

Providing Care with a Redemptive Mindset in Opioid Use Disorder

TRACY FRAME, PHARM.D., BCACP, BELMONT UNIVERSITY

JOEL FRAME, CONNECTIONS PASTOR, HOPE CHURCH

Disclosures

- Dr. Tracy Frame and Joel Frame, authors of this educational activity, have no relevant financial relationship(s) with ineligible companies to disclose.
- None of the planners for this educational activity have relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

Learning Objectives

1

Review medications used in opioid use disorder.

2

Identify the barriers to treatment for patients struggling with opioid use disorder.

3

Discuss how one could have a redemptive mindset towards those fighting an opioid use disorder.

4

Formulate a plan of action for how they might provide compassionate care to patients with opioid use disorder.



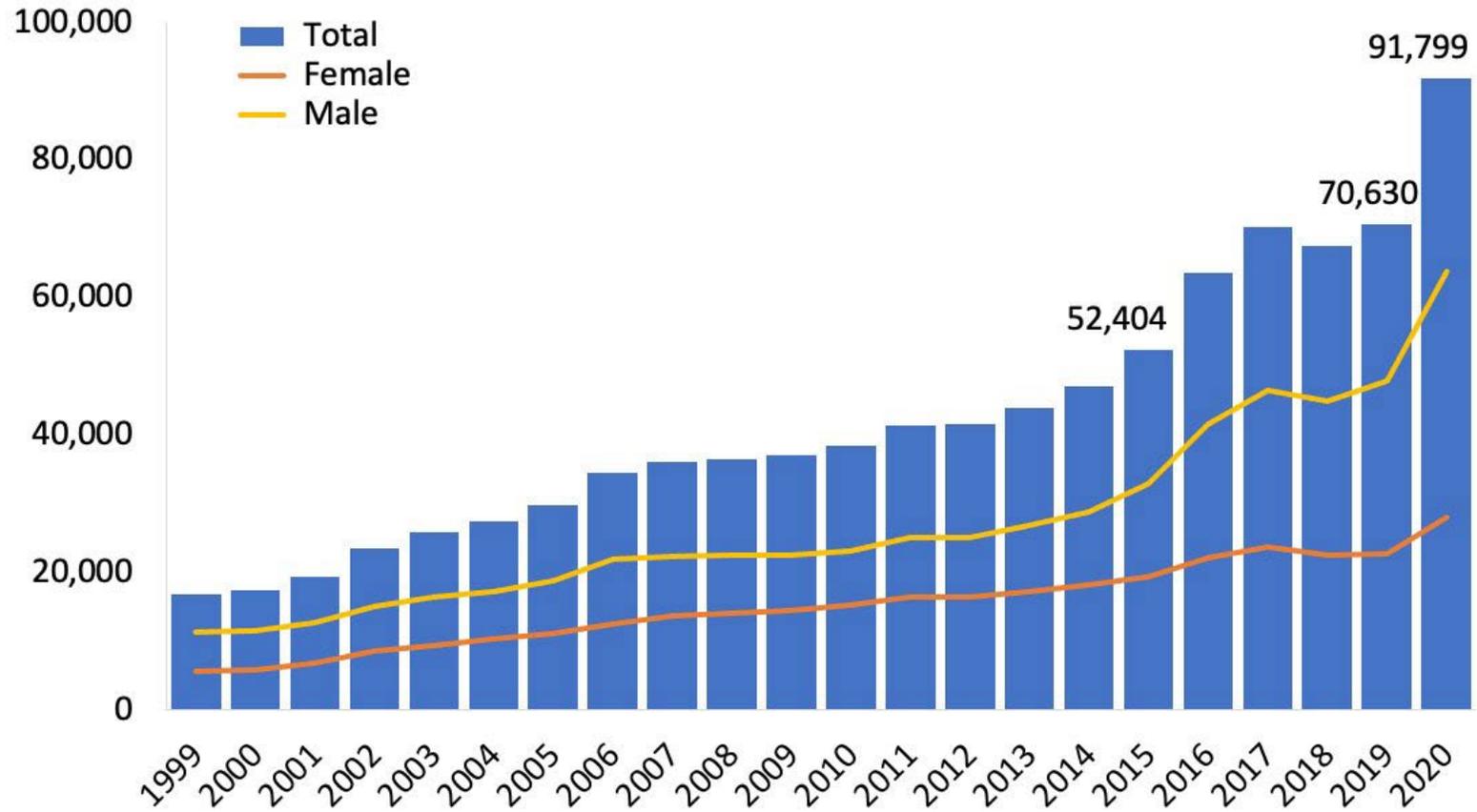
What one question do you have today about opioid use disorder or its treatment?



Quick Overview

Facts

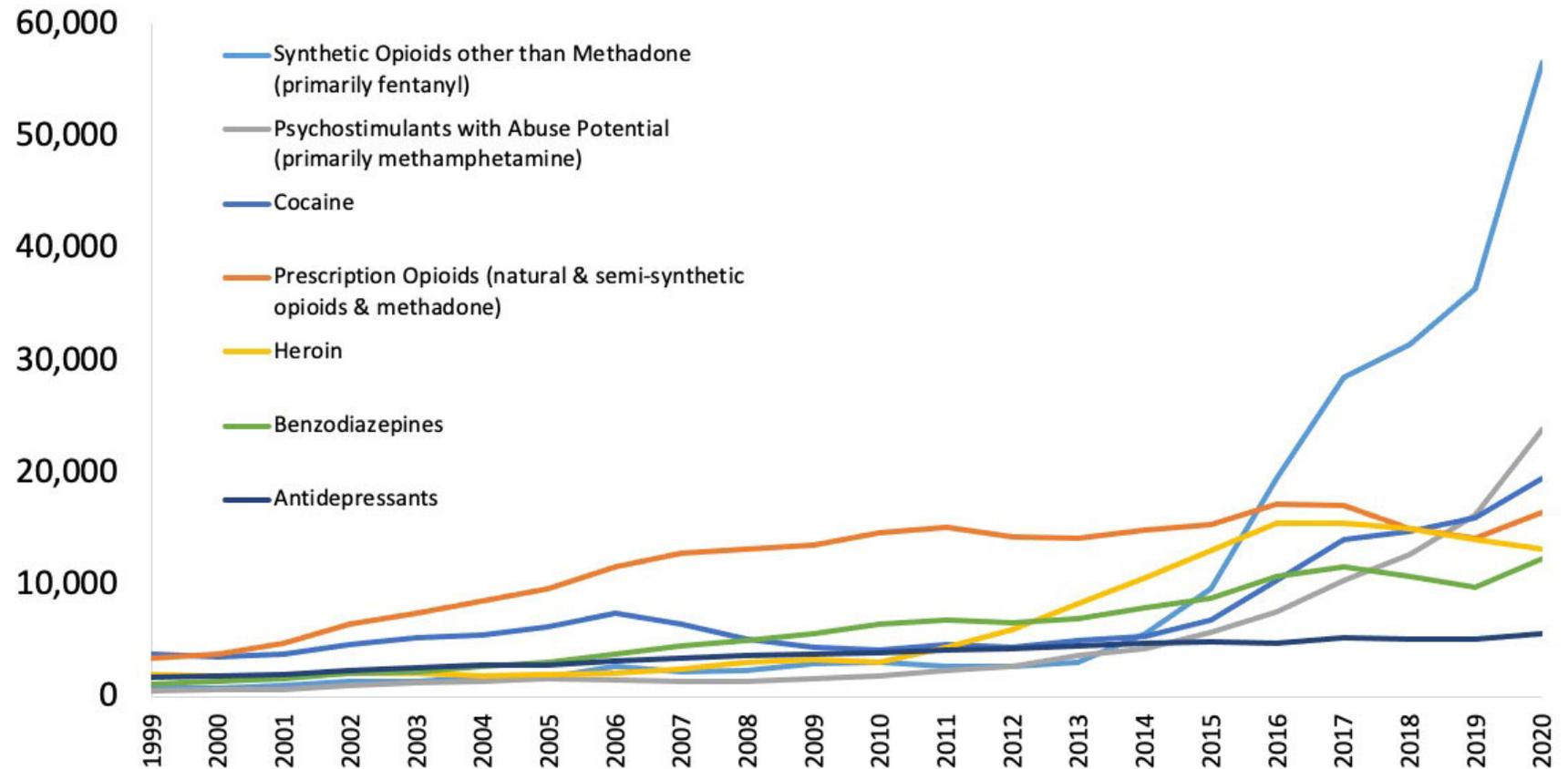
**Figure 1. National Drug-Involved Overdose Deaths*
Number Among All Ages, by Gender, 1999-2020**



*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 1999-2020 on CDC WONDER Online Database, released 12/2021.

Facts

Figure 2. National Drug-Involved Overdose Deaths*, Number Among All Ages, 1999-2020



*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 1999-2020 on CDC WONDER Online Database, released 12/2021.

Medication-Assisted Treatment

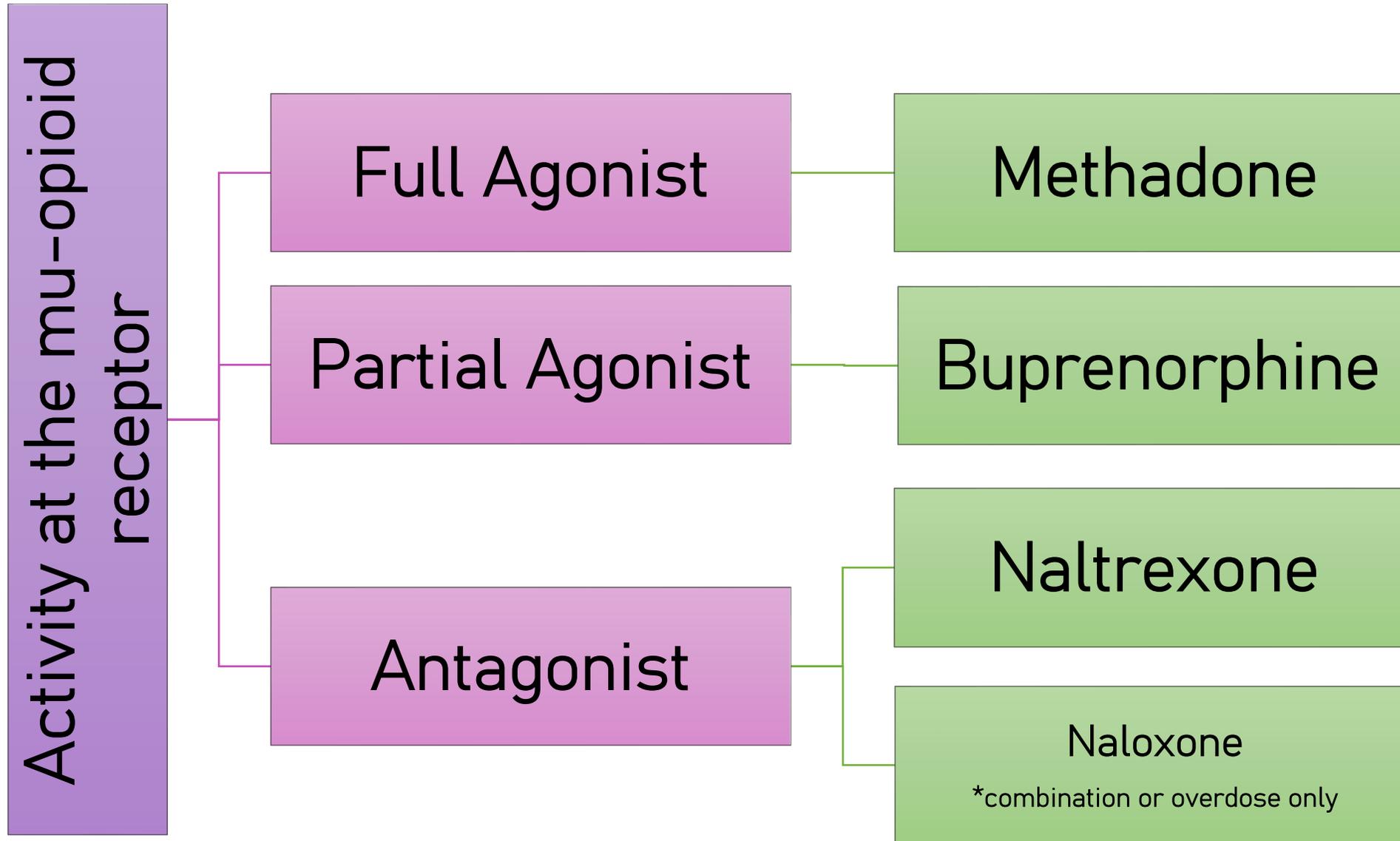
Also known as “MAT”

Use of medications, in combination with counseling and behavioral therapies, to provide a “whole-patient” approach to the treatment of substance use disorders



What medications are used to treat opioid use disorder?

MAT in Opioid Use Disorder



Methadone

Schedule II controlled substance, oral dosage form

Medically supervised withdrawal and maintenance

- Controls cravings and blunts euphoria from illicit opioids

Long-acting, usually 24-36 hours

- Wide individual variability in half-life (8 to 59 hours)
- Reaches steady state in about 5 days

Individualized dosing → begin low dose and gradually increase with daily monitoring over days to weeks

Therapeutic dose may be as high as 80-120 mg daily

Methadone

Common Adverse Effects

- Sweating
- Constipation
- Respiratory depression- especially with alcohol or benzodiazepines

Drug-Drug interactions

- With medications metabolized by CYP3A4, 2B6, 2C19
- Other medications that can cause respiratory depression

Cautions

- Prolonged QT interval
- Hepatic impairment- key role in metabolism
 - Start low and go slow
- Overdose can be fatal

Buprenorphine

Schedule III controlled substance

Requires a DATA 2000 waiver to prescribe for Opioid Use Disorder

Medically supervised withdrawal and maintenance

Initiate around 12-24 hours after last opioid or can precipitate withdrawal—typically follow Clinical Opiate Withdrawal Score (COWS)

Effective/maintenance dose is the dose that prevents withdrawal symptoms and cravings

Long elimination half-life (24 to 69 hours)

Buprenorphine

Common Adverse Effects

- Nausea, Vomiting, Dizziness, Constipation
- Peripheral edema, sedation
- Mild euphoria

Drug-Drug Interactions

- With CYP450 3A4 enzymes
- Other medications that can cause respiratory depression

Cautions

- Sedative effects (confusion, extreme sleepiness, breathing issues)
 - Especially with benzodiazepines, alcohol, other CNS depressants
- Severe liver impairment- monitor liver function
 - Combo product not recommended
 - Mono-product should reduce starting and titration dose by half

Naltrexone

ReVia® (50 mg oral tablets) or
Vivitrol® (380 mg extended-release intramuscular injection every 28 days)

- Antagonist
 - Reduces opioid cravings
 - No euphoria or sedative effects of opioids if patient were to take some

Prevention of relapse following medically supervised withdrawal

Not a control substance and not addictive

Patients need to be opioid free for at least 3–14 days before starting (depending on opioid used) or else may precipitate withdrawal

Naltrexone

Common Adverse Effects

- Oral: Nausea, vomiting, anxiety, insomnia, depression, anorexia
- Injection site reactions: pain, swelling, cellulitis, abscess, necrosis (rare, may need surgical intervention)

Drug-Drug Interactions

- Minimal

Cautions

- Risk of overdose
- Hepatotoxicity- increase in liver enzymes; monitor
 - Can cause hepatic injury; can cause further injury in patients with liver dysfunction
 - No dose adjustment with mild/moderate impairment
- Depression/ Suicidality- monitor for symptoms



A patient with Opioid Use Disorder is talking to you about treatment options. Their last use of IV heroin was this morning.



Barriers

Barriers - Overall

Stigma

Diversion/
Misuse

Medical
Complications

Induction onto
MAT

Patient Barriers

Acceptance

- Self-acceptance with having Opioid Use Disorder and desire for treatment
- Peer acceptance

Insurance coverage

Lack of mental health and social support

Missing appointments- work/childcare issues

Patient Barriers

Access to a provider

- 60.1% of rural counties in United States lack a physician with a DEA waiver to prescribe buprenorphine
- Research showed waived clinicians who were able to provide care prescribing at low rate for patient limit
- Methadone clinic daily

Access to medication

- 1 in 5 pharmacies unable/unwilling to fill buprenorphine prescription
- Difficult to find locations able to provide naltrexone injection

Transportation and travel time

- Must go to daily or weekly

Pharmacist Barriers

Distrust in provider,
pharmaceutical companies

- Opioid analgesic promotion
- Overprescribing due to incentives

Willingness to dispense
(especially buprenorphine)

Supply policies

- Monitoring for # threshold or “cap”

Lack of Education
and Training

Lack of confidence

Time

Prescriber Barriers

Insufficient:

- Training
- Education
- Experience
- Resources

Lack of Support

- Institutional
- Clinician peer support

Poor care coordination

- Lack of time
- Referral for counseling

Reimbursement

- Lifetime limits

Burdensome regulatory procedures

- Number of patients
- Waiver training course
- Record Keeping

What additional barriers have you come across when treating patients with OUD?

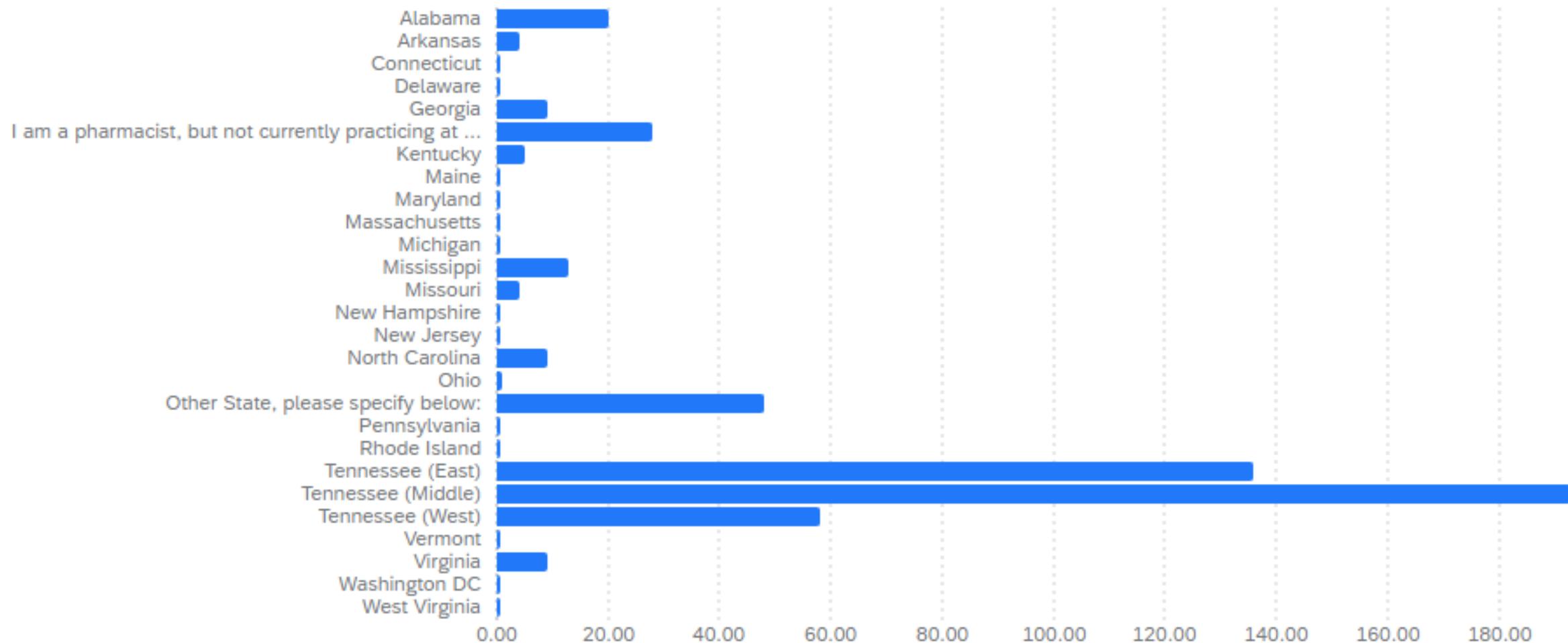
Study Preliminary Results

Frame TR, Clauson A, Hagan A. Surveyed in summer of 2019.

- 561 pharmacists consented to participate
- 480 finished survey completely
- 70% aged 18-44 years, 30% aged ≥ 45 years

- Objective of study: to gain a better understanding of pharmacists' perceptions and knowledge of dispensing buprenorphine/naloxone, naloxone and clean needles in practice.

Where are you currently practicing as a pharmacist? (Select all that apply) 480 ⓘ



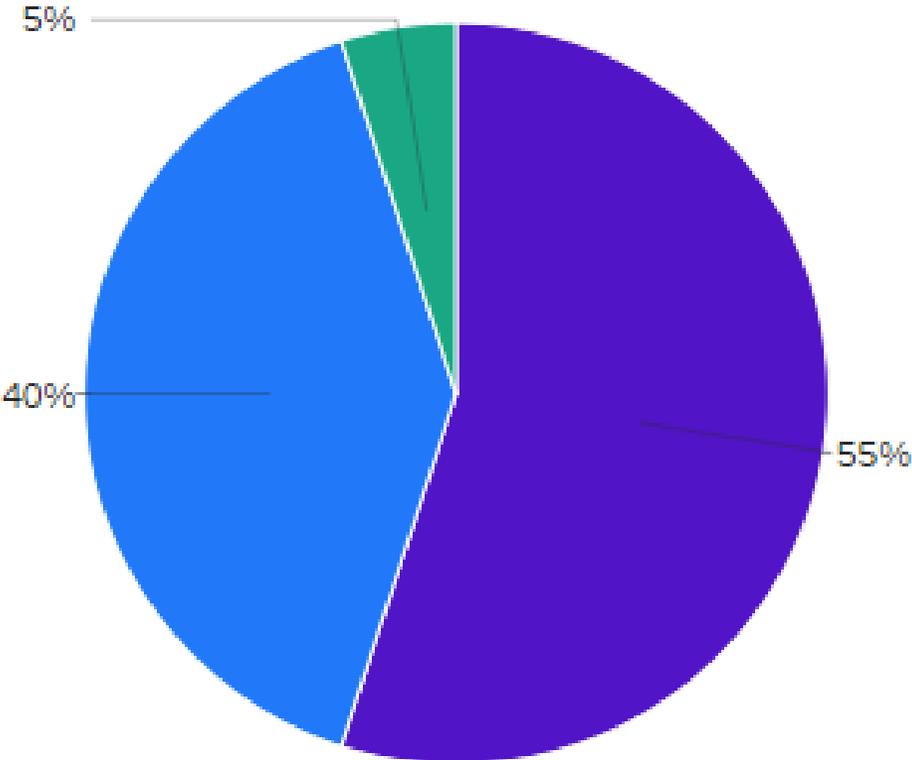
What best describes your practice site? 480 ⓘ



- Community Pharmacy- Independent
- Community Pharmacy- Large Corporation/Chain (i.e. CVS Corporation, Walgreens, Walmart, Rite Aid, Kroger Inc and A...
- Community Pharmacy- Small Corporation/Chain (i.e. Winn-Dixie, Publix, Fred's, etc.)
- Hospital Pharmacy- Outpatient/Ambulatory Care
- Hospital Pharmacy- Inpatient Pharmacy
- Other Patient Care Practice, please specify below:
- Other Non-Patient Care Practice, please specify below:

Do you personally feel addiction or substance use disorder is a disease or a choice?

480

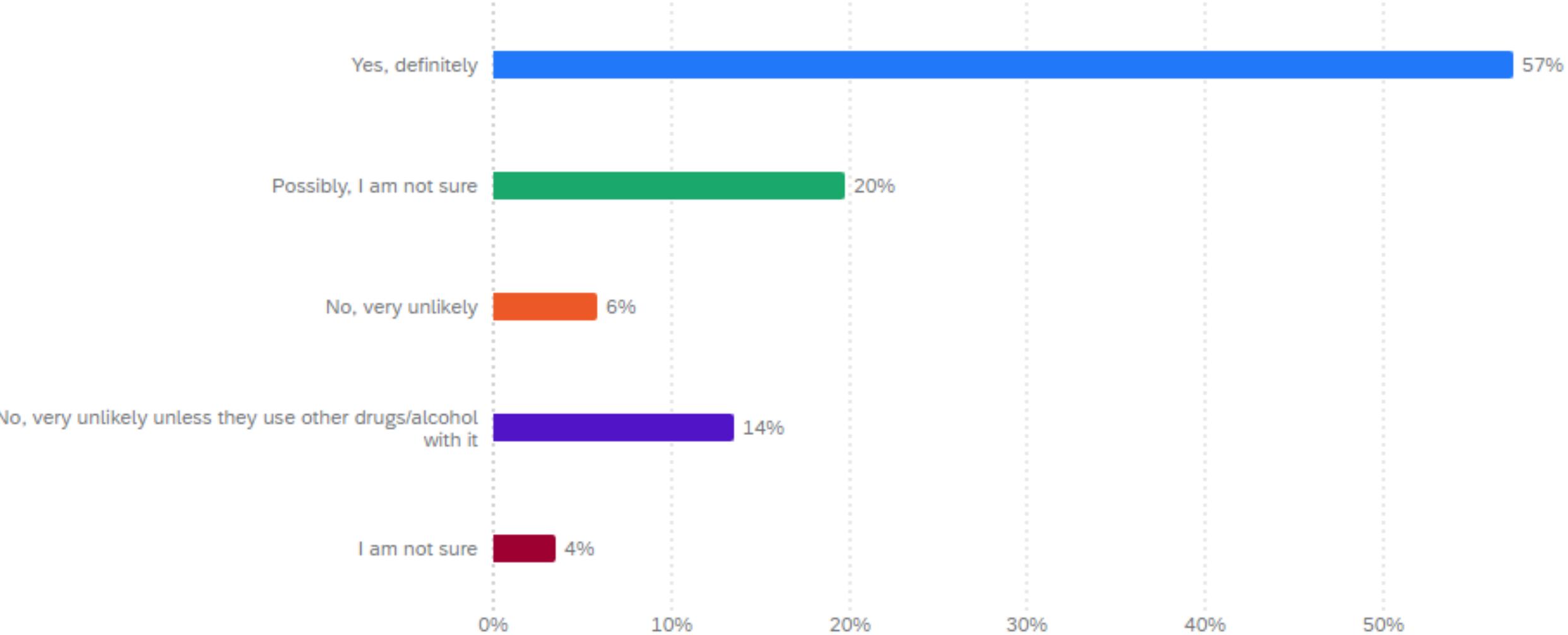


■ Choice the first time, but then turns into a disease ■ Disease ■ Choice

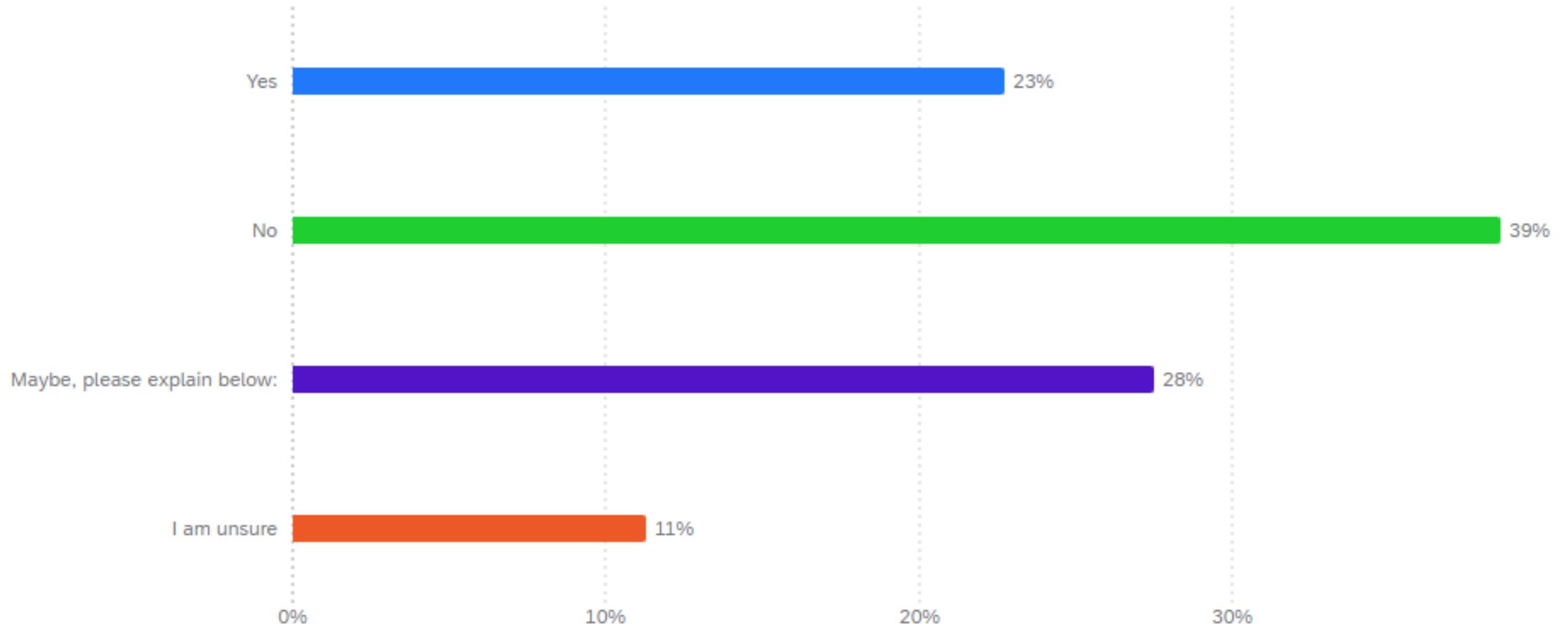
What is the mechanism of action for buprenorphine? 480 ⓘ

Q39 - What is the mechanism of action for buprenorphine?	Count ▼
I am unsure	5%
Opioid full agonist	6%
Opioid antagonist	9%
Opioid partial agonist	80%

Is it possible for someone to overdose with bupenorphine containing products? 480 ⓘ



Do you feel that giving buprenorphine/naloxone to patients perpetuates their addiction? 480 ⓘ



When dispensing a new opioid prescription for a patient, do you feel it is appropriate as a pharmacist to discuss the addiction potential of these medications with the patient?



Response	Percentage	Count
Yes	92%	440
No	8%	36

When dispensing a new opioid prescription for a patient, do you discuss the addiction potential of these medications with the patient at least 90% of the time?



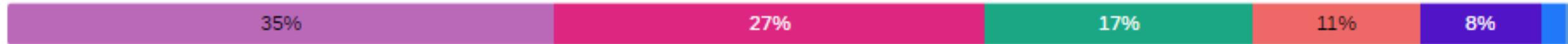
Response	Percentage	Count
Yes	50%	220
No	50%	220

When you do talk to patients, what do you discuss? (select all that apply) 220 ⓘ



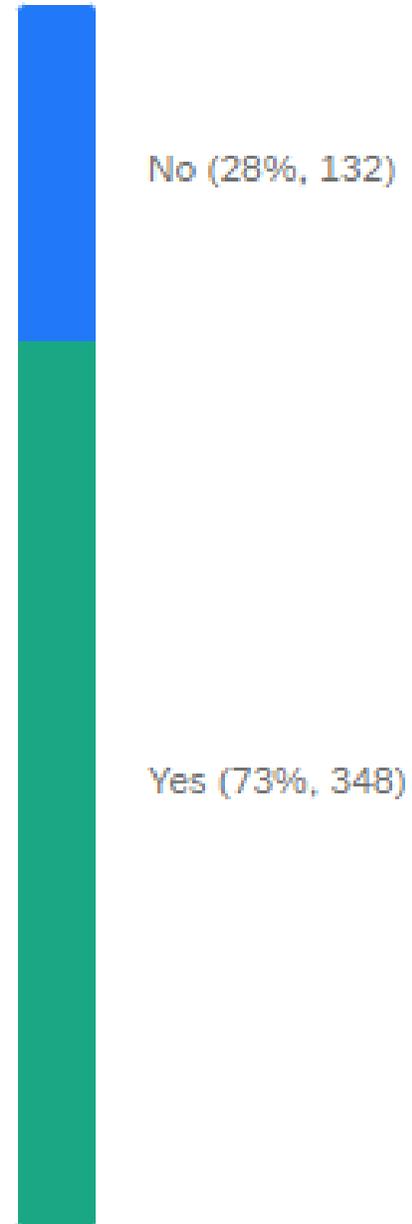
- Overuse risk
- Long-term use risk
- Personal history of substance use disorder
- Family history of substance use disorder
- Prior rehabilitation for any type of drug or alcohol
- Personal medical history of mental health conditions
- Currently living/involved in a stressful circumstance
- Other, please specify below:

What are the reasons you do not discuss the addiction potential of opioids? (select all that apply) 260 ⓘ



- Other, please specify below:
- I do not want patients to think that I am judging them
- The provider should have already talked to patients about this
- I am afraid of the patient's reaction
- It makes me nervous to talk to patients about this
- Feel it is not my job to discuss this with a patient
- I do not fully understand the addiction potential of opioids

Have you ever talked to a patient that you feel is misusing or abusing their opioid prescription (calling in for refills early, losing their medication, etc.) about concerns you may have?



Pharmacy Stocking and Dispensing Questions

Does your pharmacy routinely stock buprenorphine/naloxone? 480 ⓘ



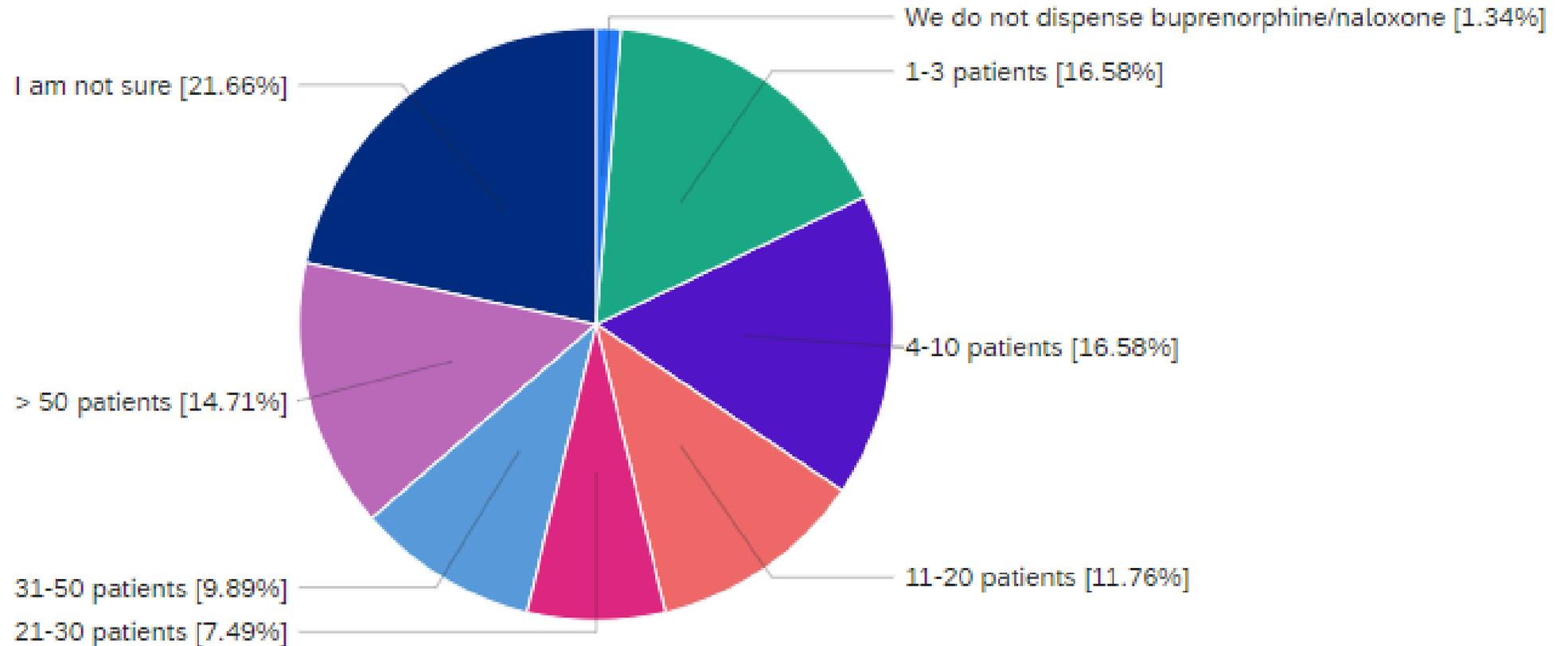
■ Yes ■ No ■ I am unsure

How often does the pharmacy you work in (the majority of the time) dispense buprenorphine/naloxone? 480 ⓘ



■ I am not sure ■ We do not dispense buprenorphine/naloxone ■ Less than once a month ■ Between once a month and every two weeks
■ Between every two weeks and weekly ■ Weekly ■ Between weekly and daily ■ Daily ■ More than once a day

How many different patients receive buprenorphine/ naloxone in a month from the pharmacy you work at the majority of the time? (374)



Personally, have you ever refused to fill or denied a prescription for buprenorphine/naloxone? 480 ⓘ



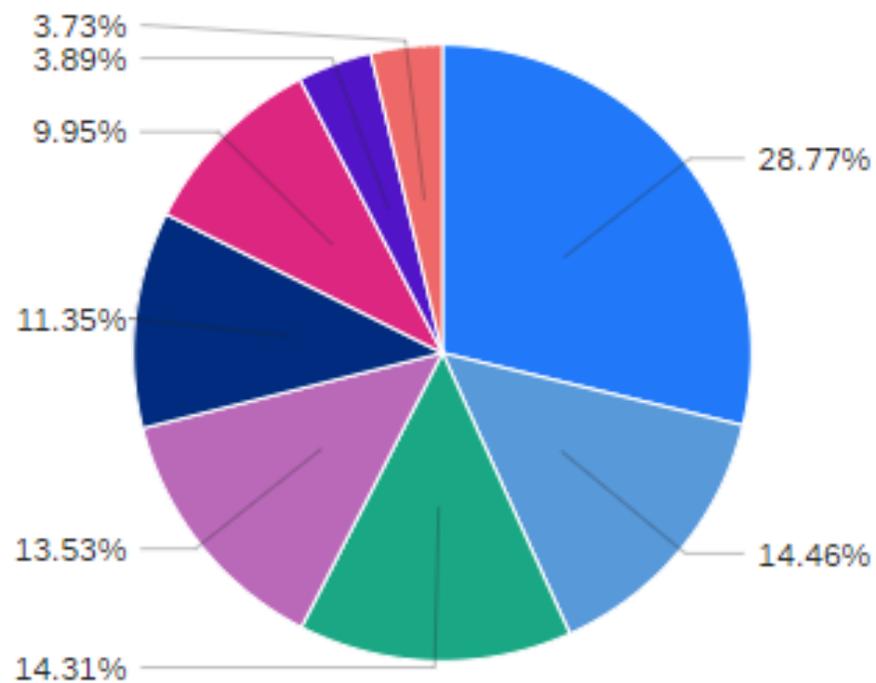
When you refuse a buprenorphine/naloxone containing prescription, do you routinely refer those patients to another pharmacy? (242)



■ Yes ■ No ■ Other, please specify below:

What were reasons as to why you refused to fill/denied the prescriptions? (Please select your top three reasons)

242



- It was too soon to fill
- Don't fill from out of state
- It was out of stock
- Don't fill from specific providers
- Other, please specify below:
- I didn't know the patient
- Patient looked disreputable
- Patient had a history of substance abuse



What is/are your major concern(s) or issue(s) with providing buprenorphine/naloxone to patients? (Please select your top three concerns) (242)



- Selling it on the streets
- Feel that the patient is not being taken care of properly by the provider (patient not being tapered down by prov...
- Perpetuating addiction
- Risk of abuse
- I know the prescribing provider is misusing their prescribing rights
- Insurance problems
- Risk of overdose
- I have no concern or issue
- Other, please specify below:



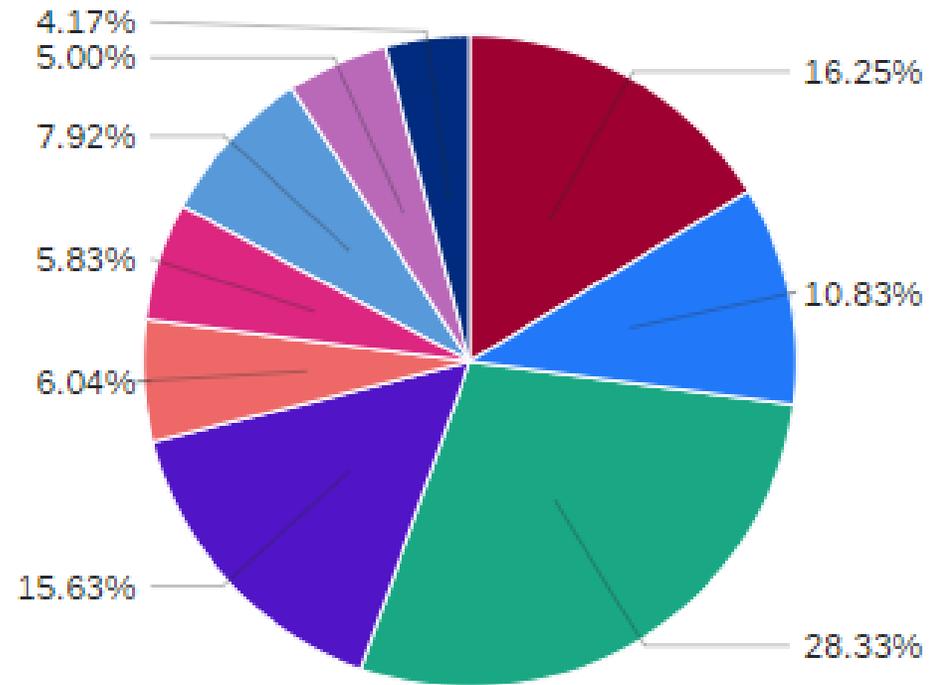
Have you ever visited a provider's office that takes care of substance use patients (that dispenses medications used for opioid use disorder or other substance use) or offered to have he/she come visit your pharmacy to foster a collaborative relationship?



Have you ever visited a substance use rehabilitation facility or offered to have someone from their organization visit your pharmacy to foster a collaborative relationship?

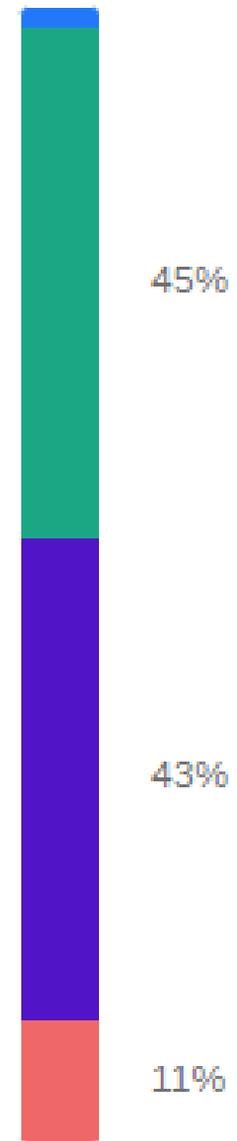


How often does the pharmacy you work in (the majority of the time) dispense naloxone? 480 ⓘ



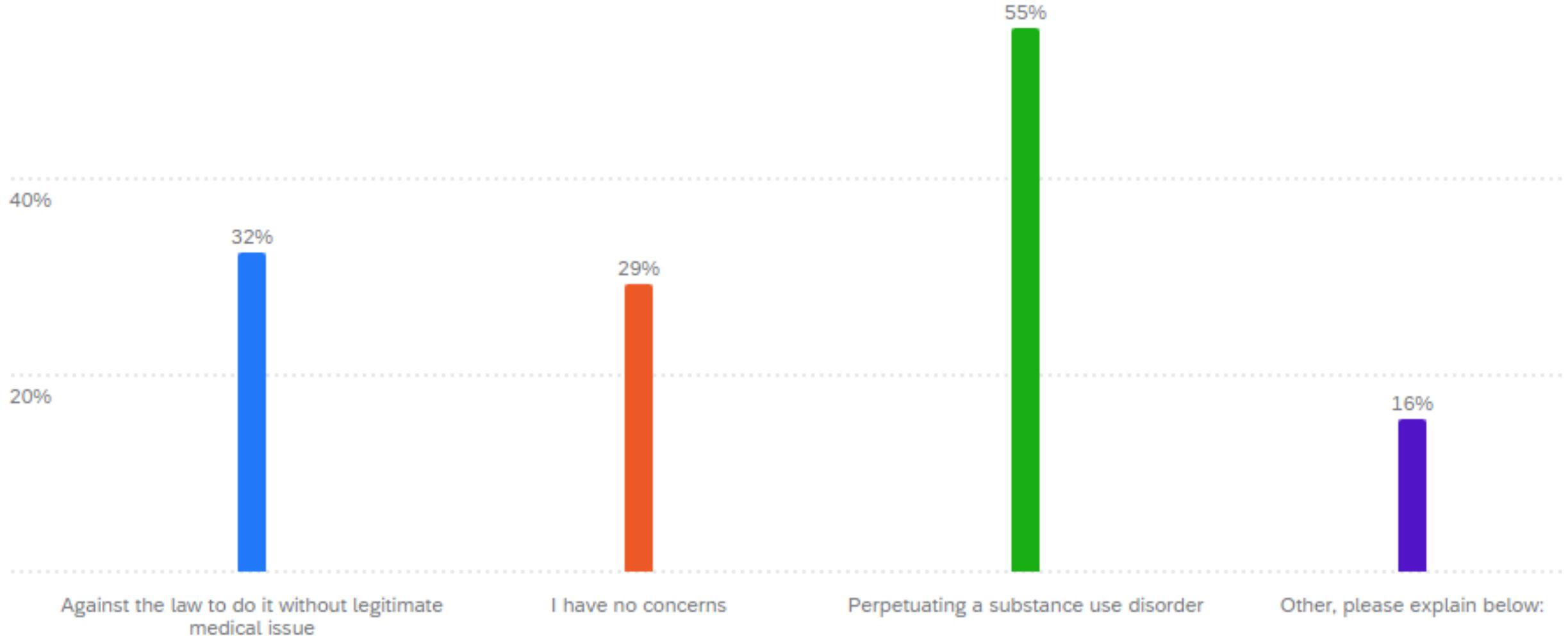
■ I am not sure ■ We do not dispense naloxone ■ Less than once a month ■ Between once a month and every two weeks
■ Between every two weeks and weekly ■ Weekly ■ Between weekly and daily ■ Daily ■ More than once a day

Does your pharmacy allow selling of syringes and/or needles without a prescription? 480



■ Yes, for free ■ Yes, at a cost ■ No ■ I am not sure

Which of the following major concerns (if any) do you have about providing syringes and/or needles? (Please sel... ⓘ)





In what ways have you potentially been a roadblock to patients with substance use disorder?

In what ways have you been an advocate for patients with substance use disorder?

Redemptive Mindset

- Choice vs Disease
- EDUCATION
- Counseling
- Collaboration
- Decreasing Fear
- Assess your own Bias
- Having a Gospel-Centric Approach

Choice vs Disease

- The National Institute on Drug Abuse (NIDA), the Substance Abuse and Mental Health Services Administration (SAMHSA), and the National Institutes of Health (NIH) describe addiction as:

“A long-term and relapsing condition characterized by the individual compulsively seeking and using drugs despite adverse consequences”

Caused by a combination of behavioral, psychological, environmental and biological factors

Genetic risk factors: estimate 23-54% hereditary for opioid use disorder based on twin and family studies

Brain disorder

- Brain imaging studies of people with addiction show physical changes in areas of the brain that are critical to judgment, decision-making, learning and memory, and behavior control

The changes are long-term and can continue long after the person has stopped using drugs

Risk and Protective Factors for Drug Use, Misuse, and Addiction

Risk Factors

- Aggressive behavior in childhood
- Lack of parental supervision
- Low peer refusal skills
- Drug experimentation/ availability of drugs at school
- Community poverty
- Genetic

Protective Factors

- Self-efficacy (belief in self-control)
- Parental monitoring and support
- Positive relationships
- Extracurricular activities
- School anti-drug policies
- Neighborhood resources

Choice vs Disease

- Initial decision typically voluntary
- If viewed as a choice:
 - Self-acquired, the person gave to themselves
 - Increased guilt, shame on patient
- If viewed as a disease:
 - Take burden off patient by understanding the change in brain
 - Realize stopping cold turkey typically never works
 - Treatable illness like diabetes, hypertension
 - Some people look at patients as if they are holding onto an excuse

Education

- Pertinent to have knowledge on:
 - Mechanism of action
 - How medications work in treatment
 - Side effects
 - Potential for overdose
 - Possibility of misuse

Potential for overdose

Buprenorphine

Possibility when using other CNS depressants, especially benzodiazepines

- Increased risk of respiratory and cardiovascular collapse
- Signs and symptoms of overdose
 - Confusion, dizziness, pinpoint pupils, hallucinations, hypotension, respiratory depression, seizures, coma
- Requires naloxone bolus of 2–3 mg followed by continuous infusion of 4 mg/hour
 - See full reversal within 40–60 minutes

Naltrexone

Possibility when trying to overcome blockade, at the end of a dosing interval, after missing a dose, after discontinuation

All

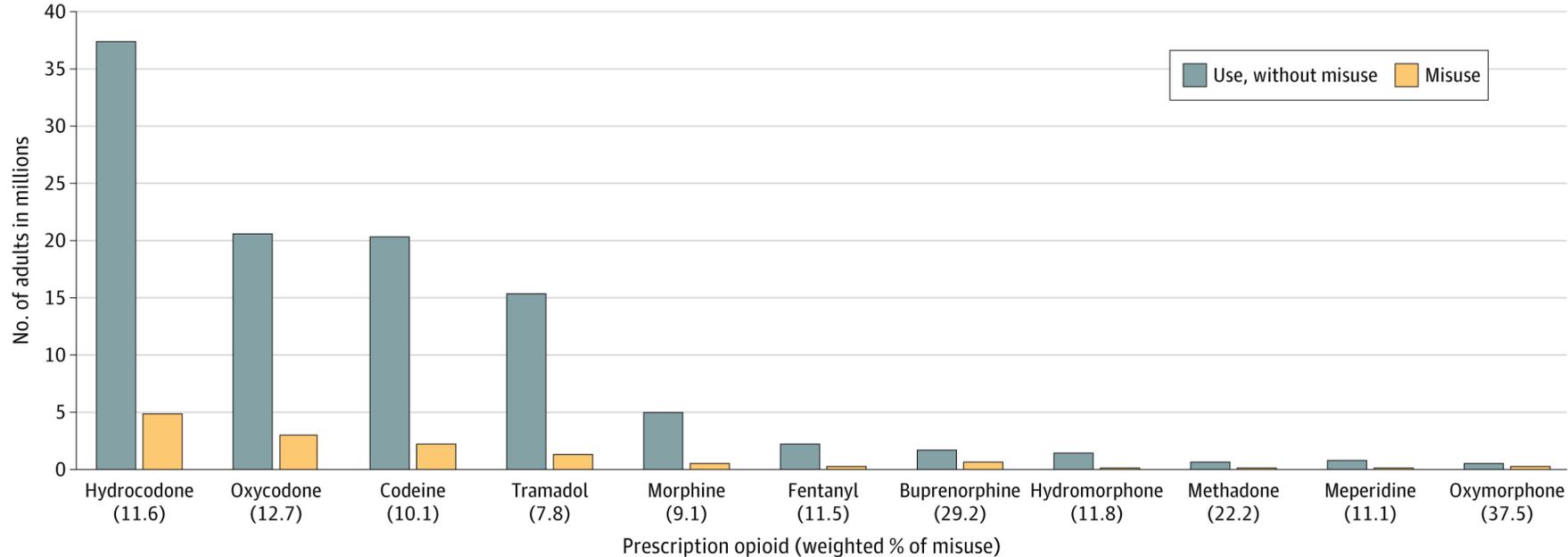
Meta-analysis of 30 cohort studies

- Patients who discontinued medication (buprenorphine, methadone, or long-acting implant naltrexone)
 - Higher risk of all-cause death (relative risk 2.33 [95% CI 2.02–2.67]) and overdose death (3.09 [95% CI 2.37–4.01]) than patients receiving medication

Possibility of misuse

- Recent study in JAMA 2021: Trends in and Characteristics of Buprenorphine Misuse among Adults in the US
- Used nationally representative data on past-year Rx opioid use, misuse, OUD and motivations
- From 2015-2019 National Survey on Drug use and Health
- 214,505 respondents

Figure 1. US Adults Who Reported Using or Misusing Prescription Opioids in the Past 12 Months (2019 Survey, 42739 respondents)



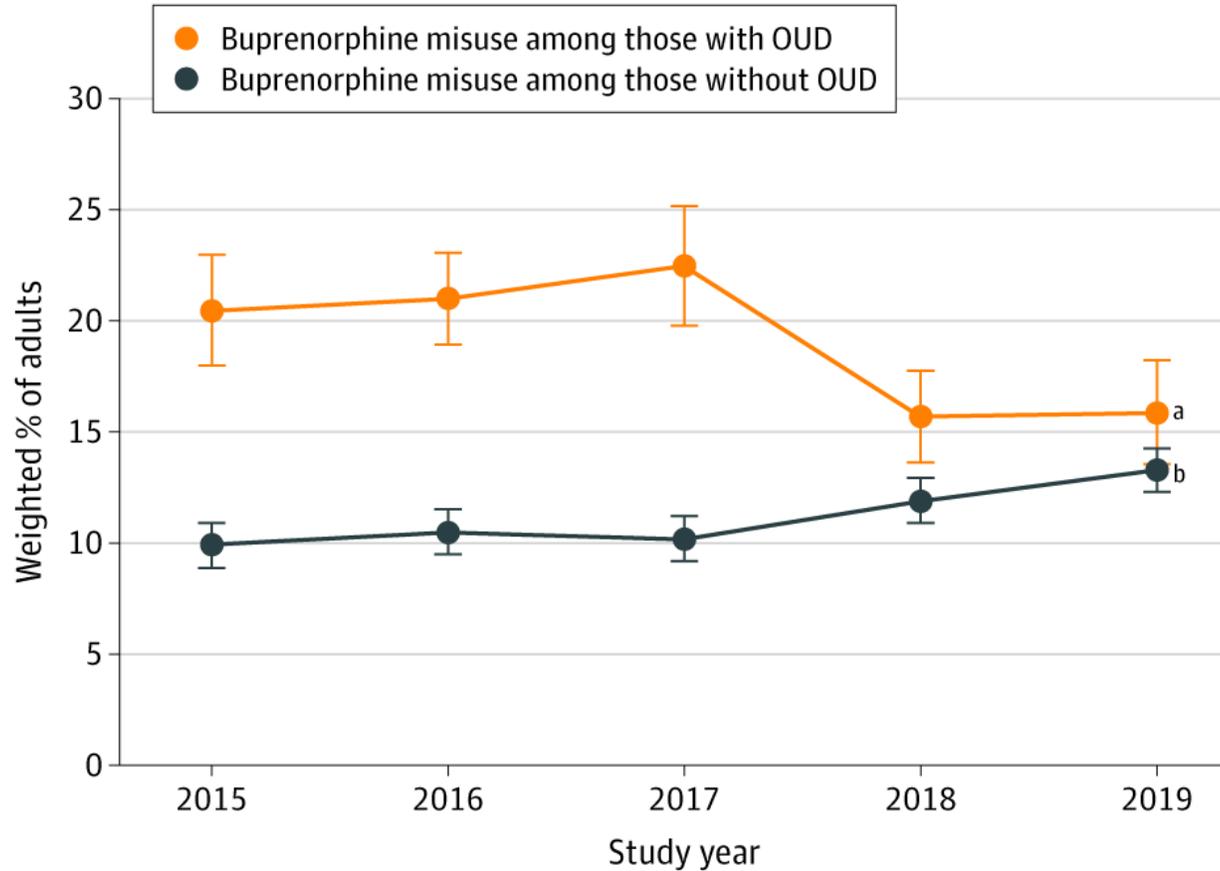


Figure Legend:

Trends in Prevalence of Past-Year Buprenorphine Misuse by Opioid Use Disorder (OUD) Status Among US Adults With Past-Year Buprenorphine Use

Data are from 2536 respondents in the 2015–2019 National Surveys on Drug Use and Health. Error bars indicate SEs.

^aLinear trend: P = .04.

^bLinear trend: P = .08.

Misuse Factors

Factors associated with misuse:

With OUD diagnosis:

- Age 24-34 and 35-49
- Residing in non-metropolitan areas
- Having past-year polysubstance use and use disorders (past-year Rx stimulant use disorder)

Without OUD diagnosis:

- 24-34 years old
- Past-year family income of <\$20,000
- Having a suicide plan
- Polysubstance use and use disorders (for example- past-year cocaine use disorder)

Negatively associated with misuse:

With OUD diagnosis:

- Past-year treatment for illicit drug use-only treatment

Without OUD diagnosis:

- Drug use-only treatment

Table 1. Differences in Main Motivation Between the Most Recent Buprenorphine Misuse and Nonbuprenorphine Prescription Opioid Misuse by Past-Year Buprenorphine Misuse and OUD Status

Main motivation for misuse	OUD status, weighted % (95% CI) ^a			
	OUD		No OUD	
	Nonbuprenorphine prescription misuse (n = 1382)	Buprenorphine misuse (n = 233)	Nonbuprenorphine prescription misuse (n = 7898)	Buprenorphine misuse (n = 213)
Relieve physical pain	52.2 (47.6-56.8) ^b	20.5 (14.0-29.0) ^{b,c}	66.6 (65.0-68.2) ^c	29.3 (21.2-39.1) ^{b,c}
Relax or relieve tension	8.9 (7.0-11.1)	3.7 (1.6-8.3) ^{b,c}	10.5 (9.4-11.7)	6.8 (3.2-14.0)
Experiment	1.4 (0.7-2.7)	1.6 (0.5-5.4)	2.4 (2.1-2.8)	8.5 (4.9-14.3) ^{b,c}
Feel good or get high	17.1 (14.4-20.2) ^b	9.4 (5.9-14.6) ^c	10.3 (9.4-11.3) ^c	18.1 (11.5-27.4) ^b
Help with my feelings or emotions	6.3 (4.8-8.2) ^b	8.2 (3.4-18.6) ^{b,d}	2.6 (2.1-3.2) ^c	11.7 (5.8-22.2) ^{b,d}
Increase/decrease effect(s) of other drugs	1.2 (0.3-4.4) ^d	15.1 (9.5-23.1) ^{b,c}	0.5 (0.3-0.8)	3.6 (2.2-5.9) ^b
Because I am hooked	7.8 (6.2-9.9) ^b	27.3 (21.6-33.8) ^{b,c}	0.2 (0.1-0.3) ^c	12.7 (7.3-21.2) ^b

Abbreviation: OUD, opioid use disorder.

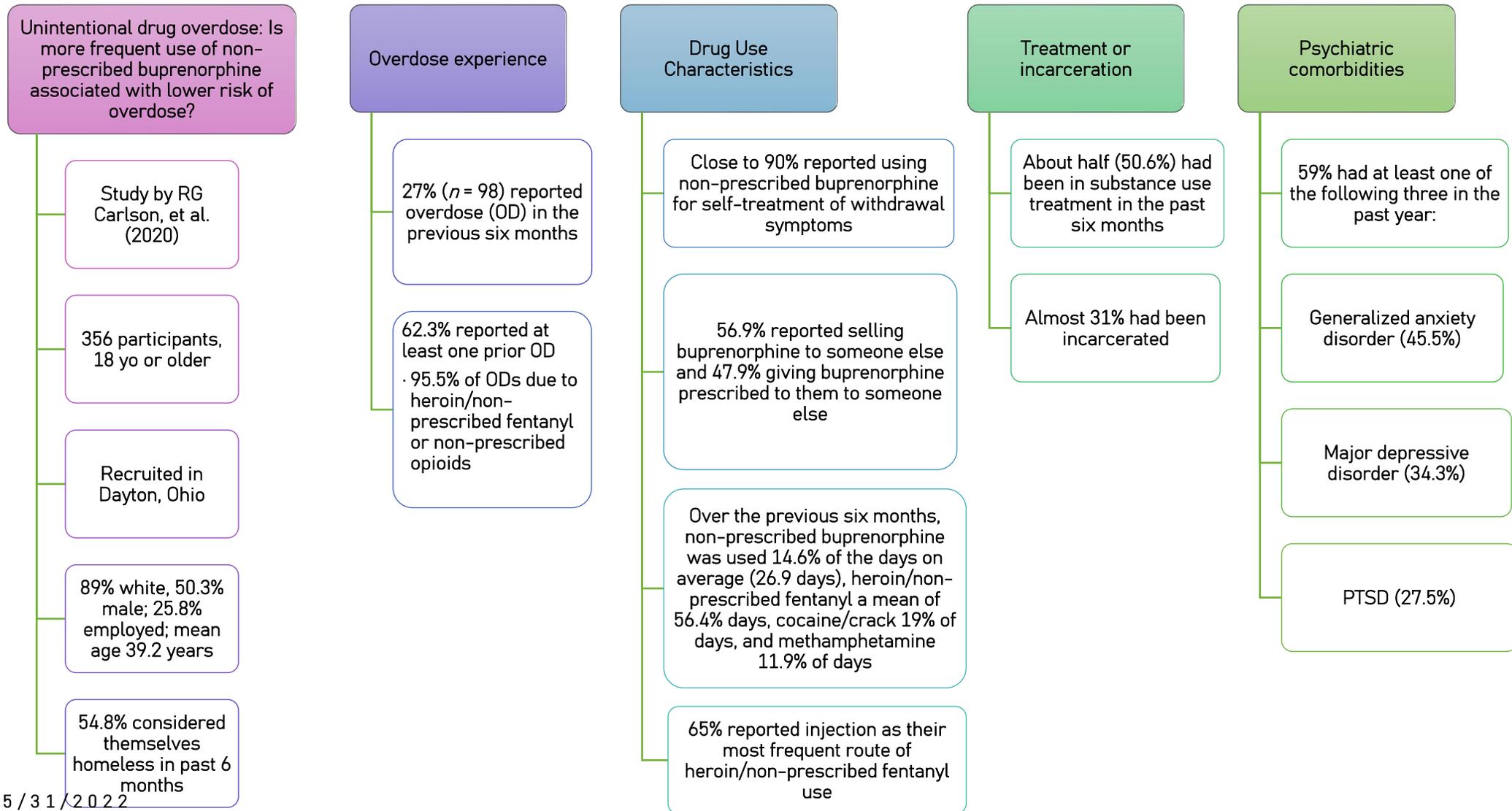
^a Data are from 9726 respondents in the 2015-2019 National Surveys on Drug Use and Health.

^b This estimate is statistically significantly ($P < .05$) different from the estimate of the corresponding adults with nonbuprenorphine prescription opioid misuse but no OUD (within each row).

^c This estimate is statistically significantly ($P < .05$) different from the estimate of the corresponding adults with nonbuprenorphine opioid misuse and with OUD (within each row).

^d Interpret with caution owing to low statistical precision.

Buprenorphine Diversion- Limited Harm?



Buprenorphine Diversion- Limited Harm?

Results:

Higher mean percentage of days of non-prescribed buprenorphine use in past six months significantly associated with:

- Decreased risk of overdose (OD) in past 6 months in both unadjusted and adjusted analyses (AOR = 0.81, 95% CI = 0.66, 0.98; $p = .0286$)

Secondary analyses showed

Individuals who used non-prescribed buprenorphine for more than 5.4% of days (10) had 33% lower odds of OD

Taking buprenorphine for 2-3 days out of 6 months reduced odds of OD by 20% compared to just 1 day

Linear trend showed more buprenorphine use resulted in greater reduction in odds of OD

Greater frequency of use of non prescribed buprenorphine is strongly associated with lower frequency of use of heroin/fentanyl

Lower frequency of use of heroin/fentanyl is strongly associated with lower risk of overdose

Patient Counseling

Genetics

- Estimates of 23-54% hereditary for opioid use disorder based on twin and family studies

Risk for overdose

- Depending on medication

Engagement in meetings

- Narcotics Anonymous
- Heroin Anonymous

Engagement with sponsor/support

Collaboration

Know your providers who work with substance use disorders

Know your treatment centers near your pharmacy

Collaborate with clinics and providers

- Study by Wu, et al- 2021
 - 3 buprenorphine treatment clinics & 3 community pharmacists
 - 88.7% treatment retention and 95.3% adherence at end of study

Be involved

- Help increase access for patients
- Patient education
- Adoption of legislation
- Volunteer!

Decreasing Fear

Empathy,
compassion and
respect

Using non-
stigmatizing
language

Non-verbal
communication
skills

Verbal
communication
skills

Asking the hard
questions

Realizing it's okay
if someone gets
upset; little risk

You could be the
only one who
cares

Develop a store
policy

Giving clean
needles does not
perpetuate
addiction

Assess your own bias

Know yourself and your own history with addiction or member of addiction community

Educate yourself on addiction

Be aware of your role as a professional and how you carry yourself → don't abuse that power

Stay alert to what informs your opinions (media, friends, family...)

Have humility

Having a Gospel-centric approach

Realize trauma may be part of their story

Connection between trauma and addiction- Adverse Childhood Experiences

Compassion

Inform your way of communication

Identify what you are responsible for

Can not shield them from natural consequences

Professional intervention

Setting boundaries

Accepting them as they are

We all are made in the image of God

We all have an invitation from Jesus

Restorative power in Jesus's healing, even if they fail

Having a Gospel-centric approach

Invite them into your community

- Church, Homes, I.D. Recovery/ Celebrate Recovery

Prayer → constantly:

- Your motives are loving and glorifying to God, for good discernment, for desires of their heart to change and lead to repentance

What if Christ were wearing the white coat?

Romans 2:1-4



In what other ways might you have more of a redemptive mindset towards patients with opioid use disorder?

Let's pause and reflect and plan together!

Think about the answer you provided to the roadblocks you have potentially caused for your patients, what steps can you take to increase your knowledge and empathy towards patients struggling with opioid use disorder?

Questions?

References

1. Overdose Death Rates. National Institutes of Health. Published January 20, 2022. Accessed April 20, 2022. <https://nida.nih.gov/drug-topics/trends-statistics/overdose-death-rates>
2. Tip 63: Medications for Opioid Use Disorder. SAMHSA. 2021. <https://store.samhsa.gov/product/TIP-63-Medications-for-Opioid-Use-Disorder-Full-Document/PEP20-02-01-006>
3. Li R, Leffers P, Doering PL. Substance Use Disorders I: Depressants, Stimulants, and Hallucinogens. In: DiPiro JT, Yee GC, Posey L, Haines ST, Nolin TD, Ellingrod V. eds. *Pharmacotherapy: A Pathophysiologic Approach, 11e*. McGraw-Hill; Accessed May 1, 2022. <https://accesspharmacy-mhmedical-com.bunchproxy.idm.oclc.org/content.aspx?bookid=2577§ionid=231921773>
4. Kumar R, Viswanath O, Saadabadi A. Buprenorphine. National Library of Medicine StatPearls. Updated August 6, 2021. Accessed May 3, 2022. <https://www.ncbi.nlm.nih.gov/books/NBK459126/>
5. Barriers to Broader Use of Medications to Treat Opioid Use Disorder. *National Academies of Sciences, Engineering, and Medicine; Health and Medicine Division; Board on Health Sciences Policy; Committee on Medication-Assisted Treatment for Opioid Use Disorder*. Published March 2019. Accessed May 12, 2022. <https://www.ncbi.nlm.nih.gov/books/NBK541389/>
6. Wright N, D'Agnone O, Krajci, et al. Addressing misuse and diversion of opioid substitution medication: guidance based on systematic evidence review and real-world experience. *J Public Health*. 2016; 38(3):e368-374.
7. What is the treatment need versus the diversion risk for opioid use disorder treatment? *NIDA*. 2021. Published December 2021. Accessed April 20, 2022. <https://www.drugabuse.gov/publications/research-reports/medications-to-treat-opioid-addiction/what-treatment-need-versus-diversion-risk-opioid-use-disorder-treatment>.
8. Cooper HLF, Cloud DH, Young AM, Freeman PR. When prescribing isn't enough—pharmacy-level barriers to buprenorphine access. *N Engl J Med*. 2020;383(8):703-705.
9. Cooper HL, Cloud DH, Freeman PR, et al. Buprenorphine dispensing in an epicenter of the U.S. opioid epidemic: a case study of the rural risk environment in Appalachian Kentucky. *Int J Drug Policy*. 2020;85: 102701.
10. Hagemeyer NE, Murawski MM, Lopez NC, Alamian A, Pack RP. Theoretical exploration of Tennessee community pharmacists' perceptions regarding opioid pain reliever abuse communication. *Res Social Adm Pharm*. 2014;10:562-75.
11. What is Addiction?: Causes, Risk Factors and Models. American Addiction Centers. Updated January 31, 2022. Accessed April 20, 2022. <https://americanaddictioncenters.org/rehab-guide/is-drug-addiction-a-disease>
12. Drugs, Brain, and Behavior: The Science of Addiction. National Institute on Drug Abuse. Updated June 2020. Accessed April 28, 2022. <https://nida.nih.gov/sites/default/files/soa.pdf>
13. Jain, P., McKinnell, K., Marino, R. et al. Evaluation of Opioid Overdose Reports in Patients Treated with Extended-Release Naltrexone: Postmarketing Data from 2006 to 2018. *Drug Saf*. 2021;44:351–359 (2021).
14. Kelty E, Hulse G. Examination of mortality rates in a retrospective cohort of patients treated with oral or implant naltrexone for problematic opiate use. *Addiction*. 2012;107:1817–24.
15. Han B, Jones CM, Einstein EB, Compton WM. Trends in and Characteristics of buprenorphine misuse among adults in the US. *JAMA Netw Open*. 2021;4(10):e2129409. doi:10.1001/jamanetworkopen.2021.29409
16. Carlson RG, Daniulaityte R, Silverstein SM, Nahhas RW, Martins SS. Unintentional drug overdose: is more frequent use of non-prescribed buprenorphine associated with lower risk of overdose?. *Int J Drug Policy*. 2020;79:102722.
17. Crist RC, Reiner BC, Berrettini WH. A review of opioid addiction genetics. *Curr Opin Psychol*. 2019;27:31-35. doi:10.1016/j.copsyc.2018.07.014
18. Wu LT, John W, Ghitza UE, et al. Buprenorphine physician-pharmacist collaboration in the management of patients with opioid use disorder: results from a multisite study of the National Drug Abuse Treatment Clinical Trials Network. *Addiction*. Published online January 11, 2021. 10.1111/add.15353.
19. Bach P, Hartung D. Leveraging the role of community pharmacists in the prevention, surveillance, and treatment of opioid use disorders. *Addict Sci Clin Pract*. 2019;14(1):30.
20. The Role of Adverse Childhood Experiences in Substance Misuse and Related Behavioral Health Problems. SAMHSA. Published June 2018. Accessed May 17, 2022. <https://mnprc.org/wp-content/uploads/2019/01/aces-behavioral-health-problems.pdf>.