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Opioid Use Disorder Treatment Integrated with Primary Care

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Conflict of Interest

- No commercial, financial or advisory relationships

Learning Objectives

1. Review the integration of SUD treatment and primary care
2. Describe the process of buprenorphine initiation as well as stabilization and maintenance (including dosing)
3. Discuss the importance of harm reduction
4. Discuss the complications of OUD related to presence of medetomidine and xylazine in the drug supply

Terms to avoid	Alternatives	Why?
Addict *User* *Substance or Drug Abuser* *Junkie* *Alcoholic/Drunk* *Substance Dependence*	• **Person with…(OUD, AUD, SUD)** • **Person with opioid addiction…** • **Patient** • **Person in recovery**	• Person-first language • Shows that a person "has" a medical problem, rather than "is" the problem • Avoids negative associations, punitive attitudes, and blame
Clean/Dirty	**For toxicology screen results:** • **Testing negative/positive**	•Accurate terminology consistent with a medical disorder
Opioid Substitution Therapy/ Replacement Therapy	• **Opioid agonist therapy** • **Evidence-Based medication for OUD** • **Pharmacotherapy**	• Avoid misconception medications substitute for another drug/addiction
Medication Assisted Treatment (MAT)	• **Medication to treat OUD** • **Pharmacotherapy for OUD**	• "Assisted treatment" -undervalues the role of medication -unlike other medical disorders

National Institute of Drug Abuse. https://www.drugabuse.gov/nidamed-medical-health-professionals/health-professions-education/words-matter-terms-to-use-avoid-when-talking-about-addiction. Accessed 04/22/2020.

Some reasons why everyone should prescribe buprenorphine

- Caring for patient in opioid withdrawal
- Patient doing well on buprenorphine and wants all care integrated
- Patient had surgery and is having difficulty coming off full opioid agonist
- Patient has been on opioid agonist for chronic pain for many years and inquires about switching to buprenorphine
- Caring for patient with opioid use disorder who asks for help
- Diagnosed patient with opioid use disorder and you want to help immediately and prevent an overdose death

Integration of substance use disorder treatment and primary care

- **In 2006, the IOM released a report recommending improvement in coordination of mental health and substance-related services into general health care services:**
- **“Available evidence suggests that integration of mental health and primary care may lead to improved care and quality of life”**
- **“Studies of health delivery, process of care, and health outcomes in integrated clinical settings will be critical to inform the process”**

What should providers expect from their patients with addiction?

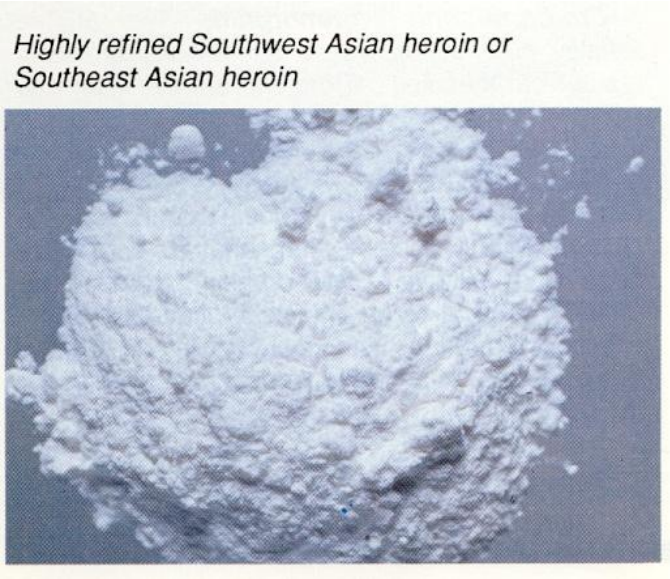
- **Desire to receive care that will improve health**
- **Engagement in care based on trust and rapport**

Press K, Zornberg G, Geller G, Carrese J, Fingerhood M. What patients with addiction disorders need from their primary care physicians: a qualitative study. Substance Abuse 2016; 37:349-55.

What do patients with addiction need from their providers

- **Knowledge about addiction**
- **Duty to treat**
- **Focus on overall health**
- **Engage patients in care**
- **Treat the full scope of illness (isolation, rejection, creating hope)**

The sap is extracted by slitting the pod



Opiates & Opioids

Opiates **= naturally present in opium**

- **e.g. morphine, codeine, thebaine**

Opioids **= manufactured**

- **Semisynthetics are derived from an opiate**
  - **–Heroin from morphine**
  - **–Buprenorphine, oxycodone from thebaine**
- **Synthetics are completely man-made to work like opiates**
  - **–Methadone**
  - **–Fentanyl**

Narcotic Regulation in US

- **1914- Harrison Narcotics Tax Act**
- **1972- Methadone approved by FDA for OUD in OTPs**
- **1978- Buprenorphine recommended as treatment for OUD**
- **1993- levo-α-acetylmethadol (LAAM) approved by FDA for OUD in OTPs**
- **2000- Drug Addiction Treatment Act of 2000 (DATA 2000)- office based physicians can prescribe "medication" for OUD - limit of 30 patients using X number**
- **2002- buprenorphine for OUD approved by FDA**
- **2003- LAAM removed from market**
- **2006- patient panel for buprenorphine increased to 100 after one year**
- **2016-patient panel increased to 275 after one year; NPs and PAs can also prescribe**
- **2020- can initiate buprenorphine using telemedicine**
- **2023- X number eliminated**

DSM5- Opioid Use Disorder

- Group 1- **Impaired control**- larger amounts and longer; desire to cut down; great deal of time spent related to using; craving
- Group **2-Social impairment**- failure to fulfill obligations; interpersonal problems; reduction in social, occupational or recreational activities
- Group 3- **Risky use-** use in hazardous situations; continued use despite negative consequences
- Group 4- **Pharmacologic dependence-** tolerance; withdrawal with cessation

Management of OUD

- Management = Treatment + Prevention
- Management = can be utilized across patient goal

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Options for Treatment

- Medication (MOUD)- methadone, buprenorphine or naltrexone
- Simple detoxification and no other treatment
- Counseling and/or peer support without MOUD
- Referral to short or long term residential treatment

SBIRT

vs

SIT (screen, intervene and treat)

Intervention- “I have joined your fan club”

- **Interventions and education are effective**
- **Interventions should emphasize health and relationship benefits**
- **Use family/friends in a positive way**
- **Avoid threats- “If you use, you will die”**
- **Give hope that life can improve**
- **Acknowledge reasons for use, but…**
- **Work together to define the benefits of change**

Effective Treatment of Opiate Addiction

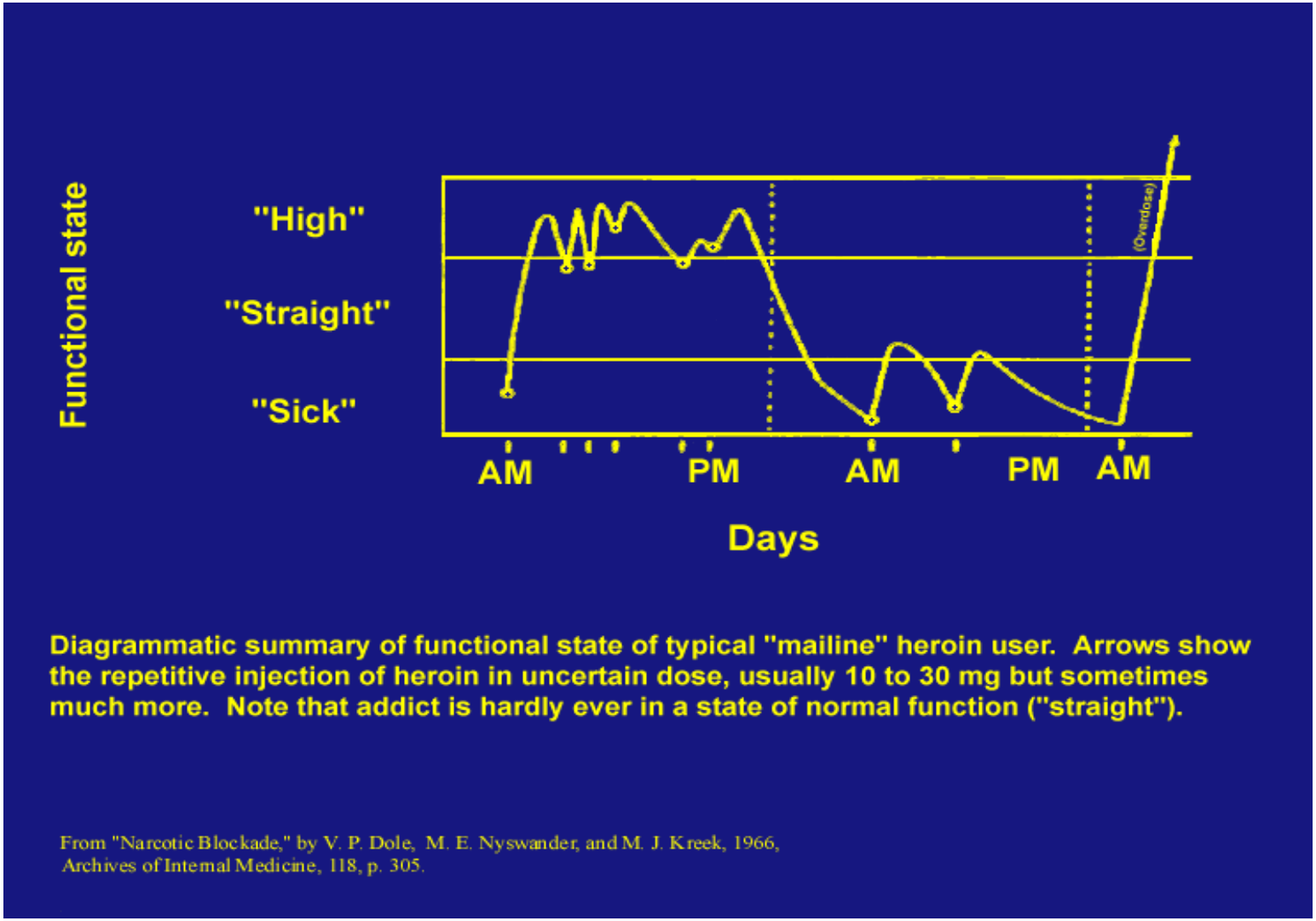
NIH Consensus Development Conference
November 17-19, 1997

- **Opiate dependence is a brain-related medical disorder**
- **Treatment is effective-**
  - **"Although a drug-free state represents an optimal treatment goal, research has demonstrated that this goal cannot be achieved or sustained by the majority of opiate-dependent people."**
- **Reduce unnecessary regulation of long-acting agonist treatment programs**
- **Improve training of health care professionals in treatment of opiate dependence**

MEDICATIONS

NOT MAT

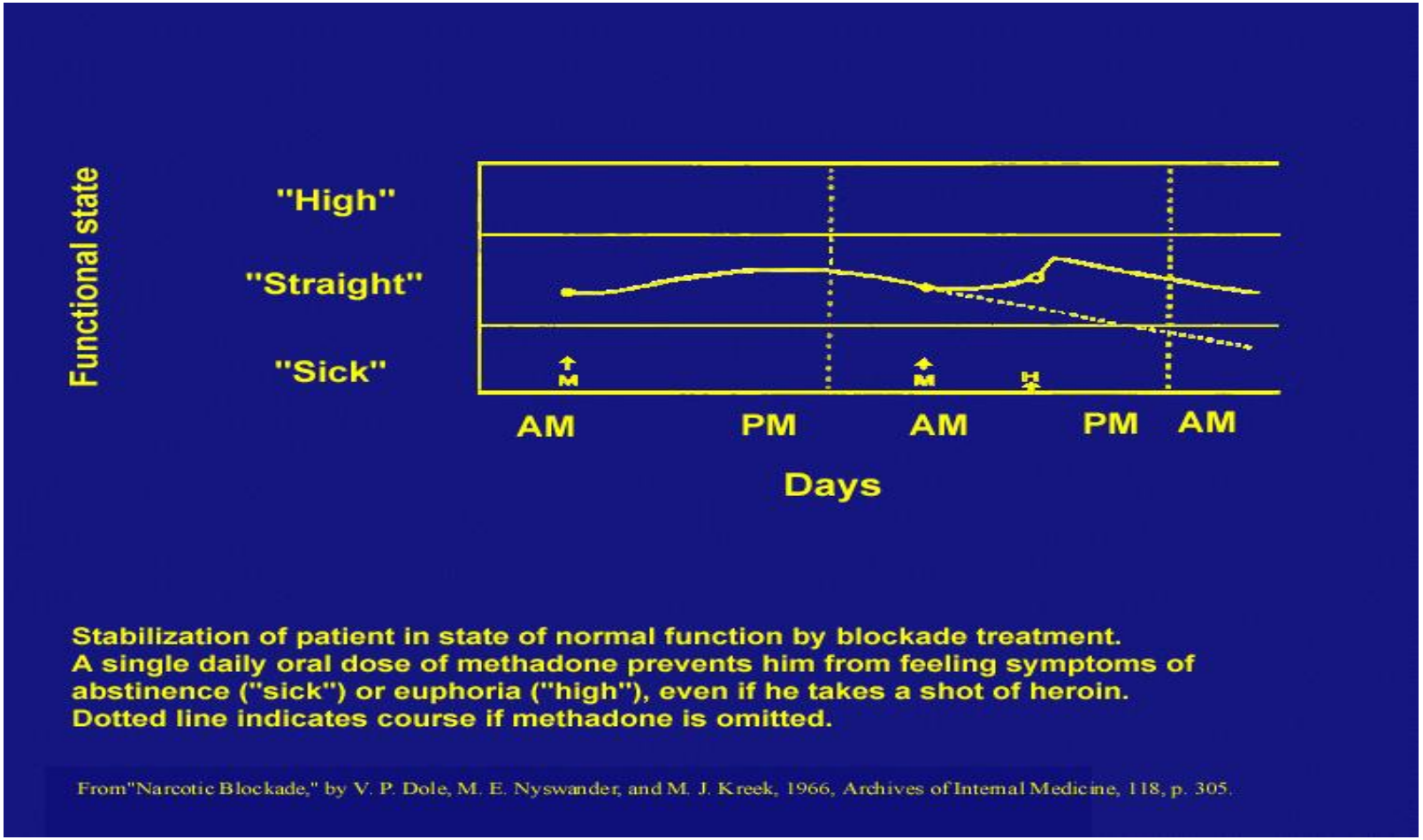
What the patient with opioid use disorder feels…



Diagrammatic summary of functional state of typical "mailine" heroin user. Arrows show the repetitive injection of heroin in uncertain dose, usually 10 to 30 mg but sometimes much more. Note that addict is hardly ever in a state of normal function ("straight").

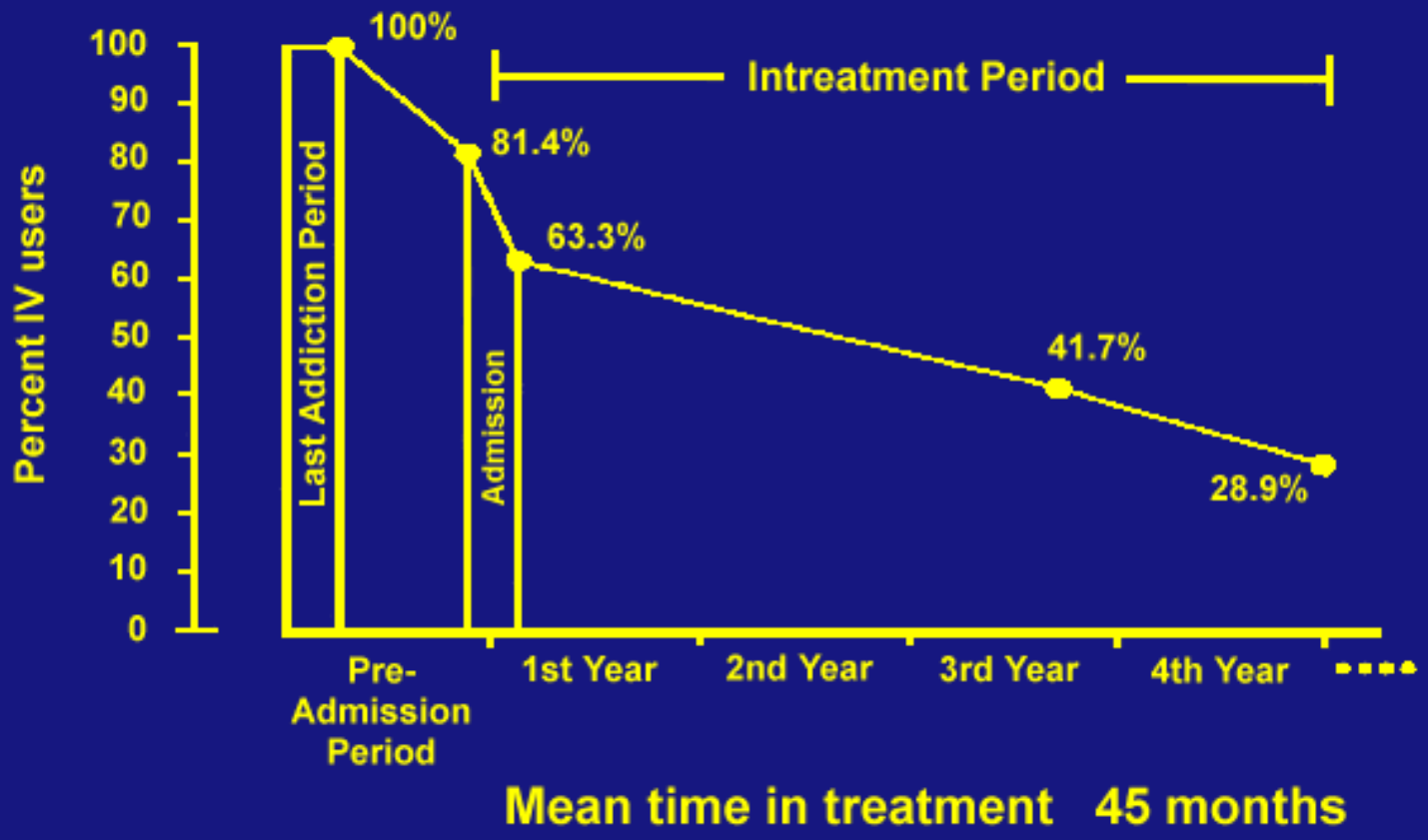
From "Narcotic Blockade," by V. P. Dole, M. E. Nyswander, and M. J. Kreek, 1966, Archives of Internal Medicine, 118, p. 305.

Stabilization by “Blockade Treatment”



Stabilization of patient in state of normal function by blockade treatment.
A single daily oral dose of methadone prevents him from feeling symptoms of abstinence ("sick") or euphoria ("high"), even if he takes a shot of heroin.
Dotted line indicates course if methadone is omitted.

From "Narcotic Blockade," by V. P. Dole, M. E. Nyswander, and M. J. Kreek, 1966, Archives of Internal Medicine, 118, p. 305.



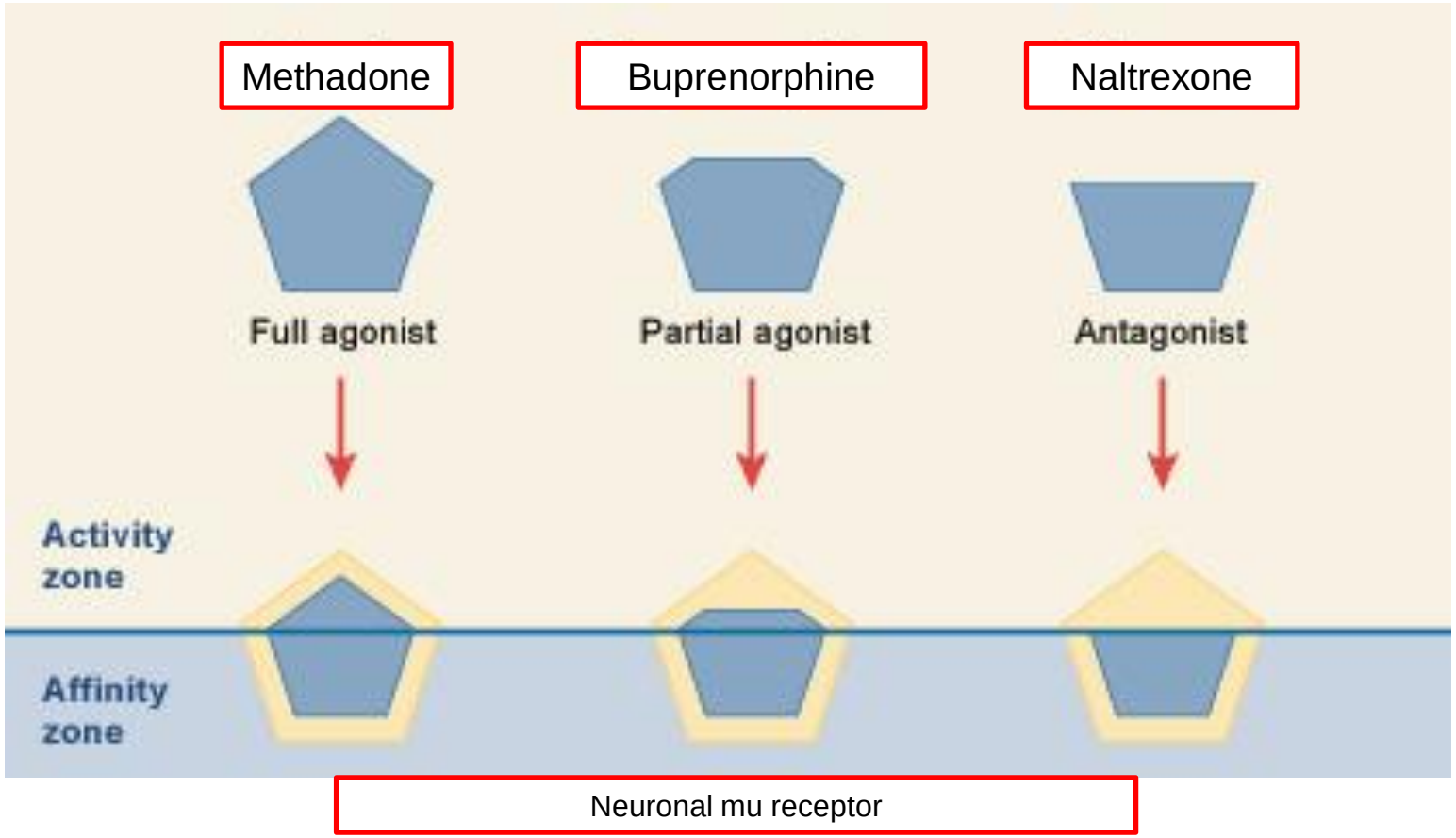
Impact of methadone maintenance treatment on intravenous drug use for 388 male methadone patients in six programs.

From the Effectiveness of Methadone Maintenance Treatment (p. 169), by J. C. Ball and A. Ross, 1991, New York: Springer-Verlag. Copyright by Springer-Verlag New York, Inc. Reprinted with permission.

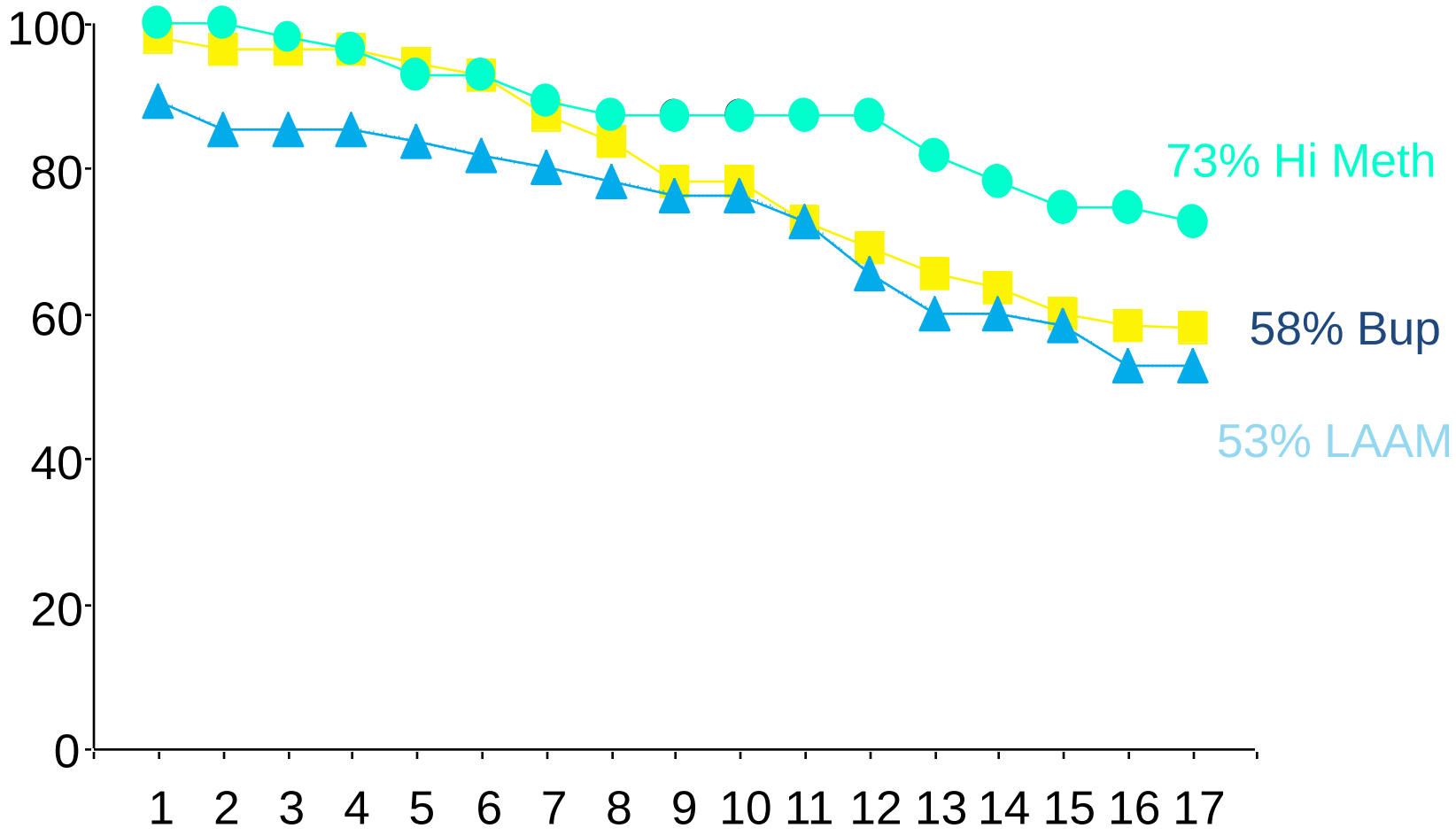
Goals of Pharmacotherapy

Mitigate withdrawal	Prevent or manage withdrawal symptoms
Reduce drug use	Reduce drug use and sustain reduction or abstinence
Improve morbidity and mortality	Prevent, reduce and/or manage the physical and social complications of continued opioid use

Medications for Opioid Use Disorder

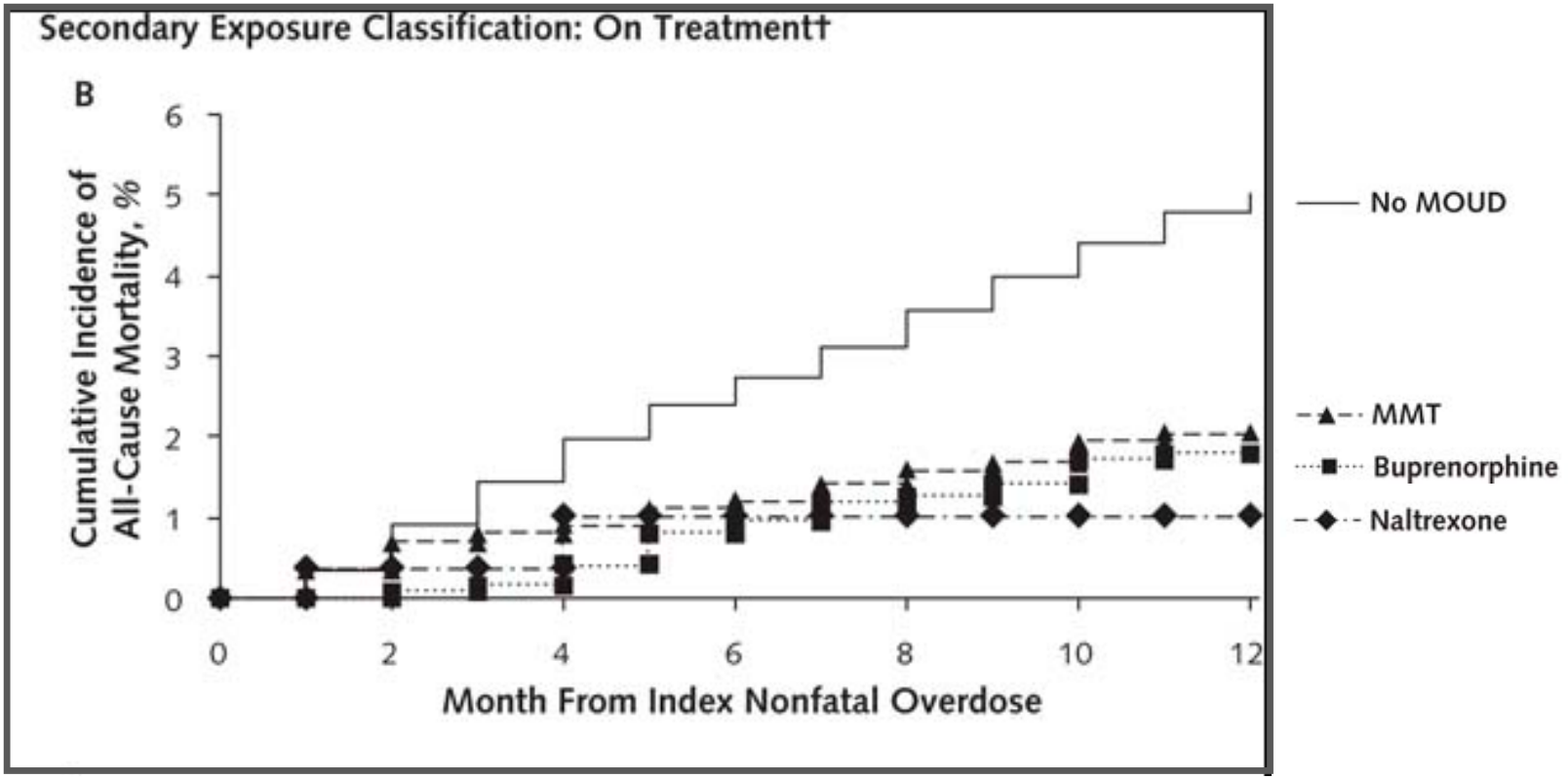


Buprenorphine, Methadone, LAAM: Treatment Retention



Johnson RE, et al NEJM 2000

MOUD Decreases Mortality



Larochelle, Annals of Internal Medicine 2018

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Major Features of Methadone

***Full Agonist* at mu receptor**

Long acting

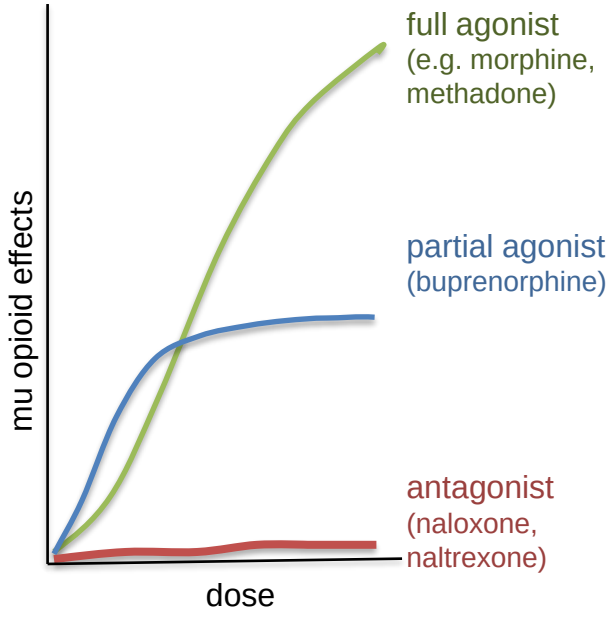
- Half-life ~ 15-60 Hours

Weak affinity for mu receptor

- *Can be displaced by partial agonists (e,g. burprenorphine) and antagonists (e.g.naloxone, naltrexone),* which can both precipitate withdrawal

Monitoring

- Significant respiratory suppression and potential respiratory arrest in overdose
- QT prolongation



Major Features of Buprenorphine

Partial agonist at mu receptor

- Comparatively minimal respiratory suppression and no respiratory arrest when used as prescribed

Long acting

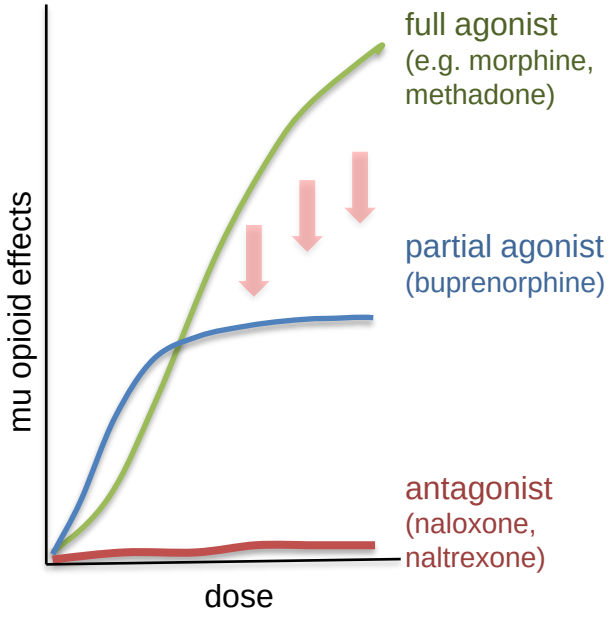
- Half-life ~ 24-36 Hours

High affinity for mu receptor

- *Blocks* other opioids
- *Displaces* other opioids
  - Can precipitate withdrawal

Slow dissociation from mu receptor

- *Stays on receptor for a long time*



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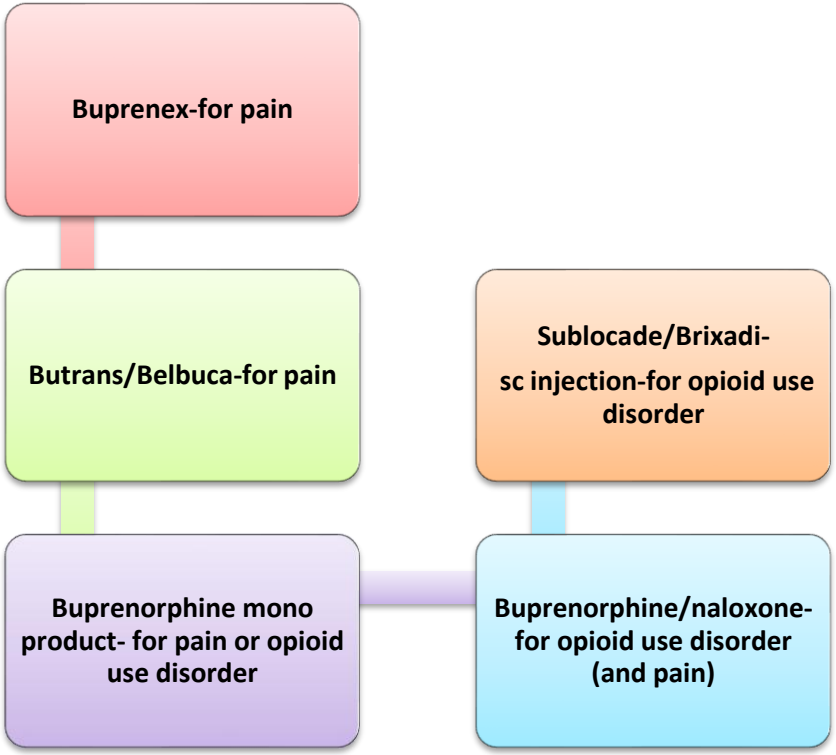
Buprenorphine Formulations



Stop using this term:

Buprenorphine Common Adverse Effects

- Headaches
  - Management: aspirin, ibuprofen, acetaminophen (if there are no contra-indications)
- Nausea
  - Management: Consider spitting the saliva out after adequate absorption instead of swallowing.
- Constipation
  - Management: Stay well-hydrated, Consume high-fiber diet, Consider stool softeners, laxatives, naloxegol
- Xerostomia (Dry mouth) –
  - Complications: Gingivitis, Periodontitis
  - Management: Stay well-hydrated, Maintain good oral hygiene

Precipitated Withdrawal

- Because of its high affinity for mu opioid receptors, buprenorphine can displace other agonists (such as heroin, methadone) that are already present and occupying the receptors

- The sudden change from full-agonist to partial-agonist activation of opioid receptors can cause sudden and severe withdrawal symptoms (precipitated withdrawal)

Starting Buprenorphine

Previous Treatment

- Prior treatment attempts
  - What type?
  - What age?
  - What happened?
  - What was your experience?
  - What was the outcome?

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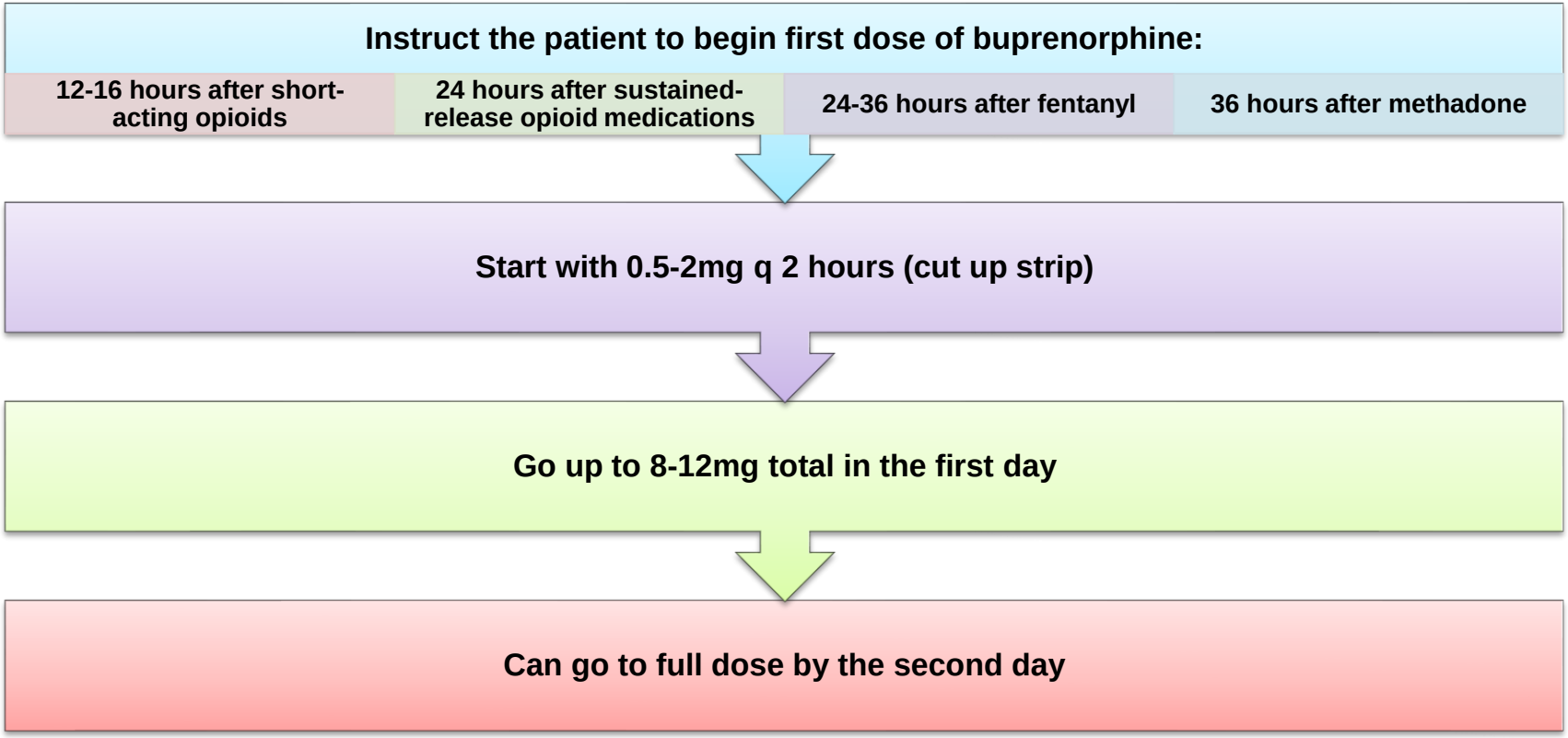
Clinical Opiate Withdrawal Scale (COWS)

- Resting Pulse
- Sweating
- Restlessness
- GI Upset
- Tremor
- Pupil Size
- Bone or Joint Aches
- Yawning
- Anxiety or Irritability
- Gooseflesh
- Runny Nose or Tearing Eyes

Wesson and Ling, 2003

To Avoid Precipitated Withdrawal



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Buprenorphine/Naloxone Instructions

Moisten mouth before taking film

Hold sublingual film/tablet (for 2 to 8 minutes) until completely dissolved

Do not swallow or spit

If administering 2 films/tablets at the same time, place the second under the tongue on the opposite side. Try to avoid having the films/tablets touch as much as possible

Don’t drink, eat, or smoke until 10 min after taking bup

Maintaining Buprenorphine

Treatment Duration

Evidence supports long term maintenance

- Studies up to 16 weeks show high relapse rates with medication withdrawal
- Improved retention rates in treatment with extended buprenorphine maintenance

Continue maintenance as long as patient is benefitting from treatment

Kakko et al., 2003
Weiss et al., 2011

Monitoring Efficacy

- **Urine toxicology- generally overused**
  - **Testing should not be to "catch" the patient**
  - **Positive UDS results**
    - **Reflect only “recent” drug use**
    - **Cannot determine exposure time, dose, or frequency of use**
    - **Should not lead to a discharge from treatment**
    - **Opportunity for discussion**

Monitoring Adherence

Urine testing for norbuprenorphine (metabolite)

Check PDMP

Pill/strip counts

Ask your patient!

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Urine Toxicology Time Limits- (may need to confirm result)

Amphetamine	2-4 days
Benzodiazepines	1-10 days
Cocaine	1-7 days
Heroin/morphine/fentanyl	1-14 days
Methadone	1-4 days
Marijuana	1-30 days
PCP	3-30 days

Optimal Management

Medications alone are efficacious and should never be delayed for individuals without access to counseling or therapy

But don’t I need to provide a counselor?

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Adjunctive Counseling During Brief and Extended Buprenorphine-Naloxone Treatment for Prescription Opioid Dependence:*A 2-Phase Randomized Controlled Trial*

Roger D. Weiss, MD; Jennifer Sharpe Potter, PhD; David A. Fiellin, MD et. al. Arch Gen Psych 2011; 68:1238-1246

- **Multicenter randomized clinical trial- n=653**

  In both phases patients randomized to standard medical management(SMM) or SMM plus counseling

  In both phases (3 &12 weeks of buprenorphine), separate counseling did not change outcomes

Support groups?

“You’re not in recovery if you’re on medication”

So now I am convinced (maybe) I should prescribe in my primary care setting…

- Prescribing is the easy part
- The conversation is the art of medicine (and the fun)

SHAME

Self-esteem

- **You- "The best thing you can do for yourself is stop using drugs"**
- **Patient- "I don't deserve the best, what else can I do?"**

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Coping


emotional
cognitive
anxiety
PTSD
flashbacks
stress
trigger
risk
treatment
trauma
veterans
guilt
anxiety
hypervigilance
fear
posttraumatic
assault
thinking
stress
survivors
behavioural
nightmares
stress
therapy
horror
guilt
irritable
behavioural
memories
CBT
fear

Visit openers:

What have you done today to make the world a better place?

What have you done today to make today better than yesterday?

Give me an update for your fan club

What if ?

- **My patient's urine drug screen is positive for…**
- **My patient's urine drug screen is negative for buprenorphine**
- **My patient misses an appointment**
- **My patient asks for a refill early**
- **My patient has an overdose**

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Recovery is about progression (not linear), not perfection

Quotes from patients on buprenorphine

“I feel normal”

“I wake up not sick”

“I have my life back”

- **Treatment in normal medical settings:**
  - **Encourages continuity of medical care**
  - **Encourages relationship building**
  - **Legitimizes opioid use disorder as a treatable, chronic illness**

So last topic…

What about dosing of buprenorphine in 2025?

(maybe 90-95% binding is no longer enough)

FDA input

- **"Current BTOD labeling has been misinterpreted by some as suggesting a maximum dosage of 16 or 24 milligrams (mg) daily although the labeling does not explicitly provide a maximum dosage. Our recommendations seek to clarify, via the labeling, that daily maintenance dosages can be incrementally adjusted for each patient based upon their individual therapeutic need and that daily doses higher than 24 mg per day may be appropriate for some patients."**

- **"Dosages higher than 24 mg buprenorphine daily have not been investigated in randomized clinical trials but may be appropriate for some patients."**

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D'Agata Mount J, Sun J, Davis A, Cover A, Sun L, Gannon C, Derenoncourt M, Garrett G, Eyasu R, Ebah E, Bijole P, Greenblatt A, Kattakuzhy S, Rosenthal E. Dose-specific clinical outcomes in patients with opioid use disorder treated with 24-32 mg/day of buprenorphine. Addiction. 2024 Nov;119(11):1964-1972.

- Low barrier buprenorphine clinic in Washington DC
- Participants were treated for HCV and offered buprenorphine at doses of 24 or 32 mg/day. 72 participants were included in the analysis: 24 (33%) patients stabilized on 24 mg, and 48 (67%) patients stabilized on 32 mg. Patients were predominantly male (78%), Black (96%), unstably housed (57%), and used opioids by injection (93%).
- Within the 32 mg cohort, increased dosing from 24 to 32 mg was associated with a decline in opioid use (68.5% at 24 mg vs 59.5% at 32 mg; P = 0.02), frequency of use per week (1.58 [0.19] at 24 mg vs. 1.15 [0.16] at 32 mg; P = 0.0002. At the end of the study period, there were significantly more patients retained in the **32 mg cohort (78.7%) compared with the 24 mg cohort (50.0%,** P = 0.02).

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Grande LA, Cundiff D, Greenwald MK, Murray M, Wright TE, Martin SA. Evidence on Buprenorphine Dose Limits: A Review. J Addict Med. 2023 Sep-Oct 01;17(5):509-516.

- **Shared decision making between prescribers and patients is important to establish a dose that meets each patient's treatment needs**
- **Pharmacological and clinical research results consistently demonstrate buprenorphine's dose-dependent benefits up to at least 32 mg/d, including reductions in withdrawal symptoms, craving, opioid reward, and illicit use while improving retention in care.**

Xylazine

- Discovered 1962 as an antihypertensive agent
- Noted to have hazardous side effects of sedation, hypotension and bradycardia
- Currently FDA approved as a common veterinary tranquilizer
- Agonist at central alpha-2 adrenergic receptor - similar effects to clonidine

Xylazine (tranq) in drug supply

- **In 2000s was described as an additive in the unregulated drug supply of Puerto Rico**
- **Usually found in conjunction with opioids**
- **2010: Increasing found in drug supply in Philadelphia**
- **Time to effect 1-2 minutes; peaks 30 minutes**
- **Duration of effect up to 4 hours**
- **Seems to be synergistic with opioids (from veterinary data)**
- **Can improve euphoria and prolong the duration of fentanyl**

Xylazine skin wounds

- **Tissue death and poor wound healing from local tissue hypoxemia**
- **Inhibition of endothelial cell proliferation**
- **Injecting at wound site to alleviate the pain (but wounds can appear at non-IDU sites)**
- **Local effect from drug extravasation or peripheral vasoconstriction**
- **Obliterative vasculitis (“shooter’s patch”)**
- **Progression to muscle with loss of limb**

Treating xylazine wounds

- **Avoid alcohol and hydrogen peroxide**
- **Clean wounds with soap (if available) and bottled/tap water or saline**
- **Keep skin around wound clean of drainage and moisturized (Vitamin A+D ointment)**
- **Black hardened wounds - chemical debridement: Santyl; Autolytic debridement: Medihoney; Mechanical debridement: wet to dry gauze**
- **Open wounds - Treat like burns: promote moist wound bed healing; Xeroform gauze or Calcium alginate dressing cut to size**

Medetomidine

- **MMWR August 1, 2024- Detection of Medetomidine Among Patients Evaluated in Emergency Departments for Suspected Opioid Overdoses- Missouri, Colorado, and Pennsylvania, September 2020–December 2023**
- **canine veterinary agent used for its anesthetic and analgesic properties**
- **alpha-2 agonist similar to xylazine**
- **Related to dexmedetomidine used in humans for sedation**
- **Seen most often in combination with xylazine when drug samples tested**
- **Unclear if contributes to skin wounds**

Patient vignette 1

- **EB is a 72 F seen for initial visit. She has a history of chronic pain in hips and knees. Her previous provider will no longer prescribe oxycodone as for the past 2 months her 30 day script ran out after 2 weeks. Tearful and fearful that providers won't help her. Cannot take NSAIDs. She admits that she often takes oxycodone when she is upset.**
- **She lives alone in senior housing apartment; 2 daughters- both with difficulties (medical and social). Non-smoker; no alcohol.**

Patient vignette 1 outcome

- **After spending time building rapport and making sure she knew my goal was to work with her, I explained I would not prescribe her oxycodone.**
- **She was open to undoing isolation, treating mood and trying buprenorphine.**
- **Almost immediately, physically more active (no longer dwelling on when next dose of pain medication is and does she have enough), remains on low dose buprenorphine, never running out before she should, with improved pain.**

Patient vignette 2

- **28F seen for first visit. Able to review in CRISP/PDMP- multiple ER visits for back pain and one opioid overdose, and many filled scripts for oxycodone from many providers. Had abnormal PAP 3 years ago. History of HIV (not addressed) and hypertension (has elevated BP today)**
- **Her agenda- getting script for oxycodone. My agenda- getting her engaged in medical care and treatment for opioid use disorder**

Patient vignette 2 outcome

- **After 3 months - seen her 7 times**
- **Doing well on buprenorphine/naloxone. No back pain. Urine drug screens all negative since the first visit.**
- **On medication for hypertension; adherent with HAART for HIV; had PAP done. No ER visits.**
- **Mood/self-esteem much improved. Better relationship with family. Working part-time.**

Harm Reduction

- **The practice of reducing the negative consequences of drug use in people who are not ready, or not able to abstain from drug use completely**

  –Needle and syringe programs

  –Safe injection practice counseling

  –Overdose education and naloxone distribution

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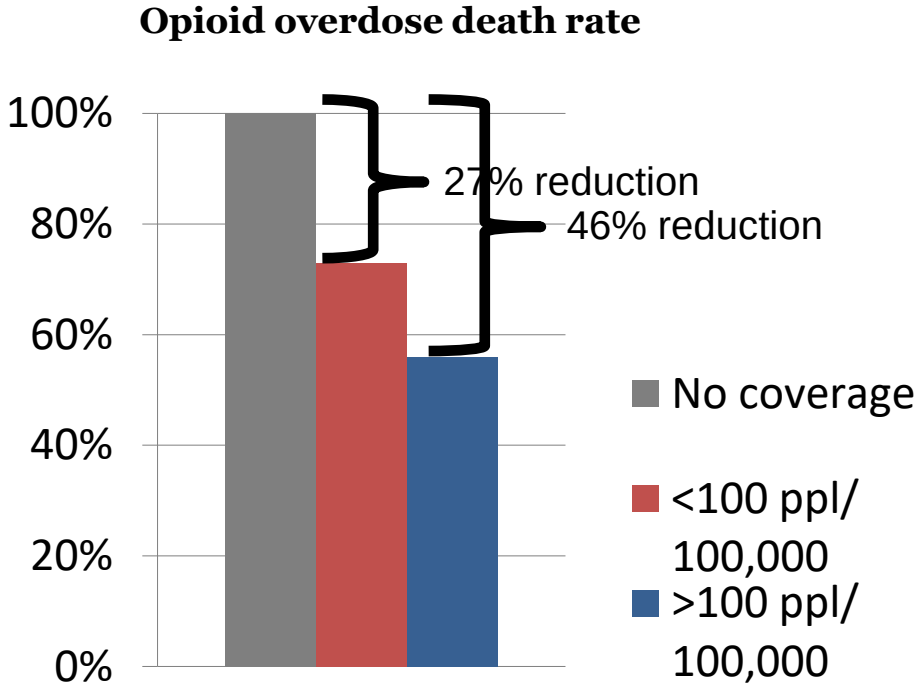
Naloxone Distribution Reduces Deaths Due to Overdose



Adapted from Alex Walley's slide, CRIT/FIT Program 2014

Summary

- **Initiating buprenorphine in the age of fentanyl is more challenging**
- **Patients initiating buprenorphine while at home offers the advantage of being able to start with lower doses (cutting a film)**
- **Buprenorphine in higher doses appears more effective in the treatment for OUD (and prevents overdose death)**
- **The reward is great when partnering with patients on their non-linear path in recovery**

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Maryland Addiction Consultation Service

Provides support to prescribers and their practices, pharmacists, and healthcare teams in addressing the needs of their patients with substance use disorders and chronic pain management.

All Services are FREE

- Phone consultation for clinical questions
- Education and training opportunities related to substance use disorders and chronic pain management
- Assistance with addiction and behavioral health resources and referrals
- Technical assistance to practices implementing or expanding office-based addiction treatment services
- MACS TeleECHO™ Clinics: collaborative medical education through didactic presentations and case-based learning

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