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Barriers and enablers to monitoring and deprescribing opioid analgesics for chronic non-cancer pain: Protocol for a qualitative evidence synthesis using the Theoretical Domains Framework

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Barriers and enablers to monitoring and deprescribing opioid analgesics for chronic non-cancer pain: Protocol for a qualitative evidence synthesis using the Theoretical Domains Framework

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Abstract

Introduction: The over-prescription and overuse of opioid analgesics for chronic non-cancer pain (CNCP) is a growing issue. Synthesis of evidence about the barriers and enablers to reducing long-term opioid prescribing and use will enable the development of tailored interventions to address both problems.

Objective: To synthesise the barriers and enablers to monitoring the ongoing appropriateness of opioid treatment and deprescribing opioids for CNCP from the clinician, patient and general public point of view, and to map the findings to the Theoretical Domains Framework (TDF).

Methods and analysis: We will perform a qualitative evidence synthesis using the TDF. We will include qualitative research that has explored clinician, patient and the general public's perceptions regarding barriers and enablers to monitoring and deprescribing opioids for CNCP. Studies not published in English will be excluded. Studies will be identified via searches in MEDLINE, EMBASE, CINAHL, AMED and PsycINFO since inception. Article selection and data extraction will be completed independently by two review authors. Methodological quality of included studies will be independently assessed by two review authors using the Critical Appraisal Skills Programme quality assessment tool. We will conduct thematic synthesis and then map identified themes and sub-themes to TDF domains. Confidence in synthesis findings will be evaluated using the GRADE Confidence in the Evidence from Reviews of Qualitative Research (CERQual) tool.

Ethics and Dissemination: Ethical approval is not required to conduct this review. We will publish the results in a peer-reviewed journal.

Review Registration number: PROSPERO reference: *pending*

Strengths and limitations

- This study will inform development of tailored, effective, theory-based interventions for reducing inappropriate use of opioid analgesics in chronic non-cancer pain.
- We will use systematic search strategies to identify relevant qualitative research.
- To minimise bias, two reviewer authors will independently select, extract data and assess the methodological quality of included studies.
- We will use GRADE CERQual to report the confidence in synthesis findings.

For peer review only

Introduction

Chronic non-cancer pain (CNCP), defined as pain persisting beyond three months unrelated to a malignancy, is highly prevalent worldwide with population estimates varying from 20 to 40%.¹⁻⁵ Optimal management of CNCP is essential to minimise the burden on individuals and the wider healthcare system. While evidence supports the use of opioid analgesics for acute and cancer-related pain, there is limited evidence supporting the long-term efficacy and safety of opioids for CNCP.⁶⁻¹¹ Furthermore, evidence suggests that potential harms such as risk of overdose, opioid abuse and opioid addiction, often outweigh potential benefits.^{12 13}

Opioid use for CNCP is common. In Australia, almost three million adults are using opioids for non-cancer pain each year,¹⁴ and there was a 15-fold increase in opioid dispensing between 1992 and 2012.¹⁵ In 2015, the amount of opioids prescribed in the United States was three times higher than in 1999,¹⁶ and the total number of opioid prescriptions peaked at more than 255 million in 2012.¹⁷ While the rates of new patients prescribed opioids in Australia and the United States have started to decline, high risk prescribing, including initiating with strong opioids and prescriptions for more than 3-days supply, is still a major problem.^{14 18}

Recent evidence-based guidelines do not recommend opioids as first-line management for CNCP.^{10 19 20} If opioids are prescribed, clinicians should monitor patient progress and evaluate benefits and harms of continuing opioid therapy with patients at least every three months (Table 1).^{10 20 21 22} If opioid treatment is ineffective or if the harms outweigh the benefits, then opioid treatment should be tapered. Unfortunately, many of the harms associated with long-term opioid use, including tolerance and addiction,⁹ can make the process of reducing or deprescribing opioids challenging for both clinicians and patients. There is also a lack of quality evidence on safe and effective interventions for deprescribing opioids in CNCP.²³

Understanding barriers and enablers to reducing the long-term prescribing and use of opioids and mapping these factors to theoretical mechanisms of behaviour change, is an important step towards developing tailored, effective approaches for reducing inappropriate use of opioids in CNCP. The Theoretical Domains Framework (TDF), which consists of 14 domains and 84 theoretical constructs drawn from over 30 theories of behaviour change, offers a systematic and theory-based approach for identifying determinants of behaviour change and facilitating design of tailored, theory-based implementation interventions.^{24 25} It allows for

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3 key factors that influence guideline recommended behaviour and clinical practice change to
4 be linked to evidence-based behaviour change techniques.²⁴
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7 To date there has been only one qualitative evidence synthesis relating to opioid use in CNCP
8 and it explored health professionals' experience of prescribing opioids for CNCP.²⁶ It found
9 that there is often a sense of uncertainty about when to prescribe opioids, and that healthcare
10 professionals struggle to balance their professional duty to 'get rid of pain' with the social
11 suspicion and hostility surrounding prescribing opioids.²⁶ This review did not focus on
12 barriers and enablers to monitoring ongoing appropriateness of opioid treatment, nor barriers
13 and enablers to reducing or deprescribing opioids. A second qualitative evidence synthesis is
14 currently underway which aims to explore patients' experiences taking opioids for CNCP but
15 does not include an explicit aim to map barriers and enablers to a behaviour change
16 framework.²⁷
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25 **Aim**

26 To synthesise available qualitative research regarding barriers and enablers to monitoring
27 ongoing appropriateness of opioid treatment and deprescribing opioids for CNCP from the
28 clinician, patient and general public point of view, and to organise the findings using the
29 TDF.
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35 **Methods**

36 We have registered this study on PROSPERO (currently pending).
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40 **Selection Criteria**

41 We will include English language full-text articles or reports (i.e. excluding conference
42 abstracts) that fulfil the following criteria:
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46 *Types of studies:* Studies that used any type of qualitative method(s) to obtain data (e.g. focus
47 group, interviews). Studies that included mixed methods will be included where the
48 qualitative data was analysed independently of the quantitative data.
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52 *Types of participants:* Clinicians (regardless of discipline), patients (previously or currently
53 being treated for CNCP with one or more opioids) and/or their carers, and the general public
54 who have been interviewed about the barriers and enablers to monitoring ongoing
55 appropriateness of opioid treatment and/or deprescribing opioids for CNCP.
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60 *Types of settings:* All healthcare settings in all countries.

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3 *Types of pain:* CNCP defined as pain lasting beyond three months unrelated to malignancy.
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6 *Types of outcome measures:* Studies that report perceptions about barriers and/or enablers to
7 guideline-recommended safe and appropriate prescribing and use of opioids in CNCP.
8

9 Specifically, we will focus on guideline recommendations related to step 6 of the World
10 Health Organization (WHO) Principles of Good Prescribing²⁸ (Table 1), including
11 monitoring ongoing appropriateness of opioid treatment (i.e. effectiveness, benefits and/or
12 harms) and stopping opioid treatment (i.e. tapering, reducing or deprescribing treatment that
13 may be ineffective or harmful). To ensure studies can provide rich data specific to the use of
14 opioids, studies will only be included where their study aim and/or methodology (e.g.
15 interview guide) specifically mention aspects of monitoring ongoing appropriateness of
16 opioid treatment or stopping opioid treatment. Where studies include participants with
17 multiple medications, we will include studies where the experiences with opioids are reported
18 separately.
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27 Studies exploring the following topics will not be a focus of this review and such studies will
28 be excluded;
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- 32 • Initiating opioid treatment
 - 33 • Opioid use and management of CNCP in the context of substance use disorder,
34 addiction or illicit opioid use.
 - 35 • Impact or evaluation of policy-, organisation-, practitioner- or patient-level
36 interventions (e.g. legislation change or experiences with a new program/intervention)
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40 Search Methods 41

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43 We will develop a search strategy with the assistance of an Information Specialist based at
44 Monash University, and with guidance from the qualitative research chapter in the Cochrane
45 Handbook.²⁹
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49 The following databases will be searched to identify relevant articles: MEDLINE, EMBASE,
50 CINAHL, AMED and PsycINFO. We will not use date limits, but will limit the search to
51 articles in English.
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55 The search will be conducted in two parts. Part 1 will combine terms related to: CNCP as
56 recommended by the Cochrane Pain, Palliative and Supportive Care group; opioids;
57 monitoring, deprescribing or reducing; and barriers and enablers. Part 2 will identify studies
58 that have utilised qualitative research methodology. Qualitative filters will be used where
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3 available to enhance sensitivity and specificity. To obtain final search results we will
4 combine part 1 and 2. The proposed MEDLINE search strategy is outlined in Appendix 1.
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7 The reference list of included studies will also be searched for relevant articles and we will
8 track citations of included studies using Web of Science to ensure we gather all relevant
9 literature. Experts in the field will also be approached to identify other potentially relevant
10 studies using the existing professional networks of the authors.
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14 Selection of studies

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16 Two review authors will independently screen all titles and abstracts yielded from the search,
17 and all full text articles considered relevant. Any disagreements will be resolved via
18 discussion or by consultation with a third review author when necessary. Search and
19 screening results will be summarised in a Preferred Reporting Items of Systematic Reviews
20 and Meta-analysis (PRISMA) flow diagram.³⁰
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26 Data collection

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28 Pairs of review authors will independently extract data from each included study using a
29 standardised data collection form. Any disagreements will be resolved by discussion or by
30 consultation with a third review author when necessary. A piloted data extraction form will
31 capture information regarding the:
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- 36 • Study details (authors, year of publication)
- 37 • Research question
- 38 • Participants (number, demographic characteristics, professional background, history
39 of opioid use, method of selection)
- 40 • Type and duration of CNCP
- 41 • Type and duration of opioid, including stage of deprescribing if applicable
- 42 • Setting (type of healthcare, country, urban/rural)
- 43 • Method of data collection (e.g. interview, focus group)
- 44 • Data analysis method (e.g. thematic analysis)
- 45 • Results (themes, sub-themes, supporting quotes, conclusions).
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55 Quality Assessment

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57 The quality of included studies will be independently assessed by two review authors using
58 the Critical Appraisal Skills Programme (CASP) Checklist.³¹ Any disagreements will be
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3 resolved via discussion or by consultation with a third review author when necessary. The
4 CASP tool uses a checklist of 10 questions, each of which includes multiple signalling
5 questions to help users interpret the items (29 signalling questions in total). Studies will not
6 be excluded based on low quality. A summary table indicating the presence or absence of
7 CASP items will be included and a narrative summary of the quality of the included studies
8 will be provided.
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10 11 12 13 14 *Data analysis and synthesis*

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16 We will initially use an inductive approach to coding and conduct thematic synthesis, as
17 outlined by Thomas and Harden.³² Each line of extracted text will be reviewed and codes will
18 be developed based on the content and meaning of each extract. As new studies are coded,
19 existing codes will be reviewed and revised with new codes added as needed. When all
20 studies have been coded, all text related to each code will be reviewed for consistency of
21 coding across studies. Two review authors will independently code an initial subset of studies
22 and then meet to discuss any discrepancies until consensus is reached. The remaining studies
23 will then be coded by one author and verified by a second author. Codes will be reviewed for
24 similarities and differences and organised into related descriptive themes. A draft summary of
25 the descriptive themes will be prepared by one author and discussed by the review team until
26 consensus is reached.
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29 Next, the emergent themes will be mapped to the domains of the TDF^{24 25} independently by
30 two review authors or if there is no relevant domain placed in an 'other' category. A draft
31 summary of the TDF-aligned themes will be prepared by one author and discussed by the
32 review team until agreement on coding interpretations is reached.
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35 In the final stage, review findings will be drafted to summarise analytical themes and
36 corresponding theoretical domains relating to barriers and enablers to ongoing monitoring of
37 opioid use and deprescribing opioids for CNCP from the clinician, patient and general public
38 point of view. The review findings will be prepared by one author and discussed by the
39 review team until consensus is reached.
40

41 42 43 44 45 46 47 48 49 50 51 52 53 *Assessment of confidence in review findings*

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55 Pairs of independent authors will use the Grading of Recommendations Assessment,
56 Development, and Evaluation (GRADE) Confidence in the Evidence from Reviews of
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3 Qualitative Research (CERQual) tool to assess the confidence in the review findings.³³ This
4 tool considers four factors that influence the confidence in synthesis of qualitative studies:
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- 7 a. Methodological limitations of the studies contributing to a review finding (based on
8 CASP assessments)
- 9 b. Relevance of studies to the review question of studies contributing to a review finding
- 10 c. Coherence of data contributing to a review finding
- 11 d. Adequacy of supporting data supporting a review finding

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16 The overall confidence in each review finding (i.e. for each theme generated) will be graded
17 as: high, moderate, low or very low (see Box 1).³³ A final decision on confidence in review
18 findings will be reached through discussion and consensus among the review team. Review
19 findings, confidence judgement for each finding and an explanation of the judgement will be
20 presented in a Summary of Qualitative Findings table (see Table 2).
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25 26 Reporting

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28 The study will be reported in accordance with the enhancing transparency in reporting the
29 synthesis of qualitative research (ENTREQ) statement.³⁴
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32 33 Discussion

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35 Here we present the design of a qualitative evidence synthesis using the TDF to explore
36 clinician, patient and general public barriers and enablers to monitoring ongoing
37 appropriateness of opioid treatment and deprescribing opioids for CNCP, and align key
38 findings with evidence-based behaviour change techniques. This is an important step towards
39 developing tailored, effective, theory-based interventions for reducing the inappropriate use
40 of opioids in CNCP.
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45 46 Authors' contributions

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48 AJC, DAO and RB conceived the idea for the study. AJC and DAO wrote the first draft of
49 the manuscript. RB, AB, CGM, SM and CWL contributed to revising subsequent drafts
50 critically for important intellectual content. All authors approved the final version of the
51 manuscript and agree to be accountable for its content.
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Table 1: World Health Organization (WHO) guide to good prescribing and opioid prescribing in CNCP guidelines

WHO Principles of Good Prescribing²⁸	Guidelines for prescribing opioids for CNCP^{10 20 21 22}
<u>Step 1</u> Define the patient's problem	<ul style="list-style-type: none"> Assess the patient using a multidisciplinary approach. Non-pharmacologic therapy and non-opioid pharmacologic therapy are preferred for CNCP
<u>Step 2</u> Specify the therapeutic objective	<ul style="list-style-type: none"> Before starting opioid therapy, clinicians should establish realistic treatment goals with the patient and set a review date. Written, structured clinician-patient agreements/contracts for opioid use could be considered.
<u>Step 3</u> Verify the suitability of the medication	<ul style="list-style-type: none"> A careful assessment of the benefits and risks of prescribing an opioid for each specific patient should be considered.
<u>Step 4</u> Write a prescription	<ul style="list-style-type: none"> Start with a low dose and adjust slowly according to response. Do not introduce an opioid at the same time as another drug.
<u>Step 5</u> Give information, instructions and warnings	<ul style="list-style-type: none"> Discuss the adverse effects, possible harms and realistic benefits of long term opioid therapy with patients.
<u>Step 6</u> Monitor (and stop?) the treatment	<ul style="list-style-type: none"> Regularly review the patient to monitor progress, evaluate benefits and harms, and assess if ongoing treatment is needed. Reviews should be within 4 weeks of starting opioid treatment or of changes in dose, and minimum every 3 months for continued treatment. If opioid treatment is ineffective, or benefits do not outweigh harms, then opioid treatment should be tapered slowly and under supervision.

Box 1: GRADE Confidence in the Evidence from Reviews of Qualitative research (CERQual) approach³³ to confidence in findings of qualitative evidence syntheses

- *High confidence*: highly likely that the review finding is a reasonable representation of the phenomenon of interest.
- *Moderate confidence*: likely that the review finding is a reasonable representation of the phenomenon of interest.
- *Low confidence*: possible that the review finding is a reasonable representation of the phenomenon of interest.
- *Very low confidence*: unclear whether the review findings is a reasonable representation of the phenomenon of interest.

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Table 2. Summary of qualitative findings

Review findings	Studies contributing to review findings	Assessment of methodological limitations	Assessment of relevance	Assessment of coherence	Assessment of adequacy	Overall GRADE CERQual assessment of confidence	Explanation of judgment
Finding 1							

CERQual, Confidence in the Evidence from Reviews of Qualitative Research

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Appendix 1: Medline Search Strategy (via Ovid)

Part 1

1. Pain, Intractable/
2. Chronic Pain/
3. exp Back Pain/
4. Neck Pain/
5. exp Arthralgia/
6. Fibromyalgia/
7. exp Headache Disorders/
8. exp Arthritis/
9. exp Musculoskeletal Pain/
10. exp Neuralgia/
11. exp Nociceptive pain/
12. exp Pain, Postoperative/
13. Pain, Referred/
14. Diabetic neuropathies/
15. (pain* or headache* or migraine* or neuralgia* or neuropath* or arthriti* or osteoarthriti* or osteoarthritis* or fibromyalg* or arthralgia* or myalgia*).mp.
16. or/1-15
17. exp Narcotics/
18. (opioid* or opiate* or opium or papaver or morphine or meperidine or methadone or buprenorphine or fentanyl or hydrocodone or hydromorphone or oxycodone or oxymorphone or codeine or tramadol or narcotic*).mp.
19. or/17-18
20. Deprescriptions/
21. Inappropriate Prescribing/
22. Prescriptions/
23. exp Drug Prescriptions/
24. exp Opioid-Related Disorders/
25. Drug Monitoring/
26. Pain Management/

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3 27. (prescrib* or prescrip* or monitor* or manag* or treat* or withdraw* or ceas* or
4 cessation or stop* or discontinu* or reduc* or taper* or titrat* or deprescrib* or
5 deprescrip* or de-prescrib* or de-prescrip* or optim*).mp.
6
7
8 28. or/20-27
9
10 29. (barrier* or enabler* or challeng* or concern* or facilitat* or belief* or believ* or
11 perception* or attitude* or perspective* or preference* or insight* or view* or
12 experience* or attitude* or factor*).mp.
13
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15 30. 16 and 19 and 28 and 29
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18 Part 2

- 19
20 31. exp Qualitative research/
21
22 32. Interview/
23
24 33. Interviews as topic/
25
26 34. Focus groups/
27
28 35. exp Decision making/
29
30 36. exp Attitude to Health/
31
32 37. Attitude of Health Personnel/
33
34 38. Nursing methodology research/
35
36 39. (Qualitative or mixed-method* or theme* or thematic).mp.
37
38 40. ((semi-structured or semistructured or unstructured or informal or in-depth or indepth
39 or face-to-face or structured or guide*) adj3 (interview* or discussion* or
40 questionnaire*)).mp
41
42 41. (focus adj3 group*).mp
43
44 42. (digital* record* or audiorecord* or taperecord* or videorecord* or videotap* or
45 audio-record* or tape-record* or video-record* or video-tap*).mp.
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47 43. or/31-42
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49 Total search strategy

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BMJ Open

Barriers and enablers to monitoring and deprescribing opioid analgesics for chronic non-cancer pain: Protocol for a qualitative evidence synthesis using the Theoretical Domains Framework

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Keywords:	PAIN MANAGEMENT, barriers and enablers, opioids, Musculoskeletal disorders < ORTHOPAEDIC & TRAUMA SURGERY, QUALITATIVE RESEARCH



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Barriers and enablers to monitoring and deprescribing opioid analgesics for chronic non-cancer pain: Protocol for a qualitative evidence synthesis using the Theoretical Domains Framework

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Conflicts of interest: The authors declare they have no competing interests.

Abstract

Introduction: The over-prescription and overuse of opioid analgesics for chronic non-cancer pain (CNCP) is a growing issue. Synthesis of evidence about the barriers and enablers to reducing long-term opioid prescribing and use will enable the development of tailored interventions to address both problems.

Objective: To synthesise the barriers and enablers to monitoring the ongoing appropriateness of opioid treatment and deprescribing opioids for CNCP from the clinician, patient and general public point of view, and to map the findings to the Theoretical Domains Framework (TDF).

Methods and analysis: We will perform a qualitative evidence synthesis using the TDF. We will include qualitative research that has explored clinician, patient and the general public's perceptions regarding barriers and enablers to monitoring and deprescribing opioids for CNCP. Studies will be identified via searches in MEDLINE, EMBASE, CINAHL, AMED and PsycINFO. Databases will be searched from inception until July 2019 and studies must be published in English. Article selection and data extraction will be completed independently by two review authors. Methodological quality of included studies will be independently assessed by two review authors using the Critical Appraisal Skills Programme quality assessment tool. We will conduct thematic synthesis and then map identified themes and sub-themes to TDF domains. Confidence in synthesis findings will be evaluated using the GRADE Confidence in the Evidence from Reviews of Qualitative Research (CERQual) tool.

Ethics and Dissemination: Ethical approval is not required to conduct this review. We will publish the results in a peer-reviewed journal.

Review Registration number: PROSPERO reference: CRD42019140784

Strengths and limitations

- This study will inform development of tailored, effective, theory-based interventions for reducing inappropriate use of opioid analgesics in chronic non-cancer pain.
- We will use systematic search strategies to identify relevant qualitative research.
- To minimise bias, two reviewer authors will independently select, extract data and assess the methodological quality of included studies.
- We will use GRADE CERQual to report the confidence in synthesis findings.
- Synthesis will be limited to quotes and themes explored in the original reports. We will not seek original data.

Introduction

Chronic non-cancer pain (CNCP), defined as pain persisting beyond three months unrelated to a malignancy, is highly prevalent worldwide with population estimates varying from 20 to 40%.¹⁻⁵ Optimal management of CNCP is essential to minimise the burden on individuals and the wider healthcare system. While evidence supports the use of opioid analgesics for acute and cancer-related pain, there is limited evidence supporting the long-term efficacy and safety of opioids for CNCP.⁶⁻¹² Furthermore, evidence suggests that potential harms such as risk of overdose, opioid abuse and opioid addiction, often outweigh potential benefits.^{13 14}

Opioid use for CNCP is common. In Australia, almost three million adults are using opioids for non-cancer pain each year,¹⁵ and there was a 15-fold increase in opioid dispensing between 1992 and 2012.¹⁶ In 2015, the amount of opioids prescribed in the United States was three times higher than in 1999,¹⁷ and the total number of opioid prescriptions peaked at more than 255 million in 2012.¹⁸ While the rates of new patients prescribed opioids in Australia and the United States have started to decline, high risk prescribing, including initiating with strong opioids and prescriptions for more than 3-days supply, is still a major problem.^{15 19}

Recent evidence-based guidelines do not recommend opioids as first-line management for CNCP.^{10 20 21} If opioids are prescribed, clinicians should monitor patient progress and evaluate benefits and harms of continuing opioid therapy with patients at least every three months (Table 1).^{10 21-23} If opioid treatment is ineffective or if the harms outweigh the benefits, then opioid treatment should be tapered. Unfortunately, many of the harms associated with long-term opioid use, including tolerance and addiction,⁹ can make the process of reducing or deprescribing opioids challenging for both clinicians and patients. There is also a lack of quality evidence on safe and effective interventions for deprescribing opioids in CNCP.²⁴

Understanding barriers and enablers to reducing the long-term prescribing and use of opioids and mapping these factors to theoretical mechanisms of behaviour change, is an important step towards developing tailored, effective approaches for reducing inappropriate use of opioids in CNCP. The Theoretical Domains Framework (TDF), which consists of 14 domains and 84 theoretical constructs drawn from over 30 theories of behaviour change, offers a systematic and theory-based approach for identifying determinants of behaviour change and facilitating design of tailored, theory-based implementation interventions.^{25 26} It allows for

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3 key factors that influence guideline recommended behaviour and clinical practice change to
4 be linked to evidence-based behaviour change techniques.²⁵
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7 To date there has been only one qualitative evidence synthesis relating to opioid use in CNCP
8 and it explored health professionals' experience of prescribing opioids for CNCP.²⁷ It found
9 that there is often a sense of uncertainty about when to prescribe opioids, and that healthcare
10 professionals struggle to balance their professional duty to 'get rid of pain' with the social
11 suspicion and hostility surrounding prescribing opioids.²⁷ This review did not focus on
12 barriers and enablers to monitoring ongoing appropriateness of opioid treatment, nor barriers
13 and enablers to reducing or deprescribing opioids. A second qualitative evidence synthesis is
14 currently underway which aims to explore patients' experiences taking opioids for CNCP but
15 does not include an explicit aim to map barriers and enablers to a behaviour change
16 framework.²⁸
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25 **Aim**

26 To synthesise available qualitative research regarding barriers and enablers to monitoring
27 ongoing appropriateness of opioid treatment and deprescribing opioids for CNCP from the
28 clinician, patient and general public point of view, and to organise the findings using the
29 TDF.
30
31
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34

35 **Methods**

36 We have registered this study on PROSPERO (CRD42019140784).
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40 **Selection Criteria**

41 We will include English language full-text articles or reports (i.e. excluding conference
42 abstracts) that fulfil the following criteria:
43
44
45

46 *Types of studies:* Studies that used any type of qualitative method(s) to obtain data (e.g. focus
47 group, interviews). Studies that included mixed methods will be included where the
48 qualitative data was analysed independently of the quantitative data.
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50
51

52 *Types of participants:* Clinicians (regardless of discipline), patients (previously or currently
53 being treated for CNCP with one or more opioids) and/or their carers, and the general public
54 who have been interviewed about the barriers and enablers to monitoring ongoing
55 appropriateness of opioid treatment and/or deprescribing opioids for CNCP.
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60 *Types of settings:* All healthcare settings in all countries.

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2
3 *Types of pain:* CNCP defined as pain lasting beyond three months unrelated to malignancy.
4

5
6 *Types of outcome measures:* Studies that report perceptions about barriers and/or enablers to
7 guideline-recommended safe and appropriate prescribing and use of opioids in CNCP.
8

9 Specifically, we will focus on guideline recommendations related to step 6 of the World
10 Health Organization (WHO) Principles of Good Prescribing²⁹ (Table 1), including
11 monitoring ongoing appropriateness of opioid treatment (i.e. effectiveness, benefits and/or
12 harms) and stopping opioid treatment (i.e. tapering, reducing or deprescribing treatment that
13 may be ineffective or harmful). To ensure studies can provide rich data specific to the use of
14 opioids, studies will only be included where their study aim and/or methodology (e.g.
15 interview guide) specifically mention aspects of monitoring ongoing appropriateness of
16 opioid treatment or stopping opioid treatment. Where studies include participants with
17 multiple medications, we will include studies where the experiences with opioids are reported
18 separately.
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26
27 Studies exploring the following topics will not be a focus of this review and such studies will
28 be excluded;
29

- 30
31
- 32 • Initiating opioid treatment
 - 33 • Opioid use and management of CNCP in the context of substance use disorder,
34 addiction or illicit opioid use.
 - 35 • Impact or evaluation of policy-, organisation-, practitioner- or patient-level
36 interventions (e.g. legislation change or experiences with a new program/intervention)
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40 Search Methods 41

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43 We will develop a search strategy with the assistance of an Information Specialist based at
44 Monash University, and with guidance from the qualitative research chapter in the Cochrane
45 Handbook.³⁰
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49 The following databases will be searched to identify relevant articles: MEDLINE, EMBASE,
50 CINAHL, AMED and PsycINFO. We will search databases from inception until July 2019,
51 but will limit the search to articles in English.
52
53

54
55 The search will be conducted in two parts. Part 1 will combine terms related to: CNCP as
56 recommended by the Cochrane Pain, Palliative and Supportive Care group; opioids;
57 monitoring, deprescribing or reducing; and barriers and enablers. Part 2 will identify studies
58 that have utilised qualitative research methodology. Qualitative filters will be used where
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60

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3 available to enhance sensitivity and specificity. To obtain final search results we will
4 combine part 1 and 2. The proposed MEDLINE search strategy is outlined in Appendix 1.

5
6
7 The reference list of included studies will also be searched for relevant articles and we will
8 track citations of included studies using Web of Science to ensure we gather all relevant
9 literature. Experts in the field will also be approached to identify other potentially relevant
10 studies using the existing professional networks of the authors.

11 Selection of studies

12
13
14
15 Two review authors will independently screen all titles and abstracts yielded from the search,
16 and all full text articles considered relevant. Any disagreements will be resolved via
17 discussion or by consultation with a third review author when necessary. Search and
18 screening results will be summarised in a Preferred Reporting Items of Systematic Reviews
19 and Meta-Analysis (PRISMA) flow diagram.³¹

20 Data collection

21
22
23 Pairs of review authors will independently extract data from each included study using a
24 standardised data collection form. Any disagreements will be resolved by discussion or by
25 consultation with a third review author when necessary. A piloted data extraction form will
26 capture information regarding the:

- 27 • Study details (authors, year of publication)
- 28 • Research question
- 29 • Participants (number, demographic characteristics, professional background, history
30 of opioid use, method of selection)
- 31 • Type and duration of CNCP
- 32 • Type and duration of opioid, including stage of deprescribing if applicable
- 33 • Setting (type of healthcare, country, urban/rural)
- 34 • Method of data collection (e.g. interview, focus group)
- 35 • Data analysis method (e.g. thematic analysis)
- 36 • Results (themes, sub-themes, supporting quotes, conclusions).

37 Quality Assessment

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40 The quality of included studies will be independently assessed by two review authors using
41 the Critical Appraisal Skills Programme (CASP) Checklist.³² Any disagreements will be
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3 resolved via discussion or by consultation with a third review author when necessary. The
4 CASP tool uses a checklist of 10 questions, each of which includes multiple signalling
5 questions to help users interpret the items (29 signalling questions in total). Studies will not
6 be excluded based on low quality. A summary table indicating the presence or absence of
7 CASP items will be included and a narrative summary of the quality of the included studies
8 will be provided.
9

14 Data analysis and synthesis

16 We will initially use an inductive approach to coding and conduct thematic synthesis, as
17 outlined by Thomas and Harden.³³ Each line of extracted text will be reviewed and codes will
18 be developed based on the content and meaning of each extract. As new studies are coded,
19 existing codes will be reviewed and revised with new codes added as needed. When all
20 studies have been coded, all text related to each code will be reviewed for consistency of
21 coding across studies. Two review authors will independently code an initial subset of studies
22 and then meet to discuss any discrepancies until consensus is reached. The remaining studies
23 will then be coded by one author and verified by a second author. Codes will be reviewed for
24 similarities and differences and organised into related descriptive themes. A draft summary of
25 the descriptive themes will be prepared by one author and discussed by the review team until
26 consensus is reached.
27

28 Next, the emergent themes will be mapped to the domains of the TDF^{25 26} independently by
29 two review authors or if there is no relevant domain placed in an 'other' category. A draft
30 summary of the TDF-aligned themes will be prepared by one author and discussed by the
31 review team until agreement on coding interpretations is reached.
32

33 In the final stage, review findings will be drafted to summarise analytical themes and
34 corresponding theoretical domains relating to barriers and enablers to ongoing monitoring of
35 opioid use and deprescribing opioids for CNCP from the clinician, patient and general public
36 point of view. The review findings will be prepared by one author and discussed by the
37 review team until consensus is reached.
38

53 Assessment of confidence in review findings

55 Pairs of independent authors will use the Grading of Recommendations Assessment,
56 Development, and Evaluation (GRADE) Confidence in the Evidence from Reviews of
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3 Qualitative Research (CERQual) tool to assess the confidence in the review findings.³⁴ This
4 tool considers four factors that influence the confidence in synthesis of qualitative studies:
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6

- 7 a. Methodological limitations of the studies contributing to a review finding (based on
8 CASP assessments)
9
10 b. Relevance of studies to the review question of studies contributing to a review finding
11
12 c. Coherence of data contributing to a review finding
13
14 d. Adequacy of supporting data supporting a review finding
15

16 The overall confidence in each review finding (i.e. for each theme generated) will be graded
17 as: high, moderate, low or very low (see Box 1).³⁴ A final decision on confidence in review
18 findings will be reached through discussion and consensus among the review team. Review
19 findings, confidence judgement for each finding and an explanation of the judgement will be
20 presented in a Summary of Qualitative Findings table (see Table 2).
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25 Reporting

26 The study will be reported in accordance with the enhancing transparency in reporting the
27 synthesis of qualitative research (ENTREQ) statement.³⁵
28
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30 Patient and public involvement

31 Patients and the public will not be involved directly in the design and conduct of the review.
32 However, the development of the review questions was informed by the Wiser Health Care
33 Research Collaboration which involves consumer advocates and health professionals.
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36 Ethics and dissemination

37 Ethical approval is not required to conduct this review. We will publish the results in a peer-
38 reviewed journal.
39
40

41 **Discussion**

42 Here we present the design of a qualitative evidence synthesis using the TDF to explore
43 clinician, patient and general public barriers and enablers to monitoring ongoing
44 appropriateness of opioid treatment and deprescribing opioids for CNCP, and align key
45 findings with evidence-based behaviour change techniques. This is an important step towards
46 developing tailored, effective, theory-based interventions for reducing the inappropriate use
47 of opioids in CNCP.
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Authors' contributions

AJC, DAO and RB conceived the idea for the study. AJC and DAO wrote the first draft of the manuscript. RB, AB, CGM, SM and CWL contributed to revising subsequent drafts critically for important intellectual content. All authors approved the final version of the manuscript and agree to be accountable for its content.

Study Status

Databases were searched in July 2019, screening and study selection occurred in August-September 2019 and data extraction is ongoing. We anticipate completion of this review by June 2020.

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Table 1: World Health Organization (WHO) guide to good prescribing and opioid prescribing in CNCP guidelines

WHO Principles of Good Prescribing²⁸	Guidelines for prescribing opioids for CNCP^{10 20 21 22}
<u>Step 1</u> Define the patient's problem	<ul style="list-style-type: none"> Assess the patient using a multidisciplinary approach. Non-pharmacologic therapy and non-opioid pharmacologic therapy are preferred for CNCP
<u>Step 2</u> Specify the therapeutic objective	<ul style="list-style-type: none"> Before starting opioid therapy, clinicians should establish realistic treatment goals with the patient and set a review date. Written, structured clinician-patient agreements/contracts for opioid use could be considered.
<u>Step 3</u> Verify the suitability of the medication	<ul style="list-style-type: none"> A careful assessment of the benefits and risks of prescribing an opioid for each specific patient should be considered.
<u>Step 4</u> Write a prescription	<ul style="list-style-type: none"> Start with a low dose and adjust slowly according to response. Do not introduce an opioid at the same time as another drug.
<u>Step 5</u> Give information, instructions and warnings	<ul style="list-style-type: none"> Discuss the adverse effects, possible harms and realistic benefits of long term opioid therapy with patients.
<u>Step 6</u> Monitor (and stop?) the treatment	<ul style="list-style-type: none"> Regularly review the patient to monitor progress, evaluate benefits and harms, and assess if ongoing treatment is needed. Reviews should be within 4 weeks of starting opioid treatment or of changes in dose, and minimum every 3 months for continued treatment. If opioid treatment is ineffective, or benefits do not outweigh harms, then opioid treatment should be tapered slowly and under supervision.

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Box 1: GRADE Confidence in the Evidence from Reviews of Qualitative research (CERQual) approach³⁴ to confidence in findings of qualitative evidence syntheses

- *High confidence*: highly likely that the review finding is a reasonable representation of the phenomenon of interest.
- *Moderate confidence*: likely that the review finding is a reasonable representation of the phenomenon of interest.
- *Low confidence*: possible that the review finding is a reasonable representation of the phenomenon of interest.
- *Very low confidence*: unclear whether the review findings is a reasonable representation of the phenomenon of interest.

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Table 2. Summary of qualitative findings

Review findings	Studies contributing to review findings	Assessment of methodological limitations	Assessment of relevance	Assessment of coherence	Assessment of adequacy	Overall GRADE CERQual assessment of confidence	Explanation of judgment
Finding 1							

CERQual, Confidence in the Evidence from Reviews of Qualitative Research

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Appendix 1: Medline Search Strategy (via Ovid)

Part 1

1. Pain, Intractable/
2. Chronic Pain/
3. exp Back Pain/
4. Neck Pain/
5. exp Arthralgia/
6. Fibromyalgia/
7. exp Headache Disorders/
8. exp Arthritis/
9. exp Musculoskeletal Pain/
10. exp Neuralgia/
11. exp Nociceptive pain/
12. exp Pain, Postoperative/
13. Pain, Referred/
14. Diabetic neuropathies/
15. (pain* or headache* or migraine* or neuralgia* or neuropath* or arthriti* or osteoarthriti* or osteoarthritis* or fibromyalg* or arthralgia* or myalgia*).mp.
16. or/1-15
17. exp Narcotics/
18. (opioid* or opiate* or opium or papaver or morphine or meperidine or methadone or buprenorphine or fentanyl or hydrocodone or hydromorphone or oxycodone or oxymorphone or codeine or tramadol or narcotic*).mp.
19. or/17-18
20. Deprescriptions/
21. Inappropriate Prescribing/
22. Prescriptions/
23. exp Drug Prescriptions/
24. exp Opioid-Related Disorders/
25. Drug Monitoring/
26. Pain Management/

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3 27. (prescrib* or prescrip* or monitor* or manag* or treat* or withdraw* or ceas* or
4 cessation or stop* or discontinu* or reduc* or taper* or titrat* or deprescrib* or
5 deprescrip* or de-prescrib* or de-prescrip* or optim*).mp.
6
7
8 28. or/20-27
9
10 29. (barrier* or enabler* or challeng* or concern* or facilitat* or belief* or believ* or
11 perception* or attitude* or perspective* or preference* or insight* or view* or
12 experience* or attitude* or factor*).mp.
13
14
15 30. 16 and 19 and 28 and 29
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17 Part 2

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19
20 31. exp Qualitative research/
21
22 32. Interview/
23
24 33. Interviews as topic/
25
26 34. Focus groups/
27
28 35. exp Decision making/
29
30 36. exp Attitude to Health/
31
32 37. Attitude of Health Personnel/
33
34 38. Nursing methodology research/
35
36 39. (Qualitative or mixed-method* or theme* or thematic).mp.
37
38 40. ((semi-structured or semistructured or unstructured or informal or in-depth or indepth
39 or face-to-face or structured or guide*) adj3 (interview* or discussion* or
40 questionnaire*)).mp
41
42 41. (focus adj3 group*).mp
43
44 42. (digital* record* or audiorecord* or taperecord* or videorecord* or videotap* or
45 audio-record* or tape-record* or video-record* or video-tap*).mp.
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47 43. or/31-42
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49 Total search strategy

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