

Rapid Evidence Product April 2021

Treatments and Technologies Supporting Appropriate Opioid Tapers

Purpose

The purpose of this topic development brief is to explore and scope the evidence on treatments and technologies supporting appropriate opioid tapers in people with pain, in order to help determine whether this topic is suitable for further action such as commissioning a systematic review or technical brief to inform clinical or policy decision making (including potential coverage determinations), or to inform future research priorities. This topic development brief is part of the Dr. Todd Graham Pain Management Study, to inform a report to Congress on acute and chronic pain management for individuals entitled to Medicare benefits.¹

Issue

Use of opioid medications has increased in older patients and other individuals with pain entitled to Medicare benefits, resulting in an expanded population of patients prescribed longterm opioid therapy.² In patients in whom an individualized assessment determines that benefits of long-term opioid therapy do not outweigh risks, the 2016 Centers for Disease Control and Prevention (CDC) guideline on long-term opioid therapy suggests that primary care clinicians in outpatient settings might consider tapering in certain patients (defined as reducing high opioid dose, though not necessarily to discontinuation).³ The Department of Health and Human Services guide on tapering recommends that clinicians review goals of opioid therapy with the patient and the risks and benefits of current therapy, to inform tapering decisions.⁴ However, even when appropriate, tapering long-term opioid therapy can be a challenge.^{4,5} Patients may experience withdrawal symptoms, negative psychological effects, worsened pain, or serious adverse events (e.g., suicide or overdose) while undergoing taper, and may not reach tapering goals. Tapering may be more challenging in Medicare populations due to higher medical complexity, presence of disability, or older age. Therefore, effective treatments and technologies to support opioid tapers in this population could improve symptoms and increase the likelihood of tapering success, while reducing adverse outcomes.

Key Findings

• Systematic reviews found that interdisciplinary pain rehabilitation, behavioral health support, and buprenorphine-assisted tapering may be effective to reduce or discontinue long-term opioid therapy; pain, function, and quality of life may improve with opioid



dose reduction in certain individuals, or populations. Buprenorphine is a partial opioid agonist that can treat pain effectively in certain patients, as well as opioid use disorders, and it has other properties including less opioid-induced hyperalgesia and easier withdrawal than full mu-agonist opioids, and less respiratory depression than other longacting opioids. However, the quality of evidence is low or very low, and few studies specifically evaluated populations potentially eligible for Medicare.

- No study evaluated the effectiveness of technological solutions to support opioid tapering in patients with chronic pain, effectiveness of interventions to mitigate risks of overdose or suicide, or how benefits and harms of tapering support interventions vary in subgroups based on demographics or clinical factors.
- Observational studies found that opioid discontinuation might be associated with increased risk of overdose and suicide or suicidal ideation, but available studies did not evaluate the indication for discontinuing opioids, the tapering strategy used, or use of strategies for mitigating risk of overdose, suicide, or suicidal ideation, and were susceptible to confounding due to these factors.

Background

Use of opioids has increased in older patients and other individuals entitled to Medicare benefits, resulting in an expanded population of patients prescribed long-term opioid therapy.² Based on the National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey, among adults 65 years of age and older, the percent of clinic visits at which an opioid was used more than doubled from 4.1 percent in 1999 to 2000 to 9.0 percent in 2009 to 2010;² since 2010, rates of opioid prescribing have generally been stable.⁶ Although long-term opioid therapy is associated with reduced pain intensity in some patients, it is also associated with adverse effects, morbidity, and overdose deaths in others; and some risks of long-term opioid therapy are dose-dependent.⁷

Tapering refers to reducing the dose of opioids in patients on long-term opioid therapy, though not necessarily to discontinuation. In patients in whom an individual assessment determines that benefits of long-term opioid therapy do not outweigh risks, the 2016 (CDC guideline recommends that primary care clinicians treating adults in outpatient settings consider tapering in certain patients, particularly if doses are above suggested thresholds.³ Other strategies in this situation include optimization of nonopioid therapies, enhanced risk mitigation, transition to buprenorphine, or evaluation for potential opioid use disorder, with appropriate evaluation or referral if indicated.⁸ However, tapering long-term opioid therapy can be a challenge.⁴ Patients may experience withdrawal symptoms, negative psychological effects, and worsened pain while undergoing taper, and tapering attempts may be unsuccessful. Inadequate access to or reimbursement of nonopioid therapies may present challenges. Tapering may even uncover underlying opioid use disorder, which requires appropriate evaluation and treatment, including opioid agonist therapy.⁹ In addition, some data suggest that discontinuation of opioids may be associated with increased risk of overdose or suicide,^{10,11} though the degree to which there is a causal association or that this finding reflects confounding factors is uncertain. In all patients, regardless of whether opioid doses are maintained or tapered, optimization of nonopioid therapies (pharmacologic and nonpharmacologic) for pain is essential.¹²

Tapering strategies and approaches vary widely. In some cases, tapering approaches are relatively unstructured and tapering is managed primarily or exclusively by the primary care clinician. More structured approaches involve: use of protocols to guide tapering (e.g., regarding rate of tapering and use of nonopioid interventions); implementation of patient-centered approaches (e.g., engagement and agreement of patients in tapering ["voluntary" tapering]¹³ and

individualization or reduction in the rate of opioid tapering, individualization of tapering goals including target dose); utilization of expertise from specialists in behavioral therapy, pain medicine, and addiction; and use of taper support interventions (including use of psychological therapies, use of the partial opioid agonist buprenorphine to assist in tapering, and use of adjunctive [nonopioid] therapies to manage pain and withdrawal during tapering).^{14,15} Technologies such as mobile applications to monitor patient symptoms enable patients to more easily communicate with clinicians, facilitate psychological or other nonpharmacological therapies, provide decision support for clinicians, or function as wearable sensors could also be useful to support opioid tapering.¹⁶ Despite the availability of these various strategies, a prior Agency for Healthcare Research and Quality- (AHRQ) funded review found a lack of evidence to inform optimal tapering approaches.¹⁷ Important research gaps included uncertainty with regard to how use of different strategies and approaches impact the likelihood of success in reaching tapering goals or effects on patient outcomes related to pain, function, or quality of life.⁵

Additionally, as tapering has become more commonplace, concerns related to potential serious harms of opioid tapering (including overdose and suicidality) have been noted, particularly with regard to inappropriate or nonconsensual tapering.^{12,18} The authors of the 2016 CDC guideline have reaffirmed¹⁹ that the guideline does not support mandatory tapering based solely on opioid dose and the Department of Health and Human Services has issued guidance on appropriate opioid dose reduction or discontinuation of long-term opioid analgesics, including when to consider tapering, important considerations and steps prior to tapering, shared decision-making with patients, individualizing the taper rate, treatment of opioid withdrawal symptoms, provision of behavioral health support, considerations in special populations, and use of opioids when benefits outweigh risks.⁴ Nonetheless, important uncertainty regarding optimal tapering approaches remain, such as the optimal dose reduction rates, appropriate tapering goals, effectiveness of patient-centered approaches, and effectiveness of interdisciplinary models, psychological therapies, buprenorphine-assisted tapering and nonopioid therapies.

Furthermore, current guidance does not specifically address tapering in Medicare populations. Tapering may be more challenging in this population due to higher medical complexity, presence of disability, or older age. Therefore, effective treatments and technologies to support appropriate opioid tapers (and pain management, overall) in this population could improve symptoms, reduce adverse outcomes, and increase the likelihood of successful tapers.

Scope

1. In patients prescribed long-term opioid therapy for chronic pain, what are the effects of treatments and technologies to support opioid tapering on pain, function, quality of life, mental health outcomes, opioid dose, likelihood of opioid discontinuation, and adverse events (including overdose and mortality)?

1a. How do the effects of treatments and technologies to support opioid tapering vary according to demographics (e.g., age, sex, race/ethnicity, socioeconomic status, insurance status) and clinical factors (e.g., pain conditions, pain duration, pain severity, comorbidities, use of opioids or other pain treatments)?

The research questions explored in this Topic Brief are listed below and are analyzed according to the PICOTS framework in Table 1.

setting)		
Questions	1. Effects of treatments and technologies	1a. Effects in subgroups
Population	Patients prescribed long-term opioid therapy for chronic pain and undergoing an opioid taper*	Subgroups defined by demographic (e.g., age, sex, race/ethnicity, socioeconomic status, insurance status) and clinical factors (e.g., pain condition, pain duration, pain severity, comorbidities, use of opioids)
Interventions	 Treatments Interdisciplinary rehabilitation Behavioral support or psychological interventions (behavior-based and cognitive behavior-based therapies) Buprenorphine-assisted tapering Non-opioid therapies (pharmacological or non-pharmacological) for pain Patient-centered approaches (engagement or agreement with tapering ["voluntary" tapering], individualized or reduced rate of tapering], individualized goal setting) Technologies (e.g., mobile applications or wearable sensors) to support tapering 	See question 1
Comparators	Usual care or no treatment/technology; other treatment or technology	See question 1
Outcomes	Pain, function, quality of life, mental health outcomes, opioid dose, likelihood of opioid discontinuation, adverse events (including overdose and mortality)	See question 1
Timing	Any	See question 1
Setting	Any	See question 1

Table 1. Questions and PICOTS (population, intervention, comparator, outcome, timing and setting)

* Not restricted to persons eligible for Medicare, though evidence in Medicare-eligible populations will be highlighted if available

Assessment Methods

We conducted a literature search (Appendix A) and assessed the topic of treatments and technologies supporting opioid tapering for people with pain for priority using a hierarchical process using assessment criteria adapted from the AHRQ Topic Development Process (Appendix B). Assessment of each criteria, based on consultation with local experts and a scan of the literature, determined the need to evaluate the next one.

- 1. Appropriateness
- 2. Importance
- 3. Current state of the evidence
- 4. Value and potential impact

For this Topic Brief, we defined value and potential impact as the potential for informing a policy/evidence action, suitability for commissioning a systematic review or technical brief, and implications for future research.

Current State of the Evidence

Based on a literature scan and consultation with local experts, this is a topic of clinical importance and appropriate for further assessment.

• Long-term opioid therapy is commonly prescribed in patients and tapering when indicated is an important clinical challenge. However, there is uncertainty with regard to optimal tapering approaches. In one large study of patients with commercial or Medicare Advantage insurance who were using long-term opioids, the annual percentage who underwent tapering of their daily dosage increased from 10.5 percent in 2008 to 22.4 percent in 2017, likely as a result of safer opioid prescribing policies.²⁰ Tapering in persons entitled to Medicare may be particularly challenging due to greater medical complexity, older age, or presence of disability.²¹⁻²³

Two systematic reviews of treatments to support opioid tapering in patients with chronic pain identified interventions that might be effective (interdisciplinary pain management programs, behavioral support, and buprenorphine-assisted tapering). However, the quality of the evidence was low or very low, and few studies specifically evaluated Medicare-relevant populations. The current evidence is summarized in Table 2 by intervention type.

- A well-conducted systematic review by Frank et al. (search date April 2017) included 67 studies (11 randomized trials and 56 observational studies) that evaluated strategies to reduce or discontinue long-term opioid therapy for chronic pain.¹⁴ Among the observational studies, there were four cohort studies, one case-control study, and 51 before-after studies. Three studies were rated good quality, 13 were rated fair quality, and 51 were rated poor quality. The three good-quality studies were all randomized trials of behavioral support interventions, though specific interventions varied (a computer and phone-based therapeutic interactive voice response program to maintain and enhance cognitive behavioral therapy skills;²⁴ mindfulness meditation plus cognitive behavioral therapy;²⁵ or motivational interviewing and pain self-management education).²⁶ The review assessed the evidence on effectiveness for all intervention types to be very low quality, due to serious risk of bias and variability across studies in settings, interventions, and populations. In addition, although all studies reported opioid dose reductions or discontinuation, tapering was not necessarily the primary goal of the evaluated interventions. Evidence was most robust for interdisciplinary pain programs (31 studies [11 fair and 20 poor], mean opioid discontinuation rate 87%), behavioral support or psychological interventions (6 studies [3 good and 3 poor], mean opioid discontinuation rate 21%) and buprenorphine-assisted tapering (10 poor studies, mean opioid discontinuation rate 91%) (Table 2). The lower rate of opioid discontinuation in the behavioral support studies could have been due in part to evaluation using more rigorous study designs: in two randomized trials^{24,26} of behavioral support interventions that reported opioid discontinuation, rates were 21 percent and 33 percent. Other therapies (ketamine-assisted dose reduction, acupuncture, detoxification, and other outpatient programs) were evaluated by three to five studies each; only poor-quality studies were available for ketamine, detoxification, and other outpatient programs. Across treatment types, the review found that more successful interventions tended to use team-based, intensive support approaches with multidisciplinary care and close (at least weekly) followup. The systematic review also found very low-quality evidence that across treatment types, dose reduction or discontinuation of opioids was associated with improved pain severity (36 studies), function (17 studies), and quality of life (12 studies); effects on these outcomes were not stratified by intervention type. Rates of opioid withdrawal symptoms were highly variable, based on 18 studies.
- A subsequent, more focused systematic review by Mackey et al. conducted for the Veterans Health Administration (VHA) utilized the systematic review by Frank et al., updated with searches conducted in May 2020.²⁷ This review differed from the Frank et

al review by focusing on studies explicitly designed to reduce opioid doses (Frank et al included studies that reported opioid dose reduction in which the intervention was not explicitly aimed at tapering), prioritizing studies assessed as being most applicable to VHA patients (based on setting and patient population), and focusing on effects of tapering on pain severity and function (effects on tapering discontinuation were not evaluated). It included 49 studies (the Frank et al systematic review, 5 randomized trials, 10 controlled observational studies, and 33 uncontrolled [before-after] studies). Thirtyfour of the studies had been included in the systematic review by Frank et al and 14 additional studies were added. Based on 19 studies (2 RCTs, 6 controlled observational studies, and 11 uncontrolled studies) considered most applicable to VHA patients, findings were consistent with the review by Frank et al. Specifically, the systematic review by Mackey et al. found that pain severity and pain-related function may improve for some patients with chronic pain on long-term opioid therapy who participate in intensive pain management interventions that incorporate opioid tapering (e.g., functional rehabilitation programs involving daily participation that incorporate physical and occupational therapy and psychotherapy components). However, the quality of evidence was assessed as low due to methodological limitations in the studies. The only two new prioritized studies in the Mackey et al. review that were not in the Frank et al. review evaluated specific (rather than unspecified or nonspecific) taper interventions. One small (n=35) randomized trial compared a tapering schedule of 10 percent per week versus usual care without tapering, but is of limited usefulness because it had very high attrition.²⁸ A before-after study of patients who voluntarily agreed to taper their opioids following education also reported high attrition; of 51 of 82 patients who completed the study, the mean opioid dose was reduced at 4 months with no change in pain intensity or function.¹³

- Two studies in the systematic reviews described above focused on Medicare-relevant populations, based on older age.
 - One before-after study found opioid tapering in older (>60 years) patients within a 3 week interdisciplinary pain rehabilitation program based on a cognitivebehavioral model was associated with reduced depression, catastrophizing, and pain interference at discharge and at 6-month followup, with significant reduction in analgesic use.²⁹
 - A retrospective cohort study (n=2,492 encounters) found similar likelihood of favorable satisfaction following tapering in patients older than 65 years and those younger than 65 years.³⁰
- One additional observational study published subsequent to the systematic reviews evaluated buprenorphine-assisted tapering, but did not evaluate a population entitled to Medicare (based on age of participants).³¹ Results were consistent with the systematic reviews.
- Another observational study published subsequent to the systematic reviews found that among patients prescribed long-term opioid therapy in the last year who underwent opioid dose reduction, there was no difference in pain severity between those who self-reported that the dose reduction was voluntary versus involuntary.³² The mean age of patients was 65 years.

Evidence on technological solutions to support opioid tapering in patients with chronic pain is not available.

• Neither systematic review specifically addressed technological solutions to support opioid tapering in patients with chronic pain and no studies of such technological

solutions were identified. We did find a third systematic review that described mobile applications for opioid use disorder (presence of pain not specified) but none of the studies evaluated the effects of mobile applications on patient outcomes.¹⁶ The applications were mainly aimed for use by clinicians and focused on opioid dose conversions. A fourth systematic review of mobile applications for chronic pain did not identify any studies focusing on patients undergoing tapering. The review identified shortcomings in the development and assessment of currently available applications, including failure to include health care providers in the development of the applications and incorporation of features that were not evidence-based or fully described.³³

Evidence on interventions to mitigate risks of harms associated with tapering is not available.

• No systematic review evaluated benefits and harms of interventions to mitigate risks of harms (overdose, suicide, suicidal ideation) associated with tapering. Two retrospective cohort studies found that discontinuation of opioids was associated with increased risk of overdose or suicide but did not evaluate the indication for discontinuing opioids, opioid tapering strategies used, or strategies for mitigating risk of overdose and were susceptible to confounding based on these factors.^{10,11}

Evidence on how benefits and harms of tapering support interventions varies in subgroups is not available.

• No systematic review evaluated how benefits and harms of tapering support interventions varied in key subgroups defined by demographic or clinical factors.

Ongoing trials may provide additional evidence to inform this topic

• A search of clinicaltrials.gov identified two ongoing RCTs^{34,35} on behavioral support interventions and one RCT³⁶ of buprenorphine-assisted tapering. The trials are scheduled to be completed in 2020, 2022, and 2024.

Strategy	Description of Interventions	Number of Studies (N)	Opioid Discontinuation Rates	Quality Ratings, Where Available*
Interdisciplinary pain program	Programs that delivered interdisciplinary pain care; variability in program components, personnel, and duration	SR: 1 SR with 31 studies (9,915) Additional studies: 0 In-progress studies: 0	Mean 87% (range 29-100%); 20 studies	Fair: 11 studies Poor: 20 studies
Behavioral support or psychological interventions	Various behavior-based and cognitive behavior-based therapies, including CBT, medication, and other complementary and integrative health methods	SR: 1 SR with 6 studies (238) Additional studies: 0 In-progress studies: 2 (200) [†]	Mean 21% (range 6-55%); 5 studies	Good: 3 studies Poor: 3 studies

Table 2. Studies of treatments to support opioid tapering in patients with chronic pain

Strategy	Description of Interventions	Number of Studies (N)	Opioid Discontinuation Rates	Quality Ratings, Where Available*
Buprenorphine- assisted tapering	Patients transitioned from long-term opioid therapy to buprenorphine; variability in induction protocol, dose, and duration of therapy	SR: 1 SR with 10 studies (470) Additional studies: 1 (240) In-progress studies: 1 (32)	Mean 91% (range 33-100%); 6 studies in SR; 45% successfully tapered and 19% successfully transitioned to buprenorphine in 1 additional study	Poor: 10 studies
Non-opioid therapies: Ketamine-assisted dose reduction	Oral, intravenous, and subcutaneous ketamine	SR: 1 SR with 4 studies (168) Additional studies: 0 In-progress studies: 0	18% and 27%; 2 studies	Poor: 4 studies
Non-opioid therapies: Acupuncture	Electroacupuncture; auricular acupuncture	SR: 1 SR with 3 studies (78) Additional studies: 0 In-progress studies: 0	66% and 86%; 2 studies	Fair: 2 studies Poor: 1 study
Patient-centered approaches	Voluntary tapering	SR: 1 SR with 1 study (51) Additional studies: 1 (290) In-progress studies: 0	Not reported; 1 study reported mean opioid dose reduced in patients who completed study following voluntary taper	Not assessed in the SR (before- after study design)
Technologies	Various mobile applications or wearable devices	No studies		
Other outpatient programs	System-wide interventions in primary care, outpatient specialty care, outpatient medical marijuana treatment	SR: 1 SR with 5 studies (1169) Additional studies: 0 In-progress studies: 0	Mean 20% (range 12-44%); 3 studies	Poor: 5 studies
Detoxification	Opioid dose reduction supported with symptomatic medications (e.g., clonidine and benzodiazepines)	SR: 1 SR with 4 (200) Additional studies: 0 In-progress studies: 0	Mean 91% (range 91-100%); 3 studies	Poor: 4 studies

Abbreviations: N = number of subjects; SR = systematic review

*For studies included in systematic reviews, based on the ratings assigned in the reviews †Planned enrollment

Summary of Assessment Criteria

Value and Impact

• Low- or very low-quality evidence could inform a policy or coverage action for several treatments (interdisciplinary pain rehabilitation programs, behavioral support, or buprenorphine-assisted tapering) to support appropriate opioid tapering. It should be noted that use of buprenorphine formulations approved for treatment of opioid use

disorder to assist in tapering of patients who have not been diagnosed with an opioid use disorder is an off-label use.⁸

- Given recent systematic reviews and limited new evidence, a new systematic review is not currently warranted. However, publication of in-progress randomized trials on behavioral support and buprenorphine-assisted tapering could warrant reconsideration of the suitability of a new systematic review.
- Research to clarify optimal tapering approaches, identify effective technologies to support tapering, identify strategies to mitigate potential harms of tapering, identify patients most likely to benefit from tapering, and confirm applicability of evidence on tapering to Medicare populations would help fill evidence gaps that could be addressed in a future systematic review and potentially inform policy or coverage actions.

See Appendix B for a summary of all EPC assessment criteria.

Related Resources

We identified additional information in the course of our assessment that might be useful.

- U.S. Department of Health and Human Services Guide for Clinicians on Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics⁴
- CDC Guideline for Prescribing Opioids for Chronic Pain United States 2016³
 - Clarification on CDC Guideline¹⁹

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Afterword

Medicare beneficiaries and other people with acute and chronic pain often receive treatment that does not successfully address pain, resulting in profound physical, emotional, and societal costs to them and their families, friends, and caregivers. Centers for Disease Control and Prevention data indicate 50 million adults in the United States have chronic daily pain, with nearly 20 million experiencing high-impact pain that interferes with daily life or work.¹ At the same time, the country is also coping with an opioid and substance use disorders crisis that involves shifting "waves" of overdose deaths associated with heroin, synthetic opioids, and prescription drugs, and intensifying polysubstance use. The country is also experiencing the COVID-19 public health emergency, which poses its own challenges for individuals, and the healthcare system.

Opioid analgesics play an essential role in treating pain, and pain management in the context of the nation's substance use crisis has rapidly evolved beyond an opioid-centric approach. Clinicians and healthcare systems need more information about multimodal pain care options in outpatient and inpatient settings to effectively treat Medicare and other patients with pain, and people with both pain and either active or historic substance use disorders, including knowledge about complementary care, analgesic medications, and medical devices that are potentially effective.

To address this challenge, AHRQ has undertaken three topic briefs and two systematic reviews to inform Medicare coverage and payment for treatment of acute and chronic pain in support of the <u>Dr. Todd Graham Pain Management Study, section 6086 of the SUPPORT Act.</u>

The topic briefs are:

- Care Coordination and Care Plans for Transitions Across Care Settings
- Treatments and Technologies Supporting Appropriate Opioid Tapers
- Treatments, Technologies, and Models for Management of Acute and Chronic Pain in People With a History of Substance Use Disorder

The systematic reviews are:

- Interventional Treatments for Acute and Chronic Pain
- Integrated Pain Management Programs

If you have comments on this report, they may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to epc@ahrq.hhs.gov.

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¹ Dahlhamer J, Lucas J, Zelaya, C, et al. Prevalence of Chronic Pain and High-Impact Chronic Pain Among Adults — United States, 2016. MMWR Morb Mortal Wkly Rep 2018;67:1001–1006. DOI: http://dx.doi.org/10.15585/mmwr.mm6736a2external icon.

Appendix A. Methods

We assessed the topic for priority for a systematic review or other AHRQ Effective Health Care report with a hierarchical process using assessment criteria adapted from the AHRQ Topic Development Criteria. Assessment of each criteria determined the need to evaluate the next one. See Appendix B for detailed description of the criteria.

Appropriateness and Importance

We assessed the nomination for appropriateness and importance, based on a preliminary literature scan for systematic reviews in Ovid MEDLINE and telephone interviews and email correspondence with six local experts with expertise in pain management and opioid tapering, in order to assess the criteria described in Appendix B.

Current State of the Evidence

We searched for high-quality, completed, or in-process evidence reviews published in the last 3 years on the questions of the nomination from these sources:

- AHRQ: Evidence reports and technology assessments
 - AHRQ Evidence Reports<u>https://www.ahrq.gov/research/findings/evidence-based-reports/index.html</u>
 - o EHC Program <u>https://effectivehealthcare.ahrq.gov/</u>
 - o US Preventive Services Task Force https://www.uspreventiveservicestaskforce.org/
 - AHRQ Technology Assessment Program https://www.ahrq.gov/research/findings/ta/index.html
- US Department of Veterans Affairs Products publications
 - o Evidence Synthesis Program https://www.hsrd.research.va.gov/publications/esp/
 - VA/Department of Defense Evidence-Based Clinical Practice Guideline Program <u>https://www.healthquality.va.gov/</u>
- Cochrane Database of Systematic Reviews https://www.cochranelibrary.com/
- PROSPERO Database (international prospective register of systematic reviews and protocols) <u>http://www.crd.york.ac.uk/prospero/</u>
- Ovid MEDLINE https://www.ovid.com/product-details.901.html
- ClinicalTrials.gov <u>https://www.clinicaltrials.gov/</u>

We conducted a search on November 11, 2020, on Ovid[®] MEDLINE[®] and The Cochrane Library. The search strategy included terms for pain and opioid tapering. Because a preliminary literature scan identified a well-conducted systematic review with searches conducted in April 2017, the search was restricted to studies published in 2015 or beyond; we utilized the systematic review for studies published prior to 2015. We reviewed all of the citations identified in the search for potentially relevant citations, and classified identified studies by study design to estimate the size and scope of a potential evidence review. We also searched ClinicalTrials.gov for in-progress reviews.

Database: Ovid MEDLINE(R) ALL <1946 to November 11, 2020> Search Strategy:

^{1 ((}opioid* or opiate* or codeine or clonidine or morphine or hydrocodone or oxycodone) adj3 (taper* or wean* or dose reduc* or reduc* dose or detox* or withdraw* or discontinuat* or cessation or tolerance or conversion or substitution or long-term)).sh,ti,ab,kw.

2 Chronic Pain/

3 exp arthralgia/ or exp back pain/ or exp headache/ or exp musculoskeletal pain/ or neck pain/ or exp neuralgia/ or exp nociceptive pain/ or pain, intractable/ or fibromyalgia/ or myalgia/

- 4 Pain/
- 5 chronic.ti,ab,kw.
- 6 4 and 5
- 7 ((chronic or persistent or intractable or refractory) adj3 pain).ti,ab,kw.

8 (((back or spine or spinal or leg or musculoskeletal or neuropathic or nociceptive or radicular) adj1 pain) or headache or arthritis or fibromyalgia or osteoarthritis).ti,ab,kw.

- 9 2 or 3 or 6 or 7 or 8
- 10 Medicare/

11 (medicare or disabled or disabilit* or kidney or renal or "lou gehrig*" or "amyotrophic lateral sclerosis" or "als").ti,ab.

- 12 10 or 11
- 13 1 and 9
- 14 1 and 12
- 15 limit 13 to yr="2015 -Current"
- 16 14 or 15
- 17 limit 16 to english language

Value and Potential Impact

Based on the literature scan, we assessed the nomination for value and potential impact, based on the quality and extent of available evidence, as summarized in the Value and Potential Impact section. We evaluated the potential for the evidence to (1) inform a policy or coverage action; (2) suitability for commissioning a new systematic review or technical brief; and (3) implications of current evidence on future research needs.

Appendix B. Assessment Criteria

Assessment Domain	Assessment Criteria	Assessment
1. Appropriateness	1a. Does the nomination represent a health care drug, intervention, device, technology, or health care system/setting available (or soon to be available) in the United States?	Yes (tapering approaches and technologies [e.g., mobile applications and wearable sensors])
	1b. Is the nomination a request for an evidence report?	No
	1c. Is the focus on effectiveness or comparative effectiveness?	Yes
	1d. Is the nomination focus supported by a logic model or biologic plausibility? Is it consistent or coherent with what is known about the topic?	Yes (evidence on treatments and technologies to support tapering on outcomes including pain, function, quality of life, impact on opioid dose, and adverse events)
2. Importance	2a. Represents a significant disease burden; large proportion of the population	Yes, long-term opioid therapy is frequently used and tapering is a commonly encountered situation in clinical practice
	2b. Is of high public interest; affects health care decision making, outcomes, or costs for a large proportion of the US population or for a vulnerable population	Yes, tapering is a challenge for clinicians and patients and can be associated with negative clinical outcomes and adverse events
	2c. Incorporates issues around both clinical benefits and potential clinical harms	Yes
	2d. Represents high costs due to common use, high unit costs, or high associated costs to consumers, to patients, to health care systems, or to payers	Yes, tapering can require high-cost treatments as well as complications that results in high costs

Assessment Domain	Assessment Criteria	Assessment
3. Current State of Evidence	3a. A recent high-quality systematic review or other evidence review is not available on this topic	Yes. A high-quality recent systematic review is available, as well as a subsequent more focused review.
	3b. Adequacy (type and volume) of research for a new systematic review or technical brief	The quality of the evidence is low but indicates that more effective approaches utilize interdisciplinary rehabilitation, behavioral support, or buprenorphine-assisted tapering.
		Evidence on technologies to support tapering is lacking.
		Evidence on strategies to mitigate serious harms of tapering (overdose, suicide) is lacking.
		Two in-progress trials on behavioral support and one in-progress trial on buprenorphine-assisted tapering may further inform this topic.
4. Value and Potential Impact	 4. Effectively utilizes existing research and knowledge by considering: Newly available evidence 	Low quality evidence could inform a policy or coverage action for treatments to support tapering.
	- Research needs	Given recent systematic review and limited new evidence, a new systematic review is not currently warranted.
		Research is needed to clarify optimal tapering approaches, identify effective technologies, identify strategies to mitigate potential harms of tapering, identify patients most likely to benefit from tapering, and confirm applicability of evidence to Medicare populations