Medication Treatment for Opioid Use Disorder

Developed collaboratively by teams at: University of Washington, Boston Medical Center, Western New York Collaborative, and University of New Mexico

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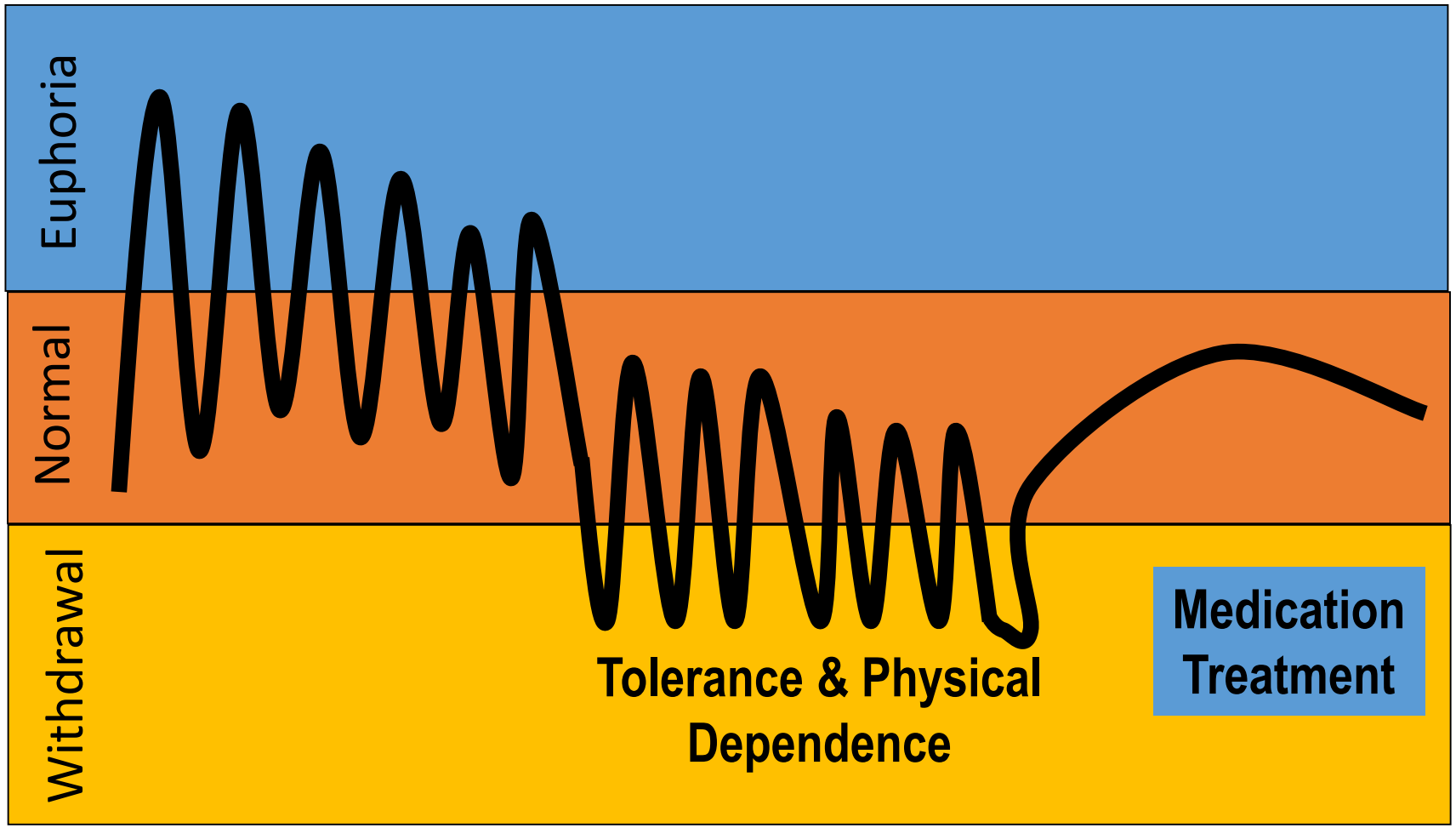
Learning Objectives

- Understand how opioids work.
- Learn what medications are available for treatment and the benefits and limitations of each.
- How to prevent overdoses.

How do Opioids Work?

- Bind to several different types of receptors in the brain, spinal cord and GI tract
- The main receptor for euphoria and for slowing breathing is the “mu” opioid receptor
- Affected areas regulate pain, mood, digestion, heart beat, blood pressure, and respirations



Acute use

Chronic use

Adapted from Alford, Boston University, 2012

Medications for Opioid Use Disorder

Goals:

- Alleviate physical withdrawal and craving
- Opioid blockade (blunt the euphoric effect of other opioids)
- Reduce or eliminate risky substance use
- Normalize deranged brain changes and physiology

Options:

- Methadone (full opioid agonist)
- Buprenorphine (partial opioid agonist)
- Naltrexone (opioid antagonist)

Economics of Treatment

- Substance use disorders cost the US > $600 billion annually
- Every dollar invested in substance use treatment programs yields a return between $4 - $7 in reduced crime and criminal justice costs
- When savings related to healthcare are included, total savings can exceed costs by a ratio of 1 to 12
- The average cost for 1 year of methadone treatment is $4,700/person, whereas 1 year of imprisonment is $24,000/person

https://www.drugabuse.gov/publications/principles-drug-addiction-treatment-research-based-guide-third-edition/frequently-asked-questions/drug-addiction-treatment-worth-its-cost 2012

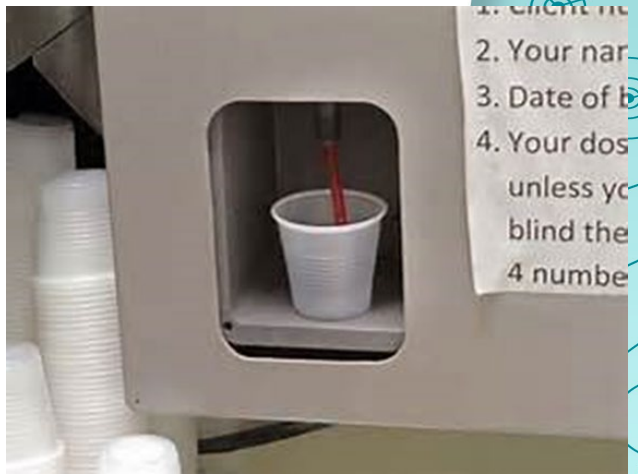
Pharmacotherapy for opioid use disorder: **Methadone**

How it works

- Full mu opioid receptor agonist
- Very long-acting; dose is titrated every 3-4 days
- Once daily dosing for substance use disorder; TID dosing for pain.

Who can prescribe for treatment of substance use disorder?

- Only designated Opioid Treatment Programs (OTP)
- **Illegal** to prescribe methadone **for substance use disorder** in general practice



Pharmacotherapy for opioid use disorder: **Methadone**

Benefits

- Daily, observed dosing
- Highly structured environment
- Multi-disciplinary approach
- High potency
- Well studied: proven to improve survival, increase employment, decrease hepatitis and HIV infections, decrease criminal activity, and to be cost-effective
- Best treatment retention rates in studies

Pharmacotherapy for opioid use disorder: **Methadone**

Limitations

- Still carries risk of overdose
- Potential medication interactions
- Slow titration results in longer time to stabilize on dose
- Poor access
- Risk of QT prolongation (Torsades de Pointes)
- Environment may be a trigger for relapse
- Stigma

METHADONE…

DECREASES RISK OF HIV AND HEPATITIS C INFECTION

Highly effective

Normalize physiology

Improves pregnancy outcomes

FACTS

Reduces relapse

One of the WHO list of 100 essential meds that should be available worldwide

Still addicted

Can't nurse your baby

Always sedated

Gets in the bones

MYTHS

Can't drive

BAD FOR YOUR BABY

Rots your teeth

Pharmacotherapy for opioid use disorder: **Buprenorphine**

How it works

- Partial mu opioid agonist
- High receptor affinity
- Formulated with naloxone – misuse deterrent
- Sublingual tablets and films, and newer injectable & implant

Who can prescribe

- Physicians who have DATA-2000 waiver (DEA-X) – requires 8 hour training course
- New as of spring 2017, NPs and PAs who have taken 24 hours of approved training

Pharmacotherapy for opioid use disorder: **Buprenorphine**

Benefits

- Lower risk of overdose and sedation
- Minimal QT prolongation
- Minimal medication interactions; but beware of benzos

Treatment can be integrated in primary care:

- Reduces stigma
- Provide medical and behavioral care, prevention
- Important tool when problems arise during chronic opioid therapy
- Home induction safe and effective

Important: very effective for pain when dose is divided TID-QID

Pharmacotherapy for opioid use disorder: **Buprenorphine**

Limitations

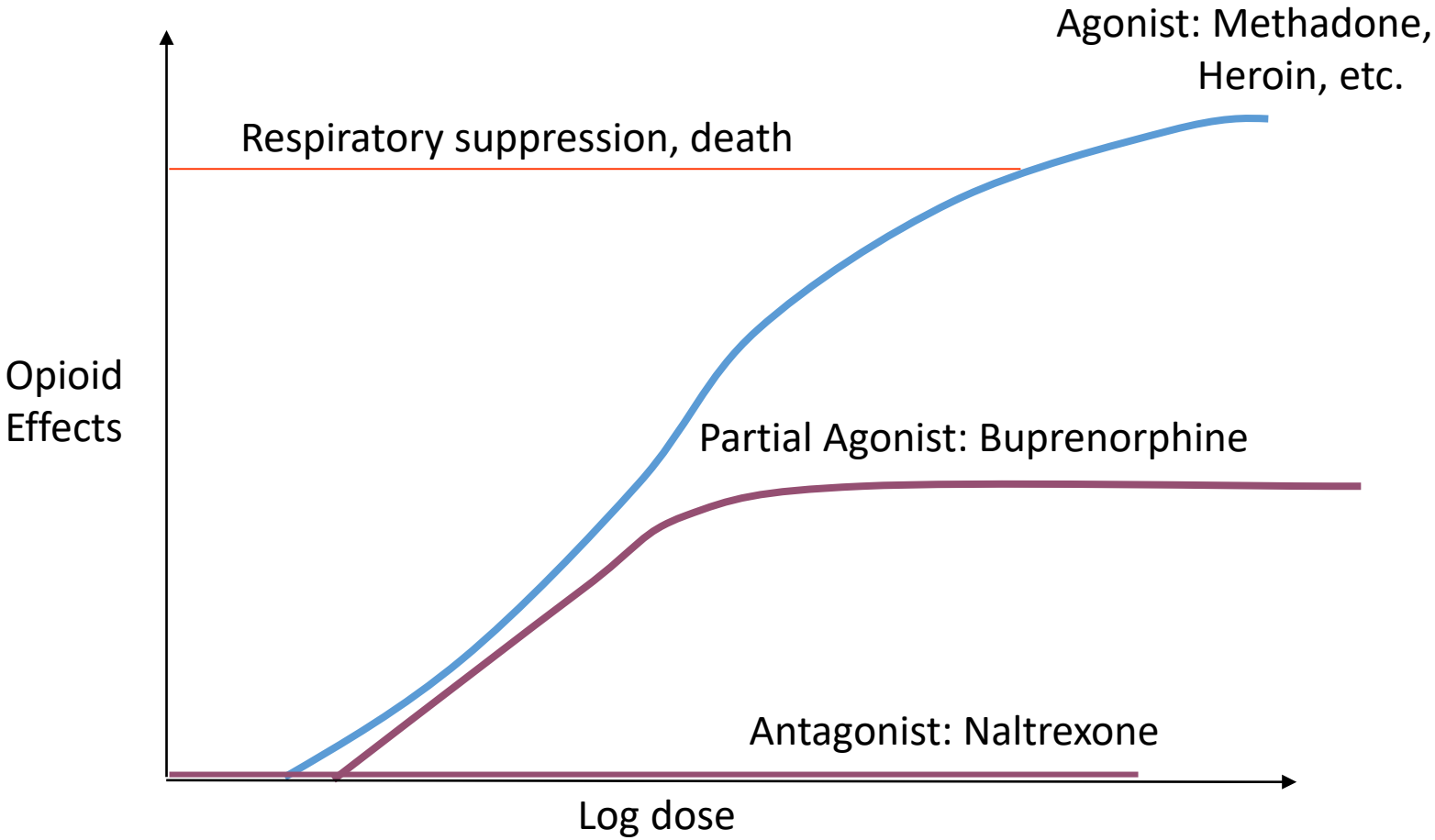
- Risk of diversion
- Possible lower retention rates compared to methadone
- Limited access due to reluctance to prescribe

Barriers in primary care include:

- Urgency of scheduling
- Induction visit and frequent early follow up
- Urine testing and prescription logistics
- Linkages to psychosocial services
- Fear of DEA visit

Highly gratifying form of treatment!

Why is overdose potential low with buprenorphine?



Trial of buprenorphine

- 40 people addicted to heroin
- Buprenorphine 16 mg/day vs

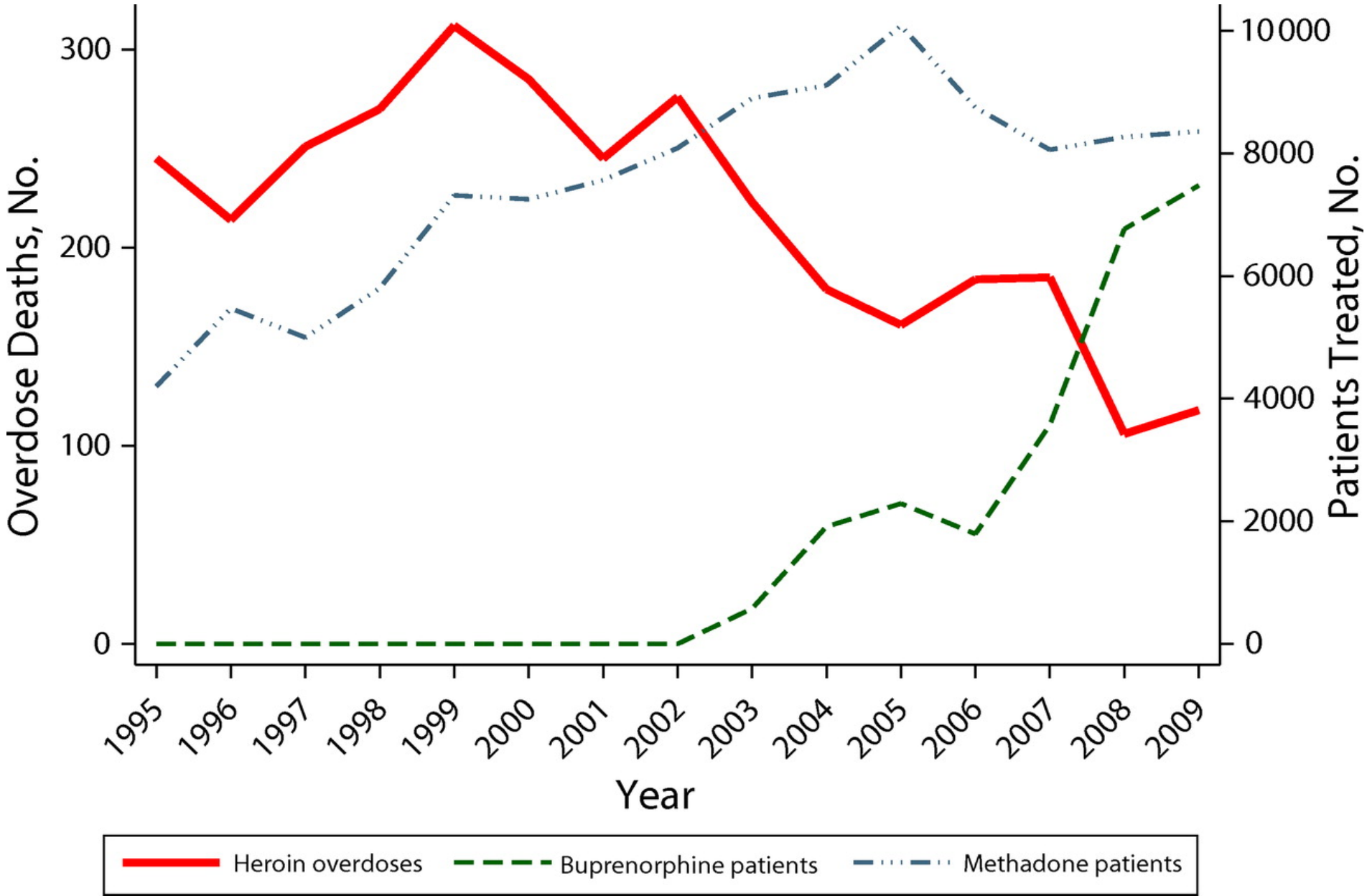
  taper + placebo
- All received indiv counseling + therapy groups
- Followed for 1 year

	Buprenorphine	Placebo
Retained at 1 yr	70%	0
% died	0	20%

Kakko et al, Lancet 2003

How effective is buprenorphine for treatment of opioid use disorder?

Author, Journal	Year	"n"	Setting	% retained in treatment
Fudala, NEJM	2003	461	Multicenter trial	57% @ 6 months
Alford, JGIM	2006	85	Acad med ctr/ community clinic; ½ patients homeless; nurse care manager	81% @ 12 month
Mintzer, Ann Fam Med	2007	99	4 primary care practices	54% @ 6 months
Soeffing, J Subst Abuse	2009	255	Urban academic health center	57% @ 12 months
Haddad, Drug Alc Dep	2013	266	Community health center network	57% @ 6 months


Overdose Deaths, No.
300
200
100
0
Patients Treated, No.
10 000
8000
6000
4000
2000
0
1995
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
Year
Heroin overdoses
Buprenorphine patients
Methadone patients

New: Long-acting buprenorphine prescribing

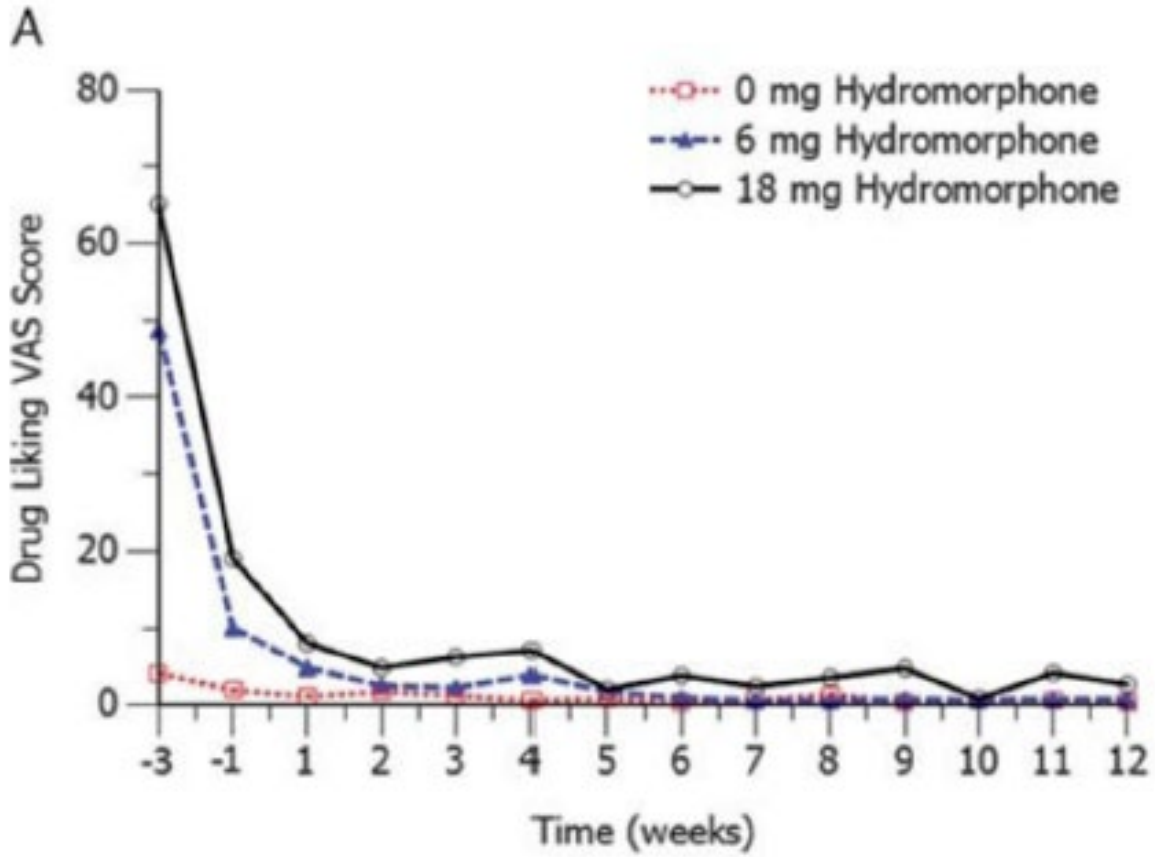
- Obtain through specialty pharmacy
- Patient must first be stabilized ≥ 7 days on SL bup
- Recommended dose is 300 mg subcut injection into abdomen monthly for two months, and then 100 mg per month
- Injection should only be done by clinical staff
- Very dangerous if injected intravenously (forms solid mass)

Long-acting injectable buprenorphine

- 39 adult patients with OUD who were not treatment-seeking
- Stablized on 4-24 mg buprenorphine
- Then given a 300 mg injection of RBP-6000 (Sublocade®), which was repeated 4 weeks later
- Tested opioid-blocking effect by having subjects report how much they “liked” hydromorphone (0, 6, or 18 mg, which is approximately equal to 135 mg morphine)

Nasser, J Clin Pharmacol, 2016

Nasser et al.



After two doses of injectable buprenorphine, blocking levels of buprenorphine maintained for at least 12 weeks

Pharmacotherapy for opioid use disorder: **Naltrexone**

How it works

- Opioid antagonist
- Causes acute withdrawal in opioid-dependent patients
- Two formulations available:
  - Oral 50 mg PO daily—not effective
  - Extended-release injectable (Vivitrol) 380 mg IM monthly

Who can prescribe

- Any prescriber
- Insurance coverage for injectable may vary
- Special injection technique

Norwegian naltrexone study by Tanum

- 159 adult patients with OUD detoxed in inpatient or jail setting
- Randomized after detox to injectable naltrexone or SL bup/nx 4-24 mg
- Followed for 12 weeks, endpoints included trial completion, UDS results, self-reported use of heroin
- Naltrexone non-inferior to bup on retention, UDS results, and use of heroin

Tanum, JAMA Psychiatry, 2017

US Naltrexone study by Lee

- 8 sites enrolled 570 adults with OUD
- Randomly assigned to naltrexone injection or SL bup/nx in inpatient setting
- Patients assigned to naltrexone were more likely to leave during initiation/detox
- 94% of bup-assigned patients were successfully inducted, vs 74% of naltrexone patients
- For patients who stayed and stabilized on meds, treatment results (retention, UDS, craving, overdose) were similar with bup/nx and naltrexone

Lee, Lancet, 2017

Pharmacotherapy for opioid use disorder: **Naltrexone**

Benefits

- No withdrawal if stopped
- Also effective in alcohol use disorder treatment
- Medication itself does not cause respiratory depression or sedation
- Not a controlled substance, no restrictions on prescribing
- Retention appears similar to buprenorphine if successful initiation is achieved

Pharmacotherapy for opioid use disorder: **Naltrexone**

Limitations

- Must abstain for opioids for 3-10 days prior to first dose
- No pain relief, and no effect from opioids
- Non-opioid approaches to pain management
- Long-term studies still lacking

Overdose prevention

- Naloxone (“Narcan”) reverses opioid overdose
- Overdose education and naloxone are an effective harm reduction strategy
- For those at high risk of overdose and their friends or family
- Populations: syringe exchange, exit from jail, in drug treatment, high risk prescribed opioids
- PrescribetoPrevent.org
- Should be provided to every patient who is being treated for opioid use disorder

Emerging models for Medication Treatment for OUD

- Massachusetts Nurse Care Manager Model
  - Full time RN and Program Manager can screen and assess, perform induction and follow closely
  - Prescriber time leveraged
  - Regular team meetings aid in decision-making
  - Allows primary care practices to involve multiple prescribers
  - RN can follow 100-125 patients
- Hub and Spoke Model (Vermont)
  - Centralized screening, assessment, stabilization
  - Transfer to primary care sites for ongoing treatment

Summary: Medications for Opioid Use Disorder

- Maintenance medications are an **essential component** of evidence-based treatment for opioid use disorder
- Strongest long-term data to support methadone and buprenorphine
- Naltrexone also highly effective, but can only be initiated in patients who are not currently physically dependent on opioids
- Primary care teams play an important role in treatment of opioid use disorders and prevention of overdose

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