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# Using a randomized controlled trial to test whether modifications to contingency management improve outcomes for heavy drinkers with serious mental illness

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ABSTRACT

*Background:* In contingency management (CM), individuals receive rewards for alcohol abstinence. CM is associated with reduced alcohol use in adults with co-occurring serious mental illnesses (SMI). Pre-treatment urine ethyl glucuronide (uEtG) levels equivalent to daily heavy drinking (uEtG > 349 ng/mL) are associated with poor response to CM. Modifications to CM are needed to improve outcomes for non-responders.
*Aims:* To determine if pre-treatment heavy drinkers, defined by uEtG, with SMI achieve higher levels of alcohol abstinence when they receive an increased magnitude of reinforcement for abstinence (High-Magnitude CM) or reinforcers for reduced drinking, prior to receiving reinforcers for abstinence (Shaping CM), relative to those who receive typical low-magnitude abstinence based CM (Usual CM). Additionally, variables in the Addictions Neuroclinical Assessment model will be examined as treatment response moderators.
*Methods:* Participants ($N$ = 400) will be recruited from two urban mental health organizations and complete a 4-week induction period where they will be reinforced for submitting samples for uEtG testing. Participants who attain a mean uEtG > 349 mg/mL will be randomized to receive either Usual CM, High-Magnitude CM, or Shaping CM for 16 weeks. Differences in abstinence, assessed by uEtG, will be examined during treatment and during a 12-month follow-up. Measures of negative emotionality, alcohol reinforcer salience, and executive functioning will be gathered at study intake and used to predict treatment outcomes.
*Discussion:* This novel approach to CM will use an alcohol biomarker to identify those at risk for treatment non-response and determine if adaptations to CM might improve outcomes for this group.

## 1. Introduction

Forty-six percent of individuals with serious mental illnesses ([SMI]; i.e.,schizophrenia spectrum, bipolar, and recurrent major depressive disorders) have a co-occurring alcohol use disorder (AUD) [1–4]. Relative to people with SMI who do not use substances, those who use alcohol or drugs experience higher levels of psychotic symptoms, inpatient psychiatric care, medical expenditures, homelessness, treatment attrition, suicidal behavior, and cognitive impairment [5–14]. Few individuals receive treatment for co-occurringSMI and AUDs, and even fewer individuals receive evidenced-based treatments [15,16].

Contingency management (CM) is a behavioral intervention that provides low-cost reinforcers (i.e.,total of $250–$400) for drug and alcohol abstinence [17] and is associated with decreased alcohol and drug use in individuals with SMI [18–21]. In a previous study of CM as a treatment for AUD in adults with SMI, we used the alcohol biomarker, urine ethyl glucuronide urine (uEtG) to assess abstinence. uEtG can detect use during the previous 2 days and heavy drinking up to 5 days

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after drinking [20,22,23]. CM participants were 3.1 times more likely to submit negative uEtG samples, relative to those receiving treatment-as-usual (TAU) and reinforcers for participation only [20]. However, participants with a pre-treatment uEtG > 499 ng/mL (i.e.,daily heavy drinking) did not respond to CM [20].

This finding is consistent with other studies that have found that biologically verified drug use immediately prior to treatment is associated with poor response to low-cost, abstinence-based CM [24–27]. Increasing reinforcer magnitude (i.e.,high-magnitude CM) is associated with improved outcomes, particularly for those who submitted drug-positive urine tests immediately prior to CM treatment [17,28–30]. Providing reinforcers for reductions in substance use before requiring abstinence (i.e.,shaping CM) is also associated with improved outcomes for people who smoke cigarettes or use drugs, who do notrespond to a typical low-cost abstinence-based CM [31–33]. However, no study has investigated the effectiveness of these CM adaptions for treating AUDs, or compared these approaches to one another.

While others have investigated predictors of treatment response, noprevious study has examined predictors of outcomes using a theoretical framework. The Addictions Neuroclinical Assessment (ANA) framework, developed by the National Institute on Alcohol Abuse and Alcoholism (NIAAA), is a neuroscience-based framework for explaining the causes and maintenance of addiction [34]. This framework postulates three domains – poor executive functioning (e.g.,working memory, impulsivity), negative emotionality (e.g.,depression, anxiety, psychological symptoms of withdrawal), and high levels of alcohol-relatedincentive salience (e.g.,thinking about alcohol, craving a drink) – asthe primary factors that cause and maintain AUDs. This model maybe particularly applicable to heavy drinkers with SMI, because these individuals experience high levels of negative emotions, poor working memory, and high levels of impulsivity and alcohol-cravings [35,36].

Funded by NIAAA (R01AA020248), we will be conducting a randomized clinical trial to determine the following aims: 1) whether levels ofalcohol abstinence during the last 3 months of treatment, and a 12-month follow-up period vary by CM condition; 2) whether groups differ on secondary alcohol outcomes, drug use, psychiatric severity, HIV risk behavior, and cigarette smoking; and 3) identify ANA-based moderators of CM treatment response across and within CM conditions.

## 2. Methods

### 2.1. Study design

Participants ($N$ = 400) recruited from two urban mental health organizations will first take part in a 4-week induction phase during which they will receive reinforcers for submitting 2 urine samples per week, regardless of uEtG results. Participants who meet secondary eligibility criteria of attendance (estimated $N$ = 240; see below) and uEtG-defined heavy drinking (uEtG > 349 ng/mL) will be randomized to receive either, a)4 months of standard-magnitude reinforcement CM for submitting alcohol-negative samples (uEtG < 150 ng/mL; Usual CM); b)4 months of high-magnitude CM for submitting alcohol-negative samples (High-Magnitude CM); or c)1 month of standard-magnitude CM for submitting urine samples that indicate light drinking (uEtG < 350 ng/mL), followed by 3 months of standard-magnitude CM for submitting alcohol-negative samples (Shaping CM). Our CM paradigm will use the variable magnitude of reinforcement procedure (VMRP), in which participants draw from a bowl for chances to receive items and gift cards. Groups will differ only on the number of drawsthey receive (Usual vs. High-Magnitude), or the contingency bywhich they are allowed to engage in draws (light drinking vs. abstinence).

Randomized participants will complete follow-up assessments at 1, 3, 6, and 12 months to assess long-term outcomes. The primary outcome will be alcohol abstinence, assessed as uEtG < 150 ng/mL, during the last 3 months of treatment (when all reinforcers are contingent on abstinence) and the 12-month follow-up period.

### 2.2. Study procedures

#### 2.2.1. Participant eligibility

Inclusion criteria include the following: 1) 4 or more standard drinks on 5 or more occasions in the past 30 days; 2) Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) diagnosis of moderate to severe AUD [37]; 3) DSM-5 diagnosis of schizophrenia or schizoaffective, bipolar I or II, or recurrent major depressive disorder (> 1 episode); 4) age 18–65 years; and 5) receipt of, or eligibility to receive TAU at study sites. Exclusion criteria include the following: 1) current DSM-5 diagnosis of a severe drug use disorder; 2) inability to demonstrate competency to provide consent on the MacAuthur Competence Assessment Tool for Clinical Research (MacCAT-CR); 3) risk of medically dangerous alcohol withdrawal (i.e.,seizure within the last 12 months, concern by participant or clinician regarding a potentially dangerous withdrawal); 4) prior diagnosis of dementia; and 5) determination by the Principal Investigator (PI) and medical director that participation would be medically or psychiatrically unsafe.

#### 2.2.2. Randomization procedures

Participants will be randomized to treatment conditions based on permuted block randomization and stratified across the following variables: 1) study site, 2) gender, and 3) baseline uEtG level > 1000 ng/mL (e.g., > 8 standard drinks), which indicates very heavy recent drinking.

### 2.3. Induction phase

Eligible participants will take part in a 4-week induction phase, during which they will engage in the VMRP procedure 2 times a week for providing urine samples. At each visit, they will receive 3 draws for prizes when they provide urine samples, regardless of whether the samples are positive for alcohol use. Those who provide at least 1 urine sample during each of these 4 weeks will receive a $20 bonus incentive. Consistent with previous studies [38] participants who 1) attain an average uEtG level of > 349 ng/mL (indicating recent heavy drinking) and 2) attend at least 1 study visit during the final week of the induction phase will be randomized. Participants who do not meet criteria for randomization will be referred to other available AUD treatments (See Fig.1). Although our published research demonstrates that uEtG > 499 ng/mL is associated with poor treatment response [20], unpublished analyses suggested that a lower cut-off of uEtG > 349 ng/mL predicts poor treatment response similar to a uEtG cut-off > 499 ng/mL. The use of a lower cut-off of uEtG > 349 ng/mL cut-off will allow increase the number of potential participants randomized into the 3 CM conditions during the treatment phase.

### 2.4. Study intervention

#### 2.4.1. Treatment-as-usual

All participants will receive psychiatric services and addiction TAU. The two urban mental health organizations provide a variety of services at multiple locations in their respective cities (Spokane and Seattle, Washington). Case management, medication management, group and individual counseling, vocational services and housing services will be available to participants based on their individual needs. These organizations also offer outpatient addiction treatment and referrals to local addiction agencies.

#### 2.4.2. Prize draws

Participants in the 3 CM conditions will engage in VMRP each time they meet criteria for obtaining reinforcers over the 16-week treatment phase. Table1 illustrates how groups will differ only by the number of times they engage in prize draws (Usual CM vs. High-Magnitude CM) or the criterion required to receive reinforcement (light drinking vs. abstinence). VMRP will involve drawing from a bowl of 500 chips, some