Embracing the Long-Term Use of Medications for Opioid Use Disorder

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The following session leader has no relevant financial relationships with ineligible companies to disclose:

- Clement Chen, PharmD

Learning Objectives

- Review literature supporting the benefits of medication for opioid use disorder (MOUD) in reducing morbidity and mortality
- Identify the role of shame in shaping the misconception of using medications for opioid use disorder long-term
- Examine recent literature providing empirical evidence for the long-term use of buprenorphine
- Develop key talking points to overcome patient resistance towards long-term MOUD
- Cite current research in the integration of evidence-based practices in communities hard hit by the opioid crisis

Poll Questions

1) A majority of my patients who are on medications for opioid use disorder expect to be on medications:
   a) Long-Term
   b) Short-Term
   c) Not Sure

2) My patients' **main** goal for being on MOUD is primarily to:
   1) Open-ended question

Review of Key MOUD Data

MOUD Reduces Mortality

Annals of Internal Medicine ORIGINAL RESEARCH

Medication for Opioid Use Disorder After Nonfatal Opioid Overdose and Association With Mortality

A Cohort Study

Marc R. Larochelle, MD, MPH; Dana Bernson, MPH; Thomas Land, PhD; Thomas J. Stopka, PhD, MHS; Na Wang, MA; Ziming Xuan, ScD, SM; Sarah M. Bagley, MD, MSc; Jane M. Liebschutz, MD, MPH; and Alexander Y. Walley, MD, MSc

- 17,568 opioid overdose survivors between 2012-2014

	Methadone	Buprenorphine	Naltrexone
All-Cause Mortality Compared to No MOUD **After 12 months**	63% reduction (CI 0.32-0.71)	37% reduction (CI 0.46-0.87)	No association (CI 0.84-2.46)
Duration of therapy	Median 5 months (IQR 2-9 months)	Median 4 months (IQR 2-8 months)	Median 1 month (IQR 1-2 months)
% of all patients receiving therapy	11%	17%	6%

Larochelle MR, et al. *Ann Intern Med.* 2018 Aug 7;169(3):13-45.

MOUD Reduces Mortality

- 15 RCTs and 36 primary cohort studies of about 750,000 participants across **different settings** documenting all-cause and cause-specific mortality
  - Rate of all-cause mortality during OAT was > ½ the rate seen during time out (RR 0.47;95% CI, 0.42-0.53) in cohort studies
    - Regardless of sex, age, geographic location, HIV and Hepatitis C status, route
    - Low risk of suicide, cancer, drug-related, alcohol-related, and cardiovascular-related mortality
- All-cause mortality was 6 times higher in the first 4 weeks after MOUD discontinuation (RR 6.01; 95% CI, 1.50-2.18)
  - Remained at nearly 2 times the rate while not receiving MOUD (RR, 1.81; 95% CI, 1.50-2.18)

Santo Jr, T, et al. *JAMA Psychiatry.* 2021 Sep 1;78(8)979-93.

Retention with MOUD

- Systematic review of 55 studies from 2010-2014
- Patients who received naltrexone or buprenorphine had better 6-month retention rates vs. placebo or no medication
- Methadone associated with better 6-month retention than buprenorphine
- Only one single study examined retention in MOUD for longer than one year

Studies mostly looked at 4-week, 3-month, 6-month retention

Timko C, et al. *J Addict Dis.* 2016;35(1):22-35.

MOUD Benefits in Reducing Opioid Harm

41000 individuals

Most common pathways:

1) **Nonintensive behavioral health (59%)**
2) **Inpatient detoxification or residential services (16%)**
3) **Buprenorphine or Methadone (13%)**

Table 2. Adjusted Hazard Ratios for Overdose and Serious Opioid-Related Acute Care Use by Initial Treatment Group Compared With No Treatment[a]

Variable	Adjusted Hazard Ratio (95% CI)	
	3 Months	12 Months
Overdose		
No treatment	1 [Reference]	1 [Reference]
Inpatient detoxification or residential services	0.82 (0.57-1.19)	1 (0.79-1.25)
BH IOP	0.81 (0.50-1.32)	0.75 (0.56-1.02)
MOUD treatment with buprenorphine or methadone	0.24 (0.14-0.41)	0.41 (0.31-0.55)
MOUD treatment with naltrexone	0.59 (0.29-1.20)	0.73 (0.48-1.11)
BH other	0.92 (0.67-1.27)	0.69 (0.56-0.85)
ED or inpatient stay		
No treatment	1 [Reference]	1 [Reference]
Inpatient detoxification or residential services	1.05 (0.76-1.45)	1.20 (0.96-1.50)
BH IOP	0.84 (0.54-1.30)	0.90 (0.67-1.20)
MOUD treatment with buprenorphine or methadone	0.68 (0.47-0.99)	0.74 (0.58-0.95)
MOUD treatment with naltrexone	1.15 (0.69-1.92)	1.07 (0.75-1.54)
BH other	0.59 (0.44-0.80)	0.60 (0.48-0.74)

Treatment duration was short: mean treatment duration for naltrexone was 74 days and 150 days for buprenorphine or methadone.

Wakeman SE, et al. *JAMA Netw Open.* 2020;3(2):e1920622

Retention with MOUD – Psychosocial and Behavioral Therapy in Conjunction

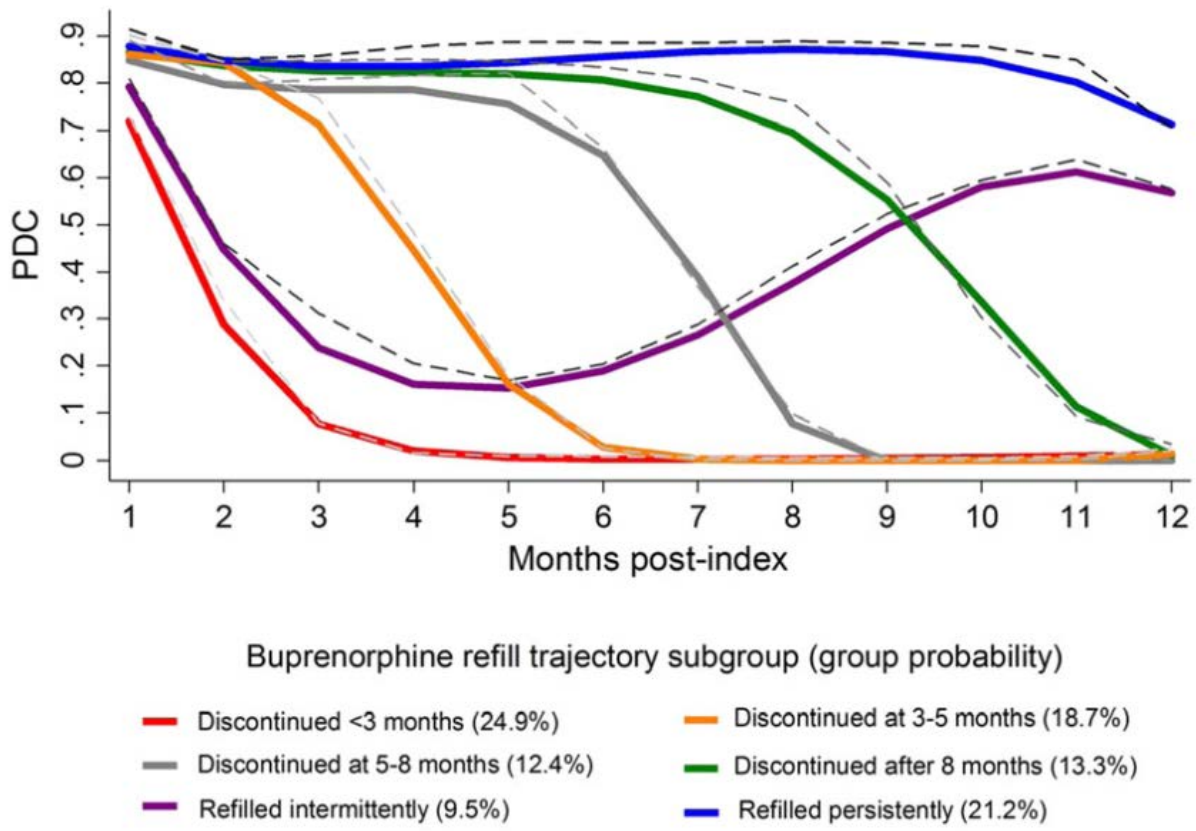
- **Aim:** Define patterns of OUD-related psychosocial and behavioral therapy services received in first 6 months of Analysis of buprenorphine initiation
- Medicaid claims data from 2013-2018
- Three trajectories: None, low-intensity, and high-intensity
- Low-intensity and high-intensity services associated with more comorbidities (behavioral health and medical treatment for opioid overdose prior to initiation of buprenorphine)
- Patients in the high-intensity therapy group had greater risk for opioid-related health care events during buprenorphine treatment (HR = 1.29; 95% CI, 1.01-1.64) vs. no therapy
- **Conclusion:** Providing therapy may help retain patients in treatment

Table 2. Adjusted hazard of buprenorphine discontinuation in the first 6 months of treatment.

	Unweighted			Weighted		
	HR	95% CI	p-Value	HR	95% CI	p-Value
No therapy	Reference			Reference		
Low-intensity therapy	0.55	0.53, 0.57	<0.001	0.55	0.54, 0.57	<0.001
High-intensity therapy	0.61	0.58, 0.63	<0.001	0.71	0.67, 0.74	<0.001

Samples H, et al. *J Subst Abuse Treat.* 2022 Mar 18;108774.

Trajectory of Buprenorphine Use



- Persistent refill trajectory associated with **18% lower risk of all-cause hospitalizations** (HR=0.82; CI 0.70-0.95) and **14% lower risk of ED visits** (HR=0.86, CI=0.78-0.95) in the following year, compared to those who stopped medications between 3-5 months.

PDC = proportion of days covered

Lo-Ciganic WH, et al. *Addiction.* 2016 May;1111(5):892-902

Key Points from Mortality Studies

- MOUD is evidence-based to reduce mortality in patients with OUD
- Optimal duration of therapy not well defined as many studies had short treatment durations to evaluate clinical outcomes in those patients who are taking MOUD beyond 6 months
- 6 months duration threshold endorsed by the National Quality Forum and based on expert consensus
  - Limits to duration may be placed by insurance

Williams AR, et al. *Am J Psychiatry.* 2020 Feb 1;177(2):117-24.

What’s causing the push for short-term MOUD?

Overcoming Myths

- **MOUD replaces one addiction with another**

- **MOUD is a bad moral choice. It is inferior to recovery without medication**

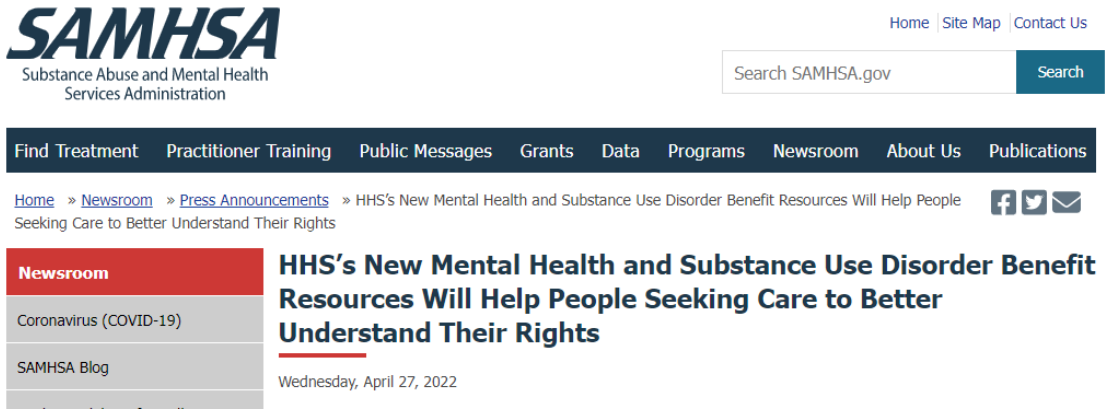
https://pcssnow.org/resource/myths-and-misconceptions-medications-for-opioid-use-disorder-moud/

Reasons for Discontinuation

- Stigma / distrust
- Expense
- Time
- Insurance restrictions (180 days max?)
- The perception that non-abstinence-based addiction recovery is not valid
- Lack of psychosocial and behavioral therapy
- Not understanding rights (ADA and new SAMHSA guidance)

- Other specific factors affecting treatment retention:
  - Younger age
  - Substance use with cocaine and heroin/HPSOs
  - Lower dose of methadone
  - Criminal activity/incarceration
  - Negative attitudes

- https://www.ada.gov/opioid_guidance.pdf



- https://www.samhsa.gov/newsroom/press-announcements/20220427/hhs-new-mental-health-substance-use-disorder-benefit-resources

Graves RL, et al. 2019. http://dx.doi.org/10.1101/971608.
O'Connor AM, et al. *PLoS One*. 2020.

Stigma → Effects on Shame

Shame: “I am bad” (limbic system)

Guilt: “I did something bad” (prefrontal cortex)

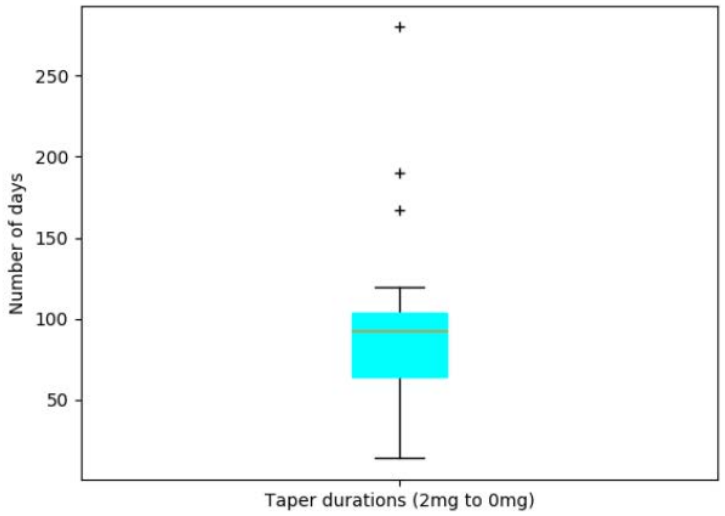
- Shame is:
  - Contagious
  - Grows stronger with secrecy, silence and judgment
  - Leads to a downward spiral of further shameful behavior
  - Correlated with addiction, depression, violence/aggression (highest shame), bullying, suicide, eating disorders
    - (Those are inversely correlated with guilt))

Attempts to Taper – Reddit Analysis of Buprenorphine-Related Posts

- **Over 16,000 posts to Reddit**
  - **Tapering, withdrawal symptoms, and adjunctive substances/behaviors for tapering**
- **Found tapering schedules were even longer than those in medical literature**
- **Challenge of tapering from 2mg → 0mg**
- **Some patients cut 2mg buprenorphine strips into "32 pieces" to facilitate further tapering**
  - **0.063mg / 0.125mg**
- **Other methods of dissolving solid buprenorphine tablets in water and patients ingesting smaller volumes to taper**
- **Fatigue, GI effects, and mood disturbances were most frequently adverse effects**
  - **Use of loperamide, vitamins/supplements, clonidine, and benzodiazepines**

- **HOWEVER**
  - **Only an estimated 15% successfully taper - most took 60-120 days (median 93 days) between 0-2mg**
  - **Patients readily share their strategies via recovery groups and social media channels**

Figure 2 Tapering durations in days from 2mg to 0mg for the subset of Reddit users for whom it was possible to curate this information (n=23).



Graves RL, et al. 2019. http://dx.doi.org/10.1101/971608.
Graves RL, et al. *J Addit Med.* 2021 Dec 3.

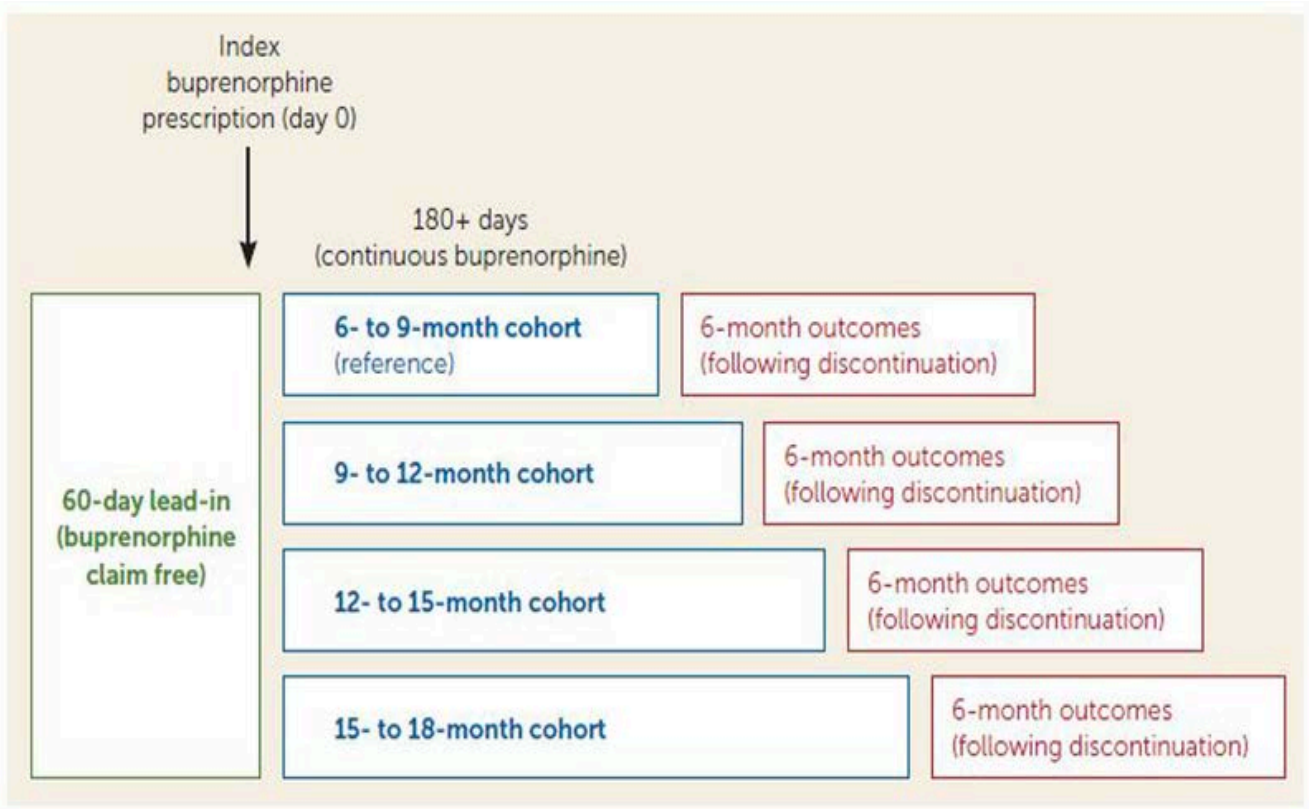
Support for Long-Term MOUD Use

CHRONIC Post-Acute Withdrawal Syndrome (PAWS)

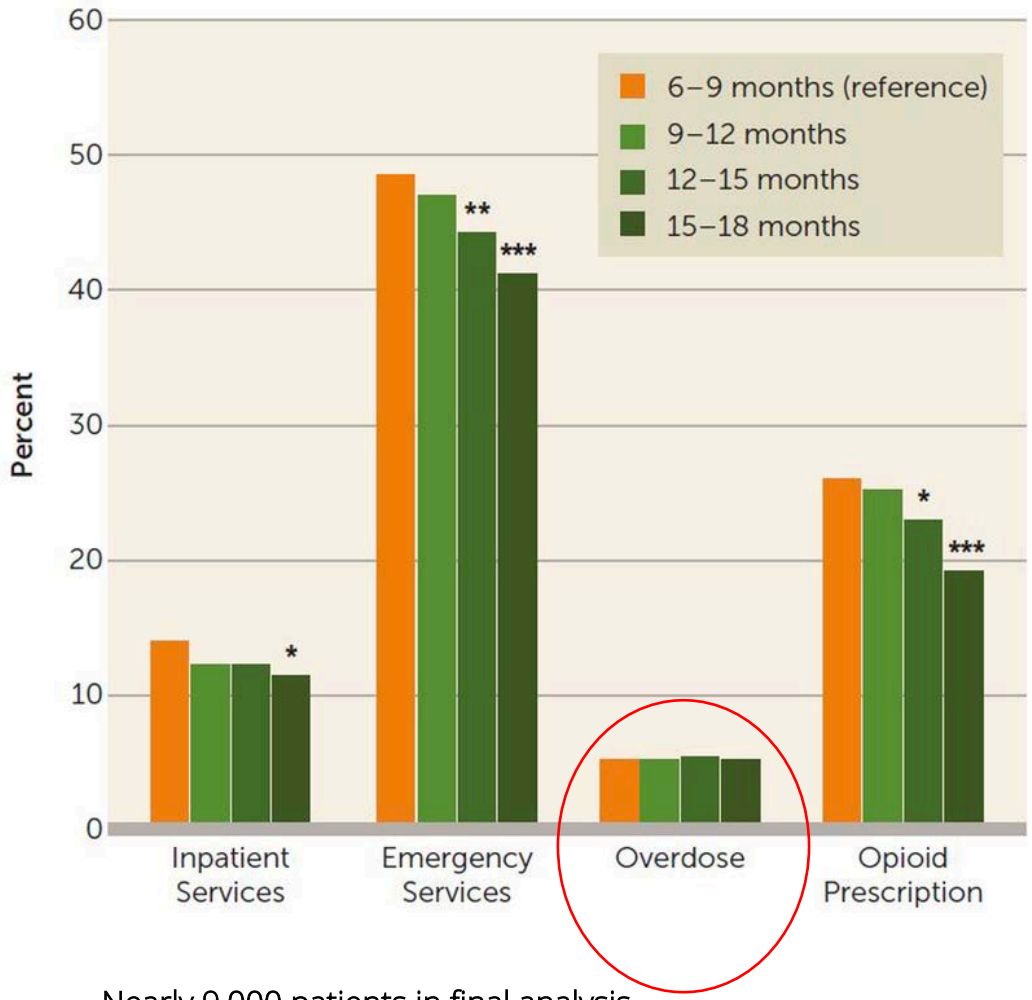
- Alcohol or drug cravings
- Irritability
- Anxiety
- Impaired decision-making skills
- Reduced control of executive functions
- Physical problems, especially pain, that may not be attributable to a specific cause

Lasts for years

Long-Term Buprenorphine Use



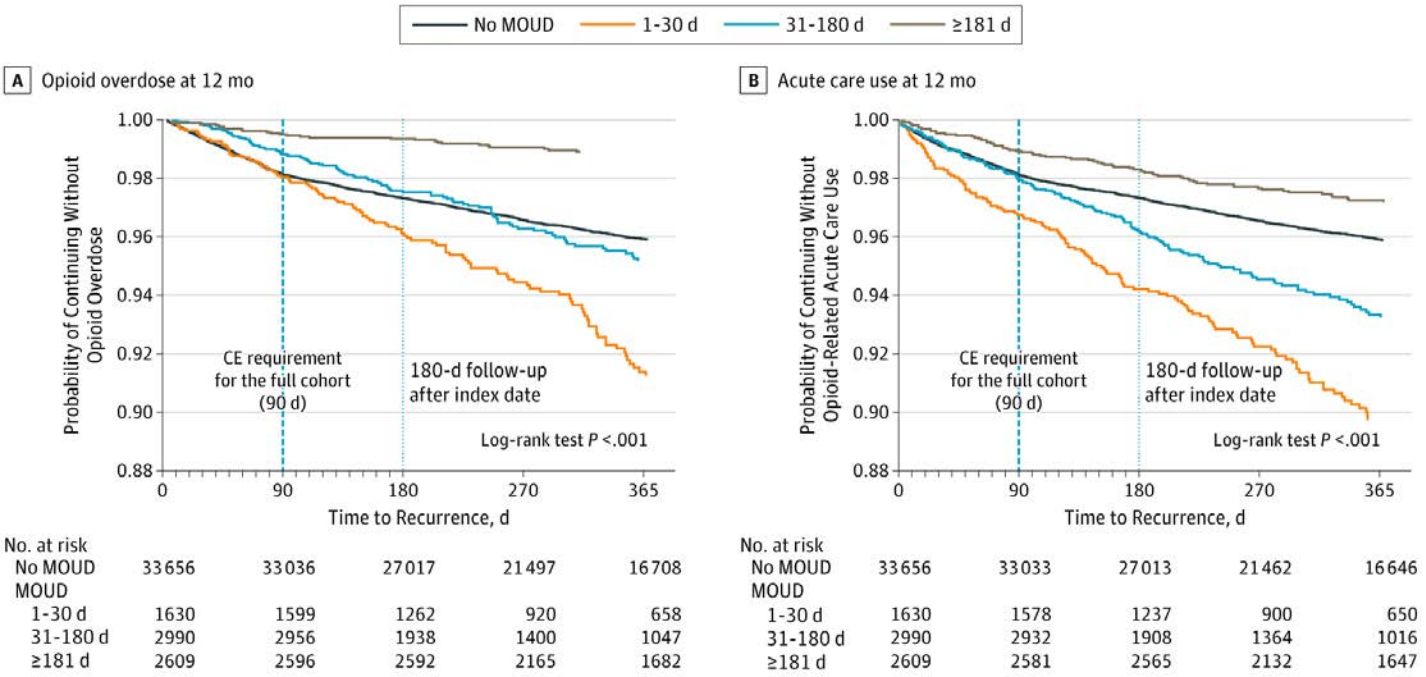
Analyzed data from 2013-2017 Medicaid claims data that includes comprehensive inpatient, outpatient , ED, and prescriptions billed to Medicaid



Nearly 9,000 patients in final analysis

Williams AR, et al. *Am J Psychiatry.* 2020 Feb 1;177(2):117-24.

Long-Term Buprenorphine Use



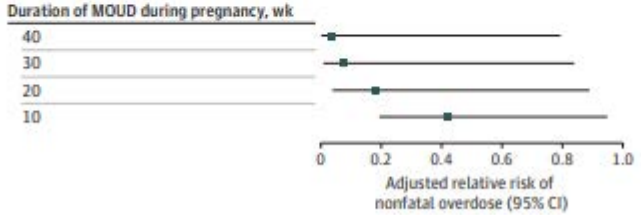
Individuals receiving <u>longer-duration (>6 months)</u> of MOUD treatment with buprenorphine or methadone had lower rates of overdose and acute care use at 12 months:

Wakeman SE, et al. *JAMA Netw Open.* 2020;3(2):e1920622
Jarlenski M, et al. *JAMA Netw Open.* 2022.

Results

This study included 2072 deliveries among 1999 female enrollees with OUD in pregnancy. A total of 1440 individuals (69.5%) had no observed MOUD use in pregnancy. Among the 632 pregnant persons (30.5%) with MOUD use, the median duration was 25.4 (IQR, 9.3-38.1) weeks (**Table**).

Figure. Association of the Duration of Medication for Opioid Use Disorder (MOUD) During Pregnancy and the Risk of Nonfatal Overdose Among Commercially Insured Pregnant Persons in the US



Retrospective cohort study of females who had a live birth between 1/2011 – 12/2019. Delivery was index date, and enrollees followed back to starting date of 12 weeks before date of conception.

MOUD Treatment Duration - Summary

- There is no evidence and no defined time limit for treating OUD
- Studies show low rate of remaining abstinent when MOUD is tapered
  - Evidence of neurobiological disease vs. disease of “moral failing”
- Presence of a post-acute withdrawal syndrome
  - Cravings
  - Irritability/anxiety
  - Presence of a dysphoric state or depression
  - Trouble sleeping
  - Anhedonia
  - Reduced control of executive functions

Bentzley BS, et al. *J Subst Abuse Treat.* 2015 May;52:48-57.
Weiss, RD, et al. *Arch Gen Psychiatry.* 2011 Dec;68(12):1238-46.

Risks of Tapering

- Advise using motivational interviewing and empathy:
  - The benefits of staying on therapy vs. risks of stopping especially in the age of highly potent synthetic opioids
  - Lack of specific guidelines - Reddit
  - The dose that makes buprenorphine most protective from overdose
  - The recurrence rates of chronic diseases and see if they have other comorbidities
  - The presence of protracted withdrawal
  - Terminology of MOUD vs. MAT
  - The difficulty of tapering especially at low doses and the rationale
  - Loss of tolerance
  - Anticipatory withdrawal, anxiety, and cravings are set-backs to brain recovery

Supporting Patients Who Wish to Taper

- Treatment goals and perception of treatment especially in those who wish to taper
  - Understand that goals are not rigid
- Provide the evidence-based recommendations and best practices and importantly, support them in their own goals!

Graves RL, et al. 2019. http://dx.doi.org/10.1101/971608.
Graves RL, et al. *J Addit Med.* 2021 Dec 3.

Case-Based Application

- TY is an **85 year-old patient** discharged from state prison after 30 years, for continuation of buprenorphine treatment. He was incarcerated for this period of time for a violent crime/shooting. Stated that this began as an argument/dispute about money re: drug deal. He denies any relapses or drug use since discharge. **He was prescribed buprenorphine 12mg daily in the prison.**
- The patient **does not have current drug use**, reports anxiety because he was just discharged from prison, and depressed because he has no place to live.
- Denies any psychotic/manic/SI/HI
- The patient was previously in prison for the criminally insane

Case-Based Application

- Substance Use History:
  - Opioids: IV heroin as a teenager*, Was using a lot because he was a dealer and was using*
    - H/o methadone: Was on methadone previously in a different prison
    - H/o buprenorphine: Initiated in prison
    - H/o XR-naltrexone: No
  - Cocaine/stimulants: IV use as a teenager
  - Sober periods (and what helped): has been sober since initiation of bupe (over 15 years)
  - Overdoses: yes , had previous overdose in the prison
  - Nicotine: current smoker; also has COPD
- Social History:
  - No reported history of trauma, no financial support, not employed, associates degree in liberal arts. Has a son and they have a good relationship – saying it has been many years since he has seen him in person. Otherwise, not in contact with any other family members.

Case-Based Application

- Initial prescription was for buprenorphine 8mg BID
- Fast forward, living in a group home and hopes to be able to move out. Also was working on getting a county/state ID.
- **F/U Visit (6 months after initial outpatient visit):** Says he is doing well on 16mg daily – cravings well-controlled and **requests decrease of buprenorphine from 16 to 12mg daily** and also working on quitting smoking which he had set a quit date on month 7 but did not achieve it.
- **Seventh month:** Says **cravings well-controlled at 12mg daily although** reported some fatigue and now wants to go to 8mg and was prescribed at 8mg daily.
  - Reported wants to taper off bupe as it does not help with his pain and this was his main reason for continuing. He is not afraid of relapse given his many years in remission.

Case-Based Application

- **Eighth Month: Taking 8mg daily** and denies drug use. Set a new quit date for smoking in in the ninth month and **wants to reduce buprenorphine to 4mg daily** over this next month.
- **Tenth Month**: Reports that he has **tapered down to 2mg daily** and denies any drug use with the exception of tobacco.
- **Twelfth Month**: Quit smoking. Hospitalized for COPD exacerbation. **Still taking buprenorphine 2mg daily** and denies drug cravings or drug use.
- **Fourteenth Month:**: Resumed smoking. **Continuing to take 2mg daily. Wants to decrease to 1mg daily.** Ultimate goal of patient is to taper off. **Moving to new apartment**
- **Sixteenth Month:**: **Continues to take 2mg daily**. Of note, follows-with a pain management physician and prescribed opioid pain medications (oxycodone 10mg QID) for arthritis. Was discussed how buprenorphine can be used for pain, but not interested in increasing dose or frequency because he has worked so long to tape his dose. Continuing to smoke 2-5 cigarettes/day.
- **Seventeenth Month**: Said he **has weaned his buprenorphine to zero** and does not want to continue treatment as he is focused on his pain due to osteoarthritis and requiring cortisone injections.

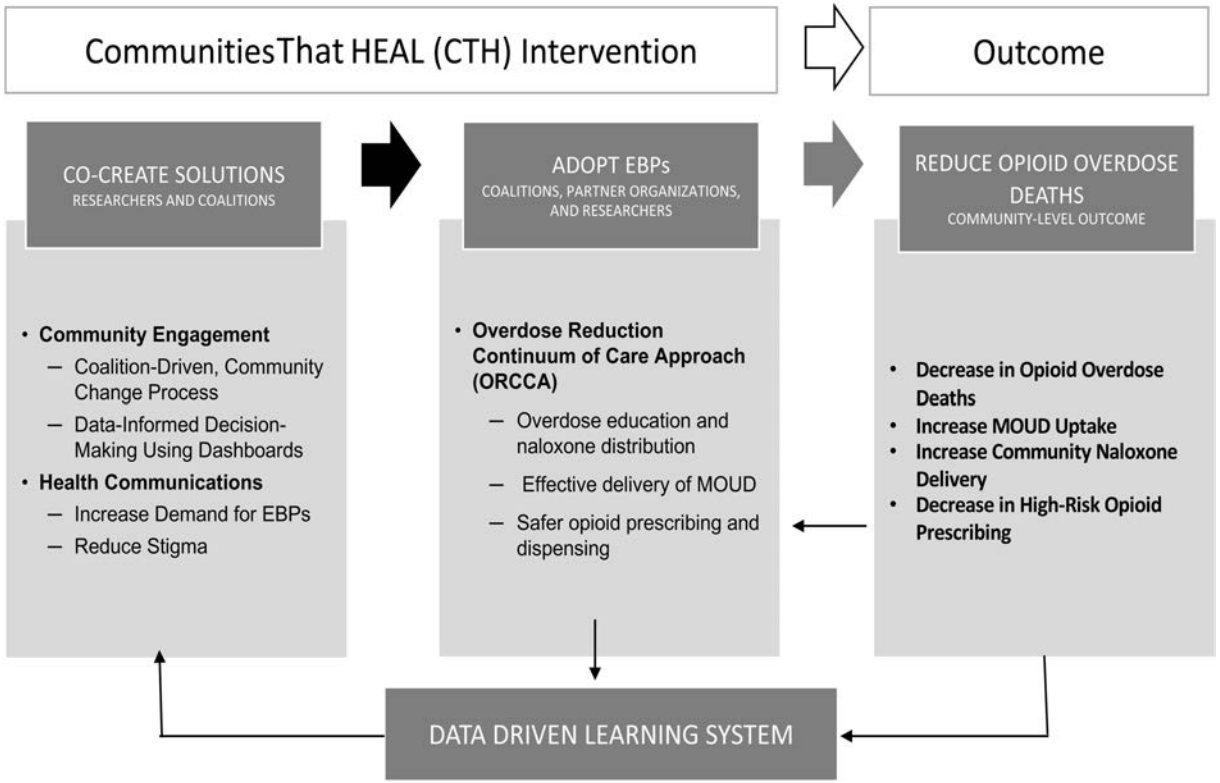
Case-Based Application – Initiating a Conversation about Tapering

- Address benefits for continuing buprenorphine and risks of stopping
  - Think about the maintenance dose especially in the age of fentanyl and the neurobiology
- Do not advise patients to stop or taper MOUD – it is always directed by the informed decision of the patient
- May take months/years
- Ask questions
  - What is the rationale for stopping buprenorphine?
  - Understand their clinical picture and risk for recurrence?
    - Environment, triggers, history of recurrence, social support
  - Are they concerned of pill burden?

Current Research Initiative

HEAL
(Helping to End Addiction Long-Term) Initiative

- Integration of evidence-based practices in communities hard hit by the opioid crisis
- Aim: Reduce opioid overdose deaths by >40% over 3 years in 67 communities
  - NY, MA, KY, OH
- Replicate results in communities nationwide



https://heal.nih.gov/research/research-to-practice/healing-communities

HEAL
(Helping to End Addiction Long-Term) Initiative

- **Putting Science into Action for People and Communities**
  - IMPOWR Program
  - JCOIN
  - ERN
  - PRISM
  - HOPE
- **Advancing Promising Therapeutics to Clinical Application**
  - Once-weekly methadone
  - 6-month implant of naltrexone

HEAL
(Helping to End Addiction Long-Term) Initiative

- **Advancing Health Equity**
  - Systemic racism, stigma, bias → poverty and lack of access to care
  - Committees including those with lived experience, advocates, or family members
- **Harnessing the Power of Novel Technologies**
  - Peer support app
  - Implanted device sensing oxygen levels
- **Identifying Promising Therapeutics and Interventions**
  - Build on existing research networks
- **Developing Tools to Facilitate Data Sharing**

HEAL Initiative

https://healingcommunitiesstudy.org/about-oud/treatment-recovery.html?utm_source=external&utm_medium=vanity_url&utm_campaign=treatment_recovery

Conclusions

- Embracing the long-term use of MOUD is critical in preventing overdose death in patients and supporting recovery, especially those who use highly potent synthetic opioids
  - Acknowledge that some patients are determined to taper off buprenorphine and be supportive
- More inclusive studies involving people who suffer the most from OUD (health equity) will likely provide more evidence to support the long-term treatment of OUD, even beyond long-term medication use
- Office-Based Addiction Treatment (OBAT) Providers and other integrated practices can help facilitate the long-term use of treatment with MOUD

Thank you!
Questions & Discussion

Discussion

- What barriers do you face in managing long-term MOUD?
- What are reasons your patients have discontinued MOUD?
- Next Step: Going beyond using long-term MOUD to facilitate recovery/sobriety towards incorporating harm reduction (for those who continue to use opioids) as part of the discussion for the rationale of long-term MOUD