Social Media Intervention to Promote Smoking Treatment Utilization and Cessation Among Alaska Native Smokers

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Study Title: Social Media Intervention to Promote Smoking Treatment Utilization and Cessation among Alaska Native Smokers

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Research Question and Aims

Developing effective interventions to decrease tobacco use among Alaska Native people is a national priority. The prevalence of smoking among US adults is highest among American Indians and Alaska Native (AI/AN) persons; however, there are a lack of tobacco cessation interventions developed specific to this disparity group.[1,2] Social media holds promise as a scalable intervention strategy to promote engagement in treatment and cessation outcomes for AN people.

We plan to develop and pilot test a culturally relevant, Facebook delivered intervention to promote smoking treatment uptake and cessation among AN people who smoke. The Facebook content will include a digital storytelling approach adapted from the effective CDC Tips™ from Former Smokers educational mass media campaign.[3] The project builds on our team's longstanding tobacco control research partnership with the AN community and was informed by our understanding of cultural factors that can both impede and encourage cessation in this population. If the pilot intervention is successful, we will have a blueprint to conduct a large randomized controlled trial. Our long-term objective is to develop interventions for AN tobacco users that will ultimately reduce their risk of tobacco-caused disease and mortality.

Hypothesis:
Phases 1-3 are exploratory and developmental phases, therefore there are no hypothesis to report. For Phase 4, we hypothesize that the intervention will be feasible and the biochemically-verified smoking abstinence rate at1, 3 and 6 months follow-up will be greater in the intervention versus control condition.

Aims, purpose, or objectives:
Specific Aim 1 (phases 1-3): To develop a culturally relevant, Facebook delivered intervention to promote smoking treatment utilization and cessation among AN adult smokers. This formative research phase will use the cultural variance and surface/deep structure frameworks[4,5] to address the influence of culture in designing health messages, and adopt qualitative (phase 1) and quantitative (phase 2) pre-testing methods to develop and beta-test the intervention prototype (phase 3).

Specific Aim 2 (phase 4): To conduct a randomized pilot trial to evaluate feasibility, uptake, consumer response, and potential efficacy of the Facebook intervention compared with a control condition. In the pilot trial, 60 adult AN people who smoke will be randomized to the Facebook intervention or to a

control condition (quitline/treatment referral). Assessments will occur at baseline, 1, 3 and 6 months follow-up.

Our sub-aims are to:

a. Examine feasibility of delivering an intervention through social media as determined by recruitment and retention rates, treatment acceptability ratings, and Facebook intervention exposure and engagement.
b. Estimate potential magnitude of the intervention effect compared to the control condition on biochemically verified, 7-day point prevalence smoking abstinence rate at 1, 3, and 6 months follow- up.
c. Explore intervention effects on secondary outcomes: self-reported abstinence from any tobacco or nicotine product, quit attempts, and use of the state quitline or any evidence-based smoking cessation treatment (pharmacological or behavioral) through 6 months follow-up.
d. Explore sex, age, and region (urban/rural) effects on Facebook exposure and engagement, smoking abstinence, smoking treatment utilization, and quit attempts.
e. Explore interdependence (relationship orientation and collaborative efforts in decision making and lifestyle changes) as a culturally relevant mediator of intervention efficacy.
f. Since the pilot testing period took place over the COVID-19 pandemic, we will explore the self-reported impact of COVID-19 perceived risks, severity, and COVID-19-related anxiety, stress, financial impacts, social isolation, and social support on our primary outcome of smoking treatment utilization and cessation at 6-months follow-up.
g. Adapt the intervention and procedures in preparation for a future large-scale efficacy randomized trial.

Supplemental Specific Aim: To assess the perceived effectiveness of social media content and communication non COVID-19 and smoking. We will use existing content on COVID-19 (e.g., CDC Tips™ campaign videos) for adaptation. Potential content adaptations for COVID-19 messaging that may impact treatment utilization and quitting as barriers or facilitators include stress, anxiety, perceived risks, social isolation, and social support. We will conduct quantitative pre-testing of content using an online survey of a new sample of 40 AN smokers recruited statewide, with stratifications based on audience segment (sex, age, and location – rural or urban).

We are submitting materials for approval for all phases of the research. All phase 1 materials are developed and submitted for review. We are submitting for review all materials for phases 2-4 with the exception of the intervention materials. This is because these subsequent phases of the research are each dependent on the previous phases, as one of the goals of this study is to conduct formative work to develop the intervention materials. Thus, before commencing phases 2-4 we will submit a modification for IRB review and approval of all intervention materials including the Facebook group postings when developed.

This project is innovative for developing a new behavioral intervention to reach AN people statewide to promote smoking treatment utilization and cessation using social media communication tools that are culturally relevant and already adopted. The proposed study is significant because it will advance research on population-specific treatments for an underserved AN tobacco use disparity group. This pilot study is the first step to an intervention that could ultimately be widely disseminated through social media, internet, and mass media channels, and serve as a model for interventions in other populations such as AI smokers, enhancing overall reach and impact. [6] Future dissemination efforts also have relevance to the Food and Drug Administration (FDA) tobacco control regulatory science research to understand effective risk communication strategies in vulnerable groups. [7]

Literature Review

Nationally, the prevalence of tobacco use is highest among Alaska Native (AN) people and tobacco cessation interventions developed specifically for this disparity group are lacking. Geographic remoteness, climate, and travel costs are key barriers to treatment delivery. Social media has promise as a scalable intervention strategy to promote smoking treatment utilization and cessation for AN people who smoke.

Background (*Include relevant experience, gaps in current knowledge, preliminary data, etc.*):

Cigarette Smoking among Alaska Native People

Cigarette smoking is the most important preventable cause of morbidity, mortality, and excess health cost in the U.S., accounting for 480,000 premature deaths yearly.[8] In 2015, smoking prevalence was 15% among U.S. adults.[8] At 22%, AI/AN persons had the highest smoking prevalence; and within this group, AN residents of Alaska (AK) had a prevalence more than double that of Alaskan Whites (42% vs. 17%).[9] Some rural AK regions also have high smokeless tobacco (ST) use rates including a homemade product, *iqmik*.[10-12] Developing effective strategies to decrease tobacco use among AN people will contribute to the U.S. public health objective of reducing tobacco-caused health disparities[13,14]; and to the Healthy Alaskans 2020 target of decreasing smoking prevalence among AN adults to 17%.[15] There is a lack of tobacco cessation interventions tailored for AN people. To address this gap, we propose to develop and pilot test a culturally relevant, Facebook intervention to promote smoking treatment utilization and cessation that builds on our longstanding tobacco control research partnership with the AN community.

Social Media as a Feasible Intervention Delivery Platform among Alaska Native People

Our previous research utilized intensive, face-to-face tobacco cessation interventions that targeted AN pregnant women and youth; these individual-based approaches had limited reach and efficacy. [16,17] AK, the largest state in the U.S., has 178 communities not connected to a road system and separated from regional hospitals by vast stretches of tundra, water, glaciers, and mountains. Geographic remoteness, climate, and travel costs are key barriers restricting access to a full spectrum of health care services for AN people. Online social networks (i.e., social media) such as Facebook, are potentially powerful tools for reaching, engaging, and connecting AN people who smoke in cessation efforts. [18] Social network platforms have a large reach at a relatively low cost, representing a distinct advantage over face-to-face approaches. Research indicates Internet (web)-based interventions are effective for smoking cessation, but are associated with very low utilization. [19-21] Highly interactive social media (i.e., web 2.0 technologies), in contrast, can increase the depth of engagement and connection with an extensive reach to underserved, diverse populations[22,23] using evidence-based content.

Nationally, Facebook is the dominant social networking platform used by 68% of U.S. adults, more than double the proportion on Twitter (21%), Instagram (28%), Pinterest (26%), or LinkedIn (25%).[24] Of Facebook users, 75% engage with the site on a daily basis. [24] Among U.S. adults online, Facebook use indicates similar high rates of engagement by sex (75% of females and 83% of males use Facebook), income (84% engagement among those with less than 30K/year vs. 77% for those reporting 75K+/year) and age groups (88%: 18-29, 84%: 30-49, 72%: 50-74 years), except for slightly less use (62%) among those 65 and older.

Of importance for the reach of our intervention is the adoption of social media and other digital technologies among AN people. The Alaska Federal Health Care Access Network (AFCAN) is a leader in providing innovative technologies and expanding telemedicine use to physicians and mid-level providers statewide to improve isolated rural community access. Moreover, Facebook and other social

media use and the use of the internet to access health information has increased among AN people, even in remote regions. Facebook is most commonly accessed on mobile phones, but also on computers and iPads. Broadband internet is needed to access social media and to upload and download videos and other links; 91% of Alaskans have access to mobile broadband service, [25] while household broadband access (excluding mobile phones) is 65% (84% of urban and 47% of rural AN households). [26] With federal stimulus funding, initiatives are underway to greatly expand home-based access to broadband internet in rural AK. [26] In a representative survey of 340 households in rural

southwest AK (73% AN adults), 87% had at least one cell phone and 60% had a smartphone. Most common reported uses were text messaging; taking or sending photos or videos; and 81% used Facebook, Twitter or other social media sites. [27,28] A survey of 362 AN females from a rural census area reported 80% used Internet, 78% had smartphones, and 90% used Facebook. [29] Rural, village-specific Facebook pages exist and are popular. We have successfully used Facebook to recruit AN tobacco users for research projects (CA164533, HL117736).

In contrast to individual-based treatments, social media platforms could lead to greater adoption and sustainability by encouraging collaborative efforts across adult generations that resonate with the AN cultural value of interdependence, defined as relationship-oriented and collaborative in decision making and lifestyle changes. [30-32] We plan to explore interdependence as a culturally relevant mediator of Facebook intervention engagement and efficacy. However, it is important to note that traditional AN lifestyle, culture, and holistic worldview are intertwined and extend beyond mere social collectivism to include interconnectedness of people with nature, the environment, and all elements of the universe. [33,34] A qualitative study assessed the acceptability of using social media for smoking cessation among Latino adults, which is of relevance because Latinos similarly conceptualize culture, health decisions, and lifestyle changes as a family or group (versus self) effort. [35] Participants valued communal aspects of social media and preferred visual, educational, and motivational messages to connect them with quitlines and other existing tobacco treatment services.

Social Media Interventions for Smoking Cessation

The importance of social network influences and social support on smoking cessation are established.[36-39] Although interventions designed to enhance social support for smokers already in treatment have found mixedresults,[40,41] a body of literature supports the efficacy of network interventions in real-world settings.[36,42,43] Further, the potential for social-media formed networks to enhance smoking cessation is an understudied and priority research area.[18,44,45]

There are only three reported trials using social media platforms for smoking cessation. An intervention with both a website and a Facebook group evaluated in a quasi-experimental design among 238 young adult smokers resulted in greater self-reported 7- and 30-day smoking abstinence rates and quit attempts, compared to an unmatched comparison group of quitline users at 3-month follow-up.[46] Participants interacted significantly more with Facebook than with the website; of Facebook users, 56% were men and 44% were women; women were more active in the group than men with respect to postings and other engagement. An analysis of sex differences in communication styles on the Facebook group revealed women emphasized support and connecting with others, while men expressed strong assertions about quitting smoking.[47]

A second study evaluated a 100-day Twitter intervention (Tweet2Quit).[48] Among 160 smokers aged 18-59 years, Tweet2Quit doubled the rate of self-reported sustained abstinence at 2-months post-quit date compared toa control condition (smokefree.gov cessation website referral + nicotine patches), 40% vs. 20%. Sex, but not age, was related to treatment outcome with women less likely to quit smoking than men in both treatment and control conditions, though both genders were highly engaged with Tweet2Quit.

The third study was uncontrolled; it was designed to test whether monetary incentives enhanced Facebook intervention engagement in a young adult smoker sample.[49] Overall engagement was high and

did not differ by incentive groups, and overall self-reported smoking abstinence rate at 6 months was 18%.

We identified only three ongoing NIH-funded randomized trials of social media interventions for smoking cessation (http://projectreporter.nih.gov): (1) Twitter supportive intervention to prevent smoking relapse in postpartum women (R21CA198036; Wen, PI), (2) Twitter intervention comparing women-only groups vs. coed groups with usual care (R01CA204356; Pechmann & Prochaska, MPI), and (3) Facebook intervention to reduce smoking and heavy drinking in young adults (R34DA04163; Ramo, PI & Prochaska, Co-I).

Three other feasibility studies examined Facebook use among smokers. Haines-Saah et al.[50] found more postings to the "Picture Me Smokefree" Facebook page among women than men (i.e., 189 total photos posted among women [mean 9.5] vs. 94 posted by men [mean 4.2]). However, content analysis revealed postings were

of similar quality for both sexes; sharing of photos and captions about experiences with tobacco use and struggles with quitting in the context of family life and relationships were the main themes. Evaluation of the Facebook page smokefreewomen.gov[51] found that increased frequency of moderator postings to facilitate dialogue and to provide support engaged existing and new users, resulting in a marked increase in user postings and reach (i.e., unique views). Finally, a Facebook intervention using health communication messaging and supportive moderator postings was associated with a decrease from baseline in cigarettes smoked per day at 2- week follow-up; increased engagement was associated with greater smoking reduction.[52]

The proposed study, focusing on AN smokers, advances the methods of published social media intervention studies through the use of biochemical verification of smoking abstinence and extended duration of follow-up. Previously, most studies have targeted only young adults, whereas we plan to include a wide age range. We will also explore potential sex, age, and regional (urban/rural) effects on Facebook engagement and quitting, as there is limited research exploring these variables within the context of social media platforms for smoking cessation.[46,48] Within smoking cessation intervention efficacy and effectiveness trials generally, a recent literature review on sex/gender differences found that of 126 tests conducted, only 2 observed that women were significantly more likely to quit smoking than men, compared to 59 that found women were significantly less likely to quit smoking than men; the remaining 65 studies reported no difference by gender.[53]

CDC Tips from Former Smokers (Tips™) Educational Campaign

The content for the proposed Facebook intervention will be culturally relevant, adapting the storytelling approach used by the effective CDC Tips™ educational, national, general audience, mass media campaign.[3] Based on factual health communication messaging, Tips™ features graphic, emotional, true stories told by former smokers to increase awareness of the harms of smoking and to encourage quitting. It has a specific call to action to use free, evidence-based state quitlines and smoking cessation website resources (www.smokefree.gov). The campaign was effective for increasing quitline utilization and quit attempts on a population-level. [3,54] Number of calls to the national quitline portal (1-800-QUIT-NOW) increased 75% over the 16-week campaign compared to pre-campaign levels, resulting in 151,536 additional quitline callers. [54] Among 4,248 smokers nationwide, the proportion making a quit attempt in the past 3 months significantly increased from 37% at baseline to 42% post-campaign (applied on a population basis, an estimated 1.83 million additional smokers made a quit attempt). [55] No sex differences were found on quit outcomes, but those with less education and African Americans were more likely to report a quit attempt compared to White smokers and those with higher education levels. The Tips™ education campaign has not been adapted for nor evaluated among AI/AN people; only 2 of the 31 available stories feature an AI/AN former smoker.

The personal story format of the Tips™ campaign promotes salience and reduces the tendency for

smokers to generate counterarguments or discount adverse health outcomes as uncommon because the stories feature real people – not actors. [56] Numerous studies, including prior work by our team, [11] suggest that storytelling is culturally congruent, making the Tips™ format ideal for social media content development. Digital storytelling and other narrative forms of communication (e.g., photonovela, photovoice) have emerged as important tools for health behavior change. [57-59] Storytelling is especially effective for AN people with a strong oral tradition[60-62] as it reinforces traditional AN knowledge systems, promotes cross-generational learning, and builds social connections. [33,63] Also of relevance to Tips™ is work conducted by our team indicating AN adults preferred graphic, factual messages on tobacco use harms compared with other appeals, but this research was limited to interventions communicating risks during pregnancy. [64,65]

Development of social media-based interventions with consideration of cultural factors (beliefs, norms and values) could lead to greater treatment participation and acceptability in AI/AN communities. [66-72] A systematic review found that indigenous smokers prefer culturally-targeted media messages. [69] Cultural tailoring increases attention to health risk messages, creates more effortful processing, and results in fewer counterarguments and greater perceived credibility of the message. [73,74] The Institute of Medicine has promoted the importance of culture as part of an integrated framework for interventions[75]; and, in particular, documented its importance for leveraging strengths and voices within AI/AN communities. [76]

The Alaska Native Tribal Health Consortium (ANTHC) conducted three focus groups of AN tobacco users (9 men, 18 women) to assess perceived effectiveness of statewide tobacco prevention and cessation media for encouraging smoking cessation. [77] Seven video concepts were reviewed, of which two featured AN people who smoke and family members (one came from Tips™: Michael, AN former smoker) and 5 targeted a general audience. The highest ratings were for the 2 videos featuring AN people. Participants reported greater cultural relevance of these two ads compared with other media because these portrayed AN individuals, communities, and activities they were familiar with; addressed the impact of tobacco use not only for themselves but for others they cared about; and conveyed emotion while providing facts on the effects of tobacco use. Participants were also asked about communication venues most likely to reach them (0-4 Likert scale from very unlikely to very likely). Facebook received the highest mean rating (3.3) compared with television (3.0), internet via computer (2.0) or smart phone (2.8), Twitter (0.8), or Instagram (0.9).

The proposed intervention will promote engagement with evidence-based smoking cessation treatment including the AK state quitline and tribal cessation programs. Promoting treatment utilization is an important issue for the tobacco research field.[2,13] In 2015, about 68% of smokers in the U.S. wanted to stop smoking and 55% made a past-year quit attempt, but only 7% quit smoking.[78] In AK, successful quit attempts are strikingly lower for AN adults compared with non-Native smokers (4% vs 10%).[9] Generally, only 4-7% of unaided quit attempts are successful, but evidence-based counseling and medication treatments boost quit rates to as high as30-40%.[38,79] Individual, group, and telephone behavioral counseling as well as 7 FDA approved medications increase smoking cessation. For example, free quitlines, now available in 50 states, double smokers' chances at quitting compared to control conditions.[38,80] However, there is a reach problem: only 1% of U.S. smokers use quitlines[81] with utilization especially low among underserved racial/ethnic minority groups.[82] A 2015 survey of U.S. state quitlines found that of the 313,505 callers receiving coaching and/or medications, only 2.4% were AI/AN adults (low given the very high prevalence of smoking among AI/AN adults).[81] Less than one-third (31%) of U.S. smokers attempting to quit use any type of evidence-based behavioral cessation counseling and/or medication.[78] Therefore, efforts to prompt more AI/AN and other diverse smokers to quit and to use evidence-based treatment methods to increase their success are important steps toward reducing tobacco-caused health disparities.

There is a lack of tobacco cessation interventions tailored for AN people. To address this gap, we propose to develop and pilot test a culturally relevant, Facebook delivered intervention to promote smoking treatment utilization and cessation that builds on our longstanding tobacco control research

partnership with the AN community.

This proposal addresses 3 of 7 gaps and priorities in tobacco research identified by the Tobacco Control Research Priorities Working Group[45]: (1) targets an underserved tobacco use disparities population, (2) develops a novel behavioral intervention using a social media platform, and (3) promotes uptake of evidence-based treatment and quitting. If effective, the proposed social media intervention has relevance for advancing the science of tobacco treatment for AI/AN communities.

Smoking and COVID-19

Underserved populations with a higher prevalence of tobacco, such as ANAI people, may be more vulnerable to the physical and mental impacts of COVID-19, enhancing the significance of the proposed supplement.[83-85] Coronavirus disease 2019 (COVID-19) is mainly a disease of the respiratory tract caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[86] As of May 05, 2020, there were 3,556,852 COVID-19 infections recorded globally, and 251,237 deaths. Tobacco smoke is a major risk factor for lung disease,[87] and cigarette smoking substantially increases risk for bacterial and viral infections.[88]

Smoking is further linked to lung inflammation and lowered immune function, and is likely associated with the negative progression and adverse outcomes of COVID-19.[89] One study found that the presence of the ACE-2 enzyme that facilitates the entry and multiplication of coronavirus into the lung cells is higher among patients with chronic obstructive pulmonary disease and in smokers.[90] Berlin et al. (2020)[91] summarized case series reports indicating that the proportion of smokers was greater among the severe cases of COVID-19, including deaths, compared with that observed among the non-severe cases.

Cigarette smoking is associated with anxiety and depressive symptoms,[92] as well as psychological stress.[93,94]These symptoms are also reported by populations affected by the COVID-19 pandemic.[86,95-98] In the absence of a medical cure for COVID-19, the global response is a simple public health strategy of isolation for those infected or at risk, reduced social contact to slow the spread, and masking and hand washing to reduce infection risk. While the primary intervention of isolation may well achieve its goals, it can also lead to loneliness, reduce access to and availability of social support, and worsen stress, anxiety, and depressive symptoms.[95,97-100] Therefore, interventions that address COVID-19 risks associated with smoking, and associated impacts including stress and reduced social connections, especially among tobacco-use disparity populations, are needed.

Study Design and Methods

Methods: *Describe, in detail, the research activities that will be conducted under this protocol*:

Informed Consent Process

Screening eligibility and study enrollment for all phases of the research will occur either online via the study's webpage, in person, or by phone or mail. All advertisements will contain the study: toll-free phone number, email address, and Qualtric's website link. Individuals will be provided a brief description of the study, and then screened in person or by phone. For further information, they can be sent a link to the study website. The website will contain a short description of the study as well as eligibility questions. Qualtrics (https://www.qualtrics.com) is a secure, online, HIPAA-compliant survey software that transmits data to and from secure firewalled data centers using Transport Layer Security encryption. We successfully used this software to obtain informed consent and to administer a tobacco use and health behavior survey study in a rural AK region with over 400 adult participants (57% AN persons). 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 at the Alaska Native Tribal Health Consortium (ANTHC) or Mayo Clinic medical facilities. The potential research participants will be given the opportunity to have any questions about the study answered and will have as much time as they need for the consent process. If anyone is

uncomfortable completing their survey via Qualtrics, they will be given the option to complete their surveys by email, phone, or in person with assistance from a study team member.
Verbal Consent: For phases 1, 2 and the supplemental aim, the research presents no more than minimal risk to subjects and involves no procedures for which written consent is normally required outside of the research context. If the potential participant is eligible and verbally consents to participate they are enrolled.

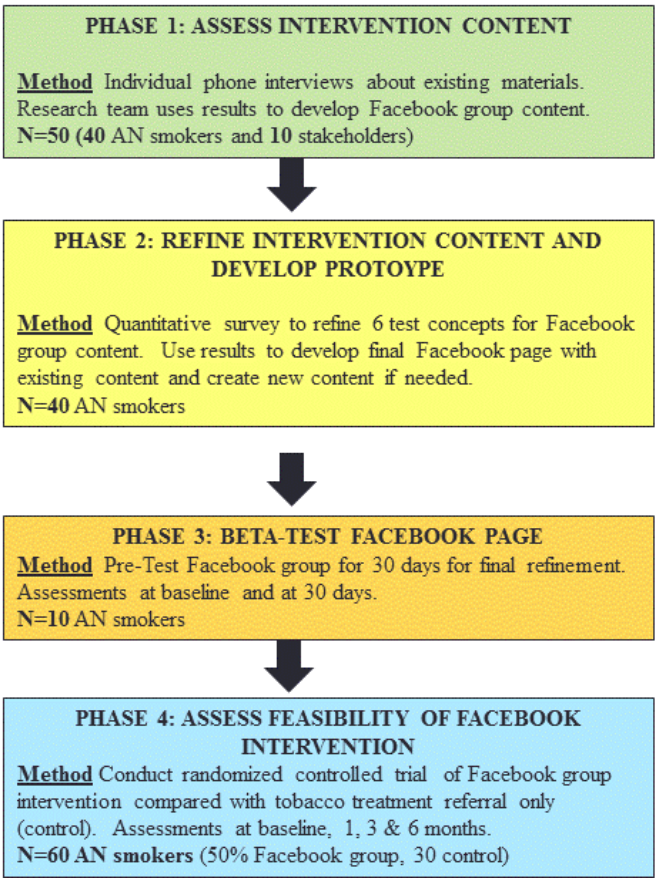
Written Consent: For phases 3 and 4, if the potential participant is eligible to participate, they will complete the informed consent in person, by mail or email, or on-line. If consent is completed on-line, to ensure they review the document, their understanding of the consent form will be assessed online through multiple choice questions with required answers before being able to proceed with the study. Questions are based on those used in studies with potentially vulnerable participants.[112] Any wrong answers during the consent will be sent to study staff who will contact the potential participant via email or phone for clarification. For those who complete their consent by mail, A study team member will mail the consent form to the participant to review, sign, and mail back in the enclosed postage-paid return envelope. Those who wish to complete consent by DocuSign, but experience difficulty, will be provided support by a study team member to complete the DocuSign process. Eligible individuals completing the informed consent process will be enrolled.

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 at the Alaska Native Tribal Health Consortium (ANTHC) or any tribal or Mayo Clinic medical facilities. All screening and consent forms/processes are approved by the Alaska Area IRB and are at the eighth grade reading level. Computer software programs are used to test the reading level of each document. Individuals will be given an opportunity to ask questions and decide whether or not s/he wishes to participate. The consenting software is designed to 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. Prior to survey administration, potential participants will be able to receive a copy of the consent information for their records. If they agree to participate they will select to proceed to the web survey, or exit if they choose to decline. The consent form will include information on the nature of the study and alternatives to taking part, and contact information (toll-free number) for the PIs of the study. Participants will be encouraged to phone with concerns or problems that might occur during the study.

Standard language in our consent procedure assures the study participants of the confidential nature of the study. Those who participate will be clearly told that they may withdraw from the study at any time without adversely affecting their current or future medical care at the Alaska Native Tribal Health Consortium (ANTHC) or any tribal or Mayo Clinic medical facilities. These standards are strictly adhered to and monitored by the Alaska Area IRB and the Mayo IRB

Figure 1: CAN Quit Study Flowchart

Connecting Alaska Native Smokers to Quit



Formative Work to Develop the Intervention: Aim 1 (Phases 1-3)

Projected Content and Structure for the Facebook Intervention

Structure and duration. The intervention will consist of a Facebook group moderated by an AN facilitator. To address potential concerns about Facebook privacy, [94] we will utilize a closed and secret Facebook group and a group policy/guideline that emphasizes confidentiality of all content. A secret group is defined as invitation only, with the group and content not visible to anyone on Facebook except participants. Thus, anyone searching on Facebook would not find the group nor be able to request to join. Also, group membership or postings through newsfeeds will not be visible on the participants' personal Facebook page.

We chose to use a moderated group based on research indicating that moderators play a critical role in directing and tailoring content to the group and enhancing overall social media engagement. [47,95] Also, the frequency of moderator Facebook postings is associated with increased participant engagement. [51]

The Facebook group will be active for 3 months. A content library of moderator postings will be developed for posting within the Facebook group for the 3 months that the group is active. The moderator will check-in with the group about 3-4 times daily to respond to comments and other user-generated content, and to prompt and direct discussions by encouraging participants to share stories about their tobacco use journey. Participants will be notified through news feeds when there is new Facebook content posted.

Content for moderator postings. Moderator postings will be developed from two existing sources.

First are the CDC Tips™ campaign digital story videos. [3] The 31 stories are based on factual appeals to quit smoking and each is about 2.5 minutes long. The stories address different phases of the quitting process, specifically: motivation (why to quit), engaging in treatment (how to quit), and relapse prevention. We anticipate creating about 8-10 new digital stories featuring AN persons. However, based on formative work, we recognize that existing Tips™ stories such as Michael's story (AN former smoker) may be acceptable, and will be included. The digital stories will be embedded in moderator postings as YouTube links.

Second, for additional content for moderator postings, we will tailor existing postings from a recently held CDC Facebook event "30 Smoke-free Days" that invited people nationwide to set a quit date and targeted adults ages 18-54 years. A moderator posted once daily for 30 days. These general audience moderator postings included images combined with text that were inspirational, celebrated quitting milestones, and included embedded YouTube links to specific Tips™ videos. The content is consistent with clinical practice guidelines for behavioral strategies to motivate, prepare and assist individuals to quit smoking, and stay tobacco free. [38] In an uncontrolled evaluation, over a 1-month period, 3,221 people nationwide received updates and posts from the Facebook page, and of these, 641 (20%) actively participated by making a quit attempt or supporting others to quit. The mean total engagement (likes, shares, replies, comments) on event content was high (36%) compared to the average monthly engagement rate of 4-6% on the CDC main Facebook wall. Moderator postings with the highest level of engagement, defined as discussion and participant sharing, were themes related to lack of family support, weight gain, and cravings.

For cultural tailoring, messaging will center on abstinence from all tobacco and nicotine products, including ST/*iqmik* and e-cigarettes. Differentiating ceremonial/traditional tobacco use from commercial use is not an issue as prior work documents that AN people do not use tobacco for such purposes. [11]

Our goal is to design a social media intervention that could be delivered on a large-scale population basis. The CDC "30 Smoke-free Days" Facebook event and the Tips™ campaign both prompted a call to positive action, specifically to use free state quitline services, a scalable approach we will use in this study. Quitlines represent a high impact approach to improve access and availability of tobacco dependence treatments because of their potential to achieve wide reach into the population, including hard-to-reach subgroups. The AK quitline services consist of free coaching calls, web coaching, supportive text messaging program, personalized web- based quit plan, a quit guide and other written materials, and/or a two week starter supply of free nicotine patches, gum, or lozenges. Quitline coaches receive cultural competency training for coaching AN people.

However, we recognize it is important to also promote other types of treatment resources in the event that federal funding for state quitlines diminishes. Thus, we will additionally promote use of evidence-based quit smoking website resources (smokefree.gov) along with regional tribal tobacco treatment programs which provide phone counseling and access to stop smoking medications. Tribal programs vary on the number of counseling sessions and duration of free nicotine replacement therapy provided.

Health Communication Framework

We will use Dr. Resnicow's cultural variance and surface/deep structure frameworks[4,5] to address the influence of culture in designing health messages. Cultural variance framework considers AN cultural influences on health behaviors including specific beliefs, norms (i.e., communication styles, social acceptance of tobacco use), values (e.g., interdependence), and AN knowledge systems/ways of knowing. [11,30,32-34,63] Surface and deep structure inform both content and format of messages. Surface structure involves matching materials and messages to observable social and behavioral characteristics such as AN people, music, and clothing. The second dimension (deep) incorporates cultural beliefs and values. Appropriate surface structure generally enhances receptivity, comprehension, and acceptance of messages whereas relevant deep structure conveys salience. Cultural variance framework largely addresses deeper level components of tailoring messages. We will use a planning framework based on

the NCI[115] and CDC[116] recommendations for developing social media and other digital health communication tools, addressing key components of message construction. This framework is in line with researcher recommendations to iteratively develop digital health interventions with user feedback.[107,108] Thus, as part of our formative work we will conduct two rounds of qualitative (phase 1) then quantitative (phase 2) pre-testing to develop message concepts and develop the intervention. Next, the intervention prototype will be developed and beta-tested (phase 3).

Phase 1

Qualitative Pre-Testing using Individual Interviews

Sample. We will use a stratified purposeful sample[119] of AN adult smokers with divisions based on audience segment (sex, age group [19-29, 30-49, 50+ years] and region [urban, rural]). Krueger[120] recommends conducting at least 10-15 interviews per major subset before reaching data saturation, whereby no new information is being learned. [120] We estimate about 40 individual interviews (20 men, 20 women; 20 urban, 20 rural; 12-13 within each age group) to achieve data saturation. Eligibility criteria for participants are described in Table 1 below. Various stakeholders will also be interviewed including AK quitline coaches, tribal cessation program counselors, and Alaska Education Advocacy members, with about 10 interviews total. There are no eligibility criteria for stakeholders, other than that they must be health professionals; stakeholders will be selected and approached for participation by the Mayo study team. The ANTHC Tobacco Cessation Program will obtain names and contact information of Tobacco Treatment Specialists and statewide Quitline personnel interested in being contacted for the interviews and provide them to the Mayo study team. Priority for stakeholder interviews will be based on length of time providing tobacco cessation counseling. Stakeholders will verbally consent and complete an interview similar to participants but it will be geared to health care professional views instead of those of an AN person who smokes.

Procedures. Interviews will be done by phone and last about 45 minutes, but may take as long as one hour. Participants will receive a $25 Visa gift card as remuneration. Eligible participants who have provided verbal consent as described above will be emailed a password-protected link to view the materials online. Materials will be available for review online on the study web site and links to the materials will also be emailed to the participant. At the end of the interview the participant will be asked if he/she would like referral information for programs and services to quit smoking. If the participant is interested, the study coordinator will mail the participant information on the Alaska Quitline and local tribal tobacco cessation program.

Moderator guide and training. A semi-structured moderator guide was developed and a project coordinator at ANTHC will conduct the interviews. Dr. Sinicrope and Ms. Hughes will provide training for the project coordinator in Anchorage including 4 hours of didactic instruction, followed by 4 hours of mock interview practice, and a certified completion interview. [120] All sessions will be audiotaped.

The interview will first cover a brief assessment of socio-demographics such as health literacy, age, sex, education, marital status, and tobacco use. The interview also covers:

(a) Tips™ digital stories: Review 4 stories from Tips™ (each about 30 seconds long) and obtain feedback. Participants will view online selected general audience videos (i.e., Terrie Bill, and Jessica's stories) and one video featuring an AN person with COPD (Michael's story) due to the strong emotional appeals about impacts of quitting on family members. [121]

Link to CDC Tips™ videos: https://www.cdc.gov/tobacco/campaign/tips/index.html

- For each story: feedback is obtained on the storyteller and story characteristics, including identification and engagement; [122] and cultural congruence (i.e., factual-based appeals from former smokers).
- Compare reactions for general audience stories versus the story featuring an AN person.

- Assess preferences for message source for new stories: AN person, sex, age, region, tobacco use, and relationship (e.g., grandparent, sibling, spouse or Elder).

(b) ANTHC digital stories: Participants will view two stories from the 7 videos below that feature AN people and are already developed by ANTHC. The research team will select 2 videos of potential videos listed below.

The video descriptions and online links are as follows:

1. Tania (community health aide, role model), time 1:38https://player.vimeo.com/video/55410351
2. Edith (cancer, quit for family), time 2:33https://vimeo.com/160043666
3. Casandra (cancer, dad quit, she quit for husband and son), time 2:33https://player.vimeo.com/video/55320782
4. Caroline (chew tobacco), time 2:25 https://player.vimeo.com/video/55 320781
5. Marie (quit smoking for son), time 2:21 https://player.vimeo.com/video/553207 84
6. Caroline (role as tobacco prevention professional), time: 1:48https://player.vimeo.com/video/55320946
7. Aubrey (she didn't start smoking until college and only smoked for a year, then quit), time: 1:38https://player.vimeo.com/video/62102834

(c) Other content for moderator postings (text and images): Four general audience postings from the CDC 30 Smoke-Free Days Facebook event will be viewed by participants that represent different themes, such as setting a quit date, celebrating milestones, family support, and cravings.

- The cultural relevance of postings is assessed and ideas for adapted or new content are gathered.
- Individual and cultural barriers to smoking treatment use or cessation that should be addressed; for example, beliefs about quitlines and stress/affective comorbidity[123, 124] are addressed.

(d) Optimizing Facebook intervention engagement: Finally the interviewer asks participants how to make the Facebook group more engaging (i.e., would text message prompts help?) and assess cultural need for groups separated by sex/age.

The stakeholder interview is similar except for brief demographic questions only and the feedback elicited is geared to health care professional views instead of those of an AN person who smokes.

Qualitative analyses. Sample characteristics will be summarized using descriptive statistics. Recordings will be transcribed by a professional transcription service. Content analysis[125] supplemented by QSR NVivo software, version 10 (Doncaster, Victoria, Australia) will be used to generate response themes. All transcribed statements will be analyzed. Codes and categories will be developed based on moderator guide topics and themes emerging from the data. Two study team members will code responses independently for each topic area; inter-rater agreement (kappa coefficient) will be assessed. During this open-coding process, themes will be extracted for analysis when there is code endorsement or elaboration by several interviews. In addition to open coding, planned comparisons within and across sex, age, and region strata will be carried out and connections made between identified categories. Coding discrepancies will be resolved through discussion with a third study team member until consensus is reached.

Concept development. From the qualitative results, the research team will develop six test concepts: 3 storylines for the digital videos with written text and graphics, and 3 image/text moderator postings representing different types of appeals and message sources. We will consult with the ANTHC media department and Mayo social media department in developing these concepts.

Inclusion/Exclusion Criteria:

Table 1:

Participant Eligibility Criteria and Rationale for Both the Formative Work and Pilot Trial: Phases 1-4

Study Inclusion/Exclusion Criteria	Rationale
Alaska Native person (based on self-reported race/ethnicity) and resides in Alaska	Study targets a population with among the highest prevalence of tobacco use in the U.S. We chose to conduct this initial study in AK to reduce sample and intervention design heterogeneity. Across the nation, there is immense cultural and geographic variability, e.g., urban vs. reservation dwelling, ceremonial vs. non-ceremonial tobacco use. Also, AK has highest percentage of AN residents vs. all other states (19% vs. 2%).[107] If effective, the intervention could be adapted for and disseminated to AI/AN adults nationwide.
Age 19 years or older	Legal smoking age in AK is 19 years. Different social media venues and content may be warranted to address developmental issues among those ≤18 years. A Twitter-based intervention for adult smokers 20-59 years found age was not related to engagement or cessation,[108] thus, we chose not to restrict the upper age limit.
Both men and women will be included	There are no preliminary data to indicate sex-specific interventions are warranted at this stage of the research. We will explore sex differences on feasibility and efficacy as a research question.
Smoked at least 1 cigarette per day over the past 7 day period	Allows for participation of AN people who smoke who report fewer cigarettes per day and are considered "light" smokers, but have cotinine concentrations equivalent to "heavy" white smokers, indicating differences in nicotine metabolism.[109,110]
If other tobacco use, cigarettes are the main tobacco product used	Cigarette smoking in combination with other tobacco product use is highly prevalent in some AK rural regions;[9] thus, results are more generalizable if other tobacco use is allowed.
Considering or willing to make a quit attempt	Intervention promotes treatment utilization and quitting. We will explore readiness to quit as a potential moderator of Facebook engagement and efficacy.
Has access to Broadband (high speed) Internet on mobile phone, at home, work, or other location.	Facebook can be accessed on a variety of technology devices such as computers, iPads, and mobile phones. Broadband internet access is needed to access social media and to upload and download videos and other links.
Has an existing Facebook account or willing to set up an account prior to study enrollment.	There is already good adoption of Facebook in rural regions of AK. Including participants familiar with regular social media interaction enhances participation, whereas non-users or those unfamiliar with Facebook are less likely to engage in the intervention.[108,111] To provide study access to a broader group, we will offer an online or paper-based tutorial for those without a Facebook account.
For past 3 months not enrolled in a program or using pharmacotherapy	Study promotes treatment uptake, utilization, and quitting.

to stop smoking	

Phase 2: Quantitative Pre-Testing of Prototype

Sample. We will test the concepts developed in Phase 1 using quantitative survey interviews conducted with a new sample of 40 AN adult smokers (eligibility criteria described above) via a stratified purposeful sample[119] with divisions based on audience segment (sex, age group, urban/rural region). [120] Participants will receive a
$25 Visa gift card as remuneration.

Procedures. Respondents will view test concepts online through pictures and text embedded in the survey. If preferred, participants will be mailed or emailed the concepts for review in advance of the survey. The survey will be done online via Qualtrics survey software or by email or phone if preferred. The survey will take about 20- 30 minutes to complete. At the end of the survey the participant will be asked to indicate if he/she would like referral information for programs and services to quit smoking. If the participant responds Yes, the study coordinator will mail the participant information on the Alaska Quitline and local tribal tobacco cessation program.

Measures. The survey will include items assessing socio-demographics such as health literacy, age, sex, education, and marital status; tobacco use, and a validated measure of perceived effectiveness (PE) to pre-test each concept. PE is useful for assessing the likelihood of success of potential messages when large scale efficacy pretesting for behavioral impact is impractical. [126] Measures of PE have been underutilized in the evaluation of message tailoring for subpopulations. We will use a 6-item validated measure of PE that was used to evaluate the Tips™ stories[121] and similar to PE measures used in other smoking cessation research. [127] After viewing each concept, respondents will rate their level of agreement on a scale from 1 (strongly disagree) to 5 (strongly agree) with the following statements: (1) this was worth remembering, (2) this grabbed my attention,
(3) this was powerful, (4) this was informative, (5) this was meaningful, (6) this was convincing. Participants will also rate each concept for "this fits with my culture." Statistical analyses. Sample characteristics and PE items will be summarized using descriptive statistics including means, percentages, and frequencies. The Chi-square goodness of fit test will be used to analyze concepts most and least preferred by participants. The association of participant sex, age, and region with message concept preferences will be examined using line regression.

Prototype Development

Mayo Clinic social media department will create the Facebook group page, develop the content library of moderator postings, and set up the software to capture participant use data. Existing Tips™ stories deemed culturally acceptable in the formative phase will be utilized for moderator postings. Moreover, ANTHC will develop new digital stories based on their extensive expertise. [60-62] Two workshops will be held in Anchorage by two trainers with about 4-5 AN participants each, with the goal of helping individuals to generate compelling stories about their tobacco use journey. Participants will be selected from our qualitative work or by the Community Advisory Board (CAB) members and invited to participate, representing both sexes and different age groups, as well as residents of urban and rural regions. The workshops will be held over 3 days lasting about 4-8 hours each day. Each participant will sign a press release and receive a $250 honorarium. Meals and beverages will be provided each day during the training. Instructions will be mailed to each participant prior to the workshop to bring a draft of their story of 1.5 pages or 250 words in length and photos/music they wish to incorporate. The talking circle is an integral part of story development. At the workshop, participants will first share their story in a circle to help facilitate dialogue and to obtain feedback to further develop their stories.
After making revisions, each participant will privately record his or her story. Next, the trainers will edit the story with the participant to create an integrated theme consistent with the formative findings. Each story

will be2.0-2.5 minutes as social media research indicates that the average duration a user will watch a video is 2.7 minutes. [128]

Additional content for moderator postings will consist of images combined with text designed to provide information and stimulate participant discussion. All text will be written in the English language at a 5th grade reading level using readability analysis software. One study found that text combined with images increased Facebook engagement 84% more than text-only posts, [129] consistent with other research. [130,131] Facebook postings for optimal engagement are about 120 characters in length. [132]

Taglines to all moderator postings will have a call to action for tobacco treatment by providing the: (1) AK state toll-free quitline number, (2) web link to regional tribal tobacco cessation programs, and (3) link to the smokefree.gov quit smoking resources website.

We will construct a content library organized similar to a treatment manual. [111] The content library will have 30postings to be used by the moderator once per day; and repeated for each month the group is active. In a future Stage II efficacy trial, we plan to fully automate these postings to increase intervention scalability. [108]

The moderator will also prompt and reinforce user-generated postings and discussion (e.g., sharing of stories of tobacco use and quitting) to sustain participant engagement. [133] Moderator guidelines for responding to participant questions and handling of inappropriate or misinformation will be included in the content library.

Phase 3

Beta-Testing of the Prototype

The intervention prototype will be beta-tested with a different sample of 10 participants (eligibility criteria above). A Facebook group size of 10 was the minimum number for optimal engagement in prior work. [49,134]The purpose of this phase will be to expose participants to the 30 days of moderator postings and obtain
feedback, to ensure that the system works as intended, to note any technical issues that need to be remedied, and to facilitate any refinements of the program. In the subsequent pilot trial, the Facebook group will be active for 3 months, but for this formative phase of the study, participation will be completed at the end of the 30-day
beta-testing period.

An online survey will be administered at baseline to assess socio-demographics such as health literacy, age, sex, education, marital status, social media use, and tobacco use. A follow-up survey will also be administered at the end of the 30 day intervention period that includes self-reported smoking status and treatment utilization, and the Social Media Usability Measure which assesses perceived ease of use, usefulness, and satisfaction rated on a 7 point scale (1-strongly disagree, 7-strongly agree); [135] as well as open-ended questions for feedback on modifications to the prototype. The baseline and follow-up surveys will be done online or by phone, or the survey will be mailed with a postage paid return envelope depending on participant preference. These surveys will take about 15-20 minutes each to complete. Participants will receive a $25 gift card for completing each assessment. Refinements will be made based on user feedback.

Phase 4

Randomized Controlled Pilot Trial (Aim 2)

Design Overview and Considerations

The pilot trial, a two-arm, parallel groups, randomized controlled design, will enroll 60 participants

Randomized with 1:1 allocation to the intervention or control condition. Participants will be randomized within stratified

blocks based on sex (male, female), age group (19-29, 30-49, 50+ years), and region (urban, rural); potential variables related to outcomes. [10,12] Assessments will be conducted for both study groups at baseline and at 1, 3,and 6 month follow-up. The primary outcomes are feasibility indicators and the 7 day, biochemically- confirmed smoking abstinence rate at 6-month follow-up. Secondary endpoints are self-reported engagement in smoking cessation treatment and quit attempts. Table 2 compares and contrasts the two study conditions.

Table 2: Design Elements of Study Groups

Intervention Components	**Intervention Condition Facebook Group + Quitline/Treatment Referral**	**Control Condition Quitline/Treatment Referral Only**
Quitline/ treatment referral (both groups)	Description of tobacco treatment services, phone numbers and web links sent via postal mail (printed materials) and email. Treatment options provide free, professional assistance based on U.S. clinical practice guidelines: (1) AK quitline, (2) regional tribal tobacco cessation programs, and (3) smokefree.gov resources (e.g., free texting program and smartphone application, quit guide)	
Facebook Intervention (developed in formative work)	• Participants join a secret (private), culturally relevant Facebook group for 3 months, and moderated by an AN tobacco research counselor • 3 months of moderator postings; plus 3-4 daily check-ins/postings to respond to participant generated content and encourage sharing of personal stories/experiences relevant to all stages of the quitting process and treatment engagement	• No additional intervention provided by research staff

Supplemental Aim: Quantitative

We will use the information we have learned in our previous phases to adapt existing content on COVID-19and smoking, and conduct quantitative testing of PE among a new sample of 40 AN smokers using identical procedures and evaluation process as was done in phase 2 of the study.

Sample. We will enroll 40 AN smokers recruited statewide, with stratifications based on audience segment (sex, age, and location – rural or urban). Recruitment procedures and study eligibility criteria are described above. Participants meeting the eligibility criteria will be provided with details on the study and asked to provide verbal consent. Participants will receive a $25 gift card for their time.

FB Content. We will use existing content (i.e., text, videos, images) on COVID-19 and smoking for adaptation from the ANTHC media department, Tips™ Campaign, and the U.S. FDA Center for Tobacco Products social media content. Informed by the cultural variance and surface/deep structure health communication frameworks,[4,5] the qualitative work completed previously provided insights into cultural tailoring for new content on COVID-19 and smoking. Qualitative analyses indicated that participants preferred culturally relevant content that included images of AN people, places, and activities that told a compelling story and was emotional. Participants tended to have less interest in content that was not relatable or that included individuals who were not AN. If a story was not AN, then it needed to include AN values, such as including family/children or telling a story in a 'real' way, with emotion and honesty. **Figure 1** below provides an example of how we modified existing content in the parent R34 grant to be relevant to the AN culture.

Figure 1

Existing CDC Tips posting

Modifications:
Include AN people, include AN activities, include family as an inspiration

New CANQuit FB posting

We will consider additional COVID-19 relevant adaptations to existing content that may impact treatment utilization and quitting, as barriers or facilitators, including stress, anxiety, perceived risks, social isolation, and social support. The research team will select 2 videos and 4 text/image postings for adaptation and evaluation for PE. We will continue to seek technical assistance from the CDC Health Communications Branch and advice from the Community Consultation Committee in selecting new content with feedback from our moderators who are interacting with CAN Quit participants daily.

Procedures. Following verbal consent, we will email each eligible candidate a link to the online survey. Participants received a $25 gift card upon survey completion. Respondents will view each of the postings then completed a 20-minute online Qualtrics (Provo, Utah, U.S.) survey assessing socio-demographic and tobacco use characteristics and an appraisal of PE of each posting using a validated measure of PE.[120] Participants will report how much they agree with the following 6 statements for each posting: "This was worth remembering," "This grabbed my attention," "This was powerful," "This was informative," "This was meaningful," and "This was convincing" using a 5-point scale from 1 (strongly disagree) to 5 (strongly agree). A total PE score is produced summing scores for the 6 items and dividing by the number of items in the scale (i.e., possible total score range 1=strongly disagree to 5=strongly agree); scores > 3.0 indicate greater PE. We added "This fits with my culture" to assess cultural relevance for each posting, with identical response options.

Statistical Methods. We will summarize sample characteristics, responses to individual items, total PE score, and the cultural relevance for each posting, with the Kruskal Wallis test to assess associations of the total PE score and cultural relevance item to sex, age group (<30, 30-49, and ≥50 years), locality (urban, rural). *P*- values ≤ 0.05 will be considered statistically significant. Postings with PE > 3.0, no substantive differences across demographic groups, and with elements considered salient to AN people who smoke, will be added to the FB intervention content library.

Interventions

All participants will receive evidence-based[38] tobacco treatment referral information by postal mail (printed materials) and email, including information on their regional tribal tobacco treatment program, state quitline, and smokefree.gov quit smoking resources (see Table 2).

Control condition will receive no additional intervention provided by research staff.

Intervention condition will additionally receive the Facebook intervention developed in Aim 1. With the enrollment letter, participants will receive instructions for joining the Facebook group. The Facebook group will be moderated on a daily basis by an AN tobacco research counselor who will be trained onsite in Anchorage by Drs. Prochaska and Resnicow using didactics and mock Facebook postings; a "refresher" training will occur 6 months after the initial training. The research team will develop a written guide for how often the moderator

should log in with expectations for his/her engagement. Moderators will also enhance engagement through prompting discussion of cultural identity and how that relates to smoking through various Facebook methods (e.g. Facebook poll, comments). 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[38] or involve inappropriate or illegal activities. [136,137] When participants enter the study they will be informed about the policies for posting content and that any inappropriate postings will be removed. In Dr. Prochaska's Twitter trial, less than 1% of postings were inappropriate. [48] The moderator will be trained to handle inappropriate or misinformation and to direct information content toward evidence-based information exchange and social support. A random sample of 20% of moderator postings and responses to participant inquiries and discussions will be selected every week for the first four weeks and monthly thereafter. [138] These transcripts will be coded by Dr. Sinicrope to assess moderator adherence to the proscribed intervention. Feedback will be provided to the moderator during weekly research team teleconferences.

Table 3: Pilot Trial Measures	**Baseline**	**1, 3, & 6 Months**
Socio-demographics and tobacco use	X	
Feasibility measures (e.g., retention, Facebook use and engagement)		X
Self-reported smoking abstinence		X
Self-reported tobacco/nicotine product use	X	X
Saliva cotinine: to verify smoking abstinence		X
Self-reported smoking treatment utilization		X
Communal Orientation Scale (mediator)	X	X

Measures

Assessments (see Table 3) will be completed at baseline and 1, 3, and 6 months follow-up. Missing data will be minimized through online assessments. With the exception of obtaining a saliva specimen for cotinine analysis, all measures will be administered online using Qualtrics. An email link will be sent automatically by the Mayo Clinic Survey Research Center to complete the assessment. If a participant does not complete online assessments, he/she will be contacted through email or by phone by the project coordinator and prompted to complete the assessment. The baseline and follow-up surveys will be done online, by phone, in person, or the survey will be mailed with a postage paid return envelope depending on participant preference. These surveys will take about 15-30 minutes each to complete. Participants will be mailed a $25 Visa gift card as remuneration for completing each assessment, the intervention group will receive their initial $25 Visa gift card after they complete the baseline assessment and join the Facebook group.

Socio-demographic and tobacco use characteristics. At baseline, we will assess participants' health literacy, sex, age, tribal group, cultural identity (language, traditionalism),[30] region of residence, marital status, education, employment, and current frequency of use of Facebook and other social media platforms. Tobacco use measures will include cigarettes per day, years of smoking, readiness to quit (Contemplation Ladder),[139] use of other tobacco and nicotine products, and the time to first cigarette after waking <30 minutes vs. ≥30 minutes,[140]which is primarily consistent with the 6-item Fagerström Test for Cigarette Dependence.[141,142]

Feasibility measures. To assess feasibility and reach, we will collect data on: # screened, # eligible based on the inclusion/exclusion criteria, # of eligible participants enrolled, and reasons for exclusion or non-

participation.
The proportion of 60 participants completing the 6 month follow-up assessment (i.e., retention) and the proportion providing a saliva cotinine specimen at each assessment will also be summarized. Treatment acceptability will be assessed with brief intervention satisfaction rating scales.[16]

Data from the Facebook application programming interface[143] will be extracted using Sprinklr software.[144] Foreach week of the study, we will extract for each intervention participant the following engagement metrics: # of logins; # digital story downloads; # user-generated posts, comments, questions and responses to the moderator or other users; # likes, shares and reactions; and time and date of each. In addition, a transcript of all participant postings will be generated for content analysis.

Smoking abstinence. At each follow-up, we will obtain the participant's self-reported cigarette use in the past 7 and 30 days, number of cigarettes smoked per day, and quit attempts. We will also assess current use of ST/*iqmik*, e-cigarettes, and other tobacco/nicotine products. All participants will be mailed a saliva kit with a collection tube and postage paid return envelope. Participants returning a saliva specimen will receive an additional $25 Visa gift card. The specimen will be shipped to and assayed by Mayo Clinic laboratories. This approach has been feasible in several NIH-funded clinical trials conducted in AK (DA 025156; CA164533; CA153605) and in other studies[148]; and biochemical verification is recommended in randomized trials with sample sizes under 500.[146] Point prevalence smoking abstinence will be defined as no smoking (not even a puff)for the last 7 days verified with salivary cotinine level <15 ng/ml.[146,147] Use of nicotine replacement therapy and ST/*iqmik* use will be assessed at follow-up because its use would elevate cotinine concentrations. If participants indicate use of e-cigarettes, saliva cotinine and reported e-cigarette use will be recorded and analyzed separately from biochemically verified cigarette smoking abstinence.

Smoking Treatment Utilization. As a secondary aim, we will document self-reported use of any evidence-based cessation aid during the 6 month study period. For this pilot study, it is not practical to objectively verify self- reported treatment use given heterogeneity of potential services/medications used.

Communal Orientation Scale (COS). The 14-item validated COS[148-149] will be administered at baseline and follow-up to examine interdependence as a culturally relevant mediator of intervention efficacy. In the intervention condition, we will also explore association of COS baseline scores with Facebook engagement. This measure assesses the extent to which individuals are relationship- versus self-oriented.

Coronavirus (COVID-19). At the 6 month follow-up assessment we will obtain information on the impacts ofCOVID-19 on smoking treatment and cessation. For those receiving the Facebook intervention we will also obtain satisfaction with the COVID-19 content and conversation.

Sample Size Calculation
The goal of the pilot trial is to obtain effect size estimates to adequately power a larger scale, Stage II efficacy trial. A sample size of 60 enrolled will be sufficient to determine the intervention's feasibility. Although not able to detect statistically significant study group differences on smoking abstinence, the study can obtain estimates of the intervention effect towards planning a definitive Stage II efficacy trial. For the dichotomous variable of point prevalence abstinence, 30 subjects per condition should provide relatively stable group proportions for effect size estimates. Effect size estimates will include odds ratios for smoking abstinence. In addition to demonstrating feasibility, a doubling of the abstinence rate for the intervention vs. control condition at 6 months will be considered to be of clinical significance and

warrant proceeding to an efficacy trial.[150] This approach is consistent with recommendations for Stage I work in behavioral addictions treatment development and for conducting small-scale trials to advance e-health interventions.[151] Given the small sample size, proposed mediational analyses are exploratory.

Data Analysis Plan

Recruitment data will be summarized, including the number of potential participants screened, number excluded for each inclusion/exclusion criteria, and number of eligible individuals agreeing to participate. To assess program reach, we will calculate proportion of subjects enrolled to total eligible subjects and compare enrollment rates by region (rural or urban) using the chi-square test. Baseline demographics will be summarized and compared between study groups using the chi-square test for categorical variables and the two-sample t- test/rank sum test for continuous variables. Percentage of enrolled participants completing each follow-up assessment (i.e., study retention) and ratings of treatment acceptability will be compared between study groups using the chi-square test (Fisher's exact test). Facebook use and engagement will be summarized using descriptive statistics and time effects over the 3 month treatment period will be assessed via mixed effects models as appropriate to explore sex, age group, and region effects respectively. The association of COS baseline scores and Facebook engagement will be evaluated using linear regression. Qualitative (content) analysis[125] will be utilized to generate themes in Facebook postings and comments.

Biochemically- confirmed 7-day point prevalence tobacco use rate at 1, 3, and 6 months follow-up will be compared between conditions using logistic regression (with odds ratio and 95% confidence interval estimates). Using an intent-to-treat approach, we will classify as smoking participants eligible but lost to follow-up or not providing biochemical verification of smoking abstinence. We will also explore multiple imputation methods[1152-154] to classify lost to follow-up as cigarette smokers or non-smokers and conduct sensitivity analyses as appropriate. For these analyses, we will adjust for stratification factors (sex, age group, urban/rural region) and any baseline differences observed between treatment conditions if data allow (i.e., adequate numbers of subjects verified as abstinent). Secondary analyses using logistic regression will explore intervention effects on self-reported abstinence from all tobacco/nicotine products, quit attempts, and self- reported tobacco treatment utilization. We will follow procedures suggested by MacKinnon[155,156] to assess mediation, fitting logistic/linear regression models to the data.

Study Dissemination Activities

After receiving Tribal review and approval, findings relevant to the community will be disseminated through presentations at regional and national community events and postings on websites and newsletters. Findings relevant for the scientific community will be presented at conferences and published in peer-reviewed journals. All manuscripts for publication and all abstracts for presentations will be submitted to ANTHC for Tribal review and approval prior to submission to a journal or other public venue.

Additionally, after receiving tribal review and approval of the following, findings relevant to the Alaska Native communities have been developed into a newsletter. In phases 3 and 4, as part of the consent process, we asked participants permission for re-contact after the study ended. We will send the newsletter only to those who provided consent for future contact in phases 3 and 4. In phases 1 and 2, we did not ask participants for permission to contact them in the future. Because sharing results is an important part in the research process, we will send the newsletter to phase 1 and 2 participants only with AAIRB approval. The newsletter only shares the results of the CAN Quit study, and does not invite people to participate in future research.

Should any 'return to sender' letters occur, we will simply recycle these letters.

Project Timeline (Table 4)

Table 4: Timeline												
Tasks	**Year 1**				**Year 2**				**Year 3**			
Month:	**3**	**6**	**9**	**12**	**15**	**18**	**21**	**24**	**27**	**30**	**33**	**36**
IRB/tribal approvals	X											
Phase 1-3												
Pre-testing		X	X	X								
Develop/beta test prototype					X	X	X					
Phase 4												
Pilot trial recruit/intervention							X	X	X			
Follow-up								X	X	X	X	
Analysis										X	X	
Dissemination												X

Resources: *Describe the available resources to conduct the research (personnel, time, facilities, mentor commitment, etc.)*:

Research Team

Collectively, the study team is uniquely suited to conduct the proposed study. Mayo Clinic and ANTHC collaborators have established and maintained a successful partnership for the past 16 years. The PI, Dr. Patten, is an expert in behavioral tobacco treatment. Other partners include Dr. Sinicrope (Co-Investigator, qualitative expert), Ms. Hughes (Research Assistant), and Mr. Decker (Biostatistician) at Mayo Clinic; and Dr. Koller (AK site PI), Zoe Merritt (Project Coordinator) and Clara McConnell (Facebook Group Moderator) at ANTHC. This team has substantial experience conducting research with AN people, including the use of mixed qualitative and quantitative methods to assess tobacco use and intervention preferences, along with development of culturally congruent tobacco cessation treatments. Dr. Resnicow (Consultant), University of Michigan, Ann Arbor, MI, is an expert in cultural messaging and tailoring of health promotion interventions. Since 2013, he has collaborated with the Mayo team and partners in rural AK to develop the social marketing campaign messaging to reduce smokeless tobacco and other tobacco use among pregnant AN women.[65,102] New collaborations were formed through developing this proposal. Dr. Prochaska (Co-Investigator), Stanford University, is an expert in designing and testing social media platforms for smoking cessation and has an ongoing R01 NHLBI funded trial using a telemedicine intervention for smoking/health behavior change among rural AN cardiology patients. Dr. Prochaska also consulted with the CDC on the 2016 Tips™ campaign with a focus on tailoring messages to smokers with depression. In addition, she was a member of the Tobacco Control Research Priorities Working Group.[45] Finally, collaborators at the CDC Health Communications Branch (that developed Tips™) contributed to this proposal and will provide guidance on intervention content.

Community Advisory Board (CAB) An existing CAB of AN adults, originally formed for a study on tobacco treatment during pregnancy,[64,103] provided input on this proposal during three meetings (two in-person and one via phone). We will form a study-specific CAB with about 10 members comprised of several existing CAB members and new members. The CAB members will be diverse, representing

various tribal health regions in AK; with experience using social media and some being former smokers. Quarterly phone or in-person meetings with CAB members will guide all study activities. Members will receive an honorarium and a meal will be provided for in-person meetings.

General Approach: Stage Model of Behavioral Therapies Development Research

Our approach follows the three-stage model of behavioral therapies development[104] and the proposed aims correspond to the two sub-stages characterizing Stage I work. In Stage Ia formative work, we will develop the Facebook intervention. In Stage Ib, we will use rigorous design and methodology to evaluate the intervention's feasibility and potential efficacy. Stage Ib results will inform a future R01, Stage II, randomized efficacy trial

A 3 year timeline is proposed. The formative work will take place in months 1-20 and recruitment for the pilot trial will occur in months 21-27, with intervention, follow-up and analyses completed by month 33. The remaining months will be spent on dissemination activities.

The study will be conducted at the ANTHC in Anchorage and at Mayo Clinic. All data collection and the intervention will be conducted by study staff at ANTHC and Mayo Clinic. Data will be collected and maintained by the Mayo Clinic Survey Research Center via Qualtrics software. Mayo Clinic will collect and maintain data electronically in a secure REDCap database.

Mayo Clinic study staff will be engaged in research activity at a non Mayo Clinic site. *Description of the activity that will be conducted by Mayo Clinic study staff.*

The study will be conducted at the ANTHC in Anchorage and at Mayo Clinic. All data collection and the intervention will be conducted by study staff at ANTHC and Mayo Clinic. Several procedures are established to monitor the quality assurance of the study. For qualitative data collection, a semi-structured interviewer guide will be developed and the Anchorage-based Project Coordinator will conduct the interviews. Dr. Sinicrope and Ms. Hughes will provide training for the project coordinator on-site in Anchorage including 4 hours of didactic instruction followed by 4 practice hours of mock interviews and a certified completion interview. All sessions will be audiotaped. These transcripts will be coded by Dr. Sinicrope to assess counselor adherence to the proscribed intervention, and feedback will be provided during weekly research team teleconferences.

Mayo Clinic social media department will create the Facebook group page, develop the content library of moderator postings, and set up the software to capture participant use data. A random sample of 20% of moderator postings and responses to participant inquiries and discussions will be selected every week for the first four weeks and monthly thereafter. These transcripts will be coded by Dr. Sinicrope to assess moderator adherence to the proscribed intervention, and feedback will be provided during weekly research team teleconferences.

A manual of study procedures will be developed for the project coordinator. Ms. Hughes, a Mayo Clinic research assistant and clinical trials coordinator, will travel with Dr. Patten to Anchorage, Alaska, to train the study staff on the data collection and other study procedures including monitoring of adverse events. We will use the same coordination, communication, and quality control procedures successfully utilized in our previous work. For ongoing trials in Alaska, we hold weekly conference calls with study staff in AK and at Mayo Clinic to discuss progress and problem solve issues related to recruitment and data collection. We also monitor quality control of the data on site through review of participant forms and procedures every 3 months. Mr. Paul Decker, Biostatistician on this protocol, will oversee the transfer of data forms, electronic data, and data storage. The Mayo Survey Research Center will electronically transfer all data to Mr. Decker. The quality of the data (data checks) including missing data and presence and frequency of outliers will be monitored once per month by Mr. Decker. For study recruitment, Ms. Hughes will track posting of ads through FB and in Alaska local newsletters and websites. AK study staff will also recruit in person using flyers and different methods of in person recruitment.

All measures will be administered online using Qualtrics software, a data security service. An email

link will be sent automatically by the Mayo Clinic Survey Research Center to complete the assessment. If a participant does not complete online assessments, he/she will be contacted through email or by phone by the project coordinator and prompted to complete the assessment. Data collected from survey responses will be handled and maintained by the Mayo Clinic Survey Research Center and a de-identified database of responses will be provided to the investigators. Interview forms and audio tapes will be labeled with subject ID numbers only; all personal identifiers will be removed before the data are sent to Mayo Clinic for analysis. At Mayo Clinic the audio tapes will be stored in a locked file drawer accessible only to the PI, Dr. Patten, Co- Investigator, Dr. Sinicrope, and the Research Assistant, Christine Hughes. These will be destroyed once the interviews are fully transcribed.

A trained research assistant at Mayo Clinic will mail the saliva sample kit to the participant; and the saliva samples, labeled with a subject ID number only, will be shipped directly back to Mayo Clinic for analysis of cotinine. Once the specimen sample is processed and results posted, the sample will be destroyed immediately.

The study staff in Anchorage and Rochester will monitor any reports or observations of medical problems or severe depression or other psychiatric symptoms in participants. Drs. Patten and Prochaska, licensed clinical psychologists, will be consulted by telephone to consult with the study staff as needed.

Subject Information

Target accrual: We will recruit up to a total of 200 Alaska Native (AN) people who smoke (100 in the formative phases, 60 for the randomized pilot trial, and 40 for the quantitative supplemental aim).
Screening for eligibility will occur online via the study's web page, by phone, or in person; and they can also use the study toll free number to answer any questions about the study. Verbal consent is adequate for phases 1, 2 and the supplemental aim since we are not collecting any personal health information, but written consent is required for phases 3 and 4. For phases 3 and 4, if respondents are eligible, they have the option to complete the informed consent in person, mail, e-mail, or on-line (i.e. DocuSign).

ANTHC will also recruit 10 stakeholders (AN and non-AN persons) for phase 1, such as quitline coaches, in person or by phone.

Subject population (children, adults, groups): We will recruit AN men and women statewide using targeted, paid, Facebook advertisements (i.e., digital targeting) or in person based on: (1) $\geq$19 years of age, (2) AN race/ethnicity and (3) keywords related to tobacco use. Ads will include an image and short text consistent with Facebook's advertising guidelines. Facebook ads are a successful method of recruiting for research studies, especially among hard-to-reach populations.[105-106] Using targeted Facebook advertisements in a rural region of AK, we have successfully recruited AN adults for studies, after learning in formative work that people preferred Facebook for outreach. Similarly, Facebook has been successful in promoting recruitment for a telemedicine project focused on smoking/health behaviors among cardiology patients in rural Nome, AK. We will partner with organizations that have a large Facebook following, such as the Alaska Federation of Natives (AFN), along with village-specific Facebook pages to advertise the study. We will also use flyers and advertise in tribal newsletters and websites.

Review of medical records, images, specimens

X (6) Video audio recording: *Plan to maintain subject privacy and data confidentiality, transcription, store or destroy, etc.*

Phase 1: Digital Videos that will be developed to use in the Facebook intervention - 8-12 Alaska Native people will record their tobacco use stories. These individuals will sign a release stating they give

permission for the study team to share their stories and they will be made aware that their stories will become a part of the public domain and will be seen by study participants on a secret Facebook page.

Phase 1: Audio Tapes of qualitative interviews to assess the development of the Facebook intervention – No names, voices, or images from the audio tapes from the interviews will be released. Permission to audio tape will be part of the verbal consent process. Confidentiality of the audio tapes will be maintained by keeping these in a locked drawer in the study office. Only the research team will review the audio tapes. Once the audio-tapes are fully transcribed and checked for accuracy, they will be destroyed.

Data Analysis

Power Statement: For the pilot RCT, the goal is to obtain effect size estimates to adequately power a larger scale, Stage II efficacy trial. Our recommended sample size, 60 enrolled AN people who smoke, will be sufficient to determine the intervention's feasibility. We recognize that the study is not adequately powered to detect statistically significant group differences on smoking abstinence, but we seek to obtain estimates of the intervention effect towards planning a definitive Stage II efficacy trial.

Data Analysis Plan: Recruitment data will be summarized, including the number of potential participants screened, number excluded for each inclusion/exclusion criteria, and number of eligible individuals agreeing to participate. To assess program reach, we will calculate proportion of subjects enrolled to total eligible subjects and compare enrollment rates by region (rural or urban) using the chi-square test. Baseline demographics will be summarized and compared between study groups using the chi-square test for categorical variables and the two-sample t-test/rank sum test for continuous variables. Percentage of enrolled participants completing each follow-up assessment (i.e., study retention) and ratings of treatment acceptability will be compared between study groups using the chi-square test (Fisher's exact test). Facebook use and engagement will be summarized using descriptive statistics and time effects over the 3 month treatment period will be assessed via mixed effects models as appropriate to explore sex, age group, and region effects respectively. The association of COS baseline scores and Facebook engagement will be evaluated using linear regression. Qualitative (content) analysis[125] will be utilized to generate themes in Facebook postings and comments.
Biochemically- confirmed 7-day point prevalence tobacco use rate at 1-, 3-, and 6-months follow-up will be compared between conditions using logistic regression (with odds ratio and 95% confidence interval estimates). Using an intent-to-treat approach, we will classify as smoking participants eligible but lost to follow-up or not providing biochemical verification of smoking abstinence. We will also explore multiple imputation methods[152-154] to classify lost to follow-up as cigarette smokers or non-smokers and conduct sensitivity analyses as appropriate. For these analyses, we will adjust for stratification factors (sex, age group, urban/rural region) and any baseline differences observed between treatment conditions if data allow (i.e., adequate numbers of subjects verified as abstinent). Secondary analyses using logistic regression will explore intervention effects on self- reported abstinence from all tobacco/nicotine products, quit attempts, and self-reported tobacco treatment utilization. We will follow procedures suggested by MacKinnon[155,156]to assess mediation, fitting logistic/linear regression models to the data.

Endpoints
Primary: The primary outcomes will be feasibility (e.g., Facebook engagement) and the biochemically- verified smoking abstinence rate at 1, 3, and 6 months follow-up.
Secondary: Secondary outcomes will include self-reported smoking cessation treatment utilization and

abstinence from all tobacco/nicotine products. We will also explore interdependence (relationship orientation and collaborative efforts in lifestyle change) as a culturally relevant mediator of intervention efficacy.

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Protection of Human Subjects

Protection of Human Subjects Training

Key personnel identified in this grant application 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.

The Alaska Area Indian Health Service Institutional Review Board requires completion of an educational course on the protection of human subjects for anyone conducting or engaged in Alaska Native research. This course is online and entitled the “Collaborative IRB Training Initiative Program

(CITI Program), available at: http://www.CITIprogram.org. All investigators and key personnel have completed this educational course. Prior to the award of this grant, the study will be reviewed and approved by the Mayo Clinic and Alaska Area Institutional Review Boards (IRBs) and Alaska Native Tribal Health Consortium (ANTHC) board of directors. Recruitment of study participants will commence after approval by all IRBs and Boards.

Recruitment and Study Inclusion/Exclusion Criteria

We will recruit up to a total of 200 Alaska Native (AN) people who smoke (100 in the formative phase, 60 for the randomized pilot trial, and 40 for the quantitative supplemental aim). Screening for eligibility will occur in person, on the phone, or online via the study's web page. If respondents are eligible, they will be taken to the study's informed consent web page. If preferred, screening will also be done by phone or in person, and they can also use the study toll free number to answer any questions about the study.

Participants will be recruited using targeted, paid, Facebook advertisements (i.e., digital targeting) or in person based on: (1) age 19 years and older, (2) AN race/ethnicity, and (3) keywords related to tobacco use. Ads will include an image and short text consistent with Facebook's advertising guidelines. Throughout Alaska, we will advertise in tribal newsletters and web sites.

Study enrollment for all phases of the research will occur either in person, online or by mail. All advertisements will contain the study: toll-free phone number, email address, and Qualtrics's website link. Individuals calling or emailing will be provided a brief description of the study and sent a link to the study website. The website will contain a short description of the study as well as eligibility questions. Qualtrics (https://www.qualtrics.com) is a secure, online, HIPAA-compliant survey software that transmits data to and from secure firewalled data centers using Transport Layer Security encryption.

Eligibility criteria for participants are (1) >19 years of age (legal smoking age), (2) Alaska Native race/ethnicity, (3) smoke at least 1 cigarette per day over the past 7-day period, (4) if other tobacco use, cigarettes are the main tobacco product used, (5) considering or willing to make a quit attempt, (6) access to internet, (7) have an existing Facebook account or willing to set up an account, and (8) is not using pharmacotherapy or has not enrolled in a program to stop smoking for past 3 months. Each person is only eligible to participate in one part of the study. Remuneration in the form of gift cards will be provided to all participants. If the individual is not eligible or not interested, he/she will be given tobacco treatment referral information.

Various stakeholders will also be interviewed including AK quitline coaches, tribal cessation program counselors, and Alaska Education Advocacy members, with about 10 interviews total. There are no eligibility criteria for stakeholders, other than that they must be health professionals; stakeholders will be selected and approached for participation by the Alaska Native Tribal Health Consortium (ANTHC) study team.

Sources of Material

Data collected from interviews, questionnaires and specimen samples (saliva) will be used for research purposes. With the exception of obtaining a saliva specimen by mail for verification of smoking abstinence, all measures will be administered by phone or online using Qualtrics. For online assessments, an email link will be sent automatically by the Mayo Clinic Survey Research Center to complete the assessment. The qualitative interviews in the first phase of the research will be audiotaped. The content of the Facebook intervention from participant postings and comments will be summarized.

Potential Risks and Procedures to Minimize Risks

Risks are minimal and include those associated with the inconvenience of completing assessment interviews and surveys, of providing saliva samples, nicotine withdrawal symptoms for those who stop smoking, and some potential risks related to confidentiality. A trained research assistant will obtain the saliva sample(s) from the participant by mail and this should not present a risk to subjects. No medications will be administered as part of

this study.

Data collected from survey responses will be handled by the Mayo Clinic Survey Research Center, which uses Qualtrics data security service and a de-identified data base of responses will be provided to the investigators. Qualtrics meets requirements set by the Federal Information security management Act of 2002, the Health Insurance Portability and Accountability Act, and the Health Information Technology for Economic and Clinical Health Act. Qualtrics servers are protected by high-end firewall systems, vulnerability scans are performed regularly, and complete backups of the data are performed nightly. Qualtrics uses Transport Layer Security (TLS) encryption (also known as HTTPS) for all transmitted data. We also protect surveys with passwords and HTTP referrer checking. Survey data is hosted by third party data centers that are SSAE-16 SOC II certified. All data are considered confidential, and treated as such, with no specific designation (such as medical (PHI), PII, or public). Finally, data entered in REDCap uses secure and certified data centers.

In our moderated Facebook intervention, it is impossible to know in advance what might be posted by users, and it is possible that incorrect postings or postings that might cause some emotional discomfort could occur. Participants will be encouraged to contact the project 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 talk about his/her own tobacco use and others' use of tobacco, and participate in discussions about moderated postings regarding AN tobacco use, readiness to quit tobacco, and tobacco treatment resources, among others. Thus, it is possible that health information or other personal information about study participants or other AN 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 in culturally appropriate postings that do not violate confidentiality or harm Facebook group members. If someone is offended by Facebook 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 arrangements, we do not anticipate any adverse consequences of participating in the secret Facebook group. The Facebook group will be secret and closed so no one 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.

Information from the participants will not be shared with anyone else except for the research team. The group moderator will emphasize confidentiality of the group discussions. Moreover, while data from this study will be published, participants will be informed that their name, village and other identifying information will not be published. No voices or images from the audio tapes from the interviews will be released. Permission to audio tape will be part of the consent form. Confidentiality of the audio tapes will be maintained by keeping these in a locked drawer in the study office. Only the research team will review the audio tapes. Once the audio-tapes are transcribed, they will be destroyed immediately.

As part of developing the Facebook intervention, 8-12 Alaska Native people will record their tobacco use stories. These individuals will sign a release stating they give permission for the study team to share their stories and they will be made aware that their stories will become a part of the public domain and will be seen by study participants on a secret Facebook page.

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 Alaska site PI and destroyed after completion of the project. All data obtained through interviews and other subject records will be kept in locked filing cabinets in offices that are kept locked when unoccupied. Subject files will be kept in a secure area, with access only by designated staff members (PIs and study staff). Any computer storage of data will be password protected and only available to the PIs 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, Facebook transcripts and the data base sent to Mayo Clinic for analysis, will be destroyed. Only summaries of group data will be reported in any publications or presentations, with no identification of individuals or villages.

All data elements and data transfer activities will be strictly compliant with HIPAA privacy regulatory requirements. Saliva samples will be shipped directly to Mayo Clinic for analysis of cotinine. These will be labeled with a subject ID number only. Once the specimen sample is processed and results posted, the sample will be destroyed immediately. Interview forms and audio tapes will be labeled with subject ID numbers only; all personal identifiers will be removed before the data are sent to Mayo Clinic for analysis. Standard security measures to store data are in place within the Mayo Clinic. Moreover, at Mayo Clinic the audio tapes will be stored in a locked file drawer accessible only to the PI Dr. Patten, Co-Investigator Dr. Sinicrope, and the Research Assistant Christine Hughes.

For participants who stop using tobacco in the pilot randomized trial, although uncomfortable, withdrawal symptoms do not pose significant health risks. Smoking cessation may result in: increased irritability, depression, anxiety, tension and increased hunger and drowsiness. Participants in both study conditions will receive written, self-help materials, which cover potential nicotine withdrawal symptoms and how to manage these. In addition, those who call the Alaska quitline, which is the goal of this study, will receive support on their quit attempt by a licensed quitline counselor, as well as a bevy of support materials in print and online. All pilot trial participants will complete online assessments via Qualtrics at baseline, 1, 3 and 6 months completion; and at these times any adverse symptoms will be assessed and those reporting adverse symptoms will be called by the project coordinator and be referred for appropriate treatment if necessary.

Clinical Management

A detailed plan is in place for clinical management of psychiatric or medical problems that might arise. The study staff in Anchorage and Rochester will monitor any reports or observations of medical problems or severe depression or other psychiatric symptoms in participants. In the event of such an occurrence, they will set into motion standard procedures for management of depression and other psychiatric or medical symptoms in research subjects. If necessary, the study staff will arrange for additional assessments of the subject's symptoms by a physician in Anchorage or at a local tribal medical facility. Individuals who report suicidal intent or other severe psychiatric or medical problems will be referred for treatment and followed throughout the study period. In the event of an emergency (e.g., suicidal plan), Anchorage staff physicians will be consulted to refer the subject for treatment at ANMC or a local tribal medical facility. Drs. Patten and Prochaska (licensed clinical psychologists) will be consulted by telephone to consult with the 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.

Potential Benefits of the Proposed Research to Subjects and Others

The study is designed to evaluate the potential effect of an intervention to promote utilization of tobacco treatment and to reduce tobacco use among AN persons. 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 tobacco use and quitting and referral information on stop smoking resources. In the next phase (randomized pilot trial), all participants will receive written tobacco treatment materials that cover cessation advice and strategies for quitting as well as referral information. The participants will have the opportunity to benefit by making behavioral changes with respect to quitting smoking or stopping their tobacco use and have access to free treatment resources. The participants randomized to the Facebook group may also receive support from others to help them quit using tobacco. If the Facebook intervention is helpful, then others may benefit if we are able to show that it works. The study will help us learn more about helping people quit tobacco.

Importance of the Knowledge to be Gained

Developing effective interventions to decrease tobacco use among AN people is a national priority. The prevalence of smoking among U.S. adults is highest among Native Americans and there is a lack of tobacco cessation interventions developed specific to this disparity group. Social media has promise as a scalable intervention strategy to promote engagement in treatment and cessation outcomes for AN people. This proposal addresses three of seven gaps and priorities in the tobacco research field identified by the Tobacco Control Research Priorities Working Group (2016), namely by: (1) targeting an underserved tobacco use disparities population, (2) developing a novel behavioral intervention using a social media platform, and (3) promoting uptake of evidence-based treatment and quitting. The proposed social media intervention, if effective, has relevance for advancing the science of tobacco treatment for Native American communities. If the intervention is found to be effective, the intervention materials and strategies could be tested in a larger scale RCT and could be readily transportable for use throughout the Alaska Native community. With some modifications, the intervention materials could also be considered for use in other Native communities and in populations with a focus on cultural interdependence.

Data Safety Monitoring Plan (DSMP)

Power Calculation and Sample Size

Sample size for each stage of this research was guided by guidelines for behavioral treatment development research. For the formative work we calculated the number of interviews necessary to cover the major subsets of interest based on audience segment (gender, age, region) and to achieve data saturation, whereby no new information is being gained by adding participants.

For the pilot RCT, the goal is to obtain effect size estimates to adequately power a larger scale, Stage II efficacy trial. Our recommended sample size, 60 enrolled AN people who smoke, will be sufficient to determine the intervention's feasibility. We recognize that the study is not adequately powered to detect statistically significant group differences on smoking abstinence, but we seek to obtain estimates of the intervention effect towards planning a definitive Stage II efficacy trial. For the dichotomous variable of point prevalence abstinence, 30 subjects per condition should provide relatively stable group proportions for effect size estimates. Effect size estimates will include odds ratios for smoking abstinence. In addition to demonstrating feasibility, a doubling of the abstinence rate for the intervention vs. control condition at 6 months will be considered to be of clinical significance and warrant proceeding to an efficacy trial. This approach is consistent with recommendations for Stage I work in behavioral addictions treatment development and for conducting small- scale trials to advance e-health interventions. Given the small sample size, proposed mediational analyses are exploratory.

TRIAL MANAGEMENT

List of Participating Enrolling Clinics or Data Collection Centers

The study will be conducted at the ANTHC in Anchorage and at Mayo Clinic. All data collection and the intervention will be conducted by study staff at ANTHC and Mayo Clinic. Data will be collected and maintained by the Mayo Clinic Survey Research Center via Qualtrics software. ANTHC will collect and maintain data electronically in a secure REDCap database.

Projected Timetable

A 3-year timeline is proposed. The formative work will take place in months 1-20 and recruitment for the pilot trial will occur in months 21-27, with intervention, follow-up and analyses completed by month 33. The remaining months will be spent on dissemination activities.

Target Population Distribution

Nearly all (98%) of participants will be of AN race. All participants will be of legal smoking age, 19 years of age or older. Both males and females will be enrolled. We expect that about half the sample (50%) will be female based on our prior studies.

DATA MANAGEMENT AND ANALYSIS

Data Acquisition and Transmission

All data collected by Mayo Clinic study staff will be done via the Qualtrics website, which is managed by the Mayo Clinic Survey Research Center. Data collected on paper forms by the ANTHC project coordinator will be entered into a secure REDCap database. Confidentiality will be maintained by all data containing only a sequentially assigned study number for each subject. The study number will not be linked to the subject's date of birth, village, hospital or any medical record number, initials, social security number, or any other identifying information. All hard copies of data will be kept in secure locked file drawers. Mr. Paul Decker, Biostatistician on this protocol, will oversee the transfer of electronic data and data storage. The quality of the data (data checks) will be monitored once per month.

Five years after publication of the results (per many journal guidelines) the paper forms and electronic databases will be destroyed. Only summaries of group data will be reported in any publications or presentations, with no identification of individuals.

Permission to audiotape the qualitative interviews in the first phase of the research will be included in the verbal consent process. Once the interviews are fully transcribed the audiotapes will be destroyed immediately.

All biospecimens for the pilot RCT will be labeled with subject ID number only. Once the result from the laboratory analysis is completed at Mayo Clinic, the biospecimen will be destroyed immediately. Test results will be posted electronically using subject ID number only.

The Mayo Clinic Division of Biostatistics has a well-developed structure for data management with over 7,000 studies currently under their control. Working data is maintained on a single large file server that services the entire section. Inactive files are moved to archival storage under control of an automated system, itself controlled by a DBMS (Ingres) based request system which ensures that all data movement is appropriately logged and commented. The archival storage is hosted on the institutional mainframe computer, which also supports billing and registration. The use of the mainframe ensures several high-level support functions for the archive system, e.g. storage of media in separate fire zones, regular copying of data to new media, guaranteed availability.

The data management will be governed by standard procedures within the division with regard to data security and access. All analyses are logged with respect to IRB authorization, accounting information, principal and secondary investigators, statistician, and data analyst involved in the analyses. All computer files and systems will be password protected and accessible by authorized personnel only.

Data Entry Methods

As the Qualtrics website is being utilized through the Mayo Clinic Survey Research Center to administer consent as well as assessments, most quantitative data will be automatically entered. Any data not automated will be entered by the Anchorage staff using a secure REDCap database. Discrepancies will be corrected by Mr. Paul Decker, Biostatistician on this protocol. Mr. Decker will oversee all data entry. All qualitative data will be transcribed by a professional transcription service and imported into QSR NVivo software, version 10, for analyses.

QUALITY ASSURANCE

A manual of study procedures will be developed for the project coordinator. Ms. Hughes, a Mayo Clinic research assistant, and clinical trials coordinator will travel with Dr. Patten to Anchorage, Alaska to train the study staff on the data collection and other study procedures. We will use the same coordination, communication and quality control procedures successfully utilized in our previous work. For ongoing trials in Alaska, we hold weekly conference calls with study staff in AK and at Mayo Clinic to discuss progress and problem solve issues related to recruitment and data collection. We also monitor quality control of the data on site through review of participant forms and procedures every 3 months.

Mr. Paul Decker, Biostatistician on this protocol, will oversee the transfer of data forms and data storage. The Mayo Survey Research Center will electronically transfer all data to Mr. Decker. The quality of the data (data checks) including missing data and presence and frequency of outliers will be monitored once per month by Mr. Decker. For study recruitment, Ms. Hughes will track posting of ads through FB and in Alaska local newsletters and websites.

For qualitative data collection, a semi-structured interviewer guide will be developed and the project coordinator in Alaska will conduct the interviews. Dr. Sinicrope and Ms. Hughes will provide training for the project coordinator on-site in Anchorage including four hours of didactic instruction followed by four practice hours of mock interviews and a certified completion interview (Krueger & Case, 2009). All sessions will be audiotaped.

The moderator for the FB-delivered intervention will report to Dr. Koller, Alaska site PI and work in tandem with the project coordinator. The moderator will be trained on-site in Alaska by Drs. Prochaska and Resnicow using didactics and mock Facebook postings and a "refresher" training will occur 6 months after the initial training. The research team will develop a written guide for how often the moderator should log in and expectations for his/her 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. A process evaluation checklist will be developed for the moderator to document delivery of specific intervention components based on existing measures. A random sample of 20% of moderator postings and responses to participant inquiries and discussions will be selected every week for the first four weeks and monthly thereafter. These transcripts will be coded by Dr. Sinicrope to assess counselor adherence to the proscribed intervention, and feedback will be provided to the moderator during weekly research team teleconferences.

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

Regulatory Issues

Reporting of Serious Adverse Events (SAEs)

Any SAE, whether or not it is related to the study intervention and for all participants, will be reported to the Mayo Clinic and Alaska Area IRBs and NIDA. A summary of the SAEs that occurred in the previous year will be included in the annual progress report to the NIDA.

Reporting of IRB Actions to the NIDA

Any action taken by the respective IRBs regarding SAEs or major changes to the protocol will be reported to the NIDA.

Report of Changes or Amendments to the Protocol

Minor changes to the protocol are allowed without prior approval, however, major design changes will be reviewed and approval sought from the NIDA Program Officer prior to seeking IRB approval and implementation.

Trial Stopping Rules

Specific stopping rules have been developed to protect the safety of our study subjects. 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 PI (Dr. Patten), Alaska site PI (Dr. Koller) or the project coordinator.

Disclosure of Any Conflict of Interest in the DSM

There are no conflicts of interest in the DSM plan that we are aware of. If such conflicts arise

during the course of the trial, the respective IRBs and the NIDA will be notified immediately.

TRIAL SAFETY

Potential Risks and Benefits for Participants

Risks are minimal and include those associated with the inconvenience of completing assessment interviews by telephone, of providing saliva samples, and online assessments. A trained research assistant at Mayo Clinic will mail the saliva sample kit to the participant; and providing and mailing the biospecimen back to Mayo Clinic for analysis (no identifiers) should not present a risk to subjects. No medications will be administered aspart of this study. Data collected from survey responses will be handled by the Mayo Clinic Survey Research Center which uses Qualtrics data security service and a de-identified data base of responses will be provided to the investigators. Qualtrics meets requirements set by the Federal Information Security Management Act of 2002, the Health Insurance Portability and Accountability Act, and the Health Information Technology for Economic and Clinical Health Act. Qualtrics servers are protected by high-end firewall systems, vulnerability scans are performed regularly, and complete backups of the data are performed nightly. Qualtrics uses Transport Layer Security (TLS) encryption (also known as HTTPS) for all transmitted data. We also protect surveys with passwords and HTTP referrer checking. Survey data is hosted by third party data centers that are SSAE-16 SOC II certified. All data are considered confidential, and treated as such, with no specific designation (such as medical (PHI), PII, or public). Finally, Mayo Clinic uses secure and certified data centers. Some data collected by ANTHC study staff will be entered by ANTHC study staff using a secure REDCap and transferred electronically to Mayo Clinic.

In our moderated Facebook intervention, it is impossible to know in advance what might be posted by users, and it is possible that incorrect postings or postings that might cause some emotional discomfort could occur.

Participants will be encouraged to contact the moderator and/or project 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 talk about his/her own tobacco use and others ‘use of tobacco, and participate in discussions about moderated postings regarding AN tobacco use, readiness to quit tobacco, and tobacco treatment resources, among others. Thus, it is possible that health information or other personal information about study participants or other AN members could be disclosed on FB postings. To ameliorate concerns, a list of do’s and don’ts for posting on the secret FB page will be posted at the front of the page so that whenever a participant joins the FB group, they will be reminded of these guidelines for sharing information, protecting confidentiality, and posting appropriately. Participants will be asked and encouraged to not mention specific names of people in their house or community. A trained moderator will monitor user postings and guide participants in culturally appropriate postings that do not violate confidentiality or harm FB group members. If someone is offended by FB postings, they can message the moderator to resolve any concerns. Any adverse events related to the FB group will also be reported as described if necessary. Despite these arrangements, we do not anticipate any adverse consequences of participating in the secret FB group. The FB group will be secret and closed so no one will be able to join the group, locate the group through a FB search, or see reactions or postings to the group through FB notification unless they are an official and invited member of the secret and closed group.

Information from the group will not be shared with anyone else except for the research team. The FB group moderator will emphasize confidentiality of the group discussions. Moreover, while data from this study will be published, participants will be informed that their name, village and other identifying information will not be published. No voices or images from the audio tapes or from the focus groups will be released. Permission to audio tape will be part of the verbal consent process. Confidentiality of the audio tapes will be maintained by keeping these in a locked drawer in the study office. Only the research team will review the audio tapes. Once the audio tapes are transcribed, they will be destroyed

immediately. In the formative phase of the research, some participants will be recording their smoking cessation stories for the intervention. These individuals (8-12) will sign a release stating they give permission for the study team to share their stories and they will be made aware that their stories will become a part of the public domain and will be seen by study participants on a secret Facebook page.

For participants who stop using tobacco in the pilot RCT, although uncomfortable, withdrawal symptoms do not pose significant health risks. Smoking cessation can result in increased irritability, depression, anxiety, tension and increased hunger and drowsiness. Participants in both study conditions will receive resources that address potential nicotine withdrawal symptoms and how to manage these. In addition, those who call the Alaska quitline will receive support on their quit attempt by a licensed quitline counselor as well as a bevy of support materials in print and online. All phase 4 subjects will complete online assessments via Qualtrics at baseline, 1, 3 and 6 months completion; and at these times any adverse symptoms will be assessed and those reporting adverse symptoms will be called by study staff and referred for appropriate treatment if necessary.

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 ID number (no identifiers) and numerically coding all data. The association of the ID-code and the participant will be kept by the research coordinator in a locked file cabinet at all times. All data obtained through interviews and other subject records will be kept in locked filing cabinets in offices that are kept locked when unoccupied. Subject files will be kept in a secure area, with access only by designated staff members (PI sand research coordinator). Any computer storage of data will be password protected and only available to the PIs and the study 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, Facebook transcripts and the data base sent to Mayo Clinic for analysis, will be destroyed. Only summaries of group data will be reported in any publications or presentations, with no identification of individuals or villages.

All data elements and data transfer activities will be strictly compliant with HIPAA privacy regulatory requirements. Saliva samples will be shipped directly to Mayo Clinic for analysis of cotinine. These will be labeled with a subject ID number only. Once the specimen sample is processed and results posted, the sample will be destroyed immediately. Interview forms and audio tapes will be labeled with subject ID numbers only; all personal identifiers will be removed before the data are sent to Mayo Clinic for analysis. Standard security measures to store data are in place within the Mayo Clinic. Moreover, at Mayo Clinic the audio tapes will be stored in a locked file drawer accessible only to the PI, Dr. Sinicrope, and the research assistant, Ms. Hughes.

Collection and Reporting of AEs and SAEs

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, ansae, whether or not it is related to the study intervention, will be reported to the Mayo Clinic IRB, the Alaska Area IRB, and NIDA. The project coordinator and FB intervention moderator both located in Alaska, and the research assistant located at Mayo Clinic, 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 Prochaska and will meet with the research staff via teleconference on a bi-weekly basis to review any new or continuing SAEs and AEs.

Management of SAEs or Other Study Risks

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 Alaska medical facility. The study staff will have a list of contacts as patient issues or concerns arise that are in need of 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 Drs. Patten and Prochaska, licensed clinical psychologists, to observe and monitor depression and psychiatric symptoms. They will be available to consult with the study staff as needed.

If the SAE involves death or a life-threatening event, the PI, 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, Chair of the Alaska Area IRB, 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 respective IRBs 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 respective IRBs and NIDA within 2 working days of when the SAE was reported. Reports of serious adverse events received by the respective IRBs will be reviewed by an institutional SAE Board, (the members of these boards are not involved in this study) to make a determination 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.

In the event that a participant withdraws from the study or the PI decides to discontinue a participant due to an SAE, the participant will be monitored by the PI 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.

Outcome of SAEs will be reported biannually 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 the respective IRBs. 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 respective IRBs.

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.

TRIAL EFFICACY

Plans for Interim Analysis

As part of the ongoing data management and statistical activities conducted by the study biostatistician, Mr. Paul Decker, the study groups will be reviewed on a quarterly basis to assess differential occurrence of the type and number of SAEs and AEs. If any significant difference is found, the relevant covariates will be thoroughly examined in order to understand more completely the relationship between the variables of interest and potential impact of the intervention on SAEs and AEs. The results of our analyses will be reported to both the respective IRBs and NIDA.

DSMP Administration

The Mayo Clinic IRB, Alaska Area IRB, the PI (Dr. Christi Patten), Alaska site PI (Dr. Kathryn Koller), and the study staff: project coordinator (Ms. Merritt), FB group moderator (Ms. McConnell) and research assistant (Christine Hughes) will all be responsible.

Responsibility for Data and Safety Monitoring

The study staff will monitor the safety of research subjects. The study staff will receive ongoing training and supervision concerning data collection and management from Drs. Patten and Koller.

Frequency of DSM Board

Every two weeks, the PI Dr. Patten, Alaska site PI Dr. Koller, Mr. Decker (study statistician), Ms. Merritt(project coordinator), Ms. McConnell (FB group moderator) and Christine Hughes (research assistant) will review the following information in detail at a study-specific meeting via teleconference:

(1) Subject accrual rate, retention and the reasons for retention failure
(2) Subject compliance with the protocol
(3) Project coordinator questions or concerns
(4) Adherence to FB protocol for moderator postings and adverse events (AEs/SAEs) and other issues reported by participants or the moderator or documented by the research assistant on FB transcripts.
(5) Adverse events (AEs/SAEs) and other issues reported by participants as documented by the project coordinator on study forms.

Decisions concerning changes, modifications, or adaptations will be decided and acted upon immediately. Annual Reviews: Protocols must be reviewed annually by the Mayo Foundation IRB and the Alaska Area
IRB. Reports will be generated regarding the study progress.

Content of DSM Report

A DSM report will be included as part of our annual progress report to the NIDA and the following will be included:

(1) Brief description of the trial
(2) Baseline sociodemographic characteristics
(3) Retention and disposition of study participants
(4) Quality assurance issues
(5) Regulatory issues
(6) AEs
(7) SAEs
(8) Efficacy