PROTOCOL

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The impact of chiropractic care on prescription opioid use for non-cancer spine pain: protocol for a systematic review and meta-analysis

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Abstract

Background In recent studies, receipt of chiropractic care has been associated with lower odds of receiving prescription opioids and, among those already prescribed, reduced doses of opioids among patients with non-cancer spine pain. These findings suggest that access to chiropractic services may reduce reliance on opioids for musculoskeletal pain.

Objective To assess the impact of chiropractic care on initiation, or continued use, of prescription opioids among patients with non-cancer spine pain.

Methods We will search for eligible randomized controlled trials (RCTs) and observational studies indexed in MED-LINE, Embase, AMED, CINAHL, Web of Science, and the Index to Chiropractic Literature from database inception to June 2024. Article screening, data extraction, and risk-of-bias assessment will be conducted independently by pairs of reviewers. We will conduct separate analyses for RCTs and observational studies and pool binary outcomes (e.g. prescribed opioid receipt, long-term opioid use, and higher versus lower opioid dose) as odds ratios (ORs) with associated 95% confidence intervals (CIs). When studies provide hazard ratios (HRs) or relative risks (RRs) for time-to-event data (e.g. time-to-first opioid prescription) or incidence rates (number of opioid prescriptions over time), we will first convert them to an OR before pooling. Continuous outcomes such as pain intensity, sleep quality, or morphine equivalent dose will be pooled as weighted mean differences with associated 95% CIs. We will conduct meta-analyses using random-effects models and explore sources of heterogeneity using subgroup analyses and meta-regression. We will evaluate the certainty of evidence of all outcomes using the GRADE approach and the credibility of all subgroup effects with ICEMAN criteria. Our systematic review will follow the PRISMA statement and MOOSE guidelines.

Discussion Our review will establish the current evidence informing the impact of chiropractic care on new or continued prescription opioid use for non-cancer spine pain. We will disseminate our results through peer-reviewed publication and conference presentations. The findings of our review will be of interest to patients, health care providers, and policy-makers.

Trial registration Systematic review registration: PROSPERO CRD42023432277.

Keywords Systematic review, Meta-analysis, Spine pain, Opioid, Chiropractic

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Background

Low back pain remains the leading cause of years lived with disability (YLD) worldwide [1]. In 2017, low back pain was responsible for around 64.9 million YLD, an increase of 47.5% since 1990; YLD due to neck pain also increased by 65.8% during the same period [1]. In North America, opioids are commonly prescribed to relieve low back and neck pain [2]; however, opioids provide only modest improvements in pain intensity, physical function, and sleep quality [3, 4]. Moreover, opioids are associated with rare but catastrophic risks, including nonfatal and fatal unintentional overdose, and 1 in 20 patients prescribed opioids for chronic pain will develop an opioid use disorder [5–7]. Accordingly, current clinical practice guidelines recommend optimization of non-opioid pharmacotherapy and non-pharmacologic treatments (e.g. education, exercise, cognitive behavioural therapy, soft-tissue massage, spinal manipulation) rather than prescription opioids as first-line therapy for acute or chronic non-cancer musculoskeletal pain [6, 8, 9].

In several recent studies, receipt of chiropractic care has been associated with lower chances of receiving prescription opioids [10–16] and, among those already prescribed, reduced opioid dose [17–19] among patients with non-cancer spine pain. A 2022 observational study of 40,929 opioid-naive persons with new-onset low back pain found that those who received chiropractic treatment early in their complaint had 12% lower odds of incident opioid use (adjusted odds ratio [OR] = 0.88; 95% confidence interval [CI], 0.80 to 0.97) and 44% lower odds of long-term opioid use (adjusted *OR* = 0.56; 95% *CI*, 0.40 to 0.77) [13]. A 2022 mixed-methods analysis of 210 opioid-using community health centre patients with chronic back or neck pain [19] found that the rate of prescription opioid fills over 12-month follow-up was 34% lower (adjusted incidence rate ratio (IRR) = 0.66; 95% *CI*, 0.52 to 0.83), and refills were 73% lower (adjusted *IRR* = 0.27; 95% *CI*, 0.17 to 0.42), among those who initiated chiropractic care (*n* = 49) versus non-recipients (*n* = 161). Recipients were also between 78 and 86% less likely to be prescribed a higher (i.e. ≥ 50-mg morphine equivalents daily [MED]) opioid dose [19]. These findings, combined with those of other reports [10–20], suggest that access to chiropractic services may reduce reliance on opioids for acute or chronic musculoskeletal pain.

A prior systematic review and meta-analysis of six uncontrolled observational studies [20] found an inverse association between attending a chiropractor and opioid receipt among patients with spinal pain (pooled *OR* = 0.36; 95% *CI*, 0.30 to 0.43). However, the literature search informing this systematic review was conducted up to April 18, 2018, the certainty of evidence was not examined, and assessments of risk of bias and heterogeneity were suboptimal [20]. Moreover, at least 10 additional studies investigating the effect of chiropractic care on new and existing opioid use have since been published [10–19]. As such, an updated systematic review and meta-analysis on chiropractic use and opioid receipt among patients with spinal pain is warranted.

Objectives

The purpose of our systematic review is to assess the impact of chiropractic care on (1) initiation, or continued use, of prescription opioids and (2) patient-important outcomes, including pain intensity, physical and emotional functioning, sleep quality, patient satisfaction, and adverse events, among adult patients with non-cancer spine pain. Our focus is on non-cancer spine pain because cancer-related spine pain is a contraindication to high-velocity, low-amplitude spinal manipulation [21]. We will explore whether our results are influenced by factors such as the year the study was conducted, methodological quality, whether pain is acute or chronic, type of opioid prescriber(s), earlier versus later chiropractic exposure, or frequency of chiropractic treatment visits.

Methods

We have reported our systematic review protocol in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) statement [22] (Additional file 1). Our protocol is also registered in the International Prospective Register of Systematic Reviews (PROSPERO) with the registration number CRD42023432277.

Eligibility criteria

Our eligibility criteria are summarized below using the PICOS (i.e. Population, Intervention, Comparison intervention, Outcome measures, Study designs) framework [23].

Participants/population

Inclusion

We will include adult patients (≥ 18 years of age) with non-cancer back or neck pain (with or without radicular symptoms) of any duration.

Exclusion

We will exclude patients with spinal neoplasms or other contraindications to chiropractic treatment (i.e. 'red flag' diagnoses such as fractures, infections, inflammatory arthritis, or cauda equina syndrome) [21].

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Intervention/exposure

Our exposure of interest will be receipt of chiropractic care, which is defined as care provided by a chiropractor, including, but not limited to spinal manipulation, soft-tissue therapy, education, reassurance, and self-care advice (e.g. icing, stretching, and strengthening exercises) [24].

Comparator/control

The comparison will be nonreceipt of chiropractic care (e.g. usual medical care, physiotherapy).

Outcomes

Primary outcomes

Our primary outcomes will be as follows: (1) prescription opioid receipt and (2) continued prescription opioid use (measured as the number and/or dose of opioid prescriptions).

Secondary outcomes

We will extract data on all other patient-important outcomes [25] that are reported, including the following: (1) pain intensity, (2) physical functioning, (3) emotional functioning, (4) sleep quality, (5) patient satisfaction, and (6) adverse events [26, 27]. We will consider outcomes for physical and emotional functioning that are reported over a minimum 4-week follow-up period.

Study designs

Inclusion

We will include both randomized and non-randomized (quasi-experimental) controlled trials and observational studies (including cohort and case–control studies) that reported an adjusted analysis exploring the association between receipt of chiropractic care and opioid use.

Exclusion

We will exclude case reports, case series, cross-sectional studies, protocols, letters, editorials, commentaries, books and book chapters, dissertations, conference abstracts, and secondary sources of evidence, including clinical practice guidelines and systematic, scoping, or narrative reviews.

We will not exclude studies based on geographic location, language, or date of publication. Studies that either were published before, or were included in, the 2020 systematic review by Corcoran et al. [20] will be re-examined to ensure a comprehensive literature search and to validate eligibility.

Information sources

We will search MEDLINE, Embase, AMED, CINAHL, Web of Science, and the Index to Chiropractic Literature without geographic or language restrictions from the inception of each database to June 2024. Our database-specific search strategies have been developed by an academic librarian (RJC) and were reviewed by a second librarian using the peer review of electronic search strategies (PRESS) checklist [28] (Additional files 2 and 3). We will also hand-search reference lists of eligible articles and related systematic reviews and contact content experts to identify additional eligible studies. We will re-run our database searches prior to our final analyses and retrieve any additional eligible studies for inclusion.

Study selection

After duplicate records have been removed (see Fig. 1), pairs of reviewers will independently screen titles, abstracts, and full-text studies for eligibility using online systematic review software (DistillerSR, Evidence Partners, Ottawa, Canada; https://www.distillersr.com/). Calibration exercises will be conducted prior to title/abstract and full-text screening to improve consistency between reviewers throughout the study selection process. Disagreements on eligibility will be resolved through discussion to achieve consensus or, when not possible, adjudication by a third reviewer. We will calculate inter-rater agreement on title/abstract and full-text screening using an adjusted kappa (κ) statistic [29] and interpret the strength of agreement at each stage as follows: poor ($\kappa \leq 0.2$), fair ($0.21 \leq \kappa \leq 0.4$), moderate ($0.41 \leq \kappa \leq 0.6$), substantial ($0.61 \leq \kappa \leq 0.8$), or almost perfect ($\kappa > 0.8$). We will adapt our screening processes (e.g. re-train or substitute raters) if κ agreement on title/abstract or full-text screening is < 0.6 [30]. A PRISMA flow diagram [31] of our study selection process is provided in Fig. 1.

Data collection process

Using standardized, pre-piloted data extraction forms, pairs of reviewers will independently extract data from included studies. We will conduct calibration exercises prior to our formal data extraction and quality assessment procedures to ensure consistency between reviewers. Extracted information will include the following: (1) the last name of first author, (2) year of publication; (3) country where the study was conducted; (4) study design; (5) number of participants; (6) participant demographics (i.e. age, sex, primary pain complaint); (7) chiropractic care and control group information (e.g. proportion of patients receiving chiropractic or usual medical care; type of usual medical care provided, such as primary or specialist care; number of days between the index visit date and initiation of chiropractic care; number of chiropractic treatment sessions attended over follow-up); (8) duration of follow-up; (9) details on opioid use
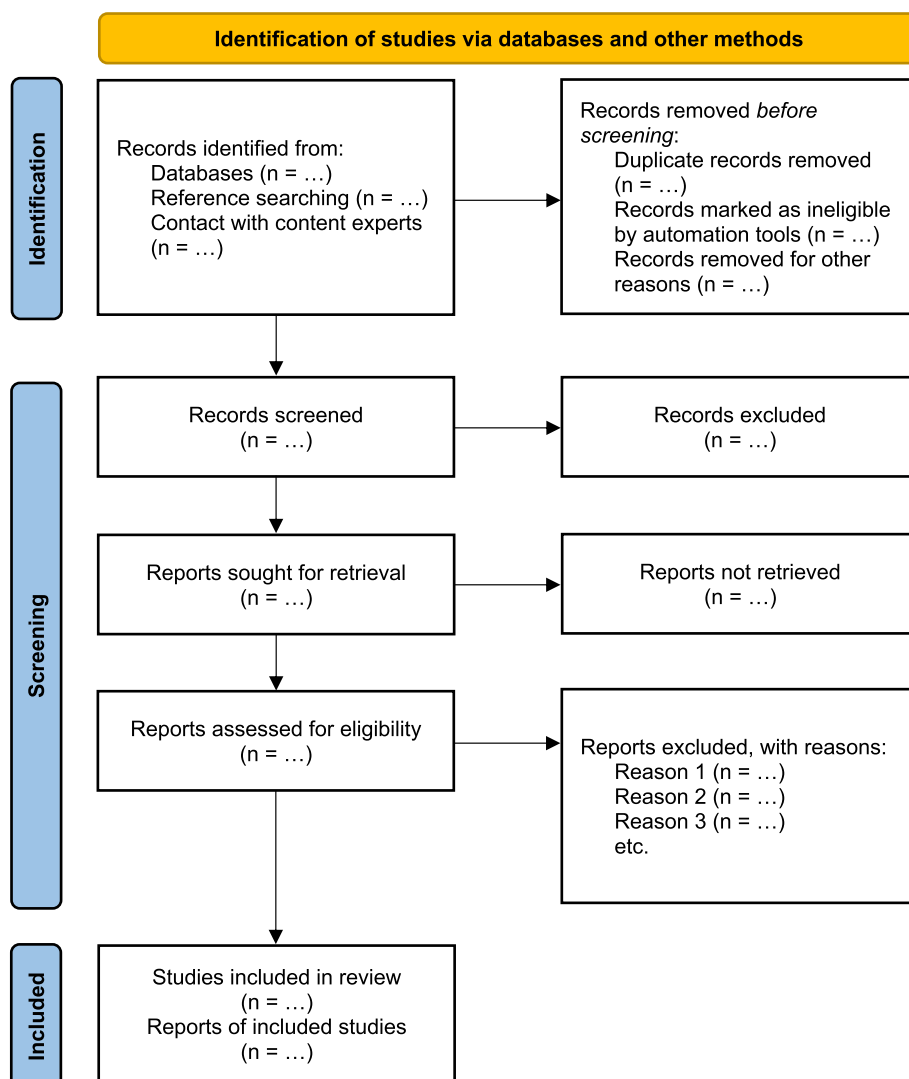
Identification of studies via databases and other methods

Identification

Records identified from:
Databases (n = …)
Reference searching (n = …)
Contact with content experts
(n = …)

Records removed *before screening*:
Duplicate records removed
(n = …)
Records marked as ineligible
by automation tools (n = …)
Records removed for other
reasons (n = …)

Screening

Records screened
(n = …)

Records excluded
(n = …)

Reports sought for retrieval
(n = …)

Reports not retrieved
(n = …)

Reports assessed for eligibility
(n = …)

Reports excluded, with reasons:
Reason 1 (n = …)
Reason 2 (n = …)
Reason 3 (n = …)
etc.

Included

Studies included in review
(n = …)
Reports of included studies
(n = …)

Fig. 1 PRISMA flow diagram

(i.e. proportion of sample prescribed opioids and, when available, total number and dose of opioid prescriptions); and (10) all patient-important outcomes including pain intensity, physical and emotional functioning, sleep quality, patient satisfaction, and adverse events. Discrepancies between reviewers will be resolved as previously described. We will also contact study authors when necessary to request unpublished or missing data or for clarification regarding eligibility.

Risk of bias in individual studies

Two reviewers will independently assess risk of bias of eligible randomized controlled trials (RCTs) and quasi-experimental studies using a risk-of-bias tool developed by the CLARITY group (https://www.distillersr.com/

resources), according to the following domains: sequence generation; allocation concealment; blinding of patients, health care providers, data collectors, outcome assessors, and data analysts; infrequent missing data (> 20% will be considered high risk of bias); and selective outcome reporting. For this final item, we will search clinical trial registries (e.g. clinicaltrials.gov) to compare studies' pre-specified outcomes with their published results. When protocols are not available, we will compare the methods and results in each trial publication. Response options for each item will be categorized as 'definitely or probably yes' (assigned as low risk of bias) and 'definitely or probably no' (assigned as high risk of bias). We will also use criteria suggested by the CLARITY group to assess the risk of bias of observational (i.e. cohort and case control)

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studies, including the following: selection bias, assessment of exposure, validity of outcome assessment(s), control of confounding variables (with adjustment for age, sex, and severity or duration of non-cancer spine pain, at a minimum, considered as an adequately adjusted model), and loss to follow-up. Disagreements between reviewers will be resolved by consensus or adjudication by a third reviewer.

Data synthesis

We will pool all binary outcomes that are reported by more than one study (e.g. prescribed opioid receipt, long-term opioid use, higher versus lower opioid dose) using ORs and associated 95% CIs. We will use a threshold of 50-mg MED to define higher versus lower opioid dose [6]. When studies provide hazard ratios (HRs) and relative risks (RRs) for time-to-event data (e.g. time-to-first opioid prescription) or incidence rates (number of opioid prescriptions over time), we will convert the HR or RR to an OR using a baseline risk (i.e. proportion of patients in the non-chiropractic care control group who had the events) before pooling [32]. Continuous outcomes such as pain intensity, physical and emotional functioning, sleep quality, or morphine equivalent dose will be pooled as weighted mean differences (WMDs) with associated 95% CIs after converting different instruments that report on the same domain (e.g. pain) into the most commonly reported scale among studies eligible for review [33, 34]. For all outcomes, we will conduct separate analyses for RCT/quasi-experimental and observational studies and prioritize adjusted over unadjusted effect estimates from observational studies if both sets of data are available.

We will conduct all meta-analyses using random-effects models [35] and the DerSimonian-Laird method [36]. We will also explore the consistency of association between our pooled results and studies reporting the same outcome domains that were unable to be pooled.

To avoid overestimating the magnitude of effect or association when restricting statistical pooling to estimates that appear in adjusted regression models, we will impute an OR of '1' or WMD of '0' for effects (from RCTs) and associations (from observational studies) that were tested in bivariable analyses but because of non-significance were excluded from adjusted analyses or were included in multivariable analyses with the only information provided being that they were 'not significant'. We will impute an associated variance for all such estimates using the hot deck approach [37].

If there are ≥ 10 studies available for meta-analysis [35], publication bias will be assessed for each outcome by visual assessment of funnel plots for asymmetry and calculation of Egger's test [38] for continuous outcomes and

Harbord's test [39] for binary outcomes. We will evaluate the certainty of evidence for all pooled measures of association using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach [40–42] (Tables 1 and 2). All analyses will be performed using Stata V.18 (StataCorp, College Station, TX, USA), and comparisons will be two-tailed using a statistical significance threshold (α) of 5%.

Subgroup, meta-regression, and sensitivity analyses

Heterogeneity will be examined through tau-squared and visual inspection of forest plots [42, 43]. When there are at least two studies in each subgroup, we will explore sources of heterogeneity with six prespecified subgroup hypotheses, assuming larger effects or associations with the following: (1) studies conducted in earlier versus later calendar years — a proxy for increased pressure on physicians to reduce opioid prescribing [6, 8]; (2) higher versus lower risk of bias, evaluated on a criterion-by-criterion basis; (3) acute versus chronic pain; (4) general practitioner versus specialist (e.g. physiatrist/pain physician) or emergency department opioid prescriber(s) [11, 13]; (5) early versus later chiropractic exposure; and (6) lower versus higher frequency of chiropractic treatment visits [14, 19, 44]. In line with previous literature [12–14, 16], we will define 'early' chiropractic exposure as receipt of chiropractic services within the first 30 days after an index visit for acute or chronic non-cancer spine pain.

When there are at least 10 studies available [35, 45], we will use meta-regression to explore the relationship between time period or chiropractic visit frequency and the association of chiropractic care on opioid use. If we find a significant slope, we will use the distribution of the scatter plot to determine an appropriate cut-off value for our subgroup analyses involving studies conducted in earlier versus later calendar years and lower versus higher frequency of chiropractic treatment visits. Tests for interaction will be performed to establish whether subgroups differ significantly from one another, and we will assess the credibility of significant subgroup effects (test for interaction $p < 0.05$) using the Instrument for Assessing the Credibility of Effect Modification Analyses (ICEMAN) criteria [46].

We will conduct sensitivity analyses to examine the impact of converting ORs from HRs or RRs, and to examine the effect of imputing data for nonsignificant effects or associations.

Patient and public involvement

We did not engage patients or the public as direct contributors to the current protocol. However, we prefaced our review with two mixed-methods studies, including interviews of people with lived and living experience of spine pain, opioid use, and chiropractic care [14,

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Table 1 GRADE evidence profile of the associations between chiropractic care and initiation, or continued use, of prescription opioids and other patient-important outcomes for non-cancer spine pain

No. of studies (design)	Risk of bias a	Inconsistency b	Indirectness c	Imprecision d	Publication bias	Effect size (95% CI)	Overall certainty of evidence
Prescription opioid receipt (yes vs. no)							
X (…)	X	X	X	X	X	X	X
Number of opioid prescriptions (i.e. unique opioid fills, subsequent refills)							
X (…)	X	X	X	X	X	X	X
Prescribed opioid dosage (mg MED)							
X (…)	X	X	X	X	X	X	X
Pain intensity (e.g. 10-cm VAS for pain)							
X (…)	X	X	X	X	X	X	X
Physical functioning (e.g. 0–100 points SF-36 physical functioning scale)							
X (…)	X	X	X	X	X	X	X
Emotional functioning (e.g. 0–100 points SF-36 mental component summary scale)							
X (…)	X	X	X	X	X	X	X
Sleep disturbance (e.g. 0–10 sleep quality scale)							
X (…)	X	X	X	X	X	X	X
Patient satisfaction (e.g. 0–10 points satisfaction scale)							
X (…)	X	X	X	X	X	X	X
Adverse events[e]							
X (…)	X	X	X	X	X	X	X

CI confidence interval, *GRADE* Grading of Recommendations Assessment, Development, and Evaluation, *MED* morphine equivalents daily, *RCT* randomized controlled trial, *SF-36* Short Form 36 Health Survey Questionnaire, *VAS* visual analogue scale

[a] We will assess risk of bias of RCTs and observational studies using tools developed by the CLARITY group (https://www.distillersr.com/resources)

[b] Inconsistency refers to unexplained heterogeneity of results. For RCTs, an I^2 of 75–100% indicates that heterogeneity may be considerable [35]. We will assess heterogeneity of pooled observational studies using tau-squared and through visual inspection of forest plots (e.g. CI overlap, difference in point estimates)

[c] Indirectness results if the patients, intervention, comparison/control, or outcomes of interest are different from the research question under investigation

[d] Serious imprecision refers to situations in which the 95% CI includes both benefit and harm

[e] Examples of manual therapy- and/or patient-important opioid-induced adverse events include the following: muscle soreness, joint pain, stiffness, headache, dizziness, nausea, vomiting, constipation, radiating symptoms, paresthesia, or fatigue [26, 27]

Table 2 Quality of evidence levels for GRADE [40]

Level	Definition
High	Further research is very unlikely to change our confidence in the estimated effect
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low	Any estimate of effect is very uncertain

GRADE Grading of Recommendations Assessment, Development, and Evaluation

19] that helped inform the current project. Further, we relied on the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials [25, 47], which was informed by patient focus groups and surveys [48], to select patient important outcomes.

Ethical considerations
This is a systematic literature review of previously published studies and does not require ethics approval.

Discussion
Opioid-related morbidity and mortality have risen in several countries over the past 25 years but particularly in Canada and the United States (US) [49]. In Canada, there were 44,592 opioid-related deaths and 42,711 opioid-related hospitalizations between January 2016 and December 2023 [50]. In the USA, there were more than 70,000 opioid-related deaths in 2020 alone [49]. Young-to middle-aged adult men have been most affected by

the opioid crisis [49–51], which has arisen partly among individuals who were initially prescribed opioids for back pain or some other musculoskeletal condition [49, 51–53]. The US Centers for Disease Control and Prevention estimated the annual cost of the opioid crisis at over US $1 trillion in 2017, equivalent to 5% of US gross domestic product [49, 54]. Recent reports from Canada and the USA also indicate that rates of opioid-related deaths and hospitalizations have worsened since before the COVID-19 pandemic [49, 50, 55].

The ongoing opioid crisis in North America has generated interest in exploring treatment options that may reduce reliance on opioids for patients with spine-related or other musculoskeletal pain. Findings from a 2020 systematic review [20] and some subsequent primary studies suggest that utilization of chiropractic services may be effective in reducing opioid prescribing [10–16, 20] and long-term opioid use [17–19]; however, the overall magnitude and certainty of these effects are unknown. The aim of our systematic review will be to assess the impact of chiropractic care on initiation, or continued use, of prescription opioids for adult patients with non-cancer spine pain. The results of our systematic review will be of interest to patients, health care providers, and policy-makers.

Strengths and limitations
Our review has several strengths. First, we will use explicit eligibility criteria and conduct a comprehensive search without date, geographic, or language restrictions to identify RCTs and observational studies exploring the impact of chiropractic care for spine pain and opioid receipt [20]. Second, we will assess the risk of bias among individual studies and evaluate the certainty of evidence using the GRADE approach. Third, we will use pre-defined subgroup analyses to explore sources of heterogeneity, and we will assess the credibility of all potential subgroup effects. Fourth, we will conduct sensitivity analyses to confirm the robustness of our meta-analyses. A limitation of our review is that we anticipate most eligible studies will be observational, which may limit the strength of inferences from our results.

Knowledge translation
The results of our review will be disseminated via a peer-reviewed publication and conference presentations.

Abbreviations

AMED	Allied and Alternative Medicine Database
CI	Confidence interval
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CLARITY	Clinical advances through research and information translation
Embase	Excerpta Medica Database
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
HR	Hazard ratio
ICEMAN	Instrument for assessing the Credibility of Effect Modification Analyses
MED	Morphine equivalents daily
MEDLINE	Medical Literature Analysis and Retrieval System Online
MOOSE	Meta-analysis Of Observational Studies in Epidemiology
OR	Odds ratio
PRESS	Peer review of electronic search strategies
PRISMA-P	Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols
PROSPERO	International Prospective Register of Systematic Reviews
RCT	Randomized controlled trial
RR	Relative risk
SF-36	Short form 36 health survey questionnaire
TX	Texas
US	United States
USA	United States of America
VAS	Visual analogue scale
YLD	Years lived with disability
WMD	Weighted mean difference

Supplementary Information
The online version contains supplementary material available at https://doi.org/10.1186/s13643-024-02654-6.

Additional file 1: PRISMA-P checklist.

Additional file 2: Literature search strategy.

Additional file 3: Completed PRESS checklist.

Availability of data and materials
The datasets to be used and/or analyzed for the current study will be available from the corresponding author on reasonable request.

Declarations

Ethical approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
PCE is supported by a postdoctoral fellowship from the Michael G. DeGroote Institute for Pain Research and Care (IPRC) at McMaster University. PCE is also supported by grants from the Canadian Institutes of Health Research (CIHR), the Michael G. DeGroote IPRC, and the Canadian Chiropractic Research Foundation for postdoctoral research outside of the submitted work. JWB is supported, in part, by a CIHR Canada Research Chair in the prevention and management of chronic pain. The other authors declare that they have no competing interests.

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References

1. GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018;392(10159):1789–1858.
2. International Narcotics Control Board. Narcotic drugs: estimated world requirements for 2020; 2019. Available from: https://www.incb.org/documents/Narcotic-Drugs/Technical-Publications/2019/Narcotic_Drugs_Technical_Publication_2019_web.pdf [Accessed 01 May 2023].
3. Busse JW, Wang L, Kamaleldin M, Craigie S, Riva JJ, Montoya L, Mulla SM Lopes LC, Vogel N, Chen E, Kirmayr K, De Oliveira K, Olivieri L, Kaushal A, Chaparro LE, Oyberman I, Agarwal A, Couban R, Tsoi L, Lam T, Vandvik PO, Hsu S, Bala MM, Schandelmaier S, Scheidecker A, Ebrahim S, Ashoorion V, Rehman Y, Hong PJ, Ross S, Johnston BC, Kunz R, Sun X, Buckley N, Sessler DI, Guyatt GH. Opioids for chronic noncancer pain: a systematic review and meta-analysis. JAMA. 2018;320(23):2448–2460.
4. Busse JW, Sadeghirad B, Oparin Y, Chen E, Goshua A, May C, Hong PJ, Agarwal A, Chang Y, Ross SA, Emary P, Florez ID, Noor ST, Yao W, Lok A, Ali SH, Craigie S, Couban R, Morgan RL, Culig K, Brar S, Akbari-Kelachayeh K, Pozdnyakov A, Shergill Y, Sivananthan L, Zihayat B, Das A, Guyatt GH. Management of acute pain from non-low back, musculoskeletal injuries: a systematic review and network meta-analysis of randomized trials. Ann Intern Med. 2020;173(9):730–8.
5. Gomes T, Greaves S, Martins D, Bandola D, Tadrous M, Singh S, Juurlink D, Mamdani M, Paterson M, Ebejer T, May D, Quercia J. Latest trends in opioid-related deaths in Ontario: 1991 to 2015. Toronto: Ontario Drug Policy Research Network; 2017. Available at: https://odprn.ca/wp-content/uploads/2017/04/ODPRN-Report_Latest-trends-in-opioid-related-deaths.pdf [Accessed 01 May 2023].
6. Busse JW, Craigie S, Juurlink DN, Buckley DN, Wang L, Couban RJ, Agoritsas T, Akl EA, Carrasco-Labra A, Cooper L, Cull C, da Costa BR, Frank JW, Grant G, Iorio A, Persaud N, Stern S, Tugwell P, Vandvik PO, Guyatt GH. Guideline for opioid therapy and chronic noncancer pain. CMAJ. 2017;189(18):E659–66.
7. Bedson J, Chen Y, Ashworth J, Hayward RA, Dunn KM, Jordan KP. Risk of adverse events in patients prescribed long-term opioids: a cohort study in the UK Clinical Practice Research Datalink. Eur J Pain. 2019;23(5):908–22.
8. Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC clinical practice guideline for prescribing opioids for pain - United States, 2022. MMWR Recomm Rep. 2022;71(3):1–95.
9. Foster NE, Anema JR, Cherkin D, Chou R, Cohen SP, Gross DP, Ferreira PH, Fritz JM, Koes BW, Peul W, Turner JA, Maher CG; Lancet Low Back Pain Series Working Group. Prevention and treatment of low back pain: evidence, challenges, and promising directions. Lancet. 2018;391(10137):2368–2383.
10. Goertz CM, Long CR, Vining RD, Pohlman KA, Walter J, Coulter I. Effect of usual medical care plus chiropractic care vs usual medical care alone on pain and disability among US service members with low back pain: a comparative effectiveness clinical trial. JAMA Netw Open. 2018;1(1): e180105.
11. Kazis LE, Ameli O, Rothendler J, Garrity B, Cabral H, McDonough C, Carey K, Stein M, Sanghavi D, Elton D, Fritz J, Saper R. Observational retrospective study of the association of initial healthcare provider for new-onset low back pain with early and long-term opioid use. BMJ Open. 2019;9(9): e028633.
12. Whedon JM, Toler AWJ, Kazal LA, Bezdjian S, Goehl JM, Greenstein J. Impact of chiropractic care on use of prescription opioids in patients with spinal pain. Pain Med. 2020;21(12):3576–673.
13. Acharya M, Chopra D, Smith AM, Fritz JM, Martin BC. Associations between early chiropractic care and physical therapy on subsequent opioid use among persons with low back pain in Arkansas. J Chiropr Med. 2022;21(2):67–76.
14. Emary PC, Brown AL, Oremus M, Mbuagbaw L, Cameron DF, DiDonato J, Busse JW. Association of chiropractic care with receiving an opioid prescription for noncancer spinal pain within a Canadian community health center: a mixed methods analysis. J Manipulative Physiol Ther. 2022;45(4):235–47.
15. Harwood KJ, Pines JM, Andrilla CHA, Frogner BK. Where to start? A two stage residual inclusion approach to estimating influence of the initial provider on health care utilization and costs for low back pain in the US. BMC Health Serv Res. 2022;22(1):694.
16. Whedon JM, Uptmor S, Toler AWJ, Bezdjian S, MacKenzie TA, Kazal LA Jr. Association between chiropractic care and use of prescription opioids among older Medicare beneficiaries with spinal pain: a retrospective observational study. Chiropr Man Therap. 2022;30(1):5.
17. Lisi AJ, Corcoran KL, DeRycke EC, Bastian LA, Becker WC, Edmond SN, Goertz CM, Goulet JL, Haskell SG, Higgins DM, Kawecki T, Kerns RD, Mattocks K, Ramsey C, Ruser CB, Brandt CA. Opioid use among veterans of recent wars receiving Veterans Affairs chiropractic care. Pain Med. 2018;19(suppl_1):S54-S60.
18. Passmore S, Malone Q, Manansala C, Ferbers S, Toth EA, Olin GM. A retrospective analysis of pain changes and opioid use patterns temporally associated with a course of chiropractic care at a publicly funded inner-city facility. J Can Chiropr Assoc. 2022;66(2):107–17.
19. Emary PC, Brown AL, Oremus M, Mbuagbaw L, Cameron DF, DiDonato J, Busse JW. The association between chiropractic integration in an Ontario community health centre and continued prescription opioid use for chronic non-cancer spinal pain: a sequential explanatory mixed methods study. BMC Health Serv Res. 2022;22(1):1313.
20. Corcoran KL, Bastian LA, Gunderson CG, Steffens C, Brackett A, Lisi AJ. Association between chiropractic use and opioid receipt among patients with spinal pain: a systematic review and meta-analysis. Pain Med. 2020;21(2):e139–45.
21. Whalen WM, Hawk C, Farabaugh RJ, Daniels CJ, Taylor DN, Anderson KR, Crivelli LS, Anderson DR, Thomson LM, Sarnat RL. Best practices for chiropractic management of adult patients with mechanical low back pain: a clinical practice guideline for chiropractors in the United States. J Manipulative Physiol Ther. 2022;45(8):551–65.
22. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA; PRISMA-P Group. Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4(1):1.
23. Stern C, Jordan Z, McArthur A. Developing the review question and inclusion criteria. Am J Nurs. 2014;114(4):53–6.
24. Beliveau PJH, Wong JJ, Sutton DA, Simon NB, Bussières AE, Mior SA, French SD. The chiropractic profession: a scoping review of utilization rates, reasons for seeking care, patient profiles, and care provided. Chiropr Man Therap. 2017;25:35.
25. Dworkin RH, Turk DC, Farrar JT, Haythornthwaite JA, Jensen MP, Katz NP, Kerns RD, Stucki G, Allen RR, Bellamy N, Carr DB, Chandler J, Cowan P, Dionne R, Galer BS, Hertz S, Jadad AR, Kramer LD, Manning DC, Martin S, McCormick CG, McDermott MP, McGrath P, Quessy S, Rappaport BA, Robbins W, Robinson JP, Rothman M, Royal MA, Simon L, Stauffer JW, Stein W, Tollett J, Wernicke J, Witter J; IMMPACT. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. Pain. 2005;113(1–2):9–19.

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26. Maiers M, Evans R, Hartvigsen J, Schulz C, Bronfort G. Adverse events among seniors receiving spinal manipulation and exercise in a randomized clinical trial. Man Ther. 2015;20(2):335–41.

27. Goshua A, Craigie S, Guyatt GH, Agarwal A, Li R, Bhullar JS, Scott N, Chahal J, Pavalagantharajah S, Chang Y, Couban R, Busse JW. Patient values and preferences regarding opioids for chronic noncancer pain: a systematic review. Pain Med. 2018;19(12):2469–80.

28. McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C. PRESS peer review of electronic search strategies: 2015 guideline statement. J Clin Epidemiol. 2016;75:40–6.

29. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics. 1977;33(1):159–74.

30. McHugh ML. Interrater reliability: the kappa statistic. Biochem Med (Zagreb). 2012;22(3):276–82.

31. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372: n71.

32. Wang Z. Converting odds ratio to relative risk in cohort studies with partial data information. J Stat Softw. 2013;55(5):1–11.

33. Thorlund K, Walter SD, Johnston BC, Furukawa TA, Guyatt GH. Pooling health-related quality of life outcomes in meta-analysis-a tutorial and review of methods for enhancing interpretability. Res Synth Methods. 2011;2(3):188–203.

34. Johnston BC, Patrick DL, Thorlund K, Busse JW, da Costa BR, Schünemann HJ, Guyatt GH. Patient-reported outcomes in meta-analyses-part 2: methods for improving interpretability for decision-makers. Health Qual Life Outcomes. 2013;11:211.

35. Higgins J, Thomas J, Chandler J, et al. Cochrane Handbook for Systematic Reviews of Interventions version 6.3 (updated August 2022). Available from: www.training.cochrane.org/handbook [Accessed 28 April 2023].

36. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials. 1986;7(3):177–88.

37. Andridge RR, Little RJ. A review of hot deck imputation for survey nonresponse. Int Stat Rev. 2010;78(1):40–64.

38. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997;315(7109):629–34.

39. Harbord RM, Egger M, Sterne JA. A modified test for small-study effects in meta-analyses of controlled trials with binary endpoints. Stat Med. 2006;25(20):3443–57.

40. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, Schünemann HJ; GRADE Working Group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008;336(7650):924–926.

41. Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, Norris S, Falck-Ytter Y, Glasziou P, DeBeer H, Jaeschke R, Rind D, Meerpohl J, Dahm P, Schünemann HJ. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. J Clin Epidemiol. 2011;64(4):383–394.

42. Iorio A, Spencer FA, Falavigna M, Alba C, Lang E, Burnand B, McGinn T, Hayden J, Williams K, Shea B, Wolff R, Kujpers T, Perel P, Vandvik PO, Glasziou P, Schunemann H, Guyatt G. Use of GRADE for assessment of evidence about prognosis: rating confidence in estimates of event rates in broad categories of patients. BMJ. 2015;350: h870.

43. Rücker G, Schwarzer G, Carpenter JR, Schumacher M. Undue reliance on I(2) in assessing heterogeneity may mislead. BMC Med Res Methodol. 2008;8:79.

44. Anderson BR, Whedon JM, Herman PM. Dosing of lumbar spinal manipulative therapy and its association with escalated spine care: a cohort study of insurance claims. PLoS ONE. 2024;19(1): e0283252.

45. Baker WL, White CM, Cappelleri JC, Kluger J, Coleman CI; Health Outcomes, Policy, and Economics (HOPE) Collaborative Group. Understanding heterogeneity in meta-analysis: the role of meta-regression. Int J Clin Pract. 2009;63(10):1426–1434.

46. Schandelmaier S, Briel M, Varadhan R, Schmid CH, Devasenapathy N, Hayward RA, Gagnier J, Borenstein M, van der Heijden GJMG, Dahabreh IJ, Sun X, Sauerbrei W, Walsh M, Ioannidis JPA, Thabane L, Guyatt GH. Development of the Instrument to assess the Credibility of Effect Modification ANalyses (ICEMAN) in randomized controlled trials and meta-analyses. CMAJ. 2020;192(32):E901–6.

47. Turk DC, Dworkin RH, Allen RR, Bellamy N, Brandenburg N, Carr DB, Cleeland C, Dionne R, Farrar JT, Galer BS, Hewitt DJ, Jadad AR, Katz NP, Kramer LD, Manning DC, McCormick CG, McDermott MP, McGrath P, Quessy S, Rappaport BA, Robinson JP, Royal MA, Simon L, Stauffer JW, Stein W, Tollett J, Witter J. Core outcome domains for chronic pain clinical trials: IMMPACT recommendations. Pain. 2003;106(3):337–45.

48. Turk DC, Dworkin RH, Revicki D, Harding G, Burke LB, Cella D, Cleeland CS, Cowan P, Farrar JT, Hertz S, Max MB, Rappaport BA. Identifying important outcome domains for chronic pain clinical trials: an IMMPACT survey of people with pain. Pain. 2008;137(2):276–85.

49. Humphreys K, Shover CL, Andrews CM, Bohnert ASB, Brandeau ML, Caulkins JP, Chen JH, Cuéllar MF, Hurd YL, Juurlink DN, Koh HK, Krebs EE, Lembke A, Mackey SC, Larrimore Ouellette L, Suffoletto B, Timko C. Responding to the opioid crisis in North America and beyond: recommendations of the Stanford-Lancet Commission. Lancet. 2022;399(10324):555–604.

50. Public Health Agency of Canada. Opioid- and stimulant-related harms in Canada (June 2024). Available from: https://health-infobase.canada.ca/substance-related-harms/opioids-stimulants/ [Accessed 17 July 2024].

51. Rummans TA, Burton MC, Dawson NL. How good intentions contributed to bad outcomes: the opioid crisis. Mayo Clin Proc. 2018;93(3):344–50.

52. Manchikanti L, Helm S 2nd, Fellows B, Janata JW, Pampati V, Grider JS, Boswell MV. Opioid epidemic in the United States. Pain Physician. 2012;15(3 Suppl):ES9-ES38.

53. Belzak L, Halverson J. The opioid crisis in Canada: a national perspective. Health Promot Chronic Dis Prev Can. 2018;38(6):224–33.

54. Luo F, Li M, Florence C. State-level economic costs of opioid use disorder and fatal opioid overdose - United States, 2017. MMWR Morb Mortal Wkly Rep. 2021;70(15):541–6.

55. Manchikanti L, Vanaparthy R, Atluri S, Sachdeva H, Kaye AD, Hirsch JA. COVID-19 and the opioid epidemic: two public health emergencies that intersect with chronic pain. Pain Ther. 2021;10(1):269–86.

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