

METHODOLOGICAL QUALITY OF CHIROPRACTIC MIXED
METHODS RESEARCH

METHODOLOGICAL QUALITY OF CHIROPRACTIC MIXED METHODS
RESEARCH: A META-EPIDEMIOLOGICAL REVIEW AND APPLICATION IN A
HEALTH SERVICES EVALUATION OF CHIROPRACTIC INTEGRATION AND
PRESCRIPTION OPIOID USE

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TITLE: Methodological Quality of Chiropractic Mixed Methods Research: A Meta-
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Integration and Prescription Opioid Use

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Lay Abstract

We reviewed the literature to assess the methodological reporting quality of mixed methods studies involving chiropractic research and found that most studies had important omissions. We applied these results to optimize methodologic reporting of two mixed methods studies on the association between chiropractic care and opioid prescribing. We found that patients with non-cancer spinal pain were less likely to receive an initial prescription for opioids if they accessed chiropractic care. Further, among chronic pain patients receiving opioids, we found that providing access to chiropractic care reduced their chances of continuing to receive opioids. The qualitative aspect of our studies provided important context to inform how patients and their primary care providers felt access to chiropractic care had reduced reliance on prescription opioids. These findings will increase awareness among researchers for opportunities to improve reporting quality of mixed methods research and highlight the potential role of chiropractic care in helping to address the opioid crisis.

Abstract

Background: An increasing number of mixed methods studies have been conducted across health care professions in recent years. However, little is known about the methodological reporting quality among mixed methods studies involving chiropractic research.

Objective: To examine the methodological quality of published chiropractic mixed methods studies, provide recommendations for improving future chiropractic mixed methods research, and apply these recommendations in two mixed methods health services evaluations of chiropractic integration and prescription opioid use for spinal pain.

Methods: We conducted a meta-epidemiological review of the chiropractic mixed methods literature and examined reporting quality using the Good Reporting of A Mixed Methods Study guideline and risk of bias using the Mixed Methods Appraisal Tool. We used generalized estimating equations to explore factors associated with higher methodological quality. We applied our findings in two sequential explanatory mixed methods investigations of the association between chiropractic care and opioid prescribing for non-cancer spinal pain.

Results: Among eligible mixed methods studies, we found that many were both poorly reported and at risk of bias. Publication in journals with an impact factor and/or more recent publication were significantly associated with higher methodological quality. In our sequential explanatory analyses, we found that receipt of chiropractic care was associated with decreases in initial opioid prescribing and long-term opioid use, and our qualitative results suggested these relationships were multi-factorial.

Conclusion: We identified areas for improvement in the methodological reporting quality of chiropractic mixed methods research. Our mixed methods studies suggest that integration of chiropractic services into primary care centres may reduce the use of opioids for spinal pain.

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List of All Abbreviations and Symbols

Abbreviations:

AIC: Akaike Information Criterion

BC: British Columbia

BMC: BioMed Central

BMI: Body Mass Index

CHC: Community Health Centre

CI: Confidence Interval

CINAHL: Cumulative Index to Nursing and Allied Health Literature

CNCP: Chronic Non-Cancer Pain

CONSORT: Consolidated Standards of Reporting Trials

COREQ: Consolidated Criteria for Reporting Qualitative Research

COVID-19: CoronaVirus Disease of 2019

CPP: Cumulative Patient Profile

DAS: Data & Analytic Services

DC: Doctor of Chiropractic

EMBASE: Excerpta Medica Database

EMR: Electronic Medical Record

ENCODE-FM: Electronic Nomenclature and Classification Of Disorders and Encounters for Family Medicine

GEE: Generalized Estimating Equation

GP: General Practitioner

GPE: Global Perceived Effect

GRAMMS: Good Reporting of A Mixed Methods Study

HR: Hazard Ratio

IBM: International Business Machines

ICES: Institute for Clinical Evaluative Sciences

ICL: Index to Chiropractic Literature

ICMJE: International Committee of Medical Journal Editors

IF: Impact Factor

IQR: Inter-Quartile Range

IRR: Incidence Rate Ratio

MAXQDA: Max Weber Qualitative Data Analysis

MED: Morphine Equivalents Daily

MEDLINE: Medical Literature Analysis and Retrieval System Online

MMAT: Mixed Methods Appraisal Tool

MSc: Master of Science

NA: Not Applicable

NP: Nurse Practitioner

NY: New York

OR: Odds Ratio

ORCID: Open Researcher and Contributor Identifier

OSF: Open Science Framework

P: Proportion

PhD: Doctor of Philosophy

PI: Principal Investigator

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PS: Practice Solutions

QIC: Quasi-likelihood under the Independence model Criterion

SD: Standard Deviation

SPOR: Strategy for Patient-Oriented Research

SPSS: Statistical Package for the Social Sciences

SR: Systematic Review

TCPS: Tri-Council Policy Statement

US: United States

USA: United States of America

VIF: Variance Inflation Factor

Symbols:

α : Alpha

χ^2 : Chi-squared

©: Copyright

\$: Dollar

=: Equals

>: Greater than

\geq : Greater than or equal to

hr: Hour

κ : Kappa

kg: Kilogram

<: Less than

\leq : Less than or equal to

m: Metre

mcg: Microgram

mg: Milligram

\times : Multiply

n: Number

#: Number

%: Percentage

r: Pearson correlation coefficient

+: Plus

\pm : Plus minus

p: Probability

ρ : Spearman rank correlation coefficient

t: Test

[™]: Trademark

v: Version

vs: Versus

Declaration of Academic Achievement

This thesis is a “sandwich thesis,” which combines a total of six individual manuscripts published or submitted for publication in peer-reviewed journals. I, Peter C. Emary, am the first author and principal contributor in each paper. This work is original research that I conducted between September 2018 and July 2022. My contributions, including those of my colleagues and others, to the research contained in this thesis are as follows:

Chapter 1: This chapter is unpublished. P.C. Emary is the sole author.

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Chapter 1:

Introduction of the Thesis

Mixed Methods Research

Mixed methods research involves the mixing or integration of various elements of quantitative and qualitative methods, including viewpoints, data collection, analysis and inference techniques, for the broad purposes of breadth and depth of understanding and corroboration (Johnson, Onwuegbuzie, & Turner, 2007). Mixed methods research is increasingly being recognized as a *third* research paradigm, distinct from purely quantitative or qualitative research (Johnson et al., 2007; Creswell & Plano Clark, 2018). Mixed methods research is particularly useful for answering questions that cannot be answered by only quantitative or qualitative methods and can serve as a powerful tool for investigating complex therapeutic interventions, educational programs, or knowledge translation strategies (Fetters, Curry, & Creswell, 2013; Creswell & Plano Clark, 2018). A common philosophical approach used in mixed methods research is ‘pragmatism,’ where the focus is on combining methods of data collection for “what works” best in answering a particular research question (Creswell & Plano Clark, 2018; p. 37). With this approach, the research question drives the study design (Creswell & Plano Clark, 2018), and both objective and subjective knowledge are valued.

Rationales for Using Mixed Methods

There are several rationales for undertaking mixed methods research (Table 1). These include, but are not limited to, a need to: (1) obtain more complete and corroborated results (e.g., to find points of convergence and divergence); (2) explain initial quantitative results (i.e., ‘complementarity’ [Greene, Caracelli, & Graham, 1989]); (3) first explore

questions, variables to be measured, or theories to guide a study before administering instruments; (4) enhance an experimental (i.e., randomized controlled) trial with a qualitative study, such as in a feasibility study or process evaluation; (5) describe and compare different types of cases; (6) involve participants in the study (i.e., participatory-social justice); or (7) develop, implement and evaluate a program (Creswell & Plano Clark, 2018).

A mixed methods study is not always preferable. Quantitative research may be the best approach when the aim is to understand the relationship between variables or determine if one group, compared to another group, performs better on a particular outcome of interest. A qualitative approach may be optimal when the aim is to explore a particular phenomenon, map the complexity of the situation, or honour the voices and convey multiple perspectives of participants (Creswell & Plano Clark, 2018).

In general, problems best suited for mixed methods research are those in which one data source (i.e., quantitative or qualitative) may be insufficient. For example, in a narrative review of the literature, I identified previously published studies on clinicians' attitudes toward medication prescription rights in chiropractic practice (Emary and Stuber, 2014). In all identified studies, traditional quantitative survey methods (e.g., Likert-scale items) were utilized for data collection. Based on the findings from these studies, we concluded that there was no clear definition or consensus on medication prescription rights within the chiropractic profession, and that further research was warranted. In a 2020 study of chiropractors in Switzerland (Emary et al., 2020), I utilized a mixed methods approach and identified four distinct viewpoints among chiropractors

toward medication prescribing not identified in previous quantitative surveys. These findings provided new insights on chiropractic prescribing rights, and consensus was reached on this topic among participants in this study (Emary et al., 2020).

Mixed Methods Study Designs

There are three core study designs used in mixed methods research, including: (1) convergent, (2) explanatory sequential, and (3) exploratory sequential (Figure 1). In a convergent design, researchers compare and combine (or ‘triangulate’) quantitative and qualitative results to obtain a richer understanding of the research problem, or to validate one set of findings with the other (Creswell & Plano Clark, 2018). For example, an online survey of students, faculty, and staff at five international chiropractic educational institutions used closed- and open-ended questions (i.e., quantitative and qualitative data collection, respectively) to evaluate patient safety attitudes among stakeholders in chiropractic teaching clinics (Pohlman et al., 2020). By combining methods, the qualitative findings in this study provided in-depth insight into the quantitative survey results and helped identify areas for improvement in patient safety education within chiropractic teaching programs.

With an explanatory sequential design, quantitative data collection and analysis are followed by qualitative data collection and analysis, and the qualitative data are used to help explain or expand on the initial quantitative results (Creswell & Plano Clark, 2018). For example, a mixed methods study on patient perceptions toward patient-centred care in chiropractic practice used an explanatory sequential design, where follow-

up qualitative interviews and focus groups were conducted to help explain initial quantitative survey results (Stuber et al., 2016). I also used an explanatory sequential mixed methods design in two separate analyses on the association between chiropractic integration and opioid use in an Ontario community health centre (Emary et al., 2021). The methods and results of this work are described in detail in Chapters 5, 6, and 7 of this thesis.

In contrast to an explanatory sequential design, an exploratory sequential design begins with an exploratory qualitative phase (i.e., qualitative data collection and analysis) followed by a developmental quantitative phase. The quantitative phase is based on the initial qualitative results, which are used to generate new quantitative variables, design a quantitative instrument, or develop activities for an intervention or digital product, such as an app or website (Creswell & Plano Clark, 2018). The developmental quantitative phase is followed by a third phase where the new feature (i.e., variable[s], instrument, or product) is tested quantitatively to see how the quantitative findings build on the initial qualitative results or provide a clearer understanding of the research problem. In either case, the development of the quantitative feature is grounded in the initial qualitative perspectives of participants (Creswell & Plano Clark, 2018). In a recent study investigating chiropractors' understanding of building trust with patients, Connell and Bainbridge (2020) used an exploratory sequential design, where initial interviews (qualitative) were conducted with chiropractors in British Columbia (BC) and used to develop a survey instrument (quantitative). The initial qualitative findings ensured that questions on the survey instrument reflected the perspectives of BC chiropractors. The

questionnaire was then distributed to all members of the provincial chiropractic association and used to measure chiropractors' perceptions of trust and confirm initial qualitative themes (Connell & Bainbridge, 2020).

Advantages and Challenges of Mixed Methods Research

There are several advantages with a mixed methods approach (Creswell & Plano Clark, 2018). Mixing quantitative and qualitative methods allows the strengths of each methodology to account for weaknesses of the other. For instance, when there is good external validity (e.g., data collected in a representative epidemiological survey or pragmatic clinical trial), quantitative research findings are generalizable to larger populations. However, findings from qualitative research allow for greater in-depth knowledge and understanding of perspectives, experiences, or beliefs of individuals or groups (Miller & Jones Harris, 2005). Therefore, by incorporating both deductive and inductive reasoning (Morgan, 2007; Creswell & Plano Clark, 2018), mixed methods research builds on the strengths of quantitative and qualitative methods and provides more complete answers to research questions. Mixed methods research can also offer new insights into investigations that go beyond the results of the separate quantitative and qualitative components (i.e., meta-inferences) (Creswell & Plano Clark, 2018), as illustrated in the following equation (Fetters & Freshwater, 2015):

$$1 + 1 = 3$$

where the first '1' is the quantitative component, the second '1' is the qualitative component, and the '3' is the combination of results and meta-inferences generated from mixing quantitative and qualitative methods.

Mixed methods research also provides opportunities for collaboration, which can help bridge the historical divide between quantitative and qualitative researchers (Creswell & Plano Clark, 2018). Mixed methods research also encourages the use of multiple worldviews, or paradigms, including those such as pragmatism that encompass both quantitative and qualitative research (Creswell & Plano Clark, 2018). A final advantage of mixed methods research is that it helps investigators develop broader skillsets or expertise in multiple forms of research methods (i.e., quantitative, qualitative, and mixed methods).

Despite its advantages, mixed methods research also entails unique challenges. For instance, mixed methods studies can often become complex, drawn-out investigations (Fetters et al., 2013; Creswell & Plano Clark, 2018). Qualitative data collection and analysis are time-intensive, and additional time is needed for mixed methods studies that incorporate a sequential explanatory (i.e., two-phase) or exploratory (i.e., three-phase) study design. There are also cost considerations in mixed methods research, such as the need to purchase additional materials or services (e.g., quantitative and qualitative analysis software programs, audio recorders, printing, transcription services), as well as the need to work in larger teams requiring qualitative and/or mixed methodologists. Mixed methods studies can also create team management issues, particularly for members with diverse levels of mixed methodological or content expertise. Further, mixed

methods investigators may need to educate team members or others (e.g., grant committees, journal editors, or peer reviewers) about mixed methods research, particularly if they are unfamiliar with this methodology.

Aim of the Thesis

The Good Reporting of A Mixed Methods Study (GRAMMS) guideline, published by O’Cathain, Murphy, and Nicholl (2008), is a commonly used reporting guideline in mixed methods research. In 2009, the Mixed Methods Appraisal Tool (MMAT) was developed and published by Pluye et al. (2009), and later validated by Pace et al. (2012), as a risk of bias tool for primary mixed methods research and systematic reviews of mixed studies (i.e., quantitative, qualitative, and mixed methods studies). Recently, there has been a dramatic increase in the conduct of primary mixed methods research across health care professions, including within the chiropractic profession (see Chapters 3 and 4). However, little is known about the methodological quality (i.e., conduct or reporting) of chiropractic studies using mixed methods. Therefore, the aim of this thesis was two-fold: (1) to examine the methodological reporting quality of published chiropractic mixed methods studies; and (2) provide recommendations for improving chiropractic mixed methods research, and apply these recommendations in a mixed methods health services evaluation of chiropractic integration and prescription opioid use for chronic pain (Emary et al., 2021).

Overview of the Thesis

This thesis is a “sandwich thesis,” consisting of six papers on the quality and use of mixed methods in chiropractic research. In Chapter 2, we provide a protocol for a meta-epidemiological review on the quality of reporting among chiropractic mixed methods studies. In Chapter 3, we present the findings of this review, including the results from our assessment of reporting quality using the GRAMMS guideline for good reporting in mixed methods research. In this review, we also examined for correlation between reporting quality and risk of bias (i.e., the GRAMMS and MMAT instruments), and we explored factors associated with reporting quality using generalized estimating equations (GEEs). In Chapter 4, using our risk of bias data, we conducted a secondary analysis of our meta-epidemiological review and explored factors associated with the quality of conduct among chiropractic mixed methods studies.

Chapter 5 includes a protocol for a mixed methods study on the association between integration of chiropractic services in an Ontario community health centre and prescription opioid use for chronic non-cancer pain. In Chapters 6 and 7, we present the results of a survival analysis (Chapter 6) and a GEE analysis (Chapter 7) from two mixed methods studies on the association of chiropractic care with opioid prescribing. Our qualitative data presented in Chapter 6 were also used in our second mixed methods analysis in Chapter 7. In Chapter 8, we provide a summary of our findings with recommendations and directions for future research.

Table 1. Rationales for undertaking mixed methods research ^a

Rationale	Description
Triangulation	<ul style="list-style-type: none">• Seeks convergence and corroboration of results from different methods (i.e., quantitative and qualitative) studying the same phenomenon.
Complementarity	<ul style="list-style-type: none">• Seeks elaboration, enhancement, illustration, or clarification of the results from one method with results from the other method.
Development	<ul style="list-style-type: none">• Seeks to use the results from one method to help inform the other method.
Initiation	<ul style="list-style-type: none">• Seeks the discovery of paradoxes and contradictions that lead to a reframing of the research question.
Expansion	<ul style="list-style-type: none">• Seeks to extend the breadth and range of inquiry by using different methods for different inquiry components.

^a Source: adapted from Greene, Caracelli, and Graham (1989).

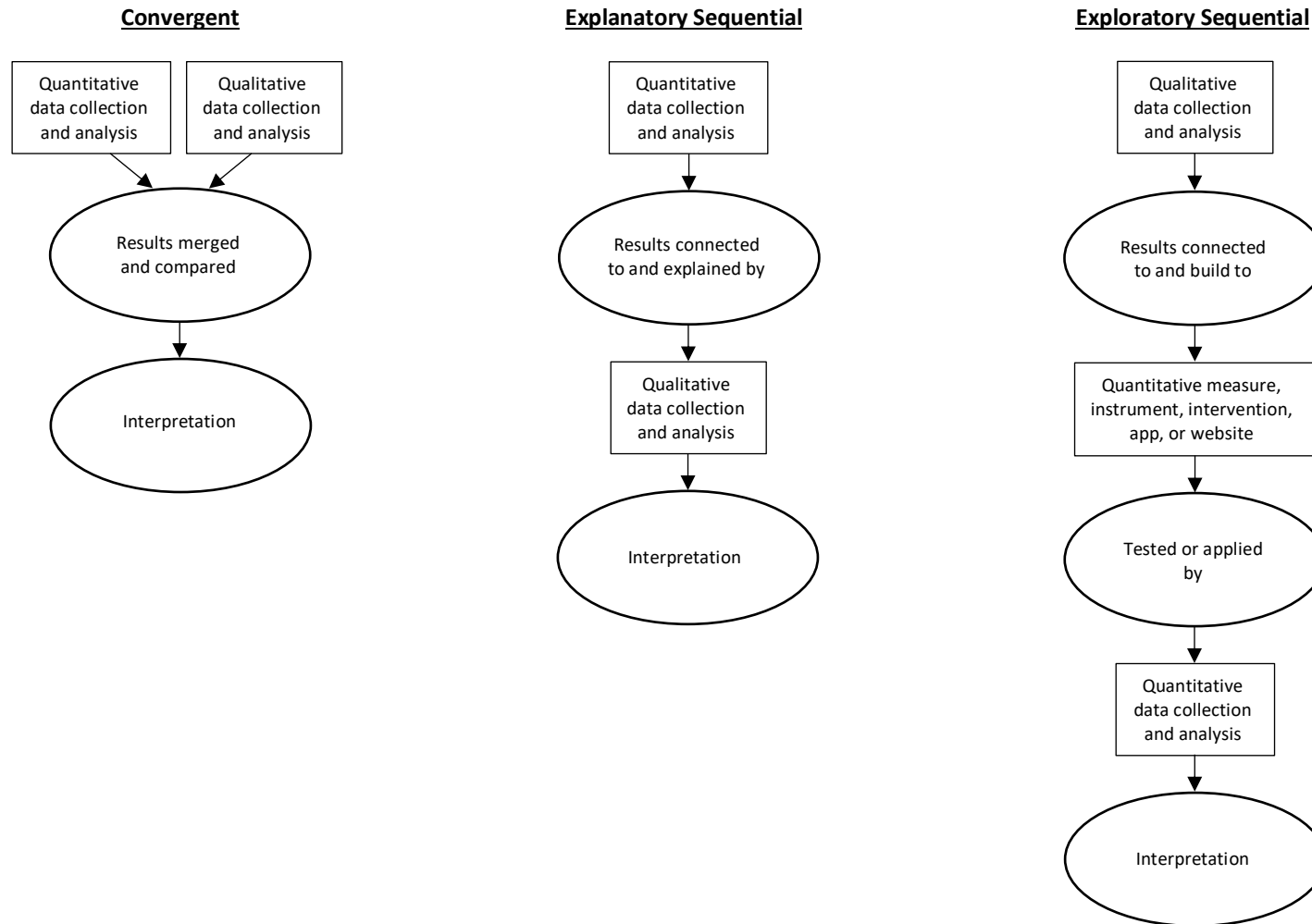


Figure 1. Core mixed methods study designs (adapted from Creswell & Plano Clark, 2018).

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Chapter 2:

Quality of reporting in chiropractic mixed methods research: a methodological review protocol

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Methods consultation: L.M., M.O., J.W.B.

Literature search: P.C.E., R.J.C.

Writing of the protocol manuscript: P.C.E.

Critical review of protocol manuscript for intellectual content: P.C.E., K.J.S., L.M., M.O., P.S.N., J.V.N., C.A.B., C.C., R.J.C., J.W.B.

All authors also read and approved the final manuscript.

STUDY PROTOCOL

Open Access



Quality of reporting in chiropractic mixed methods research: a methodological review protocol

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Abstract

Background: Mixed methods designs are increasingly used in health care research to enrich findings. However, little is known about the frequency of use of this methodology in chiropractic research, or the quality of reporting among chiropractic studies using mixed methods.

Objective: To quantify the use and quality of mixed methods in chiropractic research, and explore the association of study characteristics (e.g., authorship, expertise, journal impact factor, country and year of publication) with reporting quality.

Methods: We will conduct a systematic search of MEDLINE, EMBASE, CINAHL, and the Index to Chiropractic Literature to identify all chiropractic mixed methods studies published from inception of each database to December 31, 2020. Articles reporting the use of both qualitative and quantitative methods, or mixed qualitative methods, will be included. Pairs of reviewers will perform article screening, data extraction, risk of bias with the Mixed Methods Appraisal Tool (MMAT), and appraisal of reporting quality using the Good Reporting of A Mixed Methods Study (GRAMMS) guideline. We will explore the correlation between GRAMMS and MMAT scores, and construct generalized estimating equations to explore factors associated with reporting quality.

Discussion: This will be the first methodological review to examine the reporting quality of published mixed methods studies involving chiropractic research. The results of our review will inform opportunities to improve reporting in chiropractic mixed methods studies. Our results will be disseminated in a peer-reviewed publication and presented publicly at conferences and as part of a doctoral thesis.

Keywords: Study protocol, Mixed methods research, Reporting quality, Chiropractic, Methodological review

Background

Mixed methods designs, which include qualitative and quantitative methods, have been increasingly used in health care research to enrich findings [1, 2]. The explicit mixing or linking of qualitative and quantitative components within a mixed methods study allows researchers

to answer questions with a greater breadth and depth of understanding than would be possible with only one methodology alone [1, 2]. This integration of methods, which is central to mixed methods research [1–3], is distinct from “multi-method” research, where investigators use quantitative and qualitative methods in a study without linking or integrating the two components (e.g., adding a series of open-ended questions to the end of a quantitative survey). An integrated mixed methods approach is particularly useful for investigating

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complex, multilevel programs and interventions [3–6], and is therefore well-suited to address research problems involving knowledge translation, program evaluations, or comparisons of therapeutic interventions within the chiropractic profession. However, little is known about the frequency of use of this methodology in chiropractic research, or the quality of reporting among chiropractic studies using mixed methods.

Researchers conducting mixed methods studies need to make decisions regarding the sequencing or timing of the qualitative and quantitative components (i.e., concurrent or sequential data collection and analysis), as well as the priority or “emphasis” that will be given to each method [1, 2, 7]. For example, Stuber et al. [8] used a sequential, quantitative dominant [7] mixed methods design where supplemental interviews and focus groups (qualitative) were conducted to help explain initial survey results (quantitative) in a study of patient perceptions toward patient-centered care in chiropractic practice. In addition to the mixing or linking of two unique research paradigms—qualitative and quantitative—mixed methods studies may also involve data transformation (i.e., converting qualitative data into quantitative data [‘quantitizing’] or vice versa [‘qualitizing’] in order to further integrate the data [3]). As such, mixed methods studies can become complex investigations that require additional time and resources, and a team of researchers with expertise in quantitative, qualitative, and mixed methodologies [1, 2].

Previous methodological reviews have examined the mixed methods literature [9–14] and highlighted areas for improvement in the quality of reporting. For instance, a review of health services research [9] found that authors of mixed methods studies in health services research typically did not describe or justify the need for a mixed methods design, or integrate data and findings from the individual quantitative and qualitative components. This lack of integration inhibits new insights from being generated within mixed methods studies (i.e., beyond the results obtained from the two separate components), thereby limiting the methodological potential of this research strategy [1–3]. Currently, the quality of reporting in chiropractic mixed methods research is unknown as no methodological reviews have examined this literature.

Aim

The primary purpose of our methodological review is to examine the quality of reporting and characteristics (e.g., authorship, expertise, journal impact factor, country and year of publication) of chiropractic mixed methods studies. In addition, we will assess the risk of bias of included articles and examine the correlation between reporting

quality and risk of bias. We will also use multivariable regression analysis to explore possible factors influencing reporting quality. Our findings will be of interest to educators, researchers, publishers, editors, and consumers of the chiropractic and allied health literature.

Methods

Registration

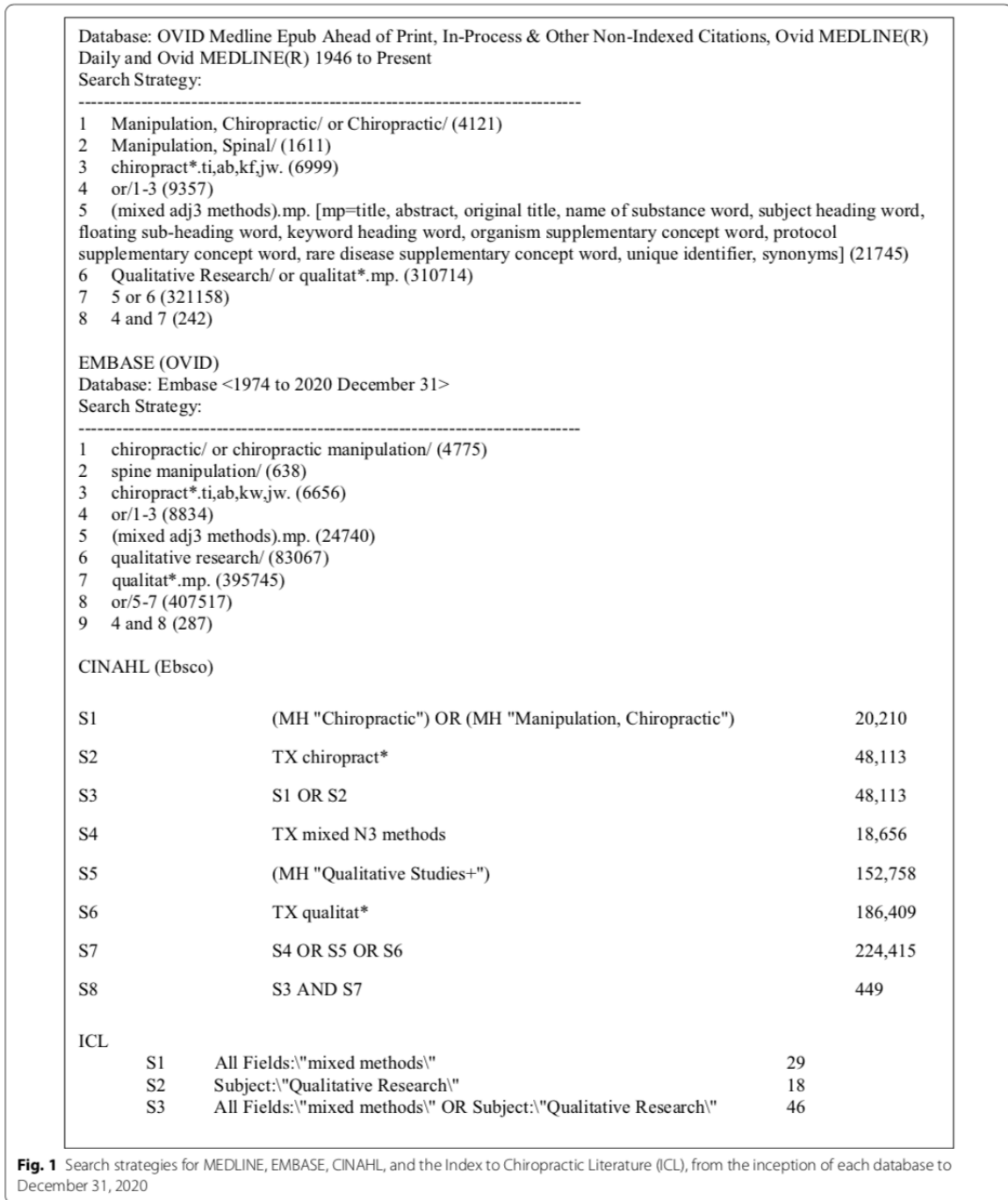
This methodological review was registered with the Open Science Framework (OSF) on December 14, 2020 (<https://osf.io/>).

Information sources

A systematic search of multiple databases including MEDLINE, EMBASE, CINAHL, and the Index to Chiropractic Literature (ICL) will be conducted to identify all published chiropractic mixed methods articles, without time limits to December 31, 2020. Our search strategy was developed by an academic librarian (RJC) (Fig. 1). The reference lists of eligible articles will also be hand-searched, and contact will be made with experts in the chiropractic mixed methods field, to identify additional eligible studies not identified in our electronic database searches. We will update our literature search if more than six months elapses between the time of our database searches and submission of results.

Eligibility criteria

Articles that meet the following criteria will be included: (1) published in a peer-reviewed journal; (2) written in the English language; (3) authored by one or more chiropractic researchers (i.e., someone with chiropractic credentials or affiliation with a chiropractic educational institution); (4) involved any type of chiropractic intervention (e.g., therapeutic, educational) or non-intervention research (e.g., policy, scope of practice); (5) reported a mixed methods approach (i.e., the use of both qualitative and quantitative methods [1, 2], or mixed qualitative methods [15], in the same research article); and (6) reports primary research. For the analysis, studies that report quantitative and qualitative results in separate papers will be combined and considered as one study. In addition, ‘mixed’ surveys (i.e., those with both closed- and open-ended questions) will only be included when the use of “mixed methods” was explicitly stated in the title or abstract. Protocols, letters, editorials, commentaries, books and book chapters, grey literature (e.g., conference proceedings, abstracts, lectures, dissertations or unpublished manuscripts), and secondary sources of evidence, e.g., clinical practice guidelines or any type of review article will be excluded.



Study selection

Each title and abstract retrieved from the database searches, as well as those identified through

bibliographic-searching and contact with experts, will be screened by pairs of independent reviewers. Online systematic review software (DistillerSR, Evidence Partners,

Ottawa, Canada; <https://www.evidencepartners.com>) will be used to facilitate the literature screening process. We will resolve discrepancies on decisions to include or exclude potentially eligible articles by discussion to achieve consensus or, when not possible, adjudication by a third reviewer. We will also complete full-text screening independently and in duplicate, with discrepancies resolved as previously described. Agreement for full-text screening will be assessed using the kappa (κ) statistic, and the strength of agreement will be interpreted as: 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 ($\kappa > 0.8$) [16].

Data collection process and assessment of reporting quality

Pairs of reviewers will independently extract data and assess reporting quality of included articles using standardized, pilot-tested data extraction forms. Discrepancies will be resolved by consensus or adjudication by a third reviewer. If a reviewer was an author on an included article, the study will be reviewed by another member of the research team. The following six items from the Good Reporting of A Mixed Methods Study (GRAMMS) criteria [9] will be used to assess reporting quality: (1) describes the justification for using a mixed methods approach to the research question; (2) describes the mixed methods design (i.e., the purpose, priority, and sequence of methods); (3) describes each method in terms of its sampling, data collection, and analysis; (4) describes the integration of the quantitative and qualitative components (i.e., where integration has occurred, how it has occurred, and who among the research team has participated in it); (5) describes any limitation of one method associated with the presence of the other method; and (6) describes any insights gained from mixing or integrating methods. An author checklist of the GRAMMS criteria is provided in Additional file 1. Selected articles will be evaluated on an item-by-item basis, with reviewers rating each item as “yes” (if the item was reported), “yes, but improvements are possible” (if the item was incompletely reported), or “no” (if the item was not reported). For the analysis (see ‘Synthesis of Results’ below), we will sum the scores for each item (1 = “yes”; 0.5 = “yes, but improvements are possible”; 0 = “no”).

The following information will also be extracted from all eligible articles: (1) the first author, (2) year of publication, (3) journal name, (4) number of authors, (5) country where the study was conducted (or, if not available, country of residence of the corresponding author), (6) type of mixed methods design, and (7) whether the list of authors included a mixed methodologist (i.e., graduate-level

training or expertise in mixed methods research). We will determine methodological expertise by examining the authors’ published details and affiliations, along with any other information given in the article that explicitly describes an author as having expertise in this area. In addition, the impact factor will be obtained at the year of publication for each journal, either directly from the journal’s website, or from the Journal Citation Report by Thompson Reuters on the Web of Science (<https://jcr.clarivate.com/>). Journals without an available impact factor will be assigned a value of zero [17].

Risk of bias of individual studies

We will assess risk of bias of included articles with the Mixed Methods Appraisal Tool (MMAT) (version 2011), which has been validated for systematic reviews of mixed studies (i.e., qualitative, quantitative, and mixed methods studies) [18–20] (Additional file 2). The MMAT is comprised of 11 items in three sections, including: (1) four items for appraising the qualitative component of a mixed methods study or a primary qualitative study; (2) four items for appraising the quantitative component of a mixed methods study or a primary quantitative study (i.e., randomized controlled, non-randomized, or descriptive); and (3) three items for appraising the mixed methods component of a mixed methods study. Pairs of reviewers will appraise each article according to the MMAT, using a similar process as described above.

Synthesis of results

We will assess all included articles for completeness of reporting on the six items of the GRAMMS instrument (i.e., 0–6 items, where 0 = no reporting of any items and 6 = complete reporting of all six items), and data will be presented as the mean (with standard deviation) or median (with inter-quartile range) number of quality items reported depending on whether the distribution is normal. Risk of bias scores obtained from the MMAT (i.e., 0–11 items) will also be summarized and presented. In addition, we will generate frequencies for individual reporting items on the GRAMMS instrument (i.e., the number of articles reporting a particular item) (Table 1) and describe extracted study characteristics as counts and percentages.

To examine correlation between the GRAMMS and MMAT instruments, we will compare the item scores for each article between the two instruments (i.e., 0–6 for GRAMMS, 0–11 for MMAT), using Pearson’s r or Spearman’s ρ for parametric and non-parametric distributions, respectively. Data distributions will be analyzed for normality by visual inspection of histograms, probability plots, and quantile–quantile plots, and then confirmed with the Kolmogorov–Smirnov test. Based on previous

Table 1 Reporting quality of included studies according to the Good Reporting of A Mixed Methods Study (GRAMMS) guideline

GRAMMS item	Reporting score and percentage of studies (n = X) reporting each GRAMMS item	
	Score ^a	Percentage
1. Describes the justification for using a mixed methods approach to the research question	X	X
2. Describes the mixed methods design (i.e., the purpose, priority, and sequence of methods)	X	X
3. Describes each method in terms of its sampling, data collection, and analysis	X	X
4. Describes the integration of the quantitative and qualitative components (i.e., where the integration has occurred, how it has occurred, and who among the research team has participated in it)	X	X
5. Describes any limitation of one method associated with the presence of the other method	X	X
6. Describes any insights gained from mixing or integrating methods	X	X

GRAMMS Good Reporting of A Mixed Methods Study

^a Count scores will be summed as 1 = "yes"; 0.5 = "yes, but improvements are possible"; and 0 = "no"

findings from research on randomized controlled trials and adherence to CONSORT guidelines [21–23], we predict that chiropractic mixed methods studies with a lower risk of bias (i.e., higher MMAT score) will be correlated with higher reporting quality.

We will use generalized estimating equations (GEEs) to explore the association between reporting quality and article characteristics (i.e., publication date, authorship, and journal impact factor). We will model the dependent variable as the number of GRAMMS items for which complete reporting occurred (maximum value of six) divided by the total number of GRAMMS items (six). The dependent variable will be regressed on the year of article publication (post-2009 versus pre-2009), journal impact factor (higher versus lower), number of co-authors (higher versus lower), and inclusion of an author with training in mixed methods (yes versus no) (Table 2).

These factors have previously been shown to be associated with methodological reporting quality [24, 25].

We will employ a binomial distribution and logit link function in our GEE models to generate crude and adjusted odds ratios, with corresponding 95% confidence intervals and *p*-values. Goodness-of-fit will be assessed by comparing our model's deviance to its degrees of freedom and by examining the residual plot. We will address over- or under-dispersion by re-running the model with a scale parameter calculated by dividing the deviance by its degrees of freedom. We will also incorporate the journal name as a grouping factor to account for potential similarity or clustering of articles published in the same journal.

We hypothesize that studies published since 2009 (i.e., ≥ 1 year after publication of the GRAMMS criteria [9]), studies published in higher impact journals,

Table 2 Unadjusted and adjusted odds ratios for the proportion of Good Reporting of A Mixed Methods Study (GRAMMS) items reported among included studies

Factor	Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Year of publication				
Pre-2009	Reference		Reference	
Post-2009	X	X	X	X
Journal impact factor ^a				
Lower	Reference		Reference	
Higher	X	X	X	X
Number of authors ^a				
Lower	Reference		Reference	
Higher	X	X	X	X
Inclusion of methodologist				
No/unclear	Reference		Reference	
Yes	X	X	X	X

CI confidence interval, OR odds ratio

^a This factor will be dichotomized at the median value, calculated across included studies

those with a greater number of authors, and those that included a mixed methodologist, will be associated with higher reporting quality. A minimum sample of 40 chiropractic mixed methods articles will be needed to guard against over-fitting of our regression model (i.e., minimum of 10 observations per independent variable) [26]. Variance inflation factors (VIFs) will also be explored to assess for multicollinearity among independent variables [27]. If we detect multicollinearity between two or more variables (i.e., $VIFs \geq 10$), we will remove the variable(s) that we deem of lower importance [28]. The two-sided statistical significance level (α) will be 5%, and all data and comparative analyses will be performed using SPSS v26.0 (IBM SPSS Statistics ©).

Reporting

Our review will be reported in accordance with an adapted version of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for meta-epidemiological research [29].

Ethical considerations

This study is a methodological literature review of previously published articles and does not require ethics approval.

Discussion

This will be the first methodological review to examine the reporting quality of published mixed methods studies involving chiropractic research. The results of this review are important because they will inform areas for improvement regarding reporting of chiropractic mixed methods studies. This may lead to important changes in the quality of evidence generated from these studies, with consequent implications for chiropractic policy, research, editorial, and clinical practice.

Mixed methods research can serve as a powerful tool for investigating complex therapeutic interventions, educational programs or knowledge translation strategies for improving clinical practice [1–6]. However, mixed methods research also requires specialized skills in qualitative and quantitative data integration and analysis [1–3]. Therefore, chiropractors conducting these types of studies should undertake graduate-level training in mixed methods research or, at a minimum, collaborate with researchers possessing mixed methodological expertise.

Previous research has shown that certain authorship factors, such as methodological expertise, as well as having multiple authors on a research project, can significantly improve the reporting quality and conduct of studies [24, 25, 30]. For example, a study on reporting quality among systematic reviews [30] found that including methodologists on research teams was associated

with greater concordance with reporting guidelines. Likewise, more recent articles or those published in journals with higher impact factors tend to meet better reporting standards [24, 25]. Yet, no research to date has investigated the influence of these or other factors on the quality of reporting among published chiropractic mixed methods studies.

Strengths and limitations

Our methodological review has several strengths. First, we will conduct a comprehensive and exhaustive search to identify all eligible studies involving chiropractic mixed methods research. To reduce errors in our methodological procedures, we will perform article screening, data extraction and quality appraisals in duplicate. Moreover, statistical adjustments will be applied at the analysis stage to control for between-group differences when exploring associations, and GEE modelling will be used to account for hierarchical clustering of articles within journals. For our regression model, we have prespecified the anticipated direction of association for each independent variable a priori to give reassurances that associations are unlikely to be spurious if detected. A limitation of this review is we will exclude non-English publications, which may lead to selection bias.

Knowledge translation

Dissemination of our review will occur via a peer-reviewed publication and a conference presentation. The review findings will also be presented publicly and defended as part of a doctoral thesis.

Abbreviations

CI: Confidence Interval; CINAHL: Cumulative Index to Nursing and Allied Health Literature; CONSORT: Consolidated Standards of Reporting Trials; EMBASE: Excerpta Medica Database; GEE: Generalized Estimating Equation; GRAMMS: Good Reporting of A Mixed Methods Study; ICL: Index to Chiropractic Literature; MEDLINE: Medical Literature Analysis and Retrieval System Online; MMAT: Mixed Methods Appraisal Tool; OR: Odds Ratio; OSF: Open Science Framework; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; SPSS: Statistical Program for the Social Sciences; SR: Systematic Review; VIF: Variance Inflation Factor.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12998-021-00395-0>.

Additional file 1. Good Reporting of A Mixed Methods Study (GRAMMS) checklist. **Additional file 2.** Mixed Methods Appraisal Tool (MMAT), version 2011.

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Authors' contributions

Concept development: PCE, LM, MO, JWB; Design: PCE, LM, MO, JWB; Supervision: LM, MO, JWB; Methods consultation: LM, MO, JWB; Literature search: PCE, RJG; Writing of protocol manuscript: PCE; Critical review of protocol manuscript for intellectual content: PCE, KJS, LM, MO, PSN, JVN, CAB, CC, RJG, JWB. All authors also read and approved the final manuscript.

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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

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

PCE is supported by grants from McMaster University, the NCMIC Foundation, and the Canadian Chiropractic Research Foundation outside of the submitted work. All authors have no competing interests to declare.

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Supplementary Material

Additional file 1: Good Reporting of A Mixed Methods Study (GRAMMS) checklist

Additional file 2: Mixed Methods Appraisal Tool (MMAT), version 2011

Additional file 1 Checklist of items for the Good Reporting of A Mixed Methods Study (GRAMMS) guideline [1,2]

Mixed methods reporting	
GRAMMS guideline	Location in manuscript where items are reported
1) Describes the justification for using a mixed methods approach to the research question	
2) Describes the design in terms of the purpose, priority and sequence of methods	
3) Describes each method in terms of sampling, data collection and analysis	
4) Describes the integration of the quantitative and qualitative components	
5) Describes any limitation of one method associated with the presence of the other method	
6) Describes any insights gained from mixing or integrating methods	

GRAMMS Good Reporting of A Mixed Methods Study

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1. O’Cathain A, Murphy E, Nicholl J. The quality of mixed methods studies in health services research. *J Health Serv Res Policy*. 2008;13:92-98.
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Additional file 2 Mixed Methods Appraisal Tool (MMAT), version 2011

Types of mixed methods study components or primary studies	Methodological quality criteria (see tutorial for definitions and examples)	Responses			
		Yes	No	Can't tell	Comments
Screening questions (for all types)	• Are there clear qualitative and quantitative research questions (or objectives*), or a clear mixed methods question (or objective*)?				
	• Do the collected data allow to address the research question (objective)? E.g., consider whether the follow-up period is long enough for the outcome to occur (for longitudinal studies or study components).				
	<i>Further appraisal may not be feasible or appropriate when the answer is 'No' or 'Can't tell' to one or both screening questions.</i>				
1. Qualitative	1.1. Are the sources of qualitative data (archives, documents, informants, observations) relevant to address the research question (objective)?				
	1.2. Is the process for analyzing qualitative data relevant to address the research question (objective)?				
	1.3. Is appropriate consideration given to how findings relate to the context, e.g., the setting, in which the data were collected?				
	1.4. Is appropriate consideration given to how findings relate to researchers' influence, e.g., through their interactions with participants?				
2. Quantitative randomized controlled (trials)	2.1. Is there a clear description of the randomization (or an appropriate sequence generation)?				
	2.2. Is there a clear description of the allocation concealment (or blinding when applicable)?				
	2.3. Are there complete outcome data (80% or above)?				
	2.4. Is there low withdrawal/drop-out (below 20%)?				
3. Quantitative non-randomized	3.1. Are participants (organizations) recruited in a way that minimizes selection bias?				
	3.2. Are measurements appropriate (clear origin, or validity known, or standard instrument; and absence of contamination between groups when appropriate) regarding the exposure/intervention and outcomes?				
	3.3. In the groups being compared (exposed vs. non-exposed; with intervention vs. without; cases vs. controls), are the participants comparable, or do researchers take into account (control for) the difference between these groups?				
	3.4. Are there complete outcome data (80% or above), and, when applicable, an acceptable response rate (60% or above), or an acceptable follow-up rate for cohort studies (depending on the duration of follow-up)?				
4. Quantitative descriptive	4.1. Is the sampling strategy relevant to address the quantitative research question (quantitative aspect of the mixed methods question)?				
	4.2. Is the sample representative of the population under study?				
	4.3. Are measurements appropriate (clear origin, or validity known, or standard instrument)?				
	4.4. Is there an acceptable response rate (60% or above)?				
5. Mixed methods	5.1. Is the mixed methods research design relevant to address the qualitative and quantitative research questions (or objectives), or the qualitative and quantitative aspects of the mixed methods question (or objective)?				
	5.2. Is the integration of qualitative and quantitative data (or results*) relevant to address the research question (objective)?				
	5.3. Is appropriate consideration given to the limitations associated with this integration, e.g., the divergence of qualitative and quantitative data (or results*) in a triangulation design?				
	<i>Criteria for the qualitative component (1.1 to 1.4), and appropriate criteria for the quantitative component (2.1 to 2.4, or 3.1 to 3.4, or 4.1 to 4.4), must also be applied.</i>				

*These two items are not considered as double-barreled items since in mixed methods research, (1) there may be research questions (quantitative research) or research objectives (qualitative research), and (2) data may be integrated, and/or qualitative findings and quantitative results can be integrated. (Source: <http://mixedmethodsappraisaltoolpublic.pbworks.com>.)

Chapter 3:

Quality of Reporting in Chiropractic Mixed Methods Research: A Methodological Review

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Contributorship:

Concept development (provided idea for the research): P.C.E., L.M., M.O., J.W.B.

Design (planned the methods to generate the results): P.C.E., L.M., M.O., J.W.B.

Supervision (provided oversight, responsible for organization and implementation, writing of the manuscript): P.C.E., L.M., M.O., J.W.B.

Data collection/processing (responsible for experiments, patient management, organization, or reporting data): P.C.E., K.J.S., P.S.N., J.V.N., C.A.B., C.C., R.J.C.

Analysis/interpretation (responsible for statistical analysis, evaluation, and presentation of the results): P.C.E.

Literature search (performed the literature search): P.C.E., R.J.C.

Writing (responsible for writing a substantive part of the manuscript): P.C.E.

Critical review (revised manuscript for intellectual content, this does not relate to spelling and grammar checking): P.C.E., K.J.S., L.M., M.O., P.S.N., J.V.N., C.A.B., C.C., R.J.C., J.W.B.

Quality of Reporting in Chiropractic Mixed Methods Research: A Methodological Review

ABSTRACT

Objective: We undertook a methodological review to examine the quality of reporting in chiropractic mixed methods research.

Methods: We searched MEDLINE, EMBASE, CINAHL, and the Index to Chiropractic Literature to December 31, 2020 for chiropractic studies reporting the use of both qualitative and quantitative methods, or mixed qualitative methods. Pairs of reviewers independently screened titles and abstracts and full-text studies, extracted data, and appraised reporting quality using the Good Reporting of A Mixed Methods Study (GRAMMS) guideline and risk of bias with the Mixed Methods Appraisal Tool (MMAT). We used generalized estimating equations to explore factors associated with reporting quality.

Results: Of 1,040 citations, 55 studies were eligible for review. Thirty-seven of these 55 articles employed either a multistage or convergent mixed methods design, and on average three of six GRAMMS items were reported among included studies. We found a strong positive correlation in scores between the GRAMMS and MMAT instruments ($r = .78$; 95% confidence interval [CI], 0.66 to 0.87). In our adjusted analysis, only publication in journals with an impact factor versus no impact factor (adjusted odds ratio = 2.71; 95% CI, 1.48 to 4.95) was associated with higher reporting quality.

Conclusion: Our findings suggest the quality of reporting in chiropractic mixed methods research is often poor, particularly among studies with a higher risk of bias. Creating awareness amongst the chiropractic research community of mixed methods reporting and quality of conduct guidelines may lead to improvements in the quality of published mixed methods chiropractic research.

Key Indexing Terms: *Chiropractic; Mixed Methods Research; Reporting Quality; Methodological Review*

INTRODUCTION

Mixed methods designs, consisting of a combination of qualitative and quantitative methods, have been increasingly used in health care research to enrich findings.^{1,2} The explicit integration of methods within a mixed methods study is distinct from research where investigators use quantitative and qualitative methods in a single study but without linking or integrating the two components (e.g., adding a series of open-ended questions to the end of a quantitative survey).¹⁻⁵ This distinction of mixed methods, that is, as an approach to research beyond simply using quantitative and qualitative methods as separate and distinct components in a single study, formally emerged within the mixed methods literature by the early 1990s.¹ Subsequently, the intentional and explicit integration of quantitative and qualitative methods has become increasingly recognized as a central tenet of mixed methods research.¹⁻⁵ An integrated mixed methods approach is particularly useful for investigating complex, multilevel programs and interventions,^{3,6-8} and is therefore well-suited to address several issues relevant to the chiropractic profession. For example, program evaluations to inform health policy decisions, knowledge translation/implementation of clinical practice guidelines, or comparisons of multi-component therapeutic interventions. However, little is known about the frequency of use of this methodology in chiropractic research, or the quality of reporting among chiropractic studies employing mixed methods.

Previous methodological reviews have examined published mixed methods studies in healthcare fields other than chiropractic;⁹⁻¹⁴ these reviews have highlighted areas for improvement in the quality of methodological reporting. For instance, one

review⁹ found that mixed methods studies in health services research typically did not describe or justify the need for a mixed methods design or integrate data and findings from the individual quantitative and qualitative components. This lack of integration inhibits new insights from being generated within mixed methods studies (i.e., beyond the results obtained from the two separate components), thereby limiting the potential of this research strategy.¹⁻³ We undertook a methodological review to examine the frequency and quality of reporting of chiropractic mixed methods studies. We also used multivariable regression analysis to explore possible factors influencing reporting quality. Our findings are important as they may guide recommendations to improve the reporting of future chiropractic research employing mixed methods designs.

METHODS

Protocol and Registration

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines adapted for meta-epidemiological research,¹⁵ and registered our protocol¹⁶ with the Open Science Framework (OSF) (<https://osf.io/mxyr8>).

Information Sources

We searched MEDLINE, EMBASE, CINAHL, and the Index to Chiropractic Literature (ICL) to identify published chiropractic mixed methods studies, from the inception of each database to December 31, 2020. We developed our search strategy with the assistance of an academic librarian (RJC) (Supplementary File 1). We also hand-

searched the bibliographies of eligible articles and contacted content experts to identify any additional references.

Eligibility Criteria

We included articles that met the following criteria: (1) published in a peer-reviewed journal; (2) written in the English language; (3) authored by one or more chiropractic researchers (i.e., someone with chiropractic credentials or affiliation with a chiropractic educational institution); (4) involved any type of chiropractic intervention (e.g., therapeutic, educational) or non-intervention research (e.g., policy, scope of practice); (5) reported a mixed methods approach (i.e., the use of both qualitative and quantitative methods,^{1,2} or mixed qualitative methods,⁵ in the same research study); and (6) was an empirical study that incorporated primary data collection. In order to help increase our yield of mixed methods studies, we only included mixed qualitative studies⁵ or ‘mixed’ surveys (i.e., those with both closed- and open-ended questions) where the use of “mixed methods” was explicitly stated in the title or abstract. We excluded protocols, letters, editorials, commentaries, case reports, books and book chapters, grey literature (e.g., conference proceedings, abstracts, lectures, dissertations or unpublished manuscripts), and secondary sources of evidence, e.g., clinical practice guidelines or any type of review article.

Study Selection

Two reviewers (PCE, CC) independently screened titles and abstracts of identified citations, and full texts of potentially eligible studies. Reviewers resolved any disagreements by discussion or, if needed, with the help of an adjudicator (KJS). We used online systematic review software (DistillerSR, Evidence Partners, Ottawa, Canada; <https://www.evidencepartners.com>) to facilitate literature screening.

Data Extraction and Assessment of Reporting Quality

Using standardized, pilot-tested data extraction forms, pairs of reviewers (PCE, KJS, PSN, JVN, CAB) independently extracted data and assessed reporting quality of included articles. Discrepancies were resolved by consensus or adjudication by a third reviewer. The following information was extracted from all eligible studies: (1) first author, (2) year of publication, (3) journal name, (4) number of authors, (5) country where the study was conducted (or country of residence of the corresponding author when not available or when the study was international), (6) type of mixed methods design, and (7) inclusion of a methodologist among the authors (rated as “yes” or “no/unclear”). A methodologist was defined as a contributing author with training in one or more health research methodology subdisciplines, including mixed methods research, qualitative research, public health, epidemiology, health technology assessment, health services research, knowledge translation/implementation science, or biostatistics. The involvement of a methodologist was determined by examining each article for authors’ qualifications or affiliations and information reported in their published digital identifiers (e.g., ORCID iD) and in the methodology section. In instances where we rated author reporting of

methodological expertise as “unclear,” we used a conservative approach and combined these counts with our “no” responses. When available, we obtained the impact factor at the time of publication for each journal in which an eligible study was published, either directly from the journal’s website or from the Journal Citation Report (<https://jcr.clarivate.com/>).

We used the six items that comprise the Good Reporting of A Mixed Methods Study (GRAMMS) guideline⁹ to assess reporting quality: (1) described the justification for using a mixed methods approach to answer the research question; (2) described the mixed methods design (i.e., the purpose, priority, and sequence of methods); (3) described the quantitative and qualitative components separately in terms of sampling, data collection, and analysis; (4) described the integration of quantitative and qualitative components (i.e., where integration occurred, how it occurred, and who among the research team participated in it); (5) described any limitation of one method that emerged from the presence of the other method; and (6) described any insights gained from mixing or integrating methods.

We chose the GRAMMS guideline over other appraisal instruments^{1,2,17} because of its explicit application to mixed methods research⁹ and widespread use.^{1,2,9,11-14} We evaluated all selected articles on an item-by-item basis, with reviewers rating each item with a “yes” (if the item was reported), “yes, but improvements are possible” (if the item was incompletely reported), or “no” (if the item was not reported).^{9,14} The decision-making rules used by reviewers for rating GRAMMS items are provided in Supplementary File 2. We assigned a score for each of the six items as follows: 1 =

“yes”; 0.5 = “yes, but improvements are possible”; 0 = “no”, for a total score ranging from 0 to 6.

Risk of Bias of Individual Studies

We assessed risk of bias of included articles with the Mixed Methods Appraisal Tool (MMAT) (version 2011), which has been validated as a risk of bias tool for systematic reviews of mixed studies (i.e., qualitative, quantitative, and mixed methods studies).¹⁸⁻²⁰

The MMAT is comprised of 11 items in three sections, including: (1) four items for appraising the qualitative component of a mixed methods study or a primary qualitative study; (2) four items for appraising the quantitative component of a mixed methods study or a primary quantitative study (i.e., randomized controlled, non-randomized, or descriptive); and (3) three items for appraising the mixed methods component of a mixed methods study. Pairs of reviewers appraised each article according to the MMAT¹⁸⁻²⁰ using a similar scoring process to the GRAMMS assessment described above, for a total score ranging from 0 to 11.

Synthesis of Results

We assessed agreement for full-text screening using the kappa (κ) statistic, and interpreted the strength of agreement as: 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 ($\kappa > 0.8$).²¹ For the purpose of analysis, studies reporting quantitative and qualitative results in separate papers were combined and included as one article. We summarized the data using mean

and standard deviation (SD) for continuous variables that were normally distributed, and median and inter-quartile range (IQR) for continuous variables that were not. All distributions were analyzed for normality by examining the data histograms, probability and quantile-quantile plots, and the Kolmogorov-Smirnov test.

We examined the correlation between total scores for the GRAMMS and MMAT instruments using Pearson's r for parametric distributions. Based on previous findings from research on randomized controlled trials and adherence to Consolidated Standards of Reporting Trials (CONSORT) guidelines,²²⁻²⁴ we hypothesized that chiropractic mixed methods articles with a lower risk of bias (i.e., higher MMAT scores) would be correlated with higher reporting quality (i.e., higher GRAMMS scores).

We built a generalized estimating equation (GEE) to explore the association between reporting quality and article or journal characteristics, including publication date, multiple authorship, inclusion of a methodologist, and availability of a journal impact factor. These variables have previously been shown to be associated with methodological reporting quality.^{25,26} Based on previous literature,²⁵⁻²⁹ we hypothesized that studies published since 2009 (i.e., ≥ 1 year after publication of the GRAMMS guideline⁹), studies published in journals with an impact factor, those with a greater number of authors, and those that included a methodologist would be associated with higher reporting quality. We modelled our dependent variable as the number of GRAMMS items for which complete reporting occurred (maximum value of six) divided by the total number of GRAMMS items (six), and used the 'events/trials' function in SPSS to generate a binary outcome. We regressed the dependent variable on the year of article publication (2009

and later versus pre-2009), availability of a journal impact factor (yes versus no), number of authors (higher versus lower), and inclusion of a methodologist (yes versus no). We dichotomized author number at the median value (four) calculated across included studies. We originally planned to explore higher versus lower journal impact factor and inclusion of a mixed methodologist as independent variables,¹⁶ but we modified our approach due to a large number of studies published in journals without an impact factor and where mixed methodological expertise was unclearly reported.

We employed a binomial distribution and logit link function for our GEE to generate a crude and adjusted odds ratio (OR), and a 95% confidence interval (CI) and corresponding *p*-value, for each independent variable. We assessed goodness-of-fit by comparing our model's deviance to its degrees of freedom and by examining the associated residual plot. Over- or under-dispersion was addressed by re-running the model with a scale parameter calculated by dividing the deviance by its degrees of freedom. To account for potential clustering or similarity of articles published in the same journal, we assumed an exchangeable working correlation matrix and specified the journal name as a grouping factor.

To guard against over-fitting of our regression model,³⁰ we required a minimum sample of 40 chiropractic mixed methods articles (i.e., minimum of 10 observations per independent variable). We tested for multicollinearity to examine correlations across predictors by calculating the variance inflation factors (VIFs) associated with each independent variable in our regression model. VIFs greater than or equal to 10 indicated the presence of multicollinearity.³¹ If we detected multicollinearity between two or more

variables, we removed the variable(s) that we deemed of lower importance.³² All data and comparative analyses were performed using SPSS v26.0 (IBM SPSS Statistics ©), and the two-sided statistical significance level (α) was 5%.

RESULTS

Our search identified 1,040 citations, and 65 articles met eligibility criteria for review (Supplementary File 3). Agreement between reviewers at the full-text screening stage was substantial ($\kappa = 0.70$). Ten studies reported quantitative and qualitative results in separate articles. As such, 55 unique mixed methods studies were analyzed (Fig 1). The frequency of articles by year of publication is shown in Figure 2.

Study Characteristics

Of the 55 eligible studies, the majority (69%) were conducted in, or had corresponding authors from, North America; over half (53%) had four or fewer authors and more than three-quarters (76%) were published after 2009 (Table 1). Twenty-nine (53%) studies were published in journals with an impact factor (median impact factor = 1.9 [IQR: 1.2 to 2.6]). Two-thirds of studies employed a complex / multistage (34%) or convergent (33%) mixed methods design, and the remainder used sequential explanatory (20%) or exploratory (13%) designs. Almost half of eligible studies (25 of 55; 45%) included a methodologist among their authors.

Reporting Quality and Risk of Bias of Included Studies

Referring to the six GRAMMS criteria, the description of the quantitative and qualitative methods (i.e., sampling, data collection, and analysis of each component) was the best reported item (77%). Authors' descriptions of the type of mixed methods design (including the purpose, priority, and sequence of methods) (23%), and specific limitations arising from the use of one method in association with the presence of the other method (16%) were the most poorly reported items (Table 2). Only three (5%) of the 55 studies fully adhered to all six GRAMMS criteria for good reporting of mixed methods research. Four studies (7%) adhered to five criteria, 10 studies (18%) adhered to four criteria, and most studies (38 of 55; 69%) adhered to three criteria or less (Supplementary File 4).

The mean number (SD) of the six GRAMMS items reported across studies was 3.0 (1.5), and the mean (SD) number of the eleven MMAT items was 6.8 (2.3). The Kolmogorov-Smirnov test was not significant for the frequencies of item scores on the GRAMMS ($p = .200$) or MMAT ($p = .173$) instruments, confirming their approximation to normal distributions. The item score between the GRAMMS and MMAT instruments was strongly and positively correlated ($r = .78$; 95% CI, 0.66 to 0.87; $p < .001$) (Fig 3). A summary table of the reporting quality and risk of bias scores for each of the 55 individual studies is provided in Supplementary File 4.

Variables Associated with Reporting Quality

In our univariate GEE analyses, publication in journals with an impact factor (OR = 2.92; 95% CI, 1.79 to 4.74; $p < .001$), inclusion of more than four authors (OR = 2.26; 95% CI, 1.37 to 3.72; $p = .001$), and having a methodologist among the study team (OR = 1.85;

95% CI, 1.11 to 3.10; $p = .019$) were associated with the odds of higher reporting quality (Table 3). In our multivariable GEE analysis, we found that only publication in journals with an impact factor (adjusted OR = 2.71; 95% CI, 1.48 to 4.95; $p = .001$) remained associated with higher reporting quality (Table 3). All VIFs were less than 1.9, suggesting no important collinearity among independent variables.

DISCUSSION

We found the quality of reporting among chiropractic mixed methods studies published in the biomedical and allied health literature is often poor. According to the GRAMMS guideline,⁹ only half of the criteria for good reporting in mixed methods research were met across the 55 eligible studies. In particular, authors' descriptions of the mixed methods design, as well as the limitations of combining qualitative and quantitative methods, were poorly reported in approximately 80% of articles. Four out of 10 studies also failed to either adequately justify the use of mixed methods research or describe the integration and insights gained from mixing qualitative and quantitative components. In addition, only 5% of studies were compliant with all six GRAMMS criteria.

Our findings are consistent with the results of methodological reviews of mixed methods reporting in other health-related (e.g., public health, palliative care) and social science disciplines.⁹⁻¹⁴ Similar to our findings, the quality of mixed methods reporting in many of the studies in these reviews was found to be deficient across various GRAMMS^{9,11-14} and MMAT¹⁰ guideline domains. With the growing number of mixed methods studies being published within the health sciences in recent years,^{1,2} the findings

of our review and others⁹⁻¹⁴ indicate an urgent need to improve the standards of reporting in mixed methods research.

We found a strong, positive correlation between higher quality of reporting and lower risk of bias (i.e., the GRAMMS and MMAT instruments). This suggests that authors who more completely report their methodology in mixed methods research are also more likely to report safeguards against risk of bias. However, because many chiropractic mixed methods studies in the current review were found to be both poorly reported and at risk of bias, we recommend that authors of future mixed methods studies be required by journal editors and reviewers to adhere to the GRAMMS guideline⁹ and the MMAT criteria.²⁰

Although some previous reviews²⁵⁻²⁹ have reported an association between higher number of authors, or inclusion of methodologists, and better reporting quality of studies, other reviews^{29,33,34} (as did ours) have failed to find an association. However, we found that publications in journals with an impact factor were 2.7 times more likely to have reported more complete details on their mixed methods compared to publications in journals without an impact factor. In our precision estimates (see Table 3), the adjusted odds ratio for this association included values between 48% and as high as nearly 5-fold. An association between reporting quality and journal impact factor has also been reported in previous methodological reviews.^{25,26} In contrast with previous research,^{25,26} we did not find a significant association between quality of reporting and the year of publication. As most journals (chiropractic and non-chiropractic) do not endorse any mixed methods

reporting guidelines,²⁰ authors of chiropractic mixed methods studies may not have been required to meet published mixed methods quality reporting standards.^{1-3,9,19}

Journal endorsement of reporting guidelines has been associated with better reporting and conduct of research studies,^{25,26} particularly if authors are obligated to meet these requirements as a condition of submission. The responsibility for enforcing compliance with reporting guidelines ultimately rests with journal editors. For example, the International Committee of Medical Journal Editors (ICMJE) has encouraged journals to request reporting standards from authors,³⁵ and when journals request authors to submit a completed reporting checklist (e.g., PRISMA for systematic reviews, CONSORT for randomized controlled trials), this has been shown to improve the quality of reporting.^{25,26} Editors of journals within the chiropractic profession could therefore play a key role in improving the reporting quality of mixed methods studies by endorsing mixed methods article reporting and quality of conduct guidelines, such as the GRAMMS⁹ and MMAT,²⁰ or other published mixed methods guideline criteria.^{1,2,17} Chiropractic journals could highlight these guidelines in their online submission instructions, and request that authors submit a completed reporting checklist highlighting where in their manuscript each item has been reported. We have provided author and peer review checklists of the GRAMMS and MMAT criteria, respectively, as supplemental material in our published methodological review protocol.¹⁶ Chiropractic journals could also reference well-presented mixed methods studies to serve as examples of good mixed methods reporting for prospective chiropractic authors. We have

identified four such examples³⁶⁻³⁹ in our review, and these studies are summarized and presented in Table 4.

Strengths and Limitations

Our review has several strengths. First, we conducted a comprehensive search in an attempt to identify all eligible studies involving chiropractic mixed methods research. To improve reliability of subjective decisions, we performed article screening, data extraction and quality appraisals in duplicate. Second, we controlled for between-group differences when exploring associations and used GEE modelling to account for hierarchical clustering of articles within journals. Third, for our regression models, we specified the anticipated direction of association for each independent variable *a priori* to give reassurances that significant associations were unlikely to be spurious.

A limitation of this review is we excluded non-English publications, which may lead to selection bias. By excluding qualitative studies and surveys that did not contain the terms “mixed methods” in their titles or abstracts, it is also possible that some chiropractic mixed methods studies may have been missed. However, our final review list (see Supplemental File 3) was reviewed by two chiropractic mixed methods experts and no additional chiropractic mixed methods studies were identified. Finally, we may not have accounted for all important variables (e.g., country of authorship), or interactions between variables,²⁶ that were relevant to the reporting quality of chiropractic mixed methods research.

CONCLUSION

Our findings suggest there is room for improvement in the reporting of chiropractic mixed methods studies. Using two different instruments, one for reporting quality and one for risk of bias, we found a strong positive correlation, indicating that studies with a lower risk of bias were strongly correlated with higher reporting quality. Creating awareness amongst the chiropractic research community of reporting and quality of conduct recommendations for mixed methods studies may improve the quality of reports. Reasons for author adherence or non-adherence to such recommendations are an important area in need of further research.

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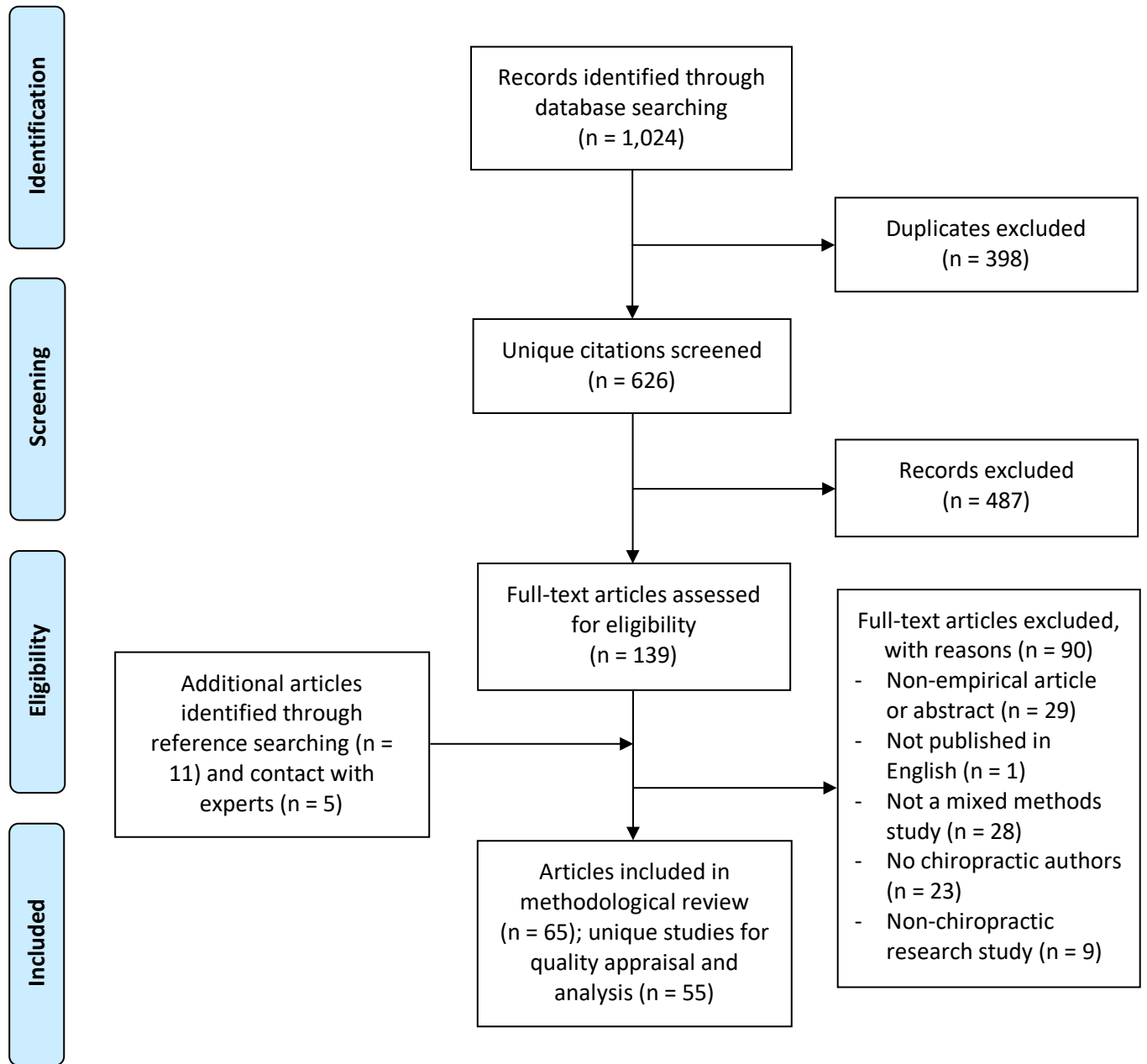


Fig 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

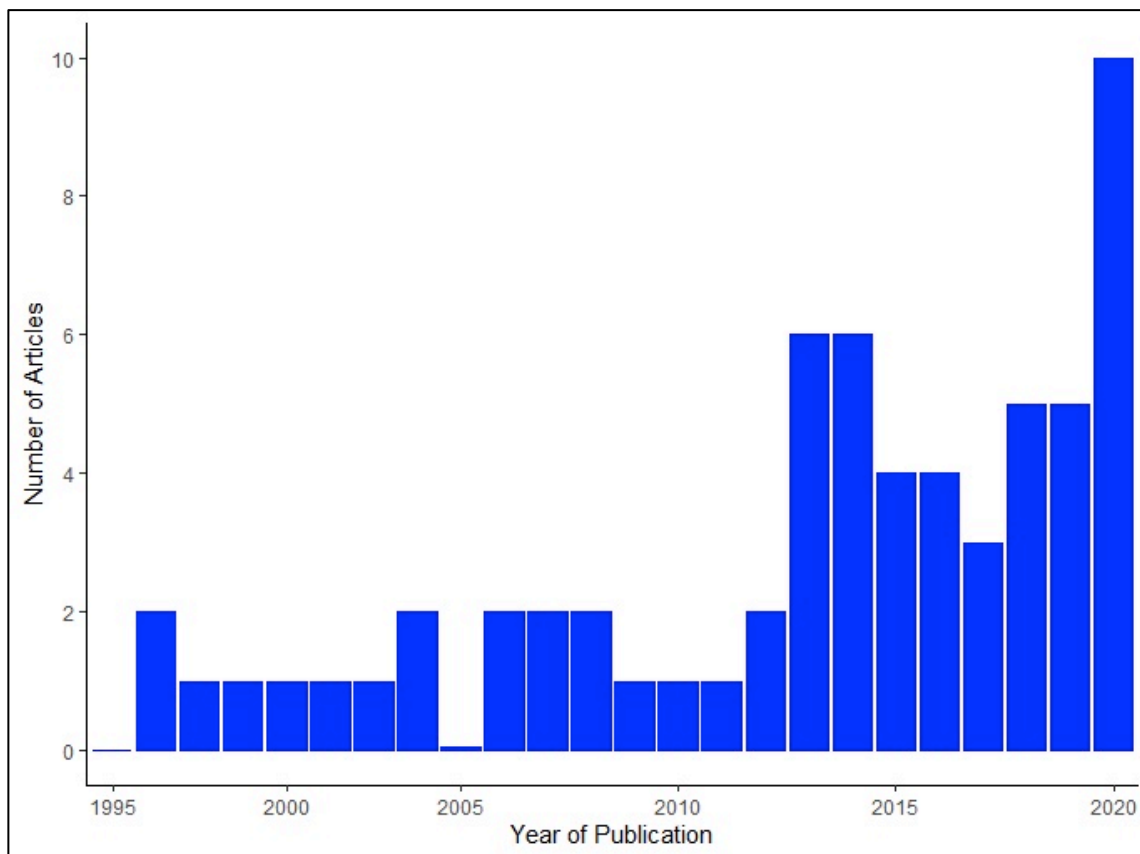


Fig 2. Histogram of the frequency of publication of chiropractic mixed methods articles (up to December 31, 2020).

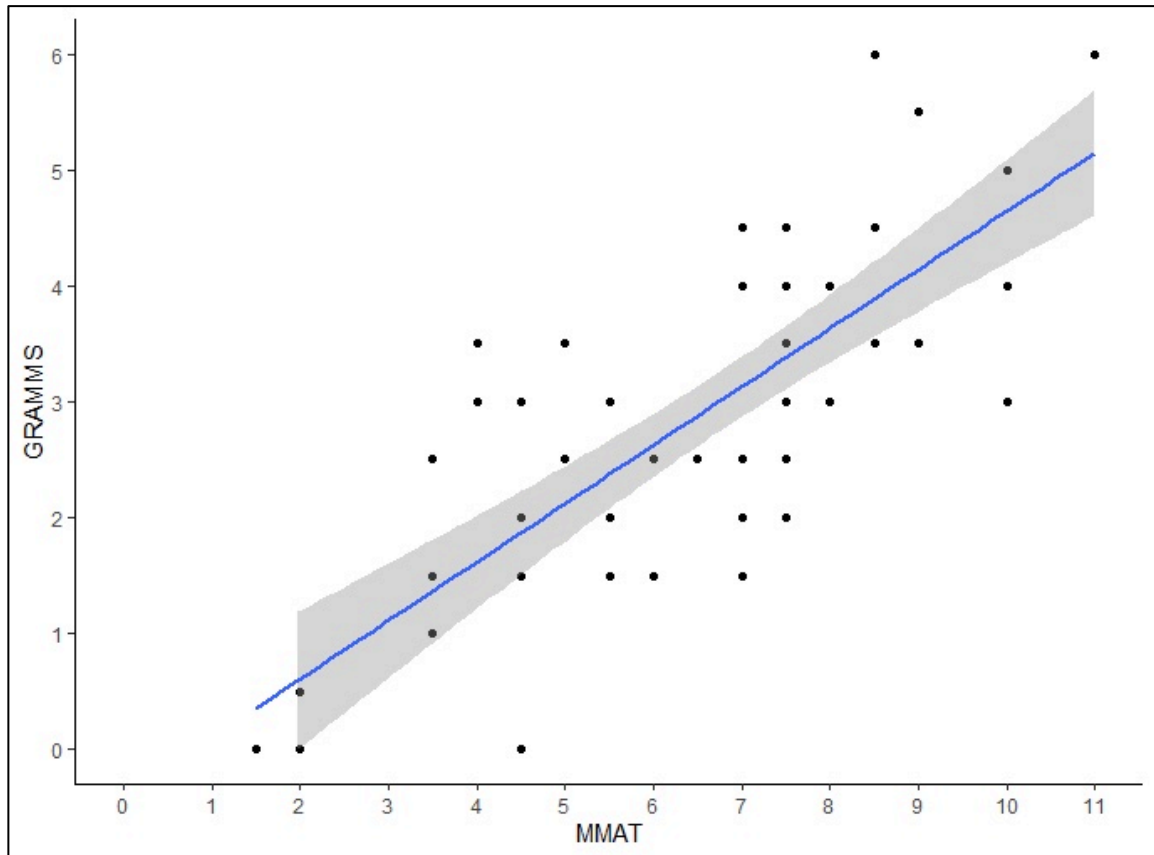


Fig 3. Correlation of item scores between the Good Reporting of A Mixed Methods Study (GRAMMS) guideline and the Mixed Methods Appraisal Tool (MMAT) for the 55 included studies.

Table 1 *Characteristics of the 55 included studies*

Study Characteristic	Category	n (%)
Year of publication	Pre-2009	13 (23.64)
	Post-2009	42 (76.36)
Number of authors ^{a,b}	≤ 4	29 (52.73)
	> 4	26 (47.27)
Country	United States of America	28 (50.91)
	Canada	10 (18.18)
	Australia	6 (10.91)
	Denmark	3 (5.45)
	United Kingdom	3 (5.45)
	Switzerland	2 (3.64)
	Germany	1 (1.82)
	South Africa	1 (1.82)
	Sweden	1 (1.82)
Mixed methods design	Complex / multistage	19 (34.54)
	Convergent	18 (32.73)
	Explanatory sequential	11 (20.00)
	Exploratory sequential	7 (12.73)
Methodologist	Yes	25 (45.45)
	No/unclear ^c	30 (54.55)
Journal impact factor	Yes	29 (52.73)
	No	26 (47.27)

^a Average values were used when studies reported quantitative and qualitative results in separate articles.

^b The cut-off point for author number was derived from the median value measured across included studies.

^c Inclusion of a methodologist was “unclear” in 15 (27.3%) of the 55 included studies.

Table 2 Reporting quality of the 55 included studies according to the Good Reporting of A Mixed Methods Study (GRAMMS) guideline

GRAMMS Item	Reporting Score and Percentage of Studies (n = 55) Reporting each GRAMMS Item	
	Score (0-55) ^a	Percentage
1) Describes the justification for using a mixed methods approach to the research question	33.0	60.0%
2) Describes the mixed methods design (i.e., the purpose, priority, and sequence of methods)	12.5	22.7%
3) Describes each method in terms of its sampling, data collection, and analysis	42.5	77.3%
4) Describes the integration of the quantitative and qualitative components (i.e., where the integration has occurred, how it has occurred, and who among the research team has participated in it)	33.5	60.9%
5) Describes any limitation of one method associated with the presence of the other method	9.0	16.4%
6) Describes any insights gained from mixing or integrating methods	34.0	61.8%
	Reporting Score and Percentage of Studies (n = 55) Reporting all 6 GRAMMS Items	
	3.0	5.4%

GRAMMS, Good Reporting of A Mixed Methods Study.

^a Count scores are summed as 1 = “yes”; 0.5 = “yes, but improvements are possible”; and 0 = “no”.

Table 3 Unadjusted and adjusted odds ratios for the association between article or journal characteristics and the proportion of Good Reporting of A Mixed Methods Study (GRAMMS) items reported among the 55 included studies

Variable	Univariate	P-value	Multivariable	P-value
	Unadjusted OR (95% CI)		Adjusted OR (95% CI)	
Year of publication <ul style="list-style-type: none"> • Pre-2009 • Post-2009 	Reference 1.78 (0.99-3.20)	.053	Reference 1.62 (0.92-2.84)	.095
Journal impact factor <ul style="list-style-type: none"> • No • Yes 	Reference 2.92 (1.79-4.74)	< .001	Reference 2.71 (1.48-4.95)	.001
Number of authors ^a <ul style="list-style-type: none"> • ≤ 4 • > 4 	Reference 2.26 (1.37-3.72)	.001	Reference 1.29 (0.70-2.38)	.420
Inclusion of methodologist <ul style="list-style-type: none"> • No/unclear • Yes 	Reference 1.85 (1.11-3.10)	.019	Reference 0.86 (0.46-1.62)	.643

CI, confidence interval; OR, odds ratio.

^a This variable was dichotomized at the median value (i.e., 4), calculated across included studies.

Table 4 *Published examples of well-reported mixed methods studies in chiropractic research*

First Author	Study Objective	Justification for Using Mixed Methods ^a	Mixed Methods Design	Data Sources	Integration of Qualitative and Quantitative Components ^b	Insights Gained from Using Mixed Methods
Connell ³⁶	Explore chiropractors' understanding of building trust with patients	Complementarity / development to inform data collection	Exploratory sequential	Interviews with chiropractors in British Columbia (BC) on perceived patient trust, and questionnaire distributed to all members of the provincial chiropractic association	Building, by using the qualitative findings to create a questionnaire; Merging, by comparing the qualitative and quantitative findings through narrative discussion	The qualitative findings ensured that survey questions reflected the perspectives of BC chiropractors; The quantitative findings were used to confirm themes related to chiropractors' perceptions of trust
Evans ³⁷	Understand Global Perceived Effect (GPE) in chronic neck pain patients	Complementarity	Complex / multistage	Patient self-report outcomes (including GPE) measured at baseline, 4, 12, 26, and 52 weeks post-randomization; Interviews with trial participants at conclusion of intervention phase (week 12)	Merging, by data transformation (i.e., quantifying qualitative data), and by comparing the quantitative and qualitative findings through joint display tables and narrative discussion	The qualitative findings provided a deeper understanding of GPE in chronic neck pain patients and allowed for better interpretation of the results from the parent clinical trial
Maiers ³⁸	Explore perceptions of spinal manipulative therapy and exercise among seniors with chronic neck pain	Complementarity	Complex / multistage	Patient self-report outcomes (pain, disability, general health, satisfaction, medication use) measured at baseline, 4, 12, 26, and 52 weeks post-randomization; Interviews with trial participants at conclusion of intervention phase (week 12)	Merging, by data transformation (i.e., quantifying qualitative data), and by comparing the quantitative and qualitative findings through narrative discussion of the results	The qualitative findings helped to identify facets of the clinical encounter that contributed to a positive therapeutic experience in the parent clinical trial (i.e., relationships and interactions with health care team members, more so than change in neck pain symptoms)
Pohlman ³⁹	Evaluate patient safety attitudes among chiropractic teaching clinic stakeholders	Complementarity / triangulation	Convergent	Online survey (closed- and open-ended questions) with students, faculty, and staff of 5 international chiropractic educational programs on attitudes toward patient safety	Merging, by comparing the quantitative and qualitative findings through joint display figures and narrative discussion	The qualitative findings provided in-depth insight into the survey results and helped identify areas for improvement in patient safety education within chiropractic teaching programs

^a *Complementarity* seeks elaboration, enhancement, illustration, clarification of the results from one method with the results from the other method. *Development* seeks to use the results from one method to help develop or inform the other method, where development is broadly construed to include sampling and implementation, as well as measurement decisions. *Triangulation* seeks convergence, corroboration, correspondence of results from the different methods. (Source: Greene JC, Caracelli VJ, Graham WF. Toward a conceptual framework for mixed-method evaluation designs. *Educ Eval Policy Anal.* 1989;11(3):255-74.)

^b Integration through *building* occurs when results from one data collection procedure informs the data collection approach of the other procedure. Integration through *merging* of data occurs when researchers bring the two databases together for analysis and for comparison. (Source: Fetters MD, Curry LA, Creswell JW. Achieving integration in mixed methods designs – principles and practices. *Health Serv Res.* 2013;48(6 Pt 2):2134-56.)

Supplementary Files

Supplementary File 1: Database search strategies

Supplementary File 2: Decision-making rules for the GRAMMS instrument

Supplementary File 3: Reference list of included articles

Supplementary File 4: GRAMMS and MMAT item scores

Supplementary File 1. *Search strategies for the Medical Literature Analysis and Retrieval System Online (MEDLINE), the Excerpta Medica Database (EMBASE), the Cumulative Index to Nursing and Allied Health Literature (CINAHL), and the Index to Chiropractic Literature (ICL), from inception of each database to December 31, 2020.*

Database: OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Search Strategy:

-
- 1 Manipulation, Chiropractic/ or Chiropractic/ (4121)
 - 2 Manipulation, Spinal/ (1611)
 - 3 chiropract*.ti,ab,kf,jw. (6999)
 - 4 or/1-3 (9357)
 - 5 (mixed adj3 methods).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (21745)
 - 6 Qualitative Research/ or qualit*.mp. (310714)
 - 7 5 or 6 (321158)
 - 8 4 and 7 (242)

EMBASE (OVID)

Database: Embase <1974 to 2020 December 31>

Search Strategy:

-
- 1 chiropractic/ or chiropractic manipulation/ (4775)
 - 2 spine manipulation/ (638)
 - 3 chiropract*.ti,ab,kw,jw. (6656)
 - 4 or/1-3 (8834)
 - 5 (mixed adj3 methods).mp. (24740)
 - 6 qualitative research/ (83067)
 - 7 qualit*.mp. (395745)
 - 8 or/5-7 (407517)
 - 9 4 and 8 (287)

CINAHL (Ebsco)

- | | | |
|----|--|--------|
| S1 | (MH "Chiropractic") OR (MH "Manipulation, Chiropractic") | 20,210 |
| S2 | TX chiropract* | 48,113 |

S3	S1 OR S2	48,113
S4	TX mixed N3 methods	18,656
S5	(MH "Qualitative Studies+")	152,758
S6	TX qualitat*	186,409
S7	S4 OR S5 OR S6	224,415
S8	S3 AND S7	449
 ICL		
S1	All Fields:"mixed methods"	29
S2	Subject:"Qualitative Research"	18
S3	All Fields:"mixed methods" OR Subject:"Qualitative Research"	46

Supplementary File 2. *Decision-making rules for rating the six items on the Good Reporting of A Mixed Methods Study (GRAMMS) guideline (adapted from Fàbregues et al.¹⁴).*

GRAMMS Guideline Item	Decision-Making Rule
1) Describes the justification for using a mixed methods approach to the research question	⇒ <i>Yes</i> – Provides an explicit justification for using mixed methods research. ⇒ <i>Yes, but</i> – Does not provide an explicit justification for using mixed methods research, but this justification can still be inferred. ⇒ <i>No</i> – Does not provide an explicit justification for using mixed methods research, and this justification cannot be inferred.
2) Describes the mixed methods design (i.e., the purpose, priority, and sequence of methods)	⇒ <i>Yes</i> – Specifies the type of mixed methods research design used and describes both the priority and the timing of the quantitative and qualitative components. ⇒ <i>Yes, but</i> – Specifies the type of mixed methods research design used and describes either the priority or the timing of the quantitative and qualitative components. ⇒ <i>No</i> – Does not specify the type of mixed methods research design used, although it may describe either the priority or the timing of the methods used, or both.
3) Describes each method in terms of its sampling, data collection, and analysis	⇒ <i>Yes</i> – Describes all (six) of the elements of the quantitative and qualitative components (i.e., type of sampling, type of data sources, type of analyses). ⇒ <i>Yes, but</i> – Describes five or four elements of the quantitative and qualitative components (i.e., type of sampling, type of data sources, type of analyses). ⇒ <i>No</i> – Describes less than four elements of the quantitative and qualitative components (i.e., type of sampling, type of data sources, type of analyses).
4) Describes the integration of the quantitative and qualitative components (i.e., where the integration has occurred, how it has occurred, and who among the research team has participated in it)	⇒ <i>Yes</i> – Reports evidence of integration. It might also provide an explicit description of where and how integration has occurred, or else this information can be inferred. ⇒ <i>Yes, but</i> – Does not report evidence of integration, but it provides an explicit description of where and how integration has occurred. ⇒ <i>No</i> – Does not report evidence of integration and does not provide an explicit description of where and how integration has occurred. It either refers to the attempt of integrating the quantitative and qualitative components or uses keywords associated with integration, or both.
5) Describes any limitation of one method associated with the presence of the other method	⇒ <i>Yes</i> – Provides an explicit description of the limitation. ⇒ <i>Yes, but</i> – Does not provide an explicit description of the limitation, but this limitation can still be inferred. ⇒ <i>No</i> – Does not provide an explicit description of the limitation and this limitation cannot be inferred.
6) Describes any insights gained from mixing or integrating methods	⇒ <i>Yes</i> – Provides an explicit description of the insights gained from mixing or integrating methods. ⇒ <i>Yes, but</i> – Does not provide an explicit description of the insights, but these insights can still be inferred. ⇒ <i>No</i> – Does not provide an explicit description of the insights and these insights cannot be inferred.

GRAMMS, Good Reporting of A Mixed Methods Study; *Yes, but*, Yes, but improvements are possible.

Supplementary File 3. Reference list of the individual 65 included articles.

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Supplementary File 4. *Good Reporting of A Mixed Methods Study (GRAMMS) and Mixed Methods Appraisal Tool (MMAT) item scores for the individual and combined 55 chiropractic mixed methods studies.*

Study No.	First Author	Year of Publication	Journal	IF at Year of Publication	GRAMMS Score n = 0-6 (%)	MMAT Score n = 0-11 (%)
1.	Waaen	2000	<i>Journal of Chiropractic Education</i>	NA	0 (0.00)	2 (18.18)
2.	Maiers	2014/2015	<i>Spine Journal/Manual Therapy</i>	2.426/1.869	3 (50.00)	8 (72.73)
3.	Jones-Harris	2010	<i>Chiropractic & Manual Therapies</i>	NA	4 (66.67)	10 (90.91)
4.	Pohlman	2020	<i>Journal of Manipulative & Physiological Therapeutics</i>	1.230	1.5 (25.00)	5.5 (50.00)
5.	Wong	2014	<i>Journal of Chiropractic Education</i>	NA	2.5 (41.67)	6.5 (59.09)
6.	Kim	2020	<i>Canadian Medical Association Journal Open</i>	NA	1 (16.67)	3.5 (31.82)
7.	Evans	2007	<i>Journal of the American Chiropractic Association</i>	NA	1.5 (25.00)	6 (54.55)
8.	Emary	2020	<i>Chiropractic & Manual Therapies</i>	1.512	4.5 (75.00)	7.5 (68.18)
9.	Stochkendahl	2018/2019	<i>Chiropractic & Manual Therapies</i>	NA/1.512	4 (66.67)	7.5 (68.18)
10.	Jamison	1996	<i>Chiropractic Technique</i>	NA	0 (0.00)	1.5 (13.64)
11.	Spegman	2007	<i>Journal of Chiropractic Education</i>	NA	2.5 (41.67)	6 (54.55)
12.	Evans	2015	<i>Global Advances in Health & Medicine</i>	NA	2 (33.33)	7 (63.64)
13.	Hestbaek	2019	<i>Chiropractic & Manual Therapies</i>	1.512	5 (83.33)	10 (90.91)

14.	Garner	2008	<i>Explore (NY)</i>	0.712	2.5 (41.67)	5 (45.45)
15.	Miller	2016	<i>Journal of Clinical Chiropractic Pediatrics</i>	NA	4.5 (75.00)	8.5 (77.27)
16.	Gudavalli	2015	<i>Trials</i>	1.859	4 (66.67)	8 (72.73)
17.	Talmage	2009	<i>Journal of Chiropractic Medicine</i>	NA	0.5 (8.33)	2 (18.18)
18.	Myburgh	2014/2016	<i>Journal of Interprofessional Care/Chiropractic & Manual Therapies</i>	1.399/NA	4 (66.67)	8 (72.73)
19.	Russell/Page	2004/2006	<i>Vaccine/Journal of Manipulative & Physiological Therapeutics</i>	2.824/0.918	3 (50.00)	8 (72.73)
20.	Goertz/Wells	2017/2020	<i>BMC Geriatrics/Journal of Patient Experience</i>	3.077/NA	3 (50.00)	10 (90.91)
21.	Goertz/Salisbury	2017/2018	<i>BMC Geriatrics/The Gerontologist</i>	2.866/NA	3.5 (58.33)	9 (81.82)
22.	Palmgren	2013	<i>Journal of Chiropractic Education</i>	NA	3.5 (58.33)	8.5 (77.27)
23.	Peterson	2019	<i>Chiropractic & Manual Therapies</i>	1.512	2.5 (41.67)	7 (63.64)
24.	Amorin-Woods	2019	<i>Journal of Chiropractic Education</i>	NA	2.5 (41.67)	7.5 (68.18)
25.	Khorsan	2013	<i>Evidence-Based Complementary & Alternative Medicine</i>	2.175	3 (50.00)	5.5 (50.00)
26.	Pohlman	2013	<i>Journal of Chiropractic Education</i>	NA	1.5 (25.00)	4.5 (40.91)
27.	Amorin-Woods	2016	<i>Chiropractic & Manual Therapies</i>	NA	2.5 (41.67)	3.5 (31.82)
28.	Pohlman	2020	<i>Chiropractic & Manual Therapies</i>	1.512	6 (100)	8.5 (77.27)

29.	Maiers	2014/2014	<i>Spine Journal/Journal of Rehabilitation Medicine</i>	2.426/1.683	6 (100)	11 (100)
30.	Pincus	2006	<i>European Journal of Pain</i>	3.333	3 (50.00)	5.5 (50.00)
31.	Rowell	2008	<i>Journal of Manipulative & Physiological Therapeutics</i>	1.102	3.5 (58.33)	4 (36.36)
32.	Stuber	2018	<i>Complementary Therapies in Medicine</i>	1.979	4.5 (75.00)	7 (63.64)
33.	Smith	2012	<i>Journal of Manipulative & Physiological Therapeutics</i>	1.647	1.5 (25.00)	6 (54.55)
34.	Peterson	1996	<i>Journal of Manipulative & Physiological Therapeutics</i>	NA	3 (50.00)	4 (36.36)
35.	Eilayyan	2018	<i>BMC Musculoskeletal Disorders</i>	2.002	3.5 (58.33)	7.5 (68.18)
36.	Cockrell	2020	<i>Gerontology & Geriatric Medicine</i>	NA	1.5 (25.00)	5.5 (50.00)
37.	Jamison	1998	<i>Chiropractic Journal of Australia</i>	NA	1.5 (25.00)	3.5 (31.82)
38.	Whitley	2019	<i>Journal of Manipulative & Physiological Therapeutics</i>	1.230	3 (50.00)	7.5 (68.18)
39.	Amorin-Woods	2017	<i>Chiropractic Journal of Australia</i>	NA	4 (66.67)	7 (63.64)
40.	Evans	2012/2014	<i>Spine/European Spine Journal</i>	2.159/2.066	6 (100)	11 (100)
41.	Bronfort/Haanstra	2011/2013	<i>Spine Journal/European Spine Journal</i>	3.290/2.437	5 (83.33)	10 (90.91)
42.	Hawk	2017	<i>Journal of Chiropractic Education</i>	NA	0 (0.00)	4.5 (40.91)
43.	Connell	2020	<i>Journal of the Canadian Chiropractic Association</i>	NA	5.5 (91.67)	9 (81.82)
44.	Testern	2015	<i>Chiropractic & Manual Therapies</i>	NA	2 (33.33)	4.5 (40.91)

45.	Ammendolia	2002	<i>Journal of Manipulative & Physiological Therapeutics</i>	1.041	3 (50.00)	4.5 (40.91)
46.	Evans/Bronfort	2003/2004	<i>Journal of Manipulative & Physiological Therapeutics</i>	0.950/0.457	5 (83.33)	10 (90.91)
47.	Bronfort/Maiers	2014/2016	<i>Annals of Internal Medicine/Manual Therapy</i>	17.810/2.158	4 (66.67)	10 (90.91)
48.	Rae	2020	<i>Journal of Chiropractic Medicine</i>	NA	1.5 (25.00)	7 (63.64)
49.	Rist/Connor	2020/2021	<i>Cephalgia/Journal of Manipulative & Physiological Therapeutics</i>	4.868/1.230	4.5 (75.00)	8.5 (77.27)
50.	Major	2020	<i>Journal of Chiropractic Education</i>	NA	1.5 (25.00)	7 (63.64)
51.	Wong	2013	<i>Journal of the Canadian Chiropractic Association</i>	NA	3.5 (58.33)	5 (45.45)
52.	Langenfeld	2018	<i>Spine</i>	2.903	3 (50.00)	5.5 (50.00)
53.	Lyons/Goertz	2013/2017	<i>BMC Complementary & Alternative Medicine/BMC Geriatrics</i>	1.877/2.866	3.5 (58.33)	8.5 (77.27)
54.	Peterson	2021	<i>Journal of Chiropractic Education</i>	NA	2 (33.33)	7.5 (68.18)
55.	Perle	1999	<i>Journal of Chiropractic Education</i>	NA	2 (33.33)	5.5 (50.00)

BMC, BioMed Central; *GRAMMS*, Good Reporting of A Mixed Methods Study; *IF*, Impact Factor; *MMAT*, Mixed Methods Appraisal Tool; *NA*, Not Applicable; *NY*, New York.

Chapter 4:

Risk of bias in chiropractic mixed methods research: a secondary analysis of a meta-epidemiological review

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Risk of bias in chiropractic mixed methods research: a secondary analysis of a meta-epidemiological review

Abstract

Objective: *To examine the risk of bias in chiropractic mixed methods research.*

Methods: *We performed a secondary analysis of a meta-epidemiological review of chiropractic mixed methods studies. We assessed risk of bias with the Mixed Methods Appraisal Tool (MMAT) and used generalized estimating equations to explore factors associated with risk of bias.*

Results: *Among 55 eligible studies, a mean of 62% (6.8 [2.3]/11) of MMAT items were fulfilled. In our adjusted analysis, studies published since 2010 versus pre-2010 (adjusted odds ratio [aOR] = 2.26; 95% confidence interval [CI], 1.39 to 3.68) and those published in journals with an impact factor versus no impact factor (aOR = 2.21; 95% CI, 1.33 to 3.68) were associated with lower risk of bias.*

Conclusion: *Our findings suggest opportunities for improvement in the quality of conduct among published chiropractic mixed methods studies. Author compliance with the MMAT criteria may reduce methodological bias in future mixed methods research.*

Key Words: methodological review, risk of bias, mixed methods research, chiropractic

Introduction

Mixed methods research involves combining quantitative and qualitative approaches in a single study. With multiple methods of data collection and analysis, research questions are answered with a greater breadth and depth of understanding than what could be achieved with only a quantitative or qualitative approach.¹⁻⁴ As such, the use of mixed methods designs in research involving the chiropractic⁵ and allied health care professions^{1,2} has increased in recent years. For instance, in the PubMed database alone, there has been an exponential rise in the number of “mixed methods” articles published since 2001 (Figure 1). However, despite the added value of mixed methods approaches, these studies can become complex investigations requiring additional time and resources and a research team with expertise in quantitative, qualitative, and mixed methodologies.^{1,2}

The explicit mixing or linking of qualitative and quantitative approaches within a mixed methods study is particularly useful for assessing multilevel programs and interventions,^{3,6-8} and is therefore a methodology well-suited to address research problems in health professions including chiropractic. For example, Maiers et al.⁹ used a multistage, experimental mixed methods design,² where interviews (qualitative) were conducted to help explain differences in outcomes (quantitative) in a randomized controlled trial of elderly patients with chronic neck pain. The four main types of study designs used in mixed methods research, namely convergent, explanatory sequential, exploratory sequential, and complex / multistage, are described in Table 1.

Previous methodological reviews have examined the mixed methods literature in healthcare fields outside chiropractic^{10,11} and have highlighted areas for improvement. One review¹⁰ of complementary and alternative medicine literature (excluding studies on chiropractic) found that most mixed methods studies did not contain adequate details on qualitative analysis, or quantitative and qualitative sampling and recruitment procedures. To date, no reviews have investigated the extent of methodological bias among published mixed methods studies involving chiropractic research. To address this knowledge gap, we undertook a secondary analysis of a meta-epidemiological review of reporting quality in chiropractic mixed methods research⁵ to examine the risk of bias among chiropractic mixed methods studies. Methodological bias is a serious threat to the internal validity of studies and limits the strength of inferences generated from primary research. As such, our findings will inform areas for improvement regarding the methodological quality of chiropractic research employing mixed methods designs.

Methods

Reporting

Our review is reported in accordance with an adapted version of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines for meta-epidemiological research.¹²

Information Sources

In line with our published protocol,⁵ we searched the Medical Literature Analysis and Retrieval System Online (MEDLINE), the Excerpta Medica Database (EMBASE), the Cumulative Index to Nursing and Allied Health Literature (CINAHL), and the Index to Chiropractic Literature (ICL) to identify all published chiropractic mixed methods studies from database inception to December 31, 2020. An academic librarian (RJC) assisted with the development of our search strategy (Online Supplementary File 1).⁵ We also hand-searched the reference lists of eligible articles and contacted two mixed methods experts to identify any additional citations. The eligibility criteria for our review are listed in Table 2.

Study Selection

Two independent reviewers (PCE, CC) screened titles and abstracts of identified citations, and full texts of potentially eligible studies. Disagreements were resolved by discussion or, when needed, with the help of an adjudicator (KJS). We used online systematic review software (DistillerSR, Evidence Partners, Ottawa, Canada; <https://www.evidencepartners.com>) to facilitate literature screening.

Data Extraction and Assessment of Risk of Bias

Pairs of reviewers (PCE, KJS, PSN, JVN, CAB) independently extracted data and assessed risk of bias of included articles using standardized, pilot-tested data extraction forms.⁵ Discrepancies were resolved by discussion to achieve consensus or, if needed, adjudication by a third reviewer with expertise in mixed methods (PCE, KJS, LM, or

MO). We extracted the following information from all eligible studies: (1) first author, (2) number of authors, (3) journal name, (4) year of publication, (5) country where the study was conducted (or country of residence of the corresponding author when the country of conduct was unavailable or when the study was international), (6) type of mixed methods design, and (7) inclusion of a methodologist among the authors (rated as “yes,” “no,” or “unclear/not reported”).

We defined a methodologist as a contributing author with training in qualitative and/or mixed methods research, public health, epidemiology, health technology assessment, health services research, knowledge translation/implementation science, or biostatistics. The involvement of a methodologist was determined by examining each article for authors’ qualifications or affiliations and information reported in the methodology section. In instances where authorship reporting of methodological expertise was “unclear or not reported,” we used a conservative approach and combined these counts with the “no” responses. When available, we also obtained the impact factor at the time of publication for each journal in which an eligible study was published, either directly from the journal’s website or from the Journal Citation Report (<https://jcr.clarivate.com/>).

We assessed risk of bias of included articles using the Mixed Methods Appraisal Tool (MMAT).^{13,14} The MMAT (version 2011) has been validated as a quality appraisal tool for systematic reviews of mixed studies (i.e., qualitative, quantitative, and mixed methods studies).¹⁴ This tool is comprised of two screening items for mixed methods research, followed by 11 appraisal items in three sections, including: (1) four items on the

qualitative component, (2) four items on the quantitative component (i.e., randomized controlled, non-randomized, or descriptive), and (3) three items on mixed methods.

Reviewers independently evaluated the risk of bias of all selected articles with the MMAT, on an item-by-item basis, rating each item with a “yes” (if the item was addressed), “can’t tell/partial” (if the item was partially addressed), or “no” (if the item was not addressed).^{14,15} Before assessing the risk of bias of articles, reviewers completed the online tutorial by Pluye et al.¹⁵ to rate MMAT items. We assigned a score for each of the eleven items as follows: 1 = “yes”; 0.5 = “can’t tell/partial”; 0 = “no”, for a total score ranging from 0 to 11.

Synthesis of Results

Agreement on full-text screening was assessed using the adjusted kappa (κ) statistic.¹⁶ Values of 0 to 0.20 represented slight agreement, 0.21 to 0.40 represented fair agreement, 0.41 to 0.60 represented moderate agreement, 0.61 to 0.80 represented substantial agreement, and greater than 0.80 represented almost perfect agreement. For the purpose of analysis, studies reporting quantitative and qualitative results in separate papers were combined and considered as a single article. We summarized article characteristics and MMAT score data across included studies using mean and standard deviation (SD) for continuous variables that were normally distributed, and median and inter-quartile range (IQR) for continuous variables that were not. All distributions were analyzed for normality by examining the data histograms, probability and quantile-quantile plots, and the Kolmogorov-Smirnov test.

We built a generalized estimating equation (GEE) to explore the association between risk of bias and article characteristics including publication date, authorship, and journal impact factor. Based on previous literature,^{17,18} we hypothesized that studies published since 2010 (i.e., ≥ 1 year after the first publication of the MMAT criteria¹³), studies published in journals with an impact factor, those with a greater number of authors, and those that included a methodologist would be associated with lower risk of bias.

We modelled our dependent variable as the number of MMAT items addressed in each article (maximum value of eleven) divided by the total number of MMAT items (eleven), and used the ‘events/trials’ function in SPSS to generate a binary outcome. We regressed the dependent variable on the year of article publication (2010 and later versus pre-2010), availability of a journal impact factor (yes versus no), number of authors (higher versus lower), and inclusion of a methodologist (yes versus no). These factors have previously been shown to be associated with reported methodological quality.^{17,18} We dichotomized author number at the median value (four) calculated across included studies. In our original protocol,⁵ we planned to explore inclusion of a mixed methodologist as an independent variable; however, we modified our approach because most studies did not clearly report mixed methodological expertise.

For our GEE, we employed a binomial distribution and logit link function to generate a crude and adjusted odds ratio (OR), and a 95% confidence interval (CI) and corresponding *p*-value, for each independent variable. We assessed goodness-of-fit by comparing our model’s deviance to its degrees of freedom and by examining the

associated residual plot. We addressed over- or under-dispersion by re-running our model with a scale parameter calculated by dividing the deviance by its degrees of freedom. To account for potential clustering or similarity of articles published in the same journal, we assumed an exchangeable working correlation matrix and specified the journal name as a grouping factor.

A minimum sample of 40 chiropractic mixed methods articles was required to guard against over-fitting of our regression model (i.e., minimum of 10 observations per independent variable).¹⁹ We also explored variance inflation factors (VIFs) to assess for multicollinearity among independent variables, and considered a $VIF \geq 10$ as problematic.²⁰ The two-sided statistical significance level (α) was 5%, and all data and comparative analyses were performed using SPSS v26.0 (IBM SPSS Statistics ©).

Results

We identified 1,040 citations, and 65 articles met our eligibility criteria for review. Ten studies reported quantitative and qualitative results in separate articles. As such, 55 unique mixed methods studies were analyzed (Figure 2). There was substantial agreement at the full-text screening stage between reviewers ($\kappa = 0.70$).

Study Characteristics

Of the 55 eligible studies, most (80%) were conducted in, or had corresponding authors from, three countries - the United States, Canada, or Australia; over half (53%) had four or fewer authors and three-quarters (75%) were published after 2010 (Table 3). Two-

thirds of studies employed a complex/multistage (34%) or convergent (33%) mixed methods design, and the remainder used sequential explanatory (20%) or exploratory (13%) designs. Over half of eligible studies (29 of 55; 53%) were published in journals that had an impact factor (median impact factor at the time of publication = 1.9 [IQR: 1.2 to 2.6]) and just under half (25 of 55; 45%) included a methodologist among their authors.

Risk of Bias of Included Studies

Referring to the eleven MMAT criteria, items pertaining to qualitative data (i.e., archives, documents, informants, observations) (89%); the qualitative analysis (86%); the mixed methods design, in terms of its relevance to addressing the research questions (86%); and the quantitative randomization, recruitment, or sampling procedures (for randomized, non-randomized, or descriptive study components, respectively) (80%) were commonly addressed. Authors' descriptions of the integration of qualitative and quantitative data (57%); how qualitative findings related to the context (e.g., the setting, in which the data were collected) (36%) or to the researchers' influence (e.g., through their interactions with participants) (26%); and specific limitations arising from the integration of qualitative and quantitative components (16%) were the most poorly addressed items (Table 4). Only two (4%) of the 55 studies met all eleven MMAT criteria for methodological quality in mixed methods research. Six studies (11%) met ten criteria, 11 studies (20%) met at least eight criteria, and most studies (36 of 55; 65%) met seven criteria or less.

The mean (SD) number of the eleven MMAT items fulfilled across studies was 6.8 (2.3). The Kolmogorov-Smirnov test was not significant for the frequency of item scores on the MMAT instrument ($p = 0.173$), confirming the approximation to a normal distribution. See Figure 3 and Appendix 1 for summaries of the risk of bias scores for the 55 included studies.

Factors Associated with Risk of Bias

In our univariate GEE analyses, studies published since 2010 (OR = 2.64; 95% CI, 1.60 to 4.34), studies published in journals with an impact factor (OR = 2.23; 95% CI, 1.45 to 3.44), those that included more than four authors (OR = 2.01; 95% CI, 1.29 to 3.14), and those that had a methodologist among the study team (OR = 1.64; 95% CI, 1.03 to 2.60) were associated with lower risk of bias (Table 5). In our multivariable GEE analysis, we found that studies published since 2010 (adjusted OR = 2.26; 95% CI, 1.39 to 3.68) and those published in journals with an impact factor (adjusted OR = 2.21; 95% CI, 1.33 to 3.68) remained associated with lower risk of bias (Table 5). As a sensitivity analysis (not reported), we ran the same model but with author number included as a continuous variable rather than a dichotomous variable and this did not change the results. All VIFs were less than 1.9, suggesting no important multicollinearity among the independent variables.

Discussion

Summary of Main Findings

The methodological quality among chiropractic mixed methods studies published in the biomedical and allied health literature is suboptimal. According to the MMAT,^{14,15} an average of only 60% of the quality criteria in mixed methods research were addressed across the 55 eligible studies. Considerations of reflexivity (i.e., the impact of research setting, or of the researchers themselves, on the qualitative methods and/or findings), as well as the limitations of combining qualitative and quantitative methods, were poorly addressed in approximately 75% of articles. Forty percent of studies also failed to either provide adequate details about allocation concealment, instrument validation, or assessment of selection bias (for studies that employed randomized, non-randomized, or descriptive quantitative components, respectively), or describe the mixing or integration of quantitative and qualitative methods. In addition, follow-up or response rates were inadequate in one-third of studies (see Table 4 for follow-up/response rate thresholds) and a similar number that employed non-randomized or descriptive study components used non-standardized outcome measures. Of the 55 eligible studies, only 4% addressed all eleven MMAT criteria.

Comparison with Relevant Literature

Our findings are consistent with the results of methodological reviews of mixed methods research in other healthcare fields, including complementary and alternative medicine¹⁰ and nursing.¹¹ Similar to our findings, the methodological rigour of many of the mixed methods studies in these reviews was found to be unsatisfactory across various MMAT domains. As most journals have yet to adopt mixed methods quality appraisal

guidelines,^{5,15} authors of chiropractic mixed methods studies have not been required to comply with published methodological standards.¹³⁻¹⁵ However, with the growing number of mixed methods studies being published within the chiropractic profession in recent years, the findings of our review indicate a need to improve the methodological quality in chiropractic mixed methods research.

In our adjusted analysis, we found that publications in journals with an impact factor and those published in 2010 or later were more than twice as likely to have reported the incorporation of stronger methodological rigour in their mixed methods compared to publications in journals without an impact factor or those published before 2010. Associations between study quality and journal impact factor or year of publication have also been reported in previous reviews.^{17,18} It is possible that authors of chiropractic mixed methods studies, particularly those who submit articles to higher impact journals, are increasingly using available risk of bias tools and methodological guidelines to assist in the conduct and reporting of their research. In contrast with previous research,^{17,18} we did not find a statistically significant association between lower risk of bias and a higher number of authors or inclusion of methodologists. However, methodological scope was broadened in our review to include additional areas of methodological expertise such as qualitative research, epidemiology, or statistics because most studies did not clearly report the inclusion of a mixed methodologist. As mixed methods research requires specialized skills in qualitative and quantitative data integration and analysis,¹⁻⁴ reporting of mixed methodological expertise would ideally be examined in future studies. Despite our lack of finding a significant association, chiropractors conducting mixed methods

studies may wish to undertake training in mixed methods research or collaborate with researchers possessing expertise in mixed methods. Details on the inclusion of mixed methodologists should also be made explicit in future publications.

Strengths and Limitations

Our review methodology has several strengths.⁵ First, we conducted a comprehensive search to identify all eligible studies involving chiropractic mixed methods research. Second, we specified the anticipated direction of association for each independent variable in our regression models *a priori* to give reassurances that significant associations were unlikely to be spurious. Third, we controlled for between-group differences when exploring associations and used GEE modelling to account for hierarchical clustering of articles within journals. Fourth, we performed article screening, data extraction and quality appraisals in duplicate, and all reviewers underwent training in the assessment of MMAT items.

A limitation of our review is we may not have accounted for all important variables (e.g., country of authorship), or interactions between variables,¹⁸ relevant to the methodological quality of chiropractic mixed methods research. In addition, the ‘methodologist’ variable as we defined it does not guarantee training in mixed methods. We originally intended to explore the inclusion of a mixed methodologist as an independent factor, but only one of the 55 included studies in our review provided this level of detail. The risk of bias assessments in our review were also limited by the reporting quality of included studies. For instance, some methodologic safeguards may

have been implemented by authors but unreported,²¹ possibly due to journal restrictions of mixed methods manuscript word counts,^{18,22} and some methodologic safeguards that were reported may not have been implemented.²³ Another limitation of our review is the exclusion of non-English publications, which may have led to selection bias.

Implications for Authors and Chiropractic Journals

To reduce the risk of bias in chiropractic mixed methods research, authors of such studies should be required by journal editors to comply with the MMAT criteria.¹⁵ Compliance with critical appraisal guidelines has been associated with reduced methodological bias in research studies,^{17,18} particularly if authors are required to meet these standards as a condition of submission. Therefore, editorial review boards of journals within the chiropractic profession could play an important role in improving the quality of conduct in chiropractic mixed methods studies by incorporating mixed methods appraisal tools, such as the MMAT checklist,¹⁵ into the peer review process. For example, the MMAT could be a supplementary review checklist, completed by peer reviewers, for each mixed methods journal submission (see MMAT version 2011 checklist in Online Supplementary File 2).¹⁵ Editors of chiropractic journals could highlight the MMAT in their online submission instructions to peer reviewers and prospective authors, and cite well-conducted mixed methods studies involving chiropractic research (e.g., Maiers et al.⁹, Evans et al.²⁴) to serve as exemplars of good methodological quality. Chiropractic journals should also ensure they have at least one mixed methodologist on their editorial board.

Conclusion

Despite a reduction in the risk of bias among chiropractic mixed methods studies in recent years, our findings suggest there is room for improvement. Adoption and utilization of the MMAT criteria by chiropractic journals is one strategy that may reduce methodological bias in future mixed methods studies.

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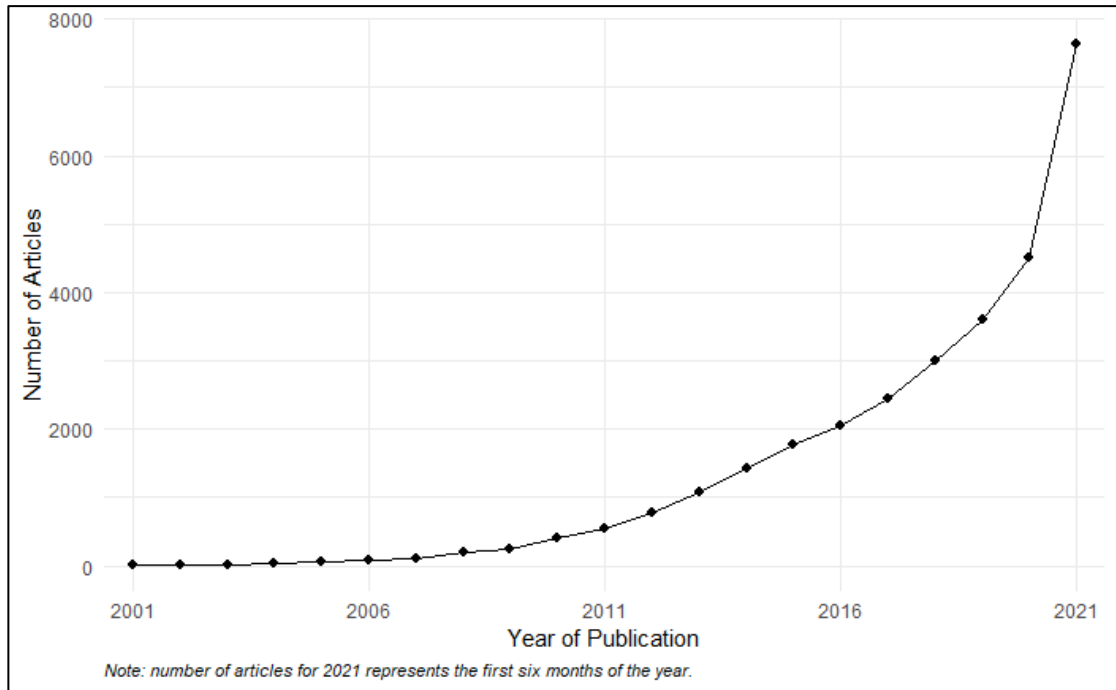


Figure 1. Frequency of “mixed methods” articles published over the last 20 years in PubMed.

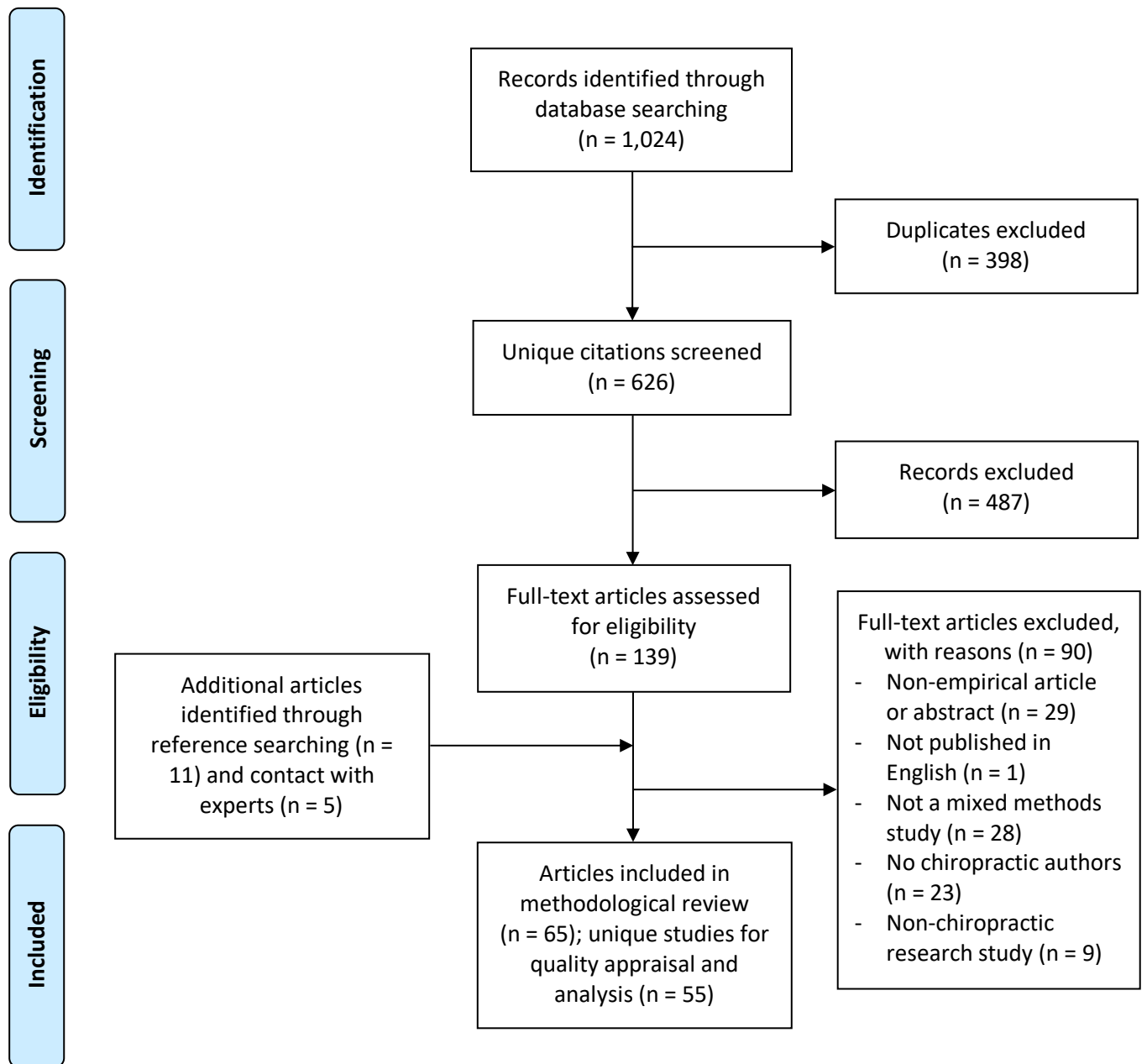


Figure 2. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

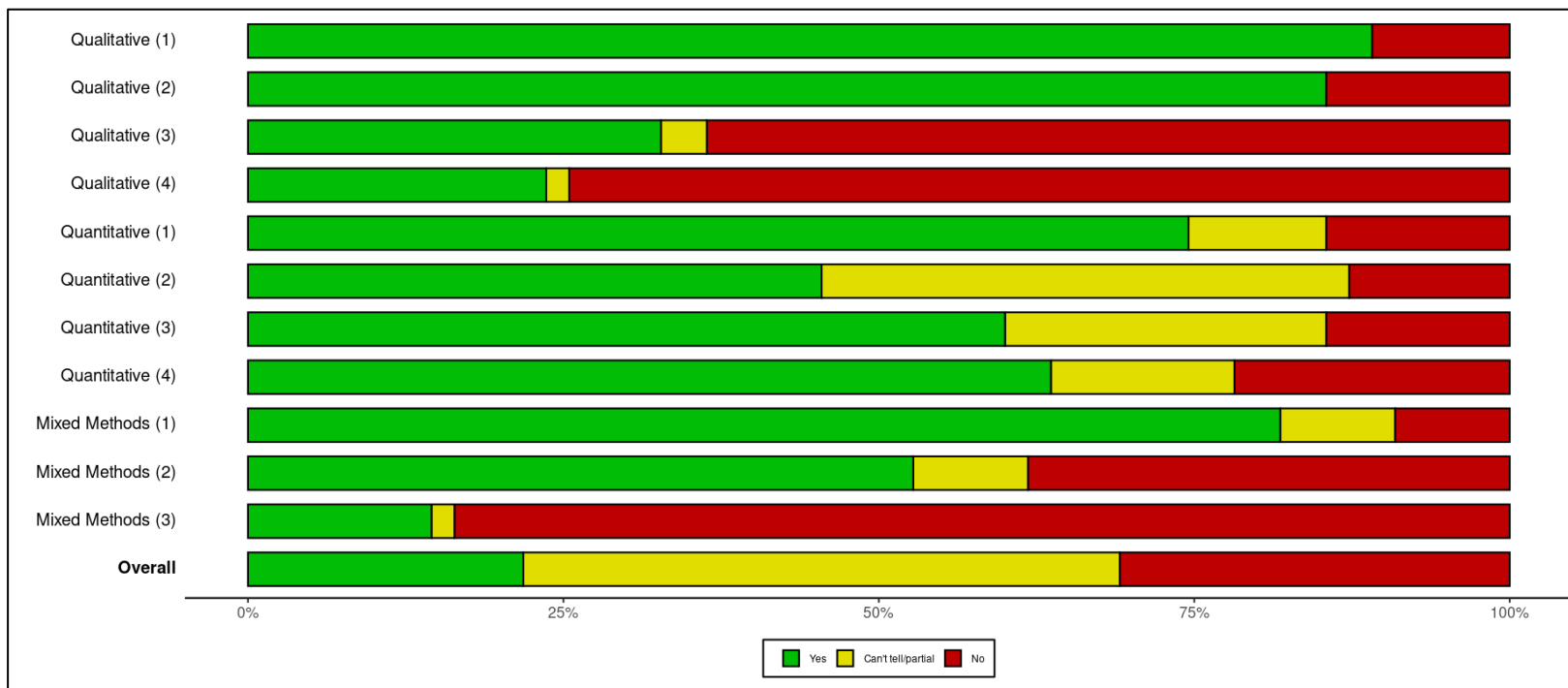


Figure 3. Summary of risk of bias assessments of the 55 eligible studies according to the Mixed Methods Appraisal Tool (MMAT), version 2011.¹⁵ Overall judgements are based on methods by Pluye et al.¹⁵ (Risk-of-bias plot was created using: McGuinness LA, Higgins JPT. Risk-of-bias VISualization (robvis): An R package and Shiny web app for visualizing risk-of-bias assessments. *Res Syn Meth.* 2020; 1-7.)

Legend:

Qualitative (1): Are sources of qualitative data (archives, documents, informants, observations) relevant to address the research question (objective)?

Qualitative (2): Is the process for analyzing qualitative data relevant to address the research question (objective)?

Qualitative (3): Is appropriate consideration given to how findings relate to the context, e.g., the setting, in which the data were collected?

Qualitative (4): Is appropriate consideration given to how findings relate to researchers' influence, e.g., through their interactions with participants?

- Quantitative (1):** a) *Randomized controlled (trials):* Is there a clear description of the randomization (or an appropriate sequence generation)?
b) *Non-randomized:* Are participants (organizations) recruited in a way that minimizes selection bias?
c) *Descriptive:* Is the sampling strategy relevant to address the quantitative research question (quantitative aspect of the mixed methods question)?
- Quantitative (2):** a) *Randomized controlled (trials):* Is there a clear description of the allocation concealment (or blinding when applicable)?
b) *Non-randomized:* Are measurements appropriate (clear origin, or validity known, or standard instrument; and absence of contamination between groups when appropriate) regarding the exposure/intervention and outcomes?
c) *Descriptive:* Is the sample representative of the population under study?
- Quantitative (3):** a) *Randomized controlled (trials):* Are there complete outcome data (80% or above)?
b) *Non-randomized:* In the groups being compared (exposed vs. non-exposed; with intervention vs. without; cases vs. controls), are the participants comparable, or do researchers take into account (control for) the difference between these groups?
c) *Descriptive:* Are measurements appropriate (clear origin, or validity known, or standard instrument)?
- Quantitative (4):** a) *Randomized controlled (trials):* Is there low withdrawal/drop-out (below 20%)?
b) *Non-randomized:* Are there complete outcome data (80% or above), and, when applicable, an acceptable response rate (60% or above), or an acceptable follow-up rate for cohort studies (depending on the duration of follow-up)?
c) *Descriptive:* Is there an acceptable response rate (60% or above)?
- Mixed Methods (1):** Is the mixed methods research design relevant to address the qualitative and quantitative research questions (or objectives), or the qualitative and quantitative aspects of the mixed methods question (or objective)?
- Mixed Methods (2):** Is the integration of qualitative and quantitative data (or results) relevant to address the research question (objective)?
- Mixed Methods (3):** Is appropriate consideration given to the limitations associated with this integration, e.g., the divergence of qualitative and quantitative data (or results) in a triangulation design?

Table 1. *Types of mixed methods study designs.*^{1,2}

Study Design	Description ^a
Convergent	A mixed methods design in which the researcher collects and analyzes two separate databases – quantitative and qualitative – and then merges the two for the purpose of comparing the results or adding transformed qualitative data as numeric variables into the quantitative database.
Explanatory sequential	A two-phase mixed methods design in which the researcher starts with the collection and analysis of quantitative data, which is then followed by the collection and analysis of qualitative data to help explain the initial quantitative results.
Exploratory sequential	A three-phase mixed methods design in which the researcher starts with the collection and analysis of qualitative data, which is then followed by a design phase of translating the qualitative findings into an approach or tool that can be tested quantitatively. Then, in the third phase, this approach or tool is tested quantitatively. This means that the approach or tool will be grounded in the views of participants.
Complex / multistage	
i) Experimental (or intervention)	A complex mixed methods approach in which the researcher combines the collection and analysis of both quantitative and qualitative data and integrates the information within an experimental quantitative research design.
ii) Case study	A type of complex mixed methods study in which both quantitative and qualitative data collection and their results are used to develop a case or multiple cases for further analysis and comparisons.
iii) Participatory-social justice	A type of complex mixed methods design in which the researcher adds a core design (i.e., convergent, explanatory sequential, or exploratory sequential) to a theoretical framework.
iv) Evaluation	A type of complex mixed methods design in which one or more core designs (i.e., convergent, explanatory sequential, exploratory sequential) are added into the steps of an evaluation procedure.

^a Source: adapted from Creswell JW, Plano Clark VL. *Designing and Conducting Mixed Methods Research*. 3rd ed. Thousand Oaks, CA: Sage 2018.

Table 2. *Article inclusion and exclusion criteria.*

Inclusion Criteria	Exclusion Criteria
<ul style="list-style-type: none"> • Published in English in a peer-reviewed journal; 	<ul style="list-style-type: none"> • Study protocols, letters, editorials, or commentaries;
<ul style="list-style-type: none"> • Authored by one or more chiropractic researchers; 	<ul style="list-style-type: none"> • Case reports or series;
<ul style="list-style-type: none"> • Was an empirical study reporting primary data collection; 	<ul style="list-style-type: none"> • Books and book chapters;
<ul style="list-style-type: none"> • Involved any type of chiropractic research (e.g., therapeutic, educational, policy, or scope of practice); and 	<ul style="list-style-type: none"> • Grey literature (e.g., conference proceedings, abstracts, lectures, dissertations or unpublished manuscripts); and
<ul style="list-style-type: none"> • Reported the use of both qualitative and quantitative methods, or mixed qualitative methods, in the same research study.^a 	<ul style="list-style-type: none"> • Secondary sources of evidence, including clinical practice guidelines, systematic, scoping or narrative reviews.

^a ‘Mixed’ surveys (i.e., those with both closed- and open-ended questions) were only included if the use of “mixed methods” was explicitly stated in the title or abstract.

Table 3. *Characteristics of the 55 included studies.*

Study Characteristic	Category	n (%)
Year of publication	Pre-2010	14 (25.5)
	Post-2010	41 (74.5)
Number of authors ^{a,b}	≤ 4	29 (52.7)
	> 4	26 (47.3)
Country	USA	28 (50.9)
	Canada	10 (18.2)
	Australia	6 (10.9)
	Other ^c	11 (20.0)
Mixed methods design	Complex / multistage	19 (34.6)
	Convergent	18 (32.7)
	Explanatory sequential	11 (20.0)
	Exploratory sequential	7 (12.7)
Methodologist	Yes	25 (45.5)
	No/unclear ^d	30 (54.5)
Journal impact factor	Yes	29 (52.7)
	No	26 (47.3)

USA = United States of America.

^a Average values were used when studies reported quantitative and qualitative results in separate articles.

^b The cut-off point for author number was derived from the median value measured across eligible studies.

^c Included studies from Denmark (n = 3), United Kingdom (n = 3), Switzerland (n = 2), Germany (n = 1), South Africa (n = 1), and Sweden (n = 1).

^d Inclusion of a methodologist was “unclear” in 15 (27.3%) of the 55 included studies.

Table 4. Risk of bias of the 55 eligible studies according to the Mixed Methods Appraisal Tool (MMAT), version 2011.¹⁵

MMAT Item	Description	Risk of Bias Score and Percentage of Studies (n = 55) fulfilling each MMAT Item	
		Score (0-55) ^a	Percentage
1. Qualitative	Are sources of qualitative data (archives, documents, informants, observations) relevant to address the research question (objective)?	49.0	89.1%
2. Qualitative	Is the process for analyzing qualitative data relevant to address the research question (objective)?	47.0	85.5%
3. Qualitative	Is appropriate consideration given to how findings relate to the context, e.g., the setting, in which the data were collected?	19.0	34.5%
4. Qualitative	Is appropriate consideration given to how findings relate to researchers' influence, e.g., through their interactions with participants?	13.5	24.5%
5. Quantitative	a) <i>Randomized controlled (trials)</i> : Is there a clear description of the randomization (or an appropriate sequence generation)? b) <i>Non-randomized</i> : Are participants (organizations) recruited in a way that minimizes selection bias? c) <i>Descriptive</i> : Is the sampling strategy relevant to address the quantitative research question (quantitative aspect of the mixed methods question)?	44.0	80.0%
6. Quantitative	a) <i>Randomized controlled (trials)</i> : Is there a clear description of the allocation concealment (or blinding when applicable)? b) <i>Non-randomized</i> : Are measurements appropriate (clear origin, or validity known, or standard instrument; and absence of contamination between groups when appropriate) regarding the exposure/intervention and outcomes? c) <i>Descriptive</i> : Is the sample representative of the population under study?	36.5	66.4%
7. Quantitative	a) <i>Randomized controlled (trials)</i> : Are there complete outcome data (80% or above)?	40.0	72.7%

	<p>b) <i>Non-randomized</i>: In the groups being compared (exposed vs. non-exposed; with intervention vs. without; cases vs. controls), are the participants comparable, or do researchers take into account (control for) the difference between these groups?</p> <p>c) <i>Descriptive</i>: Are measurements appropriate (clear origin, or validity known, or standard instrument)?</p>		
8. Quantitative	<p>a) <i>Randomized controlled (trials)</i>: Is there low withdrawal/drop-out (below 20%)?</p> <p>b) <i>Non-randomized</i>: Are there complete outcome data (80% or above), and, when applicable, an acceptable response rate (60% or above), or an acceptable follow-up rate for cohort studies (depending on the duration of follow-up)?</p> <p>c) <i>Descriptive</i>: Is there an acceptable response rate (60% or above)?</p>	39.0	70.9%
9. Mixed Methods	Is the mixed methods research design relevant to address the qualitative and quantitative research questions (or objectives), or the qualitative and quantitative aspects of the mixed methods question (or objective)?	47.5	86.4%
10. Mixed Methods	Is the integration of qualitative and quantitative data (or results) relevant to address the research question (objective)?	31.5	57.3%
11. Mixed Methods	Is appropriate consideration given to the limitations associated with this integration, e.g., the divergence of qualitative and quantitative data (or results) in a triangulation design?	8.5	15.5%
		Risk of Bias Score and Percentage of Studies (n = 55) fulfilling all 11 MMAT Items	
		2.0	3.6%

MMAT = Mixed Methods Appraisal Tool.

^a Count scores are summed as 1 = “yes”; 0.5 = “can’t tell/partial”; and 0 = “no”.

Table 5. *Unadjusted and adjusted odds ratios for the proportion of Mixed Methods Appraisal Tool (MMAT) items fulfilled among the 55 eligible studies.*

Factor	Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Year of publication <ul style="list-style-type: none"> • Post-2010 • Pre-2010 	2.64 (1.60-4.34) Reference	< 0.001	2.26 (1.39-3.68) Reference	0.001
Journal impact factor <ul style="list-style-type: none"> • Yes • No 	2.23 (1.45-3.44) Reference	< 0.001	2.21 (1.33-3.68) Reference	0.002
Number of authors ^a <ul style="list-style-type: none"> • > 4 • ≤ 4 	2.01 (1.29-3.14) Reference	0.002	1.20 (0.76-1.91) Reference	0.441
Inclusion of methodologist <ul style="list-style-type: none"> • Yes • No/unclear 	1.64 (1.03-2.60) Reference	0.036	0.79 (0.48-1.31) Reference	0.355

CI = confidence interval, OR = odds ratio.

^a This factor was dichotomized at the median value (i.e., 4), calculated across eligible studies.

Appendix 1. *Article characteristics and Mixed Methods Appraisal Tool (MMAT) item scores for the individual and combined 55 chiropractic mixed methods studies.*

First Author	Year of Publication	Journal	IF at Year of Publication	MMAT Score n = 0-11 (%)
Jamison	1996	Chiropr Tech	NA	1.5 (13.6)
Peterson	1996	J Manipulative Physiol Ther	NA	4 (36.4)
Jamison	1998	Chiropr J Aust	NA	3.5 (31.8)
Perle	1999	J Chiropr Educ	NA	5.5 (50.0)
Waalén	2000	J Chiropr Educ	NA	2 (18.2)
Ammendolia	2002	J Manipulative Physiol Ther	1.041	4.5 (40.9)
Evans/Bronfort	2003/2004	J Manipulative Physiol Ther	0.950/0.457	10 (90.9)
Russell/Page	2004/2006	Vaccine/J Manipulative Physiol Ther	2.824/0.918	8 (72.7)
Pincus	2006	Eur J Pain	3.333	5.5 (50.0)
Evans	2007	J Am Chiropr Assoc	NA	6 (54.6)
Spegman	2007	J Chiropr Educ	NA	6 (54.6)
Garner	2008	Explore (NY)	0.712	5 (45.5)
Rowell	2008	J Manipulative Physiol Ther	1.102	4 (36.4)
Talmage	2009	J Chiropr Med	NA	2 (18.2)
Jones-Harris	2010	Chiropr Man Therap	NA	10 (90.9)
Bronfort/Haanstra	2011/2013	Spine J/Eur Spine J	3.290/2/437	10 (90.9)
Smith	2012	J Manipulative Physiol Ther	1.647	6 (54.6)
Evans	2012/2014	Spine/Eur Spine J	2.159/2.066	11 (100)
Khorsan	2013	Evid Based Complement Alternat Med	2.175	5.5 (50.0)

Palmgren	2013	J Chiropr Educ	NA	8.5 (77.3)
Pohlman	2013	J Chiropr Educ	NA	4.5 (40.9)
Wong	2013	J Can Chiropr Assoc	NA	5 (45.5)
Maiers	2014/2014	Spine J/J Rehabil Med	2.426/1.683	11 (100)
Wong	2014	J Chiropr Educ	NA	6.5 (59.1)
Maiers	2014/2015	Spine J/Man Ther	2.426/1.869	8 (72.7)
Myburgh	2014/2016	J Interprof Care/Chiropr Man Therap	1.399/NA	8 (72.7)
Evans	2015	Glob Adv Health Med	NA	7 (63.6)
Gudavalli	2015	Trials	1.859	8 (72.7)
Bronfort/Maiers	2014/2016	Ann Intern Med/Man Ther	17.810/2.158	10 (90.9)
Testern	2015	Chiropr Man Therap	NA	4.5 (40.9)
Lyons/Goertz	2013/2017	BMC Complement Altern Med/BMC Geriatr	1.877/2.866	8.5 (77.3)
Amorin-Woods	2016	Chiropr Man Therap	NA	3.5 (31.8)
Miller	2016	J Clin Chiropr Pediatr	NA	8.5 (77.3)
Amorin-Woods	2017	Chiropr J Aust	NA	7 (63.6)
Hawk	2017	J Chiropr Educ	NA	4.5 (40.9)
Goertz/Salisbury	2017/2018	BMC Geriatr/Gerontologist	2.866/NA	9 (81.8)
Eilayyan	2018	BMC Musculoskelet Disord	2.002	7.5 (68.2)
Langenfeld	2018	Spine	2.903	5.5 (50.0)
Stuber	2018	Complement Ther Med	1.979	7 (63.6)
Goertz/Wells	2017/2020	BMC Geriatr/J Patient Exp	3.077/NA	10 (90.9)
Stochkendahl	2018/2019	Chiropr Man Therap	NA/1.512	7.5 (68.2)
Amorin-Woods	2019	J Chiropr Educ	NA	7.5 (68.2)

Hestbaek	2019	Chiropr Man Therap	1.512	10 (90.9)
Peterson	2019	Chiropr Man Therap	1.512	7 (63.6)
Whitley	2019	J Manipulative Physiol Ther	1.230	7.5 (68.2)
Cockrell	2020	Gerontol Geriatr Med	NA	5.5 (50.0)
Connell	2020	J Can Chiropr Assoc	NA	9 (81.8)
Emary	2020	Chiropr Man Therap	1.512	7.5 (68.2)
Kim	2020	CMAJ Open	NA	3.5 (31.8)
Major	2020	J Chiropr Educ	NA	7 (63.6)
Pohlman	2020	Chiropr Man Therap	1.512	8.5 (77.3)
Pohlman	2020	J Manipulative Physiol Ther	1.230	5.5 (50.0)
Rae	2020	J Chiropr Med	NA	7 (63.6)
Rist/Connor	2020/2021	Cephalgia/J Manipulative Physiol Ther	4.868/1.230	8.5 (77.3)
Peterson	2021	J Chiropr Educ	NA	7.5 (68.2)

BMC = BioMed Central, *IF* = Impact Factor, *MMAT* = Mixed Methods Appraisal Tool, *NA* = Not Applicable, *NY* = New York.

Online Supplementary File 1. *Search strategies for MEDLINE, EMBASE, CINAHL, and the Index to Chiropractic Literature (ICL), from the inception of each database to December 31, 2020.*

Database: OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present		
Search Strategy:		

1	Manipulation, Chiropractic/ or Chiropractic/	(4121)
2	Manipulation, Spinal/	(1611)
3	chiropract*.ti,ab,kf,jw.	(6999)
4	or/1-3	(9357)
5	(mixed adj3 methods).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	(21745)
6	Qualitative Research/ or qualitat*.mp.	(310714)
7	5 or 6	(321158)
8	4 and 7	(242)
EMBASE (OVID)		
Database: Embase <1974 to 2020 December 31>		
Search Strategy:		

1	chiropractic/ or chiropractic manipulation/	(4775)
2	spine manipulation/	(638)
3	chiropract*.ti,ab,kw,jw.	(6656)
4	or/1-3	(8834)
5	(mixed adj3 methods).mp.	(24740)
6	qualitative research/	(83067)
7	qualitat*.mp.	(395745)
8	or/5-7	(407517)
9	4 and 8	(287)
CINAHL (Ebsco)		
S1	(MH "Chiropractic") OR (MH "Manipulation, Chiropractic")	20,210
S2	TX chiropract*	48,113
S3	S1 OR S2	48,113
S4	TX mixed N3 methods	18,656
S5	(MH "Qualitative Studies+")	152,758
S6	TX qualitat*	186,409
S7	S4 OR S5 OR S6	224,415
S8	S3 AND S7	449
ICL		
S1	All Fields:"mixed methods"	29
S2	Subject:"Qualitative Research"	18
S3	All Fields:"mixed methods" OR Subject:"Qualitative Research"	46

Online Supplementary File 2. Mixed Methods Appraisal Tool (MMAT), version 2011.

Types of mixed methods study components or primary studies	Methodological quality criteria (see tutorial for definitions and examples)	Responses			
		Yes	No	Can't tell	Comments
Screening questions (for all types)	• Are there clear qualitative and quantitative research questions (or objectives*), or a clear mixed methods question (or objective*)?				
	• Do the collected data allow to address the research question (objective)? E.g., consider whether the follow-up period is long enough for the outcome to occur (for longitudinal studies or study components).				
	<i>Further appraisal may not be feasible or appropriate when the answer is 'No' or 'Can't tell' to one or both screening questions.</i>				
1. Qualitative	1.1. Are the sources of qualitative data (archives, documents, informants, observations) relevant to address the research question (objective)?				
	1.2. Is the process for analyzing qualitative data relevant to address the research question (objective)?				
	1.3. Is appropriate consideration given to how findings relate to the context, e.g., the setting, in which the data were collected?				
	1.4. Is appropriate consideration given to how findings relate to researchers' influence, e.g., through their interactions with participants?				
2. Quantitative randomized controlled (trials)	2.1. Is there a clear description of the randomization (or an appropriate sequence generation)?				
	2.2. Is there a clear description of the allocation concealment (or blinding when applicable)?				
	2.3. Are there complete outcome data (80% or above)?				
	2.4. Is there low withdrawal/drop-out (below 20%)?				
3. Quantitative non-randomized	3.1. Are participants (organizations) recruited in a way that minimizes selection bias?				
	3.2. Are measurements appropriate (clear origin, or validity known, or standard instrument; and absence of contamination between groups when appropriate) regarding the exposure/intervention and outcomes?				
	3.3. In the groups being compared (exposed vs. non-exposed; with intervention vs. without; cases vs. controls), are the participants comparable, or do researchers take into account (control for) the difference between these groups?				
	3.4. Are there complete outcome data (80% or above), and, when applicable, an acceptable response rate (60% or above), or an acceptable follow-up rate for cohort studies (depending on the duration of follow-up)?				
4. Quantitative descriptive	4.1. Is the sampling strategy relevant to address the quantitative research question (quantitative aspect of the mixed methods question)?				
	4.2. Is the sample representative of the population under study?				
	4.3. Are measurements appropriate (clear origin, or validity known, or standard instrument)?				
	4.4. Is there an acceptable response rate (60% or above)?				
5. Mixed methods	5.1. Is the mixed methods research design relevant to address the qualitative and quantitative research questions (or objectives), or the qualitative and quantitative aspects of the mixed methods question (or objective)?				
	5.2. Is the integration of qualitative and quantitative data (or results*) relevant to address the research question (objective)?				
	5.3. Is appropriate consideration given to the limitations associated with this integration, e.g., the divergence of qualitative and quantitative data (or results*) in a triangulation design?				
	<i>Criteria for the qualitative component (1.1 to 1.4), and appropriate criteria for the quantitative component (2.1 to 2.4, or 3.1 to 3.4, or 4.1 to 4.4), must also be applied.</i>				

*These two items are not considered as double-barreled items since in mixed methods research, (1) there may be research questions (quantitative research) or research objectives (qualitative research), and (2) data may be integrated, and/or qualitative findings and quantitative results can be integrated. (Source: <http://mixedmethodsappraisaltoolpublic.pbworks.com>.)

Chapter 5:

Association of chiropractic integration in an Ontario community health centre with prescription opioid use for chronic non-cancer pain: a mixed methods study protocol

Peter C. Emary, Mark Oremus, Lawrence Mbuagbaw, Jason W. Busse

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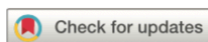
BMJ Open Association of chiropractic integration in an Ontario community health centre with prescription opioid use for chronic non-cancer pain: a mixed methods study protocol

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ABSTRACT

Introduction Emerging evidence from a number of primary care centres suggests that integration of chiropractic services into chronic pain management is associated with improved clinical outcomes and high patient satisfaction as well as with reductions in physician visits, specialist referrals use of advanced imaging and prescribing of analgesics. However, formal assessments of the integration of chiropractic services into primary care settings are sparse, and the impact of such integration on prescription opioid use in chronic pain management remains uncertain. To help address this knowledge gap, we will conduct a mixed methods health service evaluation of an integrated chiropractic back pain programme in an urban community health centre in Ontario, Canada. This centre provides services to vulnerable populations with high unemployment rates, multiple comorbidities and musculoskeletal disorders that are commonly managed with prescription opioids.

Methods and analysis We will use a sequential explanatory mixed methods design, which consists of a quantitative phase followed by a qualitative phase. In the quantitative phase, we will conduct a retrospective chart review and evaluate whether receipt of chiropractic services is associated with reduced opioid use among patients already prescribed opioid therapy for chronic pain. We will measure opioid prescriptions (ie, opioid fills, number of refills and dosages) by reviewing electronic medical records of recipients and non-recipients of chiropractic services between 1 January 2014 and 31 December 2020 and use multivariable regression analysis to examine the association. In the qualitative phase, we will conduct in-depth, one-on-one interviews of patients and their general practitioners to explore perceptions of chiropractic integration and its impact on opioid use.

Ethics and dissemination This study was approved by the Hamilton Integrated Research Ethics Board at McMaster University (approval number 2021–10930). The results will be disseminated via peer-reviewed publications, conference presentations and in-person or webinar presentations to community members and healthcare professionals.

Strengths and limitations of this study

- We will link electronic medical records with medical drug claims data from the Institute for Clinical Evaluative Sciences to validate patient opioid prescriptions and dosages.
- Generalised estimating equations will be used to account for hierarchical clustering and to control for differences in confounding factors between our exposure and comparison groups.
- For our regression models, we have prespecified the anticipated direction of association for each independent variable to provide additional reassurance that associations are unlikely to be spurious if detected.
- The qualitative component of our study will provide a richer understanding of chiropractic integration and its impact on opioid prescribing.
- Causation cannot be established with our study design, and the results may not be applicable to settings outside of Canadian community health centres.

INTRODUCTION

Chronic pain is a common condition that affects approximately 20% of the global population.^{1–4} In North America, opioids are commonly prescribed to relieve chronic pain and improve function⁵; however, opioids provide only modest benefits⁶ and are associated with important dose-dependent harms, including overdose and death.^{7–10} Accordingly, the chiropractic profession has called on governments to improve support for non-opioid approaches to managing chronic pain, particularly in vulnerable and marginalised populations.¹¹

Since 2007, a growing number of primary care centres in Canada have reported on their experiences with integration of chiropractic services into chronic pain management.^{12–19} Findings from these reports describe

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improvements in pain intensity and disability and high levels of patient satisfaction; additional outcomes include reductions in physician visits, specialist referrals, advanced imaging and prescribing of opioid and non-opioid analgesics.¹²⁻¹⁹ However, these studies¹²⁻¹⁹ employed single cohort, pre-post designs (ie, no comparison groups), thereby preventing a formal assessment of whether chiropractic integration improved chronic pain management compared with standard practice.²⁰ Comparative assessments of the integration of chiropractic services into primary care settings are sparse,^{21 22} and the impact of such integration on prescription opioid use in chronic pain management remains uncertain.

Unanswered questions also exist about specific types of integration, namely whether the impact of chiropractic services on opioid use in patients who start with chiropractic care before being prescribed opioids differs from the impact of chiropractic care on opioid use when added later to patient management. For instance, recent evidence from three studies suggests opioid-naïve patients with spine-related pain who receive chiropractic services as either standalone, or part of, first-line treatment are less likely to receive opioid prescriptions in the management of their conditions.²³⁻²⁵ In a 2020 systematic review and meta-analysis of six uncontrolled cohort studies,²³ Corcoran *et al* found that patients with acute or chronic non-cancer back or neck pain who received chiropractic services were 64% less likely than non-chiropractic users to be prescribed opioid medications (pooled OR=0.36, 95% CI 0.30 to 0.43). Similar findings have recently been reported by others^{24 25}; however, few studies have examined whether the receipt of chiropractic services can reduce opioid use in patients with existing opioid prescriptions. Similarly, few studies have examined the association between chiropractic services and opioid use among patients with chronic, non-cancer pain (CNCP) in a community health centre (CHC) setting, and none has done so using a mixed methods approach.

Aim

To help address these knowledge gaps, we will conduct a mixed methods evaluation of a chiropractic back pain programme integrated into standard physician care at the Langs CHC²⁶ in Cambridge, Ontario, Canada. Cambridge is a medium-sized urban municipality (population: ~130 000) located 82 km southwest of Toronto. CHCs provide services to communities and vulnerable populations with high unemployment rates, multiple comorbidities and high rates of musculoskeletal disorders and opioid use.^{12-15 17-19 22 26 27} Since chiropractic services are not publicly funded in Canada, these populations have traditionally faced barriers to accessing such services.^{12-15 17-19}

Conceptual framework

There are several reasons why the utilisation of chiropractic services might lead to reduced opioid use in patients with CNCP.^{13 15 16 18 19 23-25} First, chiropractic care,

including spinal manipulation, is efficacious in managing back and neck pain.²⁸⁻³⁰ Patients obtaining pain relief through chiropractic treatment might, in collaboration with their general practitioners (GPs), choose to taper opioid prescriptions. GPs might also prescribe fewer opioid medications or choose lower dosages if they can refer patients to chiropractors as a first-line treatment for pain management. In addition, patients accessing chiropractic services may be more resistant to using opioids than non-chiropractic patients and be more likely to seek out non-pharmacological pain management alternatives.

Our conceptual framework (online supplemental appendix 1) recognises that chronic spinal pain and opioid use can be associated with various comorbidities (eg, cardiovascular disease,³¹ diabetes,³² obesity,³³ depression,³²⁻³⁸ anxiety,³²⁻³⁷ somatisation³⁵ or poor general health^{34 39} as well as clinical and sociodemographic characteristics like pain severity/chronicity,^{33 38 39} smoking status,^{34 38} age³⁹ and gender.^{38 39} As such, these factors could also impact patients' utilisation of chiropractic services or opioid medications. For instance, opioid overuse/misuse has been frequently reported among individuals of low socioeconomic status and those with behavioural health problems.^{36 37} Chronic pain is prevalent among these groups,³¹⁻³⁹ and a primary motivation of chronic pain sufferers for misusing opioids is to relieve physical pain.³⁷ Therefore, our regression analyses described below ('quantitative data analysis') will control for these variables.

METHODS AND ANALYSIS

Reporting

We have reported our study protocol in accordance with the Good Reporting of A Mixed Methods Study guidelines.⁴⁰ We will report the results of our mixed methods manuscript in accordance with these guidelines, as well.

Research questions

Quantitative

In adult patients (age ≥18 years) presenting with CNCP at the Langs CHC, does adding chiropractic care to ongoing usual medical care, compared with ongoing usual medical care alone, reduce the rate of utilisation of opioid medications for up to 12 months following the index chiropractic visit?

Qualitative

How do patients and GPs at Langs perceive the integration of chiropractic services, and do they perceive this integration has impacted opioid use among persons with CNCP? For the purposes of this study, GPs will include family physicians and nurse practitioners.

Mixed methods

In what ways do the qualitative data help explain the quantitative results? For example, if an association is found between chiropractic integration at the Langs CHC and



opioid use, was it because the integration of chiropractic services allowed GPs to prescribe fewer opioids, were patients able to reduce their opioid intake because of improved pain management with access to these services or was chiropractic care implemented as part of a broader opioid-reducing strategy at the centre?

Study design

We will use a sequential explanatory mixed methods design.⁴¹ Data for the quantitative portion of the study will be obtained via chart review⁴² of electronic medical records (EMRs) of both recipients and non-recipients of chiropractic services with at least one prescribed opioid for the treatment of a CNC-related diagnosis at the Langs CHC. We will record opioid prescription data and other sample characteristics (eg, age, sex, smoking status, body mass index (BMI), healthcare visit frequency and comorbidities such as depression, anxiety, fibromyalgia, diabetes and cardiovascular disease) for all patients and tabulate the differences in opioid prescriptions (ie, opioid fills, number of refills and dosages) between the two groups. We will use multivariable regression analysis to examine whether the receipt of chiropractic services is associated with a reduction in the number or dose of opioid prescriptions. For the qualitative portion of the study, we will conduct in-depth, one-on-one interviews of patients and GPs from the Langs CHC to further explore perceptions regarding chiropractic integration and its impact on opioid prescribing. We will use pragmatism^{41 43} as the philosophical stance for mixing quantitative and qualitative methodologies. With this approach, the focus is on combining methods of data collection for 'what works' best in answering the research question.⁴¹

Rationale for mixed methods design

Our rationale for using a mixed methods design will be that of complementarity,⁴⁴ that is, the results from the qualitative portion of the study will be used to help clarify and explain the quantitative findings. The added value of mixed methods research is that multiple methods of data collection and analysis can be employed to answer questions with a greater breadth and depth of understanding than would be possible with only one methodology alone.^{41 43} As such, the interview component of our study will allow for a more complete understanding of the barriers and facilitators to incorporating chiropractic services as well as whether these services were used by patients or GPs to reduce reliance on opioid prescribing for CNC. The Langs CHC²⁶ was chosen as the setting for this study because chronic pain patients and those of low socioeconomic status tend to be frequent users of healthcare services and have high rates of opioid use in general.^{32 34 36 37} An illustrative diagram outlining our study procedures is provided in figure 1.

Chiropractic CHC programme

The chiropractic programme at the Langs CHC has been described in detail elsewhere.^{15 18} Briefly, this is a partially

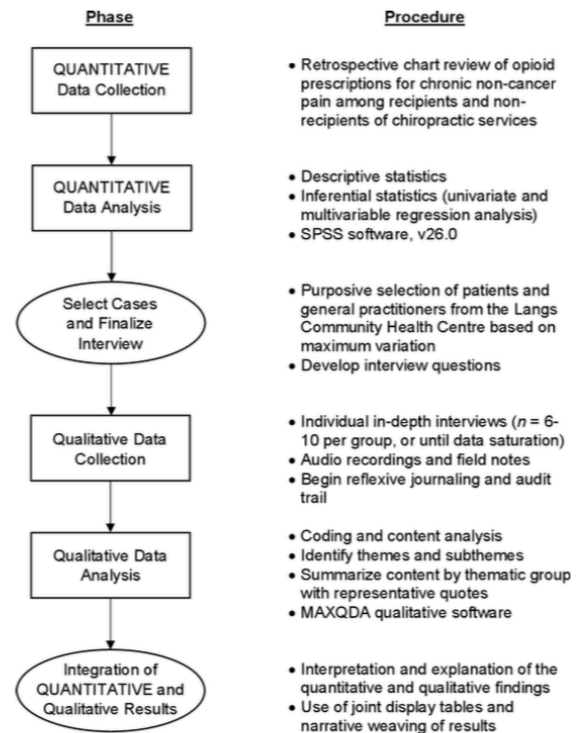


Figure 1 Study diagram of an explanatory sequential design of a mixed methods study on the association of chiropractic integration with opioid use for chronic non-cancer pain at the Langs Community Health Centre. The quantitative and qualitative data collection and analysis phases are shown along the left side of the diagram in rectangular boxes. The two points of interface (or mixing) of the quantitative and qualitative phases are shown and described in the ovals. The term 'QUANTITATIVE' is capitalised to indicate prioritisation of the quantitative phase in the study. The study procedures for each phase are listed along the right side of the diagram. MAXQDA, Max Weber Qualitative Data Analysis; SPSS, Statistical Package for the Social Sciences.

subsidised, complimentary service that operates on two separate days of the week (for a total of 4 hours per week) and is provided on a rotating basis by a team of between three to four chiropractors. The service is only accessible to patients registered at the CHC and through referral from their GP. Treatment sessions are evidence based⁴⁵ and include spinal manipulation, soft-tissue therapy, education, reassurance and home advice (eg, icing, stretching and strengthening exercises). Patients are typically discharged from care after 3 months or a maximum of 12 visits; however, some continue with treatment to address episodes of exacerbation/flare-up or chronic pain. Patients also continue to receive usual medical care at the CHC, such as GP assessment, prescription medication and referral for diagnostic testing or specialist consultation as well as other cointerventions (eg, visits

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**Table 1** Summary of variables to be used for the quantitative analysis

Variable	Category	Type	Values/units
Opioid fills	Dependent (outcome of interest)	Ratio	Fills
Opioid refills	Dependent (outcome of interest)	Ratio	Refills
Opioid dosages	Dependent (outcome of interest)	Nominal *	High dose (≥ 90 mg MED)/low dose (< 90 mg MED)
Chiropractic care	Independent (exposure of interest)	Nominal	Exposed/non-exposed
Time	Independent (potential confounder) †	Ratio	Calendar year ‡
Frequency of healthcare visits §	Independent (potential confounder) †	Ratio	Visits
Age	Independent (potential confounder) †	Ratio	Years
Sex	Independent (potential confounder) †	Nominal	Male/female
Smoking status	Independent (potential confounder) †	Nominal	Smoker/non-smoker
BMI	Independent (potential confounder) †	Nominal *	Obese (≥ 30 kg/m ²)/non-obese (< 30 kg/m ²)
Depression	Independent (potential confounder) †	Nominal	Present/absent
Anxiety	Independent (potential confounder) †	Nominal	Present/absent
Fibromyalgia	Independent (potential confounder) †	Nominal	Present/absent
Diabetes	Independent (potential confounder) †	Nominal	Present/absent
Cardiovascular disease	Independent (potential confounder) †	Nominal	Present/absent

*Opioid dosages and BMI will be dichotomised from continuous variables for comparative analysis.

†Data from the earlier years in the project's 7-year timeframe, a higher frequency of healthcare visits, younger age, male sex, smoking, obesity, depression, anxiety, fibromyalgia, diabetes and cardiovascular disease are anticipated to be positively associated with opioid use.

‡Calendar years will be measured at the patient's index visit date to the CHC for a CNCP-related diagnosis.

§Healthcare visits will constitute general practitioner and chiropractic visits.

BMI, body mass index; CHC, community health centre; CNCP, chronic non-cancer pain; MED, morphine equivalents daily.

with nurses, dieticians, social workers or physical/massage therapists) as required.

Quantitative sampling

For the quantitative phase, we will include records from adult patients, aged ≥ 18 years with one or more active prescriptions of opioid medication and who presented with CNCP (pain of ≥ 12 weeks' duration, not associated with a diagnosis of cancer) of the back or neck at the Langa CHC between 1 January 2014 and 31 December 2020. The start date for quantitative sampling was chosen as 1 January 2014 because this was the inaugural date of the CHC's chiropractic programme.¹⁵ Patients with spinal neoplasms or other contraindications to chiropractic treatment (ie, 'red flag' diagnoses such as fractures, infections, inflammatory arthritis or cauda equina syndrome) will be excluded. We will randomly select an equal number of recipients and non-recipients of chiropractic services within the aforementioned 7-year timeframe to form our exposure and comparison cohorts. Our sampling frame will be the Langa EMR database, and our sampling unit will be individual patient records. To guard against overfitting of our regression models,⁴⁶ we will set a minimum threshold of 10 events per category for each independent variable (see variable categories in table 1) to ensure that each variable has sufficient discriminant power to detect an association with opioid use, if an association exists. Based on patient recruitment numbers from our pilot

study,¹⁵ we expect to be able to select the sample from approximately 500 to 750 eligible patient charts.

Rates of missing data involving EMR extraction can vary.⁴⁷ Therefore, for validation (ie, to verify patient opioid prescriptions and dosages), the final set of EMR records will be linked with medical drug claims data from the Narcotics Monitoring System and Ontario Drug Benefit Program databases. We have confirmation from the Data and Analytic Services Department at the Institute for Clinical Evaluative Sciences (ICES) (<https://www.ices.on.ca>) that we will have access to the claims information (approval number 2020-739). ICES is an independent, non-profit research organisation that maintains a data repository of publicly funded administrative health service records for all Canadian citizens in the province of Ontario.

Quantitative data collection

Our outcome variables will be measured as the number of prescribed opioid fills, the number of prescribed opioid refills and the prescribed opioid dosages among patients in the exposure and comparison groups. These outcomes will be measured in each patient chart from both groups up to 12 months after their index visit for a CNCP-related diagnosis of the back or neck at the CHC. Although we will only extract data for patient encounters related to a back or neck pain diagnosis including opioid medications prescribed on these visit dates, it remains possible



that opioids may have been prescribed for other indications. This may attenuate the association between chiropractic care and opioid use.⁴⁸ Other variables that will be extracted from the EMR include sociodemographics (age and sex), general health (smoking status and BMI), comorbidities (depression, anxiety, fibromyalgia, diabetes and cardiovascular disease) and the total number of healthcare (ie, GP or chiropractic) visits. These variables have been shown to be associated with CNCP and opioid use.³¹⁻³⁹ In our analysis, we will explore variance inflation factors (VIFs) to assess collinearity between independent variables. If multicollinearity is detected between two or more variables (ie, VIFs ≥ 10),⁴⁹ then we will compare regression models, each separately containing one of the collinear variables, to one another and select the model containing the variable that produces the lowest Akaike information criterion. Complete lists of study variables and diagnostic codes are given in [table 1](#) and online supplemental appendix 2, respectively.

To increase the reliability of data extraction,⁴² two extractors will independently extract data from each chart and resolve differences by consensus. The principal investigator (PI) will adjudicate if necessary. The PI will also train and monitor the extractors, who will be blinded to the research questions. The PI will create standardised forms and a procedural manual to guide training and extraction. The extractors will pilot test the forms on a random sample of patient charts (eg, 10 from each of the exposure and comparison groups), and inter-rater agreement will be measured using the kappa (κ) statistic.

Quantitative data analysis

Baseline characteristics will be compared between the exposed and non-exposed groups using the χ^2 and independent t tests (or Fisher exact and Wilcoxon-Mann-Whitney tests when appropriate) for categorical and continuous variables, respectively. Generalised estimating equations (GEEs) will be used to explore the associations between exposure to chiropractic care and opioid prescribing.⁵⁰⁻⁵¹ To account for potential data clustering within-subjects or between medical or chiropractic practitioners, a robust variance estimator will be used to compute the standard errors for the coefficient estimates. In addition, because we do not know the structure of this correlation, we will conduct a sensitivity analysis and run a series of models testing different working correlation structures, including independent, autoregressive and unstructured matrices.⁵⁰⁻⁵¹ The specified link function in our GEE models will be based on the data distribution (eg, log-linear for Poisson, binomial for binary data).

GEEs with a Poisson distribution will be used when the outcomes are counts (ie, total number of opioid fills and refills over the entire course of follow-up, tabulated at the end of follow-up). Incidence density (rate) ratios for differences between the chiropractic and non-chiropractic groups will be estimated using Poisson log-linear GEEs and reported with 95% CIs and p values.

A repeated-measure GEE with a binomial distribution will be used when the outcome is opioid dosage. Opioid dosages will be assessed at 90-day intervals and dichotomised into high (≥ 90 mg) morphine equivalents daily (MED) or low (< 90 mg) MED⁶ and compared between the chiropractic and non-chiropractic groups from baseline to 12-month follow-up. We will estimate between-group differences for dosage using a binary logistic GEE and report with ORs, 95% CIs and p values. To calculate the MED for each prescribed opioid, we will multiply the quantity \times the milligrams per unit dispensed \times drug-specific conversion factors (online supplementary appendix 3).^{6,8}

For each outcome of interest, univariate and multivariable models will be built to estimate the crude and adjusted associations, respectively, between patients with and without chiropractic integration (1=with; 0=without) and the outcomes that were described above. Covariates will be grouped into blocks (ie, sociodemographic, health-related, depressive symptoms, health behaviours and healthcare visits) and sequentially entered into the models, with time (ie, calendar year) as an additional covariate and chiropractic/non-chiropractic as the main exposure variable. Based on the previous literature,^{8,31-39} we anticipate that younger age, male sex, health-related comorbidities, depressive symptoms, poor health behaviours (eg, smoking), a higher frequency of healthcare provider visits and earlier years of our 7-year project timeframe will be positively associated with opioid use. We will report all models and assess model fit using the quasi-likelihood under the independence model criterion (QIC).^{51,52} Correlation structures with the lowest QIC scores (closest to zero) will be judged as the best model fit for the data. All data and comparative analyses will be performed using SPSS V.26.0 (IBM SPSS Statistics), and the two-sided statistical significance level (α) for all quantitative analyses will be 5%.

Qualitative sampling

For the qualitative phase, we will use stratified purposive sampling to select a subsample of patients to participate in one-on-one interviews.⁵³ To maintain privacy of individuals' medical records, these patients will be chosen by their GPs and will be selected from among the sample whose charts we examined in the quantitative phase. This will be the first stage of integration (ie, connecting and building⁵⁴) between the quantitative and qualitative phases of our study. We will also recruit a purposive sample of GPs from the CHC. Maximum variation⁵³ will be used in choosing patients and GPs to ensure a range of perspectives and sociodemographic characteristics. For example, we will ask GPs to select chiropractic and non-chiropractic patients from three groups: persons whose number of opioid prescriptions has decreased over time; persons whose opioid prescriptions have remained stable or persons whose prescriptions have increased. We will provide GPs with participant recruitment guidelines. We will also recruit both medical doctors and nurse practitioners to participate in the GPs' interviews. We will select

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a minimum of 6–10 GPs and 12–20 patients (including an equal representation of chiropractic and non-chiropractic patients) on a rolling basis.⁵³ Recruitment will cease when we reach data saturation across subsamples (ie, the point at which no new information is obtained from participants in the GP, chiropractic and non-chiropractic groups).⁵⁵ We anticipate that this will happen after a total of 20–25 interviews.

Qualitative data collection

Qualitative data will be collected through the use of one-on-one (individual) semistructured interviews and framed within the principles of qualitative description.⁵⁵ Based on the findings from our quantitative analysis and relevant literature,^{12–19 22} we will develop interview guides for both patients and GPs, which will include open-ended questions asking participants about their perceptions of the integration of chiropractic services at the Langs CHC as well as how they feel these services have impacted opioid use for chronic pain. We are aware that the impact of chiropractic care on opioid use might have been affected by whether or not GPs engaged patients in a formal effort to taper their opioid prescriptions, and if patients agreed to subsequently engage in opioid tapering.⁵⁶ In addition, some patients may have engaged in other non-pharmacological pain management practices outside the CHC. Those with prior positive experience with chiropractic treatment may also have been more open to being referred by their GP for these services. As such, we will explore these issues as part of the interview process. We will also collect demographic and clinical characteristic data from interview participants, including age, sex, years in practice (for GPs) or years attending the CHC (for patients), primary pain complaint and current opioid dose.

We expect each interview to last approximately 1 hour; all interviews will be audio recorded. Field notes will be taken during the interviews to document emergent themes and other observations. To promote rigour, we will triangulate source data⁴¹ by comparing themes and subthemes generated from both the patient and GP interviews. This will help facilitate a deeper understanding of the qualitative findings.⁴¹ Trustworthiness of our qualitative data will be further assessed via member checking⁴¹ (ie, participants will be sent raw transcripts of their interviews as well as a summary of the major themes to be reviewed and affirmed). In addition, a reflexive journal and audit trail will be kept to track potential researcher bias and to document decisions made around qualitative data collection and analysis procedures.⁵⁵

Qualitative data analysis

All interview audio recordings will be transferred into the software programme, Max Weber Qualitative Data Analysis (MAXQDA) (<http://www.maxqda.com>) and transcribed verbatim. Participant identifiers will be removed. All transcripts will be independently coded by two investigators into themes and subthemes using an inductive content

analytic approach.⁵⁴ The investigators will meet after every five interviews⁵⁷ to compare their themes and arrive at a final, agreed-upon set of themes through discussion. These themes will be organised into tabular form and the investigators will select representative quotations for each theme/subtheme.⁴¹ As part of our data integration procedures (see figure 1), we will create joint display tables^{41 54} by adding a column for quotes to the tables reporting the regression models. In addition, we will integrate our qualitative and quantitative results using a weaving narrative approach (ie, the quantitative and qualitative results will be organised and presented side-by-side and discussed in terms of how they are similar or dissimilar).^{41 54} As such, our follow-up qualitative findings will be used to illuminate the statistical findings from the initial quantitative chart review.⁴¹ We will then draw on the qualitative and quantitative results jointly to come to a set of conclusions (ie, ‘meta-inferences’).^{43 53}

Patient and public involvement

Patients and the public were not involved at this stage of the project.

ETHICS AND DISSEMINATION

This study has been approved by the Hamilton Integrated Research Ethics Board at McMaster University (approval number 2021-10930). Approval to conduct this project has also been obtained from the Chief Executive Officer at the Langs CHC.²⁶

An important consideration for the EMR review will be confidentiality of patient records.⁴² To address this risk, we will have an administrator at the Langs CHC generate a list of unique identification numbers for the randomly selected patient files. The data extractors will review these files through the EMR’s ‘Cumulative Patient Profile’ page (see, eg, online supplemental appendix 4) and enter relevant data into Microsoft Excel. Furthermore, we will only report aggregate data in any publications.

Informed consent will be obtained from interview participants and the transcripts of their interviews will be deidentified prior to analysis. All chart review data will also be recorded anonymously, deidentified and coded. Audio recordings, transcripts and extracted chart data will be stored securely on a password-protected server at the Langs CHC. Any written paper records will be stored in the PI’s locked private office. All data will be destroyed after 10 years.

Dissemination of our study will occur via three peer-reviewed publications (ie, the study protocol, quantitative results and a mixed methods paper) as well as conference presentations. We will also provide written summaries and oral presentations to stakeholders (ie, patients, healthcare providers, decision-makers and community members) at the Langs CHC. We will establish connections with other stakeholder groups (eg, the Canadian Pain Society (<https://www.canadianpainsociety.ca>)) and



present our findings to them, either in-person or via webinars.

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Patient consent for publication Not applicable.

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Appendices

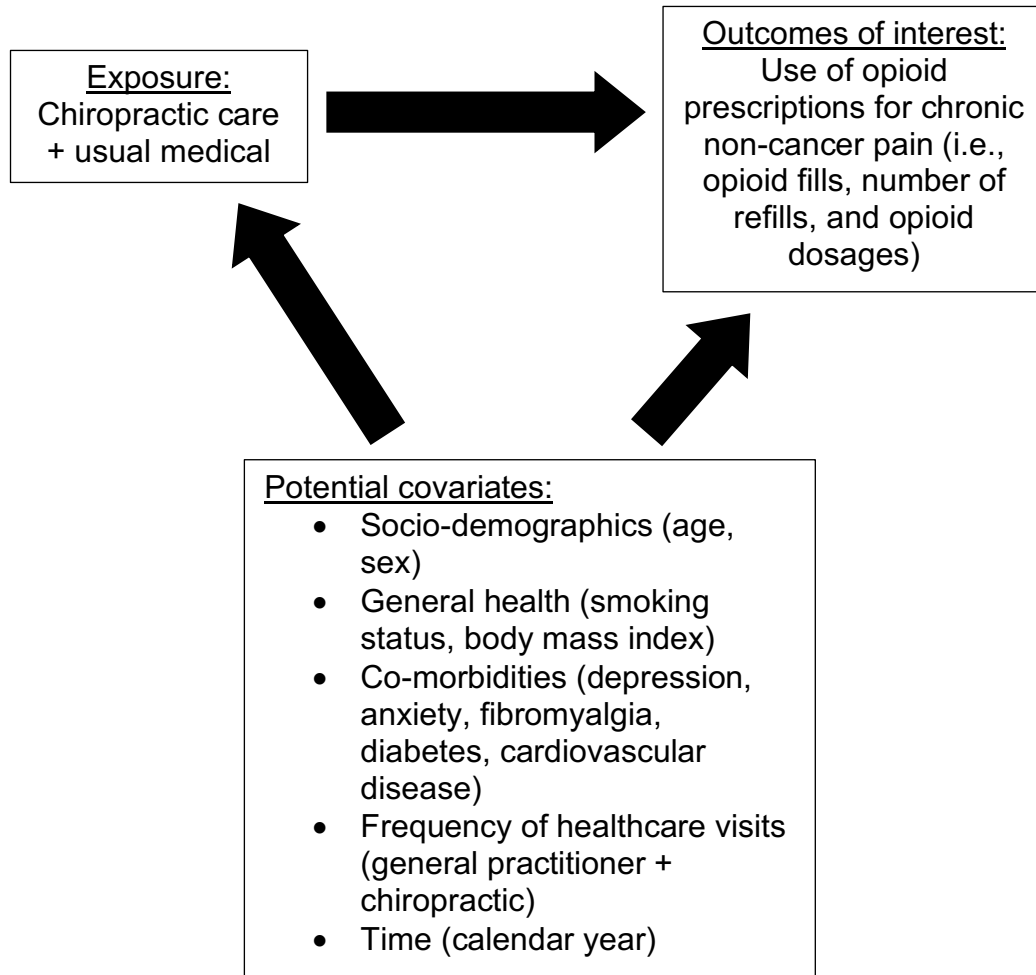
Online Supplementary Appendix 1: Conceptual framework

Online Supplementary Appendix 2: List of diagnostic chart codes

Online Supplementary Appendix 3: Morphine equivalents daily conversion factors

Online Supplementary Appendix 4: Electronic medical record ‘CPP (Cumulative Patient Profile)’ page

Online Supplementary Appendix 1 Conceptual framework for the relationship between receiving chiropractic care in addition to usual medical care and the utilization of opioid prescriptions in adult patients with chronic non-cancer pain presenting within a community health centre setting.



Online Supplementary Appendix 2 ENCODE-FM™ (Version 5.0) diagnostic codes to be used for defining the sample, exclusion criteria, and co-morbidities.

<p>Spine pain cohort Back or neck pain-related diagnoses</p>	<p>32-41, 3453-3461, 3484-3491, 3535-3540, 3560-3583, 3710-3713, 3715-3724, 3727, 3759-3789, 3839, 3858, 3866, 3867, 4002, 4258-4262, 4302-4305, 9855, 9856, 9902-9904, 9979, 9980</p>
<p>Exclusion criteria Spinal neoplasms (malignant) Spinal fractures Spinal infections Cauda equina syndrome Inflammatory arthritides</p>	<p>1264, 1265, 4091, 4092, 4113-4119 3870, 4123-4125, 4136, 4141-4145, 4179-4186 3916-3929 4819 4009-4087, 10296</p>
<p>Co-morbidities Anxiety Depression Fibromyalgia Diabetes Cardiovascular disease Smoking Obesity</p>	<p>5116-5123, 5643-5651, 9992 5129-5145, 5591-5619, 9612-9615, 10267 3841 7078-7096, 9631, 9632, 9665, 9666 3077-3380, 4645-4703, 7121-7152, 9894-9896, 9905-9907, 9977, 9978 327, 5339-5349, 9910 7182-7186, 10336</p>

ENCODE-FM™ = *Electronic Nomenclature and Classification Of Disorders and Encounters for Family Medicine.*

Online Supplementary Appendix 3 Opioid morphine equivalents daily (MED) conversion factors ^a (adapted from Busse et al.⁶).

Oral opioid formulations		
<i>Opioids</i>	<i>Oral MED conversion factors</i>	
Codeine	0.1 to 0.2	
Dihydrocodeine	0.1	
Hydrocodone	1.0 to 1.5	
Hydromorphone	5.0	
Meperidine	0.1	
Morphine	1.0	
Oxycodone	1.5	
Oxymorphone	3.0	
Tapentadol	0.3 to 0.4	
Tramadol	0.1 to 0.2	
Transdermal opioid formulations		
<i>Opioid</i>	<i>Hourly microgram dose</i>	<i>Mean MED dose (range)</i>
Fentanyl	25 mcg/hr	97 mg/day (60 to 134)
Fentanyl	37 mcg/hr	157 mg/day (135 to 179)
Fentanyl	50 mcg/hr	202 mg/day (180 to 224)
Fentanyl	62 mcg/hr	247 mg/day (225 to 269)
Fentanyl	75 mcg/hr	292 mg/day (270 to 314)
Fentanyl	87 mcg/hr	337 mg/day (315 to 359)
Fentanyl	100 mcg/hr	382 mg/day (360 to 404)

MED = morphine equivalents daily.

^a *These factors are for calculation purposes only.*

Online Supplementary Appendix 4 Example of the electronic medical record ‘CPP (Cumulative Patient Profile)’ page in PS (Practice Solutions) Suite.

The screenshot displays the 'Jomin Joseph - PSS' patient profile in the PS Suite. The interface is divided into several sections:

- Left Sidebar:** Contains navigation and filtering options such as 'Hide Demographics', 'Show Lab Table', 'Show Flowsheet', and 'Show Treatment History'. It also lists patient details like 'PSS Test Patient' and 'Family Hx'.
- Top Right:** Shows patient demographics including birthdate (Sep 2, 1945), sex (M), and health status (eligibility unknown; Not Rostered).
- Center Panel:** Displays various medical data points:
 - Counter:** MSAA, PHQ-9, GAD-7.
 - Well Baby Charts:** Perinatal Forms, Childhood Immunization.
 - Search and Links:** Search bar, Web Links, and COVID-19 related options.
 - Physical Exam:** Colonoscopy, FOBT, FIT, BMD, Pap, FBS, A1C (Jun 10, 2009), LDL.
 - Demographics:** Address, phone, and OHIP Billing information.
- Bottom Section:** Includes an 'Anatomical Area' table for joint-related referrals, a 'Note' about joint-related referrals, and a 'Physical Examination or Complaints' section.

Area	L	R	Area	L	R
Shoulder	<input type="checkbox"/>	<input type="checkbox"/>	Hip	<input type="checkbox"/>	<input type="checkbox"/>
Arm	<input type="checkbox"/>	<input type="checkbox"/>	Thigh	<input type="checkbox"/>	<input type="checkbox"/>
Elbow	<input type="checkbox"/>	<input type="checkbox"/>	Knee	<input type="checkbox"/>	<input type="checkbox"/>
Wrist	<input type="checkbox"/>	<input type="checkbox"/>	Leg	<input type="checkbox"/>	<input type="checkbox"/>
Hand	<input type="checkbox"/>	<input type="checkbox"/>	Ankle	<input type="checkbox"/>	<input type="checkbox"/>
Fingers	<input type="checkbox"/>	<input type="checkbox"/>	Foot	<input type="checkbox"/>	<input type="checkbox"/>

NOTE : All joint-related referrals must be accompanied by relevant imaging. (knee x-rays should be standing)

Physical Examination or Complaints:

Anticoagulants? Y DM? Y AIDS/HepC? Y Allergy? Y

Signature: *Jomin Joseph* Date: Feb 10, 2021

Chapter 6:

Association of Chiropractic Care with Receiving an Opioid Prescription for Non-Cancer Spinal Pain within a Canadian Community Health Center: A Mixed Methods Analysis

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Contributorship:

Concept development (provided idea for the research): P.C.E., M.O., L.M., J.W.B.

Design (planned the methods to generate the results): P.C.E., M.O., L.M., J.W.B.

Supervision (provided oversight, responsible for organization and implementation, writing of the manuscript): P.C.E., M.O., L.M., J.W.B.

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Writing (responsible for writing a substantive part of the manuscript): P.C.E.

Critical review (revised manuscript for intellectual content, this does not relate to spelling and grammar checking): P.C.E., A.L.B., M.O., L.M., D.F.C., J.D., J.W.B.

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Association of Chiropractic Care with Receiving an Opioid Prescription for Non-Cancer Spinal Pain within a Canadian Community Health Center: A Mixed Methods Analysis

ABSTRACT

Objective: The purpose of this study was to examine the association between receipt of chiropractic services and initiating a prescription for opioids among adult patients with non-cancer spinal pain in a Canadian community health center.

Methods: In this sequential explanatory mixed methods analysis, we conducted a retrospective study of 945 patient records (January 2014 to December 2020) and completed interviews with 14 patients and 9 general practitioners. We used Cox proportional hazards regression analyses, adjusted for patient demographics, co-morbidities, visit frequency, and calendar year, to evaluate the association between receipt of chiropractic care and time to first opioid prescription up to 1-year after presentation. Qualitative data were analyzed thematically and integrated with our quantitative findings.

Results: There were 24% of patients (227 of 945) with non-cancer spinal pain who received a prescription for opioids. The risk of initiating a prescription for opioids at 1-year after presentation was 52% lower in chiropractic recipients versus non-recipients (HR = 0.48; 99% CI, 0.29-0.77) and 71% lower in patients who received chiropractic services within 30 days of their index visit (HR = 0.29; 99% CI, 0.13-0.68). Patients whose index visit date was in a more recent calendar year were also less likely to receive

opioids (HR = 0.86; 99% CI, 0.76-0.97). Interviews suggested that self-efficacy, access to chiropractic services, opioid stigma, and treatment impact were influencing factors.

Conclusion: Patients with non-cancer spinal pain who received chiropractic care were less likely to obtain a prescription for opioids than patients who did not receive chiropractic care.

Key Indexing Terms: *Health Services Research; Analgesics, Opioid; Community Health Centers; Chiropractic*

INTRODUCTION

Opioid medications are commonly prescribed in North America to relieve musculoskeletal (MSK) pain and improve function.¹ However, opioids provide only modest benefits² and are associated with important harms including addiction, overdose, and death.³⁻⁶ There were 24,626 opioid-related deaths and 27,604 opioid-related hospitalizations in Canada between January 2016 and June 2021.⁷ In the United States (US), there were approximately 60,000 opioid-related deaths in 2016 alone.⁸ Young adult men have been most affected by the opioid crisis,^{7,8} which has arisen partly among individuals who were initially prescribed opioids for back pain or some other MSK condition.⁸⁻¹¹ Recent reports from Canada and the US indicate that opioid-related deaths have increased during the COVID-19 pandemic.^{7,12} Some chiropractors have called on governments, policy makers, and insurers to improve support for non-opioid approaches for managing MSK-related pain, including non-cancer back and neck pain, particularly in vulnerable or marginalized populations.¹¹

In 2017, we conducted a pilot project evaluating a newly integrated chiropractic spine pain program at the Langs Community Health Center (CHC) in Ontario, Canada¹³⁻¹⁵ and found that 82% of patients who received chiropractic care reported a significant reduction in the use of analgesics.^{13,16} However, similar to research of chiropractic integration within other Canadian primary care centers,¹⁷⁻²² our study was limited by the absence of a comparison group.^{13,16} Moreover, although several uncontrolled studies reported an association between reduced use of opioids and receipt of chiropractic care in various US populations,²³⁻²⁶ comparative assessments of the integration of chiropractic

services into primary care settings are sparse.^{27,28} In addition, the impact and understanding of such integration on prescription opioid use in non-cancer MSK pain management remains uncertain.

To address these knowledge gaps, we undertook a mixed methods analysis to examine the association between receipt of chiropractic services and opioid prescriptions among adult patients with non-cancer spinal pain in a primary care setting. We hypothesized that chiropractic care would be inversely associated with receipt of opioids. Further, we hypothesized that younger age, male sex, presenting with co-morbid depression, anxiety, fibromyalgia, diabetes or cardiovascular disease, obesity, positive smoking status, a higher frequency of healthcare provider visits, and earlier years of our 7-year study timeframe would be positively associated with opioid receipt.²⁹

METHODS

Reporting

We reported our study in accordance with the Good Reporting of A Mixed Methods Study (GRAMMS) guidelines (see Supplementary File 1).^{30,31}

Study Design

We used a sequential explanatory mixed methods design, where follow-up qualitative data were collected to clarify and explain the quantitative findings.³² This was also the second of 2 analyses undertaken in which these qualitative data were used.²⁹ Our rationale for using a mixed methods approach was that of complementarity,³³ that is, the

interview component of our study allowed for a richer understanding of whether chiropractic services were used by patients and general medical physicians/nurse practitioners (GPs/NPs) to reduce reliance on opioids. See Figure 1 for an illustrative diagram outlining our study procedures.

Ethics

The Hamilton Integrated Research Ethics Board at McMaster University approved our study (project number 2021-10930). Written informed consent was obtained from all subjects and all methods were conducted in accordance with the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2: 2020).

Quantitative Phase

Sampling

We conducted a retrospective chart review³⁴ of electronic medical records (EMRs) at the Langs CHC for all adult patients (aged ≥ 18 years) with 2 or more visits relating to a diagnosis of back or neck pain not associated with cancer between January 1, 2014 (the inaugural date of the CHC's chiropractic program¹³) and December 31, 2020. Patients with contraindications to chiropractic treatment, including fractures, infections, inflammatory arthritis, or cauda equina syndrome, were excluded from analysis. Because our exposure of interest was the addition of chiropractic care to ongoing GP/NP care, compared with ongoing GP/NP care alone,²⁹ we defined recipients of chiropractic care as any patient who received at least 1 appointment for GP/NP care and at least 1

appointment for chiropractic care during the 7-year study period. To be eligible to receive chiropractic services at the CHC, patients had to be referred by their GP/NP, thus every patient receiving chiropractic care also received ongoing GP/NP care.¹³ To account for immortal time bias,³⁵ we retained patients with opioid prescriptions after the index visit but before the first chiropractic visit in the recipient cohort.²⁶ This accounted for patients who were prescribed opioids before having a chance to receive chiropractic care. We only used first chiropractic visit as a recipient inclusion criterion in these cases.²⁶ We defined ‘non-recipients’ as those who received 2 or more appointments of GP/NP care alone. GP/NP care included assessment, prescription medication, and referral for diagnostic testing, specialist consultation or other co-interventions (ie, nursing, dietetics, social work, or physical therapy) at the CHC. Details of the chiropractic program, and our list of diagnostic codes, are described elsewhere.²⁹

Data Collection

Our main outcome variable was time to first opioid prescription, and all patients who had not received a prescription for opioids at their last follow-up were censored. An independent information technology specialist, who was blinded to our research questions,³⁴ extracted all patient data including visit and opioid prescription dates directly from the EMR. Only opioid prescription data between the time of the index and last visit dates for a non-cancer spinal pain diagnosis were included. However, it remains possible that opioids were prescribed for other indications, which would attenuate the association between chiropractic care and opioid receipt.³⁶ To increase confidence in our findings,

we defined our regression model *a priori* and selected 12 variables from the EMR database that, based on previous literature,^{23-26,37-45} we judged may be associated with time to first opioid prescription: chiropractic care, calendar year, frequency of healthcare visits, age, sex, smoking status, obesity, depression, anxiety, fibromyalgia, diabetes, and cardiovascular disease.

To prevent over-fitting of our regression model, we required a minimum sample of 120 patient records (ie, minimum of 10 events per category for each independent variable).⁴⁶ We excluded independent variables with fewer than 50 observations to ensure that each variable had sufficient discriminant power to detect an association with opioid prescribing, if such an association existed.⁴⁷ We also explored variance inflation factors (VIFs) to assess multicollinearity among independent variables and considered VIFs ≥ 5 as problematic.⁴⁸

Data Analysis

We generated frequencies for all relevant EMR data collected and reported categorical variables as proportions, normally distributed continuous data as the mean and standard deviation (SD), and skewed continuous data as the median and inter-quartile range (IQR). We compared baseline characteristics between chiropractic recipients and non-recipients using a chi-squared test for categorical variables (or Fisher's exact test if there was a cell frequency of < 5), independent *t*-tests for normally distributed continuous variables, and the Mann-Whitney U test for skewed continuous variables.

We performed a time-to-event analysis using a Cox proportional hazards regression model to assess the association between all 12 independent variables described above and time to first opioid prescription. We built a second model with the same 12 variables but with our exposure variable as ‘early’ receipt of chiropractic care (ie, receipt of chiropractic services within 30 days of the index visit). To further increase confidence in our findings, we only considered an independent variable as statistically significant if it had a p -value of $\leq .01$ in our adjusted models. We calculated unadjusted and adjusted hazard ratios (HRs) for our time-to-event analyses, their associated 99% confidence intervals (CIs), and corresponding p -values. For our Cox regression models, we tested the proportional hazards assumption by checking the p -value of the time-covariate interaction term for each independent variable using a time-dependent covariate analysis. We considered a p -value of $\leq .05$ for the interaction term as significant. Calendar year was entered into our models as a time-dependent variable. We also checked the Kaplan-Meier and log-minus-log plots for our main exposure variable (chiropractic care, or early chiropractic care) to verify the absence of non-proportionality. All data and comparative analyses were performed using SPSS v26.0 (IBM SPSS Statistics).

To help convey the magnitude of difference for our primary association of interest, we estimated the cumulative proportion of first opioid prescriptions received at 1 year among patients in our cohort who did, and did not, receive chiropractic care by using the following formula: $P_1 = 1 - (1 - P_0)^{HR}$ where P_1 is the cumulative proportion of first opioid prescriptions received by 1 year in the group that did receive chiropractic care, P_0 is the cumulative proportion of first opioid prescriptions received by 1 year in the group

of patients that did not receive chiropractic care, and HR is the association of chiropractic care with receiving an opioid prescription. We repeated this calculation for patients who did, and did not, receive early chiropractic care.

Qualitative Phase

Sampling

As described elsewhere,²⁹ we used stratified purposive sampling⁴⁹ to select a sub-sample of chiropractic and non-chiropractic patients, whose charts we examined in the quantitative phase, to participate in 1-on-1 interviews. This was the first stage of integration between the quantitative and qualitative phases of our study.⁵⁰ We also recruited a purposive sample of GPs/NPs from the Langs CHC. We obtained participant contact information from the Langs administration and the lead author (PCE) conducted recruitment via telephone or e-mail. Gift cards (\$30 for patients, \$10 for GPs/NPs) were offered as incentives. We used maximum variation,⁴⁹ based on age, sex, and the number of years in practice (for GPs/NPs) or years attending the CHC (for patients), in choosing participants to ensure a range of perspectives and sociodemographic characteristics. We aimed to interview a minimum of 6 GPs/NPs and 12 patients,⁴⁹ with interviews continuing until the occurrence of data saturation (ie, the point at which no new information was obtained from participants in the GP/NP, chiropractic, and non-chiropractic groups).⁵¹ Fundamental qualitative description^{52,53} was the methodological orientation we used to underpin the qualitative phase of our study.

Data Collection

The lead author (PCE) conducted 1-on-1 (individual) semi-structured interviews with participants. We chose individual interviews over focus groups because of the sensitive nature of our research topic and that participants could have been discouraged from sharing their full views on the subject (ie, opioid use) in the presence of other patients or peers. Interviews were conducted in a private office separate from the medical clinic at the Langs CHC and were held either in-person (n = 20) or virtually (n = 3) using the Zoom videoconferencing application (Zoom Video Communications, Inc.). Informed consent was obtained from participants before the start of each interview. Five members of our research team (PCE, ALB, MO, LM, JWB) developed the interview guides (see Supplementary Files 2 and 3) based on our quantitative findings and relevant literature.^{2,4,13-19,21-26} Three of the 5 members (PCE, ALB, JWB) had content expertise in the subject area of our study.

We audio-recorded in-person interviews using MacIntosh recording software (Audio Recorder v1.3, FIPLAB Limited, Chalfont St. Peter, Buckinghamshire, United Kingdom) and virtual interviews using Zoom's built-in recording feature. Field notes were taken after each interview by the lead author (PCE) to document emergent themes and other observations. We sent interview transcripts and a summary of the results to participants for feedback or correction.³²

Data Analysis

All interview audio recordings were transferred into the software program, MAXQDA (Max Weber Qualitative Data Analysis, VERBI Software, Sozialforschung GmbH, Berlin, Germany) and transcribed by the lead author (PCE) verbatim. Participant identifiers were removed, and a random sample of 15% of the transcripts was reviewed for accuracy by another member of the research team (JD). Two investigators (PCE, ALB) independently coded all transcripts using an inductive content analytic approach⁵² to descriptively summarize the information to ensure the ‘best fit to the data.’⁵³ We used open coding to develop concepts from the data, and axial coding to relate these codes (or concepts) to one another and identify themes and sub-themes.³²

The 2 investigators met 3 times throughout the qualitative analysis (ie, after every 7 to 8 interviews) to compare their themes and arrive at a final, agreed-upon set of themes through discussion. These themes were then organized into tabular form and representative quotes were selected for each theme/sub-theme. As part of our data integration procedures (see Figure 1),^{32,50} we created a joint display table and used a contiguous narrative approach to combine our qualitative and quantitative results. Meta-inferences^{49,51} were then drawn from the data. An audit trail of our coding and reflexive procedures was recorded throughout our analysis.⁵² For investigator reflexivity see Supplementary File 4.

RESULTS

Quantitative Findings

We identified 1,166 patient records, and 945 met eligibility criteria for inclusion in our quantitative analysis (Fig 2).

Cohort Characteristics

The baseline characteristics (n = 945) are presented in Table 1. Among patients who received an initial opioid prescription during the 7-year study period (n = 227), most (75%) were prescribed opioids within 12 months after their first visit to the CHC. The survival curve for the time to first opioid prescription among the study cohort is presented in Supplementary File 5.

Chiropractic Recipients versus Non-Recipients

There were 19% of patients (183 of 945) who received chiropractic services. Of these, 48% (87 of 183) received chiropractic services within 30 days of their index visit. In comparison to non-recipients, chiropractic recipients were more commonly female patients, depressed, or diabetic. Early chiropractic recipients had similar characteristics to those who did not receive early chiropractic services (Supplementary File 6).

Time-to-Event Analysis

The regression analysis showed an inverse association between receipt versus non-receipt of chiropractic care and opioid prescribing (HR = 0.48; 99% CI, 0.29 to 0.77) (Table 2). Thus, at 1 year, 51% of patients without chiropractic care received opioids versus 29% of patients who received chiropractic care. Among early chiropractic recipients, the risk of

initiating a prescription for opioids was lower (HR = 0.29; 99% CI, 0.13 to 0.68) (Supplementary File 7). Thus, at 1 year, 49% of patients without early chiropractic care received opioids compared to 18% of patients who received early chiropractic care (Fig 3). Patients whose index visit date was in a more recent calendar year were less likely to receive opioids (HR = 0.86; 99% CI, 0.76 to 0.97). A higher frequency of healthcare visits (HR = 1.02; 99% CI, 1.02 to 1.03), older age (HR = 1.02; 99% CI, 1.01 to 1.04), positive smoking status (HR = 1.62; 99% CI, 1.12 to 2.35) and depression (HR = 1.77; 99% CI, 1.20 to 2.61) were positively associated with receipt of opioids (Table 2). These associations were also found in our second regression model (Supplementary File 7). All VIFs were less than 1.6, suggesting no important multicollinearity among independent variables.

Contrary to our predictions, older age was positively associated with receipt of opioids. We found that male sex, obesity, anxiety, fibromyalgia, diabetes, and cardiovascular disease were not associated with receipt of opioids in our sample (Table 2 and Supplementary File 7). We explored for interaction between receipt of chiropractic care and age, smoking, depression, or healthcare visit frequency but none of the interaction terms were significant.

Qualitative and Integrated Findings

The majority (79%) of patients interviewed were women, most (86%) were either receiving disability benefits or were unemployed, and the majority (71%) had previously received at least 1 opioid prescription for non-cancer spinal pain. Among patients and

GPs/NPs, there was a large range of ages (33 to 82) and number of years in practice (GPs/NPs: 1 to 26) or years attending the CHC (patients: 2 to 43), demonstrating variability among participants (Table 3).

Twelve GPs/NPs were invited for interviews and 9 participated. Of these, 4 were medical doctors and 5 were nurse practitioners. Two medical doctors declined participation because of lack of time, and 1 nurse practitioner expressed interest but did not respond to further interview requests. Among patients, 23 were recruited and 14 completed interviews (ie, 8 of 11 chiropractic recipients and 6 of 12 non-recipients). Five patients scheduled interviews but canceled (2 chiropractic recipients, 3 non-recipients), 2 scheduled interviews but did not attend (1 recipient, 1 non-recipient), 1 was not interested and 1 declined for health reasons. In total, 23 interviews were completed (14 patients, 9 GPs/NPs). The median durations of interviews were 38 minutes (range, 20 to 40) for GPs/NPs and 25 minutes (range, 19 to 56) for patients.

Among all 23 participants, 3 GPs/NPs and 1 non-chiropractic patient made unsubstantive revisions to clarify statements from their interviews. No other participants requested corrections or content changes to their transcripts or results. We determined that data saturation had been reached when only 1 new code emerged from GP/NP interviews 7, 8 and 9; only 2 new codes emerged from chiropractic recipient interviews 7 and 8 (with no new codes from interview 8); and only 1 new code emerged from non-recipient interview 4 (with no new codes from interviews 5 and 6), which concluded patient recruitment.

Coding Tree

We identified 37 codes across interviews and categorized these into the following 4 major themes: (1) patient self-efficacy, (2) accessibility of non-pharmacological services, (3) stigma regarding use of opioids, and (4) impact of treatment. Codes pertaining to patient self-efficacy were grouped into 2 sub-themes, ‘active versus passive approaches’ and ‘resistance to taking medication.’ This latter sub-theme was more frequent among interviews of chiropractic (4 of 8) versus non-chiropractic (2 of 6) patients. For instance,

“I’ve been dealing with this pain for 10 years, and I’m not just a pill popping, believing [person]. [I’m] old school, take the pain until it’s really extreme and then – oh gee, I better take an Advil – is kinda how I deal with my pain.” Doctor of Chiropractic (DC) Patient 1

For our second theme, we created the sub-themes ‘lack of access’ and ‘access to chiropractic services at Langs.’ Lack of access to non-pharmacological services (eg, chiropractic, physical therapy) was identified in nearly all (21 of 23) participant interviews and was reported by both GPs/NPs and patients as a common facilitator of opioid use.

“It’s that scenario where you have nothing else to offer, right? So, if you’re trying to postpone heading into ‘opioid land’ and you still have something else to offer, it can definitely make a difference. ... You probably go to meds sooner than you

might otherwise because you don't have access to the intervention you'd really like." GP/NP 7

"When I was about 23 [years old], financially I wasn't able to go [to my chiropractor] anymore. So, that's when [my doctor] put me on the OxyContin and the Perc's." DC Patient 7

Our third theme captured codes related to the opioid crisis such as negative media coverage or lived experiences. Some patients also expressed a sense of judgment from others for using prescription opioids, as elucidated by the following participant:

"It's been frustrating – so frustrating. Because the [opioid] crisis seemed to just fall right on me. Like, as though I'm part of the crisis. So, [as a result] every doctor doesn't want you on any kind of pain medication. They don't believe your pain. You know what I mean? It has really affected me. ... I'm not an addict in any way. I never even ever think twice about taking that medication more than once, like, unprescribed. But I was definitely treated like I was [an addict]." Non-DC Patient 5

The remaining codes related to patients' or GPs/NPs' perspectives on the impact of treatment, including sub-themes of pain relief, functionality, and anxiety and fear surrounding opioid withdrawal. For example,

“[For] my neck, sometimes, if I didn’t go [to the chiropractor], I would really notice it in a couple months if I didn’t go every, at least every 2 months, if not every month.” DC Patient 8

“I do actually have patients on opioids that are actually working and it’s because they’re on opioids, ... that they continue to work full-time. And so, they’re not the ones that I worry about so much because they clearly have functionality, and they don’t show any behavioral stuff.” GP/NP 9

And:

“...terrifying. ... Not being able to have [my] prescription filled is very frightening – and panic. You start having anxiety.” Non-DC Patient 4

Further descriptions and frequency counts of each major theme, sub-themes, and representative participant quotes are provided in Supplementary File 8. Qualitative and quantitative findings are shown together as a joint display in Table 4.

DISCUSSION

This study was one of the first to examine the relationship between chiropractic integration and opioid use among vulnerable patients with non-cancer spinal pain in a

CHC setting,^{22,28} and the first to do so using a mixed methods approach. In our quantitative analysis, we found that receipt of chiropractic care was associated with a decreased likelihood of receiving an opioid prescription, and our follow-up interviews identified several potential influencing factors in this relationship. Our quantitative results are consistent with those of other uncontrolled observational studies.^{23-26,54} For instance, a systematic review and meta-analysis of 6 cohort studies²³ found that patients with non-cancer back or neck pain who received chiropractic services were nearly two-thirds less likely than non-chiropractic users to be prescribed opioids (pooled odds ratio = 0.36, 95% CI 0.30 to 0.43). In 2 more recent studies,^{25,26} the risk of filling an opioid prescription among US adults²⁵ and older Medicare beneficiaries²⁶ with non-cancer spinal pain was reduced by half for recipients of chiropractic services. In keeping with our findings, this reduction was greater among patients who saw a chiropractor within the first 30 days of treatment.^{25,26} An association between reduced opioid use for spinal pain with early access to non-pharmacological services (eg, chiropractic, physical therapy) has also been reported by others.^{22,24,54,55}

We gained several insights into our quantitative findings by integrating quantitative and qualitative methods. Based on our interviews, we perceive that patients who were referred for chiropractic services at the Langs CHC may have been more resistant to taking medication in general, and opioids in particular, than patients who were not referred for chiropractic services. GPs/NPs indicated that access to chiropractic treatment gave them another non-opioid pain management option. In addition, a negative stigma regarding use of prescription opioids was identified by several chiropractic

patients and GPs/NPs as a barrier to opioid use. These factors may help explain why chiropractic recipients were less likely to be prescribed opioids. We also found that when accessed as a first-line treatment, chiropractic care may have helped to delay, and in some cases prevent, opioid prescription. Our data suggest that by 1 year, access to chiropractic care resulted in an additional 22% of patients not receiving a prescription for opioids. When chiropractic care was accessed within 30 days of visiting the CHC, an additional 31% of patients avoided an opioid prescription. Thus, it appears that earlier access to chiropractic care may have had a greater protective effect in reducing the number of people obtaining opioid prescriptions.

Similar to previous research,^{4,44-46} we found that positive smoking status and co-morbid depression were strongly associated with opioid use in our sample (ie, increased risk of 62% and 77%, respectively). In the 2017 Canadian opioid guideline,⁴ we found that co-morbid mental illness was associated with an increased risk of opioid use disorder, as well as non-fatal and fatal opioid overdose when chronic pain patients were prescribed opioids. As such, a weak/conditional recommendation was made to avoid prescribing opioids to patients with active psychiatric disorders until their co-morbid mental illness has been stabilized.⁴ Our current findings suggest that patients with co-morbid depression were more likely to receive prescription opioids, which is cause for concern.

Our findings and those of other researchers suggest that chiropractic services are consistently associated with a reduced risk of opioid prescribing, as well as improved patient outcomes and potential for cost savings (eg, reductions in GP/NP visits, advanced imaging, and specialist referrals).^{13,16-26,28} As such, with further integration of

chiropractic services into primary care centers,^{13,16-26,28} the potential benefits for the opioid crisis, including how these patients are managed in CHCs and other health care settings, could be substantial.

Strengths

First, we included a robust set of potential confounders in our multivariable regression models to minimize the possibility of residual confounding. Second, we prespecified the anticipated direction of association for each independent variable in our regression models, and set our significance level to 1%, to provide greater confidence in our findings. Third, we controlled for the calendar year in our analyses to account for policy changes in opioid prescribing. Additional strengths included direct data export from the EMR to avoid extraction errors,³⁴ limited missing data (< 1%), and validation of our qualitative data via member-checking. The qualitative component of our study also provided a richer understanding of our quantitative findings.

Limitations and Future Studies

In the quantitative phase of our study, a limitation was the retrospective design, and certain variables that may be important to consider were unavailable. For example, due to the constraints of data recorded in the Langs EMR, we were unable to extract information on baseline spine-related pain (ie, severity/chronicity) or other co-interventions that patients may have received outside of the CHC. Moreover, we were unable to include race/ethnicity or other social determinants of health as possible covariates in our

analysis,⁵⁶ as these factors were not captured in the administrative database that we used. However, our findings regarding the association between receipt of chiropractic services and reduced opioid prescriptions were consistent with other studies that controlled for the duration of low back or neck pain.^{24,54,55} Moreover, due to socioeconomic disadvantages,^{13-19,21,22} most Langs CHC patients would be unlikely to have accessed private healthcare services elsewhere. A second limitation is that our primary outcome, time to first opioid prescription, is a surrogate for patient-centered outcomes, such as pain reduction or functional improvement. Third, as highlighted by our interviews, recipients of chiropractic care may have been prognostically different from non-recipients despite our adjustments for confounding. Notwithstanding, recipients had a higher prevalence of depression, which, based on our data, should have increased their risk of opioid use (see crude association under the “Univariate” column in Table 2). However, when we controlled for depression in our adjusted analyses, recipients had a lower risk of opioid receipt. Fourth, a limitation in using a sequential mixed methods design (ie, quantitative followed by qualitative) was that 11 months elapsed between our quantitative and qualitative data collection. As such, some individuals whom we attempted to recruit from the larger cohort were no longer available for interviews (eg, moved out of city, phone number no longer in service, or were deceased). Fifth, a limitation of the qualitative phase of our study is that we did not pilot-test our interview guides. However, 1-week in advance of participant interviews, patients and GPs/NPs received an information form containing examples of their interview questions. Sixth, and in line with our published protocol,²⁹ we interviewed patients and GPs/NPs to gain their perspectives on chiropractic

integration at the Langs CHC and its impact on opioid prescribing. However, the input of other stakeholders such as administrators, chiropractors, or other allied health professionals (eg, nurses, dieticians, or physical therapists) might have revealed additional themes and sub-themes to inform our research question. Seventh, as reported in Supplementary File 4 (see “Relationship with Participants”), a previous therapeutic relationship had been established between the lead author (PCE) and 2 of the 8 chiropractic patients who were interviewed for this study. This may have influenced the results in these 2 interviews; however, in neither case was care being provided at the time of the interview. A final limitation of our mixed methods study is the findings may be generalizable to some, but not all, clinic programs outside of the Langs CHC.

Although our results and those of previous studies on the association between chiropractic care and prescription opioid use are promising,^{22-26,54} observational research is prone to selection bias. As such, well-designed randomized controlled trials (eg, Goertz et al.²⁷) are urgently needed to confirm or refute these findings. A multi-stage, mixed methods, randomized controlled trial is needed to further explore our findings.

CONCLUSION

Our analysis found that patients with spine pain who received chiropractic care were less likely to receive opioids compared to patients who did not receive chiropractic care. This relationship was most pronounced among patients with early access to chiropractic services. Four themes emerged in our qualitative interviews, including patient self-

efficacy, access to chiropractic services, stigma regarding use of opioids, and impact of treatment, which provide a richer understanding of this association.

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Table 1 Demographic and clinical characteristics of patients from the quantitative chart review ($n = 945$)

Variable	Value ^a
Age in years, mean (SD)	52.4 (17.0)
Sex	
• Male	416 (44.0)
• Female	529 (56.0)
General health	
• Smoker	246 (26.0)
• Obese ^b	101 (10.7)
Co-morbidities	
• Cardiovascular disease	482 (51.0)
• Depression	420 (44.4)
• Anxiety	396 (41.9)
• Diabetes	184 (19.5)
• Fibromyalgia	57 (6.0)
Year of index visit ^c	
• 2014	299 (31.6)
• 2015	165 (17.5)
• 2016	138 (14.6)
• 2017	117 (12.4)
• 2018	71 (7.5)
• 2019	86 (9.1)
• 2020	69 (7.3)
Frequency of healthcare visits, median (IQR) ^d	4 (3-11)
Opioid prescription	227 (24.0)
Receipt of chiropractic care	183 (19.4)

CHC, community health center; GP/NP, general physician/nurse practitioner; IQR, inter-quartile range; SD, standard deviation.

^a Values are expressed as the number (%) unless otherwise indicated.

^b Patients with a body mass index of ≥ 30 kg/m² were classified as obese.

^c Year of index visit to the CHC for a non-cancer back or neck pain diagnosis.

^d Healthcare visits constitute GP/NP and chiropractic visits.

Table 2 Unadjusted and adjusted hazard ratios for the risk of opioid prescription among patients with non-cancer back or neck pain presenting between January 1, 2014 and December 31, 2020 ($n = 945$)^a

Variable	Univariate	P-value	Multivariable	P-value
	Unadjusted HR (99% CI)		Adjusted HR (99% CI)	
Chiropractic care				
• Non-exposed	Reference		Reference	
• Exposed	0.94 (0.62-1.43)	.713	0.48 (0.29-0.77)	< .001
Time (calendar year) ^b	0.81 (0.72-0.91)	< .001	0.86 (0.76-0.97)	.001
Frequency of healthcare visits ^c	1.02 (1.02-1.03)	< .001	1.02 (1.02-1.03)	< .001
Age	1.02 (1.01-1.03)	< .001	1.02 (1.01-1.04)	< .001
Sex				
• Female	Reference		Reference	
• Male	0.98 (0.70-1.39)	.904	1.06 (0.73-1.52)	.692
Smoking status				
• Non-smoker	Reference		Reference	
• Smoker	1.70 (1.19-2.43)	< .001	1.62 (1.12-2.35)	.001
Obesity				
• Non-obese	Reference		Reference	
• Obese	1.19 (0.72-1.96)	.369	0.92 (0.54-1.58)	.692
Depression				
• Absent	Reference		Reference	
• Present	1.58 (1.12-2.24)	.001	1.77 (1.20-2.61)	< .001
Anxiety				
• Absent	Reference		Reference	
• Present	1.02 (0.72-1.44)	.886	0.80 (0.54-1.18)	.136
Fibromyalgia				
• Absent	Reference		Reference	
• Present	1.74 (0.99-3.07)	.012	1.00 (0.51-1.95)	.993
Diabetes				
• Absent	Reference		Reference	
• Present	1.44 (0.98-2.12)	.014	1.07 (0.70-1.66)	.674
Cardiovascular disease				
• Absent	Reference		Reference	
• Present	1.43 (1.00-2.03)	.009	0.80 (0.52-1.23)	.181

CHC, community health center; CI, confidence interval; GP/NP, general physician/nurse practitioner; HR, hazard ratio.

^a HR > 1 indicates shorter time to first opioid prescription.

^b Calendar year was measured at the patient's index visit date to the CHC for a non-cancer spine pain diagnosis.

^c Healthcare visits constitute GP/NP and chiropractic visits.

Table 3 *Demographic and clinical characteristics of participants from the qualitative interviews (n = 23)*

Variable	Value ^a	
	Patients (n = 14)	GPs/NPs (n = 9)
Age in years, mean (SD)	56.2 (14.3)	47 (10.5)
Sex		
• Male	3 (21.4)	2 (22.2)
• Female	11 (78.6)	7 (77.8)
Years attending CHC (patients) / years in practice (GPs/NPs), mean (SD)	13 (11.6)	13.4 (6.8)
Completed post-secondary education or higher	7 (50.0)	9 (100)
Receiving disability benefits / unemployed	12 (85.7)	0 (0)
Opioid prescription	10 (71.4)	NA
Receipt of chiropractic care	8 (57.1)	NA

CHC, community health center; GP/NP, general physician/nurse practitioner; NA, not applicable; SD, standard deviation.

^a Values are expressed as the number (%) unless otherwise indicated.

Table 4 Combined display of the quantitative association between receipt of chiropractic services at the Langs Community Health Center and prescription of opioids, representative qualitative interview quotes, and meta-inferences

Variable	Quantitative Results	Qualitative Interview Quotes	Meta-Inferences
Receipt of chiropractic care (n = 183)	Negative association with receipt of opioids (adjusted HR = 0.48)	<p><u>Resistance to taking medication:</u></p> <ul style="list-style-type: none"> ● <i>“I don’t want to take any pill. It is better to bear the pain for some time rather than going for pills, or anything. [I’m] not a great believer in artificial pills.”</i> DC Patient 2 ● <i>“My thing for not wanting [opioids], I’ve lost way too many people, way too many friends, family, and I just know the destruction and devastation it does.”</i> DC Patient 6 ● <i>“[Before I came to Langs] I was on Percocet, OxyContin, Fentanyl. [I] got away from all that. It didn’t [solve anything].”</i> DC Patient 7 <p><u>Access to chiropractic services:</u></p> <ul style="list-style-type: none"> ● <i>“[The chiropractic program at Langs has] been helpful to avoid going the route of opioids sometimes. ... In some cases, people weren’t responding to what they were already on and we kind of maximized the dosing on that, and they were looking for more pain relief and one of the options might have been to add in an opioid; but because we had access to chiropractic, ... that sort of, kind of, kept things at bay and they were able to manage.”</i> GP/NP 9 ● <i>“The increased number of alternative therapies that you [have to] offer them, the more likely you are to avoid an opioid prescription.”</i> GP/NP 4 	The risk of receiving opioids was 52% lower in chiropractic recipients versus non-recipients. Patients who were referred by their GP/NP for chiropractic services at Langs may have been more resistant to taking opioids than patients who were not referred for chiropractic services. Access to chiropractic treatment also gave GPs/NPs another non-opioid pain management option.
Receipt of ‘early’ chiropractic care ^a (n = 87)	Negative association with receipt of opioids (adjusted HR = 0.29)	<ul style="list-style-type: none"> ● <i>“I see the difference between patients that have access [to non-pharmacological services] and don’t have access. ... Any patients that have access to all those</i> 	The risk of receiving opioids was 71% lower in patients who received chiropractic services

		<p><i>resources and can get them started right off the bat, I'm rarely giving them opioids. ... People that don't have access to anything, end up on opioids, just more often."</i> GP/NP 9</p> <ul style="list-style-type: none"> • <i>"I do have a patient ... who got referred [into the chiropractic program] right away and has not ever, opioids have never been on the table."</i> GP/NP 1 	<p>within 30 days of their index visit. When accessed as a first-line treatment option, chiropractic care may have helped to delay, and in some cases prevent, the prescription of opioids.</p>
<p>Index visit in more recent calendar year (n = 945)</p>	<p>Negative association with receipt of opioids (adjusted HR = 0.86)</p>	<ul style="list-style-type: none"> • <i>"I haven't started very [many] new people [on opioids]. ... That's the real shift. And I notice this in my colleagues, because my colleagues are all 20 years younger than me, and they don't start them nearly as readily as I did say 10 years ago, 15 years ago."</i> GP/NP 7 • <i>"In the last 4 or 5 years [here at Langs], we've worked even harder at getting people off opioids."</i> GP/NP 3 	<p>Patients whose index visit date was in a more recent calendar year were less likely to receive opioids. GPs/NPs at Langs have made a concerted effort in recent years to reduce opioid prescribing.</p>

DC, doctor of chiropractic; GP/NP, general physician/nurse practitioner; HR, hazard ratio.

^a Defined as receipt of chiropractic services within 30 days of the patient's index visit.

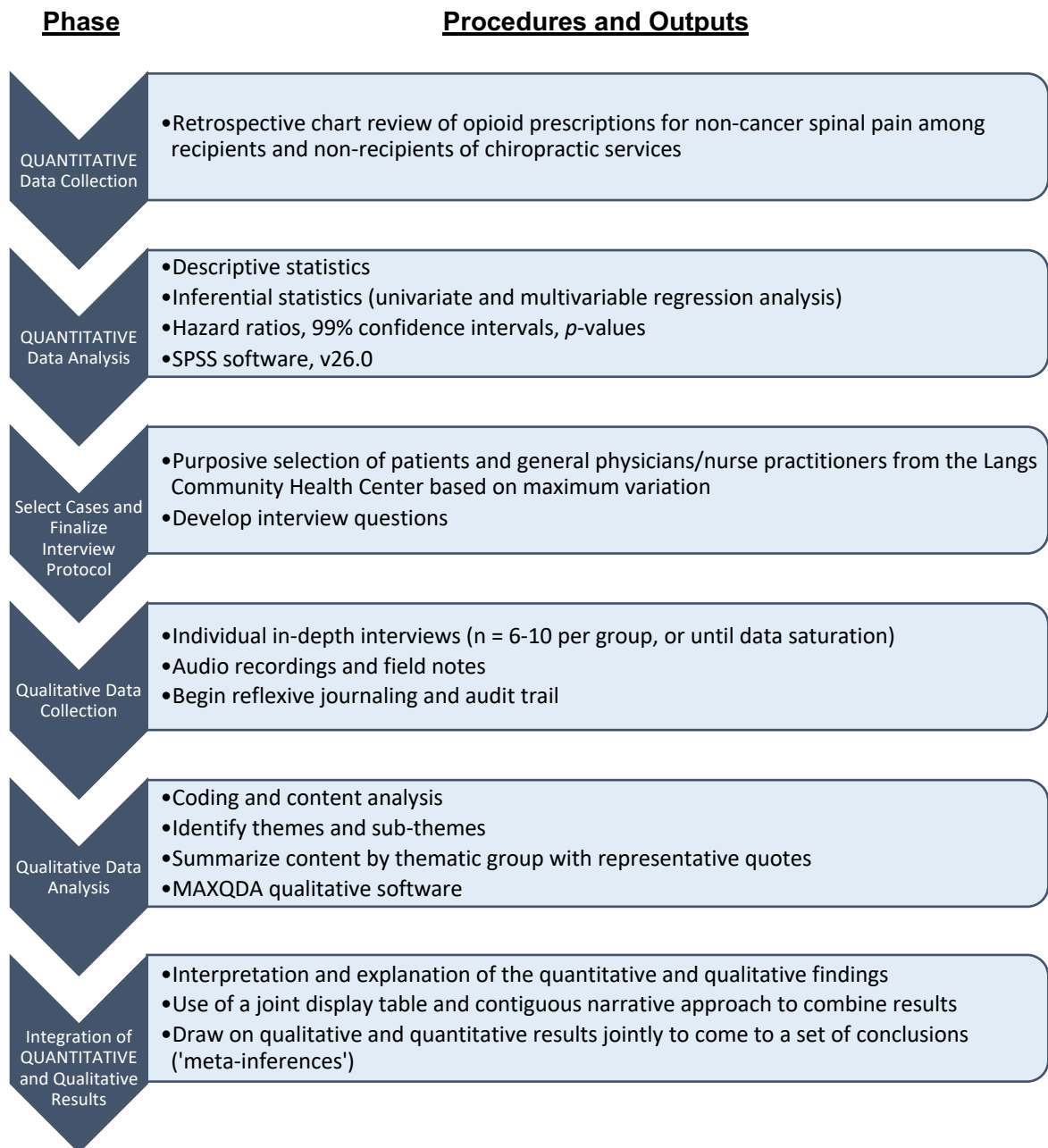


Fig 1. Study diagram of an explanatory sequential design of a mixed methods study on the association of chiropractic integration with prescription of opioids for non-cancer spinal pain at the Langs Community Health Center. The quantitative and qualitative data collection and analysis phases are shown along the left side of the diagram. The two points of interface (or mixing) of the quantitative and qualitative phases occur in the third and final steps. The term “QUANTITATIVE” is capitalized to indicate prioritization of the quantitative phase in the study. The study procedures and outputs for each phase are listed along the right side of the diagram.

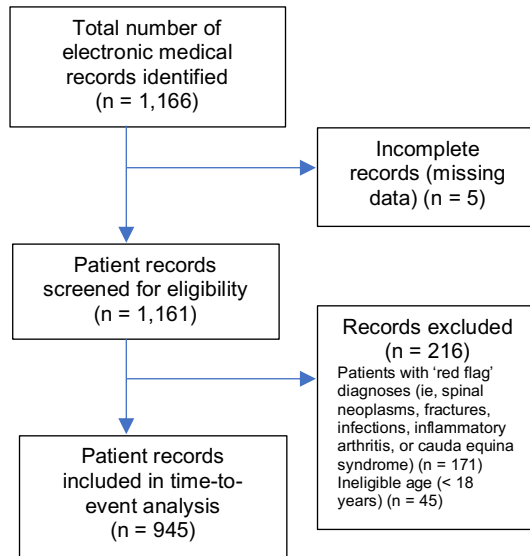


Fig 2. Flowchart of cohort inclusion for the quantitative (time-to-event) analysis.

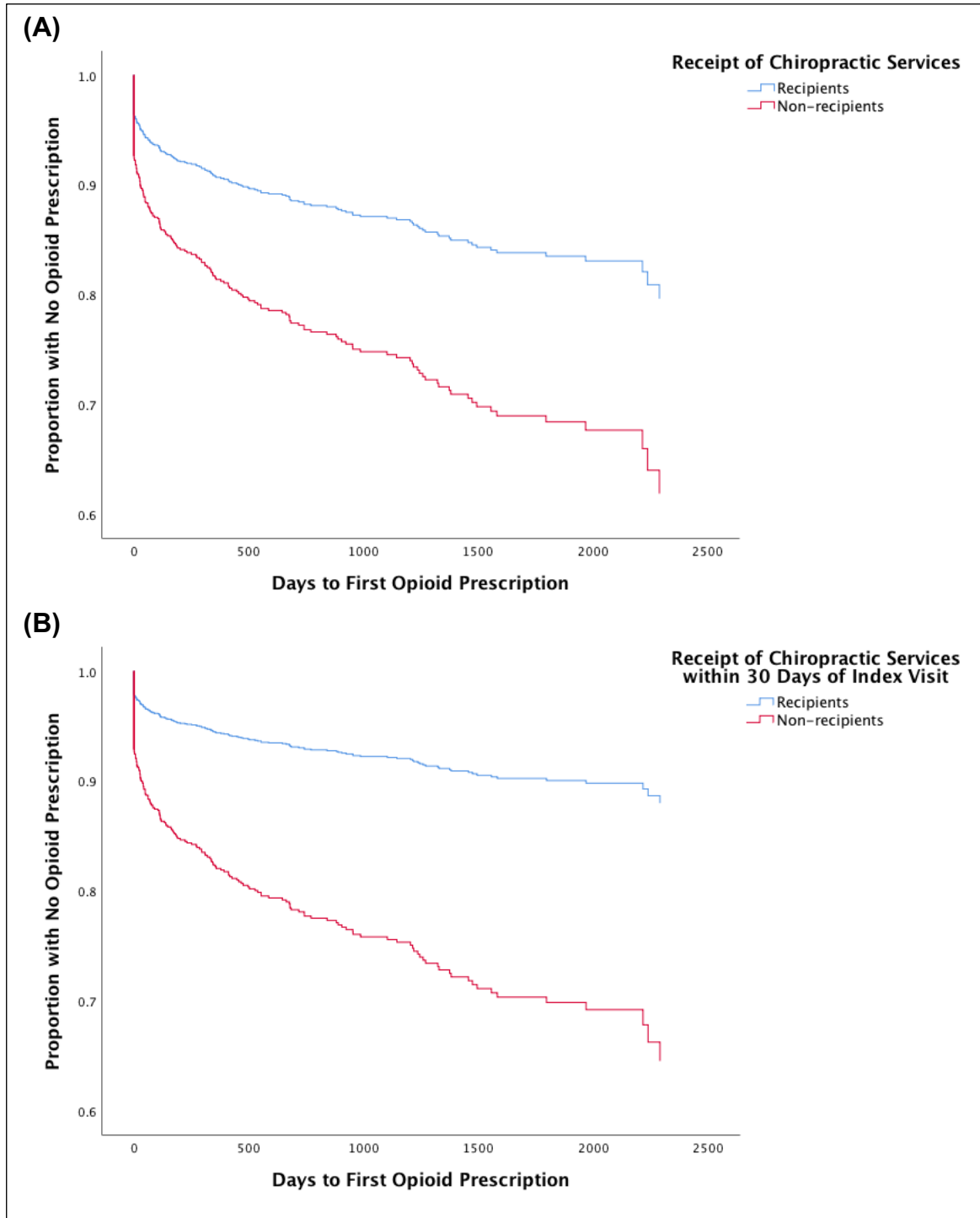


Fig 3. Survival curves of the time to first opioid prescription among recipients and non-recipients of chiropractic services (A), and recipients and non-recipients of chiropractic services within the first 30 days after an index visit for a non-cancer spinal pain diagnosis (B).

Supplementary Files

Supplementary File 1: Good Reporting of A Mixed Methods Study (GRAMMS) checklist

Supplementary File 2: Interview guide (general physicians/nurse practitioners)

Supplementary File 3: Interview guide (patients)

Supplementary File 4: Investigator reflexivity

Supplementary File 5: Survival curve for time to first opioid prescription (entire cohort)

Supplementary File 6: Comparison of recipients versus non-recipients of chiropractic services

Supplementary File 7: Cox regression of early receipt of chiropractic services (i.e., within 30 days of the index visit)

Supplementary File 8: Qualitative themes generated from semi-structured interviews

Supplementary File 1. *Checklist of items for the Good Reporting of A Mixed Methods Study (GRAMMS) guidelines.*^{30,31}

Mixed methods reporting	
GRAMMS guidelines	Location in manuscript where items are reported
1) Describes the justification for using a mixed methods approach to the research question	Methods, Study Design (pp. 124-125)
2) Describes the design in terms of the purpose, priority and sequence of methods	Methods, Study Design (p. 124-125), Figure 1 (p. 158)
3) Describes each method in terms of sampling, data collection and analysis	Methods (pp. 125-131), Figure 1 (p. 158)
4) Describes the integration of the quantitative and qualitative components	Methods (pp. 129, 131), Results (p. 137), Table 4 (pp. 156-157), Figure 1 (p. 158)
5) Describes any limitation of one method associated with the presence of the other method	Discussion, Limitations and Future Studies (p. 141)
6) Describes any insights gained from mixing or integrating methods	Discussion (pp. 138-139), Table 4 (pp. 156-157)

GRAMMS, Good Reporting of A Mixed Methods Study.

Supplementary File 2. *Interview guide for general physicians/nurse practitioners.*

Welcome:

Introductions and project overview

Before we begin, I would like to review a few items from our consent form:

- Your participation in this project is voluntary and you are free to withdraw from the study (stop the interview completely) at any time.
- Our interview will last approximately one hour.
- You do not need to answer questions that you do not want to answer or that make you feel uncomfortable.
- All of your answers are private and confidential.
- I will be recording our interview to ensure that I accurately capture your statements.
- You will receive a copy of your interview transcript and a summary of the results to confirm I have accurately represented our interview (member-checking).

Introduction:

Chiropractic services were integrated at the Langs Community Health Centre (CHC) on January 1, 2014. I would like to ask you some questions about your experience with the chiropractic services at Langs, as well as how you feel these services have affected opioid use among patients at the CHC. I will also ask you for some basic demographic information, such as your age and education. Because the chiropractic program has been put on “pause” during the COVID-19 pandemic, I'd also like to ask you about whether you feel the pandemic, including the reduced access to chiropractic services at Langs, has had any impact on patients' use of opioids.

Are you ready to begin?

1. In what year were you born?
2. How many years have you been in practice?
3. What is your highest level of education (MD [medical doctor] or NP [nurse practitioner] / other [eg, MSc or PhD])?
4. Chronic non-cancer pain (CNCP) is any painful condition that persists for at least three months and is not associated with malignant disease. Do you see a lot of patients with CNCP in your practice at Langs?

Probe: For these types of patients, what treatment(s) do you offer or recommend to them?

Probe: What types of medications do you prescribe for pain management?

Probe: For those who have been prescribed opioids, do you feel it would be desirable to have some of these patients reduce their use of opioids?

- a) If **not**, why not?
- b) If **yes**, have you attempted to engage any of your patients with CNCP in tapering their dose? Or vice versa, have any of these patients asked you about reducing their opioid prescriptions and/or dose?
- c) To the best of your knowledge, has there been any opioid-reducing strategy(ies) implemented at Langs to reduce opioid prescribing (eg, a task force to reduce opioid use, regional dashboards, tracked performance metrics related to high dose prescribing, chart audits, introduction of 2017 CMAJ [Canadian Medical Association Journal] guidelines, etc.)?

5. Chiropractic services have been integrated at Langs since January 1, 2014. Have you ever referred patients for these services?
 - a) If **not**, why not? **(Then skip to question #7.)**
 - b) If **yes**, why did you refer patients for these services (e.g., did patients request to be referred for chiropractic treatment, or did you refer them because they were not responding to medical care)?

Probe: Tell me about your experience with the chiropractic program at Langs?

Probe: Have any of your patients found these services helpful? If so, why do you think they have found these services helpful?

Probe: Can you give me any examples of where your patients have *not* found chiropractic treatment to be helpful?
6. Have you ever referred patients for chiropractic care at Langs as part of a formal effort to taper opioids?

Probe: Whether you have or not, what do you think about accessing chiropractic care as part of a strategy to help patients reduce opioid use?

Probe: Was there ever a time where you decided to reduce an opioid dose in a patient you referred for chiropractic services based on the perception that their pain was better managed and thus less opioids were required?

Probe: Do you have any examples of where you referred a patient for chiropractic services but their opioid use stayed the same or increased? If **yes**, can you elaborate on why think this was the case?
7. For this research project, we have been analyzing data on patients with CNCP who were prescribed opioid medication(s) *prior* to being referred for chiropractic treatment. Do you think that patients would be less likely to receive a prescription for opioids if they were referred for chiropractic services *first*? If so why, or if not, why not?

Probe: Can you elaborate, or give me any specific examples?
8. The chiropractic program at Langs has been on hold during the COVID-19 pandemic. How do you feel this has affected opioid use, if at all, among your patients?

Probe: Has this limited the pain management options that you can recommend to your patients?

Probe: Has the pandemic, and lack of access to chiropractic services at Langs, had any impact on the number or dose of opioid medications that you have been prescribing to your patients for pain management?
9. Thank you so much for your time. Do you have any questions, or is there anything else that you would like to share with me on this topic?

Field Notes & Emergent Themes:

Supplementary File 3. *Interview guide for patients.*

Welcome:

Introductions and project overview

Before we begin, I would like to review a few items from our consent form:

- Your participation in this project is voluntary and you are free to withdraw from the study (stop the interview completely) at any time.
- Our interview will last about an hour.
- You do not need to answer questions that you do not want to answer or that make you feel uncomfortable.
- All of your answers are private and confidential.
- I will be recording our interview so that all of your ideas are captured.
- You will receive a copy of your interview transcript and a brief summary of the results.

Introduction:

Chiropractic services have been available to patients at the Langs Community Health Centre (CHC) since January 1, 2014. I would like to ask you some questions about your experience with the chiropractic services at Langs, as well as whether you feel these services have affected your use of opioids for pain management. I will also ask you for some basic information like your age and formal education. Because the chiropractic program has been put on “pause” during the COVID-19 pandemic, I’d also like to ask you about whether you feel the pandemic, including the reduced access to chiropractic services, has had any additional effect on you with respect to your opioid use.

Are you ready to begin?

1. What year were you born in?
2. How many years have you been a patient at Langs?
3. What is your highest level of education (elementary / high school / college or university / graduate level)?
4. Are you currently working? If so, are you working part- or full-time? If you are *not* working, are you receiving disability benefits / are you retired?
5. Do you currently experience back or neck pain? If **yes**, approximately how long have you had this pain?
6. Are you currently taking any opioid medications for your pain? If so, what opioid medication(s) are you taking (eg, Tylenol with codeine [Tylenol #3], Percocet or OxyContin [oxycocet, oxycodone], Dilaudid [hydromorphone], Methadose [methadone], Stalex or MS Contin [morphine], Tramacet or Ralivia [tramadol], Suboxone [buprenorphine or naloxone], Duragesic [fentanyl patch, or oral fentanyl]) and what is the current dose?
Probe: Has this dose increased, decreased, or stayed the same since you were first prescribed opioids by your general practitioner (GP)?
7. What other types of treatment or activities do you engage in to help manage your pain?
8. Chiropractic services have been offered at Langs since January 1, 2014. Have you ever been referred by your GP for these services? (If “No,” skip to question #11.) If **yes**, tell me about your experience with the chiropractic program at Langs?
Probe: Have you found these services helpful? If so, why have you found these services helpful, or if not, why not?

- Probe: Had you ever been to a chiropractor before using the chiropractic services here at Langs? If **yes**, do you think this made you more open to being referred by your GP for chiropractic treatment at Langs?
9. Do you feel that the chiropractic services at Langs have had any effect on your opioid use? If so, why do you feel this way, or if not, why not?
Probe: Do you feel you are better able to manage your pain with access to these services?
Probe: Had your GP ever talked to you about reducing your opioid prescriptions and/or doses *before* you were referred for chiropractic treatment? If so, did you agree to work with your GP to reduce your opioid use?
10. The chiropractic program at Langs has been on hold during the COVID-19 pandemic. Has this affected your use of opioids at all? Why or why not?
Probe: If **yes**, how has it affected your use of opioids? Why do you think this is the case, or if not, why not?
Probe: Can you elaborate, or give me any specific examples?
11. **(Skip this question for those who answered “Yes” to question #7.)** If your GP has *never* referred you for chiropractic services at Langs, do you think this type of program would help you with managing your pain and possibly reduce your use of opioids?
Probe: Can you elaborate, or give me any specific examples?
Probe: Have you had any previous experience with chiropractic treatment outside of Langs?
12. Do you think that patients, such as yourself, would benefit from access to pain management services such as chiropractic treatment *before* being prescribed opioids?
Probe: Can you elaborate on why you feel this way, or can you give me any specific examples to help me understand?
13. What advice would you give to another patient who might be considering an opioid prescription to manage their pain?
14. Thank you so much for your time. Do you have any questions, or is there anything else that you would like to share with me?

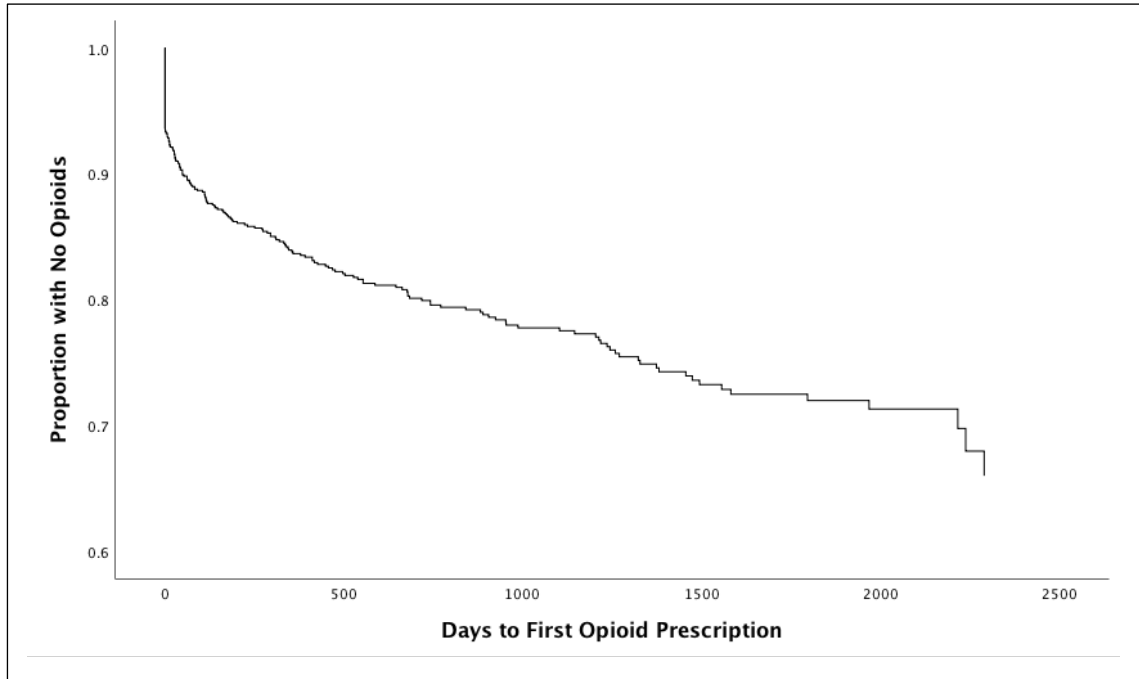
Field Notes & Emergent Themes:

Supplementary File 4. *Reporting of investigator reflexivity for the qualitative phase of our study.*

Research Team and Reflexivity^a	Description
<i>Personal Characteristics</i>	
Interviewer	All interviews were conducted by the lead author (PCE).
Credentials	At the time of the interviews, PCE was a Doctor of Philosophy (PhD) candidate in Health Research Methodology at McMaster University. He also has a Master of Science (MSc) in clinical sciences from Bournemouth University.
Occupation	The interviews were coded by two investigators (PCE, ALB). Both are practicing Doctors of Chiropractic. PCE is also an adjunct faculty member in the Chiropractic Department at D'Youville University.
Gender	PCE identifies as male and ALB identifies as female.
Experience and training	PCE has graduate-level training in health research methodology with expertise in qualitative and mixed methods research. PCE and ALB each have over 19 years of clinical and research experience.
<i>Relationship with Participants</i>	
Relationship established	PCE worked as a clinician in the chiropractic program at the Langs CHC from January 2014 to January 2016, and therefore had an established relationship with many of the GPs/NPs (6 of 9) and a few of the chiropractic patients (2 of 8) who were interviewed for this study. These established relationships seemed to facilitate trust and candid conversations during the audio-recorded interviews, particularly with the GPs/NPs. PCE did not have a prior relationship with any of the non-chiropractic patients in this study; however, early rapport was developed and established during participant recruitment telephone calls and during introductions and conversation at the start of each interview.
Participant knowledge of the interviewer	Participants were sent a form containing information about the study's aims and objectives, the lead author, and his contact details, at least 1 week in advance of each interview. Participants were also made aware that the project was being undertaken by PCE as part of a PhD thesis.
Interviewer characteristics	Both investigators (PCE, ALB) were interested in the research topic because they had prior experience (PCE – 2 years, ALB – 6 years) working as clinicians in the Langs chiropractic program. This was acknowledged as a potential source for bias in the analysis and interpretation of the data. PCE and ALB each aimed to decrease their own bias throughout the analysis by regularly reflecting on their coding decisions in relation to the study's aim, and reviewing and recording these reflections at the beginning of each of their peer debriefing meetings. Because of his clinical background as a chiropractor, PCE also practiced reflexivity during the course of conducting each interview by maintaining an awareness of how this professional background could bias his assumptions and communication with participants. Accordingly, he made a conscious effort not to stray from the interview guides or ask participants leading questions.

^a Adapted from the Consolidated Criteria for Reporting Qualitative Research (COREQ): <https://academic.oup.com/intqhc/article/19/6/349/1791966>

Supplementary File 5. *Survival curve of the time to first opioid prescription among patients (n = 945) who presented with a non-cancer spinal pain diagnosis at the Langs Community Health Center between January 1, 2014 and December 31, 2020.*



Supplementary File 6. *Baseline comparisons of recipients versus non-recipients of chiropractic services who presented at the Langs Community Health Center with non-cancer back or neck pain between January 1, 2014 and December 31, 2020.*

Variable ^a	Overall		P-value ^b	Within 30 Days of Index Visit		P-value ^b
	Recipients (n = 183)	Non-recipients (n = 762)		Recipients (n = 87)	Non-recipients (n = 858)	
Age in years, mean (SD)	54.2 (17.2)	52.0 (17.0)	.119	52.7 (16.6)	52.4 (17.1)	.872
Sex			.025 ^c			.230
• Male	67 (36.6)	349 (45.8)		33 (37.9)	383 (44.6)	
• Female	116 (63.4)	413 (54.2)		54 (62.1)	475 (55.4)	
General health						
• Smoker	48 (26.2)	198 (26.0)	.946	20 (23.0)	226 (26.3)	.497
• Obese ^d	22 (12.0)	79 (10.4)	.515	13 (14.9)	88 (10.3)	.178
Co-morbidities						
• Depression	100 (54.6)	320 (42.0)	.002 ^c	43 (49.4)	377 (43.9)	.326
• Anxiety	81 (44.3)	315 (41.3)	.472	39 (44.8)	357 (41.6)	.562
• Fibromyalgia	16 (8.7)	41 (5.4)	.086	6 (6.9)	51 (5.9)	.722
• Diabetes	47 (25.7)	137 (18.0)	.018 ^c	18 (20.7)	166 (19.3)	.763
• Cardiovascular disease	101 (55.2)	381 (50.0)	.207	44 (50.6)	438 (51.0)	.933
Year of index visit			< .001 ^c			< .001 ^c
• 2014	74 (40.4)	225 (29.5)		20 (23.0)	279 (32.5)	
• 2015	41 (22.4)	124 (16.3)		27 (31.0)	138 (16.1)	
• 2016	27 (14.8)	111 (14.6)		13 (14.9)	125 (14.6)	
• 2017	24 (13.1)	93 (12.2)		15 (17.2)	102 (11.9)	
• 2018	13 (7.1)	58 (7.6)		9 (10.3)	62 (7.2)	
• 2019	3 (1.6)	83 (10.9)		3 (3.4)	83 (9.7)	
• 2020	1 (0.5)	68 (8.9)		0 (0.0)	69 (8.0)	

SD, standard deviation.

^a Values are expressed as the number (%) unless otherwise noted.

^b Comparisons between continuous and categorical variables were measured using the independent *t*- and chi-square tests, respectively.

^c Statistically significant (2-sided) at an alpha level of 5%.

^d Patients with a body mass index of ≥ 30 kg/m² were classified as obese.

Supplementary File 7. Unadjusted and adjusted hazard ratios for the risk of opioid prescription among patients who received ($n = 87$) and did not receive ($n = 858$) chiropractic services within 30 days of their index visit for a non-cancer back or neck pain diagnosis.^a

Variable	Univariate	P-value	Multivariable	P-value
	Unadjusted HR (99% CI)		Adjusted HR (99% CI)	
Chiropractic care within 30 days of index visit				
• Non-exposed	Reference		Reference	
• Exposed	0.46 (0.21-1.02)	.012	0.29 (0.13-0.68)	< .001
Time (calendar year) ^b	0.81 (0.72-0.91)	< .001	0.88 (0.78-0.99)	.005
Frequency of healthcare visits ^c	1.02 (1.02-1.03)	< .001	1.02 (1.01-1.03)	< .001
Age	1.02 (1.01-1.03)	< .001	1.02 (1.01-1.04)	< .001
Sex				
• Female	Reference		Reference	
• Male	0.98 (0.70-1.39)	.904	1.11 (0.78-1.60)	.445
Smoking status				
• Non-smoker	Reference		Reference	
• Smoker	1.70 (1.19-2.43)	< .001	1.55 (1.07-2.25)	.002
Obesity				
• Non-obese	Reference		Reference	
• Obese	1.19 (0.72-1.96)	.369	1.00 (0.58-1.71)	.986
Depression				
• Absent	Reference		Reference	
• Present	1.58 (1.12-2.24)	.001	1.67 (1.13-2.47)	.001
Anxiety				
• Absent	Reference		Reference	
• Present	1.02 (0.72-1.44)	.886	0.81 (0.55-1.20)	.162
Fibromyalgia				
• Absent	Reference		Reference	
• Present	1.74 (0.99-3.07)	.012	1.15 (0.61-2.18)	.580
Diabetes				
• Absent	Reference		Reference	
• Present	1.44 (0.98-2.12)	.014	0.98 (0.63-1.51)	.889
Cardiovascular disease				
• Absent	Reference		Reference	
• Present	1.43 (1.00-2.03)	.009	0.82 (0.53-1.26)	.236

CHC, community health center; CI, confidence interval; GP/NP, general physician/nurse practitioner; HR, hazard ratio.

^a HR > 1 indicates shorter time to first opioid prescription.

^b Calendar year was measured at the patient's index visit date to the CHC for a non-cancer spine pain diagnosis.

^c Healthcare visits constitute GP/NP and chiropractic visits.

Supplementary File 8. *Qualitative themes generated from semi-structured interviews with patients (n = 14) and GPs/NPs (n = 9) at the Langs Community Health Center regarding perceptions of chiropractic integration and its impact on opioid prescribing.*

Figure 1. Theme ^a: Patient self-efficacy (n = 23). Patients and GPs/NPs described active and passive pain management strategies and behaviors, including a resistance among some patients toward taking medication.

<p><u>Active versus passive approaches ^b</u></p> <ul style="list-style-type: none">● “I’m continuously doing stretches, exercises, to keep myself okay.” DC Patient 2● “I try exercising, but it just makes it worse.” DC Patient 7● “It’s really hard to engage some of these folks in self-care with their chronic pain. You know? It’s just like – give me medication.” GP/NP 1● “A lot of our folks don’t feel very empowered, or don’t feel like they have much agency in their lives, which is true. ... With chronic back [pain], ... probably the greatest utility [of an active approach] is having them understand that some of this is within their control to influence.” GP/NP 7● “[For a patient who might be considering an opioid prescription to manage their pain], I would just say to start trying to feel some of your pain again so that you can learn how to manage it in a different way. You know? Instead of just, like, burying all the pain.” Non-DC Patient 5● “When [patients] come in believing that you can find the right thing that will fix their pain, and – opioid medication is one component of that belief system – I think that the more we engage in that from the get-go, the less successful we’re going to be at changing that mindset. ... Passive therapies such as opioids, or even chiropractic manipulation or massage [by themselves], are not necessarily bad; but if [passive therapy] is our starting point – and again, this is just what I’ve experienced – [I feel] it is harder to engage patients in active options later.” GP/NP 4 <p><u>Resistance to taking medication</u></p> <ul style="list-style-type: none">● “...most patients don’t want to be on a bunch of pills. They don’t want to be dependent on medication to feel better.” GP/NP 9● “I’ve been dealing with this pain for 10 years, and I’m not just a pill popping, believing [person]. [I’m] old school, take the pain until it’s really extreme and then – oh gee, I better take an Advil – is kinda how I deal with my pain.” DC Patient 1● “Most people don’t want to take pills from my perspective – for a multitude of reasons. They prefer to have all the options for treatment, and that includes non-pharm[acological] solutions.” GP/NP 2 <p><i>Legend:</i> DC, doctor of chiropractic; GP/NP, general physician/nurse practitioner. ^a Bolded phrases are for thematic emphasis. ^b Examples of active versus passive approaches include, but are not limited to, exercise, goal-setting, or education (active) versus injections, analgesics, or massage/manipulation (passive).</p>

Figure 2. Theme ^a: Accessibility of non-pharmacological services (n = 21). Lack of access to non-pharmacological services was identified as a common facilitator of opioid use.

<p><u>Lack of access</u></p> <ul style="list-style-type: none">● <i>“Most of our patients don’t have any additional coverage for extended health, like, physio, chiro, all of those things. So, unfortunately, even though those are first-line modalities for treating a lot of pain, patients can’t access it unless we have programs for it.” GP/NP 8</i>● <i>“It’s hard when you have nothing to give them. I think that’s why, in part, what’s driven opioid over-prescribing is because we have nothing else to give these people. ... I think having access to any kind of additional modalities in a timely and efficient manner for all patients would probably reduce the need for opioids in the first place.” GP/NP 9</i>● <i>“The government needs to step up and help out.” DC Patient 3</i>● <i>“It’s that scenario where you have nothing else to offer, right? So, if you’re trying to postpone heading into ‘opioid land’ and you still have something else to offer, it can definitely make a difference. ... You probably go to meds sooner than you might otherwise because you don’t have access to the intervention you’d really like.” GP/NP 7</i>● <i>“When I was about 23 [years old], financially I wasn’t able to go [to my chiropractor] anymore. So, that’s when [my doctor] put me on the OxyContin and the Perc’s.” DC Patient 7</i>● <i>“We’re told there’s a triangle of care, you know, the psychosocial, and the physical modalities, and meds, [which] are only a small part of it. But the only thing you have access to is the meds. ... It’s just ironic. The people who need [non-pharmacological] services the least, have the best access. ... But the people who are most vulnerable to [chronic pain] are the people that have the least access.” GP/NP 9</i> <p><u>Access to chiropractic at Langs</u></p> <ul style="list-style-type: none">● <i>“The [chiropractic] program at Langs was helpful in that, it allowed more access to people that didn’t have it otherwise.” GP/NP 9</i>● <i>“The evidence says you guys are as good at clearing up back pain as we are. So, we need to work together at that, and it’s helpful to have [access to chiropractic services for our patients].” GP/NP 3</i>● <i>“The folks we take care of, 95% of them couldn’t afford chiropractic on their own, or don’t have [a] benefit plan. There’s a small portion who do, but most of them don’t. So, being able to, right from the outset, present this package of care, I think [is] incredibly helpful.” GP/NP 7</i>● <i>“I’m missing the chiropractor services [since they were discontinued because of the COVID-19 pandemic]. I wish it could come back again, because I’m having pain.” DC Patient 2</i> <p>Legend: DC, doctor of chiropractic; GP/NP, general physician/nurse practitioner. ^a Bolded phrases are for thematic emphasis.</p>
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Figure 3. Theme ^a: Stigma regarding use of prescription opioids (n = 20). A negative stigma around opioids was identified by patients and GPs/NPs as a barrier to opioid use. However, patients who found benefit in using opioids often felt a sense of judgment, as well as a need to advocate for themselves to obtain an opioid prescription.

Stigma

- *“I think in our current society with news about addiction and our history of OxyContin over-prescribing, we probably have fewer people asking for opioids.”* GP/NP 3
- *“Sometimes we have people we can’t even talk into considering an opioid because they’ve taken what they’ve heard in the media so significantly they don’t want anything to do with that.”* GP/NP 7
- *“Unfortunately, patients experience a great deal of stigma, and so some of them don’t like that. And then they want to come off of their pills.”* GP/NP 9
- *“I take ... the Tylenol #3, [but] it’s no good, it’s [like] cocaine.”* DC Patient 4
- *“It’s been frustrating – so frustrating. Because the [opioid] crisis seemed to just fall right on me. Like, as though I’m part of the crisis. So, [as a result] every doctor doesn’t want you on any kind of pain medication. They don’t believe your pain. You know what I mean? It has really affected me. ... I’m not an addict in any way. I never even ever think twice about taking that medication more than once, like, unprescribed. But I was definitely treated like I was [an addict].”* Non-DC Patient 5

Legend:

DC, doctor of chiropractic; GP/NP, general physician/nurse practitioner.

^a Bolded phrases are for thematic emphasis.

Figure 4. Theme ^a: Impact of treatment (n = 19). Patients and GPs/NPs described their impressions of treatment directed at managing chronic pain.

<p><u>Pain relief</u></p> <ul style="list-style-type: none">● “[For] my neck, sometimes, if I didn’t go [to the chiropractor], I would really notice it in a couple months if I didn’t go every, at least every 2 months, if not every month.” DC Patient 8● “When you have a nerve condition, especially like mine where the nerves are hypersensitive and will shoot off through your entire body like electricity, sometimes with, you know, airflow. ... It’s literally, like, I’ve been outside and a strong wind has gone across my legs and it makes my, it just makes my heart start pounding so much because it hurts that much and I’m like – are you freaking kidding me? And in that situation, it’s just like – no, I think I actually need something very, very strong to calm these nerves down or to numb my body or these nerves.” Non-DC Patient 1● “I feel like it’s more a push from the patient to do something about [their] pain and to help [them]. ... Because ultimately, you’re trying to alleviate their suffering. That’s why they come. And, you’re trying to respond to that.” GP/NP 9 <p><u>Functionality</u></p> <ul style="list-style-type: none">● “I know that I would not be able to function without having some relief [from opioids].” Non-DC Patient 4● “I do actually have patients on opioids that are actually working and it’s because they’re on opioids, ... that they continue to work full-time. And so, they’re not the ones that I worry about so much because they clearly have functionality, and they don’t show any behavioral stuff.” GP/NP 9 <p><u>Fear or anxiety of withdrawal:</u></p> <ul style="list-style-type: none">● “...terrifying. ... Not being able to have [my] prescription filled is very frightening – and panic. You start having anxiety.” Non-DC Patient 4● “I think sometimes with the patients on opioids there’s a lot of fear and anxiety about the dosing and the reduction of the dose because it’s unpleasant. And because they’re afraid about their pain and stuff like that.” GP/NP 1● “I have to be honest, people are so anxious when you’re talking about decreasing their opioids, they don’t hear much else.” GP/NP 7 <p><u>Legend:</u> DC, doctor of chiropractic; GP/NP, general physician/nurse practitioner. ^a Bolded phrases are for thematic emphasis.</p>
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Chapter 7:

The association between chiropractic integration in an Ontario community health centre and continued prescription opioid use for chronic non-cancer pain: a sequential explanatory mixed methods study

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The association between chiropractic integration in an Ontario community health centre and continued prescription opioid use for chronic non-cancer pain: a sequential explanatory mixed methods study

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Abstract

Background: Emerging evidence suggests that access to chiropractic care may reduce the likelihood of initiating an opioid prescription for chronic pain; however, the impact of chiropractic care for patients already prescribed opioids is uncertain. We undertook a sequential explanatory mixed methods study to evaluate the association between initiating chiropractic care and continued opioid use among adult patients attending an Ontario community health centre and receiving opioid therapy for chronic pain.

Methods: We conducted a retrospective cohort study of 210 patient records between January 1, 2014 and December 31, 2020, and completed interviews with 14 patients and nine general practitioners. We used generalized estimating equations, adjusted for patient demographics, co-morbidities, visit frequency, and calendar year, to evaluate the association between receipt versus non-receipt of chiropractic services and continued opioid use (i.e., unique opioid fills, number of refills, and dosages) up to one year following the index chiropractic visit. Qualitative data were coded and analyzed using content and thematic analysis and integrated with our quantitative findings.

Results: Over 12-month follow-up, there were lower rates of opioid fills (IRR = 0.66; 95% CI, 0.52-0.83) and refills (IRR = 0.27; 95% CI, 0.17-0.42) among chiropractic recipients versus non-recipients. Although patients who did and did not receive chiropractic care began the study with the same dose of opioids, recipients were less likely to be prescribed higher-dose opioids (i.e., ≥ 50 mg morphine equivalents daily) compared to non-recipients at three months (OR = 0.14; 95% CI, 0.04-0.47), six months (OR = 0.14; 95% CI, 0.05-0.40), nine months (OR = 0.19; 95% CI, 0.07-0.57), and 12

months (OR = 0.22; 95% CI, 0.08-0.62). Interviews suggested that patient self-efficacy, limited effectiveness of opioids for chronic pain, stigma regarding use of opioids, and access to chiropractic treatment were important influencing factors.

Conclusion: We found that continued prescription opioid use among patients with chronic spine pain who received chiropractic care was lower than in patients who did not receive chiropractic care. Four themes emerged in our qualitative interviews to help provide a richer understanding of this association. A multi-stage, mixed methods randomized controlled trial is needed to confirm our findings.

Keywords: Health Services Research, Opioids, Community Health Centres, Mixed Methods, Chiropractic

Background

Chronic pain is a prevalent and global health problem associated with considerable socioeconomic burden. Worldwide, approximately one in five people live with chronic pain [1-4], with seniors, women, military veterans, indigenous populations, rural inhabitants, those with lower formal education, and individuals reporting low socioeconomic status being most affected [5-7]. In Canada, the annual economic cost of chronic pain due to medical expenditures and lost productivity was estimated between \$38 and \$40 billion in 2019, and this cost is expected to rise by more than 36% by the year 2030 [8]. The annual cost of chronic pain in the United States (US) was previously estimated to be between \$560 and \$635 billion [9]. Opioids are commonly prescribed to patients to relieve chronic pain, particularly in North America [10]; however, opioids provide only modest benefits [11] and are associated with important dose-dependent harms, including overdose and death [12-15]. Accordingly, governments, policy makers, and insurers have been called upon to improve support for non-opioid approaches to managing chronic pain, particularly in vulnerable and marginalized populations [16].

Emerging evidence suggests that early access to chiropractic treatment is associated with lower initiation of opioid prescribing among patients with spinal pain [17-21]. A 2020 systematic review and meta-analysis of six cohort studies found that patients with acute or chronic non-cancer back or neck pain who received chiropractic services early in their complaint were 64% less likely than non-chiropractic users to be prescribed opioids (pooled odds ratio [OR] = 0.36; 95% confidence interval [CI], 0.30 to 0.43) [17]. A subsequent observational study of 216,504 opioid-naive patients with new-onset low

back pain who received initial treatment from chiropractors versus primary care physicians had 90% lower odds of short-term opioid use (adjusted OR = 0.10; 95% CI, 0.09 to 0.10) and 78% lower odds of long-term opioid use (adjusted OR = 0.22; 95% CI, 0.18 to 0.26) [18,19]. Similar findings have been reported by two other recent observational studies [20,21]; however, the association between receipt of chiropractic services and continued opioid use in patients with existing opioid prescriptions is uncertain [22-24].

To help address this knowledge gap, we conducted a mixed methods health service evaluation of a chiropractic spine pain program integrated with standard physician care at the Langs Community Health Centre (CHC) [25] in Ontario, Canada. This Centre provides services to communities and vulnerable populations with high unemployment rates, multiple co-morbidities, and musculoskeletal disorders that are commonly managed with prescription opioids [23-32]. Since chiropractic services are not publicly funded in Canada, these populations have traditionally faced barriers to accessing chiropractic care [23,26-31]. We used complementarity [33] as our rationale for using a mixed methods approach, that is, the results from the qualitative phase of our study were used to help clarify and explain our quantitative findings.

Methods

We followed the Good Reporting of A Mixed Methods Study (GRAMMS) guidelines [34,35] for our study (Additional file 1).

Study design

We used a sequential explanatory mixed methods design [36]. In the quantitative phase, we obtained data via chart review [37] of electronic medical records (EMRs) of both recipients and non-recipients of chiropractic services with at least one prescribed opioid for the treatment of a chronic non-cancer pain-related diagnosis at the Langs CHC. We used generalized estimating equations (GEEs) to examine whether the receipt of chiropractic services was associated with the number or dose of opioid prescriptions. In the qualitative phase, we conducted one-on-one interviews with patients and general practitioners (GPs) to explore perceptions of chiropractic integration on opioid prescribing. See Figure 1 for a diagram outlining our study procedures. Our conceptual framework, details of the Langs chiropractic CHC program, and a complete list of diagnostic codes used for defining our study sample are provided in our study protocol [38].

Quantitative sampling

We included records for all adult patients (aged ≥ 18 years) who received one or more prescriptions for opioids dispensed over a minimum period of three consecutive months, and who attended two or more appointments relating to a diagnosis of chronic back or neck pain at the Langs CHC between January 1, 2014, and December 31, 2020. The start date for quantitative sampling was January 1, 2014, which was the inaugural date of the Langs CHC's chiropractic program [29]. Patients receiving treatment for opioid use disorder (e.g., methadone, naloxone) prior to their index visit, as well as those with spinal

neoplasms or other contraindications to chiropractic treatment (i.e., fractures, infections, inflammatory arthritis, or cauda equina syndrome), were excluded from our cohort. As we were interested in patients receiving long-term opioid therapy, we excluded individuals who had been prescribed opioids for < 90 days at their index visit, or who did not receive any opioid fills or refills after their index visit.

We linked EMR records of all patients in our study to medical drug claims data at the Institute for Clinical Evaluative Sciences (ICES) (<https://www.ices.on.ca>) with their Ontario health card number. ICES is an independent, non-profit research institute whose legal status under Ontario's health information privacy law allows for the collection and analysis of healthcare and demographic data, without consent, for health system evaluation and improvement. Patients whose health card number was incorrectly recorded in their EMR were excluded.

Quantitative data collection

Opioid prescription data were obtained from the Narcotics Monitoring System database by an independent research scientist at ICES, including the number of prescribed opioid fills, the number of prescribed opioid refills (measured in 30-day equivalents), and the prescribed opioid dosage. These outcomes were measured for up to 12 months from the date of first opioid prescription following a patient's index visit for chronic non-cancer back or neck pain. To maintain temporality, the index visit for patients who received chiropractic care was their first chiropractic visit. Other variables that were extracted from the EMR included socio-demographics (age and sex), general health (smoking status

and body mass index), co-morbidities (depression, anxiety, fibromyalgia, diabetes, and cardiovascular disease), and the total number of healthcare (i.e., GP or chiropractic) visits. These variables have been shown to be associated with opioid use [22,39-46]. To increase the reliability of data extraction [37], an independent information technology specialist, who was blinded to the research questions, extracted all patient data directly from the Langs EMR database [38].

Quantitative data analysis

Baseline characteristics were compared between the exposed (receipt of chiropractic care) and non-exposed groups using the chi-squared test for categorical variables (or Fisher's exact test if there was a cell frequency of < 5) and the Mann-Whitney U test for skewed continuous variables. We used GEEs to explore the association between exposure to chiropractic care and opioid prescribing [47,48]. To account for potential data clustering within-subjects or between medical or chiropractic practitioners, we used a robust variance estimator to compute the standard errors for our coefficient estimates. We also conducted sensitivity analyses with different working correlation structures, including independent, autoregressive, and unstructured matrices [47,48]. The specified link function in our GEE models was based on the data distribution (e.g., log-linear for data fitting a Poisson distribution, binomial for binary data).

We used GEEs with a Poisson distribution when the outcomes were counts (i.e., total number of unique opioid fills and subsequent refills over the entire course of follow-up, tabulated at the end of follow-up). We estimated incidence rate ratios (IRRs) for

differences between the chiropractic and non-chiropractic groups using Poisson log-linear GEEs and reported the associated 95% CIs and *p*-values.

We used GEEs with a binomial distribution when the outcome was opioid dosage. We assessed opioid dosages at 90-day intervals, dichotomized into higher (≥ 50 mg) morphine equivalents daily (MED) or lower (< 50 mg) MED [11] and compared these between the chiropractic and non-chiropractic groups from baseline to 12-month follow-up. We originally planned to dichotomize opioid dose using a different threshold (≥ 90 mg vs. < 90 mg MED) [38], but we modified our approach to reflect the central tendency of MED in our patient sample. We estimated between-group differences for dosage using a binary logistic GEE and reported these with ORs, 95% CIs, and *p*-values. To calculate the MED for each prescribed opioid, we multiplied the quantity \times the milligrams per unit dispensed \times drug-specific conversion factors (Additional file 2) [11,13].

For each outcome of interest, we built univariable and multivariable models to estimate the crude and adjusted associations, respectively, between patients that did or did not receive chiropractic care (1 = received; 0 = did not receive) and opioid use. We grouped covariates into blocks (i.e., socio-demographic, health-related, depressive symptoms, health behaviours, and healthcare visits) and these were sequentially entered into our models, with time (i.e., calendar year) as an additional covariate and chiropractic/non-chiropractic care as the main exposure variable. Based on previous literature [13,22,39-46], we hypothesized that younger age, male sex, health-related comorbidities, depressive symptoms, poor health behaviours (e.g., smoking), a higher frequency of healthcare provider visits, and earlier years of our 7-year study timeframe

would be positively associated with opioid use. We also hypothesized that chiropractic care would be inversely associated with opioid use.

To guard against over-fitting of our regression models [49], we set a minimum threshold of 10 events per category for each independent variable (i.e., minimum sample of 150 patient records) to ensure that each variable had sufficient discriminant power to detect an association with opioid use, if an association existed. We assessed model fit using the quasi-likelihood under the independence model criterion (QIC) [48,50].

Correlation structures with the lowest QIC scores (closest to zero) were judged as the best model fit for the data. We also explored variance inflation factors (VIFs) to assess collinearity between independent variables. If multicollinearity was detected between two or more variables (i.e., $VIFs \geq 5$) [51], we compared regression models, each separately containing one of the collinear variables, to one another and selected the model containing the variable that produced the lowest Akaike information criterion (AIC) value. The two-sided statistical significance level (α) for all quantitative analyses was 5%, and all data and comparative analyses were performed using SPSS v28.0.1.0 (IBM SPSS Statistics).

Qualitative sampling

For the qualitative phase of our study, we used stratified purposive sampling to select a subsample of chiropractic and non-chiropractic patients, whose charts we examined in the quantitative phase, to participate in one-on-one interviews [52]. This was the first stage of integration between our quantitative and qualitative study phases [53]. We also

recruited a purposive sample of GPs from the Langs CHC. The lead author (PCE) conducted recruitment via telephone or e-mail using participant contact information provided by the Langs CHC administration. We offered gift cards (\$10 for GPs, \$30 for patients) as incentives for participation. We used maximum variation [52] in choosing participants, based on age, sex, and the number of years attending the CHC (for patients) or years in practice (for GPs), to encourage a range of sociodemographic characteristics and perspectives. We also collected patients' primary pain complaint and current opioid dose. We aimed to interview a minimum of 12-20 patients and 6-10 GPs [52], with interviews continuing until saturation; the point at which no new information was obtained from participants in the GP, chiropractic, and non-chiropractic groups [54]. We used fundamental qualitative description [54,55] as our methodological orientation to underpin the qualitative phase of our study.

Qualitative data collection

The lead author (PCE), a health research methodologist with expertise in mixed methods and qualitative research, conducted one-on-one (individual) semi-structured interviews with participants. Interviews were conducted either virtually (n = 3) using the Zoom videoconferencing application (Zoom Video Communications, Inc.) or in-person (n = 20), based on participant preference. We promoted confidentiality by conducting the interviews in a private office separate from the medical clinic at the Langs CHC. We obtained informed consent from participants before the start of each interview. Five members of our research team (PCE, ALB, MO, LM, JWB) developed the patient and GP

interview guides (see Additional files 3 and 4, respectively) based on relevant literature [17-24,27] and our quantitative findings.

We audio recorded virtual interviews using Zoom's built-in recording feature and in-person interviews using MacIntosh recording software (Audio Recorder v1.3, FIPLAB Ltd.). The lead author (PCE) also took field notes after each interview to document other observations and emergent themes. To promote trustworthiness in our qualitative data, we employed member-checking [36] by sending the raw transcripts and a summary of our results to participants for feedback or correction. We also kept an audit trail of our qualitative data collection and analysis procedures [54]. A summary of our investigator reflexivity is provided in Additional file 5.

Qualitative data analysis

We transferred all interview audio recordings into the software program, MAXQDA (<http://www.maxqda.com>), and the lead author (PCE) transcribed the audio recordings verbatim. After participant identifiers were removed, another member of the research team (JD) reviewed a random sample of 15% of the transcripts for accuracy and found only a few minor typographical errors. All transcripts were then independently coded by two investigators (PCE, ALB) using an inductive content analytic approach [54]. The aim of this strategy was to descriptively summarize the information to ensure the 'best fit to the data' [55]. We used both open and axial coding in our data analysis: open coding to develop concepts from the data, and axial coding to relate these codes (or concepts) to

one another followed by the identification of themes, sub-themes and representative quotes [36].

The two investigators undertaking coding of transcripts met three times throughout the analysis (i.e., after every seven to eight interviews) to compare themes and arrive at a final, agreed-upon set of themes through discussion. We organized these themes into tabular form and selected representative quotations for each theme/sub-theme [36]. We created joint display tables as part of our data integration procedures (Figure 1), and our qualitative and quantitative results were further combined using contiguous narrative and weaving approaches [36,53]. We then drew upon our qualitative and quantitative results jointly to come to a set of conclusions (i.e., ‘meta-inferences’) [36].

Ethical considerations

Our study was approved by the Hamilton Integrated Research Ethics Board at McMaster University (project number 2021-10930). Approval to conduct this study was also obtained from the Chief Executive Officer at the Langs CHC [25].

Results

Quantitative findings

We identified a total of 1,166 patient records, and 210 met eligibility criteria for inclusion in our quantitative analysis (Figure 2).

Cohort characteristics

The majority (70%) of patients were ≥ 45 years of age, over half (58%) were female, approximately one-third (36%) were smokers, and 18% were obese. Patients presented with high rates of co-morbid conditions including cardiovascular disease (65%), depression (55%), anxiety (42%), diabetes (29%), and fibromyalgia (11%). The median number of healthcare visits per patient over 12 months was 5 (IQR, 2 to 8), and 23% received chiropractic services. In terms of opioid use, the median number of unique opioid fills over 12-month follow-up was 2 (IQR, 1 to 2), the median number of 30-day (or equivalent) opioid refills was 4 (IQR, 1 to 12), and baseline opioid dosage ranged from 2 to 840 mg MED (median = 30; IQR, 15 to 67 mg MED). Chiropractic recipients had similar baseline characteristics to those who did not receive chiropractic services (Table 1).

GEE analysis

In our adjusted regression analysis, we found inverse associations between receipt of chiropractic care and filling an opioid prescription (IRR = 0.66; 95% CI, 0.52 to 0.83) or refilling an opioid prescription (IRR = 0.27; 95% CI, 0.17 to 0.42) (Table 2). There was no difference in the odds of being prescribed a higher dose of opioids (i.e., ≥ 50 mg MED) between chiropractic recipients and non-recipients at baseline (OR = 0.61; 95% CI, 0.26 to 1.47); however, chiropractic recipients were less likely to receive a higher opioid dose compared to non-recipients at three months (OR = 0.14; 95% CI, 0.04 to 0.47), six months (OR = 0.14; 95% CI, 0.05 to 0.40), nine months (OR = 0.19; 95% CI, 0.07 to 0.57), and 12 months (OR = 0.22; 95% CI, 0.08 to 0.62). At 12-month follow-up, 29 of

49 (59%) chiropractic recipients had discontinued using opioids compared to 50 of 161 (31%) non-recipients.

Patients with an index visit date in a more recent calendar year also had a lower rate of opioid refills (IRR = 0.82; 95% CI, 0.73 to 0.93) and were less likely to be receiving higher dose opioids at three months (OR = 0.73; 95% CI, 0.57 to 0.94) and six months (OR = 0.78; 95% CI, 0.62 to 0.99) (Additional file 6 [b, d, e]). Those with a higher frequency of healthcare visits were more likely to have a higher rate of opioid refills (IRR = 1.06; 95% CI, 1.02 to 1.09) and to be receiving higher dose opioids at three months (OR = 1.11; 95% CI, 1.02 to 1.21), six months (OR = 1.09; 95% CI, 1.01 to 1.18), nine months (OR = 1.10; 95% CI, 1.02 to 1.19), and 12 months (OR = 1.12; 95% CI, 1.03 to 1.21) (Additional file 6 [b, d-g]). Male sex, depression, and fibromyalgia were positively associated with opioid dosage at various time points (Additional file 6 [c-e]). Contrary to our predictions, anxiety and obesity were negatively associated with opioid dosage (Additional file 6 [c, d, f]), while younger age was not associated with opioid use in our patient sample (Additional file 6). All VIFs were less than 1.4, suggesting no important multicollinearity among independent variables.

Qualitative and mixed methods findings

Twenty-three patients were recruited for interviews and 14 participated. Five patients scheduled interviews but cancelled (two chiropractic recipients, three non-recipients), two scheduled interviews but did not attend (one recipient, one non-recipient), one declined for health reasons and one was not interested. Of those who were interviewed, eight were

chiropractic recipients and six were non-recipients. Among GPs, four of six medical doctors and five of six nurse practitioners completed interviews. Two medical doctors declined participation because of lack of time, and one nurse practitioner expressed interest but did not respond to further interview requests. In total, 23 interviews were completed (14 patients, nine GPs). The median durations of interviews were 25 minutes (range, 19 to 56) for patients and 38 minutes (range, 20 to 40) for GPs.

The majority (79%) of the 14 patients we interviewed were female, most (86%) were either receiving disability benefits or were unemployed, and the majority (71%) had previously received at least one opioid prescription for chronic non-cancer pain. The median dosage for those currently receiving opioid medications was 19 mg MED (range, 14 to 90). Among patients and GPs, there was a large range of ages (33 to 82) and number of years attending the Langs CHC (patients: 2 to 43) or years in practice (GPs: 1 to 26), demonstrating variability among participants (Table 3).

Among all 23 participants, one non-chiropractic patient and four GPs made minor revisions to clarify statements from their interviews during member-checking. No other participants requested content changes or corrections to their transcripts or results. We determined that data saturation had been reached when only two new codes emerged from chiropractic recipient interviews 6, 7 and 8 (with no new codes from interviews 7 and 8); only one new code emerged from non-recipient interview 4 (with no new codes from interviews 5 and 6); and only one new code emerged from GP interviews 7, 8 and 9. At this point, participant recruitment was concluded.

Coding tree

We identified 37 codes across interviews which were categorized into four major themes: (1) patient self-efficacy, (2) accessibility of non-pharmacological services, (3) stigma regarding use of opioids, and (4) impact of treatment. Codes pertaining to patient self-efficacy were stratified into two sub-themes, ‘active versus passive approaches’ and ‘resistance to taking medication.’ This latter sub-theme was common among chiropractic patients, as illustrated in the following excerpt:

“Why harm your body [by taking medication]? ... I don’t want to take any pill. It is better to bear the pain for some time rather than going for pills, or anything. [I’m] not a great believer in artificial pills. ... I believe in exercises and chiropractor services, physiotherapy, rather than going for medications.” Doctor of Chiropractic (DC) Patient 2

For our second theme, we created the sub-themes ‘lack of access to non-pharmacological treatment options’ and ‘access to chiropractic services at the Langs CHC.’ Lack of access to non-pharmacological services (e.g., chiropractic, physiotherapy) was identified in nearly all (21 of 23) participant interviews and was reported as a common facilitator of opioid use. For instance,

“When I was about 23 [years old], financially I wasn’t able to go [to the chiropractor] anymore. So, that’s when [my doctor] put me on the OxyContin and the Perc’s.” DC Patient 7

“It depends on what [our patients] have access to, that’s the big limiting factor. ... It’s hard when you have nothing to give them. I think that’s why, in part, what’s driven opioid over-prescribing is because we have nothing else to give these people. ... The [chiropractic] program at Langs was helpful in that, it allowed more access for people that didn’t have it otherwise.” GP 9

Our third theme captured codes related to the opioid crisis such as negative media coverage or lived experiences. Some patients also expressed a sense of judgement from others for using prescription opioids, as elucidated by the following participant:

“It’s been frustrating – so frustrating. Because the [opioid] crisis seemed to just fall right on me. Like, as though I’m part of the crisis. So, [as a result] every doctor doesn’t want you on any kind of pain medication. They don’t believe your pain. You know what I mean? It has really affected me. ... I’m not an addict in any way. I never even ever think twice about taking that medication more than once, like, unprescribed. But I was definitely treated like I was [an addict].” Non-DC Patient 5

The remaining codes related to patients' or GPs' perspectives on the impact of treatment for chronic pain, including sub-themes of pain relief, functionality, recognition of the limited effectiveness of opioids for chronic pain, and anxiety and fear surrounding opioid withdrawal. These four sub-themes are reflected in the following participants' comments:

"[For] my neck, sometimes, if I didn't go [to the chiropractor], I would really notice it in a couple months if I didn't go every, at least every two months, if not every month." DC Patient 8

"I do actually have patients on opioids that are actually working and it's because they're on opioids, ... that they continue to work full-time. And so, they're not the ones that I worry about so much because they clearly have functionality, and they don't show any behavioural stuff." GP 9

"In my experience, the medication [Percocet] does not take the pain away. It will dull the pain so you can function, but it won't take it away. ... And that's on good days. Sometimes if it's a rough day, then even the medication is not very helpful."
Non-DC Patient 4

"There's a lot of fear around it of – if they are managed well with their opioids – that they might go back to a situation where they're feeling a lot of pain and not functioning properly." GP 5

Further descriptions and frequency counts of each of our major themes, sub-themes, and representative participant quotes are provided in Table 4. Our main quantitative findings are presented with qualitative data as joint displays in Tables 5 and 6.

Discussion

Among patients receiving long-term opioid therapy for chronic neck or back pain, we found that initiating chiropractic care was associated with fewer fills and refills for prescription opioids and, when prescribed, reduced dosage of opioids. Based on our qualitative findings, use of opioids was influenced by patients' self-efficacy and concerns about opioid-related harms, recognition of the limited effect that opioids may have on chronic pain, increasing stigma regarding use of opioids, and access to non-pharmacological treatment options.

Our findings are supported by other uncontrolled observational studies [22-24]. A retrospective analysis of quality assurance data from a CHC in Manitoba, Canada [23] found that patients referred for chiropractic services had a 22% decrease in the number of opioid tablets used after attending an average of five chiropractic visits. Between baseline and discharge, the number of chiropractic patients prescribed opioids within this health care centre decreased 26% [23]. Findings of reduced opioid usage among patients receiving chiropractic services in US Veteran Administration [22] and CHC [24] clinic settings have also been recently reported.

The integration of quantitative and qualitative methods in our study generated several insights into our results. As highlighted in our interviews, patients who were referred for chiropractic services at the Langs CHC may have been more resistant to taking opioid medication than patients not referred for chiropractic services, a sentiment supported by some published evidence [56]. In addition, GPs indicated that access to chiropractic treatment gave them another non-opioid pain management option. Lack of access to non-pharmacological services (e.g., chiropractic, physiotherapy) was reported by several participants as a facilitator of opioid use, while chiropractic patients and GPs identified negative stigma associated with the use of opioids as a common barrier. We also found in our cohort that the proportion of chiropractic recipients who discontinued using opioids was nearly double that of non-recipients. These factors may help explain why chiropractic recipients obtained fewer opioid prescriptions and were less likely to be receiving higher opioid doses up to one year after presentation.

Similar to previous research [40,42], we found that a higher frequency of healthcare visits was positively associated with opioid use. Patients with lower self-efficacy or experiencing greater difficulty coping with their pain may have been more likely to visit their healthcare providers more often and obtain opioid prescriptions on a more frequent basis and at higher doses. Recent evidence suggests that active pain self-management programs that include exercise, goal setting, education, and counselling on opioid discontinuation, as well as interventions aimed at supporting prescribers' adherence to guidelines (e.g., chart audits, tracked performance metrics related to high-dose prescribing), can increase the likelihood of patients reducing their opioid dose or

discontinuing opioid treatment [57]. However, as was frequently mentioned by both GPs and patients in our interviews (see Theme #2 in Table 4), accessibility of non-pharmacological treatment options remains a challenge, particularly for persons who are unemployed or from low income backgrounds [25-32,40-42,57].

We found that patients with an index visit date in a more recent calendar year had fewer opioid prescription refills and were less likely to receive higher opioid doses at 3- and 6-month follow-up. Current guidelines [13,58] recommend optimization of non-opioid and non-pharmacologic treatments prior to opioid use, while limiting opioid doses (when first used with patients) to less than 50 mg MED, and offering a trial of voluntary tapering if doses are already ≥ 90 mg MED. Accordingly, several GPs indicated in their interviews that a concerted effort, in the form of internal chart audits and clinical team meetings, had been made in recent years to reduce opioid prescribing at the Langs CHC. When controlling for calendar year in our analyses, however, we found that the number of opioid fills, refills, and dosages were still considerably lower among chiropractic recipients.

Several studies have reported an association between use of chiropractic services and reduced opioid prescribing [17-21] or reduced opioid use [22-24]. Previous research [26-31] also suggests that integrating chiropractic services with physician management of spine-related pain is associated with improved patient outcomes and potential for cost savings (e.g., reductions in advanced imaging, GP visits, and specialist referrals). When accessed as a first-line treatment, chiropractic services may also help to delay, and in

some cases prevent, opioid prescription [17-21]. In one of our interviews (see Theme #2, first sub-theme, Table 4), the following GP expressed that,

“...having access to any kind of additional modalities in a timely and efficient manner ... would probably reduce the need for opioids in the first place.” GP 9

A retrospective cohort study from Arkansas [59] found that early receipt of chiropractic care, though not physiotherapy, was associated with decreased odds of incident and long-term opioid use in newly diagnosed low back pain patients. As such, our findings combined with those of other researchers suggest that further integration of chiropractic services into primary care centres [23,24,26-31] and interdisciplinary spine care pathways [60] would reduce barriers in accessing these services and potentially benefit the opioid crisis and the management of patients with chronic spinal pain. However, since the efficacy of non-pharmacological interventions including chiropractic care for reducing opioid use remains uncertain [57], and observational research is susceptible to selection bias and confounding [61], well-designed mixed methods randomized controlled trials are needed to confirm our findings.

Strengths and limitations

Our study has several strengths. First, we used patient health card numbers to link EMR data with medical drug claims data from the Narcotics Monitoring System database at ICES to verify patient opioid prescriptions and dosages. Second, we specified the

anticipated direction of association for each independent variable in our regression models *a priori* to provide greater confidence in our findings. Third, we used GEEs to account for hierarchical clustering and to control for differences in confounding factors between our exposed (receipt of chiropractic care) and unexposed groups. To account for policy changes in opioid prescribing, we controlled for calendar year in our analyses. Additional strengths included limited missing data (< 1%), direct data export from the EMR to avoid extraction errors [37], and validation of our qualitative data via member-checking. A final strength of our study is our qualitative findings, which provided a richer understanding of the barriers and facilitators to opioid use and how chiropractic services may have been used by patients and GPs to reduce reliance on opioid prescribing for chronic non-cancer pain.

Our study also has several limitations. Due to the retrospective design in our quantitative phase, certain variables that may be associated with opioid use were unavailable. For example, we were unable to extract EMR data on other co-interventions that patients may have received outside of the CHC, as well as the baseline severity or chronicity of patients' spine-related pain. However, Langs CHC patients are unlikely to access private healthcare services elsewhere due to socioeconomic disadvantages [23-32]. In addition, we used receipt of opioid prescriptions over three consecutive months, combined with multiple clinic visits for a non-cancer spinal pain diagnosis at the Langs CHC, as a proxy for chronic non-cancer pain. Another limitation is that despite restricting our EMR data extraction to patient encounters related to non-cancer back or neck pain, and only including opioid medications prescribed on or between these visit

dates, it remains possible that opioids may have been prescribed for other indications. However, this would have attenuated the association between chiropractic care and opioid use [62]. Furthermore, our primary outcome measures (i.e., opioid prescriptions and dosages) are surrogates for patient-important outcomes such as functional improvement or pain reduction. An inherent limitation with using a sequential mixed methods design (i.e., quantitative followed by qualitative) is that 11 months elapsed between our quantitative and qualitative study phases, subsequently limiting our qualitative data collection. For instance, some individuals whom we attempted to recruit from the larger cohort were no longer available for interviews (e.g., moved out of city, phone number no longer in service, or were deceased). Lastly, chiropractors engaged to provide care at the Langs CHC were selected for their focus on evidence-based, time-limited management of musculoskeletal complaints [29]; practice variability among chiropractors in Canada [63] may reduce the generalizability of our findings in other settings.

Conclusion

We found that patients with chronic spinal pain who received chiropractic care obtained fewer and lower dose opioid prescriptions than patients who did not receive chiropractic care. Follow-up interviews suggested this relationship was influenced by patient self-efficacy and concerns about opioid-related harms, limited effectiveness of opioids for chronic pain, stigma regarding use of opioids, and access to non-pharmacological treatment options. Although overall results are promising, establishing the role of chiropractic care in reducing opioid use for chronic pain requires large, rigorously-

conducted randomized trials, directly addressing patient important outcomes such as pain relief, return to function and adverse events.

List of abbreviations

AIC: Akaike Information Criterion; CHC: Community Health Centre; CI: Confidence Interval; DC: Doctor of Chiropractic; EMR: Electronic Medical Record; GEE: Generalized Estimating Equation; GP: General Practitioner; GRAMMS: Good Reporting of A Mixed Methods Study; ICES: Institute for Clinical Evaluative Sciences; IRR: Incidence Rate Ratio; MAXQDA: Max Weber Qualitative Data Analysis; MED: Morphine Equivalents Daily; OR: Odds Ratio; QIC: Quasi-likelihood under the Independence model Criterion; SPSS: Statistical Package for the Social Sciences; US: United States; VIF: Variance Inflation Factor.

Declarations

Ethics approval and consent to participate

Ethics approval was obtained from the Hamilton Integrated Research Ethics Board at McMaster University (project number 2021-10930). Written informed consent was obtained from all subjects and all methods were conducted in accordance with the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2: CORE).

Consent for publication

Not applicable.

Availability of data and materials

The dataset from this study is held securely in coded form at the Institute for Clinical Evaluative Sciences (ICES). While data sharing agreements prohibit ICES from making the dataset publicly available, access may be granted to those who meet prespecified criteria for confidential access, available at www.ices.on.ca/DAS. The full dataset creation plan and underlying analytic code are available from the authors upon reasonable request, understanding that the computer programs may rely upon coding templates or macros that are unique to ICES and are therefore either inaccessible or may require modification.

Competing interests

PCE is supported by research grants from McMaster University and the NCMIC Foundation for graduate studies outside of the submitted work. All authors have no other conflicts to declare.

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Authors' contributions

Concept development: PCE, MO, LM, JWB; Design: PCE, MO, LM, JWB; Supervision: MO, LM, JWB; Methods consultation: MO, LM, JWB; Data collection/processing: PCE, ALB, DFC, JD; Analysis/interpretation: PCE, ALB; Literature search: PCE; Writing of manuscript: PCE; Critical review of manuscript for intellectual content: PCE, ALB, MO, LM, DFC, JD, JWB. All authors read and approved the final manuscript.

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Table 1 Baseline characteristics of patients from the quantitative chart review (n = 210), stratified by receipt versus non-receipt of chiropractic care

Variable ^a	Recipients (n = 49)	Non-recipients (n = 161)	P-value ^b
Age categories, in years			0.028 ^c
• 18-24	3 (6.1)	2 (1.2)	
• 25-34	7 (14.3)	14 (8.7)	
• 35-44	6 (12.2)	32 (19.9)	
• 45-54	5 (10.2)	44 (27.3)	
• 55-64	15 (30.6)	36 (22.4)	
• 65+	13 (26.5)	33 (20.5)	
Sex			0.214
• Male	17 (34.7)	72 (44.7)	
• Female	32 (65.3)	89 (55.3)	
General health			
• Smoker	13 (26.5)	63 (39.1)	0.108
• Obese ^d	6 (12.2)	31 (19.3)	0.259
Co-morbidities			
• Cardiovascular disease	34 (69.4)	102 (63.4)	0.439
• Depression	30 (61.2)	86 (53.4)	0.336
• Anxiety	20 (40.8)	69 (42.9)	0.800
• Diabetes	15 (30.6)	45 (28.0)	0.718
• Fibromyalgia	8 (16.3)	14 (8.7)	0.127
Year of index visit			0.430
• 2014	32 (65.3)	87 (54.0)	
• 2015	5 (10.2)	26 (16.1)	
• 2016	6 (12.2)	19 (11.8)	
• 2017	4 (8.2)	8 (5.0)	
• 2018	1 (2.0)	4 (2.5)	
• 2019	0 (0.0)	9 (5.6)	
• 2020	1 (2.0)	8 (5.0)	
Opioid dosage, median (IQR)	30 (13.5-56.3)	30 (15.0-75.0)	0.487

IQR inter-quartile range

^a Values are expressed as the number (%) unless otherwise noted

^b Comparisons between categorical variables or continuous variables were measured using the chi-squared test or the Mann-Whitney U test, respectively

^c Statistically significant (2-sided) at an alpha level of 5%

^d Patients with a body mass index of ≥ 30 kg/m² were classified as obese

Table 2 Unadjusted and adjusted effect sizes of the outcomes for prescription opioid use among recipients (n = 49) and non-recipients (n = 161) of chiropractic services treated for chronic non-cancer back or neck pain at the Langs Community Health Centre between January 1, 2014, and December 31, 2020

Outcome measure	Univariable	P-value	Multivariable ^a	P-value
	Effect size (95% CI)		Effect size (95% CI)	
Opioid fills ^b	0.69 (0.56 to 0.85)	< 0.001	0.66 (0.52 to 0.83)	< 0.001
Opioid refills ^c	0.38 (0.24 to 0.60)	< 0.001	0.27 (0.17 to 0.42)	< 0.001
Opioid dosages ^d				
• Baseline	0.77 (0.38 to 1.55)	0.466	0.61 (0.26 to 1.47)	0.270
• 3 months	0.42 (0.18 to 0.99)	0.049	0.14 (0.04 to 0.47)	0.001
• 6 months	0.33 (0.13 to 0.82)	0.018	0.14 (0.05 to 0.40)	< 0.001
• 9 months	0.39 (0.17 to 0.94)	0.035	0.19 (0.07 to 0.57)	0.003
• 12 months	0.52 (0.23 to 1.19)	0.123	0.22 (0.08 to 0.62)	0.004

CI confidence interval

^a Adjusted for age, sex, smoking status, obesity, depression, anxiety, fibromyalgia, diabetes, cardiovascular disease, visit frequency, and calendar year

^b Opioid prescription fills over 12-month follow-up. An incidence rate ratio < 1 indicates a lower rate of opioid fills in the recipient group

^c Opioid prescription refills (of 30 days or equivalent) over 12-month follow-up. An incidence rate ratio < 1 indicates a lower rate of opioid refills in the recipient group

^d Opioid dosage over 12-month follow-up. An odds ratio < 1 indicates a reduced likelihood of higher opioid dosage (i.e., ≥ 50 mg morphine equivalents daily) in the recipient group

Table 3 Demographic and clinical characteristics of participants from the qualitative interviews (n = 23)

Variable	Value ^a	
	Patients (n = 14)	GPs (n = 9)
Age in years, mean (SD)	56.2 (14.3)	47 (10.5)
Sex		
• Male	3 (21.4)	2 (22.2)
• Female	11 (78.6)	7 (77.8)
Years attending CHC (patients) / years in practice (GPs), mean (SD)	13 (11.6)	13.4 (6.8)
Completed post-secondary education or higher	7 (50.0)	9 (100)
Receiving disability benefits / unemployed	12 (85.7)	0 (0)
Opioid prescription	10 (71.4)	NA
Receipt of chiropractic care	8 (57.1)	NA

CHC community health centre, GP general practitioner, NA not applicable, SD standard deviation

^a Values are expressed as the number (%) unless otherwise noted

Table 4 Qualitative themes generated from semi-structured interviews with patients (n = 14) and general practitioners (n = 9) at the Langs Community Health Centre regarding perceptions of chiropractic integration and its impact on opioid prescribing

Themes	Description	Sub-themes and representative quotes ^a
1. Patient self-efficacy (n = 23)	Patients and GPs described active and passive pain management strategies and behaviours, including a resistance among some patients toward taking medication.	<p><u>Active versus passive approaches:</u></p> <ul style="list-style-type: none"> • <i>“I’m continuously doing stretches, exercises, to keep myself okay.”</i> DC Patient 2 • <i>“I try exercising, but it just makes it worse.”</i> DC Patient 7 • <i>“It’s really hard to engage some of these folks in self-care with their chronic pain. You know? It’s just like – give me medication.”</i> GP 1 • <i>“A lot of our folks don’t feel very empowered, or don’t feel like they have much agency in their lives, which is true. ... With chronic back [pain], ... probably the greatest utility [of an active approach] is having them understand that some of this is within their control to influence.”</i> GP 7 • <i>“[For a patient who might be considering an opioid prescription to manage their pain], I would just say to start trying to feel some of your pain again so that you can learn how to manage it in a different way. You know? Instead of just, like, burying all the pain.”</i> Non-DC Patient 5 • <i>“When [patients] come in believing that you can find the right thing that will fix their pain, and – opioid medication is one component of that belief system – I think that the more we engage in that from the get-go, the less successful we’re going to be at changing that mindset. ... Passive therapies such as opioids, or even chiropractic manipulation or massage [by themselves], are not necessarily bad; but if [passive therapy] is our starting point – and again, this is just what I’ve experienced – [I feel] it is harder to engage patients in active options later.”</i> GP 4 <p><u>Resistance to taking medication:</u></p> <ul style="list-style-type: none"> • <i>“...most patients don’t want to be on a bunch of pills. They don’t want to be dependent on medication to feel better.”</i> GP 9 • <i>“I’ve been dealing with this pain for 10 years, and I’m not just a pill popping, believing [person]. [I’m] old school, take the pain until it’s really extreme and then – oh gee, I better take an Advil – is kinda how I deal with my pain.”</i> DC Patient 1

		<ul style="list-style-type: none"> • <i>“Most people don’t want to take pills from my perspective – for a multitude of reasons. They prefer to have all the options for treatment, and that includes non-pharm[acological] solutions.” GP 2</i>
<p>2. Accessibility of non-pharmacological services (n = 21)</p>	<p>Lack of access to non-pharmacological services was identified as a common facilitator of opioid use.</p>	<p><u>Lack of access to non-pharmacological treatment options:</u></p> <ul style="list-style-type: none"> • <i>“Most of our patients don’t have any additional coverage for extended health, like, physio, chiro, all of those things. So, unfortunately, even though those are first-line modalities for treating a lot of pain, patients can’t access it unless we have programs for it.” GP 8</i> • <i>“It’s hard when you have nothing to give them. I think that’s why, in part, what’s driven opioid over-prescribing is because we have nothing else to give these people. ... I think having access to any kind of additional modalities in a timely and efficient manner for all patients would probably reduce the need for opioids in the first place.” GP 9</i> • <i>“The government needs to step up and help out.” DC Patient 3</i> • <i>“It’s that scenario where you have nothing else to offer, right? So, if you’re trying to postpone heading into ‘opioid land’ and you still have something else to offer, it can definitely make a difference. ... You probably go to meds sooner than you might otherwise because you don’t have access to the intervention you’d really like.” GP 7</i> • <i>“When I was about 23 [years old], financially I wasn’t able to go [to my chiropractor] anymore. So, that’s when [my doctor] put me on the OxyContin and the Perc’s.” DC Patient 7</i> • <i>“We’re told there’s a triangle of care, you know, the psychosocial, and the physical modalities, and meds, [which] are only a small part of it. But the only thing you have access to is the meds. ... It’s just ironic. The people who need [non-pharmacological] services the least, have the best access. ... But the people who are most vulnerable to [chronic pain] are the people that have the least access.” GP 9</i> <p><u>Access to chiropractic services at the Langs CHC:</u></p> <ul style="list-style-type: none"> • <i>“The [chiropractic] program at Langs was helpful in that, it allowed more access for people that didn’t have it otherwise.” GP 9</i>

		<ul style="list-style-type: none"> • <i>“The evidence says you guys are as good at clearing up back pain as we are. So, we need to work together at that, and it’s helpful to have [access to chiropractic services for our patients].”</i> GP 3 • <i>“The folks we take care of, 95% of them couldn’t afford chiropractic on their own, or don’t have [a] benefit plan. There’s a small portion who do, but most of them don’t. So, being able to, right from the outset, present this package of care, I think [is] incredibly helpful.”</i> GP 7 • <i>“I’m missing the chiropractor services [since they were discontinued because of the COVID-19 pandemic]. I wish it could come back again, because I’m having pain.”</i> DC Patient 2
3. Stigma regarding use of prescription opioids (n = 20)	<p>A negative stigma around opioids was identified by patients and GPs as a barrier to opioid use. However, patients who found benefit in using opioids often felt a sense of judgement, as well as a need to advocate for themselves to obtain an opioid prescription.</p>	<ul style="list-style-type: none"> • <i>“I think in our current society with news about addiction and our history of OxyContin over-prescribing, we probably have fewer people asking for opioids.”</i> GP 3 • <i>“Sometimes we have people we can’t even talk into considering an opioid because they’ve taken what they’ve heard in the media so significantly they don’t want anything to do with that.”</i> GP 7 • <i>“Unfortunately, patients experience a great deal of stigma, and so some of them don’t like that. And then they want to come off of their pills.”</i> GP 9 • <i>“I take ... the Tylenol #3, [but] it’s no good, it’s [like] cocaine.”</i> DC Patient 4 • <i>“It’s been frustrating – so frustrating. Because the [opioid] crisis seemed to just fall right on me. Like, as though I’m part of the crisis. So, [as a result] every doctor doesn’t want you on any kind of pain medication. They don’t believe your pain. You know what I mean? It has really affected me. ... I’m not an addict in any way. I never even ever think twice about taking that medication more than once, like, unprescribed. But I was definitely treated like I was [an addict].”</i> Non-DC Patient 5
4. Impact of treatment (n = 19)	<p>Patients and GPs described their impressions of treatment directed at managing chronic pain.</p>	<p><u>Pain relief:</u></p> <ul style="list-style-type: none"> • <i>“[For] my neck, sometimes, if I didn’t go [to the chiropractor], I would really notice it in a couple months if I didn’t go every, at least every two months, if not every month.”</i> DC Patient 8 • <i>“When you have a nerve condition, especially like mine where the nerves are hypersensitive and will shoot off through your entire body like electricity, sometimes</i>

		<p>with, you know, airflow. ... It's literally, like, I've been outside and a strong wind has gone across my legs and it makes my, it just makes my heart start pounding so much because it hurts that much and I'm like – are you freaking kidding me? And in that situation, it's just like – no, I think I actually need something very, very strong to calm these nerves down or to numb my body or these nerves.” Non-DC Patient 1</p> <ul style="list-style-type: none"> • “I feel like it's more a push from the patient to do something about [their] pain and to help [them]. ... Because ultimately, you're trying to alleviate their suffering. That's why they come. And, you're trying to respond to that.” GP 9 <p><u>Functionality:</u></p> <ul style="list-style-type: none"> • “I know that I would not be able to function without having some relief [from opioids].” Non-DC Patient 4 • “I do actually have patients on opioids that are actually working and it's because they're on opioids, ... that they continue to work full-time. And so, they're not the ones that I worry about so much because they clearly have functionality, and they don't show any behavioural stuff.” GP 9 <p><u>Recognition of the limited effectiveness of opioids for chronic pain:</u></p> <ul style="list-style-type: none"> • “In my experience, the medication [Percocet] does not take the pain away. It will dull the pain so you can function, but it won't take it away. ... And that's on good days. Sometimes if it's a rough day, then even the medication is not very helpful.” Non-DC Patient 4 • “[I've been taking pain medications since] 2012. ... It never feel[s] good. [Even though] I take three [Tylenol #3] pills every day, ... I still have a lot of pain.” DC Patient 4 • “I'm glad I'm off of the fentanyl, [but] the Butran [buprenorphine] is not holdin' all my pain. You know? It's just takin' a little bit [of it away].” Non-DC Patient 6 <p><u>Fear or anxiety of withdrawal:</u></p> <ul style="list-style-type: none"> • “There's a lot of fear around it of – if they are managed well with their opioids – that they might go back to a situation where they're feeling a lot of pain and not functioning properly.” GP 5
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		<ul style="list-style-type: none">• “...terrifying. ... Not being able to have [my] prescription filled is very frightening – and panic. You start having anxiety.” Non-DC Patient 4• “I think sometimes with the patients on opioids there’s a lot of fear and anxiety about the dosing and the reduction of the dose because it’s unpleasant. And because they’re afraid about their pain and stuff like that.” GP 1• “I was feeling more [pain] right away within the first time that I went down [in my opioid dose]. That was from the 6’s to the 3’s [6 mg of Hydromorphone to 3 mg], twice a day. And I remember that, and thinking – oh my goodness, I’m going to go back to square one if they keep doing this. Which, I didn’t want to be in that much pain.” Non-DC Patient 5• “I have to be honest, people are so anxious when you’re talking about decreasing their opioids, they don’t hear much else.” GP 7
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CHC community health centre, DC doctor of chiropractic, GP general practitioner

^a Bolded phrases are for thematic emphasis

Table 5 Joint display of the quantitative association between receipt of chiropractic services at the Langs Community Health Centre and prescription opioid use, representative qualitative interview quotes, and meta-inferences

Variable	Quantitative results	Qualitative interview quotes	Meta-inferences
Receipt of chiropractic care (n = 49)	<ul style="list-style-type: none"> • Negative association with total number of opioid fills (adjusted IRR = 0.66) • Negative association with total number of opioid refills ^a (adjusted IRR = 0.27) • Negative association with higher opioid dosage at: <ul style="list-style-type: none"> 3-month follow-up (adjusted OR = 0.14) 6-month follow-up (adjusted OR = 0.14) 9-month follow-up (adjusted OR = 0.19) 12-month follow-up (adjusted OR = 0.22) 	<p><u>Resistance to taking medication:</u></p> <ul style="list-style-type: none"> • <i>“I don’t want to take so many medicine[s]. ... It’s too much chemical going in your body, it’s no good. ... I try to take, even with my pain, [only] one Tylenol #3, and [then] I will take Advil or extra strength Aspirin or Tylenol every six hours [for the rest of the day].”</i> DC Patient 4 • <i>“I try and adhere against [taking] Tylenol #3, if I can help it.”</i> DC Patient 5 • <i>“I’ve been prescribed [opioids], ... but I just started reading about stuff, what it does to your liver and what it does to other organs in your body. I just, I chose other methods, i.e., like chiropractic, massage, I bought a hot tub – hydrotherapy. Just stuff like that. ... I’m just so not a drug guy.”</i> DC Patient 6 <p><u>Impact of chiropractic treatment on chronic pain:</u></p> <ul style="list-style-type: none"> • <i>“When I first started coming [to see the chiropractors at Langs] I couldn’t hardly walk and get in my car, to get in and out of the car, it was a challenge. And after a few chiropractor treatments, it got much better. And some days I couldn’t even turn my head sideways to see driving the car, and that got fixed. It’s gone well. Sometimes, it comes back a little bit, but then I just</i> 	<p>The rate of filling and refilling opioid prescriptions was 34% and 73% lower, respectively, among chiropractic recipients versus non-recipients. Over 12 months of follow-up, chiropractic recipients were also between 78% and 86% less likely than non-recipients to have received a higher (≥ 50 mg MED) opioid dose. Patients who were referred by their GP for chiropractic services at Langs may have been more resistant to taking opioids than patients who were not referred for chiropractic services. Access to chiropractic treatment also gave patients and their GPs another non-opioid pain management option.</p>

		<p><i>think – now I can get this fixed with the chiropractor.” DC Patient 3</i></p> <ul style="list-style-type: none"> • <i>“When I had the chiropractor [treatments], ... it wasn’t just the treatment, it was [them] givin’ me ideas of things to do to help yourself. And those kind[s] of things are so valuable.” DC Patient 5</i> • <i>“It really brings home this message of – a chemical going into your body is only one way to influence this. So, if somebody’s having a positive experience [with chiropractic treatment], and we have had lots of people who’ve had positive experiences, it can mean the difference between not increasing a dose [versus increasing a dose]. Not starting a dose? I would say that there probably are situations where we’ve had that as well.” GP 7</i> <p><u>Access to chiropractic services at the Langs CHC:</u></p> <ul style="list-style-type: none"> • <i>“A lot of our patients are from low income [backgrounds] and have transportation issues. So, having [chiropractic] services available for them here is very important.” GP 2</i> • <i>“I just didn’t have the funds to have chiropractic [treatment]. But then when it was offered to me at Langs, I was just like – yeah, I’ll take it!” DC Patient 6</i> • <i>“We definitely need those added services [for patients] who have chronic pain because it’s an option. ... We need some way of getting that patient to treat pain in non-drug ways.” GP 3</i> 	
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CHC community health centre, DC doctor of chiropractic, GP general practitioner, IRR incidence rate ratio, MED morphine equivalents daily, OR odds ratio

^a Prescription opioid refills were measured in 30-day equivalents

Table 6 Joint display of the quantitative associations of visit frequency and calendar year with prescription opioid use at the Langs Community Health Centre, representative qualitative interview quotes, and meta-inferences

Variable	Quantitative results	Qualitative interview quotes	Meta-inferences
Higher frequency of healthcare visits (n = 210) ^a	<ul style="list-style-type: none"> • Positive association with total number of opioid refills^b (adjusted IRR = 1.06) • Positive association with higher opioid dosage at: <ul style="list-style-type: none"> 3-month follow-up (adjusted OR = 1.11) 6-month follow-up (adjusted OR = 1.09) 9-month follow-up (adjusted OR = 1.10) 12-month follow-up (adjusted OR = 1.12) 	<p><u>Passive pain management strategies:</u></p> <ul style="list-style-type: none"> • <i>“I found, like, after I’d been in [for chiropractic treatment] on a Tuesday and they’d put me all back in shape again, and put my shoulder back in, I felt great by Thursday. Thursday it was time to come back in. So, it kept me even. It kept the pain down. ... With me comin’ in twice a week, I knew at least for four days out of the week I was going to be fine.”</i> DC Patient 7 • <i>“You expect the doctor to fix it, ‘cause that’s how we were brought up.”</i> Non-DC Patient 6 • <i>“Some of our people are just rather passive in their approach to their care.”</i> GP 1 • <i>“Everything is short-term. [My pain is] chronic. It’s there to stay because I try everything. ... I’ve tried physio, chiro, ... I even have steroid needles [at the] pain clinic, ... and saw a sport therapist person [physiatrist] for a different type of needle [epidural injection]. ... I take the Robaxacet if I’m in too much pain, or Advil. ... They gave me Percocet. ... [Even with regular] massage therapy [and] osteopathy, I go to bed and the day after and it’s still there. ... I wish somebody could go inside and just fix [it]. It’s just a hard place to be fixed, it’s not made to be fixed – the back.”</i> Non-DC Patient 2 	<p>Patients with a higher frequency of healthcare visits had a higher rate of refilling opioid prescriptions and were more likely to be receiving higher dose (≥ 50 mg MED) opioids over 12-month follow-up. Patients who relied on passive pain management strategies may have been more likely to visit their healthcare providers more often and obtain opioid prescriptions on a more frequent basis and at higher doses.</p>

<p>Index visit in more recent calendar year (n = 210)</p>	<ul style="list-style-type: none"> Negative association with total number of opioid refills^b (adjusted IRR = 0.82) Negative association with higher opioid dosage at: <ul style="list-style-type: none"> 3-month follow-up (adjusted OR = 0.73) 6-month follow-up (adjusted OR = 0.78) 	<p><u>Reduced opioid prescribing in recent years:</u></p> <ul style="list-style-type: none"> <i>“When I graduated [from medical school] in 1996, the overwhelming message to us was that we weren’t treating pain adequately; we weren’t treating it aggressively enough. And then of course, OxyContin was just the ‘new guy’ on the block and all that was wonderful and there was no ceiling dose, and you know the rest of that story.” GP 7</i> <i>“In the last four or five years [here at Langs], we’ve worked even harder at getting people off opioids.” GP 3</i> <i>“The goal is that opioids are not used for chronic non-cancer pain. I think over the last five [or] 10 years we’ve seen [a] reduction in use, and a lot of patients have been titrated down in their doses and are using more appropriate [levels of opioid] medications now.” GP 8</i> <i>“Having followed the sort of structure that we normally do here now in the last five years [with opioid prescribing], there’s much fewer people on [high doses].” GP 3</i> 	<p>Patients whose index visit date was in a more recent calendar year had a lower rate of refilling opioid prescriptions and were less likely to be receiving higher dose (≥ 50 mg MED) opioids at 3- and 6-month follow-up. GPs at Langs have made a concerted effort in recent years to reduce opioid prescribing.</p>
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DC doctor of chiropractic, GP general practitioner, IRR incidence rate ratio, MED morphine equivalents daily, OR odds ratio

^a Healthcare visits constitute GP and chiropractic visits

^b Prescription opioid refills were measured in 30-day equivalents

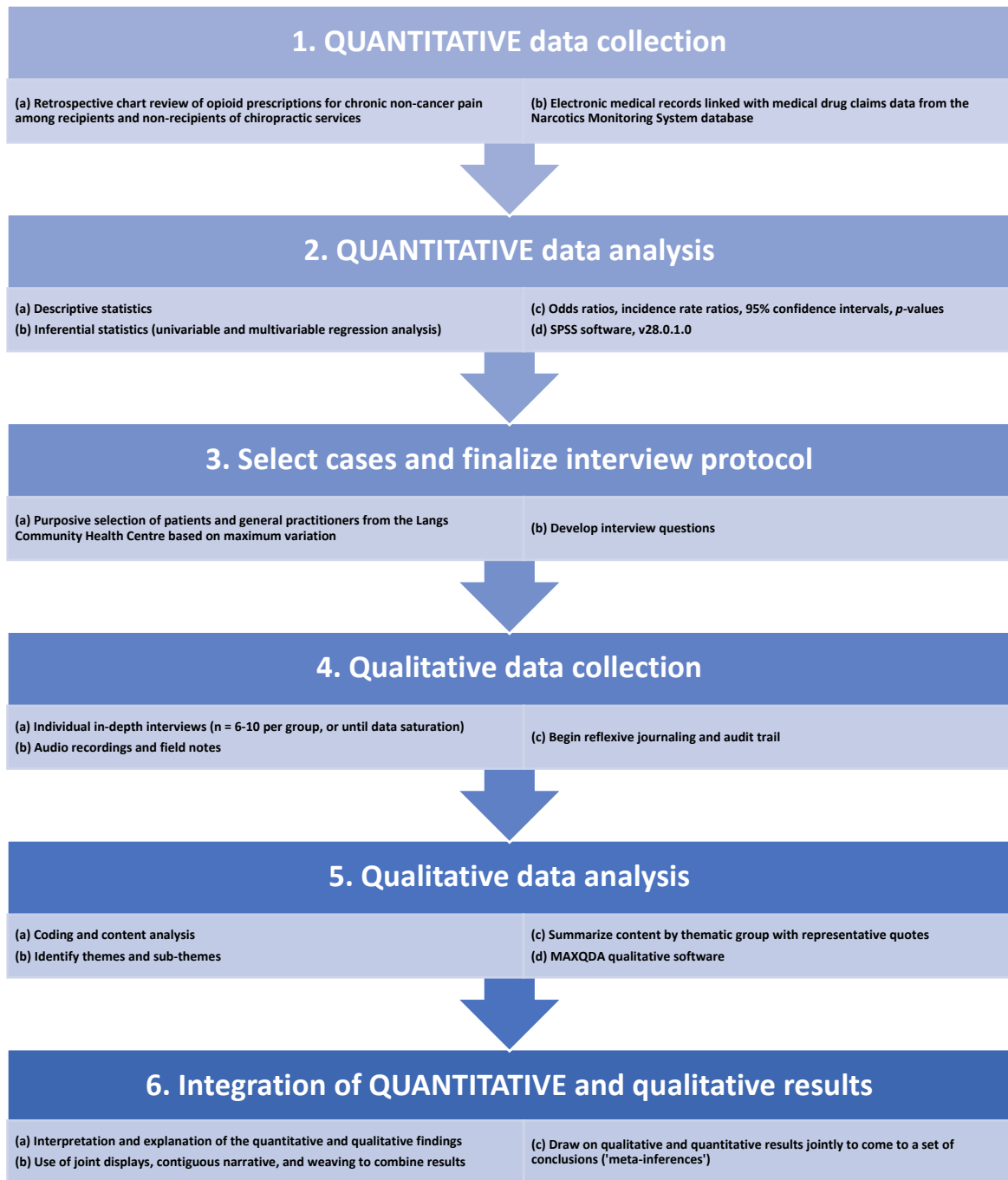


Fig. 1 Study diagram of an explanatory sequential design of a mixed methods study on the association of chiropractic integration with opioid use for chronic non-cancer pain at the Langs Community Health Centre. The quantitative and qualitative data collection and analysis phases are listed at the top of each step of the diagram. The two points of interface (or mixing) of the quantitative and qualitative phases occur in the third and final steps. The term “QUANTITATIVE” is capitalized to indicate prioritization of the quantitative phase in the study. The study procedures and outputs for each phase are listed in point-form at each step

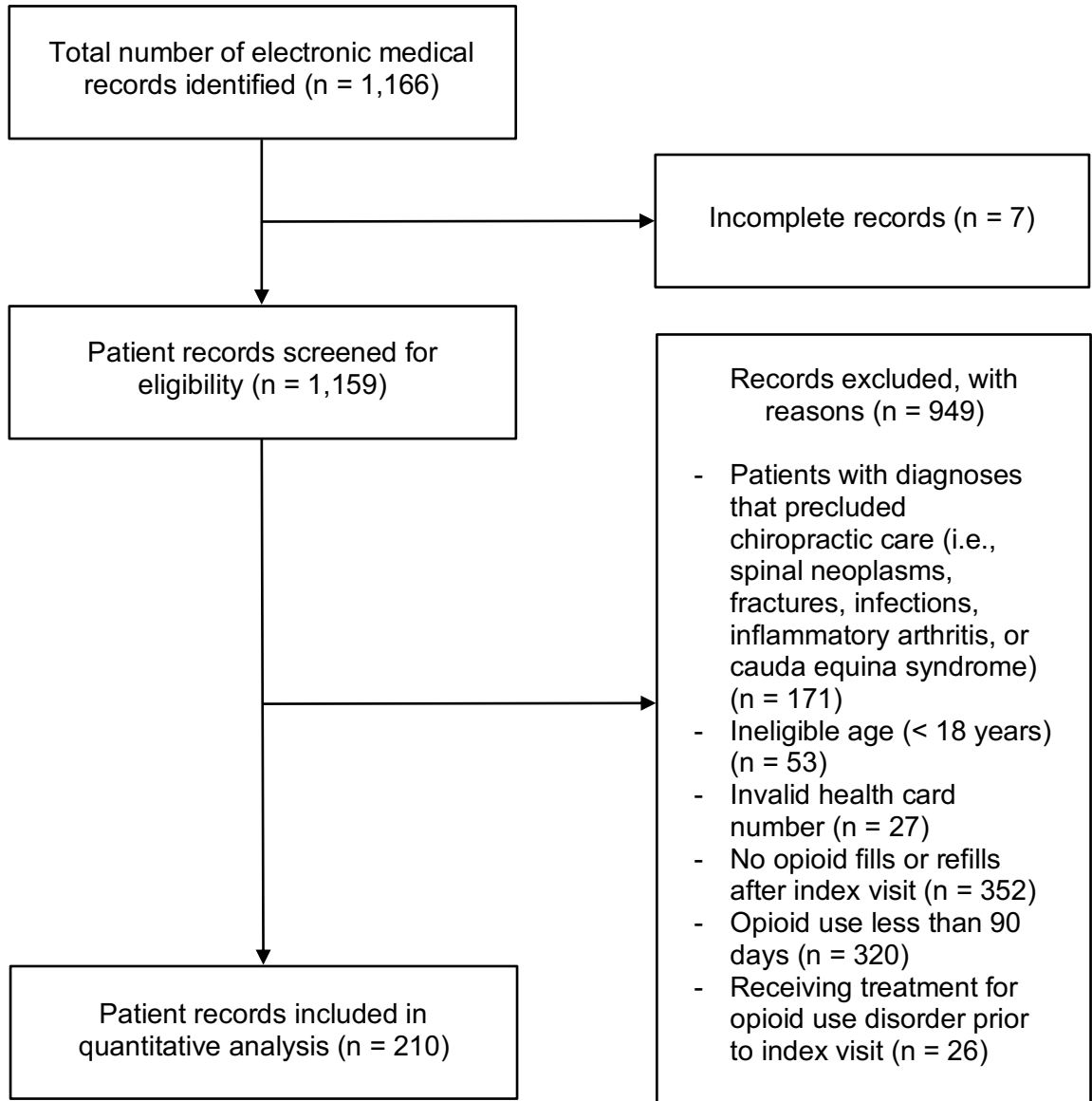


Fig. 2 Flowchart of cohort inclusion for the quantitative analysis

Supplementary Material

Additional file 1: Good Reporting of A Mixed Methods Study (GRAMMS) checklist

Additional file 2: Morphine equivalents daily conversion factors

Additional file 3: Interview guide (patients)

Additional file 4: Interview guide (general practitioners)

Additional file 5: Investigator reflexivity

Additional file 6 (a-g): Univariable and multivariable regression models for each outcome of interest

Additional file 1 Checklist of items for the Good Reporting of A Mixed Methods Study (GRAMMS) guidelines [34,35]

Mixed methods reporting	
GRAMMS guidelines	Location in manuscript where items are reported
1) Describes the justification for using a mixed methods approach to the research question	Background (p. 180)
2) Describes the design in terms of the purpose, priority and sequence of methods	Methods, Study Design (p. 181), Figure 1 (p. 226)
3) Describes each method in terms of sampling, data collection and analysis	Methods (pp. 181-188), Figure 1 (p. 226)
4) Describes the integration of the quantitative and qualitative components	Methods (pp. 185, 188), Results (p. 195), Discussion (pp. 196-197), Tables 5 and 6 (pp. 222-225), Figure 1 (p. 226)
5) Describes any limitation of one method associated with the presence of the other method	Discussion, Strengths and Limitations (p. 200)
6) Describes any insights gained from mixing or integrating methods	Discussion (pp. 196-197), Tables 5 and 6 (pp. 222-225)

GRAMMS Good Reporting of A Mixed Methods Study

Additional file 2 Opioid morphine equivalents daily (MED) conversion factors ^a
(adapted from Busse et al.[11])

Oral opioid formulations		
<i>Opioids</i>	<i>Oral MED conversion factors</i>	
Codeine	0.1 to 0.2	
Dihydrocodeine	0.1	
Hydrocodone	1.0 to 1.5	
Hydromorphone	5.0	
Meperidine	0.1	
Methadone ^b	4.0	
Morphine	1.0	
Oxycodone	1.5	
Oxymorphone	3.0	
Tapentadol	0.3 to 0.4	
Tramadol	0.1 to 0.2	
Transdermal opioid formulations		
<i>Opioid</i>	<i>Hourly microgram dose</i>	<i>Mean MED dose (range)</i>
Fentanyl	25 mcg/hr	97 mg/day (60 to 134)
Fentanyl	37 mcg/hr	157 mg/day (135 to 179)
Fentanyl	50 mcg/hr	202 mg/day (180 to 224)
Fentanyl	62 mcg/hr	247 mg/day (225 to 269)
Fentanyl	75 mcg/hr	292 mg/day (270 to 314)
Fentanyl	87 mcg/hr	337 mg/day (315 to 359)
Fentanyl	100 mcg/hr	382 mg/day (360 to 404)

MED morphine equivalents daily

^a These factors are for calculation purposes only

^b Oral dose of between 1-20 mg/day

Additional file 3 Interview guide for patients

Welcome:

Introductions and project overview

Before we begin, I would like to review a few items from our consent form:

- Your participation in this project is voluntary and you are free to withdraw from the study (stop the interview completely) at any time.
- Our interview will last about an hour.
- You do not need to answer questions that you do not want to answer or that make you feel uncomfortable.
- All of your answers are private and confidential.
- I will be recording our interview so that all of your ideas are captured.
- You will receive a copy of your interview transcript and a brief summary of the results.

Introduction:

Chiropractic services have been available to patients at the Langs Community Health Centre (CHC) since January 1, 2014. I would like to ask you some questions about your experience with the chiropractic services at Langs, as well as whether you feel these services have affected your use of opioids for pain management. I will also ask you for some basic information like your age and formal education. Because the chiropractic program has been put on “pause” during the COVID-19 pandemic, I'd also like to ask you about whether you feel the pandemic, including the reduced access to chiropractic services, has had any additional effect on you with respect to your opioid use.

Are you ready to begin?

15. What year were you born in?
16. How many years have you been a patient at Langs?
17. What is your highest level of education (elementary / high school / college or university / graduate level)?
18. Are you currently working? If so, are you working part- or full-time? If you are *not* working, are you receiving disability benefits / are you retired?
19. Do you currently experience back or neck pain? If **yes**, approximately how long have you had this pain?
20. Are you currently taking any opioid medications for your pain? If so, what opioid medication(s) are you taking (e.g., Tylenol with codeine [Tylenol #3], Percocet or OxyContin [oxycocet, oxycodone], Dilaudid [hydromorphone], Methadose [methadone], Stalex or MS Contin [morphine], Tramacet or Ralivia [tramadol], Suboxone [buprenorphine or naloxone], Duragesic [fentanyl patch, or oral fentanyl]) and what is the current dose?
Probe: Has this dose increased, decreased, or stayed the same since you were first prescribed opioids by your general practitioner (GP)?
21. What other types of treatment or activities do you engage in to help manage your pain?
22. Chiropractic services have been offered at Langs since January 1, 2014. Have you ever been referred by your GP for these services? (If “No,” skip to question #11.) If **yes**, tell me about your experience with the chiropractic program at Langs?
Probe: Have you found these services helpful? If so, why have you found these services helpful, or if not, why not?
Probe: Had you ever been to a chiropractor before using the chiropractic services here at Langs? If **yes**, do you think this made you more open to being referred by your GP for chiropractic treatment at Langs?

23. Do you feel that the chiropractic services at Langs have had any effect on your opioid use? If so, why do you feel this way, or if not, why not?
Probe: Do you feel you are better able to manage your pain with access to these services?
Probe: Had your GP ever talked to you about reducing your opioid prescriptions and/or doses *before* you were referred for chiropractic treatment? If so, did you agree to work with your GP to reduce your opioid use?
24. The chiropractic program at Langs has been on hold during the COVID-19 pandemic. Has this affected your use of opioids at all? Why or why not?
Probe: If **yes**, how has it affected your use of opioids? Why do you think this is the case, or if not, why not?
Probe: Can you elaborate, or give me any specific examples?
25. **(Skip this question for those who answered “Yes” to question #7.)** If your GP has *never* referred you for chiropractic services at Langs, do you think this type of program would help you with managing your pain and possibly reduce your use of opioids?
Probe: Can you elaborate, or give me any specific examples?
Probe: Have you had any previous experience with chiropractic treatment outside of Langs?
26. Do you think that patients, such as yourself, would benefit from access to pain management services such as chiropractic treatment *before* being prescribed opioids?
Probe: Can you elaborate on why you feel this way, or can you give me any specific examples to help me understand?
27. What advice would you give to another patient who might be considering an opioid prescription to manage their pain?
28. Thank you so much for your time. Do you have any questions, or is there anything else that you would like to share with me?

Field Notes & Emergent Themes:

Additional file 4 Interview guide for general practitioners

Welcome:

Introductions and project overview

Before we begin, I would like to review a few items from our consent form:

- Your participation in this project is voluntary and you are free to withdraw from the study (stop the interview completely) at any time.
- Our interview will last approximately one hour.
- You do not need to answer questions that you do not want to answer or that make you feel uncomfortable.
- All of your answers are private and confidential.
- I will be recording our interview to ensure that I accurately capture your statements.
- You will receive a copy of your interview transcript and a summary of the results to confirm I have accurately represented our interview (member-checking).

Introduction:

Chiropractic services were integrated at the Langs Community Health Centre (CHC) on January 1, 2014. I would like to ask you some questions about your experience with the chiropractic services at Langs, as well as how you feel these services have affected opioid use among patients at the CHC. I will also ask you for some basic demographic information, such as your age and education. Because the chiropractic program has been put on “pause” during the COVID-19 pandemic, I'd also like to ask you about whether you feel the pandemic, including the reduced access to chiropractic services at Langs, has had any impact on patients' use of opioids.

Are you ready to begin?

10. In what year were you born?
11. How many years have you been in practice?
12. What is your highest level of education (MD [medical doctor] or NP [nurse practitioner] / other [e.g., MSc or PhD])?
13. Chronic non-cancer pain (CNCP) is any painful condition that persists for at least three months and is not associated with malignant disease. Do you see a lot of patients with CNCP in your practice at Langs?
 - Probe: For these types of patients, what treatment(s) do you offer or recommend to them?
 - Probe: What types of medications do you prescribe for pain management?
 - Probe: For those who have been prescribed opioids, do you feel it would be desirable to have some of these patients reduce their use of opioids?
 - d) If **not**, why not?
 - e) If **yes**, have you attempted to engage any of your patients with CNCP in tapering their dose? Or vice versa, have any of these patients asked you about reducing their opioid prescriptions and/or dose?
 - f) To the best of your knowledge, has there been any opioid-reducing strategy(ies) implemented at Langs to reduce opioid prescribing (e.g., a task force to reduce opioid use, regional dashboards, tracked performance metrics related to high dose prescribing, chart audits, introduction of 2017 CMAJ [Canadian Medical Association Journal] guidelines, etc.)?
14. Chiropractic services have been integrated at Langs since January 1, 2014. Have you ever referred patients for these services?

- c) If **not**, why not? (**Then skip to question #7.**)
 - d) If **yes**, why did you refer patients for these services (e.g., did patients request to be referred for chiropractic treatment, or did you refer them because they were not responding to medical care)?
 - Probe: Tell me about your experience with the chiropractic program at Langs?
 - Probe: Have any of your patients found these services helpful? If so, why do you think they have found these services helpful?
 - Probe: Can you give me any examples of where your patients have *not* found chiropractic treatment to be helpful?
15. Have you ever referred patients for chiropractic care at Langs as part of a formal effort to taper opioids?
- Probe: Whether you have or not, what do you think about accessing chiropractic care as part of a strategy to help patients reduce opioid use?
 - Probe: Was there ever a time where you decided to reduce an opioid dose in a patient you referred for chiropractic services based on the perception that their pain was better managed and thus less opioids were required?
 - Probe: Do you have any examples of where you referred a patient for chiropractic services but their opioid use stayed the same or increased? If **yes**, can you elaborate on why think this was the case?
16. For this research project, we have been analyzing data on patients with CNCP who were prescribed opioid medication(s) *prior* to being referred for chiropractic treatment. Do you think that patients would be less likely to receive a prescription for opioids if they were referred for chiropractic services *first*? If so why, or if not, why not?
- Probe: Can you elaborate, or give me any specific examples?
17. The chiropractic program at Langs has been on hold during the COVID-19 pandemic. How do you feel this has affected opioid use, if at all, among your patients?
- Probe: Has this limited the pain management options that you can recommend to your patients?
 - Probe: Has the pandemic, and lack of access to chiropractic services at Langs, had any impact on the number or dose of opioid medications that you have been prescribing to your patients for pain management?
18. Thank you so much for your time. Do you have any questions, or is there anything else that you would like to share with me on this topic?

Field Notes & Emergent Themes:

Additional file 5 Reporting of investigator reflexivity for the qualitative study phase

Research team and reflexivity^a	Description
<i>Personal characteristics</i>	
Interviewer	All interviews were conducted by the lead author (PCE).
Credentials	At the time of the interviews, PCE was a Doctor of Philosophy (PhD) candidate in Health Research Methodology at McMaster University. He also has a Master of Science (MSc) in clinical sciences from Bournemouth University.
Occupation	The interviews were coded by two investigators (PCE, ALB). Both are practising Doctors of Chiropractic. PCE is also an adjunct faculty member in the Chiropractic Department at D'Youville University.
Gender	PCE identifies as male and ALB identifies as female.
Experience and training	PCE has graduate-level training in health research methodology with expertise in mixed methods and qualitative research. PCE and ALB each have over 19 years of clinical and research experience.
<i>Relationship with participants</i>	
Relationship established	PCE worked as a clinician in the chiropractic program at the Langs CHC from January 2014 to January 2016, and therefore had an established relationship with many of the GPs (6/9) and a few of the chiropractic patients (2/8) who were interviewed for this study. These established relationships seemed to facilitate trust and candid conversations during the audio-recorded interviews, particularly with the GPs. PCE did not have a prior relationship with any of the non-chiropractic patients in this study; however, early rapport was developed and established during participant recruitment telephone calls and during introductions and conversation at the start of each interview.
Participant knowledge of the interviewer	Participants were sent a form containing information about the study's aims and objectives, the lead author, and his contact details, at least one week in advance of each interview. Participants were also made aware that the project was being undertaken by PCE as part of a PhD thesis.
Interviewer characteristics	Both investigators (PCE, ALB) were interested in the research topic because they had prior experience (PCE: 2 years, ALB: 6 years) working as clinicians in the Langs chiropractic program. This was acknowledged as a potential source for bias in the analysis and interpretation of the data. PCE and ALB each aimed to decrease their own bias throughout the analysis by regularly reflecting on their coding decisions in relation to the study's aim, and reviewing and recording these reflections at the beginning of each of their peer debriefing meetings. Because of his clinical background as a chiropractor, PCE also practised reflexivity during the course of conducting each interview by maintaining an awareness of how this professional background could bias his assumptions and communication with participants. Accordingly, he made a conscious effort not to stray from the interview guides or ask participants leading questions.

^a Adapted from the Consolidated Criteria for Reporting Qualitative Research (COREQ): <https://academic.oup.com/intqhc/article/19/6/349/1791966>

Additional file 6a Unadjusted and adjusted incidence rate ratios for the total number of opioid prescription fills over 12 months among patients treated for chronic non-cancer back or neck pain between January 1, 2014 and December 31, 2020 (n = 210)

Factor	Univariable	P-value	Multivariable	P-value
	Unadjusted IRR (95% CI)		Adjusted IRR (95% CI)	
Chiropractic care • Exposed (n=49) • Non-exposed (n=161)	0.69 (0.56-0.85) Reference	< 0.001	0.66 (0.52-0.83) Reference	< 0.001
Time (calendar year) ^a	1.03 (0.98-1.08)	0.331	1.00 (0.95-1.06)	0.868
Frequency of healthcare visits ^b	1.00 (0.99-1.01)	0.847	1.01 (0.99-1.02)	0.300
Age categories • 18-34 (n=26) ^c • 35-44 (n=38) • 45-54 (n=49) • 55-64 (n=51) • 65+ (n=46)	1.28 (1.02-1.60) 1.30 (1.02-1.64) 1.24 (0.97-1.59) 1.13 (0.90-1.41) Reference	0.032 0.031 0.091 0.288	1.24 (0.98-1.58) 1.23 (0.95-1.60) 1.13 (0.85-1.51) 1.13 (0.90-1.41) Reference	0.075 0.111 0.396 0.284
Sex • Male (n=89) • Female (n=121)	0.93 (0.80-1.09) Reference	0.372	0.92 (0.78-1.08) Reference	0.298
Smoking status • Smoker (n=76) • Non-smoker (n=134)	0.98 (0.83-1.16) Reference	0.820	0.92 (0.78-1.07) Reference	0.271
Obesity • Obese (n=37) • Non-obese (n=173)	1.04 (0.86-1.25) Reference	0.716	1.04 (0.81-1.35) Reference	0.739
Depression • Present (n=116) • Absent (n=94)	1.10 (0.94-1.28) Reference	0.240	1.12 (0.91-1.36) Reference	0.282
Anxiety • Present (n=89) • Absent (n=121)	1.04 (0.89-1.21) Reference	0.653	0.98 (0.82-1.18) Reference	0.831
Fibromyalgia • Present (n=22) • Absent (n=188)	0.96 (0.76-1.22) Reference	0.741	0.93 (0.72-1.20) Reference	0.574
Diabetes • Present (n=60) • Absent (n=150)	0.87 (0.74-1.04) Reference	0.123	0.89 (0.74-1.07) Reference	0.212
Cardiovascular disease • Present (n=136) • Absent (n=74)	0.94 (0.80-1.09) Reference	0.383	0.98 (0.82-1.16) Reference	0.793

CI confidence interval, IRR incidence rate ratio

^a Calendar year was measured at the patient's index visit date for a non-cancer spine pain diagnosis

^b Healthcare visits constitute general practitioner and chiropractic visits

^c 18-24 and 25-34 age categories were collapsed and recoded as one category because of a cell frequency of < 10 in the 18-24 group

Additional file 6b Unadjusted and adjusted incidence rate ratios for the total number of opioid prescription refills over 12 months among patients treated for chronic non-cancer back or neck pain between January 1, 2014 and December 31, 2020 (n = 210) ^a

Factor	Univariable	P-value	Multivariable	P-value
	Unadjusted IRR (95% CI)		Adjusted IRR (95% CI)	
Chiropractic care • Exposed (n=49) • Non-exposed (n=161)	0.38 (0.24-0.60) Reference	< 0.001	0.27 (0.17-0.42) Reference	< 0.001
Time (calendar year) ^a	0.89 (0.76-1.03)	0.113	0.82 (0.73-0.93)	0.002
Frequency of healthcare visits ^b	1.02 (0.99-1.05)	0.139	1.06 (1.02-1.09)	0.001
Age categories • 18-34 (n=26) ^c • 35-44 (n=38) • 45-54 (n=49) • 55-64 (n=51) • 65+ (n=46)	1.15 (0.68-1.95) 1.08 (0.54-2.18) 1.60 (1.04-2.46) 1.20 (0.76-1.90) Reference	0.612 0.823 0.031 0.429	1.01 (0.59-1.72) 0.88 (0.48-1.61) 1.05 (0.65-1.69) 0.92 (0.60-1.43) Reference	0.980 0.684 0.847 0.715
Sex • Male (n=89) • Female (n=121)	1.28 (0.91-1.79) Reference	0.153	1.18 (0.87-1.61) Reference	0.281
Smoking status • Smoker (n=76) • Non-smoker (n=134)	1.42 (1.01-2.00) Reference	0.042	1.28 (0.98-1.68) Reference	0.075
Obesity • Obese (n=37) • Non-obese (n=173)	0.89 (0.61-1.29) Reference	0.537	0.80 (0.52-1.23) Reference	0.302
Depression • Present (n=116) • Absent (n=94)	1.15 (0.83-1.60) Reference	0.409	1.23 (0.83-1.82) Reference	0.315
Anxiety • Present (n=89) • Absent (n=121)	1.03 (0.73-1.46) Reference	0.854	0.86 (0.61-1.20) Reference	0.360
Fibromyalgia • Present (n=22) • Absent (n=188)	1.22 (0.66-2.27) Reference	0.529	1.22 (0.63-2.34) Reference	0.558
Diabetes • Present (n=60) • Absent (n=150)	0.98 (0.68-1.43) Reference	0.933	1.03 (0.72-1.46) Reference	0.887
Cardiovascular disease • Present (n=136) • Absent (n=74)	1.04 (0.73-1.49) Reference	0.826	1.10 (0.75-1.61) Reference	0.635

CI confidence interval, IRR incidence rate ratio

^a Opioid refills were measured in 30-day equivalents

^b Calendar year was measured at the patient's index visit date for a non-cancer spine pain diagnosis

^c Healthcare visits constitute general practitioner and chiropractic visits

^d 18-24 and 25-34 age categories were collapsed and recoded as one category because of a cell frequency of < 10 in the 18-24 group

Additional file 6c Unadjusted and adjusted odds ratios for the likelihood of higher opioid dosage at baseline among patients treated for chronic non-cancer back or neck pain between January 1, 2014 and December 31, 2020 (n = 210)

Factor	Univariable	P-value	Multivariable	P-value
	Unadjusted OR (95% CI)		Adjusted OR (95% CI)	
Chiropractic care				
• Exposed (n=49)	0.77 (0.38-1.55)	0.466	0.61 (0.26-1.47)	0.270
• Non-exposed (n=161)	Reference		Reference	
Time (calendar year) ^a	1.12 (0.95-1.32)	0.192	1.05 (0.88-1.26)	0.600
Frequency of healthcare visits ^b	1.05 (0.99-1.10)	0.085	1.05 (0.98-1.12)	0.137
Age categories				
• 18-34 (n=26) ^c	2.08 (0.75-5.76)	0.160	2.52 (0.84-7.57)	0.099
• 35-44 (n=38)	1.65 (0.65-4.20)	0.290	1.92 (0.62-5.93)	0.255
• 45-54 (n=49)	1.65 (0.68-3.96)	0.266	1.29 (0.49-3.43)	0.608
• 55-64 (n=51)	1.07 (0.44-2.64)	0.880	0.86 (0.35-2.13)	0.740
• 65+ (n=46)	Reference		Reference	
Sex				
• Male (n=89)	2.37 (1.31-4.26)	0.004	2.40 (1.27-4.55)	0.007
• Female (n=121)	Reference		Reference	
Smoking status				
• Smoker (n=76)	1.59 (0.88-2.87)	0.125	1.50 (0.75-3.01)	0.254
• Non-smoker (n=134)	Reference		Reference	
Obesity				
• Obese (n=37)	0.72 (0.33-1.58)	0.407	0.56 (0.24-1.35)	0.197
• Non-obese (n=173)	Reference		Reference	
Depression				
• Present (n=116)	1.29 (0.72-2.31)	0.394	1.62 (0.78-3.36)	0.199
• Absent (n=94)	Reference		Reference	
Anxiety				
• Present (n=89)	0.57 (0.31-1.04)	0.065	0.38 (0.18-0.80)	0.011
• Absent (n=121)	Reference		Reference	
Fibromyalgia				
• Present (n=22)	0.74 (0.28-1.99)	0.557	1.16 (0.32-4.21)	0.817
• Absent (n=188)	Reference		Reference	
Diabetes				
• Present (n=60)	1.03 (0.55-1.95)	0.926	1.19 (0.57-2.48)	0.639
• Absent (n=150)	Reference		Reference	
Cardiovascular disease				
• Present (n=136)	1.03 (0.56-1.88)	0.923	1.37 (0.65-2.89)	0.407
• Absent (n=74)	Reference		Reference	

CI confidence interval, OR odds ratio

^a Calendar year was measured at the patient's index visit date for a non-cancer spine pain diagnosis

^b Healthcare visits constitute general practitioner and chiropractic visits

^c 18-24 and 25-34 age categories were collapsed and recoded as one category because of a cell frequency of < 10 in the 18-24 group

Additional file 6d Unadjusted and adjusted odds ratios for the likelihood of higher opioid dosage at 3-month follow-up among patients treated for chronic non-cancer back or neck pain between January 1, 2014 and December 31, 2020 (n = 210)

Factor	Univariable	P-value	Multivariable	P-value
	Unadjusted OR (95% CI)		Adjusted OR (95% CI)	
Chiropractic care				
• Exposed (n=49)	0.42 (0.18-0.99)	0.049	0.14 (0.04-0.47)	0.001
• Non-exposed (n=161)	Reference		Reference	
Time (calendar year) ^a	0.89 (0.70-1.12)	0.308	0.73 (0.57-0.94)	0.015
Frequency of healthcare visits ^b	1.06 (1.00-1.11)	0.046	1.11 (1.02-1.21)	0.015
Age categories				
• 18-34 (n=26) ^c	1.08 (0.34-3.41)	0.896	0.86 (0.22-3.38)	0.825
• 35-44 (n=38)	1.12 (0.40-3.11)	0.832	0.81 (0.23-2.83)	0.740
• 45-54 (n=49)	1.75 (0.70-4.38)	0.236	0.82 (0.28-2.46)	0.727
• 55-64 (n=51)	1.11 (0.43-2.88)	0.834	0.61 (0.21-1.74)	0.352
• 65+ (n=46)	Reference		Reference	
Sex				
• Male (n=89)	2.17 (1.15-4.09)	0.016	2.58 (1.24-5.34)	0.011
• Female (n=121)	Reference		Reference	
Smoking status				
• Smoker (n=76)	1.67 (0.89-3.15)	0.113	1.52 (0.73-3.19)	0.264
• Non-smoker (n=134)	Reference		Reference	
Obesity				
• Obese (n=37)	0.52 (0.20-1.32)	0.170	0.34 (0.12-0.99)	0.048
• Non-obese (n=173)	Reference		Reference	
Depression				
• Present (n=116)	1.82 (0.95-3.49)	0.069	3.29 (1.29-8.35)	0.012
• Absent (n=94)	Reference		Reference	
Anxiety				
• Present (n=89)	0.77 (0.41-1.46)	0.429	0.35 (0.13-0.90)	0.029
• Absent (n=121)	Reference		Reference	
Fibromyalgia				
• Present (n=22)	1.82 (0.72-4.61)	0.209	3.56 (1.02-12.42)	0.047
• Absent (n=188)	Reference		Reference	
Diabetes				
• Present (n=60)	1.11 (0.56-2.20)	0.763	1.36 (0.60-3.12)	0.463
• Absent (n=150)	Reference		Reference	
Cardiovascular disease				
• Present (n=136)	0.97 (0.50-1.85)	0.914	1.03 (0.47-2.28)	0.936
• Absent (n=74)	Reference		Reference	

CI confidence interval, OR odds ratio

^a Calendar year was measured at the patient's index visit date for a non-cancer spine pain diagnosis

^b Healthcare visits constitute general practitioner and chiropractic visits

^c 18-24 and 25-34 age categories were collapsed and recoded as one category because of a cell frequency of < 10 in the 18-24 group

Additional file 6e Unadjusted and adjusted odds ratios for the likelihood of higher opioid dosage at 6-month follow-up among patients treated for chronic non-cancer back or neck pain between January 1, 2014 and December 31, 2020 (n = 210)

Factor	Univariable	P-value	Multivariable	P-value
	Unadjusted OR (95% CI)		Adjusted OR (95% CI)	
Chiropractic care				
• Exposed (n=49)	0.33 (0.13-0.82)	0.018	0.14 (0.05-0.40)	< 0.001
• Non-exposed (n=161)	Reference		Reference	
Time (calendar year) ^a	0.94 (0.76-1.16)	0.573	0.78 (0.62-0.99)	0.041
Frequency of healthcare visits ^b	1.04 (0.99-1.10)	0.137	1.09 (1.01-1.18)	0.027
Age categories				
• 18-34 (n=26) ^c	1.26 (0.44-3.64)	0.670	1.13 (0.28-4.52)	0.863
• 35-44 (n=38)	0.88 (0.33-2.38)	0.800	0.65 (0.20-2.04)	0.456
• 45-54 (n=49)	1.25 (0.51-3.06)	0.625	0.59 (0.21-1.71)	0.335
• 55-64 (n=51)	0.69 (0.27-1.80)	0.448	0.38 (0.13-1.13)	0.081
• 65+ (n=46)	Reference		Reference	
Sex				
• Male (n=89)	2.06 (1.10-3.85)	0.024	2.46 (1.21-4.96)	0.012
• Female (n=121)	Reference		Reference	
Smoking status				
• Smoker (n=76)	1.60 (0.85-3.01)	0.145	1.42 (0.67-3.01)	0.358
• Non-smoker (n=134)	Reference		Reference	
Obesity				
• Obese (n=37)	0.91 (0.40-2.09)	0.831	0.67 (0.25-1.85)	0.443
• Non-obese (n=173)	Reference		Reference	
Depression				
• Present (n=116)	1.90 (0.99-3.63)	0.052	2.67 (1.14-6.26)	0.023
• Absent (n=94)	Reference		Reference	
Anxiety				
• Present (n=89)	1.01 (0.54-1.89)	0.971	0.55 (0.24-1.22)	0.141
• Absent (n=121)	Reference		Reference	
Fibromyalgia				
• Present (n=22)	1.40 (0.54-3.64)	0.490	2.24 (0.70-7.16)	0.174
• Absent (n=188)	Reference		Reference	
Diabetes				
• Present (n=60)	1.07 (0.54-2.12)	0.842	1.14 (0.51-2.56)	0.758
• Absent (n=150)	Reference		Reference	
Cardiovascular disease				
• Present (n=136)	1.25 (0.65-2.43)	0.503	1.36 (0.62-2.99)	0.446
• Absent (n=74)	Reference		Reference	

CI confidence interval, OR odds ratio

^a Calendar year was measured at the patient's index visit date for a non-cancer spine pain diagnosis

^b Healthcare visits constitute general practitioner and chiropractic visits

^c 18-24 and 25-34 age categories were collapsed and recoded as one category because of a cell frequency of < 10 in the 18-24 group

Additional file 6f Unadjusted and adjusted odds ratios for the likelihood of higher opioid dosage at 9-month follow-up among patients treated for chronic non-cancer back or neck pain between January 1, 2014 and December 31, 2020 (n = 210)

Factor	Univariable	P-value	Multivariable	P-value
	Unadjusted OR (95% CI)		Adjusted OR (95% CI)	
Chiropractic care				
• Exposed (n=49)	0.39 (0.17-0.94)	0.035	0.19 (0.07-0.57)	0.003
• Non-exposed (n=161)	Reference		Reference	
Time (calendar year) ^a	1.01 (0.83-1.23)	0.918	0.88 (0.71-1.09)	0.234
Frequency of healthcare visits ^b	1.04 (0.99-1.09)	0.129	1.10 (1.02-1.19)	0.018
Age categories				
• 18-34 (n=26) ^c	0.84 (0.29-2.46)	0.753	0.63 (0.18-2.18)	0.469
• 35-44 (n=38)	0.71 (0.27-1.88)	0.491	0.47 (0.15-1.45)	0.189
• 45-54 (n=49)	1.01 (0.42-2.42)	0.985	0.50 (0.18-1.42)	0.194
• 55-64 (n=51)	0.56 (0.22-1.42)	0.220	0.32 (0.11-0.87)	0.026
• 65+ (n=46)	Reference		Reference	
Sex				
• Male (n=89)	1.95 (1.05-3.64)	0.035	1.63 (0.81-3.31)	0.173
• Female (n=121)	Reference		Reference	
Smoking status				
• Smoker (n=76)	1.25 (0.66-2.35)	0.494	1.41 (0.67-3.00)	0.367
• Non-smoker (n=134)	Reference		Reference	
Obesity				
• Obese (n=37)	0.89 (0.39-2.02)	0.776	0.90 (0.31-2.64)	0.848
• Non-obese (n=173)	Reference		Reference	
Depression				
• Present (n=116)	1.30 (0.70-2.43)	0.409	2.16 (0.94-4.98)	0.070
• Absent (n=94)	Reference		Reference	
Anxiety				
• Present (n=89)	0.58 (0.30-1.10)	0.094	0.34 (0.15-0.78)	0.010
• Absent (n=121)	Reference		Reference	
Fibromyalgia				
• Present (n=22)	0.81 (0.29-2.32)	0.697	1.35 (0.20-2.78)	0.654
• Absent (n=188)	Reference		Reference	
Diabetes				
• Present (n=60)	1.04 (0.53-2.04)	0.921	0.82 (0.36-5.11)	0.626
• Absent (n=150)	Reference		Reference	
Cardiovascular disease				
• Present (n=136)	0.76 (0.40-1.43)	0.390	0.69 (0.32-1.47)	0.333
• Absent (n=74)	Reference		Reference	

CI confidence interval, OR odds ratio

^a Calendar year was measured at the patient's index visit date for a non-cancer spine pain diagnosis

^b Healthcare visits constitute general practitioner and chiropractic visits

^c 18-24 and 25-34 age categories were collapsed and recoded as one category because of a cell frequency of < 10 in the 18-24 group

Additional file 6g Unadjusted and adjusted odds ratios for the likelihood of higher opioid dosage at 12-month follow-up among patients treated for chronic non-cancer back or neck pain between January 1, 2014 and December 31, 2020 (n = 210)

Factor	Univariable	P-value	Multivariable	P-value
	Unadjusted OR (95% CI)		Adjusted OR (95% CI)	
Chiropractic care				
• Exposed (n=49)	0.52 (0.23-1.19)	0.123	0.22 (0.08-0.62)	0.004
• Non-exposed (n=161)	Reference		Reference	
Time (calendar year) ^a	0.96 (0.78-1.19)	0.705	0.82 (0.66-1.04)	0.097
Frequency of healthcare visits ^b	1.06 (1.01-1.12)	0.018	1.12 (1.03-1.21)	0.006
Age categories				
• 18-34 (n=26) ^c	1.04 (0.35-3.10)	0.938	0.69 (0.19-2.55)	0.582
• 35-44 (n=38)	0.76 (0.27-2.10)	0.590	0.54 (0.17-1.78)	0.313
• 45-54 (n=49)	1.25 (0.51-3.06)	0.625	0.62 (0.24-1.64)	0.336
• 55-64 (n=51)	0.69 (0.27-1.80)	0.448	0.46 (0.16-1.31)	0.146
• 65+ (n=46)	Reference		Reference	
Sex				
• Male (n=89)	1.36 (0.72-2.55)	0.339	1.22 (0.60-2.49)	0.591
• Female (n=121)	Reference		Reference	
Smoking status				
• Smoker (n=76)	1.14 (0.60-2.17)	0.694	1.16 (0.55-2.44)	0.692
• Non-smoker (n=134)	Reference		Reference	
Obesity				
• Obese (n=37)	0.42 (0.15-1.14)	0.088	0.38 (0.12-1.22)	0.103
• Non-obese (n=173)	Reference		Reference	
Depression				
• Present (n=116)	1.57 (0.82-2.99)	0.171	2.27 (0.99-5.24)	0.054
• Absent (n=94)	Reference		Reference	
Anxiety				
• Present (n=89)	0.90 (0.47-1.70)	0.737	0.58 (0.26-1.29)	0.179
• Absent (n=121)	Reference		Reference	
Fibromyalgia				
• Present (n=22)	1.16 (0.43-3.13)	0.773	1.35 (0.39-4.69)	0.633
• Absent (n=188)	Reference		Reference	
Diabetes				
• Present (n=60)	0.79 (0.39-1.61)	0.512	0.94 (0.42-2.12)	0.880
• Absent (n=150)	Reference		Reference	
Cardiovascular disease				
• Present (n=136)	0.83 (0.43-1.59)	0.575	0.85 (0.40-1.81)	0.669
• Absent (n=74)	Reference		Reference	

CI confidence interval, OR odds ratio

^a Calendar year was measured at the patient's index visit date for a non-cancer spine pain diagnosis

^b Healthcare visits constitute general practitioner and chiropractic visits

^c 18-24 and 25-34 age categories were collapsed and recoded as one category because of a cell frequency of < 10 in the 18-24 group

Chapter 8:

Conclusion of the Thesis

Summary of Findings

This thesis included six papers (two protocols [Emary et al., 2021; Emary, Oremus, Mbuagbaw, & Busse, 2021], two methodological reviews [Emary et al., submitted November 21, 2021; Emary et al., 2022], and two mixed methods studies [Emary et al., in press; Emary et al., submitted May 28, 2022]) on the quality and application of mixed methods in chiropractic research. In Chapters 3 and 4, we reviewed the biomedical and allied health literature and found that the quality of reporting (Chapter 3) and quality of conduct (Chapter 4) among chiropractic mixed methods studies were often poor. According to the Good Reporting of A Mixed Methods Study (GRAMMS) guideline, only half of the criteria for good reporting in mixed methods research were met across eligible studies. Similarly, we found that only 60% of the criteria for risk of bias were adequately addressed in these studies according to the Mixed Methods Appraisal Tool (MMAT). We found that publication in journals with an impact factor and more recent publication were significant predictors of higher methodological quality. We also found a strong, positive correlation between the GRAMMS and MMAT instruments, indicating that studies with a lower risk of bias (i.e., higher MMAT scores) were strongly correlated with higher reporting quality.

In Chapters 6 and 7, we undertook two mixed methods analyses on the association between chiropractic integration at the Langs Community Health Centre (CHC) in Cambridge, Ontario (Langs, 2022) and opioid use among patients with non-cancer spinal pain. We incorporated mixed methods quality of reporting (GRAMMS) and conduct (MMAT) standards into these two studies. Our main quantitative findings were that

receipt of chiropractic care was associated with a decreased likelihood of receiving an opioid prescription (Chapter 6), or fewer opioid fills and refills and reduced opioid dosages among patients already receiving long-term opioid therapy for chronic spinal pain (Chapter 7). Our qualitative findings suggested these relationships were affected by patients' self-efficacy and concerns about opioid-related harms, recognition of the limited effect that opioids may have on chronic pain, increasing stigma regarding use of prescription opioids, and accessibility of non-pharmacological (e.g., chiropractic, physiotherapy) treatment options.

Methodological Contributions

Our work addresses several knowledge gaps in the literature and has made important methodological contributions to the mixed methods research field. Our methodological reviews (Emary et al., submitted November 21, 2021; Emary et al., 2022) were the first to examine reporting quality and risk of bias among published chiropractic mixed methods studies. Our review on reporting quality (Emary et al., submitted November 21, 2021) was also the first in the mixed methods literature to explore correlation between reporting quality and risk of bias (i.e., the GRAMMS and MMAT instruments). Our mixed methods studies (Emary et al., in press; Emary et al., submitted May 28, 2022) were among the first to examine the relationship between chiropractic integration and opioid use among vulnerable patients with non-cancer spinal pain in a CHC setting, and the first to do so using a mixed methods approach. Our second mixed methods study (Emary et al., submitted May 28, 2022) was also one of the first to investigate whether the receipt of

chiropractic services is associated with reduced opioid use in patients already prescribed opioid therapy for chronic non-cancer pain.

From a methodological standpoint, our sequential explanatory mixed methods analyses (Emary et al., in press; Emary et al., submitted May 28, 2022) were the first in Canada to include comparison groups in answering the aforementioned research questions. In doing so, our investigations produced a higher level of evidence (i.e., level 2b versus levels 4 and 5) (Oxford Centre for Evidence-Based Medicine, n.d.), and were therefore a substantial improvement over previous research of chiropractic integration within Canadian primary care centres (Garner et al., 2007; Mior et al., 2013; Passmore, Toth, Kanovsky, & Olin, 2015; Emary et al., 2017; Manansala et al., 2019; Emary, Brown, Cameron, & Pessoa, 2019). Unlike other comparative studies from the United States (Corcoran et al., 2020; Kazis et al., 2019; Whedon et al., 2020; Acharya et al., 2022; Whedon et al., 2022), we also controlled for calendar year in our analyses to account for policy changes in opioid prescribing (Busse et al., 2017). This helped to more clearly delineate between a reduction in opioid use associated with access to chiropractic services versus confounding by policy change. Lastly, in using a mixed methods approach, our qualitative findings provided a richer understanding of the barriers and facilitators to opioid use and how chiropractic services may have been used by patients and general practitioners to reduce reliance on opioid prescribing for non-cancer spinal pain. Previously published studies on the topic of chiropractic care and opioid prescribing have lacked in-depth, contextual understanding because they have been exclusively quantitative in nature (Garner et al., 2007; Mior et al., 2013; Passmore, Toth,

Kanovsky, & Olin, 2015; Emary et al., 2017; Kazis et al., 2019; Manansala et al., 2019; Emary, Brown, Cameron, & Pessoa, 2019; Corcoran et al., 2020; Whedon et al., 2020; Acharya et al., 2022; Whedon et al., 2022).

Recommendations and Future Research

Our findings suggest there are opportunities for improvement in the methodological quality of mixed methods studies involving chiropractic research. In particular, we found that authors of chiropractic mixed methods studies often failed to adequately describe the mixed methods study design, as well as the limitations of combining qualitative and quantitative methods. In addition, considerations of reflexivity (i.e., the impact of research setting, or of the researchers themselves, on the qualitative methods and/or findings) were often poorly addressed. Methodological issues in reporting quality and risk of bias have also been found in reviews of mixed methods research involving other health care professions (O’Cathain, Murphy, & Nicholl, 2008; Bishop & Holmes, 2013; Brown, Elliott, Leatherdale, & Robertson-Wilson, 2015; Pluye et al., 2018; Kaur, Vedel, El Sherif, & Pluye, 2019; Fábregues et al., 2020). We have summarized the methodological areas most in need of improvement among published chiropractic mixed methods studies in Table 1. Our key recommendations for improving future chiropractic mixed methods studies are also summarized and provided in Table 2.

In mixed methods research, the integration of quantitative and qualitative methods can be achieved at three levels: (1) the study design, (2) methods, and (3) interpretation and reporting (Fetters et al., 2013). In our two chiropractic mixed methods studies

(Emary et al., in press; Emary et al., submitted May 28, 2022), we integrated quantitative and qualitative methods at the *study design* level by using a sequential explanatory mixed methods design. Our quantitative and qualitative methods were integrated (or ‘connected’ [Fetters et al., 2013]) at the *methods* level through our qualitative sampling (i.e., we selected a subsample of patients from our larger cohort to participate in follow-up interviews). Our interview guides were also developed (or ‘built’) from our initial quantitative findings (Fetters et al., 2013). At the *interpretation and reporting* level, we achieved integration by presenting our quantitative and qualitative results contiguously, in joint displays, and through narrative weaving. We also adhered to the GRAMMS guideline and MMAT criteria in the reporting and conduct of these studies. For a more complete review on achieving integration in mixed methods research, we refer readers to the paper by Fetters et al. (2013).

Our main findings from our two sequential explanatory mixed methods studies (Emary et al., in press; Emary et al., submitted May 28, 2022) were that receipt of chiropractic care was associated with decreases in opioid prescribing and long-term opioid use, and our qualitative findings suggested these relationships were multi-factorial. When combined with the results of other researchers (Garner et al., 2007; Mior et al., 2013; Passmore, Toth, Kanovsky, & Olin, 2015; Emary et al., 2017; Kazis et al., 2019; Manansala et al., 2019; Emary, Brown, Cameron, & Pessoa, 2019; Corcoran et al., 2020; Whedon et al., 2020; Acharya et al., 2022; Whedon et al., 2022), our findings suggest that further integration of chiropractic services into primary care centres may positively impact the opioid crisis. However, since observational studies are prone to selection bias

and residual confounding (Choi & Noseworthy, 1992; Cook, 2009), we recommend a multi-stage, mixed methods randomized controlled trial to validate our results. An updated systematic review and meta-analysis on chiropractic use and opioid receipt among patients with spinal pain is also needed (Corcoran et al., 2020).

In conclusion, through the dissemination of our primary and secondary research findings presented in this thesis, we aim to create awareness amongst the research community of published mixed methods reporting and quality of conduct standards (i.e., the GRAMMS and MMAT criteria), and to provide two exemplar mixed methods studies for prospective mixed methods authors. Further, we have made specific recommendations to authors and journals to improve the reporting and conduct of future chiropractic mixed methods research. Together, this work may lead to important changes in the quality of evidence generated from chiropractic mixed methods studies, with consequent implications for chiropractic policy, research, editorial, and clinical practice.

Table 1. Methodological areas most in need of improvement in chiropractic mixed methods research

Reporting Quality ^a		Risk of Bias ^b	
1.	Description of the mixed methods design in terms of the purpose, priority, and sequence of methods.	1.	Considerations of reflexivity (i.e., impact of the research setting, or of the researchers themselves, on the qualitative methods and/or findings).
2.	Description of any limitation(s) of one method in association with the presence of the other method.	2.	Consideration of the limitations with combining qualitative and quantitative methods.
3.	Description of the justification for using a mixed methods approach to the research question.	3.	Details of allocation concealment, instrument validation, or assessment of selection bias (for randomized, non-randomized, or descriptive study components, respectively).
4.	Description of the integration of qualitative and quantitative components.	4.	Details regarding the mixing or integration of quantitative and qualitative methods.
5.	Description of any insights gained from mixing or integrating methods.	5.	Adequacy of follow-up or response rates (for all study types) and use of standardized outcome measures (for non-randomized or descriptive study components).

^a Assessed using the Good Reporting of A Mixed Methods Study (GRAMMS) guideline.

^b Measured with the Mixed Methods Appraisal Tool (MMAT), version 2011.

Table 2. Key recommendations for improving the methodological quality of future chiropractic mixed methods studies

Recommendations for Authors
⇒ Chiropractors conducting mixed methods studies should undertake graduate-level training in mixed methods research or, at a minimum, collaborate with researchers possessing mixed methodological expertise.
⇒ Details on the inclusion of mixed methodologists should be made explicit in future publications.
Recommendations for Journals
⇒ Editors of journals within the chiropractic profession should endorse the use of, and require adherence to, mixed methods article reporting and quality of conduct guidelines, such as the GRAMMS and MMAT criteria.
⇒ Editorial review boards of chiropractic journals should incorporate mixed methods appraisal tools, such as the MMAT checklist, into the peer review process.
⇒ Chiropractic journals should cite well-reported and well-conducted mixed methods studies involving chiropractic research to serve as exemplars of good methodological quality for prospective chiropractic mixed methods authors.
⇒ Chiropractic journals should ensure they have at least one mixed methodologist on their editorial board.

GRAMMS = Good Reporting of A Mixed Methods Study, *MMAT* = Mixed Methods Appraisal Tool.

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