Summary of Study Protocol Required by JAMA Psychiatry

1. Final Washington State University IRB Protocol
2. Statistical Analysis Plan

Principal Investigator: Michael McDonell

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Washington State University **I**nstitutional **R**eview **B**oard (**IRB**)
Office of Research Assurances
PO Box 643005 Albrook 205
Pullman, WA 99164-3005
Telephone: (509)335-3668 Fax: (509)335-6410 Email: irb@wsu.edu

Web site: http://www.irb.wsu.edu/

Human Subject Application: Non-Exempt (Expedited and Full Board Review)

IRB Use Only
IRB application No: _____

Institutional Review Board: These assurances are acceptable and this project has adequate protections for participants. This project has been properly reviewed and filed and is in compliance with federal and state law, and University regulation.

Review Status Assigned:

☐ Expedited ☐ Full Board
☐ No IRB Review Required ☐ Exempt ☐ Non-Regulatory Review

Signature:_____ Print Name:_____ Date:_____

Instructions

- ***Do NOT begin data collection prior to IRB approval.***
- ***All materials must be typed; handwritten materials will be returned.***
- ***DO NOT leave a question blank; write "n/a" if a question does not apply to the application.***
- ***WSU researchers (faculty and staff) conducting research in Deaconess Medical Center, Holy Family Hospital, Sacred Heart Medical Center, St. Luke's Rehabilitation Institute, and Valley Hospital & Medical Center should contact WSU IRB at 335-3668 or irb@wsu.edu prior to filing this application.***
- ***WSU researchers (faculty and staff) using DSHS records or facilities should contact WSU IRB at 335-3668 or irb@wsu.edu prior to filling this application.***
- ***If required, complete the addendums on the website and submit them along with the application.***

1. Principal Investigator (PI) Contact Information: (*PI must be WSU faculty or staff, and will be the study supervisor at WSU. Students, post-doctoral researchers, and visiting faculty may not serve as PI, but may be listed as co-investigators in Section 1. All correspondence will be directed to the PI listed below.*)

Last Name: McDonell First Name: Michael WSU ID #: [redacted]

Department: WSU Spokane Position: Associate Professor Campus: Spokane

Address/Mail Code: [redacted] Phone: [redacted]

E-mail: mmcdonell@wsu.edu

2. Study Title:
Contingency Management Treatment of Alochol Abuse American Indian People

SECTION 1. General Information

*Human Participants Training: WSU IRB **requires all the personnel** involved in the research to complete CITI training in the ethical use of human participants in research. The principal investigator (PI) is responsible for the training and the documentation of the personnel listed on the application. Section 1, question 2 requires the CITI training record of PI. **Re-training is required every five years**. For CITI training details visit the CITI website at http://www.citiprogram.org or http://www.irb.wsu.edu/citi.asp If you have any further questions, you can also contact the IRB coordinator at 335-3668 or irb@wsu.edu.*

1. Level of Review: ☐ Expedited (***Complete Addendum 1 and submit with the application***)

☒ Full Board

2. Human Participant Training Record (CITI –WSU) of Principal Investigator:

Date of Training: 06/24/2013 Ref #: N/A

3. Co-Investigator(s) (Co-PIs) Contact Information and Role in study*: (***Include all persons who will be directly responsible for the study management, data collection, consent process, data analysis, transcription, participant recruitment, or follow up. NOTE: If necessary, attach a list of additional Co-PI's**.)*

WSU I.D.# or indicate if it is non-WSU personnel	Last Name	First Name	Position	Role in the study
[redacted]				

See attachment of additional staff

4. Estimated Study Start Date: 8/1/2015 Duration of the study: 8/31/2018

5. ☒ Yes ☐ No Is this research supported in whole or in part by a grant or contract? If yes, complete below.

Funding Agency(s), Foundation, or Business:
National Institutes of Health-NIAAA-Office of the Director

PI on Grant/Contract: Michael G. McDonell, PhD & Dedra Buchwald, MD
OGRD #: 1R01AA022070-01A1

Grant Title/Contract:
Contingency Management Treatment of Alcohol Abuse American Indian People

6. [X] Yes [ ] No Does the research require another IRB's review (US and International)? If yes, complete below.

Name of the IRB: University of Washington; [redacted]; Alaska Area IRB -Both have reviewed and approved this protocol under full board review.
FWA number or equivalent number: University of Washington IRB – [redacted]
Alaska Area IRB - [redacted]

(***NOTE: PI is responsible for securing approval and forwarding the documentation of approval to WSU IRB)***.

7. [ ] Yes [X] No Does the PI, Co-PI, or any other person responsible for the design, conduct, or reporting of this research have an economic interest in or act as an officer or director of any outside entity whose financial interest would reasonably appear to be affected by the results of the study?

If yes, complete below:

Name of the person with potential conflict of interest (COI):

N/A

Explain the potential financial conflict of interest:

N/A

Explain how the potential conflict of interest will be managed? (*If the economic interest is a "significant economic interest" as defined in WSU's Conflict of Interest Policy, submit the management plan established with the Conflict of Interest Committee.*)

N/A

8. [X] Yes [ ] No Is the proposed research study conducted at an outside (non-WSU) facility or entity (such as hospitals, clinics, schools, school districts, factories, offices, etc..,)?

If yes, Name (s) of the facility or entity: [redacted]

The researcher has an obligation to ensure that the outside entity is aware of the proposed research study and has no objections (i.e. agrees to participate). By signing this application, the researcher indicates they will comply with this requirement. In order to respect the sovereign governments, research to be conducted on Native American tribal lands will require a letter from the Tribal Council (or equivalent authorized signatory) to the WSU IRB acknowledging the research study and their willingness to allow the proposed research.

9. ☐ Yes ☒ No Does the research require approval from other WSU compliance committees? (i.e. Radiation Safety Committee (RSC), Institutional Animal Care and Use Committee (IACUC), Institutional Biosafety Committee (IBC), etc...)

If yes, PI has responsibility to seek approval from the other committees required for this research. Work cannot start until final approval is received from **all** appropriate committees.

SECTION 2. Study Description

Provide a brief summary of the proposed research. Use lay language and avoid technical terms. IRB members not familiar with the area of research must understand the nature of the research. **The application will be returned without further review if summary is too technical.**

1. Brief (500 words or less) summary of research study:

Purpose:

American Indian and Alaska Natives (AI/ANs) are at increased risk of alcohol dependence. Higher rates of dependence in AI/AN communities results in disproportionately high rates of mortality, medical morbidity, and barriers when seeking alcohol treatment, including poverty, mistrust of typical treatments, scarcity of treating providers, and frequent rural residency. AI/ANs are more likely than other non-White races and ethnicities to drop out of alcohol treatment.

Contingency management (CM) is an intervention in which reinforcers are provided 2-3 times weekly for ~12 weeks for achieving a desired behavior. Contingency management produces one of the largest effect sizes of all mental health and educational interventions. In non-Native populations, CM is one of the most effective and well-studied behavioral treatments for illicit drug use. Compared to standard care, CM has higher rates of abstinence during treatment, 12-month post-treatment abstinence, and treatment completion.

The purpose of this study is to first use qualitative research methods to adapt the CM intervention in order to maximize cultural acceptance of the intervention in participating AI/AN communities. Second, we will perform a randomized controlled trial to evaluate the ability of a culturally-tailored contingency management (CM) intervention to increase alcohol abstinence among American Indian (AI) tribal members from three sites located in [redacted] and Anchorage, Alaska.

This innovative, culturally contingent intervention has strong potential to improve the public health of AI/ANs by reducing alcohol use and alcohol comorbidities. Our robust partnerships will ensure successful completion of this trial, while increasing our partners' knowledge of evidence-based treatment and research. To maximize generalizability, participants will be rural and urban AI/ANs representing three culturally distinct regions. Positioning AI/ANs in key roles builds local research and clinical capacity, enhancing sustainability.

Our Specific Aims are to:

1. Use qualitative research methods to adapt the CM intervention in order to maximize cultural acceptance of the intervention in participating AI/AN communities. We expect these adaptations to maximize cultural acceptability, resulting in CM attrition rates that are comparable or superior to those in non-Native populations.

2. Determine if participants randomized to the CM group more often achieve alcohol abstinence (assessed by urine-alcohol tests, breath tests and self-report) than those in the control group. We hypothesize that participants in the CM group will achieve higher rates of alcohol abstinence than controls across 12 weeks of treatment and at follow-up.

3. Quantify group differences in secondary addiction-related outcomes (e.g., cravings, illicit drug use) and alcohol-associated, health-impairing behaviors (e.g., HIV risk behavior, nicotine use). We hypothesize that the CM group will experience fewer adverse secondary outcomes and less often engage in health-impairing behaviors than controls across 12 weeks of treatment and at follow-up.

4. Identify demographic, substance use severity, psychiatric severity, health, and cultural variables that moderate the effect of CM on alcohol abstinence and attrition. We hypothesize higher substance use and psychiatric severity, poor health, as well as certain cultural and demographic variables will be associated with higher rates of alcohol use and attrition.

Design:

Qualitative Design (Aim 1): We will use qualitative research methods to adapt the CM intervention in order to maximize cultural acceptance of the intervention in participating AI/AN communities**.**

Procedures and Intervention Adaptation/Focus Groups: Prior to recruitment for the randomized controlled trial (RCT) at each study site we will conduct focus groups of community members to gather information on appropriate adaptation of the study procedures and interventions within each community. In our experience, this approach improves the quality and relevance of the materials presented for the RCT. Focus groups will consist of alcohol treatment providers, other community providers, individuals in recovery from alcohol dependence, and their family members. Up to 20 focus group members from each community (up to 60 total) will be recruited and reimbursed $20 each for their time. Focus groups will be facilitated by research staff trained by Dr. McDonell. Dr. McDonell has extensive experience conducing focus groups. Focus groups will be audio recorded and transcribed for analysis. Topics reviewed will include study information, such as study recruitment procedures and materials. Focus groups will also carefully consider the selection of reinforcers to ensure that they are desirable and compatible with cultural values of the community and practical needs of potential participants.

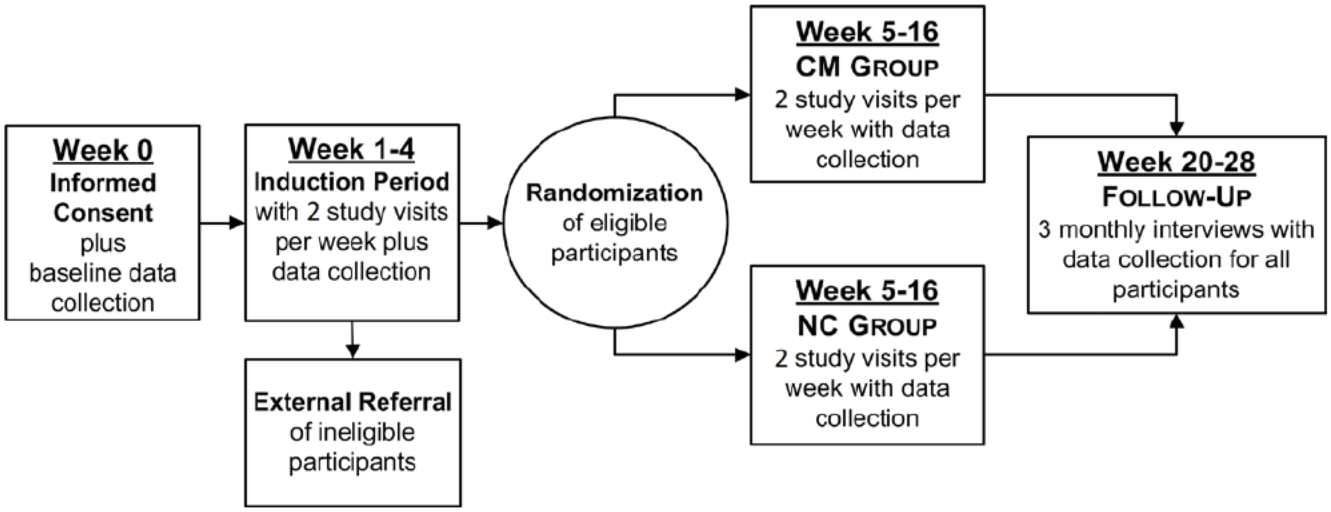
Contingency Management Randomized Controlled Trial Design (Aims 2-4): The overall design of this CM RCT, including use of the non-contingent control group and randomization procedures is similar to another project our team is conducting to evaluate CM as a treatment for alcohol and opiate abuse in American Indian communities that has been approved by Washington State University's IRB (13210---001).

We are proposing to conduct a RCT to evaluate the efficacy of a 12-week CM intervention for treating alcohol dependence in 400 AI/AN adults (Figure 1). To encourage treatment engagement and reduce dropout, participants will undergo a 4-week pre-randomization induction period during which they will receive reinforcement for providing urine tests 2 times per week. Those who regularly attend these urine testing and prize draw appointments (i.e., attend 4 of 8 visits) and have a need for treatment (e.g., have at least one alcohol-positive urine test) will be randomized (Figure 1). Those who do not meet criteria for randomization will be referred to other treatment options. Based on our previous studies and our ongoing work we estimate that 80% of the sample (n=320) will meet criteria for randomization Participants who are eligible for randomization will

be randomized to an intervention group with CM (CM group) or a control group without contingent reinforcement

(NC group). All participants will continue to receive usual treatment (described later) during the study. For the CM group, the contingency for reinforcement will be submission of alcohol-negative urine samples. Reinforcers may be vouchers (e.g., gift cards), practical items, or culturally meaningful items selected by the communities. The magnitude of reinforcement will escalate with the duration of alcohol abstinence. NC group participants will receive reinforcement each time they provide a urine sample, regardless of the results of their urine tests. Secondary outcomes will include alcohol breath tests, self-reported alcohol and drug use and their associated health risk behaviors (HIV risk behavior, nicotine use), and physical and mental health. Data collection will occur in 2 phases: during the study period (weeks 1-16, including a baseline assessment) and during the follow-up period (weeks 20-28). We will investigate predictors of CM outcomes as described in Specific Aim 4.

Figure 1 Overview of study procedures



Procedures: (***For projects involving multiple phases or complex designs, attach flow chart(s) describing the sequence of study procedures***)

The sequence and timing of each phase of the research project is described below. Study Focus Groups will occur prior to the CM RCT at each site.

Focus Groups

We will recruit up to 20 focus group members at each of the 3 participating communities (60 total) through fliers posted in the community clinics, community agencies, and centers where those interested in the topic of alcohol treatment are likely to frequent. These fliers will include a study phone number to contact study staff. Interested individuals who contact us will be screened for initial eligibility and will be asked to attend the focus group

Participants may be **included** in Focus Groups if they:

1. Are community members with a self-reported interest in alcohol treatment
2. Are age ≥18 years old
3. Have the ability to provide verbal informed consent

Participants maybe be **excluded** from Focus Groups if they:

1. Have any medical or psychiatric condition, such as organic brain disorder, dementia, or psychotic disorder, that the Site PI determines would make it difficult for the individual to participate in the focus group

Interested individuals who are eligible will be provided with the date, time, and location of the focus group. Focus groups will be held at our partnering agencies at each site. Focus groups will begin by reviewing informed consent documents and obtaining signed informed consent from participants. Then the contingency management intervention and recruitment procedures will be presented to the group via a short PowerPoint presentation and a short video demonstrating the intervention (see enclosed PowerPoint Presentation). Participants will then be allowed to ask questions. The focus group leader will then follow the attached script, asking additional probes and facilitating the discussion as appropriate. Upon completion of the focus group all participants will be provided with a $20 gift card for their time. Focus group members will be informed that they may discontinue participation at any time.

A second set of four focus groups focused on adapting CM for 18-29 year old AI/ANs with alcohol problems will be held at the partnering agencies at two of the sites ([redacted] Up to 40 participants 18 years and older will be recruited and paid $20 for their time. Focus groups will be audio recorded and transcribed for analysis. Topics reviewed will include study information, interest of young adults in CM, AUD treatment options for young adults, and potential study recruitment procedures and materials to increase CM as a potential treatment option for young AI/ANs. Questions may be tailored in an iterative fashion after each focus group based upon the comments received by participants.

Focus group audio recordings will then be transcribed and double-checked for accuracy. Demographic charactersics of focus group participants will be collected, analyzed and reported in tables, as requested by community partners.. Example demographics include age, gender, tribal affiliation, job title, housing status and education. In an effort to minimize the risk of identifying focus group participants, we will collect/report the variables in ranges/as percentages of the total group (e.g., age 20-30), use general categories (e.g., jobs "professional," laborer,"etc; education-"high school," "graduate," "some college," etc.). Characteristics will not be linked to a specific individual but will be reported in a table. When describing quotes, it will be based on the grouping of characteristics, not the specific individual that is quoted. For example, quotes would be linked to men, or individuals <29 years of age (not a specific individual). Transcripts will be transferred from each site to Washington State University using a secured network folder that is only accessible to research staff. All audio recordings will be destroyed one year after they are transcribed. Dr. McDonell as well a second coder will review each transcript and identify suggestions from group members for 1) improving the cultural acceptability of the CM intervention (e.g., rewards that are culturally appropriate) and 2) improving recruitment procedures (e.g., suggestions for how best to recruit potentially eligible participants in their community). The two coders will also independently code each focus group to identify themes related to rewards and recruitment strategies that are recommended by each community and across communities. The coders will then reconcile their codes and agree on themes that are consistent across at least three textual examples. Results of these analyses will be used to make modifications to the CM intervention and recruitment strategies across communities. Each community/Site PI in collaboration with Dr. McDonell will decide which suggestions regarding rewards and recruitment strategies are appropriate in each community. This will assure that these changes are culturally and clinically appropriate for each community. Any changes to the intervention or recruitment procedures will be reported to WSU and other relevant IRBs as modifications and will not be implemented without their approval.

CM RCT

For the remaining three years, we will recruit 400 alcohol dependent community members through advertisements in locations where alcohol dependent adults are likely to frequent (e.g., primary care clinics, social service agencies), and through radio public service announcements. We will also recruit using Facebook and study site websites where the study recruitment poster will be displayed. We will also have study staff tabling community events. We will educate all potential referral sources (e.g., community providers, courts, etc.) about the project. Data provided by our community partners indicate that ~3,700 AI/AN adults (1,000 Southcentral Foundation, Anchorage, AK; 1,200 [redacted] 2,500 [redacted]) are likely to meet study inclusion and exclusion criteria every year. Our goal is to ~33 Southcentral Foundation, 33 [redacted] and 66 [redacted] participants each year for three years (total =

400). (As of August 31, 2016, the [redacted] has discontinued participation in the study. The Research Coordinator at [redacted] resigned and [redacted] elected to discontinue participation in the WSU HONOR Project rather than hiring a replacement Research Coordinator. As of August 31, 2016 the remaining study participants at [redacted] transferred [redacted] and we continued recruitment [redacted] at [redacted]) The [redacted] study site will no longer be at [redacted] and wil be operating out of the [redacted] (See Letter of Support).

Therefore, at each site we will need to recruit 3% or less of potentially eligible individuals each year to meet our recruitment goals. Interested individuals will contact study staff who will explain the study and screen for recent alcohol and drug use. Eligible participants will be scheduled for an initial in-person baseline interview. The study will be described in detail to them and they will provide informed consent for study procedures. On the consent form, participants can opt-in to text message reminders for study appointments (see attached Text Message Reminder Script).

Participants may be **included** in the proposed study if they:

1. Self-identify as American Indian (AI)
2. Have had 4 or more standard drinks on 1 or more occasions in the last 30 days
3. Meet criteria of DSM-IV diagnosis of current alcohol dependence per the MINI psychiatric interview
4. Are English speaking
5. Have the ability to provide written informed consent

Participants may be **excluded** from the proposed study if they:

1. Self-report illicit drug use, prescription amphetamine or opioid use, or marijuana use greater than alcohol use in the last 90 days
2. Have significant risk of danger alcohol withdrawal, defined as a history of alcohol detoxification or seizure during the last 12 months AND expression of concern by the patient and/or healthcare provider
3. Show signs or symptoms of alcohol withdrawal within the past 12 months unless the potential participant's primary care provider approves their enrollment
4. Have any medical or psychiatric condition, such as organic brain disorder, dementia, or psychotic disorder that the Principal Investigator determines would compromise safe study participation. Research assistants will use the MINI interview to assess possible exclusionary cognitive or psychotic disorders.

The Site PI and Dr. McDonell will make final determination of eligibility. Eligible participants will take part in a baseline study entry interview where they will provide written informed consent and complete measures assessing eligibility, baseline characteristics and study outcomes. Following the baseline study entry interview, if the participant is determined to be eligible, they will continue into the induction period.

Induction Period for Reducing Attrition: During the induction period, all participants will receive reinforcement in the form of prize draws twice a week for providing urine samples and study related data. Therefore they can receive prize draws for providing up to eight urine samples (twice a week for 4 weeks) during the induction period. Reinforcement will be received regardless of whether their urine sample was negative or positive for alcohol use. Participants will receive five prize draws each time they submit a urine sample during the induction period. To further encourage retention, those who provide at least one urine sample each week will receive a $20 bonus in the form of a gift card to a local grocery store. Participants who do not meet criteria for randomization will be referred to available treatments for alcohol in their community. Participants who provide an alcohol breath test that is 0.05 or higher will not be receive prize draws. Instead they will be asked to return when their alcohol breath test is < 0.05 to draw for prizes.

Randomization: Eligible participants will participate in a four week induction phase and if they provide at least four urine samples out of the eight visits including at least at least one alcohol-positive urine test, they will be randomized using the REDCap randomization procedure, balancing on confounding factors that might affect outcomes. Variables to be balanced include: 1) baseline alcohol-positive urine sample; 2) community ([redacted] Southcentral Foundation). Participants will be randomized to receive 12 weeks of treatment-as-usual and either:

1. CM for alcohol abstinence
2. Non-contingent (NC) reinforcement (control condition), where abstinence is not required to receive reinforcers)

The research assistant will notify participants of their group assignment, and all notified participants will be considered part of the intent-to-treat sample. Those who drop out after randomization, defined as no contact with study staff for 3 continuous weeks, will be considered missing for future data collection.

Study Interventions

Treatment-As-Usual: All participants will be able to receive treatment-as-usual from community providers throughout the seven-month study period. Treatment-as-usual at each site is described below. This study will take place on the [redacted] at the Alaska Native Health campus and at an urban Indian healthcare facility located in [redacted]. The participants at the [redacted] site will be seen at the [redacted]. See attached letters of support from these communities, including a letter of support from the [redacted]

Contingency Management: The intervention we will utilize is similar to those previously approved by the UW and WSU IRBs and used in over 50 previous RCTs of the CM intervention. Participants randomized into the CM group will receive escalating reinforcement for alcohol abstinence. Testing will occur 2 times per week during in-person visits to the treatment facility. Consistent with previous CM interventions, participants who fail to provide a urine sample on the required days will be considered missing and therefore failing the test, unless they previously established an agreement with research staff. Urine tests will be conducted using an onsite analyzer, the Thermo Fisher Scientific Indiko. The magnitude of reinforcement will increase across consecutive weeks for which both (twice weekly) of the participant's urine tests are negative.

At every CM study visit, each participant with a negative result will be invited to draw chips out of a bowl containing 500 chips. Fifty percent of the chips will say "good job!" or a similar encouraging phrase (no prize). 41.8% of the chips will result in a small prize ($1 value), 8% will result in a large prize ($20 value), and 0.2% will result in a jumbo prize ($80 value). All chips will be replaced after all draws, so that odds of drawing any given chip are the same each time. The number of draws will occur as follows: five draws for the first week of negative urine tests, with one additional draw added for each consecutive week of negative testing. Positive or missing urine tests result in no prize draws for that week, with the number resetting to five at the first subsequent week of negative tests. After two consecutive negative tests (approximately one week) following a reset, the participant will be returned to the highest number of draws earned before the reset. The maximum number of draws possible to earn is 16, for participants who tested negative for all 12 weeks of the study period.

This escalating schedule with a reset contingency has been found to decrease the probability of relapse once abstinence has been initiated. Because up to 4 days may be needed for alcohol and opiate metabolites to completely clear the system, participants will be informed that up to 2 study appointments after substance use may be needed to assess regained abstinence by urine testing.

Participants will be allowed to schedule pre-arranged absences with study staff for cultural and/or spiritual events, doctor's appointments, or similar activities that are consistent with their recovery goals. These pre-arranged absences will not lead in a reset to 5 draws for these participants if they submit an alcohol-negative urine test immediately prior and after this pre-arranged absence. If a participant submits an alcohol-positive urine sample at either of these visits they will not receive prize draws for that visit and a reset will occur as described above.

Non-contingent Control Condition: Compensation for participants in the non-contingent (NC) control group will follow a well-established protocol used by other studies to isolate the effect of a CM intervention in large randomized trials. NC participants will also take part in the Variable Magnitude of Reinforcement Procedure, but they will receive prize draws simply for submitting urine samples, even if their samples are positive for alcohol. They will provide samples twice a week. Their level of reinforcement will be "yoked" to that of the CM group, so they will receive a number of prize draws that that is equal to the average number of prize draws earned by the CM group, but no less than five draws per sample submitted. This equates the level of reinforcement across groups while allowing us to isolate the effect of CM on alcohol use. The algorithm for this process is continually updated to accommodate the inflow of additional information from newly enrolled CM participants. This results in a compensation scheme for CM and NC participants with approximately equal numbers of prize draws over the duration of the study.

After completing the 12-week treatment period participants will take part in the three month follow-up phase of the study. During the follow-up phase participants will be scheduled for 3 visits at weeks 20, 24, and 28 after the 12-week intervention period is completed to assess the long-term efficacy of the study interventions. Each follow-up visit will take approximately 30 minutes. We will collect urine samples, breath samples and self-reported data as in the study period.

Types of Reinforcers and Maximum Treatment Earnings: Prizes will be displayed in a locked storage cabinet at study sites. Prizes will be selected with input from the focus groups as described in above. In our other non-AI studies, typical prizes include toiletries and gift cards ($1 value); gift cards, mp3 and CD players, and clothing ($20 value); and DVD players and digital cameras ($80 value). Preliminary discussions with each community indicate that reinforcers will vary from more culturally meaningful items (i.e. ceremonial objects, arts and craft supplies, tribal relevant items) to practical items (gas cards). The maximum value of reinforcers available to participants who remain continuously abstinent will be ~$500, with an average payout of $300 per participant, depending on rates of attendance and abstinence.

Participant Reimbursement: After the baseline data collection interview, each participant will receive a $30 gift card or a $30 bus pass (Southcentral Foundation site only) as compensation. Participants will then receive reinforcers for providing urine samples during the induction period, and those who provide a sample in all four weeks of the induction period will receive a $20 bonus voucher. Participants will also receive a $20 voucher for attending each of the three follow-up interviews (weeks 20, 24, and 28; total $60). Participants eligible for randomization will receive reinforcers consistent with their group assignment two times per week for 12 weeks.

Participant Study Experiences: The research team at the Southcentral Foundation has requested that we collect data on participant's experiences and motivations for participating in an alcohol treatment study. Therefore, in collaboration we have created a short assessment of patient motivations and experiences. Participants at the Southcentral Foundation site only will be asked about their motivation for participation and experience with the study. Participants will be examined using the qualitative study experience/motivation questionnaire (see HONOR Experience Questionnaire). This will be administered during the baseline interview and at each of the monthly visits. The questions will be typed directly into the RedCap database by staff. The answers will be kept in the database with only the study ID number as identifying. Data will be analyzed using a grounded theory approach, examining the data for themes that might inform motivations and perceptions about each participants experience in the study. Two independent coders will independently code these data and create separate coding hierarchies. After completing hierarchies they will meet to establish a shared hierarchy. Results will be disseminated through poster presentations and a manuscript.

Table 12 Data collection schedule

	Baseline	Induction	Treatment	Follow-up
Eligibility Criteria				
American Indian/Alaska Native	√			
Resides in participating community	√			

Age	√			
Alcohol dependence	√			
Current heavy drinking	√			
Health and risk factor exclusions	√			
Primary Outcome				
Alcohol use (ethyl glucuronide)	√	2x / week	2x / week	Every visit
Other Alcohol Outcomes				
Alcohol breath tests	√	2x / week	2x / week	Every visit
Alcohol Timeline FollowBack (self-report)	√	2x / week	2x / week	Every visit
Alcohol/Drug severity: ASI-NAV (self-report)	√	Wk 4	Wk 8,12, 16	Every visit
Alcohol cravings (self-report)	√	Wk 4	Wk 8,12, 16	Every visit
Other Secondary Outcomes				
Drug use (biochemical)	√	2x / week	2x / week	Every visit
Cigarette Timeline FollowBack (self-report)	√	2x / week	2x / week	Every visit
HIV risk behavior (self-report)	√	Wk 4	Wk 8,12, 16	Every visit
Health-related quality of life (self-report)	√	Wk 4	Wk 8,12, 16	Every visit
Attrition	√	2x / week	2x / week	Every visit
Healthcare utilization (self-report)	√	Wk 4	Wk 8,12, 16	Every visit
Enculturation (self-report)	√	Wk 4	Wk 8,12, 16	Every visit
Other Baseline Measures				
Demographics (self-report)	√			
Historical trauma/loss (self-report)	√			
Perceived discrimination(self-report)	√			
Personal trauma/stress (self-report)	√			
Psychopathology (self-report)	√			
Nicotine dependence (self-report)	√			
Readiness to change (self-report)	√			
Fetal alcohol spectrum (self-report)	√			
Medical comorbidity (self-report)	√			
Participant study experiences (self-report) at SCF site only	√	Wk 4	Wk 8,12, 16	Every visit
Adverse Events				
Alcohol Withdrawal (self-report/observation)	√	2x / week	2x / week	Every visit
Behaviors affecting participant safety	√	2x / week	2x / week	Every visit

5. What will each participant be asked to do in their role as a participant?

Focus groups: Participants in the focus groups will be asked to sign the informed consent documents. Then the contingency management intervention and recruitment procedures will be presented to the group via a short PowerPoint presentation and a short video demonstrating the intervention (see enclosed PowerPoint Presentation). Participants will then be allowed to ask questions. The focus group leader will then follow the attached script, asking additional probes and facilitating the discussion as appropriate. Upon completion of the focus group all participants will be provided with a $20 gift card for their time. Focus group members will be informed that they may discontinue participation at any time.

RCT: Initially, participants are in the induction period phase. During this phase, participants will be asked to complete study visits where they will be asked to complete study enrollment procedures, and attend data collection visits twice a week. Data collection visits include answering questions about current alcohol and cigarette use and also providing urine and breathe samples. Participants will be able to draw for prizes for completing study visits regardless of if their urine is alcohol-positive. After the four-week induction period,

participants who are randomized into the NC control group will continue the study for the next 12 weeks under the same guidelines as the induction period – they will be eligible to draw for prizes for completing study visits. CM randomized participants will be asked to complete study visits for the next 12 weeks but will only be eligible for prize draws if they provide a urine-negative sample at the study visit. Both the NC and the CM groups will complete 30-minute monthly interviews at weeks 4, 8, and 12, 16 of the study and complete 30-minute follow-up interviews at weeks 20, 24, and 28 after the completion of the 12-week treatment period. At each monthly and follow-up visit, participants will be asked to provide urine and breathe samples.

SECTION 3. Data Collection Methods

Check all method(s) to be used.

1. [X] Survey/Questionnaire
   [X] Phone [X] In person [ ] Internet [ ] E-mail [ ] Postal mail

   If checked, submit copies (if applicable, translated versions) of all the data collection methods mentioned under survey/questionnaire.

2. [X] Interview
   [X] One-on-one [X] Focus group [ ] Oral history [ ] Other: [ ]

   If checked, submit copies (if applicable, translated versions) of all the data collection methods mentioned under Interview.

3. [N/A] Observation of Public Behavior
   [ ] Classroom [ ] Public meetings [ ] Other: [ ]

4. [N/A] Examination of Archived Data/Secondary or Records

   Briefly describe the record: [ ]

5. [N/A] Taste Evaluation
   [ ] Wine/alcohol [ ] Non-wholesome food [ ] Genetically altered food

   (***Wholesome foods can be reviewed under exemption determination. Contact IRB coordinator at 509-335-3668 with any questions.***)

6. [X] Examination of Human Pathological or Diagnostic Tissue Specimens (ex: blood, bodily fluids…)

7. [N/A] Experimental (Unproven or Untested Procedures)
   [ ] Biomedical [ ] Psychological [ ] Other: [ ]

8. [X] Recordings
   [X] Voice [ ] Video [ ] Digital [ ] Image

   Check the Purpose of the recordings: [X] For transcription [ ] Other

   If checked '**other**' explain below: (Examples: For speech pattern analysis, archiving purposes, presentation at the meetings etc.,)

(Note: Confidentiality agreement is required for transcription and translation of the recordings if the job is done by project personnel such as Graduate Student, Teaching Assistant, and Undergraduate student and also for professionals hired for the work. ***Complete Addendum 10 and submit with the application****)*

9. [N/A] Other: [ ]

SECTION 4. Confidentiality and Protection of Data

1. Level of identification and confidentiality at each phase of the data in the research.

Stages of Data	Level of Confidentiality			
	Anonymous *(No identifiers that link the data to a specific subject)*	**Confidential Unlinked** *(Collected with identifier, but all identifiers & codes are removed)*	**Confidential Coded** *(Linked to a specific subject by a code, not by a direct identifier)*	**Intentionally Identified:** *(Linked to a specific subject by personal identifiers)*
Collection			**RCT**	Focus group recordings
Analysis			**RCT**	Focus group recordings
Storage			**RCT**	Focus group recordings
Dissemination	**RCT**		**Focus groups**	

(Answer for each data collection method. See example of **interview 1 and 2, recordings and survey** completed in the table. **Delete the examples and complete the methods of data for your research to match with the level of confidentiality at each stage of the data**. If you have questions, please contact IRB coordinator at 335-3668.)

2. Method(s) of protection and location of data storage: (Check all that apply)
   A. [X] Locked Office (not private)

   [X] Locked Cabinet

   [X] Coded to a Master List
   If checked, answer the following
   i. Will the master list be kept separate from the data? [X] Yes [ ] No [ ] N/A

   [ ] Restricted Computer

   [X] Password Protected

☐ Locked Private Office

☐ Encrypted Data

☒ Fire Wall System

☐ Other: ☐

B. Location of data:
Building and Room Number:

Focus Group: Focus Groups will only collect direct identifiers for recruitment and consent purposes. Transcriptions will not contain identifying information. All audio-recordings and transcriptions will be stored on a password protected WSU network folder that is only accessible to study staff. No identifying information will be included in publications, presentations, or research reports. Audio recordings will be destroyed no later than one year after they are transcribed.

CM RCT: The CM RCT research materials obtained from participants will include personal data, data derived from psychological questionnaires, drug and alcohol use information, and results from urine specimens. Names are needed for participant recruitment and tracking. Only study staff at each location will have access to direct identifiers of participants at that site. The staff at Southcentral Foundation will hold participant contact information in a separate RedCap database only accessible by SCF researchers. There will be no way to link the contact information to study ID number or other study data. Researchers at other sites will not have access to direct identifiers. The WSU research team will not have access to direct identifiers of participants recruited through study subcontractors, the South Central Foundation, [redacted] and the [redacted] However, because the WSU team is conducting all recruitment, study interventions, and data collection at the [redacted], they will have access to direct identifiers for participants recruited at the [redacted]. Site study records and materials will only be available to authorized staff at each research site. All forms with information concerning an individual participant (including self-report measures and urine samples) will be marked with a unique study ID number and not the participant's name. The link between the code and the name will be kept in a secured password-protected network location. These files will only contain the participants' names and study ID numbers and only be accessible to the Site PI and research assistant at each study site. To the extent possible, any information about a participant will never be released to outsiders without his/her explicit written consent, except that, in the event of a medical emergency, pertinent medical information will be given to the medical personnel caring for the participant, or as required by law. All data will be directly entered at each site into a password protected and secure online REDCap database using only a study ID number as an identifier. We have also obtained a Certificate of Confidentiality from NIAAA to protect participant confidentiality.

3. When will all research materials be destroyed, including voice/video/digital/image? (*WSU guidelines require all research materials (consent forms, surveys etc...) to be kept for a minimum of three years after completion of the study.)*

Focus Group: Audio recordings will be destroyed no later than one year after they are transcribed.

CM RCT: We will retain a link between study ID and participant names at each site. Keeping the link between study ID and participant name is necessary in order to address data accuracy issues that might arise during the data analyses and study dissemination phases of the research. In addition, because this is the largest RCT of a substance abuse intervention ever conducted with AI/ANs, we would like to maintain the study linkage sheets in order to contact individuals about subsequent studies that would contribute the understanding of longitudinal impacts of substance abuse treatment in Native communities. The WSU, Alaska Area, and RMTL IRBs have approved this and we have and will notify participants of this possibility in the consent form. We would additionally get approval through a modification to this application if we move forward with

contacting participants after they have completed the study.

SECTION 5. Human Subject Population

1. Approximate number of subjects to be enrolled (**Answer for each subject group.** For example: minors' #s, elderly #s.):

Group name/description	Age range of subjects	Maximum desired number of individuals (or other group unit, such as families) who will complete the research*
Focus Groups	≥18	100
Contingency Management	≥18	250
Non-Contingent Control Condition	≥18	250

2. Please identify subjects that will be recruited by **checking all that apply in 2A and 2B**. Submit additional materials as required.

   A. Children or Adult:

Age	Consent/Permission /Assent forms Required
☐ Birth to 3 years	Parental Permission Form
☐ 4-7 years	Parental Permission Form and Child's Assent
☐ 8-17 years	Parental Permission Form and Child's Written Assent
☒ 18 & over	Written Consent

   B. Populations

☐	Neonates/Fetuses
☐	Children
☐	Prisoners
☒	Pregnant women
☐	Decisionally impaired
☐	HIV/AIDS patients
☒	Native American Tribes with whom WSU has agreement
☐	Crime victims
☒	Substance abusers
☐	Persons living outside the U.S.

	☐	Non-English speaking
	☐	Terminally ill
	☐	Institutionalized individuals
	☐	College Students
	X	Men
	X	Women
	☐	Other:

3. Are there groups of people you are purposefully excluding? [X] Yes [ ] No

If yes,

A. Check all that apply:

[X] Ethnic groups

[ ] Adults 65 or older

[X] Children (under 18)

[ ] Pregnant women

[ ] Males

[ ] Females

[X] Non-English speaking

[ ] Sexual orientation

[ ] Marital status

[X] Race

[ ] Religion

[ ] Other:

B. Explain the reasons for the exclusion criteria:

Because this is a study focused on AI/ANs, we will only include individuals who identify themselves as AI/ANs, and exclude those who do not identify themselves as being part of this ethnic and racial group. We will also exclude children because of concerns about an inability to provide informed consent, as well as adverse effects on health related to alcohol use. Also this is a study focused on adults and not children. At this time, the questionnaire battery is only validated for English speakers, thus non-English speakers will be excluded.

Note: If you are conducting research with children, complete ***Addendum 2*** and submit with the application. If you are conducting research with prisoners, complete ***Addendum 3*** and submit with the application.

SECTION 6. Human Subject Recruitment

1. Recruitment/advertising methods:

Check all that apply and **attach all the materials that will be used.**

☐ Person to person solicitation

☐ Phone

☐ Postal mail

☒ E-mail

☒ Poster

☒ Media (TV, newspaper, radio, Web site)

☒ Other: tabling community events

☐ None

2. How will potential subjects be identified? How will potential subjects be approached (**Answer for each subject group**)?

Explain in detail:

Focus Group Recruitment: Before beginning the RCT we will recruit 20 community members with a vested interest in alcohol treatment for a focus group. A second set of focus groups focused on adapting CM for 18-29 year old AI/ANs with alcohol problems will be held in the two of the three site communities [redacted]) where we will recruit 40 additional AI/AN community members, 18 years and older who are interested in discussing alcohol treatment option for AI/AN young adults. We will place fliers throughout community clinics, community centers, and other places that those interested in providing feedback on alcohol treatment might frequent (see Focus Group Recruitment Flyer). Study fliers will include a study contact phone number. Interested individuals will then directly contact study staff, who will screen them over the phone for eligibility (see Focus Group Screening Script). Eligible individuals will then be provided with the time and location of the focus group. Additionally, study staff may have a recruitment table in the lobby of their facility where study staff will use a recruitment script and will answer questions and provide information to potential participants who approach the recruitment table. We will also recruit via email. Substance abuse providers and healthcare clinics will be sent an email with the study recruitment materials. Additionally, study staff may do brief presentations at clinic meetings (e.g. staff meetings) of local community substance abuse and healthcare providers.

CM RCT Recruitment: After completing the study focus groups at each site, we will recruit up to 400 participants across all sites (100 at the [redacted] (no longer participating in the study)/[redacted] up to 200 at the [redacted] up to 200 at the Southcentral Foundation, but no more than 400 total across all sites) who have documented alcohol dependence. We anticipate adding up to one more additional study site. We will use two primary strategies for recruitment, recruitment from community clinics and recruitment from the community in general. At our partnering community addiction treatment clinics and healthcare clinics staff will provide all potentially eligible participants with a study brochure and a form asking if they would like to be contacted with further information about the study (see CM RCT Brochure and Yes/No Form). All individuals who indicate that they are interested in learning more about the study using this form will be contacted by study staff and screened for initial eligibility over the phone. We will also post recruitment fliers throughout partnering addiction treatment clinics (see CM RCT Recruitment Fliers). These fliers will include the study contact information for

that site. Interested individuals can then contact study staff over the phone or in person. Study staff will then describe the study in further detail and assess for initial eligibility (see CM RCT Screening Script).

In order to recruit interested individuals who are not currently in alcohol treatment we will also post study fliers in locations where adults with alcohol use disorders are likely to frequent, such as healthcare facilities, social service agencies, community centers, courthouses, restaurants, retail locations, and at community events (see CM RCT Recruitment Flier). We will also purchase radio advertisements (see CM RCT Radio). We will also be tabling community events and utilizing Internet media, such as Facebook, where community members will have access to our recruitment material (See CM RCT Recruitment Flier). Additionally, we will also be advertising in the local newspaper (see CM RCT Newspaper). All these study recruitment materials will include a study phone number. Interested individuals can then contact study staff who will describe the study in additional detail and conduct initial study screening (see CM RCT Screening Scripts).

3. Who will obtain consent/assent and when will that be done (**Answer for each subject group**)?

Explain in detail:

Focus Groups*:* Prospective participants for the Focus Groups will be approached initially through community advertisements. Interested individuals will be asked to contact the study staff member via phone. Phone screenings will be conducted in a private manner. Clinicians at our partnering agencies will be encouraged but not required to participate in these focus groups.

CM RCT: Potential CM RCT participants will either be contacted initially by their clinician using the Yes/No Form, or through clinic and community advertisements. Fliers will be distributed and posted at amendable community organizations, including homeless shelters, clinics, libraries and other community centers. Interested individuals will then be contacted by study staff (those who indicate their interest through the Yes/No Form) or will contact study staff directly (those who learn about the study through advertisements). All recruitment procedures will be conducted in a private manner to protect confidentiality. All in-person contacts will be conducted in a confidential study office. Throughout the recruitment process potential participants will be provided with multiple opportunities to discontinue participation and will be informed that their participation or lack of participation in the study will have no bearing on the addiction care or other services they may receive. All study referral forms will be stored in a secure location at each treatment facility and will only be accessible to study staff. We have already obtained a Certificate of Confidentiality from NIAAA to protect participant confidentiality.

4. Describe any screening tools/procedures (**Answer for each subject group**):

Explain in detail:

Focus Groups*:* Initial eligibility criteria will be assessed over the phone or in-person using a screening script **(see Focus Group Screening Script).**

CM RCT: Initial eligibility criteria will again be assessed over the phone or in-person using a screening script. Each site will have a different screening script used by study staff (see CM RCT Screening Scripts). Secondary eligibility, such as alcohol dependence will be assessed at the baseline intake interview using the MINI psychiatric interview to assess for possible exclusionary cognitive or psychotic disorders.

5. Will subjects be compensated (including extra credit*)?
[X] Yes [ ] No

If yes,

A. What is the compensation, how much will the subject be offered, and how will they receive it? (i.e. extra credit, money, gift certificate, etc.)

Explain in detail:

Focus Groups: Participants will be remunerated for participating in the Focus Group, in the amount of a $20 gift card.

CM RCT: CM RCT participants will be remunerated for completing the baseline appointment with $30 gift card. Participants that attend at least one study visit per week for the induction phase (weeks 1-4) will receive a bonus voucher of $20 to a local grocery store. Participants who drop out of the post-randomization treatment phase of the study will be eligible to receive $20 for completing the monthly interviews, however, participants who drop out of the study before randomization will not be eligible to continue these monthly interviews. CM RCT participants will receive a $20 gift card for completing each of the post-treatment follow-up appointments at weeks 20, 24, and 28. If a participant drops out of the CM RCT phase, the participant may still be eligible to complete the monthly follow-up appointments and be compensated.

B. When will the participants be compensated?
☐ Before the study ☒ Installments during the study ☐ Withdraw/complete the study

**If students will be receiving extra credit for participation, they must be able to complete an alternative assignment for extra credit should they choose not to participate. This assignment must be comparable, with respect to time and effort, as participation in the research. If participants are paid by a WSU check; this requires the participants' social security number.*

SECTION 7. Informed Consent/Parental Permission/Assent Process

Choose all that apply and **attach appropriate forms to this application.** (Templates available at http://www.irb.wsu.edu/) **Note:** For a list of required elements of informed consent see the definitions at http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.116.)

1. ☒ Adult(s) ☐ Parent(s) ☐ Guardian(s)

☒ Written	A consent or permission form that contains all of the required elements of informed consent.
☐ Alteration of Informed Consent process	Requesting IRB approval for waiver of some or all of the elements of informed consent or permission (i.e. medical record review, deception research, or collection of biological specimens). **If checked,** complete ***Addendum 4*** and submit with the application.
☐ Waiver of Documentation of Informed Consent	Requesting IRB approval for waiver of the requirement for documentation of informed consent or permission (i.e. telephone survey or mailed survey, internet research, or certain international research). **If checked,** complete ***Addendum 5*** and submit with the application.
☐ Waiver of Informed Consent Process	Requesting IRB approval for waiver of the requirement for the informed consent or permission process (i.e. medical record review, deception research, or collection of biological specimens). **If checked,** complete ***Addendum 6*** and submit with the application.

2. ☐ Children ☒ Vulnerable Population

[X] Written	An assent or consent form that contains all of the required elements of informed consent.
[ ] Alteration of Informed Consent process	Requesting IRB approval for waiver of some or all of the elements of informed consent (i.e. medical record review, deception research, or collection of biological specimens). **If checked,** complete ***Addendum 4*** and submit with the application.
[ ] Waiver of Documentation of Informed Consent	Requesting IRB approval for waiver of the requirement for documentation of informed consent (i.e. telephone survey or mailed survey, internet research, or certain international research). **If checked,** complete ***Addendum 5*** and submit with the application.
[ ] Waiver of Informed Consent Process	Requesting IRB approval for waiver of the requirement for the informed consent process (i.e. medical record review, deception research, or collection of biological specimens). **If checked,** complete ***Addendum 6*** and submit with the application.

3. What steps have you taken to prevent potential coercion or undue influence in recruiting subjects and obtaining consent or assent?

Explain in detail:

Recruitment Focus Groups: Advertising for the project throughout provider offices will minimize coercion in the community and will allow interested individuals to contact study staff directly rather than having agency or community leaders approach individuals.

Recruitment CM RCT: We will begin the study by educating all providers and staff at participating agencies, as well as other referral sources, about the voluntary nature of this research project and that client participation or non-participation in this study should in no way influence the treatment they receive at the treatment agency or other services they might receive in their community. We will take other steps to minimize the possibility of coercion. Individuals will complete recruitment forms (Yes/No Form) in a confidential manner. After completing them they will place the forms face down in a labelled "Yes" or "No" envelope, such that their treating clinician and/or staff is not aware of which envelope these forms are placed in. Study staff will collect the "Yes" forms on a regular basis. They will contact these individuals to provide additional study information and screen for initial study eligibility (see RCT Screening Scripts). The potential participants will at this time have the opportunity to agree to continue with the enrollment process or decline to participate in the study and ask questions about any aspect of the study. Those who directly contact study staff via phone or in person will have the study described to them using a script and then be asked initial study screening questions in a confidential office (see RCT Screening Scripts). WSU and other relevant review organizations will approve all recruitment materials. Information regarding individuals' interest in participating in the study (i.e., their Yes/No forms) will be kept in a secure location. During the consenting procedure, participants will also have an opportunity to refuse participation and be allowed again to ask questions about the study. We will also make it clear throughout recruitment and consent documents that refusal to participate or continue participating in the study will not affect the services they receive from their clinic or other treatment they might receive. Reimbursement values have been selected to provide adequate reimbursement to participants without being coercive.

Informed Consent Focus Groups: Each participant will be provided with a consent form and the form will be read aloud by the focus group facilitator. Individuals will be allowed to ask questions and any individuals who are not interested in participating after the consent form has been read to them will be allowed to leave. Participants interested in participating will sign the consent forms for the study staff and then be provided with a copy of the consent form for their records.

Informed Consent CM RCT: Informed consent in writing will be obtained from all potential participants in the CM RCT before research participation. During the initial baseline interview, the study purpose and procedures will be explained to potential participants. If an individual decides to participate, they will read and sign the informed consent form in the presence of study staff (or the form will be read to them if they cannot read). We will emphasize that there is no pressure to participate, that referral to other treatment alternatives will be provided if participants do not wish to continue in the study, and that they are encouraged to speak to

Dr. McDonell or the Site PI about issues or concerns related to study participation. The issues of confidentiality will be discussed in detail. Two forms will be signed, one for the participant to keep and another for the study's records. This signed consent form will be kept in a separate, locked file. Participants who have any questions regarding their informed consent, or any aspects of the program at any time, will be directed to Dr. McDonell. All research assistants will be trained by Dr. McDonell in the informed consent procedures to assure that they adequately explain the risks and benefits of participating in this research in a culturally appropriate manner.

SECTION 8. Risk and Benefit Assessment

1. Potential risks to participants: **(Check all that apply)**

- [ ] Invasion of privacy to the subject or family
- [X] Breach of confidentiality
- [X] Physical harm or discomfort
- [X] Psychological/emotional discomfort or distress
- [ ] Psychological effect that is more than discomfort or distress
- [X] Social stigmatization
- [ ] Economic (e.g., employment, insurability)
- [ ] Legal
- [ ] Any study related activity which subjects might consider sensitive, offensive, threatening, or degrading?
- [ ] Withholding standard care and procedures
- [ ] Significant time or inconvenience

Other:

2. Does the study pose risk to individuals other than the participants?

Explain in detail:

No. it is a treatment study designed to assist substance users. We do not foresee it posing a risk to individuals other than participants. All research staff and clinicians are trained to work with people with substance abuse disorders. All urine samples will be handled using established safety procedures, use of gloves and other protective equipment.

3. Indicate which of the categories listed below accurately describes the specific potential risk level on over all items in Section 8, question 1 on the application:

☒ Not greater than minimal risk[1]

☐ Greater than minimal risk, but presenting the prospect of direct benefit to individual subjects

☐ Greater than minimal risk, no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition

☐ Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of subjects

4. How will you minimize these potential risks in order to protect subjects' rights and welfare?

Explain in detail:

The study is minimal risk because the procedures that participants will undergo are consistent with program development in Native communities (Focus Groups) and interventions or interviews they might receive as part of their substance use treatment (RCT) if they were not participating in the study. Many of the measures used in the study are commonly used in clinical practice, and contingency management is widely used as a clinical intervention in non-Native communities, as well as in some of our partnering Native communities.

In terms of the focus groups we will protect participant confidentiality by destroying audio recordings one year after they are transcribed. All audio recordings and transcriptions will be saved on SharePoint – a locked website that only study staff has access to. The recordings will be destroyed no later than one year after they are created. In an effort to reduce the risk of focus group participants identification through the demographic tables we will collect/report variables in ranges and report as percentages of the group total (e.g., age 20-30), use general categories (e.g., jobs "professional," laborer,"etc; education-"high school," "graduate," "some college," etc.).

If participants find any aspects of their involvement in the program psychologically, physical, or otherwise uncomfortable, they will be encouraged to discontinue participation and be assisted in finding a more acceptable form of treatment. While we will attempt to screen out (using exclusion criteria) individuals who are likely to experience alcohol withdrawal, we anticipate that withdrawal symptoms might occur, especially if the CM intervention is effective. Study staff will be trained to assess these symptoms. If withdrawal symptoms are reported or observed, participants will immediately be referred to a community medical provider. Any events that might affect participants' safety will immediately be reported to Dr. McDonell and the investigators will work with local healthcare providers to assure subject safety. If necessary, patients who experience alcohol withdrawal will be removed from the study and referred to other treatment resources.

In terms of the CM RCT, we will take extensive steps to protect participant confidentiality as described below. All data will be stripped of direct identifiers before being entered in the WSU secure web based database (REDCap). All direct identifiers will be stored at each location. WSU investigators will not have access to direct identifiers, except for participants recruited through the [redacted] by WSU employees. We have already obtained a Certificate of Confidentiality from NIAAA to protect participant confidentiality. All research findings will also be reviewed by leadership in each community in aggregate form before they are submitted for publication. The specific names and locations of participating communities will not be listed in publications and/or presentations except when permission is given by participating communities. We also have established data sharing agreements with the [redacted] and [redacted] and a research agreement with Southcentral Foundation. We are developing a similar data sharing agreement with the [redacted] that will allow them to review and approve all dissemination of study findings that include participants recruited at their site, as well as maintain data ownership of data gathered from their site.

[1] Minimal risk" means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves from those ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests. 45 CFR 46.102(i)

5. In the event that any of these potential risks occur, how will it be handled (e.g. compensation, counseling, etc.)?

Explain in detail: Dr. McDonell, in collaboration with Co-Investigators and community providers will handle adverse events. Dr. McDonell will be responsible for evaluating all Serious Adverse Events (SAEs). Participants will be questioned regularly about their wellbeing and study measures will be administered as described above. This will allow us to detect serious adverse events should they occur. Team medical doctors, such as Dr. Buchwald (Internist) and Ries (Addiction Psychiatrist) will provide medical consultation in responding to SAEs should they occur. If a participant in the study reports that they are pregnant or trying to get pregnant, study staff will inform site PI and Dr. McDonell immediately and Dr. McDonell and Site PI will work together on a plan to provide additional support to the woman. This plan was requested by our community partners. Study staff in participating communities will be trained in the assessment, reporting, and management of SAEs. This study will have a DSMB and has a DSMP plan that has been approved by NIAAA. Our approved DSMP is attached as an addendum to this application.

6. Is it possible that you will discover a subject's previously unknown physical or psychological condition (e.g. disease, depression, suicidal ideation, genetic predisposition, etc.) as a result of your procedures?

☒ YES

☐ NO

If yes, what would they be and how will you handle these situations?

Explain in detail:

Focus groups: N/A

CM RCT: It is possible that we may discover previously unknown conditions, such as suicidal ideation. We will use a set of safety procedures to ensure safe participation during the research trial. Both the clinical and the research team have medical personnel on staff available to deal with any unforeseen medical complications that may arise. Dr. McDonell is a clinical psychologist with extensive experience treating suicidal thinking and behavior. Weekly rounds will be held with the full study team (research assistants, project coordinator, Drs. McDonell, and co-investigators) and the status of each participant will be reviewed to assess medical and psychiatric safety, treatment compliance, and data completion. Consistent monitoring of participant progress provides one level of safety procedures. Another level of safety procedures involves evaluation of data collected (aggression/suicidality) and of verbal reports of suicidal and/or homicidal intent to staff members. All reports of suicidal or homicidal ideation will be immediately reported to Dr. McDonell as well as to a treating clinician or to individuals who can assure participant safety. If necessary (i.e., 911) will be called if an individual is judged to be at imminent risk of hurting themselves or others. Clinicians are available to provide a clinical assessment and management of safety concerns at each site. All research staff will receive training in identifying suicide/homicide risks and/or signs of dangerous intoxication and in following the steps needed to appropriately respond to these signs.

Participants judged by project investigators at any point to be a danger to self or others or who are judged to be in grave danger due to continued drug use and/or to medical/psychiatric problems will be discontinued from the study but actively connected with their treating clinician or to emergency services who are familiar with working with high risk situations.

7. Describe the expected benefits of this project *(NOTE: **compensation is not considered a benefit**)*:

A. To the individual subjects:

Explain in detail:

Focus Groups: N/A

CM RCT: Active alcohol abusers will receive potentially effective treatment for their alcohol dependence at no cost.

B. To society:

Explain in detail:

Focus groups: Feedback from community members regarding cultural adaptation of the contingency management intervention will help the intervention to be effective in diverse communities, broadening its generalizability.

CM RCT: Identification of effective treatment of alcohol dependence in AI/ANs, a group that is disproportionately affected by alcohol abuse, may provide the current addiction and treatment systems with useful information and thereby benefit others. Furthermore, the data collected in the proposed study will have a high level of external validity and may serve to render contingency management programs more pragmatic and accessible to AI/ANs and other populations.

8. Explain how, in your assessment, benefits of this study outweigh the risks. (e.g. risk/benefit ratio)

We will take extensive steps to mitigate the risks associated with this study. Based on the relatively low risk to participants, and the overall benefit to society, we believe the benefits of this research are greater than the risks. Identification of effective treatment of alcohol dependence in AI/ANs, a group that is disproportionately affected by alcohol and drug abuse, may provide the current addiction and treatment systems with useful information and thereby benefit others. Furthermore, the data collected in the proposed study will have a high level of external validity and may serve to render contingency management programs more pragmatic and accessible to AI/ANs and other rural populations.

SECTION 9. Research Involving Potential Reportable Activity

1. Will the project involve the potential discovery of child abuse?
[X] Yes [ ] No

If yes, there are legal obligations to disclose to the proper authorities certain information about reportable activities obtained during research. ***This obligation and intended course of action must be communicated to the participants in the consent form.***

SECTION 10. Research Involving Deception

1. [ ] Yes [X] No Will any information be purposely withheld from the participants or will they be given any misinformation?
If yes, this will require alteration of informed consent process. Complete ***Addendum 4*** and submit along with the application.

2. Why is the deception necessary?

Explain in detail: N/A

3. How and when will the subjects be debriefed after the project? **Attach debriefing script.**

Explain in detail: N/A

SECTION 11. Research Involving Health Insurance Portability and Accountability Act (HIPAA)

Address the following questions regarding the use of protected health information:

1. ☐ Yes ☒ No Will health information be obtained from a covered entity[2] (a health care provider who bills health insurers e.g., WSU Health and Wellness Services?

2. ☐ Yes ☒ No Does the research involve the provision of healthcare in a covered entity, such as WSU health services?

3. ☐ Yes ☒ No If the study involves the provision of healthcare, will a health insurer or billing agency be contacted for billing or eligibility?

4. ☐ Yes ☒ No Does the research involve use or creation of protected health information?

If **no** to all the questions above you are **not** subject to HIPAA**.**
If **yes** to any of the questions above complete ***Addendum 7*** and submit with the application.

SECTION 12. Research Involving Investigational Drugs, Devices, Alcohol, Blood, Tissue, Bodily Fluids or other Biological Specimens

1. ☐ Yes ☒ No Will any investigational new drug (IND) be used?
If yes, complete ***Addendum 8*** and attach it to the application.

2. ☐ Yes ☒ No Will any other drugs be used?
If yes, complete ***Addendum 8*** and attach it to the application.

3. ☐ Yes ☒ No Will any investigational device (IDE) be used?
If yes, complete ***Addendum 8*** and attach it to the application.

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[2] The Administrative Simplification standards adopted by Health and Human Services (HHS) under the Health Insurance Portability and Accountability Act of 1996 (HIPAA) apply to any entity that is

- a health care provider that conducts certain transactions in electronic form (called here a "covered health care provider").
- a health care clearinghouse.
- a health plan.

An entity that is one or more of these types of entities is referred to as a "covered entity" in the Administrative Simplification regulations.

4. ☐ Yes ☒ No Will alcohol be ingested by the subjects?
If yes, describe what type and how it will be administered[3]:

5. ☒ Yes ☐ No Will blood, tissue, bodily fluids, or other biological specimens be collected?
If yes, complete ***Addendum 9*** and submit with the application.

Note: if you are using blood, tissue, bodily fluids or other biological specimens, you may also need to seek Institutional Biosafety Approval before you begin the research. Contact the WSU Biosafety Manager at 509-335-4462 or ibc@wsu.edu

A. ☐ Yes ☒ No Will any of the blood, tissue, bodily fluids, or other biological specimens be used for genetic testing?

B. Do your studies involve the analysis of genes known to be implicated in the disorder(s), syndrome(s) or condition(s) you are studying? If so, what genes will you be studying?

NO

C. Alternatively, do your studies involve finding the gene(s) that may cause the condition or genetic markers that co segregate with this condition?

NO

D. Please confirm that the samples will not be used for any purpose other than to study genes related to the diseases discussed in the application and the consent form.

NO

[3] Refer to the guidelines for administration of ethyl alcohol inhuman experimentation (OGRD Memo No. 18 http://www.ogrd.wsu.edu/memos/memo18/memo18.pdf' and NIAAA.

Statistical Analysis Plan for The Honoring our Native Ongoing Recovery (HONOR) Study: A Community-Placed Multi-Site Randomized Controlled Trial

Background

Briefly, the HONOR trial seeks to determine the treatment effect of contingency management (CM) on alcohol use in American Indian and Alaska Native (AI/AN) communities.[1] Alcohol use was measured using levels of the ethyl glucuronide (EtG) biomarker in urine. This section describes both the original analytic plan and the changes made to the original analysis plan.

Analysis Plan as described in McDonell *et al* (2016)[1]

Preliminary analyses. Study participants will be characterized in terms of demographics and clinical variables using percentages for categorical variables and means and standard deviations for continuous variables. We will assess baseline characteristics by treatment group after randomization via *t*-tests and Chi-square tests. For primary and secondary outcomes, we will create indicator variables for alcohol abstinence (e.g., yes/no) at each time point.

Primary analyses. All analyses will follow intention-to-treat principles. The main outcome will be "biochemically identified abstinence" based on the EtG threshold of 150 ng/mL, which is to be assessed at each clinical visit. The model will be fit via generalized estimating equations. Our second outcome, the longest duration of abstinence (defined at the EtG level of 150 ng/mL), will be modeled using linear regression. The third outcome, time-to-return to alcohol use (EtG < 150 ng/mL) will be analyzed with the Cox proportional hazard regression. These statistical methods are based on previously conducted CM trials.[2] Estimated effects will be accompanied by 95% confidence intervals based up a two-sided alpha of 0.05. Analyses will be stratified by site, except in the case of no significant site effect (then pooled estimates will be presented). Site as an effect modifier will also be evaluated. Adjustment for potential residual confounders and precision variables will be evaluated through sensitivity analyses.

Power. Assuming a correlation between time points of 0.3 with a maximum of 36 data collection points for each participant, an alpha of 0.05, and 90% power, total necessary sample size was determined to be 320 participants (i.e., 160 per group). To allow for 20% attrition, based on previous studies, we will enroll 400 participants. Using the preceding parameters, we should be able to detect an effect size of 0.21 on the primary outcome.[3,4]

Missing data. The lead-in phase has been designed to minimize missing data after randomization.[5–7] To curb participant loss, we will also utilize study interventions that use qualitative procedures known to maximize cultural acceptability. During the statistical analysis, GEE can accommodate non-informative missingness. In the case where a substantial proportion of data is missing (over 20%), a sensitivity analysis will be performed using multiple imputation.[2,8]

Changes to the Statistical Analysis Plan

After data collection was completed, but before data analyses began, we made minor modifications to our Statistical Analysis Plan (SAP). These changes were made in order to assure that we were following best practice analytic techniques that provided the most accurate assessment and clinically meaningful assessments of our primary and secondary outcomes. Here, we describe the modifications of the SAP for

the first aim of the HONOR randomized controlled trial published previously by our research group into two major points:[1]

1. Removed additional EtG-related secondary outcomes to focus on alcohol abstinence and reduce multiple testing issues;
2. Clarified the use of multiple imputation results as the primary results

1. ***Removal of additional analyses:*** We have removed the following additional analyses from the manuscript to focus on the primary outcome and reduce multiple testing issues:
    a. Continuous EtG and heavy EtG outcomes
    b. Longest duration of abstinence
    c. Time-to-return to alcohol use
    d. Recurrent return to alcohol

2. ***Missing Data and Multiple Imputation:*** In our original SAP we proposed to present our principal analyses without multiple imputation, assuming missingness was non-informative, with multiple imputations analyses being conducted as sensitivity analyses. Due to the high level of missingness, we modified this approach to present our multiple imputation analyses as our principle approach. Traditional GEE models only satisfy the missing completely at random (MCAR) assumption (non-informative missingness). To satisfy missing at random (MAR) assumptions, we performed multiple imputation for all primary and secondary analyses with missing data and combined such analyses with GEE.[2,9,10] Therefore, all GEE model results were reported using multiple imputation to reduce potential bias induced from missingness.

References

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