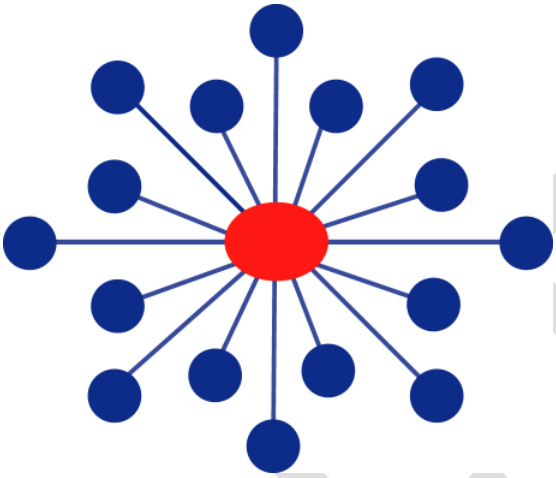
Facebook Intervention for Preventing Opioid Relapse Among American Indian Women: Wiidookaage'Win Pilot Preparatory Study (Aim 1)

NCT05340855

1/12/2023



NIDA CTN Protocol 0123

Facebook Intervention for Preventing Opioid Relapse among American Indian Women: Wiidookaage'win Pilot Preparatory Study (Aim 1)

LI: Dr. Christi Patten

Sponsor: National Institute on Drug Abuse (NIDA)
IRB approved 1/12/2023
Version 1.4

Lead Investigator (LI):	**Christi Patten, PhD** NIDA CTN NorthStar Node Mayo Clinic
Co-LI(s):	[redacted], **DrPH** NIDA CTN NorthStar Node Mayo Clinic [redacted], **PhD** NIDA CTN NorthStar Node Mayo Clinic [redacted], **PhD** NIDA CTN NorthStar Node Mayo Clinic [redacted]**MD, PhD, FACP, FASAM** NIDA CTN NorthStar Node (LI) University of Minnesota [redacted], **PhD** NIDA CTN Northeast Node Dartmouth College [redacted], **PhD** NIDA CTN Greater New York Node Columbia University Irving Medical Center [redacted], **PhD** NIDA CTN Southwest Node Center on Alcohol, Substance Use and Addictions [redacted], **MD** MIDA CTN NorthStar Node Community-University Health Care Center
CCTN Scientific Officer:	[redacted], **MS** National Institute on Drug Abuse

CONFIDENTIALITY STATEMENT

This document is confidential communication. Acceptance of this document constitutes agreement by the recipient that no unpublished information contained herein will be published or disclosed without prior approval of the LI or other participating study leadership and as consistent with the NIDA terms of award.

TABLE OF CONTENTS

1.0 LIST OF ABBREVIATIONS

Abbreviation	Definition
AE	Adverse Event
AIAN	American Indian and Alaska Native
CAC	Community Advisory Committee
CBPR	Community-Based Participatory Research
CCTN	Center for the Clinical Trials Network
CFR	Code of Federal Regulations
CHRT-SR	Concise Health Risk Tracking – Self-Report
CoC	Certificate of Confidentiality
CTN	Clinical Trials Network
eCRF	Electronic Case Report Form
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HHS	Department of Health and Human Services
HIPAA	Health Insurance Portability and Accountability Act
HSP	Human Subjects Protection
IRB	Institutional Review Board
LI	Lead Investigator
MOUD	Medication for Opioid Use Disorder
NIDA	National Institute on Drug Abuse
NIH	National Institutes of Health
OHRP	Office for Human Research Protections
OUD	Opioid Use Disorder
PTrax	Participant Tracking System
RCT	Randomized Controlled Trial

Abbreviation	Definition
REDCap	Research Electronic Data Capture
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
TLFB	Timeline Follow-Back
UDS	Urine Drug Screen
UP	Unanticipated Problem

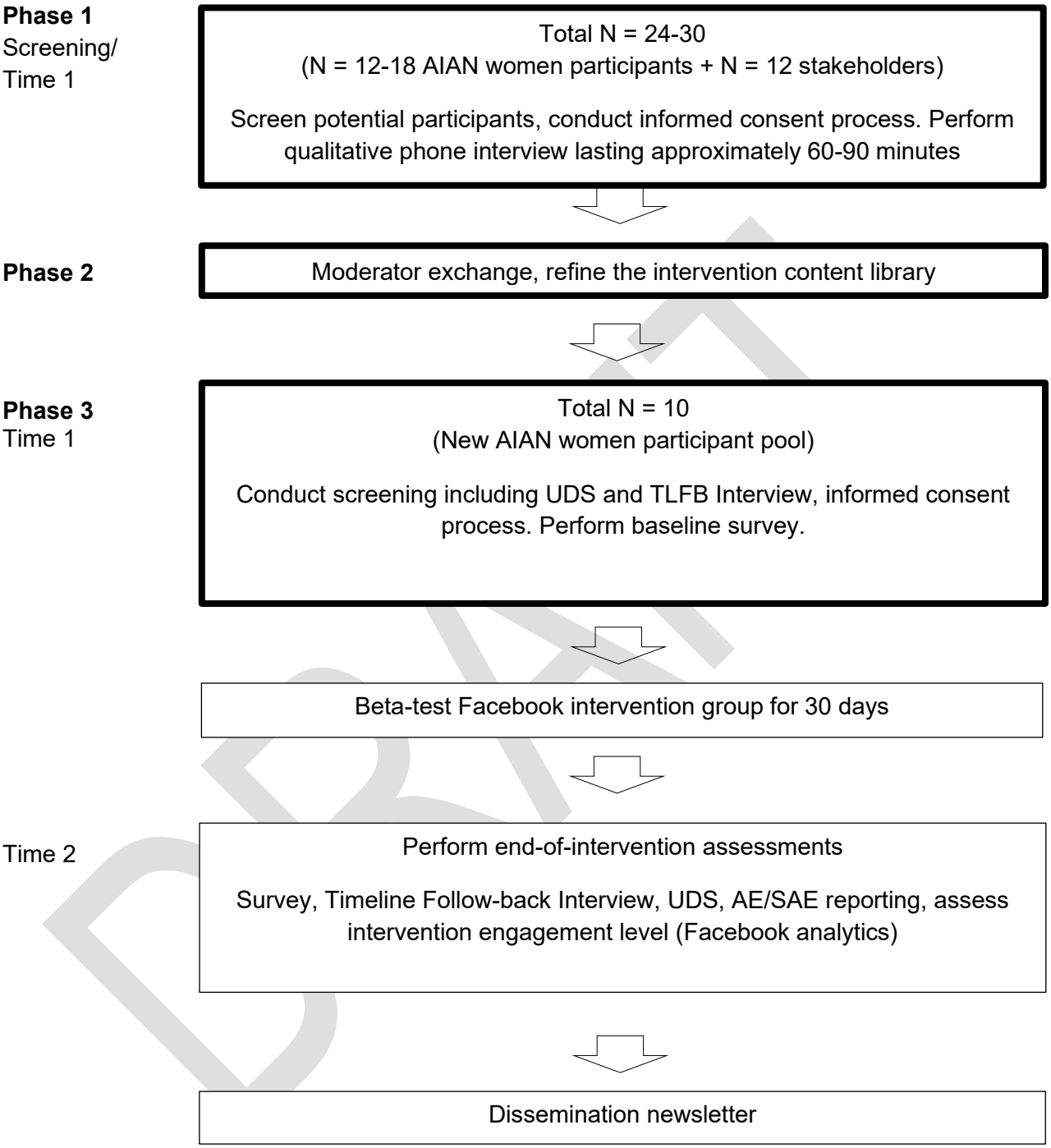
2.0 PROTOCOL SUMMARY

Synopsis

Title	Facebook Intervention for Preventing Opioid Relapse among American Indian Women: Wiidookaage'win Pilot Preparatory Study (Aim 1)
Study Number	CTN-0123
IND Number	N/A
Study Description	This Phase I, pilot preparatory study aims to develop a culturally relevant Facebook intervention for American Indian and Alaska Native (AIAN) women in Minnesota recovering from illicit opioid use. The study will consist of three phases: (1) qualitative interviews, (2) intervention content refinement and a moderator exchange (i.e., bi-directional sharing of knowledge between intervention moderators and trainers), and (3) a beta-testing period. A study-specific Community Advisory Committee (CAC) was formed whose members contributed to the study protocol and will continue to provide guidance and input on the study implementation and dissemination. At the advice of the CAC, a Native Elder woman named the study. *Wiidookaage'win* is an Ojibwe word that means "the place for help and time for helping," and reflects healing and community. We expect the participatory approach to treatment development will result in a social media intervention with cultural relevance for Native women to maintain recovery from opioid use.
Objectives	**Primary Objective:** To develop a culturally relevant Facebook intervention for AIAN women in Minnesota that will support continued recovery from illicit opioid use. **Secondary Objective:** To conduct a beta-test to assess the preliminary feasibility and acceptability of the Facebook intervention.
Outcome Measures	**Primary Outcome Measure:** A culturally relevant Facebook intervention prototype to support recovery from opioid use. **Secondary Outcome Measures:** Recruitment feasibility, study retention, level of intervention engagement and intervention satisfaction. **Exploratory Outcome Measures**: Abstinence from illicit opioid use and MOUD continuation at the end of the intervention.
Study Population	We will enroll up to 18 AIAN participants and 12 interested parties for the qualitative interview phase, and 10 different AIAN participants for the beta-testing phase. The AIAN participants will be women at least 18 years of age who reside in Minnesota, have opioid use disorder (OUD) with at least one month of opioid abstinence and are currently receiving MOUD. The interested parties will be health care providers or AIAN community partners with knowledge of AIAN culture and/or OUD treatment and recovery among AIAN people.
Phase or Stage	I

Description of Sites/Facilities Enrolling Participants	The study site is Mayo Clinic. AIAN women with OUD will be referred to this study by clinicians and staff from addiction treatment programs,community organizations and programs in and surrounding Minneapolis, Minnesota, United States, and community flyers. Interested parties will be referred primarily by our CAC.
Description of Study Intervention/Experimental Manipulation	During the qualitative phase, feedback from individual interviews with AIAN women and stakeholders will be used to develop the intervention. The web-based study intervention to be developed will be a private, hidden, moderated, Facebook group that will be active for 3 months. Moderators will post content every 1-2 days from a content library of about 30 postings each repeated twice during the 3 months. Content (moderator postings) will consist of pictures/images combined with text and videos designed to provide information and stimulate participant discussion. The intervention will be beta-tested for a 30-day period using a single arm design with assessments conducted at baseline and at the end of the intervention.
Safety Reporting	Adverse Events (AEs) and Serious Adverse Events (SAEs) that occurred within the 30-day intervention period will be self-reported by the participants in the follow-up visit.
Analyses	In the qualitative interview phase, content analysis supplemented with QSR NVivo software will be used to generate interview response themes. In the beta-testing phase, descriptive statistics will be used to summarize the sample for baseline demographic characteristics, study retention, treatment satisfaction ratings, intervention engagement level, MOUD retention, and opioid relapse, operationalized as opioid positive urine or any self-reported illicit opioid use at follow-up.
Study Duration	The duration of the study, from enrollment for the qualitative interview phase to the follow-up visit of the beta-testing phase, will be approximately 7 months.
Participant Duration	Participants in the qualitative phase will engage in one interview lasting approximately 60-90 minutes. Participants in the beta-testing phase will complete all study-related tasks, including urine collection, participation in the intervention, and surveys, within a 2-month period.

3.0 STUDY SCHEMA



3.1. Key Research Site Roles

Site LI (MD; DO; PhD)

Site Clinician (RN; NP; PA; MD; DO)

Site Psychiatrist (MD; PhD)

Program Coordinator

Study Coordinator

Intervention Moderator

Statistician

4.0 INTRODUCTION

4.1 Study Rationale

Illicit use of opioids is a major public health problem associated with significant morbidity and mortality related to HIV, hepatitis C and overdose (Nelson et al., 2011; Salomon et al., 2000; Scholl et al., 2019). As defined by the DSM-5, opioid use disorder (OUD) is "a problematic pattern of opioid use leading to clinically significant impairment or distress," including a constant desire and/or unsuccessful attempts to control opioid use (American Psychiatric Association, 2013). American Indian and Alaska Native (AIAN) adults are particularly at high risk for OUD due to elevated risk of chronic health conditions influenced by depression and anxiety, early trauma and childhood abuse, cultural displacement, unemployment, and poverty (Rieckmann et al., 2012). In 2019, AIAN adults in Minnesota were seven times more likely to die of an overdose involving opioids than white adults, representing the greatest disparity between AIANs and whites in the United States (Minnesota Department of Health, 2021).

OUD is a chronic, relapsing condition (Bell & Strang, 2020). Medication for OUD (MOUD) is an evidence-based, first-line treatment approach (Bart, 2012; Lillie et al., 2021; Mattick et al., 2009; Schuckit, 2016; Sofuoglu et al., 2019), and behavioral strategies to promote continuation of pharmacotherapy and support OUD recovery are important to prevent relapse (Bell & Strang, 2020; Nunes et al., 2018; Sofuoglu et al., 2019; U.S. Department of Health and Human Services, 2018).

Gender-specific factors affecting opioid use relapse that are more prevalent in women compared with men include perceived stress, trauma, enhanced biological stress reactivity; as well as less social support for abstinence (Becker, McClellan, & Reed, 2017; NIDA, 2020). AIAN gender-specific interventions for OUD do not exist. Research has documented the positive impact of strong ties in social networks and high levels of social support on abstinence from substance use. Strong social bonds contribute to the maintenance of behavior that is perceived as positive within a social context (Shanmugam, 2017). However, understanding how best to leverage social support remains a key challenge for the addiction treatment field (Venniro et al., 2018).

We propose to address these gaps by developing a social digital intervention to promote stress management and social network support for opioid abstinence among AIAN women. We will utilize Facebook for this platform. Now more than ever with the COVID-19 pandemic, virtual digital platforms have potential for greater reach and scale (Brewer et al., 2020; Robinson et al., 2020). Consistent with the AIAN cultural value of interdependence, social media-formed groups to prevent opioid relapse could lead to greater adoption and sustainability by encouraging collaborative efforts across generations of AIAN women and leveraging community resilience for coping with stress (Coyhis & White, 2002; Mohatt, McDiarmid, & Montoya, 2000; Teufel-Shone et al., 2016; Walters & Simoni, 2002).

The Specific Aim of this study is to develop and beta-test a Facebook group intervention prototype for AIAN women who are abstinent from illicit opioid use and receiving MOUD. We expect that the participatory approach to treatment development will result in a Facebook intervention with cultural relevance for Native women to maintain recovery from opioid use. Interventions to enhance opioid recovery among AIAN women are significant for reducing the substantial public

health burden of illicit use of opioids. A virtual Facebook platform has potential for greater intervention reach to AIAN women and scalability, enhancing the significance and overall impact.

Our approach follows the stage model of addiction therapies development (Rounsaville et al., 2001). If successful, preliminary findings from this proof-of-concept study will be used to support pilot randomized controlled trial (RCT) of the intervention within the NIDA Clinical Trials Network (CTN). This study is the first step to an intervention that could ultimately be widely disseminated through community and addiction health care settings as a treatment adjunct, as well as social media; and serve as a model for developing social digital addictions treatment in other populations, enhancing overall reach and impact.

4.2 Background and Significance to the Field

Among 91,799 drug overdose deaths in the United States in 2020, 68,630 (74.8%) involved opioid use (Hedegaard et al., 2021). OUDs have increased among US women; from 2002 to 2013, heroin use among women increased by 100% in comparison to 50% among men (Centers for Disease Control and Prevention, 2015). In 2019, women admitted for addictions treatment in Minnesota were more likely than men to report opioids as their primary substance of use (22% vs. 13%), but among AIAN women, this rate was greater (45%) (Minnesota Department of Health, 2021). AIAN women were 8.7 times more likely to be diagnosed with maternal OUD during pregnancy compared to whites, and their infants were 8.0 times more likely to be born with neonatal abstinence syndrome (March of Dimes, 2017; Minnesota Department of Health, 2021).

MOUD is the first-line treatment for OUD. Food and Drug Administration (FDA) approved medications for treating OUD are methadone, buprenorphine, and naltrexone (National Academies of Sciences, Engineering, and Medicine, 2018). MOUD has efficacy for reducing opioid use, retaining patients in care, and decreased risks of all cause and overdose-related mortality (Bart, 2012; Lillie et al., 2021; Schuckit, 2016). Relapse rates following discontinuation of medication are about 40-60% (Nunes et al., 2017; U.S. Department of Health and Human Services, 2016), thus behavioral strategies to promote continuation of MOUD and support opioid abstinence are important (Sofuoglu et al., 2019).

Women are more vulnerable to relapse to substance use than men (Becker et al., 2017; NIDA, 2020; Kennedy et al., 2013; Walitzer & Dearing, 2006); factors affecting relapse among women include stress and less social support for abstinence (Becker et al., 2017; NIDA, 2020). AIAN gender-specific interventions for OUD are lacking (Barbosa-Leiker et al., 2020; Meyer et al., 2019; Saraiya et al., 2020).

Substantial evidence documents the positive influence of social reinforcement, social networks, and social support on drug abstinence (Al Ghafri et al., 2022; Christakis & Fowler, 2008; Patten et al., 2016; Shanmugam, 2017; Venniro et al., 2018). Prior studies examined face-to-face interventions to support treatment engagement, MOUD retention and recovery involving concerned others (Brigham et al., 2014; Osilla et al., 2020) or peer outreach workers (Scott et al., 2017; Scott et al., 2020). The COVID-19 pandemic has accelerated the need for virtual digital models of care delivery (Brewer et al., 2020; Robinson et al., 2020). Social-media-formed social networks hold promise as novel and scalable platforms for providing social support for opioid

abstinence. Recent studies indicate that individuals recovering from opioid use utilize social media technologies (e.g., Reddit) for peer support and advice (Bergman et al., 2018; D'Agostino et al., 2017). Social media technologies have been adopted to be culturally relevant for AIAN people (Intahchompoo, 2018; Mathieson et al., 2017; Rushing & Stephens, 2011; Schlichting, 2016; Hensel et al., 2019). However, the use of online social networks among AIAN people for opioid recovery support has ben understudied.

The online social media platform Facebook may effectively engage AIAN people and align with AIAN value of interdependence. Facebook users can post, comment, and react to posts from other members of a group they are in. Facebook is the dominant social networking platform used by US adults across most age groups (18-29: 70%, 30-49: 77%, 50-64: 73%), with lower use among individuals >=65 years old (50%) (Auxier & Anderson, 2021). In the LI's current pilot RCT of a Facebook intervention for nicotine use enrolling AIAN people in Alaska statewide, the study is well-represented by participants of different ages (range 22 to 76 years); over half (54%) are younger than 40 years of age. Another pilot RCT of a Facebook intervention for nicotine use enrolled only young adults (18-25 years) and the researchers found high levels of intervention engagement for that population (Thrul et al., 2015). The proposed content for a Facebook intervention will be transportable to other social media platforms as indicated. For example, Instagram is predominantly used by adults aged 18-29 years (Auxier & Anderson, 2021) and groups are possible by creating a study-specific Instagram profile and setting it as private.

The LI's NIDA-funded work (DA046008) demonstrates the feasibility of a Facebook social support group for nicotine use among AIAN people (Merculieff et al., 2020; Sinicrope et al., 2019). Only 1 of 290 total screened for formative work, beta-testing, and a pilot RCT was excluded due to not having a smartphone or access to broadband internet. In the beta-testing phase (n=10; 90% women, 70% from rural villages) all completed the 1-month follow-up survey (Sinicrope et al., 2022). All 10 engaged in the intervention, e.g., the number of comments made ranged from 1-24 (median 5). Mean treatment satisfaction score based on the Social Media Usability measure was 4.1 ± 0.6 of 5.0, indicating high perceived usefulness, ease of use, and willingness to recommend the intervention to others. In the current pilot RCT, although participants were recruited during the COVID-19 pandemic, the research team exceeded the target sample of 60 (N=61) enrolled. Retention at six months follow-up is 69%. The LI's team also provided guidelines for the addictions treatment field on Facebook intervention moderator training and lessons learned (Sinicrope et al., 2022).

The Lead Investigator (LI) has experience using community-based participatory research (CBPR) to develop content (moderator postings) for Facebook group interventions for community engagement (Patten et al., 2021), and for nicotine cessation among AIAN people living in Alaska described above (Merculieff et al., 2020, Sinicrope et al., 2019). Facebook intervention content will be developed to include culturally relevant stress management strategies leveraging community strengths. Stress, trauma, and dysregulation in biologic stress response systems contribute to substance use (McCabe et al., 2016; Sinha, 2008), and women are particularly susceptible to stress-induced relapse (Kennedy et al., 2013; Walitzer & Dearing, 2005; Greenfield et al., 2010). The LI's work with AIAN women highlighted the role of stress in persistence of and relapse to nicotine use (Patten et al., 2018; Patten et al., 2020). After adjusting for covariates, Perceived Stress Scale scores were positively associated with current smoking among AIAN

women (OR=1.13, 95% CI 1.02-1.24, p=0.016), but not among men. Among pregnant AIAN women, relapse to tobacco use was 78% at 1-2 years postpartum. The primary reason reported for relapse was stress (84%) and addiction (52%) (Patten et al., 2019). Integrated interventions focused on managing stress-related symptoms (e.g., mindfulness) are effective for improving abstinence and reducing relapse to opioids and other substance use (Bowen et al., 2014; Garland et al., 2014; Vowles et al., 2019; Price et al., 2019; Witkiewitz, Bowen et al.; 2013; Witkiewitz et al., 2014); but these were evaluated using in-person delivery formats. US women reported greater use of Facebook than US men (77% vs. 61%), so AIAN women may be more likely to utilize the proposed Facebook group intervention (Auxier & Anderson, 2021). The proposed study is innovative for developing a gender-specific, socially based, opioid relapse prevention intervention using social media technologies that are culturally relevant and already adopted.

4.3 Risk/Benefit Assessment

4.3.1 Risks

Risks are minimal and include those associated with the inconvenience of completing assessment interviews and surveys by telephone/video or in-person, of providing urine samples, and some potential risks related to confidentiality. A trained member of the study staff will obtain the urine sample(s) from the participant. The urine sample test should not present risk to participants, but participants may experience discomfort if their result is positive. No medications will be administered as part of this study. The study poses no greater than minimal risk to pregnant women or fetuses if pregnant women are enrolled. No devices or drugs will be administered as part of the study.

The Facebook intervention will consist of a moderated, closed and secret (completely private) group. This means that no one aside from study participants will be able to join the group, locate the group through a Facebook search, or see reactions or postings to the group through Facebook notification unless they are an official and invited member of the secret and closed group.

In our moderated Facebook intervention, it is impossible to know in advance what might be posted by users, and it is possible that misinformation or postings that might cause emotional discomfort could occur. Participants will be encouraged to contact the study coordinator if any issue arises that causes them to feel uncomfortable. There are also some minimal risks with respect to confidentiality. As a member of a secret Facebook group, participants will be asked to discuss their own opioid recovery journeys and participate in discussions about moderated postings regarding AIAN opioid use, readiness to maintain their recovery from opioids, and opioid treatment resources, among others. Thus, it is possible that health information or other personal information about study participants or other AIAN members could be disclosed on Facebook postings. To ameliorate concerns, a list of do’s and don’ts for posting on the secret Facebook page will be posted at the front of the page so that whenever a participant joins the Facebook group, they will be reminded of these guidelines for sharing information, protecting confidentiality, and posting appropriately. Participants will be asked or encouraged to not mention specific names of people in their house or community. A trained moderator will monitor user postings and guide participants through culturally appropriate postings that do not violate confidentiality or harm intervention group members. If someone is offended by the postings,

they can message the moderator to resolve any concerns. Any adverse events related to the Facebook group will also be handled by the DSMP, if necessary. Despite these precautions, we do not anticipate any adverse consequences of participating in the intervention. In the beta-testing of a Facebook intervention for nicotine use among AIAN people (Sinicrope et al., 2022), one participant shared content outside the group on a personal Facebook page. When this occurred, the moderator sent the participant a private message, redirecting the participant to the group rules. There were no other group confidentiality or boundary violation incidents. We will remind participants in the consent form and a script in the content library to not share personal information with potential guest speakers in order to prevent confidentiality breaches.

Information from the participants will not be shared with anyone else except for the research team. No voices or images from the audio tapes from the individual qualitative interviews will be released. Permission to digitally record will be part of the consent form. Confidentiality of the recordings will be maintained by keeping these in a secure and protected computer. Only the research team will review the recordings. Once transcribed, the recordings will be destroyed after the analyses are completed. In the beta-testing phase, the posted group guidelines and intervention moderators will emphasize confidentiality of the group discussions.

Data from this study will be published and presented in aggregate form only. Participants will be informed that their name, tribal affiliation, and other identifying information; or individual comments from the individual interviews or Facebook intervention discussions or postings will not be published. This will be done to protect the confidentiality and privacy of participants.

Screening data will not include any unique identifiers and will be used for descriptive purposes only (i.e., to characterize the population of individuals screened who were found to be ineligible or not interested in participating). For enrolled participants, confidentiality will be maintained by assigning every participant a study number (no identifiers) and by numerically coding all data. All biospecimens will be labeled with the subject ID number only. The association of the ID number and the participant will be kept by the Mayo Clinic site LI and stored within Mayo's firewalls and on a secured, regularly backed-up drive. All data obtained through interviews and other subject records will be kept in locked filing cabinets in offices that are kept locked when unoccupied, or electronically within Mayo's firewalls on a secured, regularly backed-up drive. Subject files will be kept in a secure area, with access only by designated staff members (LIs and study staff). Any computer storage of data will be password protected and only available to the LIs and the project coordinator.

All information connecting study ID numbers to participant names will be destroyed after completion of the project. Five years after publication of the results (per standard journal guidelines) all paper copies of interview forms, interview transcripts and the data base, will be destroyed. Only summaries of group data will be reported in any publications or presentations, with no identification of individuals or individual statements. All data elements and data transfer activities will be strictly compliant with HIPAA privacy regulatory requirements.

Once the urine sample is processed at the point-of-contact and the study staff obtains the result, the sample will be discarded in a biohazard container and destroyed immediately. Interview forms will be labeled with subject ID numbers only; all personal identifiers will be removed before the data are coded and analyzed.

Standard security measures to store data are in place within the Mayo Clinic. Moreover, at Mayo Clinic the audio tapes from the individual interviews will be stored in a locked file drawer accessible only to the LI Dr. Patten, Co-Investigator Dr. [redacted], and the Program Coordinator Corinna Sabaque.

For participants, withdrawal symptoms from cessation of illicit opioid use do not pose significant health risks as these participants will already be receiving medication for opioid use disorder (e.g., methadone or buprenorphine). What symptoms may occur are expected to be mild and may consist of: nausea and abdominal discomfort, muscle and joint pain, sweating, runny nose and eyes, yawning, irritability, and anxiety.

4.3.2. Benefits

The study is designed develop and obtain preliminary feasibility and acceptability data on a social media intervention to promote prevention of relapse to opioid use among AIAN women. In the first phase of the research, participants will be asked for feedback in designing the intervention. All subjects will potentially benefit from discussions about opioid use and maintaining abstinence. In the third phase of the research, all participants will have access to a culturally relevant social media-formed group that aims to provide support for maintaining abstinence and information on connecting to various local resources. The participants will have the opportunity to benefit by sustaining their abstinence from opioids, continuing MOUD, and gaining new skills in mindfulness, stress management, and resiliency.

5.0 OBJECTIVES

5.1 Primary Objective

To develop a culturally relevant Facebook intervention tailored for AIAN women in Minnesota that will support continued recovery from illicit opioid use. The participatory approach to treatment development will result in a Facebook intervention with cultural relevance for Native women to maintain opioid use recovery.

5.2 Secondary Objective(s)

To conduct a beta-test to assess the preliminary feasibility and acceptability of the Facebook intervention.

5.3 Exploratory Objective(s)

To assess abstinence from illicit opioid use and MOUD retention at the end of the 30-day beta-testing of the Facebook intervention.

6.0 STUDY DESIGN

6.1 Overview of Study Design

This one-year, Phase I, single-site pilot preparatory study aims to develop a culturally relevant Facebook intervention for AIAN women in Minnesota recovering from illicit opioid use. Our approach follows the Stage model of iterative addiction therapies development (Rounsaville et al., 2001) and the study is consistent with Stage Ia. The study will consist of three phases. The first phase will consist of individual qualitative interviews conducted among AIAN women (N=18) and addiction care and interested parties (N=12) to develop the intervention content (moderator postings). The second phase will consist of development of the Facebook content library and a moderator exchange (i.e., bi-directional sharing of knowledge between intervention moderators and trainers). The third phase will consist of beta-testing and refinement of the intervention. The beta-testing phase will use a single group design enrolling 10 AIAN women participants who will have access to the Facebook intervention for a 30-day period. Assessments will be conducted for all participants at baseline and at the end of the intervention. Outcomes are recruitment feasibility, study retention, treatment satisfaction, level of intervention engagement, opioid abstinence and MOUD continuation. The feasibility of using Facebook as an intervention to maintain recovery from opioid use among AIAN women will be refined based on the beta-testing results. We have formed a Community Advisory Committee (CAC) who contributed to the study protocol and will continue to provide input and guidance on the study implementation and dissemination. We hypothesize that input from recovering AIAN women participants and the CAC, content refinement and a comprehensive moderator exchange, and a beta test of the intervention with recovering AIAN women participants will result in a culturally relevant Facebook intervention prototype to support recovery from illicit opioid use among AIAN women.

If successful, preliminary findings from this preparatory study will be used to support a pilot RCT of the intervention through the NIDA Clinical Trials Network (CTN). This study is the first step to an intervention that could ultimately be widely disseminated through community and addiction health care settings as an adjunct to treatment as well as social media.

6.2. Community-Based Participatory Research (CBPR) Approach

This study utilizes a CBPR approach to ensure the intervention and study methods are culturally relevant and acceptable for use in AIAN communities. The need for and interest in a social media intervention for maintaining opioid abstinence came from our community partners in Minneapolis, Minnesota including the Native American Community Clinic and Minnesota Indian Women's Resource Center. The study concept was co-developed with these community partners.

When developing the study protocol, we formed a CAC who provided feedback on the intervention content (moderator postings), study procedures, and measures. The members consist of AIAN women with lived experience as former opioid users, AIAN health care providers, and AIAN community members and interested parties. Health care providers and community partner organizations include the Minnesota Indian Women's Resource Center, Native American Community Clinic, Community-University Health Care Center, and Indian Health Board. We are continuing to enroll members on a rolling basis based on the CAC's recommendations on

additional members who should join. The CAC met three times virtually by Zoom to develop and design the study protocol and materials and to discuss revisions to the protocol based on the feedback from NIDA CTN reviewers. Members have the option to receive an honorarium of $150 per meeting, accept it on behalf of their organization, or donate it to a local organization or community. Members will continue to provide guidance on study implementation and dissemination.

The LI presented the study to the Healthy Nations Advisory Board (HNAB), a group of Tribal leaders representing multiple AIAN communities throughout Minnesota. Tribal leaders provided feedback on the study population, recruitment, and intervention design. The PI will meet with the Healthy Nations Advisory Board on a quarterly basis for continued guidance and feedback throughout the project.

6.3. Duration of Study and Visit Schedule

The duration of the study, from enrollment for the qualitative interview phase to the follow-up visit for the beta-testing phase, will be approximately 7 months. All visits will be conducted by phone or in-person.

Participants in the qualitative interview phase will engage in one phone interview lasting approximately 60-90 minutes, then their active participation in the study will be complete.

Participants in the beta-testing phase will complete all study-related tasks, including urine collection, participation in the Facebook intervention, and baseline and end of intervention follow-up phone surveys, within approximately two months. Their participation in the study will end after completing the follow-up visit survey and in-person UDS.

7.0. OUTCOME MEASURES

7.1 Primary Outcome Measure

A Culturally Relevant Facebook Intervention

The qualitative work of Phase 1 will result in content that will be relevant to AIAN culture. The expected outcomes are development of the intervention which includes development and refinement of the content library (yes/no), development and refinement of the Facebook intervention prototype (yes/no), development and refinement of the intervention moderator guidelines (yes/no), and moderators trained (yes/no).

The success of the Facebook intervention at supporting recovery from opioid use from the participants' perspective will be assessed in the follow-up survey. Participants will be asked for any technical problems that occurred, advice for improving the moderator postings, advice for improving the Facebook group, and the potential for gaining lay moderating skills to encourage other AIAN women to start their recovery from opioids and begin treatment.

7.2 Secondary Outcome Measures

Feasibility and Acceptability

Recruitment feasibility measures documented by study staff include the number of potential participants screened, number eligible, and number enrolled out of those eligible. Study retention will be defined as the proportion completing the end of intervention survey and a UDS. We will use the 13-item Social Media Usability scale (Lund, 2001) to assess participants' satisfaction with the intervention including perceived usefulness, ease of use, and willingness to recommend the intervention to others. The total score is the mean of all 13 items, with a potential range of 1 (low) - 5 (high) satisfaction, with higher scores indicating greater acceptability. We will also ask open-ended questions for feedback on any technical issues that occurred and suggested modifications to the prototype. For intervention engagement assessment, study staff will extract data weekly from the Facebook application programming interface (Facebook, 2020) using an extraction program based on a Python module (https://pypi.org/project/facebook-scraper/) which we have utilized in prior work (Sinicrope et al., 2022). Standard engagement metrics for social media health promotion interventions (Pagato et al, 2016) include Facebook analytics of the number of *posts* 'seen by' group members, reactions (i.e., "like", "love", "care", "haha", "wow", "sad", and "angry"), and comments. Engagement *by participant* includes the number of comments, reactions, responses to a Facebook poll or other activities, attendance at live events (e.g., guest speakers) and posts initiated (i.e., participant created a post with text, image, and/or video). A total engagement count will be calculated from these metrics. The text of participant-generated posts and comments will be exported into an excel spreadsheet for analysis of content. Unlike many web-based platforms, Facebook analytics for private groups do not provide time spent on the Facebook page.

7.3. Exploratory Outcome Measures

Abstinence from illicit opioid and other substance use will be assessed using the Timeline Follow-Back (TLFB) interview (Sobell & Sobell, 1992; Wray et al., 2016) and a UDS at the end of the intervention. Relapse will be operationalized as either a positive opioid UDS **or** self-report of any illicit opioid use in the past 30 days or since study enrollment. Secondarily, we will summarize relapse as at least seven consecutive days of self-reported illicit opioid use in the past 30 days or since study enrollment (Nunes et al., 2018). Secondarily, we will also report outcomes considering missing UDS as missing and not positive/negative (King et al., 2020). MOUD retention will be assessed using the TLFB at the end of intervention visit and summarized as the proportion of days reporting MOUD use and current use.

7.4 Study Timeline

We included a detailed study timeline with the estimated duration and deadlines for each study task per quarter. CTN-0123 was funded as a 1-year study with a timeline that included the initial formation and implementation of a CAC to co-develop the study protocol with the research team. That milestone was successfully completed.

8.0 STUDY POPULATION

8.1 Phase 1

Using a stratified purposeful sample (Patton, 2015), we estimate up to 18 interviews with AIAN women participants and 12 interviews with stakeholders (see **Section 17.2**, Rationale for Sample Size). Consistent with best practices for community engagement (CDC, 2011), we chose to include a range of diverse interested parties in the initial qualitative work, including potential end-users (AIAN women), AIAN addiction treatment and community professionals, and anybody who is otherwise knowledgeable of AIAN culture and opioid addiction and treatment within AIAN communities. AIAN addiction treatment and community professionals were included with the goal of developing a sustainable intervention for within healthcare and community settings. These individuals refer and provide addiction treatment and other services to support recovery for AIAN people and therefore have a stake in the health of AIAN women interested in maintaining their recovery.

8.1.1. AIAN Women

We will enroll up to 18 AIAN women participants for qualitative interviews participants to achieve data saturation (see **Section 17.2**, Rationale for Sample Size). If data saturation is reached at 12 AIAN women participants, we will stop accruing AIAN women participants for interviews.

8.1.2. Health Care Providers and AIAN Interested Parties

We will enroll 12 health care providers for AIAN people and AIAN interested parties for qualitative interviews.

8.2 Phase 3

A new sample of 10 AIAN women participants will be enrolled (see **Section 17.2**, Rationale for Sample Size). Participants will be recruited from (1) clinician and staff referrals from addiction treatment programs at Hennepin County Medical Center and community clinics (e.g., Native American Community Clinic, Indian Health Board, Community University Health Care Center), (2) staff referrals from community organizations and programs (e.g., Minnesota Indian Women's Resource Center, Avivo) located in Minneapolis and St. Paul, Minnesota, and (3) friends or colleagues affiliated with the CAC. A different community flyer intended for AIAN women in this phase will be posted publicly within Minneapolis containing the same information listed above, with an updated toll-free telephone number specific to Phase 3.

8.3 Participant Inclusion Criteria

Individuals must meet all the inclusion criteria to participate in the study.

8.3.1. Phase 1

8.3.1.1 AIAN Women

(1) AIAN based on self-reported race

(2) Gender identity as a woman
(3) Resides in Minnesota
(4) At least 18 years of age with no upper age limit
(5) Has OUD based on the DSM-5 Checklist (American Psychiatric Association, 2013)
(6) Self-reports at least one month of abstinence from illicit opioid use based on Timeline Follow-Back (TLFB) interview
(7) Currently receiving MOUD
(8) Is comfortable speaking and reading English
(9) Is familiar with Facebook
(10) Has access to broadband internet on a mobile phone/computer/tablet at any location

8.3.1.2 Health care providers/AIAN interested parties

(1) Health care provider or AIAN interested party
(2) Knowledge of Native culture and/or OUD treatment and recovery among AIAN people
(3) Is comfortable speaking and reading English
(4) Is familiar with Facebook
(5) Has access to broadband internet on a mobile phone/computer/tablet at any location

Having some familiarity with the Facebook platform is needed to provide feedback on content for a Facebook intervention. Access to the internet is needed to view online moderator postings for providing feedback during the interview.

8.3.2 Phase 3

(1) AIAN person based on self-reported race/ethnicity
(2) Gender identity as a woman
(3) At least 18 years of age with no upper age limit
(4) Resides in Minnesota
(5) Has OUD based on the DSM-5 Checklist (American Psychiatric Association, 2013)
(6) Self-reports at least one month of abstinence from illicit opioid use based on TLFB interview and negative urine opioid screen
(7) Currently receiving MOUD
(8) Is comfortable speaking and reading English
(9) Has an existing Facebook account or willing to set one up
(10) Is willing and able to participate in the Facebook intervention for 1 month
(11) Has access to broadband internet on a mobile phone/computer/tablet at any location
(12) Is willing and able to travel to a community clinic in Minneapolis, Minnesota for the UDS.

We carefully considered including AIAN women with OUD but not currently abstinent or receiving MOUD. However, as the first step, we are interested in developing an approach to support recovery from opioid use including MOUD retention among Native women for several reasons. First, MOUD is an evidence-based, first-line treatment and thus we want to ensure that all participants are receiving this care because MOUD will not be offered as part of the social media intervention. Research has highlighted the importance for the addictions treatment field to develop novel behavioral strategies for maintaining opioid abstinence and MOUD retention based on documented patterns of relapse. In NIDA's initial review of this protocol, the significance of

supporting recovery as an adjunct to treatment - a kind of continuing care via social support – was noted. Second, the intervention is group-based and delivered virtually without any in-person contact from the moderators. Thus, we want to ensure our participants are stable with respect to abstinence and currently receiving MOUD care to enhance the likelihood that they will engage with the Facebook group and to reduce potential adverse risks. Third, when co-designing the study concept for a social media intervention to support recovery with our AIAN community partners it was thought to be essential that women were connected to MOUD support, and that, as a treatment adjunct the proposed intervention could reinforce Native ways of knowing and cultural values to cope with stress and community resiliency for maintaining abstinence. Based on our community partner feedback it was also preferred that we did not restrict the duration of MOUD use at study enrollment so that the intervention could support MOUD initiation and continuation. Likewise, feedback from our CAC has reinforced this aspect of selecting our study population. The community-based participatory approach and working with our AIAN partner community clinics have been key to designing this study protocol and should enhance our recruitment efforts as well as all aspects of study implementation and dissemination. As the first step in this line of research, therefore, we chose to develop the intervention with a more homogenous sample of women who are abstinent from opioid use and receiving MOUD. Nonetheless, the intervention content could readily be expanded in future work for relevance to a broader population of Native women to encourage treatment-seeking and use of MOUD. In fact, our CAC discussed a pathway to later stages of the research to include Native women in recovery who can help to mentor other women to initiate abstinence within the same Facebook group.

We do not specify a maximum age limit. As discussed in the Background and Significance section, our prior work evaluating a Facebook intervention for nicotine use found a wide age range among participants. We will describe any patterns in intervention engagement by age to inform the refinement of the intervention and future research.

8.4 Participant Exclusion Criteria

AIAN potential participants in Phases 1 and 3 meeting any of the exclusion criteria listed below will be excluded from study participation. Interested party participants in Phase 1 will only fail the screening if they meet the second exclusion criterion.

(1) Self-reports current suicidality
(2) Inability or unwillingness of participant to provide verbal consent (Phase 1) or written informed consent (Phase 3)
(3) (Phase 3 only) Was a participant in Phase 1

Pregnant women, lactating women, or women who plan to become pregnant will not be excluded because the treatment being evaluated is a behavioral intervention and does not involve medication or risk to the fetus.

8.5 Strategies for Recruitment and Retention

8.5.1 Phase 1

AIAN women participants will be recruited from (1) clinician and staff referrals from addiction treatment programs (e.g., at Hennepin County Medical Center) and community clinics (e.g., Native American Community Clinic, Indian Health Board, Community University Health Care Center), (2) staff referrals from community organizations and programs (e.g., Minnesota Indian Women's Resource Center, Avivo) located in Minneapolis and St. Paul, Minnesota, and (3) friends or colleagues affiliated with the CAC. We have included a one-page study information sheet developed with the CAC that will be provided to clinicians and staff at these locations. Clinic or program staff will approach potentially eligible AIAN women to assess their interest in the study. Clinic or program staff will provide interested women with a business card with the name of the study at Mayo Clinic and dedicated study toll-free phone number and email. Interested AIAN women will contact the study staff by phone, and study staff will complete a phone screening survey with them to determine if they are eligible for the study. A community flyer intended for AIAN women will be posted publicly within Minneapolis, which will contain the study aim, translation of the study name, study logo, abbreviated eligibility criteria, horizontal flow map and brief description of their study participation, and study content information (i.e., email and toll-free telephone number). It will have a Flesch-Kincaid Reading Level at or below 8.0.

The CAC will help identify potential interested party participants who have knowledge of AIAN culture and/or OUD treatment and recovery among AIAN people. We will provide CAC members with the same 1-page study information sheet described above developed for clinic staff and business cards so that they can refer potentially interested stakeholders. Study staff will screen interested parties by phone to determine if they are eligible for the study.

8.5.2 Phase 3

We will use the same strategy for recruitment of potential AIAN women participants in recovery from illicit opioid use as described above. A toll-free telephone number will be included on the community flyer.

8.5.3 Recruitment Documentation

Potential participants will contact the study staff through the study phone number or email provided on the business card, information sheet, or community flyer.

To document recruitment, study staff will use Mayo Clinic's Participant Tracking System (PTrax). PTrax is how Mayo Clinic staff track potential participants throughout the screening and consent process. As the study staff conducts the screening process, they will enter the potential participant's name into PTrax. They will then indicate in the system how the potential participant was identified and/or referred to the study.

If the potential participant is not eligible, study staff will indicate the screen fail criteria. If the potential participant declines to participate, the study staff will indicate the reason the potential participant declines (e.g., "not interested," "not able to travel to community clinic for UDS").

If we have many potential participants declining to participate, it will be helpful to track this in PTrax so we can consult the CAC for thoughts and suggestions on how to enhance our recruitment efforts.

9.0 SITE SELECTION

9.1 Number of Sites

This is a single site study. Mayo Clinic study staff will coordinate all research activities, including participant recruitment, enrollment, interviews, assessments, the UDS, moderating the Facebook intervention, the moderator exchange, and the beta-testing of the intervention.

Though we will recruit from various community clinics and programs, they will only serve as locations for recruitment referrals and their staff will not conduct any study procedures.

The Mayo Clinic study staff will conduct the UDS at the Indian Health Board community clinic in Minneapolis, Minnesota. Indian Health Board clinic staff will not conduct any study procedures.

9.2 Site Characteristics

Mayo Clinic is a charitable, nonprofit academic medical center that provides comprehensive patient care, education in clinical medicine and medical sciences, and extensive programs in research. Mayo Clinic includes Mayo Medical School, Mayo Graduate School, Mayo School of Graduate Medical Education, Mayo School of Continuous
Professional Development and Mayo School of Health Sciences. The Mayo brothers pioneered the concept of medical group practice before the turn of the century in Rochester, Minnesota, and Mayo Clinic has grown to become the nation's largest medical group practice.

Mayo traditions encompass world-renowned clinical and surgical expertise, as well as extensive research and educational activities. Clinical support is available from 4,729 faculty in medicine, surgery, and allied sciences. In addition to the consultants, there are over 2,400 residents, fellows, and medical students among the 64,000 total personnel. In Rochester, Mayo Clinic's 2,390 physicians and scientists staff two large campuses; Mayo Clinic Hospital — Rochester, Saint Mary's Campus (1,265 beds) and Mayo Clinic Hospital — Rochester, Methodist Campus (794 beds). There is no functional distinction between hospital or clinic patients or physicians, as the entire spectrum of health care is integrated into a common practice. This organization attends over 1.3 million patients each year, who come from all over the United States and abroad.

9.3 Rationale for Site Selection

9.3.1 Mayo Clinic

The facilities and resources available to the investigative team are outstanding and include everything needed to complete the proposed project successfully. The Mayo Clinic campus in Rochester, Minnesota is a large multi-building campus; the institution is home to the Mayo Clinic NCI-designated Comprehensive Cancer Center (MCCC) and the Mayo Clinic Center for Clinical and Translational Science (CCaTS), each providing exceptional resources to support this application.

At Mayo Clinic, Drs. Patten and [redacted] hold faculty appointments in the Department of Psychiatry and Psychology. Dr. Patten directs the Behavioral Health Research Program and her research team has ample computer and office space at the Minnesota BioBusiness building. Other members of the team hold appointments in the Department of Health Sciences Research and Center for Digital Health/Connected Care. Together, MCCC, CCaTS, Center for Digital Health, and Department of Psychiatry and Psychology contribute a rich scientific environment and provide intellectual, technological, educational, and computing resources that will ensure the success of this project. Additionally, Mayo Clinic has several offices that will provide essential and unique support to carry out the proposed research, including the Office of Sponsored Projects Administration and the Office for Human Research Protection (OHRP) and IRB.

9.3.2 The Research Team

Collectively, this multidisciplinary research team brings complementary and unique expertise to the project. Dr. Patten, the LI, has experience with CBPR, AIAN women's health, social media and behavioral nicotine treatments. Dr. [redacted] (Co-I) has expertise in qualitative and mixed methods and content development and moderator training for social media interventions (Patten et al., 2020). Dr. [redacted] (Co-I) has expertise in addictions treatment among women including mindfulness and cognitive behavioral therapies for reducing addiction relapse. Other team members bring complementary expertise in addictions treatment including MOUD (Drs. [redacted]) and technology-assisted and gender-specific therapies for OUD ([redacted]) (Saraiya et al., 2020; Marsch et al., 2020). Dr. [redacted] ([redacted]) has experience with AIAN culturally adapted behavioral interventions for substance use (Dickerson, Venner, & Duran, 2014). [redacted], MD (NorthStar Node), University of Minnesota, has joined the research team as a collaborator. Dr. [redacted] is a junior health disparities researcher who provides addiction care for AIAN patients at a local clinic in Minneapolis. [redacted] PhD, Mayo Clinic, has also joined the research team as a collaborator. Dr. [redacted] is a post-doctoral clinical psychology fellow with expertise in acceptance and commitment therapy and other mindfulness-based therapies. Corinna Sabaque, MPH (Dine') will serve as the Program Coordinator and will assist with the NIDA and IRB progress reports. Corinna Sabaque and Antonia Young, BA will conduct the qualitative interviews and moderate the Facebook intervention. Additional Mayo Clinic study staff include [redacted] BA, who will assist with study design, screening, recruitment, enrollment, and assessments, and [redacted], MS, biostatistician who will assist with statistical analyses and summaries including AEs/SAEs.

10. STUDY PROCEDURES

10.1 Phase 1: Qualitative Work to Develop Facebook Content

10.1.1 Projected Facebook Content

Based on initial input from our community partners in designing the study, and subsequent advice from our CAC, potential Facebook content for the moderator postings will be derived from three sources:

(1) Mindfulness-based relapse prevention (MBRP) treatment. MBRP focuses on managing stress-related symptoms and is an evidence-based intervention for improving abstinence and reducing relapse to opioids and other substance use (Bowen et al., 2014; Garland et al., 2014; Vowles et al., 2019; Price et al., 2019; Witkiewitz, Bowen et al.; 2013; Witkiewitz et al., 2014). Topics include recognizing the role of stress/trauma in substance use, mindfulness practices in daily life and high-risk situations, acceptance, and social support (Bowen et al., 2014; Vowles et al., 2019; Witkiewitz et al., 2013; Witkiewitz et al., 2014).

(2) Stress Management and Resiliency Training (SMART) program. The SMART program has been shown to be effective in RCTs for reducing perceived stress among women and diverse populations (Bhagra et al., 2019). Topics include four key mindfulness concepts: gratitude, mindful presence, kindness, and resilient mindset translated for lay audiences (Resilient Option, 2020).

(3) Existing opioid abstinence support resources and referral information. We have developed a web link on [redacted]. It is a single webpage that includes links for participants to access existing cultural and community resources including shelters, childcare, mental/behavioral health clinics, substance use programs, and commercial tobacco cessation resources. Resources also connect or reconnect participants to MOUD and other treatments for OUD and other substance use. We have also added resources that address parenting, as well as preconception, prenatal and postpartum resources that could help to reinforce opioid abstinence. This focus aligns with the AIAN cultural value emphasizing families and interdependence in supporting addiction recovery. We worked with members of the CAC who are clinic staff from the Community-University Health Care Center, Native American Community Clinic, Indian Health Board, and Minnesota Indian Women's Resource Center to gather these opioid abstinence and community support resources. The webpage on [redacted] will also include a link to email the study team if participants have recommendations for additional resources.

We identified existing social media content such as digital story videos from Native people, images, and text that supplement the MBRP treatment and SMART program. Selection of potential content was made through feedback from the CAC. Some examples of CAC suggestions were to include pictures of nature from areas in Minnesota that were more relatable and to include artwork from local Native artists that feature Native women and spirituality. For mindfulness practices, it was important to recognize when individuals are already being mindful such as during smudging practices or watching a bird on a windowsill. In fact, it was recommended that all beta-

testing participants receive a smudge kit at study enrollment to facilitate their participation in mindfulness exercises during the intervention. Gratitude exercises that focus on a specific person might be triggering so it was suggested to have the option of gratitude toward an animal or nature. Consistent with the value placed on families among AIAN people, content will reinforce healthy parenting and families that may be especially relevant to women who have children, and/or are pregnant or planning on becoming pregnant. Furthermore, the inclusion of Native songs was thought to be healing and could reinforce culture as a way to support opioid recovery. Based on this feedback, seven potential moderator postings (text/image and video postings) were created and will be used to obtain feedback from participants in the qualitative interviews.

The CAC recommended that the study be named by a Native Elder woman to capture the essence of what the study is trying to accomplish and to have meaning in the community beyond the project. The CAC recommended Sharyl WhiteHawk (Ojibwe/Anishinaabe) who gave the study the name “Wiidookaage’win,” pronounced phonetically as “Wee doo kah gay win,” an Ojibwe word that means “the place for help and time for helping.” “Wiidookaage’win” reflects healing and community, which are values important to Native women recovering from addiction.The CAC also recommended Native artists in Minnesota for a relevant study logo, moderator postings, and Facebook cover photos. The logo was created by [redacted] featuring three Native women embracing each other and smiling, whichreflects the meaning of the study name.

10.1.2. Moderator Guides for Qualitative Interviews

We have included the semi-structured moderator guides for the individual interviews with AIAN women participants and interested parties respectively that were developed by the research team with input from our CAC. Interviews assess selected moderator postings for cultural relevance (Davis & Resnicow, 2012; Dickerson et al., 2020) and perceived effectiveness (Davis, Nonnemaker, Duke, & Farrelly, 2013) along with eliciting feedback on ways to engage AIAN women in the study and intervention. The seven moderator postings include three videos featuring digital stories from Native women and a Native song that range from 30 seconds to five minutes and 36 seconds in duration. The remaining postings are text/images encouraging mindfulness and gratitude practices and include Native artwork. For each posting, the interviewer will ask about cultural relevance. For example, “How did you relate to [the subject in the video]?” and “How, if at all, does this video relate to your values as a Native woman?” Interview questions also assess perceived effectiveness of each posting, i.e., “How do you think this posting might help in supporting Native women in their recovery from opioid use? *Do you think it would work? Why or why not?”* Other topics covered in the interview are ways to optimize engagement with the Facebook intervention and how best to appeal to women to participate in the study.

10.1.3. Interviewer Training

Interviews will be conducted by female study staff trained in qualitative interviewing. Using the moderator guides developed, Dr. [redacted] will provide training with study staff including: 4 hours of didactic instruction, 4 hours of mock interview practice, and completion of a certification interview (Krueger & Casey, 2014).

10.1.4. Screening Visit

Trained female study staff will use the Screening Form during a phone/video call with interested potential participants to determine the study eligibility criteria. For AIAN women participants only, the screening measures include the TLFB interview to assess illicit use of opioids in the past 30 days, the Concise Health Risk Tracking—Self Report (CHRT-SR) Suicidal Behavior Evaluation (Trivedi et al., 2011) to assess current suicidality, and the OUD DSM-5 Checklist, an interviewer administered instrument that consists of each DSM-5 diagnostic criterion for OUD in the form of a closed question, and staff indicate “Yes” or “No” based on the potential participant’s responses. If the potential participant answers “Yes” to at least two questions, they will be eligible for the study and will be enrolled. If they do not, they will be provided referral resources.

Those not meeting these criteria will be provided with referral resources. For those meeting the study eligibility criteria, we have included a Participant Contact Form that will be completed by study staff to obtain information to assist in contacting participants to schedule the interview. This form collects the participant’s email address and phone numbers. No information from this form is used in data analyses, nor is this information captured in the data capture system.

Study staff will either move forward to complete the consent process and qualitative interview in the same call or it will be scheduled for the near future. The participant will be sent an email or text message with a web link and attachment for viewing online materials consisting of videos and text/image postings that will be reviewed during the interview.

10.1.5. Enrollment

Individuals who are eligible and complete the informed consent process (described below) will be enrolled.

10.1.6. Interview Methods

Trained female study staff will conduct an individual semi-structured interview by phone or video call (i.e., Zoom, Facetime) lasting approximately 60-90 minutes. We have included the moderator guides for the interviews with AIAN participants and interested parties, respectively and these are described above. The interviewer will begin by obtaining verbal consent from the participant to participate in the study and to be recorded for the qualitative portion before conducting the interview. If the participant is not comfortable being recorded, they can still participate, and the study staff will take detailed field notes. The potential research participant will be informed of the details of the study, the confidential nature of the study, and the fact that participation is entirely voluntary and will not affect their current or future medical care anywhere they get health care.

If there is any sign of incoherence or report of current intoxication/substance use, the interviewer will offer referral resources and stop/reschedule the interview. If the interview is conducted by phone, the participant will be asked if they have the online link accessible to view during the interview. If not, the interviewer will resend the link by email or text. If the link cannot be accessed, the interview will be rescheduled. If the interview is done by Zoom/video call, the interviewer will share the materials on her screen so that the participant can view the postings during the interview.

First, the interviewer will begin with an icebreaker question to build rapport. For AIAN women in recovery, this will be “What was the last beautiful thing you saw?” For interested parties, this will be “Can you tell me a little bit about where you are from and how long you have worked at [organization/setting] in Minnesota?” Next, the interviewer will collect brief demographic information with items derived from the PhenX Toolkit Demographics form (Hamilton et al., 2011). For AIAN participants, this information will include race (in addition to AIAN), ethnicity, age, education, marital status, employment, and connectedness to their Native culture. The last item will be measured with the question, “For this next question, I’d like you to think of a number between zero and ten with zero meaning ‘Not at All Important’ and ten meaning ‘Very Important’. By choosing any number between zero and ten, how important is being Native to your overall identity?” (adapted from Resnicow et al 2009), and it will be scored using an 11-point Likert scale (0 = Not at all important, 10 = Very Important). For interested party participants, this will include race, ethnicity, gender identity, and their role working with AIAN women in recovery. No protected health information or identifying information will be collected from participants. For AIAN participants, the screening form will not be linked to the interview form and the interview form will contain a study ID number only with no identifiers.

Next, the interviewer will begin the audio recording and tell the participant that they started recording. In the event the participant is not comfortable being recorded, or the audio equipment is malfunctioning, the interviewer will take detailed, written notes. First, the interviewer will describe the proposed Facebook group. Second, the interviewer will watch/share each video posting with the participant and read aloud or have the participant read each text/image posting, depending on the participant’s preference. For each posting, the participant will appraise the content for cultural relevance and perceived effectiveness as described above. Third, the interviewer will inquire about best ways to recruit and engage AIAN women in recovery in this type of program. We will ask about other content that might be helpful/relevant/interesting topics to include (e.g., beading, cooking).

We pretested the moderator guides with research staff for duration, wording, and flow. We expect the interviews with AIAN women to last about 75-90 minutes and those with stakeholders about 60-90 minutes. Participation in the study is completed after the interview is conducted. Participants will receive a $[redacted] cash card as a thank you for their time. The study staff will ask the participant to provide a mailing address for the [redacted] cash card, which the study staff will document in REDCap. This information will not otherwise be included in the dataset.

At the end of the interview, all participants (AIAN women and interested parties) will be asked their permission for study staff to contact them in the future to share results from the study. All participants willing to be recontacted will be mailed a dissemination newsletter to be created with our CAC that will share the study findings.

We will also conduct a minimum of 2 member checks to increase the trustworthiness and credibility of results (Lincoln & Guba, 1985) and relevance to AIAN women. Once the interviews are transcribed and coded, for AIAN women participants who said they were willing to be re-contacted, we will conduct a brief (15-20 minute) phone interview to review her individual transcript (responses) and how these were interpreted (coded). We will ask the participant if these

interpretations resonate and if she would change or add anything. We will conduct more member checks if major discrepancies in interpretations of interview responses are noted.

10.1.7 Phase 1 Table of Assessments

Concept	Assessment
Participant eligibility measures	Screening survey
	AI/AN participants only: Meets Opioid Use Disorder criteria, based on the DSM-5 checklist (American Psychiatric Association, 2013)
	Timeline Follow-Back interview (Sobell et al., 1988) to assess illicit opioid use in past 30 days
	Current suicidality based on last 3 items from the Concise Health Risk Tracking—Self Report (CHRT-SR) Suicidal Behavior Evaluation (Trivedi et al., 2011)
Semi-structured interview	Brief demographic questions (Hamilton et al., 2011)
	Questions assessing moderator postings for cultural relevance (Davis & Resnicow, 2012; Dickerson et al., 2020) and perceived effectiveness (Davis et al., 2013)
	Questions to obtain feedback on ways to enhance study participation and Facebook group engagement

10.2 Phase 2: Prototype Development, Content Library, and Moderator Exchange

10.2.1. Prototype Development

The intervention prototype will be developed with the Mayo Center for Digital Health and guided by recommendations for social media health communications (Centers for Disease Control and Prevention, 2016). To address potential privacy concerns, we are utilizing a private and closed group (i.e., invitation only, Facebook page and postings/news feeds not visible, searchable, or accessible to anyone on Facebook except the participants) and a group policy/guideline that emphasizes confidentiality of all content. We have included a screenshot of a draft Facebook cover with the logo/study name. We have included the initial participant guidelines for the Facebook group. Based on feedback from participants and the research team during Phase 1, we will ask the Facebook group members for their input on what guidelines we should include to ensure their comfort participating in the group.

10.2.2. Content Library and Intervention Moderator Guidelines

The Facebook intervention will have a three-month duration consistent with other addiction social media intervention platforms (Meacham et al., 2021; Ramo et al., 2015; Sinicrope et al., 2019). Content (moderator postings) will be refined based on results from the qualitative interviews. We will develop a content library (digital and written) similar to a conventional treatment manual for use by the moderators (Pagoto et al., 2016). It will contain at least 30 moderator postings. Moderators will post once every 1-2 days for the three-month duration; postings will be repeated each of the three months. Content for moderator postings will consist of images, audio, and video combined with text designed to provide information and stimulate participant discussion. The postings have been refined based on the feedback from the Phase 1 qualitative interviews and CAC feedback. Some refinements included keeping posts focused on one topic, avoiding overuse. Meta-themes derived from interviews that will be addressed in the group include keeping the group a positive experience for the participants, encouraging the participants to build a toolkit of ways to deal with stress using MBRP and SMART principles, keeping the language and topics in the group authentic and relatable to the participants, and incorporating exercises or local resources for the participants to take action after viewing posts. The moderator posts will be organized by topic, and each posting will include sample text the moderators could add to initiate discussion or modify according to current group conversations. The content library will also include (1) welcome posts, group description, (2) options for Facebook covers, (3) moderator guidelines for handling challenging conversations and posting of inappropriate posts or misinformation (e.g., deleting unrelated or false posts), (4) closing posts including additional places to connect to resources after the group ends. Based on feedback from Phase 1 participants, some specific types of postings will include personal stories from AIAN women in long-term recovery, coping mechanisms provided after introducing topics such as cravings and triggers, and Facebook live event to host a guest speaker who is knowledgeable of AIAN culture and/or opioid recovery. Participant information will not be disclosed to the guest speaker, but incidental occurrences may occur. To reduce the likelihood of these occurrences, we will tell participants in the consent form and a script in the content library to not share personal information so their identity and PHI can remain protected. We will incorporate artwork from Native artists as much as possible, also consistent with Phase 1 feedback. All data collection and study accrual for Phase 1 is complete.

Although we will develop a three-month intervention, in this pilot preparatory study, we will beta-test the intervention for a 30-day period only. A 30-day intervention should allow sufficient time to determine engagement levels with Facebook and may help to determine appropriate “dosing” for a subsequent clinical trial. In prior work developing a Facebook intervention for nicotine use (Sinicrope et al., 2022), a 30-day duration was sufficient for obtaining rich feedback on the content postings and end-user experience with the intervention; to note any technical issues that need to be remedied; and to obtain preliminary data on recruitment feasibility, study retention, and level of intervention engagement. Our goal is to refine the Facebook prototype for evaluation of the three-month intervention in a subsequent pilot RCT.

10.2.3. Facebook Intervention Moderators

The intervention will be moderated by Corinna Sabaque, an AIAN woman (Navajo/Jemez Pueblo), with strong foundations in Native culture and knowledge of community resources and connections. Antonia Young will support Ms. Sabaque as a co-moderator. Dr. [redacted] will serve as a back-up moderator in the event that either Ms. Sabaque or Ms. Young is unavailable to moderate the group. In addition, as suggested by our CAC, we also plan to engage the same Native Elder woman, [redacted], who is an addictions counselor working with AIAN women and has experience using Facebook and other social media. She will act as a consultant who will assist Ms. Sabaque and Ms. Young as they moderate the group. Ms. Sabaque or Ms. Young will contact [redacted] to describe any incidents or issues that occur with no identifying information and get advice on how to address the situation. All moderators will participate in the moderator exchange described below.

10.2.4. Moderator Exchange

10.2.4.1. Overview

The success of a social media group for health behavior change is dependent upon the skills of its moderators to promote engagement among their members (Sinicrope et al., 2022; Young, 2013). Instead of a traditional training where information is sent in one direction, we have opted for a bi-directional exchange where our moderators and trainers can share knowledge with one another.

The overall goal of the training will be to ensure that our moderators have the knowledge, skills, and confidence to moderate the Facebook intervention group. In the case of Wiidookaage'win, with input from our CAC and research team, we identified that understanding, appreciation, and inclusion of AIAN culture and values must be at the forefront of all exchanges. To accomplish this goal, we have developed 5 exchanges (about 20-22 hours in total) of knowledge and skills in the areas of: 1) Supporting Recovery from Opioid Use; 2) Culture and Gender Issues in Delivery of Substance Use Interventions for Native Women; 3) Teaching Mindfulness; 4) Communication Skills for Health Behavior Change; and 5) Online Community Management Skills.

We have included a table below that details the content and length of each exchange session as well as who will lead and attend each exchange session. While each training exchange is separate, they will be provided in the sequence described here so that understanding of opioid recovery, gender, and culture issues for Native Women can be woven into all exchanges.

Faculty trainers for the moderator exchange include members of the research team. We will engage other individuals with relevant expertise as consultant trainers including Ms. [redacted] at Mayo Clinic who leads the Mayo Clinic Facebook page and is an expert at online community management (Young, 2013), and Dr. [redacted] (University of Michigan An Arbor), an expert in lay motivational interviewing skills and application of these skills to a social media forum. Both individuals trained the AIAN moderators for the LI's Alaska-based social media intervention for nicotine use (see Sinicrope et al., 2022).

10.2.4.2. Evaluation

Successful moderators will report high levels of confidence to promote engagement with and across group members, to respond to a variety of posts, and to know when to seek support from other team members as needed. To evaluate the success of our training plan, a pre-post exchange assessment will be administered measuring their levels of confidence in each area of the exchange, satisfaction with the exchange process, and recommendations for improvement. If needed, additional exchanges will be provided. All moderators will receive a certificate of completion after completing all training modules.

10.2.4.3. Beta Test Exchange

One of our faculty consultant trainers ([redacted]) will review moderator-participant discussions weekly meet with the moderators every two weeks over the beta testing period to share constructive feedback and support to one another as they hone their skills as moderators.

Wiidookaage'win Moderator Exchange Overview			
Title of Exchange	**Description**	**Time/Days**	**Faculty Trainers**
Supporting Recovery from Opioid Use	A 1-hour online workshop that covers: 1) the role of peers in recovery; 2) opioids and the brain; 3) treatment options; and 4) supporting those using opioids [redacted]. The training will include a 1-hour exchange via Zoom.	2 hour training video and 1 hour Zoom meeting to discuss and exchange information	[redacted]
Culture and Gender Considerations for Delivery of Substance Use Interventions with Native Women	A 2-hour exchange of information on how culture and gender affects opioid recovery and support, and the moderation of the Facebook group (support messaging, selection of content, and promoting engagement).	2 hours: This topic will be built into all the training modules. We will include two 1-hour Zoom meeting to discuss this topic at the beginning and then end of the training.	[redacted]
Teaching Mindfulness	Includes a 3-hour training of MBRP provided by psychotherapy.net and a 1-hour virtual training provided on SMART.	4 hours: (3-hour training video and then Zoom meeting to discuss and exchange information.	[redacted]
Online Community Management and Moderator Principles	Virtual workshop focused on ways to increase engagement in a Facebook group. Will include didactic exchange and hands-on practice.	6-8 hours	[redacted]
Communication Skills for Health Behavior Change	Virtual and face-to face workshop to build skills in lay motivational interviewing and communication. Will include didactic exchange and hands on practice	6 hours (hands-on practice will be combined with online community management training.	[redacted]
Human Subjects Training	A training about protecting human subjects in research is required by Mayo Clinic for all people engaging in medical research involving human subjects.	Study staff have already completed this training.	--

10.3. Phase 3: Beta-Testing of the Facebook Intervention

We will conduct a 30-day beta-test of the intervention prototype and study procedures with a new sample of 10 AIAN women participants in recovery from illicit opioid use. The purpose of this phase will be to expose participants to and obtain feedback on the 30 days of moderator postings, note any technical issues that need to be remedied, and facilitate any refinements of the program. This phase will use a single group design with study assessments at baseline and at the end of the intervention. Active study participation will be complete at the follow-up visit. The Facebook intervention prototype will be refined based on user feedback for use in a future pilot RCT.

10.3.1. Screening Visits and Consent Procedures

10.3.1.1. Phone Screen

The study staff will either call the participant or vice versa to begin the screening process. They will first confirm their identity with their full name provided in their email or voicemail. Trained female study staff will screen interested participants by phone to determine the study eligibility criteria with an initial set of questions. The initial set of eligibility questions will include self-reported race/ethnicity, gender identity, age, current residence, OUD DSM-5 Checklist, current use of MOUD, comfort reading and speaking English, whether the individual has a Facebook account or is willing to set one up, access to broadband Internet at any location, and willingness to travel to a community clinic in Minneapolis for the UDS. If the individual is eligible for the study, study staff will give them the option to sign the informed consent form remotely using DocuSign via PTrax or meet the study staff at the Indian Health Board community clinic to sign a hard copy of the consent form before the UDS. In addition to the study eligibility criteria, participants will be asked if they have a current prescription for opioids on the Screening Form, but this information is neither an inclusion or exclusion criterion and will only be utilized in case their urine is positive for opioids in the UDS.

At the UDS screening visit, the remaining screening procedures will include the same suicidality questions from Phase 1 and the TLFB to assess past 30 day use of opioids such as oxycodone, opiates such as heroin, and fentanyl. Those not meeting these criteria will be provided with referral resources. For those meeting the study eligibility criteria study staff will complete a Participant Contact Form. This form collects the participant's email address and phone numbers as well as secondary contact information. No information from this form is used in data analyses, nor is this information captured in the data capture system.

The study staff member will then schedule the participant for a UDS to screen them for the presence of opiates, opioids, and fentanyl. They will be asked to bring their prescription bottle to the UDS to verify that they are taking MOUD, and, if the participant indicates that they have a prescription for opioids at screening, they will be asked to bring their opioid prescription bottle as well.

10.3.1.2. In-Person Visit

Participants meeting the initial study eligibility criteria will be asked to make an in-person visit to the Indian Health Board community clinic in Minneapolis, Minnesota. Mayo Clinic study staff will

confirm their identity by asking for their full name and date of birth. If remote electronic consent was not obtained, study staff will obtain written informed consent. The participant will be asked to answer the suicidality screening questions, provide a urine sample, and verify that they are taking MOUD by presenting their prescription bottle. A member of the CAC is a clinician at the Indian Health Board who has obtained permission for Mayo Clinic staff to perform the UDS at this location. In the event the potential participant does not come to their scheduled UDS, the study staff will attempt to contact the potential participant to reschedule the visit. Three attempts will be made over 4 weeks before the potential participant will be considered ineligible.

All urine specimens will be collected using one-step temperature-controlled urine drug test cups [redacted] following the manufacturer's recommended procedures. This container is designed for safe, secure collection and transportation of biological specimens for laboratory evaluation. The container features accurate, easy-to-read, molded-in graduations on three sides. Top and bottom ribbed etchings ease the opening and closing process when wearing examination gloves. Containers are flexible, crack-resistant and are manufactured from virgin, high clarity, chemically inert, medical grade polypropylene. Heavy duty polyethylene screw caps feature a unique dual fill circle thread design which provides a tight, leak-proof seal.

The potential participant will have a private space away from the study staff to urinate into the test cup, which will have a thermometer strip attached to confirm that the sample is in the area of biological acceptance. The study staff will be required to wear protective clothing and gloves and treat it as an infectious agent. The study staff will use a script to instruct the potential participant on the minimum amount of urine necessary, that they should wash their hands after completing the sample, and how the study staff will read the result. The script will also reassure the potential participant that the urine sample will be destroyed after receiving the result, only the result will be kept if they are eligible, and they will receive a $[redacted] cash card for their time.

The study staff will use IDTC-II 12 Panel Instant Drug Test Cards [redacted] to test for recent (2-3 day window) substance use including opiates. The test will also detect amphetamine, barbiturates, buprenorphine, benzodiazepines, cocaine, methadone metabolite, methamphetamine, ecstasy, methadone, morphine, oxycodone, phencyclidine, tricyclic antidepressants, and marijuana. A separate drug test strip, the Instant Drug Test II Fentanyl, will be used to test for fentanyl (https://cliawaived.com/fentanyl-rapid-tests-20.html). The result for each substance measured with the IDTC-II cards can be “preliminary positive”, “negative”, or “invalid”. The result for the Instant Drug Test II Fentanyl can be “positive,” “negative,” or “invalid.” The study staff will be able to determine the presence of opiates and opioids within 5-60 minutes. If the result for opiates is “preliminary positive,” the woman will not be eligible for the study, and she will be provided referral resources. The UDS will only be used for research purposes, so the study staff will not share the specimen and pursue confirmation testing with a third party (i.e., CLIAwaived, Inc.). The specimen will only be used by the study staff and promptly destroyed after receiving the results.

If the urine sample result is “preliminary positive” for opioids, the woman will confirm that she has been prescribed opioids for medical use, and will show her prescription to the study staff. The purpose of presenting the prescription bottle is to support the participant’s self-report of having a prescription for opioids. However, a limitation is that we will not know if the amount of medication

consumed exceeds the prescribed amount. If they do not have a prescription, they will not be eligible for this study and will be provided referral resources.

The test will detect other commonly abused substances besides opiates, and the full results will be used to characterize the sample at baseline. Any other positive result besides opiates and opioids will be neither an inclusion nor exclusion criterion or outcome measure. Eligible participants may complete the baseline survey with the study staff immediately after the UDS during this visit, or it will be scheduled to be completed by phone in the near future. Participants will receive a $50 cash card for completing the UDS as a thank you for their time and for any travel costs incurred. 10.3.2. Informed Consent Participants will provide written informed consent via DocuSign or hard copy to participate. Study procedures and the potential risks and benefits of participating in the study will be explained by research staff. The potential research participant will be informed of the details of the study and the fact that participation is entirely voluntary and will not affect their current or future medical care anywhere they receive medical care. The study staff will ensure that all participants meet the inclusion/exclusion criteria as stated in the study protocol and that the potential participant clearly understands the study procedures and agrees to follow them. Standard language in our consent procedure assures potential participants of the confidential nature of the study. Those who participate will be clearly assured they may withdraw from the study at any time without adversely affecting current or future medical care anywhere they receive medical care. The consent form obtains HIPAA authorization from participants for use of protected health information. It also outlines the UDS procedure and sensitive questions (i.e., current suicidality) that will be asked in order to complete the screening procedure; it will note that potential participants will receive a $50 cash card in remuneration for the UDS and potential travel costs regardless of their ultimate eligibility. It will also note the potential risks of the UDS and sensitive questions, including potential discomfort in front of research staff if they receive a positive UDS result. If the woman agrees to participate, she will need to complete the UDS as part of the study screening process. Staff will answer questions about the consent form while participants are reviewing it. All screening and consent forms/processes are approved by the IRB and are at the eighth grade reading level. Potential participants will be provided with a copy of the consent form for their records. The consent form will include information on the nature of the study and alternatives to taking part, and contact information (email and toll-free number) for the LI and Program Coordinator. Participants will be encouraged to phone with concerns or problems that might occur during the study. During the informed consent process, we also ask permission to re-contact the participant in the future to share the study findings.

10.3.3. Baseline Visit

If the participant does not have time or wish to complete the baseline survey at the UDS visit, it will be scheduled for another time to be conducted by study staff by phone. We have included a copy of the Baseline Survey. Measures incorporated in this study were selected from the PhenX Toolkit version November 11, 2021, Ver 40.4 for screening and baseline demographic and substance use measures. The PhenX Demographics form (Hamilton et al., 2011) collects information about demographic characteristics of the participant, including age, ethnicity, race (in addition to AIAN), education, marital status, employment status, the number of children under the age of 18 residing in their household, and the same question from Phase 1 measuring the importance of being Native to the participant's identity. We will utilize an item from the PhenX

Toolkit that lists seven major categories of different substances including stimulants (e.g., methamphetamine, Adderall), cocaine/crack, marijuana, sedatives/tranquilizers, club drugs, hallucinogens and inhalants/solvents; and inquire about the past 30-day use of each. For each substance endorsed, we will use the TLFB to assess the days of use. We will ask how the participant used opioids (i.e., injections, pills, patches, lozenges), as Dr. Resnicow noted that their recovery experiences may differ depending on how they consumed opioids. We will collect information on OUD treatments the participant completed within 30 days before baseline, such as inpatient or outpatient services, individual or group support services, or Narcotics Anonymous. Data on substance use will be collected to characterize the sample at baseline (and again at follow-up) and to explore patterns of intervention engagement by substance use.

Based on feedback from the research team on the importance of spirituality in Native culture, the baseline survey will also include items from the World Health Organization's Quality of Life Spirituality, Religion, and Personal Beliefs (WHOQOL SRPB) scale to measure the participant's spiritual, religious, and personal beliefs and how they affect their quality of life (WHOQOL SRPB Group, 2006). Included in the PhenX toolkit (Hamilton et al., 2011), the WHOQOL SRPB was tested in a cross-cultural study and is highly correlated with psychological and social domains of Quality of Life. The items selected for the present study were based on a study that identified items with the strongest factor loadings in each facet of the WHOQOL SRPB (Skevington, Gunson, & O'Connell, 2013) as well as the study team's input on which items would be most relevant to the Facebook group. Five items from the WHOQOL SRPB were included: "To what extent does any connection to a spiritual being help you to get through hard times?" covers the *connection to the spiritual being* facet; "To what extent are you able to experience awe from your surroundings? (e.g., nature, art, music)" covers the *awe and wonder* facet and most of our MBRP content; "How much does spiritual strength help you to live better?" covers the *spiritual strength* facet; "To what extent do you have inner peace?" covers the *inner peace* facet; and "To what extent does faith give you comfort in daily life?" covers the *faith* facet. The five items will be scored on a five-point Likert scale ranging from 0=not at all to 4=an extreme amount. The total score will range from 0 to 20.

Finally, the baseline survey will include the K6 scale (Kessler et al., 2002) to characterize the sample at baseline and to monitor psychiatric symptoms at follow-up. Included in the PhenX toolkit (Hamilton et al., 2011), the K6 is a screening measure that assesses psychological distress including depressive and anxiety symptoms over the past month. The K6 measures distress with six questions (e.g., "How often did you feel nervous?" "How often did you feel hopeless?") scored on a five-point Likert scale ranging from 0=none of the time to 4=all of the time. Total scores can range from 0 to 24, with a recommended cutoff score of 13 to indicate the presence of a psychiatric disorder. The K6 scale is a widely used indicator of nonspecific psychological distress and is highly correlated with mental illness.

For individuals completing the baseline survey, the study staff will send the participant an invitation to the Facebook group by email or text message, depending on the participant's preference. If the participant does not have a Facebook account, we have included instructions that will be provided to participants on how to set one up. We developed these instructions for use in prior studies (Sinicrope et al., 2022).

Participants will receive a $[redacted] cash card for completing the baseline survey as a thank you for their time. Study staff will ask the participant to provide their mailing address for the [redacted] cash card, which the study staff will document in REDCap. This information will not otherwise be included in the dataset.

10.3.4. Enrollment

Eligible individuals providing written informed consent, completing the baseline survey, and accepting the invitation to join the Facebook group will be enrolled. Participants will be informed that the Facebook group will begin when all 10 participants have enrolled. The participant will be mailed or provided with a smudge kit and journal at the UDS visit to use for smudging and MBRP/SMART exercises posted to the Facebook group. The smudge kit is a bundle of cedar, sage, and sweetgrass inside an abalone shell approximately 2 to 3 inches in diameter, and it comes in a resealable travel bag.

10.3.5. Study Intervention Administration

The Facebook intervention was described above in **Sections 10.1 and 10.2**. Participants will receive a welcome message when they join the group and a closing message when the group ends. The intervention will be accessible for a 30-day period. Participation in the intervention is entirely virtual and asynchronous, and available 24 hours a day/7 days a week so they can comment, react, and click on posts/links on their own time. The moderators will post one selection from the intervention content library once every 1-2 days and prompt group discussions as needed. Within the 30-day period, we may host up to 2 live guest speaker events. The guest speakers would be either a member of our research team that would present on a topic relevant to our content library posts or Native experts/Elders who are knowledgeable in opioid recovery and who are well-known and respected in the community.
Moderators will check in with the group every 1-2 days to interact with the participants, monitor adherence to group guidelines, and take actions such as removing inappropriate postings and misinformation if necessary.

10.3.6. Study Intervention Adherence

Data will be extracted weekly from the Facebook application programming interface (Facebook, 2020) as described in **Section 10.3.9**. Intervention adherence will be operationalized as the level of engagement with the intervention and assessed with objective data obtained from Facebook analytics. This includes, for each of the 10 participants in the sample, Facebook group participation through number of comments, postings, reactions; attendance at live Facebook events (e.g., guest speakers), and responding to polls or other activities. These metrics will be summed to create a total engagement count. Unlike many web-based platforms, Facebook analytics for private groups do not provide time spent on the Facebook page.

10.3.7. Discontinuation of Study Intervention

If the subject never engages in the Facebook group or discontinues from the intervention but not from the study, remaining study procedures will be completed as indicated by the study protocol.

If a clinically significant finding is identified (including, but not limited to changes on the K6 scale from baseline) after enrollment, the investigator or qualified designee will determine if any change in participant management is needed. Any new clinically relevant finding will be reported as an adverse event (AE) if it meets the definition specified in Appendix A of the protocol. A plan is in place for clinical management of depression and other psychiatric symptoms or medical problems. The study staff will refer participants to the appropriate on-call physician or behavioral health clinician at the appropriate medical facility. The study staff will have a list of contacts as participant issues or concerns arise that need medical or psychiatric attention, or when other types of referral or assistance are needed. Individuals who report suicidal intent or other severe psychiatric symptoms or medical problems will be referred for treatment and followed throughout the study period. Continued participation with the study will be voluntary and in cooperation with the health care professional treating the subject's psychiatric or medical condition.

The study staff will be trained by Dr. Patten, licensed clinical psychologist, and Dr. [redacted], Mayo Clinic Board Certified Psychiatrist, to observe and monitor depression and psychiatric symptoms. They will be available to consult with the study staff as needed.

In the event a participant withdraws from the study or the LI decides to discontinue a participant due to an SAE, the participant will be monitored by the LI via ongoing status assessment until:

(1) Resolution is reached (i.e., the problem requiring treatment has resolved or stabilized with no further changes expected)
(2) The SAE is determined to be clearly unrelated to the study intervention
(3) The SAE results in death.

10.3.8 Follow-Up

Assessments will be conducted at the end of the intervention with a six-week visit window for completion (King et al., 2020). The participants will complete a UDS and a Follow-up Survey (by phone or in-person at the UDS visit). Study staff will attempt to contact the participant up to three times to complete the assessments and additionally reach out to the participant's secondary contact as needed. If the participant cannot be contacted within the six-week visit window, they will be considered lost to follow-up. Participants will receive a $[redacted] cash card for completing the Follow-Up Survey. They will receive an additional $[redacted] cash card for completing the in-person UDS as a thank you for their time and for any travel costs incurred.

Follow-up Survey measures will evaluate treatment satisfaction and user experience using the Social Media Usability scale as well as four open-ended questions. It will also ask for the participant's thoughts on the potential for the group to be used as a way to encourage women to start their recovery journey and whether the participant would be interested in a peer moderator role for a future Facebook group. The TLFB will be used to assess opioid, opiate, and fentanyl use and MOUD use for each day since the previous TLFB assessment conducted at screening. We will again collect information on other OUD treatments the participant completed within the 30 days during the intervention. Using the TLFB, we will again assess for other substance use including stimulant use such as methamphetamines, cocaine/crack and marijuana use. The UDS

will be conducted in-person and staff will follow the same procedures as described above for the screening visit.

The Follow-Up Survey will include the same items from WHOQOL SRPB as the Baseline Survey to assess any changes in how their spirituality affects their Quality of Life and the K6 scale to assess changes in psychiatric symptoms during their participation in the Facebook group. It will also ask how important the participant feels it would be for Facebook groups like the pilot group to address spirituality from 0=not at all important to 10=very important. The study staff will assess adverse events (AEs) and serious adverse events (SAEs) including self-reported trips to the emergency department (ED), hospitalizations, and overdoses since enrollment.

10.3.9. Phase 3 Table of Assessments

Concept	Assessment	Visit
Participant eligibility measures	Screening survey	Time 1
	Opioid Use Disorder diagnosis based on the DSM-5 checklist (American Psychiatric Association, 2013)	Time 1
	Timeline Follow-Back interview (Sobell et al., 1988) to assess opioid and other substance use in past 30 days	Time 1
	Current suicidality based on 3 items from the Concise Health Risk Tracking—Self Report (CHRT-SR) Suicidal Behavior Evaluation (Trivedi et al., 2011)	Time 1
	Urine drug screen ([redacted] (https://cliawaived.com/fentanyl-rapid-tests-20.html**)**	Time 1
Baseline sociodemographics	Baseline survey using PhenX Toolkit items (Hamilton et al., 2011)	Time 1
User experience measures	Social Media Usability scale (Lund, 2001) and open-ended questions	Time 2
Opioid use outcome measures	Urine drug screen ([redacted]	Time 2

	(https://cliawaived.com/fentanyl-rapid-tests-20.html)	
	Timeline Follow-Back interview (Sobell et al., 1988) to assess opioid and other substance use in past 30 days or since study enrollment	Time 2
MOUD retention	Timeline Follow-Back interview (Sobell et al., 1988) MOUD use in past 30 days or since study enrollment	Time 2
Psychiatric symptom measure	K6 scale (Kessler et al., 2002)	Time 1, Time 2
Spirituality measure	Items from World Health Organization's Quality of Life Spirituality, Religion, and Personal Beliefs measure (WHOQOL SRPB Group, 2006)	Time 1, Time 2

10.3.10. Data Collected by Study Staff

Recruitment feasibility measures documented by study staff include the number of potential participants screened, number eligible, and number enrolled out of those eligible. Study retention will be defined as the proportion completing the end of intervention Follow-up Survey and a UDS.

For intervention engagement assessment, study staff will extract data weekly from the Facebook application programming interface (Facebook, 2020) using an extraction program based on a Python module (https://pypi.org/project/facebook-scraper/) which we have utilized in prior work (Sinicrope et al., 2022). Standard engagement metrics for social media health promotion interventions (Pagato et al, 2016) include Facebook analytics of the number of *posts* 'seen by' group members, reactions (e.g., likes, loves), and comments. Engagement *by participant* includes the number of comments, reactions, responses to a Facebook poll or other activities, attendance at live events (e.g., guest speakers) and posts initiated (i.e., participant created a post with text, image, and/or video). A total engagement count will be calculated from these metrics. The text of participant-generated posts and comments will be exported into an excel spreadsheet for analysis of content. Unlike many web-based platforms, Facebook analytics do not provide time spent on the Facebook page.

10.3.11. End of Intervention Form

This form tracks the participant's status with regard to the intervention in Phase 3. It will be completed by a member of the study staff at the follow-up visit (for participants who complete study participation).

10.3.12. Study Completion Form

This form tracks the participant's status in the study. It will be completed by a member of the study staff at the follow-up visit or after the six-week visit window lapses for participants who do not complete this final follow-up. This form is used in data analyses to address variables such as treatment retention and completion. This form also provides a location for the site LI attestation of review of all study data.

11. CLINICAL AND SAFETY ASSESSMENTS

11.1. Adverse Events (AEs) and Serious Adverse Events (SAEs)

In Phases 1 and 3, AEs and SAEs may be spontaneously reported to study staff at any visit following consent. AEs and SAEs suggesting medical or psychiatric deterioration will be brought to the attention of a study clinician for further evaluation and management. AE and SAE reporting is according to the reporting definitions and procedures outlined in the protocol and in accordance with applicable regulatory requirements. For purposes of this study, the following AEs do not require reporting in the data system but is captured in the source documentation as medically indicated:
Grade 1 (mild) unrelated adverse events: This would typically include mild physical events such as headache, cold, etc., that were considered not reasonably associated with the use of the intervention.

In Phase 3, study staff will assess during the follow-up visit by asking the participant if they visited the Emergency Department (ED), were hospitalized, or had an overdose since enrollment and to briefly describe the event. The study staff will inform the participant that they should contact the study staff immediately if they have an ED visit, are hospitalized, or have an overdose at any point in the study after consent.

For AEs and SAEs, we considered obtaining objective information (e.g., on hospitalizations, ER visits, overdoses) but decided this would not be feasible for this treatment development study. We are recruiting women from the local community and will rely on staff referrals from (1) multiple addiction treatment programs, (2) community clinics and programs throughout the Metropolitan area, and (3) friends or colleagues affiliated with the CAC. We are not recruiting women at specific addictions treatment programs, or from Mayo Clinic, Hennepin Healthcare, or another health system, where medical record release forms and data-sharing agreements could be readily obtained with the permission of participants. However, through this preparatory project, we are building important relationships with community clinic providers and staff who will refer patients to the study and thus building the foundation for the next step in this research where we could work with specific clinics to provide such information. In this study, we will account for AEs using self-report as well as documenting any spontaneous reports from secondary contacts in the event we are not able to reach a participant for the follow-up visit. The risk of adverse events associated with the intervention is minimal because women are required to be currently using MOUD.

11.2. K6 Scale

In Phase 3, we will use the K6 scale (Kessler et al., 2002) at baseline and follow-up assessments. Included in the PhenX toolkit (Hamilton et al., 2011), the K6 is a screening measure that assesses psychological distress including depressive and anxiety symptoms over the past month. The K6 measures distress with six questions (e.g., “How often did you feel nervous?” “How often did you feel hopeless?”) scored on a five-point Likert scale ranging from 0=none of the time to 4=all of the time. Total scores can range from 0 to 24. The K6 scale is a widely used indicator of nonspecific psychological distress and is highly correlated with mental illness. Moreover, studies have shown that having a score of 13 or greater on the K6 is a strong indicator of the presence of a DSM

diagnosable psychiatric disorder with considerable disability (Furukawa et al., 2003; Kessler et al., 2003). The K6 has been validated in general population samples (Forman-Hoffman et al., 2014) and among AIAN adults specifically (Mitchell & Beans, 2011).

If a K6 score of >=13 is prevalent at baseline or follow-up, or if a substantial increase in scores from baseline is noted at follow-up, the LI or one of the study clinicians will follow-up with the participant for further assessment and initiate referral for additional mental health assessment and care as described in the DSMP.

11.3. Assessment of Suicidality at Screening

In the Screening for study eligibility for Phase 1 (AIAN women only) and Phase 3, the study staff will use three items from the Concise Health Risk Tracking-Self Report (CHRT-SR) Suicidal Behavior Evaluation (CHRT-SR) (Trivedi et al., 2011), a self-report assessment of suicidality and related thoughts and behaviors. The scale assesses suicidality quickly and easily in a manner consistent with the Columbia Classification Algorithm of Suicide Assessment (C-CASA) (Posner et al, 2007). The CHRT-SR will assess high risk for suicidality by a positive response (“Agree” or “Strongly Agree”) on the last three questions (thoughts of, thoughts of how, and/or a specific plan to commit suicide) and prompt a clinician assessment for suicide risk before ending the screening visit. A study clinician will complete the Concise Health Risk Tracking – Clinician Rated (CHRT-CR) (Trivedi et al, 2011) to aid in his or her assessment of symptoms and he/she will initiate referral for additional mental health assessment and care as described in the DSMP.

12. PREMATURE WITHDRAWAL OF PARTICIPANTS

Participants in either Phases 1 or 3 may withdraw voluntarily from the study at any time. If they would like to withdraw from the study, they should contact the LI. They will be advised whether they need to complete any additional tests for their safety.

All participants will be followed for the duration of the study CTN-0123 unless they withdraw consent, die, or the investigator or sponsor decides to discontinue their enrollment for any reason. Reasons for the investigator or sponsor terminating a participant from the study may include, but are not limited to

- The participant becoming a threat to self or others
- The participant not following instructions
- The participant relapses on opioids while pregnant
- Staying in the study would be harmful for the participant
- Lack of funding
- The study is canceled

The participant may choose to stay in the study if they never use or discontinue their use of the Facebook intervention.

13. STUDY HALTING RULES

Specific stopping rules have been developed to protect the safety of our study subjects enrolled in Phases 1 or 3. In the case of any SAE, the study will be stopped and no further enrollment will take place until an investigation of the event has taken place by the LI (Dr. Patten), or a Co-LI.

If the SAE involves death or a life-threatening event, the LI, Dr. Patten, will be notified immediately by the study staff. Dr. Patten will telephone, fax, and/or e-mail the Mayo Clinic IRB with follow up notifications to the NIDA Program Official within 24 hours of when she learns of the event. This telephone contact will be followed up with a standardized report form submitted to both the IRB and NIDA within 2 working days of the study staff learning of the SAE. If the SAE involves something other than death or a life-threatening event, Dr. Patten will submit a standardized, detailed report of the event to the IRB and NIDA within 2 working days of when the SAE was reported. Reports of serious adverse events received by the IRB will be reviewed by an institutional SAE Board, (the members of these boards are not involved in this study) to decide of the seriousness of the event and to determine what actions, if any, will be required. If the SAE Board determines that suspension or termination of the study is required, this information will also be reported to NIDA within 24 hours.

Outcome of SAEs will be reported bi-annually to NIDA or as otherwise specified by the NIDA Program Official. A summary of the SAEs that occurred during the previous year will be included in the annual progress report to NIDA and to IRB. All protocol changes and/or protocol amendments will be reported to NIDA, then the IRB. Additionally, a summary of all AEs will be reported in an annual progress report to the IRB. A determination of the association of the adverse event with the study intervention will be made and appropriate modifications to the protocol will be made if an association is suspected. If protocol modifications to ensure the safety of future study subjects cannot be made, the study will be terminated.

14. PARTICIPANT REIMBURSEMENT/REMUNERATION

Participants will be compensated for the participation in this study. Compensation will be in accordance with the Mayo Clinic IRB policies and procedures, and subject to IRB approval.

Participants in all phases of the study will receive compensation via a mailed Mayo Clinic Credit Union cash card. The study staff will assign a cash card ID to the participant, which will be noted in REDCap for reference when documenting payments in Mayo Clinic's Research Participant Payment Application (RPPA).

With Research Finance, the study team will document all participant payments in RPPA and the study team will ask the participant for their SSN. If they decline, the study staff will mark that the participant does not have an SSN.

15. DISSEMINATION

With input from the CAC, the research team will create a study newsletter to share the findings in aggregate from both phases of the research. This will be mailed to participants in Phases 1 and 3 who provided their permission to be re-contacted for this purpose.

16. TRAINING REQUIREMENTS

16.1 Overall

A comprehensive Training Plan will be developed to incorporate general training, study-specific training, mechanisms for competency assessment as well as a detailed description of training, supervision, and fidelity monitoring procedures. The Investigative Team is responsible for the development of a comprehensive Training Plan, instructional material, and delivery of the training, with the team comprised of the Lead Node and other participating nodes and subject matter experts, as applicable.

The CTN-0123 study staff will be trained as specified in the study Training Plan. Training will include Human Subjects Protection (HSP) and Good Clinical Practice (GCP) as well as protocol-specific training on assessments, the study intervention, safety and safety event reporting, study visits and procedures, data management, quality assurance, etc. The Lead Node is primarily responsible for development and delivery of study-specific training related to the study intervention(s) and procedures. Other parties will contribute as needed based on the subject matter and material to be covered. The various sub-teams will collaborate to deliver quality instructional material designed to prepare research staff to fully perform study procedures based on the assigned research roles and responsibilities.

In addition to general and study-specific training, the Training Plan will include a description of the delivery methods to be used for each training module (e.g., via self-study, online, webcast, or teleconference). Study staff is required to complete institutionally required training per their research site, Institutional Review Board, and authorities with regulatory oversight. Tracking of training completion for individual staff as prescribed for assigned study role(s) will be documented and endorsed by the site LI and the Lead Node. As changes occur in the prescribed training, the Training Plan and training documentation tracking forms will be amended to reflect these adjustments.

16.2 Protection of Human Subjects

Key personnel have completed the required education on the protection of human research participants at their respective institutions. The Mayo Clinic has established a formal program entitled the “Mayo Investigator Training Program” (MITP). The MITP is a web-based educational course designed to provide all personnel involved in human subject research with training about human subject protection. All Mayo personnel engaged in human subject research are required to complete the course. MITP primary objectives are to provide historical context for human subject protection regulations and explore the evolving issues for human subjects research.

17.0 STATISTICAL DESIGN AND ANALYSES

17.1 General Design

17.1.1 Study Hypothesis

We hypothesize that by using a CBPR approach, input from recovering AIAN participants and our CAC, content refinement, a comprehensive moderator exchange, and a beta test of the intervention with recovering AIAN participants will result in a culturally relevant Facebook intervention prototype to support recovery from illicit opioid use.

17.1.2 Primary and Secondary Outcomes (Endpoints)

Primary Outcome: A culturally relevant Facebook intervention prototype to support recovery from opioid use.
Secondary Outcomes: Recruitment feasibility, study retention, level of intervention engagement, and intervention satisfaction.
Exploratory Outcome Measures: Abstinence from opioid use and MOUD retention at the end of the intervention.

17.2 Rationale for Sample Size and Statistical Power

17.2.1 Projected Number of Sites

This study will have one site.

17.2.2 Projected Number of Participants

17.2.2.1 Phase 1
Using a stratified purposeful sample (Patton, 2015), we estimate up to 18 interviews with AIAN women participants and 12 interviews with interested parties, based on recommended guidelines for the number of individual qualitative interviews needed to reach data saturation (Namey et al., 2016). Data saturation is the point at which no new information is being learned (Krueger, 2014; Saunders et al., 2018). Recruitment of these additional participants should be feasible within our study timeline. We will consult with members of our Community Advisory Committee as needed as several represent AIAN healthcare and community organizations, thus we do not foresee a need to increase the number of stakeholder interviews.

17.2.2.2 Phase 3

A sample of *N*=10 AIAN women participants is consistent with recommendations for Stage Ia behavioral addictions treatment development (Rounsaville et al., 2001) and beta-testing of novel digital and mHealth interventions (Baker et al., 2014; Nielsen, 2012*)*. Moreover, 10 was the minimum number of participants for optimal Facebook intervention engagement in prior studies (Ramo et al., 2015).

17.3 Statistical Methods

17.3.1 Qualitative Analyses

17.3.1.1 Phase 1

Content analysis (Krippendorff, 2018) supplemented with QSR NVivo software version 10 (Doncaster, Victoria, Australia) will be used to generate interview response themes. The interviews will be audiotaped and professionally transcribed by a vendor approved by Mayo Clinic with a written transcript generated for each. If the participant was not comfortable being recorded, or the audio equipment was malfunctioning, the interviewer's written notes will be imported to NVivo for analysis. Two study team members will review and code the data. Initially, the coders will read 8 transcripts from the AIAN participants to decide whether 12 AIAN participants will reach data saturation. Next, 6 transcripts (~20%) will be randomly selected (3 each from the AIAN women and interested party groups respectively). These will be independently and deductively coded (Saldana, 2016) to generate code lists based on the interview content domains. These codes will be compared and reconciled before arriving at the final set of codes and the coders are calibrated. A third study team member will be brought in to aid in reaching consensus if needed. At this point, a codebook will be developed which will describe the meaning of each code and include relevant key words from the transcripts that link to each code (Miles et al., 2014). To aid in the assessment of the "acceptability" of the postings, within each code, valence coding will also be employed when relevant to track whether responses to that code are positive, negative, mixed, or neutral. The codebook will then be reviewed by the third study team member for feedback and refinement. The final codes will then be applied to all data.

Two study team members will code all interviews. The third team member will resolve discrepancies as needed until consensus is reached. The benefit of coding jointly is that there is ongoing rich discussion of the coding process, of new themes emerging from the data with continual updates of the codebook themes and keywords, and quality control of the coding process, with one person coding into NVIVO and the other person observing the coding to make sure errors are not made (Coffey & Atkinson, 1996; Patton, 2015; Wolff et al., 2019). As a part of the dual coding process, the coders will write up memos each time they meet to code. The memo-writing will be the place where discovery of patterns across themes is recorded. Through discussion ideas about potential patterns and themes will be discussed and reports will be generated using NVIVO to further explore such themes and patterns. At the end of coding, the third study team member will be asked to randomly review 5 of the interviews to assess agreement with the coding.

For AIAN women participants who give permission to be re-contacted, we will review her individual transcript (responses) and how these were interpreted (coded) (i.e., member checking). Responses will be entered and coded using the same methods as the preliminary analysis. We will conduct further qualitative analyses if there are disconfirming voices or themes where participants could not recognize or relate to the interpretations provided and/or to explore any new concepts reported.

Coded data will be examined for patterns across the AIAN women and interested party groups; as well as among AIAN women, any patterns in themes by age group, or substance use.

The qualitative findings will be discussed with the CAC who will guide us in the interpretation and integration of findings and resolving any discrepancies in themes for the AIAN women and stakeholder groups. In the LI's formative work to develop a social media intervention for nicotine use among Alaskan AIAN adults (Merculieff et al., 2021), differences were not found between AIAN smokers or community stakeholders in the acceptability of content (moderator postings) based on cultural relevance or perceived effectiveness. In addition to the feedback on the moderator postings, we expect the interested parties will provide unique information on how the intervention can best be promoted to engage AIAN women to participate in the study as well as factors in designing the intervention that would make the intervention appealing for sustained use within AIAN healthcare and community settings.

17.3.1.2 Phase 3

Survey: The Follow-up Survey contains four open-ended questions assessing the participant's experiences with the intervention, their recommendations for improving the intervention, and their thoughts on using the Facebook group as a way to learn how to mentor other AIAN women who are engaging in illicit opioid use to start their recovery. The text of survey responses will be entered into an Excel spread sheet for analysis. Analyses will generally follow the procedures described for Phase 1. Content analysis (Krippendorff, 2018) supplemented with QSR NVivo software version 10 (Doncaster, Victoria, Australia) will be used to generate response themes in the data for each of the three survey items. Coded data will be examined for any patterns in themes by age group, and substance use.

Facebook intervention group comments and postings: The text of participant-generated posts and comments will be exported into an excel spreadsheet for analysis of content. We will identify common themes of response in the data using content analysis (Krippendorff, 2018) supplemented with QSR NVivo software version 10 (Doncaster, Victoria, Australia). Analyses will generally follow the procedures described for Phase 1. We will summarize the major themes, and the frequency of topics discussed in participant comments and postings will be displayed graphically.

17.3.2 Quantitative Analyses

17.3.2.1 ***Primary Outcome*****:** A culturally relevant Facebook intervention prototype to support recovery from opioid use.

The cultural relevance of the Facebook group will be determined by valence coding with QSR NVivo software version 10. We will summarize the expected outcomes for the development of the intervention using descriptive statistics (frequencies, percentage) which are the development and refinement of the content library (yes/no), development and refinement of the Facebook intervention prototype (yes/no), development and refinement of the intervention moderator guidelines (yes/no), and intervention moderators trained (yes/no). We expect that all outcomes will be achieved at 100% implementation.

17.3.2.2 ***Secondary Outcomes****:* Recruitment feasibility, study retention, level of intervention engagement, and intervention satisfaction.

We will summarize the number of potential participants screened, number eligible, reasons for ineligibility and number enrolled out of those eligible (i.e., participation rate) using frequencies and percentages. Baseline characteristics will be summarized using descriptive statistics (means, medians, frequencies, and percentages). We will summarize the number of enrolled women reporting other substance use at baseline and at follow-up. Study retention will be summarized as the percentage of enrolled participants completing the end of intervention survey and a UDS. The Social Media Usability scale (Lund, 2001) scores will be summarized using descriptive statistics (mean, standard deviation, median and range).

The level of intervention engagement will be summarized using descriptive statistics (medians, frequencies, and percentages). The number of *posts* 'seen by' group members, their reactions, and comments will be summarized. We will also summarize participant-level engagement metrics (e.g., comments, reactions) and the total engagement count overall. The analyses will use an intent-to-treat approach including all 10 participants with those never having engaged in the Facebook group receiving a total engagement count of zero. We will describe patterns of engagement by age group (with age based on median split or <40 vs. >=40 years depending on the age distribution), substance use endorsed on the TLFB (any use: yes/no and/or median split of # of substances used) at baseline and follow-up, and relapse to opioid use (yes/no). We will summarize the total engagement count for moderator and participant-generated posts, respectively.

17.3.2.3 ***Exploratory Outcomes****:* Abstinence from opioid use and MOUD retention at the end of the intervention.

Descriptive statistics (percentages and frequencies) will be used to summarize the sample for relapse to opioids, operationalized as either a positive opiate or fentanyl UDS with missing UDS test imputed as positive **or** self-report of any illicit opioid use in the past 30 days or since study enrollment. Secondarily we will summarize relapse as at least seven consecutive days of self-reported illicit opioid use in the past 30 days or since study enrollment (Nunes et al., 2018). Secondarily, we will also summarize outcomes considering missing UDS as missing and not positive (King et al., 2020).

From the TLFB, will summarize MOUD retention as the proportion of days reporting MOUD use and current use using descriptive statistics (percentages and frequencies).

17.3.3 Missing Data and Dropouts

In Phase 1, individuals meeting the study eligibility criteria and providing informed consent will be enrolled and will not be replaced, even if they do not begin an interview. The analyses will include all enrolled participants. For some individuals in Phase 1, there may be questions that the participant prefers not to answer in which case the analysis will be conducted with available data for those questions.

In Phase 3, individuals meeting the study eligibility criteria, providing informed consent, and completing the baseline assessment will be enrolled and will not be replaced. We will use an

intent-to-treat approach with the analyses including all enrolled participants. Analyses will be conducted considering individuals with missing self-report/TLFB and/or UDS information as (1) missing=relapsed and (2) missing=missing and not relapsed.

The study team will make every effort to contact participants to complete the study tasks including reaching out to a secondary contact if needed. In Phase 3, participants will have a six-week visit window for completing follow-up study tasks including the UDS. Individuals who are not contacted or do not complete the follow-up study tasks will be considered lost to follow-up.

17.3.4 Safety Analysis

Descriptive statistics (frequencies and percentages) will be used to summarize AEs and SAEs. AEs, including SAEs, will be summarized by body system and preferred term using MedDRA codes (per The Medical Dictionary for Regulatory Activities). AEs will be presented as: (1) the number and proportion of participants experiencing at least one incidence of each event overall; and (2) the total number of each event overall in tabular form.

17.3.5 Interim Analyses

On a monthly basis, the occurrence of the type and number of SAEs and AEs will be summarized and the biostatistician will generate a report for the LI and study team for review at monthly research team meetings. Recruitment and study retention data will be summarized weekly. The Program Coordinator will generate a monthly report of the number screened, eligible, enrolled and completing the follow-up visit (Phase 3) for review at monthly research team meetings.

18.0 REGULATORY COMPLIANCE, REPORTING AND MONITORING

18.1 Statement of Compliance

This study will be conducted in accordance with the current version of the protocol, in full conformity with the ethical principles outlined in the Declaration of Helsinki, the Protection of Human Subjects described in the International Council for Harmonisation (ICH) GCP Guidelines, applicable United States (US) Code of Federal Regulations (CFR), the NIDA Terms and Conditions of Award, and all other applicable state, local, and federal regulatory requirements. The LI will assure that no deviation from, or changes to the protocol will take place without prior agreement from the Sponsor and documented approval from the IRB, except where necessary to eliminate an immediate hazard(s) to the trial participants. A Manual of Operations will be provided as a reference guide and study quality assurance tool.

18.2 Institutional Review Board Approval

Prior to initiating the study, the LI will obtain written approval from the Mayo Clinic IRB to conduct the study, which will include approval of the study protocol. If changes to the study protocol become necessary, protocol amendments will be submitted in writing by the investigators for IRB approval prior to implementation. In addition, IRBs will approve all consent forms, recruitment materials, and any materials given to the participant, and any changes made to these documents throughout study implementation. Approval of both the protocol and the consent form(s) must be obtained before any participant is consented. For changes to the consent form, a decision will be made regarding whether previously consented participants need to be re-consented. IRB continuing review will be performed annually, or at a greater frequency contingent upon the complexity and risk of the study. The LI is responsible for maintaining copies of all current IRB approval notices, IRB-approved consent documents, and approval for all protocol modifications. These materials must be received by the LI prior to the initiation of research activities at the site and must be available at any time for audit. Unanticipated problems (UPs) involving risk to study participants will be promptly reported to and reviewed by the Mayo Clinic IRB, according to its usual procedures.

18.3 Informed Consent

The informed consent process is a means of providing study information to each prospective participant and allows for an informed decision about participation in the study. Informed consent continues throughout the individual's study participation. The informed consent form in Phase 3 will include all the required elements of informed consent and may contain additional relevant consent elements and NIDA CCTN specific additional elements. The study site must have the study informed consent(s) approved by the Mayo Clinic IRB. Prior to initial submission to the IRB and with each subsequent consent revision, the consent form(s) will be sent to the Lead Node (Northstar Node, Dr. [redacted] PI) to confirm that each consent form contains the required elements of informed consent as delineated in 21 CFR 50.25(a) and CFR 46.116(b), as well as pertinent additional elements detailed in 21 CFR 50.25(b) and 45 CFR 46.116(c) and any applicable CCTN requirements. Every study participant in Phase 1 will verbally agree to

participate in the research study after listening to the study staff recite a script that includes language for HIPAA authorization. Every study participant in Phase 3 will be required to sign a valid, IRB-approved current version of the study informed consent form prior to the initiation of the screening UDS, screening suicidality questions, and any study related procedures. Because the UDS results and suicidality questions are considered PHI, the potential participant will review the written consent form if they qualify thus far after the initial set of screening questions. The site will maintain the original signed informed consent for every participant in a locked, secure location that is in compliance with all applicable IRB and institutional policies and that is accessible to the study monitors. Every study participant will be given a copy of the signed consent form.

During the informed consent process, research staff will explain the study to the potential participant. In Phase 3, the study staff will provide thepotential participant with a copy of the consent form to read and keep for reference. All participants will receive a verbal explanation in terms suited to their comprehension of the purposes, procedures, and potential risks of the study and their rights as research participants. Extensive discussion of risks and possible benefits will be provided to the participants. Phase 3 participants will have the opportunity to carefully review the written consent form and ask questions prior to signing. The participants will have the opportunity to discuss the study with their family and close friends or think about it prior to agreeing to participate. In Phase 3, if the participant is interested in participating in the study, a qualified staff member will review each section of the IRB-approved informed consent form in detail and answer any questions the participant may pose. The person obtaining consent will also sign and date the consent document. A research staff member will review the consent after it is signed to ensure that the consent is properly executed and complete. Staff members delegated by the LI to obtain informed consent will be approved by the IRB. All persons obtaining consent will have completed appropriate GCP and HSP training, as mandated by NIDA standard operating procedures (SOPs).

The informed consent form will be updated or revised whenever important new safety information is available, or whenever the protocol is amended in a way that may affect participants' participation in the trial. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study. The participant will be informed that their participation is voluntary and they may withdraw from the study at any time, for any reason without penalty. Individuals who refuse to participate or who withdraw from the study will be treated without prejudice. The site will be responsible for maintaining signed consent forms as source documents for quality assurance review and regulatory compliance.

The study does not preempt any applicable federal, state, or local laws which require additional information to be disclosed in order for informed consent to be legally effective. It is in conformance with 42 CFR 2.52, which allows for research-related provisions regarding to the disclosure of substance use disorder patient identifying information in the absence of the informed consent process and HIPAA authorization."

18.4 Quality Assurance Monitoring

In accordance with federal regulations, the study sponsor is responsible for ensuring proper monitoring of an investigation and ensuring that the investigation is conducted in accordance with

the protocol. Qualified monitors will oversee aspects of site conformity to make certain the site staff is operating within the confines of the protocol, and in accordance with GCP. This includes but is not limited to protocol compliance, documentation auditing, and ensuring the informed consent process is being correctly followed and documented. Non-conformity with protocol and federal regulations will be reported as a protocol deviation and submitted to the study sponsor and study IRB of record, (as applicable), for further review.

18.5 Participant and Data Confidentiality

Participant confidentiality and privacy are strictly held in trust by the LI, participating investigators, their staff, the safety and oversight monitor(s), and the sponsor(s) and funding agency, and will be maintained in accordance with all applicable federal regulations and/or state/Commonwealth law and regulations. This confidentiality is extended to the data being collected as part of this study. Data that could be used to identify a specific study participant will be held in strict confidence within the research team. No personally identifiable information from the study will be released to any unauthorized third party without prior written approval of the sponsor/funding agency and the participant.

All research activities will be conducted in as private a setting as possible.

The study monitor, other authorized representatives of the sponsor or funding agency, and representatives of the Mayo Clinic IRB may inspect all documents and records required to be maintained by the investigator, including but not limited to, office study records for the participants in this study. The study site will permit access to such records.

Participant records will be held confidential by use of study codes for identifying participants on CRFs, secure storage of any documents that have participant identifiers, and secure computing procedures for entering and transferring electronic data. The study participant's contact information will be securely stored at the study site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as denoted in **Section 18.14**, Records Retention and Requirements.

By signing the protocol signature page, the investigator affirms that information furnished to the investigator by NIDA will be maintained in confidence and such information will be divulged to the IRB/Privacy Board, Ethical Review Committee, or similar expert committee; affiliated institution; and employees only under an appropriate understanding of confidentiality with such board or committee, affiliated institution, and employees.

18.5.1 Certificate of Confidentiality

To further protect the privacy of study participants, the Secretary, Health and Human Services (HHS), has issued a Certificate of Confidentiality (CoC) to all researchers engaged in biomedical, behavioral, clinical or other human subjects research funded wholly or in part by the federal government. Recipients of NIH funding for human subjects research are required to protect identifiable research information from forced disclosure per the terms of the NIH Policy (see https://humansubjects.nih.gov/coc/index). This protects participants from disclosure of sensitive information (e.g., drug use). It is the NIH policy that investigators and others who have access to

research records will not disclose identifying information except when the participant consents or in certain instances when federal, state, or local law or regulation requires disclosure. NIH expects investigators to inform research participants of the protections and the limits to protections provided by a Certificate issued by this Policy.

18.6 Health Insurance Portability and Accountability Act (HIPAA)

The study site will obtain authorization from participants for use of protected health information. The study site will be responsible for communicating with the Mayo Clinic IRB and obtaining the appropriate approvals or waivers to be in regulatory compliance. Releases of participant identifying information that are permitted by the HIPAA regulations, but which are prohibited by other applicable federal regulations and/or state/Commonwealth law and regulation, are prohibited.

18.7 Investigator Assurances

The study site will have on file an active Federal wide Assurance (FWA) with the HHS OHRP setting forth the commitment of the organization to establish appropriate policies and procedures for the protection of human research subjects in alignment with 45 CFR 46, Subpart A, with documentation sent to NIDA or its designee. Research covered by these regulations cannot proceed in any manner prior to NIDA receipt of certification that the research has been reviewed and approved by the IRB provided for in the assurance (45 CFR 46.103). Prior to initiating the study, the LI will sign a protocol signature page and investigator agreement, providing assurances that the study will be performed according to the standards stipulated therein.

18.8 Financial Disclosure/Conflict of Interest

All investigators will comply with the requirements of 42 CFR Part 50, Subpart F to ensure that the design, conduct, and reporting of the research will not be biased by any conflicting financial interest. Everyone with decision-making responsibilities regarding the protocol will confirm to the sponsor annually that they have met their institutional financial disclosure requirements.

18.9 Clinical Monitoring

Investigators will host periodic visits by NIDA contract monitors who will examine whether study procedures are conducted appropriately, and that study data are generated, documented, and reported in compliance with the protocol, GCP, and applicable regulations. These monitors will audit, at mutually agreed upon times, regulatory documents, case report forms (CRFs), informed consent forms and corresponding source documents for each participant. Monitors will have the opportunity and ability to review any study-associated document or file.

NIDA-contracted monitors will assess whether submitted data are accurate and in agreement with source documentation and will also review regulatory/essential documents such as correspondence with the IRB. Areas of particular concern will be participant informed consent forms, protocol adherence, reported safety events and corresponding assessments. Reports will be prepared following the visit and forwarded to the site principal investigator, the LI and NIDA CCTN.

Qualified node personnel (Node QA monitors) or other designated party(ies) will provide site management for the study site Node QA staff or other designated party(ies) will audit source documentation, including informed consent forms and HIPAA forms. This will take place as specified by the local protocol team, node LI or lead team and will occur as often as needed to help prevent, detect, and correct problems at the study sites. Node QA personnel will verify that study procedures are properly followed and that site personnel are trained and able to conduct the protocol appropriately. If the node personnel's review of study documentation indicates that additional training of site study personnel is needed, node QA personnel will undertake or arrange for that training. Details of the contract, node QA and data monitoring are found in the study QA monitoring plan.

18.10 Inclusion of Women and Minorities

Phase 1 will enroll up to 18 participants reporting AIAN race and gender identity as a woman. Phase 1 will enroll 12 interested parties of which half (n=6) are expected to be women and about two-thirds (n=9) AIAN race. Phase 3 will enroll 10 participants reporting AIAN race and gender identity as a woman. These inclusions are scientifically justified based on the study aims and objectives to develop an intervention specific to AIAN women. Challenges encountered with recruitment will be discussed with the CAC.

18.11 Inclusion of Individuals across the Lifespan

The study team has extensive experience conducting research with ANAI adults at all ages and across the lifespan. We seek a representative distribution of adults aged 18 years and older to increase the applicability of our results and understanding of how the social media intervention can enhance recovery from opioid use among women of all adult ages. All study participants are expected to be 18 years of age or older. We are excluding children because social media interventions have been evaluated among adults, and different interventions may be warranted for children based on their developmental and cognitive abilities. We do not have a maximum age limit. Our prior work evaluating a Facebook intervention for nicotine use found a wide age range among participants. In this study we will examine descriptively any patterns in intervention engagement by age to inform the refinement of the intervention and future research.

18.12 Prisoner Certification

As per 45 CFR 46 Subpart C, there are additional protections pertaining to prisoners as study participants. A prisoner is defined as any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

If a participant in the study becomes incarcerated or otherwise meets the 45 CFR 46 Part C definition of a prisoner during the study, and the relevant research proposal was not reviewed and approved by the IRB in accordance with the requirements for research involving prisoners under Subpart C of 45 CFR 46, the LI will promptly notify the IRB. All research interactions and interventions with, and obtaining identifiable private information about, the participant must be

suspended immediately. The lone exception to this regulation is if the LI asserts that it is in the best interests of the prisoner-participant to remain in the study. The LI will promptly notify the IRB of this occurrence.

18.13 Regulatory Files

The regulatory files will contain all required regulatory documents, study-specific documents, and important communications. Regulatory files will be checked at the study site for regulatory document compliance prior to study initiation, throughout the study, as well as at study closure.

18.14 Records Retention and Requirements

Research records for all study participants (e.g., case report forms, source documents, signed consent forms, audio and video recordings, and regulatory files) will be maintained by the LI in a secure location for a minimum of 3 years after the study is completed and closed. These records are also to be maintained in compliance with IRB, state, and federal requirements, whichever is longest. The Sponsor and LI must be notified in writing and acknowledgment from these parties must be received by the site prior to the destruction or relocation of research records.

18.15 Reporting to Sponsor

The LI agrees to submit accurate, complete, legible, and timely reports to the Sponsor, as required. These include, but are not limited to, reports of any changes that significantly affect the conduct or outcome of the trial or increase risk to study participants. Safety reporting will occur as previously described. At the completion of the trial, the LI will provide a final report to the Sponsor.

18.16 Audits

The Sponsor has an obligation to ensure that this trial is conducted according to good clinical research practice guidelines and may perform quality assurance audits for protocol compliance. The LI and authorized staff from the NorthStar, Northeast, Greater New York, and Southwest Nodes; the National Institute on Drug Abuse Clinical Trials Network (NIDA CTN, the study sponsor); NIDA's contracted agents, monitors, or auditors; and other agencies such as the Department of HHS, the OHRP and the IRB of record may inspect research records for verification of data, compliance with federal guidelines on human participant research, and to assess participant safety.

18.17 Study Documentation

The study site will maintain appropriate study documentation (including medical and research records) for this trial, in compliance with ICH E6 R2 and regulatory and institutional requirements for the protection of confidentiality of participants. Study documentation includes all case report forms, workbooks, source documents, monitoring logs and appointment schedules, sponsor-investigator correspondence, and signed protocol and amendments, IRB correspondence and approved consent form and signed participant consent forms. As part of participating in a NIDA-sponsored study, each site will permit authorized representatives from NIDA and regulatory

agencies to examine (and when permitted by law, to copy) clinical records for the purposes of quality assurance reviews, audits, and evaluation of the study safety, progress, and data validity.

Source documents include all recordings of observations or notations of clinical activities and all reports and records necessary for the evaluation and reconstruction of the clinical research study. Whenever possible, the original recording of an observation should be retained as the source document; however, a photocopy is acceptable provided it is a clear, legible, and exact duplication of the original document.

18.18 Protocol Deviations

This protocol defines a protocol deviation as any noncompliance with the clinical trial protocol. The noncompliance may be either on the part of the participant, or the study site staff. As a result of deviations, corrective actions will be developed by the site and implemented promptly.

These practices are consistent with ICH GCP:

- Section 4.5 Compliance with Protocol, subsections 4.5.1, 4.5.2, and 4.5.3
- Section 5.1 Quality Assurance and Quality Control, subsection 5.1.1
- Section 5.20 Noncompliance, subsections 5.20.1, and 5.20.2.

Any departure from procedures and requirements outlined in the protocol will be classified as either a major or minor protocol deviation. The difference between a major and minor protocol deviation has to do with the seriousness of the event and the corrective action required. A minor protocol deviation is considered an action (or inaction) that by itself is not likely to affect the scientific soundness of the investigation or seriously affect the safety, rights, or welfare of a study participant. Major protocol deviations are departures that may compromise the participant safety, participant rights, inclusion/exclusion criteria or the integrity of study data and could be cause for corrective actions if not rectified or prevented from re-occurrence. The study site will be responsible for developing corrective action plans for both major and minor deviations as appropriate. Those corrective action plans may be reviewed/approved by the Lead Node with overall approval by the Mayo Clinic IRB as needed. All protocol deviations will be monitored at the study site for (1) significance, (2) frequency, and (3) impact on the study objectives, to ensure that site performance does not compromise the integrity of the trial.

All protocol deviations will be recorded in the Electronic Data Capture (EDC) system via the Protocol Deviation CRF. The LI must be contacted immediately if an unqualified or ineligible participant is randomized into the study.

Additionally, the study site is responsible for reviewing the Mayo Clinic IRB's definition of a protocol deviation or violation and understanding which events need to be reported. The study sites must recognize that the CTN and IRB definition of a reportable event may differ and act accordingly in following all reporting requirements for both entities.

18.19 Safety Monitoring

The LI may appoint a Site Medical Clinician (MD, DO, NP, or PA) for this study, who will review or provide consultation for each Adverse Event (AE) and Serious Adverse Event (SAE) as

needed. A site licensed clinical psychologist (Dr. Patten) and site board certified psychiatrist (Dr. Sharma) will also be consulted with as needed. These reviews will include an assessment of the possible relatedness of the event to the study intervention or other study procedures. The Site Medical Clinician will also provide advice for decisions to exclude, refer, or withdraw participants as required. The study staff will determine which safety events require expedited reporting to NIDA and regulatory authorities. This will include events that are serious, related and unexpected. The study staff will be trained to monitor for and report AEs and SAEs, and participants will report AEs and SAEs at the follow-up visit.

The study site has established practices for managing medical and psychiatric emergencies, and the study staff will continue to utilize these procedures. Treatment providers at the study site will be responsible for monitoring participants for possible clinical deterioration or other problems, and for implementing appropriate courses of action.

Any SAE, whether or not it is related to the study intervention and for all participants, will be reported to the Mayo Clinic IRB and NIDA. A summary of the SAEs that occurred in the previous year will be included in the annual progress report to the NIDA. Any action taken by the respective IRBs regarding SAEs or major changes to the protocol will be reported to the NIDA.

If the SAE involves death or a life-threatening event, the LI, Dr. Patten, will be notified immediately by the study staff. Dr. Patten will telephone, fax, and/or e-mail the Mayo Clinic IRB chair/vice-chair, and the NIDA Program Official within 24 hours of when she learns of the event. This telephone contact will be followed up with a standardized report form submitted to both the IRB and NIDA within 2 working days of the study staff learning of the SAE. If the SAE involves something other than death or a life-threatening event, Dr. Patten will submit a standardized, detailed report of the event to the IRB and NIDA within 2 working days of when the SAE was reported. Reports of serious adverse events received by the IRB will be reviewed by an institutional SAE Board, (the members of these boards are not involved in this study) to decide of the seriousness of the event and to determine what actions, if any, will be required. If the SAE Board determines that suspension or termination of the study is required, this information will also be reported to NIDA within 24 hours.

18.19.1 Adverse Events (AEs)

Standard definitions for adverse events and serious adverse events, their identification, characterization regarding severity and relationship to therapy and processing are described in Appendix A.

For the purpose of this study, the following AEs will not require reporting in the data system but will be captured in the source documentation as medically indicated:

Grade 1 (mild) unrelated adverse events: This would typically include mild physical events such as headache, cold, etc., that were considered not reasonably associated with the use of the intervention.

Reportable AEs will include self-reported trips to the Emergency Department or clinical deterioration (based on the K6 scale score) indicated on the end-of-intervention follow-up survey. The study staff will follow up with the participant to determine if the AE was related to the

intervention. Participants will be asked to report any reportable AEs to the study staff if they occur during their active participation.

18.19.2 Serious Adverse Events

For the purpose of this study, the following events will not be reported as an SAE but will instead be reported on study-specific forms. These events will be reported to the Mayo Clinic IRB per IRB guidelines:

- Admission for detoxification
- Admission for labor and delivery
- Admission for elective or pre-planned surgery

The following SAEs will be reported on the 30-day follow-up survey or by the participant throughout their active participation:

- Trips to the Emergency Department that resulted in hospitalization
- Hospitalizations that are not related to the admissions above
- Overdoses of any drug

The study staff will follow up with the participant to determine if the SAE was related to the intervention.

19.0 DATA MANAGEMENT

19.1 Design and Development

Data will be collected and maintained by the Mayo Clinic study team via Research Electronic Data Capture (REDCap) software. REDCap is a secure, web-based application designed exclusively to support data capture for research studies. Screening data will not include any unique identifiers and will be used for descriptive purposes only (i.e., to characterize the population of individuals screened who were found to be ineligible or not interested in participating). Only the reason for ineligibility will be kept; all other screening data from ineligible individuals will be destroyed. Data entered in REDCap uses secure and certified data centers. Thus, the risk of breeching confidentiality is low, with numerous safeguards for confidentiality in place as described.

The site study staff have access to computers and printers to conduct research and data analyses.

[redacted]

All data elements and data transfer activities within Mayo Clinic will be strictly compliant with HIPAA privacy regulatory requirements. Data shared between the study team and the study biostatistician at Mayo Clinic will be through a Research Electronic Data Capture (REDCap) database. REDCap is a secure, web-based application designed exclusively to support data capture for research studies. Data entered in REDCap uses secure and certified data centers.

19.2 Site Responsibilities

The Mayo Clinic study staff will enter all data and transfer the data files electronically to the Mayo Clinic site biostatistician. The site statistician will oversee the transfer of electronic data and data storage at Mayo Clinic, correct discrepancies in REDCap, and oversee all data entry.

19.3 Data Center Responsibilities

Mayo Clinic study staff will develop a REDCap database that will be used to track participant flow such as number of individuals screened, number ineligible/eligible and reason, and participant completion of study assessments.

The study staff will have the option of a printed or electronic Case Report Form (eCRF) for data collection. The qualitative interviews in Phase 1 will be recorded and transcribed by Landmark Transcription Services and the data imported to NVivo for analysis, or the interviewers' written notes will be imported to NVivo for analysis.

The Program Coordinator will create an SOP, and study staff collecting data will be trained on data collection and other study procedures on REDCap including monitoring of AEs.

The study staff will monitor the safety of the subjects daily. For Phase 3 participants, this includes checking on the Facebook intervention group's activities every 1-2 days. We have standard internal procedures to monitor the integrity of data collected. All staff will receive ongoing training and supervision concerning data collection and management from the Program Coordinator. Each day, the study staff will monitor the study binders from the previous day for completeness, thoroughness, accuracy, and protocol adherence. AEs will be recorded by the study staff on a CRF developed for each subject. The staff is then able to cross-reference data from the previous visits to discover any trends in existing symptoms or changes in the subject's status. The study staff will check the REDCap database once a week for accuracy and completeness. If they notice any discrepancies, they will report them to the LI.

The data will be reviewed by a member of the study staff. This will include gathering CRFs and source documents, then comparing them to entries in the database to check for accuracy before the database is locked.

19.4 Data Collection

Data collected from demographic responses prior to the interview in Phase 1 will be handled by the team using REDCap. As the REDCap website is being utilized to administer assessments, most quantitative data will be entered by those administering the interview. The baseline and follow-up survey data in Phase 3 will be entered by study staff into the REDCap database.
We will have backups of the CRFs and source documents in the study team's drive that is protected by Mayo Clinic's firewall, so the study staff will be able to recreate the data if necessary.

19.5 Data Acquisition and Entry

Study staff collecting data will have access to eCRFs and paper CRFs and will be able to enter data into the REDCap database.

19.6 Data Editing

The study statistician will correct all discrepancies in REDCap.

19.7 Data Transfer/Lock

The study staff will lock the data sheet in REDCap once all data has been confirmed (i.e., CRFs have been checked for accuracy and completeness).

Data will be transmitted by the study staff to the NIDA Central Data Repository if requested by NIDA. The final raw datasets will be returned to NIDA, if requested, for storage and archiving.

19.8 Data Training

The SOP will outline each step in the study flow from recruitment through follow-up data entry. This will ensure that the study staff enters and tracks data in a consistent manner while following the study protocol. Training may include mock-consenting, testing out study flows, and suggesting improvements while abiding to the study protocol.

19.9 Data Quality Assurance

The Manual of Operations will be developed by the Program Coordinator. We will use the same coordination, communication and quality control procedures successfully utilized in our previous work. Study staff will be trained using SOPs and the quality control of the data (accuracy and completeness of data) will be monitored monthly by the study statistician. The quality of the data (data checks) including missing data and presence and frequency of outliers. The site study team will meet weekly discuss progress and problem solve issues related to recruitment and data collection.

The interviewers for Phase 1 will be trained and certified by Dr. [redacted]. She will listen to the audio-recordings of the first four interviews conducted and provide feedback to the interviewers. She will listen to the audiotapes for another set of four interviews at the half-way point (after 15 are completed).

The intervention moderators will be trained as detailed in the procedures for Phase 2. A “refresher” training will occur every three months after the initial training. Dr. [redacted] (Co-LI) and [redacted] a consultant trainer, will review moderator-participant discussions every week after the Facebook group has been initiated and provide additional feedback to the moderators every two weeks.

The research team will develop written moderator guidelines for how often the moderator should log in, check-in and respond to comments/postings and other expectations for moderator

engagement. A potential concern about using social media for health interventions is that user postings may be of poor quality, for example, inconsistent with clinical practice guidelines or involve inappropriate or illegal activities. When participants enter the study, they will be informed about the policies for posting content and that any inappropriate postings will be removed. The moderator will be trained to handle inappropriate or misinformation, and to direct information content toward evidence-based information exchange and social support.

All study staff and volunteers will be required to complete and pass the CITI HIPPA/confidentiality course prior to any subject contact.

20.0 DATA SHARING, PUBLIC ACCESS AND PUBLICATIONS

This study will comply with the NIH Data Sharing Policy and Implementation Guidance (https://grants.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm). The LI will also register and report results of the trial in ClinicalTrials.gov, consistent with the requirements of the Policy on the Dissemination of NIH-Funded Clinical Trial Information and the Clinical Trials Registration (https://grants.nih.gov/policy/clinical-trials/reporting/understanding/nih-policy.htm).

Primary data for this study will be available to the public in the NIDA data repository, per NIDA CTN policy. For more details on data sharing please visit https://datashare.nida.nih.gov/.

The primary outcome(s) publication will be included along with study underlying primary data in the data share repository, and it will also be deposited in PubMed Central http://www.pubmedcentral.nih.gov/ per NIH Policy (http://publicaccess.nih.gov/).

The planning, preparation, and submission of publications will follow the policies of the Publications Committee of the CTN. Considerations for ensuring confidentiality of any shared data are described in **Section 18.5.**

20.1 Data Sharing Plan

Our research team fully endorses the concept data sharing as described in the National Institutes of Health Policy Statement on Data Management and Sharing dated October 29, 2020; notice # NOT-OD-21-013. Access to data generated under the project will be available for educational, research, and non-profit purposes. We will share and disseminate all products/resources from this work including surveys and intervention materials. Biospecimen samples will not be shared as specimen samples will be destroyed immediately following the assay tests and recording of results. The data emanating from research projects will be jointly owned by the researchers and tribal community partners. All requests for data sharing will be reviewed in a timely manner. Requests for materials or data sharing will be jointly reviewed and approved by the researchers and the established project-specific CAC with members representing different tribal communities. Alternatively, in the event it is not possible to hold a CAC meeting in a timely manner, requests for data sharing will be jointly reviewed and approved by the LI (Dr. Patten), Lead Node PI (Co-LI, Dr. [redacted]), and at least two community partners.

21.0 PROTOCOL AMENDMENT HISTORY

Version	Date	Description of Change	Brief Rationale
1.4		• Made changes to description of Phase 3 Facebook group based on interview and CAC feedback • Added description of the World Health Organization's Quality of Life – Spirituality, Religion, and Personal Beliefs scale for Phase 3 • Clarified that Phase 3 participants will be allowed to notify study staff of reportable AEs, not just at follow-up • Clarified that the UDS will be part of the screening procedure and not after consent is obtained • Replaced Nicole Reinicke with Ashley Brown as additional study staff	Dr. Venner noted during a moderator exchange that spirituality is important to consider when adapting to a culture. Several changes were made to reflect lessons learned during Phase 1.
1.3	06/28/2022	• Removed information for Tremendous digital/physical gift cards. Will only offer Mayo Clinic Credit Union cash cards as remuneration. • Added that study staff will ask a question about cultural connectedness during baseline in Phases 1 and 3.	Study staff has had consistent issues with Tremendous for another active study. The cash cards are ready to go. No participant has received Tremendous remuneration. The study team thought it would be useful to ask a question addressing cultural connectedness and how that informs the participants' answers in Phase 1 and the Facebook group content in Phase 3.
1.2	04/15/2022	• Clarified that the study staff will recruit up to 18 AIAN women • Added Mayo Clinic Credit Union cash card as an option	Study staff found that Tremendous funds take several weeks to be added, so Mayo Clinic Credit Union cash card will be the alternative. Also

		for remuneration, and the study staff will ask their preference • Added that the CAC can refer their friends/colleagues who work with AIAN women to the study	wanted to expand options for how CAC can refer people to the study.
1.1	02/28/2022	• Provided stronger rationale for expecting even participation among all adults ages • Added more details to qualitative analysis • Clarified that purpose of the UDS is to strengthen self-reported abstinence • For Phase 3, TLFB will assess most commonly abused substances if participant reports them • Increased interview length to 60-90 minutes • Fixed inconsistencies	NIDA requested clarification and expansion of several procedures.

22.0 REFERENCES

Al Ghafri H, Hasan N, Elarabi HF, Radwan D, Shawky M, Al Mamari S, Abdelgawad T, El Rashid A, Kodera A, Al Kathiri H, Lee AJ, Wanigaratne S. The impact of family engagement in opioid assisted treatment: Results from a randomised controlled trial. Int J Soc Psychiatry. 2022 Feb;68(1):166-170. doi: 10.1177/0020764020979026. Epub 2020 Dec 16. PMID: 33325311.

American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 2013:541.

Auxier B, Anderson M. Social Media Use in 2021. Pew Research Center. 2021 Apr 7. https://www.pewresearch.org/internet/wp-content/uploads/sites/9/2021/04/PI_2021.04.07_Social-Media-Use_FINAL.pdf

Baker, TB, Gustafson, DH, & Shah, D. How can research keep up with eHealth? Ten strategies for increasing the timeliness and usefulness of eHealth research. J Med Internet Res. 2014;16(2). doi:10.2196/jmir.2925. PMCID: PMC3961695

Barbosa-Leiker, C, Campbell, ANC, McHugh, RK, Guille, C, & Greenfield, SF. Opioid use disorder in women and the implications for treatment. Psychiatr Res Clin Pract. 2020. https://doi.org/10.1176/appi.prcp.20190051

Bart, G. Maintenance medication for opiate addiction: the foundation of recovery. J Addict Dis. 2012;31(3):207-25. doi: 10.1080/10550887.2012.694598. PMID: 22873183; PMCID: PMC3411273.

Becker JB, McClellan ML, Reed BG. Sex differences, gender and addiction. J Neurosci Res. 2017 Jan 2;95(1-2):136-147. doi: 10.1002/jnr.23963. PMID: 27870394; PMCID: PMC5120656.

Bell J, Strang J. (2020). Medication treatment of opioid use disorder. Biological Psychiatry, 87, 82-88.

Bhagra A, Medina-Inojosa JR, Vinnakota S, Arciniegas MC, Garcia M, Sood A, Mahapatra S, Lopez-Jimenez F, Bauer BA, Cha SS, Mulvagh SL. Stress management and resilience intervention in a women's heart clinic: a pilot study. J Womens Health (Larchmt). 2019 Dec;28(12):1705-1710. doi: 10.1089/jwh.2018.7216. Epub 2019 Mar 23. PMID: 30907678.

Bowen S, Witkiewitz K, Clifasefi SL, Grow J, Chawla N, Hsu SH, Carroll HA, Harrop E, Collins SE, Lustyk MK, Larimer ME. Relative efficacy of mindfulness-based relapse prevention, standard relapse prevention, and treatment as usual for substance use disorders: a randomized clinical trial. JAMA Psychiatry. 2014 May;71(5):547-56. doi: 10.1001/jamapsychiatry.2013.4546. PMID: 24647726; PMCID: PMC4489711.

Brewer LC, Fortuna KL, Jones C, Walker R, Hayes SN, Patten CA, Cooper LA. Back to the Future: Achieving Health Equity Through Health Informatics and Digital Health. JMIR. 2020 Jan 14;8 (1):e14512 PMID: 31934874 DOI: 10.2196/14512

Brigham GS, Slesnick N, Winhusen TM, Lewis DF, Guo X, Somoza E. A randomized pilot clinical trial to evaluate the efficacy of Community Reinforcement and Family Training for Treatment Retention (CRAFT-T) for improving outcomes for patients completing opioid detoxification. Drug Alcohol Depend. 2014 May 1;138:240-3. doi: 10.1016/j.drugalcdep.2014.02.013. Epub 2014 Feb 23. PMID: 24656054; PMCID: PMC4022345.

Centers for Disease Control and Prevention. *Principles of Community Engagement*. 2nd ed. Rockville, MD: NIH Publication; 2011. Retrieved from: https://www.atsdr.cdc.gov/communityengagement/pdf/PCE_Report_508_FINAL.pdf

Centers for Disease Control and Prevention (CDC). Nutrition: strategies and guidelines. 2020. Retrieved from: https://www.cdc.gov/nutrition/strategies-guidelines/index.html

Centers for Disease Control and Prevention (CDC). CDCSocialMediaWorks: Developing a Strategy for Using Social Media. 2016. Retrieved from: https://cdc.orau.gov/healthcommworks/Account/LogOn?signInArea=SocialMediaWorks#5.

Centers for Disease Control and Prevention. Today's heroin epidemic. 2015. Retrieved from: https://www.cdc.gov/vitalsigns/heroin/index.html

Christakis, NA, & Fowler, JH. The collective dynamics of smoking in a large social network. N Engl J Med, 2008;358(21):2249–2258. doi:10.1056/NEJMsa0706154.

Coffey, A. J., and P. A. Atkinson. 1996. Making sense of qualitative data: Complementary research strategies. Thousand Oaks, CA: SAGE.

Cohen, S & Williamson, G. Perceived Stress in a Probability Sample of the United States. Spacapan, S. and Oskamp, S. (Eds.) The Social Psychology of Health. Newbury Park, CA: Sage, 1988.

Comparison Between Individual Interviews and Focus Groups Based on Thematic Saturation Levels. Am J Eval, 2016;37:425-40.

Coyhis, D & White, W. Addiction and recovery in Native America: Lost history, enduring lessons. Counselor (Deerfield Beach), 2002;3(5):16-20.

Davis KC, Nonnemaker J, Duke J, Farrelly MC. Perceived effectiveness of cessation advertisements: the importance of audience reactions and practical implications for media campaign planning. Health Commun. 2013;28(5):461-472.

Davis RE, Resnicow K. The Cultural Variance Framework for Tailoring Health Messages. In: Cho H, ed. Health Communication Message Design: Theory and Practice. Thousand Oaks, CA: Sage Publications, Inc.; 2012:115-135.

Degenhardt L, Grebely J, Stone J, Hickman M, Vickerman P, Marshall BDL, Bruneau J, Altice FL, Henderson G, Rahimi-Movaghar A, Larney S. Global patterns of opioid use and dependence: harms to populations, interventions, and future action. Lancet. 2019 Oct 26;394(10208):1560-1579. doi: 10.1016/S0140-6736(19)32229-9. Epub 2019 Oct 23. PMID: 31657732; PMCID: PMC7068135.

Dickerson D, Baldwin JA, Belcourt A, et al. Encompassing cultural contexts within scientific research methodologies in the development of health promotion interventions. Prev Sci. 2020;21(Suppl 1):33-42. doi: 10.1007/s11121-018-0926-1. PMCID: PMC6311146.

Dickerson, D, Venner, KL, & Duran, B. Clinical Trials and American Indians/Alaska Natives with Substance Use Disorders: Identifying Potential Strategies for a New Cultural-Based Intervention. J Public Ment Health, 2014;13:175-178

Facebook. 2020. Retrieved from https://developers.facebook.com

FeverBee. October 15, 2017. The best lurkers an online community can have. Web page/blog post. https://www.feverbee.com/best-lurkers/

Furukawa, T. A., Kessler, R. C., Slade, T., & Andrews, G. (2003). The performance of the K6 and K10 screening scales for psychological distress in the Australian National Survey of Mental Health and Well-Being. *Psychological Medicine, 33*(2), 357-362.

Forman-Hoffman VL, Muhuri PK, Novak SP, Pemberton MR, Ault KL, Mannix D. (2014). Psychological Distress and Mortality among Adults in the U.S. Household Population. *CBHSQ Data Review. Available at: https://www.samhsa.gov/data/sites/default/files/CBHSQ-DR-C11-MI-Mortality-2014/CBHSQ-DR-C11-MI-Mortality-2014.htm*

Garland EL, Manusov EG, Froeliger B, Kelly A, Williams JM, Howard MO. Mindfulness-oriented recovery enhancement for chronic pain and prescription opioid misuse: results from an early-stage randomized controlled trial. J Consult Clin Psychol. 2014 Jun;82(3):448-459. doi: 10.1037/a0035798. Epub 2014 Feb 3. PMID: 24491075; PMCID: PMC4076008.

Greenfield SF, Back SE, Lawson K, Brady KT. Substance abuse in women. Psychiatr Clin North Am. 2010 Jun;33(2):339-55. doi: 10.1016/j.psc.2010.01.004. PMID: 20385341; PMCID: PMC3124962.

Glaser BG & Strauss AL. The Discovery of Grounded Theory. Strategies for Qualitative Research. Chicago: Aldine. 1967

Graham, A. L., Papandonatos, G. D., Erar, B., & Stanton, C. A. (2015). Use of an online smoking cessation community promotes abstinence: Results of propensity score weighting. *Health Psychology, 34*(Suppl), 1286–1295. https://doi.org/10.1037/hea0000278

Hamilton, et al. The PhenX Toolkit: Get the most from your measures. Am J Epidemiol, 2011;174(3):253-60.

Hedegaard H, Miniño AM, Spencer MR, Warner M. Drug overdose deaths in the United States, 1999–2020. NCHS Data Brief, no 428. Hyattsville, MD: National Center for Health Statistics. 2021. DOI: https://dx.doi.org/10.15620/cdc:112340external icon.

Hensel, JM, Ellard, K, Koltek, M. et al. Digital health solutions for Indigenous mental well-being. Curr Psychiatry Rep 21, 2019;68. https://doi.org/10.1007/s11920-019-1056-6

Hobfoll, SE, Jackson, A, Hobfoll, I, Pierce, CA, & Young, S. The Impact of communal-mastery versus self-mastery on emotional outcomes during stressful Resiliency and Risk 115 conditions: A prospective study of Native American women. Am J Community Psychol, 2002;30(6):853-871.

Intahchompoo C. Indigenous people, social media, and the digital divide: a systematic literature review. Am Indian Cult Res J, 2018;42(4):85-111.

Kennedy, AP, Epstein, DH, Phillips, KA, & Preston, KL. Sex differences in cocaine/heroin users: drug-use triggers and craving in daily life. Drug Alcohol Depend, 2013;132(1-2):29–37. doi:10.1016/j.drugalcdep.2012.12.025

Kessler RC, Andrews G, Colpe LJ, Hiripi E, Mroczek DK, Normand SL, et al. Short screening scales to monitor population prevalences and trends in non-specific psychological distress. Psychol Med. 2002;32(6):959-76.

Kessler, R. C., Barker, P. R., Colpe, L. J., Epstein, J. F., Gfroerer, J. C., Hiripi, E., Hiripi, E., Howes, M. J., Normand, S. L., Manderscheid, R. W., Walters, E. E., & Zaslavsky, A. M. (2003). Screening for serious mental illness in the general population. *Archives of General Psychiatry, 60*(2), 184-189.

King C, Englander H, Priest KC, Korthuis PT, McPherson S. Addressing Missing Data in Substance Use Research: A Review and Data Justice-based Approach. J Addict Med. 2020 Dec;14(6):454-456. doi: 10.1097/ADM.0000000000000644. PMID: 32142055; PMCID: PMC7483132.

Krippendorff KH. Content analysis: an introduction to its methodology. 4th ed. Thousand Oaks, CA: Sage Publications, Inc.; 2018.

Krueger RA, Casey MA. Focus Groups: A Practical Guide for Applied Research. 5th ed. Thousand Oaks, CA: Sage Publications, Inc.; 2014.

Lillie, Kate M. PhD; Shaw, Jennifer PhD; Jansen, Kelley J. MS, MAC; Garrison, Michelle M. PhD Buprenorphine/Naloxone for Opioid Use Disorder Among Alaska Native and American Indian People, Journal of Addiction Medicine: July/August 2021 - Volume 15 - Issue 4 - p 297-302 doi: 10.1097/ADM.0000000000000757

Lincoln, Y.S., & Guba, E.G. (1985). *Naturalistic inquiry*. Newbury Park, California: Sage.

Lund A. Measuring usability with the USE questionnaire. Usability Interface 2001 Jan 1;8(2):3-6.

March of Dimes. (2017, June). Neonatal Abstinence Syndrome (NAS). Retrieved from https://www.marchofdimes.org/complications/neonatal-abstinence-syndrome-(nas).aspx.

Marsch LA, Campbell A, Campbell C, Chen C-H, Ertin E, Ghitza U, Lambert-Harris C, Hassanpour S, Holtyn AF, Hser Y-I, Jacobs P, Klausner JD, Lemley S, Kotz D, Meier A, McLeman B, McNeely J, Mishra V, Mooney L, Nunes E, Stafylis C, Stanger C, Saunders E, Subramaniam G, Young S. The application of digital health to the assessment and treatment of substance use disorders: the past, current, and future role of the National Drug Abuse Treatment Clinical Trials Network. J Subst Abuse Treat, 2020;112 Suppl:4-11.

Mathieson, K, et al. "Access to Digital Communication Technology and Perceptions of Telemedicine for Patient Education among American Indian Patients with Diabetes." J Health Care Poor Underserved, 2017;28(4):1522-1536. Project MUSE, doi:10.1353/hpu.2017.0131

McCabe, SE, Cranford, JA, & Boyd, CJ. Stressful events and other predictors of remission from drug dependence in the United States: Longitudinal results from a national survey. J Subst Abuse Treat, 2016;71:41–47. https://doi.org/10.1016/j.jsat.2016.08.008

Meacham MC, Ramo DE, Prochaska JJ, Maier LJ, Delucchi KL, Kaur M, Satre DD. A Facebook intervention to address cigarette smoking and heavy episodic drinking: A pilot randomized controlled trial. J Subst Abuse Treat. 2021 Mar;122:108211. doi: 10.1016/j.jsat.2020.108211. Epub 2020 Nov 23. PMID: 33509414; PMCID: PMC7901868.

Merculieff ZT, Koller KR, Sinicrope P, Hughes CA, Bock MJ, Decker PA, Resnicow K, Flanagan CA, Meade CD, McConnell CR, Prochaska JJ, Thomas TK, Patten CA. Developing a social media intervention to connect Alaska Native people who smoke with resources and support to quit smoking: The CAN Quit study. Nicotine Tob Res, 2021;23(6):1002-1009

Meyer JP, Isaacs K, El-Shahawy O, Burlew AK, Wechsberg W. Research on women with substance use disorders: Reviewing progress and developing a research and implementation roadmap. Drug Alcohol Depend. 2019 Apr 1;197:158-163. doi: 10.1016/j.drugalcdep.2019.01.017. Epub 2019 Feb 21. PMID: 30826625; PMCID: PMC6440852.

Miles, Matthew B., et al. Qualitative Data Analysis: A Methods Sourcebook. Third edition. SAGE Publications, Inc. 2014.

Minnesota Department of Health. (2021). Differences in Rates of Drug Overdose Deaths by Race: 2019 preliminary data. Retrieved from: https://www.health.state.mn.us/communities/opioids/documents/raceratedisparity2019prelimfinal.pdf.

Mitchell, C. M., & Beals, J. (2011). The utility of the Kessler Screening Scale for Psychological Distress (K6) in two American Indian communities. *Psychological assessment*, *23*(3), 752–761. https://doi.org/10.1037/a0023288

Mohatt, GV, McDiarmid, GW, & Montoya, VC. Societies, Families, and Change: The Alaskan Example. In SM Manson & NG Dinges (Eds.), Behavioral Health Issues Among American Indians and Alaska Natives. Am Indian Alsk Native Ment Health Res Monogr Ser, 2000;1:325-365.

Namey E, Guest G, McKenna K, Chen M. Evaluating Bang for the Buck: A Cost-Effectiveness Comparison Between Individual Interviews and Focus Groups Based on Thematic Saturation Levels. Am J Eval. 2016;37(3):425-440. doi:10.1177/1098214016630406

Nielsen J. (2012). How many test users in a usability study? Retrieved from: https://www.nngroup.com/articles/how-many-test-users/#:~:text=For%20really%20low%2Doverhead%20projects,5%20users%20per%20usability%20test

Nelson PK, Mathers BM, Cowie B, et al. Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews. The Lancet. 2011;378:571–583.

NIDA. Sex and Gender Differences in Substance Use. 2020 May 28. Retrieved from https://www.drugabuse.gov/publications/research-reports/substance-use-in-women/sex-gender-differences-in-substance-use on 2020, November 29

Nunes EV, Gordon M, Friedmann PD, Fishman MJ, Lee JD, Chen DT, Hu MC, Boney TY, Wilson D, O'Brien CP. Relapse to opioid use disorder after inpatient treatment: Protective effect of injection naltrexone. J Subst Abuse Treat. 2018 Feb;85:49-55. doi: 10.1016/j.jsat.2017.04.016. Epub 2017 Apr 23. PMID: 28473233; PMCID: PMC5755382.

NVivo. QSR NVivo software, version 10. Doncaster, Victoria, Australia. 2020. Retrieved from: https://www.qsrinternational.com/nvivo-qualitative-data-analysis-software/home

Osilla, KC, Becker, K, Ecola, L. et al. Study design to evaluate a group-based therapy for support persons of adults on buprenorphine/naloxone. Addict Sci Clin Pract 2020;15(25). https://doi.org/10.1186/s13722-020 00199-2

Pagoto, S, Waring, ME, May, CN, Ding, EY, Kunz, WH, Hayes, R, & Oleski, JL. Adapting behavioral interventions for social media delivery. JMIR, 2016;18(1), e24. PMCID: PMC4752690.

Patten, C., Balls-Berry, J., Cohen, E., Brockman, T., Valdez Soto, M., West, I., . . . Eder, M. (2021). Feasibility of a virtual Facebook community platform for engagement on health research. *Journal of Clinical and Translational Science, 5*(1), E85. doi:10.1017/cts.2021.12

Patten CA, Goggin K, et al. Relationship of Autonomy Social Support to Quitting Motivation in Diverse Smokers. Addict Res Theory. 2016;24(6):477-82. doi: 10.3109/16066359.2016.1170815. PMCID: PMC5098812.

Patten CA, Koller KR, Flanagan CA, Hiratsuka V, Merritt ZT, Sapp F, Meade CD, Hughes CA,

Decker PA, Murphy N, Thomas TK. Postpartum Tobacco Use and Perceived Stress among Alaska Native Women: MAW Phase 4 Study. Int J Environ Res Public Health, 2019;16(17), 3024.

Patten CA, Lando HA, Desnoyers CA, Bock MJ, Alexie L, Decker PA, Hughes CA, Resnicow K, Burhansstipanov L, Boyer R, Klejka J. Healthy Pregnancies Project: Cluster Randomized Controlled Trial of a Community Intervention to Reduce Tobacco Use among Alaska Native Women. Int J Environ Res Public Health. 2020 Dec 12;17(24):9302. doi: 10.3390/ijerph17249302. PMID: 33322686; PMCID: PMC7764642.

Patten CA, Lando HA, Desnoyers CA, Klejka J, Decker PA, Bock MJ, et al. Association of Tobacco Use During Pregnancy, Perceived Stress, and Depression Among Alaska Native Women Participants in the Healthy Pregnancies Project. Nicotine Tob Res. 2020;22(11):2104-8.

Patten CA, Lando H, Resnicow K, Decker PA, Smith CM, Hanza MM, Burhansstipanov L, Scott M. Developing health communication messaging for a social marketing campaign to reduce tobacco use in pregnancy among Alaska Native women. J Commun Healthc. 2018;11(4):252-262. doi: 10.1080/17538068.2018.1495929. Epub 2018 Jul 16. PMID: 31548863; PMCID: PMC6756759.

Patton MQ. Qualitative Research & Evaluation Methods: Integrating Therory and Practice. 4thed. Thousand Oaks, CA: Sage Publications, Inc.; 2015.

Perrin A, Anderson M. Share of U.S. adults using social media, including Facebook, is mostly unchanged since 2018. 2019 [cited 2019 April 18]. Available from: https://www.pewresearch.org/fact-tank/2019/04/10/share-of-u-s-adults-using-social-media-including-facebook-is-mostly-unchanged-since-2018/

Price CJ, Thompson EA, Crowell S, Pike K. Longitudinal effects of interoceptive awareness training through mindful awareness in body-oriented therapy (MABT) as an adjunct to women's substance use disorder treatment: A randomized controlled trial. Drug Alcohol Depend, 2019;198:140-149.

Posner K, Oquendo MA, Gould M, Stanley B, Davies M. Columbia Classification Algorithm of Suicide Assessment (C-CASA): classification of suicidal events in the FDA's pediatric suicidal risk analysis of antidepressants. Am J Psychiatry. 2007;164(7):1035-43.

Ramo DE, Thrul J, Chavez K, Delucchi KL, Prochaska JJ. Feasibility and quit rates of the tobacco status project: a Facebook smoking cessation intervention for young adults. J Med Internet Res 2015 Dec 31;17(12):e291. PMID: 26721211. doi: 10.2196/jmir.5209

Resilient Option. 2020. Retrieved from: https://www.resilientoption.com/

Resnicow K, Davis R, Zhang N, Strecher V, Tolsma D, Calvi J, Alexander G, Anderson J, Wiese C, Cross W. Tailoring a fruit and vegetable intervention on ethnic identity: Results of a randomized study. Health Psychol. 2009 Jul;28(4):394-403. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3397196/

Richard P. Mattick et al., “Methadone Maintenance Therapy Versus No Opioid Replacement Therapy for Opioid Dependence,” Cochrane Database Syst Rev 3 (2009): CD002209, http://www.ncbi.nlm.nih.gov/pubmed/19588333

Rieckmann T, McCarty D, Kovas A, Spicer P, Bray J, Gilbert S, et al. American Indians with substance use disorders: treatment needs and comorbid conditions. Am J Drug Alcohol Abuse. 2012;38(5):498-504.

Robinson J, Borgo L, Fennell K, et al. The COVID-19 pandemic accelerates the transition to virtual care. NEJM. 2020. doi: 10.1056/CAT.20.0399.

Rounsaville, BJ, Carroll, KM, & Onken, LS. A Stage Model of Behavioral Therapies Research: Getting Started and Moving on From Stage I. Clinical Psychology: Science and Practice, 2001;8(2):133-142.

Rushing SC, Stephens D. Use of media technologies by Native American teens and young adults in the Pacific Northwest: exploring their utility for designing culturally appropriate technology-based health interventions. J Prim Prev. 2011 Aug;32(3-4):135-45. doi: 10.1007/s10935-011-0242-z. PMID: 21805055.

Saldana J. The Coding Manual for Qualitative Researchers (3rd ed.). London: SAGE Publications Ltd. 2016

Salomon N, Perlman DC, Friedmann P, Ziluck V, Des J. Prevalence and risk factors for positive tuberculin skin tests among active drug users at a syringe exchange program. Int J Tuberc Lung Dis. 2000;4:47–54.

Sanchez K, Killian MO, Mayes TL, Greer TL, Trombello JM, Lindblad R, et al. A psychometric evaluation of the Concise Health Risk Tracking Self-Report (CHRT-SR)- a measure of suicidality-in patients with stimulant use disorder. J Psychiatr Res. 2018;102:65-71.

Saraiya TC, Swarbrick M, Franklin L, et al. Perspectives on trauma and the design of a technology-based trauma-informed intervention for women receiving medications for addiction treatment in community-based settings. J Subst Abuse Treat. 2020 May;112:92-101. DOI: 10.1016/j.jsat.2020.01.011.

Saunders B, Sim J, Kingstone T, Baker S, Waterfield J, Bartlam B, Burroughs H, Jinks C. Saturation in qualitative research: exploring its conceptualization and operationalization. Qual Quant. 2018;52(4):1893-1907. doi: 10.1007/s11135-017-0574-8. Epub 2017 Sep 14. PMID: 29937585; PMCID: PMC5993836.

Schlichting, Rebekka J. "Common platforms and devices used to access news about Native Americans" Professional Projects from the College of Journalism and Mass Communications, 2016;8. http://digitalcommons.unl.edu/journalismprojects/8

Scholl L, Seth P, Kariisa M, Wilson N, Baldwin G. Drug and Opioid-Involved Overdose Deaths — United States, 2013–2017. MMWR Morb Mortal Wkly Rep 2019;67:1419–1427.

Schuckit MA. Treatment of opioid-use disorders. New Engl J Med. 2016;375(4):357–368.

Scott CK, Grella CE, Nicholson L, Dennis ML. Opioid recovery initiation: Pilot test of a peer outreach and modified Recovery Management Checkup intervention for out-of-treatment opioid users. J Subst Abuse Treat. 2018 Mar;86:30-35. doi: 10.1016/j.jsat.2017.12.007. Epub 2017 Dec 19. PMID: 29415848; PMCID: PMC5808598.

Scott CK, Dennis ML, Grella CE, Kurz R, Sumpter J, Nicholson L, Funk RR. A community outreach intervention to link individuals with opioid use disorders to medication-assisted treatment. J Subst Abuse Treat. 2020 Jan;108:75-81. doi: 10.1016/j.jsat.2019.07.001. Epub 2019 Jul 10. PMID: 31399271.

Shanmugam PK. The Influence of Social Factors in Drug Addiction–A Mini Review of Work by Miller & Carroll (2006). J Alcohol Drug Depend 5, 2017;272. doi:10.4172/2329-6488.1000272

Sinha R. Chronic stress, drug use, and vulnerability to addiction. Ann N Y Acad Sci. 2008 Oct;1141:105-30. doi: 10.1196/annals.1441.030. PMID: 18991954; PMCID: PMC2732004.

Sinicrope PS, Koller KR, Prochaska JJ, Hughes CA, Bock MJ, Decker PA, Flanagan CA, Merritt ZT, Meade CD, Willetto AL, Resnicow K, Thomas TK, Patten CA. Social Media Intervention to Promote Smoking Treatment Utilization and Cessation Among Alaska Native People Who Smoke: Protocol for the Connecting Alaska Native People to Quit Smoking (CAN Quit) Pilot Study. JMIR Res Protoc. 2019 Nov 22; 8 (11):e15155

Sinicrope PS, Young C, Resnicow K, Merritt ZT, McConnell CR, Hughes CA, Koller KR, Bock MJ, Decker PA, Flanagan CA, Meade CD, Thomas TK, Prochaska JJ, Patten CA. Sharing Lessons Learned from Beta-Testing the CAN Quit Facebook Group Prototype to Promote Smoking Treatment Utilization among Alaska Native People. JMIR. 01/12/21:28704 (2022; forthcoming/in press).

Skevington SM, Gunson KS, O'Connell KA. Introducing the WHOQOL-SRPB BREF: developing a short-form instrument for assessing spiritual, religious and personal beliefs within quality of life. Qual Life Res. 2013 Jun;22(5):1073-83. doi: 10.1007/s11136-012-0237-0. Epub 2012 Jul 27. PMID: 22836375.

Skousen T, Safadi H, Young C, Karahanna E, Safadi S, Chebib F. Successful moderation in online patient communities: inductive case study. J Med Internet Res 2020 Mar 17;22(3):e15983. PMID: 32181743. doi: 10.2196/15983.

Sobell LC, Sobell MB. Measuring alcohol consumption. Springer; 1992. Timeline follow-back; =pp. 41–72.

Sobell LC, Sobell MB, Leo GI, Cancilla A. Reliability of a timeline method: assessing normal drinkers' reports of recent drinking and a comparative evaluation across several populations. Br J Addict. 1988;83(4):393-402.

Sofuoglu, M., DeVito, E.E. and Carroll, K.M. (2019), Pharmacological and Behavioral Treatment of Opioid Use Disorder. Psych Res Clin Pract, 1: 4-15. https://doi.org/10.1176/appi.prcp.20180006

Teufel-Shone NI, Tippens JA, Mccrary HC, Ehiri JE, & Sanderson PR. Resilience in American Indian and Alaska Native Public Health: An Underexplored Framework. Am J Health Promot, 2016;32. 10.1177/0890117116664708.

Thrul J, Klein A, Ramo D. Smoking Cessation Intervention on Facebook: Which Content Generates the Best Engagement? J Med Internet Res 2015;17(11):e244

Trivedi MH, Wisniewski SR, Morris DW, Fava M, Gollan JK, Warden D, et al. Concise Health Risk Tracking scale: a brief self-report and clinician rating of suicidal risk. J Clin Psychiatry. 2011;72(6):757-64.

U.S. Department of Health and Human Services (HHS), Office of the Surgeon General, Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. Washington, DC: HHS. 2016 Nov.

Venniro M, Zhang M, Caprioli D, Hoots JK, Golden SA, Heins C, Morales M, Epstein DH, Shaham Y. Volitional social interaction prevents drug addiction in rat models. Nat Neurosci, 2018;21:1520-1529.

Vowles, KE, Witkiewitz, K, Cusack, KJ, Gilliam, WP, Cardon, KE, Bowen, S, Edwards, KA, McEntee, ML, & Bailey, RW. Integrated behavioral treatment for veterans with co-morbid chronic pain and hazardous opioid use: A randomized controlled pilot trial. J Pain. 2019;Advance online publication. https://doi.org/10.1016/j.jpain.2019.11.007

Walitzer KS, Dearing RL. Gender differences in alcohol and substance use relapse. Clin Psychol Rev. 2006;26:128–148. doi: 10.1016/j.cpr.2005.11.003.

Walters KL, Simoni JM. Re-conceptualizing Native women's health: an "indigenist" stress-coping model. Am J Public Health, 2002;92(4):520-524.

WHOQOL SRPB Group. A cross-cultural study of spirituality, religion, and personal beliefs as components of quality of life. Soc Sci Med. 2006 Mar;62(6):1486-97. doi: 10.1016/j.socscimed.2005.08.001. Epub 2005 Sep 13. PMID: 16168541.

Witkiewitz K, Bowen S, Douglas H, Hsu SH. Mindfulness-based relapse prevention for substance craving. Addict Behav. 2013 Feb;38(2):1563-1571. doi: 10.1016/j.addbeh.2012.04.001. Epub 2012 Apr 6. Erratum in: Addict Behav. 2018 Mar 21; PMID: 22534451; PMCID: PMC3408809.

Witkiewitz K, Warner K, Sully B, Barricks A, Stauffer C, Thompson BL, Luoma JB. Randomized trial comparing mindfulness-based relapse prevention with relapse prevention for women offenders at a residential addiction treatment center. Subst Use Misuse. 2014 Apr;49(5):536-46. doi: 10.3109/10826084.2013.856922. PMID: 24611849.

Wray TB, Braciszewski JM, Zywiak WH, Stout RL. Examining the reliability of alcohol/drug use and HIV-risk behaviors using Timeline Follow-Back in a pilot sample. J Subst Use. 2016;21(3):294-297. doi: 10.3109/14659891.2015.1018974. Epub 2015 Jul 8. PMID: 27293379; PMCID: PMC4896399.

Young C. Community management that works: how to build and sustain a thriving online health community. J Med Internet Res 2013 Jun 11;15(6):e119. PMID: 23759312. doi: 10.2196/jmir.2501

23.0 APPENDIX A: ADVERSE EVENT REPORTING AND PROCEDURES

The study site LI is responsible for study oversight, including ensuring human research subject protection by designating appropriately qualified and trained study personnel to assess, report, and monitor adverse events.

Definition of Adverse Events and Serious Adverse Events

An **adverse event** (AE) is any untoward medical occurrence in humans, whether or not considered study medication/intervention related which occurs during the conduct of a clinical trial. Any change from baseline in clinical status, ECGs, lab results, x-rays, physical examinations, etc., that is considered clinically significant by the site medical clinician are considered AEs.

Suspected adverse reaction is any adverse event for which there is a reasonable possibility that the study medication/intervention caused the adverse event. A reasonable possibility implies that there is evidence that the study intervention caused the event.

Adverse reaction is any adverse event caused by the study intervention.

An **adverse event, suspected adverse reaction,** or **adverse reaction** is considered "**serious**" (i.e., a serious adverse event, serious suspected adverse reaction or serious adverse reaction) if, in the view of either the site medical clinician or sponsor, it:

1) Results in death: A death occurring during the study or which comes to the attention of the study staff during the protocol-defined follow-up period, whether or not considered caused by the study intervention, must be reported.

2) Is life-threatening: Life-threatening means that the study participant was, in the opinion of the medical clinician or sponsor, at immediate risk of death from the reaction as it occurred and required immediate intervention.

3) Requires inpatient hospitalization or prolongation of existing hospitalization.

4) Results in persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions.

5) Is a congenital abnormality or birth defect.

6) Is an important medical event that may not result in one of the above outcomes but may jeopardize the health of the study participant or require medical or surgical intervention to prevent one of the outcomes listed in the above definition of serious event.

Definition of Expectedness

Any adverse event is considered "unexpected" if it is not listed in the investigator brochure or the package insert or is not listed at the specificity or severity that has been observed. If neither is available, then the protocol and consent are used to determine an unexpected adverse event.

Medical and Psychiatric History

The baseline assessment will record psychiatric symptoms using the K6 scale to assist in the assessment of worsening in intensity or severity of these conditions that would indicate an AE.

Site's Role in Eliciting and Reporting Adverse Events

Appropriately qualified and trained personnel will elicit participant reporting of AEs and SAEs at each study visit designated to collect AEs. Adverse events (medical and/or psychiatric) assessment will initiate with participant consent and follow-up of ongoing adverse events will continue through resolution or 30 days post last study visit. Study personnel will obtain as much information as possible about the reported AE/SAE to complete the AE/SAE forms and will consult with the Safety Monitor/Medical Monitor as warranted.

Standard reporting, within 7 days of our site becoming aware of the event, is required for reportable AEs. Expedited reporting (within 24 hours of their occurrence and/or our site's knowledge of the event) is required for reportable SAEs (including death and life-threatening events). Study staff are responsible for reporting SAEs to the IRB, per the Mayo Clinic IRB's guidelines.

Study staff are required to enter reportable AEs and SAEs in the Advantage eClinical system. The AE form is used to capture reportable AEs and SAEs (as defined in the protocol). Additional information may need to be gathered to evaluate SAEs and to complete the appropriate CRFs and the summary. This process may include obtaining hospital discharge reports, medical records, autopsy records or any other type records or information necessary to provide a complete and clear picture of the serious event and events preceding and following the event. If the SAE is not resolved or stable at the time of the initial report or if new information becomes available after the initial report, follow-up information must be submitted as soon as possible.

Reportable adverse events will be followed until resolution, stabilization or study end. Any serious adverse reactions will be followed until resolution or stabilization even beyond the end of the study.

Site's Role in Assessing Severity and Causality of Adverse Events

Appropriately qualified and trained study personnel will conduct an initial assessment of seriousness, severity, and causality when eliciting participant reporting of adverse events. A study medical clinician will review reportable AEs for seriousness, severity, and causality on at least a weekly basis.

Guidelines for Assessing Severity

The severity of an adverse event refers to the intensity of the event:

Grade 1	**Mild**	Transient or mild discomfort (typically < 48 hours), no or minimal medical intervention/therapy required; hospitalization not necessary (non-prescription or single-use prescription therapy may be employed to relieve symptoms, e.g., aspirin for simple headache, acetaminophen for post-surgical pain).
Grade 2	**Moderate**	Mild to moderate limitation in activity, some assistance may be needed; no or minimal intervention/therapy required, hospitalization possible.
Grade 3	**Severe**	Marked limitation in activity, some assistance usually required; medical intervention/ therapy required, hospitalization possible.

Guidelines for Determining Causality

The site medical clinician will use the following question when assessing causality of an adverse event to study intervention where an affirmative answer designates the event as a suspected adverse reaction:

Is there a reasonable possibility that the study intervention caused the event?

Site's Role in Monitoring Adverse Events

Local quality assurance monitors will review respective study data on a regular basis and will promptly advise the study staff to report any previously unreported safety issues and ensure that the reportable safety-related events are being followed to resolution and reported appropriately. Staff education, re-training or appropriate corrective action plan will be implemented at the participating site when unreported or unidentified reportable AEs or serious events are discovered, to ensure future identification and timely reporting by the site.

Regulatory Reporting for a non-IND study

If an SAE meets the expedited reporting criteria (serious and unexpected suspected adverse reactions), the sponsor will submit a volunteer MedWatch report to the FDA. The Safety Monitor/Medical Monitor will prepare an expedited report (MedWatch Form 3500 or similar) for the FDA and other regulatory authorities.

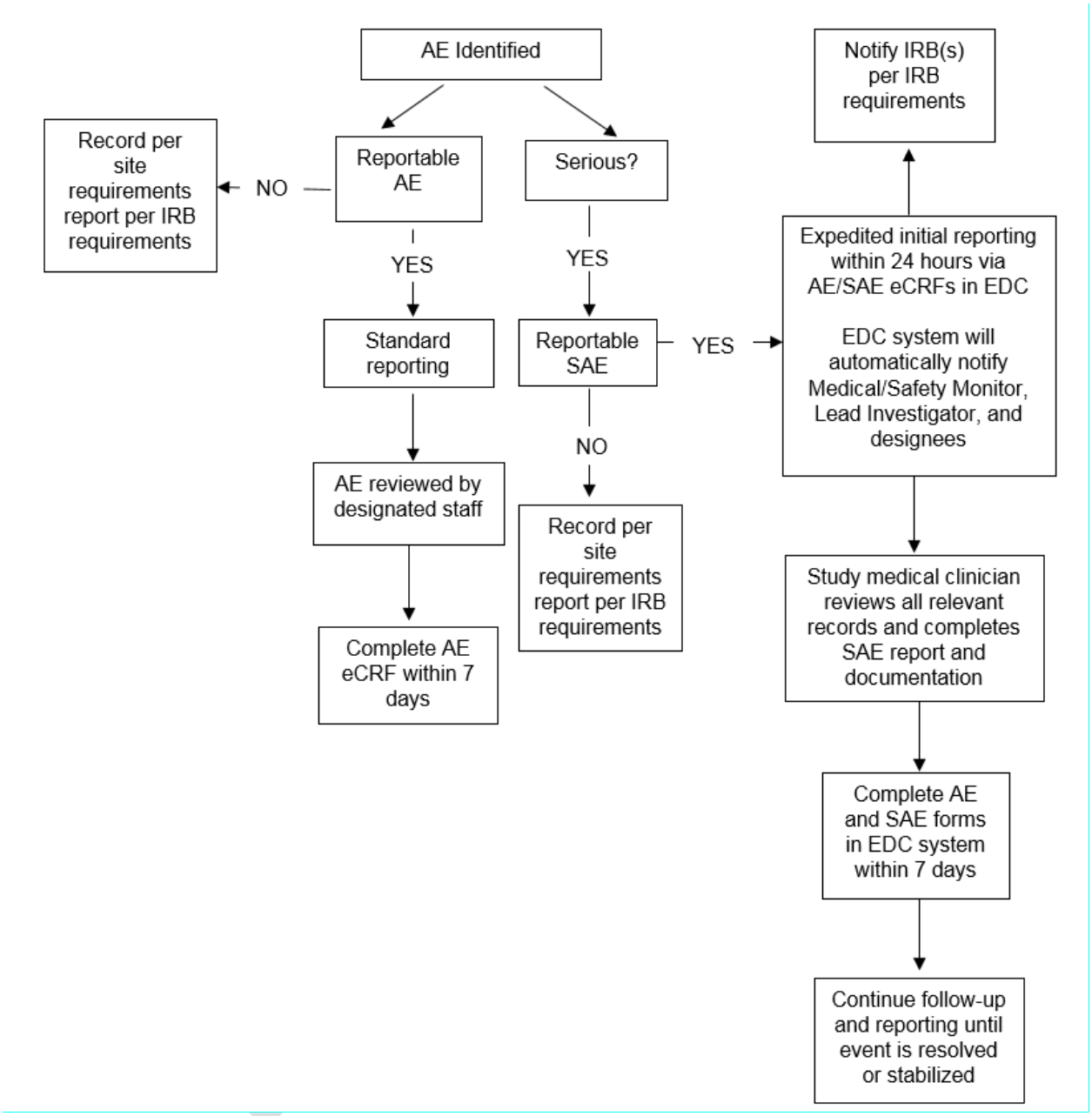
Participant Withdrawal

The site medical clinician must apply his/her clinical judgment to determine whether or not an adverse event is of sufficient severity to require that the participant be withdrawn from further study intervention. If necessary, a site medical clinician may suspend any trial treatments and institute the necessary medical therapy to protect a participant from any immediate danger. A participant may also voluntarily withdraw from treatment due to what he/she perceives as an

intolerable adverse event or for any other reason. If voluntary withdrawal is requested, the participant will be asked to complete an end-of-intervention visit to assure safety and to document end-of-intervention outcomes and will be given recommendations for medical care and/or referrals to treatment, as necessary.

Adverse Event Reporting (Chart)

1.0



24.0 APPENDIX B: DATA AND SAFETY MONITORING PLAN (DSMP)

Data and Safety Monitoring Plan Template

1.0 BRIEF STUDY OVERVIEW

In this project, we will develop and beta-test the Facebook intervention. We formed a study-specific CAC to review intervention content, measures, and recruitment messaging and provide advice on all study activities. Members are health care providers, AIAN community partners, and AIAN women, with some being former opioid users.

2.0 OVERSIGHT OF CLINICAL RESPONSIBILITIES

A. Site Lead Investigator

The site's LI (LI) is responsible for study oversight, including ensuring human research subject protection by designating appropriately qualified, trained research staff and medical clinicians to assess, report, and monitor adverse events.

All adverse events (AEs) occurring during the course of the study will be collected, documented, and reported by the investigator or sub-investigators according to the Protocol.

The occurrence of AEs and serious adverse events (SAEs) will be assessed in the follow-up survey via self-report questions on trips to the Emergency Department, hospitalizations, and overdoses. Serious adverse events will be followed until considered resolved or stable.

B. Safety Reporting

The LI (LI) may appoint a Site Medical Clinician (MD, DO, NP, or PA) or utilize the Mayo Clinic on-call physician for this study, who will review or provide consultation for each Adverse Event (AE) and Serious Adverse Event (SAE) as needed. These reviews will include an assessment of the possible relatedness of the event to the study intervention or other study procedures. The Site Medical Clinician will also provide advice for decisions to exclude, refer, or withdraw participants as required. A site clinical psychologist or psychiatrist may also review AEs and SAEs as needed. The study staff will determine which safety events require expedited reporting to NIDA and regulatory authorities. This will include events that are serious, related, and unexpected. The study staff will be trained to monitor for and report AEs and SAEs, and participants will report AEs and SAEs at the follow-up visit.

The study site has established practices for managing medical and psychiatric emergencies, and the study staff will continue to utilize these procedures. Treatment providers at the site will be responsible for monitoring participants for possible clinical deterioration or other problems, and for implementing appropriate courses of action.

Voluntary Regulatory Reporting in non-IND Trials:

For non-IND trials, if an event meets expedited reporting criteria (serious, related and unexpected) the Safety Monitor/Medical Monitor or designee will voluntarily report to FDA/Regulatory Authorities using the MedWatch Form 3500 or similar.

C. Data and Safety Monitoring

We will use the FDA definition of adverse events (AEs) and serious adverse events (SAEs). The FDA guidelines for anticipated or unanticipated SAEs will be followed. Regarding monitoring participant safety, any SAE, whether or not it is related to the study intervention, will be reported to the IRBs and NIDA. The Program Coordinator, study staff and intervention moderators located at the site, will evaluate for the presence of both SAEs and AEs at each scheduled contact, regardless of whether conducted in person, via telephone, or online. Drs. Patten and/or Bart and will meet with the research staff via teleconference on a bi-weekly basis to review any new or continuing SAEs and AEs.

D. Quality Assurance (QA) Monitoring

The Manual of Operations will be developed by the Program Coordinator. We will use the same coordination, communication and quality control procedures successfully utilized in our previous work. Study staff will be trained using the SOP and the quality control of the data (accuracy and completeness of data) will be monitored on a monthly basis by the study statistician. The quality of the data (data checks) including missing data and presence and frequency of outliers. The site study team will meet weekly discuss progress and problem solve issues related to recruitment and data collection.

The intervention moderators will be trained as detailed in the Phase 2 procedures. A “refresher” training will occur every three months after the initial training. Collen Young, a consultant trainer, will review moderator-participant discussions every week after the Facebook group has been initiated and provide additional feedback to the moderators every two weeks.

The research team will develop written intervention moderator guidelines for how often the moderator should log in, check-in and respond to comments/postings and other expectations for moderator engagement. A potential concern about using social media for health interventions is that user postings may be of poor quality, for example, inconsistent with clinical practice guidelines or involve inappropriate or illegal activities. When participants enter the study, they will be informed about the policies for posting content and that any inappropriate postings will be removed. The moderator will be trained to handle inappropriate or misinformation, and to direct information content toward evidence-based information exchange and social support. All study staff and volunteers will be required to complete and pass the CITI HIPPA/confidentiality course prior to any subject contact.

E. Management of Risks to Participants

Confidentiality

Confidentiality of participant records will be secured by use of study codes for identifying participants on CRFs, and secure storage of any documents that have participant identifiers on site, as well as secure computing procedures for entering and transferring electronic data. The documents or logs linking the study codes with the study participant on site will be kept locked/securely stored separately from the study files and records. No identifying information will be disclosed in reports, publications, or presentations.

Information That Meets Reporting Requirements

The consent form will specifically state the types of information that are required for reporting and that the information will be reported as required. These include suspected or known sexual or physical abuse of a child or elders or threatened violence to self and/or others.

Participant Protection

The site's study clinician or other designated and qualified individual will evaluate all pertinent screening and baseline assessments prior to participant enrollment to ensure that the participant is eligible and safe to enter the study. AEs will be assessed and documented at each study visit. Individuals who experience an AE that compromises safe participation in a study will be discontinued from further intervention and provided referrals for other treatment or to specialized care. Study personnel will request that the participant complete an end-of-intervention visit to assure safety and to document end-of-intervention outcomes.

A detailed plan is in place for clinical management of psychiatric or medical problems that might arise. The study staff will monitor any reports or observations of medical problems or psychiatric symptoms based on the K6 scale in participants which is administered at the baseline and follow-up visits. In the event of such an occurrence, they will set into motion procedures for referral of the participant for mental health assessment and care. Study staff will contact the LI or one of the study clinicians for further assessment of the participant's symptoms and current clinical care. Subjects who are patients at Mayo Clinic will be referred for additional mental health assessment and treatment at Mayo Clinic. However, study participants will not likely be Mayo Clinic patients. Thus, in the event of an emergency (e.g., suicidal plan), staff physicians will be consulted to refer the subject to Hennepin Healthcare or a local tribal medical facility in Minneapolis or St. Paul for further assessment and clinical care. Also, individuals who report suicidal intent or other severe psychiatric or medical problems will be referred to Hennepin Healthcare or a local tribal medical facility and followed throughout the study period. Drs. Patten, Sharma, and/or Bart (licensed clinical psychologist, board certified psychiatrist, and a physician) or the Mayo Clinic on-call site physician will be consulted by study staff as needed. Continued participation with the study will be voluntary and in cooperation with the health care professional treating the subject's psychiatric or medical condition.

Study Specific Risks

Participants may feel inconvenienced by completing study assessments and providing urine samples. They may feel uncomfortable in front of the study staff if their urine is positive for any

drugs. Facebook posts and comments may cause emotional discomfort for the participants depending on what other members and moderators post. There is a chance that the participants experience withdrawal symptoms as they continue to abstain from opioids, but this risk is minimal because they would have already abstained from illicit opioid use for at least 30 days at screening. What symptoms may occur are expected to be mild and may consist of nausea, abdominal discomfort, muscle and joint pain, perspiration, runny nose and eyes, yawning, irritability, and anxiety. Since this FB intervention is not anonymous, confidentiality of health information could be compromised. However, the intervention group moderators will emphasize that all information shared in the group should stay in the group, and any samples and identifiers outside of the intervention will be destroyed.

3.0 DATA MANAGEMENT PROCEDURES

Data will be collected and maintained by the Mayo Clinic study team via REDCap software. REDCap meets requirements set by the Federal Information security management Act of 2002, the Health Insurance and Accountability Act, and the Health Information Technology for Economic and Clinical Health Act.

4.0 DATA AND STATISTICS CENTER RESPONSIBILITIES

Mayo Clinic study staff will develop a REDCap database that will be used to track participant flow such as number of individuals screened, number ineligible/eligible and reason, and participant completion of study assessments.

The study staff will have the option of a printed CRF or eCRF for data collection. The qualitative interviews in Phase 1 will be recorded and transcribed by Landmark Transcription Services and the data imported to NVivo for analysis. If the participant is not comfortable being recorded, or the audio equipment is malfunctioning, the interviewer will take detailed, written notes that will be imported to NVivo for analysis.

Study staff will create a SOP and study staff collecting data will be trained on data collection and other study procedures on REDCap including monitoring of AEs.

The study staff will monitor the safety of the subjects daily. For Phase 3 participants, this includes checking in on the intervention group's activity every 1-2 days. We have standard internal procedures to monitor the integrity of data collected. All staff will receive ongoing training and supervision concerning data collection and management from the program coordinator. Each day, the study staff will monitor the study binders from the previous day for completeness, thoroughness, accuracy, and protocol adherence. AEs will be recorded by the study staff on a CRF developed for each subject. The staff is then able to cross-reference data from the previous visits to discover any trends in existing symptoms or changes in the subject's status. The study staff will check the REDCap database once a week for accuracy and completeness. If they notice any discrepancies, they will report them to the LI.

The data will be reviewed by a member of the study staff. This will include gathering CRFs and source documents, then comparing them to entries in the database to check for accuracy before the database is locked.

5.0 DATA COLLECTION AND ENTRY

As the REDCap website is being utilized to administer assessments, most quantitative data will be entered by those administering the interview. Discrepancies will be corrected by the study site statistician who will oversee all data entry.

6.0 DATA MONITORING, CLEANING AND EDITING

The study staff will monitor the safety of the subjects daily. For Phase 3 participants, this includes regularly checking on the Facebook group's activity. We have standard internal procedures to monitor the integrity of data collected. All staff will receive ongoing training and supervision concerning data collection and management from the program coordinator. Each day, the study staff will monitor the study binders from the previous day for completeness, thoroughness, accuracy, and protocol adherence. AEs will be recorded by the study staff on a CRF developed for each subject. The staff is then able to cross-reference data from the previous visits to discover any trends in existing symptoms or changes in the subject's status. The study staff will check the REDCap database once a week for accuracy and completeness. If they notice any discrepancies, they will report them to the LI.

The data will be reviewed by a member of the study staff. This will include gathering CRFs and source documents, then comparing them to entries in the database to check for accuracy before the database is locked.

7.0 DATABASE LOCK AND TRANSFER

The study staff will lock the data sheet in REDCap once all data has been confirmed (i.e., CRFs have been checked for accuracy and completeness).

Data will be transmitted by the study staff to the NIDA Central Data Repository if requested by NIDA. The final raw datasets will be returned to NIDA, if requested, for storage and archiving.