CADTH

CADTH RAPID RESPONSE REPORT:
SUMMARY WITH CRITICAL APPRAISAL

Mindfulness Training for Chronic Non-malignant Pain Management: A Review of the Clinical Effectiveness, Cost-effectiveness and Guidelines

Service Line:	Rapid Response Service
Version:	1.0
Publication Date:	June 25, 2019
Report Length:	34 Pages

CADTH

Authors: Chantelle C. Lachance and Suzanne McCormack

Cite As: Mindfulness Training for Chronic Non-malignant Pain Management: A Review of the Clinical Effectiveness, Cost-effectiveness and Guidelines. Ottawa: CADTH; 2019 Jun. (CADTH rapid response report: summary with critical appraisal).

ISSN: 1922-8147 (online)

About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

Questions or requests for information about this report can be directed to Requests@CADTH.ca

Abbreviations

AGREE	Appraisal of Guidelines, Research and Evaluation
AMSTAR	A MeaSurement Tool to Assess Systematic Reviews
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CRD	Centre for Reviews and Dissemination
DoD	Department of Defense
GRADE	Grading of Recommendations, Assessment, Development and Evaluation
HIT-6	Headache Impact Test-6
ICD	International Classification of Diseases
MBSR	Mindfulness-based Stress Reduction
MeSH	Medical Subject Headings
MIDAS	Migraine Disability Assessment
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCT	Randomized Controlled Trial
SF-36	36-Item Short Form Survey
VA	Department of Veterans Affairs

Context and Policy Issues

Chronic pain is a pervasive health issue that adversely affects both the patient and society, including loss of productivity, decreased quality of life, and an increased burden on the health care system.[1-4] The International Classification of Diseases (ICD) of the World Health Organization defines chronic pain as persistent or recurrent pain lasting longer than three months.[5] Non-malignant (non-cancer) related types of chronic pain may include low back pain, osteoarthritis, rheumatoid arthritis, headache, neck pain, fibromyalgia, and irritable bowel syndrome.[6] The prevalence of chronic pain is estimated to be 21% among the general Canadian population, a prevalence rate that has increased over time.[2] Chronic pain has substantial economic implications and has been estimated to cost Canada over six billion dollars per year in direct health care costs and 37 billion per year in productivity costs (e.g., job loss, sick days).[1,7,8]

Given the prevalence and burden of chronic pain, a variety of treatment options have been explored to help patients manage their symptoms of pain, including pharmacological approaches (i.e., prescription or non-prescription drugs), physical therapy, exercise, surgery, psychological therapy, and complementary and alternative therapies.[4] In order to decide what treatment is best for the patient, careful consideration should be given to the benefits and risks of the available treatment options.[9] Medications, such as opioids, are commonly prescribed for pain, with approximately three to four percent of the adult population in the United States prescribed long-term opioid therapy.[9,10] However, long-term opioid therapy presents some serious risks, including addiction, accidental overdose, hyperalgesia, and diversion for non-medical use.[10]

Mindfulness training is another potential treatment option for individuals who suffer from chronic pain.[11] Mindfulness is defined as the intentional and non-judgmental conscious awareness of the present moment.[12] A previous CADTH rapid response report that was published in 2012[11] examined the clinical effectiveness and evidence-based guidelines regarding the use of mindfulness training for chronic pain management in adults and found insufficient evidence to draw conclusions about its potential effectiveness. An update is needed to determine if the evidence surrounding mindfulness for chronic pain management is more conclusive to inform future policy decisions.

The aim of this report is to summarize the evidence regarding both the clinical and cost-effectiveness, as well as guidelines for the use of mindfulness training for chronic non-malignant pain management.

Research Questions

1. What is the clinical effectiveness of mindfulness training for chronic non-malignant pain in adults?
2. What is the cost-effectiveness of mindfulness training for chronic non-malignant pain in adults?
3. What are the evidence-based guidelines regarding the use of mindfulness training for chronic non-malignant pain in adults?

Key Findings

Two systematic reviews and three randomized controlled trials (from four publications) were identified that addressed the clinical effectiveness of mindfulness training for chronic non-malignant pain in adults, and the results were inconclusive. One relevant systematic review did not identify any relevant studies. The results from the remaining clinical studies suggested that mindfulness training may be more clinically effective than pharmacotherapy or not significantly different from pharmacotherapy for chronic non-malignant pain, depending on the outcome or population examined. No studies found mindfulness training to be significantly less effective than pharmacotherapy. More research is warranted for definitive conclusions.

No evidence regarding the cost-effectiveness of mindfulness training for chronic non-malignant pain in adults were identified.

Three evidence-based guidelines, including one Canadian guideline, satisfied the inclusion criteria for this report. All guidelines recommend the use of mindfulness training for patients with chronic pain (e.g., chronic non-malignant pain, low back pain, and multi-symptom illness). Two of the included guidelines were informed from evidence of uncertain quality, suggesting caution should be exercised in their interpretation.

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including Medline, Cumulative Index to Nursing and Allied Health Literature (CINAHL), PsycINFO, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused Internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were mindfulness and adults with chronic pain. No filters were applied to limit the retrieval by study type. The search was also limited to English language documents published between January 1, 2014 and May 28, 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	Adults with chronic non-malignant pain
Intervention	Mindfulness training (with or without pharmacotherapy)
Comparator	Q1-2: Pharmacotherapy alone (e.g., opioids, nonsteroidal anti-inflammatory drugs, acetaminophen) Q3: No comparator
Outcomes	Q1: Clinical effectiveness (e.g., pain management, reduction in pain medication use, return to work, quality of life, functioning) Q2: Cost-effectiveness (e.g., incremental cost per quality adjusted life year or health benefit) Q3: Guidelines and recommendations
Study Designs	Q1: Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials Q2: Economic evaluations Q3: Evidence-based guidelines

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published prior to 2014. Systematic reviews and clinical studies were excluded if the comparator was described as usual care or similar (e.g., treatment as usual, standard of care, waitlist control) if no context was provided regarding what usual care involved (e.g., pharmacotherapy, physical therapy, cognitive behavioural therapy). Guidelines with unclear methodology were also excluded.

Critical Appraisal of Individual Studies

The included systematic reviews were critically appraised by one reviewer using A MeaSurement Tool to Assess systematic Reviews (AMSTAR) II,[13] randomized controlled trials (RCTs) were critically appraised using Downs and Black checklist,[14] and guidelines were assessed with the Appraisal of Guidelines, Research and Evaluation (AGREE) II[15] instrument. Summary scores were not calculated for the included studies; rather, a review of the strengths and limitations of each included study were described narratively.

Summary of Evidence

Quantity of Research Available

A total of 666 citations were identified in the literature search. Following screening of titles and abstracts, 599 citations were excluded and 67 potentially relevant reports from the electronic search were retrieved for full-text review. Eight potentially relevant publications were retrieved from the grey literature search for full-text review. Of these 75 potentially relevant articles, 66 publications were excluded for various reasons, and nine publications met the inclusion criteria and were included in this report. These comprised two systematic reviews, three RCTs from four publications, and three evidence-based guidelines. Appendix 1 presents the Preferred Reporting Items for Systematic Reviews and Meta-Analyses

(PRISMA)[16] flowchart of the study selection. Additional references of potential interest are provided in Appendix 5.

Summary of Study Characteristics

Study Design

Two systematic reviews,[17,18] four publications describing three RCTs,[19-22] and three guidelines were identified.[23-25]

One of the included systematic reviews,[17] published in 2018, did not identify any relevant studies that considered the comparator of interest for this report (i.e., pharmacology). This review searched three academic databases, reference lists, and ClinicalTrials.gov for RCTs published through November 2017. The second of the included systematic reviews,[18] published in 2017, identified one relevant study for this report. The review searched four academic databases for literature through June 2016 as well as reference lists of prior systematic reviews.[18] Both reviews limited their eligibility criteria to RCTs.[17,18]

Results from three RCTs were reported in four included publications;[19-22] two of the included publications reported on the same RCT but examined different outcomes of interest.[20,21]

The three included guidelines were commissioned by two different organizations: The National Pain Center[23] and the Department of Veterans Affairs/Department of Defense (VA/DoD).[24,25] The 2017 Canadian Guideline for Opioids for Chronic Non-Cancer Pain conducted by the National Pain Center focused on providing guidance on the use of opioids, as well as other interventions (pharmacological and non-pharmacological), to manage chronic non-malignant pain for adults who are 18 years of age or older.[23] This guideline was an update to the previous 2010 guideline and the updated guideline was externally peer-reviewed.[23] The included recommendations relevant to this report were based on low to moderate quality evidence.[23] The 2017 VA/DoD guideline focused on improving patients' health and wellbeing by providing evidence-based guidance to providers who are diagnosing or treating adult patients with low back pain.[25] This guideline was an update to a previous 2007 guideline and the updated guideline was externally peer-reviewed. Relevant to this report, the guidelines included weak recommendations derived from unclear quality of evidence (i.e., quality of evidence not reported) in favour of the recommendation, classified in the guideline as "new-replaced" (i.e., the recommendation from the previous guideline was carried over to the updated guideline and modified following review of the evidence).[25] The 2014 VA/DoD guideline focused on providing guidance for primary care clinicians with a framework by which to evaluate the individual needs and preferences of patients who may be experiencing chronic multi-symptom illness or medically unexplained symptoms, leading to improved clinical outcomes.[24] This guideline was an update to a previous 2001 guideline, but it was unclear whether the updated guideline was externally peer-reviewed. Relevant to this report, the guidelines included weak recommendations based on unclear quality of evidence (i.e., quality not reported) in favour of the recommendation , classified in the guideline as "new-replaced" (as defined above).[24] All three included guidelines used the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach to assess the quality of the evidence.[23,25]

Country of Origin

The body of evidence originated from Canada (one guideline[23]), Iran (three publications describing two RCTs[19-21]), and the United States (two systematic reviews,[17,18] one RCT,[22] two guidelines[24,25]).

Patient Population

The 2018 systematic review considered studies that included patients with chronic pain conditions (i.e., chronic low back pain; chronic neck pain; osteoarthritis of the knee, hip, or hand; fibromyalgia; and tension headache).[17] This review, however, did not retrieve any relevant studies for the current report.[17] The 2017 systematic review included RCTs with adult patients with chronic pain for a minimum of three months.[18]

All of the primary studies examined adult patients with migraine and/or chronic tension-type headaches,[19-22] with two publications reporting on the same RCT.[20,21]

The target population of the 2017 National Pain Center guideline is patients with chronic non-malignant pain.[23] The intended users of the guideline are prescribers of opioids for the management of chronic non-malignant pain and those who create policy regarding this issue (e.g., primary care physicians, specialists who manage patients with chronic non-malignant pain, nurse practitioners, and regulatory agencies and other policy makers). The secondary audience of this guideline includes patients living with chronic non-malignant pain, pharmacists, and other health care professionals who manage patients with chronic non-malignant pain.[23] For the 2017 VA/DoD guideline, the target population is patients with chronic low back pain.[25] The intended users of the guideline are health care providers who manage patients with low back pain, including chronic low back pain conditions.[25] The target population for the 2014 VA/DoD guideline is patients with multi-symptom illness (e.g., migraine and tension headaches, non-cardiac chest pain, irritable bowel syndrome, and a variety of chronic pain conditions), with a focus on patients who are eligible for care in the Veterans Health Administration or the Department of Defense health care delivery system.[24] The intended users of this guideline are primary care providers who treat and manage adult patients with chronic multi-symptom illness.[24]

Interventions and Comparators

Pertinent to this report, the 2018 systematic review[17] included mindfulness practices as the intervention and pharmacotherapy as the comparator. Relevant to this report, the 2017 systematic review[18] included mindfulness-based stress reduction (MBSR) plus pharmacotherapy (i.e., over the counter and prescribed medications) as the intervention and pharmacotherapy alone as the comparator.

The three RCTs, reported in four included publications, comprised an eight-week MBSR intervention,[19-22] with two RCTs allowing for participants in the intervention group to receive usual pharmacotherapy (specific and non-specific drugs,[19] prophylactic and abortive medications[22]) in addition to the MBSR. The comparator for all RCTs was usual pharmacotherapy.[19-22] Details on the specific type, duration, dose, and frequency of pharmacotherapy were not provided for any RCT.[19-22]

Relevant to this report, all included guidelines[23-25] examined MBSR as a potential treatment for individuals who were living with chronic pain (i.e., chronic non-malignant pain, low back pain, multi-symptom illness).

Outcomes

For the systematic reviews, the outcomes of interest were function[17] and pain.[17,18] The RCTs investigated the following clinical outcomes: pain,[19] pain severity,[21] migraine/headache frequency,[22] headache severity,[22] headache duration,[22] disability (e.g., Headache Impact Test-6 or HIT-6, Migraine Disability Assessment or MIDAS),[22] quality of life (e.g., Migraine-Specific Quality of Life),[19,22] perceived stress (e.g., Perceived Stress Scale),[20,22] general mental health,[20] anxiety/depression (e.g., Patient Health Questionnaire - depression module, State Trait Anxiety Inventory),[22] mindful awareness (e.g., Five Factor Mindfulness Scale),[21,22] and headache management self-efficacy.[22] Relevant outcomes from the guidelines included pain,[23-25] function,[23,25] symptom severity,[24] and quality of life.[24,25] The minimal clinically important difference was not defined for relevant outcomes of interest with the exception of one disability outcome, HIT-6, where the authors indicated "a change of 2.3 points on HIT-6 reflects the minimum important difference that reflects meaningful clinical change" (p. 1490).[22] A detailed summary of the characteristics of included publications are provided in Appendix 2.

Summary of Critical Appraisal

Additional details regarding the strengths and limitations of included publications are provided in Appendix 3.

Systematic Reviews

Both systematic reviews used strong methodology and met the majority[18] or all[17] of the AMSTAR II checklist[13] criteria. Common strengths of the reviews include a published predefined protocol, a clear description of research questions and eligibility criteria, and systematic searches to retrieve literature performed using multiple methods (e.g., academic databases, clinical trial registries).[17,18] For transparency, the authors provided their full search strategies in the protocols and/or appendices.[17,18] In both reviews, data selection and extraction were conducted independently and in duplicate, reasons for exclusion were provided, included studies were described in adequate detail, the strength of evidence was graded for each included study, and funding sources and any potential or actual conflicts of interest were disclosed.[17,18] These strengths increase the reproducibility of the findings. The 2018 systematic review also provided a list of excluded studies in the appendix;[17] however, the 2017 review did not.[18] The 2017 review also did not justify why the review was limited to RCTs and no other study designs.[18]

Randomized Controlled Trials

The quality of evidence associated with the included RCTs was assessed using the Downs and Black Checklist.[14] Overall, the quality of the included RCTs was variable.[19-22] For all RCTs, objectives and outcomes of interest were adequately described, group assignments were randomly allocated, the number of patients included and basic characteristics of study participants were described, results were adequately reported with actual probability values (*P* values), and funding sources were disclosed when applicable.[19-22] In addition, the authors of the included studies described sample size calculations[20-22] with the exception of one RCT.[19] The investigators of one RCT prospectively registered the trial, attempted to blind patients, and also blinded the individuals who performed the data analyses;[22] the investigators of the three other publications, reporting on two RCTs, did not mention registering their trial protocol nor did they mention using blinding strategies.[19-21] For all included RCTs, more detail about the medication type, dose, and frequency used by participants in the comparator group,[19-22] and in some cases the intervention group,[19,22] was

needed to aid in interpreting the findings. Finally, it was unclear whether included participants were representative of the source population or if the staff, places, and facilities where the patients were treated were representative of the treatment most patients receive.[19-22]

Evidence-Based Guidelines

Strengths and weaknesses of the included evidence-based guidelines[23-25] were assessed using the AGREE II instrument.[15] Overall, the included guidelines met most of the AGREE II criteria. Common strengths of the guidelines included: the overall objectives and populations to whom the guidelines apply were specifically described; guideline development groups included individuals from relevant professional groups; the target users of the guidelines were defined; systematic methods were used to search for evidence; the criteria for selecting the evidence, the strengths and limitations of the body of evidence, and the methods for formulating the recommendations were clearly described; there was an explicit link between the recommendations and the supporting evidence; a procedure for updating the guidelines was provided; the different options for management of the condition or health issue were clearly presented; key recommendations were easily identifiable; and the guideline described facilitators and barriers to its application.[23-25] These features may increase the reliability of the recommendations as they demonstrate sound methodology and make these guidelines less prone to biases. A common weakness of the three guidelines was the uncertainty and/or absence of presenting monitoring and/or auditing criteria.[23-25] These criteria are important after implementation of the guideline to determine, for example, if the guidelines resulted in improved patient health care outcomes. For the 2017 National Pain Center guideline,[23] the recommendations regarding mindfulness were not specific or unambiguous; there were no explicit details on the MBSR interventions in the primary studies (e.g., no details on the duration of MBSR interventions). Also, it is uncertain whether two guidelines provided advice and/or tools on how the recommendations can be put into practice.[23,24] Moreover, for the 2014 VA/DoD guideline,[24] it was unclear if views and preferences of the target population had been sought, if the guideline was externally reviewed by experts prior to its publication or if competing interests of guideline development group members were recorded and addressed. Finally, for both VA/DoD guidelines,[24,25] it is unclear if the funding bodies influenced the content of the guideline, an important piece for the overall interpretation of the recommendations suggested by the guidelines.

Summary of Findings

Appendix 4 presents a table of the main study findings and authors' conclusions.

Clinical Effectiveness of Mindfulness Training

Two systematic reviews[17,18] and four publications on three RCTs[19-22] examined the clinical effectiveness of mindfulness training for chronic non-malignant pain. Relevant to this report, these studies examined pain, function, and wellbeing outcomes. One of the included systematic reviews did not identify relevant studies; therefore, no summary of findings can be provided from this review.[17]

Pain

Pain outcomes were assessed and reported in one systematic review[18] and three RCTs.[19,21,22]

In the systematic review,[18] one included study met the eligibility criteria of the current report; therefore, the summary of findings is reflective of one study and no meta-analytic data are presented. The systematic review included a relevant RCT that compared a modified MBSR program plus pharmacotherapy (i.e., over-the-counter and prescribed medications; intervention) to pharmacotherapy (control) for patients with chronic low back pain and found no significant difference in total pain after eight-week and 24-week follow-up periods.[18]

One RCT examined the effect of MBSR plus usual pharmacotherapy (intervention) on pain in patients with migraines and chronic tension-type headaches compared to usual pharmacotherapy alone (control).[19] Patients in the intervention group had a significant reduction in pain intensity scores compared to the control group.[19] The second RCT of patients with migraines compared standardized MBSR plus usual pharmacotherapy (intervention) to pharmacotherapy alone (control).[22] This RCT found significant reductions in headache duration in favour of the intervention immediately after the completion of the eight-week intervention, but not at one month post-intervention. The authors found no significant differences between groups for migraine frequency, headache frequency, and headache severity for both follow-up periods.[22] In another RCT, the authors found MBSR was significantly more effective than usual pharmacotherapy as evidenced by significantly lower pain severity scores, and these improvements were more pronounced at immediately following the eight-week intervention versus three months follow-up.[21]

Disability

One RCT[22] assessed disability at two different timepoints (immediately following the eight-week intervention and one month post-intervention) using two different outcomes: HIT-6 and MIDAS. This RCT compared standardized MBSR plus usual pharmacotherapy (intervention) to pharmacotherapy alone (control) and found a significant improvement in favour of the intervention for HIT-6 scores at both timepoints and MIDAS scores immediately after the eight-week intervention (no between-group differences at one month post-intervention). The study authors indicated that this magnitude of change in HIT-6 score was considered clinically meaningful.[22]

Wellbeing

Wellbeing outcomes were assessed in three RCTs (from four publications).[19-22]

One RCT revealed MBSR plus usual pharmacology (intervention) was significantly more effective than usual pharmacotherapy alone (control) as evidenced by significantly higher quality of life scores for most categories from the 36-Item Short Form Survey (SF-36): role limitation due to physical health, bodily pain, general health, energy and vitality, affect health, sum of physical health dimensions, and sum of mental health.[19] No significant differences were found for the physical functioning, role limitations due to emotional problems, and social functioning categories.[19] In the RCT that compared MBSR (intervention) to usual pharmacotherapy (control), the authors found that mindfulness awareness scores improved significantly in favour of the intervention group, and these improvements were more pronounced at immediately following the eight-week intervention versus the three month follow-up period.[21] The supporting publication of this RCT also examined perceived stress and general mental health.[20] This publication found improvements in favour of the intervention for both perceived stress and general mental health, and these improvements were also more pronounced immediately following the eight-week intervention compared to the three month follow-up period.[20] Finally, the RCT that compared standardized MBSR plus usual pharmacotherapy (intervention) to

pharmacotherapy alone (control) also reported on wellbeing outcomes.[22] This RCT found significant improvements in mindfulness awareness (both follow-up time points) and headache management self-efficacy (for eight-week follow-up) in favour of the intervention. No significant differences between groups were identified for Migraine-Specific Quality Of Life, Patient Health Questionnaire (Depression module), State Trait Anxiety Inventory or Perceived Stress Scale outcomes.[22]

Cost-Effectiveness of Mindfulness Training

No relevant evidence regarding the cost-effectiveness of mindfulness training for chronic non-malignant pain in adults was identified; therefore, no summary can be provided.

Guidelines

Three guidelines provide recommendations on the use of mindfulness training for chronic non-malignant pain in adults based on varying quality evidence.[23-25] The 2017 National Pain Center guideline provides recommendations for adults with chronic non-malignant pain.[23] The guideline provides a strong recommendation, derived from low to moderate quality of evidence, for the optimization of non-opioid pharmacotherapy and non-pharmacotherapy versus opioid use. When focusing on non-pharmacotherapy interventions, the guideline provided evidence of small to moderate short-term benefit for MBSR.[23] The 2017 VA/DoD guideline provides recommendations for adults for the management of (chronic) low back pain.[25] The guideline provides weak recommendations, derived from unclear quality of evidence (i.e., quality not reported), in favour of offering MBSR for patients with chronic low back pain. The guideline also indicates that the overall benefits of MBSR outweigh any harms or burdens to the patient.[25] The 2014 VA/DoD guideline provides recommendations for adults for the management of chronic multi-symptom illness.[24] The guideline provides weak recommendations, derived from unclear quality of evidence (i.e., quality not reported), in favour of offering MBSR delivered by trained professionals for patients with chronic multi-symptom illness.[24]

Limitations

There are certain limitations to consider when reviewing the report. Several reports, often systematic reviews, were excluded at the screening stage due to the lack of details regarding the comparator. In numerous cases, the comparator was described as usual care, treatment as usual, standard care, or waitlist control with no details regarding what these comparators involved. Since it cannot be assumed that usual care always involves pharmacotherapy, these studies were excluded from the report. Investigators of future systematic reviews on this topic may consider providing more details about the comparators and contacting authors of the original studies to obtain this information, if not provided in the publications. In addition, one of the included systematic reviews examined the clinical effectiveness of mindfulness training for chronic non-malignant pain,[17] however no relevant literature was identified, which may further highlight the lack of studies directly comparing MBSR to pharmacotherapy alone. Moreover, details on the specific type, duration, dose, and frequency of pharmacotherapy was not provided for any RCT,[19-22] which makes it difficult to precisely interpret the findings from these studies. The other systematic review that was included in this report only contained one relevant study that fulfilled the current eligibility criteria.[18] Therefore, findings from the included study were described and no meta-analytic summary data from the systematic review could be reported. Most of the clinical evidence identified included patients with chronic headache pain;[19-22] therefore, it is unclear how effective mindfulness training may be for other types of chronic non-malignant pain

(e.g., osteoarthritis, rheumatoid arthritis, neck pain, irritable bowel syndrome). For clinical studies that included MBSR plus usual pharmacotherapy as the intervention, it is not possible to discern the independent effect of mindfulness training.[18,19,22] This report did not identify any cost-effectiveness studies for inclusion. Finally, only one report (i.e., guideline) was conducted in Canada;[23] therefore, it is unclear how generalizable the results are to the Canadian context (e.g., available treatments, patient characteristics). This Canadian guideline disclosed that their recommendations were based on low- to moderate-quality evidence, but the quality of evidence that informed the other two guidelines was unclear.[24,25] These limitations warrant the use of caution when interpreting the findings of this report.

Conclusions and Implications for Decision or Policy Making

This report identified evidence on the clinical effectiveness of mindfulness training for the management of chronic non-malignant pain in adults, and three evidence-based guidelines regarding the use of mindfulness training in this population. No evidence was identified for the cost-effectiveness of mindfulness training for the management of chronic non-malignant pain.

Regarding clinical effectiveness, two relevant systematic reviews[17,18] and three RCTs from four publications[19-22] regarding mindfulness training for the management of chronic non-malignant pain were identified in the search. One of the systematic reviews did not identify any relevant studies and, therefore, no conclusions from this review can be provided. The remaining clinical studies explored pain, disability, and wellness outcomes and the clinical findings were mixed. Mindfulness training (with or without pharmacotherapy) either improved or did not significantly benefit patients with chronic pain in comparison to pharmacotherapy alone depending on the population of interest, health outcome or duration of follow-up. For example, MBSR (intervention) resulted in lower pain severity scores,[21] lower perceived stress,[20] increased mindfulness awareness,[21] and ratings of general mental health[20] compared to usual pharmacotherapy (control) for patients with chronic migraines immediately after the eight-week intervention. These findings were less apparent at three months after the intervention,[20,21] suggesting the effects of the intervention may not be retained. When comparing MBSR plus usual pharmacotherapy (intervention) with usual pharmacotherapy (control) for patients with chronic headaches, there was a significant difference between groups in favour of the intervention for 10 clinical outcomes,[19,22] a significant difference between groups in favour of the intervention immediately following the intervention but not 24 weeks post intervention for three outcomes,[22] and no significant difference between groups for 10 outcomes.[19,22] Moreover, modified MBSR plus usual pharmacotherapy did not improve total pain scores for patients with chronic low back pain immediately following an eight-week intervention nor at 24 weeks post-intervention.[18] Importantly, patients in the mindfulness training groups did not perform significantly worse than pharmacotherapy alone.[18-22]

Three evidence-based guidelines[23-25] were identified that provide recommendations regarding the use of mindfulness training for the management of chronic non-malignant pain in adults, including one Canadian guideline.[23] Generally, the guidelines development groups recommend MBSR for patients with chronic pain (i.e., chronic non-malignant pain, low back pain, multi-symptom illness).

The previous 2012 CADTH rapid response report[11] aimed to summarize clinical effectiveness and evidence-based guidelines regarding the use of mindfulness training for

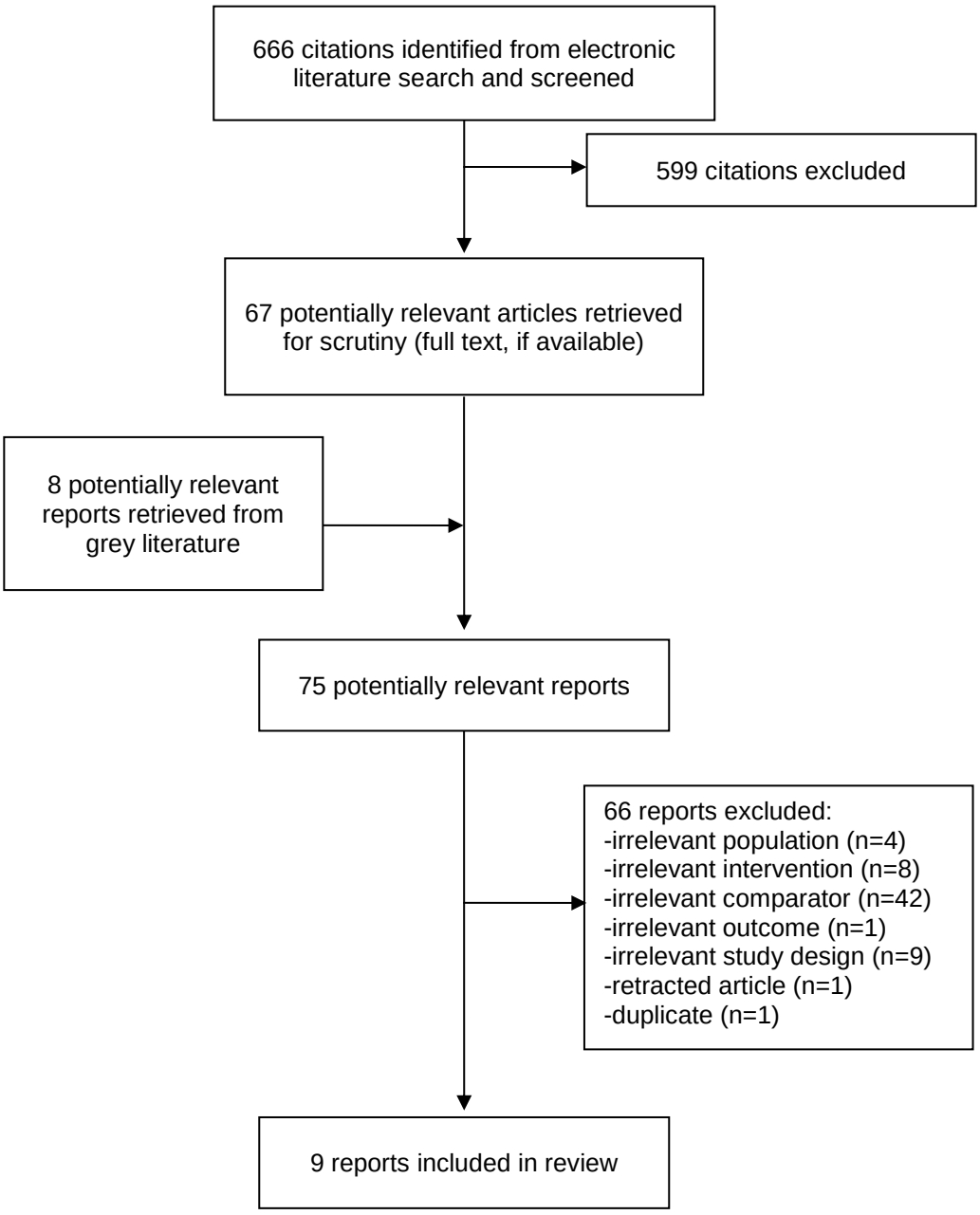
chronic pain management in adults. This report permitted mindfulness training to be compared to any other treatment. For this report, only comparisons with pharmacotherapy alone was allowed, and the search was expanded to also include cost-effectiveness literature on mindfulness training. By searching the literature from January 2014 through June 2019, nine relevant reports were identified. All these reports addressed clinical effectiveness or guideline recommendations; no relevant economic evaluations were identified. Overall, this report provided similar conclusions to the previous report in that some evidence about the potential effectiveness of mindfulness training for chronic non-malignant pain was identified, but the findings were insufficient draw definitive conclusions.

Further comparative studies evaluating the mindfulness training to pharmacotherapy alone (with details on type, dose, frequency) would enhance the utility of the evidence and better inform a determination concerning the effectiveness of mindfulness training in the care pathway for patients experiencing chronic non-malignant pain. Additional research is also required to discern the clinical effectiveness of mindfulness training alone (i.e., without a pharmacotherapy co-intervention), and the cost-effectiveness mindfulness training, for the management of chronic non-malignant pain in adults.

References

1. Lynch ME. The need for a Canadian pain strategy. *Pain Res Manag.* 2011;16(2):77-80.
2. Shupler MS, Kramer JK, Cragg JJ, Jutzeler CR, Whitehurst DG. Pan-Canadian estimates of chronic pain prevalence from 2000 to 2014: a repeated cross-sectional survey analysis. *J Pain.* 2019;20(5):557-565.
3. Hogan M-E, Taddio A, Katz J, Shah V, Krahn M. Incremental health care costs for chronic pain in Ontario, Canada: a population-based matched cohort study of adolescents and adults using administrative data. *Pain.* 2016;157(8):1626-1633.
4. Turk DC, Wilson HD, Cahana A. Treatment of chronic non-cancer pain. *Lancet.* 2011;377(9784):2226-2235.
5. Treede R-D, Rief W, Barke A, et al. A classification of chronic pain for ICD-11. *Pain.* 2015;156(6):1003.
6. National Center for Complementary and Integrative Health. Chronic Pain: In Depth. 2018; https://nccih.nih.gov/health/pain/chronic.htm.
7. Choinière M, Dion D, Peng P, et al. The Canadian STOP-PAIN project–Part 1: Who are the patients on the waitlists of multidisciplinary pain treatment facilities? *Can J Anaesth.* 2010;57(6):539-548.
8. Phillips CJ, Schopflocher D. The economics of chronic pain. In: Rashiq S, Schopflocher D, P T, Jonsson E, eds. *Chronic pain: A health policy perspective*. Weinheim (DE): Wiley-Blackwell/Wiley-VCH; 2008.
9. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain—United States, 2016. *JAMA.* 2016;315(15):1624-1645.
10. Boudreau D, Von Korff M, Rutter CM, et al. Trends in long‐term opioid therapy for chronic non‐cancer pain. *Pharmacoepidemiol Drug Saf.* 2009;18(12):1166-1175.
11. Mindfulness Training for Chronic Pain Management: A Review of the Clinical Evidence and Guidelines. *(CADTH Rapid response: summary with critical appraisal)*. Ottawa (ON): CADTH; 2012: https://www.cadth.ca/mindfulness-training-chronic-pain-management-review-clinical-evidence-and-guidelines Accessed 2019 Jun 12.
12. Kabat-Zinn J, Hanh TN. *Full catastrophe living: Using the wisdom of your body and mind to face stress, pain, and illness.* New York (NY): Delta; 2009.
13. 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.
14. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *J Epidemiol Community Health.* 1998;52(6):377-384.
15. 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 2019 Jun 25.
16. 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.
17. Pacific Northwest Evidence-based Practice Center, Skelly AC, Chou R, et al. Noninvasive nonpharmacological treatment for chronic pain: a systematic review. *(Comparative effectiveness review no 209)*. Rockville (MD): Agency for Healthcare Research and Quality; 2018: https://effectivehealthcare.ahrq.gov/sites/default/files/pdf/nonpharma-chronic-pain-cer-209.pdf Accessed 2019 Jun 25.
18. Hilton L, Hempel S, Ewing BA, et al. Mindfulness Meditation for Chronic Pain: Systematic Review and Meta-analysis. *Ann Behav Med.* 2017;51(2):199-213.
19. Bakhshani NM, Amirani A, Amirifard H, Shahrakipoor M. The Effectiveness of Mindfulness-Based Stress Reduction on Perceived Pain Intensity and Quality of Life in Patients With Chronic Headache. *Glob J Health Sci.* 2015;8(4):142-151.
20. Omidi A, Zargar F. Effects of mindfulness-based stress reduction on perceived stress and psychological health in patients with tension headache. *J Res Med Sci.* 2015;20(11):1058-1063.
21. Omidi A, Zargar F. Effect of mindfulness-based stress reduction on pain severity and mindful awareness in patients with tension headache: a randomized controlled clinical trial. *Nurs.* 2014;3(3):e21136.
22. Wells RE, Burch R, Paulsen RH, Wayne PM, Houle TT, Loder E. Meditation for migraines: a pilot randomized controlled trial. *Headache.* 2014;54(9):1484-1495.
23. Busse J, Guyatt G, Carrasco A. The 2017 Canadian guideline for opioids for chronic non-cancer pain. Hamilton (ON): Michael G. DeGroote National Pain Centre; 2017: http://nationalpaincentre.mcmaster.ca/documents/Opioid%20GL%20for%20CMAJ_01may2017.pdf Accessed 2019 Jun 25.
24. VA/DoD clinical practice guideline for the management of chronic multisymptom illness Washington (DC): Department of Veteran Affairs; Department of Defense; 2014: https://www.healthquality.va.gov/guidelines/MR/cmi/VADoDCMICPG2014.pdf Accessed 2019 Jun 14.
25. VA/DoD clinical practice guideline for diagnosis and treatment of low back pain. Washington (DC): Department of Veterans Affairs; Department of Defense; 2017: https://www.healthquality.va.gov/guidelines/Pain/lbp/VADoDLBPCPG092917.pdf. Accessed 2018 Jun 14.
26. Systematic Review Update: Noninvasive Nonpharmacologic Treatments for Chronic Pain Research Protocol *(Evidence-based Practice Center Systematic Review Protocol)*. Rockville (MD): Agency for Healthcare Research and Quality; 2019: https://effectivehealthcare.ahrq.gov/topics/noninvasive-nonpharm-pain-update/protocol. Accessed 2019 Jun 17.
27. Maglione M, Hempel S, Hilton L, et al. PROSPERO Mindfulness meditation for chronic pain (CRD42015025052). *PROSPERO: International prospective register of systematic reviews*. York (GB): University of York Centre for Reviews and Dissemination; 2015: https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=25052. Accessed 2016 Jun 25.

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
Skelly, 2018[17] United States	0 relevant studies of the 202 included RCTs	Patients with chronic pain conditions (chronic low back pain; chronic neck pain; osteoarthritis of the knee, hip, or hand; fibromyalgia; and tension headache)	Intervention: Mindfulness practices Comparator: Pharmacotherapy	Function Pain Follow-up: not applicable
Hilton, 2017[18] United States	1 relevant study of the 38 included RCTs	Adult patients with chronic pain for a minimum of 3 months (n = 40)	Intervention: Modified MBSR (body scan, sitting practice, walking meditation; 8 weeks) plus over the counter and prescribed medications Comparator: over the counter and prescribed medications	Pain Follow-up: unclear

MBSR = mindfulness-based stress reduction; RCT = randomized controlled trials.

Table 3: Characteristics of Included Primary Clinical Studies

First Author, Publication Year, Country	Study Design	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
Bakhshani, 2016[19] Iran	RCT	Patients with migraine and chronic tension-type headache according to diagnostic criteria of the International Headache Classification Committee (n = 40) Intervention: 20 participants; 70.0% female; mean age ± SD = 30.60 ± 9.08 years Comparator:	Intervention: MBSR (8 weekly sessions) plus usual pharmacotherapy (including specific and non-specific drugs) Comparator: usual pharmacotherapy (including specific and non-specific drugs)	Pain Quality of life via SF-36 (sub-outcomes include role limitation due to physical health, bodily pain, general health, energy and vitality, affect health, sum of physical health dimensions, sum of mental health, physical functioning, role limitations due to emotional problems, social functioning)

Table 3: Characteristics of Included Primary Clinical Studies

First Author, Publication Year, Country	Study Design	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
		20 participants; 65.0% female; mean age = 31.50 ± 9.57 years		
Omidi 2015[20]* Iran	RCT	Adults with tension headache according to diagnostic criteria of the International Headache Classification Committee (n = 60) Intervention: 30 participants; 76.7% female; mean age = 34.5 ± 2.41 years Comparator: 30 participants; 83.3% female; mean age = 32.0 ± 3.20 years	Intervention: MBSR (8 weekly sessions) Comparator: usual pharmacotherapy	Perceived stress General mental health Post-test: 8 weeks Follow-up: 3 months
Omidi, 2014[21]* Iran	RCT	Adults with tension headache according to diagnostic criteria of the International Headache Classification Committee (n = 60) Intervention: 30 participants; mean age: 34.5 ± 2.41 years Comparator: 30 participants; mean age = 32.0 ± 3.20 years	Intervention: MBSR (8 weekly sessions) Comparator: usual pharmacotherapy	Pain severity Mindful awareness Post-test: 8 weeks Follow-up: 3 months
Wells, 2014[22] United States	RCT	Adults with migraines (n = 19) Intervention: 10 participants; 90% female; mean age: 45.9 ± 17 years Comparator: 9 participants; 89% female; mean age = 45.2 ± 12 years	Intervention: standardized MBSR course (8 weeks) plus usual prophylactic and abortive medications Comparator: usual care, including prophylactic and abortive medications	<u>Primary outcome:</u> Migraine Frequency (number of migraines per month) <u>Secondary outcomes:</u> Headache Frequency Per Month Headache Severity Headache Duration

Table 3: Characteristics of Included Primary Clinical Studies

First Author, Publication Year, Country	Study Design	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
				Headache Impact Test-6 (HIT-6) Migraine Disability Assessment (MIDAS) Headache Management Self Efficacy Five Factor Mindfulness Migraine-Specific Quality of Life Patient Health Questionnaire - depression module State Trait Anxiety Inventory Perceived Stress Scale Initial follow-up: immediately after intervention ended (8 weeks) Final follow-up: 1-month after intervention ended

MBSR = mindfulness-based stress reduction; RCT = randomized controlled trial; SD = standard deviation; SF-36 = 36-Item Short Form Survey.

* *Note.* These two studies include the same patient population but explore different outcomes.

Table 4: Characteristics of Included Guidelines

Intended Users, Target Population	Intervention and Practice Considered	Major Outcomes Considered	Evidence Collection, Selection, and Synthesis	Evidence Quality Assessment	Recommendations Development and Evaluation	Guideline Validation
National Pain Center (Canadian Guideline for Opioids for Chronic Non-Cancer Pain), 2017[23]						
Intended Users Prescribers of opioids for the management of chronic non-malignant pain and those who create policy regarding this issue (e.g., primary care physicians, specialists who manage patients with chronic non-cancer pain, nurse practitioners, and regulatory agencies and other policy makers) Secondary audiences: • Patients living with chronic non-cancer pain • Pharmacists • Other health care professionals who manage patients with chronic non-cancer pain Target Population Patients with chronic non-cancer pain	Interventions for the management of chronic non-cancer pain, including MBSR	Relevant to this report, function and pain	Selection and prioritization of questions and outcomes Conduct systematic reviews Develop a patient values and preferences statement to complement research findings and help guide Panel in making recommendations	GRADE	Guideline development process included 4 groups: 4-member steering committee, 15-member guideline panel, 13-member multidisciplinary clinical expert committee, and 16-member patient advisory committee Conducted 2-day in-person meeting where the Guideline Panel voted anonymously after each evidence review (must be endorsed by at least 80% of panel members for acceptance of recommendation) Recommendations shared with the Clinical Expert Committee for review and feedback and solicited feedback from patients, clinicians, and other stakeholders by posting on website and through press release, social media, and email	Externally peer-reviewed
VA/DoD, 2017[25]						
Intended Users Health care providers who manage patients with low back pain,	Interventions for the management of (chronic)	Relevant to this report, function, pain and quality of life	Formulated and prioritized evidence questions	GRADE (quality of evidence not reported for recommendation	Convened a face-to-face meeting with the CPG Champions and Work Group	Externally peer-reviewed

Table 4: Characteristics of Included Guidelines

Intended Users, Target Population	Intervention and Practice Considered	Major Outcomes Considered	Evidence Collection, Selection, and Synthesis	Evidence Quality Assessment	Recommendations Development and Evaluation	Guideline Validation
including chronic low back pain <u>Target Population</u> Patients with chronic low back pain	low back pain, including MBSR		Conducted systematic review Conducted focus groups with patients	relevant to report)	CPG drafted by the Champions and Work Group sent out for internal and external peer review and comment. All feedback reviewed, discussed, and considered by the Work Group Modifications made throughout the CPG development process Final CPG approved about the diagnosis and treatment of low back pain to the VA/DoD Evidence-Based Practice Working Group	
VA/DoD, 2014[24]						
<u>Intended Users</u> Primary care providers who treat and manage adult patients with chronic multi-symptom illness (with focus on patients who are eligible for care in the Veterans Health Administration or the Department of Defense health care delivery system) <u>Target Population</u>	Management approaches for multi-symptom illness, including non-pharmacologic therapies such as mindfulness-based therapy	Relevant to this report, pain reduction, symptom severity, and quality of life	Formulated and prioritized evidence questions Conducted systematic review to update the 2001 CPG (search dates: January 2000 to October 2013)	GRADE (quality of evidence not reported for recommendation relevant to report)	Convened a face-to-face meeting with the CPG Champions and Work Group Drafted and submitted final CPG on the management of chronic multi-symptom illness to the VA/DoD Evidence-Based Practice Working Group	Unclear

Table 4: Characteristics of Included Guidelines

Intended Users, Target Population	Intervention and Practice Considered	Major Outcomes Considered	Evidence Collection, Selection, and Synthesis	Evidence Quality Assessment	Recommendations Development and Evaluation	Guideline Validation
Patients with multi-symptom illness (e.g., migraine and tension headaches, non-cardiac chest pain, irritable bowel syndrome, and a variety of chronic pain conditions)						

CPG = clinical practice guideline; DoD = Department of Defense; GRADE = Grading of Recommendations, Assessment, Development and Evaluations; MBSR = mindfulness-based stress reduction; VA = Department of Veterans Affairs.

Appendix 3: Critical Appraisal of Included Publications

Table 5: Strengths and Limitations of Systematic Reviews and Meta-Analyses using AMSTAR II[13]

Strengths	Limitations
Skelly, 2018[17]	
• Study authors published a systematic review protocol a priori[26] • Research questions clear and inclusion criteria for the review included the components of PICO • Multiple databases searched, ClinicalTrials.gov searched for unpublished trials, reference lists of included studies reviewed for includable literature • Search strategy provided in protocol[26] and appendix • Data selection and extraction conducted independently and in duplicate • Reasons for excluding studies provided in flow chart • List of excluded studies provided in appendix • Included studies described in adequate detail • Grading of the strength of evidence performed by at least two investigators independently based on Agency for Healthcare Research and Quality guidance • Methods used to combine study findings appropriate • Conflicts of interest discussed • Review authors acknowledged that this review is **"based on research conducted by the Pacific Northwest Evidence-based Practice Center under contract to the Agency for Healthcare Research and Quality"** (p. iii)	• No major limitations identified
Hilton, 2017[18]	
• Study authors published a systematic review protocol in PROSPERO[27] • Research questions clear and inclusion criteria for the review included the components of PICO • Full search strategy provided in protocol • Appropriate meta-analysis plan included a priori in protocol • Multiple databases and reference lists of systematic reviews searched • Keywords from search strategy provided • Data selection and extraction conducted independently and in duplicate • Risk of bias assessed using the Cochrane Risk of Bias tool • Other biases related to the US Preventive Services Task Force's criteria for internal validity of included studies also assessed • Reasons for excluding studies provided in flow chart • Included studies described in adequate detail • Methods used to combine study findings appropriate • Study authors disclose funding, "The systematic review was sponsored by the Department of Defense Centers of	• Did not justify why study authors included RCTs and no other study designs • List of excluded studies not provided

Table 5: Strengths and Limitations of Systematic Reviews and Meta-Analyses using AMSTAR II[13]

Strengths	Limitations
Excellence for Psychological Health and Traumatic Brain Injury (contract number 14-539.2).” (p.211) • Study authors report no conflicts of interest	

AHRQ = Agency for Healthcare Research and Quality; PICO = Population Intervention, Comparator, Outcome.

Table 6: Strengths and Limitations of Clinical Studies using Downs and Black[14]

Strengths	Limitations
Bakhshani, 2016[19]	
• Objectives, intervention, and main outcomes of the study clearly described • Patients randomly allocated to group assignment • Actual probability values (*P* values) reported for significant outcomes • Estimates of the random variability provided as standard deviations for outcomes with significant findings • Number of patients included, and basic characteristics of the patients included in the study described • Authors reported that the study was supported by Zahedan University of Medical Sciences	• More detail about the type and dose of medications used by participants in both groups was needed • Blinding not described (e.g., patients assigned to treatment allocations, evaluators who ascertained outcome data) • No sample size calculation for statistical power provided, and the authors acknowledged that the study includes a small sample • Actual probability values (*P* values) not reported for non-significant outcomes • It is unclear whether results were unbiased due to multiple testing (e.g., many subgroup analysis tests performed) • Estimates of the random variability not provided for outcomes with non-significant findings • It was unclear whether the participants were representative of the source population • It was unclear if the staff, places, and facilities where the patients were treated were representative of the treatment most of the patients receive • Any potential or actual conflicts of interest were not described
Omidi, 2015[20]	
• Objectives and main outcomes of the study clearly described • Patients in both groups were from the same institution and recruited from the same period • Patients randomly allocated to group assignment • Appropriate statistical tests used to assess outcomes • Sample size for statistical power calculated • Actual probability values (*P* values) reported for outcome of interest • Estimates of the random variability provided as standard deviations • Number of patients included, and basic characteristics of the patients included in the study described	• More detail about the comparator was needed to better understand the type and dose of antidepressant medication used and what clinical management involved • Blinding not described (e.g., patients assigned to treatment allocations, evaluators who ascertained outcome data) • It was unclear whether the participants were representative of the source population • It was unclear if the staff, places, and facilities where the patients were treated were representative of the treatment most of the patients receive

Table 6: Strengths and Limitations of Clinical Studies using Downs and Black[14]

Strengths	Limitations
• Main findings of the study described • Authors reported that they did no receive any funding to conduct the study and authors declared no conflicts of interest	
Omidi, 2014[21]	
• Objectives, intervention, and main outcomes of the study clearly described • Patients randomly allocated to group assignment • Patients in both groups were from the same institution and recruited from the same period • Appropriate statistical tests used to assess outcomes • Sample size for statistical power calculated • Actual probability values (*P* values) reported when values less than *P* = 0.001 • Estimates of the random variability provided as standard deviations • Number of patients included, and basic characteristics of the patients included in the study described • Main findings of the study described • Authors reported that they received copies of MBSR guidelines by Jon Kabat-Zinn from the Center for Mindfulness at the University of Massachusetts	• More detail about the comparator was needed to better understand the type and dose of antidepressant medication used and what clinical management involved • Blinding not described (e.g., patients assigned to treatment allocations, evaluators who ascertained outcome data) • It was unclear whether the participants were representative of the source population • It was unclear if the staff, places, and facilities where the patients were treated were representative of the treatment most of the patients receive • Any potential or actual conflicts of interest were not described
Wells, 2014[22]	
• The study was prospectively registered • Objectives and main outcomes of the study clearly described • Patients randomly allocated to group assignment • Patients in both groups were from the same institution and recruited from the same period • Sample size for statistical power calculated • Attempts to blind patients performed • Appropriate statistical tests used to assess outcomes • Data analyses were performed blind (i.e., investigator) • Actual probability values (*P* values) reported when values less than *P* = 0.001 • Estimates of the random variability provided as 95% confidence intervals • Number of patients included, and characteristics of the patients included in the study described • Main findings of the study adequately described • Authors reported that they were funded by the American Headache Society Fellowship and the Headache Research Fund of the John Graham Headache Center, Brigham and Women's Faulkner Hospital. • Conflicts of interest disclosed	• More detail about the type and dose of medications used by participants in both groups was needed (though the distinction between prophylactic and abortive medications was made) • It was unclear whether the participants were representative of the source population • It was unclear if the staff, places, and facilities where the patients were treated were representative of the treatment most of the patients receive

MBSR = mindfulness-based stress reduction.

Table 7: Strengths and Limitations of Guidelines using AGREE II[15]

Item	Guideline		
	National Pain Center, 2017[23]	VA/DoD, 2017[25]	VA/DoD, 2014[24]
Domain 1: Scope and Purpose			
1. The overall objective(s) of the guideline is (are) specifically described.	✓	✓	✓
2. The health question(s) covered by the guideline is (are) specifically described.	✓	✓	✓
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.	✓	✓	✓
Domain 2: Stakeholder Involvement			
4. The guideline development group includes individuals from all relevant professional groups.	✓	✓	✓
5. The views and preferences of the target population (patients, public, etc.) have been sought.	✓	✓	unclear
6. The target users of the guideline are clearly defined.	✓	✓	✓
Domain 3: Rigour of Development			
7. Systematic methods were used to search for evidence.	✓	✓	✓
8. The criteria for selecting the evidence are clearly described.	✓	✓	✓
9. The strengths and limitations of the body of evidence are clearly described.	✓	✓	✓
10. The methods for formulating the recommendations are clearly described.	✓	✓	✓
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.	✓	✓	✓
12. There is an explicit link between the recommendations and the supporting evidence.	✓	✓	✓
13. The guideline has been externally reviewed by experts prior to its publication.	✓	✓	unclear
14. A procedure for updating the guideline is provided.	✓	✓	✓
Domain 4: Clarity of Presentation			
15. The recommendations are specific and unambiguous.	X	✓	✓
16. The different options for management of the condition or health issue are clearly presented.	✓	✓	✓
17. Key recommendations are easily identifiable.	✓	✓	✓
Domain 5: Applicability			
18. The guideline describes facilitators and barriers to its application.	✓	✓	✓

Item	Guideline		
	National Pain Center, 2017[23]	VA/DoD, 2017[25]	VA/DoD, 2014[24]
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	unclear	✓	unclear
20. The potential resource implications of applying the recommendations have been considered.	✓	✓	✓
21. The guideline presents monitoring and/or auditing criteria.	unclear	unclear	unclear
Domain 6: Editorial Independence			
22. The views of the funding body have not influenced the content of the guideline.	✓	unclear	unclear
23. Competing interests of guideline development group members have been recorded and addressed.	✓	✓	unclear

CAD = Canadian Guideline for Opioids for Chronic Non-Cancer Pain; DoD = Department of Defense; VA = Department of Veterans Affairs.

Appendix 4: Main Study Findings and Authors' Conclusions

Table 8: Summary of Findings Included Systematic Reviews and Meta-Analyses

Main Study Findings	Authors' Conclusion
Skelly, 2018[17]	
MBSR versus Pharmacotherapy for Chronic Low Back Pain *No studies of MBSR versus pharmacotherapy met inclusion criteria.* **MBSR versus Pharmacotherapy for Fibromyalgia** *No studies of MBSR versus pharmacotherapy met inclusion criteria.*	Not applicable
Hilton, 2017[18]	
SF MPQ—total pain (24-week follow-up) Standard mean difference (95% CI) = −0.04 (−0.7 to 0.63), representing a no significant differences between groups **SF MPQ—total pain (8-week follow-up)** Standard mean difference (95% CI) = −0.01 (−0.68 to 0.65)**,** representing no significant difference between groups	Not applicable

MBSR = mindfulness-based stress reduction; SF MPQ = Short-Form McGill Pain Questionnaire.

Table 9: Summary of Findings of Included Primary Clinical Studies

Main Study Findings	Authors' Conclusion
Bakhshani, 2016[19]	

Pain results derived from analysis of covariance (ANCOVA); results presented as mean ± SD
• Significantly lower pain intensity scores in favour of intervention (53.89 ± 2.40) versus control (71.94 ± 2.20), *P* = 0.001
  ○ Covariate "pre-test of pain" was significant *P* = 0.001, indicating that level of pain intensity before MBSR intervention had a significant effect on level of pain intensity
 	
Quality of Life results derived from covariance analysis (MANCOVA); results presented as mean ± SD
• Role limitation due to physical health (RP)
  ○ Significant difference in favour of intervention group (61.62 ± 6.18) when compared to control group (40.24 ± 5.62), *P* = 0.025
• Bodily pain
  ○ Significant difference in favour of intervention group (48.97 ± 2.98) when compared to control group (33.58 ± 2.71), *P* = 0.002
• General health
  ○ Significant difference in favour of intervention group (48.77 ± 2.85) when compared to control group (36.05 ± 2.59), *P* = 0.005
• Energy and vitality
  ○ Significant difference in favour of intervention group (44.99 ± 2.81) when compared to control group (30.50 ± 2.56), *P* = 0.002
• Affect health
  ○ Significant difference in favour of intervention group (52.60 ± 1.97) when compared to control group (34.49 ± 1.80), *P* = 0001
• Sum of physical health dimensions
  ○ Significant difference in favour of intervention group (58.52 ± 2.72) when compared to control group (46.13 ± 2.48), *P* = 0.004
• Sum of mental health
  ○ Significant difference in favour of intervention group (44.82 ± 2.43) when compared to control group (33.32 ± 2.21), *P* = 0.002
• Physical functioning
  ○ No significant difference in scores between intervention and control, *P* > 0.05
• Role limitations due to emotional problems
  ○ No significant difference in scores between intervention and control, *P* > 0.05
• Social functioning
	"The findings from this study revealed that MBSR can be used non-pharmacological intervention for improvement the quality of life and development of strategies to cope with pain in patients with chronic headache. And can be used in combination with other therapies such as pharmacotherapy." (p. 142)
	
	"According to the findings of this study it can be concluded that MBSR methods generally are effective on perceived pain intensity and quality of life of patients with chronic headache. Although there was no statistically significant difference in some aspects of quality of life, such as physical functioning, role limitations due to emotional problems and social functioning, but overall changes in mean were desired to the study. Thus, the integrating of MBSR treatment with conventional medical therapy in the treatment protocol for patients with chronic headache can be advised. The researcher also believes that despite the shortcomings and deficiencies of current research, this study could be a new approach to the treatment of chronic headache and could provide a new horizon in this field of treatment." (p. 149)

Table 9: Summary of Findings of Included Primary Clinical Studies

<table>
<tr><th>Main Study Findings</th><th>Authors' Conclusion</th></tr>
<tr><td>
No significant difference in scores between intervention and control, P > 0.05
</td><td></td></tr>
<tr><td colspan="2">Omidi, 2015[20]</td></tr>
<tr><td>
Table 3. Means, SDs, and comparison of outcome measures at pre-treatment, post-treatment, and follow-up stages in the MBSR and TAU groups*
<table>
<tr><th>Outcome measure</th><th>Group</th><th>Pre-test[a]</th><th>Post-test[a]</th><th>Follow-up[a]</th><th>Time x Group (P value)</th><th>Time (P value</th><th>Group (P value</th></tr>
<tr><td>Perceived stress scale</td><td>MBSR
TAU</td><td>16.96 (2.53)
15.9 (2.86)</td><td>12.7 (2.69)
16.13 (2.44)</td><td>13.5 (2.33)
15.76 (2.22)</td><td>0.001</td><td>0.001</td><td>0.001</td></tr>
<tr><td>Total score of BSI (GSI)</td><td>MBSR
TAU</td><td>1.63 (0.56)
1.77 (0.50)</td><td>0.73 (0.46)
1.59 (0.52)</td><td>0.93 (0.34)
1.78 (0.47)</td><td>0.001</td><td>0.001</td><td>0.001</td></tr>
</table>
[a] Data presented as mean (SD). P value less than 0.05 defined as significant.
</td><td>"MBSR could reduce stress and improve general mental health in patients with tension headache." (p. 2)

"Our study supports the hypothesis that patients suffering from tension headache can enhance their general mental health by participating in the MBSR program. In summary, the results of the present study suggest that MBSR can reduce pain-related anxiety and interference in daily activities in the short term. The unique features of mindfulness exercises are easy training and no need to complex cognitive abilities." (p. 6)</td></tr>
<tr><td colspan="2">Omidi, 2014[21]</td></tr>
<tr><td>
Pain Severity (via International Headache Classification Subcommittee Diary Scale for Headache; presented as mean ± SD)

MBSR: baseline = 7.36 ± 1.25; post-test = 5.62 ± 1.74; follow-up = 6.07 ± 1.08
TAU: baseline = 7.5 ± 1.35; post-test = 7.48 ± 1.27; follow-up = 7.48 ± 1.18
Repeated measures ANOVA revealed an interaction between time and group: P < 0.001

Mindfulness Awareness (via Mindful Attention Awareness Scale; presented as mean ± SD)

MBSR: baseline = 34.9 ± 10.5; post-test = 53.8 ± 15.5; follow-up = 40.7 ± 10.9
TAU: baseline= 53.8 ± 18.1; post-test = 49.8 ± 13.4; follow-up = 50.36 ± 14.1
Repeated measures ANOVA revealed an interaction between time and group: P < 0.001

</td><td>"MBSR could reduce pain and improve mindfulness skills in patients with tension headache. It appears that MBSR is an effective psychotherapy for treatment of patients with tension headache." (p. 1)

"In summary, the results of the present study suggest that MBSR can reduce pain-related anxiety and interference in daily activities in the short term. It is suggested to perform future studies to compare efficacy of MBSR with other traditional and newer cognitive</td></tr>
</table>

Table 9: Summary of Findings of Included Primary Clinical Studies

Main Study Findings	Authors' Conclusion
	behavioral therapies in patients with tension headache. Based on this study, MBSR is recommended as an effective psychotherapy for reducing the pain in patients with tension headache and other illness with pain." (p. 4)
Wells, 2014[22]	
Note. Main results derived from independent t-tests; results presented as differential change (95% CI) **Migraine Frequency Per Month (primary outcome)** • No significant difference between groups for both initial and final follow-up **Headache Frequency Per Month** • No significant difference between groups for both initial and final follow-up **Headache Severity (0-10 scale)** • No significant difference between groups for both initial and final follow-up **Headache Duration (hours)** • Initial follow-up: 2.9 fewer hours per headache (95% CI, -4.6 to -0.02) in favour of intervention (5.1 to 2.9) versus control (6.4 to 6.1), *P* = 0.043 • Final follow-up: non-significant **Headache Impact Test-6 (HIT-6, a disability outcome)** • Initial follow-up: 4.8 fewer points (95% CI, -11.0 to -1.0) in favour of intervention (62.5 to 57.5) versus control (63.0 to 64.0), *P* = 0.043 • Final follow-up: 4.1 fewer points (95% CI, -9.0 to -1.0) in favour of intervention (62.5 to 60.0) versus control (63.0 to 63.0), *P* = 0.022 **Migraine Disability Assessment (MIDAS, a disability outcome)** • Initial follow-up: 12.6 points fewer (95% CI, -22.0 to -1.0) in favour of intervention (17.0 to 4.5) versus control (11.0 to 14.0), *P* = 0.017 • Final follow-up: non-significant **Headache Management Self Efficacy**	*"MBSR is safe and feasible for adults with migraines. Although the small sample size of this pilot trial did not provide power to detect statistically significant changes in migraine frequency or severity, secondary outcomes demonstrated this intervention had a beneficial effect on headache duration, disability, self-efficacy, and mindfulness. Future studies with larger sample sizes are warranted to further evaluate this intervention for adults with migraines."* (p. 1484) *"Nonetheless, our findings in this pilot trial support the potential safety, feasibility, and efficacy of a standardized mind/body intervention for migraineurs."* (p. 1492)

Table 9: Summary of Findings of Included Primary Clinical Studies

Main Study Findings	Authors' Conclusion
• Initial follow-up: 13.2 points increase (95% CI, 1.0 to 30.0) in favour of intervention (111.5 to 124.0) versus control (128.0 to 117.0), *P* = 0.035 • Final follow-up: non-significant **Five Factor Mindfulness** • Initial follow-up: 13.1-point increase (95% CI, 3.0 to 26.0) in favour of intervention (142.0 to 150.0) versus control (150.0 to 141.0), *P* = 0.035 • Final follow-up: 17.3-point increase (95% CI, 1.3 to 33.2) in favour of intervention (142.0 to 157.5) versus control (150.0 to 138.0), *P* = 0.045 **Migraine-Specific Quality of Life** • No significant difference between groups for both initial and final follow-up **Patient Health Questionnaire - depression module** • No significant difference between groups for both initial and final follow-up **State Trait Anxiety Inventory** • No significant difference between groups for both initial and final follow-up **Perceived Stress Scale** • No significant difference between groups for both initial and final follow-up	

ANOVA = analysis of variance; BSI = Brief Symptom Inventory; GSI = Global Severity Index; MBSR: mindfulness-based stress reduction; SD = standard deviation; TAU = treatment as usual.

* Modified from Omidi A, Zargar F. Effects of mindfulness-based stress reduction on perceived stress and psychological health in patients with tension headache. J Res Med Sci. 2015;20(11):1058–1063. Licensed under https://creativecommons.org/licenses/by/3.0/

Table 10: Summary of Recommendations in Included Guidelines

Recommendations	Strength of Evidence and Recommendations
National Pain Center (Canadian Guideline for Opioids for Chronic Non-Cancer Pain), 2017[23]	
"*We recommend optimization of non-opioid pharmacotherapy and non-pharmacotherapy, rather than a trial of opioids*." (p. 15) Supporting details which helped to inform this recommendation: "*Evidence of small to moderate short-term benefits for Tai chi, MBSR, exercise, multidisciplinary rehabilitation, spinal manipulation, massage therapy, and acupuncture. Effects on function were generally smaller than effects on pain*." (p. 15)	Strength of Recommendations: Strong Quality of Evidence: Low to moderate
VA/DoD, 2017[25]	
"For patients with chronic low back pain, we suggest MBSR." (p.6 & 33) *"The overall benefits of MSBR or CBT outweigh any harms or burdens to the patient."* (p.33)	Strength of Recommendation: "Weak For" (or "We suggest offering this option …"; i.e., weak evidence in favour of the recommendation). Recommendation category: Evidence reviewed, New-replaced (i.e., Recommendation from previous CPG that has been carried over to the updated CPG that has been changed following review of the evidence) Quality of Evidence: Not reported
VA/DoD, 2014[25]	
"The guideline panel recommends considering mindfulness-based therapy, reattribution, behavioral medical intervention, and/or brief psychodynamic interpersonal psychotherapy, delivered by trained professionals, for patients with CMI." (p.12 and p. 35)	Strength of Recommendation: "Weak For" (or "We suggest offering this option …"; i.e., weak evidence in favour of the recommendation) Recommendation category: Evidence reviewed, New-replaced (i.e., Recommendation from previous CPG that has been carried over to the updated CPG that has been changed following review of the evidence) Quality of Evidence: Not reported

CBT = cognitive behavioural therapy; CMI = chronic multi-symptom illness; CPG = clinical practice guideline; DoD = Department of Defense; MBSR = mindfulness-based stress reduction; VA = Department of Veterans Affairs.

* strong recommendations indicate that all or almost all fully-informed patients would choose the recommended course of action and indicate to clinicians that the recommendation is appropriate for all or almost all individuals. Strong recommendations represent candidates for quality of care criteria or performance indicators.

Appendix 5: Additional References of Potential Interest

Authors' response to a letter to the editor regarding guideline included in this report

Busse JW, Juurlink DN, Buckley DN, Guyatt GH. The authors respond to "Inconsistencies in the 2017 Canadian Guideline for Opioids for Chronic Noncancer Pain". CMAJ: Canadian Medical Association Journal. 2017 Oct 2;189(39):E1234.

Reviews with "treatment as usual/waitlist control" comparator

Jackson W, Zale EL, Berman SJ, Malacarne A, Lapidow A, Schatman ME, Kulich R, Vranceanu AM. Physical functioning and mindfulness skills training in chronic pain: a systematic review. J Pain Res. 2019;12:179.

Khoo EL, Small R, Cheng W, Hatchard T, Glynn B, Rice DB, Skidmore B, Kenny S, Hutton B, Poulin PA. Comparative evaluation of group-based mindfulness-based stress reduction and cognitive behavioural therapy for the treatment and management of chronic pain: A systematic review and network meta-analysis. Evid Based Ment Health. 2019 Feb 1;22(1):26-35.

Mikolasek M, Berg J, Witt CM, Barth J. Effectiveness of mindfulness-and relaxation-based eHealth interventions for patients with medical conditions: a systematic review and synthesis. Int J Behav Med. 2018 Feb 1;25(1):1-6.

Ball EF, Nur Shafina Muhammad Sharizan E, Franklin G, Rogozińska E. Does mindfulness meditation improve chronic pain? A systematic review. Curr Opin Obstet Gynecol. 2017 Dec 1;29(6):359-66.

Chou R, Deyo R, Friedly J, Skelly A, Hashimoto R, Weimer M, Fu R, Dana T, Kraegel P, Griffin J, Grusing S. Nonpharmacologic therapies for low back pain: a systematic review for an American College of Physicians Clinical Practice Guideline. Ann Intern Med. 2017 Apr 4;166(7):493-505.

Toivonen KI, Zernicke K, Carlson LE. Web-based mindfulness interventions for people with physical health conditions: systematic review. J Med Internet Res. 2017;19(8):e303.

Veehof MM, Trompetter HR, Bohlmeijer ET, Schreurs KM. Acceptance-and mindfulness-based interventions for the treatment of chronic pain: a meta-analytic review. Cogn Behav Ther. 2016 Jan 2;45(1):5-31.

Crowe M, Jordan J, Burrell B, Jones V, Gillon D, Harris S. Mindfulness-based stress reduction for long-term physical conditions: A systematic review. Aust N Z J Psychiatry. 2016 Jan;50(1):21-32.

Bawa FL, Mercer SW, Atherton RJ, Clague F, Keen A, Scott NW, Bond CM. Does mindfulness improve outcomes in patients with chronic pain? Systematic review and meta-analysis. Br J Gen Pract. 2015 Jun 1;65(635):e387-400.

Theadom A, Cropley M, Smith HE, Feigin VL, McPherson K. Mind and body therapy for fibromyalgia. Cochrane Database Syst Rev. 2015 Apr 9;(4):CD001980.

Song Y, Lu H, Chen H, Geng G, Wang J. Mindfulness intervention in the management of chronic pain and psychological comorbidity: A meta-analysis. Int J Nurs Sci. 2014 Jun 1;1(2):215-23.

Garmon B, Philbrick J, Padrick M, Goodman M. Mindfulness-based stress reduction for chronic pain: A systematic review. J Pain Manag. 2014;7(1):23.

Primary studies with unclear comparator (i.e., may include medications but description is unclear)

Simmons LA, Williams H, Silva S, Keefe F, Tanabe P. Acceptability and Feasibility of a Mindfulness-Based Intervention for Pain Catastrophizing among Persons with Sickle Cell Disease. Pain Manag Nurs. 2019 May 10.

Turner JA, Anderson ML, Balderson BH, Cook AJ, Sherman KJ, Cherkin DC. Mindfulness-based stress reduction and cognitive-behavioral therapy for chronic low back pain: similar effects on mindfulness, catastrophizing, self-efficacy, and acceptance in a randomized controlled trial. Pain. 2016 Nov;157(11):2434.

Cherkin DC, Sherman KJ, Balderson BH, Cook AJ, Anderson ML, Hawkes RJ, Hansen KE, Turner JA. Effect of mindfulness-based stress reduction vs cognitive behavioral therapy or usual care on back pain and functional limitations in adults with chronic low back pain: a randomized clinical trial. JAMA. 2016 Mar 22;315(12):1240-9.

Related CADTH reports

Non-Opioid Options for Managing Pain. Ottawa (ON): CADTH. 2019. https://www.cadth.ca/sites/default/files/pdf/non_opioid_options_for_managing_pain.pdf

Multidisciplinary Treatment Programs for Patients with Chronic Non-Malignant Pain: A Review of Clinical Effectiveness, Cost-Effectiveness, and Guidelines. *(CADTH Rapid response: summary with critical appraisal).* Ottawa (ON): CADTH; 2017. https://www.cadth.ca/multidisciplinary-treatment-programs-patients-chronic-non-malignant-pain-review-clinical

Behavioural and Psychological Interventions for Chronic Non-Cancer Pain: A Review of Guidelines. *(CADTH Rapid response: summary with critical appraisal).* Ottawa (ON): CADTH; 2016. https://www.cadth.ca/behavioural-and-psychological-interventions-chronic-non-cancer-pain-review-guidelines

Non-Drug Interventions for Chronic Non-Cancer Pain: Guidelines and Recommendations. *(CADTH Rapid response: reference list).* Ottawa (ON): CADTH; 2014. https://www.cadth.ca/non-drug-interventions-chronic-non-cancer-pain-guidelines-and-recommendations