HEALTHCARE PROVIDER KNOWLEDGE, BELIEFS, AND ATTITUDES REGARDING OPIOIDS FOR CHRONIC NON-CANCER PAIN IN NORTH AMERICA: A SYSTEMATIC REVIEW

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Abstract

The aim of this review was to identify empirically supported barriers and facilitators for prescribing opioids for Chronic Non-Cancer Pain (CNCP) through a systematic review of qualitative literature. Six databases were searched from inception to June 3, 2019 for qualitative studies reporting on provider knowledge, attitudes, beliefs, or practices pertaining to prescribing opioids for CNCP in North America. Data were extracted, risk of bias rated, and confidence in evidence graded using Cochrane Confidence in the Evidence from Reviews of Qualitative research (CERQual). Constructs identified were coded using the Theoretical Domains Framework. Twenty-six studies reporting on 599 healthcare providers were included. Fourteen constructs were identified as barriers or facilitators to prescribing opioids for CNCP that fell within seven domains. Domains and constructs identified as barriers included: (1) Environmental Context, (a) patient-related salient events (e.g., overdose), (b) provider-related salient events (e.g., threat by patient), and (c) time constraints; (2) Emotion, (a) concerns over problematic use, addiction, dependence, tolerance, and side effects, and (b) regulatory scrutiny; (3) Knowledge; (4) Beliefs About Consequences; and (5) Beliefs About Capabilities. Domains and constructs identified as facilitators included: (1) Environmental Context, (a) lack of available non-opioid alternatives, and (b) institutional pressure; (2) Social Influences, (a) patient-provider relationship, and (b) patient-provider communication; (3) Goals; and (4) Knowledge on opioid prescribing tools. Understanding the barriers and facilitators that influence opioid-prescribing offers important insight into modifiable targets for interventions that can support providers in delivering care consistent with guidelines to manage CNCP, while minimizing risks.

Keywords: Chronic non-cancer pain; Opioid prescribing; Barriers; Facilitators; Systematic Review

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Chronic Non-Cancer Pain

Chronic non-cancer pain (CNCP) is defined as pain that persists beyond three months or the typical duration of healing,[1] and is considered one of the most prevalent, debilitating and complex medical conditions to manage. [2] The World Health Organization (WHO) incorporated chronic pain as a chronic disease in May of 2019 in the International Classification of Diseases (ICD-11). [3,4] While estimates vary depending on survey methodology, nationally representative data from Canada, the United States, Germany, and other European countries indicate that 20% to 30% of adults suffer from CNCP. [5-9] Chronic pain affects approximately one in every five Canadians, or about 6 million Canadians of all ages.[9] A national survey reported that more than 50% of those affected report having experienced moderate to severe pain for more than 10 years.[9] The prevalence of chronic pain is highest among women, older adults, ethnic minorities, and Indigenous peoples.[3,9-11] Chronic pain confers a significant burden on an individual's activities of daily living, family life, and employment, which can consequently increase psychological distress and reduce quality of life. [5,10,12]

Opioids to Improve Pain Management

The primary goal for pain management is to reduce pain and improve overall functioning and quality of life for people with CNCP.[13] Given the demonstrated effectiveness of opioids for moderate to severe acute pain, and for people with cancer-related pain,[14] opioid analgesics have been commonly prescribed to treat CNCP.[15,16] A low-quality evidenced paper from 1986 initially reported that long-term opioid prescribing can be used safely for pain management with few

adverse effects.[17] This paper was widely cited, leading to the inflation of prescription opioids to manage pain.[18]

Commonly prescribed opioids include codeine, fentanyl, hydromorphone, hydrocodone, methadone, morphine, oxycodone, and tramadol.[19] Canada is one of the largest consumer of opioids per capita worldwide when measured by defined daily doses, only second to the United States.[20] Observational studies reported a four-fold increase in the sale of prescription opioids,[21] five-fold increase in drug treatment admissions for prescription opioids (from ~20,000 to ~120,000),[22] two-fold increase in emergency department visits related to pharmaceutical opioids,[23] and four-fold increase in opioid-related overdose between 1997 and 2011.[24] While prescribing rates have evidenced a slight decline since 2011,[25] the prevalence of exposure to opioids has remained high with an estimated 226 million defined daily doses (6,246 per 1,000 population) of prescription opioids dispensed in Canada in 2016.[15] This significant increase of opioid prescribing has inevitably contributed to the opioid crisis across North America.[15,16]

Efficacy of Opioids for Management of Chronic Pain

While commonly prescribed, evidence for the benefits of opioid analgesics for the management of CNCP is modest (risk difference [RD] of achieving the minimally important difference [MID] in pain relief, versus placebo, is 12%).[26] Researchers suggest that there is no benefit to using opioids over nonopioid treatments when improving pain-related function and quality of life. [27,28]Additionally, guidelines report limited evidence suggesting benefit in prescribing long-term opioid use for the management of pain.[29] It is estimated that 8 and 12 patients would need to be treated with opioids, relative to placebo, for only one to experience improved pain control and function, respectively.[26]

Adverse Effects of Opioids

Adverse effects of long-term use of opioid therapy range from low- to high-risk life threatening events. Lower-risk side effects include constipation, vomiting, nausea, sedation, dizziness, drowsiness, pruritis, and dry mouth.[26] Prolonged use of opioids can induce higher-risk side effects that can impact a variety of organ systems within the body. These include respiratory (e.g., increased chance of sleep disordered breathing), musculoskeletal (e.g., osteoporosis and increased risk of fractures), cardiovascular (e.g., higher risk of myocardial infarction or heart failure), immune, and endocrine systems.[30]

In addition to serious health risks, long term opioid use can result in opioid misuse, dependence, opioid use disorder, accidental overdose, and death.[21 31] Research indicates that there is a positive correlation between increased prescribing rates of opioids and misuse, emergency room visits, overdose, and death.[32] An estimated 92% of people who experience problematic opioid use started by taking prescription opioids,[33] and three out of four individuals who use heroin report that their misuse of narcotics began with prescription opioids.[34] Hospitalization visits have increased over 30% from 2007 to 2014 due to opioid poisoning with over 13 hospitalization visits per day in 2014 compared to 9 visits per day in 2007 in Canada.[35] Deaths attributable to opioids are responsible for 58% of drug-related deaths in Ontario – one of the most populated provinces in Canada.[36] Death rates in this province have reached nearly 3,000 individuals (8.1 per 100 000 population),[37] with one in every 133 deaths attributable to opioids.[38] Nationally, the opioid-related mortality rate in 2016 was 7.9 per 100,000 population, with one in every 91 deaths being attributed to opioids.[39]

Results from a systematic review found that the co-morbidity of substance use disorder (SUD) and CNCP was broad, ranging from 3% - 48%,[40] with highest rates of SUD found in

individuals with recurrent visits to the emergency room seeking opioid refills.[41] Problematic opioid use is reported in 10% of patients with CNCP, and 5.5% of patients prescribed opioids for CNCP meet criteria for an opioid use disorder.[42] An evidence-based review reported that 3.3% individuals with CNCP became addicted to opioids, and 11.5% reported partaking in opioid misuse, such as drug hoarding.[43] A more recent systematic review reported that the prevalence of co-morbid SUD and CNCP was found to be as high as 59.9% compared to individuals who had CNCP without SUD (44.9%). Among the individuals diagnosed with co-morbid CNCP and SUD, opioid use disorder was the most commonly diagnosed SUD (74.7%).[44] Individuals who have co-morbid SUD and CNCP are also more likely to be prescribed opioids than those without a history of SUD[40] and are more likely to experience opioid misuse.[45]

Diversion

In addition to side effects associated with opioid use, individuals will often engage in aberrant drug-related behaviours, including diversion. Drug diversion is defined as the unlawful channelling of regulated pharmaceuticals from legal sources to the illicit marketplace (e.g., selling prescribed opioids).[28] Diversion of opioids has been known to occur at any point during manufacturing and distribution phases. For example, opioids can be diverted through theft at plants or in transit to a pharmacy during the preclinical phase or through theft, selling, or sharing drugs during the post clinical phase.[46] Diversion has also been identified through double doctoring, prescription fraud/forgery, street markets, thefts and robberies, and online purchasing.[28,47] Prescription drug diversion is estimated to be a $25 billion/year industry according to the Drug Enforcement Administration of Canada.[48] Results from a systematic review and meta-analysis reported that prescription drugs are primarily sourced through friends and family with active opioid prescriptions (57% of cases of diversion), with a smaller proportion being diverted

from legitimate medical sources, such as obtaining an excess supply of prescribed opioids (29% of cases of diversion).[47] In line with the increase of opioid prescribing rates from 1997 to 2011, rates of diversion have also significantly increased from 2002 to 2010, and plateaued between 2011 and 2013.[49]

Provider Attitudes Towards Opioid Prescribing

There is contradicting evidence towards provider confidence for prescribing opioids and their willingness to prescribe opioids to people with CNCP. Results from surveys suggest that a number of providers are confident in their ability to prescribe opioids,[50-52] however, as many as 82% of providers report reluctance to prescribe opioids, and in some cases, are not willing to prescribe opioids even as a third line therapy.[53-55]

Clinical practice guidelines have been established to assist providers with the management of opioid prescribing for people with CNCP,[29,56] however, results from a meta-analysis report that almost 40% of providers do not follow these recommendations.[57] Given the trade-off between risks and benefits, healthcare providers express understandable uncertainty regarding whether, when, and how to prescribe opioid analgesics for the management of CNCP. Other factors that contribute to provider uncertainty and discomfort to manage CNCP include inadequate level of education, concerns about patient harms associated with opioids use, cognitive biases, and regulatory scrutiny.

Education

Education is a common factor that is associated with provider confidence and preparedness to prescribe opioids for people with CNCP. Providers who felt that they received an adequate amount of training or education for the management of CNCP were more willing

and more likely to prescribe opioids to patients.[58] However, many providers strongly disagree with the statement that they received an adequate education surrounding treatment of CNCP during formal education.[59,60] For example, as many as 54% and 81% of physicians surveyed reported that they received insufficient education about chronic pain management during residency and medical school, respectively,[61] and only 17% of physicians reported receiving any specialty education on pain management.[62] Canadian medical undergraduate education programs offered an average of 16-hours on pain management in 2007.[63] Further, a 2011 review of medical curricula across North America indicated that despite advances in pain science, the amount of pain education for students is limited, variable, or fragmented.[64] These reviews reflect physician responses to perceived inadequate amount of education, and consequently impacts physicians concern and preparedness towards pain management.

Familiarity of guidelines may also impact provider confidence in prescribing opioids. Despite numerous publications of guidelines to help providers effectively care for patients with CNCP,[29,56,65-67] providers report that they are not sufficiently familiar with guidelines. Being aware of clinical practice guidelines is an integral component in pain management, as those who are familiar with guidelines are less likely to believe opioids are effective, have greater concerns surrounding opioid dependence, are more likely to screen their patients for depression and substance abuse, and have greater confidence in caring for patients with CNCP.[54] Approximately 41% of health care providers across five studies reported low levels of familiarity of guidelines, or recalled reading the guidelines but did not remember the content.[54,68-71] Being unfamiliar with guidelines may lead to greater provider reluctance and uncertainty towards prescribing opioids for patients with CNCP.

Concerns About Patient Harms With Opioid Use

Evidence from surveys indicate that providers believe opioids are effective in improving pain management.[51,53,62,72-75] Nevertheless, given the varied range of the prevalence of opioid misuse and problematic opioid use disorder, [40,41,43,44] providers often report an understandable level of concern, discomfort, and frustration over problematic opioid use and will often report these concerns as a barrier to prescribing opioids.[72]

Between 23% and 84% of providers believe that patients are at risk of abuse, dependence, or addiction if prescribed opioids, and fear that their prescriptions may contribute to one or all of these three. [54,61,68,76,77] The majority of these providers indicate that the potential for addiction acts as a barrier to prescribing opioids to these patients.[61] Additionally, 16% and 42% of providers mention that they would not prescribe opioids to a patient who has previously or currently abuses substances, respectively.[71] Other side effects, including cognitive impairment, drowsiness, and physical effects additionally contribute to provider's reluctance to prescribe opioids, with more than two thirds of providers reporting concerns that these side effects will adversely affect their patients. [53,61,75,76,78]

Given the increase of societal diversion,[47,49] providers are hesitant to prescribe opioids for their patients, in fear that they will contribute to opioid diversion within the community. [50,60-62,68,75] Providers have stressed the importance on learning about evaluating and managing the risks of diversion, in addition to abuse, misuse, dependence, and tolerance amongst individuals who use opioids, and believe this should be implemented in the education system.[75]

Cognitive Biases

Cognitive biases, or heuristics, are unconscious mental shortcuts that have been found to skew medical judgements and impact clinical decision making.[79] A critical review identified 19 different heuristics that have impacted clinical decision making, including the availability and representative heuristics, two of the most common heuristics seen in medical practice.[80]

Availability heuristic. Availability heuristics occur when the perceived probability of an event is influenced by the ease to which an instance or occurrence can be brought to mind.[81] Often, events more easily recalled are due to the salient emotion attached to the event or memory. Providers will often use these past salient memories to help make their current decision, subsequently impacting present provider decision making.[81] For example, a previous study reported that physicians whose patients experienced adverse events (e.g., hemorrhaging) after being prescribed warfarin medication were 21% less likely to prescribe the same medication for future patients than physicians whose patients did not experience adverse events.[82] These previous events were easily recalled as they were salient adverse events, and subsequently impacted their current prescribing behaviours and decisions. Conversely, physician's inability to recall negative outcomes reinforced their current prescribing behaviours, such that those who do not recall previous adverse events will not change their prescribing strategies.[83] In the context of opioid prescribing, physicians may become hesitant to prescribe opioids to current patients if they recall a salient memory of a previous patient experiencing adverse events when taking opioids, such as overdose or death.

Representativeness heuristic. This heuristic represents the judgement of a present situation based off the similarities to a category or a mental prototype.[81] This could include the degree to which the characteristics of a given sample is representative of the characteristics of a

specific category.[79] For example, health care providers can assess the symptoms and characteristics of an individual, and if these characteristics are representative of a specific diagnostic criteria, providers will often make the diagnosis. [80]

In some cases, providers will base the sample off a population. For example, they will evaluate how much a presenting case's situation is representative a previous group of patients who have demonstrated similar symptoms or patterns.[84] Specifically, in a qualitative study evaluating the representative heuristic in provider decision-making, one provider quoted "You remember past experiences of similar patients with similar conditions… You know what you're looking at."[83] Provider's confidence in the diagnostic prediction can arise from the strength of the similarity between the sample and the population, thus becoming more likely to diagnose the presenting individual with the same diagnosis as the previous population's diagnosis.[84] In the context of opioid prescribing, providers may be more quickly to diagnose a patient who has CNCP with the diagnosis of substance use disorder if they present similar characteristics to a previous group of patients that have been diagnosed with CNCP and substance use disorder, which can subsequently impact prescribing decision-making.

Regulatory Scrutiny

Given the increase of opioid prescribing regulations and media coverage on the opioid epidemic, providers express concern about the potential of regulatory scrutiny when prescribing opioids, especially stronger acting (schedule II) opioids.[53,55,71,74,78,85-87] Despite the support for the appropriate prescriptions of stronger acting opioids for people with CNCP,[88,89] providers express fear of legal investigation, legal action or punishment, or sanctioning by the state medical board due to the prescribing, resulting in a reluctance or restricting of opioid prescribing for their patients.[53,78,90] In order to avoid investigation, some providers will limit the number of

refills prescribed, prescribe opioids in a lower schedule, quantity, or dose, or abruptly cease the prescription of opioids for their patients, all of which can result in patients receiving unfavourable or neglected treatment for their pain.[55,86]

Rationale for the Current Knowledge Synthesis

It is evident that there are significant provider concerns regarding the prescription of opioids to patients with CNCP that can impact the level of care given to patients. Toye and colleagues[91] have qualitatively synthesized provider's experiences of prescribing opioids for CNCP but did not focus on barriers or facilitators. The purpose of this knowledge synthesis was to identify empirically supported barriers and facilitators for prescribing opioids for CNCP (without judgment to the appropriateness of prescribing practices) through a systematic review of qualitative literature. We used a qualitative synthesis to compare the themes across studies in order to gain an in depth understanding of provider's perceptions regarding barriers and facilitators of prescribing opioids for CNCP. The identification and understanding of factors that influence provider prescription of opioids for the management of CNCP may highlight targets for improving the development and delivery of initiatives to improve the alignment between evidence-based guidelines and practice.

Method

Data Sources and Search Strategy

A detailed description of data sources and search strategies can be located in the published protocol (PROSPERO registration# CRD42018091640).[92] In brief, a search strategy was developed by an experienced information specialist in consultation with content experts from the review team and subject to peer review by an independent information specialist prior

to execution. A systematic search was performed from inception to June 3, 2019 using five electronic databases: CINAHL, Embase, MEDLINE, PsycINFO, and Cochrane CENTRAL. We searched the Cochrane library databases and the Joanna Briggs Institute for relevant systematic reviews and PROSPERO for relevant registered protocols. Manual searches of the reference lists of relevant systematic reviews were performed to identify additional eligible studies.

Inclusion Criteria

Studies were eligible if they met the following criteria: 1) qualitative in design; 2) included healthcare providers with privileges to prescribe opioids; 3) explored attitudes, beliefs or behaviours; 4) focused on the prescription of opioids for CNCP; and 5) were conducted in North America. We focused on North America because opioid-related prescribing practices, non-medical use and harms are greatest in this area of the world.[93]

Exclusion Criteria

Studies were excluded if the primary focus pertained to the management of problematic opioid use. Conference abstracts and review articles were excluded.

Screening and Data Extraction

Two teams of research assistants worked in pairs to independently screen titles and abstracts for eligibility, and full-text publications of all potentially relevant articles. The reference management software Rayyan[94] was used to remove any additional duplicates and to sort articles based on inclusion and exclusion criteria. Disagreements on inclusion and exclusion of articles between reviewers were resolved by consensus or arbitration if necessary. Inter-rater agreement was quantified using Cohen's Kappa and percentage (%) agreement.

The same four reviewers used a standardized data extraction tool to extract data from eligible studies, such that two reviewers independently extracted data from each study. Data were extracted that pertained to: 1) study methodology; 2) prescriber characteristics; 3) patient characteristics; 4) measures used; 5) methodological characteristics that informed the assessment of risk of bias; and 6) results.

Risk of Bias and Quality Assessment

Risk of bias of included studies was assessed independently and in duplicate using the 10-item Critical Appraisal Skills Programme (CASP[95]) quality assessment tool. The CASP tool is the most commonly used tool in qualitative evidence syntheses in Cochrane and the World Health Organization (WHO) guideline development processes.[96] This tool identifies three sections of issues encompassing the 10 quality assessment items that need to be considered when evaluating a critical study: Issue A: Are the results of the study valid? Questions pertaining to issue A include: 1) Was there a clear statement of the aims of the research? 2) Is a qualitative methodology appropriate? 3) Was the research design appropriate to address the aims of the research? 4) Was the recruitment strategy appropriate to the aims of the research? 5) Was the data collected in a way that addressed the research issue? and 6) Has the relationships between researcher and participants been adequately considered? Issue B: What are the results? Questions pertaining to issue B include: 7): Have ethical issues been taken into consideration? 8) Was the data analysis sufficiently rigorous? and 9) Is there a clear statement of findings? Issue C: Will the results help locally? The question pertaining to issue C includes: 10) How valuable is the research?

Approach to Evidence Synthesis

Synthesis of data from qualitative studies was conducted using a thematic analysis approach.[97] In brief, two investigators independently coded text of all eligible studies to develop descriptive themes. Meetings were held to review descriptive themes and generate analytical themes until saturation of themes were reached. Previous research has argued that the synthesis of qualitative research may not be trustworthy, as it challenges the integrity of contributing primary studies, and concepts found in one article may not contribute to others. [98,99] In line with primary qualitative research, synthesizing qualitative research is required to have a sophisticated process of analysis and interpretation. That is, review authors are encouraged to be sensitive to the importance of context and to examine possible theoretical contributions when synthesizing research.[100] By maintaining this, synthesizing qualitative research does not depend on subjective interpretation but rather a subtle realist position, allowing qualitative research synthesis to be considered trustworthy.[100]

Analytical themes were coded according to the Theoretical Domains Framework (TDF)[101] to code barriers and facilitators for prescribing opioids to manage CNCP. Originally developed to understand health professional behaviour, the TDF distills 33 theories of behaviour change into 14 domains that provide a theoretical lens through which to view cognitive, affective, social, and environmental influences on behaviour.[101] Healthcare provider statements about barriers and facilitators were assigned to a relevant TDF domain or set of domains using a process described by Cane et al.[102] Selection of the most appropriate domain(s) was based on the topic and context of statement underlying qualitative themes. Two reviewers independently categorized barriers and facilitators. Discrepancies were resolved through consensus.

Assessing Confidence in Evidence

As recommended by the Cochrane Qualitative and Implementation Methods Group,[96] confidence in themes pertaining to healthcare provider facilitators and barriers to the prescription of opioid analgesics to manage CNCP was assessed in accordance with the Grading of Recommendation, Assessment, Development, and Evaluation-Confidence in the Evidence from Qualitative Reviews (GRADE-CERQual) approach.[103] Four components are considered when grading evidence using the CERQual approach: 1) risk of bias; 2) relevance of the contributing study's aims and content to the overall review question; 3) coherence and consistency of results across included studies; and 4) quantity of data supporting a review result. Confidence ratings started at "high" and were downgraded by one or more levels if there were concerns regarding individual CERQual components.

Results

Identification of Studies

We identified 12,253 citations and reviewed 383 full-text articles. Inter-rater agreement was substantial at the title/abstract stage, $k = 0.92$ (95.98%), and moderate at the full-inclusion stage, $k = 0.62$ (80.78%). Twenty-seven qualitative studies[104-130] met inclusion criteria. Two studies reported on the same data[129,130] resulting in 26 unique studies, refer to Figure 1.

Study Characteristics

Eligible studies enrolled 599 healthcare providers (487 primary care providers, 19 specialist physicians, 35 nurse practitioners, 27 pharmacists, 13 physician assistants, 12 medical residents, and six reported as "other"; refer to Table 1). In general, risk of bias among eligible qualitative studies was low (Table 2). The CASP criterion least commonly met was "has the

relationship between researcher and participant been adequately considered?" Table 3 depicts a summary of review themes and level of confidence that themes extracted reflect the true state of affairs.

Barriers to Opioid Prescribing

Knowledge of Opioid Prescribing and Pain Management

Seven studies[108,114,117,118,121,125,126] assessed healthcare provider perceived adequacy of formal education surrounding the prescription of opioid analgesics for the management of CNCP. A sample of 140 healthcare providers (108 primary care, 7 specialist physicians and 25 pharmacists) indicated that perceived inadequate education on the prescription of opioids for pain management received during formal education was a barrier to prescribing opioids (moderate confidence). Some providers took the initiative to seek additional training on their own volition.

> *"I didn't learn [information on pain management] in school, that is for sure. We took an advanced pharm class, and we discussed [pain management] in one lecture, but that was it. Isn't that ridiculous considering how many people we see in pain?"*[114]

> *"I've basically sought out my own training because it was not something that was taught to me in medical school or residency."* [117]

Beliefs About Capabilities

Nine studies[104,106,111,118-123] assessed healthcare provider self-efficacy when prescribing opioid analgesics to manage patients with CNCP. The sample consisted of 194 providers (176 primary care, 9 specialist physicians, 7 nurse practitioners, 1 physician assistant, and 1 other).

Most healthcare providers reported low confidence in their abilities to prescribe opioids to manage patients with complex CNCP cases (moderate confidence).

> *"It's awful, and I think it's demoralizing when you leave people in pain. That's just so disrespectful. I mean you're supposed to be a doctor, you're supposed to relieve pain and suffering, and you ignore the pain."* [104]

> *"[I am uncomfortable treating] people that you classify with chronic pain syndrome... In my experience, it is a black hole."*[106]

> *"It can be a tough call sometimes. When I do prescribe, I'm a little bit uneasy."* [123]

Some providers did not feel confident in their abilities to manage pain for patients with a previous or current history of substance use.

> *"Nobody here knows how to treat pain in anybody who has a history [of addiction] and already on something like methadone… nobody knows how to treat them… It's a mistake… promoting doctors like me to [treat pain and addiction]."*[104]

> *"I am hesitant to use opioids because the patient has a history of alcoholism, uses marijuana for pain currently, and has a history of opioid abuse."*[119]

Other providers were cautious or hesitant to prescribe opioids for older patients and were uncertain in their prescribing abilities for this specific population. They were uncertain with how these individuals would respond and felt that the potential harms outweighed the potential benefits.

> *"I just have a hard time prescribing opioids in my older patients. I get frightened with 80+ year olds; how are they going to respond?"*[122]

Emotion

Eight studies[106,112-114,116,117,122,123] that reported on 188 providers (157 primary care, 19 nurse practitioners, 1 physician assistant, 10 residents, and 1 other) yielded high confidence that concerns over problematic use, addiction, dependence, tolerance, and side effects were barriers to prescribing opioid analgesics to manage CNCP. Some providers were concerned that increasing opioid doses would contribute to habituation, misuse, or addiction. This resulted in reluctance to increase the dose or avoidance of prescribing long-term opioids altogether.

> "*I always try to use medications that aren't addictive first… I try to avoid using narcotics long term for that very reason."*[114]

> *"You never get an adequate level of pain control and you keep adding the doses up and they get habituated. An end point is very difficult to achieve."*[106]

> *"So what you're telling me is you need twice as many Percocet as usual because of X, Y, Z. I hear you. On the other hand, my training in chronic pain is that this is a very high-risk thing to do, and I am uncomfortable with that high of a dose."*[117]

Some providers feared tapering or discontinuing opioids due to the choices their patients might make in response to this. They felt that they needed to continue prescribing opioids in a controlled fashion in order to avoid the possibility that patients would resort to alternative drugs or illicit opioids.

> *"In others, stimulant use and alcohol use goes way up when I titrate down their opioids. So, prescribing opioids in a controlled fashion for their pain, despite their pain risk, seems to be less risky."* [123]

"I can see [patients] going out and getting something [opioids] off the street and then overdosing because they never have done that before."[116]

Three studies[105,114,116] that reported on 38 providers (21 primary care, 3 specialist physicians, 13 nurse practitioners, 1 physician assistant) indicated that concern over regulatory scrutiny was a barrier to prescribing opioids for CNCP (moderate confidence). Providers have expressed concern over the loss of their job or license if they inadvertently harm their patient. This concern was inversely related to willingness to prescribe opioids.

"*There's always a lurking fear… certainly someone could overdose on what I prescribed and then their family member could try to press charges… My license is on the line as well*."[116]

"Every week I deal with somebody, I admit somebody, and literally I have to distrust what they tell me because if I write down on the chart and order what they tell me to order, I'll kill them. And doctors have lost their jobs, on my ward, over that issue."[105]

Beliefs About Consequences

Four studies[104,114,116,118] that reported on 78 providers (50 primary care, 17 nurse practitioners, 9 specialist physicians, 2 physician assistants) yielded moderate confidence that concern regarding diversion of prescription opioids was a barrier to prescribing for CNCP. Some providers felt that they were partly responsible for diversion because they were prescribing opioids and were concerned about who was on the receiving end.

"When I discovered my patient was selling medications… it was a feeling of like, "I am a drug dealer, I've been a drug dealer for the community for three years." And that's a

shitty, shitty feeling…. It was the actual reality that like I was contributing to that [drug use]…"[118]

"God knows where those drugs [prescribed opioids] are going and who is dying from those drugs." [116]

"If you prescribe to a population where you think diversion is going on, you definitely have a responsibility. I also worry about who is getting the drug, is it my son? I mean, we are members of the society after all."[114]

In some instances, providers immediately ceased prescribing opioids after discovering that their patients were contributing to drug diversion.

"When I found out I was also prescrbing for her sister and her mother I realized that single handedly I was probably prescribing for all of New Haven, and immediately got them off."[104]

Environmental Context

Eight studies[104,115,117,120,123,127-129] that reported on 188 providers (169 primary care, 9 specialist physicians, 7 nurse practitioners, and 3 other) yielded high confidence that inadequate appointment durations did not allow for a thorough patient assessment which was a barrier to prescribing opioids for CNCP.

Some providers felt that documentation and formal assessments took up a sufficient amount of time. Some providers reduced the number of patient encounters or cut corners during assessments and documentation because of this.

"Time. They take up an inordinate amount of time… Trying to address what the pain is and the causes for it takes up an inordinate amount of time. Let me show you the

paperwork on one, all of the paperwork that had to go into this, the consult and everything…This is why you have to limit the number, you can't see a lot of them because there's so much paperwork." [104]

"It's racing from one patient to another, and sitting down and doing formal assessments is hard to work in… but formal assessment scales and these lengthy conversations that you would think family practitioners would sit down and spend all this time, this practice isn't set up to do that. It's set up to move 35 000 patient visits through a year." [115]

"… All this stuff that I'm supposed to be doing, taking a complete history, complete addiction history… But don't have time to do what I am supposed to do in terms of proper treatment, opioid treatment, so I cut corners a bit." [127]

Other providers felt that there was insufficient time allocated to provide education about pain management, narcotics, or alternative resources.

"And I think that this is tough in our busy practices, to actually take time to really educate people about pain, and that's why we offer this chronic pain program through our family health team… But you can imagine a physician that doesn't have access to that. You don't generally have the time to spend in sessions talking about how to manage pain." [123]

"A major issue that hasn't been brought up is time and resources. And there's no way you can consistently put 20 pounds of potatoes in a five-pound bag and, you know… I think everyone around the table is very conscientious, very aware of the risks. It's a matter of resources, time, that is not allocated, and that's the nature of medicine today, and it's the nature of primary care." [117]

"*Oh the time to address and withdraw narcotics… It just takes hours."*[129]

Data from three studies[106,114,122] that reported on 60 providers (48 primary care and 12 nurse practitioners) yielded high confidence that experiencing patient-related salient events (e.g., overdose or death of a patient) lead to providers becoming hesitant to prescribe opioids to manage CNCP. These previous experiences made them become more guarded when prescribing opioids.

> *"It is both your cumulative experience and, sometimes when you've had a negative experience, it really biases how you think. I've had an experience where my patient actually overdosed. She crushed up the oxycodone we were giving her in the hospital and shot it up through her central line and died. We've all had experiences with opioids being abused. This just happened to be a very dramatic thing that happened right under my nose. It just makes me more guarded, in terms of my practice, and the lengths people will go through to do harm to themselves with opioids."*[106]

> *"I had a patient die. He took the entire bottle, and the police came to see me because they found him dead with the empty bottle with my name on it, and I say to patients now, 'I am only going to give you a small amount, because I don't want you found dead with my name on your bottle'."*[114]

> *"One of my 96 year-old female patients got an opioid and went to sleep for three days after taking it. It really clouded her sensorium, so that was a negative experience for her as well as for me."*[122]

Data from three studies[110,124,129] that reported on 62 providers (50 primary care, 8 nurse practitioner, 2 pharmacists, 2 others) yielded high confidence that the experience of healthcare

provider-related salient events (e.g., assault or threats to healthcare providers) reduced overall willingness to prescribe opioid therapy.

Some patients would threaten self-harm if opioids were tapered or discontinued.

"He [the patient] did a lot of getting up and yelling at me, just kind of laying out his frustrations and basically saying I'm not caring for him and he'll end up dying and all this and that's on me."[124]

"One guy I am thinking of said, "When I have this much pain, I feel like killing myself. My uncle killed himself because no one treated his pain." So you get this barrier of 'don't touch it or you might be causing suicide,' you know, and we are so highly attuned to that."[124]

Other patients became physically or verbally violent, or verbally threatened their provider after their opioids were tapered or discontinued.

"When I worked at a hospital I actually had a situation like that where that the man had gotten mad and he two weeks later moved into the same community that I lived in… [I told] my babysitter to watch for this man."[110]

"I've had patients come in and say, 'I know where you live.'"[110]

"… I've had someone hit me with their cane. I've had my car keyed… I already had someone that wanted to kill me several years ago about this…"[129]

Facilitators of Opioid Prescribing

Social Influences

Data from 13 studies[104,105,107,110-113,115,117,118,122,123,129] that reported on 364 providers (306 primary care, 12 specialist physicians, 19 nurse practitioners, 10 physician assistants, 2 pharmacists, 10 residents, and 5 other) yielded moderate confidence in the observation that healthcare providers are more willing to prescribe opioids when they have a trusting relationship with patients. This trust stems from the amount of years spent with the patient, having open and honest discussions about the dangers of opioids, compliance with the prescribed frequency, and when behaviours expressed from the patient represented their level of pain.

> *"The first thing is obviously I know this patient for, let's say, several years, and I never detected any suspicious specific requests for narcotic pain medications."*[113]

> *"I could trust him because he wasn't always just increasing it; sometimes he would have less, and sometimes he would ask [for] Percocet instead of Vicodin, which generally many people find it stronger, and so if the pain was worse and [he would] ask for Percocet, and he would in fact ask me to switch him back to the Vicodin at some point, so I kind of trusted… that he was getting the medications that he felt he needed at the time."*[112]

> *"Her report to me is that the narcotics help and she has not asked for meds easily... She has been savvy about her use of the medications, about asking for the narcotics, and so I'm not concerned about prescribing for her. I trust her more than some patients."*[112]

"I've known some of my patients for over 20 years. Whether it's right or wrong, I guess I have a sense of whether they're someone that I feel I could or would appropriately use these medications."[115]

Some providers recalled times when they were unsure whether they could trust their patient. Providers became reluctant to prescribe opioids when they felt that they were being lied to or were skeptical of patient motivations, when they thought that patients misrepresented their pain, had an 'addictive personality', or evidenced history of substance use.

"We have all had experiences where patients have been misrepresenting their physical findings and there's been a discrepancy between what they report and what we see. And, unfortunately, it is a very distrusting relationship inherently."[105]

"Just the being lied to when you really trust a patient and you feel like you're trying to help them."[105]

"I think there is a distrust, or a suspicion, because it is so easy for the patients to put on a show, so you don't really know if the pain is true or false." [111]

"[I have patients who report that] their back hurts all the time, but then they jump right up onto the exam table, I don't get that." [122]

"He's concerned I don't give him the pain meds; I never quite trusted him, but after the positive toxin screens for cocaine and after discovering that he was addicted to heroin, I think that was the breaking point... I stopped doing my [iatrogenic] harm from care by cutting him off from narcotics. At least I wasn't contributing to his diversion or his abuse, but I haven't found a way to help him."[112]

Some providers aimed to treat each new patient individually and ensure that their level of trust was case-dependent by avoiding letting previous experiences bias perceptions and attitudes toward new patients.

> *"… Depends on my comfort level with that patient to begin with, my relationship with that patient is probably a direct correlative to my comfort with prescribing other medications and controlled substances."*[110]

> *"I really try to look at this as a fresh new patient. They have their own set of circumstances and trying to start fresh rather than, 'this is another drug-seeking patient that I have to deal with and another chronic pain patient.' So trying to go into every [visit] with an open mind and trying to give them the benefit of the doubt, because a lot of the times we don't do that, we are just suspicious right off the bat."*[111]

Four studies[107,108,117,121] that reported on 81 providers (63 primary care, 7 specialist physicians, 7 nurse practitioners, 1 physician assistant, and 3 other) provided low confidence that risk management tools for opioid prescribing facilitated open communication with patients around opioid prescribing.

> *"So this section I've showed the patients. I've also showed the patients changes in dose. So you know, 'You can see how we've changed over time.' So I have done that with them to… say, 'We've been stable for a while, then we went up [and] what happened here?'"*[104]

> *"Sometimes I use it as a strategy, the 200mg of morphine. That's what I tell the patient: 'you're at a high dose, you've gone above the recommended dose, we need to wean you off.'"*[108]

"It has been helpful to have more people [signing the management plan] once a year. Going over stuff with the patients, like, 'We're going to review your [pain registry] report, we're going to review your urine toxicology screener'."[107]

Some providers reported that these tools can create tension in the clinical interaction and may hinder conversations about opioid misuse.

"One of the downsides to [management plans]… the conversation [about substance use] goes down, it makes it more secretive… In some ways we can't talk about, 'Are you actively using [illicit drugs or alcohol]?' as much because [patients] know it's a violation of pain management agreements. So that does limit the way we can talk about it substance use."[107]

Goals

A sample of 74 providers (64 primary care, 7 nurse practitioners, and 3 other) reported that establishing treatment-related goals with patients (e.g., tapering opioids or promoting improvement in function) facilitates opioid prescribing (moderate confidence).[117,118,126,129]

"Each time I saw him, I would tell him whether I kept the dose the same or decreased it, the goal is that by this time, you're going to be off narcotics, you know, like very consistent messaging that this is not going to be a forever thing."[117]

"… the goal is not for his pain to… his pain probably won't be gone forever. He probably won't have the strength he had in his hands when he was 20 years old either. No matter what we do the goal is just to improve as much as we can and have him functioning as much as we can."[126]

"I establish ground rules with them and now I am even saying no early refills even for legitimate reasons…"[129]

Knowledge of Opioid Prescribing Tools

Two studies that reported on 20 providers (20 primary care) indicated that training and/or education sessions on the use of opioid prescribing tools facilitates opioid prescribing.[109,121] Confidence in this interpretation was rated low due to adequacy of studies and limited breadth of providers included.

"I don't tend to need to go back and look at all of the various medications for example, or which ones I should be starting with, because I've become familiar with it. I'm very familiar with the overdose risks for example."[121]

Environmental Context

Twelve studies[104,107,117,119,120,123-128,130] that reported on 254 providers (202 primary care, 9 specialist physicians, 11 nurse practitioners, 3 physician assistants, 25 pharmacists, and 4 other) yielded moderate confidence that lack of available non-opioid treatments (e.g., substance use treatment programs, pain clinics, community resources) promoted the prescription of opioids.

"Where's the support? Yeah, but where's the multidisciplinary approach? There aren't any community resources out there to help us... It takes some time to find a resource, for physio or for massage, all those other things that could help manage pain. And it takes some time to get those in place. There's not another great alternative pain-management mechanism out there, both pharmacological and even again, non-pharmacological. Often, [patients don't qualify] and they can't get access to a lot of the other supports."[123]

"I feel completely unsupported by the substance abuse treatment community. It just doesn't exist. There's nothing… It has not been developed in such a way to become more accessible, to be less stigmatized, to be effective."[107]

"We've pretty much tried everything by the time they're on chronic narcotics… That's an incredibly difficult one because most of the time, I don't have anything else to offer people, especially at [a safety net hospital] where we don't have behavioural therapy and other things… that other places may have."[117]

"She's stable and is a single mom working and has limited access to adjunctive therapies and physical therapies."[128]

"[Chronic narcotic therapy] creates most of our problems in life, in terms of satisfaction with how we work, stuff like that. But you really don't have many other options, really."[120]

Four studies reported that reported on 82 providers (67 primary care, 13 nurse practitioner, 2 others) felt that institutional pressures acted as a facilitator to the prescription of opioids to manage CNCP.[106,110,114,128] Coherence between studies was low with some studies reporting benefits to institutional pressure, such as institutional protocols offering structure when prescribing.

"… there is a policy… no new patient is going to get a controlled prescription… I tell my patient(s) that with our policy, I cannot do anything… There are a lot of benefits to the policies and the contracts."[110]

Other studies report detriments from institutional pressure. For example, the implementation of protocols promoted quick discharge times, which has pressured providers to

prescribe opioids. Institutional pressure from managers resulted in providers feeling pressure to prescribe opioids.[106,110,114,128]

> *"If a patient tells you that they are in pain and they are receiving opioids in the hospital, and I have a strong sense that this is a person who comes back to the hospital easily and regularly if something is not right, I'm more likely to make sure that the patient has adequate pain medicine for a reasonable duration of time to reduce the chance that they get readmitted just for pain alone."*[106]

> *"I get a call from the case manager who says would you be willing to consider the following: would you be willing to consider prescribing her methadone as a pain management medication and not as a methadone maintenance for her substance abuse disorder… Looking back now it's one of these… what the heck was I thinking kind of thing… I sort of felt like I was getting stiff-armed into things."* [128]

Institutional pressure was graded low confidence due to the low coherence between studies.

Discussion

Data was reviewed from 27 qualitative studies reporting on 599 healthcare providers and identified empirically supported barriers and facilitators to prescribing opioids for CNCP with no judgment made to appropriateness of prescribing. Empirically supported barriers included: 1) perceived insufficient education on pain management and opioid prescribing during formal education (moderate confidence); 2) low perceived self-efficacy for prescribing opioids for CNCP (moderate confidence); 3) concerns over problematic use, addiction, dependence, tolerance and side effects (high confidence); 4) concern over diversion of opioids (moderate confidence); 5) concern over regulatory scrutiny (moderate confidence); 6) inadequate duration

of appointments with patients (high confidence); 7) the experience of patient-related salient events (high confidence); and 8) the experience of provider-related salient events (high confidence). Empirically-supported facilitators for the prescription of opioids to manage CNCP included: 1) presence of a trusting patient-provider working alliance (moderate confidence); 2) lack of non-opioid alternatives (moderate confidence); and 3) goal setting with patients (moderate confidence). Insufficient evidence was observed to draw confident conclusions about the influence of institutional pressure or the use of risk management tools as facilitators of opioid prescribing.

Providers reported concerns over patient adverse effects, physical tolerance, and addiction which may represent relative risk-aversion, or an accurate appreciation for potential harms. Providers from a qualitative synthesis also expressed the concern of potential misuse and addiction when prescribing opioids; however, some providers preferred to risk the potential of opioid misuse rather than risk under-treating pain – a finding that is inconsistent with our results.[91] When measured quantitatively, a large proportion of providers consider potential misuse, tolerance, or overdose as barriers to prescribing opioids.[53,61,62,71] Chronic opioid use is associated with an increase in risk for developing opioid use disorder, overdose and death.[131-134] Given the potential harms associated with opioid use, providers are justified in their concerns and uncertainty when prescribing opioids for patients with CNCP. Multidisciplinary treatment clinics including substance use treatment approaches have been recommended by guidelines to assist patients who present with complex issues. [29,56] Unfortunately, clinics may not be readily available for patients, as demand often exceeds availability. Lack of availability may result from underfunding of clinics, lack of knowledge or awareness of such pain management clinics, or lack of community access to publicly funded allied health practitioners (e.g., psychologist,

occupational therapist). [135] Healthcare providers also lack readily accessible referral pathways. As such, formal linkages between providers and treatment clinics are needed to allow for rapid access and to provide a wide variety of treatment options for patients.[107]

Providers also reported concerns over drug diversion as a barrier to prescribing opioids for CNCP. Population-based estimates indicate that the prevalence of diversion within the community is 5%[136] with rates of diversion increasing as opioid prescribing rates increase.[137] Reasons for opioid diversion vary, ranging from lack of unawareness of the consequences of opioid diversion,[138] poor education about proper storage and disposal of opioids,[139,140] to aberrant medication behaviours or misusing opioids.[47] A number of interventions have been recommended to reduce drug diversion and help identify individuals who are at risk of drug diversion, including: Education sessions; urine screening; patient contracts; low dose initiation; gradual dose titration; prescription drug monitoring programs; increasing monitoring of patients; completing multidimensional assessments with patients before prescribing opioids; and ongoing monitoring.[141-143] Clinical evidence suggests that it is unclear whether these interventions have a direct impact on reducing opioid diversion.[141] As such, there is a need to develop empirically- and clinically-based interventions to mitigate opioid diversion. In addition to this, policies could also be targeted towards focusing attention on the management of the social supply of pharmaceutical drugs, which most commonly occurs through friendships or social groups (e.g., students in fraternity/sorority environments).[47]

Providers reported that negative patient-related salient events (e.g., patients who have overdosed)[106,114,122,128] and provider-related salient events (e.g., threat to provider)[110,124,129] impacted the delivery of care. Negative events are more salient, potent, and dominant than positive events,[144] and salient negative events can result in cognitive biases that impact the

delivery of medical care.[79,80] One such bias is the availability bias which occurs when providers recall and use salient past events to influence current decision-making processes.[83] Our results support the role of this bias as numerous providers recalled previously experienced negative salient events and used these events to influence their decision making practices surrounding opioid prescribing. Previous research has demonstrated similar findings in line with this, further supporting the notion that availability bias can influence clinical decision-making.[145] Experiencing negative salient events is also supported through the representativeness bias which involves evaluating a current patient relative to previous similar patients.[84] It would appear that negative salient events lead to the creation of a mental prototype of patients with CNCP being of high potential personal risk, which influences willingness to care for future patients with CNCP.[114] While biases can often be informative and helpful when making quick clinical decisions,[80] there may be unintended consequences (e.g., undertreating pain) when providers focus specifically on previously experienced negative events. As such, it may be important for providers to critically evaluate practice behaviours, and include both successful and unsuccessful experiences with opioid prescribing when treating future patients.[106] Providers may also benefit from learning cognitive behavioural techniques to challenge biases, such as cognitive restructuring to acknowledge negative or distorted thoughts and promote reasoned practice.[146] Previous medical centres have incorporated cognitive bias awareness into their curriculum and have found promising results, demonstrating that residents were able to recognize biases and create strategies to avoid making similar errors in the future. [147-149] It is important to continue to reinforce these skills throughout the medical career as these skills can be forgotten if not practiced regularly.

Sufficient evidence was synthesized in the present review to indicate with moderate confidence that concern over regulatory scrutiny was a barrier to prescribing opioids for CNCP. Providers endorsed fear of being found liable for patient overdose leading to death which could result in the potential loss of professional licensure.[105,114,116] Evidence from surveys distributed across various providers observed similar results, indicating that fear of being found liable for patient death or fear of legal investigation resulted in reluctance to prescribe opioids. [53 78 90] While regulatory scrutiny and sanction can be effective methods for managing opioid prescribing behaviour, regulatory policies vary by province, region, territory, state, and country, and can result in barriers to prescribing[150] as well as unintended consequences, such as patients not receiving necessary prescriptions and seeking illicit opioids.[151]

Providers expressed reluctance to prescribe opioids for CNCP due to insufficient formal education on opioid prescribing.[114,121,125] Canadian medical undergraduate education programs offered an average of 16 hours on pain management in 2007,[152] and estimates suggest that only 20% of physicians in the United States have received training about recognizing drug diversion or identifying signs of substance use disorders while in medical school.[153] Healthcare providers also reported a lack of confidence in their abilities to prescribe opioids to manage CNCP, specifically when prescribing opioids to patients without a medical explanation for pain[106,122] and when treating those who have co-morbidities (e.g., substance use disorder or mental illness).[104,119] Education and training in chronic pain is necessary in order to enhance provider knowledge, confidence, and self-efficacy surrounding chronic pain management, opioid prescribing, and identifying drug abuse and addiction among people with chronic pain.[154,155] Studies evaluating education interventions have been varied with some,[156] but not all[157] interventions demonstrating improvement in knowledge and self-efficacy surrounding chronic

pain management and opioid prescribing. Increased awareness of the necessity and importance of chronic pain education across North America has led to medical schools implementing various chronic pain educational models in their curriculum, such as immersive training modules, mandatory seminars, and preclinical conferences to help physicians practice "thoughtful prescribing." [158] While these models are being implemented, the effects of such education initiatives have yet to be determined. State Boards of Nursing also provide nurse practitioners with resources and information on the mitigation of opioid misuse and diversion, in addition to information pertaining to continuing education.[159] While the majority of state websites provided at least some information on the mitigation of opioid misuse and diversion, 35% of websites included little to no information on this topic. Further, only 43% of websites provided information for continuing education links and 15% provided information on mandatory education. Finally, the majority of websites were difficult to navigate, making it hard to retrieve necessary information pertaining to continuing education, drug misuse, and diversion for opioids. Websites could be improved to ensure easy navigation and easy access of information to assist nurses when dealing with opioids for people with chronic pain.[159]

Consistent with the notion that brief medical appointments are considered a barrier to managing patients with chronic disease in primary care,[160-162] providers felt challenged to adequately assess, monitor, and weigh the risks and benefits of chronic opioid therapy with patients during brief appointments in primary care.[104,123,127] The management of chronic diseases often require more time than physicians have available, which is a significant obstacle to the delivery of quality care.[161] This is interesting given that a recent cross-sectional study of physician behaviour in primary care reported that opioid prescriptions increase by 33% as the workday progressed and by 17% when appointments ran behind schedule.[163] It would appear that

brief appointments in combination with a perceived lack of availability to discuss non-opioid therapies, influences clinical decision making when prescribing opioids. A significant proportion of providers felt that there were little to no alternative therapies available to assist patients. Those who were aware of potential alternatives felt challenged to discuss non-pharmacological options during short appointment durations.[120] In support of this, a perceived lack of non-opioid therapies was identified as a facilitator for prescribing opioids.[117,120] Canadian guidelines for opioid therapy in chronic non-cancer pain highly recommend maximizing the use of non-opioid therapies.[56] Yet, access to such therapies are difficult due to long wait list times,[164] few multidisciplinary support programs available,[165] and lack of access to publicly funded allied health professionals (e.g., physiotherapy, psychology).[135] Evidently, there is a need to initiate financial incentives to accommodate for prolonged visits, to improve availability of non-opioid pain management approaches to better align opioid prescribing practices with practice guidelines, and to connect patients with the appropriate resources necessary.[166] One potential solution is for policy makers and insurance companies to ensure access and coverage is available for various non-opioid alternatives, and to allocate resources to support these models.[117]

The patient-provider working alliance was a robust facilitator of opioid prescribing and appeared to center around trust and safety. Providers reported that patient withholding or minimization of information (e.g., history of substance use) reduced willingness to prescribe,[105,107,111] while open communication and a trusting relationship facilitated opioid prescribing.[110,112] Providers reported using risk management tools, treatment goal setting, and shared decision-making to facilitate open communication with patients. Unfortunately, confidence in using opioid risk management tools may be misplaced given that there is not a rigorous body of evidence supporting their use. Canadian physicians raised concerns about the

2017 Canadian Opioid Guideline[56] for CNCP's lack of recommendation for opioid prescribing screening tools to help inform decision-making, as it was previously mentioned in the 2010 guideline. The more recent guideline made no such recommendations because there is no empirical evidence supporting the validity of opioid prescribing screening tools.[167] Preliminary evidence suggested that factors adding complexity or uncertainty (e.g., mental-health history, comorbidity) influence clinical decision-making surrounding opioid analgesics.[119] Longstanding patient-provider relationships and shared decision-making can reduce the impact of this complexity. Research suggests that physicians demonstrating compassion, having a strong working alliance, and portraying a patient-centered approach that involves patients in treatment decision-making have been shown to improve provider clinical decision-making, positive communication, patient health, and treatment adherence.[168,169] As such, it may be of benefit to provide physicians with training programs to improve or enhance working alliance skills with patients.[169] This may help to reduce various relational difficulties that can be found when working with patients who have CNCP.[170]

The provision of education about opioid prescribing and chronic pain management have been proposed as a method for mitigating the opioid crisis.[171,172] Enhanced education initiatives have been driven at the state, provincial, and federal levels. For example, Health Canada has committed more than $2 million CAD for the development of a curriculum in chronic pain management at the medical undergraduate level. While necessary, knowledge tends to be insufficient to promote behaviour change. Clinical practice guidelines have been published to assist in the judicious prescription of opioids for CNCP;[29,56,66,67] however, provider uptake of such knowledge is less than optimal despite awareness of guidelines.[57] Interventions that focus primarily on education only address one influence of the complex clinical decision-making

algorithm involved in the prescription of opioids for CNCP. Behaviour change techniques (e.g., as summarized in the behaviour change technique taxonomy[173]) based on established theories of behaviour change (e.g., self-determination theory[174]) that map onto the TDF[101] may be required to address the barriers identified in this review. In addition to education to address gaps in knowledge,[171] such interventions could include: 1) motivational communication to address issues pertaining to motivation and self-efficacy; [175,176] 2) training in communication and shared decision-making to improve the patient-provider relationship;[177,178] 3) connecting primary care providers with specialist physicians through programs such as "Project Extension of Community Health Outcomes Chronic Pain and Opioid Stewardship" or mentorship networks such as the "Atlantic Mentorship Network – Pain & Addictions";[179] 4) cognitive behavioural approaches to circumvent cognitive biases that may undermine the timely delivery or intensification of treatment (e.g., overestimation of provider's "gut-level" assessment of risk); and 5) improving availability and access to non-opioid pain management interventions. Two recent trials have provided encouraging evidence to indicate that multifaceted interventions can be developed and tailored to the local context in order to improve provider uptake of recommendations endorsed by opioid prescribing guidelines.[180,181]

Limitations of the Literature

There are some considerations that limit the strength of conclusions drawn from this review. Primarily, almost two thirds of providers in the review consisted of general practitioners and only 3% were specialists. Although general practitioners account for the majority of prescribers, this did not allow us to capture the entire range of providers who prescribe opioids and can limit generalizability if the aim is to extrapolate to specialist providers. Additionally, sufficient evidence was available to understand the individual contribution of barriers and

facilitators, but we were unable to assess the cumulative and complex interactions between influences. Future research is needed to elucidate complex relationships and move towards a multivariate understanding anchored in a framework of behaviour change (e.g., theoretical domains framework[65]), or models of behaviour change, such as theory of planned behaviour[182] or self-determination theory.[174] Such an understanding will better elucidate influences of behaviour change, improve hypotheses regarding mechanisms of behaviour change, and inform tailored interventions.

Limitations of the Review

First, we focused on evidence from North America. Given the socio-political nature of the opioid crisis, the results of this synthesis may not extend to other geographic regions. Second, studies that focused on opioid use disorder, and the prescription of opioid agonist and antagonist treatments were excluded. Results may not generalize to the prescription of opioid agonist treatments which are included in recent clinical practice guidelines. Third, this is the first time using the TDF model to identify behaviours of prescribing practices. As such, some prescribing behaviours did not directly match up to behaviours identified in the TDF model (e.g., patient-provider relationships). Alternative coding for the framework could be used to better align with provider prescribing practices. Nevertheless, the TDF model is empirically supported, along with the CASP and CERQual ratings, which strengthen the results of the review. Fourth, publications in the review range from 2007-2019 and the results have been amalgamated. Given that prescription opioid rates have plateaued around 2011, this may have an effect on results identified in the review. Despite this concern, over half of publications in the review including more than two thirds of the sample size have been published within the last three years, highlighting the recency of the review and potential accuracy of provider beliefs. Finally, the

focus of this review pertained to prescribing opioids rather than the appropriateness of opioid prescribing (i.e., alignment of prescribing with clinical practice guidelines) due to the limited literature available on appropriate prescribing. As such, some facilitators to prescribing may represent barriers to appropriate prescribing. For example, a lack of opioid alternatives facilitates opioid prescribing, yet can be considered a barrier to the appropriate prescription of opioids for individuals with CNCP.

Conclusion

Healthcare providers have an ethical responsibility to work with patients to manage CNCP, and such management may include chronic opioid therapy. Several patient-related (i.e., concern over adverse effects, tolerance, and addiction), provider-related (i.e., knowledge, self-efficacy, concern over regulatory scrutiny), and environmental (i.e., salient events, inadequate duration of appointments) barriers to prescribing opioids for CNCP were identified, whereas facilitators pertained primarily to the patient-provider relationship and insufficient availability of non-opioid alternatives. Solutions may involve additional education, mentoring or support from experts, ensuring that regulators apply appropriate scrutiny consistent with best evidence, guidance for providers on how to best interact with challenging patients, improving accessibility to non-opioid treatments for CNCP, and ensuring that providers understand the established risk factors for various adverse events. The use of patient decision-aids for opioid prescribing may ensure better concordance between prescribing decisions and patient's values and preferences, and likely improve communication and the prescriber-patient relationship.

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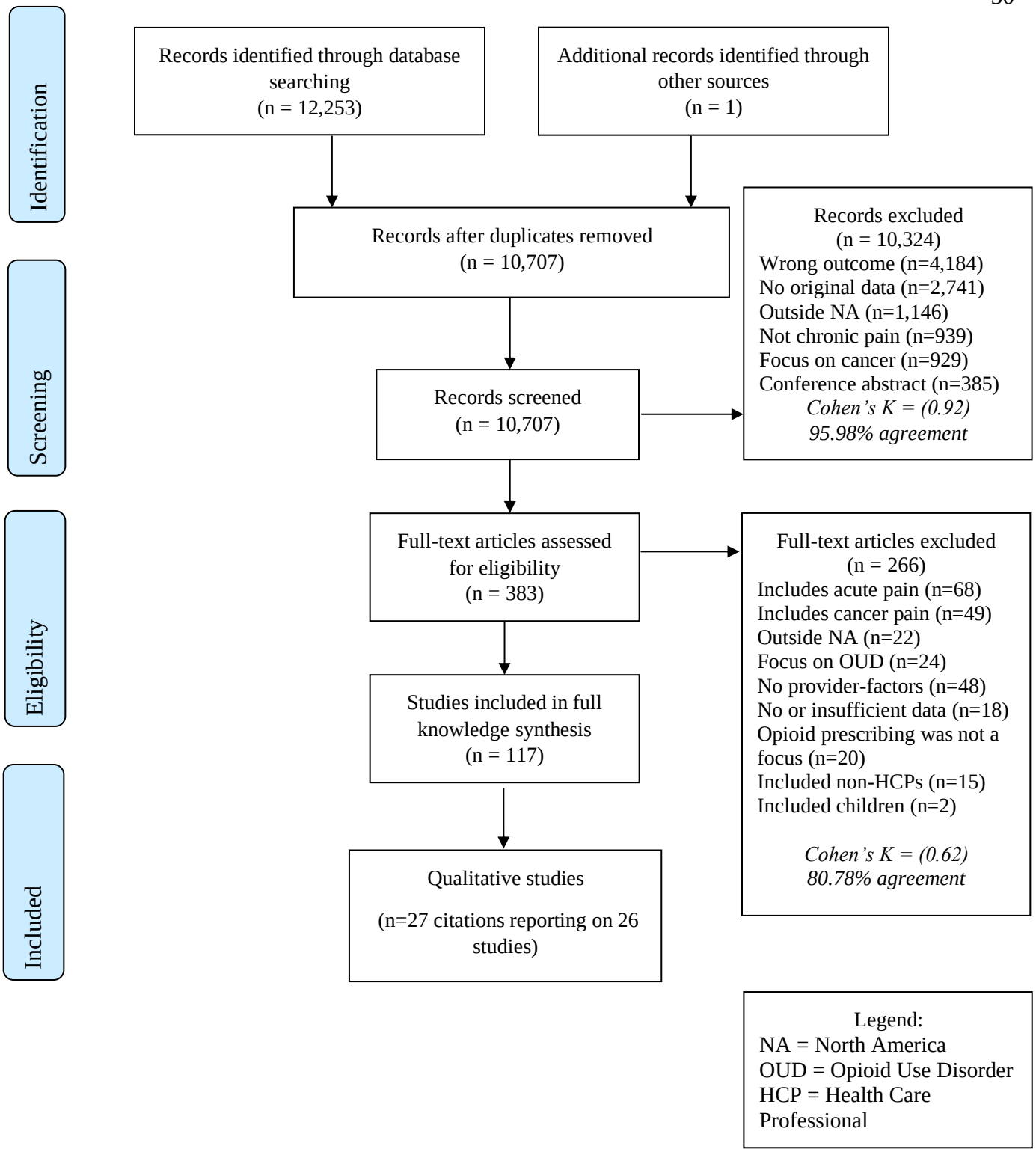

Figure 1

Flow Diagram Depicting Article Inclusion and Exclusion Along with Reasons

Table 1

Study Characteristics of Qualitative Studies

First Author (year)	Provider Characteristics	Objective of Interview	Type of Interview/ Qualitative Analysis	Constructs	Themes Relating to Opioid Prescribing	Author Implications
Barry (2010)	N=23 Internal medicine (n=10); infectious disease (n=4), addiction medicine (n=3), psychiatry (n=2), FM (n=1), did not report (n=3) Incentive: None	Examine attitudes and experiences about treating CNCP	Semi-structured/ Grounded Theory	Self-efficacy managing pain with opioids; concerns for society (diversion); short appointment duration; alternative resources; patient-provider relationship	(1) Physician factors: lack of expertise in treating pain with or without opioid addiction and/or co-existing disorders; interest in pain management, aberrant behaviours in patients, frustration of prescribing opioid analgesics, benefits of opioid agreements and continuity of care. (2) Patient factors: physician responsiveness to patients' pain, fear of addiction, concern about cost of specialty pain management, patient motivation. (3) Logistical factors: barriers of pain management referrals, addiction referrals, diagnostic workup, ancillary staff, time, and insurance coverage	To incorporate interventions into medical education to improve provider knowledge and self-efficacy in treating patients with CNCP.
Buchman (2016)	N=6 FM (n=1), internal medicine (n=2), psychiatry (n=3) Incentive: None	Examine how adults with CNCP negotiate trust and demonstrate trustworthiness with clinicians.	Semi-structured/ Grounded Theory	Fear of professional sanction or liability; patient-provider relationship	(1) Little trust in the patient due to previous lies. (2) Complicated clinical patient-practitioner relationships.	To have physicians adopt the role of epistemic humility in order to demonstrate trustworthiness and place trust wisely.

First Author (year)	Provider Characteristics	Objective of Interview	Type of Interview/ Qualitative Analysis	Constructs	Themes Relating to Opioid Prescribing	Author Implications
Calcaterra (2016)	N=25 GP (n=25) Incentive: None	To understand physicians' attitudes, beliefs and practices towards opioid prescribing during hospitalization and discharge	Semi-structured; open ended/ Mixed inductive and deductive approach	Fear for patients; institutional pressure; patient-related salient events; self-efficacy managing pain with opioids.	(1) Low confidence in prescribing opioids for CNCP and perceived limited success of managing CNCP with opioids. (2) Opioid prescribing shaped by personal experiences due to limited training. Adverse experiences (e.g., patient overdose or suspected diversion) resulted in conservative prescribing. (3) Opioids can improve unmanaged pain and prevent extended hospitalization, thus improving hospital efficiency.	(1) Management strategies (i.e., CPG-based opioid dose adjustments) are needed; involving the patient in the decision to temporarily increase their opioid dose may improve patient perceived pain control; close communication between the hospitalist and GP can help with uncertainty. (2) Focusing on successful rather than negative opioid prescribing outcomes may lead to less restrictive and more thoughtful prescribing practices; standardizing opioid prescribing to protect physicians from medico-legal consequences could lessen fears about prescribing. (3) A delicate balance between the potential benefits and drawback of using opioids may improve efficiency Overall implication: The development of evidence based strategies to promote optimal opioid prescribing for the management of acute exacerbations of chronic pain among hospitalized patients may benefit both hospital providers and patients who have a mutual goal for safe and effective pain relief.
Chang (2017)	N=23 GP (n=18); NP (n=4), PA (n=1)	Capture experiences interpreting and implementing guideline	Semi-structured/ Content analysis method	Alternative resources; patient-provider relationship;	(1) Benefits and consequences of guidelines on the clinician-patient relationship (i.e., increase honest communication when used as a tool, but can reduce trust when the focus is on risk management strategies)	(1) Educate about use of treatment agreements and urine tests to facilitate open conversations about substance use and addiction.

First Author (year)	Provider Characteristics	Objective of Interview	Type of Interview/ Qualitative Analysis	Constructs	Themes Relating to Opioid Prescribing	Author Implications
	Incentive: $50 gift card	recommendations for patients with CNCP and substance use.		patient-provider communication	(2) Provider concern about lack of substance use treatment plans available for patients	(2) Sustainable, formal and long-term alliances between primary care settings and substance use treatment programs are needed.
Chang (2016)	N=12 Anaesthesia (n=6); GP (n=5), surgeon (n=1) Incentive: None	Assess experiences, perspectives and attitudes toward the Canadian Opioid Guideline, elicit barriers and facilitators.	Semi-structured interview guide with open-ended questions/ Thematic analysis of verbatim transcripts	Patient-provider communication; education	(1) Positive attitudes but limited use of CPG. (2) Contrasting views about the 200mg watchful dose. (3) Inconsistencies in recommendations: Intervals of urine drug screening and pain severity-specific recommendations (4) Format: Guideline needs to be more user-friendly. (5) Need to improve awareness and use of CPG.	Future iterations may wish to reconsider: to validate or revise the 200mg/d watchful dose; more details regarding urine drug screening; and consideration of pain severity specific recommendations.
Clark (2007)	N=14 FM=14 Incentive: None	To determine family practice provider views of how to improve CNCP management in primary care.	Delphi panel/ Independent identification of themes from authors followed by comparison and resolution of conflicts	Education on tools	(1) The need for a physician CPG took kit with information on opioid prescribing. (2) Change in the way patients obtain monthly medications. (3) Improvement in patient self-management education and increased access to both providers and alternative interventions. (4) The importance of a nurse care manager to collaborate with providers and patients.	Further development of a “Chronic Care Model” may be a useful way to improve both provider and patient challenges in achieving adequate management of CNCP.

First Author (year)	Provider Characteristics	Objective of Interview	Type of Interview/ Qualitative Analysis	Constructs	Themes Relating to Opioid Prescribing	Author Implications
Click (2018)	N=32 GP (n=22); Osteopath (n=2); NP (n=4); Pharmacy (n=2), Other (n=2) Incentive: None	Determine what factors lead to prescribing controlled drugs for CNCP through the use of focus groups.	Semi-structured/ iterative process; transcripts combined and compared analysis of transcripts	Institutional pressure; provider-related salient events; patient-provider relationship	(1) Prescriptions have reduced since 1990s. (2) Comfort with patient, truthfulness, pain contracts, access to alternative therapies and personal safety concerns influence prescribing. (3) Lack of PDMP integration in electronic record is a barrier to use. (4) Concern of prescribing controlled drugs to women of childbearing age	Recommendation pertaining to theme 4: Prescribers should assess the possibility of pregnancy and discuss a birth control plan before initiating opioid therapy. The risk of pregnancy should be assessed at each visit and prior to any refill for long term therapies.
Desveaux (2019)	N=22 FM (n=22) Incentives: None	Understand perceived barriers and facilitators to guideline-adherent opioid prescribing.	Semi-structured/ Content analysis	Patient-provider relationship; self-efficacy managing pain with opioids; fear for patients; short appointment duration; alternative resources	(1) Fear of negative patient consequences stemming from physicians prescribing opioids (2) Provider's self-efficacy towards prescribing and patient-provider relationships play a role in physician's beliefs about their practicing capabilities (3) Behavioural regulation strategies to monitor opioid prescribing: providers report a lack of available non-opioid alternative resources (4) Professional role and identity while prescribing opioids: Struggle to balance the need to treat pain with potential harms associated with over-prescribing opioids.	a) Nonpharmacological interventions that connect patients in need with the support that may benefit them is warranted; b) There is a need for interventions that develop capacity amongst health professionals to communicate effectively about opioids with patients and other professionals. c) Solution-based strategies to support improved prescribing and management of opioids is needed (and can be used by moving beyond guideline disseminations and general education).

First Author (year)	Provider Characteristics	Objective of Interview	Type of Interview/ Qualitative Analysis	Constructs	Themes Relating to Opioid Prescribing	Author Implications
Elder (2012)	N=18 GP (n=10); PA (n=8); Incentive: None	Understand differences in pain management among adults with CNCP who are and are not prescribed opioids	Semi-structured/ Transcribed and entered into Nvivo 8 qualitative software	Patient-provider relationship; self-efficacy managing pain with opioids;	(1) Skepticism of patient motives was primary barrier to prescribing opioids. (2) Lack of communication between providers among patient prescribed opioids. (3) Implementation of risk management strategies endorsed by CPGs were identified as a means of improving patient care.	Coordination and integration of care, clinical decision support tools, patient self-management and quality of improvement are potential solutions to improve patient care.
Esquibel (2014)	N=16 Resident physician (n=10); attending physician (n=6) Incentive=None	Understand the effects of COT on the doctor-patient relationship	Semi-structured/ multistep iterative approach; immersion/crystallization process	Fear for patients; patient-provider relationship;	(1) Belief that opioids offer superficial band-aid for a wound or stepping stone to addiction. (2) Stigma about prescribing opioids for CNCP due to concerns of patient addiction and poor evidence for effectiveness on pain or function. (3) Opioid therapy can raise questions over validity of pain and become a source of conflict and mistrust that adversely impacts the patient-provider relationship.	a) A deeper understanding of the patient's complex lives may lessen physician views on drug-seeking behaviour. b) Interventions for providers and patients are needed to protect the doctor-patient relationship. c) Patient and provider may benefit from chronic pain management models to improve communication and shared decision-making. d) Physicians should use goal directed care instead of problem directed communication.
Fischer (2017)	N=96 GP (n=96) Incentive: $200	Assess effect of patient requests for specific opioid pain medication on suspected drug seeking and	Semi-structured/ thematic content analysis; Interviews	Fear for patients; patient-provider relationship	(1) Look for truthfulness across patient presentation (e.g., symptoms, demeanor, employment) to evaluate authenticity of complaint.	a) The use of initial therapy and testing to determine the severity of the pain complaint and the risk of drug seeking is worth evaluating in future research.

First Author (year)	Provider Characteristics	Objective of Interview	Type of Interview/ Qualitative Analysis	Constructs	Themes Relating to Opioid Prescribing	Author Implications
		prescribing practices.	coded quantitatively and analyzed statistically		(2) Importance of knowing the patient and their history when deciding authenticity of complaint. (3) Weighing the risks of under-treating pain and medication abuse.	b) Need for valid instruments that can be used in primary care settings assess drug seeking behaviour.
Fontana (2008)	N=9 NP (n=9) Incentive: None	Examine social and political factors affecting opioid prescribing for CNCP	Semi-structured/ Dialectical analysis	Concerns for society (diversion); institutional pressure; patient-related salient events; education; fear of professional sanction or liability; fear for patients	(1) In order of importance, NPs relied on etiology of pain, personal experience (i.e., biases), and formal education when prescribing opioids. (2) Perceived inadequacy of formal education on opioid prescribing. (3) Adverse events (e.g., overdose or death) result in reluctance to prescribe and perceived need to protect oneself by acting in the best interest of NPs. (3) Responsible to protect society from drug abuse and diversion.	N/A
Harle (2015)	N=15 FM (n=9); internal medicine (n=6)	Understand the decision to prescribe opioids for CNCP in primary care.	Semi-structured with funnelling approach/ Iterative, Open-coding	Short appointment duration; patient-provider relationship	(1) Importance of objective and consistent information about pain. (2) Importance of identifying "red flags" (e.g., history of abuse, reluctance to try non-opioid therapies).	There is potential value to EMR-based decision support to ensure physicians are able to diagnose pain conditions, weigh opioid risks and benefits and judge patient trustworthiness more objectively; need for

First Author (year)	Provider Characteristics	Objective of Interview	Type of Interview/ Qualitative Analysis	Constructs	Themes Relating to Opioid Prescribing	Author Implications
	Incentive: None		analytic approach		(3) Setting goals and expectations around patient functional outcomes can improve confidence in prescribing. (4) Longstanding relationships increase trust and willingness to prescribe. (5) Difficulty weighing benefits against risks with greatest weight given to potential abuse. (6) Time and resource constraints impede appropriate prescribing. (7) PCPs often "specialize" in chronic pain or avoid these patients.	education and policies that support high quality primary care for CNCP.
Hulen (2019)	N=6 Attending physician (N=3); Medical Residents (N=2). Health psychologist (N=1) Incentive: None	To identify sources of provider stress about prescribing opioids to manage CNCP.	Semi-structured/ Exploratory, content driven approach to applied thematic analysis	Provider-related salient events; alternative resources	(1) Challenges of pain management using opioid analgesics (objective assessments, changing guidelines, and lack of coordinated approach) (2) Patient attachment to opioids that impact patient-provider communication (e.g., threats that patients will turn to elicit sources, patient perception of entitlement to receive opioid medications, and patient perception of abandonment when tapering). (3) Provider frustration related to opioid prescribing (e.g., confrontation in clinic visits; lack of patient engagement in mental healthcare; and complex social circumstances including poverty).	Interventions (such as the CSRG) should be implemented to assist PCP prescribing, as these interventions may to help reduce stress, and improve patient safety and satisfaction

First Author (year)	Provider Characteristics	Objective of Interview	Type of Interview/ Qualitative Analysis	Constructs	Themes Relating to Opioid Prescribing	Author Implications
					(4) The role of the Controlled Substance Review Group (CSRG; communication techniques; supporting mental health engagement; structured support).	
Hurstak (2017)	N=23 GP (n=18), NP (n=4), PA (n=1) Incentive: $50 gift card	Understand perceptions of risk of opioid therapy to improve informed consent process	Semi-structured/ Grounded theory	Fear for patients; fear for professional sanction or liability	(1) Sense of personal responsibility over patient adverse events results in conservative prescribing. (2) Conservative prescribing due to fear of diversion and risk of overdose in the community. (3) Fear of liability and censure affects prescribing behaviour. (4) Contrasting views on co-prescribing naloxone (i.e., acknowledge and shift risk to patient, but is this ethical?)	a) Discuss the risks of opioid therapy and explore patients' understanding of those risks to improve safety. b) Be mindful that opioid monitoring policies can stigmatize the patient, and may harm the patient-clinician relationship. c) Benefit to incorporating information on addiction, physical dependence, and overdose risk of opioids into formal education for physicians.
Kang (2018)	N=40 Physician (N=15); Pharmacist (N=25) Incentive: None	Explore physician and pharmacist perspectives on the opioid crisis and the possibility of physician and community pharmacist collaborations to manage CNCP.	Semi-structured/ Applied thematic analysis	Education; alternative resources	(1) Challenges that lead to care deficiencies (lack of provider education and alternative treatments). (2) Using tools (drug screening, use of PDMP, obtaining patient history) to mitigate opioid abuse and diversion. (3) Increased need for interprofessional communication and support.	a) To improve provider education on non-opioid alternatives; b) To improve the ease of use of PDMPs c) To implement pharmacist-physician collaborations to enhance patient care.

First Author (year)	Provider Characteristics	Objective of Interview	Type of Interview/ Qualitative Analysis	Constructs	Themes Relating to Opioid Prescribing	Author Implications
Kennedy (2017)	N=40 GP (n=34), NP (n=3), other (n=3) Incentive: Meals	Assess experiences of opioid tapering with patients on long-term opioid therapy	Semi-structured in-person focus groups/ Mixed inductive-deductive method	Fear for patients; goal setting; short appointment durations; alternative resources; patient-provider relationship; patient-provider communication; education	(1) Patient preference and evidence of risk behaviours or adverse events can be used to identify candidates for opioid tapering. (2) Barriers to opioid tapering include: emotional burden on providers, poor patient-provider trust, and inadequate training, time and resources. (3) Facilitators of opioid tapering include: accurate empathy, individualized plan, and guidelines/policies.	a) Interventions to improve opioid tapering may include: implement routine screening for patient readiness to taper; support providers to reduce burnout; develop models for team-based care during opioid tapering. b) There is a need for patient-centered educational resources to guide discussions on tapering. c) Ensure local policies promote access to a range of effective non-pharmacological pain options.
Knight (2017)	N=23 GP (n=18), NP (n=4), PA (n=1) Incentive: None	Explore the educational, clinical, and social factors that contribute to opioid prescribing	Semi-structured/ iterative process; inductive and deductive coding	Concerns for society (diversion); patient-provider relationship; education; self-efficacy managing pain with opioids.	(1) Encouragement to be responsive to patient pain, aggressive marketing, and lack of alternative pain management options contributed to historic increase in opioids. (2) Concerns over safety of opioids and lack of evidence about efficacy have contributed to pharmacovigilance. (3) Acknowledgment that clinicians bear some responsibility in opioid epidemic. Frustration between balancing concern over health effects of withdrawing from opioids and health effects of continuing to prescribe.	a) Presenting opioid prescribing in socio-historical context in formal pain education would be beneficial. b) Address the challenges of clinical uncertainty in opioid prescribing. c) Provide students and clinicians with opportunities to problem solve opioid-related challenges common in clinician-patient interactions.

First Author (year)	Provider Characteristics	Objective of Interview	Type of Interview/ Qualitative Analysis	Constructs	Themes Relating to Opioid Prescribing	Author Implications
Liddy (2017)	N= 26 FM (n=25), other (n=1) Incentive: None	Identify themes emerging from exchanges between PCPs and specialists regarding patients with chronic pain	eConsult service between PCP and specialist/ thematic analysis of cases using a constant comparison approach	Self-efficacy; alternative resources	(1) Hesitation to prescribe opioids in patients with mental illnesses. (2) Advice sought about treatment strategies and community resources. (3) Responses provided by specialists to PCPs, including empathy and support. (4) PCPs sought advice regarding safe prescribing, deprescribing, opioid rotation, and implementation of harm reduction strategies.	N/A
Militello (2018)	N= 10 PCP (N=10) Incentive: None	Identify patient, social and provider factors that influence how providers assess and manage CNCP.	Critical decision method interviews/ Thematic analysis using framing and anchors	Education; goal setting	(1) Patient factors that influence prescribing (e.g., inappropriate use of opioid medications, resistance to non-opioid alternatives, patient condition, patient goals, therapeutic history). (2) Social and environmental factors that influence prescribing (e.g., insurance regulations, new clinical practice guidelines, unmet social needs). (3) Clinician characteristics that influence prescribing (experience and training; perception of their role; interpretation of regulations and guidelines; knowledge of resources available).	1) Future interventions that are put in place to support PCPs in chronic pain management should consider the complexity, ambiguity and uncertainty associated with pain management. They should focus on supporting sensemaking, such as aiding clinicians in identifying appropriate anchors in the context of clinical evidence and guidelines

First Author (year)	Provider Characteristics	Objective of Interview	Type of Interview/ Qualitative Analysis	Constructs	Themes Relating to Opioid Prescribing	Author Implications
Penney (2016)	N=25 GP (n=25) Incentive: None	Identify practical issues patients and providers face when assessing alternatives to opioids	Structured; focus group/ Iterative process using inductive and deductive coding	Short appointment duration; alternative resources; self-efficacy; managing pain with opioids.	(1) Alternatives to opioids are limited and difficult to access making opioids viable. (2) Patient belief in effectiveness of opioids and unwillingness to engage in lifestyle-management were barriers to tapering. (3) Acupuncture/Chiropractor can augment opioid therapy. (4) Available resources, visit duration, and patient expectations about costs and benefits influence management of CNCP, including opioid prescribing.	N/A
Robertson (2014)	N=6 FM (n=5), other (n=1) Incentive: None	To understand the impact of a point-of-care opioid tool called Opioid Manager on clinical practice	Semi-structured/ Thematic analysis; Content analysis; code-recode technique used to verify content validity	Self-efficacy managing pain with opioids; patient-provider communication; education; education on tools	(1) Use of tool improves education. (2) Lack of knowledge, discomfort, concern over regulatory sanction, and perceived poor "standards of care" were identified as challenges to CNCP management, including with opioids. (3) Tool can improve communication when information is shared with patients and other healthcare providers. (4) Tool can reduce concern over regulatory sanction and provide documentation.	N/A

First Author (year)	Provider Characteristics	Objective of Interview	Type of Interview/ Qualitative Analysis	Constructs	Themes Relating to Opioid Prescribing	Author Implications
Satterwhite (2019)	N=23 Physician, NP, Physician Assistant Incentive: None	Identify contextual factors that contribute to time scarcity and its effects on quality of care when prescribing opioids in primary care.	Semi-structured and open-ended/ Grounded theory	Short appointment durations; alternative resources;	(1) Clinician perceptions of pain as a time drain. (2) Insurance, inherited patients, and the 15-minute visit: Chronic pain management draws attention away from other patients.	(1) Tools and policies that facilitate the assessment and treatment of pain and management of opioids need to be tailored to reduce the time pressure providers feel when prescribing opioids. This can result in more effective management of CNCP; (2) Payment models that reimburse for the time necessary for CNCP assessment would help to alleviate time pressure as a barrier to appropriate pain management.
Spitz (2011)	N=26 Physician (n=23), NP (n=3) Incentive: None	Identify attitudes, and perceived barriers and facilitators to prescribing opioids among older adults	Focus group; semi-structured/ Content analysis	Patient-related salient events; patient-provider relationship; fear for patients	(1) Opioids not considered first line treatment and used with hesitation. (2) Provider barriers include fear of adverse effects and addiction; insufficient education; fear of regulatory sanction; and inability to determine organic cause. (3) Provider facilitators include studies demonstrating safety; patient and family education of risks; peer or specialist consultation; tools to assist with prescribing. (4) Expressed frustration with pressure to treat pain.	Collect data to develop evidence-based CPGs and algorithms for opioid prescribing later in life. This could improve provider confidence when prescribing opioids to older adults.
Tong (2019)	N=16 PCPs (N=16)	Understand provider factors that inform the use of opioids for	Semi-structured/ Template and emergent	Short appointment duration; alternative resources;	(1) Clinicians feel frustration and pressured to manage inappropriate amounts of opioids when inheriting patients on high doses.	New interventions must be developed to help PCPs overcome barriers (e.g., contraindications to nonopioid treatment alternatives, lack of access to adjunctive management strategies, limited time, and the

First Author (year)	Provider Characteristics	Objective of Interview	Type of Interview/ Qualitative Analysis	Constructs	Themes Relating to Opioid Prescribing	Author Implications
	Incentive: None	CNCP in primary care.	coding processes	institutional pressure	(2) Co-occurring health problems in the patient causes concern for prescribing opioids. (3) Benefits of opioids for CNCP management: chronic opioids are necessary to sustain functionality and help manage diseases. (4) Clinicians experience many challenges with weaning opioids including lack of time to properly wean opioids and justifying tapering when patients are stable at high doses.	difficulty of weaning) that prevent the successful weaning of patients off chronic opioid therapy.
Wyse (2018)	N=24 Physicians (N=18); NP (N=4); Physician Assistant (N=2) Incentive: None	To learn about the methods PCPs used to address prescription opioid misuse and aberrant opioid-related behaviours.	Semi-structured/ Content analysis	Alternative resources;	(1) Barriers to minimizing the risk of opioid prescribing and potential opioid-related harm including, resource constraints, and geographic constraints (i.e. travel time). (2) Strategies clinicians used to address common problems when caring for patients on chronic opioid therapy (e.g., ordering urine drug tests before appointments, referral to an integrated pain clinic).	a) An increase in the use of tele-medicine would improve access to pain treatment for individuals in remote areas; b) Future research should focus on accessible treatments for patients on chronic opioid therapy who show signs of substance misuse. c) Future research should design accessible and acceptable interventions for overcoming patient reluctance to receive nonpharmacologic treatment options.
Wyse (2019)	N= 24 Physicians (N=20), NP (N=4),	Identify provider strategies for managing aberrant medication behaviours among	Semi-structured/ Content analysis	Goal setting; Short appointment duration; provider related	(1) Difficult conversations between patients and providers impact opioid prescribing behaviours (e.g., objections to opioid weaning).	(1) Providers would benefit from additional guidance and support regarding how to approach the subject of addiction with patient;

First Author (year)	Provider Characteristics	Objective of Interview	Type of Interview/ Qualitative Analysis	Constructs	Themes Relating to Opioid Prescribing	Author Implications
	Incentive: None	patients prescribed chronic opioid therapy.		salient events; patient-provider relationship	(2) Clinicians experience ambivalence about enacting guideline-recommended changes	(2) Providers would benefit from support as they transition to new standards of opioid care; (3) Expanding access to resources could help reduce provider ambivalence about prescription opioid dose reduction or discontinuation and bolster guideline-recommended pain care practices.

Note: CNCP = Chronic Non-Cancer Pain; COT = Chronic Opioid Therapy; CPG = Clinical Practice Guideline; ED = Emergency Department; EMR = Emergency Medical Record; FM = Family Medicine; GP = General Practitioner; LPN = Licensed Practical Nurse; NP = Nurse Practitioner; PDMP = Prescription Drug Monitoring Program; RN = Registered Nurse; TA = Treatment Agreement; UDT = Urine Drug Test.

Table 2

Risk of Bias Ratings for Qualitative Studies Evaluated using the Critical Appraisal Skills Programme (CASP) Checklist

Author	Were research aims clearly stated?	Is qualitative methodology appropriate?	Was research design appropriate to address research aims?	Was recruitment strategy appropriate to research aims?	Were data collected in a way that addressed the issue?	Has relationship between researcher and participants been considered?	Have ethical issues been considered?	Was data analysis sufficiently rigorous?	Is there a clear statement of findings?	Is the research valuable and makes a meaningful contribution?	Number of criteria met (/10)
Barry et al. (2010)	☑	☑	☑	☑	☑	☑	☑	☑	☑	☑	10
Buchman et al. (2016)	☑	☑	☑	☑	☑	☑	☑	☑	☑	☑	10
Calcaterra et al. (2016)	☑	☑	☑	☑	☑	☒	☑	☑	☑	☑	9
Chang et al. (2017)	☑	☑	☒	☒	☒	☒	☒	☒	☑	☑	4
Chang et al. (2016)	☑	☑	☑	☑	☑	☑	☑	☑	☑	☑	10

Clark & Upshur (2007)	☑	?	☒	?	☑	☒	☒	☑	☑	☑	5
Click et al. (2018)	☑	☑	☑	☑	☑	☒	☒	☑	☑	☑	8
Desveaux et al. (2019)	☑	☑	☑	☑	☑	☑	☑	☑	☑	☑	10
Elder et al. (2012)	☑	☑	☑	☑	?	☒	?	☑	☑	☑	7
Esquibel et al. (2014)	☑	☑	☑	☑	☑	☒	☒	☑	☑	☑	8
Fischer et al. (2017)	☑	☑	☑	☑	☑	☒	☒	☑	☑	☑	8
Fontana et al. (2008)	☑	☑	☑	☑	☑	☑	☒	☑	☑	☑	9
Harle et al. (2015)	☑	☑	☑	☑	☑	☑	☑	☑	☑	☑	10
Hulen et al. (2018)	☑	☑	☑	☑	☑	☒	☑	☑	☑	☑	9

Hurstak et al. (2017)	☑	☑	☑	☑	☑	☒	☑	☑	☑	☑	9
Kang et al. (2019)	☑	☑	☑	☑	☑	☒	☑	☒	☒	?	6
Kennedy et al. (2017)	☑	☑	☑	☑	☑	☒	☑	☑	☑	☑	9
Knight et al. (2017)	☑	☑	☑	☑	☑	☑	☑	☑	☑	☑	10
Liddy et al. (2017)	☑	☑	☑	☑	☑	☒	☒	☑	☑	☑	8
Militello et al. (2018)	☑	☑	☑	☑	☑	☑	☒	☑	☑	☑	9
Penney et al. (2016)	☑	☑	☑	☑	☑	☑	☑	☑	☑	☑	10
Robertson et al. (2013)	☑	☑	☑	☑	☑	☑	☑	☑	☑	☑	10
Satterwhite et al. (2019)	☑	☑	☑	☑	☑	☒	☑	☑	☑	☑	9

Spitz et al. (2011)	☑	☑	☑	☑	☑	☒	☑	☑	☑	☑	9
Tong et al. (2019)	☑	☑	☑	☑	?	☒	☑	☒	☒	?	5
Wyse et al. (2018; 2019)	☑	☑	☑	☑	☑	☒	☑	☒	☒	?	6
Wyse et al. (2019)	☑	☑	☑	☑	☑	☒	☑	☑	☑	☑	9
Number of trials meeting criteria	28	27	26	26	25	11	19	24	25	25	

Table 3

Confidence in the Evidence from Reviews of Qualitative Research (CERQual) Rating of Qualitative Studies

Summary of review finding	Studies contributing to the theme	Methodological limitations	Coherence	Adequacy	Relevance	CERQual assessment of confidence in the evidence	Explanation of CERQual assessment
Barriers:							
Knowledge							
While some reported using knowledge from formal education to make clinical decisions regarding opioids, most providers felt their formal education was insufficient to properly prescribe opioids to patients with CNCP. The use of opioid management tools and guidelines were suggestions to improve provider education.	108,114,117,118,121,125,126	Minor concerns about methodological limitation (1 serious, 1 moderate, 3 minor, 2 none)	Moderate concerns about coherence (Some concerns about the fit between the data from the primary studies and the review finding)	Minor concerns about relevance (3 thin and 4 rich, variety of practitioners)	Minor concerns about relevance (7 different PCP specialties; majority are GPs)	Moderate confidence	Moderate concern regarding methodological limitations and coherence
Beliefs about Capabilities							
Most providers endorsed a lack of confidence in prescribing opioids for patients with CNCP, both with and without comorbid conditions. Reasons for lack of confidence include, 1) lack of biomedical explanations for pain; 2) lack of guidelines; 3) problem patients; 4) older age of patients; and 5) uncertainty of response from patients.	104,106,111,118-123	Minor concerns about methodological limitations (1 serious, 1 mod, 1 minor-mod, 1 minor, 5 none)	Minor concerns about coherence (Some concerns about the fit between the data from the primary studies and the review finding) (Knight contradicted confidence finding)	Minor concerns about adequacy (6 rich, 3 thin, variety of practitioners)	Minor concerns about relevance (9 different PCP specialties; minor contradiction)	Moderate confidence	Minor concerns about each facet

Summary of review finding	Studies contributing to the theme	Methodological limitations	Coherence	Adequacy	Relevance	CERQual assessment of confidence in the evidence	Explanation of CERQual assessment
Beliefs about Consequences							
Providers reported concern over inadvertently increasing the risk of opioid addiction among community members due to opioid diversion. Taking patients off opioid medication and the implementation of opioid policies and procedures by institutions were seen as a viable preventative measures.	104,114,116,118	Minor concerns about methodological limitations (2 minor, 2 none)	No or very minor concerns about coherence	No or very minor concerns about adequacy (3 rich, 1 thin; 8 different types of practitioners)	No or very minor concerns about relevance (no concerns because of 8 different types of PCPs, good distribution of numbers)	Moderate confidence	Minor concerns about methodological limitations
Environmental Context							
Providers found it difficult to appropriately assess and manage pain with opioids within the duration of a typical appointment. Some providers reported reducing client load or the prescription of opioids in response to this pressure.	104,115,117,120,123,127-129	Minor concerns about methodological limitations (7 none, 1 serious)	No or very minor concerns regarding coherence	No or very minor concerns about adequacy (6 rich, 2 thin,)	No or very minor concerns about relevance (8 PCP specialties, with majority being GP)	High confidence	
Providers reported experiencing negative events (e.g., death of a patient,) after providing opioids to their patients. These experiences influenced future prescribing practices, leading providers to reduce or stop prescribing opioids.	106,114,122	Minor concerns about methdological limitations (1 moderate, 2 minor)	No concerns about coherence	No concerns about adequacy (3 rich)	Minor concerns about relevance (3 PCP specialties)	High confidence	Minor concerns about methodological limitations

Summary of review finding	Studies contributing to the theme	Methodological limitations	Coherence	Adequacy	Relevance	CERQual assessment of confidence in the evidence	Explanation of CERQual assessment
Providers reported experiencing negative patient-related events (e.g., threats of violence, physical assault) after providing opioids to their patients. These threats lead to provider hesitancy to prescribe opioids in order to protect their own safety.	110,124,129	Minor concerns about methodological limitations (2 none, 1 serious)	No concerns about coherence	No concerns about adequacy (3 rich)	No concerns about relevance (7 PCP specialists)	High confidence	Minor confidence about methodological limitations
Emotion							
Providers reported concern about the risk of inadvertently contributing to the development of patient addiction and/or dependence if they prescribe opioids. Fear of opioid addiction was negatively associated with willingness to prescribe.	106,112-114,116,117,122,123	Minor concerns about methodological limitations (2 moderate, 1 minor-moderate, 4 minor, 1 none)	No or very minor concerns about coherenec	No or very minor concerns about adquacy (5 rich, 2 thin, 1 unsure)	Minor concerns about relevance (6 different PCP specialties; majority are GPs)	High confidence	Minor concerns about methodological limitations
Providers expressed concern over regulatory investigation and loss of their job as a licensed practitioner if the prescription of opioids inadvertently harmed patients. This concern was inversely associated with willingness to prescribe opioids for CNCP.	105,114,116	Minor concerns about methodological limitations (1 minor and 2 none)	No or very minor concerns about coherence	No or very minor concerns about adequacy (only 3 articles but all rich)	Minor concerns about relevance (6 PCP specialties, but number of non-GPs)	Moderate confidence	Minor concerns about methodological limitations

Summary of review finding	Studies contributing to the theme	Methodological limitations	Coherence	Adequacy	Relevance	CERQual assessment of confidence in the evidence	Explanation of CERQual assessment
Facilitators:							
Knowledge							
Educational sessions and/or training in the use of opioid prescribing tools were recommended to improve prescribing methods to students and providers.	109,121	Moderate concerns about methodological limitations (1 serious and 1 none)	No or very minor concerns about coherence	Serious concerns about accuracy (2 studies, one with thin data and one with relatively rich data)	Serious concerns about relevance (3 PCP specialties)	Low confidence	Serious concerns about accuracy, moderate concerns about methodological limitations
Goals							
Providers reported benefit from setting opioid-treatment goals with patients. These goals included tapering opioids or incorporating non-opioid treatments into pain management.	117,126,129	No concerns about methodological limitations (2 none, 1 minor)	Minor concerns about coherence (2 talking about goals of tapering with patient, 1 talking about goals of risk management)	Moderate concerns about adequacy (2 rich, 1 thin; 3 different types of practitioners)	Moderate concerns about relevance (3 PCP specialties, majority GPs)	Moderate confidence	Moderate concerns about adequacy, minor about coherence and no concerns about methodological limitations
Environmental Context							
Most providers reported insufficient availability of opioid-alternative pain management resources for their patients. Some providers utilized specialists for further resources. Others reported a lack of qualified staff or PCPs available for these patients.	104,107,117,119,120,123-128,130	Moderate concerns about methodological limitations	Minor concerns about coherence (all talking about limited alternative resources – some talking about providers/staff, some	Minor concerns about adequacy (8 rich, 4 thin; 9 different types of practitioners)	No or very minor concerns about relevance (9 PCP specialties)	Moderate confidence	Moderate concerns about methodological limitations, minor conerns

Summary of review finding	Studies contributing to the theme	Methodological limitations	Coherence	Adequacy	Relevance	CERQual assessment of confidence in the evidence	Explanation of CERQual assessment
Insufficient alternative resources were positively associated with opioid prescribing.		(4 serious, 1 minor-moderate, 1 minor, 6 none)	talking about avaliable resources, some talking about lack of knowledge of available resources)				about coherence and adequacy
Some providers reported institution pressure to facilitate patient discharges through the prescription of opioids. Some providers reported that institution protocols surrounding opioid prescribing helped prescribing practices; however, others felt that protocols impeded individualized care.	106,110,114,128	Serious concerns about methodological limitations (1 serious, 2 moderate, 1 minor)	Moderate concerns regarding coherence (these articles talk about insitutional pressure but in different ways: some pressure inhibits appropriate prescribing; some facilitates it)	Minor concerns about adequacy (3 rich, 1 thin; 5 PCP specialties)	No or very minor concerns regarding relevance (5 PCP specialties, majority are GPs)	Low confidence	Moderate concerns about methodological limitations and coherence, minor concerns about adequacy
Social Influences							
Providers prefer to have a healthy, trusting relationship with their patients and are more willing to prescribe opioids in such cases. Patient dishonesty and withholding of information is associated with distrust, suspicion, and a resistance to start or continue prescribing opioids. Some providers reported that sharing risks with patients and implementing treatment agreement plans improved the working-alliance and trust; however, others reported that patients will withhold information during such circumstances.	104,105,107,110-113,115,117,118,122,123,129	Minor concerns about methodological limitations (7 none, 2 minor, 2 moderate, 2 serious)	No or very minor concerns about coherence (some concerns about the fit between the data from primary studies and the review finding)	No or very minor concerns about adequacy (13 studies together that provided moderately rich data)	No or very minor concerns about relevance (large variety of PCP specialties)	Moderate confidence	Concerns about methodological limitations and no or very minor concerns about coherence, adequacy, and relevance

Summary of review finding	Studies contributing to the theme	Methodological limitations	Coherence	Adequacy	Relevance	CERQual assessment of confidence in the evidence	Explanation of CERQual assessment
Providers reported benefit in open conversations with patients about opioids. Most providers mentioned that risk management tools facilitate communication and shared decision-making; however, some providers felt that risk management tools will result in selective patient-reporting about opioid use and hinder communication.	[107,108,117,121]	Moderate concerns about methodological limitations (1 serious, 1 mild and 2 none)	Moderate concerns about coherence (Some contradiction between studies)	Minor concerns about adequacy (3 studies that gave rich data, 1 study that gave thin data)	Minor concerns about relevance (5 PCP specialties; majority are GPs)	Low confidence	Moderate concerns about methodological limitations and coherence