

Consequences of Reductions in Opioid Prescribing

Amy Bohnert, PhD



Abrupt Discontinuation of Opioids Dangerous, FDA Warns

Megan Brooks

DISCLOSURES | April 09, 2019

 37 Read Comments

Reports of "serious harm" in patients dependent on opioid painkillers who suddenly stop taking the medication, or rapidly decrease the dose, have prompted a drug safety [communication](#) issued today by the US Food and Drug Administration (FDA).

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- These are my own views!

Collaborators

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Background

Opioid exposure = risk of overdose

Reducing population opioid exposure = fewer new Rx + reducing long-term opioid therapy (LTOT)

Reducing LTOT = tapering

What happens to risk when patients go from exposed to unexposed?

High Dosage Prescribing is Decreasing

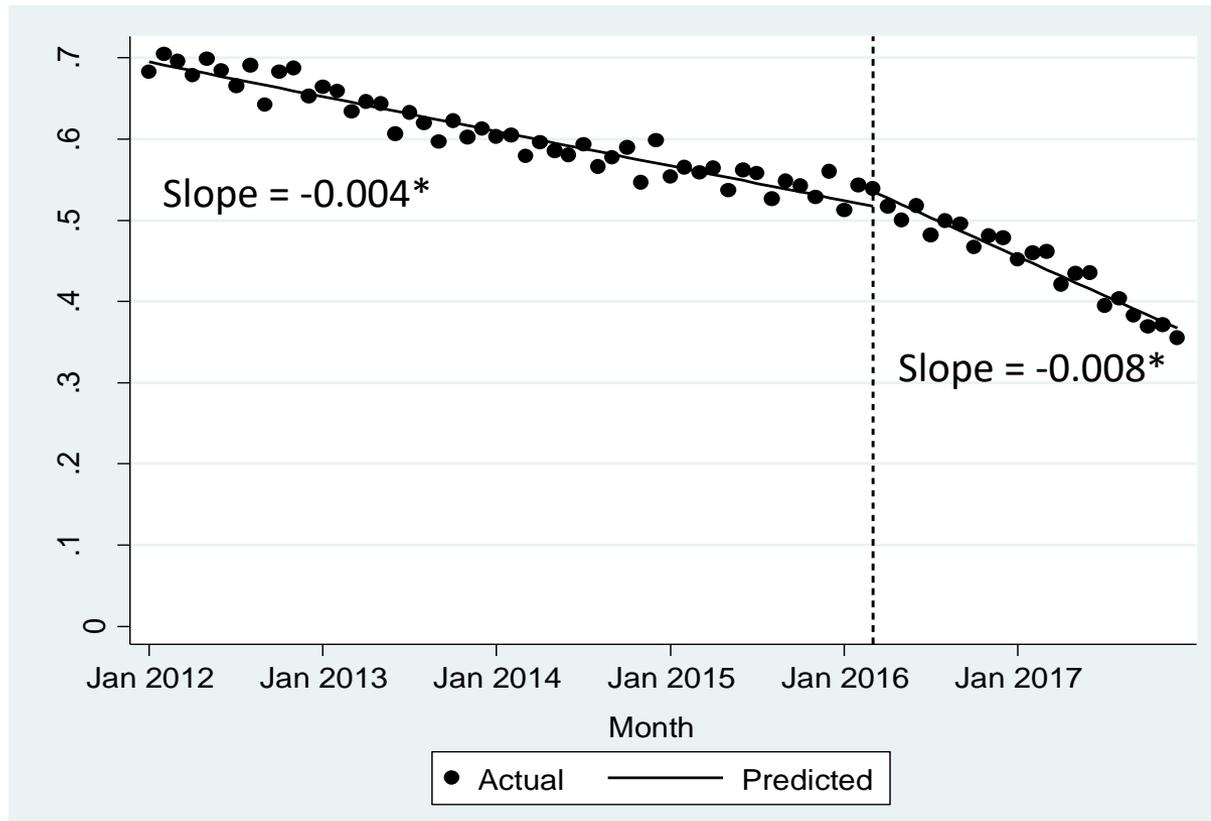
Annals of Internal Medicine

ORIGINAL RESEARCH

Opioid Prescribing in the United States Before and After the Centers for Disease Control and Prevention's 2016 Opioid Guideline

Amy S.B. Bohnert, PhD, MHS; Gery P. Guy Jr., PhD, MPH; and Jan L. Losby, PhD, MSW

Number of opioid prescriptions with a daily dosage ≥ 90 MME



Intercept
0.018*

Change in Slope
-0.004*

* $p < 0.05$

MME: milligram morphine equivalents

What is tapering?

Reduction in Daily Opioid Dosage

Can be:

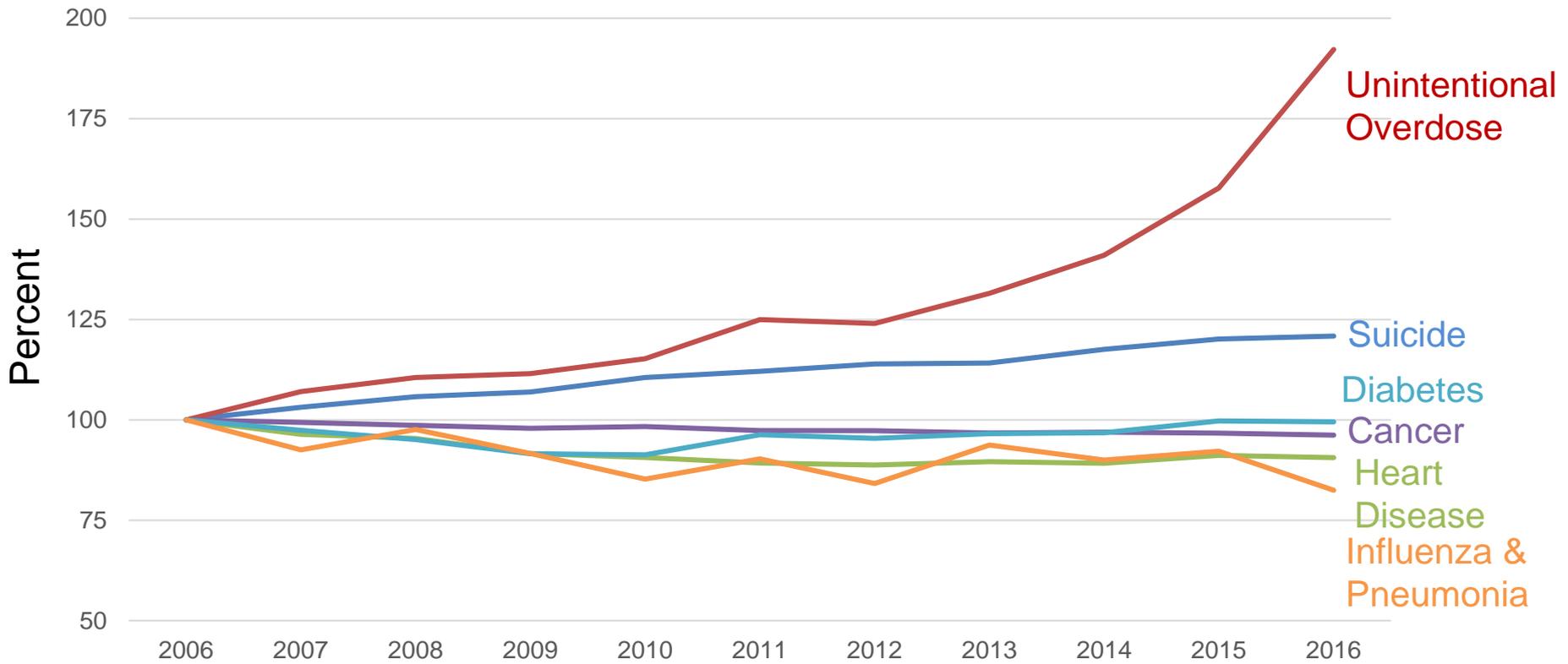
Slow vs. abrupt

Continue at a lower dose vs. discontinuation

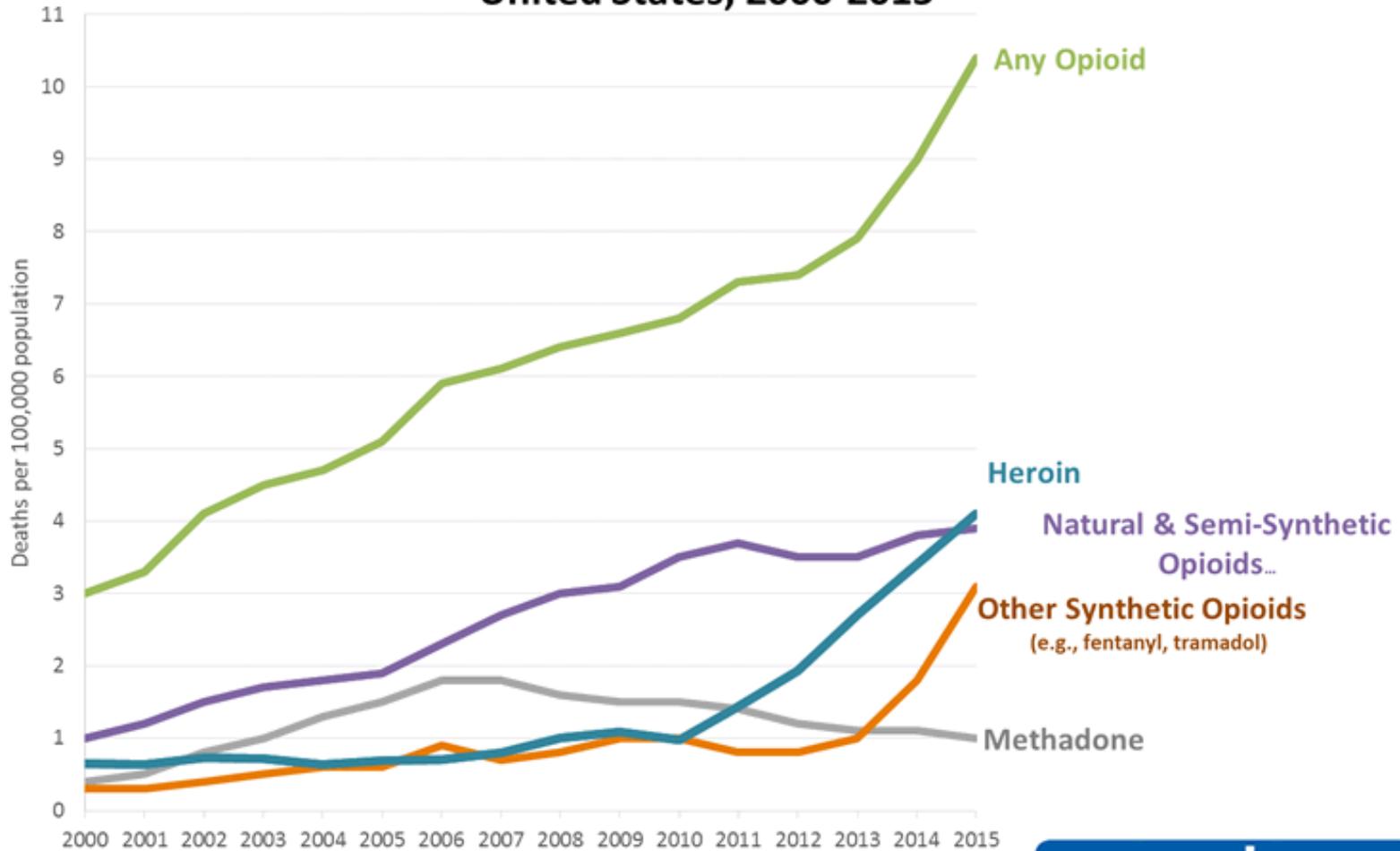
Based on policy vs. concerns

Varying degrees of patient engagement

Relative Change in Common Causes of Death



Overdose Deaths Involving Opioids, by Type of Opioid, United States, 2000-2015



SOURCE: CDC/NCHS, National Vital Statistics System, Mortality. CDC WONDER, Atlanta, GA: US Department of Health and Human Services, CDC; 2016. <https://wonder.cdc.gov/>.

www.cdc.gov
Your Source for Credible Health Information

Outline: What is the evidence?

Prescription Opioid Overdose

Transition to Non-Prescribed Opioids

Suicidal Behaviors

LIMITED HIGH QUALITY STUDIES

Measuring tapering vs. past use

Why is this so hard to study?

Rare events

Prescriber intention unclear

Confounding by indication

Optum (National Claims Data) Analysis

(Bohnert & Larochelle)

Complete analysis – not yet peer reviewed

Claims data for millions of Americans, via Optum/Clinformatics

Outcomes are measured by claims for treated conditions

Outcomes by age group				
Type	Age	N	%	Per 100,000 person-years
Heroin overdose	18 to 25	1362	53.9	18.4
	26 to 45	596	23.6	2.6
	46 and over	570	22.5	1.4
	Total	2528	100.0	3.5
Non-heroin opioid overdose	18 to 25	930	6.4	12.6
	26 to 45	2420	16.8	10.4
	46 and over	11085	76.8	26.8
	Total	14435	100.0	20.0
Suicide attempt	18 to 25	3410	22.0	46.2
	26 to 45	5349	34.5	23.1
	46 and over	6724	43.4	16.2
	Total	15483	100.0	21.5

What is the evidence?

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Bending the Prescription Opioid Dosing and Mortality Curves: Impact of the Washington State Opioid Dosing Guideline

Gary M. Franklin, MD, MPH,^{1,2*} Jaymie Mai, PharmD,² Judith Turner, PhD,^{3,4}
 Mark Sullivan, MD, PhD,³ Thomas Wickizer, PhD,⁵ and Deborah Fulton-Kehoe, PhD¹

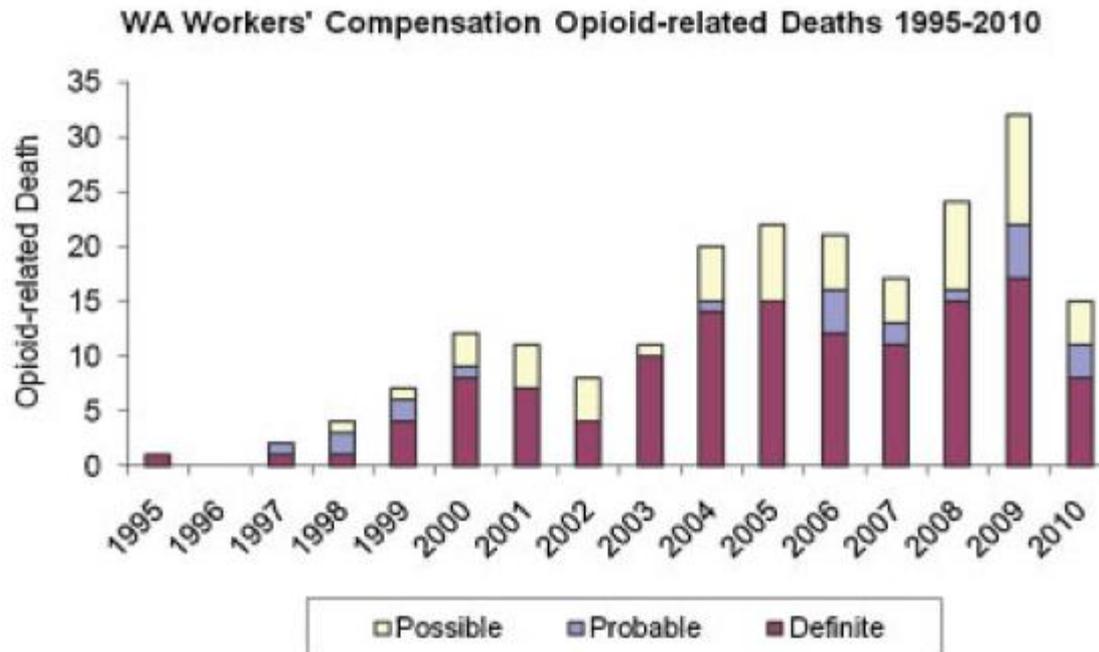


FIGURE 4. WA workers' compensation opioid-related deaths 1995–2010.



Original Investigation | Substance Use and Addiction

Association Between Opioid Dose Variability and Opioid Overdose Among Adults Prescribed Long-term Opioid Therapy

Jason M. Glanz, PhD; Ingrid A. Binswanger, MD; Susan M. Shetterly, MS; Komal J. Narwaney, PhD; Stan Xu, PhD

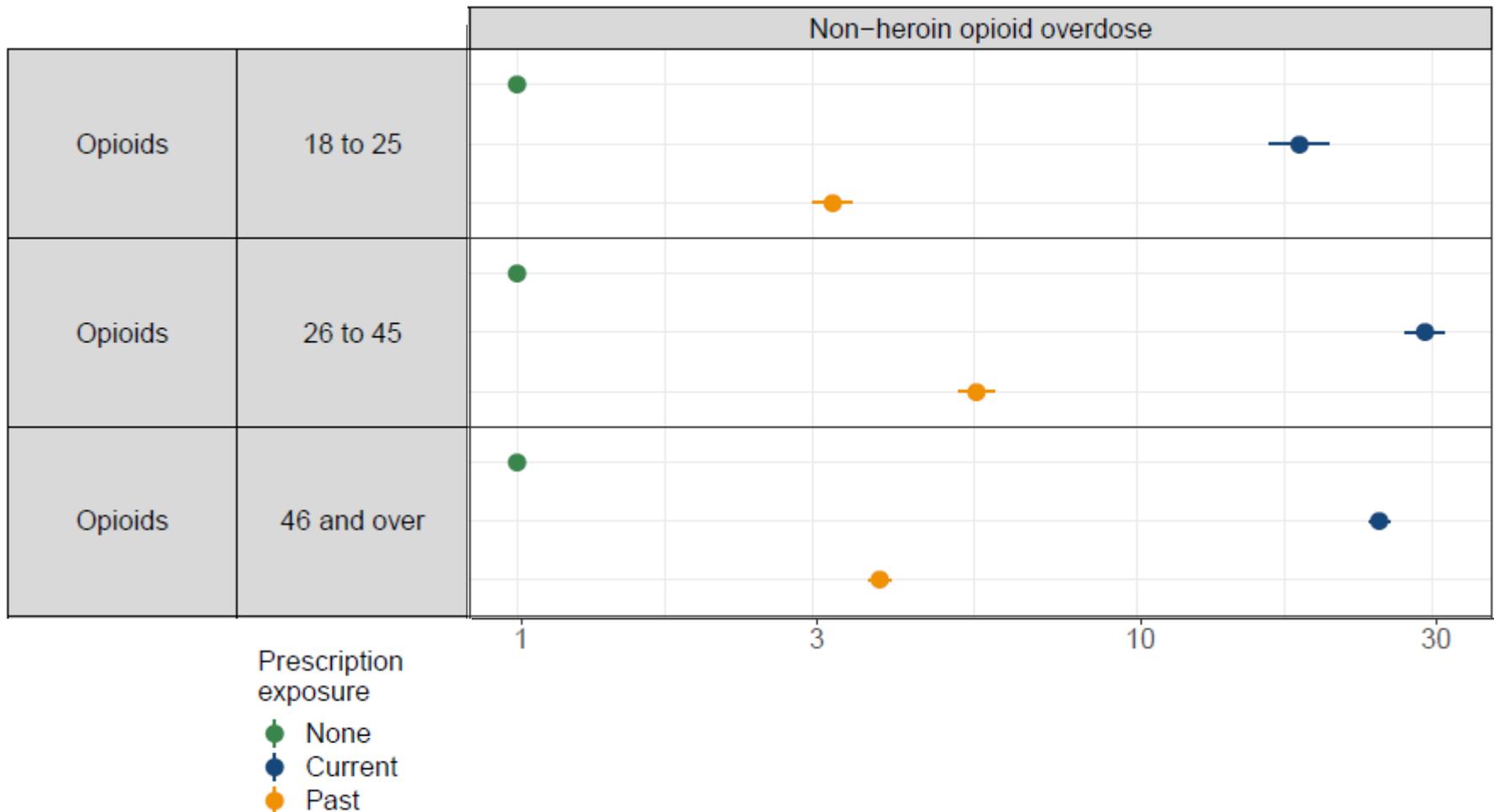
Table 2. Unadjusted and Adjusted Associations Between Opioid Dose Variability and Opioid Overdose

Characteristic	mOR (95% CIs) ^a	
	Unadjusted	Adjusted
Variability in dose, SD		
0-5.3	1 [Reference]	1 [Reference]
5.4-9.1	1.62 (0.79-3.35)	1.43 (0.68-3.01)
9.2-14.6	2.02 (1.00-4.09)	1.61 (0.79-3.31)
14.7-27.2	3.54 (1.79-6.98)	2.19 (1.08-4.43)
>27.2	6.89 (3.48-13.61)	3.32 (1.63-6.77)
Dose, mg of morphine equivalents^b		
0-20	1 [Reference]	1 [Reference]
21-50	1.68 (1.08-2.61)	1.53 (0.97-2.40)
51-100	3.36 (2.08-5.42)	2.27 (1.39-3.70)
>100	4.67 (2.83-7.72)	2.37 (1.41-3.98)

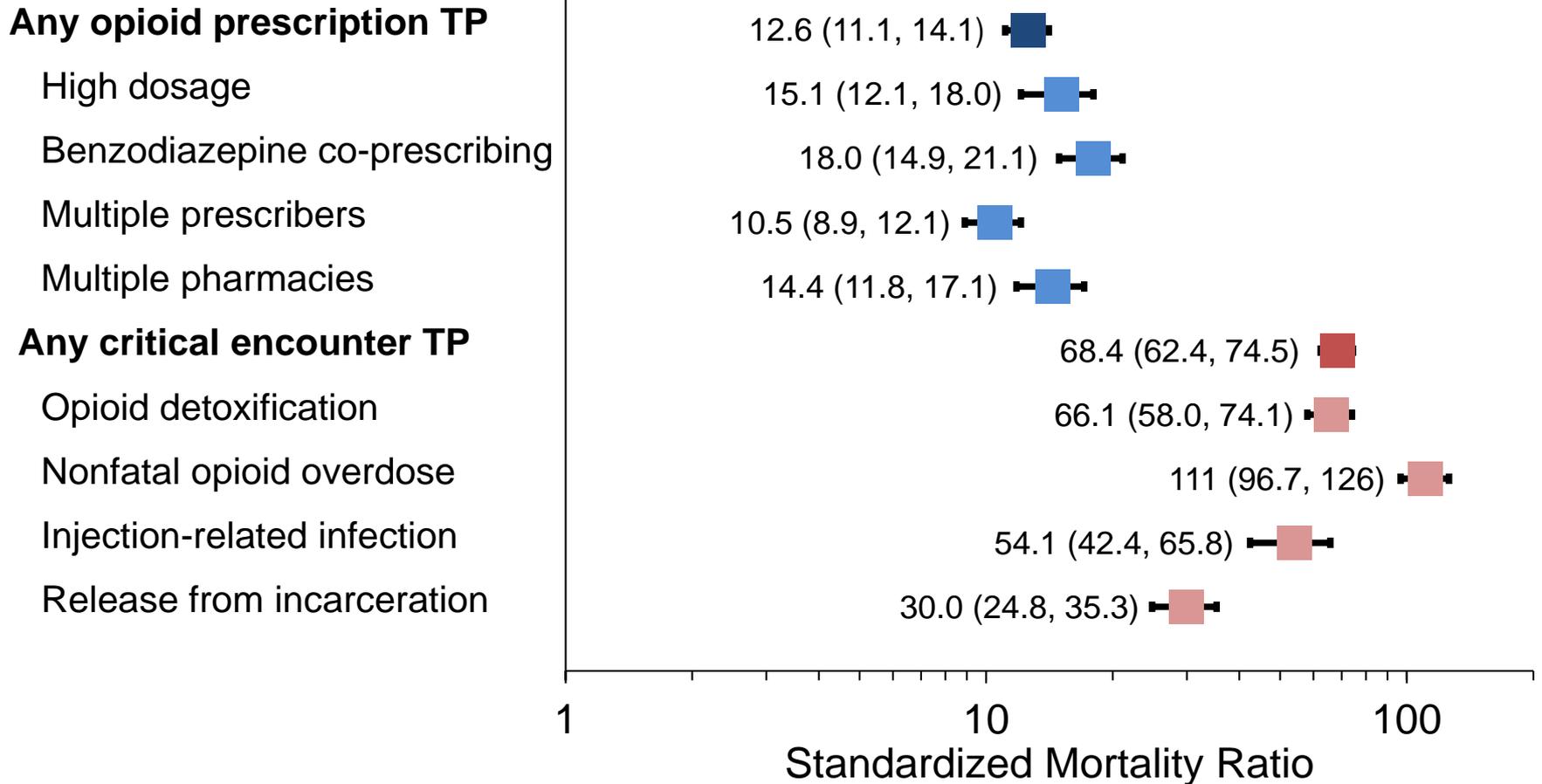
Optum (National Claims Data) Analysis

(Bohnert & Larochelle)

Hazard ratios associated with prescription exposure in the past year

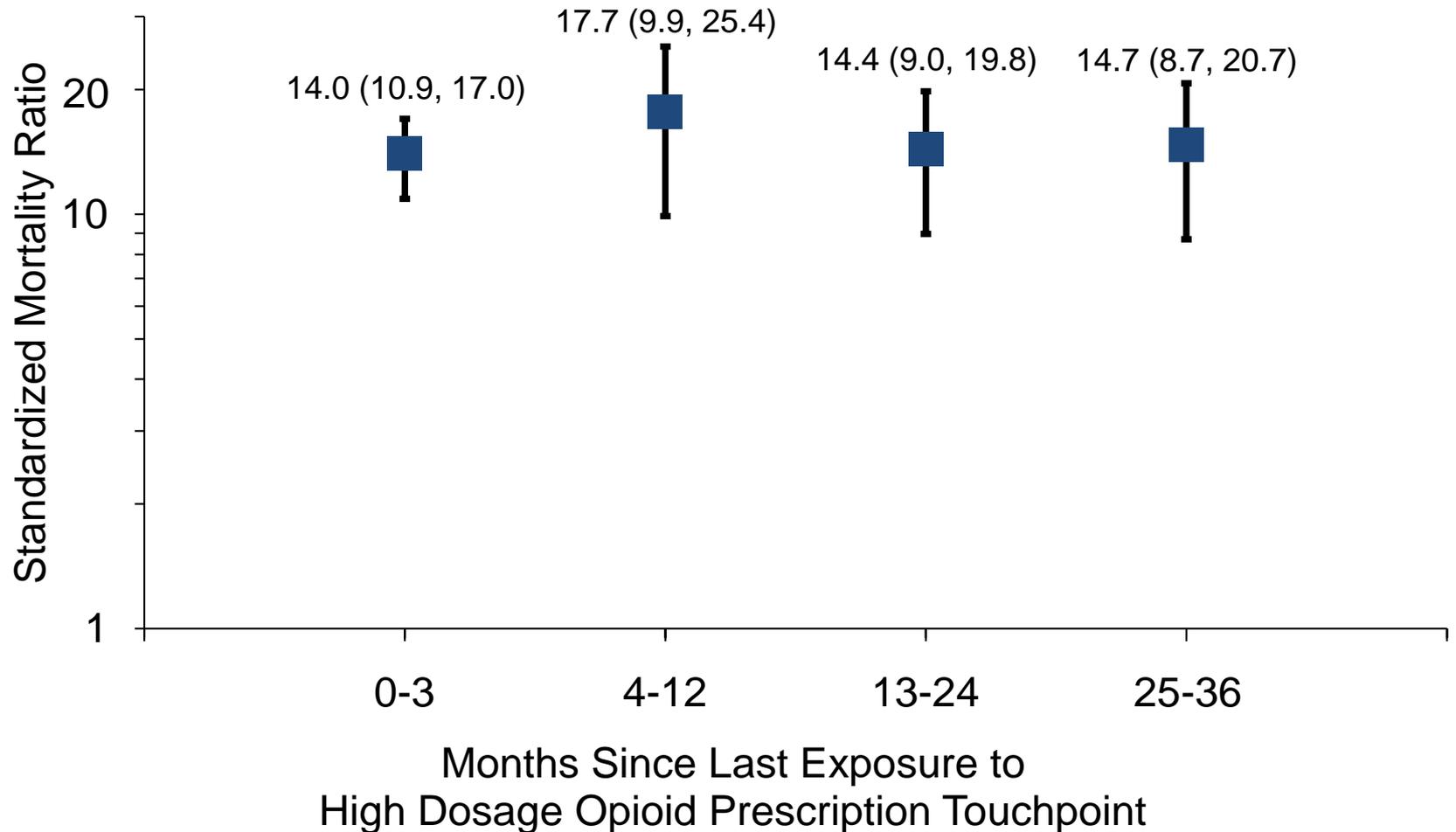


Opioid Overdose Standardized Mortality Ratios Following System Touchpoints



Source: Larochelle et al. *DRUG AND ALCOHOL DEPENDENCE*. IN PRESS.

Opioid Overdose SMR Unchanged 3 Years After Tapering High Dosage Opioids (Massachusetts, 2014, n=1,315 opioid-related deaths)



Source: Larochelle et al. *DRUG AND ALCOHOL DEPENDENCE*. IN PRESS.

What is the evidence?

Prescription Opioid Overdose

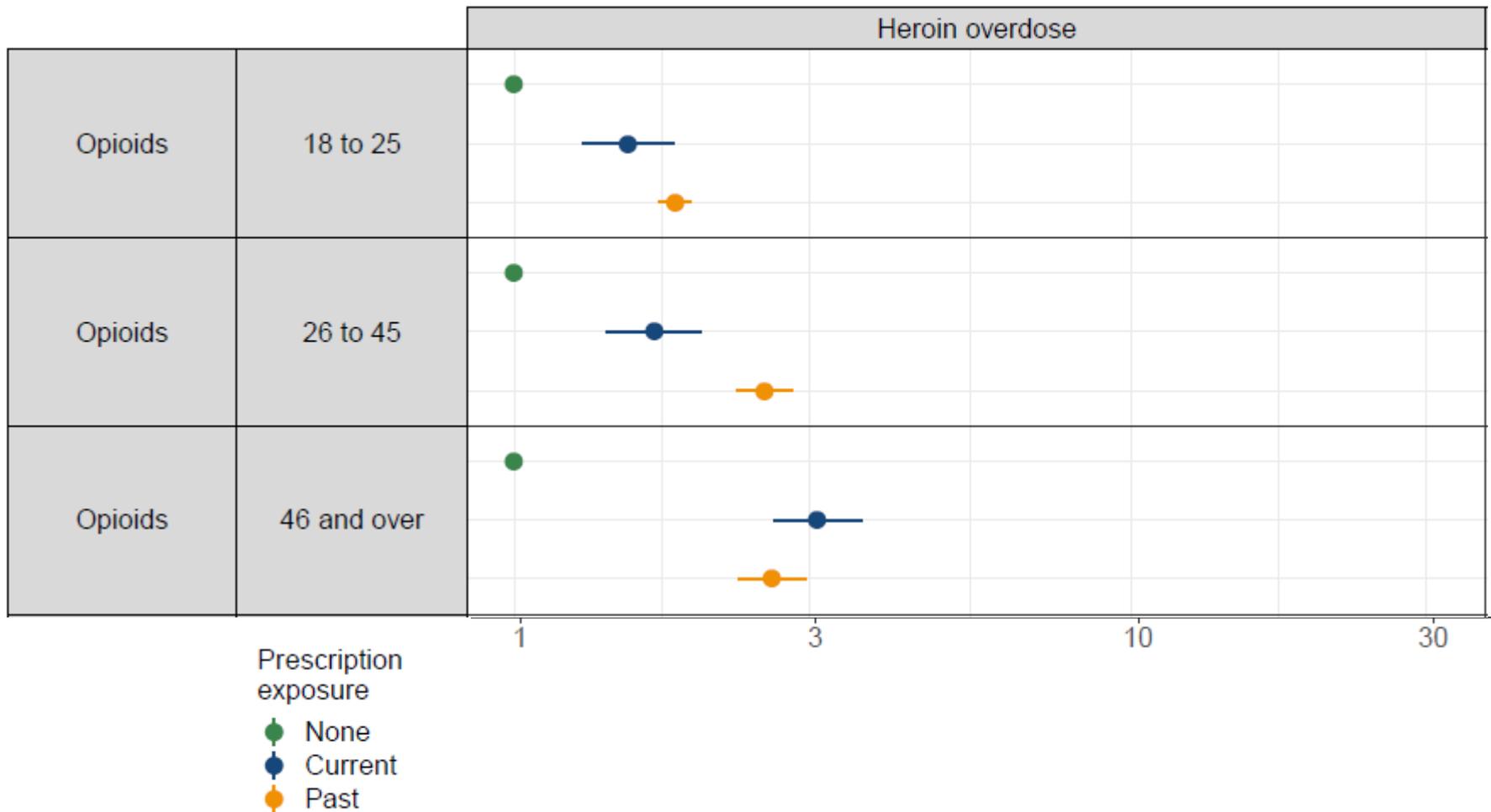
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What is the evidence?

Prescription Opioid Overdose

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Suicidal Behaviors

Opioid dose and risk of suicide

Mark A. Ilgen^{a,b,*}, Amy S.B. Bohnert^{a,b}, Dara Ganoczy^a, Matthew J. Bair^{c,d}, John F. McCarthy^{a,b}, Frederic C. Blow^{a,b}

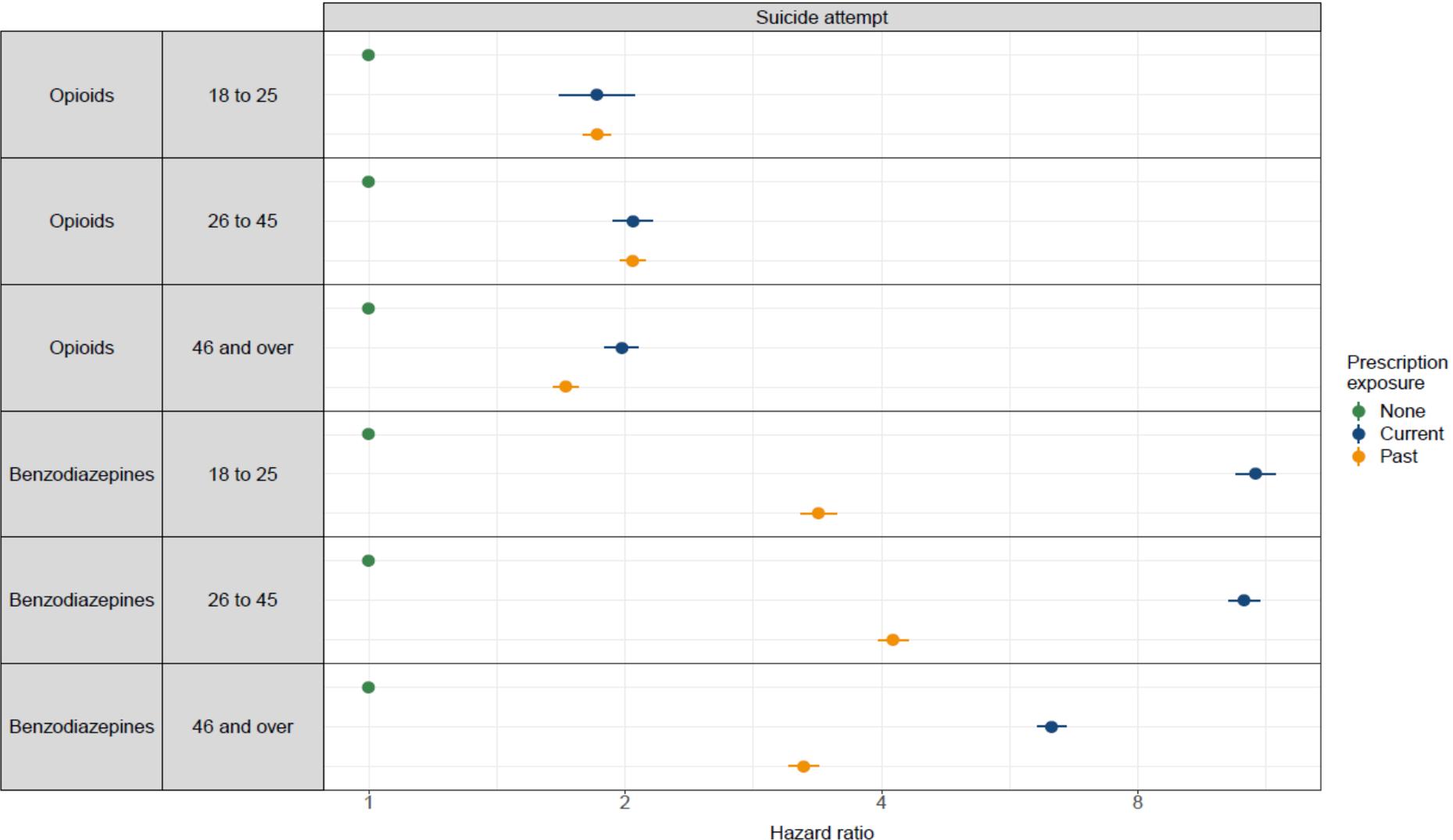
	Suicide, Any Mechanism	Intentional Overdose
	HR (95% CI)	HR (95% CI)
Prescribed Daily Opioid Dose		
1 to < 20 mg/d	1.00	1.00
20 to < 50 mg/d	1.48 (1.25, 1.75)	1.59 (1.12, 2.27)
50 to < 100 mg/d	1.69 (1.33, 2.14)	1.74 (1.09, 2.76)
100+ mg/d	2.15 (1.64, 2.81)	2.09 (1.22, 3.56)

Adjusted for age, sex, race, Hispanic ethnicity, number of pain conditions, number of psychiatric conditions, Charlson comorbidity Index, and opioid schedule.

Optum (National Claims Data) Analysis

(Bohnert & Larochelle)

Figure 2. Hazard ratios associated with prescription exposure in the past year
Suicide attempt



Summary

Need better data!

Tapering may increase transition to heroin,
but also may (or may not) decrease
prescribed opioid overdose

Unclear impact on suicide risk

How can we get better answers?

Careful measurement of tapering

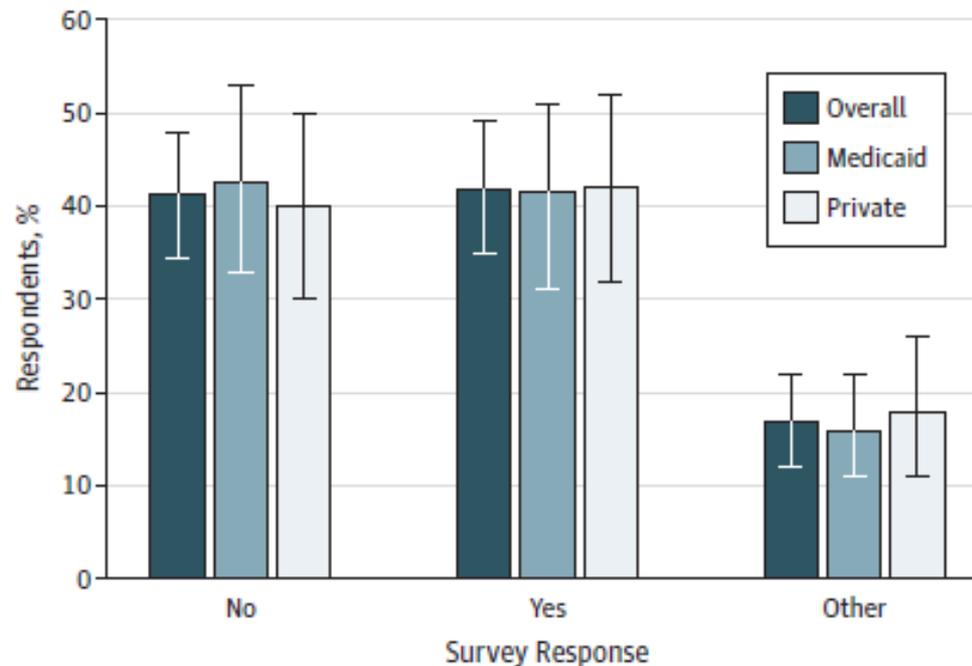
Trial emulation design

Other thoughts...

Access to Primary Care Clinics for Patients With Chronic Pain Receiving Opioids

Pooja A. Lagisetty, MD, MSc; Nathaniel Healy, BS; Claire Garpestad, BS; Mary Jannausch, MS; Renuka Tipirneni, MD, MSc; Amy S. B. Bohnert, PhD, MHS

Figure 2. Percentage of 194 Clinics Accepting New Patients Currently Taking Opioids



Other thoughts...

Suboxone, not just for classic opioid use disorder

Thank you!