

CADTH RAPID RESPONSE REPORT:
SUMMARY WITH CRITICAL APPRAISAL

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

Service Line: Rapid Response Service
Version: 1.0
Publication Date: September 20, 2019
Report Length: 24 Pages

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

ISSN: 1922-8147 (online)

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

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Abbreviations

AMSTAR	A MeaSurement Tool to Assess Systematic Reviews
BDI	Beck Depression Inventory
BDNF	brain-derived neurotrophic factor
CI	confidence interval
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CRD	Centre for Reviews and Dissemination
MBSR	Mindfulness-based Stress Reduction
MDQ	Menstrual Distress Questionnaire
MeSH	Medical Subject Headings
NS	non-significant
PICO	Population Intervention, Comparator, Outcome
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCT	randomized controlled trial
SD	standard deviation
SR	systematic review
VAS	Visual Analog Scale
WHOQOL-100	World Health Organization Quality of Life Assessment

Context and Policy Issues

Chronic pain involves persistent or recurrent pain lasting longer than three months.¹ It is a global health issue that is common in both developed and developing countries.² For example, nearly one in four Canadian adults has a chronic pain condition.^{3,4} Medications, such as opioids, are frequently prescribed for patients experiencing chronic non-malignant (i.e., non-cancer) pain to alleviate their symptoms. Given the side effects of their use (e.g., nausea, constipation, respiratory depression), potential for addiction and misuse, and uncertainty in their long-term effectiveness for treating chronic non-malignant pain, alternative strategies should be explored.⁵

Complementary and alternative medicine therapies, such as mindfulness training and yoga, are potential treatment options for individuals who have chronic non-malignant pain.^{6,7} Mindfulness is defined as the intentional and non-judgmental conscious awareness of the present moment.⁷ Yoga is a mind-body practice with three main components: physical poses/postures, breathing control, and meditation/relaxation.⁸ Most recently, two CADTH Rapid Response reports examined the clinical effectiveness, cost-effectiveness, and evidence-based guidelines regarding the use of mindfulness training (published in June 2019)⁹ and yoga (published in July 2019)¹⁰ for chronic pain management in adults. The report on mindfulness found insufficient evidence to draw conclusions about its potential clinical effectiveness.⁹ The report on yoga found evidence from one randomized study suggesting that yoga plus conventional treatment with analgesics was effective for reducing chronic pelvic pain, while conventional treatment with analgesics alone was not.¹⁰ No economic evaluations were identified in either report.^{9,10} Notably, both reviews focused on comparing mindfulness or yoga with or without pharmacotherapy to pharmacotherapy alone (e.g., opioids, nonsteroidal anti-inflammatory drugs, acetaminophen).^{9,10} To inform policy decisions, further exploration of mindfulness or yoga compared with no treatment may provide additional insight on the clinical and cost-effectiveness of these complementary and alternative medicine therapies for management of chronic non-malignant pain.

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

Research Questions

1. What is the clinical effectiveness of mindfulness training for chronic non-malignant pain in adults?
2. What is the clinical effectiveness of yoga for chronic non-malignant pain in adults?
3. What is the cost-effectiveness of mindfulness training for chronic non-malignant pain in adults?
4. What is the cost-effectiveness of yoga for chronic non-malignant pain in adults?

Key Findings

Three systematic reviews and one non-randomized controlled study were identified that addressed the research questions, and the results were mixed.

Evidence from a limited quality systematic review suggested that mindfulness training versus waitlist control significantly improved pain acceptance and depression scores for patients with chronic pain (low back pain, fibromyalgia, tension headache, general chronic pain), but did not significantly improve pain intensity, anxiety, and quality of life outcomes. More research is warranted for definitive conclusions.

Results from two systematic reviews and one non-randomized study of low to moderate quality suggested that yoga was significantly more effective than no treatment for managing chronic non-malignant pain. The included systematic reviews suggested that yoga, compared to control, significantly reduced pain intensity and psychological distress and increased general activity (e.g., daily activities, socialization, absenteeism) for patients with primary dysmenorrhea. Compared to no treatment, the nonrandomized study reported that yoga significantly reduced back pain intensity and increased back flexibility and physiologic domains (e.g., serum serotonin) for patients with chronic low back pain.

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

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including Medline, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), PsychINFO, 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 yoga or mindfulness and chronic pain. No 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 August 9, 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 (18 years or older) with chronic non-malignant pain
Intervention	Q1&3: Mindfulness training alone Q2&4: Yoga alone
Comparator	No treatment
Outcomes	Q1&2: Clinical effectiveness (e.g., pain management, reduction in pain medication use, return to work, quality of life, functioning) Q3&4: Cost-effectiveness (e.g., cost per quality-adjusted life year)
Study Designs	Q1&2: Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized controlled trials Q3&4: Economic evaluations

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, were duplicate publications, were already captured in an included systematic review (SR) or were published prior to 2014. Studies were excluded if the waitlist control group described additional treatment components (e.g., treatment as usual, pharmacological therapy, education, stress and anxiety management). Guidelines were also excluded.

Critical Appraisal of Individual Studies

The included SRs were critically appraised by one reviewer using A MeaSurement Tool to Assess systematic Reviews (AMSTAR) II¹¹ and the non-randomized study was critically appraised using the Downs and Black checklist.¹² Summary scores were not calculated for the included studies; rather, the strengths and limitations of each included study were described narratively.

Summary of Evidence

Quantity of Research Available

A total of 1,217 citations were identified in the literature search. Following screening of titles and abstracts, 1,117 citations were excluded and 100 potentially relevant reports from the electronic search were retrieved for full-text review. Two potentially relevant publications were retrieved from the grey literature search for full-text review. Of these 102 potentially relevant articles, 98 publications were excluded for various reasons, and four publications (three SRs and one non-randomized study) met the inclusion criteria and were included in this report. Appendix 1 presents the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)¹³ flowchart of the study selection. Additional references of potential interest are provided in Appendix 6.

Summary of Study Characteristics

Additional details regarding the characteristics of included publications are provided in Appendix 2.

Study Design

One SR was identified regarding the clinical effectiveness of mindfulness training for chronic non-malignant pain in adults.¹⁴ Two SRs^{15,16} and one non-randomized study¹⁷ were identified regarding the clinical effectiveness of yoga in this population. Two of the included SRs conducted meta-analyses.^{14,16} The relevant studies included within each SR were randomized controlled trials (RCTs; publication date range: 2017 to 2019).¹⁴⁻¹⁶ For two SRs, only a subset of studies were relevant for this report;^{14,15} thus, studies fulfilling the inclusion criteria for this report were described (percentage range of relevant studies captured in included SRs: 46.1% to 100.0%).¹⁴⁻¹⁶ Appendix 5 provides a detailed description of the overlap in the primary studies between the two SRs investigating yoga (Table 8).

The non-randomized study identified used a prospective, controlled study design to investigate yoga for the management of chronic non-malignant pain.¹⁷

Country of Origin

The body of evidence originated from the Republic of Korea (one SR, one non-randomized study),^{16,17} United Kingdom (one SR),¹⁴ and United States (one SR).¹⁵

Patient Population

The SR investigating mindfulness training included adult patients with a variety of chronic pain conditions (i.e., low back pain, fibromyalgia, tension headache, non-specific/general chronic pain).¹⁴ The two SRs examining yoga included patients with primary dysmenorrhea.^{15,16}

The non-randomized study exploring yoga examined premenopausal, community-dwelling patients with chronic low back pain for at least three months.¹⁷ To be eligible for the study, participants must not have (i) used pain medication; (ii) been obese; (iii) exercised regularly; or (iv) participated in other therapy for back pain.¹⁷

Interventions and Comparators

One SR investigated mindfulness training (i.e., mindfulness-based stress reduction [MBSR] program)¹⁴ and two SRs explored yoga^{15,16} as the intervention for managing chronic non-malignant pain. The included non-randomized study investigated yoga as the intervention, which comprised a 12-week Hatha yoga program (group-based, one-hour class, three times per week).¹⁷ The comparator for the included studies was either waitlist control¹⁴ or no treatment.¹⁵⁻¹⁷

Outcomes

The SRs investigated the following clinical outcomes: pain (e.g., intensity, acceptance),^{14,16} psychological morbidity (e.g., negative feelings, depression, anxiety, anger, stress, fatigue, arousal),^{14,15} quality of life,¹⁴ wellbeing,¹⁵ social and work capacity (e.g., socialization, participation in activities, absenteeism),¹⁵ and safety (i.e., adverse events).¹⁵ For the non-randomized study, the outcomes of interest were back pain intensity (measured on a Visual Analog Scale), physiological changes (in brain-derived neurotrophic factor [BDNF] and

serotonin levels), depression, and back flexibility.¹⁷ The minimal clinically important difference was not defined for relevant outcomes of interest.

Summary of Critical Appraisal

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

Systematic Reviews

The AMSTAR II checklist¹¹ was used to assess the quality of the SRs included in this report¹⁴⁻¹⁶ and the quality was moderate. Common strengths of the SRs included: a clear description of research questions and eligibility criteria were provided, multiple databases were searched, reference lists of included studies were searched to find additional potentially relevant studies, and examples of keywords used to search academic databases for literature were provided.¹⁴⁻¹⁶ All SRs described included studies in adequate detail and critically appraised the included studies using a validated tool.¹⁴⁻¹⁶ Based on how the study authors of the mindfulness SR presented their results, it was not possible to discern the quality of evidence for the subset of applicable RCTs.¹⁴ However, one yoga SR graded the four included RCTs as high-quality with a low risk of bias,¹⁶ whereas the other yoga SR graded the eight relevant RCTs as poor quality articles with high risk of bias or moderate quality articles with moderate risk of bias.¹⁵ These ratings of low methodological quality were one of the reasons why a meta-analysis was not performed for this SR.¹⁵ The study authors from each SR reported no conflicts of interest.¹⁴⁻¹⁶ These strengths increase the reproducibility of the findings. For transparency, one SR¹⁵ also provided rationale for why observational studies were excluded from the review (i.e., low level of evidence and greater potential for bias), and a full search strategy for one academic database was provided in the appendix;¹⁵ these details were not provided by the other two SRs.^{14,16} Conversely, the SR that provided more details in the above-mentioned sections did not provide reasons for excluding studies in the flow chart or any financial disclosures¹⁵ whereas the other two SRs did.^{14,16} No SR provided a list of excluded studies.¹⁴⁻¹⁶

Two SRs conducted meta-analyses.^{14,16} One SR stated that the investigators followed a prospective protocol and conducted data selection and extraction in duplicate.¹⁴ However, this review did not provide sufficient detail about the meta-analysis plan and it is unclear whether the methods used to combine study findings were appropriate.¹⁴ The investigators of the other SR did not describe following a predetermined protocol or registering the review a priori but did provide an appropriate meta-analysis plan and the methods used to combine study findings appeared appropriate.¹⁶

Non-randomized Study

The quality of evidence from the included non-randomized study¹⁷ was assessed using the Downs and Black Checklist.¹² Overall, the quality of the included study was low.¹⁷ Strengths of the study included adequately described objectives, intervention, and outcomes of interest, power calculations performed to inform the target sample size, basic characteristics of study participants described, results adequately reported with actual probability values (*P* values), and declaration of no conflicts of interest by the authors. Despite these strengths, there was no information provided to suggest that the study was prospectively registered, patients were not randomly allocated to group assignments, and blinding of evaluators who ascertained outcome data were not described. Given the nature of the intervention, it was not possible to blind the patients assigned to treatment allocations, which may contribute to performance bias (e.g., if patients anticipate a

treatment effect). Moreover, there was substantial participant dropout (39% for intervention group; 45% for control group), but the authors did not provide rationale for why this occurred. It was also unclear whether included participants were representative of the source population or if the staff, places, and facilities where the patients participated were representative of the intervention most patients receive. Finally, the authors did not report any financial disclosures to indicate how this study was funded, if applicable. Taken together, these limitations substantially decrease confidence in the results of this study.¹⁷

Summary of Findings

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

Clinical Effectiveness of Mindfulness Training

One SR examined the clinical effectiveness of mindfulness training for chronic non-malignant pain.¹⁴ Relevant to this report, this SR completed a meta-analysis on pain and psychological morbidity outcomes.¹⁴

Pain

Pain intensity and pain acceptance were assessed in the included SR.¹⁴ For these outcomes, two studies met eligibility criteria of the current report, and their findings were pooled in a meta-analysis. Relative to the waitlist control group, pain intensity was not significantly different but pain acceptance was significantly better in the MBSR group.¹⁴

Psychological morbidity

The SR included three studies which compared anxiety scores from the MBSR group to those from the waitlist control group.¹⁴ Meta-analysis results found no significant differences between groups for anxiety scores. The SR also included four studies which compared MBSR to waitlist control for depression outcomes and found a significant difference between groups in favour of the MBSR group. The SR included two studies which compared MBSR to waitlist control for quality of life (mental health) outcomes and found no significant differences between groups.¹⁴

Clinical Effectiveness of Yoga

Two SRs^{15,16} and one non-randomized study¹⁷ examined the clinical effectiveness of yoga for chronic non-malignant pain. Relevant to this report, these studies examined pain; negative feelings; social and work capacity; energy, sleep, and concentration; wellbeing; flexibility; physiological outcomes (i.e., brain-derived neurotrophic factor and serotonin; and safety outcomes.¹⁵⁻¹⁷

Pain

Pain intensity was assessed in one SR (with meta-analysis)¹⁶ and in one non-randomized study.¹⁷ By pooling data from four RCTs, the SR found pain intensity scores were significantly lower for the yoga group compared to control ($P = 0.031$).¹⁶ The non-randomized study found an interaction between time and group ($P = 0.008$), such that after a 12-week intervention the yoga group had significantly lower back pain intensity scores ($P < 0.001$) whereas the control group had significantly higher pain intensity scores ($P < 0.001$) compared to baseline.¹⁷

Negative feelings

One SR¹⁵ examined negative feeling outcomes. Three of the included RCTs found multiple aspects of psychological distress (e.g., stress relief, anger, anxiety, depression) were significantly better in the yoga group versus control group.¹⁵

The non-randomized study¹⁷ used the Beck Depression Inventory (BDI) to assess depression. Study authors found an interaction between time and group ($P = 0.018$), whereby BDI scores were maintained by the yoga group after a 12-week intervention whereas the control group's scores tended to increase (i.e., worsen; did not reach statistical significance; $P = 0.07$) compared to baseline.¹⁷

Social and work capacity

One SR investigated social outcomes.¹⁵ Four of the included RCTs from the SR found that patients in the yoga group increased socialization and improved participation in daily activities versus patients in the control group. Three of the included RCTs also found a significant reduction in absenteeism in the yoga group compared to the control group.¹⁵

Energy, sleep, and concentration

One SR examined energy, sleep, and concentration outcomes.¹⁵ One RCT included in the SR reported that the yoga group experienced a significantly lower total Menstrual Distress Questionnaire (MDQ) score and MDQ subscale scores (i.e., insomnia, fatigue, decreased efficiency, forgetfulness, confusion, and difficulty concentrating) during the premenstrual and menstrual phases compared with control group.¹⁵ Another RCT in the included SR did not find significant differences between groups (yoga versus control) for arousal outcomes, including energy and activity.¹⁵

Wellbeing

One SR examined wellbeing outcomes.¹⁵ One RCT included in the SR found wellbeing scores were significantly improved in the yoga group versus control group during the premenstrual phase.¹⁵

Flexibility

When examining back flexibility, the non-randomized study found an interaction between time and group ($P = 0.012$), such that after a 12-week intervention, the yoga group had a significant increase in back flexibility during trunk flexion ($P < 0.01$) whereas there was no significant change from baseline in the control group.¹⁷

Physiological

When examining physiological outcomes, the non-randomized study found an interaction between time and group for both serum BDNF ($P = 0.001$) and serotonin ($P = 0.035$) whereby the yoga group had a significant increase in serum BDNF levels after a 12-week intervention compared to baseline ($P < 0.01$) but serum BDNF levels were not significantly different from baseline in the control group ($P = 0.052$). Serum serotonin levels were not significantly different from baseline in the yoga group, while serum serotonin was significantly reduced from baseline in the control group ($P < 0.01$).¹⁷

Safety

One SR provided a descriptive summary of adverse events.¹⁵ Eight of the included RCTs reported no adverse events as a result of the yoga interventions.¹⁵ No details were provided about whether adverse events had occurred in the control groups.

Cost-Effectiveness of Mindfulness Training

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

Cost-Effectiveness of Yoga

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

Limitations

Certain limitations are noteworthy when reviewing the report.

When screening the literature, it was apparent that several reviews and primary studies examined either mindfulness or yoga as an added therapy to an existing treatment regime. This was also true for waitlist control groups whereby the participants could continue existing treatment options (pharmacotherapy, physiotherapy, etc.). Based on the eligibility criteria for this report, these studies were excluded. The current report sought evidence regarding the use of mindfulness or yoga alone. Notably, in “real world” circumstances many patients with chronic pain are treated with pharmacotherapy;¹⁸ therefore, the patients characterized in this report represent a small subset of the overall population of patients with chronic pain. The generalizability of these findings to patients with chronic pain more broadly is unclear.

Limited evidence from clinical studies (one SR) was identified regarding mindfulness training for chronic non-malignant pain. This review did include patients with different conditions (i.e., low back pain, fibromyalgia, tension headache, non-specific/general chronic pain), which indicates that its findings may be applicable to different populations experiencing chronic pain.¹⁴ Though two SRs^{15,16} were identified regarding the use of yoga for the management of chronic non-malignant pain, both reviews focused on patients with primary dysmenorrhea and, therefore, the results may not be applicable for patients with other types of chronic pain such as arthritis, neck pain or chronic migraine. Similarly, the non-randomized study focused on patients with low back pain,¹⁷ and the findings may not be generalizable to other chronic pain conditions.

No relevant cost-effectiveness studies were identified suggesting a lack of research regarding the comparative cost-effectiveness of mindfulness or yoga versus no treatment.

Finally, no studies included in this report were conducted in Canada; therefore, it is unclear how generalizable the results are to the Canadian context (e.g., available treatments, patient characteristics). 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 about the clinical effectiveness of mindfulness training and yoga for the management of chronic non-malignant pain in adults. No evidence was identified for the cost-effectiveness of mindfulness training or yoga for the management of chronic non-malignant pain.

Regarding clinical effectiveness of mindfulness training, one relevant SR¹⁴ was identified from the search. The SR explored pain and psychological morbidity outcomes for patients with various chronic pain conditions (low back pain, fibromyalgia, tension headache, general chronic pain) and the clinical findings were mixed. In this review, mindfulness training improved pain acceptance and depression scores, but did not improve pain intensity, anxiety or quality of life outcomes relative to waitlist control.¹⁴ It may be premature to draw conclusions about the comparative effectiveness of mindfulness training versus no treatment given the paucity of clinical evidence and inherent methodological flaws noted within the included SR.

More clinical evidence (two SRs^{15,16} and one non-randomized study¹⁷) was found regarding yoga for the management of chronic non-malignant pain. These studies explored pain; negative feelings; social and work capacity; energy, sleep, and concentration; wellbeing; flexibility; physiological outcomes (i.e., serum BDNF and serotonin; and safety outcomes.¹⁵⁻¹⁷ Compared to no treatment, the SRs reported yoga significantly reduced pain intensity and psychological distress (i.e., feelings of stress, anger, tension, anxiety, depression, mood swings), and improved wellbeing and general activity (i.e., participation in daily activities, socialization, absenteeism) for patients with primary dysmenorrhea.^{15,16} The non-randomized trial also found that yoga (12-week program) reduced back pain intensity and increased back flexibility and physiological measures (BDNF, serum serotonin) compared to no treatment for patients with chronic low back pain.¹⁷ Additional studies of high methodological quality may further aid in making definitive conclusions about yoga for the management of chronic non-malignant pain.

Previous 2019 CADTH Rapid Response reports aimed to summarize clinical effectiveness, cost-effectiveness and evidence-based guidelines regarding the use of mindfulness training⁹ or yoga¹⁰ for chronic pain management in adults. These reports compared mindfulness training or yoga with or without pharmacotherapy (intervention) to pharmacotherapy alone (control). For the current report, the interventions of interest were mindfulness training alone or yoga alone, which was compared with no treatment. The eligibility criteria were also narrowed to exclude guidelines. By searching the literature from January 1, 2014 through August 9, 2019 with these criteria, four relevant reports on clinical effectiveness were identified (one mindfulness study, three yoga studies). Overall, this report provided similar conclusions to the previous report⁹ on mindfulness training: some clinical evidence about mindfulness training for various chronic non-malignant pain was identified, but the findings were insufficient to draw definitive conclusions. Additional clinical evidence was found in favour of yoga for the management of chronic pain in the current report. For example, the previous Rapid Response found evidence from one randomized study that suggested that yoga plus conventional treatment with analgesics was effective for reducing chronic pelvic pain, while conventional treatment with analgesics alone was not.¹⁰ This report expands on these findings by identifying that yoga alone, versus no treatment, also improved several health outcome measures for patients with chronic low back pain and primary dysmenorrhea, as previously described. Although the populations represented in the current and previous reports may be fundamentally different (as

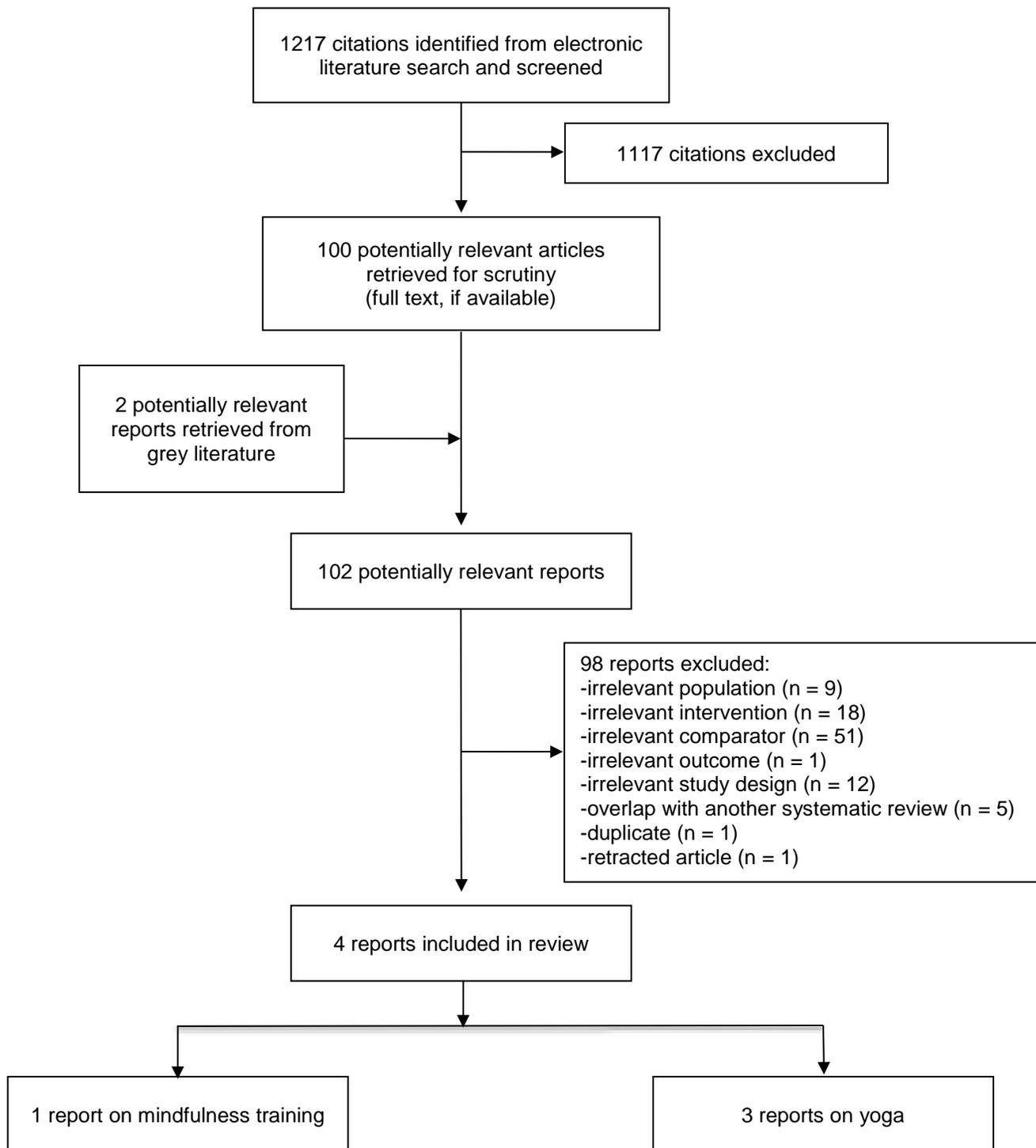
described in the limitations above), taken together these limited results suggest that mindfulness or yoga may provide some benefit for patients with chronic non-malignant pain.

Like the preceding Rapid Response reports,^{9,10} no eligible cost-effectiveness studies were identified for mindfulness training or yoga interventions. Additional research is required to discern the cost-effectiveness mindfulness training or yoga for the management of chronic non-malignant pain in adults.

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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
Mindfulness Training (n = 1)				
Ball, 2017 ¹⁴ United Kingdom	6 relevant studies of the 13 included RCTs	Adults patients with chronic pain (i.e., low back pain, fibromyalgia, tension headache, non-specific/general chronic pain)	Intervention: mindfulness program, such as MBSR Comparator: wait-list control	Pain (i.e., intensity, acceptance; primary outcomes) Psychological morbidity (i.e., anxiety and depression symptoms, quality of life [mental health]; secondary outcomes) Follow-up: unclear
Yoga (n = 2)				
Kim, 2019 ¹⁶ Republic of Korea	4 relevant studies of the 4 included RCTs	Patients with primary dysmenorrhea	Intervention: yoga Comparator: no treatment	Menstrual pain intensity (VAS) Follow-up: variable (range: 2 to 12 weeks)
McGovern, 2018 ¹⁵ United States	8 relevant studies of the 14 included RCTs	Patients with primary dysmenorrhea	Intervention: yoga Comparator: no treatment	Outcome measures corresponding to at least one of the WHOQOL-100 domains, such as negative feelings (e.g., depression, anger, anxiety, stress); social and work capacity; energy, sleep, and concentration; wellbeing Safety (i.e., adverse events) Follow-up: variable (range: 1 to 10 months)

MBSR = mindfulness-based stress reduction; RCT = randomized controlled trials; VAS = Visual Analog Scale; WHOQOL-100 = World Health Organization Quality of Life Assessment.

Table 3: Characteristics of Included Primary Clinical Study

First Author, Publication Year, Country	Study Design	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
Lee, 2014 ¹⁷ Republic of Korea	Non-randomized prospective study	<p>Premenopausal patients with chronic low back pain for ≥ 3 months who do not use pain medication, exercise regularly or participate in other therapy for back pain (n = 25)</p> <p>Intervention: 14 participants; 100.0% women; mean age \pm SD = 41.9 \pm 8.9 years</p> <p>Comparator: 11 participants; 100.0% women; mean age = 45.0 \pm 5.2 years</p>	<p>Intervention: yoga (3 times per week for 12 weeks; group-based yoga program)</p> <p>Comparator: control (no treatment)</p>	<p>Primary outcomes: back pain intensity (VAS), serum BDNF, serum serotonin</p> <p>Secondary outcomes: depression (BDI), back flexibility (trunk flexion test)</p> <p>Follow-up: 12 weeks</p>

BDI = Beck Depression Inventory; BDNF = brain-derived neurotrophic factor; SD = standard deviation; VAS = Visual Analog Scale.

Appendix 3: Critical Appraisal of Included Publications

Table 4: Strengths and Limitations of Systematic Reviews and Meta-Analyses using AMSTAR II¹¹

Strengths	Limitations
Mindfulness Training (n = 1)	
Ball, 2017 ¹⁴	
<ul style="list-style-type: none"> - Study authors stated following a prospective protocol - Research questions clear and inclusion criteria for the review included the components of PICO - Multiple databases and reference lists of SRs searched; authors also manually searched all relevant SRs for additional literature - Broad keywords from search strategy provided - Data selection and extraction conducted in duplicate and a third reviewer was used, when applicable, to settle discrepancies - Reasons for excluding studies provided in flow chart - Basic details about the included studies provided - Risk of bias assessed using the Cochrane Risk of Bias tool - Study authors acknowledged financial support - Study authors reported no conflicts of interest 	<ul style="list-style-type: none"> - Full search strategy not provided (i.e., search syntax) - Grey literature platforms, such as ClinicalTrials.gov, not searched - Did not justify why study authors included RCTs and not other study designs - Meta-analysis plan not described in adequate detail - It was unclear whether the methods used to combine study findings were appropriate - List of excluded studies not provided - Based on how the study authors presented their results, it was not possible to discern the quality of evidence from the subset of applicable RCTs
Yoga (n = 2)	
Kim, 2019 ¹⁶	
<ul style="list-style-type: none"> - Research question clear and inclusion criteria for the review included the components of PICO - Multiple databases searched, reference lists of included studies reviewed to find additional literature - Broad keywords from search strategy provided - Appropriate meta-analysis plan included - Reasons for excluding studies provided in flow chart - Included studies described in adequate detail - Risk of bias assessed using the Cochrane Risk of Bias tool - Methods used to combine study findings appropriate - Study authors discussed financial support, “<i>This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.</i>” (p.98) - Study authors reported no conflicts of interest - Study authors graded the four included RCTs as high-quality with a low risk of bias 	<ul style="list-style-type: none"> - Study authors did not describe a protocol or registering the review a priori - Full search strategy not provided (i.e., search syntax) - Grey literature platforms, such as ClinicalTrials.gov, not searched - No mention of data selection and extraction being conducted independently/in duplicate - Did not justify why study authors included RCTs and no other study designs - List of excluded studies not provided
McGovern, 2018¹⁵	
<ul style="list-style-type: none"> - Research questions clear and inclusion criteria for the review included the components of PICO - Study authors provided rationale for why observational studies were excluded from the review (i.e., low level of evidence and greater potential for bias) - Multiple databases and reference lists of SRs searched - Keywords for search strategy provided in the main text and full search strategy for one database provided in appendix 	<ul style="list-style-type: none"> - Study authors did not describe a protocol or registering the review a priori - Reasons for excluding studies not provided in flow chart - List of excluded studies not provided - Financial sources/disclosures not provided - The relevant RCTs included in this review were either poor quality articles with high risk of bias or moderate quality

Strengths	Limitations
<ul style="list-style-type: none"> - Data selection and extraction conducted independently and in duplicate - Included studies described in adequate detail - Methodological quality was appraised independently and in duplicate using the Downs and Black checklist - Study authors reported no conflicts of interest 	<p>with moderate risk of bias (a reason why a meta-analysis was not possible)</p>

PICO = Population Intervention, Comparator, Outcome; RCT = randomized controlled trial; SR = systematic review.

Table 5: Strengths and Limitations of Primary Clinical Study using Downs and Black¹²

Strengths	Limitations
Lee, 2014 ¹⁷	
<ul style="list-style-type: none"> - Objectives, intervention, and main outcomes of the study clearly described - Patients in both groups were recruited using the same method (i.e., local flyer) and from the same period - Sample size for statistical power calculated - Appropriate statistical tests used to assess outcomes - Number of patients included, and characteristics of the patients included in the study described - Main findings of the study adequately described - Actual probability values (<i>P</i> values) reported - Estimates of the random variability provided as standard deviation - Authors declared no conflict of interests 	<ul style="list-style-type: none"> - There was no information provided to suggest the study was prospectively registered - Patients were not randomly allocated to group assignments - Blinding of evaluators who ascertained outcome data not described - Blinding of the patients assigned to the treatment allocations not possible and may have contributed to performance bias - Substantial dropout (39% for intervention group; 45% or control group) without any details on the reasons for dropout - It was unclear whether the participants were representative of the source population - It was unclear if the staff, places, and facilities where the patients participated were representative of the intervention most patients receive - Authors did not report the source of funding for the study

Appendix 4: Main Study Findings and Authors' Conclusions

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

Main Study Findings	Authors' Conclusion
Mindfulness Training (n = 1)	
Ball, 2017 ¹⁴	
<p>Pain <u>Pain intensity (2 studies; primary outcome)</u> Standard mean difference (95% CI) = 0.03 (-0.26 to 0.31), representing a NS difference between groups</p> <p><u>Pain acceptance (2 studies; primary outcome)</u> Standard mean difference (95% CI) = 0.45 (0.10 to 0.80), representing a significant difference between groups in favour of the MBSR group</p> <p>Psychological morbidity <u>Anxiety (3 studies; secondary outcome)</u> Standard mean difference (95% CI) = -0.21 (-0.45 to 0.03), representing a NS difference between groups</p> <p><u>Depression (4 studies; secondary outcome)</u> Standard mean difference (95% CI) = -0.31 (-0.52 to -0.10), representing a significant difference between groups in favour of the MBSR group</p> <p><u>Quality of life (mental health; 2 studies; secondary outcome)</u> Standard mean difference (95% CI) = 0.45 (0.12 to 0.78), representing a NS difference between groups</p>	<p>Not applicable (study authors did not make any conclusions specific to the comparisons of interest for the current report).</p>
Yoga (n = 2)	
Kim, 2019 ¹⁶	
<p>Menstrual pain intensity</p> <ul style="list-style-type: none"> - Statistical heterogeneity among the trials ($Q = 87.69, P < 0.001, I^2 = 96.6$) - Standard mean difference (95% CI) = -2.09 (-3.99 to -0.19), representing a significant difference between groups in favour of the yoga group ($P = 0.031$) 	<p><i>“Yoga is an effective intervention for alleviating menstrual pain in women with primary dysmenorrhea. (p. 94)</i></p> <p><i>“In summary, a yoga intervention showed favorable outcomes on menstrual pain relief among participants with primary dysmenorrhea. These improvements were mainly in the participants’ subjective parameters, such as menstrual pain intensity in primary dysmenorrhea.” (p. 98)</i></p>
McGovern, 2018 ¹⁵	
<p>Negative feelings</p> <ul style="list-style-type: none"> - Multiple aspects of psychological distress (e.g., stress relief, anger, anxiety, depression) were significantly better in the yoga group versus control group (n = 3 studies) <p>Social outcomes</p> <ul style="list-style-type: none"> - Yoga group increased socialization and improved participation in daily activities compared to control group (n = 4 studies) - A significant reduction in absenteeism was found in the yoga group compared to control group (n = 3 studies) 	<p><i>“Practitioners may consider yoga for management of primary dysmenorrhea. However, future research using larger RCTs of high methodological quality is needed to ascertain the magnitude of yoga’s clinical significance.” (p. 470)</i></p>

Main Study Findings	Authors' Conclusion
<p>Energy, sleep, concentration</p> <ul style="list-style-type: none"> - Yoga group experienced a significantly lower total MDQ score and MDQ subscale scores (i.e., insomnia, fatigue, decreased efficiency, forgetfulness, confusion, and difficulty concentrating) during the premenstrual and menstrual phases compared with control group (n = 1 study) - NS differences between yoga and control groups for improved arousal (energy and activity; n = 1 study) <p>Wellbeing</p> <ul style="list-style-type: none"> - Wellbeing score was significantly improved in the yoga group versus control group ($P < 0.001$, n = 1 study) <p>Safety</p> <ul style="list-style-type: none"> - No adverse events reported as a result of yoga intervention (n = 8 studies) - No details about adverse events were described about the control group 	

CI = confidence interval; MBSR = mindfulness-based stress reduction; MDQ = Menstrual Distress Questionnaire; NS = non-significant; RCT = randomized controlled trial.

Table 7: Summary of Findings of Included Primary Clinical Study

Main Study Findings							Authors' Conclusion
Lee, 2014 ¹⁷							
Changes in primary and secondary outcomes ^a							<p>"We propose that BDNF may be one of the key factors mediating beneficial effects of yoga on chronic low back pain." (p. 1)</p> <p>"Our study is the first clinical study showing that yoga intervention has a significant influence on serum BDNF and serotonin levels in patients with chronic low back pain. We propose that these neuromodulators in nociceptive pathway may mediate beneficial effect of yoga on chronic low back pain." (p. 5)</p>
Variable	Group	Baseline	Week 12	2-way ANOVA with repeated measures			
				F_{time} (P value)	F_{group} (P value)	$F_{interaction}$ (P value)	
Primary							
Visual analogue scale (mm)	Yoga	48.7 ± 18.2	16.8 ± 13.2***	8.5	26.3	23.1	
	Control	48.7 ± 12.4	56.5 ± 9.9*	(0.008) ^{##}	(<0.001) ^{###}	(<0.001) ^{###}	
BDNF (pg/mL)	Yoga	23973.6 ± 6996.6	31395.9 ± 7962.7**	0.1	0	14.8	
	Control	30949.8 ± 11616.6	24422.4 ± 8206.3	-0.807	-1	(0.001) ^{##}	
Serotonin (ng/mL)	Yoga	153.8 ± 55.5	143.7 ± 61.7	11	0.2	5	
	Control	186.4 ± 86.9	134.2 ± 57.3**	(0.003) ^{##}	-0.645	(0.035) [#]	
Secondary							
Back flexibility (cm)	Yoga	4.7 ± 9.5	10.9 ± 8.4***	15.3	0.02	7.5	
	Control	7.7 ± 5.7	8.8 ± 5.2	(0.001) ^{##}	-0.892	(0.012) [#]	
Beck Depression Inventory (points)	Yoga	5.5 ± 5.1	4.2 ± 5.4	2	2.3	6.5	
	Control	5.4 ± 3.3	9.8 ± 6.8	-0.172	-0.146	(0.018) [#]	
Data are presented as mean ± standard deviation; *P < 0.05, **P < 0.01, and ***P < 0.001: paired t-test within group; #P < 0.05, ##P < 0.01, and ###P < 0.001: 2-way ANOVA with repeated measures.							

ANOVA = analysis of variance; BDNF = brain-derived neurotrophic factor.

^a Reproduced from Moseon Lee, Woongjoon Moon, and Jaehee Kim, "Effect of Yoga on Pain, Brain-Derived Neurotrophic Factor, and Serotonin in Premenopausal Women with Chronic Low Back Pain," Evidence-Based Complementary and Alternative Medicine, vol. 2014, Article ID 203173, 7 pages, 2014. <https://doi.org/10.1155/2014/203173>. Licensed under <https://creativecommons.org/licenses/by/3.0/>

Appendix 5: Overlap between Included Systematic Reviews

Table 8: Primary Study Overlap between Included Systematic Reviews Investigating Yoga

Primary Study Citation	Systematic Review Citation	
	Kim, 2019 ¹⁶	McGovern, 2018 ¹⁵
Carson 2010		
Galantino 2004		
Garfinkel 1994		
Kanojia 2013		X
Kuttner 2006		
Nag 2013a		X
Nag 2013b		X
Nag 2013c		X
Rakshae 2011	X	X
Sakuma 2012	X	X
Sridevi 1996		X
Teut 2016		
Williams 2009		
Yang 2016	X	X
Yonglitthipagon 2017	X	

Appendix 6: Additional References of Potential Interest

Ongoing Trials

Zhou Y, Charette M, Yu Y. What are the effects of mindfulness and meditation-based interventions on chronic pelvic pain management? A systematic review and meta-analysis (CRD42019123138). PROSPERO: International prospective register of systematic reviews. York (GB): University of York Centre for Reviews and Dissemination; 2019: http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42019123138

University of North Carolina, Chapel Hill. NCT03495856 Positive Mindfulness Program and Wellbeing in Chronic Pain. ClinicalTrials.gov. Bethesda (MD): U.S. National Library of Medicine; 2018: <https://clinicaltrials.gov/ct2/show/NCT03495856>

Canterbury Christ Church University. NCT03072810 4-week Mindfulness Program for Adults With Chronic Pain. ClinicalTrials.gov. Bethesda (MD): U.S. National Library of Medicine; 2018: <https://clinicaltrials.gov/ct2/show/NCT03072810>

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

Yoga for Chronic Non-Malignant Pain Management: A Review of Clinical Effectiveness, Cost-Effectiveness and Guidelines. (*CADTH Rapid response: summary with critical appraisal*). Ottawa (ON): CADTH; 2019. <https://www.cadth.ca/yoga-chronic-non-malignant-pain-management-review-clinical-effectiveness-cost-effectiveness-and>

Mindfulness Training for Chronic Non-malignant Pain Management: A Review of the Clinical Effectiveness, Cost-effectiveness and Guidelines. (*CADTH Rapid response: summary with critical appraisal*). Ottawa (ON): CADTH; 2019. <https://www.cadth.ca/mindfulness-training-chronic-non-malignant-pain-management-review-clinical-effectiveness-cost>

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>

Exercise for the Management of Back Pain: Clinical Effectiveness. (*CADTH rapid response report: summary of abstracts*). Ottawa (ON): CADTH; 2017: <https://www.cadth.ca/exercise-management-back-pain-clinical-effectiveness>

Self-Management Interventions for Back Pain: Clinical Effectiveness and Guidelines. (*CADTH rapid response report: reference list*). Ottawa (ON): CADTH; 2016: <https://www.cadth.ca/self-management-interventions-back-pain-clinical-effectiveness-and-guidelines>

Physical Therapy Treatments for Chronic Non-Cancer Pain: A Review of Guidelines. (*CADTH rapid response report: summary with critical appraisal*). Ottawa (ON): CADTH; 2016: <https://www.cadth.ca/physical-therapy-treatments-chronic-non-cancer-pain-review-guidelines>

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>

Yoga and Mindfulness: What's the Evidence from CADTH? (*CADTH tools*). Ottawa (ON): CADTH; 2015: <https://www.cadth.ca/tools/yoga-and-mindfulness-whats-evidence-cadth>

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>