

**ALCOHOL WITHDRAWAL AND CRAVING AT TREATMENT ENTRY  
PROSPECTIVELY PREDICT ALCOHOL USE OUTCOMES DURING  
OUTPATIENT TREATMENT**

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## Prevalence, Disease Burden and Mortality

Alcohol misuse and AUD are major public health problems worldwide significantly associated with consequences and global disease burden.

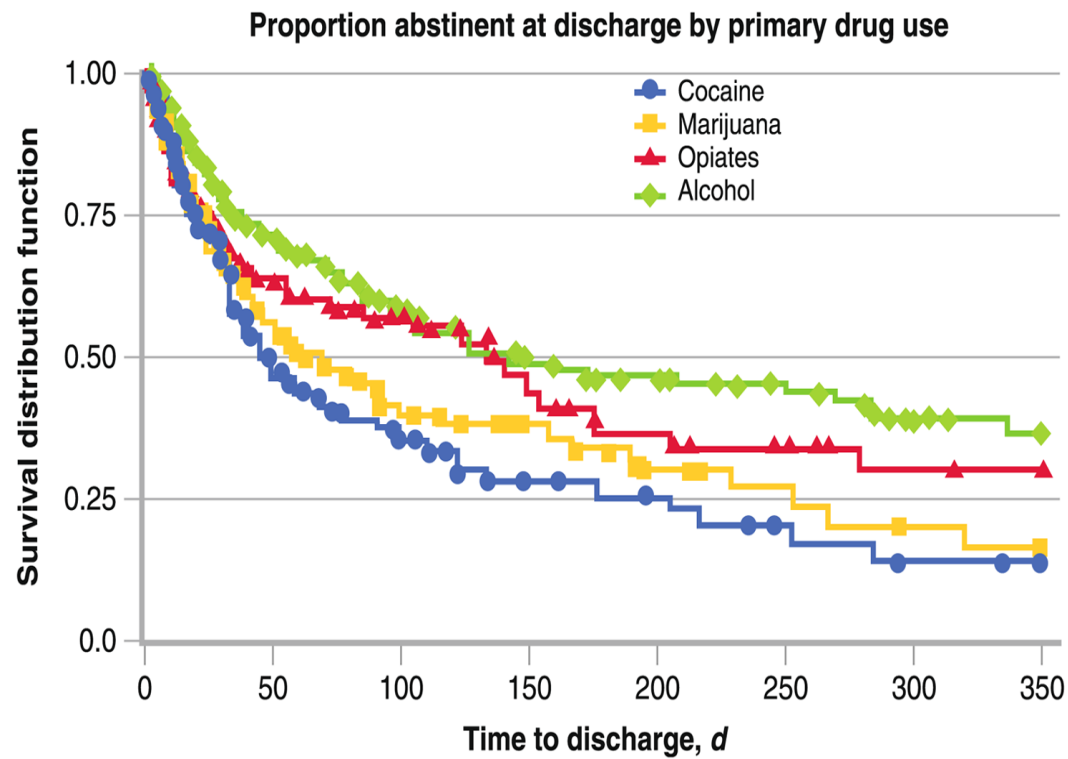
– Prevalence of alcohol use disorders:

- Globally ~ 1.4 percent of the population have AUD (107 million)
- In the US, nearly ~15 million people have AUD



# Modest Efficacy of AUD Treatments

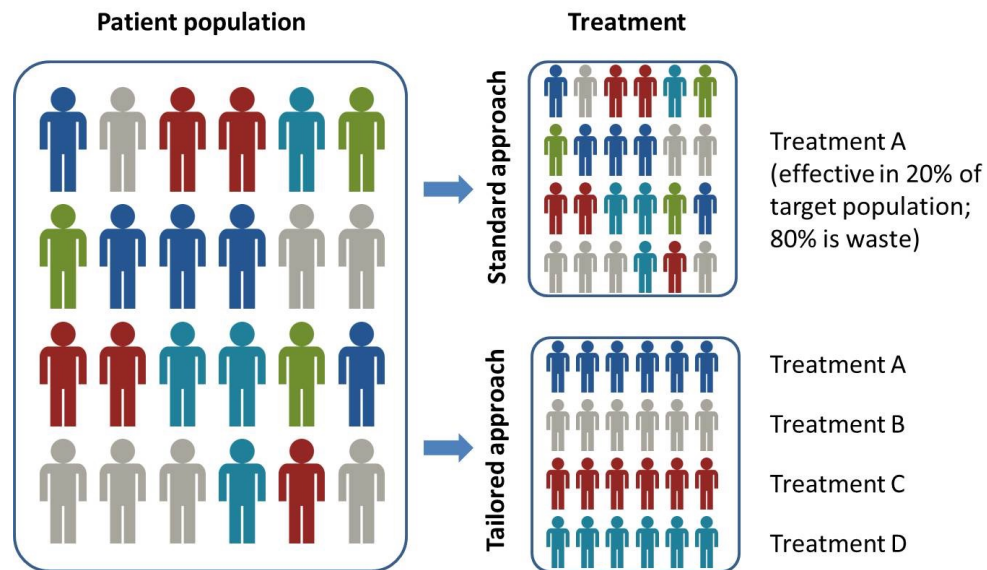
Treatment failure and high relapse rates are the norm in AUD treatment.



# Precision Medicine and Personalized Treatment of AUD

Recent initiatives (e.g., Litten et al., 2015; Witkiewitz et al. 2019) aimed at improving **personalized treatment of AUD**:

- 1) The need to identify **AUD clinical features** that differentiate those at increased risk for relapse and treatment failure.
- 2) To develop **treatments** specifically targeted for those who are at risk.



# AUD-Related Disruptions in the Stress Pathophysiology

Early alcohol abstinence in AUD:

- Altered stress and reward brain neurocircuitry (Koob, 2003; Seo, 2013)
- Disrupted prefrontal-striatal and HPA axis function (Blaine et al., 2020)
- Clinical symptoms: AW, craving, depression, anxiety, sleep difficulties



**Stress**

+



**Contextual Cues**

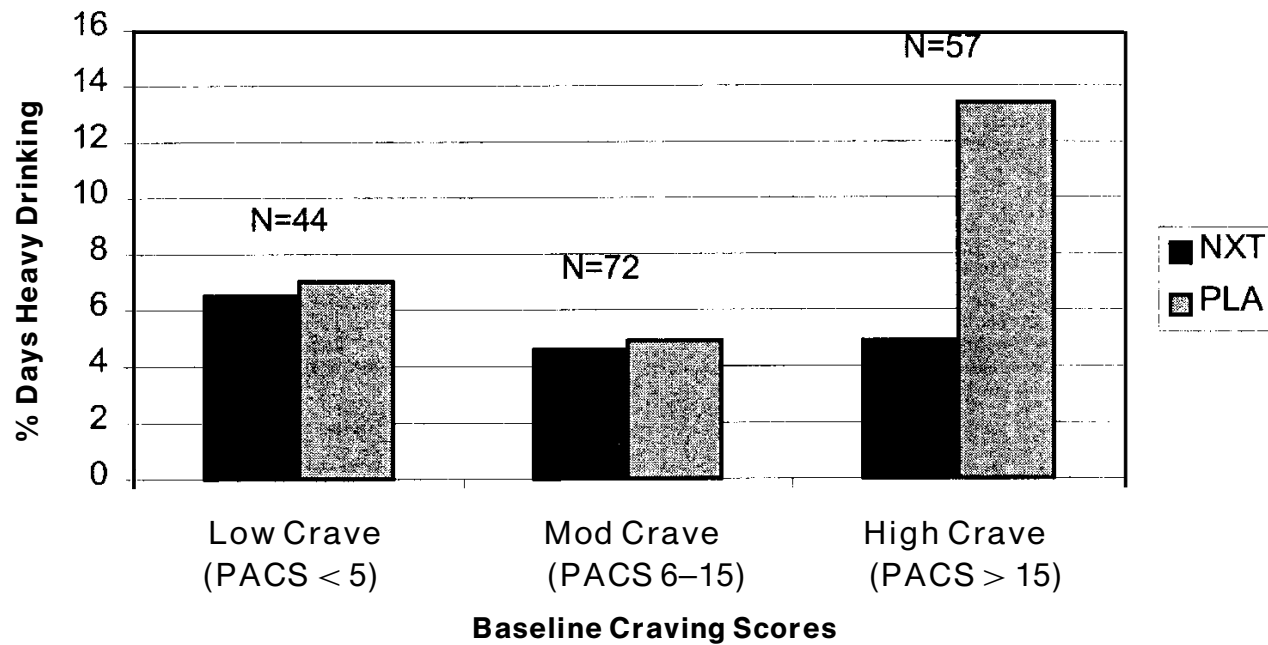
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**Relapse**

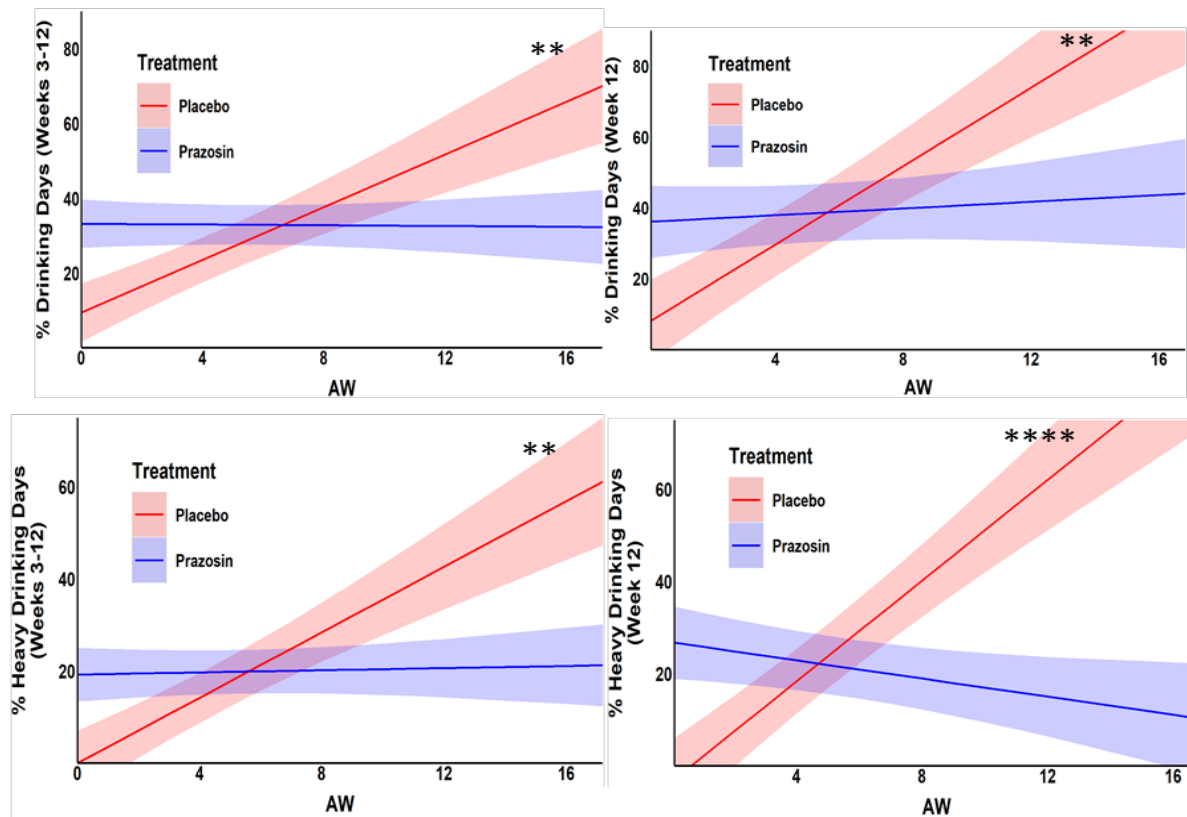
## Moderators of Medication Efficacy

Medication efficacy of **naltrexone** for AUD treatment may be moderated by **alcohol craving** (Monterosso et al., 2001).



# Moderators of Medication Efficacy

Medication efficacy of **prazosin** for AUD treatment may be moderated by **alcohol withdrawal (AW) symptoms** (Sinha et al., 2020).



Sinha et al., 2020 AJP

## Clinical Prognostic Indicators of AUD Treatment Response

Despite this evidence of relapse and treatment failure risk in those showing such stress pathophysiology of AUD, research to specifically assess whether these clinical features of AUD significantly impact alcohol use outcomes in outpatient treatment has lagged behind.



# **SPECIFIC AIMS AND OBJECTIVES**

## Specific Aims and Objectives

- ❑ **Primary Aim(s):** To examine whether clinical features of AUD–Alcohol Withdrawal (AW) and craving–would *prospectively* predict alcohol use during treatment.
- ❑ **Secondary/exploratory Aim(s):** To determine whether greater clinical symptoms of depression, anxiety, and sleep difficulties would also *prospectively* predict alcohol use outcomes during outpatient treatment.

# **METHODS**

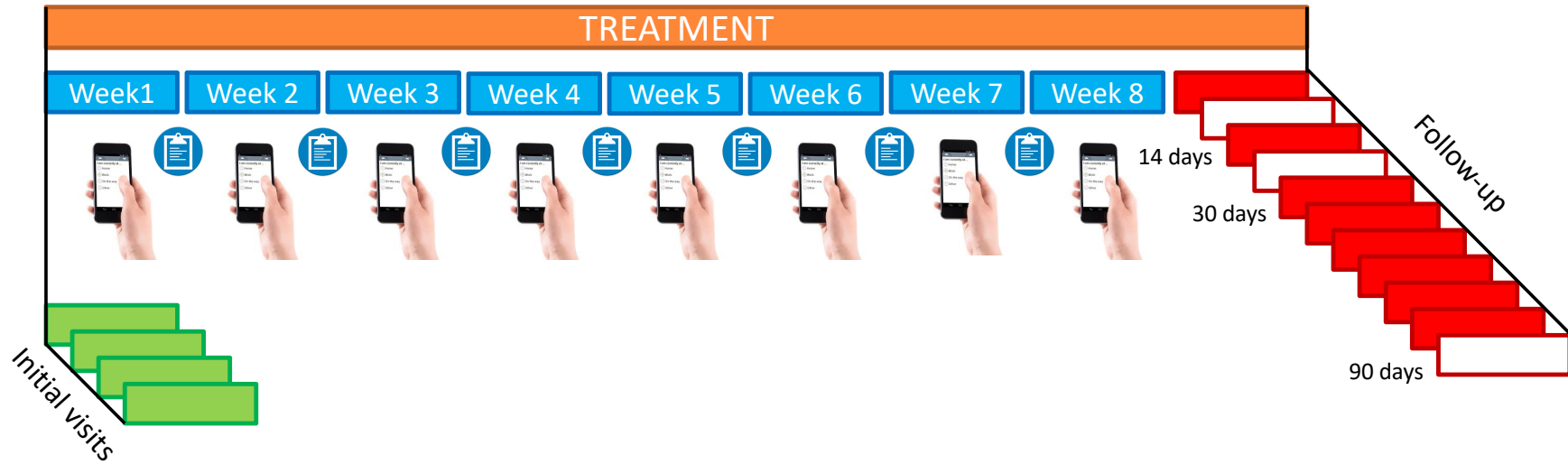
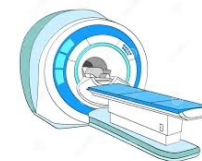
# Participants

- **80 AUD treatment-seeking community adults** with current DSM-5 moderate to severe AUD – Greater New Haven area
  - 20 to 60 years-old
  - Mean age = 36.6 (*SD* = 11.24)
  - 39.8% Female
  - 42.5% White
- **Eligibility criteria:**
  - Aged between 18 and 60
  - DSM-5 diagnosis for AUD
  - Positive alcohol urine toxicology screen at admission
- **Exclusion criteria:**
  - Current DSM-5 diagnosis for SUD
  - Severe psychiatric disorder
  - Acute untreated medical condition

# Study Design & Protocol



*Manualized 12-Step Facilitation and Relapse Prevention Therapy*



# Study Design & Protocol

## – Initial visits and baseline assessments at intake

- Demographic information (sex, age, race, and SES)
- Clinical Institute of Withdrawal Assessment for Alcohol-revised (CIWA-Ar)
- Alcohol Urge Questionnaire (AUQ)
- Hamilton Anxiety Scale (HAS)
- Beck Depression Inventory (BDI)
- The Pittsburgh Sleep Quality Index (PSQI)
- 90-day Substance Use Calendar
- The Structured Clinical Interview for DSM-5 (SCID-5)

# Study Design & Protocol

- **Weekly behavioral counseling and assessments:**
  - 1x week treatment sessions using standardized 12-Step and relapse prevention approach as outlined in the NIAAA Project MATCH manuals
  - Timeline follow-back assessments using the 7-day SUC
- **Daily ecological momentary assessment (EMA):**
  - Brief surveys administered in a smartphone application (MetricWire, Inc.)
    - Daily morning and evening prompts (and random prompts)
    - total number of drinks consumed (beer, wine, and liquor)
  - Acceptable compliance rate (approx. 69%)

# Clinical Predictors & Drinking Outcomes

## – Clinical predictors:

- Alcohol Withdrawal (AW)
- Alcohol Craving
- Depression
- Anxiety
- Sleep Problems

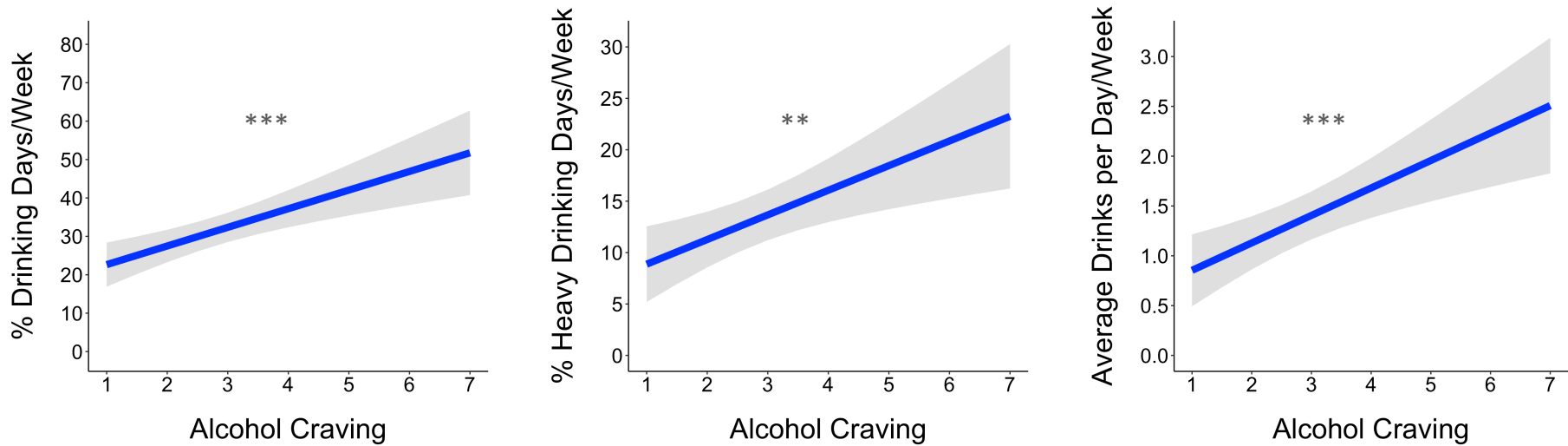
## – Drinking outcomes:

- Percent drinking days/week (DD)
- Percent heavy drinking days/week (HDD)
- Average drinks per day/week (AvgD)
- Time to dropout (i.e., time to withdraw from the study)
- Time to lapse (i.e., time to first drink),
- Time to relapse (i.e., time to first heavy drinking day).



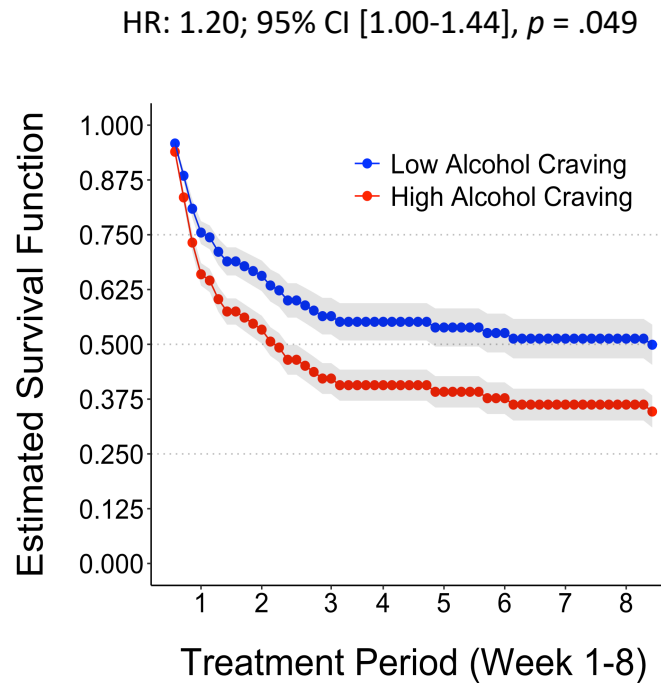
# RESULTS

# Alcohol Craving Predicting Treatment Response



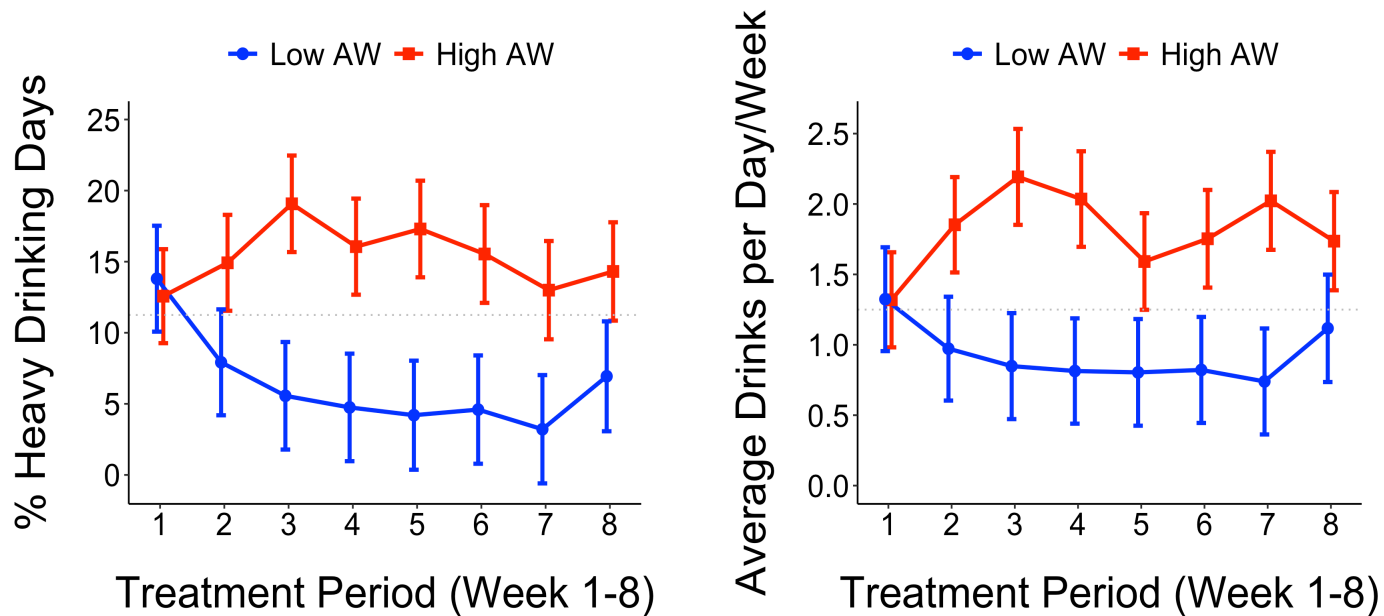
Significant main effects of craving on DD ( $p < .001$ ), HDD ( $p < .009$ ), and AvgD ( $p < .001$ ) during treatment.  
*Covariate Adjustment:* # abstinence days, past 90-day alcohol use, age, sex, race, and SES

# Alcohol Craving Predicting Treatment Response



Baseline alcohol craving (continuous scores) predicted risk of relapse to heavy drinking during treatment.  
*Covariate Adjustment:* # abstinence days, past 90-day alcohol use, age, sex, race, and SES

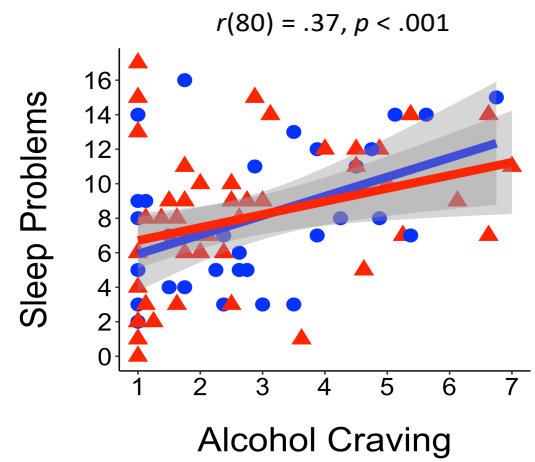
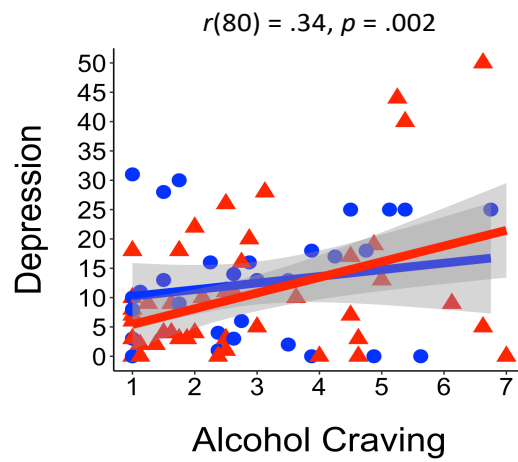
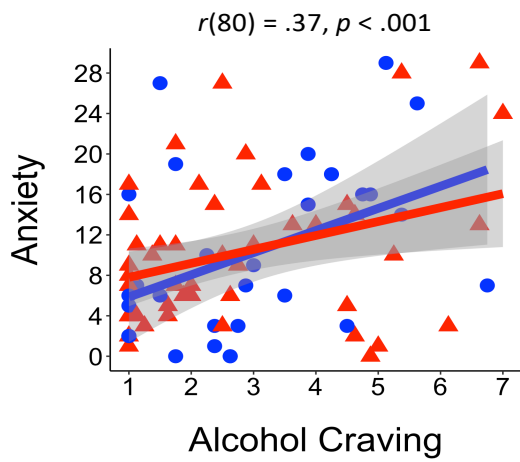
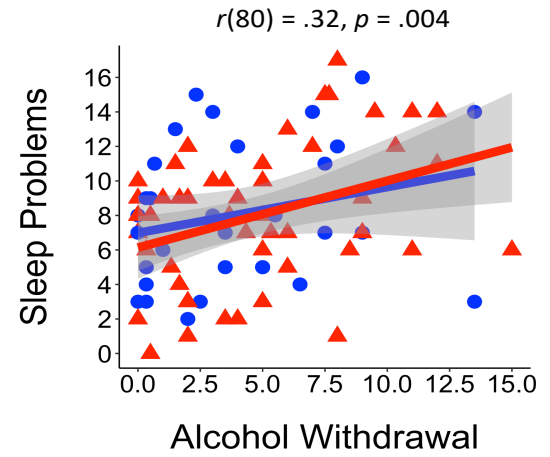
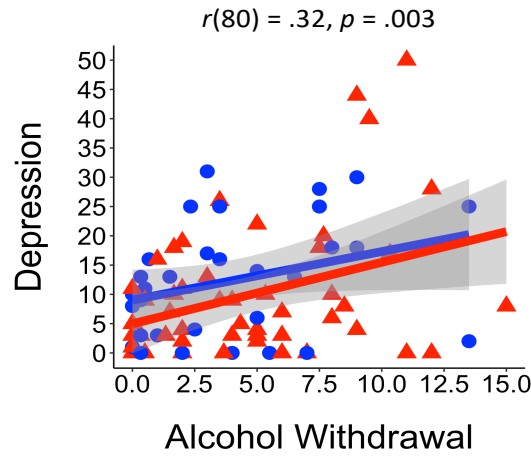
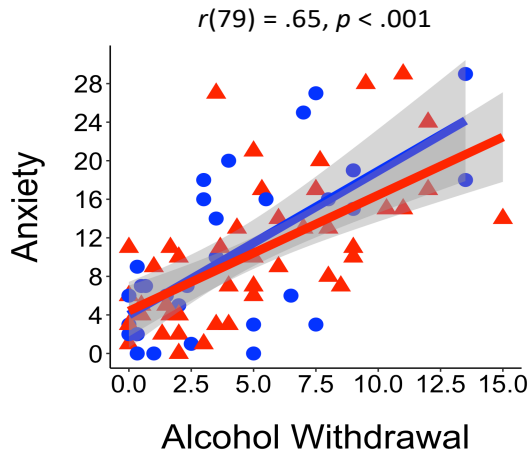
# Alcohol Withdrawal (AW) Predicting Treatment Response



Significant interaction effects of baseline AW with treatment week on HDD ( $p < .018$ ) and AvgD ( $p < .004$ )  
*Covariate Adjustment*: # abstinence days, past 90-day alcohol use, age, sex, race, and SES

# Alcohol Abstinence-Related Symptoms

Male  
Female



# Conclusion

## Conclusion

- Higher levels of craving *consistently* predicted higher levels of alcohol intake during treatment (Schlauch et al., 2019; Mchugh et al. 2017) and risk of relapse to heavy drinking (Sinha et al., 2011; Higley et al., 2011).
- Pretreatment levels of AW predict different trajectories in treatment response throughout the treatment period.
- Pretreatment symptoms of depression, anxiety, and sleep difficulties did not predict any drinking-related outcome during treatment.
- Predictive effects of AW and craving on treatment response hold up after controlling for drinking levels prior to treatment entry.

## Take Home Message

Pretreatment AW and alcohol craving, as assessed via Clinical Institute of Withdrawal Assessment for Alcohol (CIWA-Ar) and Alcohol Urge Questionnaire (AUQ), may serve as clinical prognostic indicators of alcohol use outcomes and AUD treatment response.

- Growing evidence suggesting that manifestations of **AUD-related disruptions** reflect manifestations of **stress pathophysiology**.
- Critical for understanding the wide **heterogeneity** of AUD treatment responses to improve AUD treatment outcomes.
- Treatments targeted **normalizing** and **stabilizing** AUD disruptions.



# Thank you!

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**National Institute on Alcohol  
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