Title: Smartphone-based Financial Incentives to Promote Smoking Cessation Among Alaska Native Pregnant Women

NCT Number: not yet assigned

Document Date: July 29, 2021

1 **Smartphone-based Financial Incentives to Promote Smoking Cessation Among Alaska**
2 **Native Pregnant Women**
3
4 **Project Leaders:**
5
6 **Diann Gaalema, PhD**
7 Project Principal Investigator
8 Vermont Center on Behavior and Health
9 Departments of Psychiatry and Psychological Science, University of Vermont
10
11 **Kaitlyn Browning, PhD**
12 Project Postdoctoral Fellow & Primary Project Contact
13 Vermont Center on Behavior and Health
14 Departments of Psychiatry and Psychological Science, University of Vermont
15
16 **Stephen Higgins, PhD**
17 Center Principal Investigator
18 Vermont Center on Behavior and Health
19 Center of Biomedical Research Excellence
20 Departments of Psychiatry and Psychological Science, University of Vermont
21
22 **Kathy Koller, PhD**
23 Site Principal Investigator
24 Alaska Native Tribal Health Consortium (ANTHC), Anchorage, AK
25

26 **Key Personnel:**
27 Diann Gaalema, PhD, Vermont Center on Behavior and Health, University of Vermont
28 Stephen Higgins, PhD, Vermont Center on Behavior and Health, University of Vermont
29 Allison Kurti, PhD, Vermont Center on Behavior and Health, University of Vermont
30 Kathy Koller, PhD, ANTHC
31 Timothy Thomas, MD, ANTHC
32 Christi Patten, PhD, Mayo Clinic (Rochester, MN)
33 Steven Steinhubl, MD, ANTHC
34 Christine Hughes, Mayo Clinic (Rochester, MN)
35 Norman Medina, BBA, Vermont Center on Behavior and Health, University of Vermont
36 Carolyn Evemy, BA, Vermont Center on Behavior and Health, University of Vermont
37 Kaitlyn Browning, PhD, Vermont Center on Behavior and Health, University of Vermont
38

39 **Summary:**
40 Cigarette smoking during pregnancy increases risk for catastrophic pregnancy complications,
41 growth retardation, other adverse fetal and infant health problems, and later-in-life chronic
42 conditions among exposed offspring. The most effective intervention for reducing smoking
43 during pregnancy is financial incentives whereby participants earn incentives (e.g., gift cards,
44 cash) contingent on objective evidence of smoking abstinence. However, financial incentives-
45 based interventions are typically delivered in relatively intense protocols requiring frequent
46 clinic visits, which limits the geographical range over which services can be delivered and

1   potentially denies treatment to those residing in remote or otherwise difficult to reach settings.
2
3   Dr. Steve Higgins, PhD and Dr. Allison Kurti PhD, are investigators at the University of
4   Vermont conducted a pilot clinical trial that examined the feasibility, efficacy, and cost-
5   effectiveness of a smartphone-based financial incentives intervention whereby smoking
6   monitoring and delivery of incentives were completed remotely using a mobile app (DynamiCare
7   Rewards, designed by DynamiCare Health, Inc.). For this pilot trial, pregnant women were
8   recruited via obstetrical clinics and WIC offices in Vermont, as well as Facebook ads deployed
9   nationally. Eligible participants who completed the informed consent process were assigned to
10 one of two conditions: an incentives condition wherein women receive financial incentives
11 contingent on the remote submission of breath and saliva specimens indicating abstinence from
12 recent smoking (described below), or a best practices control condition in which women receive
13 usual care for smoking cessation that is provided at their obstetrical clinics, as well as three brief
14 educational sessions and referral to their state quit line by our research staff. Data from the this
15 trial were promising, with participants in the Best Practices plus Incentives condition
16 demonstrating over three-fold higher quit rates at late pregnancy (~37%) versus Best Practices
17 participants (~11%). Dr. Higgins and Dr. Kurti are currently conducting a larger-scale version of
18 this clinical trial.
19
20 One group that is not currently being reached by this highly promising intervention approach are
21 Alaska Native women. Thus, the proposed study seeks to examine the preliminary feasibility
22 and efficacy of this remote, smartphone-based incentives intervention among 60 Alaska Native
23 pregnant women who are current cigarette smokers.
24
25 For inclusion in the study, Alaska Native women must meet the following criteria: (a) ≥ 18 years
26 of age, (b) report being smokers at the time they learned of the current pregnancy, (c) report
27 smoking in the 7 days prior to completing their eligibility screening, (d) ≤ 25 weeks pregnant, (e)
28 speak English, (f) own a smartphone (Android or iOS; 81.8% of pregnant women in wave 1
29 [2013-2014] of the Population Assessment of Tobacco and Health [PATH] reported owning a
30 smartphone). Exclusion criteria include: (a) current or prior mental or medical condition that
31 may interfere with study participation (assessed via self-report during eligibility screening), (b)
32 smoke marijuana more than once each week and not willing to quit (marijuana smoking can
33 inflate breath CO), (c) exposed to unavoidable occupational sources of CO (e.g., car mechanic),
34 and (d) self-report currently being maintained on opioid maintenance therapy (e.g., methadone,
35 buprenorphine).
36
37 Participants randomized to the Best Practices plus Incentives condition will select a quit date
38 (either the first or second Monday following their enrollment), and will submit videos of
39 themselves blowing into a breath CO monitor twice daily during week 1. They will receive
40 incentives for every sample where expired breath CO is ≤ 6 ppm. Beginning in week 2 and
41 extending through week 6, participants will submit videos twice per week (Monday/Thursday)
42 for which they will receive incentives for providing videos of themselves completing saliva
43 cotinine tests indicating smoking abstinence. From week 7 until delivery, participants will
44 submit videos once per week and will continue to receive incentives for saliva cotinine tests
45 indicating no smoking. During the postpartum period, women will submit videos twice weekly
46 for the first 4 weeks and once weekly from weeks 5-12. The first negative breath CO or salivary

cotinine sample is worth $6.25 and each consecutive negative sample will increase the value of the incentive by $1.00 up to a maximum of $33.25 per sample. Missed samples or samples that indicate smoking will be worth $0 and will reset the incentive at its starting value (i.e., $6.25). However two consecutive negative samples following the slip will restore the incentive to its value before the slip. The maximum earnings in this condition is $1,620, which is the same as our prior studies adjusting for inflation. A proposed incentive schedule is attached.

Women in both conditions will complete seven formal assessments of their smoking status during their participation (intake, early pregnancy or 1 month after enrollment, late pregnancy or $\geq$ 28 weeks gestation, and at 4-, 8-, 12-, and 24-weeks postpartum) along with a treatment acceptability questionnaire and semi-structured interview on barriers and facilitators of treatment engagement. Women will receive $50 for completing each of these ($350 total).

As the proposed study is the first examination of smartphone-based financial incentives for reducing smoking during pregnancy among Alaska Native women, it represents an exploratory study, thus power analyses were not conducted to select the sample size. However, a sample of 60 Alaska Native women (30 Best Practices plus Incentives, 30 Best Practices) is consistent with prior pilot studies on this treatment conducted at the University of Vermont (Higgins et al., 2004; Kurti et al., 2020). This sample size will be sufficient to detect significant differences in smoking abstinence at participants' late pregnancy assessment, and results of this pilot study will be used to inform power analysis calculations in larger grant applications.

Participants will be recruited from online media outlets (i.e., Facebook) targeting Alaska Native pregnant women. Recruitment materials that we propose posting online are attached. We have also attached the battery of questionnaires that we propose administering at formal assessments, the Research Information Sheet that we will read to participants over the phone to obtain verbal consent to participate in the study, as well as the full consent form that we will mail to them after obtaining their verbal consent to participate.

PURPOSE AND OBJECTIVES

Purpose

Smoking during pregnancy is the leading preventable cause of poor pregnancy outcomes in the U.S. and other developed countries, increasing risk for pregnancy complications, preterm birth, stillbirth, infant death, impaired lung development, childhood illness and developmental/behavioral problems, and lifelong increased risk for cardiovascular disease, obesity, and metabolic syndrome.[1-8] Prevalence of smoking during pregnancy among national samples of U.S. pregnant women has remained stagnant at approximately 13% over the past decade.[9-10] Because risk for maternal smoking during pregnancy is disproportionately high among economically disadvantaged women, it contributes substantially to the problem of health disparities.[11-12] Importantly, smoking prevalence is particularly high among Alaska Native women (i.e., ~ 36% (Patten et al. 2018) versus ~ 13% among U.S. pregnant women overall (Kurti et al., 2017). Alaska Native women also exhibit unique tobacco use characteristics including use of a homemade smokeless tobacco (Iqmik, Hurt et al., 2009), and very few

smoking cessation interventions have been implemented specifically among Alaska Native women (Patten et al., 2010; Patten et al., 2018).

Existing treatments for smoking cessation among pregnant smokers produce very low quit rates (< 15%) with the exception of financial incentives. Meta-analyses indicate that incentive-based treatments produce the largest effect sizes of any psychosocial or pharmacological intervention for promoting smoking cessation during pregnancy.[13-14] Additionally, two randomized, controlled trials conducted by the University of Vermont (UVM) demonstrated that incentives significantly increase sonographically estimated fetal growth, increasing abdominal circumference (cm/week), femur length (cm/week), and overall estimated fetal weight compared to control groups that received non-contingent incentives.[15] Retrospective analyses of birth outcome data aggregated across three previous trials from UVM also indicated that incentives significantly increased mean birth weight, decreased the percent of low birth weight deliveries (< 2500 g), increased the percent of women breastfeeding through 12-weeks postpartum, and decreased depressive symptoms from birth through 12-weeks postpartum among depression-prone women.[16-18] Although this evidence-based treatment has demonstrable capacity to reduce smoking and improve birth outcomes, the scalability of this approach is constrained by the frequent clinic visits necessary for biochemical verification of smoking status, which limits access to those in the immediate vicinity of clinics that can provide such care. ***Capitalizing on technological advancements may surmount such access barriers, with the potential to extend the reach of financial incentives to disadvantaged pregnant smokers nationwide.***

The overarching aim of the parent study is to develop an innovative, efficacious, remotely delivered financial incentives intervention to reduce cigarette smoking during pregnancy. Pilot data from a sample of 60 pregnant women recruited nationally (30 Best Practices plus Incentives vs 30 Best Practices) yielded promising results (Kurti et al., 2020). In brief, it was feasible to recruit and retain pregnant smokers in this smartphone-based smoking cessation pilot study, and smartphone-based financial incentives produced significantly higher quit rates during pregnancy and postpartum relative to controls. The proposed study seeks to examine the feasibility and efficacy of this treatment strategy among Alaska Native women, who were not included in completed pilot study or in the larger clinical trial led by Dr. Higgins and Dr. Kurti that is currently underway.

To enable flexible use of the intervention in diverse locations, we use a mobile-phone-based platform for delivering the incentives intervention. The platform involves a Smartphone "app" (DynamiCare Rewards) which uses video capture to verify smoking status via a breath carbon monoxide (CO) monitor along with saliva cotinine test kits, and ensures treatment fidelity by providing automated, immediate feedback, incentive calculations, and incentive delivery for abstinence. Comparable technology-based treatment delivery platforms have been used to successfully promote smoking abstinence among the general population of U.S. smokers and among other vulnerable populations including rural heavy smokers.[20]

The proposed pilot study addresses the following specific aims among Alaska Native women:

Aim 1: Examine the feasibility, efficacy, and cost-effectiveness of a mobile-phone-based incentives intervention for promoting smoking cessation among Alaska Native pregnant women.

1   We will accomplish this aim by randomly assigning 60 pregnant women who smoke to receive
2   best practices for promoting smoking abstinence plus incentives contingent on biochemically
3   verified smoking abstinence or best practices alone. Incentives will be in place from the start of
4   study enrollment through three months postpartum. Primary outcomes will be point prevalence
5   smoking abstinence and continuous abstinence during and following pregnancy. We hypothesize
6   that there will be higher abstinence rates and longer durations of abstinence in the best practices
7   plus incentives versus the best practices control condition.
8
9   **Aim 2:** Evaluate acceptability of the treatment, including barriers to and facilitators of treatment
10 engagement. We will accomplish this aim by assessing treatment enrollment and retention and
11 conducting semi-structured interviews with participants upon treatment completion. During
12 these interviews, participants will be queried about their perceived utility of the incentives for
13 promoting health-related behavior change, and other barriers and facilitators of treatment
14 engagement and success (e.g., social support networks).[21-22] Qualitative research methods will
15 be used to discern general themes.
16
17 Overall, this project has the potential to address disparities in access to efficacious, evidence-
18 based smoking cessation treatments among Alaska Native pregnant women. If the present
19 mobile-phone-based incentives intervention is acceptable and efficacious in this population, this
20 study will provide strong preliminary data for a future R01 proposal to facilitate more
21 widespread dissemination of this innovative treatment model among Alaska Native communities.
22
23 **Objectives:**
24
25 The primary objective is to examine the feasibility, efficacy, and cost-effectiveness of a mobile-
26 phone-based incentives intervention for promoting smoking cessation among Alaska Native
27 pregnant women.
28
29 The secondary objective is to evaluate the acceptability of the treatment, including barriers to
30 and facilitators of treatment engagement.
31
32
33   **METHODS AND PROCEDURES**
34
35 **Study Design:**
36 We are proposing a two condition, parallel groups, randomized controlled pilot study of a
37 mobile-phone-based financial incentives intervention targeting Alaska Native pregnant cigarette
38 smokers. The experimental group will receive financial incentives (i.e., money loaded onto a
39 debit card) contingent on the remote submission of breath carbon monoxide (CO) and saliva
40 cotinine samples indicating smoking abstinence in addition to best practices for promoting
41 smoking cessation. The control group will receive best practices alone. The use of a best
42 practices control group reflects a real-world comparison condition in that all women will receive
43 the treatment that practitioners in the community are instructed to provide (i.e., the 5As plus quit-
44 line referral) thereby enhancing the ecological validity of the study, while also minimizing
45 between-subject variability in the extent of participants' exposure to these practices by
46 implementing these treatment components ourselves (described in greater detail below).

1 Although one common alternative is to use a non-contingent incentives control group which
2 equates both groups in terms of overall earnings, a meta-analysis conducted by UVM researchers
3 showed that non-contingent incentives have no impact on abstinence levels above no-incentive
4 control conditions.[44]
5
6 This subset of 60 Alaska Native women will be randomized separately from the main trial
7 currently underway at UVM. The rationale for a separate arm targeting Alaska Native women,
8 as opposed to including them in the main trial, is that smoking prevalence is substantially higher
9 among this subpopulation (i.e., ~ 36% for AN women [Patten et al. 2018] versus ~ 13% among
10 U.S. pregnant women overall [Kurti et al., 2017]), they exhibit unique tobacco use characteristics
11 including use of a homemade smokeless tobacco (Iqmik, Hurt et al., 2009), and very few
12 smoking cessation interventions have been implemented specifically among Alaska Native
13 women (Patten et al., 2010; Patten et al., 2018).
14
15 **Procedures:**
16 *Participants* Study participants will be 60 Alaska Native pregnant women ≥ 18 years of age.
17 Participants will be recruited from online media outlets (i.e., Facebook) targeting Alaska Native
18 pregnant women. That is, participants will self-refer after seeing our ads and will complete a
19 screening online or over the telephone with research staff.
20
21 For inclusion in the study, women must meet the following criteria: (a) ≥ 18 years of age, (b)
22 report being smokers at the time they learned of the current pregnancy, (c) report smoking in the
23 7 days prior to completing their preliminary eligibility screening, (d) ≤ 25 weeks pregnant, (e)
24 speak English, (f) own a smartphone (Android or iOS; 81.8% of pregnant women in wave 1
25 [2013-2014] of the Population Assessment of Tobacco and Health [PATH] reported owning a
26 smartphone). Exclusion criteria include: (a) current or prior mental or medical condition that
27 may interfere with study participation (assessed via self-report during formal intake assessment
28 completed online or by phone using a medical and psychosocial history questionnaire), (b)
29 smoke marijuana more than once each week and not willing to quit (marijuana smoking can
30 inflate breath CO), (c) exposed to unavoidable occupational sources of CO (e.g., car mechanic),
31 (d) report currently receiving opioid maintenance therapy (e.g., methadone, buprenorphine).
32 Women who meet the inclusion criteria and complete the informed consent process will be
33 considered formally enrolled and will be mailed equipment to participate in the study, but will
34 not be randomized until they (1) confirm receipt of their equipment, (2) complete an orientation
35 session on the smartphone app used in the current study (described subsequently), and (3)
36 provide a saliva sample indicating current smoking (i.e., test strip returns a positive for cotinine,
37 a metabolite of nicotine). Upon completing these steps, women will be randomized to either the
38 best practices plus incentives condition or best practices control condition (See Treatment
39 Conditions). The only criteria for withdrawing participants after randomization occurs will be
40 pregnancy termination or fetal demise.
41
42 *General Study Procedures.*
43 **Orientation Session:** After verifying eligibility and completing the informed consent process,
44 participants will be mailed two saliva test kits. Upon receiving the saliva tests, research staff will
45 aid participants in setting up their profile (e.g., create an account, upload profile photo) on the
46 DynamiCare smartphone application ("app") which is used to submit breath and saliva samples

remotely. Participants will be trained in the operation of the app and will have the opportunity to practice submitting saliva samples. The first sample that participants submit upon receiving their saliva test kits will be used to validate smoking status and participants will be withdrawn prior to randomization if they are found to be non-smokers. Women who provide a baseline saliva test validating that they are smokers will be randomized to one of the two treatment conditions, and will be provided with information about that condition and a brief quiz (see attached) as part of their orientation session. The orientation session will be conducted by telephone. Prior to the orientation session, participants will be mailed a CO monitor, additional saliva cotinine test kits, and an instruction manual containing general information about study procedures and where to download the app that they will use during their participation, as well as specific information about how frequently they should submit breath and saliva samples and a schedule of potential earnings. Given that over 80% of pregnant women can be expected to own smartphones, these women will use their existing phone during their participation to increase the ecological validity of using a mobile phone to deliver the intervention. Women who do not own a smartphone but have access to a computer with Internet access may pursue this option instead. We will collect data on the number of participants who use mobile phones vs. computers to participate in the intervention. During the orientation session, participants will also be informed that we will cover the costs of study-related data transfer if they do not have unlimited data plans with their wireless service provider. The purpose of this is to enhance the internal validity of this efficacy study by reducing between subject variability in data coverage. We will also collect data on the number of participants who require assistance paying for data coverage. Other details covered during orientation include instructions specific to the condition to which participants are randomized (e.g., schedule for submitting breath and saliva samples, the schedule of potential earnings, and when the earnings commence). Researchers will read participants an information sheet specific to their treatment assignment (attached), which will be followed by a brief quiz (attached). The purpose of the quiz is simply to verify participant understanding of the condition to which they are randomized. Participants will respond aloud to the quiz questions over the phone and any incorrect answers will be discussed, and they will be invited to ask any additional questions upon completing the quiz. Participants will select a quit date during orientation (either the first Monday following the call or the next Monday), and research staff will contact them by phone on the Friday prior to their quit date. Staff will also inform participants to contact them in the event that their phone is lost, stolen, or broken. In sum, participants who complete the informed consent process will be mailed two saliva test kits to verify their smoking status prior to being assigned to one of the two treatment conditions. Two tests will be sent in case participants' first sample is invalid (e.g., insufficient saliva to produce a reading) and they need to complete a second test to verify smoking status. Participants who are verified to be smokers will then complete the treatment assignment phone call, after which study staff will provide them with the equipment that they will need for the remainder of the study (e.g., breath CO monitor and additional saliva test kits).

Mobile-Phone Based Financial Incentives: The intervention will be delivered on participants' smartphones via an app installed on their phone either before or during the orientation session. The process of submitting a video entails the following steps: (1) Participant opens the app, which requires them to type in a password. Their username and password (stored as a secure, "irreversible" one-way hash) will be stored in a configuration file accessible only to the application; (2) The app will verify the password and participants will be taken to the "home"

1   screen which will show their cumulative earnings to date and a "post video" button; (3) The app
2   will attempt to contact the server over the Internet (via a 3G/4G mobile network) to determine
3   the correct time and status of the participant; (4) The participant will click on the post video
4   button, thereby leading them to a simple interface for recording videos that contains a start/stop
5   recording toggle button, a play button to review the recorded video, and a post button to send the
6   video to the server; (5) After posting the video, the server will display a voucher based on the
7   voucher schedule cached from the prior video upload. The app will then create a text file
8   containing a timestamp and video file. These files will be archived, compressed, and encrypted
9   to prevent tampering and/or eavesdropping while in transit. The app will maintain a file lock on
10 the video until it is discarded or posted to prevent participants from tampering with their videos;
11 (6) If a 3G/4G or WiFi Internet connection is available, the app will poll connection status in the
12 background until an upload can be initiated; (7) When the server receives the upload, the video
13 will be extracted and the content registered with the system; (8) A text message verifying that the
14 video was received will be sent to the participant and their account will be updated; (9) Research
15 staff will review and validate videos (see Validating Videos below). Participants will be able to
16 check their recent and cumulative earnings on a mobile-friendly site. These same steps will be
17 employed among participants using the computer-based treatment delivery platform. The app
18 for use in the current study (DynamiCare Rewards) was designed by DynamiCare Health, Inc.,
19 and DynamiCare Health, Inc. has partnered with numerous universities (UVM, Johns Hopkins
20 Univ., Medical University of South Carolina) and insurance companies (e.g., Aetna) for similar
21 purposes as the proposed study.
22
23 **Abstinence Criterion:** Consistent with the parent trial underway at UVM, participants will
24 receive incentives during week 1 for all breath CO samples where CO ≤ 6 ppm. Breath CO has a
25 relatively short half-life, thus twice daily CO testing during week 1 will help detect recent
26 smoking. This frequency of testing also offers the advantage of allowing women to obtain
27 frequent access to reinforcement thereby engaging them early in the intervention. Although
28 recent studies to promote smoking cessation among pregnant women have employed cut points
29 as high as 10 ppm[87], existing data and our group's experience suggest that moderate levels of
30 smoking can go undetected when using higher cut points. After week 1, incentives will be based
31 on salivary cotinine levels. Salivary cotinine has a longer half-life and thus is more appropriate
32 for the less frequent schedule of routine smoking monitoring that will ensue following week 1.
33 The test itself simply displays a positive or negative, however the equipment specifications
34 indicate that salivary cotinine ≥ 30 ng/mL will register as positive which is consistent with the
35 cut point used in prior research conducted by UVM researchers.[45]
36
37 Participants will be informed during their orientation session about environmental sources that
38 could elevate breath CO, as well as other sources of nicotine that could elevate salivary cotinine.
39 Specifically, research staff will inform participants that they should avoid second-hand or
40 environmental smoke, as well as smoking other combustible tobacco products and/or using
41 marijuana. Thus CO readings above 6 ppm will always be considered positive during week 1 of
42 treatment (described subsequently). Similarly, participants will be informed that other sources of
43 nicotine (e.g., e-cigarettes, nicotine replacement therapy) may result in positive saliva cotinine
44 tests which may prevent them from earning incentives from week 2 onwards.
45

Smoking Monitoring: We will use the iCO™ Smokerlyzer® (coVita, Inc.), a handheld Smartphone-compatible CO monitor that connects to the phone via headphone jack or Bluetooth® technology, to monitor smoking status during week 1. Although the iCO™ Smokerlyzer® readings can be viewed using the iCO Smokerlyer® app that is freely available at both the Apple iOS App Store and Google Play Android App Store, DynamiCare Health, Inc. has interfaced the monitor with their customized app to permit researchers to validate that breath CO samples are submitted by the intended participants who are enrolled in the study. The iCO™ Smokerlyzer® permits a concentration range of 0-100 ppm and sensitivity results in individual 1 ppm increments. The operating life is approximately 200 tests or 3 years (whichever comes first), which will be adequate for the proposed study. Following week 1, we will use Alere iScreen OFD Oral Cotinine Screening tests to monitor smoking status via saliva cotinine testing. Salivary cotinine has a longer half-life than breath CO, making it a more appropriate measure with less frequent testing. Subjects will submit videos of themselves 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 $\geq$ 30 ng/mL.

Treatment Conditions.

Best Practices: The 2008 Clinical Practice Guidelines for smoking cessation recommends that pregnant smokers be provided with the 5As.[88] Briefly, these guidelines stipulate that practitioners should implement the following steps at obstetric visits: (1) Ask about smoking status at the first prenatal care visit; (2) Advise those who endorse smoking about the potential harms of smoking to mother and fetus and recommend quitting; (3) Assess the willingness of smokers to make a quit attempt during pregnancy; (4) Assist those willing to make a quit attempt by helping to establish a quit plan, referring them to a pregnancy-specific quit line and offering assistance with making the initial contact, and by providing them with a copy of the pregnancy-tailored self-help guide "Need Help Putting Out That Cigarette?", distributed by the American College of Obstetricians and Gynecologists; (5) Arrange for follow-up contacts on smoking at subsequent prenatal care visits. As there may be differences in the extent to which the 5As are implemented across obstetric clinics, research staff will implement the 5As at three assessments that take place during pregnancy (see Assessment Procedures below) to decrease between-subject variability in exposure to best practice guidelines. At the first antepartum assessment, staff will complete a fax referral form for participants to the Alaska tobacco quit line, which provides telephone-counseling calls with a trained smoking-cessation coach during pregnancy and postpartum. In addition to completing the 5As and referring women to the quit line, all women in the best practices condition will also receive the smoking cessation advice that is provided at their obstetric clinic. Note that pregnant women seeking smoking cessation treatment in the community often do not receive cessation-focused follow-up visits after endorsing that they are current cigarette smokers, nor do providers or community health workers typically submit referrals for them to a quit line. As we take these extra steps, we refer to this condition as "best practices" rather than "usual care."

Best Practices plus Financial Incentives: Women assigned to this condition will receive the best practices treatment described above plus the remote incentives intervention. As mentioned previously, participants will set a quit date during their orientation session for either the first or second Monday following the session. They may practice submitting samples (for which staff

1   will provide feedback) prior to their quit date if desired, however this is not required as they
2   would have already provided an initial sample to validate their smoking status prior to being
3   randomized. Once the quit date arrives, participants will submit two breath CO samples each
4   day, separated by 8 hours from one another. A day will start at 5:00 a.m. and end at 4:00 a.m.
5   (Alaska time). The app will indicate to participants when samples can be collected because the
6   "post video" button will be locked for 8 hours after the first sample of the day is submitted.
7
8   Beginning on the quit date and extending for one week, participants will be required to submit
9   twice daily CO samples. All samples $\leq$ 6 ppm will be considered negative and those > 6 ppm
10   will be considered positive. Requiring frequent testing during week 1 only will permit
11   participants the opportunity to earn frequent reinforcement while their salivary cotinine levels
12   decrease more gradually if participants are not smoking over the course of week 1 of treatment.
13   As with our prior and ongoing trials, including the parent trial, the value of the incentive will
14   increase with consecutive negative samples indicating smoking abstinence. If a sample has not
15   been submitted within the specified 8-hour time window, an electronic prompt will be sent to
16   submit a video two hours before the time window expires. Missed samples will be considered
17   positive unless extenuating circumstances are reported (e.g., lost, stolen, broken phone). The
18   schedule of potential earnings will be consistent with our prior trials adjusting for inflation. Thus
19   rather than a maximum potential earnings of $1,200 (2002 USD), participants in the proposed
20   study may earn up to $1,620 (2017 equivalent of $1,200 in 2002) for sustaining smoking
21   abstinence during pregnancy and for 12-weeks postpartum. The schedule of potential earnings
22   will start at $6.25 for the first negative sample and increase by $1.00 for each consecutive
23   negative sample. Thus the second negative sample will be worth $7.25, the third worth $8.25,
24   and so on, until incentive values plateau at a maximum of $33.25. If a participant submits a
25   breath CO > 6 ppm during week 1 or a positive saliva cotinine test any time after week 1, the
26   value of the incentive will be reset to the initial value of $6.25. This reset component is critical
27   to protect against relapse once an initial period of abstinence has been achieved.[89]
28
29   Following the initial quit week during which participants submit twice daily breath CO samples,
30   the schedule of monitoring will be reduced and saliva cotinine will be used to determine smoking
31   status. Only tests where the display indicates negative samples will result in participants earning
32   reinforcement. Specifically, during weeks two through six, participants will submit videos of
33   themselves completing saliva cotinine tests twice per week, then once per week from week seven
34   until delivery. During the once per week phase, the specific day on which participants are
35   required to submit a sample will be determined quasi-randomly (at least two days apart). The
36   sample will be prompted electronically via a text message at the start of the day and the
37   participant will have up to eight hours to provide the sample. This provides a balance between a
38   schedule that is sufficiently unpredictable that participants who are no longer abstinent may be
39   detected, while at the same time providing them with a reasonable time frame to submit a sample
40   upon being prompted to do so. The schedule of potential earnings during weeks two until
41   delivery will be a continuation of the escalating pay schedule from the initial quit week.
42   Importantly, intermittent reinforcement schedules induce more persistence than frequent,
43   predictable schedules,[90,91] thus the schedule we are proposing may be optimal for promoting
44   persistence and sustained abstinence.
45

As women who quit smoking during pregnancy are particularly vulnerable to relapse during the early postpartum, the frequency of monitoring will increase to twice per week for the initial four weeks postpartum. After the first month, monitoring will be returned to the weekly, quasi-random prompted monitoring schedule for the next 8 weeks. The opportunity to earn incentives will be terminated at the end of postpartum week 12, consistent with our prior and ongoing trials[45,48] thereby permitting us to compare the results of the proposed intervention to our group's traditional, in person financial incentives interventions.

Validating Videos. Key personnel will validate participant videos daily during the workweek. After logging in, the process takes less than ten minutes per video. To be considered valid, the videos of breath tests during week 1 must meet the following criteria: (a) have an authentic user (i.e., a known, enrolled participant), (b) participant can be seen holding her breath for the required duration, (d) participant can be seen and heard exhaling into the mouthpiece, and (e) participant displays CO reading at the end of the video until the monitor indicates that the reading is complete. In one recent controlled trial that required remote submission of breath CO samples, only 39 of 4,774 (0.8%) total samples submitted were problematic.[55] Regarding videos of saliva cotinine testing from week 2 through 12 weeks postpartum, videos must meet the following criteria: (a) have an authentic user (i.e., a known, enrolled participant), (b) saliva cotinine test kit is in view for entire duration of the video, (c) participant permits ample time to collect the sample and collect a reading, and (d) test result is displayed clearly at the end of video.

Delivering Incentives. Participants' account activity box on their homepage will display their recent and cumulative earnings. In our group's previous studies that used similar schedules of potential earnings to what we are proposing here, participants earned (on average) $550 during the intervention.[15] Participants in the proposed study will receive a PEX Debit Card at the beginning of the intervention onto which incentive payments will be loaded contingent on their submission of breath and saliva samples indicating smoking abstinence. These debit cards do not require a credit history check, and participants will pay no monthly fees for carrying the card. Moreover there are no costs for using the PEX Debit Cards for in-store or online shopping. Research staff will load money onto participants' study debit card after reviewing each video and determining that the video meets the criteria for validation above. Comparable methods of incentive delivery have been employed in computer-based financial incentives treatments targeting the general population of smokers,[52-54] and no participants in Dr. Kurti's parent study have experienced problems or reported complaints associated to using PEX cards. Importantly, in-person financial incentives treatments typically require research staff to venture into the community to make a incentive purchases (e.g., gift cards) in person and then deliver it to the participant. In contrast, the technology-based method that we are proposing is easy to implement and will decrease both staff travel time to redeem incentives, as well as the immediacy between engaging in the target behavior and receiving reinforcement.

Assessment Procedures. Participants in both the best practices plus incentives condition and the best practices control condition will complete a formal assessment at intake, during early pregnancy (i.e., one month after enrolling), late pregnancy (i.e., 28-weeks gestation), and at 4-, 8-, 12-, and 24-weeks postpartum. This schedule of formal assessments and the use of similar questionnaires (see Assessment Battery) will permit comparisons to prior controlled trials

1   conducted by UVM researchers.[15,45-48] Participants will receive $50 per formal assessment
2   completed regardless of their smoking status. This money may come in the form of a check
3   mailed to their home or in the form of a gift card (TangoCard) that is emailed to them.
4   TangoCard is an electronic gift card platform. If participants receive their rewards via this
5   option, the reward will be emailed to them as a unique URL. By following the URL, the
6   participant can choose from a variety of gift card brands and redeem their reward. Once they
7   select a brand, the final gift card will be emailed to them. To ensure that HIPAA security
8   standards are met and emails are kept private, TangoCard has signed a BAA (Business Associate
9   Agreement) with DynamiCare. Questionnaires will be completed remotely via computer or
10 mobile phone. Items will be administered using REDCap or SurveyGizmo, both of which
11 capture and house unique de-identified codes for study participants. Data audits will be
12 conducted monthly during the first six months of the study and then quarterly until study
13 completion to detect problems. As no personal identifying information will be collected, the
14 chance of a breach of confidentiality is very low. Regardless of whether participants complete
15 the assessment online or over the phone, participants in both treatment conditions will be
16 required to submit both a breath CO sample and a salivary cotinine sample at each formal
17 assessment to determine their smoking status.
18
19 ***Assessment Battery*** Participant's intake assessment will be conducted after they have completed
20 a preliminary eligibility screening and appear to be eligible, and will address seven areas: (a)
21 Sociodemographics (age, educational attainment, marital status, health insurance status); (b)
22 Medical/pregnancy history (height/weight, self-reported pre-pregnancy weight, weeks pregnant,
23 history of complications in prior pregnancies; (c) Smoking history (age started smoking, pre-
24 pregnancy time to first cigarette/cigarettes per day, past week time to first cigarette/cigarettes per
25 day, number of quit attempts before/during the current pregnancy, number of other smokers in
26 the household, rules about smoking in the household, nicotine dependence[92]); (d) Smoking
27 timeline follow-back (to characterize daily smoking rates and/or use of alternative tobacco
28 products or nicotine replacement therapy since learning of the current pregnancy[93]); (e) Smoking
29 attitudes (motivation to stop, confidence in ability to stop, intention to quit before the baby is
30 born, intention to remain abstinent after the baby is born, perceived stress levels); (f) Maternal
31 health/executive functioning (lifetime history of depression, general psychiatric symptoms,[94]
32 current depressive symptoms,[95] discounting of delayed hypothetical monetary rewards,[96]
33 behavioral economic measure of the reinforcing value of cigarettes,[68,97] Behavior Rating
34 Inventory of Executive Function®-Adult Form [BRIEF-A; see attached], EQ-5D Health-Related
35 Quality of Life Questionnaire [see attached]); (g) Stressful life events (SAMHSA Life Events
36 Checklist [see attached]). Appropriately modified versions of these measures will be
37 administered at the other six formal assessments identified above. In addition, at the postpartum
38 assessments we will assess breastfeeding, including initiation, duration, and different levels of
39 breastfeeding (e.g., exclusive, predominant, any).
40
41 After participants' consent to join the study, we will collect contact information over the phone
42 including their mailing address (to send them equipment), as well as the phone number for an
43 alternative contact in the case that we are unable to reach the participant. We will also ask the
44 participant to tell us how we should describe their involvement in the research study should we
45 need to reach out to their alternative contact at some point. This form is attached, and it will be

1 updated following each formal assessment. Keeping an updated mailing address is important in
2 case participants need additional equipment or paperwork mailed to them.
3
4 Regarding the cost-effectiveness analysis, we will employ the Brief Drug Abuse Treatment Cost
5 Analysis Program (Brief DATCAP;[98,99]) to estimate the cost of delivering the Incentives versus
6 Best Practices smoking cessation treatments. More specifically, we will derive the direct and
7 indirect economic cost of treatment by allocating fixed costs based upon the proportion of time
8 spent delivering these programs, as well as costs that vary by patient engagement and smoking
9 status (e.g., staff time validating breath CO samples, quit-line staff time, incentives).
10 Administration costs (e.g., postage/courier service to mail participants CO monitors) will also be
11 included. Costs will be in USD for price year 2021/2022. The time period of the cost analysis
12 will span from intake to discontinuation or completion of the program. However, since the
13 duration of treatment will vary according to where in the pregnancy a woman enters the study,
14 the economic cost per person per week will also be calculated. Research-specific resources
15 consumed over the course of the study will be excluded from the cost-effectiveness analysis.
16
17 ***Examining Acceptability.*** At the 24-week postpartum assessment or shortly thereafter,
18 participants in both the best practices plus incentives condition and best practices control
19 condition will complete a Treatment Acceptability Questionnaire (TAQ) comparable to those
20 administered in other financial incentives interventions,[21] including research conducted by Dr.
21 Kurti.[61,64] The measure will be administered on REDCap and will query participants about the
22 ease of use, helpfulness, and convenience of the intervention, as well as whether the intervention
23 was fair, fun, and whether they would recommend it. All responses will be made using a 100-
24 point visual analogue scale. Participants in the best practices plus incentives condition will
25 receive additional TAQ questions inquiring about whether they liked self-monitoring their breath
26 CO levels, liked the incentives, and whether the incentives were helpful in terms of promoting
27 smoking abstinence during treatment and sustaining abstinence following treatment withdrawal.
28 In addition, research staff will call all participants upon completing the 24-week
29 assessment/TAQ to query them about barriers and facilitators of treatment engagement
30 including: (a) features of the intervention that they felt facilitated or hindered engagement (e.g.,
31 technical difficulties/availability of technical support, self-monitoring using the CO monitor,
32 appropriateness of staff counseling surrounding smoking), (b) social/environmental variables
33 (e.g., quit support from friends/family, rules about smoking in the home, exposure to smoke-free
34 environments, social networks that promoted or discouraged quitting smoking) and (c)
35 internal/psychological variables (e.g., stress, psychological well-being, motivation to quit, self-
36 efficacy for quitting smoking). The semi-structured interview used to examine barriers and
37 facilitators of treatment engagement will use scripted prompts, however participants will be able
38 to respond freely and openly to each question. Their responses may be transcribed verbatim by
39 the research staff completing the interviews, or participants may type them into open-ended text
40 boxes.
41
42 <div align="center">**STATISTICAL CONSIDERATIONS**</div>
43
44 **Statistical Methods**
45 Study conditions will be compared on baseline demographics and other characteristics using
46 analysis of variance (ANOVA) for continuous variables and chi-square tests for categorical

1 variables. If a specific characteristic differs significantly across study conditions and is
2 predictive of the outcome, it will be considered as a potential covariate in subsequent analyses.
3 Analyses of treatment effects on smoking status will adhere to an intent-to-treat approach[100]
4 whereby all women randomized to each study condition will be included in the analyses
5 independent of early dropout, noncompliance, etc., with the exception of women excluded for
6 abortion/fetal demise as is convention in this research area. Cochran-Mantel-Haenszel tests (C-
7 M-H) will be performed for comparisons between the best practices plus incentives vs. best
8 practices alone conditions on point-prevalence smoking abstinence at the end-of-pregnancy and
9 6-months postpartum assessments. Comparisons of point-prevalence abstinence rates between
10 treatment conditions across all assessments through six months postpartum will be analyzed
11 using mixed model repeated measures for categorical data based on generalized estimating
12 equations (GEE) using a logistic link function (SAS: PROC GENMOD, SAS Institute, Cary,
13 NC). The two treatment groups will also be compared on breastfeeding and other measures
14 collected postpartum. Comparisons of treatment conditions on dichotomous outcomes (e.g., %
15 breastfeeding) will parallel categorical analyses for point prevalence abstinence using PROC
16 GENMOD to adjust potential covariate effects. The significance criterion will be set at alpha =
17 0.05 for all analyses.
18
19 Regarding the cost-effectiveness analysis (CEA), the CEA will be conducted by dividing the
20 average (mean) difference in treatment costs across the best practices plus incentives versus best
21 practices conditions by the average (mean) difference in abstinence rates in late pregnancy to
22 derive incremental cost-effectiveness ratios (ICERs).[101] Statistical significance of these ICERs
23 will be determined probabilistically by employing non-parametric bootstrapped standard
24 errors.[102] The main objective of this preliminary CEA will be to establish methods for obtaining
25 and analyzing data that pertain to treatment delivery in remote financial incentives interventions.
26 This basic CEA data will provide important preliminary data for a future RO1 application in
27 which we may propose conducting a more sophisticated cost-effectiveness analysis.
28
29 Regarding the acceptability data, TAQ items administered using a 100-point VAS will be
30 compared across the two treatment conditions using ANOVA's. Again characteristics that differ
31 across treatment condition will be considered as potential covariates. Responses to the semi-
32 structured interview questions will be analyzed afterwards using a thematic content
33 analysis.[103,104] We will employ an inductive approach whereby the content of these qualitative
34 data will direct the coding and theme development. Coding of the data will involve grouping,
35 sorting, and identifying themes that reflect barriers and facilitators of treatment engagement.
36 Two researchers will perform the content analysis independently and sort responses into themes.
37 Disagreements will be resolved through discussion until consensus is reached. Those themes
38 that emerge and reflect modifiable aspects of the intervention (e.g., provision of technical
39 support, appropriateness of staff counseling and feedback surrounding quitting smoking) will be
40 taken into account in designing future iterations of this intervention that are more responsive to
41 participant's preferences.
42
43 As our examination of the intervention among the proposed subgroup of Alaska Native women
44 represents the first feasibility and proof of concept assessment to our knowledge, power analyses
45 were not conducted to determine the sample size needed to obtain statistically significant effects
46 on the above outcomes. However, once we complete our assessment of the feasibility and

efficacy of smartphone-based financial incentives among this subset of Alaska Native women, such analyses will be conducted to determine the sample size needed in future, larger-scale studies targeting this unique subpopulation.

Sample Size Justification

A sample size of 60 Alaska Native women was selected based on initial pilot studies of the financial-incentives-based approach to promoting smoking cessation among pregnant women developed at the University of Vermont (Higgins et al., 2004), as well as Dr. Kurti's pilot study of 60 women receiving best practices plus smartphone-based financial incentives or best practices alone, which was sufficient to detect treatment differences during pregnancy and postpartum. This sample size will be sufficient to determine whether the intervention is feasible and effective at promoting late-pregnancy smoking abstinence between Alaska Native women enrolled in the best practices plus incentives versus best practices Control conditions. Results of our assessment will be used to inform power analysis calculations for larger-scale, NIH-supported research proposals focused on smoking cessation among Alaska Native pregnant women.

RISKS/BENEFITS

Risks

Participants may experience some discomfort arising from nicotine withdrawal. Participants will be informed during the informed consent process that they may experience the following symptoms of nicotine withdrawal: craving cigarettes, restlessness, irritability, increased appetite, increased eating, dizziness, difficulty concentrating, and depressed mood. There is a small risk that participants' electronic information could be accessed thereby affecting confidentiality. There is a risk that women may be uncomfortable answering some of the questions on the formal assessment batteries. There is a risk that use of other combustible tobacco products and/or marijuana during study participation may elevate participants' breath CO levels thereby preventing them from earning incentives during week 1 even if they have quit smoking cigarettes. Similarly, use of other nicotine products like e-cigarettes or nicotine replacement therapy could elevate salivary cotinine levels after week 1 and prevent subjects from earning incentives. There is also a risk that a participant may become distraught during the course of the study and become a danger to herself, or that other emergencies could arise that research staff may need to address.

Summary of Protection Against Potential Risks

We will take the following actions to protect against potential risks: (a) We will inform women during the informed consent process that reducing and/or quitting smoking may result in nicotine withdrawal symptoms however these symptoms should disappear within two weeks. (b) To ensure participant confidentiality, all study files will be stored in locked filing cabinets. All participants receive a subject identification code that is used in place of their name in all study files. The key connecting names and ID codes is kept in a locked file and stored separately from the data files. Study computers are password protected and encrypted. These protections apply only to study data collected via paper/pencil methods (e.g., phone eligibility screening data recorded by research staff). (c) For subjects who self-refer and complete their preliminary

eligibility screening online, the survey will be administered using UVM's REDCap system. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies that is hosted at UVM. REDCap has various security features, such as requiring usernames & passwords to access REDCap, and then needing permissions for the individual project. REDCap is accessed by URLs starting with HTTPS which encrypts data before being sent over the internet. (d) With respect to the assessment batteries conducted using REDCap or SurveyGizmo, we will not ask participants to self-report identifying information and both the REDCap and SurveyGizmo platforms are configured such that they do not retain identifying information (including IP addresses), thus a breach of confidentiality is exceedingly unlikely. (e) Participants will be informed during the informed consent process and again before completing the assessment batteries that they may skip questions or stop at any time should they feel uncomfortable answering some of the items. (f) Regarding the use of other tobacco products, we will inform women that the use of other combustible products could influence their breath CO and thereby limit their ability to earn incentives during week 1, and that using other nicotine-containing products following week 1 could influence saliva cotinine levels thereby preventing them from earning incentives from week 2 onwards. (g) If the investigative team or research staff are concerned that a given participant may be experiencing thoughts of harming themselves or others, this information will be immediately acted upon by staff and investigators (e.g., crisis services in the participant's community will be contacted). Research staff will be trained to deal with emergency calls. Protocols for assessing and responding to suicidality include a suicidality assessment checklist and a plan to call Crisis Services if any intent is demonstrated. If Alaska Native women are sufficiently remote that there are no local Crisis Services Centers available, study staff will contact the regional hospital operator in Alaska and request to speak with the on-call physician. The study staff in Anchorage and Rochester will monitor any reports or observations of medical problems or severe depression or other psychiatric symptoms in participants. Drs. Patten and Prochaska, licensed clinical psychologists, will be consulted by telephone to consult with study staff as needed.

The study investigators will oversee all procedures designed to continuously monitor participant safety. The investigative team will meet once each week to discuss actual or potential issues for each participant. During these meetings, investigators will review all participants' progress to ensure treatment fidelity.

Benefits
The benefits of the study are considerable. All participants will receive the 5As from research staff as well as the opportunity to have a staff member submit a fax referral form on their behalf to the Alaska tobacco quit line. Thus all participants will receive instructions about when to quit and counseling surrounding their smoking, as well as feedback about their smoking status upon providing breath CO and saliva samples. If they are successful in abstaining from smoking, all participants will receive positive feedback. Importantly, as both conditions involve treatment, the primary benefit of participating will be the potential for women to quit smoking, which may have important immediate and long-term health benefits for both the mother and her offspring. Women randomized to the contingent incentives condition have the opportunity to earn incentives that can be used to purchase goods and services that may help improve their quality of life (e.g., groceries, gas, baby clothes).

1
2 There is a reasonable likelihood that women assigned to the best practices condition will not
3 achieve outcomes as good as those assigned to the best practices plus incentives condition.
4 Nevertheless, all women will receive treatment that meets Best Practices as outlined in the 2008
5 Clinical Practice Guidelines on Treating Tobacco (Fiore et al., 2008).
6
7 Although the study is considered high-risk by definition (i.e., pregnant population), the potential
8 benefits are substantial in terms of our scientific understanding of the effectiveness of mobile-
9 phone-based financial incentives interventions targeting pregnant smokers. Overall, the
10 risk/benefit ratio appears highly favorable.
11
12 **Importance of the Knowledge to be Gained**
13 Cigarette smoking is the largest preventable risk factor for morbidity and mortality in developed
14 countries and involves considerable risks to fetal and infant health. Smoking during pregnancy
15 can lead to spontaneous abortion, preterm birth, stillbirth, low-birth weight, and sudden infant
16 death syndrome, as well as the development of later in life chronic conditions. The proposed
17 study may suggest that mobile phone based incentives hold significant clinical utility and
18 promise. If so, the platform for delivering the intervention remotely is sufficiently flexible that it
19 could be modified to treat other vulnerable populations such as those with mental illness or
20 adolescents in the future. Because distance and traveling are not limiting factors in applying the
21 treatment, the system may also prove to be especially beneficial among rural populations. In
22 short, the knowledge gained could help us develop an effective and broadly applicable treatment
23 to mitigate the morbidity and mortality associated with cigarette smoking during pregnancy.
24
25 Moreover, regarding Alaska Native women specifically, the proposed study will be the first to
26 examine the efficacy of this approach among this population. If the intervention proves to be
27 efficacious among Alaska Native women, it stands poised to make a significant contribution to
28 reducing the disproportionately high smoking rates during pregnancy among Alaska Native
29 women, and thereby reducing health disparities.
30
31 **Therapeutic Alternatives**
32 Women can utilize the free State tobacco quit line and related services outside of the context of
33 this study. They can also choose to rely on the services offered by their providers.
34
35
36   **DATA SAFETY AND MONITORING**
37
38 **Data Safety and Monitoring Plan**
39 The proposed study will utilize the same plan as the parent trial underway at UVM. This overall
40 monitoring plan consists of ongoing, close monitoring of data and safety issues by the PI and
41 other project staff and prompt reporting of any adverse events (AEs) or serious adverse events
42 (SAEs) to the institutional review board and/or NIGMS.
43
44 **Patient eligibility and status**
45 All recruitment will be managed by trained research staff under the supervision of Dr. Diann
46 Gaalema (Project PI, UVM), Dr. Kaitlyn Browning (Project Postdoctoral Fellow, UVM), Dr.

1   Stephen Higgins (Center PI, UVM), and Dr. Kathy Koller (Site PI, ANTHC) using specialized
2   forms and procedures. All information collected will be reviewed by the research staff, PI, or
3   designated representatives, who will determine participant eligibility, contact them about
4   scheduling and completing an intake assessment where appropriate. Eligible women will
5   complete the informed consent process over the phone, after which they will be mailed a paper
6   copy of the full consent form along with their equipment to participate in the study. The consent
7   procedure is described in greater detail elsewhere and recent research published in JAMA
8   demonstrates the feasibility of completing the informed consent process over the phone
9   (McConnell et al., 2017). The status of all active participants will be reviewed weekly at staff
10   meetings between the PI/Research Assistant and other trained support staff.
11
12
13   **Confidentiality**
14   Steps will be taken to ensure confidentiality of all written and electronic information. With
15   regard to written information, all study files will be stored in locked filing cabinets at UVM. All
16   participants receive a subject identification code that is used in place of their name in all study
17   files. The key connecting names and ID codes is kept in a locked file and stored separately from
18   the data files. Study computers are password protected and encrypted. With respond to
19   electronic information, the server will be protected from outside intrusion by multiple firewalls.
20   Administrative access to the machines will only occur using SSH, a secure, encrypted protocol
21   for remotely connecting to a machine. The servers will be hardened against attack using some of
22   the concepts deployed in the Bastille Linux project, a project whose purpose is to automate some
23   of the processes involved in hardening the Linux operating system. Security will be periodically
24   monitored using network mapping tools, like nmap which probe machines for vulnerabilities and
25   report the results to the system administrator. The software Port Scan Attack Detector (PSAD)
26   will be used to monitor the servers and notify administrators if they come under attack. The
27   Advanced Intrusion Detection Environment (AIDE) will be used to detect if any unauthorized
28   changes are made to the machine, allowing us to identify and fix changes that might be made to
29   critical files in the unlikely event of a break-in. Servers will be backed up nightly to external
30   hard drives using an encrypted file system. External hard drives will be rotated offsite weekly
31   and stored in the PD's office in a locked, data-safe firebox. The software vendors/developers
32   websites will be monitored for security patches and upgrades. Additionally, the server
33   appliance's Linux operating system provides a means for monitoring and regularly installing
34   security patches. See the Data Monitoring Plan for further information about protection against
35   risks. As staff training is crucial to ensuring confidentiality, all study personnel will receive
36   certification in human subjects' protection from the Collaborative Institutional Training Initiative
37   (CITI) prior to beginning work on this project.
38
39   **Auditing procedures**
40   Review of any problems related to quality of data collection, transmission or analyses, and of
41   any AEs and SAEs that occurred during the past week will occur at weekly research staff
42   meetings held by Drs. Gaalema, Browning, and Higgins at UVM.
43
44   **Adverse Event (AE) and Unanticipated Problem (UAP) Reporting**
45   In the proposed study, we will use the FDA's definition of AEs and SAEs. AEs and SAEs will be
46   assessed at each subject visit by a trained staff member, and will be discussed at the weekly

1 research staff meetings. Any SAE will be brought to the attention of the PI as soon as possible
2 and not longer than 24 hours. Any AE or SAE that is both unexpected and related to the study
3 participation will be reported to the IRB within 7 days of the event. That IRB will make a
4 determination as to whether additional reporting requirements are needed. IRB actions will be
5 reported to the funding agency by the PI no less than annually and more frequently as
6 recommended by the local IRB. Any SAEs will be summarized in the yearly Progress Reports to
7 the funding agency, including a review of frequency and severity. All SAEs will be followed
8 through ongoing consultation with the physician caring for the patient until they resolve, result in
9 death, or stabilize and are not expected to improve.
10
11 **Withdrawal Procedures**
12 Women will be free to withdraw at any point during the course of the study without penalty.
13 That will be explained during informed consent. In terms of data analysis, we will adhere to an
14 intent-to-treat approach (Armitage, 1983) wherein all women randomized to the study conditions
15 will be included in the analyses independent of early dropout, noncompliance, etc., with the
16 exception of excluding women for abortion/fetal demise prior to their late pregnancy smoking
17 assessment. Women who receive their equipment and fail to complete an orientation session, as
18 well as women who provide a baseline CO sample indicating that they are non-smokers, will be
19 withdrawn prior to randomization and thus not included in an intent-to-treat analysis.
20
21 **Sources of Materials**
22 The research materials to be obtained include interviews, questionnaires, and breath and saliva
23 specimens to verify smoking status (and serve as the basis for reinforcement in the incentives
24 condition). Materials will be collected remotely using a combination of phone calls with
25 participants, online surveys, and remote video capture via smartphone app (i.e., for submission of
26 breath CO samples and salivary cotinine samples). These data will be entered into databases with
27 no identifying information (i.e., with subject ID only). These databases are stored on password-
28 protected external hard drives in locked offices in a locked clinic accessible only to the PI and
29 research staff.
30
31   **SUBJECT CHARACTERISTICS, IDENTIFICATION AND RECRUITMENT**
32
33 **Subject Selection**
34 We are studying Alaska Native pregnant women who are currently cigarette smokers to develop
35 more effective interventions to help this population quit smoking. As noted previously, the
36 frequent biochemical verification required by in-person financial incentives interventions often
37 limits the number of individuals we can treat, as some women live in remote areas and/or lack
38 reliable transportation to a clinic. Targeting pregnant smokers in a remotely delivered
39 intervention may provide an innovative means of transcending these historical barriers to
40 treatment. Additionally, smoking prevalence is substantially higher among Alaska Native
41 pregnant women (i.e., ~ 36% [Patten et al. 2018] versus ~ 13% among U.S. pregnant women
42 overall [Kurti et al., 2017]), they exhibit unique tobacco use characteristics including use of a
43 homemade smokeless tobacco (Iqmik, Hurt et al., 2009), and very few smoking cessation
44 interventions have been implemented specifically among Alaska Native women (Patten et al.,
45 2010; Patten et al., 2018). Thus, the proposed pilot study represents the first examination of the
46 feasibility and effectiveness of financial incentives to reduce smoking targeting this specific

1 population and may provide important preliminary data for future grant applications to
2 disseminate the present intervention among Alaska Native women on a larger scale.
3
4 **Vulnerable Populations**
5 Pregnant women to develop more effective interventions to help them quit smoking.
6
7 **Number of Subjects**
8 60 Alaska Native women.
9
10 **Inclusion/Exclusion Criteria**
11 A total of 60 Alaska Native pregnant women will be recruited. The inclusion criteria include: (a)
12 $\geq$ 18 years of age, (b) report being smokers at the time they learned of the current pregnancy, (c)
13 report smoking in the 7 days prior to completing their initial eligibility screening, (d) $\leq$ 25 weeks
14 pregnant, (e) speak English, (f) own a smartphone (Android or iOS; 81.8% of pregnant women in
15 wave 1 [2013-2014] of the Population Assessment of Tobacco and Health [PATH] reported
16 owning a smartphone). The exclusion criteria include: (a) current or prior mental or medical
17 condition that may interfere with study participation (assessed via self-report), (b) smoke
18 marijuana more than once each week and not willing to quit (marijuana smoking can inflate
19 breath CO), (c) exposed to unavoidable occupational sources of CO (e.g., car mechanic), and (d)
20 currently maintained on opioid maintenance therapy. The only criteria for withdrawing someone
21 from the trial following randomization to treatment condition will be pregnancy termination or
22 fetal demise prior to participants' late-pregnancy smoking assessment ($\geq$ 28 weeks gestation).
23 Women who fail to complete an orientation session or provide an initial CO sample indicating
24 that they are smokers will be withdrawn prior to randomization. Criteria will be assessed during
25 an initial eligibility screen that can be conducted either online or by phone to determine
26 preliminary eligibility and further evaluated during the formal intake assessment.
27
28 **Inclusion of Minorities and Women**
29 This project will include only women. Smoking among pregnant and newly postpartum women
30 has sufficiently special circumstances regarding the potential toxicity to the fetus and newborn,
31 the reasons for trying to quit smoking and prevent relapse, and the patterns of smoking reduction,
32 cessation, and relapse that they need to be studied exclusively in women.
33
34 Additionally, the project will include only Alaska Native women. However, should we receive
35 referrals from non-Alaska Native women in Alaska who are pregnant and currently smoking, we
36 will refer them to the Alaska tobacco quit line.
37
38 **Recruitment**
39 As in prior and current trials conducted at UVM, including the ongoing parent trial, applicants
40 will be recruited from online media advertisements. The text for these ads, as well as exemplars
41 of pictures, are attached to this submission. These ads were developed based on prior research
42 conducted by the ANTHC involving online recruitment of Alaska Native women. These ads will
43 include a link to the preliminary screening questions administered through REDCap. If eligible,
44 we will collect the participant's contact information and schedule a time to contact them to
45 provide more information about the study and conduct the consent phone call if they choose to
46 enroll.

1
2
3
4 **FINANCIAL CONSIDERATIONS**
5
6 **Expense to Subject**
7 No known expense to subject aside from their time.
8
9 **Payment for Participation**
10 Women in both conditions will receive compensation for completing 7 formal assessments at
11 $50/assessment = $350. Women assigned to the best practices plus incentives condition will
12 have the potential to earn incentives in the form of money loaded onto a PEX Debit Card for
13 abstaining from smoking. The incentives that participants earn will vary depending on how early
14 in the pregnancy she enters the study and how well she abstains from smoking. However, the
15 maximum potential amount that a woman could earn is approximately $1620 in incentives. This
16 total is equivalent to the maximum total earnings in prior UVM trials adjusted for inflation
17 ($1,200 in 2002 USD = $1,600 today).
18
19 **Collaborating Sites**
20 The present study represents a collaboration between University of Vermont (Project PI-Diann
21 Gaalema, PhD & Center PI-Stephen Higgins, PhD) and the Alaska Native Tribal Health
22 Consortium (ANTHC), Anchorage Alaska. The Site Principal Investigator for the ANTHC is
23 Dr. Kathy Koller, Ph.D.   Dr. Koller's research focuses on developing novel, theory-based
24 behavioral interventions for tobacco cessation, including NIH-supported intervention programs
25 to reduce tobacco disparities among Alaska Native adolescents and pregnant women. The co-
26 investigators at the ANTHC are Dr. Timothy Thomas, MD (ANTHC), Dr. Christi Patten, PhD
27 (Mayo Clinic, Rochester, MN), and Dr. Steven Steinbubl, MD (ANTHC). UVM IRB approvals,
28 as well as the Human Subjects Research Protocol currently on file at UVM, are attached to this
29 submission.
30
31
32 **INFORMED CONSENT**
33
34 **Consent Procedures**
35 With respect to the informed consent process, eligible participants will be given detailed
36 information about the study including the following: (a) each study condition; (b) cash
37 compensation for their time (e.g., completing assessments); (c) the process of randomization and
38 the equal chance of being assigned to one of the two study conditions; (d) protection of
39 confidentiality and the right to withdraw at any time; (e) expectations regarding the completion
40 of formal assessments during and following their delivery (regardless of smoking status); (f)
41 risks and benefits of study participation; and (g) our procedures for dealing with any
42 endorsement of suicidality of self-harm. Contact information for the Project Postdoctoral
43 Fellow/Primary Project Contact (Dr. Browning), the Project Research Associate in Alaska at the
44 ANTHC (Lauren Gillott), the Project PI (Dr. Gaalema), Site PI (Dr. Koller), and the contact
45 person at the Alaska Area IRB will be provided during the verbal consent as well as included in
46 the paper copy of the Informed Consent Form that is mailed to subjects' homes. Participants will

1 be competent adults who can provide their voluntary informed consent. The informed consent
2 process will be completed over the phone, and we will use the attached Consent & Authorization
3 Process Documentation form to document Mom's consent to participate in a smoking cessation
4 study. Researchers will read the attached Research Information Sheet to participants and they
5 will be provided the opportunity to ask questions or postpone providing their verbal consent to
6 another time if they need more time to decide whether to participate.
7
8 After answering any questions, the participant may provide verbal consent to participate.
9 Researchers will mail a paper copy of the full consent form to participants along with equipment
10 to participate in the study. A recent study in JAMA demonstrated the feasibility of completing
11 the informed consent process remotely using Smartphones (McConnell et al., 2017).
12
13 UVM investigators will be responsible for eligibility screenings, and for moving women through
14 the informed consent process.
15
16

REFERENCES

1. Barker, D.J. (2004). The developmental origins of adult disease. J Am Coll Nutr, 23, 588S-595S.

2. Cohen, G., Jeffery, H., Lagercrantz, H., Katz-Salamon, M. (2010). Long-term reprogramming of cardiovascular function in infants of active smokers. Hypertension, 55, 722-728.

3. Dietz, P.M., England, L.J., Shapiro-Mendoza, C.K., Tong, V.T., Farr, S.L., & Callaghan, W.M. (2010). Infant morbidity and mortality attributable to prenatal smoking in the U.S. Am J Prev Med, 39, 45-52.

4. Rogers, J.M. (2009). Tobacco and pregnancy. Reproductive Toxicology, 28, 152-160.

5. Thompson BL, Levitt P, Stanwood, GD. Prenatal exposure to drugs: effects on brain development and implications for policy and education. Nat Rev Neurosci 2009;10:303-312.

6. Baba S, Wikstom AK, Stephansson O, Cnattingius S. Influence of smoking and snuff cessation on preterm birth. Eur J Epidemiol 2012;27:297-304.

7. U.S. Department of Health and Human Services. The health consequences of smoking—50 years of progress: A report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2014.

8. Leslie FM. Multigenerational epigenetic effects of nicotine on lung function. BMC Med 2013;11:27.

9. Alshaarawy, O., & Anthony, J. C. (2015). Month-wise estimates of tobacco smoking during pregnancy for the United States, 2002–2009. *Maternal and Child Health Journal*, 19(5), 1010-1015.

10. Kurti, A.N., Redner, R., Lopez, A.A., Keith, D.R., Stanton, C.A., Gaalema, D.E., &…Higgins, S.T. (in press). Tobacco and Nicotine Delivery Product Use in a National Sample of Pregnant Women. *Preventive Medicine.*

11. Higgins, S.T., Chilcoat, H.D. (2006). Women and smoking: An interdisciplinary examination of socioeconomic influences. Drug Alcohol Depend, 104 (Suppl. 1), S1-5.

12. Kandel, D.B., Griesler, P.C., & Schaffran, C. (2009). Educational attainment and smoking among women: Risk factors and consequences for offspring. Drug Alcohol Depend, 104 (Suppl. 1), S24-33.

13. Lumley, J., Chamberlain, C., Dowswell, T., Oliver, S., Oakley, L., Watson, L. (2009). Interventions for promoting smoking cessation during pregnancy. Cochrane Database Syst Rev. Jul 8;(3):CDC001055.

14. Chamberlain, C., O'Mara-Eves, A., Porter, J., Coleman, T., Perlen, S.M., & McKenzie, J.E. (2017). Psychosocial interventions for supporting women to stop smoking in pregnancy (review). Cochrane Database Syst Rev., CDC001055.

15. Higgins, S.T., Washio, Y., Lopez, A.A., Heil, S.H., Solomon, L.J., Lynch, M.E., Hanson, J.D., Higgins, T.M., Skelly, J.M., Redner, R., & Bernstein, I.M. (2014). Examining two different schedules of financial incentives for smoking cessation among pregnant women. Prev Med, 68, 51-57.

16. Higgins, S.T., Bernstein, I.M., Washio, Y., Heil, S.H., Badger, G.J., Skelly, J.M., Higgins, T.M., & Solomon, L.J. (2010a). Effects of smoking cessation with voucher-based contingency management on birth outcomes. Addiction, 105, 2023-2030.

17. Higgins, T.M., Higgins, S.T., Heil, S.H., Badger, G.J., Skelly, J.M., Bernstein, I.M., Solomon, L.J., Washio, Y., & Preston, A.M. (2010b). Effects of cigarette smoking cessation on breastfeeding duration. Nic Tob Res, 12, 483-488.

18. Lopez, A.A., Skelly, J.M., & Higgins, S.T. (2015). Financial incentives for smoking cessation among depression-prone pregnant and newly postpartum women: Effects on smoking abstinence and depression ratings. Nicotine Tob Res, 17, 455-462.

19. Kurti, A.N. Unpublished raw data. Population Assessment of Tobacco & Health (PATH) (2013-2014).

20. Stoops, W.W., Dallery, J., Fields, N.M., Nuzzo, P.A., Schoenberg, N.E., Martin, C.A., Casey, B., & Wang, C.J. (2009). An internet-based abstinence reinforcement smoking cessation intervention in rural smokers. Drug Alcohol Depend, 105, 56-62.

21. Bonevski, B., Bryant, J., Lynagh, M., & Paul, C. (2012). Money as motivation to quit: A survey of a non-random Australian sample of socially disadvantaged smokers' views of the acceptability of cash incentives. Prev Med, 55, 122-126.

22. Flemming, K., McCaughan, D., Angus, K., & Graham, H. (2015). Qualitative systematic review: Barriers and facilitators to smoking cessation experienced by women in pregnancy and following childbirth. J Adv Nurs, 71, 1210-1226.

23. LeClere, F.L. & Wilson, J.B. (1990). Smoking behavior of recent mothers, 18-44 years of age, before and after pregnancy: United States, 1990. Adv Data, 288, 1-11.

24. Higgins, S.T., Heil, S.H., Badger, G.J., Skelly, J.M., Solomon, L.J., & Bernstein, I.M. (2009). Educational disadvantage and cigarette smoking during pregnancy. Drug Alcohol Depend, 104, 100-105.

25. Tong, V.T., Dietz, P.M., Morrow, B., D'Angelo, D.V., Farr, S.L., Rockhill, K.M., et al. (2013). Trends in smoking before, during, and after pregnancy-pregnancy risk assessment monitoring system, United States, 40 sites, 2000-2010. MMWR Surveill. Summ., 62, 1-19.

26. U.S. Department of Health and Human Services: The health consequences of smoking: 50 years of progress. A report of the Surgeon General.: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion. Office on Smoking and Health, 2014.

27. Cnattingius, S. (2004). The epidemiology of smoking during pregnancy: Smoking prevalence, maternal characteristics, and pregnancy outcomes. Nicotine Tob Res, 6, 125-140.

28. Cohen, R.T., Raby, B.A., Van Steen, K., Fuhlbrigge, A.L., Celedon, J.C., Rosner, B.A., Strunk, R.C., Zeiger, R.S., & Weiss, S.T. (2010). In utero smoke exposure and impaired response to inhaled corticosteroids in children with asthma. J Allergy Clin Immunol, 126, 491-497.

29. Monteiro, P.O., & Victora, C.G. (2005). Rapid growth in infancy and childhood and obesity in later life—a systematic review. Obes Rev, 6, 143-154.

30. Dennison, B.A., Edmunds, L.S., Stratton, H.H., & Pruzek, R.M. (2006). Rapid infant weight gain predicts childhood overweight. Obes, 14, 491-499.

31. Chrestani, M.A., Santos, I.S., Horta, B.L., Dumith, S.C., Souza, M.A., & Dode, O. (2013). Associated factors for accelerated growth in childhood: A systematic review. J Matern Child Health, 17, 512-519.

32. Buka, S.L., Shenassa, E.D., & Niaura, R. (2003). Elevated risk of tobacco dependence among offspring of mothers who smoked during pregnancy: A 30-year prospective study. Am J Psychiatry, 160, 1978-1984.

33. Atluri, P., Fleck, M.W., Shen, Q., Mah, S.J., Stadfelt, D., Barnes, W., et al. (2001). Functional nicotine acetylcholine receptor expression in stem and progenitor cells of the early embryonic mouse cerebral cotex. Dev Biol, 240, 143-156.

34. Dwyer, J.B., Broide, R.S., & Leslie, F.M. (2008). Nicotine and brain development. Birth Defects Res. C: Embryo Today, 84, 30-34.

35. England, L.J., Aagaard, K., Bloch, M., Conway, K., Cosgrove, K., Grana, R., et al. (2017). Developmental toxicity of nicotine: A transdisciplinary synthesis and implications for emerging tobacco products. Neurosci Biobehav Rev, 72, 176-189.

36. Mohlman, M.K., Levy, D.T. (2016). Disparities in maternal and child health outcomes attributable to prenatal tobacco use. Matern Child Health J, 20, 701-709.

37. Sexton, M. & Hebel, J.R. (1984). A clinical trial of change in maternal smoking and its effect on birth weight. JAMA, 251, 911-915.

38. Bickel, W.K., Johnson, M.W., Koffanrus, M.N., MacKillop, J., Murphy, J.G. (2014). The behavioral economics of substance use disorders: Reinforcement pathologies and their repair. Annu Rev Clin Psychol, 10, 641-677.

39. Bickel, W.K., Odum, A.L., & Madden, G.J. (1999). Impulsivity and cigarette smoking: Delay discounting in current, never, and ex-smokers. Psychopharmacol, 146, 447-454.

40. Bickel, W.K., Jarmolowicz, D.P., Mueller, E.T., Koffanrus, M.N., & Gatchalian, K.M. (2012). Excessive discounting of delayed reinforcers as a trans-disease process contributing to addiction and other disease-related vulnerabilities: Emerging evidence. Pharmacol Ther, 134, 287-297.

41. Jaroni, J.L., Wright, S.M., Lerman, C., & Epstein, L.H. (2004). Relationship between education and delay discounting in smokers. Addict Behav, 29, 1171-1175.

42. Higgins, S.T., Delaney, D.D., Budney, A.J., Bickel, W.K., Hughes, J.R., Foerg, F., & Fenwick, J.W. (1991). A behavioral approach to achieving initial cocaine abstinence. Am J Psychiatry, 148, 1218-1224.

43. Lussier, J.P., Heil, S.H., Mongeon, J.A., Badger, G.J., & Higgins, S.T. (2006). A meta-analysis of voucher-based reinforcement therapy for substance use disorders. Addiction, 101, 192-203.

44. Davis, D.R., Kurti, A.N., Skelly, J.M., Redner, R., White, T.J., & Higgins, S.T. (2016). A review of the literature on contingency management in the treatment of substance use disorders, 2009-2014. Prev Med, 92, 36-46.

45. Higgins, S.T., Heil, S.H., Solomon, L.J., Bernstein, I.M., Lussier, J.P., Abel, R.L., Lynch, M.E., & Badger, G.J. (2004). A pilot study on voucher-based incentives to promote abstinence from cigarette smoking during pregnancy and postpartum. Nicotine Tob Res, 6, 1015-1020.

46. Heil, S.H., Higgins, S.T., Bernstein, I.M., Solomon, L.J., Rogers, R.E., Thomas, C.S., Badger, G.J., & Lynch, M.E. (2008). Effects of voucher-based incentives on abstinence from cigarette smoking and fetal growth among pregnant women. Addiction, 103, 1009-18.

47. Higgins, S.T. Unpublished trial results reported in Higgins, S.T., Washio, Y., Heil, S.H., et al. Financial incentives for smoking cessation among pregnant and newly postpartum women. Prev Med, 2012, S33-40.

48. Higgins, S.T., Washio, Y., Heil, S.H., et al. (2012). Financial incentives for smoking cessation among pregnant and newly postpartum women. Prev Med, 55, S33-40.

1
2 **49.** Ondersma, S.J., Svikis, D.S., Lam, P.K., Connors-Burge, V.S., Ledgerwood, D.M., &
3   Hopper, J.A. (2012). A randomized trial of computer-delivered brief intervention and low-
4   intensity contingency management for smoking during pregnancy. Nicotine Tob Res, 14,
5   351-360.
6
7 **50.** International Telecommunications Union (2016). ICT Facts and Figures 2016.
8   http://www.itu.int/en/ITU-D/Statistics/Pages/facts/default.aspx
9
10 **51.** Pew Research Center (2016). Mobile Facts and Figures. http://www.pewinternet.org/fact-
11   sheet/mobile/
12
13 **52.** Dallery, J., Glenn, I.M., & Raiff, B.R. (2007). An internet-based abstinence reinforcement
14   treatment for cigarette smoking. Drug Alcohol Depend, 86, 230-238.
15
16 **53.** Dallery, J., Raiff, B.R., & Grabinski, M.J. (2013). Internet-based contingency management
17   to promote smoking cessation: A randomized controlled study. J Appl Behav Anal, 46,
18   750-764.
19
20 **54.** Dallery, J., Raiff, B.R., Kim, S.J., Marsch, L.A., Stitzer, M., & Grabinski, M.J. (2016).
21   Nationwide access to an internet-based contingency management intervention to promote
22   smoking cessation: A randomized controlled trial. Addiction, doi: 10.1111/add.13715.
23   [Epub ahead of print]
24
25 **55.** Kurti, A.N., Davis, D.R., Skelly, J.M., Redner, R., & Higgins, S.T. (2016). Comparison of
26   nicotine dependence indicators in predicting quitting among pregnant smokers. Exp Clin
27   Psychopharmacol, 24, 12-17.
28
29 **56.** Methodology Committee of the Patient-Centered Outcomes Research Institute (PCORI)
30   (2012). Methodological standards and patient-centeredness in comparative effectiveness
31   research: The PCORI perspective. JAMA, 307, 1636-1640.
32
33 **57.** Whittaker, R., Merry, S., Dorey, E., & Maddison, R. (2012). A development and evaluation
34   process for mHealth interventions: Examples from New Zealand. J Health Commun, 17,
35   11-21.
36
37 **58.** Naughton, F., Jamison, J., & Sutton, S. (2013). Attitudes towards SMS text message
38   smoking cessation support: A qualitative study of pregnant smokers. Health Educ Res, 28,
39   911-922.
40
41 **59.** Sloan, M., Hopewell, S., Coleman, T., Cooper, S., & Naughton, F. (2017). Smoking
42   cessation support by text message during pregnancy: A qualitative study of views and
43   experiences of the MiQuit intervention. Nicotine Tob Res, 572-577.
44
45 **60.** Rodger, D., Skuse, A., Wilmore, M., Humphreys, S., Dalton, J., Flabouris, M., & Clifton,
46   V.L. (2013). Pregnant women's use of information and communications technologies to

access pregnancy-related health information in South Australia. Aust J Prim Health, 19, 308-312.

61. Kurti, A.N., Logan, H., Manini, T., & Dallery, J. (2015). Physical activity behavior, barriers to physical activity, and opinions about a smartphone-based physical activity intervention among rural residents. Telemedicine and eHealth, 21, 1-8.

62. Kurti, A.N., & Dallery, J. (2014). Integrating technological advancements in health-based behavior interventions: Unprecedented opportunities for behavior analysts. Mex J Behav Anal, 40, 106-126.

63. Dallery, J., Kurti, A.N., & Erb, J.P. (2014) A new frontier: Integrating behavioral and digital technology to promote health behavior. The Behavior Analyst, 38, 19-49.

64. Kurti, A.N., & Dallery, J. (2013) Internet-based contingency management increases walking in sedentary adults. J Appl Behav Anal, 46, 568-581.

65. Dallery, J., Kurti, A.N., & Martner, S. (2014). Technological approaches to assess and treat cigarette smoking. In L. Marsch, S. Lord, & J. Dallery (Eds), *Transforming Behavioral Health Care with Technology: The State of the Science.* Oxford University Press.

66. Kurti, A.N., Keith, D.R., Noble, A., Priest, J.S., & Higgins, S.T. (2016). Co-occurring risk factors for illicit drug abuse and dependence in a U.S. nationally representative sample. Prev Med, 92, 118-125.

67. Kurti, A.N., Klemperer, E., Zvorsky, I., Redner, R., Priest, J., & Higgins, S.T. (2016). Some context for understanding the place of the GED in the relationship between educational attainment and smoking prevalence. Prev Med, 92, 141-147.

68. Higgins, S.T., Kurti, A.N., Redner, R., White, T.J., Keith, D.R., Gaalema, D.E., Roberts, M.E., Doogan, N.J., & Stanton, C.A. (2015). Co-occurring risk factors for current cigarette smoking in a U.S. nationally representative sample. Prev Med, 92, 110-117.

69. Kurti, A.N., Davis, D., Skelly, J.M., Redner, R. & Higgins, S.T (2016). Comparison of nicotine dependence indicators in predicting quitting among pregnant smokers. Exp Clin Psychopharm, 24, 12-17.

70. Kurti, A.N., & Dallery, J. (2014). A laboratory-based evaluation of exercise plus contingency management for reducing cigarette smoking. Drug Alc Depend, 144, 201-209.

71. Kurti, A.N., & Dallery, J. (2014). Effects of exercise on craving and cigarette smoking in the human laboratory. Addict Behav, 39, 1131-1137.

72. Kurti, A.N., Davis, D., Redner, R., Jarvis, B., Zvorsky, I., Atwood, G.A., &…Higgins, S.T. (2016). Incorporating technology into incentive-based interventions to promote health-

related behavior change: A systematic literature review, 2004-2015. Trans Issues Psychol Sci, 2, 128-152.

73. Higgins, S.T., Reed, D.R., Redner, R., Skelly, J.M., Zvorsky, I.Z., & Kurti, A.N. (2016). Simulating demand for cigarettes among pregnant women: A low-risk method for studying vulnerable populations. J Exp Anal Behav, doi: 10.1002/jeab.232

74. Villanti, A., Boulay, M., & Juon, H.S. (2011). Peer, parent, and media influences on adolescent smoking by developmental stage. Addict Behav, 36, 133-136.

75. Villanti, A.C., Richardson, A., Vallone, D.M., & Rath, J.M. (2013). Flavored tobacco product use among U.S. young adults. Am J Prev Med, 44, 388-391.

76. Villanti, A.C., Cantrell, J., Pearson, J.L., Vallone, D.M., & Rath, J.M. (2014). Perceptions and perceived impact of graphic cigarette health warning labels on smoking behavior among U.S. young adults. Nicotine Tob Res, 16, 469-477.

77. Villanti, A.C., Pearson, J.L., Cantrell, J., Vallone, D.M., & Rath, J.M. (2015). Patterns of combustible tobacco use in U.S. young adults and potential response to graphic cigarette health warning labels. Addict Behav, 42, 119-125.

78. Villanti, A.C., Giovino, G.A., Barker, D.C., Mowery, P.D., et al. (2012). Menthol brand switching among adolescents and young adults in the National Youth Smoking Cessation Survey. Am J Public Health, 102, 1310-1312.

79. Rath, J.M., Villanti, A.C., Williams, V.F., et al. (2015). Patterns of longitudinal transitions in menthol use among U.S. young adult smokers. Nicotine Tob Res, 17, 839-846.

80. Villanti, A.C., Rath, J.M., Williams, V.F., et al. (2016). Impact of exposure to electronic cigarette advertising on susceptibility and trial of electronic cigarettes and cigarettes in U.S. young adults: A randomized controlled trial. Nicotine Tob Res, 18, 1331-1339.

81. Heil, S.H., Herrmann, E.S., Badger, G.J., Solomon, L.J., Bernstein, I.M., & Higgins, S.T. (2014). Examining of the timing of changes in cigarette smoking upon learning of pregnancy. Prev Med, 68, 58-61.

82. Vurbic, D., Higgins, S.T., McDonough, S.R., Skelly, J.M., & Bernstein, I.M. (2014). Maternal body mass index moderates the influence of smoking cessation on breastfeeding. Nicotine Tob Res, 16, 527-535.

83. Gaalema, D.E., Higgins, S.T., Pepin, C.S., Heil, S.H., & Bernstein, I.M. (2013). Illicit drug use among pregnant women enrolled in treatment for cigarette smoking cessation. Nicotine Tob Res, 15, 987-991.

84. Mullen, P.D., Carbonari, J.P., Tabak, E.R., & Glenday, M.C. (1991). Improving disclosure of smoking by pregnant women. Am J Obstet Gynecol, 165, 409-413.

85. Javors, M.A., Hatch, J.P., & Lamb, R.J. (2005). Cut-off levels for breath carbon monoxide as a marker for cigarette smoking. Addiction, 100, 159-167.

86. Higgins, S.T., Heil, S.H., Badger, G.J., Mongeon, J.A., Solomon, L.J., McHale, L., & Bernstein, I.M. (2007). Biochemical verification smoking status in pregnant and recently postpartum women. Exp Clin Psychopharmacol, 15, 58-66.

87. Tappin, D., Bauld, L., Purves, D., Boyd, K., Sinclair, L., MacAskill, S.,&…Coleman, T. (2015). Financial incentives for smoking cessation in pregnancy: Randomised controlled trial. BMJ, 350, h134.

88. Fiore, M.C., Bailey, W.C., Cohen, S.J., et al. (2008). Treating Tobacco Use and Dependence. U.S. Department of health and Human Services, Public Health Service. Rockville, MD. (Original manual published in 2000).

89. Roll, J.M., & Higgins, S.T. (2000). A within-subject comparison of three different schedules of reinforcement of drug abstinence using cigarette smoking as an exemplar. Drug Alcohol Depend, 58, 103-109.

90. Kazdin, A.E., & Polster, R. (1973). Intermittent token reinforcement and response maintenance in extinction. Behav Ther, 4, 386-391.

91. Mackintosh, N.J. (1974). The psychology of animal learning. London: Academic Press, 1974.

92. Fagerstrom, K.O., & Schneider, N.G. (1989). Measuring nicotine dependence: A review of the Fagerstrom Tolerance Questionnaire. J Behav Med, 12, 159-182.

93. Brown, R.A., Burgess, E.S., Sales, S.D., Whiteley, J.A., Evans, D.M., & Miller, I.W. (1998). Reliability and validity of a smoking timeline follow-back interview. Psychol Addict Behav, 12, 101-112.

94. Derogatis, L.R. (1993). *Brief Symptom Inventory: Administration, scoring, and procedures manual*. National Computer Systems (NCS).

95. Beck, A.T., & Beck, R.W. (1972). Screening depressed patients in family practice: A rapid technic. Postgrad Med, 52, 81-85.

96. Johnson, M.W., & Bickel, W.K. (2002). Within-subject comparison of real and hypothetical money rewards in delay discounting. J Exp Anal Behav, 77, 129-146.

97. Jacobs, E.A., & Bickel, W.K. (1999). Modeling consumption in the clinic using simulation procedures: Demand for heroin and cigarettes in opioid-dependent outpatients. Exp Clin Psychopharmacol, 7, 412-426.

98. French, M.T., Roebuck, M.C., & McLellan, A.T. (2004). Cost estimation when time and resources are limited: The Brief DATCAP. J Subst Abuse Treat, 27, 187-193.

99. French, M.T., Fang, H., & Fretz, R. (2010). Economic evaluation of a prerelease substance abuse treatment program for repeat criminal offenders. J Subst Abuse Treat, 38, 31-41.

100. Armitage, P. (1983). Trials and errors: The emergence of clinical statistics. J Roy Stat Soci, 146, 321-334.

101. Boyd, K.A., Briggs, A.H., Bauld, L., Sinclair, L., & Tappin, D. (2015). Are financial incentives cost-effective to support smoking cessation during pregnancy? Addiction, 111, 360-370.

102. Drummond, M., Manca, A., & Sculpher, M. (2005). Increasing the generalizability of economic evaluations: Recommendations for the design, analysis, and reporting of studies. Int J Technol Assess Health Care, 21, 165-171.

103. Goszczynska, E., Knol-Michalowska, K., & Petrykowska, A. (2016). How do pregnant women justify smoking? A qualitative study with implications for nurses' and midwives' anti-tobacco interventions. J Adv Nurs, 72, 1567-1578.

104. Braun, V., & Clarke, V. (2006). Using thematic analysis in psychology. Qual Res Psychol, 3, 77-101.