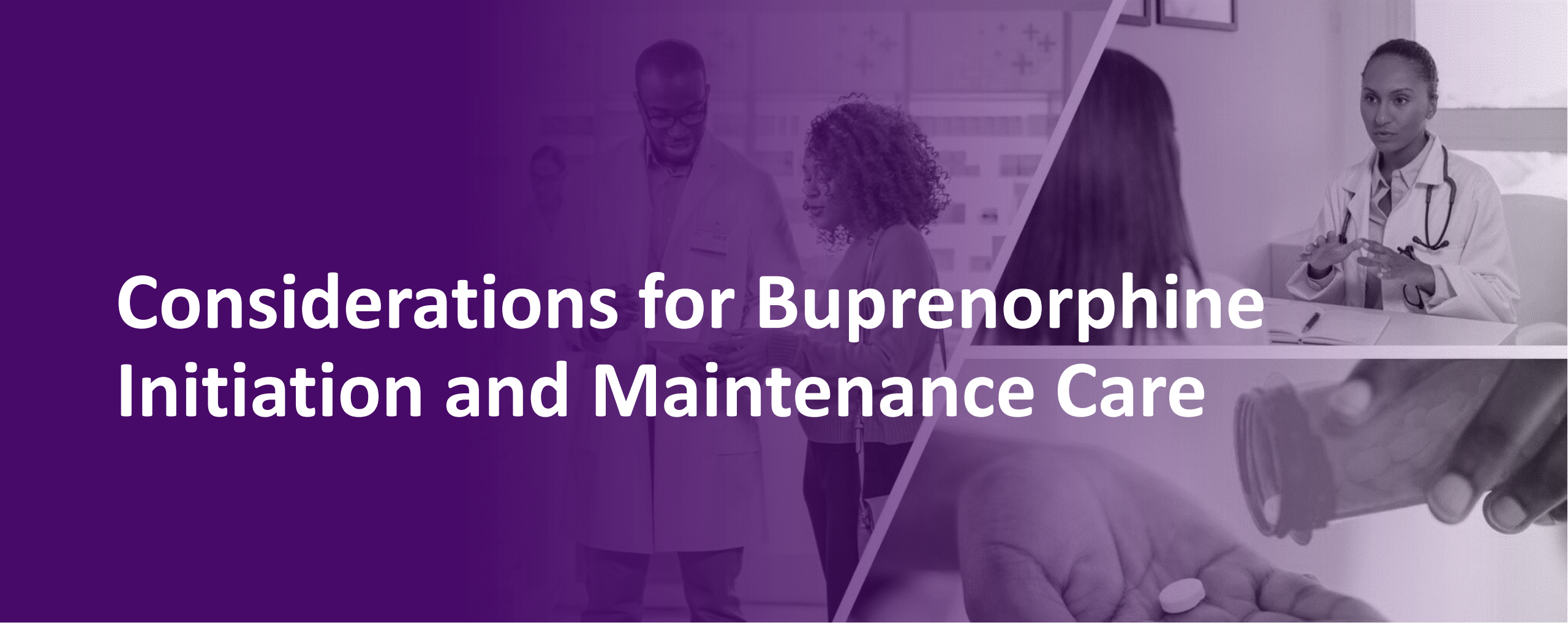


# Considerations for Buprenorphine Initiation and Maintenance Care

**The meeting will begin shortly**

REAGAN-UDALL FOUNDATION FOR THE FDA

# Housekeeping

REAGAN-UDALL FOUNDATION FOR THE FDA

Due to the meeting size, your microphone and video will remain off during the meeting.

This public meeting is being recorded. The slides, transcript, and video recording will be available on the FDA Foundation website after the meeting.

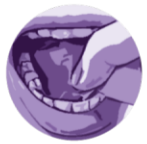
While we won't have time to directly address audience questions during today's meeting, you may use the Zoom chat function for comments.

# Today's Agenda (Eastern Time)

REAGAN-UDALL FOUNDATION FOR THE FDA

| | |
|---|---|
| **1 p.m.** | Welcome & Introduction |
| **1:05 p.m.** | Opening Remarks |
| **1:25 p.m.** | Session 1: Overview of Current Clinical Guidelines |
| **1:45 p.m.** | Session 2: Buprenorphine Initiation in the Inpatient Setting |
| **2:50 p.m.** | Break |
| **3 p.m.** | Session 3: Buprenorphine Initiation and Maintenance in the Community Setting |
| **4 p.m.** | Session 4: Buprenorphine Initiation and Maintenance in Special Populations |
| **4:45 p.m.** | Adjourn |

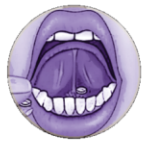
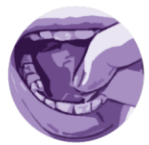
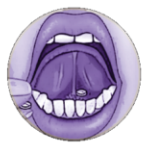
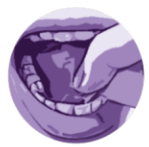
## BUPRENORPHINE MONOPRODUCT

| | Brand Name | Formulation | Strengths | Frequency | Label Indications |
|---|---|---|---|---|---|
|  | **Subutex**<br>Buprenorphine (GENERIC) | SL tablet | 2mg, 8mg | Daily to multiple times per day | Opioid Dependence |
|  | **Belbuca**<br>Buprenorphine | Buccal Film | 75mcg, 150mcg, 300mcg, 450mcg, 600mcg, 750mcg, 900mcg | Daily to multiple times per day | Pain |
|  | **Butrans**<br>Buprenorphine (GENERIC) | Transdermal | 5mcg/hr, 7.5mcg/hr, 10mg/hr, 15mcg/hr, 20mg/hr | Every 7 days | Pain |
|  | **Buprenex**<br>Buprenorphine (GENERIC) | Injection (IV, IM) | 0.3 mg/ml | Multiple times per day | Pain |
|  | **Sublocade**<br>Buprenorphine XR | Subcutaneous injection | 100mg/0.5ml syringe, 300mg/1.5mg syringe | Every 26-30 days | Moderate-Severe OUD |
|  | **Brixadi (NDA)**<br>Buprenorphine XR | Subcutaneous injection | Weekly: 8mg, 16mg, 24mg, 32mg Monthly: 64mg, 96mg, 128mg | Weekly or monthly | Moderate-Severe OUD |

**Sublingual (SL)** – tablet or film strip that dissolves under the tongue
**Buccal** – tablet or film strip that dissolves between the cheek and gums
**Transdermal** (TD) – patch that delivers medicine through the skin

**Subcutaneous injection** (SC) – medication given using a short needle into the tissue just under the skin
**Intravenous injection** (IV) – medication given into a vein
**Intramuscular injection** (IM) – medication given as a shot into the muscle

## BUPRENORPHINE/NALOXONE COMBINATION PRODUCT

| | Brand Name | Formulation | Strengths | Frequency | Label Indications |
|---|---|---|---|---|---|
|  | **Generic**<br>Buprenorphine & naloxone (GENERIC) | SL tablet | (bup/nal): 2mg/0.5mg, 8mg/2mg | Daily to multiple times per day | Opioid Dependence |
|  | **Generic**<br>Buprenorphine & naloxone (GENERIC) | Buccal/SL Film | (bup/nal): 2mg/0.5mg, 4mg/1mg, 8mg/2mg, 12mg/3mg | Daily to multiple times per day | Opioid Dependence |
|  | **Zubsolv**<br>Buprenorphine & naloxone | SL tablet | (bup/nal): 0.7mg/0.18mg, 1.4mg/0.36mg, 2.9mg/0.71mg, 5.7mg/1.4mg, 8.6mg/2.1mg, 11.4mg/2.9mg | Daily to multiple times per day | Opioid Dependence |
|  | **Suboxone**<br>Buprenorphine & naloxone (GENERIC) | Buccal/SL Film | (bup/nal): 2mg/0.5mg, 4mg/1mg, 8mg/2mg, 12mg/3mg | Daily to multiple times per day | Opioid Dependence |

https://www.asam.org/quality-care/clinical-guidelines/national-practice-guideline

### INFORMATION FROM PRODUCT PACKAGE INSERTS

**Sublingual (SL)** – tablet or film strip that dissolves under the tongue

**Buccal** – tablet or film strip that dissolves between the cheek and gums

## ENTRY POINTS

Overdose (EMS/ER)

Outpatient Clinic

Inpatient Service

**Assessment and shared decision-making between patient and provider**

## BUPRENORPHINE INITIATION

**Health System Barriers:**
- Adequate providers to take new patients?
- Adequately trained providers

**Payor Barriers:**
- May not approve treatment
- PA required so delays initiation

**Patient Barriers:**
- Fear of precipitated withdrawal
- Fear of legal action (if interacting with emergency services or health care services

## BUPRENORPHINE RX

**Payor Barriers:**
- Coverage/cost
- PA requirements

**Regulatory Barriers:**
- Influences formulation prescribed
- 72-hour rule

## PHARMACY

**Pharmacy:**
- Where to send electronic Rx?
- Will the pharmacy fill the Rx?
- Pricing
- Packaging
- Split tabs or film?
- Partial fills? (Not = bottle size)
- Repackaging (may not repackage for adherence purposes)

## MAINTENANCE/ THERAPY

**Patient Barriers**
- Adherence
- Relapse/Restart

**Payor Barriers:**
- Ongoing coverage
- Treatment time/limitations
- Formulary

**Pharmacy Barriers:**
- Stock maintenance meds?

**Provider/Health System Barriers**
- Adequate follow-up?
- Follow-up options (e.g., telehealth)

**Regulatory Barriers:**
- Available formulations
- Label restrictions

## BARRIERS THROUGHOUT THE TREATMENT JOURNEY

- Accessibility (to providers, clinics, treatment, inventory)
- Disconnect between clinical guidelines, state/local regulations, and federal regulations
- Lack of coordinated support services
- Lack of understanding about buprenorphine
- Paraphernalia laws
- Stigma
- Systemic racism/bias

# Opening Remarks

**Marta Sokolowska, PhD**
Deputy Center Director for Substance Use and Behavioral Health
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

**Yngvild K. Olsen, MD, MPH**
Director of the Center for Substance Abuse Treatment
Substance Abuse and Mental Health Services Administration

# Session 1: Overview of Clinical Guidelines

*Presenter:*
**Melissa Weimer, DO**
Yale University
American Society of Addiction Medicine

# Buprenorphine Clinical Considerations

Dr. Melissa B. Weimer, DO, MCR, DFASAM

May 10, 2023

# ASAM Clinical Practice Guidelines (CPG)

- Within the scope of Addiction Medicine, address
  - Prevention
  - Screening
  - Diagnosis
  - Treatment

# ASAM CPG Methodology Updated 2023

- Establish transparency
- Manage conflicts of interest
- Balance guideline group composition
- Use systematic review
- Establish the strength of evidence and strength of recommendations
- Articulate recommendations clearly and succinctly
- Engage stakeholder review
- Promote health equity
- Establish a process for CPG updates

# Clinical Document Types

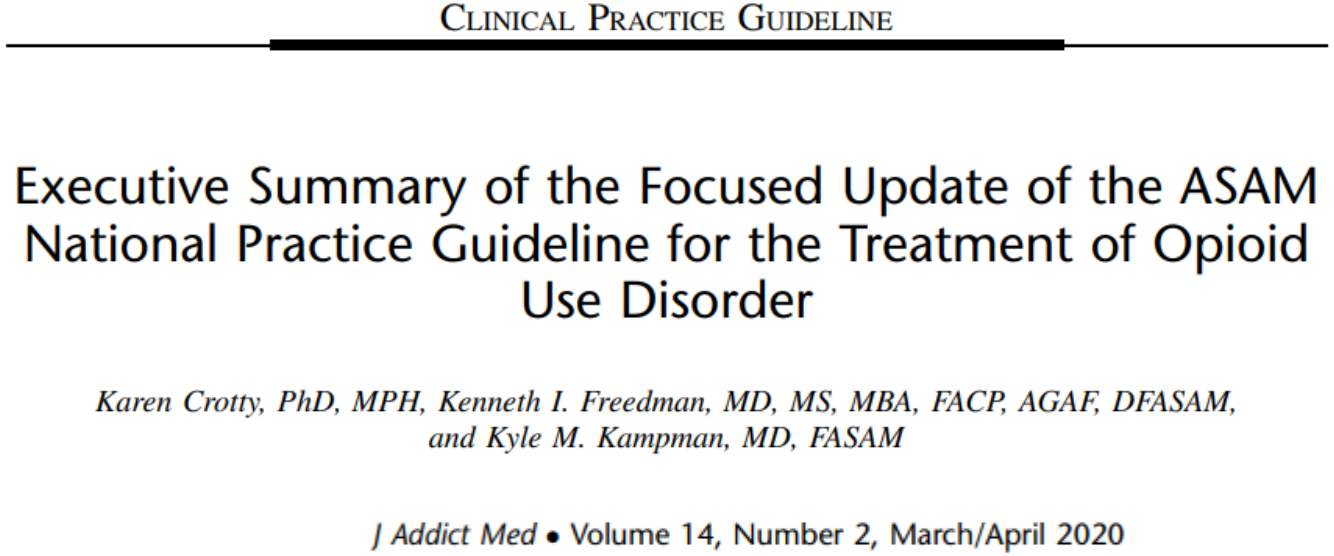
**Clinical Practice Guidelines** are the most scientifically rigorous, time-intensive documents, and require a formal systematic literature review to inform the recommendations.

**Clinical Consensus Statements** are informed by evidence, but may include a broader scope of evidence, such as case studies and reviews, including scoping literature reviews. Clinical Consensus Statements use expert clinical consensus on high-priority topics that may have conflicting or limited evidence.

**Clinical Consideration** documents address issues that are immediately clinically relevant, though they may have limited evidence. Clinical Considerations are typically informed by narrative literature reviews and based on expert clinical consensus.

# ASAM Clinical Practice Guidelines for Opioid Use Disorder

- Original CPG 2015
- Focused Update 2020
  - 35 revised recommendations
  - 13 new recommendations
  - 14 specific to buprenorphine


CLINICAL PRACTICE GUIDELINE

Executive Summary of the Focused Update of the ASAM National Practice Guideline for the Treatment of Opioid Use Disorder

*Karen Crotty, PhD, MPH, Kenneth I. Freedman, MD, MS, MBA, FACP, AGAF, DFASAM, and Kyle M. Kampman, MD, FASAM*

*J Addict Med* • Volume 14, Number 2, March/April 2020

https://www.asam.org/quality-care/clinical-guidelines/national-practice-guideline

ASAM American Society *of* Addiction Medicine

# 2020 OUD Focused Update
# Buprenorphine Initiation and Treatment Recommendations

- Initiate buprenorphine once withdrawal begins
- Starting buprenorphine dose 2-4mg, increase by 2-8mg at a time
- Office-based and home initiation are both safe and effective
- Following initiation, titrate dose to alleviate symptoms
  - 16mg or more generally needed
  - Limited evidence on doses >24 mg per day
- Do not delay or withhold treatment if patients do not engage with psychosocial treatments
- Monitor and support patients with medication management
- No time limit on treatment
- Buprenorphine taper is a slow process that needs careful monitoring

# Clinical Complexity

- High potency synthetic opioids
- Low dose initiation
- High dose initiation
- Precipitated opioid withdrawal
- Xylazine, other novel components
- Extended release buprenorphine

# Clinical Considerations

## What is a Clinical Consideration?

- High clinical relevance, addresses real-practice complexities of care
- Expert consensus-based
- Some inclusion of evidence, but does not require a systematic literature review
- Less rigorous than a Clinical Practice Guideline or Clinical Consensus document

# Buprenorphine Clinical Considerations Writing Committee

## Committee Members

Melissa B. Weimer, DO, MCR, DFASAM
Andrew Herring, MD
Sarah Kawasaki, MD
Marjorie Meyer, MD
Kelly S. Ramsey, MD, MPH, FACP, DFASAM

## Peer Reviewers

Emily Brunner, MD, DFASAM
Deepa Camenga, MD
Gail D'Onofrio, MD, MS, FACEM, FASAM
Lewis S. Nelson, MD, MBA, FASAM
Jeanmarie Perrone, MD
Sarah E. Wakeman, MD, FASAM
Stephen A. Wyatt, DO, FAOAAM, FASAM

**Table 1. Buprenorphine Clinical Considerations Scope and Key Questions Components**

| **Key Question Components** | |
|---|---|
| **P**opulation | Individuals with severe OUD chronically exposed to HPSO<br>Pregnant individuals with OUD chronically exposed to HPSO |
| **I**nterventions | Buprenorphine initiation<br>Buprenorphine stabilization<br>Buprenorphine long term treatment |
| **C**omparisons | Usual practice as specified in the ASAM 2020 Updated OUD National Practice Guideline (NPG) |
| **O**utcomes | Opioid withdrawal syndrome<br>Precipitated opioid withdrawal°<br>Opioid cravings<br>Recurrence of opioid use<br>Morbidity (e.g., non-fatal overdose, premature hospital discharge, infections)<br>All-cause mortality<br>Opioid-related mortality |
| **T**iming | Any |
| **S**etting | All outpatient/ambulatory practice settings<br>Emergency department and hospital-based practice* |

**KQ1: What specific clinical situations favor use of low or high-dose buprenorphine initiation strategies?**

**KQ2: What strategies can address patient discomfort, including precipitated withdrawal, if it occurs during buprenorphine initiation?**

**KQ3: After buprenorphine initiation, what range of buprenorphine dosing and/or dosing strategies can be considered during stabilization and long-term treatment?**

**KQ4: What are indications for injectable extended release buprenorphine for OUD treatment compared to sublingual formulations?**

**KQ5: How do other novel components affect buprenorphine initiation and stabilization?**

**KQ6: What are the OUD treatment alternatives after repeated unsuccessful attempts at buprenorphine treatment?**

# KQ1-What specific clinical situations favor use of low or high-dose buprenorphine initiation strategies?

Clinical Considerations

- Observational data suggest buprenorphine initiation is best individualized by setting and patient preference.
- Low dose buprenorphine with opioid continuation (LDB-OC) in hospital settings appears to be well tolerated in observational data.
- More evidence is needed to determine the optimal strategy for LDB-OC in ambulatory settings for patients who are ineligible for medically prescribed full agonist opioids under current regulations.
- In patients with chronic exposure to high potency synthetic opioids who are initiating buprenorphine after opioid abstinence and development of withdrawal, rapid dose escalation has been observed to be safe, primarily in the ED setting.

**Table 3. Considerations for Buprenorphine Initiation Approach Based on High Tolerance and High Potency Synthetic Opioid Exposure – Clinical Setting and Opioid Withdrawal**

| Situation | Outpatient | Emergency Department | Residential/ Hospital Setting± |
|---|---|---|---|
| **Opioid withdrawal** – COWS ≥8 with one objective sign of opioid withdrawal | Standard initiation OR HDB | Standard initiation OR HDB | Standard initiation OR HDB |
| **Opioid withdrawal** – COWS <8 | Standard initiation OR LDB-OC | Standard initiation OR LDB-OC | Standard initiation OR LDB-OC# |
| **Pain + opioid withdrawal**, COWS <8 | Standard initiation OR Prescribed FAO for pain with LDB-OC | Standard initiation OR Prescribed FAO for pain with LBD-OC | Administered FAO + LDB-OC |

HDB = High Dose Buprenorphine
LDB-OC = Low Dose Buprenorphine with Opioid Continuation
FAO = Full agonist opioid

# KQ3: After buprenorphine initiation, what range of buprenorphine dosing and/or dosing strategies can be considered during stabilization and long-term treatment?

## Clinical Considerations

- Some patients with high opioid tolerance may require buprenorphine doses > 24 mg per day during the stabilization phase of treatment.
- Physiological changes during pregnancy alter buprenorphine metabolism, necessitating adjusted buprenorphine dose and dosing intervals.
- Consider dose and frequency adjustments, psychosocial supports, and a higher level of care if individuals are unable to stabilize with buprenorphine.
- Consider a reassessment of higher (> 24 mg/day) long term doses once patients enter long term treatment without ongoing use of opioids.

# KQ4: What are indications for injectable extended-release (XR) buprenorphine for OUD treatment compared to sublingual formulations?

## Clinical Considerations

- Consider XR buprenorphine formulations for individuals who are unable to stabilize on SL buprenorphine formulations, particularly individuals who have had extensive HPSO exposure, unsafe living environments, and/or multiple opioid overdoses.
- Consider administration of XR buprenorphine soon after successful buprenorphine initiation to achieve durable opioid overdose protection.
- While XR buprenorphine is reaching steady state, consider the risks and benefits of additional SL buprenorphine, particularly for pregnant individuals.

# Session 2: Buprenorphine Initiation in the Inpatient Setting

*Presenter:*

- **Amer Raheemullah, MD**, Stanford University

*Panelists:*

- **Dionna Berkholder,** North Colorado Health Alliance
- **Gerard Carroll, MD, FAAEM, EMT-P,** Cooper University Heath Care
- **Gail D'Onofrio, MD, MS,** Yale University
- **Michael A. Smith, PharmD, BCPS,** University of Michigan Health

# Buprenorphine Initiation in the Inpatient Setting

Amer Raheemullah, MD
Clinical Associate Professor
Department of Psychiatry and Behavioral Sciences
Stanford University School of Medicine

# Goals of Induction

- Buprenorphine Maintenance
  - Decreased Mortality
  - Improved outcomes

# Goals of Induction

- Minimize withdrawal
  - Avoid precipitating withdrawal
  - Avoid prolonging opioid withdrawal unnecessarily

# Goals of Induction

- Abstain from illicit opioids
    - Provide adequate dose of buprenorphine
    - Increase as tolerated

# Menu of Buprenorphine Inductions[1]

- Standard Induction
- High-Dose Induction
- Low-Dose induction

Greenwald, M. K., Herring, A. A., Perrone, J., Nelson, L. S., & Azar, P. (2022). A neuropharmacological model to explain buprenorphine induction challenges. *Annals of Emergency Medicine*.

# Emergency Department

- First point of contact prior to admission
- Effective, low-barrier setting
- High-Dose Inductions Recommended

Greenwald, M. K., Herring, A. A., Perrone, J., Nelson, L. S., & Azar, P. (2022). A neuropharmacological model to explain buprenorphine induction challenges. *Annals of Emergency Medicine*.

# After Hospital Admission

- Opioids Not Required on Admission
  - Start buprenorphine when withdrawal develops

- Opioids Continued on Admission
  - Cannot use a standard induction

# Acutely Ill, Hospitalized Patients

- Can’t tolerate withdrawal
  - Acute psychiatric conditions
  - Post-op/trauma-related acute pain
  - Cardiac Stress

- Don’t want to tolerate withdrawal
  - Ambivalence about MOUD
  - On methadone, want to switch to buprenorphine
  - History of precipitated withdrawal

Weimer, M. B., Guerra, M., Morrow, G., & Adams, K. (2021). Hospital-based buprenorphine micro-dose initiation. *Journal of Addiction Medicine*, *15*(3), 255-257.

# Hospital is Critical Opportunity

- OUD in hospitalized patients quadrupled
  - Annual rate of hospital discharges documenting OUD without opioid overdose quadrupled during 1993–2016

- OUD in hospitalized pts increased 8% annually
  - During 2003–2016.

Peterson, C., Xu, L., Florence, C., & Mack, K. A. (2019). Opioid-related US hospital discharges by type, 1993–2016. *Journal of substance abuse treatment*, *103*, 9-13.

# Low-Dose Buprenorphine Initiation

- Names
  - Bernese Method
    - Microdose or MicroInduction
  - Low-Dose Initiation
    - Low doses don't precipitate withdrawal[1]
    - Precipitated withdrawal is a function of the starting dose of buprenorphine (not buprenorphine itself)

1. Mendelson, J.; Jones, R.T.;Welm, S.; Batki, S.L. Buprenorphine and naloxone interactions in methadone maintenance patients. Biol. Psychiatry **1997, 41, 1095–1101.**

# Low-Dose Buprenorphine Initiation

- Start with a small dose that doesn’t precipitate withdrawal
- Continue Opioids  to prevent withdrawal, and taper as tolerated
- Titrate up as tolerated

Quirk K, Stevenson M. Buprenorphine Microdosing for the Pain and Palliative Care Clinician. J Palliat Med. 2022 Jan;25(1):145-154. doi: 10.1089/jpm.2021.0378.

# Low-Dose Buprenorphine Initiation

- Transmucosal
  - Sublingual
    - Start: 0.5mg (1/4 film or tablets), 0.25mg
    - Duration: Reach 12mg dose by day 3, typically 4-7 days
  - Buccal
    - Start: 225mcg film
    - Duration: Reach 8mg SL films by day 5, 16mg by day 7

- Transdermal
    - Start: 20mcg/hr patch (or less)
    - Duration: Reach 8 mg dose by day 2, 16mg by day 3

Quirk K, Stevenson M. Buprenorphine Microdosing for the Pain and Palliative Care Clinician. J Palliat Med. 2022 Jan;25(1):145-154. doi: 10.1089/jpm.2021.0378.

# Barriers to Transdermal Inductions

- Lack of awareness of faster transdermal protocols
- Patches FDA-approved for Pain not OUD
- Patches are expensive
    - 1 Film = few dollars vs. 1 Patch = few hundred dollars
- Not covered by outpatient insurance

Sokolski, Eleasa, et al. "Rapid Low-dose Buprenorphine Initiation for Hospitalized Patients With Opioid Use Disorder." *Journal of Addiction Medicine* (2023): 10-1097.

# Barriers to Transmucosal Forms

- Many protocols take longer to get to 8mg dose
- Lowest available SL dose is 2mg
  - Requires cutting (complicated and imprecise)
    - Content uniformity only shown in films cut in half
      - high-performance liquid chromatography analysis
    - Inpatient pharmacies may not approve ¼ films
      - Buccal preparations remain an option

- Solutions
  - Consider Manufacturing Smaller SL Doses
  - Preformulated medication packaging
  - More research on faster protocols

# Research

- Speed
  - We don’t want to prolong people on illicit opioids
  - Fastest uptitration speed (for OUD)
  - Highest Starting Dose
- Routes (that lead to most adherence)
- RCT in progress
  - Clinical Practice outpacing research

# Session 2: Buprenorphine Initiation in the Inpatient Setting

*Presenter:*

- **Amer Raheemullah, MD**, Stanford University

*Panelists:*

- **Dionna Berkholder,** North Colorado Health Alliance
- **Gerard Carroll, MD, FAAEM, EMT-P,** Cooper University Heath Care
- **Gail D'Onofrio, MD, MS,** Yale University
- **Michael A. Smith, PharmD, BCPS,** University of Michigan Health

# We are taking a short break

## The meeting will resume at 3 pm ET

REAGAN-UDALL FOUNDATION FOR THE FDA

# Session 3: Buprenorphine Initiation and Maintenance in the Community Setting

*Presenter:*

- **Michelle Lofwall, MD, DFAPA, DFASAM,** University of Kentucky

*Panelists:*

- **Jeffrey Bratberg, PharmD, FAPhA,** University of Rhode Island
- **Jeremy Dubin, DO, FASAM,** Front Range Clinic
- **Eliza Hutchison, MD,** Packard Health
- **Jade Waits,** Boulder Care

# Buprenorphine Initiation and Maintenance in Communities: Dosing and Beyond

Michelle Lofwall, MD, DFAPA, DFASAM
University of Kentucky College of Medicine
Center on Drug and Alcohol Research

# Outline for today's talk

- Initiation
- Maintenance, stabilization, discontinuation and tapering
- Other management strategies
- Recognizing role of pharmacology and non-pharmacologic factors throughout
- Conclusion

# Factors to consider when initiating

- Patient level: prior preferences, Maslow hierarchy of needs (social determinants of health)
- Health care system: Payor/formulary, pharmacy access[1, 2]
- Housing status and their rules
  - Some jails have outpatient clinics see inmates– ↑ ADA suits allow opportunity for buprenorphine[3]
  - ? outpatient recovery housing allow SL
- State regulations – some have dosing limits[4]
- Provider and clinic level factors: storage of locked refrigerated injectable and admin support for required record keeping?

1. Cooper HLF et al. (2020) N Engl J Med, 383:703-705. 2. Shah R et al. (2023) Am J Health Syst Pharm, 80:e59-e66.
3. https://www.justice.gov/crt/case/fayette-county-detention-center 4. 201 KAR 9:270 Professional standards for prescribing, dispensing or administering buprenorphine monoproduct or buprenorphine with naloxone https://apps.legislature.ky.gov/law/kar/titles/201/009/270/

# Factors to consider when initiating (cont.)

- In-office vs. home initiation: home well-accepted
  - Home: ensure patient can evaluate for objective withdrawal, reassure clinic support
  - Option of in-office still helpful if available
- 1st dose of SL buprenorphine may depend on:
  - Dose:  SL: 0.5, 1, **2**, **4**, 8 or more? Injectable?
  - Micro/macro dosing outpatient? Few outpatient RCTs
  - Taking fentanyl, buprenorphine, heroin, methadone?
  - Previous experience initiating buprenorphine
  - Check own anxiety and patients' – expect success– remember placebo effect, conditioning and role of expectations

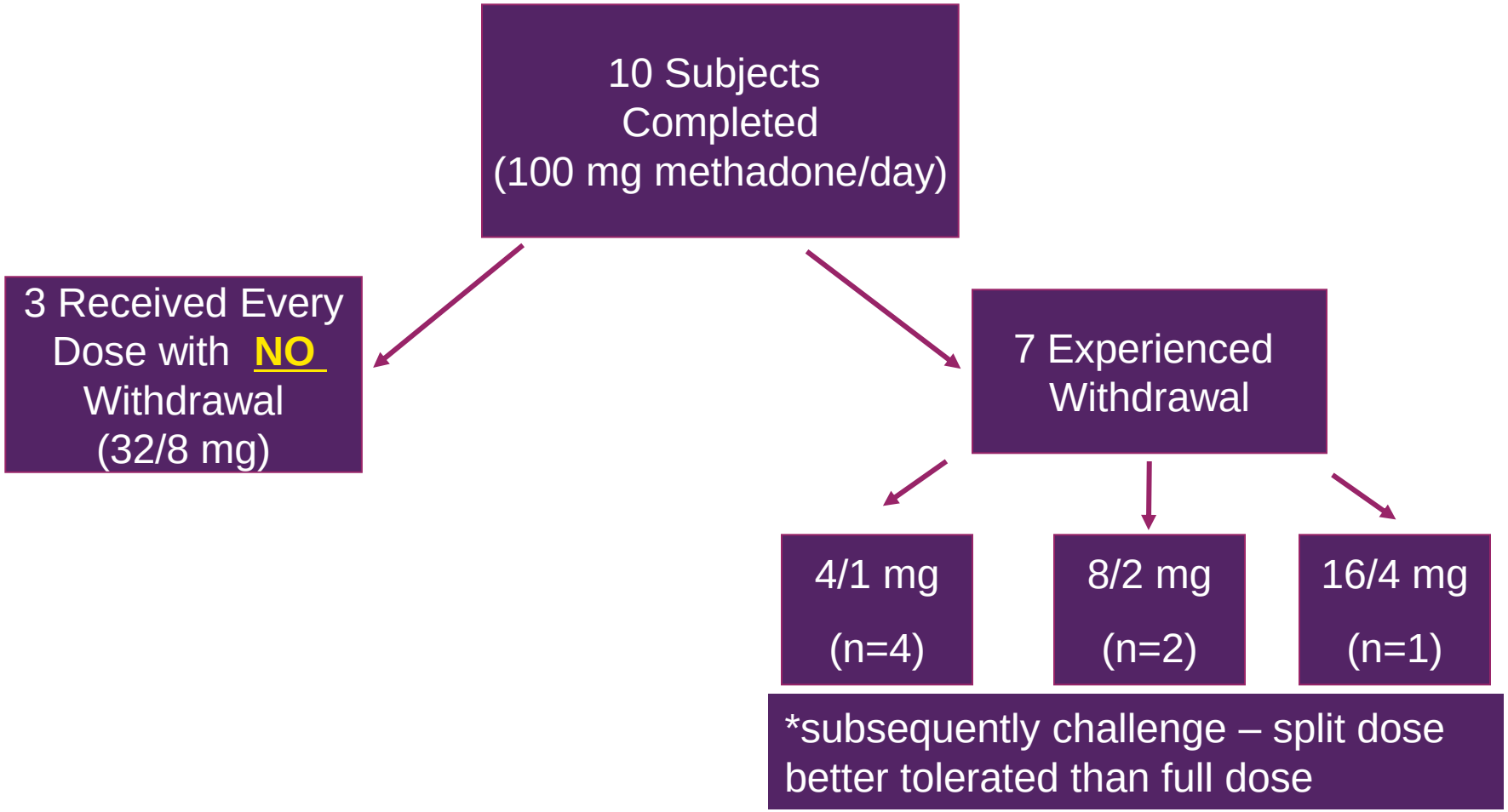
# Buprenorphine/Naloxone: Transfer from High Dose Methadone

- Subjects received rising doses UNTIL precipitated withdrawal occurred
- 2nd phase the same individualized withdrawal-producing dose was
  - Tested a second time
  - Tested as two divided doses given 2 hours apart

    For example, 8/2  4/1 → 4/1

Rosado, Walsh, et al. (2007) Drug and Alcohol Dependence, 90: 261-269. Slides from SL Walsh

# Subject Outcomes



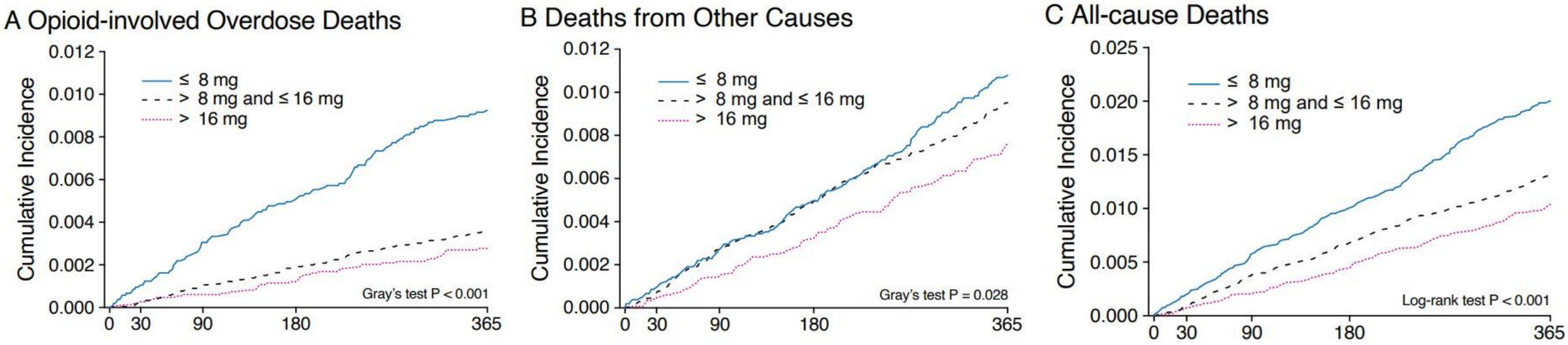

Rosado, Walsh et al (2007) Drug and Alcohol Dependence, 90: 261-269. Presented in CME program: Lofwall MR, Wunsch MJ, et al (2011). J Subst Abuse Treat. 41: 321-329.

# Considerations for initiation and maintenance dosing and management strategies (stabilization, maintenance, & discontinuation/tapering)

- SAMHSA and ASAM practice standards have dosing guidelines and instruct to individualize treatment, continue as long as patient benefiting[1,2]
- Consider a framework like other complex illnesses like Major Depressive Disorder and Diabetes Mellitus to help guide our thinking
- Clear definitions of stable? maintaining? when/who to taper? remission?
- Clinicians focus on patient outcomes like function and quality of life, preventing complications of untreated or undertreated disease (OUD) – this parallels medical management of other complex disorders

1. SAMHSA. Medications for Opioid Use Disorder. Treatment Improvement Protocol (TIP) Series 63 Publication No. PEP21-02-01-002. Rockville, MD: SAMHSA, 2021  2. The ASAM National Practice Guideline for the Treatment of Opioid Use Disorder: 2020 Focused Update. J Addict Med, 14(2S Suppl 1):1-91

# Cumulative Incidence Curves for Opioid-involved Overdose Death, Death from Other Cause, and All-cause Death, Stratified by Average Daily Dose of TM Buprenorphine for the Days Covered within the First 30 Days of Treatment




Note: The equivalence of the cumulative incidence among dose groups at all time points were compared using Gray's test for opioid-involved death and death from other causes, and Log-rank test for all-cause death. Results tests indicated differences in cumulative incidence of each outcome among the three TMbup dose groups ($p < 0.05$).

Feitong Lei, Michelle R Lofwall, Jana McAninch, Reuben, Adatorwovor, Emily Slade, Patricia R Freeman, Daniela C Moga, Nabarun Dasgupta, Sharon Walsh, Rachel Vickers-Smith, Svetla Slavova, 2023, Association between the Average Buprenorphine Dose during the First 30 Days of Treatment for Opioid Use Disorder and Mortality (*submitted*)

# Multivariable Model Associations between Average Daily Dose of TM Buprenorphine for Days Covered Within the First 30 Days of Treatment and the Incidence of Death

| Average daily dose of days covered within the initial 30-day treatment window | Opioid-involved Overdose Death | Death from Other Causes | All-cause Death |
|---|---|---|---|
| | aSHR (95% CI)[1] | aSHR (95% CI)[1] | aHR (95% CI)[2] |
| ≤8 mg | [Reference] | [Reference] | [Reference] |
| >8 to ≤ 16 mg | 0.45 (0.34, 0.60)[3] | 0.78 (0.62, 0.98)[3] | 0.63 (0.53, 0.75)[3] |
| >16 mg | 0.36 (0.25, 0.52)[3] | 0.62 (0.47, 0.80)[3] | 0.50 (0.40, 0.61)[3] |

1. aSHR = Subdistribution hazard ratio adjusted for age, gender, rural/urban residency, receipt of benzodiazepines, receipt of non-opioid controlled substances other than benzodiazepines, receipt of opioid analgesics in 180 days before initiation
2. aHR = Hazard ratio adjusted for age, gender, rural/urban residency, receipt of benzodiazepines, receipt of non-opioid controlled substances other than benzodiazepines, receipt of opioid analgesics in 180 days before initiation; CI = Confidence Interval.
3. P-value < 0.001

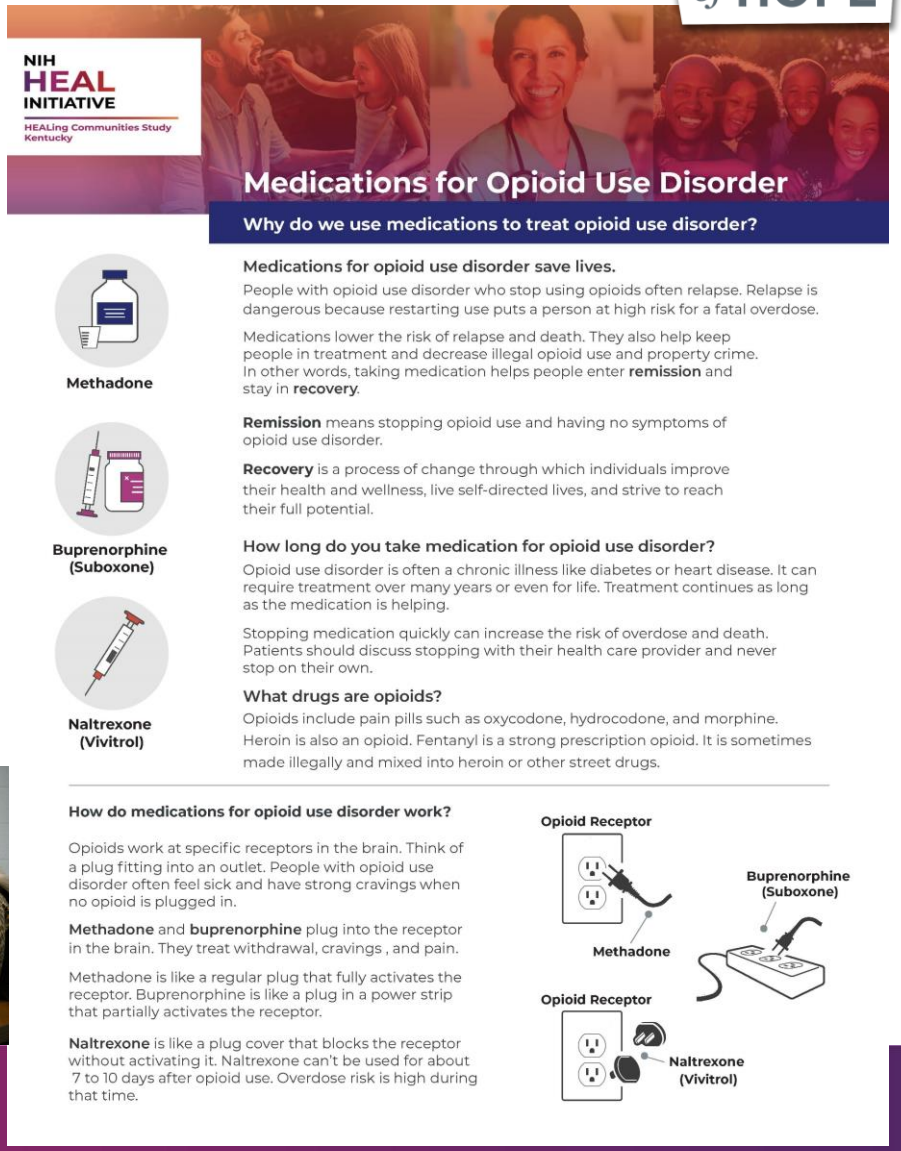
Feitong Lei, Michelle R Lofwall, Jana McAninch, Reuben, Adatorwovor, Emily Slade, Patricia R Freeman, Daniela C Moga, Nabarun Dasgupta, Sharon Walsh, Rachel Vickers-Smith, Svetla Slavova, 2023, Association between the Average Buprenorphine Dose during the First 30 Days of Treatment for Opioid Use Disorder and Mortality (*submitted*)

# Building a Well-trained Peer Support Workforce

KY HEALing Communities Study-Voices of Hope Linkage and Retention Programs

- Trained recovery coaches (RC) work to help link and retain individuals on MOUD
- RCs work in settings likely to encounter individuals with OUD who may or may not be in MOUD treatment (e.g., syringe service provider)
- Address barriers along the way

- 150+ hour <u>training curriculum</u>
  - Motivational interviewing skills, MOUD health literacy, interactive role plays, etc.
  - Competency check before field deployment
- From 12/2020 – 02/2023:
  - <u>93 RCs</u> and <u>16 supervisors</u> completed training
  - 68 agencies have RCs (anticipate 83 by study end)

NIH HEAL INITIATIVE
HEALing Communities Study Kentucky

## Medications for Opioid Use Disorder

**Why do we use medications to treat opioid use disorder?**

**Medications for opioid use disorder save lives.**

People with opioid use disorder who stop using opioids often relapse. Relapse is dangerous because restarting use puts a person at high risk for a fatal overdose.

Medications lower the risk of relapse and death. They also help keep people in treatment and decrease illegal opioid use and property crime. In other words, taking medication helps people enter **remission** and stay in **recovery**.

**Remission** means stopping opioid use and having no symptoms of opioid use disorder.

**Recovery** is a process of change through which individuals improve their health and wellness, live self-directed lives, and strive to reach their full potential.

Methadone

Buprenorphine (Suboxone)

Naltrexone (Vivitrol)

**How long do you take medication for opioid use disorder?**

Opioid use disorder is often a chronic illness like diabetes or heart disease. It can require treatment over many years or even for life. Treatment continues as long as the medication is helping.

Stopping medication quickly can increase the risk of overdose and death. Patients should discuss stopping with their health care provider and never stop on their own.

**What drugs are opioids?**

Opioids include pain pills such as oxycodone, hydrocodone, and morphine. Heroin is also an opioid. Fentanyl is a strong prescription opioid. It is sometimes made illegally and mixed into heroin or other street drugs.

**How do medications for opioid use disorder work?**

Opioids work at specific receptors in the brain. Think of a plug fitting into an outlet. People with opioid use disorder often feel sick and have strong cravings when no opioid is plugged in.

**Methadone** and **buprenorphine** plug into the receptor in the brain. They treat withdrawal, cravings , and pain.

Methadone is like a regular plug that fully activates the receptor. Buprenorphine is like a plug in a power strip that partially activates the receptor.

**Naltrexone** is like a plug cover that blocks the receptor without activating it. Naltrexone can't be used for about 7 to 10 days after opioid use. Overdose risk is high during that time.

Opioid Receptor
Buprenorphine (Suboxone)
Methadone
Opioid Receptor
Naltrexone (Vivitrol)

HCS MOUD Flyer (front page)

# Peer Supports Busting Barriers: Transportation

- Transportation reported as major barrier to starting and staying in MOUD treatment
- Peer drivers transport program participants to:
  - MOUD appointments
  - Other recovery-related appointments like counseling sessions
- Some participants eventually found personal transportation
- Opportunities to share hope while driving

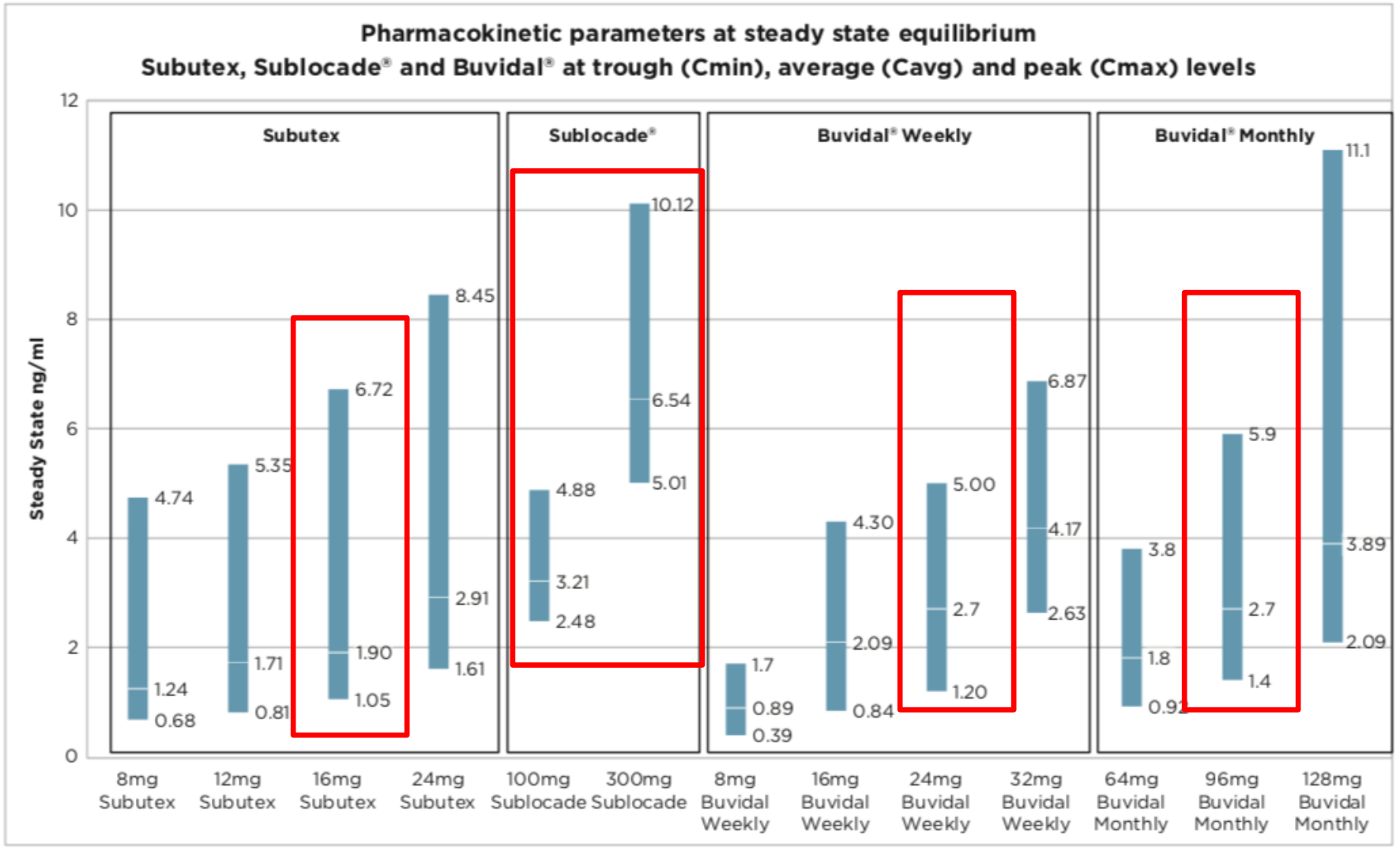



HCS peer-driver transportation in Wave 1 of HCS-KY
*transportation program focused primarily on transportation to rural OTPs

# Products, formulations, gaps in management, other considerations

- Mobile treatment especially for rural areas
- Potential for injectables including within mobile vans and pharmacy models
  - ↓ diversion risk, solves some adherence and transportation issues but $$$
  - Complex distribution/REMS: if patient no-shows – may need to waste medication
  - Some patients feel more sense of agency, but some feel the opposite
- Tapering: keep end goal in mind
  - Some patients can slowly ↓ dose over time and stay in remission
  - The '2 mg problem': Hard to go down from here
    - Europe has lower mg formulations (0.2 and 0.4 mg)
    - USA has micrograms but not approved for OUD
  - Tapering with injections – extend over time, decrease the dose?
- How about other ancillary meds to add on?

Figure 1: Pharmacokinetic parameters – steady state




*SL 16 mg and associated depot doses to use to try to achieve similar concentrations *options also to go higher or lower than typical SL 16 mg target

Lintzeris N, Dunlop A, Masters D (2019) Clinical guidelines for use of depot buprenorphine (Buvidal® and Sublocade®) in the treatment of opioid dependence. NSW Ministry of Health, Sydney Australia

# State-federal regulations alignment on “30-E”: Implications for MAT Act

- In April 2021, Health and Human Services issued buprenorphine guidelines allowing clinicians to receive a waiver exemption (30-E) to treat up to 30 patients
- Question: Will states align or are there restrictive regulations/statutes?
  - Will the licensing boards or single state agencies (SSA) require: a) waiver training and/or b) having the ability/capacity to refer patients to counseling or ancillary services for the 30-patient waiver?
  - Are the state licensing boards/single state agencies discussing the new 30 E- HHS guidelines?
  - Search Westlaw for buprenorphine regulations for all 50 states and DC
- Findings
  - Fifteen states (AL, AR, CA, CO, IN, KY, LA, ME, NJ, NM, OH, OR, VT, VA, WV) did not align
  - Findings suggest variety of reasons for non-alignment and question impact of MAT Act



Silwal, A., Talbert , J., Bohler, R., Kelsch, J., Cook , C., Blevins, D., Gallivan, M., Hunt, T., Hatcher, S., Thomas, C. P., Williams, S., Fanucchi, L., Lofwall, M. R. (2023) State alignment with federal regulations in 2022 to relax buprenorphine 30-patient waiver requirements, *Drug and Alcohol Dependence Reports*. doi: https://doi.org/10.1016/j.dadr.2023.100164

# Some responses: Opportunities and challenges

## Medical Boards

- “I cannot provide you with any further information on this matter.”
- “We are not the appropriate agency. It is rare we provide any response to this.”

## Nursing Boards

- “I do not have information regarding the new HHS buprenorphine guidance.”
- “Should be referred to private legal counsel.”
- “Not applicable because [State] remains silent on the issue.”

## Single State Agencies

- “One of the agency’s main advocates is very old school, so had not decided whether would adopt the new guidance.”
- “We are not adopting the new federal guidelines and isn’t remotely close to be up for discussion.”
- “ [State] has many prescribers, the issue is that many will still not prescribe out of fear of stigma or liability.”



Silwal, A., Talbert , J., Bohler, R., Kelsch, J., Cook , C., Blevins, D., Gallivan, M., Hunt, T., Hatcher, S., Thomas, C. P., Williams, S., Fanucchi, L., Lofwall, M. R. (2023) State alignment with federal regulations in 2022 to relax buprenorphine 30-patient waiver requirements, *Drug and Alcohol Dependence Reports*. doi: https://doi.org/10.1016/j.dadr.2023.100164

# Policy Communication, Dissemination and Implementation Strategies

- Policy changes from federal level travels through many agencies/boards and others before gets to patients
  - How to prevent communication breakdown given so many touch points and so many worries/myths?
  - What proactive dissemination and implementation science approaches are allowed and can used?
  - HHS social media platforms are followed/subscribed by more than 2.5 million people: Twitter (1.4M), YouTube (118K), Facebook (493K), Instagram (199K), and LinkedIn (495K)
- All people at the touch points are likely not OUD/MOUD experts
  - Licensing boards and pharmacies – many times volunteers on boards, boards experienced backlash from the Rx opioid epidemic  - how can another opioid really be the answer? Can the boards defend MOUD against the stigma and misinformation?
  - Public health communication campaign?

# Conclusions

- Dose matters AND so do many other things
- Perhaps principles of medical and research ethics helpful to guide as work through barriers and try to effectively address opioid epidemic: (a) do not harm, (b) beneficence, (c) justice, and (d) autonomy
- Provide a mechanism for a positive pathway forward when hit barriers and have hard conversations [diplomacy 101 class] Stay calm – don’t jump to conclusions, ask questions

# Acknowledgments


- Funding support: FDA, NIDA, SAMHSA KORE/SORE funding from our state Dept. of Behavioral Health who funds our Univ. of KY MOUD clinical services
- NIH HEAL Initiative[SM]–UM1DA049406 (KY), Site PI: Sharon Walsh, Ph.D.

  Over 100 faculty and staff at UK involved and many state/community partners
- https://www.uky.edu/healingstudy/


# Session 3: Buprenorphine Initiation and Maintenance in the Community Setting

*Presenter:*

- **Michelle Lofwall, MD, DFAPA, DFASAM,** University of Kentucky

*Panelists:*

- **Jeffrey Bratberg, PharmD, FAPhA,** University of Rhode Island
- **Jeremy Dubin, DO, FASAM,** Front Range Clinic
- **Eliza Hutchison, MD,** Packard Health
- **Jade Waits,** Boulder Care

# Session 4: Buprenorphine Initiation and Maintenance in Special Populations

*Panelists:*

- **Andrea Bonny, MD,** Nationwide Children's
- **Caitlin Martin, MD, MPH,** Virginia Commonwealth University
- **Amesika Nyaku, MD, MS,** Rutgers University
- **Chad Sabora,** Face & Voices of Recovery

# Thank you!

**Day 2 will resume tomorrow**

**Wednesday, May 11 at 1 pm ET**

REAGAN-UDALL FOUNDATION FOR THE FDA