

Comorbidity in Opioid Use Disorder: Depression, Pain

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Today's talk

- Review the role of comorbidity in the treatment of opioid use disorder: pain and depression
- Data from the U.S. multi-site Prescription Opioid Addiction Treatment Study and ongoing research at McLean Hospital/Harvard Medical School

Prescription Opioid Addiction Treatment Study (POATS)

- Compared treatments for prescription opioid dependence, using
 - buprenorphine-naloxone (bup-nx) of varying durations
 - counseling of varying intensities
- Conducted as part of National Institute on Drug Abuse Clinical Trials Network
- 10 participating sites across the U.S.
- Largest study ever conducted for prescription opioid dependence (N=653)
- Included a 3.5-year naturalistic follow-up study

**Comorbidity of opioid use
disorder and pain: data
from main trial of POATS**

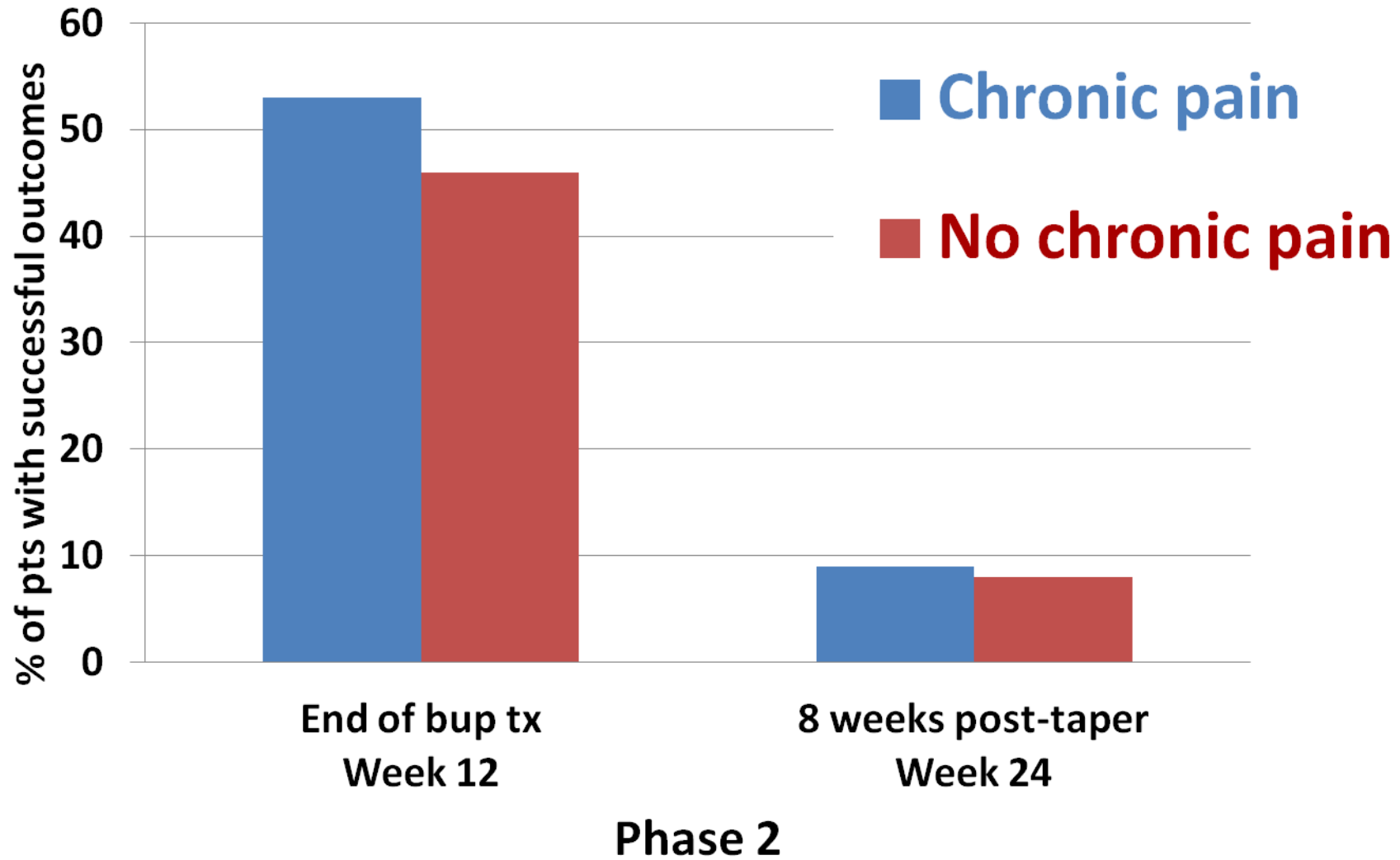
Chronic pain in POATS Patients

- Defined as pain other than every day aches and pains, not counting withdrawal pain, for >3 months
- Assessed with the Brief Pain Inventory
- 42% of patients in POATS met this criterion

Primary reason for use in chronic pain patients, past & present

- 1^o reason for **1st use**
 - Pain 83%
 - Get high 13%
- 1^o reason for **current use**
if 1st reason was pain
 - Avoid withdrawal 56%
 - Pain 23%
 - Get high 14%

Did presence of chronic pain at study entry (42%) predict successful outcome on bup-nx at 3 months?



Did pain **severity** increase **near-term** opioid use?

- Pain severity in CP patients in a given week increased likelihood of opioid use in the next week, adjusted for covariates
- Every 1-point increase in pain severity → 15% greater likelihood of next-week use
- Change in category (e.g., mild to moderate pain) → 32% increase in odds of next-week use

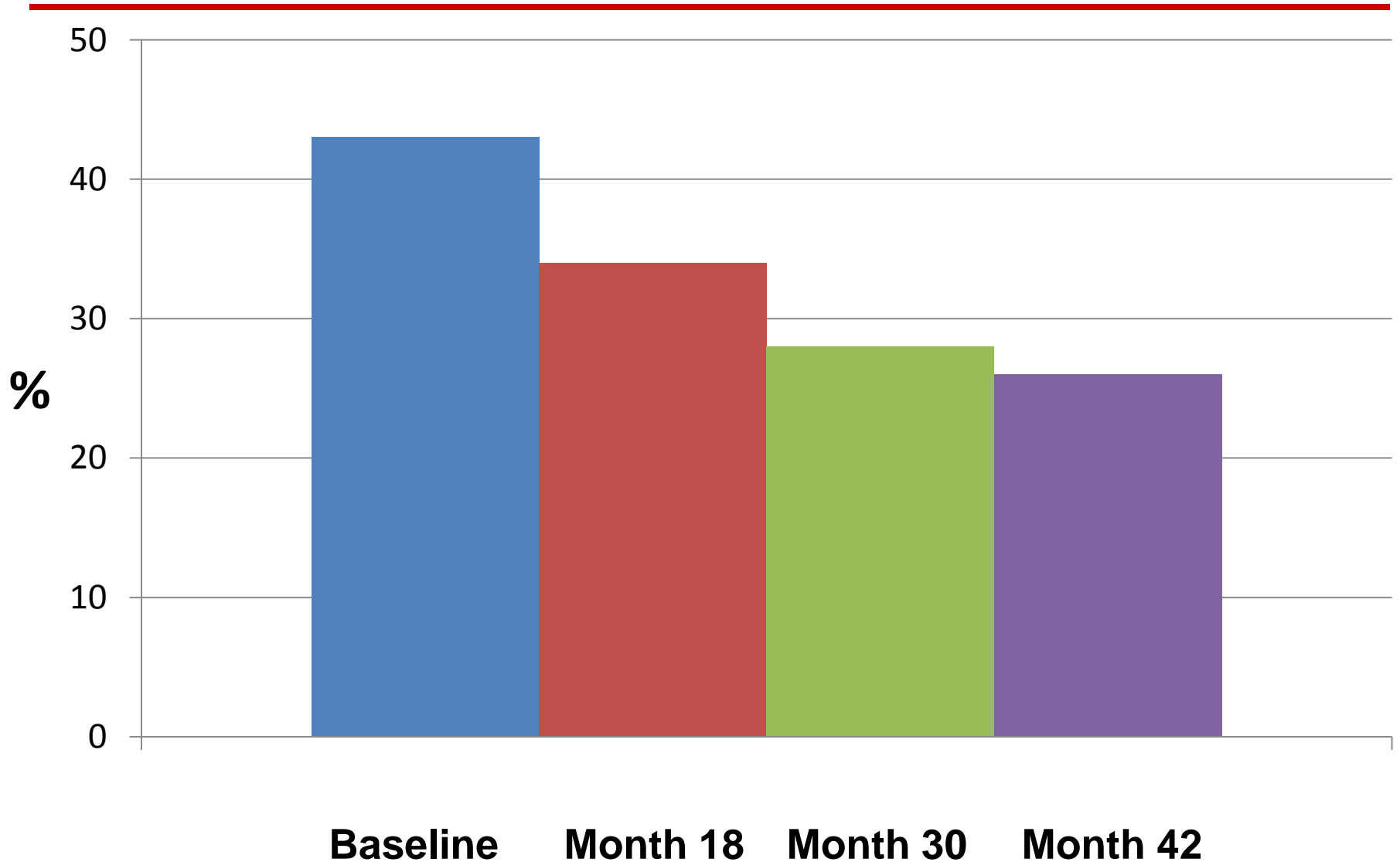
Griffin et al., Drug Alcohol Dependence, 2016

**Chronic pain over time
during the POATS 3.5-year
follow-up study**

Long-term follow-up study design

- Aim: to examine long-term outcomes of participants in the main trial
- Naturalistic, exploratory study
- Participants were interviewed at 18, 30, & 42 months post-initial randomization
 - Telephone interviews: 45-60 minutes each
 - \$75 for each interview completed

Chronic pain over time



$p < .001$

Long-term course of chronic pain

- 25% of those reporting chronic pain at study entry **never** reported chronic pain again
- 29% reporting baseline chronic pain later reported chronic pain **sometimes**, not always
- Only 18% reported chronic pain at every follow-up visit
- This is unlike course of CP in pts without OUD
- Presence of chronic pain correlated with ongoing opioid use over time, controlling for agonist tx

Opioid Use Disorder Comorbidity: Depression

Co-occurring Mood Disorders in Opioid Use Disorder

Individuals with OUD are at increased risk for mood disorders

- National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)
- N = 43,000 adults: Lifetime prevalence in OUD
 - 54% any mood disorder
 - 46% depression; 15% dysthymia; 17% mania
- **Odds ratios for specific mood disorders**
 - 5 × as likely to have any mood disorder
 - 4.4 × as likely to have major depression
 - 6.6 × as likely to have mania (9.5 F/5.5 M)

MDD is a Risk for Prescription Opioid Misuse

In 2015...

- 16 million **adults** (>18 years) had a major depressive episode
 - 12% misused prescription opioids (compared with 4% without MDD)
- 3 million **adolescents** (12–17 years) had a major depressive episode
 - 8% misused prescription opioids (compared with 3% without MDD)

Depressive Symptoms Precipitate Treatment-seeking in Pts with OUD

- Depressive symptoms differentiated those who seek treatment for OUD vs. those still using opioids in the community
- “Snowball technique”
- Significant when taking a history: “Why now?”
- MDD typically is associated with poorer treatment outcome in methadone maintenance, however

Depression and Suicidal Ideation in OUD: The Role of Buprenorphine Treatment

- MDD typically is associated with poorer treatment outcome in methadone maintenance
- However, depression and suicidality may actually be **GOOD** prognostic factors in buprenorphine treatment

Predictors of successful 12-week opioid use outcome on bup/nx in multi-site Prescription Opioid Addiction Treatment Study (N=360)

Baseline variables	Odds Ratio
Age, for every +10 years	1.28*
Lifetime major depression	1.82*
Prior opioid use disorder treatment	.62*
Lifetime route of use other than oral or sublingual	.51^

^p<.052, *p<.05

Predictors of Dropout from Buprenorphine Treatment: The Paradoxical Role of Suicidality

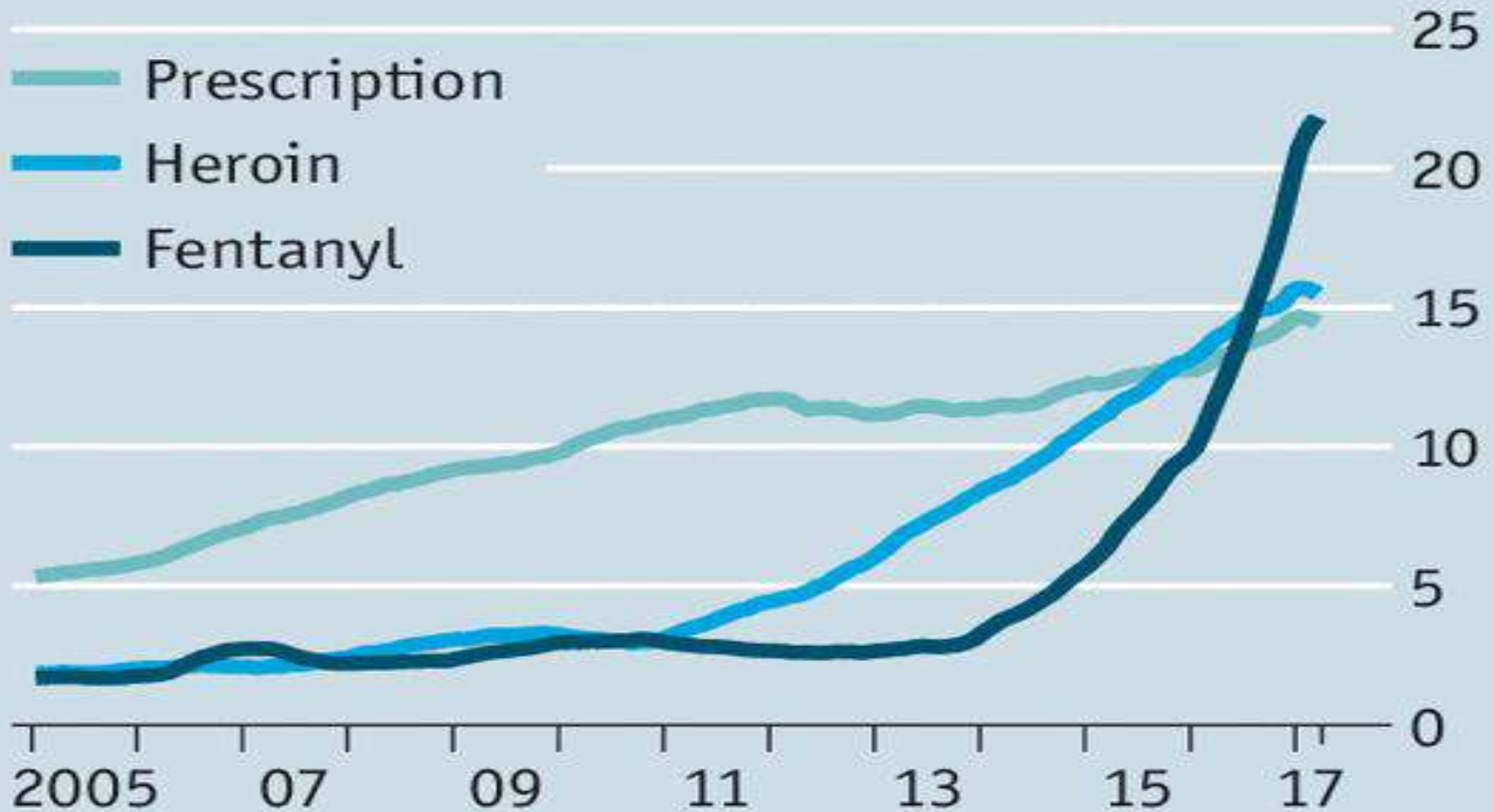
- Retrospective medical records review of 202 patients in 3 different clinics
- Age <25, opioid use in Month 1 of treatment predicted early dropout (before 3 months)
- History of a suicide attempt predicted **greater retention**

Why did MDD Predict Good Opioid Outcome in POATS?

- Was it related to reduced depressive symptoms?
 - NO
- More motivation to change (abstinence goal)?
 - NO
- More treatment engagement (mutual-help attendance)?
 - YES; Ss with MDD were 1.6x more likely to attend mutual help groups

Opioid use disorder and suicidality

Overdose Fatalities in the US, 2005-17



Source: Centres for Disease Control and Prevention

**Overdose in OUD:
Accident, suicide, or
something in between?**

Suicide Risk is Elevated in Opioid Use Disorder

- Suicide risk is higher in OUD than other SUDs
- 30% to 45% of persons with OUD report history of suicide attempt
- Among Veterans with OUD, suicide rate is 6x general population
- Magnitude of suicide risk in females with OUD is 8x that of females without OUD; in males, risk is 2x males without OUD

The Continuum from Accidental Overdose to Suicide

- “What goes through your mind after you’ve injected heroin and before you feel the effect?”
- “I’m either going to get really high or I’m going to die. I hope I get high.”
- ‘Pathological optimism’ plus fatalistic pessimism

Overdose: The Continuum from Accident to Suicide

The continuum from 'accidental' to 'intentional' overdose

- I don't want to die and I don't think I will, but I know it's possible
- Today wouldn't be the worst day to die
- I might be better off dead
- I don't care if I live or die
- I want to die today

Who is Overdosing on Opioids?

- Collected data from 120 OUD patients on inpatient detoxification/stabilization unit at McLean Hospital
- 54 have overdosed (45%) and 66 have not (55%)
- Mean # of ODs = 5.3, median = 3
- Individuals who **have overdosed (n = 54)**:
 - Mean Age: 34; Female: 41%; White 92%; Smoker: 83%
 - College graduate: 11%; Never married: 67%;
Employed full time: 28%*
- Individuals who **have not overdosed (n = 66)**:
 - Mean Age: 35; Female: 41%; White 86%; Smoker: 77%
 - College graduate: 22%; Never married: 52%;
Employed full time: 44%*

*p<.10

Overdose vs. No Overdose

Primary opioid problem***

	<u>Overdose (54)</u>	<u>No Overdose (66)</u>
Prescription opioids	8%	36%
Heroin and/or fentanyl	81%	55%
Both	11%	9%

***p<.01

Overdose vs. No Overdose (cont'd)

Treatment History

- Individuals who **have overdosed (n = 54)** vs. **not (n=66)**
 - Mean # of detoxes in lifetime: 9 vs. 3.5 ***
 - Age substance use became a problem: 17 vs. 21***
 - Age first treated for substance use disorder: 22 vs. 28 ***

Overdose vs. No Overdose (cont'd)

Other clinical characteristics

	<u>Overdose (54)</u>	<u>No Overdose (66)</u>
Co-occurring psych. disorder**	72%	50%
History of suicide attempt *	50%	17%
Chronic pain	28%	38%
Benzo misuse, past 12 months	90%	76%
Craving Score** (0-9)	6.0, 2.3	4.5, 2.8
Days of MJ use**	4.4, 8.8	9.2, 12.2
Age first BZ misuse***	19.7, 7.2	25.1, 9.3

* $p < .001$; ** $p < .02$; *** $p < .01$

Overdose and Suicidal Intent

53 participants with OUD who have overdosed responded to the following questions:

- Just before your most recent opioid overdose, how likely did you **think you would overdose**? Scale 0 (no chance) to 10 (extremely likely)
- Just before your most recent opioid overdose, how strongly did you **want to die**? Scale 0 (not at all) to 10 (very much so)

Overdose: Accident?

Just before your most recent opioid overdose, **how likely did you think you would overdose?** Scale: 0 (no chance) to 10 (extremely likely)

- 30% answered 0/10
- Mean score was 3.1, SD = 3.4
- **28%** answered $\geq 5/10$ they thought they would overdose
- **13%** of individuals answered 10/10

Overdose and Suicidal Intent

Just before your most recent opioid overdose, **how strongly did you want to die?** Scale 0 (not at all) to 10 (very much so)

- 42% answered 0/10
- 58% of those who have overdosed answered $\geq 1/10$ that they wanted to die.
- Mean score was 3.8 +/- 4.1 out of 10
- **36%** answered $\geq 7/10$
- **21%** answered 10/10

Summary

- OUD patients are at high risk of suicide, and many opioid overdoses have at least some suicidal component associated with it, if not a frank attempt
- Post-OD evaluation should address suicidal intent
- Chronic pain is common among patients with OUD and is a risk for suicide
- Depression is common and is a risk for suicide, but could actually be a good prognostic factor in buprenorphine treatment
- Attention paid to comorbidity may improve outcome in OUD patients

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Thank you.

Questions?