


National clinical guidelines for non-surgical treatment of patients with recent onset neck pain or cervical radiculopathy

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Abstract

Purpose To summarise recommendations about 21 selected non-surgical interventions for recent onset (<12 weeks) non-specific neck pain (NP) and cervical radiculopathy (CR) based on two guidelines from the Danish Health Authority.

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

Results Twelve recommendations were based on evidence and nine on consensus. Management should include

information about prognosis, warning signs, and advise to remain active. For treatment, guidelines suggest different types of supervised exercise and manual therapy; combinations of exercise and manual therapy before medicine for NP; acupuncture for NP but not CR; traction for CR; and oral NSAID (oral or topical) and Tramadol after careful consideration for NP and CR.

Conclusion Recommendations are based on low-quality evidence or on consensus, but are well aligned with recommendations from guidelines from North America. The working groups recommend intensifying research relating to all aspects of management of NP and CR.

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Background

Clinical guidelines assist clinicians' decision-making by providing recommendations for clinical procedures and interventions. The demand for clinical guidelines is steadily growing due to increased focus on evidence-based prioritising of health care services. In recent years, rigorous methods for systematically selecting and appraising the available evidence have been developed and become generally accepted [1, 2]. In 2012, the Danish Finance Act appropriated approximately 11 million EUR for the preparation of evidence-based clinical guidelines. The Danish Health Authority (DHA) was asked to lead formation of the guidelines in collaboration with the country's foremost experts in specific health areas representing a high burden of disease, high costs, large variability in care, new available technology, a change in indications for treatment, or doubt about the evidence base for established procedures and interventions. A total of 47 guidelines are now completed and in 2015 and 2016, Danish National Clinical Guidelines dealing with non-surgical treatment of recent onset (<12 weeks) non-specific neck pain (NP) [3] and recent onset (<12 weeks) cervical radiculopathy (CR) [4] were published in Danish.

Non-specific NP is defined as pain or discomfort in the neck and/or shoulder girdle with or without pain referred to the arms [5]. In most cases, a precise patho-anatomical cause for NP cannot be established, and therefore, most NP is classified as non-specific when there is no indication of specific pathology such as inflammatory rheumatic disease, osteoporosis, cancer, or radiculopathy.

CR is associated with reduced space in the nerve root canal and/or inflammatory reaction within the nerve root, which is most often triggered by a disc herniation or osseous degeneration of the facet joints [6]. Clinically, it is characterized by arm pain, in some cases paraesthesia and eventually reduced muscle strength, altered sensation and impairment of deep tendon reflexes [7]. The diagnosis of radiculopathy is based on clinical signs and symptoms, and CT scans or MRI can confirm anatomical compromise of the nerve root [7]. Establishing the diagnosis of cervical radiculopathy is, however, challenged by low diagnostic accuracy of clinical tests [8], by

a weak association between imaging findings and symptoms [9, 10], and by the phenomenon of referred pain without involvement of a nerve root that can mimic CR [11]. Therefore, at present, there is no firm definition or uniform diagnostic criteria for cervical radiculopathy, and it is challenging to separate cervical radiculopathy from non-specific neck pain with referred arm pain [3, 12].

NP is highly prevalent [13], and globally ranked number four as cause of years lived with disability [14]. Danes with NP visit their general practitioner substantially more often than people without and the costs for treatment and sick leave are approximately 400 million EUR [15]. The prevalence and incidence of CR are uncertain, but a yearly incidence of 0.83 cases per 1000 persons has been estimated in the US [16].

This paper summarizes the Danish national clinical guidelines for non-surgical treatment of recent onset (<12 weeks) non-specific NP and recent onset (<12 weeks) CR published in Danish by DHA as full reports in Danish in 2015 and 2016 [3, 4]. The mandates for the two working groups were to make recommendations concerning a maximum of ten selected interventions for NP and ten selected interventions for CR. The working groups were not asked to make recommendations for diagnostic procedures or care pathways.

Methods

Study design

The clinical 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 a recommendation related to each of the clinical questions. The method followed international standards for clinical guidelines [2], which were operationalized in a handbook from DHA and briefly summarized below [17]. This method was based on the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) approach [1]. The full clinical guidelines are available in Danish with all supportive material, including a detailed description of the methods on the DHA webpage [3, 4, 17].

Organisation of the work

Each project group consisted of a chairman, a project manager, a search specialist, a methodologist, and a lead reviewer. Members of the two multidisciplinary working groups (12 people for NP and 10 people for CR) were appointed following recommendation from professional organisations and scientific societies. The working groups

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were involved in all parts of the process including formulating the clinical questions, data extraction, risk of bias evaluation, rating the quality of the evidence, and formulating the recommendations. Reference groups with representatives from stakeholders from the Danish health care system (municipalities, regions, and hospitals), and patient organisations discussed and gave feedback and recommendations regarding selection of clinical questions and 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 and made publicly available on the DHA webpage [18].

Finally, drafts of the clinical guidelines were reviewed by two external peer-reviewers and in a public hearing. 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

Each clinical guideline addressed a maximum of ten focused clinical questions, which were structured using the patient, intervention, comparison, and outcome approach (PICO) [1].

Populations

The target populations were patients above the age of 18 years with less than 12 weeks of non-specific NP with or without associated arm pain and no signs of CR, or up to 12 weeks of symptoms and clinical signs of CR, respectively. It was assumed that the differentiation between non-specific NP and radiculopathy is based on a clinical examination without the use of diagnostic imaging. The reasons for choosing interventions in the acute stages were for NP that most people have episodes of relative short duration [13]. Similarly, we consider effects of treatment up to 12 weeks after the initial CR of special interest as patients with CR are recommended to consult a surgeon in case of no improvement after 8–12 weeks [19].

Interventions and comparisons

The mandate was restricted to non-surgical interventions. The working groups chose interventions based on perceived frequency of use, uncertainty about effectiveness, or uncertainty about superiority of one intervention over another. It was assumed that patients with either NP or CR would receive a basic intervention including information when seeking care. Therefore, the selected interventions for evaluation were to be considered a supplement to basic treatment with no further specification. Trials were, therefore, eligible for inclusion when a basic treatment was provided in both the

intervention and control groups, and the intervention under scrutiny was added in one of the groups. By doing so, the effects of adding the interventions in question to the basic treatment were reviewed, and where this was not possible, we accepted placebo- or sham-controlled trials. Because the basic treatment would vary across eligible studies, the phrase ‘in addition to other treatment’ was used in the clinical questions and recommendations. Some of the questions addressed a head-to-head comparison of two treatments when it was assumed that there is frequently a clinical situation with a choice between the two.

Outcome measures

For each of the clinical question, two or more primary outcomes and their timing were chosen a priori. In the Danish version, these are referred to as critical outcomes. The primary outcomes in both guidelines were pain and pain-related activity limitations. For these outcomes, the absolute differences between the intervention and control groups on generally accepted and validated instruments such as a visual analogue scale (VAS), a numeric pain rating scale (NRS), or the neck disability index (NDI) should be available. For questions related to medication, primary outcomes also included serious adverse events, gastrointestinal side effects, and blood pressure increase. Secondary outcomes varied across the two guidelines and included worsening of neurological signs and symptoms, pain at the end of treatment, drop-out rates, surgery during the following year, adverse effects, return to work, sick leave, and quality of life. In the Danish version, these are referred to as important outcomes.

Literature searches and inclusion criteria

The literature was systematically searched for each clinical question in three steps. First, Medline, Embase, Pedro, and a recognised national guideline database were searched for clinical guidelines 10 years back (2005 for NP and 2004 for CR). Then, Medline, Embase, Cinahl, Cochrane, and Pedro were searched for systematic reviews 10 years back, and finally, the same databases were searched for randomised clinical trials with no lower limit for the publication year. In case a high-quality 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 primary literature. All the literature searches included studies published until and including March 2016 (NP) or December 2014 (CR), published in English, Norwegian, Swedish, or Danish. The search terms and strategies are available from the DHA homepage [20, 21].

In case no RCTs were identified concerning recent onset NP, indirect evidence from populations with symptoms lasting more than 12 weeks was included in the guideline.

This was not the case for patients with CR, because the condition of long-lasting CR symptoms was considered very different from recent onset CR.

The lead reviewer screened 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 reviewers and a member of the working group or a scientific methods advisor independently assessed all included papers for quality and extracted data for each clinical question. If a high-quality systematic review was available, data were extracted from this. The quality was assessed using the AGREE-II tool [22] for clinical guidelines, the AMSTAR tool [23] for systematic reviews, and the Cochrane risk of bias tool for RCTs [24]. 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 was performed using the web-based software Covidence [25] from which data were exported to the RevMan software [26] for meta-analyses, the results of which were further transferred to MAGIC [27] or GradePro [28] for GRADE assessment [29]. Disagreements in data extraction and quality assessment were solved through consensus between the two evaluators. The quality of evidence was graded from high to very low according to the GRADE definitions (Table 1) for each of the outcomes. Downgrading was done following the standard definitions of risk of bias, inconsistency, indirectness, imprecision, publication bias, large effect, or plausible confounding [17, 29]. The overall level of evidence supporting the recommendation for each focused question was determined based on the quality for the primary outcome with the lowest quality supporting evidence.

From evidence to recommendations

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 randomised trials, a good practice recommendation was formulated based on indirect evidence, i.e., evidence from randomised trials in closely related patient populations, or consensus in the working group. Final recommendations were based on weighing the evidence of positive versus negative effects and included patient values and preferences as well as the working-groups' perceptions and experience.

Results

Altogether, the guidelines considered 19 clinical questions. Ten covered recent onset neck pain, while 9 were chosen for CR. Six interventions were covered by both clinical guidelines, namely, information/patient education, NSAIDs, opioids, manual therapy, massage, and acupuncture. Different types of exercise or combinations of exercise (individualised physical activity, motor control exercise, and directional exercise), manual therapy plus supervised exercise, and manual therapy versus medication were addressed slightly different in the two guidelines. An overview of the interventions and the general recommendations is shown in Table 3. None of the questions could be answered by existing clinical guidelines or systematic reviews and recommendations were based on RCTs in 11 of 19 questions and on consensus within the working group in eight of 19. The available evidence from RCTs was in all cases limited and of very low quality, mainly because of either high risk of bias, imprecision, small study samples, indirectness, or inconsistency. Flow charts of included literature [30], risk of bias assessments of clinical guidelines and systematic reviews, and evidence tables are available in Danish at the DHA website [31, 32].

Table 1 Definitions of grades of recommendation, assessment, development, and evaluation (GRADE) adapted from Guyatt et al. 2011 [1]

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

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 or 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

DHA Danish Health Authority

Table 3 Overview of recommendations and their level of evidence

PICO number	Intervention	Recent onset neck pain	Cervical radiculopathy
PICO 1 and 11	Patient education/information (written)	✓ For ↓ (⊕○○○○)	✓ For
PICO 12	Individualised physical activity		✓ For
PICO 13	Tramadol or NSAID?		✓ Careful consideration
PICO 8	NSAID, oral NSAID, topical	✓ Careful consideration ↑ (⊕○○○)	
PICO 9	Opioids	✓ Careful consideration	
PICO 10	Manual therapy and exercise rather than medication	↑ (⊕○○○)	
PICO 2	Supervised exercise	↑ (⊕○○○)	
PICO 14	Motor control exercise		↑ (⊕○○○)
PICO 15	Directional exercise		✓
PICO 3 and 16	Manual therapy	↑ (⊕○○○)	↑ (⊕○○○)
PICO 4	Manual therapy and supervised exercise versus supervised exercise	↑ (⊕○○○)	
PICO 5	Supervised exercise and manual therapy versus manual therapy	↑ (⊕○○○)	
PICO 17	Traction		↑ (⊕○○○)
PICO 7 and 18	Massage	↓ (⊕○○○)	✓ Against
PICO 6 and 19	Acupuncture	↑ (⊕○○○)	✓ Against

✓ Consensus recommendation, ↓ Weak recommendation against, ↑ Weak recommendation for, (⊕○○○) quality of evidence very low, see Tables 1 and 2 for definitions

Specific recommendations

Both for treatment of patients with NP and CR, weak or good clinical practice recommendations were given for information and patient education, advice to stay physically active, different types of supervised exercise, manual therapy alone or in combination with exercise, and weak recommendations were given against massage. The expert

groups recommended only using NSAID or tramadol after careful consideration and not as first choices. In patients with NP, the guideline recommends weakly for acupuncture, topical NSAID, and for exercise over NSAID. In patients with CR, there was a weak recommendation for traction and against acupuncture. A short description of eligible studies, primary outcomes, recommendations, and levels of evidence is provided in Tables 4 and 5. Forest

Table 4 PICO questions, recommendations, definitions of intervention, supporting evidence, and comments regarding patients with recent onset non-specific neck pain

Recent onset non-specific neck pain

<p>PICO 1. Should patients with recent-onset neck pain be offered advice with a focus on reassuring information in addition to other treatment?</p> <p>√ <i>It is good clinical practice to focus on reassuring information when counselling patients with recent onset neck pain. If using written information, this should be consistent with the oral information given in the consultation</i></p> <p>↓ <i>Use only written advice with a focus on reassurance after careful consideration if the written information is not supported by other elements such as oral information (⊕○○○)</i></p>	<p><i>Definition</i> Reassuring information was defined as information addressing the patient's anxiety and fear of severe illness [36] in an interactive process between patient and clinician that seeks to help the patient feel more confident through an understanding of neck pain as a benign condition in which the neck is not harmed by daily activities, work and exercise [37]</p> <p><i>Included studies</i> No evidence was found for oral information but one randomised controlled trial (RCT) addressed written information compared to usual care [38]</p> <p><i>Primary outcomes</i> The study showed a negative effect of written information on medication use but it did not report on any of the primary outcomes</p> <p><i>Comments</i> The quality of the evidence was rated very low due to only one study, risk of bias, indirectness, and imprecision. The recommendations are based mainly on consensus within the working group. The included study did not directly answer the focused question but patient's worries and concerns are known to be associated with poor prognosis. Therefore, the working group recommends reassuring information to avoid pain behaviour and promote the maintenance of physical activity, social relations and contact to the labour market</p>
<p>PICO 2. Should patients with recent onset neck pain be offered supervised exercise therapy in addition to other treatment?</p> <p>↑ <i>Consider offering supervised exercise therapy to patients with recent onset neck pain in addition to other treatment (⊕○○○)</i></p>	<p><i>Definition</i> In this guideline supervised exercise therapy was defined as any type of exercise (directional, motor control, strength or endurance) for the neck and shoulders instructed by a healthcare professional as a part of the intervention</p> <p><i>Included studies</i> Only one RCT dealing with patients with acute neck pain [39] was identified while the remaining studies included patients with varying [40] and longer duration of NP [41–46]. Supervised exercise included various exercises for strengthening of neck- and shoulder muscles [40, 42, 44, 45], motor control [42, 43], eye-neck coordination [46], posture [39], and stretching [39, 44] in various combination. These were either compared to minimal intervention [45], waiting list [45], and general practitioner care [39] or the were studied as add-ons to EMG and infrared light [42], medical treatment [46], hot/cold packs and massage [44], or acupuncture [43]</p> <p><i>Primary outcomes</i> Positive but small effects on pain and activity limitation were observed</p> <p><i>Comments</i> The quality of the evidence was downgraded for indirectness, bias in the included studies, and imprecision. The working group also suggests considering other types of physical activity taking patient reference into account. The potential positive effect on pain and disability and the low risk of harms led to the recommendation</p>
<p>PICO 3. Should patients with recent onset neck pain be offered spinal manual therapy in addition to other treatment?</p> <p>↑ <i>Consider offering spinal manual therapy in patients with recent onset neck pain in addition to other treatments (⊕○○○)</i></p>	<p><i>Definition</i> Spinal manual therapy was defined as all manual techniques (mobilisation and high velocity spinal manipulative techniques) directed at joints between the vertebrae of the neck and the upper thoracic region</p> <p><i>Included studies</i> Five RCTs [39, 47–50] were identified in which manual therapy was compared to placebo ultrasound [50], placebo manipulation [47], usual care by general practitioner [39], hot packs and electro therapy [48, 49]. One small study that included 12 patients and compared spinal manipulation directed to the contralateral side of pain to placebo ultrasound was not included because the treatment approach was considered of limited clinical relevance [50]</p>

Table 4 continued

Recent onset non-specific neck pain

	<p><i>Primary outcomes</i> The studies demonstrated a positive effect on the primary outcome pain at 4–12 week follow-up</p> <p><i>Comments</i> The quality of the evidence was very low due to risk of bias, imprecision and indirect evidence. Patient preferences, co-morbid conditions and tolerance as well as clinician skills and experience should be taken into consideration when delivering spinal manual therapy. Most patients may accept mobilisation while some may have reservations regarding high velocity thrust</p>
PICO 4. Should patients with recent onset neck pain be offered exercise therapy in combination with spinal manual therapy rather than exercise therapy alone?	
↑ <i>Consider offering exercise therapy in combination with spinal manual therapy in patients with recent onset neck pain rather than exercise therapy alone</i> (⊕○○○)	<p><i>Definition</i> The definitions of exercise therapy and spinal manual therapy were the same as above</p> <p><i>Included studies</i> No studies were found on patients with recent onset neck pain but two RCTs [41, 51] that included patients with neck pain of longer duration were identified. The studies examined the effect of adding cervical manual therapy to strength exercise [41] and motor control exercise [51]</p> <p><i>Primary outcomes</i> Small positive effects were seen at 4–12 week follow-up on the outcomes pain and activity limitation</p> <p><i>Comments</i> The quality of the evidence was very low due to risk of bias, imprecision and indirectness. The potential effect of the combined treatment led to the recommendation. This recommendation may be less relevant for patients with non-complex neck pain.</p>
PICO 5. Should patients with recent onset neck pain be offered spinal manual therapy in combination with exercise therapy in combination rather than spinal manual therapy alone?	
↑ <i>Consider offering spinal manual therapy in combination with exercise therapy in patients with recent onset neck pain rather than spinal manual therapy alone</i> (⊕○○○)	<p><i>Definition</i> The definitions of exercise therapy and spinal manual therapy were the same as above</p> <p><i>Included studies</i> We used indirect evidence from one RCT in patients with long-lasting neck pain and pain related to trauma [52]. The study compared the effect of progressive strength training in combination with manipulation of the cervical and upper thoracic spine to manipulation alone</p> <p><i>Primary outcomes</i> The study showed that the combination of interventions was more effective than manipulation alone on pain and activity limitation at 4–12 weeks</p> <p><i>Comments</i> The strength of the evidence was downgraded to very low because there was only one study, risk of bias and a mixed group of patients including long-lasting and trauma-related pain. This recommendation may be less relevant for patients with non-complex neck pain</p>
PICO 6. Should patients with recent onset neck pain be offered acupuncture in addition to other treatment?	
↑ <i>Consider offering acupuncture in patients with recent onset neck pain in addition to other treatment</i> (⊕○○○)	<p><i>Definition</i> Acupuncture was defined as any procedure where thin needles penetrate the skin, whether the aim is to affect the classical acupuncture points and meridians, or trigger-points in the muscles</p> <p><i>Included studies</i> One small RCT including 17 patients with recent onset neck pain was identified. Dry needling was compared to usual care but none of the primary outcomes for this guideline were reported [53]. Therefore, indirect evidence from nine RCTs including patients with long-lasting pain was included [54–63]. These studies compare acupuncture of varying technique, frequency and intervention period to usual care in primary care and waiting list [61, 62], sham laser [55, 56, 58], TENS [57, 60], diazepam and NSAID [54, 59, 63]</p> <p><i>Primary outcomes</i> Three studies reported no effect on the pain and activity limitation at 4–12 weeks follow-up, whereas very small effects were noted on secondary outcomes of pain at end of treatment.</p>

Table 4 continued

Recent onset non-specific neck pain

	<p><i>Comments</i> The quality of the evidence was rated very low due to bias, imprecision and indirectness. Only health care professionals with appropriate training should offer acupuncture. The potential effects on pain and activity limitations as well as mild harms lead to the recommendation.</p>
<p>PICO 7. Should patients with recent onset neck pain be offered massage in addition to other treatment?</p>	
<p>↓ <i>Only offer massage for patients with recent onset neck pain after careful consideration because no effect has been documented even with high dose treatment</i> (⊕○○○)</p>	<p><i>Definition</i> Massage was defined as all manual techniques targeting the soft tissues (muscles and connective tissue) around the neck, shoulders and upper thoracic spine regardless of the forces applied. Classical Chinese and Asian massage therapy were not considered</p>
	<p><i>Included studies</i> No RCTs were found for patients with recent onset neck pain. Indirect evidence from one RCT [64] including patients with longer duration of pain, was included</p>
	<p><i>Primary outcomes</i> There was no effect on pain after 4–12 weeks</p>
	<p><i>Comments</i> The quality of the evidence was very low due to bias, imprecisions and indirectness. The lack of effect of massage weighed against the potential risk of the patient developing passive coping strategies should be taken into account and more active strategies should be given higher priority</p>
<p>PICO 8. Should patients with recent onset neck pain be offered non-steroid anti-inflammatory drugs (NSAID) in addition to other treatment?</p>	
<p>↑ <i>Consider offering topical NSAID to patients with recent onset neck pain in addition to other treatment for immediate pain relief</i> (⊕○○○)</p>	<p><i>Definition</i> Topical and oral NSAID were included</p>
<p>√ <i>It is good clinical practice only to offer oral NSAID to patients with recent onset neck pain only after careful consideration. The treatment should be of short duration and carefully take into account harms, contra-indications and patient preference</i></p>	<p><i>Included studies</i> For topical NSAID, one RCT [65] was identified where diclofenac gel was compared to a placebo gel applied for 10 days to the neck. No direct or indirect literature was identified for oral NSAID</p>
	<p><i>Primary outcomes</i> Topical NSAID had a positive effect on the primary outcome pain at end of treatment</p>
	<p><i>Comments</i> The study had high risk of bias, and the patient group was judged not to be representative. Therefore, the quality of the evidence was downgraded to very low. For oral NSAID the recommendation followed general Danish guidelines for pharmacological treatment of pain [66] and the use of NSAID [67]</p>
	<p><i>Comments</i> If the patient has severe acute pain, per oral NSAID can be considered for short-term use. Potential harms and patient preference must be considered, particularly in the elderly and patients with coronary heart disease. A dialog with the patient about duration of treatment, the expected effect, harms and other treatment options is advised</p>
<p>PICO 9. Should patients with recent onset neck pain be offered tramadol in addition to other treatment?</p>	
<p>√ <i>It is good clinical practise only to offer tramadol to patients with recent onset neck pain after careful consideration. The treatment should be of short duration and carefully take into account harms, contra-indications and patient preference</i></p>	<p><i>Definitions</i> Tramadol in any form was included in the search</p>
	<p><i>Included studies</i> No evidence was found related to patients with recent onset neck pain. The recommendations were based on the Danish guidelines for analgesic treatment of pain [66] and use of opioids [68]</p>
	<p><i>Comments</i> In a dialog with the patients, tramadol may be considered short term if the patient has severe acute pain. The patient has to be informed about cognitive harms including sedation. Treatment of longer duration requires careful monitoring from the prescribing medical doctor and should follow national guidelines for use of opioids. The patient should be informed about duration of treatment, the expected effect, harms and alternative treatment options</p>

Table 4 continued

Recent onset non-specific neck pain

PICO 10. Should patients with recent onset neck pain be offered exercise/spinal manual therapy rather than analgesia?

↑ *Consider offering exercise therapy or spinal manual therapy rather than analgesia in patients with recent onset neck pain where more than advice and information is needed* (⊕○○○)

Definition All types of exercise, manual therapy and analgesic treatment as described in previous sections were considered

Included studies One RCT [69] was identified. The study also included patients with traumatic neck pain. Medical treatment (paracetamol, NSAID, opioids or muscle relaxants) was compared to manual therapy (manipulation, mobilisation or massage) or exercise (home exercise for flexibility without any resistance)

Primary Outcomes Exercise/manual therapy was slightly superior to pharmacological treatment on pain and activity limitation at 4–12 weeks. A number of harms were present in the pharmacological group (gastro-intestinal, increase in blood pressure, sedation) whereas in the exercise/manual therapy groups, worsening of pain was more frequent

Comments The quality of the evidence was rated low because there was only one study and because of indirectness. Exercise therapy or spinal manual therapy should be preferred over per oral analgesics, when it is clear that the individual patient needs more than information about prognosis, course, warning signs and advise to stay as active as possible

plots and risk of bias assessment are provided in Appendix 1 for all outcomes.

General recommendations

Management of people with NP and CR should always contain information about the course of the condition, prognosis, and warning signs as well as encouragement to remain as physically active as possible. In patients with non-complicated or short duration (days to weeks) NP or CR, information and advice may be sufficient. The working groups recommend that choice of any treatment should be done in consideration of patient preferences and that the amount and the intensity of treatment should be proportionate with the duration and level of pain and disability to avoid unnecessary and lengthy treatment. Both patient and health care provider should closely monitor symptoms and clinical signs and adjust treatment plans accordingly. If one of the recommended interventions fails to provide adequate effects, other guideline recommended treatments could be considered. The specific recommendations are summarised in Tables 4 and 5.

Discussion

Two Danish national clinical guidelines considered 19 clinical questions regarding the management of neck pain and cervical radiculopathy. None of the questions could be

answered by referring to existing clinical guidelines or systematic reviews. Recommendations were based on RCTs in 11 of the 19 clinical questions and on consensus in the expert groups in eight of 19. The quality of the available evidence from RCTs was consistently downgraded to very low mainly due to high risk of bias, imprecision, small study samples, and indirectness.

We found a striking lack of evidence for the efficacy of many of the interventions studied, in particular in relation to interventions for CR. Thus, either none or only small and methodologically weak studies gave supportive evidence for the use of interventions, such as information and guidance, medication, directional exercise, massage, acupuncture, motor control exercises, joint mobilisation and manipulation, and cervical traction. Therefore, the CR guideline recommendations are based mainly on indirect evidence and consensus between the members of the working groups. New high-quality clinical research, focusing on these patient groups, is likely to influence future guideline recommendations greatly.

Our recommendations are comparable to those from newer guidelines released in the USA and Canada [33–35]. In 2008, The Orthopaedic Section of the American Physical Therapy Association published clinical practice guidelines relating to assessment of impairment, clinical examination, and interventions in people with NP with and without arm pain [33], which were recently updated. In spite of slightly different definitions of the patient groups, their recommendations for treatment of patients with recent

Table 5 PICO questions, recommendations, definitions of intervention, supporting evidence and comments regarding recent onset cervical radiculopathy

Recent onset cervical radiculopathy

<p>PICO 11. Should patients with cervical radiculopathy be offered structured, individualised patient education in addition to other treatment?</p> <p>√ <i>It is good clinical practice to offer structured, individualised patient education for patients with recent onset of CR. Patient education should include information about prognosis and pain mechanisms and individualized guidance on appropriate behaviour (physical activity) and pain management</i></p>	<p>Definition Patient education was defined as structured, individualized information about the anatomical and physiological basis for cervical radiculopathy, pain mechanisms, prognosis, and/or guidance on physical activity that would enable the patient to better cope with their condition</p> <p>Included studies No randomised trials dealing with patient education were identified</p> <p>Comments It is important that the information is provided in a reassuring manner, which does not induce fear. Despite the lack of evidence, the working group believes that patient education increases the patient's understanding of their pain and condition, and thereby conveys beneficial effects</p>
<p>PICO 12. Should patients with cervical radiculopathy be offered guided, individualized exercises in addition to other treatment?</p> <p>√ <i>It is good clinical practice to guide patients with recent onset of CR about individually tailored physical activity and general training in addition to other treatment</i></p>	<p>Definitions Guided individualized exercises were defined as any advice about tailored physical activities to keep the patient active, via instructed general aerobic training and exercise to maintain, regain or improve physical performance</p> <p>Included studies No randomised trials were identified for or against an effect of guided exercises</p> <p>Comments The least pain provoking activities should be preferred. The working group believed that individual guidance in exercise might reinforce the maintenance of physical function and promote health and be helpful in coping with pain</p>
<p>PICO 13. Should patients with cervical radiculopathy be offered tramadol rather than NSAIDs?</p> <p>√ <i>It is good clinical practice to use either tramadol or NSAIDs for short-term treatment of pain in patients with recent onset CR, if paracetamol has not had sufficient effect. The choice should be made taking into account the adverse effects of both drugs and patient preferences</i></p>	<p>Definition Any type of tramadol and NSAID were included in the searches</p> <p>Included studies No randomised trials were identified</p> <p>Comments Pharmacological pain treatment should follow Danish national guidelines for acute, non-malignant pain and acute lumbar pain [70, 71]. It is the clinical experience of the working group members that the pain relieving effect of tramadol is stronger than NSAID for some patients, and vice versa, but both products have significant harms (i.e., increased risk of cardiovascular events with NSAID and addiction with tramadol). Therefore, tramadol should not be preferred over NSAID</p>
<p>PICO 14. Should patients with cervical radiculopathy be offered motor control exercises for the neck in addition to other treatment?</p> <p>↑ <i>Consider offering motor control exercises for the neck in patients with recent onset of CR in addition to other treatments (⊕○○○)</i></p>	<p>Definition Motor control exercises were defined as specific training of the deep neck muscles performed without pain aggravation [72]</p> <p>Included studies Two RCTs were identified in which motor control exercises were added to manual therapy or standard treatment [73, 74] and compared to neck collar and wait and see [73], while the other study compared to joint mobilisation and a combination of the two [74]</p> <p>Primary outcomes There was a large and clinically relevant short-term effect on pain 3–12 weeks, but no effect was seen on measures of activity limitation</p> <p>Comments The quality of the evidence was very low due to risk of bias, imprecise results and indirectness. Motor control exercises can be difficult for the patient to perform and the health care professional should consider the patients' ability to understand and adjust the exercises to avoid worsening of pain. Taking into account the possible beneficial effects on pain and function and the low risk of adverse effects, the working group considered this type of exercises safe for the patient. The patient can perform this type of exercise as an active treatment at home and thus, it allows the patient to take some responsibility for his/her own treatment</p>

Table 5 PICO questions, recommendations, definitions of intervention, supporting evidence and comments regarding recent onset cervical radiculopathy

Recent onset cervical radiculopathy

PICO 15. Should patients with cervical radiculopathy be offered treatment with directional exercise in addition to other treatment?

√ *It is good clinical practice to consider treatment with directional exercise in patients with recent onset CR in addition to other treatment*

Definition Directional exercise was defined as specific end-range movements of the neck performed in directions that reduced the patient's radiating pain [75]

Included studies No randomised trials of directional exercise in patients with CR were identified

Comments Directional exercise can be difficult for the patient to perform and the health care professional should consider the patient's ability to understand and adjust the exercises to avoid worsening of pain. Based on clinical experience among the working group members, low risk of harm, and an active patient approach, directional exercise could be a tool for patients who understand the underlying principles to gain control over their pain

PICO 16. Should patients with cervical radiculopathy be offered spinal manual therapy in addition to other treatment?

↑ *Consider offering spinal manual therapy in patients with recent onset CR in addition to other treatments* (⊕○○○)

Definition Spinal manual therapy was defined as above

Included studies One RCT was found [74].

Primary outcomes There was a positive but not statistically significant effect of adding manual therapy to exercise

Comments The quality of the evidence was low due only one study, imprecise estimates (few participants in the study) and high risk of bias

The working group agreed that use of spinal manual therapy should be combined with advice on pain relief and physical activity. It is considered good practice to initiate manual therapy using low intensity techniques and then gradually apply more intense techniques based on patient response and preference. The working group based the recommendation on consensus, because the evidence was of very low quality and the effects highly uncertain. The possibility of short-term pain relief along with the low risk of harm led to the recommendation

PICO 17. Should patients with cervical radiculopathy be offered traction in addition to other treatment?

↑ *Consider offering cervical traction for patients with recent onset CR in addition to other treatment* (⊕○○○)

Definition Traction as a treatment was defined as static or intermittent longitudinal pull applied to the patient's head in order to stretch the neck, either manually by the therapist or mechanically by using pulleys or machines

Included studies Four RCTs were identified [76–79]. Traction as an add-on to different treatment packages (physiotherapy, collar, medication) including placebo traction [76] and multimodal physiotherapy [78, 79]. The last study compared two different types of manual traction as an add-on to exercises

[77]

Primary outcomes Due to poor reporting of results, only two studies were included in the meta analysis [77, 79]. The results were neither statistically significant, nor clinically relevant. The third study showed no difference in neck or arm pain after four weeks of treatment [76], whereas the fourth study showed statistically significant and clinically relevant reduction of both neck and arm pain [78]

Comments The quality of the evidence was rated very low due to bias, heterogeneity in interventions, and inconsistency of results. Traction can be used for pain relief as an integral part of manual therapy delivered while closely monitoring of the effects. If there is no immediate effect or a deterioration of symptoms treatment should not continue. The working group placed greater emphasis on consensus on good practice than on current evidence in this clinical question. The possible positive effects on both pain and activity limitations as well as mild harms formed the basis for the recommendation

Table 5 continued

Recent onset cervical radiculopathy

PICO 18. Should patients with cervical radiculopathy be offered massage in addition to other treatment?	
√ <i>It is not good clinical practice to routinely offer massage in patients with recent onset CR in addition to other treatment</i>	<p><i>Definition</i> Massage was defined as previously described</p> <p><i>Included studies</i> No RCTs were found</p> <p><i>Comments</i> Massage can be used optionally along with joint mobilisation or manual traction in the wait for other interventions or if other treatments are ineffective or have harmful effects. The forces and the positions used during massage should be adapted to the patient's symptom responses</p>
PICO 19. Should patients with recent onset cervical radiculopathy be offered treatment with acupuncture in addition to other treatment?	
√ <i>It is not good clinical practice to routinely offer acupuncture in patients with recent onset CR in addition to other treatment</i>	<p><i>Definition</i> Acupuncture was defined as previously</p> <p><i>Included studies</i> No RCTs were found</p> <p><i>Comment</i> In some patients acupuncture may help alleviate pain in the wait for another treatment to be initiated, or in the event that other treatments are ineffective or have harms. If there is no effect, or if symptoms worsen, the treatment should not continue. The lack of evidence of efficacy and the risk of complications lead to the recommendation</p>

onset NP and mobility deficits were similar to ours and endorse thoracic manipulation, a program of neck range of motion exercises, scapula-thoracic and upper extremity strengthening and eventually cervical manipulation and/or mobilisation. Acupuncture is not recommended in the acute stage of NP. For CR, the American guideline recommends the use of mobilising and motor control exercise as well as nerve mobilisation procedures but not the use of manual mobilisation techniques. Mechanical intermittent traction and acupuncture is now only recommended for the chronic stages [33]. Differences between their and our recommendations may be explained by publication of newer research, and the focus on long-term outcomes in the American guideline. In 2010, North American Spine Society released *An evidence-based clinical guideline for the diagnosis and treatment of cervical radiculopathy from degenerative disorders* [34] and a summary of the guideline was published in 2011 [7]. This guideline included clinical questions about definitions, epidemiology, diagnosis, and a range of interventions, including physical therapy/exercise, manipulation/chiropractic, epidural steroid injections, ancillary procedures as well as a range of surgical interventions and is, therefore, not directly comparable to the new Danish guidelines. Nevertheless, for the interventions covered in both guidelines (exercise therapy and manipulation), comparable levels of evidence for effectiveness were found and recommendations were very similar indicating limited research progress between 2010 and 2015. Finally, the OPTIMa collaboration published an evidence-based guideline for the management of NP and associated disorders including CR. In this guideline structured patient education combined with range of motion

exercise, multimodal care (range of motion exercise with manipulation or mobilisation), or muscle relaxants was recommended for patients with recent onset NP, and it was recommended that clinicians not offer structured patient education alone, strain-counterstrain therapy, relaxation massage, cervical collar, electro-acupuncture, electrotherapy, or clinic-based heat. For patients with recent onset CR, clinicians were recommended to consider supervised strengthening exercises in addition to structured patient education but not structured patient education alone, cervical collar, low-level laser therapy, or traction [35].

In spite of the lack of evidence for benefit or harm for a particular intervention, physicians and professional societies look to expert groups and task forces for guidance [2]. The GRADE methodology has the potential to accommodate such circumstances, because it classifies evidence as either strong or weak and provides interpretations for patients, clinicians, and policy makers [29]. The informed clinician should choose intervention in recognition of how different choices may be appropriate for different patients and that each management decision is consistent with the patients' values or preferences [13]. The GRADE Working group encourages panels to make recommendations wherever possible whether they are based on solid evidence or not [17].

Strengths of this national clinical guideline include the commissioning and chairmanship by the DHA and the rigorous adherence to relevant scientific standards [1, 2]. Importantly, the guideline working groups were composed of clinicians and academics with a broad range of professional backgrounds and relevant professional societies and agencies were consulted during the process to ensure the

involvement of relevant stakeholders. The guideline working groups were assisted by expert research librarians and by methodologists from the Nordic Cochrane Centre and DHA. Finally, the guideline was peer-reviewed by two international experts who provided detailed comments, which resulted in revisions and clarifications prior to release of the final report.

The main weakness of these national clinical guidelines relates to the lack of high-quality clinical trials in the area, and therefore, recommendations are based on only few studies with a high risk of bias or on consensus in the guideline working groups. In addition, the working groups were limited in the number of clinical questions that they could assess; thus, the influence of individual members of the working and reference groups may have excluded an evaluation of the evidence for other potentially effective interventions. Finally, the mandate prescribed that individual studies could only be included as supportive evidence if they assessed effectiveness of interventions in addition to usual care, which may have lead the working groups to exclude studies that could potentially have strengthened the evidence base of some of the recommendations. However, only 11 RCTs were excluded from the retrieved full text papers in the last step of the study selection process.

Conclusion

Two multidisciplinary working groups were commissioned by DHA to developed new Danish National Clinical Guidelines for non-surgical treatment in patients with recent onset of NP and CR. The recommendations are generally based on weak evidence or on consensus. However, they are well aligned with recommendations from similar guidelines from North America. The guideline working groups strongly recommend to intensify research efforts in relation to all aspects of the management of NP and CR.

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