Protocol Title:	**Reducing Tobacco Use Disparities Among Adults in Safety Net Community Health Centers**
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PURPOSE OF STUDY & OBJECTIVES

An estimated 26 million smokers still receive no treatment for their smoking during their primary care visits. Given the persistent clinical system, provider, and patient barriers to addressing smoking, especially among poor populations, an EHR-automated population health management approach that links a healthcare system with community services both clinically and electronically to engage all smokers may increase access to effective treatment. Increased access is especially significant for low-income smokers who are underserved and carry a disproportionate burden of tobacco-related disease. This 2-group randomized controlled trial will evaluate the effectiveness of a person-centered population health management intervention for smoking cessation in low-income smokers. The following aims and hypotheses will be tested:

Primary Aim 1 (Effect on Treatment Engagement): Compare Choose to Change versus Usual Care for engaging low-income smokers in treatment. Hypothesis: Choose to Change will increase the proportion of smokers who complete a behavior counseling call by 6 weeks (24%), compared with Usual Care (10%).

Primary Aim 2 (Effect on Treatment Utilization): Compare Choose to Change versus Usual Care for increasing treatment utilization. Hypothesis: Choose to Change will increase the proportion of smokers who complete ≥1 additional behavior counseling calls by 14 weeks (15%), compared with Usual Care (7%).

Primary Aim 3 (Effect on Smoking Cessation): Compare Choose to Change versus Usual Care for increasing smoking cessation. Hypothesis: Choose to Change will increase the proportion of smokers

abstinent at 28 weeks (7%), as defined by bio-verified 7-day point-prevalence abstinence, compared with Usual Care (2%).

Secondary Aim 1 (Cost Evaluation): Conduct a cost-analysis to determine the cost of providing effective cessation therapy to smokers using this letter-enhanced EHR-referral and outcomes system. Evaluate the cost effectiveness of the Choose to Change letter and automated /text messages compared to usual care by calculation the cost-effectiveness ratio as the average dollars spent per successful quit.

Exploratory Aim 1 (Moderators of Intervention Effects): Evaluate motivation to quit, time since last clinic visit during which smoking was addressed, health literacy, cigarettes per day, recent smoking reduction, initial choice of cessation versus reduction, race/ethnicity, and primary language as moderators of effect of Choose to Change on treatment engagement, treatment utilization, and smoking cessation.

Exploratory Aim 2 (Mediators of Intervention Effects): Evaluate change in perceived autonomy support, autonomous motivation, confidence in ability to quit, and attitude towards NRT as mediators of intervention effects on treatment engagement, utilization, and cessation.

BACKGROUND AND RATIONALE FOR STUDY

An estimated 26 million smokers receive no treatment for their smoking during primary care visits.[1-3] Electronic health record (EHR) systems are used to increase smoking cessation treatment delivery, but at best only 65% of smokers are offered treatment.[4] Given the persistent barriers to addressing smoking, an EHR-automated population health management approach that links healthcare systems with community services electronically to engage all smokers may increase access to effective treatment. While 90% of smokers are not ready to quit abruptly, many are interested in cutting down,[4,6] and smoking reduction increases the likelihood of future quit attempts and cessation.[7] According to self-determination theory (SDT),[8] smokers who perceive themselves to be autonomous partners in their healthcare, and who are empowered to tailor their treatment goals to their level of readiness to quit, are more interested and engaged in their treatment. SDT-based intervention increases treatment utilization and smoking cessation[9], and offering smoking reduction as a treatment option increases treatment enrollment.[4] Person-centered population outreach that targets low-income smokers and encourages either quitting or cutting down as a positive first step towards cessation may increase the likelihood that they will accept (i.e., engage in) and utilize treatment and achieve abstinence.

This study will evaluate the effectiveness of a person-centered and EHR-automated population health management intervention for smoking cessation that is embedded in routine care and designed to engage low-income smokers outside of the primary care visit. The experimental approach overcomes major barriers to addressing smoking in low-income patients. Healthcare delivery and access barriers will be addressed through an EHR system that automates identification of smokers, creation of targeted engagement intervention material, referral for proactive Quitline treatment, and treatment outcomes feedback to providers to support follow-up care. Health literacy barriers will be addressed via messaging (words, graphics) targeted to low-literacy smokers. Psychological barriers (low motivation, belief that abrupt cessation is the only treatment option) will be addressed through a person-centered approach that encourages smokers to choose their own initial treatment goals. We expect that for the large proportion of low-income smokers who are ambivalent about quitting, the ability to choose between cessation and reduction, in the context of other SDT elements, will increase their interest and engagement in treatment.

We will partner with a Federally Qualified Health Center (FQHC) that serves 35,000 diverse low-income patients in Chicago. Automated via the EHR system, smokers will be mailed a one-page letter on behalf of their primary care provider encouraging smoking cessation or reduction as a first step to cessation. The letter will be paired with five automated text/ messages that reinforce the central messaging of the letter **("Choose to change and make your own goal"**). Two weeks after mailing, patients will receive a call from the Illinois Tobacco Quitline and offered free behavior counseling and free nicotine replacement therapy. Treatment outcomes will be transmitted directly to the EHR system. Our pilot data show that 24% of low-income smokers (31/132) who were sent the letter during a 3-week period accepted a Quitline call and completed ≥1 counseling session.

PARTICIPANT ELIGIBILITY: INCLUSION AND EXCLUSION CRITERIA

Target Population

Five hundred thirty adult male and female English- or Spanish-speaking current smokers who are patients at one of seven federally qualified health centers (FQHC) within the Near North Health Services Corporation (NNHSC) community clinic system will be enrolled in this clinical trial.

Inclusion Criteria
Eligible participants will be males and females who are:

1. 18 years of age or older;
2. A patient at one of the seven participating NNHSC community clinics;
3. Listed as "current someday smoker" or "current everyday smoker" in their NNHSC EHR; confirms current someday or everyday smoking status at phone screen
4. Have had ≥1 visit to their NNHSC clinic within the past 12 months

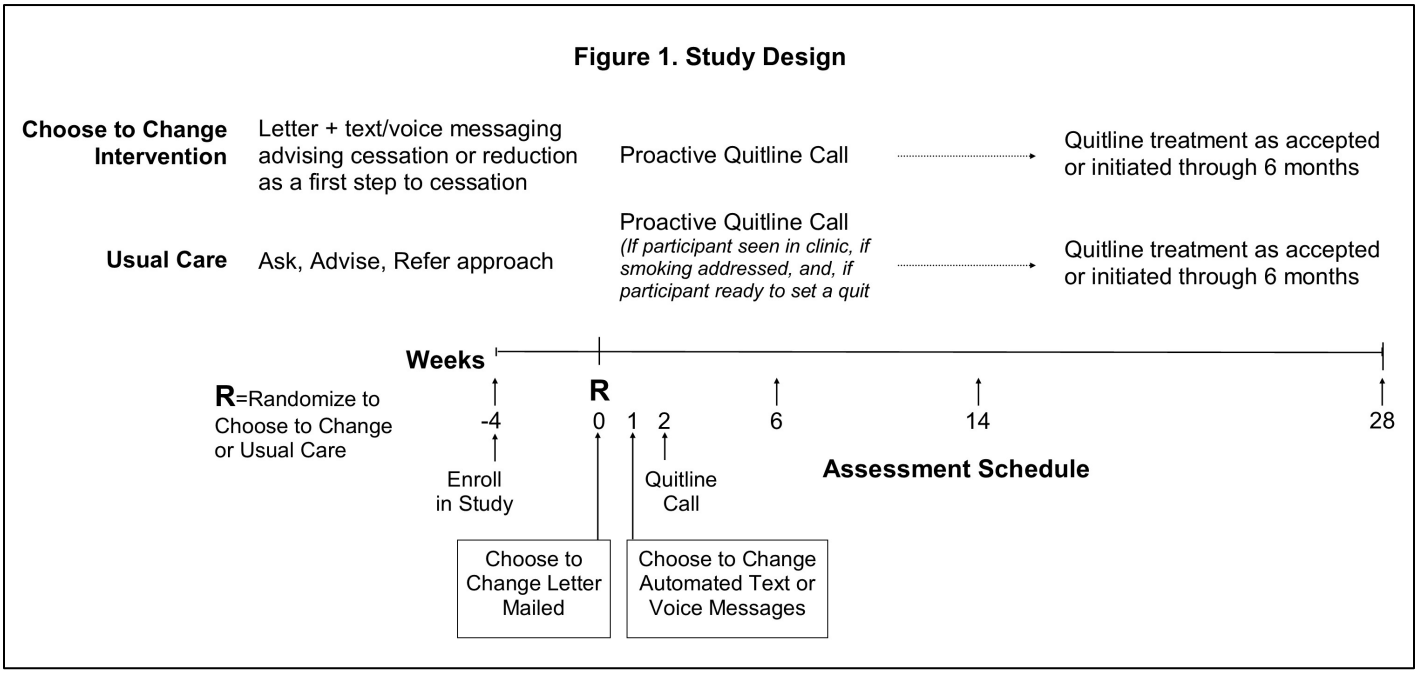
Exclusion Criteria
Participants who self-report any of the following will not be eligible to participate in the study:

1. Documented within their NNHSC EHR as preferring a language other than English or Spanish for healthcare;
2. No telephone number or address listed in the EHR;
3. Does not have a cell phone with texting capabilities;
4. Lives with another NNHSC patient who is already enrolled in the present study.

Vulnerable Populations
Children under 18 years of age, fetuses, neonates, or prisoners will not be included in this study. Pregnant women will not be actively recruited, but will be eligible for the study if they meet all other inclusion and exclusion criteria detailed above.

STUDY DESIGN
This is a 2-group randomized controlled trial to evaluate the effectiveness of the population health management intervention for low-income smokers that aims to promote Quitline treatment, engagement, utilization, and smoking cessation (Figure 1).

Figure 1. Study Design



Length of Study Participation

Participants will be involved in study-related activities for approximately 7½ months (32 weeks) from initial enrollment in the observational study and baseline assessment (week -4) through follow-up (week 28). Participants will complete four phone-based assessments during this time (Baseline/Week -4; Week 6; Week 14, Week 28) and those who report abstinence from cigarettes at the Week 28 phone interview will be asked to come in for an in-person clinic visit within 2 weeks of their Week 28 phone session in order to bioverify smoking status.

Alternative study timeline: Due to funding constraints, participants enrolled February 2018 or after will be involved in study-related activities for about 4 months (18 weeks) from initial enrollment in the observational study and baseline assessment (week -4) through a final follow-up at week 14. Participants enrolled in this alternative study timeline will complete three phone-based assessments (Baseline/Week -4; Week 6; Week 14) and those who report abstinence from cigarettes at the Week 14 phone interview will be invited to come in for an in-person clinic visit within 2 weeks of their Week 14 phone session in order to bioverify smoking status. Randomization to treatment arm and all other study procedures will be conducted in the same way as for the participants completing the full 32 week study timeline.

Study Timeline

Development of Bilateral EHR Interface with the Quitline. Led by Drs. Mohanty and Long, we will complete the testing and refinement of the bilateral EHR interface between NNHSC and the Quitline. Trainings with providers in use of the new EHR functionality will also be conducted. The integration of NNHSC and the Quitline will enable the NNHSC study care coordinator and providers to make a one-step referral to the Quitline. In turn, the Quitline will communicate patient outcomes directly to NNHSC via the EHR. The existing EHR content will be modified to automate obtaining and documenting provider approval of patient involvement and generating and documenting the mailing of the intervention letters. All clinical information will be communicated to the Quitline using Health Level Seven (HL7) standards. The Quitline will use a HL7 interface engine to receive and "translate" the information within its secure network.

Development of the EHR Query to Identify Participants. We will use structured query language (SQL) to analyze EHR data to identify eligible patients. The data query will be validated by confirming the eligibility criteria (denominator) and by performing a spot-check of positive cases (numerator) and cases determined to be negative, or failed, according to query specifications. The query will also be used to generate the following for each patient: 1) patient ID number; 2) telephone numbers (home, cell); 3) preference for method of communication about their healthcare (text message, letter); 4) primary physician; 5) preferred language for healthcare; 6) type of health insurance; 7) number of clinic visits during the past year and date of last visit; 8)

Table 2. Project Timeline

	Year 1				Year 2				Year 3			
Task/Months	1-3	4-6	7-9	10-12	13-15	16-18	19-21	22-24	25-27	28-30	31-33	34-36
Organize research team												
EHR system bilateral interface*												
EHR query development and validation												
Choose to Change Intervention and Usual Care												
Quitline counseling/medication												
Measurement of Quitline treatment outcomes												
Data cleaning and validation												
Data analysis and manuscripts												

*Development, testing, and maintenance of the EHR system bilateral interface between NNHSC and the Quitline system

date of last visit during which smoking was addressed; 9) education level; 10) household income; and 11) dates of previous referrals to smoking cessation treatment. The query will be run monthly.

STUDY PROCEDURES

Recruitment and Accrual Procedures

Study Sites

NNHSC is a FQHC comprised of eight community health clinics in Chicago. These include Cottage View Health Center, Denny Community Health Center, Komed Holman Health Center, Louse Landau Health Center, North Kostner Health Center, Reavis School-Based Health Center, Sunnyside Community Health Center (previously Uptown), and Winfield Moody Health Center. Dr. Tim Long, the Director of Performance Improvement, serves as the study Site-PI for NNHSC. NNHSC serves 35,000 patients. Racial/ethnic composition is 10% Hispanic, 66% African American, 10% Caucasian, 0.8% Asian, and 0.2% multiracial. The remainder is classified as unknown. Ninety-six percent of patients are uninsured (56%) or on Medicaid (40%). Females account for 63% of patients, and 96% live at or below the Federal Poverty Line. All study sessions, both by telephone and in-person, will be conducted at one of the NNHSC primary care home clinic of the participants listed above.

Participant Recruitment

All study participants will be patients receiving medical care at one of the seven participating NNHSC community clinics. As Reavis School-based Health Center largely serves children under the age of 18 years, we will not recruit from Reavis. We will use structured query language (SQL) to analyze EHR data to identify eligible patients. NNHSC uses the General Electric Centricity (Practice Solution 14) EHR system for all clinical encounters (supported by Alliance of Chicago). The SQL-based data query will be designed and tested by the Alliance of Chicago data team, validated by confirming the eligibility criteria (denominator) and by performing a spot-check of positive cases (numerator) and cases determined to be negative, or failed, according to query specifications. After testing, then sent to the Winfield Mood Health Center (NNHSC site) Care Coordinator via secure email. Data to be extracted for each patient will be limited to: 1) medical record number; 2) telephone numbers (home, cell); 3) preference for method of communication about their healthcare (text message, letter, home phone, etc.); 4) primary physician; 5) preferred language for healthcare; 6) type of health insurance; 7) number of clinic visits during the past year and date of last visit; and 8) date of last visit during which smoking was addressed. The query will be run monthly. We expect to complete accrual in about 15 months, enrolling about 40 participants per month.

Primary medical providers of all candidates identified as eligible for the randomized clinical trial by the SQL query will be sent an message alert with the EHR requesting that they review the list of patients identified (lists will be provider-specific) and respond within 10 days to identify any patients from the list whom they believe would not be appropriate for the survey study or potential Quitline referral. After this 10-day provider opt-out period, all patients who have not been opted out will be called by a research assistant to ask if the patient is interested in hearing about, screening and if eligible, enrolling in a quality improvement study on “health habits of primary care patients at Near North Health Services Corporation.” The study will be described as a way for “Near North Health Service Corporation and the doctors and staff to better understand the health habits, risk behaviors and wellness service needs of [their] patients” to inform possible enhancements to some of these services. Only NNHSC patients who consent to enroll in this survey study will be randomized to one of the treatment conditions (either Choose to Change or Usual Care).

We will conduct a clinic-wide awareness campaign across the seven participating NNHSC clinics describing the survey study component of the project in order to generate interest and increase enrollment. For this general clinic awareness campaign we will use posters and flyers that promote the health habits survey study and will also use small giveaways (e.g., pens, pill boxes, magnets) with graphics aligned with this theme. The goal of this general clinic campaign is only to raise awareness of the survey study, but we do not want NNHSC patients to call us regarding study enrollment. Therefore, we will not include any study personnel contact information on these general campaign flyers or posters. Postcards and magnets with the same messaging as

the posters and flyers will be bulk-mailed from NNHSC to the patients identified by the SQL query prior to outreach calls with the goal of increasing enrollment once called by the research assistant.

Additionally, for all enrolled participants, we will use a retention campaign consisting of the following:

1) Reminder letters sent one week prior to their next scheduled telephone survey appointment
2) Seasonal Newsletters providing updates about study progress on recruitment, patient testimonies about their experiences with clinical research, NNHSC clinic updates from Dr. Tim Long, health tips and information, and seasonal activities that support healthy lifestyles. The purpose of the newsletters is to keep participants engaged with the study in between their telephone interviews, thereby increasing retention and minimizing attrition.
3) Small participant incentive items using the same graphics and messaging from the general clinic campaign will be mailed with the reminder letters (e.g., water bottles, draw string bags, small ear buds, T-shirts). Consistently using the same images and themes across recruitment and retention materials will generate familiarity with the study and will serve to maintain high retention rates.

All recruitment and retention materials will be mailed from NNHSC.

Randomization and Study Conditions

Smokers identified through the SQL query from NNHSC's EHR and who consent to enroll in the NNHSC "health habits and wellness service needs study" and who complete the baseline survey will be randomized to either **Usual Care** or person-centered population management (**Choose to Change**) four weeks (week 0) after enrollment in the study (week -4). We will use a 6:6 permuted block randomization scheme to assign patients to treatment condition. Randomization will be stratified by readiness to quit, as measured using a single item question for which participants identify their level of motivation to quit smoking as measured on a 10-piont scale (1 = not at all motivated; 10 =extremely motivated), race (African American versus not), and language preferred (English versus Spanish). We plan to approach 115 patients per month to enroll 40 participants per month and achieve this randomization rate (35% response rate).

Choose to Change (CtC) Intervention:. Choose to Change will comprise two components: 1) a single page letter that messages choice of cessation or smoking reduction using words and a graphic; and 2) five automated text messages sent on behalf of the NNHSC providers that reinforce the central messaging of the letter.

CtC particicpants will be mailed the letter on behalf of their provider encouraging cessation or smoking reduction as an initial step to cessation if not ready to set a quit date, provides information about Quitline services, including safety and effectiveness, and states that a Quitline coach will be calling within two weeks to offer free treatment. The central message developed through our previous focus group work is **"Choose to change and make your own goals."** The letter also contains the other elements of SDT as well as standard evidence-based supportive and motivational statements. Participants who do not want to be called by the Quitline will be instructed to contact the NNHSC study care coordinator. Opt-outs and reasons will be recorded. In collaboration with Dr. Kenzie Cameron, the letter was designed for smokers with low health literacy based on established health communication principles. The written message is one page in length to minimize cognitive overload and burden and to maximize the effectiveness of the message.[86-89] The estimated readability according to the Flesch–Kincaid Grade Level rating is 4.8 (5th grade). The letter will be printed on NNHSC letterhead, enclosed in large-sized (6" x 9") NNHSC envelopes, and sent first-class mail.

One day after letter mailing, the first automated text message will be sent to participants notifying them that they will receive the CtC letter in coming days. During the 10 days following the letter mailing, participants will receive three more automated text messages on behalf of their healthcare provider three days apart between each message. A fifth text message will be sent 8-10 days after the Quitline's initial outreach call (i.e., Quitline outreach takes place two weeks after letter mailing). The purpose of this last text message is to provide the toll free Quitline number in case the participant has not yet been able to connect with a Quitline counselor. Also informed by SDT and patient feedback, the automated text messages will be used to sustain the motivational effects of the letter and maximize the likelihood that participants will engage in and utilize Quitline treatment. Participants who do not want to receive these messages will be able to opt-out after each message. The automated text messaging procedures were established in our prior work (P01 HS021141; Kenzie Cameron).[81] Text messaging is increasingly used in primary care to support processes of care and improve health

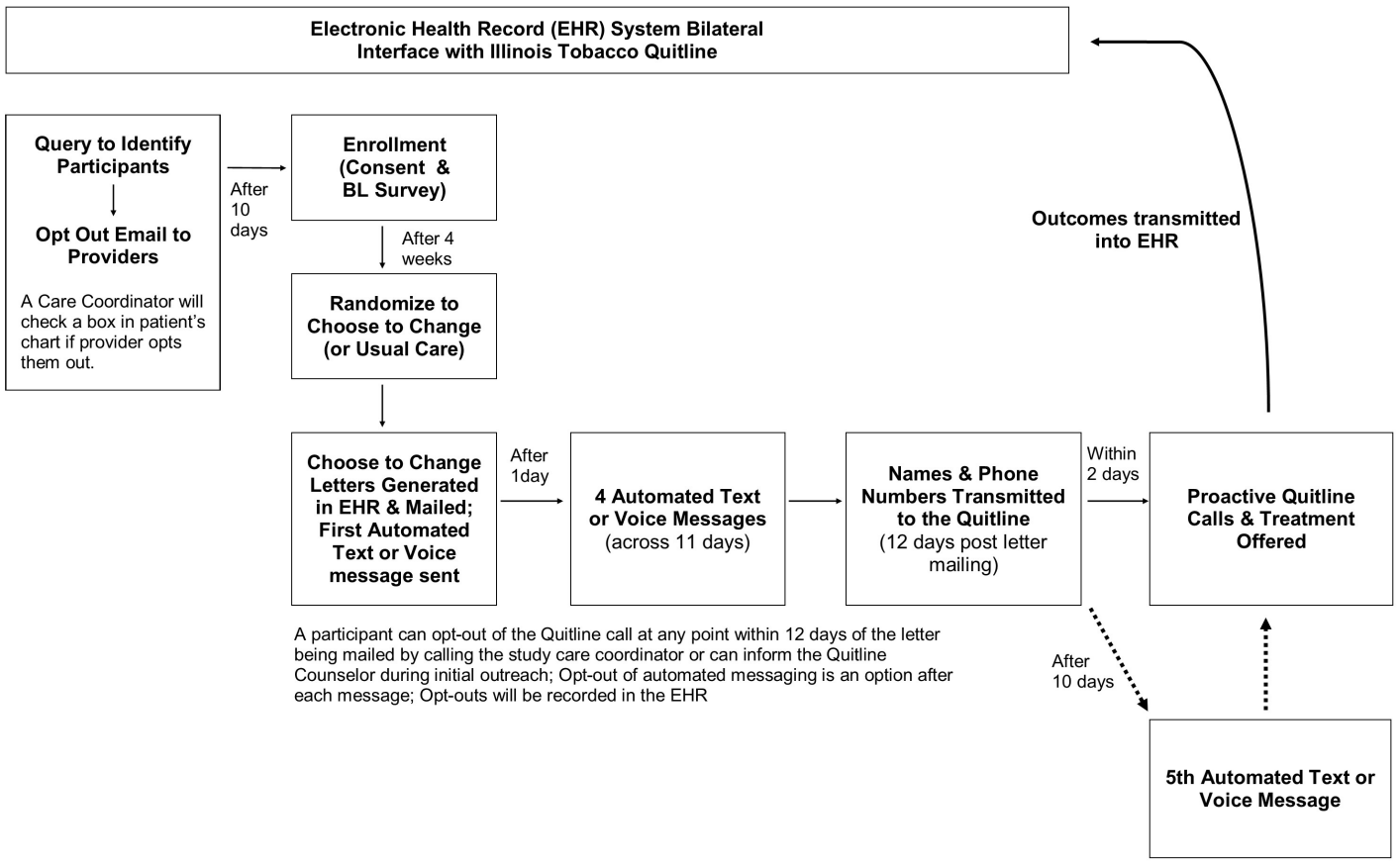
outcomes.[99] Text messaging improves attendance at healthcare visits,[100,101] adherence to diabetes self-care[102] and weight management regimens,[103] as well as the effectiveness of smoking cessation treatment.[99] Popularity of text messaging is high across racial/ethnic groups, socioeconomic levels, and ages.[102]

Two weeks after letter mailing, participants will be contacted by a Quitline counselor and offered free person-centered behavior counseling (cessation or reduction-focused depending upon patient preference) and free NRT (patch, gum, or lozenge) if determined as safe and appropriate. Please see more detail regarding the proactive Quitline treatment below.

Usual Care Condition: Participants assigned to this clinic-based control comparison will receive NNHSC clinic-based care for smoking that follows the Ask, Advise, Refer approach.[19] Following the practice adopted by NNHSC in 2011, a Usual Care participant who smokes will receive a referral for proactive Quitline treatment according to the following established clinic procedure: If the participant is seen in the clinic for a health problem or routine evaluation, a medical assistant will confirm current smoking and advise the participant to quit using clear and strong language. Current smoking and advice to quit are documented in the EHR system and the participant will be seen by the provider who addresses the purpose of the visit. If the provider also addresses the participant's smoking, establishes that the participant is motivated to set a quit date, and the participant agrees to the Quitline referral, a referral form is generated via the EHR system. Referrals are transmitted electronically via the Quitline website by the Care Coordinator. Participants who are referred will receive a call from the Quitline within 48 hours. Usual Care participants who accept Quitline treatment will receive free person-centered smoking cessation counseling and free NRT (patch, gum, or lozenge). Please note: providers may still refer patients who are not enrolled in this study to the Quitline.

In both conditions, Quitline treatment will continue as accepted or initiated by participants over 28 weeks.

Figure 3. Choose to Change Intervention Workflow



Choose to Change Intervention Clinic Workflow
All recruitment, enrollment, and data collection activities will take place at Winfield Moody Health Center, one of the NNHSC community clinics, or in the NU Preventive Medicine Research Clinic. Once eligible participants are identified by the monthly EHR query, the care coordinator will securely message the Choose to Change participants' medical providers via the NNHSC EHR messaging system stating that the identified patients "*have been selected for a smoking cessation initiative in which they may be approached to participate in a health behavior survey study and possibly offered cessation treatment through the Illinois Tobacco Quitline. You will have a period of ten days to review your patient's medical record and opt out if you believe that either the survey or the treatment would be inappropriate for this/these patient(s) at this time."* We expect this to be rare as none of the providers of patients involved in our pilot study chose to exclude them from participation. During the 10-day opt-out period, all patients will be sent recruitment postcards about the possibility of survey study participation. After the 10-day opt out period, research assistants will make recruitment calls to all patients whose providers have not opted out of the study or Quitline referral. On these recruitment calls, research assistants will ask to discuss the study in more detail, conduct initial screening, enroll those who are eligible and interested, and complete the baseline study survey. After participants have completed the baseline survey, they will be randomized to either Usual Care or the Choose to Change (CtC) intervention.

For those randomized to the CtC intervention group, the CtC letter, electronically signed on behalf of Dr. Tim Long of NNHSC, will be created by the EHR system on NNHSC letterhead and mailed by the care coordinator or research assistant. One day after CtC letter mailing, the first CtC text message will be sent to notify CtC participants of the coming letter. The remaining 4 text messages will be sent per the timeline described above. After a 12-day participant opt-out period (described in the letter), names and contact details, including best times to be called, will be sent by the EHR referral system to the Quitlineat 7:00pm each day a referral is made. Participants will be called within two days of referral. NNHSC and each of its clinics will have a unique code that will be sent via the EHR system to the Quitline along with an encrypted referral file of Choose to Change participants. A different code, but unique to NNHSC, will be used to identify and track outcomes for Usual Care participants. All codes will be specific to this study. They will serve to identify the study protocol: cessation-focused counseling and NRT or reduction-refocused counseling and NRT as a first step to smoking cessation. Once reached by the Quitline, the participant's referral data will be shown on one screen and the study protocol via the virtual library will be shown on a second screen. The protocol description and required data fields will ensure that participants are provided reduction-focused counseling if chosen, free NRT if willing and deemed safe, and that additional project-required data are collected. Patient-specific outcomes will be transmitted to NNHSC at the end of each day.

Proactive Quitline Treatment for Choose to Change and Usual Care Conditions
Participants in both treatment conditions will have the opportunity to receive the same proactive Quitline treatment consisting of person-centered behavior counseling and NRT. The Quitline protocol relies on treatment determined to be effective in the 2008 U.S. PHS Clinical Practice Guideline.[5] Participants who are reached and who accept treatment will first be asked for basic sociodemographic and smoking information. After registration and brief assessment, either smoking cessation- or reduction- focused treatment will be delivered depending on patient preference. Participants who choose reduction as their initial treatment goal will be guided toward setting a quit date aided by NRT. For all participants who engage in treatment, a self-help packet (Quit-Kit) will be mailed to provide written information on the topics covered during the initial phone session. Most calls last about 30 minutes, with the behavior counseling portion lasting about 15 minutes. A free 8-week course of NRT (patch, gum, or lozenge) will be mailed in two week allotments to participants who are willing to set a quit date and interested in and eligible to use NRT (i.e., free of medical contraindication). Per Quitline policy for Chicago residents, NRT is offered at no cost for uninsured residents and reduced cost for those who have Medicaid insurance. Because free NRT increases use of quitline treatment,[46,104] NRT will be made available at no cost to all participants to eliminate differential cost by insurance type as a potential confounder of intervention effects.

If a participant is reached by the Quitline counselor but has not received the Choose to Change letter, smoking cessation or reduction treatment will be offered and delivered according to the participant's preference. For participants not reached during the first call attempt, the Quitline counselor will make two more calls in the following two days. A voice message will only be left if the voicemail inbox belongs to the referred participant. If three calls are made without a response, the outreach process will end. The Quitline counselor will either call at times designated by the participant to be convenient or at varying times during the day. The Quitline provides services seen days per week, from 7:00 AM through 11:00 PM.

MEASURES

EHR Characterization of Population

The EHR query to identify participants will also generate information on the following characteristics: *sociodemographic* (age, gender, race, ethnicity, marital status, household income, education), *smoking history* (number of years smoking, past year quit attempts, use of multiple tobacco products, past referral for smoking cessation treatment, including quitline), and *healthcare* (e.g., date of last clinic visit, type of health insurance, most recent problem list). A second query will be run at the 8-month time point to generate number, dates, purpose of any clinic visit(s) during the study period, whether or not smoking was addressed (a required field the EHR system), and an updated problem list.

Characterization of Population that Engages in Quitline Treatment

Participants who accept the Quitline call will complete a registration process that includes brief assessment of *smoking and smoking history* to guide treatment. Information will be obtained on current smoking, including frequency and preference for menthol cigarettes. If non-daily smoking is endorsed, counselors will ask about a typical smoking day. If daily smoking is endorsed, cigarettes per day and time to first cigarette will be obtained. Counselors also ask about how long the participant has been a smoker, number of past quit attempts and, if any, by what method.

Telephone Surveys on Health Behaviors

Because many outcome, moderator, mediator, and control variables cannot be received from the Quitline via the EHR system for participants who do not engage in Quitline treatment, enrolled participants will complete the "NNHSC Health Habits and Wellness service needs survey" of smoking status and moderator, mediator, and control variables via telephone interview at baseline (week -4; 4 weeks before randomization to treatment and letter mailing), 6, 14, and 28 weeks.

Treatment Outcomes

Treatment engagement will be measured at 6, 14, and 28 (as applicable) weeks after letter mailing, and operationalized as the proportion of participants who accept the proactive Quitline call and accept treatment as defined by completing the counseling session. Participants who return a Quitline call and accept treatment also will be counted as having engaged in treatment. Further, we will assess: 1) the proportion of smokers who request cessation versus reduction counseling; and 2) the proportion of smokers who engage in treatment and who request NRT and (or) schedule a follow-up (proactive or reactive) counseling call.

Treatment utilization will be measured at 6, 14, and 28 (as applicable) weeks and will be defined as the proportion of participants who complete ≥1 additional counseling calls and receive and use NRT. The frequency and duration of sessions will also be measured.

Smoking cessation at 6 and 14 weeks will be defined as self-reported abstinence (not even a puff of a cigarette) for ≥7 days. At 28 weeks, breath CO will be used to verify abstinence for participants in the original study timeline. For participants in the alternative shorter study timeline, breath CO will be measured at 14 weeks to verify abstinence. Participants will be classified as abstinent if they report not smoking (not even a puff of a cigarette) for ≥7 days and have a CO ≤8 parts per million (ppm). Participants will be assumed to be smoking if they report smoking, cannot be reached to provide data, fail to provide a breath sample, or provide a breath sample that is >8 ppm.[105] Participants who report abstinence at 28 weeks (original timeline) or 14 weeks (alternative shorter timeline) will be invited for an in-person visit for breath carbon monoxide (CO) measurement to bio-verify abstinence status.

Moderators, Mediators, and Covariates

Hypothesized moderators of Choose to Change effects will be measured at baseline and include readiness to quit smoking,[96,97] recent smoking reduction,[51] cigarettes per day, time since last clinic visit during which smoking was addressed, initial choice of cessation versus reduction, race/ethnicity, perceived stress, , and discrimination. Hypothesized mediators of intervention effects on treatment engagement, utilization, and cessation will be measured at each survey time point and will include perceived autonomy support, autonomous motivation, confidence in ability to quit, and attitude towards NRT.

Demographic Questionnaire: Age, gender, ethnicity, and race will be measured only at baseline. Current regular smoking (daily or weekly), NHHSC home clinic for primary health care, and residential address will be confirmed. Participant residential addresses and telephone numbers will be confirmed at the baseline

assessment prior to treatment randomization to verify that the address in the EHR is accurate. This will help ensure that the participant receives the Choose to Change letter. Residential and email addresses will be confirmed at each survey.

Health Behaviors Assessment: This questionnaire will assess diet, alcohol use, physical activity, sedentary behavior, perceived stress, cigarette smoking/recent treatment (including Quitline treatment) and motivation to quit, and current desire for various health promotion services. Past week physical activity and sedentary behavior will be measured using the International Physical Activity Questionnaire short form. Health Information National Trends Survey (HINTS) items were used to assess fruit, vegetable, and sugar-sweetened beverage consumption. Alcohol consumption over the past 30 days will be assessed using the two-item PhenX Alcohol Use module. Perceived Stress will be assessed with the 4 -item Perceived Stress Scale will be used to measure general stress experienced over the last month.

Perceived Autonomy Support: The Health Care Climate Questionnaire consists of six statements that respondents must indicate the degree to which they experience their health care provider(s) as autonomy supportive versus controlling. Each HCCQ statement is scored on a 7-point Likert scale (1=Not at all True, 7=Very True). E.g., "I feel that my health-care practitioners have provided me with choices and options about smoking (including not quitting)."

Attitudes Towards Nicotine Replacement Therapy Scale (ANRT): The ANRT is a 12-item scale consisting of two subscales measuring the perception of the advantages of NRT (8-items) and drawbacks (4-items) of nicotine replacement therapy to quit smoking. "Advantages" taps beliefs that NRT will provide relief from withdrawal and craving during cessation, and "drawbacks" describes concerns about NRT dependence, side-effects, and efficacy. Scores have been associated with intention to use NRT, prior NRT use, nicotine dependence, and among those who have ever used NRT, the number of days of use.

Retention and Adherence

Based upon our past experience with clinical trial and prospective cohort studies of diverse populations (R01 DA025078; N01 HC48049), we expect at least a 60% participation rate across the four surveys. In our recent smoking cessation trial,[94] of the 1,989 sessions scheduled for the 259 participants at the Northwestern clinical site over their first 6 months, 1,604 (81%) were completed.

To maximize enrollment in this study, we will:

1) Target patients who are most likely to view one of the NNHSC clinical sites as their medical home through defining eligibility based in part on at least one clinic visit during the past year;[107]
2) Include monetary compensation for each survey completion, plus $50 for completing the in-person session at week 28 (original timeline) or week 14 (alternative shorter timeline);[107] and
3) Develop and implement strategies to engage the NNHSC community.[108,109] Drs. Alicia Matthews and Faith Fletcher, along with Dr. Melissa Simon, will provide critical guidance on best practices and issues of cultural competency related to research targeting low-income and African American populations.[110,111] For example, we plan to conduct a clinic-wide outreach campaign across the seven participating NNHC clinics to increase interest in the health habits survey. Additionally, we will use small, low-cost giveaways to increase recognition of the survey once research assistants because to recruit and enroll patients.

We have developed a plan to maximize retention of participants to overcome follow-up challenges that are often experienced in longitudinal studies of low-income populations,[112-114] such as residential instability. Strategies will include the following:

1) A user-friendly electronic tracking database of participants;
2) Elicitation at baseline and every follow-up session of relative and (or) neighbor contacts to locate participants if needed;
3) Research personnel training on team building and positive attitudes;
4) Flexible scheduling of telephone sessions, including Saturday appointments;
5) Sending personalized reminder cards and retention items (i.e., water bottles, draw string bags, earbuds, T-shirts);
6) Reminder letters with small giveaway items sent one week prior to their scheduled session and reminder calls to participants 1-2 days prior to their scheduled session
7) Establishing strong rapport with participants by providing a friendly experience during assessments;

8) Sending seasonal newsletters about living a healthy lifestyle;
9) Demonstrating a positive and caring attitude towards participants[109];
10) Rapid rescheduling of missed appointments; and
11) Acknowledgement and appreciation of participant effort.

These enrollment and retention strategies have been effective in pragmatic clinical trials and community studies of underserved populations,[112-115] as well as in our ongoing cohort study (N01 HC48049).

STATISTICAL ANALYSIS PLAN

Power

To address power for hypotheses related to **Aim 1 (Treatment Engagement at 6 Weeks),** we base our estimates for the proportion of participants completing a Quitline session by 6 weeks in the Choose to Change condition on our pilot study that resulted in a **24%** engagement rate. As for the Usual Care condition, we expect that current NNHSC Ask, Advise, Refer practice involving the Quitline as the primary referral program will result in a tripling to **10%** of the 3.3% engagement rate achieved in our EHR fax-referral project, in which our NIH-funded study of long-term nicotine patch treatment, with inclusion and exclusion criteria, served as the primary referral program.[94] Assumed rates by condition for each of the three outcomes of interest and participants per condition are presented in Table 3. We propose that a minimum of N=265 independent participants be randomized to Choose to Change versus N=265 to Usual Care, for a total N=530. Such a 1:1 allocation ratio guarantees **99% power** for the comparison of Choose to Change versus Usual Care at two-sided alpha=.05. This sample size requirement equates to 40 participants per month over the 15-month randomization period. In our three-week pilot study, 132 patients were processed through the workflow in Figure 3, a rate of 175 per month.

Table 3. Assumed Intent-to-Treat Rates by Condition for the Three Outcomes of Interest and Participants per Condition

Study Aim	Usual Care	Choose to Change
Aim 1: Engagement (6 Weeks)	10%	24%
Aim 2: Utilization (12 Weeks)	7%	15%
Aim 3: Cessation (26 Weeks)	2%	7%
Participants	265	265

Our power estimates for **Aim 2 (Treatment Utilization at 14 Weeks)** will be based on Williams et al.[9] who reported a 30% utilization rate for combined counseling and medication at a later time point than ours (6 months), following a face-to-face SDT-based intervention. Assuming 6-month utilization rates (one or more counseling calls after the initial counseling call) for the Usual Care and Choose to Change conditions of **7%** and **15%**, respectively, would be consistent with their treatment utilization odds ratio of 2.38 (95% CI=1.67-3.39), albeit at a lower baseline rate than they report. Our proposed randomization plan guarantees **84% power** for the comparison of Usual Care versus Choose to Change at two-sided alpha=.05.

Our power estimates for **Aim 3 (Smoking Cessation at 28 Weeks)** will be based primarily on Rigotti et al.[27] who reported 7-day point-prevalence abstinence rates at 14 weeks of 1% for standard care and 5% for population mail outreach under an Intent-to-Treat (ITT) approach. We expect that these 12-week ITT rates will rise to 3% in our Usual Care condition and 10% in the Choose to Change condition. Even if these rates then drop to **2%** in our Usual Care and **7%** in Choose to Change at 26 weeks, we still have **80% power** for the comparison of Choose to Change versus Usual Care at two-sided alpha=0.05

Data Analysis

All outcomes of interest for **Primary Aims 1-3** are binary (treatment engagement, treatment utilization, smoking cessation) and can be analyzed using logistic regression methods. Analyses will be conducted first using an ITT principle (missing=treatment failures). We will also conduct an adherence sample analysis that includes only participants reached at the 28-week follow-up (≥ 75% of the sample based on our experience). This approach addresses the question of effectiveness more directly, but it is subject to more bias if attrition is large or differential by treatment condition. Therefore, we will complement it by analysis of non-response patterns using sociodemographic (age, gender, race, ethnicity, marital status, household income, education), and healthcare (time since last clinic visit, type of health insurance) characteristics. These can be used to create propensity scores that allow for inverse-probability-weighing (IPW) of observed outcomes[116,117] to achieve balance across potential confounders of the treatment-to-outcome relationship. Ideally, the distribution of propensity scores will show large overlap across study conditions. If not, that will be taken as evidence that completers are not comparable on measured confounders across conditions, and that one should refrain from

further comparisons. PROC GENMOD of SAS/STAT 9.2[118] can handle subject-level probability weights. Similar findings across all three approaches would increase confidence in the results overall. Both raw and adjusted rates will be presented for each outcome by study condition. For the cessation outcome, we will also explore the impact of smoking history (e.g., past year quit attempts, past referral for Quitline treatment), race, and gender on non-response. We will also use propensity score modeling to examine the relationship between treatment utilization at 14 weeks and abstinence at 28 weeks. Since available data indicate little effect of NRT type on outcome, we will model NRT dose/duration, while controlling for patterns of utilization.

Exploratory Aim 1 (Moderators of Choose to Change Effects). We will focus our search for moderators on baseline variables such as readiness to quit, health literacy,[71] smoking level, time since the patient's last clinic visit in which smoking was addressed, and recent smoking reduction.[53] Participants who smoke more than 10 cigarettes per day, who have recently attempted to reduce their smoking, and those lower on motivational readiness to quit are expected to be disproportionately responsive to Choose to Change intervention. In addition, participants with lower literacy and those with a more recent clinic visit during which smoking was addressed are expected to be especially likely to benefit. These factors are expected to be especially responsive to the person-centered and the low-income targeted elements of the Choose to Change intervention (Figure 2), though we realize that there may be other potential moderators. Other variables to be explored as potential moderators include initial choice of smoking cessation versus reduction, and race/ethnicity. Analysis will be conducted using logistic regression, with a separate model for each outcome variable. The predictor variables will include treatment condition, the moderator variables, and their two-way interactions with condition. Sociodemographic (e.g., gender), psychosocial (e.g., perceived stress), and smoking (e.g., menthol cigarette use) variables known to influence smoking cessation will serve as covariates.

Exploratory Aim 2 (Mediators of Choose to Change Intervention Effects) hypothesizes that increases from baseline in confidence in one's ability to quit, positive attitude towards NRT, autonomy support, and autonomous motivation will mediate the effects of the Choose to Change intervention on study outcomes (Figure 2). We will establish mediation using MacKinnon's approach,[120] which is more powerful than Baron and Kenny's causal-steps method.[121] This approach is explained in Cerin and MacKinnon[122] and implemented by Papandonatos et al.[123] Simultaneous estimation of the effect of mediators (e.g., confidence in one's ability to quit, positive attitude towards NRT) will be conducted as in Napolitano et al.[124] Although we see value in building the model in a piecewise fashion (in terms of evaluating the need to adjust for potential confounders of the treatment to outcome relationship) we will complete the mediation analysis by estimating the full model in a single step using the structural equation modeling package Mplus 6.0,[125] which will allow us to assess the statistical significance of any complete mediation path evaluated via bootstrapping.

MULTIPLE SITES

This research study is part of a larger U54 grant (PI: Simon) that establishes a three-institution partnership between Northwestern University, University of Illinois at Chicago, and Northeastern Illinois University. As such, there is a Co-PI from each of the partnering institutions (Alicia Matthews, UIC; Christina Ciecierski, NEIU; both noted on page 1) for this study. Northwestern is the lead site, and Brian Hitsman serves as the lead project PI. All research activities will be conducted at one of the partnering community organizations (Near North Health Services Corporation; Tim Long, Site-PI), and the NNHSC research committee has reviewed and approved this protocol. All research activities will be conducted by NU research personnel who, in addition to the NU IRB-required human subjects protection training, have completed the human resources training and HIPAA-compliance training required by NNHSC for all NNHSC clinical personnel, thereby allowing these NU research personnel permission to access the NNHSC electronic health record and the data contained therein, and the approval to contact NNHSC patients using the procedures described in this protocol. No research activities will be conducted at either UIC or NEIU.

Alicia Matthews (UIC Co-PI) and Yamile Molina (UIC Co-I) contribute their expertise in community-based participatory research in smoking cessation among low-income and disenfranchised populations, and Dr. Matthews, specifically, designed our recruitment and retention plan. Christina Ciecierski (NEIU Co-PI) will be leading the cost evaluation component of the study.

Alliance of Chicago will provide research and EHR technical expertise for NNHSC's EHR (i.e., Alliance will build the e-Referral, e-Outcomes and letter components of the Choose to Change intervention within NNHSC's EHR.

The Illinois Tobacco Quitline will provide their evidence-based cessation treatment to all participants who accept the referral and proactive call from the Quitline counselors. The Quitline staff will conduct the same counseling to study participants that they do to any other caller or patient referred for services. They will also electronically send the treatment outcomes information to the NNHSC EHR for all participants who complete Quitline counseling sessions.

All partners, academic and community-based, will be provided with a current IRB-approved protocol. As all staff conducting the research activities are NU staff, we hold regular weekly meetings to ensure successful coordination of these activities and ongoing research protocol monitoring.

Community-Based Participatory Research
The Choose to Change intervention has benefitted from six-year collaboration with NNHSC, including Winfield Moody Health Center, Alliance, and the Illinois Tobacco Quitline. NNHSC providers and patients guided and contributed to the development of key aspects of the Choose to Change intervention, including the letter, and clinical workflow. Because of this long-term partnership, we have established a system to ensure the successful coordination of research activities across all collaborating organizations. Specifically, the PIs and research managers from NNHSC, NU, and Alliance of Chicago biweekly during the EHR-system build and through project launch. Additionally, the Alliance research manager, project director (from NU), and Quitline manager meet once monthly to address any issues that arise regarding development, study implementation, and evaluation.

Setting
The setting for this study will be Winfield Moody Health Center, which is the flagship clinic and administrative location for NNHSC, and the NU Preventive Medicine Research Clinic (680 N. Lake Shore Drive, Suite 1410, Chicago). All aspects of the study, i.e., query list identification, outreach recruitment calls, all telephone surveys, intervention letter creation, sending of intervention text messages, mailing of recruitment and retention materials, in-person clinic sessions, will take place at either Winfield Moody or the NU Preventive Medicine Research Clinic. Additionally, for participants who report abstinence at their week 28 phone session, they will be offered the option to conduct the in-person clinic visit at either their home NNHSC clinic location or the NU Preventive Medicine Research Clinic.

Prior Approvals
The NNHSC Research Committee has reviewed and approved the study protocol.

CONSENT PROCESS
Baseline and follow-up surveys will be completed by telephone; therefore, verbal informed consent will be obtained from patients prior to being enrolled. To obtain verbal informed consent, the RA will read the IRB-approved informed consent document to the candidate that includes all components of a standard informed consent form, including study description and procedures, risks and benefits of participation, alternatives to participation, financial information, protection measures taken to ensure participant confidentiality, research subject rights, and who to contact with any questions or concerns about the study. Enrolled smokers will be given the option to receive the informed consent form, via traditional mail or email, that was used to document their verbal consent and signed by the RA who obtained the consent.

During each telephone surveys, participants will be encouraged not to answer any question that makes them feel uncomfortable. It will be explained during consenting and before administration of all surveys that they may stop the survey at any time and that doing so would not negatively affect their healthcare.

Participants enrolled in the alternative/shorter study timeline will be read an edited consent that accurately explains the shorter timeline and corresponding compensation. All other aspects of the consenting process will be the same as the participants completing the original study timeline.

<u>Incomplete Disclosure</u>
The verbal consent will include information about the health habits survey only as full disclosure of the content and purpose of the Choose to Change intervention could compromise our ability to evaluate the intervention. We believe that the randomized controlled trial portion of this study is eligible for a waiver of written informed consent because it meets established criteria. First, participation in the RCT poses very low risk to participants,

i.e., no more than minimal risk to participants. Second, informed consent cannot be obtained without seriously threatening the validity of the study. The focus of this study is to evaluate the extent to which the Choose to Change letter motivates patients to engage in and use Quitlince treatment to achieve short-term smoking cessation. The Choose to Change intervention is novel in that it attempts to increase engagement in treatment through encouraging a variety of initial treatment goals, ranging from abrupt smoking cessation to gradual smoking reduction to simply learning about smoking and smoking cessation. The central idea is that smokers who are highly ambivalent about quitting will be more motivated to engage in Quitline treatment because there will be no pressure to set a quit date and abruptly quit. The usual approach to smoking cessation treatment in primary care requires a commitment to abrupt quitting. Disclosure of this flexible approach to addressing smoking cessation would expose Usual Care participants to the central message of the Choose to Change intervention and significantly undermine our ability to observe an intervention effect on Quitline engagement, utilization, and cessation. Disclosure of Quitline treatment would result in a small sample of participants who are ready to quit smoking, significantly undermining our intent to address smoking among patients who are not ready to attempt quitting (95% of all smokers). As achieved in our past randomized controlled trials,[18-20] a waiver of informed consent allows for the entire population of eligible smokers to be included in the study, thereby achieving a true assessment of the effectiveness of Choose to Change versus Usual Care without selection bias. Third, the waiver will not adversely affect the rights and welfare of participants. Patients randomized to the Choose to Change arm are given multiple opportunities to opt themselves out of the Choose to Change text messages and referral to the Quitline. After the final survey has been completed, Usual Care participants who report continued smoking will be offered a referral to the Quitline.

Debriefing
Once the study is complete and all participants have completed their last follow-up survey, all participants will be fully debriefed via newletter (emailed or traditionally mailed, based on participant preference) regarding the randomized controlled trial.

Process to Document Consent in Writing
This research study presents no more than minimal risk to participants and because survey data is collected over the telephone, we plan to obtain verbal consent to participate in the survey study and offer the participant a hard copy of the consent document.

Withdrawal of Subjects
Participation in this research study is completely voluntary. Participants do not have to answer any question that that they prefer not to and will be told this. It will be explained to participants that they can withdraw at any time, that choosing not to be in this study or to stop being in this study will not result in any penalty or loss of benefit to which participants are entitled, including health care benefits, and that withdrawal from the study will not negatively affect any rights to which they are otherwise entitled, including their right to any present or future treatment. Participants will be told that they must confirm verbally with research staff if they are choosing to withdraw from the study, after which time no more data will be collected from them. It will also be noted that if participants chose to withdraw from the study, any information/data collected prior to their withdrawal of consent can be used for research purposes.

Sharing of Results with Subjects
If requested by participants, overall study results, in aggregate, will be distributed to participants once the study has been completed.

RISK/BENEFIT ASSESSMENT

Potential Study Risks
The risks of participation in this study are very low. The established Business Associate Agreement will allow the secure integration of the NNHSC EHR and Quitline networks, effectively making a unified, HIPAA-compliant system and eliminating typical threats to confidentiality. This unified network system uses HL7, a health communication language that provides direct, secure, bi-directional transfer of protected health information between the NNHSC EHR and the Quitline's secure server. The Quitline's secure server on which patient data is stored is completely separate from its other network server that is dedicated to email and other functions that do not include protected health information. This provides a higher level of protection of patient data confidentiality and privacy. There are three stages at which NNHSC providers, on behalf of their patients, or patients themselves can decline participation in the randomized clinical trial: a) prior to any outreach to

enroll patients in the study or referral to the Quitline, all NNHSC providers will be able to exclude patients whom should not attempt smoking cessation; b) clear instructions for declining participation will be provided in the Choose to Change letter, i.e., the patient may call the study care coordinator and request that his/her name and contact information not be securely transmitted to the Quitline; and (c) patients will be given the opportunity at the start of the Quitline call to decline participation.

Patients who engage in Quitline treatment may experience mild discomfort when asked about smoking or concerns related to smoking cessation or gradual smoking reduction. Additionally, for participants who quit smoking or reduce, it is possible that they will experience symptoms of tobacco withdrawal. The most common symptoms of withdrawal are anxiety, irritability, difficulty concentrating, insomnia, and restlessness. The Quitline counselors are trained to help patients manage withdrawal symptoms. Patients will be reminded that these symptoms are typically time-limited and they will be taught behavioral strategies to manage symptoms. A free 8-week course of nicotine replacement therapy (NRT; patch, gum, or lozenge) will be mailed in two week allotments to patients who are free of medical contraindications and complete weekly counseling calls. For participants who can safely use nicotine replacement therapy (e.g, the patch, gum, or lozenge) and elect to do so, use of NRT will minimize the severity of withdrawal. Participation in the study does not otherwise involve any physical or emotional risk to study participants beyond that of everyday life.

Potential Benefits to Subjects
Potential benefits for patients are smoking cessation and the associated health and psychological benefits. We expect that successful smoking reduction will build self-confidence and substantially increase the likelihood of the smoker making a quit attempt and achieving successful smoking cessation by eight months. A potential benefit for NNHSC is improved preventive care and improved health for its patients. If the proposed intervention is determined to be effective, we will be able to disseminate it to Alliance's 11 safety net health centers throughout Chicago, comprising over 85 clinical sites that care for almost 500,000 patients.

Study Subject Compensation
Participation in this study will involve no cost to study participants. Participants enrolled prior to mid-February 2018, completing the original study timeline through Week 28 will be compensated for their time and effort up to a maximum of $195. They will earn $25 for completing the first telephone survey, $30 for completing the second survey, $40 for completing the third survey, and $50 for completing the fourth survey. Participants enrolled after mid-February 2018 into the alternative shorter study timeline through Week 14 will be compensated for their time up to $175; earning $35 for the baseline telephone survey, $40 for the second survey, and $50 for the third survey. Participant incentives will be paid as an electronic gift card after each survey. If preferred by the participant, the incentive can be provided to participants as a traditional physical gift card/pre-paid debit card to participants if they come into the clinic to pick up the card and sign paperwork confirming their receipt. Those participants who report abstinence at the week 28 (original timeline) or week 14 (alternative shorter timeline participants only) follow-up survey will be invited to attend an in-person study visit to obtain a breath carbon monoxide (CO) measurement to bio-verify abstinence status. Participants who come in for the in-person visit will be provided a gift card at the completion of that visit ($40 for the visit, $10 to cover travel). If a participant withdraws from the study, s/he will be compensated for all study sessions completed to the point at which s/he withdrew.

We expect that some participants may have cell phones as their primary method of communication with monthly plans that limit the number of voice minutes allowed. Therefore, in order to promote completion of the telephone survey sessions while not consuming their minute allotments, participants who have government-issued or pre-paid cell phones with a voice minute limits will be provided with a $5.00 minute replenishment card (worth 250 minutes) for each survey completed. The card will be sent within a few days of the completed telephone survey.

Compensation for Research-Related Injury
Not applicable. This research involves no more than minimal risk to study participants and does not involve "research-related injury."

DATA SECURITY AND MANAGEMENT
Provisions to Protect Privacy Interests of Participants
Communication of patient information for cessation referrals from Winfield Moody Health Center to the Quitline server will be transmitted by a one-step referral through the NNHSC EHR via a direct portal using Health Level

& (HL7) and HL7-compatible language directly to the Quitline internal network. By connecting directly to the internal server through this secure portal, no patient information is transmitted out of the Quitline's internal network. The email server used is completely separate from the ALA's internal email system. It is located behind a spam filter and a firewall and uses HL7 standards.

The secure electronic transmission of patient name and telephone number to the Quitline will be covered by HIPAA as there is an executed contract currently in place that has established the Quitline as a Business Associate of NNHSC and Alliance. A Business Associate is an individual or organization that performs a healthcare function involving use or disclosure of protected health information for a covered entity. One covered entity may be a Business Associate of another covered entity if it performs such services (i.e., carries out healthcare functions) for the other covered entity [HIPAA 45 CFR 164.502(e), 164.504(e), 164.532(d) and (e)]. NNHSC, Alliance, and the Quitline have completed the process to establish the necessary Business Associate Agreements (BAA) and have all committed to maintaining this clinical partnership.

The automated text messaging procedures to be used in the study were established in our ongoing work (P01 HS021141). We will use the same HIPPA-compliant, web-based service provider, Touch Point Care (www.touchpointcare.com), which specializes in secure healthcare practice-patient communication, such as appointment reminders, lab test results reporting, and other brief communications (e.g., influenza vaccine availability and clinic times). Participants' telephone numbers and preferred communication method will be uploaded via secure transmission to our study-specific, password-protected account on Touch Point Care's encrypted login page (https://www.touchpointcare.net) and will be used to place four separate text messages during the first ten days of study participation, then one final message about 9-10 days after the 4th message. Included in each message will be simple instruction on how to opt-out of further messages and the referral to the Quitline. Opting-out will require the participant to send a text reply with the word "STOP." The contact information for participants who opt-out will be permanently removed from the Touch Point Care account. The research assistant will generate a report within the touchpointcare.net interface that lists all participants who chose to opt-out of the Quitline referral. This information will be noted in the participant's EHR.

Study records generated through the telephone surveys that can identify participants will be kept confidential by assigning a unique study ID number to them. Names and identifying information will be kept completely separate from survey responses. The REDCap database and the web server are housed on secure servers operated by the Northwestern University Biomedical Informatics Center (NUBIC). Access to study data in REDCap will be restricted to the research team members by username and password. All paper data will be stored in locked cabinets in a locked office at Northwestern University Department of Preventive Medicine.

Data Collection and Management
The telephone surveys of smoking status and moderator, mediator, and control variables will be conducted at NNHSC. Data will be entered and managed using Research Electronic Data Capture software (REDCap), which uses a MySQL database via a secure web interface with data checks used during data entry to ensure data quality. REDCap includes a complete suite of features to support HIPAA compliance, including a full audit trail and user-based privileges. The MySQL database and the web server are housed on secure servers operated by the Northwestern University Biomedical Informatics Center (NUBIC). Access to study data in REDCap will be restricted to study personnel by username and password. Any paper data will be stored in locked cabinets in a locked office at Northwestern University Department of Preventive Medicine. The Alliance-hosted EHR is linked to a clinical data warehouse that provides for data analysis and reporting at the provider, health center, and population levels. Data cleaning and validation will occur in Months 25-33. The Alliance Data, Reporting, and Quality Informatics Team, led by Mr. Andrew Hamilton and overseen by Dr. Nita Mohanty, will merge the longitudinal survey data with the EHR extracted NNHSC and Quitline data. Once validated, a deidentified database will be securely transferred to a File Transfer Protocol site only accessible to Alliance and Dr. George Papandonatos at Brown University.

Provisions to Monitor the Data to Ensure the Safety of Subjects
The proposed study aims to connect patients who smoke with effective, free smoking cessation treatment. Quitline services, including behavior counseling, self-help materials, and NRT, pose low risk of adverse effects or unsafe use. The four telephone assessments of smoking status and other health behaviors is also a low risk activity. Commensurate with the low level of risk, a Data Safety and Monitoring Board (DSMB) will not be necessary. The established Business Associate Agreement between NNHSC and the Illinois Tobacco Quitline will enable the secure, encrypted network-to-network transmission of protected health information. This system

will eliminate the typical risk of threats to patient confidentiality (e.g., use of traditional fax referrals that can be misplaced). Secure systems of individualized password-protected access to network folders containing patient data provides additional security and confidentiality.

Psychological distress

Although we will not administer a formal measure of psychological distress, if any such symptoms are reported during the telephone interviews or in-person study visits, research staff are trained to offer mental health and case management resources at the conclusion of the survey to these participants. This procedure is similar to what is currently done as part of the other smoking cessation clinical trials in Dr. Hitsman's lab and include several free, low-cost/sliding scale options.

STUDY MANAGEMENT FOR HUMAN SUBJECTS PROTECTION

General Monitoring

The project will be overseen by the Principal Investigator (Dr. Brian Hitsman), the NNHSC Director of Performance Improvement, Health Information Technology, and Research (Dr. Timothy Long), the Alliance of Chicago's Director of Evidence-Based Practice (Dr. Nita Mohanty), the Senior Vice President of Helpline Services at the American Lung Association of Illinois (Mr. Michael Mark), the Northwestern project director (Ms. Anna Veluz-Wilkins), and the project statistician (Dr. George Papandonatos). Drs. Alicia Matthews (University Illinois at Chicago) and Christina Ciecierski (Northeastern Illinois University) will also assist with general monitoring, as will the project collaborators (Drs. Melissa Simon and Kenzie Cameron).

IRB Monitoring

As the official IRB of record indicated in the approved IRB authorization agreement (IAA, Federalwide Assurance #FWA00001549), the protocol will be reviewed by the Northwestern IRB and will only be implemented after successful approval. Annual reporting and auditing will be conducted by the Northwestern IRB. All procedures will be approved by the Northwestern IRB and accepted by the UIC and NEIU IRBs. The Northwestern IRB will review and monitor the research protocol detailing the study, data collection procedures, risks and benefits, the waiver of informed consent for the randomized clinical trial, and the verbal informed consent for the surveys of smoking status and behaviors. The NU IRB will monitor and review all approved protocols annually. The Research Committee at NNHSC has already reviewed and approved this research protocol.

Qualifications to Conduct Research and Resources Available

The Choose to Change intervention has benefitted from six-year collaboration with NNHSC, including Winfield Moody Health Center, Alliance, and the Illinois Tobacco Quitline. NNHSC providers and patients guided and contributed to the development of key aspects of the Choose to Change intervention, including the letter, and clinical workflow.Brian Hitsman, Ph.D., Alicia Matthews, Ph.D., and Christina Ciecierski, Ph.D., serve as PIs of the

Choose to change research project (*Reducing tobacco use disparities among adults in safety net community health centers)* as required by the U54 grant. Dr. Hitsman has a full-time appointment as assistant professor in the Department of Preventive Medicine at Northwestern University (NU) Feinberg School of Medicine. He has been a member of the NU Robert H. Lurie Comprehensive Cancer Center since 2008 and is Co-director of Responsible Conduct of Research Training in the NU Clinical and Translational Sciences Institute. Dr. Matthews has a full-time appointment as associate professor in the College of Nursing at the University of Illinois at Chicago (UIC). She also serves as Director of the Recruitment and Retention Core in the UIC Center for Clinical and Translational Science. Dr. Ciecierski has a full-time appointment as associate professor in the Department of Economics at Northeastern Illinois University (NEIU). Led by Dr. Hitsman, the proposed research project unites NU, UIC, and NEIU by extending a four-year NCI-funded collaboration with Dr. Ciecierski (P20 CA165588; PI, M. Simon) and a two-year collaboration with Dr. Matthews on the pilot studies that serve as the critical foundation for the proposed research project. Together, the PIs are committed to addressing cancer health equity through reducing racial and socioeconomic disparities in tobacco use.

Dr. Hitsman will work with Drs. Matthews and Ciecierski, in collaboration with the project community partners, on finalizing the intervention, on recruitment, enrollment, and retention of participants, and on the repeated

assessment of smoking cessation and other variables in the randomized clinical trial. Dr. Matthews will guide the implementation of best practices of cultural competency in smoking cessation research with low-income minority populations and of community-based participatory research.

Dr. Hitsman will oversee the NU project director and research personnel who will assist with all aspects of study implementation, recruitment, enrollment, and retention, and data management and quality control. Dr. Hitsman will coordinate regular meetings of the research team and will serve as the principle conduit for communication among PIs, Co-Is, and research personnel, as required. As achieved during the development of this U54 research project, the PIs and Co-Is of the community partnering organizations will meet biweekly in person to review and problem-solve study implementation, evaluation, and administration. Dr. Hitsman will hold monthly in-person meetings with the full research team to review achievement of project milestones and problem-solve issues as needed. Co-Is from outside of Chicago (Mr. Mark and Dr. George Papandonatos, Brown University) will attend by video-conference. As contact PI, Dr. Hitsman will serve will assume responsibility for the fiscal and administrative management of the project. In addition, he will be responsible for communication with NIH and submission of annual reports to NIH.

Dr. Hitsman will oversee data analysis and interpretation, but will share responsibility with Drs. Matthews and Ciecierski in writing and coordinating scientific publications and communications arising from the research project. Publication authorship will be based on the relative scientific contributions of the PIs and the rest of the research team. If a potential conflict develops, the PIs will meet and attempt to resolve the dispute. If they fail to resolve the dispute, the disagreement will be referred to an arbitration committee consisting of one impartial senior executive from each PI's department and a fourth impartial senior executive mutually agreed upon by both PIs. No members of the arbitration committee will be involved in the U54 grant.

Near North Health Service Corporation

NNHSC is a 501(c)(3) non-profit Federally Qualified Health Center (FQHC). It is one of the largest providers of community-based primary care in Chicago. NNHSC targets a primary catchment area that encompasses 68 zip code areas throughout Chicago, serving a diverse and largely underserved population. While disparate, NNHSC communities are characterized by large concentrations of Chicago Housing Authority high rise apartments, abandoned residential buildings, blighted commercial properties, and an utter absence of basic services and healthcare resources. The goal of NNHSC is to provide access to high quality healthcare and to improve the health and well-being of the diverse populations and the communities that it serves. NNHSC is a culturally sensitive, patient centered community health center that empowers individuals through education and health prevention, regardless of one's ability to pay.

A full array of primary care clinical services and comprehensive social support programs are provided through NNHSC's nine community health centers that serve over 35,000 patients. Seventeen percent of NNHSC users are smokers. Over half (56%) of the population is uninsured, 40% have Medicaid coverage, and 4% are covered through Medicare. Females account for 63% of NNHSC patients. Ninety-six percent of NNHSC users live at or below 100% of the Federal Poverty Index (FPI). Partnering with NNHSC allows the proposed study to target a diverse, underserved, low-income population.

Alliance of Chicago

Alliance of Chicago was built on partnering with community health centers and has an established relationship with NU. Alliance is a Health Resources and Services Administration-funded network of independent primary care community health centers that supports a centrally hosted electronic health record (EHR) system shared by 32 safety net health centers in 12 states. Eleven of the 32 centers are in Chicago, with over 80 clinical sites and 200,000 patients. NNHSC is one of the four founding member centers of Alliance; the others are Erie Family Health Center, Howard Brown Health Center, and Heartland Health. The target populations in Chicago are low-income and uninsured minorities: Latino, African American, Gay and Lesbian, and Immigrant and Homeless. As a network of Federally-Qualified Health Centers (FQHCs) all on a shared, centrally hosted electronic health record (EHR) system, the Alliance of Chicago is uniquely positioned to develop and implement a multifaceted, technology-based model for improving smoking rates in the city of Chicago. The Alliance EHR system for all clinical encounters (General Electric Centricity, Practice Solution 14) is distinguished by the integration of evidence-based practice recommendations into the end user interface to provide decision support at the point-of-care and facilitate routine reporting against national performance measures. The Alliance-hosted EHR is linked to a clinical data warehouse that provides for more robust data

analysis and reporting at the provider, health center, and population levels. Finally, the Alliance has invested in geo-mapping tools (ESRI software) that help convert data into actionable information, by visualizing exactly where, on the neighborhood map of Chicago, the greatest opportunities for improvement exist.

Other Members of the Research Team
The following people will be directly involved with study implementation and execution:

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