Cover page: Study protocol and statistical analysis plan and consent form

Title Babies Living Safe and Smokefree (BLiSS)

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Title of research: Babies Living Safe and Smokefree (BLiSS) Program, IRB PROTOCOL 23188

Investigator and Department: Bradley N. Collins, Ph.D., Department of Behavioral Sciences, and Stephen J. Lepore, Ph.D., Department of Behavioral Sciences

Why am I being invited to take part in this research?

We invite you to take part in a research study because you were referred by your WIC nutrition counselor, are above 18 years old, you currently smoke, and you have a child less than 6 years of age.

What should I know about this research?

- Someone will explain this research to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Who can I talk to about this research?

If you have questions, concerns, or complaints, or think the research has hurt you, contact the research team at:

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This research has been reviewed and approved by an Institutional Review Board. You may talk to them at (215) 707-3390 or e-mail them at: irb@temple.edu for any of the following:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

Why is this research being done?

This health counseling study is a partnership between the Philadelphia WIC program and behavioral health staff at Temple University. The goal of the study is to help improve your family's health.

How long will I be in this research?

We expect that you will be in this research for 1 year.

How many people will be studied?

We expect about 370 people will take part in the research.

What happens if I agree to be in this research?

Your participation will include the following:

1. You will be assigned to one of two groups: a group that focuses on reducing your children's exposure to tobacco smoke OR a group that focuses on improving your family's nutrition on a budget. The group you are assigned to will be chosen by chance, like flipping a coin. Neither you nor the study doctor will choose what treatment you get. You will have an equal chance of being in either group. Please consider whether you are open to being assigned to EITHER group.
2. You will complete three 30-minute phone interviews, and three brief in-home visits. These are scheduled at Week 1, after you finish health counseling (week 12), and 1 year after you start the program.
    a. These interviews will ask you to report information about your background, advice from your WIC counselor, and your health behavior, for example, your smoking.
    b. At the home visits, we will ask you health-related questions, and you will collect a sample of urine from your child. We will schedule these brief home meetings at a time that is convenient for you. The urine samples are used to <u>only</u> check for the amount of cotinine in your child's urine. Cotinine is a chemical that gets into children's bodies if they breathe tobacco smoke.
    c. If you report having quit smoking during your 2nd and 3rd home visits, we will collect a saliva sample from you to <u>only</u> test for cotinine. This cotinine test will verify your quit status.
    d. Your answers to these questions will be kept confidential. No one outside the study team will have access to your information, including your WIC counselor. You may refuse to answer any questions that you are not comfortable answering.
3. During this program, you will also complete up to five 15-30 minute phone calls with a health counselor over the course of approximately 8-weeks. During these meetings, you will work with your counselor to set your family's nutrition goals or goals related to protecting your children from tobacco smoke, depending on the group to which you are assigned. Your health counselor will provide you with coaching and support to help you reach your goals. You will also receive informational materials as a resource during your time in the program.
4. As part of the health counseling program, you will also download a mobile health app that will supplement the advice and support from your coach. Our staff will provide an overview of the app in your first home visit. Also, your coach may send you text messages or prompts through your app asking you to complete questions that will help you track your progress.
5. If you are randomly assigned to the group that focuses on reducing your children's exposure to tobacco smoke, you will receive up to an eight week supply of nicotine gum or nicotine lozenges.

What other choices do I have besides taking part in this research?

Instead of being in this research, your choices may include calling the Pennsylvania state Quitline for smoking counseling services or using the healthy eating services provided to you at WIC.

What happens if I agree to be in this research, but I change my mind later?

Your decision to enter this research study is voluntary, and you are not required to stay in the program. You are free to withdraw from this study at any time. Non-participation in the research or withdrawal from the study will not prejudice your future interactions with the investigator or Temple University. If you stop being in this research, already collected data may not be removed from the research database; however, no further information will be collected from you for research purposes. Your decision to not participate or discontinue participation will not affect the services you receive from WIC.

Is there any way being in this research could be bad for me?

There are no known risks associated with the counseling materials used in this study. In very rare cases, you may get upset when you hear about some health risks, such as smoking. If you do become upset, we will work with you and try to help you with any concerns. If you do quit smoking you may experience nicotine withdrawal. Symptoms of withdrawal include headache, nausea, change in mood, change in appetite, fatigue or insomnia. The risks associated with taking over-the-counter nicotine polacrilex (another word for nicotine gum or lozenges) include mouth problems, sore throat, indigestion, irregular heartbeat or, **more rarely**, nausea, vomiting, dizziness, diarrhea, weakness or rapid heartbeat.

There is minimal economic burden to you. All surveys and health counseling take place on the phone which could use up some of your phone minutes. There is a possibility you could be charged for use of the smartphone app affiliated with the study. Study payments are designed to cover the cost of phone minutes and data usage.

Those assigned to one group may not see improved smoking habits or secondhand smoke exposure compared to the other group.

Will being in this research help me in any way?

We cannot promise any benefits to you or others from taking part in this research. However, as participants in this study, you will receive advice, support, written materials, and counseling that may help you improve your health and the health of your child and family and begin healthier lifestyles.

What happens to the information collected for this research?

To the extent allowed by law, we limit the viewing of your personal information to people who have to review it. We cannot promise complete secrecy. The IRB, Temple University, North Inc., National Cancer Institute, the Food and Drug Administration and its affiliates may inspect and copy your information.

Although the study team has placed safeguards to maintain the confidentiality of your personal information, there is always a potential risk of an unpermitted disclosure. To reduce that risk, all documents and information pertaining to this research study will be kept confidential, unless required by applicable federal, state, and local laws and regulations to be disclosed. The results of this study may be published. If any data are published, you will not be identified by name.

You will also need to sign a separate "Authorization to use and disclose your protected health information" to be a part of this research. The only protected health information we collect is name, date of birth, address, phone number, your child's date of birth and, if you choose to share it, your email address.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time. Federal law provides additional protections of your personal information. These are described in another document titled "Authorization to use and disclose your protected health information" which you will receive at the first home visit

Can I be removed from this research without my OK?

The person in charge of this research or the sponsor can remove you from this research without your approval. Possible reasons for removal include no longer living with the child that is providing the urine sample, moving out of state, or exhibiting behavior that causes concern for staff safety. You may no longer be able to continue in the program if you do not complete an interview or if you do not provide cotinine (urine or saliva) samples.

What will I be paid for taking part in this research?

If you agree to take part in this research, we will pay you up to $225 for your time and effort. Specifically $100 at the beginning of the study, up to $75 at the end of treatment, and up to $50 at the end of your participation. Federal tax law requires to you to report this payment as income to the Internal Revenue Service. You may be asked to tell us your social security number. If payments are more than $599.00, we will report them to the Internal Revenue Service and send you a Form 1099-MISC. If you do not give us your social security number, you may take part in this research if you agree to not be paid.

Do you have any questions?

Signature Block for Adult Subject Capable of Consent

Your signature documents your permission to take part in this research.

Signature of subject	Date
Printed name of subject	
Signature of person obtaining consent	Date
Printed name of person obtaining consent	

Signature Block for Child Subject

Your signature documents your permission for the child named below to take part in this research.

Printed name of child

Signature of parent or individual legally authorized to consent to the child's general medical care

Date

Printed name of parent or individual legally authorized to consent to the child's general medical care

Signature of second parent

Date

Printed name of second parent

If signature of second parent not obtained, indicate why: (select one)

- ❑ The IRB determined that the permission of one parent is sufficient.
- ❑ Second parent is deceased
- ❑ Second parent is unknown
- ❑ Second parent is incompetent
- ❑ Second parent is not reasonably available
- ❑ Only one parent has legal responsibility for the care and custody of the child

Signature of person obtaining consent

Date

Signature of person obtaining consent

1) Abstract of the study

Children's secondhand smoke exposure (SHSe) remains a leading cause of avertible morbidity/ mortality, with links to asthma, otitis, SIDS, behavior problems and risk of cancer and cardiovascular disease. Addressing SHSe is a public health priority, particularly in low-income, young children–a group with excess tobacco-related risk and burden. Community clinics (e.g., Special Supplementary Nutrition Program for Women, Infants and Children [WIC]), can reach this population. WIC's standard practice for addressing SHSe includes minimal self-help advice to parents, an approach with inadequate efficacy. Clinical practice guidelines ("AAR") recommend that practitioners "Ask" parents about child SHSe, "Advise" them about harms, and "Refer" smokers to evidence-based treatments that address multiple determinants of smoking. Thus, we propose to test a multilevel, multimodal treatment model that combines a system-level WIC intervention following AAR guidelines with a more intensive, individual-level multimodal behavioral intervention (MBI) that integrates telephone SHSe reduction and cessation counseling with coaching on the National Cancer Institute's (NCI's) QuitPal mobile app and nicotine replacement therapy (NRT) use. We will train staff in Philadelphia WIC clinics to implement AAR with referrals to the trial. We will then randomize 372 eligible parents to receive AAR+MBI or AAR+CTL (attention control intervention [nutrition education]). All participants will receive AAR in WIC clinics because it is an easily adoptable, potential standard of care in community public health clinics. The primary aim is to test the hypothesis that AAR+MBI compared to AAR+CTL will result in greater reductions in child cotinine (SHSe biomarker) and reported cigarettes exposed/day at end of treatment (12 weeks) and 12-month follow-up. A secondary aim is to test the hypothesis that AAR+MBI vs. AAR+CTL will result in higher bioverified 7-day point prevalence quit rate among parents at 12-weeks (end of treatment) and 12-months. We will test the hypothesis that social support, urge coping skills, self-efficacy, and SHSe protective behaviors mediate effects of AAR+MBI on smoking outcomes and explore whether other factors moderate treatment effects.

2) Protocol Title

The protocol title is: Multilevel tobacco intervention in community clinics for underserved families. We will refer to the study as BLiSS: Babies Living Safe and Smokefree.

3) Investigators

Stephen J. Lepore Ph.D. and Bradley N. Collins Ph.D.

4) Objectives

We aim to implement and evaluate a multilevel, multimodal treatment model combining a system-level WIC clinic staff training to improve their operations involving referral practices for mothers who smoke ("Ask, Advise, & Refer" [AAR]) with an individual-level multimodal behavioral intervention (MBI) that integrates nicotine replacement therapy (NRT), an SHSe-protection and cessation quitline (with supplemental print materials for family), and a mobile application (NCI's QuitPal).

Aim 1: Test the hypothesis that our BLiSS program integrating a WIC system-level quality improvement staff training in AAR referral practices with an intensive individual-level MBI (AAR+MBI) will be more effective in reducing child SHSe (primary outcome) than a WIC AAR+attention control intervention (AAR+CTL). Hypothesis 1: Compared with control children, those in the AAR+MBI condition will have significantly greater reductions in SHSe, measured by child urine cotinine and parent-reported child daily SHSe (from all products and sources), from baseline to 12-week and 12-month follow-up.

Aim 2: Test the hypothesis that AAR+MBI will be more effective at increasing quit rates (secondary outcome) than AAR+CTL. Hypothesis 2: Compared with the control group, mothers in the AAR+MBI

group will have a significantly greater cotinine-verified, 7-day point prevalence quit rate at 12-week and 12-month follow-up.

Aim 3: Test hypotheses that changes in theoretically important variables will mediate (and precede in time) the effects of AAR+MBI on child SHSe and parent smoking outcomes. Hypothesis 3: Compared with parents in the control condition, parents in the AAR+MBI condition will evidence greater increases in SHSe protective behaviors, social support, urge management coping skills, and self-efficacy related to protecting child from SHSe and quitting smoking from baseline to 12-week follow-up. In turn, these changes in mediator variables will account for between-group differences in SHSe and cessation outcomes at 12-month follow-up.

Aim 4: Explore factors that may influence outcomes and moderate intervention effects, including presence of other smokers at home, nicotine dependence, depressive/anxious symptoms, pregnancy status, weight concerns, and intervention dosage (e.g., project quitline, NRT, and QuitPal usage).

5) Background

A systematic review[1] identified key limitations in current approaches to address SHSe: few studies produce significant SHSe reductions or use bio-verified measures; unimodal and clinic-based interventions tend to be minimal, not tailored to individuals' needs, and are generally ineffective. Our novel "high tech-warm touch" MBI approach tackles prior limitations by embedding AAR within WIC operations to increase low-income maternal smokers' access to intensive evidence-based interventions. We use technology (via prompts in electronic records) to engage WIC staff in AAR and to enhance project quitline counseling (via client-specific coaching in QuitPal app). Provision of NRT paired with education about NRT use addresses gaps in NRT access and uptake in this population. By measuring implementation of MBI components (e.g., NRT, project quitline, QuitPal) and hypothesized mediating/moderating variables, and ascertaining outcomes by multiple methods, we can test the efficacy of and improve knowledge about integrated best practices for intervening with a high-risk population.

6) Setting of the Human Research

Referrals for this trial will come from up to 10 Philadelphia WIC clinics. During routine WIC visits, WIC Nutrition Professionals will implement the AAR protocol with mothers who smoke. Moms who are not currently pregnant, and say they are interested in BLiSS will fill out a referral sheet. BLiSS staff will pick up referral sheets weekly and return them to the Temple lab in Ritter Annex 965.

Survey administration and health counseling is telephone-based. Participants will receive 3 home visits over the course of a year at baseline, end of treatment (12 weeks) and 12-month follow up. These visits facilitate delivery and overview of written intervention materials. They also allow staff to pick up the child's urine sample from the parent. This sample is used for the sole purpose of assaying cotinine, a metabolite of nicotine that provides a biomarker of child exposure to SHS.

The Data Safety and Monitoring Board will consist of two individuals, one with expertise in smoking and cessation treatments and another with expertise in smoking cessation intervention research and statistics. The role of the DSMB will be to review data regularly to monitor adherence to the data safety plan and potential adverse events from study participation. The Project Statistician will provide statistics on attrition and adverse events to the DSMB. The DSMB will review the annual statistics to determine whether there is a reason to change study procedures or terminate the study. Following any DSMB review, the DSMB will write a report outlining recommendations. These

recommendations will be forwarded to the Principal Investigators (Drs. Collins and Lepore) at Temple University and included in the annual progress report to the NIH sponsor.

7) Resources Available to Conduct the Human Research

North Inc. serves approximately 70,000 clients in the county of Philadelphia and reports that about 25% are smokers (~17,500). We propose a 5-year timeline: hiring and training (months 1-9); clinic implementation and training (months 1-9); enrollment and baseline assessments (months 9-42); 3- and 12-month follow-up assessment (months 12-54); analyses and manuscripts (months 55-60).

Facilities:

Dr. Lepore's lab comprises approximately 1600 square feet of dedicated lab and office space. This area includes two single offices for senior research staff and eight cubicles for other research staff. Staff members and research assistants have their own networked desktop computer, and access to printers, fax machines and copy machines. Dr. Collins' lab includes approximately 2000 square feet of dedicated lab and office space. His staff and research assistants have adjacent office space with access to networked desktop computers, printers and a copy machine and fax. His lab includes a secure room used for biosample handling and storage, with a -80 degree freezer for storing biosamples, and large cabinets, racks and shelving for supply storage.

Communication:

All staff complete an extensive training checklist that includes background reading, viewing PowerPoint training modules, listening to recorded interviews from previous studies, role playing mock interviews, and observing on home visits. Staff are given feedback on role plays and a senior staff member will periodically sit in on interviews for quality assurance. Inadequate performance will result in repeated quality control checks until performance has improved. Dr. Collins will oversee supervision to staff conducting smoking counseling. He will also provide treatment fidelity checks on a portion of all counseling recordings. All staff will attend weekly staff meetings where project updates will be provided.

8) Prior Approvals

Our co-investigator, who is the executive director of North Inc. (manager of the Philadelphia WIC program, where we will be enrolling participants) has agreed to our working with WIC clients in up to 10 clinics in Philadelphia. All BLiSS staff will obtain CITI certification in human subjects' research. Staff handling biosamples will have completed and will remain current in Temple's bloodborne pathogen and shipping of dangerous goods trainings so they can handle and ship urine and saliva samples.

9) Study Design

a) Recruitment Methods

Subjects will be recruited during in-person visits to Philadelphia WIC clinics. WIC staff will be trained to follow the AAR protocol whenever they encountered a mom who smokes. Moms who say they are interested in BLiSS will fill out a hard copy referral sheet providing their name, age, phone number, and if they have a smartphone. BLiSS staff will pick up referral sheets 2-3x a week and return them to the Temple office. Temple staff will then contact clients who completed the referral form for eligibility screening. All forms will be shredded after screening. Eligible participants contact information will be stored in a secure database, separate from all other data to maintain confidentiality. The secure database is encrypted and password protected on a password protected computer in lab room 965 Ritter Annex.

Participants will be eligible to receive a total of up to $225 over the course of one year as compensation for time completing assessments. Payments will be made after each home visit. Payments vary to reflect the amount of time and effort put in by the participant.

b) Inclusion and Exclusion Criteria

BLiSS staff will call WIC clients who fill out referral sheets and conduct a phone screening for eligibility. Inclusion criteria: We will recruit English-speaking mothers/female guardians (one per child) who are >17 years old, self-report smoking, own a smartphone, and have a child <6 years old who is exposed to tobacco smoke. We will use the youngest eligible child not in diapers for assessments, or the oldest child in diapers. We will include nursing mothers, but they will not receive nicotine replacement therapy (NRT) without written physician approval. Child cotinine from nursing mothers will not be analyzed because of confounding (cotinine transferred through breast milk). Exclusion criteria include pregnancy and presenting issues that can interfere with a person's ability to provide informed consent or follow and complete study procedures (active psychosis, inadequate health literacy, or (non-nicotine) drug dependence). We plan to enroll 372 subjects. We anticipate we'll need about 3,700 referrals to reach our enrollment goal.

c) Study Timelines

Subjects agree to participate for one year. We propose a 5-year (60 month) timeline: formative evaluation, hiring and training (months 1-9); clinic implementation and training (months 1-9); enrollment and baseline assessments (months 9-42); end of treatment and 12-month follow-up assessment (months 12-54); analyses, presentations, and manuscripts (months 55-60).

d) Study Endpoints

Primary outcomes. (a) Child urine cotinine will be obtained by the parent using gloves and materials provided to them to prevent contamination of the sample. Assays use validated, sensitive, high performance liquid chromatography-tandem mass spectrometry with cotinine detection limit <0.01 ng/mL urine and quantitation limit at 0.05 ng/mL. Cotinine remains the gold standard child secondhand smoke exposure (SHSe) assessment. (b) Parent-report of child's SHSe in terms of cigarettes per day (and other products affecting SHSe, such as cigars, e-cigarettes, pipes) in the home, car, and away from home by all sources will be assessed for the 7 days prior to assessment.

Secondary outcome. Parent-reported cotinine-verified 7-day point prevalence abstinence will be obtained using timeline follow-back methods incorporating a calendar to identify days abstinent since the last phone interview. During the 12-week and 12-month follow-up home visits, participants who report smoking abstinence will provide a saliva sample for validation using NicAlert cotinine test strips. Expired carbon monoxide readings will be taken as a backup to NicAlert to bioverify smoking abstinence in participants using NRT.

e) Procedures Involved in the Human Research

We will use a randomized, two-group design (AAR+MBI vs. AAR+CTL) with 3 measurement periods: pre-intervention, 12-weeks and 12-month follow-up. Follow-up periods follow standards in the field for short- and long-term follow-ups. We will recruit 1 smoker per household with a child < 6 years old from WIC clinics, where we train WIC nutrition counselors in the AAR protocol: ask about child SHSe, give print self-help SHSe and cessation resources, and refer to project staff for eligibility screening. After AAR, smokers randomized to AAR+MBI will receive the multilevel, multimodal behavioral intervention (MBI) consisting of QuitPal app, a starter supply of nicotine polacrilex also known as nicotine replacement therapy (NRT) gum or lozenge, educational materials (print, videos), text messages, and project quitline counseling. The attention control group (AAR+CTL) will receive equivalent attention through a multimodal nutrition intervention consisting of a mobile app, educational materials, text messages, and phone counseling, but will not be given NRT or information on smoking treatments beyond the AAR level.

After receiving WIC referrals, project staff will conduct eligibility screens, consent, and baseline assessment via telephone, and then schedule a face-to-face session with intervention staff at a participant's home. Randomization occurs immediately prior to this meeting to maintain blinding of assessment staff. Separate assessment and counseling staff will be used to maintain blinding. Randomization will be stratified by clinic and presence of other smokers in the home using a permuted block design.

Multilevel Behavioral Intervention (MBI) group. Staff will introduce the intervention to participants randomized to the AAR+MBI group by providing: (a) a research-ready QuitPal app with download assistance; (b) instruction in using QuitPal features; (c) enrollment in the project quitline; print materials; and (d) NRT starter and instructions.

Modified QuitPal app: Apps continually need to be updated to work with different operating systems. The clinic formative evaluation phase will provide an opportunity to modify and test our research version of the NCI QuitPal for iPhone and Android users. The app will include project quitline number; entry of quit date and daily smoking log; tracking health progress; information about health improvements related to SHSe protection and cessation; motivating users through pushed messages providing support and positive reinforcement; links to motivational and informational audiovisual messages; urge tracking; pushed urge management suggestions; scheduled reminders; and goal progress summary. For this trial, QuitPal's Facebook feature is not included because the modified app is available only to research participants to enable usage pattern data collection and evaluation. Further, we will replace the app's link to NCI's QuitLine with a link to our project quitline.

NRT starter and instructions: NRT products will be provided (nicotine polacrilex gum or lozenge). NRT is FDA approved for smoking cessation interventions and available over the counter. Following best-practice guidelines and practices implemented by state quitlines[4,5], participants will be given a free 2-week supply of NRT and counseling to use it in conjunction with a quit day set at the treatment orientation. Participants will learn how to obtain additional NRT (i.e., advice on: [a] obtaining an NRT prescription if they are insured and do not have a primary care provider; and [b] Medicaid co-pays and reimbursement procedures). Following other quitline practices, uninsured participants will receive up to 8 weeks of NRT. Project quitline counselors will give advice on NRT use based on guidelines[6,7] including benefits and harms, safe use and disposal. Free samples will only be provided to nursing mothers with written approval from a physician or other medical provider, and adverse side effects will be monitored during counseling and assessment.

Telephone counseling: The timing and frequency of telephone sessions is guided by best practices, including multiple proactive calling[4,9,10] and at least 2-3 completed calls[4,11]. We plan 5 proactive calls (unlimited client-initiated calls) to allow time to promote SHSe protections, to shape SHSe reduction achievements toward cessation, and provide the extra support for skills training and support that may be needed in our target population. Like other specialized quitlines[12], we provide flexible call scheduling and send frequent reminder messages.

Counselors will discuss participants' QuitPal usage to support ongoing usage and to reinforce their individualized treatment plans. This will increase intersession intervention dosage around tailored counseling discussion points. For example, counselors may ask about use of specific, client relevant QuitPal tracking features (e.g., tracking cigarettes smoked per day) to integrate with tailored counseling (e.g., coaching self-monitoring as a strategy to facilitate urge management).

The counseling model uses evidence-based motivational enhancement and Cognitive Behavioral Therapy (CBT) strategies for implementing telebased smoking interventions[4,10,13,14]. The telephone

counseling also is guided by recent evidence and approaches that use motivational components to promote family-level support for and adoption of SHSe protective behaviors among household members by capitalizing on parents' desire to protect young children from SHSe. Key counseling components include: (a) increasing motivation for smoking behavior change with collaborative, individualized treatment plans, support with goal setting, and guidance for building social support; (b) addressing addiction with education and navigation for accessing and using NRT; (c) improving skills (e.g., self-monitoring) to identify smoking "triggers" and to manage smoking urges with compensatory CBT strategies; and (d) improving cessation self-efficacy. (This approach mirrors common evidence-based practices implemented in state and national quitline counseling models.)

Counselor training: Our counselors have completed a 5-day program to become Certified Tobacco Treatment Specialists (CTTS) through U Penn's Perelman School of Medicine (accredited by the Association for Treatment of Tobacco Use and Dependence). An additional 30 hours of counselor training by PIs will reinforce lessons learned in the CTTS program, but importantly, will also focus on (a) how to guide SHSe protection efforts as part of a CBT-framed strategy to shape parents' behavior toward a cessation attempt, (b) how to facilitate SHSe protective behaviors and smoking behavior change in the context of challenges faced by low-income parents who smoke; and (c) how to drive a counseling process that integrates QuitPal mobile app usage to individualize the intervention to parents' particular needs. Training in CBT strategies allows for tailoring counseling to participants based on identified barriers (e.g., other smokers in the home) and catalysts (e.g., concerns for child health) of behavior change. After intensive competency-based training, counselors will refine skills in ongoing weekly supervision that includes review of fidelity monitoring feedback, discussion of current cases, and role-playing of effective session interaction.

Attention Control Intervention (CTL) Group. The purpose of the AAR+CTL group is to provide equivalent contact between the two conditions while providing distinctly different intervention content. Thus, the CTL session schedule will parallel the MBI condition. CTL health education content will focus on nutrition education. CTL clients will receive the commercially available, free mobile nutrition health app; access to Sesame Street's "Food For Thought: Nutrition on a Budget" program on the web and in hard copy, and 5 calls related to family nutrition education.

Measures

Overview. Screening, consent, and baseline assessments are conducted after receipt of referrals from WIC offices. Participant self-report data at baseline, 12-week and 12-month follow-up will be collected via structured computer assisted telephone interviewing. This method reduces literacy barriers, minimizes participant burden, and maximizes data reliability. Collection of the child's urine sample from the parent and parent biomarkers (Nicalert; CO readings) will take place during in-person meetings with parents at home visits following baseline, end of treatment (12 week) and 12 month phone assessments. Process data on QuitPal and project quitline usage will be collected in real time. Measures are tied to our theoretical model predicting reduction in child SHSe and parent smoking cessation.

See 9d above for Primary and Secondary outcomes.

Mediators. We identified several potential mediators: (a) Parental-reported exposure protection (PREP) behaviors are measured with self-report items used in our previous research and reflected in a recent meta-analysis. We operationalize PREP behavior in two measures: (1) families' current home smoking policy (0=no restrictions to 4=total indoor ban); and (2) the sum of PREP behaviors (e.g., enforce smoking restrictions; avoid smoking in rooms where child eats and sleeps; move child away from others' smoking). (b) Support for SHSe protection and smoking cessation will be measured using a modified short form of the Partner Interaction Questionnaire. The modified

measure assesses perceived intervention staff support to participants for promoting smoke-free environments and cessation (α = .91). (c) Self efficacy of smoking behavior change will be measured. We will use the Smoking Cessation Self-Efficacy Scale, which assesses confidence in one's ability to refrain from smoking in varied situations (α = .90), and a parallel form (α = .90) we developed for the KiSS trial to assess self-efficacy related to reducing child SHSe. (d) Coping with smoking urges will be assessed using the Urge Management Coping Skills measure developed for project KiSS. It captures how often smokers engaged in cognitive and behavioral coping strategies to manage smoking urges (α = .87).

Covariates and moderators. We will test five variables as potential control variables and moderators of intervention effects. (a) Nicotine dependence will be measured with the reliable and validated Fagerström Test for Cigarette Dependence. (b) Depressive symptoms will be measured with the Center for Epidemiological Studies Depression Scale, which are validated, reliable and useful in smoking studies. (c) Weight concerns will be measured using a 6-item validated scale that measures general and smoking-specific weight concerns. (d) Pregnancy/postpartum status will be measured using a single, content valid item defined as: currently pregnant, postpartum (delivered youngest child within the last 12 months), or other (youngest child delivered >12 months ago). (e) Number of individuals who smoke cigarettes daily (or other products that affect SHSe) in the home, will be assessed using a standard, content valid item. Additional demographic and smoking history variables will be measured and assessed for possible association with outcomes.

Process measures. Intervention processes will be assessed in both conditions at multiple time points, with multiple methods, and at each intervention level: AAR implementation, phone counseling, NRT utilization, and mobile app usage. Process data will include computerized tracking data from the QuitPal app, counselors' observations, participant self-reports, and WIC nutrition counselor reports. QuitPal app process data will include frequency of launching and using (e.g., inputting data) features. Counselors' observations are recorded in "session reports" completed after each participant contact, including: (1) attendance; (2) duration; (3) ratings of participant engagement. Session report data can generate a measure of total contact time over the course of the intervention. Participant self-report measures will assess their receipt and use of, and satisfaction with, clinic, counseling, app, and NRT intervention materials and advice. Similar measures have been used in our ongoing studies evaluating the efficacy and feasibility of intervention components.

f) Data Management

Data analysis:

The primary analyses will use an intention-to-treat approach. All randomized participants will be tracked in follow-up and missing outcome data will be addressed using multiple imputation methods. In sensitivity analyses, we will perform complete case analyses and we will also adapt the methods of Co-I Dr. Egleston to investigate the impact of data that is potentially missing not at random.

Analyses for Aim 1: The primary outcome will be change in cotinine between (a) baseline and 3 months and (b) baseline and 12 months. We will compare change scores between randomization arms using random-effects linear regressions in which we include randomization arm as a fixed effect and WIC clinic as a random intercept to account for potential clustering within clinic. We will assess the balance of potential confounding variables between randomization arms using linear or

logistic regressions with random intercepts to account for correlation within clinic. Potential confounders (e.g., nicotine dependence, depressive/anxious symptoms) will be added as covariates as necessary. We will also use multilevel random-effects regressions with random-effects to account for within subject correlation over time and within clinic correlation to investigate time trend trajectories. Panel time will be included in these longitudinal models. We will repeat analyses for self-reported child SHSe as a secondary outcome. We will also examine the per-protocol as-treated effect to explore dose-response relations.

Analyses for Aim 2: We will use logistic regressions with random intercepts for clinic to compare bioverified self-reported quit status (yes/no) between randomization arms at 3 and 12 months. We will use multiple logistic regressions with random intercepts for clinic to control for potential confounding variables that were not balanced between randomization arms. Similar to analyses described in Aim 1, we will also examine random-effects longitudinal logistic regressions and per-protocol as treated effects to explore dose-response relations.

Analyses for Aim 3: To investigate mediation pathways, we will use a structural equation approach that is firmly rooted in the statistical field of causal inference. Outcomes include change in SHSe and parent quit status. We will include appropriate random-effects terms to account for correlated data within clinic and participant over time. We will use cluster-adjusted bootstrap standard errors for assessment of the mediated effect. In assessment of the mediated effect, we will ensure that the intervention is associated with the potential mediators and that the mediators are associated with the outcomes. We will examine mediation pathways in which the variables are measured in a temporal ordering consistent with a causal pathway. For example, we are primarily interested in pathways in which mediators of the intervention are measured at 12 weeks end of treatment and then outcomes are measured at month 12.

Analyses for Aim 4: For moderation analyses, we will use random-effects regressions of the change in cotinine levels (SHSe) and parent quit status. In the models for Aim 4, we will include a dummy variable for randomization arm, the potential moderator variable, and an interaction term between the two (i.e. dummy variable multiplied by moderator variable). To maintain power to detect moderation, we will explore moderators separately. We will also use multiple regression models in which we include potential confounding variables, as well as the main effects and interaction terms of interest.

Power Analysis**:** We chose our sample size so that we would have at least 85% power to detect between-group differences in the primary outcomes (3- and 12-month child cotinine). Using an estimate of 20% 1-year follow-up attrition based on the KiSS trial, we expect to have 298 participants at 12 months (372*80% retention=298, or 149 per group). With 149 participants per group, we will have 85.7% power to detect an effect of 0.23 in the log cotinine change scores between randomization arms. We based the calculation on our previous counseling intervention data (mean log cotinine of 1.17 in intervention group, sd=0.58, and 1.40 in control group, sd=0.60). This also assumes a Type I error rate of 2.5% (2-sided) and the use of a random effects model in which the within clinic correlation is 0. We chose a Type I error rate of 2.5% using a Bonferroni correction for a familywise Type I error rate of 5% (0.05/2=0.025) to accommodate the two primary hypothesis tests (cotinine change at 3 and 12 months). We used R (R Software, Vienna, Austria) and PASS 11 (NCSS Software, Kaysville, UT) for calculations.

Data Security: There are two primary types of data: parent interview responses and cotinine measures obtained by parent-collected samples. Interview data will be entered on a secured computer at Temple University in Dr. Lepore's lab. A study identification number will be used to label

and track participants' data. Most interview responses will be numerical responses to multiple-response questions or rating scales. Cotinine data also will be tracked using a study identification number. Identifiers linking data to the identity of research participants will be maintained in a separate and secure area from other data. Files containing identifiers are stored in a locked cabinet in Ritter Annex Room 975. Files containing data but no identifiable information are stored in a locked cabinet in Ritter Annex Room 965. Temple study personnel have access to all paper files. The information collected in this study also will be recorded in computer files in such a manner that personal identifiers will be removed. Those computer files are encrypted and password protected and stored on a password protected computer. Such identifiers linking data to subjects will be maintained in a separate and secure area (computer in 965 Ritter Annex). At the end of the trial, all identifying information will be destroyed.

Additional data collected from the QuitPal app are transferred automatically by the mobile app from each participant's phone. The data are sent to a server via HTTPS. The data collected include statistical information about smoking habits, urges to smoke, coping mechanisms, and aggregate statistics such as frequency of application feature usage. The data collected from the mobile application do not include any personally identifying information. On the server, participants are identified only by an assigned participant ID number, which is known only to the research team. Database backups are performed regularly and are stored offsite. The encrypted data copy is performed via SSH and the backups are not accessed except in emergency. An individual's data will be securely erased 6 months after she has completed participation in the study.

Quality Control: Drs. Collins and Lepore will be responsible for overall treatment quality assurance. We will assess treatment fidelity of AAR across WIC clinics, the mobile app, and implementation of phone counseling components in experimental and control arms. Clinic-level AAR intervention fidelity will be assessed at various time points and with multiple methods. Project quitline counseling intervention fidelity will be assessed throughout the trial. Counselors will keep intervention component checklists to ensure consistent delivery of treatment components for each session in both arms. Sessions will be recorded; the project director will review checklists and a random 20% of tapes weekly against the intervention checklist. The expectation is to maintain $\geq$90% fidelity.

Storage of Specimens: Dr. Collins' lab includes a locked room used for biosample handling and storage, with a -80 degree freezer for storing urine and saliva biosamples. Samples are labeled with participant ID numbers, date, and study timepoint. Only staff who have completed Temple's bloodborne pathogens training are permitted to access the samples. Periodic UPS shipment of samples to a lab that conducts assays follows Temple's Environmental Health and Radiation Safety protocols.

g) Confidentiality

See item 12 below.

h) Provisions to Monitor the Data to Ensure the Safety of subjects

The Data Safety and Monitoring Board will consist of two individuals with expertise in smoking and cessation treatments and statistics. The DSMB will review data regularly to monitor adherence to the data safety plan and potential adverse events from study participation. The Project Statistician will provide statistics on attrition and adverse events. The DSMB will review the annual statistics to determine whether there is a reason to change study procedures or terminate the study. Following any DSMB review, the DSMB Chair will work with other board members to write a report outlining

recommendations. These recommendations will be forwarded to the Principal Investigators (Drs. Collins and Lepore) at Temple University and included in the annual progress report to the NIH sponsor.

i) Withdrawal of Subjects

Participants can be withdrawn from the research for three reasons:

1) The participant no longer lives with the child that is providing the urine sample. In previous studies, this happened when a subject was incarcerated, became a resident of a recovery house, lost custody of their child, or moved somewhere the child did not reside. This prevents us from assessing our primary outcome, child exposure to secondhand smoke by the parent.

2) The participant moves out of state.

3) The participant exhibits behavior that causes concern for staff safety. This could include mental instability, making threats or behaving aggressively, making sexual overtures or any other behavior that staff deem to be unsafe.

When a participant is withdrawn, they will be contacted by phone and receive an explanation. If staff are unable to reach them by phone, a letter will be sent. Participants will be paid any money due for study work they have already completed.

When a participant informs the project team that they wish to withdraw from the study, this action will not prejudice future interactions with study staff, Temple University, or WIC as noted in the consent form.

If a participant elects to discontinue participation in the study they will earn compensation for any completed assessments but will be informed that they are not eligible for future incentives related to the study but WIC services will not be affected. They will also be informed that they will not be contacted further.

10) Risks to Subjects

There are no known risks in using WIC nutrition counselor or telephone counselor advice and support for child SHSe reduction and parent smoking cessation. The advice provided by nutrition counselors follows nationally established guidelines for offering routine advice about the harms of smoking in clinic settings.[15] The telephone counseling protocol follows routine messages and approaches that participants would be exposed to in any freely available state-sponsored telephone quitline for smoking. The mobile app that participants have access to is freely available and distributed by the National Cancer Institute on a publicly available website. Parents may refuse advice and referrals, but none of the key personnel in this trial are aware of cases where parents refused additional clinic services because of their reaction to smoking advice provided in clinic. There are no known risks associated with the educational materials or the counseling session materials and protocols or the assessment protocols used in this project or previous projects from which procedures, protocols, and content were modeled. In rare cases, side effects of the intervention may include emotional distress from hearing about risks from smoking to one's self or one's children; however, staff and counselors are trained to deliver health messages and advice in a supportive, empathic, normalizing, and problem-solving manner that minimizes the likelihood and degree of distress a parent might experience. For parents who quit smoking, individuals may experience temporary smoking cessation withdrawal symptoms (e.g., increased appetite, cravings). However, key components of both levels of treatment and the provision of patient navigation to maximize access and use of recommended over-the-counter NRT that attenuate withdrawal

symptoms, will help participants prepare for these potential symptoms and manage them successfully. Hence, as explicitly stated in the program materials, we will make every attempt to minimize potential distress and will work with participants to lower any distress that may occur.

Subjects randomized to either group may not benefit better or at all compared to those randomized to the other group.

The risks associated with taking over-the-counter nicotine polacrilex include mouth problems, sore throat, indigestion, irregular heartbeat or, more rarely and associated with nicotine overdose, nausea, vomiting, dizziness, diarrhea, weakness, or rapid heartbeat. We will educate participants about common side effects associated with NRT use and will monitor side effects at every counseling and assessment contact. We will review these risks with participants following published clinical practice guidelines and recommendation of the US Food & Drug Administration (e.g., we will only provide NRT samples to nursing women if they present written permission of their physician or prescription to use it). We will also include flyers for participants to place in their home (e.g., beside medicine cabinet) as a reminder of NRT instructions and numbers to call if they are concerned about side effects (their physician's office, quit line, our staff phone numbers.) NRT is FDA approved for over-the-counter use and is routinely dispensed by city and state departments of public health and state-sponsored smoking cessation quitlines.

There are no identifiable risks to others who are not participants in this study. This includes participants' children.

We will make every attempt to minimize any potential risks. Exclusion criteria include self-reported major psychiatric disorders, thereby reducing the probability that the sample will present with problems or emergencies related to psychiatric disorder. However, even if parents have not received prior diagnoses of psychiatric disorders, there is a chance that they will present with symptoms of psychological distress (e.g., depressive or anxious symptoms, or stress). Such symptoms have been observed among nicotine-dependent individuals and those faced with ongoing burdens of socioeconomic and psychosocial strains of poverty and parenting young children. We plan to include the CESD to assess depressive symptoms at baseline, EOT, and follow-up. Participants who score in a range considered at risk for depression will be provided with referral information for free mental health services in their community. Program staff also will be trained to engage in a brief harm assessment interview that can be implemented at each subsequent contact with the participant in such cases. Likewise, all staff members who have contact with participants are trained in accordance with Temple University medical emergency protocols to ensure preparation of circumstances around emergent mood- or medical-related issues that could arise during telephone counseling sessions. Any time staff members are concerned about a clients' disposition, or confront an actual emergency during a session, they will contact one of the Co-PIs; and if a PI is not immediately available, they will contact the Temple University Health System psychiatrist on call. As outlined in the emergency protocol, a Co-PI (or Temple University physician/psychiatrist) will then assess the parent by phone to determine if further steps are necessary. Emergencies have not occurred in the 14 years that the Dr. Collins has been working with this and similar populations in clinical trials. Nonetheless, the following emergency protocol is in place:

(1) If a participant presents with potential depressed mood, anxiety symptoms, or distress, but expresses no intent to harm self or others, the PI will provide referral information and the phone number to the Temple University Health System's (TUHS) Psychiatry Services. This clinic offers outpatient services on a sliding scale for non-insured patients including evaluations, psychotherapy, and psychopharmacology treatment for Bipolar and Psychotic Disorders, Major Depression, and Anxiety Disorders. The PI will also provide participants with the number of TUHS Psychiatric Emergency Services center (PES) in case they escalate following the phone call and feel they need emergency services. The PES provides emergency transport to the hospital and comprehensive

psychiatric evaluation, immediate intervention and stabilization, and referral services 24 hours a day, 7 days a week. The participant will be monitored closely for the rest of their enrollment and reminded of referral information at each contact.

(2) If the PI assesses suicidal ideation or violence without a plan, the PI will follow the same steps as scenario "1". If the participant states they would feel safer under supervision, the PI will arrange for psychiatric evaluation or for an escort to the PES. He will follow-up with the patient the following day to ensure that either referral was followed through, and the participant will continue to be monitored as in "1".

(3) If the participant expresses ideation with intent to hurt him/herself or someone else, the PI will determine if a report should be sent to Protective Services in cases of suspected child abuse and/or arrange for escort to the PES. If an escort is necessary, the PI will follow-up with the participant the next day to ensure adherence to the referral and recommendations. They will continue to be monitored as in "1".

(4) If a medical, non-psychiatric emergency arises during a counseling session or interview/assessment, staff will call 911 on behalf of the family to ensure that proper medical attention is received.

11) Potential Benefits to Subjects

Direct benefits of being in this study are that participants receive advice, support, recommendations, comprehensive written materials, and counseling that is designed to improve child and family health regardless of which condition they are randomized to receive. By participating in this program, participants increase the probability they will reduce their children's SHSe and increase the chance that they will quit smoking. As a result, both short- and long-term parental and child health may improve and disease risk may diminish.

Given that tobacco use and exposure are leading causes of disease and death, the benefits of this research could include substantial public health impact.

12) Privacy and Confidentiality

This study has a very small risk of loss of privacy of personal participant information. Securing participant privacy is accomplished through several procedures and begins with the PIs' thorough training and ongoing supervision of the research staff. The primary method of ensuring security of confidential data is with the use of a highly secure database configuration administered and overseen by the Co-PIs; and any data that staff collect will be directly and immediately brought by hand to Dr. Lepore's research office and stored under lock and key. All databases are encrypted and password protected on password protected computers. Only Co-PIs and the Project Manager will have access to the passwords. Identifying information is used only for participant contact. No assessment forms, including urine and saliva cotinine assessment forms used to record collection and storage of samples, will have personal identifying information. Hard copies of identifying information will be stored in separate locked cabinets to avoid unauthorized cross-referencing of data with identifying information (and research assistants not involved with counseling will not be permitted to access counseling files.) These rules will be strictly enforced. Upon entry of data into the data management system, a participant ID will be generated. ID numbers will not be derived from identifiable information. They are generated in numerical order based on their referral site.

ID numbers and names will be located in a separate encrypted table. All tables in the study data set use an automatically generated ID as the subject identifier. Using this method, if security of the data in the study systems were to be compromised, no identifying subject information is present. Only the Project Manager (PM) will see all the data as specifically defined. Communication outside project staff will not have identifying information other than subject ID. An important note is that Dr. Lepore's and Dr. Collins' systems and individual study databases have never been compromised as a result of the rigorous and secure network firewall technologies they use in their labs. A secure server is located in a secured facility at Temple University, with dedicated uninterrupted power supply, and separate from other Temple University server systems.

The research will collect and store subject Protected Health Information and will follow HIPAA regulations. The IRB has granted a waiver of HIPAA authorization for recruiting subjects. The protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the protected health information would be permitted. A HIPAA authorization form will be signed by the subject for the remainder of the study at the first home visit. Study results will be reported in aggregate. No individuals will be identified.

Every effort will be made to help participants feel at ease with the study procedures. Interviews and phone sessions are scheduled in accordance with the participant's schedule and participants are compensated for their time. The most sensitive questions (Adverse Childhood Experiences) are administered during the 12 month follow up home visit where the participant can fill out the questionnaire herself for privacy.

13) Compensation for Research-Related Injury

Not applicable.

14) Economic Burden to Subjects

There is minimal economic burden to subjects. Survey administration and health counseling both take place on the phone which could deplete a participants' phone minutes. Study incentives are designed to offset the cost of phone minutes. Subjects may incur charges for use of smartphone apps depending on their cellular data plan. There will be no charge for downloading the apps. Both apps used are free.

15) Consent Process

We will follow INVESTIGATOR GUIDANCE: Informed Consent (HRP-802).

Infants and children: A child (age 0 to 5) of the smoking parent will be included in the study: the parent will obtain a urine sample from their child to confirm level of exposure to secondhand smoke via a cotinine assay. The permission of one parent is sufficient even if both parents are alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child. Assent of the child will not be obtained because their capability is so limited that they cannot reasonably be consulted. It will be the parent's responsibility to collect the sample from the child, not a member of the research team. At no point in time is the child required to answer any questions or directly interact with research staff in the study.

Cognitively impaired adults: During the eligibility screen, staff are trained to evaluate the participant for cognitive impairment. If there is any question, staff consult with the project manager or one of the

Principal Investigators to make a determination. If the person is deemed to have a cognitive impairment they are informed that they are ineligible for the study.

Non-English-speaking subjects: Non-English speaking subjects will not be enrolled in the research.

16) Process to Document Consent in Writing

Consent will be read during the eligibility screen if the participant wishes to know more about the study.

During the first home visit (within 2 weeks of eligibility) participants will be provided with a written copy of the consent form, which study staff will review with them. They will then be asked to sign a hard copy for study staff to keep on record.

The research staff and protocol will follow INVESTIGATOR GUIDANCE: Documentation of Informed Consent (HRP-803) to obtain documentation of consent. The IRB has granted a waiver of documentation of consent for the screening phone call. The person obtaining consent will read the consent script to the subject during the phone screen before commencing any data collection. Documented consent will be obtained with the first home visit.

17) Vulnerable Populations

Study participants will predominantly include medically underserved and minority (African American) mothers who smoke. Maternal smokers are targeted primarily because child secondhand smoke exposure (SHSe) relates primarily to maternal, not paternal smoking. African Americans are also an important group to include because tobacco- and child SHSe-related morbidity and mortality is highest in this ethnic group. Mothers 18 and older will be included. Younger parents will not be included because they represent a developmentally different subpopulation with different sets of factors associated with smoking. The present intervention is not designed to meet these developmental differences. Nursing women will be eligible to participate. Nicotine replacement therapy will not be offered to nursing women unless they have written physician approval. There is no known risk for nursing women compared to the general population of women to participate in this type of counseling intervention to facilitate smoking cessation and reduction of child SHS exposure. A child of the smoking parent will be included in the study: the parent will obtain a urine sample from their child to confirm level of exposure to secondhand smoke via a cotinine assay. It will be the parent's responsibility to collect the sample from the child, not a member of the research team. At no point in time is the child required to answer any questions or directly interact with research staff in the study. We will not enroll pregnant women, prisoners, or adults who are unable to consent.

18) Drugs or Devices

Participants randomized to the MBI intervention will receive a free 2-week supply of nicotine polacrilex replacement therapy (NRT) gum or lozenge, which is the standard practice among state quitlines. NRT will be kept in a locked cabinet in the lab and distributed directly to study participants during the baseline home visit. Following best-practice guidelines participants will receive counseling on how to use it in conjunction with a quit day set at the treatment orientation. Participants will learn how to obtain additional NRT (i.e., advice on: [a] obtaining an NRT prescription if they are insured and do not have a primary care provider; and [b] Medicaid co-pays and reimbursement procedures). Subjects in the MBI group will receive up to 8 weeks of nicotine polacrilix. Study *counselors will give advice on NRT use based on guidelines[6,7] including benefits and harms, safe use and disposal.* Special instructions will be provided for nursing women (per FDA guidelines[8]). Free samples will be provided to nursing women only with physician approval, and adverse side effects will be monitored during counseling and assessment. NRT will be purchased

online through amazon. NRT will be administered following quitline guidance but within accordance to the FDA-approved labeling and use of the drug.

With regards to the use of nicotine polacrilex: a) the investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug, b) the investigation is not intended to support a significant change in the advertising for the product, and c) the PI and other research personnel will not represent the drug as safe or effective for the purposes for which it is under investigation, or promote, commercially distribute, or test market the drug.

The QuitPal and Fooducate smartphone apps are devices being used in this research. Per FDA guidance "Mobile Medical Applications," abbreviated IDE requirements will not be followed because of functionality of these two apps does not pose a risk to a patient's safety if the mobile apps were to not function as intended.

19) Multi-Site Human Research

Temple study staff will have regular meetings with Dr. Kilby (Co-I) and the NORTH, Inc. staff to apprise them of study progress and address any questions or concerns that arise. The Project Manager will be responsible for sharing any new information or unanticipated problems with the NORTH, Inc. staff in a timely manner. Information from the study will be shared with NORTH Inc. in aggregate, no identifiable information will be shared.

20) Sharing of Results with Subjects

Study results will not be shared with participants beyond published data.

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