

BMJ Open Strategies aimed at preventing chronic opioid use in trauma and acute care surgery: a scoping review protocol

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To cite: Bérubé M, Moore L, Lauzier F, *et al*. Strategies aimed at preventing chronic opioid use in trauma and acute care surgery: a scoping review protocol. *BMJ Open* 2020;**10**:e035268. doi:10.1136/bmjopen-2019-035268

► Prepublication history for this paper is available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2019-035268>).

Received 26 October 2019
Revised 24 March 2020
Accepted 26 March 2020

ABSTRACT

Introduction Globally every year, millions of patients sustain traumatic injuries and require acute care surgeries. A high incidence of chronic opioid use (up to 58%) has been documented in these populations with significant negative individual and societal impacts. Despite the importance of this public health issue, optimal strategies to limit the chronic use of opioids after trauma and acute care surgery are not clear. We aim to identify existing strategies to prevent chronic opioid use in these populations.

Methods and analysis We will perform a scoping review of peer-reviewed and non-peer-reviewed literature to identify studies, reviews, recommendations and guidelines on strategies aimed at preventing chronic opioid use in patients after trauma and acute care surgery. We will search MEDLINE, EMBASE, PsycINFO, CINHAL, Cochrane Central Register of Controlled Trials, Web of Science, ProQuest and websites of trauma and acute care surgery, pain, government and professional organisations. Databases will be searched for papers published from 1 January 2005 to a maximum of 6 months before submission of the final manuscript. Two reviewers will independently evaluate studies for eligibility and extract data from included studies using a standardised data abstraction form. Preventive strategies will be classified according to their types and targeted trauma populations and acute care surgery procedures.

Ethics and dissemination Research ethics approval is not required as this study is based on the secondary use of published data. This work will inform research and clinical stakeholders on the required next steps towards the uptake of effective strategies aimed at preventing chronic opioid use in trauma and acute care surgery patients.

INTRODUCTION

Worldwide, close to a billion people sustain traumatic injuries every year that warrant healthcare.¹ The burden of disease secondary to acute care surgeries (surgical management of trauma patients and emergency general surgery)² is also important with 6 million procedures performed every year in the USA.³ Among trauma and acute surgery patients, a significant proportion will transition from

Strengths and limitations of this study

- Comprehensive review to identify existing strategies aimed at preventing chronic opioid use in trauma and acute care surgery.
- Results will fill an important knowledge gap on the potential role of strategies applied early after trauma and acute care surgery in the prevention of chronic opioid use.
- Adopts an integrated knowledge translation approach to ensure uptake of results by trauma and acute care surgery stakeholders from various disciplines.
- Classification of strategies according to the type of populations and contexts of application might not be feasible considering the number of studies that will be identified.
- Our work does not aim to evaluate the efficacy of the different strategies through meta-analysis.

acute to chronic pain. Indeed, the prevalence of chronic pain has been estimated to varied between 20% and 80% during the recovery trajectory of trauma and acute care surgery patients.⁴⁻⁹ Acute pain is expected to last a short time and can be clearly linked to an injury.¹⁰ Conversely, chronic pain lasts beyond the usual course of injury healing and is present on most days, or every day, over a 3-month period or more.¹¹ Considering the pain induced by traumatic injuries and acute surgical procedures, opioids are frequently prescribed in these contexts.^{12 13} However, chronic opioid use (therapy >3 months),¹⁴ has been documented in more than half of trauma and surgical patients¹⁵ and may be used up to 5 years after the initial prescription.¹⁶

The chronic use of opioids is associated with a 30% incidence of opioid use disorder,¹⁷ described as a problematic pattern of opioid consumption leading to clinically significant impairment and distress.¹⁸ In Canada, one



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of every 550 patients started on opioid therapy died of opioid-related causes.¹⁹ Moreover, in the USA, deaths from overdose, excluding those related to fentanyl, have increased by 185% (from 6158 to 17536 deaths) over the last 15 years.²⁰ Accordingly, opioid-related overdoses are now one of the primary cause of death for the 18–35-year-old age group in North America.²¹ Also, the total economic burden of opioid-related disorders due to prescription of opioids has been estimated at \$78.5 billion per year in the USA²² and \$38 billion between 2007 and 2014 in Canada.²³

The total duration of opioid prescription is the strongest predictor of opioid use disorder after surgery, with each additional week of prescribed opioids increasing the disorder rate by 44%.²⁴ Furthermore, lengthening the duration of the first prescription in opioid naïve patients is associated with a lower likelihood of opioid discontinuation after traumatic injuries.²⁵ The significant increase in opioid prescriptions, combined with a lack of patient support on how to use and wean opioids, has contributed to the alarming rise of the negative individual and social impacts associated with long-term opioid use.^{26–28}

Up to now, most efforts have been concentrated on studying the effects of strategies to reduce the use of opioid in patients already on chronic therapy.²⁹ Recently, mandatory prescription limits have been associated with a reduction of opioid use after elective surgeries.^{30–33} However, our knowledge of the potential strategies is limited, and none are currently broadly applied as standard of care interventions. The objective of our scoping review is to understand the strategies aiming at preventing chronic opioid use specific to adult trauma and acute care surgery patients.

METHODS AND ANALYSIS

Our scoping review was performed according to standard methods^{34–36} and our protocol is reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews.³⁷

Eligibility criteria

We will include studies and guidelines on strategies for preventing chronic opioid use in patients who required acute trauma and surgical services. We will include randomised controlled trials (RCTs), quasi-experimental, prospective and retrospective observational cohorts, cross-sectional and case-control studies. Preventive strategies (pharmacological or non-pharmacological) will have to target the acute care trajectory (from the hospital admission to 3 months postinjury) of adult patients (≥18 years old) after traumatic injuries or acute care surgery (ie, emergency surgery required for issues such as the surgical management of trauma patients, intestinal obstruction/perforation or abdominal organs inflammation/infection).^{2 38} Specifically, we will search for strategies applied in acute care settings (ie, intensive care unit, trauma and surgical units), rehabilitation centres and in

the community (ie, pain and family medicine clinics). Comparators will include placebo, any other intervention or no intervention (ie, standard treatment). We will consider every outcome measured 3 months after trauma or surgery. Since the opioid crisis issue has emerged at the end of the last decade, following the publication of guidelines for safe administration of opioids,³⁹ the search will be limited to documents published between 1 January 2005 and a maximum of 6 months before submission of the final manuscript. No language restriction will be applied.

Information sources

We will systematically search the following:

1. MEDLINE, Embase, PsycINFO, CINAHL, the Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science and ProQuest.
2. Websites of the following:
 - a. Injury and acute care surgery organisations including the American College of Surgeons, Orthopaedic Trauma Society, Trauma Association of Canada, International Association for Trauma Surgery and Intensive Care, Australasian Trauma Society, American Association for the Surgery of Trauma, Eastern Association for the Surgery of Trauma, American Trauma Society, British Trauma Society, Western Trauma Association, Society of Trauma Nurses, International Trauma Anaesthesia and Critical Care Society.
 - b. Pain organisations including the International Association for the Study on Pain, American Society of Anesthesiologists, Canadian Pain Society, British Pain Society and Australian Pain Society.
 - c. Healthcare quality organisations including the WHO, National Institute for Health and Care Excellence, National Association for Healthcare Quality, National Quality Forum, Agency for Healthcare Research and Quality, Australasian Association for Quality in Healthcare.

References of included articles will then be screened for any further eligible studies.

Search strategy

Using Cochrane guidelines,⁴⁰ we will develop a rigorous systematic search strategy in collaboration with an information specialist. We will use combinations of search terms under the themes of opioids and preventive strategies including text terms and MESH (Medline) or Emtree (Embase). We will adapt our search strategies for the other databases. A preliminary search strategy in MEDLINE is presented in [table 1](#).

Selection process

We will manage all citations in evidence. We will identify and remove duplicates using electronic and manual screening.⁴¹ To ensure reliability when selecting studies, two sets of 100 citations will independently be evaluated and then discussed by reviewers. Pairs of reviewers (MB,

Table 1 Search strategy in MEDLINE

Concepts	Ovid search strategy keywords	Research
Injuries and acute care surgeries	exp "Wounds and Injuries"/	#1
	(dislocation* or fracture* or injur* or traum* or "emergency surgery" OR "emergency surgeries").ab,kf,kw,sh,ti,tw. ("Acute care surgery").ab,ti. OR ("Acute care surgeries").ab,ti. OR ("Ankle surgery").ab,ti. OR ("Ankle surgeries").ab,ti. OR ("Arthroplasty").ab,ti. OR ("Arthroplasties").ab,ti. OR ("Elbow surgery").ab,ti. OR ("Elbow surgeries").ab,ti. OR ("Hip surgery").ab,ti. OR ("Hip surgeries").ab,ti. OR ("Joint surgery").ab,ti. OR ("Joint reconstruction").ab,ti. OR ("Knee surgery").ab,ti. OR ("Knee surgeries").ab,ti. OR ("Orthopedics").ab,ti. OR ("Orthopaedics").ab,ti. OR ("Orthopedic procedure").ab,ti. OR ("Orthopedic procedures").ab,ti. OR ("Orthopaedic procedure").ab,ti. OR ("Orthopaedic procedures").ab,ti. OR ("Orthopedic surgery").ab,ti. OR ("Orthopaedic surgery").ab,ti. OR ("Orthopaedic surgeries").ab,ti. OR ("Orthopaedic surgeries").ab,ti. OR ("Shoulder surgery").ab,ti. OR ("Shoulder surgeries").ab,ti. OR ("Wrist surgery").ab,ti. OR ("Wrist surgeries").ab,ti. ("Acute care surgery" OR "Acute care surgeries" OR "Ankle surgery" OR "Ankle surgeries" OR "Arthroplasty" OR "Arthroplasties" OR dislocation* OR "Elbow surgery" OR "Elbow surgeries" OR "emergency surgery" OR "emergency surgeries" OR fracture* OR "Hip surgery" OR "Hip surgeries" OR injur* OR "Joint replacement" OR "Joint surgery" OR "Joint reconstruction" OR "Knee surgery" OR "Knee surgeries" OR "Orthopedics" OR "Orthopaedics" OR "Orthopedic procedure" OR "Orthopedic procedures" OR "Orthopaedic procedure" OR "Orthopaedic procedures" OR "Orthopedic surgery" OR "Orthopaedic surgery" OR "Orthopaedic surgeries" OR "Orthopaedic surgeries" OR "Shoulder surgery" OR "Shoulder surgeries" OR traum* OR "Wrist surgery" OR "Wrist surgeries").ab,kf,kw,sh,ti,tw.	#2
	1 or 2	#3
Opioids (controlled vocabulary) (free text)	Alfentanil/ OR Buprenorphine, Naloxone Drug Combination/ OR Buprenorphine/ OR Morphine/ OR Fentanyl/ OR Hydrocodone/ OR Hydromorphone/ OR Levorphanol/ OR Meperidine/ OR Methadone/ OR Morphine Derivatives/ OR Oxycodone/ OR Oxymorphone/ OR Pentazocine/ OR Tramadol/ OR Narcotics/ OR exp Analgesics, Opioid/ OR exp Codeine/ OR Opioid-Related Disorders/	#4
	(Alfentanil or Buprenorphine or Naloxone or Morphine or Fentanyl or Hydrocodone* or Hydromorphone or Levorphanol or Meperidine or Methadone or Morphine or Oxycodone or Oxymorphone or Pentazocine or Tramadol or Narcotics or Analgesic* or Opioid* or Codeine or opiate).ab,kf,kw,sh,ti,nm,tw.	#5
	4 or 5	#6
Preventive strategies (controlled vocabulary) (free text)	"Acceptance and commitment therapy"/ OR Acetaminophen/ OR "Acupuncture Therapy"/ or Acupuncture/ OR Acupressure/ OR "Electroacupuncture"/ OR "Adaptation, Psychological"/ OR "Adrenergic alpha-2 Receptor Agonists"/ OR Clonidine/ OR "Analgesia"/ OR "Analgesics, Non-Narcotic"/ OR "Anesthetics, Local"/ OR "Anticonvulsants"/ OR "Antidepressive Agents"/ OR "Anti-Inflammatory Agents"/ OR "Biofeedback, Psychology"/ OR exp "Cognitive behavioral therapy"/ OR "Combined Modality Therapy"/ OR Counseling/ OR Cryotherapy/ OR "Decision Support Systems, Clinical"/ OR Exercise/ OR "Exercise Therapy"/ OR "Hyperthermia, Induced"/ OR Hypnosis/ OR "Immobilization"/ OR Massage/ OR Meditation/ OR "Mind-body therapies"/ or "Imagery (psychotherapy)"/ OR "Nerve Block"/ OR "Pain Clinics"/ OR Exp "Pain Management"/ OR "Organization and Administration"/ OR "Patient Education as Topic"/ OR "Patient Positioning"/ OR "Physical Therapy Modalities"/ OR "Prescription Drug Monitoring Programs"/ OR "Receptors, N-Methyl-D-Aspartate" OR Ketamine/ OR Relaxation/ OR "Relaxation Therapy"/ OR "Secondary Prevention"/ OR "Self Care"/ OR "Self-Management"/ OR "Sensory art therapies"/ or "Music therapy"/ OR "Transcutaneous Electric Nerve Stimulation"/	#7
	("acetaminophen").ab,ti. OR ("acupressure").ab,ti. OR ("acupuncture").ab,ti. OR ("adjuvant analgesics").ab,ti. OR ("adjuvant analgesic").ab,ti. OR ("analgesia").ab,ti. OR ("antidepressant").ab,ti. OR ("antidepressants").ab,ti. OR ("antiepileptic drug").ab,ti. OR ("antiepileptic drugs").ab,ti. OR ("anticonvulsant drug").ab,ti. OR ("anticonvulsant drugs").ab,ti. OR ("clonidine").ab,ti. OR ("co-analgesics").ab,ti. OR ("co-analgesic").ab,ti. OR ("cognitive strategies").ab,ti. OR ("cognitive and emotional strategies").ab,ti. OR ("cryotherapy").ab,ti. OR ("discontinuation").ab,ti. OR ("distraction").ab,ti. OR ("emotional strategies").ab,ti. OR ("gabapentin").ab,ti. OR ("guided imagery").ab,ti. OR ("health system intervention").ab,ti. OR ("hypnosis relaxation").ab,ti. OR ("interdisciplinary pain management").ab,ti. OR ("ketamine").ab,ti. OR ("local analgesics").ab,ti. OR ("massage").ab,ti. OR ("meditation").ab,ti. OR ("multidisciplinary pain management").ab,ti. OR ("multimodal analgesia").ab,ti. OR ("nerve block").ab,ti. OR ("nerve stimulation").ab,ti. OR ("non narcotic analgesic").ab,ti. OR ("non-narcotic analgesic").ab,ti. OR ("nonnarcotic analgesic").ab,ti. OR ("non narcotic analgesics").ab,ti. OR ("non-narcotic analgesics").ab,ti. OR ("nonnarcotic analgesics").ab,ti. OR ("non opioid analgesic").ab,ti. OR ("non-opioid analgesic").ab,ti. OR ("nonopioid analgesic").ab,ti. OR ("non opioid analgesics").ab,ti. OR ("non-opioid analgesics").ab,ti. OR ("nonopioid analgesics").ab,ti. OR ("pain consultation service").ab,ti. OR ("pain medication policy").ab,ti. OR ("pain medication prescribing").ab,ti. OR ("pain medication prescribing policy").ab,ti. OR ("patient positioning").ab,ti. OR ("peer support").ab,ti. OR ("peer Support-Based Groups").ab,ti. OR ("policies and procedures").ab,ti. OR ("pregabalin").ab,ti. OR ("prescriber education").ab,ti. OR ("prescription limits").ab,ti. OR ("prevention").ab,ti. OR ("public education").ab,ti. OR ("reduction").ab,ti. OR ("relapse prevention").ab,ti. OR ("restrictive opioid prescription protocol").ab,ti. OR ("self-help").ab,ti. OR ("stage of change").ab,ti. OR ("superficial cold").ab,ti. OR ("superficial heat").ab,ti. OR ("support group").ab,ti. OR ("system strategies").ab,ti. OR ("taper").ab,ti. OR ("tapering").ab,ti. OR ("topical analgesics").ab,ti. OR ("transcutaneous electric nerve stimulation").ab,ti. OR ("transitional pain service").ab,ti. OR ("weaning").ab,ti.	#8
	Opioid* adj3 (reduction or Prevention or Weaning or Discontinuation or Tapering or management or manage). tw,sh,kw,kf,oa. (Prevent* adj2 (((Continued or chronic or "long-term" or prolonged) adj2 ("use" or usage)) or misuse or overdose)). tw,sh,kw,kf,oa. ((Psychosocial* or education* or cognitive or behavior* or Acceptance or commitment or Motivational or Enhancement or Contingency or Exercise or relaxation or physical or music or acupuncture or heat or acupressure) adj2 (therap* or strateg* or management* or program* treatment* or intervention*)).tw,sh,kw,kf,oa.	#9 #10 #11
7 OR 8 OR 9 OR 10 OR 11	#12	

Continued

Table 1 Continued

Concepts	Ovid search strategy keywords	Research
Total	3 AND 6 AND 12	#13
	animals/	#14
	humans/	#15
	14 not 15	#16
	13 not 16	#17
	(2005 or 2006 or 2007 or 2008 or 2009 or 2010 or 2011 or 2012 or 2013 or 2014 or 2015 or 2016 or 2017 or 2018 or 2019).yr.	#18
	17 and 18	#19

CC, PAT and CB) will independently screen all identified records using titles, abstracts and full texts. We will settle any disagreement through discussion between reviewers and, if necessary, consultation with a fifth reviewer (AFT).

Data charting

Standardised data extraction forms for original studies (table 2) and guidelines (table 3) have been developed and piloted on a representative sample of five studies and two guidelines. Pairs of reviewers (MB, CC, PAT and CB) with methodological and content expertise will independently extract information on the following themes from original studies: setting (country, year, funding), population (age, type of injury or surgical procedure, risk factors for chronic opioid use (eg, history of substance abuse, chronic pain, mood disorders¹⁵), study design, intervention(s) (ie, preventive strategies, context of application and application timing), comparator(s), primary and secondary outcome measures and their measure time points and strategy efficacy based on measures of association, CI and significance value. The same pairs of reviewers will also independently extract data from guidelines on these themes: setting (association that developed the guidelines, year, country), population (type of injury or surgical procedure), intervention(s) (preventive strategies, context of application and application timing) and the strategies level of evidence as described in each guideline. Any disagreement will be resolved through discussion between reviewers and, if necessary, consultation with a fifth reviewer (AFT). We will contact the authors for important missing data when deemed necessary.

Quality assessment

If considered feasible, based on the number of eligible studies and guidelines, two reviewers (MB and CC) will independently critically appraise the methodological quality with the Cochrane revised tool for RCTs (RoB2),⁴² the risk of bias in non-randomised studies—of interventions (ROBINS-I) tool⁴³ and the Appraisal of Guidelines—Research and Evaluation version II (AGREE II) tool.⁴⁴ Risk of bias will be categorised as low, moderate, high and unclear. A score will be calculated for each dimension of the AGREE II tool according to reviewers' assessment.

Collate, summarise and report on results

Data collation will be conducted independently by two reviewers (MB and CC) and verified by a third reviewer (LM) and adjudicated by a fourth one in case of disagreement (AFT). Preventive strategies will be classified according to the type of preventive strategy as per pain management guidelines in trauma⁴⁵ and other fields:^{46 47} pharmacological other than opioids, educational, psychological (eg, cognitive-behavioural therapy, mindfulness therapy), rehabilitation (eg, physiotherapy, exercise programme), alternatives (eg, acupuncture, relaxation, massage), multimodal (ie, combination of pharmacological strategies or pharmacological and non-pharmacological strategies) and system-based strategies (eg, communication tools between health professionals or prescription monitoring programme). We ran our preliminary Medline strategy and screened articles published from 2017 to 2019, the 3 years associated with the greatest number of publications (n=1226) on the targeted topic. Less than 15 studies were found to be potentially eligible. Hence, we will further classify the preventive strategies according to their context of application (eg, trauma unit, pain clinic) and the timing of their efficacy testing (eg, 3–6 months, 6–12 months and ≥12 months after the trauma or acute care surgery) only if we identify a sufficient number of studies. Moreover, we will attempt to describe the type of population (eg, traumatic brain injury, orthopaedic trauma surgery, patients who required an abdominal organ resection, patients at high risk or low risk of chronic opioid use) in which each category of strategy was applied. Moreover, we will calculate the number of studies by design (eg, RCT, cohort study, expert consensus) for each preventive strategy. To describe the evidence of preventive strategies, we will summarise findings from original studies by reporting the measure of association scores along with their CI and significance value, and from guidelines by reporting strategies level of evidence. We will also report the risk of bias and AGREE II tool scores if quality assessment is performed.

Consultation

We will consult our project advisory committee comprising researchers, healthcare practitioners (surgeons,

Table 2 Data extraction form (original studies)

Author and year	Country and funding	Population (type of trauma or surgical procedure)	Age (mean and SD)	Risk factor for chronic opioid use (history of substance abuse, chronic pain, anxiety, depression)	Study design	Sample size	Strategies (pharmacological, educational, psychological, rehabilitation, alternatives, multimodal, system-based)	Context (ICU, trauma or surgical unit, rehabilitation, pain clinic, family medicine clinics)	Comparator	Measure time points (3–6, >6–12, >12 months)	Primary outcomes (measures and scores)	Secondary outcomes (measures and scores)	Efficacy (measure of association, CI, significance value)	Risk of bias (low, moderate, high, unclear)

SD, Standard deviation.

**Table 3** Data extraction form (guidelines)

Guidelines title	Author and year	Country	Population (type of trauma or surgical procedure)	Strategies (pharmacological, educational, psychological, rehabilitation, alternatives, multimodal, system-based)	Context of application (ICU, trauma or surgical unit, rehabilitation, pain clinic, family medicine clinics)	Application time points (3–6, >6–12, >12 months)	Level of evidence as per guideline	AGREE II dimensions scores (scope and purpose, stakeholder involvement, rigour, clarity, applicability, editorial independence)

physicians specialised in acute care and pain), allied health professionals (psychologists, nurses, pharmacists, physical therapists and occupational therapists), decision-makers (representatives of the *Institut National d'Excellence en Santé et en Services Sociaux* and of the Trauma Association of Canada) and patient/family partners. The objectives of the consultation will be to (1) identify any further references, (2) obtain feedback on the interpretation and presentation of results and (3) identify opportunities for knowledge transfer.

Potential limitations

Considering the objective of a scoping review, we will comprehensively appraise the scope of existing strategies aiming at preventing chronic opioid use after traumatic injuries and acute care surgery. However, as is common in scoping reviews, we will not conduct meta-analysis.^{34–36} We will only describe efficacy and/or level of evidence as reported by the authors. Nonetheless, this review will allow us to examine the extent, the range and the nature of the existing strategies on the topic to help planning future research.

Potential impact

Chronic opioid use is an important issue in trauma and acute care surgery patients. Strategies need to be implemented to prevent opioid intake beyond 3 months in this population. This scoping review will fill an important knowledge gap on the potential role of strategies offered early after trauma and acute care surgery to prevent long-term opioid use and associated negative human and social impacts. Findings will provide information on future research needed to reduce the burden associated with chronic opioid use in the trauma and acute care surgery populations.

Patient and public involvement

Two patients/family partners who have experienced a trauma or an acute care surgery will be involved in the consultation phase of this scoping review. Their feedback will be gathered on the presentation of results and strategies that should be standardised in trauma and acute care surgery in the future. Patients/family partners will be recruited in the CHU de Québec—Université Laval and trained by the *Stratégie de recherche axée sur le patients (SRAP)-Université Laval*.

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Contributors MB led the development of the protocol and drafted the manuscript. She acts as guarantor for the review. LM drafted the manuscript with the first author, critically revised and approved the final version of the manuscript. FL contributed to developing keywords, validated the search strategy, critically revised and approved the final version of the manuscript. CC contributed to the development of research objectives and elaboration of keywords, tested the search strategy and approved the final version. KV contributed to the development of research objectives, revised the manuscript and approved the final version. LT contributed to the development of research objectives, validated the search strategy, critically revised and approved the final version of the manuscript. M-OM, KP and A-MP contributed to the development of research objectives and concept definitions, critically revised and approved the final version of the manuscript. GP contributed to the development of research objectives and inclusion criteria, validated the search strategy, critically revised and approved the final version of the manuscript. P-AT contributed to the elaboration of keywords, developed and tested the search strategy, drafted parts of the methods, revised and approved the final version of the manuscript. SMH contributed to the development of research objectives, elaboration of keywords, revised and approved the final version. CS contributed to the development of research objectives and concept definitions, validated the search strategy, critically revised and approved the final version of the manuscript. CB tested the search strategy and data extraction form, revised and approved the final version of the manuscript. AFT elaborated research objectives, inclusion criteria and clinically significant outcomes, validated the search strategy, critically revised and approved the final manuscript.

Funding This research is supported by the Québec Pain Research Network (no funding number provided). The funder had no role in developing this protocol.

Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

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