Title: Evidence-based treatment recommendations for neck and low back pain across Europe: a systematic review of guidelines

Running head: Recommended treatment options for neck and back pain

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Significance

Consensus regarding evidence-based treatment recommendations for patients with neck and low back pain (NLBP) from recent European clinical practice guidelines identifies a wide range of predominantly non-pharmacological treatment options. This includes options potentially applicable to all patients with NLBP and those applicable to only specific patient subgroups. Future work within our Back-UP research team will transfer these evidence-based treatment options to an accessible clinician decision support tool for first contact clinicians.

Abstract

Background and objective: This systematic review synthesised evidence from European neck and low back pain (NLBP) clinical practice guidelines (CPGs) to identify recommended treatment options for use across Europe.

Databases and Data Treatment: Comprehensive searches of thirteen databases were conducted, from 1st January 2013 to 4th May 2020 to identify up-to-date evidence-based European CPGs for primary care management of NLBP, issued by professional bodies/organisations. Data extracted included; aim and target population, methods for development and implementation, and treatment recommendations. The AGREE II checklist was used to critically appraise guidelines. Criteria were devised to summarise and synthesise the direction and strength of recommendations across guidelines.

Results: Seventeen CPGs (11 low back; 5 neck; 1 both) from eight European countries were identified, of which seven were high-quality. For *neck pain,* there was consistent *weak* or *moderate* strength recommendations for: reassurance, advice and education, manual therapy, referral for exercise therapy/programme, oral analgesics and topical medications, plus psychological therapies or multidisciplinary treatment for specific subgroups. Notable recommendation differences between back and neck pain included, i) analgesics for neck pain (not for back pain); ii) options for back pain specific subgroups - work-based interventions, return to work advice/programmes, and surgical interventions (but not for neck pain), and iii) a greater strength of recommendations (generally moderate or strong) for back pain than those for neck pain.

Conclusions: This review of European CPGs identified a range of mainly non-pharmacological recommended treatment options for NLBP that have broad consensus for use across Europe.

1. Introduction

Neck and low back pain (NLBP) are amongst the most frequent reasons for visiting a general practitioner (GP) or physiotherapist in primary care in Europe (Bot et al., 2005; Jordan et al., 2010). The substantial burden of illness from these conditions was shown by the most recent Lancet-Global Burden of Disease study which highlighted low back pain (LBP) as the single highest cause of years lived with disability (out of 354 conditions studied), with neck pain ranked eighth (female) and twelfth (male) (GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018). Outlining potential ways to address this societal burden, the recent Lancet series on LBP (Foster et al., 2018) recommended a greater focus on improving decision-making in first-contact consultations as current treatment is highly variable (Maserejian et al., 2014) and often not in line with clinical guidelines (Darlow et al., 2014; Somerville et al., 2008), leading to suboptimal treatment outcomes (Maher et al., 2017). For example, referrals to secondary care specialists are too common, provision of self-management advice and education can be limited, opioids and imaging are over-prescribed, and sign-posting to locally available non-pharmacological options such as exercise groups is limited (Chou et al., 2017a; Koes et al., 2010; Maserejian et al., 2014). Finding solutions that promote best practice care for patients with NLBP in first-contact consultations is therefore a priority (Foster et al., 2012).

Our team is part of Back-UP, a European programme of research developing a digital health technology to support clinical decision-making for patients with NLBP based on a stratified care approach for first-contact consultations [http://backup-project.eu/]. Decision support tools have demonstrated promising results for helping clinicians to translate the most up to date recommended evidence into their practice (Murphy et al., 2014). For example, a systematic review of over 160 randomized controlled trials testing clinical decision-support systems identified improved processes of clinical care (e.g. diagnosis, treatment, disease monitoring) or patient outcomes (e.g. clinical events, quality of life) in over half of included studies (Roshanov et al., 2013).

The Keele STarT Back stratified care Tool for back pain has recently been superseded by the Keele STarT MSK Tool (Dunn et al., submitted), which has been validated in UK primary care and shown to be predictive of pain and disability across a range of common musculoskeletal (MSK) pain sites, including NLBP. In addition, a new set of recommended matched treatment options for MSK patients at low, medium and high-risk of poor outcome (Babatunde et al., 2017; Protheroe et al., 2019) have been piloted in a feasibility trial (Hill et al., accepted). However, these matched treatments were designed to evaluate stratified care in UK general practice rather than for use across European countries by a broader range of first-contact clinicians such as occupational health physicians. We therefore felt the matched treatments should be further refined for the specific context of this European project.

Recent systematic reviews of clinical practice guidelines (CPGs) for musculoskeletal pain (Lin et al., 2020), and back pain (Wong et al., 2017, Oliveira et al., 2018) aimed to summarize recommended treatments for either LBP or neck pain. However, less emphasis was placed on improving decision-making in first-contact consultations, identifying specific CPG recommendations for patient subgroups defined by their risk of persistent pain and disability and the potential relevance, and on improving the referral process. To our knowledge, no prior reviews of CPGs have assessed treatment recommendations for both neck and low back pain and explored consistencies or similarities between recommendations for these common spinal pain presentations.

The aim of this study was therefore to conduct a systematic review of published European back and neck pain clinical guidelines to describe and synthesise the evidence of recommended treatment options with broad consensus for use across Europe.

2. Methods

A systematic review of contemporary European clinical practice guidelines was conducted and reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidance (PRISMA; Moher et al., 2009).

2.1. Systematic review protocol

An *a priori* protocol was written and followed (Available at http://backup-project.eu/?page_id=84).

2.2. Search strategy

A comprehensive search strategy was conducted of eight electronic databases (EMBASE, MEDLINE, CINAHLPlus, HMIC, PsycINFO, Epistemonikos, Pedro and TRIP database) and four sources of grey

literature (National Institute for Health and Clinical Excellence (NICE), Scottish Intercollegiate Guidelines (SIGN), WHO Guidelines, Guidelines International Network (G-I-N), and DynaMed Plus) from 1st January 2013 to 4th May 2020.

The search strategy utilized both text word searching in the title, abstract or keywords and database subject headings, combining terms for neck or back pain and practice guidelines (see Supporting information Appendix S1: full search strategy for OVID MEDLINE). For the other databases, search terms were adapted to the search capabilities of the platform.

In addition, our Back UP research partners were asked to identify any relevant guidelines from their country. Reference lists of included guidelines were checked to identify additional documents relevant to the methodology of the guideline.

2.3. Eligibility criteria

Inclusion criteria

- Recent evidence-based European clinical guidelines issued by professional bodies or organisations for guideline development [published from 2013 onwards]. We included recently published guidance only, to ensure treatment recommendations emerging from the review would be based on relatively up-to-date evidence;
- Guidelines concern adult populations (18 years or over), with NLBP (including patients presenting to first contact health professionals with symptoms of whiplash related disorders or symptoms of radiculopathy such as radicular pain;
- Guidelines that include recommendations regarding treatment options for patients presenting with NLBP, in particular:
    - Treatments deliverable within primary care (as broadly considered across Europe, including occupational healthcare) or referral pathways from primary to secondary care recommended for clinical practice (in at least two European countries).
    - Treatments aiming to reduce pain, improve function and/or support return to work. Relevant outcomes also included evidence-based recommendations regarding factors (patient, clinician, environment) that may be associated with effectiveness of treatment, and recommendations regarding clinical prediction rules or decision tools supporting the selection of treatment for specific patient subgroups (where mentioned in the guideline).

Exclusion criteria

- Non-European guidelines;
- All publications that are not evidence-based clinical practice guidelines, including guidelines based solely on consensus or without an explicit literature search, and other publication types: systematic reviews, randomised trials, cohort studies, case series, editorials, protocols, letters;
- Paediatric only populations (under 18 years);
- NLBP as a result of severe trauma e.g. fracture and spinal cord injury, inflammatory arthritis including spondyloarthropathies, and those that focused on broader conditions e.g. (chronic) pain that may encompass spinal pain;
- Guidelines focused on patients managed in secondary care with an established diagnosis of radiculopathy;

- Guidelines focused specifically on surgical treatment options/comparisons or on specific interventions not limited to spinal pain e.g. analgesics in older adults;
- Guidelines that involved populations admitted to hospital (not ambulatory care);
- Guidelines for which translations could not be obtained.

2.4. Guideline selection

Results from all searches were imported into EndNote x9 (reference management software, Clarivate Analytics. Available at https://endnote.com/) and duplicates removed. Unique citations were then imported into Covidence (Veritas Health Innovation, Melbourne, Australia. Available at https://www.covidence.org/) to manage the screening process.

Two reviewers (NC and GM) independently screened all titles and abstracts for relevance against eligibility criteria and excluded ineligible publications by agreement. Full texts were independently assessed for inclusion by pairs of independent reviewers (NC, GM and DvdW). Disagreements were noted and resolved between pairs of reviewers and where necessary the involvement of a third reviewer. Reasons for exclusion at the full text stage were recorded.

2.5. Data extraction

A data extraction form was purposively designed in Excel to record relevant information from each of the clinical practice guidelines included in the review. Complementary documents were sourced where relevant, such as methodological reports and evidence syntheses. Information was extracted regarding general guideline information (e.g. country, healthcare setting, publication year, target population, and presenting symptoms); methods regarding guideline development and implementation (e.g. multidisciplinary group/single profession; how strength of evidence determined; details regarding consensus methods); and intervention recommendations, specifically only those that can be offered in primary care, and guidance for referral (e.g. [strength of] recommendations, any details regarding subgroups).

One reviewer extracted data from each guideline; in the case of guidelines in English this was independently checked by a second reviewer with any disagreements resolved through discussion. For non-English guidelines no independent check with a second experienced reviewer was feasible within the timeline of conducting this review.

2.6. Assessment of guideline quality

The AGREE II (Appraisal of Guidelines Research and Evaluation) reporting checklist was used to critically appraise guidelines (Brouwers et al., 2010a). Internationally, this is the most widely used tool for assessing guideline quality (Siering et al., 2013), with good construct validity and reliability (Brouwers et al., 2010b, c). The instrument focuses on guideline development and reporting and consists of 23 items addressing 6 domains (1. Scope and purpose; 2. Stakeholder involvement; 3. Rigour of development; 4. Clarity of presentation; 5. Applicability; and 6. Editorial independence). Each item is rated on a 7-point Likert scale from 1 (Strongly disagree) to 7 (Strongly agree). In addition, there are two final items that ask appraisers to give an overall judgement in light of ratings given for the 23 items.

The web-based platform My AGREE PLUS (https://www.agreetrust.org/my-agree/) was used to complete appraisals online, based on the user manual. Each item is presented for scoring alongside detailed guidance on how to score the item, including where to find relevant information and what to consider when deciding on the score for each item.

Critical appraisal was conducted concurrent to data extraction by the same reviewer(s). One reviewer appraised each guideline; in the case of guidelines in English this was independently checked by a second reviewer with any disagreements resolved through discussion. For non-English guidelines no independent check was feasible.

No set thresholds exist for determining high/low quality guidelines, however, AGREE II guidance suggest users decide these according to their specific context (AGREE Next Steps Consortium, 2017). Based on examples given in the AGREE II user manual, and with reference to previous studies (Bouwmeester et al., 2009; Lin et al., 2020), we considered guidelines to be of high quality if AGREE II Domain 3 *i.e.* 'Rigour of development' scored at least 70%, and the remaining five domains, along with the overall assessment, scored at least 50%.

2.7. Synthesis of guidelines and identification of consistent recommendations

All recommendations extracted from the included guidelines were collated based on the way the treatment option was described in/translated from the guideline, and then grouped according to treatment theme. Tables were drawn up to present all the recommendations, alongside details regarding the context of the guideline (i.e. professional organisation(s), country, and target population/diagnostic classification). Members of the review team, which included researchers with academic and clinical expertise in musculoskeletal pain, were presented with these tables for review. Following discussion of the many very specific intervention options *e.g.* different forms of exercise, nuanced and/or inconsistently used terms, and translation anomalies/country specific terminology (often reported in only 1 or 2 guidelines), interventions were merged by treatment type/modality. A general practitioner (physician) was invited to review the recommendations relating to medications specifically and undertook a similar process of refining the grouping of treatment options.

The direction (*i.e.* for, against, or open) and strength of recommendations was harmonised, taking into consideration the array of methods and terminologies used across included guidelines (see Supporting Information Appendix S2). The resulting nomenclature enables the reader to distinguish between strong or weak recommendations based on a formal grading system e.g. GRADE; those where no formal grading system was applied; and recommendations based on consensus/expert opinion. Treatment or referral options for which a recommendation was formulated in one guideline only, were not further considered.

To summarise and synthesise the direction and strength of recommendations across guidelines a set of criteria was devised and followed, such that:

- **Strong FOR/AGAINST recommendation** (should do/should not do): consistent recommendations in at least two high-quality guidelines from different countries (at least one guideline of which reports a 'strong' *i.e.* // or XX recommendation).

- **Moderate FOR/AGAINST recommendation** (could do/could not do): consistent recommendations in at least one high-quality (where recommendation is not based on expert opinion *i.e.* O+ or O-) and if only one high-quality, then one or more low quality guidelines.
- **Weak FOR/AGAINST recommendation:** recommendations from high quality guidelines but based on expert opinion only and/or recommendations from multiple low-quality guidelines.
- **Inconsistent**: inconsistent recommendations from guidelines of high quality (for/against).
- **Inconclusive**: open/uncertain recommendations only, or recommendations from low quality guidelines are inconsistent.

3. Results

3.1. Guideline selection

The systematic search resulted in 3941 unique citations, from which 17 clinical practice guidelines (CPGs) were identified (Fig. 1) and included in this evidence synthesis (Bier et al., 2016; Bons et al., 2017; BÄK et al., 2017; Glocker et al., 2018; Kassolik et al., 2017; Monticone et al., 2013; NICE, 2016; Pohl et al., 2018; Regione Toscana, 2015; Schaafstra et al., 2015; SFMT, 2013; Staal et al., 2017; Sundhedsstyrelsen, 2015; 2016a, b, c; van Wambeke et al., 2017).

<<Fig. 1>>

3.2. Guideline characteristics

An overview of characteristics of included CPGs and the methods used in their development and implementation is presented in Table 1, with guideline specific details provided in Supporting Information Appendices S3 & S4. The 17 contemporary CPGs originate from 8 European countries (Belgium, Denmark, France, Germany, Italy, The Netherlands, Poland, and the UK). The majority address low back pain and/or radicular pain (*n* = 12; 71%), whilst 6 (35%) are concerned with neck pain and/or radicular pain. Five guidelines (29%) focus specifically on patients presenting with symptoms of radiculopathy. Three of these guidelines (Schaafstra et al., 2015; Sundhedsstyrelsen, 2015; 2016b) are specifically developed for the management of radiculopathy in general practice or primary care. The two other guidelines were designed for healthcare professionals responsible for the management of acute lumbar (Glocker et al., 2018) or cervical (Pohl et al., 2018) radiculopathy in any ambulant, outpatient or secondary care setting". Conversely three CPGs (18%) explicitly exclude radiculopathy.

A large majority of CPGs were developed by multidisciplinary groups (*n* = 14, 82%), employed formal grading of evidence and/or recommendations (*n* = 13, 76%). Just over half the guidelines detailed timeframes for future revisions (*n* = 10, 59%), whilst just under half detailed or undertook a consensus process (*n* = 8, 47%).

In addition to treatment recommendation most guidelines addressed planning of care (*n* = 14, 82%), diagnostic assessment (*n* = 12, 71%), evaluation of red (*n* = 12, 71%) and/or yellow (psychosocial, *n* = 10, 59%) flags. Conversely, less than half the guidelines detailed the evaluation of blue/black flags

i.e. blue: individuals' perceptions of work-related factors and the relationship between work and health, black: system-level factors (context, work environment, policies) (*n* = 7, 41%), practitioner education (*n* = 8, 47%), or organisation and policy implications (*n* = 5, 29%).

<<Table 1>>

3.3. Quality appraisal

The AGREE II domain scores for each guideline are presented in Table 2, along with our designation of the overall quality *i.e.* high/low based on domain scores. Notably one guideline (Kassolik et al., 2017) was not rated highly on any of the domains, achieving at its best 44% for clarity of presentation. With the exception of this guideline, the remaining 16/17 CPGs were all highly rated *i.e.* achieved at least 50% of maximum possible score, for Domains 1 (scope and purpose) and 4 (clarity of presentation). Conversely, a minority of CPGs (*n* = 7, 41%) achieved high ratings for Domain 5 (applicability). Domains 2 (stakeholder involvement) and 6 (Editorial independence), together with overall assessment score, were each reported to a high quality in a large majority of studies (*n* = 14, 82%). Domain 3 (rigour of development) with its higher cut-off point of 70% determining high-quality was achieved by just over half the CPGs (*n* = 9, 53%).

Seven CPGs (41%) were considered high quality overall: 2 focused on neck pain, both Danish (Sundhedsstyrelsen, 2015, 2016c) and 5 on low back pain including 1 Belgian, 1 UK, 2 Danish, and 1 German (BÄK et al., 2017; NICE, 2016; Sundhedsstyrelsen, 2016a, b; van Wambeke et al., 2017), (Table 2 and Supporting Information Appendices S5 & S6).

<< Table 2 >>

3.4. Consistency of CPG recommendations for neck pain

Six guidelines provided treatment recommendations for neck pain (Bier et al., 2016; Kassolik et al., 2017; Monticone et al., 2013; Pohl et al., 2018; Sundhedsstyrelsen, 2015, 2016c). Supporting Information Appendix S5 details the specific treatment options or intervention modalities identified in each guideline together with the direction and strength of each recommendation. In total, recommendations were provided that covered a wide range of treatment options: reassurance; advice and education; medication; injection/infiltration; acupuncture; thermotherapy; manual therapy; exercise therapy; postural therapy; traction; electrotherapy; orthotics; ergonomic interventions; taping/strapping; psychological interventions; multidisciplinary treatments; referral for imaging; and referral for specialist opinion; plus a disparate group of interventions that were labelled 'miscellaneous'.

In considering the consistency of recommendations across all neck pain CPGs (Table 3), 14 treatment options were supported, while recommendations were inconsistent or inconclusive (mixed) regarding the use of 7 treatment options. For 26 treatment options a recommendation was only given in 1 guideline, and these were not further considered.

Positive (weak to moderate) recommendations from high quality (Sundhedsstyrelsen, 2015, 2016c) or multiple low quality (Bier et al., 2016; Kassolik et al., 2017; Monticone et al., 2013; Pohl et al.,

2018) guidelines supported the use of reassurance; advice and education with specific mention of physical activity, and exercise; prescription of oral analgesic medications including for neuropathic pain, and specifically paracetamol, NSAIDs, and opioids including tramadol; topical medication; exercise interventions alone or in combination with other treatments; and manual therapy in combination with another (exercise) intervention.

Psychological or multimodal (multidisciplinary) interventions were recommended for specific subgroups of patients with neck pain, with either psychosocial risk factors or for those with more persistent neck pain or disability.

Recommendations were inconsistent or inconclusive regarding manual therapies (delivered without additional active treatment); traction; electrotherapies; thermotherapies; cervical orthoses; acupuncture/dry needling; and referral for imaging.

<< Table 3>>

3.5. Consistency of CPG recommendations for low back pain

Twelve guidelines provided treatment recommendations for back pain (Bons et al., 2017; BÄK et al., 2017; Glocker et al., 2018; Kassolik et al., 2017; NICE, 2016; Regione Toscana, 2015; Schaafstra et al., 2015; SFMT, 2013; Staal et al., 2017; Sundhedsstyrelsen, 2016a, b; van Wambeke et al., 2017). Details regarding the specific treatment options or intervention modalities identified from each guideline can be found in Supporting Information Appendix S6, along with the direction and strength of each recommendation. Similar to guidelines for neck pain, recommendations were provided that covered a wide range of treatment and referral options. For many of these treatment options, the body of evidence underpinning recommendations was larger compared to neck pain, although often still inconsistent or of low quality.

Table 4 presents the summary of recommendations from high- and low-quality guidelines and the overall recommendations derived from our synthesis. A range of treatment options (n=26) were only mentioned in one guideline, and these were not considered further. Positive (weak to strong) recommendations from high quality (BÄK et al., 2017; NICE, 2016; Sundhedsstyrelsen, 2016a, b; van Wambeke et al., 2017) or multiple low quality (Bons et al., 2017; Glocker et al., 2018; Kassolik et al., 2017; Regione Toscana, 2015; Schaafstra et al., 2015; SFMT, 2013; Staal et al., 2017) guidelines supported the use of 14 treatment options, including: reassurance; advice and education with specifics for physical activity, exercises, and work; manual therapy in combination with active treatment; exercise interventions; group exercise programmes including back schools; psychological therapies including cognitive behavioural interventions as standalone interventions or in combination with exercise; work-based rehabilitation and return to work programmes.

Psychological therapies are mainly recommended for subgroups of patients with increased psychosocial risks, mood problems, or more complex, persistent back pain; while referral for surgery is only supported for cases with signs of specific pathology.

Overall, guidelines recommended strongly against the use of more than a couple of days bedrest for patients with low back pain. Referral for imaging is only supported for those with red flags, such as increased risk of fracture, infection, (metastatic) cancer, neurological emergencies including cauda

equina syndrome, aortic aneurysm or systemic inflammatory arthritis (detailed in Supporting Information Appendix S7), or deterioration of symptoms. And although mixed, moderate to strong recommendations were also given against the use of paracetamol, anti-depressants, anticonvulsants, and muscle relaxants; spinal injections for non-specific LBP; traction; orthoses; and a range of applications (e.g. electrotherapies, shortwave, laser).

Recommendations were inconsistent or inconclusive with respect to medication (NSAIDs, opioids; topical); epidural steroid and other injections; acupuncture; and manual, postural, and thermotherapies.

<< Table 4>>

3.6. Comparison of CPG recommendations for neck and low back pain

In order to examine the consistency of CPG recommendations across neck and low back pain, overall strengths of recommendation for each identified intervention (see Tables 3 & 4), were assessed (Table 5). Despite a larger body of evidence for the effectiveness of treatment for back pain and a larger number of back pain guidelines, recommendations were generally consistent for neck and back pain (Table 5), in particular regarding support for the use of advice and education, reassurance, certain oral and topical pharmacologic treatments (with the exception of paracetamol), exercise interventions, manual therapy when combined with active treatment, and psychological interventions. Guidance was also consistent in terms of the limited use of imaging (only for patients with red flags or where imaging is likely to change management), and recommendations against the use of bed rest, orthoses, traction and a range of modalities (laser therapy, electrotherapy, shortwave).

Referral for imaging or surgical intervention, bed rest, antidepressant and muscle relaxant medications, psychological or multidisciplinary interventions are recommended for specific subgroups of patients (FOR 'SPECIFIC SUBGROUP' or AGAINST 'WITH EXCEPTIONS' in Table 5).

<< Table 5>>

4. Discussion

In this review, we have systematically identified, synthesised and graded 17 European clinical guidelines relating to the management of NLBP. Based on the quality of the evidence we have identified a short list of treatment options recommended for the management of NLBP (see Table 5). This information is aimed to provide clinicians, healthcare managers, funders, policymakers and researchers with a comprehensive summary of the current consensus from clinical guidelines across Europe on the management of NLBP.

The guidelines included in our review came from 8 European countries (UK, Germany, France, Italy, Denmark, Poland, Belgium, and the Netherlands). Eleven of them addressed low back pain, five neck pain, and one both LBP and neck pain. Data extraction showed considerable variation in guideline development processes with seven guidelines (5 back, 2 neck) considered as high-quality, based on their development rigour, strong stakeholder involvement, and the applicability of their recommendations.

For ***neck pain,*** high quality guidelines consistently recommended the following evidence-based treatment options: reassurance, advice and education (including to remain active and exercise), manual therapy in combination with other treatment, referral for exercise therapy/programme, and a range of oral analgesics and topical medications, plus psychological therapies or multidisciplinary treatment for specific subgroups of patients. There was no strong evidence for use across Europe (as shown in Table 3). In contrast to the recommendations for low back pain, the neck pain guidelines included the use of painkillers such as paracetamol, NSAIDs (for acute pain only), opioids (for acute pain only), and neuropathic pain medication. However, these were only based on ***weak evidence*** (meaning the recommendations were based on expert opinion only from high quality guidelines, and/or multiple low-quality guidelines) and it should be noted that these medications are no longer consistently recommended for low back pain within the recent European guidelines. In fact, for ***low back pain*** the guidelines recommended entirely non-pharmacological treatments, additionally including work-based interventions, advice/programmes to return to work, and surgical intervention for specific subgroups. These recommendations were based on stronger evidence than those for neck pain.

In relation to previous literature, the findings of this review summarising the consensus from European guidelines, are consistent with recommendations in The Lancet back pain series (Foster et al., 2018) which advocated for greater use of non-pharmacological options for patients with back pain. The treatment options identified in this study are also broadly similar and consistent with two recent systematic reviews of clinical practice guidelines for musculoskeletal pain (Lin et al., 2020) and back pain (Oliveira et al., 2018) which identified similar key management recommendations (patient information, physical activity advice, return to work interventions, exercise interventions), although Oliveira et al., additionally identified antidepressants (for chronic LBP), NSAIDs and weak opioids for short periods of time (for acute LBP) to be frequently recommended across guidelines.

Recommendations from the European guidelines included in our review contrast notably with a systematic review of non-invasive treatments for low back pain conducted to inform the American College of Physicians Clinical Practice Guideline (Chou et al., 2016) which not only recommended 3 medication options (NSAIDs, opioids, duloxetine) with moderate to strong evidence (Chou et al., 2017b), but also included acupuncture within a group of 5 recommended non-pharmacological options (superficial heat, multi-disciplinary rehabilitation, acupuncture, exercise and manual therapy) (Chou et al., 2017a).

Many of the European guidelines included treatment recommendations related to patient subgroups: psychological therapies, multi-disciplinary treatment and referral for surgery were recommended for specific subgroups only; and very strict indications (strong recommendation against with exception given for bed rest, anti-depressants, and muscle relaxants). However, it was notable that clear assessment criteria to facilitate clinician decision-making about when to use these treatment options for specific patient subgroups were largely lacking. Similar to Lin et al. who highlighted that guidelines for patients with thoracic pain are lacking (Lin et al., 2020), we only identified one (low quality) guideline (Kassolik et al., 2017) that specifically addressed thoracic pain. We would also highlight that most guidelines lacked detail about the specific dose, duration and other detail around the delivery of the recommended treatments. For example, there was little clarity on the delivery of physical exercise or the recommended components of patient education or reassurance.

Strength and limitations

The strength of this review is that it provides a helpful overall summary of the treatment and referral recommendations from recent European guidelines for NLBP. This overview enabled us to identify treatment options that have been consistently recommended across 8 different countries and can therefore be considered to have broad European consensus. To facilitate the rigour of this evidence summary, we pre-specified inclusion and exclusion criteria for screening, quality appraised guidelines using the AGREE II checklist, and devised a set of clear criteria to summarise and synthesise the direction and strength of recommendations across guidelines. Further strengths included independent assessment of eligibility for inclusion, data extraction and appraisal of the quality of guidelines, and a standardised approach to synthesising evidence.

The guidelines included in our systematic review predominantly originate from northern and western European countries (except for the Italian guidelines), which can be considered a limitation. This may be partly explained by fewer guidelines being produced in southern or eastern Europe, but also by the fact that we only included guidelines published in the past 5 years. Whilst focusing on contemporary guidelines (2013 onwards) ensured that we identified the most relevant treatment options for current practice, we acknowledge that this meant that some earlier European guidelines, were not included. However, for the purposes of this review, we felt it was important to exclude guidelines that may not be based on up-to-date evidence of effectiveness. Although we included guidelines written in any European language, one limitation was that we were not able to carry out independent data extraction and quality appraisal by a second reviewer for guidelines not available in English. However, for most of these guidelines, the reviewer had the advantage of being involved in data extraction for English language guidelines, which helped to ensure consistency of data extraction and interpretation.

Only 7 CPGs (41%) were considered to be of overall high quality, with limitations mainly related to rigour of development (e.g. use of transparent methods to link evidence to recommendations, or processes to gain consensus regarding the strength of recommendations); and to applicability with few guidelines providing guidance on how to apply recommendations or taking into account practical and financial implications of their recommendations. Variation in the methods used to grade evidence and agree the strength of recommendations may potentially explain some of the variability in treatment recommendations across guidelines. We tried to incorporate quality as well as consistency in our synthesis of CPR, aiming to arrive at a transparent and systematic approach for summarizing and grading recommendations across guidelines.

Future work within the Back-UP research project will embed these evidence-based treatment options in an accessible clinician decision support tool for first contact clinicians, aiming to offer patients with NLBP treatment options better matched to risk of persistent pain and disability.

5. Conclusion

In conclusion, this systematic review identified seventeen contemporary clinical guidelines regarding NLBP (5 neck; 11 low back; 1 both) from 8 European countries, of which 7 were considered high quality. Recommendations were notably consistent for neck and low back pain, despite the larger evidence base and more guidelines for the latter. The implications from this review are that

clinicians have a broad range of mostly non-pharmacological evidence-based treatment options to consider for their patients with NLBP. These include some treatments which are a) potentially applicable to all patients such as advice and education and b) those applicable only to certain patient subgroups (e.g. referral to surgery).

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Author contributions

GM, DvdW and JH designed the study protocol with input from NC.
NC designed the literature search with input from DvdW.
NC, GM and DvdW performed the study selection with input from LM.
NC, GM, LM, SS and GW-J carried out data extraction and quality assessment.
NC, JH, SS and DvdW carried out the analysis and interpretation of the data.
NC and JH drafted the manuscript.
All authors critically revised the manuscript for intellectual content and read and approved the final manuscript.

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Legends for illustrations and tables

Figure 1: PRISMA Flow Diagram.

Table 1: Characteristics of included clinical practice guidelines.

Table 2: Quality appraisal of guidelines: AGREE II domain scores (%) and quality assessment. Cells in green indicate domain attained 'high' rating.

Table 3: Consistency of recommendations across guidelines for neck pain (see Supporting Information Appendix S5 for individual guidelines). ***Symbol – classification:*** // - should do; / - could do; /* - for (generic); O [O+/O-] – Open [expert opinion in favour/against]; X* - against (generic); X – should not do; XX – definitely do not do (see Supporting Information Appendix S2 for further detail).

Table 4: Consistency of recommendations across guidelines for low back pain (see Supporting Information Appendix S6 for individual guidelines). ***Symbol – classification:*** // - should do; / - could do; /* - for (generic); O [O+/O-] – Open [expert opinion in favour/against]; X* - against (generic); X – should not do; XX – definitely do not do (see Supporting Information Appendix S2 for further detail).

Table 5: Consistency of recommendations across low back pain vs neck pain guidelines

Title: Evidence-based treatment recommendations for neck and low back pain across Europe: a systematic review of guidelines

Running head: Recommended treatment options for neck and back pain

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Significance

Consensus regarding evidence-based treatment recommendations for patients with neck and low back pain (NLBP) from recent European clinical practice guidelines identifies a wide range of predominantly non-pharmacological treatment options. This includes options potentially applicable to all patients with NLBP and those applicable to only specific patient subgroups. Future work within our Back-UP research team will transfer these evidence-based treatment options to an accessible clinician decision support tool for first contact clinicians.

Abstract

Background and objective: This systematic review synthesised evidence from European neck and low back pain (NLBP) clinical practice guidelines (CPGs) to identify recommended treatment options for use across Europe.

Databases and Data Treatment: Comprehensive searches of thirteen databases were conducted, from 1st January 2013 to 4th May 2020 to identify up-to-date evidence-based European CPGs for primary care management of NLBP, issued by professional bodies/organisations. Data extracted included; aim and target population, methods for development and implementation, and treatment recommendations. The AGREE II checklist was used to critically appraise guidelines. Criteria were devised to summarise and synthesise the direction and strength of recommendations across guidelines.

Results: Seventeen CPGs (11 low back; 5 neck; 1 both) from eight European countries were identified, of which seven were high-quality. For *neck pain,* there was consistent *weak* or *moderate* strength recommendations for: reassurance, advice and education, manual therapy, referral for exercise therapy/programme, oral analgesics and topical medications, plus psychological therapies or multidisciplinary treatment for specific subgroups. Notable recommendation differences between back and neck pain included, i) analgesics for neck pain (not for back pain); ii) options for back pain specific subgroups - work-based interventions, return to work advice/programmes, and surgical interventions (but not for neck pain), and iii) a greater strength of recommendations (generally moderate or strong) for back pain than those for neck pain.

Conclusions: This review of European CPGs identified a range of mainly non-pharmacological recommended treatment options for NLBP that have broad consensus for use across Europe.

1. Introduction

Neck and low back pain (NLBP) are amongst the most frequent reasons for visiting a general practitioner (GP) or physiotherapist in primary care in Europe (Bot et al., 2005; Jordan et al., 2010). The substantial burden of illness from these conditions was shown by the most recent Lancet-Global Burden of Disease study which highlighted low back pain (LBP) as the single highest cause of years lived with disability (out of 354 conditions studied), with neck pain ranked eighth (female) and twelfth (male) (GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018). Outlining potential ways to address this societal burden, the recent Lancet series on LBP (Foster et al., 2018) recommended a greater focus on improving decision-making in first-contact consultations as current treatment is highly variable (Maserejian et al., 2014) and often not in line with clinical guidelines (Darlow et al., 2014; Somerville et al., 2008), leading to suboptimal treatment outcomes (Maher et al., 2017). For example, referrals to secondary care specialists are too common, provision of self-management advice and education can be limited, opioids and imaging are over-prescribed, and sign-posting to locally available non-pharmacological options such as exercise groups is limited (Chou et al., 2017a; Koes et al., 2010; Maserejian et al., 2014). Finding solutions that promote best practice care for patients with NLBP in first-contact consultations is therefore a priority (Foster et al., 2012).

Our team is part of Back-UP, a European programme of research developing a digital health technology to support clinical decision-making for patients with NLBP based on a stratified care approach for first-contact consultations [http://backup-project.eu/]. Decision support tools have demonstrated promising results for helping clinicians to translate the most up to date recommended evidence into their practice (Murphy et al., 2014). For example, a systematic review of over 160 randomized controlled trials testing clinical decision-support systems identified improved processes of clinical care (e.g. diagnosis, treatment, disease monitoring) or patient outcomes (e.g. clinical events, quality of life) in over half of included studies (Roshanov et al., 2013).

The Keele STarT Back stratified care Tool for back pain has recently been superseded by the Keele STarT MSK Tool (Dunn et al., submitted), which has been validated in UK primary care and shown to be predictive of pain and disability across a range of common musculoskeletal (MSK) pain sites, including NLBP. In addition, a new set of recommended matched treatment options for MSK patients at low, medium and high-risk of poor outcome (Babatunde et al., 2017; Protheroe et al., 2019) have been piloted in a feasibility trial (Hill et al., accepted). However, these matched treatments were designed to evaluate stratified care in UK general practice rather than for use across European countries by a broader range of first-contact clinicians such as occupational health physicians. We therefore felt the matched treatments should be further refined for the specific context of this European project.

Recent systematic reviews of clinical practice guidelines (CPGs) for musculoskeletal pain (Lin et al., 2020), and back pain (Wong et al., 2017, Oliveira et al., 2018) aimed to summarize recommended treatments for either LBP or neck pain. However, less emphasis was placed on improving decision-making in first-contact consultations, identifying specific CPG recommendations for patient subgroups defined by their risk of persistent pain and disability and the potential relevance, and on improving the referral process. To our knowledge, no prior reviews of CPGs have assessed treatment recommendations for both neck and low back pain and explored consistencies or similarities between recommendations for these common spinal pain presentations.

The aim of this study was therefore to conduct a systematic review of published European back and neck pain clinical guidelines to describe and synthesise the evidence of recommended treatment options with broad consensus for use across Europe.

2. Methods

A systematic review of contemporary European clinical practice guidelines was conducted and reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidance (PRISMA; Moher et al., 2009).

2.1. Systematic review protocol

An *a priori* protocol was written and followed (Available at http://backup-project.eu/?page_id=84).

2.2. Search strategy

A comprehensive search strategy was conducted of eight electronic databases (EMBASE, MEDLINE, CINAHLPlus, HMIC, PsycINFO, Epistemonikos, Pedro and TRIP database) and four sources of grey

literature (National Institute for Health and Clinical Excellence (NICE), Scottish Intercollegiate Guidelines (SIGN), WHO Guidelines, Guidelines International Network (G-I-N), and DynaMed Plus) from 1st January 2013 to 4th May 2020.

The search strategy utilized both text word searching in the title, abstract or keywords and database subject headings, combining terms for neck or back pain and practice guidelines (see Supporting information Appendix S1: full search strategy for OVID MEDLINE). For the other databases, search terms were adapted to the search capabilities of the platform.

In addition, our Back UP research partners were asked to identify any relevant guidelines from their country. Reference lists of included guidelines were checked to identify additional documents relevant to the methodology of the guideline.

2.3. Eligibility criteria

Inclusion criteria

- Recent evidence-based European clinical guidelines issued by professional bodies or organisations for guideline development [published from 2013 onwards]. We included recently published guidance only, to ensure treatment recommendations emerging from the review would be based on relatively up-to-date evidence;
- Guidelines concern adult populations (18 years or over), with NLBP (including patients presenting to first contact health professionals with symptoms of whiplash related disorders or symptoms of radiculopathy such as radicular pain;
- Guidelines that include recommendations regarding treatment options for patients presenting with NLBP, in particular:
    - Treatments deliverable within primary care (as broadly considered across Europe, including occupational healthcare) or referral pathways from primary to secondary care recommended for clinical practice (in at least two European countries).
    - Treatments aiming to reduce pain, improve function and/or support return to work. Relevant outcomes also included evidence-based recommendations regarding factors (patient, clinician, environment) that may be associated with effectiveness of treatment, and recommendations regarding clinical prediction rules or decision tools supporting the selection of treatment for specific patient subgroups (where mentioned in the guideline).

Exclusion criteria

- Non-European guidelines;
- All publications that are not evidence-based clinical practice guidelines, including guidelines based solely on consensus or without an explicit literature search, and other publication types: systematic reviews, randomised trials, cohort studies, case series, editorials, protocols, letters;
- Paediatric only populations (under 18 years);
- NLBP as a result of severe trauma e.g. fracture and spinal cord injury, inflammatory arthritis including spondyloarthropathies, and those that focused on broader conditions e.g. (chronic) pain that may encompass spinal pain;
- Guidelines focused on patients managed in secondary care with an established diagnosis of radiculopathy;

- Guidelines focused specifically on surgical treatment options/comparisons or on specific interventions not limited to spinal pain e.g. analgesics in older adults;
- Guidelines that involved populations admitted to hospital (not ambulatory care);
- Guidelines for which translations could not be obtained.

2.4. Guideline selection

Results from all searches were imported into EndNote x9 (reference management software, Clarivate Analytics. Available at https://endnote.com/) and duplicates removed. Unique citations were then imported into Covidence (Veritas Health Innovation, Melbourne, Australia. Available at https://www.covidence.org/) to manage the screening process.

Two reviewers (NC and GM) independently screened all titles and abstracts for relevance against eligibility criteria and excluded ineligible publications by agreement. Full texts were independently assessed for inclusion by pairs of independent reviewers (NC, GM and DvdW). Disagreements were noted and resolved between pairs of reviewers and where necessary the involvement of a third reviewer. Reasons for exclusion at the full text stage were recorded.

2.5. Data extraction

A data extraction form was purposively designed in Excel to record relevant information from each of the clinical practice guidelines included in the review. Complementary documents were sourced where relevant, such as methodological reports and evidence syntheses. Information was extracted regarding general guideline information (e.g. country, healthcare setting, publication year, target population, and presenting symptoms); methods regarding guideline development and implementation (e.g. multidisciplinary group/single profession; how strength of evidence determined; details regarding consensus methods); and intervention recommendations, specifically only those that can be offered in primary care, and guidance for referral (e.g. [strength of] recommendations, any details regarding subgroups).

One reviewer extracted data from each guideline; in the case of guidelines in English this was independently checked by a second reviewer with any disagreements resolved through discussion. For non-English guidelines no independent check with a second experienced reviewer was feasible within the timeline of conducting this review.

2.6. Assessment of guideline quality

The AGREE II (Appraisal of Guidelines Research and Evaluation) reporting checklist was used to critically appraise guidelines (Brouwers et al., 2010a). Internationally, this is the most widely used tool for assessing guideline quality (Siering et al., 2013), with good construct validity and reliability (Brouwers et al., 2010b, c). The instrument focuses on guideline development and reporting and consists of 23 items addressing 6 domains (1. Scope and purpose; 2. Stakeholder involvement; 3. Rigour of development; 4. Clarity of presentation; 5. Applicability; and 6. Editorial independence). Each item is rated on a 7-point Likert scale from 1 (Strongly disagree) to 7 (Strongly agree). In addition, there are two final items that ask appraisers to give an overall judgement in light of ratings given for the 23 items.

The web-based platform My AGREE PLUS (https://www.agreetrust.org/my-agree/) was used to complete appraisals online, based on the user manual. Each item is presented for scoring alongside detailed guidance on how to score the item, including where to find relevant information and what to consider when deciding on the score for each item.

Critical appraisal was conducted concurrent to data extraction by the same reviewer(s). One reviewer appraised each guideline; in the case of guidelines in English this was independently checked by a second reviewer with any disagreements resolved through discussion. For non-English guidelines no independent check was feasible.

No set thresholds exist for determining high/low quality guidelines, however, AGREE II guidance suggest users decide these according to their specific context (AGREE Next Steps Consortium, 2017). Based on examples given in the AGREE II user manual, and with reference to previous studies (Bouwmeester et al., 2009; Lin et al., 2020), we considered guidelines to be of high quality if AGREE II Domain 3 *i.e.* 'Rigour of development' scored at least 70%, and the remaining five domains, along with the overall assessment, scored at least 50%.

2.7. Synthesis of guidelines and identification of consistent recommendations

All recommendations extracted from the included guidelines were collated based on the way the treatment option was described in/translated from the guideline, and then grouped according to treatment theme. Tables were drawn up to present all the recommendations, alongside details regarding the context of the guideline (i.e. professional organisation(s), country, and target population/diagnostic classification). Members of the review team, which included researchers with academic and clinical expertise in musculoskeletal pain, were presented with these tables for review. Following discussion of the many very specific intervention options *e.g.* different forms of exercise, nuanced and/or inconsistently used terms, and translation anomalies/country specific terminology (often reported in only 1 or 2 guidelines), interventions were merged by treatment type/modality. A general practitioner (physician) was invited to review the recommendations relating to medications specifically and undertook a similar process of refining the grouping of treatment options.

The direction (*i.e.* for, against, or open) and strength of recommendations was harmonised, taking into consideration the array of methods and terminologies used across included guidelines (see Supporting Information Appendix S2). The resulting nomenclature enables the reader to distinguish between strong or weak recommendations based on a formal grading system e.g. GRADE; those where no formal grading system was applied; and recommendations based on consensus/expert opinion. Treatment or referral options for which a recommendation was formulated in one guideline only, were not further considered.

To summarise and synthesise the direction and strength of recommendations across guidelines a set of criteria was devised and followed, such that:

- **Strong FOR/AGAINST recommendation** (should do/should not do): consistent recommendations in at least two high-quality guidelines from different countries (at least one guideline of which reports a 'strong' *i.e.* // or XX recommendation).

- **Moderate FOR/AGAINST recommendation** (could do/could not do): consistent recommendations in at least one high-quality (where recommendation is not based on expert opinion *i.e.* O+ or O-) and if only one high-quality, then one or more low quality guidelines.
- **Weak FOR/AGAINST recommendation:** recommendations from high quality guidelines but based on expert opinion only and/or recommendations from multiple low-quality guidelines.
- **Inconsistent**: inconsistent recommendations from guidelines of high quality (for/against).
- **Inconclusive**: open/uncertain recommendations only, or recommendations from low quality guidelines are inconsistent.

3. Results

3.1. Guideline selection

The systematic search resulted in 3941 unique citations, from which 17 clinical practice guidelines (CPGs) were identified (Fig. 1) and included in this evidence synthesis (Bier et al., 2016; Bons et al., 2017; BÄK et al., 2017; Glocker et al., 2018; Kassolik et al., 2017; Monticone et al., 2013; NICE, 2016; Pohl et al., 2018; Regione Toscana, 2015; Schaafstra et al., 2015; SFMT, 2013; Staal et al., 2017; Sundhedsstyrelsen, 2015; 2016a, b, c; van Wambeke et al., 2017).

<<Fig. 1>>

3.2. Guideline characteristics

An overview of characteristics of included CPGs and the methods used in their development and implementation is presented in Table 1, with guideline specific details provided in Supporting Information Appendices S3 & S4. The 17 contemporary CPGs originate from 8 European countries (Belgium, Denmark, France, Germany, Italy, The Netherlands, Poland, and the UK). The majority address low back pain and/or radicular pain (*n* = 12; 71%), whilst 6 (35%) are concerned with neck pain and/or radicular pain. Five guidelines (29%) focus specifically on patients presenting with symptoms of radiculopathy. Three of these guidelines (Schaafstra et al., 2015; Sundhedsstyrelsen, 2015; 2016b) are specifically developed for the management of radiculopathy in general practice or primary care. The two other guidelines were designed for healthcare professionals responsible for the management of acute lumbar (Glocker et al., 2018) or cervical (Pohl et al., 2018) radiculopathy in any ambulant, outpatient or secondary care setting". Conversely three CPGs (18%) explicitly exclude radiculopathy.

A large majority of CPGs were developed by multidisciplinary groups (*n* = 14, 82%), employed formal grading of evidence and/or recommendations (*n* = 13, 76%). Just over half the guidelines detailed timeframes for future revisions (*n* = 10, 59%), whilst just under half detailed or undertook a consensus process (*n* = 8, 47%).

In addition to treatment recommendation most guidelines addressed planning of care (*n* = 14, 82%), diagnostic assessment (*n* = 12, 71%), evaluation of red (*n* = 12, 71%) and/or yellow (psychosocial, *n* = 10, 59%) flags. Conversely, less than half the guidelines detailed the evaluation of blue/black flags

i.e. blue: individuals' perceptions of work-related factors and the relationship between work and health, black: system-level factors (context, work environment, policies) (*n* = 7, 41%), practitioner education (*n* = 8, 47%), or organisation and policy implications (*n* = 5, 29%).

<<Table 1>>

3.3. Quality appraisal

The AGREE II domain scores for each guideline are presented in Table 2, along with our designation of the overall quality *i.e.* high/low based on domain scores. Notably one guideline (Kassolik et al., 2017) was not rated highly on any of the domains, achieving at its best 44% for clarity of presentation. With the exception of this guideline, the remaining 16/17 CPGs were all highly rated *i.e.* achieved at least 50% of maximum possible score, for Domains 1 (scope and purpose) and 4 (clarity of presentation). Conversely, a minority of CPGs (*n* = 7, 41%) achieved high ratings for Domain 5 (applicability). Domains 2 (stakeholder involvement) and 6 (Editorial independence), together with overall assessment score, were each reported to a high quality in a large majority of studies (*n* = 14, 82%). Domain 3 (rigour of development) with its higher cut-off point of 70% determining high-quality was achieved by just over half the CPGs (*n* = 9, 53%).

Seven CPGs (41%) were considered high quality overall: 2 focused on neck pain, both Danish (Sundhedsstyrelsen, 2015, 2016c) and 5 on low back pain including 1 Belgian, 1 UK, 2 Danish, and 1 German (BÄK et al., 2017; NICE, 2016; Sundhedsstyrelsen, 2016a, b; van Wambeke et al., 2017), (Table 2 and Supporting Information Appendices S5 & S6).

<< Table 2 >>

3.4. Consistency of CPG recommendations for neck pain

Six guidelines provided treatment recommendations for neck pain (Bier et al., 2016; Kassolik et al., 2017; Monticone et al., 2013; Pohl et al., 2018; Sundhedsstyrelsen, 2015, 2016c). Supporting Information Appendix S5 details the specific treatment options or intervention modalities identified in each guideline together with the direction and strength of each recommendation. In total, recommendations were provided that covered a wide range of treatment options: reassurance; advice and education; medication; injection/infiltration; acupuncture; thermotherapy; manual therapy; exercise therapy; postural therapy; traction; electrotherapy; orthotics; ergonomic interventions; taping/strapping; psychological interventions; multidisciplinary treatments; referral for imaging; and referral for specialist opinion; plus a disparate group of interventions that were labelled 'miscellaneous'.

In considering the consistency of recommendations across all neck pain CPGs (Table 3), 14 treatment options were supported, while recommendations were inconsistent or inconclusive (mixed) regarding the use of 7 treatment options. For 26 treatment options a recommendation was only given in 1 guideline, and these were not further considered.

Positive (weak to moderate) recommendations from high quality (Sundhedsstyrelsen, 2015, 2016c) or multiple low quality (Bier et al., 2016; Kassolik et al., 2017; Monticone et al., 2013; Pohl et al.,

2018) guidelines supported the use of reassurance; advice and education with specific mention of physical activity, and exercise; prescription of oral analgesic medications including for neuropathic pain, and specifically paracetamol, NSAIDs, and opioids including tramadol; topical medication; exercise interventions alone or in combination with other treatments; and manual therapy in combination with another (exercise) intervention.

Psychological or multimodal (multidisciplinary) interventions were recommended for specific subgroups of patients with neck pain, with either psychosocial risk factors or for those with more persistent neck pain or disability.

Recommendations were inconsistent or inconclusive regarding manual therapies (delivered without additional active treatment); traction; electrotherapies; thermotherapies; cervical orthoses; acupuncture/dry needling; and referral for imaging.

<< Table 3>>

3.5. Consistency of CPG recommendations for low back pain

Twelve guidelines provided treatment recommendations for back pain (Bons et al., 2017; BÄK et al., 2017; Glocker et al., 2018; Kassolik et al., 2017; NICE, 2016; Regione Toscana, 2015; Schaafstra et al., 2015; SFMT, 2013; Staal et al., 2017; Sundhedsstyrelsen, 2016a, b; van Wambeke et al., 2017). Details regarding the specific treatment options or intervention modalities identified from each guideline can be found in Supporting Information Appendix S6, along with the direction and strength of each recommendation. Similar to guidelines for neck pain, recommendations were provided that covered a wide range of treatment and referral options. For many of these treatment options, the body of evidence underpinning recommendations was larger compared to neck pain, although often still inconsistent or of low quality.

Table 4 presents the summary of recommendations from high- and low-quality guidelines and the overall recommendations derived from our synthesis. A range of treatment options (n=26) were only mentioned in one guideline, and these were not considered further. Positive (weak to strong) recommendations from high quality (BÄK et al., 2017; NICE, 2016; Sundhedsstyrelsen, 2016a, b; van Wambeke et al., 2017) or multiple low quality (Bons et al., 2017; Glocker et al., 2018; Kassolik et al., 2017; Regione Toscana, 2015; Schaafstra et al., 2015; SFMT, 2013; Staal et al., 2017) guidelines supported the use of 14 treatment options, including: reassurance; advice and education with specifics for physical activity, exercises, and work; manual therapy in combination with active treatment; exercise interventions; group exercise programmes including back schools; psychological therapies including cognitive behavioural interventions as standalone interventions or in combination with exercise; work-based rehabilitation and return to work programmes.

Psychological therapies are mainly recommended for subgroups of patients with increased psychosocial risks, mood problems, or more complex, persistent back pain; while referral for surgery is only supported for cases with signs of specific pathology.

Overall, guidelines recommended strongly against the use of more than a couple of days bedrest for patients with low back pain. Referral for imaging is only supported for those with red flags, such as increased risk of fracture, infection, (metastatic) cancer, neurological emergencies including cauda

equina syndrome, aortic aneurysm or systemic inflammatory arthritis (detailed in Supporting Information Appendix S7), or deterioration of symptoms. And although mixed, moderate to strong recommendations were also given against the use of paracetamol, anti-depressants, anticonvulsants, and muscle relaxants; spinal injections for non-specific LBP; traction; orthoses; and a range of applications (e.g. electrotherapies, shortwave, laser).

Recommendations were inconsistent or inconclusive with respect to medication (NSAIDs, opioids; topical); epidural steroid and other injections; acupuncture; and manual, postural, and thermotherapies.

<< Table 4>>

3.6. Comparison of CPG recommendations for neck and low back pain

In order to examine the consistency of CPG recommendations across neck and low back pain, overall strengths of recommendation for each identified intervention (see Tables 3 & 4), were assessed (Table 5). Despite a larger body of evidence for the effectiveness of treatment for back pain and a larger number of back pain guidelines, recommendations were generally consistent for neck and back pain (Table 5), in particular regarding support for the use of advice and education, reassurance, certain oral and topical pharmacologic treatments (with the exception of paracetamol), exercise interventions, manual therapy when combined with active treatment, and psychological interventions. Guidance was also consistent in terms of the limited use of imaging (only for patients with red flags or where imaging is likely to change management), and recommendations against the use of bed rest, orthoses, traction and a range of modalities (laser therapy, electrotherapy, shortwave).

Referral for imaging or surgical intervention, bed rest, antidepressant and muscle relaxant medications, psychological or multidisciplinary interventions are recommended for specific subgroups of patients (FOR ‘SPECIFIC SUBGROUP’ or AGAINST ‘WITH EXCEPTIONS’ in Table 5).

<< Table 5>>

4. Discussion

In this review, we have systematically identified, synthesised and graded 17 European clinical guidelines relating to the management of NLBP. Based on the quality of the evidence we have identified a short list of treatment options recommended for the management of NLBP (see Table 5). This information is aimed to provide clinicians, healthcare managers, funders, policymakers and researchers with a comprehensive summary of the current consensus from clinical guidelines across Europe on the management of NLBP.

The guidelines included in our review came from 8 European countries (UK, Germany, France, Italy, Denmark, Poland, Belgium, and the Netherlands). Eleven of them addressed low back pain, five neck pain, and one both LBP and neck pain. Data extraction showed considerable variation in guideline development processes with seven guidelines (5 back, 2 neck) considered as high-quality, based on their development rigour, strong stakeholder involvement, and the applicability of their recommendations.

For ***neck pain,*** high quality guidelines consistently recommended the following evidence-based treatment options: reassurance, advice and education (including to remain active and exercise), manual therapy in combination with other treatment, referral for exercise therapy/programme, and a range of oral analgesics and topical medications, plus psychological therapies or multidisciplinary treatment for specific subgroups of patients. There was no strong evidence for use across Europe (as shown in Table 3). In contrast to the recommendations for low back pain, the neck pain guidelines included the use of painkillers such as paracetamol, NSAIDs (for acute pain only), opioids (for acute pain only), and neuropathic pain medication. However, these were only based on ***weak evidence*** (meaning the recommendations were based on expert opinion only from high quality guidelines, and/or multiple low-quality guidelines) and it should be noted that these medications are no longer consistently recommended for low back pain within the recent European guidelines. In fact, for ***low back pain*** the guidelines recommended entirely non-pharmacological treatments, additionally including work-based interventions, advice/programmes to return to work, and surgical intervention for specific subgroups. These recommendations were based on stronger evidence than those for neck pain.

In relation to previous literature, the findings of this review summarising the consensus from European guidelines, are consistent with recommendations in The Lancet back pain series (Foster et al., 2018) which advocated for greater use of non-pharmacological options for patients with back pain. The treatment options identified in this study are also broadly similar and consistent with two recent systematic reviews of clinical practice guidelines for musculoskeletal pain (Lin et al., 2020) and back pain (Oliveira et al., 2018) which identified similar key management recommendations (patient information, physical activity advice, return to work interventions, exercise interventions), although Oliveira et al., additionally identified antidepressants (for chronic LBP), NSAIDs and weak opioids for short periods of time (for acute LBP) to be frequently recommended across guidelines.

Recommendations from the European guidelines included in our review contrast notably with a systematic review of non-invasive treatments for low back pain conducted to inform the American College of Physicians Clinical Practice Guideline (Chou et al., 2016) which not only recommended 3 medication options (NSAIDs, opioids, duloxetine) with moderate to strong evidence (Chou et al., 2017b), but also included acupuncture within a group of 5 recommended non-pharmacological options (superficial heat, multi-disciplinary rehabilitation, acupuncture, exercise and manual therapy) (Chou et al., 2017a).

Many of the European guidelines included treatment recommendations related to patient subgroups: psychological therapies, multi-disciplinary treatment and referral for surgery were recommended for specific subgroups only; and very strict indications (strong recommendation against with exception given for bed rest, anti-depressants, and muscle relaxants). However, it was notable that clear assessment criteria to facilitate clinician decision-making about when to use these treatment options for specific patient subgroups were largely lacking. Similar to Lin et al. who highlighted that guidelines for patients with thoracic pain are lacking (Lin et al., 2020), we only identified one (low quality) guideline (Kassolik et al., 2017) that specifically addressed thoracic pain. We would also highlight that most guidelines lacked detail about the specific dose, duration and other detail around the delivery of the recommended treatments. For example, there was little clarity on the delivery of physical exercise or the recommended components of patient education or reassurance.

Strength and limitations

The strength of this review is that it provides a helpful overall summary of the treatment and referral recommendations from recent European guidelines for NLBP. This overview enabled us to identify treatment options that have been consistently recommended across 8 different countries and can therefore be considered to have broad European consensus. To facilitate the rigour of this evidence summary, we pre-specified inclusion and exclusion criteria for screening, quality appraised guidelines using the AGREE II checklist, and devised a set of clear criteria to summarise and synthesise the direction and strength of recommendations across guidelines. Further strengths included independent assessment of eligibility for inclusion, data extraction and appraisal of the quality of guidelines, and a standardised approach to synthesising evidence.

The guidelines included in our systematic review predominantly originate from northern and western European countries (except for the Italian guidelines), which can be considered a limitation. This may be partly explained by fewer guidelines being produced in southern or eastern Europe, but also by the fact that we only included guidelines published in the past 5 years. Whilst focusing on contemporary guidelines (2013 onwards) ensured that we identified the most relevant treatment options for current practice, we acknowledge that this meant that some earlier European guidelines, were not included. However, for the purposes of this review, we felt it was important to exclude guidelines that may not be based on up-to-date evidence of effectiveness. Although we included guidelines written in any European language, one limitation was that we were not able to carry out independent data extraction and quality appraisal by a second reviewer for guidelines not available in English. However, for most of these guidelines, the reviewer had the advantage of being involved in data extraction for English language guidelines, which helped to ensure consistency of data extraction and interpretation.

Only 7 CPGs (41%) were considered to be of overall high quality, with limitations mainly related to rigour of development (e.g. use of transparent methods to link evidence to recommendations, or processes to gain consensus regarding the strength of recommendations); and to applicability with few guidelines providing guidance on how to apply recommendations or taking into account practical and financial implications of their recommendations. Variation in the methods used to grade evidence and agree the strength of recommendations may potentially explain some of the variability in treatment recommendations across guidelines. We tried to incorporate quality as well as consistency in our synthesis of CPR, aiming to arrive at a transparent and systematic approach for summarizing and grading recommendations across guidelines.

Future work within the Back-UP research project will embed these evidence-based treatment options in an accessible clinician decision support tool for first contact clinicians, aiming to offer patients with NLBP treatment options better matched to risk of persistent pain and disability.

5. Conclusion

In conclusion, this systematic review identified seventeen contemporary clinical guidelines regarding NLBP (5 neck; 11 low back; 1 both) from 8 European countries, of which 7 were considered high quality. Recommendations were notably consistent for neck and low back pain, despite the larger evidence base and more guidelines for the latter. The implications from this review are that

clinicians have a broad range of mostly non-pharmacological evidence-based treatment options to consider for their patients with NLBP. These include some treatments which are a) potentially applicable to all patients such as advice and education and b) those applicable only to certain patient subgroups (e.g. referral to surgery).

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Author contributions

GM, DvdW and JH designed the study protocol with input from NC.
NC designed the literature search with input from DvdW.
NC, GM and DvdW performed the study selection with input from LM.
NC, GM, LM, SS and GW-J carried out data extraction and quality assessment.
NC, JH, SS and DvdW carried out the analysis and interpretation of the data.
NC and JH drafted the manuscript.
All authors critically revised the manuscript for intellectual content and read and approved the final manuscript.

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Legends for illustrations and tables

Figure 1: PRISMA Flow Diagram.

Table 1: Characteristics of included clinical practice guidelines.

Table 2: Quality appraisal of guidelines: AGREE II domain scores (%) and quality assessment. Cells in green indicate domain attained 'high' rating.

Table 3: Consistency of recommendations across guidelines for neck pain (see Supporting Information Appendix S5 for individual guidelines). ***Symbol – classification:*** // - should do; / - could do; /* - for (generic); O [O+/O-] – Open [expert opinion in favour/against]; X* - against (generic); X – should not do; XX – definitely do not do (see Supporting Information Appendix S2 for further detail).

Table 4: Consistency of recommendations across guidelines for low back pain (see Supporting Information Appendix S6 for individual guidelines). ***Symbol – classification:*** // - should do; / - could do; /* - for (generic); O [O+/O-] – Open [expert opinion in favour/against]; X* - against (generic); X – should not do; XX – definitely do not do (see Supporting Information Appendix S2 for further detail).

Table 5: Consistency of recommendations across low back pain vs neck pain guidelines

Table 1: Characteristics of included clinical practice guidelines.

Characteristic	n	Reference
Country		
Belgium	1	van Wambeke *et al.*, 2017
Denmark	4	Sundhedsstyrelsen, 2015, 2016a-c
France	1	SFMT, 2013
Germany	3	BÄK, *et al.*, 2017; Glocker *et al.*, 2018; Pohl *et al.*, 2018
Italy	2	Monticone *et al.*, 2013; Regione Toscana, 2015
The Netherlands	4	Schaafstra *et al.*, 2015; Bier *et al.*, 2016; Bons *et al.*, 2017; Staal *et al.*, 2017
Poland	1	Kassolik *et al.*, 2017
UK	1	NICE, 2016
Pain site		
Neck	5	Monticone *et al.*, 2013; Sundhedsstyrelsen, 2015; Bier *et al.*, 2016; Sundhedsstyrelsen, 2016c; Pohl *et al.*, 2018
Low back	11	SFMT, 2013; Regione Toscana, 2015; Schaafstra *et al.*, 2015; NICE, 2016; Sundhedsstyrelsen, 2016a-b; BÄK, *et al.*, 2017; Bons *et al.*, 2017; Staal *et al.*, 2017; van Wambeke *et al.*, 2017; Glocker *et al.*, 2018
Neck & low back	1	Kassolik *et al.*, 2017
Specifically excludes radiculopathy		
Neck	1	Sundhedsstyrelsen, 2016c
Low back	3	Sundhedsstyrelsen, 2016a; BÄK, *et al.*, 2017; Bons *et al.*, 2017
Radiculopathy only focus		
Neck	2	Sundhedsstyrelsen, 2015; Pohl *et al.*, 2018
Low back	3	Schaafstra *et al.*, 2015; Sundhedsstyrelsen, 2016b; Glocker *et al.*, 2018
Multidisciplinary group or single profession		
Multidisciplinary	14	SFMT, 2013; Regione Toscana, 2015; Schaafstra *et al.*, 2015; Sundhedsstyrelsen, 2015; NICE, 2016; Sundhedsstyrelsen, 2016a-c; BÄK, *et al.*, 2017; Bons *et al.*, 2017; Kassolik *et al.*, 2017; van Wambeke *et al.*, 2017; Glocker *et al.*, 2018; Pohl *et al.*, 2018
Single	2	Bier *et al.*, 2016; Staal *et al.*, 2017
Not reported	1	Monticone *et al.*, 2013
Formal grading of evidence and/or recommendation		
Yes	13	Monticone *et al.*, 2013; SFMT, 2013; Regione Toscana, 2015; Sundhedsstyrelsen, 2015, Bier *et al.*, 2016; NICE, 2016; Sundhedsstyrelsen, 2016a-c; BÄK, *et al.*, 2017; Kassolik *et al.*, 2017; Staal *et al.*, 2017; van Wambeke *et al.*, 2017; Pohl *et al.*, 2018
No	3	Schaafstra *et al.*, 2015; Bons *et al.*, 2017; Glocker *et al.*, 2018
Not reported	1	Kassolik *et al.*, 2017
Details of consensus process given		
Yes	8	SFMT, 2013; Schaafstra et al, 2015; NICE, 2016; BÄK, *et al.*, 2017; Bons *et al.*, 2017; Glocker *et al.*, 2018; Pohl *et al.* 2018; van Wambeke *et al.*, 2017
No	9	Monticone *et al.*, 2013; Regione Toscana, 2015; Sundhedsstyrelsen, 2015; Bier *et al.*, 2016; Sundhedsstyrelsen, 2016a-c; Kassolik *et al.*, 2017; Staal *et al.*, 2017
Includes recommendations regarding		
Future revision	10	Sundhedsstyrelsen, 2015; NICE, 2016; Sundhedsstyrelsen, 2016a-c; BÄK, *et al.*, 2017; Staal *et al.*, 2017; van Wambeke *et al.*, 2017; Glocker *et al.*, 2018; Pohl *et al.*, 2018
Evaluation of red flags	12	Monticone *et al.*, 2013; SFMT, 2013; Regione Toscana, 2015; Schaafstra *et al.*, 2015; Bier *et al.*, 2016; NICE, 2016; BÄK, *et al.*, 2017; Staal *et al.*, 2017; van Wambeke *et al.*, 2017; Bons *et al.*, 2017; Glocker *et al.*, 2018; Pohl *et al.*, 2018
Evaluation of yellow flags	10	SFMT, 2013; Regione Toscana, 2015; Bier *et al.*, 2016; NICE, 2016; BÄK, *et al.*, 2017; Bons *et al.*, 2017; Staal *et al.*, 2017; van Wambeke *et al.*, 2017; Pohl *et al.*, 2018; Glocker *et al.*, 2018
Evaluation of blue/black flags	7	SFMT, 2013; Regione Toscana, 2015; Bier *et al.*, 2016; BÄK, *et al.*, 2017; Bons *et al.*, 2017; Staal *et al.*, 2017; van Wambeke *et al.*, 2017
Diagnosis	12	Monticone *et al.*, 2013; SFMT, 2013; Regione Toscana, 2015; Schaafstra *et al.*, 2015; Bier *et al.*, 2016; NICE, 2016; BÄK, *et al.*, 2017; Bons *et al.*, 2017; Kassolik *et al.*, 2017; Staal *et al.*, 2017; Pohl *et al.*, 2018; Glocker *et al.*, 2018

Planning of care	14	Monticone *et al.*, 2013; Bier *et al.*, 2016; Pohl *et al.*, 2018; Sundhedsstyrelsen, 2015, 2016a-c; BÄK, *et al.*, 2017; Bons *et al.*, 2017; NICE, 2016; Regione Toscana, 2015; Schaafstra *et al.*, 2015; Staal *et al.*, 2017; van Wambeke *et al.*, 2017[a]
Practitioner education	8	Sundhedsstyrelsen, 2015; Regione Toscana, 2015; Sundhedsstyrelsen, 2016a-c; NICE, 2016; van Wambeke *et al.*, 2017[a]; Pohl *et al.*, 2018
Organisation & policy	5	SFMT, 2013; Regione Toscana, 2015; BÄK, *et al.*, 2017; Bons *et al.*, 2017; van Wambeke *et al.*, 2017[a]

[a] subsequent clinical pathway developed that addressed this issue (Jonckheer *et al.,* 2017)

Table 2 CLEAN

Table 2: Quality appraisal of guidelines: AGREE II domain scores (%) and quality assessment. Cells in green indicate domain attained 'high' rating.

Guideline	Domain 1. Scope and Purpose	Domain 2. Stakeholder Involvement	Domain 3. Rigour of Development	Domain 4. Clarity of Presentation	Domain 5. Applicability	Domain 6. Editorial In-dependence	Overall quality of guideline	Guideline recommended for use	Quality (high/low)
Neck pain only									
Bier et al 2016	**72%**	**94%**	52%	**67%**	38%	**50%**	**67%**	Yes	**Low**
Monticone et al., 2013	**50%**	33%	38%	**100%**	0%	**50%**	33%	Yes, with modifications[a]	**Low**
Pohl et al. 2018	**61%**	**72%**	54%	**89%**	17%	**92%**	**50%**	No	**Low**
Sundhedsstyrelsen, 2015	**78%**	**67%**	**71%**	**72%**	**58%**	**83%**	**67%**	Yes, with modifications[a]	**High**
Sundhedsstyrelsen, 2016c	**89%**	**72%**	**75%**	**67%**	**63%**	**83%**	**83%**	Yes	**High**
Back pain only									
BÄK et al., 2017	**89%**	**89%**	**77%**	**94%**	**79%**	**75%**	**83%**	Yes	**High**
Bons et al., 2017	**72%**	**78%**	**81%**	**61%**	29%	**83%**	**83%**	Yes	**Low**
Glocker et al., 2018	**72%**	44%	44%	**56%**	21%	**100%**	33%	No	**Low**
NICE, 2016	**100%**	**78%**	**79%**	**94%**	**79%**	**58%**	**83%**	Yes	**High**
Regione Toscana, 2015	**83%**	**78%**	48%	**100%**	25%	17%	**50%**	Yes, with modifications[a]	**Low**
Schaafstra et al. 2015	**72%**	**78%**	65%	**50%**	29%	**83%**	**50%**	Yes with modifications[a]	**Low**
SFMT, 2013	**89%**	**72%**	65%	**100%**	13%	**100%**	**83%**	Yes	**Low**
Staal B. et al. 2017	**83%**	**83%**	**77%**	**94%**	33%	42%	**67%**	Yes with modifications[a]	**Low**
Sundhedsstyrelsen, 2016a	**78%**	**67%**	**71%**	**61%**	**63%**	**83%**	**67%**	Yes, with modifications[a]	**High**
Sundhedsstyrelsen, 2016b	**89%**	**72%**	**79%**	**72%**	**63%**	**83%**	**83%**	Yes	**High**
van Wambeke et al. 2017	**100%**	**83%**	**92%**	**94%**	**71%**	**100%**	**100%**	Yes	**High**
Neck and back pain									
Kasssolik et al. 2017	39%	22%	4%	44%	8%	42%	33%	No	**Low**

[a] AGREE II user manual provides no guidance on what this actually means and so is open to different interpretations by the different reviewers. But, broadly this was taken to mean a guideline was close to being recommended for use, but just need a little more detail in one or two areas.

Table 3 CLEAN

Table 3: Consistency of recommendations across guidelines for neck pain (see Appendix S5 for individual guidelines). ***Symbol – classification:*** // - should do; / - could do; /* - for (generic); O [O+/O-] – Open [expert opinion in favour/against]; X* - against (generic); X – should not do; XX – definitely do not do (see Supporting Information Appendix S2 for further detail).

Intervention	No. guidelines (countries)	Recommendations by guideline quality		Overall strength of recommendation	Comments
		HIGH quality	LOW quality		
FOR					
Reassurance	3(3)	1x **O+**	1x **/**; 1x **/***	Weak FOR	
Advice and Education	5(5)	1x **O+**	**For:** 1x **//**; 1x **/**; 1x **/*** **Against:** 1x **X**	Weak FOR	
Remain active (advice)	2(2)	1x **O+**	1x **/**	Weak FOR	
Encourage exercise (advice)	3(3)	1x **O+**	1x **/**; 1x **/***	Weak FOR	
Analgesics incl. for neuropathic pain	2(2)		1x **//**; 1x **/***	Weak FOR	
Paracetamol	2(2)	1x **O+**	1x **/**	Weak FOR	
NSAIDs	4(3)	2x **O+**	1x **/**; 1x **/***	Weak FOR	Short-term use
Opioids including tramadol	2(1)	2x **O+**		Weak FOR	Short-term use
Topical medications incl. NSAIDs	2(2)	1x **/**	1x **/***	Moderate FOR	
Manual therapy + other treatment	3(3)	1x **/**	1x **//** & **/**; 1x **/** & **O+**	Moderate FOR	
Exercise programs/therapy	5(5)	1x **/** & **O+**	2x **//**; 1x **/**; 1x **/***	Moderate FOR	
Exercise therapy + other treatment	2(2)	1x **/**	1x **//**	Moderate FOR	
Psychological therapies	3(3)		1x **/**; 1x **/***; 1x **O+**	Weak FOR SPECIFIC SUBGROUPS	For specific cases: mood problems, psychosocial risks, or complex, persistent pain problems
Multidisciplinary treatment	2(2)		2x **/**	Weak FOR SPECIFIC SUBGROUPS	For those with more complex or persistent pain
MIXED *i.e.* inconsistent or inconclusive					
Thermotherapy	2(2)		**For:** 1x **/*** **Against:** 1x **X***	Inconclusive	
Manual therapies	5(4)	**Mixed:** 1x **/** & **O-** **Against:** 1x X	**For:** 2x **//**; 1x **/***	Inconsistent	
Traction	3(3)	**For:** 1x **/**	**Mixed:** 1x **O+ & X*** **Against:** 1x **X**	Inconclusive	For specific cases: radiculopathy (SST, 2015), Grade III, profile D (Bier *et al.,* 2016)
Electrotherapies	4(4)		**Mixed:** 1x **/** & **O+** & **X**; 1 x **/*** & **X*** **Against:** 1x **XX**; 1x **X***	Inconclusive	
Cervical orthoses	4(4)		**For:** 1x **/*** **Mixed:** 1x **O+** & **X*** **Against:** 2x **O-**	Inconclusive	For specific cases: Grade III, profile D (Bier *et al.,*2016), or short-term in cases of severe pain (Pohl *et al.,* 2018)
Acupuncture/dry needling	4(3)	**For:** 1x **/** **Against:** 1x **O-**	**For:** 1x **//** **Against:** 1x **X***	Inconsistent	
Imaging	2(2)		**For:** 1x **//** **Against** 1x **X***	Inconclusive	

Single guideline recommendation - in favour of: O+, /*, / or //		
Avoid movement that provokes radiating pain or other symptoms in the arm (advice)	Electrotherapies + active treatment	Encourage patient to contact GP, psychologist or psychosomatic therapist
Psychosocial aspects that delay recovery (advice)	Kinesiology tape	Workplace interventions
Continue/return to work (advice)	Cervical cushion/pillow	Referral to GP and/or occupational health officer
Work-related/occupational advice	Bioptron lamps	Referral to GP or referring specialist
Thermotherapy + other treatment	Ledotherapy lamps	Referral to physical therapist specialized in worker rehabilitation
Steroids	Infra-red lamps	Referral to occupational health and safety service
Spinal epidural steroid injection (transforaminal route with imaging)	Bath salts with mud extracts, special water-pearling inserts or ozone	Referral to occupational health officer or a physical therapist specialised in worker rehabilitation
Postural re-education	Magnetic mattress	Referral to surgeon/surgery
Single guideline recommendation - against: O-, X*, X or XX		
Bed rest (advice) [1-2 days, selected cases only]	Written information (advice)	

Table 4 CLEAN

Table 4: Consistency of recommendations across guidelines for low back pain (see Appendix S6 for individual guidelines). ***Symbol – classification:*** // - should do; / - could do; /* - for (generic); O [O+/O-] – Open [expert opinion in favour/against]; X* - against (generic); X – should not do; XX – definitely do not do (see Supporting Information Appendix S2 for further detail)

Intervention	No. guidelines (countries)	Recommendations by guideline quality		Overall strength of recommendation	Comments
		HIGH quality	LOW quality		
FOR					
Reassurance	4(4)	1x **O+**	1x **//**; 2x **/***	Weak FOR	
Advice and Education (including individualised)	10(8)	1x **//**; 1x **/**; 2x **O+**	**For**: 1x **//**; 4x **/***; **Mixed**: 1x **O+** & **O**	Strong FOR	
Remain active	9(6)	1x **//** & **O+;** 2x **/**; 2x **O+**	1x **//** & **O+;** 3x **/***	Strong FOR	
Encourage physical exercise (unsupervised)	7(6)	2x **O+**	1x **//**; 1x **//** & **O+**; 3x **/***	Weak FOR	
Continue/return to work	2(2)		1x **//** & **O+**; 1x **/***	Weak FOR	
Manual therapy in combination with other treatment	4(3)	2x **/**; 1x **O+**	1x **/***	Moderate FOR	
Exercise programs/therapy	9(6)	**For**: 3x **/** **Mixed**: 1x **//** & **O**	**For:** 4x **/*** **Against:** 1x **XX**	Strong FOR	
Group exercise programmes/back schools	3(3)	1x **/**; 1x **/** & **O+.**	1x **/***	Moderate FOR	
Psychological therapies including behavioural and CBT	4(3)	1x **//**	3x **/***	Strong FOR SPECIFIC SUBGROUPS	For specific cases: mood problems, psychosocial risks, or complex, persistent pain problems
Psychological therapies in combination with other treatment (exercise)	2(2)	2x /		Moderate FOR	
Multidisciplinary treatment including MBR programs, and multidisciplinary rehabilitation involving work focus	7(5)	1x **//**; 2x **/**	**For**: 2x **/***; 1x **O+** **Mixed:** 1x **/** & **O**	Strong FOR SPECIFIC SUBGROUPS	For specific cases: subacute and chronic LBP with patient strongly motivated to resolve and/or psychosocial obstacles to recovery.
Work-based interventions including rehabilitation programmes	3(3)	1x **/**	1x **//**; 1x **//** & **/**	Moderate FOR	
Return to work programmes	3(3)	1x **//**; 2x **O+**		Strong FOR	
To surgeon/surgery	8(6)	**For**: 1x **//**; 1x **/;** 1x **O+** **Against:** 1x **XX**	**For**: 2x **/***; **Against**: 1x **X*** **Mixed:** 1x **O+** & **O**	Strong FOR SPECIFIC SUBGROUPS	For specific cases: failure of non-surgical treatment, moderate/severe persistent pain; specific indications e.g. cauda equine, severe neurological symptoms etc.
AGAINST					
Bed rest	6(4)	1x **XX**	1x **XX**; 4x **X***	Strong AGAINST WITH EXCEPTIONS	Except: for a few days in severe/acute cases
Paracetamol	8(6)	**Against:** 3x **X,** 1x **X***	**For:** 1x **//** & **O+** & **O**; 3x **/***	Moderate AGAINST	
Antidepressants including SSRIs, SNRIs, Tricyclics	6(5)	**Against:** 1x **X***; 1x **XX** & **X** **Mixed:** 1x **O+** & **X**	**Against:** 1x **X*** **Mixed:** 1x **/*** & **X*** **Open:** 1x **O**	Strong AGAINST WITH EXCEPTIONS	For specific cases: comorbid depression (BÄK, *et al.*, 2017, high quality) or chronic pain [tricyclics only] (Glocker *et al.*, 2018, low quality)

Anticonvulsants/Antiepileptics including gabapentin, pregablin, carbamazepine, topiramat	5(5)	**Against:** 1x **XX**; 1x **X**; 1x **X***	**Against:** 1x **X*** **Mixed:** 1x **XX** & **O-** & **O**	Strong AGAINST	
Muscle relaxants including diazepines/benzodiazepines	5(4)	**Against**: 1x **XX** **Mixed:** 1x **XX** & **X** & **O+**	**Against**: 2x **X*** **Mixed:** 1x **//** & **O**	Strong AGAINST WITH EXCEPTIONS	For specific cases: non-specific LBP where non-drug and non-opioid treatments ineffective (BÄK, *et al.*, 2017, high quality); 2nd line medication for acute non-specific LBP (Regione Toscana, 2015, Low quality)
Spinal injections [for non-specific LBP]	6(5)	**Against:** 1x **XX;** 1x **X***	2x **X***, 2x **O**	Strong AGAINST	
Traction	6(6)	**Against:** 2x **XX**; 1x **X***	**For:** 1x **/*** **Against:** 1x **O-** **Open**: 1x **O**	Strong AGAINST	
Electrotherapy including laser therapies, TENS, PENS, shortwave diathermy, US, ultra-shortwave, inferential, magnetic field, electromagnetic, light therapy, shockwave, electrostimulation	6(6)	**Against:** 2x **XX**; 1x **X***	**Against:** 1x **O-**; **Mixed:** 1x **/*** & **X*;** 1x **XX** & **O-** & **O**	Strong AGAINST	
Orthoses including belts, corsets, foot orthotics, insoles, rocker shoes, pull-ups, walking stick, elbow crutches and bands	6(6)	**Against:** 2x **XX**; 1x **X***	**For:** 1x **/*** **Against:** 1x **X** **Mixed:** 1x **XX** & **O-** & **O**	Strong AGAINST	
Imaging	9(6)	**Against**: 3x **X** **Mixed**: 1x **XX** & **//**	**Against**: 1x **XX**; 4x **X***	Strong AGAINST WITH EXCEPTIONS	Except: in cases of red flags
MIXED					
NSAIDs	9(7)	**For:** 2x **/**; 1x **/** & **O+** **Against:** 1x **X**	**For:** 4x **/***; 1x **//** & **O**	Inconsistent	
Opioids (including tramadol) +/- paracetamol (or NSAIDs)	8(6)	**Mixed:** 1x **//** & **X**; 1x **O+** & **X**; 1x **/** & **X*** **Against:** 1x **X**	**For:** 3x **/*** **Mixed:** 1x **//** & **O+** & **O**	Inconsistent	Generally, 'Against' for chronic LBP (unless severe limitations) and 'For' where other analgesics ineffective, contraindicated, or not tolerated.
Topical medications/NSAIDS	3(3)	**Against**: 1 x **XX**	**For:** 2x **/***	Inconclusive	
Spinal epidural steroid injection	5(5)	**For:** 1x **/** **Mixed**: 1x **/** & **X*** **Against**: 1x **X**	**For:** 1x **/*** **Mixed**: 1x **O+** & **O**	Inconsistent	
Other injections including intravenous, intramuscular, infiltration of trigger points and ligaments, intradiscal infiltration, prolotherapy, Botulium toxin	2(2)	1x **XX**	1x **O**	Inconclusive	
Thermotherapy including local heat, hot/cold compresses, baths, sauna	5(4)	**Mixed:** 1x **O+** & **X**	**For:** 2x **/***; **Open:** 1x **O** **Mixed**: 1x **//** & **O**	Inconsistent	
Manual therapy including mobilisation, manipulation and soft-tissue techniques	8(6)	**For:** 2x **/** **Mixed:** 1x **XX & O**	**For:** 1x **/*** **Against:** 2x **X***	Inconsistent	

			Mixed: 1x **XX** & **O**; 1x (**XX** & **O-** & **O**) & (**//** & **O**)	
Postural therapies e.g. Alexander therapy, postural re-education	3(3)	**Open:** 2x **O**	**For:** 1x **/***	Inconclusive
Acupuncture	5(4)	**For**: 1x **O+** **Against**: 1x **X**; 1x **X***; 1x **O-** **Open:** 1x **O**		Inconsistent

Single guideline recommendation	
FOR	**AGAINST**
Analgesics (general)	Antibiotics
Metamizol	Flurpirtin
Collaborate with company doctor, company physical therapist or occupation health and safety service	Uridine monophosphate (UMP)
CAM (general *ie* acupuncture and TCM, phytotherapy, homeopathy, manual therapies)	Kinesiotaping
Referral to family doctor	Shock-absorbing or anti-fatigue flooring
Referral to manual therapist	**MIXED**
Referral to family doctor, company doctor and/or psychologist	Steroids
Referral for specialist assessment	Progressive muscle relaxation
Bioptron lamps (SC)	Phytotherapeutics
Ledotherapy lamps (SC)	Topical phytotherapeutics
Infra-red raditation (SC)	**OPEN**
Bath salts with mud extracts or special water-pearling inserts or even ozone (SC)	Spa treatments
Magnetic mattress (SC)	Ozone therapy
	Medullary stimulations
	'Taking it slowly/easy'

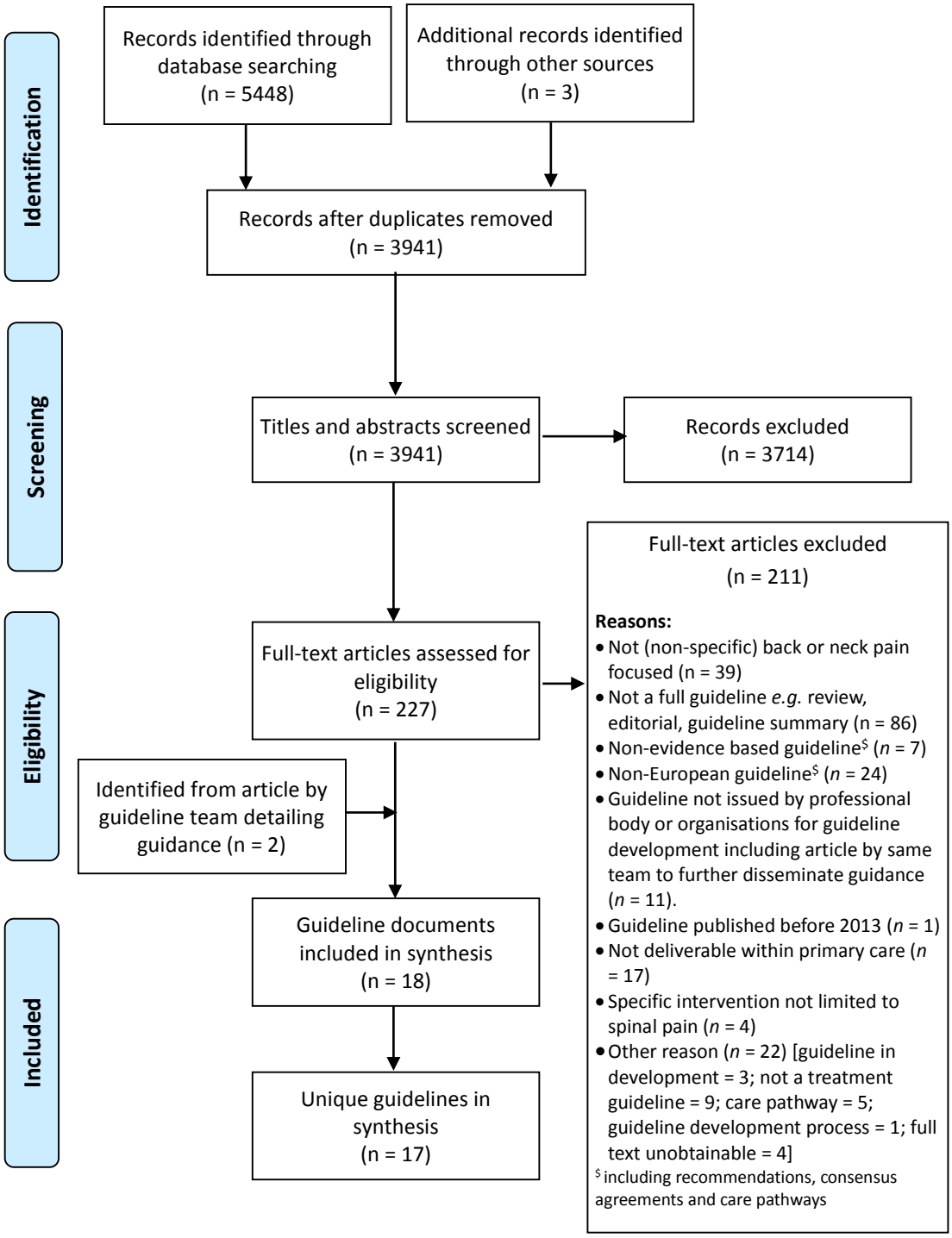
Table 5 CLEAN

Table 5: Consistency of recommendations across low back pain vs neck pain guidelines

	Low Back Pain		Neck Pain	
Intervention	**No. guidelines (countries)**	**Overall strength of recommendation**	**No. guidelines (countries)**	**Overall strength of recommendation**
Reassurance (advice)	4(4)	Weak FOR	3(3)	Weak FOR
Advice and Education (advice)	10(8)	Strong FOR	5(5)	Weak FOR
Remain active (advice)	9(6)	Strong FOR	2(2)	Weak FOR
Encourage physical exercise (advice)	7(6)	Weak FOR	3(3)	Weak FOR
Continue/return to work (advice)	2(2)	Weak FOR	1(1)	(For)
Bed rest (advice)	6(4)	Strong AGAINST WITH EXCEPTIONS	1(1)	(Against)
Analgesics incl. for neuropathic pain	1(1)	(For)	2(2)	Weak FOR
Paracetamol	8(6)	Moderate AGAINST	2(2)	Weak FOR
NSAIDs	9(7)	Inconsistent	4(3)	Weak FOR
Opioids (including tramadol) +/- paracetamol (or NSAIDs)	8(6)	Inconsistent	2(1)	Weak FOR
Antidepressants	6(5)	Strong AGAINST WITH EXCEPTIONS		
Anticonvulsants/Antiepileptics	5(5)	Strong AGAINST		
Muscle relaxants	5(4)	Strong AGAINST WITH EXCEPTIONS		
Topical medications incl. NSAIDS	3(3)	Inconclusive	2(2)	Moderate FOR
Spinal injections [for non-specific LBP]	6(5)	Strong AGAINST		
Spinal epidural steroid injection	5(5)	Inconsistent	1(1)	(For)
Other injections	2(2)	Inconclusive		
Thermotherapy	5(4)	Inconsistent	2(2)	Inconclusive
Manual therapy	8(6)	Inconsistent	5(4)	Inconsistent
Manual therapy combined with other treatment	4(3)	Moderate FOR	3(3)	Moderate FOR
Exercise programs/therapy	9(6)	Strong FOR	5(5)	Moderate FOR
Exercise therapy combined with other treatment			2(2)	Moderate FOR
Group exercise programmes/back schools	3(3)	Moderate FOR		
Postural therapies	3(3)	Inconclusive		
Traction	6(6)	Strong AGAINST	3(3)	Inconclusive
Electrotherapy	6(6)	Strong AGAINST	4(4)	Inconclusive
Orthoses	6(6)	Strong AGAINST	4(4)	Inconclusive
Acupuncture	5(4)	Inconsistent	4(3)	Inconsistent
Psychological therapies	4(3)	Strong FOR SPECIFIC SUBGROUPS	3(3)	Weak FOR SPECIFIC SUBGROUPS
Psychological therapies combined with other treatment	2(2)	Moderate FOR		
Multidisciplinary treatment	7(5)	Strong FOR SPECIFIC SUBGROUPS	2(2)	Weak FOR SPECIFIC SUBGROUPS
Work-based interventions	3(3)	Moderate FOR		
Return to work programmes	3(3)	Strong FOR		
Imaging	9(6)	Strong AGAINST WITH EXCEPTIONS	2(2)	Inconclusive
To surgeon/surgery	8(6)	Strong FOR SPECIFIC SUBGROUPS		

Figure 1 CLEAN

Figure 1: PRISMA Flow Diagram



Supporting Information Appendix S1: MEDLINE (Ovid) Search strategy

The following table is an explanation of the symbols used in the search strategy below.

/	indicates an index term (MeSH heading)
exp	before an index term indicates that all subheadings were selected
.ab.	indicates a search for a term in the abstract only
.ti,ab,kw.	indicates a search for a term in the title, abstract and keyword
.ti,ab,kw,kf.	indicates a search for a term in the title, abstract, keyword and word in keyword
$	at the end of a term indicates that this term has been truncated
$*n*	at the end of a term indicates that this term has been truncated
adj	indicates a search for two terms where they appear adjacent to each another
adj*n*	indicates a search for two terms where they appear within *n* words of each another

1	exp Back Pain/
2	dorsalgia.ti,ab,kw.
3	(backache or back ache).ti,ab,kw.
4	((back or lumb$) adj3 pain).ti,ab,kw.
5	((spine or spinal) adj3 pain).ti,ab,kw.
6	coccyx.ti,ab,kw.
7	coccydynia.ti,ab,kw.
8	exp Sciatic Neuropathy/
9	sciatica.ti,ab,kw.
10	spondylosis.ti,ab,kw.
11	lumbago.ti,ab,kw.
12	back disorder$.ti,ab,kw.
13	Neck Pain/
14	((neck or cervical) adj3 pain).ti,ab,kw.
15	(neck adj3 ache).ti,ab,kw.
16	neckache.ti,ab,kw.
17	cervicalgia.ti,ab,kw.
18	cervicodynia.ti,ab,kw.
19	Whiplash Injuries/
20	whiplash.ti,ab,kw.
21	neck disorder$.ti,ab,kw.
22	intervertebral disc displacement/
23	((disk$ or disc$) adj3 (herniat$ or prolapse$ or slipped)).ti,ab,kw.
24	radiculopathy/
25	radicul$.ti,ab,kw.
26	or/1-25
27	practice guideline/
28	Health Planning Guidelines/
29	guideline$1.ti,kw,kf.
30	guidance.ti,kw,kf.
31	standards.ti,kw,kf.
32	((practice or treatment$ or clinical) adj standard).ti,kw,kf.

33 recommendation$1.ti,kw,kf.
34 ((practice or treatment$ or clinical) adj3 consensus).ti,kw,kf.
35 Consensus Development Conference.pt.
36 (practice adj (guideline$1 or guidance or standard$1 or recommendation$1)).ab.
37 (clinical adj (guideline$1 or guidance or standard$1 or recommendation$1)).ab.
38 (treatment$ adj3 (guideline$1 or guidance or standard$1 or recommendation$1)).ab.
39 (CPG or CPGs).ti,kw,kf.
40 Critical Pathways/
41 position statement$1.ti,ab,kw,kf.
42 policy statement$1.ti,ab,kw,kf.
43 (practice adj3 parameter$1).ti,ab,kw,kf.
44 (((critical or clinical or practice) adj3 (path$1 or pathway$1 or protocol$1)) and (guideline$1 or guidance or standard$1 or recommendation$1)).ab.
45 ((care adj3 (path$1 or pathway$1 or map$1 or plan or plans)) and (guideline$1 or guidance or standard$1 or recommendation$1)).ab.
46 ((care adj3 standard$1) and (guideline$1 or guidance or recommendation$1)).ab.
47 or/27-46
48 26 and 47
49 limit 48 to yr="2013 -Current"

Supporting Information Appendix S2 – Classification of recommendations

	Symbol - Classification	Definition	Possible terminology and associated guidelines
FOR	// - Should do	Recommendations that are strongly endorsed and should be applied in all circumstances unless there is reason not to. Based on strong evidence reporting clinically relevant benefit that outweighs risk.	• 'strong' (Sundhedsstyrelsen, 2015, 2016a-c), with wording 'should' (Pohl et al., 2018; Bier et al., 2016), or 'offer' (NICE, 2016; van Wambeke et al., 2017). • Recommendation strength A (Monticone et al., 2013; Regione Toscana, 2015; SFMT, 2013), with wording 'do' (BÄK et al., 2017) • Level 1 (Staal et al., 2017)
	/ - Could do	Recommendations where there are doubts as to whether the intervention should always be applied and therefore implementation should be carefully considered. Based on consistent but weak evidence reporting clinically relevant benefit that outweighs risk.	• 'weak' (NICE, 2016; Pohl et al., 2018; Sundhedsstyrelsen, 2015, 2016a-c; van Wambeke et al., 2017), with wording 'can be used' (Bier et al., 2016) • Recommendation strength B (Regione Toscana, 2015; Monticone et al., 2013) • Recommendation B/'weak' (BÄK et al., 2017) • Recommendation strength B or C (SFMT, 2013) • Level 2 (Staal et al., 2017)
	/* - For (generic)	Recommendation in favour of intervention, where no formal grading system has been used.	• For (Bons et al., 2017; Glocker et al., 2018; Kassolik et al., 2017; Schaafstra et al., 2015)
OPEN	O [O+/O-] – Open	Where no recommendation for or against an intervention can be made, because of an insufficient or inconsistent/conflicting evidence-base. Where expert opinion was then employed to indicate in favour of or against an intervention, this is indicated with a plus (O+) or minus (O-), respectively.	• Open (Pohl et al., 2018; BÄK et al., 2017) • 'no recommendation' (NICE, 2016; van Wambeke et al., 2017) • 'no advice either way' (Glocker et al., 2018) • Recommendation strength C (Monticone et al., 2013; Regione Toscana, 2015) • 'unclear evidence' (SFMT, 2013) • Level 3 or 4 (Staal et al., 2017) • For: expert opinion (van Wambeke et al., 2017); Good practice (Sundhedsstyrelsen, 2015, 2016a-c); Open: may be used (BÄK et al., 2017); 'may be used' (Bier et al., 2016); GDG agreed (NICE, 2016); 'Seems to be effective' (SFMT, 2013); Recommendation strength A* (Regione Toscana, 2015) • Not good practice (Sundhedsstyrelsen, 2015, 2016c); 'Evidence of ineffectiveness' (Regione Toscana, 2015)
AGAINST	X* - Against (generic)	Recommendation against an intervention, where no formal grading system used, or applied to recommendations against.	• Against (Bier et al., 2016; Bons et al., 2017; Glocker et al., 2018; Kassolik et al., 2017; Schaafstra et al., 2015) • 'Do not offer' (NICE, 2016)
	X – Should not do	Recommendations where there are doubts as to whether the intervention should not always be applied and should be carefully consideration. Based on consistent but weak evidence reporting no clinically relevant benefit, and/or harms that outweigh benefit.	• 'weak' (Pohl et al., 2018; Sundhedsstyrelsen 2015, 2016a-c) with wording 'do not routinely offer' (van Wambeke et al., 2017); • Recommendation strength B (BÄK et al., 2017); Pohl), • Recommendation strength B or C (SFMT, 2013) • Recommendation D (Monticone et al., 2013) • Level 2 (Staal et al., 2017)
	XX - Definitely do not do	Recommendations where there is strong evidence of no clinically relevant benefit and/or harms outweighing benefits.	• 'strong' with wording 'do not offer' (van Wambeke et al., 2017), or 'should not' (Pohl et al., 2018) • Recommendation strength A (SFMT, 2013; Pohl et al., 2018) with wording 'do not' (BÄK et al., 2017) • Recommendation E/'strongly discouraged' (Monticone et al., 2013) • Level 1 (Staal et al., 2017)

Supporting Information Appendix S3: Basic characteristics of included clinical practice guidelines

Guideline ID, publication date	Country	Organisation(s)	Target Population	Diagnostic classification (incl./excl.)
Neck pain				
Bier *et al.,* 2016 [Nov-16]	Netherlands	Royal Dutch Society for Physical Therapy	Neck pain (Grades I-IV); Physical and manual therapists.	Neck pain defined as "an unpleasant sensory and emotional experience that is associated with actual or potential tissue damage" in the neck region (from superior nuchal line to scapular spine), potentially accompanied by pain in the head, shoulder, and/or arm. Severity is classified into Grades I-IV.
Monticone *et al.,* 2013	Italy	The Italian Society of Physical and Rehabilitation Medicine (SIMFER)	Neck pain; Specialists in physical and rehabilitation medicine, or involved in treating spinal disorders (orthopaedists, neurologists, rheumatologists), rehabilitation team members (occupational therapists, physical therapists, psychologists, general practitioners), and patients and their families.	Neck pain
Pohl *et al.,* 2018	Germany	German Association of Scientific Medical Societies	Degenerative cervical radiculopathy (CR); All health professionals involved in the management of CR.	Degenerative cervical radiculopathy, confirmed by imaging (MRI)
Sundhedsstyrelsen 2015 [20-May-15, ver 1.0]	Denmark	Danish Health Authority	Patients >18 years; Pain <12 weeks; Clinical signs of cervical radiculopathy caused by disk herniation or degenerative changes; Primary care	Recent onset cervical radiculopathy, excluding radiculopathy caused by cancer, infections, traumas, circulatory insufficiency, osteoporosis or arm pain that does not stem from changes in the cervical spine. *nb*: no distinction is made between cervical radiculopathy caused by disc herniation and other degenerative conditions, as treatment is usually undertaken without existing imaging.
Sundhedsstyrelsen 2016c [29-Nov-16, ver 1.0]	Denmark	Danish Health Authority	Adult patients; Pain <12 weeks located in the neck region; Primary care	Recent onset neck pain, excluding radiculopathy, traumatic neck pain, and specific causes of neck pain including cancer, inflammatory muscle and joint disease, infections, circulatory insufficiency, and osteoporosis.
Low back pain				
BÄK, *et al.,* 2017 (2nd edition, ver. 1) [update from Oct-15]	Germany	30 health organisations, including German Medical Association, National Association of Statutory Health Insurance Physicians, and Scientific Medical Societies	Low back pain in all settings; All medical and allied health professionals, adults with LBP and their relatives, healthcare decision-makers, and members of the general public.	Nonspecific low back pain: pain in the back between costal arch and gluteal fold, with or without radiating pain, but excluding radiculopathy, tumours, infection, and fractures.

Bons *et al.,* 2017 (2nd revision) [Feb-17; update from 2005]	Netherlands	Dutch College of General Practitioners	Low back pain; General Practitioners, primary care.	Non-specific low back pain: back pain between the lower ribs and buttocks, where no specific physical cause can be identified, thus excluding malignancy, vertebral fracture, axial spondyloarthritis, and lumbosacral radicular syndrome.
Glocker *et al.*, 2018 [11-Jan-18]	Germany	German Society for Neurology in collaboration with associations for neurosurgery, orthopaedics and orthopaedic surgery	Adults with acute back/leg pain due to lumbar radiculopathy (lumbar nerve compression or damaged), presenting in 1° or 2° care, or rehabilitation	Lumbar radiculopathy (established pathology, not radicular or referred pain only). Imaging required in patients with symptoms and neurological signs indicating radiculopathy.
National Institute for Health Care Excellence (NICE), 2016 [30-Nov-16]	UK	National Institute for Health and Care Excellence (NICE)	Low back pain and sciatica; Individuals ≥ 16 years old; Primary and secondary care settings (invasive and non-invasive treatment options.	Low back pain including discogenic pain, degenerative disc disease, lumbar disc herniation, secondary to lumbar degenerative disease, and facet joint pain. Sciatica including sciatica/lumbago, radicular pain/radiculopathy, pain radiating to the leg, neurogenic claudication, and nerve root compression/irritation. Exclusion: pregnancy-related back pain, spondylolisthesis, osteoarthritis, sacroiliac joint dysfunction, adjacent-segment disease, failed back surgery syndrome, and serious underlying pathologies. Mixed populations, unless data for people with low back pain only can be extractable.
Regione Toscana, 2015 [update from 2005]	Italy	Consiglio Sanitario Regionale, Regione Toscana	Back pain	Back pain including acute non-specific low back pain; acute radiculopathy (sciatica or cruralgia); persistent acute back pain, subacute and chronic non-specific back pain, and specific chronic low back pain.
Schaafstra *et al.* 2015 (2nd revision) [update from 2005]	Netherlands	Dutch College of General Practitioners	Lumbosacral radicular syndrome; General practitioners, primary care	Lumbosacral radicular syndrome, defined as radiating pain in one buttock or leg, with or without other stimulation phenomena (paraesthesia) and neurological deficits (hypaesthesia/hypalgesia, paresis, reduced reflexes), which is suggestive of stimulation of one (sometimes two) specific lumbosacral nerve root(s).
Société Française de Médecine du Travail (SFMT) (2013) [21-Oct-13]	France	French Society of Occupational Medicine. Partners: National Institute of Research and Security, French Society of Rheumatology (Spine section), National Institute of Health and Medical Research, French Society of Physical Medicine and Rehabilitation, Department of Occupational Health and Health Education, University of Liège.	Adult workers exposed to manual handling and lifting; Lumbar spine	Recommendations relate to the lumbar spine (though some of the studies reviewed relate to other areas)

Staal B. *et al*. 2017 [update from 2013]	Netherlands	Royal College of Physiotherapists together with professional organisation for manual therapists	Low back pain; Physiotherapists and manual therapists	Low back pain, including non-specific LBP and pain due to specific spinal pathology
Sundhedsstyrelsen 2016a [20-Jun-16, ver 1.0]	Denmark	Danish Health Authority	Patients>16 years; Pain <12 weeks regardless of prior episodes; Localised from Th12 to inferior glut fold with or without leg pain; Primary Care	Non-specific low back pain with or without leg pain, excluding lumbar radiculopathy.
Sundhedsstyrelsen 2016b [19-Jan-16, ver 1.0]	Denmark	Danish Health Authority	Patients >18 years; Pain <12 weeks; Clinical signs of lumbar radiculopathy with or without MRI verification; Primary care	Recent onset lumbar radiculopathy whether due to disc herniation or facet joint (or unclear from MRI), but excluding radiculopathy due to other causes e.g. tumours, spinal stenosis, spondylolisthesis and diabetes mellitus.
van Wambeke *et al.* 2017 [27-Nov-17, 2nd ed]	Belgium	Belgian Health Care Knowledge Centre	Low back pain and sciatica; Individuals ≥ 16 years old; Primary and secondary care settings (invasive and non-invasive treatment options.	Low back pain defined as pain between the bottom of the rib cage and the buttock creases, without serious underlying cause (red flags), and radicular pain (incl. neurogenic claudication). Covers acute (0-6 weeks), sub-acute (6-12 weeks) and chronic (from 12 weeks) phases. Exclusion of serious spinal pathology (infection, malignancy and fractures), inflammatory conditions (ankylosing spondylarthritis), potentially serious neurological sequelae of sciatica (progressive neurological deficit and cauda equina syndrome), pregnancy-related back pain, sacroiliac joint dysfunction, adjacent-segment disease, failed back surgery syndrome, and spondylolisthesis.
Neck and low back pain				
Kasssolik *et al.,* 2017	Poland	Polish Society of Physiotherapy, Polish Society of Family Medicine and College of Family Physicians in Poland	Back pain syndromes; Primary care.	Cervical back pain syndrome: as defined by the International Association for the Study of Pain *i.e.* neck pain below the nuchal line and above the line marked by the transverse line running through the 1st spinous process of the thoracic spine and laterally through the sagittal plane adjacent to lateral surface of the neck. Thoracic back pain syndrome: Pain experienced in the upper and middle back of the torso between the Th1–Th12 vertebrae. Lumbar-sacral back pain syndrome *i.e.* low back pain (LBP): below 12th rib and above lower gluteal folds, associated with possible radiation to the lower limbs.

Supporting Information Appendix S4 - Development and implementation methods used in clinical practice guidelines

Guideline ID	Multi-disciplinary group committee or single profession?	Date or timeframe for future revision	How was level of evidence determined and/or strength of recommendation determined	Consensus (details)	includes recommendations regarding (Y/N):						
					Evaluation of flags						
					red	yellow	blue/ black	Diagnosis	Planning of care	Practitioner education	Organisation and policy
Neck pain											
Bier et al., 2016	9 authors in total; 8 describe themselves as physiotherapists and/or manual therapists, 1 describes themselves as an epidemiologist. 4 of the physiotherapists/manual therapists additionally describe themselves as epidemiologists; 2 physiotherapists/manual therapists additionally describe themselves as policy advisors.	Not reported	GRADE (High, Moderate, Low, Very low) Based on: High quality evidence; Low quality evidence; and expert opinion. Recommendation wording ranging from: recommended to use (should be used - A); can be used - B; may be used - 0; recommended against	Specific interventions searched for; best evidence sought through specific guidelines and Cochrane databases; additional electronic searches also conducted; quality appraisal conducted	Y	Y	Y	Y	Y	N	N
Monticone et al., 2013	Not reported	Not reported	Evidence graded: I (highest) – VI (lowest) Strength of recommendation: A (strongly recommend) – E (strongly discourage)	Not reported, it is unclear whether this was undertaken	Y	N	N	Y	Y	N	N
Pohl et al., 2018	Multidisciplinary: experts from neurology, orthopaedics, physiotherapy, emergency medicine, trauma surgery, neurosurgery, pain medicine, occupational therapy, and patient organisation.	Valid for 3 years (until 2021)	Recommendations graded: "soll" (should = strong); "sollte" (may = weak); or "kann" (open)	Consensus achieved through Nominal Group Technique (2 meetings and Delphi survey). Recommendations adopted with at least 88% agreement	Y	Y	N	Y	Y	N	N
Sundhedsstyrelsen, 2015	Development/Working group consisting of 10 interdisciplinary clinicians. Reference group consisting of 11 interdisciplinary clinicians. Secretariat consisting of 5 persons from Danish Health Authority	Every 3 years, or if new evidence emerges	Overall level of evidence (high, moderate, low, very low) and strength of recommendations (Strong, weak, good practice) determined using GRADE	The guideline used the Danish Health Authorities recommendations that are based on the GRADE system	N	N	N	N	Y	Y	N

Sundhedsstyrelsen, 2016c	Development/Working group consisting of 12 interdisciplinary clinicians. Reference group consisting of 11 interdisciplinary clinicians. Secretariat consisting of 3 persons from Danish Health Authority	Every 3 years, or if new evidence emerges	Overall level of evidence (high, moderate, low, very low) and strength of recommendations (Strong, weak, good practice) determined using GRADE	The guideline used the Danish Health Authorities recommendations that are based on the GRADE system	N	N	N	N	Y	Y	N
Low back pain											
BÄK et al., 2017	Multidisciplinary: Aimed at all medical professions involved in the detection, diagnosis and treatment of patients with low back pain, treatment-support specialists (e.g. occupational therapy, physiotherapy, psychotherapy, social work); specialty hospitals and departments, acute and rehabilitative hospitals	update planned 5 years after publication	Oxford Centre of Evidence 2011 levels of evidence: level 1 to 5, with type of study design depending on type of research question + AMSTAR score for each review Recommendations graded using GRADE approach: A (strong), either 'do' or 'do not'; or B (weak), either 'should do' or 'should not do'; or 0 (open): 'may do'.	Multi-part nominal group process with representatives of different healthcare specialties and organisations. Each organisation had one vote. process includes 6 steps: (i) silent review of the guideline manuscript; (ii) opportunity to propose changes to recommendations and grading; (iii) moderator records the judgements and alternative proposals; (iv) preliminary voting on all recommendations; (v) discussion on issues where there is no consensus; (vi) final vote	Y	Y	Y	Y	Y	N	Y
Bons et al., 2017 (2nd revision)	Single profession: general practitioners, but aligned with the multidisciplinary (CBO) guidance for non-specific LBP and developed together with national organisations for neurologists, orthopedists, physiotherapist, etc. Patient involvement through meeting with patient organisation.	Not reported	Narrative summaries of the evidence. Recommendations not graded.	Literature searches conducted by College of GPs. Working group reviews evidence and formulates recommendations. Feedback requested from number of specialists and experts; followed by round of feedback from random sample of (n=50) GPs.	Y	Y	Y	Y	Y	N	Y
Glocker et al., 2018	Multidisciplinary, aimed at neurologists, neursurgeons, orthopedic doctors and surgeons, and for information for rehabilitation physicians and physiotherapists	2023	Not used	First round send to panel members for comments; teleconference to discuss disagreements; final draft distributed. Agreement scored on 1-6 scale; but results not reported for each treatment option.	Y	Y	N	Y	N	N	N

National Institute for Health Care Excellence (NICE), 2016	Multidisciplinary group including: neurosurgeon, GP, nurse, psychologist, physiotherapist, osteopath, patients, researchers, orthopaedic surgeon, rheumatologist, Pain medicine consultant, and health economist	Review of evidence base after publication, to establish if it has progressed significantly to alter recommendations and thus warrant update.	Overall level of evidence determined using GRADE (high, moderate, low, very low). Strength of recommendation based on GRADE. Wording in guideline to reflect strength: 'offer' - strong recommendation (usually where there is clear evidence of benefit); 'consider' - a recommendation for which the evidence of benefit is less certain.	Systematic reviews conducted. Recommendations drafted on the basis of the GDG's interpretation of the available evidence, or expert opinion (agreed though discussion) where evidence was of poor quality, conflicting or absent. Recommendation wording was agreed by the GDG taking into consideration the actions health professionals need to take, the information readers need to know, the strength of the recommendation, the involvement of patients (and their carers if needed) in decisions on treatment and care, and consistency with NICE's standard advice on recommendations about drugs, waiting times and ineffective interventions	Y	Y	N	Y	Y	Y	N
Regione Toscana, 2015	Multi-professional team: doctors (general medicine, orthopaedics, rheumatology), psychologists and psychotherapists	Not reported	Evidence graded: I (highest) – VI (lowest) Recommendations graded: • A. Strong; • A*. Strong, where evaluation with RCT not possible, or based on irrefutable clinical experience • B. Doubts as to whether recommendation should always be implemented and should be carefully considered. • C. Substantial uncertainty; where no studies found, or studies report conflicting results.	**Check this is the right information and if so summarise?**	Y	Y	Y	Y	Y	Y	Y

Schaafstra et al., 2015 (2nd revision)	Single profession: general practitioners but aligned with the multidisciplinary (CBO) guidance for lumbar radicular syndrome and developed together with national organisations for neurologists, orthopaedists, and physiotherapists. Patient involvement through meeting with patient organisation.	Not stated	Narrative summaries of the evidence. Recommendations not graded.	Literature searches conducted by College of GPs. Working group reviews evidence and formulates recommendations. Feedback requested from number of specialists and experts; followed by round of feedback from random sample of GPs (*n* = 50).	Y	N	N	Y	Y	N	N
Société Française de Médecine du Travail (SFMT), 2013	Working group consisting of medical practitioners (n=24): specialists in rheumatology, industrial medicine, osteopathy, rehabilitation, physiotherapy, ergonomics, occupational therapy, nursing, physiology, and epidemiology. Service users also involved. 'Reading group' (n=50) to review the literature: similar composition to working group.	Not stated	Overall level of evidence graded: 1 (highest) to 4 (lowest). Recommendations graded: A. level of evidence 1 (highest); B. level of evidence 2; C. levels of evidence 3 and 4 (lowest). 'Expert consensus' in the absence of relevant studies.	A method proposed by the Haute Autorité de Santé (HAS) was used (HAS, 2010). This is based on critical review of the literature and the views of a multidisciplinary group of professionals.	Y	Y	Y	Y	N	N	Y

Staal et al., 2017	Physiotherapy and Manual therapy	3-5 years, update planned for 2018 at the latest	Evidence level: A1 (systematic review); A2 (RCT of good quality); B (RCT of poorer quality or other comparative study, e.g. matched cohort, non-RCT), C (non-comparative study); D (expert opinion) Recommendation level: Level 1 (A1 or multiple A2 studies) - "*It has been demonstrated that*.."; Level 2 (multiple B studies) – "*It is possible that*.."; Level 3 (1 x A2 or B study) - "*There are indications that*.."; Level 4 (C studies or consensus only) - "*The working group is of the opinion that* .."	Not described	Y	Y	Y	Y	Y	N	N
Sundhedsstyrelsen, 2016a	Development/Working group consisting of 12 interdisciplinary clinicians; Reference group consisting of 11 interdisciplinary clinicians; Secretariat consisting of 4 persons from the Danish Health Authority	Every 3 years, or if new evidence emerges	Overall level of evidence (high, moderate, low, very low) and strength of recommendations (Strong, weak, good practice) determined using GRADE.	The guideline used the Danish Health Authorities recommendations that are based on the GRADE system	N	N	N	N	Y	Y	N
Sundhedsstyrelsen, 2016b	Development/Working group consisting of 11 interdisciplinary clinicians; Reference group consisting of 12 interdisciplinary clinicians; Secretariat consisting of 6 persons from the Danish Health Authority	Every 3 years, or if new evidence emerges	Overall level of evidence (high, moderate, low, very low) and strength of recommendations (Strong, weak, good practice) determined using GRADE.	The guideline used the Danish Health Authorities recommendations that are based on the GRADE system	N	N	N	N	Y	Y	N

van Wambeke et al., 2017	Multidisciplinary including GP, psychologists, physiotherapists, orthopaedic surgeon, anaesthesiologist, neurosurgeons	Ideally reviewed 5 years after publication to determine if all or part should be updated. (may be earlier if important new evidence published)	Overall level of evidence determined using GRADE (high, moderate, low, very low). Strength of recommendation based on GRADE (strong/weak). Wording in guideline to reflect strength: 'offer'/'do not offer' - strong recommendation for/against; 'consider'/'do not routinely offer' - weak recommendation for/against. Nb: based on NICE guideline.	NICE evidence and recommendations checked, summarised and added, and discussed in GDG meetings. Before each meeting, GDG members asked to agree or not with NICE recommendation and strength suggested by KCE team. KCE made an overview of the agreement scores and the comments formulated by the GDG members. This structured the GDG meeting and enabled discussion of each comment (including of GDG members not present). In cases of disagreement, the topic was proposed for re-discussed at the next GDG meeting. Minutes highlighted changes made to recommendations and the reasons and were sent to every GDG member after each meeting. Four consultation rounds which each contained roughly 15 recommendations to be scored and commented were needed. Final list of NICE and Belgium recommendations checked during the final GDG meeting (24 Jan 2017).	Y	Y	Y	N	N[$]	N[$]	N[$]
Neck and low back pain											
Kasssolik et al. 2017	Experts from the Polish Society of Physiotherapy, Polish Society of Family Medicine and College of Family Physicians in Poland	Not reported	Not reported	Not reported	N	N	N	Y	N	N	N

[$] - following this guideline, a clinical pathway was developed by KCE that addressed planning of care, practitioner education, and organisation and policy.

Supporting Information Appendix S5: Neck pain recommendations in European practice guidelines

Direction and strength of recommendations for each guideline (for symbol definition see Supporting Information Appendix S2). Green columns represent guidelines rated as high quality. **Abbreviation:** SC – self-care, SST – Sundhedsstyrelsen

Guideline ID	SST 2016c	Bier 2016	Monticone 2013	Kasssolik 2017	Pohl 2018	SST 2015
Country	**DK**	**NL**	**IT**	**PL**	**DE**	**DK**
	Recent onset non-specific neck pain	Neck pain (Grades I-IV; Profiles A-D)[a]	Neck pain	Cervical back pain syndrome	Cervical radiculopathy	Recent onset cervical radiculopathy
Guideline quality	**High**	**Low**	**Low**	**Low**	**Low**	**High**
Reassurance						
Reassurance	**O+**	**/** - I-III (A-D)		**/*** - acute		
Advice and Education						
Advice and Education		**/** - I-III (A-D)	**X**	**/*** - acute	**//**	**O+**
Written information	**X**					
Bed rest				**X*** - 1-2 days selected cases		
Remain active		**/** - I-III (A-D)				**O+**
Encourage exercise		**/** - I-III (A-D)		**/***		**O+**
Avoid movement/activity that provokes radiating pain or other symptoms in the arm		**/** - III (D)				
Continue/return to work		**/** - I-III (A-D)				
Work-related/occupational advice		**/** - I-III (A-D)				
Psychosocial aspects that delay/inhibit recovery		**/** - I/II (C)				
Medication						
Analgesics incl. for neuropathic pain				**/*** - incl. SC	**//** - offer early	
Paracetamol			**/** - short-term			**O+**
NSAIDs	**O+** - short term		**/** - short-term	**/*** - SC		**O+** - short term
Opioids including tramadol	**O+** - short term					**O+** - short term
Steroids			**/** - short-term			
Topical medications incl. NSAIDs	**/**			**/*** - SC		
Injection/infiltration						
Spinal epidural steroid injection (transforaminal route with imaging)					**/** - severe persistent symptoms	
Thermotherapy						
Thermotherapy incl. hot/ cold compress, bath, sauna		**X***- I-III (B-D)		**/***		
Thermotherapy + other treatment		**O+** - I-III (B-D) - short-term				
Manual therapies						
Manual therapy including mobilisation, manipulation and soft-tissue techniques	**X**		**//** - acute	**/***	**//**	Massage: **O-;** Mobilisations: **/**
Manual therapy + other treatment	**/**	Massage: **O+** - I-III (B-D), short-term; Mobilisation + exercise: **O+** - III (D), Thoracic mobilisation + exercise: **/** - III (D)	Manipulation/ mobilisation + exercise: **//** - chronic; Massage with exercise + manipulation/ mobilization: **/** - chronic			
Exercise						
Exercise programs/therapy		**/** - I/III (B-D)	**//** - chronic	**/***	**//**	Neuro-muscular

						exercises: **/;** McKenzie Method exercises**: O+**
Exercise therapy + other treatment	**/**	**//** - I/III (B-D)				
Postural therapies						
Postural re-education				**/***		
Traction						
Traction		**O+** - III (D); **X*** - I/II (B-C)	**X**			**/**
Electrotherapies						
Electrotherapy incl. light, laser, Low Level Laser Therapy (LLLT), pulsed electromagnetic, TENS, Ultrasound (US), shockwave, Magnetic, electromagnetic		**X* -** I-III (B-D)	LLLT: **/** - acute and chronic - short term; Pulsed electro-magnetic therapy: **O+** - acute and chronic, short term; TENS: **X** - acute and chronic	TENS (SC), Light, US, magnetic field, electro-magnetic: **/***; Intensive physical therapy e.g. high energy laser, shock-wave, electro-stimulation: **X*** - chronic	**XX**	
Electrotherapies + other treatment			**/** - chronic			
Orthotics						
Cervical orthoses (soft and stiff collars)		**O+** - III (D), short-term**;** **X*** - I-II (B-C)	**O-**	**/***	**O-** - intermittent use, severe pain, max 10-25 days	
Ergonomic						
Cervical cushion		**O+** - I-III (B-D)				
Taping/strapping						
Kinesiology tape		**O+ -** I-III (B-D) trauma-related, short-term				
Acupuncture						
Acupuncture/dry needling	**/**	**X* -** I-III (B-D)	**//** - sub-acute and chronic, short term			**O-**
Psychological interventions						
Psychological therapies incl. behavioural and cognitive-behavioural therapies		**O+ -** I-III (B-D)	**/** - chronic	**/*** - chronic		
Multidisciplinary treatment/programs						
Multidisciplinary treatment			**/** - chronic		**/** - chronic w/o indication for surgery	
Work-related interventions						
Workplace interventions		**O+** - I-III (B-D), if work-related				
Imaging						
Imaging				**X***	**//** - to confirm diagnosis	
Referral						
To GP and/or occupational health officer		**O+** - I-III (B-D), after 6 weeks if treatment not effective				
To GP or to the referring specialist		**O+** - IV				
To physical therapist specialized in worker rehabilitation		**O+** - I-III (A-D), where absenteeism				

		or production loss without absenteeism		
To occupational health officer or a physical therapist specialised in worker rehabilitation		**O+** - I-III (B-D) - where work-related factors suspected to impede recovery		
To occupational health and safety service (Arbodienst)		**O+** - I-III (B-D) - in cases of absenteeism		
Encourage patient to contact GP, psychologist and/or psychosomatic therapist		**O+** - I/II (C) - where psychosocial factors hinder recovery		
To surgeon/surgery			**/** - chronic, refractory (appropriate method for anatomical findings)**; O+** - severe neurological symptoms	
Miscellaneous				
Bioptron lamps		**/*** - SC		
Ledotherapy lamps		**/*** - SC		
Infra-red lamps		**/*** - SC		
Bath salts with mud extracts, special water-pearling inserts or ozone		**/*** - SC		
Magnetic mattress		**/*** - SC		

[a] **Profile A**, neck pain grade I/II, normal course; **Profile B**, neck pain grade I/II, delayed course without dominant psychosocial influence; **Profile C**,

Supporting Information Appendix S6: Low back pain recommendations in European practice guidelines

Direction and strength of recommendations for each guideline (for symbol definition see Supporting Information Appendix S2). Green columns represent guidelines rated as high quality. **Abbreviation:** SC – self-care, SST - Sundhedsstyrelsen

Guideline ID	Bons, 2017	SFMT, 2013	BAK, 2017	Staal, 2017	SST, 2016a	van Wambeke, 2017	NICE, 2016	Kassolik, 2017	Regione Toscana, 2015	Glocker, 2018	Schaafstra, 2015	SST, 2016b
Country	**NL**	**FR**	**DE**	**NL**	**DK**	**BE**	**UK**	**PL**	**IT**	**DE**	**NL**	**DK**
	NSLBP	Lumbar spine, in context of workers exposed to lifting and handling	NSLBP +/- radiating, w/o radiculopathy	LBP, including specific and non-specific (profile 1-3)[a]	recent onset NSLBP +/- leg pain	LBP and radicular pain	LBP and sciatica	Lumbar-sacral back pain syndrome (LBP)	LBP +/- radiculopathy (sciatica or cruralgia)[$]	lumbar radiculopathy	Lumbo-sacral radicular syndrome	recent onset lumbar radiculopathy
Guideline quality	**Low**	**Low**	**High**	**Low**	**High**	**High**	**High**	**Low**	**Low**	**Low**	**Low**	**High**
Reassurance												
Reassurance				**/*** - Profiles 1-3		**O+**		**/*** - acute	**//** - general LBP & acute NSLBP			
Advice and Education												
Advice and Education (including individualised)	**/***	**O+** - acute and subacute LBP; **O** - cLBP	**//**	**/*** - Profiles 1-3	**/**	**O+**	**O+**	**/*** - acute	**//** - general LBP		**/*** - for a period of 6-8 weeks	
Bed rest			**XX**	**X*** - max 2 days if only way to control pain - Profiles 1-3				**X*** - acute, but in selected cases 1-2 days	**XX** - general LBP, acute NSLBP; **O-** - acute radiculopathy (a few days if severe sciatica)	**X***- max 4 days	**X*** - only for a few days if symptoms severe	
Remain active	**/***		**//** - subacute and chronic; **O+** acute LBP	**/*** - Profiles 1-3	**/**	**O+**	**O+**		**//** - general LBP & acute NSLBP; **O+** acute radiculopathy	**/***		**/**
Encourage physical exercise (unsupervised)		**//**		**/*** - Profiles 1-3		**O+**	**O+**	**/***	**//** - general LBP		**/*** - for a period of 6-8 weeks	
Continue/return to work				**/*** - Profiles 1-3					**//** - general LBP & acute NSLBP; **O+** -			

							acute radiculopathy				
Medication											
Analgesics (general)							**/*** - incl. SC				
Paracetamol	**/***[b]	**X**		**X**	**X** - as single medication	**X** * - as single medication		**//** - acute nsLPB; **O+ -** acute radiculopathy ; **O** - cLBP	**/*** [b]	**/*** [b]	
NSAIDs	**/***[b]	**/** - traditional NSAIDs**; O+** - COX2i		**X**	**/**	**/**	**/*** - SC	**//** - acute nsLPB; **O+** - acute radiculopathy **; O** – cLBP	**/*** [b]	**/*** [b]	
Opioids (including tramadol) +/- paracetamol (or NSAIDs)	**/***[b] – weak opioids for severe acute LBP; weak or strong opioids for cLBP with severe limitation. Short-term	**//** - weak opioids if other analgesics not effective; **X** – transdermal		**X**	**O+** - acute LBP +/- radicular pain if NSAID contraindicated, not tolerated or ineffective; **X** - cLBP	**/**- acute LBP only if an NSAID is contraindicated, not tolerated or ineffective; **X*** - cLBP		**//** - acute NSLBP; **O+** - acute radiculopathy ; **O** - cLBP	**/*** [b]	**/*** [b]	
Steroids								**XX** - acute NSLBP; **O+** - acute radiculopathy , short term; **O** – chronic pain			
Antidepressants including SSRIs, SNRIs, Tricyclics	**X***	**X** - in general; **O+** if depressive comorbid symptoms			**XX** - SSRIs; **X** - Tricyclics & SNRIs	**X*** - SNRIs, SSRIs, Tricyclics		**O** - cLBP	**X*** - SSRIs; **/***- Tricyclics. chronic pain		
Anticonvulsants/Antiepileptics including gabapentin, pregablin, carbamazepine, topiramat	**X***	**X**			**XX** - LBP +/- radicular pain in absence of neuropathic pain	**X***		**XX** - acute NSLBP; **O-** - acute radiculopathy ; **O** - cLBP			

Muscle relaxants including diazepines/benzodiazepines	**X***	**X** - acute, **XX** - chronic NSLBP. BUT **O+** - acute and chronic if non-drug measures or non-opioid analgesics not effective		**XX** - (skeletal MRs)		**//** - (centrally acting MRs) acute NSLPB. 2nd line only; **O** - cLBP		**X***	
Antibiotics				**XX**					
Metamizol		**O+** - short term if NSAIDs not effective							
Flurpirtin		**XX**							
Uridine monophosphate (UMP)		**XX**							
Topical medications/NSAIDS	**/*** - NSAIDs	**XX** - NSAIDs				**/*** - SC			
Injection/infiltration									
Spinal injections [for non-specific LBP]	**X***			**XX**	**X***	**O** - cLBP	**O**	**X***	
Spinal epidural steroid injection				**/** - [sub-]acute (at least 2-3 weeks) and severe radicular pain	**/ -** acute, severe sciatica; **X*** - neurogenic claudication in central spinal canal stenosis	**O+** - acute radiculopathy ; **O** - cLBP		**/*** - if symptoms severe, > 6-8 weeks' duration, and surgery not indicated	**X**
Other injections including intravenous, intramuscular, infiltration of trigger points and ligaments, intradiscal infiltration, prolotherapy, Botulium toxin		**XX**				**O** - cLBP			
Thermotherapy									
Thermotherapy including local heat, hot/cold compresses, baths, sauna		heat: **O+;** cold: **X**	**/* -** Profile 2, if impaired joint function			heat/cold: **/*** Local heat: **//** - acute NSLBP; **O** - cLBP	heat: **O**		
Manual therapies									

Manual therapy including mobilisation, manipulation and soft-tissue techniques		**XX** - acute (massage); **O** - manipulation/ mobilisation	**/* -** Profile 2, if impaired joint functionality; **X*** - Profiles 1&3	**/**			**/***	**Massage: XX** - acute NSLBP **O-** - acute radiculopathy ; **O** - cLBP. **Manipulation** : **//** - acute NSLBP (after 2-3 weeks and before 6 from onset); **O** - cLBP	**X***	**X***	**/**
Manual therapy in combination with other treatment		**O+** - subacute/ chronic			**/**	**/**			**Massage + exercise: /*** - - subacute & chronic; **Massage + electro-therapies: /*** - acute radiculopathy with limited mobility		
Exercise											
Exercise programs/therapy	**/*** - especially for those who have been unable to stay active	**// -** subacute/ chronic; **O** - acute	**/*** - Profiles 2 & 3	**/**	**/**		**/***	**XX -** specific exercises - acute NSLBP		**/***	**/**
Group exercise programmes/back schools		**/ -** subacute and chronic**; O+** - chronic recurrent				**/**			**/*** - chronic only		
Postural therapies											
Postural therapies e.g. Alexander therapy, postural re-education					**O**	**O**	**/*** - SC				
Traction											
Traction		**XX**	**O- -** Profiles 1-3		**XX**	**X***	**/***	**O -** cLBP			
Taping/strapping											
Kinesiotaping		**XX**									

Electrotherapies										
Electrotherapy including laser therapies, TENS, PENS, shortwave diathermy, ultrasound (US), ultrashortwave, inferential, magnetic field, electromagnetic, light therapy, shockwave, electrostimulation		**XX**	**O- -** Profiles 1-3		**XX**	**X***	TENS (incl SC), US, (electro)-magnetic field, light therapy - **/*; I**ntensive physical therapy (e.g. shockwave, high energy laser or electro-stimulation) - **X***	**XX** - acute NSLBP; **O-** - acute radiculopathy ; **O** - cLBP		
Orthotics										
Orthoses including belts, corsets, foot orthotics, insoles, rocker shoes, pull-ups, walking stick, elbow crutches and bands	**X**	**XX**			**XX**	**X***	**/***	**XX** - acute NSLBP; **O-** - acute radiculopathy ; **O** - cLBP		
Complementary and alternative therapies (CAM)										
Acupuncture		**O+** - acute (if other treatments not effective, short term) and chronic		**X**	**O**	**X***				**O-**
CAM (acupuncture and TCM, phytotherapy, homeopathy, manual therapies)								**O+**		
Phytotherapeutics		**O+; X –** Harpago-phytum procumbens								
Topical phytotherapeutics		**X** - *Symphytum officinale*; **O+** - Capsaicin								
Psychological interventions										
Psychological therapies including behavioural and cognitive behavioural therapies	**/*** - after 12 weeks, especially if struggling to manage	**//** - subacute LBP depending on psycho-social risk profile					**/***	**/*** - chronic pain		

Psychological therapies + other treatment (exercise)							/	/	
Progressive muscle relaxation			**O-** - acute LBP, **O+ -** subacute LBP or those with stress, anxiety etc, - may prevent chronic pain in this group; **/ -** chronic LBP						
Multidisciplinary treatment/program									
Multidisciplinary treatment including multidisciplinary biopsychosocial rehabilitation (MBR) programs	**/*** - cLBP and motivated to receive further treatment	**/** - subacute or cLBP, **O -** acute LBP	**//** - cLBP	**/*** - profiles 2 & 3 with delayed recovery		**/** - persistent LBP or radicular pain: with psychosocial obstacles to recovery, or when previous evidence-based management has not been effective	**/ -** persistent LBP or sciatica with significant psychosocial obstacles to recovery or when previous treatments have not been effective.	**O+** - subacute & chronic NSLBP: disability is high, or recent onset and patient strongly motivated to resolve	
Work-related interventions									
Work-based interventions including rehabilitation programmes (exercises, preferably with workplace visits, workplace adjustments, or other interventions on the part of the employer)		**// -** employees; **/** - for employers (context of 1º or 2º prevention)	**/**					**//** - acute NSLBP	
Return to work programmes			**//**			**O+**	**O+**		
Collaborate with company doctor, company physical therapist or occupation health and safety service				**/* -** Profile 2 - if sick leave >4 weeks; **/*** - Profile 3 - if					

				recovery impeded by heavy physical work, prolonged sick leave, a labour dispute, or if collaboration expected to promote the recovery						
Imaging										
Imaging	**X*** - unless suspicion of serious pathology[†]	**XX** - except if red flags[†]; Repeat imaging not recommended within a year, unless there is a new clinical indication for it	**XX** - acute or persistent LBP if no red flags[†], OR repeat imaging (w/o change in clinical presentation); **//** - severe and disabling LBP not improved after 6 weeks treatment OR Referral for further investigations, including appropriate imaging if red flags[†]		MRI: **X**	**X -** unless red flags[†], or if its expected result may lead to change in management	**X***	**X*** - unless red flags[†]	**X*** - unless red flags/ suspicion of serious pathology[†]	MRI: **X**
Referral										
To family doctor				**/* -** Profile 3, if treatment has had no effect after 3-6 weeks						
To manual therapist				**/* -** Profile 2, if impaired joint functionality						

To family doctor, company doctor and/or psychologist			**/*** - Profile 3, if serious or persistent psychosocial factors hamper recovery						
For specialist assessment (neurophysiopathological evaluation)						**O+** - acute radiculopathy, if persistent pain, or atypical lower limb responses, or new or progressive motor deficits			
To surgeon/surgery (also included here where guideline addresses a particular surgical intervention and gives context e.g. failure of non-surgical intervention)	**X***	**XX**		**//** - only after failure of a non-surgical evidence-based multimodal management, and after evaluation in a multi-disciplinary consultation	**/** - for failed non-surgical treatment, and source of pain from structures supplied by the medial branch nerve and moderate or severe LBP at the time of referral OR for sciatica with failed non-surgical treatment with sciatica consistent radiological findings	**O+** - acute radiculopathy, only after 1 month of conservative therapy if severe and disabling, with no improve-ment or worsening or clinical evidence of compressed nerve root; <1 month if neurological worsening, severe pain and resistant to conservative therapy or appearance	**/*-** specific indications only [cauda equina symptoms, severe neurological signs, or in case of persistent problems and clear nerve compression and no response to conservative treatment]	**/*** - after 12 weeks, if persistent (severe) symptoms	**O+** - within 12 weeks in cases where severe and disabling pain persists despite non-surgical treatment

					of red flags; **O** – cLBP	
Miscellaneous						
Spa treatments					**O -** cLBP	
Ozone therapy					**O -** cLBP	
Medullary stimulations					**O -** cLBP	
'Taking it slowly/easy'					**O -** cLBP	
Bioptron lamps					**/*** - SC	
Ledotherapy lamps					**/*** - SC	
Infra-red lamps					**/*** - SC	
Bath salts with mud extracts, water-pearling inserts or ozone					**/*** - SC	
Magnetic mattress					**/*** - SC	
Shock-absorbing or anti-fatigue flooring	**X**					

[$] recommendation strength given en masse per type of back pain (For and against), not on individual intervention basis

† further details regarding red flags given in Supporting Information Appendix S7

[a] **Profile 1:** normal course; **Profile 2 / 3:** abnormal course, without / with dominant presence of psychosocial factors impeding recovery respectively

[b] stepwise according to guidance: paracetamol, NSAIDs, opiate

Supporting Information Appendix S7: Red flags in the context of imaging in low back pain recommendations

Guideline ID, publication date	Condition	Imaging recommendations	Red flags/serious pathologies
BÄK, *et al.*, 2017	Nonspecific low back pain with or without radiating pain	Referral for further investigations, including appropriate imaging if there are red flags / warning signs.	(1) **fracture/osteoporosis**: severe trauma, minor trauma in older people or those wit (likely) osteoporosis; treatment with systemic steroids; (2) **infection**: general malaise, previous bacterial infection, immune suppression, recent back surgery, severe pain at night; (3) radiculopathy: severe progressive symptoms, **cauda equina symptoms** (sensory deficits, incontinence, paresis); (4) **tumour/metastases**: older age, cancer history, unexplained weight loss, loss of appetite, severe night pain; (5) **axial spondylitis**: morning stiffness, peripheral arthritis, etc
Bons *et al.*, 2017	Non-specific low back pain	Imaging in case of suspected serious pathology.	(1) suspicion of **rupture aneurysm of aorta**: age >40, acute severe pain, history of aorta aneurysm, symptoms or signs of threatened circulation (fainting, dizziness, etc); (2) symptoms of **cauda equina**: sensory deficits; severe radicular pain; incontinence; recent back surgery; (3**) unexplained progressive course; fever and night sweats; cancer history**
Glocker *et al.*, 2018	Lumbar radiculopathy	CT or MRI only in case of red flags.	(1) previous trauma in older people with increased risk of fragility **fracture**, including those with osteoporosis; (2) suspicion of **tumour** or **infection**: fever, unexplained weight loss, increasing pain at night; (3) **cauda equina syndrome:** progressive paresis, incontinence
Schaafstra *et al.* 2015	Lumbo-sacral radicular syndrome	Imaging when there is suspicion of serious pathology.	Red flags/signs and symptoms: (1) **severe pain, cancer history, recent back surgery, unexplained weight loss, fever, possible Lyme's disease**; (2) **cauda equina symptoms**: incontinence, severe sensory deficits or loss of strength; (3) when surgery may be indicated .
Société Française de Médecine du Travail (SFMT) (2013)	Lumbar spine, in context of workers exposed to lifting and handling	Standard X-ray generally not recommended in patients 20 to 55 years old, except if there are suspect clinical signs /red flags. Second-line imaging (CT, MRI, scintigraphy, PET) not recommended in the absence of suspicious clinical signs / red flags.	(1) **Progressively worsening non-mechanical pain**, present at rest and in particular during night; (2) **widespread neurological symptoms** (deficit in the control of the bladder or anal sphincters, motor impairment of the legs, cauda equina syndrome); (3) **paraesthesia in the pubis or perineum**; (4) **Significant trauma** e.g. fall from a height; (5) **Unexplained weight loss**; (6) **History of cancer**, **presence of febrile syndrome**; (7) **IV drug use, or prolonged use of corticosteroids**; (8) **Significant structural deformation of the spinal column**; (9) **Chest pain (= back pain)**; (10) **Age of onset <20 years or >55 years**; (11) **Fever**; (12) **Altered of general condition**.
van Wambeke *et al.* 2017	LBP and radicular pain	Do not routinely offer imaging in the absence of red flags. Only refer for imaging if expected results may lead to change in management (e.g. if an invasive intervention is being considered).	(1) **Neurological emergencies:** widespread neurological symptoms; progressive neurological symptoms; cauda equina symptoms: saddle anaesthesia/hypoesthesia, urinary retention, urinary or faecal incontinence, isolated sexual disfunction; (2) **Fracture (traumatic)**: severe low back pain following significant/high-energy trauma; back pain following trauma with ankylosing spondylitis; (3) Vascular signs indicative of **torn aortic aneurysm** alongside low back pain or sock; (4) **Fracture (pathological):** history/risk of osteoporosis, long-term corticosteroid use, thoracic pain, older age, unexplained weight loss, cancer history; (5) **infection:** objective signs, IV drug use, patient immunocompromised, unexplained weight loss, previous/concurrent systematic infection or risk of infection, recent surgical intervention, urinary or cutaneous infection.

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Section/topic	#	Checklist item	Reported on page #
TITLE PAGE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
Funding	2	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review on your title page.	1
Bulleted statements	3	'Database?' and ' what does this review add?'.	1
ABSTRACT			
Structured summary	4	Provide a structured summary including, as applicable: background and objective; databases and data treatment; results, conclusion; systematic review registration number.	2
INTRODUCTION			
Rationale	5	Describe the rationale for the review in the context of what is already known.	2-3
Objectives	6	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	7	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	3
Eligibility criteria	8	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4-5
Information sources	9	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	3-4
Search	10	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supporting Information Appendix S1
Study selection	11	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	12	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5
Data items	13	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
Risk of bias in individual studies	14	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5-6

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Section/topic	#	Checklist item	Reported on page #
Summary measures	15	State the principal summary measures (e.g., risk ratio, difference in means).	n/a
Synthesis of results	16	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6-7
Risk of bias across studies	17	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	5-6
Additional analyses	18	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	n/a
RESULTS			
Study selection	19	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7, Figure 1
Study characteristics	20	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	7-8, Table 1, Supporting information Appendices S3 & S4
Risk of bias within studies	22	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	8, Table 2
Results of individual studies	23	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Supporting information Appendices S5, S6 & S7
Synthesis of results	24	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	8-10, Tables 3-4
Risk of bias across studies	25	Present results of any assessment of risk of bias across studies (see Item 15).	8, Table 2
Additional analysis	26	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	n/a
DISCUSSION			
Summary of evidence	27	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	10-11
Limitations	28	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	12
Conclusions	29	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	12-13

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097