

CADTH RAPID RESPONSE REPORT:
SUMMARY WITH CRITICAL APPRAISAL

Multidisciplinary Treatment Programs for Patients with Acute or Subacute Pain: A Review of Clinical Effectiveness, Cost-Effectiveness, and Guidelines

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Authors: Srabani Banerjee, Charlene Argáez

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Context and Policy Issues

Pain can be categorized as acute or chronic and also sometimes as acute, subacute and chronic pain. Definitions for each of these categories vary, and there is overlap in definitions for “acute” and “subacute” pain. For instance, acute pain is defined as pain that presents for less than three months,¹ pain that lasts from one day to 12 weeks,² or as pain that restricts daily activities and duration of one month or less.³ Subacute pain is defined as pain that presents for less than three months,¹ or as pain duration of one to two months,³ or pain of duration of six to 12 weeks.⁴ Chronic pain is defined as pain that presents for more than three months,^{1,3} or pain that restricts daily activities for longer than 12 weeks.

Chronic pain is a global health problem. In Canada, approximately 25% adults have a chronic pain condition.⁵ The prevalence estimates for chronic pain are likely to vary depending on the sample population surveyed, and the assessment method.⁶ Costs associated with chronic pain include both direct and indirect costs.^{4,5} It is estimated that in Canada the annual direct cost to the health care system is over six billion dollars and the annual indirect cost due to job loss and sick days is over 37 billion dollars.⁵ Chronic pain is a problem for the individual suffering and also a societal burden.⁴

If not appropriately managed, acute and subacute pain may turn into chronic pain. Hence there is increasing recognition of the importance of intervening before symptoms reach the chronic stage.⁴ Interventions for alleviating pain include several options such as pharmacologic agents, and non-pharmacologic treatments related to physical, psychological, and social functioning. There is growing interest in multidisciplinary treatment programs. Multidisciplinary treatment program encompasses medical therapy, behavioral therapy, physical reconditioning and education.⁷ There appear to be some variations in the definitions of multidisciplinary treatment. Multidisciplinary treatment can be defined as including at least three of the following categories: psychotherapy, physiotherapy, relaxation techniques, medical treatment, patient education, or vocational therapy.^{8,9} Multidisciplinary treatment can also entail a physical component (e.g., exercise programs) and at least one other element from psychological, social and occupational dimensions.⁹ These treatments are often delivered by a team of healthcare professionals with different skills.⁴ Multidisciplinary treatment may also be referred to as interdisciplinary treatment, multimodal treatment, or inter-professional treatment.

These multidisciplinary treatment programs may be labor-intensive, time consuming, not easily available, and costly. Hence the evidence regarding multidisciplinary treatment programs would be useful for decision making purposes.

The purpose of this report is to review the clinical effectiveness and cost-effectiveness of multidisciplinary treatment programs for patients with acute or subacute pain in outpatient settings. Additionally, this report aims to review the evidence-based guidelines regarding multidisciplinary treatment programs for patients with acute or subacute pain in outpatient settings.

Research Questions

1. What is the clinical effectiveness of multidisciplinary treatment programs for patients with acute or subacute pain in outpatient settings?
2. What is the cost-effectiveness of multidisciplinary treatment programs for patients with acute or subacute pain in outpatient settings?
3. What are the evidence-based guidelines regarding multidisciplinary treatment programs for patients with acute or subacute pain in outpatient settings?

Key Findings

One systematic review reported that for subacute low back pain, multidisciplinary treatments were generally statistically significantly more effective than usual care, but with respect to other treatments the comparative effectiveness was unclear; the evidence was reported to be of low or very low quality. A second systematic review reported that there was conflicting evidence on the effectiveness of multimodal care for osteoporotic vertebral compression fracture pain in comparison to no treatment or waitlist.

For acute and/or subacute low back pain, three guidelines (two of which were included in a systematic review) suggest that multidisciplinary treatment may be used, however the recommendations were either not graded or what evidence was used to inform the guidelines was unclear. For recent onset neck pain, one guideline suggests that multimodal treatment may be used; however, the recommendation was weak.

Methods

Literature Search Methods

A limited literature search was conducted on key resources including PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No methodological filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2014 and April 8, 2019.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Patients (any age) with acute or subacute pain in outpatient settings
Intervention	Multidisciplinary treatment or multidisciplinary treatment programs for managing acute and subacute pain (may also be called multi-professional, multimodal, interdisciplinary, inter-professional, multidisciplinary primary care teams, lower-back pain program, neck pain program)
Comparator	Q1& Q2: Alternative treatments or programs for pain management, or usual care; no treatment; waitlist; placebo Q3: No comparator necessary
Outcomes	Q1: Clinical benefits and harms (e.g., pain, physical function, social function [including return to school or work], emotional and psychological functioning (e.g., anxiety, depression, sleep), health-related quality of life, opioid use, opioid prescribing practices) Q2: Cost-effectiveness outcomes (e.g., incremental cost per QALY or health benefit gained, health care resource utilization) Q3: Evidence-based guidelines and recommendations
Study Designs	Health technology assessments, systematic reviews/meta-analyses, randomized controlled trials, non-randomized studies, economic evaluations, and evidence-based guidelines

QALY = quality adjusted life year.

Exclusion Criteria

Studies were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published prior to 2014. Studies on acute and chronic pain which did not report results for acute pain separately were excluded. Studies on pain which did not specify acute pain or subacute were excluded, as were studies using multimodal analgesic drugs (i.e. combination of drugs with different mechanisms of action) were excluded. Guidelines with unclear methodology were excluded.

Critical Appraisal of Individual Studies

The included systematic reviews were critically appraised by one reviewer using AMSTAR 2,¹⁰ and evidence-based guidelines were critically assessed using AGREE II.¹¹ Summary scores were not calculated for the included studies, rather, the strengths and limitations of each individual study were described narratively.

Summary of Evidence

Quantity of Research Available

A total of 482 citations were identified in the literature search. Following screening of titles and abstracts, 457 citations were excluded and 25 potentially relevant reports from the electronic search were retrieved for full-text review. Three potentially relevant publications were retrieved from the grey literature search for full-text review. Of these 28 potentially relevant articles, 23 publications were excluded for various reasons, and five publications met the inclusion criteria and were included in this report. These comprised three systematic reviews,^{4,12,13} and two evidence-based guidelines.^{2,3} No relevant randomized controlled trial, non-randomized study, or economic evaluation was identified. Appendix 1 presents the PRISMA¹⁴ flowchart of the study selection.

Summary of Study Characteristics

Study characteristics are summarized and additional details are provided in Appendix 2, Table 2 and Table 3.

Study Design

Of the three included systematic reviews,^{4,12,13} two systematic reviews^{12,13} had a broad focus; hence, only the included primary studies relevant for the current report are discussed here. One systematic review¹² with a broad focus was a review of systematic reviews and included three relevant primary studies (design not specified) published between 2004 and 2010. The second systematic review⁴ included nine randomized controlled trials (RCTs) published between 2006 and 2012. The third systematic review¹³ with a broad focus was a systematic review of guidelines and included two guidelines relevant for this current report.

Two relevant evidence-based guidelines^{2,3} published in 2018 and 2016 were identified. For both guidelines, the guideline development groups were multidisciplinary teams, comprehensive literature searches were conducted to identify evidence, and recommendations were formulated based on consensus using a modified Delphi technique, and graded using the Grading of Recommendation, Assessment, Development and Evaluation (GRADE) approach. Details of the GRADE approach were not reported in the guideline reports, however details of the GRADE approach are available in other publications.^{15,16}

Country of Origin

Of the three included systematic reviews,^{4,12,13} in two systematic reviews^{4,12} published in 2018¹² and 2017,⁴ the first author was from Canada and in one systematic review¹³ published in 2018 the first author was from Brazil. This systematic review¹³ which was a review of guidelines, included two relevant guidelines with one published from Finland in 2011 and one published from Spain in 2012.

Both the included evidence based guidelines^{2,3} were published from Canada.

Population

One systematic review¹² included adults with osteoporotic vertebral compression fracture pain, one systematic review⁴ included adults with subacute back pain, and the systematic review¹³ of guidelines included patients with non-specific low back pain. For two systematic reviews, in the included primary studies the number of patients varied between 20 and 351, the mean ages were greater than 30 years, and the proportions of females ranged from <20% to 99%. In the systematic review¹³ of guidelines there was no mention of age or gender.

One guideline² applies to adults with non-specific low back pain and one guideline³ applies to adults with neck pain-associated disorders and whiplash-associated disorders. Both guidelines are intended for use by health care providers.

Interventions and Comparators

One systematic review¹² compared multimodal care (exercise, manual therapy and education) with no intervention or exercise only, and one systematic review⁴ compared multidisciplinary biopsychosocial rehabilitation with other therapies or usual care. In the

systematic review¹³ of guidelines one of the treatments considered was multidisciplinary treatment.

Both the guidelines^{2,3} provide recommendations for several treatment options of which one is multimodal care. One guideline² provides recommendations for a combination of spinal manipulation therapy and commonly used treatments. These commonly used treatments may include advice on posture and physical activity, and usual medical care. One guideline³ provides recommendations for multimodal manual therapy, which includes manipulation and mobilization, assisted stretching, hot and cold packs, and advice. It also provides recommendations for a multimodal approach comprised of manual therapy, education and exercise.

Outcomes

In both systematic reviews,^{4,12} pain and quality of life were reported. Additionally, in one systematic review,¹² physical function, psychological symptoms, thoracic kyphosis and trunk extension strength were reported. Also, in the second systematic review⁴ disability, sick leave, and return to work were reported. In the systematic review¹³ of guidelines recommendations on multidisciplinary treatment were reported.

Both guidelines^{2,3} present recommendations for multimodal care. Recommendations were graded.

Summary of Critical Appraisal

The critical appraisal of the included studies is summarized below and details are presented in Appendix 3, Table 2 and Table 3.

Overall, the three included systematic reviews^{4,12,13} appeared to be well conducted. In all three systematic reviews the objective was stated, a comprehensive literature search was undertaken, a list of included studies was provided, article selection was done by more than one reviewer, data extraction was done by two reviewers independently or done by one reviewer and checked by a second reviewer, and quality assessment of the studies were conducted. In one systematic review¹² the included studies were reported to be of good quality, and in the second systematic review⁴ the evidence was reported to be of low or very low quality. In the systematic review¹³ of guidelines, the two relevant guidelines satisfied most or all the quality assessment criteria. A list of excluded studies was provided in one systematic review⁴ but not provided in two systematic reviews.^{12,13} Analysis of publication bias was not conducted in any of the systematic reviews, however considering the small number of included studies an analysis does not seem feasible. In two systematic reviews,^{4,13} conflicts of interest were declared and do not appear to be of concern, and in one systematic review¹² conflicts of interest were not presented, hence it is unclear if there could be any issue.

In the two included guidelines^{2,3} the scope and purpose were stated, the guideline development group included individuals from relevant professional groups, patient perspectives were considered, systematic methods were used to search for evidence and develop the guidelines, the recommendations were clear, a process for updating the guidelines was in place, and conflicts of interest were declared and addressed. However, for one guideline² the evidence on which conclusions and recommendations were based was unclear. For both guidelines applicability of the guidelines was presented but details were lacking.

Summary of Findings

Relevant study findings are summarized and details of the main study findings and authors' conclusions are presented in Appendix 4, Table 6 and Table 7.

Clinical Effectiveness

Two systematic review,^{4,12} were identified regarding the clinical effectiveness of multidisciplinary treatment programs for adult patients with acute or subacute pain. Relevant study findings are summarized below and a table of the main study findings and authors' conclusions are presented in Appendix 4, Table 6.

Low back pain

One systematic review⁴ reported that overall, patients with subacute low back pain appeared to do better (in terms of pain intensity, disability, and sick leave) with multidisciplinary biopsychosocial rehabilitation compared with usual care, however the comparative effectiveness of multidisciplinary biopsychosocial rehabilitation and other treatments was unclear. In this systematic review it was mentioned that the evidence was of low or very low quality.

Osteoporotic vertebral compression fracture pain

One systematic review¹² found evidence of conflicting results and reported that there was insufficient evidence on the effectiveness of multimodal care for acute osteoporotic vertebral compression fracture pain.

Cost-Effectiveness

No relevant evidence regarding the cost-effectiveness of multidisciplinary treatment programs for patients with acute or subacute pain was identified; therefore, no summary can be provided.

Guidelines

Two evidence-based guidelines^{2,3} were identified regarding recommendations for multidisciplinary treatment programs for patients with low back pain,² and neck pain-associated disorders and whiplash-associated disorders.³ In addition, a systematic review¹³ of guidelines reported recommendations from two guidelines on multidisciplinary treatment and multidisciplinary rehabilitation for low back pain.

Relevant recommendations are summarized below and related details are presented in Appendix 4, Table 7.

Low back pain

For acute low back pain, one guideline² suggests spinal manipulation therapy, commonly used treatments, or a combination of spinal manipulation therapy and commonly used treatments to decrease pain and disability in the short-term, based on patient preference and practitioner experience. This is a conditional recommendation based on low quality evidence. This guideline concluded that a multimodal approach including spinal manipulation therapy, other commonly used active interventions, self-management advice, and exercise is an effective treatment strategy for acute and chronic back pain, with and without leg pain however, the evidence on which this was based was not clearly reported. The systematic review¹³ of guidelines mentioned that one guideline (from Spain) recommends multidisciplinary rehabilitation for any duration of symptoms of low back pain

and one guideline (from Finland) recommends multidisciplinary treatment for subacute and chronic low back pain.

Neck pain

For recent onset neck pain (grades I to II) one guideline suggests³ a range-of-motion home exercise, medication or multimodal manual therapy for reduction of pain and disability. This is a weak recommendation based on moderate quality evidence.

For recent whiplash-associated disease (grades I to III) one guideline³ suggests multimodal care over education alone. This is a weak recommendation based on moderate quality evidence.

Limitations

Although the systematic reviews were well conducted, the amount of available evidence was limited, in that the number of studies providing information on a particular outcome was small. Furthermore, the comparator interventions were sparsely described.

The included studies in the systematic reviews addressed either back pain, or osteoporotic vertebral compression fracture pain; hence the impact of multidisciplinary treatment on pain associated with other health conditions is unclear.

In most (80%) of the included publications, adults were eligible for inclusion, and in one publication participant age was not specified; hence, the impact of treatment on managing pain in the pediatric population is unclear.

The majority of the included primary studies in the systematic reviews were conducted in Europe, some in the US and one in Canada. Generalizability of the findings to the Canadian setting is unclear. However, since all of these primary studies were conducted in developed countries it is possible that findings may be applicable to the Canadian setting.

No evidence was identified on the cost-effectiveness of multidisciplinary treatment for acute or subacute pain; the impact on health care resources is unclear.

In one guideline though rigorous methods were used, due to a paucity of evidence, the strength of the recommendations was weak.

Conclusions and Implications for Decision or Policy Making

Two systematic reviews^{4,12} were identified regarding the clinical effectiveness of multidisciplinary treatment programs for patients with acute or subacute pain. One systematic review¹³ of evidence-based guidelines and two evidence-based guidelines^{2,3} were identified regarding multidisciplinary treatment programs for patients with acute or subacute pain. No relevant economic studies were identified regarding the cost-effectiveness of multidisciplinary treatment programs for patients with acute or subacute pain.

Based on low quality or very low quality evidence, one systematic review⁴ reported that for subacute low back pain multidisciplinary treatments were generally statistically significantly more effective than usual care but with respect to other treatments the comparative effectiveness was unclear. A second systematic review reported that there was insufficient evidence on the effectiveness of multimodal care for osteoporotic vertebral compression fracture pain.

For acute and/or subacute low back pain, three guidelines² (two of which were included in a systematic review)¹³ suggest that multidisciplinary treatment may be used, however the recommendations are either conditional or not graded. For recent onset neck pain, one guideline³ suggests that multimodal treatment may be used, however this is a weak recommendation. When considering these recommendations, it is important to bear in mind that these recommendations are weak, conditional or not graded.

The findings need to be interpreted in the light of limitations such as there being a limited quantity of evidence and also the evidence being of low quality.

One additional guideline¹⁷ did not specifically report on multidisciplinary treatment programs so did not satisfy the inclusion criteria for the current report. It presented some information that may be useful so is discussed here. According to this guideline:

“Given that most patients with acute or subacute low back pain improve over time regardless of treatment, clinicians and patients should select nonpharmacologic treatment with superficial heat (moderate-quality evidence), massage, acupuncture, or spinal manipulation (low-quality evidence). If pharmacologic treatment is desired, clinicians and patients should select nonsteroidal anti-inflammatory drugs or skeletal muscle relaxants (moderate-quality evidence). (Grade: strong recommendation)” (p521)¹⁷

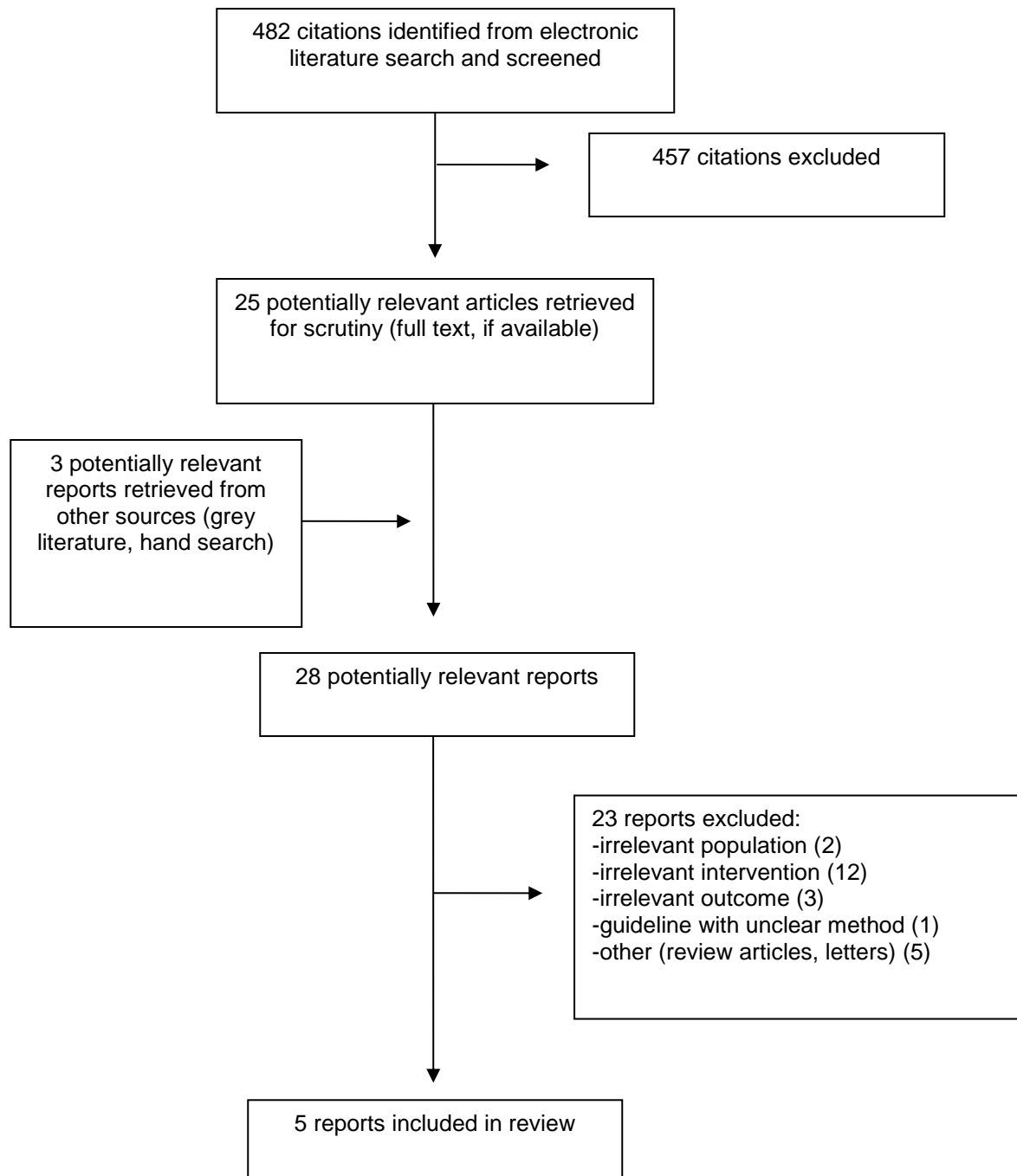
A second guideline¹ was excluded because of unclear methodology. This guideline, however, recommends multidisciplinary treatment programs for occupationally-related subacute low back pain. It reports that for subacute low back pain, intensive multidisciplinary rehabilitation (intervention that includes a physician consultation coordinated with psychological, physical therapy, social, or vocational intervention) is moderately effective. Also, this guideline reported that there was no evidence identified to recommend interdisciplinary rehabilitation for acute low back pain. These recommendations should be considered with caution because the guideline methodology was unclear.

High-quality studies are needed to definitively determine the clinical effectiveness and cost-effectiveness of multidisciplinary treatments compared with other treatment modalities for individuals with acute or subacute pain.

References

1. Toward Optimized Practice. Evidence-informed primary care management of low back pain: clinical practice guideline. Edmonton (AB): Institute of Health Economics, Toward Optimized Practice; 2017: http://www.topalbertadoctors.org/download/1885/LBPguideline.pdf?_20190402160705 Accessed 2019 May 06.
2. Bussi eres A, Stewart G, Al-Zoubi F, et al. Spinal manipulative therapy and other conservative treatments for low back pain: a guideline from the Canadian Chiropractic Guideline Initiative. *J Manipulative Physiol Ther.* 2018 May;41(4):265-293.
3. Bussi eres A, Stewart G, Al-Zoubi F, et al. The treatment of neck pain–associated disorders and whiplash-associated disorders: a clinical practice guideline. *J Manipulative Physiol Ther.* 2016 Oct;39(8):523-564.e527.
4. Marin TJ, Van Eerd D, Irvin E, et al. Multidisciplinary biopsychosocial rehabilitation for subacute low back pain. *Cochrane Database Syst Rev.* 2017;6:CD002193.
5. Fashler S, Cooper L, Oosenbrug E, Burns L, Razavi S, al. e. Systematic review of multidisciplinary chronic pain treatment facilities. *Pain Res Manag.* 2016.
6. Schopflocher D, Taenzer P, Jovey R. The prevalence of chronic pain in Canada. *Pain Res Manag.* 2011;16(6):445-450.
7. Jeffrey M, Butler M, Stark A, Kane R. Multidisciplinary pain programs for chronic noncancer pain. *Effective Health Care Program, Technical Brief (no. 8).* Rockville (MD): Agency for Healthcare Research and Quality; 2011 Sep: https://effectivehealthcare.ahrq.gov/sites/default/files/pdf/pain-chronic_technical-brief.pdf. Accessed 2019 May 06.
8. Scascighini L, Toma V, Dober-Spielmann S, Sprott H. Multidisciplinary treatment for chronic pain: a systematic review of interventions and outcomes. *Rheumatology (Oxford).* 2008 May;47(5):670-678.
9. Scottish Intercollegiate Guidelines Network. Management of chronic pain: a national clinical guideline. *Guideline no. 136.* New Edinburgh (UK): SIGN; 2013 Dec: <https://www.sign.ac.uk/assets/sign136.pdf> Accessed 2019 May 06.
10. Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ.* 2017;358:j4008. <http://www.bmj.com/content/bmj/358/bmj.j4008.full.pdf>. Accessed 2019 May 06.
11. Agree Next Steps Consortium. The AGREE II Instrument. [Hamilton, ON]: AGREE Enterprise; 2017: <https://www.agreetrust.org/wp-content/uploads/2017/12/AGREE-II-Users-Manual-and-23-item-Instrument-2009-Update-2017.pdf>. Accessed 2016 May 06.
12. Ameis A, Randhawa K, Yu H, et al. The Global Spine Care Initiative: a review of reviews and recommendations for the non-invasive management of acute osteoporotic vertebral compression fracture pain in low- and middle-income communities. *Eur Spine J.* 2018;27(Suppl 6):861-869.
13. Oliveira CB, Maher CG, Pinto RZ, et al. Clinical practice guidelines for the management of non-specific low back pain in primary care: an updated overview. *Eur Spine J.* 2018;27(11):2791-2803.
14. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *J Clin Epidemiol.* 2009;62(10):e1-e34.
15. GRADE Handbook: handbook for grading the quality of evidence and the strength of recommendations using the GRADE approach. 2013; <https://gdt.gradepro.org/app/handbook/handbook.html>, 2019 May 06.
16. Table: GRADE strength of recommendations and quality of evidence (1-6). Arlington (VA): Infectious Diseases Society of America; 2008: <https://www.idsociety.org/globalassets/idsa/topics-of-interest/lyme/grade-table-and-reference.pdf> Accessed 2019 May 6.
17. Qaseem A, Wilt TJ, McLean RM, Forcica MA. Noninvasive treatments for acute, subacute, and chronic low back pain: a clinical practice guideline from the American College of Physicians. *Ann Intern Med.* 2017;166(7):514-530.

Appendix 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Table 2: Characteristics of Included Systematic Reviews and Meta-Analyses

First Author, Publication Year, Country	Study Designs and Numbers of Primary Studies Included	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
Ameis, ¹² 2018, Canada	<p>Systematic review of reviews and recommendations. It included two systematic reviews which included three relevant primary studies (study design not specified) published between 2004 and 2010. Of these 3 studies, 2 were from Europe and 1 from the US.</p> <p>(This systematic review had a broad focus and only publications relevant for the current report are considered here)</p> <p>Aim: To develop recommendations for pain management strategies for pain due to OVCF for underserved regions</p>	<p>Adults with acute OVCF pain</p> <p>N = 253 (48 + 20 + 185)</p> <p>Age (years): ≥ 50 (mean ages in years in the primary studies were: 76, ≥ 50, and 80)</p> <p>% Female: 99</p>	<p>Intervention: Multimodal care (exercise + manual therapy + education)</p> <p>Comparator: no intervention (for 2 studies) and exercise (for 1 study)</p>	<p>For the primary studies: Change in pain and physical function; change in thoracic kyphosis, pain and QoL; and change in trunk extension strength and psychological symptoms</p> <p>FU: NR</p>
Oliveira, ¹³ 2018, Brazil	<p>Systematic review of guidelines. It included 2 relevant guidelines published in Finland in 2011 and from Spain in 2012.</p> <p>(This systematic review had a broad focus. It included 15 guidelines published between 2010 and 2017. One guideline from each of the countries: Africa (multinational), Australia, Brazil, Belgium, Canada, Denmark, Finland, Germany, Malaysia, Mexico, the Netherlands, Philippines, Spain, the US, and the UK. Of these, one guideline by Finland and one guideline by Spain were relevant for this current report.)</p>	<p>Patients with non-specific LBP (acute or any symptom duration)</p> <p>N = NA</p> <p>Age: NR</p> <p>% Female: NA</p> <p>(Note: In the 15 guidelines, the population was patients with acute LBP [10 guidelines] or chronic LBP [1 guideline], or LBP regardless of symptom duration [4 guidelines]; two of these guidelines had information relevant for this current report)</p>	<p>Multidisciplinary rehabilitation, multidisciplinary treatment</p>	<p>Recommendations</p>

Table 2: Characteristics of Included Systematic Reviews and Meta-Analyses

First Author, Publication Year, Country	Study Designs and Numbers of Primary Studies Included	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
	<p>Aim: To provide an overview of recommendations regarding the diagnosis and treatment of patients with non-specific LBP.</p> <p>(Additional details are presented in Table 3)</p>			
Marin, ⁴ 2017, Canada	<p>Systematic review included 9 RCTs of which 7 were included in quantitative analyses. The RCTs were published between 2006 and 2012; 5 RCTs were conducted in Europe and 4 RCTs were conducted in North America. Of the 7 RCTs included in the analysis, 4 studies were conducted in Europe, 2 studies in USA, and 1 study in Canada.</p> <p>Aim: To assess the effectiveness of MBR for subacute LBP.</p>	<p>Adults with subacute low back pain (with a mean duration for the current episode greater than 6 weeks and less than 12 weeks)</p> <p>Across the included RCTs:</p> <p>N = 33 to 351</p> <p>Age (mean; years): 32 to 44</p> <p>% Female: 40% to 60% in 7 studies and < 20% in 2 studies.</p> <p>Baseline symptom intensity: <60% on pain and disability scale for 8 RCTs and not categorized for 1 RCT.</p>	<p>MBR vs. other therapies or usual care.</p> <p>Intervention: MBR therapy included a physical component (e.g. pharmacological, physical therapy) in combination with either a psychological, social, or occupational component (or any combination of these) and involved healthcare professionals from at least two different clinical disciplines.</p> <p>Comparator: Usual care or other intervention</p>	<p>Primary outcomes: Pain intensity, disability, sick leave.</p> <p>Secondary outcomes: QoL; psychological and cognitive function (such as depression, fear avoidance)</p> <p>Duration of treatment: 2 to 18 weeks with the exception of one included study for which the duration was 1.25 hour + 75 minutes.</p> <p>FU after randomization: Short term (up to 3 months); Medium term (greater than 3 months and less than 12 months); Long term (12 months or more)</p>

FU = follow-up; LBP = low back pain; MBR = multidisciplinary biopsychosocial rehabilitation; NA = not applicable; NR = not reported; OVCF = osteoporotic vertebral compression fractures; QoL = quality of life; RCT = randomized controlled trial.

Table 3: Characteristics of Included Guidelines

Objective	Intended Users, Target Population	Guideline Development Group	Methodology
Oliveira, ¹³ 2018, Brazil			
<p>To provide an overview of recommendations regarding the diagnosis and treatment of patients with non-specific LBP.</p> <p>(This publication was a systematic review of guidelines and additional details are available in Table 2)</p>	<p>The included guidelines were intended for a multidisciplinary audience in primary care.</p> <p>The target population was patients with non-specific LBP.</p>	<p><u>Guideline from Spain, 2012:</u> The GDG comprised a multidisciplinary working group through a Management Committee comprised of experts in the area of LBP, appointed by the Governments of 14 countries participating in the European Union</p>	<p><u>Guideline from Spain, 2012:</u> Evidence was obtained through literature searches on electronic databases.</p> <p>Quality of the evidence was assessed using the AHCPR guide and “The levels of Evidence” recommended for The Back Group of the Cochrane Collaboration.</p> <p>Consensus was reached via discussion in the working group.</p> <p>The guideline is the Spanish version of the COST B13 European Program. The document is available in English on the website. The guideline provides a care pathway for LBP.</p>
		<p><u>Guideline from Finland, 2011:</u> The GDG included experts in psychiatry, orthopedic surgery, neurosurgery, radiology, general medicine, psychiatry, and physiotherapy</p>	<p><u>Guideline from Finland, 2011:</u> Evidence was obtained through a comprehensive literature search.</p> <p>Strength of evidence was determined using an explicit weighting procedure.</p> <p>Consensus was reached using consensus methods such as group discussion when the evidence was weak or not available.</p> <p>The guideline is published in the national Duodecim journal and is available on the websites</p>
Bussi�eres, ² 2018, Canada			
<p>To provide guidance on the conservative management of non-specific LBP. It addresses the use of SMT alone or in combination with other frequently used conservative therapies.</p>	<p>The guideline is intended for primary care physicians (chiropractors, general, physicians, physiotherapist).</p> <p>The target population is adult patients with acute and chronic back pain, and back-related leg pain LBP.</p>	<p>The GDG comprised clinicians, clinician researchers, lead methodologist, and one patient advocate.</p>	<p>Evidence was obtained through literature searches on electronic databases.</p> <p>Strength of evidence was determined using GRADE.</p> <p>Consensus was reached using a modified Delphi technique.</p> <p>A plan was in place for dissemination and implementation of the guidelines.</p>
Bussi�eres, ³ 2016, Canada			
<p>To provide guidance on the management of</p>	<p>The intended users are chiropractors and other primary care health care</p>	<p>The GDG comprised clinicians, clinician researchers, a lead</p>	<p>Evidence was obtained through literature searches on electronic databases.</p>

Table 3: Characteristics of Included Guidelines

Objective	Intended Users, Target Population	Guideline Development Group	Methodology
neck-pain-associated disorders and whiplash-associated disorders.	<p>providers delivering conservative care, and policy makers.</p> <p>The target population is adult patients with neck-pain-associated disorders and whiplash-associated disorders.</p>	methodologist, one decision maker and one patient advocate.	<p>Strength of evidence was determined using GRADE.</p> <p>Consensus was reached using a modified Delphi technique.</p> <p>A plan was in place for dissemination and implementation of the guidelines.</p>

AHCPR = Agency for Health Care Policy and Research; GDG = guideline development group; GRADE = Grading of Recommendation Assessment, Development and Evaluation; LBP = low back pain; SMT = spinal manipulation therapy.

Appendix 3: Critical Appraisal of Included Publications

Table 4: Strengths and Limitations of Systematic Reviews and Meta-Analyses using AMSTAR 2¹⁰

Strengths	Limitations
Ameis, ¹² 2018, Canada	
<ul style="list-style-type: none"> The objective was clearly stated Multiple databases (MEDLINE, EMBASE, AMED, several guidelines databases) were searched January 1990 to May 2015 Study selection was described and a flow chart was presented A list of included studies was provided Article selection was done independently by two reviewers Quality assessment (risk of bias) was done independently by two reviewers. The relevant included studies were judged to be of good quality Data extraction was conducted by one reviewer and checked by a second reviewer Characteristics of the included studies were presented 	<ul style="list-style-type: none"> A list of excluded studies was not provided Publication bias does not appear to have been examined Meta-analysis was not conducted (not feasible considering the small number and heterogeneity of studies) Conflicts of interest of the authors were not presented
Oliveira, ¹³ 2018, Brazil	
<ul style="list-style-type: none"> The objective was clearly stated Multiple databases (MEDLINE and PEDro, and from National Guideline Clearing house and NICE) were searched between 2008 and 2017. In addition reference lists of relevant reviews and guidelines, and Web of Science citations, were searched and experts in the field were consulted. A list of included studies (guidelines) was provided. Article selection was done independently by two reviewers. Data extraction was done independently by two reviewers. Quality assessment of the included guidelines was conducted. Quality assessment was based on the following criteria: multidisciplinary group committee, systematic literature search, strength of evidence, consensus, direct link of evidence to recommendation, external review, clear recommendation, time of updating, strategies as well as barriers and facilitators for implementation, and additional material for implementation. All of these 10 criteria were addressed in the guideline from Finland, and 80% of these 10 criteria were addressed in the guideline from Spain. Characteristics of the included guidelines were presented but studies providing the evidence were not discussed 	<ul style="list-style-type: none"> Study (i.e., guideline) selection was not described and a flow chart was not presented A list of excluded studies (i.e., guidelines) was not provided Unclear if quality assessment of the studies (i.e., guidelines) was conducted Publication bias does not appear to have been examined Conflicts of interest were declared. Of the eight authors, seven authors had no conflicts of interest relevant to their report, and one author received lecture fees from a pharmaceutical company.
Marin, ⁴ 2017, Canada	
<ul style="list-style-type: none"> The objective was clearly stated Multiple databases (MEDLINE, EMBASE, PsycINFO, Cochrane Central Register of Controlled trials, Clinical trials registry, and others) were searched up to July 2016 Study selection was described and a flow chart was presented 	<ul style="list-style-type: none"> Publication bias was not investigated as there were too few studies to conduct an analysis Conflicts of interest were declared .Seven of the authors had no known conflicts of interest and one author was consultant to AO Spine for an unrelated study Conflicts of interest were declared. Of the eight authors,

Table 4: Strengths and Limitations of Systematic Reviews and Meta-Analyses using AMSTAR 2¹⁰

Strengths	Limitations
<ul style="list-style-type: none"> • A list of included studies was provided • A list of excluded studies was provided • Article selection was done independently by four reviewers • Data extraction and quality assessment were done independently by four reviewers working in pairs. The quality of the included studies was judged to be of low or very low quality. • Characteristics of the included studies were presented • Meta-analysis was conducted when appropriate 	<p>seven authors had no conflicts of interest and one author had association with industry but it was unrelated to the report.</p>

Table 5: Strengths and Limitations of Guidelines using AGREE II¹¹

Item	Guideline	
	Bussi�eres, ² 2018, Canada	Bussi�eres, ³ 2016, Canada
Domain 1: Scope and Purpose		
1. The overall objective(s) of the guideline is (are) specifically described.	yes	yes
2. The health question(s) covered by the guideline is (are) specifically described.	yes	yes
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.	yes	yes
Domain 2: Stakeholder Involvement		
4. The guideline development group includes individuals from all relevant professional groups.	yes	yes
5. The views and preferences of the target population (patients, public, etc.) have been sought.	yes	yes
6. The target users of the guideline are clearly defined.	yes	yes
Domain 3: Rigour of Development		
7. Systematic methods were used to search for evidence.	yes	yes
8. The criteria for selecting the evidence are clearly described.	yes	yes
9. The strengths and limitations of the body of evidence are clearly described.	unclear	yes
10. The methods for formulating the recommendations are clearly described.	yes	yes
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.	unclear	yes
12. There is an explicit link between the recommendations and the supporting evidence.	unclear	yes (however, some discrepancies in the reporting of evidence in different sections of the report)
13. The guideline has been externally reviewed by experts prior to its publication.	yes	yes
14. A procedure for updating the guideline is provided.	yes	yes
Domain 4: Clarity of Presentation		
15. The recommendations are specific and unambiguous.	yes	yes
16. The different options for management of the condition or health issue are clearly presented.	unclear	yes
17. Key recommendations are easily identifiable.	yes	yes
Domain 5: Applicability		
18. The guideline describes facilitators and barriers to its application.	yes, but not in detail	yes, but not in detail

Table 5: Strengths and Limitations of Guidelines using AGREE II¹¹

Item	Guideline	
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	yes, but not in detail	yes, but not in detail
20. The potential resource implications of applying the recommendations have been considered.	yes, but not in detail	yes, but not in detail
21. The guideline presents monitoring and/or auditing criteria.	unclear	unclear
Domain 6: Editorial Independence		
22. The views of the funding body have not influenced the content of the guideline.	no	no
23. Competing interests of guideline development group members have been recorded and addressed.	yes	yes

Appendix 4: Main Study Findings and Authors' Conclusions

Table 6: Summary of Findings Included Systematic Reviews and Meta-Analyses

Main Study Findings		Authors' Conclusion																																								
Ameis, ¹² 2018, Canada																																										
<p>Findings are from 3 primary studies included in 2 systematic reviews</p> <p>One study (multimodal care versus no intervention): Mean change in pain (using NRS 0 to 10) was 1.8 (95% CI, 0.1 to 3.5) on movement and 2.0 (95% CI, 0.2 to 3.9) at rest favoring multimodal care. Mean change in physical function (using QUA-LEF00-41) was 4.8 (95% CI, 0.5 to 9.2) favoring multimodal care.</p> <p>Second study (multimodal care versus waitlist): Greater improvement in thoracic kyphosis with multimodal care ($P = 0.017$) and no difference with respect to QoL or pain</p> <p>Third study (multimodal care versus education): Change in trunk extension strength was 10.68 (95% CI, 6.98 to 14.39) favoring multimodal care. Change in psychological symptoms was -0.03 (95% CI, -0.20 to -0.10) favoring multimodal care.</p>		<p><i>"There is insufficient evidence of effectiveness of multimodal care for acute OVCFs."</i> (p. 5865)</p>																																								
Oliveira, ¹³ 2018, Brazil																																										
<p>Evidence on which the recommendations in the guidelines were based was not presented. Of the 15 guidelines reviewed, two guidelines (one each from Spain and Finland) provided relevant recommendations.</p>		<p>The authors mentioned that one guideline (from Spain) recommends multidisciplinary rehabilitation for any duration of symptoms for LBP and one guideline (from Finland) recommends multidisciplinary treatment for subacute and chronic LBP.</p>																																								
Marin, ⁴ 2017, Canada																																										
<p>Comparison of impact on pain intensity with MBR versus usual care</p> <table border="1"> <thead> <tr> <th>FU term</th> <th>No. of studies</th> <th>No. of patients</th> <th>SMD (95% CI)</th> <th>Heterogeneity I² (%)</th> </tr> </thead> <tbody> <tr> <td>Short</td> <td>4</td> <td>272</td> <td>-0.40 (-0.74 to -0.06) Favors MBR</td> <td>44</td> </tr> <tr> <td>Medium</td> <td>2</td> <td>155</td> <td>-0.34 (-1.00 to 0.31) Difference not significant</td> <td>73</td> </tr> <tr> <td>Long</td> <td>4</td> <td>336</td> <td>-0.46 (-0.70 to -0.21) Favors MBR</td> <td>17</td> </tr> </tbody> </table> <p>Comparison of impact on disability with MBR versus usual care</p> <table border="1"> <thead> <tr> <th>FU term</th> <th>No. of studies</th> <th>No. of patients</th> <th>SMD (95% CI)</th> <th>Heterogeneity I² (%)</th> </tr> </thead> <tbody> <tr> <td>Short</td> <td>4</td> <td>272</td> <td>-0.38 (-0.63 to -0.14) Favors MBR</td> <td>0</td> </tr> <tr> <td>Medium</td> <td>2</td> <td>151</td> <td>-0.44 (-1.09 to 0.22) Difference not significant</td> <td>72</td> </tr> <tr> <td>Long</td> <td>3</td> <td>240</td> <td>-0.44 (-0.87 to -0.01)</td> <td>61</td> </tr> </tbody> </table>		FU term	No. of studies	No. of patients	SMD (95% CI)	Heterogeneity I ² (%)	Short	4	272	-0.40 (-0.74 to -0.06) Favors MBR	44	Medium	2	155	-0.34 (-1.00 to 0.31) Difference not significant	73	Long	4	336	-0.46 (-0.70 to -0.21) Favors MBR	17	FU term	No. of studies	No. of patients	SMD (95% CI)	Heterogeneity I ² (%)	Short	4	272	-0.38 (-0.63 to -0.14) Favors MBR	0	Medium	2	151	-0.44 (-1.09 to 0.22) Difference not significant	72	Long	3	240	-0.44 (-0.87 to -0.01)	61	<p><i>"On average, people with subacute LBP that receive MBR will do better than if they receive usual care, but it is not clear whether they do better than people who receive some other type of treatment. However, the available research provides mainly low to very low low-quality evidence, thus additional high-quality trials are needed before we can make definitive recommendations for clinical practice."</i> (p. 25)</p>
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Table 6: Summary of Findings Included Systematic Reviews and Meta-Analyses

Main Study Findings					Authors' Conclusion
Favors MBR					
Comparison of impact on outcomes in the long-term with MBR versus usual care					
Outcome	No. of studies	No. of patients	Effect size (95% CI)	Heterogeneity I ² (%)	
Return to work	3	170	OR (95% CI): 3.19 (1.46 to 6.98) Favors MBR	0	
Sick leave period	2	210	SMD (95% CI); -0.38 (-0.66 to -0.10) Favors MBR	41	
Comparison of impact on pain intensity with MBR versus other treatments					
FU term	No. of studies	No. of patients	SMD (95% CI)	Heterogeneity I ² (%)	
Short	2	165	-0.09 (-0.50 to 0.33) Difference not significant	44	
Medium	2	162	-0.64 (-1.85 to 0.57) Difference not significant	92	
Long	2	336	-0.14 (-0.36 to 0.07) Difference not significant	0	
Comparison of impact on disability with MBR versus other treatments					
FU term	No. of studies	No. of patients	SMD (95% CI)	Heterogeneity I ² (%)	
Short	2	165	-0.00 (-0.34 to 0.34) Difference not significant	17	
Medium	2	162	-0.49 (-1.50 to 0.51) Difference not significant	89	
Long	2	345	-0.03 (-0.24 to 0.18) Difference not significant	0	
Comparison of impact on sick leave period in the long term with MBR versus other treatments					
No. of studies	No. of patients	SMD (95% CI)	Heterogeneity I ² (%)		
2	158	-0.25 (-0.98 to 0.47) Difference not significant	77		
Quality of Life (QoL)					
<p>One study showed that in terms of QoL (assessed using SF-36), the MBR group showed improvement in physical functioning when compared with usual care group, however there was no between-group difference for mental functioning. A second study showed that MBR was no more effective than usual care in improving QoL at 12 and 24 months. A third study showed that compared to another treatment, MBR was no more effective in reducing fear avoidance or improving physical functioning but was more effective in improving mental health (assessed using SF-36).</p>					

CI = confidence interval; FU = follow up; LBP = low back pain; MBR = multidisciplinary biopsychosocial rehabilitation; OR = odds ratio; OVCF = osteoporotic vertebral compression fractures; QoL = quality of life; SF-36 = 36 item short form survey; SMD = standardized mean difference.

Table 7: Summary of Recommendations in Included Guidelines

Evidence	Strength of Evidence and Recommendations
Bussi�eres,² 2018, Canada	
<p>The authors concluded that a multimodal approach including SMT, other commonly used active interventions, self-management advice, and exercise is an effective treatment strategy for acute and chronic back pain, with or without leg pain, but the evidence on which the conclusion was based was not clearly reported.</p>	<p><i>“Recommendation: For patients with acute (0-3 months) LBP, we suggest SMT, other commonly used treatments, or a combination of SMT and commonly used treatments to decrease pain and disability in the short term, based on patient preference and practitioner experience (low quality of evidence, conditional recommendation).</i></p> <p><i>Remarks. Other commonly used treatments may include advice on posture and physical activity, and usual medical care when deemed beneficial.” (p. 9)</i></p>
Bussi�eres,³ 2016, Canada	
<p>One RCT showed that in adults with acute or subacute neck pain, multimodal care and home exercises and advice were as effective as medication in reducing pain and disability in the short term (26 weeks). However, compared with home exercise, medication was associated with a higher risk for adverse events.</p> <p>One RCT (that included patients with WAD [grades I to III], N = 507) showed that there was greater decrease in disability with multimodal care versus education.</p>	<p><i>“Recommendation: For patients with recent (0-3 months) neck pain grades I to II, we suggest either range-of-motion home exercises, medication, or multimodal manual therapy for reduction in pain and disability. (Weak recommendation, moderate quality evidence)</i></p> <p><i>Remark: Home exercises included education self-care advice, exercises, and instruction on activities of daily living. Medication included NSAIDs, acetaminophen, muscle relaxant, or a combination of these. Multimodal manual therapy included manipulation and mobilization with limited light soft tissue massage, assisted stretching, hot and cold packs, and advice to stay active or modify activity as needed.” (p. 544)</i></p> <p><i>“Recommendation: For adult patients with recent (0-3 months) WAD grades I to III, we suggest multimodal care over education alone. (Weak recommendation, moderate-quality evidence)</i></p> <p><i>Remark: Multimodal care may consist of manual therapy (joint mobilization, other soft tissue techniques), education, and exercises.” (p. 545)</i></p> <p>With respect to the multimodal care versus intramuscular ketorolac for recent NAD (grade I to III), the authors mentioned that overall, the balance between the desirable and undesirable consequences is uncertain and more research is warranted in this area before any recommendation can be made.</p>

FU = follow up; LBP = low back pain; NAD = neck pain associated disease; NSAID = non-steroidal anti-inflammatory drug; RCT = randomized clinical trial; SMT = spinal manipulation therapy; WAD = whiplash associated disease