Health Evidence Review Commission's Chronic Pain Task Force

September 20, 2018

9:30 AM - 11:30 AM

Wilsonville Holiday Inn, Candlewood Room
25425 SW 95th Ave
Wilsonville, Oregon 97070

Section 1.0

Call to Order

AGENDA
Chronic Pain Task Force
September 20, 2018
9:30-11:30 a.m.
Wilsonville Holiday Inn, Candlewood Room
25425 SW 95th Avenue
Wilsonville, Oregon 97070
(All agenda items are subject to change and times listed are approximate)

#	Time	Item	Presenter
1	9:30	Call to Order / Introduction of new members / Review of June minutes	Ariel Smits
2	9:35	Introduction • Objections of proposal • Summary of proposal to date Feedback: VBBS and public comment, specific issues raised re proposal Supplementary evidence review	Ariel Smits
3	10:00	Presentation on public health impact of opioids	Tom Jeanne
4	10:10	Presentation on opioid guidelines and opioid tapering	Beth Darnall
5	10:25	Q&A with presenters	all
6	10:30	Input on key questions for review of opioid tapers by the Center for Evidence-based Policy	all
7	10:40	Input on HERC Pain Treatment Implementation Survey of CCOs	all
8	10:45	Public Comment	
9	11:15	Next steps – direction for staff regarding required evidence reviews, direction for proposed line/guideline, etc.	Ariel Smits
10	11:30	Adjournment	Ariel Smits

MINUTES

Chronic Pain Task Force
Wilsonville Training Center
Wilsonville, OR
June 7, 2018
9:30-11:30 a.m.

Members Present: Kevin Cuccaro DO, Laura Ocker, Kim Jones, Nora Stern (via phone), Tracy Muday MD, Amber Rose Dullea (via phone), Cat Buist, Jim Shames MD (via phone); Ben Marx (via phone); Holly Jo Hodges MD (via phone)

Members Absent: David Sibell MD, Andrew Gibler, David Eisen, Mitch Haas

Staff Present: Ariel Smits, MD, MPH; Jason Gingerich

Also Attending: Sheila Moran; Beth Martin, Oregon Association of Naturopathic Physicians; Dan Cushing, Pac West

1. CALL TO ORDER

The meeting was called to order at 9:30 AM. The minutes from the April, 2018 Chronic Pain Taskforce meeting were reviewed. They were updated to reflect that David Eisen was not in attendance. Staff will post the minutes on the HERC website.

2. DISCUSSION

Smits reviewed the discussions of the Taskforce to date. She also reported to the group regarding the May VBBS/HERC discussions of the Taskforce recommendations. The HERC adopted the Statement of Intent proposed by the Taskforce with a minor edit. Smits then reviewed the requested evidence on Tai Chi and mindfulness therapy. The evidence is inadequate to support Tai Chi, but slightly stronger to support mindfulness therapy.

The group moved directly into discussion of the staff proposals. First, the group discussed the revised staff proposal for a new chronic pain line. The group again discussed the inclusion of fibromyalgia on the new line. There was discussion that fibromyalgia was reviewed by the HERC with the last biennial review and insufficient evidence was found for effectiveness of treatment for this condition. However, the group felt that the therapies that had evidence for fibromyalgia (exercise, sleep education) were included on the new line. Patients with fibromyalgia are very similar to patients with chronic pain syndrome, and should not be singled out. Additionally, the group noted that fibromyalgia patients would be treated through providers simply changing their diagnosis to chronic pain syndrome. The

decision was to add fibromyalgia to the proposed new line, and have Kim Jones give a presentation regarding evidence for treatment during the August HERC discussion of the new chronic pain line.

There was discussion that if fibromyalgia was moved to the new line, then current line 528 FIBROMYALGIA, CHRONIC FATIGUE SYNDROME, AND RELATED DISORDERS would only have chronic fatigue syndrome on it as a unique placement. Smits was directed to look at the procedures on this line; if there was nothing but medical visits and behavioral health interventions, then 528 should be changed to CHRONIC FATIGUE SYNDROME.

The group reviewed the proposed new guideline for the new chronic pain line. There was discussion about the type of pain education that patients should receive. It was decided to add knowledge of pain "as a biopsychosocial phenomenon" to the guideline. There was discussion about including massage as a PT modality later in the guideline. The group felt that massage by non-PT providers should be included in the 30-visit PT/acupuncture limit because massage was a passive modality and should be used sparingly. Smits was concerned about including massage in the 30-visit limit as this might limit what the CCOs could offer through their flex spending. If massage was included as a medical benefit, then the CCOs might have to use medical funds for it, and this would be difficult as massage therapists generally do not have Medicaid billing IDs and there being other barriers to this type of payment.

Next, the group discussed line scoring. Cuccaro proposed increasing the score for tertiary prevention to 2 to match the back line, as the ability to prevent future problems would be similar. Muday suggested decreasing the need for service to 0.8 to match the back line and current chronic pain/fibromyalgia line. These changes were agreed on by the group. The new scoring placed the new line at approximately line 443.

The group approved the suggested changes to the back guideline (Guideline Note 56). There was discussion about the table at the end of the back guideline. It was noted that it was quite out of date, and HERC staff was directed to look at the updated AHRQ review to see if the table was updated and, if so, modify the guideline table to match the updated one. If AHRQ did not update the table from the previous Chou paper, then the group recommended taking out benzodiazepines and opioids from the table in the guideline and otherwise updating the table based on the 2016 AHRQ reviews of pharmacologic and non-pharmacologic therapy for back pain. *[Editorial note: There was no similar table in the 2016AHRQ review for low back pain or a 2018 review of noninvasive, nonpharmacologic treatments for chronic pain; therefore staff will be recommending to HERC that the table be removed in its entirety from Guideline Note 56.]*

The group next discussed the opioid guideline (Guideline Note 60). Smits reported that the evidence search for the optimal length of an opioid taper found no evidence. The CDC opioid prescribing guidelines use 10% per week reductions based on expert opinion. The group agreed that there was no evidence on best taper length. The group felt that the optimal taper length was very dependent on the patient, the dose of opioids, the length of time on opioids, etc. The group felt that the taper length for the guideline should be no more than one year. This allows faster tapers for patients that are able, but allows slower tapers for those patients that require a slower rate. Additionally, one year would be consistent with the previous version of the guideline. Muday noted that her CCO approves opioid therapy for 3 months, then checks in with the patient and provider. In her experience, very high dose patients need more time to taper.

The modifications to the acupuncture guideline did not elicit any comments.

The final chronic pain line proposal was approved. Smits reviewed the next steps—the proposal will be reviewed at the August VBBS meeting and, if approved, at the August HERC meeting. The proposal may require further discussion and in that case will be discussed again at a fall VBBS/HERC meeting. If approved, the proposed new line would go into effect January 1, 2020. There will need to be actuarial review prior to implementation of the new line.

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3. PUBLIC TESTIMONY

Sheila Moran, an acupuncturist and chronic pain patient who worked in an federally-qualitied health center (FQHC) treating chronic pain patients, testified. She noted that acupuncture was not being covered for various conditions because it was not found to be evidence-based, but she said this is because the wrong data is being collected. She also noted that prior authorizations for acupuncture in her CCO were a barrier to patients accessing this type of care. She feels that the 30-visit limit for acupuncture is way off for chronic pain patients. The 30-visit limit is based on acute injury, not difficult patients with a long history of pain. She also did not feel that asking for a functional assessment after the first visit makes sense. Function plateaus at some point when in maintenance phase and functional assessments are not helpful. She noted that it is not practical to get patients off opioids who have been on them for many, many years. Pain patients are psychologically abused by the medical system. Also, chronic pain is a chronic disease that needs maintenance treatment for life.

Beth Martin, from Oregon Association of Naturopathic Physicians, testified. NDs are primary care providers and have proscribing rights. However, NDs have Issues with opioid tapering and suboxone. NDs cannot prescribe suboxone for opioid use disorder. She requested support to add suboxone to the ND formulary.

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4. ADJOURNMENT

The meeting was adjourned at 11:30am.

Appendix A
New Chronic Pain Line Proposal

LINE: XXX
CONDITION: CHRONIC PAIN SYNDROME AND FIBROMYALGIA
TREATMENT: LIMITED PHYSICAL MODALITIES, COGNITIVE BEHAVIORAL THERAPY, MEDICAL THERAPY
ICD-10: G89.21 (Chronic pain due to trauma), G89.28 (Other chronic postprocedural pain), G89.29 (Other chronic pain), G89.4 (Chronic pain syndrome), M79.7 (fibromyalgia)
CPT: 90785, 90832-90840, 90853 (psychotherapy—for CBT and ACT), 96150-96155 (Health and behavior assessment and intervention), 97110-97124, 97140-97168, 97530, 97535 (PT/OT), 97810-97814 (acupuncture), 98966-98969, 99051, 99060, 99070, 99078, 99201-99215, 99281-99285, 99304-99337, 99340-99404, 99408-99449, 99487-99490, 99495, 99496, 99605-99607 (medical office visits, including ER and SNF)
HCPCS: G0157-G0160 (PT/OT assistant), G0396-G0397 (alcohol and substance abuse screening), G0463-G0467, G0469, G0470 (FQHC care), G0490, G0511-G0513 (RFQHC care), G0514 (prolonged office visit)

GUIDELINE NOTE XXX, CHRONIC PAIN THERAPY

Lines XXX, 528

Chronic pain conditions are included on Line XXX when symptoms have been present for at least 3 months and have not responded to conservative management.

The following treatments are included on Line XXX:

- Office evaluation, consultation and education.
    - Pain education, if done, should include, but not be limited to: sleep, nutrition, stress reduction/mood, exercise, and knowledge of pain as a biopsychosocial phenomenon. All providers seeing chronic pain patients should be trained in pain science (e.g., a contemporary understanding of the central and peripheral nervous system in chronic pain), motivational interviewing, culturally sensitive care, and trauma informed care. Care should be multidisciplinary and focus on active therapies.
- Cognitive behavioral therapy (CBT)/acceptance and commitment therapy (ACT). The necessity for CBT and/or ACT should be re-evaluated every 90 days and coverage will only be continued if there is documented evidence of decreasing depression or anxiety symptomatology, improved ability to work/function, increased self-efficacy, or other clinically significant, objective improvement.
- The following therapies, when available, may be provided: yoga, mindfulness training, massage, supervised exercise therapy (land-based and aquatic), intensive interdisciplinary rehabilitation. HCPCS S9451 is only included on Line XXX for the provision of yoga or supervised exercise therapy.
- A total of 30 visits per year of any combination of the following therapies when available and medically appropriate. These therapies are only included on these lines if provided by a provider licensed to provide the therapy and when there is documentation of measurable clinically significant progress toward the therapy plan of care goals and objectives using evidence-based objective tools. Once the pre-determined goals of care have been achieved, an additional two visits may be authorized for maintenance therapy to maintain these improvements. These 30

visits count toward the visit totals in GUIDELINE NOTE 56 NON-INTERVENTIONAL TREATMENTS FOR CONDITIONS OF THE BACK AND SPINE if the patient has comorbid back or spine conditions.

1) Rehabilitative therapy (physical and/or occupational therapy), if provided according to Guideline Note 6 REHABILITATIVE AND HABILITATIVE THERAPIES. Rehabilitation services provided under this guideline also count towards visit totals in Guideline Note 6. CPT 97124 is included in this category.
2) Acupuncture

Non-opioid medications are only included on Line XXX if all of the following apply:

1) The medication is FDA approved or supported by compendia for treatment of chronic, non-neuropathic pain
2) The patient is also being treated with active therapy (e.g., physical therapy, CBT) or is continuing maintenance of self-management strategies learned from such therapy.
3) The benefit of non-opioid medication is re-evaluated at least every 90 days and medications are only continued if there is documented evidence of improvement of function of at least fifteen percent as compared to baseline based on a validated tool (e.g., Oswestry, SF-MPQ, and MSPQ). Less frequent monitoring may be appropriate for certain medications after safety and efficacy are established.

Opioids are included on this line according to GUIDELINE NOTE 60 OPIOIDS FOR CONDITIONS OF THE BACK AND SPINE AND CHRONIC PAIN.

Line Scoring

Line XXX CHRONIC PAIN SYNDROME AND FIBROMYALGIA
Category: 7
HL: 4
Suffering: 3
Population effects: 0
Vulnerable population: 0
Tertiary prevention: 2
Effectiveness: 2
Need for service: 0.8
Net cost: 2
Score: 288
Approximate line placement: 443

Line 528 CHRONIC FATIGUE SYNDROME
Category: 7
HL: 4
Suffering: 3
Population effects: 0
Vulnerable population: 0
Tertiary prevention: 0
Effectiveness: 1
Need for service: 0.8
Net cost: 2
Score: 112
Line placement: 528

Line 401 CONDITIONS OF THE BACK AND SPINE
Category: 7
HL: 4
Suffering: 3
Population effects: 0
Vulnerable population: 0
Tertiary prevention: 2
Effectiveness: 3
Need for service: 0.8
Net cost: 2
Score: 438
Approximate line placement: 401

Line: 528

Condition: ~~FIBROMYALGIA,~~ CHRONIC FATIGUE SYNDROME~~, AND RELATED DISORDERS~~ (See Guideline Notes 64,65,135)

Treatment: MEDICAL THERAPY

ICD-10: ~~G89.21,G89.28-G89.29,G89.4,M79.7,~~R53.82

CPT: 90785,90832-90840,90846-90853,93792,93793,98966-98969,99051,99060,99070,99078, 99201-99215,99281-99285,99341-99378,99381-99404,99408-99449,99487-99490,99495-99498,99605-99607

HCPCS: G0248-G0250,G0396,G0397,G0463-G0467,G0490,G0511,G0513,G0514

GUIDELINE NOTE 56, NON-INTERVENTIONAL TREATMENTS FOR CONDITIONS OF THE BACK AND SPINE

Lines 361,401

Patients seeking care for back pain should be assessed for potentially serious conditions ("red flag" symptoms requiring immediate diagnostic testing), as defined in Diagnostic Guideline D4. Patients lacking red flag symptoms should be assessed using a validated assessment tool (e.g. STarT Back Assessment Tool) in order to determine their risk level for poor functional prognosis based on psychosocial indicators.

For patients who are determined to be low risk on the assessment tool, the following services are included on these lines:

- Office evaluation and education,
- Up to four total visits, consisting of the following treatments: OMT/CMT, acupuncture, and PT/OT. Massage, if available, may be provided as part of these four total visits.
- First line medications: NSAIDs, acetaminophen, and/or muscle relaxers. Opioids may be considered as a second line treatment, subject to the limitations on coverage of opioids in Guideline Note 60 OPIOIDS FOR CONDITIONS OF THE BACK AND SPINE. See evidence table.

For patients who are determined to be medium- or high risk on the validated assessment tool, as well as patients undergoing opioid tapers as in Guideline Note 60 OPIOIDS FOR CONDITIONS OF THE BACK AND SPINE, the following treatments are included on these lines:

- Office evaluation, consultation and education
- Cognitive behavioral therapy/acceptance and commitment therapy. The necessity for cognitive behavioral therapy/acceptance and commitment therapy should be re-evaluated every 90 days and coverage will only be continued if there is documented evidence of decreasing depression or anxiety symptomatology, improved ability to work/function, increased self-efficacy, or other clinically significant, objective improvement.
- Prescription and over-the-counter medications; opioid medications subject to the limitations on coverage of opioids in Guideline Note 60 OPIOIDS FOR CONDITIONS OF THE BACK AND SPINE. See evidence table.
- The following evidence-based therapies, when available, may be provided: yoga, massage, supervised exercise therapy, intensive interdisciplinary rehabilitation. HCPCS S9451 is only included on Line 401 for the provision of yoga or supervised exercise therapy.
- A total of 30 visits per year of any combination of the following evidence-based therapies when available and medically appropriate. These therapies are only included on these lines if provided by a provider licensed to provide the therapy and when there is documentation of measurable clinically significant progress toward the therapy plan of care goals and objectives using evidence based objective tools (e.g. Oswestry, Neck Disability Index, SF-MPQ, and MSPQ). These 30 visits count toward the visit totals in GUIDELINE NOTE XXX CHRONIC PAIN THERAPY if the patient has comorbid chronic pain conditions.
    3) Rehabilitative therapy (physical and/or occupational therapy), if provided according to Guideline Note 6 REHABILITATIVE AND HABILITATIVE THERAPIES. Rehabilitation services provided under this guideline also count towards visit totals in Guideline Note 6. CPT 97124 is included in this category.
    4) Chiropractic or osteopathic manipulation
    5) Acupuncture

Mechanical traction (CPT 97012) is not included on these lines, due to evidence of lack of effectiveness for treatment of back and neck conditions.

The development of this guideline note was informed by HERC coverage guidances on Low Back Pain Non-Pharmacologic, Non-Invasive Intervention, Low Back Pain, Pharmacological and Herbal Therapies. See http://www.oregon.gov/oha/HPA/CSI-HERC/Pages/Evidence-based-Reports.aspx.

Evidence Table of Effective Treatments for the Management of Low Back Pain

[Editor's note: CPTF recommendation was to update or replace this table; staff recommendation is to simply remove it.]

Intervention Category*	Intervention	Acute < 4 Weeks	Subacute & Chronic > 4 Weeks
Self-care	Advice to remain active	•	•
	Books, handout	•	•
	Application of superficial heat	•	
Nonpharmacologic therapy	Spinal manipulation	•	•
	Exercise therapy		•
	Massage		•
	Acupuncture		•
	Yoga		•
	Cognitive-behavioral therapy		•
	Progressive relaxation		•
Pharmacologic therapy (Carefully consider risks/harms)	Acetaminophen	•	•
	NSAIDs	•(▲)	•(▲)
	Skeletal muscle relaxants	•	
	Antidepressants (TCA)		•
	*Benzodiazepines***	•(▲)	•(▲)
	*Tramadol, opioids***	•(▲)	•(▲)
Interdisciplinary therapy	Intensive interdisciplinary rehabilitation		•

• Interventions supported by grade B evidence (at least fair-quality evidence of moderate benefit, or small benefit but no significant harms, costs, or burdens). No intervention was supported by grade "A" evidence (good-quality evidence of substantial benefit).

▲ *Carries greater risk of harms than other agents in table.*

NSAIDs = nonsteroidal anti-inflammatory drugs; TCA = tricyclic antidepressants.

*These are general categories only. Individual care plans need to be developed on a case by case basis. For more detailed information please see: http://www.annals.org/content/147/7/478.full.pdf

**Associated with significant risks related to potential for abuse, addiction and tolerance. This evidence evaluates effectiveness of these agents with relatively short term use studies. Chronic use of these agents may result in significant harms.

GUIDELINE NOTE 60, OPIOIDS FOR CONDITIONS OF THE BACK AND SPINE AND CHRONIC PAIN

Lines 346,361,401,527,XXX

Opioid medications are only included on these lines under the following criteria:

For acute injury, ~~acute flare of chronic pain,~~ or after surgery:

1) During the first 6 weeks opioid treatment is included on these lines ONLY:
   a) When each prescription is limited to 7 days of treatment, AND

b) For short acting opioids only, AND
c) When one or more alternative first line pharmacologic therapies such as NSAIDs, acetaminophen, and muscle relaxers have been tried and found not effective or are contraindicated, AND
d) When prescribed with a plan to keep active (home or prescribed exercise regime) and with consideration of additional therapies such as spinal manipulation, physical therapy, yoga, or acupuncture, AND
e) There is documented verification that the patient is not high risk for opioid misuse or abuse.

2) Treatment with opioids after 6 weeks, up to 90 days after the initial injury/~~flare/~~surgery is included on these lines ONLY:
a) With documented evidence of improvement of function of at least thirty percent as compared to baseline based on a validated tool (e.g. Oswestry, Neck Disability Index, SF-MPQ, and MSPQ).
b) When prescribed in conjunction with therapies such as spinal manipulation, physical therapy, yoga, or acupuncture.
c) With verification that the patient is not high risk for opioid misuse or abuse. Such verification may involve
i) Documented verification from the state's prescription monitoring program database that the controlled substance history is consistent with the prescribing record
ii) Use of a validated screening instrument to verify the absence of a current substance use disorder (excluding nicotine) or a history of prior opioid misuse or abuse
iii) Administration of a baseline urine drug test to verify the absence of illicit drugs and non-prescribed opioids.
d) Each prescription must be limited to 7 days of treatment and for short acting opioids only

3) Chronic opioid treatment (>90 days) after the initial injury/~~flare/~~surgery is not included on these lines except for the taper process described below.

Transitional coverage for patients on long-term opioid therapy ~~as of July 1, 2016~~:

For patients ~~on covered chronic~~ receiving long-term opioid therapy ~~as of July 1, 2016, opioid medication is included on these lines only from July 1, 2016 to December 31, 2016. During the period from January 1, 2017 to December 31, 2017~~, continued coverage of opioid medications requires an individual treatment plan ~~developed by January 1, 2017~~ which includes a taper with an end to opioid therapy no later than one year from the start of the taper ~~no later than January 1, 2018~~. Taper plans must include nonpharmacological treatment strategies for managing the patient's pain ~~based on Guideline Note 56 NON-INTERVENTIONAL TREATMENTS FOR CONDITIONS OF THE BACK AND SPINE~~. If a patient has developed dependence and/or addiction related to their opioids, treatment is ~~available~~ included on Line 4 SUBSTANCE USE DISORDER**.**

GUIDELINE NOTE 92, ACUPUNCTURE

Lines 1,5,202,361,401,409,461,538

Inclusion of acupuncture (CPT 97810-97814) on the Prioritized List has the following limitations:

Line 1 PREGNANCY

Acupuncture pairs on Line 1 for the following conditions and codes.

Hyperemesis gravidarum

ICD-10-CM: O21.0, O21.1

Acupuncture pairs with hyperemesis gravidarum when a diagnosis is made by the maternity care provider and referred for acupuncture treatment for up to 12 sessions of acupressure/acupuncture per pregnancy.

Breech presentation

ICD-10-CM: O32.1

Acupuncture (and moxibustion) is paired with breech presentation when a referral with a diagnosis of breech presentation is made by the maternity care provider, the patient is between 33 and 38 weeks gestation, for up to 6 sessions per pregnancy.

Back and pelvic pain of pregnancy

ICD-10-CM: O99.89

Acupuncture is paired with back and pelvic pain of pregnancy when referred by maternity care provider/primary care provider for up to 12 sessions per pregnancy.

Line 5 TOBACCO DEPENDENCE

Acupuncture is included on this line for a maximum of 12 sessions per quit attempt up to two quit attempts per year; additional sessions may be authorized if medically appropriate.

Line 202 CHRONIC ORGANIC MENTAL DISORDERS INCLUDING DEMENTIAS

Acupuncture is paired with the treatment of post-stroke depression only. Treatments may be billed to a maximum of 30 minutes face-to-face time and limited to 12 total sessions per year, with documentation of meaningful improvement; patients may have additional visits authorized beyond these limits if medically appropriate.

Line 361 SCOLIOSIS

Acupuncture is included on this line with visit limitations as in Guideline Note 56 NON-INTERVENTIONAL TREATMENTS FOR CONDITIONS OF THE BACK AND SPINE.

Line 401 CONDITIONS OF THE BACK AND SPINE

Acupuncture is included on this line with visit limitations as in Guideline Note 56 NON-INTERVENTIONAL TREATMENTS FOR CONDITIONS OF THE BACK AND SPINE.

Line 409 MIGRAINE HEADACHES

Acupuncture pairs on Line 409 for migraine (ICD-10-CM G43.0, G43.1, G43.5, G43.7, G43.8, G43.9), for up to 12 sessions per year.

Line XXX CHRONIC PAIN SYNDROME AND FIBROMYALGIA

Acupuncture is included on this line with visit limitations as in Guideline Note XXX CHRONIC PAIN THERAPY

Line 461 OSTEOARTHRITIS AND ALLIED DISORDERS

Acupuncture pairs on Line 461 for osteoarthritis of the knee only (ICD-10-CM M17), for up to 12 sessions per year.

*Line 538 TENSION HEADACHES

Acupuncture is included on Line 538 for treatment of tension headaches (ICD-10-CM G44.2), for up to 12 sessions per year.

The development of this guideline note was informed by a HERC coverage guidance. See http://www.oregon.gov/oha/HPA/CSI-HERC/Pages/Evidence-based-Reports.aspx.

*Below the current funding line.

Section 2.0

Discussion of CPTF proposal

The HERC Chronic Pain Taskforce

September 20, 2018

Oregon Health Authority

Objectives

- Consider adjusting OHP coverage to improve treatment for fibromyalgia and other chronic pain conditions
  - Currently no treatments available other than office visits and non-PA'd medications
  - Consider whether evidence of effectiveness or other factors justify reprioritization
  - Ensure appropriate limitations on therapies that have limited evidence of effectiveness/risks (e.g., opioids)

CPTF June 2018 proposal

- Recommendation
  - Add new line for specific diagnoses, with evidence-based treatments for chronic pain conditions
    - Cognitive behavioral therapy, PT, acupuncture, other active modalities.
  - Add guideline to limit opioid therapy
    - Limited acute prescribing
    - Limit therapy for up to 90 days with criteria
    - Taper plan required for patients on long-term opioid therapy (complete in 1 year after initiated)

Public comment and media attention

- 400+ patient emails, 14 provider emails
- In-person protests at VbBS meetings and OHA offices
- Op Eds in Wall Street Journal, coverage in Bend Bulletin, Portland Business Journal, Oregon Public Broadcasting and others
- Most feedback was negative and focused on the perception that all patients with any chronic pain (regardless of diagnosis) would be tapered off currently prescribed opioids

Major themes of comments

Services proposed for addition (PT, acupuncture, yoga, massage, NSAIDs etc.)

- Patients and Providers : Therapies did not work or were helpful but not sufficient, had side effects

Conditions mentioned included:

- Back pain (including failed back surgery, arachnoiditis), fibromyalgia, arthritis, post-accident pain, other musculoskeletal pain, bladder pain, ocular pain, migraines, PTSD

Major themes of comments (continued)

Opioid limitations

- Opioids are effective in improving function, tapers reduce function
- Patients taking opioids as prescribed are not addicts, are treated as such, are discriminated against
- Concerns about (or consideration of) suicide, illicit substance use if a taper requirement is put in place
- Taper policy is overreaction to some patients (not all)
- Doctors, not payers should make these decisions
- Requirements should not apply to specific conditions (cancer, autoimmune, rare conditions)

Issues to address

- Clarify rationale, evidence for opioid limitation
- Address specifics of CPTF proposal
  - –Central pain syndrome (ICD-10 G89.0)
  - –Clarification of population included
  - –Inclusion of/guideline for fibromyalgia
    - P&T medication review this fall

Issues to address

- Questions about the effectiveness of long term opioid therapy for treatment of chronic pain
  - –SPACE trial
  - –Chou systematic review
  - –Noble Cochrane review
  - –Els 2017 and 2018 Cochrane reviews
  - –CDC prescribing guidelines

Issues to address

- Prescription opioids and heroin
  - –NIDA 2018
    - Majority (75-80%) of heroin users first use prescription opioids
    - Only 4% of prescription opioid users start using heroin within 5 years

Issues to address

- Effects of opioid taper on pain and function
  - MED 2017 (to be updated)
  - Frank 2017 systematic review
  - McPherson 2018 retrospective VA study
  - Darnall 2018 prospective study

Informational presentations

- Dr. Tom Jeanne, Oregon Public Health Division
- Dr. Beth Darnall, Stanford University

Evaluate research plan

- Center for Evidence Based Policy to update its systematic review on effectiveness and harms of opioid taper
  - CPTF to review scope today
- Survey of CCOs
  - How were back coverage changes implemented?
  - Lessons learned from back coverage expansion
  - Feedback about new potential line, implementation issues

Next Steps

- Additional information required
- Direction on changes to proposal
- Other direction for staff

Oregon Health Authority

Chronic Pain Taskforce
September 2018

The Chronic Pain Taskforce approved a proposal to create a new line for a limited number of chronic pain conditions at their June, 2018 meeting. This proposal was presented at the August VbBS meeting, and a large amount of written and verbal public testimony was received. Please refer to the following for more details:

1. Appendix A: June 2018 CPTF proposal to VbBS/HERC
2. Appendix B: summary of themes from written public testimony
3. Appendix C: VbBS minutes section on CPTF proposal

Written and oral public testimony focused on concerns regarding limitations on opioids and the requirement to taper patients on long term opioid therapy. To assist in the deliberations of the Taskforce, HERC staff have reached out to various experts in addictions and treatment of chronic pain, at OHSU, Outside In, and other community providers. We are excited to have two new members of the Taskforce. Dr. Amanda Risser is joining the Taskforce as an addictions expert. Lisa Boyle is also joining the Taskforce as a pharmacist with expertise in managing prior authorizations.

<u>Issues that have arisen with the proposal details, with plans to address them</u>:

1) There is a fibromyalgia guideline that needs to be incorporated into the new line guideline in some manner or deleted if appropriate

   GUIDELINE NOTE 135, FIBROMYALGIA
   Line 528
   Fibromyalgia (ICD-10-CM M79.7) treatment should consist of a multi-modal approach, which should include two of more of the following:
   A) medications other than opioids
   B) exercise advice/programs
   C) cognitive behavioral therapy.
   Care should be provided in the primary care setting. Referrals to specialists are generally not required. Use of opioids should be avoided due to evidence of harm in this condition.

   The Pharmacy and Therapeutics Committee will conduct a review of fibromyalgia medications to inform VbBS's decision about whether to reprioritize fibromyalgia and inform possible updates to this guideline note. This review is anticipated to be done prior to the December CPTF meeting.

2) Consider inclusion of central pain syndrome (ICD-10 G89.0) based on CCO feedback. Central pain syndrome is a neurological condition caused by damage to or dysfunction of the central nervous system (CNS), which includes the brain, brainstem, and spinal cord. This syndrome can be caused by stroke, multiple sclerosis, tumors, epilepsy, brain or spinal cord trauma, or Parkinson's disease. It is typically difficult to treat, but can respond to tricyclic antidepressants. Currently, G89.0 is on line 317 STROKE.
3) Need to specify that cancer, arthritis, and other currently funded conditions are not included in the guideline for the new line

Chronic Pain Taskforce
September 2018

Additional evidence review

Evidence review on effectiveness and harms of opioids for treatment of chronic pain

1) **Krebs 2018**, SPACE trial of opioids vs NSAIDs vs Tylenol for chronic pain
   a) N=240 pts, RCT
   b) Groups did not significantly differ on pain-related function over 12 months (overall *P* = .58); mean 12-month BPI interference was 3.4 for the opioid group and 3.3 for the nonopioid group (difference, 0.1 [95%CI, −0.5 to 0.7]). Pain intensity was significantly better in the nonopioid group over 12 months (overall *P* = .03); mean 12-month BPI severity was 4.0 for the opioid group and 3.5 for the nonopioid group (difference, 0.5 [95%CI, 0.0 to 1.0]). Adverse medication-related symptoms were significantly more common in the opioid group over 12 months (overall *P* = .03); mean medication-related symptoms at 12 months were 1.8 in the opioid group and 0.9 in the nonopioid group (difference, 0.9 [95%CI, 0.3 to 1.5]).
   c) CONCLUSIONS AND RELEVANCE Treatment with opioids was not superior to treatment with nonopioid medications for improving pain-related function over 12 months. Results do not support initiation of opioid therapy for moderate to severe chronic back pain or hip or knee osteoarthritis pain.
2) **Chou 2015**, systematic review of the safety and effectiveness of long term opioids for the treatment of chronic pain
   a) No study of opioid therapy versus no opioid therapy evaluated long-term (>1 year) on outcomes related to pain, function, quality of life, opioid abuse, or addiction.
   b) Good- and fair-quality observational studies suggest that opioid therapy for chronic pain is associated with increased risk for overdose, opioid abuse, fractures, myocardial infarction, and markers of sexual dysfunction, although there are few studies for each of these outcomes; for some harms, higher doses are associated with increased risk.
   c) Evidence on the effectiveness and harms of different opioid dosing and risk mitigation strategies is limited.
   d) Conclusion: Evidence is insufficient to determine the effectiveness of long-term opioid therapy for improving chronic pain and function. Evidence supports a dose-dependent risk for serious harms.
3) **Noble 2010**, Cochrane review of opioids for treatment of chronic non-cancer pain
   a) N=26 studies (4892 patients)
      i) 25 case series, 1 RCT comparing two opioids
      ii) Various administrative routes (oral, patch, intrathecal)
   b) Many participants discontinued due to adverse effects (oral: 22.9% [95% confidence interval (CI): 15.3% to 32.8%]; transdermal: 12.1% [95% CI: 4.9% to 27.0%]; intrathecal: 8.9% [95% CI: 4.0% to 26.1%]); or insufficient pain relief (oral: 10.3% [95% CI: 7.6% to 13.9%]; intrathecal: 7.6% [95%CI: 3.7% to 14.8%]; transdermal: 5.8%[95% CI: 4.2% to 7.9%]).
   c) Signs of opioid addiction were reported in 0.27% of participants in the studies that reported that outcome.
   d) All three modes of administration were associated with clinically significant reductions in pain, but the amount of pain relief varied among studies. Findings regarding quality of life and functional status were inconclusive due to an insufficient quantity of evidence

for oral administration studies and inconclusive statistical findings for transdermal and intrathecal administration studies.

e) **Authors' conclusions** Many patients discontinue long-term opioid therapy (especially oral opioids) due to adverse events or insufficient pain relief; however, weak evidence suggests that patients who are able to continue opioids long-term experience clinically significant pain relief. Whether quality of life or functioning improves is inconclusive. Many minor adverse events (like nausea and headache) occurred, but serious adverse events, including iatrogenic opioid addiction, were rare.

Els 2018, Cochrane review of adverse events associated with medium- and long-term use of opioids for chronic

a) N=14 reviews, most with data in the 6 to 16 week range
   i) 61 studies, 18,679 patients
b) A GRADE assessment of the quality of the evidence for specific adverse events led to a downgrading (to very low- to moderate-quality evidence depending on study) due to risk of bias, indirectness, and imprecision.
c) there was a significantly increased risk of experiencing any adverse event with opioids compared to placebo (risk ratio (RR) 1.42, 95% confidence interval (CI) 1.22 to 1.66) as well as with opioids compared to a non-opioid active pharmacological comparator, with a similar risk ratio (RR 1.21, 95% CI 1.10 to 1.33). There was also a significantly increased risk of experiencing a serious adverse event with opioids compared to placebo (RR 2.75, 95% CI 2.06 to 3.67). Furthermore, there were significantly increased risk ratios with opioids compared to placebo for a number of specific adverse events: constipation, dizziness, drowsiness, fatigue, hot flushes, increased sweating, nausea, pruritus, and vomiting.
d) There was no data on any of the following prespecified adverse events of interest in any of the included reviews in this overview of Cochrane Reviews: addiction, cognitive dysfunction, depressive symptoms or mood disturbances, hypogonadism or other endocrine dysfunction, respiratory depression, sexual dysfunction, and sleep apnoea or sleep-disordered breathing.
e) Authors' conclusions: A number of adverse events, including serious adverse events, are associated with the medium- and long-term use of opioids for CNCP. The absolute event rate for any adverse event with opioids in trials using a placebo as comparison was 78%, with an absolute event rate of 7.5% for any serious adverse event. Based on the adverse events identified, clinically relevant benefit would need to be clearly demonstrated before long-term use could be considered in people with CNCP in clinical practice.

5) **Els 2017**, Cochrane review of high dose opioids for chronic non cancer pain
   a) No studies met inclusion criteria
   b) Authors' conclusions**:** There is a critical lack of high-quality evidence regarding how well high-dose opioids work for the management of chronic non-cancer pain in adults, and regarding the presence and severity of adverse events. No evidence-based argument can be made on the use of highdose opioids, i.e. 200 mg morphine equivalent or more daily, in clinical practice. Trials typically used doses below our cut-off; we need to know the efficacy and harm of higher doses, which are often used in clinical practice.

Expert recommendations of use of opioids for chronic pain

1) **CDC 2016**, opioid prescribing guidelines

a) Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate
b) Opioids are not first-line or routine therapy for chronic pain
c) If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

Evidence on prescription opioids and subsequent heroin use

1) **NIDA 2018**, Prescription Opioids and Heroin
    a. Of people entering treatment for heroin addiction who began abusing opioids in the 1960s, more than 80 percent started with heroin. Of those who began abusing opioids in the 2000s, 75 percent reported that their first opioid was a prescription drug
    b. Examining national-level general population heroin data (including those in and not in treatment), nearly 80 percent of heroin users reported using prescription opioids prior to heroin
    c. While prescription opioid abuse is a growing risk factor for starting heroin use, only a small fraction of people who abuse pain relievers switch to heroin use. According to general population data from the National Survey on Drug Use and Health, less than 4 percent of people who had abused prescription opioids started using heroin within 5 years

Evidence on opioid tapering on pain and functionality

1) **MED 2017,** systematic review of effectiveness and harms of opioid dose reduction
    a. Confidence is limited by the very low quality of evidence overall, but there is scarce evidence on harms associated with tapering strategies, and the findings suggest that pain, function, and quality of life might improve during and after opioid discontinuation or dose reduction.
2) **Frank 2017**, systematic review of patient outcomes after taper from long term opioid therapy
    a. N=67 studies (11 randomized trials and 56 observational studies) examining 8 intervention categories, including interdisciplinary pain programs, buprenorphine assisted dose reduction, and behavioral interventions,
        i. Study quality was good for 3 studies, fair for 13 studies, and poor for 51 studies.
        ii. the overall quality of evidence was very low.
    b. Among 40 studies examining patient outcomes after dose reduction (very low overall quality of evidence), improvement was reported in pain severity (8 of 8 fair-quality studies), function (5 of 5 fair-quality studies), and quality of life (3 of 3 fair-quality studies).
    c. Conclusion: Very low quality evidence suggests that several types of interventions may be effective to reduce or discontinue LTOT and that pain, function, and quality of life may improve with opioid dose reduction.

3) **McPherson 2018**, changes in pain intensity after discontinuation of long term opioid therapy for non cancer pain
    a. Retrospective VA study
    b. N=5,551 patients
    c. Pain measured on a 0-10 pain scale (NRS scale). The unadjusted linear slope describing the 12-month post discontinuation pain trajectory was -0.07 points (P< 0.01), indicating that pain scores decreased, on average across all patients, by approximately one-tenth of a point on the NRS per month for the year after opioid discontinuation.
    d. After controlling for patient demographic, clinical, and pain treatment utilization variables, average pain scores did not significantly change over the 12 months after LTOT discontinuation.
    e. Conclusion: Pain intensity after discontinuation of LTOT does not, on average, worsen for patients and may slightly improve, particularly for patients with mild-to-moderate pain at the time of discontinuation.
4) **Darnall 2018**, opioid tapering for patients with chronic pain
    a. Prospective cohort study of patient outcomes with voluntary opioid taper
        i. N=51 patients, median 6 year duration of opioid use, median MEDD was 288mg.
        ii. Median pain intensity was moderate (5 out of 10 on a numeric pain rating). After 4 months, the median MEDD was reduced to 150 (IQR, 54-248) mg (*P* = .002). The likelihood of a greater than 50%o opioid dose reduction was not predicted by starting dose, baseline pain intensity, years prescribed opioids, or any psychosocial variable.
        iii. Neither pain intensity (*P* = .29) nor pain interference (*P* = .44) increased with opioid reduction.

Chronic Pain Taskforce
September 2018

Additional information being collected by HERC staff for Taskforce

1) Center for Evidence Based Policy systematic review on effectiveness and harms of opioid taper update
    a. See PICO and key questions
2) Survey of CCOs regarding observed benefits and harms of opioid reduction for back/neck pain; lessons learned regarding implementation of such a taper policy

Appendix A

June 2018 Task Force Proposal

Taskforce recommendations:

1) Create a new line for chronic pain and fibromyalgia for the 2020 Biennial Review as shown below
2) Adopt a new guideline for this line as shown below
3) Score this new line as shown below
4) Modify line 528 FIBROMYALGIA, CHRONIC FATIGUE SYNDROME, AND RELATED DISORDERS as shown below
    i. Remove all diagnoses other than chronic fatigue syndrome and modify line title
5) Modify GUIDELINE NOTE 56, NON-INTERVENTIONAL TREATMENTS FOR CONDITIONS OF THE BACK AND SPINE as shown below
    i. Matches changes in the new chronic pain conditions guideline
6) Modify GUIDELINE NOTE 60, OPIOIDS FOR CONDITIONS OF THE BACK AND SPINE as shown below
    i. Adds chronic pain line to the guideline
    ii. Modifies the paragraph on tapering for chronic opioid use
    iii. Removes flares of chronic pain as an indication for opioids
7) Modify GUIDELINE NOTE 92, ACUPUNCTURE as shown below
    i. Adds the new chronic pain line to the guideline

LINE: XXX
CONDITION: CHRONIC PAIN SYNDROME AND FIBROMYALGIA
TREATMENT: LIMITED PHYSICAL MODALITIES, COGNITIVE BEHAVIORAL THERAPY, MEDICAL THERAPY
ICD-10: G89.21 (Chronic pain due to trauma), G89.28 (Other chronic postprocedural pain), G89.29 (Other chronic pain), G89.4 (Chronic pain syndrome), M79.7 (fibromyalgia)
CPT: 90785, 90832-90840, 90853 (psychotherapy—for CBT and ACT), 96150-96155 (Health and behavior assessment and intervention), 97110-97124, 97140-97168, 97530, 97535 (PT/OT), 97810-97814 (acupuncture), 98966-98969, 99051, 99060,99070,99078,99201-99215,99281-99285,99304-99337, 99340-99404,99408-99449,99487-99490,99495,99496,99605-99607 (medical office visits, including ER and SNF)
HCPCS: G0157-G0160 (PT/OT assistant), G0396-G0397 (alcohol and substance abuse screening), G0463-G0467,G0469,G0470 (FQHC care), G0490, G0511-G0513 (RFQHC care),G0514 (prolonged office visit)

GUIDELINE NOTE XXX, CHRONIC PAIN THERAPY

Lines XXX, 528

Chronic pain conditions are included on line XXX when symptoms have been present for at least 3 months and have not responded to conservative management.

The following treatments are included on line XXX:

- Office evaluation, consultation and education.
    - Pain education, if done, should include but not be limited to sleep, nutrition, stress reduction/mood, exercise, and knowledge of pain as a biopsychosocial phenomenon. All providers seeing chronic pain patients should be trained in pain science (e.g. a contemporary understanding of the central and peripheral nervous system in chronic

pain), motivational interviewing, culturally sensitive care, and trauma informed care. Care should be multidisciplinary and focus on active therapies.

- Cognitive behavioral therapy (CBT)/acceptance and commitment therapy (ACT). The necessity for CBT and/or ACT should be re-evaluated every 90 days and coverage will only be continued if there is documented evidence of decreasing depression or anxiety symptomatology, improved ability to work/function, increased self-efficacy, or other clinically significant, objective improvement.
- The following therapies, when available, may be provided: yoga, mindfulness training, massage, supervised exercise therapy (land based and aquatic), intensive interdisciplinary rehabilitation. HCPCS S9451 is only included on Line XXX for the provision of yoga or supervised exercise therapy.
- A total of 30 visits per year of any combination of the following therapies when available and medically appropriate. These therapies are only included on these lines if provided by a provider licensed to provide the therapy and when there is documentation of measurable clinically significant progress toward the therapy plan of care goals and objectives using evidence based objective tools. Once the pre-determined goals of care have been achieved, an additional two visits may be authorized for maintenance therapy to maintain these improvements. These 30 visits count toward the visit totals in GUIDELINE NOTE 56 NON-INTERVENTIONAL TREATMENTS FOR CONDITIONS OF THE BACK AND SPINE if the patient has comorbid back or spine conditions.
    1) Rehabilitative therapy (physical and/or occupational therapy), if provided according to Guideline Note 6 REHABILITATIVE AND HABILITATIVE THERAPIES. Rehabilitation services provided under this guideline also count towards visit totals in Guideline Note 6. CPT 97124 is included in this category.
    2) Acupuncture

Non-opioid medications are only included on line XXX if all of the following apply:

1) The medication is FDA approved or supported by compendia for treatment of chronic, non-neuropathic pain
2) The patient is also being treated with active therapy (e.g. physical therapy, CBT, etc.) or is continuing maintenance of self-management strategies learned from such therapy.
3) The benefit of non-opioid medication is re-evaluated at least every 90 days and medications are only continued if there is documented evidence of improvement of function of at least fifteen percent as compared to baseline based on a validated tools (e.g. Oswestry, SF-MPQ, and MSPQ). Less frequent monitoring may be appropriate for certain medications after safety and efficacy are established.

Opioids are included on this line according to GUIDELINE NOTE 60, OPIOIDS FOR CONDITIONS OF THE BACK AND SPINE AND CHRONIC PAIN.

Appendix A

June 2018 Task Force Proposal

Line Scoring

Line XXX CHRONIC PAIN SYNDROME
Category: 7
HL: 4
Suffering: 3
Population effects: 0
Vulnerable population: 0
Tertiary prevention: 2
Effectiveness: 2
Need for service: 0.8
Net cost: 2
Score: 288
Approximate line placement: 443

Line 528 FIBROMYALGIA, CHRONIC FATIGUE SYNDROME, AND RELATED DISORDERS
Category: 7
HL: 4
Suffering: 3
Population effects: 0
Vulnerable population: 0
Tertiary prevention: 0
Effectiveness: 1
Need for service: 0.8
Net cost: 2
Score: 112
Line placement: 528

Appendix A

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Line 401 CONDITIONS OF THE BACK AND SPINE
Category: 7
HL: 4
Suffering: 3
Population effects: 0
Vulnerable population: 0
Tertiary prevention: 2
Effectiveness: 3
Need for service: 0.8
Net cost: 2
Score: 438
Approximate line placement: 401

Line: 528

Condition: ~~FIBROMYALGIA,~~ CHRONIC FATIGUE SYNDROME~~, AND RELATED DISORDERS~~ (See Guideline Notes 64,65,135)
Treatment: MEDICAL THERAPY
ICD-10: ~~G89.21,G89.28-G89.29,G89.4,M79.7,~~R53.82
CPT: 90785,90832-90840,90846-90853,93792,93793,98966-98969,99051,99060,99070,99078, 99201-99215,99281-99285,99341-99378,99381-99404,99408-99449,99487-99490,99495-99498,99605-99607
HCPCS: G0248-G0250,G0396,G0397,G0463-G0467,G0490,G0511,G0513,G0514

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GUIDELINE NOTE 56, NON-INTERVENTIONAL TREATMENTS FOR CONDITIONS OF THE BACK AND SPINE

Lines 361,401

Patients seeking care for back pain should be assessed for potentially serious conditions ("red flag" symptoms requiring immediate diagnostic testing), as defined in Diagnostic Guideline D4. Patients lacking red flag symptoms should be assessed using a validated assessment tool (e.g. STarT Back Assessment Tool) in order to determine their risk level for poor functional prognosis based on psychosocial indicators.
For patients who are determined to be low risk on the assessment tool, the following services are included on these lines:

- Office evaluation and education,
- Up to four total visits, consisting of the following treatments: OMT/CMT, acupuncture, and PT/OT. Massage, if available, may be provided as part of these four total visits.
- First line medications: NSAIDs, acetaminophen, and/or muscle relaxers. Opioids may be considered as a second line treatment, subject to the limitations on coverage of opioids in Guideline Note 60 OPIOIDS FOR CONDITIONS OF THE BACK AND SPINE. See evidence table.

For patients who are determined to be medium- or high risk on the validated assessment tool, as well as patients undergoing opioid tapers as in Guideline Note 60 OPIOIDS FOR CONDITIONS OF THE BACK AND SPINE, the following treatments are included on these lines:

- Office evaluation, consultation and education
- Cognitive behavioral therapy/acceptance and commitment therapy (ACT). The necessity for cognitive behavioral therapy/ acceptance and commitment therapy should be re-evaluated every 90 days and coverage will only be continued if there is documented evidence of decreasing depression or anxiety symptomatology, improved ability to work/function, increased self-efficacy, or other clinically significant, objective improvement.
- Prescription and over-the-counter medications; opioid medications subject to the limitations on coverage of opioids in Guideline Note 60 OPIOIDS FOR CONDITIONS OF THE BACK AND SPINE. See evidence table.
- The following evidence-based therapies, when available, may be provided: yoga, massage, supervised exercise therapy, intensive interdisciplinary rehabilitation. HCPCS S9451 is only included on Line 401 for the provision of yoga or supervised exercise therapy.
- A total of 30 visits per year of any combination of the following evidence-based therapies when available and medically appropriate. These therapies are only included on these lines if provided by a provider licensed to provide the therapy and when there is documentation of measurable clinically significant progress toward the therapy plan of care goals and objectives using evidence based objective tools (e.g. Oswestry, Neck Disability Index, SF-MPQ, and MSPQ). These 30 visits count toward the visit totals in GUIDELINE NOTE XXX CHRONIC PAIN THERAPY if the patient has comorbid chronic pain conditions.
    3) Rehabilitative therapy (physical and/or occupational therapy), if provided according to Guideline Note 6 REHABILITATIVE AND HABILITATIVE THERAPIES. Rehabilitation services provided under this guideline also count towards visit totals in Guideline Note 6. CPT 97124 is included in this category.
    4) Chiropractic or osteopathic manipulation
    5) Acupuncture

Mechanical traction (CPT 97012) is not included on these lines, due to evidence of lack of effectiveness for treatment of back and neck conditions.

The development of this guideline note was informed by HERC coverage guidances on Low Back Pain Non-Pharmacologic, Non-Invasive Intervention, Low Back Pain, Pharmacological and Herbal Therapies. See http://www.oregon.gov/oha/HPA/CSI-HERC/Pages/Evidence-based-Reports.aspx.

[delete the table below]

~~**Evidence Table of Effective Treatments for the Management of Low Back Pain**~~

Intervention Category*	Intervention	Acute < 4 Weeks	Subacute & Chronic > 4 Weeks
Self-care	Advice to remain active	●	●
	Books, handout	●	●
	Application of superficial heat	●	
Nonpharmacologic therapy	Spinal manipulation	●	●
	Exercise therapy		●
	Massage		●
	Acupuncture		●
	Yoga		●
	Cognitive-behavioral therapy		●
	Progressive relaxation		●
Pharmacologic therapy (Carefully consider risks/harms)	Acetaminophen	●	●
	NSAIDs	●(▲)	●(▲)
	Skeletal muscle relaxants	●	
	Antidepressants (TCA)		●
	*Benzodiazepines***	●(▲)	●(▲)
	*Tramadol, opioids***	●(▲)	●(▲)
Interdisciplinary therapy	Intensive interdisciplinary rehabilitation		●

- ● Interventions supported by grade B evidence (at least fair-quality evidence of moderate benefit, or small benefit but no significant harms, costs, or burdens). No intervention was supported by grade "A" evidence (good-quality evidence of substantial benefit).

▲ *Carries greater risk of harms than other agents in table.*

NSAIDs = nonsteroidal anti-inflammatory drugs; TCA = tricyclic antidepressants.

*These are general categories only. Individual care plans need to be developed on a case by case basis. For more detailed information please see: http://www.annals.org/content/147/7/478.full.pdf

**Associated with significant risks related to potential for abuse, addiction and tolerance. This evidence evaluates effectiveness of these agents with relatively short term use studies. Chronic use of these agents may result in significant harms.

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GUIDELINE NOTE 60, OPIOIDS FOR CONDITIONS OF THE BACK AND SPINE AND CHRONIC PAIN

Lines 346,361,401,527,XXX

Opioid medications are only included on these lines under the following criteria:

For acute injury, ~~acute flare of chronic pain,~~ or after surgery:

1) During the first 6 weeks opioid treatment is included on these lines ONLY:
   a) When each prescription is limited to 7 days of treatment, AND
   b) For short acting opioids only, AND
   c) When one or more alternative first line pharmacologic therapies such as NSAIDs, acetaminophen, and muscle relaxers have been tried and found not effective or are contraindicated, AND
   d) When prescribed with a plan to keep active (home or prescribed exercise regime) and with consideration of additional therapies such as spinal manipulation, physical therapy, yoga, or acupuncture, AND
   e) There is documented verification that the patient is not high risk for opioid misuse or abuse.
2) Treatment with opioids after 6 weeks, up to 90 days after the initial injury/~~flare/~~surgery is included on these lines ONLY:
   a) With documented evidence of improvement of function of at least thirty percent as compared to baseline based on a validated tools (e.g. Oswestry, Neck Disability Index, SF-MPQ, and MSPQ).
   b) When prescribed in conjunction with therapies such as spinal manipulation, physical therapy, yoga, or acupuncture.
   c) With verification that the patient is not high risk for opioid misuse or abuse. Such verification may involve
      i) Documented verification from the state's prescription monitoring program database that the controlled substance history is consistent with the prescribing record
      ii) Use of a validated screening instrument to verify the absence of a current substance use disorder (excluding nicotine) or a history of prior opioid misuse or abuse
      iii) Administration of a baseline urine drug test to verify the absence of illicit drugs and non-prescribed opioids.
   d) Each prescription must be limited to 7 days of treatment and for short acting opioids only

3) Chronic opioid treatment (>90 days) after the initial injury~~/flare/~~surgery is not included on these lines except for the taper process described below.

Transitional coverage for patients on long-term opioid therapy ~~as of July 1, 2016~~:

For patients ~~on covered chronic~~ receiving long-term opioid therapy ~~as of July 1, 2016, opioid medication is included on these lines only from July 1, 2016 to December 31, 2016. During the period from January 1, 2017 to December 31, 2017~~, continued coverage of opioid medications requires an individual treatment plan ~~developed by January 1, 2017~~ which includes a taper with an end to opioid therapy no later than one year from the start of the taper ~~no later than January 1, 2018~~. Taper plans must include nonpharmacological treatment strategies for managing the patient's pain ~~based on Guideline Note 56 NON-INTERVENTIONAL TREATMENTS FOR CONDITIONS OF THE BACK AND SPINE~~. If a patient has

developed dependence and/or addiction related to their opioids, treatment is ~~available~~ included on Line 4 SUBSTANCE USE DISORDER**.**

GUIDELINE NOTE 92, ACUPUNCTURE

Lines 1,5,202,361,401,409,461,538

Inclusion of acupuncture (CPT 97810-97814) on the Prioritized List has the following limitations:

Line 1 PREGNANCY

Acupuncture pairs on Line 1 for the following conditions and codes.

Hyperemesis gravidarum

ICD-10-CM: O21.0, O21.1

Acupuncture pairs with hyperemesis gravidarum when a diagnosis is made by the maternity care provider and referred for acupuncture treatment for up to 12 sessions of acupressure/acupuncture per pregnancy.

Breech presentation

ICD-10-CM: O32.1

Acupuncture (and moxibustion) is paired with breech presentation when a referral with a diagnosis of breech presentation is made by the maternity care provider, the patient is between 33 and 38 weeks gestation, for up to 6 session per pregnancy.

Back and pelvic pain of pregnancy

ICD-10-CM: O99.89

Acupuncture is paired with back and pelvic pain of pregnancy when referred by maternity care provider/primary care provider for up to 12 sessions per pregnancy.

Line 5 TOBACCO DEPENDENCE

Acupuncture is included on this line for a maximum of 12 sessions per quit attempt up to two quit attempts per year; additional sessions may be authorized if medically appropriate.

Line 202 CHRONIC ORGANIC MENTAL DISORDERS INCLUDING DEMENTIAS

Acupuncture is paired with the treatment of post-stroke depression only. Treatments may be billed to a maximum of 30 minutes face-to-face time and limited to 12 total sessions per year, with documentation of meaningful improvement; patients may have additional visits authorized beyond these limits if medically appropriate.

Line 361 SCOLIOSIS

Acupuncture is included on this line with visit limitations as in Guideline Note 56 NON-INTERVENTIONAL TREATMENTS FOR CONDITIONS OF THE BACK AND SPINE.

Line 401 CONDITIONS OF THE BACK AND SPINE

Acupuncture is included on this line with visit limitations as in Guideline Note 56 NON-INTERVENTIONAL TREATMENTS FOR CONDITIONS OF THE BACK AND SPINE.

Line 409 MIGRAINE HEADACHES

Acupuncture pairs on Line 409 for migraine (ICD-10-CM G43.0, G43.1, G43.5, G43.7, G43.8, G43.9), for up to 12 sessions per year.

Line XXX CHRONIC PAIN SYNDROME

Acupuncture is included on this line with visit limitations as in Guideline Note XXX CHRONIC PAIN THERAPY

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Line 461 OSTEOARTHRITIS AND ALLIED DISORDERS

Acupuncture pairs on Line 461 for osteoarthritis of the knee only (ICD-10-CM M17), for up to 12 sessions per year.

*Line 538 TENSION HEADACHES

Acupuncture is included on Line 538 for treatment of tension headaches (ICD-10-CM G44.2), for up to 12 sessions per year.

The development of this guideline note was informed by a HERC coverage guidance. See http://www.oregon.gov/oha/HPA/CSI-HERC/Pages/Evidence-based-Reports.aspx.

*Below the current funding line.

Appendix B

Public Comment Summary

Qualitative summary of a sample of written public testimony from patients and experts (most common themes):

1) Alternative therapies have been tried in the past and didn't work or had adverse effects; these therapies are beneficial but not sufficient to address pain adequately
2) Benefits of long-term opioid therapy:
    a) improved function
    b) improved ability to work or care for self/family
3) Harms of involuntary taper from long-term opioid therapy:
    a) reduced function
    b) increased pain
    c) reduced ability to work
    d) increased disability
    e) increased risk of suicide
    f) increased use of illicit opioids/drugs
4) Patients on chronic opioids are not addicts
5) The proposed taper policy is an overreaction to a few bad patients/doctors/illegal drug users
6) Stories of bad experiences with forced tapers
7) Opioid tapers should be decided between doctors and patients, not payers
8) This discriminates against low-income patients/OHP patients
9) Long term use of opioids is not the best strategy for treating chronic pain. It leads to tolerance which reduces patients' ability to be effectively treated for painful events such as fractures or surgery

Appendix C

Excerpt from August, 2018 VbBS minutes

- **Topic: Chronic Pain Task Force report**

Discussion: Smits gave an overview of the Task Force recommendations, including details of the proposed new line for fibromyalgia and chronic pain (diagnoses and treatments), the proposed accompanying guideline note, and changes recommended to the opioid guideline. She also summarized the major themes in the large number of public comments received on this topic. Saboe asked for clarification regarding lack of coverage for chiropractic care. Smits responded that the spinal manipulation CPT codes were not proposed for inclusion on the new line; however, if a chiropractor did PT services or office visit care, those CPT codes would be covered.

Kim Jones, PhD gave a presentation regarding the state of the evidence supporting coverage for treatments for fibromyalgia.

Public testimony
Carolyn Concion, NP, testified that patients are stabilized on opioids for years. Then providers taper medications, frequently involuntarily. Patients are also rejected by providers due to their chronic pain.
Rob Twillman, Academy of Integrated Pain Management, testified in support of moving chronic pain above the current funding line, but opposes forcing opioid tapers. He requested that the subcommittee look at outcomes for chronic back pain patients tapered off opioids: functionality, suicides, mental health issues, etc. He noted that improved function is a criterion for the first 90 days of opioids in the opioid guideline, but improved function is not considered after 90 days. He feels that the opioid guideline needs criteria for pausing, stopping or reversing tapers.

Karen Yeargain, patient/public health nurse from Prineville, testified that it's not diverted prescription drugs that are causing overdose problems, but rather street drugs. Oregon has decreased prescribing of opioids and is seeing increased suicides, but no increase in street drugs in chronic pain patients. Opioids increase functionality.

Ginevra Liptan, MD, an internal medicine physician with a focus on fibromyalgia, testified, noting that she is also a chronic pain patient. Opioids are imperfect. She agreed that the HERC should cover fibromyalgia and noted that Oregon is the only state without Medicaid funding for fibromyalgia care. She requested that the commission add tools that are helpful but do not take away the tool that has been helpful (opioids).

Allan Chino, PhD, a clinical health psychologist and pain specialist, testified about the need to move fibromyalgia above the line and have tools to help these patients. He noted that outcomes are superior when a range of treatment options are available, including opioids. Decisions should be based on individual patients. He noted that he has never seen hyperalgesia in his practice.

Karl Probst, a VA patient, testified about the new VA policy that requested patients get off opioids. Patients are offered suboxone instead. He feels that he has a better quality of life though opioids.

Appendix C

Excerpt from August, 2018 VbBS minutes

Patrick Starnes, an independent candidate for Oregon Governor, testified. He asked that the Committee not lump addicts with chronic pain sufferers. He stated that the commission needs more pain patient representation on the Task Force.

Steven Hix, a patient, testified. He is very frightened about what is happening locally and nationally with opioids. He has tried all of the proposed modalities without success. Hydrotherapy was the most successful. He notes that it is very easy to lose hope, and become depressed. The most vulnerable people in this country are suffering. Taking away people's medicine will not magically make their pain go away. This is a matter of human decency. There is a huge problem when one is labeled as a drug seeker. Health care insurance is a huge expense.

Helen Turner, a clinical nurse specialist caring for children with chronic pain, testified that opioids help children go to school and have improved quality of life. Evidence for opioids is messy at best, and does not apply to all patients. She is trying to get as many kids off opioids as she can, but some cannot be taken off.

Amanda Siebe, a patient with complex regional pain syndrome, testified. She brought in boxes of medical records, which include her treatment with all types of modalities. Only methadone helps her pain. Taking away opioids drives patients to suicide and street drugs. This takes away hope and functionality, giving nothing in exchange. <3% of patients on opioids become addicted.

BJ Cavnor, the executive director of One in Four, testified about his concern about restrictions on opioids in the guideline note. Pain patients are not addicts. Chronic pain patients are stigmatized. The PDMP database monitors drugs. Patients and providers should decide the best treatment strategy between them. This is a reactive policy at the state and national level, and does not help the overall opioid crisis.

Julia (no last name given) testified that this conversation was not public knowledge. She has tried all non-opioid medications, procedures and modalities; none work other than opioids.

Coffman gave the next steps in the process, as well as how to find out public meeting information, materials for public meetings, and how to provide written and oral testimony. The next meeting of the Chronic Pain Task Force will be September 20, 2018. The Task Force will have one or more meetings, and then forward their revised recommendations to VBBS at a future meeting. Any changes regarding chronic pain will need to be made by the March 2019 HERC meeting and would take effect with the January 1, 2020 Biennial Review changes.

Recommended Actions:

1) HERC staff will take the public testimony, subcommittee input, and HERC input to the September Chronic Pain Task Force meeting and work with the Task Force to revise their recommendations

JAMA | Original Investigation

Effect of Opioid vs Nonopioid Medications on Pain-Related Function in Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain
The SPACE Randomized Clinical Trial

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IMPORTANCE Limited evidence is available regarding long-term outcomes of opioids compared with nonopioid medications for chronic pain.

OBJECTIVE To compare opioid vs nonopioid medications over 12 months on pain-related function, pain intensity, and adverse effects.

DESIGN, SETTING, AND PARTICIPANTS Pragmatic, 12-month, randomized trial with masked outcome assessment. Patients were recruited from Veterans Affairs primary care clinics from June 2013 through December 2015; follow-up was completed December 2016. Eligible patients had moderate to severe chronic back pain or hip or knee osteoarthritis pain despite analgesic use. Of 265 patients enrolled, 25 withdrew prior to randomization and 240 were randomized.

INTERVENTIONS Both interventions (opioid and nonopioid medication therapy) followed a treat-to-target strategy aiming for improved pain and function. Each intervention had its own prescribing strategy that included multiple medication options in 3 steps. In the opioid group, the first step was immediate-release morphine, oxycodone, or hydrocodone/acetaminophen. For the nonopioid group, the first step was acetaminophen (paracetamol) or a nonsteroidal anti-inflammatory drug. Medications were changed, added, or adjusted within the assigned treatment group according to individual patient response.

MAIN OUTCOMES AND MEASURES The primary outcome was pain-related function (Brief Pain Inventory [BPI] interference scale) over 12 months and the main secondary outcome was pain intensity (BPI severity scale). For both BPI scales (range, 0-10; higher scores = worse function or pain intensity), a 1-point improvement was clinically important. The primary adverse outcome was medication-related symptoms (patient-reported checklist; range, 0-19).

RESULTS Among 240 randomized patients (mean age, 58.3 years; women, 32 [13.0%]), 234 (97.5%) completed the trial. Groups did not significantly differ on pain-related function over 12 months (overall $P = .58$); mean 12-month BPI interference was 3.4 for the opioid group and 3.3 for the nonopioid group (difference, 0.1 [95% CI, −0.5 to 0.7]). Pain intensity was significantly better in the nonopioid group over 12 months (overall $P = .03$); mean 12-month BPI severity was 4.0 for the opioid group and 3.5 for the nonopioid group (difference, 0.5 [95% CI, 0.0 to 1.0]). Adverse medication-related symptoms were significantly more common in the opioid group over 12 months (overall $P = .03$); mean medication-related symptoms at 12 months were 1.8 in the opioid group and 0.9 in the nonopioid group (difference, 0.9 [95% CI, 0.3 to 1.5]).

CONCLUSIONS AND RELEVANCE Treatment with opioids was not superior to treatment with nonopioid medications for improving pain-related function over 12 months. Results do not support initiation of opioid therapy for moderate to severe chronic back pain or hip or knee osteoarthritis pain.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT01583985

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Supplemental content

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Long-term opioid therapy became a standard approach to managing chronic musculoskeletal pain despite a lack of high-quality data on benefits and harms.[1]

Rising rates of opioid overdose deaths have raised questions about prescribing opioids for chronic pain management. Because of the risk for serious harms without sufficient evidence for benefits, current guidelines discourage opioid prescribing for chronic pain.[2-4] Systematic reviews cited by guidelines identified no randomized trials of opioid therapy that reported long-term pain, function, or quality-of-life outcomes.[4,5]

The Strategies for Prescribing Analgesics Comparative Effectiveness (SPACE) trial was a pragmatic randomized trial that compared opioid therapy vs nonopioid medication therapy over 12 months for primary care patients with chronic back pain or hip or knee osteoarthritis pain of at least moderate severity despite analgesic use. Hypotheses were that opioids compared with nonopioid medications would lead to better pain-related function and pain intensity and more adverse effects.

Key Points

Question For patients with moderate to severe chronic back pain or hip or knee osteoarthritis pain despite analgesic use, does opioid medication compared with nonopioid medication result in better pain-related function?

Findings In this randomized clinical trial that included 240 patients, the use of opioid vs nonopioid medication therapy did not result in significantly better pain-related function over 12 months (3.4 vs 3.3 points on an 11-point scale at 12 months, respectively).

Meaning This study does not support initiation of opioid therapy for moderate to severe chronic back pain or hip or knee osteoarthritis pain.

Methods

The Minneapolis Veterans Affairs (VA) institutional review board approved the trial protocol and patients provided written informed consent. Recruitment details and the trial protocol have been published.[6] The trial protocol and statistical analysis plan are in Supplement 1.

Pragmatic Trial Design

To maximize applicability to primary care, the trial was designed to be pragmatic.[6,7] Eligibility criteria facilitated enrollment of diverse patients from primary care. Interventions were delivered with flexibility in medication selection and dosage. Patients were allowed to participate in nonpharmacological pain therapies outside of the study and were encouraged to complete outcome assessments regardless of their participation in the active interventions.

Participants

Eligible patients had chronic back pain or hip or knee osteoarthritis pain that was moderate to severe despite analgesic use. Chronic pain was defined as pain nearly every day for 6 months or more. Moderate or greater severity was defined by a score of 5 or more on the 3-item pain intensity, interference with enjoyment of life, and interference with general activity (PEG) scale (range, 0-10).[8]

Patients on long-term opioid therapy were excluded. Other reasons for exclusion included contraindications to all drug classes in either group, including class-level opioid contraindications (eg, active substance use disorder), and conditions that could interfere with outcome assessment (eg, life expectancy <12 months).[6] Patients with severe depression or posttraumatic stress disorder symptoms were not excluded because these patients often receive opioids in practice.

Patients were recruited from 62 Minneapolis VA primary care clinicians from June 2013 to December 2015 (**Figure**). Primary care clinicians were located at multiple clinics affiliated with the Minneapolis VA Health Care System, including clinics in the main medical center building and 4 outpatient clinics in the greater Minneapolis-Saint Paul metropolitan area. Potentially eligible patients were identified by searching the electronic health record (EHR) for back, hip, or knee pain diagnoses at a primary care visit in the prior month. Study personnel screened patients by telephone and then conducted a focused chart review.

Randomization and Blinding

To ensure balanced numbers of patients with back and osteoarthritis pain in each group, randomization was stratified by primary pain diagnosis. The SAS (SAS Institute), version 9.4, uniform random number generator was used to produce a computerized randomization table. Approximately 1 week after the enrollment visit, patients met with the study clinical pharmacist, who initiated random group assignment using a programmed study application that automatically assigned the next unused position in the randomization table. This process simultaneously informed the pharmacist and patient of group assignment. EHR documentation informed patients' primary care clinicians of study participation and group assignment. Study medications were visible in the EHR. Outcome assessors were blinded to group assignment.

Intervention Delivery

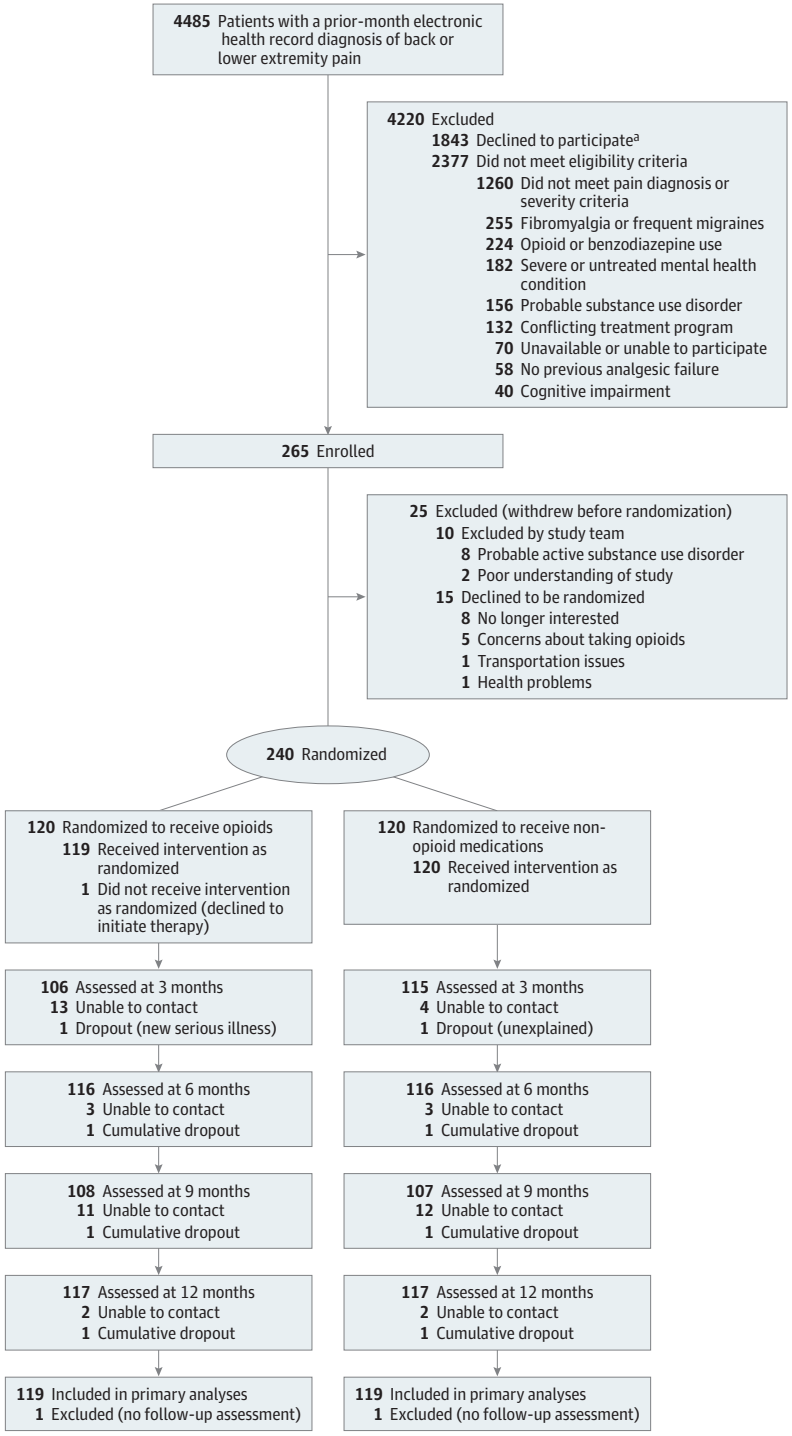
Medication was delivered using a collaborative pain care model with demonstrated effectiveness.[9,10] In both groups, patients received structured symptom monitoring and a treat-to-target approach to medication management delivered primarily by a single pharmacist. After randomization, the pharmacist reviewed past medications and identified individual functional goals. The initial medication regimen was determined by the assigned group and considerations such as patient preference and comorbidities. Follow-up visits were monthly until a stable regimen was established, then visits occurred every 1 to 3 months. Visits were in-person at 6 and 12 months when possible and otherwise mostly by telephone.

Both interventions used 3 medication steps. Medications were adjusted within the assigned group to achieve targets of improved PEG scores and progress toward individual goals. Study medications were dispensed from the VA pharmacy.

Opioid Prescribing Strategy

Per protocol, patients in the opioid group started taking immediate-release (IR) opioids. Step 1 was morphine IR,

Figure. Flow of Participants Through the Study



[a] Patients could decline to participate at any point in the screening process, including before the telephone eligibility interview; therefore, patients who declined to participate were not necessarily eligible.

hydrocodone/acetaminophen, and oxycodone IR. Step 2 was morphine sustained-action (SA) and oxycodone SA. Step 3 was transdermal fentanyl. Single-opioid therapy was preferred, but dual therapy with a scheduled SA opioid and as-needed IR opioid was considered based on patient needs and preferences. Opioids were titrated to a maximum daily dosage of 100 morphine-equivalent (ME) mg. If dosages were titrated to 60 ME mg/d without a response, rotation to another opioid was considered before dosage escalation.[11]

Nonopioid Prescribing Strategy

In the nonopioid medication group, step 1 was acetaminophen (paracetamol) and nonsteroidal anti-inflammatory drugs (NSAIDs). Step 2 included adjuvant oral medications

(ie, nortriptyline, amitriptyline, gabapentin) and topical analgesics (ie, capsaicin, lidocaine). Step 3 included drugs requiring prior authorization from the VA clinic (ie, pregabalin, duloxetine) and tramadol. Patients were initially prescribed a step 1 medication, unless all were clinically inappropriate. Subsequent changes included titrating, replacing, or adding medications.

Intervention Adherence

Patients were instructed to receive medications for back, hip, or knee pain only from the study. Nonpharmacological therapies were allowed outside of the study. If patients desired discontinuation of all study medications, they were transitioned back to preenrollment pain medications. Medication adherence was monitored by discussion with patients and checking the state prescription monitoring program website.

Descriptive Measures

Before randomization, patients were asked to state their preferred treatment group, perceptions of effectiveness and safety of opioid and nonopioid medications, and expectations for improvement on 0 to 10 scales (higher scores = more favorable).[12,13] To characterize the study population and provide data required by federal funders, self-identified race/ethnicity was assessed by asking patients to select from 6 categories.

Main Outcomes

The primary outcome was pain-related function, assessed with the 7-item Brief Pain Inventory (BPI) interference scale.[14] Pain intensity, the main secondary outcome, was assessed with the 4-item BPI severity scale. Both BPI scales yield 0 to 10 scores (higher score = worse function or intensity). A prior study of chronic pain in primary care estimated a minimal clinically important difference (MCID) of 0.7 points for both BPI interference and BPI severity.[15] Following consensus guidelines, this trial used a 1-point difference as the MCID for BPI interference and BPI severity, and used a 30% reduction from baseline as MCID for moderate improvement.[16] The primary adverse outcome was a patient-reported checklist of 19 medication-related symptoms,[17] modified from the original version by adding common analgesic adverse effects (eg, memory problems, sweating).[18]

Secondary Health Outcomes

Secondary outcomes were as follows: the Veterans RAND 12-item Health Survey (VR-12) quality-of-life measure (range, 0-100; higher score = better quality of life, standardized to mean of 50),[19] the 11-item Roland-Morris Disability Questionnaire (RMDQ) measure of pain-related physical function (range, 0-11; higher score = worse function, MCID = 2.0),[20] the 8-Item Patient Health Questionnaire (PHQ-8) depression measure (range, 0-24; higher score = worse depression, MCID = 5), the 7-Item Generalized Anxiety Disorder measure (GAD-7; range, 0-21; higher score = worse anxiety, MCID = 5)[21]; the Patient-Reported Outcomes Measurement Information System (PROMIS) sleep disturbance short form (range, 8-32; higher score = worse sleep disturbance)[22]; the Migraine Disability Assessment (MIDAS) questionnaire (range, 0-270; higher score = worse headache disability),[23] the Arizona Sexual Experience Scale (ASEX; range 5-30; higher score = worse sexual function)[24]; and the Multidimensional Fatigue Inventory (MFI) general fatigue, mental fatigue, physical fatigue, reduced activity, and reduced motivation scales (for each scale: range, 4-20; higher score = worse, MCID = 2).[25] Additional secondary outcomes not reported here were the global impression of pain change, the Fullerton Advanced Balance scale, 6-m gait speed, chair stand, grip strength tests, cold pain tolerance, free testosterone, and the Indiana University Telephone-Based Assessment of Neuropsychological Status.

Assessment for Adverse Events and Potential Opioid Misuse

At each assessment, patients reported new hospitalizations, emergency department (ED) visits, and falls. VA hospitalizations and ED events were identified by searching EHR databases from enrollment to 13 months after randomization. Two independent raters determined whether events were analgesic-related.[26] Discrepancies were resolved by discussion.

Opioid misuse describes use of prescription opioids in a manner other than as prescribed. This study used multiple approaches to evaluate for potential misuse, including medical record surveillance for evidence of "doctor-shopping" (seeking medication from multiple physicians), diversion, substance use disorder, or death; checking the state prescription monitoring program website at each visit and as needed; and completing the Addiction Behavior Checklist[27] at each intervention visit. The Addiction Behavior Checklist measures aberrant medication-related behaviors that may indicate misuse (range, 0-20; higher score = more aberrant behavior; 3 = threshold for opioid misuse). At 6-month and 12-month assessments, patients completed self-report measures and had urine drug testing. Substance use was assessed with the Alcohol Use Disorders Identification Test (AUDIT) and drug use questions from a National Institute on Drug Abuse screening tool.[28,29]

Assessment of Study Treatment Received and Nonstudy Co-Interventions

Pain medication dispensing data were obtained from EHR databases. Total study visit duration was calculated for each patient as the sum of minutes from clinician-entered *Current Procedural Terminology* (*CPT*) codes for all intervention encounters; for *CPT* codes that include a range of minutes (ie, 5-10, 11-20, 21-30), the highest value was used. Nonstudy co-interventions were obtained from patient report and EHR data.

Statistical Analysis

Assuming a 2-sided α level of .05 and a standard deviation of 2.7,[30] 115 patients completing the study per group were required for 80% power to detect a 1-point between-group difference in mean BPI interference at 12 months.[16] The initial target was 276 randomized patients, but enrollment was stopped at 265 due to difficulty recruiting and better-than-anticipated retention.

Analyses were intention-to-treat, with all patients included in their assigned treatment group. Scales were not scored if less than 70% of items were completed. When less than 30% of items were missing, the average of nonmissing

Table 1. Baseline Characteristics of Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain Randomized to Opioid vs Nonopioid Medication

Characteristic	Opioid Group, No. (%) (n = 120)	Nonopioid Group, No. (%) (n = 120)
Age, y		
Mean (SD)	56.8 (13.3)	59.7 (14.0)
Median (IQR)	59.5 (46.5-67.0)	64.0 (53.0-69.0)
Women	36 (13)	36 (13)
Race/ethnicity		
White	105 (88)	102 (86)
Black	7 (6)	11 (9)
Other or multiple	7 (6)	6 (5)
Education ≥4-y degree	29 (24)	31 (26)
Employment		
Employed for wages	50 (42)	31 (26)
Self-employed	7 (6)	7 (6)
Retired	43 (36)	56 (47)
Other	19 (16)	24 (20)
Primary pain diagnosis[a]		
Back pain	78 (65)	78 (65)
Hip or knee osteoarthritis pain	42 (35)	42 (35)
Substance use assessment		
Current smoker	25 (21)	13 (11)
Hazardous alcohol use (AUDIT score ≥8)	3 (3)	2 (2)
Past-year illicit drug use	8 (7)	15 (13)
Mental health measures		
Moderate depression (PHQ-9 score ≥10)	28 (23)	25 (21)
Moderate anxiety (GAD-7 score ≥10)	11 (9)	11 (9)
Positive PTSD screen (PC-PTSD score ≥3)	25 (21)	25 (21)
Prerandomization treatment group preference[b]		
Unsure or no preference	72 (60)	51 (43)
Opioid medication group	25 (21)	44 (37)
Nonopioid medication group	23 (19)	25 (21)
Prerandomization perceptions of treatment groups, mean (SD)[c]		
Opioid effectiveness	7.8 (2.1)	7.8 (2.0)
Opioid safety	5.8 (2.5)	5.8 (2.8)
Nonopioid effectiveness	5.7 (2.7)	5.6 (2.8)
Nonopioid safety	6.6 (2.7)	6.5 (2.8)
Expectations for improvement[d]	7.6 (1.8)	7.4 (2.0)

Abbreviations: AUDIT, Alcohol Use Disorders Identification Test; GAD-7, 7-Item Generalized Anxiety Disorder Questionnaire; IQR, interquartile range; PHQ-9, 9-Item Patient Health Questionnaire; PC-PTSD, primary care posttraumatic stress disorder screener.

[a] Patients self-identified 1 condition as their most bothersome pain problem.

[b] Patients were asked, "Now, imagine if you were given a choice between groups. Considering what you know so far, which treatment group would you choose?"

[c] Patients were asked, "In general, how (effective or safe) do you consider (opioid medications or nonopioid medications) for long-term treatment of pain?" (range, 0-10; 0 = not at all [effective or safe], 10 = most [effective or safe] possible).

[d] Patients were asked, "In terms of your pain, how much improvement do you think is likely for you personally during this study?" (range, 0-10; 0 = no improvement to 10 = a great deal of improvement).

items was used for measures scored as an average, and missing "count" data were scored as 0.

Two-sided *t* tests and χ^2 tests were used for unadjusted between-group comparisons of primary and secondary outcomes at each assessment time point. Main analyses included data from all time points in mixed models (logistic, Poisson, Gaussian) for repeated measures to compare mean scores between treatment groups over 12 months, adjusting for baseline values, with time as fixed effects and intercept as random effects. For medication-related symptoms, groups were compared using a statistical test for treatment × time interaction. Individual patient-level functional response and pain intensity response were defined as 30% or more reduction from baseline to 12-month follow-up in BPI interference and severity, respectively.[16] χ^2 Tests were used to compare response rates as a secondary measure of effectiveness. The threshold for statistical significance was a *P* value less than .05. Analyses of secondary outcomes were exploratory and not adjusted for multiple testing. Post hoc treatment group by primary pain diagnosis interaction tests were used to explore possible differential treatment effects. Post hoc sensitivity analyses adjusting for smoking status were conducted to examine potential effects of the baseline group imbalance in current smoking. SAS (SAS Institute), version 9.2, was used for statistical analysis.

Results

Of 265 enrolled patients, 25 withdrew prior to randomization and 240 were randomized (Figure). Follow-up rates were 92% at 3 months (106 in the opioid group and 115 in the nonopioid group), 97% at 6 months (116 in each group), 90% at 9 months (108 in the opioid group and 107 in the nonopioid group), and 98% at 12 months (117 in each group). Two patients dropped out before completing follow-up assessments and were excluded; 1 patient randomized to opioids declined to initiate opioid therapy; all others received assigned therapy (Figure).

Mean age was 58.3 years (range, 21-80) and 32 patients (13.0%) were women (**Table 1**). For primary pain diagnosis, 156 patients (65%) had back pain and 84 patients (35%) had hip or knee osteoarthritis pain. The opioid group had 25 current smokers (21%) and the nonopioid group had 13 current smokers (11%). Regarding treatment group preference, in the opioid group, 72 patients (60%) had no preference and 25 patients (21%) preferred opioids. In the nonopioid group, 51 patients (43%) had no preference and 44 patients (37%) preferred opioids.

Pain and Health Outcomes

There was no significant difference in pain-related function between the 2 groups over 12 months (overall *P* = .58). At 12 months, mean BPI interference was 3.4 in the opioid group (SD, 2.5) vs 3.3 in the nonopioid group (SD, 2.6); difference, 0.1 (95% CI, −0.5 to 0.7). Pain intensity was significantly better in the nonopioid group over 12 months (overall *P* = .03). At 12 months, mean BPI severity was 4.0 in the opioid group (SD, 2.0) vs 3.5 in the nonopioid group (SD, 1.9); difference, 0.5 (95% CI, 0.0 to 1.0).

Table 2. Patient-Reported Primary and Secondary Outcomes Among Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain Randomized to Opioid vs Nonopioid Medication

Outcome	Opioid Group, Mean (SD) (n = 119)	Nonopioid Group, Mean (SD) (n = 119)	Between-Group Difference (95% CI)[a]	Overall *P* Value[b]
Pain-Related Function (Primary Outcome)				
BPI interference scale (range, 0-10; higher score = worse)[c]				.58
Baseline	5.4 (1.8)	5.5 (2.0)	−0.1 (−0.6 to 0.4)	
3 mo	3.7 (2.1)	3.7 (2.2)	0.0 (−0.6 to 0.6)	
6 mo	3.4 (2.1)	3.6 (2.4)	−0.2 (−0.8 to 0.4)	
9 mo	3.6 (2.2)	3.3 (2.4)	0.4 (−0.2 to 1.0)	
12 mo	3.4 (2.5)	3.3 (2.6)	0.1 (−0.5 to 0.7)	
Pain Intensity (Secondary Outcome)				
BPI severity scale (range, 0-10; higher score = worse)[d]				.03
Baseline	5.4 (1.5)	5.4 (1.2)	0.0 (−0.4 to 0.3)	
3 mo	4.3 (1.8)	4.0 (1.7)	0.3 (−0.2 to 0.7)	
6 mo	4.1 (1.8)	4.1 (1.9)	0.0 (−0.5 to 0.5)	
9 mo	4.2 (1.7)	3.6 (1.7)	0.7 (0.2 to 1.2)	
12 mo	4.0 (2.0)	3.5 (1.9)	0.5 (0.0 to 1.0)	
Additional Secondary Health Outcomes				
VR-12 physical health (range, 0-100; lower score = worse)				.23
Baseline	27.2 (9.0)	27.0 (7.2)	0.2 (−1.9 to 2.2)	
3 mo	32.5 (9.8)	33.5 (9.9)	−1.0 (−3.6 to 1.6)	
6 mo	33.3 (9.7)	33.6 (10.0)	−0.3 (−2.8 to 2.2)	
9 mo	32.0 (10.5)	34.8 (10.9)	−2.9 (−5.8 to 0.0)	
12 mo	32.7 (10.1)	33.9 (9.9)	−1.3 (−3.8 to 1.3)	
VR-12 mental health (range, 0-100; lower score = worse)				.40
Baseline	47.3 (11.2)	47.8 (13.0)	−0.3 (−3.4 to 2.8)	
3 mo	51.8 (10.1)	50.5 (12.0)	1.3 (−1.6 to 4.3)	
6 mo	51.6 (9.8)	50.3 (12.5)	1.4 (−1.5 to 4.3)	
9 mo	51.8 (10.7)	52.6 (11.5)	−0.8 (−3.8 to 2.2)	
12 mo	51.2 (11.6)	50.4 (12.6)	0.7 (−2.4 to 3.8)	
RMDQ-11 pain-related physical function (range, 0-11; higher score = worse)[e]				.47
Baseline	8.0 (2.5)	8.6 (1.9)	−0.5 (−1.1 to 0.0)	
6 mo	6.3 (3.3)	7.1 (3.1)	−0.8 (−1.7 to 0.0)	
12 mo	5.8 (3.4)	5.9 (3.5)	−0.1 (−1.0 to 0.8)	
PHQ-8 depression symptoms (range, 0-24; higher score = worse)[f]				.13
Baseline	6.3 (4.5)	5.8 (5.0)	0.5 (−0.7 to 1.7)	
6 mo	4.4 (3.9)	4.8 (5.2)	−0.4 (−1.6 to 0.8)	
12 mo	4.3 (4.0)	4.5 (5.3)	−0.2 (−1.5 to 1.1)	
GAD-7 anxiety symptoms (range, 0-21; higher score = worse)[g]				.02
Baseline	4.0 (3.6)	3.5 (4.0)	0.5 (−0.5 to 1.4)	
6 mo	3.0 (3.5)	3.2 (4.5)	−0.2 (−1.3 to 0.8)	
12 mo	2.5 (3.3)	2.8 (4.2)	−0.4 (−1.4 to 0.7)	
PROMIS sleep disturbance (range, 8-32; higher score = worse)[g]				.33
Baseline	25.5 (7.8)	24.2 (8.4)	1.2 (−0.8 to 3.3)	
6 mo	22.2 (8.8)	22.0 (9.0)	0.2 (−2.2 to 2.5)	
12 mo	23.4 (8.2)	21.0 (8.3)	2.3 (0.1 to 4.6)	

(continued)

Functional response (≥30% improvement in BPI interference) occurred in 69 patients (59.0%) in the opioid group vs 71 patients (60.7%) in the nonopioid group; difference, −1.7% (95% CI, −14.4 to 11.0); *P* = .79. Pain intensity response (≥30% improvement in BPI severity) occurred in 48 patients (41.0%) in the opioid group vs 63 patients

Table 2. Patient-Reported Primary and Secondary Outcomes Among Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain Randomized to Opioid vs Nonopioid Medication (continued)

Outcome	Opioid Group, Mean (SD) (n = 119)	Nonopioid Group, Mean (SD) (n = 119)	Between-Group Difference (95% CI)[a]	Overall *P* Value[b]
MIDAS headache disability (range, 0-270; higher score = worse)[h]				
Baseline	6.1 (16.5)	6.1 (16.2)	−0.1 (−4.2 to 4.1)	.82
6 mo	3.8 (12.6)	5.5 (18.8)	−1.7 (−6.0 to 2.5)	
12 mo	3.7 (11.6)	3.2 (11.6)	−0.5 (−2.7 to 3.6)	
ASEX sexual function (range, 5-30; higher score = worse)[i]				
Baseline	17.4 (5.6)	17.7 (6.0)	−0.3 (−1.8 to 1.3)	.49
12 mo	17.9 (6.0)	19.0 (6.5)	−1.1 (−2.8 to 0.7)	
MFI general fatigue (range, 4-20; higher score = worse)[j]				
Baseline	13.8 (3.8)	12.8 (4.1)	1.0 (−0.0 to 2.0)	.68
6 mo	12.7 (3.9)	12.5 (4.3)	0.2 (−0.9 to 1.3)	
12 mo	12.5 (3.9)	12.0 (4.4)	0.6 (−0.6 to 1.7)	
MFI mental fatigue (range, 4-20; higher score = worse)[j]				
Baseline	10.0 (4.2)	9.6 (4.7)	0.4 (−0.7 to 1.6)	.39
6 mo	9.0 (4.2)	9.3 (4.4)	−0.3 (−1.4 to 0.9)	
12 mo	9.2 (3.9)	9.3 (4.3)	0.1 (−1.3 to 1.0)	
MFI physical fatigue (range, 4-20; higher score = worse)[j]				
Baseline	13.6 (4.1)	12.9 (4.1)	0.7 (−0.3 to 1.8)	.73
6 mo	12.9 (4.4)	12.5 (4.5)	0.4 (−0.8 to 1.5)	
12 mo	12.4 (4.3)	11.8 (4.3)	0.7 (−0.5 to 1.9)	
MFI reduced activity (range, 4-20; higher score = worse)[j]				
Baseline	11.4 (4.1)	10.9 (4.6)	0.5 (−0.7 to 1.6)	.74
6 mo	10.6 (4.6)	10.5 (4.5)	0.2 (−1.0 to 1.4)	
12 mo	10.6 (4.2)	10.3 (4.5)	0.3 (−1.0 to 1.5)	
MFI reduced motivation (range, 4-20; higher score = worse)[j]				
Baseline	9.8 (3.6)	8.8 (3.8)	1.0 (0.0 to 2.0)	.09
6 mo	9.1 (3.6)	8.9 (4.0)	0.2 (−0.8 to 1.2)	
12 mo	8.6 (3.2)	8.8 (3.7)	−0.2 (−0.7 to 1.6)	

Abbreviations: ASEX, Arizona Sexual Experience Scale; BPI, Brief Pain Inventory; GAD-7, 7-Item Generalized Anxiety Disorder Questionnaire; MFI, Multidimensional Fatigue Inventory; MIDAS, Migraine Disability Assessment Scale; PHQ-8, 8-Item Patient Health Questionnaire; PROMIS, Patient Reported Outcomes Measurement Information System; RMDQ-11, 11-Item Roland-Morris Disability Questionnaire; VR-12, Veterans RAND 12-item Health Survey.

[a] Unadjusted time-specific between-group comparisons.

[b] *P* values are from mixed models for repeated measures comparing between-group difference during the 12-mo trial, controlling for baseline and including all available time points.

[c] Missing data for 1 patient in the opioid group at 9 mo.

[d] Missing data for 1 patient in the opioid group at 3 mo.

[e] Missing data for 2 patients in the nonopioid group at 12 mo.

[f] Missing data for patients: at 6 mo, 3 in the opioid group and 9 in the nonopioid group; at 12 mo, 12 in the opioid group and 15 in the nonopioid group.

[g] Missing data for patients: at 6 mo, 2 in the opioid group and 8 in the nonopioid group; at 12 mo, 11 in the opioid group and 12 in the nonopioid group.

[h] Missing data for patients: at 6 mo, 3 in the opioid group and 8 in the nonopioid group ; at 12 mo, 13 in the opioid group and 14 in the nonopioid group.

[i] Missing data for patients: at baseline, 11 in the opioid group and 9 in the nonopioid group; at 12 mo, 19 in the opioid group and 17 in the nonopioid group.

[j] Missing data for patients: at baseline, 2 in the opioid group and 3 in the nonopioid group; at 6 mo, 2 in the opioid group and 9 in the nonopioid group; at 12 mo, 14 in the opioid group and 18 in the nonopioid group.

(53.9%) in the nonopioid group; difference, −12.8% (95% CI, −25.6 to 0.0); *P* = .05.

Health-related quality of life did not significantly differ between the 2 groups (physical health overall: *P* = .23; difference at 12 months, −1.3 [95% CI, −3.8 to 1.3]; mental health overall: *P* = .40; difference at 12 months, 0.7 [95% CI, −2.4 to 3.8]). Of the remaining secondary outcomes, only anxiety significantly differed between groups (**Table 2**; eTables 1-2 in Supplement 2).

Adverse Outcomes and Potential Misuse

The opioid group had significantly more medication-related symptoms over 12 months than the nonopioid group (overall: *P* = .03; difference at 12 months, 0.9 [95% CI, 0.3 to 1.5]) (**Table 3**).

There were no significant differences in adverse outcomes or potential misuse measures (Table 3). Two hospitalization or ED visit events were determined analgesic-related: 1 hospitalization in the nonopioid group and 1 ED visit in the

Table 3. Adverse Outcomes and Measures of Potential Misuse Among Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain Randomized to Opioid vs Nonopioid Medication

Outcome	Opioid Group	Nonopioid Group	Between-Group Difference (95% CI)[a]	*P* Value
Primary Adverse Outcome				
Medication-related symptom checklist (0-19; higher score = worse), mean (SD)[b]				
Baseline	1.2 (1.9)	1.2 (1.9)	0.0 (−0.5 to 0.5)	.03[c]
3 mo	2.3 (2.5)	1.3 (1.8)	1.0 (0.5 to 1.6)	
6 mo	2.1 (2.7)	1.3 (2.3)	0.7 (0.1 to 1.4)	
9 mo	1.9 (2.8)	0.9 (1.9)	1.0 (0.4 to 1.6)	
12 mo	1.8 (2.6)	0.9 (1.8)	0.9 (0.3 to 1.5)	
Secondary Adverse Outcomes				
All-cause hospitalization, No.(%)[d]				
0	99 (83)	99 (83)	0 (−10 to 10)	.94[e]
1	15 (13)	16 (13)	1 (−9 to 8)	
≥2	6 (5)	5 (4)	1 (−5 to 6)	
All-cause ED visit, No.(%)[d]				
0	60 (50)	73 (61)	−11 (−24 to 2)	.18[e]
1	34 (28)	30 (25)	3 (−8 to 15)	
≥2	26 (22)	17 (14)	8 (−2 to 17)	
Number of falls in 12 mo after enrollment, No.(%)[f]				
0	63 (53)	63 (53)	0 (−13 to 13)	.19[e]
1	26 (22)	17 (14)	8 (−2 to 17)	
≥2	29 (25)	39 (33)	−8 (−20 to 3)	
Potential Misuse Measures				
Patients with ≥1 positive urine drug tests for an illicit drug or unexplained prescription drug, No. (%)[g]				
Illicit drug positive	6 (5)	12 (11)	−5 (−12 to 2)	.13[e]
Unexplained prescription drug positive	11 (10)	9 (8)	3 (−5 to 10)	.67[e]
Clinician-assessed behaviors, No.(%)				
Significant PMP finding at any visit[h]	6 (5)	4 (3)	2 (−3 to 7)	.75[i]
Misuse behavior at any visit[j]	11 (9)	8 (7)	3 (−4 to 9)	.47[e]
Patient-reported substance use at 12 mo, No.(%)				
Hazardous alcohol use[k]	2 (2)	4 (4)	−2 (−6 to 3)	.44[i]
Past-year drug use[l]	17 (16)	13 (13)	3 (−6 to 13)	.56[e]

Abbreviations: ED, emergency department; PMP, Prescription Monitoring Program.

[a] Unadjusted time-specific between-group comparison of means or percentages.

[b] Missing data for patients: at 3 mo, 1 in the nonopioid group; at 6 mo, 1 in the opioid group and 1 in the nonopioid group; at 12 mo, 3 in the opioid group and 3 in the nonopioid group (n = 119 in each group).

[c] *P* value for treatment by time interaction.

[d] Hospitalization and ED visit events were counted until 13 mo after randomization for all randomized patients (n = 120 in each group). Events that started in the ED and resulted in hospitalization were counted as hospitalizations and do not contribute to the ED visit count.

[e] *P* value from χ^2 test.

[f] The sum of falls reported at each follow-up interview. Missing data for 1 patient in the opioid group.

[g] Illicit drugs are illegal substances, including cannabis. Unexplained prescription drugs are potentially prescribed substances for which there was no known prescription. Missing data for patients: 4 in the opioid group and 6 in the nonopioid group.

[h] Significant PMP finding is any prescription that was not disclosed and for which there was no clear acute pain-related indication (n = 119 in each group).

[i] *P* value for Fisher exact test.

[j] Misuse behavior was an Addiction Behavior Checklist score of 3 or more at any visit (n = 119 in each group).

[k] Hazardous alcohol use is Alcohol Use Disorders Identification Test score of 8 or more. Missing data for patients: 4 in the opioid group and 6 in the nonopioid group.

[l] Positive result was defined as a patient report of any past-year use of cannabis, cocaine, methamphetamine, inhalants, hallucinogens, street opioids, or prescription medications (opioids, sedatives, or stimulants) for nonmedical purposes. Missing data for 13 opioid patients and 17 nonopioid patients.

opioid group. No deaths, "doctor-shopping," diversion, or opioid use disorder diagnoses were detected.

Intervention Adherence and Retention

Number and duration of study visits were similar in the 2 groups (**Table 4**). Twenty-three patients (19%) in the opioid group and 10 patients (8%) in the nonopioid group discontinued study medication (eTable 6 in Supplement 2). Most patients in the opioid group received low or moderate dosage therapy (eTables 7-8 in Supplement 2). In each 90-day follow-up period, fewer than 15% of patients in the opioid group had a mean dispensed dosage of 50 ME mg/d or more. In the

Table 4. Medications and Visits Over 12 Months From the Electronic Health Records of Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain Randomized to Opioid vs Nonopioid Medication

	Opioid Group (n = 119)		Nonopioid Group (n = 119)	
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)
Study drugs, No.[a]	1.7 (0.8)	2.0 (1.0-2.0)	3.8 (1.7)	4.0 (3.0-5.0)
Study prescribed analgesic, months, No.[b]				
Acetaminophen	0.1 (0.5)	0.0 (0.0-0.0)	2.6 (3.2)	1.0 (0.0-4.0)
Oral NSAID	0.4 (2.0)	0.0 (0.0-0.0)	5.9 (4.9)	5.0 (0.5-10.0)
Analgesic adjunct	0.2 (1.4)	0.0 (0.0-0.0)	3.3 (4.3)	1.0 (0.0-6.2)
Topical	0.0 (0.6)	0.0 (0.0-0.0)	3.5 (3.5)	3.0 (1.0-6.0)
Tramadol	0.1 (0.6)	0.0 (0.0-0.0)	0.4 (1.3)	0.0 (0.0-0.0)
Opioid[c]	8.1 (4.1)	8.4 (5.6-11.2)	0.0 (0.0)	0.0 (0.0-0.0)
Study visits, No.				
In-person visits	2.8 (2.0)	2.0 (2.0-3.0)	2.8 (2.2)	2.0 (2.0-3.0)
Telephone visits	6.2 (2.9)	7.0 (5.0-8.0)	6.2 (2.5)	7.0 (5.0-8.0)
Total study visit duration, min[d]	231 (95)	230 (159-289)	217 (82)	197 (155-267)
Nonstudy outpatient visits, No.[e]				
Primary care	6.8 (6.5)	5.0 (2.0-8.0)	7.1 (7.1)	4.0 (2.0-9.0)
Specialty	6.7 (12.0)	3.0 (1.0-8.0)	6.3 (6.4)	4.0 (1.0-9.0)
Mental health	4.8 (10.3)	0.0 (0.0-6.0)	7.5 (22.1)	0.0 (0.0-5.0)
Rehabilitation	4.5 (15.8)	1.0 (0.0-3.0)	3.1 (6.1)	1.0 (0.0-4.0)

Abbreviations: IQR, interquartile range; NSAIDs, nonsteroidal anti-inflammatory drugs.

[a] Number of unique study-prescribed medication formulations during the intervention, regardless of duration of use.

[b] Analgesic months is the sum of the number of months of medication dispensed from Veterans Affairs outpatient pharmacies for each discrete medication within a category during the 12-mo intervention period. For example, a patient dispensed analgesic A for 6 mo and analgesic B for 12 mo would have 18 analgesic months. Crossover (ie, nonopioid medications in the opioid group and vice versa) is accounted for by patients who desired discontinuation of all medications in their assigned study group. Study clinicians restarted preenrollment medications if requested by these patients, but did not manage or adjust these off-protocol medications.

[c] Opioid months do not include tramadol.

[d] The sum of minutes extracted from clinician-entered *Current Procedural Terminology* codes for all study encounters.

[e] Outpatient visits include both in-person and telephone encounters with any type of clinician, including physicians, mental health providers, physical therapists, and nurses. Encounters for diagnostic testing (eg, radiology examinations, endoscopy) and nonmedical ancillary services (eg, social work, nutrition, education) are not included.

nonopioid group, tramadol was dispensed to 4 patients (3%), 6 patients (5%), 8 patients (7%), and 13 patients (11%) in the first, second, third, and fourth 90-day follow-up windows, respectively. eTables 9 to 10 in Supplement 2 show nonstudy pain treatments.

Subgroup and Sensitivity Analyses

Post hoc tests for interaction of primary pain diagnosis (ie, back pain, osteoarthritis pain) by treatment group on pain outcomes were not statistically significant (P = .25 for BPI interference, P = .34 for BPI severity). For the back pain subgroup at 12 months, BPI interference was 2.9 in the opioid group (SD, 2.1) vs 3.3 in the nonopioid group (SD, 2.6); difference, −0.4 (95% CI, −1.2 to 0.3); BPI severity was 3.7 in the opioid group (SD, 1.8) vs 3.6 in the nonopioid group (SD, 2.0); difference, 0.1 (95% CI, −0.5 to 0.8). For the hip or knee osteoarthritis pain subgroup at 12 months, BPI interference was 4.4 in the opioid group (SD, 2.8) vs 3.4 in the nonopioid group (SD, 2.6); difference, 1.1 (95% CI, −0.1 to 2.3); BPI severity was 4.5 in the opioid group (SD, 2.2) vs 3.4 in the nonopioid group (SD, 1.8); difference, 1.1 (95% CI, 0.2 to 2.0).

In a post hoc sensitivity analysis, adjusting for baseline smoking status, results did not substantially change (BPI interference adjusted overall, P = .65; BPI severity adjusted overall, P = .05; medication-related adverse symptoms adjusted overall, P = .03).

Discussion

Among patients with chronic back pain or hip or knee osteoarthritis pain, treatment with opioids compared with nonopioid medications did not result in significantly better pain-related function over 12 months. Nonopioid treatment was associated with significantly better pain intensity, but the clinical importance of this finding is unclear; the magnitude was small (0.5 points on the 0-10 BPI severity scale) and was less than the MCID of 1.0. Opioids caused significantly more medication-related adverse symptoms than nonopioid medications. Overall, opioids did not demonstrate any advantage over nonopioid medications that could potentially outweigh their greater risk of harms.

Among the secondary outcomes, only anxiety symptoms were statistically better in the opioid group. This finding is consistent with the role of the endogenous opioid system in stress and emotional suffering.[31] The importance of this finding is uncertain because the magnitude of the difference in anxiety was small and the overall level of anxiety

was low (9% of patients had moderate severity anxiety symptoms at baseline).

Recent systematic reviews have concluded that opioids have small beneficial effects on pain compared with placebo that may be outweighed by common adverse effects.[5,32-34] Observational studies have found that treatment with long-term opioid therapy is associated with poor pain outcomes, greater functional impairment, and lower return to work rates.[35-37] In this trial, pain-related function improved for most patients in each group. Poor pain outcomes associated with long-term opioids in observational studies may be attributable to overprescribing and insufficient pain management resources rather than to direct negative effects of opioids.[31,38] This trial did not have sufficient statistical power to estimate rates of death, opioid use disorder, or other serious harms associated with prescribed opioids.[39-41]

This trial's pragmatic design has several advantages. First, enrolled patients had characteristics similar to those of patients receiving opioids in VA primary care, including patients with depression and posttraumatic stress disorder.[6] Second, flexibility of treatment within assigned groups facilitated high study retention. Third, the treat-to-target approach reflects clinical practice more closely than approaches comparing single drugs or fixed dosages and allowed maximized benefit for patients.[9,10] Because individual medications are effective for only a minority of patients with chronic pain,[33,42] structured reassessment and adjustment of medications is likely necessary for effective pharmacological treatment.

Few data are available regarding optimal opioid dosing for pain, function, and tolerability. A meta-analysis of chronic back pain trials found incremental benefits of larger opioid dosages, but concluded benefits were too small "to be clinically important even at high doses."[32] Another meta-analysis of opioid trials for musculoskeletal pain in older adults found no association of dosage with pain or function.[34] Recent opioid prescribing guidelines recommend keeping daily dosages low.[2-4] This study was designed to identify the medication regimen with the best balance of benefits and tolerability for each patient and allowed treatment with a range of low to moderately high opioid dosages.

By pragmatic design, this trial did not require high levels of adherence to study medications. This study had high active treatment continuation and study retention rates, so results reflect outcomes across a range of treatment adherence.

Limitations

This study has several limitations. First, the complexity of interventions precluded masking of patients. Because primary outcomes were patient-reported, results are subject to potential reporting bias that would likely favor opioids. Second, there was an imbalance in prerandomization treatment preference. Any effect of this imbalance would likely favor opioids. Third, because this study was conducted in VA clinics, patient characteristics differ from those of the general population, most notably in sex distribution. Fourth, patients with physiological opioid dependence due to ongoing opioid use were excluded, so results do not apply to this population.

Conclusions

Treatment with opioids was not superior to treatment with nonopioid medications for improving pain-related function over 12 months. Results do not support initiation of opioid therapy for moderate to severe chronic back pain or hip or knee osteoarthritis pain.

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Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Krebs, Jensen, DeRonne, Bair.
Critical revision of the manuscript for important intellectual content: Gravely, Nugent, DeRonne, Goldsmith, Kroenke, Bair, Noorbaloochi.
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REFERENCES

1. Reuben DB, Alvanzo AA, Ashikaga T, et al. National Institutes of Health Pathways to Prevention Workshop: the role of opioids in the treatment of chronic pain. *Ann Intern Med*. 2015;162(4):295-300.

2. Department of Veterans Affairs/Department of Defense. Management of opioid therapy for chronic pain. https://www.healthquality.va.gov/guidelines/Pain/cot/VADoDOTCPG022717.pdf. Accessed February 7, 2018.

3. Busse JW, Craigie S, Juurlink DN, et al. Guideline for opioid therapy and chronic noncancer pain. *CMAJ*. 2017;189(18):E659-E666.

4. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain—United States, 2016. *MMWR Recomm Rep*. 2016;65(1):1-49.

5. Chou R, Turner JA, Devine 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(4):276-286.

6. Krebs EE, Jensen AC, Nugent S, et al. Design, recruitment outcomes, and sample characteristics of the Strategies for Prescribing Analgesics Comparative Effectiveness (SPACE) trial. *Contemp Clin Trials*. 2017;62:130-139.

7. Loudon K, Treweek S, Sullivan F, Donnan P, Thorpe KE, Zwarenstein M. The PRECIS-2 tool: designing trials that are fit for purpose. *BMJ*. 2015;350:h2147.

8. Krebs EE, Lorenz KA, Bair MJ, et al. Development and initial validation of the PEG, a 3-item scale assessing pain intensity and interference. *J Gen Intern Med*. 2009;24(6):733-738.

9. Kroenke K, Krebs E, Wu J, et al. Stepped Care to Optimize Pain care Effectiveness (SCOPE) trial study design and sample characteristics. *Contemp Clin Trials*. 2013;34(2):270-281.

10. Kroenke K, Krebs EE, Wu J, Yu Z, Chumbler NR, Bair MJ. Telecare collaborative management of chronic pain in primary care: a randomized clinical trial. *JAMA*. 2014;312(3):240-248.

11. Department of Veterans Affairs/Department of Defense. Management of opioid therapy for chronic pain. https://www.va.gov/painmanagement/docs/cpg_opioidtherapy_summary.pdf. Accessed February 7, 2018.

12. George SZ, Robinson ME. Preference, expectation, and satisfaction in a clinical trial of behavioral interventions for acute and sub-acute low back pain. *J Pain*. 2010;11(11):1074-1082.

13. Linde K, Witt CM, Streng A, et al. The impact of patient expectations on outcomes in 4 randomized controlled trials of acupuncture in patients with chronic pain. *Pain*. 2007;128(3):264-271.

14. Keller S, Bann CM, Dodd SL, Schein J, Mendoza TR, Cleeland CS. Validity of the brief pain inventory for use in documenting the outcomes of patients with noncancer pain. *Clin J Pain*. 2004;20(5):309-318.

15. Krebs EE, Bair MJ, Damush TM, Tu W, Wu J, Kroenke K. Comparative responsiveness of pain outcome measures among primary care patients with musculoskeletal pain. *Med Care*. 2010;48(11):1007-1014.

16. Dworkin RH, Turk DC, Wyrwich KW, et al. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. *J Pain*. 2008;9(2):105-121.

17. Weingart SN, Gandhi TK, Seger AC, et al. Patient-reported medication symptoms in primary care. *Arch Intern Med*. 2005;165(2):234-240.

18. Jonsson T, Christrup LL, Højsted J, et al. Symptoms and side effects in chronic noncancer pain: patient report vs systematic assessment. *Acta Anaesthesiol Scand*. 2011;55(1):69-74.

19. Selim AJ, Rogers W, Fleishman JA, et al. Updated US population standard for the Veterans RAND 12-item health survey (VR-12). *Qual Life Res*. 2009;18(1):43-52.

20. Stroud MW, McKnight PE, Jensen MP. Assessment of self-reported physical activity in patients with chronic pain: development of an abbreviated Roland-Morris disability scale. *J Pain*. 2004;5(5):257-263.

21. Kroenke K, Spitzer RL, Williams JB, Löwe B. The Patient Health Questionnaire Somatic, Anxiety, and Depressive Symptom Scales: a systematic review. *Gen Hosp Psychiatry*. 2010;32(4):345-359.

22. Yu L, Buysse DJ, Germain A, et al. Development of short forms from the PROMIS sleep disturbance and Sleep-Related Impairment item banks. *Behav Sleep Med*. 2011;10(1):6-24.

23. Stewart WF, Lipton RB, Dowson AJ, Sawyer J. Development and testing of the Migraine Disability Assessment (MIDAS) Questionnaire to assess headache-related disability. *Neurology*. 2001;56(6)(suppl 1):S20-S28.

24. McGahuey CA, Gelenberg AJ, Laukes CA, et al. The Arizona Sexual Experience Scale (ASEX): reliability and validity. *J Sex Marital Ther*. 2000;26(1):25-40.

25. Smets EM, Garssen B, Bonke B, De Haes JC. The Multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. *J Psychosom Res*. 1995;39(3):315-325.

26. Uppsala Monitoring Center. The use of the WHO-UMC system for standardised case causality assessment. https://www.who-umc.org/media/2768/standardised-case-causality-assessment.pdf. Accessed February 7, 2018.

27. Wu SM, Compton P, Bolus R, et al. The addiction behaviors checklist: validation of a new clinician-based measure of inappropriate opioid use in chronic pain. *J Pain Symptom Manage*. 2006;32(4):342-351.

28. National Institute of Drug Abuse. Resource guide: screening for drug use in general medical settings. https://www.drugabuse.gov/publications/resource-guide-screening-drug-use-in-general-medical-settings/introduction. Accessed February 7, 2018.

29. Fiellin DA, Reid MC, O'Connor PG. Screening for alcohol problems in primary care: a systematic review. *Arch Intern Med*. 2000;160(13):1977-1989.

30. Kroenke K, Bair MJ, Damush TM, et al. Optimized antidepressant therapy and pain self-management in primary care patients with depression and musculoskeletal pain: a randomized controlled trial. *JAMA*. 2009;301(20):2099-2110.

31. Sullivan MD, Ballantyne JC. What are we treating with long-term opioid therapy? *Arch Intern Med*. 2012;172(5):433-434.

32. Abdel Shaheed C, Maher CG, Williams KA, Day R, McLachlan AJ. Efficacy, tolerability, and dose-dependent effects of opioid analgesics for low back pain: a systematic review and meta-analysis. *JAMA Intern Med*. 2016;176(7):958-968.

33. Chou R, Deyo R, Friedly J, et al. Systemic pharmacologic therapies for low back pain: a systematic review for an American College of Physicians Clinical Practice guideline. *Ann Intern Med*. 2017;166(7):480-492.

34. Megale RZ, Deveza LA, Blyth FM, et al. Efficacy and safety of oral and transdermal opioid analgesics for musculoskeletal pain in older adults: a systematic review of randomized, placebo-controlled trials [published online December 11, 2017]. *J Pain*. doi:10.1016/j.jpain.2017.12.001

35. Sjøgren P, Grønbæk M, Peuckmann V, Ekholm O. A population-based cohort study on chronic pain: the role of opioids. *Clin J Pain*. 2010;26(9):763-769.

36. Turner JA, Shortreed SM, Saunders KW, LeResche L, Von Korff M. Association of levels of opioid use with pain and activity interference among patients initiating chronic opioid therapy: a longitudinal study. *Pain*. 2016;157(4):849-857.

37. Volinn E, Fargo JD, Fine PG. Opioid therapy for nonspecific low back pain and the outcome of chronic work loss. *Pain*. 2009;142(3):194-201.

38. Finestone HM, Juurlink DN, Power B, Gomes T, Pimlott N. Opioid prescribing is a surrogate for inadequate pain management resources. *Can Fam Physician*. 2016;62(6):465-468.

39. Bohnert AS, Valenstein M, Bair MJ, et al. Association between opioid prescribing patterns and opioid overdose-related deaths. *JAMA*. 2011;305(13):1315-1321.

40. Edlund MJ, Martin BC, Russo JE, DeVries A, Braden JB, Sullivan MD. The role of opioid prescription in incident opioid abuse and dependence among individuals with chronic noncancer pain: the role of opioid prescription. *Clin J Pain*. 2014;30(7):557-564.

41. Ray WA, Chung CP, Murray KT, Hall K, Stein CM. Prescription of long-acting opioids and mortality in patients with chronic noncancer pain. *JAMA*. 2016;315(22):2415-2423.

42. Moore A, Derry S, Eccleston C, Kalso E. Expect analgesic failure; pursue analgesic success. *BMJ*. 2013;346:f2690.

Cochrane Library

Cochrane Database of Systematic Reviews

Long-term opioid management for chronic noncancer pain (Review)

Noble M, Treadwell JR, Tregear SJ, Coates VH, Wiffen PJ, Akafomo C, Schoelles KM, Chou R

Noble M, Treadwell JR, Tregear SJ, Coates VH, Wiffen PJ, Akafomo C, Schoelles KM, Chou R.
Long-term opioid management for chronic noncancer pain.
Cochrane Database of Systematic Reviews 2010, Issue 1. Art. No.: CD006605.
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[Intervention Review]

Long-term opioid management for chronic noncancer pain

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ABSTRACT

Background

Opioid therapy for chronic noncancer pain (CNCP) is controversial due to concerns regarding long-term effectiveness and safety, particularly the risk of tolerance, dependence, or abuse.

Objectives

To assess safety, efficacy, and effectiveness of opioids taken long-term for CNCP.

Search methods

We searched 10 bibliographic databases up to May 2009.

Selection criteria

We searched for studies that: collected efficacy data on participants after at least 6 months of treatment; were full-text articles; did not include redundant data; were prospective; enrolled at least 10 participants; reported data of participants who had CNCP. Randomized controlled trials (RCTs) and pre-post case-series studies were included.

Data collection and analysis

Two review authors independently extracted safety and effectiveness data and settled discrepancies by consensus. We used random-effects meta-analysis' to summarize data where appropriate, used the I^2 statistic to quantify heterogeneity, and, where appropriate, explored heterogeneity using meta-regression. Several sensitivity analyses were performed to test the robustness of the results.

Main results

We reviewed 26 studies with 27 treatment groups that enrolled a total of 4893 participants. Twenty five of the studies were case series or uncontrolled long-term trial continuations, the other was an RCT comparing two opioids. Opioids were administered orally (number of study treatments groups [abbreviated as "k"] = 12, n = 3040), transdermally (k = 5, n = 1628), or intrathecally (k = 10, n = 231). Many participants discontinued due to adverse effects (oral: 22.9% [95% confidence interval (CI): 15.3% to 32.8%]; transdermal: 12.1% [95% CI: 4.9% to 27.0%]; intrathecal: 8.9% [95% CI: 4.0% to 26.1%]); or insufficient pain relief (oral: 10.3% [95% CI:

7.6% to 13.9%]; intrathecal: 7.6% [95% CI: 3.7% to 14.8%]; transdermal: 5.8% [95% CI: 4.2% to 7.9%]). Signs of opioid addiction were reported in 0.27% of participants in the studies that reported that outcome. All three modes of administration were associated with clinically significant reductions in pain, but the amount of pain relief varied among studies. Findings regarding quality of life and functional status were inconclusive due to an insufficient quantity of evidence for oral administration studies and inconclusive statistical findings for transdermal and intrathecal administration studies.

Authors' conclusions

Many patients discontinue long-term opioid therapy (especially oral opioids) due to adverse events or insufficient pain relief; however, weak evidence suggests that patients who are able to continue opioids long-term experience clinically significant pain relief. Whether quality of life or functioning improves is inconclusive. Many minor adverse events (like nausea and headache) occurred, but serious adverse events, including iatrogenic opioid addiction, were rare.

PLAIN LANGUAGE SUMMARY

Opioids for long-term treatment of noncancer pain

The findings of this systematic review suggest that proper management of a type of strong painkiller (opioids) in well-selected patients with no history of substance addiction or abuse can lead to long-term pain relief for some patients with a very small (though not zero) risk of developing addiction, abuse, or other serious side effects. However, the evidence supporting these conclusions is weak, and longer-term studies are needed to identify the patients who are most likely to benefit from treatment.

BACKGROUND

This systematic review differs in several ways from a previous systematic review on this topic that our group performed (Noble 2008). Because reviews in *The Cochrane Library* have fewer restrictions on the size of the review than a traditional peer-reviewed article, we were able to include the outcomes health-related quality of life and functional status in this review. The evidence base changed, with the inclusion of newly published studies (Collado 2008; Pascual 2007; Rauck 2008; Shaladi 2007; Thorne 2008) and non-English-language studies (Bettoni 2006; Klapetek 1971; Pimenta 1998), one study that we have reclassified as prospective (Kumar 2001), and one study that was not identified in our earlier searches (Thimineur 2004). In addition, two studies that were included in our previous review were excluded in this review, because we recently found that they were actually retrospective studies through personal communications with the study authors (Kanoff 1994; Tutak 1996). However, the differences in the studies that met general inclusion criteria did not impact the conclusions of the review in any important way. In addition, we updated our methodology to reflect more current methods by reducing the minimum number of studies needed to perform a meta-regression from 10 to five, implementing an updated quality-assessment approach using a revised instrument, not excluding studies with particularly low scores, and using each of the instrument items as a covariate to investigate heterogeneity where appropriate.

Chronic noncancer pain

The International Association for the Study of Pain (IASP) defines chronic pain as "pain which persists past the normal time of healing," which is considered to be pain lasting for three months or longer (IASP 1986). Chronic pain is a common problem worldwide. A World Health Organization survey of primary care patients seeking care at 15 centers in 14 countries across Asia, Africa, Europe, South America, and North America found that 22% of primary care patients reported pain lasting longer than 6 months (Gureje 1998). A systematic review of four international studies conducted in developed countries found prevalence rates of any type and severity level of chronic pain ranging from 10.5% to 55.2% of the population (Harstall 2003). The Pain in Europe survey of 46,000 individuals showed that one in five people suffer from chronic pain (Breivik 2006). In this survey, chronic pain sufferers reported 7 years of chronic pain on average, with some reporting pain lasting more than 20 years (Breivik 2006). An estimated 9% of Americans (Clark 2002) and 19% of Europeans (Breivik 2006) have moderate to severe chronic noncancer pain (CNCP). Women are more likely than men to experience chronic pain, and the overall prevalence of chronic pain increases with age

GUIDELINE FOR PRESCRIBING OPIOIDS FOR CHRONIC PAIN

IMPROVING PRACTICE THROUGH RECOMMENDATIONS

CDC's *Guideline for Prescribing Opioids for Chronic Pain* is intended to improve communication between providers and patients about the risks and benefits of opioid therapy for chronic pain, improve the safety and effectiveness of pain treatment, and reduce the risks associated with long-term opioid therapy, including opioid use disorder and overdose. The Guideline is not intended for patients who are in active cancer treatment, palliative care, or end-of-life care.

DETERMINING WHEN TO INITIATE OR CONTINUE OPIOIDS FOR CHRONIC PAIN

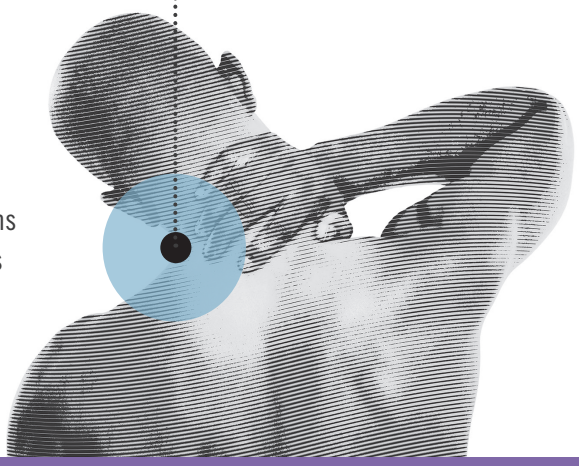
1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.

2. Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how opioid therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.

3. Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy.

CLINICAL REMINDERS

- **Opioids are not first-line or routine therapy for chronic pain**
- **Establish and measure goals for pain and function**
- **Discuss benefits and risks and availability of nonopioid therapies with patient**



U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

LEARN MORE | www.cdc.gov/drugoverdose/prescribing/guideline.html

OPIOID SELECTION, DOSAGE, DURATION, FOLLOW-UP, AND DISCONTINUATION

CLINICAL REMINDERS

- Use immediate-release opioids when starting
- Start low and go slow
- When opioids are needed for acute pain, prescribe no more than needed
- Do not prescribe ER/LA opioids for acute pain
- Follow-up and re-evaluate risk of harm; reduce dose or taper and discontinue if needed

4 When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.

5 When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when considering increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day.

6 Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed.

7 Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

ASSESSING RISK AND ADDRESSING HARMS OF OPIOID USE

8 Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present.

9 Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months.

10 When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.

11 Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.

12 Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder.

CLINICAL REMINDERS

- Evaluate risk factors for opioid-related harms
- Check PDMP for high dosages and prescriptions from other providers
- Use urine drug testing to identify prescribed substances and undisclosed use
- Avoid concurrent benzodiazepine and opioid prescribing
- Arrange treatment for opioid use disorder if needed

LEARN MORE | www.cdc.gov/drugoverdose/prescribing/guideline.html

Research Paper

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Changes in pain intensity after discontinuation of long-term opioid therapy for chronic noncancer pain

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Abstract

Little is known about changes in pain intensity that may occur after discontinuation of long-term opioid therapy (LTOT). The objective of this study was to characterize pain intensity after opioid discontinuation over 12 months. This retrospective U.S. Department of Veterans Affairs (VA) administrative data study identified N = 551 patients nationally who discontinued LTOT. Data over 24 months (12 months before and after discontinuation) were abstracted from VA administrative records. Random-effects regression analyses examined changes in 0 to 10 pain numeric rating scale scores over time, whereas growth mixture models delineated pain trajectory subgroups. Mean estimated pain at the time of opioid discontinuation was 4.9. Changes in pain after discontinuation were characterized by slight but statistically nonsignificant declines in pain intensity over 12 months after discontinuation (B = −0.20, P = 0.14). Follow-up growth mixture models identified 4 pain trajectory classes characterized by the following postdiscontinuation pain levels: no pain (average pain at discontinuation = 0.37), mild clinically significant pain (average pain = 3.90), moderate clinically significant pain (average pain = 6.33), and severe clinically significant pain (average pain = 8.23). Similar to the overall sample, pain trajectories in each of the 4 classes were characterized by slight reductions in pain over time, with patients in the mild and moderate pain trajectory categories experiencing the greatest pain reductions after discontinuation (B = −0.11, P = 0.05 and B = −0.11, P = 0.04, respectively). Pain intensity after discontinuation of LTOT does not, on average, worsen for patients and may slightly improve, particularly for patients with mild-to-moderate pain at the time of discontinuation. Clinicians should consider these findings when discussing risks of opioid therapy and potential benefits of opioid taper with patients.

Keywords: Chronic noncancer pain, Prescription opioid discontinuation, Pain intensity, Veterans, Long-term opioid therapy

1. Introduction

U.S. epidemiologic data characterize rising trends in opioid prescribing nationally from the early 1990s through 2012 with subsequent modest year-over-year declines from 2013 through 2016.[11,26] Declining rates of overall and unsafe opioid prescribing are the result of fewer new opioid initiations and, in large part, discontinuation of existing opioid therapy.[20] Although prescription opioids have demonstrated short-term efficacy in placebo-controlled clinical trials at reducing pain intensity in patients with some chronic pain conditions,[1] little evidence exists for their efficacy beyond 3 months,[2] and even less is known about changes in pain after discontinuation of long-term opioid therapy (LTOT).

For patients with chronic pain, pain intensity may follow distinct trajectories over time.[4,9,17,29] Results from a recent systematic review of pain trajectories in patients with low back pain found that, overall, chronic low back pain is characterized by slight reductions in pain after initial presentation for treatment in ambulatory outpatient settings, followed by stable levels of pain over time.[17] A minority of patients (<15%) have pain characterized as fluctuating over time. Notably, within-patient variability of pain scores over time is high, with scores for some patients fluctuating across the entire 0 to 10 pain intensity numeric rating scale (NRS).[9] These findings have been extended to other chronic musculoskeletal pain conditions including knee and hip pain, and over continuous longitudinal follow-up of 5 to 6 years.[4,29]

Despite evidence that chronic pain, on average, remains consistent over time, few studies have examined pain trajectories after important therapeutic changes to patients' pain management plans, such as tapering or discontinuing prescription opioid therapy. A recent systematic review examined patient outcomes after interventions aimed to taper or discontinue LTOT.[10] Thirty-six studies, the majority (n = 28) of which were rated as "poor" quality observational studies, assessed pain intensity outcomes.

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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Letters

RESEARCH LETTER

Patient-Centered Prescription Opioid Tapering in Community Outpatients With Chronic Pain

The risks associated with prescription opioids are well described.[1,2] Although reducing opioid use is a national priority, existing opioid tapering models use costly interdisciplinary teams that are largely inaccessible to patients and their physicians.[3,4] Patients and physicians need solutions to successfully reduce long-term prescription opioid dosages in settings without behavioral services. We conducted a study of voluntary, patient-centered opioid tapering in outpatients with chronic pain without behavioral treatment.

Methods | Patients with non–cancer-related chronic pain prescribed long-term opioids at a community pain clinic were provided education about the benefits of opioid reduction (reduced health risks without increased pain) by their prescribing physician. Physicians offered to partner with patients to slowly reduce their opioid dosages over 4 months. The only exclusion was current treatment for substance use disorder. The study was approved by the Stanford University institutional review board; participants provided written or electronic informed consent, and no compensation was provided to participants.

Of the 110 eligible patients, 82 (75%) agreed to taper their opioid dosages; of those, 68 provided baseline demographics, information on opioid use, pain, marijuana use and psychosocial measures. Patients received a self-help book on reducing opioid use, and a slow, individually designed taper. Opioid dosages were reduced up to 5% for up to 2 dose reductions in month 1 to minimize negative physical and emotional response, withdrawal symptoms, and to facilitate patient confidence in the process. In months 2 to 4, patients were asked to further reduce use by as much as 10% per week; dose decrements were tailored to the patient. Patient responses were monitored with close clinical follow-up (at least monthly) and doses adjusted accordingly. Follow-up surveys were administered at 4 months; patients who provided data at 4 months were considered study completers. We confirmed patient-reported opioid prescription with medical record review. We documented patient compliance and accuracy of reported medication use with periodic urine drug testing and continuous monitoring of the state Prescription Drug Monitoring Program (PDMP). No compliance issues or aberrant prescriptions were noted. We converted opioid doses to morphine equivalent daily dose (MEDD). Change in MEDD from baseline was the primary outcome and pain intensity was a secondary outcome. Kruskal-Wallis rank sum test was used for continuous variables and χ^2 test for polychotomous variables.

Results | The patients' mean (SD) age was 51 (12) years, and 41 (60%) were female. Thirty-one of 82 enrolled patients

Table. Characteristics and Outcomes[a]

	Completers (n = 51)					Dropouts[b]		
	Baseline		4 mo			Baseline		
Variable	Median (IQR)	NA	Median (IQR)	NA	*P* Value[c]	Median (IQR)	NA	*P* Value[d]
Age	52 (43-50)	1				57 (50-63)	0	.12
Opioid duration[e]	6 (3-11)	10				6 (5-8)	4	.57
Opioid dose[f]	288 (153-587)	0	150 (54-248)	0	.002	244 (147-311)	1	.45
Pain intensity	5.0 (3.0-7.0)	0	4.5 (3.0-7.0)	3	.29	3.5 (3.0-6)	1	.10
PCS	22 (10-30)	1	15 (7-23)	5	.04	22 (20-30)	0	.39
Fatigue[g]	60 (54-65)	4	59 (51-65)	3	.64	63 (59-66)	2	.45
Anxiety[g]	60 (53-64)	1	54 (46-62)	3	.06	62 (59-63)	1	.35
Depression[g]	56 (49-64)	1	55 (48-61)	2	.31	62 (57-65)	1	.05
Sleep disturbance[g]	59 (54-70)	2	56 (50-64)	2	.13	62 (53-67)	1	.66
Pain interference[g]	63 (58-67)	1	63 (57-67)	2	.44	66 (61-68)	1	.13
Pain behavior[g]	60 (57-63)	2	59 (56-64)	2	.47	62 (60-64)	1	.14
Physical function[g,h]	39 (34-41)	1	39 (34-43)	2	.78	36 (34-41)	1	.07

Abbreviations: IQR, interquartile range; NA, not applicable; PCS, Pain Catastrophizing Scale.

[a] Completers provided 4-month data, dropouts enrolled but did not provide month 4 data.

[b] Thirty-one enrolled; 17 provided the baseline data.

[c] Probability of difference between week baseline and 4 months for completers where null hypothesis is true.

[d] Probability of baseline difference between completers and dropouts where null hypothesis is true.

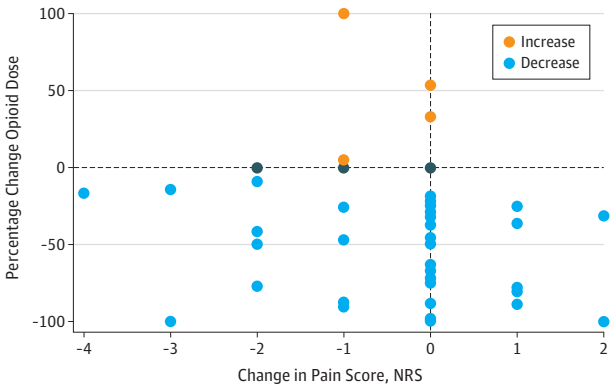
[e] Opioid duration (years taking opioids).

[f] Opioid dose (morphine equivalent daily dose).

[g] Patient Reported Outcomes Information System (PROMIS) measure.

[h] Lower scores reflect worse function, pain (numeric rating scale).

Figure. Change in Opioid Morphine Equivalent Daily Dose and Absolute Change in Pain Intensity Score From Baseline to Month 4 for Study Completers



NRS indicates numeric rating scale.

(38%) did not complete a 4-month follow-up survey and therefore were considered to have dropped out of the study. Depression negatively correlated (P = .05) and baseline marijuana use positively correlated (P = .04) with study completion. The **Table** provides characteristics and results for the sample; we found no sex association with study completion or opioid reduction.

Among study completers (n = 51) baseline median MEDD (interquartile range [IQR]) was 288 (153-587) mg, with a median 6-year duration (IQR, 3-9) duration of opioid use. Median pain intensity was moderate (5 out of 10 on a numeric pain rating). After 4 months, the median MEDD was reduced to 150 (IQR, 54-248) mg (P = .002). The likelihood of a greater than 50% opioid dose reduction was not predicted by starting dose, baseline pain intensity, years prescribed opioids, or any psychosocial variable. Neither pain intensity (P = .29) nor pain interference (P = .44) increased with opioid reduction. The **Figure** shows the relationship between percentage change in MEDD and pain intensity in study completers.

Discussion | Our findings suggest that a substantial fraction of patients at a pain clinic may wish to engage in voluntary opioid tapering. Our data challenge common notions that patients taking high-dose opioids will fail outpatient opioid tapers or that duration of opioid use predicts taper success. Combining patient education about the benefits of opioid reduction with a plan that reduces opioids more slowly than current tapering algorithms[5] with close clinician follow-up may help patients engage and succeed in voluntary outpatient tapering. Because our data are generated from a single pain clinic, studies are needed to assess how well our protocol would generalize to other types of patients and settings.

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Author Contributions: Dr Darnall had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
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Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Darnall, Mackey, Flood.
Critical revision of the manuscript for important intellectual content: Darnall, Ziadni, Stieg, Kao.
Statistical analysis: Darnall, Kao, Flood.
Administrative, technical, or material support: Darnall, Ziadni, Stieg, Mackey, Kao.
Study supervision: Darnall, Stieg.

Conflict of Interest Disclosures: None reported.

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1. Edlund MJ, Martin BC, Russo JE, DeVries A, Braden JB, Sullivan MD. The role of opioid prescription in incident opioid abuse and dependence among individuals with chronic noncancer pain: the role of opioid prescription. *Clin J Pain*. 2014;30(7):557-564.

2. Darnall BD, Stacey BR, Chou R. Medical and psychological risks and consequences of long-term opioid therapy in women. *Pain Med*. 2012;13(9):1181-1211.

3. Murphy JL, Clark ME, Banou E. Opioid cessation and multidimensional outcomes after interdisciplinary chronic pain treatment. *Clin J Pain*. 2013;29(2):109-117.

4. 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(3):308-318.

5. Berna C, Kulich RJ, Rathmell JP. Tapering long-term opioid therapy in chronic noncancer pain: evidence and recommendations for everyday practice. *Mayo Clin Proc*. 2015;90(6):828-842.

Using Chaplains to Facilitate Advance Care Planning in Medical Practice

Although many patients do not want aggressive care at the end of life (EoL),[1] such care is not uncommon[2] and may be associated with poorer quality of life and psychological distress.[3] Advance care planning (ACP) permits patients to express preferences for EoL care and increase concordance between care that is desired and care that is delivered at EoL.[4] Rather than waiting for an urgent health crisis, regular office visits are a preferred time for ACP discussions.[4] With the new Centers for Medicare policy, lack of reimbursement for time spent in ACP discussions should no longer be a barrier to conducting them.[5] However, other structural (eg, competing demands) and professional barriers (eg, lack of

[Overview of Reviews]

Adverse events associated with medium- and long-term use of opioids for chronic non-cancer pain: an overview of Cochrane Reviews

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ABSTRACT

Background

Chronic pain is common and can be challenging to manage. Despite increased utilisation of opioids, the safety and efficacy of long-term use of these compounds for chronic non-cancer pain (CNCP) remains controversial. This overview of Cochrane Reviews complements the overview entitled 'High-dose opioids for chronic non-cancer pain: an overview of Cochrane Reviews'.

Objectives

To provide an overview of the occurrence and nature of adverse events associated with any opioid agent (any dose, frequency, or route of administration) used on a medium- or long-term basis for the treatment of CNCP in adults.

Methods

We searched the Cochrane Database of Systematic Reviews (the Cochrane Library) Issue 3, 2017 on 8 March 2017 to identify all Cochrane Reviews of studies of medium- or long-term opioid use (2 weeks or more) for CNCP in adults aged 18 and over. We assessed the quality of the reviews using the AMSTAR criteria (Assessing the Methodological Quality of Systematic Reviews) as adapted for Cochrane Overviews. We assessed the quality of the evidence for the outcomes using the GRADE framework.

Main results

We included a total of 16 reviews in our overview, of which 14 presented unique quantitative data. These 14 Cochrane Reviews investigated 14 different opioid agents that were administered for time periods of two weeks or longer. The longest study was 13 months in duration, with most in the 6- to 16-week range. The quality of the included reviews was high using AMSTAR criteria, with 11 reviews meeting all 10 criteria, and 5 of the reviews meeting 9 out of 10, not scoring a point for either duplicate study selection and data extraction, or searching for articles irrespective of language and publication type. The quality of the evidence for the generic adverse event outcomes according to GRADE ranged from very low to moderate, with risk of bias and imprecision being identified

for the following generic adverse event outcomes: any adverse event, any serious adverse event, and withdrawals due to adverse events. A GRADE assessment of the quality of the evidence for specific adverse events led to a downgrading to very low- to moderate-quality evidence due to risk of bias, indirectness, and imprecision.

We calculated the equivalent milligrams of morphine per 24 hours for each opioid studied (buprenorphine, codeine, dextropropoxyphene, dihydrocodeine, fentanyl, hydromorphone, levorphanol, methadone, morphine, oxycodone, oxymorphone, tapentadol, tilidine, and tramadol). In the 14 Cochrane Reviews providing unique quantitative data, there were 61 studies with a total of 18,679 randomised participants; 12 of these studies had a cross-over design with two to four arms and a total of 796 participants. Based on the 14 selected Cochrane Reviews, there was a significantly increased risk of experiencing any adverse event with opioids compared to placebo (risk ratio (RR) 1.42, 95% confidence interval (CI) 1.22 to 1.66) as well as with opioids compared to a non-opioid active pharmacological comparator, with a similar risk ratio (RR 1.21, 95% CI 1.10 to 1.33). There was also a significantly increased risk of experiencing a serious adverse event with opioids compared to placebo (RR 2.75, 95% CI 2.06 to 3.67). Furthermore, we found significantly increased risk ratios with opioids compared to placebo for a number of specific adverse events: constipation, dizziness, drowsiness, fatigue, hot flushes, increased sweating, nausea, pruritus, and vomiting.

There was no data on any of the following prespecified adverse events of interest in any of the included reviews in this overview of Cochrane Reviews: addiction, cognitive dysfunction, depressive symptoms or mood disturbances, hypogonadism or other endocrine dysfunction, respiratory depression, sexual dysfunction, and sleep apnoea or sleep-disordered breathing. We found no data for adverse events analysed by sex or ethnicity.

Authors' conclusions

A number of adverse events, including serious adverse events, are associated with the medium- and long-term use of opioids for CNCP. The absolute event rate for any adverse event with opioids in trials using a placebo as comparison was 78%, with an absolute event rate of 7.5% for any serious adverse event. Based on the adverse events identified, clinically relevant benefit would need to be clearly demonstrated before long-term use could be considered in people with CNCP in clinical practice. A number of adverse events that we would have expected to occur with opioid use were not reported in the included Cochrane Reviews. Going forward, we recommend more rigorous identification and reporting of all adverse events in randomised controlled trials and systematic reviews on opioid therapy. The absence of data for many adverse events represents a serious limitation of the evidence on opioids. We also recommend extending study follow-up, as a latency of onset may exist for some adverse events.

PLAIN LANGUAGE SUMMARY

Side effects of opioid drugs when used to treat chronic non-cancer pain in the medium- or long-term

Bottom line

There is good-quality evidence showing that side effects can occur in people with chronic non-cancer pain who use opioid medicines for longer than two weeks.

Background

Opioids are a type of pain medicine related to opium. We conducted an overview of Cochrane Reviews, which are a type of scientific paper, to learn what these papers said about the side effects of opioid drugs. We were interested in the medium- and long-term side effects with this treatment for pain in adults who use opioid medicines who have chronic pain that is not due to cancer. We studied opioid medications compared to pills that do not contain any medicine (placebos) and opioid medications compared to other treatments.

Key results

In March 2017, we found 16 Cochrane Reviews of 14 different opioid medicines, including codeine, morphine, and oxycodone. These papers included 61 studies with more than 18,000 participants. We found that people who take opioids have a higher risk of having any side effect, such as constipation, dizziness, and nausea, as well as having a serious side effect. We did not find any information in the Cochrane Reviews about many of the known and sometimes serious side effects of opioids, such as addiction, depression, and sleep problems.

Quality of the reviews and the evidence

[Overview of Reviews]

High-dose opioids for chronic non-cancer pain: an overview of Cochrane Reviews

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ABSTRACT

Background

Chronic pain is typically described as pain on most days for at least three months. Chronic non-cancer pain (CNCP) is any chronic pain that is not due to a malignancy. Chronic non-cancer pain in adults is a common and complex clinical issue where opioids are routinely used for pain management. There are concerns that the use of high doses of opioids for chronic non-cancer pain lacks evidence of effectiveness and may increase the risk of adverse events.

Objectives

To describe the evidence from Cochrane Reviews and Overviews regarding the efficacy and safety of high-dose opioids (here defined as 200 mg morphine equivalent or more per day) for chronic non-cancer pain.

Methods

We identified Cochrane Reviews and Overviews through a search of the Cochrane Database of Systematic Reviews (*The Cochrane Library*). The date of the last search was 18 April 2017. Two review authors independently assessed the search results. We planned to analyse data on any opioid agent used at high dose for two weeks or more for the treatment of chronic non-cancer pain in adults.

Main results

We did not identify any reviews or overviews meeting the inclusion criteria. The excluded reviews largely reflected low doses or titrated doses where all doses were analysed as a single group; no data for high dose only could be extracted.

Authors' conclusions

There is a critical lack of high-quality evidence regarding how well high-dose opioids work for the management of chronic non-cancer pain in adults, and regarding the presence and severity of adverse events. No evidence-based argument can be made on the use of high-dose opioids, i.e. 200 mg morphine equivalent or more daily, in clinical practice. Trials typically used doses below our cut-off; we need to know the efficacy and harm of higher doses, which are often used in clinical practice.

MED Scope Statement

Topic

Tapering or Discontinuing Opioid Use among Patients with Chronic Noncancer Pain: Update Report

Date: September 14, 2018

Nominated by: Oregon (Participant Request)

Center researcher: Susan Carson

Background

According to the Centers for Disease Control and Prevention (CDC), there were more than 22,000 deaths from prescription opioids in 2015.[1] Despite the potential for harm and a lack of evidence of effectiveness, opioids are frequently prescribed to treat chronic noncancer pain.[2,3] Clinical practice guidelines recommend tapering and discontinuing opioid therapy for patients with chronic noncancer pain whenever possible.[1,4-6]

As state Medicaid and public health program administrators develop approaches to encourage tapering and discontinuing opioid medications, they need up-to-date information on the benefits and harms of these practices. A 2017 Medicaid Evidence-based Decisions Project (MED) report on this topic concluded that there was limited evidence on harms associated with tapering strategies, and the findings suggested that pain, function, and quality of life might improve during and after opioid discontinuation or dose reduction.[7] Confidence in these findings was limited by the overall very low quality of evidence.[7] This MED report will update the evidence and clinical practice guidelines sections of the previous report and will include any available information on voluntary versus involuntary opioid tapering and discontinuation.

PICO

Population:

- Adult patients (18 years and older) using opioids for chronic (6 months or longer) noncancer pain

Intervention:

- Interventions to taper opioid dose or discontinue opioid treatment

Comparators:

- No tapering
- Different opioid discontinuation or tapering strategies (head-to-head comparisons)

- No comparison

Effectiveness and Harms Outcomes:

- Opioid abstinence (successful discontinuation)
- Dose reduction as a percentage of morphine equivalents (a measure of success with tapering)
- Self-reported pain
- Quality of life
- Function
- Mortality (including suicide, accidental overdose, other causes)
- Adverse events (e.g., overdose)

Key Questions

1. What is the evidence for the effectiveness and harms of various strategies for tapering or discontinuing opioids among adult patients with chronic noncancer pain? Do the effectiveness or harms of these strategies vary by:
    a. Medication type or dosing level (e.g., particular agent, long- vs. short-acting formulation, single-drug vs. combination agent)
    b. Morphine milligram equivalents at the time of taper initiation or discontinuation
    c. Population characteristics (e.g., diagnosis, length of time of opioid use, age, gender, comorbidities)?
    d. Whether tapering or discontinuation is voluntary (i.e., patient decision) or involuntary (i.e., the decision of someone other than the patient)?
    e. Tapering supports (e.g., behavioral interventions, additional therapeutic modalities)
    f. Rapid vs. slow tapering

Proposed Approach

We will search MED clinical evidence sources (e.g., Ovid MEDLINE, Cochrane library) starting from the end date of searches in the last report (August 29, 2017). Studies involving only patients who are incarcerated or who are under court order related to opioid use will be excluded. For the adverse event outcome, we will report any event that was found to be statistically significantly different between groups or had at least a 10% difference between groups.

References

1. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain--United States, 2016. *Jama.* 2016;315(15):1624-1645.

2. Chou R, Turner JA, Devine 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(4):276-286.

3. Krebs EE, Gravely A, Nugent S, et al. Effect of opioid vs nonopioid medications on pain-related function in patients with chronic back pain or hip or knee osteoarthritis pain: the SPACE randomized clinical trial. *Jama.* 2018;319(9):872-882.

4. Berna C, Kulich RJ, Rathmell JP. Tapering long-term opioid therapy in chronic noncancer pain: evidence and recommendations for everyday practice. *Mayo Clin Proc.* 2015;90(6):828-842.

5. Busse JW, Craigie S, Juurlink DN, et al. Guideline for opioid therapy and chronic noncancer pain. *Cmaj.* 2017;189(18):E659-e666.

6. Washington State Agency Medical Directors' Group. Interagency guideline on prescribing opioids for pain. 2015; http://www.agencymeddirectors.wa.gov/Files/2015AMDGOpioidGuideline.pdf.

7. Leof A, Crabtree E, McDonagh M, Lazur BH, King V. Tapering or discontinuing opioid use among patients with chronic noncancer pain. 2017; https://www.medclearinghouse.org/topicfiles/pain/tapering_or_discontinuing_opioid_use_among_patients_with_chronic_noncancer_pain_evidence_guidelines_and_policy/.

HERC Pain Treatment Implementation Survey

About This Survey

The Health Evidence Review Commisson (HERC) is considering a proposal to add certain chronic pain conditions (including fibromyalgia, chronic pain due to trauma, other chronic postprocedural pain, other chronic pain and chronic pain syndrome) to a funded line. The proposal would add nonpharmacologic and pharmacologic treatments to this line, with guideline notes which have some similarities to the current guidelines for back pain (Guideline notes 56 and 60).

As it considers making these changes, the Commission seeks information from CCOs about their choices and experiences related to implementing the 2016 back pain changes, including the addition of therapeutic care as well as the limitations on coverage of opioids and other medicaitons.

A version of this survey was conducted in early 2016. Some questions address similar issues in order to be able to compare data with the prior survey results.

Note: Responses will be summarized in public meeting materials and redacted responses will be available by public records request. All information identifying any CCO, provider group or individual will be kept confidential.

Validated assessment tool (e.g. STarT Back Assessment Tool) in order to determine risk level for poor functional prognosis based on psychosocial indicators.

1. Regarding the Validated assessment tool (e.g. STarT Back Assessment Tool) in order to determine risk level for poor functional prognosis based on psychosocial indicators:
Are you requiring providers to document use of an assessment tool for coverage?

- ◯ Yes
- ◯ No
- ◯ We did but have stopped doing so

If you don't currently require this, why not?

* 2. Regarding differentiating benefits for uncomplicated back pain based on risk of poor functional prognosis (e.g. offering cognitive behavioral therapy, additional therapeutic modalities for higher risk patients as recommended in the new HERC guideline):
Are you doing this now?

- ◯ Yes - unlimited access for all members
- ◯ Yes - for selected members
- ◯ Yes - pilot program currently involving members (please provide # of members in comment box below)
- ◯ Planning to cover differentiated benefits
- ◯ Not planning to cover in a differential manner

If you answered "yes - pilot program currently involving members," please provide the number of members in the comment box.

Covering for uncomplicated back pain a range of therapeutics modalities. Please check all that apply.

* 3. Osteopathic manipulation (please check all that apply)

- [ ] Yes, unlimited access for all members
- [ ] Yes, for selected members
- [ ] Yes, pilot program currently involving members
- [ ] Planning to cover in the future
- [ ] Provider supply is adequate
- [ ] Covered in the past but stopped covering

If you are not planning to cover and/or if you are experiencing any barriers to coverage or stopped covering it, please explain.

* 4. Chiropractic manipulation (please check all that apply)

- [ ] Yes, unlimited access for all members
- [ ] Yes, for selected members
- [ ] Yes, pilot program currently involving members
- [ ] Planning to cover in the future
- [ ] Provider supply is adequate
- [ ] Covered in the past but stopped covering

If you are not planning to cover and/or if you are experiencing any barriers to coverage or stopped covering it, please explain.

* 5. Acupuncture (please check all that apply)

- [ ] Yes, unlimited access for all members
- [ ] Yes, for selected members
- [ ] Yes, pilot program currently involving members
- [ ] Planning to cover in the future
- [ ] Provider supply is adequate
- [ ] Covered in the past but stopped covering

If you are not planning to cover and/or if you are experiencing any barriers to coverage or stopped covering it, please explain.

* 6. Physical therapy (please check all that apply)

- [ ] Yes, unlimited access for all members
- [ ] Yes, for selected members
- [ ] Yes, pilot program currently involving members
- [ ] Planning to cover in the future
- [ ] Provider supply is adequate
- [ ] Covered in the past but stopped covering

If you are not planning to cover and/or if you are experiencing any barriers to coverage or stopped covering it, please explain.

* 7. Occupational therapy (please check all that apply)

- [ ] Yes, unlimited access for all members
- [ ] Yes, for selected members
- [ ] Yes, pilot program currently involving members
- [ ] Planning to cover in the future
- [ ] Provider supply is adequate

If you are not planning to cover and/or if you are experiencing any barriers to coverage or stopped covering it, please explain.

* 8. Cognitive behavioral therapy (please check all that apply)

- [ ] Yes, unlimited access for all members
- [ ] Yes, for selected members
- [ ] Yes, pilot program currently involving members
- [ ] Planning to cover in the future
- [ ] Provider supply is adequate

If you are not planning to cover and/or if you are experiencing any barriers to coverage or stopped covering it, please explain.

* 9. Yoga (please check all that apply)

- [ ] Yes, unlimited access for all members
- [ ] Yes, for selected members
- [ ] Yes, pilot program currently involving members
- [ ] Planning to cover in the future
- [ ] Provider supply is adequate
- [ ] Covered in the past but stopped covering

If you are not planning to cover and/or if you are experiencing any barriers to coverage or stopped covering it, please explain.

* 10. Massage (please check all that apply)

- [ ] Yes, unlimited access for all members
- [ ] Yes, for selected members
- [ ] Yes, pilot program currently involving members
- [ ] Planning to cover in the future
- [ ] Provider supply is adequate

If you are not planning to cover and/or if you are experiencing any barriers to coverage or stopped covering it, please explain.

* 11. Supervised exercise therapy (please check all that apply)

- [ ] Yes, unlimited access for all members
- [ ] Yes, for selected members
- [ ] Yes, pilot program currently involving members
- [ ] Planning to cover in the future
- [ ] Provider supply is adequate

If you are not planning to cover and/or if you are experiencing any barriers to coverage or stopped covering it, please explain.

* 12. Intensive interdisciplinary rehabilitation (please check all that apply)

- [ ] Yes, unlimited access for all members
- [ ] Yes, for selected members
- [ ] Yes, pilot program currently involving members
- [ ] Planning to cover in the future
- [ ] Provider supply is adequate

If you are not planning to cover and/or if you are experiencing any barriers to coverage or stopped covering it, please explain.

13. Regarding implementing expanded coverage of therapeutic modalities (PT/OT, manipulative therapies, massage, supervised exercise, yoga, CBT), has your organization tracked outcomes (such as cost, satisfaction, medication use or health outcomes)? If so what did you find?

- [ ] No, we did not track outcomes
- [ ] Positive health outcomes
- [ ] Negative health outcomes
- [ ] Higher-than-predicted costs
- [ ] Lower-than-predicted costs
- [ ] Positive patient satisfaction
- [ ] Lower patient satisfaction
- [ ] Lower opioid use
- [ ] Higher opioid use

Please add a brief narrative description of your findings.

Documentation of measurable clinically significant progress toward the therapeutic plan goals and objectives using evidence based objective tools (e.g. Oswestry, Neck Disability Index, SF-MPQ, and MSPQ).

* 14. Are you requiring this now for approval of additional physical interventions?

- ◯ Yes
- ◯ No
- ◯ Previously required, but dropped requirement now

If you are not requiring the above, please explain.

* 15. Are you requiring this now for opiates?

- ◯ Yes
- ◯ No
- ◯ Previously required, but have dropped requirement now
- ◯ If you are not requiring the above, please explain.

The therapies in the back pain guidelines are specified as allowed and counting toward the 30 visit limit in Guideline Note 6.

* 16. Are you doing this now?

- ◯ Yes
- ◯ No
- ◯ Previously combined, but no longer combine

If you are not combining these limits, please explain why.

* 17. If you answered no to question 16, are you likely to?

- ◯ Yes
- ◯ No

If you answered no to the above question, please explain.

GUIDELINE NOTE 60, OPIOID PRESCRIBING FOR CONDITIONS OF THE BACK SPINE has several elements:

* 18. First 6 weeks post trauma: 7 day maximum opioid prescription, short acting, alternative meds tried, plan to keep active, consider alternative therapies, lack of current or prior opioid misuse

- ◯ You are implementing now
- ◯ You are planning to implement
- ◯ You are not planning to implement
- ◯ Implemented in the past, but are no longer enforcing this requirement

If you are not enforcing this requirement, please explain why.

* 19. After 6 weeks restrict to cases with documented improved function of at least 30%, in conjunction with alternative therapies, verification (specified) of lack of risk for opioid misuse

- ◯ You are implementing now
- ◯ You are planning to implement
- ◯ You are not planning to implement
- ◯ You implemented this in the past but are no longer enforcing this requirement

If you are not enforcing this requirement, please explain why.

* 20. Other prescription requirements for 45-90 days (short acting only, failure of other medications, Rx for activity plan)

- ◯ You are implementing now
- ◯ You are planning to implement
- ◯ You are not planning to implement
- ◯ Implemented in the past but no longer enforce these provisions

If you are not enforcing these provisions, please explain why.

* 21. Verification of no active opioid misuse/abuse (45-90 days)

- ◯ You are implementing now
- ◯ You are planning to implement
- ◯ You are not planning to implement
- ◯ You implemented this in the past but no longer enforce this requirement

If you are not enforcing this requirement, please explain why.

* 22. Tapering for chronic back pain (please check all that apply)

- ◯ You are implementing now
- ◯ You are planning to implement
- ◯ You are not planning to implement
- ◯ Partially implemented
- ◯ Previously implemented but no longer enforce this requirement

If you are not enforcing this requirement, or have partially implemented it, please explain why.

23. If similar guideline were written to apply to chronic pain that is not back pain (with exclusions for certain funded diagnoses, including cancer), which response most accurately reflects your view.

- ☐ This would simplify administration
- ☐ This would complicate administration
- ☐ This would benefit our patients
- ☐ This could harm our patients
- ☐ The existing guideline needs to be reworked for implementability; then consider whether it should apply to other forms of chronic pain
- ☐ The existing guideline should be eliminated; coverage controls are not the best way to manage opioid therapy
- ☐ Other (see below)
- ☐ Please add any additional thoughts below

* 24. Does the CCO have a plan for developing and adopting opioid prescribing guidelines among prescribers?

- ◯ Yes
- ◯ No

* 25. If you answered yes to question 24:

When do you plan to implement?

What guidelines will you be using?

* 26. If you answered no to question 24, will you be?

- ◯ Yes
- ◯ No

If you answered no, please explain why

* 27. What percentage of controlled substances providers have integrated opioid prescribing guidelines into clinical practice in your CCO - approximate?

Which of the following medications for non-specific back pain are you currently covering?

* 28. Opioids

- ◯ Currently covering
- ◯ Planning to cover
- ◯ Not planning to cover
- ◯ Stopped covering

Comments

* 29. Lidocaine patches

- ◯ Currently covering
- ◯ Planning to cover
- ◯ Not planning to cover
- ◯ Stopped covering

Comments

* 30. Lyrica

- ◯ Currently covering
- ◯ Planning to cover
- ◯ Not planning to cover
- ◯ Stopped covering

Comments

* 31. NSAIDS

- ◯ Currently covering
- ◯ Planning to cover
- ◯ Not planning to cover
- ◯ Stopped covering

Comments

* 32. Gabapentin

- ◯ Currently covering
- ◯ Planning to cover
- ◯ Not planning to cover
- ◯ Stopped covering

Comments

* 33. Benzodiazapines

- ◯ Currently covering
- ◯ Planning to cover
- ◯ Not planning to cover
- ◯ Stopped covering

Comments

* 34. Muscle relaxants (e.g. cyclobenzaprine, robaxin, soma)

- ◯ Currently covering
- ◯ Planning to cover
- ◯ Not planning to cover
- ◯ Stopped covering

Comments

* 35. Would your CCO prefer HERC add specific classes of meds (e.g. gabapentin, Lyrica, lidocaine patches, etc.) to the back guideline (medical or narcotic or both)?

- ◯ Yes
- ◯ No

36. If chronic pain diagnoses (including fibromyalgia, chronic pain due to trauma, other chronic postprocedural pain, other chronic pain and chronic pain syndrome) were added to a funded line, what (if any) classes of drugs would need to be addressed with a guideline?

- ☐ Opioids
- ☐ Benzodiazipines
- ☐ Lyrica
- ☐ Gabapentin
- ☐ Lidocaine patches
- ☐ Tramadol
- ☐ Duloxetine
- ☐ NSIADs
- ☐ Acetominiphen
- ☐ None

Please list other classes or briefly describe your concerns for any of the classes you checked above.

* 37. Can you share any cost-analysis you have of the changes in coverage (e.g. expanding physical therapy, or acupuncture, or restricting opioids) for back pain?

38. Please describe any thoughts or concerns about expanding coverage for fibromyalgia, chronic pain due to trauma, other chronic postprocedural pain, other chronic pain and chronic pain syndrome.

* 39. Address

Name	
Title	
CCO	
Email Address	
Phone Number	

Thank you for participating!