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CADTH RAPID RESPONSE REPORT:
SUMMARY WITH CRITICAL APPRAISAL

Multidisciplinary Treatment Programs for Patients with Chronic Non-Malignant Pain: A Review of Clinical Effectiveness, Cost-Effectiveness, and Guidelines – An Update

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Abbreviations

AGREE II	Appraisal of Guidelines for Research and Evaluation Instrument
OCC	Osher Clinical Center
RCT	randomized controlled trial
SF-36	Short Form Health Survey Questionnaire

Context and Policy Issues

Chronic pain, typically referring to pain that persists for more than three months,[1] is a significant healthcare concern.[2-5] Patients suffering from chronic pain may experience considerable disability leading to substantial psychosocial and socioeconomic consequences.[6] In addition, there is growing concern among decision-makers and healthcare providers regarding the current epidemic overuse of opioids,[5] a class of medication often prescribed to provide pain relief,[7] but the use of which remains controversial in the context of chronic pain.[7,8]

Pain can be defined as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” according to the International Association for the Study of Pain.[9] In the presence of long-lasting pain, patients may experience changes in pain perceptions and threshold levels, coping abilities, social and professional activities, as well as significant impact on quality of life.[2] Therefore, the multi-dimensional aspect of chronic pain suggests that optimal management may be best achieved using multimodal approaches. These include multidisciplinary treatment programs delivered by at least two healthcare professionals of different backgrounds.[10,11] Multidisciplinary treatment programs can include various combinations of medical therapy, psychotherapy or behavioral therapy, exercise programs for physical reconditioning, relaxation techniques and patient education.[9,10] Therefore, multidisciplinary treatment programs can encompass a wide variety of treatment programs.

It is important to assess the evidence regarding the clinical effectiveness and cost-effectiveness of multidisciplinary treatment programs to assist in objective decision making in pain management. There is a need for evidence regarding how to provide optimal management services for patients with chronic pain that go beyond the only use of medication. This an update to a 2017 CADTH Rapid Response report[2] in which the evidence for multidisciplinary treatment programs for patients with chronic, non-malignant pain was assessed. Findings regarding clinical effectiveness showed that multidisciplinary treatment programs were associated with significant improvements from baseline in pain and function or disability. The difference between the intervention and control groups for this outcome did not always reach statistical significance; however, the control groups included a wide range of strategies that also provided improvement compared to baseline pain levels. With respect to quality of life, anxiety, and depression, the report concluded that there seemed to be improvements with multidisciplinary treatments but the difference compared with control treatments was not always significant. No relevant cost-effectiveness studies were identified. One evidence-based guideline recommended multidisciplinary management of chronic non-malignant pain. Two other guidelines recommended such programs in the following circumstances: patients significantly affected by chronic low back pain and with no improvement with primary care management, or patients with chronic non-cancer pain who were using opioids and experiencing serious challenges in tapering.

The purpose of this report is to update the 2017 CADTH Rapid Response report[2] previously mentioned and to review the comparative clinical effectiveness, cost-effectiveness, and evidence-based guidelines regarding the use of multidisciplinary treatment programs for patients with chronic, non-malignant pain in outpatient settings.

Research Questions

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

Key Findings

Two systematic reviews,[4,5] two randomized controlled trials,[12,13] and one economic evaluation[14] regarding multidisciplinary treatment programs for patients with chronic, non-malignant pain in outpatient settings were included. No relevant evidence-based guidelines were identified.

Overall, findings from the included studies suggest that the multidisciplinary management of chronic non-malignant pain is associated with significant improvements in pain intensity, and may be associated with significant improvements in quality of life and function. There was substantial variation in the types of multidisciplinary treatment programs and control interventions among studies. This suggests that various combinations of individual components in multidisciplinary programs may result in effective pain management.

Findings from one economic evaluation suggested that the cost-effectiveness of multidisciplinary pain management programs is uncertain. The difference in quality-adjusted life-years between multidisciplinary treatment and control treatment was not statistically meaningful, and the higher costs associated with multidisciplinary treatment of patients with chronic low back pain resulted in an incremental cost-effectiveness ratio exceeding standard willingness-to-pay thresholds.

Findings from the current report are consistent with those from the 2017 CADTH Rapid Response report.[2] Evidence regarding optimal pain management services suggests that there is a benefit from moving beyond the only use of medication to more comprehensive programs. However, further research is needed to identify the type of components and combinations that would provide optimal benefits for patients with chronic pain.

Methods

Literature Search Methods

This report makes use of a literature search strategy developed for a previous CADTH report.[2] For the current report, a limited literature search was conducted on key resources including PubMed, the Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit retrieval by study type. Where possible, retrieval was limited to the human population. The search was

limited to English-language documents published between January 1, 2017 and April 11, 2019 to capture any articles published since the previous report.

Selection Criteria and Methods

Studies were eligible for inclusion if they were published between May 25, 2017 (i.e., the date of the search in the previous report that is being updated in the current report)[2] and April 11, 2019. One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Patients (any age) with chronic, non-malignant pain in outpatient settings
Intervention	Multidisciplinary treatment or multidisciplinary treatment programs for managing chronic, non-malignant pain (may also be called multi-professional, multimodal, interdisciplinary, inter-professional, multidisciplinary primary care teams, lower-back pain program, neck pain program)
Comparator	Q1-2: Alternative treatments or programs for pain management, or usual care; no treatment; waitlist; placebo Q3: No comparator necessary
Outcomes	Q1: Clinical benefits and harms (e.g., pain, physical function, social function [including return to school or work], emotional and psychological functioning (e.g., anxiety, depression, sleep), health-related quality of life, opioid use, opioid prescribing practices) Q2: Cost-effectiveness outcomes (e.g., incremental cost per quality-adjusted life-years (QALY) or health benefit gained) Q3: Evidence-based guidelines
Study Design	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, economic evaluations, and 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 May 25, 2017. As per the study design criteria, non-randomized studies were not eligible for inclusion; however, a list of non-randomized studies identified from the literature search is provided in Appendix 5 as additional references of potential interest. Guidelines that were not evidence-based (i.e. for which the recommendations were not based on a systematic approach to identify and evaluate the supporting evidence) or with unclear methodology were also excluded, as well as position statements and consensus documents that did not describe a formal literature search for evidence upon which the recommendations were based.

Critical Appraisal of Individual Studies

The included systematic reviews were critically appraised by one reviewer using the Risk of Bias in Systematic Reviews (ROBIS),[15] randomized studies were critically appraised using the Cochrane Risk of Bias Tool,[16] economic studies were assessed using the Drummond checklist,[17] and guidelines were assessed with the Appraisal of Guidelines for Research and Evaluation Instrument (AGREE II).[18] 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 546 citations were identified in the literature search. Following screening of titles and abstracts, 504 citations were excluded and 42 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 potentially relevant articles, 39 publications were excluded for various reasons, and 5 publications met the inclusion criteria and were included in this report. These comprised 2 systematic reviews, 2 randomized controlled trials (RCTs) and 1 economic evaluation. Appendix 1 presents the PRISMA[19] flowchart of the study selection. Additional references of potential interest are provided in Appendix 5.

Summary of Study Characteristics

A summary of the characteristics of the included systematic reviews, clinical studies and economic evaluation is provided below. Additional details are available in Appendix Table 2 to Table 4.

Study Design

Two systematic reviews were included.[4,5] Liossi et al. 2019[4] included 9 RCTs and 19 studies with single group pre-post design. The literature was searched from database inception to March 22, 2018. Peterson et al. 2018[5] included 8 RCTs and 1 retrospective cohort study. The literature was searched from 1996 to October 2016. There was no overlap in the primary studies included in the systematic reviews.

Two clinical studies (both RCTs) were also included: Monticone et al. 2017[12] and Ronzi et al. 2017.[13]

The economic evaluation (Wayne et al. 2019)[14] was an observational-based study evaluation. The background, study design and research methods were based on a previously published study by the same author with the clinical inputs being utilized from this publication while cost inputs were based on resource consumption estimates from Blue Cross Shield of Massachusetts databases. The study was non-model based with a societal perspective. The only identified assumption in the study, that the cost of work absence ($30 per hour) was similar for all subjects, was based on previous studies.

Country of Origin

The primary authors of the two systematic reviews were from the United Kingdom (Liossi et al. 2019)[4] and the United States (Peterson et al. 2018).[5] The primary authors of the two RCTs were from Italy (Monticone et al. 2017)[12] and France (Ronzi et al. 2017).[13] The primary authors of the economic evaluation (Wayne et al. 2019)[14] were from the United States.

Patient Population

One systematic review (Liossi et al. 2019)[4] included pediatric patients with mixed chronic pain diagnoses (high prevalence of chronic headache, abdominal pain, and complex

regional pain syndrome). Patients had a mean age of 13.8 years (ranged from 3 to 22 years across studies). The second systematic review (Peterson et al. 2018)[5] included adult patients with chronic musculoskeletal pain. Patients had a mean age that ranged from 37 to 62 years across studies. The sample size in the individual RCTs ranged from 63 to 1,066 patients. Baseline pain intensity ranged from 5.1 to 7.7 on a 10-point scale.

One RCT (Monticone et al. 2017)[12] included 170 adult patients with chronic neck pain (> 3 months). Patients had a mean age of 53 years and 61% were women. Patients reported a moderate level of disability and pain at baseline. The second RCT (Ronzi et al. 2017)[13] included 159 working-aged patients with chronic low back pain (> 3 months) and at least 1 month of sick leave in preceding year and/or 3 months in preceding two years. Patients had a mean age of 42 years and 59% were men. Pain duration exceeded 5 years in 60% of patients and almost all patients were on sick leave at baseline.

The economic evaluation (Wayne et al. 2019)[14] was conducted in a patient population in the United States at the Osher Clinical Center (OCC) at a tertiary academic hospital and other clinics. The study compared the cost-effectiveness of multidisciplinary care at OCC versus conventional care at non-OCC clinics among patients with chronic low back pain. The analysis included 278 patients and included patients if they had a diagnosis of non-specific chronic-low back pain (> 3 months), over 21 years of age, English speaking and agreed to three follow-up assessments over a 12 month period. Patients in the OCC group had a mean age of 50 years and were 69% female while patients in the non-OCC group had a mean age of 52 years, and were 74% female.

Interventions and Comparators

One systematic review (Liossi et al. 2019)[4] compared interdisciplinary interventions (with various content, number of sessions, and follow-up time-points) coordinated by two or more healthcare professionals of different disciplines with a control or comparison group that included placebo, waiting list or single-disciplinary intervention. Most primary studies included in the systematic review reported treatment durations varying from 3 to 12 weeks. The second systematic review (Peterson et al. 2018)[5] compared multimodal chronic pain care models in primary care setting with usual care (regular access to primary and specialty care). Treatment durations in the primary studies were not reported.

One RCT (Monticone et al. 2017)[12] compared a multidisciplinary rehabilitation program (multimodal exercises combined with psychologist-led cognitive-behavioral therapy sessions) with general physiotherapy for 10 weeks. The study had a 12-month follow-up period. The second RCT (Ronzi et al. 2017)[13] was a three-arm study comparing the following 5-week interventions: an intensive and multidisciplinary program conducted in a rehabilitation center; a less intensive outpatient program conducted by a trained private physiotherapist; and a mixed strategy combining the same outpatient program associated with a weekly multidisciplinary intervention. The study had a 12-month follow-up period.

The economic evaluation (Wayne et al. 2019)[14] evaluated the costs and benefits of integrative care treatment (OCC group) compared to conventional treatment (non-OCC group) in patients with chronic low back pain.

Outcomes

Pain intensity and/or pain-related function were reported in all systematic reviews and RCTs. Other reported outcomes included quality of life, depression, anxiety, sick leave and

school attendance. Details regarding the outcome measures used are provided in Appendix 2.

The economic evaluation estimated the incremental cost-effectiveness ratio (ICER) of integrative care compared to conventional treatment in patients with chronic low back pain using the cost per quality adjusted life year (QALY) metric for each group.

Summary of Critical Appraisal

Additional details regarding the strengths and limitations of the included publications are provided in Appendix 3, Table 5 to Table 7.

Systematic Reviews

Both systematic reviews (Liossi et al. 2019[4] and Peterson et al. 2018[5]) were well conducted. The objective and eligibility criteria were clear and relevant. One systematic review (Liossi et al. 2019)[4] included uncontrolled studies, which may provide lower quality evidence than RCTs.

In both systematic reviews (Liossi et al. 2019[4] and Peterson et al. 2018[5]), comprehensive literature searches were undertaken. Article selection was described and was done in duplicate for Liossi et al. 2019,[4] and data extraction was done by one reviewer and checked by a second reviewer. For Peterson et al. 2018,[5] the authors reported that the review process was streamlined to meet a condensed timeframe by focusing on a subset of high-priority outcomes and settings, and by using sequential instead of independent dual review process to minimize bias. Therefore, both article selection and data extraction were completed by one reviewer and checked by a second reviewer.

One of the two systematic reviews (Liossi et al. 2019)[4] conducted meta-analyses despite the fact that considerable variation was reported across the included studies in term of multidisciplinary interventions and control groups, as well as in the clinical outcome measures. This resulted in high levels of heterogeneity observed in most analyses; however, the robustness of the results was explored through funnel plots and sensitivity analyses.

One systematic review (Peterson et al. 2018)[5] provided limited information regarding the choice and definitions of control groups in the primary studies, resulting in uncertainty regarding interpretation of the findings from between-group analyses.

Both systematic reviews (Liossi et al. 2019[4] and Peterson et al. 2018[5]) reported that there were no conflicts of interest.

RCTs

In both RCTs (Monticone et al. 2017[12] and Ronzi et al. 2017[13]), the study objectives were clear, inclusion and exclusion criteria were described, and details regarding the interventions and comparators were provided. One RCT (Ronzi et al. 2017)[13] included three treatment arms: two multidisciplinary interventions of various intensities and one group undergoing individual rehabilitation with a physiotherapist. Randomization appeared to be appropriate; however, patients and healthcare professionals were not blinded to treatment allocation due to the nature of the intervention and control strategies. Reported baseline characteristics were similar between groups. Both RCTs (Monticone et al. 2017[12] and Ronzi et al. 2017[13]), used appropriate outcome measures and intention to treat analyses were conducted.

For one of the two RCTs (Monticone et al. 2017),[12] similar proportions of patients in each group discontinued from the study. In Ronzi et al. 2017,[13] there was imbalance between groups in the proportions of patients discontinuing from the study (a higher number of patients were lost to follow-up in the Private Intervention Strategy arm compared with patients from the Intensive Intervention Strategy arm). This could impact the findings; however, the direction of the bias in uncertain.

Both RCTs (Monticone et al. 2017[12] and Ronzi et al. 2017[13]) reported that there were no conflicts of interest.

Economic Evaluation

Although the identified economic evaluation (Wayne et al. 2019)[14] was not a model-based study (e.g., decision tree, markov model, etc.) the authors clearly stated the research question, perspective and time frame of the study. However, the type of analysis (observational prospective cohort study) was not clearly justified over other conventional economic evaluations (e.g. cost-effectiveness analysis or cost-utility analysis), and a rationale for not conducting a model-based evaluation was not provided. The clinical and cost outcomes were clearly stated as well as the type of statistical analysis used. The study was conducted in the US and may not be generalizable to the Canadian context due to significant differences in healthcare structure and cost of care and treatment (i.e., medication costs, insurance coverage and out-of-pocket expenses). Additionally, there was variability among patient group characteristics that were not controlled for which may affect the overall outcomes of the study.

Summary of Findings

A detailed summary of study findings is available in Appendix 4, Table 8 to Table 10.

Clinical Effectiveness of Multidisciplinary Treatment Programs

Pain Intensity and Pain-Related Function

A systematic review (Liossi et al. 2019)[4] investigated the effect of interdisciplinary interventions coordinated by two or more healthcare professionals of different disciplines compared with a control or comparison group in pediatric patients with mixed chronic pain diagnoses. Results of the meta-analysis showed that interdisciplinary interventions were superior to control groups in reducing pain intensity after a one-month follow-up. The difference between groups on this outcome did not reach statistical significance after 12 months. However, the meta-analysis demonstrated that participation in interdisciplinary interventions was associated with sustained benefits, as reflected by a significant within-group reduction in pain intensity after 12 months compared to baseline pain levels.

The other systematic review (Peterson et al. 2018)[5] evaluated the benefits of multimodal chronic pain care models compared with usual care in adult patients with chronic neck pain. No meta-analysis was performed considering the high levels of heterogeneity inherent to multidisciplinary programs. The authors concluded that models including both decision support and proactive treatment monitoring were associated with clinically relevant improvement in pain intensity or pain-related function compared with usual care, as reflected by the significantly greater proportion of patients participating in multimodal chronic pain care models who achieved clinically significant improvement from baseline (≥ 30%) at 12 months.

One RCT (Monticone et al. 2017)[12] demonstrated the superiority of a multidisciplinary rehabilitation program compared with general physiotherapy in reducing pain and disability after 12 months in adult patients with chronic neck pain. In addition, participation in a multidisciplinary rehabilitation program was associated with a significant within-group benefit for these outcomes at 12 months compared to baseline.

The other RCT (Ronzi et al. 2017)[13] compared three different intervention strategies: an intensive and multidisciplinary program, an individual rehabilitation program with a private physiotherapist, and a mixed program, in working-aged patients with chronic low back pain and sick leave. The study did not show significant differences among the three intervention strategies for pain intensity. However, results demonstrated that patients from the intensive and mixed intervention strategies, both considered multidisciplinary programs, reported significant within-group improvements at 12 months compared to baseline in almost all evaluated outcomes. The authors concluded that various combinations of individual components in multidisciplinary programs may result in effective pain management. Patients from the private intervention strategy reported no significant improvement over 12 months for several physical and psychosocial outcomes, including pain intensity.

Quality of Life, Including Depression and Anxiety

A systematic review in a pediatric population (Liossi et al. 2019)[4] did not show significant differences between intervention and control groups in terms of quality of life. However, the study demonstrated that participation in interdisciplinary interventions was associated with significant within-group benefits on the outcomes of functional disability, anxiety, depression and catastrophizing at various time points compared to baseline.

Another systematic review (Peterson et al. 2018)[5] reported that 3 out of 6 multimodal chronic pain care models with results on quality of life showed significant benefits of these interventions compared with usual care in adult patients with chronic neck pain, The differences between groups in these primary studies ranged from 8.8 to 19.9 on the Short Form Health Survey Questionnaire (SF-36), a validated outcome measure commonly used to assess health-related quality of life. Results regarding depression and anxiety were reported in 4 models; of these, 3 models showed a statistically significant difference between intervention and control groups on at least one of the outcomes of depression or anxiety.

One RCT (Monticone et al. 2017)[12] demonstrated the superiority of a multidisciplinary rehabilitation program over general physiotherapy on quality of life, kinesiophobia, and pain catastrophizing at 12 months in adult patients with chronic neck pain. For quality of life, results from each of the eight domain scores of the SF-36 showed a mean between-group difference of at least 15% favoring the multidisciplinary intervention strategy ($P < 0.001$). In addition, participation in a multidisciplinary rehabilitation program was associated with a significant within-group benefit at 12 months compared to baseline for the same outcomes of quality of life, kinesiophobia, and pain catastrophizing.

Sick Leave and School Attendance

A systematic review (Liossi et al. 2019)[4] showed that participation in interdisciplinary interventions was associated with significant within-group benefits on school attendance and school functioning in pediatric patients after 3 months. No comparisons were reported between intervention and control groups.

One RCT (Ronzi et al. 2017)[13] did not show significant differences among the three intervention strategies in the number of days of sick leaves in working-aged patients with chronic low back pain. However, results demonstrated that the three different intervention strategies were all associated with a significant within-group decrease in duration of sick leaves 12 months after treatment compared with the 12 months preceding treatment.

Cost-Effectiveness of Multidisciplinary Treatment Programs

The economic evaluation (Wayne et al. 2019)[14] identified a willingness-to-pay threshold of $100,000 per QALY which was not met by calculated incremental cost-effectiveness ratio (ICER) of $436,676 per QALY. The unadjusted chronic low back pain-related costs were higher in the OCC group compared to the non-OCC group while the difference in QALYs between groups was not considered statistically meaningful. A number of variables were adjusted for by descriptive statistical analysis including age, sex, marital status, duration of chronic low back pain treatment, number of days with pain in the last 180 days, smoking status, body mass index and baseline outcome. Bootstrapping analysis determined that cost-savings associated with multidisciplinary care (OCC group) was very unlikely as a majority of bootstrapped QALY differences had better effectiveness at a higher cost. Overall, the researchers concluded that integrative treatment was not cost-effective as the ICER was substantially over the willingness-to-pay threshold with more research required to identify potential benefits of integrative care models for chronic low back pain.

Evidence-Based Guidelines Regarding Multidisciplinary Treatment Programs

No relevant evidence-based guidelines regarding multidisciplinary treatment programs for patients with chronic, non-malignant pain in outpatient settings were identified; therefore, no summary can be provided.

Limitations

Multidisciplinary interventions used in the studies were of different types, and the definition of multidisciplinary treatment varied; the comparators were also variable, so comparisons between studies were difficult.

There was limited evidence for various outcomes such as social function, effect on opioid use, treatment satisfaction and adverse events.

No Canadian studies were identified. Generalizability of the findings from the included studies to the Canadian population of patients who experience chronic, non-malignant pain is uncertain.

No relevant evidence-based guidelines were identified.

Conclusions and Implications for Decision or Policy Making

Two systematic reviews,[4,5] two RCTs,[12,13] and one economic evaluation[14] were included. No relevant evidence-based guidelines were identified.

Overall, findings from the included studies suggested that the multidisciplinary management of chronic non-malignant pain was associated with significant improvements in pain intensity, and may be associated with significant improvements in quality of life and function. Several different outcome measures were used to assess quality of life and function, and a statistically significant difference between multidisciplinary treatment and

control treatment was not always observed for all outcome measures. However, there was substantial variation in the types and definitions of multidisciplinary treatment programs, as well as control interventions, among studies. This suggests that various combinations of individual components in multidisciplinary programs may result in effective pain management. Further research addressing the comparative effectiveness of individual components of multidisciplinary pain management programs may help to determine which combinations provide optimal benefits.

Findings from one economic evaluation suggested that the cost-effectiveness of multidisciplinary pain management programs is uncertain. The difference in quality-adjusted life-years between multidisciplinary treatment and control treatment was not statistically meaningful, and the higher costs associated with multidisciplinary treatment of patients with chronic low back pain resulted in an incremental cost-effectiveness ratio exceeding standard willingness-to-pay thresholds. The researchers concluded that multidisciplinary treatment was not cost-effective based on the available data and that additional research was required to adequately assess potential benefits of multidisciplinary pain management programs.

This an update to a 2017 CADTH Rapid Response report[2] in which the evidence for multidisciplinary treatment programs for patients with chronic, non-malignant pain was assessed. Findings from that previous report regarding clinical effectiveness showed that multidisciplinary treatment programs were associated with significant improvements from baseline in pain and function or disability. The difference between the intervention and control groups for this outcome did not always reach statistical significance; however, the control groups included a wide range of strategies that also provided improvement compared to baseline on pain levels. With respect to quality of life, anxiety, and depression, the report concluded that there seemed to be improvements with multidisciplinary treatments but the difference compared with control treatments was not always significant. No relevant cost-effectiveness studies were identified. One evidence-based guideline recommended multidisciplinary management of chronic non-malignant pain. Two other guidelines recommended such programs in the following circumstances: patients significantly affected by chronic low back pain and with no improvement with primary care management, or patients with chronic non-cancer pain who were using opioids and experiencing serious challenges in tapering.

Findings from the current report are consistent with those from the 2017 CADTH Rapid Response report.[2] Evidence regarding optimal pain management services suggests that there is a benefit from moving beyond the only use of medication to more comprehensive programs. However, further research is needed to identify the type of components and combinations that would provide optimal benefits for patients with chronic pain.

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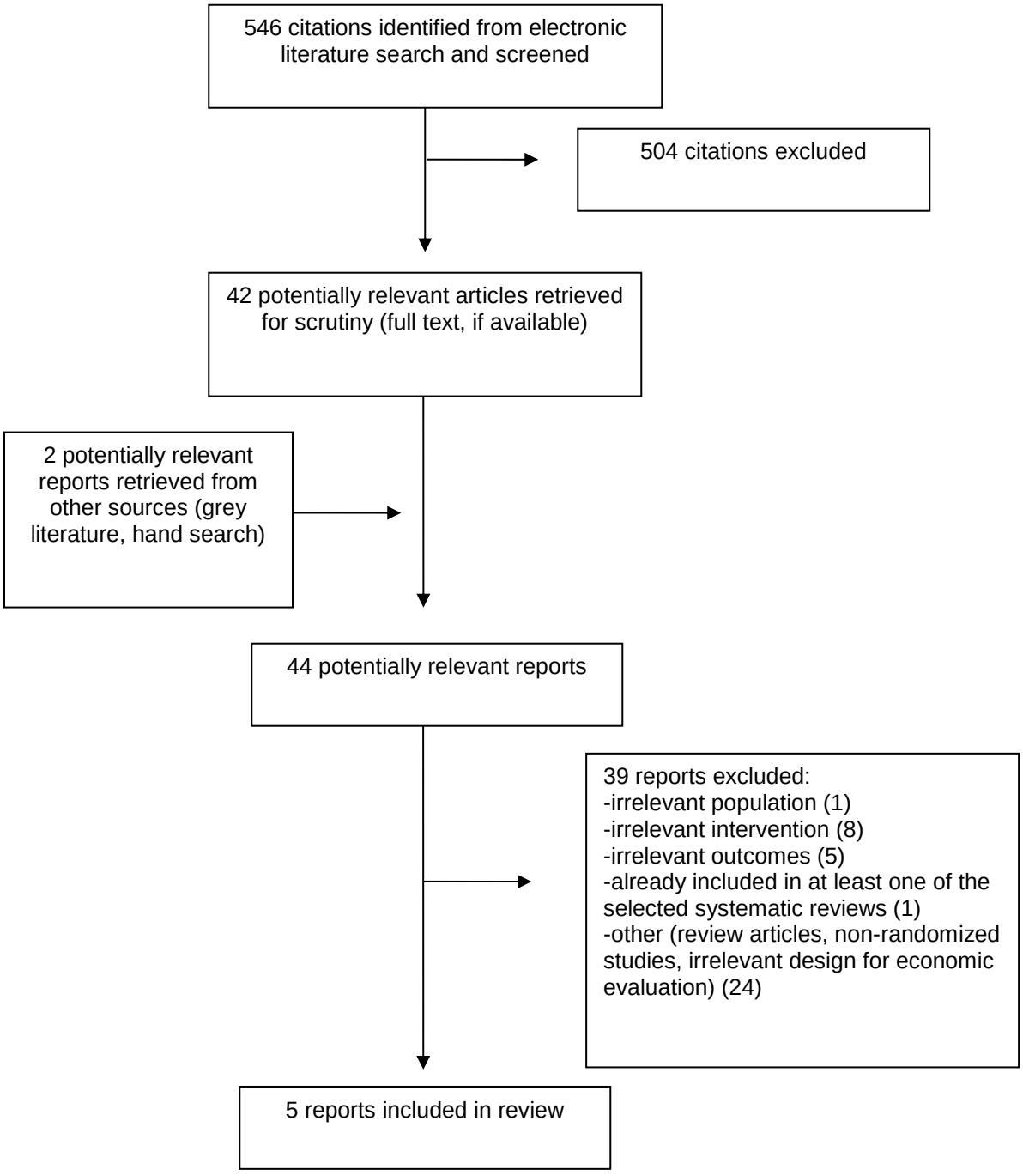
Appendix 1: Selection of Included Studies



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
Liossi et al. 2019[4] **UK**	Systematic review design. Included: 9 RCTs and 19 studies with single group pre-post design.	Pediatric patients with mixed chronic pain diagnoses. High prevalence of chronic headache, abdominal pain, and complex regional pain syndrome. Mean age: 13.8 years (ranged from 3 to 22 years across studies).	Intervention: Interdisciplinary interventions in outpatient or inpatient setting of various content, number of sessions, and follow-up time-points, all coordinated by two or more healthcare professionals of different disciplines. Comparator: Control or comparison group (placebo, waiting list, single disciplinary intervention).	Clinical outcome: Pain intensity Follow-up time points: • Immediately post-treatment • 1 month • 3 months • 12 months
Peterson et al. 2018[5] **US**	Rapid Review design with systematic review methods. Included: 8 RCTs and 1 retrospective cohort study.	Adult patients with chronic musculoskeletal pain. N ≤ 250 in most studies (ranged from 63 to 1,066 patients). Mean age ranged from 37 to 62 years. Baseline pain intensity ranged from 5.1 to 7.7 on a 10-point scale. Mental health comorbidities prevalence ranged from 1 to 24%. Most frequently reported: major depressive disorder, post-traumatic stress disorder, substance use disorder.	Intervention: Multimodal chronic pain care models in primary care setting organized in four system Interventions: • Decision support • Additional care coordination resources • Enhanced patient education and activation • Increased access to a broader range of treatments. Comparator: Usual care (regular access to primary and specialty care).	Clinical outcomes: • Pain intensity or pain-related function • QOL Length of follow-up: 12 months in most studies (ranged from 6 to 18 months).

QOL = quality of life; RCT = randomized controlled trial.

Table 3: Characteristics of Included Clinical Studies

First Author, Publication Year, Country	Study Design	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
Monticone et al. 2017[12] **Italy**	RCT Setting: outpatients specialized rehabilitation center. Methods details: •Permuted-block randomization •Principal investigator and biostatistician blinded to treatment allocation.	Adult patients with chronic neck pain (> 3 months). N=170 85 in intervention; 85 in control group. Age (mean ± SD): 53.8 ± 13.3 years (intervention group) 52.0 ± 12.1 years (control group). Gender: 61% women. Moderate level of disability and pain reported at baseline.	Intervention: Multidisciplinary rehabilitation program combining multimodal exercises with psychologist-led cognitive-behavioural therapy sessions. Two sessions of 1 hour / week for 10 weeks. Comparator: General physiotherapy. One session of 1 hour / week for 10 weeks. Major pharmacological agents prohibited (opioids, steroids, anticonvulsants, antidepressant analgesics).	Clinical outcomes: •Neck Disability Index •Kinesiophobia •Pain catastrophizing •Pain (NRS) •QOL (Short-Form Health Survey) Follow-up time points: •Before training •After training •12 months
Ronzi et al. 2017[13] **France**	RCT Three-arm trial. Setting: mixed outpatient rehabilitation center and private ambulatory treatment. Methods details: •Computerized randomization •Open label treatment allocation.	Working-aged patients with chronic low back pain (> 3 months); and ≥ 1 month of sick leave in preceding year and/or 3 months in preceding 2 years. N=159 49 in intervention 1 54 in intervention 2 56 in intervention 3 Age, mean ± SD (range): 41.5 ± 10.3 (range 23 to 58) years. Sex: 59% men. Pain duration > 5 years in 60% of patients. Almost all patients on sick leave.	Interventions: 1. Intensive and multidisciplinary program conducted in a rehabilitation center. 2. Less intensive outpatient program conducted by a trained private physiotherapist. 3. Mixed strategy combining the same outpatient program associated with a weekly multidisciplinary intervention. Duration: 5 weeks.	Clinical outcomes: •Number of days of sick leave •QOL •Social ability Length of follow-up: 12 months

NRS = numerical rating scale; QOL = quality of life; RCT = randomized controlled trial; SD = standard deviation.

Table 4: Characteristics of Included Economic Evaluation

First Author, Publication Year, Country	Type of Analysis, Time Horizon, Perspective	Decision Problem	Population Characteristics	Intervention and Comparator(s)	Clinical and Cost Data Used in Analysis	Main Assumptions
Wayne et al. 2019[14] **US**	Observational-based study evaluation 12 month time period Societal perspective	*"To report the results of health economic analyses comparing two treatment approaches for CLBP."* (p. 1)	Patients with CLBP who received CIT or usual care at OCC at the same tertiary hospital. Inclusion criteria: > 21 years of age, English speaking, agreed to 3-month follow-up over 12 months. N=278 134 OCC patients 38 non-OCC patients Mean Age: 50.2 years in OCC group 52.1 years in non-OCC group Sex: 31.3% male in OCC group 26.4% male in Non-OCC group	Intervention: CIT (OCC group) Comparator: Usual Care (Non-OCC)	Outcomes: • QALYs • Back pain-related outcomes (RDQ and BOP) Cost data: • daily activities • devices • hospital stays • surgeries • ER visits • injections • medications • office visits	A value of $30 per hour absent from work as used in other studies

BOP = bothersomeness of pain; CIT = coordinated and integrated therapies; CLBP = chronic low back pain; ER = Emergency room; OCC = Osher Clinical Center; RDQ = Roland disability questionnaire.

Appendix 3: Critical Appraisal of Included Publication

Table 5: Strengths and Limitations of Systematic Reviews and Meta-Analyses using ROBIS (Risk of Bias in Systematic Reviews)[15]

Strengths	Limitations
Liossi et al. 2019[4]	
• Objectives and eligibility criteria clear, relevant, reasonable. • Multiple databases (MEDLINE, PsycINFO, CINAHL, Web of Science, SCOPUS, Cochrane Library, PubMed, PubPsych) and grey literature searched until March 22, 2018. • Search strategy described and developed with research team and medical librarian. • Study selection described and performed independently by two review authors. Data extraction completed by one reviewer and checked by at least one second reviewer. • Flow chart of study selection and list of included studies provided. Study characteristics described. • Risk of bias assessed using the Cochrane Risk of Bias tool for randomized and non-randomized controlled trials, and the Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group for the single-group studies. • Meta-analyses conducted. • Funnel plots and sensitivity analyses performed. • It was mentioned that there were no conflicts of interest.	• Considerable variation was reported across the included studies in term of multidisciplinary interventions and control groups, as well as in the clinical outcome measures. High levels of heterogeneity were observed in most analyses. • Inclusion of uncontrolled studies, which may provide lower quality evidence than RCTs.
Peterson et al. 2018[5]	
• Objectives and eligibility criteria clear, relevant, reasonable. • Multiple databases (MEDLINE, CINAHL, Cochrane Database of Systematic Reviews), as well as Agency for Healthcare Research and Quality, Google Scholar and additional grey literature searched from 1996 to October 2016. Additional hand searches of reference list. • Search strategy described. • Study selection and data extraction completed by one reviewer and checked by a second reviewer. • Flow chart of study selection and list of included studies provided. Study characteristics described. • Risk of bias assessed using the Drug Effectiveness Review Project methods for RCTs and risk of bias using the Cochrane's Risk of Bias Tool for cohort studies. • It was mentioned that there were no conflicts of interest.	• The authors reported that the review process was streamlined to meet a condensed timeframe by focusing on a subset of high priority outcomes and settings, and by using sequential instead of independent dual review process to minimize bias. • Meta-analyses were not conducted given the heterogeneity inherent to complex multicomponent interventions such as multidisciplinary programs for chronic pain. • Limited information was provided regarding the control groups that were selected the primary studies, affecting interpretation of the between-group comparisons.

CINAHL = Cumulative Index to Nursing and Allied Health Literature; RCT = randomized controlled trial.

Table 6: Strengths and Limitations of Clinical Studies using the Cochrane Risk of Bias Tool[16]

Strengths	Limitations
Monticone et al. 2017[12]	
Study Design, Intervention and Comparator •Study objective clear with relevant context provided. •Inclusion and exclusion criteria described. •Details regarding intervention and comparator provided. **Selection, Allocation and Disposition of Patients** •Allocation sequence random (permuted-block randomization). •Researchers blinded to treatment allocation. •Baseline characteristics reported and similar between groups. •Similar proportions of patients in each group discontinued from the study. **Outcome Measures** •Use of appropriate outcome measures. **Statistical Analysis** •Intention to treat analysis conducted. •Sufficient power to demonstrate statistical significance for testing of the primary outcome. **Other** •It was mentioned that there were no conflicts of interest.	•Patients and healthcare professionals were not blinded to treatment allocation. •Risk of attention bias due to the differences between groups in terms of time spent with healthcare professionals. •Patient population with moderate levels of pain and disability undergoing rehabilitation for chronic neck pain. Generalizability of the findings to other patient populations is unknown.
Ronzi et al. 2017[13]	
Study Design, Intervention and Comparator •Study objective clear with relevant context provided. •Inclusion and exclusion criteria described. •Details regarding intervention and comparator provided. **Selection, Allocation and Disposition of Patients** •Allocation sequence random (computerized randomization). •Baseline characteristics reported and similar between groups. **Outcome Measures** •Use of appropriate outcome measures. **Statistical Analysis** •Intention to treat analysis conducted. **Other** •It was mentioned that there were no conflicts of interest.	•Open-label treatment allocation. Patients, healthcare professionals and researchers were not blinded to treatment allocation. •Imbalance between groups in the proportions of patients discontinuing from the study (a higher number of patients were lost to follow-up in the Private Intervention Strategy arm compared with patients from the Intensive Intervention Strategy arm). •Population of working-aged patients with chronic low back pain and sick leave. Generalizability of the findings to other patient populations is unknown.

Table 7: Strengths and Limitations of Economic Studies using the Drummond Checklist[17]

Strengths	Limitations
Wayne et al. 2019[14]	
Study design • The research question, economic importance of the research questions, viewpoints of analysis and rationale for choosing alternative programs were clearly stated • The alternative compared was clearly stated • The form of economic evaluation used was stated **Data Collection** • The sources of effectiveness were provided • The primary outcome measures were clearly stated • Methods to value benefits were stated • Details of the subjects from who valuations were obtained were given • Currency and price data were recorded **Analysis and interpretation of results** • Time horizon of costs and benefits was stated • Statistical analysis and confidence intervals were given • The answer to the study question was given • Conclusions followed from data reported • Conclusions were accompanied by appropriate caveats	• The choice of economic evaluation was not justified • No adjustments were made for price inflation • The choice of not using a discount rate was not specified • The findings of this US-based study may not be generalizable to other health system and treatment measures for chronic pain management. • Between-study comparisons of cost-effectiveness were difficult due to variability in populations studied, therapeutic exposures, costs considered and time frames of observation • Most patients in the intervention group were treated at the OCC only during the first 3 months of the study, suggesting a potential delayed impact on disability • Residual confounders, unknown or unmeasured, could have contributed to the overall findings and differences between groups • Unable to obtain information about referral patterns to the OCC and other non-OCC clinics and may result in selection bias • Baseline characteristics of subjects could influence the type of care the subject received and overall health costs and not accounted for

OCC = Osher Clinical Center.

Appendix 4: Main Study Findings and Authors' Conclusions

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

<table>
<tr><th colspan="4">Main Study Findings</th><th>Authors' Conclusion</th></tr>
<tr><td colspan="5">Liossi et al. 2019[4]</td></tr>
<tr><td colspan="4">Pediatric patients with mixed chronic pain diagnoses (high prevalence of chronic headache, abdominal pain, and complex regional pain syndrome).
Meta-Analyses Results
<table>
<tr><th>Clinical Outcome</th><th>Time Point</th><th>Number of Studies (Participants)</th><th>Effect Size (95% CI)</th></tr>
<tr><td colspan="4">Between-Group Analysis</td></tr>
<tr><td rowspan="3">Pain intensity</td><td>0 – 1 month</td><td>4 (194)</td><td>-1.07 (-2.12, -0.01)</td></tr>
<tr><td>3 months</td><td>2 (60)</td><td>-1.12 (-2.68, 0.44)</td></tr>
<tr><td>12 months</td><td>2 (54)</td><td>-0.20 (-1.62, 1.22)</td></tr>
<tr><td>Anxiety</td><td>0 – 1 month</td><td>2 (134)</td><td>-0.06 (-0.40, 0.28)</td></tr>
<tr><td>Catastrophizing</td><td>Post-intervention</td><td>2 (133)</td><td>-0.23 (-0.57, 0.11)</td></tr>
<tr><td>Functional disability</td><td>Post-intervention</td><td>2 (133)</td><td>0.34 (-1.71, 2.39)</td></tr>
<tr><td colspan="4">Within-Group Analysis (Pre – Post)</td></tr>
<tr><td rowspan="5">Pain intensity</td><td>0 – post-intervention</td><td>11 (698)</td><td>0.42 (0.14, 0.69)</td></tr>
<tr><td>0 – 1 month</td><td>4 (299)</td><td>0.93 (0.58, 1.28)</td></tr>
<tr><td>0 – 3 months</td><td>7 (396)</td><td>0.95 (0.39, 1.50)</td></tr>
<tr><td>0 – 6 months</td><td>2 (67)</td><td>0.78 (-0.30, 1.87)</td></tr>
<tr><td>0 – 12 months</td><td>4 (334)</td><td>1.45 (0.70, 2.20)</td></tr>
<tr><td rowspan="2">Functional disability</td><td>0 – post-intervention</td><td>10 (869)</td><td>1.11 (0.70, 1.51)</td></tr>
<tr><td>0 – 3 months</td><td>4 (271)</td><td>0.77 (0.01, 1.53)</td></tr>
<tr><td rowspan="3">Anxiety</td><td>0 – post-intervention</td><td>3 (164)</td><td>0.30 (-0.10, 0.70)</td></tr>
<tr><td>0 – 3 months</td><td>3 (204)</td><td>0.46 (0.32, 0.60)</td></tr>
<tr><td>0 – 12 months</td><td>2 (156)</td><td>0.57 (0.40, 0.74)</td></tr>
<tr><td rowspan="4">Depression</td><td>0 – post-intervention</td><td>8 (564)</td><td>0.36 (0.17, 0.55)</td></tr>
<tr><td>0 – 1 month</td><td>2 (264)</td><td>0.65 (0.52, 0.79)</td></tr>
<tr><td>0 – 3 months</td><td>3 (230)</td><td>0.31 (-0.04, 0.66)</td></tr>
<tr><td>0 – 12 months</td><td>2 (152)</td><td>0.31 (-0.18, 0.79)</td></tr>
<tr><td rowspan="2">Catastrophizing</td><td>0 – post-intervention</td><td>5 (328)</td><td>0.75 (0.53, 0.97)</td></tr>
<tr><td>0 – 3 months</td><td>3 (132)</td><td>0.76 (0.30, 1.22)</td></tr>
<tr><td>School attendance</td><td>0 – 3 months</td><td>4 (304)</td><td>0.64 (0.11, 1.17)</td></tr>
<tr><td>School functioning</td><td>0 – 3 months</td><td>2 (188)</td><td>0.35 (0.20, 0.49)</td></tr>
</table>
CI = confidence interval.</td><td>"Patients randomized to interdisciplinary interventions reported significantly lower pain intensity 0-1 month post-intervention compared with patients randomized to the control groups. Within-groups analysis of patients receiving interdisciplinary interventions showed significant improvements pre- to post-intervention in pain intensity, functional disability, anxiety, depression, catastrophizing, school attendance, school functioning, and pain acceptance. Few differences were found between interventions delivered in inpatient vs outpatient settings." (p. 1)</td></tr>
<tr><td colspan="5">Peterson et al. 2018[5]</td></tr>
<tr><td colspan="4">Adult patients with chronic musculoskeletal pain.</td><td>"Multimodal chronic pain care</td></tr>
</table>

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

Main Study Findings	Authors' Conclusion
Meta-analyses were not conducted. **Results – Intervention versus Control Group**	*delivery models coupling decision support with proactive treatment monitoring consistently provide clinically relevant improvement in pain and function.*" (p S71)

Clinical Outcome	Findings
Decision support coupled with case management (N=7 models of multimodal care)	

Pain intensity / Pain-related function	• Results reported for N=5 models.
	• Assessed as the proportion of patients with clinically significant improvement from baseline (≥ 30%).
	• Between-group difference reached statistical significance in 4 models of multimodal care at 12 months (NNT ranged from 4.1 to 12.7).
	• Outcome measures included:
	  ○ Roland-Morris Disability Questionnaire (RMDQ)
	  ○ Brief Pain Inventory (BPI)
	  ○ Outcome Measures in Rheumatology-Osteoarthritis Research Society International (OMERACT-OARSI).

QOL	• QOL results reported for N=6 models. • Between-group differences reached statistical significance in 3 models and ranged from 8.8 to 19.9 on the SF-36.

Depression and anxiety	• Results reported for N=4 models.
	• Between-group difference reached statistical significance on at least one of the outcomes of depression or anxiety in 3 models.
	• Outcome measures included:
	  ○ Patient Health Questionnaire (PHQ-9)
	  ○ Hospital Anxiety and Depression Scale (HADS)
	  ○ Generalized Anxiety Disorder (GAD-7)

Opioid use	• Results reported for N=3 models. • No statistically significant difference was reported between groups in the primary studies in opioid prescription or treatment duration.
Risk/complexity-matched treatment pathways (N=1 model of multimodal care)	
Pain intensity / Pain-related function	• Assessed as the proportion of patients with clinically significant improvement from baseline (≥ 30%). • The between-group difference reached statistical significance assessed with the Roland-Morris Disability Questionnaire (RMDQ).
QOL	The between-group difference reached statistical significance for the Short Form 12 (SF-12) physical score, but not for the mental score.
Depression and anxiety	The between group difference reached statistical significance for the outcome of depression, but not anxiety (assessed with HADS).
Increasing access via group multidisciplinary intervention sessions (N=1 model of multimodal care)	
QOL	The between-group difference reached statistical significance for the SF-36 physical score. Statistical significance was not reached for the other SF-36 reported domains.

EQ-5D = EuroQol health-related quality of life; NNT = number needed to treat; QOL = quality of life; SF-36 = Short Form Health Survey Questionnaire.

RCT = randomized controlled trial.

Note: This is a summary table of the most relevant outcomes assessed in the included studies. Additional outcome results are found in the publications.

Table 9: Summary of Findings of Included Clinical Studies

Main Study Findings	Authors' Conclusion
Monticone et al. 2017[12]	

RCT in adult patients with chronic neck pain and moderate level of disability and pain reported at baseline.

Clinical Outcome, Estimated marginal means (95% CI)	Time Point	Intervention Strategy (10-week duration)		SS*
		Multidisciplinary N=85	General Exercise N=85	
Neck Disability Index (0–100)	Baseline	41.9 (40.7 - 43.2)	41.1 (39.8 - 42.3)	*P* < 0.001
	Post-Intervention	24.3 (22.4 - 26.2)	36.7 (34.8 - 38.6)	
	12 months	21.7 (19.7 - 23.6)	37.3 (35.4 - 39.3)	
Tampa Scale for Kinesiophobia (13–52)	Baseline	28.0 (26.2 - 29.7)	28.2 (26.5 - 30.0)	*P* < 0.001
	Post-Intervention	18.2 (16.6 - 19.8)	28.3 (26.7 - 29.8)	
	12 months	16.8 (15.3 - 18.2)	29.1 (27.7 - 30.6)	
Pain Catastrophizing Scale (0–52)	Baseline	20.4 (19.0 - 21.9)	20.8 (19.4 - 22.2)	*P* < 0.001
	Post-Intervention	13.4 (12.9 - 14.8)	20.2 (18.8 - 21.6)	
	12 months	12.2 (10.9 - 13.5)	21.2 (19.9 - 22.5)	
Pain intensity on NRS (0–10)	Baseline	6.0 (5.7 - 6.2)	6.1 (5.9 - 6.3)	*P* < 0.001
	Post-Intervention	2.1 (1.8 - 2.3)	5.3 (5.1 - 5.6)	
	12 months	2.1 (1.8 - 2.3)	5.6 (5.3 - 5.8)	
SF-36 Physical function domain (0–100)	Baseline	49.4 (47.1 - 51.7)	51.1 (48.8 - 53.4)	*P* < 0.001
	Post-Intervention	80.1 (77.5 - 82.7)	62.0 (59.4 - 64.6)	
	12 months	86.4 (83.7 - 89.0)	64.5 (61.9 - 67.2)	
SF-36 Mental health domain (0–100)	Baseline	51.3 (48.8 - 53.9)	52.0 (49.4 - 54.5)	*P* < 0.001
	Post-Intervention	84.8 (82.5 - 87.2)	62.7 (60.3 - 65.1)	
	12 months	88.2 (85.7 - 90.7)	67.9 (65.4 - 70.4)	

CI = confidence interval; NRS = numerical rating scale; SF-36 = Short Form Health Survey Questionnaire; SS = statistical significance.
*P-values are for time effect, for group effect and for time by group interaction effect (linear mixed model). All p-values reported were statistically significant with p<0.001.

Authors reported the following findings:

- The within-group improvements observed over 12 months in the clinical outcomes of disability and pain intensity were significantly greater in the Multidisciplinary Intervention Strategy group compared to the General Exercise group.
- Results from the eight domain scores of the SF-36, a quality of life measure, showed a mean between-group difference of at least 15% in favor of the Multidisciplinary Intervention Strategy (*P* < 0.001).
- Patients assessed treatment effectiveness at 12 months using the 5-point Likert Global Perceived Effect scale. Patients from the Multidisciplinary Intervention Strategy group were

"*The present study showed that a group-based multidisciplinary program including both multimodal exercises and cognitive-behavioral therapy was superior to a group-based general physiotherapy in the management of subjects with chronic neck pain. The between-group differences were clinically meaningful for disability, pain relief, quality of life, kinesiophobia and catastrophizing, and were maintained at long-term.*" (p 749)

Table 9: Summary of Findings of Included Clinical Studies

<table>
<tr><th>Main Study Findings</th><th>Authors' Conclusion</th></tr>
<tr><td>statistically significantly more satisfied with the intervention compared with patients from the General Exercise group (P < 0.001).
• At 12 months, all patients (n = 78) from the Multidisciplinary Intervention Strategy group returned to their work activities. Five patients (out of n = 77) from the General Exercise group remained on sick leave.</td><td></td></tr>
<tr><td colspan="2">Ronzi et al. 2017[13]</td></tr>
<tr><td>Three-arm RCT in working-aged patients with chronic low back pain and sick leave.

Change from Baseline to 12 Months
<table>
<tr><th rowspan="2">Clinical Outcome, Median (Interquartile Range Q1-Q3)</th><th colspan="3">Intervention Strategy (5-week duration)</th><th rowspan="2">SS*</th></tr>
<tr><th>Intensive N=49</th><th>Mixed N=56</th><th>Private N=54</th></tr>
<tr><td>Sick leave days over 12 months</td><td>50.5 (0.0-200.0)</td><td>47.0 (10.0-199.0)</td><td>45.0 (0.0-98.0)</td><td>ns</td></tr>
<tr><td>Pain intensity on VAS</td><td>45 (25-59)</td><td>37 (15-61)</td><td>33 (19-48)</td><td>ns</td></tr>
<tr><td>SF-36 PCS</td><td>39.1 (33.8-50.4)</td><td>41.6 (34.2-49.9)</td><td>37.5 (33.0-46.8)</td><td>ns</td></tr>
<tr><td>SF-36 MCS</td><td>48.3 (42.1-53.4)</td><td>46.6 (38.7-56.6)</td><td>48.9 (41.4-54.8)</td><td>ns</td></tr>
</table>
ns = non-significant; SF-36 MCS = Mental Component Summary of the Short Form Health Survey Questionnaire; SF-36 PCS = Physical Component Summary of the Short Form Health Survey Questionnaire; SS = statistical significance; VAS = visual analog scale.
*Between-group statistical significance assessed with p-value (Kruskal–Wallis test).
Note: Within-group statistical testing not reported.

Authors reported the following within-group findings (no numerical results reported):
• In the three intervention groups, duration of sick leaves decreased significantly during the 12 months that followed treatment interventions compared with the 12 months preceding treatment.
• In the Intensive and Mixed Intervention Strategy treatment groups, there was a significant improvement at 12 months compared to baseline in almost all evaluated outcomes.
• In the Private Intervention Strategy treatment group, there was no significant improvement over 12 months for several physical and psychosocial outcomes, including pain intensity.</td><td>"This study confirms that disparate treatments might show similar effectiveness because they could all work through concomitant changes in beliefs, attitudes, and coping mechanisms. The original mixed strategy can treat a larger number of chronic low back pain patients, at a lower cost and provide local community-based care." (p 1364-5)</td></tr>
</table>

RCT = randomized controlled trial.
Note: This is a summary table of the most relevant outcomes assessed in the included studies. Additional outcome results are found in the publications.

Table 10: Summary of Findings of Included Economic Evaluation

Main Study Findings	Authors' Conclusion
Wayne et al. 2019[14]	
Cost outcomes • At 3 months, the total unadjusted mean costs per patient were higher for OCC group than non-OCC group (difference per patient $947) • At 3 to 6 months, the cost difference was reduced to $235 per patient (95% CI: -282 to 752) • At 6 to12 months, the cost difference increased to $391 per patient (95% CI: -1,078 to 1,861) • Annual unadjusted mean costs per patient was higher for OCC group than non-OCC group $9,106 (95% CI: 6,233 to 11,980) versus $6,283 (95% CI: 4,522 to 8,043) • Annual adjusted mean costs per were significantly higher for OCC group than non-OCC group $11,527 (95% CI: 7,766 to 15,287) versus $6,811 (95% CI: 3,763 to 9,858) **Effectiveness outcomes** • Unadjusted QALYs were higher in OCC group compared to non-OCC group over 12 months (0.6989 versus 0.6205) • Adjusted QALYs were not statistically different between OCC group and non-OCC group (0.6420 versus 0.6312) **Cost effectiveness** • ICER: $436,676 per QALY gained in OCC group • Cost savings with intervention is unlikely	• Primary back-pain specific clinical outcomes (RDQ and BOP) improved and were statically greater in OCC groups compared to non-OCC group • ICER was not below the WTP threshold ($100,000 per QALY) and not considered cost-effective • Patients who utilized integrative care in a hospital setting may have differed from those who utilized usual care treatments • Overall, self-reported costs (e.g. frequency of medication, medication costs, doctor visits) were higher in the integrative care group with no relative effect on QALYs compared to conventional treatment although RDQ and BOP outcomes significantly improved for the integrative care group • It may be beneficial for future studies to consider randomization of subjects and longer study design to evaluate the cost-effectiveness of integrative care for CBLP

BOP= bothersomeness of pain; CI = confidence interval; CLBP = chronic low back pain; ICER = incremental cost-effectiveness ratio; OCC = Osher Clinical Center; QALY = quality adjusted life years; RDQ = Roland disability questionnaire; WTP = willingness to pay.

Appendix 5: Additional References of Potential Interest

Non-Randomized Studies

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Revivo G, Amstutz DK, Gagnon CM, McCormick ZL. Interdisciplinary pain management improves pain and function in pediatric patients with chronic pain associated with joint hypermobility syndrome. *PM R*. 2019 Feb;11(2):150-157.

Guildford BJ, Daly-Eichenhardt A, Hill B, Sanderson K, McCracken LM. Analgesic reduction during an interdisciplinary pain management programme: treatment effects and processes of change. *Br J Pain*. 2018 May;12(2):72-86.

Joypaul S, Kelly FS, King MA. Turning pain into gain: evaluation of a multidisciplinary chronic pain management program in primary care. *Pain Med*. 2018 Dec 12.

Patwardhan A, Matika R, Gordon J, Singer B, Salloum M, Ibrahim M. Exploring the role of chronic pain clinics: potential for opioid reduction. *Pain Physician*. 2018 Nov;21(6):E603-e610.

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White LD, Summers P, Scott A. Changes in clinical status after completion of an interdisciplinary pain management programme incorporating pain neurophysiology education. *Physiother Can*. 2018 Fall;70(4):382-392.

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