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National Clinical Guidelines for non-surgical treatment of patients with recent onset low back pain or lumbar radiculopathy

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Title Page

Title:

National Clinical Guidelines for non-surgical treatment of patients with recent onset low back pain or lumbar radiculopathy.

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National Clinical Guidelines for non-surgical treatment of patients with recent onset low back pain or lumbar radiculopathy.

Abstract

Purpose

To summarise recommendations about twenty non-surgical interventions for recent onset (< 12 weeks) non-specific low back pain (LBP) and lumbar radiculopathy (LR) based on two guidelines from the Danish Health Authority.

Methods

Two multidisciplinary working groups formulated recommendations based on the GRADE approach.

Results

Sixteen recommendations were based on evidence, and four on consensus. Management of LBP and LR should include information about prognosis, warning signs, and advise to remain active. If treatment is needed, the guidelines suggest using patient education, different types of supervised exercise, and manual therapy. The guidelines recommend against acupuncture, routine use of imaging, targeted treatment, extraforaminal glucocorticoid injection, paracetamol, NSAIDs, and opioids.

Conclusion

Recommendations are based on low to moderate quality evidence or on consensus, but are well aligned with recommendations from international guidelines. The guideline working-groups recommend that research efforts in relation to all aspects of management of LBP and LR be intensified.

Keywords

Clinical Guideline, low back pain, lumbar radiculopathy, non-surgical intervention, recommendations, conservative treatment

Background

In 2012, the Danish Finance Act appropriated a total of €10.8 Mio for the preparation of clinical guidelines. The Danish Health Authority (DHA) was subsequently commissioned to formulate 47 national clinical guidelines to support evidence-based decision making within health areas with a high burden of disease, a perceived large variation in practice, or uncertainty about which care was appropriate [1]. Two of these areas were low back pain (LBP) and lumbar radiculopathy (LR). Consequently in 2014, two working groups were formed with the aim of developing national clinical guidelines for non-surgical interventions for recent onset (< 12 weeks) LBP and for recent onset (< 12 weeks) LR. The primary target groups for these guidelines were primary sector healthcare providers, i.e. general practitioners, chiropractors, and physiotherapists, but also medical specialists or others in the primary or secondary healthcare sector handling patients with LBP or LR.

An estimated 15% of the Danish population suffers from low back pain (LBP) [2], and most will experience LBP during their lifetime [3], which is in accordance with estimates globally [4]. Both globally [5] and in Denmark [6], LBP with or without LR is a leading cause of years lived with disability, and consequently has major socioeconomic impact on society. For example, out of the 2.9 million Danes in the workforce, those with LBP have 5.5 million more days off work annually when compared to those without LBP, which accounts for 20% of all sick days, and LBP with or without LR is the most common reason for seeing a general practitioner, accounting for almost one in ten visits [2]. In addition, Danes with LBP visit their general practitioner 3.3 times more often compared to Danes without LBP, and they consult approximately 30% more often chiropractors and physiotherapists [2]. Once you have had an episode of LBP, most will experience recurrences [7], and only a minority will stay pain free for longer periods of time [8]. Additionally, 1-10% of patients with LBP will experience LR, which is associated with a poorer prognosis compared to LBP without LR [9].

This paper summarises the two Danish national clinical guidelines, which were published in 2016 as full reports in Danish [10, 11]. The mandates for the two working groups were to make recommendations based on a maximum of ten clinical questions for LBP and LR each. The working groups were not asked to make recommendations for diagnostic procedures or care pathways.

Methods

Study design

The guidelines were based on systematic reviews of the scientific literature and subsequent meta-analyses. The evidence of effect was balanced against the risk of harms and patient preferences to make recommendations related to each of the clinical questions. The method followed international standards for clinical guidelines [12], which were operationalised in a handbook from DHA [13] and briefly summarised below. This method was based on the Grades of Recommendations, Assessment, Development, and Evaluation (GRADE) approach [14]. The full clinical guidelines are available with all supportive material, including a description of the methods on the DHA webpage (in Danish) [13].

Organisation of the work

For each guideline, a project group within DHA consisting of a chairman, a project manager, a lead reviewer, a search specialist, a methodologist, and a multidisciplinary working group with 10 (LBP) and 12 (LR) members was set up. Working group members were appointed by invitation from professional organisations and scientific societies. They were involved in all parts of the process including formulating the clinical questions, selecting literature, data extraction, rating the quality of evidence, and formulating recommendations. Reference groups with representatives from stakeholders from the Danish healthcare system (municipalities, regions and hospitals), and patient organisations discussed and gave suggestions to the clinical questions and feedback on the recommendations. The lead reviewers coordinated the tasks of the working groups and drafted the reports. Potential conflicts of interest were declared by all involved partners and made publicly available on the DHA webpage (in Danish) [10, 11].

Finally, drafts of each of the clinical guidelines were in a public hearing and reviewed by two external peer-reviewers. The comments and feedback were considered by the working groups and taken into consideration when formulating the final versions of the guidelines.

Formulating the clinical questions

The clinical guidelines addressed a maximum of ten clinical questions, which were structured according to the Patient, Intervention, Comparison, and Outcome approach (PICO) framework [14].

Populations

The target populations were 1) patients above the age of 16 years suffering from non-specific LBP with or without associated leg pain but no signs of LR, and 2) patients with symptoms and clinical signs of LR above the age of 18 years. The symptoms had to have lasted less than 12 weeks for both populations. It was assumed that the differentiation between non-specific LBP and LR could be based on anamnestic information and a clinical examination without diagnostic imaging. Therefore, no distinction was made between LR caused by disc herniation and other degenerative conditions. Studies were eligible for the clinical guideline on LBP if at least 75% of the participants in a study matched the inclusion criteria. No such cut point was used in the LR guideline.

Interventions and comparisons

The mandate restricted the clinical guidelines to non-surgical interventions, and for the clinical guideline on LR only to non-pharmacological interventions. The choice of clinical questions was based on the working group's perceived frequency of use, uncertainty about effectiveness, or uncertainty about whether one intervention was superior to another. Because it was assumed that all patients would receive basic information regarding disease progression, prognosis and danger signals, advice on activity and possible medical pain management when seeking care, it was decided to make recommendations about the interventions as a supplement or add-on to this basic treatment with no further specification, hereafter named 'usual care'. Thus, trials were eligible for inclusion when usual care was provided in both the intervention and the control group, and the intervention in question was added in the intervention group. By doing so, the effects of adding the interventions to usual care were reviewed; if this was not possible, a comparison of treatments or sham-controlled trials was accepted. Some clinical questions addressed a head-to-head comparison of two interventions when it was assumed that clinicians often will choose between the two.

Outcome measures

For each of the clinical questions, two or more primary outcome measures and their timing were chosen a priori by the working groups. For most LBP questions, back pain intensity and back pain-related activity limitation were deemed primary outcomes. Back pain intensity, leg pain intensity, back pain-related activity limitation, and neurological deficits were considered primary outcome measures for the LR questions. For all outcome measures, the absolute differences between intervention and control groups on generally accepted and validated instruments such as a visual analogue scale (VAS), a numeric pain rating scale (NRS), Roland-Morris Disability Questionnaire (RMDQ) or Oswestry Disability Index (ODI) should be available. In the LBP guideline, the pharmacological questions also included as primary outcomes were serious adverse events. Secondary outcomes measures included fear-avoidance, work status, health-related quality of life, study drop outs, recurrence, and surgery rates.

The working groups defined minimally clinically relevant effects as a difference of 15 mm on a 100 mm on a VAS-scale, two points on an 11-point NRS, and 10 points on a 100-point scale of back pain-related disability [15].

Literature searches and inclusion of literature

For each of the clinical questions, the literature was systematically searched in three-steps: Firstly, Embase, Medline, Cinahl (LBP only), Psycinfo (LBP only), PEDRO (LBP only) as well as national and international guideline databases were searched for clinical guidelines ten years back (2004 and 2005 included respectively for LR and LBP). Secondly, Medline, Embase, Cinahl, PsycInfo and Pedro (LBP only), and the Cochrane Library were searched for systematic reviews ten years back, and thirdly, the same databases were searched for randomised clinical trials (RCTs) with no lower limit for publication year. In case a high-quality clinical guideline or systematic review would have covered earlier studies, the date for the last search for this review was used as the lower limit for the new search for randomised trials. All literature searches included studies published until and including December 2014 (LR) or March 2016 (LBP) published in English, German (LBP only), Norwegian, Swedish, or Danish. The search terms and strategies are available at the DHA website [10, 11].

Where no RCTs dealing with recent onset LR could be identified, indirect evidence from LR populations with symptoms lasting for more than 12 weeks informed consensus recommendations.

The lead reviewer screened and retrieved titles and abstracts. Potentially eligible papers were then collected in full text. Subsequently, the lead reviewer and a member of the working group independently screened the full text papers for inclusion or exclusion. Disagreements were resolved by discussion until consensus was reached.

Data extraction and quality assessment

The lead reviewer and a member of the working group or a scientific methods advisor independently extracted data for each clinical question and assessed all included papers for quality. If a high quality clinical guideline or systematic review was available, data were extracted from these. The quality was assessed using the AGREE-II tool [16] for clinical guidelines, the AMSTAR tool [17] for systematic reviews, and the Cochrane risk of bias tool for RCTs [18]. When a risk of bias assessment was available from a Cochrane review, it was transferred directly to the clinical guideline. The handling of references and data extractions were performed using the web-based software Covidence [19], from which data were exported to the RevMan software [20] for meta-analyses; the results of which were further transferred to either GradePro [21] (LR) or MAGIC [22] (LBP) for GRADE assessment. Disagreements in data extraction and quality assessment were solved by consensus between the two evaluators in all instances. The quality of evidence was graded from very low to high according to the GRADE definitions (Table 1) for each outcome. Downgrading was done following standard definitions of risk of bias, inconsistency, indirectness, imprecision, and publication bias [23]. The overall level of evidence supporting the recommendation for each clinical question was determined based on the quality for the primary outcome with the lowest quality evidence.

From evidence to recommendations

Finally, the evidence was summarised in evidence tables, and forest plots were constructed when meta-analyses were feasible. Based on the available evidence, strong or weak recommendations for or against an intervention were proposed following the criteria outlined in Table 2. Each recommendation was annotated with the strength of the recommendation and the level of evidence according to GRADE. In case no evidence was available from RCTs, a good practice recommendation was formulated based on clinical experience and consensus in the working group. The recommendations were based on weighing the quality of evidence, positive versus negative effects, patient values and preferences as well as the perception and experience of the working groups.

[Insert Table 2 around here]

Results

The guidelines considered ten clinical questions concerning LBP and ten concerning LR. Six interventions were covered by both clinical guidelines, two of which were stand-alone interventions (advice to stay active vs rest; routine use of Magnetic resonance imaging [MRI] and/or X-ray vs. no imaging), and four were evaluated as an add-on to usual care vs. usual care (individualised patient information, supervised exercise, acupuncture, and manual therapy). In addition, the clinical guideline for LBP covered three questions addressing pharmacological interventions (paracetamol, opioids and Non-Steroidal Anti-inflammatory Drugs [NSAIDs]) as add-on to usual care, and targeted group-based care vs. non-targeted care. For LR, three head-to-head comparisons of exercise and manual therapy interventions (directional exercise vs. neuromuscular control training; directional exercise in combination with neuromuscular control training vs directional exercise alone; supervised exercises vs. manual therapy) were performed. An overview of the clinical questions and recommendations are provided in Table 3.

[Insert Table 3 around here]

A short description of eligible papers, primary outcomes, recommendations, and levels of evidence are provided in Tables 4 and 5. Forest plots of all outcomes and risk of bias assessments are provided in Appendix 1 and 2. Evidence tables are available in the complete clinical guidelines following each clinical question at the DHA website (in Danish) [10, 11].

[Insert Table 4 and 5 around here]

Generally, recommendations from the two guidelines endorse patient enablement through information and education, advice to remain physically active and supervised exercise in addition to usual care. For pain relief, manual therapy including joint mobilisation and manipulation in addition to usual care was recommended, whereas the expert groups recommended only using pain medication in the form of paracetamol, NSAID, and opioids in addition to usual care after

careful consideration in patients with LBP. No recommendations were made for the use of pain medication in relation to LR because this was outside of the mandate of the group.

Acupuncture was not endorsed for routine use in the two conditions. The groups recommended against routine imaging, i.e. X-ray or MRI, in patients presenting with both recent onset LBP and/or LR, and against the use of extraforaminal glucocorticoid injections in addition to usual care in patients with LR. Finally, it was recommended that patients with LR are referred for surgical consultation within 12 weeks if severe and disabling pain persists despite non-surgical treatment.

Of the 20 clinical questions, none could be answered by any of the clinical guidelines or systematic reviews that were retrieved. Recommendations were based on RCTs when available (16 out of 20 questions) and the remaining on professional consensus (four questions). Flow charts of included literature, quality assessments of clinical guidelines, systematic reviews, and RCTs and evidence tables are available at the DHA website (in Danish) [10, 11].

DISCUSSION

Multidisciplinary expert groups formulated two national clinical guidelines for the DHA covering non-surgical treatment of recent onset LBP and LR in adults and found a striking lack of evidence for the effectiveness of the interventions examined. Thus, commonly used interventions like information and guidance; medication; mechanical diagnosis and therapy; massage; acupuncture; motor control exercise; and spinal manual therapy had either no or limited quality supporting evidence. Consequently, guideline recommendations are to a large extent based on consensus between members of the working groups; therefore, new high quality trials focusing on LBP and LR patients are likely to impact future guideline recommendations greatly.

Wong et al reviewed clinical practice guidelines for non-surgical management of LBP with or without LR published between 2005 and 2014 and found that advice and education about self-management and reassurance as well as advice for staying active, supervised exercise, and manual therapy were universally recommended for people presenting to health care professionals with these conditions [108]. They also found that paracetamol, and NSAID were recommended as treatment options in all guidelines reviewed, whereas muscle relaxants, and a short course of opioids were recommended in some but not all guidelines [108]. In 2016, new guidelines for non-invasive treatments for LBP and sciatica were published from The National Institute for Health Care Excellence (NICE) in the UK [109]. These guidelines are more comprehensive than the Danish national guidelines because they also deal with chronic LBP, clinical examination and surgical treatments. However, for recent onset LBP and sciatica they also recommend providing people with advice and

education as well as encouragement to stay active and continue with normal activities, to consider group exercises, and to consider manual therapy treatments as part of treatment that also include exercise [109]. With respect to pharmacological treatment, the NICE guidelines are similar to the Danish guidelines when they recommend against routine use of paracetamol as a stand-alone treatment, that NSAID is only to be used after careful consideration of co-morbidities and other risk-factors for side-effects and if used, then only in the lowest effective dose. Finally, they recommended that opioids should not be given routinely for managing LBP or sciatica [109].

Expert groups have used lack of evidence for benefit or harm for a particular intervention as an argument for not putting forward a recommendation [110]. Such interpretation of the evidence, however, has been met with frustration by health care professionals and professional societies who look to expert groups and task forces for guidance [111]. Fortunately, the GRADE methodology accommodates these circumstances as it classifies evidence as either strong or weak and provide interpretations for patients, clinicians, and policy makers [112]. Faced with either no or weak evidence, it is important that patients know that their particular preference among the various therapies should guide choice of intervention. Clinicians must therefore acknowledge that different choices may be appropriate for different patients and must help each patient choose a management option consistent with his or her values or preferences. Finally, policy makers must involve all relevant professional groups and stakeholders when determining how best to design care pathways [112]. Importantly, guideline panels should not refrain from making recommendations because individual patients and clinicians will make different choices when faced with a weak recommendation. In fact, this is to be expected. Consequently, the GRADE Working Group encourage panels to make recommendations wherever possible whether they are based on solid evidence or not [113].

Strengths of this national clinical guideline include the chairmanship by the DHA and the rigorous adherence to relevant scientific standards. Furthermore, the guideline working-groups were composed of clinicians and academics with a range of professional backgrounds, as well as relevant professional societies and agencies were consulted during the process, which together aims to ensure buy-in by relevant stakeholders in the country. The guideline working-groups were assisted by expert research librarians and guideline methodologists. Finally, the guidelines were peer-reviewed by international experts who provided detailed comments which resulted in revisions and clarifications prior to release of the final report. The main weakness of this work relates to the lack of clinical trials in some areas; therefore, the weak recommendations are mostly based on consensus in the guideline working-groups. The DHA recommend that the guidelines are updated

three years after the publication unless new developments warrant an earlier update.

CONCLUSION

Two multidisciplinary working-groups developed two national clinical guidelines for non-surgical treatment in adult patients with LBP and LR of less than 12 weeks' duration under the Danish Health Authority. The recommendations are based on limited evidence or on consensus but are well aligned with recommendations from similar international guidelines. The guideline working-groups strongly recommend that research efforts in relation to all aspects of the management of LBP and, in particular, LR be intensified.

Funding and Conflicts of Interest

Funding was provided by The Danish Finance Act (2012), and the DHA was commissioned to formulate the national clinical guidelines. Funding was provided to members of the project groups, i.e. lead reviewers (MJS and PK), project manager (BH), methodologists (JA and ST), search specialists, and chairmen. No funding was provided to the working or reference group members. Potential conflicts of interest have been declared by all involved partners and made publicly available on the DHA webpage (in Danish) [10, 11]. The funders had no role in the design, collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the article for publication.

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Table 1. Definitions of Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) adapted from Balshem et al. 2011 [24].

| Quality of Evidence | Definition |
|------------------------|---|
| High (⊕⊕⊕⊕) | We are very confident that the true effect lies close to that of the estimate of the effect. |
| 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. |
| Low (⊕⊕○○) | Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect. |
| 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. |

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Table 2. Recommendations and their definitions by the Danish Health Authority (DHA).

| Recommendation | Definition |
|--|--|
| Strong recommendation for ↑↑ | The DHA makes a strong recommendation in favour of an intervention when evidence of high quality shows that its desirable effect clearly outweighs undesirable effect. |
| Weak / conditional recommendation for ↑ | The DHA makes a weak/conditional recommendation in favour of an intervention when the desirable effect of an intervention is judged to marginally outweigh the undesirable effects <i>or</i> when the available evidence cannot rule out a significant benefit of an intervention and the harms are judged to be few or absent. |
| Weak / conditional recommendation against ↓ | The DHA makes a weak/conditional recommendation against an intervention when the undesirable effects are judged to outweigh the desirable effects, but where this is not supported by strong evidence. This recommendation is also made in case of strong evidence for both beneficial and harmful effects when the balance between them is difficult to determine. Also used when it is considered that patients' preferences vary. |
| Strong recommendation against ↓↓ | The DHA makes a strong recommendation against an intervention in case of high-quality evidence showing that the undesirable effects of an intervention clearly outweigh the desirable effects. The DHA also makes a strong recommendation against an intervention when the review of the evidence shows with great certainty that the intervention is useless. |
| Good practice √ | Good practice recommendations are based on professional consensus among the members of the working group when relevant evidence is not available. The recommendation may be either for or against the intervention. Therefore, this type of recommendation is weaker than the evidence-based recommendations irrespective of whether these are strong or weak. |

Table 3. Overview of recommendations and their level of evidence.

| PICO | Intervention | Recent onset low back pain | Lumbar radiculopathy |
|--|---|----------------------------|-----------------------|
| PICO 1 and 11 | Advice to stay active | ↑ (⊕⊕○○) | ↑ (⊕⊕○○) |
| PICO 2 | Patient educations | ↑ (⊕○○○) | |
| PICO 3 | Targeted interventions | √ against routine use | |
| PICO 4 + 18 | Routine imaging MRI and x-ray MRI | ↓ (⊕○○○) | ↓ (⊕○○○) |
| PICO 5 and 15 | Spinal manual therapy | ↑ (⊕⊕○○) | ↑ (⊕○○○) |
| PICO 6 +12 | Supervised exercise | ↑ (⊕⊕○○) | ↑ (⊕⊕○○) |
| PICO 13 | Directional exercise vs. motor control exercise | | ↑ (⊕○○○) |
| PICO 14 | Directional exercise + motor control exercise vs Directional exercise | | √ for |
| PICO 16 | Supervised exercise or spinal manual therapy | | ↑ (⊕○○○) equal effect |
| PICO 7 and 17 | Acupuncture | ↓ (⊕○○○) | √ against routine use |
| PICO 8 | Paracetamol | ↓ (⊕⊕⊕○) | |
| PICO 9 | Opioids | ↓ (⊕⊕○○) | |
| PICO 10 | NSAIDs | ↓ (⊕⊕○○) | |
| PICO 19 | Extraforaminal glucocorticoid injection | | ↓ (⊕⊕○○) |
| PICO 20 | Surgical consultation before 12 weeks | | √ for |
| √ Consensus recommendation, ↓ Weak recommendation against, ↑ Weak recommendation for. See Tables 1 and 2 for definitions of level of evidence. | | | |

Table 4. PICO questions, recommendations, definitions of interventions, supporting evidence and comments regarding recent onset low back pain.

| PICO 1. Should patients with recent onset low back pain be advised to stay active as compared to rest? | |
|--|---|
| <p>↑ <i>Consider offering patients with recent onset LBP advice about staying active rather than advice about rest (⊕⊕○○).</i></p> | <p><i>Definition:</i> Stay active was defined as maintaining usual levels of daily activity, including work, despite pain. Advice should include information regarding benefits of staying active (including continued work participation), the potential harm of inactivity, and information regarding gradual increase in levels of activity. Advice should be given individually and in dialogue with the patient.</p> <p><i>Included studies:</i> For advice to stay active, we identified four randomised studies [25-28]. Advice to stay active was compared to bed rest [26, 27], advice about activity within pain limits [28], and no advice [25].</p> <p><i>Primary outcomes:</i> Two studies showed a small, statistically significant effect in favour of staying active on short term pain intensity and activity limitation [15, 29].</p> <p><i>Comment:</i> The level of evidence was downgraded due to lack of a clinically relevant effect, risk of bias, and imprecise effect estimate.</p> <p>The working group agreed that the overall positive effects of staying active outweigh the potential harmful effects, which led to a recommendation in favour of advice to stay active.</p> |
| PICO 2. Should patients with recent onset low back pain be offered individualised patient education in addition to usual care? | |
| <p>↑ <i>Consider offering individualised patient education in addition to usual care in patients with recent onset low back pain and the ability to increase self-efficacy (⊕○○○).</i></p> | <p><i>Definition:</i> Patient education was defined as education regarding health literacy, competencies, and adaptation of behaviour [30]. Patient education should consist of reassurance facilitated by elements of cognitive behavioural therapy. Reassurance was defined as a process taking place during the interaction between the clinician and the patient, during which information, instruction, or persuasions are exchanged with the purpose of reducing patients worries and fears of illness, and where recommendations are translated into action in daily life [31, 32].</p> <p><i>Included studies:</i> We identified nine RCTs published in 10 papers [25, 29, 33-40]. Patient education consisted of dialogue only [33-35], or dialogue in combination with exercise therapy [25, 29, 36-40]. Patient education was compared to usual care in the form of usual general practice [33-35, 37], advice [29, 36], manual therapy [38], and exercise therapy [25, 39].</p> <p><i>Primary outcomes:</i> Six papers reported on the primary outcomes [25, 34, 36-39]. We saw a small, statistically significant improvement in short term fear-avoidance in favour of patient education in addition to usual care compared with usual care alone [36]. No difference in effect was observed in short term pain intensity [25, 34, 36-39].</p> <p><i>Comments:</i> The level of evidence was downgraded due to lack of a clinically relevant effect, risk of bias, imprecise effect estimate, only one study (short term fear-avoidance); and small sample size (short term fear-avoidance)</p> <p>In addition to the recommendation, the working group agreed that individual patient education should be offered specifically to patients who are worried about their LBP, show signs of fear-avoidance or passive behaviour. The intervention should only be offered to patients who are motivated, are able to change their level of self-efficacy, and be based on a patient-centred dialogue.</p> |

PICO 3. Should patients with recent onset low back pain be offered targeted interventions compared to usual (non-targeted) care?

| | |
|--|---|
| <p>√ <i>It is not good practice to routinely offer targeted treatment in patients with new onset LBP in addition to usual care over usual care, as the effect is unknown</i></p> | <p><i>Definition:</i> The working group operationalized targeted treatment, as treatment targeting subgroups of patient with similar pre-identified, modifiable prognostic factors.</p> <p><i>Included studies:</i> We identified six RCTs [34, 41-45]. Four studies [41-44] grouped patients according to physical prognostic factors and evaluated the effect of physical interventions (spinal manipulation or exercises). Two studies [34, 45] grouped according to psychological factors or duration of symptoms, and evaluated the effect of cognitive behaviour therapy or graded activity.</p> <p><i>Comments:</i> All six studies compared the intervention to a non-matched intervention, and were considered to have low risk of bias, but none were designed or had adequate power to address the effect of targeting treatment to subgroups (primary outcomes: short term pain intensity and activity limitations). The working group also found that the studies were too heterogeneous in terms of definitions of subgroups and interventions. Thus, the recommendation is based on consensus.</p> <p>The working group further recommends that clinicians consider psychosocial aspects of LBP, as it may lead to identification of patients with specific needs.</p> |
|--|---|

PICO 4. Should patients with recent onset low back pain be offered routine imaging (MRI or x-ray) compared to no imaging?

| | |
|---|--|
| <p>↓ <i>Do not routinely offer imaging (MRI or x-ray) to patients with recent onset LBP, as the evidence does not support a positive effect (⊕○○○).</i></p> | <p><i>Definition:</i> Routine use of either lumbar magnetic resonance imaging or conventional x-ray.</p> <p><i>Included studies:</i> We identified four randomised studies [46-49]. The effect of routine MRI was evaluated in two studies [46, 47] and x-ray in two studies [48, 49] combined with usual care in all four studies. This was compared to imaging on specific indication or lack of improvement, [47-49] and to a delayed information about findings [46].</p> <p><i>Primary outcomes:</i> Only one papers reported on the primary outcomes [46]. Long term sick leave was not statistically different in the two groups in one study [46].</p> <p><i>Comments:</i> The level of evidence was downgraded due to lack of a clinically relevant effect, no reporting of the primary outcome health care utilization, only one study, and risk of bias.</p> <p>The working group agreed that imaging without indications of serious underlying conditions does not improve clinical outcomes. Further, the potential harm (i.e. radiation exposure and risk of labelling patients with diagnoses that might not be the actual cause of their pain) outweigh the potential positive effects, which led to a recommendation against routine imaging.</p> |
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PICO 5. Should patients with recent onset low back pain be offered spinal manual therapy in addition to usual care?

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| <p>↑ <i>Consider offering patients with recent onset LBP spinal manual therapy in addition to usual care (⊕⊕○○).</i></p> | <p><i>Definition:</i> Spinal manual therapy was defined as any manual technique that moves one or more joints within normal ranges of motion and aims at improving spinal joint motion or function, i.e. any mobilization or spinal manipulation technique.</p> <p><i>Included studies:</i> Four studies were included [50-53], all of which evaluated spinal manipulation as an add on to usual care. No studies evaluated spinal mobilisation. This was compared to four different usual care packages; ultrasound [52], myofascial release [51], information and paracetamol [53], or information, muscle relaxants or low dose opioids, and physiotherapy [50].</p> <p><i>Primary outcomes:</i> We observed a small, statistically significant effect in favour of manual therapy on short term pain intensity [50-53], but no difference in effect on short term activity limitations [50-53].</p> <p><i>Comments:</i> The level of evidence was downgraded due to lack of a clinically relevant effect, risk of bias, and inconsistent results.</p> |
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PICO 6. Should patients with recent onset low back pain be offered supervised exercise in addition to usual care?

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| <p>↑ Consider offering patients with recent onset LBP supervised exercise in addition to usual care (⊕⊕○○).</p> | <p><i>Definition:</i> Supervised exercise was broadly defined as exercises or physical activity, which were aimed directly at the back or general health and fitness, e.g. back-specific strengthening, stretching, motor control exercise or mobilizing exercises, and cardiovascular training. The exercises had to be adapted to the individual, be progressive as per patient improvement, and be delivered by a trained healthcare professional.</p> <p><i>Included studies:</i> Seven RCTs reported in eight papers [25, 36, 54-59] were included. The intervention consisted of either general strengthening, coordination and mobility exercises [25, 36, 54-56], directional exercise [57, 59], and endurance training of spinal musculature [58]. This was compared to usual care consisting of advice and paracetamol as needed [54, 55, 57-59], standard GP care [36, 56], and a dialogue based consultation [25].</p> <p><i>Primary outcomes:</i> Four papers reported on the primary outcomes [25, 54, 56, 57]. We did not observe differences in effects in long term pain intensity [25, 54, 56] or long term activity limitations [25, 56, 57].</p> <p><i>Comments:</i> The level of evidence was downgraded due to lack of a clinically relevant effect, risk of bias, and imprecise effect estimate.</p> <p>A recommendation in favour of the intervention was formulated based on the observation that there was a trend in all the included studies in favour of supervised exercise. This uniform trend was neither statistically significant nor clinically relevant, but a positive effect of supervised exercise cannot be conclusively dismissed. In addition, it was emphasized that exercise has a potential positive effect on the patients' general health, it may prevent recurrent episodes, and serious adverse events are rare.</p> |
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PICO 7. Should patients with recent onset low back pain be offered acupuncture in addition to usual care?

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| <p>↓ Do only offer patients with recent onset LBP acupuncture in addition to usual care after careful consideration, as the effect is uncertain (⊕○○○).</p> | <p><i>Definition:</i> Acupuncture was defined as any treatment that involves penetrating the skin with fine needles without the use of injection of substrates, i.e. as in concordance with traditional eastern medicine or in the form of dry-needling.</p> <p><i>Included studies:</i> We included two RCTs [60, 61]. One study evaluated traditional Chinese acupuncture [60] and one evaluated dry needling [61]. Both compared the intervention with usual care defined as information and advice regarding usual activity.</p> <p><i>Primary outcomes:</i> A small, statistically significant effect in favour of acupuncture intervention was found on short term pain intensity [60, 61]. No difference in effect was seen on short term activity limitations [60, 61].</p> <p><i>Comments:</i> The level of evidence was downgraded due to lack of a clinically relevant effect, risk of bias, and imprecise effect estimate, and small sample size.</p> <p>A recommendation against the intervention was formulated based on the observations that the effect of the intervention was not clinically relevant regarding short term pain intensity, there were no differences in effects regarding short and long term function, a possible negative effect regarding sick leave, and an overall very weak evidence base.</p> |
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PICO 8. Should patients with recent onset low back pain be offered paracetamol in addition to usual care?

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| <p>↓ Do only offer patients with recent onset LBP paracetamol in addition to usual care after careful consideration, as the evidence points towards no short-term effect (⊕⊕⊕○).</p> | <p><i>Definition:</i> Oral paracetamol taken between 2 and 21 days at an equivalent dose of 2000-4000 mg/d.</p> <p><i>Included studies:</i> One RCT was identified [62]. The intervention consisted of four weeks of paracetamol 3990 mg/day in addition to usual care. This was compared to usual care alone, defined as placebo plus advice and information.</p> <p><i>Primary outcomes:</i> There was no difference in effects using short term pain intensity, short term activity limitations, or serious adverse events [62].</p> <p><i>Comments:</i> The level of evidence was downgraded due to lack of a clinically relevant effect and only one study eligible.</p> |
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PICO 9. Should patients with recent onset low back pain be offered opioids in addition to usual care?

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| <p>↓ Do only offer patients with recent onset LBP opioids in addition to usual care after careful consideration, as the evidence points towards no short-term effect (⊕⊕○○).</p> | <p><i>Definition:</i> Oral opioids taken between 1 and 14 days at an equivalent dose of 50-100 mg 4 times daily for tramadol or 10 mg maximum every 4 hours for morphine.</p> <p><i>Included studies:</i> We identified one RCT [63]. The intervention consisted of 1-2 tablets of 5 mg oxycodone combined with 325 mg of acetaminophen every 8 hour in addition to usual care. The intervention was compared to placebo plus usual care defined as 500 mg of naproxen twice daily plus advice regarding exercises, heat, cold, physiotherapy, massage and acupuncture [63].</p> <p><i>Primary outcomes:</i> There was no difference in effect on short term activity limitations [63].</p> <p><i>Comments:</i> The level of evidence was downgraded due to lack of a clinically relevant effect, only one study eligible, and no reporting of the primary outcomes short term pain intensity and serious adverse events.</p> |
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PICO 10. Should patients with recent onset low back pain be offered Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) in addition to usual care?

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| <p>↓ Do only offer patients with recent onset LBP NSAIDs in addition to usual care after careful consideration, as the evidence points towards no short-term effect (⊕⊕○○).</p> | <p><i>Definition:</i> Oral ibuprofen (1200-1800 mg/d) or naproxen (500-1000 mg/d) taken between 5 and 14 days.</p> <p><i>Included studies:</i> One RCT was identified [53]. The intervention consisted of 50 mg of oral diclofenac twice daily until the patient was pain free or no more than four weeks in combination with usual care. This was compared to placebo and usual care defined as advice and 1 g of paracetamol four times a day. Both groups also received deactivated ultrasound.</p> <p><i>Primary outcomes:</i> There were no differences in effects on short term pain intensity and short term activity limitations [53].</p> <p><i>Comments:</i> The level of evidence was downgraded due to lack of a clinically relevant effect, only one eligible study, and no reporting of the primary outcome serious adverse events.</p> |
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Table 5. PICO questions, recommendations, definitions of interventions, supporting evidence and comments regarding recent onset lumbar radiculopathy.

| PICO 11. Should patients with recent onset lumbar radiculopathy be advised of physical activity compared to rest? | |
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| <p>Recommendation 11 and level of evidence</p> <p>↑ <i>Consider recommending normal physical activity rather than reduced activity in the form of bed rest to patients with recent onset lumbar nerve root compression (⊕⊕○○).</i></p> | <p><i>Definition:</i> Physical activity was defined as any physical activity as tolerated by the patient, e.g. walking, working, participating in leisure time activities, or exercises, with the purpose of staying active.</p> <p><i>Included studies:</i> We identified two RCTs [64, 65]. Advice to stay active was compared to one [64] or two [65] weeks of bed rest.</p> <p><i>Primary outcomes:</i> We did not observe any differences in effects on short term leg pain intensity [64, 65], back pain intensity [65], or activity limitations [64, 65].</p> <p><i>Comment:</i> The level of evidence was downgraded due to lack of a clinically relevant effect, imprecise effect estimate; and only one study (back pain intensity).</p> <p>A recommendation in favour of the intervention was formulated based on the potential positive effects of physical activity and the potential negative effects of rest on the patients' general health.</p> |
| PICO 12. Should patients with recent onset lumbar radiculopathy be offered supervised exercise therapy in addition to usual care? | |
| <p>↑ <i>Consider offering supervised exercise therapy to patients with recent onset lumbar nerve root compression as an add-on to usual treatment (⊕⊕○○).</i></p> | <p><i>Definition:</i> Supervised exercise therapy was defined as exercises or physical activities, which had a therapeutic focus, were tailored and adjusted to the individual patient, and delivered by a trained healthcare professional. These included directional exercises, motor control exercise, nerve mobilisation, or strength exercises.</p> <p><i>Included studies:</i> In total, six RCTs were identified [29, 66-70]. The intervention consisted of motor control exercises [66, 70], directional exercises combined with advice [67] or neuromuscular control exercises [69], isometric exercises [68], or general exercises [29]. This was compared to advice [66, 67], advice and general exercises [70], sham exercises [69], rest [68], and usual GP care [29].</p> <p><i>Primary outcomes:</i> A clinically relevant effect in favour of the intervention was observed on short term leg pain intensity [29, 66-70], and a small, statistically significant effect on short term back pain intensity [29, 67, 70]. We did not observe differences in effects on short term activity limitations [29, 67, 69, 70] or neurological deficits [69, 70].</p> <p><i>Comments:</i> The level of evidence was downgraded due to lack of transferability (inconsistent comparisons) and imprecise effect estimate.</p> |

PICO 13. Should patients with recent onset lumbar radiculopathy be offered directional exercise compared to motor control exercise?

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| <p>↑ <i>Consider offering directional exercise or motor control exercise to patients with recent onset lumbar nerve root compression. There is no documentation of a clinically relevant difference between the two types of treatment (⊕○○○).</i></p> | <p><i>Definitions:</i> Directional exercise was defined as repeated movement in a specific direction that alleviate referred pain based on the concept of mechanical diagnosis and therapy (MTD) [71] Motor control exercise was defined as core stability training exercises focussing on the deep core musculature supporting the spine, and performed without pain provocation and typically with the spine in a neutral position.</p> <p><i>Included studies:</i> Based on the literature search of PICO 12, four RCTs were included [66, 67, 69, 70]. None of the included studies did a head-to-head comparison, and consequently an indirect comparison was made.</p> <p><i>Primary outcomes:</i> We did not observe a statistically significant difference between the two interventions on short term leg pain intensity [66, 67, 69, 70] back pain intensity [67, 70], activity limitations [67, 69, 70], or neurological deficits [69].</p> <p><i>Comments:</i> The level of evidence was downgraded due to indirect comparisons, lack of transferability (variation in populations, interventions, and comparisons).</p> |
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PICO 14. Should patients with recent onset lumbar radiculopathy be offered directional exercise in combination with neuromuscular control training compared to directional exercise alone?

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| <p>√ <i>It is good practice to consider combining directional exercises with motor control exercises rather than directional exercises alone for patients with recent onset lumbar nerve root compression, since a synergistic effect of the two interventions cannot be ruled out.</i></p> | <p><i>Definition:</i> Combined exercise therapy was defined as treatment consisting of a combination of various exercises tailored to the individual patient and adjusted per his or her symptoms, and delivered by a healthcare professional. The focus of this question was specifically on directional exercises and motor control as defined in PICO 13.</p> <p><i>Included studies:</i> None identified.</p> <p><i>Comments:</i> In the recommendation, consideration was given to the potential positive effect of both direction-specific exercises and neuromuscular control training. The working group agree that it is likely that, in combination, the two interventions may have a greater effect than individually and they are probably often given together.</p> |
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PICO 15. Should patients with recent onset lumbar radiculopathy be offered spinal manual therapy in addition to usual care?

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| <p>↑ <i>Consider offering spinal manual therapy to patients with recent onset lumbar nerve root compression as an add-on to the usual treatment (⊕○○○).</i></p> | <p><i>Definition:</i> Manual therapy is defined in PICO 5.</p> <p><i>Included studies:</i> We did not identify any studies that matched the patient population. Instead, three RCTs [67, 72, 73] identified from the literature search were included as indirect evidence; the first included patients with disc protrusion but intact annulus verified by MRI [72], the second study included patients with radiating leg pain of mixed duration (mean 24 months) with or without neurological symptoms [73], and one RCT included patients with and without radiating leg pain of mixed duration [67]. The interventions consisted of manipulation [72, 73] or manipulation, mobilization and muscle stretching techniques [67]. Usual care was defined as advice alone [67], advice and sham manipulation [72], and home exercise [73].</p> <p><i>Primary outcomes:</i> We observed a small, statistically significant effect in favour of the intervention on short term leg pain intensity [67, 72, 73], back pain intensity [67, 72, 73] and activity limitations [67, 73]. No difference was observed on neurological deficits [67, 73].</p> <p><i>Comments:</i> The level of evidence was downgraded due to lack of transferability (downgraded twice due to mixed populations) and imprecise effect estimate.</p> |
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PICO 16. Should patients with recent onset lumbar radiculopathy be offered one of supervised exercise therapy or spinal manual therapy over the other?

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| <p>↑ <i>Consider recommending supervised exercise therapy or manual therapy to patients with recent onset lumbar nerve root compression. There is no documentation of a clinically relevant difference between the two interventions (⊖○○○).</i></p> | <p><i>Definition:</i> Supervised exercise therapy is defined in PICO 12 and spinal manual therapy in PICO 5.</p> <p><i>Included studies:</i> We did not identify any studies that did a head-to-head comparison of the interventions in the target population. Instead, indirect evidence was considered. We identified two RCTs that made a head-to-head comparison of directional exercises and manual therapy in patients with LBP > 3 months with and without radiating leg pain and/or neurological symptoms [67, 74]. We further included indirect evidence from PICO 12 [29, 66-70] and PICO 15 [67, 72, 73] and based the recommendation on a comparison via usual care.</p> <p><i>Primary outcomes:</i> In patients with LBP >3 months, we did not observe differences in effects on short term leg pain intensity [67], back pain intensity [67, 74] or activity limitations [67, 74]. Same results were found in the indirect comparisons (short term leg pain intensity [29, 66-70, 72, 73], back pain intensity [29, 67, 70], activity limitations [29, 67, 69, 73], neurological deficits [69, 70]).</p> <p><i>Comments:</i> The level of evidence was downgraded due to indirect comparisons, lack of transferability (population, symptom duration, and presence of leg pain), imprecise effect estimates and lack of reporting of the primary outcome neurological deficits.</p> |
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PICO 17. Should patients with recent onset lumbar radiculopathy be offered acupuncture in addition to usual care compared to usual care?

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| <p>Recommendation 17 and level of evidence</p> <p>√ <i>It is not good practice to offer acupuncture on a routine basis to patients with recent onset lumbar nerve root compression.</i></p> | <p><i>Definitions:</i> Acupuncture is defined in PICO 7.</p> <p><i>Included studies:</i> None identified.</p> <p><i>Comments:</i> The recommendation was formulated based on clinical experience and indirect evidence from two systematic reviews dealing with acupuncture for non-specific LBP [75] and complementary and alternative treatment [76].</p> |
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PICO 18. Should patients with recent onset lumbar radiculopathy be offered MRI in addition to usual treatment compared to usual care?

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| <p>↓ <i>MRI should only be offered to patients with recent onset lumbar nerve root compression upon due consideration, since the beneficial effect is uncertain (⊕○○○).</i></p> | <p><i>Definition:</i> Lumbar MRI within 1 to 12 weeks after start of symptoms, and relevant information to the patient regarding imaging findings.</p> <p><i>Included studies:</i> We identified one RCT [46], in which patients were offered a clinical examination, MRI and usual care, and followingly randomized to either receive information regarding MRI findings or not. Usual care consisted of advice, medication, exercises and physiotherapy. Further, one cohort study [77] was included as indirect evidence.</p> <p><i>Primary outcomes:</i> We did not observe any differences in effect on short term activity limitations, and short- and long term fear-avoidance [46].</p> <p><i>Comments:</i> The level of evidence was downgraded due to lack of transferability (mixed population), only one study, and lack of reporting of primary outcomes (short term leg pain intensity, short term back pain intensity, and lumbar surgery).</p> <p>The working group emphasised that information regarding imaging findings does not appear to improve clinical outcomes. Further, the potential harm (i.e. negative iatrogenic effects, increased surgical rates and overtreatment) outweigh the potential positive effects [77], which led to a recommendation against the intervention.</p> |
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PICO 19. Should patients with recent onset lumbar radiculopathy be offered extraforaminal glucocorticoid injection in the lumbar nerve root area in addition to usual treatment compared to usual care?

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| <p>↓ <i>Extraforaminal glucocorticoid injection in the lumbar nerve root area should only be offered to patients with recent onset lumbar nerve root compression upon due consideration, since the beneficial effect is probably short-lived and very low (⊕○○○).</i></p> | <p><i>Definition:</i> X-ray guided glucocorticoid injection (with or without local anaesthetics) in the musculature adjacent to the nerve root of the affected nerve root (i.e. without penetration of the dura) in patients with a pre-existing MRI that excluded other pathologies and visualized the intervertebral space.</p> <p><i>Included studies:</i> We did not identify any studies that evaluated this question. As indirect evidence, we identified a systematic review [78] and a health technology evaluation [79], including one RCT [80] that compared extraforaminal to epidural injections, and 24 studies comparing steroidal injection compared to placebo [81-104].</p> <p><i>Primary outcomes.</i> The overall result on short term pain intensity was a statistically significant, but clinically small, effect in favour of the intervention [78, 79]. No clinically relevant effect was seen on short term activity limitations [78, 79].</p> <p><i>Comments:</i> The level of evidence was downgraded due to indirect evidence, lack of transferability (procedures not routinely used in Denmark), imprecise effect estimate, and risk of bias.</p> <p>The evidence profile presented for this question in the Danish report and the above recommendations are based on Chou et al [79] pp.155, 156, 163, 165 and 170.</p> <p>In the recommendation, consideration was given to the time and effort that is required to perform the procedure, and the lack of clinically relevant short and long term effects, which led to a recommendation against the intervention.</p> |
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PICO 20. Should patients with recent onset lumbar radiculopathy and no effect of conservative treatment be offered a surgical consultation before 12 weeks compared to after 12 weeks?

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| <p>√ It is good practice that patients with recent onset lumbar nerve root compression are assessed by a back surgeon within 12 weeks in cases where severe and disabling pain persists despite non-surgical treatment</p> | <p><i>Definition:</i> A consultation with a surgical specialist within 12 weeks from the start of symptoms and with the aim to evaluate the potential need for lumbar surgery. This should be offered to patients who have undergone non-surgical treatment without improvement.</p> <p><i>Included studies:</i> None identified.</p> <p><i>Comments:</i> As indirect evidence, a systematic review on the timing of surgery [105], which included two studies on surgical versus non-surgical treatment [106, 107] informed a good practice recommendation.</p> |
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