

Predictors of Treatment Allocation Guesses in a Double-blind RCT testing Injectable Hydromorphone vs. Diacetylmorphine for Opioid Use Disorder

Kirsten Marchand, PhD (Candidate)
University of British Columbia
Vancouver, Canada

Conflict of Interest

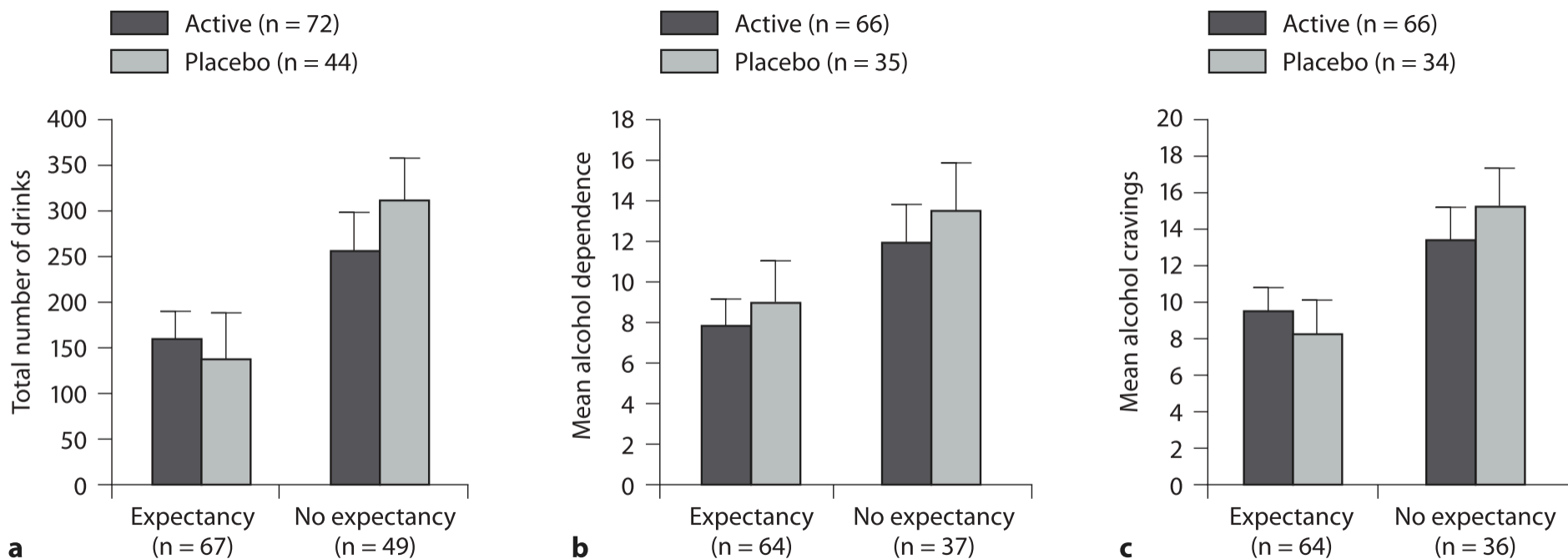
- None to declare.

Study to Assess Longer-term Opioid Medication Effectiveness (SALOME trial)

- For people with long-term opioid use disorder, not benefitting from available treatments (n=202)
- Double-blind randomization to injectable hydromorphone (HDM) or diacetylmorphine (DAM) treatment for 6 months
- Demonstrated the non-inferiority of injectable HDM vs. DAM

Motivation to Consider Expectancies in RCTs

Beliefs about treatment allocation are associated with trial outcomes, independent of the treatment received.



SALOME: Success of the Blinding Evaluation

Among trial participants:

- Tested if treatment assignment expectancy (guess) was associated with treatment outcomes
 - “What treatment do you think you are receiving?”

- Explored reasons for guesses
 - “Why do you think you are receiving X treatment?”

- Tested predictors of guess, including open reasons

Analytic Methods

- Guess groups created:
 - ✧ DAM definitely + DAM possibly = DAM
 - ✧ HDM definitely + HDM possibly = HDM
 - ✧ Unsure

- Thematic coding of open comments (n=471 codes generated from 198 participants)

- Pairwise comparisons testing differences in treatment outcomes by guess group

- Multinomial logistic regression for predictors of guess

Relevant Descriptive Data

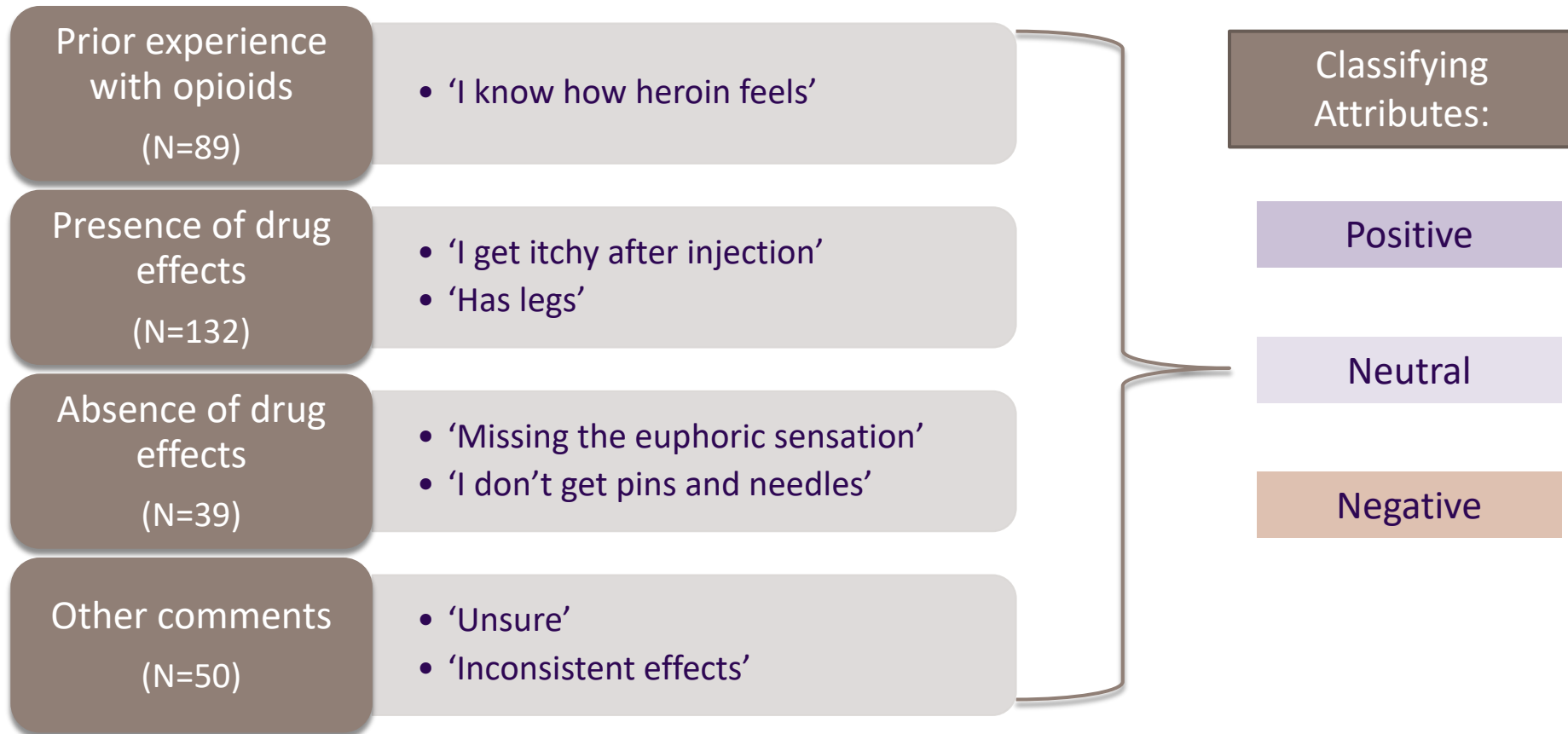
- 83% preferred DAM at baseline (before randomization)
- 82% would take HDM in real-world setting if DAM were not available
- 91% perceived the medication to be effective at T6

	Treatment Guess			
Randomization Arm	HDM	DAM	Unsure	Total
HDM	51	29	19	99
DAM	44	35	19	98
Total	95	64	38	197

Key Findings I

Why do you think you are receiving DAM, HDM or Unsure?

- Major categories and classifying attributes



Key Findings II

Efficacy Outcomes by Treatment Guess:

- Physical health: $p < 0.05$ for DAM vs. HDM and Unsure
- Psych health: $p < 0.05$ for DAM vs. HDM and Unsure

Outcome variable	Gussed DAM $n = 64$	Gussed HDM $n = 95$	Unsure $n = 39$
Prior 30 days street heroin use	4.33 ± 7.94	4.58 ± 8.82	3.33 ± 6.10
Positive for street heroin markers	15 (23.8%)	24 (26.4%)	10 (25.6%)
Prior 30 days any street opioid use ^a	5.47 ± 9.02	5.36 ± 9.24	4.74 ± 7.55
Prior 30 days crack cocaine use	7.03 ± 11.23	8.14 ± 11.22	8.79 ± 12.14
Prior 30 days illegal activities	5.41 ± 10.44	2.76 ± 6.59	3.53 ± 8.53
MAP Physical health score ^{b,d,e}	9.59 ± 7.58	12.57 ± 8.39	12.61 ± 8.51
MAP Psychological health score ^{b,d,e}	6.98 ± 7.30	9.35 ± 8.44	9.00 ± 9.40
SALOME compliance ^c	54 (84.4%)	76 (80.0%)	27 (69.2%)

Key Findings III

Predictors of guess (adjusted results):

- Drug-related high = higher odds guessing DAM vs. HDM
- Observed drowsiness event = higher odds guessing DAM vs. HDM
- Negative reasons for guess = lower odds guess DAM vs. HDM; higher odds guessing HDM vs. Unsure
- Neutral or positive reasons = higher odds guessing DAM or HDM vs. Unsure

Predictor	DAM vs. HDM OR (95% CI)	DAM vs. unsure OR (95% CI)	HDM vs. unsure OR (95% CI)
Week 1 VAS drug-related high score	1.02 (1.00, 1.03) ^a	1.01 (1.00, 1.03)	1.00 (0.98, 1.01)
Had an observed drowsiness event related to the medication: Yes vs. no	3.32 (1.44, 7.97) ^a	1.81 (0.60, 5.68)	0.54 (0.18, 1.65)
Any negative reason for perceived treatment assignment: Yes vs. no	0.14 (0.06, 0.31) ^a	2.52 (0.75, 9.29)	18.30 (6.12, 64.33) ^a
Any neutral or positive reason for perceived treatment assignment: Yes vs. no	1.91 (0.68, 5.84)	34.77 (10.8, 132.54) ^a	18.22 (6.02, 65.39) ^a

Key Message: Expectancies Matter

- Guessing DAM was associated with better self-reported health:
 - Recall that blinding and non-inferiority were demonstrated
 - Might be that people felt better and attributed this to DAM, and/or
 - People who believed they were on DAM, expected and then experienced health improvements

Key Message: Expectancies Matter

- Guesses were based on cues from prior experiences with opioids and drug-related effects:
 - Cues were not guess specific (e.g., pins and needles used by both DAM and HDM guessers)
 - Preference for DAM might have influenced expectancy
- **Suggests that the overall treatment experience and clinical outcomes could be enhanced via discussions about treatment expectations and perceived drug effects.**

Thank you!

A few key references:

- Oviedo-Joekes E, Guh D, Brissette S, Marchand K, MacDonald S, Lock K, Harrison S, Janmohamed A, Anis AH, Krausz M, et al. 2016. Hydromorphone compared with diacetylmorphine for long-term opioid dependence. A randomized clinical trial. *JAMA Psychiatry*. 73:1-9.
- Colagiuri B, Morley K, Boakes R, Haber P. 2009. Expectancy in double-blind placebo-controlled trials: an example from alcohol dependence. *Psychother Psychosom*. 78:167–171.
- Dar R, Barrett SP. 2014. The effects of beliefs regarding drug assignment in experimental and field studies of nicotine delivery devices: a review. *J Psychopharmacol (Oxford)*. 28:1071–1079.
- Crow R, Gage H, Hampson S, Hart J, Kimber A, Thomas H. 1999. The role of expectancies in the placebo effect and their use in the delivery of health care: a systematic review. *Health Technol Assess*. 3:1–110.