# Opioids, Addiction, and Pain: State of the Art in VA

Keith Humphreys, PhD William Becker, MD Evelyn Chang, MD, MSHS: Katherine Mackey, MD, MPP Stephanie Veazie, MPH





U.S. Department of Veterans Affairs

### **HSR&D SOTA XV**. Effective Management of Pain and Addiction: Strategies to Improve Opioid Safety

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### **Opioid SOTA JGIM Supplement**



SAFETY

Effective Management of Pain and Addiction: Strategies to Improve Opioid Safety

### A VA Health Services Research & Development Service State of the Art Conference



Corresponding Author	Article Title	Article Type
Becker	Mounting a Scientifically-Informed Response to the Opioid Crisis in the Veterans Health Administration	Editorial
Priest	Expanding Access to Medications for Opioid Use Disorder: Program and Policy Approaches from Outside the Veterans Health	Perspective
	Administration	
Compton	The Importance of Learning Health Systems in Addressing the Opioid Crisis	Perspective
Morasco	Prospective Investigation of Factors Associated with Prescription Opioid Dose Escalation Among Patients in Integrated Health	Original
	Systems	
Minegishi	Opioid Discontinuation among High-Dose Long-Term Patients in the Veterans Health Administration	Original
Frank	Association Between Opioid Dose Reduction Against Patients' Wishes and Change in Pain Severity	Original
Chang	Increasing Access to Medications for Opioid Use Disorder and Complementary and Integrative Health Services in Primary Care	Original
Sandbrink	Opioid Prescribing and Opioid Risk Mitigation Strategies in the Veterans Health Administration	Original
Mackey	Benefits and harms of long-term opioid dose reduction or discontinuation in patients with chronic pain: A rapid review	Systematic Review
Veazie	Managing acute pain in patients taking medication for opioid use disorder: A rapid review	Systematic Review
Mackey	Barriers and facilitators to use of medications for opioid use disorder: A rapid review	Systematic Review
Manhapra	Complex persistent opioid dependence with long-term opioids: A gray area that needs definition, better understanding,	Perspective
	treatment guidance and policy changes.	
Kertesz	Promoting patient-centeredness in opioid deprescribing: a blueprint for (de)implementation science	Perspective
Becker	A Research Agenda for Advancing Strategies to Improve Opioid Safety: Findings from a VHA state of the art conference	Perspective
Frank	Implementation and Policy Recommendations from the VHA State of the Art Conference on Strategies to Improve Opioid Safety	Perspective





# Spotlight on Pain: Increasing Access to Opioid Use Disorder Treatment in VISN 22

VA Cyberseminar Series

December 8, 2020

Evelyn Chang, MD, MSHS



**CSHIIP** Center for the Study of Healthcare Innovation, Implementation & Policy



### Objectives

- Describe project to implement access to Medications for Opioid Use Disorder (MOUD) in partnership with VISN 22
- Describe implementation challenges to increasing access to MOUD and lessons learned

# Problem Statement and Goal

- Opioid-related mortality can be reduced by treating addiction to opioids, or Opioid Use Disorder (OUD), using medications for Opioid Use Disorder (MOUD)
  - Methadone
  - Buprenorphine/naloxone
  - ER-naltrexone
- Uptake of MOUD has been slow, particularly in primary care settings
- Goal: To increase awareness, access, and implementation of OUD treatment in primary care, where many patients are already seen for chronic disease management

## **QUERI VISN 22 Partnered Implementation Initiative**

- VISN 22 partnered with researchers on an initiative to increase access to MOUD and complementary and integrative health (CIH, e.g., yoga, acupuncture, mindfulness) among patients with OUD with the goal of decreasing opioid-related overdoses and deaths
  - "No wrong door"
- Implementation Strategy: Evidence-Based Quality Improvement (EBQI)
- Pilot Sites: Phoenix, Tucson
- Funding: Start-up funding from QUERI (4/1/18 9/30/19)

### **VISN 22 Pilot Implementation Sites**



### Evidence-Based Quality Improvement (EBQI)



# **Implementation Timeline**

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October 2019: Stakeholder exit interviews completed

# Where are the opportunities for treatment?



Patients diagnosed with OUD but **not on MOUD within past three years Data Source: CDW, PIT** 

	Southern Arizona (TUC) (n=584)	Phoenix (PHX) (n= 941)
% who had a VA encounter in Primary Care in the past six months	62.5%	64.7%
% who had a <b>VA</b> encounter in <b>Mental Health</b> in the past six months	49.3%	57.0%
% who had a <b>VA</b> encounter in <b>Emergency Room</b> in the past six months	34.6%	37.4%
% who had a <b>VA</b> encounter in <b>Pain clinic</b> in the past six months	17.1%	10.6%
% who have had <u>any med/surg/psych</u> <sup>+</sup> hospitalizations in past six months	22.9% (20.8% TUC)	18.7% (12.7% PHX)

<sup>+</sup> includes fee-basis hospitalizations; <sup>‡</sup> Includes MH, Psych and SUD IND and GRP Outpatient encounter info VA only based on primary encounter stop code

## Capacity to Provide MOUD

Data Source: Academic Detailing Report



	Southern Arizona	Phoenix	
Number of clinicians with X-waiver	21	32	
Pain clinic	2 (surgical service) (10%)	2 (MH and ambulatory care) (6%)	
Number of X-waiver clinicians who have p			
O patients	2 (10%)		
• <b>1-30</b> patients	14 (67%)	22 (69%)	
• <b>31-100</b> patients	4 (19%)		
• 101-275 patients			

Data as of May 3, 2018. This excludes data from providers who are no longer at VA Includes X-waivers presented to Credentialing and recorded in VISTA

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### Stakeholders at VISN 22 Pilot Sites (Phoenix, Tucson)



### Stakeholder Interviews: Patients



• Expressed satisfaction with the buprenorphine program in the addiction treatment setting, but reported lack of education about buprenorphine as an option from primary care.

"I was actually going to go to a private clinic with a Suboxone program. And the clinic, the first thing they said was, 'Why aren't you going to the VA? The VA has this program.' And I had no idea at all that the VA even offered the program... back in the day, primary care physicians were not saying anything about it. They weren't saying, 'Hey, we have a Suboxone program if you would like to get off pain meds.' I was never told that."



# Stakeholder Interviews: Clinicians

- Barriers to prescribing MOUD:
  - Stigma
  - Lack of knowledge and training
  - Lengthy process for credentialing and privileging

# Stakeholder Interviews: Clinicians



 Strong reluctance to prescribing MOUD in primary care due to insufficient support, PCP turnover and burnout, and nursing burnout.

"No PCPs want to do it. At our facility, PCPs don't have enough support. Lots of non-clinical work falls on them- the nursing leadership does not want to help with the workload.... Because of this, there's lots of turnover. PCPs burn out because they are constantly being asked to take on more. Honestly, my reaction to this idea is 'no frickin' way- you're not going to put more on my docs or I will lose them. This always happens – a good idea comes down that gets dumped on Primary Care because no one else wants to do it."

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# **Training for Clinicians**



- Grand Rounds aimed at PCPs about how to recognize Opioid Use Disorder (OUD) in the primary care population
  - Phoenix: 2 Grand Rounds attended by >100 providers
  - Tucson: 1 Grand Rounds attended by 22 providers
- X-Waiver trainings
  - Phoenix: 4 trainings attended by a total of 19 PCPs, 26 pharmacists, 20 nurses, 18 specialty providers
  - Tucson: 2 trainings, attended by 9 PCPs and 5 specialty providers

## Clinical Preceptorship for Newly X-Waivered Providers



### Sample Buprenorphine Provider Training

Adapted from Anita Karnik, MD Phoenix VA

- Training can be either a full day or half day, depending on the PCP's preference (full day is ideal).
- Try to schedule training for the busiest clinic days, to maximize shadowing opportunities.
- Review of material below is fit in around clinic flow.
- Ideally, providers will be able to:
  - o Observe an initial evaluation, including assessment of Opioid Use Disorder (1-6 below).
  - o Observe an induction appt with provider
  - o Observe induction with nursing staff
  - Observe follow-up appts with patients at different stages (Induction, Titration, Maintenance, Weaning)

### **Buprenorphine Training Components**

- 1. Review Opioid Use Disorder (OUD) diagnosis and concepts (Many PCPs have not seen what opioid withdrawal looks like and can't describe it well)
- 2. Review Complex Persistent Opioid Dependence
- 3. Indications to start Buprenorphine
- 4. Buprenorphine evaluation appointment
  - a. Liver Function Tests (LFTs)
  - b. Labs: HIV, HCV, STDs
- 5. 24 hours off all opioids; not magic number, just easier
- 6. Clinical Opiate Withdrawal Scale (COWS) and teaching nursing to complete
- 7. Day of induction
  - a. Assessment
    - i. Date/Time of last use and COWS
    - ii. Assess Mood
    - iii. Assess for Suicidal Ideation (SI)/update Suicide Risk Assessment (SRA) if needed (might do after induction)
    - iv. Cravings (usually best to do when come in for induction)
  - b. Informed consent completed by provider (*this is can be very confusing especially for the* 
    - "grey zone" pts but they really need to understand it)
      - i. Buprenorphine prescribed for OUD/complex dependence not pain
      - ii. Can't take opioids
      - iii. Can't use alcohol
      - iv. Benzodiazepines are relative contraindication
      - v. Notify me if planning surgery
      - vi. Responsible for safe keeping
    - vii. Will be performing random urine drug testing
    - viii. We perform random pill counts
    - ix. We don't give early refills (assess on case by case basis)
    - x. We don't mail prescriptions
  - c. Nursing
    - i. Education on addiction and active/ non-pharmacologic treatments for pain
    - ii. Nursing note
    - iii. Clinical warning note

### d. Clinic vs Home induction

- 8. Indications for referrals back to Addiction or Pain
- Language related to stigma, OUD, complex dependence, buprenorphine (Stigma has been a major issue with pts not wanting to accept MAT- try to help PCPs destigmatize)
- Should consider mental health optimization- opportunity to do screening for depression/anxiety, substance abuse counseling, active care for chronic pain/pain rehabilitation programing (e.g. Cognitive Behavioral Therapy-Chronic Pain, or pain program)
- 11. Opioid Overdose Education and Naloxone including how to order
- 12. Discussion about "grey zone" issues, how to have the conversation about MAT, patient concerns, site-specific logistical issues
- 13. Review articles and documents:
  - The conundrum of opioid tapering in long-term opioid therapy for chronic pain: A commentary. <u>Manhapra</u>, A. et al. (2017)
- The next stage of buprenorphine Care for Opioid Use Disorder: Martin, SA et al. (2018)
- Printed copy of buprenorphine education for patients found in IMED consent patient education section
- Printed copy of the buprenorphine imed consent that the patient would be signing
- Any site-specific VA guidelines for buprenorphine
- For those that are not familiar at all with Opioid Use Disorder, VA academic detailing brochure, Opioid Use Disorder: A VA Clinician's Guide to Identification and Management of Opioid Use Disorder (2016)

### **Tools for Patients Outreach**





#### Dear Veteran,

This informational letter is being sent out as part of a national initiative to Veterans who have experienced longterm pain and may be interested in learning about treatment options for those whose bodies have become dependent on medications like opioids, as well as alternative non-medication treatment options (yoga, tai-chi, acupuncture, mindfulness, medication) that can help with stress and pain.

Opioids are one type of pain medicine and are also known as narcotics. Examples of opioids are: hydrocodone. oxycodone, methadone, fentanyl, hydromorphone, and

morphine. Over the past decade due to overprescribing opioid medications in the United States, many patients ended up on prescription

opioid medications for years and years, and even overdosing on them. When more evidence came out showing the risks with these medications and how they can change your brain, providers began moving away from opioid medications and started using alternative treatment options. Because of the way these medications work, people can develop an opioid use disorder even if they are taking these medications for pain.

Ask your provider about opioid use disorder or if alternative treatments might be right for you.

#### Sincerely,

Dr. Francisco Rivera-Pabon, Chief of Primary Care Southern Arizona VA Health Care System

### **Veteran Perspectives**



"I came to the VA in 2003 with a neck injury and from the first five milligram Percocet that I got, it blew up to a massive addiction. And that's something that I'd never had an issue with-I'd never been addicted, never even tried any hard drugs! With a spinal injury, it just didn't get better. It progressively got worse. So over time, we had to increase the dosage for it to

Once I finally had my spinal surgery I was thinking that I could just stop taking the medication- but as soon as I tried it. I realized real quick. I need help. At first I wasn't sure about Suboxone- 'another version of an opiate? I don't want to get on another opiate'- but I did my research and I saw the success stories. As soon as I found out the VA had a program, I jumped in head first. I was done. I wanted to get off pain medication.

Across the board, everybody that I've spoken to that is going through this program says the same thing - without it they would probably be either dead or homeless. For me, literally, it's changed my life. I have a phenomenal job. I have a trajectory of massive success ahead of me. I was definitely spiraling down very fast. And now, my future looks amazing."

### **Could Your Pain Medications Be** Harming you?

If you are a Veteran who has experienced long-term pain, you may be interested in learning about treatment options that can help with stress and pain. These can include treatments for those whose bodies

have become dependent on medications like opioids, as well



as alternative non-medication treatment options (voga, tai-chi, acupuncture, mindfulness, meditation).

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### **VA** DESERT PACIFIC HEALTHCARE NETWOR



### Flyer

### Veteran Perspectives



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### VA Dashboard Manual

### Data Source: Academic Detailing reports, Online operations reports

1 Page



### User's Guide: Best Practices in using VA Dashboards for OUD/MAT

#### Introduction

#### 1. Background

This user guide was developed to help spread best practices for use of the various opioid dashboards available to VA providers. It was developed based on guidance from a provider who used these practices to singlehandedly improve their facility's SUD16 metrics to > 90<sup>th</sup> percentile in 6 months. This can be used to understand:

- Which patients might benefit from Medication-Assisted Treatment (MAT) for opioid use disorder (OUD)?
- Which patients might benefit from additional OUD risk mitigation strategies (e.g., drug screen, informed consent, naloxone)?
- Which patients might have been inappropriately diagnosed with OUD based on encounter coding?
- Which patients on buprenorphine have been lost to follow-up?

#### 2. Target User

 Facility: a facility may have designated staff to monitor their SUD16 metrics via the dashboards Preferably a provider with X-waiver training o Ideally, one person should be consistently reviewing these dashboards to make it easier to spot new patients/trends. Provider or Care Team: a provider or care team may monitor

SUD-16 Measure dashboards to identify patients TN 40.95 40.95 44.85 41.45 10.15 10.85 17.05 16.05 54.25 54.65 10.85 10.15 10.1 Preferably a provider who regularly sees OUD patients.

#### 3. High-Yield Dashboards (in priority order)

that may benefit from

engagement in MAT

intervention or need re-

- a. Psychotropic Drug Safety Initiative (PDSI)
- b. Stratification Tool for Opioid Risk Mitigation (STORM)
- c. Overdose Education and Naloxone Distribution (OEND)
- d. OUD Patient Report
- e. Buprenorphine Dashboard can be reserved for buprenorphine review

#### 4. Case Examples:

There are 2 things to consider: a) is this a patient who may be in need of an intervention, or b) is this a provider who may need training to code appropriately?

#### a. Case 1: Offering MAT to Patients

By using a combination of dashboards and chart review, an addiction specialist identified patients on longterm opioids who might benefit from medication review and adjustment of treatment plans, including

	PDSI Dashboard	STORM Dashboard	OFND Dashboard	OUD Patient Report	Bunrenorphine
	(Psychotropic Drug	(Stratification Tool for	(Overdose Education	And the sector of the sector of the sector	Dashboard
	Safety Initiative)	Opioid Risk Mitigation) and Dist	and Naloxone Distribution)		12
URL Link:	Ctrl+Click to Open	Ctrl+Click to Open	Ctrl+Click to Open	Ctrl+Click to Open	Ctrl+Click to Open
Assessment:	SUD16 Score	STORM Risk Score	RIOSORD Risk Score	OUD diagnosis or risk based on long term opioid therapy	Buprenorphine prescription history
Organized by:	Facility; Provider; Patient	Facility; Provider; Care Team; Patient	National; VISN; Facility; Provider	National, VISN, Facility, Provider, Patient level	Provider; Patient
Use for:			9) 9		
Identify patients that may benefit from MAT.	1	2	3	4	
ldentify patients that were <u>coded</u> <u>inappropriately</u> .	1	2	3		
Identify patients that may benefit from <u>OUD</u> <u>risk mitigation</u> <u>strategies</u> (i.e., MAT, Naloxone, etc.).		1	2	3	
Identify patients with expired Buprenorphine <u>coverage</u> that may benefit from reengagement.					1

\*Numbers listed in order of priority

VA Dashboards for OUD/MAT

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### SAIL SUD-16 Measure



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## Stakeholder Exit Interviews: MOUD



• Stakeholders reported shifts in attitudes and processes around MOUD, particularly acceptability within primary care:

"... I have definitely noticed an organizational shift. This is something that went from something very super-specialty care, like, it really just needs a buprenorphine consult ... to something that people see ... as possibly being able to be managed. If it's mild to moderate opiate use disorder, people can view it as something that can be managed within a primary care setting or primary psychiatry setting as well, and then ... triaging more complicated cases to specialty care."

# Key elements

- Providing data to front-line staff, facility leadership, VISN leadership, and advisory committee helped with understanding the problem and potential solutions
  - Primary Care and Mental Health are potential OUD treatment locations
  - Very little capacity in Primary Care to prescribe buprenorphine
- Research-clinical partnership enabled front-line staff creativity and problem-solving
  - Tool development for education, mass media, audit and feedback
- Primary care-specialty partnerships were key for training and implementation
- Provider review of dashboards with feedback was a very powerful tool

## Next Steps

- We have received funding to disseminate tools developed by pilot sites to the rest of the VAMCs within VISN22
- During FY20-22, we are partnering with medical centers across VISN22 to increase access to MOUD and CIH in primary care.
- The VISN22 effort is part of a Phase 2 VISN-Partnered Implementation Initiative (PII)- a nationally integrated initiative that spans six VISNs and 57 sites called "Consortium to Disseminate and Understand Implementation of Opioid Use Disorder Treatment (CONDUIT)," led by Will Becker, MD

# Acknowledgments Project Team Members

### **VISN** members

- Kenneth R. Browne
- Kamonica L. Craig, PharmD,
- Frank Evans, PharmD, MBA
- Laurie Graaff, RN, MBA, MS-ISM
- Karen L. MacKichan, MD
- Margaret Mendes, PharmD
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- Araceli Revote, MD, MPH
- Shawn Toy, PharmD
- Lucretia Vaughan, MD

### **Evaluation Team**

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- Stephanie Taylor, PhD
- Britney Lewkowitz, MPH
- Larissa Mooney, MD
- Rebecca Oberman, MSW, MPH
- Adam Resnick, MPH
- Elizabeth Yano, PhD, MSPH

# Acknowledgements Site QI Teams

### Tucson

- Karen Atencio, MD
- Eve Broughton, MSN, APN, CNS
- Kristina De Los Santos, PharmD
- Rebecca Dawson, MD
- Elissa Gumm, DO
- Stephanie Lee, PharmD
- Sally Petty, RN
- Kristyn Straw-Wilson, PharmD
- Dinah (Lea Anne) Weigel, RN

### Phoenix

- Matthew Ahuett, PharmD, BCPS
- Patrick Flyte, MD
- Anita Karnik, MD
- Show Lin, MD
- Aram Mardian, MD
- Shannon Mentzel, PharmD, BCPS
- Jolyn Moeller, RN, CDE



# Questions? Email <u>Evelyn.Chang@va.gov</u>

Further details will be included in the manuscript in the JGIM Special Supplement



### Benefits and Harms of Long-term Opioid Dose Reduction or Discontinuation in Patients with Chronic Pain: a Rapid Review

Kate Mackey, MD, MPP

ESP Coordinating Center Portland VA Medical Center

December 2020



- This report is based on research conducted by the Evidence Synthesis Program (ESP) Coordinating Center located at the **Portland VA Medical Center, Portland, OR**, funded by the Department of Veterans Affairs, Veterans Health Administration, Health Services Research and Development.
- The findings and conclusions in this document are those of the author(s) who are responsible for its contents; the findings and conclusions do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs.
- No investigators have any affiliations or financial involvement (*eg*, employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.



# The Problem: A Difficult Balance



- Ongoing crisis of morbidity, mortality, and misuse due to opioids
- VA/DoD and CDC guidelines recommend considering LTOT tapers when risks > benefits
- Patients with chronic pain on longterm opioid therapy (LTOT) and the providers who care for them are at the center of a difficult balance

Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain — United States, 2016. Morbidity and Mortality Weekly Report. 2016;65(1):1-49. Department of Veterans A, Department of D. VA/DoD Clinical Practice Guideline for Opioid Therapy for Chronic Pain. 2017; https://www.healthquality.va.gov/guidelines/Pain/cot/VADoDOTCPG022717.pdf





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### VA/DoD and CDC Tapering Recommendations

- Emphasize shared decision-making regarding LTOT tapers
- Individualize taper speeds and suggest gradual tapers with pauses in the tapering process as needed
- Similar approaches are recommended by the American Academy of Family Physicians, the Washington State Agency Medical Directors' Group, and the Oregon Pain Guidance Clinical Advisory Group

Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain — United States, 2016. Morbidity and Mortality Weekly Report. 2016;65(1):1-49. Department of Veterans A, Department of D. VA/DoD Clinical Practice Guideline for Opioid Therapy for Chronic Pain. 2017; https://www.healthquality.va.gov/guidelines/Pain/cot/VADoDOTCPG022717.pdf



U.S. Department of Veterans Affairs

Evidence Synthesis Program





April 2019

"Recently, the FDA has received *reports of serious harm*, including serious withdrawal symptoms, uncontrolled pain and suicide, in patients who are physically dependent on opioid pain medicines *when these medicines are suddenly discontinued or when the dose is reduced too quickly*, often without adequate patient communication, follow-up or support."




**Key Question 1:** Among patients prescribed long-term opioid therapy for chronic pain, what are the benefits and harms of opioid dose reduction or discontinuation?

# **Key Question 2:** Do the benefits and harms of opioid dose reduction or discontinuation vary by:

- Patient characteristics
- Patient engagement in tapering
- LTOT regimen
- Tapering characteristics



## **Previous Evidence**

#### **Annals of Internal Medicine**



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## REVIEW

### Patient Outcomes in Dose Reduction or Discontinuation of Long-Term Opioid Therapy A Systematic Review

Joseph W. Frank, MD, MPH; Travis I. Lovejoy, PhD, MPH; William C. Becker, MD; Benjamin J. Morasco, PhD; Christopher J. Koenig, PhD; Lilian Hoffecker, PhD, MLS; Hannah R. Dischinger, BS; Steven K. Dobscha, MD; and Erin E. Krebs, MD, MPH

- Included 40 mostly fair- or poor-quality studies
- Inconclusive evidence on the impact of LTOT tapers on pain severity, pain-related function, quality of life, withdrawal symptoms, substance abuse, and adverse effects





**Population:** Adults prescribed long-term opioids (≥ 3 months) for chronic pain

Intervention: Dose reduction or discontinuation

**Comparator:** Any

Outcomes: Pain severity, pain-related function, quality of life, patient satisfaction\*, healthcare utilization\*, opioid withdrawal symptoms, substance use, opioid overdose\*, suicidal ideation and suicidal self-directed violence\*

Timing, Setting, Study Design: Any

\*New since Frank et al review





- Search: MEDLINE, PsycINFO, Cochrane databases and other sources (January 2017 – May 2020)
- Study selection: Based on eligibility criteria
- Data abstraction: Study characteristics and results
- Critical appraisal: Use of standardized tools
- Quality control: Assessments first completed by one reviewer and checked by at least one additional reviewer. Disagreements resolved by consensus.
- Peer Review: Topic and methodological experts commented, responses are publicly available



## GRADE Criteria to Evaluate Body of Evidence





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# **Prioritization of Evidence**



## **19 Prioritized Studies**

2 RCTs, 6 controlled observational studies, and 11 uncontrolled observational studies

## VHA and outpatient settings

- Other settings with sufficiently described populations and interventions
- Evaluated serious harms of tapering (*eg* overdose and suicide)

All other studies





**Key Question 1:** Among patients prescribed long-term opioid therapy for chronic pain, what are the benefits and harms of opioid dose reduction or discontinuation?



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## Results Summary: Opioid Dose Reduction Benefits and Harms

	Patient Outcomes						Adverse Events		
Author, Year	Pain Severity	Pain-related Function	Quality of Life	Patient Satisfaction	Healthcare Utilization or Retention	Depression or Anxiety	Withdrawal Symptoms	SUD or Opioid Overdose	Suicidal Ideation or SSV
High Intensity Co-interventions (e.g. multimodal pain management programs with daily attendance over several weeks)									
Darchuk, 201018	✓	✓				×			
Hooten, 2007b27	✓	✓	×			×			
Hooten, 200930				_					
Huffman, 201732	✓	1				✓			
Murphy, 201334	✓	1	✓	✓					
Nicholas, 201936*	✓	✓							
Townsend, 200840	✓	1	✓			<ul> <li>✓</li> </ul>			
Moderate Intensity Co-interventions (e.g. outpatient pain management combined with enhanced psychosocial supports)									
Kurita, 2018*46	=		1			=	×		
Sullivan, 201750	✓	✓							
Low Intensity Co-Intervention (e.g. use of a self-help book)									
Darnall, 2018*54	=	=							
Undefined Co-intervention	on or Usual	Care							
Demidenko, 2017*55									×
DiBenedetto, 2019*	=	=							
Harden, 201556	<ul> <li>✓</li> </ul>								
Hundley, 2018*57					=			×	x
James, 2019*58					×			×	
Mark, 2019*59					×			×	
McPherson, 2018*61	=								
Perez, 2019*					×				
Von Korff, 2019*63								×	
Overall Evidence Quality		Low		Very I	Low			Very Low	



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# Patient Outcomes by Intervention Intensity



#### Pain and Pain-Related Function

#### **High Intensity Interventions:**

7 observational studies describing multimodal programs requiring daily participation for 3-4 weeks

#### **Moderate Intensity Intervention:**

2 RCTs embedded in multidisciplinary pain clinics, 1 with medication optimization prior to a scheduled taper and 1 with enhanced psychosocial supports

#### Low Intensity Intervention:

1 observational study of a self-help book paired with individual clinician guidance

#### Unclear:

9 studies did not describe a specific tapering intervention



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## Limitations:

- Most studies did not have a control group
- Common measures of pain severity (*eg* Pain Numerical Rating Scale) do not tell us whether a change was clinically meaningful
- Most studies did not report whether patients with worse pain and function required a change in clinical management
- Opioid dose reductions in these studies were mostly *voluntary*



# LTOT Tapers and Substance Use

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- Evidence is unclear; studies have not directly examined this outcome
- <u>Best evidence</u>: 2019 study by Mark et al of Medicaid claims data in Vermont
  - Between 2013-17 opioids were discontinued in 494/694 patients on ≥ 120mg MEDD
  - $\circ~$  Prior to discontinuation, 60% of patients had a diagnosis of substance use disorder
  - After discontinuation, almost half (49%) of patients had an ED visit or hospitalization due to opioid poisoning or substance use disorder
  - <1% of patients were transitioned onto an opioid use disorder medication</li>
- Limitations: study does not describe LTOT discontinuation reasons or exclude reverse causation
- Highlights a real-world pattern of abrupt opioid discontinuation and undertreatment of substance use disorders





# LTOT Tapers and Opioid Overdose



- Evidence is unclear; few studies have examined this outcome
- <u>Best evidence</u>: 2019 large retrospective cohort study by Von Korff et al examining opioid overdose rates following different phases of an opioid risk reduction initiative in Washington
  - Overdose rates decreased by 17% per year within the intervention group (patients in Washington's Group Health practice) after a dose reduction effort
  - Reduction was not significantly different when compared to the control group (patients followed at Group Health's contracted community clinics)
- Provides inconsistent support that reducing opioid doses leads to lower overdose rates
- Limitation: Does not exclude possibility of reverse causation



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# LTOT Tapers and Suicide Risk

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- Evidence is unclear; few studies have examined this outcome
- <u>Best evidence</u>: 2017 retrospective study by Demidenko et al
  - 509 VA patients with substance use disorders and matched controls underwent clinician-initiated tapers (75% due to aberrant behaviors)
  - o 47 (9.2%) had new-onset suicidal ideation and 12 patients (2.4%) had suicidal selfdirected violence in the year following opioid discontinuation
  - $_{\odot}$  Risk was higher in patients with PTSD and psychotic disorders
- Limitations include the exclusion of patients who died or who had no VHA contact in the year following discontinuation



# Key Question 2: Variation in Outcomes?

- Very limited evidence on how outcomes vary by patient characteristics or taper approaches
- Important evidence gap



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# Summary of Key Findings



Pain severity and function may improve with voluntary intensive pain management interventions and may not change with less intensive interventions, but our confidence in these findings is low.

In real-world practice, opioid discontinuation is often occurring abruptly without shared decision-making and without linking patients to additional supports.

Important evidence gaps relate to potential harms.

We know the least about outcomes with clinician-initiated and involuntary opioid dose reductions.



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Evidence is inadequate to fully weigh the balance of the benefits and harms of LTOT for chronic pain against the benefits and harms of opioid tapering, primarily due to *limited information on harms*.





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## **Citation:**

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## Managing Acute Pain in Patients Taking Medication for Opioid Use Disorder: A Rapid Review

Stephanie Veazie, MPH Kate Mackey, MD, MPP ESP Coordinating Center Portland VA Medical Center

December 2020

## Disclosure



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The findings and conclusions in this document are those of the author(s) who are responsible for its contents; the findings and conclusions do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs.

No investigators have any affiliations or financial involvement (*eg*, employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.







- **Opioid Use Disorder** (OUD) is a problematic pattern of opioid use leading to clinically significant impairment or distress.
- **Medications for OUD** (*ie*, Medication-Assisted Treatment) are opioid agonists and ٠ antagonists.
- Acute pain is a "sudden-onset, time-limited pain that can vary in intensity, modulating factors, and impact on functionality and quality of life."



## Challenges in Managing Acute Pain in OUD



Cooper R, Vanjani R, Trimbur MC. Acute Pain Management in Patients Treated With Buprenorphine: A Teachable Moment. JAMA Intern Med. Published online July 29, 2019. doi:10.1001/jamainternmed.2019.3103

Becker WC, Fiellin DA. When Epidemics Collide: Coronavirus Disease 2019 (COVID-19) and the Opioid Crisis. Ann Intern Med. 2020;173(1):59-60. doi:10.7326/M20-1210



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Medication	Opioid receptor activity	Considerations for pain management
Methadone	Full activation	Unpredictable effects with dose changes
Buprenorphine/naloxone	Partial activation	May reduce the effectiveness of other opioids
Naltrexone	Blocks the effects of opioids	Extended-release injectable form lasts up to 30 days

Connery HS. Medication-assisted treatment of opioid use disorder: review of the evidence and future directions. *Harvard review of psychiatry*. 2015;23(2):63-75. Alford DP, Compton P, Samet JH. Acute pain management for patients receiving maintenance methadone or buprenorphine therapy. *Ann Intern Med*. 2006;144(2):127-134. Vickers AP, Jolly A. Naltrexone and problems in pain management. *BMJ (Clinical research ed)*. 2006;332(7534):132-133.



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# **Guidance from Professional Societies**



#### Methadone

• Higher doses of full agonist opioids may be needed.

#### Buprenorphine/naloxone

- For mild pain, temporarily increase and add another opioid if needed.
- For severe pain, discontinue and replace with a high potency opioid.

#### Naltrexone

- Discontinue prior to planned surgery.
- · Use nonopioid pain management for unexpected acute pain.

Similar guidance from: Perioperative Pain and Addiction Interdisciplinary Network (PAIN)



Goel A, Azargive S, Weissman JS, et al. Perioperative Pain and Addiction Interdisciplinary Network (PAIN) clinical practice advisory for perioperative management of buprenorphine: results of a modified Delphi process. Br J Anaesth. 2019;123(2):e333-e342.





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## Rapid Review: Managing Acute Pain

#### Managing Acute Pain in Patients Taking Medication for Opioid Use Disorder: a Rapid Review

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BACKGROUND: Managing acute pain in patients with opioid use disorder (OUD) on medication (methadone, buprenorphine, or naltrexone) can be complicated by patients' higher baseline pain sensitivity and need for higher opioid doses to achieve pain relief. This review aims to evaluate the benefits and harms of acute pain management strategies for patients taking OUD medications and whether strategies vary by OUD medication type or cause of acute pain.

METHODS: We systematically searched multiple bibliographic sources until April 2020. One reviewer used prespecified criteria to assess articles for inclusion, extract data, rate study quality, and grade our confidence in the body of evidence, all with second reviewer checking. RESULTS: We identified 12 observational studies-3 with control groups and 9 without. Two of the studies with control groups suggest that continuing buprenorphine and methadone in OUD patients after surgery may reduce the need for additional opioids and that ineffective pain management in patients taking methadone can result in disengagement in care. A third controlled study found that patients taking OUD medications may need higher doses of additional opioids for pain control, but provided insufficient detail to apply results to clinic practice. The only case study examining naltrexone reported that postoperative pain was managed using tramadol. We have low confidence in these findings as no studies directly addressed our question by comparing pain management strategies and few provided adequate descriptions of the dosage, timing, or rationale for clinical decisions.

DISCUSSION. We lack rigorous evidence on acute pain management in patients taking medication for OUD; however, evidence supports the practice of continuing methadone or buprenorphine for most patients during acute pain episodes. Well-described, prospective studies of adjuvant pain management strategies when OUD medications are continued would add to the existing literature base. Studies on nonopioid treatments are also needed for patients taking naltrexone.

Prior presentations: The full report this work is based on is available on the RSP website at https://www.bsrl.mseanth.wa.gov/publications/esp/ reports.cfm. The full report was presented during an HSR&D Cyberseminar on August 27, 2019.

Electronic supplementary material The online version of this article (https://dot.org/10.1007/s11606-020-06256-5) contains supplementary material, which is available to authorized users.

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#### **PROTOCOL REGISTRATION:** PROSPERO; CRD42019132924

REYWORDS: opioid use disorder; buprenorphine; methadone; nalirexone; acute pain.

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#### BACKGROUND

Managing acute pain (such as from surgery or injury) in patients taking medications for opioid use disorder (OUD) can be difficult due to patients' increased pain sensitivity and higher opioid tolerance, as well as clinicians' fear that the use of an opioid during an acute pain episode could trigger an OUD relapse.1-3 The potential for serious adverse events when methadone and buprenorphine/naloxone (referred to as buprenorphine for brevity) are changed or combined with additional opioids adds to the complexity of acute pain management. Methadone (a full opioid agonist) can cause serious, unpredictable effects such as respiratory depression or overdose when the dose is changed or when other opioids are added.4, 5 Buprenomhine (a partial opioid agonist) partially activates these receptors and reduces the effect of other opioids. Both medications can cause withdrawal when discontinued.4, 6 Naltrexone (an opioid antagonist) blocks the effect of other opioids and is often administered in an extended-release injectable format which cannot be withdrawn or reversed in cases of unexpected acute pain.7,1

Guidance from professional societies such as the American Society of Addiction Medicine (ASAM) and the Periopentive Pain and Addiction Interdisciplinary Network (PAIN) suggests possible approaches to managing pain in OUD patients taking medications; however, these approaches are primarily based on expert consensus due to the paucity of available research.<sup>9,10</sup> For those taking methadone, the 2015 ASAM guidelines comment that higher doses of full opioid agonists in addition to methadone may be needed tor manage acute pain and that short-acting opioids may be needed for those undergoing surgery, cifing two observational studies.<sup>11, 12</sup> For those taking buprenophine, ASAM comments that temporarily increasing buprenophine dosing may JGIM paper summarizes 2019 ESP rapid review findings + updated search in April 2020



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**Key Question 1:** What are the benefits and harms of strategies to manage acute pain in adults taking medication for OUD?

Key Question 2: Do these benefits and harms vary by patient characteristics such as type of medication or type of acute pain (emergency condition vs planned surgery)?



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**Population:** Nonpregnant adults taking medication for OUD who have acute (sudden-onset, time-limited) pain

**Intervention:** Any pain management approach (*e.g.*, OUD medication discontinuation or dose change, use of other opioid, or non-opioid therapies)

#### **Comparator:** Any

Outcomes: Pain severity, pain-related function, quality of life, patient satisfaction, healthcare utilization, opioid withdrawal symptoms, substance use relapse, opioid overdose, suicidal ideation and suicidal self-directed violence, other adverse events

#### Timing, Setting, Study Design: Any







**Search:** MEDLINE, PsycINFO, CINAHL, and CENTRAL (inception through April 2020) and consulted with experts

> Study selection: Based on eligibility criteria

> Data abstraction: Study characteristics (PICOs) and results

>Critical appraisal: Use of standardized tools

>Quality control: Assessments first completed by one reviewer and checked by at least one additional reviewer. Disagreements resolved by consensus.



## **12 Included Studies**

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- No systematic reviews or RCTs
- No studies among Veterans.
- 3 observational studies with control groups & 9 observational studies with no control groups.
- Most examined buprenorphine or methadone- only 1 case study examined naltrexone.





# 3 Controlled Studies: Overview



- Provide the best available evidence, although evidence is indirect.
- Characteristics of 3 controlled studies-
  - Study type: All retrospective cohort
  - # of participants: 236
  - Follow-up: 24 hours 2 years
  - **Populations:** Primarily surgical patients
  - Comparisons:
    - 1 compared pain management in pts taking methadone vs. buprenorphine
    - 2 compared pain management in pts taking methadone or buprenorphine vs. non-OUD patients.
  - Interventions: Summaries of the % of patients who received certain medications
  - Outcomes: Pain, functionality, quality of life, length of hospital stay, adverse events



### MacIntyre 2013:

- Compared pts who were undergoing surgery taking methadone vs. buprenorphine.
- ½ to ¾ of pts received their OUD medication the day after surgery; similar, high doses of opioids in both groups; both groups used adjuvant analgesics.
- Methadone and buprenorphine pts, and those that did and did not receive OUD medications the day after surgery, were similar in terms of pain, functionality, and adverse events (nausea, vomiting, sedation).
   However, those who didn't receive usual dose the day after surgery used more patient-controlled analgesia for longer periods of time than those who did receive their usual dose.
- <u>Major limitations</u>: Some differences between groups at baseline & unclear why some pts had OUD medications discontinued after surgery.

### • Hansen 2016:

- Compared pts undergoing knee & hip surgery taking methadone or buprenorphine vs. those without OUD
- Unclear if OUD medications were continued; OUD medication group received 8x opioid dosage at discharge; similar use of adjuvant analgesics.
- Similar pain, functionality, and quality of life at 6 weeks and 1 year, except OUD medication group had worse knee range of motion at 1 year compared to those without OUD.
- <u>Major limitations</u>: Unclear if OUD medications were continued for all, some or no patients, and no subgroup analysis by medication type.



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#### • Hines 2008

- Compared pts with surgical or acute condition taking methadone vs. non-OUD pts.
- 12% of methadone pts had dose increased; similar opioid doses; similar use of adjuvant analgesics.
- Similar reports of pain in both groups. However, pts taking methadone had longer hospital stays, and were more likely to have behavioral problems, discharge against medical advice, and transfer to another hospital.
- <u>Major limitations</u>: Pain assessments based on how often the word "pain" appears in a patient's ward notes, unclear why some patients had methadone dose increased.



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#### Lessons learned:

- Continuing the use of buprenorphine and methadone for patients with OUD after surgery may reduce the need for additional opioids.
- Patients taking medication for OUD are opioid-tolerant and need higher doses of opioid agonists for effective pain control compared to patients without OUD.
- Ineffective management of acute pain in OUD patients taking methadone can lead to disengagement in care.

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These studies have **major** methodological limitations, including:

- Pain management strategies not adequately described (*i.e.*, timing, dosage)
- Inadequate methods used to assess pain severity outcomes
- Few studies reported other patient-important outcomes



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# 9 Uncontrolled Studies

- ESP Evidence Synthesis Program
- Study characteristics: 2 case series & 7 case studies (# of participants=14)
- What these studies add:
  - Additional causes of acute pain (ie, emergency conditions)
  - Naltrexone
  - More detailed descriptions of timing, dosage, and sequence of acute pain management
- Lessons learned: Tramadol may be used to manage pain in patients on extended-release naltrexone undergoing planned surgery.
- Limitations: These studies have critical methodological limitations, including:
  - No control groups
  - Small number of participants
  - Rarely using measurement tools to assess outcomes
  - High risk of both selection and reporting bias



See reference slide for list of uncontrolled studies





- This review confirmed there is a lack of rigorous evidence on the management of acute pain in patients taking methadone, buprenorphine, or naltrexone.
- Although limited, the best available evidence suggests that continuing methadone or buprenorphine during an acute pain episode is preferable to discontinuing these medications.
- More research is needed that evaluates patient outcomes following wellcharacterized acute pain management interventions including OUD medication dose and schedule adjustments and use of adjunctive non-opioid pain management strategies.



# Citations for 12 Included Studies



#### **3 Controlled Studies:**

- MacIntyre PE, Russel RA, Usher KAN, Gaughwin M, Huxtable CA. Pain relief and opioid requirements in the first 24 hours after surgery in patients taking buprenorphine and methadone opioid substitution therapy. Anaesth Intensive Care. 2013;41:222-230.
- Hansen LE, Stone GL, Matson CA, et al. Total joint arthroplasty in patients taking methadone or buprenorphine/naloxone preoperatively for prior heroin addiction: A prospective matched cohort study. J Arthroplasty. 2016;31(8):1698-1701.
- Hines S, Theodorou S, Williamson A, Fong D, Curry K. Management of acute pain in methadone maintenance therapy in-patients. Drug Alcohol Rev. 2008;27(5):519-523

#### 9 Uncontrolled Studies:

- Barelli R, Morelli Sbarra G, Sbaraglia F, Zappia L, Rossi M. Prevention of post-operative hyperalgesia in a heroin-addicted patient on methadone maintenance. J Clin Pharm Ther. 2019;44(3):397–399.
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## **Operational Partners**

Operational partners are system-level stakeholders who have requested the ESP report to inform decision-making. They recommend TEP members; assure VA relevance; help develop and approve final project scope and timeframe for completion; provide feedback on draft report; and provide consultation on strategies for report dissemination.

William Becker, MD Director, Opioid Reassessment Clinic VA Connecticut Healthcare System

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