

Objectives

- Overview of the pathophysiology of withdrawal
- Review induction strategies for buprenorphine
- Review additional adjunct medications to treat withdrawal

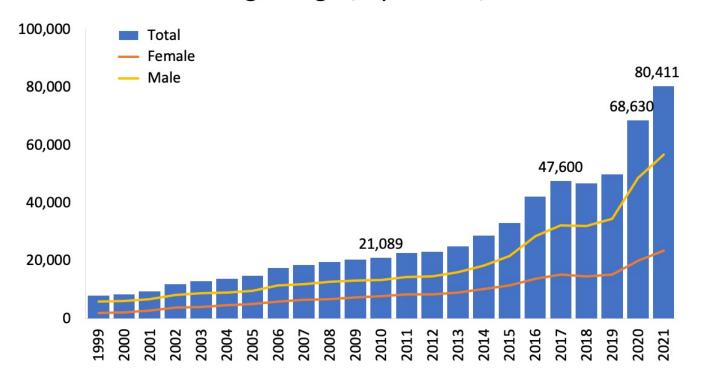
Disclaimers

- I have no financial disclosures
- Ijust discovered Alart
- Thanks to Dr. Joseph Carpenter for his help with this talk

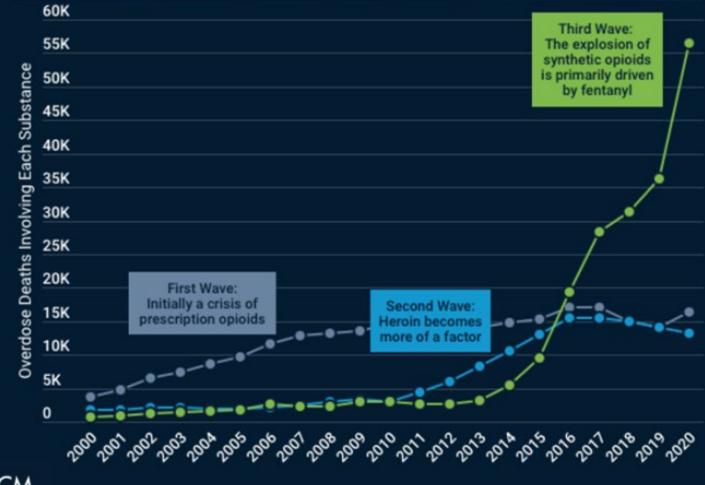




Figure 3. National Overdose Deaths Involving Any Opioid*, Number Among All Ages, by Gender, 1999-2021



^{*}Among deaths with drug overdose as the underlying cause, the "any opioid" subcategory was determined by the following ICD-10 multiple cause-of-death codes: natural and semi-synthetic opioids (T40.2), methadone (T40.3), other synthetic opioids (other than methadone) (T40.4), or heroin (T40.1). Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2021 on CDC WONDER Online Database, released 1/2023.



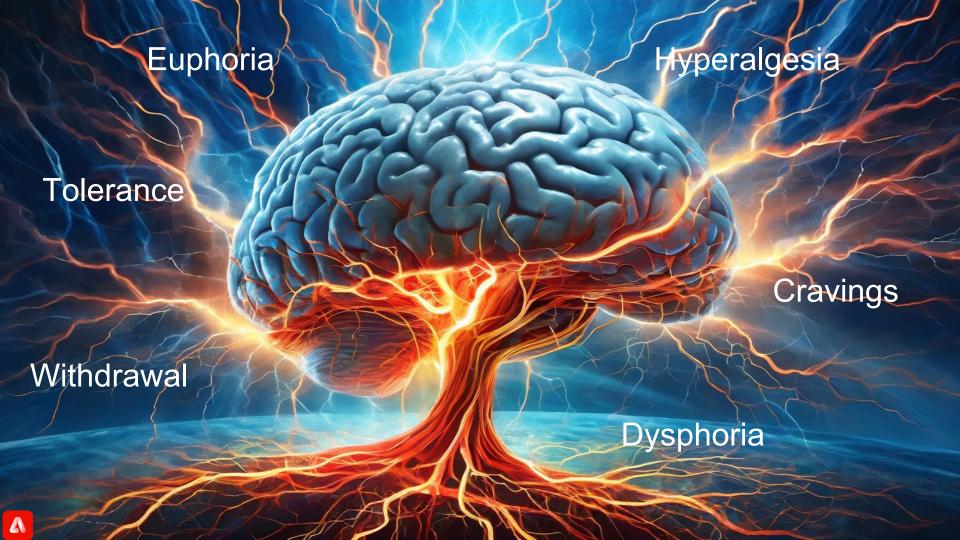






HEROIN









Opioid Withdrawal

Spontaneous

- Most common
- Abrupt cessation of opioid use

Precipitated

- Introduction of opioid antagonist
- Most severe

Protracted

Long-term, subjective symptoms



Symptoms

- Vomiting & Diarrhea
- Tachycardia
- Mydriasis
- Myalgias
- Yawning
- Tremors
- Diaphores is
- Piloerection
- Restlessness
- Normal Mental Status







COWS Wesson & Ling, J Psychoactive Drugs. 2003 Apr-Jun;35(2):253-9. Clinical Opiate Withdrawal Scale

Resting Pulse Rate: beats/minute		GI Upset: over last 1/2 hour		
Measured after patient is sitting or lying for one minute		0 No GI symptoms		
0	Pulse rate 80 or below	1	Stomach cramps	
1	Pulse rate 81-100	2	Nausea or loose stool	
2	Pulse rate 101-120	3	Vomiting or diarrhea	
4	Pulse rate greater than 120	5	Multiple episodes of diarrhea or vomiting	
Sweating: over past 1/2 hour not accounted for by room temperature or patient		Tremor observation of outstretched hands		
activity.		0 No tremor		
0	No report of chills or flushing	1	Tremor can be felt, but not observed	
1	Subjective report of chills or flushing	2	Slight tremor observable	
2	Flushed or observable moistness on face	4	Gross tremor or muscle twitching	
3	Beads of sweat on brow or face	123	2000 000 000 000 000 000 000 000 000 00	
4	Sweat streaming off face			
Restlessness Observation during assessment		Yawning Observation during assessment		
0	Able to sit still	0	No yawning	
1	Reports difficulty sifting still, but is able to do so	1	Yawning once or twice during assessment	
3	Frequent shifting or extraneous movements of legs/arms	2	Yawning three or more times during assessment	
5	Unable to sit still for more than a few seconds	4	Yawning several times/minute	
Pupil size		Anxiety or irritability		
0	Pupils pinned or normal size for room light	0	None	
1	Pupils possibly larger than normal for room light	1	Patient reports increasing irritability or anxiousness	
2	Pupils moderately dilated	2	Patient obviously irritable anxious	
5	Pupils so dilated that only the rim of the iris is visible	4	Patient so irritable or anxious that participation in the	
3	rupus so duated that only the rim of the iris is visible		assessment is difficult	
Bone or Join	t aches If patient was having pain previously, only the additional	Gooseflesh skin		
component a	attributed to opiates withdrawal is scored	0	Skin is smooth	
0	Not present	3	Piloerrection of skin can be felt or hairs standing up on	
1	Mild diffuse discomfort		arms	
2	Patient reports severe diffuse aching of joints/ muscles	5	Prominent piloerrection	
4	Patient is rubbing joints or muscles and is unable to sit	15	V200506-100-00-00-4-1-00-00-00-00-00-00-00-00-00-00-00-00-0	
	still because of discomfort			
Runny nose	or tearing Not accounted for by cold symptoms or allergies	Description of the second		
0	Not present	Total Score		
1	Nasal stuffiness or unusually moist eyes	The total score is the sum of all 11 items Initials of person completing Assessment:		
2	Nose running or tearing			
4	Nose constantly running or tears streaming down cheeks	D. 18 (19 (19 (19 (19 (19 (19 (19 (19 (19 (19	2 5.05.00 (1. 7. 03) (1. 10. 10. 10. 10. 10. 10. 10. 10. 10. 1	

Score: 5-12 mild; 13-24 moderate; 25-36 moderately severe; more than 36 = severe withdrawal





Managing Withdrawal



Detoxification Only

70% return to use within 6 months



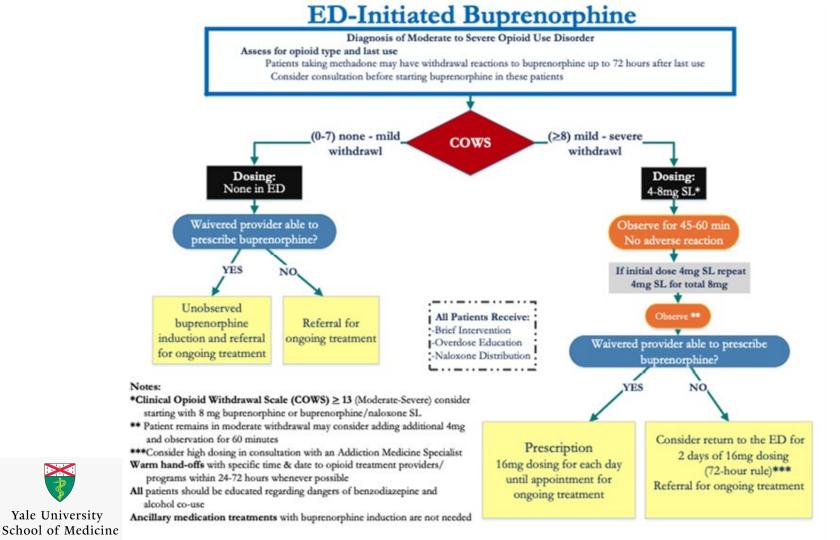


Medication Assisted Treatment (MAT)

<u>Medication</u>	<u>Mu Act ivit y</u>	<u>Init iat ion</u>	<u>Dosing</u>	<u>Cost</u>	<u>Risks</u>
Buprenorphine	Part ial Agonist	Int er mediat e	1-3 x/day (Mont hly)	\$ (\$\$\$)	Precipit at ed Wit hdrawal
Met hadone	Full Agonist	Easy	Da ily	\$	Overdose, QTc prolongation
Naltrexone	Ant a gonis t	Difficult	Mont hly	\$\$\$	Precipit at ed Wit hdrawal



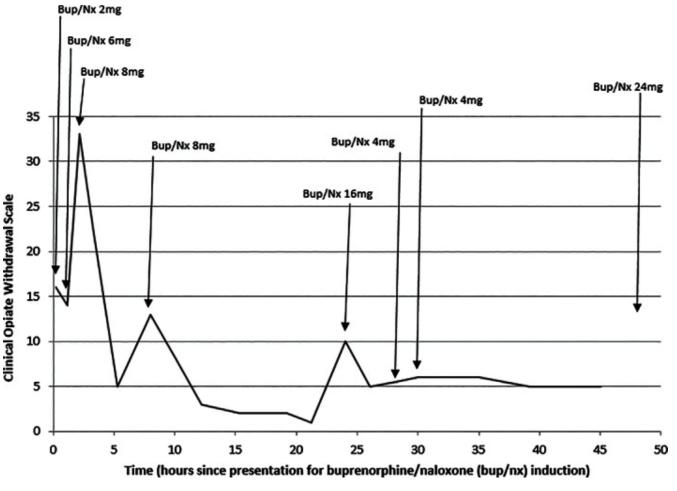




Precipitated Withdrawal

- 9% of inductions
- Induced too soon
- Long acting opioids
- Chronic fentanyl user
- Answer
 - More Buprenorphine
 - Adjunct medications
 - Coaching



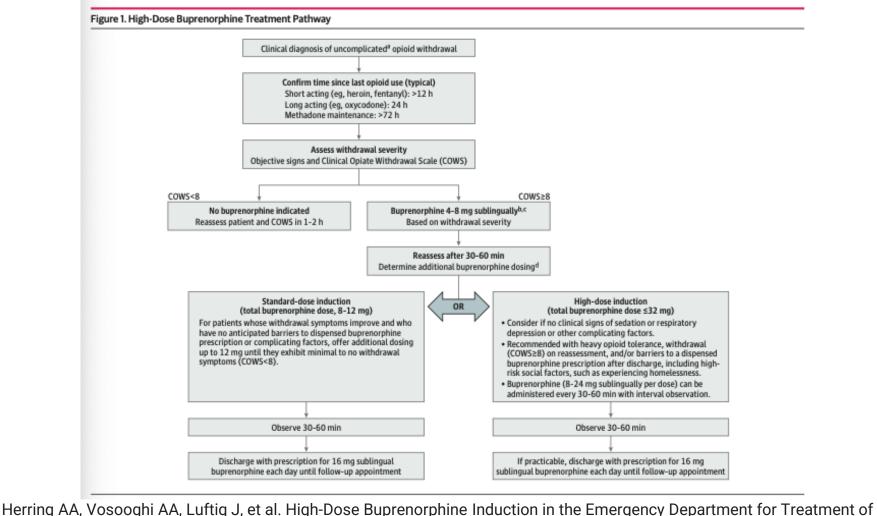


Oakley B, Wilson H, Hayes V, Lintzeris N. Managing opioid withdrawal precipitated by buprenorphine with buprenorphine. Drug Alcohol Rev. 2021 May;40(4):567-571. doi: 10.1111/dar.13228. Epub 2021 Jan 21. PMID: 33480051; PMCID: PMC8248003.



Buprenorphin	Day	Dose	Route		
Start BUP microdosing	Once BUP reaches a maintenance dose,	Maintain BUP	1	0.1	IV
overlapping with full MOR agonist	stop full MOR agonist		1	0.2	IV
Cell Membrane	2	0.3	IV		
Desensitized MOR	Cytoplasm Desensitized MOR				
Full MOR Agonist Buprenorphine	Resensitized and Upregulated MOR		2	0.3	IV
	R R R	000000	3	0.3	IV
7 9 934			3	0.3	IV
	3	2	SL		
Downregulated MOR	4	2	SL		
Rev	4	4	SL		
900	500	O _O	5	4	SL
			5	8	SL
		6	8	SL	
		7	8	SL	
	7	8	SL		





Opioid Use Disorder. *JAMA Netw Open*. 2021;4(7):e2117128. Published 2021 Jul 1. doi:10.1001/jamanetworkopen.2021.17128

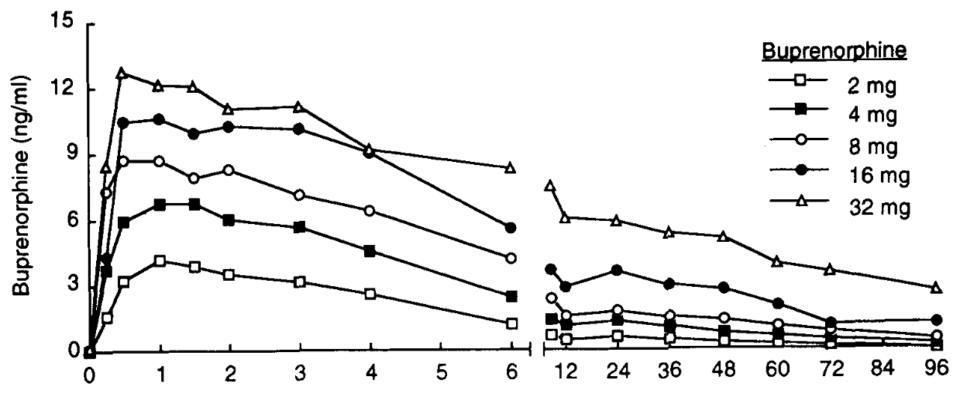


Fig. 5. The time course of plasma drug levels is illustrated for buprenorphine (upper panel) and methadone (lower panel) for 96 hours. Each *data point* represents the mean score for the group.

Walsh SL, Preston KL, Stitzer ML, Cone EJ, Bigelow GE. Clinical pharmacology of buprenorphine: ceiling effects at high doses. *Clin Pharmacol Ther*. 1994;55(5):569-580. doi:10.1038/clpt.1994.71

Now What

Fat al Overdose after ED Treatment

- 5-15% within 1 year
 - 0 1% within 1 month
- o 0.25% within 2 days







Addiction Medicine. Saving Lives.

