ECHO IDAHO

Opioids, Pain and Substance Use Disorders

Managing Adverse Effects of MOUD

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Project ECHO

Learning Objectives

- Review the pharmacology of MOUDs
- Identify the most common adverse effects of methadone, buprenorphine, and naltrexone
- Discuss clinical strategies to monitor and manage these adverse effects

Confusing pharmacology terms and what they actually mean

Type of Drug	What It Does	Example	How Strong Is the Signal?	Analogy
Full Agonist	Turns the receptor **all the way on**	Methadone	🚨 Full strength	Like turning a light switch **all the way on**
Partial Agonist	Turns the receptor **partly on**	Buprenorphine	🟡 Medium strength	Like using a **dimmer switch** — light, but not full power
Antagonist	**Blocks** the receptor so other drugs can't turn it on	Naltrexone	⛔ No signal	Like **putting a lock on the light switch** so it can't be turned on

Opioid Receptors and Functions

Mu

- [ ] **Analgesia**
- [ ] Respiratory depression
- [ ] **Euphoria**
- [ ] Physical dependence
- [ ] Constipation
- [ ] Sedation

Kappa

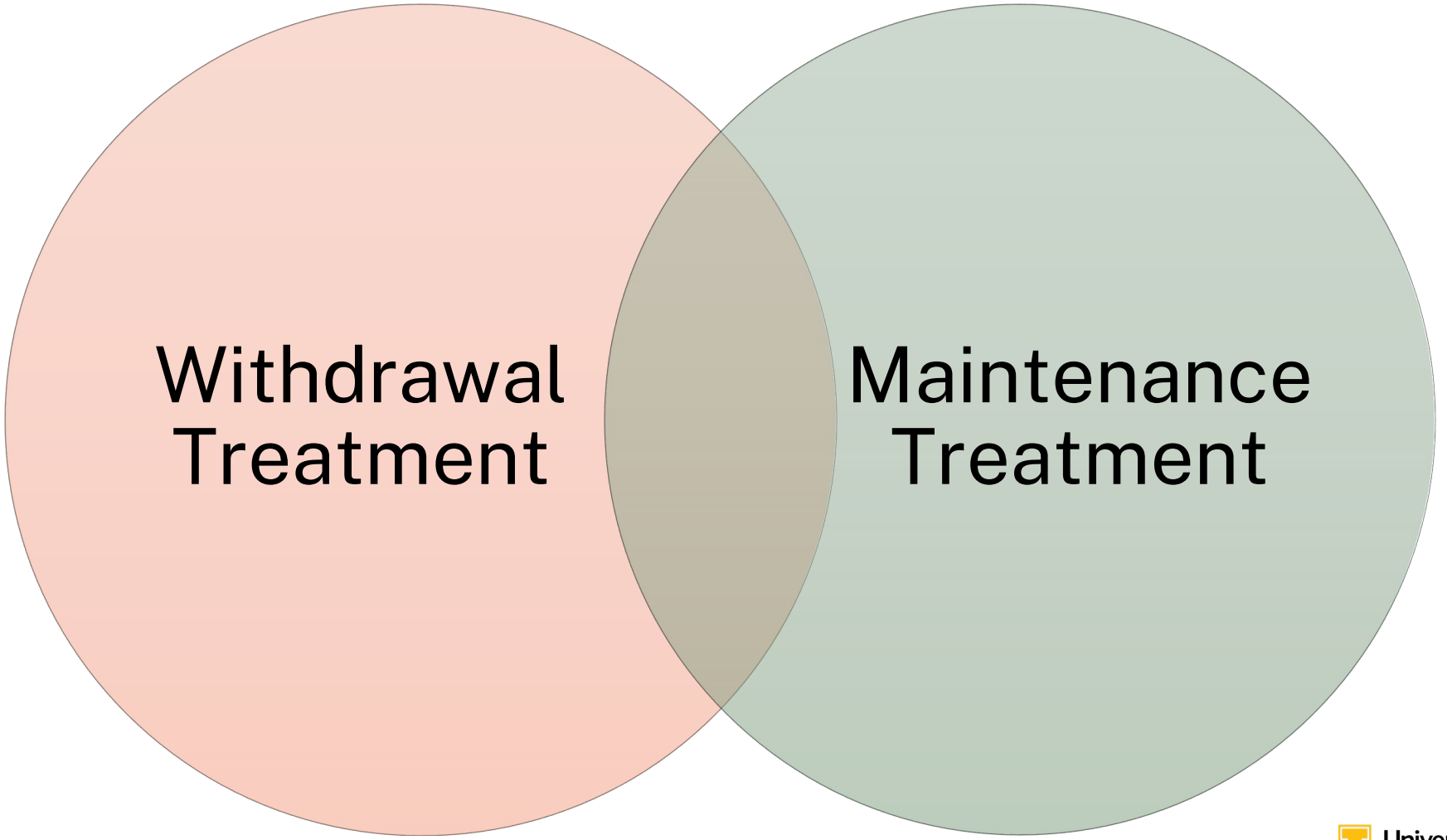
- [ ] Analgesia
- [ ] Sedation
- [ ] Miosis
- [ ] Dysphoria

Delta

- [ ] Analgesia

Fine, Perry G.; Russell K. Portenoy (2004) "Chapter 2: The Endogenous Opioid System." A Clinical Guide to Opioid Analgesia. McGraw Hill.

Pharmacotherapy:
<u>Two</u> different pharmacologic aspects of SUD treatment



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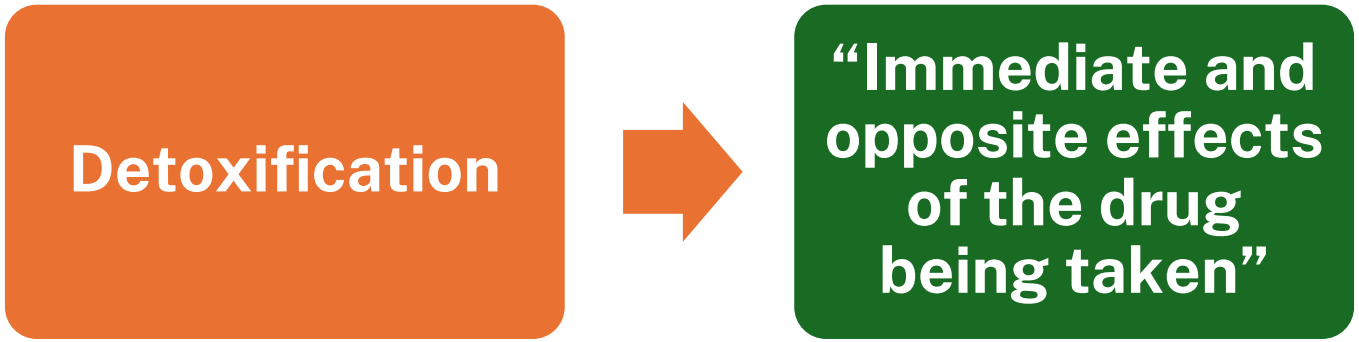
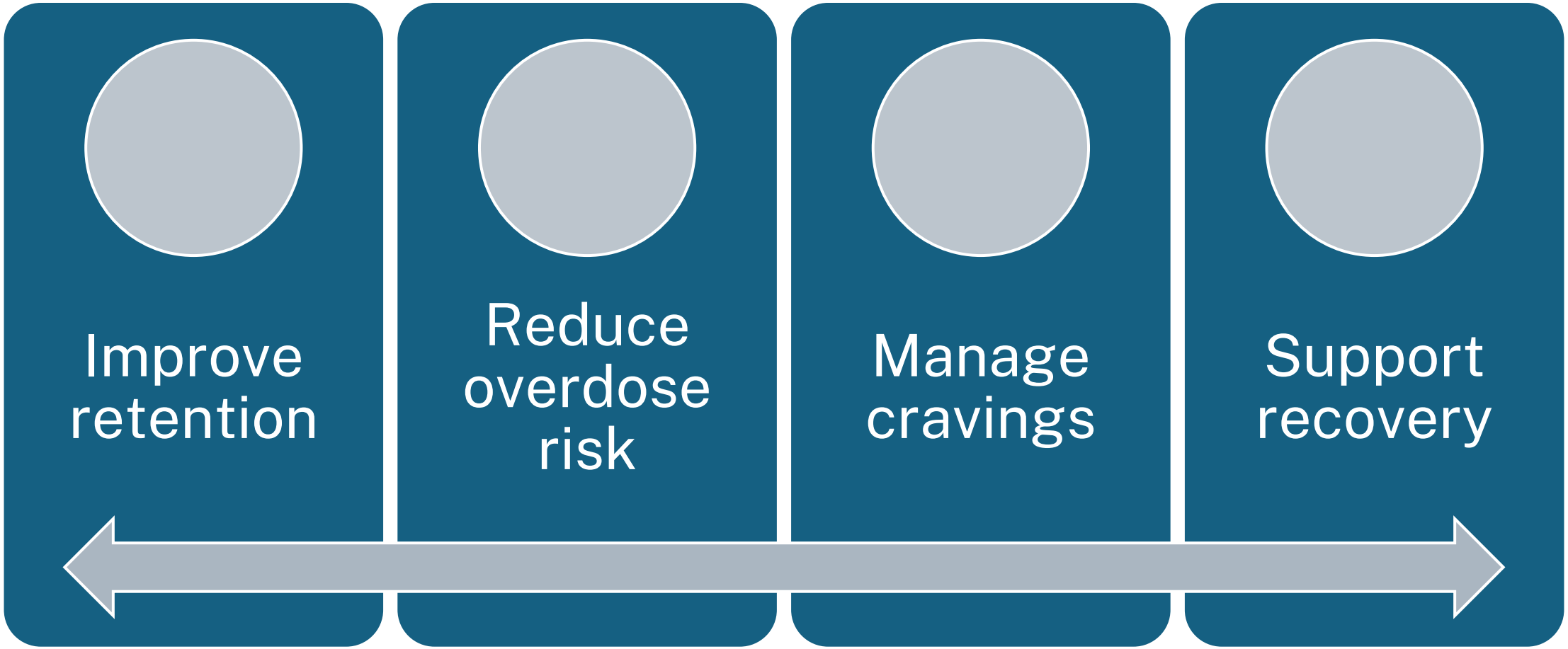
Withdrawal: Definition



Why MOUD?


Improve retention
Reduce overdose risk
Manage cravings
Support recovery

Maintenance: Definition

- Medication Assisted Treatment (old, not preferred term) → MOUD
  - May be similar pharmacology of drug of abuse (i.e., methadone, buprenorphine) OR
  - May be targeted at preventing intoxication or “reward and reinforcement” (i.e., naltrexone)
  - May be targeted at adverse associations with using (i.e. disulfiram, naloxone detox (please don’t do this))
- Harm Reduction
  - Can include pharmacological and nonpharmacological measures
  - Community-based naloxone (Narcan®) access

What medications do we use for OUD?

Naltrexone (oral tablets, long acting injection)

- Opioid receptor antagonist (blocker)
- Used to block euphoric effects and improve retention
- Requires full detoxification prior to initiation

Buprenorphine (sublingual, depot injection, implants)

- Opioid receptor partial agonist (it stimulates Mu kind of like other opioids, but not to the same degree)
- Used to block euphoric effects, improve retention, manage cravings
- Sometimes used for withdrawal management, used as maintenance

Methadone (oral tablets)

- Opioid receptor agonist
- Used to block effects of other opioids, improve retention, prevent withdrawal, manage cravings
- Burdensome for patients with OUD, but can be highly effective

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☐ Respiratory depression	☐ Sedation	
☐ **Euphoria**	☐ Miosis	
☐ Physical dependence	☐ Dysphoria	
☐ Constipation		
☐ Sedation		

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MOUD Adverse Effect Comparison Table

Adverse Effect	Methadone	Buprenorphine	Naltrexone
Constipation	✓✓✓	✓✓	✓
Sedation	✓✓✓	✓	Rare
Sweating	✓✓✓	Rare	No
QT prolongation	✓✓✓	No	No
Nausea	✓	✓✓	✓✓✓
Hepatotoxicity	Rare	Rare	✓✓✓

Naltrexone Pearls

- Opioid receptor blocker
- Because it is a blocker, it has a very different adverse effect profile when compared to methadone or buprenorphine:
- Most common ADRs:
  - Nausea, vomiting (by far)
  - Headache
  - Fatigue
  - Hepatotoxicity (dose related) → requires ongoing monitoring
  - Injection site reactions (inj only)
- Must educate on adherence, pain management, and risks of recurrent drug use

Buprenorphine Pearls

- Partial Mu agonist (high affinity, slow dissociation “like a bad ex”)
- Adverse effects can mirror that of methadone kind of, but to a much lesser degree
- Common adverse effects:
  - HA
  - N/V, constipation
  - Insomnia
  - Mild euphoria
  - Precipitated withdrawal (some patients conclude that this effect is from naloxone in combo products, but it is generally not)
  - Inj site reactions (long acting inj formulation)

Methadone Pearls

- Full receptor agonist
- OG treatment for OUD that revolutionized the approach to managing OUD as a medical condition, not a flaw of the character
- Very efficacious, but burdensome due to OTP requirements and adverse effects
- Common adverse effects:
  - Sedation (especially during initiation and titration)
  - Constipation (ongoing problem)
  - Sweating (dose related)
  - Weight gain
  - QT prolongation (dose related, can be very serious)
  - Respiratory depression (esp during induction)

Medication	Common Adverse Effect	Intervention	Monitoring
Naltrexone	Nausea	Take with food, try depot before oral, anti-nausea meds if severe	Track nausea frequency and med adherence
	Fatigue	Rule out other causes, encourage gradual activity increase	Screen for depression or other conditions
	Headache	OTC pain relievers (acetaminophen), dose adjustment if persistent, hydration	Monitor frequency and severity
	Liver enzyme elevation	Avoid alcohol, lower dose, discontinue if enzymes triple ULN	Baseline and periodic ALT/AST
	Injection site reaction (XR)	Warm compress, topical steroids, rotate sites	Visual inspection, patient comfort

Medication	Common Adverse Effect	Intervention	Monitoring
Buprenorphine	Nausea, constipation	Dietary changes, bowel regimen, hydration	Ask about bowel habits, check for GI distress
	Insomnia	Dose in morning, sleep hygiene, avoid caffeine late in day	Patient report of sleep patterns. R/O other causes like depression or anxiety.
	Headache	OTC pain relievers (acetaminophen), dose adjustment if persistent	Monitor frequency and severity
	Precipitated withdrawal	Ensure appropriate induction timing (wait until moderate withdrawal)	Monitor COWS or subjective reports
	Injection site reaction (XR)	Warm compress, topical steroids, rotate sites	Visual inspection, patient comfort

Medication	Common Adverse Effect	Intervention	Monitoring
Methadone	Nausea, constipation	Dietary changes, laxatives, hydration	Ask about bowel habits, check for GI distress
	Sedation & respiratory depression	Lower dose, split dosing, caution with other sedating meds	Observe alertness, COWS, UDS, drug inx checker
	Sweating	Clothing changes, reassure, possible dose adjustment	Patient report, quality of life impact
	Weight gain	Diet/exercise counseling, metabolic labs, GLP1s??	Monitor weight, lipids, glucose, other metabolically offensive meds
	QT prolongation	Avoid other QT drugs, monitor ECG, electrolyte balance	Baseline & follow-up ECGs, esp. if >100 mg/day

Clinical Pearls of MOUD

- As with most medications, adverse effects of MOUD are often dose related and in some instances transient
- Supportive care and education are some of the most important interventions in improving adherence to treatment
- Tailor therapy accounting for patient presentation, preferences, and comorbidities (pay special attention to psych comorbidities, chronic pain, and other common medical conditions like DMII)
- Monitor labs and EKGs (even when there is not a problem)

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