

# LOW BACK PAIN AND RADICULAR PAIN: ASSESSMENT AND MANAGEMENT





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Acknowledgements:	Nicolas Fairon (KCE)



Particular acknowledgements:

The authors of this guideline wish to thank the National Institute for Health and Care Excellence (NICE) for the impressive work they have devoted to the preparation of a low back pain guideline, and their permission for the KCE and the Belgian health care workers to make use of this work.

The original NICE (National Institute for Health and Care Excellence) guideline to which this document refers, was produced by the British National Collaborating Centre for Cancer in 2016. It is available from <http://www.nice.org.uk/guidance/ng2>. NICE guidance is prepared for the National Health Service in England and Wales and does not necessarily apply to Belgium. NICE has not been involved in the development or adaptation of any guidance for use in Belgium.

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Fees or other compensation for writing a publication or participating in its development: Luc Ailliet (grant for doctoral degree VU Amsterdam 2011 - 2015)

Participation in scientific or experimental research as an initiator, principal investigator or researcher: Luc Ailliet (doctoral degree VU Amsterdam 2011 – 2015 «*Rol van biopsychosociale factoren in het herstel van mensen met nekpijn en/of low back pain*»), Anne Berquin (validation French version of questionnaire Örebro (OMPSQ)), Mieke Dolphens (investigator IWT-TBM financed project «*A modern neuroscience approach to chronic spinal pain*» (1 nov. 2013 – 31 oct 2017)), Lode Godderis (development of instruments for the evaluation of needs of disabled people (financed by FPS Social Security) ; development of questionnaire to evaluate the prognosis for resumption of work), Aline Ollevier (coordinator and principal investigator of «*eUlift*»), Veerle Stevens (manager of the programme «*Optimizing physical and psychosocial assessment in patients with non-specific chronic low back pain*»), Maurits Van Tulder (multiple scientific studies in the field of low back pain, financed by ZonMW ; principal investigator of studies about radiofrequency denervation for facet joint pain and sacro-iliacale joints, endoscopic transforaminal discectomy and epidural injections McKenzieplus ; investigator at NHMRC in Australia), Johan Vlaeyen (Methusalem programme «*From acute aversive sensations to chronic bodily symptoms*» (FNO)).

A grant, fees or funds for a member of staff or another form of compensation for the execution of research: Aline Ollevier (Erasmus + EPOS fund)



Consultancy or employment for a company, an association or an organisation that may gain or lose financially due to the results of this report: Lode Godderis (Knowlegde, Information and Development Manager at IDEWE), Virginie Fraselle (BPS), Martine Jeunehomme (Keep Moving; Commission Risk prevention)

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Other possible interests that could lead to a potential or actual conflict of interest: Martine Jeunehomme (thesis), Maurits van Tulder (co-editor of the Cochrane Back and Neck Group)

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- **The external experts were consulted about a (preliminary) version of the scientific report. Their comments were discussed during meetings. They did not co-author the scientific report and did not necessarily agree with its content.**
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Publication date:

27 November 2017 (2<sup>nd</sup> edition; 1<sup>st</sup> edition: 19 May 2017)

Domain:

Good Clinical Practice (GCP)

MeSH:

Low back pain, sciatica, practice guideline

NLM Classification:

WE 755

Language:

English



Format: Adobe® PDF™ (A4)  
Legal depot: D/2017/10.273/36  
ISSN : 2466-6459  
Copyright: KCE reports are published under a “by/nc/nd” Creative Commons Licence  
<http://kce.fgov.be/content/about-copyrights-for-kce-reports>.



How to refer to this document?

Van Wambeke P, Desomer A, Ailliet L, Berquin A, Demoulin C, Depreitere B, Dewachter J, Dolphens M, Forget P, Fraselle V, Hans G, Hoste D, Mahieu G, Michielsen J, Nielens H, Orban T, Parlevliet T, Simons E, Tobbackx Y, Van Schaeybroeck P, Van Zundert J, Vanderstraeten J, Vlaeyen J, Jonckheer P. Low back pain and radicular pain: assessment and management. Good Clinical Practice (GCP) Brussels: Belgian Health Care Knowledge Centre (KCE). 2017. KCE Reports 287. D/2017/10.273/36.

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







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## LIST OF ABBREVIATIONS

ABBREVIATION	DEFINITION
<b>ACOEM</b>	American College of Occupational and Environmental Medicine
<b>AGREE</b>	Appraisal of Guidelines Research and Evaluation
<b>AMSTAR</b>	Assessing the Methodological quality of Systematic Reviews
<b>APBMT- BBVAG</b>	Association professionnelle belge des médecins du travail – Belgische Beroepsvereniging voor Arbeidsgeneesheren
<b>APTA</b>	American Physical Therapy Association
<b>AQuMed</b>	Agency for Quality in Medicine (Joint Institution of the German Medical Association and the National Association of Statutory Health Insurance Physicians in Germany)
<b>AXXON</b>	Representative association of Belgian physiotherapists
<b>AZ</b>	General hospital (Algemeen Ziekenhuis)
<b>BBS</b>	Belgian Back Society
<b>BMI</b>	Body mass index
<b>BPS</b>	Belgian Pain Society
<b>BSN</b>	Belgian Society of Neurosurgery
<b>BSS</b>	Belgian Spine Society
<b>BVAS - ABSYM</b>	Belgische Vereniging van Artsensyndicaten - Association Belge des Syndicats Médicaux
<b>BVC - UBC</b>	Belgische Vereniging van Chiropractors – Union Belge des Chiropractors
<b>CBIP – BCFI</b>	Centre Belge d'Information Pharmacothérapeutique – Belgisch Centrum voor Farmacotherapeutische Informatie
<b>CBR</b>	Consensus based recommendation
<b>CDC</b>	Centers for Disease Control and Prevention (US)
<b>CEBAM</b>	Belgian Centre for Evidence-Based Medicine



<b>CENTRAL</b>	The Cochrane Central Register of Controlled Trials
<b>CHC</b>	Centre Hospitalier Chrétien
<b>CHU - UVC</b>	Centre Hospitalier Universitaire – Universitair Verplegingscentrum (University Hospital Centre)
<b>CI</b>	Confidence interval
<b>COI</b>	Conflict of Interest
<b>DARE</b>	Database of Abstracts and Reviews of Effectiveness
<b>e.g.</b>	Exempli gratia; Example given
<b>EMBASE</b>	Name of an International biomedical database that covers journals and conferences
<b>FBZ - FMP</b>	Fonds voor de beroepsziekten - Fonds des maladies professionnelles
<b>FMP – FBZ</b>	Fonds des maladies professionnelles- Fonds voor de beroepsziekten
<b>Fedris</b>	Federaal Agentschap voor beroepsrisico's – Agence fédérale des risques professionnels
<b>FNO</b>	Fonds Nuts Ohra
<b>FOD – SPF - FPS</b>	Federale Overheidsdienst – Service Public Fédéral - Federal Public Service
<b>FPS – FOD - SPF</b>	Federal Public Service - Federale Overheidsdienst – Service Public Fédéral
<b>GBS - VBS</b>	Groupement des unions professionnelles Belges de médecins spécialistes - Verbond der Belgische beroepsverenigingen van artsen-specialisten
<b>GDG</b>	Guideline Development Group
<b>GRADE</b>	Grading of recommendations assessment, development and evaluation
<b>GRID</b>	Groupe Régional Interdisciplinaire Douleur
<b>HQE</b>	High quality evidence
<b>ICSI</b>	Institute for Clinical Systems Improvement (U.S)
<b>IDEWE</b>	Belgische Externe Dienst voor Preventie en Bescherming op het Werk
<b>i.e.</b>	Id est; that is



<b>IMA – AIM</b>	InterMutualistisch Agentschap – Agence Intermutualiste
<b>INAMI – RIZIV – NIHDI</b>	Institut National d'Assurance Maladie-Invalidité – Rijksinstituut voor Ziekte- en Invaliditeitsverzekering - National Institute for Health and Disability Insurance
<b>ISP – WIV</b>	Institut scientifique de santé publique – Wetenschappelijk instituut volksgezondheid (Scientific institute of public health)
<b>KNGF</b>	Koninklijk Nederlands Genootschap voor Fysiotherapie (The Netherlands)
<b>KU</b>	Catholic University (Katholieke Universiteit)
<b>LBP</b>	Low back pain
<b>LQE</b>	Low quality evidence
<b>LR</b>	Likelihood ratio
<b>LR-</b>	Negative likelihood ratio
<b>LR+</b>	Positive likelihood ratio
<b>MD</b>	Mean difference
<b>MEDLINE</b>	Medical Literature Analysis and Retrieval System Online (International biomedical database)
<b>MeSH</b>	Medical subject headings
<b>MID</b>	Minimum important difference
<b>mm</b>	millimetre
<b>Mo</b>	Months
<b>MQE</b>	Moderate quality evidence
<b>MRC</b>	Medical Research Council Scale for muscle strength
<b>MRI</b>	Magnetic Resonance Imaging
<b>NA</b>	Not applicable
<b>NCGC</b>	National Clinical Guideline Centre
<b>NHMRC</b>	National Health and Medical Research Council (Australian)



<b>NICE</b>	National Institute for Health and Clinical Excellence (United Kingdom)
<b>NIDHI</b>	National Institute for Health and Disability Insurance - Rijksinstituut voor Ziekte- en Invaliditeitsverzekering – Institut National d'Assurance Maladie-Invalidité
<b>NNT</b>	Number Needed to Treat
<b>NR</b>	Not reported
<b>NRS</b>	Numeric rating scale
<b>NS</b>	Not significant
<b>NSAID</b>	Non-Steroidal Anti-Inflammatory Drugs
<b>ODI</b>	Oswestry disability index
<b>OKE</b>	Het Ondersteunings-en Kenniscentrum Ergotherapie
<b>OR</b>	Odds ratio
<b>PENS</b>	Percutaneous electrical nerve stimulation
<b>Q1</b>	Lower (25%) quartile
<b>Q3</b>	Upper (75%) quartile
<b>RBSPRM</b>	Royal Belgian Society of Physical and Rehabilitation Medicine
<b>RCT</b>	Randomised controlled trial
<b>RIZIV – INAMI – NIHDI</b>	Rijksinstituut voor Ziekte – en Invaliditeitsverzekering – Institut National d'Assurance Maladie-Invalidité – National Institute for Health and Disability Insurance
<b>RMDQ</b>	Roland Morris disability questionnaire
<b>RoB</b>	Risk of bias
<b>RR</b>	Relative risk
<b>RRR</b>	Relative risk reduction
<b>RZ</b>	Regional Hospital (Regionaal Ziekenhuis)
<b>SAE</b>	Serious adverse event
<b>SIGN</b>	Scottish Intercollegiate Guidelines Network





<b>SPF – FOD - FPS</b>	Service Public Fédéral - Federale Overheidsdienst – Federal Public Service
<b>SR</b>	Systematic review
<b>SS</b>	Sample size
<b>SSBe</b>	Spine Society of Belgium
<b>SSMG</b>	Société Scientifique de Médecine Générale
<b>SSST</b>	Société Scientifique de Santé au Travail
<b>TENS</b>	Transcutaneous electric nerve stimulation
<b>UA</b>	Universiteit Antwerpen
<b>UCL</b>	Université catholique de Louvain
<b>ULB</b>	Université libre de Bruxelles
<b>UGent</b>	University Ghent
<b>UKO</b>	Unie voor gediplomeerden in Kinesitherapie en Osteopathie
<b>UBC - BVC</b>	Union Belge des Chiropractors – Belgische vereniging van Chiropractors
<b>UVC – CHU</b>	University hospital center (Universitair Verplegingscentrum – Centre Hospitalier Universitaire)
<b>UZ</b>	University Hospital (Universitair ziekenhuis)
<b>VAS</b>	Visual analogue scale
<b>VAVP</b>	Vlaamse Anesthesiologische Vereniging voor Pijnbestrijding
<b>VBS – GBS</b>	Verbond der Belgische beroepsverenigingen van artsen-specialisten – Groupement des unions professionnelles Belges de médecins spécialistes
<b>VE</b>	Vlaams Ergotherapeutenverbond
<b>VHQE</b>	Very high quality evidence
<b>VLQE</b>	Very low quality evidence
<b>Vs.</b>	Versus



<b>VUB</b>	Vrije Universiteit Brussel
<b>VWVA</b>	Vlaamse Wetenschappelijke Vereniging Arbeidsgeneeskunde
<b>WHO</b>	World Health Organization
<b>WIP</b>	World Institute of Pain
<b>WIV – ISP</b>	Wetenschappelijk Instituut Volksgezondheid – Institut Scientifique de Santé Publique
<b>wk(s)</b>	Week(s)
<b>WVVK</b>	Wetenschappelijke vereniging van Vlaamse kinesitherapeuten
<b>yrs</b>	Years
<b>ZNA</b>	Ziekenhuis Netwerk Antwerpen
<b>ZOL</b>	Ziekenhuis Oost-Limburg



## ■ SCIENTIFIC REPORT

### 1 INTRODUCTION

#### 1.1 Background

Low back pain (LBP) is a considerable public health problem which combines high frequency, healthcare consumption and societal cost. In Belgium, according to the 2013 Health interview survey, 21% of the 15 years old and plus declared to have suffered from low back disorder or other chronic back defect in the past 12 months.<sup>1</sup> Low back pain is a common cause for seeking health care. In 2004, in Belgium, one-fourth of patients between 18 and 75 years had visited a GP in the preceding 10 years because of LBP and 40.000 multiple-day and 46.000 one-day hospitalizations were reported for patients with LBP problems.<sup>2</sup>

Episodes of back pain are usually transient. For many patients with acute LBP or radicular pain, the complaints will disappear without any intervention. However for up to one third of patients, a pain of at least moderate intensity persists one year after the onset, leading to an important use of healthcare services and work absenteeism.<sup>3, 4</sup> The National Institute for Health and Disability Insurance (RIZIV/INAMI) is aware of the costs linked to low back pain in terms of interventions' reimbursement but also sickness leave.

In 2006, the KCE had published a report (KCE report n° 48) on chronic low back pain focusing on the evaluation and treatment of patients, as well as on the incidence, costs and (occupational) consequences of this disorder<sup>2</sup>. Ten years later, one could wonder whether new evidence is available and if the recommendations should be changed. A focus on non-invasive and non-pharmacological treatment was initially proposed since several conservative multidisciplinary therapeutic programmes exist without a definition of the precise composition of such programs. The invasive treatment was however also considered to be important, because, in the Belgian situation, injections and surgery appeared frequently used as treatment option for LBP with regional variations highlighting professional uncertainty and controversy.<sup>5</sup>



## 1.2 The need for a guideline

Currently, the management of low back pain is fragmented in Belgium across modes of care, e.g. outpatient in primary care, emergency department, specialists' consultation, and pain clinics. Moreover a variation of the quality of care is suspected. A guideline based on recent evidence and validated by Belgian clinicians should allow to offer the best care to each patient and to reduce the number of people with disabling long-term back pain; and so the personal, social, and economic impact of low back pain to society. This guideline is also necessary to standardize the practices and build an ideal care pathway for the management of low back pain which is another KCE project (see website of KCE).

## 1.3 Scope

The scope of this guideline was defined in collaboration with experts and stakeholders (see list in Appendix 1) during an initial scoping meeting held on September 2015. The initial scope was proposed by physiotherapists and focused on non-invasive interventions (medication not included) in the treatment of chronic low back pain. It appeared indeed that several conservative multidisciplinary therapeutic programs based on physical reactivation (exercise) and cognitive-behavioral interventions existed without a definition of the precise composition of such programs and without consensual recommendations (see list of interventions in Appendix 2). However, the cost of surgery for low back pain and the regional variation in surgery rate observed in Belgium stressed the need to include invasive interventions in the guideline. Moreover, another KCE project focusing on the elaboration of a care pathway for low back pain had to be based on recent Belgian recommendations. Therefore it was decided to enlarge the scope to the evaluation and the management of low back pain by all kind of interventions.

Another point of discussion was the definition of the affection aimed by this guideline. It was decided to focus on low back pain and radicular pain not attributable to a recognisable, known specific pathology (for example infection, tumour, osteoporosis, fracture, structural deformity, inflammatory disorder, cauda equina syndrome or serious neurological disorder).

Low back pain is defined as a pain in the back between the bottom of the rib cage and the buttock creases. The term non-specific was not used because it appeared to have inconsistent significations in the literature. Radicular pain evokes a pain in the lower extremity with a dermatomal distribution. In some patients, radicular pain can be dominant over the back pain or can be isolated. Radicular pain can be associated with neurological symptoms and signs (numbness and/or tingling, in a dermatome pattern, reflex disturbances or motor weakness in an associated myotome), although this is not always the case. Not all radicular pain have a neuropathic pain component, i.e. pain caused by a lesion or a disease affecting the somatosensory nervous system.

All phases of the affection are covered by the guideline: acute phase from 0 to 6 weeks, sub-acute from 6 to 12 weeks and chronic from 12 weeks.

### **This guideline covers:**

- Low back pain without serious underlying cause (red flags)
- Radicular pain (including neurogenic claudication)

### **This guideline does not address:**

- Low back pain and radicular pain in children (<16 years old)
- Serious spinal pathology (infection, malignancy and fractures)
- Inflammatory causes of low back pain (ankylosing spondylarthritis)
- Potentially serious neurological sequelae of sciatica (progressive neurological deficit and cauda equina syndrome).
- Pregnancy-related back pain
- Sacroiliac joint dysfunction
- Adjacent-segment disease
- Failed back surgery syndrome
- Spondylolisthesis



## 1.4 Remit of the guideline

### 1.4.1 Overall objectives

The guidelines provides recommendations based on current scientific evidence for the evaluation and management of low back pain and radicular pain in adult population. Clinicians are encouraged to interpret these recommendations in the context of the individual patient situation and her own values and preferences.

### 1.4.2 Multidisciplinary approach

In this report we focused on the effectiveness of specific interventions, without taking into account the organization of health services. In clinical practice, a multidisciplinary approach by different health care professionals is encouraged for some patients with specific risk factors. Another KCE project is dedicated to the elaboration of a care pathway for the management of low back and radicular pain.

### 1.4.3 Patient-centered care

The choice of a treatment should not only consider medical aspects but also patient preferences. Patients should be well and timely informed about all treatment options and the advantages and disadvantages they offer. Indeed, patient representatives involved in the development of the care pathway emphasized the need for patient information. This information should be clear and repeated over time. Patients' perspectives are more in depth taken into account in the KCE project on care pathways for low back pain and radicular pain.

### 1.4.4 Target users of the guideline

This guideline is intended to be used by care providers involved in the care for adults with low back pain and radicular pain, such as general practitioners, specialists in physical medicine and rehabilitation, physiotherapists, pain therapists, orthopedic surgeons, neurosurgeons, psychologists and other clinicians. It is also of interest for patients, hospital managers and policy makers. Moreover some recommendations may not always be in line with the current criteria for NIHD (RIZIV/INAMI) reimbursement of diagnostic and therapeutic interventions. The NIHD may consider adaptation of reimbursement/funding criteria based on these recommendations.

## 1.5 Statement of intent

Clinical Guidelines are designed to improve the quality of health care and decrease the use of unnecessary or harmful interventions. This guideline has been developed by healthcare professionals and researchers for use within the Belgian context. It provides advice regarding the evaluation and management of low back and radicular pain in adults.

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



## 1.6 Funding and declaration of interest

KCE is a federal institution funded for the largest part by INAMI – RIZIV, but also by the Federal Public Service of Health, Food chain Safety and Environment, and the Federal Public Service of Social Security. The development of clinical practice guidelines is part of the legal mission of the KCE. Although the development of guidelines is paid by KCE's budget, the sole mission of the KCE is providing scientifically valid information. KCE has no interest in companies (commercial or non-commercial i.e. hospitals and universities), associations (e.g. professional associations, unions), individuals or organisations (e.g. lobby groups) that could be positively or negatively affected (financially or in any other way) by the implementation of these guidelines. All care providers involved in the Guideline Development Group (GDG) or the peer-review process completed a declaration of interest form. Information on potential conflicts of interest is published in the colophon of this report. All members of the KCE researchers make yearly declarations of interest and further details of these are available upon request.

## 2 METHODOLOGY

### 2.1 The Guideline Development Group

This guideline is the result of a collaboration between a multidisciplinary group of practising healthcare professionals and KCE researchers. Before the start of the project (summer 2015), each Belgian organisation of general practitioners, physiotherapists, physicians specialized in physical medicine and rehabilitation, and multidisciplinary organisations focusing on spine such as the Spine Society of Belgium (SSB) or the Belgian Back Society (BBS) were contacted in order to identify experts combining knowledge in evidence-based medicine and low back pain. Additional professionals with acknowledged scientific expertise in low back pain were identified by snowball sampling. The final composition of the whole GDG is documented in Appendix 1.

The roles assigned to the GDG were:

- To delimit the scope, in close collaboration with the stakeholders;
- To define the clinical questions, in close collaboration with the KCE Expert Team and stakeholders;
- To identify critical and important outcomes;
- To provide feedback on the selection of studies and identify further relevant manuscripts which may have been missed;
- To provide judgement about indirectness of evidence;
- To provide feedback on the draft recommendations;
- To specify the Belgian context and address additional concerns to be reported under a section on 'other considerations'.

Guideline development and literature review expertise, support, and facilitation were provided by the two KCE researchers (P. Jonckheer, A. Desomer).



## 2.2 General approach

The KCE guideline is produced according to highly codified principles, based on scientific information regularly updated from the international literature. This guideline was developed using a standard methodology based on a systematic review of the evidence. Further details about KCE and the guideline development methodology are available at <https://kce.fgov.be/content/kce-processes>.

If recent high-quality guidelines from other institutions are available on the topic to be updated, the KCE standard guideline development process proposes to adapt their recommendations to the local Belgian context according to a formal methodology developed by the ADAPTE group, an international group of guideline developers and researchers. This approach generally includes three major phases ([www.adapte.org](http://www.adapte.org)):

- **Set-up Phase:** In which an outline of the necessary tasks to be completed prior to beginning the adaptation process (e.g., identifying necessary skills and resources) is prepared.
- **Adaptation Phase:** In which guideline developers move from the selection of a topic to the identification of specific clinical questions; search for and retrieve guidelines; assess the consistency of the evidence considered, its quality, validity, content and applicability; decide how to best adapt the evidence found; and prepare a draft of the adapted guideline.
- **Finalization Phase:** which guides guideline developers through getting feedback on the document from stakeholders who will be impacted by the guideline, consulting with the source developers of guidelines used in the adaptation process, establishing a process for review and updating of the adapted guideline and the process of creating a final document.

## 2.3 Search for existing guidelines

The search strategy for guidelines was performed in Augustus 2015 and focused on guidelines published after the 1st January 2010. Twelve search engines were used such those of the guidelines international network, the National Guideline Clearinghouse, the National Institute for Health and Care Excellence or the Scottish Intercollegiate Guidelines Network (full list in Appendix 3).

Seventeen guidelines were identified and were appraised by two independent researchers (*PJ and AD*) with the 8 items of the third domain on rigour of development from the AGREE II checklist ([www.agreetrust.org](http://www.agreetrust.org)). Detailed results are presented in Appendix 4.

This appraisal allowed to identify three guidelines of (very) high quality but with relatively old search dates (most recent search date was until 2012). In the same time, NICE announced the publication of a comprehensive guideline on the assessment and management of low back pain and sciatica, scheduled for September 2016. It was decided, in consensus with the GDG, to wait the draft of the NICE guideline that was available for public consultation in March 2016. Based on this draft, an assessment of the methodological quality ([www.agreetrust.org](http://www.agreetrust.org)) of the NICE guideline was performed by two independent researchers (*PJ and AD*). Each item was scored and disagreement was discussed. Based on this overall assessment (Appendix 5), the NICE 2016 guideline on low back pain and sciatica was rated as high quality. It was concluded that the NICE guideline outweighed the three preselected guidelines due to its comprehensive scope (in contrast to the SIGN guideline which was scored as high quality but focused on chronic LBP only) and its recent search date (December 2015).



## 2.4 Clinical research questions

The KCE 2017 guideline encompasses all the clinical research questions from the NICE 2016 guideline (Table 1). Full literature searches, critical appraisal and evidence reviews were completed by NICE for all the 23 specified review questions. These clinical research questions were presented to the GDG in June 2016 in order to identify lacking topics which should be added in the KCE guideline. No major topics were identified. During the elaboration of the Belgian guideline, some additional interventions were evoked (e.g. andullation therapy) and are listed in the synthesis under the chapter "topics not studied".





**Table 1 – List of the NICE 2016 clinical research questions**

**Review questions**

- In people with suspected (or under investigation for) sciatica, what is the clinical and cost effectiveness of clinical examination compared to history alone or history with imaging, when each is followed by treatment for sciatica, in improving patient outcomes?
- Which validated risk assessment tools are the most accurate for identifying people with low back pain with or without sciatica at risk of poor outcome/delayed improvement?
- What is the clinical and cost effectiveness of stratifying management of non-specific low back pain with or without sciatica according to outcome of a risk assessment tool/questionnaire?
- What is the clinical and cost effectiveness of performing imaging (X-ray or MRI) compared with no investigation to improve functional disability, pain or psychological distress in people with low back pain with or without sciatica?
- What is the clinical and cost effectiveness of self-management strategies in the management of non-specific low back pain with or without sciatica?
- What is the clinical and cost effectiveness of exercise interventions in the management of non-specific low back pain with or without sciatica?
- What is the clinical and cost effectiveness of postural therapies in the management of non-specific low back pain with or without sciatica?
- What is the clinical and cost effectiveness of orthotics and appliances in the management of non-specific low back pain with or without sciatica?
- What is the clinical and cost effectiveness of manual therapies in the management of non-specific low back pain with or without sciatica?
- What is the clinical and cost effectiveness of acupuncture in the management of non-specific low back pain with or without sciatica?
- What is the clinical and cost effectiveness of electrotherapies in the management of non-specific low back pain with or without sciatica?
- What is the clinical and cost effectiveness of psychological interventions in the management of non-specific low back pain with or without sciatica?
- What is the clinical and cost effectiveness of pharmacological treatments in the management of non-specific low back pain with or without sciatica?
- What is the clinical and cost effectiveness of MBR programmes in the management of non-specific low back pain with or without sciatica?
- What is the clinical and cost effectiveness of return to work programmes in the management of non-specific low back pain with or without sciatica?
- What is the clinical and cost effectiveness of spinal injections in the management of non-specific low back pain
- What is the clinical and cost effectiveness of radiofrequency denervation in the management of non-specific low back pain
- What is the clinical and cost effectiveness of epidural injections in the management of sciatica
- Does history of previous fusion surgery, smoking status, BMI or psychological distress predict response to surgery in people with non-specific low back pain?
- Does image concordant pathology or presence of radicular symptoms predict response to surgery in people with suspected sciatica?
- What is the clinical and cost-effectiveness of disc replacement surgery for people with non-specific low back pain?
- What is the clinical and cost effectiveness of spinal fusion/arthrodesis in people with non-specific low back pain?
- What is the clinical and cost effectiveness of spinal decompression in people with sciatica?



The questions are presented above in their initial presentation. The term “non-specific” was removed by NICE during the finalisation of the guideline since it was considered unclear and confusing. The word *sciatica* proposed by NICE was judged not accurate for the Belgian experts who preferred to replace it by radicular pain. This was done in each concerned Belgian recommendation.

## 2.5 NICE methodology

### 2.5.1 Searching for evidence

According to the authors of the NICE guideline 2016 on low back pain and sciatica, systematic searches of literature were conducted in Medline, Embase, and The Cochrane Library. Additional subject specific databases were used for some questions: CINAHL (lifestyle interventions, combinations of interventions, non-invasive interventions); PsycINFO (combinations of interventions and psychological interventions); AMED (non-invasive interventions); the NHS Economic Evaluations Database (NHS EED), the Health Technology Assessment (HTA) database and the Health Economic Evaluation Database (HEED). Papers published after the 15 December 2015 (last updated date) and papers published in languages other than English were not reviewed. Unpublished literature, including the drug manufacturers' unpublished clinical trial results was not considered. All references sent by stakeholders were reviewed.

A first selection was performed on titles and abstracts based on the inclusion criteria for each research question. Full texts were assessed also for relevance (inclusion and exclusion criteria). Each relevant full text was critically appraised using the appropriate study design checklist as specified in the NICE guidelines manual. Key information was extracted and summaries of evidence were generated by outcome.

An overview of the steps followed by the searchers of NICE is presented in Figure 1. More information is available on the NICE website (<https://www.nice.org.uk/guidance/cg88>).

Figure 1 – Step-by-step process of review of evidence in the guideline



Source: NICE guideline 2016 – Low back pain and sciatica (lay-out adapted by KCE)



2.5.2 Grading evidence

Outcome data were combined, analysed and reported by NICE according to study design:

- Randomised data and prognostic data were meta-analysed where appropriate and reported in GRADE profile tables.
- Observational data were presented as a range of values in GRADE profile tables or meta-analysed if appropriate.

Some explanation on the GRADE approach is presented below in Table 2, Table 3, Table 4 and Table 5.

Table 2 – A summary of the GRADE approach to grading the quality of evidence for each outcome

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

Source: Guyatt GH, Oxman AD, Sultan S, Glasziou P, Akl EA, Alonso-Coello P, et al. GRADE guidelines: 9. Rating up the quality of evidence. *J Clin Epidemiol.* 2011;64(12):1311-6.

Table 3 – Levels of evidence according to the GRADE system

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

Source: Balshem H, Helfand M, Schünemann HJ, Oxman AD, Kunz R, Brozek J, et al. GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol.* 2011;64(4):401-6.

**Table 4 – Downgrading the quality rating of evidence using GRADE**

Quality element	Reasons for downgrading
<b>Limitations</b>	For each study reporting the selected outcome, possible risk of bias introduced by lack of allocation concealment, lack of blinding, lack of intention-to-treat analysis, loss of follow-up and selective outcome reporting were assessed. Additionally, other limitations such as stopping early for benefit and use of unvalidated outcome measures were taken into consideration. Level of evidence was downgraded if studies were of poor quality. Downgrading was omitted if studies with low risk of bias were available that lead to similar conclusions as the studies with a high risk of bias.
<b>Inconsistency</b>	Downgrading the level of evidence for inconsistency of results was considered in the following situations: point estimates vary widely across studies, confidence intervals show minimal or no overlap, the statistical test for heterogeneity shows a low p-value or the $I^2$ is large.
<b>Indirectness</b>	Quality rating was downgraded for indirectness in case the trial population or the applied intervention differed significantly from the population or intervention of interest. Also, the use of surrogate outcomes could lead to downgrading. A third reason for downgrading for indirectness occurred when the studied interventions were not tested in a head-to-head comparison.
<b>Imprecision</b>	<p>Evaluation of the imprecision of results was primarily based on <u>examination of the 95%CI</u>. Quality was rated down if clinical action would differ if the upper versus the lower boundary of the 95%CI represented the truth. In general, 95%CIs around relative effects were used for evaluation, except when the event rate was low in spite of a large sample size. To examine the 95%CIs, the clinical decision threshold (CDT) was defined. When the 95%CI crossed this clinical decision threshold, the quality level was rated down. A relative risk reduction (RRR) of 25% was defined as CDT by default and adapted if deemed appropriate e.g. in case of a low risk intervention.</p> <p>Even if 95%CIs appeared robust, level of evidence could be rated down because of fragility. To judge fragility of results, it is suggested to calculate the number of patients needed for an adequately powered (imaginary) single trial, also called the <u>optimal information size (OIS)</u>. If the total number of patients included in a systematic review was less than the calculated OIS, rating down for imprecision was considered. For calculations, a RRR of 25% was used, unless otherwise stated. When the OIS could not be calculated, a minimum of 300 events for binary outcomes and a minimum of 400 participants for continuous outcomes were used as a rule of thumb.</p>
<b>Reporting bias</b>	Quality rating was downgraded for reporting bias if publication bias was suggested by analysis using funnel plots or searching of trial registries. Publication bias was also suspected if results came from small, positive industry-sponsored trials only.



**Table 5 – Downgrading the quality rating of evidence for diagnostic accuracy using GRADE**

Quality element	Reasons for downgrading
<b>Limitations</b>	Risk of bias were assessed by considering the majority of the evidence. This method took into account the size of the studies, as well as the number of studies.
<b>Inconsistency</b>	Inconsistency was assessed by examining the paired sensitivity and specificity plots.
<b>Indirectness</b>	Indirectness were assessed by considering the majority of the evidence. This method took into account the size of the studies, as well as the number of studies.
<b>Imprecision</b>	Imprecision was assessed by considering the confidence interval around the sensitivity; regions of acceptability were defined – so that if the confidence interval lay wholly within a region the evidence was considered precise. But if the confidence interval crossed into two or three regions, the evidence was downgraded by one and two increments respectively. These regions were arbitrarily defined as 90-100%, 80-90% and below 80%.
<b>Reporting bias</b>	Quality rating was downgraded for reporting bias if publication bias was suggested by analysis using funnel plots or searching of trial registries. Publication bias was also suspected if results came from small, positive industry-sponsored trials only.

## 2.6 Analysis of NICE review

The KCE team checked and summarized the evidence provided by NICE for each clinical question (see Appendix 7. Summary sheets). We used the evidence tables and forest plots provided by NICE in order to understand the results. Per topic, we developed one or more overview tables in order to present, in an easily understanding way, the clinical effectiveness of each intervention and comparison for each outcome. The level of evidence underlying each recommendation came from the original source.

Some methodological aspects were discussed with the GDG such as the minimal importance difference used by NICE. The main point of criticism was the very low cut off value of 1 point on a numeric rating scale (NRS 0-10) to determine the difference in pain intensity between groups. A quick search in literature revealed no consensus on this cut off value. A low Minimum important difference (MID) could eventually lead to an overestimation of the effect, however NICE took into account a combination of different outcomes in the evidence statement and the formulation of the recommendation is also depending of other factors (costs, benefits/harms, quality of evidence, preferences).

Moreover regarding the differences over time between groups, NICE applied a MID of 30 or 50% improvement (outcome: responder criteria) which was agreed by the Belgian GDG members.

For some topics, additional evidence was provided by the Belgian GDG members or by the KCE searchers. This evidence was checked by the KCE team and discussed during a GDG meeting.

NICE emphasized that the pharmacological interventions presented in the guideline 2016 concerns patients with low back pain only and referred to a previous guideline on neuropathic pain (CG 173 Neuropathic pain in adults: pharmacological management in non-specialist settings, last updated in December 2014) for the pharmacological management of patients with sciatica. A similar methodological approach was followed for the NICE recommendations specific for neuropathic pain as for the other recommendations included in the Belgian guideline, i.e. presenting to the GDG the clinical effectiveness of each intervention and comparison for each outcome.



Nevertheless the good quality of the recent NICE guideline (see section on quality appraisal), some limitations were encountered during the development process of the Belgian guideline, such as:

- The term “sciatica” used by NICE was considered by the Belgian GDG as unclear and preferred “radicular pain” (see scope)
- Some definitions were imprecise or encompassed many interventions without distinctions between them (e.g. multidisciplinary biopsychosocial rehabilitation (MBR) programmes, exercises programmes, postural therapy (Alexander therapy included).
- For some interventions, the difference between acute and chronic low back pain are mentioned but not for all. In some cases (exercises, manual therapy, MBR), the KCE team had to search this difference directly in the primary studies.
- Searches were restricted by NICE to articles published in English.
- The link between the evidence and the recommendation was not always clearly made, mostly for interventions with unclear clinical benefit.
- Back schools were considered out of scope in the NICE guideline because the NICE GDG considered this to be outdated and no longer in use. However there is a difference between the UK and the Belgian definition of ‘Back schools’.
- These potential limitations of the NICE guideline were discussed with the Belgian GDG and taken into account during the analysis of the NICE findings.

## 2.7 Formulation of recommendations

Each recommendation proposed by NICE was discussed in GDG meetings. In order to prepare this discussion, every GDG member received access to an on-line survey (Lime Survey), presenting the comprehensive summary of the evidence (with additional tables), the NICE GDG considerations and the NICE recommendations (see an example of a survey in Appendix 6). In some cases Belgian additional information was also provided such as the BCFI/CBIP recommendation on analgesic medications. All GDG members were invited to mark if they agree or not with the proposed NICE recommendations. A strength of each recommendation was also suggested by the KCE team on the basis of the NICE formulation (“Offer” for strong and “Consider” for a weak). Open questions were added for allowing the respondent to explain his/her disagreement or to comment his/her answer. Before the start of each GDG meeting, the KCE researchers made an overview of the agreement scores and the comments formulated by the Belgian GDG members. This overview structured the GDG meeting and gave the opportunity to discuss every comment (also from the GDG members who were not present at one of the GDG meetings). In case of disagreement, the topic was proposed to be re-discussed in the following GDG meeting. Minutes clearly mentioning which changes were made to the recommendation and on which base were sent to every GDG member after each meeting. Four consultation rounds which each contained roughly 15 recommendations to be scored and commented using were needed. A similar methodological approach was followed for the NICE recommendations specific for neuropathic pain in a fifth round.

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



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

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

Source: Andrews JC, Schunemann HJ, Oxman AD, Pottie K, Meerpohl JJ, Coello PA, et al. GRADE guidelines: 15. Going from evidence to recommendation—determinants of a recommendation's direction and strength. *J Clin Epidemiol.* 2013;66(7):726-35.

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

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

Sources: Schünemann HJ, Jaeschke R, Cook DJ, Bria WF, El-Solh AA, Ernst A et al. An Official ATS Statement: Grading the Quality of Evidence and Strength of Recommendations in ATS Guidelines and Recommendations. *Am J Respir Crit Care Med* 2006; 174:605–14.£  
Guyatt G, Gutterman D, Baumann MH, Addrizzo-Harris D, Hylek EM, Phillips B et al. Grading Strength of Recommendations and Quality of Evidence in Clinical Guidelines - Report From an American College of Chest Physicians Task Force. *Chest* 2006; 129:174-81.

A strong recommendation implies that most patients would want the recommended course of action. A weak recommendation implies that the majority of informed patients would want the intervention, but many would not. Specifically, a strong negative recommendation means the harms of the recommended approach clearly exceed the benefits whereas a weak negative recommendation implies that the majority of patients would not want the intervention, but many would. In the case of a weak recommendation, clinicians are especially required to spend adequate time with patients to discuss patients' values and preferences. Such an in-depth



discussion is necessary for the patient to make an informed decision. This may lead a significant proportion of patients to choose an alternative approach. Fully informed patients are in the best position to make decisions that are consistent with the best evidence and patients' values and preferences.

For policy-makers, a strong recommendation implies that variability in clinical practice between individuals or regions would likely be inappropriate whereas a weak recommendation implies that variability between individuals or regions may be appropriate, and use as a quality of care criterion is inappropriate. We offer the suggested interpretation of "strong" and "weak" recommendations in Table 8.

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

Implications	Strong recommendation	Weak recommendation
<b>For patients</b>	Most individuals in this situation would want the recommended course of action, and only a small proportion would not. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	The majority of individuals in this situation would want the suggested course of action, but many would not.
<b>For clinicians</b>	Most individuals should receive the intervention. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.	Recognize that different choices will be appropriate for individual patients and that you must help each patient arrive at a management decision consistent with his or her values and preferences. Decision aids may be useful helping individuals making decisions consistent with their values and preferences.
<b>For policy makers</b>	The recommendation can be adopted as policy in most situations.	Policy-making will require substantial debate and involvement of various stakeholders.

\* the terms "conditional" and "weak" can be used synonymously

Source: Andrews JC, Schunemann HJ, Oxman AD, Pottie K, Meerpohl JJ, Coello PA, et al. GRADE guidelines: 15. Going from evidence to recommendation-determinants of a recommendation's direction and strength. *J Clin Epidemiol.* 2013;66(7):726-35.

The strength of the recommendations is translated in the formulation in the following way:

- "Offer" for strong recommendation pro
- "Consider" for weak recommendation pro
- "Do not offer" for strong recommendation against
- "Do not routinely offer" for weak recommendation against

- Other verbs for consensus-based experts opinion

The results of the Lime survey were presented and discussed during four GDG meetings (29 June 2016, 15 September 2016, 12 October 2016 and 10 December 2016). A change in the formulation or in the strength of the NICE recommendation was made only if the arguments were clear and a consensus between the Belgian GDG members was obtained. The major changes are underlined in the results chapter of this scientific report.





The final version of the NICE guideline was published at the end of November 2016, including the comments of the stakeholders. These comments, the final list of the NICE recommendations (which contained some small modifications compared to the draft version) and the final set of the Belgian recommendations were checked during the final GDG meeting on the 24 January 2017.

For each clinical question, a summary sheet is available in Appendix 7 gathering the material provided by the NICE 2016 guideline (evidence and GDG considerations), the NICE recommendations, the comments of the Belgian GDG (from the Lime surveys and the different meetings), the comments of the NICE stakeholders and the NICE answers, the Belgian GDG comments from the last meeting on the 24 January 2017 and the final Belgian recommendations in three languages (English, French and Dutch).

## 2.8 External review

### 2.8.1 Healthcare professionals (stakeholders)

The recommendations prepared by the guideline development group were circulated to relevant representatives of professional associations or other clinical experts not involved in the GDG (see Appendix 1) but involved in the elaboration of the care pathway. All expert referees made declarations of interest. Their comments were gathered and discussed during three working groups the 7, 8 and 9 February 2017.

## 2.9 Final validation

As part of the standard KCE procedures, an external scientific validation of the report was conducted prior to its publication. This validation was done in two phases. First, the content was evaluated by two clinicians on the 9 March 2017. Second, the methodology was validated making use of the AGREE II checklist. This validation process was chaired by CEBAM on the 21 March 2017.

# 3 CLINICAL RECOMMENDATIONS

## 3.1 Assessment of low back pain and radicular pain

### 3.1.1 History taking and clinical examination

Comprehensive history taking and clinical examination are important parts of the process for the management of people with back pain or radicular pain. This is the first step for excluding differential diagnoses (e.g. nephritis colitis, hip osteoarthritis, aortic dissection) and for identifying symptoms or signs suggestive of possible serious underlying pathology. NICE mentioned different clinical examinations such as straight leg raise (may be referred to as sciatic nerve stretch test), femoral nerve stretch test, crossed straight leg raise, motor muscle strength, dermatome sensory loss, reflex impairment and, slump test.

The NICE search question focused on the clinical and cost effectiveness of clinical examination (compared to history alone or history with imaging) for people with suspected (or under investigation for) sciatica.

The NICE evidence review can be found on p.61-63 in the **full guideline on assessment and non-invasive treatments** (<https://www.nice.org.uk/guidance/ng59/evidence>). A summary sheet in Appendix 7.1 gathered the evidence findings, the NICE GDG considerations, the results of the online survey and the discussion with the Belgian GDG.

### Scientific evidence regarding specific examination for sciatica

No relevant clinical studies were identified by NICE who decided not to extend the search to diagnostic accuracy studies. According to NICE, given the fact that there is no agreed reference standard for diagnosis of sciatica, such a review would therefore not be informative for setting guideline recommendations. No relevant economic evaluations were identified.



## Conclusions

**No evidence was found by NICE regarding the clinical and cost-effectiveness of clinical examination in people with suspected radicular pain. No evidence was searched regarding the clinical and cost-effectiveness of clinical examination in people with low back pain without radicular pain.**

## Other considerations regarding specific examination for sciatica

Factor	Comment
<b>Balance between clinical benefits and harms</b>	<ul style="list-style-type: none"><li>• The Belgian GDG highlighted <b>the lack of a single physical test</b> that would combine high sensitivity and sensibility to identify a radiculopathy.</li><li>• Some GDG members reminded the results of the Cochrane review on clinical examination from Van Der Windt DAWM 2010<sup>6</sup>. In this review, it was stressed that several aspects of physical examination in isolation (scoliosis, paresis or muscle weakness, muscle wasting, impaired reflexes, sensory deficits) do not accurately distinguish between low-back pain patients with or without lumbar radiculopathy due to disc herniation. For other tests (forward flexion, hyper extension test, and slump test), there was insufficient evidence to provide recommendations regarding their diagnostic accuracy or usefulness. The Straight Leg Raising (SLR) or Lasègue's test showed high sensitivity (and variable specificity), whereas the XSLR showed high specificity in surgical studies but coupled with low sensitivity. The crossed SLR (XSLR) or crossed Lasègue's test was usually only positive in patients with major nerve root impingement, and the authors of the Cochrane review emphasised that "these results were obtained in populations characterised by a very high prevalence of disc herniation (&gt;75% in nearly all studies) and a severe spectrum of disease, and cannot be generalised to populations with a lower prevalence of the target condition". This is why they concluded that there was still insufficient evidence for the clinical usefulness of the SLR and XSLR in the diagnosis of disc herniation in primary care populations and other populations of patients not (yet) referred for surgery.</li><li>• The GDG agreed that there was <b>insufficient evidence</b> to recommend a substantial change to normal clinical practice and therefore agreed not to make a recommendation in favour of a specific text for radicular pain.</li><li>• The Belgian GDG highlighted however the <b>potential utility of a combination of clinical tests</b> and confirmed that a <b>history taking and a clinical examination</b> (including testing motor) is needed to exclude the presence of symptoms or signs suggestive of possible serious underlying pathology (red flags). This is linked with another NICE recommendation based on consensus and included in the NICE chapter on imaging: "Think about alternative diagnoses when examining or reviewing people with low back pain, particularly if they develop new or changed symptoms. Exclude specific causes of low back pain, for example, cancer, infection, trauma or inflammatory disease such as spondyloarthritis. If serious underlying pathology is suspected, refer to relevant NICE guidance on: Metastatic spinal cord compression in adults, Spinal injury, Spondyloarthritis, Suspected cancer."</li></ul>



- **A list of red flags is proposed in the box 1** in the synthesis of this guideline. This list was based on an expert opinion consensus. The Belgian GDG was aware that the sensitivity and specificity of these flags are limited if they are used as single but it was considered that a cluster of red flags can support the formulation of hypothesis, beside the clinical expertise. However, the absence of specific affection should be always regarded as a hypothesis, not as a definitive diagnosis and red flags remain useful for clinicians to keep an awareness for possible underlying serious pathology.
- Therefore it was proposed to use the recommendation proposed by NICE as above in order to emphasise the place of a comprehensive history taking and clinical examination for low back pain, whatever there is a radicular pain or not.
- A systematic review from Downie et al (BMJ 2013)<sup>7</sup> focusing on screening for malignancy and fracture in patients with low back pain confirmed the need of being cautious with the use of red flags (few are informative and the probability of detection for spinal fracture is higher when multiple red flags were present).

<b>Quality of evidence</b>	Not applicable.
<b>Patients values and preferences</b>	People consulting healthcare professionals may expect an examination as part of the consultation, and this examination contributes highly to satisfaction with the consultation.
<b>Costs (resource allocation)</b>	History taking and clinical examination request mainly time dedicated by clinicians. This cost is broadly counterweighted by the benefit of gathering information on the patient, his/her history and his/her symptoms.

Recommendation	Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"> <li>• Always take into account differential diagnoses when examining or reviewing patients with low back or radicular pain, particularly if they develop new or changed symptoms. Exclude signs suggestive of possible serious underlying pathology (identified as red flags)*, for example, cancer, infection, trauma, inflammatory disease such as spondyloarthritis, or severe neurological problems such as cauda equina syndrome.</li> </ul>	Experts opinion	Not applicable

\* The sensitivity and specificity of these flags are very limited if they are used as single but a cluster of red flags, beside the clinical expertise, can support the formulation of hypothesis. The probability of serious underlying pathology is low.



### Change in comparison with the NICE recommendation

Minor changes have been proposed by the Belgian GDG

6. ~~Think about~~ Always take into account ~~alternative differential~~ diagnoses when examining or reviewing ~~people~~ patients with low back pain or radicular pain, particularly if they develop new or changed symptoms. Exclude ~~specific causes of low back pain signs suggestive of possible serious underlying pathology~~ (identified as red flags), for example, cancer, infection, trauma or inflammatory disease such as spondyloarthritis or severe neurological problems such as cauda equina syndrome. ~~If serious underlying pathology is suspected, refer to relevant NICE guidance on: Metastatic spinal cord compression in adults, Spinal injury, Spondyloarthritis, Suspected cancer.~~

The reasons underlying these changes are described in Appendix 7.1.

#### 3.1.2 Risk assessment and stratification

The aim of risk assessment is to identify risk factors or prognostic features that may make a person more likely to suffer from chronic, disabling back pain. Several tools exist that are used to predict delayed improvement or poor outcome. A first question is which among them are the most accurate for identifying people with low back pain or radicular pain at risk of poor outcome. A second question is whether management stratified according to the tool is effective rather than a 'one size fits all' approach'. Two aspects were therefore analysed in this chapter: the accuracy of the risk assessment and the impact of management adapted to the risk stratification.

The NICE evidence review can be found on p.64-117 in the full guideline on assessment and non-invasive treatments and the forest plots in Appendix K p.5-26 (<https://www.nice.org.uk/guidance/ng59/evidence>). A summary sheet in Appendix 7.2 gathered the evidence findings, the NICE GDG considerations, the results of the online survey and the discussion with the Belgian GDG.

### Scientific evidence regarding the research question: Which validated risk assessment tools are the most accurate for identifying people with low back pain or sciatica at risk of poor outcome/delayed improvement?

**Risk assessment:** 16 studies reporting evidence for 11 risk assessment tools were selected by NICE. All of the studies were conducted in a low back pain population except 2 which had a mixed population of people with or without additional sciatica. NICE selected several outcomes such as sensitivity, specificity, predictive values, discrimination (by calculating the area under the receiver operating characteristic curve) and calibration (predicted risk versus observed risk). The quality of evidence was low or very low except for the Örebro and STarT Back screening tools (high level of evidence in some cases). According to NICE, the STarT Back screening tool is the single tool gathering sufficient evidence on discrimination (DIS) and calibration (CAL): high discrimination and moderate calibration for predicting functional improvement; moderate discrimination and low calibration for predicting pain. Detailed results are presented in Table 5 in Appendix 7.2. No economic evaluation was found.

### Scientific evidence regarding the research question: What is the clinical and cost effectiveness of stratifying management of non-specific low back pain or sciatica according to outcome of a risk assessment tool/questionnaire?

**Risk stratification:** 6 studies (published in 8 papers) were included by NICE for the analysis on effectiveness of stratifying management. All of the studies were conducted in a population of low back pain with or without sciatica. As there was only one randomised trial identified, cohort studies were also searched for. However, none of the cohort studies identified met the inclusion criteria specified in the NICE protocol. Three economic evaluations, reported in seven papers, were identified and included in the review.



Three tools were compared with the absence of risk tool; one of them (STarT Back screening tool) was analysed in two different settings:

- Hicks/Delitto classification versus no risk tool
  - no clinical difference for quality of life (mental and physical component scores of the SF-36) (2 studies, very low quality, n=234) except a **clinical benefit favouring stratified treatment at ≤ 4 month for the physical component score**.
  - a **clinical benefit for stratified management for responders to pain improvement at ≤ 4 months** (a single low quality study, n=156) and **responders to function improvement at > 4 months** (1 study, very low quality, n=156) but no clinical difference for the majority of outcomes reported (pain, function and healthcare utilisation).
- O'Sullivan classification system versus no risk tool
  - clinical benefit of stratified treatment for pain in both the short (≤ 4 months) and long term (> 4 months) (low-very low quality, 1 study, n=94) and a clinical benefit of stratified treatment for function in the short term only (low-very low quality, 1 study, n=94). No other outcomes measured.
- STarT Back risk tool versus no risk tool in secondary care
  - no clinical difference for most of the outcomes: quality of life (mental component score), pain, function and psychological distress (a single, low quality study<sup>a</sup>, n=851); a clinical benefit was observed with the stratified treatment for quality of life measured by the physical component score of the SF-12 at both the short (≤ 4 months) and long (>4 months) term (a single, low quality study, n=851). Overall, adjusted mean changes in RMDQ 0-24 scale scores were not significantly higher (MID>2) in the intervention group than in the control group at 4 months (MID 1.81 [95% CI 1.06–2.57]) and at 12 months (MID 1.06 [0.25–1.86]).

When the individual stratified groups from the STarT Back classification of low, medium and high risk category patients were compared with no risk tool, several clinical benefit were observed:

- a clinical benefit favouring stratified treatment for quality of life (EQ-5D) in the high risk category patients at ≤ 4 months (1 study, very low quality, n=236) and in the medium and high risk category patients at > 4 months (1 study, very low quality, n=394 and n=236).
  - a clinical benefit favouring stratified treatment for quality of life (physical component score of the SF-12) in both the medium and high risk patients at the ≤ 4 months' time point (1 study, very low quality, n=394 and n=236) as well as in the medium risk patients at > 4 months (1 study, very low quality, n=392).
  - a clinical benefit in responder criteria for improvement in pain and function in the overall group as well each stratified risk group at the ≤ 4 month follow up (1 study, low-very low quality, n=99).
  - no clinical difference between the STarT Back risk tool compared to no risk tool for all other outcomes reported at any time point.
- **STarT Back risk tool (IMPACT cohort) versus no risk tool in primary care**
    - no clinical difference for any outcome reported (quality of life, pain, function and psychological distress) (a single study, very low quality evidence, n=922).

<sup>a</sup> NICE downgraded the RCT of Hill due to very serious risk of bias (e.g. loss of follow-up, slight imbalance in attrition group) and very serious imprecision



When the individual stratified groups from the STarT Back classification of low, medium and high risk, several clinical benefits were found:

- a clinical benefit favouring stratified treatment for quality of life (EQ-5D) in the high risk category patients at  $\leq 4$  months and  $> 4$  months (1 study, very low quality, n=922).
- a clinical benefit for stratified treatment in patients identified as being at high risk for quality of life measured (physical component score of the SF-12), pain and function at the  $> 4$  month follow-up (very low quality, n=189).
- no clinical difference between the STarT Back risk tool compared to no risk tool for all other outcomes reported at any time point.

#### **Economic evidence**

No evidence was found for risk assessment. Regarding risk stratification, one cost-utility analysis found that in adults with low back pain (with or without sciatica) Hicks/Delitto classification based intervention dominated (less costly and more effective) compared to usual physical therapy care. This analysis was assessed as partially applicable with potentially serious limitations. Two cost-utility analysis found that in adults with low back pain (with or without sciatica) STarT Back stratification based interventions dominated (less costly and more effective) compared to current best practice/usual care. These analyses were assessed as directly applicable with potentially serious limitations (due to methodological limitations: not all risk stratification tools from the review protocol are included in the studies; within-trial analysis; bootstrapping of ICER from NHS and PSS perspective not undertaken...).

#### **Conclusions**

- **Regarding the risk assessment, analysis showed evidence in terms of discrimination and calibration for the STarT Back screening tool. Evidence for the other tools is judged insufficient. The results regarding the effectiveness of the risk stratification found poor evidence for the use of the Hicks/Delitto classification (few clinical benefits), some evidence for the use of the O'Sullivan classification (clinical benefit in pain in both short and long term and in function at short term in a single study).**
- **With the STarT Back screening tool, when the individual stratified groups of low, medium and high risk category were compared with no risk tool, a clinical benefit was mentioned, in several outcomes for the medium and the high risk groups. The economic evaluations highlighted two instruments: the Hicks/Delitto classification based interventions dominated compared to usual physical therapy care and the STarT Back stratification based interventions dominated compared to current best practice/usual care.**



## Other considerations regarding risk assessment and stratification

Factor	Comment
<b>Balance between clinical benefits and harms</b>	<ul style="list-style-type: none"> <li>• The Belgian GDG acknowledged that evidence found by NICE showed a better accuracy for the risk assessment of poor outcomes in low back pain with the STarT Back Screening tool than other tools. However, a recent meta-analysis<sup>9</sup> tempered this results and concluded that the STarT Back screening tool and the Örebro Musculoskeletal Pain Screening Questionnaire obtained similar results for function. Moreover, the authors of the review mentioned that the Örebro tool should be recommended for absenteeism outcomes.</li> <li>• Another aspect is the efficacy of management adapted to the risk stratification. Positive results favouring stratified care with the STarT Back screening tool was found by NICE for some critical outcomes. These positive results were also supported by the non-randomised study IMPaCT study.</li> <li>• The Belgian GDG agreed that stratification should be considered not only for identifying subgroups at risk of poor outcome but also for tailoring the management to risk profile. The value of the risk stratification is to offer a more complex and intensive treatment in higher risk patients and decrease the risk of overtreatment in the lower risk patients.</li> <li>• The Örebro was considered by some Belgian GDG member as a better prognostic tool than the SBT (confirmed by the results of Karan 2017<sup>8</sup>), while the STarT Back tool appeared more accurate than the Örebro for treatment allocation in a stratified perspective. The STarT Back tool encompassed indeed potentially treatment-modifiable prognostic indicators and allowed to define three potential patients subgroups with three corresponding treatment approaches: low risk subgroup (suitable for primary care management according to guidelines), medium risk subgroup (high levels of physical prognostic indicators, appropriate for physiotherapy), and high risk subgroup (high levels of psychosocial prognostic indicators, appropriate for a combination of physical and cognitive-behavioural treatments). By contrast, the Örebro tool did not make any distinction between physical and psychosocial risk factors, making specific treatment allocation more difficult.</li> <li>• The Belgian GDG acknowledged that both tools have their advantages and inconveniences and could be used for different purposes (e.g. first risk stratification in primary care for the STarT Back screening tool; assessment of disability and work-absenteeism risk in varied settings for the Örebro). Both are validated in either solely low back pain populations or mixed populations of people with low back pain and/or radicular pain, but none are validated for radicular pain specifically.</li> <li>• Given the fact that no tool has a perfect sensitivity, specificity and predicting value, the likelihood for misclassifying some people exists and should be reminded. Both tools have false positive and false negative results. The Belgian GDG emphasised that an assessment tool should never replace the clinical decision-making based on a comprehensive interview and that patients in the low risk group who continue to experience pain should be re-assess in order to offer further treatment.</li> <li>• Moreover, the risk factors or prognostic features that may make a person more likely to suffer from chronic, disabling back pain are not all encompassed in the proposed risk stratification tools. Several psychological, psychiatric, contextual and work-related factors, identified as yellow, orange, blue and black flags, should be included in the clinical decision-making process. A list of these flags is presented in the box 2 of the synthesis of this guideline.</li> <li>• The tailored management proposed by NICE are described in two categories of risk. The Belgian GDG agreed with this proposition but stressed that this should be adapted regarding the cut-off of each tool (e.g. the higher risk category encompassed the medium and high risk profiles in the STarT Back tool). Independently the amount of risk classes determined by the stratification</li> </ul>



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tools, the main message is that low risk patients need a simpler approach and that patients at higher risk need a more intensive and complex management.

- The timing of risk stratification and tailored treatment was discussed by the Belgian GDG because this should take into account the feasibility for the care providers (may be uneasy in hyper-acute phase), the formulation of some questions and the risk of overtreatment if performed too early (before spontaneous evolution). In the Belgian care pathway, it is proposed not to perform the risk stratification at the first contact, certainly if this one occurs before 48 hours after the pain onset, but rather during a second encounter (around 2 weeks).

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**Quality of evidence**

- For the risk assessment, the evidence was rated as low or very low quality for all of the outcomes and risk assessment tools (due to outcome reporting bias, and attrition bias), except for STarT Back and Örebro tools which was graded as high quality (for both discrimination and calibration).
- For the risk stratification, the evidence was rated as low or very low quality for all of the outcomes, mainly due to risk of bias (and sometimes due to additional imprecision): mainly lack of appropriate blinding to the key confounders for randomized studies and selection bias coupled with lack of appropriate blinding for the single non-randomised study.
- The three economic analyses presented potentially serious limitations.

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**Patients values and preferences**

- The aim of the risk stratification is to tailor the management to each patient, taken into account several personal factors. Therefore the management is based more on patients' needs than on the complaints characteristics.
- The Belgian GDG discussed the importance of tools that are easy and quick to conduct in practice (for the clinicians but also for the patients). It was noted that the STarT Back tool is short and can be completed in a few minutes. For the Örebro, the long version was considered not acceptable and the short version was preferred. The STarT Back and the Örebro short version gather around 10 questions both.
- Several translations of the STarT Back tool are proposed <http://www.keele.ac.uk/sbst/startbacktool/translations/>: one formal translation in French, another formal translation in Dutch and an informal translation in German. The short version of the Örebro is also translated in French and Dutch although this versions were not formally validated yet.

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**Costs (resource allocation)**

- The cost-utility analyses found that in adults with low back pain (with or without sciatica) STarT Back stratification based interventions could be cost-effective compared to current best practice/usual care.
  - The time dedicated by the clinicians for obtaining answers to the questionnaire is the major cost linked to the instrument use.
  - Given that the STarT Back and the Örebro tools are poorly used by the Belgian general practitioners, specific training should be organised for the clinicians. This represents maybe an additional cost due to the Belgian context.
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Recommendation	Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"> <li>Consider using risk stratification (with for example the STarT Back risk assessment tool or the Örebro Musculoskeletal Pain Screening Questionnaire, short version) for each new episode of low back pain with or without radicular pain. This risk stratification should not be performed during the first 48h after the pain onset*. The aim of the risk stratification is to inform shared decision-making about stratified management. *It is advised to perform the risk stratification during the second consultation, approximately 2 weeks after onset.</li> </ul>	Weak (RCTs)	Low to very low
<ul style="list-style-type: none"> <li>Based on risk stratification, consider:               <ul style="list-style-type: none"> <li>Simpler and less intensive support for patients with low back pain with or without radicular pain likely to improve quickly and have a good outcome (for example, reassurance, advice to keep active and guidance on self-management)</li> <li>More complex and intensive support for patients with low back pain with or without radicular pain at higher risk of a poor outcome (for example, exercise programmes with or without manual techniques and a psychological intervention such as cognitive-behavioral approach).</li> </ul> </li> </ul>	Weak (RCTs)	Low to very low

**Change in comparison with the NICE recommendation**

Some important changes have been proposed by the Belgian GDG, in particular the addition of the Orebro Musculoskeletal Pain Screening Questionnaire as example and a specification regarding the timing for the first risk stratification. Minor changes are also presented for consistency in the formulation of all recommendations (sein other topics).

1. Consider using risk stratification (for example, the STarT Back risk assessment tool and the Örebro Musculoskeletal Pain Screening Questionnaire) at first point of contact with a healthcare professional for each new episode of low back pain (with or without sciatica radicular pain). This risk stratification should not be performed during the first 48h after the pain onset. The aim of the risk stratification is to inform shared decision-making about stratified management.

2. Based on risk stratification, consider:
  - o simpler and less intensive support for ~~people~~ patients with low back pain with or without ~~sciatica~~ radicular pain likely to improve quickly and have a good outcome (for example, reassurance, advice to keep active and guidance on self-management)
  - o more complex and intensive support for ~~people~~ patients with low back pain with or without ~~sciatica~~ radicular pain at higher risk of a poor outcome (for example, exercise programmes with or without manual ~~therapy techniques~~ or using and a psychological ~~approach~~ intervention such as cognitive-behavioural approach)."

The reasons underlying these changes are described in Appendix 7.2.



### 3.1.3 Imaging

In patients with low back or radicular pain **with NO signs of possible serious underlying pathology**, the benefit of imaging in terms of improving patient related outcomes, either at initial presentation or later in the pathway, was considered as an area of uncertainty.

The use of **imaging in presence of symptoms or signs suggestive of possible serious underlying pathology (red flags)** is beyond the scope of this guideline and not included in this chapter.

The NICE evidence review can be found on p.118-153 in the full guideline on assessment and non-invasive treatments and the forest plots in Appendix K p.27-39 (<https://www.nice.org.uk/guidance/ng59/evidence>).

A summary sheet in Appendix 7.3 gathered the evidence findings, the NICE GDG considerations, the results of the online survey and the discussion with the Belgian GDG.

#### **Scientific evidence regarding imaging in low back pain and radicular pain**

Five randomised trials and five additional cohort studies were mentioned by NICE. Most of the studies concerned mixed populations of people with low back pain with and without sciatica. One of the trials included an indirect population (including people from 14 years of age). The search was extended by NICE to cohorts for all comparisons due to insufficient evidence and 4 additional studies were identified that met the inclusion criteria. One economic evaluation relating to imaging versus no imaging has also been included in this review.

As shown in the Table 6 in Appendix 7.3:

#### LBP WITH OR WITHOUT SCIATICA

- No clinical benefit of imaging compared to no imaging or deferred imaging was found in the majority of the included studies (low to very low quality): no difference in pain severity, in function or in psychological distress, both at short ( $\leq 4$  months) and long terms ( $> 4$  months).
- Inconsistent results were showed in term of quality of life at short and long terms: a clinical benefit of imaging (X-rays or MRI or CT) versus no imaging was suggested by RCTs (low to very low quality) but no difference was found for X-ray versus no imaging in one cohort study (very low quality).
- There was conflicting evidence regarding the healthcare utilisation at short and long term:
  - At  $\leq 4$  months, no clinical difference for X-ray versus no imaging (1 or 2 RCTs; low to very low quality) but clinical benefit favouring no imaging compared to either X-ray or MRI or CT (2 cohort studies; very low quality).
  - At  $> 4$  months, no clinical difference or clinical benefit favouring no imaging (3 RCTs; 2 comparing X-ray to no imaging, 1 comparing MRI to no imaging; low to very low quality) and (2 observational studies; 1 comparing X-ray to no imaging, 1 comparing MRI to no imaging; very low quality).
  - At both  $\leq 4$  and  $\geq 4$  months, clinical benefit of deferred imaging (MRI at 41-180 days post-onset) versus earlier imaging (MRI within the first 30 days post-onset) for most healthcare utilisation outcomes (1 cohort study, very low quality); the same cohoert study showed no clinical difference between imaging and deferred imaging in healthcare utilisation of injections at  $\leq 4$  months and nerve testing at  $> 4$  months (very low quality).



#### LBP WITHOUT SCIATICA

- One cohort study (very low quality) showed a clinical benefit at long term favouring no MRI or deferred MRI (>6 weeks of injury) compared to MRI (within 6 weeks of injury) for quality of life and function. No clinically important difference was demonstrated in pain severity at > 4 months

#### LBP WITH SCIATICA

- One cohort study (very low quality) showed a clinical benefit at long term favouring no MRI or deferred MRI (>6 weeks of injury) compared to MRI (within 6 weeks of injury) for quality of life and function. No clinically important difference was demonstrated in pain severity at > 4 months.

#### Economic evidence

- One cost-utility analysis found that early imaging is cost effective compared to delayed, selective imaging (ICER: £1,527 per QALY gained. This analysis was assessed as partially applicable with potentially serious limitations

#### Conclusions

**No clear evidence favouring imaging (compared to no imaging or deferred imaging) was found in people with low back pain or radicular pain. In terms of healthcare utilization, no clinical difference or a clinical benefit favouring no imaging or deferred imaging was shown compared to imaging within the first 30 days (very low quality evidence). In the single cost-utility analysis, limited evidence suggested that early imaging was cost-effective to delayed imaging.**



### Other considerations regarding imaging in low back pain and radicular pain

Factor	Comment
<b>Balance between clinical benefits and harms</b>	<ul style="list-style-type: none"><li>• The evidence in favour of imaging was obtained mostly from a RCT performed in a secondary care setting and was not confirmed by a cohort study in primary care. The positive results observed in specialized setting maybe not generalizable to all patients with low back pain and/or radicular pain (more severe or chronic disease; more specialized clinicians with greater abilities to diagnose specific low back pain disease justifying an imaging)..</li><li>• The Belgian GDG agreed with NICE that imaging is not useful per se but only where it is likely to change future management of the condition (for example if epidural infiltration or spinal surgery was being considered).</li><li>• Moreover, the Belgian GDG emphasised that imagining could be iatrogenic, favouring patients' misbeliefs that his/her symptoms are linked to the findings of imaging even if this findings are also present in asymptomatic individuals. Moreover, unnecessary imaging may generate anxiety if benign findings are interpreted by the patient (or the clinician) as indicating a serious or clinically relevant pathology.</li><li>• Imaging is also associated with a risk of cumulative medical radiation exposure.</li><li>• The Belgian GDG discussed the utility to formulate different recommendations according to the setting such as NICE (who specify in one recommendation "Do not routinely offer imaging in a non-specialist setting" and in another recommendation "Explain to people with low back pain (with or without radicular pain) that they may not need imaging, even if they are being referred for a specialist opinion"). In Belgium, since the primary care is not a gatekeeper and patients have direct access to physicians, specialized clinicians can be the first health care provider consulted by a patient with a first episode of low back pain. Thus there is no reason to make a distinction between the settings in Belgium.</li></ul>
<b>Quality of evidence</b>	<ul style="list-style-type: none"><li>• Due to insufficient evidence, the review was extended by NICE to cohort studies (4 additional studies included). However, for most of the comparisons, evidence came from a small number of studies.</li><li>• A piece of the available evidence could be outdated, because the imaging modality studied was x-rays rather than MRI. Moreover one RCT used bed rest as concomitant treatment to imaging.</li><li>• The economic evaluation was assessed as partially applicable with potentially serious limitations.</li></ul>
<b>Values and preferences</b>	<ul style="list-style-type: none"><li>• The Belgian GDG stressed that in low back pain without sign of severity, imaging is often used by physician for self-reassurance in response to diagnostic uncertainty. However, many of the imaging findings one would associate with low back pain causation (for example; disc and joint degeneration) are frequently found in asymptomatic individuals and imaging is often unable to confirm or refute a provisional diagnosis.</li><li>• A lot of patients with low back pain expect also imaging for reassurance, as the clinical diagnosis is uncertain. However, on the basis of the clinical and cost-effectiveness evidence reviewed, in instances where imaging was not likely to change management, it was considered that people might accept the decision not to receive imaging.</li><li>• This implies a need for patients' information. This information could be provided during the encounter with the clinician but also, by some public health campaigns using different media.</li></ul>
<b>Costs (resource allocation)</b>	<ul style="list-style-type: none"><li>• One cost-utility analysis was mentioned by NICE but assessed as partially applicable with potentially serious limitations. This analysis showed that early imaging (MRI/CT) was cost effective compared to delayed, selective imaging in secondary setting</li></ul>



but the level of evidence was assessed as low to very low by NICE. The NICE GDG noted that the conclusions of this study were not consistent with cohort studies evidence, which indicated no clinically important difference or clinically important benefit favouring no imaging.

- Further resource may be required to convince patients that an imaging is not needed in low back pain without suspected serious underlying pathology.

Recommendations	Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"> <li>• In the absence of red flags, do not routinely offer imaging for people with low back pain with or without radicular pain. Only prescribe imaging if its expected result may lead to change management, e.g. when an invasive intervention is being considered.</li> </ul>	Weak (RCTs & cohort studies)	Low to very low
<ul style="list-style-type: none"> <li>• Explain to people with low back pain with or without radicular pain that they may not need imaging, even if they are being referred for a specialist opinion.</li> </ul>	Experts opinion	Not applicable

### Change in comparison with the NICE recommendations

Minor changes have been proposed by the Belgian GDG regarding the 3 clinical recommendations proposed in the NICE 2016 guidelines.

- In the absence of red flags, Do not routinely offer imaging ~~in a non-specialist setting for people with~~ low back pain with or without ~~sciatica~~ radicular pain.
- Consider Only prescribe imaging ~~in a specialist care setting for people with low back pain with or without sciatica only~~ if its expected result is likely may lead to change management, e.g. when an invasive intervention is being considered.
- Explain to people with low back pain with or without ~~sciatica~~ radicular pain that even if they are being referred for a specialist opinion, they may not need imaging.

The reasons underlying these changes are described in Appendix 7.3.

## 3.2 Non-invasive treatment (medication excluded)

### 3.2.1 Self-management

If pain complaints become long-term, it can impact on people's physical condition and their ability to undertake normal activities of daily living.

The lack of a clear definition of (non-specific) low back pain and the lack of sufficient accurate information/advice of the caregiver(s) on the actual complaints of the patient, can produce increasing confusion, distress and, for many people, may result in an inability to adopt positive coping strategies. This can quickly result in vicious cycles of physical deconditioning, low mood, withdrawal from normal activity and, increased anxiety.

Moreover if pain complaints become long-term, it can impact on people's physical condition and their ability to undertake normal activities of daily living.

According to the International Association for the Study of Pain, chronic pain is typically managed, but not cured. In this shift in treatment paradigm, self-management has been considered as a promising treatment package.



### Definition of self-management

Self-management has been defined as “the individual’s ability to manage the symptoms, treatment, physical and psychological consequences and lifestyle changes inherent in living with a chronic condition”. This emphasizes the importance of interactive, collaborative care between patient and health care professional allowing for patient empowerment, rather than one-way, passive care from expert to patient. Also personal responsibility is encouraged for one’s day-to-day management over the duration of disease.<sup>9</sup>

In this review, self-management includes self-management advice (including advice to stay active or contrary to bed rest), self-management programs (including patient education and reassurance by written information, e.g. the Back Book), and unsupervised exercise regimes (including exercise prescription, advice to exercise at home).

The NICE evidence review can be found on p.154-202 in the full guideline on assessment and non-invasive treatments and the forest plots in Appendix K p.40-57 (<https://www.nice.org.uk/guidance/ng59/evidence>).

A summary sheet in Appendix 7.4 gathered the evidence findings, the NICE GDG considerations, the results of the online survey and the discussion with the Belgian GDG.

### Scientific evidence regarding self-management programs

Twenty-eight studies with self-management as single intervention and seven studies looking at combinations of non-invasive interventions (with self-management as the adjunct) were included in the NICE review. Different kinds of self-management programs (patient education and reassurance, advice to stay active, advice to bed rest and unsupervised exercise) were compared to placebo/sham, usual care, each other, any other non-invasive intervention or to combined interventions in order to assess the clinical and cost effectiveness of self-management. One economic evaluation including unsupervised exercise (exercise prescription) as a comparator has been included in this review. No relevant economic evaluations were identified that included self-management programmes, advice to stay active or advice for bed rest as a comparator. Several other economic evaluations were

identified by NICE but not retained due to limited applicability or serious methodological limitations.

### Self-management program as a single intervention

#### LOW BACK PAIN WITHOUT SCIATICA:

- *Self-management program (education, reassurance, advice)*: No studies found on comparisons to sham, usual care or bed rest. The studies on the comparison to other non-invasive interventions, showed either no clinical differences between comparators or some clinical benefit in some of the reported outcomes in favour of the comparator (e.g. more patients with a >50% improved function score in favour of exercise, increased function in favour of massage, less medication use in group who received yoga lessons).
- *Advice to stay active*: A single study reported only one outcome and found a clinical benefit of bed rest over advice to stay active in responder criteria (number of days to full activity at short term). No other outcomes were reported and the quality of the evidence was assessed as very low.
- *Advice to bed rest*: No evidence was available.
- *Unsupervised exercise*: Similar to the evidence on self-management programs, the studies comparing unsupervised exercise to usual care, postural therapy or massage, revealed either no clinical differences or some benefit in favour of the comparator (e.g. improved QoL scores after 6 or 24 sessions of Alexander technique). Only one study per comparison was included.



#### LOW BACK PAIN WITH SCIATICA:

- Self-management program (education, reassurance, advice): No studies found on comparisons to sham, usual care or bed rest. The studies on the comparison to other non-invasive interventions, showed no differences compared to biomechanical exercises, only at long term a clinical benefit for pain was found in favour of self-management (in a single study).
- Advice to stay active: No evidence was available.
- Advice to bed rest: The few studies comparing advice to bed rest to usual care, revealed no clinical differences. Even a small benefit in favour of usual care was found in leg pain at short term.
- Unsupervised exercise: No evidence was available.

#### MIXED POPULATION (WITH OR WITHOUT SCIATICA):

- *Self-management program (education, reassurance, advice):* Comparison to usual care, sham or bed rest revealed no major differences in pain, function and responder criteria (in pain and function). Only a small benefit in QoL was seen in favour of self-management compared to usual care. In the comparison to other non-invasive interventions, no clinical differences could be demonstrated.
- *Advice to stay active:* In the single small RCTs comparing advice to stay active versus bed rest the majority of the critical and important outcomes were not reported. Patients who received the advice to stay active perceived an increased function, at short term. These results should be interpreted with caution due to the very small number of studies and the many not reported outcomes
- *Advice to bed rest:* The single study comparing advice to bed rest to usual care found no clinical differences between both groups.
- *Unsupervised exercise:* Similar to the evidence on self-management programs, the studies comparing unsupervised exercise to usual care or exercises, revealed either no clinical differences or some benefit in favour of the comparator (e.g. improved pain scores and less pain relapses after biomechanical exercises). Only one study per comparison was included.

#### Combined interventions with self-management as adjunct

##### LOW BACK PAIN WITHOUT SCIATICA:

- One study examined the effectiveness of the combination of self-management (exercise prescription) and postural therapy (Alexander technique) in different modalities (6 or 24 lessons of postural therapy) and found no differences for most of the outcomes (QoL, pain, function, healthcare utilisation). Only long-term data were reported and other outcomes (psychological distress, adverse events and responder criteria) were not reported.

##### LOW BACK PAIN WITH SCIATICA:

- No studies were found.

##### MIXED POPULATION (WITH OR WITHOUT SCIATICA):

- Conflicting evidence was found on the effect of the addition of home exercises to laser therapy: 2 small studies found no clinical benefit on short term pain and function, whereas another study found a clinical benefit on short term pain (not on function). No clinical important benefits (on pain and function) were seen in the combination of self-management and biomechanical exercises compared to biomechanical exercises alone. No long term data and other outcomes (psychological distress, adverse events, and responder criteria) were reported.

#### Economic evidence

- One cost-utility analysis (partially applicable with potentially serious limitations) in people with low back pain without radicular pain found that the combination of unsupervised exercises and usual care was cost effective compared to usual care alone, independently if they received massage or Alexander technique lessons. Among a selection of active treatment, the combination of Alexander technique (24 lessons) with unsupervised exercise was the most effective and cost effective option
- No economic evaluation were found in people with radicular pain or the mixed population of people with or without radicular pain.



## Conclusions

**No convincing evidence was found in favour of tailored self-management programs compared to sham, usual care or other non-invasive interventions. The economic evaluation showed that adding exercise prescription to other interventions was more cost effective than each intervention alone.**

## Other considerations regarding self-management programs

GRADE Factors	Comments
<b>Balance between clinical benefits and harms</b>	<ul style="list-style-type: none"><li>• The NICE GDG discussed the necessity of a body of evidence to show specific intervention effects, that is, over and above any contextual or placebo effects. It was therefore agreed that if placebo or sham-controlled evidence is available, this should inform decision making in preference to contextual effects. However, if there was a lack of placebo or sham-controlled evidence, evidence against usual care will be given priority when decision making.</li><li>• The NICE GDG acknowledged there was no conclusive evidence in favour of self-management and highlighted that:<ul style="list-style-type: none"><li>○ Compared to usual care: some benefit in QoL, but not for pain and function. Healthcare utilisation was reduced by the use of self-management but this could be biased by taking part in a trial.</li><li>○ Compared to supervised activity: additional benefit of supervised activity could be due to contact with healthcare professional and the associated contextual effects</li><li>○ Advice to stay active versus bed rest: the beneficial effects of bed rest in days to full activity are explained by the GDG by the study characteristics (single study, specific population of combat trainees). Review showed that there was no evidence that bed rest in the short term was harmful, but also no evidence to suggest that it was beneficial to do so.</li></ul></li><li>• Although the direct evidence was far from convincing, the NICE and Belgian GDG considered that, based on evidence from combination and multidisciplinary programmes reviews, self-management plays an important role in the management of a variety of chronic conditions (and to reduce the risk for chronicity).</li><li>• The GDG agreed that although there was no conclusive evidence in favour of self-management (provided in isolation), it was still important to provide advice to people about their condition and encourage them to continue with normal activities.</li><li>• It was noted that there is no evidence from this review that a more complex intervention was any more effective than simple advice.</li><li>• The Belgian GDG agreed with NICE that self-management was justified and should be applied as a principal element alongside all treatment for people with low back pain and radicular pain as part of routine practice.</li></ul>



**Quality of evidence**

- The quality of the 35 RCTs ranged from very low to moderate with serious or very serious risk of bias due to small trials, difficulty of adequate blinding, and lack of information on background care increasing the risk of overestimating effects.
- The NICE and Belgian GDG noted that the included studies were not optimally designed to test self-management.
- The economic evidence was assessed as partially applicable with potentially serious limitations.

**Values and preferences**

- It was agreed important for clinicians to take into account people's concerns about their back pain and radicular pain, and tailor the advice to the individual.
- The Belgian GDG mentioned also that the provision of information on the nature of low back pain with or without radicular pain and the encouragement to continue with normal activities as far as possible, might not be sufficient if kinesiophobia is present. This should be tackled explicitly and a behavioural change is pursued.
- The biopsychosocial approach should be formally recommended.
- An overlap with multidisciplinary biopsychosocial rehabilitation programs was noticed.
- The importance of correct information and advice on the condition of the patient was emphasised. The members suggested to add a box with good and harmful advice proposed in O'Sullivan et al, 2014<sup>10</sup>. This box is inserted in the synthesis of the guideline.
- Regarding the potential barriers to self-management, NICE referred to two existing NICE guidances related to this area: NICE public health guidance on managing long term sickness and incapacity to work and NICE guideline on patient experience in adult NHS services: improving the experience of care for people using adult NHS services.

**Costs (resource allocation)**

- Addition of exercise prescription to other interventions was more cost effective than the other interventions alone.
- The provision of advice would not be a change of practice. Promotion of self-management may incur some minimal costs, but is an essential part of good patient care to ensure patients are adequately informed.

**Recommendations**

- Provide each patient with advice and information, tailored to their needs and capabilities, to help them self-manage their low back pain with or without radicular pain, at all steps of the treatment pathway. Include:
  - Information on the benign nature of low back pain and radicular pain
  - Encouragement to continue with normal activities, exercise included.

**Strength of Recommendation**

Experts opinion

**Level of Evidence**

Moderate to very low



### Change in comparison with the NICE recommendations

- Provide ~~people~~ each patient with advice and information, tailored to their needs and capabilities, to help them self-manage their low back pain with or without ~~sciatica~~ radicular pain, at all steps of the treatment pathway. Include:
  - Information on the benign nature of low back pain and radicular pain
  - Encouragement to continue with normal activities, exercise included.

The reasons underlying these changes are described in Appendix 7.4.

### 3.2.2 Exercise therapies

Exercise therapies make use of various forms of physical exercise to prevent or treat low back pain. The term 'exercise therapy' encompasses a wide range of different exercise types, environments and theoretical models. What they have in common is the engagement of the person with a programme of physical exercise that the person is encouraged to perform on a regular basis.

Exercise therapy may be delivered by a range of healthcare professionals, on a one to one basis or in a group environment. The focus may vary from exercise using specialist gym equipment to exercises conducted at home or in the outdoor environment. Exercise may be directed at improving a variety of parameters of fitness and function including muscle strength, timing or endurance, flexibility and range of motion, precision of movement, cardiovascular fitness, functional task performance and confidence.

In the current clinical practice, the modalities of the exercise program remain unclear, resulting in a variety of practices.

#### Definition of exercise therapies as included in the review

- **Biomechanical exercise:** any exercise intervention that is primarily directed at altering or improving spinal mechanics, by muscle strengthening, stretching, range of motion exercise, motor control exercise (core stability programmes and Pilates) or programmes aimed

at addressing specific problem movements (McKenzie exercise and Feldenkrais method)

- **Aerobic exercise:** any exercise intervention that is primarily directed at improving cardiovascular fitness and endurance
- **Mind-body exercise:** any exercise intervention that includes a combined physical, mental and spiritual focus, often with connection to metaphysical and cultural philosophies. Examples include the various forms of Yoga and Tai Chi.
- **Mixed exercises:** any exercise intervention that incorporates a combination of any of the previous three categories (biomechanical exercises, aerobic exercises, mind-body exercises)

The NICE evidence review can be found on p.203-309 in the full guideline on assessment and non-invasive treatments and the forest plots in Appendix K p.57-100 (<https://www.nice.org.uk/guidance/ng59/evidence>).

A summary sheet in Appendix 7.5 gathered the evidence findings, the NICE GDG considerations, the results of the online survey and the discussion with the Belgian GDG.

#### Scientific evidence regarding exercise therapies

A total of 75 RCTs on single interventions and 16 RCTs on combined interventions was included in the review in order to assess the clinical and cost-effectiveness of different types of exercise. One economic evaluation was identified in patients with low back pain without sciatica and four economic evaluations were found in the mixed population (low back pain with or without sciatica). Within the evidence reported by NICE, the KCE researchers looked at differences in efficacy of exercise therapy between acute and chronic low back pain. The same definition of acute has been applied as in NICE: acute low back pain is less than 3 months, chronic low back pain is at least 3 months. For clarity reasons, no distinction has been made between acute and subacute low back pain.



### Biomechanical exercises as single intervention or as adjunct

#### LOW BACK PAIN WITHOUT SCIATICA:

(see Tables 7 and 16 in Appendix 7.5)

- *Individual biomechanical exercises:* Compared to usual care, a clinically important improvement of biomechanical exercises was found in QoL (at both time points). For pain and function the results are less consistent but overall more beneficial in favour of biomechanical exercises for pain improvement than for function. More adverse events were reported in the group undertaking the biomechanical exercises. In the pooled data, studies on acute and chronic low back pain patients were mixed. Re-analysis of these data showed that the single RCT on acute low back pain patients (individual biomechanical exercise versus usual care) reported no clinical difference in **pain** change score (VAS 0-85) at both time points and in **function** (RMDQ 0-24, only at short term reported). No other outcomes were reported.
- *Group biomechanical exercises:* A clinical benefit was found for QoL and function in favour of (group) biomechanical exercises compared to usual care, but no differences for pain. No long-term data were reported. No evidence was found on acute low back pain patients.
- *Biomechanical exercises as adjunct in combined interventions:* Adding biomechanical exercises to electrotherapy (TENS) revealed no clinical differences in pain and function at short term. A clinical improvement in pain and function was noted in a combined intervention of biomechanical exercises and self-management (education) compared to self-management (education) alone. No evidence was found on acute low back pain patients.

#### LOW BACK PAIN WITH SCIATICA:

(see Table 8 in Appendix 7.5)

- *Individual biomechanical exercises:* The single study comparing biomechanical exercises to usual care found a clinical benefit for pain severity in favour of the biomechanical exercises (only reported outcome and no long-term data reported). The duration of the pain complaints was not clearly stated in the study, therefore no distinction can be made between the efficacy in acute and chronic low back pain patients. No clinical differences were found at both time points for QoL (except for long-term physical component in favour of biomechanical exercises), pain and function when biomechanical exercises were compared to spinal manipulations (low-amplitude-high velocity). This single study considered low back pain patients with at least 6 weeks of pain complaints, this group of patients is considered as a mixed population of acute and chronic pain patients, therefore no statement can be made on the efficacy in acute low back pain patients.
- *Group biomechanical exercises:* No evidence was available.
- *Biomechanical exercises as adjunct in combined interventions:* The combination of biomechanical exercises and self-management (unsupervised exercises) showed a clinical benefit in pain and function (at short term) compared to a combined intervention of electrotherapy (TENS and laser), soft tissue techniques (massage) and self-management (unsupervised exercises). No evidence was found on acute low back pain patients.



#### MIXED POPULATION (WITH OR WITHOUT SCIATICA):

(see Tables 9 and 17 in Appendix 7.5)

- *Individual biomechanical exercises:* Comparison to usual care, showed only a short term benefit in QoL and psychological distress, both in favour of biomechanical exercises. No clinical differences were found for overall score on pain and function. Within the pooled data, one RCT was included on acute low back pain patients, but the results were in line with the overall conclusion (no clinical difference in overall pain and in function at both time points). Comparison to active comparators (self-management (advice), or interferential therapy) found a clinically benefit in short term pain (compared to IFT) and a long-term benefit in function (compared to self-management). In both studies, the duration of the pain complaints was not clearly stated, therefore no separate statement can be made on its efficacy in patients with acute low back pain.
- *Group biomechanical exercises:* The comparison to usual care showed at short term only an improvement in function, and at long-term a clinical benefit in pain and in healthcare utilisation (NSAID use) in favour of biomechanical exercises. No evidence was found on this comparison in patients with acute low back pain. In the comparison to active comparators (only one RCT found on unsupervised exercises) only the outcome pain was reported and showed at short term no difference but at long term a clinical improvement in favour of biomechanical exercises. In this study the duration of the pain complaints was not clearly stated, therefore no separate statement can be made on the efficacy of biomechanical exercises (compared to unsupervised exercises) in patients with acute low back pain.
- *Biomechanical exercises as adjunct in combined interventions:* Across the different comparison of combined interventions of biomechanical exercises and orthotics/self-management/manual therapy, no consistent beneficial effect was found in favour of the combined intervention with biomechanical exercises. Often the improvement in pain was not associated with an improvement in function. Drawing a conclusion on its effectiveness is also hampered by the single small studies per comparison, not reporting all critical (and/or important) outcomes at both time points. No clear statement can be made on the

efficacy in acute low back pain due to lack of separate studies on this patient group. In the retrieved studies either only chronic patients were included or the duration was not clearly stated.

#### Aerobic exercises

##### LOW BACK PAIN WITHOUT SCIATICA:

(see Tables 10 and 16 in Appendix 7.5)

- *Individual aerobic exercises:* Only studies comparing different types of aerobic exercises (walking, treadmill running, deep water running) to usual care were retrieved, with a clinical improvement in function and pain (only for deep water running), but no differences in QoL and psychological distress. No evidence was found on the efficacy of individual aerobic exercises in patients with acute low back pain.
- *Group aerobic exercises:* The studies on aerobic exercises compared to usual care, found at short term a benefit in QOL and pain in favour of aerobic exercises, but not in function and psychological distress. At long term no differences were anymore found (only pain and function reported). One study comparing aerobic exercises to (group) biomechanical exercises showed only a short term benefit in pain after aerobic exercises but no differences were found at long term nor for function (at both time points). No evidence was found on the efficacy of group aerobic exercises in patients with acute low back pain.
- *Aerobic exercises as adjunct in combined interventions:* The combination of aerobic exercises and a psychological intervention (behavioural therapy) revealed no difference in pain (only reported outcome) compared to the psychological intervention alone. When aerobic exercises were added to a combined intervention of a psychological intervention (cognitive behavioural therapy) and self-management (education) no differences were found in pain and even a beneficial effect on function was noted in favour of the combined intervention without exercises. No evidence was found on acute low back pain patients.



## LOW BACK PAIN WITH SCIATICA:

- No evidence was available.

## MIXED POPULATION (WITH OR WITHOUT SCIATICA):

(see Table 11 in Appendix 7.5)

- *Individual aerobic exercises*: In the comparisons to usual care and to active comparator (individual biomechanical exercises), no differences were found in short term pain (only reported in comparison to usual care) and function. No evidence was found on the efficacy of individual aerobic exercises in patients with acute low back pain.
- *Group aerobic exercises*: Only comparisons to active comparators were found in this patient group: whereas no differences in pain and function (at both time points) were found between aerobic or (group) biomechanical exercises, a clinical benefit in short-term pain was noted in the aerobic exercise group compared to the group who received self-management (advice to bed rest). No evidence was found on the efficacy of group aerobic exercises in patients with acute low back pain.
- *Aerobic exercises as adjunct in combined interventions*: No evidence was available.

**Mind-body exercises**

## LOW BACK PAIN WITHOUT SCIATICA:

(see Table 12 in Appendix 7.5)

- *Individual mind-body exercises*: No evidence was available.
- *Group mind-body exercises*: The single study on the comparison to usual care, reported more pain reduction (at both time points, only reported outcome) in the mind-body exercise group. Compared to self-management (advice to stay active) a short term benefit of the mind-body exercises on function and on responder criteria (improvement in function) was shown. However, this beneficial effect is not anymore seen at long-term. No difference in function was found between mind-body exercises and (group) mixed exercises (aerobic and biomechanical). In both comparisons (self-management or mixed exercises) an important decreased medication use was found in the

group mind-body exercises. No evidence was found on the efficacy of mind-body exercises in patients with acute low back pain.

- *Mind-body exercises as adjunct in combined interventions*: No evidence was available.

## LOW BACK PAIN WITH SCIATICA:

- No evidence was available.

## MIXED POPULATION (WITH OR WITHOUT SCIATICA):

(see Table 13 in Appendix 7.5)

- *Individual mind-body exercises*: Only studies on the comparison of mind-body exercises to (individual) biomechanical exercises were retrieved. Evidence from 1 small study showed short term clinical benefit of yoga on pain and function, whereas a study on tai chi found no clinically important differences on short-term pain (no data on function reported).
- *Group mind-body exercises*: Different types of yoga were compared to usual care, but no clear conclusion can be drawn on its potential beneficial effects due to inconsistent results for QoL, pain, function, psychological distress and healthcare utilisation. A clinically important improvement in pain (at both time points) was found in the group mind-body exercises compared to the group who received (individual) biomechanical exercises.
- In the retrieved studies either the duration of the pain complaints was not clearly stated or only patients with chronic low back pain were considered, therefore no conclusion can be made on the efficacy of mind-body exercises in patients with acute low back pain.
- *Mind-body exercises as adjunct in combined interventions*: No evidence was available.



### Mixed exercises

#### LOW BACK PAIN WITHOUT SCIATICA:

(see Tables 14 and 16 in Appendix 7.5)

- *Individual mixed exercises:* No evidence was available.
- *Group mixed exercises:* In the comparison to usual care, some beneficial effect of mixed exercises was seen in QoL, but not in pain, function and psychological distress. No evidence was found in patients with acute low back pain. Whereas no differences were found compared to self-management (Back Book), some benefit of a similar mix of aerobic and biomechanical exercises was found on pain and function (but not on psychological distress) compared to cognitive behavioural therapy. In both comparisons, no evidence was found for acute low back pain patients.
- *Mixed exercises as adjunct in combined interventions:* The combined interventions of mixed exercises (biomechanical and aerobic) and electrotherapy (PENS) compared to sham or real electrotherapy (PENS) could not demonstrate any beneficial effect (in QoL, pain and function) on the addition of mixed exercises to electrotherapy. The only reported outcome in the comparison of group mixed exercises (biomechanical and aerobic), self-management (education) and manual therapy (spinal manipulation) versus the combination of individual biomechanical exercises, self-management (education) and manual therapy (spinal manipulation) showed no difference in analgesic use between both interventions. No evidence was found on acute LBP patients.

#### LOW BACK PAIN WITH SCIATICA:

- *Individual mixed exercises:* The only reported outcome in the comparison to waiting list showed a beneficial effect of individual mixed exercises on (leg) pain. No long term data or other outcomes were reported. This study involved only chronic low back pain patients, therefore no conclusion can be made for acute low back pain patients.
- *Group mixed exercises:* At short term, no clinical difference in overall pain and function were found between mixed exercises and usual care. Some benefit of mixed exercises were seen in pain at rest and pain on movement. At long term, the results are more conflicting with a benefit in overall pain favouring mixed exercises whereas function improved more in the usual care group. No evidence was found in patients with acute low back pain.
- *Mixed exercises as adjunct in combined interventions:* No evidence was available.

#### MIXED POPULATION (WITH OR WITHOUT SCIATICA):

(see Tables 15 and 17 in Appendix 7.5)

- *Individual mixed exercises:* Studies comparing mixed exercises to active comparators (unsupervised exercises of biomechanical exercises), showed a short term improvement in pain compared to unsupervised exercises, however, no differences in pain and function were found between mixed or biomechanical exercises. No evidence was found in patients with acute low back pain.
- *Group mixed exercises:* The results on the comparison with usual care is somewhat inconsistent, but overall could be stated that in the mixed exercise group an improvement in QoL, pain (at both time points) and function (only at short term) was noted. No differences were found in pain, function, psychological distress and healthcare utilisation between group mixed exercises and cognitive behavioural therapy. No evidence was found in patients with acute low back pain.
- *Mixed exercises as adjunct in combined interventions:* The evidence on the addition of mixed exercises to other interventions was limited to a single study comparing the combination of mixed exercises



(biomechanical and aerobic) and Alexander technique to Alexander technique alone, but no differences were found in short-term function. No long-term nor other outcomes were reported. The duration of the complaints was not clearly stated, therefore no differentiation could be made between chronic and acute low back pain patients.

### Economic evidence

- One economic evaluation was identified in patients with low back pain without sciatica: The combination of biomechanical exercise and self-management was dominated by combination of biomechanical exercise, manual therapy and self-management. If manual therapy (spinal manipulation) is not available, combination of biomechanical exercise and self-management was cost-effective compared to self-management alone.
- Four economic evaluations were found in the mixed population (low back pain with or without sciatica) and found that:
  - group mind-body exercise + usual care was cost effective compared to usual care alone
  - biomechanical exercise was dominated (more effective and less costly) by a 3 element MBR programme (physical, psychological and educational)
  - group mixed modality exercise (biomechanical + aerobic) was dominated (more costly and less effective) by cognitive behavioural approaches
  - mixed modality manual therapy in combination with self-management and biomechanical exercise showed no statistically significant increase in costs or outcomes compared to self-management
- No economic evaluations were found in patients with sciatica. Also no economic evaluations considered the cost-effectiveness of aerobic exercises.

### Conclusions

- **Biomechanical exercises:** Some beneficial effect of biomechanical exercises could be noted but the evidence is inconsistent across the different outcomes. The outcomes improved (slightly) when the exercises were performed in group and/or in combination with other active interventions.
- **Aerobic exercises:** The inconsistency across the outcomes (e.g. improvement in pain severity not associated with improvement in function) hampers to draw a clear conclusion on the clinical effectiveness of aerobic exercises. The evidence on aerobic interventions as adjunct was restricted to people with low back pain without sciatica and could not demonstrate any beneficial effect. No evidence was found in people with low back pain and sciatica.
- **Mind-body exercises:** The majority of the evidence focused on the effectiveness of group mind-body exercises. Some improvement in pain severity was shown compared to usual care or self-management, however the effects faded out at long term. No clear conclusion can be made if mind-body exercises are more beneficial than biomechanical exercises. No evidence was found in people with low back pain and sciatica.
- **Mixed exercises:** In the studies on mixed exercises often aerobic and biomechanical exercises were combined, however the evidence is not clear cut in favour of this mix of exercises. If some short-term effect was noted in one of the outcomes, this effect was no longer seen at long term.



- 
- In summary, it can be stated that some evidence of clinically important effects was found for the critical outcomes, but insufficient evidence that one form of exercise was superior to another. Also no clear distinction in efficacy between acute and chronic low back pain patients could be demonstrated. The majority of the studies included chronic low back pain patients. Therefore no clear statement can be made on the efficacy of exercise therapy in acute low back pain patients. This should not be interpreted as “no effect”.
  - Cost-effectiveness: Based on the economic evidence across the different patient subgroups, it could be stated that the cost-effectiveness of exercise therapy increased in combined interventions with self-management and manual therapy. A 3-element multidisciplinary rehabilitation program with a physical, psychological and educational component seemed to be more effective and less costly.
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## Other considerations regarding exercise therapies

GRADE Factors	Comments
<b>Balance between desirable and undesirable effects</b>	<ul style="list-style-type: none"> <li>• The NICE GDG discussed the necessity of a body of evidence to show specific intervention effects, that is, over and above any contextual or placebo effects. It was therefore agreed that if placebo or sham-controlled evidence is available, this should inform decision making in preference to contextual effects. However, if there was a lack of placebo or sham-controlled evidence, evidence against usual care will be given priority when decision making.</li> <li>• Although some trials were identified that had sham exercise as a comparator, on consideration of these, the NICE GDG agreed none met the protocol criteria for appropriate sham interventions for this review. Some shams were interventions being considered elsewhere within the guideline, and are considered under the relevant comparators, whereas others were comparing different forms of exercise and have been excluded. There was consequently no evidence available for exercise compared to placebo/sham.</li> <li>• The Belgian GDG agreed that the evidence compared to usual care did show that exercise is likely to be of value, although with some uncertainty about the effect size and that effect of exercise compared to usual care or self-management could be due to imbalance of therapeutic attention.</li> <li>• In the absence of a feasible sham control, the GDG agreed that this was sufficient evidence for a recommendation to consider exercise for people with low back pain with or without sciatica.</li> <li>• The Belgian GDG noted that the high number of studies, even of low quality, showed good results. Also the clinical importance of exercises and staying active was emphasised.</li> <li>• However, there was insufficient evidence that one form of exercise was superior to another and a recommendation for a specific exercise modality was not supported from the current evidence base. <ul style="list-style-type: none"> <li>○ The GDG agreed that aerobic exercise has many additional health benefits and therefore, would not discourage anyone from partaking in such exercise programmes, but were not able to support a recommendation for aerobic exercise alone.</li> <li>○ The Belgian GDG noted that the evidence on group sessions is not superior to evidence on individual sessions and agreed that “group” should be removed from the recommendation.</li> </ul> </li> <li>• Data on adverse events were very limited and exercise, if conducted appropriately, should be safe.</li> </ul>
<b>Quality of evidence</b>	<ul style="list-style-type: none"> <li>• The quality of the evidence ranged from moderate to low.</li> <li>• Contextual factors, such as therapist’ attention, might explain, at least in part, the observed effects to the likelihood of overestimating the effect.</li> <li>• The NICE GDG agreed that the pooling of studies with widely differing interventions, despite strengthening the body of evidence, would make it difficult to draw a conclusion about what type of exercise to offer, and to which populations.</li> <li>• The economic evidence was assessed as partially applicable with potentially serious limitations</li> </ul>
<b>Values and preferences</b>	<ul style="list-style-type: none"> <li>• This review was unable to tease out which type of exercise modality was effective and the frequency and duration of the exercise to be given. The Belgian GDG agreed with NICE that it is important to consider tailoring the programme to the individual, including taking into account an intensity that was feasible for the individual to be able to undertake and sustain. It was noted that the majority of exercise considered in this review was delivered by clinical providers. The GDG emphasised the need for an individualized</li> </ul>



approach and that it would be useful to recommend an intervention that the person with back pain would be likely to participate in and that promotes self-management.

- The Belgian GDG suggested to replace the terms “biomechanical, aerobic, mind-body” by “specific” exercises: the specification of type of exercises seemed unnecessary due to the lack of superior effect of one type of exercises and it leaves more open to the clinicians to adapt the treatment plan to the individual needs of the patient.
- Regarding the recommendation to consider offering exercise in a group environment (based on the likely cost savings of that approach and the lack of evidence for the superior efficacy of individually delivered exercise), the Belgian GDG mentioned that group exercises may not be suitable or acceptable for all patients and highlighted the need for clinicians to be sensitive to this (e.g. cultural, psychological or functional ability).
- Other comments formulated by the Belgian GDG members were:
  - The wording “within the NHS” is not relevant for Belgian clinical practice and should be removed. Also it was unclear why the payment should be mentioned in the recommendation. Currently in Belgium there are already nomenclature codes available for exercise therapy in patients with low back pain.
  - It is not clear why the recommendation is focused on “specific episode”. According to NICE, the importance of keeping active with normal activities outside specific episodes or flare-ups is addressed by the self-management recommendation. However, the Belgian GDG suggested to remove this concepts “with a specific episode or flare-up” because the link between the evidence and the recommendation is unclear and it is important to remind that chronic patients can also benefit from exercise therapy.
  - There was some discussions if individualised therapy will lead to a more passive approach. The GDG members agreed on the fact that exercise therapy requires an active participation of the patient.

#### Costs (resource allocation)

- There is uncertainty about the cost effectiveness of exercise programmes, largely depending on the number of sessions and in group or individually but the benefits of exercise are likely and therefore appropriate to recommend group exercise.
- Evidence was not strong enough for strong recommendation with regards to optimal type, dose or duration of any exercise programme.
- Despite uncertainties it was likely that the benefits of exercise to people with a specific episode or flare-up with or without sciatica would justify the costs.
- Given the additional costs and uncertainties regarding the benefits of individual exercise, NICE considered appropriate to recommend group exercise since they could incur fewer costs than individual exercise. However, the Belgian GDG did not agree on this perception and preferred to leave open if exercises should be performed alone or in group.

#### Recommendation

- Consider an exercise programme (specific exercises or a combination of approaches) for people with low back pain with or without radicular pain. Take patient’s specific needs, capabilities and preferences into account when choosing the type of exercise programme.

#### Strength of Recommendation

Weak (RCTs)

#### Level of Evidence

Moderate to low



### Change in comparison with the NICE recommendations

- Addition of “people with” and “sciatica” replaced by “radicular pain”
- Deleted “group”, “within the NHS”, “a specific episode or flare-up of”
- Replaced “biomechanical, aerobic, mind-body” by “specific”
- “program” added, “people’s” replaced by “patients”
- Consider a ~~group~~ exercise programme (~~biomechanical, aerobic, mind-body~~ specific or a combination of approaches) ~~within the NHS~~ for people with a ~~specific episode or flare-up of~~ low back pain with or without ~~sciatica~~ radicular pain. Take ~~people’s~~ patient’s specific needs, preferences and capabilities into account when choosing the type of exercise programme.

The reasons underlying these changes are described in Appendix 7.5.

### 3.2.3 Postural therapies

Within the non-invasive therapeutic options, postural therapy and its potential beneficial effect in the management of patients with low back pain with or without radicular pain, is not yet well known in the Belgian clinical practice.

#### Definition of postural therapies

- **Postural therapies** aim to prevent or reduce low back pain by focusing on the correction of postures that are theorised to be suboptimal and place excessive or damaging loads upon the spine. They generally involve the encouragement of postures considered by the therapist or discipline to be healthier with a focus on education regarding which postures are considered optimal and detrimental. Postural therapy also focuses on exercises and practice at adopting the postures and movements that are considered healthy. There are various disciplines of postural therapy and, while they share similarities, they may differ on aspects of what are considered optimal and suboptimal postures and the techniques used to address this.

- The **Alexander Technique** a taught practical method and an embodied, contemplative practice. Alexander lessons help people to free themselves from unhelpful postural and movement habits and develop a more intelligent and skilled control of the manner in which they respond to stimuli and engage in activity. Alexander Technique teachers focus on restoring the working of the postural supporting mechanisms through experiential learning aided by hands-on guidance and encouraging changes in an individual's own thinking and attitude. They help people attend to postural sensory feedback and make use of this information; show them how to allow the neuromuscular mechanisms to determine appropriate postural support and the pathways of skilled movement without habitual interference in the underlying non-conscious processes; and how to initiate movement through clarity of intention in a way that is compatible with current theories of skilled motor control.<sup>11</sup>

The NICE evidence review can be found on p.310-334 in the full guideline on assessment and non-invasive treatments and the forest plots in Appendix K p.100-110 (<https://www.nice.org.uk/guidance/ng59/evidence>).

A summary sheet in Appendix 7.6 gathered the evidence findings, the NICE GDG considerations, the results of the online survey and the discussion with the Belgian GDG.

#### Scientific evidence regarding postural therapies

In this section, the evidence on the clinical and the cost-effectiveness of postural therapies (including Alexander technique) has been considered in comparison to usual care or active interventions. Two randomised trials were identified comparing Alexander technique lessons (of various durations) with usual care, massage or mixed exercise in people with a recurrent episode of low back pain, in a population without sciatica, and an overall population with or without sciatica. A further search for cohort studies was conducted, from which 2 studies were identified and full copies ordered. Both these cohorts were excluded, the first due to inappropriate outcomes (physiological measures of muscle activity) and the second due to the study design (non-comparative study). One economic evaluation was identified that included Alexander technique lessons as a comparator and has been included in this review.



#### LOW BACK PAIN WITHOUT SCIATICA:

- *Single interventions:* An RCT comparing 6 lessons of Alexander technique to usual care, massage of self-management (exercise prescription) revealed a potential important benefit in QoL but no differences in pain, function and healthcare utilisation (primary care contacts and prescriptions). When the number of Alexander technique lessons was increased to 24, improvements were seen for QoL, pain and function (for all 3 comparisons). However, no difference was found in healthcare utilisation (primary care contacts and prescriptions). The comparison of 6 lessons versus 24 lessons of Alexander technique, showed a clinically important benefit for the physical domain of QoL and for function, but not differences were found for the mental health domain of QoL, pain intensity and healthcare utilisation. In none of the comparisons, short term outcomes were reported.
- *Postural therapies as adjunct in combined interventions:* The combination of 6 lessons of Alexander technique with self-management (home exercise prescription) showed a beneficial effect on function, pain and the physical domain of QoL in favour of the combined intervention, no difference was observed in the mental domain of QoL. When the number of Alexander lessons were increased to 24 and combined with self-management (home exercise prescription), a clinical benefit was found in all reported outcomes (pain, function and QoL).

#### LOW BACK PAIN WITH SCIATICA:

- *Single interventions:* No evidence was available.
- *Postural therapies as adjunct in combined interventions:* A single RCT reported one comparison: the combination of postural therapy (head posture corrective exercise program) and multidisciplinary rehabilitation program (physical, cognitive and educational component) versus the multidisciplinary rehabilitation program only. No clinical differences were found in pain (leg and back) severity and function. No long term data were reported, nor other outcomes.

#### MIXED POPULATION (WITH OR WITHOUT SCIATICA):

- *Single interventions:* Ten lessons of Alexander technique showed no short term clinical benefit in pain and function, only at long term a clinical benefit for function was found in favour of the postural therapy compared to usual care. In the same RCT the 10 lessons of Alexander technique were also compared to mixed exercises (biomechanical + aerobic). Only the results for the outcome of short-term function were reported and no difference was observed between both comparators.
- *Postural therapies as adjunct in combined interventions:* The same RCT as in the results section on single interventions, reported also the results for the comparison of a combination of 10 lessons of Alexander technique with mixed exercises (biomechanical + aerobic) to usual care or to group mixed exercises (biomechanical + aerobic). Compared to usual care, only a clinical benefit in long-term function was observed in favour of the combination of Alexander technique with exercises. However, no differences were found for short term function or pain at any time point. Compared to group mixed exercises, the only reported outcome (short term function) showed no difference between both treatment arms.

#### Economic evidence

- One economic evaluation concerned Alexander technique lessons in patients with low back pain without sciatica:
  - Compared to usual care: Alexander technique lessons were cost effective (both alone and as an adjunct to an exercise prescription). There was some uncertainty (depending on concurrent treatment) but 24 lessons is probably the most cost effective option (over 6 lessons).
  - Compared to active interventions: the combination of Alexander technique (24 lessons) with self-management (exercise prescription) was the most effective (highest QALYs) and most cost effective option from usual care, soft tissue techniques (massage), Alexander technique (6 or 24 lessons), usual care + self-management (exercise prescription), self-management (exercise prescription) + massage, or Alexander technique lessons (6 lessons) + self-management (exercise prescription).



## Conclusions

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- In the evidence review a distinction is made by NICE between the evidence on postural education and on Alexander technique.
  - No studies were found on the effectiveness of postural education/exercise (as single) intervention.
  - No studies were found on Alexander technique compared to placebo or sham therapy. The increase of Alexander technique lessons from 6 to 24 showed an improvement in (physical) quality of life, pain and function compared to usual care or active interventions.
  - The combination of postural therapy with multidisciplinary rehabilitation program revealed no clinical differences compared to the rehabilitation program alone. A similar tendency was found in the study comparing the combination of Alexander technique lessons and self-management to usual care: the increase in number of lessons from 6 to 24 improved the pain, function and quality of life scores.
  - The single economic evaluation suggested that the Alexander technique lessons may be cost effective.
-



### Other considerations regarding postural therapies

GRADE Factors	Comments
<b>Balance between desirable and undesirable effects</b>	<ul style="list-style-type: none"><li>• Given that no RCT or observational study evidence was identified relating to the effectiveness of <b>postural education/exercise</b>, the Belgian GDG agreed with NICE that a recommendation should not be made on this topic as single intervention.</li><li>• <b>Regarding the Alexander technique</b>, overall could be stated that the increase from 6 to 24 lessons improved the outcome measures. The study reporting results on 10 lessons of Alexander technique in a mixed population (with or without sciatica) was a feasibility trial with a small number of participants which was taken into account when weighing up the evidence. The combination of postural therapy with a MBR program revealed no clinical differences, but the combination of Alexander technique lessons with self-management (exercise prescription) showed improved scores on pain, function and QoL.</li><li>• A small increase in healthcare utilisation was observed with the Alexander technique, but the NICE GDG considered the benefits of a longer course of treatment to outweigh the harms. Indeed, although no evidence was reported on the occurrence of adverse events, the NICE highlighted that the Alexander technique was a low risk treatment for patients and serious adverse events were unlikely.</li><li>• The NICE GDG agreed that the evidence reviewed was promising in terms of potential quality of life for people with low back pain, however the evidence in favour of the Alexander technique was taken from a single study which it is not sufficient to recommend a significant change in practice.</li><li>• Given the potential benefit demonstrated for the Alexander technique in the evidence reviewed, the NICE GDG considered making a research recommendation on this therapy to be conducted in order to re-evaluate its use in the future. It was however noted that following completion of the ASPEN feasibility trial (included in this review), it is likely that a larger trial will follow and therefore a research recommendation was not prioritised for this topic.</li><li>• The GDG stressed that no evidence was found for patients with low back pain and sciatica.</li><li>• The exclusion of other postural therapy techniques was also questioned by the Belgian GDG, e.g. the global postural re-education, Pilates exercises. (KCE note: Pilates has been considered in the exercise chapter)</li></ul>
<b>Quality of evidence</b>	<ul style="list-style-type: none"><li>• The quality for all outcomes ranged from moderate to very low due to high risk of bias (absence of description of usual care, high rates of missing data, inadequate blinding).</li><li>• Due to the limited information about the usual care, it is not possible to tell if it is the Alexander technique itself or simply the contact with a therapist that is causing any effects seen in the first trial. All the data reported from this trial were longer-term follow-up data (&gt; 4 months - 1 year), and none of the outcomes were measured at ≤4 months.</li><li>• It was recognised that the nature of the intervention itself may preclude designing an adequate placebo-controlled study, however, it was agreed that concurrence of results in more than one pragmatic trial with clear descriptions of comparator interventions and intention to treat analyses would give greater confidence to the GDG in recommending the intervention than the single trial currently available.</li></ul>



	<ul style="list-style-type: none"> <li>The economic analysis was judged to be partially applicable with potentially serious limitations, due to the limitations in reporting of uncertainty within the analysis. However, the available information does suggest that the conclusion is probably reasonable robust.</li> </ul>
<b>Values and preferences</b>	<ul style="list-style-type: none"> <li>The Belgian GDG considered that Alexander technique is more than a postural therapy (see Appendix 7.6). NICE was aware that the two interventions included in the review (alexander technique and head posture corrective exercises) are distinct, but felt that both fall under the overarching heading of postural therapy, in the same way that yoga and aerobic exercise are distinct but both fall under exercise.</li> <li>The Belgian GDG preferred to consider Alexander technique rather as a separate intervention. Nevertheless, for both interventions, no recommendation was formulated.</li> <li>Moreover the Alexander techniques are currently not included in the training of physiotherapists.</li> <li>Problems related to this type of exercises is the potential impact of the caregiver.</li> </ul>
<b>Costs (resource allocation)</b>	<ul style="list-style-type: none"> <li>No economic evaluations were identified relating postural education/exercise.</li> <li>The potential cost-effectiveness of Alexander technique lessons was considered as relevant by the NICE GDG members, although the evidence for effectiveness is based on a single trial (the ATEAM trial). Recommending the intervention would lead to a significant change in practice and more evidence is needed to recommend its use in clinical practice.</li> </ul>

Recommendation	Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"> <li>No recommendation was formulated on postural therapies.</li> </ul>	NA	NA
<ul style="list-style-type: none"> <li>No recommendation was formulated on Alexander technique lessons.</li> </ul>	NA	NA

#### Change in comparison with the NICE recommendations

- Nevertheless the formulation of a separate recommendation on Alexander technique, for both kinds of therapies, no clear recommendation was formulated.
- The reasons underlying these changes are described in Appendix 7.6.



### 3.2.4 Orthotics and appliances

Orthotics and specialist footwear may be used for a number of reasons to treat or prevent back pain (correction of proposed leg length or foot posture abnormalities, with the goal of normalising or altering lower limb, pelvis and trunk mechanics and load, training and enhancing balance and proprioception or reducing the lumbar lordosis). There is a broad range of products, and the materials used vary, with soft, semi-rigid and rigid orthotics available.

There is also a wide range of lumbar corsets, belts and supports available, which are considered as appliances or devices. They vary widely in design, materials, the degree of rigidity and the area to which they are designed to provide support. The devices are commonly used with the aim of providing support to or reducing the load on the lower back and/or pelvic joints. They can also be used to attempt to correct deformity, limit motion or provide a type of massage or heat to the area.

Nevertheless the widespread use of orthotics and appliances, its clinical effectiveness remains uncertain.

The NICE evidence review can be found on p.335-351 in the full guideline on assessment and non-invasive treatments and the forest plots in Appendix K p.110-114 (<https://www.nice.org.uk/guidance/ng59/evidence>).

A summary sheet in Appendix 7.7 gathered the evidence findings, the NICE GDG considerations, the results of the online survey and the discussion with the Belgian GDG.

#### Scientific evidence regarding orthotics and appliances

A search was performed to assess the clinical and cost-effectiveness of orthotics (i.e. orthopaedic shoes) and appliances (i.e. belts and corsets) in the management of low back pain and sciatica. Twelve randomised controlled trials were included by NICE: Three of the trials compared foot orthotics to placebo, sham or usual care, 7 trials compared a variety of corsets and belts to either usual care, analgesics, massage or manual therapy. Each trial was investigating the effectiveness of orthotics and appliances in people with low back pain with or without sciatica. Due to the limited data available from randomised trials included in this review, the

search was widened by NICE to include cohort studies. One cohort study relevant to the protocol was identified which compared foot orthotics and usual care and has been included in the review. One study looking at combinations of non-invasive interventions (with orthotics as the adjunct) was also included in this review. Five Cochrane reviews were identified but they could not be included for different methodological reasons. No relevant economic evaluations were identified.

#### Scientific evidence regarding belts/corsets

##### LOW BACK PAIN WITHOUT SCIATICA:

- *Single interventions:* The single small study comparing lumbar belts to usual care (only comparison found) showed no clinical difference in function, pain and responder criteria for pain improvement. In the comparison of corsets to usual care, a different result was found depending on the type of corset: a small clinical benefit in function was found with inextensible corsets, while no difference was found with extensible corsets. With both corset types no clinical difference in pain could be demonstrated. Corsets compared to active comparators (spinal manipulation, massage or non-opioid analgesics) revealed only a short term improvement in function in favour of corsets compared to massage (but this was not associated with an improvement in pain). All studies were on small sample sizes, inducing a serious imprecision of the results. In none of the comparisons a clinical benefit in pain scores was observed.
- *Belts/corsets as adjunct in combined interventions:* No evidence was available.

##### LOW BACK PAIN WITH SCIATICA:

- No evidence was available.





## MIXED POPULATION (WITH OR WITHOUT SCIATICA):

- *Single interventions:* No evidence was available.
- *Belts/corsets as adjunct in combined interventions:* The addition of a corset to a treatment package of electrotherapy and manual therapy (massage + traction) improved the pain and functions score significantly more than the combination of electrotherapy and manual therapy alone. Only one study was found on this single comparison, and no other relevant outcomes measures were reported

**Scientific evidence regarding foot orthotics**

## LOW BACK PAIN WITHOUT SCIATICA:

- *Single interventions:* The only RCT found in this patient group, compared rocker sole shoes to sham shoes (flat soles) and found no clinical difference in function, pain, anxiety scores and depression scores, at both time points. Only a small clinical benefit at both time points was found in QoL in favour of flat sole shoes.
- *Foot orthotics as adjunct in combined interventions:* No evidence was available.

## LOW BACK PAIN WITH SCIATICA:

- *Single interventions:* Foot orthotics (customized insoles) compared to placebo orthotics showed a short-term clinical benefit in function and pain in favour of the foot orthotics. The randomized and non-randomized studies comparing foot orthotics to usual care found no difference in function. Only a short term improvement in pain was seen.
- *Foot orthotics as adjunct in combined interventions:* No evidence was available.

## MIXED POPULATION (WITH OR WITHOUT SCIATICA):

- No evidence was available.

**Economic evidence**

- No relevant economic evaluations were identified.
- For the consideration of cost-effectiveness, not only unit costs for the orthotics but also additional costs, e.g. appointment for fitting, needs to be taken into account.

**Conclusions**

- 
- **There is insufficient evidence to support a positive recommendation for the use of belts or corsets as a treatment for low back pain. No studies were found on the potential use of belts or corsets in patients with low back pain and sciatica.**
  - **No good evidence was available that foot orthotics or rocker soles were of benefit to patients with low back pain with or without sciatica.**
  - **No conclusion can be drawn on the cost-effectiveness of orthotics due to lack of economic evaluations.**
-



**Other considerations regarding belts or corsets**

GRADE Factors	Comments
<b>Balance between desirable and undesirable effects</b>	<ul style="list-style-type: none"> <li>The Belgian GDG acknowledged that there was very limited evidence of clinical benefit for belts or corsets. Only a benefit was observed for lumbosacral belts when compared to massage in terms of function but not pain and the evidence for the use of corsets when given as part of a combined treatment with electrotherapy and manual therapy did indicate some benefit for pain and function but this evidence was all from single small studies.</li> <li>The Belgian GDG agreed with NICE that there was insufficient evidence to support a positive recommendation for the use of belts or corsets as treatment for low back pain and agreed that a research recommendation was not a priority for this intervention.</li> <li>The GDG stressed that all of the evidence identified was for patients with low back pain. No studies were retrieved in patients with sciatica.</li> </ul>
<b>Quality of evidence</b>	<ul style="list-style-type: none"> <li>The quality evidence was low or very low quality due to serious or very serious risk of bias (inadequate blinding)</li> <li>It was not possible in some cases to assess whether the care in both groups was comparable, inducing the risk of overestimating effects on subjective outcomes such as pain and function.</li> </ul>
<b>Values and preferences</b>	<ul style="list-style-type: none"> <li>Following consideration was mentioned by the NICE stakeholders, which are also applicable for the Belgian clinical practice:               <ul style="list-style-type: none"> <li>In clinical practice, these orthotics are often prescribed as an aid for the patient to self-manage the condition and to encourage participation in an active lifestyle and aid to return to work. But according to NICE, this proposition is to be rejected given the lack of beneficial effects.</li> <li>Orthotics and appliances are also considered by some clinicians as an ancillary support in improving stability and integrity of the spine and its adjacent structures. NICE rejected this proposition based on the lack of beneficial effects.</li> </ul> </li> <li>Among the Belgian GDG members, some beneficial effects of corsets were mentioned by lowering the pressure on the discs in older people but this does not change the Belgian GDG agreement for a recommendation against their use (as formulated by NICE).</li> </ul>
<b>Costs (resource allocation)</b>	<ul style="list-style-type: none"> <li>No economic evaluations were identified.</li> <li>Orthotics are often purchased by the patient. However, if prescribed by the healthcare system, a cost will be associated with the orthotics themselves and the potentially healthcare professional time if a referral is made to a podiatrist, orthotics or similar.</li> <li>Given the lack of sufficient evidence of clinical benefit for belt/corset, intervention costs were not considered justified by NICE.</li> </ul>

Recommendation	Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"> <li>Do not offer belts or corsets for managing low back pain with or without radicular pain.</li> </ul>	Strong (RCTs)	Very low to low

**Change in comparison with the NICE recommendations**

- “sciatica” replaced by “radicular pain”: Do not offer belts or corsets for managing low back pain with or without sciatica radicular pain.
- The reasons underlying these changes are described in Appendix 7.7.

**Other considerations regarding foot orthotics and rocker sole shoes**

GRADE Factors	Comments
<b>Balance between desirable and undesirable effects</b>	<ul style="list-style-type: none"> <li>• The Belgian GDG acknowledged that there was some evidence of benefit from the use of customised insoles compared to placebo in improving pain and function in patients with low back pain and sciatica. It was noted that this evidence was from a single small study.</li> <li>• Compared to usual care some improvement in pain scores were found with foot orthotics but without improvement in function.</li> <li>• The comparison of rocker sole shoes to flat soles revealed no clinical differences, except a small improvement in QoL scores in the flat sole group.</li> <li>• The Belgian GDG agreed with NICE that there was no good evidence to support a positive recommendation for the use of belts or corsets as treatment for low back pain and agreed that a research recommendation was not a priority for this intervention.</li> </ul>
<b>Quality of evidence</b>	<ul style="list-style-type: none"> <li>• The quality ranged from moderate to very low due to serious or very serious risk of bias (inadequate blinding)</li> <li>• It was not possible in some cases to assess whether the care in both groups was comparable, inducing the risk of overestimating effects on subjective outcomes such as pain and function.</li> <li>• The attempt to achieve blinding by the use of placebo foot insoles in one study was considered insufficient to resolve this risk of bias due to the explicit visual differences between both types of insoles that would have a negative impact on the blinding of the participants.</li> <li>• A possible error in outcome reporting is possible in a study that measured pain severity on a 0-10 scale but reported as a scale of 0-100.</li> </ul>
<b>Values and preferences</b>	<ul style="list-style-type: none"> <li>• Following consideration was mentioned by the NICE stakeholders, which are also applicable for the Belgian clinical practice: <ul style="list-style-type: none"> <li>○ In clinical practice, these orthotics are often prescribed as an aid for the patient to self-manage the condition and to encourage participation in an active lifestyle and aid to return to work. But according to NICE, this proposition is to be rejected given the lack of beneficial effects.</li> <li>○ Orthotics and appliances are also considered by some clinicians as an ancillary support in improving stability and integrity of the spine and its adjacent structures. NICE rejected this proposition based on the lack of beneficial effects.</li> </ul> </li> <li>• The Belgian GDG members mentioned that foot orthotics can be eventually necessary in the treatment of low back pain and may have a place in case of associated knee or foot problems, but this is specific cases and all GDG members agreed on the recommendation against its use (as formulated by NICE).</li> </ul>
<b>Costs (resource allocation)</b>	<ul style="list-style-type: none"> <li>• No economic evaluations were identified.</li> </ul>



- Orthotics are often purchased by the patient. However, if prescribed by the healthcare system, a cost will be associated with the orthotics themselves and the potentially healthcare professional time if a referral is made to a podiatrist, orthotics or similar.
- Given the lack of sufficient evidence of clinical benefit for belt/corset, intervention costs were not considered justified by NICE.

Recommendation	Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"> <li>• Do not offer foot orthotics for managing low back pain with or without radicular pain.</li> </ul>	Strong (RCTs & cohort studies)	Very low to moderate
<ul style="list-style-type: none"> <li>• Do not offer rocker sole shoes for managing low back pain with or without radicular pain.</li> </ul>	Strong (RCTs)	Very low to moderate

#### Change in comparison with the NICE recommendations

- “sciatica” replaced by “radicular pain”: Do not offer foot orthotics/rocker sole shoes for managing low back pain with or without ~~sciatica~~ radicular pain.
- The reasons underlying these changes are described in Appendix 7.7.

#### 3.2.5 Manual Therapies

Manual therapy interventions use passive or active assisted movements, usually delivered by the hands of the practitioner. Typically, they aim to act on the neuromusculoskeletal system focussing on joints and soft tissues to improve mobility and function, and to decrease pain.

#### Definition of manual therapies as included in this review

- **Spinal manipulation:** a gapping motion of a synovial joint within a spinal segment in response to a force of typically short duration
- **Spinal mobilisation:** joint movement within the normal range of movement
- **Soft tissue techniques:** manual manipulation/mobilisation of soft tissues (including but not restricted to massage)

Mobilisation and soft tissue techniques are performed by a wide variety of practitioners; whereas manipulation is usually performed by chiropractors or osteopaths, and by doctors or physiotherapists who have undergone additional training in manipulation. Manual therapists often combine a range of techniques in their approach and may also include exercise interventions and advice about self-management

The NICE evidence review can be found on p.352-457 in the full guideline on assessment and non-invasive treatments and the forest plots in Appendix K p.115-152 (<https://www.nice.org.uk/guidance/ng59/evidence>).

A summary sheet in Appendix 7.8 gathered the evidence findings, the NICE GDG considerations, the results of the online survey and the discussion with the Belgian GDG.



### Scientific evidence regarding manual therapies

In the NICE review on the clinical and cost-effectiveness of manual therapies following interventions were considered: soft-tissue techniques, manual traction, spinal manipulation/mobilisation (including Spinal Manipulation Therapy (SMT) and Maitland technique), and mixed modality manual therapy (soft tissue technique +/- traction +/- manipulation/mobilisation). The evidence on single interventions was extracted from 48 RCTs, the combined interventions were reported in 18 RCTs. Non-randomised trials were not considered. One economic evaluation with soft tissue techniques as a comparator, another with manipulation/mobilisation and one that compared manipulation/mobilisation in combination with biomechanical exercise and self-management compared to self-management alone (were included in the review. In addition, two economic evaluations were identified that included mixed manual therapy – one includes mixed manual therapy in combination with self-management and in combination with both self-management and biomechanical exercise compared to self-management alone and a combination of self-management and biomechanical exercise (and the other looks at biomechanical exercise, a combination of mixed manual therapy and self-management, and an MBR programme. No relevant economic evaluations were identified that included traction or mixed modality manual therapy as a comparator.

In addition to the evidence review performed by NICE, the KCE researchers also looked at differences in efficacy of manual therapy (manipulation/mobilisation and soft-tissue techniques) between acute and chronic low back pain. The same definition of acute has been applied as in NICE: acute low back pain is less than 3 months, chronic low back pain is at least 3 months. For clarity reasons, no distinction has been made between acute and subacute low back pain.

### Scientific evidence regarding traction

#### LOW BACK PAIN WITHOUT SCIATICA:

- *Single interventions:* Only one comparison (versus sham) was found (in 1 RCT): no clinical difference was observed in short term pain. No long-term data were reported.
- *Traction as adjunct in combined interventions:* No evidence was available.

#### LOW BACK PAIN WITH SCIATICA:

- *Single interventions:* Two studies were retrieved in this patient group, one study on the efficacy of weight-bath traction and one study on mechanical traction, both compared to usual care. After discussion with the GDG president, it was decided to exclude the study on mechanical traction from this evidence review. Mechanical traction is not considered as a manual therapy and is currently in Belgium not widely anymore used. In the study on weight-bath traction: a clinically important short-term benefit was reported on all domains of QoL and pain, both in favour of traction. However no clinical difference was found for function. No long term data were reported.
- *Traction as adjunct in combined interventions:* No evidence was available.

#### MIXED POPULATION (WITH OR WITHOUT SCIATICA):

(see Table 19 in Appendix 7.8)

- *Single interventions:* In the comparison of traction versus sham, a clinically important reduction in (short-term) pain was demonstrated in patients who received inversion traction (only outcome reported on inversion traction), but not among those who received mechanical traction (at short and long term). Neither a clinical difference was found in function after mechanical traction at both time points. Use of other medical treatments (healthcare utilisation) was increased in the mechanical traction group in the short term, but this between group difference was not sustained at long term. When compared to usual care, no differences were found for pain and function (at short term, no



long-term data reported). In the single study comparing traction to biomechanical exercises, a decreased healthcare utilisation (visits to other healthcare practitioners) was noted in those receiving traction.

- *KCE note:* The primary study on the comparison of traction to biomechanical exercises could not be retrieved in the NICE documents.
- *Traction as adjunct in combined interventions:* The addition of traction to a combination of infra-red therapy and biomechanical exercises (stretching) showed no clinical differences in pain, function and healthcare utilisation (medication use) at both time points.

### Scientific evidence regarding manipulation/mobilisation

#### LOW BACK PAIN WITHOUT SCIATICA:

(see Tables 20, 22 and 23 in Appendix 7.8)

- *Single interventions:* Comparison with sham, revealed only a short term clinical benefit on the physical component of QoL in favour of manipulation/mobilisation (other reported outcomes were pain and function, at both time points). Within the three included studies on the sham comparison, one study considered acute low back pain patients, but the findings are in line with the overall conclusion (i.e. no clinical difference in pain and function, at short term). The two other RCTs included either chronic low back pain patients or a mixed duration of pain (>50 days or >6 episodes in last 12 months). Comparison with usual care found a short term pain improvement and a higher number of patients who reported a 30% or 50% improvement in pain and function in favour of manipulation/mobilisation. These benefits were found in the study on acute low back pain patients. Comparison with active comparators (massage, belts/corsets, ultrasound (US), NSAIDs) showed, across all reported outcomes, a clinical benefit only in pain at both time points (compared to US). Within these comparisons either chronic low back pain patients or a mixed population of acute and chronic low back pain patients were included, therefore no clear conclusion can be drawn on the efficacy of manipulation/mobilisation compared to active comparators in patients with acute low back pain.
- *Manipulation/mobilisation as adjunct in combined interventions:*
  - In the three RCTs comparing the combination of manipulation and biomechanical exercises (McKenzie or stretching) to biomechanical exercises (core stability or stretching), only a short term clinical benefit in pain was found in favour of the combination of manipulation and stretching compared to core stability exercises. In all three studies, no clinical differences in function were found. The benefit in pain was shown in the study on chronic low back pain patients; in the two studies on acute low back pain patients no differences were found in function (only reported outcome).
  - When the combination of manipulation and biomechanical exercises (stretching) were compared to aerobic exercises (walking) a short term clinical benefit in pain and function was found in favour of the combination with manipulation. No long-term data were reported in this single study on acute low back pain patients.
  - The two RCTs, both in chronic low back pain patients and comparing the combination of manipulation and aerobic exercises to other types of exercises (aerobic or biomechanical), demonstrate only a short term benefit in function in favour of the combined intervention with manipulation compared to aerobic exercises.
  - The combination of manipulation with biomechanical exercises compared to manipulation combined with aerobic exercises did not reveal any clinical differences in pain and function (only short term data reported). In this study only chronic low back pain patients were included.



#### LOW BACK PAIN WITH SCIATICA:

- *Single interventions:* A single study comparing manipulation/mobilisation to sham in acute low back pain patients, showed a long term clinical benefit of spinal manipulation for QoL in the majority of the domains (except for general health domain in favour of sham and no differences in the role physical and bodily pain domains). Also a clinical benefit of spinal manipulation was found in terms of responder criteria (>30% improvement in (local back and radiating) pain) in the long term. No results were reported on function. When manipulation/mobilisation was compared with usual care, one study showed no differences in pain and QoL (except for the physical health composite at short term) (at both time points), but fewer adverse events were reported in the spinal manipulation group. The same study showed clinical benefit for function at short term but not at long-term. The patients included in this study consisted of a mixed population of acute and chronic low back pain patients with a current episode of 4 weeks or more.
- *Manipulation/mobilisation as adjunct in combined interventions:* Adding manipulation/mobilisation to a combination of self-management (education) and (aerobic) exercises revealed no clinical differences in pain and function (at short term) (no long-term data or other outcomes were reported, 1 RCT on acute low back pain patients).

#### MIXED POPULATION (WITH OR WITHOUT SCIATICA):

(see Tables 21, 24 and 25 in Appendix 7.8)

- *Single interventions:* Compared to usual care, the clinical benefit depended on the manipulation modality (spinal adjusting mobilisation, high velocity thrust, traction gap manipulation) but overall could be stated that the retrieved evidence (on pain, function, adverse events, QoL) was not consistent in favour or against manipulation. Only an increased number of healthcare visits were found in patients who received manipulation/mobilisation. Only the study on traction gap manipulation was on acute low back pain patients, which reported a short term clinical benefit in function in favour of manipulation (only reported outcome). Comparison with active comparators ((biomechanical) exercises, interferential therapy, self-management

(education, advice, reassurance), NSAIDs, combined intervention of exercise + education) showed inconsistent results for QoL and only a short term clinical benefit in pain and function in favour of manipulation compared to biomechanical exercises and the combined intervention of exercise + education. The study on the comparison to interferential therapy included acute low back pain patients and reported inconsistent results for QoL and no clinical benefit in pain and function. The studies on the other comparisons included either chronic low back pain patients or a mixed population of acute and chronic low back pain patients.

- *Manipulation/mobilisation as adjunct in combined interventions:* Eight RCTs were found on the combined interventions with manipulation/mobilisation as an adjunct versus usual care or active comparators (combinations of self-management, exercises, NSAIDs, or interferential therapy), with one study per comparison. Three of the 8 studies reported results on QoL and demonstrated an overall (but small) clinical benefit of the addition of manual therapy in a combined intervention. Only one (small study) of the 6 studies reporting pain, found a clinical benefit in favour of manipulation. The results for function are less consistent: in 4 of the 6 studies a short term benefit was found in favour of manipulation, however at long term only 2 of the 5 studies reported this benefit. In the majority of the studies (5/8) results for both time points were not reported, which hampers the overall conclusion of the potential effect of manipulation on functioning of the patient. Regarding healthcare utilisation, only a long term benefit was found for medication use in favour of manipulation. Three studies included acute low back pain patients but no consistent conclusion can be drawn on the potential effect of manipulation as a therapy adjunct in this subgroup of patients due to inconsistent results per outcome and only one study found per comparison.



### Scientific evidence regarding soft-tissue techniques

#### LOW BACK PAIN WITHOUT SCIATICA:

(see Table 18 in Appendix 7.8)

- *Single interventions:* Studies which compared soft-tissue techniques as a single intervention to sham, usual care or active comparators reported no consistent results on a potential clinical benefit. Compared to sham, conflicting results were found for (short-term) pain (due to different scales) but no clinical difference in function. In the comparison with usual care and active comparators (acupuncture and self-management (education)), only a short term clinical benefit on function was found in favour of massage (compared to usual care or self-management). The retrieved studies included either chronic low back pain patients or a mixed population of acute and chronic low back pain patients.
- *Soft-tissue techniques as adjunct in combined interventions:* A combined intervention of massage and self-management (exercise prescription) versus postural therapy (Alexander technique 6 or 24 lessons, 2 RCTs) in chronic low back pain patients revealed only a long-term benefit in the physical component of QoL in the postural therapy group (24 lessons Alexander technique). No clinical differences were found in the other reported outcomes (pain, function and healthcare utilisation). No studies were found on acute low back pain patients.

#### LOW BACK PAIN WITH SCIATICA:

- *Single interventions:* No evidence was available.
- *Soft-tissue techniques as adjunct in combined interventions:* In this patient group, 2 comparisons were found on the effectiveness of a treatment package with muscle energy technique (in 2 small RCTs on chronic low back pain patients). The addition of muscle energy techniques to a combined intervention of self-management (unsupervised exercise) and biomechanical exercises (McKenzie) revealed no difference in pain and function, both at short term (only data reported). However, when muscle energy techniques were combined with self-management (unsupervised exercise) and biomechanical exercises (McKenzie) a clinical benefit in pain and function in favour of this combined intervention was observed compared to the combination of self-management (unsupervised exercise), biomechanical exercises (McKenzie) and standard treatment (TENS + laser + massage). No studies were found on acute low back pain patients.

#### MIXED POPULATION (WITH OR WITHOUT SCIATICA):

- No evidence was available.

### Scientific evidence regarding mixed modality manual therapy (combination of soft-tissue techniques, traction, manipulation/mobilisation)

#### LOW BACK PAIN WITHOUT SCIATICA:

- *Single interventions:* Comparison with sham and usual care, showed a clinically important benefit of the mixed modality in pain (compared to usual care) and in (>30%) improvement in pain (compared to sham). Comparison with active comparators (manipulation/mobilisation, massage, traction, biomechanical exercise) showed a short term improvement in pain in favour of the mixed modality (compared to traction and biomechanical exercise) and a short term improvement in function (compared to massage). The retrieved studies included either patients with chronic low back pain, a mixed population or the duration of the pain was not clearly stated, therefore no conclusion can be drawn





on the efficacy of a mixed modality manual therapy in acute low back pain patients.

- *Mixed modality as adjunct in combined interventions:* The combined intervention of manual therapies (manipulation + massage) showed no clinical differences in short term pain and function (no long-term data reported). The patient population consisted of a mixed population of patients with subacute or chronic low back pain.
- *KCE note:* this comparison is presented in the NICE review as a comparison of a mixed modality as adjunct in combined interventions, however the study considers only the combination of manipulation and (trigger point) therapy, this kind of intervention is rather a mixed modality. In the study the comparator was a sham intervention and should rather be reported in the bullet above (single interventions).

#### LOW BACK PAIN WITH SCIATICA:

- No evidence was available.

#### MIXED POPULATION (WITH OR WITHOUT SCIATICA):

- *Single interventions:* Only one comparison was retrieved in a single study on chronic low back pain patients: no clinical difference in pain and function was found between the mixed modality and sham, at both time points.
- *Mixed modality as adjunct in combined interventions:* Three RCTs compared different combinations of mixed modality manual therapy and self-management and/or exercises to self-management or self-management and exercises in a mixed population of at least 4 weeks of low back pain. Overall could be stated that no clinical difference was found for short term and long term pain, function and healthcare utilisation. Nevertheless the lack of difference in function, a significant higher number of patients reported more than 30% improvement in function after the mixed modality intervention (responder criteria) (in 2 of 3 studies). The results for QoL are less consistent in between the studies: a clinical benefit of the combined intervention with the mixed modality was seen in the physical component of SF-36 (either at short term or at both time points) and in EQ-5D (at both time points), but no differences were found for the mental component of SF-36.

#### Economic evidence

- Four economic evaluations were identified in patients with low back pain without sciatica on:
  - *Soft-tissue techniques:* One cost-utility analysis found that massage + usual care was not cost effective but became cost effective when used as an adjunct to unsupervised exercise.
  - *Manipulation/mobilisation:* One cost-utility analysis found that manipulation (12 sessions) was cost effective compared to sham manipulation.
  - *Mixed modality manual therapy:*
    - One cost-consequence analysis found that the combination of mixed modality with self-management and exercise did not show any statistically significant increase in costs or outcomes.
    - One cost-utility analysis found that mixed modality + self-management was cost effective compared to combination of mixed modality, exercise and self-management, self-management + exercise or self-management alone
- One economic evaluation was found in the mixed population (low back pain with or without sciatica)
  - One cost-utility analysis (Critchley 2007) found that manual therapy + self-management was dominated by a 3 element MBR programme (physical, psychological, educational).
- No economic evaluations were found in patients with sciatica. Also no economic evaluations considered the cost-effectiveness of traction.



## Conclusions

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- The few studies on traction could not demonstrate any beneficial effect of this type of manual therapy in comparison to sham, usual care or active comparators.
  - The majority of the RCTs on manual therapies concerned the effectiveness of manipulation/mobilisation as single intervention or in combination with other interventions. The limited, inconsistent clinical benefit of manipulation/mobilisation as single intervention improved when manipulation/mobilisation was combined with other interventions, and mainly in combination with (different types of) exercises. The retrieved evidence could not demonstrate any serious harmful effects of manipulation/mobilisation.
  - The evidence on soft-tissue techniques was limited to studies on massage. The few studies showed that massage as stand-alone intervention was less effective than in combination with other interventions.
  - The majority of the retrieved evidence considered the effectiveness of mixed modality manual therapy as adjunct in combined interventions. No convincing evidence was found on the beneficial effects of mixed modality manual therapy.
  - No clear conclusion can be drawn on a potential difference in efficacy of manual therapy between patients with acute and chronic low back pain. Only in some pooled results, studies on acute low back pain patients were included. Analysis of these studies revealed that the findings were in line with the pooled results. Also in the majority of the comparisons only one study was often included (sometimes on acute low back pain patients) so no comparison between population groups could be made. Therefore, one could state that based on the retrieved evidence no clear distinction can be made in the efficacy of manual therapy between acute or chronic low back pain.
- 
- Based on the uncertainty in the economic evidence, manual therapies as standalone may not be cost-effective, but in combination with other interventions (as treatment package including exercises) it might be more likely to become cost effective.
-



## Other considerations regarding traction

GRADE Factors	Comments
<b>Balance between desirable and undesirable effects</b>	<ul style="list-style-type: none"> <li>The NICE GDG discussed the necessity of a body of evidence to show specific intervention effects, that is, over and above any contextual or placebo effects. It was therefore agreed that if placebo or sham-controlled evidence is available, this should inform decision making in preference to contextual effects. However, if there was a lack of placebo or sham-controlled evidence, evidence against usual care will be given priority when decision making.</li> <li>Only very limited evidence of benefit was found for traction as a single intervention. Based on the single study on one comparison, no solid conclusion can be drawn on the effectiveness of traction in the management of low back pain with or without sciatica.</li> <li>If some benefit was demonstrated compared to usual care, the NICE and Belgian GDG considered this not as sufficient evidence due to the small sample size of the single retrieved study and the very low quality of the evidence. Also in the study on weight-bath traction versus usual care, the patients were admitted in hospital due to sciatica but therefore unlikely to be representative of the broader population with sciatica.</li> <li>Adverse events were not reported in the included studies.</li> <li>In conclusion, the Belgian GDG agreed with NICE that traction should not be offered for low back pain or sciatica.</li> </ul>
<b>Quality of the evidence</b>	<ul style="list-style-type: none"> <li>The quality ranged from very low to high quality, downgrading mainly due to imprecision of effect and/or high risk of bias (unclear allocation concealment and lack of blinding).</li> </ul>
<b>Values and preferences</b>	<ul style="list-style-type: none"> <li>According to some NICE stakeholders, traction can be considered as an ancillary procedure to improve the functional stability and integrity of the spine and its adjacent structures. But NICE replied that there was very limited evidence of benefit for traction as a single therapy, and therefore could not be recommend it as an ancillary procedure.</li> <li>The Belgian GDG agreed with the recommendation against the use of traction proposed by NICE.</li> </ul>
<b>Costs (resource allocation)</b>	<ul style="list-style-type: none"> <li>No economic evaluations were identified relating to traction.</li> <li>Use of traction will be associated with costs relating to the equipment and personnel time required to deliver the therapy. If effective, upfront costs may be offset by downstream cost savings due to reduced healthcare utilisation or may be justified due to the benefits to the patient. Although some indications of possible benefit were seen for traction in a sciatica population, overall the GDG concluded that it was insufficient to support a conclusion of evidence of clinical benefit and thus also insufficient to justify intervention costs.</li> </ul>

Recommendation	Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"> <li>Do not offer traction for managing low back pain with or without radicular pain.</li> </ul>	Strong (RCTs)	Very low to high



### Change in comparison with the NICE recommendations

- Addition of “people with” and “sciatica” replaced by “radicular pain”: Do not offer traction for managing low back pain with or without sciatica radicular pain
- The reasons underlying these changes are described in Appendix 7.8.

### Other considerations regarding soft-tissue techniques/manipulation/mobilisation

GRADE Factors	Comments
<b>Balance between desirable and undesirable effects</b>	<ul style="list-style-type: none"><li>• The NICE GDG discussed the necessity of a body of evidence to show specific intervention effects, that is, over and above any <b>contextual or placebo effects</b>. It was therefore agreed that if placebo or sham-controlled evidence is available, this should inform decision making in preference to contextual effects. However, if there was a lack of placebo or sham-controlled evidence, evidence against usual care will be given priority when decision making.</li><li>• There was <b>mixed evidence</b> for the effectiveness of manual therapy modalities, particularly with function outcomes not correlating with quality of life outcomes.</li><li>• It was also difficult to assess evidence from <b>a wide variety of interventions</b> for manipulation/mobilisation.</li><li>• <b>Compared to sham</b>: there was some limited evidence of benefit of soft-tissue techniques, spinal manipulation and mixed modality manual therapies in pain or quality of life, however, these benefits were only shown at short term (and even somewhat inconsistent at short term).</li><li>• <b>Compared to usual care</b>: Conflicting results did not show consistently benefit when manual therapy was offered as single treatment. However, a large multicentre study demonstrated benefits in quality of life and in responder criteria for function when manual therapy was combined with self-management and exercise. Only little effect was seen beyond four months in single interventions, in a mixed modality trial a more prolonged beneficial effect on QoL was noted.</li><li>• <b>Mixed modality manual therapies</b>: The majority of the evidence was from a mixed population (low back pain with or without sciatica). The results were conflicting and inconsistent over the different comparisons.</li><li>• <b>Combination of interventions</b>: the NICE and Belgian GDG noted that the clinical effects of manual therapy in pain and function improved when provided in combination with exercises. Several, single studies compared different modalities of active comparators in combination with manual therapy, resulting in an inconsistent overview of evidence in which it is difficult to determine which combination of modalities showed the most clinical benefit. Compared to the limited evidence of manual therapy as a single intervention, <b>the combination of the latter with active comparators increased its potential clinical benefits</b>. There was some inconsistent evidence of clinical benefit when the intervention contained mixed modality manual therapy or a spinal manipulation component.</li><li>• <b>Soft-tissue techniques</b>: The majority of the evidence was on massage. Considering that a comparison with usual care should result in a greater effect estimate than the specific effect of the intervention (as demonstrated in placebo comparisons), the GDG</li></ul>



GRADE Factors	Comments
	<p>felt that the absence of a clinically important improvement in quality of life and pain in this comparison indicated sufficient evidence of <b>absence of effect</b> to recommend against the use of soft tissue techniques (massage) on its own.</p> <ul style="list-style-type: none"> <li>• The NICE GDG discussed whether the <b>passive nature</b> of manual therapies might explain the lack of long-term effects.</li> <li>• No <b>serious events</b> attributable to manual therapy were reported but common minor and transient adverse events (mainly muscle soreness for a few days following treatment). The NICE GDG were aware of possible serious but very rare adverse events that may be related to spinal manipulation and took this into account when making a recommendation. The Belgian GDG confirmed this concern. Moreover, the Belgian GDG members mentioned the potential harms of manipulation in patients with radicular pain. Due to the imprecision of the definition of non-specific low back pain with sciatica, the Belgian GDG preferred to be clear and to include a reminder of the potential harmful effects of manipulation in case of radicular pain in a text in front of the recommendation.</li> <li>• The NICE GDG concluded that due to the possible risk of adverse events and conflicting nature of the evidence, manual therapy (soft-tissue techniques and manipulation/mobilisation) should be considered <b>as part of a treatment package</b>, rather than a sole intervention to all people with low back pain with or without sciatica. The different components in a treatment package are less defined as in a MBR program, involving a physical component and at least one other element from a biopsychosocial approach, offered as an integrated programme. Also was agreed that manual therapy should <b>not be a mandatory component of a treatment package</b>, but that it is one optional modality that might be considered <b>alongside exercises</b>.</li> <li>• There was sufficient evidence to assume the effects for a combination of therapies would apply equally to those with low back pain with or without sciatica and therefore recommended these should be considered for either condition.</li> </ul>
<b>Quality of evidence</b>	<ul style="list-style-type: none"> <li>• The quality level ranged from high to very low quality, downgrading mainly due to imprecision of effect and/or high risk of bias (unclear allocation concealment and lack of blinding).</li> <li>• One large trial (UK Beam trial, n=1334) showed clinical benefit of mixed modality manual therapy. However, the GDG did note that the evidence from this study was mostly rated as low quality (due to high drop-out rates and lack of blinding) and that the clinical benefit for function came from a post hoc analysis of the data.</li> <li>• The responder analyses for pain and function from two large trials informed the GDG's recommendations, but there were also concerns about the limitations of responder analyses (reduced power to detect differences, 'responders' have not necessarily improved due to the intervention etc). The NICE GDG noted also that some of the responder analyses post-hoc analyses were, which further raised concerns about reliability of these analyses. These concerns are reflected in the wording of the recommendation and the NICE GDG chose to advise 'consider' (weak recommendation).</li> </ul>
<b>Values and preferences</b>	<ul style="list-style-type: none"> <li>• The Belgian GDG preferred to not mention massage within the recommendation. This could give the impression that the evidence is more robust than it actually is and soft-tissue techniques involves much more than only massage.</li> <li>• The definition of manual therapy was discussed in the Belgian context. IFOMT defined manual therapy as an integrated approach combined with exercises and education. NICE, however, considered manual therapy mainly as the manual actions performed by the practitioner. A first suggestion was to add the IFOMT definition in the text according to the recommendation but no consensus was obtained regarding the relevance of this unique professional definition. It was therefore suggested to use the wording "manual techniques" rather than "manual therapy" in the Belgian guideline to avoid confusion with the professional identity of the manual therapists and to avoid discussion if other therapists may also perform this kind of intervention (e.g. osteopaths). The manual</li> </ul>



GRADE Factors	Comments
	<p>therapist must be member of the treatment team and fully adhere to the treatment approach (rationale that must be given to the patient).</p> <ul style="list-style-type: none"> <li>• The Belgian GDG stressed that because patients with low back pain and/or sciatica need an individual approach in function of the needs, manual therapy can be useful for some, but mostly also other strategies will be necessary.</li> <li>• Following NICE stakeholders' feedback on the definition of a multimodal package, the wording has been changed into "treatment package including exercise with or without psychological therapy".</li> <li>• In the final version of the NICE guideline, the recommendations on manual techniques and psychological therapies were gathered in one recommendation, but the Belgian GDG preferred to split up again this recommendation.</li> <li>• Addition of "integrated" in the multimodal treatment packages has been discussed: this emphasises the need of an integrated approach in which the manual therapists (including osteopaths and chiropractors) work in line with the other care disciplines and to avoid parallel care approaches. However, this organisational aspect will be discussed in the pathway.</li> <li>• One of the GDG members revealed the potential use of imaging before manipulation, but the GDG agreed not to change the recommendation based on the lack of evidence concerning this topic.</li> </ul>
<b>Costs (resource allocation)</b>	<ul style="list-style-type: none"> <li>• <b>Soft-tissue techniques:</b> found not to be cost effective when given alone (it had lower QALYs and higher costs), but was cost effective when used as an adjunct to self-management (unsupervised exercise). Given the wide use of self-management in low back pain these results suggest uncertainty in the cost effectiveness of massage. The NICE GDG concluded that based on the uncertainty around the cost-effectiveness and the overall lack of clinical evidence, there was insufficient evidence around the cost-effectiveness of soft-tissue techniques.</li> <li>• <b>Manipulation/mobilisation:</b> The only economic evaluation found that manipulation (12 sessions) may be cost-effective compared to sham, but there are a large number of uncertainties in this evidence.</li> <li>• <b>Mixed modality manual therapy:</b> In the UK BEAM trial, self-management and mixed modality manual therapy had most QALY's and the most costs. Another study showed that the combination of self-management and mixed modality therapy if more cost effective than biomechanical exercises alone, however when all comparisons were considered, a three-element MBR programme was the cheapest and more effective option.</li> <li>• The uncertainty in the economic evidence and manual therapy may not be cost effective as a standalone intervention but might be more likely if <b>manual therapy is provided as part of a treatment package including exercise with or without psychological therapy.</b></li> </ul>

Recommendation	Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"> <li>• Consider manipulation, mobilisation, or soft-tissue techniques for managing low back pain with or without radicular pain, but only as part of a multimodal treatment with a supervised exercise programme.</li> </ul>	Weak (RCTs)	High to very low



### Change in comparison with the NICE recommendations

- “sciatica” replaced by “radicular pain”
- “massage” has been removed
- A separate recommendation has been formulated on psychological therapy.

Consider ~~manual therapy~~ (manipulation, mobilisation or soft-tissue techniques ~~such as massage~~) for managing people with low back pain with or without ~~sciatica~~ radicular pain, but only as part of a multimodal treatment with a supervised exercise programme ~~treatment package including exercise, with or without psychological therapy.~~

The reasons underlying these changes are described in Appendix 7.8.

### 3.2.6 Acupuncture

Acupuncture originated in China approximately 2000 years ago, but in Belgium the most common form of acupuncture used, is defined as “Western medical acupuncture”, which is more based on neurophysiological mechanisms. The proposed mechanisms of action of acupuncture are complex in terms of neurophysiology, and involve various effects including the release of endogenous opioids. There has been considerable research into the use of acupuncture for pain relief; however uncertainty remains as to the benefit of acupuncture in the management of low back pain and radicular pain.

#### Definition of acupuncture

Acupuncture involves treatment with needles, and is most commonly used for pain relief. The needles are either manipulated to produce a particular ‘needle sensation’, or stimulated electrically (electroacupuncture) for up to 20 minutes. Some practitioners also use moxa, a dried herb which is burned near the point to provide heat. A course of treatment usually consists of six or more sessions during which time, if a response occurs, pain relief gradually accumulates.

The NICE evidence review can be found on p.458-498 in the full guideline on assessment and non-invasive treatments and the forest plots in Appendix K p.153-172 (<https://www.nice.org.uk/guidance/ng59/evidence>).

A summary sheet in Appendix 7.9 gathered the evidence findings, the NICE GDG considerations, the results of the online survey and the discussion with the Belgian GDG.

#### Scientific evidence regarding acupuncture

The clinical and cost-effectiveness of acupuncture has been considered in comparison to sham/placebo, usual care and active comparators. Twenty-nine RCTs were found by NICE on single interventions of acupuncture, and 3 RCTs on combined interventions. Two Cochrane reviews were identified but could not be included since the stratification of the population, i.e. low back pain only, low back pain with or without sciatica and low back pain with sciatica, did not match that of the review protocol. However the studies included in the Cochrane reviews were individually assessed and included by NICE if they matched the review protocol. One economic evaluation was also included in the review.

#### LOW BACK PAIN WITHOUT SCIATICA:

- *Single interventions:* In the comparison to **sham** acupuncture, only a benefit in healthcare utilisation (decrease in analgesic use) was found in favour of acupuncture, whereas no consistent results were found for QoL and psychological distress, and no differences between acupuncture and sham for pain, function and adverse events. Compared to **usual care**, a short term clinical benefit of acupuncture was found in function and pain, but these effects were not anymore seen at long term. Regarding QoL, a benefit was seen for the composite physical score (at both time points) but not for the composite mental health score. No differences were seen in psychological distress, healthcare utilisation (number of care visits and number of pain medication prescriptions) and number of adverse events. Two comparisons were found on acupuncture versus **active comparators** (TENS or massage): only for pain a clinically improvement (at short term) was noted (compared to TENS). In the other reported outcomes



(function, healthcare utilisation, and adverse events) no clinical differences could be detected.

- *Acupuncture as adjunct in combined interventions* (see Table 26 in Appendix 7.9): A very small study compared the combination of **acupuncture and electrotherapy** (TENS) to usual care or to electrotherapy (TENS). In both treatment arms, no clinical differences were found in pain and function. Only short term data and no other outcomes were reported. Another small study assessed the effectiveness of **acupuncture with massage** but could not detect any difference in short term pain compared to usual care. Only short term data and no other outcomes were reported. The addition of acupuncture to a combined intervention of group (biomechanical and aerobic) **exercises and self-management** (education, Back Book and unsupervised exercise) resulted in contrasting findings: at short term, a clinical improvement in QoL and in pain scores was seen in the group without acupuncture, and no differences were found for function. At long term, the clinical improvement in QoL and in pain scores was now seen in the group with acupuncture and also at long term no differences were found for function. Other outcomes were not reported.

#### LOW BACK PAIN WITH SCIATICA:

- No evidence was available.

#### MIXED POPULATION (WITH OR WITHOUT SCIATICA):

- *Single interventions*: Across any of the reported outcomes (pain, function, responder criteria for function and adverse events) no clinical differences were found compared to **sham** acupuncture. At short term, a clinically important improvement in QoL (across all domains and measures), pain, function and responder criteria for function with acupuncture compared to **usual care** was demonstrated. At long term the results are less in favour of acupuncture with inconsistent results for QoL and no clinical benefit anymore in pain and function. One study

comparing acupuncture to **waiting list control**, found no consistent results for all component scores for QoL and no differences in healthcare utilisation. When acupuncture is compared to NSAID as active comparator, some differences were found on the type of NSAID. With intramuscular Diclofenac, a short term pain improvement was found but not anymore at long-term. No clinical differences in function were found (at both time points). The comparison with oral Diclofenac showed no clinical differences in pain, function (both at both time points) and healthcare utilisation (only reported at short term).

- *Acupuncture as adjunct in combined interventions*: No evidence was available.

#### Economic evidence

- One cost-utility analysis found that acupuncture + usual care was cost effective compared with usual care alone for LBP with or without sciatica. This analysis was assessed as partially applicable with potentially serious limitations.

#### Conclusions

- **Compared to sham: Overall it could be stated that no clinical differences in the critical outcomes were reported, indicating a lack of treatment-specific effect of acupuncture.**
- **Compared to usual care or active comparators: No consistent, compelling evidence was found in favour of acupuncture. When a short term effect was noticed in one of the outcomes, this effect was not anymore seen at long term.**
- **Cost-effectiveness: The addition of acupuncture to usual care increased costs and improved health and could indicate the potential cost-effectiveness of acupuncture.**





## Other considerations regarding acupuncture

GRADE Factors	Comments
<b>Balance between desirable and undesirable effects</b>	<ul style="list-style-type: none"> <li>• The NICE GDG discussed the necessity of a body of evidence to show specific intervention effects, that is, over and above any contextual or placebo effects. It was therefore agreed that if placebo-controlled evidence (or sham acupuncture) is available, this should inform decision making in preference to contextual effects, but that the effect sizes compared with usual care would be important to consider if effectiveness relative to placebo, or sham, has been demonstrated.</li> <li>• <b>Placebo/sham:</b> In patients without sciatica, no clinical benefit was seen for pain and function and results were inconsistent for quality of life and psychological distress. No differences in adverse events were noticed between both groups. In the mixed population, the results were clearer: no improvement for any of the reported outcomes.</li> <li>• <b>Usual care/waiting list:</b> some short term improvements in pain, function and (in some subdomains of) QoL was found in the acupuncture group but not anymore at long-term. Many of the observed benefits were not sustained beyond 4 months, however the study treatment durations were a maximum of 15 weeks and the NICE GDG debated whether a long term follow up would be expected from a shorter course of treatment.</li> <li>• In the sensitivity analysis for pain in acupuncture versus sham or usual care, the mean differences were less favourable towards acupuncture but the NICE GDG agreed that it did not change their conclusion to recommend against the use of acupuncture.</li> <li>• <b>Active comparators:</b> The conflicting results and the uncertainty around made it difficult to determine the clinical beneficial effectiveness of acupuncture. The combination of acupuncture with other treatments didn't show any additional benefit of the addition of acupuncture.</li> <li>• <b>Adverse events:</b> Although acupuncture was considered a relatively safe intervention, it was acknowledged that lack of detail on the nature of the adverse events as reported by the trials is a concern with regard to interpreting results appropriately.</li> <li>• <b>In summary,</b> the Belgian GDG noted the very heterogeneous results and found it difficult to draw a clear conclusion on the potential use of acupuncture in the management of low back pain. The lack of consistent clinically important effects compared to sham, led to the conclusion that the effects of acupuncture were probably the results of contextual effects.</li> </ul>
<b>Quality of evidence</b>	<ul style="list-style-type: none"> <li>• The quality of the evidence ranged from very low to high (only in sham comparisons). The lower rating of the evidence was due to high risk of bias (lack of blinding of patient and therapist).</li> <li>• Subgroup analysis according to type of acupuncture and chronicity of pain did not explain the heterogeneity found in the meta-analyses.</li> <li>• The comparison to sham/placebo/usual care was hampered by the included populations in the studies (e.g. acute low back pain in emergency departments), and therefore not necessarily generalizable to the general population.</li> <li>• Some of the included studies on usual care were rather a waiting list comparison, which may over-estimate the effects of treatment as people may become disheartened whilst waiting to start active treatment, and may be a cause for the</li> </ul>



GRADE Factors	Comments
<b>Values and preferences</b>	<p>observed heterogeneity in the meta-analysis. In many of the usual care studies the patients in the usual care received management that was not representative of UK primary care practice or even received more than usual care.</p> <ul style="list-style-type: none"><li>• The <b>Belgian GDG</b> noted the weak quality of the evidence.</li></ul> <hr/> <ul style="list-style-type: none"><li>• The NICE GDG considered whether it was acceptable to recommend an intervention that was thought unlikely (on the basis of reported results) to have a specific treatment effect but was thought to be acting through contextual mechanisms. The GDG acknowledged that this was a controversial issue. The GDG considered that other treatments reviewed in the guideline had specific and clinically important treatment effects, beyond <b>contextual effects</b>, although acknowledged that for treatments where no “sham” comparison was available it was not possible to distinguish specific effects. The majority view of the group was to recommend “do not offer” acupuncture.</li><li>• The NICE GDG thought that it was more likely that contextual effects rather than pain reduction were driving the observed outcomes for acupuncture.</li><li>• The NICE GDG discussed whether acupuncture could be considered for those not responding to other treatment options, rather than as a routine treatment. However, the GDG did not find any evidence to support treatment in such sub-groups and chose not to make a recommendation in this regard.</li><li>• The GDG considered that there was a substantial body of evidence relating to acupuncture and that further research was unlikely to alter conclusions.</li><li>• The <b>Belgian GDG</b> confirmed the weak evidence on the potential benefit of acupuncture but emphasized also the lack of evidence on harmful effects, concluding that a strong recommendation against the use of acupuncture would be exaggerated.</li><li>• The <b>Belgian GDG</b> noted also that NICE completely changed his point of view in comparison to the 2009 version of their guideline, in which was stated: “Consider offering a course of acupuncture needling comprising up to a maximum of 10 sessions over a period of up to 12 weeks”.</li><li>• In the <b>KCE report 2011</b> on acupuncture practice in Belgium, a proven limited effect of acupuncture was shown for specific indications. Sham acupuncture also provided better results than no therapy. In this report the importance of potential beneficial effects of placebo in the treatment of a (chronic) pain complaint was also considered.</li><li>• Other comments formulated by the <b>Belgian GDG members</b> were:<ul style="list-style-type: none"><li>○ Since 2008 STRICTA norms for scientific research in acupuncture has been implemented, this will increase the methodological quality of the trials.</li><li>○ In some sham comparisons, invasive needling is used, but this cannot be considered as a real sham comparison, due to the potential specific treatment effects of this kind of sham needling.</li><li>○ The evidence for other non-invasive treatments is also limited or even less effective than acupuncture, but no recommendation against these interventions was made (e.g. spinal manipulations, exercise therapy). Often the combination of acupuncture with other interventions is more effective than the other interventions alone.</li><li>○ Acupuncture is in clinical practice often used for radicular pain, but no evidence was found on this patient group.</li></ul></li></ul>



GRADE Factors	Comments		
	<ul style="list-style-type: none"> <li>• After discussion in the Belgian <b>GDG meeting</b>, a consensus was reached not to formulate a recommendation on the use of acupuncture in low back patients. Following issues were the basis for this decision:               <ul style="list-style-type: none"> <li>○ The difference between the NICE 2009 and the 2016 recommendation (going from a pro to an against recommendation)</li> <li>○ No clear superior effect of acupuncture versus sham</li> <li>○ No evidence available on harmful effects</li> <li>○ Not sufficient evidence on the potential benefits and harms to formulate a clear recommendation. Not formulating a recommendation gives the clinician more free choice to offer acupuncture to his/her patient, if needed. As a reminder, in a previous KCE-report it was recommended that only certain clinicians could perform acupuncture (physicians, physiotherapists, nurses and midwives)<sup>12</sup>.</li> <li>○ No preference for a research recommendation.</li> </ul> </li> <li>• Following considerations (synthesis) were mentioned by the <b>NICE stakeholders</b>, which are also applicable for the Belgian clinical practice               <ul style="list-style-type: none"> <li>○ Many stakeholders did not agree with the conclusion of NICE to formulate a strong recommendation against acupuncture based on the lack of beneficial effect compared to placebo/sham. However, NICE did not change the recommendation.</li> <li>○ Other guidelines continue to support the use of acupuncture as an effective treatment.</li> <li>○ NICE mentioned in one of his responses that the decision to update the review was partially influenced by the lack of implementation of some of the 2009 recommendations.</li> </ul> </li> </ul>		
<b>Costs (resource allocation)</b>	<ul style="list-style-type: none"> <li>• The only retrieved economic evaluation found that the addition of acupuncture to usual care increased costs and improved health.</li> <li>• The NICE GDG decided that the best comparator to prove treatment-specific effects over and above contextual or placebo effects, would be a placebo or sham. The GDG concluded that there was <b>insufficient evidence of an overall treatment-specific effect</b> to support a recommendation for acupuncture and so <b>consideration of cost-effectiveness was not considered relevant</b>.</li> <li>• Also in the trial behind the economic evaluation only benefit for QoL was found and not for pain, function or psychological distress, questioning by which mechanism quality of life would be improved.</li> </ul>		
Recommendation		Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"> <li>• No recommendation on acupuncture has been formulated.</li> </ul>		NA	NA



### Change in comparison with the NICE recommendations

- The recommendation “Do not offer acupuncture for managing low back pain with or without sciatica” has been removed.
- The reasons underlying these changes are described in Appendix 7.9.

### 3.2.7 Electrotherapies

Electrotherapy is an umbrella term that defines a variety of interventions with the common feature that they all involve the application of forms of energy to the body. These all aim to produce various physiological effects with the goal of improving symptoms or recovery.<sup>13</sup> However, the exact mechanism of electrical stimulation’s beneficial effect remains controversial. It may directly block transmission of pain signals along nerves and it has been shown to promote the release of endorphins (natural painkillers produced by the body).<sup>14</sup> Electrotherapies are widely used as a therapeutic adjunct in the management of low back pain. However despite the widespread use, the analgesic effectiveness of electrotherapies remains uncertain.

#### Definition of electrotherapy

In this review following electrotherapies were considered:

- **Transcutaneous electrical nerve stimulation (TENS)** = delivery of a small current to pads on the skin to produce a tingling sensation. Mechanisms for TENS-induced pain relief are thought to be multifactorial and due to the effect of controlling the activity of the peripheral, spinal and supra-spinal nervous systems.
- **Percutaneous electrical nerve stimulation (PENS)** = same principle as TENS, but with electrode needles are inserted through the skin into the subcutaneous tissue to produce a sensation in the tissue itself.
- **Interferential therapy** = application of medium frequency electrical currents by several electrodes on the skin over the affected area, sometimes with the use of suction cups. It is used to stimulate local nerves with the aims of modulating pain, reducing swelling, stimulating local muscles or to promote healing.
- **Low level laser therapy (LLLT)** = non-invasive application of a single wavelength of light to the skin over the injured area using a probe with

the hypothesis that this results in local heating and effects on local chemical activity and cellular behaviour (anti-inflammatory effect and promote tissue repair).

- **Therapeutic ultrasound** = delivery of mechanical energy in the form of high frequency sound waves to the site of injury, usually through a probe applied to the skin with the hypothesis that a thermal or mechanical stimulation may generate improved blood flow and may also facilitate the inflammatory process and tissue healing.

The NICE evidence review can be found on p.499-568 in the full guideline on assessment and non-invasive treatments and the forest plots in Appendix K p.173-200 (<https://www.nice.org.uk/guidance/ng59/evidence>).

A summary sheet in Appendix 7.10 gathered the evidence findings, the NICE GDG considerations, the results of the online survey and the discussion with the Belgian GDG.

#### Scientific evidence regarding electrotherapy

In the NICE evidence review the clinical and cost-effectiveness of electrotherapy as a non-invasive intervention in the management of low back pain and sciatica has been considered. This review focused on the effectiveness of TENS, PENS, interferential therapy, ultrasound and laser therapy. Other forms of electrotherapy were not considered. Forty studies were included in the review for electrotherapy as single intervention and thirteen studies looking at combinations of non-invasive interventions. Two Cochrane reviews were identified by NICE but they were not included due to the population definition. No relevant economic evaluations were identified. One economic evaluation relating to TENS was identified but excluded due to limited applicability.

In Appendix 7.10 the clinical review with summarizing tables on the clinical effectiveness per comparison, the GDG considerations and the results of the online survey are gathered.



### Scientific evidence regarding TENS (Transcutaneous Electrical Nerve Stimulation)

#### LOW BACK PAIN WITHOUT SCIATICA:

(see Tables 27 and 30 in Appendix 7.10)

- *Single interventions:* Overall could be stated that only some clinical benefit is seen in QoL and pain (change score) in favour of TENS compared to sham. The other reported outcomes showed either no difference or conflicting results (due to different measurement scales). Comparison with usual care or active comparators (acupuncture, corsets, spinal manipulation, massage) revealed no clinical differences in the majority of the reported outcomes or even a clinical benefit in pain in favour of the active comparator (acupuncture and manipulation).
- *TENS as adjunct in combined interventions:* There was some evidence of improvement in the short-term for QoL when TENS was given in addition to (biomechanical) exercise (in a single small study) compared to (biomechanical) exercise alone, however there was no difference in pain, function and psychological distress in combination with other interventions (TENS + acupuncture versus acupuncture; TENS + (biomechanical) exercise versus sham TENS).
- In none of the comparisons long-term data were reported.

#### LOW BACK PAIN WITH SCIATICA:

- No evidence was available.

#### MIXED POPULATION (WITH OR WITHOUT SCIATICA):

(see Tables 28 and 31 in Appendix 7.10)

- *Single interventions:* No clinical differences in QoL, pain and function at short term (<4months) were seen compared to sham or usual care. Only in the comparison with massage and sham (in a single study with small sample size), a clinical benefit was found in pain and in responder criteria (improvement in pain) in favour of TENS. These two outcomes were the only reported outcomes.

- *TENS as adjunct in combined interventions:* Only one study was found which compared a combination of BEMER (Bio-Electro-Magnetic-Energy-Regulation therapy), TENS, (mixed) exercise and massage versus placebo BEMER, TENS, (mixed) exercise and massage: conflicting results (no difference or in favour of sham) were found for QoL, but no difference in pain and function.
- In none of the comparisons long-term data were reported

### Scientific evidence regarding PENS (Percutaneous Electrical Nerve Stimulation)

#### LOW BACK PAIN WITHOUT SCIATICA:

(see Table 30 in Appendix 7.10)

- *Single interventions:* Patients who received PENS, showed a clinical important improvement at short term (<4 months) in QoL, pain and function compared to sham. However, no differences were anymore seen at long term (>4 months). Compared to TENS, the evidence is less clear cut, with some clinical benefit at short term (<4 months) in QoL but not for pain and function. No long-term data were reported for this comparison.
- *PENS as adjunct in combined interventions:* In terms of QoL, there was some evidence that PENS in addition to exercise was less beneficial than exercise with sham PENS, both at short and long term. No clinical difference was found for the other reported outcomes (pain and function), both at short and long term.

#### LOW BACK PAIN WITH SCIATICA:

- No evidence was available.

#### MIXED POPULATION (WITH OR WITHOUT SCIATICA):

- *Single interventions:* No clinical benefit in pain and function was found for PENS compared to usual care or TENS. In both comparisons (one study per comparison) no long term data were reported, nor on the other critical or important outcomes.
- *PENS as adjunct in combined interventions:* No evidence was available.



- A single RCT comparing the combination of *electro-acupuncture*, self-management (education and home exercises) and (mixed) exercises to self-management (education and home exercises) and (mixed) exercises, showed a short term clinical benefit in pain in favour of electro-acupuncture, but no differences were found in function and in healthcare utilisation (analgesic use).

#### Scientific evidence regarding Interferential therapy (IFT)

##### LOW BACK PAIN WITHOUT SCIATICA:

- *Single interventions*: No clinical benefit of IFT on pain (in comparison to sham, 2 RCTs) or function (in comparison to traction, 1 RCT) could be demonstrated. Per comparison only one outcome at short term was reported.
- *IFT as adjunct in combined interventions*: No evidence was available.

##### LOW BACK PAIN WITH SCIATICA:

- No evidence was available.

##### MIXED POPULATION (WITH OR WITHOUT SCIATICA):

(see Table 31 in Appendix 7.10)

- *Single interventions*: No evidence was available.
- *IFT as adjunct in combined interventions*: A clinical benefit was found in the longer term for QoL in the combination of IFT and spinal manipulation compared to spinal manipulation alone, but not in the short term. There was no clinical benefit at both time points for pain and function. Only one comparison was found, reported in a single RCT.

#### Scientific evidence regarding Low Level Laser Therapy (LLLT)

##### LOW BACK PAIN WITHOUT SCIATICA:

(see table 26 in Appendix 7.10)

- *Single interventions*: In the single comparison retrieved (LLT versus sham, 3 RCTs), conflicting results were reported for pain: whereas 2 RCTs found no clinical difference on overall pain score, a clinical benefit of laser therapy was found in reduced pain intensity in the last 24 hours and in responder criteria (>60% pain improvement) (reported in single studies). No clinical difference in function was found.
- *LLLT as adjunct in combined interventions*: One study was found that compared a combination of laser therapy with self-management (education) and biomechanical exercises to self-management (education) and biomechanical exercises. The only reported short term outcome (pain) showed a clinical benefit in favour of laser therapy. No long term data nor other outcomes were reported.

##### LOW BACK PAIN WITH SCIATICA:

(see Table 29 in Appendix 7.10)

- *Single interventions*: Some inconsistency in the results were found in the comparison of laser therapy versus sham: the overall scores on function and pain showed no clinical benefit of laser therapy (reported in 2 small studies). However, a large RCT reported a benefit of laser therapy in pain change score and in responder criteria (improvement in function). A similar inconsistency was found in the comparison to usual care: no clinical short term benefit was found for pain in contrast to a clinical benefit in responder criteria for function in favour of laser therapy. The single small study on the comparison to traction, found no clinical difference in (back and radicular) pain, whereas a short term improvement in function scores was found in the group who received laser therapy. No long-term data were reported for all retrieved comparisons.
- *LLLT as adjunct in combined interventions*: No evidence was available.



#### MIXED POPULATION (WITH OR WITHOUT SCIATICA):

(see Table 31 in Appendix 7.10)

- **Single interventions:** Both in the comparison to usual care and to exercise, a clinical short term benefit of laser therapy in pain was found, but without clinical difference in function.
- **LLLT as adjunct in combined interventions:** Laser therapy combined with self-management revealed no clinical difference in short-term pain and function compared to self-management alone. The comparison of HILT laser therapy and self-management (home exercises) with a placebo HILT laser therapy and self-management (home exercises), showed a short term improvement in pain in favour of laser therapy but without clinical difference in function scores. No long-term data were reported.

#### Scientific evidence regarding Therapeutic Ultrasound (US)

##### LOW BACK PAIN WITHOUT SCIATICA:

- **Single interventions:** Compared to sham, no clinical differences were found in the reported outcomes (pain, function and responder criteria in pain) (reported in a single study). Compared to usual care, some inconsistent results were found for QoL, a clinical benefit in pain in favour of US and no clinical differences in function and psychological distress (reported in a single study).
- **US as adjunct in combined interventions:** Two RCTs were found that compared the combination of US with biomechanical exercises (and self-management (semi-supervised exercises)) to biomechanical exercises (and self-management). In both studies no clinical differences were found for QoL, pain, function and psychological distress. No long-term data were reported.

##### LOW BACK PAIN WITH SCIATICA:

- **Single interventions:** In both comparisons (US versus sham (1 RCT) and US versus traction (1 RCT)), no clinical differences were found in pain, function and healthcare utilisation (use of paracetamol).
- **US as adjunct in combined interventions:** The combination of US and (biomechanical and aerobic) exercises showed a short term clinical benefit in pain and healthcare utilisation (medication use) but without improvement in function compared to waiting list control. However, if the same combination of US and exercises is compared to exercises, no clinical difference were anymore found for pain, function and healthcare utilisation (medication use).

##### MIXED POPULATION (WITH OR WITHOUT SCIATICA):

- **Single interventions:** Only one comparison (versus laser therapy) was found in a single RCT that reported only one outcome: no clinical difference in pain was found.
- **US as adjunct in combined interventions:** No evidence was available.

#### Economic evidence

- No relevant economic evaluations were identified.

#### Conclusions

- 
- **Inconsistent and insufficient evidence, including lack of retrieved studies on patients with low back pain and sciatica, was found in favour of TENS, PENS, interferential therapy, laser therapy and therapeutic ultrasound.**
  - **No conclusion can be drawn on the cost-effectiveness of electrotherapy due to lack of economic evaluations.**
-



**Other considerations regarding TENS**

GRADE factors	Comments
<b>Balance between desirable and undesirable effects</b>	<ul style="list-style-type: none"> <li>The Belgian GDG acknowledged that conflicting results or lack of clinical difference was found when TENS was compared to sham TENS, usual care or to active comparators.</li> <li>No adverse effects were reported by the GDG members (both NICE and the Belgians).</li> </ul>
<b>Quality of evidence</b>	<ul style="list-style-type: none"> <li>The quality evidence was low or very low quality, mainly due to risk of bias (difficulty of adequate blinding, high drop-out and switching rates, difficulties with selection bias and issues with comparability of care).</li> <li>The NICE GDG also highlighted problems with the sham for TENS: given that the effectiveness of TENS is widely thought to be related to the intensity of the stimulus, a true sham that establishes robust blinding is not achievable.</li> </ul>
<b>Values and preferences</b>	<ul style="list-style-type: none"> <li>Following considerations were mentioned by the <b>NICE stakeholders</b>, which are also applicable for the Belgian clinical practice:               <ul style="list-style-type: none"> <li>One of the NICE stakeholders emphasised the potential benefit of TENS as part of a range of self-management strategies, as it can be delivered independently by the patient.</li> <li>The lack of long-term data can be explained by the working mechanism of TENS: i.e. via the pain gate mechanism only a temporary pain relief can be achieved during the time it is operated by the patient. The value of TENS lies particularly in helping to manage pain flare ups.</li> <li>TENS can be helpful for reducing pain enabling to exercise and allowing return to normal function and it can reduce the need for pharmacological intervention.</li> <li>A proposition was made to change the recommendation that TENS should only be offered as part of a multimodal package, but this proposition has been rejected by NICE due to lack of evidence of the combined interventions with TENS as adjunct.</li> </ul> </li> <li>Nevertheless the lack of evidence in favour of TENS, some of the <b>Belgian GDG</b> members mentioned the use of TENS for short term relieve in case of failure of medical treatment or in patients with very severe pain (very small subgroup of patients). However, all GDG members agreed to recommend against the use of TENS in the management of low back pain (with or without radicular pain).</li> </ul>
<b>Costs (resource allocation)</b>	<ul style="list-style-type: none"> <li>Currently, TENS machines are often purchased by the patient in the UK, however they may also be provided on loan to the patient.</li> <li>Given the conflicting evidence on its clinical benefit, the cost of providing this intervention (provided on loan to the patient at a cost to the NHS in terms of the machine itself and also related personnel time explain how to use it) were not considered justified by the NICE GDG.</li> <li>In Belgium, the TENS machine does not have to be purchased by the patient, but can be borrowed or the patient can come to the clinical practice of the physiotherapist for an additional session of TENS to his/her conventional therapy sessions. This clinical practice does not necessarily imply additional costs for the patient, nor for the society. Sometimes patients with chronic pain by a TENS machine for personal use, after a positive trial.</li> </ul>

Recommendation	Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"> <li>Do not offer transcutaneous electrical nerve stimulation (TENS) for managing low back pain with or without radicular pain.</li> </ul>	Strong (RCTs)	Low to very low





**Change in comparison with the NICE recommendations**

- “sciatica” replaced by “radicular pain”: Do not offer transcutaneous electrical nerve stimulation (TENS) for managing low back pain with or without ~~sciatica~~ radicular pain.

The reasons underlying these changes are described in Appendix 7.1

**Other considerations regarding PENS**

GRADE Factors	Comments
<b>Balance between desirable and undesirable effects</b>	<ul style="list-style-type: none"> <li>• The Belgian GDG acknowledged that there was insufficient evidence on benefit for PENS.</li> <li>• The potential adverse events related to the penetration of the skin was considered by the NICE GDG members, but this risk would be similar to acupuncture which has an acceptable safety profile.</li> </ul>
<b>Quality of evidence</b>	<ul style="list-style-type: none"> <li>• The quality of evidence ranged from moderate to very low due to risk of bias.</li> <li>• The NICE GDG also highlighted problems with the sham for PENS: given that the effectiveness of PENS is widely thought to be related to the intensity of the stimulus, a true sham that establishes robust blinding is not achievable.</li> </ul>
<b>Values and preferences</b>	<ul style="list-style-type: none"> <li>• The NICE GDG mentioned that PENS is currently not widely used in UK and so a recommendation for its use would imply a significant change in practice. No comments were formulated by the NICE stakeholders.</li> <li>• The <b>Belgian GDG</b> members agreed on the strong formulation of the recommendation against PENS due to the conflicting evidence in combination with the more invasive therapy with possible adverse events and the fact it is not common used.</li> </ul>
<b>Costs (resource allocation)</b>	<ul style="list-style-type: none"> <li>• No economic evaluations were retrieved.</li> <li>• Given that PENS is not widely used, higher implementation costs are expected and there is insufficient evidence according to NICE 2016 to justify intervention costs.</li> </ul>

Recommendation	Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"> <li>• Do not offer percutaneous electrical nerve stimulation (PENS) for managing low back pain with or without radicular pain.</li> </ul>	Strong (RCTs)	Moderate to very low



**Change in comparison with the NICE recommendations**

- “sciatica” replaced by “radicular pain”: Do not offer percutaneous electrical nerve stimulation (PENS) for managing low back pain with or without ~~sciatica~~ radicular pain.

The reasons underlying these changes are described in Appendix 7.10.

**Other considerations regarding interferential therapy**

GRADE Factors	Comments
<b>Balance between desirable and undesirable effects</b>	<ul style="list-style-type: none"> <li>• The Belgian GDG acknowledged the lack of evidence of clinical benefit for IFT (few studies): only evidence on effectiveness of IFT as single intervention found in patients with low back pain without sciatica.</li> <li>• The <b>Belgian GDG</b> members mentioned the importance of a strong recommendation against the use of IFT, considering the absence of effectiveness reported in literature and the controversial rationale of this kind of current.</li> <li>• Another Belgian GDG members noted that the lack of evidence on the comparison to sham in 2 high quality RCTs, are reasons to formulate a strong recommendation against its use.</li> </ul>
<b>Quality of evidence</b>	<ul style="list-style-type: none"> <li>• There was high and low quality of the evidence</li> </ul>
<b>Values and preferences</b>	<ul style="list-style-type: none"> <li>• Following considerations were mentioned by <b>the NICE stakeholders</b>, which are also applicable for the Belgian clinical practice:               <ul style="list-style-type: none"> <li>○ Based on the study on the comparison of manual therapy and IFT, it can be concluded that IFT was found to be effective as manual therapy when used alone or in combination. This conclusion has been rejected by NICE, based on the lack of clinical difference in reported outcome (QoL).</li> <li>○ IFT is already considered inappropriate modality in modern NHS physiotherapy due to lack of evidence.</li> </ul> </li> </ul>
<b>Costs (resource allocation)</b>	<ul style="list-style-type: none"> <li>• No economic evaluations were retrieved.</li> <li>• Use of IFT will be associated with costs relating to equipment and personnel time required to deliver the therapy, although the NICE GDG noted that IFT units are already available in most physiotherapy departments.</li> <li>• Given the lack of evidence of clinical benefit for interferential therapy, intervention costs were not considered justified.</li> </ul>

Recommendation	Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"> <li>• Do not offer interferential therapy for managing low back pain with or without radicular pain.</li> </ul>	Strong (RCTs)	High to low

**Change in comparison with the NICE recommendations**

- “Sciatica” replaced by “radicular pain”: Do not offer interferential therapy for managing people with low back pain with or without ~~sciatica~~ radicular pain.

The reasons underlying these changes are described in Appendix 7.10.

**Other considerations regarding Therapeutic Ultrasound**

GRADE Factors	Comments
<b>Balance between desirable and undesirable effects</b>	<ul style="list-style-type: none"> <li>• The only evidence of benefit was of low quality and based on low patient numbers; for the majority outcomes no benefit was seen.</li> </ul>
<b>Quality of evidence</b>	<ul style="list-style-type: none"> <li>• There was low to very low quality of the evidence due to risk of bias and imprecision of the effect estimate.</li> </ul>
<b>Values and preferences</b>	<ul style="list-style-type: none"> <li>• Following consideration was mentioned by the <b>NICE stakeholders</b>, which are also applicable for the Belgian clinical practice:             <ul style="list-style-type: none"> <li>○ US is already considered an inappropriate modality in modern NHS physiotherapy due to lack of evidence.</li> </ul> </li> <li>• No additional comments were formulated by the <b>Belgian GDG</b> members.</li> </ul>
<b>Costs (resource allocation)</b>	<ul style="list-style-type: none"> <li>• No economic evaluation was retrieved.</li> <li>• Use of US will be associated with costs relating to equipment and personnel time required to deliver the therapy, although the NICE GDG noted that US units are already available in most physiotherapy departments.</li> <li>• Given the lack of evidence of clinical benefit for ultrasound therapy, intervention costs were not considered justified.</li> </ul>

Recommendation	Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"> <li>• Do not offer ultrasound for managing low back pain with or without radicular pain.</li> </ul>	Strong (RCTs)	Very low to low

**Change in comparison with the NICE recommendations**

- “Sciatica” replaced by “radicular pain”: Do not offer ultrasound for managing low back pain with or without sciatica radicular pain.

The reasons underlying these changes are described in Appendix 7.10.

**Other considerations regarding Low Level Laser Therapy**

GRADE Factors	Comments
<b>Balance between desirable and undesirable effects</b>	<ul style="list-style-type: none"> <li>• The Belgian GDG acknowledged that conflicting evidence was found comparing laser with sham and usual care for pain and function outcomes. However, the evidence of clinical benefit was of moderate quality in a reasonable large patient group whereas the evidence of no benefit was of lower quality and in smaller patient groups.</li> <li>• The NICE GDG noted that the larger trial was conducted in an inpatient setting in Serbia and questioned the applicability of this evidence to a UK healthcare context.</li> <li>• Also no clear conclusion can be drawn on the effectiveness of laser when comparisons were made with active interventions of exercise and traction.</li> <li>• The NICE GDG concluded that the evidence was conflicting and insufficient to base a recommendation on, but it was considered as an area for future research.</li> <li>• A review by Glazov in 2016<sup>15</sup> focused on low-level laser therapy mentioned a useful reduction in pain in chronic LBP for up to 3 months with few adverse effects but recommended further rigorously blinded trials using adequate laser doses before formulating a recommendation.</li> </ul>
<b>Quality of evidence</b>	<ul style="list-style-type: none"> <li>• The quality of evidence was moderate (in the large trial).</li> <li>• The applicability of the trial and its relevance to decision-making was questioned due to the very intensive treatment regimen and the inpatient care setting.</li> </ul>
<b>Values and preferences</b>	<ul style="list-style-type: none"> <li>• In the online survey the Belgian GDG members were not convinced of the importance to formulate a research recommendation on laser therapy. However, during the GDG meeting one of the GDG members mentioned the recent systematic review of Huang 2015<sup>16</sup>, which showed significantly lower pain scores after laser therapy compared with placebo. No significant treatment effect was found for function or spinal range of motion outcomes.</li> <li>• It was agreed to maintain the research question, as formulated by NICE with the addition that new trials on this topic should be monitored.</li> <li>• No comments were formulated by the NICE stakeholders</li> </ul>
<b>Costs (resource allocation)</b>	<ul style="list-style-type: none"> <li>• No economic evaluation was retrieved.</li> <li>• Use of laser will be associated with costs relating to equipment and personnel time required to deliver the therapy, although the NICE GDG noted that laser therapy units are already available in most physiotherapy departments.</li> <li>• Given the lack of evidence of clinical benefit for ultrasound therapy, intervention costs were not considered justified.</li> </ul>



- It was also highlighted that the regimen in the key trial was very intensive (5 daily sessions for 3 weeks) and cost effectiveness may depend on whether or not clinical benefit is maintained when treatment stops. No long-term data were available to justify this.

**Recommendation for research**

**Actions needed**

- What is the clinical and cost-effectiveness of laser therapy in the management of low back pain and radicular pain?

Monitoring of new high quality trials

**Change in comparison with the NICE recommendations**

- “Sciatica” replaced by “radicular pain”: What is the clinical and cost-effectiveness of laser therapy in the management of low back pain and sciatica radicular pain?

The reasons underlying these changes are described in Appendix 7.10.

*3.2.8 Psychological interventions*

Low back pain is a complex phenomenon that cannot be reduced to its physical aspects and is influenced by an interaction of sensitive, motivational-affective, and cognitive-evaluative components. The psychological aspects of treatment, in particular cognitive behavioural approaches, have been developed as a result of an intense understanding of this complexity and play a role increasingly important in the management of chronic pain. Cognitive-behavioural approaches are aimed at altering unhelpful or inappropriate beliefs as a basis for changing ‘illness-behaviour’ and encourage ‘well behaviour’ and a return to normal function.

The NICE evidence review can be found on p.569-604 in the full guideline on assessment and non-invasive treatments and the forest plots in Appendix K p.201-210 (<https://www.nice.org.uk/guidance/ng59/evidence>).

A summary sheet in Appendix 7.11 gathered the evidence findings, the NICE GDG considerations, the results of the online survey and the discussion with the Belgian GDG.

**Scientific evidence regarding psychological interventions**

Twenty-one RCTs (reported in twenty-five papers) were included by NICE for single interventions. No RCT was found for acceptance and commitment therapy and the search was extended to cohort studies for these two topics and for mindfulness. No relevant cohort studies were identified. Comparators were usual care, waiting list, sham or other psychological therapy. No evidence was identified for responder criteria or adverse events from the included studies. Three studies (reported in six papers) looking at combinations of non-invasive interventions (with psychological therapy as the adjunct) were also included. Results are presented separately for 4 kinds of psychological interventions: Cognitive behavioural approaches, Behavioural therapy, Mindfulness and Cognitive therapy. Three economic evaluations concerned cognitive behavioural approach were included. No studies were identified relating to behavioural therapies, cognitive therapies, mindfulness or acceptance and commitment therapy. One additional economic evaluation (Critchley et al 2007) of a MBR programme which included a psychological component was identified. This is included in the MBR chapter.



**Cognitive behavioural approaches (mixed of cognitive therapy, education, engaging in fear-provoking activities, stress reduction, wellbeing therapy) as single intervention** (see Table 32 in Appendix 7.11)

- Compared to sham or usual care or waiting list controls: No clinical benefit was observed in mixed population (with and without sciatica) with measures of pain and function being the most commonly outcomes reported (moderate to very low quality; total of 7 studies; range of n = 47–458). The one exception was **function** as measured by RMDQ at ≤4 months, which showed a **clinical benefit** of cognitive behavioural approaches compared with waiting list control (low quality; 2 studies; n = 240).
- Compared to behavioural therapy (positive reinforcement of healthy behaviours, education, activity quotas): No difference was found in mixed population (with and without sciatica) in terms of pain at either time point (1 study; low quality; n=73). Potential **clinical benefit** in favour of **cognitive behavioural approaches** at >4 months when function measured by RMDQ (1 study; low quality; n=73), but not by the Quebec back pain disability scale (1 study; very low quality; n=73).

**Behavioural therapy (EMG biofeedback or relaxation or operant conditioning, with participation of spouses, group discussion, role playing, feedback)** (see Table 33 in Appendix 7.11)

- Compared with sham biofeedback: Potential **clinical benefit** of behavioural therapy for improving **pain** at short term (low quality; 1 study; n = 24) in mixed population (with and without sciatica).
- Compared with waiting list controls: No clinical benefit of behavioural therapy approach for pain intensity measured on the McGill scale (very low quality; 2 studies; n = 122) but **potential clinical benefit of behavioural therapy in improving pain** measured by Back pain log at short term when compared to usual care in mixed population (with and without sciatica) (very low quality; 1 study; n = 20). No clinically important difference for function or healthcare utilisation (very low quality; n = 103).

- Only one study (Turner 1990; exercise therapy vs Waiting list; n=96) concerned low back pain population without sciatica and is included in the exercise chapter.

**Mindfulness (meditation sessions and meditation homework assignments) versus usual care or waiting list controls**

- No clinically important benefit of a mindfulness intervention was found in mixed population (with or without sciatica) compared to waiting list control on pain (very low quality; 2 studies; n=124), function (low quality; 1 study; n=37) or the majority of quality of life outcomes reported (very low to low quality; 1 study; n=37) except for the quality of life composite measures of mental health and physical health, which showed a clinical benefit of mindfulness (2 studies, very low quality, n=124) at short term.

**Cognitive therapies (explanation of pain mechanisms, illness perception, functional examination with individual feedback and advice)**

LOW BACK PAIN POPULATION WITHOUT SCIATICA

- Compared to usual care/waiting list: Potential **clinical benefit** of cognitive therapy in terms of **quality of life** (SF-36) and **pain** at long term but no difference for function (very low quality; 1 study; n = 63).
- Compared with biomechanical plus aerobic exercise: Conflicting evidence on the clinical benefit of cognitive therapy for the quality of life components at long term (**clinical benefit** favouring cognitive therapy on physical function, bodily pain, vitality, social function, role emotional and mental health but clinical benefit in favour of exercise on role function, and no clinically important difference seen for general health or health transition). There was also no clinical benefit observed for function or pain (very low quality; n = 64).



#### MIXED POPULATION (WITH OR WITHOUT SCIATICA)

- Compared with waiting list control: Potential **clinical benefit** of cognitive therapy in terms of **pain intensity** (VAS 0-10) at short term, but no clinical difference on psychological distress or function assessed with the sickness impact profile (very low quality; 1 study; n = 34).

#### Combination of psychological therapy (behavioural therapy) and aerobic exercise

- Compared to waiting list controls or aerobic exercise alone: No clinical benefit of psychological therapy (behavioural therapy) in combination with aerobic exercise in terms of pain (McGill 0-78) at long term (very low quality; 1 study; n=37 or 39) in low back pain population without sciatica.

#### Combination of psychological therapy (cognitive behavioural approaches) plus aerobic exercise

- Compared to aerobic exercise alone: No clinical benefit in the short-term but benefit in the longer term for the psychological therapy on both pain and function (low quality; 1 study; n=84) in mixed population (with or without sciatica).

#### Combination of psychological therapy (cognitive behavioural approaches) plus self-management

- Compared to self-management alone: **Clinically important benefit** of cognitive behavioural approaches in terms of **quality of life** when assessed by EQ-5D and SF-12 physical component in both the short and longer term, but not for the mental component of the SF12 in mixed population (with or without sciatica); No difference between treatments in terms of pain and function with the exception of function assessed by the von Korff scale at longer term follow up when self-management alone was more beneficial in terms of improvements in function (moderate and low quality evidence, 1 study, n=545 to 598).

#### Economic evaluation

- One cost-utility analysis found that **usual care was dominant** (less costly and more effective) compared to cognitive behavioural approach for the management of low back pain (with or without sciatica). This analysis was assessed as partially applicable with potentially serious limitations.
- One cost-utility analysis found that **cognitive behavioural approach was dominant** (less costly and more effective) compared to mixed modality exercise for the management of low back pain (with or without sciatica). This analysis was assessed as partially applicable with potentially serious limitations.
- One cost-utility analysis found that **cognitive behavioural approach was dominant** (less costly and more effective) when compared to a 2-element MBR (physical, psychological) programme and mixed manual therapy plus self-management for treating low back pain (with or without sciatica). This analysis was assessed as partially applicable with potentially serious limitations.

#### Conclusions

**No evidence was found of clinical benefit of the cognitive behavioural approach except for function measured by RMDQ (at  $\leq 4$  months compared to waiting list control and at  $>4$  months compared to behavioural therapy) but not for pain. There was evidence of a potential clinical benefit of behavioural therapy for improving pain but not for function. Cognitive therapy showed inconsistent results (with clinical benefit in pain and in several aspects of quality of life). No clinically important benefit was demonstrated for mindfulness and few clinical benefits were observed in quality of life with a combination of psychological therapy and self-management compared to self-management alone. Evidence focused mostly on mixed population (with and without sciatica). The economic evaluation showed that cognitive-behavioural approach was dominant compared to mixed modality exercise or MBR programme and mixed manual therapy + self-management but was less dominant compared to usual care.**



### Other considerations regarding psychological interventions

GRADE Factors	Comments
<b>Balance between clinical benefits and harms</b>	<ul style="list-style-type: none"><li>• The Belgian GDG acknowledged that most of the evidence is based on individual studies for each comparison and there was too poor evidence to recommend any psychological intervention in isolation.</li><li>• The Belgian GDG highlighted some limitations in the NICE review that can lead to an under-estimation of the effect:<ul style="list-style-type: none"><li>○ The inappropriate outcome measurements: rather than pain and function, one should be review whether the intervention reduce the fear of pain for example.</li><li>○ The possible misclassification of interventions: e.g. cognitive therapies dedicated to explain pain mechanisms should be considered as education rather than psychological intervention.</li><li>○ The risk that interventions included in the studies were not provided by a qualified clinical psychologist.</li></ul></li><li>• Since the Belgian present guideline recommends to use a risk stratification that takes into account psychological factors, it is consistent to propose a psychological approach, certainly for patient at high risk for psychological factors.</li><li>• Moreover, the clinical benefit observed from a large trial where cognitive behavioural therapy was offered in combination with self-management suggested that psychological interventions should be integrated in a package of treatment. This suggestion is confirmed in the chapter on MBR programmes.</li></ul>
<b>Quality of evidence</b>	<ul style="list-style-type: none"><li>• The quality of evidence ranged from moderate to very low; serious or very serious risk of bias (due mostly to the difficulty of adequate blinding with such interventions) in most of the studies included.</li><li>• NICE highlighted that the comparator was waiting list controls groups in a number of the studies although this is not reflective of usual practice and often lead to inflated estimates of effect sizes in the intervention groups due to the negative effect on people randomised to delayed treatment.</li><li>• NICE stressed also the lack of detail about the background care that the participants received apart from the intervention, and therefore impossibility to assess in some cases whether the care in the two groups was comparable, with a risk of overestimating effects in subjective outcomes such as pain and function.</li><li>• For behavioural therapies, all included studies published prior to 1990 but according to NICE, this treatment is now less commonly used to treat people with low back pain).</li><li>• For mindfulness, evidence was very limited (1 small study compared to waiting list control, and 1 compared to sham which only reported data in graphical format and therefore could not be analysed within this review). No observational studies identified.</li></ul>
<b>Values and preferences</b>	<ul style="list-style-type: none"><li>• The patients' needs and preferences are a crucial element to include in the risk stratification and the shared-decision making process.</li></ul>
<b>Costs (resource allocation)</b>	<ul style="list-style-type: none"><li>• The 3 economic analysis showed uncertainty regarding the cost-effectiveness of cognitive behavioural approach as a standalone intervention and they were assessed by NICE as partially applicable with potentially serious limitations.</li><li>• The main cost of delivering psychological interventions will be the personnel costs. NICE proposed that psychological interventions may be delivered by a psychologist or another health care professional trained to give the therapy such as a nurse or physiotherapist.</li></ul>





Recommendations	Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"> <li>Consider a psychological intervention using a cognitive behavioural approach for managing low back pain with or without radicular pain, but only as part of a multimodal treatment* with a supervised exercise programme.</li> </ul>	Weak (RCTs)	Moderate to very low

\*Psychological interventions are optional and are only applied to certain patients at certain time period and depending on their risk stratification

### Change in comparison with the NICE recommendations

Minor changes have been proposed by the Belgian GDG regarding the clinical recommendations proposed in the NICE 2016 guidelines. The end of the NICE recommendation concerned another recommendation and was not retained in the Belgian version for clarity.

19. Consider a psychological ~~therapies~~ intervention using a cognitive behavioural approach for managing low back pain with or without ~~sciatica~~ radicular pain but only as part of a multimodal treatment ~~package~~ including a supervised exercise programme, ~~with or without manual therapy (spinal manipulation, mobilisation or soft tissue techniques such as massage).~~

More detailed on the reasons underlying these changes are described in Appendix 7.11.

### 3.2.9 Multidisciplinary biopsychosocial rehabilitation (MBR) programs

The MBR approach combines education and physiotherapy, with different forms of cognitive-behavioural psychology to address participants' unhelpful beliefs about their pain, reduce 'fear-avoidance' behaviours and catastrophic thinking and improve mood, thus decreasing disability and improving function. Currently in Belgium a MBR program has already been rolled out in hospital setting with following treatment modalities: functional and psychosocial evaluation (including questionnaires), information/education (biopsychosocial influencing factors), ergonomics (including work-related adjustments if applicable), individualized exercise program. This program is described more in detail in the Belgian pathway of low back pain.

### Definition of multidisciplinary biopsychosocial rehabilitation (MBR) programs

Multidisciplinary biopsychosocial rehabilitation (MBR) was defined as an intervention that involves a physical component (such as specific exercise modalities, mobilisation, massage) and at least one other element from a biopsychosocial approach, that is psychological or social and occupational or educational (defined educational intervention e.g. education on anatomy, psychology, imaging, coping, medication, family, work and social life).

The different components of the intervention had to be offered as an integrated program involving communication between the providers responsible for the different components. These programs may in fact include various components delivered by one individual, and the multidisciplinary aspect can apply to the interventions included in the package (across disciplines), not to the number of people/disciplines delivering this.

The NICE evidence review can be found on p.670-737 in the full guideline on assessment and non-invasive treatments and the forest plots in Appendix K p.232-254 (<https://www.nice.org.uk/guidance/ng59/evidence>).

A summary sheet in Appendix 7.12 gathered the evidence findings, the NICE GDG considerations, the results of the online survey and the discussion with the Belgian GDG.



### Scientific evidence regarding MBR programs

The clinical and cost effectiveness of different kinds of MBR programs have been considered. Twenty-two RCTs were included in this review by NICE. One Cochrane review was identified but it was excluded as the definition of MBR programme was different, requiring a minimum of two healthcare professionals from different professional backgrounds, and the review included studies comparing MBR to surgery, however the studies included in this Cochrane review were individually assessed and included if they matched the review protocol. A comparison between a 3-element MBR program and disc replacement can be found in the disc replacement chapter. Two economic evaluations were identified that included an MBR programme as a comparator and have been included in this review.

In addition to the evidence review performed by NICE, the KCE researchers also looked at differences in efficacy of MBR programs between acute and chronic low back pain. The same definition of acute has been applied as in NICE: acute low back pain is less than 3 months, chronic low back pain is at least 3 months. For clarity reasons, no distinction has been made between acute and subacute low back pain.

### Scientific evidence regarding MBR program 3 elements: physical + psychological + education

#### LOW BACK PAIN WITHOUT SCIATICA:

- *Compared to usual care:* A single RCT compared a MBR program (delivered by a monodisciplinary team; physical (stretching, aerobic exercises and strength) + psychological (cognitive-behavioural principles) + education (educational message encouraging self-reliance)) to usual care (referral to physiotherapy possible, including spinal manipulation) in a mixed population of acute and chronic low back pain patients but found no differences in pain and function, at both time points. Other outcomes were not reported.
- No studies were found on the comparison to single interventions, combined interventions or other MBR programs. Also no studies were found in acute low back pain patients.

#### LOW BACK PAIN WITH SCIATICA:

- No evidence was available.

#### MIXED POPULATION (WITH OR WITHOUT SCIATICA):

(see Table 34 in Appendix 7.12)

- *Compared to usual care:* An MBR program (delivered by a multidisciplinary team; physical (postural therapy, strength, stretching) + psychological (relaxation) + education (information in group discussions)) was compared to a waiting list control and found a benefit of the MBR program in pain but an improvement in function in the waiting list control, both at long term. No short-term data or other outcomes were reported. The single study included only chronic low back pain patients.
- *Compared to single interventions:* No clinical differences in QoL, pain and function were found (at both time points) between an MBR program (delivered by a monodisciplinary team; physical (mobility training, interferential therapy) + psychological (cognitive therapy) + education (Back Care booklet)) and individual aerobic exercises (walking) in acute low back pain patients.
- *Compared to combined interventions:* Two studies were found with different combined interventions:
  - Monticone 2015: 3-element MBR (delivered by a multidisciplinary team; physical (group exercises on mobility and muscle awareness, task oriented exercises, exercises to recover coordination, balance and walking stability) + psychological (group-based cognitive-behavioural approaches) + education (information, ergonomic advice)) versus combination of biomechanical exercise (strength) + manual therapy (mobilisation) + postural therapy (postural control exercises) + self-management (educational booklet)
  - Critchley 2007: 3-element MBR (delivered by a monodisciplinary team; physical (group strength, stretching and light aerobic exercises) + psychological (cognitive-behavioural approach) + education (structured back pain education)) versus combination of biomechanical home exercises (stretching) + manual therapy (mobilisation, manipulation, massage) + self-management (advice)



- Compared to a combined intervention of exercise, manual therapy, postural therapy and self-management (Monticone 2015), a clinical important benefit was found in QoL and pain (both at both time points) in favour of the MBR program, however not in function (at short and long term). The study of Critchley 2007 revealed no clinical difference (at long-term) between the MBR program and the combined intervention (exercise, manual therapy and self-management) in QoL, pain and function. No short term data were reported in this study. Both studies included only chronic low back pain patients.
- *Compared to other MBR programs:* Two comparisons were found in which a 3-element MBR program (delivered by a multidisciplinary team; physical (strength, aqua therapy) + psychological (cognitive therapy or behavioural therapy) + education (written handouts)) was compared to a 2-element MBR program with the same physical and educational component. Both comparisons differ in the psychological component in the 3-element MBR program. Evidence from the 2 studies on the 3-element MBR programme with a cognitive component showed no clinical benefit for any of the outcomes reported. The single study on the 3-element MBR programme with a behavioural component found among the other reported outcomes, only a long term clinical benefit in psychological distress in favour of the 2-element MBR programme. Both studies included only chronic low back pain patients.

### **Scientific evidence regarding MBR program 2 elements: physical + psychological**

#### LOW BACK PAIN WITHOUT SCIATICA:

- *Compared to usual care:* The single study comparing a 2-element MBR programme with physical (muscle relaxation, strength) and psychological (cognitive restructuring techniques) component found a clinical benefit in short term pain and function. For psychological distress, conflicting results were found. No long term data or other outcomes were reported. Also only chronic low back pain patients were included.
- No studies were found on the comparison to single interventions, combined interventions or other MBR programs.

#### LOW BACK PAIN WITH SCIATICA:

- No evidence was available.

#### MIXED POPULATION (WITH OR WITHOUT SCIATICA):

(see Table 35 in Appendix 7.12)

- Compared to usual care: Two studies was found:
  - A 2-element MBR program consisting of a physical (active physical training with graded activity) and psychological (problem solving training) component (delivered by multidisciplinary team) was compared to a waiting list control: no clinical difference in pain and in psychological distress was shown, only a short-term clinical benefit was found in function. No long term data were reported in this study and only chronic low back pain patients were included.
  - A 2-element MBR program consisting of a physical (physical reconditioning: stretching, strength, relaxation, aerobic exercises, recreational activities) and psychological (psychosocial and return to work issues) component (delivered by multidisciplinary team) compared to usual care ('non-intervention group') reported only results on the number of patients who returned to work and a clinical benefit was shown in the MBR group. This study included only acute low back pain patients.
- *Compared to single interventions:* Three studies (4 comparisons) were found with different single interventions (all on chronic low back pain patients)
  - A 2-element MBR (physical (aerobic and biomechanical exercises) + psychological (cognitive-behavioural therapy/problem solving training), delivered by a monodisciplinary team) versus mixed exercises (biomechanical + aerobic, 12 weeks)



- A 2-element MBR (physical (active physical training with graded activity) + psychological (problem solving training), delivered by a multidisciplinary team) versus mixed exercises (biomechanical + aerobic, 10 weeks)
  - A 2-element MBR (physical (active physical training with graded activity) + psychological (problem solving training), delivered by a multidisciplinary team) versus psychological therapy (cognitive behavioural approach-CBA)
  - A 2-element MBR (physical (stretching, strength, aerobic exercises, balneotherapy) + (psychological (individual cognitive therapy), delivered by a multidisciplinary team) versus individual biomechanical exercises (core stability)
  - Across all comparisons, only a clinical benefit was found in short term pain relief and function in favour of the 2-element MBR programme compared to a mixed modality exercise intervention (Khan 2014). No long term data were reported in this study. The other studies found no differences for pain, function, psychological distress, return to work and healthcare utilisation at short and long term.
  - *Compared to combined interventions:* Three studies were found with different combined interventions (all on chronic low back pain patients)
    - A 2-element MBR program (physical (biomechanical exercises, postural control, mobilisation) + psychological (cognitive-behavioural approach), delivered by a multidisciplinary team) versus combined intervention of (biomechanical) exercises + manual therapy (mobilisation): a clinical benefit favouring MBR programme was found in QoL, pain and function for both time points.
    - A 2-element MBR (physical (specific movement exercises and physical activity programme tailored to movement classification) + psychological (behavioural management approach), delivered by a monodisciplinary team) versus combined intervention of (biomechanical) exercises + manual therapy (mobilisation + manipulation) showed at both time points a clinical benefit in pain and in healthcare utilisation (care-seeking after intervention) in favour of the MBR programme but no difference was found in function.
  - A 2-element MBR (physical (motor training, stability) + psychological (cognitive-behavioural approach), delivered by a multidisciplinary team) versus combined intervention of (biomechanical) exercises + manual therapy (mobilisation) + postural therapy (postural control) showed a short term clinical benefit in QoL and pain in favour of the MBR programme but no difference in function and healthcare utilisation (medication use). No long term data were reported in this study.
  - No studies were found on the comparison to other MBR programs.
- Scientific evidence regarding MBR program 2 elements: physical + education**
- LOW BACK PAIN WITHOUT SCIATICA:
- No evidence was available.
- LOW BACK PAIN WITH SCIATICA:
- No evidence was available.
- MIXED POPULATION (WITH OR WITHOUT SCIATICA):
- (see Table 36 in Appendix 7.12)
- *Compared to single interventions:* Three studies were found with different single interventions (on chronic low back pain patients or a mixed population of acute and chronic low back pain patients).
    - A 2-element MBR (physical (aerobic, strength exercise, ball games, training in hot water, fitness centre) + education (postural techniques and pain management) (delivered by a multidisciplinary team) versus exercise (biomechanical-core stability): conflicting results were found for QoL, no clinical difference in pain (at both time points) and in short term function, whereas only at long term a clinical benefit in function was found.



- In the studies of Preyde 2000 the physical component of the 2-element MBR programme comprised exercise and spinal manipulation or exercise alone combined with education on posture and body mechanics (delivered by a mono-disciplinary team) in comparison to manual therapy (spinal manipulation). The addition of manipulation to the physical component in the MBR program revealed conflicting results for pain but no clinical difference for function and psychological distress. The MBR programme with only exercise in the physical component showed only a clinical benefit in function in favour of the single intervention (manipulation). No long term data were reported in both studies.
- No studies were found on the comparison to usual care, combined interventions or other MBR programs.

### Economic evidence

Two economic evaluations were found:

- One cost-utility analysis found that a 3-element MBR (physical, psychological, education) program was dominant (less costly and more effective) compared to biomechanical exercises and a combination of mixed manual therapy + self-management for treating low back pain (with or without sciatica). This analysis was assessed as partially applicable with potentially serious limitations.
- One cost-utility analysis found that a 2-element MBR (physical, psychological) programme was dominated (more costly and less effective) compared to cognitive behavioural approaches and mixed manual therapy plus self-management for treating low back pain (with or without sciatica). This analysis was assessed as partially applicable with potentially serious limitations.

### Conclusions

- **The majority of the evidence was found in the mixed population (with or without sciatica). No studies were reported in patients with low back pain and sciatica. Most studies included either chronic or a mixed population of acute and chronic low back pain patients. Two studies were found (a 3-element MBR program versus aerobic exercise and a 2-element (physical and psychological) versus usual care in an acute population with low back pain with or without sciatica. No reliable statement can be made on the efficacy of MBR program in acute low back pain patients based on these two studies.**
- **3-element MBR program (physical, psychological and educational elements): Mixed evidence was found for the comparison to usual care. In patients without sciatica no differences were found, whereas in the mixed population some benefit in pain was found in favour of the MBR program but also an improvement in function in the waiting list control. The beneficial effects of MBR program compared to single or combined interventions or to other MBR programs is very small and not consistent.**
- **2-element MBR program (physical and psychological elements): In the comparison to usual care, some short term benefit on pain and function was found in patients with low back pain without sciatica, but these results were less consistent in the mixed population. Comparisons to single interventions, revealed only a short term benefit in pain and function compared to mixed exercises. More beneficial effects in pain and function of a MBR program was seen in the comparisons to combined interventions.**
- **2-element MBR program (physical and educational elements): Only comparisons to a single intervention in the mixed population were found but could not show a consistent beneficial effect of a MBR program. The limited evidence hampers a clear conclusion if an educational component should be part of a MBR program.**
- **Cost-effectiveness: A 3-element MBR program is less costly and more effective compared to biomechanical exercises and a combination of mixed manual therapy and self-management for treating low back pain.**



## Other considerations regarding MBR programs

GRADE Factors	Comments
<b>Balance between desirable and undesirable effects</b>	<ul style="list-style-type: none"><li>• The NICE GDG discussed the necessity of a body of evidence to show specific intervention effects, that is, over and above any contextual or placebo effects. It was therefore agreed that if placebo or sham-controlled evidence is available, this should inform decision making in preference to contextual effects. However, if there was a lack of placebo or sham-controlled evidence, evidence against usual care will be given priority when decision making. The GDG noted that there was very little evidence for usual care comparisons and no studies were identified that could be classified as a placebo/sham comparison.</li><li>• <b>Clinical benefit:</b> There was mixed evidence with no clear benefits of MBR program compared to usual care or other interventions. In some instances the benefit was in favour of the comparator. Based on the mixed evidence or even the lack of effect, the NICE GDG were unable to recommend that an educational component should be part of an MBR program.</li><li>• <b>Adverse events:</b> No potential harms were identified.</li><li>• <b>In summary,</b> the NICE GDG considered this evidence alongside the evidence from the individual non-invasive intervention reviews involving cognitive behavioural approaches, and agreed that MBR programs should be recommended. It was not clear from the evidence reviewed if 3-element MBR offered benefits over the 2-element MBR. However the NICE GDG noted that the consistent components of the programmes with benefit were physical and psychological components. The recommendation was therefore made for MBR with a physical and psychological element and that the psychological component should incorporate a cognitive behavioural approach.</li></ul>
<b>Quality of evidence</b>	<ul style="list-style-type: none"><li>• The quality of the evidence ranged from very low to moderate due to high risk of bias (inadequate blinding, high drop-out rates).</li><li>• The high drop-out rate may underestimate the effect of an MBR program.</li><li>• The evidence consisted of single studies with small sample sizes per comparison.</li></ul>
<b>Values and preferences</b>	<ul style="list-style-type: none"><li>• Some NICE stakeholders questioned the criteria used to determine if a placebo intervention was critical for decision-making or not. NICE replied that some benefit was shown over usual care/waiting list comparator. Although there was no clinical difference between groups for pain and psychological distress outcomes, there was evidence of benefit of a 2-element MBR programme for the function and return to work outcomes compared to usual care/waiting list in people with or without sciatica. There was also clinical benefit there of a 2-element MBR for pain and function in people with low back pain without sciatica. The GDG acknowledged that the evidence for 3-element MBR versus usual care/waiting list was mixed. Overall the NICE GDG felt that combined physical and psychological program should nonetheless be recommended on the basis of the evidence showing benefit over waiting list, single and combined interventions, alongside evidence from single intervention chapters.</li><li>• For all interventions it was agreed important to note that the person delivering the therapy would have a large effect on the outcome of treatment. The NICE GDG discussed that in practice the psychological element of this type of intervention may be delivered by a psychologist or by another healthcare professional trained in these techniques. It was considered important that the individual was appropriately trained with the competency to deliver the intervention.</li><li>• The NICE GDG felt that a psychologically informed physiotherapy or rehabilitation programme would be particularly useful for people with chronic pain and psychosocial distress, i.e. people with low back pain or sciatica and significant psychosocial obstacles to recovery (for example, avoidance of normal activities based on inappropriate beliefs about their condition).</li></ul>



However, the GDG advised that main focus for their recommendation for combined physical and psychological treatments was for people with psychosocial distress resulting from chronic low back pain and sciatica, rather than people presenting with pain and additional psychological problems. The GDG therefore felt that people who have not responded to previous treatments, for example when they have failed to improve pain adequately, or have not helped enough to enable people to return to normal activity of daily life, including work, would also benefit from a psychologically informed rehabilitation programme, as part of a risk assessment-based, stepped care approach.

- Following comments were formulated by the **Belgian GDG** members:
  - MBR is probably the best of care we can offer, although improvements are possible and need to be further developed.
  - However a MBR programme should not be considered for every LBP patient but is only offered to subacute (to avoid chronicity) and chronic LBP patients, otherwise it would be too expensive to provide this kind of care services to every LBP patient. Also access (and reimbursement) to the MBR programs in hospitals is currently restricted for patients with at least 6 weeks of low back pain (K60 nomenclature). The GDG members referred also to the recommendations on risk stratification and stressed the importance to offer this program only to patients who have a high risk for poor outcome.
  - Also a preference for a weak recommendation was made as a result of the mixed evidence, the rather low quality of the evidence and the questionable cost-effectiveness.
  - There are psychological obstacles to recovery and a reference to yellow flags are needed. However the word “significant” should be removed because significant could be interpreted as a result of a measurement, but it is unclear how to measure the degree of psychological obstacles and the necessity of its measurement. The Belgian GDG members agreed on the importance to take into account the psychological factors in the chronicity of low back pain but preferred not to put emphasis on the severity of these psychological obstacles in this recommendation.
  - Could it be assumed that persistent LBP patients have received all appropriate treatments? In the discussion, it was mentioned that every caregiver should verify if the previous treatments were appropriated for his/her patient. After discussion, it is concluded not to add “appropriate” in the recommendation because it has been considered a good clinical practice to check up all previous treatments before starting a new one.
  - Different to a combined intervention in which different treatment are put next to each other, is the integration of different disciplines in an interdisciplinary way (combination of two or more disciplines into one activity) by crossing boundaries and thinking across them. NICE emphasised that MBR is defined as interventions involving a physical component and at least one other element from a biopsychosocial approach, offered as an integrated programme. In this respect they are different from simple combinations of interventions but the involvement of different disciplines is not clear..
  - “Persistent non-specific low back pain or sciatica” should be replaced by “persistent low back pain or radicular pain”.
  - The terms “preferable in a group context” should be removed to be in line with the Belgian recommendation on exercise therapy).
  - Given the mixed results concerning the effects of MBR, the Belgian GDG agreed with NICE that further research into tailoring multidisciplinary programs to specific patient subgroups/profiles is needed. In the draft version of the NICE guideline a **research recommendation** was proposed “What is the cost-effectiveness of providing long term support (>12 months) for people with chronic, non-specific low back pain with or without sciatica, in reducing health care utilization?” The Belgian GDG members discussed on the relevance of this research recommendation and proposed following research recommendation: “What is the ideal duration of a MBR program?”. This research could be carried out in Belgium.



**Costs (resource allocation)**

- Taking into account the overall body of clinical effectiveness evidence for MBR programmes the NICE GDG concluded there was mixed evidence of its effectiveness and cost-effectiveness, in particular in the economic study showing MBR to be cost effective the EQ5D and pain outcomes were not clinically important. However, the GDG considered MBR to be likely to be cost effective. If MBR is effective, upfront intervention costs may be offset by downstream cost savings due to reduced healthcare utilisation or may be justified due to the benefits to the patient.
- In Belgium, a MBR program is already implanted (with a NIHDI nomenclature code) but with restricted access and conditions. Offering such a MBR program to all LBP patients would be too expensive.

**Recommendation**

**Strength of Recommendation**

**Level of Evidence**

- Consider a multidisciplinary rehabilitation programme, which combines a physical and a psychological component, incorporating a cognitive behavioural approach, and which takes into account a person’s specific needs and capabilities, for people with persistent low back pain or radicular pain:
  - when they have psychosocial obstacles to recovery
  - or
  - when previous evidence-based management has not been effective

Weak (RCTs)

Moderate to very low

**Recommendation for research**

**Strength of Recommendation**

**Level of Evidence**

- What is the ideal duration of a MBR program?

NA

NA

**Change in comparison with the NICE recommendations**

- “sciatica” replaced by “radicular pain”
- “preferably in a group context”, “significant” deleted
- “(for example, avoiding normal activities based on inappropriate beliefs about their condition)” replaced by “see yellow flags”
- “treatment” replaced by “evidence-based management”
- Consider a multidisciplinary rehabilitation programme which combines combined—a physical and psychological component programme, incorporating a cognitive behavioural approach (preferably in a group context) and which takes into account a person’s specific needs and

capabilities) for people with persistent low back pain or sciatica-radicular pain:-

- when they have significant psychological obstacles to recovery (for example, avoiding normal activities based on inappropriate beliefs about their condition) (see Yellow flags)
- or
- when previous treatments evidence-based management has not been effective

The reasons underlying these changes are described in Appendix 7.12.





### 3.2.10 Return to work programs

Most people with low back pain continue to work whether or not with impaired productivity. Inability to work contributes to poverty through loss of income, and work and socioeconomic status are the main drivers of social gradients in health. Loss of employment can contribute to altered self-image, psychological distress and social exclusion.

There is strong epidemiological and clinical evidence that (long-term) sickness absence and disability depend more on individual and work-related psychosocial factors than on biomedical factors or the physical demands of work.

Modern clinical management for most musculoskeletal conditions emphasises advice and support to remain in work or to return as soon as possible in order to mediate improvements in pain and other aspects of health, quality of life and well-being. Organisational interventions, such as transitional work arrangements (temporary modified work or progressive resumption of work) and improving communication between health care and the workplace, can facilitate early and sustained return to work.

Importantly, physical activity and early return to work interventions do not seem to be associated with any increased risk of recurrences or further sickness absence.<sup>17</sup>

#### Definition of return to work programs

Return to work programs are structured interventions with the specific aim of facilitating return to gainful employment. They share much with programs designed to improve clinical outcomes, often being multidisciplinary and including components of exercise and education, as well as commonly addressing psychological factors. However, their primary focus is on vocational rehabilitation and engaging corresponding specialised skills.

The NICE evidence review can be found on p.738-761 in the full guideline on assessment and non-invasive treatments and the forest plots in Appendix K p.254-259 (<https://www.nice.org.uk/guidance/ng59/evidence>).

A summary sheet in Appendix 7.13 gathered the evidence findings, the NICE GDG considerations, the results of the online survey and the discussion with the Belgian GDG.

#### Scientific evidence regarding return to work programs

Eight RCTs (reported in a total of 12 papers) were included by NICE in the review. Four further papers were found reporting data from 2 studies. Most studies provided programmes to individuals; two provided therapy in both group and individual formats. One Cochrane review on return to work programmes was identified but it was not included as it included studies in people with back pain but not specifically low back pain. The studies included in this Cochrane review were individually assessed by NICE and included if they matched the review protocol. Three economic evaluations were identified that included a return to work intervention as a comparator and have been included in this review.

#### Scientific evidence regarding individual delivered return to work programs

##### LOW BACK PAIN WITHOUT SCIATICA:

(see Table 37 in Appendix 7.13)

- Only one study per comparison was found: the multidisciplinary programs, consisting of physical exercise programs with graded activity and based on cognitive behavioural approach, were compared to usual care or to a combined intervention of physiotherapy modalities (interferential therapy, TENS, traction, manual therapy, exercise therapy) whereas the monodisciplinary RTW program, which focused on counselling sessions by an occupational physician was compared to usual care. All studies found no clinical difference in pain, function and healthcare utilisation, only a small benefit was seen in QoL and in number of days of sickness leave in patients receiving counselling sessions (monodisciplinary RTW program) compared to usual care.



#### LOW BACK PAIN WITH SCIATICA

- No evidence was found.

#### MIXED POPULATION (WITH OR WITHOUT SCIATICA)

- Three RCTs were found on the comparison of an individual RTW program versus usual care however due to the different interventions within the RTW programs, the results could not be pooled. Overall could be stated that the majority of the evidence reported no clinically important differences of RTW programs compared to usual care or to a combined interventions of physiotherapy modalities.
- Evidence from 1 study (Anema 2007) suggested clinical harm of a multidisciplinary programme with a return to work focus for quality of life, when compared to usual care (high quality; n=186). There was no evidence of clinical difference in pain at short and long term (3 single studies; low to moderate quality; n=188, n=117, n=141) and psychological distress at > 4 months (1 study; moderate quality; n=141). Benefit in favour of usual care compared to return to work programmes was observed for function in the longer term follow up (1 study (Lambeek 2010), n=117, low quality) but not at short term (1 study (Anema 2007); moderate quality; n=188). Other evidence was mixed for days to return to work, absenteeism from unpaid work (very low quality; n=196), return to work (2 single studies, low to very low quality) and healthcare utilisation outcomes (2 single studies; very low to moderate quality; n=134, n=57).

#### **Scientific evidence regarding mixed group and individually return to work programmes**

#### LOW BACK PAIN WITHOUT SCIATICA

- In the single study, a multidisciplinary RTW program (graded activity, education and CBT) was compared to a similar RTW program, only CBT was been replaced by group education. In the only reported outcome of number of persons who returned to work, no difference was found between both types of RTW programs.

#### LOW BACK PAIN WITH SCIATICA

- No evidence was found.

#### MIXED POPULATION (WITH OR WITHOUT SCIATICA)

- No difference was found between the RTW program (physical treatment, CBT and workplace-based intervention) compared to usual care for the (only reported) outcome 'return to work at greater than 4 months'.

#### **Conclusions**

**The few studies found comparing RTW programs to usual care, combined intervention of physiotherapy modalities or other RTW programs, reported no clinical benefit of tailored RTW programs.**



## Other considerations regarding return to work programs

GRADE Factors	Comments
<b>Balance between clinical benefits and harms</b>	<ul style="list-style-type: none"> <li>• There was little evidence of benefit from certain programmes suggesting a need for treatment programs to be tailored to the individual.</li> <li>• The Belgian GDG agreed that facilitation of returning patients to work, where applicable, should be encouraged and this should be considered in consultation with people with low back pain to suggest this as one of the goals of treatment.</li> <li>• However, the included studies used tailored intervention programs that could be too intensive to be relevant to the Belgian healthcare context.</li> <li>• Some types of RTW programs, such as stay at work programs, were not included in the review, therefore no conclusion can be drawn on these kind of interventions.</li> <li>• Due to the lack of evidence for a specific intervention or programme that could be recommended to enable people to return to work and the existing services available, alongside the broader evidence highlighting benefits of enabling people to return to work or their usual activities, the GDG agreed that a consensus recommendation should be made for this to be encouraged as part of all treatment for people with low back pain and/or radicular pain and should even be considered a one of the top priorities in the management of low back pain (with or without radicular pain).</li> </ul>
<b>Quality of evidence</b>	<ul style="list-style-type: none"> <li>• The quality of the evidence, from 8 RCTs, ranged from high to very low, mainly downgraded for high risk of bias due to lack of appropriate blinding and high number of drop-outs.</li> </ul>
<b>Values and preferences</b>	<ul style="list-style-type: none"> <li>• The Belgian GDG emphasised that a lack of evidence does not negate the importance of returning to work.</li> <li>• Moreover, return to work is not the single aspect to be considered; the return to activities of daily living and social participation was considered as equally important.</li> </ul>
<b>Costs (resource allocation)</b>	<ul style="list-style-type: none"> <li>• It was difficult to come to a conclusion regarding the cost effectiveness of return to work interventions:             <ul style="list-style-type: none"> <li>○ In patients with low back pain without radicular pain, one cost-consequence analysis found that a RTW program was less costly and more effective than usual care.</li> <li>○ In the mixed population (low back pain with or without radicular pain) conflicting evidence was found: one cost-utility analysis found that RTW program was cost effective compared to usual care whereas another cost-utility analysis found that usual care was dominant (less costly and more effective) compared to RTW programmes.</li> <li>○ All economic studies were based on studies performed in the Netherlands but were assessed as partially applicable with potential serious limitations.</li> </ul> </li> <li>• The GDG decided not to recommend specific return to work programs separate from other clinical interventions as they may not be cost effective.</li> <li>• Encouraging people who are absent from work due to their acute low back pain and/or radicular pain to return to work or usual activities could be done as part of usual care and therefore unlikely to incur additional costs to the Belgian healthcare system, therefore this would be cost effective and should be recommended.</li> <li>• The Belgian GDG completed the above-mentioned statement with: In chronic pain patients who are long-term absent from work, the change of return-to-work becomes rather low and mostly needs facilitating strategies like tailored treatment depending on the needs of the patient (work-related-CBT), guidance and coaching to and in the workplace (need for aid of external partners) and finally consensus between all involved parties (patient, treatment team, employer, occupational physician etc). This may lead to additional costs.</li> </ul>



Recommendations	Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"> <li>Promote and facilitate return to work or normal activities of daily living as soon as possible for people with low back pain with or without radicular pain.</li> </ul>	Experts opinion	High to very low

### Change in comparison with the NICE recommendations

- No changes are made  
The reasons underlying these changes are described in Appendix 7.13.

#### 3.2.11 Back schools

Within the list of topics not covered by the NICE guideline, back schools were mentioned by the Belgian GDG.

In the most recent Cochrane review on the effectiveness of back schools for acute and subacute non-specific low back pain, a back school has been defined as a therapeutic program which included both education and exercise, and is given to groups of participants and supervised by a healthcare provider. It was introduced in Sweden in 1969 as an intervention protocol consisting of an educational program (e.g. theoretical lessons given by the care provider on the clinical relevant anatomy and the biomechanics) and skills acquisition program, including physical exercises. The content and length of back schools seem now to vary widely.<sup>18</sup> In this review only 4 studies were included that were already assessed in a previous version of the Cochrane review from 1999. Pooling of the findings was not possible due to the dissimilarities between the studies and half of the studies were at high risk of bias. The single study comparing back school to placebo found no differences in short term pain, only a shorter duration of sick-leave was noticed in the back school-group. Four studies comparing back school to another intervention (physical therapy, myofascial therapy, joint manipulation, advice) found no differences in pain, function, work status and adverse events. Only the combination of back school to a back care program was more effective for function than the back school alone. The authors concluded that the studies were insufficient to give a clear statement on the

effectiveness of back school and its potential role in the management of low back pain.

This kind of therapeutic intervention has been explicitly excluded from the update of the NICE guideline as the NICE GDG considered that “it is outdated and no longer used”. Whilst in Belgian practice, this concept is still applied in the management of low back pain.

However, when looking further into detail what is behind this concept of back school in the Belgian practice, it became clear that the original modalities of the back school has changed into a more multidisciplinary approach. Many of the rehabilitation programs in Belgian hospitals are still called “back schools” but covers far more aspects of the management of low back pain, including physical reconditioning and more psychosocial aspects than the original definition of back school which is rather focused on patient education and some ergonomic advice and exercises. Currently it is thus more a semantic discussion than a real difference in clinical practice between the UK and Belgium. A proposition could be to avoid the use of the term back school and give it a more appropriate name covering the different aspects of the treatment program, e.g. back rehabilitation program.



### 3.3 Medications

The NICE guideline 2016 considered only the pharmacological interventions for low back pain and referred to another guideline for sciatica (CG 173 Neuropathic pain in adults: pharmacological management in non-specialist settings, last updated in December 2014). However, this guideline was not assessed as acceptable by the Belgian GDG. The arguments for rejecting this reference were:

- The scope that covered all types of neuropathic pain and encompassed a very low number of studies on lumbar radicular pain (only 2 small studies on chronic lumbar radiculopathy). The recommendations were mainly based on evidence in patients with diabetic neuropathy or post-herpetic neuralgia, which are different conditions compared to radicular pain. Moreover, not every radicular pain has a neuropathic pain component.
- The outdated data: this guideline was published in 2013 (search date July 2012). In the latest update of December 2014, just a footnote has been added to the first treatment recommendation to clarify the use of generic pregabalin and off-label status. An update of literature would be needed before including these recommendations in the Belgian guideline.
- The fact that the guideline focused on non-specialist settings, although this distinction is difficult to retrieve in the studies. The difference between non-specialist and specialist settings is considered as less important for the Belgian guideline.
- The formulation of the recommendations: in contrast to other guidelines on the pharmacological management of neuropathic pain, the stepwise approach is less clear in this guideline while it is very useful according to the Belgian GDG.

Therefore, the Belgian GDG decided to review the formulation of the NICE recommendations on the pharmacological management of low back pain and verify whether they can be applied to radicular pain also. A lot of recommendations were indeed based on a literature review encompassing patients with LBP with or without sciatica. As showed below, the Belgian GDG members indicated when a specific recommendation for radicular pain was needed (chronic radicular pain or with a neuropathic pain component).

The management of radicular pain by injections of medications is developed in another chapter of this guideline.

The NICE evidence review can be found on p.605-670 in the full guideline on assessment and non-invasive treatments and the forest plots in Appendix K p.210-232 (<https://www.nice.org.uk/guidance/ng59/evidence>).

A summary sheet in Appendix 7.14 gathered the evidence findings, the NICE GDG considerations, the results of the online survey and the discussion with the Belgian GDG.

#### 3.3.1 Non-steroidal anti-inflammatory drugs (NSAIDs)

Non-steroidal anti-inflammatory drugs (NSAIDs) block the synthesis of prostaglandins that are induced during inflammatory processes by inhibiting the activity of cyclooxygenase-2 (COX-2). Classic (i.e. not COX-selective) NSAIDs inhibit in a quite similar way both isoenzymes COX-2 and COX-1 which is involved in the synthesis of prostaglandins with a role in the protection of the mucosa gastric. So-called COX-2 selective NSAIDs preferentially inhibit COX-2. Although it is noted there are different side effect profiles, NSAIDs and selective COX-2 inhibitors were regarded by NICE as a single drug class of 'NSAIDs'.



### Scientific evidence regarding NSAIDs in low back pain and radicular pain

Fifty five studies were included by NICE in the review focusing on all kind of medications as single intervention. Among them, seven RCTs concerns the comparison NSAIDs versus placebo. One study looking at a combination of drugs versus NSAIDs and two studies looking at combinations of non-invasive interventions (with pharmacological therapy including NSAIDs as the adjunct) were also included in this review. Randomised controlled trial evidence for pharmacological treatments compared to other non-invasive interventions has been reported in other chapters, e.g. NSAIDs versus acupuncture and NSAIDs versus manipulation/mobilisation. Finally, one economic evaluation (cost-utility analysis model) compared various pharmacological treatments, among which there were 2 NSAIDs.

#### NSAIDs as single intervention versus placebo

##### LBP WITH OR WITHOUT SCIATICA

- Evidence from 2 studies suggested a **small clinical benefit at short term of etoricoxib** compared to placebo in terms of pain severity and function at both analysed doses (60 and 90mg during 12 weeks; MID for pain 60mg -1.13 [95%CI -1.57, -0.70]; MID for pain 90 mg -1.02 [95%CI -1.45, -0.59]; Difference in least-squares for function 60 mg -2.64 [95%CI -3.61, -1.67] ; Difference in least-squares for function 90 mg -2.23 [95%CI -3.19, -1.26]; low to moderate quality; n = 427 and 422). There was also a clinical benefit for quality of life on the physical subscale of the SF- 12 at both doses but this was not seen for the mental subscale (moderate quality; n = 427 and 422). The included population in both studies consisted on patients aged 18-75 years, with low back pain for at least 3 months, used an NSAID or paracetamol for treatment of their low back pain regularly (at least past 30 days).

##### LBP WITHOUT SCIATICA

- Evidence from a single study found a **potential benefit of ibuprofen** (max 6x200 mg/day 7 days) **or diclofenac** (max 6x12,5 mg/day 7 days) compared with placebo for pain intensity at short-term (7 days) (MID Ibuprofen -1.13 [95%CI -1.85, -0.41], MID diclofenac -1.09 [95%CI -1.83, -0.35] low quality; n = 195 and 200). This study included patients

aged 18 to 60 years with untreated acute low back pain without sciatica and onset within 2 days.

- Another single study focused on tenoxicam 20 mg (one intramuscular injection followed by 20 mg oral, during 15 days) in patients with acute LBP (<2 weeks) and showed **no difference** on pain intensity at 15 days compared to placebo (low quality; n = 68). However, this study was old (1994) and encompassed s concurrent care, 7 days of bed rest followed by 7 days light activity at home.
- Evidence from 4 studies showed **no clinical difference** of etoricoxib, piroxicam, diclofenac or indomethacin in the rate of **adverse events** (low quality; n = 1344).

#### Combination of drugs versus NSAIDs

##### LBP WITHOUT SCIATICA

- One study compared opioid (codeine) plus paracetamol versus NSAID (ketorolac) in acute low back pain and showed **no difference** in pain outcomes at less than 4 months, but **adverse events** were more common with the combination codeine + paracetamol (1 study, high quality, n=121).

#### Combinations of non-invasive interventions – pharmacological adjunct

##### LBP WITH SCIATICA

- There was evidence from one RCT showing that when NSAIDs (not specified) were combined with massage, there was a **clinical benefit** for pain (MID VAS -1.16 [95%CI -2.31, -0.01] in the short-term, compared to massage alone (very low quality, n=54). However, no difference was observed for function measured in RMDQ or ODI.
- Another RCT compared a combination of NSAID (valdecoxib 20 mg) plus exercise (biomechanical) versus acupuncture in chronic LBP and showed **no difference** in pain (very low quality, n=60). There was no evidence available for any of the other outcomes.



**Economic evidence**

- One economic evaluation (Wielage et al., 2013) compared various pharmacological treatments (head to head studies): duloxetine (SNRI), two NSAIDs (celecoxib and naproxen), pregabalin and four opioid analgesics. This cost-utility analysis model found that duloxetine was dominant (less costly and more effective) compared to pregabalin, celecoxib, oxycodone/paracetamol, oxycodone, tapentadol and tramadol for treating low back pain (with or without sciatica) post paracetamol. It also found that duloxetine was not cost effective compared to naproxen treatment (ICER: £41,521 per QALY gained). This analysis was assessed as partially applicable with potential serious limitations.
- In addition, one cost-effectiveness analysis comparing paracetamol to ibuprofen found that paracetamol was dominant (less costly and more effective) compared to ibuprofen for acute low back pain (without sciatica). This analysis was assessed as partially applicable with potential serious limitations

**Conclusions**

**The included evidence comparing NSAIDs versus placebo concerned piroxicam, etoricoxib, diclofenac, ibuprofen, indomethacin, tenoxicam and valdecoxib. A short-term slight clinical benefit in terms of pain severity and function was found by some studies and no difference in adverse events was demonstrated compared to placebo. One study comparing codeine + paracetamol versus ketorolac in acute low back pain showed no difference in pain outcomes at less than 4 months, but more adverse events with the combination codeine + paracetamol. Further evidence demonstrated benefit of pain when NSAIDs were combined with massage but this was from a single small study. Economic evidence suggested that naproxen is more cost effective than duloxetine while celecoxib was less cost effective than duloxetine and ibuprofen less cost-effective than paracetamol.**

**Other considerations regarding NSAIDs in low back pain and radicular pain**

GRADE Factors	Comments
<b>Balance between clinical benefits and harms</b>	<ul style="list-style-type: none"> <li>• The Belgian GDG acknowledged that NICE literature review found evidence of benefit of NSAIDS compared to placebo at short-term regarding pain severity and function. This applied to both acute and chronic LBP with or without radicular pain.</li> <li>• However, the Belgian GDG stressed that:               <ul style="list-style-type: none"> <li>○ Two recent systematic reviews published in 2016 (one OPTIMA review by Wong et al.<sup>19</sup> and one Cochrane review by Enthoven et al.<sup>20</sup>) tempered the positive results of NSAIDs. The efficacy of NSAIDs appeared to be unclear in acute LBP and was only suggested by low quality evidence for chronic LBP with small effect (see Table 38 in Appendix 7.14).</li> <li>○ The doses of celecoxib used in the included studies (400 mg/day) was a maximal dose according to the CBIP/BCFI.</li> <li>○ A strong recommendation as initially proposed by NICE could wrongly suggest that a medication is always indicated in LBP such as a standard.</li> </ul> </li> <li>• The evidence review did not demonstrate any increase in adverse events in those receiving NSAIDs but the Belgian GDG agreed with NICE that the randomised controlled trials reviewed were not likely to pick up long term complications, toxicity due to co-morbidities or drug interactions. All physicians should be aware of the considerable toxicity of NSAIDs. Moreover,</li> </ul>



GRADE Factors	Comments
	<p>the side-effect profile of NSAIDs varied between drugs (some NSAIDs have mostly a gastro-intestinal toxicity, other a cardio-renal...), and therefore it should be considered when determining which drug was most appropriate for the individual according to his/her risk factors.</p> <ul style="list-style-type: none"><li>• No analysis by type of NSAIDs was performed which precluded to show a superiority of one to other in term of efficacy. The selection of one NSAID rather than another should be influenced by the patient profile of risk.</li><li>• The Belgian GDG agreed that physicians have to monitor risk factors because NSAIDs are frequently used, even by patients with high blood pressure or renal failure. For example, in patient with cardio-renal risk, the development of oedema should be monitored because it can occur (in link or not with the NSAIDs and effect on the renal function).</li><li>• The Belgian GDG emphasised that gastro protective treatment is not always needed. It is depending of the kind of NSAIDS (not for COXIB), the treatment duration (not in short term), and the patient characteristics.</li><li>• The Belgian GDG agreed with the need to be cautious but was not convinced by the terms “the lowest effective dose for the shortest possible period of time.” It was considered confusing: Do physicians have to start with a lower dose than recommended or with a standard dose that will be decreased as soon as possible? In Belgium, it appears that physicians usually start with a recommended dose and decrease the dose in case of improvement some days later (decreasing adaptation) because medication is only one part of the management of LBP. In some cases however, due to the patient's risk factors, the clinicians start with a lower dose than recommended and increase it if not sufficiently effective but well tolerated (increasing adaptation). In other situations, it is also possible to prescribe a medication as needed rather than a fixed dose.</li><li>• The GDG mentioned that valdecoxib was withdrawn from the Belgian market.</li><li>• The review of Rasmussen-Barr<sup>21</sup> was published online the 15th October 2016 (after the last discussion on medication with the Belgian GDG). However, this review only included two additional trials, Herrmann 2009 and Kanayama 2005, to the original review by Roelofs 2008 and Roelofs 2008 was included in the SR of Wong 2016 discussed by the Belgian GDG. The review of Rasmussen-Barr focused on patients with sciatica and concluded that the efficacy of NSAIDs for pain reduction was not significant but that NSAIDs showed a better global improvement compared to placebo. Therefore, this new evidence was not considered sufficient to imply a change in the Belgian recommendation.</li><li>• The Belgian GDG acknowledged that NICE has not found evidence on the potential role of topical NSAIDs in the management of low back pain although this kind of administration was included within the protocol and search for the review. It is proposed to quote the topical NSAIDs in a list of topics without clear recommendation due to the lack of evidence.</li></ul>
<b>Quality of evidence</b>	<ul style="list-style-type: none"><li>• The quality of evidence ranged mainly from a GRADE rating of moderate to low. According to NICE, this was due to the high number of drop outs in some of the included studies, resulting in a high risk of bias rating, as well as the imprecise nature of the results extracted and analysed in this review. Evidence for opioid plus paracetamol versus NSAIDs in a low back pain population had a high quality GRADE rating for the pain severity and adverse events outcome. The high quality GRADE rating for these outcomes was due to the low risk of bias in the study outcomes and the precision of the results.</li><li>• It was noted no heterogeneity when the data was pooled.</li></ul>





GRADE Factors	Comments
<b>Patients values and preferences</b>	<ul style="list-style-type: none"> <li>According to the Belgian GDG, it appeared that in practice physicians prefer to prescribe the NSAID they well know or the NSAID that is the patient's preference (already used and tolerated by him or her). The prescription is done for a limited duration (about 1 week).</li> </ul>
<b>Costs (resource allocation)</b>	<ul style="list-style-type: none"> <li>Two economic analysis were quoted by NICE. Both were assessed partially applicable with potentially serious limitations. Results were conflicting: according to one, naproxen (NSAID) appeared cost effective compared to duloxetine (SNRI), celecoxib (NSAID), pregabalin (gabapentinoid anticonvulsant) and four opioid analgesics in the management of low back pain post a first line treatment with paracetamol. According to the other, paracetamol was dominant (less costly and more effective) compared to ibuprofen. The NICE GDG considered both studies and agreed that, when considering the limitations of these analyses, the unit cost of NSAIDs and the clinical evidence for etoricoxib (NSAID), NSAIDs were likely to be cost-effective for the treatment of non-specific low back pain.</li> </ul>

Recommendations	Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"> <li>If a medication is required for managing low back pain with or without radicular pain (e.g. due to severity of the pain and patients' preferences), consider oral NSAIDs taking into account potential differences between NSAIDs in gastrointestinal, liver and cardio-renal toxicity and the person's risk factors, including age.</li> </ul>	Weak (RCTs)	Moderate to very low
<ul style="list-style-type: none"> <li>When prescribing oral NSAIDs for low back pain, think about appropriate clinical assessment, ongoing monitoring of the evolution of risk factors, and the use of gastro protective treatment.*</li> </ul>	Experts opinion	NA
<ul style="list-style-type: none"> <li>When prescribing oral NSAIDs for low back pain, select the lowest effective dose for the shortest possible period of time.**</li> </ul>	Experts opinion	NA

\* The Belgian GDG emphasises that gastro protective treatment is not always needed. It depends on the kind of NSAID (usually not for coxib), the treatment duration (usually not in short term), and the patient' characteristics.

\*\*The lowest effective dose means the lowest dose that has an effect according to each individual patient. The Belgian GDG stresses the risk of under- or over-dose and suggests to start in most situations with a recommended dose, to assess the result and in case of improvement to test a decrease of this dose.



### Change in comparison with the NICE recommendations

Minor changes have been proposed by the Belgian GDG regarding the 3 clinical recommendations proposed in the NICE 2016 guidelines.

- If a medication is required for managing low back pain with or without radicular pain (e.g. due to severity of the pain and patients' preferences), consider oral non-steroidal anti-inflammatory drugs (NSAIDs), taking into account potential differences between NSAIDs in gastrointestinal, liver and cardio-renal toxicity, and the person's risk factors, including age.
- When prescribing oral NSAIDs for low back pain, think about appropriate clinical assessment, ongoing monitoring of risk factors, and the use of gastroprotective treatment.
- When prescribing oral NSAIDs for low back pain, select ~~Prescribe oral NSAIDs for low back pain at~~ the lowest effective dose for the shortest possible period of time.

The reasons underlying these changes are described in more details in Appendix 7.14.2.

### 3.3.2 Paracetamol

Paracetamol has analgesic and anti-inflammatory effects. This medication combines good tolerance and favourable safety profile. The CBIP/BCFI underlined that the advantage of paracetamol as a modified release preparation is not clear.

### Scientific evidence regarding paracetamol in low back pain and radicular pain

Fifty five studies were included by NICE in the review focusing on all kind of medication as single intervention. Among them, there were only two studies on paracetamol versus placebo (with one not analysed because pain outcomes only presented graphically) and one study comparing amitriptyline and paracetamol. Several studies looking at a combination of paracetamol and opioid versus placebo or versus another drugs were also included in this review. Moreover, due to insufficient randomised trial evidence, a further search of cohort studies on paracetamol was carried out by NICE. This

search did not identify additional relevant studies. Two economic analysis was found for paracetamol, both assessed as partially applicable with potential serious limitations.

### Paracetamol as single intervention versus placebo

#### LOW BACK PAIN WITH OR WITHOUT SCIATICA

- Evidence from 1 study concerned new episode of acute low back pain with or without leg pain (radicular pain 20%), at least moderate-intensity pain. No clinical benefit with paracetamol (two times 665 mg modified-release paracetamol tablets 3 times a day) was found for any of the reported outcomes at 4 weeks – pain (low quality; n = 1011), function (low quality; n = 1007), quality of life (low quality; n = 495) or adverse events (very low quality; n = 1065).
- No data were available for psychological distress, nor for the comparison with usual care.

#### Head-to-head comparison

- A comparison between amitriptyline 150mg daily and paracetamol (2000mg daily) found a clinical benefit in favour of amitriptyline for improving pain intensity at 5 weeks (MID -1.83 [95%CI -3.66, 0.00], 1 study, moderate quality; n = 39), but no clinical difference for psychological distress (1 study, low and moderate quality; n = 39). The population of this second study encompassed acute and chronic LBP (max 6 months) with or without sciatica.

### Combinations of drugs versus placebo

#### LBP WITHOUT SCIATICA

- Evidence was inconsistent: some results suggested a **clinical benefit (CIB) at short term for pain in favour of the combination opioids (tramadol) and paracetamol** vs placebo (VAS; MID -1.55 [95%CI -2.47, -0.63]; 1 study; low and moderate quality; n = 327) while other results showed a **CIB at short term for placebo** regarding pain (meaningful pain relief: HR 1.57 [95%CI 1.05, 2.35; 1 study; low quality, n = 277). Concerning the other outcomes, a **CIB in favour of placebo** was observed for the SF-36 domains of bodily pain, general health,



physical function, and physical role (low and moderate quality; n = 327) and no clinical difference for pain on the McGill score, function and other SF-36 items.

- There was a clinical harm with the combination for **increased adverse events** (2 studies; moderate quality; n = 613).

#### LOW BACK PAIN WITH OR WITHOUT SCIATICA

- A **CIB** was suggested at short term with a **combination tramadol plus paracetamol** for **responder criteria** (pain reduction >30%; RR 1.4 [95%CI 1.03, 1.91]; 1 study; moderate quality; n=175) but a CIB in favour of **placebo for some measurement of quality of life** (general health, physical function, physical role, social function and vitality; 1 study; low and moderate quality; n = 170) and no difference for other measurements of quality of life and for function.
- There was a clinical harm with the combination for **increased adverse events** (2 studies; high quality; n = 295).

#### Combinations of drugs versus other drugs

##### LOW BACK PAIN WITHOUT SCIATICA

- One study compared opioid (codeine) plus paracetamol versus NSAID (ketorolac) in acute low back pain and showed **no difference in pain** outcomes at less than 4 months, but **adverse events** were more common with the combination codeine + paracetamol (1 study; high quality; n=121).

##### LOW BACK PAIN WITH SCIATICA

- One study compared a combination of opioids (tramadol) plus paracetamol versus an anticonvulsant (pregabalin 75 mg). This study only reported **adverse events** and showed **no clinical difference** between the groups (moderate quality; n = 60).

#### Economic evidence

- One economic evaluation (Wielage 2013) comparing various pharmacological treatments found that duloxetine was dominant (less costly and more effective) compared to oxycodone/paracetamol (and other drugs) for treating low back pain (with or without sciatica) post first line treatment with paracetamol.
- Another cost-effectiveness analysis found that paracetamol was dominant (less costly and more effective) compared to ibuprofen for acute low back pain without sciatica.

#### Conclusions

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**No clinical benefit was found for paracetamol compared to placebo at short term for any outcomes in acute LBP. There was some evidence suggesting a clinically important benefit of a combination opioid plus paracetamol for the critical outcome pain severity when compared to placebo. However, other results were not consistent with this findings and there was a clinical harm with the combination for increased adverse events. Evidence from a comparison between codeine + paracetamol versus ketorolac showed no difference in pain outcomes, but more adverse events in the combination group. By contrast, evidence from a comparison between tramadol + paracetamol versus pregabalin found no difference in adverse events. Finally, two economic evidence reported that paracetamol appeared more cost-effective compared to ibuprofen but less cost-effective compared to duloxetine.**

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**Other considerations regarding paracetamol in low back pain and radicular pain**

GRADE Factors	Comments
Balance between clinical benefits and harms	<ul style="list-style-type: none"> <li>The Belgian GDG acknowledged there was no clinical benefit observed at short term in any of the reported outcomes with paracetamol compared to placebo.</li> <li>Two additional systematic reviews (The Cochrane review by Saragiotto et al. in 2016<sup>22</sup> and the meta-analysis by Machado et al published in the BMJ in 2015<sup>23</sup>) were mentioned by the GDG (see Table 39 in Appendix 7.14.3). They confirmed that no effect was found with paracetamol compared to placebo in acute low back pain and that it was uncertain if paracetamol has any effect on chronic LBP.</li> <li>However, the Belgian GDG considered that the NICE recommendation against the use of paracetamol alone sounds too hard and should be softened (by adding the word “routinely”). The arguments for this change were:               <ul style="list-style-type: none"> <li>The lack of efficacy of paracetamol vs placebo in LBP is demonstrated by a single study (Williams 2014) in patients with acute low back pain with or without leg pain (radicular pain 20%), at least moderate-intensity pain, since a mean duration of 10 days. This is not generalizable for all patients with LBP.</li> <li>Paracetamol may be the single option if NSAIDs or opioids are contra-indicated or poorly tolerated.</li> <li>The Belgian clinicians used to start analgesic treatment by paracetamol, as recommended by the CBIP/BCFI and there is a risk of high resistance in front of a strong recommendation.</li> </ul> </li> <li>The Belgian GDG highlighted that there was some evidence suggesting a clinically important benefit of a combination opioid plus paracetamol for the critical outcome pain severity when compared to placebo but this was not confirmed by other results. Moreover the risk of adverse events with this combination should be lead to be cautious (see chapter 3.3.3. Opioids).</li> <li>Finally, the Belgian GDG agreed that an important message for the clinicians is that usually paracetamol should not be offered alone or more precisely as a single medication.</li> </ul>
Quality of evidence	<ul style="list-style-type: none"> <li>The quality of evidence ranged mainly from a GRADE rating of moderate to very low. According to NICE, this was due to the high number of drop outs in some of the included studies, resulting in a high risk of bias rating, as well as the imprecise nature of the results extracted and analysed in this review. Evidence for opioid plus paracetamol versus placebo in a low back pain with or without sciatica population had a high quality GRADE rating for the adverse events outcome and opioid plus paracetamol versus NSAIDs in a low back pain only population had a high quality GRADE rating for the pain severity and adverse events outcome. The high quality GRADE rating for these outcomes was due to the low risk of bias in the study outcomes and the precision of the results.</li> </ul>
Patients values and preferences	<ul style="list-style-type: none"> <li>Belgian patients used to manage pain with paracetamol and some of them are satisfied with this. This should be taken into account during the shared decision-making.</li> </ul>
Costs (resource allocation)	<ul style="list-style-type: none"> <li>The NICE economic evaluation did not allow to conclude clearly regarding the cost-efficacy of paracetamol.</li> </ul>

Recommendations	Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"> <li>Do not routinely offer paracetamol (as single medication) for managing low back pain with or without radicular pain.</li> </ul>	Weak (RCTs)	High to very low



### Change in comparison with the NICE recommendations

Changes have been proposed by the Belgian GDG regarding the 2 clinical recommendations proposed in the NICE 2016 guidelines.

Do not routinely offer paracetamol (as single medication) alone for managing low back pain with and without radicular pain.

The reasons underlying these changes are described in Appendix 7.14.3.

#### 3.3.3 Opioids

Opioids include natural and synthetic alkaloid derivatives of poppy plant resin. The principle mode of action on pain relief is by binding to opioid receptors in the central and peripheral nervous system. Opioids vary in potency and side-effects, based on the relative activation of different receptors and pathways. The effect of opioids on non-cancer pain is limited by tolerance (decreasing effectiveness of a given dose with repeated use), side-effects (typically constipation, nausea), dependence and addiction.

#### Scientific evidence regarding opioids in low back pain and radicular pain

Fifty five studies were included by NICE in the review focusing on all kind of medication as single intervention. Among them, 13 studies concerned opioids as single intervention. Several studies looking at a combination of drugs versus placebo and one study looking at combinations of drugs versus other drugs were also included in this review. Finally, one economic evaluation (cost-utility analysis model) compared various pharmacological treatments, among which there were 4 opioids.

### Opioids as single intervention versus placebo

#### LOW BACK PAIN WITHOUT SCIATICA

- Evidence from 1 study (low quality, n = 389) demonstrated **conflicting results**: a clinical benefit favouring opioids (oxycodone xtampza ER  $\geq 40$  to  $\leq 160$  mg oxycodone HCL equivalents daily) for physical component (MID 3.90 [95%CI 1.95, 5.85] but favouring placebo for mental quality of life score (MID -3.22 [95%CI -5.37, -1.07] at 12 weeks. Results were **beneficial with opioids for responder criteria for improvement in pain severity** (>30% improvement in pain intensity on NRS scale MID 1.48 [95%CI 1.16, 1.90]; (>50% improvement in pain intensity on NRS scale MID 1.57 [95%CI 1.16, 2.12]. The population consisted in male and non-pregnant females, aged 18 to 75, with a clinical diagnosis of moderate-to-severe CLBP (ie. pain intensity score of  $\geq 5$  to  $\leq 9$  on an 11-point pain intensity-numerical rating scale [PI-NRS]) for a minimum of 6 months before the screening visit.
- Consistent evidence across a large number of studies suggested that there was **no clinically important benefit in terms of pain** (12 studies; moderate quality; n = 3268) **or function** (7 studies; moderate quality; n = 1510) for opioids compared with placebo but a clinically important harm in terms of **increased adverse events with opioids** (7 studies; very low quality; n = 1804). The included drugs were mainly tramadol (200-400 mg/day), oxycodone (20-80mg) and morphine 15 mg. All patients had chronic low back pain (at least 3 months duration)
- No data were available for psychological distress, nor for the comparison with usual care.

#### LOW BACK PAIN WITH SCIATICA

- A single study reported only results for **adverse events** and no clinical differences were found between oxycodone/codeine (10 or 20mg every 12h) and placebo.



## Combinations of drugs versus placebo

### LBP WITHOUT SCIATICA

- Evidence was inconsistent: some results suggested a **clinical benefit (CIB) at short term for pain in favour of the combination opioids (tramadol) and paracetamol** vs placebo in acute & chronic LBP (VAS; MID -1.55 [95%CI -2.47, -0.63]; 1 study; low and moderate quality; n = 327 while other results showed a **CIB at short term for placebo** regarding pain in acute LBP (meaningful pain relief: HR 1.57 [95%CI 1.05, 2.35; 1 study; low quality, n = 277). Concerning the other outcomes, a **CIB in favour of placebo** was observed for the SF-36 domains of bodily pain, general health, physical function, and physical role (low and moderate quality; n = 327) and no clinical difference for pain on the McGill score, function and other SF-36 items.
- There was a clinical harm with the combination for **increased adverse events** (2 studies; moderate quality; n = 613).

### LOW BACK PAIN WITH OR WITHOUT SCIATICA

- A **CIB** was suggested at short term with a **combination tramadol plus paracetamol** for **responder criteria** (pain reduction >30%; RR 1.4 [95%CI 1.03, 1.91]; 1 study; moderate quality; n=175) but a **CIB** in favour of **placebo for some measurement of quality of life** (general health, physical function, physical role, social function and vitality; 1 study; low and moderate quality; n = 170) and no difference for other measurements of quality of life and for function. Both studies concerned patients with chronic LBP.
- There was a clinical harm with the combination for **increased adverse events** (2 studies; high quality; n = 295).

## Combinations of drugs versus other drugs

### LOW BACK PAIN WITHOUT SCIATICA

- One study compared opioid (codeine) plus paracetamol versus NSAID (ketorolac) in acute low back pain and showed **no difference in pain** outcomes at less than 4 months, but **adverse events** were more common with the combination tramadol + paracetamol (1 study; high quality; n=121).

### LOW BACK PAIN WITH SCIATICA

- One study compared a combination of opioids (tramadol) plus paracetamol versus an anticonvulsant (pregabalin 75 mg). This study only reported **adverse events** and showed **no clinical difference** between the groups (moderate quality; n = 60).

### Economic evidence

- The economic evidence for opioids (Wielage et al 2013) comparing various pharmacological treatments found that duloxetine was dominant (less costly and more effective) compared to oxycodone/paracetamol, oxycodone, tapentadol and tramadol (and other drugs) for treating low back pain (with or without sciatica) post paracetamol. This study was based on clinical evidence of people with chronic low back pain. No economic evidence for opioid use for the management of acute low back pain was identified.

### Conclusions

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**Compared to placebo, there is low quality evidence of benefit of opioids in some indicators of quality of life and in responder criteria for pain but there is also consistent evidence across a large number of studies suggesting no clinically important benefit in terms of pain or function. All these evidence was provided by studies on population with chronic LBP. The combination tramadol + paracetamol showed also inconsistent results when compared to placebo: clinically important benefit for the critical outcome pain severity in some analysis but not all, and negative findings for quality of life. The very few trials that compared opioids to non-steroidal anti-inflammatory drugs (NSAIDs) or antidepressants did not show any differences regarding pain and function. Moreover a clinically important harm in terms of increased adverse events was observed with opioids. Economic evidence showed that duloxetine was dominant in chronic LBP compared to the 3 opioids included in the analysis.**

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## Other considerations regarding opioids in low back pain and radicular pain

GRADE Factors	Comments
<b>Balance between clinical benefits and harms</b>	<ul style="list-style-type: none"> <li>• The lack of evidence for the benefit of opioids versus placebo in acute low back pain or for the management of acute episodes of low back pain was stressed by the Belgian GDG. The GDG highlighted also that in chronic LBP, although some evidence showed a clinical benefit at short term with opioids compared to placebo, these positive findings were not observed for all important outcomes. A similar conclusion could be drawn for the combination opioid plus paracetamol.</li> <li>• Besides the NICE analysis, two additional reviews were quoted by the Belgian GDG (a Cochrane review by Chaparro et al. in 2013<sup>24</sup> and a review by Abdel Shaheed et al. published in the JAMA Intern Med in 2016<sup>25</sup>) (see Table 40 in Appendix 7.14.4). These reviews found no more evidence for the use of opioids in acute low back pain and showed a potential effect of opioid analgesics in terms of short and/or intermediate pain relief in people with chronic low back pain, although the effect is small and not clinically important even at higher doses. None systematic review distinguish weak and strong opioids effects within the results.</li> <li>• The Belgian GDG acknowledged that an increased risk of adverse events is observed in patients receiving opioids, including risk of addiction. This outweighed the potential benefits of these medications and the Belgian GDG agreed that opioids should not be routinely used in the management of low back pain. Nevertheless, the Belgian GDG discussed the utility of opioids in few cases and the strength of a recommendation against their use.</li> <li>• In acute low back pain or for the management of acute episodes of low back pain, although no evidence was found, the Belgian GDG agreed with NICE to formulate a consensus based recommendation. According to the Belgian GDG, it is almost not possible to avoid opioids (with or without paracetamol) in the management of some patients with acute pain, in particular where an NSAID could not be used, or had been ineffective or poorly tolerated. Some GDG members highlighted that closing the door for all kinds of opioids would jeopardize the use of the weak opioids although the balance between side effects and benefits is not so bad with this kind of opioids (compared to the strong ones). Therefore the proposed recommendation was added with several limitations :             <ul style="list-style-type: none"> <li>○ with weak opioids only</li> <li>○ for the shortest period possible,</li> <li>○ for those who cannot tolerate or for whom NSAIDs are unsuitable.</li> </ul> </li> <li>• In chronic low back pain, the GDG agreed with a recommendation against the use of opioids but disagreed with a strong recommendation. The GDG was aware of the high risk of adverse events with opioids but stressed the potential benefit observed in the review and also the need to provide an alternative treatment in patient not improved by other intervention.</li> </ul>
<b>Quality of evidence</b>	<ul style="list-style-type: none"> <li>• The quality of evidence ranged mainly from a GRADE rating of moderate to very low. According to NICE, this was due to the high number of drop outs in some of the included studies, resulting in a high risk of bias rating, as well as the imprecise nature of the results extracted and analysed in this review. Evidence for opioid plus paracetamol versus placebo in a low back pain with or without sciatica population had a high quality GRADE rating for the adverse events outcome and opioid plus paracetamol versus NSAIDs in a low back pain only population had a high quality GRADE rating for the pain severity and adverse events outcome. The high quality GRADE rating for these outcomes was due to the low risk of bias in the study outcomes and the precision of the results.</li> </ul>



	<ul style="list-style-type: none"> <li>The review protocol defined that opioids would be pooled unless heterogeneity was observed. Therefore strong and weak opioids were combined within this review. It was noted that there was no heterogeneity in the pooled data.</li> </ul>
<b>Patients values and preferences</b>	<ul style="list-style-type: none"> <li>With the known side effects of NSAIDs, the GDG acknowledged the need for an alternative treatment option for people with contraindications to NSAIDs use.</li> <li>The Belgian GDG emphasised the use of the combination tramadol + paracetamol in Belgium rather than codeine + paracetamol as quoted by the NICE GDG and decided not to support the NICE research recommendations on the efficacy of codeine. Moreover, the GDG considered that codeine should not be prescribed at first line given its characteristics and the existence of rapid and poor metabolizers.</li> <li>The Belgian GDG stressed that a fixed association “paracetamol-tramadol” is not recommended by the CBIP/BCFI.</li> </ul>
<b>Costs (resource allocation)</b>	<ul style="list-style-type: none"> <li>The economic evidence for opioids found by NICE (Wielage et al 2013) indicated that opioids were not cost-effective for the management of chronic low back pain. No economic evaluation was found regarding the cost-efficacy of weak opioids in acute low back pain.</li> </ul>

Recommendations	Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"> <li>Think about weak opioids (with or without paracetamol) for the shortest period possible for managing acute low back pain with or without radicular pain only if an NSAID is contraindicated, not tolerated or has been ineffective.</li> </ul>	Experts opinion	NA
<ul style="list-style-type: none"> <li>Do not routinely offer opioids for managing chronic low back pain with or without radicular pain.</li> </ul>	Weak (RCTs)	High to very low

### Change in comparison with the NICE recommendations

Changes have been proposed by the Belgian GDG regarding the 2 clinical recommendations proposed in the NICE 2016 guidelines.

24. ~~Consider~~ Think about weak opioids (with or without paracetamol) for the shortest period possible for managing acute low back pain with and without radicular pain only if an NSAID is contraindicated, not tolerated or has been ineffective.

26. Do not routinely offer opioids for managing acute low back pain (see recommendation 24).

27. Do not routinely offer opioids for managing chronic low back pain with and without radicular pain.

The reasons underlying these changes are described in Appendix 7.14.4. The research recommendation “What is the clinical and cost-effectiveness of codeine with and without paracetamol for the acute management of low back pain?” was not retained in the Belgian guideline.





### 3.3.4 Antidepressants

Antidepressants are used for analgesic purpose in chronic and neuropathic pain, separate from their antidepressant actions. They are subdivided according to their chemical structure and their mode of action although the selectivity is never quite specific. In this chapter, we use the following classification: selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs) and tricyclic antidepressants (TCAs).

#### Scientific evidence regarding antidepressants in low back pain and radicular pain

Fifty five studies were included by NICE in the review focusing on all kind of medication as single intervention. Among them, 10 studies concerned antidepressants. No study was found that looked at a combination of drugs including antidepressants versus placebo or versus other drugs. Due to insufficient randomised trial evidence further search for cohort studies on antidepressants was carried out but without identifying relevant studies. Finally, one economic evaluation (cost-utility analysis model) compared various pharmacological treatments, including one SNRI (duloxetine). No relevant economic evaluations were identified that included SSRI and tricyclic antidepressants.

#### Antidepressants as single intervention versus placebo

##### MIXED POPULATION (LOW BACK PAIN WITH OR WITHOUT SCIATICA)

- **SSRIs versus placebo:**
  - No clinically important difference was observed for any of the reported critical outcomes (pain, function and psychological distress) for fluoxetine 100 ng/mL, 200 ng/mL, 400ng/mL (duration 12 weeks) or paroxetine 20 mg, duration 56 days compared with placebo (1 or 2 studies; very low to moderate quality; range of n = 53-162).
- **SNRIs versus placebo:**
  - No difference was observed for duloxetine 20 or 60 or 120 mg/day (duration 12 or 13 weeks) compared with placebo, in terms of pain measured on Brief pain inventory (3 studies; moderate quality; n = 1004) and function (3 studies; moderate quality; n = 1004). However, a high proportion of patients reported a responder criteria of more than 30% reduction of pain with SNRI (2 studies; n = 630; low quality; RR 1.22 [95%CI 1.05, 1.43]). For quality of life, results were conflicting: no difference on SF-36 (1 or 2 studies; low and moderate quality; range of n = 162-588), but a benefit of SNRIs on EQ-5D in (2 studies, moderate quality; n = 742). One study (moderate quality; n = 357) showed fewer healthcare utilisation (at least one treatment for adverse events) in favour of placebo.
- **TCAs versus placebo:**
  - No clinically important difference was observed for any of the reported critical outcomes (pain, function and psychological distress) for nortriptyline, dose escalation: 25 mg for 3 days; 50 mg for 4 days; 75 mg for 3 days; 100 mg for 4 days (duration 8 weeks) or for trazodone (50 mg tablets: 1 tablet a day for 3 days, 1 tablet 2 times a day for 3 days, 1 tablet 3 times a day for 3 days, then continue increasing dose by 1 tablet every 3 days on a 3-times-a-day schedule, barring significant side effects, to a maximum of 4 tablets 3 times a day (600 mg/day), average daily dose: 201 mg, (duration 6 weeks) compared with placebo (1 or 2 studies; very low to moderate quality; range of n = 53-162).
  - In terms of **adverse events**, a clinically important harm of both **SSRIs** (Risk ratio 3.22 [95%CI 1.04, 10.01], 1 study; very low quality; 11 n = 69) and **SNRIs** (Risk ratio 1.39 [95%CI 1.17, 1.65], 3 studies; n = 1041; low quality) was seen compared with placebo.
- The included population in all studies encompassed adult patients with **chronic LBP** (at least 6 months).



## LOW BACK PAIN WITHOUT SCIATICA

- SSRIs versus placebo: One study of high risk of bias using benzotropine mesylate was analysed but not reported in the results.

### Head to head comparison

- A **clinical benefit** was found for the TCA amitriptyline 150mg daily compared with paracetamol (2000mg daily) for improving pain intensity was observed at 5 weeks (MID -1.83 [95%CI -3.66, 0.00], 1 study, moderate quality; n = 39), but no clinical difference for psychological distress (1 study, low and moderate quality; n = 39). The population of this second study encompassed acute and chronic LBP (max 6 months) with or without sciatica.
- A **clinical harm** in terms of increased adverse events (sedation, dry mouth and vertigo) with anticonvulsant (pregabalin 75mg twice daily for 2 weeks, followed by 150mg twice daily for 4 weeks then 300mg twice daily) compared with antidepressants TCA (amitriptyline 12.5mg for 2 weeks, followed by 25mg for 4 weeks and increased to 50mg) was demonstrated at 14 weeks in evidence from a single study (low quality; n = 200) in chronic LBP patients with or without sciatica.

### Economic evaluation

- The economic evaluation (Wielage 2013) compared various pharmacological treatments (head to head studies) and found that duloxetine was dominant (less costly and more effective) compared to pregabalin, celecoxib, oxycodone/paracetamol, oxycodone, tapentadol and tramadol for treating low back pain (with or without sciatica) post paracetamol. It also found that duloxetine was not cost effective compared to naproxen treatment (ICER: £41,521 per QALY gained). This analysis was assessed as partially applicable with potential serious limitations.

## Conclusions

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**All evidence was provided by studies on population with chronic LBP. No clinically important difference was observed for any of the reported critical outcomes for SSRIs or TCAs compared with placebo. Similar results were observed for SNRIs compared with placebo except for reduction of pain >30% and quality of life measured on EQ-5D where a benefit of SNRIs was seen. In terms of adverse events, a clinically important harm of both SSRIs and SNRIs was observed compared with placebo. The head-to-head comparison showed a clinical benefit with TCA compared to paracetamol for improving pain intensity and also more clinical harms compared to anticonvulsants. One economic model, partially applicable with potential serious limitations, showed that duloxetine was dominant compared to several drugs but less cost effective compared to naproxen.**

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**Other considerations regarding antidepressants in low back pain and radicular pain**

GRADE Factors	Comments
<b>Balance between clinical benefits and harms</b>	<ul style="list-style-type: none"> <li>The Belgian GDG acknowledged that no clinically important difference was observed for SSRIs versus placebo for any of the reported critical outcomes except for adverse events which were seen to increase in the intervention group. Therefore the GDG agreed that the balance benefit risk is negative for the SSRIs.</li> <li>The results is less clear for the TCAs and the SNRIs since some clinical benefits were showed by the NICE review. Moreover, some recent RCTs appeared to confirm the benefit of duloxetine compared to placebo in chronic low back pain (especially if there is a neuropathic pain component).</li> <li>Because the Belgian guideline on low back pain and radicular pain did not refer to a specific guideline on the pharmacological interventions for neuropathic pain, a door should be opened to other medications than NSAIDs and opioids (with or without paracetamol). In chronic pain, where central sensitisation and/or a neuropathic pain component may be present, TCAs and SNRIs could be useful. The CBIP/BCFI mentioned that TCA (amitriptyline) and duloxetine can be indicated in neuropathic pain and other chronic pain.</li> <li>However the Belgian GDG was aware of the risk of adverse events and proposed to keep a recommendation against the use of antidepressants in LBP but to soften it by adding routinely for TCAs and SNRIs only.</li> <li>The Belgian GDG emphasised that antidepressants are not indicated for acute low back pain</li> </ul>
<b>Quality of evidence</b>	<ul style="list-style-type: none"> <li>The quality of evidence ranged from a GRADE rating of moderate to very low. According to NICE, this was due to the high number of drop outs in some of the included studies, resulting in a high risk of bias rating, as well as the imprecise nature of the results extracted and analysed in this review.</li> </ul>
<b>Values and preferences</b>	<ul style="list-style-type: none"> <li>According to the Belgian GDG, it is important to be able to consider a pharmacological option for people with chronic low back pain or radicular pain, outside NSAIDs or opioids. Some of these patients have a long painful pathway and expect help from clinicians.</li> </ul>
<b>Costs (resource allocation)</b>	<ul style="list-style-type: none"> <li>The economic study found by NICE did not demonstrated a clear positive cost-effectiveness report for antidepressants.</li> </ul>

Recommendations	Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"> <li>Do not offer selective serotonin reuptake inhibitors (SSRI) for managing low back pain with or without radicular pain.</li> </ul>	Strong (RCTs)	Moderate to very low
<ul style="list-style-type: none"> <li>Do not routinely offer tricyclic antidepressants or non-selective serotonin–norepinephrine reuptake inhibitors (SNRI) for managing low back pain with or without radicular pain. This recommendation is applicable only for chronic pain; the use of antidepressants is not recommended in acute pain.</li> </ul>	Weak (RCTs)	Moderate to very low



### Change in comparison with the NICE recommendations

Changes have been proposed by the Belgian GDG regarding the 2 clinical recommendations proposed in the NICE 2016 guidelines.

28. Do not offer selective serotonin reuptake inhibitors, ~~serotonin-norepinephrine reuptake inhibitors or tricyclic antidepressants~~ for managing low back pain with or without radicular pain.

+ Do not routinely offer tricyclic antidepressants or serotonin-norepinephrine reuptake inhibitors for managing low back pain with or without radicular pain. This recommendation is applicable only for chronic pain; the use of antidepressants is not recommended in acute pain.

More detailed on the reasons underlying these changes are described in Appendix 7.14.5.

### 3.3.5 Anticonvulsants

Antidepressants are used for analgesic purpose in chronic and neuropathic pain, separate from their anticonvulsant actions. They have diverse pharmacological properties including binding to sodium and calcium ion channels and decreasing the release of neurotransmitters in the brain and spinal cord.

### Scientific evidence regarding anticonvulsants in low back pain and radicular pain

Fifty five studies were included by NICE in the review focusing on all kind of medication as single intervention. Among them, 2 studies concerned anticonvulsants. One study was found that looked at a combination of drugs versus anticonvulsant. Due to insufficient randomised trial evidence further search for cohort studies on anticonvulsants was carried out which allow to identify one relevant cohort study. Finally, two economic studies were included in the review: one economic evaluation that compared gabapentinoid anticonvulsants to usual care and one cost-utility analysis model comparing duloxetine (SNRI), two NSAIDs, pregabalin (gabapentinoid anticonvulsant) and four opioid analgesics.

### Anticonvulsants as single intervention versus placebo or usual care

#### LOW BACK PAIN POPULATION WITH SCIATICA:

- **Gabapentinoids versus placebo:** Evidence from 1 randomised, placebo-controlled RCT with gabapentinoids (dosage increasing from 300 mg to 1200 mg per day over a period of 6 weeks) demonstrated no clinical benefit (low quality; n = 65) in pain intensity at 6 weeks (unclear duration of pain). A clinically significant harm with gabapentinoids in terms of **increased risk of adverse events** was showed (Risk ratio 1.60 [95%CI 0.96, 2.67], (low quality; n = 65),
- **Gabapentinoids versus usual care:** One observational study on chronic LBP patients with pregabalin (mean dose 189.9 mg/d, duration 12 weeks) demonstrated a **clinically important improvement** at 12 weeks on pain intensity (MID -1.40 [95%CI -1.81, -0.99]) and responder criteria (pain reduction>50%: Risk ratio 1.66 [95%CI 1.30, 2.12]) (very low quality; n = 683). This observational study showed also no clinical benefit for depression or anxiety and a **clinical harm** for quality of life on SF-12 (MID for physical health 3.90 [95%CI 2.21, 5.59], MID for mental health score 5.30 [95%CI 3.71, 6.89], very low quality; n = 683).

#### MIXED POPULATION (WITH AND WITHOUT LBP)

- **Topiramate versus placebo:** One further RCT compared topiramate (titrated at 50 mg/week to a dose of 300 mg/day in the sixth week and then remained constant, duration 10 weeks) with placebo in adults with chronic LBP with or without leg pain for at least 6 months. Evidence showed a **clinically important benefit** at 10 weeks of topiramate for pain severity (MID -11.40 [95%CI -12.16, -10.64]) and, no clinically important difference for function but a **harm** in terms of increased rate of adverse events (risk ratio 1.80 [95%CI 0.93, 3.49], low and moderate quality; n = 96).



### Head-to-head comparison

- A **clinical harm** in terms of increased adverse events (sedation, dry mouth and vertigo) with anticonvulsant (pregabalin 75mg twice daily for 2 weeks, followed by 150mg twice daily for 4 weeks then 300mg twice daily) compared with antidepressants TCA (amitriptyline 12.5mg for 2 weeks, followed by 25mg for 4 weeks and increased to 50mg) was demonstrated at 14 weeks in evidence from a single study (low quality; n = 200) in chronic LBP patients with or without sciatica.

### Combinations of drugs versus other drugs

- One study compared a combination of opioids (tramadol) plus paracetamol versus an anticonvulsant (pregabalin 75 mg) in older people with chronic low back pain (with sciatica). This study only reported adverse events and showed no clinical difference between the groups (moderate quality; n = 60).

### Economic evaluation

- One cost–consequence analysis found that care including pregabalin was less costly and more effective than care excluding pregabalin for low back pain with sciatica (£68 more per patient, pain (BPI): MID -1.40, quality of life (SF-12 physical summary score): MID 3.90, quality of life (SF-12 mental summary score): MID 5.30, psychological distress (HADS - anxiety): MID -1.80 and psychological distress (HADS - depression): MID -1.90 per patient). This analysis was assessed as partially applicable with potential serious limitations.
- Another economic evaluation (Wielage 2013) found that duloxetine was dominant (less costly and more effective) compared to pregabalin, celecoxib, oxycodone/paracetamol, oxycodone, tapentadol and tramadol for treating low back pain (with or without sciatica) post paracetamol. This analysis was assessed as partially applicable with potential serious limitations.

### Conclusions

**All studies focused on patient with sciatica. There was inconsistent evidence for the impact of gabapentinoids on pain intensity. One RCT demonstrated no clinical benefit while one observational study demonstrated a clinically important improvement compared with usual care. Harm in terms of increased risk of adverse events or negative impact on anxiety, depression and quality of life was also found with gabapentinoids. One further RCT showed confusing results for topiramate versus placebo. Anticonvulsants appeared to present an increase adverse event compared to antidepressants but no difference compared to a combination of opioids + paracetamol. Finally the economic evidence showed that care including pregabalin was less costly and more effective than care excluding pregabalin in people with sciatica but duloxetine was dominant compared to pregabalin in another study in a mixed population (with and without sciatica).**



**Other considerations regarding anticonvulsants in low back pain and radicular pain**

GRADE Factors	Comments
<b>Balance between clinical benefits and harms</b>	<ul style="list-style-type: none"> <li>The Belgian GDG acknowledged that the evidence relative to gabapentinoids on pain was from 1 small placebo controlled RCT (n=65) and 1 observational cohort study which provided inconsistent results. The evidence of a clinically important effect of topiramate for both function and pain severity was considered surprising since this drug is not commonly used for low back pain and has a significant side effect profile.</li> <li>The Belgian GDG discussed the potential efficacy for anticonvulsants in LBP especially if there is a neuropathic pain component since there is a physiological explanation of this efficacy (working action on central sensitization).</li> <li>Both studies included by NICE focused on people with low back pain with sciatica.</li> <li>Moreover, because the Belgian guideline on low back pain and radicular does not refer to a specific guideline on the pharmacological interventions for neuropathic pain, a door should be opened to other medications than NSAIDs and opioids (with or without paracetamol).</li> <li>The CBIP/BCFI mentioned that anticonvulsants (carbamazepine, gabapentin and pregabalin) can be indicated in neuropathic pain and other chronic pain.</li> <li>However the Belgian GDG was aware of the risk of adverse events and proposed to keep a strong recommendation against the use of anticonvulsants in LBP but to add an exception (in case of neuropathic pain).</li> </ul>
<b>Quality of evidence</b>	<ul style="list-style-type: none"> <li>There are only two studies: one small RCT (n=80) and one cohort study with a large sample size but considered at high risk of bias in part due to being an un-blinded study.</li> <li>The quality of evidence ranged from a GRADE rating of moderate to low for anticonvulsants.</li> </ul>
<b>Values and preferences</b>	<ul style="list-style-type: none"> <li>According to the Belgian GDG, it is important to be able to consider a pharmacological option for people with neuropathic pain. Some of these patients have a long painful pathway and expect help from clinicians.</li> </ul>
<b>Costs (resource allocation)</b>	<ul style="list-style-type: none"> <li>There was uncertainty regarding the costs and effects of gabapentinoid anticonvulsant (pregabalin) with two analysis with serious limitations showing inconsistent results.</li> </ul>

Recommendations	Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"> <li>Do not offer anticonvulsants for managing low back pain with or without radicular pain in absence of a neuropathic pain component.</li> </ul>	Strong (RCTs & cohort studies)	Moderate to low



### Change in comparison with the NICE recommendations

Changes have been proposed by the Belgian GDG regarding the clinical recommendations proposed in the NICE 2016 guidelines.

29. Do not offer anticonvulsants for managing low back pain with or without radicular pain in absence of a neuropathic pain component.

More detailed on the reasons underlying these changes are described in Appendix 7.14.6.

### 3.3.6 Skeletal muscle relaxants

Guidelines from many countries have advocated that muscle relaxants be considered for short-term use in patients with low back pain when the paraspinal muscles are in spasm. These drugs bind to different receptors and exert their effect on muscles by central nervous system mechanisms.

#### Scientific evidence regarding skeletal muscle relaxants in low back pain and radicular pain

Fifty five studies were included by NICE in the review focusing on all kind of medication as single intervention. Among them, 6 studies concerned muscle relaxants with 3 studies for tizanidine and old single studies for diazepam, baclofen and orphenadrine citrate. Due to insufficient randomised trial evidence on skeletal muscle relaxants further search for cohort studies on was carried out but without identifying any relevant cohort study. No relevant economic evaluations were identified that included muscle relaxants and one economic evaluation relating to NSAIDs, opioid analgesics and muscle relaxants was identified but was selectively excluded due to a combination of applicability and methodological limitations.

### Skeletal muscle relaxants as single intervention versus placebo

- There was conflicting evidence in relation to pain intensity on tizanidine:
  - Evidence from 2 placebo controlled studies showed no clinical benefit on pain intensity with tizanidine 4 mg three times a day, duration 7 days (moderate quality; n = 193) in *acute LBP population with or without sciatica*;
  - However, 1 study comparing tizanidine (2 mg + aceclofenac 100 mg fixed dose, duration 7 days) with usual care found clinical benefit on pain severity (MID -2.11 [95%CI -2.72, -1.5], low to very low quality; n = 185) in adults with *acute low back pain without sciatica* of at least moderate severity and of recent onset.
- No data were available for quality of life, function or psychological distress.
- There was evidence of a clinically relevant increased incidence of adverse events in the groups treated with muscle relaxants compared with placebo (3 studies; moderate quality; n = 412), but not compared with usual care (1 study; very low quality; n = 197).

### No economic evaluation

### Conclusions

**Evidence identified was for tizanidine mainly, with pain severity and occurrence of adverse events as only outcomes. There was conflicting evidence in relation to pain with one study versus placebo showing no clinical benefit and one study versus usual care showing clinical benefit. There was evidence of an increased incidence of adverse events in the group treated with muscle relaxants compared to placebo. No economic evidence was found.**



**Other considerations regarding skeletal muscle relaxants in low back pain and radicular pain**

GRADE Factors	Comments
<b>Balance between clinical benefits and harms</b>	<ul style="list-style-type: none"> <li>The Belgian GDG acknowledged the lack of evidence of a clinical benefit regarding the skeletal muscle relaxants. Moreover several drugs included in the review by NICE were not available in the Belgian market (e.g. orphenadrine and tetrazepam).</li> <li>The evidence found concerned mainly tizanidine and showed conflicting results regarding a potential benefit on pain. By contrast, an increase of adverse events was noticed.</li> <li>The NICE GDG had highlighted that it was surprising the only available evidence for diazepam, which is widely prescribed for people with low back pain, was from 1 small RCT (n = 76) in 1978, which only reported change in muscle spasms. The addition of an RCT published in German (not included in this review due to being a non-English language study) would remain a very weak evidence base for this drug. This led the NICE GDG to write a research recommendation for the use of diazepam in the management of non-specific low back pain.</li> <li>However given the lack of clinical evidence in favour of the muscle relaxant in low back pain and the risk of adverse events, the Belgian GDG disagreed with the NICE proposition. For some GDG members this research question was already outdated, whereas other members were interested in the effect on other outcomes than pain, e.g. anxiety, particularly because they are commonly used although they have a lot of side effects.</li> <li>Finally, given the risk of adverse events, the Belgian GDG preferred to recommend that muscle relaxants should not be used for the management of low back and radicular pain. A recommendation against muscle relaxants should support a change in practice among the Belgian physicians who are usually prescribing benzodiazepines for low back pain.</li> </ul>
<b>Quality of evidence</b>	<ul style="list-style-type: none"> <li>The quality of evidence ranged from a GRADE rating of moderate to very low for muscle relaxants.</li> </ul>
<b>Values and preferences</b>	<ul style="list-style-type: none"> <li>People may be anxious as a result of a sudden onset of disabling back pain and could have difficulty relaxing with the result that muscles involved in the problem may go into spasm. However, this did not justify the use of muscle relaxants. Information that muscle spasm pain does not signify increasing harm to any structure should be provided.</li> </ul>
<b>Costs (resource allocation)</b>	<ul style="list-style-type: none"> <li>No economic studies were found for muscle relaxants. However a cost could be inevitably associated with providing this drug and given the conclusion of lack of clinical benefit and increased incidence of adverse events observed in the clinical evidence, this cost appeared to be not justified.</li> </ul>

Recommendations	Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"> <li>Do not offer skeletal muscle relaxants for managing low back pain with or without radicular pain</li> </ul>	Strong (RCTs)	Moderate to very low





### Change in comparison with the NICE recommendations

The research recommendation proposed in the NICE 2016 guidelines “What is the clinical and cost-effectiveness of benzodiazepines for the acute management of low back pain?” was not accepted and a clinical recommendation against skeletal muscle relaxants was formulated instead by the Belgian GDG.

More detailed on the reasons underlying these changes are described in Appendix 7.14.7.

#### 3.3.7 Antibiotics

Recently, antibiotics have been used to treat chronic low back pain. However, it is not known whether it is the antimicrobial or anti-inflammatory properties of antibiotics that are important clinically for this purpose.

#### Scientific evidence regarding antibiotics in low back pain and radicular pain

Fifty five studies were included by NICE in the review focusing on all kind of medication as single intervention. Among them, one study concerned antibiotics. Due to insufficient randomised trial evidence on skeletal muscle relaxants further search for cohort studies on was carried out but without identifying any relevant cohort study. No relevant economic evaluations were identified that included antibiotics.

### Antibiotic as single intervention versus placebo

- There was evidence from 1 RCT of the use of antibiotics (amoxicillin-clavulanate (500mg/125 mg) three times a day) in people with MRI confirmed disc prolapse, subsequent vertebral end plate oedema and *chronic low back pain of more than 6 months duration with or without sciatica*. This evidence suggested an improvement in health care utilisation (doctor consultation for back pain, risk ratio 0.56 [95%CI 0.34, 0.92], but also an increase in adverse events (risk ratio 2.78 [95% 1.79, 4.32]) (low and moderate quality; n = 162).
- No data were available for quality of life, pain severity, function or psychological distress, nor for the comparison with usual care.

### No economic evaluation

### Conclusions

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**Evidence from one RCT only showed an improvement in health care utilisation but also an increase in adverse events. This RCT focused on chronic low back pain with MRI confirmed disc prolapse. No economic evidence was found.**

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### Other considerations regarding antibiotics in low back pain and radicular pain

GRADE Factors	Comments
<b>Balance between clinical benefits and harms</b>	<ul style="list-style-type: none"><li>• The Belgian GDG acknowledged the lack of evidence of a clinical benefit regarding the use of antibiotics in low back pain. One RCT only was found that showed improvement but also an increase of adverse events with antibiotic in low back pain. Moreover, the population included in this RCT was very specific (MRI confirmed disc prolapse) and the recruitment of the population was unclear. Consequently, this population may not be a representative sample.</li><li>• By contrast with NICE who decided not to formulate a recommendation on antibiotics, the Belgian GDG preferred to recommend against this use in low back pain with or without radicular pain. The arguments were mainly<ul style="list-style-type: none"><li>○ The importance of adverse events in individual level but also for the public health in terms of antibiotic resistance</li><li>○ The current overwhelming overuse of antibiotics in Belgium where the control of antibiotic prescription is a real problem.</li></ul></li></ul>
<b>Quality of evidence</b>	<ul style="list-style-type: none"><li>• The quality of evidence ranged from a GRADE rating of moderate to low for antibiotics, from a single study.</li></ul>
<b>Values and preferences</b>	<ul style="list-style-type: none"><li>• There are regular public information campaigns on the overuse of antibiotics in Belgium. People are informed that antibiotics is not needed in routine (mainly in an infection context).</li></ul>
<b>Costs (resource allocation)</b>	<ul style="list-style-type: none"><li>• No economic studies were found for antibiotics. However a cost could be inevitably associated with providing this drug and given the conclusion of lack of clinical benefit and increased incidence of adverse events observed in the clinical evidence, this cost appeared to be not justified.</li></ul>

Recommendations	Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"><li>• Do not offer antibiotics for managing low back pain with or without radicular pain</li></ul>	Strong (RCTs)	Moderate to low

### Change in comparison with the NICE recommendations

There was no NICE final recommendation on antibiotics

More detailed on the reasons underlying these changes are described in Appendix 7.14.8.



### 3.3.8 Oral Methylprednisolone

During the GDG meeting on the 12th October 2016, one member of the Belgian GDG asked if oral methylprednisolone was sometimes used in Belgium in the treatment of LBP (for example in case of slight motor deficit).

According to the other member of the GDG however, its use appeared to be not usual.

Moreover, it was not studied by NICE.

Therefore, KCE proposed to add this medication in the list of “treatments not included in the Belgian guideline on LBP because not covered by NICE” (as andullation, shock waves, etc.).

More detailed on the reasons underlying these changes are described in Appendix 7.14.9.

## 3.4 Invasive treatments

### 3.4.1 Spinal injections

Several different types of spinal injections can be performed for low back pain with different techniques and drugs. Usually the injected agents aim to sooth inflamed tissue or calm excessive nerve activity, but some (sclerosants) aim to induce inflammation and stimulate healthy new tissue growth. In general, spinal injections are used in conjunction with other therapies, for example exercise programmes.

#### Definition of spinal injections

- **Facet joint injections** target the small joints linking the spinal vertebrae, known as the facet joints. Each vertebra has 2 connections below, one each side, and 2 above. Injections of local anaesthetic or steroid into selected joints are used to try to temporarily reduce or stop back pain. It is usually used in conjunction with an exercise programme. It is unlikely that the substances injected would remain for long.

- **Medial branch blocks** are injections of local anaesthetic on to the medial branch nerves that supply the facet joints. It is usually done to define those who would respond to radiofrequency denervation of the positive tested levels.
- **Intradiscal therapy** is aimed at treating internal disc disruption (IDD), which some therapists believe can be a cause of low back pain. Both steroids and non-steroidal anti-inflammatory drugs have been injected into the disc in an attempt to suppress inflammation and reduce pain.
- **Prolotherapy** (also known as proliferation therapy or regenerative injection therapy) involves injecting tissue with an irritant solution. This may be a joint, ligament or tendon insertion, or injected into connective tissue or muscle.
- **Trigger Point Injections** use various mixtures of local anaesthetics (and/or a steroid, or botulinum toxin). A trigger point is argued to be a painful or irritable knot in a muscle. Injections are usually carried out in an outpatient setting, and repeated at intervals.

The NICE evidence review can be found on p.12-42 in the full guideline on invasive treatments and the forest plots in Appendix K p.260-270 (<https://www.nice.org.uk/guidance/ng59/evidence>).

A summary sheet in Appendix 7.15 gathered the evidence findings, the NICE GDG considerations, the results of the online survey and the discussion with the Belgian GDG.

#### Scientific evidence regarding spinal injections in low back pain

The clinical and cost effectiveness of spinal injections have been considered as monotherapy in comparison to saline or other single interventions or as combination therapy in comparison to other interventions. Thirty-one RCTs were included in the review. The search was extended to cohort studies for all comparisons due to insufficient evidence and 2 studies were identified that met the inclusion criteria. Four Cochrane reviews were identified, but were not included due to methodological reasons. The individual studies were assessed and included if they matched the review protocol. No relevant economic evaluations were identified.



## Image-guided facet joint injections

### MONOTHERAPY

(see Table 41 in Appendix 7.15)

- *Steroid versus saline*: A single RCT reported a clinical benefit in pain and function at long term in favour of steroid injections (methylprednisolone), but not at short term.
- *Steroid versus hyaluronans*: A single RCT reported a short term clinical benefit in pain favouring steroids (triamcinolone acetonide) but this benefit was not anymore seen at long term. Also no clinical differences were found for (different measures of) function.

### COMBINATION THERAPY

(see Table 41 in Appendix 7.15)

- *Steroid + biomechanical exercise (home stretching exercises) vs biomechanical exercise (home stretching exercises)*: No clinically important difference were seen in pain, function and responder criteria (>50% improvement in pain or function) in one RCT. No long term data were reported.
- *Steroid + anaesthetic vs biomechanical exercise (McKenzie exercises)*: One cohort study found a clinical benefit in pain at both time points in favour of the steroid injection (methylprednisolone + bupivacaine), but not in function.

## Image-guided intradiscal injections

### MONOTHERAPY

(see Table 42 in Appendix 7.15)

- *Steroid versus saline*: Evidence from 3 studies showed a clinical benefit in terms of improving pain and function in the group receiving a steroid injection (bethametasone or dexamethasone) in the short term. Evidence from 2 studies also showed clinical benefit of steroid injections (betamethasone) for pain and function in the long term, but this was not observed in the case of function when dexamethasone (1 study), or

methylprednisolone acetate (1 study, only reported outcome), was used as injectate.

### COMBINATION THERAPY

(see Table 42 in Appendix 7.15)

- *Steroid + anaesthetic vs anaesthetic*: Evidence from 3 studies showed no clinically important difference between treatments for all outcomes reported (pain, function, responder criteria >50% pain improvement when steroid plus anaesthetic (betamethasone + bupivacaine) was injected compared to anaesthetic injection alone irrespective of route of administration being caudal epidural, medial branch blocks or interlaminar injections.
- *Steroid + anaesthetic vs mixed modality exercise*: The single study comparing steroid plus anaesthetic (methylprednisolone + bupivacaine) versus mixed modality exercise (self-management (back education and home exercise), biomechanical exercise (McKenzie and stability), manual therapy (manipulation/mobilisation, Maitland and mulligan), electrotherapy (ultrasound) and heat/ice) reported no benefit of the injection for QoL, pain or function in the short term.

## Prolotherapy/sclerosants

### MONOTHERAPY

(see Table 43 in Appendix 7.15)

- *Sclerosant vs anaesthetic*: A single RCT (on glycerol versus bupivacaine) reported only one outcome: no clinical difference was found for pain at short term. No long term data were reported.



## COMBINATION THERAPY

(see Table 43 in Appendix 7.15)

- *Sclerosants + anaesthetic vs saline*: Evidence from a single study demonstrated a clinical benefit favouring the injection of sclerosant plus anaesthetic (phenol + lignocaine) for pain and function in both the short and long term.
- *Sclerosants + anaesthetic vs anaesthetic*: A single RCT (phenol + lidocaine versus lidocaine) reported no clinical differences in long term pain and function. No short term data were reported.

## Other non-image guided injections

### MONOTHERAPY:

- *Botulinum toxin vs saline*: Evidence from 1 study showed clinical benefit of botulinum toxin for responder criteria in pain (>50% pain improvement) at short term (moderate quality; n=30). No long term data were reported.

### COMBINATION THERAPY:

- *Steroid + anaesthetic vs steroid*: Evidence from 1 study on methylprednisolone + levobupivacaine versus methylprednisolone alone demonstrated no clinically important difference between the treatments for pain (first or second block) at either short or long term.

## Economic evidence: none

## Conclusions

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**Only few studies were found per comparison across the different types of spinal injections. Evidence showed inconsistent results on a potential clinical benefit of spinal injections in the management of low back pain. No economic evaluation was identified which allowed to assess the cost beneficial effect of spinal injections.**

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### Other considerations regarding spinal injections in low back pain

GRADE Factors	Comments
<b>Balance between desirable and undesirable effects</b>	<ul style="list-style-type: none"><li>• The Belgian GDG acknowledged there was very limited evidence of benefit from spinal injections, with inconsistent findings and single study for each comparison.</li><li>• Although the included studies in the NICE review did not demonstrate a clear harmful effect of spinal injections, the Belgian GDG mentioned several arguments against this intervention:<ul style="list-style-type: none"><li>○ In Belgium, most spinal injections are image-guided. Avoiding unnecessary exposure to radiation is an additional argument to formulate a recommendation against the use of spinal injections for low back pain.</li><li>○ A clear recommendation could counteract the current (over)use of spinal injections in clinical practice.</li><li>○ Apart from the lack of evidence to support injections, invasive treatments shift the patient away from the key message that back pain should be dealt with activity.</li></ul></li><li>• The NICE and Belgian GDG consequently agreed that it was appropriate to recommend against the use of spinal injections for people with low back pain.</li><li>• Regarding specifically <b>facet joint injections</b>, several Belgian GDG members suggested a potential efficacy although poorly demonstrated by the analysis of the retrieved studies by NICE: (due to the very low number of RCTs). A subgroup differentiation for patients with suspected facet syndrome was suggested. Additional literature was cited by the GDG members, or additionally searched by KCE researchers:<ul style="list-style-type: none"><li>○ The review of Poetcher et al, in Spine 2014<sup>26</sup>: the forest plots comparing corticoid facet injections with facet joint radiofrequency denervation were more favourable for radiofrequency denervation.</li><li>○ A primary study by Lakemeier 2013<sup>27</sup>: no clear differences were found between spinal injections and radiofrequency denervation (a similar pain improvement was found in both groups). This study was incorrectly excluded in the review of NICE due to wrong population, i.e. patients with facet joint osteoarthritis), but in the primary study is clear mentioned that only patients with non- specific low back pain of at least 24 months duration were included.</li><li>○ Several guidelines mentioned the lack of evidence (on short and long term) and recommended against the use of spinal injections. However, none of the studies reported harmful effects.</li></ul></li><li>• The Belgian GDG emphasised other issues concerning the use of facet joint injections, such as:<ul style="list-style-type: none"><li>○ The diagnosis of facet joint pain syndrome is difficult to establish, because there is no clear definition.</li><li>○ Often facet injections do not exactly reach the facet joint, this is why the technique remains controversial.</li></ul></li><li>• After all, the GDG members agreed that no clear recommendation could be formulated on the potential use of spinal injections for facet joint pain syndrome, due to the low level of evidence on the benefits and potential harms of these injections.</li><li>• The Belgian GDG mentioned also that the present recommendation focuses on the therapeutic use of spinal injections, and does not encompass the diagnostic purposes (see discussion on radiofrequency denervation).</li></ul>
<b>Quality of evidence</b>	<ul style="list-style-type: none"><li>• Overall, the quality of the evidence ranged from moderate to very low, due to risk of bias (and additional imprecision)</li></ul>



	<ul style="list-style-type: none"> <li>For facet joint injections, the quality of the evidence ranged from low to very low.</li> <li>Several limitations of the studies were listed, e.g. questionable applicability to the UK setting, no biological reason for a long term effect without effect on short term, small sample sizes etc.</li> </ul>
<b>Values and preferences</b>	<ul style="list-style-type: none"> <li>The NICE stakeholders mentioned that in clinical practice, this kind of injections are often given within a multimodal approach according to a biopsychosocial model and with assessment if benefit occurs. NICE refused to formulate a recommendation pro spinal injections (see reasons above-mentioned in benefits and harms) but confirmed that the assessment of post-administration responsiveness should be part of routine practice for every intervention.</li> </ul>
<b>Costs (resource allocation)</b>	<ul style="list-style-type: none"> <li>No economic evaluations were identified. Some costs relating to the drugs, consumables and equipment (e.g. imaging), personnel time will be associated with its use and will also depend on the number of injections given. Given the NICE and Belgian GDG's conclusion that there was a lack of evidence of clinical benefit for injections, intervention costs were not considered justified.</li> </ul>

Recommendation	Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"> <li>Do not offer spinal injections for managing low back pain.</li> </ul> <p>*No clear recommendation could be formulated on the potential use of facet joint injections for facet joint pain syndrome, due to the low level of evidence on the benefits and potential harms of these injections.</p>	Strong	Very low to moderate

**Change in comparison with the NICE recommendations**

- No changes in the wording of the recommendation.
- A footnote has been added that no clear recommendation on facet joint injections for facet joint pain syndrome could be formulated.
- The reasons underlying these changes are described in Appendix 7.15.

*3.4.2 Radiofrequency denervation for facet joint pain*

The lumbar facet joints are pairs of joints that stabilize and guide motion in the spine. These joints are well innervated by the medial branches of the dorsal rami. In current clinical practice, people with low back pain may be offered facet joint nerve blockade with a local anaesthetic to determine the presence or absence of a facet joint pain component. Those who experience significant but short term pain relief may then be offered a neuro-destructive procedure called 'radiofrequency denervation' in an attempt to achieve longer term pain relief.



### Definition of radiofrequency denervation

Radiofrequency denervation has evolved as a treatment for spinal pain over the last 40 years and is a minimally invasive and percutaneous procedure performed under local anaesthesia or light intravenous sedation. Radiofrequency energy is delivered along an insulated needle in contact with the target nerves. This focussed electrical energy heats and denatures the nerve. This process may allow axons to regenerate with time requiring the repetition of the radiofrequency procedure.

The NICE evidence review can be found on p.43-66 in the full guideline on invasive treatments and the forest plots in Appendix K p.271-275 (<https://www.nice.org.uk/guidance/ng59/evidence>).

A summary sheet in Appendix 7.16 gathered the evidence findings, the NICE GDG considerations, the results of the online survey and the discussion with the Belgian GDG.

### Scientific evidence regarding radiofrequency denervation in low back pain and radicular pain

The clinical and cost effectiveness of radiofrequency denervation in the management of facet joint pain has been considered. Eight RCTs were included by NICE in the review. Studies on people with low back pain and sciatica were excluded from this review and also pulsed radiofrequency was not considered. Two Cochrane reviews were identified but could not be included. One review included studies in people with neck as well as back pain. The other review included people with low back pain other than facet joint pain. The studies included in these Cochrane reviews were individually assessed and included if they matched the review protocol. One economic evaluation was identified that included radiofrequency denervation as comparator and has been included in this review.

### Radiofrequency denervation versus placebo/sham (see Table 44 in Appendix 7.16)

- **A clinical benefit favouring radiofrequency denervation** was found for pain, both at short term and long term (VAS 0-10; 4 RCTs; low to moderate quality, n=96-160). However, a single study which measured pain with the McGill questionnaire reported no clinical difference in pain at both time points (low to very low quality; n=30). Additionally a benefit for radiofrequency denervation in responders to pain reduction measured by global perceived effect was demonstrated by 2 studies at both time points although this was not seen for pain reduction measured by VAS at less than 4 months reported by a single study (low quality, n=111).
- **No differences** between RF denervation and placebo/sham were found for function; healthcare utilisation and in two of the reported adverse events. No long term data for adverse events were reported.
- **Conflicting evidence** from 1 study for quality of life at short term showed clinical benefit for radiofrequency denervation for the SF-36 domains of general health and vitality. Radiofrequency denervation was inferior to sham for the domains of physical functioning and no differences between treatments was found for the domains mental health, pain and social functioning (moderate to very low quality, n=81). No long term data for QoL were reported.
- **Harms:** Evidence from a single study demonstrated an increase in adverse events for radiofrequency denervation in terms of the number of patients with moderate or severe treatment related pain (at short term; low quality, n=78).





### Radiofrequency denervation versus medial branch block (see Table 44 in Appendix 7.16)

- A single study reported a short term and long term clinical benefit in favour of radiofrequency denervation for pain (VNS 0-10; very low quality; n=100). No clinical differences were found for QoL (EQ-5D 5-15; very low quality; n=100). The outcome QoL was reported in the forest plots but not in evidence statements (text) due to difficulties to interpret the EQ-5D data (analysis in a non-typical format).

### Economic evidence

- One cost-consequence analysis on the comparison of RF denervation versus placebo/sham found that radiofrequency denervation was more costly and more effective compared to sham for treating low back pain (with or without sciatica). This analysis was assessed as partially applicable with potentially serious limitations.
- One original economic model found that radiofrequency denervation was cost effective compared to usual care (i.e. active management in primary care) for treating low back pain suggestive of facet joint origin that has not resolved despite non-invasive management. This analysis was assessed as partially applicable with potentially serious limitations

### Conclusions

**A clinical benefit of radiofrequency denervation has been shown in pain based on 4 small RCTs in favour of RF denervation compared to placebo, mainly in patients with chronic low back pain. No difference was observed in function and findings were conflicting for quality of life. Some adverse events were reported associated with the RF denervation. Compared to medial branch block, RF denervation showed a clinical benefit on pain but no difference for quality of life. According to the economic evaluation, RF denervation is more costly and more effective than placebo/sham but more cost effective than usual care for treating low back pain suggestive for facet joint origin.**



**Other considerations regarding radiofrequency denervation in low back pain**

GRADE Factors	Comments
<b>Balance between desirable and undesirable effects</b>	<ul style="list-style-type: none"> <li>• The Belgian GDG acknowledged the potential benefit of radiofrequency denervation on pain compared to placebo or medial branch block. Other results were inconsistent.</li> <li>• Regarding the adverse events, more treatment-related pain was found in the RF denervation group (however also in the sham group as well) at short term. However, the limitations of the evidence found (very small event rate, small study size, only one study reported this outcome) made it difficult to extrapolate this data to clinical practice.</li> <li>• The NICE GDG highlighted that all of the evidence came from populations with chronic pain (ranging from 2 to 3 years duration or longer) who had failed to respond to conservative treatment. The mean pain scores in the studies reviewed was &gt;5 and the NICE GDG considered that this would reflect the population for which RF denervation might be appropriate. It was agreed, also by the Belgian GDG, that the recommendation should emphasize that this treatment should be considered only for that population (people with chronic pain with a score of 5 or more on a numeric rating scale, or equivalent) and not for all people with low back pain.</li> <li>• The Belgian GDG stressed that the previous conservative treatment should have been appropriate and suggested to specify that the management should have been an evidence-based multimodal management.</li> <li>• The uncertainty regarding the diagnosis is mentioned. The NICE GDG noted that it would be helpful for clinicians to be able to identify patients who may be suitable for this interventions. Some features may be helpful in identifying those patients:               <ul style="list-style-type: none"> <li>○ Increased pain unilaterally or bilaterally on lumbar paraspinal palpation</li> <li>○ Increased back pain on 1 or more: extension (more than flexion), rotation, extension/side flexion, extension/rotation and,</li> <li>○ No radicular symptoms and,</li> <li>○ No sacroiliac joint pain elicited using a provocation test</li> </ul> </li> </ul> <p>The Belgian GDG proposed to add in the recommendation the terms “with suspected facet joint pain” as a mean to take the diagnosis uncertainty into account.</p> <ul style="list-style-type: none"> <li>• There was a small discussion on the potential harm of performing a medial branch block in patients with missed red flags but this is rather a rare exception and in most cases a comprehensive history taking and clinical examination will already rule out potential risks and red flags. This question is important because in Belgium, there is only reimbursement for RF denervation after a positive diagnostic medial branch block.</li> <li>• The NICE GDG emphasised also that this technically demanding procedure should only be performed by appropriately trained clinicians.</li> </ul>
<b>Quality of evidence</b>	<ul style="list-style-type: none"> <li>• The quality of the evidence ranged from moderate to low.</li> <li>• Assessment of the retrieved evidence was hampered by methodological issues, e.g. difference in baseline scores for function (with both groups in the minimal disability group), reporting of outcomes in a non-standardized manner, selective reporting of domains of SF-36 (QoL), small sample sizes etc.</li> <li>• Not much confidence was placed in the study comparing RF denervation with medial branch block, because the methods used did not follow current clinical practice.</li> </ul>



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<hr/> <b>Values and preferences</b>	<ul style="list-style-type: none"><li>• No comparisons to usual care or waiting list control were found (which are the most common comparisons in the other interventions in this guideline).</li><li>• The economic evaluation was assessed as partially applicable with potentially serious limitations.</li><li>• In current clinical practice a single initial diagnostic medial branch block is administered to identify the population who might respond to RF denervation, and that the majority of the included studies conformed to this practice. Both NICE and Belgian GDG agreed that patients who experience prolonged pain relief from medial branch block should be offered RF denervation rather than repeated medial branch blocks when seeking further treatment.</li><li>• NICE mentioned that the trials reviewed did not suggest that increasing age was associated with a poorer response to RF denervation.</li><li>• The Belgian GDG members agreed to move the third recommendation proposed by NICE on imaging “Do not offer imaging for people with low back pain with specific facet joint pain as a prerequisite for radiofrequency denervation” as a footnote to the first recommendation on RF denervation and to leave out “in people with low back pain with specific facet joint pain” because redundant.</li><li>• Following considerations (synthesis) were mentioned by the NICE stakeholders, which are also applicable for the Belgian clinical practice<ul style="list-style-type: none"><li>○ Most clinicians would lean differently towards RF in different age groups given the limited evidence of long-term benefit. The recommendation would put overemphasis on RF denervation in young patients. NICE replied that the trials reviewed did not suggest that increasing age was associated with a poorer response to RF denervation.</li><li>○ In clinical practice every patients’ response to the treatment is assessed. NICE replied that the assessment of responsiveness post-administration should be a part of routine practice of any intervention.</li><li>○ In clinical practice the injections are provided with ongoing multimodal support. NICE replied that the review protocol included also combinations of treatment but no such trials were identified relevant to the review.</li><li>○ The assessment of responsiveness post-administration should be a part of routine practice of any intervention. Indeed, the duration of pain relief following radiofrequency denervation is uncertain. Data from randomised controlled trials suggests relief is maintained for at least 6-12 months but no study has reported longer term outcomes. The NICE and Belgian GDG agreed that a research recommendation is required to inform long term (&gt;2years) outcomes from RF ablation, beyond the timeframe in the included studies.</li></ul></li></ul>
<hr/> <b>Costs (resource allocation)</b>	<ul style="list-style-type: none"><li>• In Belgium, there is only reimbursement for RF denervation after a positive diagnostic medial branch block.</li><li>• The single economic evaluation on RF denervation compared with sham, reported higher costs with RF denervation, but this study did not report function or pain outcomes, it is therefore difficult to determine whether or not this study reflects the wider body of evidence.</li><li>• The health economic model suggests that RF denervation is cost effective over usual care if the duration of pain relief exceeds 16 months. No conclusion was made on repeated RF denervation but in Belgium, the RF denervation reimbursement is restricted to a maximum of 3 per year.</li><li>• <b>No imaging before the procedure</b> was considered in the model as the GDG experts advised this would not be required and therefore would be an inefficient use of resources.</li><li>• The NICE GDG expressed concern about the potential cost impact of a strong recommendation.</li></ul>

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Recommendation	Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"> <li>Consider assessment for radiofrequency denervation for people with chronic low back pain with suspected facet joint pain when:               <ul style="list-style-type: none"> <li>non-surgical evidence-based multimodal management has not worked for them, and</li> <li>the main source of pain is thought to come from structures innervated by the medial branch nerve and</li> <li>they have moderate or severe levels of localised back pain (rated as 5 or more on a numeric rating scale (NRS 0-10)) at the time of referral.</li> </ul>               Imaging for people with low back pain with specific facet joint pain is NOT a prerequisite for radiofrequency denervation.             </li> </ul>	Weak (RCTs)	Moderate to very low to
<ul style="list-style-type: none"> <li>Only do radiofrequency denervation in people with chronic low back pain after a positive response to a diagnostic medial branch block.</li> </ul>	Expert opinion	Not applicable

**Change in comparison with the NICE recommendations**

Minor changes have been performed. A footnote has been added what is considered behind non-surgical treatment.

- Consider ~~referral for~~ assessment for radiofrequency denervation for people with chronic low back pain with suspected facet joint pain when:
  - non-surgical evidence-based multimodal management has not worked for them, and
  - the main source of pain is thought to come from structures applied by the medial branch nerve and
  - they have moderate or severe levels of localised back pain (rated as 5 or more on a ~~visual analogue~~ numeric rating scale (NRS 1-10)) at the time of referral.

- Only ~~perform~~ do radiofrequency denervation in people with chronic low back pain after a positive response to a diagnostic medial branch block. The reasons underlying these changes are described in Appendix 7.16.

Recommendation for research	Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"> <li>What is the clinical and cost effectiveness of radiofrequency denervation for chronic low back pain in the long term?</li> </ul>	NA	NA



### Change in comparison with the NICE recommendations

- No changes in the wording of the recommendation.
- The reasons underlying these changes are described in Appendix 7.16.

### 3.4.3 Epidural injections

- Epidural injection consists of injecting a therapeutic substance into the epidural space close to the spinal canal which contains notably the spinal nerve roots. There are three administration modes of injections: caudally at the base of the spine, in the midline between the vertebral laminae (interlaminar epidural) or laterally, through the intervertebral foramen (transforaminal epidural, nerve root injection, dorsal root ganglion injection).
- The pharmacological substance most commonly used in epidural injection for the management of sciatica is corticosteroid, with or without local anaesthetic. Anti-TNF (Tumour Necrosis Factor) agents are more recently be proposed in patients with sciatica.

The NICE evidence review can be found on p.67-124 in the full guideline on invasive treatments and the forest plots in Appendix K p.275-302 (<https://www.nice.org.uk/guidance/ng59/evidence>).

A summary sheet in Appendix 7.17 gathered the evidence findings, the NICE GDG considerations, the results of the online survey and the discussion with the Belgian GDG.

### Scientific evidence regarding epidural injections in radicular pain

Twenty randomised controlled trials were included in the review, encompassing several comparisons of single interventions. Given the lack of RCT data for the comparison of steroid versus placebo/sham, the search was extent to cohort study data for this comparison; however no relevant cohort studies were identified. A combined search for the epidurals injections for sciatica review and the spinal injections review identified four Cochrane reviews. None of them was included: one due to the studied population (people with neuropathic pain syndromes and not low back pain) and the others because the stratification of people with low back pain, low back pain with or without sciatica and sciatica was unclear. All relevant

studies included in the reviews were re-extracted by NICE where appropriate, individually assessed and included if they matched the protocol. Two economic evaluations were also identified.

### Scientific evidence for image-guided epidurals injection

SCIATICA PRIMARILY CAUSED BY ( $\geq 70\%$ ) DISC PROLAPSE

(see Tables 45 and 46 in Appendix 7.17)

- Anaesthetic versus sham/placebo (saline): A single study (*fluoroscopy guided injections of 0.75ml of 0.5% bupivacaine*) reported a **short term clinical benefit in leg pain** (low quality; n=64) in favour of sham/placebo, however no difference was found in the proportion of patients reporting a more than 50% reduction in pain (responder criteria; low quality; n=64). No long term data were reported.
- Anti-TNF (mean of 3 doses) versus sham/placebo (saline): A single RCT (*contrast flow/fluoroscopy guided injections of 0.5-2.5mg or 12.5mg etanercept*) reported a **clinical benefit in leg pain** (very low quality; n=37) **at short term** in favour of anti-TNF. Another study reported the adverse events but found none in both groups (low quality; n=24) at both time points.
- Anti-TNF + anaesthetic versus anaesthetic: A single study (*fluoroscopy guided injections of 4mg etanercept + 0.5% bupivacaine versus 0.5% bupivacaine + saline*) found no difference in short term pain (low quality; n= 56) and function (moderate quality; n=56), nor in healthcare utilisation (surgery and >20% opioid use or cessation non-opioids; low quality; n=56-23) or in responder criteria (>50% reduction in pain at short and long term; low quality; n=56).
- Steroid + anaesthetic versus placebo/sham: **A clinical benefit** of the combination of steroids and anaesthetics (*fluoroscopy guided injections of 1.75ml triamcinolone 40mg/ml + 0.75ml of 0.5% bupivacaine*) compared to placebo (saline) was found for **(leg) pain** (1 RCT; moderate quality; n=65) and for **responder criteria** (number of patients reporting >50% pain reduction; high quality; n=65)). However, no difference in function (ODI 0-100; low-moderate quality; n=160) was found at both time points.



- **Steroid + anaesthetic** versus anaesthetic. Within this comparison, 3 different approaches of epidural injections were found: transforaminal, caudal and interlaminar approach.
  - Studies on the transforaminal approach (4 RCTs; *fluoroscopy-guided injections of methylprednisolone/triamcinolone/betamethasone + bupivacaine/lidocaine*) revealed no differences in pain (3-1 RCTs; moderate-high quality; n=233-120), function (2-1 RCTs; low-moderate quality; n=178-120) and healthcare utilisation (opioid intake; 1 RCT; moderate quality; n=120) at both time points. **Two outcomes of responder criteria** (number of patients reporting a >50% pain reduction at short term; 3 RCTs; very low quality; n=233 and number of patients who underwent surgery at long term; 1 RCT; low quality; n=55) showed a **clinical benefit** in favour of the combination of steroids and anaesthetics. Other outcomes of responder criteria (function improvement; 1 RCT; low-moderate quality; n=120) revealed no differences.
  - A study on the caudal approach (1 RCT; *fluoroscopy-guided injections of 6mg betamethasone or 40mg methylprednisolone + 0.5% lidocaine*) showed no difference in pain (low quality; n=353-120), function (low-moderate quality; n=120), healthcare utilisation (opioid intake; moderate quality; n=120) and responder criteria (>50% improvement in pain or function; moderate-low quality; n=120) at both time points.
  - One study reported on the interlaminar approach (1 RCT; *fluoroscopy-guided injections of 80mg methylprednisolone + 0.5% lidocaine*) and found a **clinical benefit in responder criteria** (>50% pain reduction; very low quality; n=69) in favour of the combination of steroids and anaesthetics, both at short and long term. No differences in long-term healthcare utilisation (additional injections; very low quality; n=69) and in adverse events (complications; very low quality; n=69) were found.
- **Steroid + anaesthetic** versus anti-TNF + anaesthetic. A single RCT (*fluoroscopy-guided injections of 60mg methylprednisolone + 0.5% bupivacaine*) reported a short term **clinical benefit in pain** (moderate quality; n=54) **and function** (moderate quality; n=54) in favour of the combination of steroids and anaesthetics. However, no differences were found for responder criteria (>50% pain reduction; low quality; n=54) and healthcare utilisation (surgery; low quality; n=54 and medication reduction; moderate quality; n=54-23).
- **Steroid + anaesthetic** epidural versus combination of non-invasive interventions (pharmacological (Tizanidine, Diclofenac, amitriptyline), manual therapy (traction), physiotherapy (TENS, short wave diathermy) and biomechanical exercises (Back extension exercises)). A single RCT (injections of saline + 2% xylocaine + 2ml triamcinolone acetate) reported a **long-term clinical benefit in QoL** (numerical pain intensity of HRQoL; moderate quality; n=100), **pain** (moderate quality; n=100), **function** (moderate quality; n=100), **responder criteria** (complete pain relief; high quality; n=102) in favour of the combination of steroids and anaesthetics. No difference was found for psychological distress (BDI 0-63; moderate quality; n=100). No short term data were reported.

#### SCIATICA PRIMARILY CAUSED BY NON-DISC LESION

- **Steroid + anaesthetic** versus anaesthetic: Three studies compared steroids and anaesthetics (*fluoroscopy-guided injections of triamcinolone/betamethasone/methylprednisolone + lidocaine*) to anaesthetics alone and found **no clinical differences for all reported outcomes**: QoL (at short term; 1 RCT; low quality; n=386), pain (both time points; 3-2 RCTs; low-moderate quality; n=606-202), function (RMDQ 0-24; short term; 1 RCT; very low quality; n=386 and ODI 0-100; both time points; 1 RCT; moderate quality; n=100), responder criteria for pain (>30% reduction; short term; 1 RCT; low quality; n=386 and >50% reduction; both time points; 1 RCT; very low quality; n=100) and for function (>30% reduction; short term; 1 RCT; very low quality; n=386 and >50% reduction; both time points; 1 RCT; low-very low quality; n=100), healthcare utilisation (opioid intake; both time points; 1 RCT; moderate-low quality; n=100) and serious adverse events (both time points; 2-1 RCTs; very low-moderate quality; n=500-100).



### SCIATICA PRIMARILY CAUSED BY UNCLEAR SPINAL PATHOLOGIES

- **Steroid + anaesthetic** versus anaesthetic: Four studies compared steroids and anaesthetics (*fluoroscopy-guided injections of methylprednisolone/betamethasone + bupivacaine/lidocaine*) to anaesthetics in a mixed population and found **no clinical differences for all reported outcomes**: pain (VAS 0-10; short term; 2 RCTs; very low quality; n=205 and PPI 0-5; short term; 1 RCT; very low quality; n=69), function (ODI 0-100; short term; 2 RCTs; very low quality; n=263), healthcare utilisation (surgery; both time points; 2-1 RCTs; very low quality; n=127-129 and medication reduction; both time points; 1 RCT; moderate quality; n= 58-24) and adverse events (both time points; 1 RCT; low quality; n=129-124). In 3 of the 4 studies, the transforaminal approach was applied. In the fourth study the approach was not specified.
- **Subanalysis** (see Table 46 in Appendix 7.17), comparing the effectiveness of epidural injections with steroids and anaesthetics to anaesthetics in the three included populations (sciatica caused by disc prolapse, sciatica caused by non-disc lesion and mixed population) revealed some clinical benefits (in responder criteria for >50% pain reduction and a reduced number of patients who underwent surgery) in the population with disc prolapse, although the effects are small, reported in a small number of studies with moderate to very low quality.

### Scientific evidence for non-image guided epidural injections

#### SCIATICA PRIMARILY CAUSED BY (≥70%) DISC PROLAPSE

(see Table 47 in Appendix 7.17)

- **Steroid** epidural versus placebo: Two RCTS reported no short term clinical difference between steroids epidural (injections of methyl prednisolone) and placebo for pain (VAS 1-10; 2 RCTs; moderate quality; n=174 and McGill 1-5; 1 RCT; high quality; n=156 and McGill 0-50; 1 RCT; high quality; n=156), function (ODI/RMDQ 0-100; 2 RCTs; low quality; n=221) and (minor) adverse events (2 RCTs; low quality; n=232). No long term data were reported.
- **Steroid + anaesthetic** epidural versus combination of non-invasive interventions (self-management + static and dynamic exercises): A single study (*injections of methyl prednisolone + bupivacaine*) reported only one outcome: no clinical difference for pain (VAS 1-10; short term; moderate quality; n=139) was found.
- **Steroid + anaesthetic** epidural versus pharmacological treatment (NSAIDs): A single study (injections of methyl prednisolone + prilocaine) reported no clinical differences in pain, function and healthcare utilisation (paracetamol use; low quality; n=64). No long term data were reported.
- **Steroid + anaesthetic** epidural versus pharmacological treatment (combination of NSAIDs + opioids+ muscle relaxants): A single study (*injections of methyl prednisolone + xylocaine*) reported no clinical differences in pain (VAS 1-10; at both time points; very low-low quality; n=50) and long term (minor) adverse events (low quality; n=50).
- **Steroid + anaesthetic** epidural versus anaesthetic: No critical outcomes were reported for this comparison. A single RCT (*injections of carbocaine + hydrocortisone*) reported no clinical differences in responder criteria (>75% pain reduction at both time points; very low quality; n= 30) and in healthcare utilisation (number of patients who underwent surgery; at long term; very low quality; n=30).
- **Steroid + anaesthetic** epidural versus anaesthetic epidural: One RCT compared different modalities of steroids and anaesthetics and found following results (no long term data were reported):
  - Dexamethasone + Bupivacaine vs anaesthetic: no differences in short term pain (VAS 1-10; moderate quality; n=105) and healthcare utilisation (use of physiotherapy; low quality; n=82).
  - Triamcinolone + Bupivacaine vs anaesthetic: a clinical benefit in short term pain (VAS 1-10; moderate quality; n=107) and healthcare utilisation (use of physiotherapy; low quality; n=84).
  - Methyl prednisolone vs bupivacaine: a clinical benefit in short term pain (VAS 1-10; moderate quality; n=105) and healthcare utilisation (use of physiotherapy; low quality; n=81). Another RCT (injections of carbocaine + hydrocortisone) found no differences in healthcare utilisation (number of patients who underwent surgery; very low quality; n=33) and in responder criteria (>75% pain reduction: at both time points; very low quality; n=33).



## SCIATICA PRIMARILY CAUSED BY UNCLEAR SPINAL PATHOLOGIES

(see Table 48 in Appendix 7.17)

- Steroid epidural versus placebo: A single study reported only one outcome: no long term difference in healthcare utilisation (discontinuation of analgesics; very low quality; n=51) was found between steroids epidurals (methyl prednisolone) and placebo. No short term data were reported.
- Steroid epidural versus usual care: A single study (injections of triamcinolone) reported a short term **clinical benefit in leg pain** (NRS 1-10; low quality; n=63) **and function** (RMDQ 0-24; low quality; n=63) in favour of steroids. However, no difference was anymore seen at long term. Other measures of pain severity showed no differences compared to usual care (back pain, pain during day/night, overall pain; low quality; n=63), at both time points. Regarding QoL, some conflicting results were found: at short, the majority of the subdomains of SF-36 0-100 showed a clinical benefit in favour of steroids, however a harmful affect was seen for subdomain vitality and no difference for emotional well-being. At long term, no differences were found for 3 subdomains (mental composite, vitality and pain) and a harmful effect for emotional well-being (low-moderate; n=50).
- Steroid epidural versus anaesthetic epidural: The single RCT (injections of depromedrone) reported only one outcome: no difference was found in patients who underwent back surgery (healthcare utilisation) at short term. No long term data were reported.
- Steroid + anaesthetic epidural versus placebo: A single RCT (injections of triamcinolone acetamide + bupivacaine) reported no differences compared to placebo for (leg or back) pain (VAS 1-10; at both time points; moderate quality; n=228), function (ODI 1-100; at both time points; moderate-low quality; n=228), psychological distress (HAD 0-21 anxiety and depression; at both time points; low-moderate quality; n=228), healthcare utilisation (mean analgesic use/week, referred for surgery, further physiotherapy, referral to pain management services, further epidurals; moderate-low quality; n=228), responder criteria (>75% leg or back pain reduction; at short term; low quality; n=228) and (minor) adverse events (low quality; n=228).

- Steroid + anaesthetic epidural versus anaesthetic epidural: A single RCT (injections of methyl prednisolone + lignocaine) reported only one outcome: no difference was found in healthcare utilisation (reduced drug intake; very low quality; n=29 and back surgery; very low quality; n=30) compared to anaesthetic epidural.
- A sub analysis, comparing the efficacy of steroids epidural versus placebo in the different populations, was hampered by the lack of reported outcomes. In the mixed population only healthcare utilisation was reported and this outcome was not reported in the 2 RCTs on patients with disc prolapse.

### Economic evidence

- One cost-utility analysis on the comparison of non-image guided epidural injections of steroids + local anaesthetics versus placebo found that the epidural injections of steroids was not cost effective compared to placebo for adults with low back pain and sciatica (ICER: £44,701 per QALY gained). This analysis was assessed as partially applicable with potentially serious limitations.
- One cost-effectiveness analysis on the comparison of non-image guided steroids epidural versus usual care found that steroids are more costly and more effective than placebo in adults with sciatica (ICER: £60 per 1 point improvement in NRS back pain score). This analysis was assessed as partially applicable with potentially serious limitations.





**Conclusions**

**No difference was found in the majority of comparisons except a clinical benefit at short term on pain with imaged-guided epidural injections, notably for the combination of steroid and anaesthetic compared to placebo for patient with sciatica primarily caused by (≥70%) disc prolapse. In population with sciatica caused by non-disc lesion or with unclear spinal pathologies, only comparison between a combination of steroid and anaesthetic versus anaesthetic was analysed and no difference was found for any outcome. In non-imaged guided epidural injections, no clinical benefit was observed for patient with patient with sciatica primarily caused by (≥70%) disc prolapse but no study comparing the combination of steroid and anaesthetic versus placebo was found. Inconsistent results was showed for people with unclear spinal pathologies. Regarding epidural injections using anti-TNF, no evidence was found for non-image guided anti-TNF and limited evidence showed a positive effect of image-guided anti-TNF epidurals on pain and function but from three studies not pooled together because different comparisons were used). The two economic analysis included in the review focus on non-image guided epidural injections and suggested that they are not cost-effective compared to placebo.**

**Other considerations regarding epidural injections in radicular pain**

GRADE Factors	Comments
<b>Balance between clinical benefits and harms</b>	<ul style="list-style-type: none"> <li>• The Belgian GDG acknowledged that there was few evidence of some clinical benefit at short term on pain with the epidural injection. This results concern mainly image-guided epidurals of local anaesthetic and steroid versus placebo/sham. There was insufficient/lack of evidence for effectiveness to support epidural injections using anti-TNF.</li> <li>• The GDG agreed with NICE that epidural injection is a relatively safe and routinely used procedure:</li> <li>• It was noticed that according to NICE, the evidence suggested that epidural injection of local anaesthetic and steroid may reduce the number of people who would require surgical intervention. This evidence was reinforced by evidence from 2 trials that were included in the spinal decompression review that compared decompression to epidurals showing that 50% of people who had an epidural did not go on to have surgery.</li> <li>• The Belgian GDG stressed that radicular symptoms usually improve over the course of a few months in the majority of people without treatment. Given that, it is important to identify the patient who could receive true benefit with epidural injections. Most of the RCT</li> </ul>



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evidence came from people with acute and moderately severe radicular pain (rated as 5 or more on a numeric rating scale from less than 3 months), primarily caused by disc prolapse.

- In patients with chronic radicular pain due to a stenotic condition, there was no evidence that epidural injections of local anaesthetic and steroid were effective. The Belgian GDG disagreed however with the NICE proposition to make a recommendation against using epidurals in people with claudicant leg symptoms caused by central spinal canal stenosis. Several reasons were provided for explaining this disagreement:
  - NICE based this recommendation on studies mainly comparing steroids + anaesthetic versus anaesthetic in patients with stenosis. But the similar comparison in patients with disc prolapse provided the same results and did not preclude a potential efficacy of the injections. NICE mentioned this recommendation is mostly based on a consensus.
  - The terms "central spinal stenosis" is considered as incorrect because spinal stenosis contains several subgroups, including some with mixed pathologies (central, lateral and/or foraminal stenosis, severe or moderate, unilateral or bilateral, static or dynamic symptoms). Then, a global/systematic/strong recommendation cannot be drawn from these data and "central" is not accurate.
  - In patients with severe neurogenic claudication, surgery is the first option. However, in chronic, elderly patients who are not suitable for surgery, epidural injections could be an option.
  - Given the relative safety of epidural injection, an absence of evidence of clinical benefit should not lead to formulate a strong recommendation against the intervention but rather not to formulate any recommendation.

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**Quality of evidence**

- The overall quality, based on 20 RCTs, ranged from moderate to low quality due to risk of bias caused by selection or performance bias, small sample sizes and imprecision
- Evidence showing an effect of anti-TNF (image-guided) was only from single studies, which mostly had small sample sizes. Some of the other studies had incomplete reporting of outcome data (for example, no standard deviations were reported for some outcomes and 1 study only had data for 1 participant in the comparison arm). This also meant that the evidence was rated as being at high risk of bias and so overall the confidence in the findings is very low.
- The economic evaluations were assessed as partially applicable with potentially serious limitations.

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**Values and preferences**

- In the Belgium context, where specialised physicians are directly accessible for patients, even within 3 days after the onset of pain, it appears important to specify that an epidural injection is an option for acute radicular pain but does not concern the first week after the pain onset.
  - The Belgian GDG acknowledged there was limited evidence for a difference in effectiveness of image guided compared to non-image guided epidural injections from the NICE review. In Belgium however, since the 1st November 2016, only the transforaminal injections, standardized as image-guided are reimbursed. Therefore, the suggested research question from NICE on the image-guided injections is useless in the Belgian context.
  - The Belgian GDG discussed the effectiveness of giving multiple / subsequent epidural injections and mentioned that the reimbursement criteria edited since the 1<sup>st</sup> November 2016 restricted the number of epidural injections to a maximum of 3 injections per year.
  - The patients' needs and preferences are a crucial element to include in the shared-decision making process. In patients with severe radicular pain, it is important to be able to offer an option for managing their pain.
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**Costs (resource allocation)**

- The economic evidence found by NICE suggested that epidural injections were not cost-effective compared to placebo. However, if epidural injections allow to reduce the number of people with severe sciatica requiring surgical intervention; this would generate some cost savings.

**Recommendations**

**Strength of Recommendation**

**Level of Evidence**

- Consider epidural injections of local anaesthetic and steroid\* in people with (sub)acute (at least 2-3 weeks) and severe\*\* radicular pain.  
 \* Since the 1<sup>st</sup> of November 2016, only image-guided radicular and transforaminal injections are reimbursed in Belgium.  
 \*\*Severe radicular pain should be defined on an individual basis with the patient but a score rated as 5 or more on a numeric rating scale (NRS 0-10) could be considered as a reasonable yardstick.

Weak (RCTs)

Moderate to very low

**Change in comparison with the NICE recommendations**

Minor changes have been proposed by the Belgian GDG regarding the first clinical recommendations on epidural injections proposed in the NICE 2016 guidelines. The second NICE recommendation on the same topic was not retained in the Belgian version for clarity.

36. Consider epidural injections of local anaesthetic and steroid in people with (sub)acute (at least 2-3 weeks) and severe radicular pain sciatica (rated as 5 or more on a numeric rating scale (NRS 1-10)).

~~37. Do not use epidural injections for neurogenic claudication in people who have central spinal canal stenosis~~

The NICE research proposition R3.” What is the clinical and cost effectiveness of image guided compared to non-image guided epidural injections for people with acute sciatica?” was removed from the Belgian guideline.

More detailed on the reasons underlying these changes are described in Appendix 7.17.

**3.4.4 Surgery and prognostic factors**

Surgery for low back pain and sciatica is most commonly carried out when more conservative treatments have failed. As with most major invasive procedures, surgery to manage back pain and sciatica carries with it an inherent risk of serious harm.

For surgery in people with low back pain, a number of prognostic factors are thought to be linked to better or worse response to surgery. These include a history of previous spinal fusion surgery, smoking status, BMI and psychological distress. In people with suspected sciatica however, the prognostic factors for response to surgery are thought to be distinct and may be more affected by the presence of radicular symptoms and presence of pathology on imaging.

The NICE evidence review can be found on p.125-137 in the full guideline on invasive treatments and the forest plots in Appendix K p.302-305 (<https://www.nice.org.uk/guidance/ng59/evidence>).

A summary sheet in Appendix 7.18 gathered the evidence findings, the NICE GDG considerations, the results of the online survey and the discussion with the Belgian GDG.



Two research questions were included in the review.

**Scientific evidence regarding the question “Does history of previous fusion surgery, smoking status, BMI or psychological distress<sup>b</sup> predict response to surgery in people with low back pain with or without sciatica who have failed to respond to appropriate conservative therapy?”**

#### SMOKING

- Low quality evidence from a single cohort study (population with spinal stenosis with or without sciatica) with a multivariable analysis, showed smoking status was a prognostic factor after adjusting for duration of symptoms in predicting improvement in function after surgery (standard open decompressive laminectomy compared to non-operative treatment of usual care), favouring not smoking, in people with low back pain.

#### BMI > 30

- Very low quality evidence from a single cohort study (LBP with or without sciatica) with multivariable analysis gave some indication that a BMI greater than 30 may be a prognostic factor in predicting poorer response to surgery (surgery not defined) in terms of improving function in people with low back pain after adjusting for duration of complaints before surgery. This was highly imprecise with an adjusted odds ratio of 0.79 [0.21, 2.97].

#### PSYCHOLOGICAL DISTRESS

- Low-very low quality evidence from a single cohort study (LBP with or without sciatica) with multivariable analysis, suggested that psychological distress was a prognostic factor in predicting response to surgery in terms of improving back pain after adjusting for duration of

complaints before surgery (surgery not defined), with lower levels of distress predicting better outcome, in people with low back pain or sciatica.

#### HISTORY OF PREVIOUS FUSION SURGERY

- No relevant evidence was identified.

**Scientific evidence regarding the question “Does image concordant pathology or presence of radicular symptoms predict response to surgery in people with suspected sciatica?”**

#### RADICULAR SYMPTOMS

- Very low quality evidence from a single cohort study (LBP with or without sciatica) with multivariable analysis suggested presence of radicular symptoms was a prognostic factor for predicting the response to surgery (surgery not defined) (leg pain) at less than or equal to 4 months after adjusting for duration of symptoms.
- Low-very low quality evidence from 4 cohort studies with multivariable analyses, suggested presence of radicular symptoms was a prognostic factor in predicting response to surgery (function at 4y; leg pain at 12 months; function at 1y; 50% improvement in pain in 1y; 30% and 50% improvement in function in 1y) at greater than 4 months in people with sciatica after adjusting for duration of symptoms, duration of complaints before surgery and duration of pain. This evidence indicated that greater radicular symptoms / higher leg pain scores indicated better response to surgery.

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<sup>b</sup> Psychological distress is largely defined as a state of emotional suffering characterized by symptoms of depression (e.g., lost interest; sadness; hopelessness) and anxiety (e.g., restlessness; feeling tense) (Mirowsky and Ross 2002) (on Internet). This concept is not defined by NICE 2016.



IMAGE-CONCORDANT PATHOLOGY

- No relevant evidence was identified.

**Economic evidence**

- No relevant economic evaluations were identified.

**Conclusions**

**There is a paucity of evidence to effectively explore the effect of prognostic factors on the outcomes of people with low back pain or sciatica following surgery. There is a trend towards worse outcomes in the groups of people who has prognostic factors identified, e.g. smoking and high BMI. Based on the evidence, no answer can be provided to the second question about the link between image concordant pathology or presence of radicular symptoms and prediction response to surgery in people with suspected sciatica.**

**Other considerations regarding prognostic factors and surgery**

GRADE Factors	Comments
<b>Balance between desirable and undesirable effects</b>	<ul style="list-style-type: none"> <li>• The Belgian GDG was aware that only evidence for the outcomes of pain and function was available.</li> <li>• Differences in surgical outcomes could possibly be due to the surgical technique rather than the prognostic factor (despite adjustments for confounders in the multivariate analyses).</li> <li>• There was insufficient evidence to suggest that smoking and obesity reliably impacted the prognosis for patients undergoing surgical treatment. It was however acknowledged that weight loss and smoking cessation have public health benefits and therefore should be encouraged.</li> <li>• The NICE GDG mentioned that there may be other factors, for example, age and the presence of co-morbidities, not identified in the protocol.</li> <li>• It was agreed that the prognostic factors identified should not preclude a surgical opinion where the benefits of surgery might outweigh the potential risks.</li> </ul>
<b>Quality of evidence</b>	<ul style="list-style-type: none"> <li>• The quality of the evidence ranged from low to very low.</li> </ul>
<b>Values and preferences</b>	<ul style="list-style-type: none"> <li>• The NICE GDG agreed that using the limited evidence to deny treatment to certain people would be unethical.</li> <li>• The Belgian GDG discussed the relevance of the NICE recommendation “Do not allow a person’s BMI, smoking status or psychological distress to influence the decision to refer them for surgical opinion for sciatica”. Based on the possible confusing</li> </ul>



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interpretation of the recommendation and the lack of added-value, it was decided to **remove this recommendation in the Belgian guideline**. Following issues were mentioned to argue this decision:

- It was not clear if these prognostic factors influence the decision taken by the surgeon to perform surgery or if these factors only could influence the decision to refer the patient to the surgeon.
- In Belgium, there is no gatekeeper, every patient can go directly to the surgeon, without a mandatory referral.
- The decision to perform surgery should be a process of shared decision making of the benefits and risks
- BMI, smoking or psychological distress should not be used to deny people from surgery for low back pain or radicular pain.
- Other articles were mentioned which emphasised the important and recognized influence of psychosocial outcomes
- In spite of the poor evidence, we know that there are people with psychosocial risk factors that have worse outcomes of surgery. Given the poor evidence, such recommendation should simply not be made and it should be at the discretion of the care provider to judge.
- This recommendation is valid if and only if the surgeon takes these risk factors into account before making a decision. As formulated, it could suggest that these factors are not important to assess.
- It should be clear that "surgical opinion for radicular pain" is not the same as "surgery for radicular pain". Before any invasive treatment, risk factors need to be assessed.

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**Costs (resource allocation)**

- No relevant economic evaluations were identified.
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**Change in comparison with the NICE recommendations**

- The NICE recommendation: "Do not allow a person's BMI, smoking status or psychological distress to influence the decision to refer them for surgical opinion for sciatica" has been removed in the Belgian guideline.
- The reasons underlying these changes are described in Appendix 7.18.

**3.4.5 Disc replacement**

Disc replacement, or spine arthroplasty, is an operation which replaces intervertebral units with artificial discs that can act as a functional prosthetic replacement. The aim is to remove the painful disc. Single discs can be replaced, or alternatively, several levels can be replaced during the same surgery. The indications and rationale are similar to those of spinal fusion but by contrast with spinal fusion, the disc arthroplasty preserves movement.

The NICE evidence review can be found on p.138-156 in the full guideline on invasive treatments and the forest plots in Appendix K p.306-311 (<https://www.nice.org.uk/guidance/ng59/evidence>).

A summary sheet in Appendix 7.19 gathered the evidence findings, the NICE GDG considerations, the results of the online survey and the discussion with the Belgian GDG.



### Scientific evidence regarding disc replacement in low back pain and radicular pain

A search was undertaken by NICE for randomised trials comparing the clinical and cost effectiveness of performing disc replacement surgery in people with low back pain. Five randomised controlled trials were included in the review; 2 of the studies were published as multiple papers. All studies included people with low back pain with or without sciatica, and compared disc replacement to other treatment. Four studies compared disc replacement to spinal fusion while 1 compared disc replacement to a 3-element MBR programme. The search was extended by NICE to cohort studies due to insufficient evidence and 2 further studies were included. Two economic evaluations were identified: one on total disc replacement versus fusion and one on total disc replacement versus multidisciplinary rehabilitation.

### Disc replacement versus spinal fusion in patients with LBP with or without sciatica

- Total disc replacement versus anterior lumbar interbody fusion: A clinical benefit for the QoL SF-36 physical component summary score was found at short term (<4 mo) and at long term (at 1y and at 2y) in favour of disc replacement but not for the SF-36 mental component summary score (both at short term and at long term) (SF-36 0-100; 1 RCT; low to very low quality; n=577). No clinical differences between disc replacement and spinal fusion were found for pain (back and leg pain, NRS 0-10; 1 RCT; low to very low quality; n=577) and for function (ODI 0-100; 1 RCT; very low quality; n=577) both at short term and long term. The number of patients who reported adverse events was higher in the disc replacement group (only reported at short term, 1 RCT; low to very low quality; n=577) but no differences were found in number of reoperations (at 2 y; low to very low quality; n=577).
- Total disc replacement versus posterior lumbar interbody fusion: A clinical benefit for QoL was shown at 1y in favour of disc replacement but not anymore at 2y (EQ-5D 0-1; 1 RCT; low to very low quality; n=152). Similar to the anterior approach, no clinical difference was found for function (ODI 0-100; 1 RCT; very low quality; n=152) and pain (back and leg pain; VAS 0-10; 1 RCT; low to very low quality; n= 152).

No clinical difference was found for the reoperation outcome, only a lower number of device-related reoperations were found at 5y in the disc replacement group (1 RCT; very low quality; n=152). No short term data were reported.

### Disc replacement versus 3-elements MBR (multidisciplinary biopsychosocial rehabilitation programme with cognitive, physical and education components) in patients with LBP without sciatica

- A single study reported a clinically important benefit of disc replacement for QoL (EQ-5D 0-1 and SF-36 0-100 physical component; low to very low quality; n=172) in the long term (at 1y and at 2y) but not for the SF-36 0-100 mental component (low quality; n=172). Also a benefit of disc replacement was shown for back pain severity in the long term (at 1y and at 2y) (VAS 0-10; low to very low quality; n=172). There was no clinical difference for function in the short or longer term (ODI 0-100; low to very low quality; n=172). No short term data were reported for QoL and pain.

### Economic evaluation

- One cost-utility analysis found that total disc replacement was dominant (less costly and more effective) compared to spinal fusion in people with low back pain with or without sciatica. This study was partially applicable with potentially serious limitations.
- One cost-utility analysis found that total disc replacement was cost-effective compared to multidisciplinary rehabilitation (ICER: £9,544 per QALY gained). This study was partially applicable with potentially serious limitations.
- This economic evaluation was assessed as partially applicable with potentially serious limitations: The real extent of uncertainty around the conclusion could not be assessed as the probabilistic sensitivity analyses were conducted using societal costs and the 2 comparators were not considered cost effective, therefore disc replacement might have been compared to cost-ineffective interventions and that could explain why it is cost effective.



## Conclusions

**Compared to spinal fusion (anterior or posterior), evidence showed a clinical benefit at short and long term for disc replacement in some components of quality of life but no difference for pain, function and other components of quality of life. The number of patients who reported adverse events was higher in the disc replacement group. Compared to 3-elements MBR, evidence showed a clinical benefit for disc replacement at long term in pain and some components of quality of life but no difference for function and other components of quality of life. The economic analysis suggested that disc replacement was cost effective compared to spinal fusion and multidisciplinary rehabilitation, two comparators judged as not effective.**

## Other considerations regarding disc replacement in low back pain and radicular pain

GRADE Factors	Comments
<b>Balance between clinical benefits and harms</b>	<ul style="list-style-type: none"><li>• The Belgian GDG acknowledged that there was some evidence of clinical benefit for disc replacement compared to other interventions (spinal fusion and MBR) but the confidence of the results was low.<ul style="list-style-type: none"><li>○ Evidence for the comparison of disc replacement versus fusion was limited, with outcomes analysed from 2 RCTs only.</li><li>○ The comparison between disc replacement and 3-elements MBR could be inappropriate, as people with low back pain would often take part in a MBR programme before undergoing surgery.</li></ul></li><li>• The Belgian GDG agreed with the NICE GDG concern that the benefits observed came mainly from a study comparing disc replacement to anterior lumbar interbody fusion, a procedure that is not commonly performed due to perceived lack of effectiveness. The comparison with a MBR programme was also considered as inappropriate, as people with low back pain would often take part in a MBR programme before undergoing surgery. The GDG noted that evidence for this comparison came from a single RCT.</li><li>• The risk of severe adverse events with disc replacement is stressed by the Belgian GDG. It was noted that a high occurrence of adverse events was observed in studies not powered to detect harm but could be reflective of the risk observed in practice.</li><li>• Despite seeing some signs of benefit from disc replacement compared to other interventions, the GDG felt the risk of harms associated with disc replacement outweighed the potential benefits.</li></ul>
<b>Quality of evidence</b>	<ul style="list-style-type: none"><li>• Evidence from 3 RCTS, quality ranged from low to very low, mainly downgraded for high risk of bias due to incomplete blinding, high drop-out rates and baseline differences between the groups for several characteristics (including baseline values of critical outcomes).</li><li>• The GDG expressed particular concern over the high number of patients that dropped out of the disc replacement group during the trial comparing 3-element MBR versus disc replacement (30% versus 17%). As the trial featured ITT analysis with</li></ul>





	<p>last value carried forward (assuming patients had no improvement after dropout), this raised a concern about data interpretation. The imprecise nature of the outcomes included in this review further contributed to decreasing the GRADE quality rating.</p> <ul style="list-style-type: none"> <li>The GDG raised concerns about the comparators in the included studies as they were either procedures without proven efficacy, or in the case of MBR, would be expected to be offered earlier in the pathway as an option prior to surgery.</li> </ul>
<b>Values and preferences</b>	<ul style="list-style-type: none"> <li>The patients' needs and preferences are a crucial element to include in the shared-decision making process. The importance of harm and the balance benefit-risk deserve detailed explanation to the patient.</li> </ul>
<b>Costs (resource allocation)</b>	<ul style="list-style-type: none"> <li>The economic analysis suggested that disc replacement was cost effective compared to spinal fusion and multidisciplinary rehabilitation but serious limitations were associated with this evaluation.</li> <li>The KCE report in 2015 emphasised the lack of difference in efficacy and safety between disc replacement and fusion. There was a recommendation to reimburse spinal disc replacement in line with the current reimbursement for spinal fusion.</li> <li>A while ago reimbursement for lumbar disc prosthesis was achieved (but not for cervical disc prosthesis), then it was considered as a long standing entitlement and this is difficult to turn back.</li> <li>However, the GDG members agree that the NICE recommendation should not be modified due to the limited evidence and the potential risk of harms.</li> </ul>

Recommendations	Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"> <li>Do not offer disc replacement in people with low back pain.</li> </ul>	Strong (RCTs)	Low to very low

### Change in comparison with the NICE recommendations

No change have been proposed by the Belgian GDG regarding the clinical recommendations proposed in the NICE 2016 guidelines.

More detailed on the reasons underlying these changes are described in Appendix 7.19.

### 3.4.6 Spinal fusion

- Spinal fusion is an operation that aims to achieve solid bone union between spinal vertebrae by using the patient's own bone or artificial bone substitutes. The procedure of spinal fusion is a common component part of many types of spinal operation (e.g. deformity correction, tumours removal and fractures treatment). It can also be used as a component part of an operation aiming to decompress the spinal neurological structures. In clinical practice, spinal fusion can sometimes be proposed for the management of severe and persistent low back pain not improved by non-invasive treatments.



- Spinal fusion can be performed according to different surgical approaches to the spine (from the back, the front or the side) with potential differences in the risk of harm.

The NICE evidence review can be found on p.157-184 in the full guideline on invasive treatments and the forest plots in Appendix K p.311-319 (<https://www.nice.org.uk/guidance/ng59/evidence>).

A summary sheet in Appendix 7.20 gathered the evidence findings, the NICE GDG considerations, the results of the online survey and the discussion with the Belgian GDG.

### **Scientific evidence regarding spinal fusion in low back pain and radicular pain**

Nine randomised controlled trials and 1 cohort studies were included in the review. As there was only 1 RCT for the comparison of spinal fusion versus usual care, the search was extended to cohort studies for this comparison as well as spinal fusion versus no surgery for which there were no randomised trials. One cohort study was identified that met the inclusion criteria for fusion versus usual care and was included in the review. One Cochrane review was identified but was not included as the stratification of the people with low back pain, low back pain with/without sciatica and sciatica was unclear, however the individual studies from the Cochrane review were individually assessed and included in this review if they matched the review protocol. One non-randomised study was identified comparing spinal fusion with spinal decompression. Four RCTs were found for the comparison with other non-invasive treatments and 2 RCTs for the comparison with different types of surgery. The results of two RCTs are pooled with previous reported results of the same trial. Two economic evaluations were identified: one on spinal fusion versus 3-elements MBR programme and one on spinal fusion versus total disc replacement. No economic evaluations were identified comparing spinal fusion to no surgery or usual care.

### **Spinal fusion versus usual care (physical therapy, epidural injections and medication) in mixed population (LBP with or without sciatica)**

- A single RCT reported a clinical benefit at long term (2 year) of spinal fusion for pain (VAS 0-10; Mean diff: -1.51 [95%CI -2.09, -0.93], very low quality; n=264) and for function measured by the General Function Score and the Million VAS (low to very low quality; n=264). However, function measured by the ODI 0-100 demonstrated no clinical difference (very low quality, n=264). A greater number of adverse events (complications) and reoperations were seen at 2 year in the spinal fusion group (OR 5.00 [95%CI 2.45, 10.19] and OR 4.12 [95%CI 1.30, 13.10], low quality, n=283). No short term data were reported.
- One cohort study showed no clinical differences found at 1y for quality of life (SF-12 0-100, PCS and MCS; very low quality, n=96), pain (NRS 0-10; very low quality; n=96) and function (ODI 0-100; very low quality; n=96). No short term data were reported.

### **Spinal fusion versus other non-invasive treatments in patients with LBP without sciatica**

- Spinal fusion versus 3-elements MBR programme (exercise, education, cognitive behaviour therapy): Evidence from 3 RCTs showed no clinical difference at long term for pain (at 1y, 2 RCTs; very low quality; n=118), function (at 1 y, 2 RCTs; low-very low quality; n=118 & at 2y; 1 RCT; low quality; n=349), and the majority of the QoL domains (except for general health perception and pain) (1 RCT; low quality; n=246). In addition, there was no difference for healthcare utilisation (unplanned hospital admissions for spinal surgery; GP consultations, practice nurse consultations, GP home visits; practice nurse home visits) (1 RCT; low to very low quality; n=349). No short term data were reported.
- Spinal fusion versus mixed modality exercise: A single RCT comparing spinal fusion with mixed modality exercise (aerobic + biomechanical exercise) demonstrated a clinical benefit in pain at 1y and at 2y (VAS 0-100, very low quality, n=41) and function at 1y and at 2y (ODI 0-100 and JOAS 0-3; very low quality; n=41) in favour of spinal fusion. No short term data were reported.



### **Spinal fusion versus different types of surgery (disc replacement) in mixed population (LBP with or without sciatica)**

- Two RCTs reported no clinical difference in pain (very low quality; n=577-729) and in function (low quality; n=577-729) at short term (3 months) and long term (1y and 2y). In terms of QoL (EQ-5D 0-1 at 1y; 1 RCT; very low quality; n=152 & SF-36 0-100 physical component score at 3mo, 1y and 2y; 1 RCT; low to very low quality; n=577), spinal fusion was shown to be less effective than disc replacement. However, no clinical difference in QoL was found for other measurements (EQ-5D 0-1 at 2y; 1 RCT, low quality; n=152) & SF-36 0-100 mental component score at 3mo, 1y and 2y; 1 RCT, low quality; n=577). Statistically no clinical differences were found for adverse events (mortality, complications) (2 RCTs; low to very low quality; n=577-729) and number of re-operations (very low quality; n=152). However, some conflicting tendencies were noticed: whereas a tendency towards a clinical benefit for fusion was noticed for less complications at 5y (1 RCT; very low quality; n=152), the same study reported more occurrences of surgery at adjacent level at 2y in the spinal fusion group (very low quality; n=152).

### **Economic evidence**

- One cost-utility analysis found that spinal fusion was not cost-effective compared to a 3-elements MBR programme for treating LBP with or without sciatica (ICER: £48,515 per QALY gained). This study was partially applicable with potentially serious limitations.
- One cost-utility analysis found that spinal fusion was dominated (more costly and less effective) compared to total disc replacement in people with low back pain with or without sciatica. This study was partially applicable with potentially serious limitations.

### **Conclusions**

**Most studies encompassed population with and without sciatica (spinal fusion compared to non-invasive treatments focused rather on population without sciatica). Conflicting evidence is observed when spinal fusion is compared to usual care: one RCTs showed some clinical benefits at long term for pain and for function according to certain instruments while a cohort study found no difference. A greater number of adverse events and reoperations were seen in the spinal fusion group. No clinical benefit at long term was showed when spinal fusion was compared to a 3-element MBR programme but a clinical benefit in pain and function was observed with spinal fusion compared to mixed modality exercise. Compared to disc replacement, no difference was found for pain and function at short and long term and results are inconsistent for quality of life and adverse events. Spinal fusion appeared to be less cost-effective than a 3-elements MBR programme or a total disc replacement.**



### Other considerations regarding spinal fusion in low back pain and radicular pain

GRADE Factors	Comments
<b>Balance between clinical benefits and harms</b>	<ul style="list-style-type: none"><li>• The Belgian GDG acknowledged that although a clinical benefit in pain was observed with spinal fusion compared to usual care in one large RCT, the majority of evidence found by NICE was not in favour of this operation in patients with low back pain (with or without radicular pain).</li><li>• Moreover, the GDG stressed the potential harm of spinal fusion for patients in terms of complication and reoperation rate. This broadly out weights the potential benefit of the operation.</li><li>• However, one cannot preclude that there are some rare subgroups of patients (e.g. degenerative anterolisthesis with marked instability, degenerative severe deformities) who can benefit from fusion surgery if well selected and after failed appropriate conservative management. The Belgian GDG considered this exceptions and agree with the NICE proposition to allow spinal fusion in very few cases. Three conditions were formulated by the Belgian GDG for this exception:<ul style="list-style-type: none"><li>○ Surgery might be proposed only in patient with complaints persistent after an evidence-based non-invasive multimodal treatment.</li><li>○ Because the identification of the few patients eligible for spinal fusion is not easy, a multidisciplinary consultation should precede the decision.</li><li>○ Given the limited number of studies from which data could be evaluated and the uncertainties in benefit-risk in this population, an assessment of all spinal fusions in low back pain patients should be systematically organised (national spine registry).</li></ul></li><li>• The Belgian GDG agreed with NICE that further research is needed regarding the role of spinal fusion in patient with low back pain without underlying disease. However, rather than carry out a large, multi-centre randomized trial with sufficient power such as proposed by NICE, a systematic record of the patient data in a national registry is suggested because more feasible in Belgium. The analysis of these data should allow to identify the patients which can benefit of spinal fusion. This is translated in a proposition for further research.</li></ul>
<b>Quality of evidence</b>	<ul style="list-style-type: none"><li>• The quality of evidence from 9 RCTS ranged from low to very low, mainly downgraded for high risk of bias and uncertainty of the effect size.</li><li>• In the study comparing spinal fusion versus usual care, population was randomised to more of the same treatment (physiotherapy and advice) or surgery. The NICE GDG discussed that the control group appeared to be a severely disadvantaged group that had not been offered a new treatment and had been selected on the grounds of strict inclusion criteria of mandatory sick leave or equivalent disability for a year, as well as previous failure of non-surgical treatments. The NICE GDG felt that this could result in a risk of bias due to a 'negative contextual effect' and also raised concerns that the study only reported outcomes at 2 years. The surgical group in this study was also much larger than the usual care group (n=211 versus n=72). It was also noted that Million Visual Analogue Scale (MVAS) used to measure function in the study reported a final score of 0-100 whereas commonly the MVAS comprises of 15 questions with a scale of 0-150.</li><li>• In the comparison to other treatments (3-elements MBR programmes with varying intensity and mixed modality exercise), one study in particular was noted by the NICE GDG to be a very small trial and used a less intensive comparator than the</li></ul>



	<p>other trials. The small benefit in pain and function favouring spinal fusion reported in this study was not observed in the larger studies with more intensive comparator interventions.</p> <ul style="list-style-type: none"> <li>• In the comparison with other types of surgery (total disc replacement), the larger of the 2 studies was an industry funded investigational device exemption trial for an artificial lumbar disc and had an incomplete outcome data rate of 15.1% in the control arm compared to 5.7% in the disc replacement group which cast doubt on the results reported.</li> <li>• The economic evidence was assessed as partially applicable with potentially serious limitations.</li> </ul>
<b>Values and preferences</b>	<ul style="list-style-type: none"> <li>• The patients' needs and preferences are a crucial element to include in the shared-decision making process. The importance of harm and the balance benefit-risk deserve detailed explanation to the patient.</li> </ul>
<b>Costs (resource allocation)</b>	<ul style="list-style-type: none"> <li>• Two economic analysis showed that spinal fusion are less effective and more costly than a 3-elements MBR programme or disc replacement. Both studies were assessed by NICE partially applicable with potentially serious limitations.</li> </ul>

Recommendations	Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"> <li>• Do not offer spinal fusion for people with low back pain unless within following preconditions:               <ul style="list-style-type: none"> <li>○ after failure of a non-surgical evidence-based multimodal management, and</li> <li>○ after evaluation in a multidisciplinary consultation and</li> <li>○ preferably with data registration in a register</li> </ul> </li> </ul>	Strong (RCTs & cohort studies)	Low to very low

Recommendation for research	Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"> <li>• Based on an analysis of the register of patients who underwent spinal fusion for low back pain, in which patient subgroups spinal fusion could be offered as a surgical option</li> </ul>	NA	NA



### Change in comparison with the NICE guidelines

Changes have been proposed by the Belgian GDG regarding the clinical recommendations proposed in the NICE 2016 guidelines.

40. Do not offer spinal fusion for people with low back pain unless ~~as part of a randomised controlled trial~~ within following preconditions:

- after failure of a non-surgical evidence-based multimodal management and
- after evaluation in a multidisciplinary consultation and
- preferably with data registration in a register

More detailed on the reasons underlying these changes are described in Appendix 7.20.

#### 3.4.7 Spinal decompression

- Spinal decompression aims to remove pressure on the nervous structures within the spinal column. Compression may be due to an abnormality of vertebral body, disc and ligaments at the front, facet joints and foramen at the sides, and the lamina and ligaments at the back. According to NICE, the most common cause of the narrowing of the spinal canal is degenerative lumbar disease i.e. spondylosis.
- There have been other techniques for removing the disc material, including laser, thermo-coagulation radiofrequency and many others. No review of the comparative effectiveness of these methods was performed and NICE mentioned that this has to be determined by the individual surgeon and by clinical appropriateness.

The NICE evidence review can be found on p.185-225 in the full guideline on invasive treatments and the forest plots in Appendix K p.320-338 (<https://www.nice.org.uk/guidance/ng59/evidence>).

A summary sheet in Appendix 7.21 gathered the evidence findings, the NICE GDG considerations, the results of the online survey and the discussion with the Belgian GDG.

### Scientific evidence regarding spinal decompression in radicular pain

Nine randomised controlled trials (published in 14 papers) were included in the review. The search was extended to cohort studies for comparisons where there was insufficient evidence (specific forms of decompression versus a valid comparator) and 4 further studies were included (published in 6 papers). Four techniques were analysed with different comparators: discectomy versus usual care (2 RCTs and 2 cohort studies), versus combined intervention (4 RCTs), versus fusion (1 cohort study); percutaneous disc decompression versus usual care (1 RCT); plasma disc decompression versus other treatment (epidural steroid injection) (1 RCT) and laminectomy versus usual care (1 RCT and 1 cohort study). All studies concerned patients with sciatica. Three economic evaluations were identified with the relevant comparison and have been included in this review.

**Discectomy versus usual care (conservative treatment to resume daily activities; or active physical therapy, education, NSAIDs)** (see Table 49 in Appendix 7.21)

- **Quality of life**
  - At ≤4 months, clinical benefit for discectomy was shown for quality of life (SF-36 bodily pain, physical function (2 RCTs; very low quality; n=696), mental health, vitality and general health (1 RCT; low quality; n=281) and for EQ-5D (1 study, low quality, n=283).
  - At >4 months-1y, clinical benefit for discectomy was shown in quality of life for the majority of domains of the SF-36 apart from physical functioning and mental health for which there was no clinical difference between treatments (2 RCTs; low to very low quality; n=696-281). There was no clinical difference with the EQ-5D 0-1 (1 RCT; low quality; n=283).
  - At 2y, clinical benefit for discectomy was shown in quality of life for the SF-36 domain bodily pain but not for physical function (1 RCT; very low quality; n=373).
  - A cohort study reported a clinical benefit in two subdomains of the QoL SF-36 0-100 (bodily pain and physical function) and in function



in favour of discectomy at any time point (1 study, very low quality; n=656-621).

- **Leg and back pain**

- At short term (<4months), clinical benefit was seen in pain in the discectomy group, (VAS 0-10; 2 RCTs, low to very low quality; n=333-50) and in function measured by RMDQ 0-24 (1 RCT; low quality; n=281); but no difference with ODI 0-100 (2 RCTs; low quality; n=467).
- At long term (1y and 2y), no clinical difference was anymore seen in pain (VAS 0-10; 2 RCTs, low to very low quality; n=333-50) nor in function (RMDQ 0-24, 1 RCT; low quality; n=281 & ODI 0-100, 2 RCTs; low quality; n=467). No differences were found in number of patients with additional physical therapy visits (healthcare utilisation) (at 2y; 1 RCT; very low quality; n=50).
- At both short and long term, no clinical difference for pain measured with the sciatica bothersomeness index 0-24 was observed (1 RCT; very low quality; n=409-373) but a clinical benefit in number of patients who reported a complete or nearly complete disappearance of symptoms in the discectomy group (responder criteria) (1 RCT; low quality; n=281).
- A cohort study reported a clinical benefit in favour of discectomy at short term and at 1y (sciatica bothersomeness index 0-24; 1 study; very low quality; n=656 and back pain bothersomeness 0-6; 1 study; very low quality; n=1191), but no clinical difference was anymore found for back pain at 2y.
- A higher number of patients with more reported diagnostic test use was found in the discectomy group (1 study; low quality; n=1191), but no differences were found in the other measures of healthcare utilisation (number of patients with additional physical therapy visits, number of patients with reported healthcare visits and medication use) (1 study; very low quality; n=1191).

- **Discectomy versus combined intervention (manual therapy + biomechanical exercise + self-management)**

- At short term, conflicting evidence was found from 1 RCT for QoL at short term (<4mo): clinical benefit for discectomy was found for the subdomains of bodily pain, vitality, physical function and general health but clinical harm for discectomy for the domains of physical role, emotional role and social function and no difference for the subdomain mental health (SF-36 0-100; low to very low quality; n=40). No clinical difference was found for pain (McGill 0-78; 1 RCT; low quality; n=40) and function (RMDQ 0-24; 1 RCT; low quality; n=40). No long term data were presented for the reported outcomes.

- **Percutaneous disc decompression versus usual care (conservative therapy of analgesics, NSAIDs, muscle relaxants, physiotherapy, education)**

- A single RCT reported only results for the pain outcome: a clinical benefit in leg pain was found at short term (<4months) and at long term (1y and at 2y) in favour of the percutaneous disc decompression (NVS 0-10; low to very low quality; n=62).

- **Plasma disc decompression versus other treatment (epidural steroid injection)**

- A single RCT compared plasma disc decompression to epidural steroid injection and found a clinical benefit in leg and back pain (VAS 0-10; 1 RCT; low to moderate quality; n=85) at both short term (3 months) and long term (6 months) in favour of the plasma disc decompression. However, there was no clinical difference in function at any time point (low to moderate quality; n=85) or in procedure related adverse events (at 6 months; very low quality; n=55).



### Laminectomy versus usual care (active physical therapy, education, NSAIDs)

- **Quality of life**
  - At short term, conflicting evidence was showed for the SF-36 0-100: no difference for the submain of bodily pain but a clinical benefit in favour of usual care for the submain of physical function (1 RCT; low quality; n=246).
  - At long term, a clinical benefit was found in favour of laminectomy for the SF-36 0-100 submain of bodily pain (at 1 y and ta 2y; 1 RCT; low quality; n=246) but no differences for submain of physical function (1 RCT; low quality; n=246).
  - A combined cohort-RCT study showed a clinical benefit for the SF-36 0-100 subdomains of bodily pain and physical function (very low quality; n=691-448) both at short and long term in favour of laminectomy.
- Leg and back pain
  - No differences for pain (both leg and back pain) (low back pain bothersomeness index 0-24; sciatica bothersomeness index 0-24; 1 RCT; low quality; n=246-221) and for function (ODI 0-100; 1 RCT; low quality; n=251-221) were found at any time point.
  - The combined cohort-RCT study showed a clinical benefit for function both at short and long term in favour of laminectomy (ODI 0-100; 1 study; very low quality; n=691-532). For pain, only a clinical benefit in favour of laminectomy was found for back pain at 1y (Back pain bothersomeness index 0-24; 1 study; low to very low quality; n=691-532). For the other time points (short term and at 2y) and for leg pain at any time point, no differences could be found between laminectomy and usual care (sciatica bothersomeness index 0-24; 1 study; very low quality; n=691-533).

### Economic evidence

Three cost–utility analyses found that spinal decompression was not cost-effective compared to usual care treating patients with disc herniation or spinal stenosis. These analyses were assessed as partially applicable with potentially serious limitations.

### Conclusions

**When discectomy was compared with usual care, some evidence showed clinical benefits on certain (but not all) components of quality of care at short and long term and conflicting results for pain, function and healthcare utilization. When discectomy was compared with combined intervention, evidence was also conflicting: clinical benefit for discectomy in some components of quality of life but clinical harm for others and no difference in pain and function. Regarding percutaneous disc decompression versus usual care, a clinical benefit was observed for the intervention in leg pain at short and long term but it is based on 1 RCT only. For plasma disc decompression versus epidural steroid injection, a clinical benefit was found for the intervention in leg and back pain at both short and long term but not in function and adverse events. Finally, when laminectomy was compared to usual care, conflicting evidence was observed for quality of life with a clinical benefit in favour of usual care for some components at short term and in favour of laminectomy at short and long term for some others; clinical benefit was found in function for laminectomy but the results were less clear for pain. Economic evidence suggested that spinal decompression was not cost-effective compared to usual care in the treatment of patients with disc herniation or spinal stenosis. All studies concerned patients with sciatica.**





## Other considerations regarding spinal decompression in radicular pain

GRADE Factors	Comments
<b>Balance between clinical benefits and harms</b>	<ul style="list-style-type: none"> <li>The Belgian GDG acknowledged there was limited evidence showing effectiveness on certain outcomes such as quality of life with discectomy, leg pain for percutaneous disc decompression and plasma disc decompression, and function for laminectomy.</li> <li>There was few evidence of harms associated with the intervention and discectomy appeared as a relative safe procedure although the risk of adverse events should not be neglected.</li> <li>The Belgian GDG was aware that radicular symptoms tend to improve naturally with time without treatment but in rare cases, when people suffer from severe radicular pain and failed to respond to conservative management, earlier symptom resolution with surgical intervention should be an option.</li> <li>The optimal time window for performing spinal decompression is controversial and the Belgian GDG emphasised this should be determined case by case. In order to give enough time to allow spontaneous favourable evolution and/or a sufficiently longer period of conservative management, it appeared advisable to wait at least 6 weeks before proposing spinal decompression. In practice, it is rare that surgery is done before 6 weeks in Belgium but it appeared also useful for the GDG to suggest not to wait systematically until more than 3 months, certainly if there are significant neurological deficits or if the pain is uncontrollable in spite of evidence-based pain management.</li> <li>The Belgian GDG agreed with NICE that imaging before the intervention was a pre-requisite (because prior imaging was an inclusion criteria for all of the included studies and because operating without concordant imaging would carry a significant risk of harm to the patient). Moreover, the radiological findings should be consistent with the current clinical findings.</li> <li>The place of electrophysiological diagnostic before surgery was also questioned: it was not mentioned by NICE but widely used in Belgium. Therefore the Belgian GDG proposed to mention electrophysiological diagnostic in a list of topics for which "no clear recommendation can be formulated because not studied by NICE.</li> </ul>
<b>Quality of evidence</b>	<ul style="list-style-type: none"> <li>Quality evidence of the 9 RCTS and 4 cohort studies, ranged from low to very low, mainly downgraded for high risk of bias due to lack of appropriate blinding.</li> <li>The non-randomised evidence was rated as very low quality, due to inherent selection bias in non-randomised studies as well as a lack of appropriate blinding. This meant it was considered to be at serious risk of bias and therefore NICE placed low confidence in the effects reported.</li> </ul>
<b>Values and preferences</b>	<ul style="list-style-type: none"> <li>The patients' needs and preferences are a crucial element to include in the shared-decision making process. The importance of harm and the balance benefit-risk deserve detailed explanation to the patient. In particular, it appears crucial to provide information on the natural course of radicular symptoms, which improves naturally in time or with conservative management in the majority of cases.</li> </ul>
<b>Costs (resource allocation)</b>	<ul style="list-style-type: none"> <li>The 3 economic analysis found by NICE showed suggested that spinal decompression was not cost-effective compared to usual care in the treatment of patients with disc herniation or spinal stenosis. However the NICE GDG concluded that there was a high uncertainty around the conclusions of the economic studies because the cost of surgery was overestimated in the USA studies and the effectiveness was likely to be underestimated in the European study. According to the NICE GDG, decompression surgery could be cost effective in patients with sciatica when other treatments have failed.</li> </ul>



Recommendations	Strength of Recommendation	Level of Evidence
<ul style="list-style-type: none"><li>Consider spinal decompression for people with radicular pain (at least 6-12 weeks after the onset) when non-surgical evidence-based multimodal management has not improved pain or function and their radiological findings are consistent with the current clinical symptoms.</li></ul>	Weak (RCTs & cohort studies)	Low to very low

### Change in comparison with the NICE recommendations

Changes have been proposed by the Belgian GDG regarding the clinical recommendations proposed in the NICE 2016 guidelines.

41. Consider spinal decompression for people with sciatica radicular pain (at least 6-12 weeks after the onset) when non-surgical evidence-based multimodal management treatment has not improved pain or function and their radiological findings are consistent with sciatic the current clinical symptoms.

More detailed on the reasons underlying these changes are described in Appendix 7.21.



## 4 IMPLEMENTATION AND UPDATING OF THE GUIDELINE

### 4.1 Implementation

#### 4.1.1 Actors of the implementation of this guideline

The dissemination and implementation of this guideline at a national level but also at regional levels will be ideally performed in collaboration with partners whose mission is the improvement of the quality of care. Several professional and scientific organisations could be involved in this process. Several representatives of the professional organisations, universities, hospitals and primary care settings, and governmental structures were involved in the development of the guideline. Next to their collaboration to this project, they have also the role to disseminate this guideline in their field of practice and/or to implement the recommendation in the training of (para)medical students.

This guideline should be disseminated through diverse channels such as websites or programmes of continuing education. The dissemination of this guideline can further be supported by transforming this material into attractive and user-friendly tools tailored to specific caregiver groups and patient associations. The synthesis can be used as a guide. This guideline will be also available on the website of the KCE and on EBMPPracticeNet, which is a dissemination platform of high-quality labelled guidelines for the Belgian primary care.

Moreover, another KCE project develops also in 2017 a care pathway for low back pain patients. This pathway is based on each clinical recommendation providing by this guideline. Two algorithms (one for low back pain and another for radicular pain) are proposed to synthesis the management process of these two entities.

#### 4.1.2 Barriers and facilitators for implementation of this guideline

Potential barriers and facilitators for the implementation of this guideline can be related to the level of evidence underlying the clinical recommendations, the health practitioners, the patients themselves or to the health system as a whole.

The level of evidence underlying the clinical recommendations can be a facilitator or a barrier for the implementation of the clinical guidelines. It is more difficult to motivate health practitioners and patient to adopt specific constraining behaviours or abandon diagnostic interventions where a low level of scientific evidence leads to the formulation of 'weak' recommendations. On the contrary, a high level of evidence and strong recommendations are incentives to change a current practice.

Regarding the barriers linked with health care providers, the deep discussion with the GDG, a multidisciplinary team of Belgian clinicians allowed us to identify several concerns and to take them into account within the formulation of the recommendation. Some specific actions have been identified that are needed to reduce certain barriers. An example is a training on the risk stratification for many of the healthcare providers involved in the management of low back pain.

The patients' expectations will deserve also attention. The paradigm shift from a biomedical to a biopsychosocial approach could be difficult, and the patients' pressure for imaging will require specific public information.

The organisational aspect needed for implementing the clinical recommendations implies a deep reflection on each step of the management. Several initiatives exist in Belgium aiming to improve the quality of care for pain, in terms of accessibility to multidisciplinary programs but also promotion to stay at work. These initiatives are described in the KCE project on pathway for low back pain.

*The best way to **effect** change is to work with existing stakeholders.*



## 4.2 Monitoring the quality of care

A KCE project on PROMs and PREMS indicators has start in 2016 with a part dedicated to low back pain. This project should provide a list of indicators to be recorded in order to monitor the quality of care delivered to low back pain patients. More information will be available at the end of 2017 on the KCE website.

## 4.3 Guideline update

Clinical guidelines need a periodic evaluation of scientific literature that may impact the formulation of the recommendations for clinical practice (quality of the evidence, balance between benefits and harms, patients' values and preferences, or resource use and cost). Any decision to update a guideline must balance the need to reflect changes in the evidence against the need for constancy, because regular changes to guideline recommendations would make implementation difficult.

KCE clinical guidelines are updated as needed so that recommendations take into account important new information. This guideline would ideally be reviewed at 5 years after publication to determine whether all or part of it should be updated. If important new evidence is published earlier, we may decide to do a more rapid update of some recommendations.



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