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Focus Article

Non-Surgical Interventions for Lumbar Spinal Stenosis Leading To Neurogenic Claudication: A Clinical Practice Guideline

André Bussières,[*,†] Carolina Cancelliere,[‡] Carlo Ammendolia,[§] Christine M. Comer,[¶] Fadi Al Zoubi,[‖] Claude-Edouard Châtillon,[#] Greg Chernish,[**] James M Cox,[††] Jordan A Gliedt,[‡‡] Danielle Haskett,[§§] Rikke Krüger Jensen,[¶¶] Andrée-Anne Marchand,[‖‖] Christy Tomkins-Lane,[##] Julie O'Shaughnessy,[***] Steven Passmore,[†††] Michael J. Schneider,[‡‡‡,§§§] Peter Shipka,[¶¶¶] Gregory Stewart,[‖‖‖] Kent Stuber,[###,****] Albert Yee,[††††] and Joseph Ornelas[‡‡‡‡,§§§], In collaboration with the Canadian Chiropractic Guideline Initiative in collaboration and Bone and Joint Canada

[*]*School of Physical Medicine & Occupational Therapy, McGill University, Montreal, Quebec, Canada*
[†]*Département Chiropratique, Université du Québec à Trois-Rivières, Quebec, Canada*
[‡]*Faculty of Health Sciences, University of Ontario Institute of Technology, Oshawa, Canada*
[§]*Faculty of Medicine, University of Toronto and Mount Sinai Hospital, Ontario, Canada*
[¶]*Leeds Community Healthcare NHS Trust, Leeds, United Kingdom/ Faculty of Medicine, University of Leeds, United Kingdom*
[‖]*Department of Rehabilitation Sciences, The Hong Kong Polytechnic University, Hung Hom, Hong Kong*
[#]*CIUSSS MCQ CHAUR, Trois-Rivières, Quebec, Canada*
[**]*Family Medicine at the University of Manitoba, Winnipeg, Manitoba, Canada*
[††]*Private Practice, Fort Wayne, Indiana*
[‡‡]*Department of Neurosurgery, Medical College of Wisconsin, Milwaukee, Wisconsin*
[§§]*Private Practice, Halifax, Nova Scotia, Canada*
[¶¶]*NIKKB and Department of Sports Science and Clinical Biomechanics, University of Southern Denmark, Denmark*
[‖‖]*Département Chiropratique, Université du Québec à Trois-Rivières, Quebec, Canada*
[##]*Department of Health and Physical Education, Mount Royal University, Calgary, Canada*
[***]*Département Chiropratique, Université du Québec à Trois-Rivières, Quebec, Canada*
[†††]*Faculty of Kinesiology & Recreation Management, University of Manitoba, Winnipeg, Manitoba, Canada*
[‡‡‡]*Department of Physical Therapy, University of Pittsburgh, Pennsylvania*
[§§§]*Clinical and Translational Science Institute, University of Pittsburgh, Pennsylvania*
[¶¶¶]*Private Practice, Saint Albert, Alberta, Canada*
[‖‖‖]*Private Practice, Winnipeg, Manitoba, Canada*
[###]*Canadian Memorial Chiropractic College, Toronto, Ontario, Canada*

Description: We aimed to develop an evidence-based guideline for the non-surgical management of patients with lumbar spine stenosis causing neurogenic claudication. Using the GRADE approach, the 20-member multidisciplinary guidelines panel based recommendations on evidence from a systematic review of randomized controlled trials and systematic reviews published through June 2019, or expert consensus if not trials could be identified. The literature was monitored up to October 2020. Clinical outcomes evaluated included pain, disability, and walking capacity. This guideline provides updated recommendations from 2 previous guidelines (North American Spine Society, Danish Health Authority) based on the best available evidence. Implementing recommendations issued in this guideline should help clinicians deliver more consistent care and may help improve patient and healthcare system outcomes.

Disclosures: Funding for this guideline was provided by the Canadian Chiropractic Research Foundation. The views of the funding body have not influenced the content of the guideline. A conflict of interest disclosure or declaration form was completed by all participants involved in this guideline. Three conflicts of interest were reported for this study (J. C. is the developer of the Cox Flexion-Distraction table used to treat conditions of the lumbar spine; C.A. and M.J.S. published RCTs on the treatment of LSS); these panel members abstained from voting on related recommendations.

Address reprint requests to André Bussières, DC, PhD, School of Physical and Occupational Therapy, Faculty of Medicine and Health Sciences, McGill University, 3630 Promenade Sir-William-Osler, Hosmer House, Room 205 Montreal, Quebec, Canada H3G 1Y5. E-mail: Andre.bussieres@mcgill.ca, Andre.bussieres@uqtr.ca

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[****]Sunnybrook Health Sciences Centre, Toronto, Ontario
[††††]Health Systems Management, Rush University, Chicago, Illinois
[‡‡‡‡]American Hip Institute, Des Plaines, Illinois

Abstract: **Lumbar spinal stenosis (LSS) causing neurogenic claudication (NC) is increasingly common with an aging population and can be associated with significant symptoms and functional limitations. We developed this guideline to present the evidence and provide clinical recommendations on nonsurgical management of patients with LSS causing NC. Using the GRADE approach, a multidisciplinary guidelines panel based recommendations on evidence from a systematic review of randomized controlled trials and systematic reviews published through June 2019, or expert consensus. The literature monitored up to October 2020. Clinical outcomes evaluated included pain, disability, quality of life, and walking capacity. The target audience for this guideline includes all clinicians, and the target patient population includes adults with LSS (congenital and/or acquired, lateral recess or central canal, with or without low back pain, with or without spondylolisthesis) causing NC. The guidelines panel developed 6 recommendations based on randomized controlled trials and 5 others based on professional consensus, summarized in 3 overarching recommendations: (Grade: statements are all conditional/weak recommendations)** Recommendation 1. ***For patients with LSS causing NC, clinicians and patients may initially select multimodal care nonpharmacological therapies with education, advice and lifestyle changes, behavioral change techniques in conjunction with home exercise, manual therapy, and/or rehabilitation (moderate-quality evidence), traditional acupuncture on a trial basis (very low-quality evidence), and postoperative rehabilitation (supervised program of exercises and/or educational materials encouraging activity) with cognitive-behavioral therapy 12 weeks post-surgery (low-quality evidence).*** Recommendation 2. ***In patients LSS causing NC, clinicians and patients may consider a trial of serotonin–norepinephrine reuptake inhibitors or tricyclic antidepressants. (very low-quality evidence).*** Recommendation 3. ***For patients LSS causing NC, we recommend against the use of the following pharmacological therapies: nonsteroidal anti-inflammatory drugs, methylcobalamin, calcitonin, paracetamol, opioids, muscle relaxants, pregabalin (consensus-based), gabapentin (very low-quality), and epidural steroidal injections (high-quality evidence).***

Perspective: ***This guideline, on the basis of a systematic review of the evidence on the nonsurgical management of lumbar spine stenosis, provides recommendations developed by a multidisciplinary expert panel. Safe and effective non-surgical management of lumbar spine stenosis should be on the basis of a plan of care tailored to the individual and the type of treatment involved, and multimodal care is recommended in most situations.***

Key words: *Practice guideline, lumbar spine stenosis, neurogenic claudication, disease management, nonsurgical treatment, rehabilitation.*

Background

Spinal pain remains the leading cause of global disability.[17] Lumbar spinal stenosis (LSS), a frequent cause of chronic low back and leg pain, is associated with significant disability and functional limitations. The mean prevalence estimates for LSS based on clinical or radiological diagnoses vary between 11% and 38% in the general population (mean age 62, age range 19–93), 15 to 25% in primary care and 29 to 32% in secondary care populations.[61] The prevalence and economic burden associated with LSS are expected to increase dramatically given the aging population.[30,31,123]

Lumbar spinal stenosis (LSS) is commonly a degenerative process causing the narrowing of the central spinal canal, lateral recesses, or intervertebral foramen (or a combination thereof), progressively compressing the neurovascular structures in the spinal canal or foramen. Lumbar spinal stenosis can be classified as acquired or congenital (developmental) or both and may be associated with degenerative spondylolisthesis or scoliosis.[10,69,75] Symptomatic LSS is typically described as neurogenic claudication (NC), characterized by unilateral or bilateral buttock, thigh or calf symptoms (aching, cramping, pain or sensory/balance problems with paresthesia, numbness and weakness) precipitated by prolonged standing or walking and relieved by sitting, lumbar flexion and lying down.[64,122] Low back pain (LBP) may or may not be present with NC.[69] These symptomatic individuals report significant limited walking ability that impacts their capacity to engage in recreational and social activities, all leading to an important emotional impact on their lives.[4,92,96]

Diagnostic decisions require complex judgments that integrate advanced imaging and clinical findings along with knowledge of the patient's clinical course.[4,30] Clinical classification criteria to identify patients with LSS causing NC include age over 60 years, positive 30-second extension test, negative straight leg test, pain in both

legs, and leg pain relieved by sitting, leaning forward or flexing the spine.[44]

Although the natural history of mild to moderate degenerative LSS causing NC tends to be favorable in approximately 60% of patients (ie, improved or unchanged back or leg pain),[69,85,134] with approximately 30% of patients with LSS expected to worsen,[28] this condition remains the most common reason for spinal surgery in patients aged over 65 years.[31] While surgery may rapidly improve pain and disability over nonsurgical treatments in the first 3 months for some patients with LSS causing NC,[40,78] the clinical benefits may not be sustained beyond 4 to 8 years.[58,76]. Reoperation rates at 8-year (18%) [63,78] have been reported. Some studies have demonstrated a larger proportion of adverse events in people undergoing surgical (10−24%) versus nonsurgical (0−3%) care.[78,141] Lumbar spinal stenosis surgery is almost always an elective procedure.[75,76] A referral for special investigations (eg, advanced imaging procedures, neurological and/or vascular investigations) and/or surgical consultation is recommended if the patient presents with severe intermittent claudication (walking $\leq$ 100 meters), new or progressive lower limb weakness,[127] and failure to respond to an appropriate/intensive course of nonsurgical care, as determined by the patient's quality of life and expectations.

The clinical management of LSS causing NC is challenging. The North American Spine Society (NASS) clinical practice guidelines[74] found insufficient evidence to recommend for or against the use of pharmacological or nonpharmacological treatments, while the Danish Health Authority (DHA) guideline[105] recommended against paracetamol, nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, neurogenic pain medication, muscle relaxants or manual therapy to treat these patients. The 2 guidelines currently available need to be updated because their recommendations were informed by evidence published more than 10 (NASS)[74] and 4 (DHA)[105] years ago respectively. Considering the substantial lack of high-quality evidence for the effectiveness of the interventions addressed in these guidelines, new trials are likely to impact the recommendations. Therefore, an updated, evidence-based clinical practice guideline is warranted to inform the nonsurgical management of LSS causing NC.

Methods

Panel Composition

The project lead of the Canadian Chiropractic Guideline Initiative (A.B.) appointed 2 co-chairs (J.O. and G.S.) for the guideline panel and nominated the project executive committee and the remaining guideline panelists. J.O. served as the lead methodologist, and G.S. helped ensure multidisciplinary and geographic representation of the panel and advised on specific duties of panel members, time commitment, and decision-making process for reaching consensus (development of key questions and of recommendations). The multidisciplinary guideline panel included 19 individuals representing chiropractic (K.S., J.M.C., J.A.G., S.P., P.S., J.O.), physiotherapy (C.M.C., F.A.Z), general physician (G.C), acupuncture (S.P., P.S., G.C.), kinesiology (D.H.), orthopedic surgery (A.Y.) neurosurgery (C.-É.C.), clinical epidemiology (C. A., A.-A.M), motor control and learning (S.P.), health services and clinical research (C.T-L, M.J.S.), methodologists (C.C., A.B., C.T-L.), decision maker (G.S.), and consumer representative (D.H.) to ensure that stakeholder and patient values and preferences were considered. The panel also included R.K.J., a member of the Danish Health Authority Clinical Guidelines for surgical and nonsurgical treatment of patients with spinal stenosis (DHA). Three observers nonvoting members, an epidemiologist with expertise in knowledge translation (C. C.) and 2 decision makers (B.G, R.M.) monitored the face-to-face meetings of the guideline panel held in Toronto (February 2018). To ensure wide representation, a general physician (G.C.) and a chiropractor (P.S.), both licensed acupuncturists joined the panel in May 2018. Three panel members (J.C., C.A., M.J.S) reported a conflict of interest through self-declaration. They were not involved in the voting where they were potentially conflicted. Two information specialists (J.B., A.T) contributed to searching, and 5 research assistants (H.Y., L. V., J.J.W., H.M.S., G.C.) were involved in selecting studies and assessing quality.

Scope and Purpose

We used the best available evidence to develop a clinical practice guidelines document for the nonsurgical management of patients with LSS causing NC. Specifically, we developed clinical recommendations based on systematic reviews using the Grades of Recommendation, Assessment, Development (GRADE) approach.[50]

The target population is adults ($\geq$18 years of age) with LSS (acquired, congenital, lateral or central) leading to NC with or without associated spondylolisthesis. Excluded from this guideline are adults presenting with associated radicular symptoms (ie, leg pain secondary to lumbosacral nerve root pathology) not relieved by sitting or lumbar flexion.

The target users of this guideline are primarily rehabilitation clinicians caring for patients with LSS causing NC in primary, secondary and tertiary health care settings (eg, physicians, physiotherapists, chiropractors, occupational therapists, acupuncturists, athletic therapists, massage therapists, nurse practitioners), but also medical specialists (physiatrists, rheumatologists orthopedic surgeons, neurosurgeons), and decision-makers involved with the organization and delivery of health care (eg, third party payers, professional associations, and regulatory boards). The recommendations in this guideline aim to: 1) promote restoration of function; 2) reduce the intensity of symptoms; 3) improve health-related quality of life; 4) prevent or reduce chronic pain and disability; 5) promote active participation of patients in their care; and 6) promote consistent high-quality care for adults with LSS causing NC.

The guideline was developed by the Canadian Chiropractic Guideline Initiative in collaboration with the Bone

and Joint Canada and the International Taskforce on Diagnosis and Management of Lumbar Spinal Stenosis.

Ethics

Because no novel human participant intervention was required, and secondary analyses were considered, this guideline is exempt from institutional ethics review board approval.

Systematic Review of the Evidence

We updated the systematic reviews previously conducted for the NASS evidence-based clinical guidelines for multidisciplinary spine care specific to nonsurgical interventions,[69] and the DHA[105] up to June 2019.

Our guideline panel initially developed 11 standardized key questions in a PICO format (ie, population, intervention, comparator, outcome)[49] on December 02, 2017. Due to the paucity of literature, the guideline panel revisited key questions in February 2018 as follows. Key question 1 on multimodal rehabilitation interventions covers lifestyle changes, behavioral change techniques in conjunction with other rehabilitation methods, manual therapy, exercise and/or rehabilitation, and ancillary nonpharmacological treatments. To better reflect usual care, a question on medication was split into 8 distinct key questions (nonsteroidal anti-inflammatory drugs (NSAID), adjunctive analgesics (methylcobalamin, paracetamol, and calcitonin), antidepressant agents including serotonin–norepinephrine reuptake inhibitors (SNRIs) or tricyclic antidepressants (TCAs), opioid, muscle relaxants, and antiseizure neuropathic medication (pregabalin and gabapentin). Supervised training after surgery (Key question 12) covers presurgical and postsurgical rehabilitation, and postsurgical manual therapy. Key questions 2 on acupuncture, and 10 on Epidural Steroid Injections (ESI) remained unchanged. See Table 1. Standardized key questions.

Inclusion Criteria

- Population: Adults (≥18 years of age) with LSS (acquired, congenital with or without spondylolisthesis, lateral or central) causing NC, verified with relevant spine imaging (anatomical evidence of central canal and/or lateral recess stenosis on MRI and/or CT). Patients' symptoms included NC characterized by radiating leg or buttock pain, numbness, fatigue or loss of sensation in the lower limbs, balance disturbances, diminished walking capacity, limited function and loss of activities of daily living, and worsening of the symptoms by standing and walking and relieved by sitting, lumbar flexion or lying down. 7,75,114. Intervention: Non-surgical interventions including non-pharmaceutical and pharmaceutical treatments alone or in combination, and perisurgical rehabilitation:
  - Non-pharmacological interventions included but were not limited to: self-management (eg, relaxation, information/discussions on pain and stress self-management, body awareness exercise, sedentary and nutritional lifestyle change interventions, coping, problem solving, improving self-efficacy), education/behavioral approaches (eg, cognitive

Table 1. Topics and Key Questions Addressed by the Guideline Development Group

1. For patients with lumbar spinal stenosis, should multimodal rehabilitation interventions[†] versus another treatment be used to decrease pain, and improve function, quality of life, and return to participation?
2. For patients with lumbar spinal stenosis, should acupuncture versus another treatment be used to decrease pain, and improve function, quality of life, and return to participation?
3. In patients who underwent spinal fusion with or without decompression, should supervised training after surgery[⍰] versus another treatment be used to decrease pain, and improve function, quality of life, and return to participation?
4. For patients with lumbar spinal stenosis, should nonsteroidal anti-inflammatory drugs (NSAID)[‡] be used?
5. For patients with lumbar spinal stenosis, should adjunctive analgesics (methylcobalamin, paracetamol)[‡] versus another treatment be used to decrease pain, and improve function, quality of life, and return to participation?
6. For patients with lumbar spinal stenosis, should adjunctive analgesics (calcitonin)[‡] versus another treatment be used to decrease pain, and improve function, quality of life, and return to participation?
7. For patients with lumbar spinal stenosis, should serotonin–norepinephrine reuptake inhibitors (SNRIs) or tricyclic antidepressants (TCAs)[‡] versus another treatment be used to decrease pain, and improve function, quality of life, and return to participation?
8. For patients with lumbar spinal stenosis, should opioid[‡] versus another treatment be used to decrease pain, and improve function, quality of life, and return to participation?
9. For patients with lumbar spinal stenosis, should muscle relaxants[‡] be used to decrease pain, and improve function, quality of life, and return to participation?
10. For patients with lumbar spinal stenosis, should anti-seizure neuropathic medication (pregabalin)[‡] versus another treatment be used to decrease pain, and improve function, quality of life, and return to participation?
11. For patients with lumbar spinal stenosis, should anti-seizure neuropathic medication (gabapentin)[‡] versus another treatment be used to decrease pain, and improve function, quality of life, and return to participation?
12. In patients who underwent spinal fusion with or without decompression, should Epidural Steroid Injections (ESI) versus another treatment be used to decrease pain, and improve function, quality of life, and return to participation?

**The searches encompassed all key questions. Retrieved citations downloaded in EndNote were screened based on the inclusion criteria. Admissible articles were then separate in RYYAN according to proposed key questions.

behavioral approach, motivational interviewing), home and/or supervised exercise, manual therapy (eg, spinal manipulation, mobilization, massage therapy), acupuncture, passive physical modalities (eg, transcutaneous electrical nerve stimulation (TENS), laser, ultrasound, diathermy), back braces or supports (eg, strapping and taping), multimodal rehabilitation intervention (eg, a combination of advice/education, lifestyle changes, exercise therapy, manual therapy), and perioperative rehabilitation (eg, pre or post-surgical supervised exercise programs).
  - Pharmacological interventions included but were not limited to: oral medications such as non-steroidal anti-inflammatory drugs (eg, ibuprofen, celecoxib, diclofenac or misoprostol), adjunctive analgesics (eg, vitamin B12, paracetamol, nasal or intramuscular calcitonin, topical lidocaine), antidepressant agents (eg, SNRIs, TCAs, nortriptyline, duloxetine, sertraline, trazodone or mirtazapine), opioids (eg, morphine, OxyContin, trenodal, codeine), muscle relaxants (eg, cyclobenzaprine), prostaglandins, neuropathic drugs, anticonvulsant - neuropathic medications (eg, gabapentin, pregabalin or lereica), and epidural injections (with or without steroid or anesthetic, or both).

- *Comparison:* control (no or delayed treatment, or sham/placebo eg, light massage, detuned ultrasound), usual care or other non-pharmacological or pharmacological interventions.
- *Outcomes:* Outcomes were categorized according to these follow-up periods: immediate (up to one week), short-term (between 1 week and 3 months), intermediate (between 3 months and 1 year), and long-term (1 year or longer): [6] leg/back pain intensity (eg, visual analog scale, numerical rating scale), walking capacity or performance[27,62] (eg, Zurich Claudication Questionnaire (ZCQ)), disability (eg, Oswestry, Roland Morris Disability, SF-36, PROMIS global health and well-being questionnaires), quality of life (eg, EuroQol 5, SF-36),[25,55,62]. Secondary outcomes were risk of falls, the need for pain medication, and adverse events (Appendix 1).

Study designs: Systematic reviews and meta-analyses; RCTs with an inception cohort of at least 30 participants per treatment arm at baseline with the specified condition, because this sample size is considered the minimum needed for non-normal distributions to approximate the normal distribution;[93] and observational studies (cohort, case-control), nonrandomized controlled trials (NRCTs), controlled before-after (CBA), and before-after (BA) studies.

Exclusion Criteria

- *Population:* Patients with: 1) LSS associated with LBP or radicular symptoms not relieved by sitting or lumbar flexion (usually due to lateral recess stenosis) or worsen with flexion and a positive SLR (usually due to disc herniation); 2) other conditions causing radiating leg pain such as vascular claudication or hip arthrosis; or 3) radiological instability of the spine.
- *Intervention/comparison:* The surgical management of LSS, with the exception of perisurgical rehabilitation.

Search Strategy and Study Selection

To identify articles published since the search performed for the updated NASS guideline[69] (1966-July 2010) and DHA[105] (July 2016 to December 2017) (see Appendix A. NASS[69] and Appendix B. Danish Health Authority (DHA)[32]), an information specialist (J.B.) updated and adapted the search strategies from July 1, 2010 to December 31, 2017 in MEDLINE, ACP Journal Club, Cochrane Database of Systematic reviews (DCSR), Database of Abstracts of Reviews of Effectiveness (DARE), Cochrane Central Register of Controlled Trials, EMBASE, CINAHL, and US and International Trials registries. We used subject headings and key terms related to LSS, nonsurgical interventions, and rehabilitation (Appendix 2. MEDLINE search strategy).

Electronic search results were downloaded into Endnote X9 reference manager software (Clarivate Analytics, Philadelphia, Pennsylvania, USA), and duplicates were removed. Random pairs of reviewers independently screened citations and abstracts based on the eligibility criteria using a standardized screening sheet. They first double screened 15% of the references in order to establish coder reliability. If the Cohen's kappa inter-rater reliability for inclusion or exclusion, as indicated by Cohen's kappa, was satisfactory (> 0.80), the remaining references were split in half and screened by either the first or second coder. If the inter-rater reliability was <0.80 the 2 screeners went through their conflicts and agreed on the criteria before continuing screening. Any disagreements were resolved through discussions and by consulting a third reviewer. If the abstracts did not provide sufficient information to determine inclusion or exclusion, we reviewed the full-text article, using the same process.

Our initial search yielded 7621 articles (Fig 1). Of the 162 records screened for eligibility, 2 admissible RCTs by Kim et al (2016),[66] and Monticone et al (2014)[87], and 3 systematic reviews (SRs) by Ammendolia et al (2013),[6] Enthoven et al (2016),[35] and Liu et al (2015),[74], with relevant RCTs (Friedly et al (2014),[39] Yaksi (2007)[140]) were included in our synthesis. Seven additional studies, including 5 SRs (Podichetty et al (2011)[100] van Tulder, et al (2003),[129] Chou et al (2017),[24] Kuijpers et al (2011),[70] Staiger et al (2003)[117]), and 2 RCTs (Rodrigues et al (2014),[104] Waikakul et al (2000)[132]) were considered in the narrative synthesis when developing consensus-based recommendations. The articles included and

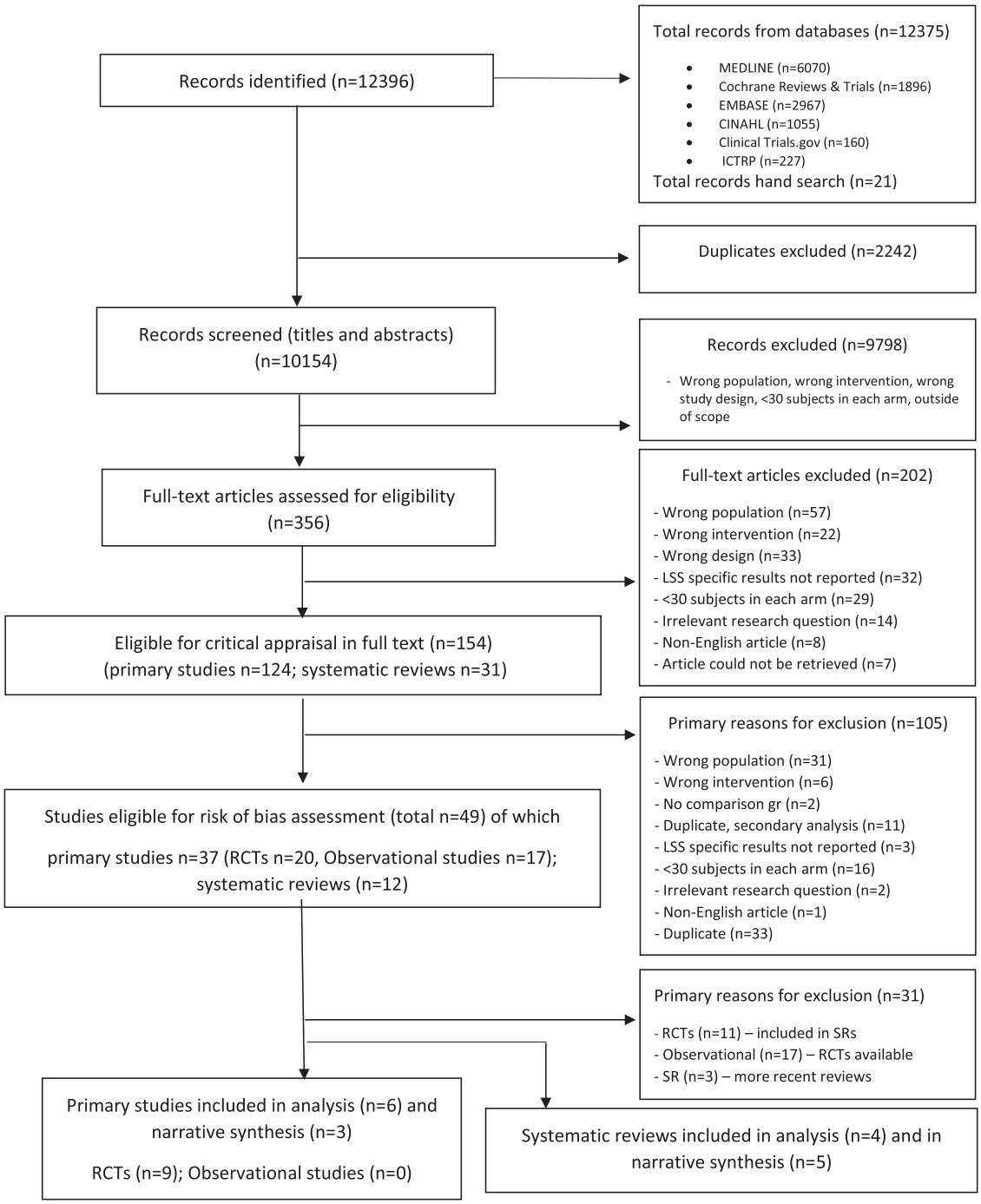

Figure 1. PRISMA flow diagram: conservative treatment for lumbar spinal stenosis
Search strategies updated in MEDLINE, ACP Journal Club, Cochrane Database of Systematic reviews (DCSR), Database of Abstracts of Reviews of Effectiveness (DARE), Cochrane Central Register of Controlled Trials, EMBASE, CINAHL, and US and International Trials registries from 1 July 2010 to 31 December 2017; updated from 1 Jan 2014 to 6 June 2019. The literature was monitored up to October 2020.

excluded after full-text review from this search are listed in Appendix 3.

Our updated search on June 6th, 2019 in MEDLINE and Cochrane Central Register of Controlled Trials (Appendix 2) yielded 4775 articles' (Fig 1). Of the 194 records screened for eligibility, 4 scientifically admissible RCTs by Ammendolia et al (2018), [3] Minetama et al (2019),[86] Oka et al (2018),[94] and Schneider et al (2019),[108] and RCTs from a systematic review by Machado et al (2017)[79] were also included in the synthesis. Coauthors (C.A., J.O., A.B., C.C., K.S.) involved in updating a 2013 Cochrane review on LSS[6] monitored the literature for new RCTs (up to June 2020), leading to the including of an RCT by Qin et al (2020).[103] The articles included and excluded after full-text review from the updated search are listed in Appendix 4.

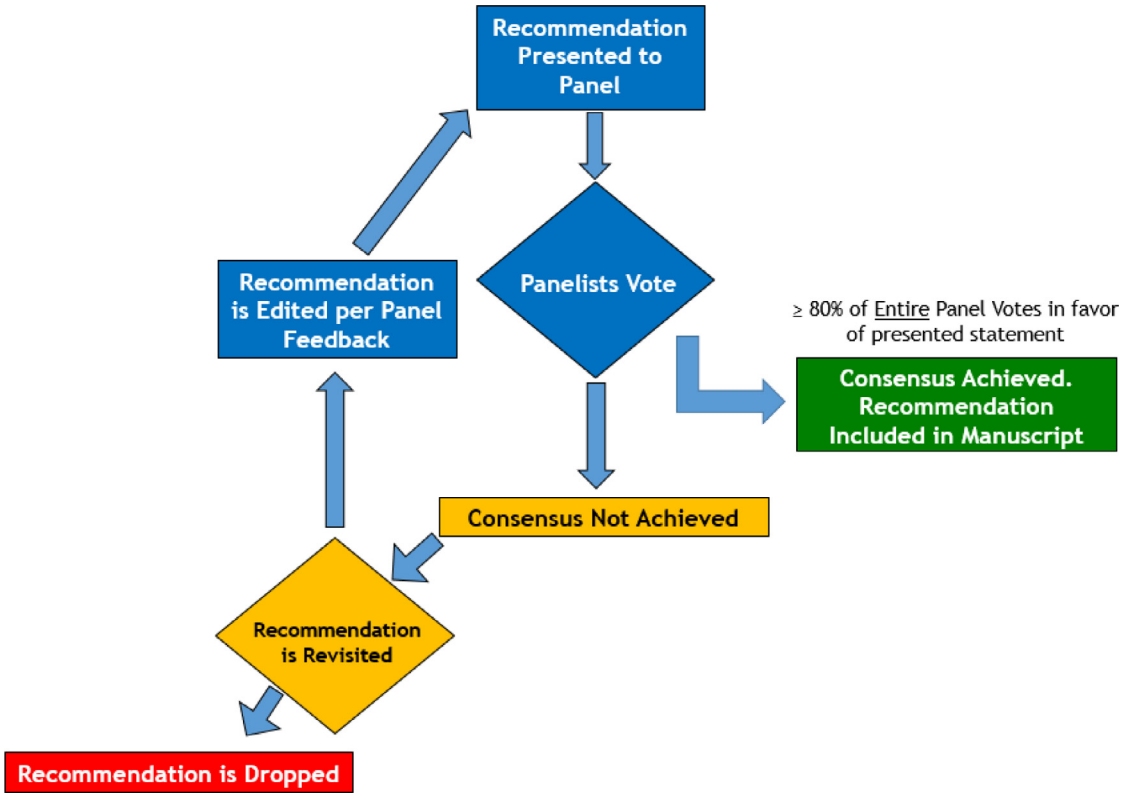

Figure 2. Consensus Development Process
Adapted from Hsu CC, Sandford BA. The Delphi Technique: Making Sense of Consensus. J Advanced Nursing 32:1008-15. 2007.

Risk of Bias Assessment

Eligible studies were critically appraised for quality by 2 independent reviewers reaching consensus, with adjudication by a third reviewer if needed, using A Measurement Tool to Assess Systematic Reviews (AMSTAR II),[113] Cochrane RoB 2 revised tool for assessing RCTs,[119] and Scottish Intercollegiate Network (SIGN) checklists for observational studies.[115] Studies were deemed to have a low risk of bias if 2 independent reviewers judged that selection bias, information bias and confounding likely did not threaten the internal validity of the study. (Appendix 5. Tables 1-2). The risk of bias was incorporated into an evidence profile table of the associated outcomes for corresponding key question. The GRADE approach provides a defined framework for critically appraising the body of evidence for each outcome.[48]

Data Extraction

Data from eligible studies were extracted into a prepiloted standardized form. Study authors were contacted to obtain missing data. The data extraction form included: author, year, country, study design, study population, intervention description and dosage, setting of intervention, comparison group, primary outcomes: leg pain, walking ability (distance, time), disability, quality of life, and secondary outcomes: risk of falls, the need for pain medication, and adverse events. Pairs of reviewers independently extracted data and reached consensus through discussion. A third reviewer was used to resolve disagreements if consensus could not be reached.

Development of Guideline Recommendations

Grading the Evidence and Developing Recommendations

We used the Guideline Development Tool (GDT) (http://www.guidelinedevelopment.org/), and assessed the quality of the body of evidence for our outcomes of interest by applying the GRADE methodological approach.[47] (see definitions in Table 2).

The results section provides the PICO questions along with recommendations, definitions of interventions, supporting evidence, comments and remarks regarding LSS. Evidence profiles were used to summarize the evidence [48] (Appendix 6, Tables 1-6). The quality of evidence rating (high, moderate, low or very low) reflects our confidence in the estimate of the effect to support a recommendation and considers the strengths and limitations of the body of evidence stemming from risk of bias, imprecision, inconsistency, indirectness of results, and publication bias. [48] The evidence profiles serve to describe the grading of each recommendation and the outcomes used to address a key question. The outcome estimates and study used for each key question are described in Appendix 7. Both of these resources provided the supporting evidence gathered for each recommendation.

Using the Evidence to Decisions Framework (EtD),[109] the panel formally met twice (February 2018, Toronto, Canada and May 2018, Montreal, Canada) to consider

Table 2. Significance of the Four Levels of Evidence According to Grades of Recommendation, Assessment, Development, and Evaluation (GRADE)

Quality of evidence	*Definition*
High (⊕⊕⊕⊕)	We are very confident that the true effect lies close to the estimate of the effect.
Moderate (⊕⊕⊕O)	We are moderately confident of the estimated effect: The true effect is likely to be close to the estimate, but there is a possibility that it is substantially different.
Low (⊕⊕OO)	We have limited confidence of estimated effect: The true effect may be substantially different from the estimated effect.
Very low (⊕OOO)	We have very little confidence in the estimated effect: The true effect is likely to be substantially different from the estimate.

Adapted from Balshem H, Helfand M, Schünemann HJ, Oxman AD, Kunz R, Brozek J, Vist GE, Falck-Ytter Y, Meerpohl J, Norris S, Guyatt GH. GRADE guidelines: 3. Rating the quality of evidence. J Clin Epidemiol 64:401-406, 2011.

the balance of desirable and undesirable consequences to determine the strength of each recommendation, using informed judgment on the quality of evidence and effect sizes, resource use, acceptability and feasibility. To make a recommendation, the panel needed to express an average judgment with respect to the balance of desirable (eg, reduced pain and disability, walkability) and undesirable (eg, adverse reactions) consequences of an intervention; confidence in the values and preferences for the target population based on recent qualitative studies;[18,77] and resource implications (costs)[98] as outlined in the EtD.[8] We defined the strength rating of a recommendation (strong, weak/conditional) as the extent to which the desirable consequences of an intervention outweigh its undesirable consequences. A strong recommendation can be made when the desirable consequences *clearly* outweigh the undesirable consequences. In contrast, a conditional or weak recommendation is made when the desirable consequences *likely* outweigh the undesirable consequences.[50,126] If the evidence was not compelling, the decision to write or not write a recommendation was based on consensus of the panel.

In absence of scientific evidence from admissible RCTs, the guideline panel considered available studies (low quality RCTs, observational studies, systematic reviews of small RCTs), before producing consensus-based recommendations. These "good practice" recommendations are based on professional consensus among the multidisciplinary members of the working group. The recommendation may be either for or against the intervention. These types of recommendations are weaker than the evidence-based recommendations irrespective of whether these are strong or weak.

Where available, the panel used randomized clinical trials (RCTs) only to inform recommendations. For questions where no RCT could be identified, the panel considered nonexperimental designs. For PICO questions on pharmaceutical therapy (nonsteroidal anti-inflammatories, adjunctive analgesics, antidepressant agents, opioids, muscle relaxants, neuropathic medications and epidural injections), the panel either: 1) updated the DHA recommendations[105] where new evidence was available; 2) adopted DHA recommendations[105] for which no new evidence existed; or 3) made no recommendation. For patients with LSS causing NC with LBP, the panel relied on indirect evidence from recent guidelines[19,22,88,102] and systematic reviews.[33,80,82,106,138] addressing the management of LBP.

The panel provided recommendations based on the evidence if statistically and clinically significant differences were found. The panel followed a 2-step process in making a recommendation. First, in the absence of standardized cut-off values to determine minimal clinically important differences (MCIDs) when quantifying treatment effectiveness,[133] the panel reached a consensus decision that a 20% within-group change in the outcome of interest in any arm of a study was required to make a recommendation. The decision to use a 20% within-group threshold was informed by current published reports and relevant available MCIDs.[15,23,54,118] However, MCIDs can vary across populations, settings, and conditions and depending on whether within-group or between-group differences are being assessed. Therefore, the panel considered MCID values for the most relevant outcomes.

We reached a consensus decision that the thresholds for MCIDs should reach a between-group difference following treatment of 10 points on 0- to 100-point Visual Analogue Scale (VAS), 1 point on 0- to 10-point Numerical Rating Scale (NRS), 2 points on 0- to 24-point Roland-Morris Disability Questionnaire (RMDQ), 10 points on 0- to 100-points for Oswestry Disability Index (ODI), at least 0.52 for the physical component and 0.48 for symptom variability on the Zurich Claudication Questionnaire (ZCQ), and a difference of at least 0.12 on the EuroQol 5 Dimensions (EQ-5D). Definitions for these outcome measures are provided in the glossary of terms. Finally, the panel agreed to a MCID of 30% between-group difference for walking distance, and a standardized mean difference (SMD)/effect size of 0.2 to 0.5 between groups for any outcomes. These thresholds were informed by the methods in the DHA,[105] and the Agency for Healthcare Research and Quality (AHRQ) Comparative Effectiveness Review (CER).[23]

Secondly, the results from relevant studies were used to formulate a recommendation where appropriate. A detailed summary of evidence for each key question is

available in Appendix 8. A treatment found to be effective was recommended by our panel when we found statistically significant between group differences and clinical significance based on the MCID applied in the study. If a study found 2 or more treatments together to be effective compared to a control based on our threshold, then the panel recommended all effective treatments together.

The EtD frameworks were completed and recommendations were drafted over a series of conference calls with panel members after making judgments about 4 decision domains: quality of evidence (confidence in estimates of effect); balance of desirable (eg, reduced pain and disability) and undesirable outcomes (eg, adverse reactions); confidence about the values and preferences for the target population; and resource implications (costs).[8,9] A synthesis of our judgments about the domains determined the direction (ie, for or against an intervention) and the strength of recommendations (the extent to which one can be confident that the desirable consequences of an intervention outweigh the undesirable consequences and are acceptable and feasible). A specific format was followed to formulate recommendations using patient description and the treatment comparator.[8] Remarks were added for clarification, if needed. If the desirable and undesirable consequences were judged to be evenly balanced and the evidence was not compelling, the panel decided not to write any recommendation.

A modified Delphi technique was used at an in-person meeting to achieve consensus on each recommendation (HYPERLINK "http:// Fig 2).[14,56] Using an online tool (www.polleverywhere.com), panelists voted their level of agreement with each recommendation (including quality of evidence and strength of recommendation) based on the 3-point scale (yes, no, neutral). Before voting, panelists were encouraged to discuss and provide feedback on each recommendation in terms of suggested wording edits or general remarks. To achieve consensus and be included in the final manuscript, each recommendation had to have at least 80% agreement with a response rate of at least 75% of eligible panel members. It was further decided to restrict the Delphi process to 2 rounds, as the previous guidelines[69,105] were already based upon careful reviews of the literature. All recommendations achieved consensus in the first round.

Peer Review

A 9-member external committee composed of stakeholders, expert clinicians, and researchers from Canada, United States, Europe, Asia, and Australasia (Appendix 9) independently reviewed the draft manuscript, recommendations, supporting evidence, applicability and feasibility. The AGREE II instrument (rating scales and open-ended questions) was used to assess the methodological quality of the guideline.[18]

For a list of abbreviations and glossary of terms, please see Appendix 10.

Results

Recommendations on the Nonsurgical Management of Lumbar Spine Stenosis Causing Neurogenic Claudication (GRADE)

Evidence-based and expert consensus recommendations were developed to improve the conservative management and health outcomes (pain, disability, quality of life walking distance) of people with LSS managed in the primary care setting (Tables 3 and 4). For each PICO question, we first assessed any relevant RCTs, and other designs only if no RCTs were available. Thus, recommendations for 6 PICO questions were based primarily on RCTs (Appendix 6, Tables 1-6), while 5 others based on expert consensus, supported by systematic reviews or observational studies or indirect evidence from systematic reviews or RCTs where available.

Discussion

We developed an evidence-based clinical practice guideline to help clinicians deliver effective interventions to individuals with LSS causing NC. Our recommendations, based on the best available evidence, expert opinion, and in consideration of patient values and preferences, intend to assist clinical decision making and promote healthcare system efficiency.

Our recommendations state which interventions should be offered; as well as those that should not be offered because their effectiveness has not been clearly established.

For patients with LSS causing NC, our recommendations are primarily based on low to moderate level evidence or consensus from a multidisciplinary working group. As such, the true treatment effect may differ from the estimated effects, therefore the results should be interpreted with caution.

Summary of Recommendations

Clinicians should work in partnership with patients to develop a patient-centered care plan that considers the patient's values and preferences, discussing with them effective intervention options, as well as risks and benefits of the care plan, and come up with a shared decision. We suggest clinicians consider offering a multimodal rehabilitation intervention consisting of a combination of education, sedentary and nutrition lifestyle modification for patients with limited walking ability and overweight or obese individuals with related comorbidities, behavioral change techniques in conjunction with manual therapy (spinal mobilization, manipulation, massage) of the thoracic and lumbar spine, pelvis, and lower extremities, and individually tailored supervised and home exercise program (stretches and strength training, cycling, and body weight-supported treadmill walking), a trial of acupuncture or antidepressants (SNRIs, TCAs), and, in cases where surgery was performed, postoperative rehabilitation with CBT. On the other hand, we cannot recommend the use of

Table 3. Benefits and Comparative Benefits of Nonpharmacological Therapies

Key question/Intervention	*Recommendation*	*Strength of recommendation*	*Quality of evidence*
PICO 1. For patients with lumbar spinal stenosis, should multimodal rehabilitation interventions versus another treatment be used to decrease pain, and improve function, quality of life, and return to function?			
Multimodal therapy	For patients with LSS and neurogenic claudication with or without LBP, we suggest offering a combination of education and advice, manual therapy and home-based exercise for improvement in walking capacity and symptoms/physical function in the short and long term.	Conditional/Weak	Moderate (⊕⊕⊕O)

Definition: Multimodal rehabilitation interventions may include sedentary and nutrition lifestyle changes, [71,125] behavioral change techniques in conjunction with manual therapy, exercise and/or rehabilitation, and ancillary non-pharmacological treatment.

Included studies: We identified 3 RCTs [3,86,108] in which a comprehensive program, including various combination of self-management strategy, with or without cognitive behavioral approach, patient education and advice to stay active, supervised and home exercises (strengthening, stretching, and conditioning exercises, and stationary cycling), and manual therapy (thrust and non-thrust manipulation, manual spine stretching) was compared to home exercises or to medical care plus exercise (Appendix 6, Table 1).

Primary outcomes: Functional disability (ODI), leg pain (NRS), physical performance scale of the Zurich Claudication Questionnaire (ZCQ) or Swiss Spinal Stenosis (SSS) questionnaire, physical function (SF-36), and walking distance (Self-Paced Walk Test (SPWT))/gait disturbance (Japanese Orthopaedic Association Back Pain Evaluation Questionnaire).

Key results: In one RCT (Ammendolia 2018) [3], the adjusted mean difference (MD) in walking distance in the comprehensive group vs the self-directed group was 304.1 m (95% CI, 77.9 to 530.3) at 3 mo and 421.0 m (95% CI, 181.4 to 660.6) at 6 mo. At 6 mo, 82% of participants in the comprehensive group and 63% in the self-directed group achieved the MCID, (adjusted RR 1.3; 95% CI, 1.0 to 1.7). Both primary treatment effects persisted at 12-mo favoring the comprehensive program. At 6-mo, the comprehensive program showed significantly greater improvements in the ODI walk scale (-0.8; 95% CI, -1.3 to -0.4) and at 12-mo in the ZCQ, SF-36 physical function and bodily pain scores.

In one other RCT (Schneider 2019), [108] manual therapy/individualized exercise had greater, but non-clinically important improvement of symptoms/physical function (Swiss Spinal Stenosis (SSS) questionnaire) at 2 mo, compared to medical care (adjusted mean difference -2.0; 95% CI: -3.6 to -0.4) or group exercise (-2.4; 95% CI: -4.1 to -0.8). Using the >30% responder criterion (secondary responder analyses), manual therapy/exercise had a greater proportion of responders in symptoms/physical function (20%; omnibus $P = .002$) and walking capacity (Self-Paced Walking Test) (65.3%; omnibus $P = .04$) at 2-mo compared to medical care (7.6% and 48.7%) or group exercise (3% and 46.2%). Group exercise also had greater improvement in average daily physical activity (armband accelerometer) at 2 -mo compared to medical care (28.7; 95% CI: 2.7 to 54.7). At 6-mo, there were no between-group differences in mean outcome scores or responder rates.

In the third RCT (Minetama (2019),[86] the supervised physical therapy group showed significant greater improvement at 6 wk vs home exercise in ZCQ symptom severity and physical function (mean difference (MD) −0.4; 95% CI: −0.6 to −0.2), walking distance on the SPWT (MD 455.9 m; 95% CI: 308.5 to -603.2), leg pain (MD −1.4; 95%CI: −2.5 to −0.3), gait disturbance (MD 16.0; 95%CI: 5.4 to -26.7), and physical functioning (MD 9.2; 95%CI: 2.1 to -16.3).

Comment: The panel determined a moderate certainty in the evidence, with minor and transitory undesirable effects and no major adverse events reported.

Remarks: Multimodal rehabilitation intervention was delivered twice weekly over 6 wk. It included individualized instruction on exercise and self-management strategies using a cognitive behavioral approach. At the end of the program, daily home exercise (30 min cycling plus 30 min of structured exercises) and self-care strategies should be maintained.[3,108]

PICO 2. For patients with lumbar spinal stenosis, should acupuncture versus another treatment be used to decrease pain, and improve function, quality of life, and return to function?			
Acupuncture	For patients with LSS and neurogenic claudication with or without LBP, we suggest considering traditional acupuncture on a trial basis to improve pain and physical function in the short-term.	Conditional/Weak	Very low (⊕000)

Definition: Needle acupuncture (eg, Hwato Acupuncture, Suzhou, China; 0.30×40 mm/0.30×75 mm) at various sites (eg, Acupoints of Shenshu (BL23), Dachangshu (BL25), Weizhong (BL40), Chengshan (BL57), and Taixi (KI3)) [103] or outward from the spinous process bilaterally at L2, L4, S2, and S4, middle of the popliteal fossa, inferior recess in the fibular head, lower end of the groove of the inner and outer head of the gastrocnemius).[87]

Included studies: We identified 2 RCTs [87,103] investigating the effect of acupuncture in patients with NC caused by LSS (Appendix 6 Table 2).
Primary outcomes: Physical function (RMDQ) and physical performance (ZCQ)

(*continued on next page*)

Table 3. Continued

Key question/intervention	Recommendation	Strength of recommendation	Quality of evidence
Key results: A RCT by Qin et al (2020) [103] compared acupuncture to noninsertive sham acupuncture for 24 treatments over 8-wk in patients LSS with NC. The acupuncture group showed significant greater improvement in disability at 8 wk (adjusted mean difference (MD) -2.6 [95% CI, -3.7 to -1.4]) and at 3 mo (MD -2.3 [95% CI, -3.9 to -0.7], but not at 6-mo. The acupuncture group also showed greater improvement in leg and buttock pain intensity (NRS) at 8 wk (MD -2.9 [95% CI, (-3.8 to -2.0)], 3 mo MD -2.4 [95% CI, -3.3 to -1.4)] and 6 mo (MD -2.1 [95% CI, -3.0 to -1.2]), and back pain (NRS) at 8 wk (MD -2.3 [95% CI, -3.0 to -1.5]) and 3 mo [95% CI -1.7 (-2.6 to -0.8]).			
A low-quality comparative study by Oka et al (2018) [87] assigned 119 Japanese patients with LSS and L5 radiculopathy (mixed population) to receive either acupuncture (5 sessions in one month), back flexion exercises and an educational manual or pain medication (acetaminophen). Significant reduction in symptom severity was observed in all 3 groups, while improved physical function was found in the acupuncture group only (MD − 2.1, 95% CI − 0.40 to − 0.01). The acupuncture group also demonstrated better physical function compared to exercise group at 1 month (between-group difference in ZCQ least-square mean = 2.17, P = .02).			
Comment: The panel determined a moderate certainty in the evidence, with minor and transitory undesirable effects and no major adverse events reported. The most frequently reported transient minor adverse events were worsening of symptoms, general discomfort, pain at the treated areas, and body ache. [57] The resources required for an acupuncture intervention are relatively small (cost of care and equipment needed), with the exception of training and certification to provide the technique.			
Remarks: There is very low quality evidence from 2 small trials that acupuncture provides marginal short-term improvement in pain and functional recovery for degenerative LSS. Current evidence provides borderline clinically important short-term improvement and is insufficient to suggest long-term benefit.			
PICO 3. In patients who underwent spinal fusion with or without decompression, should supervised training after surgery versus another treatment be used to decrease pain, and improve function, quality of life, and return to function?			
Supervised training after surgery	For patients with LSS and neurogenic claudication, we suggest offering post-operative rehabilitation with CBT to reduce pain and improve function at 1 month and 12 mo postsurgery.	Conditional/Weak	Low (⊕⊕00)
Definition: Post-operative rehabilitation was defined as a supervised program of exercises and/or educational materials encouraging activity 12 wk after surgery. Supervised exercise may include active spinal mobilization, strengthening of spinal deep muscles, stretching of lower limb and low back, functional exercise, walking, and ergonomic advice.			
Included studies: A RCT by Monticone et al (2014) [87] compared individual 60-min sessions twice/wk of cognitive-behavioral therapy (CBT) for 4 wk combined with exercise (90-min session 5 times/wk for 4 wk) to exercise therapy alone in of patients with post-operatively following lumbar fusion due to LSS with NC (Appendix 6, Table 3).			
Outcomes: Functional disability (ODI), back and leg pain intensity (NRS)			
Key results: At 1 month, CBT + exercise had significantly less disability (MD: 11.37 (95% CI, 8.68 to 14.07) and back pain (MD: 1.98 (95% CI, 1.62 to 2.34) compared to exercise alone. At 12 mo, CBT + exercise had significantly less disability (MD: 11.1 (95% CI, 8.72 to 13.81), back pain (MD: 2.77 (95% CI, 2.41 to 3.13), and leg pain (MD: 1.13 (95% CI, 1.03 to 1.65) compared to exercise alone. A small proportion of participants in both groups reported minor transitory pain worsening and mood alterations.			
Comments: The panel determined a low certainty in the evidence, with minor and transitory undesirable effects and no major adverse events reported.			

SSS, Swiss spinal stenosis questionnaire; ZCQ, Zurich claudication questionnaire; SF-36, Short Form 36; NPRS, The Numeric Pain Rating Scale; RMDQ, Roland Morris Disability Questionnaire; ODI, Oswestry Disability Index; CBT, cognitive-behavioral therapy; MD, mean difference; MCID, minimal clinically important difference; RCT, randomized controlled trial; RR, relative risk.
PICO questions, recommendations, definitions of interventions, supporting evidence, comments and remarks regarding LSS.

Table 4. Benefits and Comparative Benefits of Pharmacological Therapies

Key question/Intervention	*Recommendation*	*Strength of recommendation*	*Quality of evidence*
PICO 4. For patients with lumbar spinal stenosis, should nonsteroidal anti-inflammatory drugs (NSAID) be used for patients with lumbar spine stenosis?			
NSAIDs	For patients with LSS and neurogenic claudication with or without LBP, we do not suggest the use of NSAIDs for any duration.	Conditional/Weak	Low (⊕⊕OO)
Definition: Anti-inflammatory drugs in the form of NSAIDs (eg, naproxen 250–500 mg or ibuprofen 400–600 mg 3–4 times or twice daily) with treatment duration from 4 to 12 wk.			
Included studies: We did not identify any RCT investigating the effect of NSAID in patients with NC caused by LSS (Appendix 6, Table 4). Patients with LSS often presents with LBP. The panel considered indirect evidence from 2 systematic reviews (Enthoven et al (2016), [35] Machado et al (2017) [79]) reporting a statistically, but non-clinically significant immediate and short-term benefit favoring NSAIDs compared to placebo in reducing LBP. NSAIDs increased the risk of gastrointestinal adverse effect.[73,74].			
Comment: The panel determined a low certainty in the evidence, with small desirable effects (many of the estimates did not meet MCID), and a moderate risk of undesirable effects reported.			
Remarks: Consider possible drug interactions and potential differences in gastro-intestinal, liver, cardiovascular and renal toxicity, and the person's risk factors, including age. [62,139]			
PICO 5. For patients with lumbar spinal stenosis, should adjunctive analgesics (methylcobalamin, paracetamol) versus another treatment be used to decrease pain, and improve function, quality of life, and return to function?			
Adjunctive Analgesics (Methylcobalamin, Paracetamol)	For patients with LSS and neurogenic claudication with or without LBP, we do not suggest the use of Methylcobalamin or Paracetamol (acetaminophen).	Conditional/weak	Consensus-based
Definition: Pain medication in the form of oral Methylcobalamin/vitamin B12 (0.5 mg, 3 times/d for 6 mo) or paracetamol (max 4 grams daily for 4-12 wk).			
Studies considered: One RCT by Waikakul et al (2000) [132] compared oral Methylcobalamin along with usual care to conventional treatment only (education, activity modification, strengthening exercises for the trunk and abdominal muscles, physical therapy, and NSAIDs, analgesics and muscle relaxant as needed), and another RCT by Rodrigues et al (2014) [104] compared Paracetamol to either oral corticoid (1 mg/kg/d with a 1/3 dose reduction weekly) or placebo for 3 wk.			
Primary outcomes: Walking distance (Meters), pain (VAS), functional disability (RMDQ and 6-min walk test), quality of life (SF-36).			
Key results: No between group difference was observed in those trials.			
Comments: The panel determined a very low certainty in the evidence, with uncertain desirable effects and a risk of undesirable effects. The panel decided to pursue consensus-based recommendation.			
Remarks: Paracetamol cannot be recommended at this time for neurogenic pain. Further, Paracetamol is unlikely to provide clinical benefit for concurrent acute or chronic LBP. Other treatment options should be considered in case of persistent and function-limiting symptoms considering potential adverse effects.			
PICO 6. Should Adjunctive Analgesics (Calcitonin) be Used for Patients with LSS vs other therapies or placebo?			
Adjunctive analgesics (Calcitonin)	For patients with LSS and neurogenic claudication with or without LBP, we do not suggest the use of Calcitonin.	Conditional/Weak	Consensus-based
Definition: Pain medication in the form of nasal salmon calcitonin spray or intramuscular calcitonin (variable doses)			
Studies considered: A review of four small RCTs by Podichetty (2011) [100] found no significant improvement when comparing calcitonin with placebo for pain (VAS) or walking distance. About 5% of patients reported minor transient side effects (nausea and flushing).			
Primary outcomes: Pain (VAS) and walking distance (Meters).			
Comments: Although the panel considered this review, it was eventually excluded from the analysis due to a lack of reported data with unclear pooled estimates. The panel decided to pursue consensus-based recommendation.			
Remarks: Calcitonin releases β-endorphins and can be used as an analgesic agent. The most frequently reported transient minor adverse events were nausea and flushing. Other treatment options should be considered in case of persistent and function-limiting symptoms.			
PICO 7. For patients with lumbar spinal stenosis, should serotonin–norepinephrine reuptake inhibitors (SNRIs) or tricyclic antidepressants (TCAs)‡ versus another treatment be used to decrease pain, and improve function, quality of life, and return to function?			
SNRIs or TCAs	For patients with LSS and neurogenic claudication with or without LBP, we suggest to consider a trial of serotonin–norepinephrine reuptake inhibitors (SNRIs) or tricyclic antidepressants (TCAs).	Conditional/Weak	Consensus-based

(*continued on next page*)

Table 4. Continued

Key question/Intervention	*Recommendation*	*Strength of recommendation*	*Quality of evidence*
Definition: SNRIs and TCA are a class of anti-depressant medication commonly used to treat chronic pain. *Included studies:* No RCT investigated the effect of SNRIs or TCAs in patients with NC. *Studies considered:* The panel considered indirect evidence on the use of SNRIs and TCAs in chronic LBP and neuropathic pain. [59, 65,102,117, 128, 130, 136] *Comment:* The panel pursued a consensus-based recommendation, with moderate risk of adverse events considered. The panel concludes that a trial of SNRI or TCA should be considered in patients with LSS causing NC with LBP. *Remarks:* Consider side effects including, but not limited to, cognitive and physical function, cardiovascular issues and postural instability (eg, falls).			
PICO 8. For patients with lumbar spinal stenosis, should opioid versus another treatment be used to decrease pain, and improve function, quality of life, and return to function?			
Opioids	For patients with LSS and neurogenic claudication with or without LBP, we do not suggest the use of opioids as first line treatment.	Conditional/Weak	Consensus-based
Definition: Opioids (eg, morphine 10 mg 3–4 times/d, oxycodone 5–10 mg twice/d or tramadol 50–100 mg 3–4 times/d in addition to non-opioid pain medication and with a treatment duration from 4 to 12 wk) [105]. *Studies included:* No eligible RCTs investigated the effect of opioids for the treatment of NC caused by LSS. *Studies considered:* The panel considered indirect evidence from opioid therapy guidelines for chronic noncancer pain [19], and consensus-based recommendation from the DHA guideline on managing LSS [105]. Comment: The panel pursued a consensus-based recommendation, with strong risk of adverse events considered. Opioids may only be used for patients who have failed to respond to the aforementioned treatments and only if the potential benefits outweigh the risks for individual patients and after a discussion of known risks and realistic benefits with patients. [19,37] While the potential benefit of opioids for neurogenic claudication due LSS is unknown, there is strong evidence for the potential side effects of opioid use [19,102]. *Remarks:* Should a trial of opioids be considered in selected patients who have persistent, problematic pain despite optimized non-opioid therapy, caution should be used with respect to side effects including, but not limited to cognition, balance, narcotic habituation, overdose and death [19,102].			
PICO 9. For patients with lumbar spinal stenosis, should muscle relaxants be used to decrease pain, and improve function, quality of life, and return to function?			
Muscle relaxants	For patients with LSS and neurogenic claudication with or without LBP, we do not suggest the use of muscle relaxants.	Conditional/Weak	Consensus-based
Definition: Skeletal muscle relaxants (eg, tizanidin 2–4 mg 3–4 times/d, chlorzoxazone 250 mg 3–4 times/d) for 4–12 wk [105]. *Studies included:* No RCTs investigated the use of muscle relaxants in patients with NC caused by LSS. *Studies considered:* Patients with LSS often presents with LBP. The panel considered indirect evidence from systematic reviews (van Tulder, et al (2003),[129] Chou et al (2017),[24] and guidelines [102,105] addressing the management of LBP. For acute LBP, there was moderate to strong evidence that different muscle relaxants performed similarly to each other, and are more effective than placebo for short-term pain relief for patients. However, evidence was insufficient to determine effects on function. For chronic LBP, there was insufficient evidence with inconsistent results and methodological shortcomings to determine the effects of muscle relaxants. Adverse events however were significantly more prevalent in the muscle relaxants group (RR = 1.50; 95% CI, 1.14 to 1.98), and especially the central nervous system (RR = 2.04; 95% CI, 1.23 to 3.37). *Comment:* The panel pursued a consensus-based recommendation, with known undesirable consequences greater than the uncertain desirable effects of muscle relaxants. For patients with LSS causing NC with LBP, the panel determined there was a low certainty of evidence, with existing studies focusing on LBP of various etiologies. Muscle relaxants may provide short-term pain relief for acute and subacute LBP, though adverse events secondary to muscle relaxant use should be considered. *Remarks:* Important to differentiate true muscle relaxants vs psychogenic relaxants. Psychogenic relaxants are more commonly prescribed and may help improve sleep. For patients with claudication type pain, it is important to consider the anti-spasm properties of these agents. Risks of transient adverse events should be considered and patients should be monitored. van Tulder et al (2003),[129] Chou et al (2017),[24]			
PICO 10. For patients with lumbar spinal stenosis, should anti-seizure neuropathic medication (pregabalin) versus another treatment be used to decrease pain, and improve function, quality of life, and return to function?			
Pregabalin	For patients with LSS and neurogenic claudication with or without LBP, we do not suggest the use of pregabalin for short-term reduction in pain and improved function.	Conditional/Weak	Consensus-based

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Table 4. Continued

Key question/Intervention	*Recommendation*	*Strength of recommendation*	*Quality of evidence*

Definition: Medication for neurogenic pain (eg, fixed and flexible doses of Pregabalin between 75 mg/d and 600 mg/d)
Studies considered A non-inferiority RCT by Kim et al (2016) [61] compared limaprost, pregabalin or a combination of limaprost and pregabalin.

Primary outcomes: Functional disability (ODI), leg pain (VAS), walking distance (Meters).

Key results: There was no between-group difference in disability between the pregabalin and limaprost (MD: 3.39 (95% CI, -1.28 to 8.06) at 2 mo. Limaprost did not result in inferior outcomes compared with treatment with pregabalin or pregabalin+limaprost on the ODI. There were no differences in the improvement of leg pain or walking distance among the 3 groups. All groups reported drug-related adverse events. Compared with the limaprost group, the pregabalin, and limaprost+pregabalin groups showed a significantly higher incidence of drug related adverse events.

Comment: The panel pursued a consensus-based recommendation, with uncertain desirable effects and a risk of undesirable effects reported.

Remarks: Despite their widespread use, recent systematic reviews, meta-analysis and guidelines advise against the use of anti-seizure neuropathic medication (eg, pregabalin and gabapentin) due to limited evidence and significant risk of adverse effects without any demonstrated benefit [34,102,111].

PICO 11: For patients with lumbar spinal stenosis, should anti-seizure neuropathic medication (gabapentin)‡ versus another treatment be used to decrease pain, and improve function, quality of life, and return to function?

Gabapentin	For patients with LSS and neurogenic claudication with or without LBP, we do not suggest the use of gabapentin.	Conditional/Weak	Very low ⊕OOO)

Definition: Medication for neurogenic pain (eg, Gabapentin 300 mg 3 times/d, increasing to 900 mg, 3 times/d)

Studies included: One small RCT by Yaksi et al (2007) [140] compared gabapentin to placebo (Appendix 6, Table 5).This trial was identified in 2 systematic reviews (Ammendolia et al 2013, [6] and the Danish National Guideline by Rousing et al (2019) [105].

Primary outcomes: Leg pain (VAS), walking distance (Meters)

Key results: A statistically significant improvement in leg pain and walking distance in favor of gabapentin at 3 and 4 mo follow-up, but the effect size did not reach clinical significance. Patients in both groups were treated with therapeutic exercises, lumbosacral corset with steel bracing, and NSAIDs. This trial reported that some participants randomized to the gabapentin group (no data specified) experienced mild to moderate drowsiness or dizziness, or both.

Comments: The panel determined very low certainty in the evidence. Because of this lack of evidence and moderate risk of side effects the recommendation did not favor gabapentin neurogenic pain medication.

Remarks: Despite their widespread use, recent systematic reviews, meta-analysis and guidelines advise against the use of anti-seizure neuropathic medication (eg, pregabalin and gabapentin) for managing patients with associated due to limited evidence and significant risk of adverse effects without any demonstrated benefit [34,45,102,111].

PICO 12. In patients who underwent spinal fusion with or without decompression, should Epidural Steroid Injections (ESI) versus another treatment be used to decrease pain, and improve function, quality of life, and return to function?

Epidural steroid injections (ESI)	For patients with LSS and neurogenic claudication with or without LBP, we do not suggest the use of epidural steroidal injections for short-term reduction in pain and improved function.	Conditional/Weak	High (⊕⊕⊕⊕)

Definition: Lumbar epidural steroid injections can be performed using 3 approaches: translaminar, caudal, or interlaminar. Injections typically contain a glucocorticoid (eg, triamcinolone (60−120 mg), betamethasone (6−12 mg), dexamethasone (8−10 mg), or methylprednisolone (60 to 120 mg) with or without an anesthetic (eg, 1−3 mL of 0.25% to 1% lidocaine) under fluoroscopic guidance [39].
Studies included: One RCT by Friedly et al (2014) [39] compared 2 injections of either epidural steroid injection (glucosteroid plus lidocaine) or lidocaine alone. This trial was identified in a systematic review and meta-analysis by Liu et al (2015) [74] which included 10 RCTs comprising 1010 patients (mixed population) comparing ESI and local anesthetic (Appendix 6, Table 6).

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Table 4. Continued

KEY QUESTION/INTERVENTION	RECOMMENDATION	STRENGTH OF RECOMMENDATION	QUALITY OF EVIDENCE
Outcomes: Function (RMDQ, walking ability), pain (VAS). *Key results:* Friedly et al (2014) [39] found no short (6 wk) or long-term (up to 12 mo) between-group differences in either function (RMDQ) or pain. Responder analysis revealed that about a third of patients in both arms were RMDQ responders and about half were pain responders (≥30% improvement at 6 wk). Repeated epidural injections of either type did not offer any additional long-term benefit if the injections in the first 6 wk did not improve pain. ESI was not superior to lidocaine alone. In the Liu et al (2015) [74] review, ESIs did not significantly improve pain or function (walking ability) compared with local anesthetic alone. Few adverse events were reported in the trials included in the Liu et al (2015) review. [74] However, a review by Kerezoudis et al (2018) [65] and case reports of complications following interlaminar epidural steroid injections [112] suggest that ESIs can lead to decreased bone mineral density and increased risk for vertebral fracture. *Comment:* The panel determined that there was moderate certainty in the evidence, with unclear desirable effect (some of the estimates did not meet MCID) and small undesirable effects with rare reporting of adverse events. Results differed depending on study design, approach (transforaminal, interlaminar, or caudal), outcome measures, and comparison groups evaluated. Resource, cost, and training requirements to perform epidural steroid injections are not inconsequential and this treatment is not readily available in all areas, particularly in remote or smaller centers. *Remarks:* Epidural steroidal injections may have minor adverse events such as subarachnoid entries, nerve root irritation, or pain and swelling at the site of injection. Patients with more severe structural changes as less likely to respond and may be at higher risks of adverse events.			

SSS, Swiss spinal stenosis questionnaire; ZCQ Zurich claudication questionnaire; SF-36, Short Form 36; NPRS, The Numeric Pain Rating Scale; RMDQ, Roland Morris Disability Questionnaire; ODI, Oswestry disability index; CBT, cognitive-behavioral therapy; MD, mean difference; MCID, minimal clinically important difference; RCT, randomized controlled trial; RR, relative risk.
PICO questions, recommendations, definitions of interventions, supporting evidence, comments and remarks regarding LSS.

NSAIDs, analgesics (methylcobalamin, paracetamol, calcitonin), opioids as a first-line treatment, muscle relaxants, antiseizure neuropathic medication (pregabalin), or epidural steroidal injections.

All recommendations included in this guideline are based on very low to high risk of bias RCTs. Further, the overall quality of evidence ranged from very low to moderate considering other factors suggested by GRADE, such as imprecision and risks of bias, and thus the strength of recommendations is weak at this time. Nonetheless, given that the natural history of mild to moderate degenerative LSS tends to be favorable for about two-third of patients,[69,85,134] the inconclusive evidence about the moderate to long-term effectiveness of surgical interventions for people with LSS causing NC,[5,28,78,105,141] the higher risk of adverse events of surgical compared to nonsurgical interventions,[78,141] and evidence that delaying surgery is not detrimental to surgical outcome,[143] a reasonable trial of multimodal rehabilitation intervention with or without selected medication is warranted for most symptomatic LSS patients prior to recommending more invasive interventions.

Comparisons With Other CPGs and Reviews on the Management of LSS

While our findings agreed with the DHA[105] and NASS[68,69] guidelines regarding the common medications assessed, divergence in opinion with these 2 guidelines[68,69,105] can largely be explained by the use of different eligibility criteria, and the inclusion of recently published evidence on multimodal rehabilitation intervention[3,86,108] and acupuncture[103] upon which we were able to base our recommendations.

First, this guideline included a wider population of adults (≥18 years of age), is restricted to neurogenic claudication, and applies to a specific audience. Neurogenic claudication is due to neuroischemia where the radicular type is due to nerve root inflammation. The differing pathophysiology may require different treatment approaches. Further, only RCTs with an inception cohort of at least 30 participants per arm at baseline were admissible for non-normal distributions to approximate the normal distribution.[93] Importantly, three recent high to moderate quality RCTs[3,86,108] investigated the effectiveness of various combination of multimodal rehabilitation that have informed our guideline recommendations, but were not available when the NASS[68,69] and DHA[105] guidelines were developed.

Second, the NASS guideline[68,69] recommended a limited course of active physical therapy (education and exercise), while the DHA[105] recommended tailored supervised exercise as an option for patients with LSS . This guideline suggests clinicians consider offering a stepped-wise treatment approach with multimodal rehabilitation as first line treatment (and possibly acupuncture), alone or in combination with selected medication after considering potential risks and patient preference and values. Interestingly, the proposed sequential treatment approach parallels

recommendations from recent guidelines on the management of adults with low back pain.[38,102] Using the GRADE approach, the panel determined that the balance of desirable and undesirable outcomes favored multimodal rehabilitation consisting of manual therapy (spinal mobilization, manipulation, massage) of the thoracic and lumbar spine, pelvis, and lower extremities, and individually tailored supervised and home exercise program (stretches and strength training, cycling, and body weight-supported treadmill walking) combined with cognitive-behavioral therapy. All patients in Ammendolia (2018)[3] and Minetama (2019)[86] RCTs were allowed to continue with previously prescribed medications, while those in the trial by Schnieder (2019)[108] were randomly allocated to usual medical care, group exercise or manual therapy/individualized exercise. Results favored "intense" rehabilitation programs of care. A detailed description of the multimodal rehabilitation program is available elsewhere.[2]

Third, the NASS guideline[68,69] found insufficient evidence to support the use of acupuncture while the DHA guideline[105] did not assess this modality. While this guideline suggest acupuncture may be recommended if patients have a preference for or willingness to receive acupuncture, this is based on very low quality evidence from small RCTs showing borderline clinically important short-term improvement and is insufficient to suggest long-term benefit. Whether the results from the trials conducted in Asia would generalize to another or larger LSS population remains to be determined.[2]

Lastly, this guideline recommend against the use of NSAIDs, methylcobalamin, paracetamol, calcitonin, opioids, muscle relaxants, pregabalin, or gabapentin. As patients with LSS often present with LBP, clinicians may want to considered a review of systematic reviews by Wong et al (2016)[137] concluding that oral NSAIDs are more effective than placebo for nonspecific chronic LBP, but not for acute LBP. Guidelines generally advise prescribing oral NSAIDs at the lowest effective dose for the shortest time possible. Any potential benefits should be weighed against the risk of harm.[80] A Cochrane review by Saragiotto et al (2016)[106] concluded that Paracetamol does not produce better outcomes than placebo for people with acute LBP, and it is uncertain if it has any effect on chronic LBP.

Based on consensus, this guideline and the DHA guideline[105] suggest that opioids should only be used for patients with LSS who have failed to respond to the aforementioned treatments, and only if the potential benefits outweigh the risks for individual patients. Shared decision making should include a discussion of known risks and realistic benefits with these patients.[19,33,75,82] The American College of Physician (ACP) guidelines for LBP including radiculopathy recommended against the use of opioids as a first or second line treatment.[102] Based on indirect evidence,[24,129] we recommend against the routine use of skeletal muscle relaxants in patients with LSS considering the risks of transient adverse effects. The DHA[105] state in their guideline "It is good practice to avoid use of muscle relaxants in these patients, since the beneficial effect is uncertain and there is a risk of adverse reactions, including dizziness, fatigue, dry mouth, muscle weakness and gastrointestinal effects, may outweigh the unknown potential benefit of muscle relaxants." The ACP guideline[102] recommended skeletal muscle relaxants as a second line treatment for acute and subacute LBP if pharmacologic therapy is desired.

We also recommended against the use of epidural steroid injections (ESI) for patients with LSS and NC. While ESI was not covered in DHA guideline,[105] the NASS [68,69] guideline recommended interlaminar ESI for short-term (2 weeks to 6 months) symptom relief in patients with NC or radiculopathy. There is, however, conflicting evidence concerning long-term (21−24 months) effectiveness. The difference between our recommendation for ESI and the NASS guideline[68,69] can be explained by the fact that the NASS inclusion criteria allowed for inclusion of studies of patients with lumbosacral radicular pain, in addition to those with LSS and NC.[72] In contrast, our inclusion criteria required that patients in the study were diagnosed specifically with LSS and NC.

Function and Participation

Symptomatic LSS strongly impacts individuals' emotional state, quality of life, and physical function including walking, recreational activities such as sports and exercise, standing, social activities, household activities, managing comorbid health conditions, working, sleeping and lifting.[4,77,96] Thus, health care providers should be prepared to address negative emotional responses to LSS and related misconceptions, and provide advice and education about LSS, including individualized care based on self-management techniques and lifestyle changes.[77] Sedentary and nutrition lifestyle modification for patients with limited walking ability and overweight or obese individuals with related comorbidities may include low-cost wearable accelerometer or pedometer-based physical activity promotion, nutrition education by a dietician, and advice from an exercise physiologist over a 12-week intervention.[71,120,125] In a pilot trial, participants logged on to the e-health Web site to access personal step goals, nutrition education videos, and a discussion board.[125]

Despite the benefits of physical activity for reducing the risk of chronic health conditions, only 32% of clinicians advise older adult patients to begin or continue to do exercise or physical activity during office visits. [12] Clinicians' reluctance to prescribe physical activity to older patients may be attributable to a lack of knowledge regarding appropriate exercise prescription for older adults in light of the potential risks and benefits of various doses and types of exercise.[142] Barriers to exercise participation among older adults include fear of pain or exacerbation of existing pain, low self-efficacy, fear of injury, lack of social support, and social isolation.[29,142] Perhaps as a result, patients with chronic musculoskeletal pain prefer individually tailored information and support when prescribed physical activity. [63] Interventions that combine both behavioral and cognitive behavior change techniques are more effective

than interventions that only use one for older adults.[11] Frameworks and guidelines for exercise prescription in older adults and modification of these guidelines for patients with the most common age-associated comorbidities are available to assist clinicians.[11,142] Pre-exercise screening prior to initiating an exercise program is recommended, along with considerations to modify medications if necessary.

Dissemination and Implementation Plan

While the potential resource implications (specialized staff, cost) of applying the guideline recommendations are considered small, a recent manual by the National Institute for Health and Care Excellence (NICE) can be used to assess the financial change in the use of resources (cost or saving) as a result of implementing this guideline.[89]

Once a decision to disseminate and/or implement this guideline has been made to help improve the management of patients with LSS leading to NC, the following 6 steps of the Knowledge-to-Action framework may be considered: [46]

Adapting knowledge to local context: Clinicians, insurers and policymakers should consider using the ADAPTE framework to adapt this guideline to their needs and jurisdictions.[26] Resource-constrained settings may prefer using alternative approaches described elsewhere.[83]

Assessing barriers/enablers to knowledge use: Uptake of guideline recommendations in clinical practice can be impeded by a wide range of professional (eg lack of time, knowledge, skills, self-capacity, misperceptions about evidence-based CPGs,)[20,51,116] and organizational/environmental barriers (eg leadership, organizational culture, years involved in quality improvement, data infrastructure/information systems, and resources).[52] Stakeholders and researchers may use the recently developed Clinician Guideline Determinants Questionnaire, a validated tool that addresses multiple potential determinants specific to guideline use from a clinician perspective.[41]

Selecting, tailoring, implementing interventions: Knowledge Translation (KT) strategies to increase the likelihood of successful guideline uptake and reduce knowledge-practice gaps should aim to target problem behaviors of care providers,[1,13,95,110] patients,[43,107] and wider health care organizations.[53] Numerous theories, models, and frameworks can be used to inform each step of the KT process (planning/design, dissemination and implementation, evaluation, and sustainability) or across the full KT spectrum (from planning to sustainability).[91,121] The Expert Recommendations for Implementing Change (ERIC) taxonomy propose a systematic approach to specifying active components of implementation strategies when planning small- and large-scale implementation efforts.[99,101] Depending on the specific barriers to uptake and available resources, interventions can range from low cost manually-generated reminders delivered to providers on paper,[97] audit and feedback,[60]and use of local opinion leaders. [37] Ongoing and frequent theory-based implementation interventions are recommended to effectively change clinical practice and improve patient health.[84,26] As with prior guidelines,[21,22] we considered the Guideline Implementation Planning Checklist [42] and available strategies and supporting evidence to increase guideline uptake.[36] To raise awareness, professional organizations are encouraged to inform their members of this new guideline and companion documents for practitioners (Appendix 11) and patients (Appendix 12) easily accessible at: https://www.ccgi-research.com/ and http://boneandjointcanada.com/ to help with "front line" dissemination.

Monitoring the use of the guideline, 5) evaluating its impact, and 6) assessing sustained use: These steps may be done through surveys, chart reviews or electronic health records, and intervention studies to evaluate impact.[60] For instance, the Clinician Guideline Determinants Questionnaire[41] can be used at multiple time points to assess determinants of the use of our new guideline, before and after implementation of an intervention to demonstrate impact on guideline use or following audit showing failure to routinely apply guideline recommendations to plan interventions to sustain guideline use. Identifying indicators of success should be defined a priori (eg, outcomes related to clinician learning and performance, patient outcomes and cost-effectiveness of care).

Research Implications

Future research should aim to identify and validate LSS clinical phenotypes (NC pain symptoms; NC claudication sensory /balance symptoms; NC radicular unilateral leg pain) and associated severity of symptoms/disability (ie, mild, moderate, severe) in relationship to the severity of structural anatomical changes that may more likely be predictive of those patients who may to benefit from conservative versus surgical treatment approaches. Research should also prioritize high quality RCTs testing various combinations of modalities of nonpharmacological (eg, education about self-care, home vs supervised exercise, manual therapy, acupuncture, CBT and other psychological interventions, perioperative rehabilitation) and pharmacological treatments (eg, serotonin −norepinephrine reuptake inhibitors, tricyclic antidepressants) and dosage (duration and intensities) required for optimal benefits for each phenotype, while considering patient preference,[4,16,67,77] and determining the most important (objective) outcomes that are meaningful to patients to gauge treatment success aligned with patients' goals (eg, participating in recreational and social activities).[81] The completion of RCTs comparing best medical management with or without antidepressants (SNRIs or TCAs) in patients with symptomatic LSS is also encouraged. Ongoing trials may provide partial answers.[7,124,135]

Guidelines Update

Methods for updating these guidelines are as reported in our prior guidelines[21] and others.[90,114] The Canadian Chiropractic Guideline Initiative will follow the following process: (1) monitoring changes in

evidence, available interventions, importance and value of outcomes, resources available, and relevance of the recommendations to clinicians (limited systematic literature searches each year for 3-5 years and survey to experts in the field annually); (2) assessing the need to full or partial update (relevance of the new evidence or other changes, type and scope of the update); and (3) communicating the process, resources, and timeline to the Guideline Advisory Committee of the CCGI, who will submit a recommendation to the Guideline Steering Committee to make a decision to update and schedule the process. Further, a recently developed checklist (CheckUp) will be used to improve the reporting of the updated guideline.[131]

Strengths and Limitations

This clinical practice guideline was based on comprehensive literature search and updated the evidence from 2 previous guidelines. We used the GRADE approach providing clear link between recommendations and evidence. This guideline was peer-reviewed by international experts who provided detailed comments prior to release of the final report. Nonetheless, our guideline also has limitations. First, given that we were also interested in pharmacological interventions, we may have missed studies published in Embase related to the effectiveness of pharmacological therapies in individuals with LSS causing NC. Second, we only searched for articles published in English. Third, only 2 databases (MEDLINE and Cochrane Central) were searched in our updated search (January 2014 through June 2019). However, the 3-year search overlap (2014-2017) between the initial and updated search did not uncover any new admissible articles, and 4 coauthors (CA, JO, KS, AB) involved in a parallel Cochrane review using several additional databases identified only 2 additional admissible RCT[86,103] which were incorporated in this guideline. Forth, although the composition of the guideline panel was diverse, with experienced methodologists, expert clinicians and surgeons, stakeholder and patient representatives, a majority of the panel members had clinical training in chiropractic. When updating this guideline, the future panel should include a larger proportion of GPs, rheumatologists, physiatrists, experts in pain and interventional radiology, physiotherapists, occupational therapists, massage therapists, and naturopaths. Expanding the multidisciplinary nature of a future panel will ensure a broader forum for discussion among panelists. Additional efforts should be made to include participants from South America, Asia and Africa. Fifth, patient experiences or expectations were mainly informed by recent qualitative studies.[16,77]; Sixth, the scope of this guideline focused on selected outcomes such as pain, disability and function although included studies assessed additional patient outcomes. In addition, poor descriptions of the interventions evaluated by included studies were common; Seventh, our recommendations were limited by the amount and quality of evidence published in the literature. The low quality of evidence mainly related to the randomization process, and deviations from the intended interventions in RCTs; blinding, incomplete outcome data, and selective outcome reporting in observational studies. Therefore, new high-quality trials are likely to impact the recommendations in future guidelines.[8] Given the limited number of RCTs addressing LSS patients matching our inclusion criteria, studies did not always explicitly fit our inclusion criteria. Any differences in LSS patient population were accounted for in both the wording of the recommendation/remarks, and the full description of the evidence precluding to support the recommendation/remark statement.

Guideline Disclaimer

The evidence-based practice guidelines published by the Canadian Chiropractic Guideline Initiative (CCGI) in collaboration with Bone and Joint Canada include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options. Guidelines are intended to inform clinical decision making, are not prescriptive in nature, and do not replace professional care or advice, which always should be sought for any specific condition. Furthermore, guidelines may not be complete or accurate because new studies that have been published too late in the process of guideline development or after publication are not incorporated into any particular guideline before it is disseminated. CCGI and its working group members, executive committee, and stakeholders (the "CCGI Parties") disclaim all liability for the accuracy or completeness of a guideline and disclaim all warranties, expressed or implied. Guideline users are urged to seek out newer information that might impact the diagnostic and/or treatment recommendations contained within a guideline. The CCGI Parties further disclaim all liability for any damages whatsoever (including, without limitation, direct, indirect, incidental, punitive, or consequential damages) arising out of the use, inability to use, or the results of use of a guideline, any references used in a guideline, or the materials, information, or procedures contained in a guideline, based on any legal theory whatsoever and whether or not there was advice of the possibility of such damages.

Through a comprehensive and systematic literature review, CCGI evidence-based clinical practice guidelines incorporate data from the existing peer-reviewed literature. This literature meets the pre specified inclusion criteria for the clinical research question, which CCGI considers, at the time of publication, to be the best evidence available for general clinical information purposes. This evidence is of varying quality from original studies of varying methodological rigor. CCGI recommends that performance measures for quality improvement, performance-based reimbursement, and public reporting purposes should be based on rigorously developed guideline recommendations.

Contributorship Information

Concept development (provided idea for the research): A.B., G.S., J.O., C.M.C.

Design (planned the methods to generate the results): A.B., G.S., J.O., C.M.C.

Supervision (provided oversight, responsible for organization and implementation, writing of the manuscript): A.B., G.S., J.O.

Data collection/processing (responsible for organization, or reporting data): A.B., F.A.-Z., G.S., J.O.

Analysis/interpretation (responsible for statistical analysis, evaluation, and presentation of the results): A.B., J.O.

Literature search (performed the literature search): A.B., F.A.-Z., A.T-W.

Writing (responsible for writing a substantive part of the manuscript): A.B., C.C., G.S., F.A.-Z., P.D., D.H., C. H., I.P., S.P., J.S., M.S., J.W., J.O., A.Y.

Critical review (revised manuscript for intellectual content, this does not relate to spelling and grammar checking): A.B., C.C., G.S., F.A.-Z., P.D., M.D., D.H., C.H., I.P., S.P., J.S., M.S., J.W., J.O., A.Y.

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Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jpain.2021.03.147.

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