

Opioid Dose Reduction in Patients Prescribed Long-term Opioid Therapy for Chronic Pain

Travis Lovejoy, PhD, MPH

Center to Improve Veteran Involvement in Care (CIVIC),
VA Portland Healthcare System

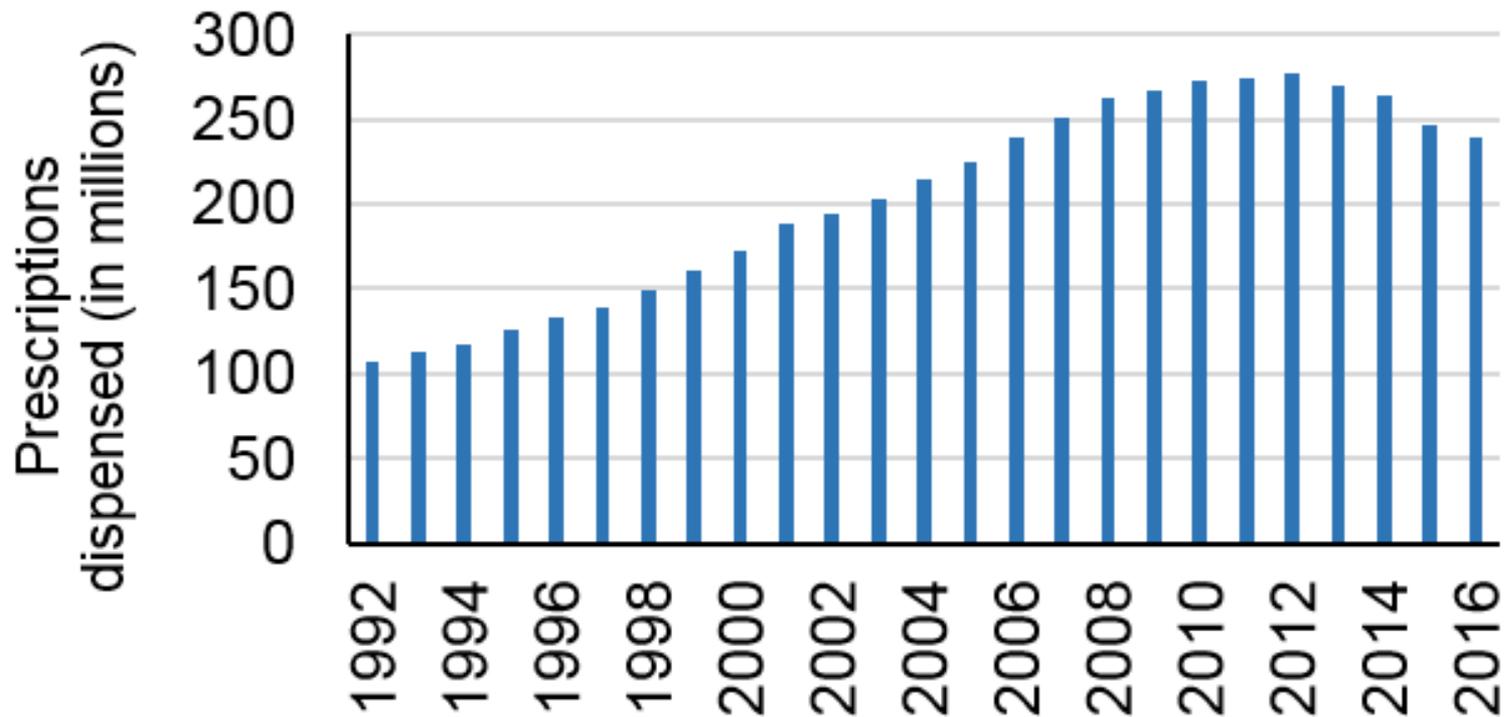
Disclosures and Conflicts of Interest

I have no financial, personal, or other relationships that would cause conflicts of interest with the information reported here.

Overview

- Background on opioid tapering and discontinuation
- Results of a study examining care process and patient outcomes following complete opioid discontinuation
- Clinical approaches to opioid taper and discontinuation

Opioid Prescriptions Dispensed in the U.S. Annually, 1992-2016



Pezalla et al., 2017

Why might this be?

- Clinical practice guidelines (VA/DoD, CDC, APS/AAPM)
- Greater awareness of the opioid “epidemic” through media portrayals (Borwein et al., 2013)
- Limited evidence of the long-term efficacy of opioid therapy for chronic non-cancer pain (Abdel et al., 2016)
- Significant risk of adverse harms (Chou et al., 2015)
- Monitoring for aberrant behaviors (e.g., PDMPs)
- Local, state, and national initiatives to increase safer opioid prescribing

Patient outcomes following opioid taper or discontinuation

- Systematic review (Frank et al., Epub ahead of print)
 - 36 studies that assessed pain intensity outcome, 17 functioning, and 12 quality of life
 - All were observational studies of poor quality, a few were fair quality
- Among fair quality studies, opioid dose reduction was associated with reduced pain intensity and improved functioning and quality of life
- Many patients received interdisciplinary pain treatment concurrent with taper

Unintended negative consequences of opioid taper and discontinuation

- Substitution of heroin or other substances for prescription narcotics (Compton et al., 2016)
- Onset of new, or exacerbation of existing, mental health symptoms (Demidenko et al., 2017)
- Negatively impact relationships between patients and members of their clinical care teams (Frank et al., 2016)
- Patients discontinue care (Lovejoy et al., 2017)

Poll Question

What is your primary role?

- A. Clinician – Prescriber
- B. Clinician – Non-prescriber (e.g. PT, OT, psychologist)
- C. Researcher
- D. Administrator

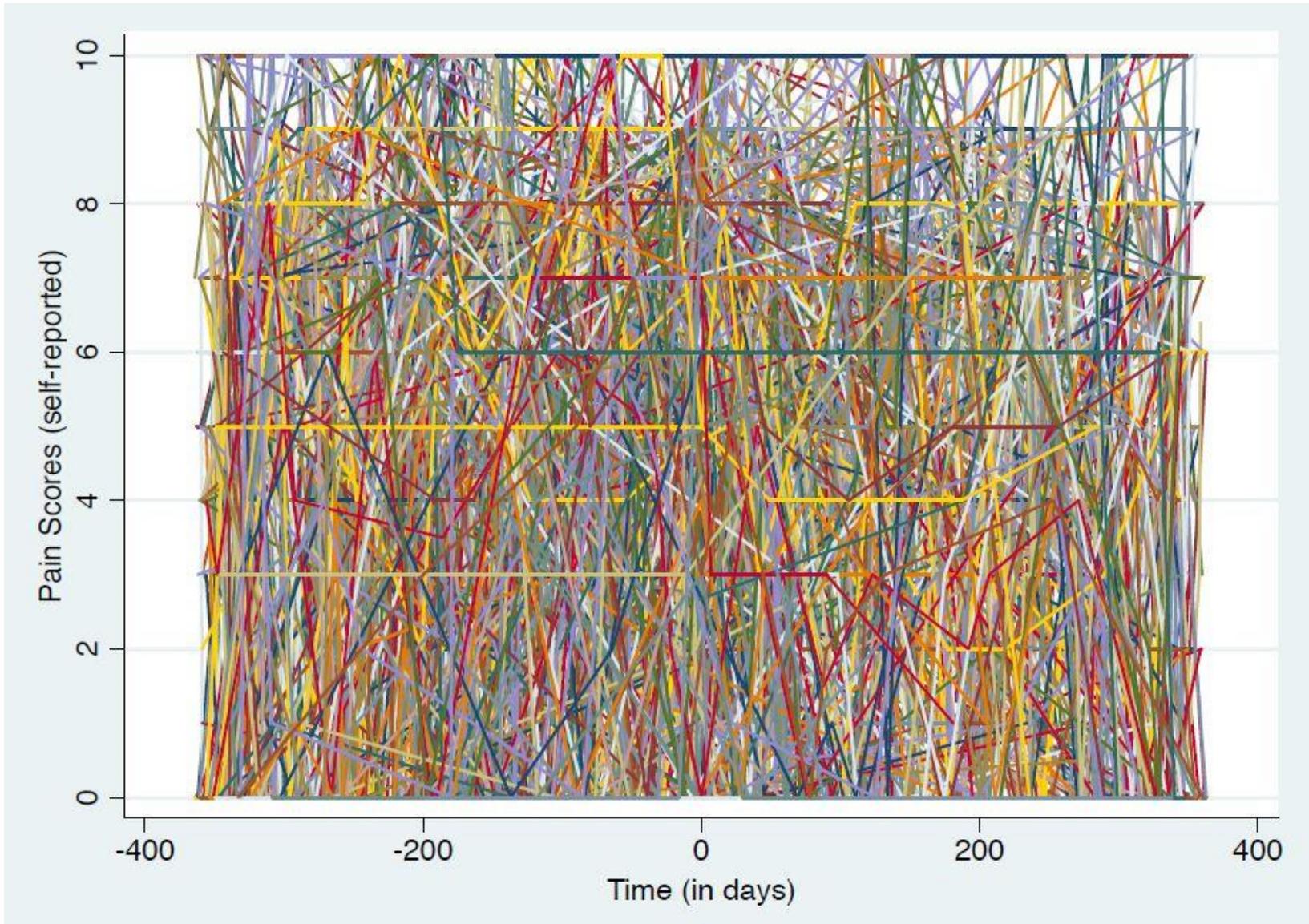
Study of opioid discontinuation in Veterans with and without substance use disorders

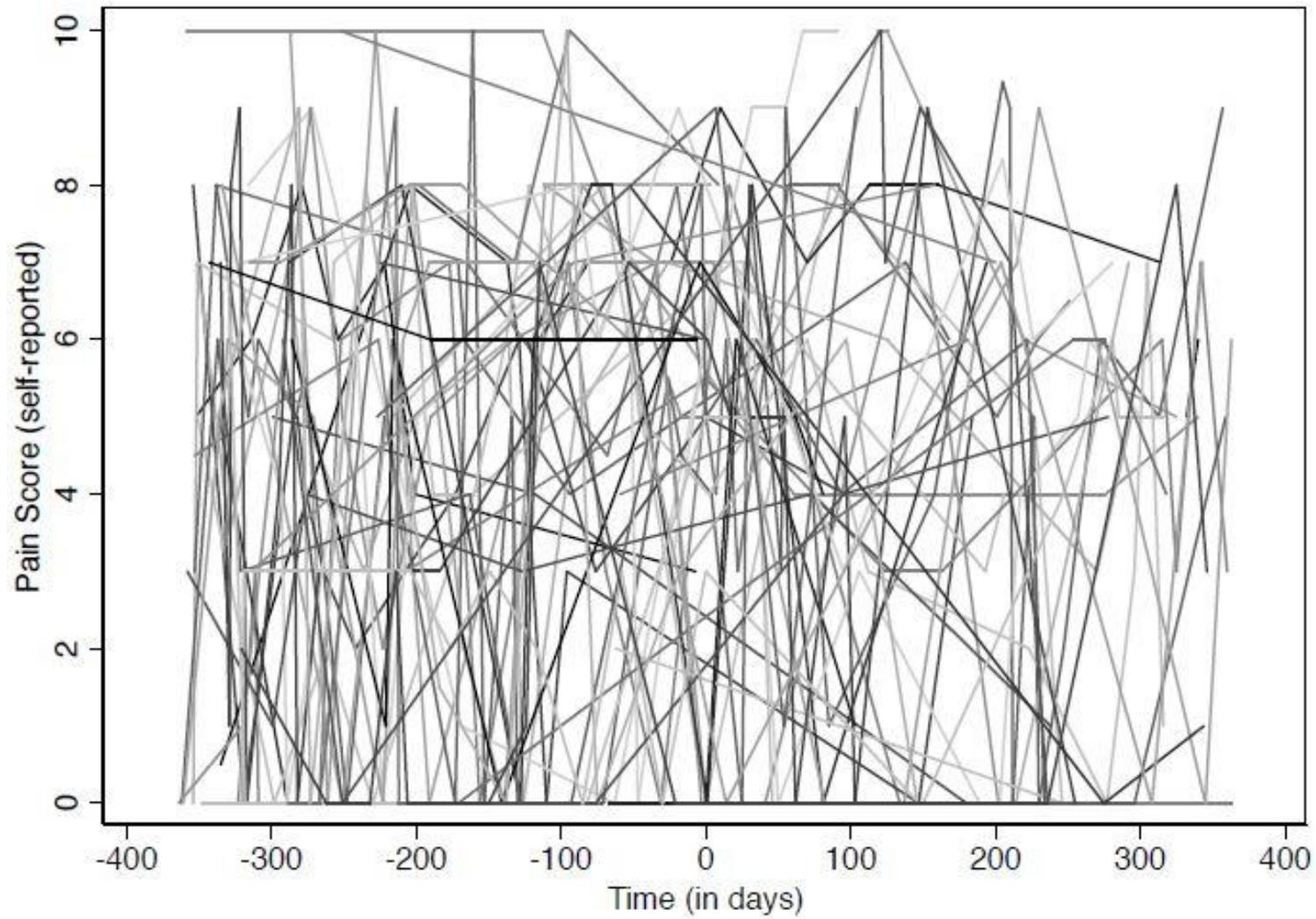
- Retrospective electronic medical record review and administrative data abstraction
- Cohort of Veterans prescribed LTOT through VA in 2011
- Discontinued LTOT in 2012
- Randomly sampled 300 with SUD diagnosis
- Propensity score matched 300 without SUD diagnosis

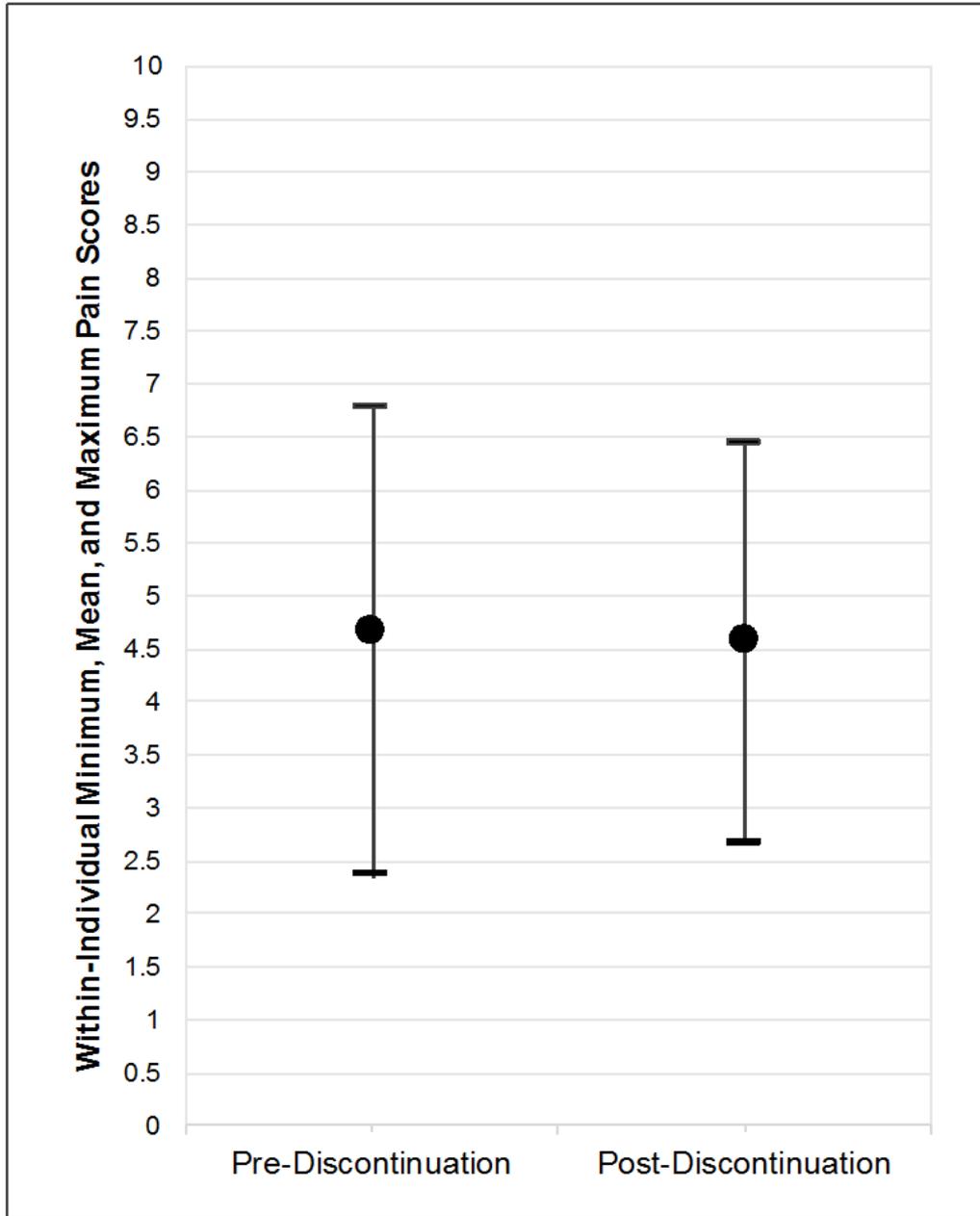
Likelihood of LTOT discontinuation between patients with and without SUD, n = 600

Discontinuation Reason	SUD, % (n)	No SUD, % (n)	Unadjusted odds ratio (95% confidence interval)	Adjusted odds ratio (95% confidence interval)
<u>Aberrant behaviors</u>	70% (211)	57% (171)	1.79 (1.28-2.51)*	1.93 (1.34-2.80)*
Known or suspected substance abuse	52% (157)	35% (105)	2.04 (1.47-2.83)*	2.26 (1.58-3.22)*
Aberrant urine drug test	39% (118)	35% (105)	1.20 (0.86-1.68)	1.21 (0.85-1.73)
Opioid misuse	18% (53)	13% (39)	1.44 (0.92-2.25)	1.31 (0.80-2.14)
Nonadherence to pain plan of care	9% (27)	14% (41)	0.63 (0.37-1.05)	0.59 (0.33-1.04)
Known or suspected opioid diversion	5% (14)	2% (7)	2.05 (0.82-5.15)	1.65 (0.61-4.48)

*Estimate significant at the $P < 0.05$ level







Pain intensity following discontinuation of LTOT

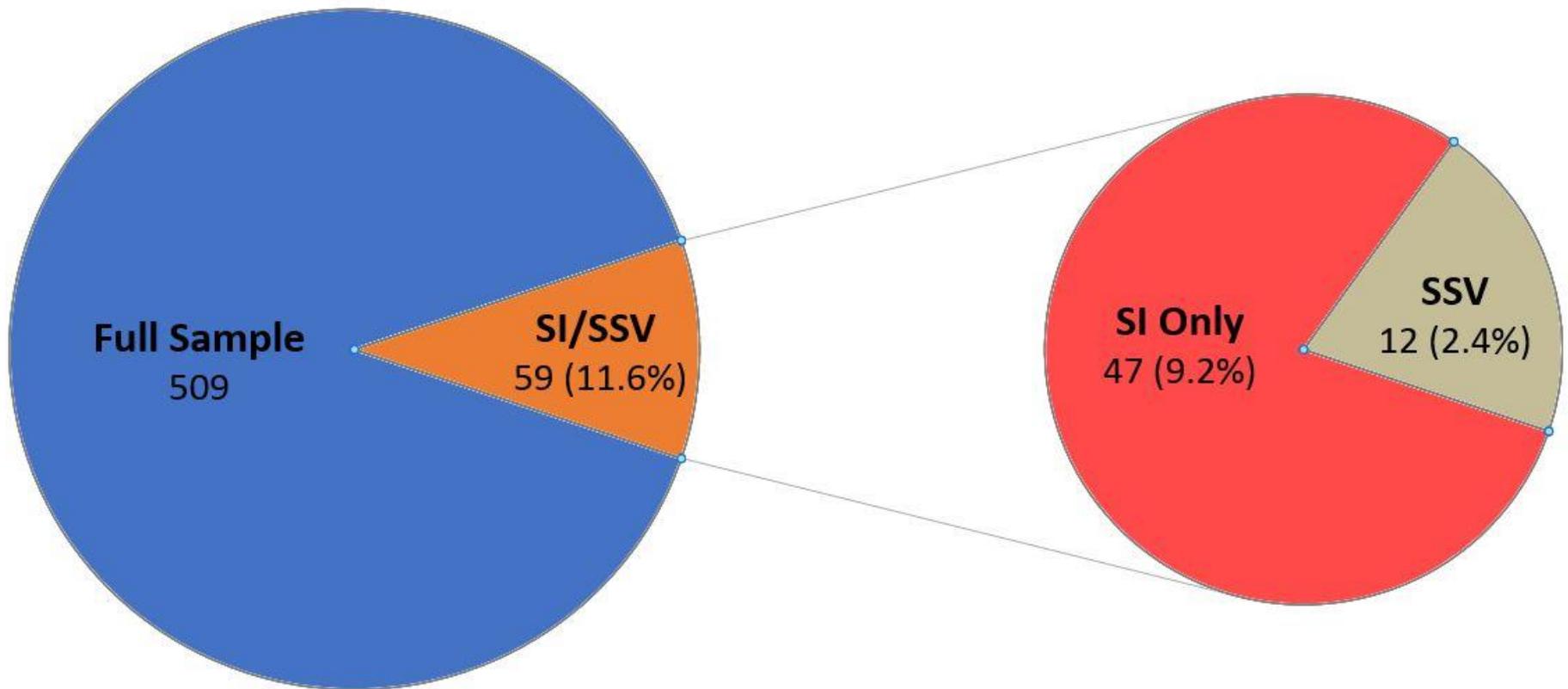
	At time of Discontinuation B (SE)	Change over 12 months B (SE)
Pre-discontinuation pain	0.61 (0.06) *	-0.02 (0.01) *
Patient reason for LTOT discontinuation	-1.16 (0.36) *	0.04 (0.05)

* $p < 0.05$.

Adjusted models controlled for age, gender, race, and pre-discontinuation mental health and SUD diagnoses, pain treatment utilization, medical comorbidity, and LTOT discontinuation reason.

- Pain rating of 4.68, on average across patients, at the time of discontinuation
- Decrease in pain intensity of 0.25 points on average in the year following discontinuation of LTOT (non-statistically significant)

Suicidal ideation and suicidal self-directed violence in patients discontinued from LTOT by the opioid-prescribing clinician

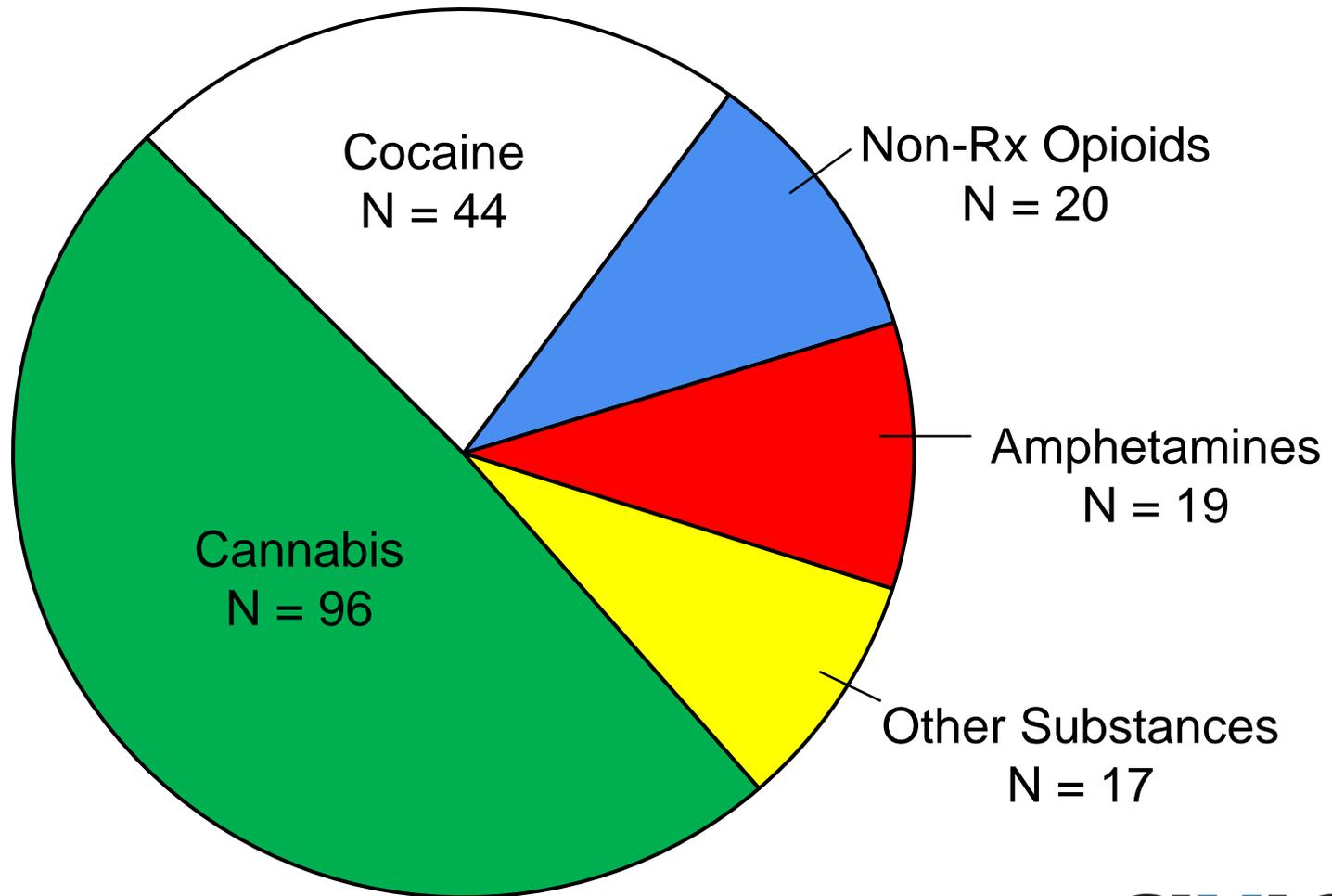


New onset suicidal ideation or suicidal self-directed violence following LTOT discontinuation by the opioid-prescribing clinician, n = 509

	Model 3
Mental health diagnoses	
Depressive disorder	0.93 (0.38–2.31)
Bipolar disorder	0.28 (0.03–2.37)
PTSD	3.78 (1.41–10.14)*
Other anxiety disorders	1.06 (0.43–2.60)
Psychotic-spectrum disorders	6.72 (1.73–26.17)*
Substance use disorder diagnosis	0.86 (0.39–1.87)
Prescribed benzodiazepine in the year prior to discontinuation	0.73 (0.21–2.59)
Average MEDD in the year prior to discontinuation	1.00 (1.00–1.01)

* p < 0.05.

LTOT discontinuation due to a positive urine drug test



Likelihood of SUD treatment referral and engagement following substance-related LTOT discontinuation

Substance leading to discontinuation	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Association with SUD treatment clinician referral		
Cannabis	0.53 (0.28–0.98)	0.44 (0.23–0.84)
Cocaine	2.73 (1.35–5.53)	3.32 (1.57–7.06)
Association with SUD treatment engagement		
Cannabis	0.53 (0.25–1.13)	0.42 (0.19–0.94)
Cocaine	1.76 (0.78–3.94)	2.44 (1.00–5.96)

*Adjusted models controlled for age, gender, race, pre-discontinuation mental health diagnosis, and pre-discontinuation SUD diagnosis.

Limitations

- Data obtained exclusively from the electronic medical record likely underestimates prevalence of some clinical phenomena (e.g., SI, SUD)
- Focused on patients at risk of discontinuation due to aberrant behaviors (SUD and matched controls)
- Conservative definitions of LTOT and discontinuation were applied
- Discontinuation occurred in 2012 and may not capture the full spectrum of discontinuation reasons in more contemporary samples

Conclusions

- There may not be a clear “risk profile” for patients who will engage in opioid-related aberrant behaviors
- Little change in pain following LTOT discontinuation
- Other adverse outcomes may be present, such as onset of new or exacerbation of existing mental health symptoms
- Differential approaches to treatment based on the type of substance use that leads to discontinuation

Acknowledgments

- Collaborators

- Steven Dobscha, MD
- Benjamin Morasco, PhD
- Sterling McPherson, PhD
- Joe Frank, MD, MPH
- Mark Ilgen, PhD
- Shannon Nugent, PhD
- Jessica Wyse, PhD
- Michael Demidenko, BS
- Thomas Meath, MPH
- Julia Holloway, BS
- Crystal Lederhos Smith, MS

- Funding

- Locally Initiated Project Award # QLP 59-048 (PI: Lovejoy) from the United States (U.S.) Department of Veterans Affairs Substance Use Disorder Quality Enhancement Research Initiative
- Career Development Award IK2HX001516 from the U.S. Department of Veterans Affairs Health Services Research and Development (PI: Lovejoy).

References

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 Int Med.* 2016;176:958-968.

Borwein A, Kephart G, Whelan E, Asbridge M. Prescribing practices amid OxyContin crisis: examining the effect of print media coverage on opioid prescribing among physicians. *J Pain.* 2013;14:1686-1693.

Chou R, Turner JA, Devine EB, Hansen RN, Sullivan SD, Blazina I, Dana T, Bougatsos C, Deyo RA. 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 Int Med.* 2015;162:276-286.

Compton WM, Jones CM, Baldwin GT. Relationship between nonmedical prescription-opioid use and heroin use. *N Engl J Med.* 2016;374:154-163.

Demidenko MI, Dobscha SK, Morasco BJ, Meath THA, Ilgen MA, Lovejoy TI. Suicidal ideation and behaviors following clinician-initiated prescription opioid discontinuation among long-term opioid users. *Gen Hosp Psychiatry.* 2017;47:29-35.

Frank JW, Levi C, Matlock DD, Calcaterra SL, Mueller SR, Koester S, Binswanger IA. Patients' perspectives on tapering of chronic opioid therapy: a qualitative study. *Pain Med.* 2016;17:1838-1847.

Frank JW, Lovejoy TI, Becker WC, Morasco BJ, Koenig CJ, Hoffecker L, Dischinger HR, Dobscha SK, Krebs EE. Patient outcomes in dose reduction or discontinuation of long-term opioid therapy: a systematic review. *Ann Intern Med.* July 18, 2017. Epub ahead of print.

Lovejoy TI, Morasco BJ, Demidenko MI, Meath THA, Frank JW, Dobscha SK. Reasons for discontinuation of long-term opioid therapy in patients with and without substance use disorders. *Pain.* 2017;158:526-534.

Pezalla EJ, Rosen D, Erensen JG, Haddox JD, Mayne TJ. Secular trends in opioid prescribing in the USA. *J Pain Res.* 2017;10:383-387.

Tapering/Discontinuing Long-Term Opioid Therapy (LTOT) for Chronic Pain: Why, When, How

William C. Becker, MD

Assistant Professor, General Internal Medicine

VA Connecticut Healthcare System

Yale University School of Medicine

July 26, 2017



I have no conflicts of interest related to the content of this presentation.

Poll Question

Complex chronic pain and related opioid issues are:

- A) The most challenging thing I treat clinically
- B) Among the most challenging things I treat
- C) Sometimes challenging, sometimes not
- D) Not particularly challenging
- E) Downright easy
- F) N/A; I'm not a clinician

When to taper

- Clinicians should taper or wean patients off of COT who engage in repeated aberrant drug-related behaviors or drug abuse/diversion, experience no progress toward meeting therapeutic goals, or experience intolerable adverse effects. (AAPM/APS, 2009)
- 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. (CDC, 2016)

Special Communication

**CDC Guideline for Prescribing Opioids for Chronic Pain—
United States, 2016**

Deborah Dowell, MD, MPH; Tamara M. Haegerich, PhD; Roger Chou, MD

Benefit vs. harm

Evaluation of this balance fundamental to every (pharmaco)therapy we provide.

Acting on the results of the evaluation in a patient-centered yet decisive way is our duty.

Assessing benefit

- Goal of LTOT for chronic pain: *Maintain or improve function; reduce pain-related functional interference.*
- Recommendations:
 - Establish specific, measurable, action-oriented, realistic, time-bound goals with the patient and frequently monitor over time.
 - Use a validated measure of pain-related functional interference (e.g. the 3-item PEG¹) and follow over time.
- Observe and listen to the patient; observe and listen to the patient's companions.

¹Krebs EE et al. JGIM, 2009.

Assessing harm/safety

- Typically early in therapy or with dose escalation: constipation, nausea/vomiting, sedation/drowsiness, mental clouding, itching, euphoria/dysphoria → *ask explicit questions*
- Usually longer-term: hypogonadism, osteoporosis, hyperalgesia, worsened sleep apnea, declining function, anhedonia/MDD, opioid use disorder → *chart review, detailed assessment*
- Concerning behaviors/use inconsistent with treatment agreement → *urine drug testing, querying prescription drug monitoring program*
- Always highly relevant: falls, motor vehicle accidents, overdose → *ask explicit questions, chart review*

Morphine equivalent dose

- Method of standardizing potency across various opioid compounds
- Based on equianalgesic tables from dose ranging studies

- Example:
20 mg oxycodone TID
=
90 mg morphine
equivalent daily dose

Equianalgesic dose (MG)	Opioid (oral)
30	Morphine
7.5	Hydromorphone
20	Oxycodone
30	Hydrocodone

Odds of overdose by increasing dose



	Dunn	Gomes	Bohnert
Dose* (mg/day)	HR (95% CI)	OR (95% CI)	HR (95% CI)
1-<20	1.00 (REF)	1.00 (REF)	1.00 (REF)
20-<50	1.2 (0.4-3.6)	1.3 (0.9-1.8)	1.9 (1.3-2.7)
50-<100	3.1 (1.0-9.5)	1.9 (1.3-2.9)	4.6 (3.2-6.7)
≥100 or 100-199	11.2 (4.8-26.0)	2.0 (1.3-3.2)	7.2 (4.9-10.7)
≥200		2.9 (1.8-4.6)	

*morphine equivalent

Dunn et al. Annals IM 2010; Gomes et al. Archives IM 2011; Bohnert et al. JAMA 2011

Slide courtesy of Joe Frank, MD

Opioid use disorder (DSM-5)

Physiologic sequelae

- Tolerance
- Withdrawal
- Opioid craving

Loss of control

- Greater amounts of use or longer period of use than intended
- Persistent desire but unsuccessful efforts to cut down
- Inordinate amount of time obtaining, using, or recovering

Adverse consequences

Summary of 5 criteria:

- Important social, occupational or recreational activities given up or reduced due to opioid use or recurrent opioid use despite physical or psychological problems caused or worsened by use

DSM-5 criteria vs. pain literature guided criteria

<u>DSM-5</u>	<u>Pain literature</u>
• Failure to fulfill major roles	• Multiple prescribers
• Use in physically hazardous situations	• Frequent ED visits
• Persistent interpersonal problems	• Multiple drug “allergies”
• Unsuccessful efforts to cut down	• Running out of meds early
• Great deal of time obtaining	• Frequent phone calls to clinic
• Giving up activities	• Prescription losses
• Craving	• Anger/temper with clinicians/staff
• Continued use despite knowledge of harm	

Identifying opioid use disorder

- Prescriber's role:
 - Partner with the patient
 - Be transparent/forthright/non-judgmental
- In the treatment agreement/signature informed consent:
 - I want to ensure your safety.
 - I will be monitoring [*in these ways*].
 - Specifically, I'm looking for [*safe use behavior*].
 - If you demonstrate lack of safety, it is my duty to stop the therapy and transition you to safer therapy.
- *If patient evidences recurrent problematic behavior, that suggests loss of control; OUD dx needs to be strongly considered.*

Weighing benefit vs. harm

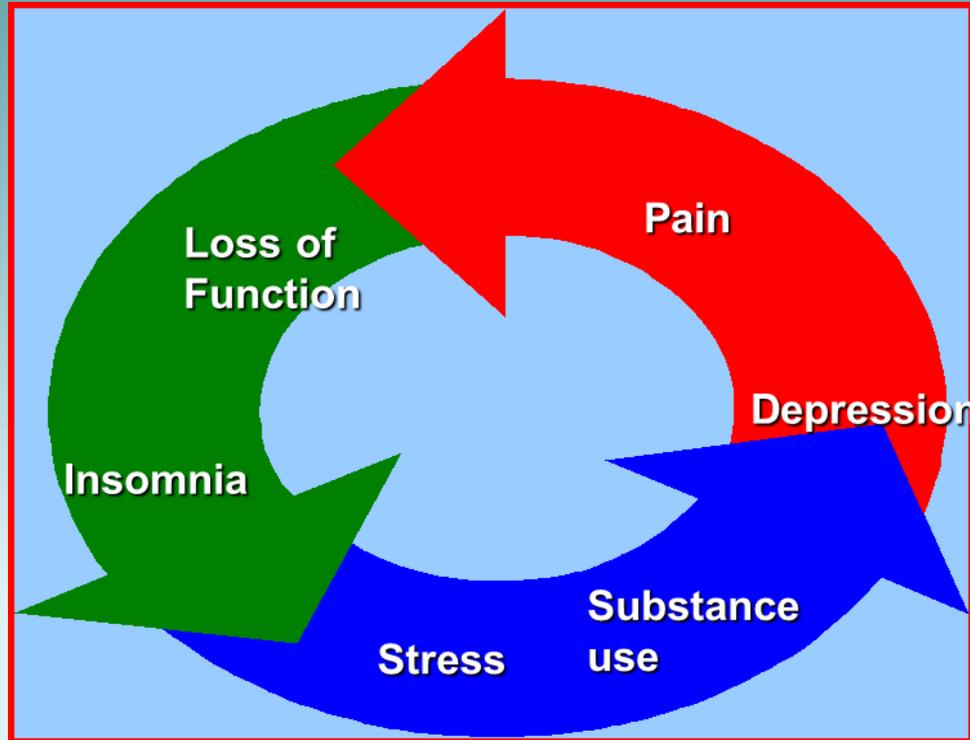
Prohibitive harm

- **Life-threatening harm:** non-fatal overdose, serious or recurrent fall, serious or recurrent motor vehicle accident. *Opioids must be tapered markedly and/or discontinued.*
- **Incident opioid use disorder.** *Opioids must be discontinued; pharmacotherapy for OUD should be offered/initiated.*
- **Hazardous drug/alcohol use that patient cannot discontinue and/or will not accept treatment for.** *Opioids should be discontinued.*

Prohibitive harm, cont'd

- Taper should be fast, e.g. 25% per week (or even per day).
- If recent rx, consider advising taper of supply patient already has on hand.
- In OUD → feasible, accessible linkage to evidence-based pharmacotherapy **mandatory**.
- We need to get better at seizing opportunities to transition patients to buprenorphine.

Benefit absent/negligible



- If benefit needs to outweigh harm to continue LTOT and benefit is absent, recommendation = taper.
- If patient disagrees with assessment of absent benefit, try to educate; unilateral taper decision may be necessary.

“Doing reasonably well” on high to ultra-high dose

- Decent, non-declining function
- Dose ≥ 90 mg MEDD; risk accumulating
- *At present time,* recommend bringing to bear all resources at your disposal to help patient choose to initiate a taper.
- *Involuntary taper not recommended*
- Increased vigilance for:
 - Opportunities to lower dose (esp. pts entering system)
 - Evident harm that is tipping balance towards necessary taper

Framing the low benefit conversation

- Empathic tone
- Concern
- Shared responsibility
- Optimism

“We know more about safety problems related to opioids and **we are concerned** about your health and safety. We recognize that we/the system prescribed you these medications so now **we want to help you be safer** while still managing your pain. The good news -- **many patients feel better** once they’re on lower doses.”

Tapering/discontinuing in low benefit

- Fairly limited evidence to guide¹
- Patients report increased willingness when offered empathy, support, reassurance, team-based approach^{2,3}
- Recommendations/observations:
 - Offer choice/flexibility when possible: e.g. which med would you like to decrease first? Which dose of the day could you most easily lower?
 - Almost no such thing as “too slow”
 - Success in each step down breeds success
 - Offer patients option to “pause” PRN

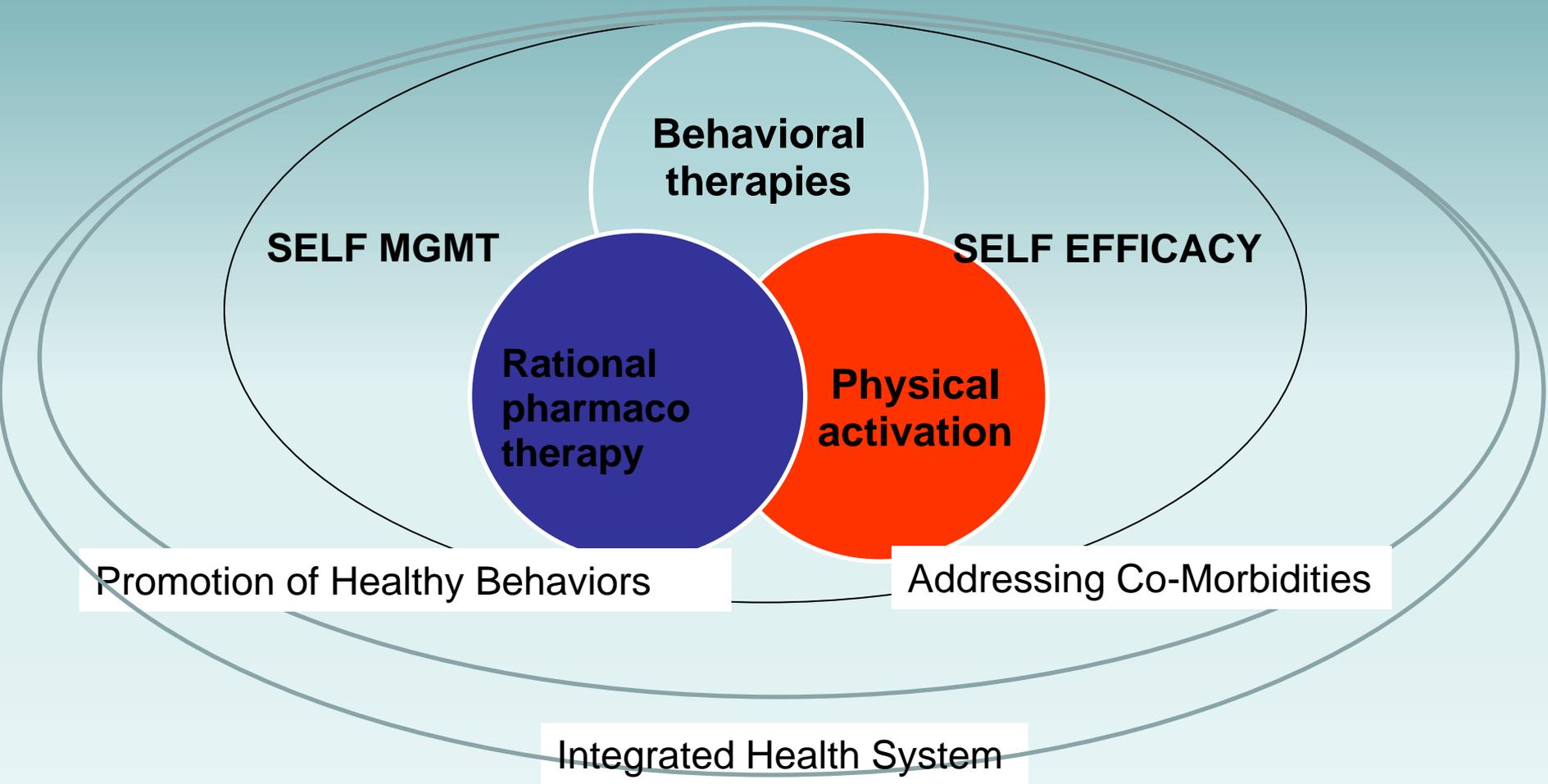
¹Frank, JW et al. Annals IM, 2017. ²Frank JW et al. Pain Medicine, 2016.

³Becker et al. BMC Family Practice, 2017.

Patient outcomes post-taper

- In 40 studies of 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)
 - Quality of life (3 of 3 fair-quality studies)

Evidence-based high value chronic pain care



Evidence-based non-pharmacologic treatments for chronic pain



Physical activation

- Structured exercise
- Physical therapy
- Yoga
- Tai Chi

Manual techniques

- Chiropractic
- Acupuncture

Behavioral treatments

- Cognitive behavioral therapy
- Mindfulness based stress reduction

Non-opioid pharmacologic options

- NSAIDs
- Acetaminophen
- Gabapentanoids (gabapentin, pregabalin)
- SNRIs (duloxetine, venlafaxine)
- Topicals (capsaicin, NSAIDs, lidocaine)
- *NB: many of these medications also have neurocognitive side effects; observe best practices in med management*

Optimizing treatment of co-occurring conditions

- Major depression, anxiety, other MH conditions
- Diabetes, OSA and other chronic conditions
- Substance use disorders

Team-based care/collaborative care

- PCPs strongly endorse need for support¹
- Integrated pain team (IPT) model:
 - Multidisciplinary: PCP/prescriber, Psychologist, Pharmacist, RN Case Manager, Physical Therapist
 - Time/space for more in depth assessment, closer follow-up
 - Biopsychosocial orientation, motivational interviewing stance
 - Assume pain care responsibilities on time-limited basis
 - Early evidence for dose lowering (SFVAHCS,² VACHS³)
- Collaborative care → Pharmacist or RN Care Manager collaborating with single or group of PCPs.
 - Narrower model than IPT but similar biopsychosocial orientation
 - More reliance on referrals for multi-modal care

¹Becker et al BMC Fam Pract, 2017. ²Grasso J et al. HSRD Nat'l Mtg, 2017.

³Becker et al. Pain Medicine, 2017.

Primary-care Integrated Pain Support

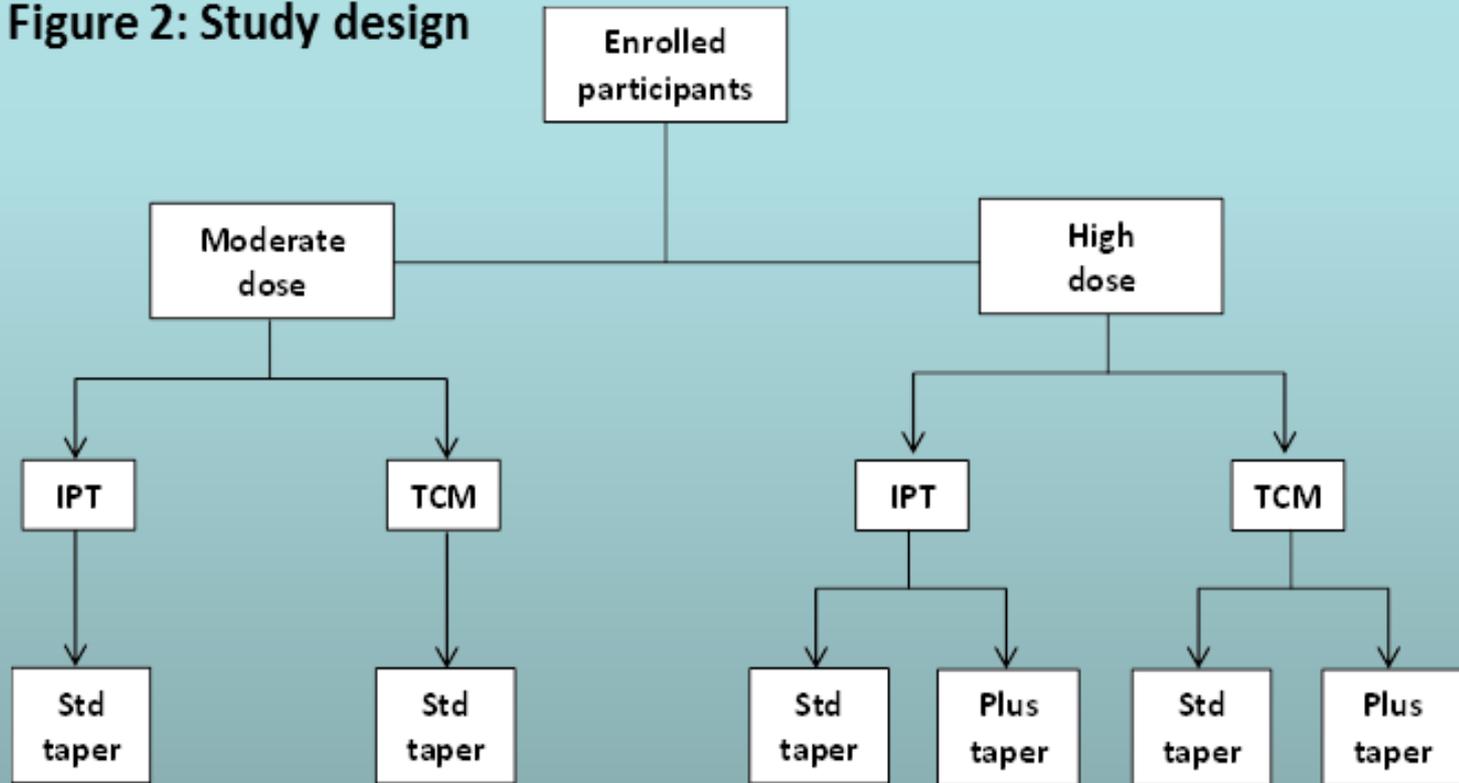
- Hybrid III implementation/effectiveness trial pharmacist-primary care provider collaborative care program to support voluntary reduction of high-risk opioid regimens and engagement with non-pharmacologic treatment

Site	Care team activated	Dashboard functional	Letters mailed	Consults initiated	Opioids/ opi + bzds
Denver	X	X	132	6	4/2
Little Rock	X	X	52	5	4/1
TN Valley	X	X	*	*	*

- Denver PCP: “I can’t imagine trying to do this without PIPS support”
- Little Rock Primary Care Chief: “Team-based care in action.”
- Denver patient: “I feel clearer...better.”

VOICE design

Figure 2: Study design



- Aim 1: Compare TCM vs IPT on improving pain and reducing opioid use
- Aim 2: To compare standard versus expanded taper options for reducing opioid use

Summary

- Opioids should be tapered/discontinued when benefit does not outweigh harm.
- Carefully and frequently assess benefit and harm.
- When to taper: 1) prohibitive harm; 2) absent benefit; 3) decent function but high dose; 1 & 2 can be involuntary *if necessary*; 3 should be voluntary.
- How to taper: Speed guided by degree of current harm; offer options when available; patient-centered; collaborative; bolster other multi-modal treatment
- Emergence of models of care that improve tapering rates

Thank you

*I'd be happy to take any non-marijuana
related questions.*

william.becker4@va.gov

References

- Krebs, E. E., et al. (2009). "Development and initial validation of the PEG, a three-item scale assessing pain intensity and interference." Journal of General Internal Medicine **24(6): 733-738.**
- Dunn, K. M., et al. (2010). "Opioid Prescriptions for Chronic Pain and Overdose." Annals of Internal Medicine **152: 85-92.**
- Gomes, T., et al. (2011). "Opioid dose and drug-related mortality in patients with nonmalignant pain." Archives of Internal Medicine **171(7): 686-691.**
- Bohnert, A. S. B., et al. "Association Between Opioid Prescribing Patterns and Opioid Overdose-Related Deaths." JAMA: 305(13): 1315-1321.
- Dowell, D., et al. (2016). "CDC guideline for prescribing opioids for chronic pain—United States, 2016." JAMA 315(15): 1624-1645.
- Ballantyne, J. C. and C. Stannard (2013). "New addiction criteria: Diagnostic challenges persist in treating pain with opioids." Pain 21: 1-7.
- Frank, J. W., et al. (2017). "Patient outcomes in dose reduction or discontinuation of long-term opioid therapy: A systematic review." Annals of Internal Medicine.
- Frank, J. W., et al. (2016). "Patients' perspectives on tapering of chronic opioid therapy: A qualitative study." Pain Medicine 17(10): 1838-1847.
- Becker, W. C., et al. (2017). "Barriers and facilitators to use of non-pharmacological treatments in chronic pain." BMC Family Practice 18(1): 41.
- Grasso J et al (2017). Implementation and evaluation of the IPT: pain outcomes, opioid safety, treatment satisfaction among veterans in primary care. Oral presentation, HSRD Nat'l Mtg. June 19, 2017.
- Becker, W. C., et al. (2017). "Evaluation of an Integrated, Multidisciplinary Program to Address Unsafe Use of Opioids Prescribed for Pain." Pain Medicine.

Resources

- <http://www.agencymeddirectors.wa.gov/Calculator/DoseCalculator.htm>
- The Opioid Therapy for Chronic Pain Work Group (2017). "VA/DoD CLINICAL PRACTICE GUIDELINE FOR OPIOID THERAPY FOR CHRONIC PAIN." Retrieved May 16, 2017, from <http://www.healthquality.va.gov/guidelines/Pain/cot/>.
- <https://www.cdc.gov/drugoverdose/prescribing/clinical-tools.html>
- https://www.pbm.va.gov/PBM/academicdetailingservice/Pain_and_Opioid_Safety.asp

QUESTIONS/COMMENTS?

Travis.Lovejoy@va.gov

william.becker4@va.gov