Addiction Medicine Updates for the Hospitalist

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Disclosures

- Elsevier honorarium for OUD Discussion Guide

Objectives

- Describe the urgency of our addiction crisis and why leveraging hospitalization is critical.
- Implement alcohol, opioid, and stimulant use disorder treatment in hospitalized patients.
- Identify frontiers in hospital addictions care

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Roadmap

- **Background**
- Diagnosis, Treatment, and Care Transitions
- Frontiers

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Why Hospital-Based Addiction Care?

More than 107,000 died of drug-related overdoses in 2021– the highest in a 1-year period

The 4th Wave: Multiple Substances & Stimulant-related deaths

Gregory Rec/Portland Press Herald via Getty Images

Fentanyl is 50X-100X stronger than heroin and morphine and it's everywhere

New Hampshire State Police Forensic Lab. STAT 2016.

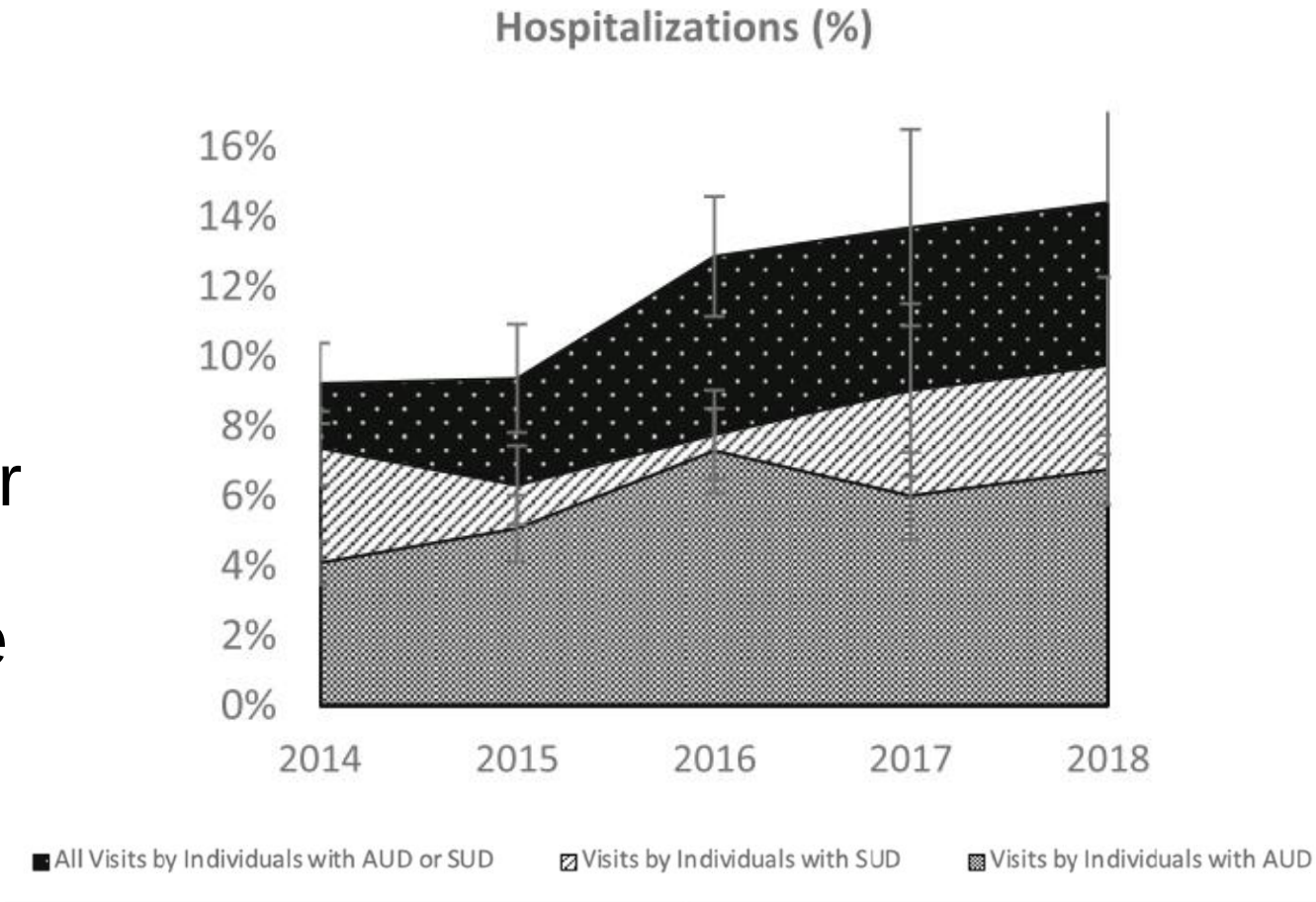
Addiction Crisis

- More than 480,000 tobacco-, 95,000 alcohol-, and 107,000 drug-related deaths yearly

Alcohol and Public Health, ARDI. Kariisa M. MMWR 2019;68:388–395
Spillane S, JAMA Network Open 2020. Grant BF, JAMA Psychiatry 2017.

SUD Prevalent in Hospitals

- 1 in 9 hospitalizations involves an SUD
- 12-month mortality after hospital discharge is 7.8%
- We spend $13.2 billion/year in healthcare spending on addiction related acute care visits



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Suen LW, JGIM 2021. King C, JAM 2022.
Peterson C, JAMA Network Open, 2021.

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Why treat addiction in the hospital?

2/3 Patients are Motivated to Reduce Use

Benefits of Treating SUD During Hospitalization

Patient

Healthcare system

Velez CM, JGIM 2017. Trowbridge P 2017. Wakeman S, JGIM 2017. Englander H, JHM 2018. Wilson JD, JGIM 2022. Kimmel SD, JAMA Open 2020.

POSITION STATEMENT

Journal of Hospital Medicine
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Management of opioid use disorder and associated conditions among hospitalized adults: A Consensus Statement from the Society of Hospital Medicine

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Richard Bottner DHA, PA-C[3] | Honora Englander MD[4] | Zoe Weinstein MD[5] |
Melissa B. Weimer DO, MCR[6] | Eugene Lambert MD[7] | Shoshana J. Herzig MD, MPH[7,8]

Identifying and treating OUD & opioid withdrawal

Managing perioperative pain in the setting of OUD

Optimizing care transitions

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Roadmap

- Background
- **Diagnosis, Treatment, and Care Transitions**
- Frontiers

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35 Y woman admitted with right upper extremity cellulitis and started on vancomycin

- On morning signout you're paged that she is complaining of diarrhea, abdominal pain, headache, and nausea
- You see her and note she is yawning and her pupils are dilated. She shares she used fentanyl 12 hours before

Does she have OUD?

DSM-5 Criteria for SUD Diagnosis

Impaired Control	Inability to **C**ut down	**R**isk of harm	**Risky Use**
	Loss of **C**ontrol—use more/longer than intended	Continued use despite health **C**onsequences	
	Compulsion—much time using/ recovering	Tolerance	**Pharmacologic Criteria**
	Craving	Withdrawal	
Social Impairment	**R**ole failure—school, work, home		
	Relationship trouble		
	Give up meaningful activities		

2-3: Mild
4-5: Moderate
6 or more: Severe

She uses fentanyl 5 times daily and has been unable to cut back. She lost her job due to missing work and has distanced herself from her parents due to her use. Does she have OUD?

A) Yes
B) No
C) Need more information

Control**:** Exceeded own limits
Can’t **C**ut down
Compulsion: Time using, getting, recovering
Craving
Role failure
Relationship trouble
Gave up other meaningful activities
Risk of bodily harm
Consequences: Physical/psychological
Tolerance
Withdrawal

General Approach to Substance Use Conversations

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She expresses interest OUD treatment. What would you offer?

A) Buprenorphine
B) Methadone
C) Clonidine, diphenhydramine, loperamide, acetaminophen
D) Extended-release naltrexone
E) Psychosocial treatment (residential, mutual help group)
F) Nothing; he should follow up with his PCP
G) Need more information

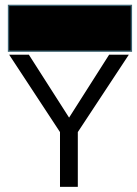
Medications for OUD

Mu receptor →

Opioids: full mu agonist
heroin, oxycodone, fentanyl

Methadone: full mu agonist

Buprenorphine: <u>partial</u> mu agonist
High affinity, ceiling effect



Extended-release naltrexone:
Full antagonist, high affinity

She expresses interest OUD treatment. What would you offer?

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G) Need more information

We can start OUD treatment in the hospital

(c) This section is **not intended to impose *any* limitations on a physician or authorized hospital staff to administer or dispense narcotic drugs in a hospital to maintain or detoxify a person *as an incidental adjunct to medical or surgical treatment of conditions other than addiction*,** or to administer or dispense narcotic drugs to persons with intractable pain in which no relief or cure is possible or none has been found after reasonable efforts.

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Title 21 Code of Federal Regulations

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PART 1306 — PRESCRIPTIONS

GENERAL INFORMATION

§1306.07 Administering or dispensing of narcotic drugs.

(a) A practitioner may administer or dispense directly (but not prescribe) a narcotic drug listed in any schedule to a narcotic dependant person for the purpose of maintenance or detoxification treatment if the practitioner meets both of the following conditions:

(1) The practitioner is separately registered with DEA as a narcotic treatment program.

(2) The practitioner is in compliance with DEA regulations regarding treatment qualifications, security, records, and unsupervised use of the drugs pursuant to the Act.

(b) Nothing in this section shall prohibit a physician who is not specifically registered to conduct a narcotic treatment program from administering (but not prescribing) narcotic drugs to a person for the purpose of relieving acute withdrawal symptoms when necessary while arrangements are being made for referral for treatment. Not more than one day's medication may be administered to the person or for the person's use at one time. Such emergency treatment may be carried out for not more than three days and may not be renewed or extended.

(c) This section is not intended to impose any limitations on a physician or authorized hospital staff to administer or dispense narcotic drugs in a hospital to maintain or detoxify a person as an incidental adjunct to medical or surgical treatment of conditions other than addiction, or to administer or dispense narcotic drugs to persons with intractable pain in which no relief or cure is possible or none has been found after reasonable efforts.

(d) A practitioner may administer or dispense (including prescribe) any Schedule III, IV, or V narcotic drug approved by the Food and Drug Administration specifically for use in maintenance or detoxification treatment to a narcotic dependent person if the practitioner complies with the requirements of §1301.28 of this chapter.

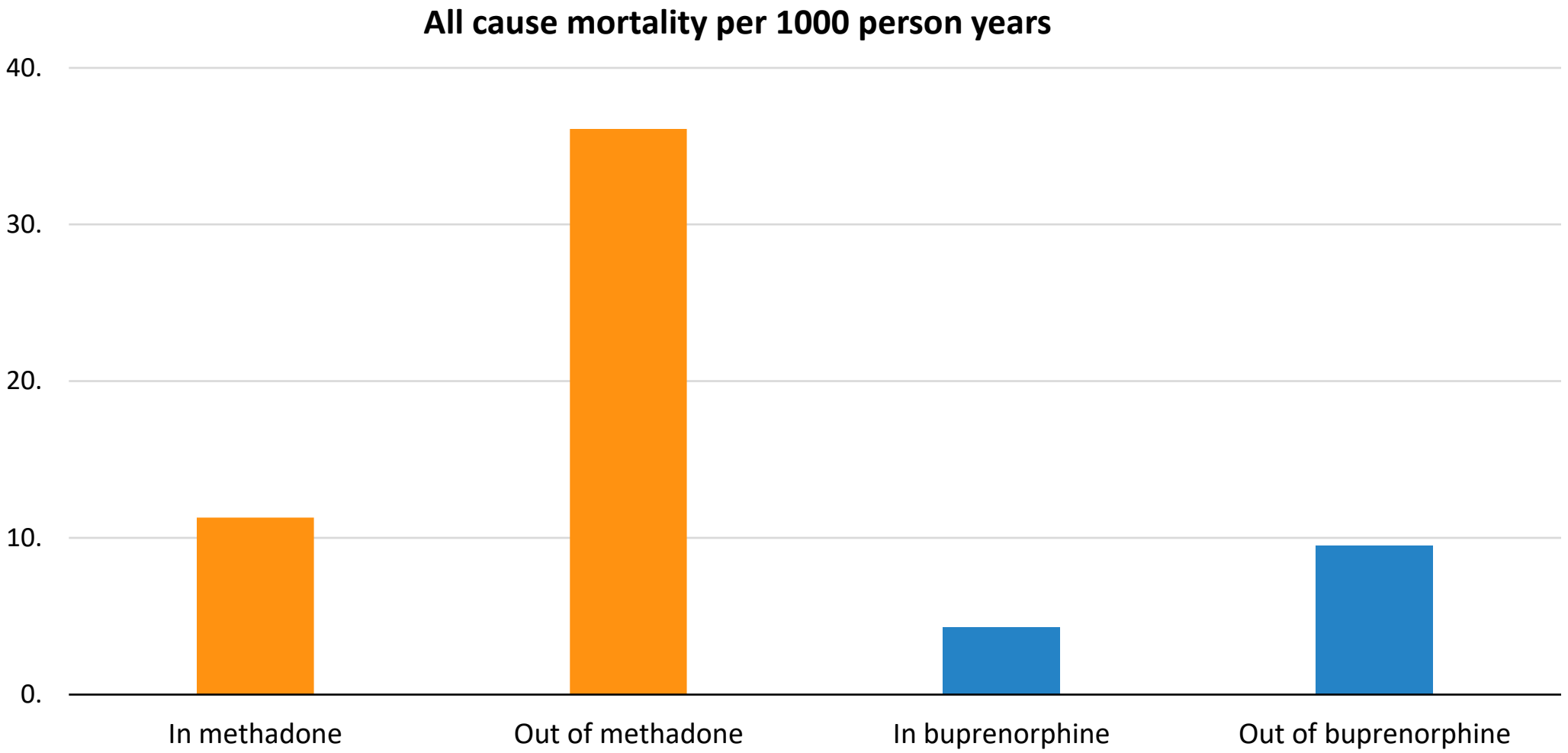
[39 FR 37986, Oct. 25, 1974, as amended at 70 FR 36344, June 23, 2005]

Cases Against Doctors
Chemical Control Program
CMEA (Combat Meth Epidemic Act)
Controlled Substance Schedules
DATA Waived Physicians
Drug Disposal Information
Drug and Chemical Information
E-commerce Initiatives
Federal Agencies & Related Links
Federal Register Notices
National Prescription Drug Take Back Day
NFLIS
Publications & Manuals
Questions & Answers
Significant Guidance Documents
Synthetic Drugs
Title 21 Code of Federal Regulations
Title 21 USC Codified CSA

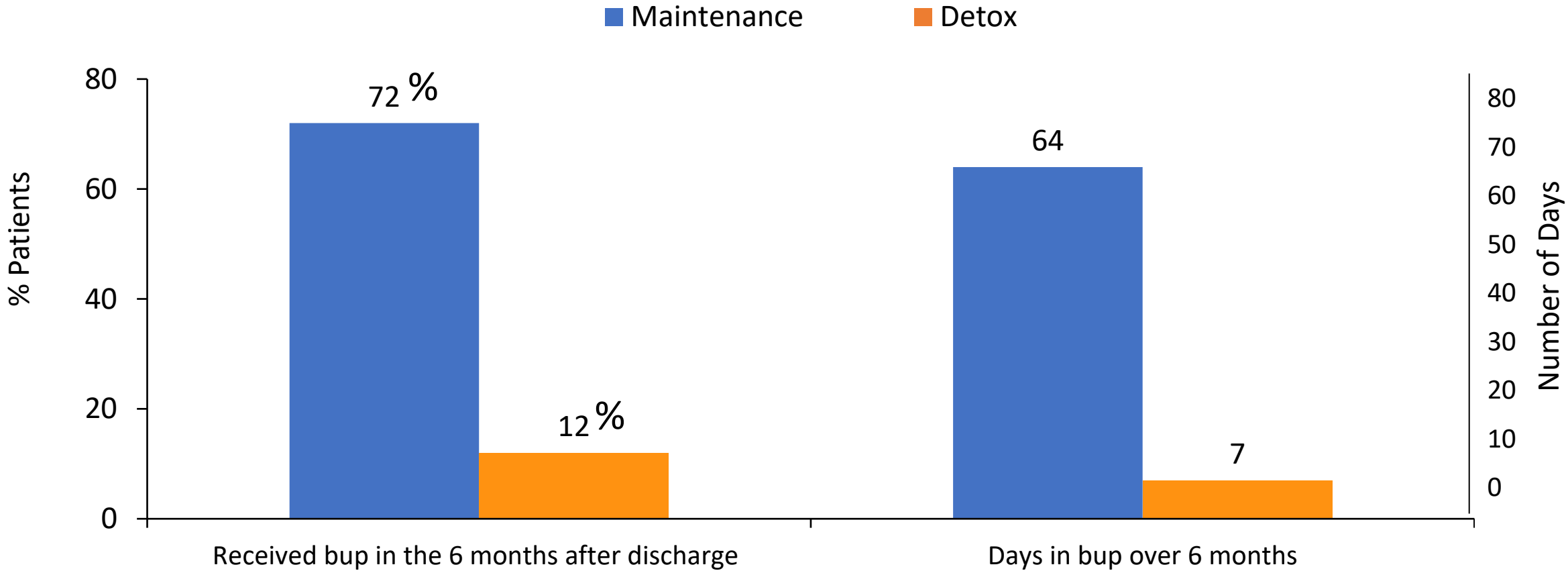
Medications for OUD

	Methadone	Buprenorphine
Treatment retention	Higher than buprenorphine	Increased retention at doses >16mg
Office visits	Daily visits to Opiate Treatment Program (OTP – methadone clinic)	Daily-monthly; some OTPs carry it as DOT
Prescribe in acute care?	Any inpatient clinician during hospitalization	Any inpatient clinician during hospitalization
Prescribe at discharge?	**OTP** **3-day dispensing**	**Any clinician**
Sedation	Yes at high doses, non-tolerant patients or slow metabolizers	Ceiling effect for respiratory depression
Withdrawal when starting	**Start anytime. Takes days to reach treatment dose**	**Withdrawal or low-dose/microdose**

Decreased Mortality



Hospital Initiation of Buprenorphine



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Buprenorphine Starts

Traditional Initiation

- Can tolerate opioid free period
- In opioid withdrawal (COWS score 8-11)
- Use short acting opioids (e.g., heroin, oxycodone)

Low-dose/Microdosing

- Avoid opioid free period (acute pain/post-op)
- Regular fentanyl use/long-acting opioids
- + Minimizes risk of opioid withdrawal
- - Takes longer to get someone on a therapeutic dose

Huhn AS, Drug and Alcohol Dependence 2020.
Varshneya NB, JAM 2022.

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Traditional Buprenorphine Initiation

1. When COWS ≥8, give 2-8 mg
2. Reassess in 2 hours. Give additional 2-8mg if continued withdrawal or cravings. Reassess q4-6 hours thereafter.
    - Max day 1: 16-24 mg
3. Therapeutic dose 16-24mg/day; some may need more

- **Increase dose:** craving, withdrawal, pain
- **Decrease dose:** insomnia, mania, sedation
- **Split dose:** every 6-8 hours in setting of pain

Works well with pill-based OUD and heroin use disorder

COWS Score for Opioid Withdrawal

Sign or Symptom	Score
Heart Rate	< 80 = 0 81-100 = 1 101-120 = 2 > 120 = 4
Sweating	None = 0 Subjective report = 1 Flushed or moist face = 2 Beads of sweat on face = 3 Sweat streaming of face = 4
Restlessness	Able to sit still = 0 Subjective reports of restlessness = 1 Frequent shifting or extraneous movements = 3 Unable to sit still for longer than a few seconds = 5
Pupil size	Normal or small = 0 Pupils possibly larger than appropriate = 1 Pupils moderately dilated = 2 Pupils so dilated that only rim or iris visible = 5
Bone or joint aches	None = 0 Mild diffuse discomfort = 1 Subjective reports = 2 Patient actively rubbing joints or muscles = 4
Rhinorrhea or lacrimation	None = 0 Congestion or moist eyes = 1 Rhinorrhea or lacrimation = 2 Nose constantly running or tears streaming = 4
Yawning	None = 0 Yawning 1-2 times = 1 Yawning > 3 times = 2 Yawning several times per minute = 4
Anxiety or irritability	None = 0 Subjective report = 1 Patient appears anxious = 2 So irritable that cannot participate in assessment = 4
Gooseflesh	Smooth skin = 0 Piloerection can be felt = 3 Prominent piloerection = 5

Withdrawal Assessment

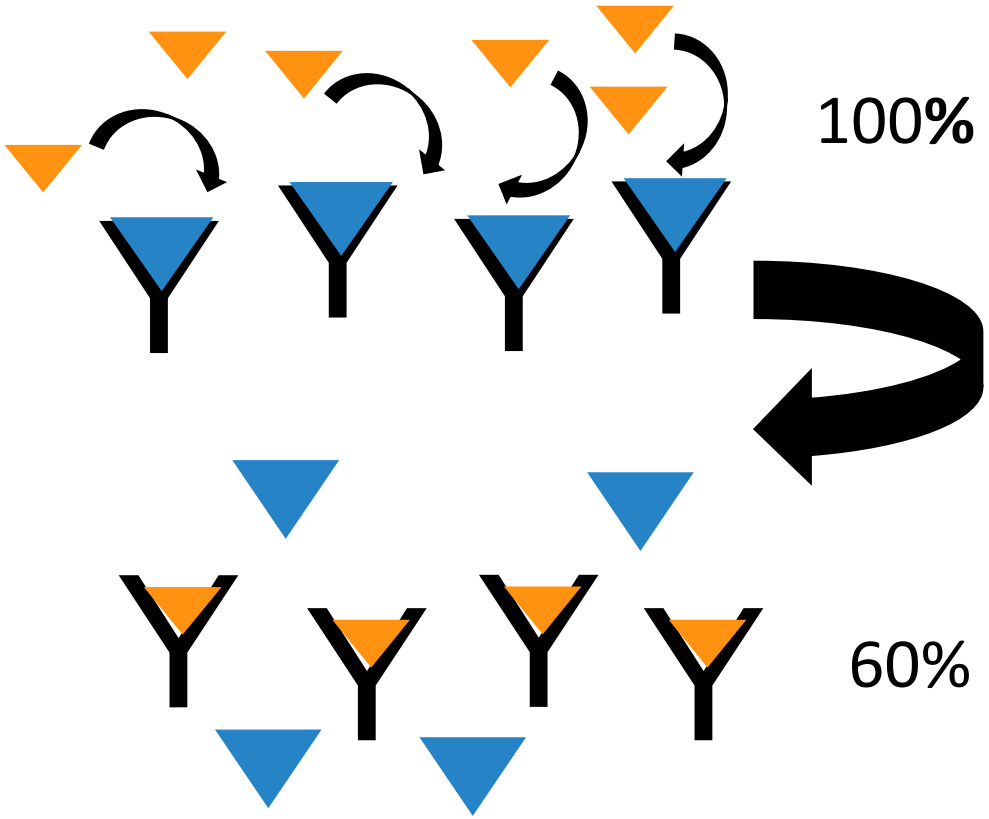
COWS shortcut: Subjective symptoms AND at least 1 objective sign of withdrawal

- Subjective: Nausea, abdominal pain, myalgias, chills
- Objective (≥1): Restlessness, sweating, rhinorrhea, dilated pupils, watery eyes, tachycardia, yawning, goose bumps, vomiting, diarrhea, tremor

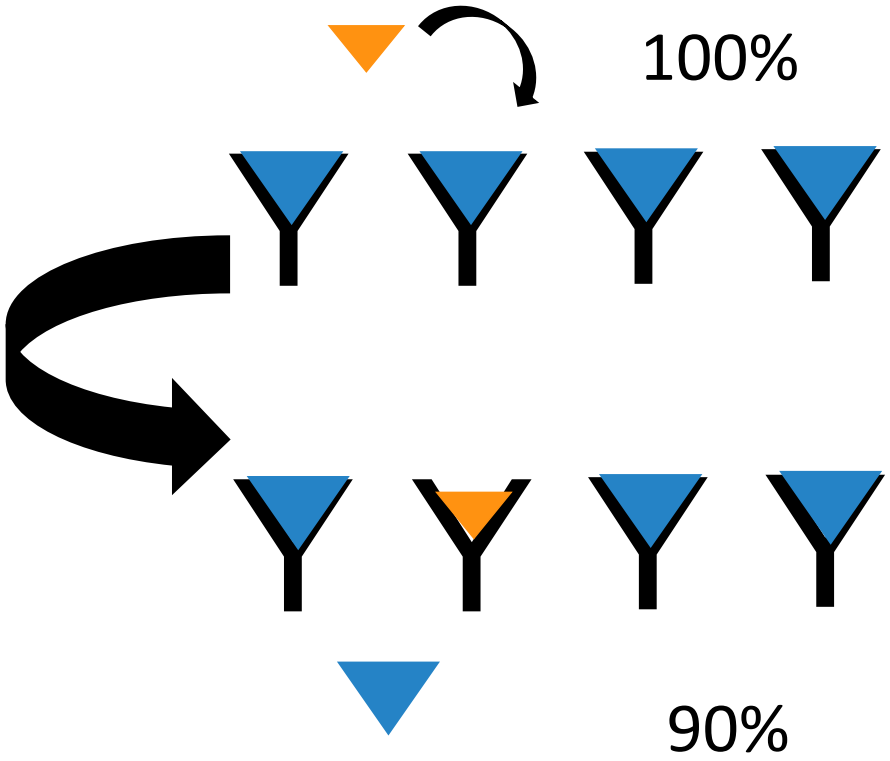
Precipitated Withdrawal

= Full opioid agonist

= Buprenorphine, partial opioid agonist



Microdosing to Avoid Withdrawal



Spreen LA, Pharmacotherapy 2022.

Example Microdose Titration

	Buprenorphine SL film dose	Full Agonists
Day 1	0.5mg QID	Scheduled and/or PRN opioids
Day 2	1 QID	
Day 3	2QID	
Day 4 and on	8 BID-TID	Start decreasing or stop opioids unless acute pain

Depends on formulations available in your hospital

Barriers you may encounter:

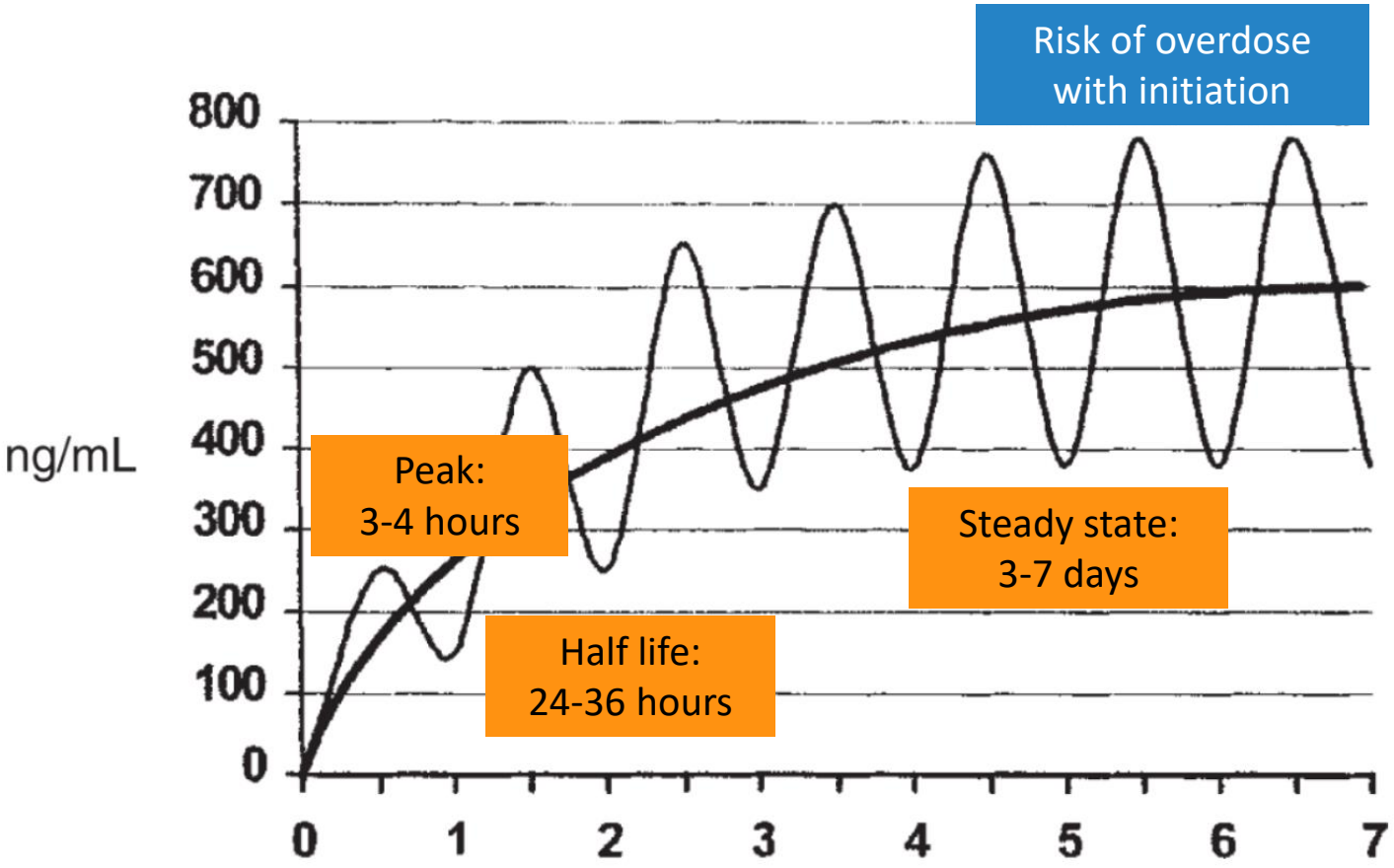
- Cutting 2mg films into quarters
- Not enough full opioid agonists

Weimer MB, Addiction 2022. Cohen SM, JAM 2022. Button D, JAM 2022. Thakrar AP, JAM 2022. Weimer MB, JAM 2021. Robbins JL, JABFM 2021.

Buprenorphine formulations for microdosing starts

Generic	Route	Brand Name	Approved for OUD	Used in hospital microdose starts
Buprenorphine-naloxone	SL film	Suboxone	Yes	Yes
Buprenorphine-naloxone	SL tab	Zubsolv	Yes	Yes
Buprenorphine	SL tab	Subutex	Yes	Yes
~~Buprenorphine~~	~~SQ injection~~	~~Sublocade~~	~~Yes~~	~~No~~
Buprenorphine	buccal	Belbuca	**Chronic Pain**	Yes
Buprenorphine	Transdermal patch	Butrans	**Chronic Pain**	Yes
Buprenorphine	IV	Buprenex	Pain	Yes

Methadone


Risk of overdose with initiation
ng/mL
800
700
600
500
400
300
200
100
0
Peak: 3-4 hours
Steady state: 3-7 days
Half life: 24-36 hours
0
1
2
3
4
5
6
7
Days at steady dose

Methadone Initiation in the Hospital

Day 1 Start with 10-30 mg, reassess in 3-4 hrs, add 10mg if withdrawal or cravings, max 40 mg Check for sedation at 4 hours.
Day 2 Total Day 1 + 5-10mg in 3-4 hrs if withdrawal or cravings, max 50 mg
Day 3 Today Day 2+ 5-10 mg in 3-4 hrs if withdrawal or cravings, max 60 mg
Thereafter Monitor on 60mg daily for 3-5 days before increasing again by 5-10mg. Hold for 3-5 more days and repeat this process as needed. Target daily dose 80-120mg.

Ok to give additional short acting opioids during hospitalization

46 Y woman admitted with alcohol withdrawal and mild alcohol-related hepatitis. You diagnose her with AUD using the DSM-5 criteria. What AUD treatment would you offer?

A) Naltrexone
B) Extended-release naltrexone
C) Acamprosate
D) Topiramate
E) Gabapentin
F) Psychosocial treatment (e.g., residential, mutual help group)
G) Need more information

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1st Line AUD Medications

Medication	Dose	Mechanism	Adverse Effects	Contraindications	Liver disease	Renal disease	Evidence
Naltrexone or Extended-Release Naltrexone	50mg daily or 380mg/ month	• Mu-opioid antagonist • Reduces cravings, blocks pleasurable effects of EtOH, reduces binges	GI upset Transaminitis	• LFTs>5 ULN • Decompensated cirrhosis • Opioids	Not in Child Pugh C	Ok to use unless severe CKD	• NNT=12 to reduce heavy drinking • NNT=20 for abstinence • High cravings, early AUD, fam history
Acamprosate	666mg TID	• Modulates glutamate hyperactivity • Improves dysphoria, promotes abstinence • Best if already s/p detox and aims abstinence	Diarrhea Fatigue	• Dose reduce CKD	Yes	Dose reduce to 333 TID	• NNT=12 to prevent return to any drinking • Not useful in heavy drinking
Disulfiram	250-500 daily	• Aldehyde dehydrogenase inhibitor • Causes negative physical effects if EtOH intake	Diarrhea Headache Dermatitis Rare hepatitis	• LFTs> 5 ULN • EtOH in past 24h • Severe CV disease	No	Yes, as long as not severe	• Only effective in RCT of directly observed treatment (DOT)

2nd Line AUD Medications

Medication	Dose	Mechanism	Adverse Effects	Contraindications	Liver disease	Renal disease	Evidence
Gabapentin	600 TID	• Facilitates GABA • Improves anxiety, sleep dysphoria	• Somnolence • Dizziness	Dose reduce CKD	Yes	Dose reduce	• Reduces binges • Increases abstinence • NNT 8 for abstinence, 5 for decreased binge drinking • Can combine with naltrexone
Topiramate	25 BID → 150 BID	• Facilitates GABA, decreases glutamate. • Improves dysphoria, cravings, impulsivity	• Cognitive slowing • Paresthesias • Somnolence • Rare metabolic acidosis • Kidney stones • Glaucoma	H/o kidney stones, narrow-angle glaucoma	Yes	Dose reduce	• Reduces heavy drinking days, drinks/day. • NNT 7.5 for return to heavy drinking, adjust for NNH • Can use with ESLD • Useful in PTSD, seizures, weight loss • Can combine with naltrexone

AUD Medications

MAINTAIN ABSTINENCE

- **Naltrexone / extended-release naltrexone**
- **Acamprosate**
- Gabapentin*
- **Disulfiram**

* Not FDA approved for AUD

DECREASE USE

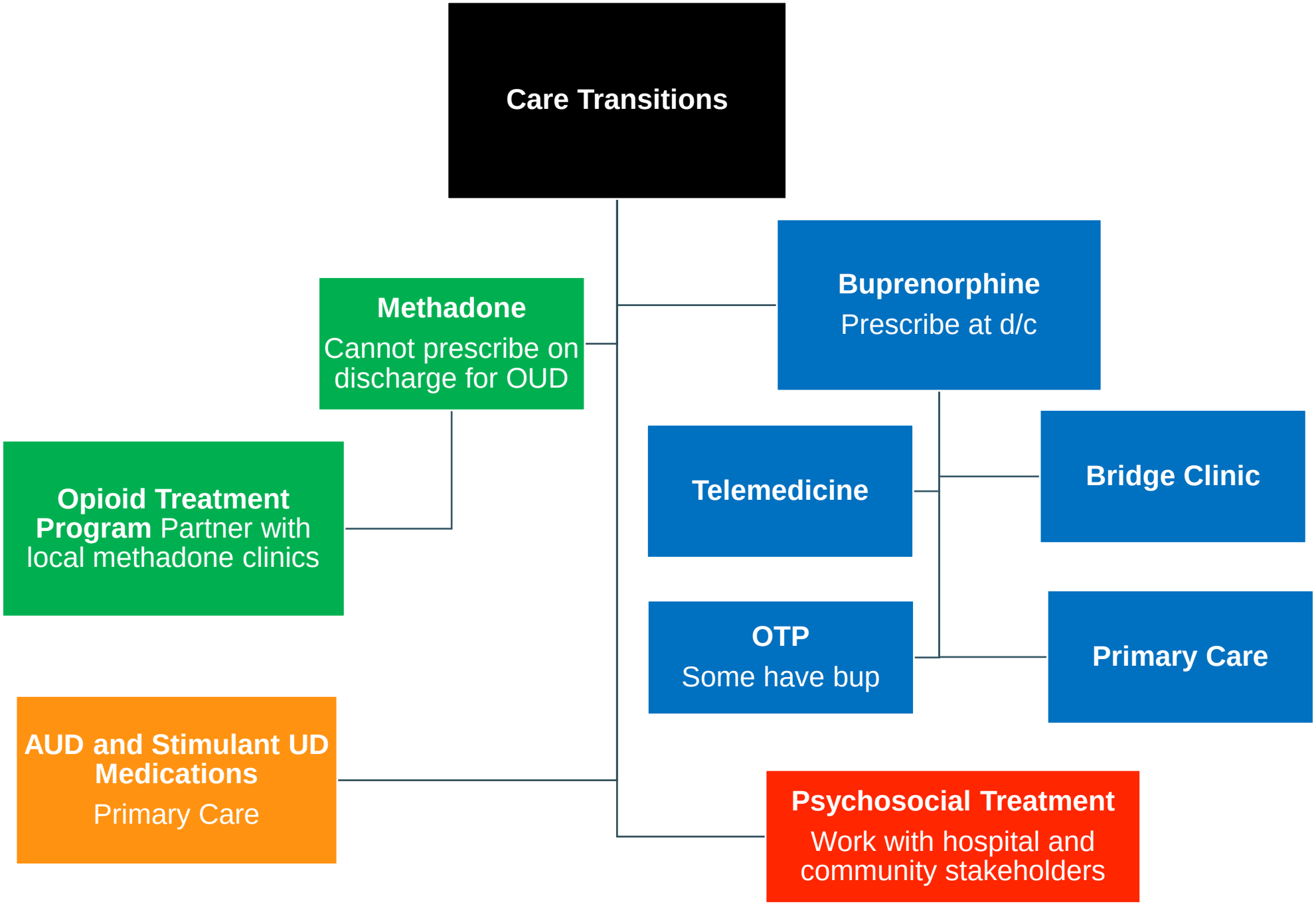
- **Naltrexone / extended-release naltrexone**
- Gabapentin*
- Topiramate*
- ~~Baclofen*~~
- Prazosin*
- Ondansetron*
- Varenicline*

Chaignot C, Pharmacoepidemiology and Drug Safety 2018.

Non-FDA approved, off-label meds for Stimulant Use Disorder

Medication	Dose	Mechanism	Adverse Effects	Contraindications	Renal disease	Evidence
Bupropion	150 daily x 3D then 150 BID	• Norepinephrine-dopamine reuptake inhibitor, nicotinic acetylcholine antagonist • May blunt stimulant-induced catecholamine release and reinforcement	Nausea, dry mouth, insomnia	• Reduces seizure threshold • Dose reduce to 75-100mg in setting of liver disease	Cr Cl <60 dose reduce to max 150 daily	• 29% v 14% achieved abstinence; 54% in medication adherence. With counseling. • <daily meth use • Smoking, depression
Mirtazapine	15 qHS x 1W then 30 qHS	• Atypical antidepressant • Enhances serotonin, increases dopamine release, antihistamine	Drowsiness, weight gain, anticholinergic	• Dose reduce CKD	Severe CKD max 30	• Reduction in utox with methamphetamine in tx group. Risk Ratio .75 at 24 weeks • Depression, insomnia
Extended-Release Naltrexone + Bupropion	380mg q3W XR-NTX +450 qD Bupropion	• Mu-opioid antagonist • Reduces cravings, blocks pleasurable effects	GI upset Transaminitis	• LFTs>5 ULN • Decompensated cirrhosis/Child Pugh C • Opioids	Ok to use unless severe CKD	• High bupropion adherence, NNT 9 (3/4 NR utox for Meth UD) • Concurrent AUD, high risk for opioid OD

Heinzerling KG, Addiction 2014. Coffin PO, JAMA Psychiatry 2020. Trivedi MH, NEJM 2021. SAMHSA TIP 33 2021.


Care Transitions
Methadone
Cannot prescribe on discharge for OUD
Buprenorphine
Prescribe at d/c
Opioid Treatment Program Partner with local methadone clinics
Telemedicine
Bridge Clinic
OTP
Some have bup
Primary Care
AUD and Stimulant UD Medications
Primary Care
Psychosocial Treatment
Work with hospital and community stakeholders

Roadmap

- Background
- Diagnosis and Treatment
- **Harm Reduction and Overdose Prevention**
- Care Transitions

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Stimulant Use Disorder

- Best evidence = **Contingency Management**
  - Positive reinforcement for desired behaviors
  - In stimulant use desired behaviors may be:
    - Urine toxicology non-reactive for stimulants
    - Patients attends appointments to discuss stimulant use
  - California is piloting contingency management through Medicaid
- Other psychosocial treatment (e.g., residential, groups)
- Non-FDA approved, off-label medications

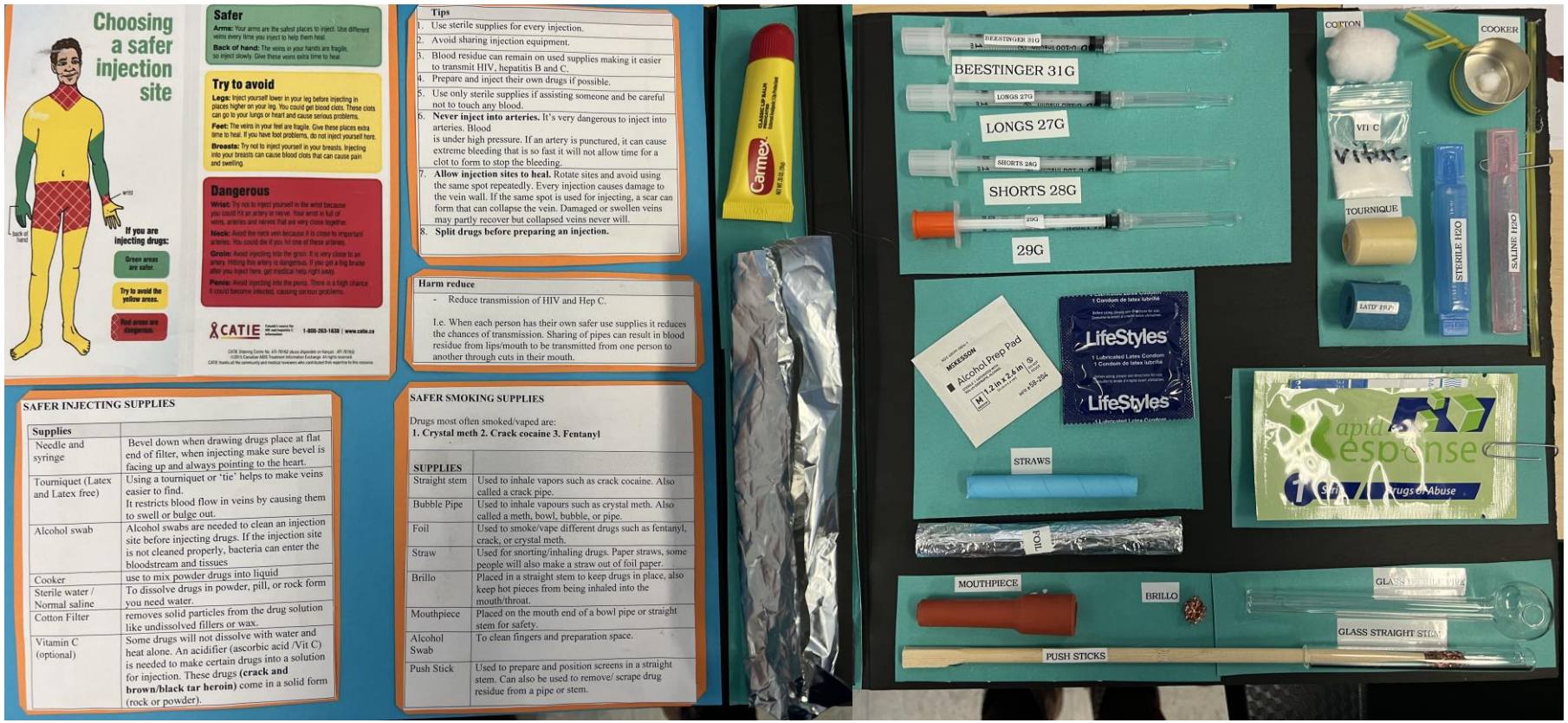
AshaRani PV. Drug Alcohol Dependence, 2020.
Bach P. JAM 2020.

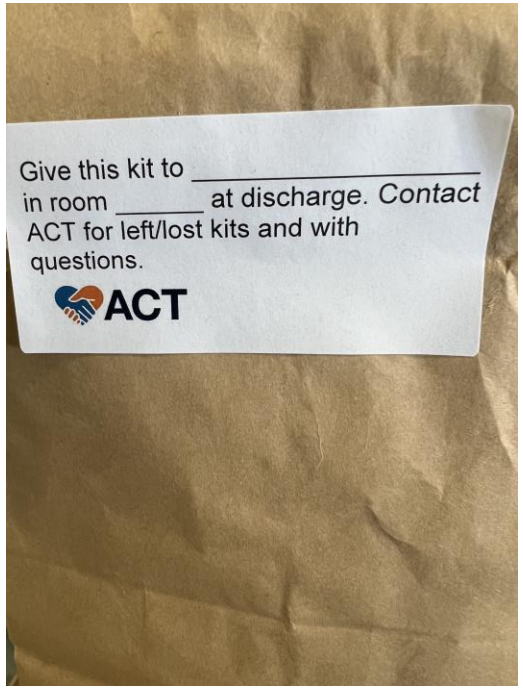
Harm Reduction in Hospitals

Syringe Service Program Information	Review injection practices	Link to Overdose Prevention Centers	Never Use Alone 800-484-3731
HCV and HIV education, screening, and treatment	Fentanyl test strips/harm reduction supplies	Naloxone	Stimulants warrant overdose prevention

Perera R, HRJ 2022.

Harm Reduction is…





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Harm Reduction Evidence

- Reduces HIV, hepatitis and skin and soft tissue infections
- SAVES LIVES by reducing overdose deaths!
- Builds trust
- Reduce stigma
- 5X likelier to enter addiction treatment and 3X likelier to stop substance use

HIV and Injection Drug Use , Vital Signs, 2016. Rachlis BS, HRJ 2009. Logan DE, Journal of Clin Psychology 2010.

Roadmap

- Background
- Diagnosis, Treatment, and Care Transitions
- **Frontiers**

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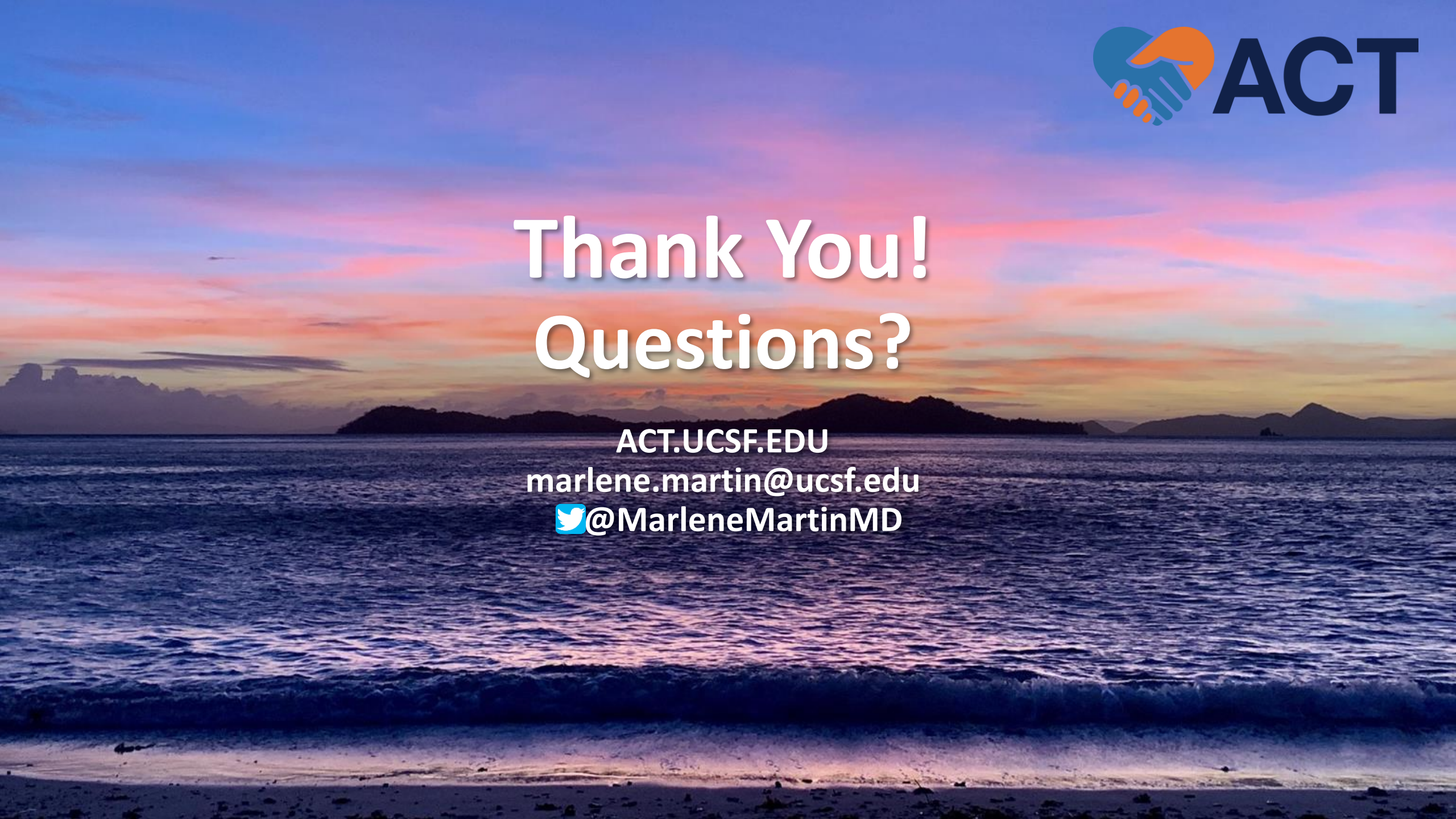
Opportunities for us to improve SUD care

DIAGNOSE & TREAT SUD

PRESCRIBE NALOXONE

BECOME AN SUD CHAMPION


ACT
Thank You!
Questions?
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@MarleneMartinMD

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