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.a,c, Jennifer S. Potter, Ph.D.a,e, Elise Marino, B.A.d
Roger D. Weiss, M.D.a, Swetha S. Mulpur, B.A.b, Robrina Walker, Ph.D.a, & Madhukar Trivedi, M.D.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 Addictive 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: 663 individuals meeting criteria for opioid dependence for prescription opioids were randomized to outpatient standard medical management (SMM) or SMM + opioid dependence counseling (SMM+ODC).
- 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, 10.
- SMM+ODC had two additional 45-minute drug counseling sessions in weeks 1-4, 6, 8.

Measures

- The Opiate Craving Scale (OCS) is a 3-item unidimensional scale; scores range from 0 to 70; and, greater scores indicate higher levels of craving.
- The Clinical Opiate Withdrawal Scale (COWS) is an 11-item measure; scores range from 0 to 60, 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.

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 Gleyzal et al. (2007) were followed:
1. Examine fit indices for models with increasing numbers of classes.
2. After identifying the model with the best fit (using the BIC) qualitatively examine classes.
3. Examine graphs of all 3 processes (craving, withdrawal, lapse-free survival) for clinical parsimony.
4. 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

- 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.

Conclusions

References & Acknowledgements

- Full references are available from the 1st author by e-mail request.
- POATS (CTN-0330) was supported by the National Institute on Drug Abuse of the National Institutes of Health under Award Numbers U01 DA15831 and K24 DA02288 (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.

Sample Characteristics

- **Characteristics**
  - Age, M(SD): 33.2 (10.2)
  - Ever used heroin, n(%): 75.1 (23.0)
- **Opioid Use-Pain**
  - White, n(%): 596 (91.3)
  - Years opioid use, M(SD): 5.1 (4.7)

- **Education (years), MSID:**
  - Class 5: 13.0 (2.2)

- **Never married, n(%):**
  - Class 5: 326 (49.9)

- **Employed full-time, n(%):**
  - Class 5: 411 (62.9)

- **Craving by Latent Class**
  - Class 1: 20.2
  - Class 2: 25.2
  - Class 3: 15.1
  - Class 4: 30.1
  - Class 5: 10.8

- **Withdrawal by Latent Class**
  - Class 1: 20.2
  - Class 2: 25.2
  - Class 3: 15.1
  - Class 4: 30.1
  - Class 5: 10.8

- **Lapse by Latent Class**
  - Class 1: 4.2%
  - Class 2: 3.8%
  - Class 3: 7.3%
  - Class 4: 9.7%
  - Class 5: 1.5%

- **Free Survival by Model**
  - Class 1: 34477.1
  - Class 2: 34638.4
  - Class 3: 34524.1
  - Class 4: 34581.4
  - Class 5: 34618.1

- **Notes:**
  - 1. Gleyzal et al. (2007) recommended the use of the BIC for selecting the best model.
  - 2. The BIC is a measure of model fit that penalizes for model complexity.
  - 3. Chi-square (χ²) tests were not used for model selection because they are sensitive to sample size and may not be reliable for complex models.
  - 4. Theoretical Model: There is finer separation of individuals in times at which they fail.

Sample Sizes

- **Class:**
  - Class 1: 269 (44)
  - Class 2: 282 (42)
  - Class 3: 93 (15)
  - Class 4: 71 (12)
  - Class 5: 35 (6)

References & Acknowledgements

- Full references are available from the 1st author by e-mail request.
- POATS (CTN-0330) was supported by the National Institute on Drug Abuse of the National Institutes of Health under Award Numbers U01 DA15831 and K24 DA02288 (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.

References & Acknowledgements

- Full references are available from the 1st author by e-mail request.
- POATS (CTN-0330) was supported by the National Institute on Drug Abuse of the National Institutes of Health under Award Numbers U01 DA15831 and K24 DA02288 (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.