Study Protocol
NCT05740098
July 21, 2020

Below is a copy of the protocol reviewed by the University of Vermont Institutional review Board. Information in red font reflects changes made to continue the project after the onset of the COVID pandemic. A chronological list of dates for IRB approved protocol changes is listed immediately below.

10/29/2015: Dropped plan to offer non-contingent incentives to women in the Best Practices alone condition.

2/17/16: Added a 2nd baseline child urine specimen to increase the accuracy of our estimate of pretreatment secondhand smoke exposure.

4/19/2016: Eliminated breastfeeding as an exclusion criterion as it was determined that nicotine is transferred in breastmilk at insufficient levels to be detected in child urine specimens as due to secondhand smoke exposure.

8/17/2016: Discontinued use of public insurance (Medicaid or equivalent) as a study inclusion criterion

3/30/2020: Revised data collection methods to minimize physical contact between study staff and participants due to the COVID pandemic.

7/21/2020: Further adjustments in data collection methods to minimize physical contact between study staff and participants due to the COVID pandemic.

Human Subjects Research Protocol

PROTOCOL SUMMARY

Project Title:	**Protocol Version Date (required for each protocol modification):**
Behavioral Economic Approach to Reducing Maternal Smoking in Disadvantaged Women	7/10/2020

Principal Investigator: Stephen T. Higgins

TYPE OF REVIEW

Which type of IRB review are you requesting? Full [ ] Expedited [X] Complete category.

Your research may be expeditable if the research activities (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories: (CHECK THE CATEGORY(IES) THAT APPLY.

[ ] (1) **Clinical studies of drugs and medical devices only when condition (a) or (b) is met.**
(a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (NOTE: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review).
(b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

[ ] (2) **Collection of blood samples** by finger stick, heel stick, ear stick, or venipuncture as follows: (a) from healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week: or (b) from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

[X] (3) Prospective **collection of biological specimens** for research purposes by noninvasive means.

[ ] (4) **Collection of data through noninvasive procedures** (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves.

[ ] (5) Research involving **materials** (data, documents, records, or specimens) that have been collected, or will be **collected solely for nonresearch purposes** (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 .CFR 46.101 (b)(4). This listing refers only to research that is not exempt.)

[ ] (6) **Collection of data from voice, video, digital, or image recordings** made for research purposes.

[X] (7) **Research on individual or group characteristics or behavior or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.** (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3)).

PURPOSE AND OBJECTIVES

Purpose: The importance of the research and the potential knowledge to be gained should be explained in detail. Give background information.

Maternal Smoking and Child Secondhand Smoke Exposure (SHSe)

Smoking among women is sufficiently important to the U.S. public health to have warranted two separate reports of the U.S. Surgeon General devoted exclusively to the topic (USDHHS,1980; 2001). Smoking prevalence is unevenly distributed in the U.S. population, being highly concentrated among individuals with low

socioeconomic status, especially low educational attainment. Such differential smoking rates contribute directly to the unsettling problems of health disparities that are growing in the U.S. (e.g., Margerison-Zilko, 2012). Not surprisingly, there is considerable consensus on the need to reduce smoking among disadvantaged women, especially maternal smokers (e.g., Graham et al., 2007; Higgins & Chilcoat, 2009; Kandel et at., 2009).

Despite widespread knowledge of the harmful effects of second-hand-smoke exposure (SHSe), estimates are that 85% of children from low-income U.S. families experience chronic exposure (Cornelius et al., 2003; Halterman et at., 2010; USDHHS, 2007). Children exposed to SHS are at increased risk for numerous serious health problems, including sudden infant death syndrome, more severe asthma, lower respiratory infections, and chronic middle ear disease, and maternal smoking is a particularly significant contributor to this increased morbidity and mortality (Blackburn et at., 2005; Schoenberger et at., 2003; USDHHS, 2007). SHSe is also a substantial economic burden on the U.S. healthcare system, being estimated to increase direct medical and life-lost costs by » $5 billion annually (Aligne & Stoddard, 1997; Sisko et al., 2009).

Interventions developed to reduce children's SHSe have aimed to (1) decrease parental smoking around their children, (2) increase parental smoking cessation, or (3) both. Since smoking by a child's mother is a particularly significant contributor to SHSe, interventions have typically targeted smoking mothers. Regarding efforts to decrease smoking around children, studies testing relatively low-intensity interventions (e.g., written materials, brief advice) have failed to change exposure levels (e.g., Irvine et at., 1999; Wakefield et al., 2002), while those testing more intensive interventions have had more success decreasing children's SHSe, with at least some instances of biochemically-verified changes (see Hovell et at., 2009).

The results of Hovell et al. suggest that interventions to help mothers smoke away from their children may yield important benefits. Still, as the Surgeon General's report on children and SHSe notes, "the single best way [for a smoker] to protect their family from secondhand smoke is to quit smoking." Unfortunately, that is where substantial improvements are sorely needed in treatment development efforts. We know of only two reports focused exclusively on developing a smoking cessation intervention for mothers of young children (Curry et at., 2003; Wall et at., 1995). The interventions tested were brief, low-cost interventions (e.g., brief advice, written materials, telephone outreach) that could be readily integrated into pediatric care. Both Curry et al. and Wall et at. reported differences in self-reported point-prevalence smoking levels (14% vs. 7% at 12 mos, and 6% vs. 3% at 6 mos, respectively), but in neither case could those self-reported changes be biochemically verified. Of course, there is considerable social pressure on parents to underreport smoking (e.g., Hovell et al., 2009; Lund et at., 2004) and hence it is not unexpected that self-reported cessation rates might be inflated.

Clearly, more effective smoking-cessation interventions for mothers are needed to meet the public health priority of reducing SHSe among children (USDHHS, 2010). We recognize that maternal smoking cessation will not eliminate SHSe among children since many (-40%) live with more than one smoker (King et at., 2009). However, the evidence is clear that smoking mothers are the primary contributors to their children's SHSe, making them the obvious first target (Blackburn et al., 2005; Schoenberger et al., 2003; USDHHS, 2007). The overarching goal of this project is to develop an efficacious, cost-effective incentive-based smoking cessation intervention that is combined with state-of-the-art smoking-cessation pharmacotherapy practices to optimize outcomes.

More Intensive and Effective Cessation Interventions

Brief, low-cost interventions. A notable limitation discernible in the literature on smoking-cessation for mothers of young children is an over-reliance on brief, low-cost interventions with broad reach that can be readily delivered as part of routine medical care, etc. This is a public health approach where the overarching goal is to improve population health over time. The dramatic decline in smoking prevalence in the U.S. over the past 45 years is evidence of the effectiveness of that approach (Irvin Vidrine et al., 2009). While there is widespread recognition of the importance of that accomplishment, there is also growing recognition of the need to compliment the public-health approach with more intensive interventions targeting the most vulnerable populations who often are underserved by this public health model (Abrams, 2007; Frohlich & Potvin, 2008; Hiscock et al., 2012; Irvin Vidrine et al., 2009; Satchel & Higginbotham, 2008). What is driving much of this recognition of the need for adjustments in tobacco-control strategies is the leveling off of the declines in smoking prevalence in the U.S. and other developed countries during the past decade, largely attributable to the difficulties encountered in decreasing smoking among more economically-disadvantaged individuals.

This same heavy reliance on brief, low-cost interventions is also true of efforts to promote smoking cessation during pregnancy where results have similarly fallen short. For example, we know of at least 16 controlled trials in that area examining variations of brief advice and pregnancy-specific self-help materials (see Lumley et at., 2009; Melvin & Gaffney, 2004). Only four of those trials resulted in significant differences in antepartum cessation rates (Ershoff et al., 1989; Hjalmarson et at., 1991; Windsor et al., 1985; 1993) and just one trial produced a demonstrable improvement in birth outcomes (Ershoff et al., 1990). Such exclusive focus on brief interventions seems incompatible with the extensive evidence linking cigarette smoking with serious adverse health

consequences for infants and children (Rogers, 2009).

Regarding the general population of smokers, the 2008 Clinical Practice Guidelines on Treating Tobacco are quite clear in concluding that intensive treatment is more effective than brief treatment, intensive treatments are appropriate for all tobacco users willing to participate in them, and that patient satisfaction is higher with intensive compared to brief interventions (Fiore et al., 2008). We believe that these same recommendations need to be followed with maternal smokers. There are at least two areas of treatment development research for smoking cessation during pregnancy where investigators are examining more intensive treatment interventions (i.e., pharmacotherapies and financial incentives). Regarding pharmacotherapies, there have been several promising trials reported on NRT with pregnant smokers and important ongoing research (see Oncken & Kranzler, 2009 for a review). Two of the more promising findings have involved increased cessation rates with combined behavioral and pharmacological interventions (Pollak et al., 2007) and improved birth outcomes with NRT despite modest treatment effects on abstinence (Oncken et at., 2008). There is little question that pharmacotherapy has an important contribution to make to improving smoking-cessation outcomes with maternal smokers.

Incentives

We feel the same is true regarding financial incentives. Several controlled trials conducted by our research group and another group at Oregon State University have demonstrated that an incentive-based intervention where women earn vouchers exchangeable for retail items contingent on biochemically-verified abstinence significantly increases antepartum and postpartum smoking abstinence, improves birth outcomes, and increases breastfeeding duration among economically disadvantaged women (Donatelle et at., 2000; Heil et al., 2008; Higgins et al., 2004; Higgins et al., 2010a; Higgins et al., 2010b). That is the model that we are proposing in this application. The treatment effects obtained with incentives in pregnant smokers, a notoriously difficult population of smokers to treat, are encouraging regarding the potential utility of this approach for treating other groups of recalcitrant smokers as well. In the most comprehensive meta-analysis on cessation treatments for pregnant smokers, financial incentives produced a 24% average difference between experimental and control conditions compared to 6% across all treatment approaches (Lumley et al., 2009). Additionally, in an economic analysis of the interventions reviewed in that comprehensive meta-analysis comparing financial incentives, cognitive behavioral strategies, stages of change, feedback, pharmacotherapies, and "other" therapies that was commissioned by the United Kingdom's National Institute for Health and Clinical Excellence (NICE), financial incentives produced the highest net cost benefit per intervention, with a net benefit of 2,261 pounds or $3,482 after accounting for the cost of the intervention (Taylor, 2009, http://www.nice.org.uk/nicemedia/live/13023/49421/49421.pdf}. We believe it is important to include cost-effectiveness analyses in this next generation of incentives treatment-outcome studies and we are proposing to do so in the proposed study with mothers of young children. Importantly, there is evidence from the smoking-cessation literature that cost-effectiveness increases with increasing intensity of smoking-cessation interventions (Cromwell et at., 1997).

Pharmacotherapy

We know of only four controlled studies that experimentally investigated the effects of combining abstinence-contingent incentives with smoking-cessation pharmacotherapy and all examined only short-term abstinence (< 3 wks). Our group conducted a controlled study with 14 schizophrenic outpatients using a within-subjects design, another challenging population with high smoking prevalence and notoriously poor quit rates (Tidey et al., 2002). During three 5-day periods, patients were exposed to incentives for smoking abstinence combined with transdermal 21 mg NRT, incentives combined with placebo, and non-contingent incentives combined with placebo. Incentives increased abstinence compared to the non-contingent control, but NRT did not improve outcomes above incentives plus placebo. Similarly, Tidey et al. (2011) reported a between-groups study with 57 schizophrenic smokers randomized to 300 mg/day bupropion SR or placebo in combination with incentives for reductions in urinary cotinine levels or to a non-contingent control condition. Over a 22-day study period, incentives decreased cotinine levels compared to the control condition, but bupropion did not reduce cotinine or improve outcomes above levels achieved with incentives. The two other studies were conducted with smokers without serious mental illness (Perkins et al., 2008; 2010). Both studies used a 2 x 2 crossover design involving 5-day study periods comparing incentives vs. no incentives and active medication vs. placebo. The medications were 21 mg transdermal NRT (Perkins et al., 2008) and 1 mg b.i.d. varenicline (Perkins et al., 2010). Across both studies, treatment effects were additive: incentives and medication each independently increased abstinence and when combined produced abstinence levels greater than those observed with either alone. To our knowledge, the proposed trial will represent the first experimental examination of the effects of combining incentives with pharmacotherapy compared to incentives alone on longer-term abstinence.

Behavioral Economics as a Conceptual Framework for Understanding Parental Smoking

The high rates of SHSe described above can be difficult to comprehend considering that the adverse consequences are increasingly well known and there are more effective smoking-cessation treatments available now than ever before. Studies indicate that parents are well aware of the adverse consequences of SHSe on

children's health (Halterman et al., 2010), including smoking parents (Johansson et al., 2005). A report by Mahabee-Gittens (2002) also provides insight into the smoking-cessation intentions of parents with young children. In this study of 102 disadvantaged parents, 82% had intentions to quit but only 21% actually made a quit attempt. Importantly, 66% reported that they would be interested in joining a smoking- cessation program and/or trying a smoking-cessation medication. Despite knowledge of the adverse consequences of continued smoking and intentions to quit, why don't these mothers stop smoking?

Behavioral economics offers potential answers to that question. Results from several studies demonstrate that smokers discount the value of delayed reinforcement more than nonsmokers, a phenomenon known as delay discounting (DD) (Bickel et al., 2007). This difference can be summarized as smokers showing a greater preference for more immediate, smaller magnitude rewards (e.g., smoking a cigarette) *over* more delayed, larger-magnitude rewards (e.g., a healthy child). Moreover, other studies have shown that individuals with less education discount more than those with more education (e.g., de Wit et al., 2007). Additionally, two studies by our group have demonstrated that greater discounting predicts poorer treatment outcomes in pregnant smokers (Washio et al., 2011; Yoon et al., 2007). Yoon et al. (2007) demonstrated that among women who quit smoking during pregnancy (N=48), those who discounted more at baseline were also more likely to relapse back to smoking by 6-months postpartum. Using data from our research clinic for cocaine abusers, Washio et al. (2011) demonstrated that DD of hypothetical monetary reinforcers predicted the amount of abstinence achieved among 36 outpatients receiving incentives with relatively low- or high-magnitude monetary value. DD predicted the number of weeks of cocaine abstinence, adjusting for treatment condition ($p = .02$). Interestingly, greater discounters achieved less abstinence in the low-magnitude ($p = .02$), but not in the high-magnitude ($p = .30$) incentive conditions, suggesting that the high-magnitude incentives were helping individuals abstain despite their steeper discounting.

Other behavioral-economic tasks also have important potential contributions to make toward understanding persistent smoking among disadvantaged populations and individual differences in response to incentives and other interventions. One instrument that we are proposing to examine in this application uses a simulated cigarette purchase task (CPT) to generate demand curves for smoking-produced reinforcement (e.g., Murphy et al., 2011). Individuals report the number of cigarettes they would smoke in a hypothetical day across a range of prices per cigarette. In approximately 20 min, the task generates a rich array of measures of demand and price sensitivity, including breakpoint, and intensity and elasticity of demand among others. The same task has been used effectively to assess individual price sensitivity with alcohol and opioid consumption (Jacobs & Bickel, 1999; Murphy et at., 2009), differences between smokers with vs. without serious mental illness (Mackillop & Tidey, 2011), and has been shown to predict treatment outcome in problem drinkers (MacKillop & Murphy, 2007).

Incentives can be conceptualized as altering the price of smoking by adding the opportunity cost of forfeiting the incentive available for abstinence to the price of purchasing the cigarettes. As such, there is a sound theoretical rationale to anticipate that individual differences in elasticity of demand (i.e., sensitivity to price) may predict sensitivity to the incentives, with successful treatment response corresponding to greater price sensitivity. Similarly, NRT can be conceptualized as substituting an inferior form of nicotine reinforcement for cigarette smoking. As such, there is a sound theoretical rationale for anticipating that individuals who are already more sensitive to price in the absence of the inferior substitute (at baseline) may show even greater elasticity of demand when NRT is available to substitute for smoking. That is, they would be expected to benefit more from the combined incentives + NRT intervention than those with more inelastic baseline demand curves. We will explore such relationships in the proposed study and believe that doing so has the potential to enhance understanding of the processes underpinning successful treatment with these and other interventions, individual differences in treatment response, differences between treatment conditions, and provide future targets for improving interventions with disadvantaged smokers.

Summary
Developing efficacious and cost-effective interventions to increase smoking cessation among disadvantaged mothers and reducing SHSe among their children is an important U.S. public health priority. The financial incentives model that we are proposing is effective with other treatment-recalcitrant populations and we believe has the potential to meet this important public-health challenge. Indeed, results from the subsets of mothers who have participated in our prior trials on incentives for smoking-cessation among pregnant women provide preliminary empirical support for that position. Because of the prevalence of heavy smoking among disadvantaged smokers, we will also examine whether combining incentives with pharmacotherapy improves outcomes above incentives alone. Behavioral-economic theory suggests that the efficacy of the cessation intervention that we are proposing is at least in part attributable to providing smaller, more immediate incentives for success that acts to bridge the temporal delay to the larger naturalistic rewards of improved health outcomes for mother and child. We will continue to investigate the behavioral-economic processes involved in smoking among disadvantaged women and how these processes relate to individual differences in treatment response.

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Objectives: Clearly state the primary and secondary objective(s) of the study.

Primary aim # 1: develop an efficacious, cost-effective smoking-cessation intervention for mothers of young children. 250 smoking mothers of children ages 11 yrs will be recruited from our University hospital pediatric service and other community practices and randomly assigned to one of three treatment conditions: (1) usual care for quitting smoking and protecting children from SHSe; (2) usual care combined

with financial incentives for biochemically-verified maternal smoking abstinence; (3) usual care combined with financial incentives plus pharmacotherapy using innovative procedures to optimize medication efficacy. We will conduct cost-effectiveness analyses of the three interventions. We hypothesize that each of the interventions with incentives will increase smoking abstinence compared to usual care alone, but that the largest magnitude and most cost- effective treatment effects will be achieved by combining incentives with pharmacotherapy.

Primary aim # 2: determine whether maternal smoking cessation decreases objective measures of SHSe in children. Urine samples will be collected from the youngest child of each maternal participant at each follow-up assessment *for* determination of cotinine levels. We will examine this outcome by (a) comparing between treatment conditions and (b) comparing children of abstainers versus smokers independent of treatment condition. We hypothesize that (a) both incentives interventions will decrease child cotinine levels significantly more than usual care alone and (b) that SHSe levels will be significantly lower among children of abstainers than smokers.

Secondary aim: utilize behavioral-economic measures to improve understanding of treatment process and predict outcomes. Women will complete smoking-price sensitivity and delay-discounting tasks at study intake and follow-up assessments. We hypothesize that cigarette price sensitivity will increase as an orderly function of treatment intensity and differ between treatment conditions, and that steeper baseline discounting (i.e., greater impulsivity) will predict smoking abstinence at follow- up assessments after controlling for the influence of treatment.

METHODS AND PROCEDURES

Study Design: Describe the research design, including a description of any new methodology and its advantage over existing methodologies.

This study is a randomized clinical trial with three treatment conditions. Treatment conditions will last for 12 weeks and consist of either **A:** usual care for reducing SHSe**. B:** provisions of incentives contingent upon biochemically-verified maternal smoking abstinence or **C:** the incentive program combined with provision of and support in using of pharmacotherapies. Outcome measures will include maternal abstinence rates, child cotinine exposure and the interaction of behavioral economic measures and treatment success. This extended treatment period of combined incentive and pharmacotherapy support represents a novel and intense approach to reducing smoking and second-hand smoke exposure in these vulnerable populations.

Procedures: Describe all procedures (sequentially) to which human participants will be subjected. Identify all procedures that are considered experimental and/or procedures performed exclusively for research purposes. Describe the types, frequency and duration of tests, study visits, interviews, questionnaires, etc.

Note: A clinical research protocol may involve interventions that are strictly experimental or it may involve some aspect of research (e.g., randomization among standard treatments for collection and analysis of routine clinical data for research purposes). It is important for this section to distinguish between interventions that are experimental and/or carried out for research purposes versus those procedures that are considered standard therapy. In addition, routine procedures performed solely for research purposes (e.g., additional diagnostic/follow-up tests) should be identified.

Screening:
Participants will be recruited primarily from our university-affiliated hospital's pediatric practice but also other pediatric and family medicine practices throughout the county in which our clinic is located as well as from the local office for Women, Infants, and Children (WIC). All mothers attending a pediatric visit with their child will complete a brief self-administered smoking- screening form (attached). Those who endorse smoking in the prior 7 days and having a child s 11 years of age will be invited for an intake assessment.

Intake Assessment:
The study intake assessment battery will examine the following seven areas: (1) Socio-demographics: age, yrs of education, race/ethnicity, height/weight, marital status, and health insurance status. (2) Smoking history: age started smoking, average number of cigarettes smoked per day, time to first cigarette in the morning, number of previous quit attempts, number of other smokers in the household, nicotine dependence/tolerance (Fagerstrom & Schneider, 1989),

and nicotine withdrawal (Hughes & Hatsukami, 1986). Smoking Timeline Follow-back (TLFB) interviews will be conducted (Brown et at., 1998) to characterize fluctuations in daily smoking rates and associated child SHSe. (3) Smoking attitudes: motivation to stop, confidence in ability to stop, intention to quit, and measures of perceived stress. (4) Biochemical verification of maternal smoking status and baseline SHSe of the child: Maternal breath CO (piCO Breath CO Monitor, Bedfont Scientific Ltd) and urine cotinine levels (Viva-E Enzyme Immunoassay Testing (EMIT) System, Seimens) will be measured. The urine cotinine level of each target child will be measured to establish a baseline of SHSe. For children still in diapers, urine samples will be collected by placing a sterile cotton pad in the diaper (e.g., Hovell et al., 2009). (5) SHSe: Mothers will be queried regarding their smoking in the house during workdays and non-workdays in the past 7 days, their child's SHSe during the past 7 days related to their smoking and that of others in the home as well as outside the home (e.g., grandparents home) (Hovell et al., 2009). Exposure will be quantified as # of cigs smoked while the child was in the room or car. (6) Medical history/Mental health status: any current medical concerns problems, prescription and over-the-counter medications currently used, allergies, surgical, gynecologic, and family history, immunizations, substance abuse history, and review of systems, lifetime history of depression, general psychiatric symptoms (Brief Symptom Inventory, Derogatis, 1993), and current depressive symptoms (Beck Depression Inventory, Beck & Beck, 1972). If a subject expresses any thoughts of harm to self or others the subject will be taken to a private room and the staff member will sit with them and call Crisis Services (7) Behavioral economics: mothers will complete the delay discounting task (Johnson & Bickel, 2002) and the simulated cigarette purchase task (Murphy et al., 2011). Permission will be requested of all mothers for project staff to review child health records through 48 wks after the quit date, but permission will not be a requirement for participation.

Treatment Conditions

Participants will be randomly assigned to one of three treatment conditions: (1) usual care for smoking cessation and protecting children from SHSe, (2) usual care combined with incentives for objectively verified smoking abstinence, and (3) usual care combined with incentives and pharmacotherapy using innovative procedures to enhance its efficacy. We will stratify assignment on four variables that may influence maternal and child outcomes: (1) maternal smoking *level* (< vs. > 20 cigs/day), (2) maternal educational attainment (< vs. > 12 yrs), (3) the number of smokers living with the target child (1 vs. a 2), and (4) whether the target child is < vs. > 6 yrs of age. We will pilot test an initial 10 participants in the combined incentives and pharmacotherapy condition for training and protocol refinement purposes as that is the most complex of the interventions and includes the protocols to be used in the other treatment conditions.

Usual care. The 2008 Clinical Practice Guidelines for smoking cessation recommends that medical providers should at a minimum implement the 5As (Fiore et al., 2008). To assure that referring pediatric services are at least acquainted with the 5As, our staff will conduct office-based training sessions with all referring practices prior to the start of study recruitment and once annually throughout the course of the study using training procedures developed previously by our research team and utilized in our prior studies. As part of training in the 5As, providers will be encouraged to refer smokers to the Vermont Quit Network that is supported by the Vermont Department of Health (http://www.vtquitnetwork.org). This network offers a wide range of free cessation services, including nicotine replacement therapy wherein free nicotine patches, gum, or lozenges will be mailed directly to the participant's home. There are basic web-based modules on preparing to quit, motivating oneself during the quit process, a review of the reasons that people smoke, evaluating whether pharmacotherapy may help, developing a quit plan, and sustaining abstinence. Additionally, they provide free online coaching that includes forums with former smokers and others who are currently trying to quit, or individual smoking-cessation phone counseling, or in-person smoking-cessation group counseling offered in the local community hospitals. Importantly, we will have no involvement with the content of counseling or other smoking-cessation services that might be routinely offered through the referring medical practices aside from us providing the once yearly workshop on how to implement the 5As and recommending them to refer women to the Vermont Quit Network. Our goal is for this condition to represent usual care and not standard of care as stipulated in the Clinical Practice Guidelines. As discussed above in the section on follow-up assessments, we will assess all mothers on smoking-cessation recommendations and services received through their children's health-care providers, which is information that can be considered in cost-effectiveness and other analyses.

Usual care + incentives. Participants in this condition will receive the usual-care services from their providers described above plus a 12-week program of monetary incentives for verified smoking abstinence (maximum earnings = $810 over 12 wks) that will be implemented by our clinic staff. The initial smoking negative test (< 6 ppm) will be worth $10. Each consecutive negative test increases the incentive by $2.50, with the 2nd consecutive negative test worth $12.50, the 3rd negative test $15, the 4th test $17.50, etc. Incentive value continues to escalate upward based on consecutive negative test results with a maximum value of $50. A positive test or failure to submit a specimen for a scheduled test resets incentive value back to the initial $10. This reset contingency protects against relapse once a period of abstinence has been achieved (Roll & Higgins, 2000). Two consecutive negative tests following a reset will return incentives back to the value that they were at prior to the positive test result. Based on prior studies (Heil et at., 2008), we anticipate mothers will earn about 40% ($324) of the maximum possible. Use of NRT or other

pharmacotherapies in this condition will not be prohibited in keeping with usual care being a component of this condition, but study staff will not offer them the pharmacotherapy protocol described below. Based on our prior studies with incentives for smoking cessation and those of others in disadvantaged populations, we are confident that there will be minimal ongoing pharmacotherapy use in this condition or the usual care condition above (<10%) (Coleman et at., 2012; Heil et al., 2008; Hiscock et at., 2012; Yoon et at., 2009). Economically disadvantaged smokers under-utilize smoking-cessation pharmacotherapies (e.g., Coleman et at., 2012; Hiscock et at., 2012).

Usual care + incentives + pharmacotherapy. Mothers in this condition will receive the counseling and incentives protocols described above and the following pharmacotherapy protocol: (1) A clear recommendation will be provided by our clinic staff to use NRT. For those who agree, we will immediately register them with the Vermont Quit Network if they have not already done so asking for a supply of free NRT as part of the registration and using our clinic address as the delivery site. We will have NRT already available onsite that we will use so that the pharmacotherapy protocol can be implemented immediately after a woman agrees to use it. That supply can be replenished as needed when the requested package arrives from the state. We will use the medications provided through the Vermont Quit Network (over-the-counter NicoDerm CQ, GlaxoSmithKline Consumer Healthcare). (2) Following their quit date, participants will be encouraged to follow a standard 10-wk course of transdermal NRT, using the 21 mg/24 hr patch for 6 more wks, the 14mg/24 hr patch for 2 wks, and the 7 mg/24 hr patch for the final 2 wks. Additionally, participants will be encouraged to use nicotine lozenges (or gum if someone objects to the lozenges) in combination with transdermal NRT beginning on their quit date as a behavioral substitute for smoking. We will use Commit (GlaxoSmithKline Consumer Healthcare) brand of 2 or 4 mg lozenges in various flavors, with those who smoke within 30 min of awaking using the higher dose and those who first smoke later than 30 min using the lower dose as per package insert. We will encourage use of the lozenges for 10 wks. Women will pick up one-week supplies of NRT patch and lozenges at their first clinic visit each week. The project nurse will assess medication side effects at each visit, and recommend adjustments in dose and other aspects of the regimens described above as warranted and in consultation with the clinic medical director.

Abstinence-monitoring schedule. Beginning with the quit date, all mothers will report to the clinic or be met at a convenient location according to a predetermined 12-week schedule. Week 1 of the cessation effort includes five consecutive days of 1 x daily abstinence monitoring. In Weeks 2-8, abstinence monitoring will be reduced to twice weekly and then to once weekly for the remaining 4 weeks (Weeks 9-12). Abstinence will be defined as a breath carbon monoxide level < 6 ppm for purposes of implementing the incentives program. To keep the frequency of clinic contacts and data collected comparable across treatment conditions in this trial, women assigned to the usual-care only condition will receive $15 vouchers independent of smoking status for attending the abstinence-monitoring sessions. This will assure comparable levels of attendance across conditions. When the influence of such non-contingent incentives on smoking or other drug abstinence was examined in a meta-analysis, it was identical to providing no incentives at all (Lussier et al., 2006). Thus, this will be done in the proposed study for research purposes only. TLFB assessments will be completed at each visit to assess any smoking since last visit as well as use of NRT or other smoking-cessation medications. Following this assessment subjects will be randomized to one of three treatment groups.

Follow-up Assessments

The assessment battery will be completed with all mothers and children again at 6, 12, 24, and 48 wks after intake by staff blind to treatment condition. All subjects will be compensated $35 per follow-up assessment independent of smoking status to assure high compliance. We have achieved high rates of follow-up compliance (85-90%) in prior studies with this level of compensation and anticipate the same in the proposed study. Urine specimens collected from mothers and children at the follow-up assessments will be sent to an outside laboratory for cotinine testing using gas chromatography (GC) with maternal and liquid chromatography-mass spectrometry (LC-MS/MS) for child specimens; maternal specimens will also be assessed for tobacco alkaloids anabasine and anatabine using LC-MS/MS to discriminate between cotinine from smoking vs. NRT use (Jacob et al., 2002). Participants will complete a brief yes-no questionnaire consisting of five questions adapted from prior studies with women on smoking-cessation services received (e.g., Sherman et al., 2005): (1) Has your child's doctor talked with you about smoking cessation since last assessment? (2) Has your child's doctor referred you to a smoking-cessation clinic or related service (e.g., online/phone counseling) since last assessment? (3) Have you attended a smoking-cessation clinic (or online or phone counseling) since last assessment? (4) Has your child's doctor recommended or prescribed a smoking- cessation medication (e.g., nicotine patch/gum/lozenges, Zyban) since last assessment? (5) Have you used any smoking- cessation medications since last assessment? Those reporting use of a pharmacotherapy will complete a TLFB interview to characterize use since last assessment. Importantly, in an effort to minimize physical contact between research personnel and existing participants in light of the COVID-19 pandemic, we will be conducting follow-up surveys over the phone. Additionally, video monitoring will be used to verify the smoking status of the mothers. This procedure involves video chatting with participants to monitor them as they self-test saliva samples for cotinine (i.e., a metabolite of nicotine) using Alere iScreen OFD Oral Cotinine Screening tests. Participants will video chat with research personnel while completing the tests, with each test taking approximately 5 minutes (i.e., 2-3 minutes of swabbing the mouth and tongue, and up to 3 minutes

to produce a result). The display indicates whether the sample is either positive or negative, with a positive test registering for salivary cotinine levels > 30 ng/ml. Video interactions between participants and research personnel will not be recorded or stored as data. Finally, because the cotinine tests are not designed to detect SHSe in children, child urine samples will be collected via curbside pickup. Staff will wear facial coverings and gloves during curbside pickup. Urine samples will be placed in a location greater than 10 feet away from the participant and collected by staff at a designated time. Urine samples will be sanitized thoroughly before being returned to the laboratory.

Health record review:
During consent mothers will be given the option to allow us to review their child's health records (see consent form). If the mother agrees we will have her sign a records release form. The release will specify that we are requesting a copy of the child's health record from date of intake through 48 weeks following the quit date. We will send the record release to the child's pediatrician or family practice who is the main provider for the child during that 48-week period. We will then review the records with oversight by our pediatric experts to identify illness that may have occurred or been exacerbated by secondhand smoke exposure (e.g., asthma, bronchitis, pneumonia or other respiratory infections, wheezing/coughing, ear infections).

Describe required screening procedures performed before enrollment and while on study.

As described above, participants will be recruited primarily from our university-affiliated hospital's pediatric practice but also other pediatric and family medicine practices throughout the county in which our clinic is located as well as from the local office for Women, Infants, and Children (WIC). All mothers attending a pediatric visit with their child will complete a brief self-administered smoking- screening form (attached). Those who endorse smoking in the prior 7 days and having a child s 11 years of age will be invited for an intake assessment.

For research involving survey, questionnaires, etc.: Describe the setting and the mode of administering the instrument and the provisions for maintaining privacy and confidentiality. Include the duration, intervals of administration, and overall length of participation.

[ ] **Not applicable**

Assessments (Intake and 6-, 12-, 24- and 48-week Follow-up):
Assessments will be conducted in private rooms in our treatment center located in the UHC building to maximize privacy and confidentiality. Assessments will take approximately 1 hour and will occur 5 times over a period of 48 weeks. All assessments consist of the same set of questionnaires and tasks.

The Fagerström Test for Nicotine Dependence (FTND; Heatherton et al., 1991) will be administered to assess nicotine dependence severity; The Minnesota Nicotine Withdrawal Scale (MNWS; Hughes & Hatsukami, 1986), will be administered to assess withdrawal symptoms; Lifetime history of depression and general psychiatric symptoms will be assessed using the Brief Symptom Inventory (Derogatis, 1993); Current depressive symptoms will be assessed using the Beck Depression Inventory (Beck & Beck, 1972); A computerized delay discounting task will be used to measure preferences for delay versus immediate rewards (Johnson & Bickel, 2002); A simulated cigarette purchase task will be used to measure a subject's willingness to pay varying amounts for cigarettes (Murphy et al., 2011); The Client (Outpatient) version of the DATCAP (French 2005; Salomé et al., 2003) will be used to quantify time and effort costs to the participant in attending the study visits; The Smoking Stage of Change questionnaire will be administered to characterize readiness to quit smoking.

TYPES OF PROCEDURES (Please do not use the "other" option unless the procedure is not listed.)
Check all that apply.

[X]	Survey (mail, telephone, in-person, on-line)	[ ]	Blood drawing:	Vol.		Over days, weeks?	
[X]	Medical exams/history					Type & Amt.	
[ ]	Deception ***see below**	[ ]	Surgery			[X]	Collection of Urine and/or Feces
[X]	Observation	[ ]	Drug Administration			[ ]	HIV Testing
[ ]	Photographs	[ ]	Device Use			[ ]	Ultrasound (e.g. echocardiogram)
[ ]	Audio Recording	[ ]	Exercise			[ ]	Imaging (e.g. CT scan, DEXA, mammogram, PET scans, SPECT)
[ ]	Video Recording	[ ]	Diet			[ ]	Use of Radiation treatment
[ ]	Interviews in person or by phone	[ ]	Pathology Specimens (retrospective)			[ ]	Use of Radioactive substances (e.g. radiolabeled antibodies, drugs or contrasts)
[ ]	Focus Groups	[ ]	Genetic Materials (DNA)*			[ ]	MRI (for treatment studies)

☐	Review of prospective data	☒	Questionnaires	☐	MRI (not for treatment studies)
☐	Review of retrospective data	☐	Diaries	☐	Tissue (obtained for clinical purposes)
☐	Recording of Identifiable Data	☐	Pregnancy Tests	☐	Tissue (obtained solely for research)
☐	Electrocardiograms				
☐	Sensitive Data (criminal or sexual conduct, drug or alcohol conduct or use)	(specify):			

***If genetic information is being collected, GINA language must be added to the consent form.**
*****Deception typically involves withholding information from the potential subject and would require an alteration to the consent process.

Statistical Considerations: Delineate the precise outcomes to be measured and analyzed. Describe how these results will be measured and statistically analyzed. Delineate methods used to estimate the required number of subjects. Describe power calculations if the study involves comparisons. Perform this analysis on each of the primary and secondary objectives, if possible.

Treatment conditions will be compared for differences in baseline characteristics using I-tests for continuous measures and chi-square tests for categorical variables. If specific characteristics differ significantly across treatment conditions and are predictive of treatment outcomes, they will be considered as potential covariates in subsequent analyses. Primary analyses will include *all* subjects randomized to treatment conditions independent of early dropout, noncompliance, etc., consistent with an intent-to-treat approach to randomized clinical trials (Armitage, 1983). The primary outcome measures in this trial will be point prevalence smoking abstinence at the 12- and 24-week assessments. We will analyze abstinence at 48 weeks for an estimate of relapse rates and for use in comparing SHSe levels and secondhand smoke-related illness rates in children of abstainers and smokers but are not developing this initial trial with thoseat assessments as a primary outcome. We will also assess continuous abstinence from the quit date through 24-week assessment. Abstinence will be defined as a self-report of no smoking in the past 7 days, breath CO < 6 ppm, confirmed by urine cotinine testing (< 50 ng/ml) of specimens collected at the 12- and 24-week assessments by an independent laboratory. The study is designed to have sufficient power to have a greater than 80% chance of detecting treatment difference at each assessment point through 24-weeks. Abstinence rates at each assessment will be compared across the treatment conditions using chi square tests or Fisher's Exact tests, if small expected cell frequencies are present. Comparison of point-prevalence abstinence rates among treatment conditions across all periodic assessments will be analyzed using mixed model repeated measures for categorical data based on generalized estimating equations utilizing a logistic link function (SAS: PROC GENMOD, SAS Institute, Cary, NC) with assessment time, treatment condition, and their interaction as factors. Treatment comparisons and temporal changes in children's mean urine cotinine will be examined using repeated measures analysis of variance (PROC MIXED) across assessments. Group comparisons at each time point will be based on Fisher's protected LSD. Because cotinine levels are typically skewed, data will be log transformed prior to analyses. Analysis of variance will be used to compare SHSe levels by maternal smoking status at specific follow-up assessments. Logistic regression will be used to examine the association between baseline temporal discounting and other measures of price sensitivity and subsequent abstinence. Baseline DD will be expressed as the logarithm of each participant's estimated parameter k, and elasticity of demand in the models from the cigarette purchase task. Additional explanatory variables in the models will include treatment condition and subject demographic and smoking characteristics. Additional models will examine potential interactions between treatment condition *and* measures from the demand curves as well as target child characteristics such as baseline cotinine level.

Sample Size Justification
Sample size was determined based on having sufficient power to detect differences between treatment conditions corresponding to our first specific aim on point prevalence abstinence differences at the 12-week end-of-treatment assessment and the 24-week follow-up assessment. Our completed trials on smoking cessation among pregnant women provide relevant information for estimating sample size for the proposed study. Across three trials, biochemically-verified, 7-day point-prevalence abstinence in the contingent and non-contingent conditions at the end-of-pregnancy were ~35% in the contingent conditions and ranged from 9-23% in the non-contingent conditions. We estimate that the incentive condition will produce 35% abstinence rates and the usual care condition will produce 15% abstinence rates. The proposed sample size of 240 trial participants (80/condition) will result in estimated power .95 using O = 0.05 for detecting differences among the treatment conditions (i.e., 40% vs. 15%) at 12-week end-of-treatment assessment. Power is estimated to be .80 to detect a 15% (i.e., 20% vs. 5%) difference between treatment conditions at the 24-week follow-up assessment. For the second specific aim relating to the objective measure of SHSe in children, power is estimated to be .80 using O = 0.05 to detect treatment differences of approximately 35% with respect to the mean decrease in urine cotinine levels from baseline and > .80 in comparisons by maternal smoking status. This computation is based on variability estimates from Hovell et al. (2009) which corresponds to a log transformed analysis and geometric means. This assumes moderate correlation (r = .50) between cotinine levels within subjects across assessment times. If our average baseline levels are similar to theirs, this relative difference translates to an absolute mean difference of approximately 4.2 ng/ml between treatment conditions and larger effects in comparisons by maternal smoking status. For the logistic regression analyses corresponding to the secondary aim on behavioral economic predictors, power is estimated to be .80 using O=.05 for detecting explanatory variables that have odds ratios ranging from 2.0 to 2.5 per one SD change from their mean assuming total model R2 ranging from .20 to .40. This exact estimate is dependent on the total number of predictors and the overall R2 of the model with lower detectable OR's associated with smaller overall R2.

Economic Evaluation, Cost analysis.
We will conduct a cost-effectiveness analysis (CEA) from the societal perspective (Drummond et al., 2005). First, to determine

the cost of each intervention, we will employ the Brief Drug Abuse Treatment Cost Analysis Program (Brief DATCAP; French et al., 2004), which has been widely used in the area of substance abuse (e.g., French et al., 2008; Roebuck et al., 2003; 2009; 2011; http://datcap.com/), including incentives projects (Knealing et al., 2008). The economic cost of treatment will be derived by allocating fixed costs based upon the proportion of time or space utilized by the programs and costs that vary by patient engagement and smoking status (e.g., drug tests, financial incentives). The total cost per treatment episode will be individual-specific, and will also include the opportunity cost of the patient's time while in treatment as measured by the Client (Outpatient) version of the DATCAP (French 2005; Salomé et al., 2003). The time period of the cost analysis will span from intake to discontinuation or completion of the program. The cost of all research-specific resources consumed will be excluded from the evaluation. All costs and benefits will be expressed in a common dollar year. Estimated treatment costs will be combined with the estimated child healthcare utilization costs to represent total costs per treatment condition. Cost-effectiveness analysis. CEA will be conducted wherein the average (mean) difference in treatment costs across the three treatment conditions will be divided by the average (mean) difference in each outcome to derive incremental cost-effectiveness ratios (ICERs). Statistical significance of these ICERs will be determined by employing non-parametric bootstrapped standard errors (Drummond et al., 2005). A special form of CEA, cost-utility analysis (CUA), will be performed. Based upon smoking status from the quit date through the 48-week assessment, the number of quality-adjusted life years (QALYs) gained by the mother—as measured by the proportion of time spent in 'smoking' and/or 'non-smoking' status will be derived using QALY weights recommended in the extant literature (e.g., Cromwell et al., 1997; Flack et al., 2007). We will estimate relapse curves beyond the 48-week assessment from the literature to estimate longer-term outcomes. QALYs gained by each child based on changes in their biochemically verified SHSe will be similarly calculated using QALY weights recommended in the literature (Taylor, 2009). The incremental cost per QALY gained between the three treatment conditions will be calculated and compared for mothers and children separately and also summed across mothers and children. In conducting analyses for children, we will assume that all children residing fulltime with the mother share the same smoking status as the target child.

Risks/Benefits: Describe any potential or known risks. This includes physical, psychological, social, legal or other risks. Estimate the probability that given risk may occur, its severity and potential reversibility. If the study involves a placebo or washout period, the risks related to these must be addressed in both the protocol and consent. Describe the planned procedures for protecting against or minimizing potential risks and assess their likely effectiveness. Where appropriate, discuss plans for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects. Discuss the potential benefits of the research to the subjects and others. Discuss why the risks to the subjects are reasonable in relation to the anticipated benefits to subjects and others. Discuss the importance of the knowledge gained or to be gained as a result of the proposed research and why the risks are reasonable in relation to the knowledge that reasonably may result. If there are no benefits state so.

Risks:
- The participant may feel uncomfortable answering some of the questions. We will work with them to minimize this discomfort and no one has to answer any question that they do not wish to.
- There is a risk that confidential information might accidentally be disclosed, including illegal drug use results. Professional standards for protecting confidential information (detailed below) will be used to minimize this risk.
- Participants in this study may experience withdrawal. These symptoms can include anger, irritability, frustration, anxiousness, depressed mood, craving for cigarettes, difficulty concentrating, increased appetite, weight gain, sleep problems, restlessness, impatience, constipation, dizziness, coughing, nightmares, nausea, and sore throat. If these mood changes appear to put a participant's health at risk they will be asked to stop participating in the study.
- There is a risk of COVID-19 transmission during curbside pickup of urine samples. Research staff will conduct wellness checks before scheduled visits. If either the participant or the staff person reports any symptoms of COVID-19, curbside pickup of the sample will be postponed until a later date. If no symptoms are reported, staff will use the social distancing protocol detailed above in the Methods and Procedures section to collect the sample while minimizing physical contact with the participant.

Benefits:
- Participation in any of the three treatment conditions could result in cessation of maternal smoking. This would have health benefits both for the mother and the child.

Therapeutic Alternatives: List the therapeutic alternatives that are reasonably available that may be of benefit to the potential subject and include in the consent form as well.

☐ **Not Applicable**

Subjects could attempt to quit on their own, without the support of this study. Contact information for the Vermont Quit Network is included in the consent form.

Data Safety and Monitoring: The specific design of a Data and Safety Monitoring Plan (DSMP) for a protocol may vary extensively depending on the potential risks, size, and complexity of the research study. For a minimal risk study, a DSMP could be as simple as a description of the Principal Investigator's plan for monitoring the data and performance of safety reviews or it could be as complex as the initiation of an external, independent Data Safety and Monitoring Board (DSMB). The UVM/UVM Medical Center process for review of adverse events should be included in the DSMP.

All efforts will be made to maintain confidentiality. All assessments will be conducted privately. All data will be coded by identification number, with the codes known only by the investigators on this project. Names will not be connected with any results. All data from this project will be kept in a confidential form at the UHC building. The security of these records will be maintained by keeping paper files in a locked file cabinet and by keeping computer files in a password protected file on the UVM College of Medicine computer network. The results of this study will eventually be published and information may be exchanged between medical investigators, but patient confidentiality will be maintained.

The sponsors (NICHD) as well as the Institutional Review Board and regulatory authorities could be granted direct access to original medical and research records for verification of clinical trial procedures and/or data. If this is required, it will be done under the conditions that will protect privacy to the fullest extent possible consistent with laws relating to public disclosure of information and the law-enforcement responsibilities of the agency. Data resulting from this research will be kept for 10 years following publication as is recommended by APA.

Define criteria to be used for decision making regarding continuation, modification, or termination of the entire study (not individual participation) (i.e. "stopping rules).

In the proposed study, we will use the FDA's definition of Adverse Events (AEs) and Serious Adverse Events (SAEs). AEs and SAEs will be assessed at each subject visit by a trained staff member and copies of all reports noting AEs and SAEs will be kept in a central file as well as in the individual subject's chart. AEs and SAEs will be discussed at the weekly research meetings. There are no predefined "stopping" rules for this study. However, the study may be terminated if the investigators determine that the frequency of AEs and SAEs warrants discontinuation.

Modifications may be made to the study if the PI determines that participants recruitment is not progressing satisfactorily. Specifically, recruitment may be expanded to partners outside of WIC or the UVM Health Network in an effort to meet recruitment goals.

What will be the frequency of the review? Please note that the frequency of reviews should be commensurate with the risk of the study. At a minimum, a review of the data should be conducted annually at time of continuing review. **Forward copies of the data and safety monitoring reports to the 1) IRB, 2) CRC (if applicable), and/or 3) UVMCC (if applicable).**

☐	Monthly	☒	Annually
☐	Quarterly	☐	Other (e.g. by dosing level, no. of subjects enrolled):
☐	Bi-annually		

Will the sponsor be conducting data monitoring visits for this study?

☐ Yes ☒ No ☐ NA

If yes, how often?

Adverse Event, Unanticipated Problem (UAP), Reportable New Information (RNI): Describe how events and UAPs will be evaluated and reported to the IRB. All protocols should specify that, in the absence of more stringent reporting requirements, the guidelines established in the "Adverse Event and Unanticipated Problems Reporting Policy" will be followed. The UVM/UVM Medical Center process for review of adverse events and UAPs to subjects or others should be included in the DSMP.

Any SAE will be brought to the attention of the PIs and the study physician as soon as possible and not longer than 24 hours. Any AE or SAE that is both unexpected and related to study participation will be reported to the IRB within 7 days of the event. The IRB will make a determination as to whether additional reporting requirements are needed. IRB actions will be reported to the funding agency by the PIs no less than annually and more frequently as recommended by the local IRB. Any SAEs will be summarized in the yearly Progress Reports to the funding agency, including a review of frequency and severity. All SAEs will be followed through ongoing consultation with the physician caring for the patient until they resolve, result in death, or stabilize and are not expected to improve. The study staff will be in close contact with participants and health care providers throughout the study to monitor for potential unanticipated problems. Any unanticipated problems will be discussed at the weekly research staff meetings and reported as required to the CHRMS using the Report of Protocol-Related Problems & Deviations Form.

Withdrawal Procedures: Define the precise criteria for withdrawing subjects from the study. Include a description of study requirements for when a subject withdraws him or herself from the study (if applicable).

There are no predefined criteria for withdrawal from the study. However, participants may be withdrawn if the PI determines it is not advisable that they continue on in the program. Participants may withdraw themselves at any time, for any reason.

Sources of Materials: Identify sources of research material obtained from individually identifiable human subjects in the form of specimens, records or data. Indicate whether the material or data will be obtained specifically for research purposes or whether use will be made of existing specimens, records or data.

Sources of material will include:

- Questionnaires on demographics (age, marital status, education, etc.) and physical and mental health
- Questionnaires about cigarette use, withdrawal and cravings, as well as thoughts and feelings about smoking
- Urine and breath samples that measure recent cigarette use and exposure to tobacco byproducts
- Questionnaires about the time and effort required to attend study-related visits
- Tasks that measure the value of cigarettes and the strength of preference for money available now compared to money available later

DRUG INFORMATION

Investigators are encouraged to consult the UVM Medical Center Investigational Pharmacy Drug Service (847-4863) prior to finalizing study drug/substance procedures.

Drug (s) [X] **Not applicable**

Drug name – generic followed by brand name and common abbreviations. Availability – Source and pharmacology; vial or product sizes and supplier. If a placebo will be used, identify its contents and source.

Preparation: Reconstitution instructions; preparation of a sterile product, compounded dosage form; mixing guidelines, including fluid and volume required. Identify who will prepare.

Storage and stability – for both intact and mixed products.

Administration – Describe acceptable routes and methods of administration and any associated risks of administration.

Toxicity – Accurate but concise listings of major toxicities. Rare toxicities, which may be severe, should be included by indicated incidence. Also adverse interactions with other drugs used in the protocol regimen as well as specific foods should be noted. Address significant drug or drug/food interactions in the consent form as well. List all with above details.

Is it FDA approved: (include FDA IND Number)

1. in the dosage form specified? If no, provide justification for proposed use and source of the study drug in that form.
2. for the route of administration specified? If no, provide justification for route and describe the method to accomplish.
3. for the intended action?

SUBJECT CHARACTERISTICS, IDENTIFICATION AND RECRUITMENT

Subject Selection: Provide rationale for subject selection in terms of the scientific objectives and proposed study design.

Despite widespread awareness of the adverse health consequences of SHSe, almost 60% of all U.S. children and 85% of those from low-income families are chronically exposed (Cornelius et al., 2003; Halterman et al., 2010; USDHHS, 2007). SHSe, especially from maternal smoking, increases risk for infant death, chronic respiratory infections, asthma, and other longer-term medical problems. Thus, studying potential treatment approaches to reduce maternal smoking in disadvantaged populations is of the utmost importance.

Vulnerable Populations: Explain the rationale for involvement of subjects (e.g., cognitively impaired, Non-English speaking, prisoners, students). Discuss what procedures or practices will be used in the protocol to minimize their susceptibility to undue influences and unnecessary risk (physical, psychological, etc.).

[ ] **Not applicable**

This study aims to compare different treatments to minimize exposure to children of second-hand-smoke. As such, we must include minor children in this protocol. Risk to these children is minimal as their participation consists solely of providing urine samples **via curbside exchange**. Alternatively, risk to these children may actually be reduced by participation in this study as they may experience a decrease in second-hand-smoke exposure.

Inclusion/Exclusion Criteria: Eligibility and ineligibility criteria should be specific. Describe how eligibility will be determined and by whom. Changes to the eligibility criteria at a later phase of the research have the potential to invalidate the research.

Inclusion criteria:

- Having a child ≤ 11 years of age who resides with them full time
- Report having smoked ≥ 10 cigarettes per day for at least the last year, confirmed by urine cotinine testing
- Uninsured or insured by Medicaid or another state-supported insurance indicative of low SES
- Express interest in quitting smoking and willingness to initiate NRT
- Currently use no other tobacco products or NRT
- At least 18 years of age
- Reside in the county where the clinic is located, with no plans to move in the next year
- English speaking

Exclusion criteria

- Failure to meet the aforementioned criteria
- Medical contraindications to transdermal NRT/lozenges
- Meeting DSM-IV criteria for alcohol of drug dependence other than nicotine in the prior 12 months
- Having a current (past month) affective disorder, current/past psychotic disorder, or being suicidal
- Currently pregnant, breastfeeding, or planning to become pregnant in the next 12 months
- Incarceration
- Refusal to participate
- Refusal to allow child to participate

Inclusion of Minorities and Women: Describe efforts to include minorities and women. If either minorities or women are excluded, include a justification for the exclusion.

As we are targeting mothers for our smoking-cessation efforts, women will make up the majority of the subject pool for this project. All efforts will be made to include minorities in this study. As we are targeting disadvantaged women we are likely to recruit a more diverse group than expected given the local population.

Inclusion of Children: Describe efforts to include children. Inclusion is required unless a clear and compelling rationale shows that inclusion is inappropriate with respect to the health of the subjects or that inclusion is inappropriate for the purpose of the study. If children are included, the description of the plan should include a rationale for selecting or excluding a specific age range of children. When included, the plan must also describe the expertise of the investigative team in working with children, the appropriateness of the available facilities to accommodate children, and the inclusion of a sufficient number of children to contribute to a meaningful analysis relative to the purpose of the study. Provide target accrual for this population. Identify whether children are wards of the state. **If children are excluded** then provide appropriate justification.

Children under 12 will be included in this study. As this study aims to measure reduction in child exposure to second-hand-smoke, inclusion of children is crucial. Children 12 and older will not be included as the chances of children using tobacco products themselves increase substantially at that age.

For protocols including the use of an investigational drug, indicate whether women of childbearing potential have been included and, if not, include appropriate justification.

n/a

If HIV testing is included specifically for research purposes explain how the test results will be protected against unauthorized disclosure. Include if the subjects are to be informed of the test results. If yes, include the process and provision for counseling. If no, a rationale for not informing the subjects should be included.

[X] **Not applicable**

Will the SONA psychology Pool be utilized? *Include documentation indicating permission to use this recruiting tool* Yes [ ] No [X]

FINANCIAL CONSIDERATIONS

Describe all potential research related expenses to subjects:

There will be no added expense to the participant for participation in this study.

Compensation for participation: Describe all plans to pay subjects, either in cash, a gift or gift certificate. Please note that all payments must be prorated throughout the life of the study. The IRB will not approve a study where there is only a lump sum payment at the end of the study because this can be considered coercive. The amount of payment must be justified. Clarify if subjects will be reimbursed for travel or other expenses.

☐ **Not applicable**

All subjects will receive $35 compensation for their time for each of the 5 assessments. Subjects in Treatment A will receive $15 in financial incentives for each of the 23 study visits. Subjects in Treatments B or C will receive financial incentives for the 23 study visits only if they demonstrate biochemically-verified smoking abstinence. Incentives for these visits start at $10 and max out at $50 (details of schedule are described above). Important to clarify is we consider the $35 for each follow-up assessment as compensation. However, we consider financial incentives for attending sessions and abstaining from smoking as therapeutic interventions (i.e., therapy) and not compensation for study participation.

Collaborating Institutions

Will this research be conducted in collaboration with other sites at other locations? Yes ☐ No ☒ X

If so, complete the following for all collaborating institutions:

Institution Name	Describe Involvement	Is there an IRB? If yes, attach approval or explanation	Are other permissions required? If yes, attach approval or explanation

INFORMED CONSENT

a. Type of Consent

i. Are you obtaining Written Consent? ☒ X Yes ☐ No

If yes, will there be more than one consent document? ☒ X Yes ☐ No

If yes, how many consent documents and for what populations.

Two consent forms will be used, one for the mother and one for the child. One HIPAA form will be used for the child.

ii. Are you requesting a Waiver of Informed Consent? ☐ Yes ☒ X No

This request means that you will not be obtaining verbal nor written consent. **If yes**, complete the form Request for a Waiver of Informed Consent/Authorization/Documentation in UVMClick.

iii. Are you requesting an Alteration of Informed Consent Procedures? ☐ Yes ☒ X No

This is a request to alter an individual's informed consent or elements of informed consent. Deception in research would be one example when consent would be altered. See Policies and Procedures Manual for more information about when a subject's consent may be altered. **If yes**, complete the smart form Request for a Waiver of Informed

Consent/ Authorization/ Documentation in UVMClick.

iv. Are you requesting a Waiver of Documentation of Informed Consent? [ ] Yes [X] No
This request means you are obtaining verbal or implied consent without obtaining the subject's signature on a consent form. See manual for the criteria required to obtain this type of waiver.

If yes, complete the form Request for a Waiver of Informed Consent/Authorization/Documentation in UVMClick.

v. Do you intend to obtain consent from a legally authorized representative? [ ] Yes [X] No
If yes, describe the process.

vi. Are you requesting a short form consent process for non-English speaking subjects? [ ] Yes [X] No
If yes, please describe. Guidance available in the Policies and Procedures Manual.

b. Consent Process

i. Once a prospective subject is identified, who initiates the informed consent discussion and answers questions presented by the subject or the subject's family?

The PI or an authorized representative will initiate the informed consent discussion and answer questions presented by the subject or subject's family.

ii. Where (in what setting) is the informed consent process initiated? How much time is the subject given to decide?

Those who are eligible will be invited to the clinic for an in-person session. Those eligible may have as much time as they need to review the informed consent form before deciding to participate.

iii. Is the principal investigator present for the initial and subsequent informed consent discussions with the subject?

The PI or an authorized representative will be present for the initial and subsequent informed consent discussions with the subject.

iv. What other method of documentation is used to record the informed consent process, in addition to the executed consent form? See an example of documentation of the informed consent **process** under consent templates on our forms page. *(This separate documentation is required to document the consent process with the research subject)*

One HIPAA form will be used to the child.

Information Withheld From Subjects: Will any information about the research purpose and design be withheld from potential or participating subjects? If so, explain and justify the non-disclosure and describe plans for post-study debriefing.

[X] **Not applicable**

Research Data Management Plan: The Research Data Management and Security Plan form must be completed. The form, along with guidance, can be found in our forms library and must be submitted with your initial application.