

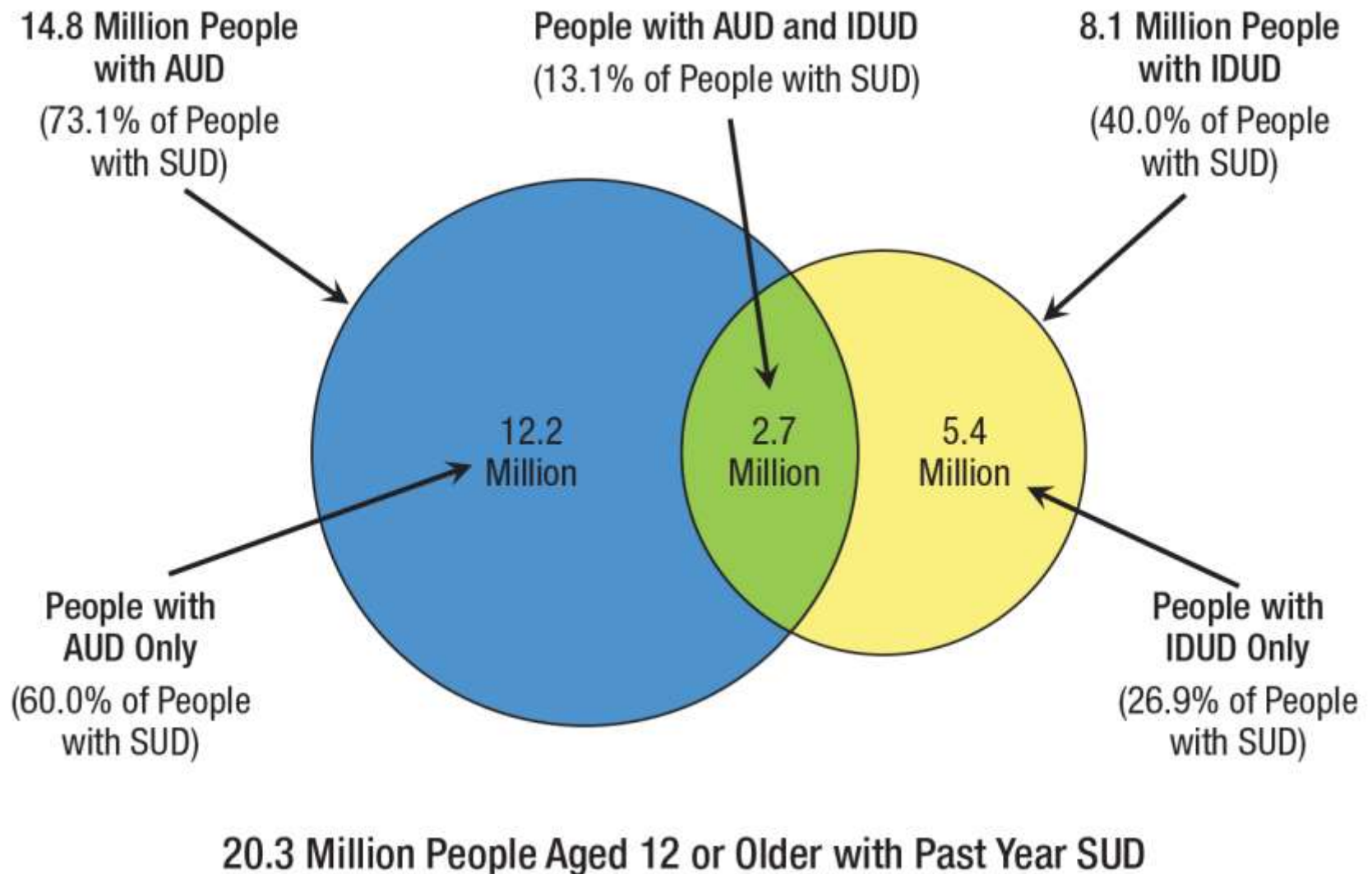
Gabapentin as a Potential Treatment for Co-abuse of Opioids and Alcohol: Human Laboratory Study

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Professor of Neurobiology

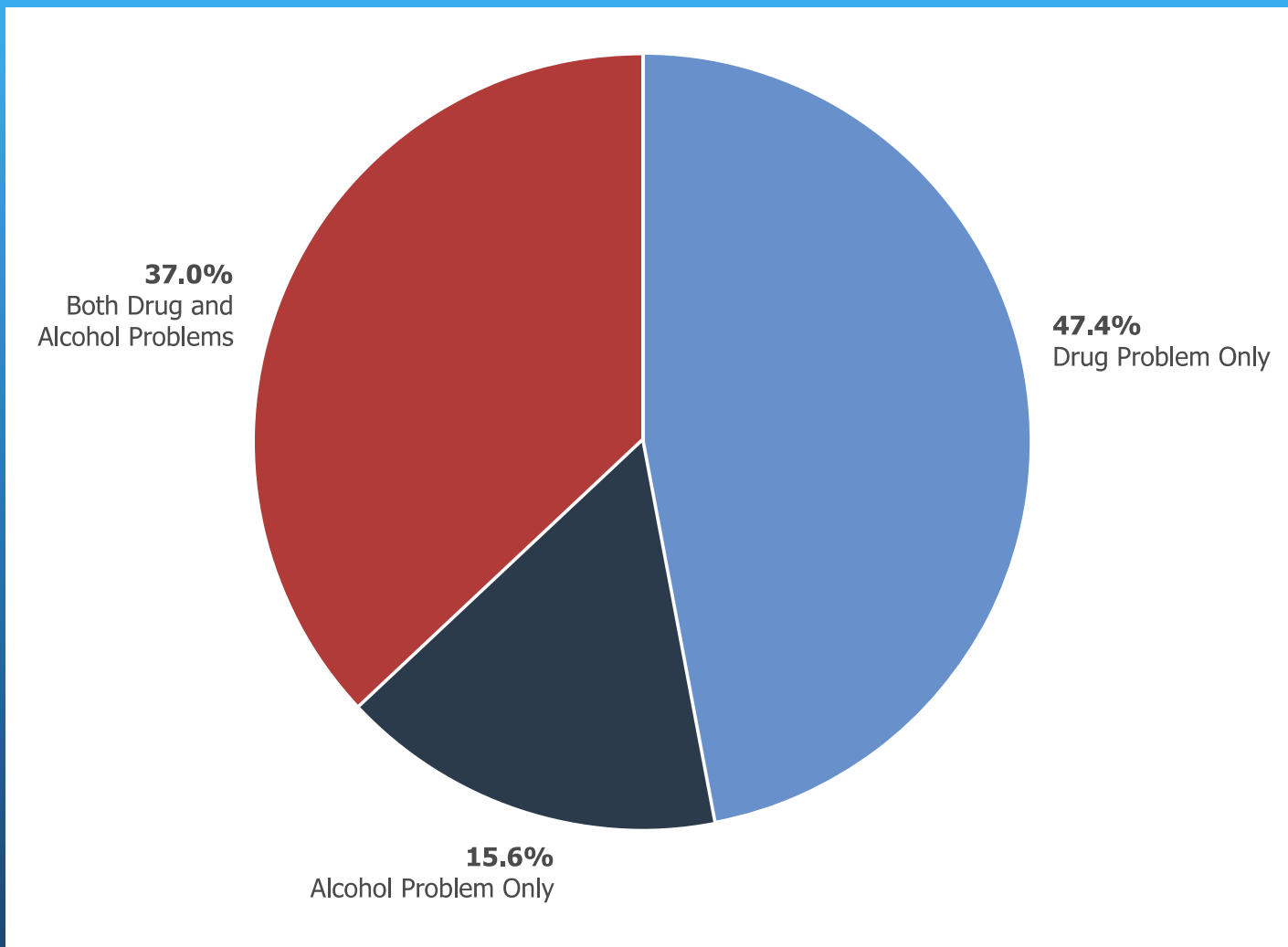
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Department of Psychiatry
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No conflicts of interest

Alcohol Use Disorder (AUD) and Illicit Drug Use Disorder (IDUD) in the Past Year among People Aged 12 or Older with Past Year Substance Use Disorder (SUD): 2018



Single-day count of patients enrolled in substance use treatment in 2017



Behavioral Health Barometer: U.S., Vol 5: Indicators as measured through the 2017 NSDUH and NSSATS, HHS Pub No SMA-19-Baro-17-US, 2019

OPIOIDS ARE FREQUENTLY USED WITH ALCOHOL



- Both are CNS depressants
- Can be lethal when used together
- Treatment outcomes are poor among patients on medication-assisted therapy who are problem drinkers (Ferri et al., 2014; Marcovici et al., 1980; Stapleton and Comiskey, 2010)

RATIONALE FOR TESTING GABAPENTIN

- Is thought to inhibit the $\alpha 2\delta$ subunit of presynaptic Ca^{2+} channels, which may indirectly modulate γ -aminobutyric acid (GABA) and perhaps glutamate neurotransmission (Sills, 2006)
- Good safety and tolerability profile and is in widespread clinical use for several indications (seizures, neuralgia, pain, anxiety, sleep disorders)
- Acute administration of gabapentin (0, 1000, 2000 mg) did not alter subjective effects of alcohol (0.75 g/kg) or alcohol craving in heavy drinkers (Bisaga and Evans, 2006)
- But maintenance on gabapentin (0, 900, and 1800 mg/day) did increase rates of complete abstinence from alcohol in alcohol-dependent patients and it improved mood, sleep and craving (Mason et al., 2014); it also reduced alcohol withdrawal symptoms (Malcolm et al., 2007; Mason et al., 2009)
- In rodent models, gabapentin prevented the development of morphine-induced conditioned place preference and blocked morphine-induced dopamine release in the nucleus accumbens (Andrews et al., 2001)

ISSUES

ADDICTION

SSA SOCIETY FOR THE
STUDY OF
ADDICTION

REVIEW

doi:10.1111/add.13324

Gabapentin misuse, abuse and diversion: a systematic review

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METHODS

- 8-week, inpatient, within-subjects study
- Non-treatment-seeking participants with OUD and AUD
- Must use opioids and alcohol simultaneously
- Morphine maintenance dose: 30 mg QID
- Gabapentin maintenance doses: 0 and 1800 mg/day
- 9 test doses (randomized, double-blind oral solutions):
 - Placebo (0 g/kg alcohol + 0 mg/70 kg oxycodone)
 - 0.5 g/kg alcohol
 - 0.75 g/kg alcohol
 - 15 mg/70 kg oxycodone
 - 30 mg/70 kg oxycodone
 - 0.5 g/kg alcohol + 15 mg/70 kg oxycodone
 - 0.5 g/kg alcohol + 30 mg/70 kg oxycodone
 - 0.75 g/kg alcohol + 15 mg/70 kg oxycodone
 - 0.75 g/kg alcohol + 30 mg/70 kg oxycodone
- **PRIMARY DEPENDENT MEASURE: Visual analog scale rating of Drug Liking**
- **SECONDARY DEPENDENT MEASURES: Other VAS, physiological responses**

Representative Study Design																
1st MAINTENANCE DOSE (0 or 1800 mg/day Gabapentin)	Test Week 1					Test Week 2					Test Week 3					
	Mon	Tue	Wed	Thu	Fri	Mon	Tue	Wed	Thu	Fri	Mon	Tue	Wed	Thu	Fri	
Stabilization on morphine and the first dose of study medication	Oxy (mg/70kg)	0		30		15	15		30		0	30		15		0
	Alcohol (g/kg)	0		High		0	High		Low		High	0		Low		Low
2nd MAINTENANCE DOSE (1800 or 0 mg/day Gabapentin)	Test Week 4					Test Week 5					Test Week 6					
	Mon	Tue	Wed	Thu	Fri	Mon	Tue	Wed	Thu	Fri	Mon	Tue	Wed	Thu	Fri	
Stabilization on the second dose of study medication	Oxy (mg/70kg)	15		30		0	30		15		0	30		0		15
	Alcohol (g/kg)	Low		High		Low	0		High		0	Low		High		0

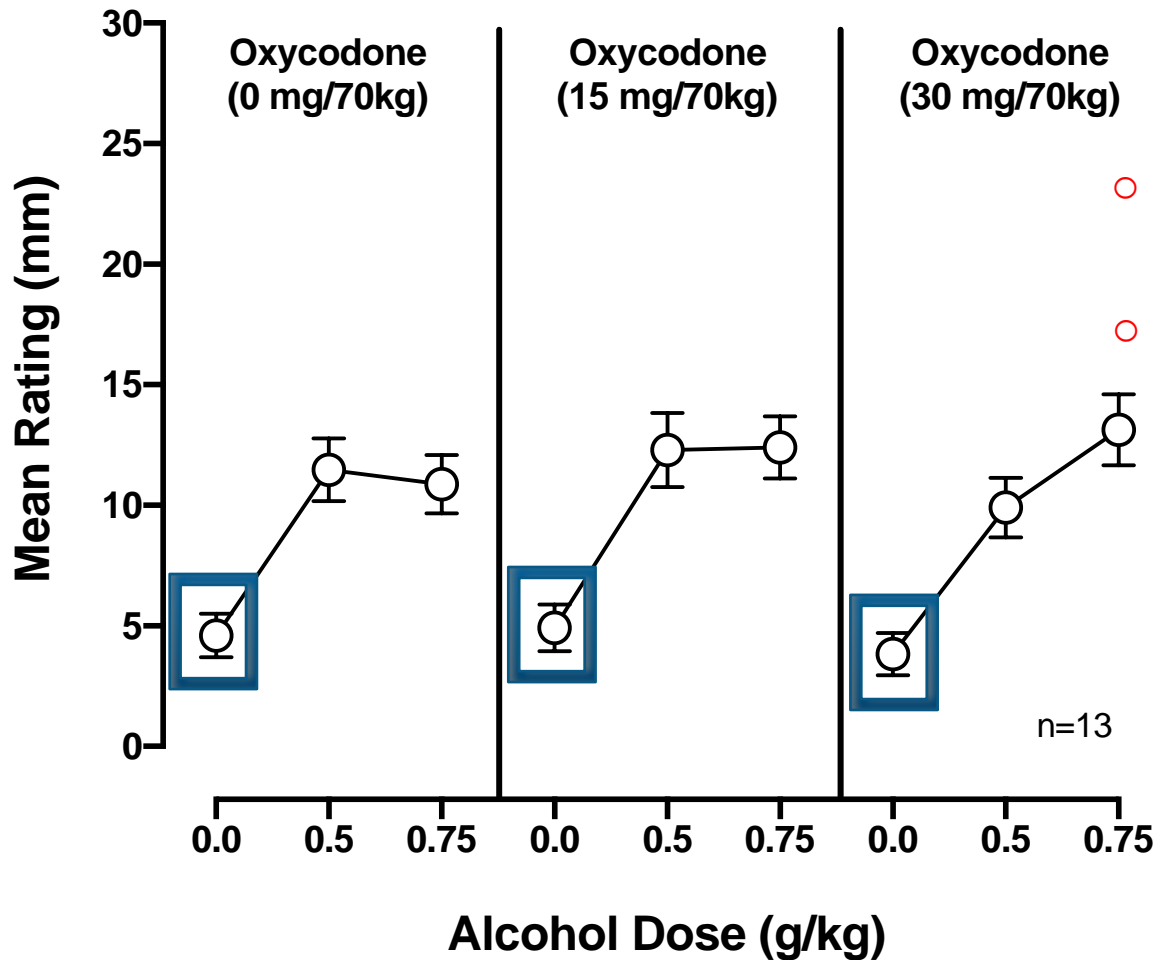
DEMOGRAPHICS of COMPLETERS (n=13)

- 13 men
- 44.1 ± 3.0 years of age
- 7 Black, 3 White, 2 Hispanic
- 10 IN heroin user, 3 IV and IN heroin user
- 6.6 ± 0.3 days per week heroin (range: 4-7 days)
- 7.6 ± 0.9 bags per day heroin
- 5.6 ± 0.5 days per week alcohol (range: 3-7 days)
- 5.3 ± 0.6 drinks per occasion (range: 2-9 drinks)

- 4 discontinued early: 2 for personal reasons, 2 for elevated blood pressure

Does GABAPENTIN alter the abuse liability of oxycodone and alcohol, alone or in combination?

Liking



- Alcohol significantly increased Liking
- Oxycodone did not affect Liking

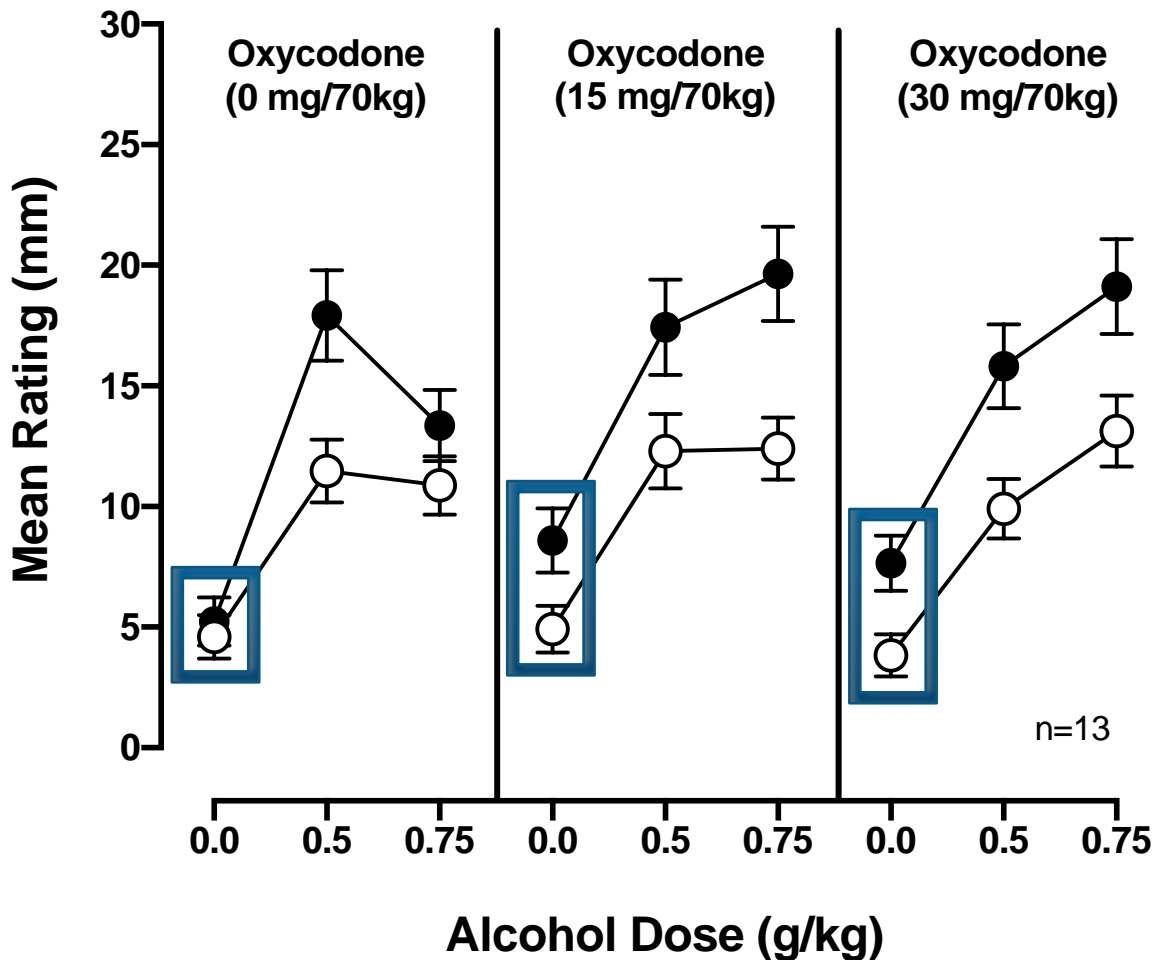
n=13

Main Effect of
Gabapentin Dose:
Alcohol Dose: $p=0.04$

Gabapentin Dose (PO)

○ 0 mg QD

Liking

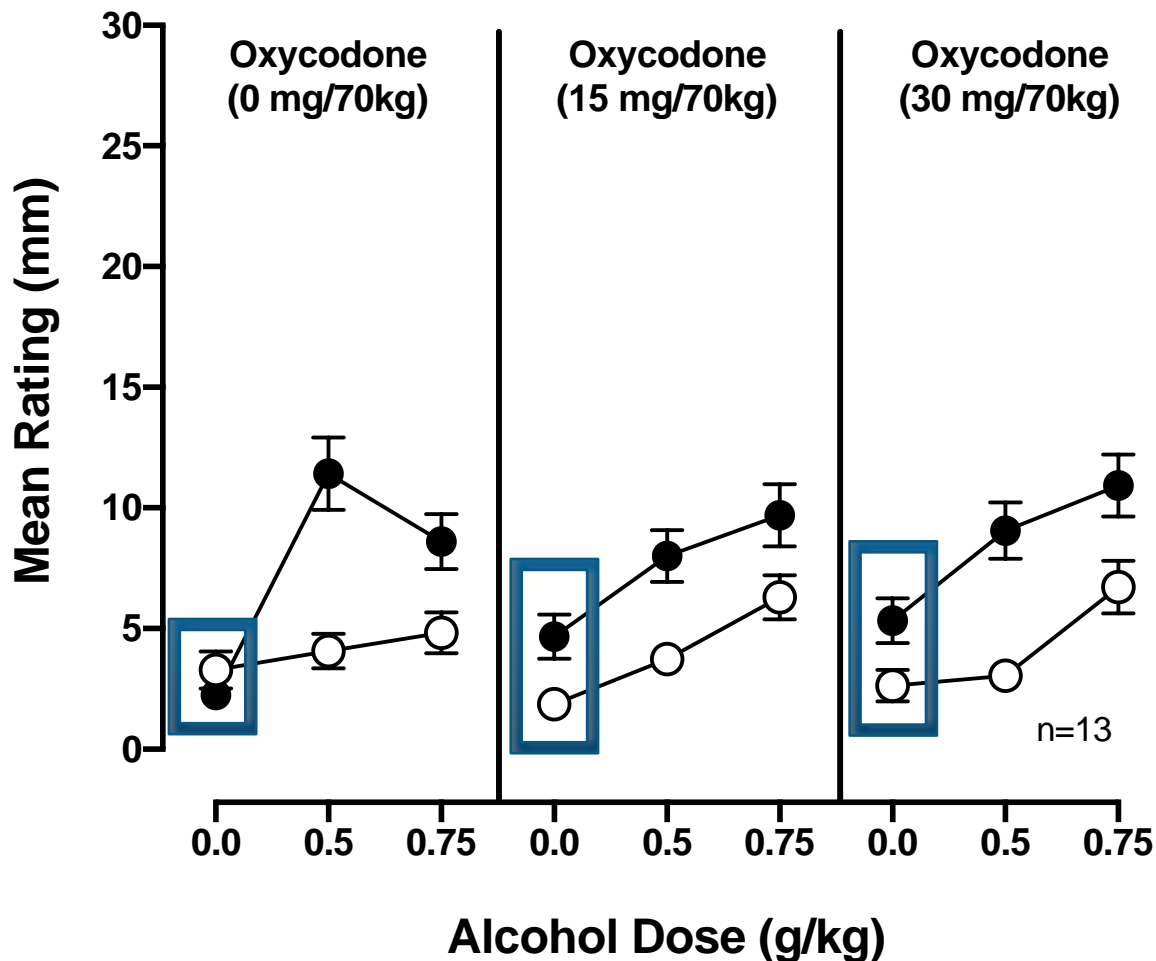


- Gabapentin alone did not affect Liking
- But it appeared to increase Liking of oxycodone alone
- Overall gabapentin significantly increased Liking

Main Effect of
Gabapentin Dose: $p=0.04$
Alcohol Dose: $p=0.04$

Gabapentin Dose (PO)
○ 0 mg QD
● 1800 mg QD

High

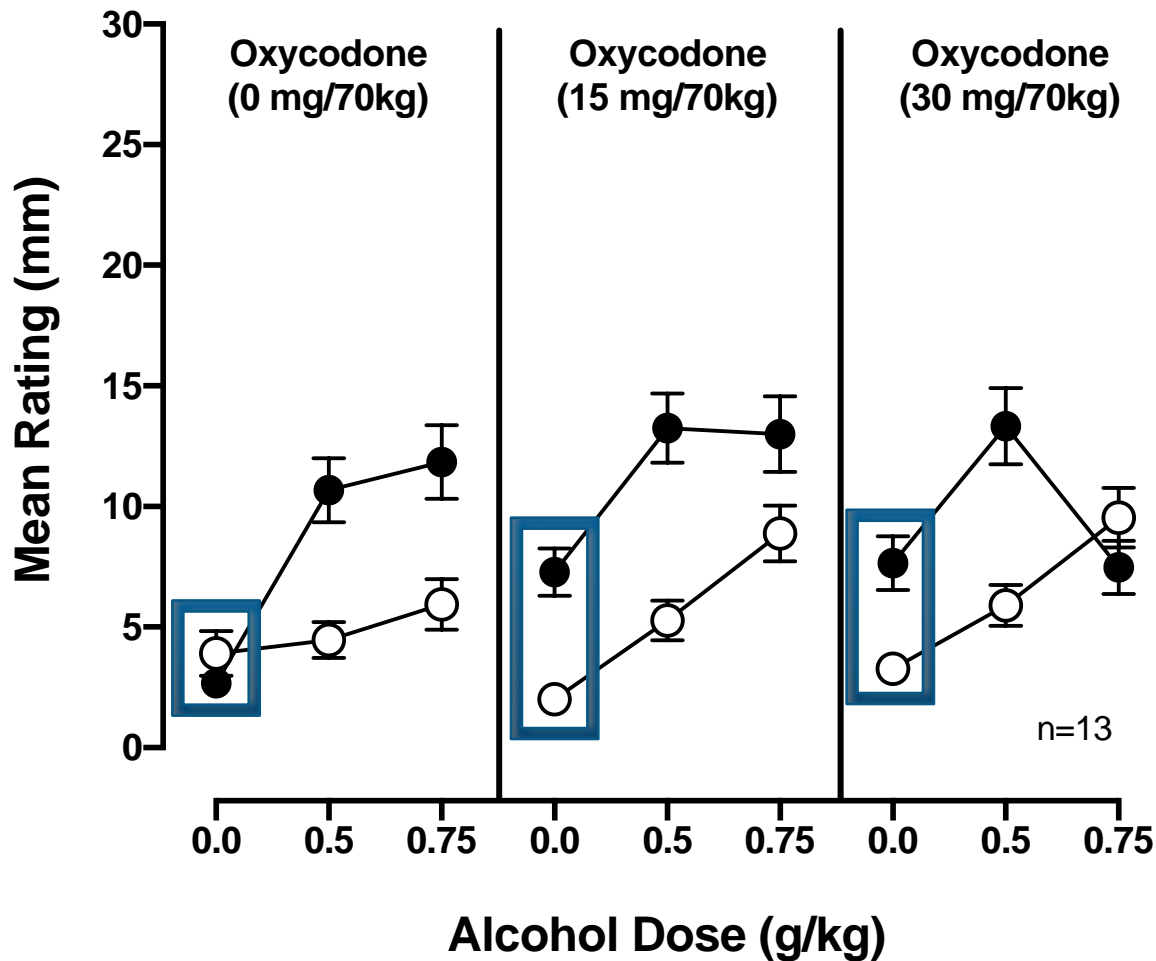


- Gabapentin alone did not affect ratings of High
- But it appeared to increase ratings of High with oxycodone alone
- Overall gabapentin significantly increased ratings of High

Main Effect of
Gabapentin Dose: $p=0.03$
Alcohol Dose: $p=0.02$

Gabapentin Dose (PO)
○ 0 mg QD
● 1800 mg QD

Sedated



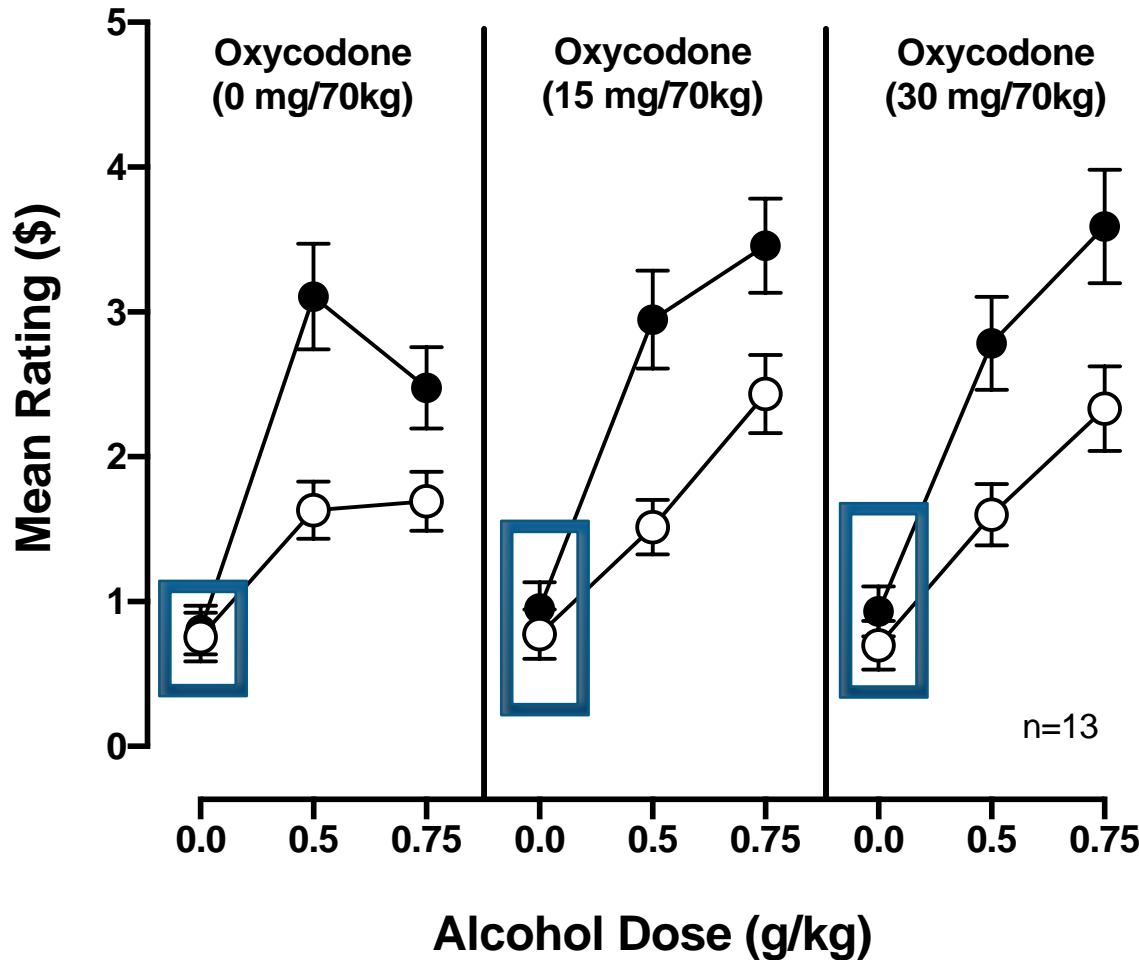
Main Effect of
Gabapentin Dose: $p=0.03$
Alcohol Dose: $p=0.005$

Gabapentin Dose (PO)

- 0 mg QD
- 1800 mg QD

- Gabapentin alone did not affect ratings of Sedated
- But it appeared to increase oxycodone-induced ratings of Sedated
- Overall gabapentin significantly increased ratings of Sedated

Would Pay

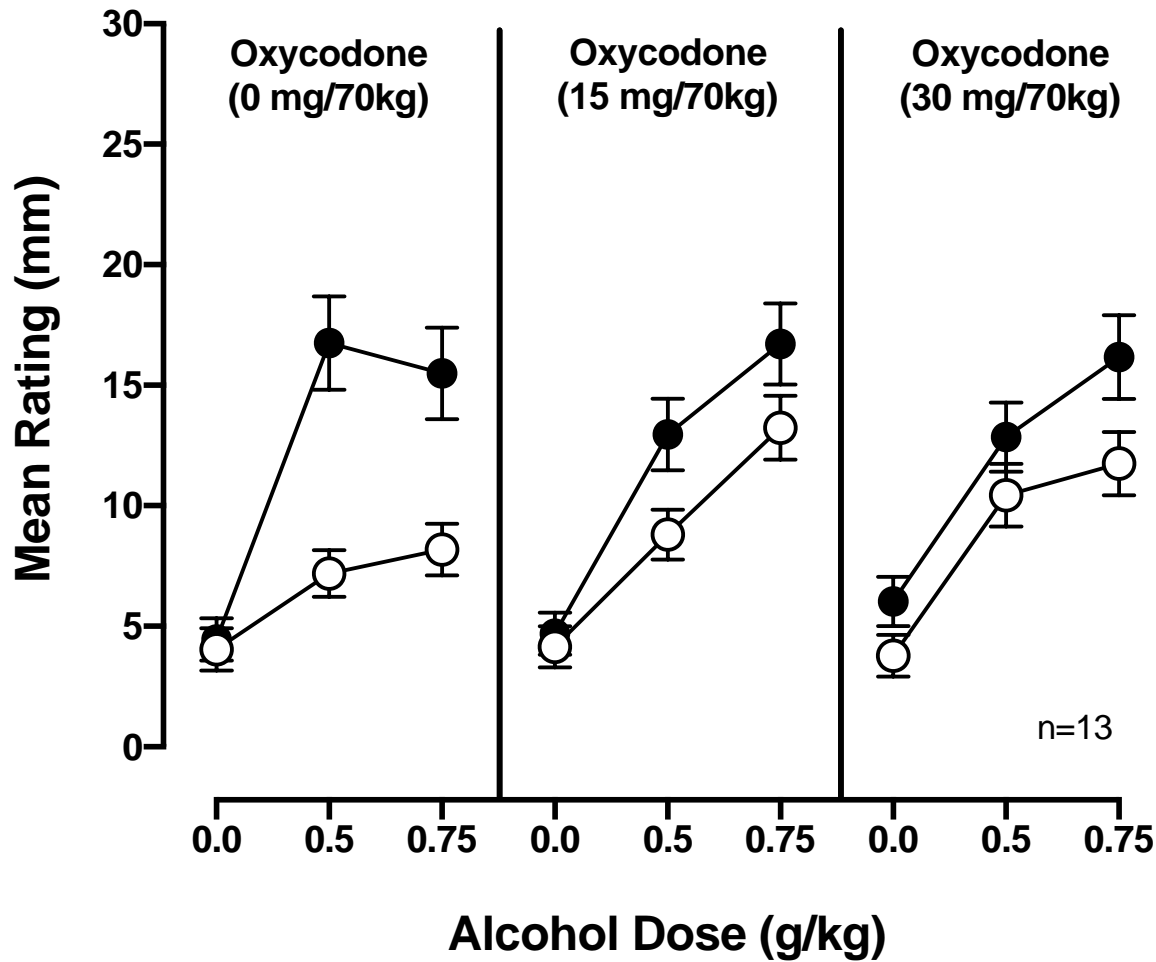


- Gabapentin alone did not affect the amount subjects would pay for the drugs
- Unlike the other effects, it did not affect the amount they would pay for oxycodone alone
- But overall gabapentin increased the amount subjects would pay for the drugs

Main Effect of
 Gabapentin Dose: $p=0.06$
 Alcohol Dose: $p=0.03$

Gabapentin Dose (PO)
 ○ 0 mg QD
 ● 1800 mg QD

Potent



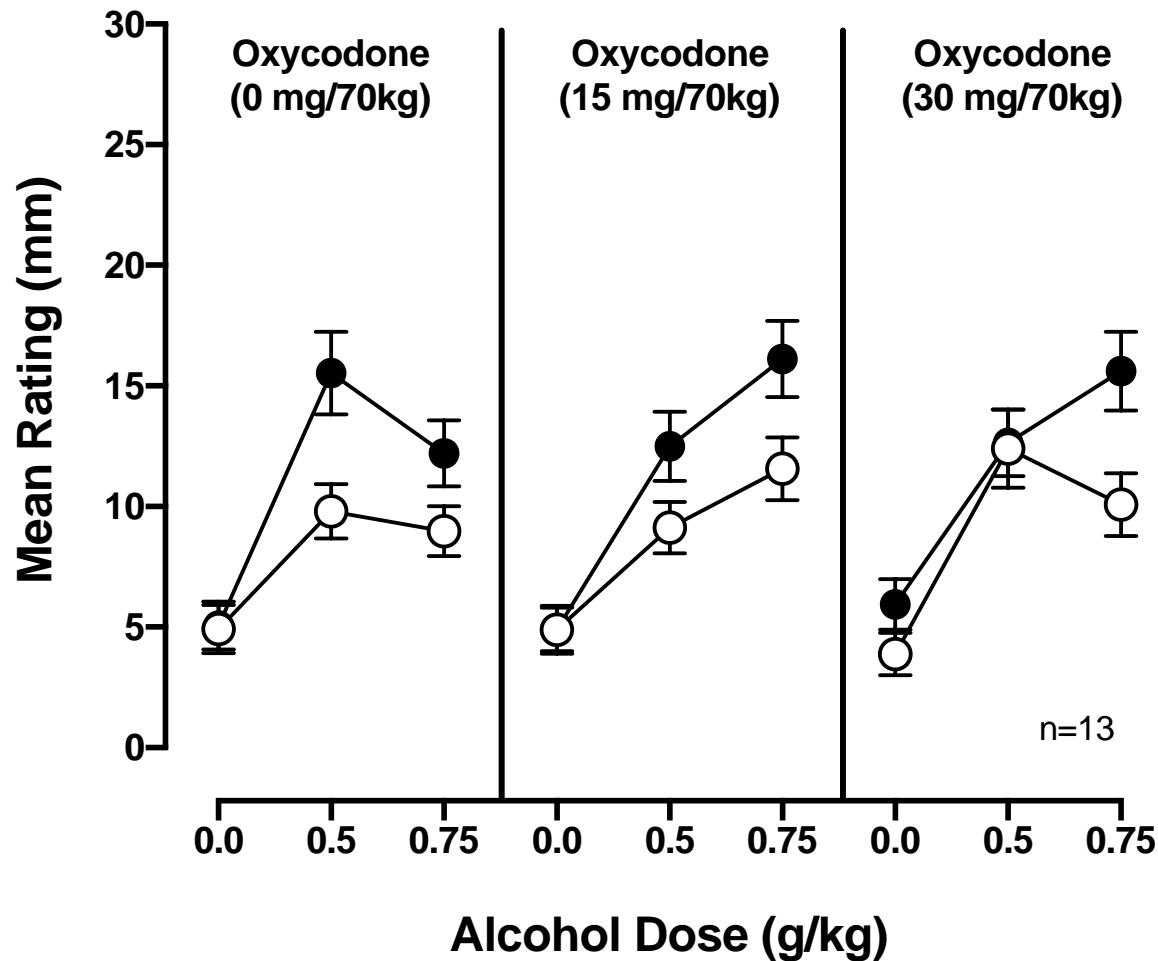
○ Similar findings were observed for ratings of potency

Main Effect of
Gabapentin Dose: $p=0.11$
Alcohol Dose: $p=0.03$

Gabapentin Dose (PO)

○ 0 mg QD
● 1800 mg QD

High Quality



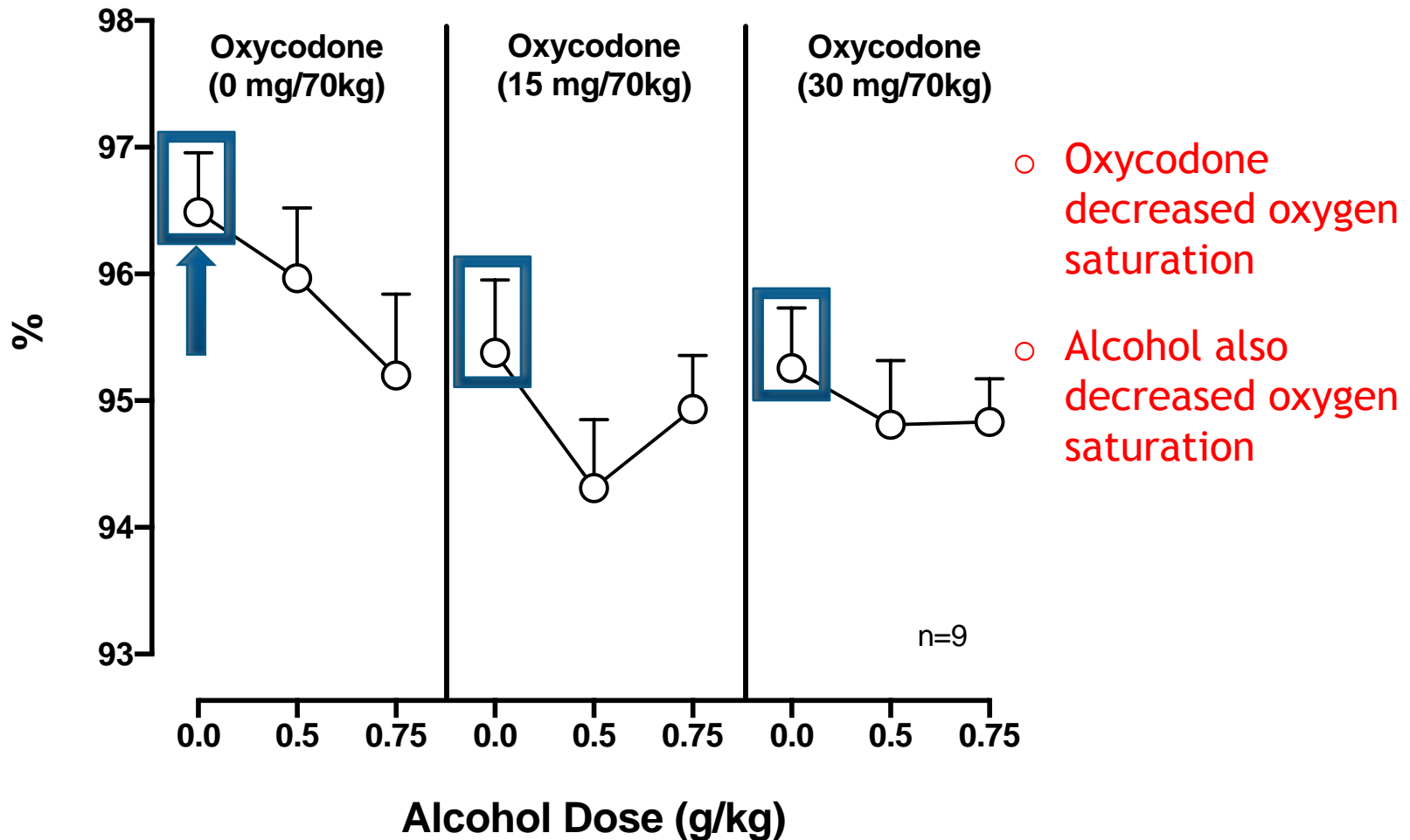
○ Similar findings also were observed for ratings of high quality

Main Effect of
Gabapentin Dose: $p=0.14$
Alcohol Dose: $p=0.02$

Gabapentin Dose (PO)
○ 0 mg QD
● 1800 mg QD

**WHAT ABOUT POTENTIAL TOXIC
EFFECTS OF THE COMBINATION?**

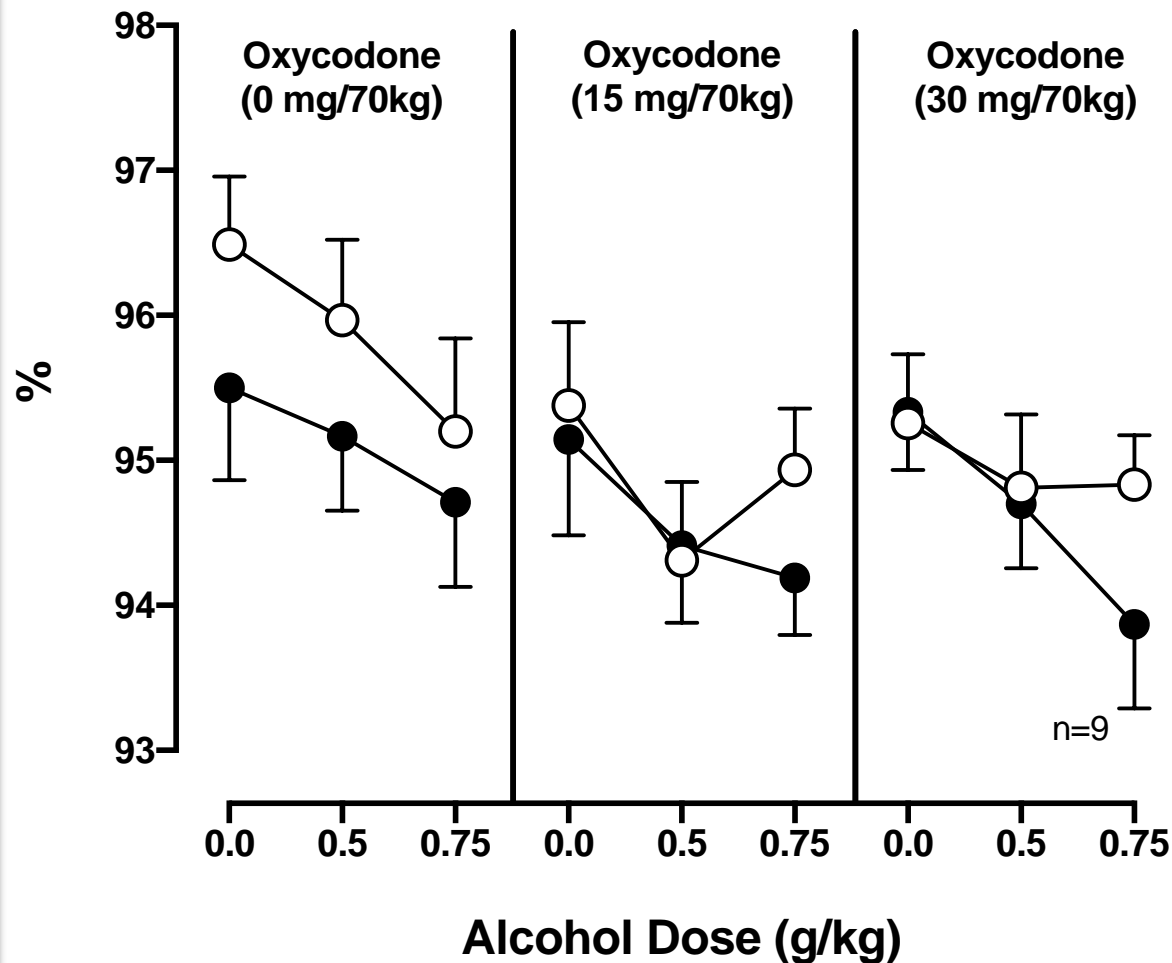
Trough Oxygen Saturation



Main Effect of
Oxycodone Dose: $p=0.02$
Alcohol Dose: $p=0.01$

Gabapentin Dose (PO)
○ 0 mg QD

Trough Oxygen Saturation

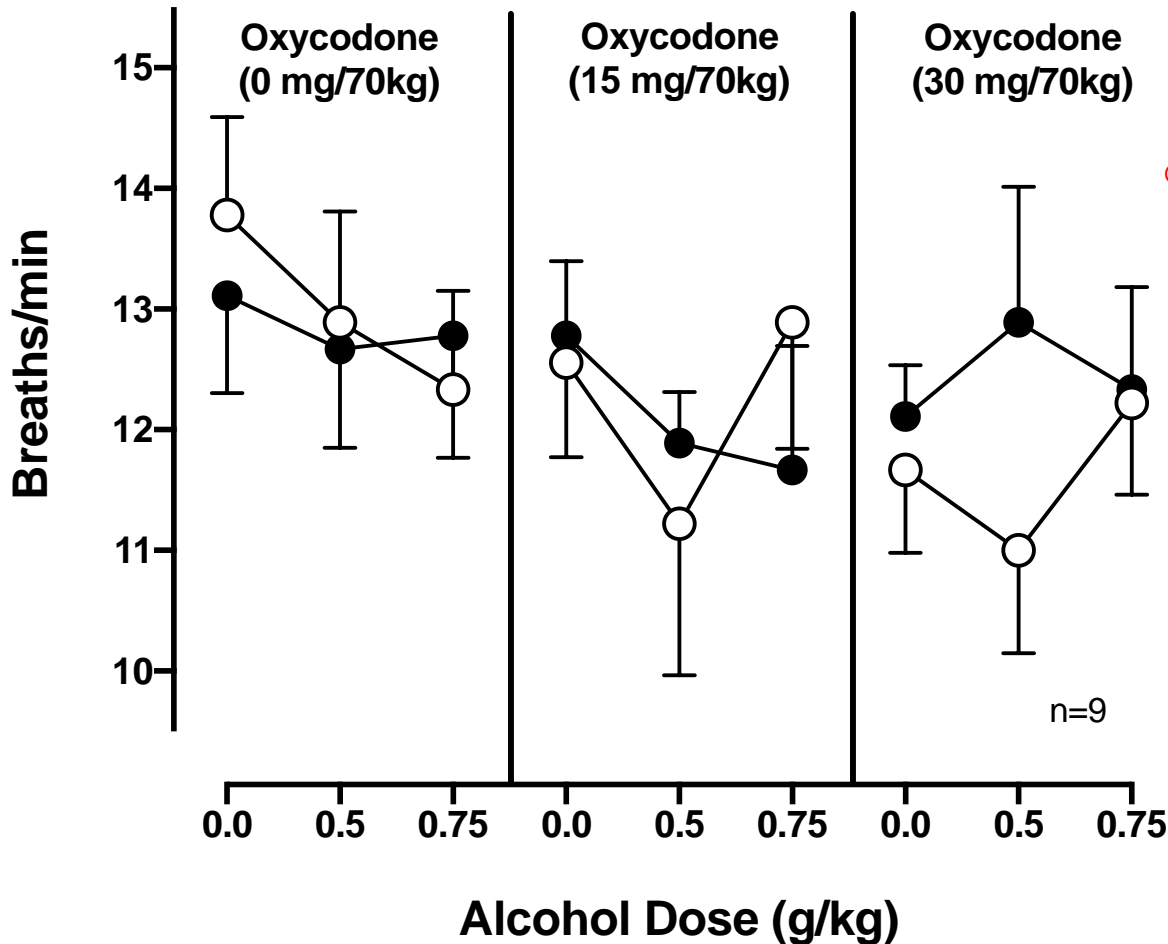


○ Gabapentin did not significantly alter oxygen saturation

Main Effect of
Oxycodone Dose: $p=0.02$
Alcohol Dose: $p=0.01$

Gabapentin Dose (PO)
○ 0 mg QD
● 1800 mg QD

Trough Respiratory Rate



○ Gabapentin did not significantly alter respiratory rate

Main Effect of Oxycodone Dose: $p=0.05$

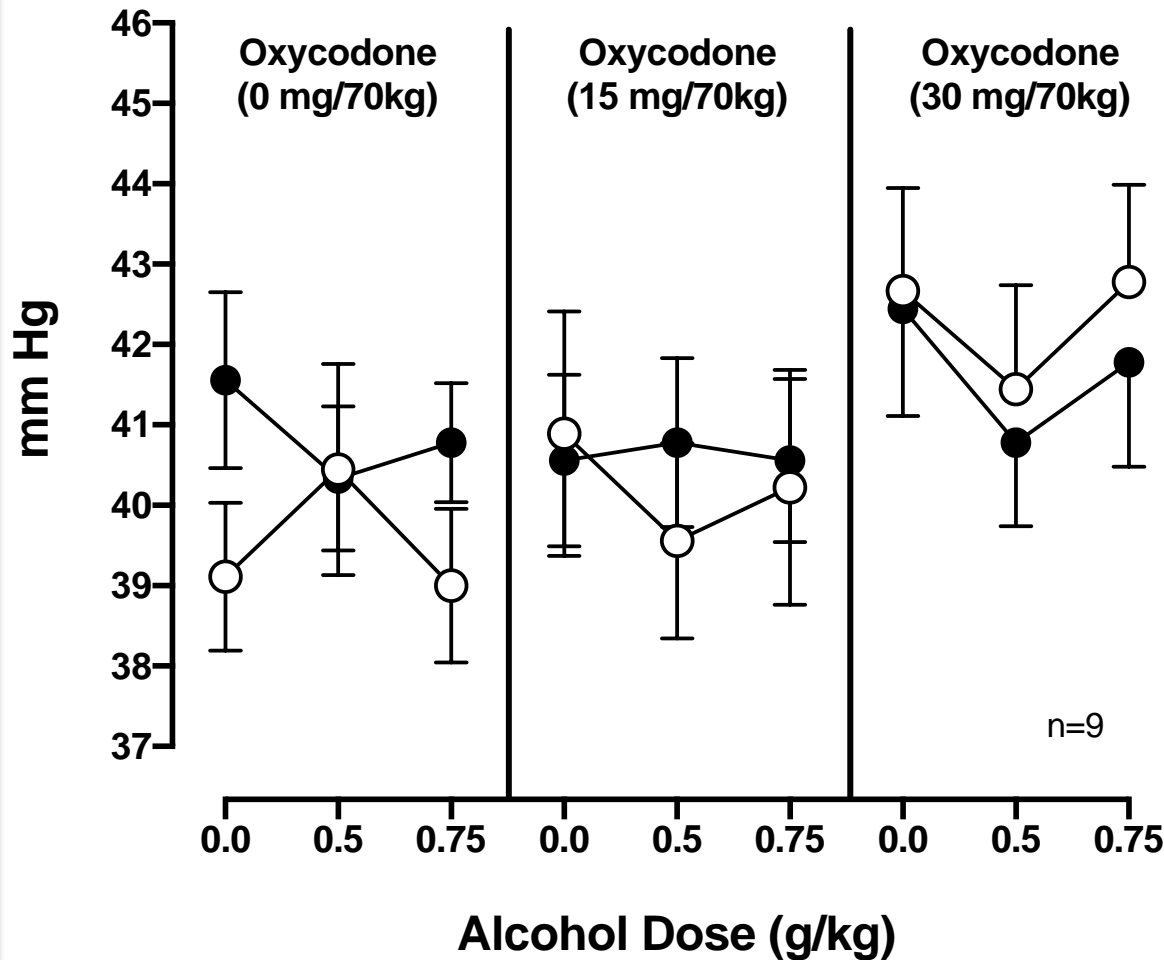
Gabapentin Dose (PO)

○ 0 mg QD

● 1800 mg QD

n=9

Peak End Tidal CO₂



○ Gabapentin did not significantly alter end tidal CO₂

Main Effect of Oxycodone Dose: $p=0.0002$

Gabapentin Dose (PO)

○ 0 mg QD

● 1800 mg QD

CONCLUSIONS

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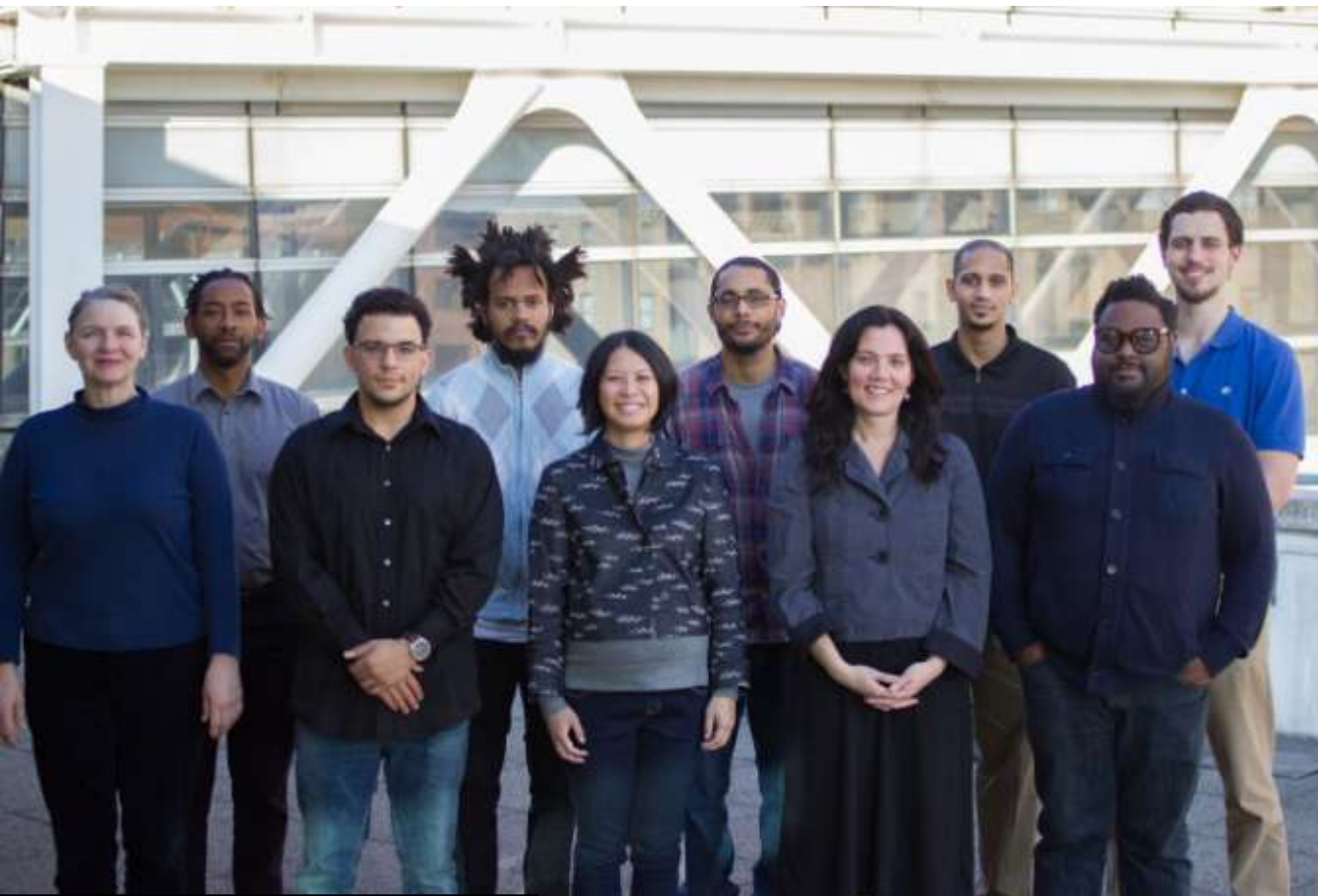
Gabapentin prescribed during substance abuse treatment: The perspective of treatment providers

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ONLINE

Google Doodle honors Herbert Kleber, who changed how we view drug addiction

The American psychiatrist saved countless lives in the process.

BY STEVEN MUSIL | SEPTEMBER 30, 2019 7:00 PM PDT

