The Healing and Empowering Alaskan Lives Toward Healthy-Hearts (HEALTHH) Project: Study protocol for a randomized controlled trial of an intervention for tobacco use and other cardiovascular risk behaviors for Alaska Native People

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A R T I C L E   I N F O

A B S T R A C T

Background: Tobacco use and tobacco-related diseases disproportionately affect Alaska Native (AN) people. Using telemedicine, this study aims to identify culturally-tailored, theoretically-driven, efficacious interventions for tobacco use and other cardiovascular disease (CVD) risk behaviors among AN people in remote areas.
Design: Randomized clinical trial with two intervention arms: 1) tobacco and physical activity; 2) medication adherence and a heart-healthy AN diet.
Participants: Participants are *N* = 300 AN men and women current smokers with high blood pressure or high cholesterol.
Interventions: All participants receive motivational, stage-tailored, telemedicine-delivered counseling sessions at baseline and 3, 6, and 12 months follow-up; an individualized behavior change plan that is updated at each contact; and a behavior change manual. In Group 1, the focus is on tobacco and physical activity; a pedometer is provided and nicotine replacement therapy is offered. In Group 2, the focus is on medication adherence for treating hypertension and/or hypercholesterolemia; a medication bag and traditional food guide are provided.
Measurements: With assessments at baseline, 3, 6, 12, and 18 months, the primary outcome is smoking status, assessed as 7-day point prevalence abstinence, biochemically verified with urine anabasine. Secondary outcomes include physical activity, blood pressure and cholesterol, medication compliance, diet, multiple risk behavior change indices, and cost-effectiveness.
Comments: The current study has the potential to identify novel, feasible, acceptable, and efficacious interventions for treating the co-occurrence of CVD risk factors in AN people. Findings may inform personalized treatment and the development of effective and cost-effective intervention strategies for use in remote indigenous communities more broadly.
Clinical Trial Registration # NCT02137902

1. Introduction

Tobacco use remains the leading preventable cause of morbidity and mortality and contributes to significant racial/ethnic group health disparities [1]. Alaska Native (AN) people have high smoking prevalence and an increased risk for cardiovascular disease (CVD) and early death [2, 3]. The smoking prevalence in Alaska is 18% overall [4]. In contrast, 1 in 2 AN men and 1 in 3 AN women smoke cigarettes [5]. Effectively, the smoking prevalence among AN adults today is what the smoking prevalence was for US adults in the 1960s [1]. Efforts and

progress in addressing the US tobacco epidemic have not been equitably distributed.

Tobacco use clusters with additional CVD risk behaviors, and attention to multiple risks is recommended to optimize health and well-being [6–8]. Previous research has identified smoking, obesity, lipids, and psychosocial factors as accounting for 90% of the population-attributable risks for myocardial infarction [9, 10]. Lower education and racial/ethnic minority status predict engagement in multiple risks; struggling with multiple risks is related to greater nicotine dependence; and clustering of behavioral risks is associated with CVD treatment noncompliance. National data on AN/American Indian adults indicated that 79% had at least one CVD behavioral risk factor and 46% had two or more [11]. Existing research to date has been largely cross-sectional and limited in the behaviors assessed. Greater understanding of the co-occurrence of multiple risks in AN people and effective intervention strategies are needed.

In the literature, multibehavioral intervention trials have mixed evidence. A 2011 review reported a nonsignificant reduction in smoking; change in other behaviors (e.g., physical activity) was unreported [12]. A separate review indicated secondary prevention and interventions with a thematic focus on a disease state (e.g., cancer) achieved greater success on multiple risks [13]. More research is needed to examine multi-behavioral interventions and with a focus on understudied and high-risk communities [13–15].

Engagement in one behavior may support change in another. Specifically, physical activity may reduce cravings to smoke, withdrawal symptoms, and cessation-related weight gain [16]. Changing two or more behaviors at once, however, may be overwhelming. In a review of 20 randomized controlled trials of physical activity as an adjunct to tobacco treatment, nearly half the studies had under 30 participants per group; interventions varied in intensity, duration, format, and setting [17]; only 4 trials significantly increased fitness at end of treatment. Greater tobacco abstinence in the physical activity condition was reported in 4 of 20 studies at posttreatment, and only 1 study at 12 months. Notably, the study with the sustained effect tailored the intervention to participants' stage of change, informed by the transtheoretical model (TTM). Other research, targeting safe sun practices and healthy diet, found that TTM interventions can successfully support changes in multiple behaviors while aiding tobacco cessation [18, 19].

In 2011, the National Heart, Lung and Blood Institute requested applications for indigenous-health focused research on multiple health behavior change for secondary prevention of CVD. [20] With a focus on AN smokers and treatment of multiple risk behaviors, the current trial seeks to translate advances in telemedicine, personalized medicine, and computerized chronic disease interventions for the prevention of CVD among AN people.

2. Methods

Our interdisciplinary team brings expertise in cardiology, psychology, public health, nutrition, health economics, statistics, and pharmacogenomics. Investing in local capacity and fostering bidirectional learning, two team members, both of AN descent, received diversity supplements to support their dissertation projects linked to the main award. Notable study features include: (i) use of video telemedicine, at the invitation of tribal leadership, to address leading risk behaviors for CVD in AN people in the rural clinics they own and operate; (ii) application of culturally-tailored, theoretically-driven, TTM computer-assisted interventions to guide provider counseling for efficient and systematic attention to multiple risk behaviors for change (Table 1); (iii) comparing interventions on health behaviors (tobacco/physical activity) versus health factors (hypertension and high cholesterol); (iv) evaluation of effectiveness using objective measures (urine anabasine to biochemically confirm tobacco abstinence, lipid profile, blood pressure); (v) examination of cost-effectiveness of the

Table 1
Example Alaska Native (AN)-tailored intervention counseling activities by behavior and stage of change.

Intervention topic		Stage of change				
		Pre-contemplation	Contemplation	Preparation	Action	Maintenance
G 1	Smoking cessation	Sharing the facts: Tobacco is not native to Alaska and was not involved in any traditional practices; Tobacco accounts for 20% of Alaskan deaths; Heart benefits of quitting smoking are immediate	Comebacks for cons: Assesses key concerns and highlights strategies for treating nicotine withdrawal and the stress of quitting	Action plan: Selecting a quit date, sharing commitment with family/friends, identifying change strategies and medications	Avoid relapse: Identifying triggers and developing a plan to avoid relapse; identifying smoke-free environments	Maintain motivation: Encourages engagement in pleasant activities (AN dance, connecting with friends/family) to reward self for staying smoke-free
	Physical activity	Exercise in nature: Participant identifies natural opportunities for physical activity in the environment (e.g., fishing, berry picking, hunting)	Behavior awareness: Encourages use of study-provided pedometer to see that each step counts for health	Family activities: References AN respect for family and encourages exercising with others	Reaping rewards: Outlines a contract for success with goals, target dates, and self-identified rewards	Slipup recovery: Reframes setbacks as part of the process; helps identify situational and seasonal challenges to exercising and strategies for the future
G 2	AN heart-healthy diet	Food in nature: Highlights AN foods such as seal and salmon as rich in heart healthy fats with contrast to highly processed, high-sodium commercialized food options	Return to AN dietary ways: "Traditional Food Guide" provides simple, heart-healthy meal and snack ideas; encourages connecting with elders to learn more about AN traditional diets	Family activities: Encourages family engagement in AN traditional cooking practices to continue heart-healthy traditions across generations	Eat this not that: Identifies common unhealthy food choices (e.g, *Spam*), with heart healthier AN food substitutes, (e.g. *Muktuk*)	Check your thinking: Provides testimonies from AN people sharing how they maintained their motivation to sustain heart healthy dietary practices
	Medication adherence	Stories like me: Letters from AN people sharing their stories about managing their heart health with medications	Behavior awareness: Guides tracking of current medication adherence to identify best change practices	Finding inspiration: Offers 10 creative ideas for supporting adherence, such as the study medication bag	Connecting to care: Encourages seeking additional support from community health aides and providers	Staying on track: Encourages forward thinking to sustain attention and motivation to heart health adherence

intervention to inform clinical practice, health care policy, and dissemination; and (vi) evaluation of theoretical mediators and moderators of treatment outcome including village size and individuals' rate of nicotine metabolism. The trial will be the first to test a biomarker of the rate of nicotine metabolism as a moderator of treatment outcome in a sample of AN people, in smokers unmotivated to quit, and in those at high risk of CVD. Rather than requiring immediate action for behavior change, the intervention is tailored to motivation. The counseling is therefore flexible and inclusive, relevant to community members at any stage in the process of changing a behavior, particularly relevant when targeting multiple risk behaviors for change.

Specifically, we aim to test the efficacy of two technology-mediated interventions for supporting change in multiple risk behaviors in AN people for secondary disease prevention living in remote communities. The two interventions, one focused on tobacco use and physical activity and the second focused on medication adherence and a heart-healthy AN diet, are directly informed by the research team's prior fieldwork in rural Alaska and continued community partnership with tribes [21–23]. Further the interventions are responsive to AN cardiovascular health needs and traditional values and target 5 of the American Heart Association's 7 Strategic Impact Goals for 2020 [24, 25].

The primary hypothesis is that group 1 (tobacco use and physical activity) will significantly outperform group 2 (medication adherence and heart-healthy AN diet) through 18-months follow-up in producing biochemically-confirmed tobacco abstinence and secondarily will increase physical activity. The secondary hypotheses are that group 2 will significantly outperform group 1 in producing greater control of hypertension and hypercholesterolemia through medication compliance and dietary change. Secondary aims will compare the interventions on overall behavior change; model cost-effectiveness and budgetary impact of each intervention; and examine moderators/mediators of treatment outcome, including the trans-3′-hydroxycotinine to cotinine ratio, a noninvasive measure of nicotine metabolism rate (NMR). The trial combines technology, pharmacology, behavioral science, and health economics for advancing the health of AN people.

2.1. Study design, setting, and recruitment

This study is a 2-group randomized controlled trial (RCT) with 300 AN men and women smokers recruited in the Norton Sound Region of Alaska, which has a population of approximately 9492 and covers over 23,000 mile^2 in Northwestern Alaska on the Seward Peninsula (Fig. 1). The largest town is Nome (population 3598) and there are 15 villages with populations ranging from 150 to 900 residents. [26, 27] Approximately 76% of the population is of AN heritage. The AN people in Norton Sound are primarily Inupiaq and Yup'ik. A rural and remote area, the main form of transportation between Nome and the region's 15 villages is by commuter "bush" planes. Utilizing video teleconference (VTC) and TTM-tailored interventions, the trial aims to reach at-risk AN people regardless of residential location or current motivation for health behavior change.

Participants are recruited though intensive community outreach that includes, but is not limited to: public radio announcements; communications from the Norton Sound Health Corporation to communities; flyers posted in gathering areas; VHF (very high frequency) radio communications in the villages; and study information letters mailed to patients from the clinic providers. Interested individuals are directed to call the study's toll-free line in Anchorage for description of the study, eligibility screening, and overview of informed consent procedures. Interested and eligible individuals who provide signed informed consent are randomized to one of two active interventions, both targeting multiple risks for CVD prevention, after completing the baseline survey and providing baseline biological samples. A computer generated stratified random assignment program individually randomizes participants based on their village size (Nome vs. other), cigarettes per day (cut-point of 8), and stage of change for quitting smoking, the last two

variables known to be related to outcomes and addressed by the intervention [19, 28]. Participants living at the same address are randomized to the same treatment intervention group to address potential contamination concerns (i.e., sharing of study materials). The design of the trial is in accordance with the Consolidated Standards of Reporting Trials (CONSORT) statement; the trial is registered with the Clinical Trials Registry (NCT02137902). Institutional review board (IRB) approval was obtained from Stanford University; the University of California, San Francisco; the Alaska Area IRB; the Alaska Native Tribal Health Consortium Board and its manuscript and proposal review committee; and the Norton Sound Board of Directors and its Research Ethics Review Board, the latter which has closely guided the HEALTHH project.

2.2. Sample

Study inclusion criteria are AN heritage; English speaking; aged 19 years or older (i.e., legal smoking age in AK); residing in the Norton Sound region; currently smoking 5 or more cigarettes per day; with high blood pressure (systolic/diastolic BP ≥ 140 mmHg/90 mmHg) or high cholesterol (LDL ≥ 160) or currently prescribed antihypertensives or cholesterol medication. Study exclusion criteria are active pregnancy; currently in a tobacco cessation treatment program or taking cessation medications; and body mass index (BMI) > 50.

2.3. Interventions

Intervention strategies are informed by our team's 6-year Community Based Participatory Research project in the Bristol Bay Region of Alaska [21–23]. Both groups receive active interventions with behavioral counseling; the counseling and print materials are highly individualized, thereby minimizing the likelihood of cross-condition contamination. The print materials for both groups are culturally tailored to reflect traditional AN values, including respect for elders, the land, and family, and have photos of Alaskan traditional food, land, and people. As part of the tailoring process, the materials were reviewed by three team members of AN heritage; two data safety monitoring board members of AN and American Indian heritage; by the Norton Sound Research Ethics Review Board, comprised of tribal stakeholders; and the Alaska Area Institutional Review Board. All feedback was recorded and incorporated into enhancements and tailoring of the intervention including imagery (photos), language and cultural terms, and AN stories.

Evaluated in Norton Sound, the intervention is designed to be more broadly relevant to smokers of AN heritage. Nutrition materials were adapted from USDA guidelines [29], to recommendations based on AN traditional diets rich in heart healthy omega-3 polyunsaturated fats from marine mammals and fish [30–33]. The counseling is guided by TTM-tailored computer-assisted programs completed interview-style by counselors based in Anchorage or at Stanford University via VTC with the study participants in the village clinics. Counseling by phone is used as back-up if the internet connectivity is poor and not sufficient for a VTC counseling session. Study counselors are skilled in motivational interviewing, TTM principles, and tobacco treatment clinical practice guidelines. Group 1 participants receive tailored counseling focused on increasing intrinsic motivation, goal setting for tobacco and physical activity, adherence with nicotine replacement therapy (NRT), and self-monitoring with a pedometer-based walking program. The study provides 12-weeks of combination NRT (patch plus gum or lozenge) and a pedometer for participants randomized to group 1. Group 2 participants receive tailored counseling focused on increasing intrinsic motivation for blood pressure and cholesterol management, medication adherence and practices consistent with a heart-healthy AN diet, that includes traditional foods. Participants have regular access to traditional foods through subsistence activities (spring and summer), food sharing (e.g., successful hunting of a moose by one is shared with community/

Fig. 1. Norton Sound region: HEALTHH Study Recruitment Communities.

village), public eateries (e.g., the Norton Sound Health Corporation Hospital cafeteria in Nome serves traditional foods such as reindeer or fish), and community celebrations/gatherings. Participants in group 2 receive support on blood pressure and cholesterol medication management, a medication bag to organize their medications, and a cookbook with heart-healthy AN recipes. Table 1 provides examples of intervention strategies by behavioral target and stage of change. The online TTM computer intervention tracks completed research sessions with time duration and flags sessions due but not yet completed, allowing for process monitoring from a distance and in real-time.

2.4. Assessments

Assessments are at baseline and 3, 6, 12, and 18-month's follow-up, conducted at the village clinics or via a toll-free phone line (Table 2). For their time, participants are paid $30 at baseline; $40 at months 3, 6, and 12; and $50 at 18-months, for a total possible stipend of $200 provided via gift cards. A comprehensive contact form collects information for tracking participants, used in longitudinal studies with long-term follow-up rates exceeding 80%. At each follow-up, changes in contact information are elicited.

The primary outcome is smoking status, assessed as number of cigarettes smoked in the last 7 days, coded as abstinent only for participants reporting "no tobacco, not even a puff." Consensus guidelines from the Society for Research on Nicotine and Tobacco recommend use of 7-day point prevalence abstinence in cessation-induction studies with smokers unmotivated to quit, who will be quitting at different time points within the trial [34]. For participants reporting 7-day abstinence at follow-up assessments, biochemical verification involves a urine sample for evaluation of anabasine, a biomarker of tobacco exposure with half-life of 8-h that is not present in NRT. Liquid chromatography-mass spectrometry will determine concentrations of anabasine in urine, corrected for urine creatinine concentration. Values < 2 ng/ml will be considered a confirmed nonsmoker. As a secondary tobacco outcome,

we will assess 6-month prolonged abstinence from the 12- to 18-month assessment, applying the National Heart, Lung, and Blood Institute definition of failure of smoking on 7 consecutive days or smoking at least once each week over 2 consecutive weeks [34].

Secondary outcomes include blood pressure, cholesterol ratio, nicotine metabolism ratio (trans-3′-hydroxycotinine to cotinine ratio, abbreviated NMR), BMI, medication compliance, physical activity, diet, and multiple risk behavior change. Nonadherence measures are: (1) the Medication Adherence Scale (MAS) and (2) 5-items measured on a 5-point Likert scale of the frequency of various forms of non-adherence in the last month (e.g., taking less than recommended, taking a break; reliability = 0.67) [35]. Dietary quality is measured with an adaptation of the National Cancer Institute Food Frequency (FFQ) nutrition scale, with regional and cultural-tailoring to assess the intake frequency and estimate portions of both foods purchased in village stores and acquired from subsistence activities or shared with participants by family, friends, and neighbors [36]. The FFQ was shortened and modified to assess Native foods from the region and processed foods with a balance of food options that were heart healthy and heart unhealthy. Multiple risk behavior change will be calculated as the: 1) Framingham Risk Factor Score (an estimate of the 10-year CVD risk of an individual based on gender-specific formulas with age), total and HDL cholesterol, smoking status, and systolic BP; 2) Multiple Risk Behavior Change Impact Factor, calculated as intervention efficacy summed over the multiple behavioral targets, $I = \Sigma_{\# \text{ of behaviors(n)}}(E_n)$; intervention efficacy will be defined as the proportion in action/maintenance (e.g., nonsmokers) for each targeted risk behavior; and 3) linear index of multiple behavior change computed by subtracting baseline scores from follow-up scores for each risk behavior, dividing by the standard deviation of the difference (i.e., z-score), and summing across the individual risks (smoking, exercise, diet, medication adherence) [37, 38]. Stage of change was assessed by survey for each behavior individually using standard questions and asked as part of the VTC session to guide the counseling [19, 39].

Table 2
Baseline and follow-up assessments in the HEALTHH Study.

Measures	Baseline	3-month	6-month	12-month	18-month
Sociodemographics (e.g., age, gender, education, income, marital status)	x				
MacArthur Social Ladder Scales [50]	x				
Cigarettes smoked past 7 days	x	x	x	x	x
Other tobacco and nicotine use	x	x	x	x	x
Secondhand smoke exposure	x				
Quit attempts	x	x	x	x	x
Time to first cigarette [41]	x				
Nicotine metabolism ratio (NMR) [22]	x				
Minnesota Nicotine Withdrawal Scale [42]	x	x	x	x	x
Stages of change for smoking, physical activity, diet, and mediation adherence [43–45]	x	x	x	x	x
Items from the Alcohol Severity Index [46]	x	x	x	x	x
CES-Depression Scale [47]	x	x	x	x	x
Leisure Time Activity Categorical Item [49]	x	x	x	x	x
Modified FFQ nutrition scale [36]	x	x	x	x	x
Health related quality of life, CDC HRQOL 14 [48]	x	x	x	x	x
Anabasine to confirm tobacco abstinence		x	x	x	x
Blood pressure and heart rate	x	x	x	x	x
Full lipid profile, cholesterol ratio	x		G2		x
Medication Adherence Scale [35]	x	x	x	x	x
Medication side effects		x	x	x	x
Measures of multiple risk behavior change (MRBC)	x	x	x	x	x
Framingham Risk Factor Score					
MRBC Impact Factor					
Linear index of MRBC					
Telemedicine Intervention acceptability	x	x	x	x	

Note: G2 = group 2 only.

Our measure of cost-effectiveness is the Health Care Utilization (HCU) inventory, which assesses frequency, duration, and cause of emergency room, inpatient, and outpatient care. Adapted from the Treatment Services Review, the HCU uses established methods and was used successfully in our previous studies [40]. Staff time spent on different activities is tracked for each intervention component to enable estimation of the real cost of intervention materials and dissemination. Data are routinely collected on all intervention-related costs of materials and services, such as manuals, cessation pharmacotherapy, pedometers, postage, and printing. Staff activity logs track labor costs for delivering intervention materials to differentiate intervention costs from research-related costs of recruitment, assessment, start-up, and development costs. The cost estimate will reflect all costs needed to replicate the treatments in clinical practice, including identifying smokers and introducing the treatment program.

Descriptive measures include demographics (age, gender, education, income, employment); tobacco co-use (e.g., smokeless), addiction (e.g., cigarettes/day, time to first cigarette upon waking) [41], environmental tobacco exposure, prior quit attempts, the Minnesota Nicotine Withdrawal Scale [42], and stages of change measures [43–45]; alcohol use (items from Alcohol Severity Index) [46], the Center for Epidemiologic Studies Depression Scale [47], physical and emotional well-being (CDC HRQOL 14) [48, 49] and perceived social and community standing (MacArthur Social Ladder Scales) [50].

Lastly, process measures are tracking the extent to which the treatments are delivered to participants as intended and will be examined as mediators of treatment outcomes. Participants complete brief evaluations of treatment acceptability after each VTC counseling session. Adverse Effects (e.g., headache, skin sensitivity, insomnia, nervousness) are assessed. We measure engagement in in-study and outside-of-study, tobacco cessation, exercise, medication adherence, and dietary interventions.

2.5. Data analysis

We will run standard diagnostic statistics and graphical analysis for all variables to check for outliers and out-of-range values and to confirm that distributions meet assumptions of the statistical tests to be used. The psychometric properties of measures with scale scores will be examined for internal consistency and factor structure to ensure the measures are operating as desired with this diverse sample. Preliminary analyses will test the correlation between order of study entry and outcome. Dropout rates will be examined by condition. If differences for any of these variables are noted, they will be statistically controlled as a covariate in model testing or as a stratification variable. The use of these statistical techniques will be taken into account in interpretation of the outcomes.

Every effort will be made to limit the amount of missing data, including completion of most surveys by interview. If it appears missingness is related to a measured aspect of the participants, we will include those measures as covariates in the hypothesis-testing models. Sensitivity analyses will check that methods of dealing with missing data do not have a major impact on study conclusions. We also will conduct outcome analyses based on coding missing subjects as "smoking" to allow direct comparison of findings with the research literature.

A repeated-measures, mixed-effects model of the dichotomous outcome variable, will be estimated and tested to examine the primary outcome of abstinence versus smoking status, indexed as 7-day point prevalence, at 3- through 18-months follow-up by condition. The independent variables will be study condition, home village, stage of change plus covariates as identified in preliminary data analyses. A test of the coefficient on treatment condition will be a direct test of the primary hypothesis. The SAS Proc NLMIXED will be used for computation. A parallel model, using logistic regression, will examine 6-month prolonged abstinence from 12- to 18-months follow-up. The study is designed and powered to test a single primary hypothesis. The identified secondary aims, however, are of interest, theoretically driven, and proposed a priori. Intervention effects on level of physical activity, blood pressure, cholesterol ratio, BMI, medication adherence, dietary change, Framingham Risk, and the multibehavioral impact factor will be tested in a similar fashion, using separate linear models via Proc MIXED given that the outcomes will be continuously distributed.

An important outcome for purposes of subsequent intervention diffusion is cost effectiveness, often reported as cost per gain in quality

adjusted life year in smoking cessation trials. If the treatment effect is significant, cost-effectiveness will be evaluated. We will determine the incremental cost-effectiveness ratio by determining the difference in cost incurred by the tobacco/physical activity intervention relative to the active control, and dividing this by the difference in the incremental effectiveness, expressed in quality adjusted life years. Costs will be evaluated from the societal perspective and will include intervention and healthcare costs. Intervention costs, including screening and counseling activities, will be estimated using a micro-costing method. We will combine logs of staff activity on randomly selected dates with wage and benefit data to determine labor costs, use prevailing rental rates to determine the cost of space, and hospital cost report data for administrative overhead. The cost of treatment groups will be compared using log-link generalized linear models. Since the effect of the intervention is not realized in the follow-up period, we will construct a Markov model of lifetime costs and benefits using the substantial literature on the long-term effect of risk factors on survival and healthcare costs. We will discount cost and benefits at a 3% annual rate and evaluate the uncertainty associated with model parameters using a probabilistic sensitivity analysis. We also will consider whether results are sensitive to changes in the discount rate. A bootstrap approach will estimate the confidence region surrounding cost-effectiveness and estimate the cost effectiveness acceptability curve (i.e., the statistical significance of the intervention over a range of critical cost-effectiveness ratios) [51]. Provided the treatment effect is significant, a Budget Impact Analysis will be conducted following best practices identified by the International Society of Pharmacoeconomics and Outcomes Research task force. First, we will estimate the direct short-term cost of screening patients and providing the interventions from the perspective of the hospital providing the service. Second, we will subtract from these estimates, literature-based estimates of the offsetting effect of smoking cessation on healthcare utilization, adopting the healthcare payer perspective. We will use trial data to estimate the percent of patients that actually engages in treatment. Scenario analysis will estimate budget impacts under different risk prevalence and engagement rates.

We will examine whether treatment effects differ for patient subgroups including: substance use, tobacco co-use, depression symptoms, demographics, baseline stage of change, time to first cigarette, and NMR. Lastly, we will examine process measures as potential treatment mediators including: intervention acceptability ratings; NRT use; attention to behavior risks by outpatient providers; and number of telehealth sessions completed. Analysis of mediation will be based on the structural equation modeling framework.

3. Discussion

Targeting racial/ethnic disparities in tobacco use and other CVD-related risk behaviors, this study aims to identify effective and cost-effective interventions for AN people in remote villages. In a RCT, the study will compare interventions using telemedicine to promote the American Heart Association's identified ideal health behaviors (nonsmoking and physical activity) related to ideal health factors (managing cholesterol and blood pressure). The study is innovative in its use of telemedicine to reach AN people in remote locations. Key strengths of the study include an AN-tailored, theoretically-driven TTM computer-assisted intervention aimed at multiple behavior change and a collaborative partnership with AN communities.

Results from this study will need to be considered in light of limitations which may impact generalizability of findings. The study focus is on tobacco use and other CVD risk behaviors; hence, smokers without hypertension and/or hypercholesterolemia are not included, which may skew the sample slightly older. Also, nondaily and "light" smokers (i.e., < 5 cigarettes/day) as well as exclusive smokeless tobacco users are excluded, because NRT has not been shown to be effective for light/nondaily smokers and smokeless tobacco users. Although designed to

be relevant to smokers of AN heritage more broadly, for feasibility, the evaluation is centered in a single region of Alaska. Despite these limitations, this first study will yield important information to guide future research.

This study aims to identify and treat the co-occurrence of CVD risks in AN people. Findings may inform personalized treatment and the development of effective and cost-effective intervention strategies delivered to AN people in their communities. Study findings will be disseminated to community members in the Norton Sound region by mail and internet postings in lay language, will be presented to the Norton Sound Health Corporation Board of Directors and other community leaders, to the Alaska Native Tribal Health Consortium leadership, and will be presented at state and national, cardiovascular health and behavioral science conferences.

Conflict of interest declaration

Drs. Prochaska and Benowitz have served as expert witnesses against the tobacco companies in lawsuits for which they have received fees for the work and have provided consultation to pharmaceutical and technology companies that make medications and other treatments for quitting smoking. No other authors have any disclosures to report related to this work.

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