

Opioid withdrawal and craving trajectories following buprenorphine taper: A latent class and growth mixture model of time-to-first opioid lapse



Thomas F. Northrup, Ph.D.^a, Angela L. Stotts, Ph.D.^{a,b}, Charles Green, Ph.D.^{b,c}, Jennifer S. Potter, Ph.D.^{d,e}, Elise Marino, B.A.^d
 Roger D. Weiss, M.D.^e, Swetha S. Mulpur, B.A.^a, Robrina Walker, Ph.D.^f, & Madhukar Trivedi, MD^f



^a University of Texas Medical School-Houston, Department of Family & Community Medicine ^b University of Texas Medical School-Houston, Psychiatry and Behavioral Science ^c University of Texas Medical School-Houston, Department of Pediatrics ^d University of Texas Health Science Center at San Antonio, Department of Psychiatry ^e McLean Hospital, Division of Alcohol and Drug Abuse & Harvard Medical School, Department of Psychiatry ^f University of Texas Southwestern Medical Center, Department of Psychiatry

Contact Information: Thomas.F.Northrup@uth.tmc.edu

Introduction & Aim

- Patients who detoxify from opioid agonist therapy typically lapse to opioids (Tuten, 2011), and a majority of lapses occur within 1 month (Gossop et al., 2002).
- Two opioid-detoxification processes (i.e., craving and withdrawal) have been studied in relationship to opioid outcomes (e.g., Ziedonis et al., 2009).
- Subtype (or "latent class") analyses have shown promise to explain heterogeneous substance dependence treatment outcomes and offer novel targets for clinical intervention.
- Aim:** This secondary data analysis of the Prescription Opioid Addiction Treatment Study (POATS; Weiss et al., 2011), characterized heterogeneity among prescription opioid-dependent individuals based on trajectories of craving, withdrawal, and time-to-first lapse during buprenorphine stabilization and taper.

Participants and Procedures

- POATS was a 2-phase multisite, randomized clinical trial (NCT00316277).
- In phase 1: 653 individuals meeting criteria for opioid dependence for prescription opioids were randomized to outpatient standard medical management (SMM) or SMM + opioid dependence counseling (SMM+ODC).
- All participants were inducted on buprenorphine at the start of week 1 (max dose = 32 mg), stabilized for weeks 1 and 2 and tapered during weeks 3 and 4.
- Assessments were conducted weekly from baseline to week 4 and biweekly thereafter to week 12.
- SMM and SMM+ODC each had brief weekly visits at weeks 1-4, 6, & 8.
- SMM + ODC had two additional 45-minute drug counseling sessions in weeks 1-4, 6, & 8.
- Only phase 1 data is analyzed herein; therefore, no details on phase 2 are given.

Measures

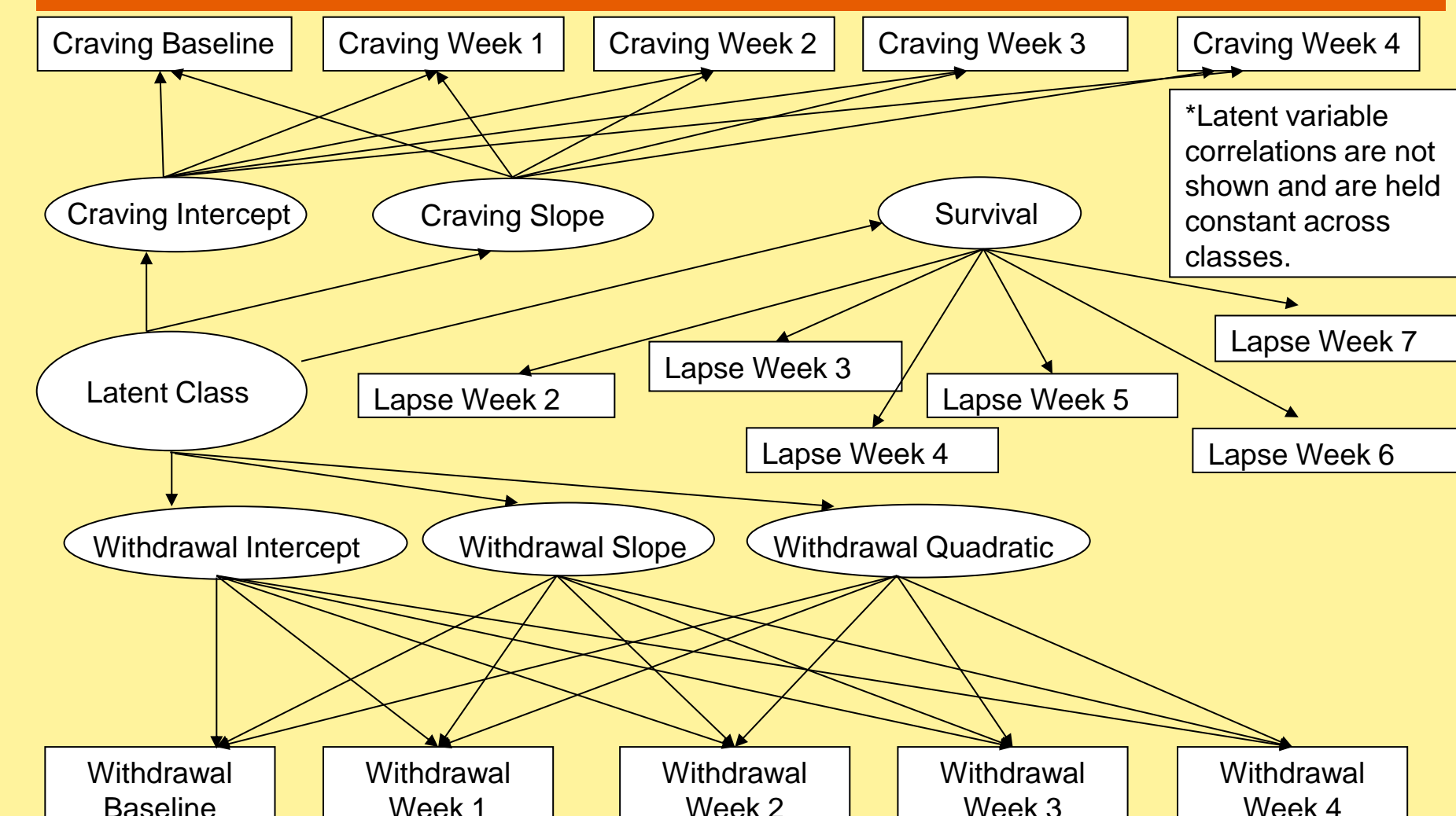
- The Opiate Craving Scale (OCS) is a 3-item unidimensional scale; scores range from 0 to 30; and, greater scores indicate higher levels of craving.
- The Clinical Opiate Withdrawal Scale (COWS) is an 11-item measure; scores range from 0 to 46; and, greater scores indicate higher levels of withdrawal.
- Drug use was measured through urine drug screens (UDS) and self-report as collected with timeline followback (TLFB) procedures.
- An opioid lapse was defined as the "week" in which ANY of the following occurred: 1) any opioid-positive UDS, 2) any missing UDS, 3) self-reported opioid use, or 4) failure to complete the TLFB.

Data Preparation and Analysis

- Time to first lapse was truncated at week 7 and COWS and OCS were truncated at week 4 due to sparse data after these time points.
- Data were analyzed with Mplus version 7 (Muthen & Muthen, 2012).
- Time to first lapse, and trajectories of craving and withdrawal were modeled simultaneously to identify latent classes of individuals using a growth-mixture model.
- Recommendations from Nylund et al. (2007) were followed:
 - Examine fit indices for models with increasing numbers of classes.
 - After identifying the model with the best fit (using the BIC) qualitatively examine classes.
 - Examine graphs of all 3 processes (craving, withdrawal, lapse-free survival) for clinical parsimony.
 - Select the model with the best balance of statistical fit and clinical relevance.

*Note: Clustering due to site was accounted for in the model.

Theoretical Model



Sample Characteristics

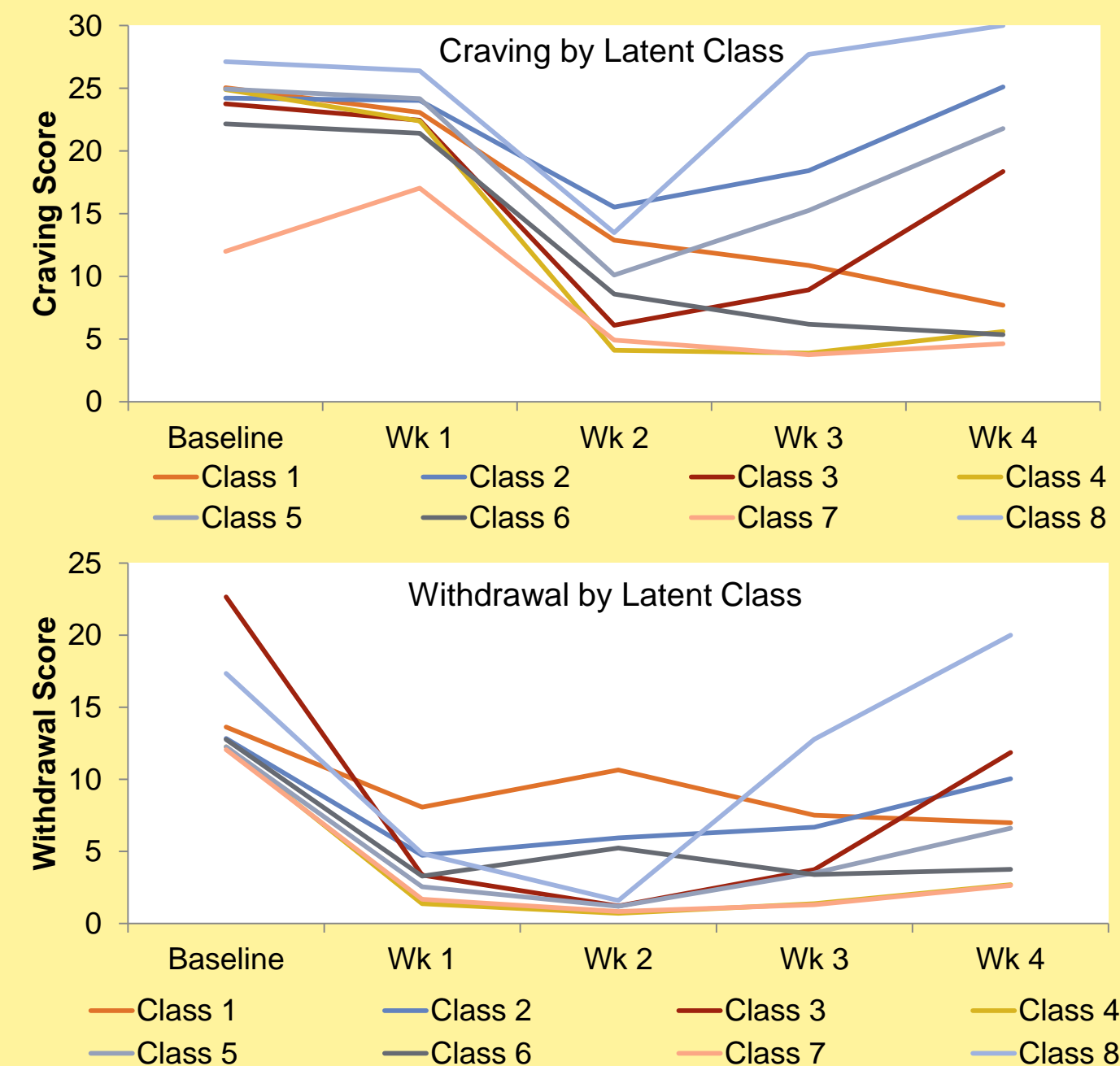
Socio-demographics		Opioid Use/Pain	
Characteristic	Value	Characteristic	Value
Age, M(SD)	33.2(10.2)	Ever used heroin, n(%)	150(23.0%)
Female, n(%)	261(40.0%)	Years opioid use, M(SD)	5.1(4.7)
White, n(%)	596(91.3%)	Opioid analgesic use (past 30 days), M(SD)	26.9(6.6)
Education (years), M(SD)	13.0(2.2)	Heroin use (past 30 days), M(SD)	0.1(0.6)
Never married, n(%)	326(49.9%)	Prior opioid use disorder treatment, n(%)	210(32.2%)
Employed full-time, n(%)	411(62.9%)	Current chronic pain, n(%)	274(42.0%)

Fit Indices by Model

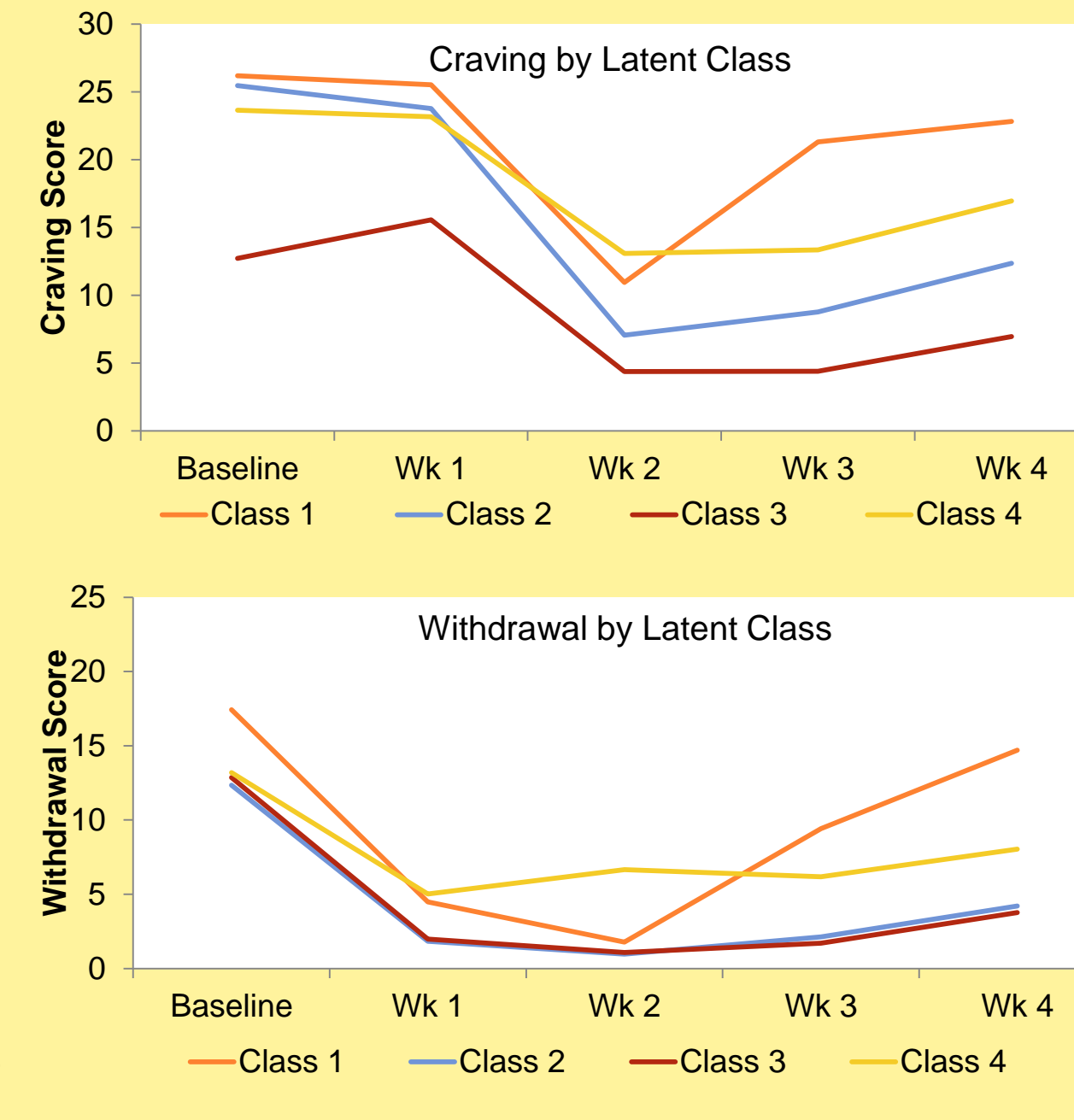
Model	AIC	BIC	aBIC	ΔBIC	Entropy	Parameters
2 Class	34477.1	34638.4	34524.1	264.1	0.63	36
3 Class	34599.3	34792	34655.5	-153.6	0.84	43
4 Class	34516.1	34740.1	34581.4	51.9	0.82	50
5 Class	34126.6	34395.5	34205.0	344.7	0.78	60
6 Class	34047.1	34351.9	34136.0	43.6	0.80	68
7 Class	33982.9	34323.4	34082.1	28.4	0.81	76
8 Class	33935.3	34311.8	34045.1	11.7	0.79	84
9 Class	33910.9	34323.2	34031.1	-11.4	0.77	92

Note. AIC = Akaike's Information Criterion; BIC = Bayesian Information Criterion; aBIC = Adjust BIC; ΔBIC = Change in BIC scores from one class to the next

8-Class Model (Best Statistical Fit)



4-Class Model (Most Clinically Parsimonious)



4-Class and 8-Class Model Comparisons

Sample Sizes:
4-Class: 1(n=45), 2(n=442), 3(n=95), 4(n=71)
8-Class: 1(n=10), 2(n=32), 3(n=25), 4(n=19), 5(n=35), 6(n=85), 7(n=261), 8(n=185)

- Craving**
- 8-Class Model:** It is hard to distinguish the craving intercept (i.e., baseline levels) and change over time across 8 classes.
 - 4-Class Model:** 4 separate patterns emerge:
 - Low baseline craving, moderate decrease, & no early rebound craving at week 3 (class 3, red line).
 - High baseline craving, large decrease, slow rebound craving at week 3 (Class 2, blue line).
 - High baseline craving, moderate decrease, slow rebound craving (Class 4, yellow line).
 - High baseline craving, moderate decrease, quick rebound at week 3 (Class 1, orange line).

- Withdrawal**
- 8-Class Model:** It is hard to distinguish the withdrawal intercept (i.e., baseline levels) and change over time.
 - 4-Class Model:** 3 separate patterns emerge:
 - Moderate baseline withdrawal, large decrease, & slow early rebound withdrawal at week 3 (Classes 2 and 3, red and blue lines).
 - Moderate baseline withdrawal, moderate decrease, and no early rebound withdrawal at week 3 (Class 4, yellow line).
 - High baseline withdrawal, large decrease, & quick early rebound withdrawal at week 3 (Class 1, orange line).

- Lapse-Free Survival**
- 8-Class Model:** There is finer separation of individuals into times at which they fail.
 - 4-Class Model:**
 - Class 1 (orange) – highest craving and withdrawal group = all failed by week 5.
 - Class 4 (yellow) – intermediate craving and withdrawal group = all failed by week 6.
 - Class 2 (blue) – relatively low craving and withdrawal group = 3.8% survive beyond week 6.
 - Class 3 (red) – lowest craving and withdrawal group = 4.2% survive beyond week 6.

Note. 5 classes were smaller than n = 35

Conclusions

- The overwhelming majority of individuals dependent on opioids who detoxify from opioid agonist therapy in an outpatient setting will experience a lapse within 6 weeks; however, individuals were successfully parsed into clusters experiencing similar levels of craving and withdrawal, and lapse episodes.
- Individuals who report lower initial and ongoing craving and withdrawal tend to have longer times to first opioid use.
- Monitoring craving and withdrawal during buprenorphine induction, stabilization, and detoxification may allow more individually tailored and timely interventions to be developed and delivered to extend time-to-first opioid lapse.
- This was the first latent class analysis to our knowledge that simultaneously modeled craving, withdrawal, and opioid use and needs to be replicated in future research.

References & Acknowledgements

- Full references are available from the 1st author by e-mail request.
- POATS (CTN-0030) was supported by the National Institute on Drug Abuse of the National Institutes of Health under Award Numbers U10 DA15831 and K24 DA022288 (PI: Weiss).
- The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.
- The authors have no conflicts of interest to disclose.