Medications for Opioid Use Disorder

Speakers:
Ericka L. Crouse, PharmD
Sharon Gatewood, PharmD

Accreditation Statement

In support of improving patient care, VCU Health Continuing Education is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

This activity provides 2 contact hours (0.2 CEUs) of continuing education credit.

ACPE Universal Activity Number (UAN): JA4008237-0000-23-059-L01-P

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ACPE

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Disclosures

- The Planning Committee Members disclose the following relevant financial relationships:
  - Lauren Pamulapati, PharmD, BCACP – Nothing to disclose
  - Sharon Gatewood, PharmD, BCACP, FAPhA – Nothing to disclose
  - Ericka L. Crouse, PharmD, BCPP, BCGP, FASHP, FASCP – Paid consultant for Wolters-Kluwer/Lexicomp; Editorial Board Member for The Medical Letter (All relationships have been mitigated)
- The Presenting Faculty Members disclose the following relevant financial relationships:
  - Sharon Gatewood, PharmD, BCACP, FAPhA – Nothing to disclose
  - Ericka L. Crouse, PharmD, BCPP, BCGP, FASHP, FASCP – Paid consultant for Wolters-Kluwer/Lexicomp; Editorial Board Member for The Medical Letter (All relationships have been mitigated)
- No commercial support was used in the development and implementation of this activity

<u>Presenters will discuss the off-label use of:</u>

Naloxone injection via nasal administration; clonidine in opioid withdrawal; fentanyl test strips; buprenorphine/naloxone films; lidocaine for injection site pain

Meet Your Speakers

Sharon Gatewood

Ericka Crouse

Also practices on Inpatient Psychiatry at VCUHealth

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E Crouse personal photo; https://www.vcuhealth.org/locations/location-details?id=14; https://dailyplanetva.org/2020/05/daily-planet-converts-recently-purchased-building-into-covid-assessment-center/

Objectives

1. Describe trends in opioid overdose
2. Recognize signs and symptoms of opioid overdose and opioid withdrawal
3. Summarize treatment strategies to manage opioid withdrawal.
4. Compare and contrast dosage forms of medications utilized in treating opioid overdose and opioid use disorder (OUD).
5. Identify adverse effects of medications for opioid use disorder (MOUD).
6. Recognize myths regarding MOUD.
7. Describe prevention mitigation strategies for medication errors.
8. Select a MOUD treatment plan through patient cases.

Audience Assessment

What is your practice area?

A. Academia
B. Ambulatory care
C. Community pharmacy
D. Independent pharmacy
E. Hospital pharmacy - inpatient
F. Hospital pharmacy - clinical
G. Investigational
H. Nuclear
I. Other

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Analogy: Diabetes versus Opioid Use Disorder

- Mishka Terplan, MD

Interprofessional Communication

A survey of providers qualitatively describing communication between DATA waivered providers (N = 85) and community pharmacists in Northeast TN identified:

- **<u>Education and Understanding:</u>** Providers noted community pharmacists **did not** fully understand the meaning of recovery [noting "patients are not on this medication because they enjoy it"]
  - One provider noted educating patients to be polite to pharmacists
- **<u>Stigma:</u>** Providers perceived community pharmacists as holding stigmatizing attitudes toward MOUD and negative judgements of providers who worked in MAT/MOUD clinics as "Buprenorphine Pill Mills"
- Patients are often the mediary of communication between pharmacist and provider

MAT = medication assisted therapy; MOUD = medications for opioid use disorder

Ventricelli DJ, et al. Subst Use Misuse 2020; 55(3):349-57.

Reducing Stigma

A study by the Recovery Research Institute surveyed 315 respondents

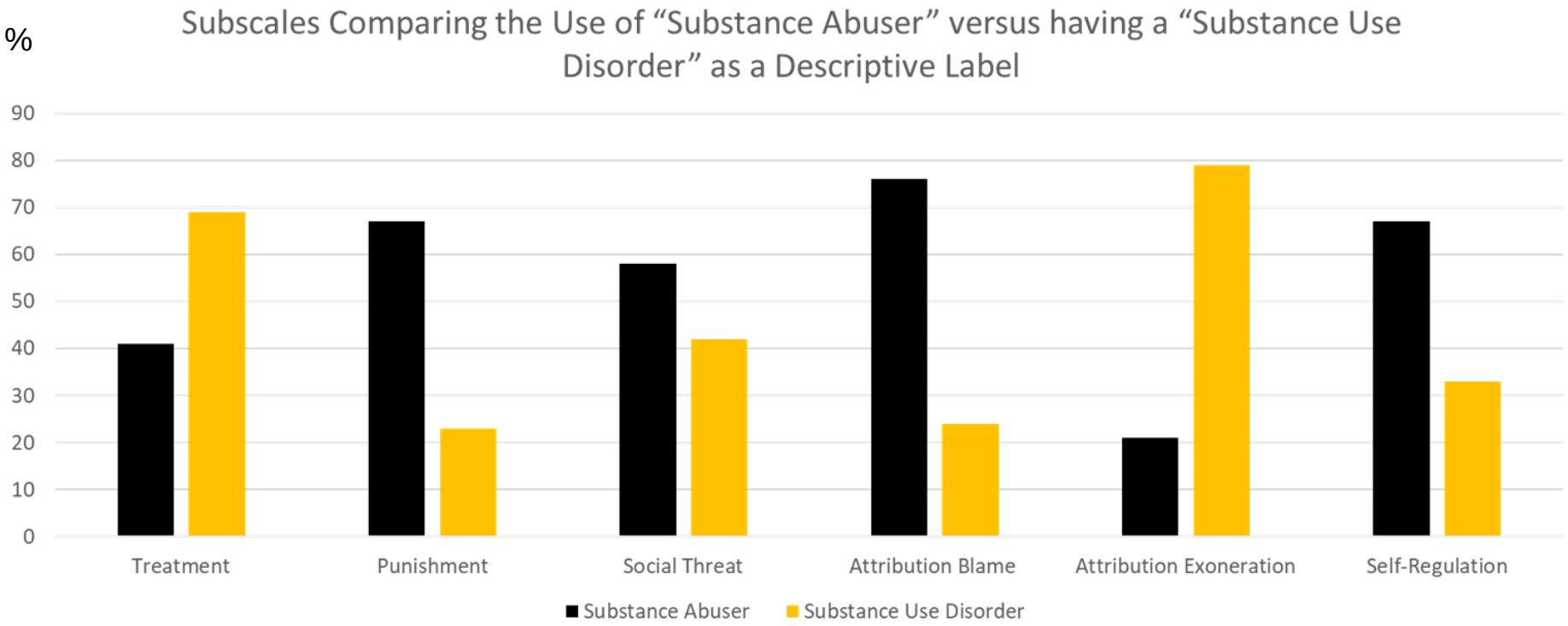
Use of Substance Abuser vs. Having a Substance Use Disorder

The Substance Abuser

- Less likely to benefit from treatment
  - That their “problem” was a result of “innate dysfunction” over which they did not have control
- More likely to:
  - Benefit from punishment
  - Socially threatening
  - Blamed for their substance-related difficulties and e able to “control” their Substance use without help

Acknowledgement: Tom Bannard, Ally Training and Rams in Recovery;
Recoveryanswers.org/research-post/the-real-stigma-of-substance-use-disorders/

Impact of Our Words



Survey of 314 participants: 50% who worked in Health Care; 20% were students, 29% worked outside healthcare or were unemployed or retired, and 5% did not report an occupation. Average participant 31 years old white (81%) female (76%) ~ 50% had a bachelor's degree or higher level of education.

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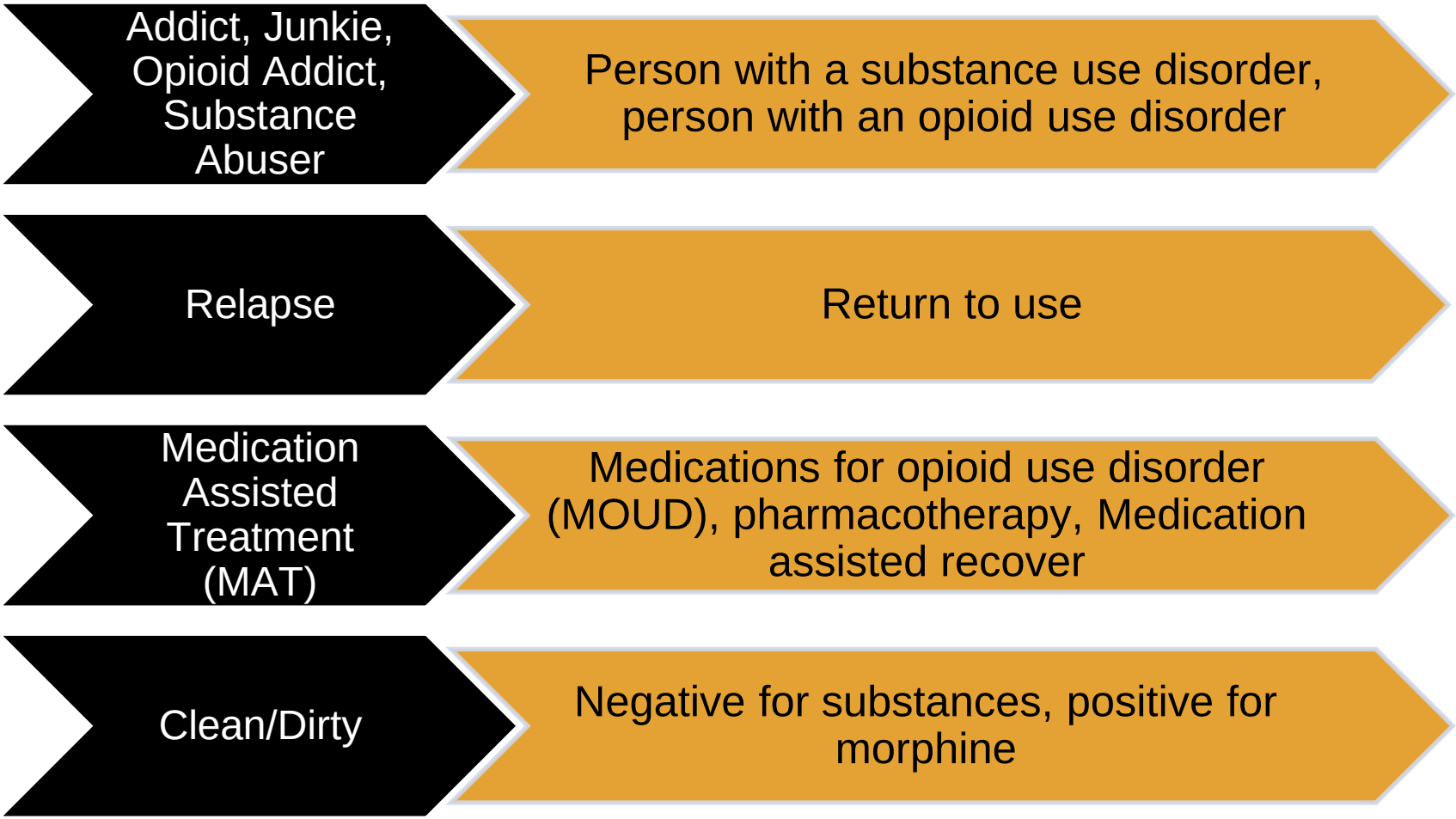
https://www.recoveryanswers.org/research-post/the-real-stigma-of-substance-use-disorders/ Accessed April 2023

Reducing Stigma: Words Matter

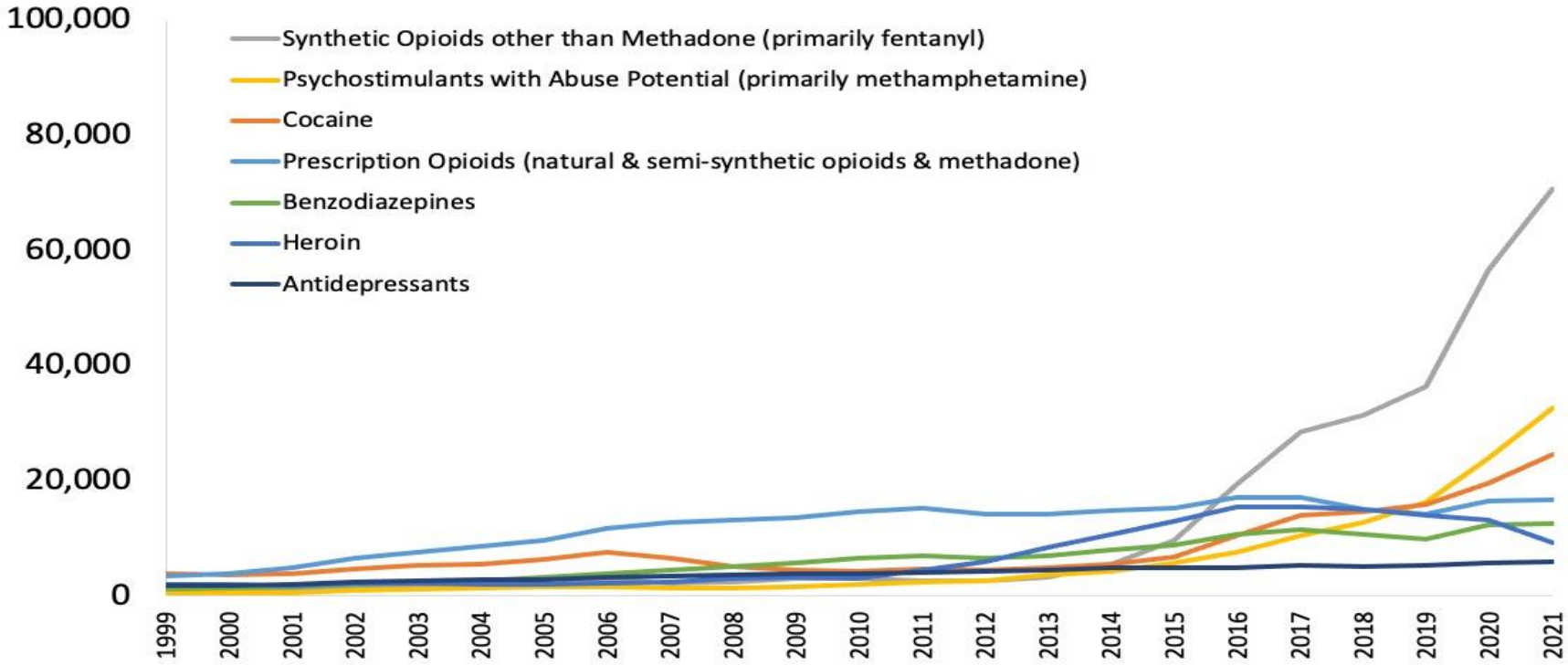


Acknowledgement: Tom Bannard, Ally Training and Rams in Recovery and University of the Sciences - Substance Use Disorder Institute
Acknowledgement: M. Geier, PharmD CPNP Slides Annual Meeting

Trends

National Data

Figure 2. National Drug-Involved Overdose Deaths*, Number Among All Ages, 1999-2021

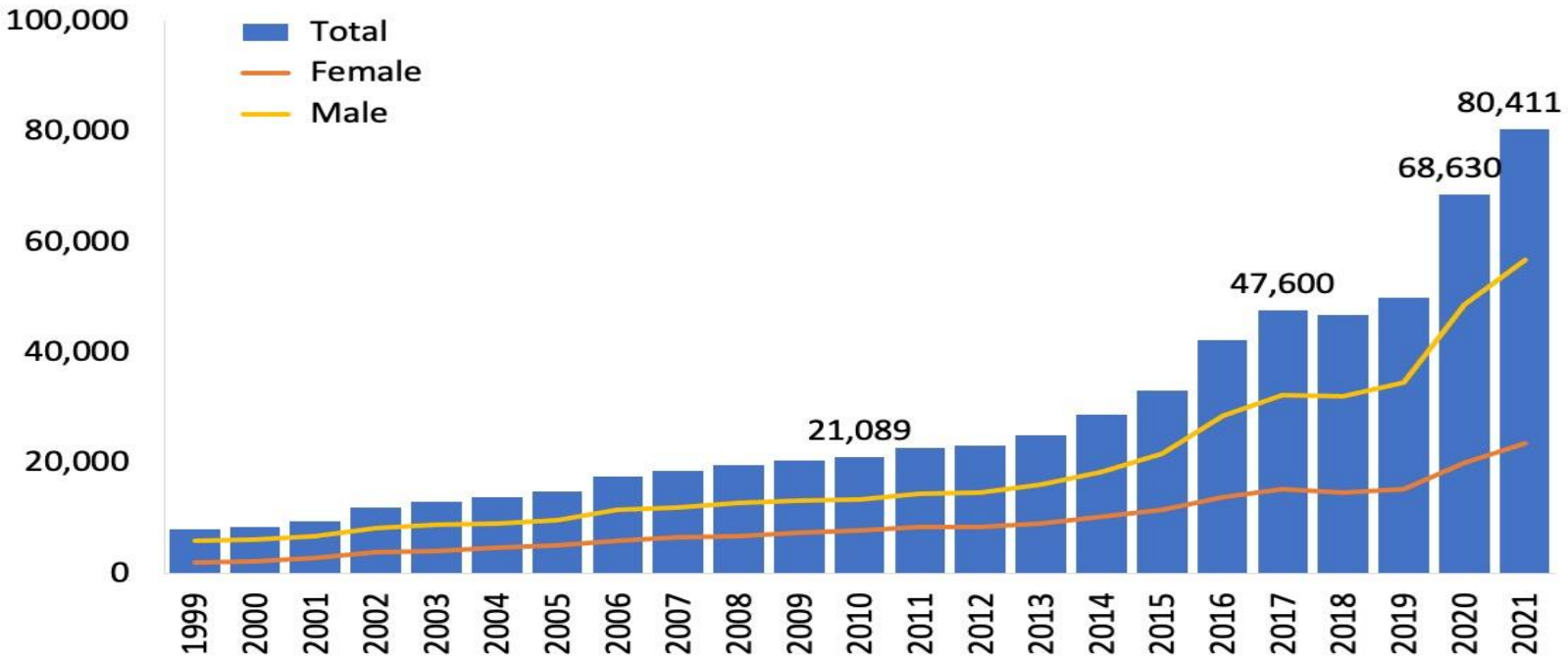


*Includes deaths with underlying causes of unintentional drug poisoning (X40–X44), suicide drug poisoning (X60–X64), homicide drug poisoning (X85), or drug poisoning of undetermined intent (Y10–Y14), as coded in the International Classification of Diseases, 10th Revision. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2021 on CDC WONDER Online Database, released 1/2023.

https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates

National Data

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

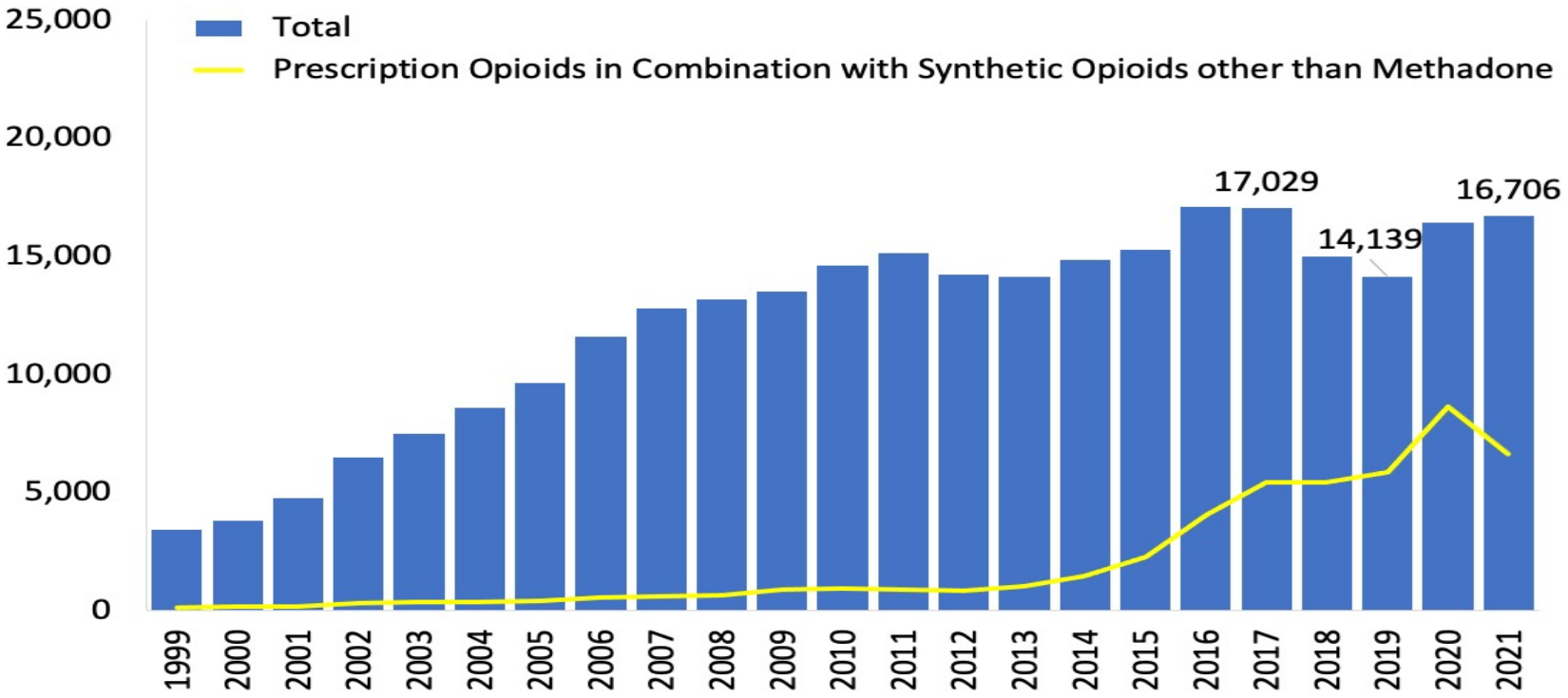


*Among deaths with drug overdose as the underlying cause, the "any opioid" subcategory was determined by the following ICD-10 multiple cause-of-death codes: natural and semi-synthetic opioids (T40.2), methadone (T40.3), other synthetic opioids (other than methadone) (T40.4), or heroin (T40.1). Source: 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.

https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates

National Data

Figure 4. National Overdose Deaths Involving Prescription Opioids*, Number Among All Ages, 1999-2021

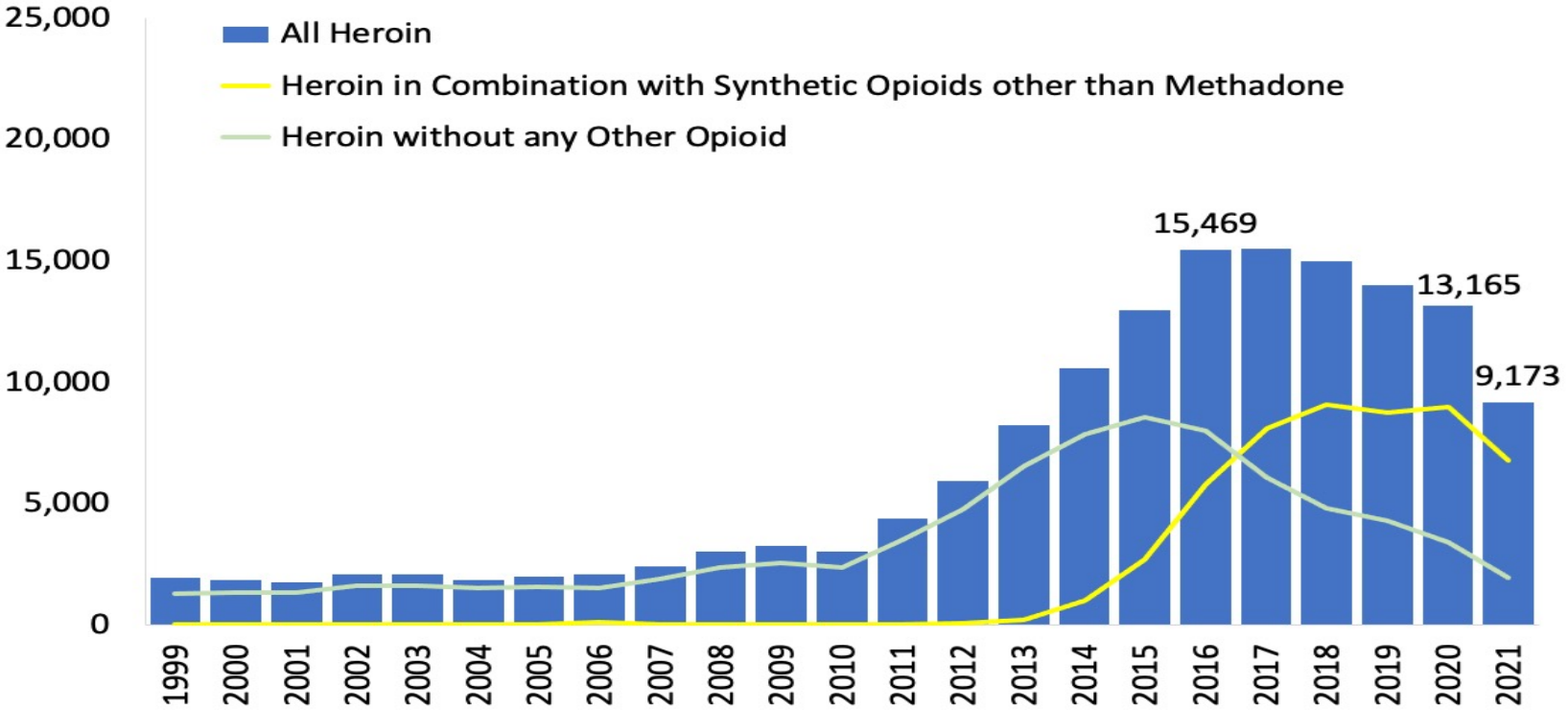


*Among deaths with drug overdose as the underlying cause, the prescription opioid subcategory was determined by the following ICD-10 multiple cause-of-death codes: natural and semi-synthetic opioids (T40.2) or methadone (T40.3). Source: Centers for Disease Control and Prevention, National Center for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

https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates

National Data

Figure 5. National Overdose Deaths Involving Heroin*, by other Opioid Involvement, Number Among All Ages, 1999-2021



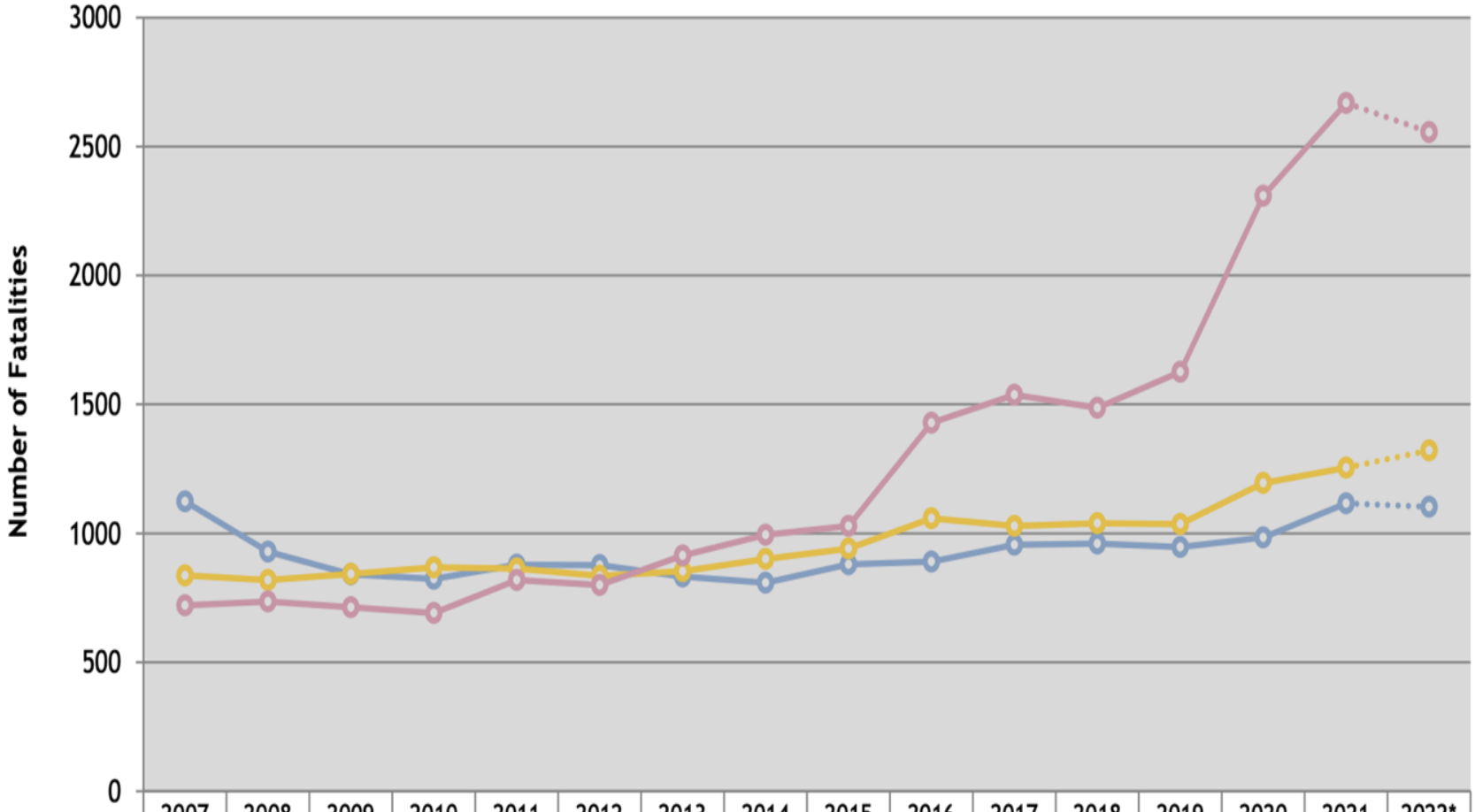
*Among deaths with drug overdose as the underlying cause, the heroin category was determined by the T40.1 ICD-10 multiple cause-of-death code. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2021 on CDC WONDER Online Database, released 1/2023.

https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates

Virginia Data

Total Number of Motor Vehicle, Gun, and Drug Related Fatalities by Year of Death, 2007-2022*

Data for 2022 is a Predicted Total for the Entire Year



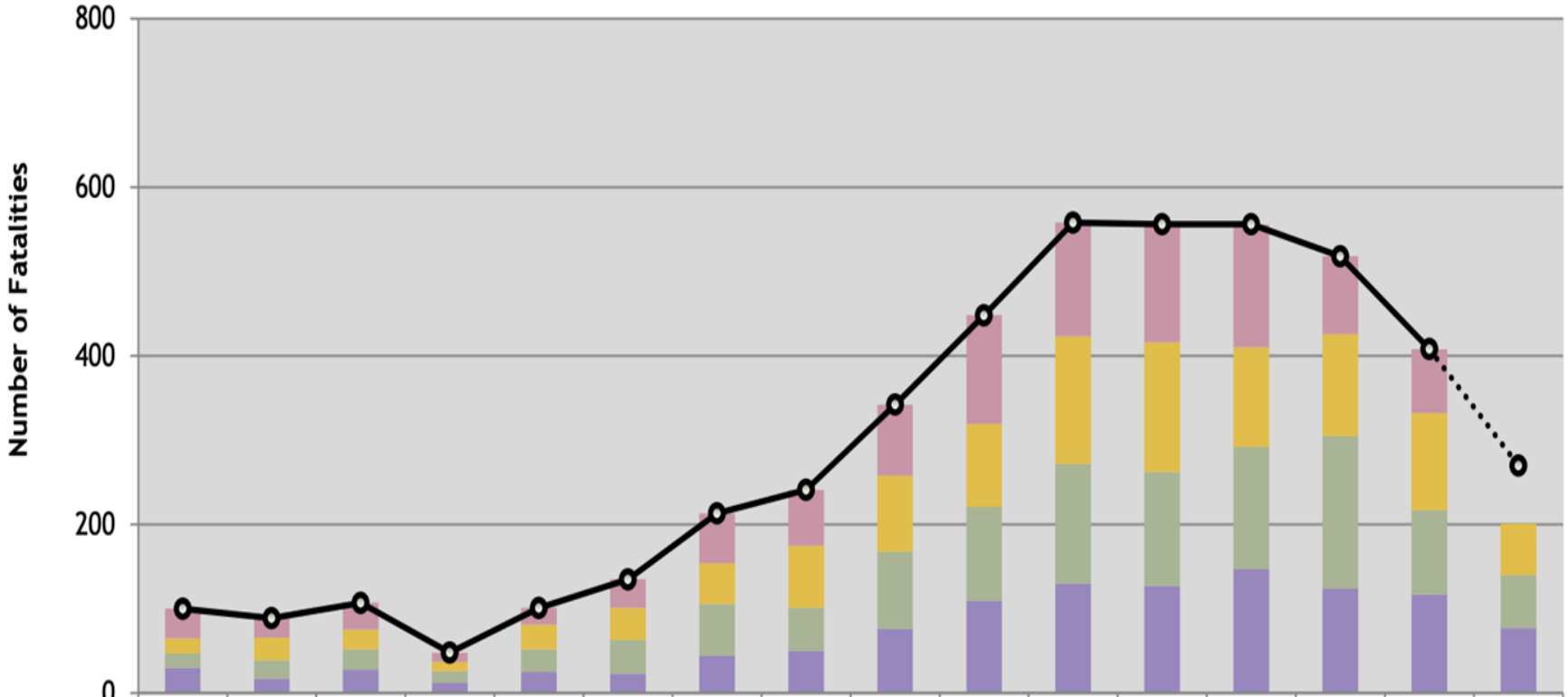
	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022*
Motor Vehicle Related	1124	928	841	823	878	877	832	808	879	890	955	960	947	984	1116	1103
Gun Related	836	818	843	868	863	835	852	901	940	1058	1028	1038	1036	1195	1255	1322
Fatal Drug Overdose	721	735	713	690	819	799	914	994	1028	1428	1537	1486	1627	2309	2669	2557

https://www.vdh.virginia.gov/

Virginia Data

Total Number of Fatal Heroin Overdoses by Quarter and Year of Death, 2007-2022*

Data for 2022 is a Predicted Total for the Entire Year

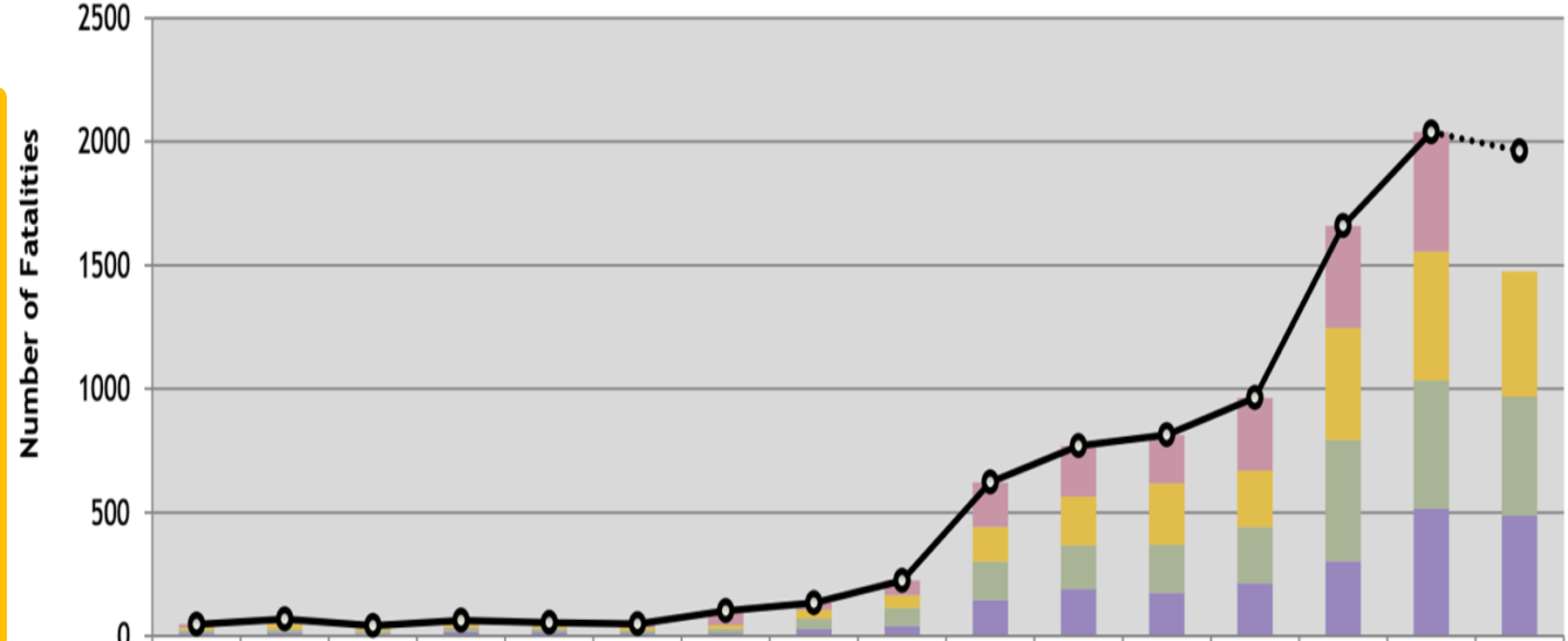


	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022*
Q4	35	23	32	11	20	34	59	66	84	129	135	140	146	92	76	
Q3	18	27	23	11	29	38	48	74	90	98	151	154	118	121	115	61
Q2	17	22	24	14	27	40	62	51	92	111	142	135	145	181	100	63
Q1	30	17	28	12	25	23	44	50	76	110	130	127	147	124	117	77
Total Fatalities	100	89	107	48	101	135	213	241	342	448	558	556	556	518	408	270

Total Number of Fatal Fentanyl Overdoses by Quarter and Year of Death, 2007-2022*

Data for 2022 is a Predicted Total for the Entire Year

Virginia Data

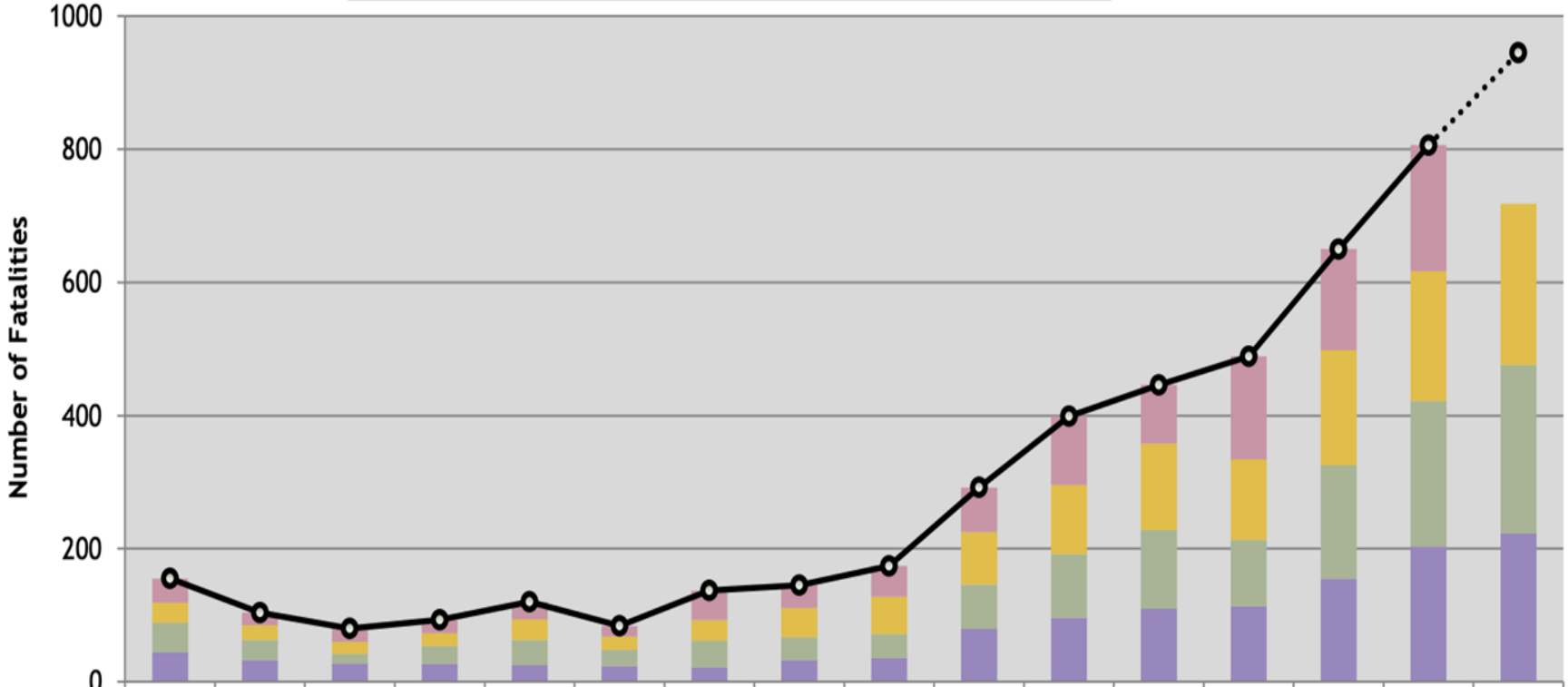


	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022*
Q4	14	19	13	19	11	15	58	28	59	180	203	194	294	413	482	
Q3	8	22	8	9	11	11	14	35	53	140	199	248	228	453	523	506
Q2	14	12	12	18	16	13	19	42	72	157	175	195	227	489	519	480
Q1	12	15	10	18	16	11	11	29	41	145	192	176	215	304	515	488
Total Fatalities	48	68	43	64	54	50	102	134	225	622	769	813	964	1659	2039	1963

Virginia Data

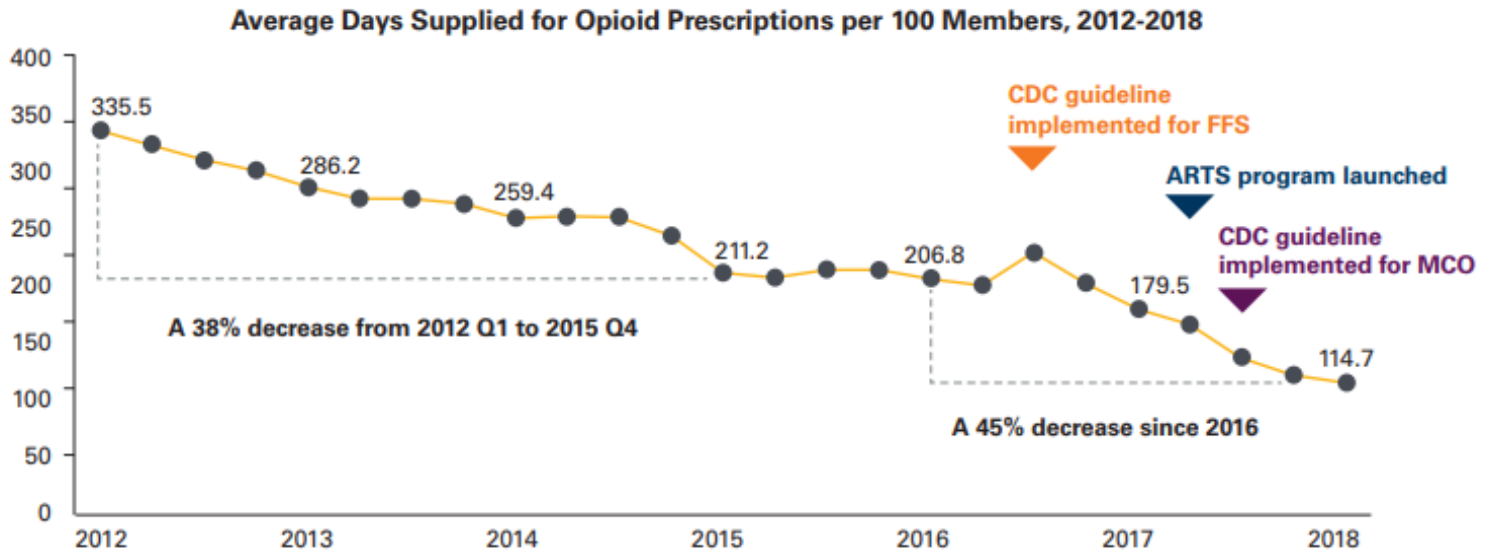
Total Number of Fatal Cocaine Overdoses by Quarter and Year of Death, 2007-2022*

Data for 2022 is a Predicted Total for the Entire Year



	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022*
Q4	36	19	20	20	26	16	44	34	46	67	103	88	155	152	189	
Q3	30	22	18	19	31	20	31	44	56	79	104	130	121	173	195	242
Q2	44	30	14	27	38	24	40	34	36	66	96	118	99	170	219	253
Q1	45	33	28	27	25	24	22	33	36	80	96	110	114	155	203	223
Total Fatalities	155	104	80	93	120	84	137	145	174	292	399	446	489	650	806	945

Impact of National and State-Wide Programs on Opioid Prescribing in Virginia



ARTS = Addiction & Recovery Treatment Services

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http://www.dmas.virginia.gov/files/links/2583/HBP_ARTS%20Issue%2003_(01.29.2019).pdf

The 3 Waves of the Opioid Epidemic

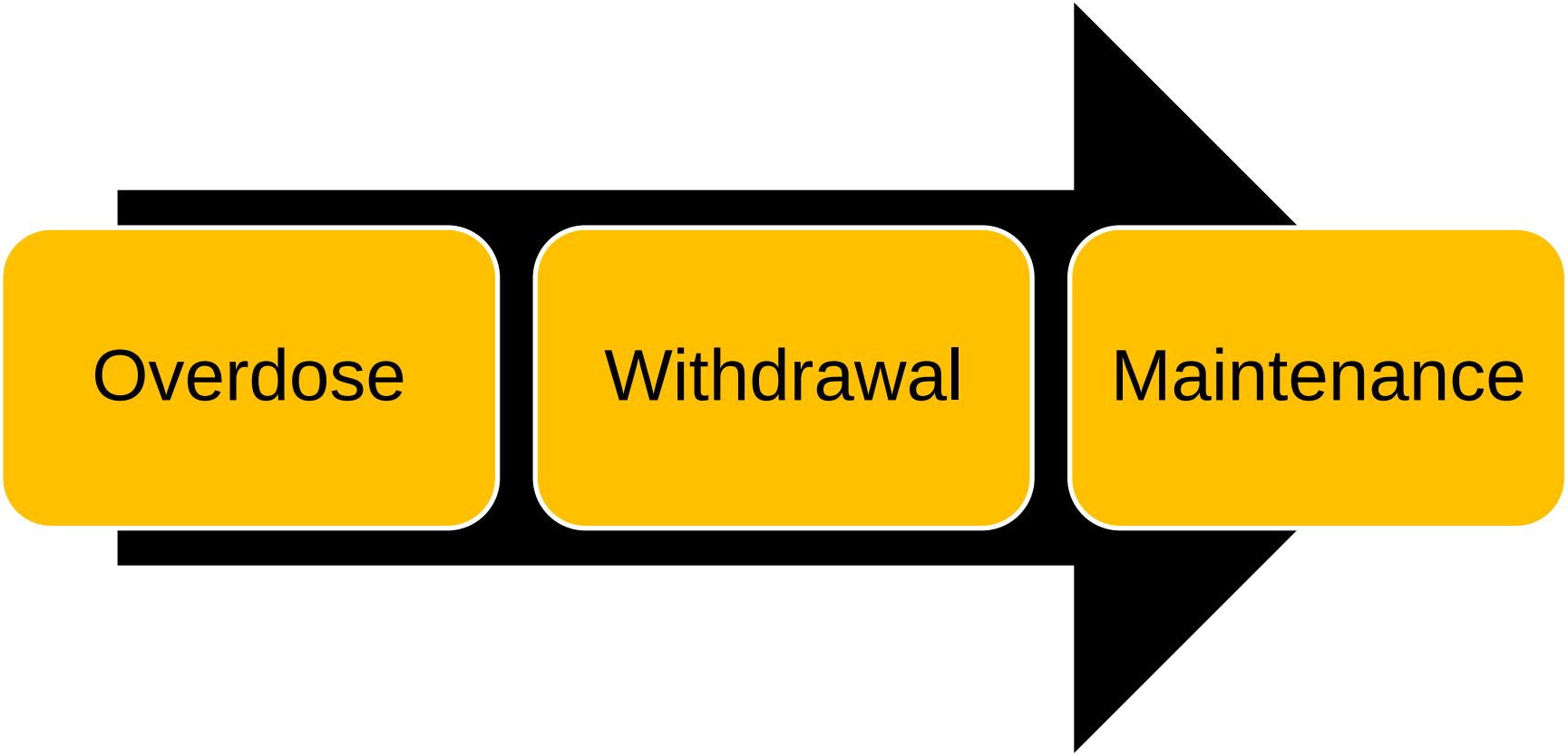
Summary

https://www.cdc.gov/opioids/basics/epidemic.html

Fentanyl Impact on Overdose

- DEA One Pill Can Kill Campaign
- Fentanyl-laced fake “prescription pills” including oxycodone, alprazolam, stimulants
  - 2022: 6 of 10 samples
  - 2021: 4 of 10 samples

Treatment of Opioid Use Disorder (OUD) Across the Spectrum



Medications in OUD

Publicly available at: https://www.drugabuse.gov/drug-topics/trends-statistics/infographics/medications-opioid-overdose-withdrawal-addiction

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Opioid Overdose

Signs & Symptoms of Opioid Overdose

Really High	Overdose (OD)
• Muscles relaxed • Slow/slurred speech • Responsive (shouting or painful stimuli) • Normal heart rate (HR)/pulse • Normal skin tone	• Pale, clammy skin • Breathing is infrequent or stopped (~ 3 breaths/min) • Pinpoint pupils • Deep snore, gurgle, or “death rattle” • Unresponsive to stimuli • Slowed or no HR/pulse • Blue fingers or lips

Higher risk for Opioid Overdose (OD) if:

- Overdosed in the past
- Been abstinent
- Recently changed the opioid they are using
- Concurrent benzodiazepines and/or alcohol

From the Revive! Training Guide: Available at: http://dbhds.virginia.gov/behavioral-health/substance-abuse-services/revive

Assessment

A 37-year-old is reports using heroin intravenously 2 to 3 times daily.

Which medication can be used to reduce the risk of an opioid overdose occurrence?

A. Methadone
B. Buprenorphine
C. Naltrexone
D. Naloxone

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Which medication can be used to reduce the risk of an opioid overdose occurrence?

A. Methadone

B. Buprenorphine

C. Naltrexone

D. Naloxone → Opioid Antagonist

Audience Check-in: Select All

Which of the following ways can someone obtain naloxone?

A. Over-the-Counter
B. Health department
C. Prescription from provider
D. Automatic dispensing machine
E. Request from outpatient pharmacy

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Naloxone Treatment Options

Brand Name	Strength	Route of Administration	Onset	Half Life	Time to Peak
Narcan®	4 mg/0.1 mL	Nasal	8-13 min	2 hours	20-30 min
Kloxxado®	8 mg/0.1 mL	Nasal	8-13 min	2 hours	15 min
Zimhi®	5 mg/0.5 mL	IM	2-5 min	0.5-1.5 hours	15 min
Naloxone generic	0.4 mg/1 mL 2 mg/2 mL	IV IM SQ	1-2 min 2-5 min 2-5 min	~ 3 hours	15 min

From prescribing information. Kloxxado Hima Pharmaceuticals 2021; Zimhi Adamis Pharmaceuticals 2021; https://www.narcan.com/home#resources; https://www.fda.gov/media/100429/download#:~:text=Naloxone%20has%20an%20onset%20of,or%20more%20breaths%20per%20minute).; Lexicomp online, naltrexone 2023

Breaking News!!

FDA NEWS RELEASE

FDA Approves First Over-the-Counter Naloxone Nasal Spray

https://www.fda.gov/news-events/press-announcements/fda-approves-first-over-counter-naloxone-nasal-spray#:~:text=Today%2C%20the%20U.S.%20Food%20and,for%20use%20without%20a%20prescription

REVIVE!

Opioid Overdose & Naloxone Education for Virginia

- Trains how to recognize and treat opioid overdose
- Educates how to administer naloxone

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https://dbhds.virginia.gov/behavioral-health/substance-abuse-services/revive/

Photo courtesy of: Sarah Melton Thomason, PharmD, BCPP

Audience Assessment

Who should be trained on naloxone?

A. The patient
B. Caregivers
C. Family and friends
D. Health care providers

Audience Assessment

Who should be trained on naloxone?

A. *The patient*
B. **Caregivers**
C. **Family and friends**
D. **Health care providers**

Who Needs Naloxone?

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Acknowledgement: M. Geier. CPNP annual meeting.
Permission received to reuse
https://www.sfdph.org/dph/comupg/oservices/mentalHlth/cbhs/default.asp

Naloxone

Mechanism of Action: Opioid Antagonist

Administration:

1. Identify the signs of overdose and attempt to arouse patient
2. If the patient cannot be aroused, perform rescue breathing and CPR
3. Properly administer the naloxone product
4. Place patient in the “recovery position”
5. Call 9-1-1 and watch patient closely
6. Watch for worsening of overdose signs
   - If breathing does not return to normal after 2-3 minutes
7. If necessary administer a 2nd dose of naloxone

From the Revive! Training Guide: Available at: http://dbhds.virginia.gov/behavioral-health/substance-abuse-services/revive

VDH VIRGINIA DEPARTMENT OF HEALTH

Statewide Standing Order for Naloxone
Virginia Department of Health
109 Governor Street, 13th Floor
Richmond, VA 23219

Date Issued: **February 10th, 2023**

https://www.vdh.virginia.gov/content/uploads/sites/3/2022/01/Naloxone-Standing-Order_1-14-2022.pdf

Approved Options for Intranasal, Auto-Injector or Injectable Administration:

Intranasal	Auto-injector*	Intranasal	Intranasal	Injection** (Pharmacists Only)
Naloxone 2mg/2ml prefilled syringe, #2 syringes Directions: Spray one-half of the syringe into each nostril upon signs of opioid overdose. Call 911. Additional doses may be given every 2 to 3 minutes until emergency medical assistance arrives. **Mucosal Atomization Device (MAD** Directions: Use one auto-injector upon signs of opioid overdose. Call 911. Additional doses may be given every 2 to 3 minutes until emergency medical assistance arrives.	**Naloxone 2mg #1 twin pack auto-injector*** Directions: Use one auto-injector upon signs of opioid overdose. Call 911. Additional doses may be given every 2 to 3 minutes until emergency medical assistance arrives.	**Naloxone Nasal Spray 4mg, #1 twin pack** Directions: Administer a single spray intranasally into one nostril. Administer additional doses using a new nasal spray with each dose, if the patient does not respond or responds and then relapses into respiratory depression. Call 911. Additional doses may be given every 2 to 3 minutes until emergency medical assistance arrives.	**Naloxone nasal spray, 8mg, #1 twin pack** Directions: Administer a single spray intranasally into one nostril upon signs of opioid overdose. Administer additional dose in other nostril using a new nasal spray with each dose, if patient does not respond or response, then releases into respiratory depression. Call 911. Additional doses may be given every 2 to 3 minutes until emergency medical assistance arrives.	**Naloxone 0.4mg/ml #2 single-use 1ml vials (Pharmacists Only)**** Directions: inject 1 ml in shoulder or thigh upon signs of opioid overdose. Call 911. Repeat after 2-3 minutes if no or minimal response. Must dispense with 2 single-se 1 ml vials, 2 (3 ml) syringes and 2 (23-25 gauge) hypodermic needles and instructions for administration. Directions: Use as directed for naloxone administration.

*Persons dispensing naloxone auto-injector formulations shall follow the Board of Pharmacy's protocol for the naloxone auto-injector formulations provided in the Board of Pharmacy's Guidance Document 110-44.
**Except for pharmacists, persons authorized to dispense under this standing order shall only dispense formulations for intranasal administrations or an auto-injector formulation.

May refill as long as order remains effective.

Prescriber: DocuSigned by: Laura Forlano [redacted] Date: 2/10/2023 | 4:42:29 PM EST

Laura G. Forlano
NPI Number: 1346391406
Virginia Medical License Number: 0102202858

Publicly available at: https://www.vdh.virginia.gov/content/uploads/sites/3/2022/01/Naloxone-Standing-Order_1-14-2022.pdf Accessed April 2023

Virginia Statewide Protocol

Protocol went into effect in January 2021

Inclusion criteria

- 18 years of age or older, experiencing or at risk of experiencing an opioid-related overdose
- 18 years of age or older, in a position to assist an individual who is experiencing or at risk of experiencing an opioid-related overdose

https://www.dhp.virginia.gov/pharmacy/
accessed on 04/14/2023

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Opioid Withdrawal

- A patient just received naloxone
- Fear of withdrawal often perpetuates the cycle of continued use

Patient Quotes:

"You don't get high after a while. You just need it so you're not sick. You have to have that balance. There are some days where you're so dope sick, you can't even get out of bed"

"I was purely seeking the drug to stay well"

Kosten TR and Baxter LE. Am J Addict 2019;28(2):55-62

Case Scenario

A 28-year-old male who uses intravenous heroin daily presents to the hospital with an abscess on his arm. He is admitted to internal medicine for intravenous antibiotics.

Which scale do recommend using to monitor for symptoms of withdrawal?

A. Clinical Opioid Withdrawal Scale (COWS)
B. Objective Opioid Withdrawal Scale (OOWS)
C. Clinical Institute Narcotic Assessment (CINA)
D. Clinical Institute Withdrawal Assessment for Alcohol - revised (CIWA-Ar)

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B. Objective Opioid Withdrawal Scale (OOWS)
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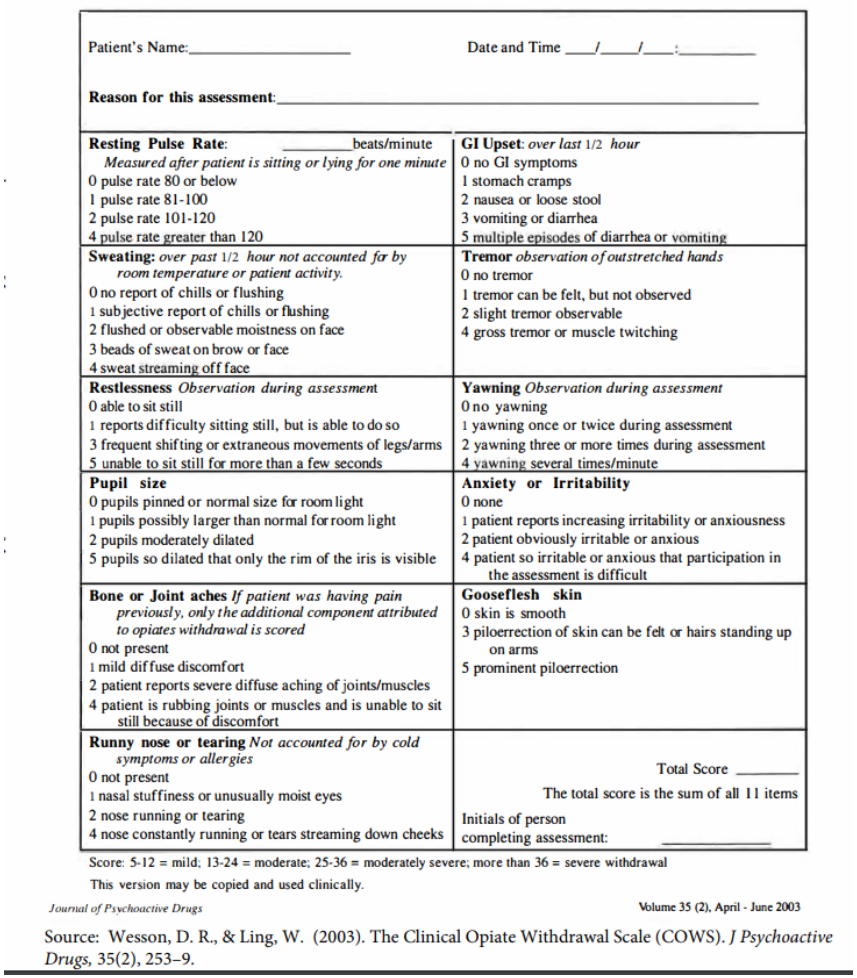
Scales Used in Opioid Withdrawal

	Title of Scale	Description	Each symptom Scored
CINA	Clinical Institute Narcotic Assessment	11 symptoms (subj/obj); also determines severity of symptoms	0-2, 0-3, 0-6 0: absent
COWS	Clinical Opioid Withdrawal Scale	11 symptoms (subj/obj) Takes ~ 2 mins	0-4 or 0-5 0: absent
OOWS	Objective Opioid Withdrawal Scale	13 symptoms (obj) Takes ~ 5 minutes	0: absent 1: present
SOWS	Subjective Opioid Withdrawal Scale	16 symptoms, Likert 5-point scale (subj)	0: absent – 4: extreme

Cunningham et al. Am Society of Addiction Medicine OUD Guidelines Update 2020

Wesson DR and Ling W. 2003. J Psychoactive Drugs 35:2:253-59.

Clinical Opiate Withdrawal Scale (COWS)



Patient's Name:_____ Date and Time ___/___/___:_____

Reason for this assessment:_____

Resting Pulse Rate: _____beats/minute *Measured after patient is sitting or lying for one minute* 0 pulse rate 80 or below 1 pulse rate 81-100 2 pulse rate 101-120 4 pulse rate greater than 120	**GI Upset**: *over last 1/2 hour* 0 no GI symptoms 1 stomach cramps 2 nausea or loose stool 3 vomiting or diarrhea 5 multiple episodes of diarrhea or vomiting
Sweating: *over past 1/2 hour not accounted for by room temperature or patient activity.* 0 no report of chills or flushing 1 subjective report of chills or flushing 2 flushed or observable moistness on face 3 beads of sweat on brow or face 4 sweat streaming off face	**Tremor** *observation of outstretched hands* 0 no tremor 1 tremor can be felt, but not observed 2 slight tremor observable 4 gross tremor or muscle twitching
Restlessness *Observation during assessment* 0 able to sit still 1 reports difficulty sitting still, but is able to do so 3 frequent shifting or extraneous movements of legs/arms 5 unable to sit still for more than a few seconds	**Yawning** *Observation during assessment* 0 no yawning 1 yawning once or twice during assessment 2 yawning three or more times during assessment 4 yawning several times/minute
Pupil size 0 pupils pinned or normal size for room light 1 pupils possibly larger than normal for room light 2 pupils moderately dilated 5 pupils so dilated that only the rim of the iris is visible	**Anxiety or Irritability** 0 none 1 patient reports increasing irritability or anxiousness 2 patient obviously irritable or anxious 4 patient so irritable or anxious that participation in the assessment is difficult
Bone or Joint aches *If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored* 0 not present 1 mild diffuse discomfort 2 patient reports severe diffuse aching of joints/muscles 4 patient is rubbing joints or muscles and is unable to sit still because of discomfort	**Gooseflesh skin** 0 skin is smooth 3 piloerrection of skin can be felt or hairs standing up on arms 5 prominent piloerrection
Runny nose or tearing *Not accounted for by cold symptoms or allergies* 0 not present 1 nasal stuffiness or unusually moist eyes 2 nose running or tearing 4 nose constantly running or tears streaming down cheeks	Total Score _____ The total score is the sum of all 11 items Initials of person completing assessment: _____

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

This version may be copied and used clinically.

Journal of Psychoactive Drugs Volume 35 (2), April - June 2003

Source: Wesson, D. R., & Ling, W. (2003). The Clinical Opiate Withdrawal Scale (COWS). *J Psychoactive Drugs*, 35(2), 253–9.

Yellow highlighted /underlined symptoms are unique to Opioid Withdrawal

1. Pulse rate
2. Sweating
3. Restlessness
4. Pupil size → dilation (mydriasis)
5. Bone/joint aches
6. Runny nose or tearing
7. GI upset
8. Tremor
9. Yawning
10. Anxiety/Irritability
11. Gooseflesh Skin

Scoring:
5-12: Mild
13-24: Moderate
25-36 Mod/severe
> 36 severe

https://www.drugabuse.gov/sites/default/files/ClinicalOpiateWithdrawalScale.pdf;
https://www.ndafp.org/image/cache/27B.pdf

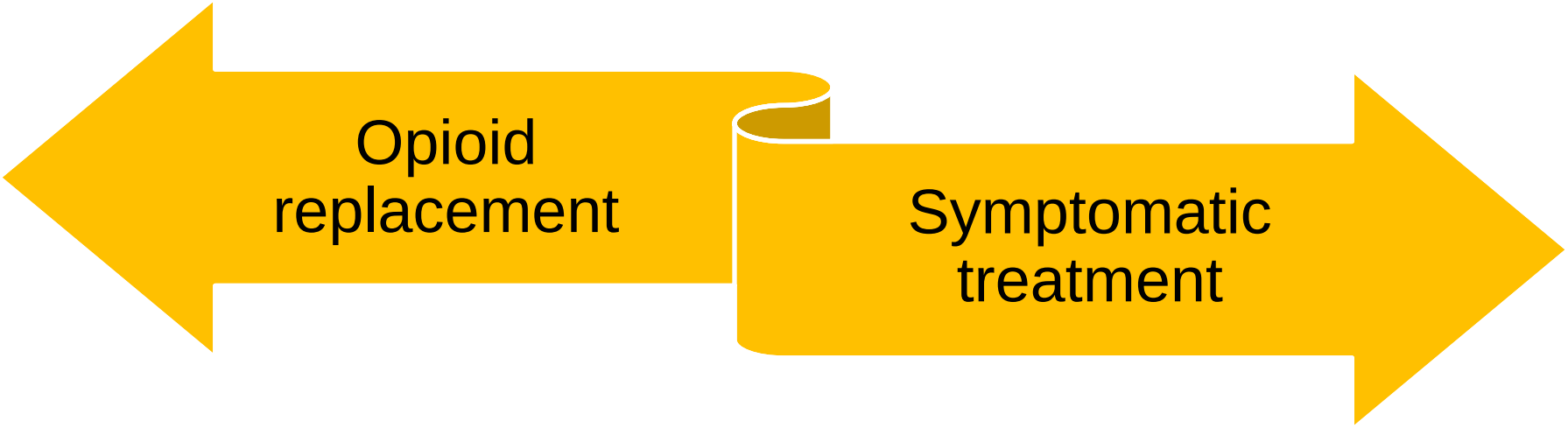
Case Scenario

A 28-year-old male who uses intravenous heroin daily presents to the hospital with an abscess on his arm. He is admitted to internal medicine for intravenous antibiotics.

His COWS score is 17. How do you recommend managing his symptoms of withdrawal?

A. Clonidine
B. Methadone
C. Lorazepam
D. Buprenorphine/naloxone

Differing Approaches to Managing Opioid Withdrawal



Cunningham et al. Am Society of Addiction Medicine OUD Guidelines Update 2020; Accessed at: https://sitefinitystorage.blob.core.windows.net/sitefinity-production-blobs/docs/default-source/guidelines/npg-jam-supplement.pdf?sfvrsn=a00a52c2_2 Accessed on April 14, 2023

Withdrawal Management with Opioid Replacement

	Buprenorphine or Buprenorphine/Naloxone	Methadone
COWS scores	Want in moderate withdrawal ideally COWS ≥ 13* to avoid precipitated withdrawal	Want in mild withdrawal; usually treat once COWS ≥ 5
Based on COWs Score	Initial dose: 2 to 4 mg, titrated up to 4 to 16 mg/day Day 1: not to exceed 8 mg/24 hours – generally given as 4 mg in 2 separate doses Day 2: many protocols. keep patient at 8 mg can increase to 16 mg **ASAM:** Initial dose of 2 to 4 mg up to 8 mg total Day 1 titrated as needed to suppress withdrawal (WD) (4 to 16 mg/day)	Day 1: Once COWS > 5 give a dose → medicate Roughly one point = 1 mg (rounded) 5-8 pts → 5 mg; 9 -12 points → 10 mg; 13-16 pts → 15 mg; etc… Once stable – calculate previous 24 hour dose, and give as a single dose in AM….then taper **ASAM:** Day 1: 10-30 mg, with 1st day max of 30-40 mg. Can give incremental doses of 5-10 mg every 3-6 hours PRN. Taper off in 6 to 10 days
Taper	↓ Usually by 2 mg/day over 3 to 5 days	↓5-10 mg/day over 6 to 10 days
Limitations	**Risk of precipitating withdrawal Cannot use in ICU populations who are on narcotic (e.g. fentanyl drips for sedation)	QTc prolongation; Reports of QTc and torsade de pointes with fluoxetine with high-dose maintenance methadone; Drug interactions (primarily CYP3A4 substrate; also 2B6 & 2C19)
Comparison to alpha-agonists?	Buprenorphine may be more effective ↓ WD symptoms, retaining patients in WD management, and may support completion of WD management than alpha-agonists	Methadone may result in similar severity of WD symptoms when compared to alpha agonists

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* For OBOT based – can start at COWS of 11-12 is generally sufficient to prevent precipitated WD
Cunningham et al. Am Society of Addiction Medicine (ASAM) OUD Guidelines Update 2020
Vieweg WVR Ther Adv Psychopharm 2013;3:219-32.
Also includes dosing example from hospital protocols, VCUHealth, Richmond VA

What About the 3-day Rule?

- If a patient is admitted to the hospital primary medical diagnosis **other than** OUD (e.g. endocarditis, suicidal ideation, psychosis)
  - An inpatient (~~non-DATA waivered~~) provider may initiate or maintain buprenorphine/naloxone or methadone to prevent withdrawal symptoms that may complicate the primary condition
  - Discharge planning ideally should arrange follow-up for MOUD
  - *Note there is **not** a time limit on this*
- Versus if primary reason/diagnosis for hospitalization is OUD: must adhere to the 3-day rule (Title 21, Code of Federal Regulations, **Part 1306.07(b))**

  Providers may administer but not prescribe provided
  - Not more than one day's medication may be administered or given to a patient at one time
  - This treatment may not be carried out for more than 72 hours
  - This 72-hour period cannot be renewed or extended*
  - Cannot write a discharge Rx for methadone

https://www.ecfr.gov/current/title-21/chapter-II/part-1306/subject-group-ECFR1eb5bb3a23fddd0/section-1306.07

COWS - Symptoms

Anxiety/ Irritability	Yawning	Tearing/ Runny nose	Piloerection/ Goosebumps
Sweating/ Perspiration	Tremor	Nausea/ Vomiting	Mydriasis
Abdominal Cramps	Joint aches	Pulse rate	

What medications can help with these symptoms?

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https://www.ndafp.org/image/cache/27B.pdf; Cunningham et al. Am Society of Addiction Medicine OUD Guidelines Update 2020; Wesson DR and Ling W. 2003. J Psychoactive Drugs 35:2:253-59.

Symptomatic Management

Opioid Withdrawal Symptom	Pharmacologic Strategies	MOA/classification
Overall Withdrawal Symptoms	Clonidine, lofexidine	Alpha-2 agonist
Nausea/Vomiting	Ondansetron Prochlorperazine, metoclopramide	Antiemetic – 5HT3 antagonist Antiemetic – D2 antagonist, anticholinergic
Diarrhea	Loperamide Bismuth salicylate	Anticholinergic
Muscle Cramps & headache	Ibuprofen, naproxen, ketorolac Acetaminophen	NSAIDs APAP
Muscle spasms	Baclofen, cyclobenzaprine, methocarbamol	Muscle relaxants
Abdominal Cramps/spasms	Dicyclomine	Antispasmodic/anticholinergic
Anxiety/Irritability	Hydroxyzine, diphenhydramine ? Lorazepam, clonazepam	Antihistamines Benzodiazepines (with caution)

Cunningham et al. Am Society of Addiction Medicine OUD Guidelines Update 2020; Gowing L, et al. Cochrane Database Syst Rev 2016;216(5):CD002024; Kosten TR and Baxter LE. Am J Addict 2019;28(2):55-62; E Crouse Clinical Experience and VCUHealth hospital protocols

Alpha-2 Agonists

Clonidine*

&

Lofexidine

Help reduce:

- Sweating
- Diarrhea
- Intestinal cramps
- Nausea
- Anxiety and irritability
  - May also help with tearing, runny nose, and piloerection
  - **Not as effective** for muscle cramps, restlessness, insomnia, or craving!!

In acute withdrawal: Norepinephrine (NE) hyperactivity

Mechanism of Action: Work by restoring NE balance

Can be used in combo with Buprenorphine/Naloxone or Methadone

*Clonidine is off-label; lofexidine is FDA approved

Lofexidine prescribing information US WorldMeds Sept 2020 and manufacturer website hcp.lucemyra.com, accessed April 2023; www.uptodate.com Wolters-Kluwer/Lexicomp online 2023; Gowing L, et al. Cochrane Database Syst Rev 2016; May 3;2016(5):CD002024; Kosten TR and Baxter LE. Am J Addict 2019;28(2):55-62

Comparing Alpha-2-Agonists

	Clonidine (Oral)	Lofexidine (Oral)
FDA approved for mitigation of opioid withdrawal	No – "off-label"	Yes – 1st drug
T1/2	12 – 16 hours	17 – 22 hours
Peak	1 – 3 hours	3 – 5 hours
Bioavailability	70 – 80%	72%
Adverse Effects	Hypotension, dizziness, sedation *Hold parameters	Orthostatic hypotension, hypotension, dizziness, bradycardia, dry mouth, somnolence/sedation; *Hypotension may be less than clonidine*
Cost	0.1 mg tabs $4-12 for a 10-day supply	0.18 mg tabs $2,300- 2,500 for a 96 tabs (8-day supply)

Lexi-drugs; Lofexidine prescribing information Sept 2020: Also available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/209229s000lbl.pdf
Pricing from: Goodrx.com April 2023

Comparing Alpha-2 Agonists: Dosing

Clonidine "off-label"

- Day 1: 0.1 mg every 4 hours
- Day 2: 0.1 mg every 6 hours
- Day 3: 0.1 mg every 8 hours
- Alternative:
  - 1 tablet every 4 to 6 hours PRN
- By COWS score:
  - 0.1 mg for COWS 8-12; 0.2 mg for COWS > 12
- ASAM: 0.1-0.3 mg every 6 to 8 hours; Max 1.2 mg/24 hours

Lofexidine

- 0.18 mg – Take 3 tablets (0.54 mg) four times daily for up to 14 days
- Taper dose over 2-4 days

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Lofexidine prescribing information US WorldMeds Sept 2020 and manufacturer website hcp.lucemyra.com, accessed April 2023
Paula B, J Subst Abuse Treat 2002;23(3)163-9.; Cunningham ASAM 2020; Gowing L, et al. Cochrane Database Syst Rev 2016; May 3;2016(5):CD002024; Kosten TR and Baxter LE. Am J Addict 2019;28(2):55-62

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What do you recommend?

A. Methadone
B. Buprenorphine
C. Buprenorphine/naloxone
D. Naltrexone
E. Naloxone

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Medications for Opioid Use Disorder (MOUD)

Goal of Treatment

Treatment Settings
OTP versus OBOT

OTP = Opioid Treatment Program

- Primarily methadone
  - Referred to as MMT = methadone maintenance treatment
- Federal regulations

OBOT = Outpatient-based Opioid Treatment

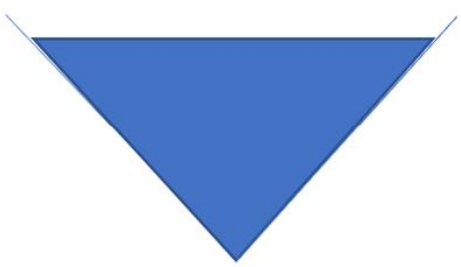
- Primarily buprenorphine/naloxone or naltrexone

OBAT = Outpatient-based Addiction Treatment

- Primarily buprenorphine/naloxone and other substance use disorders

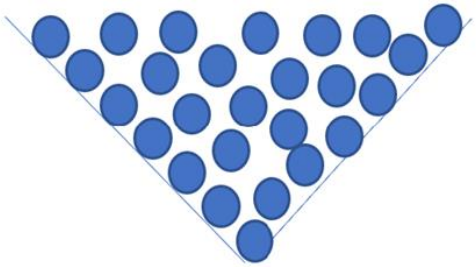
https://store.samhsa.gov/sites/default/files/d7/priv/pep15-fedguideotp.pdf

Mechanism of Action for Agents Used in MOUD



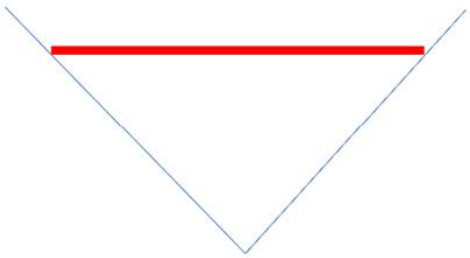
Methadone

Full Agonist



Naltrexone:

Full Antagonist



Buprenorphine:

Partial Agonist

Figure adapted from:
https://www.npr.org/sections/health-shots/2017/06/12/523774660/a-drugmaker-tries-to-cash-in-on-the-opioid-epidemic-one-state-law-at-a-time

Methadone

Mechanism of Action: Full opioid agonist

Pharmacokinetics

- Half-life = 36-48 hours
- Onset of action = 30 minutes after oral ingestion
  - Peak plasma levels seen at 2-4 hours & persist for 24+ hours
- Metabolized by CYP450: 3A4, 2B6, 2C19 (interactions with antiretrovirals, anticonvulsants, rifampin)

Dosing

- Initial maintenance dose = 10 – 30mg daily
- Dose increases can be made every 4 – 7 days in 10 mg increments
- Average daily maintenance dose is 60 – 120mg

Cunningham et al. Am Society of Addiction Medicine OUD Guidelines Update 2020;
From prescribing information. Roxane Laboratories 2015.

Methadone

Contraindications

- Hypersensitivity, respiratory depression, severe bronchial asthma

Warnings

- Concurrent use with medications that cause respiratory depression
- Liver disease
- Adrenocortical insufficiency
- Serotonin syndrome with antidepressants and anti-migraine meds
- Medications with risk to prolong QT interval
- Neonatal withdrawal after use of methadone during pregnancy

Cunningham et al. Am Society of Addiction Medicine OUD Guidelines Update 2020;
From prescribing information. Roxane Laboratories 2015.

Buprenorphine (SL)

Mechanism of Action:

- Combined opioid partial agonist/antagonist

Pharmacokinetics

- Rapid absorption in the oral mucosa
  - 3 minutes to dissolve films; 5-10 minutes to dissolve the tablet
  - Peak plasma concentrations are reached within 90 minutes

Dose

- Initial 2-4mg, max 24 mg per day (strips or tablets)
- Should only initiate therapy when signs and symptoms of withdrawal are present
  - Can precipitate withdrawal if other opioids are still active

Cunningham et al. Am Society of Addiction Medicine OUD Guidelines Update 2020;
From prescribing information. Suboxone Indivior Inc. 2023.

Buprenorphine (SL)

Contraindication

- Hypersensitivity
- Severe hepatic impairment

Warnings

- Respiratory depression
- Sedation
- Severe hepatic impairment not recommended
- CYP3A4 inhibitor medications
- Neonatal withdrawal after use during pregnancy
- Serotonin syndrome with antidepressants and anti migraine meds

Cunningham et al. Am Society of Addiction Medicine OUD Guidelines Update 2020;
From prescribing information. Suboxone Indivior Inc. 2023.

Buprenorphine/Naloxone REMS for Pharmacists:

Verify the Rx from a DATA 2000 Waivered prescriber

X is no longer required as of 2023

Keep in mind that a **limited supply of buprenorphine-containing products should be dispensed** during the initiation of therapy. This is due to the need for prescribers to closely and frequently assess the patients' needs, their symptoms, and potential risk of misuse, diversion, and abuse.

Check state Prescription Drug Monitoring Programs, → review all medications (e.g., benzodiazepines, other opioids, and CNS depressants) to assess for appropriateness of co-prescribing.

Provide the Medication Guide to patients each time the medicine is dispensed and discuss the risks and side effects associated with buprenorphine products, including what to do if patients experience side effects.

Buprenorphine/Naloxone REMS for Pharmacists:

- **Remind** patients who are picking up induction doses to return as directed to the doctor's office so that they can be supervised while taking the medication. → *Versus we have started doing a lot more "Home inductions"*
- **Explain** how to safely store the medication out of the sight and reach of all others, especially children.
- Provide appropriate patient counseling on safe use of buprenorphine-containing products and **encourage patients to seek psychosocial counseling and support for safe and effective treatment.**

https://www.suboxonerems.com/pharmacist-information

When to consider mono-product buprenorphine SL?

Mono-product should only be prescribed on extremely rare occasions:
In OBOTs/OBATs: combo product >>>>monoproduct

1. **Pregnancy**
   - However, after delivery switch back to combination with naloxone [even if breastfeeding – naloxone transfer is very low]
2. **Severe liver disease/cirrhosis**

- ***As of Aug 2017 (VA board of Medicine):
  - Prescriptions for the mono-product **should not exceed 3% of total prescriptions for buprenorphine written by the prescriber**
  - [This does not include the long-acting formulations]
  - Otherwise buprenorphine/naloxone is the preferred product and used in >97% of patients
- Why?
  - The mono-product is more likely to be diverted.
  - Combined with naloxone as the "abuse deterrent" – With PO or SL administration – naloxone has poor bioavailability; Goal is to prevent melting and injecting.

Lavinghousez C. Substance-related disorders in BCPP study guide, Am Assoc of Psychiatric Pharmacists (AAPP/CPPN) 2017 Ed: Kirkwood CK and Ehret M.
https://www.dhp.virginia.gov/Medicine/docs/FAQPrescribingBuprenorphine.pdf

Subcutaneous Buprenorphine

- Long-acting buprenorphine injection every 4 weeks by a healthcare professional
- Refrigerated product
- Dosage
  - Initial – 300 mg every 4 weeks for 2 months
  - Maintenance – 300 mg to 100 mg every 4 weeks
- Must be 16 years of age or older (no pediatric data)
- Transmucosal buprenorphine-containing (at least 8 mg) product followed by a dose adjustment for a minimum of 7 days
- Participating in psychosocial counseling (individual or group) at least once per week
- Not recommended in moderate to severe hepatic impairment

Cunningham et al. Am Society of Addiction Medicine OUD Guidelines Update 2020;
From prescribing information. Sublocade Indivior Inc. 2023.

Buprenorphine Subcutaneous: Injection Site Reactions

Injection Site Pain:

- 100 mg (0.5 mL): 1.8-4.9%
- 300 mg (1.5 mL): 3.5-8%

19 Gauge 5/8-inch needle

Management Options:

- Ice the area
- No evidence for lidocaine – used “off-label”

Pruritis:

- Up to 9.5%

Manufacturer prescribing information; Sublocade Indivior Inc. 2023.Data on file from drug manufacturer

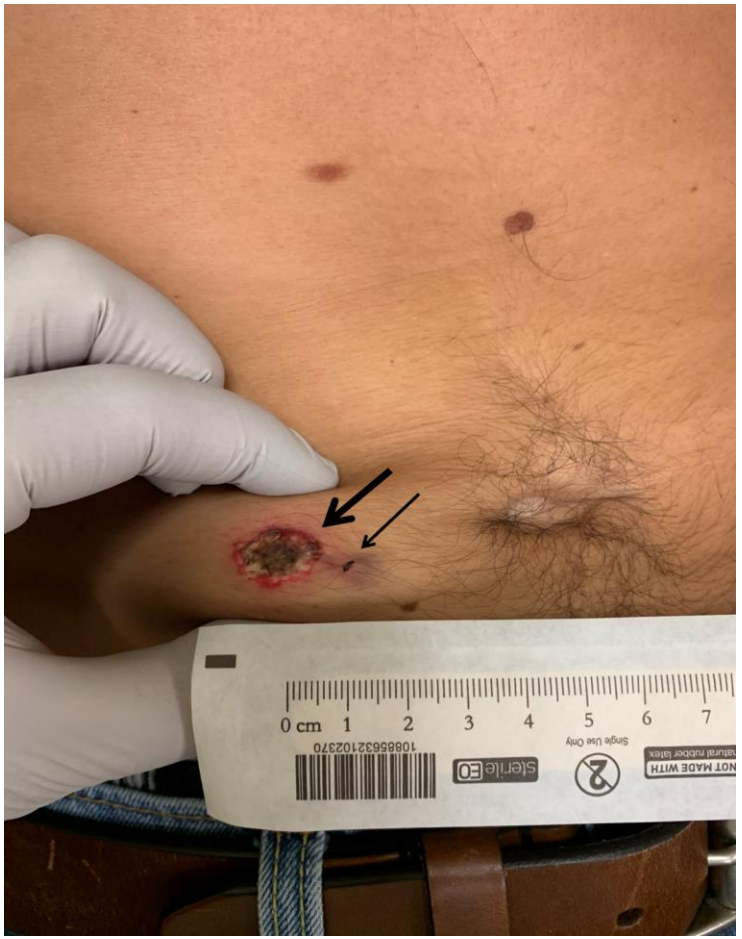
Buprenorphine Subcutaneous

Published Adverse Event

- Intradermal reaction
- More than just an injection site reaction!

Injection should have been 45 degrees

Injection should never be dispensed directly to the patient



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Crouse EL, et al. J Addic Med 2022; 16(2):242-4.
Permission to use photo obtained

Naltrexone XR (IM injection)

- Naltrexone extended-release injectable suspension for intramuscular administration
  - Indicated for the prevention of relapse to opioid dependence following opioid detoxification
  - Opioid antagonist with highest affinity for the μ-opioid receptor
  - 380 mg once monthly
  - Refrigerate
  - Must be administered by a healthcare professional
  - Alternate buttocks with each injection

Cunningham et al. Am Society of Addiction Medicine OUD Guidelines Update 2020;
From prescribing information. Vivitrol Alkermes Inc. 2022.

Naltrexone Warnings and Precautions

- Opioid overdose potential following discontinuation of therapy
- When reversal of injectable naltrexone blockade is required for pain management
- Opioid-free for a minimum of 7-10 days prior to administering
  - Oral challenge test
- Patient access to naloxone

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Cunningham et al. Am Society of Addiction Medicine OUD Guidelines Update 2020;
From prescribing information. Vivitrol Alkermes Inc. 2022.

Naltrexone Intramuscular: Injection Site Reactions

- 4.2 mL deep IM injection into the gluteal muscle with a 20-gauge needle.
- Incidence:
  - Injection site pain: 17%
  - Injection site pruritus: 10%
  - Injection site ecchymosis: 7%
- Prevention: Awareness, Education
- There was a naltrexone REMs regarding severe injection site reactions (including necrosis); however this was removed in May 2021

Vivitrol prescribing information; Alkermes Sept 2022.
https://www.pdr.net/risk-evaluation-and-mitigation-strategies-summary/vivitrol?druglabelid=1199#:~:text=The%20goals%20of%20this%20REMS%20are%3A&text=To%20inform%20patients%20and%20healthcare,with%20the%20use%20of%20VIVITROL.
https://www.hhs.texas.gov/sites/default/files/documents/oct-2022-durb-agenda-item3aa.pdf

Naltrexone Intramuscular: Common Adverse Effects

- Nausea: more common after initial injection (33%); usually mild and improves with a few days after injection.

- Should improve within with each subsequent injection. Other: tiredness, headache (25%), vomiting, decreased appetite (14%), painful joints and muscle cramps

From prescribing information. Vivitrol Alkermes Inc. 2022.

Summary of MOUD

	Pros	Cons	Other Considerations	Frequency of Visit
Methadone **agonist**	• Long-history of efficacy, can be started any time during treatment, high patient retention rates • Evidence for use in pregnancy • Less cost • Volume not restricted	• Overdose potential • QTc prolongation • Only available in a regulated OTP • Daily travel to appointments • Does not show up on PDMP • Reports of feeling “high” • Oversedation • Daily cost	Consider in patients who continue to use with buprenorphine treatment Poor response to buprenorphine Misuse/diversion of buprenorphine Contraindications: asthma, ileus Caution with OSA, breathing disorders, liver disease	Daily in clinic Observed treatment Can graduate to “take homes”

Summary of MOUD

	Pros	Cons	Other Considerations	Frequency of Visit
Buprenorphine **agonist/ antagonist**	• Lower potential for overdose • Monoproduct can be used in pregnancy • Is on PDMP • Option for long-acting injection	• Lack of data for buprenorphine/naloxone in pregnancy • Can be diverted • Multiple co-pays per month	Proper administration	Can graduate to less frequent visits
Naltrexone **antagonist**	• Not an opioid • Available as a long-acting injection or oral	• Must be opioid-free to initiate • Not ideal for non-adherent patients • Not ideal for pregnancy	Option for persons who do not want any opioid Option to transition to when tapering methadone or buprenorphine	Monthly

Case Scenario

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What do you recommend?

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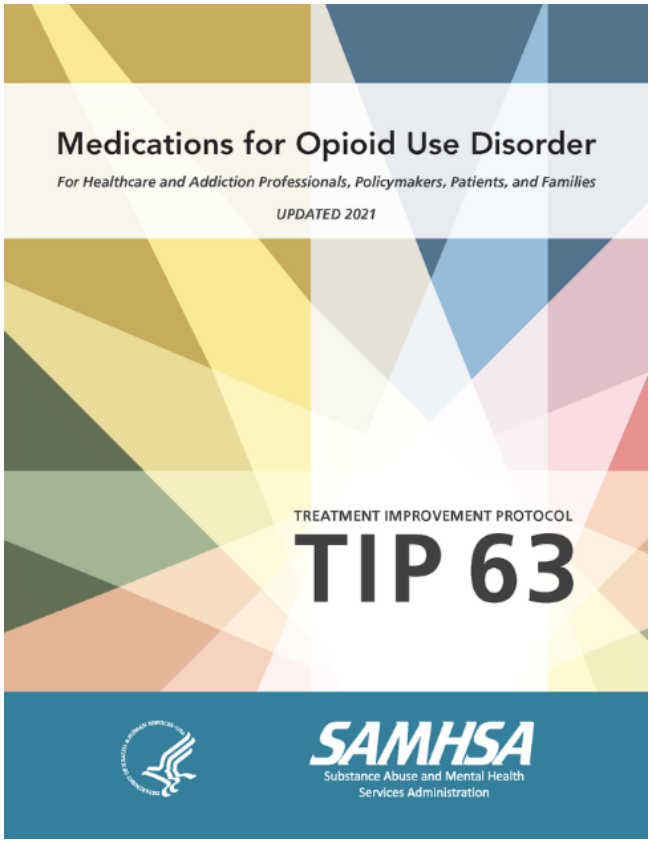
MOUD Guidelines



The ASAM
NATIONAL PRACTICE GUIDELINE
For the Treatment of Opioid Use Disorder
2020 Focused Update

Cunningham et al. Am Society Addiction Med Guidelines 2020
Available at: https://sitefinitystorage.blob.core.windows.net/sitefinity-production-blobs/docs/default-source/guidelines/npg-jam-supplement.pdf?sfvrsn=a00a52c2_2
https://store.samhsa.gov/sites/default/files/pep21-02-01-002.pdf

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Transition of MOUD Options

Medication From → To	Buprenorphine	Methadone	Naltrexone
Buprenorphine		No delay needed	7-14 days after last dose of buprenorphine
Methadone	Better tolerated when on <30-40 mg/day of methadone; microdosing protocols may be used		Must be completely withdrawn from opioids
Naltrexone	Wait 1 day for PO; 30 days for extended-release naltrexone	Wait 1 day for PO; 30 days for extended-release naltrexone Start with low initial methadone dose	

Cunningham et al. Am Society Addiction Med Guidelines 2020

Opioid Abstinence Rates

Study	Medication	% opioid free on medication	% opioid free on placebo/detox
Krupitsky et al. 2011	Naltrexone ER (inj)	36	23
Fudala et al. 2003 Weiss et al. 2011*	Buprenorphine/naloxone	20 -50	6
Woody et al. 2008 Age 14-21 years	Buprenorphine/naloxone	60	20
Mattick et al. 2009	Methadone	60	30

* Rx opioid dependent patients;
Adapted from: Connery HS. Harv Rev Psychiatry; 2015:23:63-75

Role of Urine Drug Screens (UDS)

Depending on the clinic and where they are in treatment -

UDS - completed every visit or monthly

UDS in OBOTs/OTPs are more sensitive than general UDS used in hospital settings

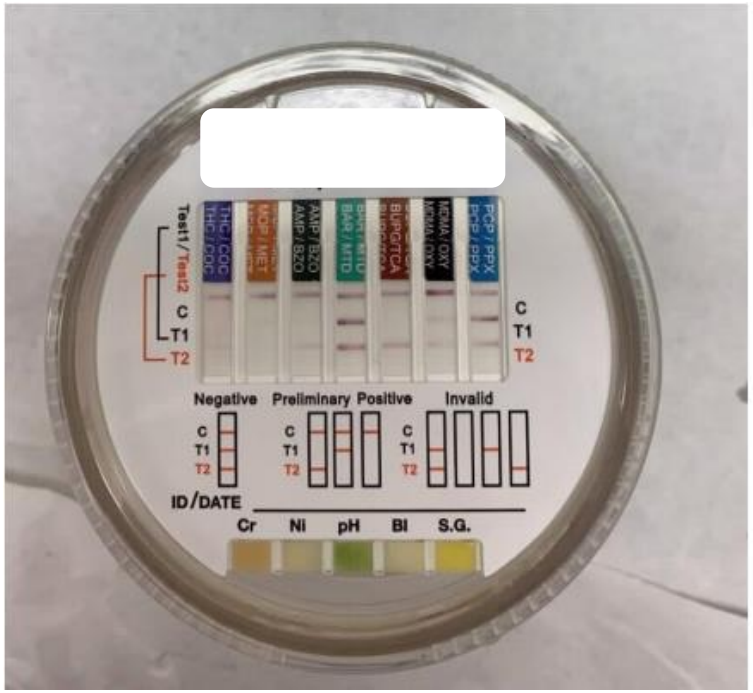
UDS used to confirm adherence and abstinence

Limitations:

- Observed versus non-observed
- Does **not** detect fentanyl
- Does **not** clarify if buprenorphine is buprenorphine or norbuprenorphine
  - Thus this may require a confirmatory “send out” lab to determine ratio of buprenorphine:norbuprenorphine

Personal Experience; SAMHSA Guidelines Tip 63 2021

Urine Drug Screen Cups



Photos courtesy of E Crouse and S Melton Thomason

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Adverse Reactions & Management

Sedation

Incidence:

- Methadone >>> Buprenorphine > Naltrexone

Management:

- Methadone: Lower dose if possible, may be a reason to consider switching to buprenorphine.
- Try to avoid prescribing stimulants
- Buprenorphine: tolerance develops over time

Cunningham et al. Am Society of Addiction Medicine OUD Guidelines Update 2020

MOUD-Induced Constipation

- A survey of 105 patients in “opioid substitution therapy”* at time of survey 81% reported **constipation** and 58% reported having been counseled on it being a side effect and only 20% were satisfied with how it was treated
  - Direct quote: “Although constipation is a frequent side-effect of OST [MOUD], it is an under-recognized, underdiagnosed & undertreated problem in the field of addiction”

*Publication did not specify which OST/MOUD used

Lugoboni F, et al. Drugs Context. 2021;10:2021-7-2.

Constipation

Incidence:

- Methadone >>> buprenorphine/naloxone > buprenorphine > naltrexone [negligible]

Opioid-Induced Constipation Management:

- Stimulants (senna, bisacodyl)
- Softeners (docusate)
- Polyethylene glycol
- Increase fluids
- Role of fiber

"Mush and Push"

Lugoboni F et al. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8547547/pdf/dic-2021-7-2.pdf

Lugoboni F, et al. Drugs Context. 2021;10:2021-7-2.

Webster et al. Substance Abuse and Rehabilitation 2016:7 81–86. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4913538/pdf/sar-7-081.pdf

https://www.hhs.texas.gov/sites/default/files/documents/oct-2022-durb-agenda-item3aa.pdf

Methadone & QTc Prolongation

Boxed warning

- QT prolongation and serious arrhythmia including torsades de pointes

Dose dependent adverse effect

- Increased with doses > 100 mg/day

Risk factors:

- Female sex
- CYP3A4 inhibitors
- Drug-drug interaction with concomitant QTc medications
- Electrolyte abnormalities: Low K, Low Mag, Low Calcium

Presenting symptoms:

- Seizures or syncopal episodes

Management

- If QTc > 500 msec, consider reducing dose, eliminating modifiable risk factors, or evaluate if switching medications is indicated

Mujtaba S, et al. J Cardiovasc Dis Research 2013;229-35.

Methadone & Sleep Apnea

Mechanism: Respiratory depressant effect

Incidence:

- **Obstructive Sleep Apnea:**
  - 35.2% in methadone in maintenance treatment (MMT)
  - Higher rates in higher BMI and longer time on methadone
- **Central Sleep Apnea:**
  - Reported as 30% of patients with stable MMT
  - Another review (N = 71) reported 14.1% and did not find it to be dose dependent

Management:

- Avoid benzodiazepines
- Role for switching to buprenorphine?

Badr MS, et al. Curr Pulmonol Rep. 2019 March ; 8(1): 14–21.
Sharkey KM, et al Drug Alcohol Depend. 2010 April 1; 108(1-2): 77–83.

Buprenorphine/Naloxone SL: Taste

Time to dissolve:	• Films: ~ 2.88 minutes • Tabs: up to 10 minutes
Taste:	• Buprenorphine: bitter • Suboxone®: metallic, bitter, salty flavor; orange • Zubsolv®: minty
Management:	• Candies, coffee, dark chocolate, juices • Do not brush teeth immediately!

Zubsolv product website Available at: https://zubsolv.com/; https://www.workithealth.com/blog/suboxone-tastes-bad-tips-to-cope-with-the-flavor/

Buprenorphine/Naloxone SL: Dental Problems

Jan 2022 FDA Warning on buprenorphine products dissolved in the mouth

- Tooth decay, cavities, dental abscesses, tooth erosion, tooth loss
- Benefits outweigh risk - oral care can help

2013 case series of 11 patients reporting since starting buprenorphine an average of:

- 5.2 dental caries per patient
- 3.6 dental fillings
- 2.4 cracked teeth

https://www.fda.gov/drugs/drug-safety-and-availability/fda-warns-about-risks-dental-problems-associated-buprenorphine-medicines-dissolved-mouth-treat; Suzuki J et al Prim Care Companion CNS Disord 2013 https://www.fda.gov/drugs/drug-safety-and-availability/fda-warns-about-dental-problems-buprenorphine-medicines-dissolved-mouth-treat-opioid-use-disorder

Buprenorphine/Naloxone SL: Dental Problems

- Prevention is key!
- After it is completely dissolved counsel patients to:
  1. Take a large sip of water
  2. Swish it gently around teeth & gums
  3. Wait at least 1 hour before brushing their teeth after use
     - Why? because it is acidic making teeth more “vulnerable”
- Regular dental follow ups!

https://www.fda.gov/drugs/drug-safety-and-availability/fda-warns-about-risks-dental-problems-associated-buprenorphine-medicines-dissolved-mouth-treat; https://www.bicyclehealth.com/suboxone-faq/why-does-suboxone-taste-bad

Precipitated Withdrawal

Risk: Buprenorphine, Naltrexone and Naloxone

Buprenorphine

- Must be in mild-moderate withdrawal before initiating buprenorphine/naloxone
- Illicit fentanyl has proven new challenges
  - Role for microinduction

Naltrexone

- Should be opioid free 7 to 10 days before injection

Naloxone

- if a person has overdosed, the benefit far exceeds risk of withdrawal

Long Acting Injections - Wearing Off Effect

Buprenorphine Subcutaneous

- Half-life: 43 to 60 days
- Builds up with continued use; tests positive on a UDS for ~ 6 months up to 1 year

Naltrexone

- Half-life: 5 to 10 days
- Some patient's describe increased cravings ~ 1 week before injection is due

Prescribing information: Sublocade Indivior 2023; Vivitrol Alkermes 202

Risk of Overdose

Buprenorphine

- Opioid naive patients - cases of overdose with just 2 mg
- SQ - Serious harm or death if injected intravenously (IV)

Naltrexone

- Risk factors - trying to overcome the blockade by taking more opioids
- Risk if dose is missed; days leading up to injection

Methadone

- Risk if misused, opioid-naive or use other opioids while on

Vivitrol prescribing information Alkermes Sept 2022
Sublocade prescribing information Indivior

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Medication Errors with MOUD

Medication Error

Mary Johnson 3/23/23

Buprenorphine/naloxone 8 mg/ 2 mg films
Take 1 film by mouth twice a day

#14 films

T. Nguyen
DEA X1234567

Buprenorphine Bioavailability

Extensive first-pass metabolism

- Oral: If swallowed, only 10% of IV is absorbed → thus less effective
- Sublingual (SL) film/tab: bioavailability ranges from 28 to 51% across studies (most often cited as 29-30%)
- Naloxone SL: bioavailability 3 to 10% of IV*

* If naloxone is inhaled – increases to about 30%

Elkader A and Sproule B Clin Pharmacokinet 2005;44:661-80,
Coe MA, et al. J Addict Med. 2019;13:93-103

Med Error

Suzie Mikeworth 3/23/23

Methadone 40 mg tablets

Take 3 tablets daily for opioid dependence

#21

M. Thompson

DEA T1234567

Can you fill this Rx?

Potential Med Error: Product Selection in Inpatient Pharmacy

New order for methadone 100 mg PO daily

Which product should be used to fill this order?

A. 10 mg tablets – 10 tablets per dose
B. 40 mg tablets – 2.5 tablets per dose
C. 10 mg/mL oral solution – 10 mL per dose
D. 10 mg/mL parenteral solution – 10 mL per dose

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B. 40 mg tablets – 2.5 tablets per dose
c. **10 mg/mL oral solution – 10 mL per dose**
D. 10 mg/mL parenteral solution – 10 mL per dose

Med Error: Duplicate Therapy

- A patient was complaining of the horrible taste with Suboxone®
- Provider converted:
  - Suboxone® 8 mg/2 mg - 2 films SL daily → Zubsolv® 11.4 mg/2.9 mg
- Contacted pharmacy to confirm they had Zubsolv® and was told they did not have in stock, so provider resumed the Suboxone®.
- Next week in clinic - Patient reported picking up and proceeding to take **BOTH** products
  - Dose equivalent of buprenorphine 32 mg/day!

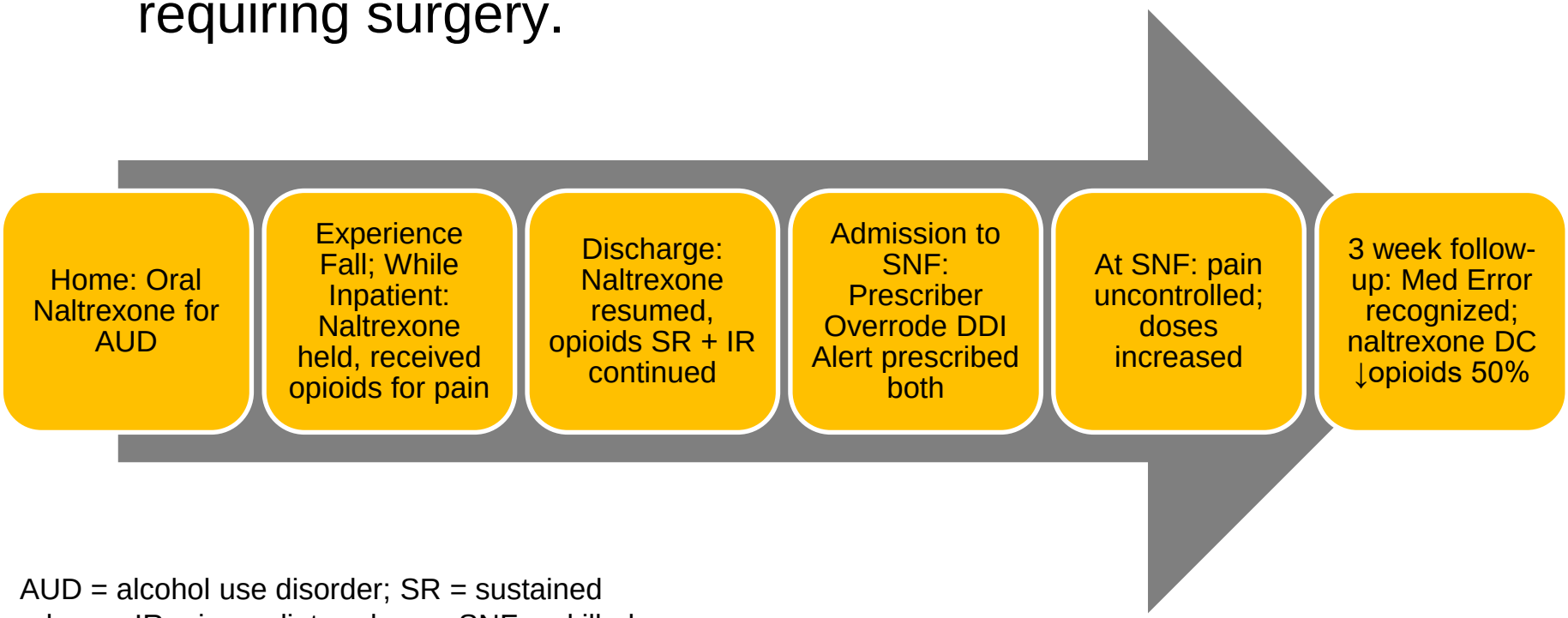
Buprenorphine Products Approved for OUD

	Brand Name	Strengths (mg)	Considerations
Buprenorphine/naloxone combination products			
SL film	Suboxone® Generics	2/0.5, 4/1, 8/2, 12/3	Most commonly used and cited
SL tab	Zubsolv®	0.7/0.18, 1.4/0.36, 2.9/0.71, 5.7/1.4, 8.6/2.1, 11.4/2.9	Higher bioavailability thus lower doses prescribed
SL tab	Generic	2/0/5, 8/2	Similar ratio as films
Buprenorphine monoproduct			
SL tab	Subutex® (discontinued) Generic only	2, 8	Less than 3% of your patients should be prescribed monoproduct in Virginia
Subcutaneous injection	Sublocade®	100 mg/0.5 mL 300 mg/1.5 mL	Shipped directly to clinic site form specialty pharmacies

Suboxone prescribing information Indivior 2023, Zubsolv product website accessed April 2023, Lexicomp Online, Wolters Kluwer, 2023 Sublocade prescribing information Indivior 2023

Med Error: Transitions of Care

- 56-year-old F on **naltrexone** for alcohol use disorder fell while intoxicated and had a cervical spine fracture requiring surgery.



AUD = alcohol use disorder; SR = sustained release; IR = immediate release; SNF = skilled nursing facility; DDI = drug-drug-interactions

Chou R. AHRQ PSNet Web M&M Case studies: 2018 Available at: https://psnet.ahrq.gov/web-mm/painful-medication-reconciliation-mishap .

Potential Med Error

Patient on buprenorphine 300 mg subcutaneous monthly is arrested.

When the next dose is due, the jail called the clinic to see if they could give naltrexone IM instead.

How do you respond?

A. Yes

B. No

Potential Med Error

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How do you respond?

A. Yes
B. No

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Common Misperceptions Surrounding MOUD

What's On the Prescription Drug Monitoring Program (PDMP)?

When reviewing the PDMP for MOUD related medications, which of the following are included (Select All)?

A. Naloxone
B. Naltrexone
C. Methadone
D. Buprenorphine subcutaneous
E. Buprenorphine (+/- naloxone) sublingual

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Just Completed Rehabilitation

Family perception - Now at a low risk of overdose

- Many programs are 28 days or less
- Safely get patients through withdrawal symptoms
- However, during rehabilitation tolerance goes down

MOUD is “just replacing one opioid with another”

Many persons with OUD experience stigma regarding using MOUD

- The attitude that receiving “medication assisted therapy” or maintenance opioids reflects an illness, a defect, or moral weakness needs to change

https://www.careinnovations.org/wp-content/uploads/Discontinuing_Methadone_and_Buprenorphine.pdf

Fentanyl Test Stips

- Can detect for presence of fentanyl
- Considered illegal and “drug paraphernalia” in most states
- Since 2019 Virginia fentanyl test strips have been legalized/decriminalized
  - Criminal penalties for test strip possession and distribution were removed
  - Can be obtained from local health department or authorized comprehensive harm reduction sites
- Virginia Department of Health website has instructions on how to use

https://www.facingsouth.org/2022/01/fight-legalize-life-saving-fentanyl-test-strips-southern-states; https://www.vdh.virginia.gov/epidemiology/naloxone/#:~:text=Fentanyl%20test%20strips%20are%20also,authorized%20comprehensive%20harm%20reduction%20sites.
https://www.vdh.virginia.gov/content/uploads/sites/3/2022/11/Fentanyl-Test-Strip-Instructions-English.pdf

Audience Assessment: Benzodiazepine Interaction?

A patient has been treated with clonazepam 1 mg TID for as far back as the PDMP and your pharmacy records go. They present with a new prescription for:
buprenorphine/naloxone 8 mg/2 mg - 1 film SL BID.

What do you do?

A. Ensure the patient has access to naloxone
B. Contact clonazepam provider and ask them to discontinue
C. Refuse to fill the buprenorphine while on concurrent clonazepam
D. Contact buprenorphine prescriber and request switching to a non-opioids MOUD product

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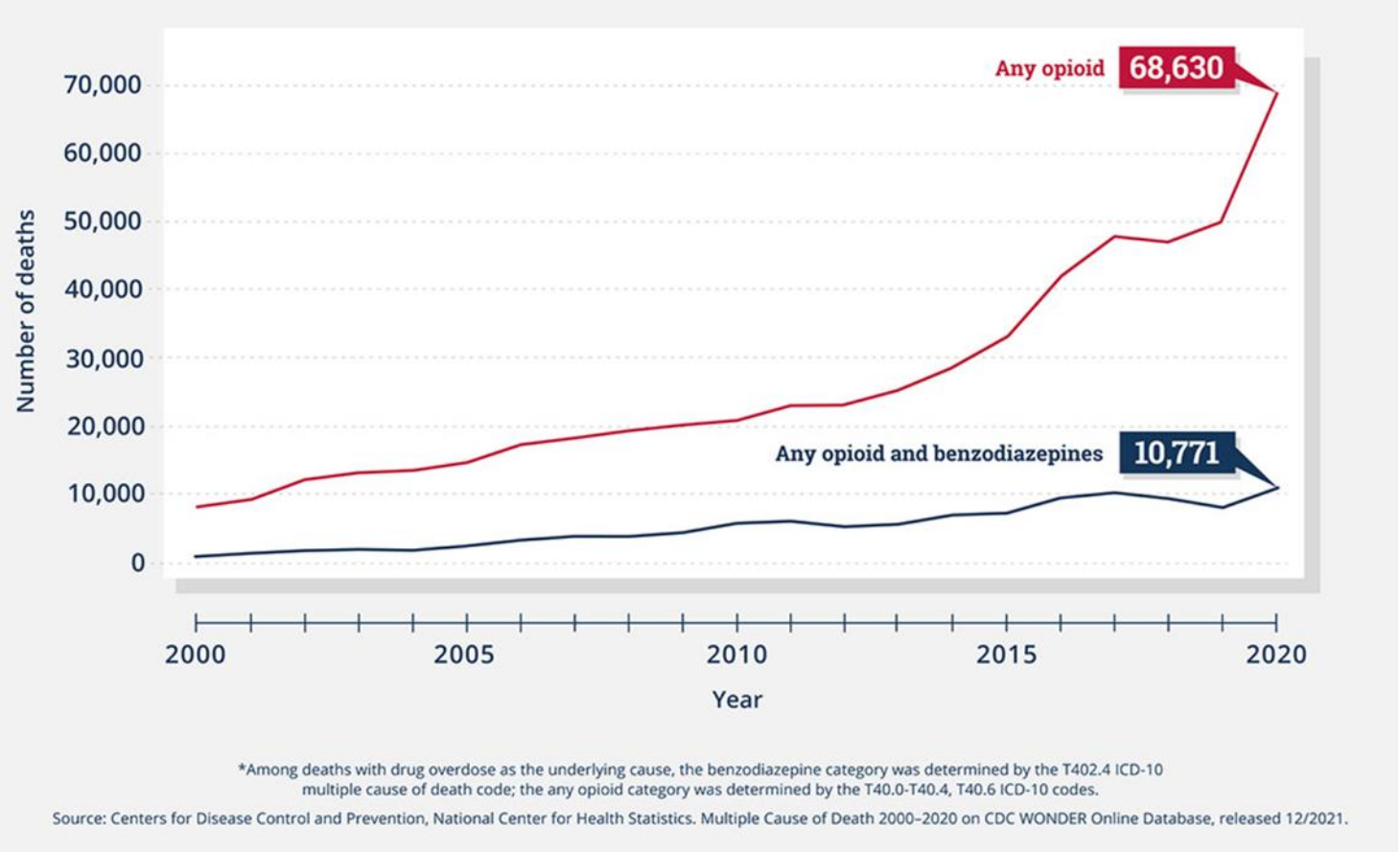
Benzodiazepines in Overdose



Public domain: nida.nih.gov
ttps://nida.nih.gov/research-topics/opioids/benzodiazepines-opioids. Accessed January 21, 2023

Warning on Opioids and Benzodiazepines (BZD) or Alcohol

Aug 2016:

Concomitant use of [Insert Opioid] with BZDs or other CNS depressants, including alcohol, may result in profound sedation, respiratory depression, coma and death…

2017 Amended their warning – to NOT withhold MOUD in patients taking BZDs

In 2020 updated to include BZDs have a risk of abuse and misuse; addiction, dangerous withdrawal

Mixing with alcohol can lead to life-threatening side effects

https://www.center4research.org/fda-updates-black-box-warning-for-benzodiazepines/; www.dailymed.nlm.nih.gov

https://www.drugabuse.gov/drug-topics/trends-statistics/overdose-death-rates

Audience Assessment

You receive a prescription for (or inpatient order for)

Buprenorphine/naloxone 8 mg/2 mg

½ film SL BID

Can you cut buprenorphine films?

A. Yes
B. No
C. Unsure

Suboxone prescribing information, Indivior 2018

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½ film SL BID

Can you cut buprenorphine films?

A. Yes
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C. Unsure

Suboxone prescribing information, Indivior 2018

Can you Cut Buprenorphine Films?

The prescribing information: “Do not cut, chew or swallow buprenorphine or buprenorphine/naloxone films”

However…buprenorphine and naloxone are spread evenly throughout the strip

Off-label:

On the street: People take “pieces”

In clinical practice:

- Providers prescribe 0.5 or 0.25 films
- They can be cut in half or quarters

Suboxone prescribing information, Indivior 2018; https://www.drugs.com/medical-answers/bunavail-cut-half-3538222/

How Long?

Case Vignette 1	Case Vignette 2
• 42-year-old with opioid use disorder admitted for depression on buprenorphine/naloxone 8 mg/2 mg - 2 films daily x 3 years	• 61-year-old with OUD on methadone maintenance x 14 years admitted for diabetic foot ulcer requiring IV antibiotics

In both scenarios a provider on the team entering the orders asked:
Why? Why is this person still on MOUD so many years later??

Buprenorphine Discontinuation & Rates of Relapse

Study	Total pop; prior heroin use (%)	Maintenance period	Mean dose	Abstinent maintenance	Taper duration	Follow-up time; Naltrexone Y/N	Abstinant post taper?
Sigmon et al. 2013	N = 70; ~50%	2 weeks	11.5 mg	82%	1 wk 2 wk 4 wk	9 wk Yes 8 wk Yes 6 wk Yes	21% 17% 50%
Weiss et al. 2011	N = 32; 26%	12 weeks	20.8 mg	54%	4 wk	8 wk None	9.6%
Ling et al 2009	N = 516; 83%	4 weeks	20.3 mg	37%	1 wk 4 wk	4 wk None	18%
Woody et al. 2009	N = 55; 76%	8 weeks	15.1 mg	54%	4 wk	6 mos None	34%
Breen et al. 2003	N = 50; 100%	2 weeks (> 6 mo methadone)	8.6 mg	NR	11 wk	4 wk optional	44%

Table adapted from: Bentzley BS, et al. J Subst Abuse Treat. 2015 May;52:48-57.

Methadone Discontinuation & Relapse

- 1970s - Dr. Dole's "vision" was life-long treatment
- A 2001 Review on post-discharge outcomes of patients exiting:
  - Extended methadone detoxification
  - "Abstinence-oriented" methadone programs
  - Methadone maintenance programs

Findings:

→ High rates of relapse to opioid use after methadone discontinuation

→ Consequences of leaving methadone treatment increased death rates following discharge.

Quinones S. Dreamland, 2015.
Bentzley BS, et al. J Subst Abuse Treat 2015; 52:48-57.

True or False:
DATA Waiver is Required

You must have an X-waiver, DEA number "X" to write a prescription for buprenorphine or buprenorphine/naloxone

True or False:
DATA Waiver is Required

You must have an X-waiver, DEA number "X" to write a prescription for buprenorphine or buprenorphine/naloxone

From SAMHSA

Starting June 27, 2023 - per the Consolidated Appropriations Act of 2023 (PDF | 3.8 MB):

New or Renewing Drug Enforcement Administration (DEA) registrants are required to have at least one of the following:

- A total of 8 hours of training from certain organizations on opioid or other substance use disorders for practitioners renewing or newly applying for a registration from the DEA to prescribe any Schedule II-V controlled medications;
- Board certification in addiction medicine or addiction psychiatry from the American Board of Medical Specialties, American Board of Addiction Medicine, or the American Osteopathic Association; or
- Graduation within five years and status in good standing from medical, advanced practice nursing, or physician assistant school in the United States that included successful completion of an opioid or other substance use disorder curriculum of at least eight hours.

https://www.samhsa.gov/medications-substance-use-disorders/removal-data-waiver-requirement

From SAMHSA

https://store.samhsa.gov/sites/default/files/pep21-06-01-002.pdf

Take Home Points

- Overdoses from opioids including fentanyl continue to rise. Distribution of naloxone remains an important tool to reduce overdose mortality
- A primary reason persons continue to use is fear of withdrawal. Withdrawal can be managed symptomatically or with opioid replacement.
- The 3 primary medications used to treat OUD are buprenorphine(+/- naloxone) methadone, and naltrexone
- Educate yourself and patients

Ways to Learn More:

Documentaries Available on:

- Netflix:
  - The Pharmacist
  - Heroin(e)
- Hulu: Dopesick
- Youtube: Virginia - Hardest Hit available at: https://hardesthitva.com/

Books:

- Dreamland by Sam Quinones
- Dopesick by Beth Macy

Resources for Patients & Family

Themselves:

- Decisions in Recovery: Treatment for Opioid Use Disorder: https://store.samhsa.gov/product/SMA16-4993
- Never use alone: https://neverusealone.com/

Their families and friends:

- Medication Assisted Treatment for Opioid Addiction: Facts for Families and Friends: https://portal. ct.gov/-/media/DMHAS/Opioid-Resources/MATInfoFamilyFriendspdf.pdf

Any Questions?

https://www.fentanylawarenessday.org/