Using Buprenorphine to Treat Opioid Use Disorder

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Objectives

- Explain the complexities of buprenorphine prescribing in the age of fentanyl
- Describe the evidence supporting buprenorphine for opioid use disorder

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Disclosures

- No financial relationships to disclose

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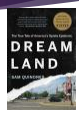
Historical Context

- **1898** – Bayer company begins production of heroin on a commercial scale
- **1912** – Harrison Narcotics Act prohibits prescription of narcotics to treat addiction
- **1969** – first methadone clinic opens in the United States
- **1990s** – greater awareness of untreated pain as a problem, research published supposedly demonstrating lack of addictive potential for opioids when prescribed for pain
- **1996** – pain declared the "5th vital sign" by the American Pain Society, OxyContin® (oxycodone) patented by Purdue Pharma
- **2000s** – proliferation of doctor shopping, pill mills, diversion of prescribed medications
- **2000s** – heroin decreases in price, heroin from South America dominates the US market
- **2000** – Drug Addiction Treatment Act permits use of buprenorphine to treat opioid use disorder
- **2010s** – heroin from Mexico begins to dominate the US market
- Late **2010s** – fentanyl begins to take off in the US market
- **2021** – overdose deaths (including from opioids) peak at 107,000



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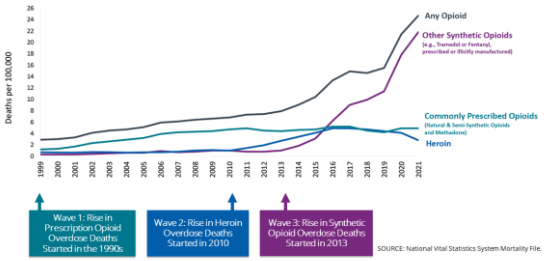
Three Waves of Opioid Overdose Deaths



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American Society of Addiction Medicine (ASAM) Definition of Addiction

Addiction is a **primary, chronic disease of brain reward, motivation, memory** and related circuitry.

Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors.

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Diagnosis of Opioid Use Disorder – DSM V Criteria

Taken in **larger amounts** or over a **longer period of time** than intended

Persistent desire or unsuccessful efforts to cut down or control opioid use

Great deal of **time spent in activities to obtain**, use or recover from effects

Craving, or strong desire to use

Resulted in **failure to fulfill major role obligations** at work, school or home

Continued use despite **social or interpersonal problems** caused or exacerbated by opioids

Important social, occupational or recreational **activities given up**

Recurrent use in **physically hazardous situations**

Continued use **despite physical or psychological problems**

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Diagnosis of Opioid Use Disorder – DSM V Criteria

How much are opioids ruining this person's life?

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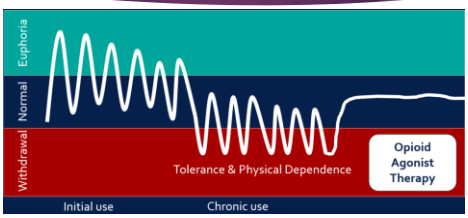
Clinical Rationale for Opioid Agonist Therapy



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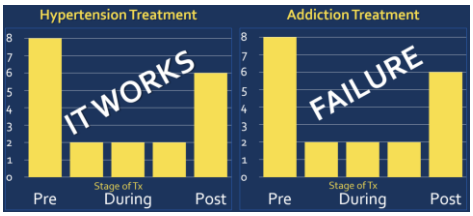
Clinical Rationale for Opioid Agonist Therapy



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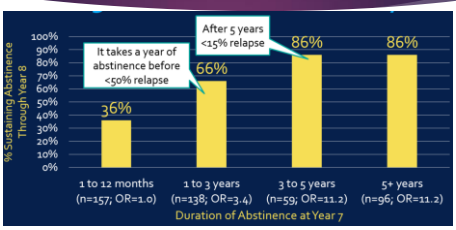
Longitudinal Trends In Recovery



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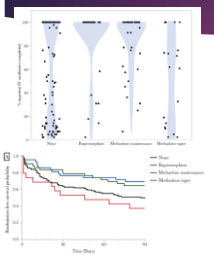
Evidence Rationale for Starting MOUD in the Hospital



- Greater proportion of patients completing antibiotic therapy (64% vs 46%)
- Greater number of days of gold-standard antibiotic therapy
- Reduced 30-day & 90-day hospital readmission
- More likely to attend outpatient follow up appointments after discharge
- Higher likelihood of attending an outpatient addiction treatment program after hospital discharge
- Reduction in AMA discharge, post discharge higher odds of medication adherence, reduced emergency department visits and reduced opioid overdoses

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Medications for Opioid Use Disorder

	Methadone	Buprenorphine	Naltrexone
Mechanism	**Full agonist** for mu opioid receptor	**Partial agonist** for mu opioid receptor, antagonist for the kappa receptor	**Antagonist** for the mu receptor
Typical effective dose	80-180mg	16-32mg or monthly LAI (300mg and 100mg doses)	50-150mg or monthly LAI (380mg)
Advantages	Full agonist activity works better for some patients Structure of methadone program helps unstable patients No risk of precipitated withdrawal Decades of data	Low risk of respiratory depression Can be prescribed by primary care physicians, access for patients Partial agonist activity avoids sedation	No risk of respiratory depression Not an opioid Also treats alcohol use disorder Short-term non-inferiority trial with buprenorphine
Drawbacks	Safety & drug interactions Only available through methadone treatment program (4 in MT)	Lack of provider familiarity Partial agonist activity requires planning around precipitated withdrawal	Requires 7 days of abstinence from opioids Complicates pain management Likely less effective than opioid agonist therapy

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Why would **anyone** be on Methadone???

1. **More effective** at keeping people from using illicit opioids compared to buprenorphine/suboxone
2. Some patients **need full mu-agonist therapy** to remain sober and remain in treatment
   - Methadone effective dose 80-150mg, some patients may need more
   - Buprenorphine/suboxone 24mg = 50-60mg methadone
3. **Daily observed dosing** works better for some patients
   - Patients who need additional supervision
   - Homeless
   - Living with still-using family member or partner
   - More severe opioid use disorder
4. Still provides **mu receptor blockade** when dosed appropriately

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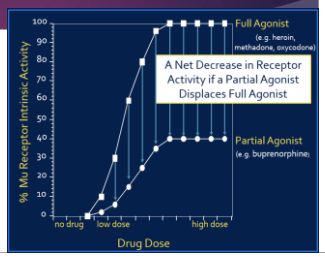
Precipitated Withdrawal Phenomenon

- Buprenorphine has extremely high receptor affinity, higher than almost all other opioids
- Unidirectional – precipitated withdrawal is only a concern when transitioning FROM full agonist opioids TO buprenorphine
- Giving full agonist opioids to someone who is on buprenorphine will NOT cause precipitated withdrawal



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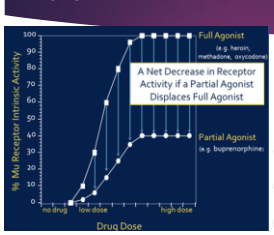
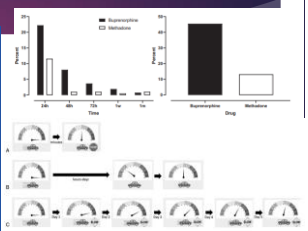
Fentanyl & Precipitated Withdrawal in Buprenorphine Initiation





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Low Dose Buprenorphine With Full Agonist Overlap

- Slow up-titration of buprenorphine dose over a week while continuing the full-agonist
- Avoids many symptoms of precipitated withdrawal

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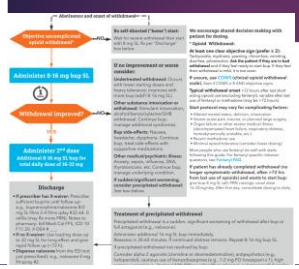
High-Dose Buprenorphine Initiation



- Patient waits until they are in bad withdrawal, encouraged to wait as long as possible
- Buprenorphine initiation with higher doses (8-16mg), total daily dose maximum of 32mg
- Aggressive loading strategy overcomes precipitated withdrawal with high doses of buprenorphine

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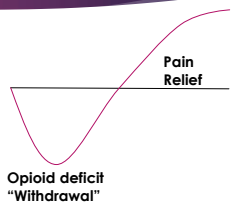
Acute Pain Management on Opioid Agonist Therapy

- Reassure and gain trust early
- Fill the opioid deficit
- Treat acute pain aggressively – treating acute pain will NOT make the patient's opioid use disorder worse!!



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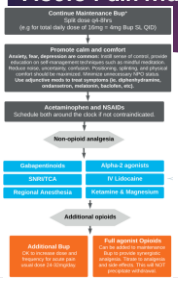
Acute Pain Management: Inpatient



- Try every available strategy before reducing the dose of buprenorphine or discontinuing buprenorphine,
- Adding full agonist opioids on top of maintenance buprenorphine will NOT precipitate withdrawal
- For patients on methadone, call the methadone program to confirm the dose, continue full daily dose, consider split dosing for help with pain control. Do not use buprenorphine!
- For patients on Naltrexone, stop 72 hours prior to elective surgery, stop LAI one month prior. In emergent situations, may need aggressive multi-modal pain control, high-affinity opioids

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Don't forget!

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Acute Pain Management: Outpatient

- Continue maintenance buprenorphine dose
  - Consider temporarily increasing total daily dose and taking smaller doses more frequently to help with pain control
- Utilize NSAIDs, Tylenol, other multi-modal medications unless contraindicated
- Close coordination of care with specialists, if involved
- Patients with opioid use disorder on buprenorphine may need higher doses and/or more high affinity opioids compared to opioid-naïve patients, but the duration of treatment should be the same

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Non-Opioid Medications for Opioid Withdrawal

- Appropriate to treat opioid withdrawal symptoms while the patient is transitioning to definitive treatment with either buprenorphine or in select patients, Naltrexone
- Managing opioid withdrawal symptoms with the intended endpoint of total abstinence is NOT recommended by most professional medical societies
- A treatment strategy of withdrawal management or "detox" followed by treatment without medications like methadone, buprenorphine or naltrexone in select patients INCREASES the patient's risk of death by overdose

TABLE 1
Therapy Guidelines

Supportive Therapy	
Anxiety/autonomic symptoms of withdrawal	Clonidine 0.1mg po q6h prn for SBP > 160, opioid withdrawal HOLD if BP less than 100/70 or HR less than 60
Myalgia/pain	Tylenol 650mg po q6h prn mild pain
Diarrhea	Loperamide 4mg po x 1, then 2mg po prn loose stools Max 16mg in 24 hours
Abdominal cramps	Dicyclomine 10mg po q6h prn abdominal cramps
Anxiety related to opioid withdrawal	Hydroxyzine 50mg po q6h prn anxiety
Nausea	Ondansetron 4mg po q8h prn nausea
Sleep/insomnia	Melatonin 3mg po qhs prn sleep Mirtazapine 7.5mg po qhs prn insomnia

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Resources

- UCSF National Substance Use Warmline 855-300-3595 9am-8pm ET
- Montana Primary Care Association MAT Chat – Webinar – Monthly on 2nd Wednesday – 8am-9am
- CA BRIDGE program - https://bridgetotreatment.org/wp-content/uploads/protocol-packet.pdf

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