Nicotine Replacement Therapy Sampling & Selection

Study Statistical Analysis Plan

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A. Significance.

Smoking Prevalence in Low Income Populations. Cigarette smoking is responsible for 1 in 5 overall deaths and remains the leading cause of death and disability in the United States (U.S)[1,2]. While smoking prevalence has declined from a high of 45% in the 1960s to 16.4% in 2014 among the general population[1,2], smoking prevalence has remained high (26.3%) among those living in poverty as well as those with less than a high school education (22.9%-43%)[1]. Alabama has one of the highest rates of poverty (19.3% of the Alabama population lives in poverty compared to 14.8% in the U.S. generally) and is ranked 48th in the nation with only New Mexico, Louisiana, and Mississippi having higher poverty rates in the U.S.[3,4]. Not surprisingly, Alabama also has some of the highest prevalence rates of smoking (22.1%; 42nd among states[5]) in the U.S., with the highest prevalence rates among those without a high school diploma (40.9%)[5]. Alabama ranks among the worst for state-wide initiatives to limit tobacco use and exposure[5]. For example, Alabama does not have statewide smoke-free laws, the state allows sampling and the display of tobacco products in commercial venues, does not provide state Medicaid-covered tobacco treatment (and rejected Medicaid expansion under the Affordable Care Act), and also has some of the lowest cigarette taxes nationally ($0.425 per pack; 46th among states) relative to almost any other state in the nation[5]. The decline in smoking in Alabama has been much slower than the national average, likely due to the lack of prevention messaging and treatment availability as well as the high rates of poverty and low educational attainment[5].

Smoking Interventions among Low Income Populations. Few interventions have been specifically designed or tested in low income smokers. The few interventions that have been tested generally were pilot studies[6-9]. Overall, these pilot studies find that it is feasible and acceptable to intervene with low income smokers in a variety of settings including psychiatric patients in an urban public hospital[6], parents of Head Start children[7], and primary care safety net settings[8-9]. Larger clinical trials with low income populations have either focused on increasing motivation to utilize existing smoking cessation resources (e.g., tobacco quit lines) [10-14] or have used proactive tobacco cessation outreach[13-14] to increase engagement in treatment. Use of motivational interviewing (MI) was found to increase tobacco quit line calls over standard referrals[10] as well as abstinence[11;13]. However, MI was not found to increase abstinence compared to standard of care when both groups received NRT[12]. African American smokers engaged in care at a Veteran's Administration setting had higher cessation relative to White smokers, regardless of provision of proactive or standard cessation treatment[14], suggesting no racial differences when provision of care is equally available. Similarly, in our own smoking cessation study of individuals under criminal justice supervision, no racial differences were found among participants who were adherent to bupropion[15], regardless of the amount of behavioral counseling received. Importantly, standard behavioral counseling did not enhance adherence to medication, despite the focus on the importance of adherence during counseling sessions. In summary, while motivational approaches and proactive referrals did not generally increase cessation on their own, they did improve access to existing services. Further, standard smoking cessation counseling did not improve medication adherence and novel interventions are needed to increase adherence to medications, particularly in low income populations.

Medication Adherence. More than 75% of individuals prescribed medications for chronic diseases do not use them as directed and medication non-adherence costs the healthcare system more than $300 billion annually in preventable hospitalizations.[16] Several factors have been found to be associated with non-adherence including low perceived efficacy of the medication, side effects, complicated medication regimens, poor relationship with the provider, low health literacy, and medication costs and co-pays for prescriptions[17-19]. Adherence is particularly low among individuals from disadvantaged communities due to negative perceptions of the healthcare system including less trust in medical providers, lower belief about the efficacy of medication, difficulty accessing services, and lower health literacy[20-21]. In fact, <u>developing interventions to improve medication adherence in these populations has been identified as the single best means to reduce health disparities over other targets such as equalizing access to healthcare or reducing provider discrimination</u>[22].

Adherence to smoking cessation pharmacotherapies is similarly poor as most people do not use pharmacotherapy when attempting to quit smoking[23], and among individuals who use smoking cessation medication, 69% prematurely quit use of medication[24]. Rates of non-adherence to NRT are particularly high with approximately 76% prematurely discontinuing NRT[24]. However, medication adherence is critical for successful cessation and adherence to smoking pharmacotherapies triples the rates of cessation[25-27]. Similar to medication adherence generally, misperceptions about the safety and efficacy of NRT has undermined effective use of these medications, particularly among disadvantaged populations[24-25; 28-29]. African American smokers report less lifetime use of smoking cessation pharmacotherapy[30], hold less positive attitudes about

the use of pharmacotherapy for cessation, report more concerns about the addiction potential, efficacy, potential for interactions with other medications and harms of pharmacotherapy, and are uncertain about the need for pharmacotherapy for cessation relative to White, non-Hispanic smokers[31-32]. This mistrust of medications among disadvantaged populations may be a leading factor contributing to racial disparities in smoking cessation and finding novel mechanisms to increase adherence is a critical step to reduce disparities.

Despite the known problems associated with medication adherence for NRT use in smoking cessation, we found only a few published studies that targeted adherence to pharmacotherapy specifically as an intervention. These studies showed that brief psychoeducation about NRT can both improve attitudes toward NRT[33-34] as well as increase intentions for future use[35]. Similarly, a recent Cochrane review of eight studies on interventions designed to increase adherence to smoking pharmacotherapy (all educational in nature) noted an increase in reported adherence among the intervention over control conditions (RR:1.14); although this dropped to a non-significant difference when using a random-effects model to account for heterogeneity among study designs and characteristics[36]. However, this review and other studies measuring more important clinical changes such as smoking cessation did not find psychoeducation alone to be effective[34,36]. These findings mirror results from adherence interventions with chronic diseases[37-43] which noted that while self-reported adherence improved with educational interventions, only 8 out of 57 studies demonstrated improvements in measurable clinical outcomes (e.g., a decrease in blood pressure. etc.). The lack of meaningful clinical change in both studies of chronic disease as well as smoking cessation demonstrated the lack of efficacy for educational interventions alone for improving adherence[42]. However, experiential interventions appear to be a more promising approach for increasing NRT adherence.

Experiential Approaches for Increasing Adherence. While education about the benefits and safety of NRT do not appear to lead to improved utilization of smoking pharmacotherapy during quit attempts, more "hands on" experiences with NRT do appear to increase utilization and cessation. For example, participants who previously used pharmacotherapy in a quit attempt were more likely to be adherent with pharmacotherapy in subsequent attempts[44]. This suggests that experience with smoking pharmacotherapy may be one way to increase medication adherence and subsequent abstinence. Indeed, support for such a strategy has been found in studies that have examined the effects of NRT sampling. In at least two clinical trials testing a sampling intervention, providing 1-2 week NRT samples for practice quit attempts (PQAs) was shown to produce positive change in process measures as well as actual cessation[45-46]. Thus, providing medication to increase experience with pharmacotherapy, even among non-treatment seeking smokers, may be an important mechanism to increase motivation and adherence in a future quit attempt. Similarly, providing NRT for in-session sampling improved perceptions of NRT over psychoeducation without in-session sampling of NRT[47-48].

Although these studies provided nicotine samples to use in practice quit attempts or to improve perceptions of NRT in-session[47-48], they did not investigate using NRT in-session with the goal of increasing experience with NRT to boost cessation. Further, these studies did not examine how patient preference may impact cessation. A study that provided participants with different forms of NRT to use at home and then select their preferred NRT to use for cessation demonstrated smoking reduction[49]. However, a subsequent study targeting cessation using a patient's preferred product versus randomized product did not find significant differences for cessation[50], suggesting results of using a preferred NRT product are mixed and in need of additional study. Preferred product selection is an important clinical practice issue since patient preference for specific medications is likely a consideration when prescribing treatment. Importantly, and most relevant to the proposed project, these studies did not provide in-session experience with these products as part of the patient preference process. Our novel approach combines the most promising elements of all of these NRT sampling approaches. We will prospectively pilot a 4 week intervention providing in-session NRT sampling of four short acting NRT products (gum, inhaler, lozenge, nasal spray) in combination with nicotine patch. Use of these products will occur in real time during session and expectancies about NRT will be discussed and perceptions of NRT explored. Participants will be given a one week sample of these products for at home practice quit attempts to acclimate to these medications. At the end of the 4 week sampling period, participants will select their preferred short acting NRT to use in conjunction with nicotine patch to make a sustained quit attempt. Importantly, we believe that in-session experience with NRT coupled with at home PQAs are both critical as it is experience with medication and determining subsequent NRT preference that may be most strongly associated with adherence and subsequent meaningful clinical outcomes such as medication uptake and abstinence. But first we need to pilot this intervention to determine if this experiential intervention coupled with counseling about NRT expectancies as well as the positive and negative effects of NRT can increase adherence over standard cessation treatment.

B. Innovation

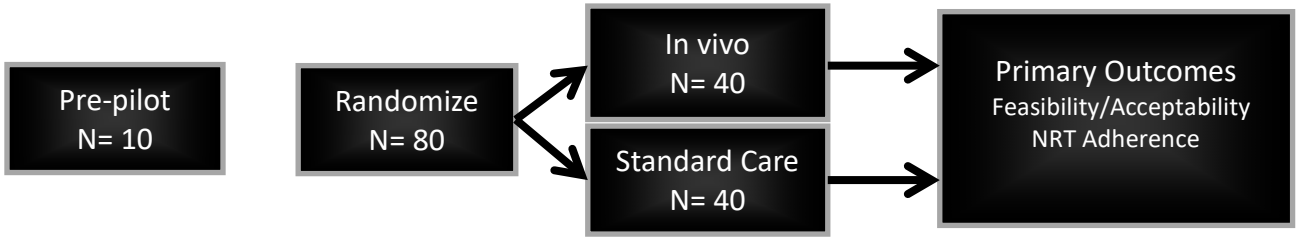
This proposal builds on and extends previous NRT sampling research. First, while NRT sampling has been shown to increase quit attempts, abstinence, indicators of cessation readiness, and perceptions about NRT, this approach still relies on the patient to use the NRT on their own after session[45-46; 49-50]. Even the previous studies that have provided NRT in-session have done so for the purpose of determining participant preferences and did not use these sessions for addressing misperceptions or experiences of using NRT or follow-up on adherence or cessation outcomes[47-48]. Sampling interventions that allowed participants to take home various forms of NRT and then select their preferred NRT did not provide the NRT in-session to determine actual use of the medication or address misperceptions of these products[49-50]. Thus, the most important and innovative aspect of our proposed study is that this approach will provide in-session use of NRT in a prescriptive and controlled fashion for the purposes of addressing misperceptions and providing experience with the medication, thereby increasing medication adherence. Then participants will practice use of these medications at home in a naturalistic environment to acclimate and make PQAs. This combined approach has several benefits including a) the assurance that the smoker actually tries NRT, b) the ability to highlight positive aspects of NRT experiences (e.g., relief of withdrawal and urge), c) the capacity to address misperceptions and provide feedback and guidance on any experienced adverse events in real time NRT use, d) and the chance to use NRT for PQAs in a naturalistic environment. Smokers on their own may never actually try the medication or may discontinue their brief use of NRT if they experience negative effects [e.g., 29,35]. This In vivo approach with PQAs remedies these shortcomings. A second innovation is that we will have allow participants to sample all available acute acting NRT formulations in combination with nicotine patch both in session and at home for PQAs and then select their preferred acute product to use with the patch for optimal effectiveness. Combined NRT has been shown to be as effective as varenicline for smoking cessation[51] and providing In vivo experience with using these products in combination may be particularly effective to promote adherence and cessation. Allowing the participant to select their preferred short acting product is believed to increase engagement and abstinence self-efficacy, both of which are believed to increase medication adherence. Finally, this intervention can be provided by non-therapy professionals as it does not require extensive training in motivational interviewing, cognitive-behavioral therapy, or other significant therapeutic skills. This element makes this intervention very translatable to low resource settings. Importantly, In vivo approaches may be particularly important for low income smokers who have limited experience with use of medications, low health literacy, and a distrust of the medical community[18,20].

C. Approach

Design and Overview. This pilot study will examine the feasibility, acceptability, and preliminary impact of providing an In vivo intervention with NRT to increase NRT adherence compared to the control group. The intervention will be tested and refined initially with 10 participants in the In vivo NRT group (In vivo). Following the pre-pilot testing, 80 participants will be randomized to either the 1) In vivo or 2) Standard of Care (SC). All participants will complete approximately 60 minutes of baseline assessment to determine smoking history and characteristics prior to randomization, including previous experience with NRT. In vivo participants will be provided with each of the four forms of acute NRT (gum, lozenge, nasal spray, inhaler per week; counterbalanced across sessions by participant) to use in each 30 minute session in conjunction with a nicotine patch. In session, they will discuss their In vivo experience of using each combination NRT at each of the four sessions. To bolster their in vivo NRT experience, participants will be provided with a weekly sample of each NRT product to use between sessions to acclimate to the medication and to make PQAs. After the 4 week In vivo intervention period, participants will select their preferred acute NRT product to use with the nicotine patch (combination NRT; cNRT) to use for cessation over the next eight weeks. SC participants will receive four sessions of standard behavioral smoking cessation counseling and will select their preferred acute NRT (gum, lozenge, nasal spray, inhaler) based on product description. Thus, both groups will receive cNRT for 8 weeks total to make a quit attempt. All participants will continue to receive medication and monitoring for side effects, regardless of their medication adherence. Study visits occur at baseline (Week 0), intervention Weeks 1-4, medication selection/quit goal setting visit at Week 5, medication check (Week 6) Weeks 9 and 13 (end-of-treatment), and follow-up at one month later (Week 17; see Figure 1 for Study Design).

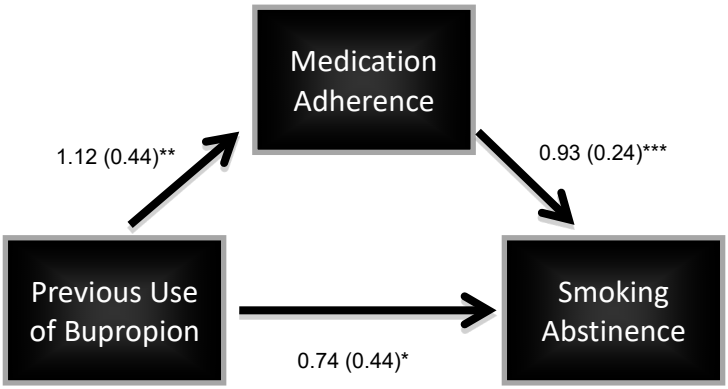
Preliminary Studies. The PI and her team have completed studies directly relevant to the current proposal and have worked with several different low income and disadvantaged populations such as individuals in the criminal justice system and Persons Living with HIV (PLWH).

Figure 1: Proposed Study Design from Recruitment to One Month Follow-up



1. Importance of Medication Adherence. Our group was the first to provide a cessation intervention to smokers under community corrections supervision at their point of monitoring (R01CA141663). We provided 12 weeks of bupropion to smokers, and randomized them to either four 30 minute sessions of standard smoking cessation counseling or brief physician advice to quit smoking. We randomized 500 smokers in 40 months and our results demonstrate the feasibility and acceptability of enrolling low income smokers for cessation. Although the majority of our participants reduced their cigarettes smoked per day (cpd) by the end-of-treatment (EOT) from baseline levels (reduced from 15 cpd to 7 cpd), only about 6% were abstinent at any particular time point (EOT: 9.3%) with no differences in cessation between our two groups. The most important predictor of successful cessation was medication adherence, with individuals who reported at least 80% adherence to 12 weeks of bupropion treatment (44% adherence) demonstrating an EOT quit rate of 17% vs. 4% for non-adherent participants with a biochemical CO verified cutoff of ≤3 ppm (p<0.001). To compare to the existing treatment literature which generally uses a CO cutoff of 10 ppm, quit rates were 48% vs. 13% (p<0.001) for adherent and non-adherent participants, respectively, at EOT. In either scenario, smoking cessation rates was quadrupled among adherent individuals and suggests adherence as critical target for low income smokers[15].

Figure 2: Mediation Model



Sobel Test: 2.13 (0.49), p =.033
*p<0.10; **p<0.01; ***p<0.001

2. Prior Medication Use, Adherence, and Cessation. In a follow-up analysis, we examined prior use of bupropion in relationship to adherence and cessation. While only 26 participant (5%) reported prior use of bupropion, smokers with prior bupropion use were significantly more likely to rate bupropion as helpful for smoking cessation at baseline (p=0.025) compared to smokers without prior experience with bupropion. We ran univariate analyses to determine the factors associated with adherence. Of the almost 50 variables examined including demographics (age, sex, race, income, etc.), dependence, withdrawal, craving, and smoking history, (e.g., age of first smoking, number of previous quit attempts, etc.) only five variables were significantly associated with bupropion adherence: race, age, prior bupropion use, treatment group, and percentage of friends who smoke. When these variables were simultaneously entered into a logistic regression model, prior use of bupropion was the single best predictor of adherence (OR=3.50; CI: 1.45-8.47; p=0.005).

We examined univariate predictors of being abstinent (7 days abstinent, CO ≤ 3ppm) at any time during treatment ("floating abstinence") and found several variables associated with abstinence including age, race, age of first tried smoking, cigarettes per day, abstinence self-efficacy, motivation, nicotine dependence, craving, difficulty of prior quit attempt, medication adherence, desire to quit in the next 30 days, and prior bupropion use. Using logistic regression, we found that medication adherence was the single best predictor of abstinence (OR=2.29; 1.32-3.97; p=0.003). Cigarettes per day was the only other variable associated with abstinence (OR=0.939; 0.898-0.981; p=0.005).

Given the associations between a) prior use of bupropion and medication adherence and b) medication adherence and abstinence, we were interested in testing a mediation model of these relationships. We found evidence of mediation such that the relationship between previous use of bupropion and smoking abstinence was significantly mediated by medication adherence (see Figure 2)[53]. We also tested mediation models that included motivation to quit, abstinence self-efficacy, interest in quitting, and belief in the efficacy of bupropion

and did not find significant mediation effects of these variables for the relationship between previous use of medication and smoking cessation. Thus, it appears that previous experience with medication is related to improvements in medication adherence, which is then associated with smoking abstinence and these associations are not accounted for by motivation, abstinence self-efficacy, or self-reported belief in the efficacy of medication. ***In other words, it is the concrete experience of using a medication that is most strongly associated with downstream uptake, adherence, and abstinence.***

3. A Pilot of In vivo Nicotine Sampling with PQAs. We randomized 47 community corrections smokers to either 4 sessions of In vivo NRT sampling with PQAs between sessions: Session 1 (S1): patch, S2: gum, S3: combination, S4: review quit attempt or 4 sessions of standard smoking cessation counseling (SC) with combination patch and gum. Both interventions were delivered by undergraduate students with minimal training in smoking cessation interventions but who were trained to follow the treatment manual. Medication was provided up to 12 weeks with additional study visits at weeks 8 and 12. In vivo participants demonstrated in session decreases in both withdrawal and craving relative to SC which illustrates the feasibility and acceptability of administering NRT in session to effect. When good adherence was calculated (defined as use of 80% of prescribed doses), participants in the In vivo group had a higher adherence rates to the patch (78.9% vs. 56.3%; p=0.15; converted Cohen's d=0.502), gum (57.9% vs. 20%; p=0.026; converted Cohen's d=0.828) and combination NRT (cNRT; 42.1% vs. 20%; p=0.17; converted Cohen's d=0.483) relative to Controls at Week 4. By Week 8, good adherence to nicotine patch had attenuated, although differences for adherence to gum (54.5% vs. 15.4%; p=0.04; converted Cohen's d=0.91) and cNRT (36.4% vs. 15.4%, p=0.237; converted Cohen's d=0.498) remained present between groups. By Week 12, no significant differences on good adherence were noted between the groups. A trend for better short-term abstinence was found for In vivo participants versus SC (10% vs. 0%, p=0.19; converted Cohen's d=0.44) at Week 4, although these differences attenuated by Week 12. While this study demonstrated good effects of the In vivo construct, this approach has several limitations compared to the proposed approach. First, participants only sampled gum and did not have a choice in the short-acting NRT to use with patch which does not reflect the real-world options for short-acting NRT. In addition, this pilot recruited only participants in community corrections and did not recruit low income participants without criminal justice involvement. While developing effective interventions for criminal justice populations is important, testing this approach with more general populations of low income smokers is needed initially. Finally, this project was a pilot trial with small numbers of participants and did not examine long-term outcomes after the 12 weeks of NRT administration and long-term outcomes are necessary to determine real-world impact.

These studies demonstrate our experience developing interventions with low income populations and the significance of the proposed approach. However, while our data as well as previous NRT sampling interventions are suggestive of the importance of NRT experience for subsequent cessation, pilot data are needed to determine the mechanisms of action associated with medication adherence. We will examine whether providing an In vivo NRT sampling intervention increases adherence over SC and whether this is due to increased positive NRT expectancies and abstinence self-efficacy as well as decreases in withdrawal and cravings. This is a necessary first step prior to launching a larger clinical trial examining this In vivo intervention for increasing abstinence.

Participant Availability, Feasibility and Rate of Enrollment. Participants will be recruited from the Birmingham metro community with flyers hanging at different community locations that serve low income smokers (e.g., bus stops, medical student run medical clinic servicing indigent patients, etc.). Based on our previous studies with similar populations as well as the high rates of smoking in Alabama, we do not anticipate any problems in recruiting the necessary study population. In our previous study with community corrections smokers, we screened 650 potential participants in 40 months to randomize 500, with most participants excluded due to medical contraindications for bupropion. Recruiting 10 participants in 3 months and 80 participants over 20 months would require enrollment of approximately 3-4 participants per month. Given that our team recruited a similar low income population of 500 participants within 40 months of recruitment (8 months earlier than projected), enrollment is very feasible. Further, while we will not focus specifically on participants with criminal justice involvement, individuals in the criminal justice system but serving their time in the community will not be excluded if they meet the other enrollment criteria.

Inclusion Criteria. a) 18 years or older; b) qualifying as low income (as defined by making <150% above the poverty line or <$22,260 as a single or <$45,570 for a family of four); c) Smoking at least 5 cpd for the past year and a CO>10ppm to ensure daily smoking. This relatively low cutoff was chosen due to the expectation of

enrolling a large ≥50% African-American average <10 CPD compared to Whites who average ~15 CPD.; and d) English speaking.

Exclusion Criteria. a) Living in a restricted environment (e.g., prison or jail facility, etc.); b) Pregnant or nursing (all women will be required to use an acceptable form of contraception); c) Currently enrolled in a smoking cessation treatment program, using NRT products, or prescribed bupropion or varenicline; d) Known sensitivity to any of the nicotine replacement products or sensitivity to adhesive used in nicotine patches; e) Trouble breathing, a pulmonary condition, or sinus problems; f) Within one month post-myocardial infarction or untreated severe angina; g) poor dentation or temporomandibular joint (TMJ) problems such as unable to use nicotine gum; h) Cognitive impairment or unstable psychiatric condition that interferes with the informed consent process (individuals stable on psychiatric medications will be included); or i) Daily or exclusive use of other tobacco products (e.g., electronic cigarettes, little cigars, etc.).

Pre-Pilot Intervention Refinement. We will conduct a pre-pilot intervention with 10 open-label In vivo participants to finalize study procedures and determine therapy fidelity prior to launch of the pilot RCT. All sessions will be audio-taped and 50% of the pre-pilot tapes will be coded for treatment fidelity to using the Yale Adherence and Competence Guidelines[54] to ensure adherence to the In vivo intervention. We will also solicit feedback from participants about satisfaction with treatment through a survey that will ask to rate their satisfaction with various aspects of treatment as well as assess treatment credibility and expectancy. We will make any refinements to the intervention or therapist training prior to initiating the pilot RCT.

Intervention. In vivo Group. Participants in the intervention group will receive In vivo experience with four different forms of short acting NRT combined with patch and counseling focused on their experience of using NRT, including positive experiences, side effects and smoking cessation expectancies. For each session, participants will be instructed to arrive to session wearing the nicotine patch and to have gone as long as possible without smoking. The rationale for instructing patch use from the beginning is to promote the use of combination NRT as the expectation. Further, instructing participants to go as long as possible without smoking is to demonstrate the additive effect of short acting NRT for relieving cravings and withdrawal effects. Prior to each session and receipt of the short acting NRT, participants will complete the brief withdrawal (Minnesota Nicotine Withdrawal Scale [MNWS]) and craving (Questionnaire of Smoking Urges; QSU) measures; see Table 1 for a brief description. Participants will repeat these assessments at the end of their session. All sessions (In vivo or SC) will be approximately 30 minutes and will be conducted individually by research assistants (RAs) trained to use the In vivo manual and who are not tobacco treatment specialists to increase real-world application and dissemination of this approach (see In vivo manual in Appendix A).

Session 1: At the end of the Baseline assessment (described below), In vivo participants will be given one nicotine patch and instructed to place it on their upper arm the day of their next appointment. If they arrive without the patch, they will immediately have a patch placed on their upper arm. They will then complete the assessment measures to allow the nicotine patch to demonstrate initial medication effects. The peak effects of nicotine patch occurs at 3.8 hours; however, initial detection of the drug occurs at 11.8 minutes[55]. Thus, participants will be wearing the patch for at least 30 minutes of assessment or longer which should be sufficient to experience at least some of the effects of the patch for relieving withdrawal. Our pilot work demonstrated that In vivo participants experienced reduced withdrawal and craving within 30 minutes of administration. After assessment, the first few minutes of the intervention will focus on their in vivo experience of wearing the nicotine patch and will query previous experiences with the patch. We will solicit both positive (e.g., “the patch helps with cravings”) as well as negative perceptions (e.g., “it makes my arm itch”) of the patch. Participants will discuss any side effects they experience with using the nicotine patch in session. Next, participants will be given one of four short-acting forms of NRT (gum, lozenge, inhaler, nasal spray; counterbalanced across participants by session). Thus some participants may receive gum first, while others will receive inhaler, lozenge, or nasal spray. This will wash out any primacy or recency effects of NRT across participants for product selection. The gum, lozenge and inhaler demonstrate initial effects for relief of withdrawal around 5 minutes and peak effects after about 15 minutes, while the nasal spray occurs more rapidly and more closely mimics the relief from smoking[56-57]. Thus, the delivery of nicotine in these short-acting products should be fast enough for participants to experience the effects of the medication on withdrawal and craving symptoms during session, as we noted with gum in our previous pilot study. Safety and efficacy results specific to both the patch and the specific short-acting NRT administered will be reviewed with the participant. They will also discuss their expectancies for the effectiveness of these products for cessation. Participants will be given a week supply of nicotine patches and whichever short-acting product they were randomized to receive first to use

after session and will be instructed on its use. The purpose of providing a seven day supply of cNRT product will be to encourage participants to use and acclimate to the cNRT and to use for PQAs. They will not be required to abstain during the week, but can use the cNRT however they wish, which may include concurrent use with smoking, or during practice or legitimate quit attempts. They will be instructed to wear the patch the day of their Session 2-4 visits but not to use the short-acting NRT on the day of study visits.

Sessions 2-4: Before completion of assessment measures, participants will be checked to make sure they are wearing a nicotine patch and will have a patch placed on their upper arm if they are not wearing it. After the assessment, they will be asked about their experience during the past week with using the nicotine patch and their experience with their short-acting NRT product, including any positive or negative experiences with the either medication and how they have used the NRT (e.g., to reduce) as well as any quit attempts they experienced. After this point, they will be given the next short-acting nicotine product and provided instructions on how to use the medication in session. They will discuss any prior experiences using the specific short-acting NRT as well as their expectancies for the medication to reduce their withdrawal or cravings. Safety and efficacy information specific to the use of that specific short-acting NRT will be reviewed with the participant. They will discuss any side effects that they notice with use of the specific short-acting NRT in session. Similar to above, participants will be given a week supply of both the patch and the assigned short-acting NRT at each session to use for practice during the week. They will always be instructed to wear a patch but not use the short-acting NRT during the morning of their subsequent sessions.

Standard of Care Group. Participants in the SC group will receive behavioral smoking cessation counseling based on best practice guidelines[26]. This same four session counseling intervention was used in our previous smoking cessation intervention with participants in the criminal justice system and was found to be acceptable and feasible with low income populations. While this intervention does not focus exclusively on use of NRT, proper NRT use is covered as part of any standard behavioral intervention for smoking cessation[26]. However, NRT will not be used in vivo during control sessions. Participants will be given a description of all four short-acting NRTs and will select one during their product selection session to use with the patch for smoking cessation throughout the intervention along with standard instructions for use. All counseling sessions will be approximately 30 minutes to match for therapeutic contact in the intervention group and will be conducted by RAs trained in the intervention and following the treatment manual (see draft client workbook in Appendix B).

Session 1: This session focuses on the harms of smoking and benefits of quitting. It will also cover behavioral factors associated with smoking including smoking as a habit, smoking cues, cognitive strategies to avoid smoking (e.g., distraction) and the physical symptoms related to nicotine withdrawal. Participants will learn coping strategies to deal with withdrawal and craving.

Session 2: Session 2 will focus on problem solving strategies to use for successful abstinence. The counselor will review common pitfalls associated with quitting such as refusing cigarettes from friends, weight gain, and sleep problems. Participants will be taught behavioral and cognitive strategies to combat these pitfalls. In addition, participants will be taught a brief relaxed breathing exercise to use during times of craving or when they have difficulties with sleep.

Session 3: This session of counseling will focus on behavioral changes made during the intervention (e.g., reducing number of cpd) and will discuss the importance of complete abstinence as the goal. Participants will be provided with strategies to reward themselves for abstinence including taking the money saved from buying cigarettes and using it for short-term and long-term rewards. In addition to reinforcements for abstinence, the counselor will review lapse behaviors and will stress the importance of abstinence as the goal.

Session 4: The session will cover basic information for preparing to quit including setting a quit date, eliciting social support from friends/family, and behavioral strategies to quit (e.g., discarding unused cigarettes, etc.). Participants will be educated on the use of all of the short-acting NRT products with the patch and will be told that they can use these products together for maximal effectiveness, although they will not use these products in-session. The importance of using cNRT will be emphasized during this session. Participants will take home a description of each NRT product to decide which product they want to use for their quit attempt.

Product Selection. At Week 5, after four weeks of product sampling of the four different NRT products and review of experiences with the final product, In vivo participants will select which short-acting NRT medication to use in conjunction with the patch. SC participants will select a short-acting NRT to use with the patch based on the product description only. All participants will be encouraged to continue to use their selected cNRT, assisted with setting a quit date, and provided with eight weeks NRT medication to use for cessation.

One Week Follow-up. All participants will return at Week 6 to check for any adverse effects of the medication, medication adherence, and initial abstinence status. Any problems with the medication will be checked and addressed and problem solving around quit attempts and maintaining abstinence will be covered. This session is expected to be 30 minutes.

Interventionist Training and Fidelity. Interventionists will be undergraduate level research assistants (RAs) with degrees in psychology or a related field. They will be trained to follow the manual and deliver both behavioral interventions by the PI, although they will not have extensive tobacco training. All sessions will be audio-taped and 20% will be coded for treatment fidelity to using the Yale Adherence and Competence Guidelines[54] to ensure no contamination between behavioral interventions. The choice to utilize non-therapist interventionists was made to approximate the therapy skill level of most professionals in low resource settings.

Combination Nicotine Replacement (cNRT). Participants will be screened at the time of their baseline appointment for the appropriateness of all NRT products. Our physician collaborator will be available to answer any questions that may arise when screening participants and will assist the PI in evaluating any adverse events believed to be related to the use of NRT. All participants will be evaluated for their initial NRT dose based on Federal Drug Administration guidelines. Participants who smoke 10 or fewer cpd will start at 14mg patch while smokers who use 11 or more cpd will start at 21mg patch. The nicotine inhaler delivers 4 mg of nicotine per cartridge (inhaling for 20 minutes on each cartridge) with participants using about 6 cartridges daily. Nicotine nasal spray delivers 0.5mg of nicotine per spray with one spray per nostril (1mg total) recommended 1-2 times per hour. Participants will be given the 2mg nicotine gum or lozenge to use. The safety and tolerability of using NRT products together or smoking while using NRT has been demonstrated[e.g.51]. Further, the rationale for using combination NRT over a single agent is two-fold. First combination NRT has demonstrated the best efficacy for promoting abstinence over all other single agents with the exception of varenicline[58]. Second, NRT is short-acting and can be administered in-session to demonstrate the effect of this medication in relieving withdrawal symptoms, including craving. NRT can also be used sporadically as is proposed during the sampling weeks. Other smoking cessation pharmacotherapies (e.g., bupropion, varenicline) take about a week to titrate to full effect[26]. Both groups will receive 8 weeks of medication for a sustained quit attempt, although the In vivo group will be sampling four different short acting NRT products during the first four weeks of the intervention.

Baseline and Assessment Measures. After eligibility determination and consent to participate, the baseline assessment will be administered. This assessment is expected to take about 60 minutes and will provide basic smoking history, smoking behavior, and proposed mediators and moderators such as treatment interest, expectancies for NRT, previous use of NRT, craving, withdrawal, and side effects associated with NRT use (see Table 1 description) and will be repeated during the study period (see Table 2 for assessment schedule).

Table 1: Instrument Description
Screening Questionnaire. Participants will be asked basic screening questions prior to consent for the study to determine initial eligibility including: age, income, currently pregnant or nursing, average CPD, latex allergy, myocardial infarction in past month, and years of smoking. (3 min)
Demographics. Basic demographic information will be collected including age, gender, race/ethnicity, education level, employment status, marital and living situation, monthly income, and history of substance use and mental illness. (1 min)
Urine Drug Screen. All participants will be screened for drug use during baseline assessment. We will test for alcohol (using ethyl glucuronide) as well as amphetamines, barbiturates, benzodiazepines, cannabis, cocaine, opiates, and methadone. (1 min)
Smoking History. Questions about smoking history will include age of smoking initiation, age of regular use, us of other tobacco products, number of years of smoking, average cigarettes smoked per day, previous quit attempts, time since last quit attempt, difficulty of last quit attempt, previous smoking cessation treatment (e.g., use of NRT, bupropion, varenicline), family members who smoke, and family and personal medical problems related to smoking. (10 min)
Treatment Expectancies. This assessment queries expectancies about the efficacy of various forms of smoking pharmacotherapy (e.g., nicotine gum, patch, lozenge, inhaler, nasal spray, varenicline, and bupropion) as well as behavioral interventions (e.g., group, individual, self-help materials, hypnosis) using the question, "How much do you think _____ will help you to quit smoking". These questions are answered using 1-7 Likert scale. This is a scale we developed and used in our studies with this population. (5 min)
Perceived Stress Scale – 10 Item (PSS-10[59]). This is a self-report questionnaire that assesses a person's stress in the past month. It utilizes a 5-point Likert scale ranging from "Never" to "Very Often". (1 min)
Thoughts About Abstinence Questionnaire – 4 Items (TAA) [60]. This survey assesses 1) motivation to quit; 2) expected difficulty quitting; 3) confidence in one's ability to quit (abstinence self-efficacy); and 4) abstinence goals. (1 min)
Smoking Abstinence Questionnaire (SAQ[61]). The SAQ assesses a smoker's expectancies for the process of smoking cessation on 10 scales. The SAQ scales have demonstrated good reliability and robust relationships with tobacco dependence, motivation to quit and abstinence self-efficacy, and withdrawal. (5 min)
Abstinence-Related Motivational Engagement (ARME[62]). This 16-item scale assesses motivational changes after a quit attempt

on a 0-7 Likert scale. (5 min)

Attitudes about Nicotine Replacement-12 scale (ANRT-12[63]***).*** This 12-item scale asses smoker's attitudes about NRT and measures two factors: advantages (e.g., NRT will help with withdrawal symptoms and cravings) and disadvantages of NRT (e.g., NRT is addictive, side effects, etc). (5 min)

Fagerström Test for Nicotine Dependence **(FTND**[64]**)**. The FTND is a 6-item self-report measure of nicotine dependence from the Fagerström Tolerance Questionnaire[65]. The FTND has satisfactory internal consistency and high test-retest reliability. (5 min)

Brief Wisconsin Inventory of Smoking Dependence Motives (WISDM-37[66]**)**. The Brief WISDM has 37 items that load onto 11 subscales. The psychometric properties of the reduced-item WISDM subscales is comparable to the WISDM-68. (10 min)

Questionnaire of Smoking Urges-Brief Form **(QSU**[67]**)**. The shortened version of the QSU assesses cravings associated with quitting smoking. The 10-item scale is scored on a Likert-style scale ranging from 1 (strongly disagree) to 7 (strongly agree). During Sessions 1-4, participants will complete this measure before and after their counseling sessions. (5 min)

Minnesota Nicotine Withdrawal Scale (MNWS[68]**)** using DSM-IV criteria it assesses the physical and psychological symptoms associated with withdrawal. During Sessions 1-4, participants will complete this measure before and after their sessions. (5 min)

Treatment Satisfaction Survey (TSS). This survey will be administered at the Product Selection session and subsequent sessions to determine satisfaction with both treatments. In addition to standard questions about different aspects of treatment (e.g., satisfaction with medication, satisfaction with therapy, etc.), participants will queried about what aspects of the intervention they would change and how they would change it. (5 min).

Credibility and Expectancy Questionnaire (CEQ)[69]***.*** This 6-item brief scale asks patients about how they think and feel about the treatment. It is broken down into two main scales; credibility and expectancy for treatment. It has demonstrated good internal consistency and good test-retest reliability. (2 min).

Side Effects. We will use a side effect scale to determine common side effects associated with pharmacotherapy and quitting smoking. This self-administered, 1-7 Likert scale instrument was used during our previous smoking cessation trial with correctional populations and captured the range of side effects experienced during the trial. (5 min)

Carbon Monoxide **(CO) and Tobacco Use Assessment.** Expired breath samples will be obtained at every study visit. Participants will be asked questions related to recent smoking behavior, including time since last cigarette, 24 hour quit attempts, overnight abstinence status, number of cpd, and average cpd smoked for that week. CO >3 ppm will be considered smoking[70-72]. (1 min)

NRT Adherence. All participants will be assessed on their self-reported daily use of NRT using a Time Line Follow-Back (TLFB) method during the 8 weeks of treatment. All participants will also be assessed during all intervention weeks for their use of NRT by returning used patches and returning used blister packaging/used canisters/cartridges from short-acting NRT. Use of 80% of more of the medication will be considered adherent. We used a similar technique to assess NRT adherence in our pilot trial with good compliance with returning used patches/blister packaging. (5 min)

Table 2: Study Assessment Schedule

	BL		Post-Randomization Assessment Schedule								
Measures or Procedures (weekly compensation)	**Day 0 ($10)**	**RANDOMIZATION**	**WK1 S1 ($20)**	**WK2 S2 ($20)**	**WK3 S3 ($20)**	**WK4 S4 ($20)**	**WK5 PS ($20)**	**WK6 ($20)**	**WK9 ($40)**	**WK13 ($40)**	**M1 FU ($40)**
Screening Questionnaire	X										
Demographics	X										
Urine Drug Screen	X										
Smoking History	X										
Treatment Expectancies	X		X	X	X	X	X	X	X	X	X
PSS – 10 Item	X		X	X	X	X	X	X	X	X	X
TAA	X		X	X	X	X	X	X	X	X	X
SAQ	X						X	X	X	X	X
ARME	X		X	X	X	X	X	X	X	X	X
ANRT-12	X		X	X	X	X	X	X	X	X	X
FTND	X						X	X	X	X	X
WISDM	X						X	X	X	X	X
QSU	X		X[1]	X[1]	X[1]	X[1]	X	X	X	X	X
MNWS	X		X[1]	X[1]	X[1]	X[1]	X	X	X	X	X
TSS							X			X	X
CEQ							X			X	X
Side Effects	X		X	X	X	X	X	X	X	X	
Carbon Monoxide **(CO)**	X		X	X	X	X	X	X	X	X	X
NRT Adherence	X		X	X	X	X	X	X	X	X	

Note: BL=Baseline Assessment; S=session; WK=week; M=month; PS=Product Selection; [1]All participants will complete these surveys twice (at the beginning and end of session) during sessions 1-4.

Randomization. We anticipate enrolling 10 pre-pilot participants in 3 months and 80 participants in 20 months and, based on our previous study with this population, expect to retain at least 70% through the one month follow-up point. Randomization will occur after completion of the initial screening and assessment.

Primary Outcomes. Feasibility and acceptability will be measured through high study retention (70%) and recruitment (recruitment of all participants within 24 months) in our groups. Additional items of acceptability include high scores on treatment satisfaction and credibility/expectancies that are equal or higher to the SC

group. Medication adherence is a third primary outcome with expected differences between our groups. Adherence is notoriously difficult to determine. Self-reported adherence is not always reliable, particularly during treatment studies where there is a demand characteristic to report the desired targeted behavior[73-74] (e.g., adherence to NRT). The behavioral methods described under the assessment section represent the best available self-report tools for determining NRT adherence (e.g., TLFB report, returning used NRT patches and used product blister packs/packaging). Adherence will be defined by self-report using the TLFB and verified through returned patches and packaging. Good adherence is defined by taking greater than 80% of doses of medication at each time point. We have used these techniques in previous studies with low income populations with good compliance for use of TLFB verified by return of NRT materials[75].

Participant Tracking and Retention. Participants will attend four weekly intervention sessions and a Product Selection session at Week 5. They will receive a one week follow-up after starting medication as well as monthly follow-up at weeks 9 and 13 during the NRT administration. The final follow-up will occur one month post-intervention. For this study, we will follow our participants for one month after the end of NRT administration (~4 months total in the study). We will continue to use our standard methods for ensuring high retention including collecting contact information on the participant as well as obtaining the contact information of three close friends or family members and providing follow-up and reminder phone calls. We have used these methods with good success with our ongoing and previous projects with this population. Thus, we believe we can maintain high retention and follow-up throughout the study.

Data Management and Statistical Analysis. Data will be entered and stored on the UAB secured network. Data analyses will performed by the PI who has a master's degree in biostatistics using SPSS.

To test Aim 1, the development and refinement of the In vivo intervention, we will pre-pilot the intervention with 10 participants. We will examine participant's responses on the Treatment Satisfaction Survey as well as examine other factors that participants mention to improve treatment. As the intervention is already developed, this phase will be primarily used to finalize study procedures and make modifications to the study protocol. We will not conduct any in depth interviews or use qualitative methods, but will rather use this is an opportunity to make minor adjustments to the protocol.

To Test Aim 2, feasibility and acceptability of the intervention, we will determine our rate of recruitment, retention and the credibility and expectancies for the intervention using descriptive statistics. We expect that the novel In vivo intervention will be both feasible and acceptable as evidenced by a high rate of recruitment and over 70% retention through follow-up, with no differences in attrition between the groups. In addition, we expect that In vivo intervention will be rated as high on treatment satisfaction, credibility, and expectancies for treatment relative to SC. We will use Chi-Square analyses to examine attrition and t-tests to examine treatment satisfaction scores, credibility, and expectancy differences between the groups.

To test Aim 3, we will examine medication adherence during the 8 week intervention period between the intervention groups using Chi Square analyses at weeks 6, 9 and 13. Medication adherence will be defined as a self-reported use of taking 80% of medication as prescribed at each time point for both groups (adherent or not adherent). We can also look at adherence as a continuous proportion variable: adherence = number of doses taken / the number of doses given. We will also examine demographic and smoking characteristics (particularly withdrawal, cravings, abstinence self-efficacy, and NRT perceptions) that would be associated with medication adherence at weeks 6, 9 and 13 using logistic regression. These analyses will allow us to examine important associations with medication adherence in these groups.

To examine underlying factors believed to be important for medication adherence, particularly withdrawal, craving, self-efficacy, and perceptions of NRT, we will also examine these factors by intervention groups across time using paired t-tests, as appropriate. We are primarily interested in determining if our In vivo group had decreases in withdrawal and cravings, while increasing abstinence self-efficacy and NRT perceptions relative to the SC group. Given the pilot nature of this intervention, we will be able to examine 24-hour quit attempts and abstinence, but these factors are not the main focus on analyses as we will likely be underpowered to find significant differences on these outcomes with this small of a sample. While 80 participants may seem like a fairly large sample for a pilot study, a sample size between 500-600 participants is typical for most smoking cessation interventions and would be needed to examine important moderators and mediators of cessation. However, we will be able to obtain initial effect sizes that will be useful for determining the appropriate sample size for a fully-scaled R01 project in the future, if this intervention appears promising.

Missing data. There is a high likelihood that we will have participants who may miss an appointment, do not complete the study, or are otherwise lost to follow-up. Because of the potential of bias due to non-missing

completely at random data, we will perform sensitivity analyses to assess whether differences in treatment outcome are a function of study completion. We will assess the magnitude of missing data upon completion of the study. If the amount of missing data is large (>30%), we will utilize multiple imputation (MI) methods in order to not suffer a loss of power due to the loss in sample. However, our previous smoking cessation intervention with a criminal justice sample had the same number of intervention sessions had a 74% retention rate at one year. We expect to have a 70-80% retention rate throughout the time of this study.

Study Design Considerations. We made several design choices that should be discussed. First, as is appropriate for a pilot trial, issues of feasibility and acceptability are the primary outcomes of interest. In addition, adherence to NRT is the smoking-related primary outcome of interest, rather than cessation. In our sample of participants and using a CO cutoff of 3 ppm, we generally only achieve about a 6-10% abstinence rate at any one time. While this seems low to researchers who are used to using 10 ppm cutoffs, our previous studies do achieve similar abstinence rates when we use the higher cutoff point of 10 ppm as other smoking cessation interventions. We believe that a 10 ppm cutoff is artificially high and classifies light smokers or chippers as abstinent[70-72] and we would rather be rigorous in our outcome of cessation. We know from previous studies as well as the existing literature on adherence that approximately half of smokers are adherent to their medications. Given these proportions, we will be able to do better comparisons to determine the underlying factors associated with adherence with a small sample such as 80 participants and would need much larger samples (N=500-600) to examine factors associated with cessation. Further, evidence suggests that adherence to medications is a critical factor in cessation and no interventions have been developed to successfully increase adherence as well as smoking abstinence. This project is the first step in developing an adherence intervention that we believe will also increase cessation. In addition, some may question the rationale for giving the patch with acute NRT product at all sessions and not separating the experience of these products. This design choice was made for two reasons: First, we wanted to normalize the use of combination NRT by setting the expectation from the start that the patch is to be used with short acting NRT. Second, we want smokers to realize that the patch alone may be insufficient to reduce all cravings and withdrawal but that a short acting NRT can be used to relieve these symptoms acutely. Finally, we considered doing a standard NRT education intervention as our control group such as has been tried in the past to examine the impact on adherence and cessation and this would be a good comparator. However, we wanted to pilot this In vivo intervention against what is considered the best practices for smoking cessation as we believe In vivo could potentially be a stand-alone treatment for cessation that would require less therapeutic knowledge and training to implement relative to standard smoking cessation counseling. This is important for dissemination in low-resource settings and for broad dissemination and adoption.

Strengths and Limitations of the Study. This study has modest limitations that should be mentioned. First, given the special nature of low income smokers, a criticism of this approach may be that this intervention should first be tested in a "general" population of smokers to examine initial effects before being tailored to a specialty population such as low income smokers. However, testing this approach with low income and disadvantaged smokers targets the population with the lowest rates of medication adherence who are the least likely to use NRT during quit attempts and the most likely to hold negative perceptions of NRT, all the proposed targets of this intervention. Thus, testing an adherence intervention in this population provides a smoking cessation intervention that is specifically responsive to the needs of this population. If we first tested this intervention among general/middle-upper income population of smokers who already have good rates of NRT adherence, we may not detect differences between our groups in NRT adherence or changes in NRT perceptions due to a ceiling effect. Further, smoking is now concentrated in low income and other disadvantaged smokers[76] (e.g., substance users, mentally ill, incarcerated, etc.) and few interventions have been developed to help these smokers, likely due to this "trickle-down science" mentality of first testing all interventions with general, non-disadvantaged smokers. Given that low income smokers now represent the "new majority" of smokers[76], testing smoking cessation interventions first in a general population of smokers who are at least middle income with no substance use or mental illness actually makes these interventions less "real world" and unable to generalize to the actual population of smokers present today. Second, a related criticism may be that our intervention is not intensive enough to bring about changes in such a difficult to treat smoker. This is an issue that we constantly struggle with and an argument can be made on both sides of this issue. Interventions that are very intensive in terms of time and resources are unlikely to be implemented in busy clinical or low resource settings; while interventions that are brief may not have the desired impact. We selected an intervention that is brief and simple enough to implement in busy settings by non-therapist providers but still intensive and targeted to bring about change. Third, we are comparing two different

behavioral interventions that primarily differ on the mode of delivery and product selection of NRT, making it more challenging to find an effect. However, we feel that having an active control group which delivers a best practices intervention will more fully test the premise that this approach is superior for increasing adherence in this disadvantaged population. Obviously, comparing our active intervention to a no treatment or inferior control group would maximize our ability to find a significant difference between our groups, but it would not answer the question of superiority of this approach for this population. It is analogous in medication development to the developing of another SSRI medication to treat depression versus developing a new class of medications. We were most interested in determining if this approach could be a "new class" behavioral approach for smoking adherence that is superior to current best practices. Finally, other concerns that may be raised center around our ability to obtain the necessary sample of participants or other methodological choices. We have demonstrated experience with recruiting similar samples of smokers as proposed in this application and have been able to maintain excellent retention in our studies with challenging populations. We have been conducting research with disadvantaged populations for over 15 years and have made the best choices we could, realizing that alternative methods could also be considered and debated.

The proposed intervention has several important strengths. First, the intervention is fairly straightforward, and if successful, could be implemented within low resource settings with minimal training or expertise needed by the interventionist. In fact, we are using non-therapists for this intervention to underscore the translation of this intervention in low resource settings. Second, the intervention is also very novel and expands from more traditional psychoeducational interventions as a mode for increasing adherence (which has limited results, at best) to a more experiential model similar to previous NRT sampling interventions that expose motivated and non-motivated smokers to NRT as a mechanism for increasing medication adherence and ultimately cessation. Low income smokers have lower health literacy and hold negative perceptions of medications. Importantly, they also appear to have limited experience with using such medications during smoking cessation. Providing an intervention that provides experience with the medication in a controlled, supervised session (in which negative experiences can be contained and reframed in real time) may be an important strategy to increase NRT adherence, particularly in this population. Allowing participants the opportunity to then select their preferred short acting NRT is believed to maximize abstinence self-efficacy, motivation, and engagement in the quit process. Third, few smoking cessation interventions have been developed for low income smokers and the proposed study represents the next logical step in developing an effective intervention to help these smokers increase adherence and attain abstinence. To our knowledge, no medication adherence studies have been developed or conducted with a low income population, despite the fact that low income populations hold negative NRT perceptions and have the lowest medication adherence and use during quit attempts. Fourth, low income and other disadvantaged groups of smokers now represent the majority of the population who are current smokers and suffer from disproportionate disease burden. Despite this fact, interventions continue to be developed that target general smokers and exclude these disadvantaged smokers from clinical trials. However, developing effective smoking cessation interventions with this population has the potential to reduce health disparities to significantly improve health and reduce death and disease in this underserved population. Finally, this proposal is led by an experienced PI as well as a team of investigators who have worked together over the years. Thus, the ability to implement and complete this important study within the three year proposed timeframe is assured. See study timeline below.

Timeline: Month 1 we will hire/train staff; Months 2-6 we will enroll 10 participants and begin the pre-pilot intervention. We will make any changes to the intervention during Month 7. During Months 8-30 we will recruit and complete follow-up of our participants. Months 31-33 will be for completing follow-up appointments, data cleaning, and data analysis. Months 34-36 will be for completing data analysis and disseminating results.

Impact. Development of a novel, experiential intervention that can be delivered by non-therapists to increase NRT adherence through improved NRT expectancies, perceptions and self-efficacy would be a significant advancement in smoking cessation for low income smokers. Increasing medication adherence is believed to be the single most important factor for reducing racial disparities in smoking cessation and disease outcomes. Developing an intervention to increase NRT adherence is critical to increase smoking abstinence in low income, disadvantaged smokers. This project represents an important first step in developing an effective intervention to improve NRT adherence that could be widely adopted and disseminated by non-therapists in low resource settings.