NIHR | National Institute for Health and Care Research

Journals Library

Check for updates

Health Technology Assessment

*Volume 30 • Issue 27 • March 2026*

*ISSN 2046-4924*

# Interventions to safely and effectively reduce (taper) use of opioids in chronic non-cancer pain: a systematic review

*Ruaraidh Hill, Michelle Maden, Rui Duarte, Sam Eldabe, Su Golder, Marty Chaplin, Beth Shaw, Katy Sutcliffe, Adam Todd, Rebecca Bresnahan, Katherine Edwards, Janette Greenhalgh, Juliet Hounsome, Jack Trafford and Nefyn Williams*

*DOI 10.3310/GDWP3572*

NIHR | National Institute for Health and Care Research

Health Technology Assessment

Check for updates

Extended Research Article

# Interventions to safely and effectively reduce (taper) use of opioids in chronic non-cancer pain: a systematic review

Ruaraidh Hill[1*] Michelle Maden[1] Rui Duarte[1] Sam Eldabe[2] Su Golder[3] Marty Chaplin[1] Beth Shaw[4] Katy Sutcliffe[5] Adam Todd[6] Rebecca Bresnahan[1] Katherine Edwards[1] Janette Greenhalgh[1] Juliet Hounsome[1] Jack Trafford[1] and Nefyn Williams[7]

[1]Liverpool Reviews and Implementation Group, Health Data Science, Institute of Population Health, University of Liverpool, Liverpool, UK
[2]Department of Anaesthesia and Pain Management, South Tees Hospitals NHS Foundation Trust, Middlesbrough, UK
[3]Department of Health Science, The University of York, York, UK
[4]Center for Evidence-based Policy, Oregon Health and Science University, Portland, OR, USA
[5]Evidence for Policy and Practice Information and Coordination Centre, Social Research Institute, University College London, London, UK
[6]School of Pharmacy, University of Newcastle upon Tyne, Newcastle upon Tyne, UK
[7]Primary Care and Mental Health, Institute of Population Health, University of Liverpool, Liverpool, UK

[*]**Corresponding author** rahill@liverpool.ac.uk

Published March 2026
DOI: 10.3310/GDWP3572

This report should be referenced as follows:

Hill R, Maden M, Duarte R, Eldabe S, Golder S, Chaplin M, *et al*. Interventions to safely and effectively reduce (taper) use of opioids in chronic non-cancer pain: a systematic review. *Health Technol Assess* 2026;**30**(27). https://doi.org/10.3310/GDWP3572

# Health Technology Assessment

ISSN 2046-4924 (Online)

Impact factor: 4

A list of Journals Library editors can be found on the NIHR Journals Library website

Launched in 1997, *Health Technology Assessment* (HTA) has an impact factor of 4 and is ranked 30th (out of 174 titles) in the 'Health Care Sciences & Services' category of the Clarivate 2022 Journal Citation Reports (Science Edition). It is also indexed by MEDLINE, CINAHL (EBSCO Information Services, Ipswich, MA, USA), EMBASE (Elsevier, Amsterdam, the Netherlands), NCBI Bookshelf, DOAJ, Europe PMC, the Cochrane Library (John Wiley & Sons, Inc., Hoboken, NJ, USA), INAHTA, the British Nursing Index (ProQuest LLC, Ann Arbor, MI, USA), Ulrichsweb™ (ProQuest LLC, Ann Arbor, MI, USA) and the Science Citation Index Expanded™ (Clarivate™, Philadelphia, PA, USA).

This journal is a member of and subscribes to the principles of the Committee on Publication Ethics (COPE) (www.publicationethics.org/).

Editorial contact: journals.library@nihr.ac.uk

The full HTA archive is freely available to view online at www.journalslibrary.nihr.ac.uk/hta.

**Criteria for inclusion in the *Health Technology Assessment* journal**
Manuscripts are published in *Health Technology Assessment* (HTA) if (1) they have resulted from work for the HTA programme, and (2) they are of a sufficiently high scientific quality as assessed by the reviewers and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

## HTA programme

Health Technology Assessment (HTA) research is undertaken where some evidence already exists to show that a technology can be effective and this needs to be compared to the current standard intervention to see which works best. Research can evaluate any intervention used in the treatment, prevention or diagnosis of disease, provided the study outcomes lead to findings that have the potential to be of direct benefit to NHS patients. Technologies in this context mean any method used to promote health; prevent and treat disease; and improve rehabilitation or long-term care. They are not confined to new drugs and include any intervention used in the treatment, prevention or diagnosis of disease.

The journal is indexed in NHS Evidence via its abstracts included in MEDLINE and its Technology Assessment Reports inform National Institute for Health and Care Excellence (NICE) guidance. HTA research is also an important source of evidence for National Screening Committee (NSC) policy decisions.

## This article

The research reported in this issue of the journal was funded by the HTA programme as award number NIHR128842. The contractual start date was in September 2020. The draft manuscript began editorial review in July 2023 and was accepted for publication in October 2024. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' manuscript and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this article.

This article presents independent research funded by the National Institute for Health and Care Research (NIHR). The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, the HTA programme or the Department of Health and Social Care. If there are verbatim quotations included in this publication the views and opinions expressed by the interviewees are those of the interviewees and do not necessarily reflect those of the authors, those of the NHS, the NIHR, the HTA programme or the Department of Health and Social Care.

This article was published based on current knowledge at the time and date of publication. NIHR is committed to being inclusive and will continually monitor best practice and guidance in relation to terminology and language to ensure that we remain relevant to our stakeholders.



Published by the NIHR Journals Library (www.journalslibrary.nihr.ac.uk), produced by Newgen Digitalworks Pvt Ltd, Chennai, India (www.newgen.co).

# Abstract

**Background:** Opioids are prescribed for the management of chronic non-cancer pain, but they have important limitations and evidence does not support long-term use. People taking opioids therefore need support to reduce or stop use.

**Objectives:** The research aimed to inform better practice, pathways and service design to support people to reduce or stop their use of opioids and address inequalities.

Our objectives were to evaluate evidence on:

- effectiveness, safety (including adverse effects, adverse event) and acceptability of interventions to reduce opioid use
- barriers and facilitators to effective intervention
- inequalities in access to, acceptability of and benefiting from interventions.

**Methods:** We undertook four systematic reviews of published evidence on effectiveness; safety and acceptability; barriers and facilitators and inequalities. Searches included databases [MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, PsycInfo® (American Psychological Association, Washington, DC, USA)], trial registries (EU-CTR, International Standard Randomised Controlled Trial Number, Australian New Zealand Clinical Trials Register, ClinicalTrials.gov), websites (National Institute for Health and Care Research – be part of research, National Institute for Health and Care Excellence Evidence Search, Health Management Information Consortium, British Pain Society Members area) and repositories (Google Scholar, CORE.ac.uk) up to September 2022.

Records were independently assessed for inclusion using prespecified criteria: (1) adults with chronic non-cancer pain, with (2) prescription opioid use of at least 3 months experiencing an (3) intervention aiming reduce or discontinue the use of opioids. Cochrane Risk-of-Bias tool for randomised controlled trials and the appropriate Critical Appraisal Skills Programme tool were used for cohort, case-control and qualitative studies.

For the reviews of effectiveness and safety, data were synthesised and presented using tables and narrative synthesis. Meta-analysis was not appropriate. The barriers and facilitators review used thematic synthesis.

**Results:** A total of 44 studies (reported across 52 papers) were included in at least 1 of the reviews: 27 studies were included in the effectiveness, 7 in safety and 16 in the barriers and facilitators reviews. All but two studies provided evidence for the inequalities review.

*Effectiveness and safety:* The characteristics of the included studies were heterogeneous with different intervention approaches examined.

Fifteen studies reported effects on pain. There was no difference in pain severity between intervention and control groups across seven of eight comparative studies. All but two studies reported change in opioid use. The proportion of patients who ceased opioid use varied across studies and some studies reported evidence of later relapse. Other outcomes, including anxiety and depression and sleep quality, were examined across the included studies but there was no clear pattern of effect. No adverse event studies reported serious adverse event and no participants reportedly withdrew due to adverse event. Few studies examined intervention acceptability.

*Barriers and facilitators:* Eight barriers and eight facilitators were identified. They highlight the complex nature of the tapering process with the potential for multiple interdependent, behavioural, structural and contextual barriers to arise.

*Inequalities:* Most studies reported on PROGnosis RESearch Strategy partnership-Plus categories, but few considered impact. Our findings suggest males and older patients experience poorer tapering outcomes.

**Conclusions:** Evidence to support any specific opioid tapered reduction intervention is mixed and uncertain. Our findings reinforce that service design and delivery require careful consideration of individual-level factors and highlight the potential to widen inequalities.

Stakeholders consulted on the evidence suggest valuing relationships, addressing fear and stigma and upskilling in behaviour change techniques are key.

**Study registration:** This study is registered as PROSPERO CRD42020171135.

**Funding:** This award was funded by the National Institute for Health and Care Research (NIHR) Health Technology Assessment programme (NIHR award ref: NIHR128842) and is published in full in *Health Technology Assessment*; Vol. 30, No. 27. See the NIHR Funding and Awards website for further award information.

# Contents

# List of tables

# List of figures

# List of boxes

# List of abbreviations

| | |
|---|---|
| AE | adverse events |
| BPI | Brief Pain Inventory |
| CASP | Critical Appraisal Skills Programme |
| CBT | cognitive–behavioural therapy |
| CERQual | Confidence in the Evidence from Reviews of Qualitative Research |
| CES-D | Centre for Epidemiological Studies Depression Scale |
| COVID-19 | coronavirus disease 2019 |
| COWS | Clinical Opioid Withdrawal Scale |
| C-SOSI | Calgary Symptoms of Stress Inventory |
| GP | general practitioner |
| GRADE | Grading of Recommendations, Assessment, Development and Evaluations |
| HADS | Hospital Anxiety and Depression Scale |
| IASP | International Association of the Study of Pain |
| MCID | minimum clinically important differences |
| MED | morphine equivalent dose |
| MedSIP | National Patient Safety Team's Medicines Safety Improvement Programme |
| MI | motivational interviewing |
| MPI | Multidimensional Pain Inventory |
| NICE | National Institute for Health and Care Excellence |
| OOWS | Objective Opiate Withdrawal Scale |
| OSI | Opioid Safety Initiative |
| PHQ-9 | Patient Health Questionnaire-9 items |
| PI | principal investigator |
| PMC | prospective matched cohort |
| PRISMA | Preferred Reporting Items for Systematic Reviews and Meta-Analyses |
| PROGRESS-Plus | PROGnosis RESearch Strategy partnership-Plus |
| PSC | Patient Safety Collaboratives |
| QCA | qualitative comparative analysis |
| RCT | randomised controlled trial |
| SEM | socio-ecological model |
| SF-36 | Short Form questionnaire-36 items |
| SOWS | Subjective Opiate Withdrawal Scale |
| STORM | Support Team Onsite Resource for Management of Pain |
| TDF | Theoretical Domains Framework |
| VA | Veteran Affairs |
| WHO | World Health Organization |

# Plain language summary

## What was the question?

Opioids are often prescribed for chronic non-cancer pain, but evidence does not support their long-term use and people taking opioids may need support to reduce or stop their use. Our research aimed to inform the design of better National Health Service care and services and address inequalities.

## What did we do?

We used systematic reviews to thoroughly examine existing research on:

- how well different interventions work, their safety profiles, and how acceptable they are to patients
- factors that hinder (barriers) or support (facilitators) successful interventions
- differences (inequalities) in access to or receiving a benefit from these interventions.

What we found:

Like other research teams, we found that the evidence about how well interventions work, their safety, and how acceptable they are to patients to be of low quality. We are not sure which intervention approaches (or the components of these) affect patients' opioid use and pain, but there is some evidence that tapering combined with support interventions may make *some difference* to opioid use *without increasing* reported pain. We also found that patients may benefit from extra support during tapering. None of the studies we found reported any serious problems (adverse events). Safe and effective reductions in opioid use may be more likely when care is *patient-centred*, acknowledges the *complexity* of the process, both the patient and healthcare professional are *willing* to taper, and the patient is able to maintain their *ability* to taper.

Patients may experience differences ('inequalities') in access to tapering or in outcomes. We found that some patients may experience less benefit, including people who are *male*, *older* or have *another disease or condition* (a comorbidity) in addition to pain may. We did not find enough evidence about how other important equity characteristics affect outcomes.

The evidence does not let us recommend a specific approach, but it suggests the need to consider the overall wraparound support for patients reducing or tapering their opioid use. Our stakeholders suggested that practitioners prefer *evidence-informed options* over a single fixed pathway.

# Scientific summary

## Background

It is estimated that chronic pain affects between one-third to a half of the UK population. Chronic pain is thought to arise as a dynamic interaction between biological, psychological and social factors and is difficult to treat. Opioids are commonly prescribed for the management of chronic non-cancer pain, but they have important limitations and current evidence does not support their long-term use. People taking opioids may therefore need support to reduce or stop their use. Low-quality evidence indicates that people can reduce or stop their opioid use and experience reduced pain, but research has focused on limited effectiveness outcomes and not on the factors that influence outcomes for, and the experiences of, different groups of people who require opioid tapering.

## Objectives

The main aims of the research were to inform better practice, pathways and service design to support people with chronic non-cancer pain to reduce or stop their use of opioids and address inequalities in access.

Our objectives were to evaluate published evidence on:

- effectiveness, safety [including adverse effects, adverse event (AE)] and acceptability of interventions to reduce opioid use
- barriers and facilitators (B&F) to effective intervention
- inequalities in access to, acceptability of and benefiting from interventions.

## Methods

We undertook four systematic reviews of the published evidence on effectiveness, safety (including adverse effects, AE) and acceptability of interventions to reduce opioid use; the B&F to effective intervention and inequalities in access to or benefiting from interventions. Searches were conducted in four databases [MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, PsycInfo® (American Psychological Association, Washington, DC, USA)], four trial registries (EU-CTR, ISRCTN, Australian New Zealand Clinical Trials Register, ClinicalTrials.gov), four websites (National Institute for Health and Care Research – be part of research, National Institute for Health and Care Excellence Evidence Search, Health Management Information Consortium, British Pain Society Members area) and two academic repositories (Google Scholar, CORE.ac.uk). Additional strategies included searching the reference lists of topic-relevant systematic reviews and our included studies, citation searches and suggestions from experts and clinicians working in the field. All searches were updated in September 2022.

Articles were independently assessed for inclusion by at least two reviewers using prespecified eligibility criteria: (1) adults with chronic non-cancer pain, (2) prescription opioid use of at least 3 months and (3) the intervention aimed to reduce or discontinue the use of opioids. The relevant outcomes differed between the four reviews as did the eligible study designs. Exclusion criteria for all reviews were: papers published prior to 2000, non-English language papers and publications that were editorials, theses, conference abstracts, letters or commentaries. Both data extraction and assessment of risk of bias were conducted by one reviewer and checked for accuracy by a second. Data extraction was done using pre-piloted forms. Risk of bias was assessed using the Cochrane Risk-of-Bias tool for randomised controlled trials and the appropriate Critical Appraisal Skills Programme tool was used for cohort, case-control and qualitative studies.

For the reviews of effectiveness and safety, data were synthesised and presented using tables and narrative review. Meta analyses were not appropriate for the effectiveness or adverse effects reviews. For the B&F review, qualitative data were analysed following methods for thematic synthesis.

## Results

A total of 44 studies (reported across 52 papers) were included in at least 1 of the 4 reviews. In total, 27 studies were included in the effectiveness review, 7 in the adverse effects review and 16 in the B&F review. All but two studies provided evidence for the inequalities review.

### *Effectiveness and safety of interventions to reduce opioid use*

The characteristics of the included studies were heterogeneous and different intervention approaches were examined. We identified similar limitations to previous reviews, in that there was variation across the functions of the interventions investigated and in the reported outcomes. Many studies were non-comparative, had short follow-up periods and/or experienced high dropout rates. Two studies were of taper-only interventions (i.e. sequential dose reduction), 6 studies examined interventions that could be used as adjuncts to tapering (including acupuncture and mindfulness training), 11 studies were of interventions that involved tapering plus support and 8 studies were of an intervention aimed at changing health services. Overall, 11 studies included a comparator, and 16 studies were non-comparative.

Fifteen studies reported effects on pain. There was no difference in pain severity between intervention and control groups across seven of eight comparative studies that reported effects on pain. All but two of the included studies reported at least one measure of change in opioid use, and across many of the studies, patients achieved reductions in opioid dose. The proportion of patients who ceased opioid use varied across studies and some studies reported evidence of later relapse. While cessation of opioid use is an outcome that is clinically important, defining the level of reduction in opioid use that is clinically relevant is problematic. A range of other outcomes, including anxiety and depression and sleep quality, were examined across the included studies but there was no clear pattern of effect. None of the seven studies that reported AEs reported any serious AEs, and no patients were reported to have withdrawn from a study due to an AE. Few studies examined intervention acceptability. Further, at least two studies experienced significant issues related to dropouts and slow enrolment into the trial respectively.

### *Barriers and facilitators of effective intervention*

Eight barriers and eight facilitators were identified. They highlight the complex nature of the tapering process with the potential for multiple interdependent, behavioural, structural and contextual barriers to arise. To improve the chances of a successful tapering outcome, there is a need for a whole systems approach that is patient-centred and recognises that tapering is a dynamic, individualistic, intensive process. Our findings reinforce the perspective that the design and delivery of successful opioid-tapering initiatives requires careful consideration of individual-level factors and that these individual-level factors have implications for interpersonal, organisational and environmental level approaches to opioid tapering. Crucial to the success of opioid tapering, is both a patient and provider's willingness to taper and the ability of a patient to maintain a taper.

### *Inequalities in access to or benefitting from intervention*

Most studies collected and reported baseline data according to the PROGnosis RESearch Strategy partnership-Plus categories, but few considered the impact of patient demographics on effectiveness or whether inequalities existed in access to opioid tapering. Consequently, little is known about opioid-tapering interventions and their impact on inequalities. Our findings suggest that patients who are male and older experience a worse tapering outcome. Mixed results were found for the impact of comorbidities on tapering outcomes. For race/ethnicity, occupation and socioeconomic status, no significant differential associations were observed.

## Conclusions

Our evidence synthesis shows that evidence to support any opioid reduction intervention for the tapering of opioids in people with chronic non-cancer pain is mixed and uncertain. With none of the studies done in the UK, the generalisability of our findings to NHS clinical practice is uncertain. No included study reported serious AEs, and no patients were reported to have withdrawn from a study due to an AE. Our review findings also reinforce the perspective that the design and delivery of successful opioid-tapering interventions require careful consideration

of individual-level factors and demonstrate the potential for interventions to widen inequalities in relation to both effectiveness and access.

Stakeholders commenting on our findings suggest that practitioners agree that valuing relationships and addressing fear and stigma are key, and that upskilling in the use of behaviour change techniques and support for both patients and practitioners in readiness for change would support tapering.

## Study registration

This study is registered as PROSPERO CRD42020171135.

## Funding

This award was funded by the National Institute for Health and Care Research (NIHR) Health Technology Assessment programme (NIHR award ref: NIHR128842) and is published in full in *Health Technology Assessment*; Vol. 30, No. 27. See the NIHR Funding and Awards website for further award information.

# Chapter 1 Background

## Chronic pain

Pain is defined by the International Association of the Study of Pain (IASP) as an unpleasant sensory and emotional experience associated with actual or potential tissue damage.[1] Under the latest World Health Organization (WHO) *International Classification of* Diseases, Eleventh edition, chronic pain is classified as either chronic primary pain or chronic secondary pain.[2] Chronic primary pain is defined as pain that persists or recurs for longer than 3 months and is associated with significant emotional distress or functional disability and that cannot be better accounted for by another chronic pain condition. Chronic secondary pain syndromes are linked to other diseases as the underlying cause, for which pain may initially be regarded as a symptom.

Pain has a significant impact globally, with the Global Burden of Disease study 2016 finding pain and pain-related diseases to be a leading cause of disability and disease burden.[3] Estimates of the prevalence of chronic pain vary in the literature but experiences of chronic pain, a complex and distressing condition, are common. A systematic review of UK studies estimated a pooled prevalence of chronic pain of 43.5% and prevalence of moderate-severely disabling chronic pain between 10.4% and 14.3%.[4] More recent estimates, drawn from electronic health records (2016–7), suggest that 31.9% of adults with musculoskeletal disorders in England experience 'high impact' chronic pain.[5]

Chronic pain can have a significant impact on peoples' lives and more broadly on society. People who are permanently unable to work because of long-term sickness or disability are more likely to report having chronic pain and people who report chronic pain are less likely to be in employment.[6] Chronic pain does not affect people equally. Women report a higher prevalence than men and people living in more deprived areas of England are more likely to report having chronic pain than those living in the least deprived areas.[6] Black people are more likely to experience chronic pain than people of other ethnicities.[6]

## Opioid therapy for chronic non-cancer pain

Opioid therapy has been the mainstay of pain management for centuries. Although only a small dose may be required initially to manage someone's pain, the nervous system rapidly develops tolerance to the effects of opioids,[7] including the analgesic effect, which means that the opioid dose needs to be increased over time to achieve the same level of pain relief. Some people may experience hypersensitivity to pain because of long-term opioid use.[8]

The use of opioids in acute and end-of-life pain is well established, but evidence does not support the clinical effectiveness of longer-term (particularly high-dose) opioid treatment for chronic pain.[9] Furthermore, treatment carries a dose-dependent risk for serious harms, which increase substantially at doses above an oral morphine equivalent of 120 mg/day.[10] The long-term use of opioid therapy for the management of non-cancer pain has therefore been questioned, and in 2018, IASP published a statement recommending caution against continuous, longer-term use of opioids because of issues with efficacy and safety.[11]

There has also been increasing recognition in the USA, Canada, Australia and many European countries (including the UK) that efforts to improve pain management have led to continuous increases in opioid prescribing.[12–14] In England, opioid prescriptions were found to have increased by 34% between 1998 and 2016.[13] A UK-wide study found evidence of wide variation in prescribing practices, with older age groups and social deprivation associated with an incremental increase in long-term opioid use.[15] An alarming rise in the number of deaths associated with the use of prescription opioids in the USA and Canada,[16] have renewed global calls for the reduction of new prescriptions of opioids and high-dose prescribing.

Recent international guidelines place a greater emphasis on treating chronic non-cancer pain with non-pharmacological therapies. For example, Almeida *et al.*[17] examined changes in the management recommendations for low back pain in

national clinical practice guidelines from the UK, Denmark, Belgium and the USA, finding that non-pharmacological treatments were now more consistently encouraged over pharmacological treatments. New National Institute for Health and Care Excellence (NICE) guidelines for chronic primary pain published in 2021 recommend that patients be offered psychological therapies, acupuncture or group-based exercise.[18]

## Tapering and stopping opioid therapies

The National Patient Safety Team's Medicines Safety Improvement Programme (MedSIP) has recognised the harms of high-dose opioid prescribing (> 120 mg oral morphine equivalent) and set ambitions to reduce this practice by 50% by March 2024.[19] The Faculty of Pain Management 'Opioids Aware' prescribing resource[20] provides indications for the gradual reduction (tapering) of opioids and/or discontinuation (summarised in *Box 1*).

**BOX 1** 'Opioids Aware' prescribing resource on tapering and stopping

It is important to taper or stop the opioid regimen if:

- The medication is not providing useful pain relief. The dose above which harms outweigh benefits is 120 mg oral morphine equivalent/24 hours. Increasing opioid load above this dose is unlikely to yield further benefits but exposes the patient to increased harm.
- The underlying painful condition resolves.
- The patient receives a definitive pain-relieving intervention (e.g. joint replacement).
- The patient develops intolerable side effects.
- There is strong evidence that the patient is diverting his/her medications to others.

Systematic reviews that have examined the effectiveness of interventions aimed at reducing opioid prescribing have however been limited by the low quality of the evidence available.[21–23] Very little published research has been conducted in the UK to date. At the end of 2021, the 15 Patient Safety Collaboratives (PSC) in England carried out an intelligence gathering exercise on behalf of the MedSIP.[24] This exercise identified 112 examples of service activities across England that were being provided with the specific aim of reducing the prescribing of opioids. The pathway that emerged from their analysis covered five stages for tapering and stopping opioids:

- *prevent initiation*, strategies and practices that divert treatment away from the prescribing of opioids while still effectively managing pain
- *de-escalate*, activity that prevents increasing doses of opioids or minimises the duration of treatment
- *find chronic use*, methods used to identify patients who are at risk of dependence or harm from continuing opioid use
- *treat (taper and support)*, interventions aimed at reducing opioid prescribing
- *sustain*, interventions designed to maintain the lowest possible opioid use.

The Medicines Optimisation Group at the University of East Anglia drew on this local and national evidence to develop a toolkit for opioid tapering. They identified seven key features that should be included in all opioid-tapering interventions (shown in *Box 2*).

**BOX 2** Medicines Optimisation Group East Anglia toolkit for tackling chronic opioid use in non-cancer pain

- There needs to be a clear expectation that opioid deprescribing is the responsibility of prescribers. . . .and programmes should incorporate. . .
- Information about the consequences of excess opioid use.
- Information about how to taper (guidelines).
- Prescribers with appropriate knowledge and skills to initiate tapering discussions and navigate the patient pathway.
- A consistent approach by all members of the healthcare team.
- Comprehensive education for patients.
- A pathway for patient management including access to appropriate levels of psychological and physical support.

Only limited attention has been given in systematic reviews to the consideration of adverse events (AEs). Further, the conflict between the physician's desire to relieve the patient's pain and fear of inducing addiction persists and can influence the selection of therapies including opioids. By exploring barriers and facilitators to, the safe and effective reduced use of prescribed opioids for chronic non-cancer pain, we can more easily identify strategies that will support patients, carers and healthcare professionals to safely and effectively taper opioids, where appropriate. Furthermore, analysis of barriers and facilitators can contribute to an improved understanding of how multiple levels of the healthcare system (i.e. individual, interpersonal, organisational and environmental factors) may influence 'transformation and change processes' (Williamson and Nelson, 2017, p. 1249)[25] to hinder or enable an opioid taper. One recent systematic review explored barriers and facilitators in the broader context of opioid deprescribing and monitoring;[26] however, no systematic reviews were located focusing specifically on factors impacting on the success of opioid tapering.

The target populations for opioid-tapering interventions are likely to be heterogeneous with different sociodemographic characteristics, which may affect their response to opioid-tapering interventions. Consequently, this may result in a widening of social and health inequalities. However, little is known about opioid-tapering interventions and their impact on inequalities. Furthermore, more opioids are prescribed in the north than in the south of England and more opioids are prescribed in areas of greater social deprivation.[13,27] It is therefore paramount to consider and evaluate potential inequalities in access to interventions that aim to reduce the use of opioids. To date, no systematic reviews have focused on inequalities in effectiveness or patient experience for different groups of people accessing or undergoing opioid tapering.

# Chapter 2 Aim and objectives

## Study aim

The overarching aim of this study is to inform better practice, pathways and service design within the NHS to support people with chronic non-cancer pain to reduce their use of opioids and reduce inequalities in relation to clinical effectiveness of, and access to opioid tapering.

## Objectives to support the study

Conduct evidence syntheses to:

- Determine the effectiveness, safety profile and patient acceptability of interventions to effectively reduce use of opioids (Reviews 1 and 2).
- Identify barriers to, and facilitators of, the safe and effective reduced use of opioids from patient, professional and service perspectives (Review 3).
- Assess inequalities in relation to access to, acceptability of and benefit from interventions to effectively reduce use of opioids (Review 4).

# **Chapter 3** Systematic review methods

The review methods followed the general principles outlined in the Centre for Reviews and Dissemination guidance[28] for conducting reviews in health care (Reviews 1–4), Thomas and Harden's[29] 'Methods for the thematic synthesis of qualitative research in systematic reviews' (Review 3) and the Joanna Briggs Institute mixed-methods guidance[30] (Review 3). The reviews are reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist.[31]

## Search strategy

The search strategies were designed by an experienced information specialist (MM) in collaboration with the wider review team and stakeholders to ensure that the search terms (particularly the opioid terms) were relevant to our requirements (e.g. relevant to NHS clinical practice). The following information sources were searched: databases, websites, academic repositories, references of topic relevant systematic reviews, citation searches, reference lists of included studies, trials registries (Review 1 only) and suggestions from experts and clinicians working in the field. *Table 1* outlines the specific sources searched for each of the reviews. We also used an adapted version of the CLUSTER approach[32] using citation searching, tracking lead authors, targeted Google Scholar searches and PubMed-related articles, to identify sibling or related studies.

**TABLE 1** Search sources for effectiveness (Review 1), adverse effects (Review 2) and barriers and facilitators (Review 3)

| Search sources | Review 1<br>Effectiveness | Review 2<br>Adverse effects | Review 3<br>Barriers and facilitators |
|---|---|---|---|
| MEDLINE | ✔ | ✔ | ✔ |
| EMBASE | ✔ | ✔ | ✔ |
| CENTRAL | ✔ | ✔ | ✔ |
| CINAHL | ✔ | ✔ | ✔ |
| PsycInfo® (American Psychological Association, Washington, DC, USA) | ✔ | ✔ | ✔ |
| Science Citation Index | | ✔ | |
| ICTRP Unavailable at this time redirected to primary sources: | | | |
| EU-CTR<br>www.clinicaltrialsregister.eu/ | ✔ | ✔ | |
| ISRCTN<br>www.isrctn.com/ | ✔ | ✔ | |
| ANZCTR<br>www.anzctr.org.au/ | ✔ | ✔ | |
| ClinicalTrials.gov | ✔ | ✔ | |
| NIHR be part of research[3]<br>https://bepartofresearch.nihr.ac.uk/ | ✔ | ✔ | |
| NICE Evidence Search | ✔ | ✔ | ✔ |
| HMIC | | | ✔ |
| Repository searches via Google Scholar<br>CORE.ac.uk[3] | | | ✔ |
| British Pain Society Members area | ✔ | ✔ | ✔ |

ANZCTR, Australian New Zealand Clinical Trials Register; CENTRAL, Cochrane Central Register of Controlled Trials; CINAHL, Cumulative Index to Nursing and Allied Health Literature; HMIC, Health Management Information Consortium; ICTRP, International Clinical Trials Registry Platform; NIHR, National Institute for Health and Care Research.

Three searches were conducted in parallel: Search 1: identified relevant studies for the effectiveness review (Review 1); Search 2: identified relevant studies for the adverse effects review (Review 2); and Search 3: identified papers that were either barrier and facilitator studies or were qualitative studies (Review 3). Studies used to inform the inequalities review (Review 4) were identified from the studies included in Reviews 1–3.

Initial exploratory searches were developed in an iterative manner in MEDLINE from keywords identified by the review team and published topic-relevant systematic reviews. Keywords included opioid terms AND tapering terms AND pain terms. This structure was then adapted to identify relevant studies for each review according to the relevant eligibility criteria (see *Appendix 1* for search strategies). All databases were searched from inception to 11 January 2021. All searches were updated on 20 September 2022. Search results were downloaded into EndNote [Clarivate Analytics (formerly Thomson Reuters), Philadelphia, PA, USA] and records were deduplicated and exported to a specialist systematic review management system, Rayyan[33] for screening.

## Eligibility criteria

The population, intervention, comparators, outcomes, study designs process was used to frame the inclusion/exclusion criteria for the effectiveness and adverse effects reviews (Reviews 1 and 2) (*Table 2*). The SPICE framework[34] was used to frame the inclusion criteria for the barriers and facilitator review (Review 3) and the inequalities review (Review 4) (*Table 3*). For the inequalities review (Review 4), the PROGnosis RESearch Strategy partnership-Plus (PROGRESS-Plus)[35] framework was used to consider socially stratifying factors that may widen inequalities (*Table 4* for defining PROGRESS-Plus characteristics).

**TABLE 2** Eligibility criteria for effectiveness review (Review 1) and adverse effects review (Review 2)

| | Inclusion | Exclusion |
|---|---|---|
| Population | Adults (18 years and older) with chronic non-cancer pain and prescription opioid use of at least 3 months | People with a diagnosis of opioid use disorder (opioid addiction) |
| | | People using illicit opioids |
| Intervention | Any intervention (pharmacological or non-pharmacological) focused on managed reduction of opioid use over time | Interventions not focused on managed reduction of opioid use |
| | Aim of the study must include a treatment goal of dose reduction or cessation of opioid medication | (Rapid detoxification – such as over 1 up to × days) |
| Comparator | Any comparator or none | Not applicable |
| Outcomes | *Effectiveness* | Other reported outcomes |
| | Pain intensity/severity, measured using a validated scale (e.g. NRS, VAS) | |
| | Physical functioning, measured using a validated scale (e.g. ODI, BPI) | |
| | Prescribed opioid use | |
| | Psychological functioning/emotional functioning, measured using a validated scale (e.g. BDI, HAD, SF-36) | |
| | Opioid withdrawal symptoms, measured using a validated scale (e.g. ShOWS) | |
| | Quality of life, measured using a validated scale (e.g. EQ-5D, SF-36) | |
| | Dropout rates and reasons | |

**TABLE 2** Eligibility criteria for effectiveness review (Review 1) and adverse effects review (Review 2) (*continued*)

| | Inclusion | Exclusion |
|---|---|---|
| | Mortality | |
| | Patient global impression of change, measured using a validated scale (e.g. PGIC) | |
| | Sleep quality, measured using a validated scale (e.g. Pittsburgh Sleep Quality Index) | |
| | Social or economic activities (e.g. work) | |
| | Rescue treatment use | |
| | Non-prescribed medication use | |
| | *Adverse effects* | |
| | AEs | |
| | Mortality | |
| Design | *Effectiveness* | *Effectiveness* |
| | RCTs | Uncontrolled observational studies and case series with fewer than 25 participants |
| | Controlled observational studies | Case reports |
| | Uncontrolled observational studies (with at least 25 participants) | Qualitative studies |
| | | Reviews (systematic, non-systematic) |
| | *Adverse effects* | *Adverse effects* |
| | RCTs | Qualitative studies |
| | Controlled observational studies | Reviews (systematic, non-systematic) |
| | Uncontrolled observational studies (with no limit on participant numbers) | |
| | Case reports | |
| Limits | Published in 2000 and onwards | Pre-2000 |
| | English-language publications | Non-English language |
| | | Publication types: editorials, theses, conference abstracts, letters, commentaries |

BDI, Beck Depression Inventory; BPI, Brief Pain Inventory; EQ-5D, EuroQol-5 Dimensions; NRS, Numeric Rating Scale; ODI, Oswestry Disability Index; PGIC, patient global impression of change; RCT, randomised controlled trial; SF-36, Short Form questionnaire-36 items; VAS, visual analogue scale.

**TABLE 3** Eligibility criteria for barriers and facilitators review (Review 3) and inequalities review (Review 4)

| | Inclusion | Exclusion |
|---|---|---|
| Setting | Any community or health or social care setting using prescription opioids for management of chronic non-cancer pain | |
| Perspective | Adults (18 years or older) with chronic non-cancer pain and prescription opioid use of at least 3 months<br>or | People with a diagnosis of opioid use disorder (opioid addiction) |

continued

**TABLE 3** Eligibility criteria for barriers and facilitators review (Review 3) and inequalities review (Review 4) (*continued*)

| | Inclusion | Exclusion |
|---|---|---|
| | Healthcare providers/carers of patients with chronic non-cancer pain and prescription opioid use of at least 3 months | People using illicit opioids |
| Intervention | Opioid tapering – any intervention (pharmacological or non-pharmacological) focused on managed reduction of opioid use over time | Interventions not focused on managed reduction of opioid use |
| Comparison | Not applicable | Not applicable |
| Evaluation | Studies that reported (explicit or non-explicit) barriers or facilitators to safe and effective reduced use of prescribed opioids for chronic non-cancer pain from patient, professional and service perspectives | Conference abstracts |
| | Qualitative, quantitative, mixed-method or case series study designs as long as they reported barriers/facilitators in the results (rather than reported anecdotally within the discussion) | |
| | Relevant systematic reviews and study protocols were retained only for checking for completed primary studies | |
| | English language only studies | |

**TABLE 4** Included measures of PROGRESS-Plus characteristics

| PROGRESS-Plus factor | Definition |
|---|---|
| Place of residence | Rural, urban and inner-city places of residence |
| Race, ethnicity, culture and language | Racial, ethnic and cultural background and language (e.g. patient does not speak the same language as the healthcare provider) |
| Occupation | Unemployed/employed/retired; full-time or part-time employment; graded hierarchies measuring occupational status; skilled or unskilled work |
| Gender and sex | Male or female |
| Religion | Religious affiliation, beliefs or values held |
| Education | Level of educational attainment or qualifications; institutions attended (e.g. school/further education/higher education); years in full-time education |
| Socioeconomic status | Poverty or income level (continuous level or proportion falling into income brackets), asset-based measures (e.g. housing tenure) or receipt of state welfare or health payment assistance |
| Social capital | Social support (e.g. marital status, social support from friends, family or provider) or social network |
| Plus factors | Age |
| | Comorbidities |
| | Status as long-term opioid user (inequalities in access to opioid tapering only) |

## Study selection

A single screening process was adopted across all reviews. Two reviewers independently screened all titles and abstracts to identify studies for inclusion against all review eligibility criteria (see *Tables 2* and *3*). The full text of papers was retrieved if studies fulfilled the eligibility criteria for at least one review, or if it was unclear from the abstract whether or not the paper fulfilled the inclusion criteria. The full-text papers were independently reviewed by two reviewers. The full text had to fulfil the eligibility criteria for at least one of the reviews (see *Tables 2* and *3*) to be included. In the event of disagreement, a third reviewer or clinical expert was consulted.

## Quality assessment

For each review, quality assessment was undertaken by one reviewer and cross-checked by a second reviewer. Any disagreements about risk of bias were resolved by discussion, or by consulting with a third reviewer.

For the effectiveness and AEs review (Reviews 1 and 2), randomised controlled trials (RCTs) were assessed using the Cochrane tool for assessing risk of bias in randomised trials,[36,37] whereas cohort studies and case-control studies were assessed using the relevant Critical Appraisal Skills Programme (CASP) checklists.[38]

For the barriers and facilitators review (Review 3), the methodological limitations of qualitative studies and qualitative data from mixed-methods studies were assessed using an adapted version of the CASP Qualitative tool[39] based on the following CASP domains: context, sampling strategy, data collection, data analysis, support of individual study findings in the underlying data, reflexivity, ethical considerations and other concerns. For the quantitative studies, the relevant CASP tool was applied.[38,40] CASP tools were modified to use 'can't tell' when insufficient information was available to make a judgement (i.e. a reporting issue) and an additional category was added ('somewhat') and used when relevant information including both strengths and limitations was reported (i.e. a methodological issue).[41] We made a judgement on the overall assessment of the limitations of the study[42] as follows:

- where assessments for most items in the tool were 'yes', this indicated *no or few limitations*
- where assessments for most items in the tool were 'somewhat' or 'cannot tell', this indicated *minor limitations*
- where assessments for one or more items in the tool were 'no', this indicated *major limitations*.

## Data extraction

Data from the included studies were entered into a pre-piloted data extraction form tailored to the effectiveness and AEs reviews (Reviews 1 and 2) and the barriers and facilitators review (Review 3). Data were extracted by one reviewer and independently checked for accuracy by a second reviewer. Data from multiple publications of the same study were extracted and reported as a single study. The data extraction elements for the effectiveness and AE reviews (Reviews 1 and 2) and barrier and facilitators review (Review 3) are presented in *Appendices 1* and *3*. Relevant data extracted and included in these reviews were examined for evidence of inequalities in access to, acceptability of and benefit from interventions to reduce use of opioids (Review 4).

## Data synthesis

### *Effectiveness and adverse effects reviews (Reviews 1 and 2)*

Meta-analysis was not possible for this review because of significant differences in study designs, methods, timing of assessment and definition of outcomes. Consequently, a narrative synthesis was performed. Outcomes are presented in evidence tables with an accompanying description of the evidence.

### *Barriers and facilitators review (Review 3)*

Qualitative data were analysed following Thomas and Harden's three-step approach to thematic synthesis of qualitative research in systematic reviews:[29] (1) coding of text line by line; (2) development of descriptive themes; and (3) development of analytical themes. First, text was coded on a line-by-line basis. An iterative approach to coding was undertaken and codes were reviewed and revised as new data emerged. A single reviewer coded the data, and a second reviewer checked the assigned codes. Any discrepancies were resolved by discussion. Second, the codes were reviewed and arranged into related descriptive themes. Finally, analytical themes were derived from the related descriptive themes in collaboration with the wider review team. A convergent integrated approach to synthesis was adopted that was consistent with the Joanna Briggs Institute mixed-methods guidance of 'qualitising' quantitative data, that is 'qualitizing refers to quantitative data being converted into themes, categories, typologies, or narratives'.[30]

## Confidence in review findings

Currently, there is no guidance on how to assess confidence/certainty in mixed-methods reviews. By transforming quantitative data into qualitative data,[30] we aimed to be inclusive when assessing confidence in the review findings. Confidence in the Evidence from Reviews of Qualitative Research (CERQual) uses four components to assess confidence in review findings: methodological limitations, adequacy of data, coherence and relevance. For each review finding, each component was assessed as either having 'no, or very minor', 'minor', 'moderate' or 'serious' concerns. An overall assessment of confidence in the review findings was then assessed as 'high', 'moderate', 'low' or 'very low'.[43,44,45,46,47] Confidence in the review findings were assessed using the information available in the thematic analysis and results from the CASP quality assessment.

## Mapping barriers and facilitators to theoretical frameworks

Identifying barriers and facilitators is enhanced by using theoretical frameworks to guide the process.[48,49,50] Framing barriers and facilitators within theoretical domains can help explain why an intervention works[49,51] and can aid in the identification of tailored implementation strategies for successful opioid tapering. Opioid-tapering initiatives are more likely to be effective if they target the determinants (barriers and facilitators) of tapering. To facilitate implementation of the review findings, we mapped identified barriers and facilitators to opioid tapering in people with chronic non-cancer pain to two theoretical frameworks; the Theoretical Domains Framework (TDF)[52,53,54] and a modified version of the Levesque *et al.* conceptual framework of access to health care.[55,56]

## Theoretical domains framework

The TDF version 2 [TDF(v2)][52,53,54] was used to identify *what* affective, cognitive, social and environmental barriers and facilitators to tapering exist. The TDF(v2) is a validated framework based on psychological theory that has been used to identify determinants of behaviour change. The TDF(v2) consists of 84 constructs organised into 14 theoretical domains (knowledge; skills; social/professional role and identity; beliefs about capabilities; optimism; beliefs about consequences; reinforcement; intentions; goals; memory, attention and decision processes; environmental context and resources; social influences; emotions; and behavioural regulation) focusing on individual- and group-level behaviours derived from 33 behaviour change theories. The TDF(v2) offers advantages for assessing barriers and facilitators to interventions that operate at individual, group/team or organisational level. This framework has been used to guide recent evidence synthesis on barriers and facilitators to opioid monitoring and deprescribing,[26] a recent realist review[57] on opioid tapering and in primary research on the use of opioid prescribing.[58]

We followed the guidance on analysing data using the TDF(v2) of behaviour change to investigate implementation problems.[59]

### *Developing a coding guideline*

To increase the reliability of coding, we developed a coding framework. One reviewer developed the coding framework; a second reviewer checked the coding. Any discrepancies in the interpretation of the codes were resolved by discussion.

### *Deductive analysis*

Data were extracted and coded according to which TDF domain they were judged to represent. Coding was undertaken in an iterative manner, with modifications made upon familiarisation with the data.

#### *Inductive analysis*

If data did not fit any of the TDF domains, a new theme was created.

#### *Identifying important domains*

Barriers and facilitators (coded to constructs) were rank-ordered according to the numbers of studies that reported them to identify the most common determinants to opioid tapering. To facilitate recommendations for practice, barriers and facilitators within each TDF domain were organised using the socio-ecological model (SEM).[60] The SEM allowed us to highlight barriers and facilitators to opioid tapering within multiple levels of the healthcare system (i.e. at the individual, interpersonal, organisational and environmental levels).

### Levesque's conceptual framework of access to health care

Review findings were also mapped to a modified version of Levesque's conceptual model of access to health care[56] for two reasons. First, to help gain a deeper understanding of whether barriers and facilitators arise from dimensions of accessibility of services, from the abilities of healthcare workforce (provider-related barriers and facilitators) and/or from the abilities of patients to interact with the dimensions of accessibility to generate access (patient-related barriers and facilitators). Second, the model allows for the exploration of barriers and facilitators at various time points in the patient's care pathway, thereby enabling a greater understanding of when barriers and facilitators may arise during the opioid-tapering process. A modified version[56] of Levesque *et al.*'s. conceptual framework[55] was used as it recognised the '"human fit" between the needs and abilities of the population with the capacity and abilities of the healthcare workforce',[56] (p. 7) highlighting that 'organisational structures and processes are mediated by individuals with different capabilities and with varying capacity to engage'[56] (p. 4). Thus, the modified version allowed for consideration of barriers relating to the abilities of providers (e.g. confidence in their ability to taper, fears of difficult patient interactions) as well as the abilities of patients.

### *Inequalities review (Review 4)*

Due to the clinical heterogeneity observed in opioid-tapering outcomes in studies reporting quantitative data, we adopted a two-stage narrative approach to synthesis. In stage 1, all studies included in Reviews 1–3 were reviewed for PROGRESS-Plus characteristics (see *Table 4*) reported in baseline characteristics and PROGESS-Plus characteristics controlled for, or adjusted for, in statistical analysis. In stage 2, only studies that explored one or more of the following were narratively synthesised in detail:

- stratifying effect analyses by different categories of a PROGRESS-Plus characteristic
- associations between PROGRESS-Plus characteristics and changes in opioid use or tapering trajectory following a tapering intervention
- the impact of opioid-tapering initiatives on PROGRESS-Plus-related outcomes (e.g. ability to work)
- any patient PROGRESS-Plus factor identified as a barrier or facilitator to opioid-tapering interventions or any PROGRESS-Plus factor associated with participation (e.g. number of dropouts/completers, reasons for dropout).

Data within each PROGRESS-Plus factor were then organised using the SEM[60] to present the findings. The SEM allowed for highlighting of inequalities in the effectiveness of, and access to, opioid tapering within multiple levels of the healthcare system. Findings were also mapped to a modified version of Levesque's conceptual model of access to health care[55,56] for two reasons. Firstly, to help gain a deeper understanding of whether inequalities in access arise from dimensions of accessibility of services or abilities of healthcare workforce and/or from the abilities of patients to interact with the dimensions of accessibility to generate access. Secondly, the model allows for the exploration of inequalities at various time points on the tapering pathway, thereby enabling a greater understanding of when inequalities may arise during the opioid-tapering process.

## Stakeholder engagement

To explore the completeness of and to contextualise the findings of the evidence reviews, a summary of findings was presented to stakeholders and discussed at an online workshop using an approach based on NICE fieldwork methods.[61]

## Deviations from the protocol

We specified in the protocol that we would use an emerging method, qualitative comparative analysis (QCA) to complement the synthesis of quantitative and qualitative evidence. The QCA would have been used to identify components of interventions that were linked to the safe reduction of opioids. However, QCA was not feasible as we did not find sufficient evidence. The heterogeneity and reporting of the evidence also hampered our use of other novel methods specified in the protocol (harvest plots and a menu of intervention effects) that would have provided a visual extension to the results of the synthesis.

When we developed the project, two UK intervention trials, I-WOTCH and the EMPOWER study, were in progress. We intended to have access to the I-WOTCH study data, but this was not forthcoming, and the EMPOWER study did report within the time frame for inclusion of data in our project.

# **Chapter 4** Search results for all reviews

The results of the searches and study selection are presented in *Figure 1*. The initial and updated searches identified 16,434 unique records to be screened, and of these 15,574 papers were excluded as they did not fulfil the inclusion criteria. The full-text copies of the remaining 860 papers, plus an additional 6 papers identified through hand-searching, were obtained and the inclusion criteria were applied independently by at least 2 reviewers. At this stage, 728 papers were excluded as they did not fulfil the inclusion criteria. A further 52 studies were excluded once reviewers began to extract data. The reasons for exclusions during data extraction are shown in *Appendix 4*. A further 30 papers reported on ongoing studies that were yet to report their results.

Four papers[62,63,64,65] reporting barriers and facilitators data were identified in the update searches, but as these papers did not contribute any new data to the review they were excluded but retained for inclusion in a future update. Overall, 52 papers (44 studies) were included in at least 1 of the 3 reviews (Reviews 1–3). The overlap between the reviews is shown in *Figure 2* and a list of the studies included in each review is shown in *Table 5*.

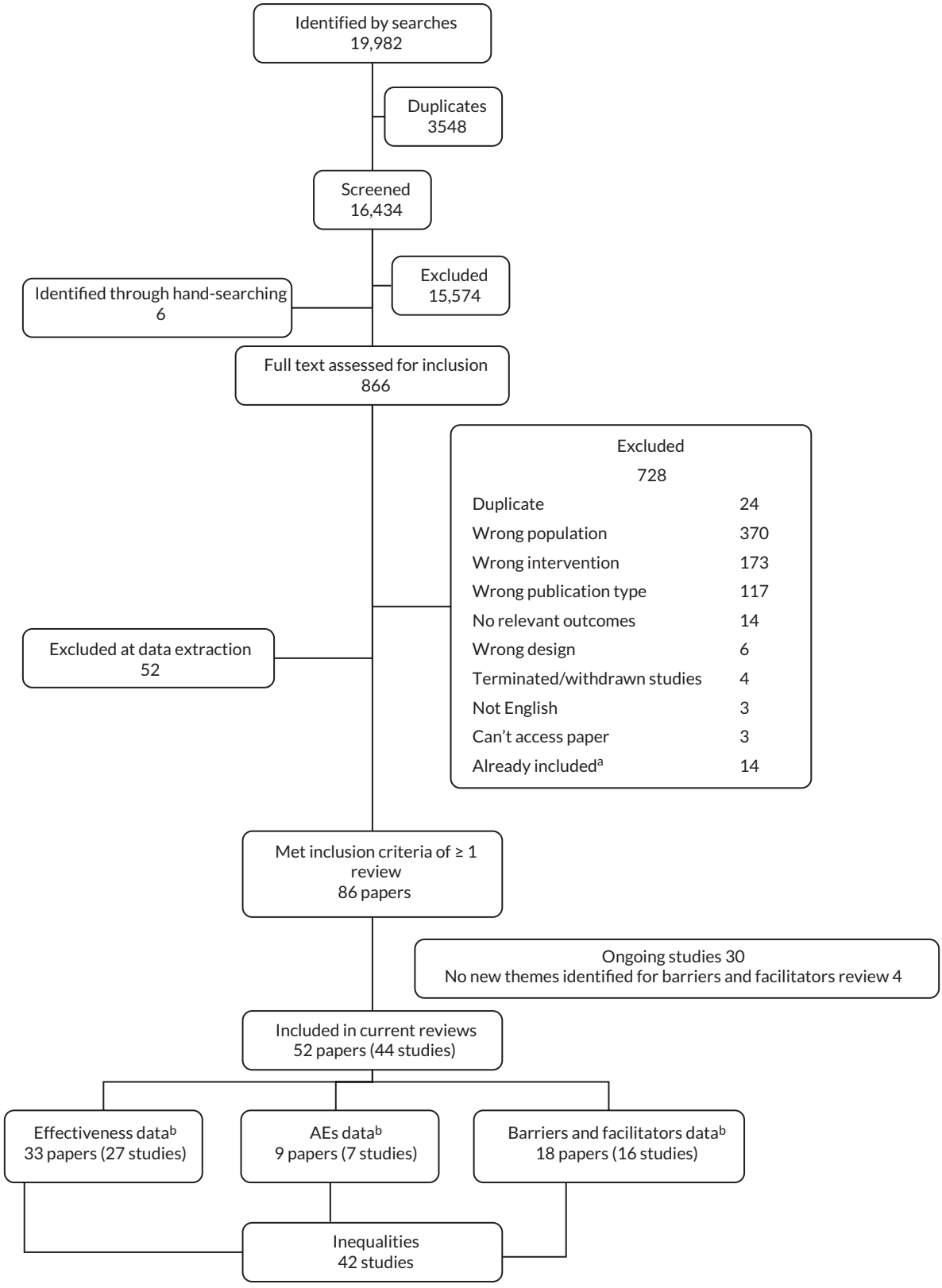


**FIGURE 1** Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram. a, Only applies to updated search where studies may have been identified in the earlier search. b, Some studies provided data that contributed to ≥ 1 review.

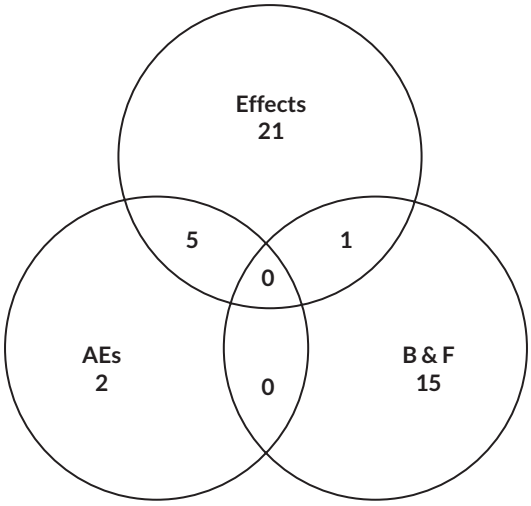


**FIGURE 2** Overlap of studies between reviews. B&F, barriers and facilitators.

**TABLE 5** Studies contributing data to each of the four reviews

| Review data | Included studies (*N*) | References |
|---|---|---|
| ***Individual data*** | | |
| Effects only | 21 | Austin 2019,[66] Bienek 2019,[67] Cunningham 2016,[68] Garland 2014,[69] Gersch 2021,[70] Hudak 2020,[71] Huffman 2017,[72] Jacobs 2016,[73] Krumova 2013,[74] Kurita 2018,[75] Laigaard 2020,[76] Montgomery 2020,[77] Murphy 2013,[78] Panicker 2022,[79] Rivich 2018,[80] Seal 2020,[81] Sharp 2018,[82] Thakral 2018[83] (linked papers: Von Korff 2016,[84] 2017,[85] Sherman 2018,[86] Thakral 2018[87]), Townsend 2008,[88] Twillman 2018,[89] Zhou 2017[90] |
| AEs only | 2 | Caldera 2020,[91] Lalanne 2016[92] |
| Barriers and facilitators only | 15 | Benintendi 2021,[93] Firemark 2021,[94] Kuntz 2021,[95] Frank 2016,[96] Giannitrapani 2018[97] (linked paper: Giannitrapani 2018[98]), Henry 2019,[99] Henry 2019[100] (linked paper: Henry 2017[101]), Kennedy 2018,[102] Langford 2020,[103] Magee 2021,[104] Matthias 2017,[105] McNeilage 2022,[106] Quinlan 2021,[107] White 2020,[108] Wu 2019[109] |
| ***Combined data*** | | |
| Effects and AEs | 5 | Capano 2020,[110] Jackson 2021,[111] Zheng 2008,[112] Sullivan 2017[113] (linked paper: NCT 2013[114]),[115] Zheng 2019[116] (linked paper: Xue 2012[115]) |
| Effects and barriers and facilitators | 1 | Westanmo 2015[117] |
| Inequalities | 42 | Austin 2019,[66] Benintendi 2021,[93] Bienek 2019,[67] Capano 2020,[110] Cunningham 2016,[68] Firemark 2021,[94] Frank 2016,[96] Garland 2014,[69] Gersch 2021,[70] Giannitrapani 2018,[97,98] Henry 2019,[99] Henry 2019,[100,101] Hudak 2020,[71] Huffman 2017,[72] Jackson 2021,[111] Jacobs 2016,[73] Kennedy 2018,[102] Krumova 2013,[74] Kuntz 2021,[95] Kurita 2018,[75] Laigaard 2020,[76] Langford 2020,[103] Magee 2021,[104] Matthias 2017,[105] McNeilage 2022,[106] Montgomery 2020,[77] Murphy 2013,[78] Panicker 2022,[79] Quinlan 2021,[107] Rivich 2018,[80] Seal 2020,[81] Sharp 2018,[82] Sullivan 2017,[113] Thakral 2018[83,87] (linked papers: Von Korff 2016,[84] 2017,[85] Sherman 2018[86]), Townsend 2008,[88] Twillman 2018,[89] Westanmo 2015,[117] White 2020,[108] Wu 2019,[109] Zheng 2008,[112] Zheng 2019,[116] Zhou 2017[90] |

# Chapter 5 Effectiveness of interventions to reduce opioid use

## Summary of study characteristics

Thirty-three papers, reporting on 27 studies, assessed the effectiveness of tapering of opioids in people with chronic non-cancer pain. Five of those studies also reported on AEs.[110,111,112,113,116] Eleven papers reported on comparative studies. Of these, seven were RCTs,[69,71,75,111,112,113,116] one was a prospective matched cohort (PMC) study,[81] one was a retrospective randomly matched cohort study[70] and two were retrospective cohort studies.[67,77] Sixteen papers were non-comparative studies; 14 were single cohorts (6 were prospective and 8 were retrospective) and 2 were studies that did not follow a patient cohort but reported on changes in outcomes following a change in practice.[83,117]

None of the included studies were done in the UK. Twenty-one studies were done in the USA,[66,68,69,70,71,72,73,77,78,79,80,81,82,83,88,89,90,110,111,113,117] two each were done in Australia,[112,116] Denmark[75,76] and Germany.[67,74] All comparative studies except one,[67] were done in outpatient clinics and three studies[71,77,81] were done in US Department of Veteran Affairs (VA) facilities. Two non-comparative studies[74,78] were done in inpatient facilities and three[73,80,117] were done in US VA facilities. The recruitment period of the studies varied from 1 month to 6 years and the earliest study started recruiting in 2001.[74]

The type of intervention and the comparator varied across the studies. Of the comparative studies, two studies[67,75] examined a tapering-only intervention based on sequential dose reduction, four studies[77,111,112,116] examined acupuncture, three studies[69,71,113] examined cognitive, psychological and behavioural interventions, and two studies[70,81] examined pain management programmes. The comparator groups received treatment as usual in six studies,[70,75,77,81,111,113] support groups in two studies,[69,71] sham acupuncture in two studies,[112,116] and the remaining study[67] assessed two different dose reduction schedules. Of the 16 non-comparative studies, 7 studies[66,73,80,82,83,89,117] examined interventions aimed at changing a service (e.g. linked to the US Opioid Safety Initiative [OSI]), 3 studies[78,90,110] examined a pharmacological intervention and 6 studies[68,72,74,76,79,88] examined pain management programmes.

None of the authors of the comparative studies reported receiving commercial funding. Eleven non-comparative studies reported a funding source and one study[110] received funding from a commercial company that manufactured the intervention under study (CBD Hemp extract).

Of the comparative studies, one[69] reported a conflict of interest due to the author being 'the Director of the Center on Mindfulness and Integrative Health Intervention Development', which indicated a potential commercial interest in the intervention under study. Two non-comparative studies reported that members of the research teams either were in receipt of grants from private companies or were principal investigators (PIs) in commercially funded studies.[83,88] For four studies,[66,69,80,112] there was no information about whether there were conflicts or not. For the remaining 19 studies, it was reported that there were no conflicts of interest.

All studies reported outcome measures at baseline, the end of treatment/discharge and at least one later follow-up assessment. The length of follow-up varied between 3 and 8 months. A range of outcome measures were used in the studies but all but two studies[68,69] reported on the change in opioid use. The timing of outcomes was not always reported clearly, although most studies reported values at baseline and the end of the intervention.

Details of the study characteristics are shown for comparative studies in *Table 6* and non-comparative studies in *Table 7*.

## Intervention characteristics

### *Comparative studies*

Details of the intervention characteristics are shown in *Table 8*.

**TABLE 6** Study characteristics of the comparative studies (Review 1)

| Author, year | Design, no. of arms | Country, setting | Recruitment period | Funding, conflicts of interest | Timing of assessments | Outcome measures |
|---|---|---|---|---|---|---|
| Garland, 2014[69] | RCT | USA | 2011–2 | Grants from the National Institute on Drug Abuse and the Fahs-Beck Fund for Research and Experimentation | Baseline | Pain severity (BPI) |
| | 2 | Outpatient | | Conflicts = NR | End of treatment | Pain interference (BPI) |
| | | | | | 3-month follow-up | Changes in opioid use disorder status |
| | | | | | | Desire for opioids |
| | | | | | | Self-reported opioid misuse |
| | | | | | | Non-reactivity |
| | | | | | | Reinterpretation of pain sensations |
| | | | | | | Reappraisal |
| | | | | | | Affective and somatic symptoms of stress |
| | | | | | | Treatment credibility |
| Hudak, 2020[71] | RCT | USA | October 2016–22 | Department of Defence National Institute on Drug Abuse | Baseline | Opioid dose reduction |
| | 2 | Outpatient | | Conflicts = Dr Garland is the Director of the Center on Mindfulness and Integrative Health Intervention Development. Dr Garland has received honoria and payment for seminars, lectures and teaching engagements, also royalties from the sale of books | End of treatment period | |
| | | VA primary care and pain clinics | | | 2 and 4 months follow-up | |
| Jackson, 2021[111] | RCT | USA | October 2017–October 2018 | Vanderbilt Institute for Clinical Translational Research Grant | Baseline | Change in MED |
| | 2 | Outpatient | | Conflicts = none | Monthly until completion | HADS-A |
| | | | | | | HADS-D |
| | | | | | | CINA |

continued

**TABLE 6** Study characteristics of the comparative studies (Review 1) (*continued*)

| Author, year | Design, no. of arms | Country, setting | Recruitment period | Funding, conflicts of interest | Timing of assessments | Outcome measures |
|---|---|---|---|---|---|---|
| | | | | | | NRS |
| Kurita, 2018[75] | RCT | Denmark | February 2009–December 2014 | The Danish Agency for Science, Technology and Innovation and Hørslev-Fonden | Baseline | QoL |
| | 2 | Outpatient | | Conflicts = none | 2–3 weeks after randomisation | Risk for opioid medication misuse |
| | | Multidisciplinary team of the pain centre | | | 4–6 weeks after randomisation | Symptoms of opioid withdrawal |
| | | | | | 3–6 months after randomisation | Pain intensity |
| | | | | | | Equivalent daily oral morphine dose in milligrams |
| | | | | | | Other medications |
| | | | | | | Hours of sleep in the previous night before assessment |
| | | | | | | Sensation of rest |
| | | | | | | Anxiety |
| | | | | | | Depression |
| | | | | | | Measures of cognitive function |
| Sullivan, 2017[113,114] | RCT | USA | May 2013–September 2015 | National Institute of Drug Addiction | Baseline | Opioid use, pain severity and pain interference subscales (BPI) |
| | 2 | Outpatient | | Conflicts = none | End of treatment period | Prescription Opioid Difficulties Scale |
| | | Multidisciplinary pain centre | | | 34 weeks follow-up | Prescription Opioid Misuse Index |
| | | | | | | Patient Health Questionnaire-9 |
| | | | | | | Generalized Anxiety Disorder-7 |

**TABLE 6** Study characteristics of the comparative studies (Review 1) (*continued*)

| Author, year | Design, no. of arms | Country, setting | Recruitment period | Funding, conflicts of interest | Timing of assessments | Outcome measures |
|---|---|---|---|---|---|---|
| | | | | | | Insomnia Severity Index |
| | | | | | | Pain Self-Efficacy Questionnaire |
| | | | | | | Patient Health Questionnaire-15 |
| | | | | | | Opioid craving |
| | | | | | | Patient global impression of change |
| | | | | | | Perceived helpfulness of opioid taper support |
| | | | | | | Feasibility – no. of sessions attended, in person or telephone |
| | | | | | | AEs |
| Zheng, 2008[112] | RCT | Australia | 2005–6 | Research Grant Australian Acupuncture and Chinese Medicine Association | Baseline | Dosage of opioid like medication |
| | 2 | Outpatient | | Royal Melbourne Institute of Technology University | End of treatment period | Type and incidence of related side effects |
| | | Pain management clinic | | Australian Postgraduate Award | Every 4 weeks until 20 weeks follow-up | Pain intensity (VAS) |
| | | | | Conflicts = NR | | MPQ |
| | | | | | | SF-36 |
| | | | | | | BDI |
| Zheng, 2019[115,116] | RCT | Australia | July 2009 and February 2013 | National Health and Medical Research Council, Australia (555411) and partially funded by the Helen MacPherson Smith Trust (No. 6549) | Baseline | Dosage of opioid medication (diary) |
| | 3 | Outpatient | | Conflicts = none | End of the treatment period | BDI |
| | | Three pain clinics and from the public | | | Every 4 weeks for 12 weeks follow-up | SF-36 v2 |

continued

**TABLE 6** Study characteristics of the comparative studies (Review 1) (*continued*)

| Author, year | Design, no. of arms | Country, setting | Recruitment period | Funding, conflicts of interest | Timing of assessments | Outcome measures |
|---|---|---|---|---|---|---|
| | | | | | | Roland Morris Disability Questionnaire ~(functionality) |
| | | | | | | SOWS |
| | | | | | | Change of attitudes |
| | | | | | | Pain and non-pain signs and symptoms (Chinese Medicine Chronic Pain Questionnaire) |
| Seal, 2020[81] | PMC | USA | November 2015–January 2018 | Department of Veterans Affairs Quality Enhancement Research Initiative award (Grant no: 15-283) | Baseline | Changes in MEDD |
| | 2 | Outpatient | | Conflicts = none | 3 months after randomisation | Opioid risk mitigation |
| | | San Francisco Veterans affairs Medical Centre | | | 6 months after randomisation | |
| Bienek, 2019[67] | Retrospective cohort (change in clinical practice) | Germany | 2010–6 | None | Baseline | Length of hospital stay |
| | 2 | Inpatient | | Conflicts = none | Daily | Duration of opioid withdrawal |
| | | Hospital | | | Discharge | Completed taper |
| | | | | | 6 weeks post discharge | Reduction in MED |
| | | | | | | Attrition |
| | | | | | | Serious AEs |
| | | | | | | Pain intensity |
| | | | | | | SOWS |
| Gersch, 2021[70] | Retrospective randomly matched cohort study | USA | 1 April 2016 and 30 June 2017 | Kaiser Permanente Pharmacy Department | Baseline, 3, 6 and 12 months | Primary: 6-month change from daily MME from baseline |

**TABLE 6** Study characteristics of the comparative studies (Review 1) (*continued*)

| Author, year | Design, no. of arms | Country, setting | Recruitment period | Funding, conflicts of interest | Timing of assessments | Outcome measures |
|---|---|---|---|---|---|---|
| | 2 | Kaiser Permanente Colorado (KPCO), healthcare delivery system | | Conflicts = none | | Secondary: 3- and 12-month change in daily MME<br><br>6- and 12-month reduction ≥ 20% reduction in daily MME<br><br>6-month change of non-opioid medications (benzodiazepine/ hypnotic, anticonvulsant, antidepressant, muscle relaxant and prescription NSAIDs)<br><br>6-month non-medication pain management healthcare utilisation |
| Montgomery, 2020[77] | Retrospective cohort | USA | August 2017–January 2019 | No funding | 3 months prior | Pain (NRS) |
| | 2 | Outpatient<br><br>Fargo Veterans Affairs Health Care system facilities | | Conflicts = none | Baseline<br><br>End of treatment<br><br>6 months follow-up | Daily dosage of MME |

BDI, Beck Depression Inventory; BPI, Brief Pain Inventory; CINA, Clinical Institute Narcotic Assessment; HADS-A, Hospital Anxiety Depression Scale-Anxiety; HADS-D, Hospital Anxiety Depression Scale-Depression; MED/MEDD, morphine equivalent (daily) dose; MME, morphine milligram equivalent; MPQ, McGill Pain Questionnaire; NR, not reported; NRS, Numeric Rating Scale; NSAIDs, non-steroidal anti-inflammatory drugs; QoL, Quality of Life; SF-36, 36-Item Short Form Health Survey; SOWS, Subjective Opiate Withdrawal Scale; VAS, visual analogue scale.

**TABLE 7** Study characteristics of the non-comparative studies (Review 1)

| Author<br>Year | Country<br>Setting | Recruitment period | Funding<br>Conflicts of interest | Timing of assessments | Outcome measures |
|---|---|---|---|---|---|
| ***Prospective cohort*** | | | | | |
| Capano<br>2020[110] | USA<br>Private pain management centre | September–December 2018 | Ananda Professional.<br>Conflicts = Alex Capano is employed by Ecofibre Ltd, which wholly owns the sponsor company, Ananda Professional | Baseline<br>4 and 8 weeks | Pain Disability Index (PDI-4),<br>Pittsburgh Sleep Quality Index (PSQI)<br>Pain intensity and inference (PEG)<br>Patient Health Questionnaire (PHQ-4)<br>Dependence on opioids for pain control measured via the opioids' dose<br>Readiness to taper (VAS) |
| Cunningham<br>2016[68] | USA<br>Outpatient | January 2006–December 2012 | NR<br>Conflicts = none | Admission<br>Dismissal | Clinical Opioid Withdrawal Scale (COWS)<br>Clinical Institute Withdrawal Assessment (CIWA)<br>Pain (NRS)<br>MPI<br>SF-36<br>Pain catastrophising (PCS)<br>Depressive symptoms (CES-D) |
| Jacobs<br>2016[73] | USA<br>Veterans' Health Association primary care clinic<br>Outpatient | 15 December 2014–31 March 2015 | Funded by intramural support for quality improvement projects<br>Conflicts = none | NR | Adverse outcomes (NR in paper)<br>Non-VA controlled substance prescriptions<br>Pharmacist recommendations for regimen change cohort<br>Discontinuation of COT |
| Krumova<br>2013[74] | Germany<br>Inpatient<br>Pain management department hospital | January 2001–December 2006 | PhD Thesis<br>Conflicts = none | Baseline<br>End of intervention<br>1–2 years | Opioid withdrawal/reduction<br>Pain intensity average, maximum and current (11-point scale)<br>Depression (the Allgemeine Depression scale, equivalent to the CES-D)<br>PDI<br>Self-report instrument on pain-related disability<br>SF-36 (Mental Component Summary Score and Physical Component Summary Score) |
| Laigaard<br>2020[76] | Denmark<br>Hospital<br>Outpatient | January 2018 (Zealand University Hospital) and July 2018 (Holbæk Hospital) – May 2019 | Grant from Kong Christian den Tiendes Fond<br>Conflicts = none | Baseline<br>50% reduction of daily opioid consumption<br>When no further reductions were feasible | Median opioid dose oral morphine milligram equivalents<br>Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)<br>Trail Making Test (TMT) A and B<br>HADS<br>SF-36 |

**TABLE 7** Study characteristics of the non-comparative studies (Review 1) (*continued*)

| Author<br>Year | Country<br>Setting | Recruitment period | Funding<br>Conflicts of interest | Timing of assessments | Outcome measures |
|---|---|---|---|---|---|
| Townsend<br>2008[88] | USA<br>Pain rehabilitation centre<br>Outpatient | January 2005–February 2006 | The Department of Psychiatry and Psychology Research Committee<br>Conflicts = W. M. Hooten: Sucampo Pharmaceutical – site PI, clinical trial; Eli Lilly – site PI, clinical trial; Pfizer – site PI, clinical trial. Other authors had no relevant financial relationships to disclose | Admission<br>Discharge<br>6-month post treatment | Withdrawn from opioids<br>Pain severity (MPI)<br>Pain interference (MPI)<br>Perceived control over pain and life events (MPI)<br>General activity level (MPI)<br>Depression – CES-D<br>Health status (SF-36)<br>Pain catastrophising scale (PCS) |
| ***Retrospective cohort*** | | | | | |
| Austin<br>2019[66] | USA<br>Health Education Center<br>Outpatient | 2016–17 | NR<br>Conflicts = NR | NR | COT cessation<br>Change in MED<br>% of patients on > 50 MED and > 90 MED<br>Number of patients on concomitant benzodiazepines. |
| Huffman<br>2017[72] | USA<br>Pain clinic<br>Outpatient | 2007–12 | Partially supported by the Cleveland Clinic Neurological Center for Outcomes Research.<br>Conflicts = none | Discharge<br>6 and 12 months post treatment | Pain severity (NRS)<br>Depression (DASS)<br>Anxiety (DASS)<br>Functional impairment (PDI)<br>Treatment completion<br>Opioid resumption at 6, 12 months post treatment |
| Murphy<br>2013[78] | USA<br>Inpatient<br>Veterans Affairs tertiary care hospital | July 2006–March 2011 | NR<br>Conflicts = None | Within 2 days of admission and within 2 days of discharge | Ceased opioids<br>Pain numeric rating scale: pain intensity<br>Pain outcomes questionnaire for veterans: pain severity, interference in activities of daily living, mobility, negative affect, vitality and pain-related fear<br>Chronic Pain Coping Inventory<br>Coping strategies coping questionnaire catastrophising subscale<br>Sleep<br>Satisfaction with treatment |

continued

**TABLE 7** Study characteristics of the non-comparative studies (Review 1) (*continued*)

| Author<br>Year | Country<br>Setting | Recruitment period | Funding<br>Conflicts of interest | Timing of assessments | Outcome measures |
|---|---|---|---|---|---|
| Panicker 2022[79] | USA<br>Multidisciplinary pain clinic | June 2019–December 2019 | NR<br>Conflicts = none | The Advanced Practice Registered Nurse (APRN) evaluated the patient during the initial and follow-up visits (note: not clear when follow-up visits occurred) | Prescribed opioid dose<br>Self-reported pain scores |
| Rivich 2018[80] | USA<br>Outpatient<br>Veterans Affairs Eastern Colorado Health Care System | 1 January 2015–31 March 2015 | The study was not funded.<br>Conflicts = NR | 12 months following initial review | Change in total daily opioid dose<br>Concurrent prescribing of opioids and benzodiazepines<br>Adherence to local VA/Veterans Integrated Service Network (VISN) policy<br>Monitoring practices |
| Sharp 2018[82] | USA<br>Setting = NR | 2009–14 | Internal funding for the KPSC Care Improvement Research Team supported the project<br>Conflicts = none | NR | Reduction in opioid prescribing<br>Proportion of encounters with unfavourable satisfaction scores |
| Twillman 2018[89] | USA<br>Advocacy organization<br>Setting = NR | 25 September –17 October 2017 | Collegium Pharmaceutical, Inc., Canton, MA, USA<br>Conflicts = none | 6 months | ER/LA opioid medications<br>Pain severity<br>Level of function<br>Side effects |
| Zhou 2017[90] | USA<br>Treatment at outpatient rehabilitation and pain management clinic and review at private physician office for physical medicine and rehabilitation | 1 December 2011 and 31 December 2014 | NR<br>Conflicts = none | Admission<br>Discharge | Pain intensity<br>Successful opioid discontinuation |

**TABLE 7** Study characteristics of the non-comparative studies (Review 1) (*continued*)

| Author<br>Year | Country<br>Setting | Recruitment period | Funding<br>Conflicts of interest | Timing of assessments | Outcome measures |
|---|---|---|---|---|---|
| ***Non-patient cohort*** | | | | | |
| Thakral 2018[83,84,85,86,87] | Washington, USA<br>Outpatient<br>Primary care clinics of the Group Health Cooperative | 2006–14 | Patient-Centered Outcomes Research Institute<br>National Institute of Aging<br>Conflicts = Dr Von Korff was PI to GHRI that concerned opioids. Grants also supported work on opioids by Dr Shortreed, Ms Saunders and Mr Walker. Von Korff and Shortreed co-investigators GHRI grants. Dr Shortreed funding from GHRI grants.<br>Ms Saunders stock in Merck | Baseline period (2006–7)<br>Dose reduction period (1 January 2008–30 September 2010)<br>Risk mitigation period (1 January 2010–30 September 2014) | Average daily MED<br>Interference with activities and enjoyment of life, and depressive symptoms |
| Westanmo 2015[117] | USA<br>Outpatient<br>Veterans association outpatient hospital and community-based outpatient clinics | 1 April 2011–1 October 2014 | Not reported<br>Conflicts = none | Baseline (90 days prior to 1 April 2011)<br>Post (90 days prior to 1 October 2014)<br>That is 3.5 years | Prescribing rates of high dose opioid therapy (> 200 MED daily)<br>Prescribing of specific opioid drugs<br>Provider beliefs and attitudes |

CES-D, Centre for Epidemiological Studies Depression Scale; COT, chronic opioid therapy; DASS, The Depression, Anxiety and Stress Scale; ER, extended-release; LA, long-acting; MED, morphine equivalent dose; MPI, Multidimensional Pain Inventory; NR, not reported; NRS, Numeric Rating Scale; SF-36, Short Form questionnaire-36 items; VAS, visual analogue scale.

**TABLE 8** Intervention characteristics of the comparative studies (Review 1)

| Study ID | Type of intervention | Brief intervention description | Type of comparator | Brief comparator description | Aim of intervention | Setting | Mode(s) of delivery | Group/ individual | Duration/intensity |
|---|---|---|---|---|---|---|---|---|---|
| ***RCTs*** | | | | | | | | | |
| Garland 2014[69] | Behavioural; no active tapering | Mindfulness-orientated recovery enhancement (MORE) – mindfulness training, third-wave CBT and principles from positive psychology | Active control: support group | Support group: 2-hour conventional SG sessions 8–12 participants; social worker-led discussion on topics pertinent to chronic pain and long-term opioid use that were selected to roughly match corresponding themes in the MORE intervention | Reduction | Outpatient | Face to face | Group | 2 hours/week 8 weeks |
| Hudak 2020[71] | Behavioural; no active tapering | MORE (see above) | Active control: supportive group psychotherapy | Supportive group psychotherapy: 2-hour Rogerian group psychotherapy sessions; psychologist facilitated emotional expression and discussion on topics pertinent to chronic pain and long-term opioid use. Plus 15 minutes/day journaling | Reduction | Outpatient | Face to face | Group | 2 hours/week 8 weeks |
| Jackson 2021[111] | Acupuncture + standard of care | Participants received standard of care in addition to the NADA protocol (standard of care consists of medication management with opioid weaning) | Standard of care | Standard of care (consists of medication management with opioid weaning) | Reduction | Outpatient | Face to Face | Individual | Monthly for 12 months |
| Kurita 2018[75] | Sequential opioid dose reduction | Reduction of 10% of the daily opioid dose every week until discontinuation of opioid treatment for up to 6 months | TAU | Maintained on the same treatment for the next 6 months without changes of medications | Discontinuation | Outpatient | Face to face and telephone | Individual | NA |
| Sullivan 2017[113,114] | Sequential opioid dose reduction and behavioural intervention | 10% reduction of the original dose per week until 30% of the original dose was reached. At that point, the 10% was recalculated on the basis of this dose and the taper then proceeded by 10% of this new dose per week. Motivational interviewing and CBT | TAU | Usual care | Reduction | Outpatient | Face to face and telephone | Group and individual | 30 minutes/week for 18 weeks |

**TABLE 8** Intervention characteristics of the comparative studies (Review 1) (*continued*)

| Study ID | Type of intervention | Brief intervention description | Type of comparator | Brief comparator description | Aim of intervention | Setting | Mode(s) of delivery | Group/ individual | Duration/intensity |
|---|---|---|---|---|---|---|---|---|---|
| Zheng 2008[112] | Acupuncture; no active tapering | Electroacupuncture | Sham | Sham electroacupuncture | Reduction | Outpatient | Face to face | Individual | 20 minutes, twice/ week for 6 weeks |
| Zheng 2019[115,116] | Acupuncture; no active tapering | Electroacupuncture | C1 = Sham<br>C2 = Education only | Sham electroacupuncture<br>Education only | Reduction | Outpatient | Face to face | Individual | 20 minutes, twice/ week for 4 weeks, then 20 minutes, once/week for 2 weeks then 20 minutes/fortnightly for 4 weeks.<br>Total, 12 sessions within 10 weeks.<br>Pain specialists provided pain and medication education to each participant once in the whole trial |
| *PMC* | | | | | | | | | |
| Seal 2020[81] | Interdisciplinary | Integrated Pain Team (IPT) clinic encourages behavioural health strategies, physical modalities and exercise | TAU | Usual primary care | Reduction | Outpatient | Face to face *or* telephone | NR | Median of 4 visits in 6 months; 60 minutes for an initial visit with 30-minute follow-up visits |
| ***Retrospective cohort*** | | | | | | | | | |
| Bienek 2019[67] | Sequential opioid dose reduction | Fixed opioid withdrawal, 30% first day and then approximately 10% each day until completely tapered | Controlled opioid withdrawal | Individualised opioid withdrawal | Discontin-uation | Inpatient | Face to face | Individual | N/A |
| Gersch 2021[70] | Pain e-consult program (PEP) | PEP through which primary care clinicians can request pain management consultations | Usual care (provided by clinical pharmacy specialists) | Usual care | Reduction | Outpatient | Internet, other | Individual | 12 months or KPCO membership termination, whichever came first |
| Montgomery 2020[77] | Acupuncture; no active tapering | Battlefield acupuncture | TAU | Usual care | Reduction | Outpatient | Face to face | Individual | NR |

CBT, cognitive–behavioural therapy; KPCO, Kaiser Permanente Colorado; N/A, not applicable; NADA, National Acupuncture Detoxification Association; NR, not reported; SG, support group; TAU, treatment as usual.

Of the 11 comparative studies, 2 examined sequential opioid dose reduction interventions ('taper only'),[67,75] 4 examined acupuncture (only 1 of which combined acupuncture with active tapering),[77,111,112,116] 3 examined cognitive, psychological and behavioural interventions (only 1 of which combined the intervention with active tapering),[69,71,113] 1 examined a pain e-consult programme[70] and 1 examined an integrated pain team.[81]

The comparator groups received treatment as usual in six studies,[70,75,77,81,111,113] support groups in two studies,[69,71] and sham acupuncture in two groups.[112,116] The remaining study assessed two different dose reduction schedules, that is fixed opioid withdrawal compared to individualised withdrawal.[67]

Interventions could aim to either reduce or discontinue opioid use. The aim of the intervention in this respect is important when looking at the outcomes on opioid use. For nine of the comparative studies the aim was to reduce opioid use, whereas two aimed to discontinue opioid use.[67,75] One study[70] aimed to improve prescriber education and practice.

All but 1 study[67] was conducted in an outpatient setting and 10 used face-to-face delivery.[67,69,71,75,77,81,111,112,113,116] For three of these studies, telephone contact was also used.[75,81,113] The intervention in one study was based on e-consults.[70]

Most interventions were delivered individually, though the two studies assessing mindfulness delivered the intervention in groups;[69,71] the motivational interviewing (MI) and cognitive–behavioural therapy (CBT) element of the Sullivan 2017 study[113] was also delivered in groups.

The duration and intensity of the interventions ranged from 6 weeks[112] to 12 months.[111]

### *Non-comparative studies*

Details of the intervention characteristics are shown in *Table 9*.

Of the 16 non-comparative studies, 7 were interventions aimed at changing the service, for example OSIs.[66,73,80,82,83,89,117] Two of these did not follow the same cohort of patients through the study.[83,117] Of the remaining nine studies aimed at the individual, three used a pharmacological intervention[78,90,110] and six were pain rehabilitation programmes.[68,72,74,76,79,88] The aim of 10 studies was to reduce the level of opioid use,[66,68,76,79,80,82,83,89,110,117] whereas 5 studies aimed for participants to discontinue opioids.[72,74,78,88,90] The remaining study aimed to reduce opioid prescribing rates.[73]

Where applicable, interventions were conducted in outpatient settings for all but two studies.[74,78] The interventions that focused on individuals instead of changing a system were all conducted face to face, predominantly individually, although four studies also reported using group sessions.[68,72,79,88]

The duration of therapy was reported by seven of the nine studies aimed at the individual and ranged from 15 days[88] to 0.8 years.[90] Two studies did not report the duration or intensity of the intervention.[76,79]

### *Further analysis of intervention components*

We examined the composition of the interventions examined across the included studies to understand more about what components of behaviour change were involved. Studies were first grouped by type of intervention as follows:

- pain management programme, eight studies[68,70,72,74,76,79,81,88]
- tapering curriculum/guidelines/initiative, six studies[66,73,80,83,89,117]
- pharmacological-assisted opioid tapering, three studies[78,90,110]
- tapering only, two studies[67,75]
- acupuncture, four studies[77,111,112,116]
- cognitive, psychological and behavioural, three studies[69,71,113]
- clinical encounter, one study.[82]

Two studies were excluded from the further analysis as insufficient information was provided about the components of the intervention.[82,89] In 19 studies,[67,68,69,71,72,74,75,76,77,78,79,81,88,90,110,111,112,113,116] the intervention components targeted patient

**TABLE 9** Intervention characteristics of the non-comparative studies (Review 1)

| Study ID | Type of intervention | Brief intervention description | Aim of intervention | Setting | Mode(s) of delivery | Group/ individual | Duration/intensity |
|---|---|---|---|---|---|---|---|
| ***Prospective cohort*** | | | | | | | |
| Capano 2020[110] | Pharmacological; no active tapering | CBD hemp extract<br>Participants self-titrated their dose of CBD | Reduction | Outpatient | Face to face | Individual | N/A |
| Cunningham 2016[68] | Sequential opioid dose reduction + interdisciplinary | Tapering protocol as part of interdisciplinary pain rehabilitation program | Reduction | Outpatient | Face to face | Group and individual | 8 hours/day for 3 weeks Monday–Friday |
| Jacobs 2016[73] | Quality improvement project | Chronic Opioid Assessment Program (COAP), a pharmacy-driven initiative to assess and document patient risk factors and monitor appropriateness of chronic opioid therapy at the time of prescription renewal | Opioid prescribing | Outpatient | Telephone | Individual | N/A |
| Krumova 2013[74] | Sequential opioid dose reduction + interdisciplinary | Pain rehabilitation programme. Opioid taper followed by an individualised interdisciplinary treatment (i.e. CBT, physiotherapy, mirror therapy, invasive procedures) 30% reduction on the first day then gradually reduced until zero | Discontinuation | Inpatient | Face to face | Individual | 22.8 ± 11.2 days |
| Laigaard 2020[76] | Interdisciplinary | Opioid reduction through a range of individualised therapeutic options | Reduction | Outpatient | Face to face | Individual | NR |
| Townsend 2008[88] | Interdisciplinary | Pain rehabilitation programme. Physical therapy, occupational therapy, biofeedback and relaxation training, stress management, wellness instruction, chemical health education and pain management training | Discontinuation | Outpatient | Face to face | Group and individual | 8 hours/day for 15 consecutive days |
| ***Retrospective case review*** | | | | | | | |
| Austin 2019[66] | OSI | A three-pronged opioid-tapering curriculum: awareness, direct instruction, and guided instruction | Reduction | N/A | N/A | N/A | N/A |
| Huffman 2017 | Interdisciplinary | Interdisciplinary chronic pain rehabilitation outpatient programme: daily medical management, individual psychotherapy (2–3 × per week), group psychotherapy (~7 hours per week), cognitive–behavioural group interventions and psychoeducation, physical and occupational therapy, substance use education, weaning from habituating medications and optional monthly aftercare Opioid weaning schedules were based on daily examination for withdrawal signs and symptoms | Discontinuation | Outpatient | Face to face | Group and individual | 9½ hours/day, 5 days a week for 3–4 weeks |

continued

**TABLE 9** Intervention characteristics of the non-comparative studies (Review 1) (*continued*)

| Study ID | Type of intervention | Brief intervention description | Aim of intervention | Setting | Mode(s) of delivery | Group/ individual | Duration/intensity |
|---|---|---|---|---|---|---|---|
| Murphy 2013[78] | Pharmacological + inter-disciplinary | Pain rehabilitation programme + hydromorphone in sweetened fruit juice | Discontinuation | Inpatient | Face to face | NR | 6 hours/day for 15 weekdays plus 2–3 hours/ day independent assignments, twice daily exercise, walking and relaxation sessions at weekend |
| Panicker 2022[79] | Advanced practice registered nurse-led multidisciplinary programme | Advanced practice registered nurse-led multidisciplinary programme | Reduction | Outpatient | Face to Face | Group and individual | NR |
| Rivich 2018[80] | OSI | OSI; multidisciplinary chart reviews of patients to provide safety recommendations to prescribers through the electronic medical record | Reduction | N/A | N/A | N/A | N/A |
| Sharp 2018[82] | Clinical encounter | Clinical encounters | Reduction | N/A | N/A | N/A | N/A |
| Twillman 2018[89] | OSI | Introduction of CDC guidelines | Reduction | N/A | N/A | N/A | N/A |
| Zhou 2017[90] | Pharmacological + inter-disciplinary | Comprehensive opioid taper treatments (including interventional pain management techniques, psychotherapy, acupuncture, physical modalities and exercises, and adjuvant medications) on top of the medication-assisted treatment using methadone | Discontinuation | Outpatient | Face to face | Individual | Average number of clinic visits 11.5 (12.2) in 0.8 (1.1) years |
| ***Non-patient cohort*** | | | | | | | |
| Westanmo 2015[117] | OSI | OSI implementation | Reduction | Outpatient | N/A | N/A | N/A |
| Thakral 2018[83,84,85,86,87] | OSI | Dose reduction and risk mitigation initiative | Reduction | Outpatient | N/A | N/A | N/A |

N/A, not applicable; NR, not reported.

behaviour only, in 5 studies intervention components targeted healthcare professional's behaviour only,[66,70,73,80,83] and in 1 study,[117] intervention components targeted both patient and healthcare professional behaviour. Using the Behaviour Change Wheel book as a guide,[118] each study was examined to identify which of nine possible intervention functions (education, training, environmental restructuring, modelling, persuasion, coercion, incentivisation, restriction and enablement) were used in the intervention.

### Patient behaviour

For 20 studies that targeted patient behaviours, interventions had between 1 and 3 intervention functions (*Table 10*). The most frequent functions were Enablement (18 studies) and Restriction (12 studies). Restriction refers to the use of rules to reduce the opportunity to engage in the target behaviour and interventions that involved opioid dose reduction or cessation were mapped to this function. Enablement functions aim to increasing means or reduce barriers to increase capability and were mapped to interventions that aimed to bring about a change in psychological capability. Intervention functions identified less frequently were Training (four studies) and Education (three studies). In 15 studies, interventions were mapped to more than 1 function and 5 combinations of functions were found:

- Training + Restriction + Enablement, five studies[68,72,78,81,88]
- Restriction + Enablement, five studies[67,74,76,90,111]
- Education + Restriction + Enablement, two studies[75,79]
- Training + Enablement, two studies[69,71]
- Education + Training + Restriction + Enablement, one study.[113]

**TABLE 10** Behavioural intervention components (Review 1)

| Reference | Whose behaviour targeted? Primary behavioural aim (i.e. cessation or reduction) | Intervention Intervention components | Intervention function(s)[a] |
|---|---|---|---|
| *Pain management programmes (including tapering and pain management only)* | | | |
| Cunningham 2016[68] | **Patient behaviour** To reduce or cease opioid use | **Sequential opioid dose reduction, pain rehabilitation programme** Physical therapy, occupational therapy, biofeedback and relaxation training, and group therapies; group session CBT, management of stress, the emotional impact of pain, and understanding pain sensitisation. | Training; Restriction; Enablement |
| Krumova 2013[74] | **Patient behaviour** To reduce or cease opioid use | **Sequential opioid dose reduction, pain rehabilitation programme** Individual basis for nonmedical treatments, included supportive CBT and physiotherapy, special interventions and invasive procedures. | Restriction; Enablement |
| Laigaard 2020[76] | **Patient behaviour** To reduce opioid use | **Opioid reduction at a multidisciplinary pain centre** Individualised therapeutic options; Various treatment modalities used (but not described). | Restriction; Enablement |
| Townsend 2008[88] | **Patient behaviour** To cease all opioids and simple analgesics taken for relief of chronic pain | **Pain rehabilitation programme** Pre-candidacy evaluation to assess physical and emotional stability; incorporated a range of therapies and training approaches (e.g. physical therapy, biofeedback and relaxation training, and stress management); patients focus on functional restoration goals and learn how to self-manage their chronic pain symptoms (group setting); identification and treatment of comorbid psychiatric illnesses; family education programme and aftercare planning. | Training; Restriction; Enablement |

continued

**TABLE 10** Behavioural intervention components (Review 1) (*continued*)

| Reference | Whose behaviour targeted? Primary behavioural aim (i.e. cessation or reduction) | Intervention Intervention components | Intervention function(s)[a] |
|---|---|---|---|
| Huffman 2017[72] | **Patient behaviour**<br>To cease opioid use | **Pain rehabilitation programme**<br>Daily medical management; individual and group psychotherapy and cognitive–behavioural group interventions; psychoeducation, physical and occupational therapy, substance use education, weaning from habituating medications, and optional monthly aftercare. | Training; Restriction; Enablement |
| Seal 2020[81] | **Patient behaviour**<br>To improve pain and decrease opioid risk through dose reduction and risk mitigation strategies | **Integrated Pain Team**<br>Multimodal pain care planning; behavioural health strategies (e.g. CBT), physical modalities (e.g. acupuncture, chiropractic care, heat, and ice) and exercise (e.g. physical therapy, yoga, Tai Chi). | Training; Restriction; Enablement |
| Gersch 2021[70] | **Health professional behaviour**<br>To improve prescriber education and practice | **Pain e-consult programme, based on ECHO tele-monitoring/mentoring model**<br>Primary care physicians received intensive training on how to approach pain e-consults; primary care physicians worked collaboratively to review a patient's electronic health record to provide mentoring 'recommendations' for pain management and individual patient recommendations; note placed in the patient's electronic health record. | Training; Environmental restructuring; Enablement |
| Panicker 2022[79] | **Patient behaviour**<br>To reduce or cease opioid use | **Advanced practice registered nurse led multidisciplinary pain clinic**<br>Opioid reduction based on patient inclusion in decision-making; patient education concerning the risks and side effects of opioid use and the use of non-pharmacological therapies to manage chronic pain; complementary and integrative therapies; addressed psychosocial and behavioural factors affecting pain, patient preference and concerns, and family involvement; risk mitigation strategies. | Education; Restriction; Enablement |
| ***Tapering curriculum/guidelines/initiatives*** | | | |
| Jacobs 2016[73] | **Health professional behaviour**<br>Consistent implementation of clinical guidelines | **Chronic Opioid Assessment Programme**<br>Two clinical pain pharmacist positions created to perform monthly risk assessments of patients requesting COT renewal; protocol and note template developed to assess patient's chronic opioid regimen via monthly telephone calls. Pharmacists documented recommendations in the patient's electronic medical record. Primary care provider alerted to note. | Environmental restructuring; Enablement |
| Austin 2019[66] | **Health professional behaviour**<br>To increase concordance with national practice guidelines | **Opioid-tapering curriculum (OSI). Needs assessment and three-pronged opioid-tapering curriculum.**<br>All providers given practice-wide and provider-specific data on the primary end points; annual, required 1-hour session was incorporated into the didactics and was repeated as a required faculty development seminar; each resident spent 4 half-days at minimum in the practice's interdisciplinary pain clinic and participated in one chronic pain group medical visit each year. | Education; Training |
| Rivich 2018[80] | **Health professional behaviour**<br>To reduce high-dose prescribing | **Multidisciplinary chart reviews (OSI)**<br>Chart reviews provided specific recommendations that were documented in the electronic medical record; initial chart reviews were completed by multidisciplinary team members with experience in chronic pain management and included a nurse practitioner, a clinical pharmacist and multiple clinical health psychologists. | Environmental restructuring; Enablement |

**TABLE 10** Behavioural intervention components (Review 1) (*continued*)

| Reference | Whose behaviour targeted? Primary behavioural aim (i.e. cessation or reduction) | Intervention Intervention components | Intervention function(s)[a] |
|---|---|---|---|
| Thakral 2018[83,84,85,86,87] | **Health professional behaviour** Increase compliance with updated recommendations in an interagency guideline for opioid prescribing for chronic non-cancer pain | **OSI implementation** Primary care providers received lists of primary care patients at or above the dosing threshold. Providers with greater numbers of high-dose COT patients received feedback from medical directors; lowering COT doses was strongly supported by medical staff leadership and consulting specialists in Physical and Rehabilitation Medicine, including voluntary in-service continuing education sessions regarding chronic pain management attended by many primary care providers; practice tools were integrated in the electronic medical record, an online course and onsite resources for consultation. | Education; Persuasion; Environmental restructuring |
| Westanmo 2015[117] | **Health professional behaviour and patient behaviour** To reduce high-dose prescribing | **Dose reduction and risk mitigation initiative (OSI)** Preparatory phase included planning, pain management education and training, and baseline evaluation; trained clinical pharmacist met with primary care-based clinical pharmacists to discuss OSI goals and processes and review clinical procedures for opioid dose tapering; information about existing non-pharmacological pain management services disseminated; full day pain education course for patients; active support and endorsement from executive leadership of the healthcare system; Opioid dose reduction strategies implemented including monitoring of prescribing with feedback and pharmacist support for pain medication changes and opioid tapering. | Education; Persuasion; Training; Enablement |
| Twillman 2018 | – | **Introduction of CDC guidelines** | – |
| ***Pharmacological assisted tapering*** | | | |
| Capano 2020[110] | **Patient behaviour** To reduce opioid use and improve QoL indicators | **CPD Hemp extract** | Enablement |
| Murphy 2013[78] | **Patient behaviour** To cease use of all opioids | **Pain rehabilitation programme + hydromorphone** Taught self-management skills; focus on active treatment modalities that include graduated physical therapy, aquatic therapy, daily paced walking, relaxation techniques, daily exercise sessions, occupational therapy, recreational therapy, individual psychotherapy, educational classes and family interventions as appropriate. | Training; Restriction; Enablement |
| Zhou 2017[90] | **Patient behaviour** To cease opioid use | **Comprehensive opioid taper treatments, medication-assisted treatment** All patients received the comprehensive opioid taper treatments (including interventional pain management techniques, psychotherapy, acupuncture, physical modalities and exercises, and adjuvant medications) on top of the medication-assisted treatment using methadone (transient use). | Restriction; Enablement |
| ***Tapering only*** | | | |
| Kurita 2018[75] | **Patient behaviour** To stabilise and discontinue opioids | **Sequential opioid dose reduction** Scheduled opioid dose decrease to opioid discontinuation; encouragement from research nurses based on simple reminders of when to start the next dose reduction; possible advantages and disadvantages of opioid discontinuation explained to patients. | Education; Restriction; Enablement |

continued

**TABLE 10** Behavioural intervention components (Review 1) (*continued*)

| Reference | Whose behaviour targeted? Primary behavioural aim (i.e. cessation or reduction) | Intervention Intervention components | Intervention function(s)[a] |
|---|---|---|---|
| Bienek 2019[67] | **Patient behaviour** To reduce opioid dose/use | **Sequential opioid dose reduction** Patients were evaluated by a psychologist for motivation for withdrawal, psychic comorbidities and presence of dependence syndrome; contract between the physician and patient was signed, declaring the patient's intrinsic motivation and commitment to withdrawal; could request psychological support and physiotherapeutic treatment for relaxation. | Restriction; Enablement |
| ***Acupuncture*** | | | |
| Zheng 2008[112] | **Patient behaviour** To reduce opioid use/dose | Electroacupuncture | Enablement |
| Zheng 2019[115,116] | **Patient behaviour** To reduce opioid use/dose | Electroacupuncture | Enablement |
| Montgomery 2020[77] | **Patient behaviour** To reduce opioid use/dose | Battlefield acupuncture | Enablement |
| Jackson 2021[111] | **Patient behaviour** Improve the psychological distress of patients undergoing an opioid taper | **Acupuncture, medication management with opioid weaning** Gradual reductions in combination with adjuvant non-opioid medications and therapies; additional therapies recommended and/or referrals provided. for example physical therapy and psychological support; auricular acupuncture. | Restriction; Enablement |
| ***Cognitive, psychological and behavioural*** | | | |
| Garland 2014[69] Hudak 2020[71] | **Patient behaviour** To reduce chronic pain and prescription opioid misuse | **Mindfulness-orientated recovery enhancement** Mindfulness training to target automatic habit behaviour and foster non-reactivity; positive reappraisal training; training in savouring pleasant events and emotions | Training; Enablement |
| Sullivan 2017[113,114] | **Patient behaviour** To reduce opioid use/dose | **Sequential opioid dose reduction, MI and CBT** MI-based sessions; pain self-management training (modelled on CBT interventions for chronic pain) including behavioural goal setting, education/training in relaxation, behavioural activation techniques, and sleep hygiene education; patients completed 'personal action plans'. | Education; Training; Restriction; Enablement |
| ***Clinical encounter*** | | | |
| Sharp 2018[82] | – | **Clinical encounters** | – |

COT, chronic opioid therapy; ECHO, Extension for Community Healthcare Outcomes; QoL, quality of life.

a Intervention functions based on the Behaviour Change Wheel:[118] *Education* = increasing knowledge or understanding; *Persuasion* = using communication to induce positive or negative feelings or stimulate action; *Incentivisation* = creating expectation of reward; *Coercion* = creating expectation of punishment or cost; *Training* = imparting skills; *Restriction* = using rules to reduce the opportunity to engage in the target behaviour (or to increase the target behaviour by reducing the opportunity to engage in competing behaviours); *Environmental restructuring* = changing the physical or social context; *Modelling* = providing an example for people to aspire to or imitate; *Enablement* = increasing means/reducing barriers to increase capability or opportunity.

## Healthcare professional behaviour

For six studies that targeted healthcare professional behaviours, interventions had between two and three intervention functions (see *Table 10*). The most frequent functions were Environmental restructuring (four studies) and Enablement (four studies). The functions Training (three studies), Education (three studies) and Persuasion (two studies) were also identified. Environmental restructuring refers to functions which aim to change the physical or social context. In the context of the interventions that targeted healthcare professional behaviour, an example of this function involved notes

or recommendations being placed on patient's electronic health record. All the interventions across the six studies were mapped to more than one intervention function as follows:

- Training + Environmental restructuring + Enablement, one study[70]
- Education + Persuasion + Training + Enablement, one study[117]
- Education + Persuasion + Environmental restructuring, one study[83]
- Education + Training, one study[66]
- Environmental restructuring + Enablement, two studies.[73,80]

## Population characteristics

### *Comparative studies*

Details of the population characteristics are shown in *Table 11*.

The 11 comparative studies included a total of 1606 participants, with individual studies ranging from 35[75,112,113] to 665 participants.[70] The participants were evenly divided between the intervention and comparator groups for seven studies, whereas three studies[70,111,116] enrolled more participants to the intervention group than the comparator group and one study enrolled more participants to the comparator group than the intervention group.[67]

Four studies reported notably more females than males in the study, three studies reported notably more males than females and four studies reported equal proportions of males and females. The mean ages of participants ranged from 47.4[69] to 65 years.[77]

The type of chronic pain that participants were experiencing was reported by six studies and was varied. The mean duration of pain was reported by four studies and varied from 10.8[116] to 19.8 years.[112]

The types of opioids participants were taking was only reported by three studies and differed between studies. For the five studies reporting the duration of opioid treatment, the values varied between 6.6[75] and 14.1 years.[81] The average daily opioid dose was reported by seven studies and varied between 76.9[70] and 367 mg/day.[75] Two further studies reported weekly doses of 461 and 295 mg/week[112] and 463 and 620 mg/week.[116]

### *Non-comparative studies*

Details of the population characteristics are shown in *Table 12*.

The two non-comparative studies that did not follow a cohort of patients are not included in the description of the population characteristics, though the sample sizes and details of opioid use are reported in *Table 12*. The remaining 14 studies included 5710 participants and individual studies ranged from 34[79] to 2492[82] participants.

The sex of participants in the non-comparative studies was less evenly spread than in the comparative studies with seven studies reporting notably more females than males, five studies reporting notably more males than females and only two studies reporting equal proportions of males and females. Two studies failed to report the proportion of males and females. The ages of participants ranged from 44.5[88] to 64 years.[73] Three studies did not report the average age of participants.[72,82,89]

The type of chronic pain that participants were experiencing was reported by six studies and was varied. The mean duration of pain was reported by four studies and varied from 8.6[68] to 12.7 years.[78]

The types of opioids participants were taking was only reported by two studies[68,74] and differed between the studies. For the five studies reporting the duration of opioid treatment, the values varied between 3.9[88] and 10 years.[76] The average daily opioid dose was reported by 11 studies and varied between 41.04[79] and 367 mg/day.[74]

**TABLE 11** Population characteristics of the comparative studies (Review 1)

| Author year | Total *N* | Arm | *N*, females, males | Age (years) Mean (SD), range | Type of chronic pain, *n* (%) | Duration (years) of chronic pain Mean (SD), range | Types of opioids, *n* (%) | Duration (years) of opioid use Mean (SD), range | Level of opioid use (mg/daily) Mean (SD), range |
|---|---|---|---|---|---|---|---|---|---|
| Garland 2014[69] | 115 | I | *N* = 57<br>F = 40<br>M = 17 | 49.3 (13.68) | Lumbago: 30 (53%)<br>Fibromyalgia: 11 (19%)<br>Arthritis: 4 (7%)<br>Cervicalgia: 5 (9%)<br>Other: 7 (12%) | NR | NR | NR | NR |
| | | C | *N* = 58<br>F = 38<br>M = 20 | 47.4 (13.56) | Lumbago: 35 (60%)<br>Fibromyalgia: 12 (21%)<br>Arthritis: 4 (7%)<br>Cervicalgia: 2 (3%)<br>Other: 5 (9%) | | | | |
| Hudak 2020[71] | 62 | I | *N* = 34<br>F = 3<br>M = 31 | 60.2 (9.8) | Back: 19 (55%)<br>Legs/feet: 2 (6%)<br>Joints: 6 (18%)<br>Neck/shoulders: 3 (9%)<br>Other: 4 (12%) | 16.4 (12.9) | Oxycodone: 10 (29%)<br>Hydrocodone: 8 (24%)<br>Tramadol: 13 (38%)<br>Morphine: 3 (9%)<br>Methadone: 3 (9%)<br>Other: 4 (12%) | 9.4 (7.1) | 94.6 (207.9) |
| | | C | *N* = 28<br>F = 6<br>M = 22 | 58.1 (10.3) | Back: 15 (56%)<br>Legs/feet: 2 (7%)<br>Joints: 3 (11%)<br>Neck/shoulders: 6 (22%)<br>Other: 1 (4%) | | Oxycodone: 9 (33%)<br>Hydrocodone: 9 (33%)<br>Tramadol: 7 (26%)<br>Morphine: 3 (11%)<br>Methadone: 1 (4%)<br>Other: 3 (11%) | 8.7 (9.2) | 98.4 (216.6) |
| Jackson 2021[111] | 15 | I and C[a] | *N* = 15<br>F = 7<br>M = 8 | 56.5 (17.3) | NR | NR | NR | NR | I = 112 (71)<br>C = 191 (121) |

**TABLE 11** Population characteristics of the comparative studies (Review 1) (*continued*)

| Author year | Total *N* | Arm | *N*, females, males | Age (years) Mean (SD), range | Type of chronic pain, *n* (%) | Duration (years) of chronic pain Mean (SD), range | Types of opioids, *n* (%) | Duration (years) of opioid use Mean (SD), range | Level of opioid use (mg/daily) Mean (SD), range |
|---|---|---|---|---|---|---|---|---|---|
| Kurita 2018[75] | 35 | I | *N* = 15<br>F = 6<br>M = 9 | 56.3 (9.2), 33–69 | Neuropathic: 2 (13.3%)<br>Nociceptive somatic: 4 (26.7%)<br>Nociceptive visceral: 0 (0%)<br>Neuropathic + nociceptive somatic: 8 (53.3%)<br>Neuropathic + nociceptive visceral: 1 (6.7%) | 15.1 (11.6), 2–40 | NR | 9.9 (7.1), 2–30 | 367.4 (369.8), 60–1500 |
| | | C | *N* = 20<br>F = 15<br>M = 5 | 50.6 (14.4), 25–71 | Neuropathic: 3 (15%),<br>Nociceptive somatic: 8 (40%)<br>Nociceptive visceral: 0 (0%)<br>Neuropathic + Nociceptive somatic: 9 (45)<br>Neuropathic + Nociceptive visceral: 0 (0%) | 11.4 (7.6), 2–25 | | 6.6 (4.7), 1–16 | 220.8 (169.1), 60–740 |
| Sullivan 2017[113,114] | 35 | I | *N* = 18<br>F = 12<br>M = 6 | 54.4 (10.1) | NR | NR | NR | 10.2 (4.3) | 207.2 (269.3) |
| | | C | *N* = 17<br>F = 13<br>M = 4 | | | | | | 245.2 (347.3) |
| Zheng 2008[112] | 35 | I | *N* = 17<br>F = 8<br>M = 9 | 51.1 (13) | NR | 19.8 (24.5) | Codeine: 10<br>Methadone: 1<br>Oxycodone: 4<br>Morphine: 4<br>Tramadol: 6 | NR | 461.6 (462.6) |
| | | C | *N* = 18<br>F = 9<br>M = 9 | 48.4 (10.5) | | 13 (1.1) | Codeine: 14<br>Methadone: 0<br>Oxycodone: 5<br>Morphine: 3<br>Tramadol: 4 | | 295.5 (288) |

continued

**TABLE 11** Population characteristics of the comparative studies (Review 1) (*continued*)

| Author year | Total *N* | Arm | *N*, females, males | Age (years) Mean (SD), range | Type of chronic pain, *n* (%) | Duration (years) of chronic pain Mean (SD), range | Types of opioids, *n* (%) | Duration (years) of opioid use Mean (SD), range | Level of opioid use (mg/daily) Mean (SD), range |
|---|---|---|---|---|---|---|---|---|---|
| Zheng 2019[115,116] | 108 | I | *N* = 48<br>F = 28<br>M = 20 | 55.9 (11.3) | NR | 10.8 (9.4) | NR | NR | 463.3 (438.6) |
| | | C | *N* = 29<br>F = 18<br>M = 11 | 58.4 (12.8) | | 13.3 (9.6) | | | 620.8 (792.4) |
| | | C2 | *N* = 31<br>F = 16<br>M = 15 | 58.4 (12.8) | | 16.3 (12.5) | | | 871.41 (1772.3) |
| ***PMC*** | | | | | | | | | |
| Seal 2020[81] | 294 | I | *N* = 147<br>F = 15<br>M = 132 | 62.1 (12.4) | NR | NR | NR | 14.1 (5.3) | 124.1 (241.1) |
| | | C | *N* = 147<br>F = 15<br>M = 132 | 62.9 (11.4) | | | | 13.6 (5.1) | 124.5 (231.5) |
| ***Retrospective cohort*** | | | | | | | | | |
| Bienek 2019[67] | 195 | I | *N* = 68<br>F = 30<br>M = 38 | 51 (13) | Neuropathic: 18 (25.5%)<br>CRPS: 3 (4.4%)<br>Muscle or joint: 18 (26.5%)<br>Back pain: 20 (29.4%)<br>Other: 8 (11.8%) | NR | Morphine: 8 (11.8%)<br>Hydromorphone: 18 (26.5%)<br>Oxycodone: 15 (22.1%)<br>Oxycodone/naloxone: 4 (5.9%)<br>Fentanyl: 8 (11.8%) | NR | 185 (194) |
| | | C | *N* = 127<br>F = 53<br>M = 74 | 54 (12) | Neuropathic: 49 (38.6%)<br>CRPS: 7 (5.5%)<br>Muscle or joint: 32 (25.2%)<br>Back pain: 29 (22.8%)<br>Other: 11 (8.7%) | | Morphine: 21 (16.5%)<br>Hydromorphone: 23 (18.1%)<br>Oxycodone: 26 (20.5%)<br>Oxycodone/naloxone: 18 (14.2%)<br>Fentanyl: 21 (16.5%) | | 253 (385) |

**TABLE 11** Population characteristics of the comparative studies (Review 1) (*continued*)

| Author year | Total *N* | Arm | *N*, females, males | Age (years) Mean (SD), range | Type of chronic pain, *n* (%) | Duration (years) of chronic pain Mean (SD), range | Types of opioids, *n* (%) | Duration (years) of opioid use Mean (SD), range | Level of opioid use (mg/daily) Mean (SD), range |
|---|---|---|---|---|---|---|---|---|---|
| Gersch 2021[70] | 665 | I | *N* = 125<br>F = 83<br>M = 42 | 58.9 | Abdominal pain: 4 (3.2%)<br>Back pain: 19 (15.2%)<br>Burn: 0 (0.0%)<br>Dislocation/sprain/strain: 6 (4.8%)<br>Fibromyalgia: 16 (12.8%)<br>Fracture: 10 (8.0%)<br>Internal injury: 0 (0.0%)<br>Joint pain: 14 (11.2%)<br>Migraine: 0 (0.0%)<br>Nerve damage: 1 (0.8%)<br>Open wound: 3 (2.4%)<br>Other injury: 14 (11.2%)<br>Trauma complication: 1 (0.8%)<br>Superficial injury: 3 (2.4%)<br>No pain indication: 85 (68.0%) | NR | NR | NR | 88.4 (58) |
| | | C | *N* = 540<br>F = 361<br>M = 179 | 59.3 | Abdominal pain: 13 (2.4%)<br>Back pain: 85 (15.7%)<br>Burn: 0 (0.0%)<br>Dislocation/sprain/strain: 67 (5.0%)<br>Fibromyalgia: 49 (9.1%)<br>Fracture: 34 (6.3%)<br>Internal injury: 0 (0.0%)<br>Joint pain: 39 (7.2%)<br>Migraine: 1 (0.2%)<br>Nerve damage: 2 (0.4%)<br>Open wound: 8 (1.5%)<br>Other injury: 20 (3.7%)<br>Trauma complication: 5 (0.9%)<br>Superficial injury: 4 (0.8%)<br>No pain indication: 403 (74.6%) | NR | NR | NR | 76.9 (44.8) |

continued

**TABLE 11** Population characteristics of the comparative studies (Review 1) (*continued*)

| Author year | Total *N* | Arm | *N*, females, males | Age (years) Mean (SD), range | Type of chronic pain, *n* (%) | Duration (years) of chronic pain Mean (SD), range | Types of opioids, *n* (%) | Duration (years) of opioid use Mean (SD), range | Level of opioid use (mg/daily) Mean (SD), range |
|---|---|---|---|---|---|---|---|---|---|
| Montgomery 2020[77] | 47 | I | *N* = 24<br>F = 4<br>M = 20 | 61 (8.88) | Back: 14 (58.3%)<br>Joint: 6 (25%)<br>Neck: 4 (16.7%)<br>Chronic pain syndrome: 5 (20.8%)<br>Myofascial pain: 5 (20.8%) | NR | NR | NR | NR |
| | | C | *N* = 23<br>F = 1<br>M = 22 | 65 (8.5) | Back: 12 (52.2%)<br>Joint: 7 (30.4%)<br>Neck: 8 (34.7%)<br>Chronic pain syndrome: 3 (13.1%)<br>Myofascial pain: 2 (8.7%) | | | | |

C, comparator; F, females; I, intervention; M, males; NR, not reported.
a Not reported for each group.

**TABLE 12** Population characteristics of the non-comparative studies (Review 1)

| Author year | Sample size No. of females/ males | Age years Mean (SD), range | Type of chronic pain, *n* (%) | Duration of chronic pain Mean (SD) | Types of opioids, *n* (%) | Duration (years) of opioid use Mean (SD) | Level of opioid use ~~Mean (SD),~~ range | Concomitant medications Overall |
|---|---|---|---|---|---|---|---|---|
| ***Prospective cohorts*** | | | | | | | | |
| Capano 2020[110] | *N* = 97<br>F = 66<br>M = 31 | 56.1 (NR), 39–70 | NR | NR | NR | NR | NR | NR |
| Cunningham 2016[68] | *N* = 55<br>F = 46<br>M = 9 | 48.6 (13.2) | Fibromyalgia | 8.6 (11.3) | Hydrocodone/acetaminophen: 16 (29%)<br>Oxycodone/acetaminophen: 7 (13%)<br>Oxycodone extended release: 11 (20%)<br>Oxycodone: 8 (15%)<br>Fentanyl patches: 5 (9%)<br>Methadone: 6 (11%)<br>Morphine: 8 (15%)<br>Others: 15 (27%) | 4.6 (5.8) | 99 (143), 500–600 | Patients on multiple daily opioids = 21 (38%) (range 2–4) |

**TABLE 12** Population characteristics of the non-comparative studies (Review 1) (*continued*)

| Author year | Sample size No. of females/ males | Age years Mean (SD), range | Type of chronic pain, *n* (%) | Duration of chronic pain Mean (SD) | Types of opioids, *n* (%) | Duration (years) of opioid use Mean (SD) | Level of opioid use ~~Mean (SD),~~ range | Concomitant medications Overall |
|---|---|---|---|---|---|---|---|---|
| Jacobs 2016[73] | *N* = 148<br>F = 2<br>M = 146 | 64 | NR | NR | NR | NR | 117.8, 4–1092 | NR |
| Krumova 2013[74] | *N* = 102<br>F = 47<br>M = 55 | 51 (13), 22–79 | Neuropathic pain syndromes: 37 (36.3%)<br>Non-neuropathic pain syndromes: 54 (52.9%)<br>Others: 11 (10.8%) | NR | WHO step-3 opioids:<br>Morphine: 95 (93.1%)<br>Fentanyl TTS: 25 (24.5%)<br>Hydromorphone: 18 (17.6%)<br>Oxycodone: 14 (13.7%)<br>Buprenorphine: 7 (6.9%)<br>Pethidine: 1 (1%)<br>L-methadone: 1 (1%)<br>WHO step-2 opioids:<br>Tilidine + naloxone: 4 (3.9%)<br>Tramadol: 3 (2.9%) | 3.6 (3.8) | 366.5 (524), 20–4200 | NSAIDs and cyclo-oxygenase 2-inhibitors = 25.5%<br>Metamizole and paracetamol = 26.5%<br>Anticonvulsants = 36%<br>Antidepressant = 31%<br>Benzodiazepines = 5%<br>Fluoirtine = 4% |
| Laigaard 2020[76] | *N* = 51<br>F = 34<br>M = 17 | 55.9 (13) | Musculoskeletal: 18 (35%)<br>Musculoskeletal and neuropathic: 23 (45%)<br>Functional: 6 (12%)<br>Visceral: 4 (8%) | NR | NR | Median 10 | 80 | Paracetamol: 29 (57%)<br>NSAID: 4 (8%)<br>Gabapentin/pregabalin: 22 (43%)<br>Antidepressant: 15 (29%)<br>Benzodiazepine: 2 (4%) |
| Townsend 2008[88] | *N* = 213<br>F = 170<br>M = 43 | 44.5 (14.2), 13–83 | Low back (29.6%)<br>Fibromyalgia (13.6%)<br>Chronic headache (10.8%)<br>Generalised (not fibromyalgia) (9.4%)<br>Abdominal (9.4%)<br>Neck (6.6%)<br>Other (i.e. lower/upper extremity, face, foot, jaw, chest wall, pelvis, hip, mouth) (20.6%) | 8.9 (8.3) | NR | 3.9 (4.2) | 99 (141.7), 1–1060 mg Median 45.0 mg | NSAIDs: 100 (46.9%)<br>Benzodiazepines: 85 (39.9%)<br>Muscle relaxants: 52 (24.4%)<br>Anticonvulsants: 94 (44.1%)<br>SSRI antidepressants: 70 (32.9%)<br>Tricyclic antidepressants: 50 (23.5%)<br>Other antidepressants: 99 (46.5%) |
| ***Retrospective cohorts*** | | | | | | | | |
| Austin 2019[66] | *N* = 707<br>F = 463<br>M = 244 | 62.5 (15.2) | NR | NR | NR | NR | 53.4 (76.9), 1.5–747.5 mg Median 30 mg | Benzodiazepine use: 212 (30.0%) |

continued

**TABLE 12** Population characteristics of the non-comparative studies (Review 1) (*continued*)

| Author year | Sample size No. of females/ males | Age years Mean (SD), range | Type of chronic pain, *n* (%) | Duration of chronic pain Mean (SD) | Types of opioids, *n* (%) | Duration (years) of opioid use Mean (SD) | Level of opioid use ~~Mean (SD),~~ range | Concomitant medications Overall |
|---|---|---|---|---|---|---|---|---|
| Huffman 2017[72] | *N* = 941<br>F = 577<br>M = 364 | NR | NR | NR | Opioids, *n* = 836 (89%)<br>Tramadol only, *n* = 66 (7%)<br>Buprenorphine, *n* = 39 (4%) | NR | 176.54 (384.22) | NR |
| Murphy 2013[78] | *N* = 221<br>F = 39<br>M = 182 | 49.08 (10.97) | Back: 133 (60.2%)<br>Extremity: 34 (15.4%)<br>Neck: 22 (10.0%)<br>Head: 14 (6.3%)<br>Other: 18 (8.1%) | 12.69 (10.45) | NR | NR | 61.14 (61.17), 8–360 | NR |
| Panicker 2022[79] | *N* = 34<br>F = 3<br>M = 31 | 63.18 (15.39) | Low back pain (93%) | NR | NR | NR | 41.04 | NR |
| Rivich 2018[80] | *N* = 147<br>F = 15<br>M = 132 | Median = 61, 33–84 | Back, spinal pain, nonspecific: 94 (64%)<br>Lower body and extremities (hip, knee, ankle, foot): 42 (29%)<br>Upper body and extremities (shoulder, wrist, neck): 23 (16%)<br>Chronic pain syndrome: 20 (14%)<br>Neuropathy, nonspecific: 8 (5.4%)<br>Abdominal pain: 2 (1.4%) | NR | NR | NR | 315 | NR |
| Sharp 2018[82] | *N* = 2492<br>F = 1415<br>M = 1077 | NR | NR | NR | NR | NR | NR | NR |
| Twillman 2018[89] | *N* = 362<br>F = NR<br>M = NR | NR | NR | NR | NR | NR | NR | NR |

**TABLE 12** Population characteristics of the non-comparative studies (Review 1) (*continued*)

| Author year | Sample size No. of females/ males | Age years Mean (SD), range | Type of chronic pain, *n* (%) | Duration of chronic pain Mean (SD) | Types of opioids, *n* (%) | Duration (years) of opioid use Mean (SD) | Level of opioid use ~~Mean (SD),~~ range | Concomitant medications Overall |
|---|---|---|---|---|---|---|---|---|
| Zhou 2017[90] | *N* = 140<br>F = 87<br>M = 53 | 46.7(12.7) | NR | 9.6 (8.4) | NR | 7.7 (6.1) | 83.5 (123.4) | Acupuncture: 9.3%<br>Bupropion: 42.1%<br>Clonidine: 77.9%<br>Epidural injection: 7.9%<br>Manipulation: 40.0%<br>Mirtazapine 23.6%<br>Sacroiliac joint injections: 16.4%<br>Selective serotonin receptor inhibitors: 85.7%<br>Topiramate: 15.7%<br>Trigger point injections: 26.4% |
| ***Non-patient cohort*** | | | | | | | | |
| Thakral 2018[83,84,85,86,87] | *N* = 23,809<br>F = 15,190<br>M = 8619 | NR | NR | NR | NR | NR | NR | Sedative use: 32.4% |
| Westanmo 2015[117] | *N* = 50,749<br>F = NR<br>M = NR | NR | | NR | Fentanyl (transdermal): 94 (0.19%)<br>Methadone: 286 (0.56%)<br>Morphine (sustained action): 831 (1.64%)<br>Oxycodone (sustained action): 292 (0.58%)<br>Hydrocodone (acetaminophen): 4058 (8.00%)<br>Hydromorphone (immediate release): 164 (0.32%)<br>Morphine (immediate release): 100 (0.20%)<br>Oxycodone (acetaminophen): 1562 (3.08%)<br>Oxycodone (immediate release): 679 (1.34%) | NR | < 200 MED/day *or* > 200 MED/day | NR |

C, comparator; F, females; I, intervention; M, males; MED, morphine equivalent dose; NR, not reported; NSAIDs, non-steroidal anti-inflammatory drugs; SSRI, selective serotonin reuptake inhibitor; TTS, transdermal therapeutic system.

## Quality assessment

### *Comparative studies*

#### Randomised controlled trials

For the RCTs, the Cochrane Risk of Bias 2 tool[36] was used and overall quality was assessed rather than for each outcome. The results are shown in *Table 13* and *Figure 3*. Only one RCT was rated as being at low risk of bias, with low risk across all domains;[69] all other RCTs had an overall rating of 'some concerns', with at least one domain assessed as having some concerns. No studies were assessed as being at high risk of bias for any domain.

**TABLE 13** Results of Risk of Bias 2 assessment for the RCTs (Review 1)

| Study ID | Treatment | Comparator | D1 | D2 | D3 | D4 | D5 | Overall |
|---|---|---|---|---|---|---|---|---|
| Sullivan 2017[113,114] | MI | Usual care | | | | | | Low risk |
| Kurita 2018[75] | Taper | Usual care | | | | | | Some concerns |
| Zheng 2008[112] | EA | Sham EA | | | | | | High risk |
| Zheng 2019[115,116] | EA | Sham EA | | | | | | |
| Hudak 2020[71] | MORE | Supportive group | | | | | | |
| Garland 2014[69] | MORE | Supportive group | | | | | | |
| Jackson 2021[111] | Auricular acupuncture | Standard of care | | | | | | |

D1, randomisation process; D2, deviations from the intended interventions; D3, missing outcome data; D4, measurement of the outcome; D5, selection of the reported result; EA, electroacupuncture; MORE, mindfulness-orientated recovery enhancement.

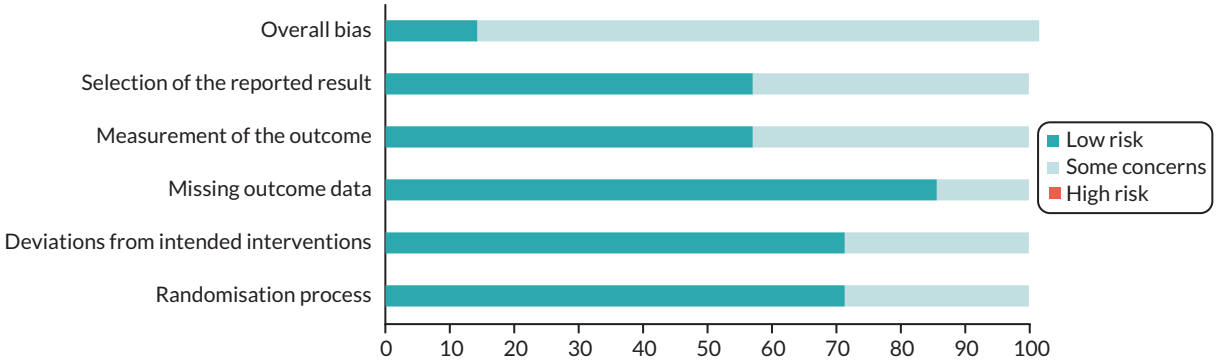


**FIGURE 3** Percentage of RCTs in each risk category overall and for each domain (Review 1).

#### Non-random comparative studies

For non-random comparative studies, CASP tools were used to assess study quality. For the PMC study, the CASP case-control checklist was used.[119] For the two retrospective cohort studies, the CASP cohort study checklist was used.[38] The results for these studies are shown in *Table 14*.

### *Non-comparative studies*

As all of the non-comparative studies were single cohort studies, the CASP cohort study checklist was used.[38] The results for these studies are shown in *Table 15*.

## Outcomes

Of the outcomes of interest to this review (see *Table 2*), seven were reported by three or more studies and are synthesised in this section. Full data extraction tables for each outcome are included in *Appendix 5* with brief summary tables shown here for pain outcomes (*Table 16*) and change in opioid dose (*Table 17*).

**TABLE 14** Summary table of the CASP quality assessments – non-RCTs (Review 1)

| Study ID | 1 Clearly focused issue | 2 Appropriate method | 3 Recruitment | 4 Selection of controls | 5 Exposure | 6a Groups treated equally | 6b Confounders | 9 Believable results | 10 Local population | 11 Inline | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ***PMC*** | | | | | | | | | | | |
| Seal 2020[81] | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✗/✔ | |
| **Study ID** | **1 Clearly focused issue** | **2 Recruitment** | **3 Exposure** | **4 Outcome** | **5a Confounders identified** | **5b Confounders considered** | **6a Follow-up complete** | **6b Follow-up adequate** | **9 Believable results** | **10 Local population** | **11 Inline** | **12 Implications** |
| ***Retrospective cohorts*** | | | | | | | | | | | | |
| Bienek 2019[67] | ✔ | ✗ | ✔ | ✔ | ✗ | ✗ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ |
| Gersch 2021[70] | ✔ | ✗/✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✗/✔ | ✗/✔ | ✗/✔ |
| Montgomery 2020[77] | ✔ | ✔ | ✔ | ✔ | ✗ | ✗ | ✔ | ✔ | ✔ | ✗/✔ | ✔ | ✗/✔ |

**Note**
✔, yes; ✗, no; ✗/✔, can't tell.

**TABLE 15** Summary table of the CASP quality assessments – single cohort studies (Review 1)

| Study ID | 1 Clearly focused issue | 2 Recruitment | 3 Exposure | 4 Outcome | 5a Confounders identified | 5b Confounders considered | 6a Follow-up complete | 6b Follow-up adequate | 9 Believable results | 10 Local population | 11 Inline | 12 Implications |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ***Single prospective cohort*** | | | | | | | | | | | | |
| Capano 2020[110] | ✔ | ✔ | ✗/✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✗/✔ | ✔ | ✔ | ✗/✔ |
| Cunningham 2016[68] | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✗/✔ | ✔ | ✗/✔ | ✔ | ✗/✔ |
| Jacobs 2016[64] | ✔ | ✗/✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✗ | ✔ | ✗/✔ | ✗/✔ | ✔ |
| Krumova 2013[74] | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✗/✔ | ✗/✔ |
| Laigaard 2020[76] | ✔ | ✔ | ✔ | ✔ | ✔ | ✗/✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✗/✔ |
| Townsend 2008[88] | ✔ | ✔ | ✔ | ✔ | ✗/✔ | ✗/✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✗/✔ |
| ***Single retrospective cohort*** | | | | | | | | | | | | |
| Austin 2019[66] | ✔ | ✔ | ✗ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✗/✔ |
| Huffman 2017[72] | ✔ | ✔ | ✔ | ✔ | ✗ | ✔ | ✔ | ✔ | ✔ | ✔ | ✗/✔ | ✔ |
| Murphy 2013[78] | ✔ | ✗ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✗ | ✔ | ✔ |
| Panicker 2022[79] | ✔ | ✗/✔ | ✔ | ✔ | ✗/✔ | ✗ | ✗/✔ | ✗/✔ | ✔ | ✗/✔ | ✗/✔ | ✗/✔ |
| Rivich 2018[80] | ✔ | ✔ | ✔ | ✔ | ✗/✔ | ✗/✔ | ✔ | ✔ | ✔ | ✗/✔ | ✔ | ✔ |
| Sharp 2018[82] | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✗/✔ | ✗/✔ | ✔ | ✔ | ✔ | ✗/✔ |
| Twillman 2018[89] | ✔ | ✔ | ✗/✔ | ✗/✔ | ✗ | ✗ | ✔ | ✔ | ✔ | ✔ | ✔ | ✗/✔ |
| Zhou 2017[90] | ✔ | ✔ | ✗/✔ | ✗/✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✗/✔ | ✗/✔ |
| ***Non-patient cohort*** | | | | | | | | | | | | |
| Thakral 2018[83,84,85,86,87] | ✔ | ✔ | ✔ | ✔ | ✗/✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✔ | ✗/✔ |
| Westanmo 2015[117] | ✔ | ✔ | ✔ | ✔ | ✗ | ✗ | ✔ | ✔ | ✔ | ✔ | ✗/✔ | ✗/✔ |

Note
✔, yes; ✗, no; ✗/✔, can't tell.

**TABLE 16** Summary outcomes table for pain severity and interference

| Study | Study design | Intervention (I) | Comparator (C) | FU | Change in points from baseline | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Pain severity | | | | Pain interference | | | |
| | | | | | Scale | I | C | I vs. C | Scale | I | C | I vs. C |
| ***Pain management programmes (including tapering and pain management only)*** | | | | | | | | | | | | |
| Cunningham 2016 | SRC | Rehabilitation programme | None | PT | NRS | **−2.0** | … | N/A | MPI | −10.2 | … | N/A |
| Krumova 2013 | SRC | Rehabilitation programme | None | 12–24 months | NRS | −1.2 | … | N/A | … | … | … | … |
| Townsend 2008 | SRC | Rehabilitation programme | None | 6 months | MPI | −10.2 | … | N/A | MPI | −14.2 | … | N/A |
| Panicker 2022 | SRC | Nurse led pain clinic | None | PT | NS | **−3.0** | … | N/A | … | … | … | … |
| ***Pharmacological-assisted tapering*** | | | | | | | | | | | | |
| Murphy 2013 | SRC | Rehabilitation programme | None | PT | NRS | −0.5 | … | N/A | POQ-VA ADL | −2.8 | … | N/A |
| Zhou 2017 | SRC | Comprehensive taper | None | PT | VAS | **−2.6** | … | N/A | … | … | … | … |
| Capano 2020 | SRC | Hemp extract | None | PT | … | … | … | N/A | PEG | −0.8 | … | N/A |
| ***Tapering only*** | | | | | | | | | | | | |
| Kurita 2018[66] | RCT | Taper only | Stabilisation | 4–6 weeks | VNS | + 0.2 | + 0.9 | *No difference* | … | … | … | … |
| Bienek 2019[58] | RC | Taper only | FSD vs. ISD | 6 weeks | NRS | −0.9 | −0.9 | N/A | … | … | … | … |
| ***Cognitive, psychological and behavioural*** | | | | | | | | | | | | |
| Garland 2014[60] | RCT | Mindfulness training | Support group | 3 months | BPI | −0.6 | + 0.6 | *Favours intervention* | BPI | −1.3 | + 0.4 | *Favours intervention* |
| Sullivan 2017[54] | RCT | Taper + MI/CBT | Taper only | 34 weeks | BPI | −1.0 | −0.1 | *No difference* | BPI | −1.5 | −0.5 | *Favours intervention* |

continued

**TABLE 16** Summary outcomes table for pain severity and interference (*continued*)

| Study | Study design | Intervention (I) | Comparator (C) | FU | Change in points from baseline | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Pain severity | | | | Pain interference | | | |
| | | | | | Scale | I | C | I vs. C | Scale | I | C | I vs. C |
| ***Acupuncture*** | | | | | | | | | | | | |
| Zheng 2008[56] | RCT | Electroacupuncture | Sham | 20 weeks | VAS | −0.8 | −0.7 | *No difference* | … | … | … | … |
| Zheng 2019[55] | RCT | Electroacupuncture | Sham | PT | VAS | + 0.1 | −0.3 | *No difference* | … | … | … | … |
| Jackson 2021 | RCT | Taper + acupuncture | No acupuncture | PT | NRS | + 0.4 | + 0.7 | *No difference* | … | … | … | … |
| Montgomery 2020[68] | RC | Acupuncture | None | PT | NRS | −1.3 | 0.0 | *No difference* | … | … | … | … |

BPI, Brief Pain Inventory (0–10 points); FSD, fixed starting dose; FU, follow-up; ISD, individualised starting dose; MPI, Multidimensional Pain Inventory (52-item, 12 scales); N/A, not applicable; NRS, Numerical Rating Scale (0–10 points); NS, not specified; PEG, 3-Item scale assessing pain intensity and interference (0–10 points); POQ-VA, Pain Outcomes Questionnaire-for veterans Interference in activities of daily living scale (0–10 points); PT, immediately post-treatment/discharge; RC, retrospective cohort; SRC, single retrospective cohort; VAS, visual analogue scale (0–10 points); VNS, verbal numerical scale (0–10).

**Notes**
*Favours intervention* = statistically significant effect in favour of intervention group ($p < 0.05$); *No difference* = no statistically significant difference in effect between intervention and control groups.
**Bold** values indicate a change from the baseline value of 2.0 points or more on a 0–10 pain scale.

**TABLE 17** Summary outcomes table for change in opioid outcomes: reduction and cessation

| Study | Study design | Intervention (I) | Comparator (C) | FU | Reduction, change in mean MEDD or equivalent | | | Cessation, % tapered off opioids | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | I | C | I vs. C | I | C | I vs. C |
| ***Pain management programmes (including tapering and pain management only)*** | | | | | | | | | | |
| Seal 2020[72] | PMC | Integrated Pain Team | Usual care | 6 months | −55.7 | −17.4 | *Favours intervention* | … | … | … |
| Gersch 2021[70] | RC | Pain e-consult programme | Usual care | 12 months | −23.0 | −9.1 | *Favours intervention* | … | … | … |
| Cunningham 2016[59] | SPC | Rehabilitation programme | … | 3 weeks | … | … | … | 100.0% | … | N/A |
| Krumova 2013[65] | SPC | Rehabilitation programme | … | PT | … | … | … | 76.5% | … | N/A |
| | | | | 12–24 months | … | … | … | 48.0% | … | N/A |
| Laigaard 2020[67] | SPC | Multidisciplinary pain centre | … | PT | −61.0[a] | … | N/A | … | … | … |
| Townsend 2008[79] | SPC | Rehabilitation programme | … | PT | … | … | … | 82.6% | … | N/A |
| | | | | 6 months | … | … | … | 77.3% | … | N/A |
| Huffman 2017[63] | SRC | Rehabilitation programme | … | PT | −54.4 | … | N/A | 69.5% | … | N/A |
| | | | | 6 months | … | … | … | 29.9% | … | N/A |
| Panicker 2022[79] | SRC | Nurse-led pain clinic | … | PT | −18.1 | … | N/A | … | … | … |
| ***Tapering curriculum/guidelines/initiative*** | | | | | | | | | | |
| Jacobs 2016[64] | SPC | Chronic Opioid Assessment Programme | … | Chart review | … | … | … | 9.5% | … | N/A |
| Austin 2019[57] | SRC | Opioid-tapering curriculum | … | Chart review | + 5.1[b] | … | N/A | 26.6% | … | N/A |
| Rivich 2018[71] | SRC | Multidisci-plinary chart reviews | … | 3 months | −37.0[a] | … | N/A | … | … | … |
| Westanmo 2015[101] | NPC | OSI implementation | … | 42 months | −20.0 | … | N/A | … | … | … |

continued

**TABLE 17** Summary outcomes table for change in opioid outcomes: reduction and cessation (*continued*)

| | | | | | Reduction, change in mean MEDD or equivalent | | | Cessation, % tapered off opioids | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Study** | **Study design** | **Intervention (I)** | **Comparator (C)** | **FU** | **I** | **C** | **I vs. C** | **I** | **C** | **I vs. C** |
| ***Pharmacological assisted tapering*** | | | | | | | | | | |
| Murphy 2013[69] | SRC | Rehabilitation programme | … | PT | … | … | … | 100% | … | N/A |
| Zhou 2017[81] | SRC | Comprehensive taper | … | PT | … | … | … | 27.9% | … | N/A |
| ***Tapering only*** | | | | | | | | | | |
| Kurita 2018[66] | RCT | Taper only | Stabilisation | PT | −140.8 | + 80.0 | *No difference*[c] | 0.0% | 0.0% | N/A |
| Bienek 2019[58] | RC | Taper only | FSD vs. ISD | PT | −127.7 | −206.9 | N/A | 64.8% | 50.2% | N/A |
| ***Cognitive, psychological and behavioural*** | | | | | | | | | | |
| Hudak 2020[62] | RCT | Mindfulness training | Support group | 4 months | −14.9 | −2.2 | *Favours intervention* | … | … | … |
| Sullivan 2017[54] | RCT | Taper + MI/CBT | Taper only | 12 weeks | −107.7 | −107.0 | *No difference* | 11.1% | 11.8% | *No difference* |
| ***Acupuncture*** | | | | | | | | | | |
| Zheng 2008[56] | RCT | Electroacupuncture | Sham | 20 weeks | −116.9 | −56.5 | *No difference* | … | … | … |
| Zheng 2019[55] | RCT | Electroacupuncture | (1) Sham + PMM; (2) PMM | 26 weeks | −125.2 | (1) −92.4; (2) −42.0 | *No difference* | … | … | … |
| Jackson 2021[53] | RCT | Taper + acupuncture | No acupuncture | PT | −34.0 | −66.0 | *No difference* | … | … | … |
| Montgomery 2020[68] | RC | Battlefield acupuncture | No intervention | 6 months | + 3.9 | + 8.7 | *No difference* | … | … | … |

FSD, fixed starting dose; FU, follow-up; ISD, individualised starting dose; MEDD, morphine equivalent daily dose; N/A, not applicable; NPC, non-patient cohort; PMM, pain and medication management plan only; PT, post-treatment; RC, retrospective cohort; SPC, single prospective cohort; SRC, single retrospective cohort.

a Change in median dose.

b Change is between baseline cohort and patients who remained on opioid therapy.

c Study underpowered because of dropouts.

**Note**

*Favours intervention* = statistically significant effect in favour of intervention group ($p < 0.05$); *No difference* = no statistically significant difference in effect between intervention and control groups.

### *Pain*

Pain was reported by 15 studies either in terms of severity and/or interference.

Four non-comparative studies that assessed pain management programmes reported pain severity as an outcome.[68,74,79,88] Three studies used an 0- to 10-point scale and one study used the Multidimensional Pain Inventory (MPI), a 52-item, 12-scale inventory. All four studies reported a decrease in pain scores from baseline to discharge/end of the intervention. A decrease was still apparent at follow-up in two studies that reported outcomes at 6 months and 12–24 months, respectively.[74,88] Neither of the comparative studies assessing pain management programmes reported pain severity or pain interference as an outcome.[70,81]

Three non-comparative studies that assessed pharmacological-assisted opioid tapering[78,90,110] all reported at least one pain outcome. Two studies reported decreases in pain severity from baseline to discharge/end of intervention, both on a 0- to 10-point scales. Two studies also reported a decrease in pain interference. None of the studies reported outcomes over a longer follow-up period.

Two studies of tapering-only interventions reported pain severity, both at discharge/end of the intervention and over a longer follow-up period. One study[75] compared a taper intervention with stabilisation finding no significant difference between groups at follow-up. The other study[67] of different starting doses found a reduction in pain scores from baseline in both groups at follow-up.

Two comparative studies assessing cognitive, psychological and behavioural interventions reported both pain severity and interference; measured in both studies with the Brief Pain Inventory (BPI). The study of mindfulness training compared to a support group, found statistically significant effects in favour of the intervention for both pain severity and interference.[69] The study of tapering and MI/CBT found no difference in pain severity between the intervention and taper-only control at follow-up.[113] For pain interference, a statistically significant effect in favour of the intervention was found at follow-up.

Four comparative studies that assessed acupuncture reported pain severity as an outcome. None of the studies found a statistically significant difference between the intervention and control groups.

As statistically significant evidence by itself is insufficient to indicate whether the magnitude of the effect on pain is clinically important,[120] we explored minimally important differences across the studies that reported pain outcomes. This exploratory analysis was based on a reduction of at least 2 points on 0- to 10-point scale. The change from baseline reached a difference of 2.0 points or more in three non-comparative studies: two studies[68,79] of pain management programmes and one study[90] of pharmacological-assisted tapering.

### *Change in opioid dose (including cessation)*

All but two studies[68,69] reported at least one measure of change in opioid use. Twenty-two studies reported on the outcome of reduction in opioids with differences in how the outcome was reported. The different outcome types are reported in separate tables in *Appendix 5*.

#### Change in mean morphine equivalent daily dose or equivalent

Five studies that examined pain management programmes reported on the reduction of opioid dose. Two comparative studies found statistically significant effects in favour of the intervention at follow-up.[70,81] Seal *et al.*[81] compared an integrated pain team with usual care and Gersch *et al.*[70] a pain e-consult programme with usual care. Three non-comparative studies all reported reductions in opioid dose between baseline and the end of treatment/discharge.[72,79] Two further studies[74,88] reported details for participants still taking opioids at the end of treatment, with all patients having reduced their doses.

Three studies[66,80,117] that examined an opioid-tapering curriculum, guideline or curriculum reported changes in opioid dose. Austin *et al.*[66] reported the change in dose between a baseline cohort and patients who remained on opioid therapy, finding no significant change. Two studies[80,117] about the implementation of recommendations related to the

US OSI reported reductions in opioid dose. One further study[83] of OSI implementation reported 'modest reductions' in the annual rate of opioid prescribing.

One study that examined pharmacological-assisted opioid-tapering interventions reported that 51.5% of participants using the CBD hemp extract were able to reduce opioid medications at week 8.[110]

Both studies that examined tapering-only interventions reported on the reduction of opioid dose. Kurita *et al.*[75] reported a reduction in dose in the taper-only intervention group, but there was no significant difference between the taper only and stabilisation groups at follow-up. The authors state that the taper phase of the study was underpowered due to dropout. Bienek *et al.* reported reductions in dose in both the fixed starting dose group and individualised starting dose group.[67]

Two comparative studies[71,113] that examined cognitive, psychological and behavioural interventions reported changes in opioid use. Hudak *et al.*[71] found a statistically significant reduction in opioid dose that favoured mindfulness training compared to a support group. Sullivan *et al.*[113] reported reductions in opioid dose in both the taper and MI/CBT intervention group and taper-only control group but found no statistically significant difference between the groups at the end of treatment or at follow-up.

All four comparative studies that examined the use of acupuncture reported on the reduction of opioid dose.[77,111,112,116] Three studies, including two that examined electroacupuncture and one that examined taper and acupuncture, reported reductions in the both the intervention and control groups. However, none of the studies found a statistically significant difference between the intervention and comparator groups at the end of treatment or follow-up.

One study that examined clinical encounters reported that 29% of clinical encounters were followed by a reduction in opioid prescribing.[82]

### Cessation of opioid use

All but one study[75] whose aim was for cessation reported on the number of participants succeeding in ceasing opioid use. An additional study that aimed to reduce opioid use also reported cessation rates.[66]

Four non-comparative studies that examined pain management programmes reported cessation rates. The studies reported a high proportion of participants ceasing use at the end of the intervention – ranging from 69.5%[72] to 100%.[68] Three studies reported cessation rates at follow-up and a proportion of patients had relapsed to opioid use following cessation; the proportion of patients that remained opioid free in these three studies were 48.0%,[74] 77.3%[88] and 29.9%,[72] respectively.

Two studies that examined tapering curriculums, guidelines or initiatives reported low proportions of participants ceasing use – 9.5%[73] and 26.6%,[66] respectively.

Two studies that examined pharmacological-assisted opioid tapering reported that 100% of participants[78] and 27.9% of participants,[90] respectively, had ceased opioid use at the end of treatment.

One comparative study of a cognitive, psychological and behavioural intervention that compared taper plus MI/CBT with taper only found that only two participants in each group ceased opioid use. Two comparative studies that examined tapering interventions reported cessation rates. Kurita *et al.*[75] reported that no participants in either the taper-only intervention group or stabilisation comparison group ceased opioid use. Bienek *et al.*[67] compared a fixed starting dose taper regimen with an individualised starting dose regimen, finding that 64.8% and 50.2% of participants, respectively, ceased opioid use.

#### *Opioid withdrawal-related symptoms or dependence*

Opioid withdrawal-related symptoms were poorly reported across the studies with only three studies[67,68,75] reporting symptoms assessed using a validated scale.

One non-comparative study[68] reported that the peak score on the Clinical Opioid Withdrawal Scale (COWS) was higher for patients on higher opioid doses but not significantly different based on the morphine equivalent dose (MED). The mean peak COWS score occurred at 80% reduction from the initial opioid dose for patients on a MED dose of 100 mg/day or less, 64% for a MED dose of 100–200 mg/day, and 72% for a MED dose of > 200 mg/day.

Two comparative studies examined tapering-only interventions. One study[75] did not report the results of either the Objective Opiate Withdrawal Scale (OOWS) or Subjective Opiate Withdrawal Scale (SOWS) that they used. The final study did report that those on a fixed starting dose had a significantly lower 10-day mean daily SOWS scores than those on an individualised starting dose (comparator group).[67]

### *Acceptability of the intervention and patient satisfaction*

Acceptability of the intervention and patient satisfaction were reported in four studies. One study examined pharmacological-assisted tapering, and participants were asked to score overall satisfaction on a scale of 0–10, the average rating was 8.3.[78] Two studies examined cognitive, psychological and behavioural interventions. Garland *et al.*[69] measured treatment credibility based on three items about attitudes towards treatment. There was no statistically significant difference between the intervention and control groups on this measure (21.4 vs. 19.3). In the study by Sullivan *et al.*,[113] intervention group participants were asked to rate the helpfulness of the taper plus MI/CBT intervention on a 1- to 5-point scale. The intervention was rated as very or extremely helpful by 81.3% of participants at the end of the intervention and by 73.3% at 34 weeks follow-up. Finally, Sharp *et al.*[82] reported that the number of patients with a mean satisfaction score > 9 was 88.9%.

### *Emotional functioning*

Eight studies reported the outcome depression,[68,69,74,75,76,88,111,113] and of those, four also reported anxiety outcomes.[75,76,111,113]

Four of the studies reporting depression as an outcome were evaluations of pain management programmes. Two non-comparative studies[74,76] reported no change in depression measures, at 12- to 24-month follow-up or at the final visit, respectively. Two further non-comparative studies, both of 3-week rehabilitation programmes reported statistically significant reductions in depression on the Centre for Epidemiological Studies Depression Scale (CES-D) at the end of the programme.[68,88] Townsend *et al.*[88] followed patients up at 6 months post treatment, finding that the significant reduction in depression remained.

Four comparative studies[69,75,111,113] reported depression outcomes measured with the Hospital Anxiety and Depression Scale (HADS),[75,111] Calgary Symptoms of Stress Inventory (C-SOSI)[69] and the Patient Health Questionnaire-9 items (PHQ-9).[113] The intervention types explored in these studies varied and included two studies of cognitive, psychological and behavioural interventions,[69,113] acupuncture[111] and sequential opioid dose reduction.[75] None of the studies found a statistically significant difference between the intervention and comparator groups at the end of treatment or follow-up.

Four studies reported anxiety outcomes. Three were comparative studies (of acupuncture,[111] sequential opioid dose reduction[75] and a cognitive, psychological and behavioural intervention[113]) and one was a non-comparative study of a pain management programme.[76] None of the comparative studies found a statistically significant difference between the intervention and comparator groups at the end of treatment or follow-up.[75,111,113] The non-comparative study did not find a statistically significant change between baseline and the end of treatment.[76]

### *Sleep quality*

Sleep quality was reported by four studies.[75,78,110,113] Two non-comparative studies examined pharmacological interventions[78,110] and both reported statistically significant improvements in sleep quality from baseline to the end of the intervention. Two comparative studies[75,113] that examined sequential opioid dose reduction and acupuncture interventions, respectively, found no statistically significant difference between the intervention and comparator groups at either the end of the intervention or at longer-term follow-up.

### *Quality of life*

Quality-of-life outcomes measured with the 36-item Short Form Survey (SF-36) were reported by five studies.[68,74,75,76,112] Two comparative studies, of sequential opioid dose reduction[75] and electroacupuncture,[112] respectively, reported no statistically significant difference between the intervention and comparator groups at either the end of the intervention or at longer-term follow-up.

The three remaining studies were all non-comparative studies of pain management programmes.[68,74,76] One study reported a statistically significant improvement from baseline in the mental component summary of the SF-36 but not in the physical component at 12–24 months follow-up.[74] Another study[68] reported a statistically significant improvement from baseline on the general health perceptions domain of the SF-36. One study reported no significant changes from baseline.[76]

Two further studies reported that they assessed SF-36 scores but did not report results in their published papers.[75,112]

## Summary

The literature searches identified 27 relevant studies, including 11 comparative studies and 16 non-comparative studies. There were some concerns about the risk of bias across the included studies but only significant concerns about the quality of one study.[67] With differences in population, such as the number of recruited patients and patient characteristics, study design (including intervention), collected outcome data and duration of follow-up, it was unsurprising that for the outcomes of pain severity, emotional functioning, sleep quality and quality of life, some studies reported improvements while other studies reported no differences. Although only reported by two studies, there was consistency in terms of the acceptability of interventions which was high. Confidence in this finding is enhanced by the safety review results (see Chapter 7) as none of the seven studies that reported AEs reported any serious AEs, and no patients were reported to have withdrawn from a study due to an AE.

All except two of the included studies[68,69] reported at least one measure of change in opioid use. While cessation of opioid use is an outcome that is clinically important, defining the level of reduction in opioid use that is clinically relevant is problematic. Findings from a systematic literature review[121] of minimum clinically important differences (MCID) for chronic pain relief showed that reported MCID levels vary considerably, although baseline pain was strongly associated with absolute, but not relative, measures. Further, but to a much lesser degree, MCID was also influenced by the operational definition of relevant pain relief and possibly by clinical condition.

The relevance to NHS practice of some of the interventions described in the included studies is unclear. For example, four of the comparative studies assessed the effect of acupuncture on reduction of opioid use; however, acupuncture is only sometimes available on the NHS, access is limited and most patients wanting acupuncture pay for private treatment. Further, five of the non-comparative studies examined how the introduction of OSIs affected patient use of opioids; such initiatives will only be relevant if the assessed measures are not already implemented in the NHS.

# Chapter 6 Safety of interventions to reduce opioid use

## Search results

Of the 52 papers included in at least 1 of the reviews, 9 papers, reporting on 7 studies,[91,92,110,111,112,113,116] reported on AEs because of an intervention used for the tapering of opioids in people with chronic non-cancer pain. Five of those studies[110,111,112,113,116] also reported on the effectiveness of the intervention and have been reported in Chapter 5. Of the 52 papers included in at least 1 of the reviews, 9 papers, reporting on 7 studies,[90,91,109,110,111,112,115] reported on AEs because of an intervention used for the tapering of opioids in people with chronic non-cancer pain. Five of those studies[109,110,111,112,115] also reported on the effectiveness of the intervention and have been reported in Effectiveness of interventions to reduce opioid use.

## Study characteristics

The two publications not included in the effectiveness review were both case reports.[91,92] Four studies were RCTs[111,112,113,116] and one was a non-comparative prospective cohort study.[110] The study characteristics of all seven studies are shown in *Table 18*.

Four studies were conducted in the USA,[91,110,111,113] two in Australia[112,116] and one in France.[92] The length of follow-up was reported by five studies[91,110,112,113,116] and varied from 8[110] to 34 weeks.[113] The number of participants in the studies were generally small (*N* = 1,[91] *N* = 1,[92] *N* = 15,[111] *N* = 35[113]) though two studies reported ~100 participants (*N* = 97[110] and *N* = 108[116]). Most studies had more female participants, though all but the case studies included some male participants. The mean age of participants ranged from 36[92] to 58.4 years.[116] The type and duration of chronic pain that participants were experiencing was poorly reported by the studies as were details on the types and the duration of use of opioids. The baseline levels of opioid use were reported but ranged greatly from 112[111] to 871.41 mg/daily.[116]

## Intervention characteristics

The intervention characteristics of the included studies are shown in *Table 19*.

All but one study aimed to reduce the dose of opioids, whereas one study aimed for the participant to discontinue use of opioids.

Three studies assessed the use of acupuncture,[111,112,116] three used pharmacological interventions (CBD[91,110] and ketamine[92]) and one used a combination of a sequential opioid dose reduction with MI and CBT.[113] For four comparative studies, the comparator was usual care in two studies[111,113] and sham acupuncture in two studies.[112,116] For all but one study,[113] the intervention was delivered individually and face to face. The duration of the intervention varied; for the two studies using CBD to taper opioid use participants continued to use CBD,[91,110] for the participant in Lalanne *et al.*,[92] ketamine was used for 4 days and then withdrawn (there are no details on length of time). The three studies using acupuncture varied in their duration from 8 weeks[112] to 12 months.[111]

## Quality assessment

The quality assessment for the four RCTs[111,112,113,116] and the comparative study[110] are shown in *Tables 13* and *15*. The overall rating in the Risk of Bias 2[36] showed that there were some concerns; no study had a rating of high risk in any of the domains. For the comparator study, the CASP cohort checklist[38] showed that the study was of good quality.[110] Single case reports were not quality assessed.

**TABLE 18** Study characteristics (Review 2)

| Study | Design<br>~~Number of arms~~ | ~~Country~~<br>~~Setting~~ | Timing of assessments | *N* | Arm | *N*<br>~~Females~~<br>~~Males~~ | Age (years), mean (SD) | Type of chronic pain | Duration (years) of chronic pain, mean (SD) | Types of opioids | Duration (years) of opioid use, mean (SD) | Level of opioid use (mg/daily), mean (SD) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Jackson 2021[111] | RCT<br>2 | USA<br>Outpatient | Baseline<br>NR | 15 | I and C | *N* = 15<br>F = 7<br>M = 8 | 56.5 (17.3) | NR | NR | NR | NR | I = 112 (71)<br>C = 191 (121) |
| Sullivan 2017[113] | RCT<br>2 | USA<br>Outpatient<br>Multidisciplinary pain centre | Baseline<br>End of treatment period<br>34 weeks follow-up | 35 | I | *N* = 18<br>F = 12<br>M = 6 | 54.4 (10.1) | NR | NR | NR | 10.2 (4.3) | 207.2 (269.3) |
| | | | | | C | *N* = 17<br>F = 13<br>M = 4 | | | | | | 245.2 (347.3) |
| Zheng 2008[112] | RCT<br>2 | Australia<br>Outpatient<br>Pain management clinic | Baseline<br>End of treatment period<br>Every 4 weeks until 20 weeks follow-up | 35 | I | *N* = 17<br>F = 8<br>M = 9 | 51.1 (13) | NR | 19.8 (24.5) | Codeine 10<br>Methadone = 1<br>Oxycodone 4<br>Morphine 4<br>Tramadol 6 | NR | 461.6 (462.6) |
| | | | | | C | *N* = 18<br>F = 9<br>M = 9 | 48.4 (10.5) | | 13 (1.1) | Codeine 14<br>Methadone 0<br>Oxycodone 5<br>Morphine 3<br>Tramadol 4 | | 295.5 (288) |
| Zheng 2019[116] | RCT<br>3 | Australia<br>Outpatient<br>Three pain clinics and from the public | Baseline<br>End of the treatment period<br>Every 4 weeks for 12 weeks follow-up | 108 | I | *N* = 48<br>F = 28<br>M = 20 | 55.9 (11.3) | NR | 10.8 (9.4) | NR | NR | 463.3 (438.6) |
| | | | | | C | *N* = 29<br>F = 18<br>M = 11 | 58.4 (12.8) | | 13.3 (9.6) | | | 620.8 (792.4) |
| | | | | | C2 | *N* = 31<br>F = 16<br>M = 15 | 58.4 (12.8) | | 16.3 (12.5) | | | 871.41 (1772.3) |
| Capano 2020[110] | Prospective cohort<br>1 | USA<br>Private pain management centre | Baseline<br>4 and 8 weeks | 97 | N/A | *N* = 97<br>F = 66<br>M = 31 | 56.1 (NR), 39–70 | NR | NR | NR | NR | NR |
| Caldera 2020[91] | Case report | USA<br>Outpatient<br>University hospital | Baseline<br>Six months follow-up | 1 | N/A | 1<br>F = 1 | 43 | Right-sided headaches and neck and shoulder pain | 14 years | Morphine | 14 years | 150 |

**TABLE 18** Study characteristics (Review 2) (*continued*)

| Study | Design<br>~~Number of arms~~ | ~~Country~~<br>~~Setting~~ | Timing of assessments | *N* | Arm | *N*<br>~~Females~~<br>~~Males~~ | Age (years), mean (SD) | Type of chronic pain | Duration (years) of chronic pain, mean (SD) | Types of opioids | Duration (years) of opioid use, mean (SD) | Level of opioid use (mg/daily), mean (SD) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Lalanne 2016[92] | Case report | France<br>Inpatient<br>University Hospital | Baseline<br>NR | 1 | N/A | 1<br>F = 1 | 36 | Lumbar pain | NR | Diazepam 10 mg three times per day, hydroxyzine 100 mg twice daily, venlafaxine 150 mg in the morning, oxycontin® extended-release 60 mg twice daily, oxycodone 10 mg every 4 hours, and acetaminophen/codeine 300 mg/25 mg six times per day | 1 year | NR |

C, comparator group; F, females; I, intervention group; M, males; NR, not reported.

**TABLE 19** Intervention characteristics (Review 2)

| Study | Aim of intervention | Type of intervention | Brief intervention description | Type of comparator | Brief comparator description | Mode(s) of delivery<br>~~Group/individual~~ | Duration/intensity |
|---|---|---|---|---|---|---|---|
| Jackson 2021[111] | Reduction | Acupuncture + standard of care | Participants received standard of care in addition to the National Acupuncture Detoxification Association protocol (standard of care consists of medication management with opioid weaning, and also received acupuncture sessions with each visit). | Standard of care | Standard of care (consists of medication management with opioid weaning). | Face to face<br>Individual | Monthly for 12 months |
| Sullivan 2017[113,114] | Reduction | Sequential opioid dose reduction and behavioural intervention | 10% reduction of the original dose per week until 30% of the original dose was reached. At that point, the 10% was recalculated on the basis of this dose and the taper then proceeded by 10% of this new dose per week.<br>MI and CBT | TAU | Usual care | Telephone<br>Group and individual | 30 minutes/week for 18 weeks |

continued

**TABLE 19** Intervention characteristics (Review 2) (*continued*)

| Study | Aim of intervention | Type of intervention | Brief intervention description | Type of comparator | Brief comparator description | Mode(s) of delivery Group/individual | Duration/intensity |
|---|---|---|---|---|---|---|---|
| Zheng 2008[112] | Reduction | Acupuncture | Electroacupuncture | Sham | Sham electroacupuncture | Face to face Individual | 20 minutes, twice/week for 6 weeks |
| Zheng 2019[115,116] | Reduction | Acupuncture | Electroacupuncture | C1 = Sham<br>C2 = Education only | Sham electroacupuncture<br>Education only | Face to face Individual | 20 minutes, twice/week for 4 weeks, then 20 minutes, once/week for 2 weeks then 20 minutes/fortnightly for 4 weeks.<br>Total, 12 sessions within 10 weeks.<br>Pain specialists provided pain and medication education to each participant once in the whole trial. |
| Capano 2020[110] | Reduction | Pharmacological | CBD hemp extract<br>Participants self-titrated their dose of CBD. | N/A | N/A | Face to face Individual | N/A |
| Caldera 2020[91] | Discontinuation | Pharmacological | 15 mg per week weaning protocol for daily morphine conducted over 1 month.<br>Then a weaning protocol for the immediate relief morphine<br>Medical cannabis | N/A | N/A | Face to face Individual | Medical cannabis 500 mg which had a 2 : 1 CBD to THC ratio in vape form.<br>It had 26.3% CBD and 17% THC.<br>These were divided into 2.5 mg doses per inhalation. |
| Lalanne 2016[92] | Reduction | Pharmacological | Ketamine oral solution for 2 days, then gradual reduction of opioid treatment over 2 days | N/A | N/A | Face to face Individual | Ketamine oral solution (5 mg/ml, magistral formulae) 1 mg/kg, and 2 days after ketamine initiation her opioid treatment was gradually reduced (10% reduction in the initial dosage each 2 days). |

C, comparator group; CBD, Cannabidiol; N/A, not applicable; TAU, treatment as usual; THC, tetrahydrocannabinol.

## Outcomes

The AEs reported in each of the studies is shown in *Table 20*. No study reported serious AEs. Five studies did report some AEs with two of the acupuncture studies reporting incidence rates of between 15% and 21%. No study reported that an AE resulted in withdrawal from the study.

## Summary

Nine papers, reporting on seven studies,[91,92,110,111,112,113,116] reported on AEs. All but one study aimed to reduce the dose of opioids, whereas one study aimed for the participant to discontinue use of opioids. Three studies assessed the use of acupuncture, three used pharmacological interventions (CBD and ketamine) and one used a combination of a sequential opioid dose reduction with MI and CBT. No study reported serious AEs.

**TABLE 20** Adverse event data reported in studies (Review 2)

| Study | Intervention | AE data |
|---|---|---|
| Jackson 2021[111] | Acupuncture + standard of care | *'There were no adverse outcomes such as skin irritation, inflammation, or vagal responses throughout this study'.* |
| Sullivan 2017[113,114] | Sequential opioid dose reduction and behavioural intervention | One AE in the taper support group; was classified as severe and study-related. A patient prescribed nortriptyline developed an allergic reaction 2 days later (including difficulty breathing, a swollen uvula, redness in neck and flushed face); primary care physician discontinued the medication and the symptoms resolved. |
| Zheng 2008[112] | Electroacupuncture | No serious AEs were reported. Overall incidence rate of AEs was 52/345 = 15%.<br>Intervention = 33; comparator = 19. |
| Zheng 2019[115,116] | Electroacupuncture | No serious AEs were reported. The most common AEs were pain at the site of needling, lethargy and bruising. No group differences.<br>Intervention = 86, 17% incidence rate, 1.8 (3.1) per person<br>Comparator = 70, 21% incidence rate, 2.4 (5.1) per person |
| Capano 2020[110] | CBD hemp extract | One participant reported that CBD 'made her heart race' and combined twice-daily dosing into one dose to manage the side effect. One participant reported nausea from CBD but continued using the product. One participant reported 'heart burn and dry mouth' after initiating CBD. One participant reported CBD increased her night-time anxiety and disturbed sleep. No significant AEs were reported. |
| Caldera 2020[91] | Medical cannabis | Reported no side effects from the medical cannabis. |
| Lalanne 2016[92] | Ketamine oral solution | *'She complained of no side effects of ketamine other than an unusual weakness'.* |

# Chapter 7 Barriers and facilitators of effective intervention

## Search results

Eighteen papers[93,94,95,96,97,98,99,100,101,102,103,104,105,106,107,108,109,117] reporting on 16 studies[93,94,95,96,97,99,100,102,103,104,105,106,107,108,109,117] were included in the barriers and facilitators review. One of the studies[117] was also included in the effects review (Review 1). The PRISMA flow chart is reported in *Figure 1*. Four studies[62,63,64,65,122] were identified in the update search; none of these studies identified any additional barriers or facilitators in addition to those reported in the papers identified in the original search, suggesting that data saturation had been reached. Consequently, these additional studies were not incorporated into this review.

## Study characteristics

*Table 21* outlines the included study characteristics. All studies were published between 2015 and 2022, of which, eight studies were published between 2020 and 2022. Studies were undertaken in three countries, predominantly in USA. Eleven studies were conducted in the USA, four studies in Australia and one study in the UK.

Of the 16 studies, 10 were qualitative,[93,94,96,97,99,100,102,103,105,106] 5 were mixed methods[95,104,107,108,109] and 1 was quantitative.[117] Qualitative data were extracted from all five mixed-methods studies and quantitative data were extracted from two mixed-methods studies.[95,107]

Qualitative methods used included interviews in 11 studies,[93,94,95,96,99,103,104,105,106,108,109] focus groups in 4 studies,[97,99,102,103] audio-recorded clinical visits in 1 study,[105] video-recorded clinical visits in 1 study[100] and open-ended survey in 2 studies.[104,107] Quantitative methods used included surveys in two studies[107,117] and data collected from patients, records and pharmacy dispensing in one study.[95]

Nine studies[94,95,97,100,103,104,105,117] explored barriers to, and facilitators of, opioid tapering in chronic non-cancer pain as part of their study aims. Two studies[96,102] reported results on barriers and facilitators more widely by examining patient/provider experiences of opioid tapering. In five studies,[93,99,106,108,109] barriers and facilitators were inferred from results that described wider patient/provider experiences of opioid tapering.

Thirteen studies[93,95,96,97,99,100,102,104,105,106,107,108,117] declared no conflicts of interest and one study[109] did not report whether there were any conflicts of interest. Two studies reported a conflict of interest. Firemark *et al.*[94] reported that '8 authors received grant funding from the National Institute on Drug Abuse of the National Institutes of Health as part of the grant that is funding this study' and Langford *et al.*[103] declared 'non-financial support from Pfizer Australia, outside the submitted work'.

### *Population characteristics*

Participants were sampled from primary care clinics,[93,96,99,100,102,104,105,106,108] pain management clinics,[93,107] VA medical centres,[102,117] other multiple/integrated healthcare systems (e.g. pain addiction treatment services, pharmacy, community-based outpatient clinics, public tertiary pain clinic, family health services)[93,94,95,97,104,106,109] and via a deprescribing conference.[103]

Seven studies focused on patient perspectives,[93,96,99,104,106,107,109] five studies[94,97,102,103,117] focused on healthcare professional's perspectives and four studies[95,100,105,108] included both patients and healthcare professional perspectives. No studies explored views from a carer perspective.

Of the 12 studies that involved a patient perspective, 5 studies[93,95,96,99,109] included patients who had tapered/discontinued opioids, 6 studies[96,99,100,104,106,109] included patients actively tapering, 1 study[107] included patients about to

**TABLE 21** Included study characteristics for barriers and facilitators review (Review 3)

| Author, date | Country | Aim | Study design | Theoretical approach (if reported) | Method of data collection (relevant to our review) | Method of data analysis (relevant to our review) | Setting | Perspective | Sample |
|---|---|---|---|---|---|---|---|---|---|
| Benintendi 2021[93] | USA | To describe the ways in which well-intentioned **taper** initiatives impacted people living with chronic pain, a population already experiencing a well-documented and significant burden of stigma. | Qualitative | Framework of structural stigma used to guide analysis[a] | 41 interviews | Thematic analysis (deductive and inductive) | Primary care clinics at Boston Medical Center in Boston, MA, and the High Dose Opioid Tapering Initiative, pain management clinic, addiction treatment services, and primary care clinics of the University of Michigan Health System (UMHS, also called Michigan Medicine) in Ann Arbor, MI | Patients | *N* = 41 patients who had undergone an opioid taper in the last 2 years<br>Age range 28–76<br>18 males, 23 females |
| Firemark 2021[94] | USA | To identify **factors that influence or interfere** with referrals by primary care providers (PCPs) to a pharmacist-led telephone-based programme to assist patients undergoing opioid tapering | Qualitative | RE-AIM implementation framework[b] | 35 interviews | Thematic analysis (inductive) | An integrated healthcare system (HCS) in Oregon and Southwest Washington | Provider | *N* = 35 20 PCPs, 15 STORM staff (12 pharmacists, 3 non-pharmacists; 9 current STORM staffs, 6 former STORM staffs)<br>15 males, 20 females |
| Frank 2016[96] | USA | To explore patients' perspectives on opioid tapering. | Qualitative | Health Belief Model | 24 semistructured interviews | Thematic analysis (deductive and inductive) | Primary care clinics affiliated with three health systems in Denver, Colorado: (1) an academic medical centre, (2) an urban, safety-net medical centre and (3) a Veterans Affairs medical centre | Patients | *N* = 24 patients, of which 6 currently on opioid medications without tapering, 12 currently tapering chronic opioid therapy (COT), 6 discontinued COT within the past 3 years<br>Mean age 52 (range 31–73)<br>11 males, 13 females |

continued

**TABLE 21** Included study characteristics for barriers and facilitators review (Review 3) (*continued*)

| Author, date | Country | Aim | Study design | Theoretical approach (if reported) | Method of data collection (relevant to our review) | Method of data analysis (relevant to our review) | Setting | Perspective | Sample |
|---|---|---|---|---|---|---|---|---|---|
| Giannitrapani 2018[97,98] | USA | To understand providers' **perceptions of barriers** to reducing opioid use and improving the use of non-pharmacological pain management therapies for chronic pain | Qualitative | Fortney, Burgess[123] dimensions of access[c] | Nine focus groups | Thematic analysis (deductive)<br>Post hoc analysis of barriers and facilitators | Two academically affiliated CA Medical Centres, California and Oregon and associated community-based outpatient clinics | Providers | *N* = 60 primary care providers, registered nurses, licensed practical nurses, clerks, psychologists and social workers.<br>Mean age: NR<br>Male/female: NR |
| Henry 2019[99] | USA | To characterise patients' experiences with opioid tapering and identify communication strategies that **are likely to foster** productive, patient-centred discussions of opioid tapering. | Qualitative | Health Belief Model | Focus groups (*n* = 4) and interviews | Thematic analysis (inductive) | 13 different primary care clinics within the University of California, Davis Health System located in the greater Sacramento area | Patients | *N* = 21 patients took part in focus groups, of which 14 had completed tapering, 4 were currently tapering and 3 had been recommended to taper<br>*N* = 7 patients also interviewed, of which 4 had completed tapering, 2 were currently tapering, and 1 had been recommended to taper<br>Mean age 58.2<br>10 males, 11 females |
| Henry 2019b[100,101] | USA | To identify patient statements about opioids that indicate potential **openness to tapering opioids** or trying non-opioid pain treatments | Qualitative | – | 86 video-recordings of clinical visits | Thematic analysis (inductive) | Two academic primary care clinics at the University of California, Davis Medical Center in Sacramento, California | Patients and providers | *N* = 86 patients, of which 8 were currently undertaking tapering and 49 physicians<br>Patients<br>Mean age: 59.6<br>31 males, 55 females<br>Physicians<br>Mean age: 29.6<br>12 males, 37 females |

**TABLE 21** Included study characteristics for barriers and facilitators review (Review 3) (*continued*)

| Author, date | Country | Aim | Study design | Theoretical approach (if reported) | Method of data collection (relevant to our review) | Method of data analysis (relevant to our review) | Setting | Perspective | Sample |
|---|---|---|---|---|---|---|---|---|---|
| Kennedy 2018[102] | USA | To explore PCPs' experiences discussing and implementing opioid tapering with patients on long-term opioid therapy | Qualitative | – | Focus groups (*n* = 6) | Thematic analysis (inductive) | Six academically affiliated primary care clinics in university, urban safety net, and Veterans Health Administration medical centres in Colorado | Providers | *N* = 40, of which 34 physicians, 3 physician assistants/ nurse practitioners, 3 others (nurses/clinical pharmacist)<br>Mean age: 40<br>21 male, 19 female |
| Kuntz 2021[95] | USA | To identify factors from patients and pharmacists, that were cited as **hindering or contributing** to successful opioid tapering | Mixed methods | – | Qualitative: Interviews<br>Quantitative: Baseline and follow-up data collected from patients, records and pharmacy dispensing data | Qualitative: Thematic analysis (inductive)<br>Quantitative: Multilevel hierarchical modelling to evaluate predictors of a successful taper, defined as a 50% decrease from baseline opioid use during the 12 months following the index date. | Kaiser Permanente Northwest (KPNW) an integrated health system in northwest Oregon and southwest Washington | Qualitative: Patients and providers<br>Quantitative: Patients | Qualitative: *N* = 25 patients who had undergone STORM tapering and *N* = 12 former and current STORM pharmacists<br>Patients<br>Mean age: 58<br>5 males, 20 females<br>Pharmacists<br>Mean age NR<br>2 males, 10 females<br>Quantitative:<br>*N* = 1384 patients<br>Age:<br>24% 21–49 years<br>50% 50–64 years<br>26% ≥ 65 years<br>37% male, 63% female |

continued

**TABLE 21** Included study characteristics for barriers and facilitators review (Review 3) (*continued*)

| Author, date | Country | Aim | Study design | Theoretical approach (if reported) | Method of data collection (relevant to our review) | Method of data analysis (relevant to our review) | Setting | Perspective | Sample |
|---|---|---|---|---|---|---|---|---|---|
| Langford 2020[103] | Australia | To explore the perspectives of healthcare professional stakeholders on the **challenges associated with opioid deprescribing** and **factors to be considered in the development of** opioid deprescribing guidelines | Qualitative | – | Focus groups (*n* = 2) and interviews | Thematic analysis (inductive) | Australian National Deprescribing Network conference (focus groups), Healthcare professional's place of work (interviews) | Providers | *N* = 20 (focus groups) of which 2 GPs, 1 general physician, 1 geriatrician, 1 rheumatologist, 3 clinical pharmacologists, 12 clinical pharmacists<br>*N* = 11 (interviews) of which 2 GPs, 1 anaesthetist, 2 geriatricians, 1 addiction specialist, 2 clinical pharmacists, 3 registered nurses |
| Magee 2021*[104] | Australia | To examine patients' use of mobile technologies in health care, interest in using mHealth support, preferences for the form and content of mHealth support, and potential **barriers to and facilitators of engagement** with mHealth support for opioid tapering. | Mixed methods | | Survey and interviews | | Private primary care practice in regional New South Wales and a public tertiary pain clinic in a metropolitan area in Australia | Patients | *N* = 21 patients currently or planning to taper<br>Age range: 29–83<br>10 males, 11 females |
| Matthias 2017[105] | USA | To understand communication processes related to opioid tapering, **to identify best practices and opportunities for improvement**. | Qualitative | – | 95 audio-recordings of clinical visits and interviews | Thematic analysis (inductive) | Four of 9 primary care clinics at an academic, safety-net hospital serving primarily low-income patients | Patients and providers | *N* = 37 patients, 9 PCPs<br>Patients (tapering status not reported)<br>Mean age: 58<br>12 males, 25 females<br>PCPs<br>Mean age: 45<br>1 males, 8 females |

**TABLE 21** Included study characteristics for barriers and facilitators review (Review 3) (*continued*)

| Author, date | Country | Aim | Study design | Theoretical approach (if reported) | Method of data collection (relevant to our review) | Method of data analysis (relevant to our review) | Setting | Perspective | Sample |
|---|---|---|---|---|---|---|---|---|---|
| McNeilage 2022*[106] | Australia | To identify patterns in individuals' experience of tapering and explore whether patient characteristics, readiness to taper, opioid tapering self-efficacy, or psychosocial context were related to tapering trajectory | Longitudinal study (Qualitative data) | – | 173 Semistructured phone interviews with 21 patients. Patients interviewed an average of 8 (range 2–12) over mean duration 12 weeks (range 2–20) | Phase 1: Between subject thematic analysis (inductive) Phase 2: Global ratings of tapering readiness and self-efficacy before commencement of taper (low, moderate, high) Phase 3: A within-subject longitudinal analysis of participants' experience of pain, distress, interference (low, moderate, high), and withdrawal symptoms (yes/no) together with changes in opioid dose (oral morphine equivalent daily dose) and psychosocial context | A tertiary public pain clinic in a metropolitan research hospital and a private primary care practice in a regional area | Patients | *N* = 21 patients currently tapering Age range: 29–83 10 males, 11 females |
| Quinlan 2020[107] | UK | To investigate the extent of the psychological comorbidity of patients with chronic pain and long-term opioid use and their hopes and fears before embarking on opioid tapering. | Mixed methods | Un-named theory used to inform analysis | Survey (Questionnaire) | Qualitative: Thematic analysis (inductive and deductive) Quantitative: Descriptive statistics | Opioid clinic in the Pain Management Centre of the Oxford University Hospitals NHS Foundation Trust | Patients | *N* = 49/60 patients just before commencing tapering |

continued

**TABLE 21** Included study characteristics for barriers and facilitators review (Review 3) (*continued*)

| Author, date | Country | Aim | Study design | Theoretical approach (if reported) | Method of data collection (relevant to our review) | Method of data analysis (relevant to our review) | Setting | Perspective | Sample |
|---|---|---|---|---|---|---|---|---|---|
| Westanmo 2015[117] | USA | To describe processes and outcomes of a health system quality improvement initiative designed to reduce opioid-related harms | Non-patient cohort | – | Survey (Questionnaire) | Frequency analysis | A Veterans Affairs healthcare system in Minneapolis | Providers | *N* = 34/46 responded before initiative, 31/48 responded after initiative |
| White 2020[108] | Australia | To evaluate patient and provider perspectives regarding the opioid-tapering intervention Assess, Inform, Manage and Monitor. | Mixed methods | Behaviour Change Wheel[d] | Semistructured telephone interviews | Thematic analysis | Two general practices in New South Wales, Australia (ranked in bottom 30% of Australian local government areas) | Patients and providers | *N* = 6 patients (unclear tapering status)<br>*N* = 4 providers, of which 1 GP, 1 practice nurse, 1 dietitian, 1 pharmacist |
| Wu 2019[109] | USA | To evaluate the effect of this prescribing policy, with secondary aims to gain insight into the patient experience of undergoing opioid tapering and to generate hypotheses for further study | Mixed methods | SEM | Semistructured telephone/face to face interviews | Grounded theory thematic analysis (inductive) | Solano County Family Health Services | Patients | *N* = 6 patients (3 actively tapering, 3 discontinued)<br>Mean age 55.8, Age range: 53–61<br>4 males, 2 females |

GP, general practitioner; NR, not reported; PCPs, primary care providers; STORM, Support Team Onsite Resource for Management of Pain.
* Used same sample, different study aims/design.
a Hatzenbuehler *et al.*[124]
b Glasgow *et al.*[125]
c Fortney and Burgess.[123]
d Michie *et al.*[126]

commence tapering and 4 studies[96,99,100,104] included patients who had not tapered. In two studies, the tapering status of the patient was not reported[105]or was unclear.[108]

### *Intervention characteristics*

Twelve studies[93,96,97,99,100,102,103,105,106,107,109,117] reported on barriers and facilitators around tapering in general (i.e. not on any specific tapering intervention). Four studies[94,95,104,108] reported on barriers and facilitators in the context of a specific tapering intervention. Two studies[94,95] reported on the Support Team Onsite Resource for Management of Pain (STORM) programme, STORM is a phone-based, pharmacist-led programme providing tailored care to patients tapering off opioids and supporting primary care physicians who support them. White *et al*.[108] reported on a multimodal opioid-tapering intervention, 'Assess Inform Manage Monitor' involving general practitioners (GPs), nurses, community pharmacists, psychologists, dietitians and exercise physiologists. Magee *et al*.[104] assessed potential barriers to and facilitators of mobile health technologies (mHealth) for providing opioid-tapering support.

### *Phenomena of interest*

Fifteen studies[93,94,95,96,97,99,100,102,103,104,105,106,107,108,109] reported on both barriers and facilitators to opioid tapering, while one study reported on barriers only.[117]

### *Theoretical frameworks*

Seven theoretical frameworks were used across eight studies[93,94,96,97,99,107,108,109] to guide methods and analyses. Two studies[96,99] used the Health Belief Model,[60,108] used the Behaviour Change Wheel,[123] Wu *et al.*[109] used SEM, Benintendi *et al.*[93] used a framework of structural stigma,[124] Firemark *et al.*[94] used the RE-AIM implementation framework,[125] Giannitrapani *et al.*[97] used the dimensions of access framework[123] and Quinlan *et al.*[107] used an unnamed theoretical framework.

## Quality assessment

*Tables 22* and *23* outline the quality assessment of the included studies. Overall, the quality of 13 studies reporting qualitative data was moderate to high and 2 studies had major limitations. The CASP qualitative item most consistently overlooked was consideration of the relationship between participants and researchers. Five studies[97,99,100,107,109] only somewhat addressed data analysis, and four of these studies[97,100,107,109] also only somewhat addressed ethical issues. One study[104] somewhat addressed data collection considerations. Two studies[94,103] clearly addressed all CASP qualitative items. In Giannitrapani *et al*.,[97] the study design (based on a post hoc analysis of a RCT) was not appropriate to address the aim of the research and only somewhat addressed a clear statement of findings. Wu *et al.*[109] did not clearly state their findings. The single cohort study[117] was of low quality as it did not identify or account for all confounding factors in the analysis.

### *Confidence in the review findings*

Confidence in the review findings derived using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) CERQual approach are shown in the Summary of Findings and Evidence Profile in *Appendix 6* (see *Table 38*) . We had high confidence in 21 subthemes, moderate confidence in 13 subthemes, low confidence in 7 subthemes and very low confidence in 4 subthemes. The main reasons for downgrading were concerns about data adequacy and relevance.

## Barriers to opioid tapering in adults with chronic non-cancer pain

Overall, we identified eight barriers to opioid tapering in adults with chronic non-cancer pain. (*Table 38*) in *Appendix 6* outlines the key themes and subthemes with supporting quotes and confidence judgements. *Figure 4* highlights the barriers and facilitators to opioid tapering within multiple levels of the healthcare system (i.e. at the individual, interpersonal, organisational and environmental levels) according to the SEM.[60]

### *Theme B1: Lack of knowledge, beliefs and poor understanding about opioid use, tapering and perceived risks associated with opioid use*

At an individual level, both providers and patients described a perceived or actual lack of knowledge and understanding among patients around tapering and the risks and side effects associated with long-term opioid use (subtheme B1.1,

**TABLE 22** Quality assessment for barriers and facilitators review (Review 3)

| Study | 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? | 6 Has the relationship between researcher and participants been adequately considered? | 7 Have ethical issues been taken into consideration? | 8 Was the data analysis sufficiently rigorous? | 9 Is there a clear statement of findings? | Overall quality assessment |
|---|---|---|---|---|---|---|---|---|---|---|
| *CASP Qualitative Quality Assessment Criteria* | | | | | | | | | | |
| Benintendi 2021[93] | Yes | Yes | Yes | Yes | Yes | Can't tell | Yes | Yes | Yes | Few limitations |
| Firemark 2021[94] | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No limitations |
| Frank 2016[96] | Yes | Yes | Yes | Yes | Yes | Can't tell | Yes | Yes | Yes | Few limitations |
| Giannitrapani 2018[97,98] | Yes | Yes | No | Yes | Yes | Can't tell | Somewhat | Somewhat | Somewhat | Major limitations |
| Henry 2019a[99] | Yes | Yes | Yes | Yes | Yes | Can't tell | Yes | Somewhat | Yes | Few limitations |
| Henry 2019b[100,101] | Yes | Yes | Yes | Yes | Yes | Can't tell | Somewhat | Somewhat | Yes | Few limitations |
| Kennedy 2018[102] | Yes | Yes | Yes | Yes | Yes | Somewhat | Yes | Yes | Yes | Few limitations |
| Kuntz 2021[95 a] | Yes | Yes | Yes | Yes | Yes | Can't tell | Yes | Yes | Yes | Few limitations |
| Langford 2020[103] | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Few limitations |
| Magee 2021[,104,a] | Yes | Yes | Yes | Yes | Somewhat | Can't tell | Yes | Yes | Yes | Few limitations |
| Matthias 2017[105] | Yes | Yes | Yes | Yes | Yes | Can't tell | Yes | Yes | Yes | Few limitations |
| McNeilage 2022[106] | Yes | Yes | Yes | Yes | Yes | Can't tell | Yes | Yes | Yes | Few limitations |
| Quinlan 2020[,107,a] | Yes | Yes | Yes | Yes | Yes | Somewhat | Somewhat | Somewhat | Yes | Few limitations |
| White 2020[,108,a] | Yes | Yes | Yes | Yes | Yes | Can't tell | Yes | Yes | Yes | Few limitations |

**TABLE 22** Quality assessment for barriers and facilitators review (Review 3) (*continued*)

| Study | 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? | 6 Has the relationship between researcher and participants been adequately considered? | 7 Have ethical issues been taken into consideration? | 8 Was the data analysis sufficiently rigorous? | 9 Is there a clear statement of findings? | Overall quality assessment |
|---|---|---|---|---|---|---|---|---|---|---|
| Wu 2019[109,a] | Yes | Yes | Yes | Yes | Yes | Can't tell | Somewhat | Somewhat | No | Major limitations |

a Mixed-methods study – only qualitative methods where assessed using CASP checklist for qualitative research.

**Note**
Assessment notes: Where the assessments for most items in the tool were 'yes' = no or few limitations.
Where the assessments for most items in the tool were 'somewhat' or 'cannot tell' = minor limitations.
Where the assessments for one or more questions in the tool were 'no' = major limitations.
Overall assessment based on Pollock *et al.*[42]

**Source**
This report is licensed under a Creative Commons Attribution 4.0 International license (CC-BY). However, the CASP Checklist, developed by the Critical Appraisal Skills Programme (CASP), is available under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International license (CC BY-NC-SA). CASP checklists can be accesed at https://casp-uk.net.

**TABLE 23** Quality assessment for barriers and facilitators review (Review 3) – a cohort study

| Study | 1 Did the study address a clearly focused issue? | 2 Was the cohort recruited in an acceptable way? | 3 Was the exposure accurately measured to minimise bias? | 4 Was the outcome accurately measured to minimise bias? | 5a Have the authors identified all important confounding factors? | 5b Have they taken account of the confounding factors in the design and/or analysis? | 6 Follow-up long enough? | Overall quality assessment |
|---|---|---|---|---|---|---|---|---|
| ***CASP Cohort Quality Assessment Criteria*** | | | | | | | | |
| Westanmo 2015[117] | Yes | Yes | Yes | Yes | No | No | Yes | Major limitations |

**Note**
Assessment notes: Where the assessments for most items in the tool were 'yes' = no or few limitations.
Where the assessments for one or more questions in the tool were 'no' = major limitations.
Overall assessment based on Pollock *et al.*[42]

**Source**
This report is licensed under a Creative Commons Attribution 4.0 International license (CC-BY). However, the CASP Checklist, developed by the Critical Appraisal Skills Programme (CASP), is available under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International license (CC BY-NC-SA). CASP checklists can be accesed at https://casp-uk.net.

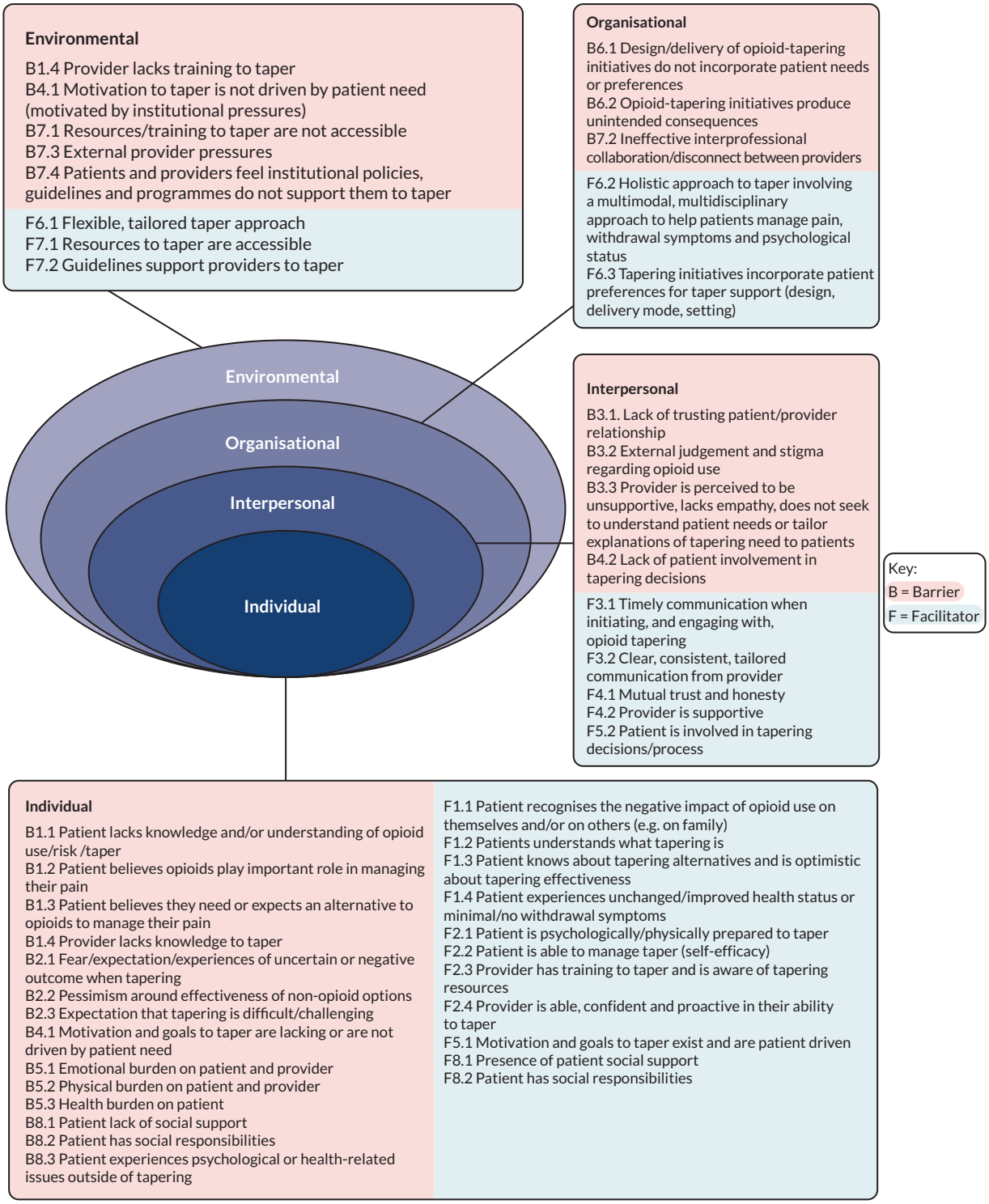


**FIGURE 4** Barriers and facilitators to opioid tapering in patients with chronic non-cancer pain according to the SEM (Review 3).

high confidence).[93–95,98,99,101,102,104–106] Generally, patients were aware of the risks and side effects of opioid use but did not associate these risks with their own opioid use. For example, patients either viewed risk of addiction as being associated with illegal drug behaviour, had been on opioids for a long time without overdosing or they attributed their side effects to other causes. These beliefs along with a misunderstanding of tapering (often viewed as stopping opioids abruptly or completely, rather than a gradual reduction in opioid use) resulted in a general lack of understanding around why some patients need to taper and, ultimately, to an unwillingness to taper.

Patients described opioids as playing an important role in their pain management (subtheme B1.2, moderate confidence). For some patients, the fact that opioids were thought to be effective in controlling their pain and, in some cases, was the only way to control their pain, led to contentment about their current opioid use or a feeling of dependence on opioids. Patients considered that the current benefits from opioids (e.g. reduced pain) outweighed the risk of opioid harms in the future. For those who considered tapering opioids, some patients believed they needed, or expected, an alternative treatment (pharmaceutical or non-pharmaceutical) to opioids to manage their pain (subtheme B1.3, moderate confidence).

Providers also believed that they lacked the knowledge and skills to taper patients (subtheme B1.4, moderate confidence). From a 'knowledge' perspective, providers described not knowing 'how to taper' due to a lack of adequate opioid taper training, as well as a lack of awareness or understanding around the resources available to support opioid tapering.

### *Theme B2: Fears and negative expectations of, or beliefs around, opioid tapering*

At the individual level, both patients and providers identified fears, or expectations of, an uncertain or negative outcome as a significant barrier to opioid tapering (subtheme B2.1, high confidence).[93–96,98,101–107,116] Both patients and providers feared that patients may experience an adverse health outcome from tapering, for example, a fear of a return of, or increase in pain, worse quality of life, loss of function or opioid withdrawal symptoms. Patient expectations of an uncertain or negative outcome were partly driven by past bad experiences of opioid tapering. Provider expectations of an uncertain or negative outcome centred on the worsening of the patient–provider relationship (e.g. feeling threatened during patient interactions, patient discontinues health care or changes provider) and was largely based on previous experiences.

Patients and providers were pessimistic about the effectiveness of non-opioid medication options in managing pain or improving quality of life (subtheme B2.2, low confidence). In addition, providers felt some of the alternative analgesics on offer would not be suitable for specific patients with contraindications.

There was an expectation among providers that opioid tapering was challenging for both the patient and the provider, requiring substantial effort on both parts (subtheme B2.3 moderate confidence). Observations were largely made based on provider tapering experience. Providers described difficulty in changing existing patient preferences and expectations around using opioids to manage pain and felt that some patients were hard to motivate. Patient interactions were described as emotionally exhausting or draining, leading some providers to avoid tapering discussions altogether.

### *Theme B3: Strained patient–provider relationship*

At an interpersonal level, both patients and providers described a lack of a trust in the patient–provider relationship as a barrier to opioid tapering (subtheme B3.1, moderate confidence).[92–94,98,101,102,104–108] Patients described a lack of trust of providers in several ways. First, patients were particularly distrustful of their GPs when they had been on opioids for a long time, and now were suddenly being asked to taper. Conversely, some patients trusted their GPs, but did not trust other healthcare professionals. In these instances, a lack of trust arose from a lack of understanding of either the individual's need to taper or the role of pharmacists and others in the tapering process. In addition, a lack of trust arose when patients felt that their providers were not being honest with them about their motives to taper. Some providers, on the other hand, did not trust patients to share their pain-related symptoms or opioid-related side effects in the belief that patients feared having their opioids withdrawn. Consequences of a lack of trust between patients and providers include providers being unable to accurately assess a patient for tapering and patients feeling betrayed and choosing to discontinue health care with their provider.

Patients also described feeling stigmatised or judged by providers who they felt labelled them as 'addicts' or as being dependent on opioids (subtheme B3.2, high confidence). As a result, patients felt their pain was disbelieved or invalidated by providers. In one instance, this experience of being disbelieved and stigmatised particularly affected a patient who felt marginalised due to their race.

When providers were, or were perceived to be, unsupportive, this was considered as a patient-reported barrier to tapering (subtheme B3.3, moderate confidence). Patients felt providers were unsupportive in the way they responded, for example, that they lacked empathy, did not listen to them or were inflexible, and in a proactive way, for example, they did not seek to understand patient needs during tapering discussions, did not explain the rationale for tapering or provide advice or guidance on managing a taper. This led to patients feeling abandoned by providers.

### *Theme B4: Lack of patient motivation or involvement in tapering process*

Motivation to taper was considered a barrier at individual and wider environmental levels.[92–94,98,104,105] Barriers to tapering arose when motivations and goals for tapering were lacking or not driven by patient need (subtheme B4.1, moderate confidence). Patients were less receptive to tapering when providers did not consider their needs and were motivated to taper by external institutional pressure. On the other hand, providers were not motivated to offer tapering to patients they thought were not open to tapering for fear of failure.

A lack of patient involvement in tapering decisions and processes was a patient-reported barrier to tapering (subtheme B4.2, low confidence) at the interpersonal level. Patients did not feel empowered to taper if they lacked choice or control over the taper or if they perceived a power imbalance between the provider and patient over tapering decisions.

### *Theme B5: Burden of tapering*

Both patients and providers described several sources of burden of tapering relating to the individual and environmental level. First, they described the emotional burden (subtheme B5.1, high confidence).[93–96,98,101–105,108] For patients, a poor emotional status either prior to or during tapering due to withdrawal symptoms was considered detrimental to tapering success, with increased stress making their pain worse. For some providers, tapering was an overwhelming experience for them. They described trying to balance competing demands and expectations around the need to balance safe prescribing, with a need to maintain patient satisfaction made decisions around tapering opioids more difficult.

Tapering was also physically burdensome (subtheme B5.2, low confidence) requiring a sustained effort from both patients and providers. Patients expended energy trying to regulate their behaviour to manage their pain and often found it difficult or were unable to regulate their behaviour. Providers described tapering as time-intensive, referring to both the time it took to have tapering discussions with patients and then to help them to manage pain with non-pharmacological alternatives.

Patients also described the health burden of tapering (subtheme B5.3, high confidence) with some experiencing an increase in pain, withdrawal symptoms or loss of function.

### *Theme B6: Opioid-tapering initiatives are not tailored to incorporate patient need or preference*

Organisational-level barriers were observed when the design and delivery of opioid-tapering initiatives were not tailored to, or did not consider, patient needs and preferences (subtheme B6.1, very low confidence).[92,98,101–103,105,108] One study reported on patient-reported potential barriers to an app-based opioid-tapering initiative.[104] Study patients felt the content of the text messages sent to support the self-management of their pain were impersonal, or they disliked having to respond to text messages. Issues of accessibility were raised that included the patient not having the means to access taper support (e.g. no/poor internet access) or having poor vision and, therefore, not being able to read the text messages. For providers, the fact that tapering support did not include methods of improving patient motivation was considered a barrier. A failure to incorporate patient preferences around opioid-tapering implementation activities resulted in an individual-level barrier arising because of a lack of patient experience of, or confidence in, using the mode of tapering support to self-manage their pain.[104]

Furthermore, a potential consequence of the poor design and delivery of opioid-tapering initiatives was the production of unintended consequences (subtheme B6.2, high confidence). Patients felt that the constant monitoring of opioid use (e.g. via pill counts or urine testing) reinforced perceptions of stigma around addiction, reduced patient autonomy and increased mistrust. On some occasions, this resulted in patients changing provider, discontinuing health care or seeking alternative opioid supplies.

### *Theme B7: Unsupportive health-system-related tapering environmental context*

Studies reported a range of interpersonal-, organisational- and environmental-level barriers relating to the availability of, and access to, tapering resources.[92,93,96,98,101–103,108] Above all, a lack of access to resources and training inhibited providers from initiating a taper (subtheme B7.1, high confidence). Providers complained of a lack of availability of alternative pain management therapies to help taper opioids, and even when alternatives were available, they described a lack of timely access to them, or had concerns that the resources would be discontinued or were understaffed. This resulted in providers referring only their most challenging patients for fear of overwhelming the service. Barriers relating to affordability and accessibility (e.g. transportation, setting) prevented patients accessing tapering resources. Providers also felt there was a lack of adequate tapering training available to them.

Even when resources were available, some providers felt that their attempts to taper were hindered by ineffective interprofessional collaboration (subtheme B7.2, very low confidence). Providers discussed a sense of disconnect between primary care and the acute sector over the management of patients on long-term opioids for chronic pain. Prescribers in the inpatient setting did not see opioid reduction as their responsibility; rather, they were more concerned with managing acute pain. Therefore, GPs felt they had less control over opioid reduction. PCPs felt their lack of understanding around tapering initiatives was compounded when other healthcare professionals involved in tapering patients were not co-located within their healthcare settings.

External pressures on providers (subtheme B7.3, moderate confidence) due to workload or pressure to demonstrate productivity to leadership meant providers felt that they lacked time to help patients taper opioids.

Both patients and providers felt that institutional polices, guidelines and initiatives did not support them to taper (subtheme B7.4, moderate confidence). Providers felt current guidance inadequately addressed opioid discontinuation. When it was addressed, there was an underlying assumption that all patients would follow the same tapering trajectory, thereby failing to account for fluctuations in patients' pain and the need for tapering initiatives to be individualised. Patients, on the other hand, felt marginalised by the wider context, specifically policies around the US opioid epidemic which they felt unfairly targeted them (i.e. labelled them as 'opioid addicts').

### *Theme B8: Patient experiences poor or unexpected life circumstances*

At an individual level, patients' social networks and social support played an important part in preventing patients from accessing a taper.[92,94,98,105] Patients described the absence of a social support (i.e. friends or family) as a barrier to opioid tapering (subtheme B8.1, low confidence). This was sometimes due to the side effects of tapering (e.g. keeping a partner awake when a patient struggled to sleep) or a lack of understanding from the patient's spouse. Others felt socially isolated; some had a desire to hide away during a taper, or their family and friends lived far away.

Personal social responsibilities (i.e. work, money and family commitments) also impeded the ability of patients to taper opioids (subtheme B8.2, high confidence).

Personal events occurring outside of opioid tapering experienced by patients also impacted on a patient's desire/ability to continue with a taper (subtheme B8.3, high confidence). Patients described experiencing psychological stress or health-related issues due to reasons not associated with tapering as a barrier to taper, for example, death of family members or receiving a cancer diagnosis.

## Facilitators of opioid tapering in adults with chronic non-cancer pain

Overall, we identified eight facilitators of opioid tapering in adults with chronic non-cancer pain. *Appendix 6* outlines the key themes and subthemes with supporting quotes and confidence judgements.

### *Theme F1: Patient recognises the negative impact of opioids, understands what tapering is and perceives/experiences the benefits of tapering*

At the individual level, patient recognition of the negative impact of opioid use on themselves and/or on others (e.g. on family) facilitated the initiation of a taper (subtheme F1.1, high confidence).[94,95,98,99,101,102,104–107] For example, this

occurred when patients associated bad side effects with opioid use, were concerned about possible dependence or addiction, spoke of not feeling in control or were aware of the impact their opioid use was having on those close to them. Patients recognised why they needed to taper when providers tailored the rationale to taper to individual circumstances.

Patients were more willing to taper opioids when they understood what tapering was and why they themselves needed to taper (subtheme F1.2, very low confidence). Patients who understood that tapering was a gradual, dynamic process, rather than an abrupt cessation of opioids were more open to tapering. Experience of a taper was a factor associated with a successful outcome.[106]

Patient knowledge about tapering alternatives and beliefs around tapering effectiveness were also important (subtheme F1.3, very low confidence). Patients were optimistic about tapering effectiveness when they could see the value of referral for non-medication behavioural treatment.

Perhaps unsurprisingly, an improved or unchanged health status (e.g. decrease/no change in pain, improvements in functioning) or minimal/no withdrawal symptoms while tapering (subtheme F1.4, high confidence) were facilitators of opioid tapering.

### *Theme F2: Ability to initiate, manage/cope with taper*

The ability of patients and providers to manage and cope with a taper were reported at the individual level.[93,94,96,98,101–105,108] Being psychologically and physically prepared to taper (subtheme F2.1, high confidence) was described as an enabling factor by patients. Patients understood that tapering may lead to an increase in their pain or withdrawal symptoms but were accepting of the consequences and were emotionally stable.

Self-efficacy, a patient's belief in their ability to manage a taper (subtheme F2.2, moderate confidence), was described as a facilitator to successful opioid tapering. Once patients recognised that tapering would require effort on their behalf, they adopted pharmaceutical and/or non-pharmaceutical strategies (including behavioural changes such as planning their day more effectively) to help them manage their pain.

From a provider perspective, an awareness of tapering resources and training (subtheme F2.3, moderate confidence) was seen to facilitate initiation of tapering discussions with patients and/or referral of patients for tapering support.

Providers also described being able, confident in their own ability to taper and being proactive (subtheme F2.4, low confidence) as enabling factors. Provider confidence in their ability to taper increased when patients were open to tapering or when interactions with patients went well. Providers described being proactive in identifying opportunities to initiate a taper, choosing their moment when patients were experiencing serious adverse effects from opioid use or when they inherited a patient from another provider.

### *Theme F3: Clear, consistent, supportive and timely communication in preparing patients to taper*

Interpersonal-level factors describing the need for timely communication when initiating and during opioid tapering to manage patient expectations were highlighted by both patients and providers (subtheme F3.1, high confidence).[93,94,101–104] Providers spoke of a need to discuss opioid tapering at the same time as opioids are prescribed, thereby managing patient expectations, preparing them for tapering and easing provider burden around the need to initiate a taper discussion in the future. Providers also highlighted the need for timely and responsive reminders about the tapering support available to them. Patients, on the other hand, described a preference for communications from providers to be responsive to patient needs rather than disrupting their day unnecessarily.

Clear, consistent, tailored communication from providers (subtheme F3.2, high confidence) was also a facilitator to successful tapering. Providers tried to focus their conversations on patient-relevant side effects and were consistent with their messages during tapering discussions over time. Patients sought reassurance from providers that first, they would not be abandoned and, second, that what they were experiencing during tapering was normal. Patients suggested this could be achieved at an organisational level by providers tailoring the information sent to the patients to the stage of tapering. As a result, effective provider communication increased patient trust in providers.

### *Theme F4: Strong, open, supportive patient–provider relationship*

At the interpersonal level, both patients and providers discussed the importance of a strong, open and supportive patient–provider relationship as a facilitator to successful opioid tapering.[94,95,98,99,101,104,105,107] Mutual honesty and trust between patient and provider (subtheme F4.1, moderate confidence) facilitated the initiation of, and engagement with, opioid tapering.

Patients and providers also described the characteristics of a supportive provider (subtheme F4.2, high confidence) as being someone who is non-judgemental, empathetic, flexible and responsive to patient needs, and who seeks to listen to and understand patients' concerns and offers guidance on managing a taper.

### *Theme F5: Decision to initiate and manage taper involves patient and is driven by patient need*

A patient-centred shared decision-making approach to the initiation and management of opioid tapering was discussed by both patients and providers as a facilitator of opioid tapering.[92,94,98,101,102,104–108] At the individual level, patients who were motivated to taper (e.g. had experienced a serious AE on opioids, risked being excluded from family life or felt their lives revolved around opioids) or who had set themselves personal goals (e.g. wanted better health/quality of life or to be more involved in family life) (subtheme F5.1, high confidence) were more likely to achieve a successful taper. In addition, patients were more willing to taper when providers were motivated by individual patient need. Providers described being more willing to taper if they believed patients were open to tapering or requested to taper.

At an interpersonal level, patient involvement in tapering decisions was also considered important (subtheme F5.2, high confidence), both at the point of initiating a taper and throughout the taper process, with both patients and providers discussing the need for patients to be offered options and control over a taper.

### *Theme F6: Taper initiative is tailored to incorporate patient need/preferences*

Patients and providers both mentioned the benefits of organisational-level facilitators when a tailored approach to tapering opioids is required (subtheme F6.1, high confidence).[92–94,98,101–105,108] For example, providers sought to schedule the timing of a taper initiation to coincide with patient having some 'down time'. Providers also recognised the need to adjust the dose and/or speed of the taper based on patient response to maintain patient engagement.

Providers discussed the importance of adopting a holistic, multimodal and multidisciplinary approach to tapering (subtheme F6.2, moderate confidence). Providers discussed the need to include non-opioid analgesic alternatives to opioids and pain management strategies and involve pharmacists, physiotherapists, psychologists and others to help patients manage their pain, withdrawal symptoms, comorbidities and emotional health. Providers particularly appreciated support from other healthcare professionals when dealing with more complex tapering patients.

In studies that examined facilitators of a specific tapering intervention, patients often expressed preferences for the design and delivery of taper support (subtheme F6.3, low confidence). Patients expressed preferences around the content of taper support and the delivery mode (e.g. face-to-face vs. mobile technologies), suggesting that active patient involvement in the tapering process is an important enabler.

### *Theme F7: Supportive health system environment*

At the organisational and wider environmental levels, a supportive health system environment, which provided tapering resources and guidance, was essential to enable opioid tapering in chronic pain patients.[93–96,101–103,105,107] Accessibility to resources was often discussed by both providers and patients as a facilitator to opioid tapering (subtheme F7.1, high confidence). Providers stressed the need not only for access, but also for timely access to alternative treatments and multidisciplinary support in managing patients' chronic pain. The co-location of providers and multidisciplinary teams offering taper support was suggested as a solution. Involving a multidisciplinary team also helped to address provider workload pressures that could have prevented them from initiating a taper. Providers also recognised that adequate funding was necessary to enable accessibility. From a patient perspective, accessibility related to out-of-hours access to tapering support, regular contact with the same provider and low cost were important facilitators.

Providers also appreciated the availability of tapering guidelines and policies to support them to initiate taper discussions with patients (subtheme F7.2, high confidence). However, there was also some recognition that the

existence of guidelines alone is not sufficient and that a guideline implementation strategy would be beneficial. Providers also felt that guidelines should recognise the need for a tailored, multimodal approach to tapering opioids.

### *Theme F8: Life circumstances*

Patients' individual-level life circumstances played an important role in facilitating successful opioid tapering.[94,95,98,101,103,105] Both patients and providers highlighted the benefits of a patient social support system such as family, friends, other tapering patients and providers in providing moral support and encouragement (subtheme F8.1, high confidence).

Patients who had social responsibilities were more open to opioid tapering (subtheme F8.2, low confidence). Providers noted that patients to whom family were important were more receptive to tapering discussions. Patients themselves also highlighted family responsibilities (e.g. need to care for sick relatives) as reasons for embarking on an opioid taper.

## Mapping barriers and facilitators to the Theoretical Domains Framework

Individual, interpersonal, organisational and environmental barriers and facilitators to the successful tapering of opioids in chronic non-cancer patients were mapped to all 14 domains of the TDF (see *Table 39* in *Appendix 7*). At the individual level, patient barriers were mapped to 12 TDF domains and patient facilitators to 12 TDF domains. Patient barriers were not identified for 'Social/professional role and identity' and 'Intentions', while patient facilitators were not identified for 'Social/professional role and identity' and 'Optimism'.

Provider barriers were mapped to seven TDF domains and facilitators to seven TDF domains. Provider barriers were not identified for 'Skills', 'Reinforcement', 'Intentions', 'Goals', 'Environmental context and resources', 'Social influences', 'Behavioural regulation' while facilitators were not identified for 'Social/professional role and identity', 'Beliefs about consequences', 'Intentions', 'Memory, attention, and decision processes', 'Environmental context and resources', 'Emotion' or 'Behavioural Regulation'.

At the interpersonal level, barriers mapped to four TDF domains ('Skills', 'Beliefs about capabilities', 'Social influences', 'Emotions') and facilitators to eight TDF domains ('Skills', 'Beliefs about capabilities', 'Reinforcement', 'Intentions', 'Memory, attention, and decision processes', 'Environmental context and resources', 'Social influences', 'Emotions').

At the organisational level, barriers were mapped to three TDF domains ('Beliefs about consequences', 'Environmental context and resources', 'Social influences') and facilitators to two TDF domains ('Environmental context and resources', 'Social influences'). At the environmental level, barriers were mapped to four TDF domains (Social/professional role and identity', 'Beliefs about consequences', 'Reinforcement', 'Environmental context and resources') and facilitators to one TDF domain ('Environmental context and resources').

## Mapping barriers and facilitators to the conceptual model of healthcare access

*Figure 5* maps the barriers and facilitators to opioid tapering that influence the realisation of access from both a patient and provider perspective to Levesque *et al.*'s modified conceptual model of healthcare access.[55,56]

From a patient perspective, most factors influencing healthcare access were predominantly individual level and focused around three dimensions of healthcare access: 'ability to perceive' (related to a patient's health literacy and beliefs about tapering),[55] 'ability to seek' (related to personal autonomy and ability to choose to seek care)[55] and 'ability to engage' (related to patient participation and involvement in decision-making around tapering).[55] Patients reported fewer organisational-/environmental-level barriers around the dimensions of access, 'ability to reach' (related to personal mobility and freedom to access tapering) and 'ability to pay' (related to ability to afford tapering, e.g. the ability to take time off work to attend tapering appointments).

Most provider factors influencing healthcare access were concentrated around the dimension, 'ability to be appropriate' (related to the fit between a patient's tapering need and services offered) and were a mix of individual-,

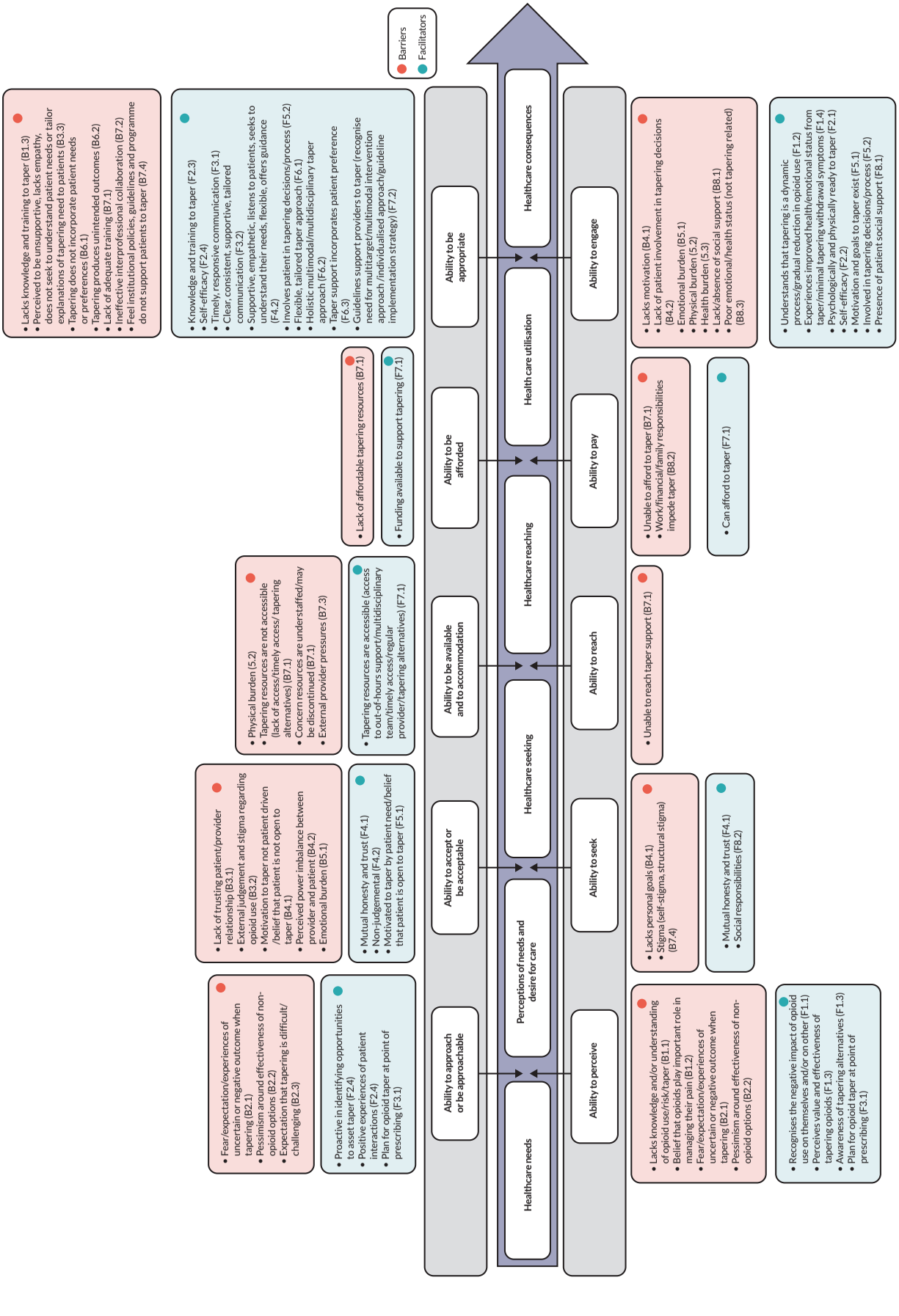


**FIGURE 5** Conceptual model of healthcare access with domains of barriers and facilitators of tapering opioids in adults with chronic pain (Review 3).

organisational- and environmental-level factors. However, a number of barriers and facilitators were also evenly spread across another three dimensions: 'ability to approach and be approachable' (related to the fact that patients know that they need to taper),[55] 'ability to accept or be acceptable' (related to cultural and social factors that determine whether tapering is acceptable and appropriate[55]) and 'ability to be available and to accommodate' (related to the existence of tapering support and its ability to be reached in a timely manner).[55]

Complementary patient and provider barriers were noted. Both patients and providers talked about the need for trust and honesty when seeking to taper ('ability to accept or be acceptable'/'ability to seek'), accessibility of tapering resources ('ability to be available and to accommodate'/ability to reach) and the need for patient involvement during a taper ('ability to be appropriate'/'ability to engage').

## Summary

To our knowledge, this is the first systematic review of barriers and facilitators to focus specifically on opioid tapering in patients with chronic non-cancer pain. Eighteen papers reported in 16 studies were included in a mixed-methods synthesis. Most included studies were conducted in the USA. This is not surprising given the extent of the opioid epidemic[127] and calls from the Center of Disease Control and Prevention[128] to limit the use of high-dose opioids. Over half the studies included in this review were published within the last 2 years, which reflects the growing concern around long-term opioid use in patients with chronic non-cancer pain and the current lack of suitable solutions to the problem. Overall, eight barriers and eight facilitators of opioid tapering in chronic non-cancer pain patients were identified across multiple levels of the healthcare system (i.e. at the individual, interpersonal, organisational and environmental levels, see *Figure 4*) and across multiple TDF domains.

Individual-level factors acting as barriers to opioid tapering were predominant and focused around patient and provider beliefs (subtheme B1.1, high confidence, subthemes B1.2/B1.4, moderate confidence), expectations of tapering (sub-theme B2.1, high confidence, subtheme B2.2, low confidence, subtheme B2.3 moderate confidence), a lack of patient motivation (subtheme B4.1, moderate confidence), tapering burden (subthemes B5.1/b5.3, high confidence, subtheme B5.2, low confidence) and the influence of social factors (subtheme B8.1, low confidence, subthemes B8.2/B8.3, high confidence). In addition, most patient barriers and facilitators clustered around the first and last dimensions of Levesque *et al.*'s[55] conceptualisation of healthcare access framework (see *Figure 5*). Crucial to the success of opioid tapering therefore, is both a patient and provider's willingness to taper and the ability of a patient to maintain a taper.

Our review findings suggest several factors operating at an interpersonal level [i.e. trusting, supportive patient–provider relationship (subtheme F4.1, moderate confidence, subthemes F4.2, high confidence), effective communication of opioid risk so patients can relate to their need to taper (subtheme F3.2, high confidence) and environmental level (provider training (subtheme F2.3, moderate confidence)] that may help to increase patient and provider willingness to taper. Crucially, trust needs to be established early in the patient–provider relationship, before tapering becomes necessary.[86] Planning to taper opioids at the point at which they are prescribed (subtheme F3.1, high confidence) may help to alleviate providers' anxiety over initiating tapering conversations. This finding supports the UK NICE guidelines[129] on the withdrawal management of medicines associated with dependence or withdrawal symptoms in adults; this guidance recommends that conversations around risks associated with taking opioids and tapering opioids are initiated before the point at which tapering becomes necessary and, ideally, at the point of prescribing.

Our findings suggest that individual-level barriers, including patient motivation (subthemes B2.3/B4.1 moderate confidence, subtheme F5.1, high confidence), social factors (subtheme B8.1/F8.2, low confidence, subthemes B8.2/F8.1, high confidence) and stigma (subtheme B3.2, high confidence), may play an important role in whether a patient not only seeks to initiate a taper but also remains engaged throughout the taper (see *Figure 5*). Such barriers may be addressed at the interpersonal and organisational levels, for example, having a supportive, non-judgemental provider (subtheme F4.2, high confidence), use of motivational interview techniques[130] and consideration of patient preference in the design/delivery of tapering support (subtheme B6.1, very low confidence) such as in the EMPOWER study,[131]

may help to ensure that tapering interventions and providers do not unintentionally reinforce perceptions of stigma around addiction (subtheme B6.2, high confidence). In addition, part of successful tapering requires skilful consulting behaviours using techniques such as MI.

There are many opportunities for tapering in NHS GP practices. Repeat prescriptions are updated regularly, but our findings show that these may be missed opportunities due to organisational and environmental barriers including lack of time (subtheme B5.2, low confidence), lack of access to non-pharmacological treatments, especially psychological treatments (subtheme B7.1, high confidence), lack of timely access to deprescribing interventions (subtheme B7.1, high confidence) and ineffective inter-professional collaboration (subtheme B7.2, very low confidence). Many of these organisational- and environmental-level barriers are consistent with those often reported in other studies evaluating barriers to health care.[132] Currently in the UK, there is limited provision of services to specifically support patients tapering opioids.[129]

Our focus on tapering, as opposed to wider deprescribing and monitoring, strengthens the applicability of the identified barriers and facilitators to an opioid-tapering non-cancer pain population and, in some cases, increases confidence in the findings of recent broad systematic reviews on barriers and facilitators to opioid monitoring and deprescribing.[26] Furthermore, our review identifies additional factors to those reported by Cross *et al*.,[26] for example, providers should be motivated to taper by individual patient need rather than institutional pressure, tapering initiatives should avoid reinforcing perceptions of stigma around addiction. The influence of patients' social responsibilities (work, financial, family commitments) and patients' experiences of psychological stress and/or health-related issues due to reasons not associated with tapering are also key factors.

While several barrier and facilitator themes are common across different healthcare contexts [e.g. the lack of time (subtheme B7.3, moderate confidence) and the need for a trusting patient–provider relationship (subtheme F4.1, moderate confidence)],[132,133,134,135,136] there are some contextual factors that make opioid tapering particularly challenging for both patient and providers. First, the way in which a patient's ability to taper fluctuates depending upon a patient's health and emotional status (subthemes B5.1/B5.3/F1.4/F2.1, high confidence) and social factors (subtheme B8.1/F8.2, low confidence, subthemes B8.2/B8.3/F8.1, high confidence). Fluctuations of state may arise either as a consequence of tapering- or non-tapering-related events including changes in life circumstances (subthemes B8.2/B8.3/F8.1, high confidence). Therefore, it is essential that tapering is tailored to take account of changes in individual circumstances (subtheme F6.1, high confidence) and that there is timely access to tapering resources, including psychosocial support (subtheme F6.2, moderate confidence). These findings provide qualitative evidence for the NICE guidelines[129] which recommend considering a patient's individual circumstances, available support and timely access, when planning an opioid taper. Second, opioid tapering may be even more challenging for patients on multiple medications when providers need to consider how these additional medications (e.g. anti-depressant, anti-psychotic, non-narcotic pain medications) may affect a patient's response to tapering or how to taper more than one medication. Finally, there is a need to achieve a balance between not letting patients feel abandoned, for example, by offering more regular reviews with the need to avoid increasing feelings of stigma, for example, through closer monitoring of taper patients.

Progress on addressing health system barriers to opioid tapering can already be seen in the UK where recent NICE guidelines[129] recognise the need for an individualised, flexible approach to opioid tapering, trust within the patient–provider relationship, avoidance of terminology that may be interpreted as stigmatising language and consideration of a patient's circumstance and available support. However, barriers and facilitators to opioid tapering are often complex and context dependent. Given the current wider adverse environmental contexts [coronavirus disease discovered in 2019 (COVID-19) pandemic, current downturn in the worldwide economic situation], the greatest challenges to successful opioid tapering may be the implementation of guidance recommendations by providers and organisations.

Current wider contextual events, such as the COVID-19 pandemic, may impact both individual- and system-level barriers to opioid tapering, thus severely hindering timely initiation of opioid tapering. The pandemic has placed immense pressures on the NHS and health systems worldwide with an increasing backlog of patients waiting to access

healthcare treatment. Two studies[104,106] in our review referred to the pandemic. One study[106] highlighted the potential for it to exacerbate a known barrier to tapering – social isolation. The other study[104] highlighted the potential for the pandemic to accelerate the acceptance of new digital health technologies to facilitate opioid tapering. However, in adopting new technologies, practitioners must ensure that they do not widen inequalities in access to tapering support (see *Chapter 8*).

# **Chapter 8** Inequalities in access to or benefiting from intervention

## Search results

Forty-two studies were included from the parallel reviews examining effectiveness and AEs of opioid-tapering interventions and barriers and facilitators to tapering of opioids in adults with chronic non-cancer pain. The PRISMA flow chart is reported elsewhere (see *Figure 1*).

## Study characteristics

Included study characteristics are presented in *Table 24*. Included studies were conducted across 5 countries (31 USA, 6 Australia, 2 Denmark, 2 Germany and 1 UK). Only two studies[105,108] reported on outcomes of tapering initiatives delivered exclusively to a disadvantaged PROGRESS-Plus population subgroup (low income) and one study[83] specifically aimed to examine the differential impact of opioid tapering on average daily opioid doses of patients at higher risk for opioid-related adverse outcomes compared with lower-risk patients.

*Figure 6* displays the PROGRESS-Plus characteristics collected at baseline versus analysed. Thirty-nine (93%)[66,67,68,69,70,71,72,73,74,75,76,77,78,79,80,81,82,83,88,90,93,94,95,96,99,100,102,103,104,105,106,107,108,109,110,111,112,113,116] collected baseline data on PROGRESS-Plus characteristics (see *Figure 6*) and 30 (71%)[66,68,69,72,74,75,76,82,83,88,89,90,93,94,95,96,97,99,102,103,104,105,106,107,108,109,110,111,113,116] undertook analysis involving PROGRESS-Plus factors.

In the 30 studies that analysed PROGRESS-Plus factors, the most frequent factor analysed was comorbidity (24 studies), followed by social capital (17 studies) and gender (11 studies). No studies were located that examined the impact of 'Religion' on inequalities. Five studies analysed 1 factor, 6 studies analysed 2 and 18 studies analysed 3 or more factors.

Altogether, 17 studies[66,68,69,74,75,76,82,83,88,89,90,95,106,110,111,113,116] examined whether opioid-tapering initiatives were more or less effective across disadvantaged populations (see *Table 3*) and 15 studies[93,94,95,96,97,99,102,103,104,105,106,107,108,109,110] reported on whether opioid-tapering initiatives were more or less accessible across disadvantaged populations. The quality of the included studies is reported elsewhere (see *Figure 3*, *Tables 13*–*15*, *22* and *23*). In brief, the quality of the 13 studies reporting qualitative data in the barriers and facilitators review was moderate to high and 2 studies had major limitations. The overall quality of the studies included in the effectiveness review was moderate.

The effects of PROGRESS-Plus characteristics were analysed further in three ways: (1) by stratifying effect analyses by different categories of a PROGRESS-Plus characteristic; (2) by exploring associations between PROGRESS-Plus characteristics and changes in opioid use or tapering trajectory following a tapering intervention (including differential associations, e.g. male vs. female; low vs. high SES); and (3) by assessing the impact of opioid-tapering initiatives on PROGRESS-Plus-related outcomes (e.g. ability to work).

Of the 17 studies that examined whether opioid-tapering initiatives were more or less effective across disadvantaged populations, 7 studies[66,82,83,90,95,106,110] examined the association of PROGRESS-Plus characteristics with tapering outcomes, of which, 4 studies[83,90,95,110] assessed differential associations (e.g. male vs. female; younger vs. older patients). Four studies[66,82,90,95] assessed associations of PROGRESS-Plus characteristics with tapering outcomes and 10 studies[68,69,74,75,76,88,89,111,113,116] assessed the impact of tapering on PROGRESS-Plus-related outcomes. One study[106] assessed descriptive associations with tapering outcomes. Ten studies[66,67,69,74,75,76,88,112,113,116] reported on the number of dropouts or reasons for dropout in relation to PROGRESS-Plus characteristics

PROGnosis RESearch Strategy partnership-Plus characteristics were analysed on 8 tapering outcomes: (1) mental health/depression/anxiety (10 studies[68,69,74,75,76,88,89,111,113,116]); (2) reduction or change in opioid dose/use/withdrawal (3

**TABLE 24** Study characteristics for inequalities review (Review 4)

| Author, date, country | Study design | Included in effects/AE/ barriers and facilitators review | Aim | PROGRESS-Plus inclusion/exclusion criteria | PROGRESS-Plus sample characteristics and author-reported generalisability issues considerations relating to PROGRESS-PLUS sample characteristics (overall figures unless otherwise stated) | Control variables | Inequalities assessed on effects | | | Inequalities assessed on access |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Association of PROGRESS-Plus with tapering outcome | Effect of tapering on PROGRESS-Plus outcome | Effect of PROGRESS-Plus on participation | |
| Austin, 2019,[66] USA | Retrospective case review | Effects | To assess the impact of an opioid-tapering curriculum | *Inclusion*<br>Age: ≥ 18 years<br>*Exclusion*<br>No PROGRESS-Plus | *N* = 707 patients<br>G: 34.5% male, 65.5% female<br>+A (mean ± SD): 62.5 ± 15.2 years | | G, +A | | +G, +A | |
| Benintendi, 2021,[93] USA | Qualitative | Barriers and facilitators | To describe the ways in which well-intentioned taper initiatives impacted people living with chronic pain | *Inclusion*<br>Age: ≥ 18 years<br>*Exclusion*<br>Not specified | *N* = 41 patients<br>R: 2.44% American Indian/ Alaska Native<br>• 21.95% Black/African American<br>• 65.85% White<br>• 7.32% Other<br>• 2.44% Mixed (> 1 race)<br>G: 44% male, 56% female<br>+A: 31.71% 25–44 years<br>• 21.95% 45–54 years<br>• 26.83% 55–64 years<br>• 19.51% 65 years+ | | | | | P, R, So, +Co, +St |
| Bienek, 2019,[67] Germany | Retrospective cohort | Effects/AEs | To compare the tolerability, efficacy and safety of opioid withdrawal under a fixed dose and individualised dose protocol | *Inclusion*<br>No PROGRESS-Plus<br>*Exclusion*<br>Not specified | *N* = 195 patients<br>G: 57.44 male, 42.56 female<br>+A (mean ± SD): 54 ± 12 years individualised<br>Starting dose<br>51 ± 13 years fixed starting dose | | | | +Co | |

**TABLE 24** Study characteristics for inequalities review (Review 4) (*continued*)

| Author, date, country | Study design | Included in effects/AE/ barriers and facilitators review | Aim | PROGRESS-Plus inclusion/exclusion criteria | PROGRESS-Plus sample characteristics and author-reported generalisability issues considerations relating to PROGRESS-PLUS sample characteristics (overall figures unless otherwise stated) | Control variables | Inequalities assessed on effects | | | Inequalities assessed on access |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Association of PROGRESS-Plus with tapering outcome | Effect of tapering on PROGRESS-Plus outcome | Effect of PROGRESS-Plus on participation | |
| Capano, 2020,[110] USA | Prospective cohort | Effects/AEs | To investigate the impact of full hemp extract cannabidiol on opioid use and quality-of-life indicators among chronic pain patients. | *Inclusion*<br>Age: 30–65 years<br>*Exclusion*<br>Comorbidities: Any psychotic disorder, any epileptic activity in the last 12 months, incapacitating systemic disorder (cardiac, renal or hepatic) | *N* = 97 patients<br>G: 30.07% male, 64.03% female<br>+A (mean): 56.1 years | | G | | | S |
| Cunningham, 2016,[68] USA | Prospective cohort | Effects | To describe opioid tapering and withdrawal symptoms in fibromyalgia patients on opioids | *Inclusion*<br>No PROGRESS-Plus<br>*Exclusion*<br>No PROGRESS-Plus | *N* = 55 patients<br>R: 91% ethnicity, Caucasian<br>O: 18% currently working<br>G: 16% male, 84% female<br>E (mean, ± SD): 16.6 ± 2.42 years of education<br>+A (mean, ± SD): 48.6 ± 13.2 years | | | +Co | | |
| Firemark, 2021,[94] USA | Qualitative | Barriers and facilitators | To identify factors that influence or interfere with referrals by PCPs to a pharmacist-led telephone-based programme to assist patients undergoing opioid tapering | *Inclusion*<br>No PROGRESS-Plus<br>*Exclusion*<br>No PROGRESS-Plus | *N* = 35 providers<br>G: 42.86% male, 57.14% female<br>O: For PCPs (*N* = 20) duration of healthcare system employment (mean, range): 11.9 years, 1.3–26.5 years | | | | | So |

continued

**TABLE 24** Study characteristics for inequalities review (Review 4) (*continued*)

| Author, date, country | Study design | Included in effects/AE/ barriers and facilitators review | Aim | PROGRESS-Plus inclusion/exclusion criteria | PROGRESS-Plus sample characteristics and author-reported generalisability issues considerations relating to PROGRESS-PLUS sample characteristics (overall figures unless otherwise stated) | Control variables | Inequalities assessed on effects | | | Inequalities assessed on access |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Association of PROGRESS-Plus with tapering outcome | Effect of tapering on PROGRESS-Plus outcome | Effect of PROGRESS-Plus on participation | |
| Frank, 2016,[96] USA | Qualitative | Barriers and facilitators | To explore patients' perspectives on opioid tapering | *Inclusion*<br>Age: ≥ 18 years<br>R: English speaking<br>*Exclusion*<br>No PROGRESS-Plus<br>'This purposive sampling strategy also sought to achieve a diverse sample according to gender and age'. p. 1839 | *N* = 24 patients<br>R: 79% White race<br>G: 46% male, 54% female<br>E: 21% high school or general educational development<br>29% some college<br>50% college graduate<br>+A: (mean, ± SD): 52 ± 10 years | | | | | So, +St |
| Garland, 2014,[69] USA[a] | RCT | Effects | To evaluate the feasibility of developing a clinical trial comparing acute (pre–post) and longer term (3-month follow-up) efficacy of mindfulness-orientated recovery program MORE with that of a conventional support group (SG) in reducing chronic pain and prescription opioid misuse. | *Inclusion*<br>No PROGRESS-Plus<br>*Exclusion*<br>Not specified | *N* = 115 patients<br>R: 3.48% American Indian<br>18.26% African American<br>65.22% Caucasian<br>3.48% other<br>9.56% no response<br>O: 25.21% work status full time<br>G: 32% male, 68% female<br>E: 70.43% some college<br>S (income level): 23.48% below $20,000<br>23.48% $20,000–39,9999<br>8.70% $40,000–59,9999<br>7.83% $60,000–79,9999<br>6.96% over $80,0000<br>25.57% no response<br>A (mean, ± SD): 49.3 ± 13.68 years MORE Group vs.<br>47.4 ± 13.56 years Support Group | R, G, E, S, +A, +Co | | +Co | G, E, S, +A, +Co | |

**TABLE 24** Study characteristics for inequalities review (Review 4) (*continued*)

| Author, date, country | Study design | Included in effects/AE/ barriers and facilitators review | Aim | PROGRESS-Plus inclusion/exclusion criteria | PROGRESS-Plus sample characteristics and author-reported generalisability issues considerations relating to PROGRESS-PLUS sample characteristics (overall figures unless otherwise stated) | Control variables | Inequalities assessed on effects | | | Inequalities assessed on access |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Association of PROGRESS-Plus with tapering outcome | Effect of tapering on PROGRESS-Plus outcome | Effect of PROGRESS-Plus on participation | |
| Gersch, 2021,[70] USA | Retrospective matched cohort study | Effects | To assess the effectiveness of a PEP, a multidisciplinary tele mentoring service based on the Extension for Community Healthcare Outcomes (ECHO) model to reduce opioid use in the outpatient setting | *Inclusion*<br>+A: 18 years and above and below 80 years<br>*Exclusion*<br>No PROGRESS-Plus | *N* = 665 patients<br>*Intervention (N = 125) vs. control (N = 540)*<br>R: 78.4% vs. 77.8% White race<br>G: 33.6% vs. 33.1% male, 66.4% vs. 66.9% female<br>+A (mean, ± SD): 58.9 ± 10.8 years vs. 59.3 ± 10.6 years<br>+Co: 4.8% vs. 1.1% alcohol abuse<br>28% vs. 23.2' chronic pulmonary disease<br>5.6% vs. 5.6% congestive heart failure<br>22.4% vs. 17.8% diabetes<br>44.8% vs. 33.3% hypertension<br>8.8% vs. 4.1% liver disease<br>4.0% vs. 4.4% myocardial infarction<br>20% vs. 10.6% renal insufficiency<br>Charlson Comorbidity Index (mean, ± SD): 1.5 ± 1.6 vs. 1.2 ± 1.7<br>Chronic Disease Score (mean, ± SD): 6.4 ± 4.1 vs. 5.7 ± 4.0 | | | | | |

continued

**TABLE 24** Study characteristics for inequalities review (Review 4) (*continued*)

| Author, date, country | Study design | Included in effects/AE/ barriers and facilitators review | Aim | PROGRESS-Plus inclusion/exclusion criteria | PROGRESS-Plus sample characteristics and author-reported generalisability issues considerations relating to PROGRESS-PLUS sample characteristics (overall figures unless otherwise stated) | Control variables | Inequalities assessed on effects | | | Inequalities assessed on access |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Association of PROGRESS-Plus with tapering outcome | Effect of tapering on PROGRESS-Plus outcome | Effect of PROGRESS-Plus on participation | |
| Gianni-trapani, 2018,[97,98] USA | Qualitative | Barriers and facilitators | To understand providers' perceptions of barriers to reducing opioid use and improving the use of non-pharmacological pain management therapies for chronic pain | *Inclusion*<br>No PROGRESS-Plus<br>*Exclusion*<br>Not specified | *N* = 60 providers<br>No PROGRESS-Plus characteristics specified | | | | | P, S, +Co |
| Henry, 2019a,[99] USA | Qualitative | Barriers and facilitators | To characterise patients' experiences with opioid tapering and identify communication strategies that are likely to foster productive, patient-centred discussions of opioid tapering | *Inclusion*<br>A: 35–85 years<br>*Exclusion*<br>No PROGRESS-Plus | *N* = 21 patients<br>R: 10% African American<br>5% Asian/Pacific Islander<br>76% Caucasian<br>5% Native American<br>5% American/Mexican/Indian<br>10% Hispanic<br>O: 19% full-time employment<br>5% Out of work<br>57% Not able to work<br>19% Retired<br>G: 48% male, 52% female<br>E: 14% high school or less<br>57% some college<br>19% bachelor's degree<br>10% master's degree<br>S (annual household income):<br>24% < $40,000<br>48% $40,000–80,000<br>29% > $80,000<br>+A (mean, ± SD): 58.2 ± 8.3 years | | | | | O, So, +Co, +St |

**TABLE 24** Study characteristics for inequalities review (Review 4) (*continued*)

| Author, date, country | Study design | Included in effects/AE/ barriers and facilitators review | Aim | PROGRESS-Plus inclusion/exclusion criteria | PROGRESS-Plus sample characteristics and author-reported generalisability issues considerations relating to PROGRESS-PLUS sample characteristics (overall figures unless otherwise stated) | Control variables | Inequalities assessed on effects | | | Inequalities assessed on access |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Association of PROGRESS-Plus with tapering outcome | Effect of tapering on PROGRESS-Plus outcome | Effect of PROGRESS-Plus on participation | |
| Henry, 2019b,[100,101] USA | Qualitative | Barriers and facilitators | To identify patient statements about opioids that indicate potential openness to tapering opioids or trying non-opioid pain treatments | *Inclusion*<br>A: Adults<br>*Exclusion*<br>R: Spoke a language other than English | *N* = 86 patients, 49 providers<br>Patients:<br>R: 14% Hispanic<br>65.1% White<br>27.9% Black<br>0% Asian<br>2.3% Native American<br>4.7% multirace/other<br>O: 12.8% working full time or part time<br>1.2% not working<br>34.9% retired<br>51.2% disabled/unable to work<br>G: 36.1% male, 43.9% female<br>E: 17.4% did not finish high school<br>18.6% high school graduate<br>34.9% some college<br>12.8% associate or technical degree<br>16.3% bachelor's degree or more<br>S (annual household income):<br>24.7% ≤ $10,000<br>35.3% $10,001–20,000<br>12.9% $20,001–40,000<br>8.2% $40,001–60,000<br>10.6% $60,001–80,000<br>8.2% > $80,000<br>+A (mean, ± SD): 59.6 ± 10.5 years ≤ $10, 000<br>Providers:<br>R: 2% Hispanic<br>49% White<br>4.1% Black<br>42.9% Asian<br>0% Native American<br>4.1% multirace/other<br>G: 24.5% male, 75.5% female<br>+A (mean, ± SD): 29.6 ± 3.6 years | | | | | |

continued

**TABLE 24** Study characteristics for inequalities review (Review 4) (*continued*)

| Author, date, country | Study design | Included in effects/AE/ barriers and facilitators review | Aim | PROGRESS-Plus inclusion/exclusion criteria | PROGRESS-Plus sample characteristics and author-reported generalisability issues considerations relating to PROGRESS-PLUS sample characteristics (overall figures unless otherwise stated) | Control variables | Inequalities assessed on effects | | | Inequalities assessed on access |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Association of PROGRESS-Plus with tapering outcome | Effect of tapering on PROGRESS-Plus outcome | Effect of PROGRESS-Plus on participation | |
| Hudak, 2021,[71] USA | RCT | Effects | To test whether participation in MORE vs. supportive group (SG) psychotherapy would occasion increased alpha and theta power as well as frontal midline theta (FMT) coherence during a laboratory-based mindfulness-meditation session. | *Inclusion*<br>No PROGRESS-Plus<br>*Exclusion*<br>No PROGRESS-Plus | *N* = 62 patients<br>R: 3.23% African American<br>4.84% Hispanic/Latino<br>82.26% White<br>4.84% Native American/ American Indian<br>3.23% other<br>G: 85.5% male, 14.5% female | | | | | |
| Huffman, 2017,[72] USA[b] | Retrospective cohort | Effects/ barriers and facilitators | To examine outcomes of patients weaned from opioids in an interdisciplinary chronic pain rehabilitation programme | *Inclusion*<br>No PROGRESS-Plus<br>*Exclusion*<br>Not specified | *N* = 941 patients<br>G: 36.68% male, 61.32% female<br>So (marital status):<br>57.49% married<br>20.5% single<br>11.8% divorced<br>7.86% other<br>+A: (mean, ± SD): 59.3 ± 9.9 years | G, So, +A | | | | |
| Jacobs, 2015,[73] USA | Prospective cohort pilot study | Effects/AEs | To describe the development and implementation of the Chronic Opioid Assessment Program (COAP), and provide an analysis of initial findings and the impact of COAP on opioid prescribing practices. | *Inclusion*<br>No PROGRESS-Plus<br>*Exclusion*<br>No PROGRESS-Plus | *N* = 148 patients<br>G: 98% male, 2% female<br>+A (mean): 64 years<br>+Co: 33.8% depression<br>19.6% substance use disorder<br>32% post-traumatic stress disorder (PTSD) | | | | | |

**TABLE 24** Study characteristics for inequalities review (Review 4) (*continued*)

| Author, date, country | Study design | Included in effects/AE/ barriers and facilitators review | Aim | PROGRESS-Plus inclusion/exclusion criteria | PROGRESS-Plus sample characteristics and author-reported generalisability issues considerations relating to PROGRESS-PLUS sample characteristics (overall figures unless otherwise stated) | Control variables | Inequalities assessed on effects | | | Inequalities assessed on access |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Association of PROGRESS-Plus with tapering outcome | Effect of tapering on PROGRESS-Plus outcome | Effect of PROGRESS-Plus on participation | |
| Jackson, 2021,[111] USA | Pilot RCT | Effects/AEs | To integrate acupuncture within the standard of care during outpatient opioid tapering and assess impact of this treatment on cumulative withdrawal symptoms, psychological distress, and pain. | *Inclusion*<br>G: males or females<br>R: English speaking<br>+A; 18–65 years<br>*Exclusion*<br>Significant psychological disease requiring ongoing treatment | *N* = 15 patients<br>R: 93.3% White<br>6.7% Black<br>0% Hispanic<br>100% not Hispanic<br>G: 53% male, 47% female<br>+A (mean, ± SD): 56.5 ± 17.3 years | | | +Co | | |
| Kennedy, 2018,[102] USA | Qualitative | Barriers and facilitators | To explore PCPs' experiences discussing and implementing opioid tapering with patients on long-term opioid therapy | *Inclusion*<br>No PROGRESS-Plus<br>*Exclusion*<br>Not specified | *N* = 40 providers<br>R: 70% non-Hispanic White<br>3% non-Hispanic Black<br>10% Hispanic<br>18% other<br>G: 53% male, 47% female<br>+A: (mean, ± SD): 44 ± 20 years | | | | | So, +Co |
| Krumova, 2013,[74] Germany[c] | Prospective cohort | Effects | To evaluate the relation between the pain intensity shortly after OW and the probability for long-term opioid non-use. | *Inclusion*<br>No PROGRESS-Plus<br>*Exclusion*<br>Psychiatric diseases with increased risk of withdrawal complication | *N* = 102 patients<br>G: 53.9% male, 46.1% female<br>So (marital status): 55.9% married<br>+A (mean, ± SD): 51 ± 13 years | | | +Co | G | |

continued

**TABLE 24** Study characteristics for inequalities review (Review 4) (*continued*)

| Author, date, country | Study design | Included in effects/AE/ barriers and facilitators review | Aim | PROGRESS-Plus inclusion/exclusion criteria | PROGRESS-Plus sample characteristics and author-reported generalisability issues considerations relating to PROGRESS-PLUS sample characteristics (overall figures unless otherwise stated) | Control variables | Inequalities assessed on effects | | | Inequalities assessed on access |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Association of PROGRESS-Plus with tapering outcome | Effect of tapering on PROGRESS-Plus outcome | Effect of PROGRESS-Plus on participation | |
| Kuntz, 2021,[95] USA | Mixed methods | Barriers and facilitators | To identify factors from patients and pharmacists, that were cited as hindering or contributing to successful opioid tapering | *Inclusion*<br>A: ≥ 21 years<br>*Exclusion*<br>No PROGRESS-Plus | *N* = 25 patients, 12 providers<br>*Patients*<br>R: 91% non-Hispanic White<br>G: 37% male, 63% female<br>S (Neighbourhood Deprivation Index):<br>25% quintile 1 (lowest)<br>25% quintile 2<br>25% quintile 3<br>25% quintile 4 (highest)<br>So:<br>+A: 24% 21–49 years<br>50% 50–65 years<br>26% > 65 years<br>+Co:<br>Charlson Comorbidity Index:<br>41% 0<br>23% 1<br>14% 2<br>23% ≥ 3<br>11% substance use disorder<br>53% depression<br>34% anxiety<br>6% PTSD<br>29% fibromyalgia<br>Chronic pain diagnoses, mean (SD): 3.8 (1.7)<br>*Providers*<br>G: 16.7% male, 83.3% female | | R, G, S, +A, +Co | | | O, S, So, +Co, +St |

**TABLE 24** Study characteristics for inequalities review (Review 4) (*continued*)

| Author, date, country | Study design | Included in effects/AE/ barriers and facilitators review | Aim | PROGRESS-Plus inclusion/exclusion criteria | PROGRESS-Plus sample characteristics and author-reported generalisability issues considerations relating to PROGRESS-PLUS sample characteristics (overall figures unless otherwise stated) | Control variables | Inequalities assessed on effects | | | Inequalities assessed on access |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Association of PROGRESS-Plus with tapering outcome | Effect of tapering on PROGRESS-Plus outcome | Effect of PROGRESS-Plus on participation | |
| Kurita, 2018,[75] Denmark[d] | RCT | Effects | To evaluate the efficacy of stabilising opioid therapy followed by a sequential opioid tapering off programme in chronic non-cancer pain patients | *Inclusion*<br>E: At least 7 years of schooling<br>A: ≥ 18 years<br>*Exclusion*<br>R: Not fluent in Danish language<br>+Co: Poor general health condition, dementia, encephalopathy, brain damage, cranial base trauma, renal or hepatic failure, other metabolic disturbances (medical diagnose) | *N* = 35 patients<br>O: 22.9% working<br>G: 40% male, 60% female<br>E (mean, ± SD): 11.5 ± 3.6 years education in years<br>S (income in DKK): 11.8% < 200,000<br>64.7% 200,000–499,000<br>23.5% ≥ 500,000<br>So: 68.6% co-habitation<br>+A (mean, ± SD): 53.0 ± 12.6 years | | +Co | | G, +A, +Co | , |
| Laigaard, 2020,[76] Denmark | Prospec-tive cohort | Effects | To investigate cognitive function and health-related quality of life in patients with chronic non-cancer pain during opioid reduction | *Inclusion*<br>A: > 18 years<br>*Exclusion*<br>E: Patients not able to speak and understand Danish | *N* = 51 patients<br>G: 33.3% male, 66.7% female<br>O (any employment): 22%<br>E (highest education):<br>35% primary/secondary school<br>49% vocational<br>16% university<br>So (living alone): 41%<br>A (mean, ± SD): 55.9 ± 13 years | | | Co | O, G, E, So, +A | |

continued

**TABLE 24** Study characteristics for inequalities review (Review 4) (*continued*)

| Author, date, country | Study design | Included in effects/AE/ barriers and facilitators review | Aim | PROGRESS-Plus inclusion/exclusion criteria | PROGRESS-Plus sample characteristics and author-reported generalisability issues considerations relating to PROGRESS-PLUS sample characteristics (overall figures unless otherwise stated) | Control variables | Inequalities assessed on effects | | | Inequalities assessed on access |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Association of PROGRESS-Plus with tapering outcome | Effect of tapering on PROGRESS-Plus outcome | Effect of PROGRESS-Plus on participation | |
| Langford, 2020,[103] Australia | Qualitative | Barriers and facilitators | To explore the perspectives of healthcare professional stakeholders on the challenges associated with opioid deprescribing and factors to be considered in the development of opioid deprescribing guidelines | *Inclusion*<br>No PROGRESS-Plus<br>*Exclusion*<br>Not specified | *N* = 31 providers<br>G: 48.4% male, 51.6% female<br>O (profession):<br>4 GPs<br>1 anaesthetist<br>1 general physician<br>3 geriatricians<br>1 addiction specialist<br>1 rheumatologist<br>3 clinical pharmacologists<br>14 clinical pharmacists<br>3 registered nurses | | | | | P, S, +Co, +St |
| McNeilage, 2021,[106] Australia | Qualitative (longitudinal study) | Barriers and facilitators | To identify patterns in individuals' experience of tapering and explore whether patient characteristics, readiness to taper, opioid-tapering self-efficacy, or psychosocial context were related to tapering trajectory | *Inclusion*<br>No PROGRESS-Plus<br>*Exclusion*<br>A: < 18 years<br>R: Insufficient English<br>+Co: major psychiatric conditions | *N* = 21 patients<br>P (geographic location):<br>10 cities, 11 rurals<br>O (employment status):<br>4 working<br>17 not working<br>G: 10 male, 11 female<br>E (educational level):<br>6 vocational training<br>3 high school<br>7 bachelor's degree<br>1 master's degree<br>1 PhD<br>3 NR<br>S (Neighbourhood Deprivation Index):<br>So (in a relationship):<br>13 yes<br>8 no<br>+A (mean, range): 55 years, 29–83 years<br>+St (opioid therapy duration, range): 4 months to 25 years | | P, O, E, So, +A | | | P,O, S, So, +Co, +St |

**TABLE 24** Study characteristics for inequalities review (Review 4) (*continued*)

| Author, date, country | Study design | Included in effects/AE/ barriers and facilitators review | Aim | PROGRESS-Plus inclusion/exclusion criteria | PROGRESS-Plus sample characteristics and author-reported generalisability issues considerations relating to PROGRESS-PLUS sample characteristics (overall figures unless otherwise stated) | Control variables | Inequalities assessed on effects | | | Inequalities assessed on access |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Association of PROGRESS-Plus with tapering outcome | Effect of tapering on PROGRESS-Plus outcome | Effect of PROGRESS-Plus on participation | |
| Magee, 2021,[104] Australia | Mixed methods (qualitative data only) | Barriers and facilitators | To explore patients' access to and use of mobile technology, interest in mHealth support for opioid tapering, preferences for the form and content of mHealth support, and potential barriers to and facilitators of engagement with mHealth support for opioid tapering | *Inclusion*<br>A: > 18 years<br>*Exclusion*<br>R: insufficient English<br>+CoM: Major psychiatric conditions, comorbid opioid use disorder | *N* = 21 patients<br>O (employment status):<br>19% employed<br>78% unemployed or not working<br>5% NR/data missing<br>G: 48% male, 52% female<br>E: 14% high school graduate<br>29% vocational training<br>33% bachelor's degree<br>10% postgraduate degree<br>14% NR/data missing<br>S (Neighbourhood Deprivation Index):<br>So (relationship status):<br>10% single<br>48% married<br>14% in a relationship<br>10% widowed<br>19% NR/data missing<br>+A (mean, ± SD): 55 ± 12.26 years<br>+St duration of opioid treatment, years [mean (SD)]:<br>9.3 ± 7.5 years | | | | | P, S, So, +Co |

continued

**TABLE 24** Study characteristics for inequalities review (Review 4) (*continued*)

| Author, date, country | Study design | Included in effects/AE/ barriers and facilitators review | Aim | PROGRESS-Plus inclusion/exclusion criteria | PROGRESS-Plus sample characteristics and author-reported generalisability issues considerations relating to PROGRESS-PLUS sample characteristics (overall figures unless otherwise stated) | Control variables | Inequalities assessed on effects | | | Inequalities assessed on access |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Association of PROGRESS-Plus with tapering outcome | Effect of tapering on PROGRESS-Plus outcome | Effect of PROGRESS-Plus on participation | |
| Matthais, 2017,[105] USA | Qualitative | Barriers and facilitators | To understand communication processes related to opioid tapering, to identify best practices and opportunities for improvement. | *Inclusion*<br>A: ≥ 18 years<br>R: Speaks English<br>*Exclusion*<br>Not specified | *N* = 37 patients, 9 providers<br>*Patients*<br>R: 41% White<br>46% Black<br>2.5% American Indian<br>8% other<br>2.5% don't know/refused<br>O (employment):<br>16% employed<br>8% not employed<br>19% retired<br>54% unable to work<br>3% other/refused<br>G: 32% male, 25% female<br>E: 38% some high school or less<br>30% high school/GED<br>27% some college/technical or business school<br>5% college degree or above<br>S (income): 11% comfortable<br>43% just enough<br>43% not enough<br>3% refused<br>+A (mean): 58 years<br>*Providers*<br>R: 78% White<br>11% Black<br>1% Asian<br>O (employment):<br>100% employed<br>E: 89% MD<br>11% physician assistant<br>+A (mean): 45 years | | | | | So, Co |

**TABLE 24** Study characteristics for inequalities review (Review 4) (*continued*)

| Author, date, country | Study design | Included in effects/AE/ barriers and facilitators review | Aim | PROGRESS-Plus inclusion/exclusion criteria | PROGRESS-Plus sample characteristics and author-reported generalisability issues considerations relating to PROGRESS-PLUS sample characteristics (overall figures unless otherwise stated) | Control variables | Inequalities assessed on effects | | | Inequalities assessed on access |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Association of PROGRESS-Plus with tapering outcome | Effect of tapering on PROGRESS-Plus outcome | Effect of PROGRESS-Plus on participation | |
| Montgomery, 2020,[77] USA | Retrospective cohort | Effects | To analyse the effectiveness of battlefield acupuncture to decrease chronic pain immediately and 6 months after treatment and to decrease the number of opioids needed to manage chronic pain | *Inclusion*<br>No PROGRESS-Plus<br>*Exclusion*<br>No PROGRESS-Plus | *N* = 47 patients<br>*Intervention vs. control*<br>R: 96% vs. 96% White race/ethnicity<br>G: 83.3% vs. 95.6% male, 16.7% vs. 0.04% female<br>S (Neighbourhood Deprivation Index):<br>+A (mean, ± SD): 61 ± 8.8 years vs. 65 ± 8.5 years | | | | | |
| Murphy, 2013,[78] USA[e] | Retrospective cohort | Effects | To evaluate the associations between opioid cessation and subsequent multidomain treatment outcomes | *Inclusion*<br>No PROGRESS-Plus<br>*Exclusion*<br>+Co-M: Current medical or psychiatric status precluded them from full benefit and engagement | *N* = 221 patients<br>O (employment):<br>13.6% full time<br>4.1% part time<br>7.3% unemployed<br>75.1% disabled/retired<br>G: 82.4% male, 17.6% female<br>R: 66.1% White<br>18.1% African American<br>9.5% Hispanic<br>6.4% other<br>E (mean, ± SD): 13.86 ± 2.45<br>So (marital status):<br>55.2% married<br>12.2% never married<br>28.1 divorced or separated<br>2.7% cohabiting not married<br>1.8% widowed<br>+ A (mean, ± SD):<br>49.08 ± 10.97 years | | | | | |

continued

**TABLE 24** Study characteristics for inequalities review (Review 4) (*continued*)

| Author, date, country | Study design | Included in effects/AE/ barriers and facilitators review | Aim | PROGRESS-Plus inclusion/exclusion criteria | PROGRESS-Plus sample characteristics and author-reported generalisability issues considerations relating to PROGRESS-PLUS sample characteristics (overall figures unless otherwise stated) | Control variables | Inequalities assessed on effects | | | Inequalities assessed on access |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Association of PROGRESS-Plus with tapering outcome | Effect of tapering on PROGRESS-Plus outcome | Effect of PROGRESS-Plus on participation | |
| Panicker, 2022,[79] USA | A retrospective quality improvement (QI) project | Effects | To evaluate chronic non-cancer pain management of veterans using an advanced practice registered nurse (APRN)-led multidisciplinary team approach to incorporate non-opioid and non-pharmacological modalities to affect self-reported pain and use of prescribed opioids | *Inclusion*<br>+A: > 19 years<br>*Exclusion*<br>Not specified | *N* = 34 patients<br>G: 91.8% male, 8.2% female<br>O (employment status):<br>36.4% retired<br>27.3% disability<br>18.9% unemployed<br>18.9% employed<br>So (marital status):<br>52.9% married<br>+ A (mean, ± SD): 63.18 ± 5.39 years<br>+St: 21% receiving prescription opioids < 12 months and similarly for patients receiving opioids 1–5 years.<br>32% were prescribed opioids for 5–10 years<br>26% prescribed beyond 10 years<br>+Co: Of the 34 veterans' only 8 did not have a mental health diagnosis. Depression and PTSD were found equally at 35% and anxiety among 1%. | | | | | |

**TABLE 24** Study characteristics for inequalities review (Review 4) (*continued*)

| Author, date, country | Study design | Included in effects/AE/ barriers and facilitators review | Aim | PROGRESS-Plus inclusion/exclusion criteria | PROGRESS-Plus sample characteristics and author-reported generalisability issues considerations relating to PROGRESS-PLUS sample characteristics (overall figures unless otherwise stated) | Control variables | Inequalities assessed on effects | | | Inequalities assessed on access |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Association of PROGRESS-Plus with tapering outcome | Effect of tapering on PROGRESS-Plus outcome | Effect of PROGRESS-Plus on participation | |
| Quinlan, 2021,[107] UK | Mixed methods (qualitative and quantitative data) | Barriers and facilitators | To investigate the extent of the psychological comorbidity of patients with chronic pain and long-term opioid use and their hopes and fears before embarking on opioid tapering | *Inclusion*<br>No PROGRESS-Plus<br>*Exclusion*<br>Not specified | *N* = 49 patients<br>G: 48% male, 52% female<br>O: few were in employment<br>+A (mean, range): 52.5 years, 23–76 years<br>+Co: Generalised Anxiety Disorder (mean, median, IQR): 12.41–13.50, 8.00–17.00<br>+St: many having been on these doses for over 10 years. | | | | | So, +Co, +St |
| Rivich, 2018,[80] USA | Retrospective cohort | Effects | To identify the impact of OSI chart reviews on total daily opioid dose, prescribing practices of opioids and benzodiazepines, and adherence to VA/VISN policy and monitoring parameters. | *Inclusion*<br>No PROGRESS-Plus<br>*Exclusion*<br>No PROGRESS-Plus | *N* = 147 patients<br>G: 90% male, 10% female<br>+A (median, range): 61 years, 33–84 years | | | | | |

continued

**TABLE 24** Study characteristics for inequalities review (Review 4) (*continued*)

| Author, date, country | Study design | Included in effects/AE/ barriers and facilitators review | Aim | PROGRESS-Plus inclusion/exclusion criteria | PROGRESS-Plus sample characteristics and author-reported generalisability issues considerations relating to PROGRESS-PLUS sample characteristics (overall figures unless otherwise stated) | Control variables | Inequalities assessed on effects | | | Inequalities assessed on access |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Association of PROGRESS-Plus with tapering outcome | Effect of tapering on PROGRESS-Plus outcome | Effect of PROGRESS-Plus on participation | |
| Seal, 2020,[81] USA[f] | PMC | Effects | To evaluate the effectiveness of an Integrated Pain Team (IPT) clinic in decreasing opioid dose and mitigating opioid risk. | *Inclusion (patients matched on)*<br>G: male or female<br>+A: < 55 or ≥ 55<br>+Co: number and type of psychiatric diagnoses (PTSD, depression, bipolar disorder, and/or other psychiatric diagnosis)<br>*Exclusion*<br>No PROGRESS-Plus | *N* = 294 patients<br>*Intervention vs. control*<br>R: 6.8% vs. 6.8% Hispanic or Latino<br>81% vs. 82.3% not Hispanic or Latino<br>59.9% vs. 70.1% White<br>17% vs. 6.8% Black or African American<br>6.8% vs. 4.1% American Indian or Alaska Native<br>1.4% vs. 1.4% Native Hawaiian or other Pacific Islander, or Asian multirace<br>G: 89.8% vs. 89.8% male, 10.2% vs. 10.2% female<br>So (marital status): 37.4% vs. 44.2% married<br>35.4% vs. 32.7% divorced or separated<br>21.1% vs. 18.4% never married<br>4.8% vs. 4.1% widowed/ widow/widower<br>+A (mean, ± SD): 62.1 ± 12.4 years vs. 62.9 ± 11.4 years<br>+CoM: psychiatric and substance use disorders: 34% vs. 38.1% depressive disorder | | | | | |

**TABLE 24** Study characteristics for inequalities review (Review 4) (*continued*)

| Author, date, country | Study design | Included in effects/AE/ barriers and facilitators review | Aim | PROGRESS-Plus inclusion/exclusion criteria | PROGRESS-Plus sample characteristics and author-reported generalisability issues considerations relating to PROGRESS-PLUS sample characteristics (overall figures unless otherwise stated) | Control variables | Inequalities assessed on effects | | | Inequalities assessed on access |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Association of PROGRESS-Plus with tapering outcome | Effect of tapering on PROGRESS-Plus outcome | Effect of PROGRESS-Plus on participation | |
| | | | | | 26.5% vs. 25.9% PTSD<br>12.2% vs. 9.5% alcohol use disorder<br>17.0% vs. 6.1% opioid use disorder<br>7.5% vs. 2.7% other drug use disorder<br>Chronic medical conditions:<br>12.9% vs. 12.2% sleep apnoea<br>22.5% vs. 15.7% chronic pulmonary disease<br>2.7% vs. 1.4% cognitive impairment<br>8.8% vs. 6.1% chronic kidney disease<br>10.2% vs. 8.8% hepatic disease<br>+St (duration of VA opioid therapy (years): 14.1 (5.3) vs. 13.6 (5.1) | | | | | |

continued

**TABLE 24** Study characteristics for inequalities review (Review 4) (*continued*)

| Author, date, country | Study design | Included in effects/AE/ barriers and facilitators review | Aim | PROGRESS-Plus inclusion/exclusion criteria | PROGRESS-Plus sample characteristics and author-reported generalisability issues considerations relating to PROGRESS-PLUS sample characteristics (overall figures unless otherwise stated) | Control variables | Inequalities assessed on effects | | | Inequalities assessed on access |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Association of PROGRESS-Plus with tapering outcome | Effect of tapering on PROGRESS-Plus outcome | Effect of PROGRESS-Plus on participation | |
| Sharp, 2018,[82] USA[d] | Retrospective cohort | Effects | Whether reducing opioid prescriptions for patients without cancer to safer levels is associated with low satisfaction scores among patients with high opioid use in a real-world managed care setting. | *Inclusion*<br>No PROGRESS-Plus<br>*Exclusion*<br>+A: younger than 18 years | *N* = 2492 patients<br>R:72% White<br>9.3% African American<br>15.1% Hispanic<br>2.2% Asian/PI or Native American<br>1.4% unknown<br>G: 43.2% male, 56.8% female<br>+A: 54.5% < 65 years<br>45.6% ≥ 65 years<br>+Co (Elixhauser score):<br>70.26% < 3<br>29.7% ≥ 3 | | R, G, +A, +Co | | | |

**TABLE 24** Study characteristics for inequalities review (Review 4) (*continued*)

| Author, date, country | Study design | Included in effects/AE/ barriers and facilitators review | Aim | PROGRESS-Plus inclusion/exclusion criteria | PROGRESS-Plus sample characteristics and author-reported generalisability issues considerations relating to PROGRESS-PLUS sample characteristics (overall figures unless otherwise stated) | Control variables | Inequalities assessed on effects | | | Inequalities assessed on access |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Association of PROGRESS-Plus with tapering outcome | Effect of tapering on PROGRESS-Plus outcome | Effect of PROGRESS-Plus on participation | |
| Sullivan, 2017,[113,114] USA | RCT | Effects/AEs | Does a prescription opioid taper support intervention for patients receiving moderate or higher dose long-term opioid therapy for chronic non-cancer pain work? | *Inclusion*<br>No PROGRESS-Plus<br>*Exclusion*<br>+Co: considered medically unstable (as judged by the referring physician); report of suicide attempt or psychiatric hospitalisation in the past 10 years or current suicidal ideation with specific plan or intent; report of psychotic symptoms on the modified Mini International Neuropsychiatric Interview; report of current abuse of substances other than nicotine or marijuana according to the National Institute on Drug Abuse Alcohol, Smoking, and Substance Involvement Screening Test | *N* = 35 patients<br>*Intervention vs. control*<br>R: 72.2% vs. 100% white<br>5.6% vs. 0% black<br>11% vs. 5.6% Asian<br>5.6% vs. 0% Native American, Alaska Native, or Pacific Islander<br>5.6% vs. 0% Hispanic<br>G: % male, % female<br>E: 11.1% vs. 23.5% high school<br>44.4% vs. 47.1% some college<br>27.8% vs. 23.5% college graduate<br>16.7% vs. 5.9% graduate or professional school<br>+Co Score of > 10 on the PHQ-9 (moderate or greater depressive symptom severity): 61% vs. 53%<br>*Overall*<br>+A (mean, ± SD): 54.4 ± 10.1 years<br>+St (duration of their current use of opioid medication, mean, ± SD): 10.2 ± 4.3 years | | | +Co | +Co | |

continued

**TABLE 24** Study characteristics for inequalities review (Review 4) (*continued*)

| Author, date, country | Study design | Included in effects/AE/ barriers and facilitators review | Aim | PROGRESS-Plus inclusion/exclusion criteria | PROGRESS-Plus sample characteristics and author-reported generalisability issues considerations relating to PROGRESS-PLUS sample characteristics (overall figures unless otherwise stated) | Control variables | Inequalities assessed on effects | | | Inequalities assessed on access |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Association of PROGRESS-Plus with tapering outcome | Effect of tapering on PROGRESS-Plus outcome | Effect of PROGRESS-Plus on participation | |
| Thakral, 2018,[83,84,85,86,87] USA[d] | Non-patient cohort Interrupted time series | Effects/AEs | To determine if opioid risk reduction initiatives including dose reduction and risk mitigation strategies for chronic non-cancer pain patients receiving COT had a differential impact on average daily opioid doses of COT patients at higher risk for opioid-related adverse outcomes compared with lower-risk patients. | *Inclusion*<br>S: At least 12 months of continuous enrolment in the health insurance plan prior to and including the current quarter<br>+A: ≥ 26 years<br>*Exclusion*<br>No PROGRESS-Plus | *N* = 23,809 patients<br>P: 87.6% Western Washington<br>G: 36.2% male, 63.8% female<br>+A: 24.3% 26–45 years<br>47.1% 46–64 years<br>28.7% 65 +years<br>+Co:<br>9.9% substance use disorders<br>56.2% mental disorders<br>Comorbidity score:<br>57.4% 0<br>8.6% 1<br>14.8% 2<br>19.3% 3 + | | G, +A, +Co | | | |
| Townsend, 2008,[88] USA[g] | Prospective cohort | Effects | We test the hypothesis that patients with chronic pain and long-standing opioid use who undergo opioid withdrawal in the course of rehabilitative treatment will experience significant and sustained improvement in pain and functioning similar to patients who were not taking opioids. | *Inclusion*<br>No PROGRESS-Plus<br>*Exclusion*<br>No PROGRESS-Plus | *N* = 213 patients<br>R: 96.7% white<br>O (% working for a wage): 26.3%<br>G: 21.2% male, 79.8% female<br>E (mean no. of years ± SD):14.6 ± 2.9 years<br>92.5% completed high school<br>So (marital status): 64.8% married<br>+ A (mean, ± SD): 44.5 ± 14.2 years | | | P, +Co, | +Co, So | |

**TABLE 24** Study characteristics for inequalities review (Review 4) (*continued*)

| Author, date, country | Study design | Included in effects/AE/ barriers and facilitators review | Aim | PROGRESS-Plus inclusion/exclusion criteria | PROGRESS-Plus sample characteristics and author-reported generalisability issues considerations relating to PROGRESS-PLUS sample characteristics (overall figures unless otherwise stated) | Control variables | Inequalities assessed on effects | | | Inequalities assessed on access |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Association of PROGRESS-Plus with tapering outcome | Effect of tapering on PROGRESS-Plus outcome | Effect of PROGRESS-Plus on participation | |
| Twillman, 2018,[89] USA | Retrospective cohort | Effects/AEs | Patients with chronic pain receiving long-term opioid therapy were surveyed to assess the incidence and impact of opioid dose reduction following this guideline's promulgation. | *Inclusion*<br>No PROGRESS-Plus<br>*Exclusion*<br>No PROGRESS-Plus | *N* = 362 patients | | | O, So, +Co | | |
| Westanmo, 2015,[117] USA | Non-patient cohort before and after | Effects | To describe processes and outcomes of a health system quality improvement initiative designed to reduce opioid-related harms | *Inclusion*<br>No PROGRESS-Plus<br>*Exclusion*<br>Not specified | *N* = 6942/50,749 patients (April 2011) and 5981/54,636 (October 2014) patients received opioid prescriptions | | | | | |
| White, 2020,[108] Australia | Mixed methods (qualitative data only) | Barriers and facilitators | To evaluate patient and provider perspectives regarding the opioid-tapering intervention Assess, Inform, Manage and Monitor. | *Inclusion*<br>R: English speaking<br>+A: Adults<br>*Exclusion*<br>+Co: Serious underlying pathology, physically or mentally unable to complete survey; current abuse of illicit substances; unable to use a telephone due to cognitive or hearing impairment<br>S: in receipt of workers compensation benefits | *N* = 6 patients, 4 providers<br>*Patient*<br>Not reported separately for qualitative data<br>*Provider*<br>O: 25% GP<br>25% practice nurse<br>25% dietitian<br>25% pharmacist | | | | | So |

continued

**TABLE 24** Study characteristics for inequalities review (Review 4) (*continued*)

| Author, date, country | Study design | Included in effects/AE/ barriers and facilitators review | Aim | PROGRESS-Plus inclusion/exclusion criteria | PROGRESS-Plus sample characteristics and author-reported generalisability issues considerations relating to PROGRESS-PLUS sample characteristics (overall figures unless otherwise stated) | Control variables | Inequalities assessed on effects | | | Inequalities assessed on access |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Association of PROGRESS-Plus with tapering outcome | Effect of tapering on PROGRESS-Plus outcome | Effect of PROGRESS-Plus on participation | |
| Wu, 2019,[109] USA | Mixed methods (case series design, qualitative data only) | Barriers and facilitators | To evaluate the effect of this prescribing policy, with secondary aims to gain insight into the patient experience of undergoing opioid tapering and to generate hypotheses for further study | *Inclusion*<br>R: Speak English<br>+A: older than 18 years<br>*Exclusion*<br>No PROGRESS-Plus | *N* = 6 patients<br>R: 2 white<br>2 African American<br>2 Hispanic<br>G: 4 males, 2 females<br>+A (range): 53–61 years | | | | | So, +St, +Co |
| Zheng, 2008,[112] Australia | RCT | Effects/AEs | Does real electroacupuncture reduce the use of opioid-like medications consumption and associated side effects in patients with chronic pain when compared to sham electroacupuncture | *Inclusion*<br>+A: 18–80 inclusive<br>*Exclusion*<br>Not specified | *N* = 35 patients<br>*Intervention vs. control*<br>G: 53% vs. 50% male, 47% vs. 50% female<br>+ A (mean, ± SD): 51.1 ± 13 years vs. 48.4 ± 10.5 years | | | | So | |
| Zheng, 2019,[115,116] Australia | RCT | Effects/AEs | To assess if electroacupuncture is an effective adjunct therapy to standard pain and medication management in reducing opioids use by patients with chronic musculoskeletal pain. | *Inclusion*<br>R: confident in conversational and reading English<br>+A: aged between 18 and 85 years<br>*Exclusion*<br>+Co: suffering from chronic musculoskeletal pain; severely depressed with suicidal tendency as judged by pain specialists, unstable heart condition, brain tumour, current cancer, haemophilia or wearing cardiac pacemakers | *N* = 108 patients<br>*Intervention vs. control vs. pain management*<br>G: 41.7% vs. 37.9% vs. 51.6% male, 58.3% vs. 62.1% vs. 48.4% female<br>E (education level): 20.8% vs. 27.6% vs. 19.4% University of higher<br>68.8% vs. 55.2% vs. 64.5% ≥ 9 year of formal education<br>4.2% vs. 13.8% vs. 9.7% < 9 years<br>6.3% vs. 3.4% vs. 6.5% missing<br>So (marital status): 44.7% vs. 57.1% vs. 53.3% partnered<br>55.3% vs. 42.9% vs. 46.7% single | | | +Co | P, G, E, So, +A, +Co | |

**TABLE 24** Study characteristics for inequalities review (Review 4) (*continued*)

| Author, date, country | Study design | Included in effects/AE/ barriers and facilitators review | Aim | PROGRESS-Plus inclusion/exclusion criteria | PROGRESS-Plus sample characteristics and author-reported generalisability issues considerations relating to PROGRESS-PLUS sample characteristics (overall figures unless otherwise stated) | Control variables | Inequalities assessed on effects | | | Inequalities assessed on access |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Association of PROGRESS-Plus with tapering outcome | Effect of tapering on PROGRESS-Plus outcome | Effect of PROGRESS-Plus on participation | |
| | | | | | 1 vs. 1 vs. 1 missing<br>+A (mean, ± SD): 55.9 ± 11.3 years vs. 54.8 ± 13.7 years vs. 58.4 ± 12.8 years<br>+Co [Beck Depression Inventory, mean (SD)]: 11.5% vs. 7.8% vs. 14.7% | | | | | |
| Zhou, 2017,[90] USA | Retrospective cohort | Effects | To explore the success rate and important adjuvant medications in the medication-assisted treatment with temporary use of methadone for opioid discontinuation in patients with prescription opioid use disorder. | *Inclusion*<br>+A: ≥ 18 years at first clinic visit<br>*Exclusion*<br>No PROGRESS-Plus | *N* = 140 patients<br>R: %<br>O (employment status):16.5% employed<br>83.5% not employed<br>G: 37.9%% male, 62.1%% female<br>S (Neighbourhood Deprivation Index):<br>So (marriage status): 49.5% single<br>27.8% married<br>22.7% other<br>Living status:<br>33% alone<br>67% with other<br>+ A (mean, ± SD): 46.7 ± 12.7 years<br>+Co (anxiety, depression, or both): 90% yes, 10% no<br>+St (unit: years): 7.7 ± 6.1 | | O, G, So, +A, +Co | | | |

+A, age; Co, comorbidities; E, education; G, gender; O, occupation; OW, opioid withdrawal; P, place of residence; R, race, ethnicity, language; S, socioeconomic status; So, social capital. Plus factors: St, status as long-term opioid user.

a Employed an active control condition which attempted to control for non-specific therapeutic factors such as social interaction and support, inequalities associated with dropout vs. completion.

b PROGRESS-Plus variables analysed for participation and impact on pain, depression, anxiety and functional impairment but data not available separately for opioid users, statistical models adjusted for PROGREESS-Plus variables.

c Assessed influence of PROGRESS-Plus on relapse/stable.

d Adjusted for PROGRESS-Plus characteristics.

e Assessed difference in PROGRESS-Plus characteristics across for completers and non-compliance but data not available separately for opioid users.

f Tapering groups were matched on PROGRESS-Plus characteristics, adjusted for PROGRESS-Plus characteristics.

g Looked at differences in PROGRESS-Plus characteristics for participation but data not available separately for opioid users, looked at impact on return to work, but compared with non-opioid group.

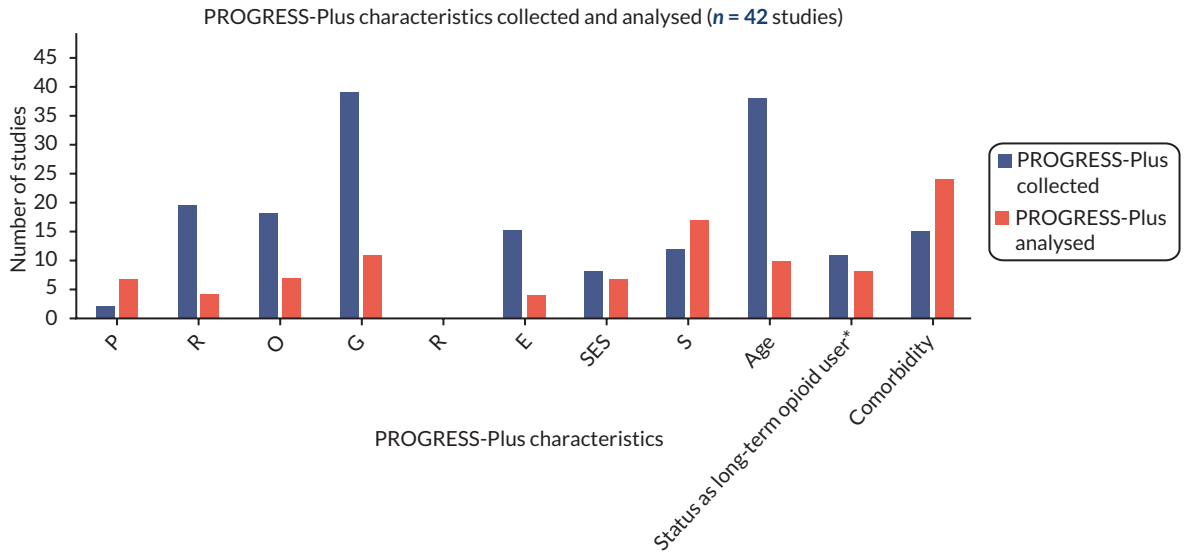


**FIGURE 6** PROGRESS-Plus characteristics collected at baseline vs. analysed (Review 4). E, education; G, gender; O, occupation; P, place of residence; R, race, ethnicity, language; R, religion; S, social capital; SES, socioeconomic status.

studies[82,83,95]); (3) opioid discontinuation (1 study[90]); (4) quality of life (1 study[110]); (5) tapering trajectory (1 study[106]); (6) ability to work (1 study[89]); (7) relationship with medical professionals/family/friends (1 study[89]); and (8) remaining on chronic opioid therapy (1 study[66]).

### *Impact of PROGRESS-Plus characteristics on inequalities in effectiveness of, and access to, opioid tapering*

Factors relating to inequalities in effectiveness of, and access to, opioid tapering were reported across nine PROGRESS-Plus characteristics (see *Tables 40–42* in *Appendix 8*) and related to individual (pertaining to the patient), interpersonal (interaction with provider), organisational and wider environmental contexts. Factors associated with inequalities in effectiveness of opioid tapering operated at an individual level only. Inequalities in access were found that may arise from dimensions of accessibility of services or abilities of healthcare workforce and/or from the abilities of patients to interact with the dimensions of accessibility to generate access (*Figures 7* and *8*).

### *Impact of 'Place of Residence' on inequalities in opioid tapering*

Factors relating to 'Place of Residence' that may potentially widen inequalities were reported for both effectiveness of and access to opioid tapering across seven studies.[88,93,97,103,104,106,116] The evidence suggested that inequalities in access due to 'Place of Residence' may widen as a result of individual, organisational and environmental factors and may affect a patients' ability to reach an opioid taper. At an individual level, inequalities may widen when a patient lives in a rural area[106] or in areas with poor mobile phone reception.[104] Organisational factors relating to the way in which opioid tapering is implemented and wider environmental factors may help to explain why these individual factors widen inequalities, for example, when patients are forced to travel long distances to attend face-to-face opioid-tapering appointments,[93,97,103] or when tapering support is delivered by mobile phone apps.[104] Wider environmental factors external to tapering that may increase inequality in access include a lack of or poor transportation,[93] or living in an area prone to natural disaster occurrences.[106] In addition, the way in which resources were distributed appeared to increase inequalities when tapering resources or alternative therapies were not available to providers in certain locations.[97,102,103] Three studies,[97,103,106] highlighted factors relating to 'Place of Residence' that may potentially reduce inequalities in access at the organisational level, including the availability of tapering resources and delivering tapering initiatives in home or community settings.

### *Impact of 'Race, Ethnicity and Language' on inequalities in opioid tapering*

Three studies[69,82,95] reported on factors relating to 'Race, Ethnicity, Language' that may potentially widen inequalities on the effectiveness of opioid tapering at the individual level. Two studies[82,95] did not find an association between race or ethnicity and opioid reduction. In addition, one RCT[69] did not find a significant difference in race among patients

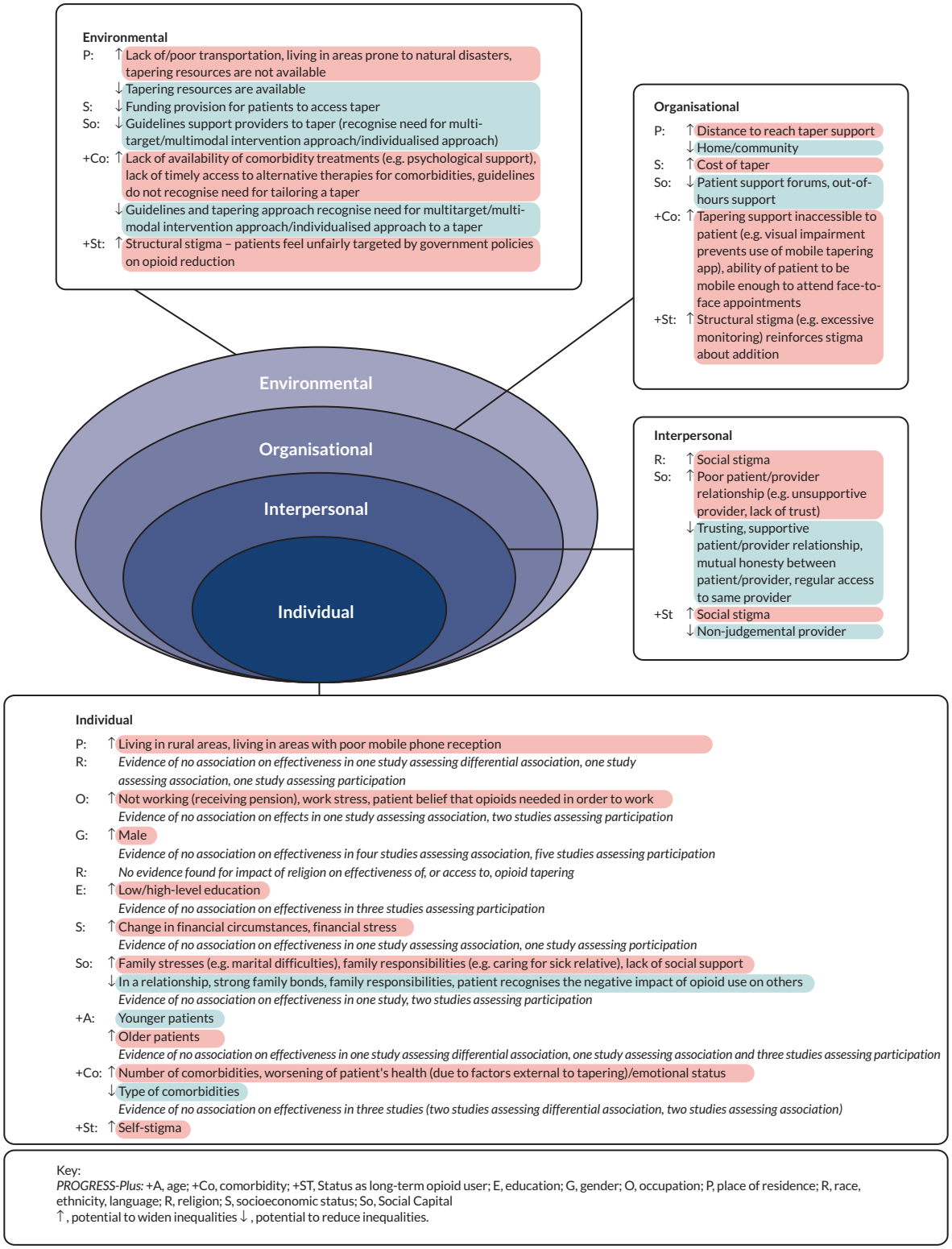


**FIGURE 7** Inequalities in effectiveness of, and access to, opioid tapering in patients with chronic non-cancer pain according to the SEM (Review 4).

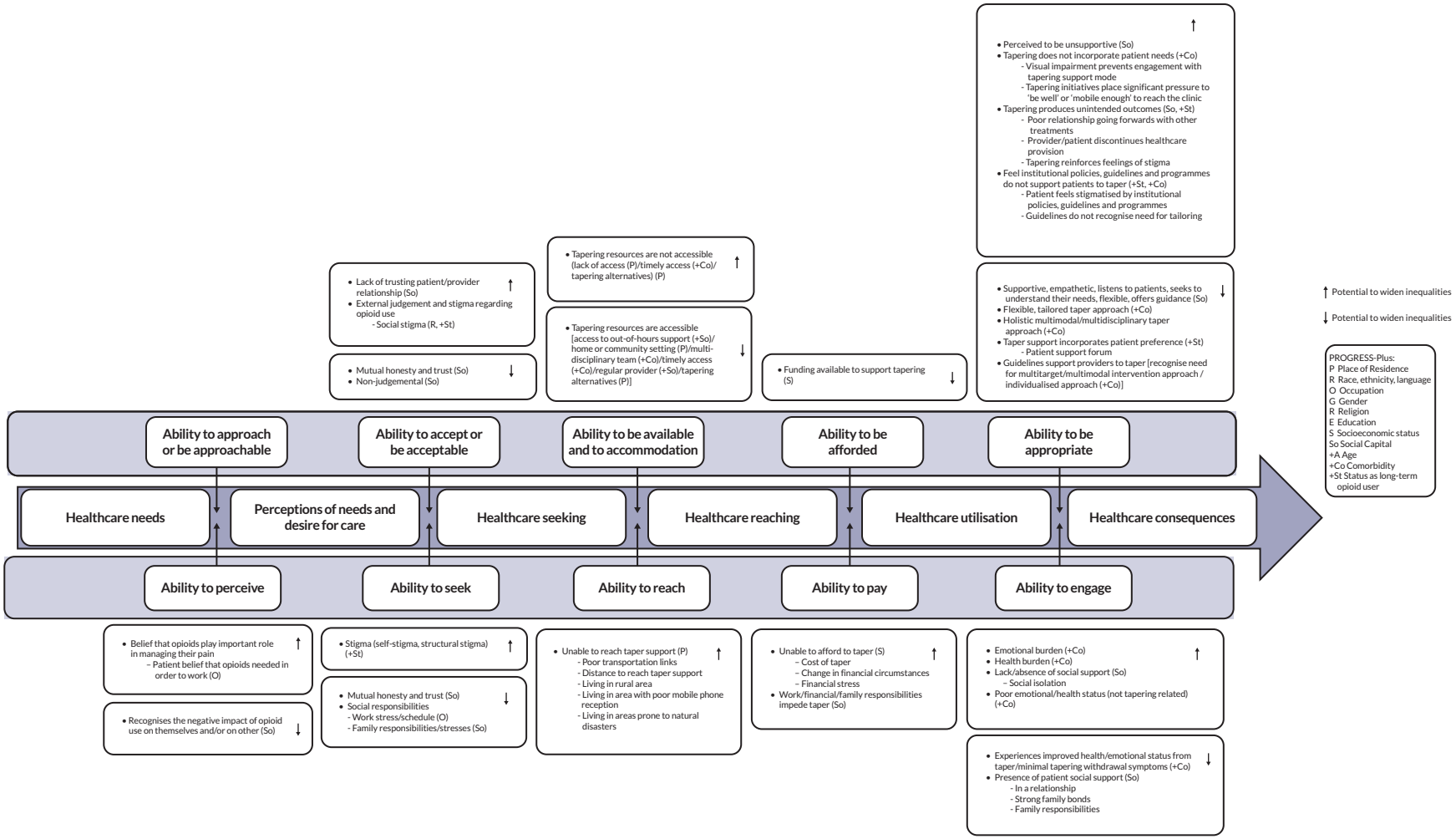


**FIGURE 8** Conceptual model of healthcare access of tapering opioids in adults with chronic pain (Review 4).

who dropped out of the tapering trial compared to those who completed. Interpersonal factors relating to race that may widen inequalities in patients seeking treatment to taper were noted in one study. For example, Benintendi *et al.*[93] found that fear of racial discrimination may compound existing stigma around opioid use, and that this may prevent patients from seeking help to taper. No studies were found that examined the impact of 'language' on effectiveness or access to opioid tapering; however, six studies[76,96,105,108,109,111] included language as an inclusion/exclusion criteria.

### *Impact of 'Occupation' on inequalities in opioid tapering*

'Occupation' was considered a factor that could widen inequalities in both the effectiveness of and access to opioid tapering in three studies.[89,95,106] Individual-level factors relating to 'occupation' that may widen inequalities in tapering effectiveness were found in two studies. For example, McNeilage *et al.*[106] reported a descriptive association between 'not working (all receiving pension)' and a distressing tapering trajectory and Twillman *et al.*[89] assessed the impact of tapering on an occupation-related outcome and found that opioid tapering significantly worsened a patient's ability to work. One study[90] did not find a significant association between employment status (yes/no) and opioid discontinuation and there was no significant impact of occupational status found in two further studies[69,76] among patients who dropped out or were lost to follow-up compared to those who completed the study. Factors relating to 'occupation' that could widen inequalities in access included individual factors relating to work stress or patient beliefs that opioids were needed in order to work.[95,99] Wider environmental factors related to busy work schedules.[106] These factors may also act as a barrier to access at the point at which the patient perceives a need to taper, or seeks to taper.

### *Impact of 'Gender' on inequalities in opioid tapering*

Factors relating to the impact of 'Gender' on inequalities were only reported for tapering effectiveness. At an individual level, a widening of inequalities in opioid-tapering effectiveness due to 'Gender' was noted in four studies,[82,83,95,110] all of which reported significantly worse tapering outcome for males. Of these, one study[83] found a lower dose reduction in males compared to females, one study[82] found that patients in the dose reduction group were more likely to be female and one study[95] found that the odds of a 50% reduction in opioid use at 12 months were decreased among men compared to women. One further study[110] found that males reported a worse PHQ-4 score at week 8 post taper compared to females (though not at baseline or 4 weeks). There were no significant associations between 'Gender' and tapering outcomes reported in four studies.[66,83,90,110] No significant difference was found between males and females with regards to study participation in six studies.[66,69,74,75,76,116]

### *Impact of 'Religion' on inequalities in opioid tapering*

No evidence of impact of 'Religion' on either tapering effectiveness or access was found.

### *Impact of 'Education' on inequalities in opioid tapering*

One study[106] reported an individual-level factor association of 'Education' with tapering effectiveness, finding that patients with low levels of education were associated with a 'surviving' opioid-tapering trajectory, while patients with a university education were associated with a 'resilient' tapering trajectory. Three studies[69,76,116] found no significant difference in study participation due to 'Education'.

### *Impact of 'Socioeconomic status' on inequalities in opioid tapering*

Six studies[95,97,103,104,106,110] reported on individual-, organisational- or wider environmental-level factors that have the potential to widen inequalities in access to opioid tapering. Individual-level factors across three studies were related to changes in individual financial circumstances, including financial stress,[95,106] changes in/loss/alteration of patient insurance plans/policies,[110] and having their phone service cancelled.[110] Organisational and environmental factors examined in five studies included the cost to the patient to taper[97,103,104,106,110] (which in one instance prevented a patient from participating in the study[110]) and the availability of funding provision for patients to access tapering support.[97]

Based on the findings of one study,[95] there was no evidence of an impact of socioeconomic status on tapering effectiveness, which resulted in a widening of inequalities at an individual level. Another study[69] also found no significant difference in socioeconomic status between participants who dropped out of the study compared to those who completed.

### *Impact of 'Social capital' on inequalities in opioid tapering*

'Social capital' was the most reported factor that may widen or reduce inequalities in access to opioid tapering. With regards to tapering effectiveness, 'social capital' was assessed at the individual level in three studies,[89,90,106] which reported mixed effects of social capital on tapering effectiveness which may potentially widen or reduce inequalities. One study[89] reported a negative impact of tapering on social capital-related outcomes which may widen inequalities, including observing a significant worsening of relationships with medical professionals and friends/family among patients whose dose decreased compared to patients whose dose was unchanged. On the other hand, characteristics relating to social capital had a positive association with a tapering outcome, with one study[106] reporting a descriptive association between patients in a relationship and a 'thriving' tapering trajectory. One study[90] did not find a significant association between marriage or living status and opioid discontinuation. Further, while no significant differences were found in two studies[76,116] on dropouts/loss to follow-up due to social status, two other studies[88,112] reported family issues as reasons for why patients dropped out of tapering.

Eleven studies[88,93,94,95,99,102,105,106,108,109,112] highlighted characteristics relating to both the existence of, or lack of, social support at an individual and interpersonal level that may widen inequalities at different points along a tapering trajectory. At an individual level, one study[106] found that a lack of social support from family or friends may widen inequalities if increased feelings of social isolation resulted in a lack of motivation among patients to initiate and sustain a taper. Conversely, two studies[95,106] found that patients who had strong family relationships experienced barriers when external family stresses and responsibilities, such as caring for sick or dying relatives/friends or marital problems, prevented them from tapering. On an interpersonal level, eight studies[93,94,99,102,105,106,108,109] highlighted that a poor patient–provider relationship may widen inequalities in tapering provision when an unsupportive provider or lack of trust between patients and providers leads to unintended consequences such as an ongoing poor relationship with providers on other treatments and, in some instances, patients changing healthcare providers, or providers discontinuing healthcare provision with patients.[102]

The existence of 'social capital' may also help reduce inequalities in access to opioid tapering on an individual, interpersonal and organisational level. Individual-level factors were examined across seven studies.[95,96,99,102,104,106,107] Patients with strong family bonds or family responsibilities were more likely to initiate and sustain a taper than patients who felt isolated. Among these patients, either the patients themselves recognised the impact opioids were having on their relationships or family members raised concerns about their opioid use, thereby motivating them to initiate a taper. At the interpersonal level, across seven studies[95,96,99,104,105,106,108] it was found that a trusting patient–provider relationship was helpful in reducing inequalities in access to opioid tapering. Findings from four studies[94,95,99,108] also suggested that mutual honesty between patient and provider and regular access to the same provider were key to building a trusting patient–provider relationship. At the organisation level, across two studies,[96,104] it was found that patient support forums[96,104] and out-of-hours support[104] have the potential to reduce inequalities associated with social capital. These findings show that 'social capital' has the potential to impact on every stage of the patient's tapering pathway.

### *Impact of 'Age' on inequalities in opioid tapering*

A widening of inequalities in opioid-tapering effectiveness due to 'Age' at the individual level was observed in three studies[82,83,95] which found significant associations of age in favour of younger patients and one study[106] reported a descriptive association between being aged 50 years and older and a 'resilient' tapering trajectory. No significant difference on opioid use was found on mean age in one study,[90] between younger populations (26–45 vs. 45–64 years) in another,[83] or for those ≥ 65 years compared to 50–64 years.[95] With regards to inequalities in participation, one study[66] found a significant association of younger age with remaining an active patient but no association between age and remaining on chronic opioid therapy. Three further studies[69,75,76] found no significant difference in study participation due to 'Age'.

### *Impact of 'Comorbidities' on inequalities in opioid tapering*

Thirteen studies[68,69,74,75,76,82,83,88,89,95,111,113,116] assessed the impact of 'Comorbidities' and tapering effectiveness at an individual level. Of these, three studies[68,88,89] measured the impact of tapering on comorbidity outcomes. Mixed results were noted with one study[89] reporting that mental health worsened among patients whose dose decreased compared to patients whose dose was unchanged, whereas two other studies found a statistically significant improvement on

depression at 3 weeks post taper[68] and immediately following opioid withdrawal and at 6 months post treatment.[88] Mixed results were also noted for studies examining an association between 'Comorbidities' and tapering outcomes. A differential impact which may lead to a widening of inequalities was reported in one study,[95] which found significantly greater odds of a 50% reduction in opioid use at 12 months in patients with no Charlson Comorbidities compared to one. Conversely, three studies[82,83,95] reported better tapering outcomes for patients with existing comorbidities, including mental disorders,[83] substance use disorders,[83,95] anxiety[95] and an Elixhauser comorbidity score of ≥ 3.[82] There was no association of tapering with comorbidities related to depression and anxiety in seven studies[69,74,75,76,111,113,116] and in three studies[83,90,95] which assessed an association between comorbidities and tapering outcomes.

With regards to participation, five studies[67,69,75,88,113] reported issues in participation relating to comorbidities which may widen inequalities. Two studies[69,88] reported dropouts due to 'comorbidity issues', and one study[67] reported late cessation of opioids due to aggravated depressive symptoms and escalating levels of pain, anxiety and depression.[113] In addition, one study[75] found that patients who dropped out presented significantly worse scores of anxiety, depression, general health as assessed by SF-36 and a higher risk for opioid misuse as assessed by the Pain Medication Questionnaire (PMQ). Two studies[69,116] found no significant differences between participants who dropped out compared to those who completed.

Factors relating to 'comorbidities' that could widen inequalities in access were highlighted at the individual, organisational and environmental levels across 11 studies.[93,95,97,99,102,103,104,105,106,107,109] Five studies[95,99,104,106,107] found that a worsening of a patient's health (due to factors external to tapering) or emotional status was more likely to lead to a disruption or discontinuation of tapering, resulting in a widening of inequalities relating to access. Evidence from four studies[97,102,103,106] indicated that such inequalities at the individual level were further compounded by environmental-level factors relating to availability of comorbidity treatments, including a lack of timely access to alternative therapies for comorbidities or the lack of recognition for an individualised approach to tapering, thus resulting in patients slowing down or stopping a taper. In addition, two studies[93,104] indicated that organisational factors relating to intervention design and setting may inadvertently widen inequalities when a patient's health status (visual impairment and ability to be mobile enough to attend tapering appointments) prevented them from accessing tapering support. At an individual level, three studies[99,104,106] found that improvements in a patients' emotional state were also seen as characteristics enabling a successful taper. Based on findings from across three studies,[99,103,105] a flexible, tailored, tapering approach which recognises changes in patient's health and emotional status may help reduce inequalities relating to 'Comorbidities'. Four studies[97,103,106,109] highlighted environmental factors around increased availability and access to multidisciplinary care (e.g. pain specialists, psychologists) and alternative therapies to help patients manage their health and emotional issues while tapering.

### *Impact of 'Status as a long-term opioid user' on inequalities*

Seven studies,[93,95,99,103,106,107,109] which assessed the impact of a patient's status as a long-term opioid user on tapering, found evidence that tapering interventions may widen inequalities in access. Across these studies, stigma associated with 'status as a long-term opioid user' was found to arise directly as a result of opioid tapering on a number of levels (individual, interpersonal and environmental), and sometimes occurring across multiple levels simultaneously. On an individual level (relating to self-stigma), one study[93] found that some patients felt that their pain was invalidated or disbelieved, resulting in feelings of shame, guilt and humiliation. Findings across seven studies[93,95,99,103,106,107,109] suggested that this self-stigma could be perpetuated on an interpersonal level by discriminatory behaviours and negative attitudes of providers resulting in patients fearing, or experiencing, being labelled a 'drug addict' by their providers (relating to social stigma). On a wider environmental level, one study[93] reported that some patients felt unfairly targeted by wider government policies to reduce opioid use without consideration for their individual circumstances. The same study[93] also highlighted that an unintended consequence of the design of opioid-tapering interventions (e.g. monitoring of opioid use, urine toxicology screening) was that they may reinforce stigma about addiction. As a result of stigmatisation, patients may be reluctant to seek help to taper or engage with the tapering process, thus widening inequalities in access. Conversely, the study[93] indicated that monitoring of opioid use was also seen as an opportunity to distance oneself from social stigma. In one study,[96] a non-judgemental provider was seen as an interpersonal factor noted as having the potential to reduce inequalities in access.

## Summary

To our knowledge, this is the first systematic review to synthesise evidence on whether and how inequalities (as defined by PROGRESS-Plus) impact on the effectiveness of, and access to, opioid tapering in adults with chronic non-cancer pain. Forty-two studies included across the three parallel reviews were of varying quality. We found that most studies had collected and reported baseline data with regards to PROGRESS-Plus categories, but less than half considered the impact of them on effectiveness, and just over a third considered them in relation to inequalities in access to opioid tapering. Only two studies[105,108] focused specifically on a disadvantaged group in their study population and only one study[83] aimed to assess differential effects of opioid tapering albeit, comparing patients at high risk of adverse effects with lower-risk patients. Of those that assessed PROGRESS-Plus characteristics in relation to effectiveness, no studies reported on differential effectiveness of opioid-tapering interventions across the selected PROGRESS-Plus characteristics. Instead, inequalities in effectiveness were explored by: (1) stratifying effect analyses by different categories of a PROGRESS-Plus characteristic; (2) exploring associations between PROGRESS-Plus characteristics and changes in opioid use or tapering trajectory following a tapering intervention; or (3) assessing the impact of opioid-tapering initiatives on PROGRESS-Plus-related outcomes (e.g. ability to work).

Only four studies assessed the differential effects of opioid tapering across PROGRESS-Plus characteristics. Our findings agree with those of Lehne and Bolte,[137] who highlight that many studies frequently measure PROGRESS-Plus factors such as race/ethnicity, social status and education, but that few actually consider them in the analysis. This is likely due to researchers not considering the impact of their research on inequalities when planning their studies.[138] Differential effect analyses were more frequently considered for gender, age and comorbidities, with significant findings of a worse tapering outcome for patients who are male and older. Mixed evidence for differential effects was found for comorbidities. For race/ethnicity, occupation and socioeconomic status, no significant differential associations were observed on opioid dose reduction. No differential associations were measured for place of residence, education or social capital. There is also evidence suggesting significant associations (not differential) between gender, age, occupation, social capital and comorbidities on tapering outcomes. Ultimately, any widening of inequalities in access to opioid tapering will likely impact on a widening of inequalities in the effectiveness of opioid tapering. Factors that may potentially widen inequalities in relation to access were highlighted at the individual, interpersonal and wider structural levels and may arise at any point across the entire spectrum of the tapering process, from the point of recognition of a need to taper, initiation of and engagement with a taper. Of note is the influence of 'social capital' which is clearly visible at every stage in a patient's opioid-tapering pathway.

Given that the findings of this review indicate significant associations of some PROGRESS-Plus characteristics, in particular, 'Gender', 'Age' and 'Comorbidities' with changes in opioid use or tapering trajectory, it is imperative that researchers consider including demographic representation of disadvantaged populations in research on opioid tapering. The review findings on inequalities in participation, in particular, reasons for patients dropping out/not completing an opioid taper also have important implications for the way in which interventions are designed and implemented to avoid excluding underserved populations. The NIHR 'Improving inclusion of underserved groups in clinical research: Guidance from the NIHR INCLUDE project[139] supports this view, stating that the 'principle of "no decision about me, without me" provides the moral justification for ensuring that under-served groups are always included in research' regardless of the subject matter being researched. In addition, one of the review findings highlighted inequalities in access to alternative tapering options depending upon where patients access tapering support (place of residence). However, in a survey of patient engagement in RCTs of tapering chronic opioid therapy, James *et al*.[140] found that in order to improve engagement, patients wanted access to alternative pain management options.

While some PROGRESS-Plus characteristics were well reported (e.g. age, gender), other PROGRESS-Plus characteristics that may potentially widen inequalities were less well reported and less frequently analysed. This may indicate a lack of diversity in the sampling approach within the included studies, resulting in an under-representative sample. For example, mental health comorbidities are common among patients prescribed long-term opioid use for chronic non-cancer pain,[95] and the results of this review indicate an association of mental health comorbidities with tapering outcomes. However, only 12 studies (31%) in this review reported on the comorbidity status of participants. Important differences in how comorbid populations respond to or engage with opioid tapering compared to other groups may not therefore have been captured. The current state of research on opioid tapering may not, therefore, accurately reflect the high healthcare burden of opioid tapering within this group.[139]

# **Chapter 9** Discussion

## Summary

This systematic review has examined evidence to inform better practice, pathways and service design in the NHS to support people with chronic non-cancer pain to reduce or stop their use of opioids and address inequalities in access. A review of effectiveness was combined with reviews of safety, barriers and facilitators and inequalities.

Twenty-seven studies were identified that examined the effects of interventions to reduce (or cease) opioid use. Like other research teams who have evaluated the effectiveness of interventions to taper opioid use, we found the published evidence to be of low quality. In agreement with Sandhu 2018, our assessment of the evidence was limited by the variation in intervention investigated, reported outcomes, the low quality of studies, short follow-up and high dropout rates. Similarly, the studies included in our review reported results from behavioural interventions, acupuncture, sequential opioid dose reduction programmes, interdisciplinary programmes, a pain e-consult, pharmacological programmes, a quality improvement project and an OSI. Contact with patients varied from long sessions, over a short duration (e.g. 8 hours per day for 3 weeks) to unspecified input over a longer time period (12 months). Interventions were generally delivered in an outpatient setting but could be delivered face-to-face, over the internet or via telephone; they could be delivered to individuals, groups or, in the case of two programmes, to individuals and groups. We are therefore uncertain about which intervention approaches or their components effect peoples' opioid use and pain but found some evidence that tapering plus support interventions may make some difference to opioid use while not increasing reported pain. Seven studies reported on AEs. None reported any serious AEs, and no patients were reported to have withdrawn from a study due to an AE. We found few studies that examined intervention acceptability but noted at least two studies that experienced significant issues related to patients leaving the study early and slow enrolment into the study, respectively.

By exploring barriers of and facilitators, we can more easily identify strategies that will support patients, carers and healthcare professionals to safely and effectively taper opioids. Sixteen studies were identified for inclusion, and eight barriers and eight facilitators were identified across multiple levels (individual, interpersonal, organisational and environmental levels) of the healthcare system. The use of theoretical frameworks to guide the analysis ensured that our research is comparable with previous research using the same frameworks and makes it easier to advance knowledge and identify gaps. At an individual level, the mapping of barriers and facilitators to the TDF[59] provides practitioners with the opportunity to identify and modify patient/provider behaviours to increase the chance of a successful taper, whereas the Levesque *et al.*[55] amended access to healthcare framework helps providers to identify when and where barriers and facilitators may arise during the opioid-tapering pathway. Tapering is a complex process. The chances of safely and effectively tapering opioids are likely to be increased where the care provided recognises this *complexity* and is *patient-centred*. Crucial to the success of opioid tapering is a *willingness* among both the patient and healthcare professional to taper, and *ability* of a patient to maintain a taper. Use of MI techniques[130] and considering patient preference in the design/delivery of tapering support also appear important, as demonstrated in the EMPOWER study[131] which considered patient- and provider-specific individual-level barriers in the design and delivery of an opioid taper programme. This may also help to ensure that tapering interventions and providers do not unintentionally reinforce perceptions of stigma around addiction. In addition, successful tapering concerns skilful consulting behaviours using techniques such as MI.

Little is known about opioid-tapering interventions and deferral access or outcomes according to equality groups' characteristics and their impact on inequalities. We found that although most studies collected and reported baseline data relevant to PROGRESS-Plus categories, few considered the impact on effectiveness or in relation to inequalities in access to opioid tapering. Ultimately, any widening of inequalities in access to opioid tapering will likely impact on a widening of inequalities in the effectiveness of opioid tapering. Factors that may potentially widen inequalities in relation to access were highlighted at the individual, interpersonal and wider structural levels and may arise at any point across the entire spectrum of the tapering process, from the point of recognition of a need to taper, initiation of and engagement with a taper. Of note is the influence of 'social capital', which is clearly visible at every stage in a

patient's opioid-tapering pathway. While the review is comprehensive, it may not show the true impact of inequalities on the effectiveness of, and access to, opioid tapering. In particular, this review found a similar limitation to that reported in a previous review of inequalities in the uptake of, adherence to and effectiveness of behavioural weight management interventions in adults[138] of low statistical power of the individual studies to detect differential effects of interventions. As reported in Birch *et al.*,[138] this is likely because an investigation of inequalities was not the focus of the analysis. In addition, due to the small sample sizes of many of the studies assessing the effectiveness of opioid tapering, and in some studies a lack of reporting on some PROGRESS-Plus characteristics (e.g. 'Social status'), inequalities in effectiveness may have been present but not detected.

## What considerations should be made in service delivery and practice?

We found that the skills of healthcare professionals were an important theme in the barriers and facilitators review. This referred to both the *skills* of healthcare professionals in tapering opioids and in relation to building a *positive relationship* with the patient undergoing tapering. However, we do not know from the effectiveness review what training for healthcare professionals is effective. For patients, we found that a lack of knowledge and understanding about tapering was a barrier, as well as a perception that opioids play an important role in pain management. Four studies from the effectiveness review examined an intervention that involved a patient education component. One study provided detail on these components, which included education about dose-related risk, the neuropsychology of pain and how to manage pain. Training patients in skills to manage their pain without opioids was a component in eight studies. However, we are unclear what contribution, if any, education and training components make to any intervention effect on opioid use or pain.

Patients' life circumstances play an important role in facilitating successful opioid tapering and social factors affecting patients was an important theme in the barriers and facilitators review. Seven studies from the effectiveness review, all of taper plus support interventions, were based on a model of CBT. CBT relies on a collaborative process between patients and healthcare professionals and so may address the need for trusting, non-judgemental and supportive patient-professional relationships. Among healthcare professionals, the barriers and facilitators review highlighted the need for a supportive health system environment for tapering. Five studies included intervention components that involved collaborative working or dedicated posts (such as pharmacists) to support patient management, for example, by reviewing patient records and developing recommendations. A common component of these interventions was a note or prompt being placed on patients' health records alerting the provider to the recommendation for tapering.

Through the barriers and facilitators review, we found that negative expectations of tapering and an overarching view that tapering was a burden affected patient's motivation for tapering. Twelve studies from the effectiveness review examined interventions that included components which targeted negative emotions. These commonly involved providing patients with access to physical, psychological or alternative therapies, including acupuncture. We also found through the barriers and facilitators review that the motivation of healthcare professionals to taper was impacted by their patient's *motivation*. Few studies involved intervention components that appeared to directly target the motivation of healthcare professionals. Two studies, which were both linked to US OSI, involved *feedback* on prescribing practices and *endorsement* for opioid dose reduction from *peers or senior leadership*.

## Patient and public involvement

A patient and public adviser was involved as a co-applicant. We included a person with lived experience in the research team, and they advised on the development of the funding application and early stages of our project. They did not have further input into the project when they left the service they had supported. Our stakeholder consultation also included people with lived experience. The stakeholders helped us contextualise our findings and consider implementation issues.

## Equality, diversity and inclusion

The research looked to serve a heterogeneous population with a range of sociodemographic characteristics. There is wide variation in opioid prescribing practices in the UK,[15] but more opioids are prescribed in areas of greater social deprivation. For this reason, it was important that we considered and evaluated the potential inequalities in access to interventions that aim to reduce the use of opioids. The use of the PROGRESS-Plus framework in our review enabled a comprehensive exploration of inequalities across a wide range of sociodemographic characteristics, beyond the most investigated measures of gender and age. In addition, we considered various 'Plus' factors (age, comorbidities and status as a long-term opioid user) known to impact on the effectiveness of, and access to, opioid-tapering interventions.

## Strengths

This evidence synthesis has many strengths and we conducted our reviews in accordance with international systematic review guidance.[28,29,30] The reviews of effectiveness, safety and acceptability build on previous systematic reviews[21,23] and the reviews of barriers and facilitators and inequalities add novelty. To our knowledge, the review of barriers and facilitators is the first to focus specifically on opioid tapering in patients with chronic non-cancer pain and the review of inequalities the first to comprehensively review the impact of inequalities across the whole tapering pathway.

We took a sensitive approach to searching to ensure that all voices (i.e. participant, provider and carer) were heard and that all types of barriers and facilitators were captured (individual, organisational, wider contextual). We aimed to minimise publication bias by searching for both published and unpublished literature. To minimise selection bias, two reviewers screened all studies. Studies were included where barriers and facilitators were not the primary focus, for example, studies that explored broader issues around experiences of opioid tapering.

Further strengths included the consideration of a comprehensive range of effectiveness outcomes ($n$ = 49). These outcomes were chosen based on data collected as part of previous systematic reviews on this topic,[21,23] with the addition of consideration of Initiative on Methods, Measurement and Pain Assessment in Clinical Trials, recommendations for core outcome measures for chronic pain clinical trials (Dworkin 2005). This approach ensured that the review collected data relating to outcomes of importance to patients. In line with recommendations by Bach-Mortensen *et al.*,[141] we clearly defined the concept of 'barrier' and 'facilitator' in our review of barriers and facilitators, described how factors were identified and extracted from included studies and assessed the level of confidence in our findings.

## Limitations of the research

All of the studies identified for inclusion were done in USA, Europe or Australia, and none were done in the UK. This raises an important question about the generalisability of the interventions to NHS practice. Generalisability is of particular concern in relation to the six studies that were undertaken in VA facilities. While the VA is reported to often (but not always) perform better than, or similarly to, other US systems of care with regards to the safety and effectiveness of care, analyses have shown that VA users are more likely than non-VA users to be elderly, non-Hispanic black, lower income, in poorer health and live in non-metropolitan areas.

Factors including type of chronic pain, duration of pain, type and duration of opioid use and level of opioid use may influence the efficacy of a tapering intervention. These factors tended to be poorly reported in the included studies, and the included studies tended to recruit patients with multiple types of chronic pain. Further, in each study, patients were taking a range of different opioids at a range of different doses.

Currently, there is no guidance on how to assess confidence/certainty in the results of mixed-methods reviews using GRADE. By transforming quantitative data into qualitative data,[30] we aimed to be inclusive in making a judgement on the confidence in the review findings applied GRADE-CERQual[45] to provide some consistency, although we accept this is a somewhat modified approach. In addition, none of the five studies located in the update search identified any new

themes that would change the findings of the review (i.e. data saturation had been achieved) and were therefore not incorporated into the review. However, the addition of these studies may increase confidence in some of the findings and can be incorporated in future updates.

For the review of inequalities, we did not look to analyse intersectionality of two or more PROGRESS-Plus factors. Patients may experience multiple inequalities which may add unique consequences to their health status during and following an opioid taper, and/or access to tapering support. Furthermore, we did not look at how inequalities are impacted over time, for example, whether the impact of opioid tapering on inequalities changes over time. Finally, the studies included in the review of inequalities were taken from a set of studies included in two parallel reviews on the effectiveness of, barriers and facilitators to, opioid tapering. As a result, relevant studies which did not meet the inclusion criteria for these two reviews may have been missed.

# Chapter 10 Conclusions

Our evidence synthesis shows that evidence to support any opioid reduction intervention for the tapering of opioids in people with chronic non-cancer pain is mixed and uncertain, with some interventions showing promise and others showing limited or no effect. However, with none of the studies done in the UK, the generalisability of our findings to NHS clinical practice is uncertain.

Our review findings highlight the complex nature of the tapering process with the potential for multiple interdependent, behavioural (individual/interpersonal level), structural (organisational level) and contextual (environmental) barriers to arise. To improve the chances of a successful outcome for patients with chronic non-cancer pain who are tapering opioids, there is a need for a whole systems approach to opioid tapering that is patient-centred and recognises that tapering is a dynamic, individualistic, intensive process. Our review findings also reinforce the perspective that the design and delivery of successful opioid-tapering initiatives require careful consideration of individual-level factors and that these individual-level factors have implications for interpersonal, organisational and environmental level approaches to opioid tapering.

Our review highlights the extent to which social inequalities (as defined by the PROGRESS-Plus framework) are considered in studies examining the effectiveness of, and access to, opioid-tapering interventions in adults with chronic non-cancer pain. The findings of this review demonstrate the potential for opioid-tapering interventions to widen inequalities in relation to both effectiveness and access and that inequalities may arise at various points along a tapering pathway, occurring at an individual, interpersonal, organisational or environmental level. Consequences of inequalities in access may include delays in seeking treatment due to anticipated stigma from providers, patient/provider-initiated discontinuation of health care, ultimately resulting in inequalities in effectiveness. It is imperative, therefore, that researchers and practitioners consider the impact on inequalities in the design and implementation of opioid-tapering initiatives.

## Implications for research

Further research to identify the most effective method(s) of opioid withdrawal should be a priority. Data are needed from RCTs that consider the effect of theoretically grounded behaviour change interventions. Data should be collected from patients who have similar baseline characteristics. Treatment arms should be balanced in terms of use of other medications and multidisciplinary team input. Collected data should be used to explore how length of time taking opioids, baseline opioid dose and type of pain impact withdrawal programme effectiveness. The collection of long-term follow-up data would show whether any reduction in opioid use is sustained over time.

Our findings support the calls made by Mardian *et al.*[131] for researchers, practitioners, patients and managers to work together to co-produce evidence on opioid-tapering initiatives to improve patient acceptability. Very few studies included in our review focused on patient acceptability or, indeed, the feasibility of specific opioid-tapering interventions. All long-term prescribing in the NHS is in primary care, so the lack of studies from a UK primary care perspective is striking and has important future research implications. The PSC report carried out on behalf of the MedSIP identified many examples of service activities across England, so activity is not lacking. There therefore needs to be evaluation to generate the evidence needed to understand and maximise the value of different approaches to tapering across the NHS. Given the importance placed on the existence of social support as a facilitator to achieving a successful taper, our review also echoes calls of previous review findings[26] for more research on this factor.

In line with other systematic reviews that have investigated the impact of various interventions on inequalities,[137,138] we echo calls for researchers to consider and report on the differential effects of opioid-tapering initiatives across wider PROGRESS-Plus characteristics, with sufficiently powered studies to detect significant differences should they exist. Furthermore, researchers should ensure their sampling strategies are inclusive and are representative of underserved populations (across the entire PROGRESS-Plus spectrum) that may be disadvantaged. The inclusion of qualitative

studies examining barriers and facilitators to opioid tapering was useful in highlighting inequalities in relation to access; however, most of the qualitative studies explored experiences of opioid tapering in general, rather than in response to a specific tapering intervention. Process evaluations of opioid-tapering interventions undertaken as part of an effectiveness study therefore may be a valuable source of equality data.

## Implications for practice/decision-makers

For clinicians and those organising and implementing tapering initiatives, these findings can help them to understand and address potential barriers that prevent patients initiating and engaging with an opioid taper. Knowing what barriers may arise at each stage of the tapering process can help providers better prepare for tapering, by identifying what facilitators may need to be put in place, at which points, to overcome the barriers. Our review findings validate the amendments made to the Levesque *et al.*[55] framework by Voorhees *et al.*[56] to consider both provider abilities to taper opioids and provider capacity to deliver opioid tapering. Due to the low quality and variability of the evidence identified, we are unable to come to any certain conclusions about the effectiveness of interventions for tapering opioids among people with chronic non-cancer pain. Interventions that combine dose tapering with support appear to be the most promising approach. Our findings also highlight the extent to which inequalities matter in relation to opioid tapering. The interpersonal characteristics of healthcare professionals may impact on inequalities, including the need to avoid stigmatising patients on chronic long-term opioid therapy and the importance of building trust to maintain a supportive patient–provider relationship. In addition, the findings of this review have important implications for the design and delivery of opioid-tapering interventions in avoiding widening inequalities to ensure access and accessibility to all. These findings have particular importance given the context of provision of care during the COVID-19 pandemic and move towards more remote forms of health care. Technology-based remote tapering initiatives should be careful not to discriminate against disadvantaged populations. In considering the impact of tapering implementation on inequalities, practitioners should remember that equal access does not necessarily equate with equality and, therefore, additional support for more disadvantaged populations may be required to reduce inequality gradients.

# Additional information

## CRediT contribution statement

**Ruaraidh Hill (https://orcid.org/0000-0002-2801-0505):** Conceptualisation (lead), Investigation (equal), Formal analysis (equal), Funding acquisition (lead), Investigation (lead), Methodology (lead), Supervision (equal), Writing – reviewing and editing (lead).

**Michelle Maden (https://orcid.org/0000-0003-4419-6343):** Conceptualisation (equal), Investigation (lead), Data curation (lead), Formal analysis (equal), Funding acquisition (supporting), Methodology (equal), Supervision (equal), Writing – original draft (lead), Writing – reviewing and editing (equal).

**Rui Duarte (https://orcid.org/0000-0001-6485-7415):** Conceptualisation (equal), Funding acquisition (equal), Investigation (equal), Data curation (supporting), Formal analysis (supporting), Methodology (supporting), Supervision (equal), Writing – original draft (supporting), Writing – reviewing and editing (supporting).

**Sam Eldabe (https://orcid.org/0000-0002-9250-1886):** Conceptualisation (supporting), Formal analysis (supporting).

**Su Golder (https://orcid.org/0000-0002-8987-5211):** Methodology (equal).

**Marty Chaplin (https://orcid.org/0000-0002-7097-8704):** Data curation (supporting), Formal analysis (supporting), Writing – original draft (supporting).

**Beth Shaw (https://orcid.org/0000-0003-4693-9956):** Conceptualisation (supporting), Investigation (supporting), Formal analysis (supporting), Methodology (equal), Writing – original draft (supporting).

**Katy Sutcliffe (https://orcid.org/0000-0002-5469-8649):** Methodology (equal), Formal analysis (supporting), Writing – original draft (supporting).

**Adam Todd (https://orcid.org/0000-0003-1496-9341):** Conceptualisation (supporting), Formal analysis (supporting).

**Rebecca Bresnahan (https://orcid.org/0000-0001-5578-1535):** Data curation (supporting), Investigation (equal), Formal analysis (supporting), Writing – original draft (supporting).

**Katherine Edwards (https://orcid.org/0000-0002-1092-0092):** Investigation (equal), Data curation (supporting), Formal analysis (supporting). Writing – original draft (supporting).

**Janette Greenhalgh (https://orcid.org/0000-0003-4812-1904):** Investigation (equal), Data curation (supporting), Writing – original draft (supporting).

**Juliet Hounsome (https://orcid.org/0000-0002-2026-3778):** Investigation (lead), Data curation (lead), Formal analysis (equal), Writing – original writing (equal).

**Jack Trafford (https://orcid.org/0009-0005-3904-2165):** Data curation (supporting).

**Nefyn Williams (https://orcid.org/0000-0002-8078-409X):** Conceptualisation (equal), Investigation (equal), Data curation (supporting), Formal analysis (supporting), Methodology (equal), Writing – original draft (supporting).

## Acknowledgements

The principal investigator (Dr Ruaraidh Hill) thanks the research team for applying their expertise and for their consistent commitment to this project. The research team are grateful to the following people for their important contributions: We thank our expert advisory panel for excellent support to the early development of this project. Carmen Smith for patient advisory support to initial stages of this project. Our stakeholders, who offered insight to completeness and usefulness of the report findings and to Katherine Cowan (Katherine Cowan Consulting Ltd) for facilitating our stakeholder engagement. Drs Angela Boland (University of Liverpool) and Sophie Beale (Hare Research) for editorial support. Lisa Jones (Liverpool John Moores University) for extensive proof reading and quality assurance activities in the editorial phase.

## Data-sharing statement

Due to the nature of this study and the type of data collected, there are a limited number of data that can be shared further. All requests on search results and the libraries screened in the systematic review platform are available on request and should be submitted to the corresponding author for consideration.

## Ethics statement

The research did not require ethical approval as it was wholly secondary research using existing reports both published and unpublished.

## Information governance statement

University of Liverpool is committed to handling all personal information in line with the UK Data Protection Act (2018) and the General Data Protection Regulation (EU GDPR) 2016/679. Under the Data Protection legislation, University of Liverpool is the Data Controller, and you can find out more about how we handle personal data, including how to exercise your individual rights and the contact details for our Data Protection Officer here www.liverpool.ac.uk/policy-centre/governance/ and here www.liverpool.ac.uk/it/records-management/information-management-policy/

## Disclosure of interests

***Full disclosure of interests:*** Completed ICMJE forms for all authors, including all related interests, are available in the toolkit on the NIHR Journals Library report publication page at https://doi.org/10.3310/GDWP3572.

***Primary conflicts of interest:*** Nefyn Williams – Deputy chair of NIHR HTA Funding Committee (Commissioned Research) 1 November 2022 to 31 October 2025.

Adam Todd – NIHR HTA Prioritisation Committee A (out of hospital) 1 March 2020–31 February 2024.

## Disclaimer

Every effort has been made to obtain the necessary permissions for reproduction, to credit original sources appropriately and to respect copyright requirements. However, despite our diligence, we acknowledge the possibility of unintentional omissions or errors and we welcome notifications of any concerns regarding copyright or permissions.

## Publications

Bresnahan R, Hill R, Maden M, Duarte R, Eldabe S, Golder S, *et al. WE688 Safe and Effective Reduction of Opioids in Chronic Non-cancer Pain: A Systematic Review of Effects*. IASP 2024 World Congress on Pain, August 2024, Amsterdam, Netherlands, 2024.

Bresnahan R, Maden M, Hill R, Duarte R, Eldabe S, Golder S, *et al. WE688 WE709 Tapering Opioids in Chronic Non-cancer Pain: A Systematic Review of Barriers and Facilitators*. IASP 2024 World Congress on Pain, August 2024, Amsterdam, Netherlands. 2024.

# References


1. Raja SN, Carr DB, Cohen M, Finnerup NB, Flor H, Gibson S, *et al*. The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises. *Pain* 2020;**161**:1976–82.
2. Treede RD, Rief W, Barke A, Aziz Q, Bennett MI, Benoliel R, *et al*. Chronic pain as a symptom or a disease: the IASP Classification of Chronic Pain for the International Classification of Diseases (ICD-11). *Pain* 2019;**160**:19–27.
3. Vos T, Allen C, Arora M. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 2017;**390**:1211–59.
4. Fayaz A, Croft P, Langford RM, Donaldson LJ, Jones GT. Prevalence of chronic pain in the UK: a systematic review and meta-analysis of population studies. *BMJ Open* 2016;**6**:e010364.
5. Yu D, Peat G, Jordan KP, Bailey J, Prieto-Alhambra D, Robinson DE, *et al*. Estimating the population health burden of musculoskeletal conditions using primary care electronic health records. *Rheumatology (Oxford)* 2021;**60**:4832–43.
6. NHS Digital. *Health Survey for England 2017*. London: NHS Digital; 2018.
7. Christie MJ. Cellular neuroadaptations to chronic opioids: tolerance, withdrawal and addiction. *Br J Pharmacol* 2008;**154**:384–96.
8. Tompkins DA, Campbell CM. Opioid-induced hyperalgesia: clinically relevant or extraneous research phenomenon? *Curr Pain Headache Rep* 2011;**15**:129–36.
9. Els C, Jackson TD, Hagtvedt R, Kunyk D, Sonnenberg B, Lappi VG, Straube S. High-dose opioids for chronic non-cancer pain: an overview of Cochrane Reviews. *Cochrane Database Syst Rev* 2017;**10**:CD012299.
10. ChouDana T, Bougatsos C, Deyo RA, Turner R, Devine JA, Hansen EB, *et al*. The effectiveness and risks of long-term opioid therapy for chronic pain: a systematic review for a National Institutes of Health Pathways to Prevention Workshop. *Ann Intern Med* 2015;**162**:276–86.
11. International Association for Study of Pain. *IASP Statement on Opioids for Pain Management*. 2018. URL: www.iasp-pain.org/advocacy/iasp-statements/opioids-for-pain-management/?navItemNumber=7225 (accessed April 2023).
12. GuyMurphy LB, Dowell D, Zhang GP Jr, Bohm K, Losby MK, Lewis J, *et al*. Vital signs: changes in opioid prescribing in the United States, 2006–2015. *MMWR Morb Mortal Wkly Rep* 2017;**66**:697–704.
13. Curtis HJ, Croker R, Walker AJ, Richards GC, Quinlan J, Goldacre B. Opioid prescribing trends and geographical variation in England, 1998–2018: a retrospective database study. *Lancet Psychiatry* 2019;**6**:140–50.
14. Royal Australian College of General Practitioners. *Australian GPs Call for Reform in Pain Management to Protect Patients and Reduce Risky Opioid Use [Press Release]*. Melbourne, VIC: Royal Australian College of General Practitioners; 2017.
15. Jani M, Yimer B, Sheppard T, Lunt M, Dixon WG. Birlie Time trends and prescribing patterns of opioid drugs in UK primary care patients with non-cancer pain: a retrospective cohort study. *PLOS Med* 2020;**17**:e1003270.
16. Centers for Disease Control and Prevention. Vital signs: overdoses of prescription opioid pain relievers – United States, 1999–2008. *MMWR Morb Mortal Wkly Rep* 2011;**60**:1487–92.
17. Almeida M, Saragiotto B, Richards B, Maher CG. Primary care management of non-specific low back pain: key messages from recent clinical guidelines. *Med J Aust* 2018;**208**:272–5.
18. National Institute for Health and Care Excellence. *Chronic Pain (Primary and Secondary) in over 16s: Assessment of All Chronic Pain and Management of Chronic Primary Pain. NG193*. Manchester: National Institute for Health and Care Excellence; 2021.

19. NHS England. *The National Patient Safety Improvement Programmes*. 2021. URL: www.england.nhs.uk/patient-safety/patient-safety-improvement-programmes/#MedSIP (accessed April 2023).
20. Faculty of Pain Medicine. *Opioid Aware*. Updated January 2022. URL: www.fpm.ac.uk/opioids-aware (accessed April 2023).
21. EcclestonKnaggs R, Moore RA, Fisher C, Thomas E, Hearn KH, Derry L, *et al*. Interventions for the reduction of prescribed opioid use in chronic non-cancer pain. *Cochrane Database Syst Rev* 2017;**11**:CD010323.
22. Frank JW, Lovejoy TI, Becker WC, Morasco BJ, Koenig CJ, Hoffecker L, *et al*. Patient outcomes in dose reduction or discontinuation of long-term opioid therapy: a systematic review. *Ann Intern Med* 2017;**167**:181–91.
23. Fishbain DA, Pulikal A. Does opioid tapering in chronic pain patients result in improved pain or same pain vs increased pain at taper completion? A structured evidence-based systematic review. *Pain Med* 2019;**20**:2179–97.
24. NHS National Patient Safety Improvement Programmes. *Improving Chronic Pain Management by Reducing Harm from Opioids: Report on an Analysis of Published Literature and Real-World Case Studies from across England*. London: NHS England; 2021.
25. Williamson TB, Nelson HW. Reply to the comment by Wellstead et al. on "Barriers to enhanced and integrated climate change adaptation and mitigation in Canadian forest management". *Can J Forest Res* 2018;**48**:1246–50. https://doi.org/10.1139/cjfr-2018-0205
26. Cross AJ, Buchbinder R, Mathieson S, Bourne A, Maher CG, Lin CC, O'Connor DA. Barriers and enablers to monitoring and deprescribing opioid analgesics for chronic non-cancer pain: a systematic review with qualitative evidence synthesis using the Theoretical Domains Framework. *BMJ Qual Saf* 2022;**31**:387–400.
27. Mordecai L, Reynolds C, Donaldson LJ, de C Williams AC. Patterns of regional variation of opioid prescribing in primary care in England: a retrospective observational study. *Br J Gen Pract* 2018;**68**:e225–33.
28. Centre for Reviews and Dissemination. *Systematic Reviews. CRD's Guidance for Undertaking Reviews in Health Care*. York: University of York; CRD; 2009.
29. Thomas J, Harden A. Methods for the thematic synthesis of qualitative research in systematic reviews. *BMC Med Res Methodol* 2008;**8**:45.
30. Stern C, Lizarondo L, Carrier J, Godfrey C, Rieger K, Salmond S, *et al*. Methodological guidance for the conduct of mixed methods systematic reviews. *JBI Evid Implement* 2021;**19**:120–9.
31. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, *et al*. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;**372**:n71.
32. Booth A, Harris J, Croot E, Springett J, Campbell F, Wilkins E. Towards a methodology for cluster searching to provide conceptual and contextual 'richness' for systematic reviews of complex interventions: case study (CLUSTER). *BMC Med Res Methodol* 2013;**13**:118.
33. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. *Syst Rev* 2016;**5**:210.
34. Booth A, Cleyle S. Clear and present questions: formulating questions for evidence based practice. *Libr Hi Tech* 2006;**24**:355–68.
35. O'Neill J, Tabish H, Welch V, Petticrew M, Pottie K, Clarke M, *et al*. Applying an equity lens to interventions: using PROGRESS ensures consideration of socially stratifying factors to illuminate inequities in health. *J Clin Epidemiol* 2014;**67**:56–64.
36. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, *et al*. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019;**366**:l4898.
37. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, *et al*.; Cochrane Bias Methods Group. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011;**343**:d5928.

38. Critical Appraisal Skills Programme. *CASP Cohort Study Checklist*. 2022. URL: https://casp-uk.net/casp-tools-checklists/ (accessed April 2023).

39. Critical Appraisal Skills Programme. *CASP Qualitative Checklist*. 2020. URL: https://casp-uk.net/casp-tools-checklists/ (accessed April 2023).

40. Critical Appraisal Skills Programme. *CASP Randomised Controlled Trial Checklist*. 2020. URL: https://casp-uk.net/casp-tools-checklists/ (accessed April 2023).

41. Long HA, French DP, Brooks JM. Optimising the value of the critical appraisal skills programme (CASP) tool for quality appraisal in qualitative evidence synthesis. *Res Methods Med Health Sci* 2020;**1**:31–42.

42. Pollock A, Campbell P, Cheyne J, Cowie J, Davis B, McCallum J, *et al*. Interventions to support the resilience and mental health of frontline health and social care professionals during and after a disease outbreak, epidemic or pandemic: a mixed methods systematic review. *Cochrane Database Syst Rev* 2020;**11**:CD013779.

43. Colvin CJ, Garside R, Wainwright M, Munthe-Kaas H, Glenton C, Bohren MA, *et al*. Applying GRADE-CERQual to qualitative evidence synthesis findings-paper 4: how to assess coherence. *Implement Sci* 2018;**13**:13.

44. Glenton C, Carlsen B, Lewin S, Munthe-Kaas H, Colvin CJ, Tunçalp O, *et al*. Applying GRADE-CERQual to qualitative evidence synthesis findings-paper 5: how to assess adequacy of data. *Implement Sci* 2018;**13**:14.

45. Lewin S, Bohren M, Rashidian A, Munthe-Kaas H, Glenton C, Colvin CJ, *et al*. Applying GRADE-CERQual to qualitative evidence synthesis findings-paper 2: how to make an overall CERQual assessment of confidence and create a summary of qualitative findings table. *Implement Sci* 2018;**13**:10.

46. Munthe-Kaas H, Bohren MA, Glenton C, Lewin S, Noyes J, Tunçalp O, *et al*. Applying GRADE-CERQual to qualitative evidence synthesis findings-paper 3: how to assess methodological limitations. *Implement Sci* 2018;**13**:9.

47. Noyes J, Booth A, Lewin S, Carlsen B, Glenton C, Colvin CJ, *et al*. Applying GRADE-CERQual to qualitative evidence synthesis findings-paper 6: how to assess relevance of the data. *Implement Sci* 2018;**13**:4.

48. Thompson W, Reeve E. Deprescribing: moving beyond barriers and facilitators. *Res Social Adm Pharm* 2022;**18**:2547–9.

49. Booth A, Carroll C. Systematic searching for theory to inform systematic reviews: is it feasible? Is it desirable? *Health Info Libr J* 2015;**32**:220–35.

50. Noyes J, Hendry M, Booth A, Chandler J, Lewin S, Glenton C, Garside R. Current use was established and Cochrane guidance on selection of social theories for systematic reviews of complex interventions was developed. *J Clin Epidemiol* 2016;**75**:78–92.

51. Graham-Rowe E, Lorencatto F, Lawrenson JG, Burr JM, Grimshaw JM, Ivers NM, *et al*. Barriers to and enablers of diabetic retinopathy screening attendance: a systematic review of published and grey literature. *Diabet Med* 2018;**35**:1308–19.

52. Cane J, O'Connor D, Michie S. Validation of the theoretical domains framework for use in behaviour change and implementation research. *Implement Sci* 2012;**7**:37.

53. Michie S, Johnston M, Abraham C, Lawton R, Parker D, Walker A; 'Psychological Theory' Group. Making psychological theory useful for implementing evidence based practice: a consensus approach. *Qual Saf Health Care* 2005;**14**:26–33.

54. Michie S, Johnston M, Francis J, Hardeman W, Eccles M. From theory to intervention: mapping theoretically derived behavioural determinants to behaviour change techniques. *Appl Psychol* 2008;**57**:660–80.

55. Levesque JF, Harris MF, Russell G. Patient-centred access to health care: conceptualising access at the interface of health systems and populations. *Int J Equity Health* 2013;**12**:18.

56. Voorhees J, Bailey S, Waterman H, Checkland K. Accessing primary care and the importance of 'human fit': a qualitative participatory case study. *Br J Gen Pract* 2022;**72**:e342–50.

57. Bhattacharya D, Whiteside H, Tang E, Kantilal K, Loke Y, Atkins B, Hill C. A review of trial and real-world data applying elements of a realist approach to identify behavioural mechanisms supporting practitioners to taper opioids. *Br J Clin Pharmacol* 2022;**88**:4019–42.
58. Desveaux L, Saragosa M, Kithulegoda N, Ivers NM. Understanding the behavioural determinants of opioid prescribing among family physicians: a qualitative study. *BMC Fam Pract* 2019;**20**:59.
59. Atkins L, Francis J, Islam R, O'Connor D, Patey A, Ivers N, *et al*. A guide to using the theoretical domains framework of behaviour change to investigate implementation problems. *Implement Sci* 2017;**12**:77.
60. Bronfenbrenner U. Ecological Systems Theory. In Vasta R, editor. *Annals of Child Development*, vol. **6**. London: Jessica Kingsley Publishers; 1989. pp. 187–249.
61. National Institute for Health and Care Excellence. *Developing NICE Guidelines: The Manual*. URL: www.nice.org.uk/process/pmg20/chapter/introduction (accessed April 2023).
62. HamiltonBlyth F, Mathieson S, Gnjidic M, Christine Lin D, Jansen CW, Weir J, *et al*. Opioid deprescribing: qualitative perspectives from those with chronic non-cancer pain. *Res Social Adm Pharm* 2022;**18**:4083–91.
63. Hamilton M, Mathieson S, Gnjidic D, Jansen J, Weir K, Shaheed CA, *et al*. Barriers, facilitators, and resources to opioid deprescribing in primary care: experiences of general practitioners in Australia. *Pain* 2022;**163**:e518–26.
64. Schneider JL, Firemark AJ, Papajorgji-Taylor D, Reese KR, Thorsness LA, Sullivan MD, *et al*. 'I really had somebody in my corner'. Patient experiences with a pharmacist-led opioid tapering program. *J Am Pharm Assoc* 2022;**63**:241–51.e1.
65. Kosakowski S, Benintendi A, Lagisetty P, Larochelle MR, Bohnert ASB, Bazzi AR. Patient perspectives on improving patient-provider relationships and provider communication during opioid tapering. *J Gen Intern Med* 2022;**37**:1722–8.
66. Austin RC, Fusco CW, Fagan EB, Drake E, Pacious J, Dickens H, *et al*. Teaching opioid tapering through guided instruction. *Fam Med* 2019;**51**:434–7.
67. Bienek N, Maier C, Kaisler M, Michel-Lauter B, Schwarzer A, Meyer-Friesem CH. Intensity of withdrawal symptoms during opioid taper in patients with chronic pain-individualized or fixed starting dosage? *Pain Med* 2019;**20**:2438–49.
68. Cunningham JL, Evans MM, King SM, Gehin JM, Loukianova LL. Opioid tapering in fibromyalgia patients: experience from an interdisciplinary pain rehabilitation program. *Pain Med* 2016;**17**:1676–85.
69. Garland EL, Manusov EG, Froeliger B, Kelly A, Williams JM, Howard MO. Mindfulness-oriented recovery enhancement for chronic pain and prescription opioid misuse: results from an early-stage randomized controlled trial. *J Consult Clin Psychol* 2014;**82**:448–59.
70. Gersch WD, Delate T, Bergquist KM, Smith K. Clinical effectiveness of an outpatient multidisciplinary chronic pain management telementoring service. *Clin J Pain* 2021;**37**:740–6.
71. Hudak J, Hanley AW, March RW, Nakamura Y, Yabko B, *et al*. Endogenous theta stimulation during meditation predicts reduced opioid dosing following treatment with mindfulness-oriented recovery enhancement. *Neuropsychopharmacology* 2020;**46**:836–43.
72. Huffman KL, Rush TE, Fan Y, Sweis GW, Vij B, Covington EC, *et al*. Sustained improvements in pain, mood, function and opioid use post interdisciplinary pain rehabilitation in patients weaned from high and low dose chronic opioid therapy. *Pain* 2017;**158**:1380–94.
73. Jacobs SC, Son EK, Tat C, Chiao P, Dulay M, Ludwig A. Implementing an opioid risk assessment telephone clinic: outcomes from a pharmacist-led initiative in a large Veterans Health Administration primary care clinic, December 15, 2014–March 31, 2015. *Subst Abus* 2016;**37**:15–9.
74. Krumova EK, Bennemann P, Kindler D, Schwarzer A, Zenz M, Maier C. Low pain intensity after opioid withdrawal as a first step of a comprehensive pain rehabilitation program predicts long-term nonuse of opioids in chronic noncancer pain. *Clin J Pain* 2013;**29**:760–9.

75. Kurita GP, Hojsted J, Sjogren P. Tapering off long-term opioid therapy in chronic non-cancer pain patients: a randomized clinical trial. *Eur J Pain* 2018;**22**:1528–43.

76. Laigaard J, Bache N, Stottmeier S, Mathiesen O, Estrup S. Cognitive function during opioid tapering in patients with chronic pain: a prospective cohort study. *J Pain Res* 2020;**13**:3385–94.

77. Montgomery AD, Ottenbacher R. Battlefield acupuncture for chronic pain management in patients on long-term opioid therapy. *Med Acupunct* 2020;**32**:38–44.

78. Murphy JL, Clark ME, Banou E. Opioid cessation and multidimensional outcomes after interdisciplinary chronic pain treatment. *Clin J Pain* 2013;**29**:109–17.

79. Panicker L, Prasun MA, Stockmann C, Simon J. Evaluation of chronic, noncancer pain management initiative in a multidisciplinary pain clinic. *Pain Manag Nurs* 2022;**23**:122–7.

80. Rivich J, McCauliff J, Schroeder A. Impact of multidisciplinary chart reviews on opioid dose reduction and monitoring practices. *Addict Behav* 2018;**86**:40–3.

81. Seal KH, Rife T, Li Y, Gibson C, Tighe J. Opioid reduction and risk mitigation in VA primary care: outcomes from the integrated pain team initiative. *J Gen Intern Med* 2020;**35**:1238–44.

82. Sharp AL, Shen E, Wu YL, Wong A, Menchine M, Kanter MH, *et al*. Satisfaction with care after reducing opioids for chronic pain. *Am J Manag Care* 2018;**24**:e196–9.

83. Thakral M, Walker RL, Saunders K, Shortreed SM, Dublin S, Parchman M, *et al*. Impact of opioid dose reduction and risk mitigation initiatives on chronic opioid therapy patients at higher risk for opioid-related adverse outcomes. *Pain Med* 2018;**19**:2450–8.

84. Von Korff M, Dublin S, Walker RL, Parchman M, Shortreed SM, Hansen RN, *et al*. The impact of opioid risk reduction initiatives on high-dose opioid prescribing for patients on chronic opioid therapy. *J Pain* 2016;**17**:101–10.

85. Von Korff M, Walker RL, Saunders K, Shortreed SM, Thakral M, Parchman M, *et al*. Prevalence of prescription opioid use disorder among chronic opioid therapy patients after health plan opioid dose and risk reduction initiatives. *Int J Drug Policy* 2017;**46**:90–8.

86. Sherman KJ, Walker RL, Saunders K, Shortreed SM, Parchman M, Hansen RN, *et al*. Doctor-patient trust among chronic pain patients on chronic opioid therapy after opioid risk reduction initiatives: a survey. *J Am Board Fam Med* 2018;**31**:578–87.

87. Thakral M, Walker RL, Saunders K, Shortreed SM, Parchman M, Hansen RN, *et al*. Comparing pain and depressive symptoms of chronic opioid therapy patients receiving dose reduction and risk mitigation initiatives with usual care. *J Pain* 2018;**19**:111–20.

88. Townsend CO, Kerkvliet JL, Bruce BK, Rome JD, Hooten WM, Luedtke CA, *et al*. A longitudinal study of the efficacy of a comprehensive pain rehabilitation program with opioid withdrawal: comparison of treatment outcomes based on opioid use status at admission. *Pain* 2008;**140**:177–89.

89. Twillman RK, Hemmenway N, Passik SD, Thompson CA, Shrum M, DeGeorge MK. Impact of opioid dose reduction on individuals with chronic pain: results of an online survey. *J Pain Res* 2018;**11**:2769–79.

90. Zhou K, Jia P, Bhargava S, Zhang Y, Reza T, Peng YB, Wang GG. Opioid tapering in patients with prescription opioid use disorder: a retrospective study. *Scand J Pain* 2017;**17**:167–73.

91. Caldera FE. Medical cannibus as an alternative for opioids for chronic pain: a case report. *SAGE Open Med Case Rep* 2020;**8**:907015.

92. Lalanne L, Nicot C, Lang JP, Bertschy G, Salvat E. Experience of the use of Ketamine to manage opioid withdrawal in an addicted woman: a case report. *BMC Psychiatry* 2016;**16**:395.

93. Benintendi A, Kosakowski S, Lagisetty P, Larochelle M, Bohnert ASB, Bazzi AR. 'I felt like I had a scarlet letter': recurring experiences of structural stigma surrounding opioid tapers among patients with chronic, non-cancer pain. *Drug Alcohol Depend* 2021;**222**:108664.

94. Firemark AJ, Schneider JL, Kuntz JL, Papajorgji-Taylor D, Dickerson JF, Thorsness LA, *et al*. 'We need to taper' interviews with clinicians and pharmacists about use of a pharmacy-led opioid tapering program. *Pain Med* 2021;**22**:1213–22.

95. Kuntz JL, Dickerson JF, Schneider JL, Firemark AJ, Papajorgji-Taylor D, Slaughter M, *et al*. Factors associated with opioid-tapering success: a mixed methods study. *J Am Pharm Assoc* 2021;**61**:248–57.e1.

96. Frank JW, Levy C, Matlock DD, Calcaterra SL, Mueller SR, Koester S, Binswanger IA. Patients' perspectives on tapering of chronic opioid therapy: a qualitative study. *Pain Med* 2016;**17**:1838–47.

97. Giannitrapani KF, Ahluwalia SC, McCaa M, Pisciotta M, Dobscha S, Lorenz KA. Barriers to using nonpharmacologic approaches and reducing opioid use in primary care. *Pain Med* 2018;**19**:1357–64.

98. Giannitrapani KF, Ahluwalia SC, Day RT, Pisciotta M, Dobscha S, Lorenz K. Challenges to teaming for pain in primary care. *Healthc (Amst)* 2018;**6**:23–7.

99. Henry SG, Paterniti DA, Feng B, Iosif AM, Kravitz RL, Weinberg G, *et al*. Patients' experience with opioid tapering: a conceptual model with recommendations for clinicians. *J Pain* 2019;**20**:181–91.

100. Henry SG, Gosdin MM, White AEC, Kravitz RL. 'It sometimes doesn't even work': patient opioid assessments as clues to therapeutic flexibility in primary care. *J Gen Intern Med* 2019;**35**:1635–40.

101. Henry SG, Bell RA, Fenton JJ, Kravitz RL. Goals of chronic pain management: do patients and primary care physicians agree and does it matter? *Clin J Pain* 2017;**33**:955–61.

102. Kennedy LC, Binswanger IA, Mueller SR, Levy C, Matlock DD, Calcaterra SL, *et al*. 'Those conversations in my experience don't go well': a qualitative study of primary care provider experiences tapering long-term opioid medications. *Pain Med* 2018;**19**:2201–11.

103. Langford AV, Gnjidic D, Lin CWC, Bero L, Penm J, Blyth FM, *et al*. Challenges of opioid deprescribing and factors to be considered in the development of opioid deprescribing guidelines: a qualitative analysis. *BMJ Qual Saf* 2020;**30**:10881.

104. Magee MR, Neilage AG, Avery N, Glare P, Ashton-James CE. McmHealth interventions to support prescription opioid tapering in patients with chronic pain: qualitative study of patients' perspectives. *JMIR Form Res* 2021;**5**:e25969.

105. Matthias MS, Johnson NL, Shields C, Bair MJ, MacKie P, Huffman M, *et al*. 'I'm not gonna pull the rug out from under you': patient-provider communication about opioid tapering. *J Pain* 2017;**18**:1365–73.

106. McNeilage AG, Avery NS, Holliday S, Glare PA, Ashton-James CE. A qualitative trajectory analysis of patients' experiences tapering opioids for chronic pain. *Pain* 2022;**163**:e246–60.

107. Quinlan J, Willson H, Grange K. Hopes and fears before opioid tapering: a quantitative and qualitative study of patients with chronic pain and long-term opioids. *Br J Pain* 2021;**15**:120–8.

108. White R, Hayes C, Boyes AW, Paul CL. Integrated primary healthcare opioid tapering interventions: a mixed-methods study of feasibility and acceptability in two general practices in New South Wales, Australia. *Int J Integr Care* 2020;**20**:6.

109. Wu CA, Simon AJ, Modrich MA, Stacey MW, Matyas BT, Shubrook JH. Adapting the social-ecological framework for chronic pain management and successful opioid tapering. *J Am Osteopath Assoc* 2019;**119**:793–801.

110. Capano A, Weaver R, Burkman E. Evaluation of the effects of CBD hemp extract on opioid use and quality of life indicators in chronic pain patients: a prospective cohort study. *Postgrad Med* 2020;**132**:56–61.

111. Jackson HJ, Walters J, Raman R. Auricular acupuncture to facilitate outpatient opioid weaning: a randomized pilot study. *Med Acupunct* 2021;**33**:153–8.

112. Zheng Z, Guo RJ, Helme RD, Muir A, Da Costa C, Xue CCL. The effect of electroacupuncture on opioid-like medication consumption by chronic pain patients: a pilot randomized controlled clinical trial. *Eur J Pain* 2008;**12**:671–6.

113. Sullivan MD, Turner JA, DiLodovico C, D'Appollonio A, Stephens K, Chan YF. Prescription opioid taper support for outpatients with chronic pain: a randomized controlled trial. *J Pain* 2017;**18**:308–18.

114. ClinicalTrials.gov. *Pilot Trial of Opioid Taper Support (POTS)*. 2013. URL: https://clinicaltrials.gov/show/NCT01883882 (accessed April 2023).

115. Xue CC, Helme RD, Gibson S, Hogg M, Arnold C, Somogyi AA, *et al*. Effect of electroacupuncture on opioid consumption in patients with chronic musculoskeletal pain: protocol of a randomised controlled trial. *Trials* 2012;**13**:169.

116. Zheng Z, Gibson S, Helme RD, Wang Y, Lu DSC, Arnold C, *et al*. Effects of electroacupuncture on opioid consumption in patients with chronic musculoskeletal pain: a multicenter randomized controlled trial. *Pain Med (Malden, Mass)* 2019;**20**:397–410.

117. Westanmo A, Marshall P, Jones E, Burns K, Krebs EE. Opioid dose reduction in a VA health care system: implementation of a primary care population-level initiative. *Pain Med (Malden, Mass)* 2015;**16**:1019–26.

118. Michie S, Atkins L, West R. *The Behaviour Change Wheel: A Guide to Designing Interventions*. London: Silverback Publishing; 2014.

119. Critical Appraisal Skills Programme. *CASP Case Control Checklist*. 2022. URL: https://casp-uk.net/casp-tools-checklists/ (accessed April 2023).

120. Smith SM, Dworkin RH, Turk DC, Dermott MP, Eccleston C, Farrar JT, *et al*. McInterpretation of chronic pain clinical trial outcomes: IMMPACT recommended considerations. *Pain* 2020;**161**:2446–61.

121. Olsen MF, Bjerre E, Hansen MD, Tendal B, Hilden J, Hróbjartsson A. Minimum clinically important differences in chronic pain vary considerably by baseline pain and methodological factors: systematic review of empirical studies. *J Clin Epidemiol* 2018;**101**:87–106.e2.

122. Buonora M, Perez HR, Stumph J, Allen R, Nahvi S, Cunningham CO, *et al*. Medical record documentation about opioid tapering: examining benefit-to-harm framework and patient engagement. *Pain Med* 2020;**21**:2574–82.

123. Fortney JC, Burgess JF Jr, Bosworth HB, Booth BM, Kaboli PJ. A re-conceptualization of access for 21st century healthcare. *J Gen Intern Med* 2011;**26**:639–47.

124. Hatzenbuehler ML. Structural stigma: research evidence and implications for psychological science. *Am Psychol* 2016;**71**:742–51.

125. Glasgow RE, Vogt TM, Boles SM. Evaluating the public health impact of health promotion interventions: the RE-AIM framework. *Am J Public Health* 1999;**89**:1322–7.

126. Michie S, van Stralen MM, West R. The behaviour change wheel: a new method for characterising and designing behaviour change interventions. *Implement Sci* 2011;**6**:42.

127. The Lancet. A time of crisis for the opioid epidemic in the USA. *Lancet* 2021;**398**:277.

128. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain: United States, 2016. *JAMA* 2016;**315**:1624–45.

129. National Institute for Health and Care Excellence. *Medicines Associated with Dependence or Withdrawal Symptoms: Safe Prescribing and Withdrawal Management for Adults. NG215*. 2022. URL: www.nice.org.uk/guidance/ng215/resources/medicines-associated-with-dependence-or-withdrawal-symptoms-safe-prescribing-and-withdrawal-management-for-adults-pdf-66143776880581 (accessed April 2023).

130. Crawley A, Murphy L, Regier L, McKee N. Tapering opioids using motivational interviewing. *Can Fam Physician* 2018;**64**:584–7.

131. Mardian A, Perez L, Pun T, Cheung M, Porter J, De Bruyne K, *et al*. Engagement in prescription opioid tapering research: the EMPOWER study and a coproduction model of success. *J Gen Intern Med* 2022;**37**:113–7.

132. Doherty AJ, Boland P, Reed J, Clegg AJ, Stephani AM, Williams NH, *et al*. Barriers and facilitators to deprescribing in primary care: a systematic review. *BJGP Open* 2020;**4**:bjgpopen20X101096.

133. Waddell A, Lennox A, Spassova G, Bragge P. Barriers and facilitators to shared decision-making in hospitals from policy to practice: a systematic review. *Implement Sci* 2021;**16**:74.

134. Boland L, Graham ID, Légaré F, Lewis K, Jull J, Shephard A, *et al*. Barriers and facilitators of pediatric shared decision-making: a systematic review. *Implement Sci* 2019;**14**:7.

135. Rushforth B, McCrorie C, Glidewell L, Midgley E, Foy R. Barriers to effective management of type 2 diabetes in primary care: qualitative systematic review. *Br J Gen Pract* 2016;**66**:e114–27.

136. Sohal T, Sohal P, King-Shier KM, Khan NA. Barriers and facilitators for type-2 diabetes management in south Asians: a systematic review. *PLOS ONE* 2015;**10**:e0136202.

137. Lehne G, Bolte G. Impact of universal interventions on social inequalities in physical activity among older adults: an equity-focused systematic review. *Int J Behav Nutr Phys Act* 2017;**14**:20.

138. Birch JM, Jones RA, Mueller J, McDonald MD, Richards R, Kelly MP, *et al*. A systematic review of inequalities in the uptake of, adherence to, and effectiveness of behavioral weight management interventions in adults. *Obes Rev* 2022;**23**:e13438.

139. NIHR. *Improving Inclusion of under-Served Groups in Clinical Research: Guidance from the NIHR-INCLUDE Project*. London: NIHR; 2020.

140. James J, Lai B, Witt T. Patient engagement survey regarding future double-blinded, randomized controlled trial of tapering of chronic opioid therapy. *J Prim Care Community Health* 2019;**10**:9890231.

141. Bach-Mortensen AM, Lange BCL, Montgomery P. Barriers and facilitators to implementing evidence-based interventions among third sector organisations: a systematic review. *Implement Sci* 2018;**13**:103.

# Appendix 1 Literature search strategies

## Review 1 (clinical effectiveness)

**MEDLINE** (Ovid MEDLINE(R) ALL < 1946–20 September 2022 >)

1 Analgesics, Opioid/ (46,131)
2 exp Buprenorphine/ (5550)
3 exp Codeine/ (7134)
4 exp Dextropropoxyphene/ (1465)
5 exp Fentanyl/ (16,035)
6 exp Hydrocodone/ (637)
7 exp Hydromorphone/ (1321)
8 exp Meperidine/ (5790)
9 exp Meptazinol/ (187)
10 exp Methadone/ (12,560)
11 exp Morphine/ (38,400)
12 exp Nalbuphine/ (687)
13 exp Opiate Alkaloids/ (87,065)
14 exp Oxycodone/ (2350)
15 exp Oxymorphone/ (497)
16 exp Pentazocine/ (2234)
17 exp Tapentadol/ (327)
18 exp Tramadol/ (3194)
19 (opioid* or opiate*).mp. (138,206)
20 (codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or codydramol or co-proxamol or hydromorphone or nalbuphine or oxymorphone).mp. (119,880)
21 or/1-20 (218,473)
22 Opiate Substitution Treatment/ (3266)
23 (taper* or wean* or detox* or withdraw* or discontinu* or cease or cessation or terminat* or remove* or stop* or substitut* or deprescri*).mp. (1,348,899)
24 ((dose or dosage or medicine* or medication) adj1 (reduc* or consumption or lower* or decreas*)).mp. (39,564)
25 (("opiate use" or "opioid use" or OLM) adj3 (reduc* or change* or decreas*)).mp. (1162)
26 or/22-25 (1,382,888)
27 exp Pain/ (402,869)
28 exp Arthritis/ (263,296)
29 Fibromyalgia/ (8582)
30 exp Headache Disorders/ (35,118)
31 pain*.mp. (813,659)
32 (neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*).mp. (603,586)
33 or/27-32 (1,381,008)
34 21 and 26 and 33 (8554)
35 exp animals/ (23,717,900)
36 humans.sh. (18,943,220)
37 35 not 36 (4,774,680)
38 34 not 37 (6694)
39 limit 38 to english language (6193)
40 letter.pt. (1,116,589)

41 editorial.pt. (553,178)
42 comment.pt. (885,663)
43 case reports.pt. (2,147,225)
44 clinical conference.pt. (7420)
45 consensus development conference nih.pt. (790)
46 consensus development conference.pt. (11,887)
47 congress.pt. (66,493)
48 review.pt. (2,744,229)
49 or/40-48 (6,504,602)
50 39 not 49 (4525)
51 limit 50 to "all adult (19 plus years)" (2502)
52 adult*.mp. (5,996,128)
53 50 and 52 (2192)
54 51 or 53 (2718)
55 limit 54 to yr="2000 -Current" (2256)

**EMBASE** (Ovid 1974–20 September 2022)

1. exp opiate/
2. narcotic analgesic agent/
3. exp buprenorphine/
4. exp codeine/
5. exp dextropropoxyphene/
6. exp fentanyl/
7. exp hydrocodone/
8. exp hydromorphone/
9. exp pethidine/
10. exp meptazinol/
11. exp methadone/
12. exp morphine/
13. exp nalbuphine/
14. exp oxycodone/
15. exp oxymorphone/
16. exp pentazocine/
17. exp tapentadol/
18. exp tramadol/
19. exp butorphanol/
20. exp dipipanone/
21. exp dihydrocodeine/
22. exp diamorphine/
23. exp cocodamol/
24. exp codydramol/
25. exp dextropropoxyphene plus paracetamol/
26. (opioid* or opiate*).mp.
27. (codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or co-dydramol or co-proxamol or hydromorphone or nalbuphine or oxymorphone).mp.
28. or/1-27
29. exp drug detoxification/
30. exp drug withdrawal/
31. exp drug substitution/
32. exp deprescription/

33. (taper* or wean* or detox* or withdraw* or discontinu* or cease or cessation or terminat* or remove* or stop* or substitut* or deprescri*).mp.
34. ((dose or dosage or medicine* or medication) adj1 (reduc* or consumption or lower* or decreas*)).mp.
35. (("opiate use" or "opioid use" or OLM) adj3 (reduc* or change* or decreas*)).mp.
36. or/29-35
37. exp Pain/
38. exp arthritis/
39. fibromyalgia/
40. exp "headache and facial pain"/
41. pain*.mp.
42. (neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*).mp.
43. or/37-42
44. 28 and 36 and 43
45. exp animal/ or exp nonhuman/ or exp animal experiment/ or exp animal model/
46. human/
47. 45 not 46
48. 44 not 47
49. limit 48 to (books or chapter or conference abstract or conference paper or "conference review" or editorial or letter or note or review)
50. 48 not 49
51. limit 50 to english language
52. limit 51 to (adult <18 to 64 years> or aged <65+ years>)
53. adult*.mp.
54. 51 and 53
55. 52 or 54
56. limit 55 to yr="2000 -Current"

**Cochrane Central Register of Controlled Trials** (CENTRAL via The Cochrane Library www.cochranelibrary.com/, September 2022)

#1 MeSH descriptor: [Analgesics, Opioid] this term only
#2 MeSH descriptor: [Buprenorphine] explode all trees
#3 MeSH descriptor: [Codeine] explode all trees
#4 MeSH descriptor: [Dextropropoxyphene] explode all trees
#5 MeSH descriptor: [Fentanyl] explode all trees
#6 MeSH descriptor: [Hydrocodone] explode all trees
#7 MeSH descriptor: [Hydromorphone] explode all trees
#8 MeSH descriptor: [Meperidine] explode all trees
#9 MeSH descriptor: [Meptazinol] explode all trees
#10 MeSH descriptor: [Methadone] explode all trees
#11 MeSH descriptor: [Morphine] explode all trees
#12 MeSH descriptor: [Nalbuphine] explode all trees
#13 MeSH descriptor: [Opiate Alkaloids] explode all trees
#14 MeSH descriptor: [Oxycodone] explode all trees
#15 MeSH descriptor: [Oxymorphone] explode all trees
#16 MeSH descriptor: [Pentazocine] explode all trees
#17 MeSH descriptor: [Tapentadol] explode all trees
#18 MeSH descriptor: [Tramadol] explode all trees
#19 opioid* or opiate*
#20 codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or co-dydramol or co-proxamol or hydromorphone or nalbuphine or oxymorphone

#21 25-#20
#22 MeSH descriptor: [Opiate Substitution Treatment] explode all trees
#23 taper* or wean* or detox* or withdraw* or discontinu* or cease or cessation or terminat* or remove* or stop* or substitut* or deprescri*
#24 (dose or dosage or medicine* or medication) NEAR/1 (reduc* or consumption or lower* or decreas*)
#25 ("opiate use" or "opioid use" or OLM) NEAR/3 (reduc* or change* or decreas*)
#26 142-#25
#27 MeSH descriptor: [Pain] explode all trees
#28 MeSH descriptor: [Arthritis] explode all trees
#29 MeSH descriptor: [Fibromyalgia] this term only
#30 MeSH descriptor: [Headache Disorders] explode all trees
#31 pain*
#32 neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*
#33 (OR #27-#32)
#34 #21 AND #26 AND #33 in Trials
#35 MeSH descriptor: [Animals] explode all trees
#36 MeSH descriptor: [Humans] this term only
#37 #35 not #36
#38 #34 not #37

**CINAHL (EBSCO*host*)**

S1 (MH "Analgesics, Opioid")
S2 (MH "Buprenorphine")
S3 (MH "Codeine+")
S4 (MH "Propoxyphene")
S5 (MH "Fentanyl+")
S6 (MM "Dihydromorphinone")
S7 (MH "Meperidine")
S8 (MH "Methadone")
S9 (MH "Morphine+")
S10 (MH "Nalbuphine")
S11 (MH "Oxycodone")
S12 (MH "Pentazocine")
S13 (MH "Tramadol")
S14 (MH "Butorphanol")
S15 TI (opioid* or opiate*) OR AB (opioid* or opiate*) OR SU (opioid* or opiate*)
S16 TI (codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or co-dydramol or co-proxamol or hydromorphone or nalbuphine or oxymorphone) OR AB (codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or co-dydramol or co-proxamol or hydromorphone or nalbuphine or oxymorphone) OR SU (codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or co-dydramol or co-proxamol or hydromorphone or nalbuphine or oxymorphone)
S17 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16
S18 (MH "Substance Withdrawal, Controlled")
S19 TI (taper* or wean* or detox* or withdraw* or discontinu* or cease or cessation or terminat* or remove* or stop* or substitut* or deprescri*) OR AB (taper* or wean* or detox* or withdraw* or discontinu* or cease or cessation or

terminat* or remove* or stop* or substitut* or deprescri*) OR SU (taper* or wean* or detox* or withdraw* or discontinu* or cease or cessation or terminat* or remove* or stop* or substitut* or deprescri*)
S20 TI (((dose or dosage or medicine* or medication) N1 (reduc* or consumption or lower* or decreas*))) OR AB (((dose or dosage or medicine* or medication) N1 (reduc* or consumption or lower* or decreas*))) OR SU (((dose or dosage or medicine* or medication) N1 (reduc* or consumption or lower* or decreas*)))
S21 TI (((“opiate use” or “opioid use” or OLM) N3 (reduc* or change* or decreas*))) OR AB (((“opiate use” or “opioid use” or OLM) N3 (reduc* or change* or decreas*))) OR SU (((“opiate use” or “opioid use” or OLM) N3 (reduc* or change* or decreas*)))
S22 S18 OR S19 OR S20 OR S21
S23 (MH “Pain+”)
S24 (MH “Arthritis+”)
S25 (MH “Fibromyalgia”)
S26 (MH “Headache+”)
S27 TI pain* OR AB pain* OR SU pain*
S28 TI (neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*) OR AB (neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*) OR SU (neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*)
S29 S23 OR S24 OR S25 OR S26 OR S27 OR S28
S30 S17 AND S22 AND S29
S31 (MH “Animals+”)
S32 (MH “Human”)
S33 S31 not S32
S34 S30 NOT S33
S35 PT book OR PT book chapter OR PT book review OR PT commentary OR PT doctoral dissertation OR PT editorial OR PT letter OR PT proceedings OR PT review
S36 S34 NOT S35
S37 S34 NOT S35Limiters - Publication Year: 2000-2020, Narrow by Language: - English, Narrow by SubjectAge: - all adult

**PsycInfo (EBSCO)**

S1 DE “Opiates” OR DE “Buprenorphine” OR DE “Codeine” OR DE “Endogenous Opiates” OR DE “Fentanyl” OR DE “Morphine” OR DE “Oxycodone”
S2 DE “Meperidine”
S3 DE “Methadone”
S4 DE “Morphine”
S5 DE “Pentazocine”
S6 DE “Tramadol”
S7 TI (opioid* or opiate*) OR AB (opioid* or opiate*) OR SU (opioid* or opiate*)
S8 TI (codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or codydramol or co-proxamol or hydromorphone or nalbuphine or oxymorphone) or AB (codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or codydramol or co-proxamol or hydromorphone or nalbuphine or oxymorphone) OR SU (codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or codydramol or co-proxamol or hydromorphone or nalbuphine or oxymorphone
S9 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8
S10 DE “Drug Withdrawal”

S11 TI (taper* or wean* or detox* or withdraw* or discontinu* or cease or cessation or terminat* or remove* or stop* or substitut* or deprescri*) OR AB (taper* or wean* or detox* or withdraw* or discontinu* or cease or cessation or terminat* or remove* or stop* or substitut* or deprescri*) OR SU (taper* or wean* or detox* or withdraw* or discontinu* or cease or cessation or terminat* or remove* or stop* or substitut* or deprescri*)
S12 TI ((dose or dosage or medicine* or medication) N1 (reduc* or consumption or lower* or decreas*)) OR AB ((dose or dosage or medicine* or medication) N1 (reduc* or consumption or lower* or decreas*)) OR SU ((dose or dosage or medicine* or medication) N1 (reduc* or consumption or lower* or decreas*))
S13 TI (("opiate use" or "opioid use" or OLM) N3 (reduc* or change* or decreas*)) OR AB (("opiate use" or "opioid use" or OLM) N3 (reduc* or change* or decreas*)) OR SU (("opiate use" or "opioid use" or OLM) N3 (reduc* or change* or decreas*))
S14 S10 OR S11 OR S12 OR S13
S15 DE "Pain" OR DE "Aphagia" OR DE "Back Pain" OR DE "Chronic Pain" OR DE "Headache" OR DE "Myofascial Pain" OR DE "Neuralgia" OR DE "Neuropathic Pain" OR DE "Somatoform Pain Disorder"
S16 DE "Arthritis" OR DE "Rheumatoid Arthritis"
S17 DE "Fibromyalgia"
S18 TI (pain*) OR AB (pain*) OR SU (pain*)
S19 TI (neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*) OR AB (neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*) OR SU (neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*)
S20 S15 OR S16 OR S17 OR S18 OR S19
S21 S9 AND S14 AND S20
S22 PO animal NOT PO human
S23 S21 NOT S22
S24 PZ (Column/Opinion OR Comment/Reply OR Dissertation OR Editorial OR Letter OR Review-Any)
S25 S23 NOT S24
S26 S23 NOT S24Limiters - Published: 20000101-20211231, Narrow by SubjectAge: - adulthood (18 yrs & older), Narrow by Language: - english

**ClinicalTrials.gov**

Search 1: Opiate withdrawal syndrome (Condition) Limit to Adults
Search 2: Opioid Use (Condition) AND (taper* OR wean* OR detox* OR withdraw* OR discontinu* OR cease OR cessation OR terminat* OR remove* OR stop* OR substitut* OR deprescri) (Other terms) Limit to Adults
Search 3: Opioid Use, Unspecified (Condition) AND (taper* OR wean* OR detox* OR withdraw* OR discontinu* OR cease OR cessation OR terminat* OR remove* OR stop* OR substitut* OR deprescri) (Other terms) Limit to Adults

Notes

1. Doesn't accept long complex search strategies – limits use of Boolean to combine concepts

**EU Clinical Trials Register (EU-CTR)** (www.clinicaltrialsregister.eu/)

(Opioid* OR opiate* OR codeine OR oxycodone OR tramadol OR hydromorphone OR morphine OR fentanyl OR meperidine OR pethidine OR dextropropoxyphene OR methadone OR buprenorphine OR pentazocine OR hydrocodone OR butorphanol OR tapentadol OR papaveretum OR meptazinol OR dipipanone OR dihydrocodeine OR diamorphine OR co-codamol OR codydramol OR co-proxamol OR hydromorphone OR nalbuphine OR oxymorphone) AND (pain* OR neuralgi* OR myalgi* OR neuropath* OR arthriti* OR osteoarthri* OR arthralgi* OR sciatica OR headache* OR migrain*) AND (taper* OR wean* OR detox* OR withdraw* OR discontinu* OR cease OR cessation OR terminat* OR remove* OR stop* OR substitut* OR deprescri*) Limit by date from 2000-

**Australian New Zealand Clinical Trials Registry (ANZCTR)** (www.anzctr.org.au/)

Search 1: (opioid* or opiate*) AND (pain*) AND (taper* or wean* or detox* or withdraw* or discontinu*)
Search 2: (opioid* or opiate*) AND (pain*) AND (cease or cessation or terminat* or remove* or stop*)
Search 3: (opioid* or opiate*) AND (pain*) AND (substitut* or deprescri*)

Notes

1. Doesn't accept long complex search strategies - limited to 100 characters

**ISRCTN** (www.isrctn.com/)

(Opioid* OR opiate* OR codeine OR oxycodone OR tramadol OR hydromorphone OR morphine OR fentanyl OR meperidine OR pethidine OR dextropropoxyphene OR methadone OR buprenorphine OR pentazocine OR hydrocodone OR butorphanol OR tapentadol OR papaveretum OR meptazinol OR dipipanone OR dihydrocodeine OR diamorphine OR co-codamol OR codydramol OR co-proxamol OR hydromorphone OR nalbuphine OR oxymorphone) AND (pain* OR neuralgi* OR myalgi* OR neuropath* OR arthriti* OR osteoarthri* OR arthralgi* OR sciatica OR headache* OR migrain*) AND (taper* OR wean* OR detox* OR withdraw* OR discontinu* OR cease OR cessation OR terminat* OR remove* OR stop* OR substitut* OR deprescri*) Limit to adult

**NIHR be part of research** (https://bepartofresearch.nihr.ac.uk/)

Opioid or opioids or opiate or opiates or codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or codydramol or co-proxamol or hydromorphone or nalbuphine or oxymorphone

## Adverse events review

### MEDLINE

Database: Ovid MEDLINE(R) ALL <1946–6 January 2021>

1. Analgesics, Opioid/
2. exp Buprenorphine/
3. exp Codeine/
4. exp Dextropropoxyphene/
5. exp Fentanyl/
6. exp Hydrocodone/
7. exp Hydromorphone/
8. exp Meperidine/
9. exp Meptazinol/
10. exp Methadone/
11. exp Morphine/
12. exp Nalbuphine/
13. exp Opiate Alkaloids/
14. exp Oxycodone/
15. exp Oxymorphone/
16. exp Pentazocine/
17. exp Tapentadol/
18. exp Tramadol/
19. (opioid* or opiate*).mp.

20. (codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or co-dydramol or co-proxamol or hydromorphone or nalbuphine or oxymorphone).mp.
21. or/1-20
22. Opiate Substitution Treatment/
23. (taper* or wean* or detox* or withdraw* or discontinu* or cease or cessation or terminat* or remove* or stop* or substitut* or deprescri*).mp.
24. ((dose or dosage or medicine* or medication) adj1 (reduc* or consumption or lower* or decreas*)).mp.
25. (("opiate use" or "opioid use" or OLM) adj3 (reduc* or change* or decreas*)).mp.
26. or/22-25
27. exp Pain/
28. exp Arthritis/
29. Fibromyalgia/
30. exp Headache Disorders/
31. pain*.mp.
32. (neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*).mp.
33. or/27-32
34. 21 and 26 and 33
35. exp animals/
36. humans.sh.
37. 35 not 36
38. 34 not 37
39. limit 38 to english language
40. letter.pt.
41. editorial.pt.
42. comment.pt.
43. clinical conference.pt.
44. consensus development conference nih.pt.
45. consensus development conference.pt.
46. congress.pt.
47. review.pt.
48. or/40-47
49. 39 not 48
50. limit 49 to "all adult (19 plus years)"
51. adult*.mp.
52. 49 and 51
53. 50 or 52
54. limit 53 to yr="2000 -Current"
55. "Drug-Related Side Effects and Adverse Reactions"/
56. exp Product Surveillance, Postmarketing/
57. Drug Monitoring/
58. exp Drug Eruptions/
59. Abnormalities, Drug-Induced/
60. ae.fs.
61. co.fs.
62. to.fs.
63. ci.fs.
64. (adverse adj2 (interaction$ or response$ or effect$ or event$ or reaction$ or outcome$)).mp.
65. (unintended adj2 (interaction$ or response$ or effect$ or event$ or reaction$ or outcome$)).mp.
66. (unintentional adj2 (interaction$ or response$ or effect$ or event$ or reaction$ or outcome)).mp.
67. (unwanted adj2 (interaction$ or response$ or effect$ or event$ or reaction$ or outcome$)).mp
68. (unexpected adj2 (interaction$ or response$ or effect$ or event$ or reaction$ or outcome$)).mp.

69. (undesirable adj2 (interaction$ or response$ or effect$ or event$ or reaction$ or outcome$)).mp.
70. (serious adj2 (interaction$ or response$ or effect$ or event$ or reaction$ or outcome$)).mp.
71. (toxic adj2 (interaction$ or response$ or effect$ or event$ or reaction$ or outcome$)).mp.
72. (adrs or ades).mp.
73. side effect$.mp.
74. complication$.mp.
75. pharmacovigilance.mp.
76. (harm or harms or harmful).mp.
77. tolerability.mp.
78. ((drug or product or postmarketing or post marketing) adj2 surveillance).mp.
79. ((drug or product) adj2 monitoring).mp.
80. safe.mp.
81. safety.mp.
82. toxicity.mp.
83. Substance-related disorders/
84. Substance withdrawal syndrome/
85. mo.fs.
86. or/55-85
87. exp animals/ not humans.sh.
88. 86 not 87
89. 54 and 88

**EMBASE** (Ovid 1974–6 January 2021)

1. exp opiate/
2. narcotic analgesic agent/
3. exp buprenorphine/
4. exp codeine/
5. exp dextropropoxyphene/
6. exp fentanyl/
7. exp hydrocodone/
8. exp hydromorphone/
9. exp pethidine/
10. exp meptazinol/
11. exp methadone/
12. exp morphine/
13. exp nalbuphine/
14. exp oxycodone/
15. exp oxymorphone/
16. exp pentazocine/
17. exp tapentadol/
18. exp tramadol/
19. exp butorphanol/
20. exp dipipanone/
21. exp dihydrocodeine/
22. exp diamorphine/
23. exp cocodamol/
24. exp codydramol/
25. exp dextropropoxyphene plus paracetamol/
26. (opioid* or opiate*).mp.
27. (codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol

or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or co-dydramol or co-proxamol or hydromorphone or nalbuphine or oxymorphone).mp.
28. or/1-27
29. exp drug detoxification/
30. exp drug withdrawal/
31. exp drug substitution/
32. exp deprescription/
33. (taper* or wean* or detox* or withdraw* or discontinu* or cease or cessation or terminat* or remove* or stop* or substitut* or deprescri*).mp.
34. ((dose or dosage or medicine* or medication) adj1 (reduc* or consumption or lower* or decreas*)).mp.
35. (("opiate use" or "opioid use" or OLM) adj3 (reduc* or change* or decreas*)).mp.
36. or/29-35
37. exp Pain/
38. exp arthritis/
39. fibromyalgia/
40. exp "headache and facial pain"/
41. pain*.mp.
42. (neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*).mp.
43. or/37-42
44. 28 and 36 and 43
45. exp animal/ or exp nonhuman/ or exp animal experiment/ or exp animal model/
46. human/
47. 45 not 46
48. 44 not 47
49. limit 48 to (books or chapter or conference abstract or conference paper or "conference review" or editorial or letter or note or review)
50. 48 not 49
51. limit 50 to english language
52. limit 51 to (adult <18 to 64 years> or aged <65+ years>)
53. adult*.mp.
54. 51 and 53
55. 52 or 54
56. limit 55 to yr="2000 -Current"
57. exp Adverse Drug Reaction/
58. exp Drug Eruption/
59. Drug Fatality/
60. Drug Fever/
61. exp Drug Hypersensitivity/
62. exp Drug Induced Disease/
63. Unspecified Side Effect/
64. Drug Surveillance Program/
65. Postmarketing Surveillance/
66. Drug Induced Malformation/
67. adverse drug reaction.fs.
68. complication.fs.
69. drug interaction.fs.
70. drug toxicity.fs.
71. side effect.fs.
72. (adverse adj2 (interaction$ or response$ or effect$ or event$ or reaction$ or outcome$)).mp.
73. (unintended adj2 (interaction$ or response$ or effect$ or event$ or reaction$ or outcome$)).mp.
74. (unintentional adj2 (interaction$ or response$ or effect$ or event$ or reaction$ or outcome)).mp.
75. (unwanted adj2 (interaction$ or response$ or effect$ or event$ or reaction$ or outcome$)).mp.
76. (unexpected adj2 (interaction$ or response$ or effect$ or event$ or reaction$ or outcome$)).mp.

77. (undesirable adj2 (interaction$ or response$ or effect$ or event$ or reaction$ or outcome$)).mp.
78. (serious adj2 (interaction$ or response$ or effect$ or event$ or reaction$ or outcome$)).mp.
79. (toxic adj2 (interaction$ or response$ or effect$ or event$ or reaction$ or outcome$)).mp.
80. (adrs or ades).mp.
81. side effect$.mp.
82. complication$.mp.
83. pharmacovigilance.mp.
84. (harm or harms or harmful).mp.
85. tolerability.mp.
86. ((drug or product or postmarketing or post marketing) adj2 surveillance).mp.
87. ((drug or product) adj2 monitoring).mp.
88. safe.mp.
89. safety.mp.
90. toxicity.mp.
91. or/57-90
92. (exp animal/or exp nonhuman/or exp animal experiment/or exp animal model/) not exp human/
93. 91 not 92
94. 56 and 93

**CENTRAL**

Cochrane Central Register of Controlled Trials

Issue 1 of 12, January 2021

#1 MeSH descriptor: [Analgesics, Opioid] this term only
#2 MeSH descriptor: [Buprenorphine] explode all trees
#3 MeSH descriptor: [Codeine] explode all trees
#4 MeSH descriptor: [Dextropropoxyphene] explode all trees
#5 MeSH descriptor: [Fentanyl] explode all trees
#6 MeSH descriptor: [Hydrocodone] explode all trees
#7 MeSH descriptor: [Hydromorphone] explode all trees
#8 MeSH descriptor: [Meperidine] explode all trees
#9 MeSH descriptor: [Meptazinol] explode all trees
#10 MeSH descriptor: [Methadone] explode all trees
#11 MeSH descriptor: [Morphine] explode all trees
#12 MeSH descriptor: [Nalbuphine] explode all trees
#13 MeSH descriptor: [Opiate Alkaloids] explode all trees
#14 MeSH descriptor: [Oxycodone] explode all trees
#15 MeSH descriptor: [Oxymorphone] explode all trees
#16 MeSH descriptor: [Pentazocine] explode all trees
#17 MeSH descriptor: [Tapentadol] explode all trees
#18 MeSH descriptor: [Tramadol] explode all trees
#19 opioid* or opiate*
#20 codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or co-dydramol or co-proxamol or hydromorphone or nalbuphine or oxymorphone
#21 25-#20
#22 MeSH descriptor: [Opiate Substitution Treatment] explode all trees
#23 taper* or wean* or detox* or withdraw* or discontinu* or cease or cessation or terminat* or remove* or stop* or substitut* or deprescri*
#24 (dose or dosage or medicine* or medication) NEAR/1 (reduc* or consumption or lower* or decreas*)

#25 ("opiate use" or "opioid use" or OLM) NEAR/3 (reduc* or change* or decreas*)
#26 142-#25
#27 MeSH descriptor: [Pain] explode all trees
#28 MeSH descriptor: [Arthritis] explode all trees
#29 MeSH descriptor: [Fibromyalgia] this term only
#30 MeSH descriptor: [Headache Disorders] explode all trees
#31 pain*
#32 neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*
#33 (OR #27-#32)
#34 #21 AND #26 AND #33 in Trials
#35 MeSH descriptor: [Animals] explode all trees
#36 MeSH descriptor: [Humans] this term only
#37 #35 not #36
#38 #34 not #37
#39 MeSH descriptor: [Drug-Related Side Effects and Adverse Reactions] explode all trees
#40 MeSH descriptor: [Product Surveillance, Postmarketing] explode all trees
#41 MeSH descriptor: [Drug Monitoring] explode all trees
#42 MeSH descriptor: [Drug Eruptions] explode all trees
#43 MeSH descriptor: [Abnormalities, Drug-Induced] explode all trees
#44 (adverse NEAR/2 (interaction* or response* or effect* or vent* or reaction* or outcome*)):ti,ab,kw
#45 (unintended near/2 (interaction* or response* or effect* or event* or reaction* or outcome*)):ti,ab,kw
#46 (unintentional near/2 (interaction* or response* or effect* or event* or reaction* or outcome*)):ti,ab,kw
#47 (unwanted near/2 (interaction* or response* or effect* or event* or reaction* or outcome*)):ti,ab,kw
#48 (unexpected near/2 (interaction* or response* or effect* or event* or reaction* or outcome*)):ti,ab,kw
#49 (undesirable near/2 (interaction* or response* or effect* or event* or reaction* or outcome*)):ti,ab,kw
#50 (serious near/2 (interaction* or response* or effect* or event* or reaction* or outcome*)):ti,ab,kw
#51 (toxic near/2 (interaction* or response* or effect* or event* or reaction* or outcome*)):ti,ab,kw
#52 ((adrs or ades or "side effect*" or complication* or pharmacovigilance or harm or harms or harmful)):ti,ab,kw
#53 (tolerability or ((drug or product or postmarketing or post marketing) near/2 surveillance) or ((drug or product) near/2 monitoring) or safe or safety or toxicity):ti,ab,kw
#54 (OR #39-#53)
#55 #38 AND #54 in Trials

**CINAHL (EBSCO)**

S1 (MH "Analgesics, Opioid")
S2 (MH "Buprenorphine")
S3 (MH "Codeine+")
S4 (MH "Propoxyphene")
S5 (MH "Fentanyl+")
S6 (MM "Dihydromorphinone")
S7 (MH "Meperidine")
S8 (MH "Methadone")
S9 (MH "Morphine+")
S10 (MH "Nalbuphine")
S11 (MH "Oxycodone")
S12 (MH "Pentazocine")
S13 (MH "Tramadol")
S14 (MH "Butorphanol")
S15 TI (opioid* or opiate*) OR AB (opioid* or opiate*) OR SU (opioid* or opiate*)
S16 TI (codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or co-dydramol

or co-proxamol or hydromorphone or nalbuphine or oxymorphone) OR AB (codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or co-dydramol or co-proxamol or hydromorphone or nalbuphine or oxymorphone) OR SU (codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or co-dydramol or co-proxamol or hydromorphone or nalbuphine or oxymorphone)

S17 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16

S18 (MH "Substance Withdrawal, Controlled")

S19 TI (taper* or wean* or detox* or withdraw* or discontinu* or cease or cessation or terminat* or remove* or stop* or substitut* or deprescri*) OR AB (taper* or wean* or detox* or withdraw* or discontinu* or cease or cessation or terminat* or remove* or stop* or substitut* or deprescri*) OR SU (taper* or wean* or detox* or withdraw* or discontinu* or cease or cessation or terminat* or remove* or stop* or substitut* or deprescri*)

S20 TI (((dose or dosage or medicine* or medication) N1 (reduc* or consumption or lower* or decreas*))) OR AB (((dose or dosage or medicine* or medication) N1 (reduc* or consumption or lower* or decreas*))) OR SU (((dose or dosage or medicine* or medication) N1 (reduc* or consumption or lower* or decreas*)))

S21 TI ((("opiate use" or "opioid use" or OLM) N3 (reduc* or change* or decreas*))) OR AB ((("opiate use" or "opioid use" or OLM) N3 (reduc* or change* or decreas*))) OR SU ((("opiate use" or "opioid use" or OLM) N3 (reduc* or change* or decreas*)))

S22 S18 OR S19 OR S20 OR S21

S23 (MH "Pain+")

S24 (MH "Arthritis+")

S25 (MH "Fibromyalgia")

S26 (MH "Headache+")

S27 TI pain* OR AB pain* OR SU pain*

S28 TI (neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*) OR AB (neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*) OR SU (neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*)

S29 S23 OR S24 OR S25 OR S26 OR S27 OR S28

S30 S17 AND S22 AND S29

S31 (MH "Animals+")

S32 (MH "Human")

S33 S31 not S32

S34 S30 NOT S33

S35 PT book OR PT book chapter OR PT book review OR PT commentary OR PT doctoral dissertation OR PT editorial OR PT letter OR PT proceedings OR PT review

S36 S34 NOT S35

S37 S34 NOT S35Limiters - Publication Year: 2000-2020, Narrow by Language: - English, Narrow by SubjectAge: - all adult

S38 (MH "Adverse Drug Event+")

S39 (MH "Abnormalities, Drug-Induced")

S40 TX adverse N2 (interaction* or response* or effect* or event* or reaction* or outcome*)

S41 TX unintended N2 (interaction* or response* or effect* or event* or reaction* or outcome*)

S42 TX unintentional N2 (interaction* or response* or effect* or event* or reaction* or outcome*)

S43 TX unwanted N2 (interaction* or response* or effect* or event* or reaction* or outcome*)

S44 TX unexpected N2 (interaction* or response* or effect* or event* or reaction* or outcome*) OR TX undesirable N2 (interaction* or response* or effect* or event* or reaction* or outcome*)

S45 TX serious N2 (interaction* or response* or effect* or event* or reaction* or outcome*)

S46 TX toxic N2 (interaction* or response* or effect* or event* or reaction* or outcome*)

S47 TX (adrs or ades) OR TX side effect* OR TX complication* OR TX pharmacovigilance OR TX (harm or harms or harmful) OR TX tolerability
S48 TX ((drug or product or postmarketing or post marketing) N2 surveillance) OR TX ((drug or product) N2 monitoring) OR TX safe OR TX safety OR TX toxicity
S49 (MH "Pharmacovigilance")
S50 S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49
S51 S37 AND S50

**PsycInfo® (American Psychological Association, Washington, DC, USA) (EBSCO)**

S1 DE "Opiates" OR DE "Buprenorphine" OR DE "Codeine" OR DE "Endogenous Opiates" OR DE "Fentanyl" OR DE "Morphine" OR DE "Oxycodone"
S2 DE "Meperidine"
S3 DE "Methadone"
S4 DE "Morphine"
S5 DE "Pentazocine"
S6 DE "Tramadol"
S7 TI (opioid* or opiate*) OR AB (opioid* or opiate*) OR SU (opioid* or opiate*)
S8 TI (codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or codydramol or co-proxamol or hydromorphone or nalbuphine or oxymorphone) or AB (codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or codydramol or co-proxamol or hydromorphone or nalbuphine or oxymorphone) OR SU (codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or codydramol or co-proxamol or hydromorphone or nalbuphine or oxymorphone)
S9 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8
S10 DE "Drug Withdrawal"
S11 TI (taper* or wean* or detox* or withdraw* or discontinu* or cease or cessation or terminat* or remove* or stop* or substitut* or deprescri*) OR AB (taper* or wean* or detox* or withdraw* or discontinu* or cease or cessation or terminat* or remove* or stop* or substitut* or deprescri*) OR SU (taper* or wean* or detox* or withdraw* or discontinu* or cease or cessation or terminat* or remove* or stop* or substitut* or deprescri*)
S12 TI ((dose or dosage or medicine* or medication) N1 (reduc* or consumption or lower* or decreas*)) OR AB ((dose or dosage or medicine* or medication) N1 (reduc* or consumption or lower* or decreas*)) OR SU ((dose or dosage or medicine* or medication) N1 (reduc* or consumption or lower* or decreas*))
S13 TI (("opiate use" or "opioid use" or OLM) N3 (reduc* or change* or decreas*)) OR AB (("opiate use" or "opioid use" or OLM) N3 (reduc* or change* or decreas*)) OR SU (("opiate use" or "opioid use" or OLM) N3 (reduc* or change* or decreas*))
S14 S10 OR S11 OR S12 OR S13
S15 DE "Pain" OR DE "Aphagia" OR DE "Back Pain" OR DE "Chronic Pain" OR DE "Headache" OR DE "Myofascial Pain" OR DE "Neuralgia" OR DE "Neuropathic Pain" OR DE "Somatoform Pain Disorder"
S16 DE "Arthritis" OR DE "Rheumatoid Arthritis"
S17 DE "Fibromyalgia"
S18 TI (pain*) OR AB (pain*) OR SU (pain*)
S19 TI (neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*) OR AB (neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*) OR SU (neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*)
S20 S15 OR S16 OR S17 OR S18 OR S19
S21 S9 AND S14 AND S20

S22 PO animal NOT PO human
S23 S21 NOT S22
S24 PZ (Column/Opinion OR Comment/Reply OR Dissertation OR Editorial OR Letter OR Review-Any)
S25 S23 NOT S24
S26 S23 NOT S24Limiters - Published: 20000101-20211231, Narrow by SubjectAge: - adulthood (18 yrs & older), Narrow by Language: - english
S27 DE "Side Effects (Drug)" OR DE "Drug Addiction" OR DE "Drug Allergies" OR DE "Drug Dependency" OR DE "Drug Sensitivity"
S28 DE "Drug Interactions"
S29 DE "Monitoring"
S30 TX adverse N2 (interaction* or response* or effect* or event* or reaction* or outcome*)
S31 TX unintended N2 (interaction* or response* or effect* or event* or reaction* or outcome*)
S32 TX unintentional N2 (interaction* or response* or effect* or event* or reaction* or outcome*)
S33 TX unwanted N2 (interaction* or response* or effect* or event* or reaction* or outcome*)
S34 TX unexpected N2 (interaction* or response* or effect* or event* or reaction* or outcome*)
S35 TX undesirable N2 (interaction* or response* or effect* or event* or reaction* or outcome*)
S36 TX serious N2 (interaction* or response* or effect* or event* or reaction* or outcome*)
S37 TX toxic N2 (interaction* or response* or effect* or event* or reaction* or outcome*)
S38 TX (adrs or ades) OR TX side effect* OR TX complication* OR TX pharmacovigilance OR TX (harm or harms or harmful) OR TX tolerability
S39 TX ((drug or product or postmarketing or post marketing) N2 surveillance) OR TX ((drug or product) N2 monitoring) OR TX safe OR TX safety OR TX toxicity
S40 S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39
S41 S26 AND S40

**Science Citation Index (Web of Science)**

# 35 #32 AND #8 Refined by: [excluding] PUBLICATION YEARS: (1997 OR 1996 OR 1995 OR 1994 OR 1993 OR 1992 OR 1999 OR 1991 OR 1998 OR 1990) AND [excluding] DOCUMENT TYPES: (MEETING ABSTRACT OR REVIEW OR EDITORIAL MATERIAL OR LETTER OR PROCEEDINGS PAPER)
Indexes=SCI-EXPANDED Timespan=All years
# 34 #32 AND #8 Refined by: [excluding] PUBLICATION YEARS: (1997 OR 1996 OR 1995 OR 1994 OR 1993 OR 1992 OR 1999 OR 1991 OR 1998 OR 1990)
# 33 #32 AND #8
# 32 #31 OR #30 OR #29 OR #28 OR #27 OR #26 OR #25 OR #24 OR #23 OR #22 OR #21 OR #20 OR #19 OR #18 OR #17 OR #16 OR #15 OR #14 OR #13 OR #12 OR #11 OR #10 OR #9
# 31 TOPIC: (("drug induced malformation"))
# 30 TOPIC: (("drug induced disease*"))
# 29 TS=((drug NEAR/2 (eruption or fatality or fever or hypersensitivity)))
# 28 TOPIC: ((toxicity))
# 27 TOPIC: ((safety))
# 26 TOPIC: ((safe))
# 25 TS=(((drug or product) NEAR/2 recall))
# 24 TS=(((drug or product) NEAR/2 monitoring))
# 23 TS=(((drug or product or postmarketing or "post marketing") NEAR/2 surveillance))
# 22 TOPIC: ((tolerability))
# 21 TOPIC: ((harm or harms or harmful))
# 20 TOPIC: ((pharmacovigilance))
# 19 TOPIC: ((complication*))
# 18 TOPIC: (("side effect*"))
# 17 TOPIC: ((adrs or ades))
# 16 TOPIC: ((toxic NEAR/2 (interaction* or response* or effect* or event* or reaction* or outcome*)))
# 15 TOPIC: ((serious NEAR/2 (interaction* or response* or effect* or event* or reaction* or outcome*)))

# 14 TOPIC: ((undesirable NEAR/2 (interaction* or response* or effect* or event* or reaction* or outcome*)))
# 13 TOPIC: ((unexpected NEAR/2 (interaction* or response* or effect* or event* or reaction* or outcome*)))
# 12 TOPIC: ((unwanted NEAR/2 (interaction* or response* or effect* or event* or reaction* or outcome*)))
# 11 424 TOPIC: ((unintentional NEAR/2 (interaction* or response* or effect* or event* or reaction* or outcome*)))
# 10 TOPIC: ((unintended NEAR/2 (interaction* or response* or effect* or event* or reaction* or outcome*)))
# 9 TOPIC: ((adverse NEAR/2 (interaction* or response* or effect* or event* or reaction* or outcome*))) # 8 #7 AND #6
# 7 TOPIC: (pain* or neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*)
# 6 #5 AND #1
# 5 #4 OR #3 OR #2
# 4 TOPIC: (((“opiate use” or “opioid use” or OLM) NEAR/3 (reduc* or change* or decreas*)))
# 3 TOPIC: (((dose or dosage or medicine* or medication) NEAR/1 (reduc* or consumption or lower* or decreas*)))
# 2 TOPIC: (taper* or wean* or detox* or withdraw* or discontinu* or cease or cessation or terminat* or remove* or stop* or substitut* or deprescri*)
# 1 TOPIC: (opioid* or opiate* or codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or codydramol or co-proxamol or hydromorphone or nalbuphine or oxymorphone)

## Barriers and facilitators review (Review 2)

**MEDLINE** (Ovid MEDLINE(R) ALL < 1946–20 September 2022 >)

1 Analgesics, Opioid/ (46,162)
2 exp Buprenorphine/ (5552)
3 exp Codeine/ (7135)
4 exp Dextropropoxyphene/ (1465)
5 exp Fentanyl/ (16,036)
6 exp Hydrocodone/ (637)
7 exp Hydromorphone/ (1322)
8 exp Meperidine/ (5790)
9 exp Meptazinol/ (187)
10 exp Methadone/ (12,563)
11 exp Morphine/ (38,403)
12 exp Nalbuphine/ (689)
13 exp Opiate Alkaloids/ (87,073)
14 exp Oxycodone/ (2351)
15 exp Oxymorphone/ (497)
16 exp Pentazocine/ (2234)
17 exp Tapentadol/ (327)
18 exp Tramadol/ (3196)
19 (opioid* or opiate*).mp. (138,261)
20 (codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or codydramol or co-proxamol or hydromorphone or nalbuphine or oxymorphone).mp. (119,899)
21 or/1-20 (218,530)
22 Opiate Substitution Treatment/ (3266)
23 (taper* or wean* or detox* or withdraw* or discontinu* or cease or cessation or terminat* or remove* or stop* or substitut* or deprescri*).mp. (1,348,899)
24 ((dose or dosage or medicine* or medication) adj1 (reduc* or consumption or lower* or decreas*)).mp. (39,564)

25 (("opiate use" or "opioid use" or OLM) adj3 (reduc* or change* or decreas*)).mp. (1162)
26 or/22-25 (1,382,888)
27 exp Pain/ (402,869)
28 exp Arthritis/ (263,296)
29 Fibromyalgia/ (8582)
30 exp Headache Disorders/ (35,118)
31 pain*.mp. (813,659)
32 (neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*).mp. (603,586)
33 or/27-32 (1,381,008)
34 21 and 26 and 33 (8554)
35 exp animals/ (23,717,900)
36 humans.sh. (18,943,220)
37 35 not 36 (4,774,680)
38 34 not 37 (6694)
39 limit 38 to english language (6193)
40 letter.pt. (1,116,589)
41 editorial.pt. (553,178)
42 comment.pt. (885,663)
43 clinical conference.pt. (7420)
44 consensus development conference nih.pt. (790)
45 consensus development conference.pt. (11,887)
46 congress.pt. (66,493)
47 review.pt. (2,744,229)
48 or/40-48 (6,504,602)
49 39 not 49 (4525)
50 limit 50 to "qualitative (maximizes sensitivity)" (1729)
51 barrier*.mp. (326,342)
52 facilitat*.mp. (558,610)
53 qualitative.mp. (261,594)
54 51 or 52 or 53 (1,075,573)
55 49 and 54 (269)
56 50 or 55 (1847)
57 limit 56 to yr="2000 -Current" (1704)

Notes

1. Adapted qualitative search filter applied – barrier* or facilitator* or qualitative free-text terms added.

**EMBASE** (Ovid 1974– 20 September 2022)

1. exp opiate/
2. narcotic analgesic agent/
3. exp buprenorphine/
4. exp codeine/
5. exp dextropropoxyphene/
6. exp fentanyl/
7. exp hydrocodone/
8. exp hydromorphone/
9. exp pethidine/
10. exp meptazinol/
11. exp methadone/
12. exp morphine/

13. exp nalbuphine/
14. exp oxycodone/
15. exp oxymorphone/
16. exp pentazocine/
17. exp tapentadol/
18. exp tramadol/
19. exp butorphanol/
20. exp dipipanone/
21. exp dihydrocodeine/
22. exp diamorphine/
23. exp cocodamol/
24. exp codydramol/
25. exp dextropropoxyphene plus paracetamol/
26. (opioid* or opiate*).mp.
27. (codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or co-dydramol or co-proxamol or hydromorphone or nalbuphine or oxymorphone).mp.
28. or/1-27
29. exp drug detoxification/
30. exp drug withdrawal/
31. exp drug substitution/
32. exp deprescription/
33. (taper* or wean* or detox* or withdraw* or discontinu* or cease or cessation or terminat* or remove* or stop* or substitut* or deprescri*).mp.
34. ((dose or dosage or medicine* or medication) adj1 (reduc* or consumption or lower* or decreas*)).mp.
35. (("opiate use" or "opioid use" or OLM) adj3 (reduc* or change* or decreas*)).mp.
36. or/29-35
37. exp Pain/
38. exp arthritis/
39. fibromyalgia/
40. exp "headache and facial pain"/
41. pain*.mp.
42. (neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*).mp.
43. or/37-42
44. 28 and 36 and 43
45. exp animal/or exp nonhuman/or exp animal experiment/or exp animal model/
46. human/
47. 45 not 46
48. 44 not 47
49. limit 48 to (books or chapter or conference abstract or conference paper or "conference review" or editorial or letter or note or review)
50. 48 not 49
51. limit 50 to english language
52. limit 51 to "qualitative (maximizes sensitivity)"
53. barrier*.mp.
54. facilitat*.mp.
55. qualitative.mp.
56. 53 or 54 or 55
57. 51 and 56
58. 52 or 57
59. limit 58 to yr="2000 -Current"

1. Adapted qualitative search filter applied – barrier* or facilitator* or qualitative free-text terms added.

**CINAHL (EBSCO*host*)**

S1 (MH "Analgesics, Opioid")
S2 (MH "Buprenorphine")
S3 (MH "Codeine+")
S4 (MH "Propoxyphene")
S5 (MH "Fentanyl+")
S6 (MM "Dihydromorphinone")
S7 (MH "Meperidine")
S8 (MH "Methadone")
S9 (MH "Morphine+")
S10 (MH "Nalbuphine")
S11 (MH "Oxycodone")
S12 (MH "Pentazocine")
S13 (MH "Tramadol")
S14 (MH "Butorphanol")
S15 TI (opioid* or opiate*) OR AB (opioid* or opiate*) OR SU (opioid* or opiate*)
S16 TI (codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or co-dydramol or co-proxamol or hydromorphone or nalbuphine or oxymorphone) OR AB (codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or co-dydramol or co-proxamol or hydromorphone or nalbuphine or oxymorphone) OR SU (codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or co-dydramol or co-proxamol or hydromorphone or nalbuphine or oxymorphone)
S17 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16
S18 (MH "Substance Withdrawal, Controlled")
S19 TI (taper* or wean* or detox* or withdraw* or discontinu* or cease or cessation or terminat* or remove* or stop* or substitut* or deprescri*) OR AB (taper* or wean* or detox* or withdraw* or discontinu* or cease or cessation or terminat* or remove* or stop* or substitut* or deprescri*) OR SU (taper* or wean* or detox* or withdraw* or discontinu* or cease or cessation or terminat* or remove* or stop* or substitut* or deprescri*)
S20 TI (((dose or dosage or medicine* or medication) N1 (reduc* or consumption or lower* or decreas*))) OR AB (((dose or dosage or medicine* or medication) N1 (reduc* or consumption or lower* or decreas*))) OR SU (((dose or dosage or medicine* or medication) N1 (reduc* or consumption or lower* or decreas*)))
S21 TI ((("opiate use" or "opioid use" or OLM) N3 (reduc* or change* or decreas*))) OR AB ((("opiate use" or "opioid use" or OLM) N3 (reduc* or change* or decreas*))) OR SU ((("opiate use" or "opioid use" or OLM) N3 (reduc* or change* or decreas*)))
S22 S18 OR S19 OR S20 OR S21
S23 (MH "Pain+")
S24 (MH "Arthritis+")
S25 (MH "Fibromyalgia")
S26 (MH "Headache+")
S27 TI pain* OR AB pain* OR SU pain*
S28 TI (neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*) OR AB (neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*) OR SU (neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*)
S29 S23 OR S24 OR S25 OR S26 OR S27 OR S28
S30 S17 AND S22 AND S29

S31 (MH "Animals+")
S32 (MH "Human")
S33 S31 not S32
S34 S30 NOT S33
S35 PT book OR PT book chapter OR PT book review OR PT commentary OR PT doctoral dissertation OR PT editorial OR PT letter OR PT proceedings OR PT review
S36 S34 NOT S35
S37 S34 NOT S35Limiters - Publication Year: 2000-2021; English Language; Clinical Queries: Qualitative - High Sensitivity
S38 TI (barrier* or facilitat* or qualitative) OR AB (barrier* or facilitat* or qualitative) OR SU (barrier* or facilitat* or qualitative)Limiters - Publication Year: 2000-2021; English Language
S39 S36 AND S38
S40 S37 OR S39

**PsycInfo (EBSCO*host*)**

S1 DE "Opiates" OR DE "Buprenorphine" OR DE "Codeine" OR DE "Endogenous Opiates" OR DE "Fentanyl" OR DE "Morphine" OR DE "Oxycodone"
S2 DE "Meperidine"
S3 DE "Methadone"
S4 DE "Morphine"
S5 DE "Pentazocine"
S6 DE "Tramadol"
S7 TI (opioid* or opiate*) OR AB (opioid* or opiate*) OR SU (opioid* or opiate*)
S8 TI (codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or codydramol or co-proxamol or hydromorphone or nalbuphine or oxymorphone) or AB (codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or codydramol or co-proxamol or hydromorphone or nalbuphine or oxymorphone) OR SU (codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or codydramol or co-proxamol or hydromorphone or nalbuphine or oxymorphone)
S9 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8
S10 DE "Drug Withdrawal"
S11 TI (taper* or wean* or detox* or withdraw* or discontinu* or cease or cessation or terminat* or remove* or stop* or substitut* or deprescri*) OR AB (taper* or wean* or detox* or withdraw* or discontinu* or cease or cessation or terminat* or remove* or stop* or substitut* or deprescri*) OR SU (taper* or wean* or detox* or withdraw* or discontinu* or cease or cessation or terminat* or remove* or stop* or substitut* or deprescri*)
S12 TI ((dose or dosage or medicine* or medication) N1 (reduc* or consumption or lower* or decreas*)) OR AB ((dose or dosage or medicine* or medication) N1 (reduc* or consumption or lower* or decreas*)) OR SU ((dose or dosage or medicine* or medication) N1 (reduc* or consumption or lower* or decreas*))
S13 TI (("opiate use" or "opioid use" or OLM) N3 (reduc* or change* or decreas*)) OR AB (("opiate use" or "opioid use" or OLM) N3 (reduc* or change* or decreas*)) OR SU (("opiate use" or "opioid use" or OLM) N3 (reduc* or change* or decreas*))
S14 S10 OR S11 OR S12 OR S13
S15 DE "Pain" OR DE "Aphagia" OR DE "Back Pain" OR DE "Chronic Pain" OR DE "Headache" OR DE "Myofascial Pain" OR DE "Neuralgia" OR DE "Neuropathic Pain" OR DE "Somatoform Pain Disorder"
S16 DE "Arthritis" OR DE "Rheumatoid Arthritis"
S17 DE "Fibromyalgia"
S18 TI (pain*) OR AB (pain*) OR SU (pain*)

S19 TI (neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*) OR AB (neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*) OR SU (neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*)
S20 S15 OR S16 OR S17 OR S18 OR S19
S21 S9 AND S14 AND S20
S22 PO animal NOT PO human
S23 S21 NOT S22
S24 PZ (Column/Opinion OR Comment/Reply OR Dissertation OR Editorial OR Letter OR Review-Any)
S25 S23 NOT S24
S26 S23 NOT S24Limiters - Published: 20000101-20211231; Methodology: FIELD STUDY, INTERVIEW, -Focus Group, QUALITATIVE STUDY
S27 TI (qualitative or barrier* or facilitat* or interview* or experience*) OR AB (qualitative or barrier* or facilitat* or interview* or experience*) OR SU (qualitative or barrier* or facilitat* or interview* or experience*)Limiters - Published: 20000101-20211231
S28 S25 AND S27
S29 S26 OR S28
S30 S26 OR S28Narrow by Language: - english

Notes

1. Qualitative filter based on maximally sensitive qualitative search strategy for PsycInfo (Ovid) by Haynes et al. with additional terms barrier* or facilitat* added http://hiru.mcmaster.ca/hiru/HIRU_Hedges_PsycINFO_Strategies.aspx

**Health Management Information Consortium** (Ovid HMIC <1979–September 2022>)

1. opiates/or morphine/or morphine derivatives/
2. (opioid* or opiate*).mp.
3. (codeine or oxycodone or tramadol or hydromorphone or morphine or fentanyl or meperidine or pethidine or dextropropoxyphene or methadone or buprenorphine or pentazocine or hydrocodone or butorphanol or tapentadol or papaveretum or meptazinol or dipipanone or dihydrocodeine or diamorphine or co-codamol or codydramol or co-proxamol or hydromorphone or nalbuphine or oxymorphone).mp.
4. 1 or 2 or 3
5. (taper* or wean* or detox* or withdraw* or discontinu* or cease or cessation or terminat* or remove* or stop* or substitut* or deprescri*).mp.
6. ((dose or dosage or medicine* or medication) adj1 (reduc* or consumption or lower* or decreas*)).mp.
7. (("opiate use" or "opioid use" or OLM) adj3 (reduc* or change* or decreas*)).mp.
8. 5 or 6 or 7
9. 4 and 8
10. exp Pain/
11. exp Arthritis/
12. exp Fibromyalgia/
13. exp Headaches/
14. pain*.mp.
15. (neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*).mp.
16. or/10-15
17. 9 and 16

**NICE Evidence Search** (searched 11 January 2021 only, source discontinued 2021)

(opioid* or opiate*) "chronic pain*" (taper* or wean* or withdraw* or discontinu* or cease or cessation or terminat* or remove* or stop* or substitut* or deprescri*) Limit to 2000-, Secondary evidence, Primary Evidence, Safety alerts, Case Studies, Ongoing Trials

1. Doesn't accept long complex search strategies, short targeted search required

## Websites/Internet

**Google Scholar** (https://scholar.google.com/)

allintitle: opioid tapering "chronic pain" Limit to date 2000-2021
allintitle: opioid taper "chronic pain" Limit to date 2000-2021
allintitle: opioid tapered "chronic pain" Limit to date 2000-2021
allintitle: opioids tapering "chronic pain" Limit to date 2000-2021
allintitle: opioids taper "chronic pain" Limit to date 2000-2021
allintitle: opioids tapered "chronic pain" Limit to date 2000-2021
allintitle: opioids withdrawal "chronic pain"
allintitle: opioid withdrawal "chronic pain"

**CORE.ac.uk**

Advanced search in title field
Search 1:
All words (opioid*)
Exact phrase (Chronic pain)
At least one word (taper* wean* withdraw* discontinu* cease cessation terminat* remove* stop* substitut* deprescri*)
Search 2:
All words (opiate*)
Exact phrase (Chronic pain)
At least one word (taper* wean* withdraw* discontinu* cease cessation terminat* remove* stop* substitut* deprescri*)

Notes

1. Short targeted searches accepted only – cannot narrow down simple Boolean searches.

# **Appendix 2** Data extraction for effectiveness and adverse events review (Review 1)

We extracted the following information:

- Research question
- Author year
- Brief intervention description
- Brief comparator description
- Design
- Number of arms
- Setting
- Country
- Recruitment period
- Funding
- Conflicts of interest
- Duration of intervention
- Timing of assessments
- Outcome measures
- Sample size
- Number in intervention group 1
- Number in comparator group
- Inclusion criteria
- Exclusion criteria
- Number of females
- Number of males
- Age years: mean, standard deviation, median, lowest, highest
- Type of chronic pain
- Duration of chronic pain: mean, standard deviation, median, lowest, highest
- Types of opioids
- Duration of opioid use: mean, standard deviation, median, lowest, highest
- Level of opioid use: mean, standard deviation, median, lowest, highest
- Concomitant medications
- Outcome type
- Definition of outcome
- Baseline value intervention group 1
- Baseline value comparator group
- Outcome time point
- End of intervention value group 1
- End of intervention value comparator group
- Test
- Value
- *p*-value
- Significant
- Longer outcome definition
- Longer outcome value group 1
- Stats test
- Test value
- *p*-value 2

- Significant 2
- Notes
- AE outcomes types
- AE outcomes assessed how
- Longer outcome value comparator group

# **Appendix 3** Data extraction for barriers and facilitators review (Review 2)

We extracted the following information:

- Author
- Year
- Country
- Aim (overall)
- Study design
- Theory (theory that informs the study)
- Setting (e.g. primary care, secondary care)
- Perspective (e.g. patient, healthcare professional, etc.)
- Sample size
- Method of data collection relevant to our review [method used to obtain information on barriers and facilitators, e.g. questionnaire – closed format (face-to-face)]
- Method of data analysis relevant to our review (e.g. thematic, frequency)
- Type of intervention if reported (using the Template for Intervention Description and Replication framework)
- Documented barriers/facilitators
- Source of barrier/facilitator (e.g. direct participant quote)
- Author-reported theme (if reported)
- Number of people endorsing barrier/facilitator (if reported)
- Demographic source of variation (if reported e.g. age, length of time on opioids, more/less experienced physicians)

We classified reported barriers and facilitators sources as:

- 'Author interpreted patient/provider summary if the source of the data came from a statement of the author's interpretation (e.g. 'Providers noted the importance of preparing patients both for an upcoming discussion of opioid tapering and for the implementation of an opioid taper'.)
- 'Patient quote' if the source of the data came direct from a patient (e.g. 'I feel more able to taper with the support of my family and doctor')
- 'Provider quote' if the source of the data came from a healthcare professional/GP etc. (e.g. 'I don't have the time to sit and have a proper discussion about tapering with my patient')
- 'Statistical data' if the source of the data came from statistical analysis (e.g. '35% said doctor didn't discuss tapering with them')
- Participant quotes (provider and patient) were analysed to inform CERQual judgements on data adequacy. One reviewer (MM) completed the coding for all coded data, which was then checked by a second reviewer (KE).

# **Appendix 4** Papers excluded from the reviews at data extraction

**TABLE 25** Papers excluded at data extraction and reasons for exclusion

| Reference | Reason for exclusion | Review |
|---|---|---|
| Acceptability of a primary care-based opioid and pain review service: a mixed-methods evaluation in England. *Br J Gen Pract* 2019. | Not tapering | B and F |
| Agarwal V, Louw A, Puentedura EJ. Physician-delivered pain neuroscience education for opioid tapering: a case report. *Int J Environ Res Public Health* 2020;**17**:3324. | No relevant outcomes | B and F |
| Baron MJ, McDonald PW. Significant pain reduction in chronic pain patients after detoxification from high-dose opioids. *J Opioid Manag* 2006;**2**:277–82. | Not tapering | All three |
| Becker WC, Mattocks KM, Frank JW, Bair MJ, Jankowski RL, Kerns RD, *et al.* Mixed methods formative evaluation of a collaborative care program to decrease risky opioid prescribing and increase non-pharmacologic approaches to pain management. *Addict Behav* | Not tapering | B and F |
| Bourgeois HC, Proteau RC, Vielma C, Hartung DM, Irwin AN. Evaluation of an Interdisciplinary Controlled Substance Review Committee on opioid prescribing in a community health center. *Pain Med* 2020;**21**:1840–6. | No relevant outcomes | B and F |
| Buono FD, Savage SR, Cerrito B, O'Connell J, Garakani A, Ackerman S, *et al.* Chronic pain, mood disorders and substance use: outcomes of interdisciplinary care in a residential psychiatric hospital. *J Pain Res* 2020;**13**:1515–23. | Not tapering | B and F |
| Buonora M, Perez HR, Stumph J, Allen R, Nahvi S, Cunningham CO, *et al*. Medical record documentation about opioid tapering: examining benefit-to-harm framework and patient engagement. *Pain Med* 2020;**21**:2574–82. | No relevant outcomes | B and F |
| Comerci G, Marr L, Finlay E. End stage chronic pain (ESCP): naming complex suffering in the opioid crisis era. *Am J Hosp Palliat Care* 2020:1049909120969623. | AEs not measured | AE |
| Crum IT, Karre VMM, Balasanova AA. Transitioning from intrathecal hydromorphone to sublingual buprenorphine–naloxone through microdosing: a case report. *A A Pract* 2020;**14**:e01316. | Not tapering | Effects and AE |
| Darchuk KM, Townsend CO, Rome JD, Bruce BK, Hooten WM. Longitudinal treatment outcomes for geriatric patients with chronic non-cancer pain at an interdisciplinary pain rehabilitation program. *Pain Med (Malden, Mass)* 2010;**11**:1352–64. | Length of opioid use NR | Effects |
| Del Tredici S, Iacoviello A. Use of a simple pain assessment tool in a shared decision-making approach to tapering chronic, high-dose opioids. *Cureus* 2021;**13**:e18892. | AEs not measured | AE |
| Garland EL, Hudak J, Hanley AW, Nakamura Y. Mindfulness-oriented recovery enhancement reduces opioid dose in primary care by strengthening autonomic regulation during meditation. *Am Psychol* 2020;**75**:840–52. | Not tapering | Effects |
| Garland EL, Hanley AW, Kline A, Cooperman NA. Mindfulness-oriented recovery enhancement reduces opioid craving among individuals with opioid use disorder and chronic pain in medication assisted treatment: Ecological momentary assessments from a stage 1 randomized controlled trial. *Drug Alcohol Depend* 2019;**203**:61–5. | Population – non-prescribed opioids in large proportion of participants | Effects |
| Gimbel JS, Rauck RL, Bass A, Wilson J, Pixton G, Malhotra B, *et al.* Effects of naltrexone exposure observed in two phase three studies with ALO-$0_2$, an extended-release oxycodone surrounding sequestered naltrexone. *J Opioid Manag* 2019;**15**:417-27. | Not tapering | Effects and AE |
| Goodman MW, Guck TP, Teply RM. Dialing back opioids for chronic pain one conversation at a time. *J Fam Pract* 2018;**67**:753–7. | Length of opioid use NR | Effects |
| Grus I, Firemark A, Mayhew M, McMullen CK, DeBar LL. Taking opioids in times of crisis: institutional oversight, chronic pain and suffering in an integrated healthcare delivery system in the U.S. *Int J Drug Policy* 2019;**74**:62–8. | Not tapering | B and F |

continued

**TABLE 25** Papers excluded at data extraction and reasons for exclusion (*continued*)

| Reference | Reason for exclusion | Review |
|---|---|---|
| Guille C, Barth KS, Mateus J, McCauley JL, Brady KT. Treatment of prescription opioid use disorder in pregnant women. *Am J Psychiat* 2017;**174**:208–14. | No relevant outcomes | B and F |
| Hassamal S, Haglund M, Wittnebel K, Danovitch I. A preoperative interdisciplinary biopsychosocial opioid reduction program in patients on chronic opioid analgesia prior to spine surgery: a preliminary report and case series. *Scand J Pain*. | AEs not measured/ reported < 25 pts | All three |
| Henry SG, Feng B, Verba S, Kravitz RL, Iosif AM. The story vs. the storyteller: factors associated with the effectiveness of brief video-recorded patient stories for promoting opioid tapering. *Health Expect* 2021;**24**:991–9. | No relevant outcomes | B and F |
| Huffman KL, Sweis GW, Gase A, Scheman J, Covington EC. Opioid use 12 months following interdisciplinary pain rehabilitation with weaning. *Pain Med (Malden, Mass)* 2013;**14**:1908–17. | Population – a proportion of patients were already weaned of opioids prior to starting the intervention (unclear how many) | Effects |
| Hundley L, Spradley S, Donelenko S. Assessment of outcomes following high-dose opioid tapering in a Veterans Healthcare System. *J Opioid Manag* 2018;**14**:89–101. | Population – 36 patients (83.7%) were prescribed methadone which is used for opioid addiction and not pain | All three |
| James J, Lai B, Witt T. Patient engagement survey regarding future double-blinded, randomized controlled trial of tapering of chronic opioid therapy. *J Prim Care Commun Health* 2019;**10**:N.PAG–N.PAG. | Wrong design | B and F |
| Johnson B, Faraone SV. Outpatient detoxification completion and one-month outcomes for opioid dependence: a preliminary study of a neuropsychoanalytic treatment in pain patients and addicted patients. *Neuropsychoanalysis* 2013;**15**:145–60. | AEs not measured | AE |
| Kapural L, Kapural M, Bensitel T, Sessler DI. Opioid-sparing effect of intravenous outpatient ketamine infusions appears short-lived in chronic-pain patients with high opioid requirements. *Pain Physician* 2010;**13**:389–94. | Not tapering | All three |
| Larance B, Campbell G, Moore T, Nielsen S, Bruno R, Lintzeris N, *et al.* Concerns and help-seeking among patients using opioids for management of chronic noncancer pain. *Pain Med* **20**:758–69. | Not tapering | B and F |
| Liebschutz JM, Xuan ZM, Shanahan CW, LaRochelle M, Keosaian J, Beers D, *et al.* Improving adherence to long-term opioid therapy guidelines to reduce opioid misuse in primary care: a cluster-randomized clinical trial. *JAMA Intern Med* **177**:1265–72. | 21 days opioids < 3 months opioids | Effects |
| McCann KS, Barker S, Cousins R, Franks A, McDaniel C, Petrany S, *et al.* Structured management of chronic nonmalignant pain with opioids in a rural primary care office. *J Am Board Fam Med* 2018;**31**:57–63. | No relevant outcomes | B and F |
| Muriel J, Margarit C, Barrachina J, Ballester P, Flor A, Morales D, *et al.* Pharmacogenetics and prediction of adverse events in prescription opioid use disorder patients. *Basic Clin Pharmacol Toxicol* 2019;**124**:439–48. | Intervention – opioid rotation followed by tapering but unclear how tapering performed | All three |
| Naylor MR, Naud S, Keefe FJ, Helzer JE. Therapeutic interactive voice response (TIVR) to reduce analgesic medication use for chronic pain management. *J Pain* 2010;**11**:1410–9. | Not tapering | Effects |
| ClinicalTrials.gov. *Discontinuation from Chronic Opioid Therapy for Pain Using a Buprenorphine Taper*. 2016. URL: https://clinicaltrials.gov/show/NCT02737826 | No relevant outcomes | All three |
| ClinicalTrials.gov. *Meditation-CBT for Opioid-Treated Chronic Low Back Pain*. 2013. URL: https://clinicaltrials.gov/show/NCT01775995 | Not tapering | All three |
| ClinicalTrials.gov. *Structured Discontinuation vs. Continued Therapy in Suboptimal and Optimal Responders to High-Dose Long-Term Opioids for Chronic Pain*. 2016. URL: https://clinicaltrials.gov/show/NCT02741076 | Terminated early due to lack of recruitment | Effects |
| Nicholas MK, Asghari A, Sharpe L, Beeston L, Brooker C, Glare P, *et al.* Reducing the use of opioids by patients with chronic pain: an effectiveness study with long-term follow-up. *Pain* 2020;**161**:509–19. | Wrong population | Effects and B and F |

**TABLE 25** Papers excluded at data extraction and reasons for exclusion (*continued*)

| Reference | Reason for exclusion | Review |
|---|---|---|
| Nilsen HK, Stiles TC, Landrø NI, Fors EA, Kaasa S, Borchgrevink PC. Patients with problematic opioid use can be weaned from codeine without pain escalation. *Acta Anaesthesiol Scand* 2010;**54**:571–9. | AEs not measured | AE |
| Ocker AC, Shah NB, Schwenk ES, Witkowski TA, Cohen MJ, Viscusi ER. Ketamine and cognitive behavioral therapy for rapid opioid tapering with sustained opioid abstinence: a case report and 1-year follow-up. *Pain Pract* 2020;**20**:95–100. | Rapid tapering | All three |
| Perez HR, Buonora M, Cunningham CO, Heo M, Starrels JL. Opioid taper is associated with subsequent termination of care: a retrospective cohort study. *J Gen Intern Med* 2020;**35**:36–42. | No relevant outcomes | Effects |
| Pullen S. Chronic pain mitigation and opioid weaning at a multidisciplinary AIDS clinic: a case report. *Rehabil Oncol* 2019;**37**:37–42. | No relevant outcomes | B and F |
| Pullen SD, Del Rio C, Brandon D, Colonna A, Denton M, Ina M, *et al.* An innovative physical therapy intervention for chronic pain management and opioid reduction among people living with HIV. *BioResearch Open Access* 2020;**9**:279–85. | AEs not measured | AE |
| Ritvo AD, Calcaterra SL, Ritvo JI. Using extended release buprenorphine injection to discontinue sublingual buprenorphine: a case series. *J Addict Med* 2020. | Not tapering | All three |
| Schumann ME, Lapid MI, Cunningham JL, Schluenz L, Gilliam WP. Treatment effectiveness and medication use reduction for older adults in interdisciplinary pain rehabilitation. *Mayo Clin Proc Innov Qual Outcomes* 2020;**4**:276–86. | Length of opioid use NR | Effects |
| Scott LJ, Kesten JM, Bache K, Hickman M, Campbell R, Pickering AE, *et al.* Evaluation of a primary care-based opioid and pain review service: a mixed-methods evaluation in two GP practices in England. *Br J Gen Pract* | Not tapering | Effects and B and F |
| Setting expectations, following orders, safety, and standardization: clinicians' strategies to guide difficult conversations about opioid prescribing. *J Gen Intern Med* 2019. | Not tapering | B and F |
| Sihota A, Smith BK, Ahmed SA, Bell A, Blain A, Clarke H, *et al.* Consensus-based recommendations for titrating cannabinoids and tapering opioids for chronic pain control. *Int J Clin Pract* 2020. | Not B and F (wrong objective) | B and F |
| Sturgeon JA, Sullivan MD, Parker-Shames S, Tauben D, Coelho P. Outcomes in long-term opioid tapering and buprenorphine transition: a retrospective clinical data analysis. *Pain Med (Malden, Mass)* 2020. | Not tapering | Effects |
| Terasaki D, Klie K. Tramadol withdrawal in the setting of buprenorphine induction: a case report. *J Addict Med* 2020;**14**:264–6. | Not tapering | Effects and AE |
| Tong ST, Hochheimer CJ, Brooks EM, Sabo RT, Jiang V, Day T, *et al.* Chronic opioid prescribing in primary care: factors and perspectives. *Ann Fam Med* 2019;**17**:200–6. | Not tapering | B and F |
| Wang H, Akbar M, Weinsheimer N, Gantz S, Schiltenwolf M. Longitudinal observation of changes in pain sensitivity during opioid tapering in patients with chronic low-back pain. *Pain Med* 2011;**12**:1720–6. | Population – analysis on 20 participants/34 (14 dropped out) so below 25 participant threshold | All three |
| White R, Hayes C, Boyes AW, Chiu S, Paul CL. General practitioners and management of chronic noncancer pain: a cross-sectional survey of influences on opioid deprescribing. *J Pain Res* 2019;**12**:467–75. | No relevant outcomes | B and F |
| White RA, Hayes C, Boyes AW, Chiu S, Paul CL. Therapeutic alternatives for supporting GPs to deprescribe opioids: a cross-sectional survey. *BJGP Open* 2018;**2**:bjgpopen18X101609. | No relevant outcomes | B and F |
| Younger J, Barelka P, Carroll I, Kaplan K, Chu L, Prasad R, *et al.* Reduced cold pain tolerance in chronic pain patients following opioid detoxification. *Pain Med (Malden, Mass)* 2008;**9**:1158–63. | AEs not measured/ reported; < 25 pts | Effects and AE |
| Ziadni M, Chen AL, Krishnamurthy P, Flood P, Stieg RL, Darnall BD. Patient-centered prescription opioid tapering in community outpatients with chronic pain: 2-to 3-year follow-up in a subset of patients. *Pain Rep* 2020;**5**:e851. | AEs not measured | AE |

B and F, barriers and facilitators; NR, not reported.

# **Appendix 5** Outcome tables for effectiveness review (Review 1)

**TABLE 26** Pain severity

| Author year | Pain scale | Intervention/ comparator | Baseline value, mean (SD) | Time point 1 | Pain intensity, mean (SD) | Test, *p*-value | Time point 2 | Pain intensity, mean (SD) | Test, *p*-value |
|---|---|---|---|---|---|---|---|---|---|
| Cunningham 2016[68] | NRS | Interdisciplinary rehabilitation programme with individualised opioid tapering (3 weeks; *N* = 55) | 7.2 (1.6) | 3 weeks (at discharge) | 5.2 (2.2) | *t*-test $p < 0.01$ | – | – | – |
| Krumova 2013[74] | NRS | Inpatient opioid tapering followed by individualised pain management (NS; *N* = 102) | 7.1 (1.8) | 22.8 (11.2) days (end of intervention); mean (SD) | 5.4 (2.1) | Cohen's *d* $p < 0.001$ | 12–24 months follow-up | 5.9 (2.3) | Cohen's *d* $p < 0.001$ |
| Townsend 2008[88] | MPI | Pain rehabilitation programme (3 weeks; *N* = 213) | 49.3 (8.6) | 3 weeks (at discharge) | 40.0 (12.9) | NR | 6 months post intervention | 39.1 (14.5) | NR |
| Panicker[79] | NS (0- to 10-point scale) | APRN-led multidisciplinary pain clinic (NS; 34) | 6.11 (2.46) | Post tapering | 3.1 (2.57) | *t*-test ($t = 4.99$, df = 28, $p < 0.0001$) | – | – | – |
| Murphy 2013[78] | NRS | Interdisciplinary pain programme with tapering using hydromorphone (3 weeks; *N* = 221) | 7.0 (1.8) | 3 weeks from entry (within 2 days of discharge) | 6.5 (1.7) | ANOVA < 0.001 | – | – | – |
| Zhou 2017[90] | VAS | Comprehensive opioid taper treatments including medication-assisted treatment using methadone: patients who successfully tapered (NS; *N* = 39) | 8.0 (1.2) | Last visit (time not specified) | 5.4 (2.6) | $p < 0.001$ | – | – | – |

continued

**TABLE 26** Pain severity (*continued*)

| Author year | Pain scale | Intervention/ comparator | Baseline value, mean (SD) | Time point 1 | Pain intensity, mean (SD) | Test, *p*-value | Time point 2 | Pain intensity, mean (SD) | Test, *p*-value |
|---|---|---|---|---|---|---|---|---|---|
| Kurita 2018[75] | VNS | 10% reduction of daily opioid dose until discontinuation (up to 6 months; *N* = 15) | 6.3 (1.8) *N* = 13 | 2–3 weeks post randomisation | 6.3 (1.6) *N* = 15 | Wilcoxon *p* = 0.245 | 4–6 weeks post randomisation | 6.5 (1.8) *N* = 10 | Wilcoxon *p* = 1.00 |
| | | Usual care (*N* = 20) | 5.4 (2.5) *N* = 19 | | 5.4 (2.3) *N* = 19 | | | 6.3 (2.5) *N* = 19 | |
| Bienek 2019[67] | NRS | Fixed starting dose (90 mg morphine/day) protocol (NS; *N* = 68) | 6.6 (1.9) | 19.7 (7.5) days (at discharge) | 6.2 (2.3) | NR | 6 weeks post discharge | 5.7 (2.4) | Wilcoxon *p* < 0.01 |
| | | Individualised starting dose (70% of patient's MED) protocol (NS; *N* = 127) | 6.3 (1.7) | 15 (4.7) days (at discharge) | 6.0 (2.0) | | | 5.4 (2.4) | Wilcoxon *p* < 0.05 |
| Zheng 2008[112] | VAS | Electroacupuncture (6 weeks; *N* = 17) | 4.6 (1.6) | 8 weeks from entry (end of intervention) | 3.8 (2.0) | ANOVA *p* = 0.960 | 20 weeks | NR | NR *p* > 0.05 |
| | | Sham electroacupuncture (6 weeks; *N* = 18) | 5.5 (1.7) | | 4.8 (1.9) | | | | |
| Zheng 2019[115,116] | VAS | Pain and medication management plan plus electroacupuncture (12 weeks; *N* = 48) | 5.0 (1.6) | 14 weeks post randomisation (end of intervention) | 5.1 (0.3) | ANCOVA *p* = 0.783 | – | – | – |
| | | Pain and medication management plan plus sham electroacupuncture (12 weeks; *N* = 29) | 5.7 (2.1) | | 5.4 (0.5) | | | | |
| | | Pain and medication management only (12 weeks; *N* = 31) | 5.7 (2.0) | | 5.8 (0.4) | | | | |

**TABLE 26** Pain severity (*continued*)

| Author year | Pain scale | Intervention/ comparator | Baseline value, mean (SD) | Time point 1 | Pain intensity, mean (SD) | Test, *p*-value | Time point 2 | Pain intensity, mean (SD) | Test, *p*-value |
|---|---|---|---|---|---|---|---|---|---|
| Jackson 2021[111] | NRS | Acupuncture and standard of care (12 months; *N* = 9) | 4.8 (1.9) | Post intervention | 5.2 (1.7) | Wilcoxon nonparametric test *p* = 0.07 | – | – | – |
| | | Standard of care (12 months; *N* = 6) | 6.2 (2.2) | | 6.9 (1.5) | | | | |
| Montgomery 2020[77] | NRS | Battlefield acupuncture (NS; *N* = 24) | 5.2 (1.89) | Immediately post-BFA treatment | 3.9 (2.07) | ANOVA *p* < 0.01 | 6 months post-BFA treatment | Mean difference = −0.2 | ANOVA *p* > 0.01 |
| | | Usual care (*N* = 23) | 7 (NR) | | 7 (NR) | ANOVA *p* > 0.01 | | 7 (NR) | ANOVA *p* > 0.01 |
| Garland 2014[69] | BPI | Mindfulness-Oriented Recovery Enhancement (8 weeks; *N* = 57) | 5.4 (1.4) | 8 weeks (end of intervention) | 4.9 (1.4) | ANCOVA *p* = 0.04 | 3 months | 4.8 (2.0) | ANCOVA *p* = 0.04 |
| | | Support group (8 weeks; *N* = 58) | 5.5 (1.5) | | 5.7 (1.6) | | | 6.1 (1.5) | |
| Sullivan 2017[113,114] | BPI | MI and CBT (22 weeks; *N* = 18) | 5.7 (1.4) | 22 weeks (end of intervention) | 4.7 (1.6) | Adjusted mean difference *p* = 0.30 | 34 weeks | 4.7 (1.8) | Adjusted mean difference *p* = 0.19 |
| | | Usual care (*N* = 17) | 6.3 (1.5) | | 5.8 (1.9) | | | 6.2 (2.6) | |

ANCOVA, analysis of covariance; ANOVA, analysis of variance; BFA, battlefield acupuncture; NRS, numerical rating scale (0–10); NS, not specified; SD, standard deviation; SE, standard error; VAS, visual analogue scale (0–10); VNS, verbal numerical scale (0–10).
a Mean (SE).

**TABLE 27** Pain interference

| Author year | Definition of outcome | Intervention/ comparator | Baseline value, mean (SD) | Time point 1 | Value, mean (SD) | Test, *p*-value | Time point 2 | Value, mean (SD) | Test, *p*-value |
|---|---|---|---|---|---|---|---|---|---|
| Cunningham 2016[68] | MPI | Interdisciplinary rehabilitation programme with individualised opioid tapering (3 weeks; *N* = 55) | 55.2 (5.3) | 3 weeks (at discharge) | 45.0 (11.9) | *t*-test two sided $p < 0.001$ | – | – | – |
| Townsend 2008[88] | MPI | Pain rehabilitation programme (3 weeks; *N* = 213) | 51.3 (9.1) | 3 weeks (at discharge) | 37.1 (12.7) | | – | – | – |
| Capano 2020[110] | PEG | Hemp extract cannabidiol (8 weeks; *N* = 97) | 6.5 (1.9) | 8 weeks (end of intervention) | 5.7 (2.0) | ANOVA 0.006 | – | – | – |
| Murphy 2013[78] | POQ-VA ADL | Interdisciplinary pain programme with tapering using hydromorphone (3 weeks; *N* = 221) | 16.1 (11.9) | 3 weeks (within 2 days of discharge) | 13.3 (11.7) | ANOVA time effect $p < 0.001$ | – | – | – |
| Garland 2014[69] | BPI | Mindfulness-Oriented Recovery Enhancement (8 weeks; *N* = 57) | 5.9 (2.2) | 8 weeks (end of intervention) | 5.2 (1.9) | ANCOVA $p = 0.003$ | 3 months | 4.60 (2.66) | ANCOVA $p = 0.005$ |
| | | Support group (8 weeks; *N* = 58) | 6.4 (2.0) | | 6.9 (1.5) | | | 6.75 (1.86) | |
| Sullivan 2017[113,114] | BPI | MI and CBT (22 weeks; *N* = 18) | 6.0 (1.9) | 22 weeks (end of intervention) | 4.6 (2.4) | Adjusted mean difference $p = 0.049$ | 34 weeks | 4.5 (2.1) | Adjusted mean difference $p = 0.05$ |
| | | Usual care (*N* = 17) | 6.6 (2.4) | | 6.4 (2.1) | | | 6.1 (2.7) | |

ANCOVA, analysis of covariance; ANOVA, analysis of variance; PEG, 3-Item scale assessing pain intensity and interference (0–10); POQ-VA, pain outcomes questionnaire-for veterans Interference in activities of daily living scale; SD, standard deviation.

**TABLE 28** Acceptability of the intervention and patient satisfaction

| Author year | Definition of outcome | Intervention/ comparator | Time point 1 | Value, *n*/*N* (%) | Test, *p*-value | Time point 2 | Value, $/*N* (%) | Test *p*-value |
|---|---|---|---|---|---|---|---|---|
| Murphy 2013[78] | Overall satisfaction (0–10) | Interdisciplinary pain programme with tapering using hydromorphone (3 weeks; *N* = 221) | 3 weeks (within 2 days of discharge) | 8.3 (2.0) | N/A | – | – | – |
| Garland 2014[69] | Treatment credibility three items based on Attitudes Towards Treatment | Mindfulness-Oriented Recovery Enhancement (8 weeks; *N* = 57) | 8-weeks (end of intervention) | 21.4 (4.0) | ANCOVA *p* = 0.08 | – | – | – |
| | | Support group (8 weeks; *N* = 58) | | 19.3 (4.9) | | – | – | – |
| Sullivan 2017[113,114] | Number of patients rated the intervention as very or extremely helpful | MI and CBT (22 weeks; *N* = 18) Usual care (*N* = 17) | 22 weeks post randomisation (end of intervention) | 13/16 (81.3) NR | N/A | 34 weeks post randomisation | 11/15 (73.3) NR | – |
| Sharp 2018[82] | Number of patients with mean satisfaction score > 9 | Clinical 'encounters' | NR | 2216/2492 (88.9) | – | – | – | – |

ANCOVA, analysis of covariance; N/A, not applicable; NR, not reported.

**TABLE 29** Emotional functioning: depression

| Author year | Definition of outcome | Intervention/comparator | Baseline value | Time point 1 | Value, mean (SD) | Test, *p*-value | Time point 2 | Value, mean (SD) | Test, *p*-value |
|---|---|---|---|---|---|---|---|---|---|
| Cunningham 2016[68] | CES-D | Interdisciplinary rehabilitation programme with individualised opioid tapering (3 weeks; *N* = 55) | 30.4 (12.8) | 3 weeks (at discharge) | 18.0 (12.6) | *t*-test $p < 0.001$ | – | – | – |
| Krumova 2013[74] | CES-D | Inpatient opioid tapering followed by individualised pain management (NS; *N* = 102) | 25.9 (11) | – | – | – | 12–24 months follow-up | 25.6 (10.9) | Cohen's *d* $p > 0.05$ |
| Laigaard 2020[76] | HADS median (IQR) | Multidisciplinary pain centre with individualised therapeutic options (NS; *N* = 51) | 4 (2–7) | Final visit: 254 (106–357) days from baseline | 3 (2–5) | Linear mixed-effects RE model $p = 0.05$ | – | – | – |
| Townsend 2008[88] | CES-D | Pain rehabilitation programme (3 weeks; *N* = 213) | 29.3 (12.4) | 3 weeks (at discharge) | 16.3 (11.7) | $p < 0.001$ | 6 months post intervention | 17.8 (13.4) | $p < 0.001$ |
| Kurita 2018[75] | HADS | 10% reduction of daily opioid dose until discontinuation (up to 6 months; *N* = 15) | 6.3 (4.9) *n* = 13 | 2–3 weeks post randomisation | 5.0 (4.7) *n* = 15 | Wilcoxon $p = 0.651$ | 4–6 weeks post randomisation | 6.4 (4.7) *n* = 11 | Wilcoxon $p = 0.856$ |
| | | Usual care (*N* = 20) | 6.2 (3.3) *n* = 19 | | 5.0 (3.3) *n* = 20 | | | 6.0 (3.7) *n* = 18 | |
| Jackson 2021[111] | HADS-D | Acupuncture and standard of care (12 months; *N* = 9) | 5.8 (5.0) | Post intervention | 5.3 (4.1) | Wilcoxon nonparametric test $p = 0.20$ | – | – | – |
| | | Standard of care (12 months; *N* = 6) | 5.8 (3.3) | | 7.2 (1.3) | | | | |
| Garland 2014[69] | C-SOSI | Mindfulness-Oriented Recovery Enhancement (8 weeks; *N* = 57) | 10.63 (6.82) | 8 weeks (end of intervention) | 8.20 (7.09) | NS | – | – | – |
| | | Support group (8 weeks; *N* = 58) | 11.50 (7.37) | | 10.76 (6.44) | | | | |
| Sullivan 2017[113,114] | PHQ-9 | MI and CBT (22 weeks; *N* = 18) | 12.56 (8.33) | 22 weeks (end of intervention) | 8.88 (7.49) | Adjusted mean difference −2.21 (−6.62 to 2.21) $p = 0.32$ | 34 weeks post randomisation | 9.00 (5.80) | Adjusted mean difference −1.89 (−6.23 to 2.44) $p = 0.38$ |
| | | Usual care (*N* = 17) | 12.29 (6.93) | | 11.27 (6.58) | | | 11.13 (7.53) | |

HADS-D, Hospital Anxiety Depression Scale-Depression; IQR, interquartile range; NR, not reported; NS, not specified; RE, random effects; SD, standard deviation.

**TABLE 30** Emotional functioning: anxiety

| Author year | Definition of outcome | Intervention/ comparator | Baseline value, mean (SD) | Time point 1 | Value, mean (SD) | Test, *p*-value | Time point 2 | Value, mean (SD) | Test, *p*-value |
|---|---|---|---|---|---|---|---|---|---|
| Laigaard 2020[76] | HADS median (IQR) | Multidisciplinary pain centre with individualisedther-apeutic options (NS; *N* = 51) | 6 (4–10) | Final visit: 254 (106–357) days from baseline | 5 (3–8) | Linear mixed-effects RE model *p* = 0.18 | – | – | – |
| Kurita 2018[75] | HADS | 10% reduction of daily opioid dose until discontin-uation (up to 6 months; *N* = 15) | 7.6 (3.6) *n* = 13 | 2–3 weeks post randomisation | 6.9 (3.7) *n* = 15 | Wilcoxon *p* = 0.867 | 4–6 weeks post andomisation | 6.7 (4.0) *n* = 11 | Wilcoxon *p* = 0.964 |
| | | Usual care (*N* = 20) | 7.2 (3.4) *n* = 19 | | 6.6 (4.3) *n* = 20 | | | 6.3 (3.6) *n* = 18 | |
| Jackson 2021[111] | HADS | Acupuncture and standard of care (12 months; *N* = 9) | 8.5 (4.9) | Post intervention | 7.4 (4.2) | Wilcoxon nonparametric test *p* = 0.74 | – | – | – |
| | | Standard of care (12 months; *N* = 6) | 6.3 (3.0) | Post intervention | 7.4 (4.2) | Wilcoxon nonparametric test *p* = 0.74 | – | – | |
| Sullivan 2017[113,114] | GAD-7 | MI and CBT (22 weeks; *N* = 18) | 8.39 (7.18) | 22 weeks post randomisation (end of intervention) | 5.94 (5.59) | *p* = 0.10 | 34 weeks post randomisation | 6.00 (4.38) | *p* = 0.16 |
| | | Usual care (*N* = 17) | 8.82 (7.34) | | 9.07 (7.31) | | | 8.75 (6.97) | |

GAD-7, Generalised Anxiety Disorder-7; IQR, interquartile range; NS, not specified; RE, random effects; SD, standard deviation.

**TABLE 31** Sleep quality

| Author year | Outcome definition | Intervention/ comparator | Baseline value | Time point 1 | Value, mean (SD) | Test, *p*-value | Time point 2 | Value, mean (SD) | Test, *p*-value |
|---|---|---|---|---|---|---|---|---|---|
| Capano 2020[110] | PSQI | Hemp extract cannabidiol (8 weeks; *N* = 97) | 12.1 (4.1) | Week 8 (end of intervention) | 10.3 (4.3) | ANOVA *p* = 0.03 | – | – | – |
| Murphy 2013[78] | Overall sleep rating (0 'best' to 10 'worst') | Interdisciplinary pain programme with tapering using hydromorphone (3 weeks; *N* = 221) | 7.1 (1.9) | 3 weeks (within 2 days of discharge) | 6.3 (2.5) | ANOVA time effect *p* < 0.001 | – | – | – |
| Kurita 2018[75] | Sleep in minutes | 10% reduction of daily opioid dose until discontinuation (up to 6 months; *N* = 15) | 321.9 (104.8) *n* = 13 | 2–3 weeks post randomisation | 380.0 (146.0) *n* = 15 | Wilcoxon *p* = 0.167 | 4–6 weeks post randomisation | 360.4 (121.1) *n* = 12 | Wilcoxon *p* = 0.718 |
| | | Usual care (*N* = 20) | 288.6 (94.6) *n* = 18 | | 312.0 (96.1) *n* = 20 | | | 353.3 (168.9) *n* = 18 | |
| Sullivan 2017[113,114] | Insomnia severity (ISI) | MI and CBT (22 weeks; *N* = 18) | 15.6 (7.5) | 22 weeks (end of intervention) | 12.4 (6.4) | Adjusted mean difference −3.13 (−7.22 to 0.96) *p* = 0.13 | 34 weeks | 13.38 (6.74) | Adjusted mean difference −1.19 (−5.49 to 3.11) *p* = 0.58 |
| | | Usual care (*N* = 17) | 17.1 (6.6) | | 16.8 (7.1) | | | 15.50 (7.11) | |

ANOVA, analysis of variance; ISI, insomnia severity; PSQI, Pittsburgh Sleep Quality Index; SD, standard deviation.

**TABLE 32** Quality of life

| Author year | Intervention/comparator | Baseline value | Time point 1 | Value, mean (SD) | Test, *p*-value | Time point 2 | Value, mean (SD) | Test, *p*-value |
|---|---|---|---|---|---|---|---|---|
| ***SF-36 PCS*** | | | | | | | | |
| Krumova 2013[74] | Inpatient opioid tapering followed by individualised pain management (NS; *N* = 102) | 26.1 (7.7) | – | – | – | 12–24 months follow-up | 27.8 (9.8) | Cohen's *d* *p* > 0.05 |
| Laigaard 2020[76] | Multidisciplinary pain centre with individualised therapeutic options (NS; *N* = 51) | Median 28.4 (IQR 24.2–33.7; *n* = 51) | Final visit: 254 (106–357) days from baseline | 28.3 (24.6–35.1; *n* = 40) | Linear mixed-effects RE model *p* = 0.42 | – | – | – |
| Kurita 2018[75] | 10% reduction of daily opioid dose until discontinuation (up to 6 months; *N* = 15) | 31.2 (19.7) *n* = 13 | 2–3 weeks after randomisation | NR | NR | 4–6 weeks after randomisation, | NR | NR |
| | Usual care (*N* = 20) | 37.0 (20.8) *n* = 19 | | NR | NR | | NR | NR |
| Zheng 2008[112] | Electroacupuncture (6 weeks; *N* = 17) | NR | 8 weeks from entry (end of intervention) | NR | > 0.05 | Week 20 | NR | > 0.05 |
| | Sham electroacupuncture (6 weeks; *N* = 18) | NR | | NR | | | NR | |
| ***SF-36 MCS*** | | | | | | | | |
| Krumova 2013[74] | Inpatient opioid tapering followed by individualised pain management (NS; *N* = 102) | 36.7 (11.1) | – | – | – | 12–24 months follow-up | 41.9 (12.5) | Cohen's *d* *p* < 0.01 |
| Laigaard 2020[76] | Multidisciplinary pain centre with individualised therapeutic options (NS; *N* = 51) | Median 46.4 (IQR 38.8–55.3; *n* = 51) | Final visit: 254 (106–357) days from baseline | 49.5 (43.5–55.5; *n* = 40) | Linear mixed-effects RE model *p* = 0.42 | – | – | – |
| ***SF-36 Health Perception*** | | | | | | | | |
| Cunningham 2016[68] | Interdisciplinary rehabilitation programme with individualised opioid tapering (3 weeks; *N* = 55) | 33.3 (12.6) | 3 weeks (at discharge) | 42.9 (12.7) | *t*-test *p* < 0.001 | – | – | – |

IQR, interquartile range; MCS, mental component summary; NR, not reported; NS, not specified; PCS, physical component summary; RE, random effects; SD, standard deviation.

**TABLE 33** Ceased use

| Author year | Intervention/comparator (duration, *N*) | Time point 1 | Cessation of opioid use, *n*/*N* (%) | Time point 2 | Cessation of opioid use, *n*/*N* (%) |
|---|---|---|---|---|---|
| Cunningham 2016[68] | Interdisciplinary rehabilitation programme with individualised opioid tapering (3 weeks; *N* = 55) | End of treatment (3 weeks) | 55/55 (100%) | – | – |
| Krumova 2013[74] | Inpatient opioid tapering followed by individualised pain management (NS; *N* = 102) | 22.8 (11.2) days (at discharge); mean (SD) | 78/102 (76.5) | 12–24 months post-opioid cessation | 42/102 (48.0) |
| Townsend 2008[88] | Pain rehabilitation programme (3 weeks; *N* = 213) | 3 weeks (at discharge) | PP: 176/190 (92.6)<br>ITT: 176/213 (82.6) | 6 months post intervention | 102/132 (77.3%) |
| Huffman 2017[72] | Interdisciplinary chronic pain rehabilitation programme (3–4 weeks; *N* = 941) | 3–4 weeks (at discharge) | PP: 654/754 (86.74)<br>ITT: 654/941 (69.5) | 6 months | PP: 281/406 (69.2)<br>ITT: 281/941 (29.9) |
| | | | | 12 months | PP: 222/343 (64.7)<br>ITT: 222/941 (23.6) |
| Jacobs 2015 | Pharmacist-led telephone risk assessment clinic (NS; *N* = 148) | Retrospective chart review: December 2014–March 2015 (maximum 3.5 months) | 14/148 (9.5) | – | – |
| Austin 2019[66] | Opioid-tapering curriculum (NS; *N* = 707) | Retrospective chart review: July 2016–July 2017 (maximum 12 months) | PP: 188/648 (29.0)<br>ITT: 188/707 (26.6) | – | – |
| Murphy 2013[78] | Interdisciplinary pain programme with tapering using hydromorphone (3 weeks; *N* = 221) | 3 weeks (within 2 days of discharge) | 221/221[100] | – | – |
| Zhou 2017[90] | Comprehensive opioid taper treatments including medication-assisted treatment using methadone (NS; *N* = 140) | 8.8 (7.2) months[b] | 39/140 (27.9) | 14.3 (13.0) months | PP: 39/39[100]<br>ITT: 39/140 (27.9) |
| Bienek 2019[67] | Fixed starting dose (90 mg morphine/day) protocol (NS; *N* = 68) | 19.7 (7.5) days (at discharge) | PP: 59/68 (86.8)<br>ITT: 59/91 (64.8) | – | – |
| | Individualised starting dose (70% of patient's MED) protocol (NS; *N* = 127) | 15 (4.7) days (at discharge) | PP: 109/127 (85.8)<br>ITT: 110/219 (50.2) | | |

ITT, intention-to-treat; NS, not specified; PP, per protocol; SD, standard deviation.
a Mean (SD).
b Mean time taken by patients to successfully taper off all opioids.

**TABLE 34** Change in morphine equivalent daily dose

| Author year | Intervention/ comparator (duration, *N*) | Baseline value, mean (SD) | Time point 1 | MEDD, mean (SD) | Test, *p*-value | Time point 2 | MEDD, mean (SD) | Test, *p*-value | Summary |
|---|---|---|---|---|---|---|---|---|---|
| Seal 2020[81] | Integrated Pain Team (IPT) clinic (6 months; *N* = 147) | 124.1 (241.1) | 3 months post baseline | 82.5 (157.7) | Unadjusted *p* = 0.15 Adjusted *p* = 0.03 | 6 months post baseline | 68.4 (166.1) | Unadjusted *p* = 0.03 Adjusted *p* < 0.0 | IPT group achieved greater opioid dose reductions vs. usual care at 3 and 6 months |
| | Usual primary care clinic (6 months; *N* = 147) | 124.5 (231.5) | | 116.4 (230.0) | | | 107.1 (223.4) | | |
| Gersch 2021[70] | Pain e-consult programme (12 months; *N* = 125) | 88.4 (58.0) | 6 months | Change = −13.8 (IQR: −27.5 to 5.9) | *p* = 0.001 (*p* = 0.002) | 12 months | Change = −23.0 (IQR: −36.9 to 1.5) | *p* < 0.001 (*p* < 0.001) | Pain e-consult group had a greater opioid dose reduction at 6 and 12 months |
| | Usual care (12 months; *N* = 540) | 76.9 (44.8) | | Change = −2.8 (IQR: −12.7 to 9.6) | | | Change = −9.1 (IQR: −20.5 to 4.4) | | |
| Panicker 2022[79] | APRN-led multidisciplinary pain clinic (NS; 34) | 41.1 (58.69) | Post tapering | 23.05 (31.78) | Wilcoxon ranked sum test *p* < 0.0001 | – | – | – | Significant reduction in MEDD |
| Austin 2019[66] | Opioid-tapering curriculum (NS; *N* = 707) | 53.4 (76.9), median 30 (range 1.5–747.5) | Retrospective chart review: July 2016–July 2017 (maximum 12 months) | 58.5 (89.1) median 30 (range 0.83–840) | Baseline cohort vs. patients who remained on COT (*N* = 460) *p* = 0.053 | – | – | – | Average MEDD did not change among patients remaining on COT |
| Rivich 2018[80] | OSI – chart reviews (12 months; *N* = 147) | Median 315 (NR) | 12 months from initial review | Median 278 | Wilcoxon *p* < 0.05 | – | – | – | Reduction in median opioid dose pre- vs. 12 months post chart review |
| Westanmo 2015[117] | OSI – guideline implementation (NS; April 2011, *N* = 50,749; October 2014, *N* = 54,636) | 43 (NR; *n* = 6942) | April 2011–October 2014 (post OSI implementation; max. 3.5 years) | Pre 43 vs. post 23 (NR; *n* = 5981) | 47% difference pre vs. post NR | - | - | - | (Focus on reduction of high doses) |

continued

**TABLE 34** Change in morphine equivalent daily dose (*continued*)

| Author year | Intervention/ comparator (duration, *N*) | Baseline value, mean (SD) | Time point 1 | MEDD, mean (SD) | Test, *p*-value | Time point 2 | MEDD, mean (SD) | Test, *p*-value | Summary |
|---|---|---|---|---|---|---|---|---|---|
| Bienek 2019[67] | Fixed starting dose (FSD; 90 mg morphine/day) protocol (NS; *N* = 68) | 185 (194) | 19.7 (7.5) days (at discharge) | 57.3 (55.1) | Mann–Whitney U *p* = 0.96 | – | – | – | No difference between group at discharge. Both groups reduced their dose (unclear whether pts. Who ceased are included) |
| | Individualised starting dose (70% of patient's MEDD) (ISD) protocol (NS; *N* = 127) | 253 (385) | 15 (4.7) days (at discharge) | 46.1 (25.7) | | | | | |
| Jackson 2021[111] | Acupuncture and standard of care (12 months; *N* = 9) | 112 (71) | Post intervention | 78 (44) | Wilcoxon nonparametric test *p* = 0.43 | – | – | – | No difference between groups at end of treatment |
| | Standard of care (12 months; *N* = 6) | 191 (121) | | 125 (124) | | | | | |
| Sullivan 2017[113,114] | MI and CBT (22 weeks; *N* = 18) | 207.2 (269.4) | 22 weeks (end of intervention) | 111.9 (153.6) | *p* = 0.09 | 34 weeks post randomisation | 99.5 (152.0) | *p* = 0.34 | No difference between groups at end of treatment or FU |
| | Usual care (*N* = 17) | 245.2 (347.4) | | 169.9 (201.4) | | | 138.2 (155.9) | | |

APRN, advanced-practice registered nurse; COT, chronic opioid therapy; FU, follow-up; IQR, interquartile range; MEDD, morphine equivalent daily dose; NR, not reported; NS, not specified; SD, standard deviation.

**TABLE 35** Reduction in dose (measures other than morphine equivalent daily dose)

| Author year | Definition of outcome | Intervention/comparator (duration, *N*) | Baseline value, mean (SD) | Time point 1 | Outcome value, mean (SD) | Test *p*-value | Time point 2 | Outcome value, mean (SD) | Test *p*-value | Summary |
|---|---|---|---|---|---|---|---|---|---|---|
| Laigaard 2020[76] | OME, median (IQR) | Multidisciplinary pain centre with individualised therapeutic options (NS; *N* = 51) | 80 (IQR 45–161; *n* = 51) | Final visit: 254 (106–357) days from baseline | Median 19 (IQR 0–60; *n* = 40) | | | | | (Focus of study is on cognitive assessment) |
| Huffman 2017[72] | Daily opioid dose | Interdisciplinary chronic pain rehabilitation programme (3–4 weeks; *N* = 941) | 87.7 (153.0) | 3–4 weeks (at discharge) | 33.26 (19.57) *N* = 70 | *t*-test $p < 0.01$ | NR | | | Of the 70 pts still on COT mean dose was significantly reduced |
| Thakral 2018[83–87] | Estimated change per year in average daily opioid dose, mean (95% CIs) | Opioid dose and risk reduction initiative: females (NS; *N* = 15,197) | −3.7 (−5.6 to −1.9) | Dose reduction phase (January 2008–September 2010): Implementation of guidelines to discourage ≥ 120 mg MED daily | −5.9 (−7.0 to −4.8) | N/A | Risk mitigation phase (October 2010–September 2014) | −1.3 (−2.1 to −0.6) | N/A | Only modest reductions in annual rate of dose reduction among COT patients |
| | | Opioid dose and risk reduction initiative: males (NS; *N* = 8612) | −5.3 (−9.4 to −1.3) | | −8.8 (−10.8 to −6.9) | | | −1.5 (−2.7 to −0.3) | | |
| Kurita 2018[75] | Opioid dose, mg | 10% reduction of daily opioid dose until discontinuation (up to 6 months; *N* = 15) | 367.4 (369.8) | 2–3 weeks post randomisation | 230.6 (142.6) | Wilcoxon $p = 0.230$ | 4–6 weeks post randomisation | 226.6 (144.4) *n* = 12 | Wilcoxon $p = 0.446$ | Phase 2 (taper) underpowered because of dropouts |
| | | Usual care (*N* = 20) | 220.8 (169.1) | | 345.8 (273.3) | | | 300.8 (238.5) *n*-18 | | |
| Zheng 2008[112] | Opioid-like medication (mg/week) | Electroacupuncture (6 weeks; *N* = 17) | 461.6 (462.6) | 8 weeks from entry (end of intervention) | 281.4 (401.9) | ANOVA $p = 0.056$ | 20 weeks | 344.7 (396.8) | NR | By 20 weeks, OLM had increased in REA group and no change in SEA group, |
| | | Sham electroacupuncture (SEA; 6 weeks; *N* = 18) | 295.5 (288.0) | | 219.1 (293.0) | | | 239.0 (294.5) | | |

continued

**TABLE 35** Reduction in dose (measures other than morphine equivalent daily dose) (*continued*)

| Author year | Definition of outcome | Intervention/comparator (duration, *N*) | Baseline value, mean (SD) | Time point 1 | Outcome value, mean (SD) | Test *p*-value | Time point 2 | Outcome value, mean (SD) | Test *p*-value | Summary |
|---|---|---|---|---|---|---|---|---|---|---|
| Zheng 2019[115,116] | Adjusted mean opioid dosage (SE) | Pain and medication management plan plus electroacupuncture (EA) (12 weeks; *N* = 48) | 48,463.3 (63.3) | 14 weeks post randomisation (post treatment; average of weeks 11–14) | 48,526.6 (24.0) | EA vs. SEA ANCOVA *p* = 0.585 | 26 weeks (week 26) | 25,410.4 (25.5) | EA vs. SEA ANCOVA *p* = 0.1 | No difference between intervention groups at end of treatment or FU |
| | | Pain and medication management plan plus SEA (12 weeks; *N* = 29) | 29,620.8 (147.2) | | 29,537.4 (30.7) | | | 20,475.5 (28.6) | | |
| | | Pain and medication management only (PMM) (12 weeks; *N* = 31) | 31,871.4 (318.3) | | 31,585.2 (29.9) | EA vs. PMM ANCOVA *p* = 0.19 | | N/A | | |
| Montgomery 2020[77] | Mean change in MME | Battlefield acupuncture (NS; *N* = 24) | 31.0 | 6 months post BFA | + 3.9 | NR | | | | No significant changes in MME in either group |
| | | Usual care (*N* = 23) | 45.05 | | + 8.7 | | | | | |
| Hudak 2020[71] | Estimated marginal mean MME (SE) | MORE (8 weeks; *N* = 34) | 94.6 (36.1) | – | – | – | 4 months | 79.7 (36.2) | Linear mixed model *p* = 0.02 | MORE participants had greater reduction in opioid dose over time |
| | | Supportive group psychotherapy (8 weeks; *N* = 28) | 100.4 (40.5) | | | | | 98.2 (40.6) | | |

ANOVA, analysis of variance; BFA, battlefield acupuncture; CI, confidence interval; COT, chronic opioid therapy; FU, follow-up; IQR, interquartile range; MME, morphine milligram equivalents; MORE, mindfulness-orientated recovery enhancement; N/A, not applicable; NR, not reported; NS, not specified; OLM, opioid-like medications; OME, oral morphine equivalents; REA, real electroacupuncture; SD, standard deviation; SE, standard error.

**TABLE 36** Number of patients who reduced opioid dose

| Author year | Intervention/comparator | Time point | Outcome value, *n*/*N* (%) | Summary |
|---|---|---|---|---|
| Krumova 2013[74] | Inpatient opioid tapering followed by individualised pain management (NS; *N* = 102) | 22.8 (11.2) days (end of intervention); mean (SD) | 24/24 (still taking opioids) | Of the 24 patients who were still taking opioids, all had a relevant dose reduction |
| | | 12–24 months follow-up | 18/55 (still taking opioids) | At 12–24 months follow-up of 55 pts were taking opioids, though 18 were still on unchanged low doses |
| Townsend 2008[88] | Pain rehabilitation programme (3 weeks; *N* = 213) | 3 weeks (at discharge) | 14/14 (100%) | 14 pts who were still taking opioids all were on reduced dose |
| Rivich 2018[80] | OSI (12 months; *N* = 147) | 12 months from initial review | 50/147 (34.0) | 12 months after initial review 34% of patients had a reduction in opioid dose |
| Twillman 2018[89] | Introduction of CDC guidelines | 6 months | 149/362 (41.2) | 41.2% of respondents reported that their opioid dose was reduced |
| Capano 2020[110] | Hemp extract cannabidiol (8 weeks; *N* = 97) | Week 8 (end of intervention) | PP: 50/94 (53.2)<br>ITT: 50/97 (51.5) | 53.2% of participants using the CBD hemp extract were able to reduce opioid medications at week 8. |
| Sharp 2018[82] | Clinical 'encounters' | NS | 722/2492 (29) | The sample included 2492 encounters, 29% of which were followed by a reduction in opioid prescribing. |

CDC, Centers for Disease Control and Prevention; ITT, intention-to-treat; NS, not specified; PP, per protocol; SD, standard deviation.

**TABLE 37** Opioid withdrawal-related symptoms or dependence

| Author year | Definition of outcome | Intervention/ comparator | Time point 1 | Value | Test, *p*-value | Time point 2 | Value | Test, *p*-value |
|---|---|---|---|---|---|---|---|---|
| Cunningham 2016[68] | Peak COWS | Interdisciplinary rehabilitation programme with individualised opioid tapering (3 weeks; *N* = 55) | Peak COWS were higher for patients on higher opioid doses but not significantly different based on MED ($p = 0.22$). The mean peak COWS score occurred at 80% reduction from the initial opioid dose for patients on a MED dose of 100 mg/day or less, 64% for a MED dose of 100–200 mg/day, and 72% for a MED dose of > 200 mg/day. | | | | | |
| Kurita 2018[75] | OOWS | 10% reduction of daily opioid dose until discontinuation (up to 6 months; *N* = 15) | 2–3 weeks after randomisation | NR | NR | 4–6 weeks after randomisation, | NR | NR |
| | | Usual care (*N* = 20) | | NR | NR | | NR | |
| Kurita 2018[75] | SOWS | 10% reduction of daily opioid dose until discontinuation (up to 6 months; *N* = 15) | 2–3 weeks after randomisation | NR | NR | 4–6 weeks after randomisation, | NR | NR |
| | | Usual care (*N* = 20) | | NR | NR | | NR | |
| Bienek 2019[67] | 10-day mean of daily SOWS scores, mean (SD) | Fixed starting dose (90 mg morphine/ day) protocol (NS; *N* = 68) | Day 0–Day 10 of opioid withdrawal | 14.91 (9.42) | RM ANOVA $p < 0.01$ | – | – | – |
| | | Individualised starting dose (70% of patient's MED) protocol (NS; *N* = 127) | | 16.11 (9.97) | | – | – | – |

NR, not reported; NS, not specified; RM ANOVA, repeated measures analysis of variance; SD, standard deviation.

# **Appendix 6** Summary of findings and evidence profile (Review 3)

**TABLE 38** Summary of findings and evidence profile (Review 3)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| ***Barriers*** | | | | | | | | | |
| B1. Lack of knowledge, beliefs and poor understanding about opioids use, tapering and perceived risks associated with opioid use | *B1.1 Patient lacks knowledge and/or understanding of opioid use/risk/taper* | 'When asked about specific concerns related to opioid medications, patients were generally aware of opioid overdose as a potential complication but did not perceive themselves to be at risk' (Author-interpreted patient summary).[96]<br>'So I've taken this medicine, I've been fine for 10 years. It works for me. why in the world would you change it?' (Patient quote).[105]<br>'A lot of times when I bring up side effects of opiates for patient[s] that are already on it, they say, "Well, I don't have that side effect" or "I have it, but it's from something else"' (Provider quote).[102]<br>'Everybody thinks they're unique and they're not gonna overdose, and they're not addicted, and they never did anything wrong, and they need their medicine, and they've never had any of those side effects, and [the opioid] helps them' (Provider quote).[105]<br>'Patients who understood tapering to mean a gradual or partial reduction in opioid medications were generally more receptive to tapering than those who understood it to mean stopping "cold turkey" or stopping opioids completely' (Author-interpreted patient summary).[99] | Matthias 2017[105]<br>Firemark 2021[94]<br>Kennedy 2018[102]<br>Frank 2016[96]<br>Henry 2019[99]<br>Henry 2019[100] | No or very minor concerns | Minor concerns<br>Rich data from different perspectives including data from five studies (patients: nine summaries, eight quotes; providers: three summaries, three quotes) | No or very minor concerns<br>Data are consistent and supported by information from patient and providers | Minor concerns<br>Finding largely supported by two studies that explicitly reported on barriers and facilitators and from patient/provider perspective, but unclear whether their population of chronic pain patients also included cancer patients | High confidence | Six studies with minor concerns about adequacy of data and relevance. No or very minor methodological limitations andcoherence concerns. |

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | *B1.2 Patient believes opioids play important role in managing their pain* | 'The majority of patients expressed concerns over pain worsening without opioids, even though they recorded very high pain scores (despite large opioid doses), with most claiming that the opioids were helpful in controlling their pain and ability to manage daily life' (Author-interpreted patient summary).[107]<br>'I was thankful to have it. And I never, ever misused. I think opiates have been demonized there's still a very legitimate need for pain. . . relief in the chronic pain population. . .' (Patient quote).[95]<br>'When I think about some of my more recent patients, it was their belief that their pain needed opioids and there were no other options. They put a high value in the opioids as being the only thing that is going to manage their pain' (Provider quote).[95]<br>'If [opioids] work for you, what are the negatives? Balance it out. Like I said, if they even got rid of half the pain in my knees, I'd keep taking them. I'm kind of an advocate for, if you need them, take them. . .' (Patient quote).[99]<br>'Potential future adverse effects were described as less salient than the risk of increased pain with decreased opioid medication' (Author interpreted patient summary).[96] | Henry 2019[100]<br>Kuntz 2021[95]<br>Quinlan 2020[107]<br>Langford 2020[103]<br>Frank 2016[96]<br>Henry 2019[99] | Minor concerns<br>Methods of data collection/analysis not fully reported in three studies, contributing to 1/3 of quotes to study finding | Minor concerns<br>Rich data from different perspectives (patients: 10 summaries, 11 quotes; providers: 4 summaries, 1 quotes) | Moderate concerns<br>Elements of the underlying data are defined in slightly different ways across different studies | Minor concerns<br>Finding largely supported by three studies that did not explicitly report on barriers and facilitators | Moderate confidence | Six studies with moderate concerns about coherence. Minor concerns with methodological limitations, data adequacy and relevance. Downgraded due to concerns about coherence. |

continued

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | *B1.3 Patient believes they need or expects an alternative to opioids to manage their pain* | 'I've been on opiates, you know, for most of my adult life now, and I'm probably going to be on them for the rest of my life. I mean you're not going to cure what's wrong with me. so I'm always going to need something' (Patient quote).[96]<br>'I have a tremendous fear in a doctor saying I want you to taper off the methadone and get totally off the methadone with no alternative whatsoever. I think that would be an irrational decision by a doctor, and I probably wouldn't take that advice' (Patient quote).[96]<br>'In my experience, it's really hard to take something away from people without giving them something in return. So, if you are saying I am taking away your candy and not give you anything, people aren't going to react very well to that' (Provider quote).[103] | Langford 2020[103]<br>Frank 2016[96]<br>McNeilage 2022[106] | No or very minor concerns | Moderate concerns<br>Relatively rich data but from a limited number of studies and small number of observations (patients: one summary; four quotes) | No or very minor concerns<br>Data are clear and consistent | Minor concerns<br>Two studies are unclear whether their population of chronic pain patients also included cancer patients | Moderate confidence | Three studies with moderate concerns about data adequacy, minor concerns about relevance. No or very minor concerns about methodological limitations and coherence. Downgraded due to small number of studies and data contributing to finding. |

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | *B1.4 Provider lacks knowledge and training to taper* | 'Patients tapering off methadone are routinely referred to STORM because most PCPs are unfamiliar with this process' (Author interpreted provider summary).[94]<br>'I think there is an assumption that everyone knows how to *[taper]* – but the reality is they don't' (Provider quote).[103]<br>'STORM pharmacists described how some PCPs confuse the STORM program with other pain services and either do not know how to refer to STORM or unintentionally refer to another resource. PCPs also report forgetting about the STORM program' (Author-interpreted provider summary).[94]<br>'Many PCPs described a lack of specialized training in chronic pain management' (Author-interpreted provider summary).[94] | Langford 2020[103]<br>Firemark 2021[94] | No or very minor concerns | Moderate concerns<br>Relatively rich data but from a limited number of studies and small number of observations (providers: five summaries, three quotes) | No or very minor concerns<br>Data are clear and consistent | No or very minor concerns<br>Data mostly from one directly relevant study | Moderate confidence | Two studies with moderate concerns about data adequacy. No or very minor concerns about methodological limitations, coherence and relevance. Downgraded due to small number of studies and data contributing to finding. |

continued

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| B2. Fears and negative expectations of, or beliefs around, opioid tapering | *B2.1 Fear/ expectation/ experiences of uncertain or negative outcome when tapering* | 'Fear of withdrawal was mentioned by 10 (17%) patients, with some patients referring to previous experiences' (Author-interpreted patient summary, Statistical data).[107]<br>'I have that fear that if I stop, things are going to go to hell. I don't want to be in that situation again' (Patient quote).[99]<br>'I don't think they're aware of how bad withdrawals are. I mean there's vomiting bile, there's stomach cramps, there's the cold shakes and fever. I mean it's pretty bad' (Patient quote).[96]<br>'It automatically sets up this punitive conversation when you say, you know you were doing great, [but] I'm going to cut off your medicines. Because we don't do that in any other disease. We don't do that in hypertension. We don't do that with insulin' (Provider quote).[105]<br>'If I try to lower doses to < 200 ME/day, my patients may become upset and perhaps threatening or violent: Pre-tapering initiative: 21 (62%) vs. Post-tapering initiative: 20 (64%)' (Statistical data).[117]<br>'Some providers reported feeling threatened by patients who were angry about providers' recommendations on opioid dosing' (Author interpreted provider summary).[102] | Frank 2016[96]<br>Henry 2019[99]<br>Kuntz 2021[95]<br>Quinlan 2020[107]<br>White 2020[108]<br>Langford 2020[103]<br>Matthias 2017[105]<br>McNeilage 2022[106]<br>Kennedy 2018[102]<br>Firemark 2021[94]<br>Giannitrapani 2018[97]<br>Westanmo 2015[117] | Minor concerns<br>4/12 studies with methodological limitations, of which 2 contribute high number of quotes | No or very minor concerns<br>Rich data from different perspectives from a large number of studies and observations (patients: 15 summaries, 16 quotes; providers: 13 summaries, 12 quotes; statistical data: 4; predictive data: 1) | No or very minor concerns<br>Data are clear and consistent across many studies and finding title incorporates a range of actual outcomes | No or very minor concerns<br>Finding largely supported by directly relevant data | High confidence | 12 studies with minor concerns about methodological limitations. No or very minor concerns about adequacy of data, coherence and relevance. |

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | *B2.2 Pessimism around effectiveness of non-opioid options* | 'Throughout my life, the doctors have done everything, trying to get me to exercise, to stretch, things that shocked my muscles. In the '70s, they put some kind of body cast on me that I wore for months. Gosh, I've had everything' (Patient quote).[96]<br>'Patients identified suboptimal effectiveness with previous trials of alternative methods for pain control such as nonopioid medications, injections, and surgery. This led to pessimism about their ability to adequately manage pain without opioid medications' (Author-interpreted provider summary).[96]<br>'Paracetamol and non-steroidal anti-inflammatory agents were identified as possible alternative analgesics; however, participants saw limited clinical utility of these agents as opioid substitutes due to a perceived lack of efficacy, clinical contraindications in specific patient cohorts and concerns about long-term use' (Author-interpreted provider summary).[103]<br>'All participants in this group expressed frustration at the lack of effective pain management alternatives available to them' (Author interpreted patient summary).[106] | Frank 2016[96]<br>McNeilage 2022[106]<br>Langford 2020[103] | No or very minor concerns | Moderate concerns<br>Data from a limited number of studies and observations (patient: four summaries, four quotes; provider: one summary, two quotes) | No or very minor concerns<br>Data are clear and consistent and supported by information from patient and providers | Moderate concerns<br>Finding supported largely supported by 1 directly relevant study from a patient perspective only | Low confidence | Three studies with moderate confidence about data adequacy and relevance. No or very minor concerns about methodological limitations and coherence. Downgraded due to small number of studies and data contributing to finding and findings largely supported from a patient perspective only. |

continued

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | *B2.3 Expectation that tapering is difficult/challenging* | 'Opioid deprescribing was viewed as a challenging and time-intensive activity with little incentive and substantial effort required from both healthcare professionals and patients' (Author-interpreted provider summary).[103]<br>'You see the person on your schedule and you know it's going to be. . . one of those just draining conversations' (Provider quote).[102]<br>'Providers assume it is difficult to change existing patient preferences and expectations about using opioid medications to manage their chronic pain' (Author-interpreted provider summary).[97] | Langford 2020[103]<br>Giannitrapani 2018[97]<br>White 2020[108]<br>Firemark 2021[94]<br>Kennedy 2018[102] | No or very minor concerns | Moderate concerns<br>Fairly superficial data (provider: seven summaries, eight quotes) | No or very minor concerns<br>Data are varied across the studies in terms of reasons why tapering is difficult/challenging, but clearly supports the finding | Minor concerns<br>Findings largely supported by three studies in which it is unclear whether their population of chronic pain patients also included cancer patients, or patients with acute pain | Moderate confidence | Five studies with moderate concerns about data adequacy. Minor concerns about relevance. No or very minor concerns about methodological limitations and coherence. Downgraded due to superficial data. |

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| B3. Strained patient–provider relationship | *B3.1. Lack of trusting patient/provider relationship* | 'Patients don't want to talk to anybody else but their doctor. They don't trust anybody else' (Author interpreted patient summary/ patient quote).[94]<br>'. . .patients reporting negative interactions with clinicians felt clinicians were not entirely honest about their reasons for tapering' (Author-interpreted patient summary).[99]<br>'First, providers noted a concern that their patients may not fully share pain-related symptoms and opioid-related side effects. . .' (Author-interpreted provider summary).[102]<br>'People [are] trying to figure out how to answer the questions so that they're not going to be taken off their medicine' (Provider quote).[102] | Kennedy 2018[102]<br>McNeilage 2022[106]<br>Firemark 2021[94]<br>Henry 2019[99] | No or very minor concerns | Moderate concerns<br>Lack of depth in data from a limited number of studies and observations (patient: three summaries, one quote; provider: three summaries, two quotes) | Minor concerns<br>Data are mostly clear and supported by information from patient and providers | Moderate concerns<br>In two studies barriers and facilitators are inferred. In three studies it is unclear whether their population of chronic pain patients also included cancer patients, or patients with acute pain | Moderate confidence | Four studies with moderate concerns about data adequacy and relevance. Minor concerns about coherence. No or very minor concerns about methodological limitations. Downgraded due to lack of depth in data from a limited number of studies and observations |

continued

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | *B3.2 External judgement and stigma regarding opioid use* | 'Participants also described challenges with having their previously acceptable medical care newly perceived as troublesome, unacceptable, or even criminal by providers. These participants articulated feelings of guilt, shame, and humiliation when providers' perceptions were communicated to them. Some felt unfairly accused during conversations about various tapering initiatives' (Author-interpreted patient summary).[93]<br>'They were just throwing them [opioids] at me and now all the sudden I'm made to feel like a criminal. I think the system, the state, the way everything happened, was badly done' (Patient quote).[93]<br>'Dependence and addiction were issues alluded to by 16 (27%) patients, either reflecting their own concerns or the judgement of others' (Statistical data).[107]<br>'Patient feels angry about referral and treated "like an addict"' (Author-interpreted patient summary/patient quote).[95]<br>'In addition, they reported feeling stigmatised ("Is he saying I'm a drug addict or something now?" P14)' (Author-interpreted patient summary/patient quote).[106] | Langford 2020[103]<br>Benintendi 2021[93]<br>Kuntz 2021[95]<br>McNeilage 2022[106]<br>Quinlan 2020[107]<br>Matthias 2017[105] | No or very minor concerns | No or very minor concerns<br>Rich data from a large number of observations (patient: 16 summaries, 12 quotes; provider: 2 summaries, 1 quote) | No or very minor concerns<br>Data are clear and consistent | No or very minor concerns<br>Data are largely supported by one directly relevant study | High confidence | Six studies with no or very minor concerns about methodological limitations, adequacy of data, coherence and relevance. |

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | | 'In one instance, a participant described her fear that her pain would be disbelieved or invalidated by providers: ' 'You always have that fear of 'are they going to believe you' or 'are they going to think that you just want to stay at these higher doses'?' (Patient quote).[93]<br>'The experience of being dually disbelieved and stigmatized as 'drug 'seeking' was additionally burdensome for Black women in the sample. Several described the ways in which dominant cultural norms interacted with other forms of marginalization including racism' (Author-interpreted patient summary).[93] | | | | | | | |

continued

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | *B3.3 Provider is perceived to be unsupportive, lacks empathy, doesn't seek to understand patient needs or tailor explanations of tapering need to patients* | '*[patient]* feeling that they were not being heard ("He was on the phone half the time I was there", P14)' (Author-interpreted patient summary/patient quote).[106]<br>'However, some patients expressed negative experiences in relation to the support provided: "I saw her twice, then I actually stopped going because she (the psychologist) wasn't dealing with any of the different things I could do for the pain"' (Author-interpreted patient summary/patient quote).[108]<br>'Others described having conversations with their providers that addressed general reasons for tapering but did not apply to them specifically (e.g. addiction is a potential risk)' (Author-interpreted patient summary).[105]<br>'This has been my doctor for almost 20 years and he treated me like a stranger, like nothing' (Patient quote).[99]<br>'Some participants reported receiving inadequate communication or explanation from providers about their decisions to taper, resulting in some feeling abandoned and "orphaned by the system" as a result of various tapering initiatives' (Author-interpreted patient summary).[93] | McNeilage 2022[106]<br>White 2020[108]<br>Henry 2019[99]<br>Benintendi 2021[93]<br>Matthias 2017[105]<br>Wu 2019[109] | No or very minor concerns | Minor concerns<br>Fairly rich data from adequate number of observations (patient: 14 summaries, 7 quotes; provider: 2 summaries, 1 quote) | Minor concerns<br>Data are clear and varied across the studies in terms of reasons why tapering is perceived as unsupportive | Moderate concerns<br>Largely based on findings of five studies in which barriers and facilitators are inferred. In two studies it is unclear whether their population of chronic pain patients also included cancer patients, or patients with acute pain | Moderate confidence | Six studies with moderate concerns about relevance. Minor concerns about data adequacy and coherence. No or very minor concerns about methodological limitations. Downgraded due to 5/6 studies in which barriers and facilitators were inferred. |

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| B4. Lack of patient motivation or involvement in tapering process | *B4.1 Motivation and goals to taper are lacking or are not driven by patient need* | 'Despite tapering being voluntary, these participants were very reluctant to do so – they often had trouble articulating their motivations' (Author interpreted patient summary).[106]<br>'patients reporting negative interactions with clinicians felt clinicians were not entirely honest about their reasons for tapering (e.g. clinicians were motivated by institutional anti-opioid pressures rather than patients' best interests)' (Author-interpreted patient summary).[99]<br>'PCPs are saying "the CDC is making me do this, or [the health system] is making me do this, and I don't believe in it, but I have to do it". And so then, when you have to taper a patient. . . it's not going to go well' (Author-interpreted provider summary).[95]<br>'Sometimes the doctors would literally tell their patients, "Well, Kaiser is making me do this. I wouldn't do it [referral] if Kaiser wasn't making me do it" which is always a bad way to start someone on a taper' (Pharmacist) (Provider quote).[94]<br>'PCPs and STORM team interviewees noted that PCPs do not want to set the STORM team up for failure with a patient who is not open to working with the program' (Author interpreted provider summary).[94] | Henry 2019[99]<br>McNeilage 2022[106]<br>Benintendi 2021[93]<br>Firemark 2021[94]<br>Kuntz 2021[95] | No or very minor concerns | Minor concerns<br>Relatively rich data supported by an adequate number of observations (patient: 11 summaries, 8 quotes; provider: 2 summaries, 2 quotes) | No or very minor concerns<br>Data are clear and supported by information from patient and providers | Moderate concerns<br>In three studies barriers and facilitators are inferred.<br>In two studies it is unclear whether their population of chronic pain patients also included cancer patients, or patients with acute pain | Moderate confidence | Five studies with moderate concerns about relevance.<br>Minor concerns about data adequacy.<br>No or very minor concerns.<br>Downgraded due to 3/6 studies in which barriers and facilitators were inferred providing the most data observations for finding. |

continued

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | *B4.2 Lack of patient involvement in tapering decisions* | 'Not all patients felt involved in the process. One patient believed that her doctors were conferring with each other and making decisions without her – "He had lowered it and I didn't even realize it. He didn't even tell me it was getting lowered again. I wondered why I ran out even earlier than what I normally did"' (Author-interpreted patient summary/Patient quote).[105] 'In turn, both patients and pharmacists perceived feelings of lack of control or choice during the taper' (Author-interpreted patient/provider summary).[95] 'Patients explicitly discussed the power differential between patients and clinicians – only clinicians can prescribe (or refuse to prescribe) opioids – when they described negotiating about opioid dosing or the rate of tapering' (Author-interpreted patient summary).[99] | Matthias 2017[105] Henry 2019[99] Kuntz 2021[95] | No or very minor concerns | Moderate concerns Relatively rich data and adequate number of observations, but supported by small number of studies (patient: nine summaries, four quotes; provider: three summaries) | Moderate concerns Data were sometimes more varied and the finding in these cases is an oversimplified description | No or very minor concerns Data are supported by two directly relevant studies | Low confidence | Three studies with moderate concerns about adequacy of data and coherence. No or very minor concerns about methodological limitations and relevance. Downgraded due to small number of studies and data contributing to finding and data variation in coherence assessment. |

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| B5. Burden of tapering | *B5.1 Emotional burden on patient and provider* | 'I also had lots of fears about let's say there was an apocalypse in our society, what would happen to me?. I would get so sick not having those drugs 'cause I was physically dependent on these drugs, you know. It's a very insecure feeling' (Patient quote).[96]<br>'Fear and anxiety over loss of pain management approach/uncertain how will function or cope without opioid medication' (Author-interpreted patient summary).[95]<br>'Other than pain, the main taper-related challenge that participants reported was withdrawal symptoms, with a few participants finding insomnia and mood-related symptoms (i.e. irritability, anxiety, and low mood) particularly unpleasant' (Author-interpreted patient summary).[106]<br>'Sometimes I have to just check myself in terms of, you know, is this my issue? Is this just that I don't like the numbers? Because, there's data and we know that [opioids are] not good for elderly, but then people are also individuals' (Provider quote).[106]<br>'It's very hard to sit in front of a patient who identifies a medicine, an opiate, as being helpful and tell them, 'I care about you. I don't want you to be in pain, and also I think that these medicines are wrong for you. . .' (Provider quote).[102] | Frank 2016[96]<br>McNeilage 2022[106]<br>Henry 2019[99]<br>Kuntz 2021[95]<br>Magee 2021[104]<br>Giannitrapani 2018[97]<br>Firemark 2021[94]<br>Matthias 2017[105]<br>Langford 2020[103]<br>Kennedy 2018[102] | No or very minor concerns | No or very minor concerns<br>Rich data from a large number of studies and observations (patient: 14 summaries, 12 quotes; provider: 8 summaries, 10 quotes) | No or very minor concerns<br>Data incorporate a range of reasons for emotional burden, all of which clearly supports the finding | No or very minor concerns<br>Data are supported by four directly relevant studies | High confidence | 10 studies with no or very minor concerns about methodological limitations, adequacy of data, coherence and relevance. |

continued

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | | 'it takes a huge psychological toll on providers and teams to deal with a lot of these challenging cases' (Author-interpreted provider summary).[97] | | | | | | | |
| | *B5.2 Physical burden on patient and provider* | 'Nearly all patients noted that managing opioids became more difficult as tapering progressed. In addition to timing opioid consumption around daily activities and contacting clinics for refills, patients expended more energy monitoring their day-to-day opioid supply' (Author-interpreted patient summary).[99]<br>'So perhaps there is a behavioural thing, it seems easier to pop a pill than to try a heat pack or what not. (P6, SI)' (Provider quote).[103]<br>'I think the biggest barrier for them is the time that it can take to have this conversation' (Provider quote).[94]<br>'Opioid deprescribing was viewed as a challenging and time-intensive activity with little incentive and substantial effort required from both healthcare professionals and patients' (Author-provider summary).[103]<br>'In comparison with medications, providers perceive offering nonpharmacologic pain management strategies as more time consuming' (Author-interpreted patient summary).[97] | Henry 2019[99]<br>Langford 2020[103]<br>Wu 2019[109]<br>Giannitrapani 2018[97]<br>Firemark 2021[94] | Moderate concerns. Findings based largely on two poor-quality studies | Moderate concerns<br>Lack of depth of data and limited number of observations (patient: five summaries, two quotes; provider: three summaries, two quotes) | No or very minor concerns<br>Data are clear and varied across the studies in terms of reasons for physical burden, but clearly supports finding | Moderate concerns<br>Largely based on findings of two studies in which barriers and facilitators are inferred. In three studies it is unclear whether their population of chronic pain patients also included cancer patients, or patients with acute pain | Low confidence | Five studies with moderate concerns about methodological limitations, data adequacy and relevance. No or very minor concerns about coherence. Downgraded due to findings supported largely by two poor quality studies and lack of depth of data and limited number of observations. |

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | *B5.3 Health burden on patient* | 'Other than pain, the main taper-related challenge that participants reported was withdrawal symptoms' (Author-interpreted patient summary).[106]<br>'In addition to high levels of distress, participants within this group reported high and often increasing levels of pain intensity and deteriorating functioning' (Author-interpreted patient summary).[106]<br>'not being able to help my wife do a bit of housework or do the mowing' (Patient quote).[106]<br>'Each reported persistent pain, withdrawal symptoms, and decreased quality of life' (Author-interpreted patient summary).[109]<br>'Experiences of increased pain or withdrawal symptoms' (Author-interpreted patient summary).[95] | Henry 2019[99]<br>McNeilage 2022[106]<br>Kuntz 2021[95]<br>Magee 2021[104]<br>Wu 2019[109] | Minor concerns | No or very minor concerns<br>Rich data with adequate number of patient observations (patient: 20 summaries, 7 quotes; provider: 1 summary) | No or very minor concerns<br>Data are clear and varied across the studies in terms of reasons for health burden, but clearly supports finding | No or very minor concerns<br>Finding fully supported by two directly relevant studies | High confidence | Five studies with minor concerns about methodological limitations. No or very minor concerns about adequacy of data, coherence and relevance. |

continued

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| B6. Opioid-tapering initiatives are not tailored and produce unintended consequences | *B6.1 Design/delivery of opioid-tapering initiatives do not incorporate patient needs or preferences* | 'I just hate texting. [P16, female, 46 years, pain clinic, metropolitan area]' (Patient quote).[104]<br>'Several participants described perceived barriers toward phone-based digital interventions including limited phone reception or access to internet' (Author-interpreted patient summary).[104]<br>'I use glasses and my phone is a very cheap phone. If it's in the middle of the day I can't read them. [P14, male, 56 years, primary care, regional area]' (Patient quote).[104]<br>'You don't go driving on your own for the first time. You have to get the license. You need your lessons first.I would hate to have to do this [pain self-management] and not know how' (Patient quote).[104]<br>'Methods preclude patient motivation' (Author-interpreted patient summary).[109] | Henry 2019[99]<br>Wu 2019[109]<br>Magee 2021[104] | Moderate concerns. Findings largely based on one study of moderate quality | Serious concerns Relatively thin data largely based on observations from a single study (patient: eight summaries, seven quotes; provider: one summary) | Moderate concerns Elements of the underlying data may be defined in slightly different ways across different studies | No or very minor concerns Finding fully supported by one directly relevant study | Very low confidence | Three studies with serious concerns about data adequacy. Moderate concerns about methodological limitations and coherence. No or very minor concerns about relevance. Downgraded due to relatively thin data largely based on observations from a single study and concerns over methodological limitations and coherence. |

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | *B6.2 Opioid-tapering initiatives produce unintended consequences* | 'A few patients considered seeking alternative opioid sources during tapering when their pain or withdrawal was severe' (Author-interpreted patient summary).[99]<br>'another (P14) expressed concern that their doctor had a 'blanket approach to cut everyone off painkillers' and that they were 'forcing people onto illegal drugs or, worse, self-harm' (Author-interpreted patient summary/patient quote).[106]<br>'Yes, it is stigmatising, and I don't think the current system is good enough to help address that stigma. (P15, FG)' (Provider quote).[103]<br>'These taper initiatives produced unintended consequences including reduced patient autonomy, facilitating mistrust, and reinforcing stigma about addiction' (Author-interpreted patient summary).[93] | Langford 2020[103]<br>Benintendi 2021[93]<br>Henry 2019[99]<br>McNeilage 2022[106]<br>Kennedy 2018[102] | No or very minor concerns<br>Findings largely based on one study with few concerns and one with minor concerns | Minor concerns<br>Relatively rich data supported by an adequate number of studies and observations (patient: 12 summaries, 4 quotes; provider: 1 summary, 1 quote) | No or very minor concerns<br>Data incorporate a range of unintended consequences | Minor concerns<br>Finding largely supported by two studies in which barriers and facilitators are inferred. | High confidence | Five studies with minor concerns about adequacy of data and relevance. No or very minor concerns about methodological limitations and coherence. |

continued

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| B7. Unsupportive health-system-related tapering environmental context | *B7.1 Resources/ training to taper are not accessible* | 'Providers highlighted insufficient availability to multiple types of services, including surgical services. . . complementary and integrative medicine modalities such as acupuncture, massage, chiropractic, or biofeedback. . .physical and occupational therapy. . . behavioral and mental health services' (Author-interpreted provider summary)[97]<br>'Providers described multiple logistical barriers to implementing opioid tapering in primary care, including inadequate training and resources to support opioid tapering and nonopioid chronic pain management' (Author-interpreted provider summary).[102]<br>'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 behavioral therapy and other things ... that other places may have' (Provider quote).[102]<br>'It's under resourced. There is a very long waiting list for pain clinics and it's a problem. (P2, SI)' (Provider quote).[103]<br>'We didn't know how long | Kennedy 2018[102]<br>Giannitrapani 2018[97]<br>Langford 2020[103]<br>Magee 2021[104]<br>Benintendi 2021[93]<br>Firemark 2021[94] | No or very minor concerns<br>One study contributes most to findings, three good-quality ones also provide ample support | No or very minor concerns<br>Rich data with large number of studies and observations (patient: 3 summaries, 1 quote; provider: 21 summaries, 12 quotes) | No or very minor concerns<br>Data are clear and varied across the studies in terms of reasons for non-access, but clearly supports finding | No or very minor concerns | High confidence | Six studies with no or very minor concerns about methodological limitations, adequacy of data, coherence and relevance. |

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | | it [STORM program] would be funded. We always knew that it was a precious resource, so you tended not to use it routinely. It would be sort of something you would save for a more challenging case'. (Provider quote).[94]<br>'One provider described this challenge in a hypothetical interaction with a patient: "I live 200 miles away and I'm not coming to physical therapy"' (Author-interpreted provider summary/provider quote).[97]<br>'Some described the inconvenience of randomly assigned "pill counts", citing difficulty accessing transportation or living many hours away. These "pill counts"placed significant pressure to "be well" or 'mobile enough to reach the clinic and coordinate logistics with insufficient time to prepare (e.g. "a day's notice")' (Author-interpreted patient summary).[93]<br>'We do not have the ability to really offer those [NPT] options to them A lot of our patients have limited resources. And we are their medical providers. We're the only people they see. They don't go into the community because they can't afford it' (Provider quote).[97] | | | | | | | |

continued

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | *B7.2 Ineffective interprofessional collaboration* | 'That has been pointed out year after year – the disconnect between the hospital and the community' (Participant 1, semistructured interview) (Provider quote).[103]<br>'(Hospital) is not the right time to try and institute a deprescribing program – I mean you might think so from the outside. . . but we would generally continue their dose of medication throughout their stay and we would generally discharge them on the same dose they came in on' (Provider quote).[103]<br>'Some participants expressed concern that specialised and multidisciplinary services, once engaged, decrease general practitioner agency to deprescribe opioids' (Author-reported provider summary).[103]<br>'(Hospital) is not the right time to try and institute a deprescribing program – I mean you might think so from the outside. . . but we would generally continue their dose of medication throughout their stay and we would generally discharge them on the same dose they came in on' (Provider quote.)[103] | Langford 2020[103] | No or very minor concerns | Serious concerns Adequate data supported by a single study and very limited observations (provider: two summaries, two quotes) | Serious concerns Finding is supported by some limited data but for some observations the link is rather vague | Moderate concerns Finding supported by one study on deprescribing (including both tapering and discontinuation) which included both chronic and acute patients | Very low confidence | 1 study with serious concerns about data adequacy and coherence. Moderate concerns about relevance. No or very minor concerns about methodological limitations. Downgraded due to finding based on a single study with very limited observations and concerns over coherence and relevance. |

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | *B7.3 External provider pressures* | 'Lack of time during a typical clinic visit was frequently noted as a barrier to discussing tapering' (Author-interpreted provider summary).[102]<br>'Because of pressure to demonstrate productivity, providers did not feel they had the support from their leadership to spend adequate visit time on pain' (Author-interpreted provider summary).[97]<br>'And they do not encourage us to make follow-up visits. They don't encourage a lot of clinic visits for the patients. They want to do everything by secure messaging or telephone. So yes, I could do my annual exam. "Oh, you're having pain?" In another practice, I might say, "Okay, well, let's make a follow-up visit for you to talk about the pain", and I would do that. That's kind of discouraged here. . .' (Provider quote).[97]<br>'STORM pharmacists expressed a recognition that PCPs are overburdened' (Author-interpreted provider summary).[94]<br>'Workload pressures. . . were viewed as barriers to opioid deprescribing' (Author-interpreted provider summary).[103] | Langford 2020[103]<br>Firemark 2021[94]<br>Kennedy 2018[102]<br>Giannitrapani 2018[97] | No or very minor concerns | Moderate concerns<br>Relatively rich data from a small number of observations across four studies (provider: four summaries, four quotes) | No or very minor concerns<br>Data are clear and varied across the studies, but clearly supports finding | Minor concerns<br>In all studies it is unclear whether their population of chronic pain patients also included cancer patients, or patients with acute pain | Moderate confidence | Four studies with moderate concerns about data adequacy. Minor concerns about relevance. No or very minor concerns about methodological limitations and coherence. Downgraded due to small number of observations. |

continued

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | *B7.4 Patients and providers feel institutional policies, guidelines and programmes do not support them to taper* | 'Participants identified that current opioid prescribing guidelines provide advice regarding initiation of treatment, yet they rarely address monitoring or medication discontinuation. Participants felt that currently available resources provide inadequate cessation guidance and support, requesting novel approaches to ensure appropriate opioid use' (Author-interpreted provider summary).[103]<br>'You have to treat these patients individually, I think a pathway as such for pain management doesn't work, I think the pathway is saying all patients are following the same trajectory in their dose reduction and that sort of thing. . .' (Provider quote).[103]<br>'Due to the dynamic nature of these factors, patients' pain and perceived need for opioids fluctuate daily, a reality that may be at odds with recommendations to taper opioids by a fixed percentage every 2–4 weeks' (Author-interpreted provider summary).[99]<br>'The interviewed participants expressed concerns of not being able to enjoy participating in life because of pain and were frustrated with the US Food and Drug Administration's laws, which they felt did not consider the patients as individuals' (Author-interpreted provider summary).[93] | Langford 2020[103]<br>Benintendi 2021[93]<br>Wu 2019[109]<br>Henry 2019[99] | No or very minor concerns | Moderate concerns<br>Relatively rich data from small number of studies and observations (patient: six summaries, one quote; provider: two summaries, two quotes) | No or very minor concerns<br>Data are clear and consistent in supporting finding | Minor concerns<br>Finding largely supported by three studies in which barriers and facilitators are inferred. | Moderate confidence | Four studies with moderate concerns about adequacy of data. Minor concerns about relevance. No or minor concerns about methodological limitations and coherence. Downgraded due to concerns over small number of studies and observations from three studies in which barriers and facilitators were not explicitly reported. |

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | | 'Participants spoke with similar displeasure about the U.S. opioid epidemic's influence on their care, perceiving that their individual opioid tapers occurred as a direct result of the epidemic, "the government clamping down", "the government watching people", and negative publicity thrust upon doctors' (Author-interpreted patient summary/patient quotes).[93] | | | | | | | |
| B8. Patient experiences poor or unexpected life circumstances | *B8.1 Patient lack of social support* | 'Adversity experienced by participants included relationship difficulties ("I keep turning over a lot at night and that is hard on our relationship because he has to go to work", P03)' (Author-interpreted patient summary).[106]<br>'My husband is not understanding so it makes it a bit hard', and participant 06 explained 'All my family are overseas, and they are just completely unaware of what's going on' (Patient quote).[106]<br>'Patients experienced tapering as dynamic because their pain and perceived need for opioids varied from day to day and because their pain was frequently affected (either positively or negatively) by changes in their social relationships' (Author-interpreted patient summary).[99] | Henry 2019[99]<br>McNeilage 2022[106] | Minor concerns | Moderate concerns<br>Adequate data mostly from a single study (patient: six summaries, five quotes) | No or very minor concerns<br>Data are clear and consistent with findings | Moderate concerns<br>Finding supported by two studies in which barriers and facilitators are inferred. | Low confidence | Two studies with moderate concerns about data adequacy and relevance. Minor concerns about methodological quality. No or very minor concerns about coherence. Downgraded due to finding based largely on data from a single study and based entirely on data from studies in which barriers and facilitators are inferred. |

continued

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | *B8.2 Patient has social responsibilities* | 'Two of the most common dynamics impacting tapering were patients' ability to fulfil their roles and responsibilities related to their work and family. For example, one patient deferred tapering until after retirement because he needed opioids in order to work' (Author-interpreted provider summary).[99]<br>'Patients and pharmacists both noted that opioid tapering can be hampered or halted because of other ongoing health issues, *caretaker responsibilities*, *or other family*, *career*, *or financial struggles*' (Author-interpreted provider summary).[95]<br>'Significant caretaker role and responsibilities (e.g. taking care of dying spouse or ill child)' (Author-interpreted provider summary).[95]<br>'Adversity experienced by participants. . . Financial stress ("My husband doesn't have a lot of work", P16)' (Patient quote).[106]<br>'. . .one patient deferred tapering until after retirement because he needed opioids in order to work' (Author-interpreted provider summary).[99] | Kuntz 2021[95]<br>Henry 2019[99]<br>McNeilage 2022[106] | No or very minor concerns | Minor concerns<br>Fairly rich data mostly from two studies with adequate number of observations (patient: 10 summaries, 3 quotes; provider: 5 summaries) | No or very minor concerns<br>Finding title incorporates a range of social responsibilities | No or very minor concerns<br>Finding fully supported by one directly relevant study | High confidence | Three studies with minor concerns about data adequacy. No or very minor concerns about methodological limitations, coherence and relevance. |

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | *B8.3 Patient experiences psychological or health-related issues outside of tapering* | 'One patient reported starting, escalating, and then tapering off opioids 3 separate times; the last 2 episodes were due to injuries during car accidents' (Author-interpreted patient summary).[99]<br>'Another participant described a situation in which she contracted the flu and could not take her pain medication for a day or two' (Author-interpreted patient summary).[93]<br>'There are people that have some sort of event happen where it's really not appropriate to keep tapering all the way through they are having major surgery or they have a significant death in the family' (Provider quote).[95]<br>'Other ongoing health issues (e.g. surgery, influenza) that slowed or stopped taper' (Author-interpreted patient/provider summary).[95]<br>'a few participants noted that opioids could act as an emotional crutch and could be used inadvertently to self-medicate for stress, depression, and anxiety' (Author-interpreted patient summary).[106]<br>'Adversity experienced by participants . . . other health complications' (Author-interpreted patient summary).[106] | Kuntz 2021[95]<br>Henry 2019[99]<br>McNeilage 2022[106]<br>Benintendi 2021[93] | No or very minor concerns | Minor concerns<br>Rich data from 4 studies with large numbers of observations (patient: 15 summaries, 10 quotes; provider: 5 summaries, 2 quotes) | No or very minor concerns<br>Finding title incorporates a range of non-tapering-related health/psychological issues | Minor concerns<br>Finding supported by three studies in which barriers and facilitators are inferred. | High confidence | Four studies with minor concerns about data adequacy and relevance. No or very minor concerns about methodological limitations and coherence. |

continued

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| ***Facilitators*** | | | | | | | | | |
| F1. Patient recognises the negative impact of opioids, understands what tapering is and perceives/ experiences the benefits of tapering | *F1.1 Patient recognises the negative impact of opioid use on themselves and/or on others* (e.g. *on family)* | 'Providers noted that patients to whom family is highly important or who expressed concern about taking medications were more likely to be receptive to a discussion about tapering opioids' (Author-interpreted provider summary).[102]<br>'if I have to take more I'll be in serious trouble' (Patient quote).[99]<br>'I don't like feeling – I like to stay in control of me' (Patient quote).[99]<br>'Patient notices adverse effects/has concerns regarding possible addiction' (Author-interpreted patient summary).[95]<br>'Patient Quote: 'I had times where I would just fall asleep on the couch . . . and I wanted to get off oxycodone because [it was] not working well for me . . . it made me tense and uptight' (Patient quote).[95]<br>'Dependence and addiction were issues alluded to by 16 (27%) patients, either reflecting their own concerns or the judgement of others' (Statistical data).[107]<br>'Many statements suggest that long-term opioids are having a negative impact on the patient's quality of life and, likely, on that of their family and friends' (Author-interpreted patient summary).[107] | Henry 2019[99]<br>Langford 2020[103]<br>Henry 2019[100]<br>Quinlan 2020[107]<br>Kennedy 2018[102]<br>Kuntz 2021[95]<br>Matthias 2017[105] | No or very minor concerns<br>Finding supported largely by one good quality study and two with some concerns | No or very minor concerns<br>Rich data with large number of studies and observations (patient: 27 summaries, 17 quotes; provider: 2 summaries, 2 quotes; statistical data: 2) | No or very minor concerns<br>Finding title incorporates a range of negative impacts seen across the data | No or very minor concerns<br>Finding fully supported by directly relevant data | High confidence | Seven studies with no or very minor concerns about methodological limitations, adequacy of data, coherence and relevance. |

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | *F1.2 Patients understand what tapering is* | 'Patients who understood tapering to mean a gradual or partial reduction in opioid medications were generally more receptive to tapering than those who understood it to mean stopping "cold turkey" or stopping opioids completely' (Author-interpreted patient summary).[99] 'Patients experienced tapering as dynamic because their pain and perceived need for opioids varied from day to day and because their pain was frequently affected (either positively or negatively) by changes in their social relationships and emotional state' (Author-interpreted patient summary).[99] | Henry 2019[99] | Minor concerns | Serious concerns Adequate data from a limited number of observations in one study (patient: four summaries, predictive: two) | Moderate concerns Elements of some underlying data are vaguely described | Moderate concerns Finding supported by only one study in which barriers and facilitators are inferred. | Very low confidence | One study with serious concerns about data adequacy. Moderate concerns about coherence and relevance. Minor concerns about methodological limitations. Downgraded due to finding based entirely on data from a single study, based in which barriers and facilitators are inferred and vague descriptions of underlying data. |

continued

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | *F1.3 Patient knows about tapering alternatives and is optimistic about tapering effectiveness* | 'Referrals for non-medication behavioural treatments were also found to be acceptable for short term treatment intervention when the patient could see the value in the referral' (Author-interpreted patient summary).[108]<br>'"yeah, they've actually given me a referral to see their dietitian and because my arthritis is . . . I've put on a little bit of weight so it's hurt my knees" (Female age 47)' (Patient quote).[108]<br>'The techniques participants used were typically influenced by factors such as their knowledge of nonopioid alternatives as well as cost and availability' (Author-interpreted patient summary).[106] | McNeilage 2022[106]<br>White 2020[108] | No or very minor concerns | Moderate concerns<br>Adequate data from a small number of studies and very limited number of observations (patient: two summaries, two quotes) | Moderate concerns<br>Supporting data are not always sufficiently described to be sure that the data clearly supports the finding | Moderate concerns<br>Finding supported by studies in which barriers and facilitators are inferred. In one study it is unclear whether their population of chronic pain patients also included cancer patients | Very low confidence | Two studies with moderate concerns about data adequacy, coherence and relevance. No or very minor concerns about methodological limitations. Downgraded due to limited supporting data, lack of clarity of data and finding supported entirely by studies in which barriers and facilitators are inferred. |

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | *F1.4 Patient experiences unchanged/ improved health status or minimal/ no withdrawal symptoms* | 'It's not much worse without the medication as it is with it. After you've taken it for a while, it doesn't do any good. That's what I've found. But that's hard to convince people of it. . .' (Patient quote).[96]<br>'My family is really pleased too. Like, I'm more alert now. They say I'm engaged more again and talking to them. I don't just sit there and zone out' (Patient quote).[96]<br>'Patients who experienced minimal withdrawal symptoms or increases in pain during tapering perceived greater success with taper' (Author-interpreted patient/ provider summary).[95]<br>'These participants generally reported steadily decreasing opioid doses, steady improvements in functioning. . .' (Author-interpreted patient summary).[106]<br>'They reported unchanged or improved functioning and unchanged or improved mood' (Author-interpreted patient summary).[106] | Frank 2016[96]<br>Henry 2019[99]<br>McNeilage 2022[106]<br>Kuntz 2021[95] | No or very minor concerns | Minor concerns<br>Rich data from small number of studies with adequate number of observations (patient: 13 summaries, 11 quotes; provider: 2 summaries) | No or very minor concerns<br>Finding title incorporates a range of patient experiences relating to health status/ withdrawal symptoms | No or very minor concerns<br>Finding fully supported by two directly relevant studies | High confidence | Four studies with minor concerns about data adequacy. No or very minor concerns about methodological limitations, coherence and relevance. |

continued

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| F2. Ability to initiate, manage/ cope with taper | *F2.1 Patient is psychologically/ physically prepared to taper* | 'It's just I've had to re-learn how to do things and to accept that some things I'm not gonna be able to do.. . . I'm a huge Disneyland fan.. . . And I realized I can't ride some of the rides I always did' (Patient quote).[99]<br>'participant 03 explained that by learning to accept their pain, they were able to "forget about it and just live like normal"' (Author-interpreted patient summary/patient quote).[106]<br>'Similarly, during pain flare-ups, participants' approach to pain coping was to "grit my teeth and bear it" (P09), "get on with it" (P11), and "put up with it" (P19)' (Author-interpreted patient summary/patient quote).[106]<br>'I could feel the with-drawals, but they weren't anything I couldn't handle' (Patient quote).[95]<br>'Successful surgery and/ or implant that greatly decreased pain levels and need for opioid medication' (Author-interpreted patient/ provider summary).[95] | Henry 2019[99]<br>McNeilage 2022[106]<br>Kuntz 2021[95]<br>Magee 2021[104] | No or very minor concerns | Minor concerns<br>Rich data from small number of studies with adequate number of observations (patient: 12 summaries, 9 quotes; provider: 1 summary) | No or very minor concerns<br>Finding title incorporates a range of psychological and physical approaches patients adopted to cope with pain | Minor concerns<br>Finding partially supported by two studies in which barriers and facilitators are inferred. | High confi-dence | Four studies with minor concerns about data adequacy and rele-vance. No or very minor concerns about meth-odological limitations and coher-ence. |

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | *F2.2 Patient is able to manage taper (self-efficacy)* | 'Participants used a range of pharmacological (e.g. over-the counter analgesics, gabapentinoids, antidepressants, and alcohol) and nonpharmacological (e.g. distraction, rest, exercise, cognitive behavioural techniques, heat and ice packs, and massage) strategies to cope with opioid tapering' (Author-interpreted patient summary).[106]<br>'Tapering prompted some patients to curtail or re-think activities, while others adopted new strategies (e.g. staying physically and socially active) to manage pain and get through the day' (Author-interpreted patient summary).[99]<br>'The reality of tapering off medication, for me, has been that if I'm careful, and I really follow the plan of taking a pill every six hours, or every eight hours, I'm going to be okay.. . . I may be somewhat physically uncomfortable, but I'm not in screaming pain.. . .' (Patient quote).[99] | Henry 2019[99]<br>McNeilage 2022[106] | Minor concerns | Minor concerns<br>Rich data from small number of studies with adequate number of observations and statistically significant data (patient: 19 summaries, 13 quotes; statistical data: 1) | Minor concerns<br>Studies generally addressed self-efficacy though some did not sufficiently describe how patients were able to manage taper | Moderate concerns<br>Finding fully supported by two studies in which barriers and facilitators are inferred. In one study it is unclear whether their population of chronic pain patients also included cancer patients | Moderate confidence | Two studies with moderate concerns about relevance. Minor concerns about methodological considerations, data adequacy and coherence. Downgraded due to finding based entirely on studies in which barriers and facilitators are inferred. |

continued

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | *F2.3 Provider has training to taper and is aware of tapering resources* | '. . . providers need training to successfully make a shift away from opioids' (Author-interpreted provider summary).[97]<br>'But I think that we need more resources and better education' (Provider quote).[97]<br>'All PCPs interviewed reported awareness of STORM due to participation in standard training about STORM' (Author-interpreted provider summary).[94]<br>'But I feel like once I had a handle on what the STORM team was and what they could offer and how to get in touch with them, it's so smooth. It runs so easily. It just took care of itself' (Provider quote).[94]<br>'PCPs generally appreciated the training provided by the STORM program and the resource of specialized staff for consultation and support' (Author-interpreted provider summary).[94]<br>'Motivational interviewing practice' (Author-interpreted provider summary).[109] | Firemark 2021[94]<br>Giannitrapani 2018[97]<br>Wu 2019[109] | No or very minor concerns<br>Finding supported fully by one high quality study | Moderate concerns<br>Adequate data from small number of studies and observations (provider: five summaries, one quote) | Minor concerns<br>Finding is generally consistent across data | No or very minor concerns | Moderate confidence | Three studies with moderate concerns about data adequacy. Minor concerns about coherence. No or very minor concerns about methodological limitations andrelevance. Downgraded due to limited number of observations. |

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | *F2.4 Provider is able, confident and proactive in their ability to taper* | 'Providers additionally identified serious adverse events or crises as opportunities to assert a more urgent indication to taper opioid therapy' (Author-interpreted provider summary).[102]<br>'"I've been pleasantly surprised when people don't get angry, and they say, 'Well, I guess that's a reasonable place to start.' And I'm a little bit bowled over because there were years when I would just get beat up". (Interview: PCP 9)' (Provider quote).[105]<br>'"The number of people who do profess the fact that they are aware of a degree of dependence and they would like to do something about it, and I think they are the ones we can target". (P1, SI)' (Provider quote).[103]<br>'Within the community setting, it was suggested that prescribers need to be more proactive in initiating opioid deprescribing when they "inherit" a patient from another prescriber' (Author-interpreted provider summary).[103] | Firemark 2021[94]<br>Matthias 2017[105]<br>Kennedy 2018[102]<br>Langford 2020[103] | No or very minor concerns | Moderate concerns<br>Adequate data from small number of studies and reasonable number of observations (provider: seven summaries, nine quotes) | Serious concerns<br>Key aspects of the underlying data are sometimes vaguely defined or described and we cannot always be sure that the data in fact clearly support the review finding | Moderate concerns<br>In all four studies it is unclear whether their population of chronic pain patients also included cancer patients and one also included acute pain patients | Low confidence | Four studies with serious concerns about coherence. Moderate concerns about data adequacy and relevance. No or very minor concerns about methodological limitations. Downgraded due to concerns over coherence, small number of studies and relevance. |

continued

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | | '"If it's brought to my attention from the administrators here or other powers that be, that they are on too much opioids, then I would engage [the patient] and then talk to them about decreasing. I guess the best way I can put it is – if it isn't broken and it's working for them and no one is telling me that they're taking too much, I just kind of keep it as is" (PCP)' (Provider quote).[94] | | | | | | | |
| F3. Clear, consistent, supportive and timely communication in preparing patients to taper | *F3.1 Timely communication when initiating and engaging with, opioid tapering* | 'The key is to establish the expectations upfront when you're prescribing . . . It helps the patient understand where things are going on that trajectory and makes the conversation about deprescribing much easier' (Provider quote).[103] 'The most important thing from my perspective is thinking about deprescribing from the point of initiation. So, having an exit plan. Part of that is having a deprescribing strategy at the point of initiating opioids, not when you realise that they aren't working' (Provider quote).[103] 'pharmacists described how PCPs are reminded of and encouraged to use the program during STORM team check ins through rounding and consultation about patients' (Author-interpreted provider summary).[94] | Kennedy 2018[102] Kuntz 2021[95] Magee 2021[104] Langford 2020[103] Firemark 2021[94] | No or very minor concerns Finding fully supported from good quality studies | Minor concerns Rich data from adequate number of studies and observations (patient: two summaries, one quote; provider: eight summaries, three quotes) | No or very minor concerns Data relates directly to the finding | No or very minor concerns Finding supported in full by directly relevant studies | High confidence | Five studies with minor concerns about data adequacy. No or very minor concerns about methodological limitations, coherence and relevance. |

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | | 'They identified quick responsiveness by STORM pharmacists to meet PCP and patient needs as facilitating use of the program' (Author-interpreted provider summary).[94] 'Participants' views regarding the acceptability of mHealth interventions for opioid tapering were influenced by factors such as the frequency of the messages and pattern of delivery. One participant preferred receiving messages at night, whereas another was concerned about receiving too frequent or too repetitive messages' (Author-interpreted provider summary/provider quote).[104] | | | | | | | |
| | *F3.2 Clear, consistent, tailored communication from provider* | 'some PCPs successfully tailored their messages about opioid tapering to their patients' individual circumstances. For example, the following PCP described how she helped a patient with pulmonary disease better understand why she was reducing her opioids' (Author-interpreted provider summary).[105] 'Well, it's easier to talk about stuff like erectile dysfunction and no testosterone because that is a more direct thing than, let's say, the overdose issue, which is going to be rare for any individual patient' (Provider quote).[102] | Kennedy 2018[102] Matthias 2017[105] McNeilage 2022[106] Magee 2021[104] | No or very minor concerns | No or very minor concerns Very rich data from small number of studies with a large number of observations (patient: 3 summaries, 2 quotes; provider: 7 summaries, 17 quotes) | No or very minor concerns Data relates directly to the finding | Minor concerns Finding largely based on three studies in which it is unclear whether their population of chronic pain patients also included cancer patients | High confidence | Four studies with minor concerns about relevance. No or very minor concerns about methodological limitations, data adequacy and coherence. |

continued

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | | 'We were able to very directly talk about the [opioid] medication's effects potentially on her respiratory system. So that was very clear to her. [I said], "Listen, you have a decreased respiratory drive. You are on oxygen. We don't want anything else to suppress that"' (Provider quote).[105]<br>'I tell all my chronic pain patients [opioids] don't work. "They don't work well, you know. I'd like to help you get off them" You know what? They don't hear it the first time' (Provider quote).[102]<br>'I don't usually stop anyone cold turkey, so then I'll say, "When we taper, you'll feel a little bit of [opioid withdrawal symptoms] with each dose reduction, but it's temporary". I try to say the word temporary as many times as I can' (Provider quote).[102]<br>'other participants also described supportive relationships with a pain specialist and other allied health professionals. They reported feeling reassured by encouragement from clinicians as well as information about their pain diagnosis, opioids, and symptoms of tapering' (Author-interpreted patient summary).[106] | | | | | | | |

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | | 'One participant recommended tailoring the information to reflect the user's stage of tapering to reassure them that what they were experiencing was normal' (Author-interpreted patient summary).[104] | | | | | | | |
| F4. Strong, open, supportive patient–provider relationship | *F4.1 Mutual trust and honesty* | 'Many patients who had experienced opioid tapering identified a positive relationship with a trusted provider as a key to their willingness to initiate and their ability to sustain opioid tapering' (Author-interpreted patient summary).[96]<br>'First, they expressed the importance of mutual honesty – clinicians being honest with patients, and patients being honest with clinicians and with themselves' (Author-interpreted patient summary).[99]<br>'This patient described mutual honesty as a pre-requisite for successful opioid tapering' (Author-interpreted patient summary).[99]<br>'If you're struggling with your doctor, or struggling with the relationship with your doctor, I would first begin asking yourself, am I being completely honest with my doctor, and if I'm not, why not' (Patient quote).[99] | Henry 2019[99]<br>Frank 2016[96]<br>Kuntz 2021[95] | Minor concerns | Moderate concerns<br>Rich data from small number of studies and observations (patient: four summaries, one quote; provider: two summaries) | No or very minor concerns<br>Data relates directly to the finding | No or very minor concerns | Moderate confidence | Three studies with moderate concerns about data adequacy. Minor concerns about methodological limitations. No or very minor concerns about coherence and relevance. Downgraded due to small number of studies and observations. |

continued

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | *F4.2 Provider is supportive* | 'Providers emphasized the essential role of acknowledging patients' experience with chronic pain and expressing empathy during these discussions' (Author-interpreted provider summary).[102]<br>'Patience, empathy and compassion from pharmacists/patients feel listened to and advocated for' (Author-interpreted patient/provider summary).[95]<br>'Providers were praised for attributes such as being supportive, non- judgmental, flexible, and accessible' (Author-interpreted patient summary).[96]<br>'[my doctor] is very supportive. If I was in more pain, I feel like I could go back to her and say, "I need more"' (Patient quote).[99]<br>'important part of productive opioid tapering conversations, for patients as well as for providers, was ensuring that patients did not feel abandoned during tapering . . . PCPs frequently reassured patients that they would be with them through the entire tapering process' (Author-interpreted summary).[105]<br>'participants in this trajectory commonly reported supportive relationships with their prescribing doctor, clinical team, friends, and family. For example, participant 05 reported receiving support from their partner, prescribing doctor' (Author-interpreted patient summary).[106] | Kennedy 2018[102]<br>Frank 2016[96]<br>Henry 2019[99]<br>Henry 2019[100]<br>Kuntz 2021[95]<br>McNeilage 2022[106]<br>Matthias 2017[105]<br>White 2020[108] | No or very minor concerns | No or minor concerns<br>Relatively rich data from large number of studies and observations (patient: 18 summaries, 13 quotes; provider: 10 summaries, 7 quotes) | No or very minor concerns<br>Finding title incorporates a range of supportive behaviour/attributes described across the data | No or very minor concerns | High confidence | Eight studies with no or very minor concerns about methodological limitations, data adequacy, coherence and relevance. |

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | | 'I did want to get off of them. I just didn't want to feel attacked with "Hey, this is going to happen". I wanted to go down. I didn't want to get off of it, but I was willing to go down' (Patient quote).[96]<br>'And I just try and reassure them that I hear them, how bad the pain is, and. What we do have to offer, and some kind of hope, and try and you know I want to work with you' (Provider quote).[105]<br>'these patients described clinicians who took the time to learn about their needs, build mutual trust, and devise individualized tapering plans' (Author-interpreted patient summary).[99]<br>'Elicits more information or patient perspective' (Author interpreted provider summary).[100]<br>'Providers sought . . . to counsel patients on the potential for increased pain and opioid withdrawal symptoms during dose reduction'. (Author interpreted provider summary).[102] | | | | | | | |

continued

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| F5. Decision to initiate and manage taper involves patient and is driven by patient need | *F5.1 Motivation and goals to taper exist and are patient driven* | 'I can probably count on one hand the number of patients that have come to my office in 20 years and said, "Hey, I really want to cut down the dose". Almost inevitably when I run into this, it's precipitated by some sort of a crisis' (Provider quote).[102]<br>'I think the defining moment for me was, I was standing holding one of the babies and I fell asleep . . . [My family] had had it so I wasn't allowed to see the kids, none of my grandkids, until I decided what I was going to do' (Patient quote).[99]<br>'Other patients cited the goal of better health as a motivation for tapering' (Author-interpreted patient summary).[99]<br>'"Tapering dose is something that I would be happy to do with a patient if they wanted to". (P5, SI)' (Provider quote).[103]<br>'Patients and pharmacists noted that openness to reduce opioid use, a concern about adverse effects or addiction, an aversion to the idea of being on opioids, and observations that opioids were less effective over time facilitated successful tapering' (Author-interpreted patient/provider summary).[95] | Kennedy 2018[102]<br>Henry 2019[99]<br>Kuntz 2021[95]<br>Wu 2019[109]<br>Benintendi 2021[93]<br>Langford 2020[103]<br>Quinlan 2020[107]<br>White 2020[108] | Minor concerns | No or minor concerns<br>Relatively rich data from a large number of studies and observations (patient: 12 summaries, 11 quotes; provider: 5 summaries, 6 quotes; statistical data: 3) | No or very minor concerns<br>Studies clearly described specific motivation/goals for tapering | No or very minor concerns | High confidence | Eight studies with minor concerns about methodological limitations. No or very minor concerns about data adequacy, coherence and relevance. |

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | | 'It comes back to attitude that patients who want to make the change or are willing to work with you, willing to be open to new pain management strategies, tend to be more successful'. (Provider quote).[95]<br>'hope for a better quality of life was expressed by five (8%) patients' (Statistical data).[107]<br>'Reduction of side effects such as effect on sperm quality as we are trying for a baby' (Patient quote).[107]<br>'Yeah, so I just had that determination in me so, because I've got a cruise in February, so I'm like,- right, I've got a cruise and I'm sick of being on this medication, so I was just like, bang' (Patient quote).[108] | | | | | | |

continued

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | *F5.2 Patient is involved in tapering decisions/process* | 'She put me down to 2 and a half [pills per day]. Then she said, okay, we'll go down to half a pill. I told her I didn't think that just 2 a day would do it, and she said okay' (Patient quote).[105]<br>'patient input in the tapering process also emerged as an important theme' (Author interpreted provider summary).[105]<br>'Patients as well as PCPs described a desire for patients to be given options and thereby have some control over the tapering process' (Author-interpreted patient/provider summary).[105]<br>'I'll always give people options, I think that's really important, so they don't feel trapped or hemmed in and often people feel very angry towards the health professionals for getting them on such a high dose of opioids or they feel angry at themselves' (Provider quote).[103]<br>'Patient experienced their PCP as "partnering" with them regarding the referral' (Author-interpreted patient summary).[95]<br>'"Mentally it's important for me to be very much part of the process and feel like I'm in control", P01' (Patient quote).[106] | Matthias 2017[105]<br>Kuntz 2021[95]<br>McNeilage 2022[106]<br>Langford 2020[103] | No or very minor concerns | Minor concerns<br>Rich data from a small number of studies with a large number of observations (patient: 10 summaries, 12 quotes; provider: 8 summaries, 7 quotes) | No or very minor concerns<br>Data are consistent across studies from both patients and providers | No or very minor concerns | High confidence | Four studies with minor concerns about data adequacy. No or very minor concerns about methodological limitations, coherence and relevance. |

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| F6. Taper intervention is tailored to incorporate patient need/ preferences | *F6.1 Flexible, tailored taper approach* | 'Providers sought to tailor the timing and speed of the opioid tapering plan and to counsel patients on the potential for increased pain and opioid withdrawal symptoms during dose reduction' (Author-interpreted provider summary).[102]<br>'I try to set them up for success by having any kind of taper start on a time when they might have some down time' (Provider quote).[102]<br>'Second, these patients described clinicians who took the time to . . . devise individualized tapering plans' (Author-interpreted patient summary).[99]<br>'PCPs frequently reassured patients that they would be with them through the entire tapering process, and sometimes even told patients that if the pain became intolerable, they could discuss increasing the opioid dose again for a time. This seemed to provide an important safety net for patients' (Author-interpreted patient summary).[105]<br>'I knew she wasn't just going to take me completely off of [the opioids] because I would be miserable. She just said, "We'll try this, but if you need to go back to where you were, I'll do that" (Interview: patient 20)' (Patient quote).[105] | Kennedy 2018[102]<br>Henry 2019[99]<br>Kuntz 2021[95]<br>Matthias 2017[105]<br>Langford 2020[103]<br>McNeilage 2022[106] | No or very minor concerns | Minor concerns<br>Rich data from adequate number of studies and observations (patient: seven summaries, three quotes; provider: seven summaries, three quotes) | No or very minor concerns<br>Data are consistent across studies from both patients and providers | No or very minor concerns | High confidence | Six studies with minor concerns about data adequacy. No or very minor concerns about methodological limitations, coherence and relevance. |

continued

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | | 'For these participants, their opioid dose was negotiated each time they were due for a new prescription, and, as a result, their taper was generally slower than those in other trajectories' (Author-interpreted patient summary).[106]<br>'Participant 19 reduced their dose by half (albeit from a low starting dose), P17 reduced their dose by 6% (albeit from a very high starting dose), and participants 09 and 11 reduced their opioid dose by around 50% and 75%, respectively' (Statistical data).[106] | | | | | | | |

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | *F6.2 Holistic approach to taper involving a multimodal, multidisciplinary approach to help patients manage pain, withdrawal symptoms and psychological status* | 'A structured and holistic approach to deprescribing was considered optimal, with adjunct or alternate analgesic agents, non-pharmacological pain management strategies and involvement of multidisciplinary healthcare members' (Author-interpreted provider summary).[103]<br>'PCPs described relying on the STORM team to work with those complex patients who may require longer tapers or more support than PCPs can offer' (Author-interpreted provider summary).[94]<br>'A distinguishing feature of this group was that every participant received pain education and multidisciplinary care' (Author-interpreted patient summary).[106]<br>'The other participant had requested a referral to a pain specialist to completely taper opioids and was making progress' (Author-interpreted patient summary).[109]<br>'Benefit of pain or addiction specialist care' (Author-interpreted patient summary).[109] | Langford 2020[103]<br>Wu 2019[109]<br>McNeilage 2022[106]<br>Kennedy 2018[102]<br>Firemark 2021[94]<br>Kuntz 2021[95] | No or very minor concerns | Minor concerns<br>Relatively rich data from adequate number of studies with adequate number of observations (patient: four summaries, one quote; provider: six summaries, one quote; statistical data: one) | No or very minor concerns<br>Data are consistent across studies from both patients and providers | Moderate concerns<br>Finding partially supported by two studies in which barriers and facilitators are inferred. In four studies in which it is unclear whether their population of chronic pain patients also included cancer patients and one study included patients with acute pain | Moderate confidence | Five studies with moderate concerns about data adequacy and relevance. No or very minor concerns about methodological limitations and coherence. Downgraded due to concerns over data adequacy and relevance. |

continued

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | *F6.3 Tapering initiatives incorporate patient preferences for taper support (design, delivery mode, setting)* | 'One patient was so afraid of withdrawal that she would only attempt tapering in an inpatient facility' (Author-interpreted patient summary).[99]<br>'Relatedly, some participants suggested that ease of use and simplicity of content would facilitate engagement' (Author-interpreted patient summary).[104]<br>'Participants provided recommendations for content that they believed would be helpful in an mHealth intervention' (Author-interpreted patient summary).[104]<br>'I think it would be really useful to have maybe different things on there like techniques to help. "If you've got really bad pain, why don't you try this?" [P08, female, 32 years, pain clinic, metropolitan area]' (Patient quote).[104]<br>'In line with the preference for face-to-face and nonautomated services outlined earlier, several participants recommended that an option for personal follow-up be built into the service' (Author-interpreted patient summary).[104]<br>'I think the phone call thing is better than any social media, better than anything you just type in or anything because it's human. [P04, male, 57 years, pain clinic, metropolitan area]' (Patient quote).[104] | Magee 2021[104]<br>Henry 2019[99]<br>Benintendi 2021[93] | Serious concerns<br>Finding largely based on one study with unclear data collection | Moderate concerns<br>Relatively rich data supported mostly with observations from 1 study (patient: 14 summaries, 15 quotes) | No or very minor concerns<br>Finding title incorporates a patient preferences at the broadest level to capture contradictory patient preferences for taper support | No or very minor concerns<br>Finding fully supported by one directly relevant study | Low confidence | Three studies with serious concerns about methodological limitations. Moderate concerns about adequacy of data. No or very minor concerns about coherence and relevance. Downgrade due to finding based largely on data from on one study with unclear data collection methods. |

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | | 'The text messaging I think would be really good because the thing that probably scares me most is to speak to someone about it. [P08, female, 32 years, pain clinic, metropolitan area]' (Patient quote).[104]<br>'I can use [SMS] easier. because I don't use my phone much for that sort of thing [apps]. [P09, male, 61 years, primary care, regional area]' (Patient quote).[104] | | | | | | | |
| F7. Supportive health system environment | *F7.1 Resources to taper are accessible* | 'A primary benefit of an mHealth intervention reported by participants was increased access to support for opioid tapering during periods when other services were not available (i.e. out of office hours)' (Author-interpreted patient summary).[104]<br>'I think it would be better if the appointments were closer together . . . it'd be good if more things could happen' (Patient quote).[108]<br>'Other providers, by contrast, perceived having a range of available options and emphasized that NPTs offered an important alternative to opioids for pain management' (Author-interpreted provider summary).[97]<br>'Providers endorsed the importance of allowing patients to receive care in their own community and allotting funds for community-based services and programs' (Author-interpreted provider summary).[97] | Langford 2020[103]<br>McNeilage 2022[106]<br>Giannitrapani 2018[97]<br>Firemark 2021[94]<br>Magee 2021[104]<br>Kuntz 2021[95]<br>White 2020[108]<br>Frank 2016[96] | No or very minor concerns | No or minor concerns<br>Relatively rich data from a large number of studies and observations (patient: six summaries, five quotes; provider: nine summaries, nine quotes) | No or very minor concerns<br>Data are clear and varied across the studies in terms of reasons for accessibility, but clearly supports finding | No or very minor concerns | High confidence | Eight studies with no or very minor concerns about methodological limitations, data adequacy, coherence and relevance. |

continued

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | | 'I do have the other referral options more easily available to me' (Provider quote).[103]<br>'Specialist and multidisciplinary care were largely seen as enablers to opioid deprescribing' (Author-interpreted provider summary).[103]<br>'STORM pharmacists also noted that colocation has allowed them to meet patients in person, improving patients' receptivity to the referral' (Author-interpreted provider summary).[94]<br>'So [the patient] is looking at this as confirmation that what I had decided is appropriate, because now they're hearing it from somebody else [STORM pharmacist] as well' (Provider quote).[94]<br>'Regular contact and easy access to same pharmacist (e.g. both scheduled and unscheduled calls)' (Author-interpreted provider summary).[95]<br>'I think the mobile system would be good for that because it feels like you have some way of reaching someone or some way of someone reaching you to check in' (Patient quote).[104] | | | | | | |

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | *F7.2 Guidelines support providers to taper* | 'We do have a contract, and it's really spelled out what we're supposed to be doing. I just give them the contract and I say, "Whether I agree with it or not, it's something that I have to follow, and so the patient has to follow as well"' (Provider quote).[102]<br>'PCPs described how access to CDC opioid prescribing guidelines makes it easier to initiate conversations with patients about tapering' (Author-interpreted provider summary).[94]<br>'When I first came [to HCS] it was before the CDC gave their recommendations. So, it was much more difficult. Now it's very nice with the CDC because there's strict guidelines – it's just made it a little bit easier' (Provider quote).[94]<br>'I don't think a guideline on its own will fix this problem . . . you need to think about how to get people to actually use the guideline' (Author-interpreted provider summary).[103]<br>'Consideration of individual patient psychosocial factors was emphasised as being integral to the deprescribing approach. Due to the variability of patients and their individual circumstances, participants highlighted that prospective opioid deprescribing guidelines would need to address patient psychosocial factors while allowing clinicians to tailor care to patients' personal circumstances' (Author-interpreted provider summary).[103] | Kennedy 2018[102]<br>Langford 2020[103]<br>Firemark 2021[94] | No or very minor concerns | Minor concerns<br>Rich data supported by a small number of studies with a large number of observations (provider: 14 summaries, 7 quotes) | No or very minor concerns<br>Data are clear and consistent in supporting finding | Minor concerns<br>Finding supported fully by three studies in which it is unclear whether their population of chronic pain patients also included cancer patients and one study included patients with acute pain | High confidence | Three studies with minor concerns about data adequacy and relevance. No or very minor concerns about methodological limitations and coherence. |

continued

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | | 'In potential contrast to the facilitators above that supported individualized opioid tapering, providers also acknowledged the supportive role of local policies and expert guidelines that they applied universally to all patients on long-term opioid therapy' (Author-interpreted provider summary).[102] | | | | | | | |
| F8. Patient has social responsibilities and a strong social support system | *F8.1 Presence of patient social support* | 'Patients experienced tapering as dynamic because their pain and perceived need for opioids varied from day to day and because their pain was frequently affected (either positively or negatively) by changes in their social relationships' (Author-interpreted patient summary).[99]<br>'Tapering success was linked to the presence of a patient social support system and the use of additional resources to cope with challenges that may arise during tapering' (Author-interpreted patient summary).[95]<br>'Having a supportive wife. She'd point out things, and she was more aware than I and that helped me recognize the pros [of tapering]' (Patient quote).[95]<br>'A number of participants commented more generally on the importance of social support when tapering, either from friends and family, a group within a treatment program, or clinicians' (Author-interpreted patient summary).[104] | Henry 2019[99]<br>Kuntz 2021[95]<br>Frank 2016[96]<br>Magee 2021[104]<br>McNeilage 2022[106] | No or very minor concerns | No or minor concerns<br>Rich data supported by adequate number of studies with large number of observations (patient: 12 summaries, 8 quotes; provider: 3 summaries, 1 quote) | No or very minor concerns<br>Data are clear and consistent in supporting finding | No or very minor concerns | High confidence | Five studies with no or very minor concerns about methodological limitations, data adequacy, coherence and relevance. |

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | | 'Participants often attributed their ability to taper their opioids safely and successfully to the support of friends, family, and clinicians' (Author-interpreted patient summary).[106]<br>'Although they typically had less frequent contact with healthcare providers than those with other trajectories, the survivors described supportive relationships with family and friends in their community' (Author-interpreted patient summary).[106] | | | | | | | |
| | *F8.2 Patient has social responsibilities* | 'Providers noted that patients to whom family is highly important or who expressed concern about taking medications were more likely to be receptive to a discussion about tapering opioids' (Author-interpreted provider summary).[102]<br>'Well, she has a partner who has a lot of medical problems herself and is going to need more care and she didn't feel like she was able to do that with the amount of pain medication that she was on' (Provider quote).[102] | Kennedy 2018[102]<br>Henry 2019[99] | Minor concerns | Moderate concerns<br>Relatively rich data from two studies with limited number of observations (patient: one summary, two quotes; provider: one summary, one quote) | No or very minor concerns<br>Data are clear and consistent in supporting finding | Minor concerns<br>Finding fully supported by two studies in which barriers and facilitators are inferred | Low confidence | Two studies with moderate concerns about data adequacy. Minor concerns about methodological limitations and relevance. No or very minor concerns about coherence. |

continued

**TABLE 38** Summary of findings and evidence profile (Review 3) (*continued*)

| Overarching theme | Review finding | Illustrative quotes | Supporting studies | Methodological limitations | Adequacy of data | Coherence | Relevance | CERQual rating | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | | 'My mother-in-law came to live with us about three months ago. She needs care, so guess who's having to take care of her when I get home? That means I've got to take less medication to be able to function when I get home' (Patient quote).[99]<br>'I still try to be productive around the house, and part being a taxi for the family, you're driving people and stuff like that, so coherence is my responsibility . . .' (Patient quote).[99] | | | | | | | Downgraded due to limited number of studies and observations and findings based entirely on studies in which barriers and facilitators were inferred. |

# **Appendix 7** Barriers and facilitators to opioid tapering mapped to the Theoretical Domains Framework (Review 3)

**TABLE 39** Barriers and facilitators to opioid tapering mapped to the TDF (Review 3)

| TDF domain | | Individual (patient) | Individual (provider) | Interpersonal | Organisational | Environmental |
|---|---|---|---|---|---|---|
| 1. Knowledge (an awareness of the existence of something) | Barriers | • Lack of understanding of what tapering is and why they need to taper opioids[94,99,105] (B1.1) HC | • Lack of knowledge about tapering opioids[94,103] (B1.4) MC | | | |
| | | • Believes they need or expects an alternative to opioids to manage their pain[96,103,106] (B1.3) MC | • Lack of awareness/ understanding of tapering support available[94] (B1.3) MC | | | |
| | Facilitators | • Recognises the negative impact of opioid use on themselves[95,99,100,102,103,107] and on others[107] (F1.1) HC | • Awareness of tapering resources[94] (F2.3) MC | | | |
| | | • Understands what tapering is and why it applies to them[99,105] (F1.2) VLC | | | | |
| | | • Awareness of non-opioid alternatives[106] (F1.3) VLC | | | | |
| 2. Skills (an ability or proficiency acquired through practice) | Barriers | • Lack of experience in using mode of opioid taper initiative[104] (B6.1) VLC | | • Poor provider communication with patients[93,105] (B3.3) MC | | |
| | Facilitators | | • Trained to taper opioids in chronic pain patients[94,97,109] (F2.3) MC | • Provider prepares patient for tapering[95,102] (F3.1) HC | | |
| | | | | • Provider explains reasons for need to taper to patient focusing on relevant, unpleasant side effects[102,105] (F3.2) HC | | |

**TABLE 39** Barriers and facilitators to opioid tapering mapped to the TDF (Review 3) (*continued*)

| TDF domain | | Individual (patient) | Individual (provider) | Interpersonal | Organisational | Environmental |
|---|---|---|---|---|---|---|
| | | | | • Provider is consistent in tapering messages,[102] balances empathy with concern for safety[102] and reassures patients[105,106] during tapering discussions (F3.2) HC<br>• Provider listens to patient[105] (F4.2) HC<br>• Provider is empathetic[95,100,102,105,106] (F4.2) HC | | |
| 3. Social/professional role and identity (a coherent set of behaviours and displayed personal qualities of an individual in a social or work setting) | Barriers | | • Resistant to tapering patients below a specified threshold[94] (B5.1) HC | | | • Competing demands and expectations make decisions about tapering patients more difficult[94,102,103] (B5.1) HC |
| | Facilitators | | | | | |
| 4. Beliefs about capabilities (acceptance of the truth, reality, or validity about an ability, talent, or facility that a person can put to constructive use) | Barriers | • Feel dependent on opioids[95,103] (B1.2) MC | • Belief that tapering is challenging for patient[103] (B2.3) MC | • Patient does not feel provider involves them in tapering process/ decisions[105] (B4.2) LC | | |
| | | • Lack of confidence in use of opioid taper initiative[104] (B6.1) VLC | • Belief that it is difficult to change existing patient preferences/ expectations about using opioids to manage chronic pain[97,103] (B2.3) MC<br>• Belief that patient is hard to motivate[108] (B2.3) MC | | | |

continued

**TABLE 39** Barriers and facilitators to opioid tapering mapped to the TDF (Review 3) (*continued*)

| TDF domain | | Individual (patient) | Individual (provider) | Interpersonal | Organisational | Environmental |
|---|---|---|---|---|---|---|
| | Facilitators | | • Confident in ability to manage an opioid taper[94] (F2.4) LC | • Patients should be involved[95,105] or feel involved in tapering decisions/process[105,106] (F5.2) HC | | |
| 5. Optimism (the confidence that things will happen for the best or that desired goals will be attained) | Barriers | • Content with current opioid use and its role in managing pain[95,107] (B1.2) MC | • Pessimistic about efficacy and use of non-opioid alternatives to manage pain[103] (B2.2) LC | | | |
| | | • Pessimistic about effectiveness of non-opioid/medication options to manage pain/improve quality of life[96,103,106] (B2.2) LC | • Belief that patient is not open to tapering[94] (B4.1) MC | | | |
| | Facilitators | | • More willing to taper if patient is open to taper[95,103] or requests to[102] (F5.1) HC | | | |
| 6. Beliefs about consequences (acceptance of the truth, reality, or validity about outcomes of a behaviour in a given situation) | Barriers | • Low perceived risk of opioid use/side effects[96,100,102] (B1.1) HC | • Experience/expectation of negative/uncertain outcome of tapering[94,97,102,103,105,108,117] (B2.1) HC | | • Concern that resource is understaffed[94] (B7.1) HC | • Concern that tapering resource will be discontinued[94] (B7.1) HC |
| | | • Belief that opioids play important role in managing pain[95,100] (B1.2) MC | | | | |
| | | • Experience/expectation of negative/uncertain outcome of tapering[106,108] (B2.1) HC | | | | |
| | | • Tapering worsens patient's health status[95,99,104,106,109] (B5.3) HC | | | | |

**TABLE 39** Barriers and facilitators to opioid tapering mapped to the TDF (Review 3) (*continued*)

| TDF domain | | Individual (patient) | Individual (provider) | Interpersonal | Organisational | Environmental |
|---|---|---|---|---|---|---|
| | Facilitators | • Perceives value of referral for non-medication behavioural treatment[108] (F1.3) VLC<br>• Tapering improves health/emotional status[96,99,106] (F1.4) HC<br>• Experiences no/minimal withdrawal symptoms[95,96] (F1.4) HC<br>• Acceptance of consequences (e.g. can cope with pain)[95,99,106] (F2.1) HC<br>• Recognises effort needed to taper[99] (F2.2) MC | | | | |
| 7. Reinforcement (increasing the probability of a response by arranging a dependent relationship, or contingency, between the response and a given stimulus) | Barriers | • Lack of clear motivation to taper[99,106] (B4.1) MC<br>• Tapering worsens health status[95,99,104,106,109] (B8.3) HC | | | | • Provider motivated to taper by institutional pressure[93,94,95] or desire to reduce opioids[99] (B4.1) MC |
| | Facilitators | • Motivated to taper[95,99,102,109] (F5.1) HC | | • Provider motivated to taper by individual patient need[93] (F5.1) HC | | |
| 8. Intentions (a conscious decision to perform a behaviour or a resolve to act in a certain way) | Barriers | | | | | |

continued

**TABLE 39** Barriers and facilitators to opioid tapering mapped to the TDF (Review 3) (*continued*)

| TDF domain | | Individual (patient) | Individual (provider) | Interpersonal | Organisational | Environmental |
|---|---|---|---|---|---|---|
| | Facilitators | | • Proactive in identifying opportunities to asset taper[102,103] (F2.4) LC | • Mutual honesty between patient and provider[99] (F4.1) MC<br>• Provider works to build mutual trust with patient[99] (F4.1) MC<br>• Provider seeks to understand patient needs[99,100,105] is responsive[106] and flexible[96,106] (F4.2) HC<br>• Provider seeks to involve patient in tapering process/ decisions[95,105] (F5.2) HC | | |
| 9. Goals (mental representations of outcomes or end states that an individual wants to achieve) | Barriers | • Lack of personal goal(s) for tapering[106] (B4.1) MC | | | | |
| | Facilitators | • Has personal goal(s) for tapering[99,107,108] | | | | |
| 10. Memory, attention and decision processes (the ability to retain information, focus selectively on aspects of the environment, and choose between two or more alternatives) | Barriers | • Trade-off between pain management and opioid risk[96,99] (B1.2) MC<br>• Lacks control or choice over taper[95] (B4.2) LC | • Belief that tapering may not be appropriate for some patients[103,105] (B5.1) HC | | | |
| | Facilitators | • Patient has some control[95,105,106] or choice[95,103,105] of taper (F5.2) HC | | • Provider and patient plan for opioid reduction at the point of prescribing[103] (F3.1) HC | | |

**TABLE 39** Barriers and facilitators to opioid tapering mapped to the TDF (Review 3) (*continued*)

| TDF domain | | Individual (patient) | Individual (provider) | Interpersonal | Organisational | Environmental |
|---|---|---|---|---|---|---|
| 11. Environmental context and resources (any circumstance of a person's situation or environment that discourages or encourages the development of skills and abilities, independence, social competence, and adaptive behaviour) | Barriers | • Accessibility issues (e.g. poor vision)[104] (B6.1) VLC | | | • Opioid-tapering initiative does not incorporate patient need or preferences[99,104,109] (B6.1) VLC | • Non-pharmacological pain management is more time intensive compared to medications[94,97,103] (B5.2) LC |
| | | • Unable to afford to taper[97,104] (B7.1) HC | | | • Lack of access to taper support (e.g. no internet)[104] (B6.1) VLC | • Lack of availability of resources[97,102,103] (B7.1) HC |
| | | • Experiences traumatic event (e.g. death of family member)[95,106](B8.2) HC | | | • Patients feel stigmatised by tapering initiative[93,103] (B6.2) HC | • Lack of timely access to tapering resources/ support[102,103] (B7.1) HC |
| | | • Health status declines due to reasons not associated with tapering[93,95,99,106] (B8.2) HC | | | • Tapering initiatives facilitate mistrust/ provider abandonment/patient disconnect from health care/reduction of patient autonomy/ change of clinicians/ patient seeking alternative opioids supply[93,99,102,106] (B6.2) HC | • Resources are not affordable/costly[103] (B7.1) HC |
| | | • Work/financial responsibilities prevent initiation or engagement with taper[95,99,106] (B8.2) HC | | | • Lack of co-location of provider and taper support (MDT team)[94] (B7.1) HC | • Lack of adequate opioid-tapering training[102] (B7.1) HC |
| | | | | | • Unable to reach taper support (distance/lack of transport)[93,97] (B7.1) HC | • Unsupportive local tapering policy and expert tapering guidelines[103] which don't recognise need for tailoring[99,103] or are stigmatising[93,109] (B7.4) MC |

continued

**TABLE 39** Barriers and facilitators to opioid tapering mapped to the TDF (Review 3) (*continued*)

| TDF domain | Individual (patient) | Individual (provider) | Interpersonal | Organisational | Environmental |
|---|---|---|---|---|---|
| | | | | | • Workload pressures (e.g. providers feel pressured to demonstrate productivity rather than spend adequate time on taper)[94,97,103] and lack of time to manage taper[102] (B7.3) MC |
| Facilitators | | | • Timely communication[104] (F3.1) HC | • Tailored information to reflect patient stage of tapering[104] (F3.2) HC | • Flexible, tailored taper appro ach[95,99,102,103,105,106] (F6.1) HC |
| | | | • Responsive interprofessional communication[94] with reminders about tapering support available[94] (F3.1) HC | • Use of alternative therapies (non-opioid analgesics, non-pharmacological pain management)[103,106,109] (F6.1) HC | • Treatment of patient comorbidities[109] (F6.1) HC |
| | | | | • Supported by a multi-disciplinary team (e.g. pharmacist, psychologist)[94,95,102,103,106] (F6.2) HC | • Accessibility of resources[103] including alternatives treatments for pain[97] access to a MDT[94,103] and co-location of provider and MDT[94] (F7.1) HC |
| | | | | • Patient expresses preferences for taper support (design, delivery mode, setting)[93,99,104] (F6.3) LC | • Affordability of tapering[106] (F7.1) HC |
| | | | | • Accessibility of resources,[96,106] including out-of-hours access[104]and access to same/regular provider[94,95,108] (F7.1) HC | • Tapering guideline implementation strategy[103] (F7.2) HC |

**TABLE 39** Barriers and facilitators to opioid tapering mapped to the TDF (Review 3) (*continued*)

| TDF domain | | Individual (patient) | Individual (provider) | Interpersonal | Organisational | Environmental |
|---|---|---|---|---|---|---|
| | | | | | • Taper support delivered in community/home[97] (F7.1) HC | • Supportive local tapering policy and expert tapering guidelines[94,102,103] which recognise need for tailoring[103] and a multimodal tapering approach[103] (F7.2) HC |
| 12. Social influences (those interpersonal processes that can cause individuals to change their thoughts, feelings, or behaviours) | Barriers | • Feel stigmatised[93,95,103,105,106,107] or racially discriminated against[93] (B3.2) HC | | • Lack of trusting patient/provider relationship with patient[94,102,106] (B3.1) MC | • Lack of advice/guidance on managing taper[99] (B3.3) MC | |
| | | • Fears pain would be disbelieved or invalidated by provider[93,106] (B3.2) HC | | • Perceived power imbalance between the clinician and patient[99] (B4.2) LC | | |
| | | • Lack of social support[99,106] (B8.1) LC | | • Disconnect between providers[103] (B7.2) VLC | | |
| | | • Family responsibilities prevent initiation of, or engagement with, taper[95] (B8.2) HC | | | | |
| | Facilitators | • Presence of social support[95,96,99,104,106] (F8.2) LC | • Positive experiences of patient interactions (interactions with patients are not difficult)[105] (F2.4) LC | • Trusting patient–provider relationship[95,96] (F4.1) MC | | |
| | | • Family responsibilities facilitate initiation of, or engagement with taper[99,102] (F8.2) LC | | • Supportive[95,96,99,100,102,106] non-judgemental[96] providers (F4.2) HC | • Patient given advice/guidance on managing taper[99,108] (F7.2) HC | |

continued

**TABLE 39** Barriers and facilitators to opioid tapering mapped to the TDF (Review 3) (*continued*)

| TDF domain | | Individual (patient) | Individual (provider) | Interpersonal | Organisational | Environmental |
|---|---|---|---|---|---|---|
| 13. Emotion (a complex reaction pattern, involving experiential, behavioural, and physiological elements, by which the individual attempts to deal with a personally significant matter or event) | Barriers | • Fear of uncertain or negative outcome when tapering[95,96,99,107,108] (B2.1) HC | • Fear patient may experience an adverse tapering outcome[103,105] (B2.1) HC | • Feel providers are not being honest with them[99] (B3.1) MC | | |
| | | • Poor emotional status prior to taper initiation or during taper[95,96,99,104,106] (B5.1) HC | • Feel patient interactions are emotionally draining/exhausting/difficult to manage[102] (B2.3) MC | • Feel unsupported,[106,108] betrayed or abandoned[93,99] (B3.3) MC | | |
| | | | • Feel overwhelmed trying to manage a taper[94,97] (B5.1) HC | • Patient/provider don't listen to each other,[99,105,106] lacks empathy[109] or is inflexible[99] (B3.3) MC | | |
| | Facilitators | • Emotionally stable/has a good psychological state[99,104,106] | | • Patient feels listened to[95] (F4.2) HC | | |
| 14. Behavioural regulation (anything aimed at managing or changing objectively observed or measured actions) | Barriers | • Expends energy during tapering to regulate behaviour[99] (B5.2) LC | | | | |
| | | • Unable/finds it difficult to regulate behaviour[103,109] (B5.2) LC | | | | |
| | Facilitators | • Adopts strategies to manage their pain or is able to regulate their behaviour[99,102] (F2.2) MC | | | | |

HC, high confidence; LC, low confidence; MC, moderate confidence; VLC, very low confidence.

**Note**
Key – Confidence in review finding.

# **Appendix 8** Inequalities and opioid-tapering effectiveness across PROGRESS-Plus factors (Review 4)

**TABLE 40** Inequalities and opioid-tapering effectiveness across PROGRESS-Plus factors

| PROGRESS-Plus (number of studies) | Potential to widen inequalities | No evidence of widening of inequalities on opioid-tapering effectiveness |
|---|---|---|
| Place of residence (1) | *Descriptive association of place of residence with tapering outcome*<br>Living in a rural area was associated with a surviving trajectory[106]<br>*Study participation*<br>• *N* = 3 dropouts due to transportation problems[88]<br>• *N* = 2 dropouts due to difficulty with travelling[116] | |
| Race, ethnicity, language (2) | | *No differential association of race/ethnicity/language with tapering outcome*<br>• Odds of a 50% reduction in opioid use at 12 months were not statistically significant in racial/ethnic minorities compared to White non-Hispanics (OR 0.98, $p = 0.98$)[95]<br>*No association of race/ethnicity/language with tapering outcome*<br>• No association found between race and dose reduction ($p < 0.36$)[82]<br>*Study participation*<br>• No significant differences between participants who dropped out vs. those who completed[69] |
| Occupation (3) | *Impact of tapering on occupation*<br>• Ability to work got worse among patients whose dose decreased compared to patients whose dose was unchanged (62.9% vs. 33.8%, $p \leq 0.05$)[89]<br>*Descriptive association of occupation with tapering outcome*<br>• Not working (all receiving pension) was associated with a surviving trajectory (descriptive analysis)[106] | *No association of occupation with tapering outcome*<br>• No significant difference was found between employment status (yes/no) on opioid discontinuation (10.3/89.7 vs. 19.0/81.0, $p = 0.213$)[90]<br>*Study participation*<br>• No significant differences between participants who dropped out vs. those who completed[69]<br>• No statistically significant differences on lost to follow-up/completers[76] |
| Gender/sex (6) | *Differential association of gender with tapering outcome*<br>• PHQ-4 score showed a significant decline in males compared with females at week 8 (but not at baseline or 4 weeks)[110]<br>• Statistically significant effect of gender (males vs. females) on estimated change per year in average daily opioid dose Mean change (95% CI): −8.8 (−10.8 to −6.9) vs. −5.9 (−7.0 to 4.8), $p = 0.010$[83] | *No differential association of gender with tapering outcome*<br>• Effect of gender (males vs. females) on other quality-of-life outcomes not statistically significant[110]<br>• No statistically significant effect of gender on relative change per year in proportion of COT patients receiving ≥ 120 mg MED by male vs. female, relative risk (95%CI): 0.84 (0.81 to 0.87) vs. 0.85 (0.82 to 0.88), $p = 0.684$[83] |

**TABLE 40** Inequalities and opioid-tapering effectiveness across PROGRESS-Plus factors (*continued*)

| PROGRESS-Plus (number of studies) | Potential to widen inequalities | No evidence of widening of inequalities on opioid-tapering effectiveness |
|---|---|---|
| | *Association of gender with tapering outcome*<br>• Patients in the dose reduction group were more likely to be female ($p = 0.003$)[82]<br>• Odds of a 50% reduction in opioid use at 12 months were decreased among men (OR 0.83, $p < 0.021$)[95] | *No association of gender with tapering outcome*<br>• No significant association of gender on opioid discontinuation ($p = 0.493$)[90]<br>• No association found between female and remaining on chronic opioid therapy ($p < 0.127$)[66]<br>*Study participation*<br>• No association found between female and remaining an active patient ($p < 0.601$)[66]<br>• No significant differences between participants who dropped out vs. those who completed[69]<br>• No significant difference in completion of withdrawal between men and women[74]<br>• No significant difference in participation between sex[75]<br>• No statistically significant differences on lost to follow-up/completers[76]<br>• No statistically significant differences on drop-outs[116] |
| Religion (0) | | |
| Education (1) | *Descriptive association of education with tapering outcome*<br>• University education was associated with a resilient trajectory[106]<br>• Low levels of education were associated with a surviving trajectory (descriptive analysis)[106] | *Study participation*<br>• No significant differences between participants who dropped out vs. those who completed[69]<br>• No statistically significant differences on lost to follow-up/completers[76]<br>• No statistically significant differences on drop-outs[116] |
| SES (1) | | *No differential association of SES with tapering outcome*<br>• Odds of a 50% reduction in opioid use at 12 months were not statistically significant in Quartile 1 (lowest neighbourhood deprivation index) (OR 0.83, $p = 0.067$), Quartile 2 (OR 0.91, $p = 0.356$), or Quartile 4 (highest Neighbourhood Deprivation Index) (OR 0.89, $p = 0.263$) compared to Quartile 3[95] |

continued

**TABLE 40** Inequalities and opioid-tapering effectiveness across PROGRESS-Plus factors (*continued*)

| PROGRESS-Plus (number of studies) | Potential to widen inequalities | No evidence of widening of inequalities on opioid-tapering effectiveness |
|---|---|---|
| | | *Study participation*<br>• No significant differences between participants who dropped out vs. those who completed[69] |
| Social capital (3) | *Impact of tapering on social capital*<br>• Relationships with medical professionals got worse among patients whose dose decreased compared to patients whose dose was unchanged (55% vs. 14.6%, $p \leq 0.05$)[89]<br>• Relationships with friends/family got worse amongst patients whose dose decreased compared to patients whose dose was unchanged (48.3% vs. 25.8%, $p \leq 0.05$)[89] | *No association of social capital with tapering outcome*<br>• No statistically significant difference found for marriage status ($p = 0.281$) or living status ($p = 0.622$) on opioid discontinuation[90]<br>*Study participation*<br>• No statistically significant differences on lost to follow-up/completers[76]<br>• No statistically significant differences on dropouts[116] |
| | *Association of social capital with tapering outcome*<br>• Patients in a relationship were associated with a thriving trajectory[106] | |
| Plus: Age (6) | *Differential association of age with tapering outcome*<br>• Odds of a 50% reduction in opioid use at 12 months were increased among patients aged 21–49 years compared to 50–64 years (OR 1.32, $p < 0.004$)[95]<br>• Significant difference in estimated change per year in average daily opioid dose 65+ years vs. 46–64 years, relative risk (95% CI): −3.5 (−4.7 to −2.3) vs. −8.4 (−10.0 to −6.8), $p < 0.001$[83]<br>• Significant difference in estimated change per year in average daily opioid dose 65 +years vs. 26–45 years, relative risk (95% CI): −3.5 (−4.7 to −2.3) vs. −8.5 (−13.0 to −4.0), $p = 0.001$[83] | *No differential association of age with tapering outcome*<br>• Odds of a 50% reduction in opioid use at 12 months were not significant among patients aged ≥ 65 years compared to 50–64 years (OR 1.32, $p < 0.004$)[95]<br>• No difference in estimated change per year in average daily opioid dose 46–64 years vs. 26–45 years, relative risk (95%CI): −8.4 (−10.0 to −6.8) vs. −8.2 (−10.7 to −5.8), $p = 0.916$[83]<br>*No association of age with tapering outcome*<br>• No statistically significant difference for mean age ($p = 0.509$) on opioid discontinuation[90]<br>• No association found between age and remaining on chronic opioid therapy ($p < 0.083$)[66] |
| | *Association of age with tapering outcome*<br>• Patients in the dose reduction group were more likely to be < 65 years old than patients in the no dose reduction group ($p = 0.001$)[82]<br>• > 50 years old was associated with a resilient trajectory (descriptive analysis)[106] | *Study participation*<br>• No significant differences between participants who dropped out vs. those who completed[69]<br>• No significant difference in participation between age[75] |

**TABLE 40** Inequalities and opioid-tapering effectiveness across PROGRESS-Plus factors (*continued*)

| PROGRESS-Plus (number of studies) | Potential to widen inequalities | No evidence of widening of inequalities on opioid-tapering effectiveness |
|---|---|---|
| | *Study participation* | • No statistically significant differences on lost to follow-up/ completers[76] |
| | • Remaining an active patient associated with younger age ($p < 0.001$).[66] | • No statistically significant differences on drop-outs[116] |
| Plus: Comorbidity (mental health/poor health status not due to taper) (13) | *Impact of tapering on comorbidity* | *No impact of tapering on comorbidity* |
| | • Mental health got worse among patients whose dose decreased compared to patients whose dose was unchanged (64.4% vs. 32.9%, $p \leq 0.05$)[89] | • No significant difference between treatment groups (real vs. sham electroacupuncture) on mental health ($F_{2101} = 0.82$, $p = 0.444$)[116] |
| | • Significant improvement on depression following opioid withdrawal ($p < 0.001$) and 6-month post treatment ($p < 0.001$)[88] | • No significant difference between stable and relapsed groups on depression[74] |
| | • Significant improvement on depression at 3 weeks post tapering ($p < 0.001$)[68] | • No significant difference on mental self-reported health-related quality of life, including depression and anxiety scores (all $p \geq 0.05$)[76] |
| | *Differential association of comorbidity with tapering outcome* | • No significant difference between treatment groups (standard outpatient management with opioid weaning vs. standard outpatient management with opioid weaning + acupuncture) on depression or anxiety (HADS-D $p = 0.30$, HADS-A $p = 0.74$)[111] |
| | • Odds of a 50% reduction in opioid use at 12 months were statistically significant for 0 Charlson Comorbidities compared to 1 Charlson Comorbidities (OR 0.72, $p = 0.001$)[95] | • No significant difference between treatment groups (Mindfulness-Orientated Recovery Program vs. Support Program) on depression[69] |
| | • Statistically significant effect of substance use disorder on estimated change per year in average daily opioid dose yes vs. no, mean change (95% CI): −10.7 (−14.9 to −6.5) vs. −6.5 (−7.6 to −5.5), $p = 0.064$[83] | • No significant difference between treatment groups (taper/no taper) on depression ($p = 0.076$) or anxiety ($p = 0.806$)[75] |
| | • Statistically significant effect of mental disorder on estimated change per year in average daily opioid dose yes vs. no, mean change (95% CI): −8.2 (−9.7 to −6.7) vs. −5.2 (−6.6 to −3.8), $p = 0.005$[83] | • No significant difference between treatment groups (MI and CBT vs., usual care) on depression post treatment ($p = 0.32$), or at 34 weeks ($p = 0.38$) or on anxiety post treatment ($p = 0.1$) and at 34 weeks ($p = 0.16$)[113] |
| | *Association of comorbidity with tapering outcome* | *No significant differential impact of comorbidity with tapering* |
| | • Odds of a 50% reduction in opioid use at 12 months were increased in patients with an anxiety diagnosis (OR 1.32; $p < 0.003$), history of substance use disorder (OR 1.62, $p < 0.001$)[95] | • Odds of a 50% reduction in opioid use at 12 months were not statistically significant for 2 Charlson Comorbidities (OR 1.18, $p = 0.184$) or ≥ 3 Charlson Comorbidities (OR 1.04, $p = 0.714$) compared to 1 Charlson Comorbidities[95] |

continued

**TABLE 40** Inequalities and opioid-tapering effectiveness across PROGRESS-Plus factors (*continued*)

| PROGRESS-Plus (number of studies) | Potential to widen inequalities | No evidence of widening of inequalities on opioid-tapering effectiveness |
|---|---|---|
| | • Patients in the dose reduction group were more likely to have an Elixhauser comorbidity score of ≥ 3 compared to patients in the no dose reduction group ($p$ = 0.006)[82] | • No statistically significant effect of substance use disorder on relative change per year in proportion of COT patients receiving ≥ 120 mg MED yes vs. no, relative risk (95%CI): 0.86 (0.80 to 0.92) vs. 0.84 (0.82 to 0.87), $p$ = 0.694[83] |
| | *Study participation* | • No statistically significant effect of mental disorders on relative change per year in proportion of COT patients receiving ≥ 120 mg MED yes vs. no, relative risk (95%CI): 0.85 (0.82 to 0.88) vs. 0.84 (0.80 to 0.89), $p$ = 0.900[83] |
| | • Late cessation due to aggravated depressive symptoms ($N$ = 3)[67] | *No significant association of comorbidity with tapering* |
| | • $N$ = 1 dropped out due to unrelated medical issue[69] | • Odds of a 50% reduction in opioid use at 12 months were not statistically significant in patients with depression (OR 1.07; $p$ = 0.399), PTSD (OR 1.11, $p$ = 0.576), fibromyalgia (OR 1.01, $p$ = 0.879, or no. of chronic pain diagnoses (OR 0.97, $p$ = 0.212)[95] |
| | • $N$ = 1 withdrew from the taper support sessions to have her opioid dose increased because of escalating levels of pain, anxiety, and depression[113] | No statistically significant difference found between anxiety, depression, or both ($p$ = 0.572) on opioid discontinuation[90] |
| | • $N$ = 2 dropout due to emotional stability[88] | *Study participation* |
| | • Patients who dropped out presented worse scores of anxiety ($p$ = 0.019), depression ($p$ = 0.106), general health ($p$ = 0.047) assessed by SF-36 and higher risk for opioid misuse assessed by PMQ ($p$ = 0.015)[75] | • No significant differences between participants who dropped out vs. those who completed[69] |
| | | • No statistically significant differences on dropouts[116] |

**TABLE 41** Inequalities and access to opioid tapering across PROGRESS-Plus factors

| PROGRESS-Plus (number of studies) | Factors that may widen inequalities in access to tapering | Factors that may reduce inequalities in access to tapering |
|---|---|---|
| Place of residence (5) | Long distance to travel to access taper support[93,97,103] | Tapering initiatives delivered in home/community settings[97,103] |
| | Lack of transportation[93] | Resources to taper are accessible[97,103,106] |
| | Tapering support delivered via mobile phones limits access for patients living in areas with poor phone reception[104] | |
| | Living in close proximity to natural disasters[106] (external) | |
| | Lack of availability of resources and alternative therapies[97,102,103] | |
| Race, ethnicity, language (1) | Fear of racial discrimination compounding existing stigma around opioid use[93] | |
| Occupation (3) | Work stress/schedule prevent patients accessing tapering support[95,106] (external) | |
| | Opioids needed in order to work[99] | |
| Gender/sex (1) | | |
| Religion (0) | | |
| Education (0) | | |
| SES (6) | • Cost of tapering[97,103,104,106,110]<br>• Financial stress[95,106] (external) | • Funding provision for patients to access tapering support[97] |
| | • Patient's phone service cancelled[110] | |
| | • Changes in/loss/alterations of patient insurance plans/policies[110] | |
| Social capital (12) | • Lack of social support, social isolation (COVID)[106]<br>• Lack of supportive provider[99,105,106,108,109]<br>• Family responsibilities or stresses (e.g. caring for a dying relative, sick child, death of relative or friend, marital problems)[95,106] (external)<br>• Lack of trust in patient–provider relationship[94,99,102,106] | • Patients with strong family bonds or family responsibilities were more likely to initiate and sustain a taper[95,96,99,102,104,106,107] |
| | • Lack of honesty in patient–provider relationship[102]<br>• Poor relationship going forwards with other treatments[102]<br>• Provider/patient discontinues healthcare provision[102] | • Patient recognises the negative impact of opioid use on others[107] |

continued

**TABLE 41** Inequalities and access to opioid tapering across PROGRESS-Plus factors (*continued*)

| PROGRESS-Plus (number of studies) | Factors that may widen inequalities in access to tapering | Factors that may reduce inequalities in access to tapering |
|---|---|---|
| | • *N* = 2 dropouts due to family stressor[88]<br>• *N* = 2 dropouts family issues[112] | • Provision of a supportive, trusting patient-provider relationship is crucial[95,96,99,104,105,106,108]<br>• Support forum to share tapering experiences with other patients[96,104]<br>• Mutual honesty between patient and provider[99]<br>• Regular contact and easy access to same provider[94,95,108]<br>• Out-of-hours support (e.g. via mHealth)[104] |
| Plus: Age (1) | | |
| Plus: Comorbidity (mental health/poor health status not due to taper) (11) | • Inadequate access/timely access to alternative therapies[97,102,103,106]<br>• Worsening health status (not associated with tapering)[95,99,104,106]<br>• Worsening emotional status[95,99,104,106,107]<br>• Visual impairment prevents engagement with tapering support mode[104] | • Access to multidisciplinary care/alternative therapies (e.g. pain specialist, psychologist)[97,103,106,109]<br>• Treatment for comorbidities[109]<br>• Flexible tapering approach in response to changes in health and emotional status[99,105]<br>• Improvement in emotional status[99,104,106] |
| | | Equity |
| | • Tapering initiatives place significant pressure to 'be well' or 'mobile enough' to reach the clinic[93]<br>• Guidelines do not recognise need for tailoring[99,103] | • Guidelines support providers to taper (recognise need for multitarget/multimodal intervention approach/ individualised approach)[103] |
| Plus: Status as long-term opioid user (8) | • Self-stigma (feeling guilt, humiliation, shame)[93]<br>• Social stigma (fear of being labelled a drug addict, having pain disbelieved or invalidated)[95,99,103,106,107,109]<br>• Structural stigma[93]<br>• Tapering initiative is stigmatising (e.g. monitoring opioid use reinforces stigma around addiction)[93,103] | • Non-judgmental provider[96]<br>• Monitoring opioid use seen as opportunity to distance oneself from social stigma[93] |

**TABLE 42** Examples of data supporting review findings on inequalities in access to opioid tapering in patients with chronic non-cancer pain

| PROGRESS-Plus category | Examples of data |
|---|---|
| Place of residence (P) | Some described the inconvenience of randomly assigned 'pill counts', citing difficulty accessing transportation or living many hours away.[93] |
| | One provider described this challenge in a hypothetical interaction with a patient: 'I live 200 miles away and I'm not coming to physical therapy'.[97] |
| | 'And it would be nice if they could get physical therapy at home. If they could get, you know, massage therapy at home'.[97] |
| | 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.[102] |
| | Community-based care was considered by most participants as the preferred setting for opioid deprescribing due to patient accessibility and the opportunity for regular follow-up.[103] |
| | Other providers, by contrast, perceived having a range of available options and emphasised that NPTs offered an important alternative to opioids for pain management.[97] |
| Race (R) | The experience of being dually disbelieved and stigmatised as 'drug 'seeking' was additionally burdensome for black women in the sample. Several described the ways in which dominant cultural norms interacted with other forms of marginalisation including racism.[93] |
| | 'I had the hardest time getting my medicine every month. You got the stress of trying to get out of pain while you're at heightened of pain, then you have the stress of being treated like a dope addict [and] of being treated in a racially discriminatory way'.[93] |
| Occupation (O) | Two of the most common dynamics impacting tapering were patients' ability to fulfil their roles and responsibilities related to their work and family. For example, one patient deferred tapering until after retirement because he needed opioids in order to work.[99] |
| | Other stressors such as: work schedule. . .[95] |
| Gender | None reported. |
| Religion | None reported. |
| Education | None reported. |
| SES | Direct out of pocket cost to patients was highlighted as a financial barrier to access.[97] |
| | We do not have the ability to really offer those [NPT] options to them. A lot of our patients have limited resources . . . So therefore they can't opt into a program like Humana where they can get into, you know, a gym or something like that.[97] |
| | And that the VA would give them, even if it's just an allotted amount of money every year to spend on these alternative programmes.[97] |
| | Several participants described perceived barriers toward phone-based digital interventions including limited phone reception or access to internet: I don't have Wi-Fi. I can't afford it.[104] |
| | . . .financial stress ('You've got no money, you can't do anything, you live week to week)'[106] |
| Social capital | Patients experienced tapering as dynamic because their pain and perceived need for opioids varied from day to day and because their pain was frequently affected (either positively or negatively) by changes in their social relationships. . .[99] |
| | Adversity experienced by participants . . . social isolation and other issues related to COVID-19 ('I think when you haven't got anything else to concentrate on the pain just seems to be worse than it normally would.[106] |
| | Participants often attributed their ability to taper their opioids safely and successfully to the support of friends, family, and clinicians.[106] |
| | 'My mother-in-law came to live with us about three months ago. She needs care, so guess who's having to take care of her when I get home? That means I've got to take less medication to be able to function when I get home'.[99] |

continued

**TABLE 42** Examples of data supporting review findings on inequalities in access to opioid tapering in patients with chronic non-cancer pain (*continued*)

| PROGRESS-Plus category | Examples of data |
|---|---|
| | Finally, patients and pharmacists noted that life circumstances were particularly influential on the tapering process and its success. Tapering success was linked to the presence of a patient social support system and the use of additional resources to cope with challenges that may arise during tapering.[95] |
| | Providers noted that patients to whom family is highly important or who expressed concern about taking medications were more likely to be receptive to a discussion about tapering opioids.[102] |
| | Many statements suggest that long-term opioids are having a negative impact on the patient's quality of life and, likely, on that of their family and friends: 'things would be better at home. My wife thinks I've been on opioids too long', 'feel healthier, easier to be around.[107] |
| | Participant 16 remarked 'My husband is not understanding so it makes it a bit hard', and participant 06 explained 'All my family are overseas, and they are just completely unaware of what's going on'. Participant 20 described feeling socially isolated ('I've been staying pretty close to home, which I don't think helps really').[106] |
| | Adversity experienced by participants . . . the death or illness of loves ones ('It's got very tough the last 18 months because [wife] has a brain tumour', P01).[106] |
| | Significant caretaker role and responsibilities (e.g. taking care of dying spouse or ill child)[95] |
| | 'You have to get people to people. On paper, [patients] don't care. They really don't. They have to have some one-on-one quality time with a real person who talks about real issues'.[96] |
| | Providers noted a concern that their patients may not fully share pain-related symptoms and opioid-related side effects, limiting providers' ability to accurately assess risk and benefit [and] providers described potential negative effects of opioid tapering on the patient-provider relationship going forward.[102] |
| | Providers were praised for attributes such as being supportive, non- judgmental.[96] |
| | Patients described clinicians who took the time to learn about their needs, build mutual trust, and devise individualised tapering plans.[99] |
| | Patients who described positive relationships with their clinicians, and who identified clinicians as a source of support during tapering, gave similar answers about effective patient-clinician communication around tapering.[99] 'There were several times I called [pharmacist] to talk and she was always available and ready to listen'.[95] |
| | Patients reporting negative interactions with clinicians felt clinicians were not entirely honest about their reasons for tapering (e.g. clinicians were motivated by institutional anti-opioid pressures rather than patients' best interests), did not listen to patients or individualise tapering plans, or were inflexible once tapering started.[99] |
| | These taper initiatives produced unintended consequences including reduced patient autonomy, facilitating mistrust, and reinforcing stigma about addiction.[93] |
| | Relatedly, many participants reported that tensions in these relationships made their tapering journey more difficult.[106] |
| +Age | None reported |
| +Comorbidities | Patients who reported positive experiences received anticipatory guidance about tapering and described clinicians willing to adjust tapering plans based on patients' experience or in response to changes in patients' emotional state or health status.[99] |
| | Other ongoing health issues (e.g. surgery, influenza) that slowed or stopped taper.[95] 'During the taper I had a couple of procedures done a lot of breast biopsies. I just wasn't comfortable coming off the morphine until all the other pain-type of things happening at the time were taken care of'.[95] |
| | Participants predicted that their level of interest and engagement with mHealth support may fluctuate over the course of their taper depending on their mood, pain, and state of mind.[104] |
| | These 'pill counts' placed significant pressure to 'be well' or 'mobile enough to reach the clinic and coordinate logistics with insufficient time to prepare (e.g. 'a day's notice'). These clinical encounters both eroded patients' trust while providing opportunities, for some participants, to 'prove' their compliance.[93] |
| | Providers at both the VA and the safety net hospital noted that inadequate access to alternative treatments for pain limited their ability to taper opioid medications.[102] |

**TABLE 42** Examples of data supporting review findings on inequalities in access to opioid tapering in patients with chronic non-cancer pain (*continued*)

| PROGRESS-Plus category | Examples of data |
|---|---|
| | 'The VA has been a little slower to catch up.in the participation of mental health in pain management'.[97] |
| | Providers' frustrations with time delays in access were not limited to surgery but were also aimed at other options such as pool therapy.[97] |
| | Specialist and multidisciplinary care were largely seen as enablers to opioid deprescribing; however, effectiveness of a multidisciplinary approach was thought to be limited by accessibility and lengthy wait times for referrals to pain clinics.[103] |
| | A structured and holistic approach to deprescribing was considered optimal, with adjunct or alternate analgesic agents, non-pharmacological pain management strategies and involvement of multidisciplinary healthcare members.[103] |
| | Consideration of individual patient psychosocial factors was emphasised as being integral to the deprescribing approach. Due to the variability of patients and their individual circumstances, participants highlighted that prospective opioid deprescribing guidelines would need to address patient psychosocial factors while allowing clinicians to tailor care to patients' personal circumstances.[103] |
| | Ongoing mental health issues (e.g. depression)/often relying on opioid medications to manage mental health symptoms.[95] |
| | All participants who followed a resilient trajectory struggled to meet their tapering goals and temporarily increased or delayed reducing their medication at times of stress.[106] |
| | Participants predicted that their level of interest and engagement with mHealth support may fluctuate over the course of their taper depending on their mood, pain, and state of mind[104] |
| Status as long-term opioid user | Opioid-related stigma was thought to prevent patients from initiating conversations with clinicians about deprescribing, potentially limiting the opportunity for intervention, engagement and education.[103] |
| | The presence of unintended consequences in the context of various tapering initiatives is summarized by the following quote: I feel very stigmatized. I feel like I'm wearing a scarlet letter. I'm angry. I'm angry at the system, the pharmaceutical company, and my old doctor.[93] |
| | Nearly all participants reported experiencing being perceived as 'drug-seeking', a 'junkie', or an 'addict' in both clinical contexts and pharmacies.[93] |
| | Patient feels angry about referral and treated 'like an addict'[95] |
| | Less concern re addiction, or more specifically, people including health professionals, thinking I am overly dependent'; 'being spoken to like a heroin addict'; 'Clear thinking, not become addicted'.[107] |
| | Other participants' narratives echoed this experience, including descriptions of being perceived as lying about pain in order to receive opioids. For many, this underlying tension resulted in feeling unheard, uncared for, and accused within clinical contexts.[93] |
| | Efforts to monitor patients' opioid use were received differently across participants, although all described heightened awareness of providers' monitoring of their opioid use.[93] |
| | Providers were praised for attributes such as being supportive, non- judgmental.[96] |

EME
HSDR
**HTA**
PGfAR
PHR

Part of the NIHR Journals Library
www.journalslibrary.nihr.ac.uk



***Published by the NIHR Journals Library***