

PROTOCOL

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Healthcare provider knowledge, attitudes, beliefs, and practices surrounding the prescription of opioids for chronic non-cancer pain in North America: protocol for a mixed-method systematic review

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Abstract

Background: Evidence from diverse areas of medicine (e.g., cardiovascular disease, diabetes) indicates that healthcare providers (HCPs) often do not adhere to clinical practice guidelines (CPGs) despite a clear indication to implement recommendations—a phenomenon commonly termed clinical inertia. There are a variety of reasons for clinical inertia, but HCP-related factors (e.g., knowledge, motivation, agreement with guidelines) are the most salient and amenable to intervention aimed to improve adherence. CPGs have been developed to support the safe and effective prescription of opioid medication for the management of chronic non-cancer pain. The extent of physician uptake and adherence to such guidelines is not yet well understood. The purpose of this review is to synthesize the published evidence about knowledge, attitudes, beliefs, and practices that HCPs hold regarding the prescription of opioids for chronic non-cancer pain.

Methods: An experienced information specialist will perform searches of CINAHL, Embase, MEDLINE, and PsycINFO bibliographic databases. The Cochrane library, PROSPERO, and the Joanna Briggs Institute will be searched for systematic reviews. Searches will be performed from inception to the present. Quantitative and qualitative study designs that report on HCP knowledge, attitudes, beliefs, or practices in North America will be eligible for inclusion. Studies reporting on interventions to improve HCP adherence to opioid prescribing CPGs will also be eligible for inclusion. Two trained graduate-level research assistants will independently screen articles for inclusion, perform data extraction, and perform risk of bias and quality assessment using recommended tools. Confidence in qualitative evidence will be evaluated using the Grades of Recommendation, Assessment, Development, and Evaluation-Confidence in the Evidence from Qualitative Reviews (GRADE-CERQual) approach. Confidence in quantitative evidence will be assessed using the GRADE approach.

Discussion: The ultimate goal of this work is to support interventions aiming to optimize opioid prescribing practices in order to prevent opioid-related morbidity and mortality without restricting a HCP's ability to select the most appropriate treatment for an individual patient.

Systematic review registration: PROSPERO [CRD42018091640](https://www.prospero.org/registration/CRD42018091640).

Keywords: Clinical inertia, Clinical practice guideline adherence, Opioids, Chronic pain, Systematic review

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Background

The prescription of opioid analgesics represents a double-edged sword. On the one hand, opioid analgesics (e.g., morphine, oxycodone, fentanyl) have been shown to provide modest improvement in pain and function for patients with chronic non-cancer pain. On the other hand, prescription opioids may lead to opioid-induced algesia [1, 2], addiction, or diversion, particularly at high doses (e.g., ≥ 200 mg morphine equivalents/day) [3]. As such, prescription opioids are associated with serious and increasing public health problems, such as addiction treatment admissions and overdose death [4].

Opioid prescribing within the context of chronic pain management

In 2011, the United States Institute of Medicine concluded that chronic pain, defined as pain that persists longer than 3 months, or beyond the expected duration of healing [5], is a public health concern and should be treated as a disease itself [6]. While estimates vary depending on survey methodology, nationally representative data from Canada, the USA, Germany, and other European countries indicates that 20 to 30% of adults (≥ 18 years of age) suffer with chronic non-cancer pain [7–11]. The prevalence of chronic pain is higher among women [12] and ethnic minorities [13] and increases with age. Approximately 65% of community-dwelling seniors and 80% of older adults living in care facilities experience chronic pain, including cancer-related pain [14].

The goal of pain management is to decrease pain and improve function while monitoring for adverse effects [15]. In the late 1980s and early 1990s, the under-treatment of pain, including among patients with chronic non-cancer pain, garnered national attention in both the USA and Canada. A classic 1986 publication describing the treatment of chronic pain in 38 patients concluded that opioid pain relievers could be prescribed safely on a long-term basis [16]. Further, a letter to the editor of the *New England Journal of Medicine* asserted that the rate of addiction in patients receiving opioids was low [17]. This letter was heavily and uncritically cited as evidence that addiction was rare with long-term opioid therapy, many citing rates $\leq 1\%$ [18]. Despite low-quality evidence, these sources were widely cited to support the expanded use of opioid medication for the management of chronic pain [4]. By the late 1990s, healthcare providers (HCPs) were encouraged by pharmaceutical companies and medical boards to be more proactive in treating all types of pain (e.g., acute, palliative, chronic) to alleviate suffering, including the prescription of opioid analgesics at relatively high doses for long durations [19]. The potential adverse effects of long-term opioid use were under-appreciated and often based on beliefs that opioids were safe for extended use

in patients with chronic pain with no known dosing threshold. Opioid prescribing increased in a marked linear fashion until 2013 when it began to plateau in the USA [20] and Canada [21].

Trends in opioid prescribing morbidity and mortality

The past two decades have been characterized by a linear increase in the prescription of opioid medications. A twofold increase in the consumption of hydrocodone and fivefold increase in the use of oxycodone was observed in the USA between 1999 and 2011 [22]. Observational data show a mean increase from 180 mg morphine equivalents per person in the US population per year in 1997 to 710 mg per person per year in 2010 [23]. This corresponded with a fourfold increase in the sale of prescription opioids [23], a fivefold increase in drug treatment admissions for prescription opioids (from $\sim 20,000$ to $\sim 120,000$) [24], more than a twofold increase in emergency department visits related to pharmaceutical opioids [25], and a fourfold increase in opioid-related overdose [26]. Although there is an undeniable rise in the availability of illicit opioids [27, 28], it has also been argued that opioid-related mortality is directly associated with the increase in opioid prescriptions observed in Canada, the USA, Europe, the UK, Spain, France, and Australia [21, 29–31]. Beyond the direct association, prescriber adjustment and tapering of opioid analgesics have been associated with risk of non-medical use, morbidity, and mortality as individuals turn to illicit opioids in an attempt to manage their pain [32].

A systematic review of data from the USA and Canada identified three interacting factors associated with opioid-related mortality: (1) prescriber behaviors, (2) patient characteristics, and (3) systemic determinants [33]. Pertinent for this protocol, four ways that prescriber behaviors influence opioid-related mortality were elucidated. First, results from seven studies indicated that prescribing higher doses of opioids is associated with opioid-related mortality. Second, seven studies reported an association between more potent opioids, such as fentanyl, and opioid-related mortality. Third, 14 studies reported that the co-prescription of opioids with sedatives or more than one opioid was associated with the observed increase in opioid-related mortality. This was particularly relevant with the co-prescription of methadone which has a small window between therapeutic and fatal doses. Finally, eight studies reported that an increase in the number of opioid prescriptions played a role in opioid mortality through increased availability. The top quintile of prescribers was observed to issue opioid prescriptions 4.5 times more frequently than the next quintile and wrote the final prescription in 63% of opioid-related deaths [34].

Clinical practice guidelines for the prescription of opioid medication

Clinical practice guidelines (CPGs) have been developed by several countries, including the USA [35] and Canada [2], to support evidence-based prescription of opioid medication for the management of chronic non-cancer pain. A systematic review of opioid prescribing CPGs identified 13 guidelines reporting on recommendations for the prescription of opioids for chronic pain between 2007 and 2013 [36]. While there is between-guideline variability, clinical practice guidelines consistently recommend that HCPs (1) avoid doses ≥ 90 –200 mg per day, (2) acquire additional training prior to prescribing methadone, (3) recognize risk of fentanyl patches, (4) titrate cautiously, and (5) reduce doses by at least 25 to 50% when switching opioid [36]. Based on expert consensus rather than rigorous supporting evidence, CPGs also regularly support the use of risk assessment tools, written treatment agreements, and urine drug tests to mitigate risks.

Clinical inertia in the context of prescribing opioids for chronic pain management

Despite their widespread availability and strong evidence supporting the benefits of their use [37–39], there is a long history of poor uptake of CPGs for chronic disease management by HCPs, with many studies reporting rates of non-adherence at or exceeding 50% [40–42]. HCP non-adherence to CPGs is increasingly referred to as “clinical inertia” [43]. Practically speaking, clinical inertia refers to a HCP’s decision not to initiate, intensify, titrate, or stop treatment despite an indication and recognition of the need to do so. Clinical inertia has most commonly been studied within the context of managing chronic diseases, such as diabetes, cardiovascular disease, hypertension, and dyslipidemia. Within this area, it has been estimated that clinical inertia is responsible for up to 80% of myocardial infarctions and strokes within the context of sub-optimally treated hypertension, diabetes, and dyslipidemia [44].

Our team recently published a review of clinical inertia in the context of chronic disease management where we elucidated the factors associated with this behavior [45]. In brief, clinical inertia is influenced by HCP factors (e.g., knowledge, agreement with guidelines, cognitive biases, motivation), patient factors (e.g., sociodemographics, medical history, lifestyle factors, treatment adherence), and system factors (e.g., time constraints, resources, setting) [45]. System- and patient-level interventions are often mistakenly perceived as being more important or resulting in greater benefit than HCP-level interventions. This protocol will focus on HCP-related factors given that HCP influences (1) account for 50% of variability in clinical inertia [44], (2) are less well understood than system- and

patient-factors, (3) often require more sophisticated behavioral corrective interventions, (4) are particularly relevant given the difficult balance between under-prescribing within the context of pain management and over-prescribing within the context of aberrant use, and (5) partially address a priority identified by patients and clinicians who have taken part in a national chronic pain research priority setting process [46].

It is difficult to estimate the impact of clinical inertia on pain, opioid-related morbidity, and mortality because of the relative paucity of available data. Consistent with other chronic diseases, the available evidence suggests that HCP adherence to opioid prescribing guidelines is less than optimal [47]. For example, a survey of more than 200 physicians in Wisconsin reported that only 38% were aware of at least one clinical practice guideline for prescribing opioids in the management of chronic pain [48]. Similarly, an assessment of HCP behavior in a sample of 1300 physicians and residents in Massachusetts reported only partial compliance with national opioid prescribing guidelines (e.g., 43% had a controlled substance agreement, 34% provided > 2 early refills, 63% utilized urine drug tests) [49].

There are many reasons why HCPs deviate from CPGs. One obvious reason is insufficient knowledge. Many HCPs are unaware that evidence of long-term effectiveness for opioids is lacking [4] or that risks include hyperalgesia [50], androgen deficiency [51], and serious fractures from falls [52]. A study of more than 700 family physicians in Canada reported that only 40% of physicians correctly answered two of nine questions pertaining to knowledge of opioid prescribing [53]. Inadequate training and a consequent lack of self-efficacy (i.e., a belief in one’s own ability to personally affect change) are other reasons. More than 70% of 636 family physicians in the province of Quebec surveyed did not feel confident that they could properly prescribe opioids for chronic non-cancer pain, despite 75% of the sample having received continuing education on the topic within the previous year [54]. A similar study observed that 54% of primary care providers surveyed in Massachusetts did not feel sufficiently trained to prescribe opioids [55]. Large volume and inaccessibility of guidelines also contribute to HCP deviation from CPGs. A qualitative study of 12 pain physicians in Ontario identified excessive length and poor formatting as a deterrent to the implementation of the 2010 CPGs for the safe and effective use of opioids for chronic non-cancer pain [56]. An additional reason is fear; nearly 50% of 226 physicians surveyed in Wisconsin reported altering opioid prescribing practices (e.g., limiting refills, lowering dose, reducing prescribed quantity) due to fear of investigation by regulatory agencies [48]. This is also problematic as it may lead to under-treatment of pain or use of an

inappropriate opioid tapering schedule contributing to unnecessary suffering, such as aggressive tapering.

In summary, it is safe to assume that adherence to the current guidelines for the prescription of opioid medication for the management of chronic non-cancer pain will make no exception to the general observation that adherence to recommendations detailed in CPG is suboptimal, and would therefore benefit from interventions to improve adherence.

Objective of the proposed systematic review

To date, there has been no literature synthesis pertaining to factors associated with HCP clinical inertia in the context of prescribing opioid medication for chronic non-cancer pain. A systematic review of this nature is needed for at least four reasons:

1. To elucidate the factors associated with prescribing opioid analgesics in accordance with CPGs.
2. To explore the relative effectiveness of interventions intended to improve the uptake of CPG recommendations for the prescription of opioids to manage chronic non-cancer pain.
3. To guide the development of novel interventions to optimizing the prescription of opioid analgesics.
4. To identify gaps in knowledge pertaining to clinical inertia for the prescription of opioid analgesics.

Methods

Protocol reporting and registration

This review protocol was prepared in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analyses Protocol (PRISMA-P) guidelines [57] (refer to Additional file 1). The protocol is registered with Prospective Register of Systematic Reviews (PROSPERO; registration#CRD42018091640).

Structured clinical question(s)

1. What are the knowledge, attitudes, beliefs, and practices that HCPs hold regarding the prescription of opioids for chronic non-cancer pain?
2. Do knowledge, attitudes, beliefs, and practices pertaining to prescribing opioids for the management of chronic non-cancer pain differ by HCP characteristics (e.g., sex, discipline, duration of practice) or patient factors (e.g., sex, history of addiction)?
3. What is the prevalence of clinical inertia for prescribing opioids for the management of chronic non-cancer pain?
4. Have interventions been developed that have an impact on opioid prescribing behavior for the management of chronic non-cancer pain?

Data sources and search strategy

A preliminary search strategy will be created under the guidance of an experienced information specialist (BS; refer to Additional file 2). A second information specialist will peer-review the strategy prior to execution using the Peer Review for Electronic Search Strategies (PRESS) checklist [58]. Using the OVID platform, we will search Ovid MEDLINE® (1946 to April 23, 2018), including Epub Ahead of Print and In-Process & Other Non-Indexed Citations, Embase Classic + Embase (1947 to April 23, 2018), and PsycINFO (1806 to April 23, 2018). We will also search the Cochrane Library on Wiley and CINAHL (1981 to present) on Ebsco. The Joanna Briggs Institute EBP Database and PROSPERO (2011 to present) will be searched for completed systematic reviews.

Search strategies will incorporate controlled vocabulary for relevant themes (e.g., “Analgesics,” “Opioid,” “Health Personnel,” “Guideline Adherence”) and keywords (e.g., “opioid,” “physician,” “clinical inertia”). Vocabulary and syntax will be adjusted across databases. No language restriction will be imposed, but where possible, animal-only studies will be removed from the results. No study-specific filters will be applied given the wide range of study designs of interest.

Study eligibility criteria

Population

Our population of interest is HCPs who prescribe opioid medication (e.g., physician, dentist, nurse practitioner). Studies that include medical residents will also be eligible for inclusion.

Interest

Clinical inertia (i.e., barriers and facilitators of adherence to long-term opioid prescribing guidelines) for the management of chronic non-cancer pain. We also aim to capture interventions that have been conducted to improve adherence to opioid prescribing guidelines within the context of chronic pain.

Context

Primary and specialist care of patients with chronic non-cancer pain in North America.

Outcomes

HCP knowledge, attitudes, beliefs, and practices pertaining to opioid prescribing guidelines for the management of chronic non-cancer pain. HCP behavior will be coded for clinical inertia.

Designs

A range of study designs will be eligible. Survey and epidemiological, qualitative, and uncontrolled studies

reporting on facilitators and barriers towards implementing long-term opioid prescribing guidelines will be eligible given that such research can maximize the value of a systematic review to inform clinical practice, policy, and decision-making [59, 60]. Controlled studies, experimental designs, non-randomized controlled studies, and retrospective and prospective cohort studies that include a control group, including before-after studies, will be eligible for inclusion in order to evaluate the efficacy/effectiveness of interventions designed to improve adherence to long-term opioid prescribing guidelines.

The following inclusion criteria will be applied:

- Study involves the prescription of opioid medication for adults (≥ 18 years of age). We chose to focus on adults given that comparable guidelines have not been published for children and youth [61]. As such, practice and clinical inertia would likely be quite different for children/youth compared to adults.
- The study concerned at least one of the following: knowledge, attitudes, beliefs, or practices pertaining to long-term opioid prescribing for the management of chronic non-cancer pain.
- The study reported data from HCPs who prescribes opioid medication (e.g., physician, specialist (MD), dentist, pharmacist, nurse practitioner). Studies that include medical residents are also considered eligible for inclusion.
- The study reports on original data. Multiple reports of single studies will be handled avoiding duplication of source data.
- The study was conducted in North America. We chose this distinction because opioid-related prescribing practices, non-medical use, and harms are greater in North America than anywhere else in the world [62]. Differences in the organization of health systems, prescription practices, dispensing and medical cultures, and patient expectations have been proposed as factors that contribute to the differences observed [62].

The following exclusion criteria will be applied:

- The primary focus of the study pertains to non-medical opioid use (i.e., opioid abuse and dependence).
- The primary focus of the study pertains to the prescription of medication to prevent or manage non-medical opioid use (e.g., naloxone, suboxone, methadone). Studies focusing on the prescription of these medications will be eligible if they are prescribed specifically for pain management.
- Conference abstracts.

Screening and data extraction

Two trained graduate-level research assistants will independently screen titles and abstracts of all identified search results for potential inclusion. The reviewers will select all potentially relevant citations reporting on HCP knowledge, attitudes, beliefs, or practices regarding prescribing opioid medication for chronic non-cancer pain. In doubt, references will be included at the title and abstract level. Full-text publications of all potentially relevant articles, selected by either reviewer, will be retrieved and examined for eligibility. The reference management software Rayyan [63] will be used to remove duplicates and sort inclusions and exclusions. Agreement between reviewers will be quantified using the Kappa statistic [64] before proceeding to solve disagreements. Disagreements on inclusion and exclusion of articles between reviewers will be resolved by consensus or arbitration by a third reviewer (JAR) if necessary. The study selection process will be documented using a PRISMA flow diagram [65].

In duplicate, the same two reviewers will independently extract information from all potentially eligible studies using a pre-designed data extraction Excel spreadsheet. Interpreters will be enlisted to screen and translate non-English language studies as required. Two levels of extraction will occur. Limited extraction will be implemented for all articles that were identified as potentially eligible after the initial screening of titles and abstracts for inclusion and exclusion criteria and will include the following:

1. Journal article information (i.e., first author, journal, publication year).
2. Basic screening of inclusion and exclusion criteria as outlined in the “[Study eligibility criteria](#)” section.

The reviewers will then categorize the articles as “in” or “out” and list the reason for exclusion. Excluded articles will be listed in the PRISMA diagram, grouped by reasons for exclusion.

Following the brief extraction, full-data extraction of included articles will be completed independently by each reviewer. The following information will be extracted for each article:

1. Information on methodology (i.e., study design, length of follow-up, country, incentives offered)
2. Participant information (i.e., total sample size, recruitment method, defined sub-groups, provider discipline)
3. Details on the measures used (i.e., instruments used, intervention characteristics, method of delivery)

4. Outcomes: Similar to other systematic reviews of physician beliefs [66], knowledge, attitudes, beliefs, and practice will be extracted verbatim and coded in accordance with the 14 domains defined by the Theoretical Domains Framework [67, 68]. Inter-rater reliability of these categories will be assessed using the Kappa statistic [64].
5. Results of the study (e.g., response rate, missing data, handling of missing data, sub-groupings, proportion of HCPs endorsing beliefs along with range and confidence intervals).
6. Risk of bias. Risk of bias will be collected using validated tools, refer to the “[Risk of bias and quality assessment](#)” section.

Once completed, the full extractions will be compared across raters to ensure accuracy. Discrepancies will be resolved by an independent arbiter (JAR).

Risk of bias and quality assessment

The methodological quality and risk of bias of included studies will be assessed independently and in duplicate by the same two trained research assistants. Risk of bias in randomized trials will be assessed using a modified version [69] of the Cochrane risk of bias tool [70]. The domains assessed include random sequence generation, allocation concealment, blinding of participants and personnel, attrition, reporting bias, and other sources of bias. Each domain will be assigned a judgment of “high risk of bias” or “low risk of bias” [70]. Corresponding authors of studies assessed will be contacted for clarification when insufficient evidence is reported to assess risk of bias. No study-level summary judgment of risk of bias will be performed given that such summative judgments do not correspond with treatment outcomes [71].

Methodological quality of cross-sectional studies will be assessed using the “instrument for risk of bias in cross-sectional studies of attitudes and practices” available from Evidence Partners and contributed by the Clinical Advances Through Research and Information Translation (CLARITY) Group at McMaster University [72]. Five domains are assessed for cross-sectional survey studies, including representativeness of sample to the population of interest, adequacy of response rate, missing data, clinical sensibility, and reliability and validity of the instrument used. Each domain is assigned a judgment of “definite risk of bias,” “probable risk of bias,” “probable risk of low bias,” or “definite risk of low bias.” A table will be constructed that depicts risk of bias.

Methodological quality of cohort studies will be assessed using Joanna Briggs Institute checklist for cohort studies [73]. Eleven domains are assessed, including similarity of groups recruited, timing of exposure,

validity and reliability of exposure, identification of confounding factors, mitigation of confounds, validity and reliability of outcome measured, adequacy of follow-up, completeness of follow-up, appropriateness of statistical analyses. Each domain is assigned a rating of “yes,” “no,” “unclear,” or “not applicable.” A table will be constructed that depicts risk of bias.

Confidence in information obtained from qualitative studies will be assessed in accordance with recommendations made by the Cochrane Qualitative and Implementation Methods Group [74] using a multi-dimensional concept of quality that includes (1) clarity of aims and research question, (2) congruence between questions and methods, (3) rigor of sampling and data collection, and (4) overall conceptual depth and breadth are reflected in study design, process, and results. As recommended [74], information will be collected by having two independent raters appraise study quality using the 10-item Critical Appraisal Skills Programme (CASP; [75]) quality assessment tool for qualitative studies. Each item will be rated as “yes,” “no,” or “unclear.” Quality assessment will be depicted using a table.

Approach to evidence synthesis

Included studies will be categorized according to study design. Frequencies and percentages will be reported for categorical variables. Means and standard deviations (SDs) or median and interquartile range will be reported for continuous data as appropriate. The extracted proportions of studies that include the same category of knowledge, beliefs, attitudes, and practices will be pooled. A Q-test adapted for proportions will be used to test for heterogeneity of proportions [64]. As recommended [64], random effects models will be performed to account for the imperfect measurement of knowledge, beliefs, attitudes, and practices. The proportions from each study will be weighted by the size of the respective sample. If a single study uses several items to measure the same underlying construct (e.g., “prescribing guidelines are developed using populations that are not representative of the chronic pain presentations that I see in my practice”), then the most commonly used item will be utilized. Results will be presented as pooled proportions, 95% confidence intervals, range, and pooled frequencies for each category of knowledge, attitudes, beliefs, and practices. If sufficient data is obtained, results will be broken down by HCP characteristics (e.g., sex, discipline) to perform sub-group analysis. Sensitivity analyses will be performed on studies that are deemed “low risk of bias.”

If studies are identified that evaluate the effect of an intervention to change HCP adherence to recommendations in CPGs for the prescription of opioid medication, relevant statistics (e.g., F-values, means and SDs) will be

used to calculate standardized mean differences using formulae described previously [76]. A meta-analysis will be performed if ≥ 3 studies are identified that evaluate a theoretically and methodologically similar intervention [77]. Analytic computations will be performed using Comprehensive Meta-Analysis software (CMA; [78]). Evidence for publication bias will be assessed through visual inspection of a funnel plot, and fail-safe N_s will be calculated using Orwin's formula [79] with the recommended criterion of effect size of 0.20.

Assessing confidence in evidence

As per recommendations [74], the Grades of Recommendation, Assessment, Development, and Evaluation-Confidence in the Evidence from Qualitative Reviews (GRADE-CERQual) approach [80] will be used to assess confidence in synthesized qualitative results. The CERQual approach includes four components: (1) methodological limitations of individual studies, (2) relevance of the review question of individual studies, (3) coherence of review results, and (4) adequacy of data supporting a review result. Confidence in quantitative evidence will be evaluated using the GRADE approach [81].

Discussion

This will be the first knowledge synthesis to elucidate the factors associated with clinical inertia with respect to HCP guideline adherence for the safe prescription of opioid medication for the management of chronic non-cancer pain. The knowledge generated by this synthesis is vital for better understanding the concerns that HCPs have about prescribing opioid medications. Such knowledge will be used to elucidate theory-driven and evidence-based behavior change principles that specifically target the various facets of clinical inertia identified. Identified behavior change principles can be integrated into existing interventions that have proven effective (e.g., education) or used to develop novel interventions (e.g., education delivered using motivational communication—a broad set of evidence-based, patient-centered techniques designed to promote motivation for behavior change [82]). The ultimate goal of this work is to optimize opioid prescribing practices in order to prevent opioid-related morbidity and mortality without restricting a HCP's ability to select the most appropriate treatment for an individual patient.

Additional files

Additional file 1: Preferred Reporting Items for Systematic Review and Meta-Analyses Protocol (PRISMA-P) checklist. (DOCX 32 kb)

Additional file 2: Sample search strategy. (DOCX 15 kb)

Abbreviations

CASP: Critical Appraisal Skills Programme; CIHR: Canadian Institutes of Health Research; CPG: Clinical practice guideline; HCP: Healthcare provider; PRESS: Peer Review of Electronic Search Strategies; PRISMA-P: Preferred Reporting Items for Systematic Review and Meta-Analyses Protocol; PROSPERO: Prospective Register of Systematic Reviews

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Registration

This systematic review is registered with PROSPERO, an international prospective register of systematic reviews (registration #CRD42018091640), available at https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=91640.

Author's contributions

JAR, TSC, KC, DF, and PAP are members of the core investigative team and were involved in review conceptualization and design, refinement of clinical questions and methodologies, and development of data extraction tools. NB, JWB, LC, AI, and KLL are members of the study advisory committee and were involved in refinement of the clinical questions and methodologies and development of data extraction tools. BS is responsible for development, refinement, and implementation of the search strategy. JAR is responsible for coordinating the review. All authors will provide continued feedback throughout the review process and be involved in the interpretation of data and writing of the first manuscript. All authors reviewed, provided critical feedback, and approved this protocol.

Competing interests

The authors declare that they have no competing interests, financial or otherwise.

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