Opioid Use Disorder: An Evidence-Based, Public Health-Oriented Approach

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1

Disclosures

No conflicts of interest or relevant financial relationships with ineligible companies to disclose

2

Learning Objectives

- Describe the epidemiology of opioid use disorder and opioid-related mortality, with a focus on how increased heroin use and fentanyl in the drug supply has changed the dynamics of the epidemic.
- Define opioid use disorder, and explain how to diagnose opioid use disorder.
- Describe options for treatment of opioid use disorder, including detox, behavioral therapies and medications for opioid use disorders (buprenorphine, methadone, naltrexone), and discuss the evidence for effectiveness of these interventions.
- Understand the mechanism of action of buprenorphine, and describe key principles of managing opioid use disorder with buprenorphine.
- Describe how principles of harm reduction can be applied to treating opioid use disorder, including naloxone prescribing and access to syringe services programs.
- Describe the impact of stigma on people with opioid use disorder, and discuss ways to reduce stigma related to opioid use disorders in clinical practice.
- Describe a public health-oriented approach to opioid use disorder, and explain how public health practitioners can advocate for policies that improve morbidity and mortality from opioid use disorder

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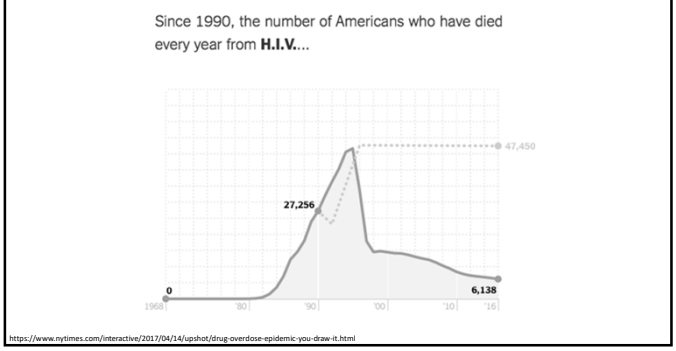

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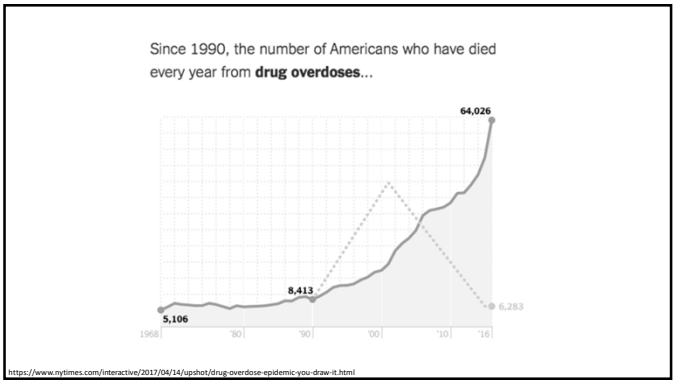

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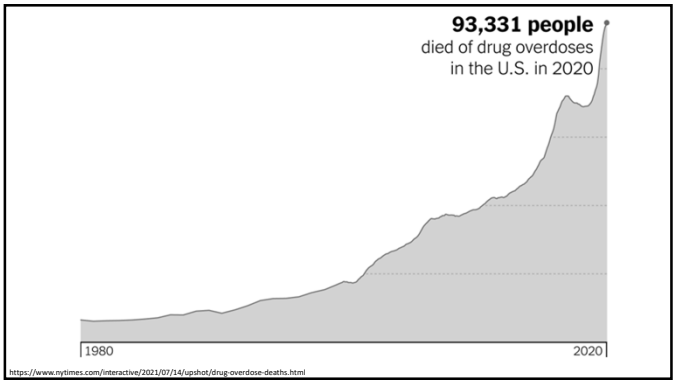

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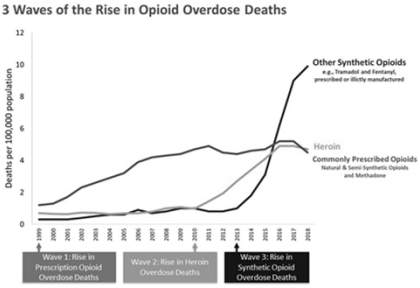
Opioid Overdose Crisis in US



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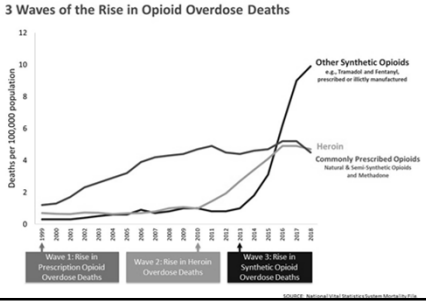


9

HEALTH • FENTANYL

Fentanyl Is Causing Almost Half of All Overdose Deaths, Research Shows

BY BRITTANY SHOOT
July 2, 2018 6:36 PM CDT

The shadow of U.S. Sen. Lindsey Graham (R-SC) is cast on a photograph of heroin and fentanyl during a news conference the U.S. Capitol March 22, 2018 in Washington, DC.

https://fortune.com/2018/07/02/fentanyl-is-causing-almost-half-of-all-overdose-deaths-research-shows/

10

Opioid-Related Mortality in Missouri

- Drug overdose = leading cause of death among adults 18-44 in Missouri
- Many overdose deaths involve multiple substances, but majority (70%) involve opioids
- In 2020, there were 1,375 Missourians who lost their lives to an opioid overdose

https://health.mo.gov/data/opioids/

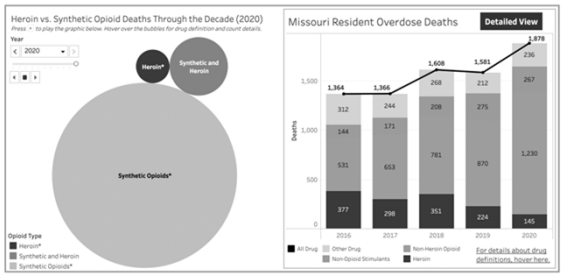
11

Other Complications from Opioid Use Disorder

- Endocarditis
- Hepatitis C
- HIV
- Narcotic bowel syndrome
- Serious social/interpersonal problems
- Job loss
- And many more…

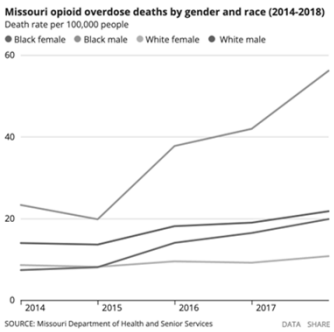
12

Missouri Drug Overdose Dashboard



https://health.mo.gov/data/opioids/

13



https://www.stltoday.com/news/local/govt-and-politics/missouri-s-opioid-epidemic-hits-african-americans-hardest-especially-in-st-louis/article_a2fcb27a-11a3-5518-8301-639fb0f324e3.html

14

A Critical Need

- ~80% of Americans with OUD don't get treatment
- People with OUD lack access to proven treatments, particularly medications for opioid use disorder
- Not enough psychiatrists and addiction specialists to meet demand → can be managed in primary care
- Policy barriers to delivering most evidence-based treatments for opioid use disorder

Wakeman S, Barnett M. NEJM 2018; 279(1):1-4.

15

DIAGNOSING OPIOID USE DISORDER

16

Jane

- Jane is a 48-year-old female presenting to primary care clinic to establish with new PCP after moving
- MVA in 2015, started on oxycodone for management of pain by PCP
- Has taken oxycodone 5 mg TID for past 7 years (confirmed with PMP)
- This dose controls pain and allows her to work
- Does not use ETOH or other substances (confirmed with UDS)
- Always takes oxycodone as prescribed, never takes more, does not get in way of family or work life

QUESTION: Does Jane have an opioid use disorder?

17

Opioid Use Disorder

- Addiction is not simply about use of substances, but behaviors and symptoms surrounding drug use
- Many people use drugs, only some develop addiction
- 3 C's of addiction
  - Loss of **C**ontrol
  - Continued Use in spite of negative **C**onsequences
  - **C**raving/**C**ompulsion

18

Diagnosing Opioid Use Disorder

DSM 5 Criteria

– More/longer than intended – Unable to cut back/control – Time dedicated to obtaining, using, recovering from – Physical or psychological consequences	Loss of Control	NO
– Activities given up – Failure to fulfill major obligations – Social or interpersonal problems caused or made worse by	Continued Use in spite of consequences	NO
– Use in hazardous situations – Craving/strong desire/urge	Craving/Compulsion	NO
– Tolerance (unless taken solely under appropriate medical supervision) – Withdrawal (unless taken solely under appropriate medical supervision)	Physical dependence	?

APA. 2013. Diagnostic and Statistical Manual of Mental Disorders (5th ed).

Mild = 2-3 symptoms, **Moderate** = 4-5 symptoms, **Severe** = 6+ symptoms

19

Jane #2

- Jane is a 48-year-old female presenting to primary care clinic to establish with new PCP after moving
- MVA in 2015, started on oxycodone for management of pain by PCP
- Started craving higher and higher doses, PCP initially escalated and then stopped prescribing
- Bought rx pain pills on street for a while, then couldn't afford → switched to heroin
- Heroin use has led to loss of job, loss of spouse, several overdoses
- Tried to quit on own but withdrawal too hard. Not sure how to quit.

QUESTION: Does Jane #2 have an opioid use disorder?

20

Diagnosing Opioid Use Disorder

DSM 5 Criteria

– More/longer than intended – Unable to cut back/control – Time dedicated to obtaining, using, recovering from – Physical or psychological consequences	Loss of Control	☑
– Activities given up – Failure to fulfill major obligations – Social or interpersonal problems caused or made worse by	Continued Use in spite of consequences	☑
– Use in hazardous situations – Craving/strong desire/urge	Craving/Compulsion	☑
– Tolerance (unless taken solely under appropriate medical supervision) – Withdrawal (unless taken solely under appropriate medical supervision)	Physical dependence	☑

APA. 2013. Diagnostic and Statistical Manual of Mental Disorders (5th ed).

Mild = 2-3 symptoms, **Moderate** = 4-5 symptoms, **Severe** = 6+ symptoms

21

Additional History

Chief Complaint(s):
- interested in suboxone

HPI:

New/Follow-up Patient Consult

Patient is here for substance use disorder evaluation and management.
- Last opioid use:
- History of opioid use (age started, route?):
- Consequences of use:
- Prior h/o sobriety:
- Treatment hx / prior pharmacotherapy:
- H/o overdose:
- Other drugs / ETOH:
- Medical complications of use:
- HCV status:
- Child-bearing status:
- Medical comorbidities
- Psych hx:

Social hx (housing, employment, supports, legal issues):.

22

DSM-IV vs DSM-V

DSM-IV	DSM-V
Substance use disorders were broken up into categories of ***substance dependence*** and ***substance abuse***	These categories were combined to create a single category of ***substance use disorder***, with severity (mild to severe) depending on number of symptoms

23

Language Matters

Contents lists available at ScienceDirect

International Journal of Drug Policy

journal homepage: www.elsevier.com/locate/drugpo

Research paper

Does it matter how we refer to individuals with substance-related conditions? A randomized study of two commonly used terms☆

John F. Kelly*, Cassandra M. Westerhoff

Center for Addiction Medicine, Department of Psychiatry, Massachusetts General Hospital, 60 Staniford Street, Boston, MA 02114, United States

24

Language Matters

"Substance Abuser"

Mr. Williams is a substance abuser and is attending a treatment program through the court. As part of the program Mr. Williams is required to remain abstinent from alcohol and other drugs. He has been compliant with program requirements, until one month ago, when he was found to have two positive urine toxicology screens which revealed drug use and a breathalyzer reading which revealed alcohol consumption. Within the past month there was a further urine toxicology screen revealing drug use. Mr. Williams has been a substance abuser for the past few years. He now awaits his appointment with the judge to determine his status.

"Substance Use Disorder"

Mr. Williams has a substance use disorder and is attending a treatment program through the court. As part of the program Mr. Williams is required to remain abstinent from alcohol and other drugs. He has been compliant with program requirements, until one month ago, when he was found to have two positive urine toxicology screens which revealed drug use and a breathalyzer reading which revealed alcohol consumption. Within the past month there was a further urine toxicology screen revealing drug use. Mr. Williams has had a substance use disorder for the past few years. He now awaits his appointment with the judge to determine his status.

Fig. 1. Study vignettes.

25

Study Summary

- **Methods:**
  - 516 clinicians attending two mental health conferences completed the study
  - Randomized to read one of two vignettes
  - Completed likert-scale questionnaire assessing perceptions of the person in the vignette
- **Results:**
  - Those who read the "substance abuser" vignette were significantly more likely to agree that the person in the vignette was personally culpable for their addiction and that punitive (rather than therapeutic) measures should be taken
- **Conclusion**
  - *Even among highly trained mental health professionals*, language may trigger implicit biases → perpetuate stigma against people with addiction

26

Language Matters

Changing the Language of Addiction ASAM

Terms that stigmatize addiction can affect the perspective and behavior of patients, clients, scientists, and clinicians. Clinicians especially need to be aware of person-first language and avoid more stigmatizing terms.

Terms Not to Use	Terms to Use
• addict, abuser, user, junkie, druggie	• person with a substance use disorder
• alcoholic, drunk	• person with an alcohol use disorder
• oxy-addict, meth-head	• person with an opioid use disorder
• ex-addict, former alcoholic	• person in recovery
• clean/dirty (drug test)	• negative/positive result(s)

27

Language Matters

AMERICAN OSTEOPATHIC ASSOCIATION

Policy Statement, American Osteopathic Association, 2020

The American Osteopathic Association (AOA) commit to the use of clinically-accurate, non-stigmatizing, person-first language ("substance use disorder," "recovery," "substance misuse," "positive or negative urine screen," and "person with a substance use disorder") and discourage the use of stigmatizing terminology ("substance abuse," "substance abuser," "addict," "alcoholic," and "clean/dirty") in future publications, resolutions, and educational materials both in print and online; and, that the AOA encourages its members and organizational partners to incorporate clinically-accurate, non-stigmatizing, person first language into their clinical practice.

28

EVIDENCE-BASED TREATMENT FOR OPIOID USE DISORDER

29

Jane #2

- Jane is a 48-year-old female presenting to primary care clinic to establish with new PCP after moving
- MVA in 2015, started on oxycodone for management of pain by PCP
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- Heroin use has led to loss of job, loss of spouse, several overdoses
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30

Question

Which of the following treatments would give Jane the best chance of long-term success (reduced OUD-associated morbidity/mortality)?

A. Detox
B. Buprenorphine
C. Methadone
D. Naltrexone
E. Cognitive-behavioral therapy
F. B or C

31

Question

Which of the following treatments would give Jane the best chance of long-term success (reduced OUD-associated morbidity/mortality)?

A. Detox
B. Buprenorphine
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E. Cognitive-behavioral therapy
F. B or C

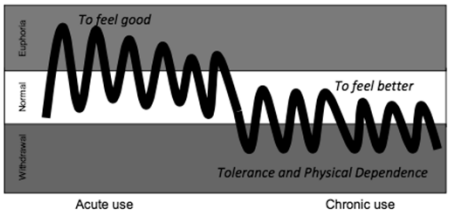
32

Options for Treating Opioid Use Disorder

- Behavioral treatment (formal treatment program, individual counseling)
- Opioid Agonists
  - Buprenorphine
  - Methadone
- Opioid Antagonists
  - Naltrexone
- Detox

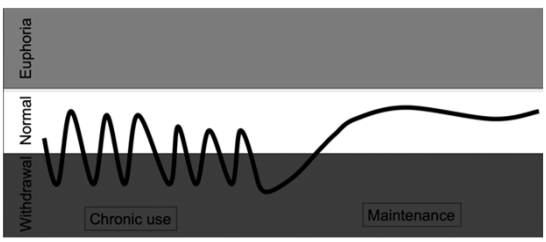
33

Why People Use Opioids?



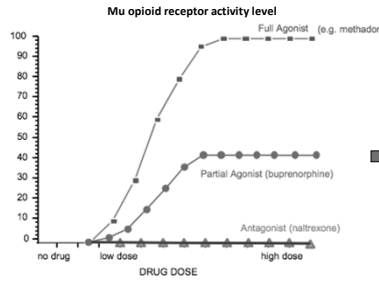
34

How Medication Treatment Works



35

A bit of pharmacology…



Methadone = full agonist at mu opioid receptor

Buprenorphine = partial agonist at mu opioid receptor

Naltrexone = antagonist at mu opioid receptor

36

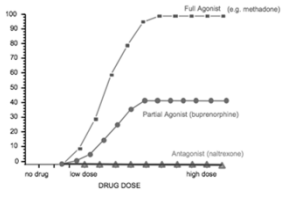
Goals of Medication Treatment for OUD

1) Relief of withdrawal symptoms
   - Methadone, buprenorphine
2) Opioid blockade
   - Methadone, buprenorphine, naltrexone
3) Reduce opioid craving
   - Methadone, buprenorphine, naltrexone
4) Restore reward pathway
   - Methadone, buprenorphine, naltrexone

37

Buprenorphine

- **Partial agonist** at mu opioid receptor
- High affinity, but low activity
  - **Low activity** = treats withdrawal, reduce cravings
  - **Low activity** → CEILING EFFECT
    - Euphoria unusual
    - Overdose risk low and only occurs with other substances (BDZs and ETOH)
    - Patients feel normal while taking
  - **High affinity** = blocks other opioids from stimulating receptor in presence of buprenorphine

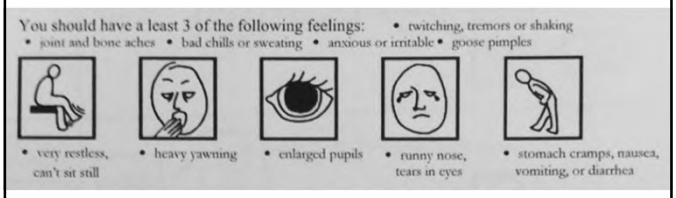


38

Buprenorphine

39

Buprenorphine Induction

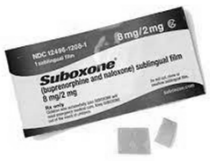


Precipitated withdrawal: occurs if buprenorphine induction started before patients start having withdrawal symptoms

40

SUBOXONE (buprenorphine-naloxone)

- Buprenorphine co-formulated with naloxone (opioid blocker)
- Naloxone not orally bioavailable
- If crushed and injected, naloxone counteracts effect of buprenorphine (safety mechanism)
- Buprenorphine solo product sold as *Subutex*
  - Somewhat higher diversion risk



41

Buprenorphine – regulations

- FDA approved for OUD in 2002
- Prescriber must have **DEA X waiver** to prescribe in outpatient settings
- Each prescriber has limit to how many patients can prescribe to at given time (30, 100, 275)
- Historically, obtaining waiver required 8-hour training course
  - As of 2021, MD/DO's can get waiver to treat up to 30 patients in first year without required training course

SAMHSA Substance Abuse and Mental Health Services Administration

https://www.samhsa.gov/medication-assisted-treatment/become-buprenorphine-waivered-practitioner

42

Buprenorphine – regulations

- December 2022 Congress passed "Omnibus Bill" → signed into law by President Biden
- Removal of federal requirement for practitioners to have a "waiver" to prescribe buprenorphine
- **All practitioners with a DEA license that includes Schedule III authority may now prescribe buprenorphine**
- New training requirements on opioid use disorder treatment for all DEA application go into effect June 2023 (more to come…)

43

A Quick Comparison…

	Buprenorphine	Methadone	Naltrexone
Mechanism of action	Partial agonist	Full agonist	Antagonist
Key facts	• Strong data to support efficacy • Can be prescribed in primary care setting with X waiver • Excellent safety profile, low overdose risk	• Strong data to support efficacy • Can only be prescribed for OUD in **highly structured treatment settings** where patients have to come daily • Higher overdose risk (due to full agonism of opioid receptor), more drug interactions	• **Weaker data to support efficacy** • Requires 7 days of abstinence from opioid use before starting (this is really hard!) • Option for individuals seeking to avoid any opioids

44

Show Me the Data!!

JAMA Psychiatry

- Systematic review and meta-analysis including 36 cohort studies and 15 RCTs, encompassing >700,000 patients
- Among cohort studies, treatment with opioid agonist therapies (buprenorphine or methadone) was associated with **lower risk of all-cause mortality** compared with no opioid agonist use (RR 0.47, 95% CI 0.42-0.53)
- While receiving opioid agonist treatment, individuals were also at lower risk of injury and poisoning, suicide, cancer, alcohol-related mortality, and cardiovascular mortality

Santo et al, JAMA Psychiatry, 2021

45

What about detox?

- **Detoxification:** use of medications to bring patient from opioid-dependent to opioid-free state
  - Examples of treatments = short term buprenorphine (to treat withdrawal symptoms only)
- **The problem = detox without maintenance therapy doesn't work**
  - Even when paired with psychosocial counseling and other supports!!
  - Patients undergoing acute detox have very poor retention in care (Kakko, 2003)
  - Patients undergoing acute detox may actually have INCREASED risk of overdose due to loss of opioid tolerance (Strang et al, 2003)

Kakko et al, Lancet, 2003
Strang et al, BMJ, 2003

46

What about counseling?

- Counseling alone without pharmacotherapy is ineffective and leads to high rates of relapse
- Studies of counseling combined with pharmacotherapy compared with buprenorphine or methadone alone have not shown consistent benefit
- Clinical bottom line = patients on medication for opioid use disorder should be offered psychosocial therapy
  - But it should <u>not</u> be a prerequisite for treatment

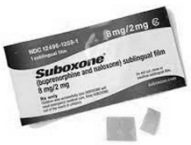
Wakeman, JAMA, 2020

47

"So how long do I have to be on this?"

LONG ENOUGH!

- Weigh overall low risk of long-term maintenance treatment VS high risk of relapse and associated morbidity/mortality



48

Myths – Medication-based Treatments

- **Substituting one addiction for another**
  - "Addiction" defined by compulsive use despite harm
  - Patients may become *dependent* on buprenorphine, but this is not addiction
    - Would you consider long-term use of anti-depressants, insulin, blood pressure meds "addiction"?
- **It's dangerous**
  - These medications REDUCE mortality!
- **Abstinence-based treatment is better**
  - There is no data to support 30-day OUD treatment or detox
  - There is good data supporting medication-based treatment with buprenorphine or methadone
- **Takes too much time/resources**
  - Short office visits
  - BH support important but not a deal-breaker ("medication first" model)

49

Chronic Disease Model of Care

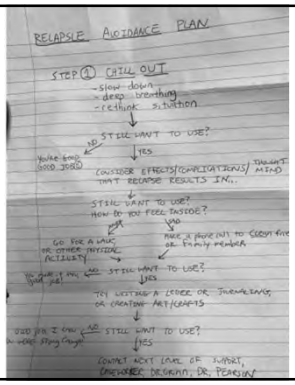
- Opioid use disorder is a **chronic, relapsing illness** associated with significant morbidity and mortality
  - Like hypertension or diabetes, OUD has genetic, environmental and behavioral components
- Maintenance medication-based treatment for OUD is the standard of care
  - Like metformin for diabetes or amlodipine for hypertension

50

Relapse and Continued Use

- Some patients on medication for opioid use disorder will struggle to remain abstinent from illicit opioid use
- Relapse is not an indication to stop treatment!
- Over time treatment works!

51



52

HARM REDUCTION

53

Harm Reduction

- **Harm reduction =** a set of practical strategies aimed at reducing negative consequences from drug use
- **Goal** is to meet patients where they are at, reduce harm, and prevent death
- Examples of harm reduction for patients with opioid use disorder
  - Overdose education and naloxone distribution
  - Syringe services programs
  - Fentanyl test strips
- Data shows harm reduction approaches *reduce risk of infection* and *reduce overdose risk*

Wakeman, JAMA, 2020

54

Prescribe naloxone to:
- Patients with opioid use disorder
- Patients with history of opioid overdose
- Patients on high doses of prescribed opioids
- Friends and family of individuals who use opioids

55

56

A PUBLIC HEALTH APPROACH

57

OUD thru a Public Health Lens

https://www.yourrecoverysolutions.com/projects1.html

58

Public Health Solutions

- Expand access to evidence-based OUD treatments
  - Removal of X waiver
  - Low barrier buprenorphine
  - Increased training for healthcare providers
  - Access to MOUD for incarcerated persons
- Remove policy barriers to effective harm reduction modalities
  - Syringe services programs
  - Fentanyl test strips
  - Expand naloxone access

Gupta R, Levine RL, Cepeda JA, Holtgrave DR. Transforming Management of Opioid Use Disorder with Universal Treatment. N Engl J Med. 2022 Oct 13;387(15):1341-1344. doi: 10.1056/NEJMp2210121. Epub 2022 Sep 21. PMID: 36129991.

59

Public Health Solutions

- Decrease stigma associated with opioid use disorder
  - At structural, community, and individual levels
- Improve access to healthcare for people with OUD
  - Medicaid expansion
- Address the broader social determinants of health
  - Food insecurity, homelessness, stigma/discrimination all contribute to opioid use disorder morbidity/mortality, and create real barriers to treatment

Gupta R, Levine RL, Cepeda JA, Holtgrave DR. Transforming Management of Opioid Use Disorder with Universal Treatment. N Engl J Med. 2022 Oct 13;387(15):1341-1344. doi: 10.1056/NEJMp2210121. Epub 2022 Sep 21. PMID: 36129991.

60

Questions?

61