HIC# 2000024740

HRP-503B – BIOMEDICAL RESEARCH PROTOCOL
(2017-1)

Protocol Title: Evaluating the feasibility and efficacy of a real-time smoking intervention using wearable technology

Principal Investigator: Krysten W. Bold, Ph.D.

Version Date: 5/29/2020

(*If applicable*) Clinicaltrials.gov Registration #: NCT04172623

INSTRUCTIONS
This template is intended to help investigators prepare a protocol that includes all of the necessary information needed by the IRB to determine whether a study meets approval criteria. **Read the following instructions before proceeding:** 1. Use this protocol template for a PI initiated study that includes direct interactions with research subjects. Additional templates for other types of research protocols are available in the system Library. 2. If a section or question does not apply to your research study, type "Not Applicable" underneath. 3. Once completed, upload your protocol in the "Basic Information" screen in IRES IRB system.

APPROVED BY THE YALE UNIVERSITY IRB 6/26/2020

SECTION I: RESEARCH PLAN

1. **Statement of Purpose:** State the scientific aim(s) of the study, or the hypotheses to be tested.

The proposed project will use wearable technology to test the feasibility and efficacy of delivering a novel real-time smoking intervention to improve standard tobacco treatment. 50 adult daily smokers will be recruited from an outpatient tobacco treatment center to participate in an 8-week pilot intervention. Participants will be randomly assigned to a control group (standard treatment ST, n=25) or experimental group (standard treatment plus real-time smoking intervention ST+, n=25). The control group (ST) will not receive real-time feedback about their smoking. The experimental group (ST+) will receive real-time feedback as soon as smoking is detected using wearable technology during the 8-week intervention. Specific aims include:

Aim 1: Evaluate the feasibility, acceptability, and helpfulness of the real-time smoking intervention. We will characterize rates of adherence (i.e., number of days wearing the smartband) and evaluate participant satisfaction and perceived usefulness of the intervention using post-treatment interviews and ratings.

Aim 2: Assess the preliminary efficacy of the real-time intervention as an adjunct to standard tobacco treatment. We will compare biochemically confirmed 7-day point prevalence abstinence at the end of treatment (week 8) to estimate effect sizes for ST+ vs. ST. Additional outcomes will compare total number of days abstinent and changes in cigarettes per smoking day from baseline to end of treatment between ST+ and ST as proximal indices of good clinical response that are related to long-term cessation outcomes.

2. **Probable Duration of Project:** State the expected duration of the project, including all follow-up and data analysis activities.

2 years. We anticipate recruiting and enrolling 50 subjects over 20 months and will complete data entry and analysis by the end of 2 years.

3. **Background:** Describe the background information that led to the plan for this project. Provide references to support the expectation of obtaining useful scientific data.

Cigarette smoking is the leading cause of preventable death[1]. The majority of current smokers want to quit[2], but most smoking quit attempts are unsuccessful[2-4], suggesting treatment innovations are needed. Mobile smoking treatments are gaining popularity and have many benefits, including that treatments are highly accessible, scalable, and can be provided in the user's natural environment[5,6]. However, existing mobile interventions require users to manually record smoking behavior and decide if and when to access support[7], limiting the accuracy of information and the timeliness of the intervention. Recent innovations in wearable technology (e.g., smartbands) now allow for passive, automatic identification of smoking behavior through geospatial sensors and adaptive learning algorithms. Preliminary research indicates smoking can be identified reliably in real time using smartband technology[8], yet no studies have tested

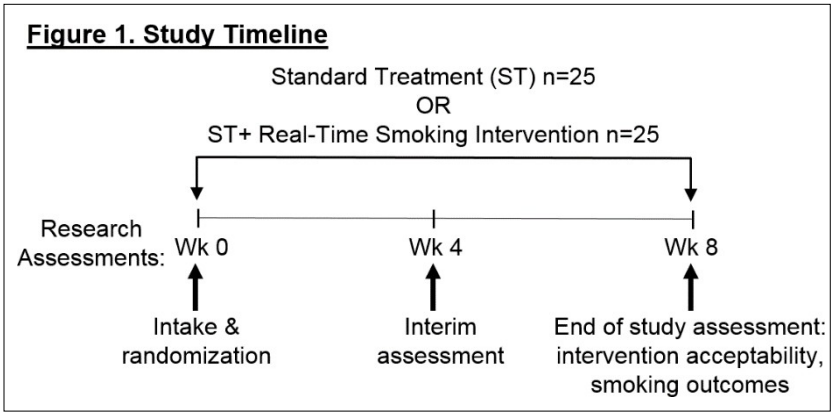
whether intervening in the moment when smoking is detected can promote cessation during a quit attempt.

Real-time notifications as soon as smoking is detected may improve the timeliness of intervention delivery and enhance quitting success. According to cognitive theories of drug use, smoking behavior becomes highly automatic over time, such that smoking occurs quickly, efficiently, and without deliberate intention or awareness[9-11]. Real-time notifications when smoking is detected may help promote cessation by bringing awareness to the smoking event, thereby reducing the automaticity of smoking and providing an opportunity to practice alternative coping strategies. Even after a lapse, or initial return to smoking after quitting, this real-time feedback may help individuals recover abstinence and protect against a return to smoking.

4. Research Plan: Summarize the study design and research procedures using non-technical language that can be readily understood by someone outside the discipline. Be sure to distinguish between standard of care vs. research procedures when applicable, and include any flowcharts of visits specifying their individual times and lengths. Describe the setting in which the research will take place.

Overview: The proposed study will evaluate the feasibility and efficacy of a real-time smoking intervention as an adjunct to enhance standard tobacco treatment. 50 adult smokers will be randomly assigned to a control group (standard tobacco treatment, ST, n=25) vs. an experimental group (standard treatment plus a real-time smoking intervention, ST+, n=25). Randomization to group (1:1) will be stratified by average number of cigarettes smoked per day at baseline (< or ≥ 10 cigarettes per day) to balance groups on smoking intensity. Enrolled participants will complete research visits at 4 weeks and 8 weeks (see Figure 1). Participants will receive financial compensation for their time spent completing research activities: $20 for each appointment (week 0,4,8) for a total of $60. Participants will earn a $20 bonus for attending the last visit (week 8) and returning the smartband and charger. These visits will take place remotely in which the participant will speak with our research staff by phone or video call, at the tobacco clinic, at our research office, or at a location that is convenient, such as a public place.

Figure 1. Study Timeline



Recruitment: We will recruit from the Yale Tobacco Treatment Service (TTS) and the Winchester chest clinic. These programs are a specialized outpatient services at Yale-New Haven Hospital that provides individual tobacco treatment to a large patient

population of current smokers. New patients referred to the TTS and Winchester chest clinic will be informed about the study and will be invited to set up a screening appointment if interested. To facilitate participant enrollment and retention, study procedures may take place in person or remotely (e.g., phone, secure video conference) when possible.

Screening Assessments: To screen for eligibility, participants will complete the following assessments including: 1) Smoking history to assess smoking quantity and frequency such as number of cigarettes per day and number of years smoked, 2) self-reported other tobacco and drug use for the past 30 days. Participants may also complete biochemical verification of smoking status, such as breath carbon monoxide (CO) measured in parts per million or cotinine measured in a small sample of urine or saliva.

Participants: Eligibility criteria include: (a) age 18 or older, (b) daily cigarette smoker, (c) seeking smoking cessation treatment at Yale TTS or Winchester chest clinic, (d) able to read and write in English, (d) owning a smartphone (smartphone ownership is estimated to be over 80% among adult smokers who are motivated to quit[12]). Exclusion criteria include: (a) unstable psychiatric/medical conditions (e.g., suicidal ideation, acute psychosis, dementia), (b) current use of other tobacco products assessed via self-report, (c) current daily use of combustible marijuana. We exclude participants who use other tobacco products or smoke marijuana because the smartband system is only validated to detect and respond to cigarette smoking. We exclude participants who are regular users of combustible marijuana because this can elevate expired breath carbon monoxide (CO) making CO an inaccurate measure to confirm cigarette smoking status.

Experimental Methods: Eligible participants will be randomized to one of two treatment conditions (ST vs. ST+). All participants will receive standard outpatient tobacco treatment (ST) at the Yale Tobacco Treatment Service (TTS) or Winchester chest clinic following clinical practice guidelines[13]. All patients receive up to 8 sessions of one-on-one counseling which focuses on setting a quit date within the first 2 weeks of treatment and discusses coping strategies and relapse prevention. Patients are encouraged to try smoking cessation pharmacotherapy and can obtain these medications over the counter or by prescription from the TTS or Winchester chest clinic. The experimental group (ST+) will receive standard care plus an adjunct treatment which involves wearing a smartband for the 8-week study and receiving real-time notifications as soon as smoking is detected with the embedded geospatial movement sensors in the smartband. There are multiple commercially available smartbands/smartwatches that are compatible with the real- time smoking monitoring system; for example, the Asus Zenwatch 2 pairs with the user's smartphone via Bluetooth connection. When smoking is detected, an alert is sent to the user through the band (vibration) and their smartphone app (alert) with a message indicating that smoking was just detected. The user can indicate yes/no if this smoking detection was accurate. Real-time smoking data is recorded for the user to review in their smartphone app and is available for the research team to view on a password-protected secure online dashboard. Data include only the timing and number of smoking events, labeled by subject ID. This real-time notification may disrupt the automaticity of smoking behavior and help bring awareness to smoking and related cues in the moment, which may enhance the individual's ability to anticipate and respond adaptively to cues in the future. The control group will also receive the smartband to wear for the 8 week study to control for demands associated with remembering to wear the band and charge it.

Measures: Baseline measures will be used to characterize the sample. Repeated measures will be used to assess changes in smoking and related constructs during treatment.

Demographic Questionnaires (week 0): Age, gender, marital status, employment status, occupation.

Smoking History (week 0): Smoking characteristics will be assessed, including the number of years of cigarette use, length of prior quit attempts, and prior treatments used.

Quitting Motivation and Confidence (week 0): Readiness to quit smoking and confidence quitting smoking will be measured on an 11-point scale (0=not at all, 10=extremely) using the contemplation ladder[14].

Discounting task (week 0): A brief computerized discounting task will be administered (5 questions each) to assess choice preference for cigarettes and money. Participants choose between a hypothetical smaller sooner reward or larger later reward, which is a validated measure of decision-making that has been shown to relate to treatment outcomes[15,16].

Timeline Follow-Back Interview (TLFB)[17,18] (week 0,4,8): A standardized, validated, and reliable interview will be used to obtain quantity and frequency estimates of tobacco use, alcohol, and other drugs for the 30-days prior to baseline and at each research visit.

Biochemical Verification of Smoking Status (week 0,4,8): Assessed when needed to confirm reported abstinence via either expired breath carbon monoxide (CO) levels, which have a half-life of 2 hours or cotinine measured in a small sample of urine or saliva.

Nicotine Dependence (week 0,8): Measured by the Fagerström Test for Nicotine Dependence[19] and the 4-item NIH PROMIS® measure for daily smokers[20].
Craving (week 0,4,8): Measured by the Questionnaire of Smoking Urges-Brief[21] (QSU-Brief).

Strength of Smoking Habit (week 0,4,8): Measured with a 6-item Self-Report Habit index adapted and validated for smoking behavior[22,23], e.g. “Smoking is something I do automatically” rated on a 5-point scale (1=strongly disagree, 5=strongly agree).

Perceived Control Over Smoking (week 0,4,8): Measured with 3 valid, reliable items rated on a 7-point scale[24] that have demonstrated associations with smoking outcome[25,26], e.g., “How much control do you feel you have over not smoking?” (1=no control, 7=complete control).

Approach-Avoidance Task (AAT) (week 0, 4, 8): An objective behavioral task that measures the tendency to automatically approach smoking stimuli (e.g., cigarettes). Our research team has used an adapted version of the approach-avoidance task (AAT[27]) to measure smoking approach and avoidance action tendencies[28-30]. The task starts with 20 practice trials in which participants learn to push or pull the joystick in response to picture format (landscape or portrait). The practice phase is followed by 160 test trials in which pictures of cigarette stimuli (e.g., cigarettes, cigarette packages) and non-cigarette stimuli (e.g., pencil) come equally in

push- or pull-format (this takes 5 to 10 minutes). Picture format (landscape or portrait) to response assignment (push or pull) is counterbalanced, with half the participants pulling landscape pictures and half portrait pictures. The smoking approach bias represents the relative difference between pushing and pulling the joystick in response to the smoking stimuli, measured as mean reaction time. Evidence supports reliable approach tendencies related to substance use and indicates that meaningful changes in automatic approach tendencies related to substance use outcomes can be detected after one week[27,28,31-35].

End of Treatment Ratings (week 8): We will evaluate participant satisfaction and perceived usefulness of the treatment across both conditions with post-treatment interviews and ratings.

Analytical Plan:

Data Management and Statistical Analyses: The proposed study will follow HIPAA guidelines for data collection, management, and monitoring. Data analyses will use the intention-to-treat (ITT) principle[36], where missing data will be treated as smoking. Data analyses will be conducted under the supervision of Dr. Gueorguieva who is a biostatistician. Data on quantitative outcomes will be examined for conformity to the normal distribution and transformation or non-parametric methods will be used if necessary.

Aim 1: Evaluate the feasibility, acceptability, and helpfulness of the real-time smoking intervention. We will use descriptive statistics to summarize participant ratings of satisfaction and perceived usefulness of the intervention at the end of treatment, including characterizing adherence and feasibility of using the smartband device based on self-report and objective adherence (i.e., number of days wearing the smartband).

Aim 2: Assess the preliminary efficacy of the real-time intervention as an adjunct to standard tobacco treatment. We will compare biochemically confirmed 7-day point prevalence abstinence at the end of treatment (i.e., reported abstinence from cigarettes during the last week of the study that is confirmed with CO≤ 4ppm or cotinine measured in a small sample of urine or saliva) to estimate effect sizes for ST+ vs. ST. We will also compare continuous outcome measures between ST+ and ST that are proximal indices of good clinical response: number of days abstinent and changes in cigarettes per smoking day from baseline to week 8. We will use independent sample t-tests to compare total days abstinent between ST+ and ST and a 2x2 mixed ANOVA (time x condition) to compare changes in cigarettes per smoking day from baseline to week 8.

5. Genetic Testing N/A ☒

A. Describe

i. the types of future research to be conducted using the materials, specifying if immortalization of cell lines, whole exome or genome sequencing, genome wide association studies, or animal studies are planned *Write here*

ii. the plan for the collection of material or the conditions under which material will be received *Write here*

iii. the types of information about the donor/individual contributors that will be entered into a database *Write here*

iv. the methods to uphold confidentiality *Write here*

B. What are the conditions or procedures for sharing of materials and/or distributing for future research projects? *Write here*

C. Is widespread sharing of materials planned? *Write here*

D. When and under what conditions will materials be stripped of all identifiers? *Write here*

E. Can donor-subjects withdraw their materials at any time, and/or withdraw the identifiers that connect them to their materials? *Write here*

i. How will requests to withdraw materials be handled (e.g., material no longer identified: that is, anonymized) or material destroyed)? *Write here*

F. Describe the provisions for protection of participant privacy *Write here*

G. Describe the methods for the security of storage and sharing of materials *Write here*

6. Subject Population: Provide a detailed description of the types of human subjects who will be recruited into this study.
   Write here

We will recruit current adult (at least 18 years old) daily smokers who are seeking smoking cessation treatment at Yale TTS or Winchester chest clinic. See detailed inclusion and exclusion criteria below (section 8).

7. Subject classification: Check off all classifications of subjects that will be specifically recruited for enrollment in the research project. Will subjects who may require additional safeguards or other considerations be enrolled in the study? If so, identify the population of subjects requiring special safeguards and provide a justification for their involvement.

☐Children	☐ Healthy	☐Fetal material, placenta, or dead fetus
☐Non-English Speaking	☐ Prisoners	☐Economically disadvantaged persons
☐Decisionally Impaired	☐ Employees	☐Pregnant women and/or fetuses
☐Yale Students	☐ Females of childbearing potential	

NOTE: Is this research proposal designed to enroll children who are wards of the state as potential subjects?

Yes ☐ No ☒

8. Inclusion/Exclusion Criteria: What are the criteria used to determine subject inclusion or exclusion?

Inclusion Criteria:
(a) age 18 or older
(b) daily cigarette smoker
(c) seeking smoking cessation treatment at Yale TTS or Winchester chest clinic
(d) able to read and write in English
(d) owning a smartphone

Exclusion Criteria:
(a) Unstable psychiatric/medical conditions (e.g., suicidal ideation, acute psychosis, dementia)
(b) Current use of other tobacco products or regular use of combustible marijuana assessed via self-report

How will eligibility be determined, and by whom? Write here

Patients who are referred to tobacco treatment at TTS or Winchester chest clinic who are interested in participating will be contacted by our research staff and will be provided with additional information about the project. Interested participants will be initially screened by telephone to assess age, smoking status, and to ensure they are currently seeking smoking cessation treatment. Participants who meet initial eligibility screening will be scheduled for an intake session either remotely or in person. During the intake session, participants will complete an informed consent form. Following this, a research assistant will obtain medical and substance use histories, and may collect breath CO levels or cotinine measured by a small sample of urine or saliva. If study criteria are met, the participant will be randomized and scheduled for the subsequent sessions.

9. **Risks:** Describe the reasonably foreseeable risks, including risks to subject privacy, discomforts, or inconveniences associated with subjects participating in the research.

We feel that this research poses minimal risks to adults who are seeking treatment to stop smoking.

We provide a detailed description of risks below.

Smoking Intervention Components: The smoking intervention components pose minimal risk. All participants will receive standard outpatient tobacco treatment (ST) at the Yale Tobacco Treatment Service (TTS) or Winchester chest clinic following clinical practice guidelines. Patients receive up to 8 sessions of one-on-one counseling with a trained tobacco treatment specialist which focuses on setting a quit date within the first 2 weeks of treatment and discusses coping strategies and relapse prevention. Participants can obtain smoking cessation pharmacotherapy over the counter or by prescription from the smoking cessation provider. Participants will meet routinely with their provider to discuss their medication use. Additionally, wearing the smartband to track smoking behavior poses minimal risk. This technology passively monitors smoking behavior through wrist and arm movements using sensors in the smartband. When smoking is detected, an alert is sent to the users in the experimental condition through the band (vibration) and their smartphone app (alert) with a message indicating that smoking was just detected. The user can indicate yes/no if this smoking detection was accurate. Real-time smoking data is recorded for the user to review in their smartphone app and is available for the research team to view on a password- protected secure online dashboard. Data include only the timing and number of smoking events, labeled by subject ID.

Interviews/Self-Report Questionnaires: These are all noninvasive and should add no risk. The major disadvantages are the time taken to complete them, and possible breach of confidentiality. We have done our best to make the assessment schedule in this study as brief as possible. Also, our past experience with these measures indicates that they are acceptable to subjects. Dr. Bold, a licensed clinical psychologist, will be available to meet with individuals and will provide staff with consultation should the need arise. Careful efforts aimed at maintaining confidentiality will be made, which are described below, and only participants' study numbers will be recorded on the forms themselves in order to protect confidentiality.

Breath, saliva and urine collections: Breath screening, saliva collections and urine collections should add no risks other than those normally associated with these procedures. Breath and

urine screens will be performed by appropriately trained research staff during the screening and research visits.

Loss of Confidentiality: Participants will be providing sensitive information, including their smoking and alcohol use behaviors. There are potential risks to subjects if such information were to be made public. Several procedures will help reduce the risk of disclosure of sensitive information, described in detail below.

Limits to Confidentiality: Participants will be informed that we will aim to protect their confidentiality and not reveal any personal information collected as part of the research procedures, including their reported smoking and other substance use history. All personnel to be involved in this study are already or will be certified by the Yale Human Investigation Committee (HIC) as having completed training in the protection of the rights of human subjects who participate in research. However, participants will be informed that if they report any information to us about child abuse or homicidal/suicidal behavior, we will be required to report this information to the appropriate authorities. These limits to confidentiality will be clearly stipulated in the consent form.

10. Minimizing Risks: Describe the manner in which the above-mentioned risks will be minimized.
Write here

A. Recruitment and Informed Consent

We will recruit individuals from the Yale Tobacco Treatment Service (TTS) and the Winchester chest clinic. Yale TTS is a specialized outpatient service at Yale-New Haven Hospital that provides individual tobacco treatment to a large patient population of current smokers. New patients referred to the TTS will be offered the opportunity to participate in the study via clinician referrals and will provide verbal consent to be contacted by research staff. Research staff will meet with interested participants for an intake visit either remotely or in person. At the start of the intake visit, consent to participate will be obtained from all participants after the research procedures and risks associated with participation have been explained. The entire consent form will be reviewed in detail with the participant in a private, one-on-one setting with a research staff member. The consent form will provide clear and explicit language about the smoking intervention components, smoking- monitoring procedures, and smartband use. Any questions the participant may have will be addressed. If participants wish, they may take the consent form home and consider it further before signing. They may also request to speak to anyone on the research team about questions they have or to consult others, including their physician and family members. Participants will sign 2 copies of the consent, retain one, and the researchers will keep the second copy on file. Participants will be informed that they are free to decline participation and withdraw from the study at any time and that neither action will adversely affect their relationship with any study personnel. Following resolution of any questions, the participant will be asked to sign the consent form, if he/she agrees to participate.

For remote intake visits, the approved informed consent form will be provided online via Qualtrics to subjects in advance of participation. Research staff will review the consent form by phone or video conference with the potential participant, and research staff will answer any questions regarding the study or consent form at this time. Subjects who wish to participate will click “I accept” and electronically sign the document by initialing the Qualtrics form. A copy of the consent form will be automatically emailed to the participant.

B. Protection Against Risk

The research team are trained regarding proper guidelines for ethical human research, and they will ensure that all research activities are in full compliance. All research subjects will be competent adults who willingly provide their written agreement to participate prior to research participation during a formal informed consent process. A copy of the signed consent form will be provided to all subjects. All participants will be assured that research participation is voluntary, and that even after enrollment, they are free to discontinue without penalty at any point during the study. The investigative team has decades of clinical research experience with human subjects, including conducting similar study procedures in individuals with nicotine dependence and other substance use disorders. Additional treatment referrals or continued support through the Tobacco Treatment Service will be made available to participants following study completion, as needed.

Specific protections against risks include:

1. All personnel to be involved in this study will be certified by the Yale Human Investigation Committee (HIC) as having completed training in the protection of the rights of human subjects who participate in research.
2. Effective screening will exclude all participants who would be at greater risk for complications from smoking interventions and/or study participation because of medical or specific psychiatric illnesses. Dr. Bold, a licensed clinical psychologist, will evaluate all potential participants for inclusion. If participants are not eligible for the study and/or request further assistance with quitting smoking once the study is completed, appropriate referrals will be provided.
3. Upon study enrollment, numerous safeguards will be used to monitor participants. Participants will be seen routinely during treatment by TTS staff and research team members. Dr. Bold will be available to meet with participants as needed and will provide participants with additional treatment referrals if they are interested. The TTS will be available to consult with participants and review medical concerns as needed. The TTS team consists of experts with decades of experience including: a licensed clinical psychologist who serves as the clinical director, a medical director, a pulmonologist, a team of advanced practice nurses, clinical psychology fellows, and administrative support staff.
4. Right to privacy and confidentiality for participation in this research will be protected through alphanumeric coding of data (in place of names) and proper storage of research records, including study exit interviews. Collected materials will be maintained via an alphanumeric reference system maintained by Dr. Bold. Participants' names will appear only on the consent form and a master list maintained in a physically locked file that is separate from research data. Our data collection and management procedures are fully compliant with HIPAA. Access will be limited to personnel intimately involved in the study. Participants will be informed of our efforts to maintain privacy and confidentiality. However, they will be told that if they present with suicidal or homicidal ideation and/or report any form of child/elder abuse or report plans to damage property then we will have to report this to the appropriate authorities and/or provide them with referrals for immediate treatment. Electronic data will be de-identified and password protected. Only members of the study team will have access to the physical or electronic data.

11. Data and Safety Monitoring Plan: Include an appropriate Data and Safety Monitoring Plan (DSMP) based on the investigator's risk assessment stated below. (Note: the HIC will make the final determination of the risk to subjects.)
    a. What is the investigator's assessment of the overall risk level for subjects participating in this study? Minimal risk
    b. If children are involved, what is the investigator's assessment of the overall risk level for the children participating in this study? N/A
    c. Include an appropriate Data and Safety Monitoring Plan. Examples of DSMPs are available here http://your.yale.edu/policies-procedures/forms/420-fr-01-data-and-safety-monitoring-plans-templates for
        i. Minimal risk
        ii. Greater than minimal

Dr. Bold, the PI, will be responsible for monitoring the data, assuring protocol compliance, and conducting the safety reviews at the specified frequency that must be conducted at a minimum of every 6 months (including when reapproval of the protocol is sought). During the review process, Dr. Bold (i.e., the study monitor) will evaluate with key personnel whether the study should continue unchanged, require modification or amendment, continue or close to enrollment. Dr. Bold, the Yale University IRB, and the funding agency have the authority to stop or suspend the study or require modifications.

Although we have assessed the proposed study as one of minimal risk, the potential exists for anticipated and/or unanticipated adverse events, serious or otherwise, to occur since it is not possible to predict with certainty the absolute risk in any given individual or in advance of first-hand experience with the proposed study methods. Therefore, we provide a plan for monitoring the data and safety of the proposed study.

Dr. Bold will reduce the potential for risks by being part of the screening process of all participants and reviewing eligibility criteria to rule out participants whose clinical characteristics would be adversely affected by the smoking interventions and/or participation in the research study. Frequent in-person or remote assessment and ongoing visits with treatment staff at the TTS and Winchester chest clinic will allow for close regular monitoring of participants. Research staff will check participants' data sources for clinically significant changes and alert Dr. Bold and the TTS/Winchester team as needed.

Attribution of Adverse Events:
Adverse events will be monitored for each individual participating in the study and attributed to the study procedures/design by Dr. Bold, the PI, in collaboration with key personnel according to the following categories:

1. Definite: Adverse event is clearly related to investigational procedures(s)/agent(s).
2. Probable: Adverse event is likely related to investigational procedures(s)/agent(s).
3. Possible: Adverse event may be related to investigational procedures(s)/agent(s).
4. Unlikely: Adverse event is likely not to be related to the investigational procedures(s)/agent(s).
5. Unrelated: Adverse event is clearly not related to investigational procedure(s)/agent(s).

Plan for Grading Adverse Events:
The following scale will be used in grading the severity of adverse events noted during the

study:

1. Mild adverse event
2. Moderate adverse event
3. Severe

Plan for Determining Seriousness of Adverse Events: In addition to grading the adverse event, Dr. Bold, the PI will determine with key personnel whether the adverse event meets the criteria for a Serious Adverse Event (SAE). An adverse event is considered serious if it:

1. is life-threatening
2. results in in-patient hospitalization or prolongation of existing hospitalization
3. results in persistent or significant disability or incapacity
4. results in a congenital anomaly or birth defect OR
5. results in death
6. based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition, OR
7. adversely affects the risk/benefit ratio of the study

An adverse event may be graded as severe but still not meet the criteria for a Serious Adverse Event. Similarly, an adverse event may be graded as moderate but still meet the criteria for an SAE. Dr. Bold, the PI, will consider the grade of the event as well as its "seriousness" when determining whether the event meets criteria for an SAE and requires a report to the Yale University IRB or funding agency.

Adverse Event Reporting:
Every event that is reported by participants to either Dr. Bold, the PI, or the designated research staff and that meets criteria above will be documented. Dr. Bold will report serious adverse events and unanticipated problems to the Yale University IRB within 5 days of it becoming known using the required documentation. An adverse event report will be generated for each event and will include details of the event in the report (e.g., description of the event, when and how it was reported, as well as any official records or documentation to corroborate the event; determination of attribution). Any action resulting in a temporary or permanent suspension of this study (e.g., IRB actions, or actions by the investigators) will be immediately reported to the funding agency. Dr. Bold, the PI, will conduct a review of all adverse events upon completion of every study participant with key personnel. Dr. Bold will evaluate the frequency and severity of the adverse events with key personnel and determine if modifications to the protocol or consent form are required or if a stop in protocol is required. Dr. Bold will submit an annual report summarizing all adverse events.

Safety and Study Progress Reviews:
Dr. Bold will lead a weekly research meeting with key personnel to review the status of all enrolled participants and discuss the eligibility of potential participants. At this weekly meeting, Dr. Bold will review study progress (i.e., recruitment goals, retention, protocol adherence). Any adverse events will be reviewed at this meeting, including serious adverse events that may have been attended to outside of this weekly meeting. An annual progress

report will be submitted to Yale University IRB and the funding agency that lists and summarizes adverse events, documents whether adverse event rates are consistent with pre-study assumptions, summarizes recruitment and retention and reason for dropouts, and summarizes study progress related to the stated aims.

Data Quality and Management:
Dr. Bold will supervise and train the Research Assistant and all key personnel on study procedures to ensure that all procedures are followed and are in compliance with the approved Yale University IRB protocol. Dr. Bold will also provide training and oversight to study staff to ensure data are generated, documented, and reported according to requirements by the Yale University IRB and the funding source. The Biostatistician, Dr. Gueorguieva, will also oversee quality assurance of data.

d. For multi-site studies for which the Yale PI serves as the lead investigator:
   i. How will adverse events and unanticipated problems involving risks to subjects or others be reported, reviewed and managed? *Write here*
   ii. What provisions are in place for management of interim results? *Write here*
   iii. What will the multi-site process be for protocol modifications? *Write here*

12. Statistical Considerations: Describe the statistical analyses that support the study design.
Write here

Aim 1: Evaluate the feasibility, acceptability, and helpfulness of the real-time smoking intervention. We will use descriptive statistics to summarize participant ratings of satisfaction and perceived usefulness of the intervention at the end of treatment, including characterizing adherence and feasibility of using the smartband device based on self-report and objective adherence (i.e., number of days wearing the smartband).

Aim 2: Assess the preliminary efficacy of the real-time intervention as an adjunct to standard tobacco treatment. We will compare biochemically confirmed 7-day point prevalence abstinence at the end of treatment (i.e., reported abstinence from cigarettes during the last week of the study that is confirmed with CO≤ 4ppm) to estimate effect sizes for ST+ vs. ST. We will also compare continuous outcome measures between ST+ and ST that are proximal indices of good clinical response: number of days abstinent and changes in cigarettes per smoking day from baseline to week 8. We will use independent sample t-tests to compare total days abstinent between ST+ and ST and a 2x2 mixed ANOVA (time x condition) to compare changes in cigarettes per smoking day from baseline to week 8.

Sample Size Justification & Power Calculation: This study is a developmental project testing the feasibility and potential efficacy of adding a novel intervention to enhance standard smoking cessation treatment. Sample size for the current study is based on guidelines for Stage 1 treatment development studies that suggest a minimum of 15 participants per experimental arm to obtain a reliable effect size estimate[37]. Our target sample (25 per group) is sufficient to determine preliminary efficacy and estimate effect sizes for the binary cessation outcome, 7-day point prevalence abstinence at the end of treatment. This sample size produces two-sided 95% confidence intervals for the difference in population proportions with a half-width that is equal to 22%-24% when the difference in abstinence rates between groups (ST+ vs. ST) in estimated sample proportions is 10%-15% (e.g., 25% vs. 15%, 30% vs. 15%,

35% vs. 20%). For the continuous smoking outcomes, based on power=.80 and two-tailed alpha=.05, we can detect a statistically significant difference between groups of 4 days abstinent (SD=5) and a difference of 6 cigarettes per smoking day (SD=8) between baseline and end of treatment by group.

SECTION II: RESEARCH INVOLVING DRUGS, BIOLOGICS, RADIOTRACERS, PLACEBOS AND DEVICES

If this section (or one of its parts, A or B) is not applicable, check off N/A and delete the rest of the section.

A. RADIOTRACERS ☒N/A
B. DRUGS/BIOLOGICS ☒N/A
C. DEVICES ☒N/A

SECTION III: RECRUITMENT/CONSENT AND ASSENT PROCEDURES

1. Targeted Enrollment: Give the number of subjects:
   a. Targeted for enrollment at Yale for this protocol: 50 adults
   b. If this is a multi-site study, give the total number of subjects targeted across all sites: N/A

2. Indicate recruitment methods below. Attach copies of any recruitment materials that will be used.

☒ Flyers	☐ Internet/web postings	☐ Radio
☐ Posters	☐ Mass email solicitation	☐ Telephone
☐ Letter	☐ Departmental/Center website	☐ Television
☐ Medical record review*	☐ Departmental/Center research boards	☐ Newspaper
☐ Departmental/Center newsletters	☐ Web-based clinical trial registries	☒ Clinicaltrails.gov
☐ YCCI Recruitment database	☐ Social Media (Twitter/Facebook):	
☒ Other: Referral from Yale TTS		

* Requests for medical records should be made through JDAT as described at
http://medicine.yale.edu/ycci/oncore/availableservices/datarequests/datarequests.aspx

3. Recruitment Procedures:

a. Describe how potential subjects will be identified. We will recruit individuals from the Yale Tobacco Treatment Service (TTS) and the Winchester chest clinic. Yale TTS is a specialized outpatient service at Yale-New Haven Hospital that provides individual tobacco treatment to a large patient population of current smokers. New patients referred to the TTS or Winchester will be informed about the research study by their clinician or the administrative staff who schedules their appointments. Interested patients will provide verbal consent to be contacted by research staff.

b. Describe how potential subjects are contacted. Research staff will first contact interested participants by phone to complete initial screening. If participants meet initial eligibility criteria, they will be scheduled for an intake visit. At the start of the intake visit, consent to participate will be obtained from all participants after the research procedures and risks associated with participation have been explained.

c. Who is recruiting potential subjects? The PI and research staff will recruit potential subjects.

HIC# 2000024740

4. Assessment of Current Health Provider Relationship for HIPAA Consideration:
Does the Investigator or any member of the research team have a direct existing clinical relationship with any potential subject?

☐ Yes, all subjects

☒ Yes, some of the subjects

☐ No

If yes, describe the nature of this relationship. We will recruit patients who are receiving tobacco treatment from the Yale TTS service and the Winchester chest clinic so we will be collaborating with their clinical providers (e.g., APRN tobacco treatment specialists, clinical pharmacists) and the administrative staff who schedules appointments and manages referrals for tobacco treatment. The tobacco treatment providers will be providing clinical services to each patient in addition to being part of the research team. Participation in the study is completely voluntary and does not impact the patient relationships with the tobacco counselors or their other healthcare providers. This is outlined in detail in the consent form.

5. Request for waiver of HIPAA authorization: (When requesting a waiver of HIPAA Authorization for either the entire study, or for recruitment purposes only. Note: if you are collecting PHI as part of a phone or email screen, you must request a HIPAA waiver for recruitment purposes.)
Choose one:

☐ For entire study

☒ For recruitment/screening purposes only

☐ For inclusion of non-English speaking subject if short form is being used and there is no translated HIPAA research authorization form available on the University's HIPAA website at hipaa.yale.edu.

i. Describe why it would be impracticable to obtain the subject's authorization for use/disclosure of this data: *Write here*

ii. If requesting a waiver of signed authorization, describe why it would be impracticable to obtain the subject's signed authorization for use/disclosure of this data: We request a waiver of signed authorization only for initial participant recruitment/screening purposes to obtain interested participants' phone numbers and/or email for voice and text communication to make initial contact with the research team. At the first phone contact with the research team, participants will provide verbal consent for the screening process. If participants prefer to complete the online screener through the Yale Qualtrics system, participants will indicate their consent to be screened by answering questions in the online screening survey.

The investigator assures that the protected health information for which a Waiver of Authorization has been requested will not be reused or disclosed to any person or entity other than those listed in this application, except as required by law, for authorized oversight of this research study, or as specifically approved for use in another study by an IRB.

Researchers are reminded that unauthorized disclosures of PHI to individuals outside of the Yale HIPAA-Covered entity must be accounted for in the "accounting for disclosures log", by subject name, purpose, date, recipients, and a description of information provided. Logs are to be forwarded to the Deputy HIPAA Privacy Officer.

6. Process of Consent/Assent: Describe the setting and conditions under which consent/assent will be obtained, including parental permission or surrogate permission and the steps taken to ensure subjects' independent decision-making.

   The entire consent form will be reviewed in detail with the participant in a private, one-on-one setting with a research staff member. The consent form will provide clear and explicit language about the smoking intervention components, smoking-monitoring procedures, and smartband use. Any questions the participant may have will be addressed. If participants wish, they may take the consent form home and consider it further before signing. They may also request to speak to anyone on the research team about questions they have or to consult others, including their physician and family members. Participants will sign 2 copies of the consent, retain one, and the researchers will keep the second copy on file. Participants will be informed that they are free to decline participation and withdraw from the study at any time and that neither action will adversely affect their relationship with any study personnel. Following resolution of any questions, the participant will be asked to sign the consent form, if he/she agrees to participate. For remote intake visits, the approved informed consent form will be provided online via Qualtrics to subjects in advance of participation. Research staff will review the consent form by phone or video conference with the potential participant, and research staff will answer any questions regarding the study or consent form at this time. Subjects who wish to participate will click "I accept" and electronically sign the document by initialing the Qualtrics form. A copy of the consent form will be automatically emailed to the participant.

7. Evaluation of Subject(s) Capacity to Provide Informed Consent/Assent: Indicate how the personnel obtaining consent will assess the potential subject's ability and capacity to consent to the research being proposed.
   We will not be enrolling participants with limited decision-making capacity. We plan to exclude individuals with current serious psychiatric or medical illnesses. During the consenting process, the research assistant will read and review the consent form with the prospective participant. The research assistant will then ask the potential participant various questions about the consent form and study protocol to ensure the prospective participant sufficiently understands the study and the nature of their consent to participate.

8. Non-English Speaking Subjects: Explain provisions in place to ensure comprehension for research involving non-English speaking subjects. If enrollment of these subjects is anticipated, translated copies of all consent materials must be submitted for approval prior to use.
   N/A

As a limited alternative to the above requirement, will you use the short form* for consenting process if you unexpectedly encounter a non-English speaking individual interested in study participation and the translation of the long form is not possible prior to intended enrollment? YES ☐ NO ☒

Note* If more than 2 study participants are enrolled using a short form translated into the same language, then the full consent form should be translated into that language for use the next time a subject speaking that language is to be enrolled.

Several translated short form templates are available on the HRPP website (yale.edu/hrpp) and translated HIPAA Research Authorization Forms are available on the HIPAA website (hipaa.yale.edu). If the translation of the short form is not available on our website, then the translated short form needs to be submitted to the IRB office for approval via modification prior to enrolling the subject. ***Please review the guidance and presentation on use of the short form available on the HRPP website.***

If using a short form without a translated HIPAA Research Authorization Form, please request a HIPAA waiver in the section above.

9. Consent Waiver: In certain circumstances, the HIC may grant a waiver of signed consent, or a full waiver of consent, depending on the study. If you will request either a waiver of consent, or a waiver of signed consent for this study, complete the appropriate section below.

☐Not Requesting any consent waivers

☒Requesting a waiver of signed consent:

☒ Recruitment/Screening only *(if for recruitment, the questions in the box below will apply to recruitment activities only)*

☐ Entire Study (Note that an information sheet may be required.)

For a waiver of signed consent, address the following:

- Would the signed consent form be the only record linking the subject and the research? YES ☐ NO ☒
- Does a breach of confidentiality constitute the principal risk to subjects? YES ☐ NO ☒

OR

- Does the research pose greater than minimal risk? YES ☐ NO☒
- Does the research include any activities that would require signed consent in a non-research context? YES ☐ NO ☒

☐ Requesting a waiver of consent:

☐ Recruitment/Screening only *(if for recruitment, the questions in the box below will apply to recruitment activities only)*

☐ Entire Study

For a full waiver of consent, please address all of the following:

SECTION IV: PROTECTION OF RESEARCH SUBJECTS

☐ Yes ***If you answered yes, stop. A waiver cannot be granted.***

☐ No

- Will the waiver adversely affect subjects' rights and welfare? YES ☐ NO☐
- Why would the research be impracticable to conduct without the waiver?
- Where appropriate, how will pertinent information be returned to, or shared with subjects at a later date?

Confidentiality & Security of Data:

1. What protected health information (medical information along with the HIPAA identifiers) about subjects will be collected and used for the research? We will collect names and demographic information. Identifiable information will be collected and used to enroll, treat, and contact participants. It will only be used for this purpose. This information will be stored in locked cabinet apart from the research records. Given that this trial involves adding an intervention to the clinical care of the Tobacco Treatment Service at Smilow Cancer Hospital or Winchester Chest Clinic, all participants will have a medical record as part of their clinical care. The medical records are in an electronic format on a secure server apart from the paper research records. Additional medical information collected for research will be recorded only with the subject ID number.

   This includes information on smoking status, smoking cessation medication used during the study,

and the schedule of visits with the tobacco treatment clinical team.

2. How will the research data be collected, recorded and stored? Research data will be collected using in-person interviews, survey assessments, objective measures of smoking behavior (via the smartband), and self-reports. All identifiable information (names and demographic information) will be stored in a locked file cabinet. All participants will be assigned a study participant ID made up of numbers and letters. Subsequently, participants will be identified in the Case Report Forms (CRFs) only by that number (e.g., CM24). A list of IDs and the corresponding names will be maintained by the Principal Investigator and stored in a locked research cabinet. All other research data (interviews, survey assessments, objective measures of smoking behavior, and self-reports) will not contain identifiable information and will be labeled only with the subjects' unique numerical indicator. The smoking data captured from the smartband includes the time and date of smoking episodes. These data are available for the research team on a password-protected secure online dashboard.

3. How will the digital data be stored? ☐CD ☐DVD ☐Flash Drive ☐Portable Hard Drive ☒Secured Server ☒Laptop Computer ☒Desktop Computer ☐Other
Digital data with PHI will be stored on a secured server. Digital data without PHI may be stored and analyzed on a laptop or desktop computer.

What methods and procedures will be used to safeguard the confidentiality and security of the identifiable study data and the storage media indicated above during and after the subject's participation in the study? Several steps will be taken to safeguard the confidentiality of subjects and their data. Right to privacy for participation in this research will be protected through coding of data and proper storage of research records. All research data that is collected will be assigned a study participant number and that number will be the only link between participant names/identifying information and the digital databases. The names of participants will not be associated with these data and assessments will be maintained according to participant study number. A master list connecting participant study numbers to participant names will be kept in a locked file cabinet where it can only be accessed by senior level project staff. Any information published as a result of the study will be in aggregate and such that it will not permit identification of any participant.

We are not directly assessing incidents of child abuse or elderly abuse. However, if this information is disclosed by a participant or volunteer in the context of this research, a report will be made to the Department of Child and Families Services or other agency as required by law. Subjects will be informed of this limit to confidentiality as it is stated in the informed consent document.

All investigators and key personnel have taken the required Yale University HIPAA training. Right to privacy for participation in this research will be protected through coding of data and proper storage of research records. A list of numbers and the corresponding names will be maintained by the Principal Investigator in a locked research cabinet.

Individually identifiable health information will be protected in accordance with the Health Insurance Portability and Accountability Act of 1996 and by additional protections of substance abuse treatment records afforded under Code of Federal Regulations (CFR) Part 2, Subpart E. All research personnel will be trained on human subjects protection and HIPAA procedures.

All portable devices must contain encryption software, per University Policy 5100. If there is a technical reason a device cannot be encrypted please submit an exception request to the Information Security, Policy and Compliance Office by clicking on url http://its.yale.edu/egrc or email it.compliance@yale.edu

4. What will be done with the data when the research is completed? Are there plans to destroy the identifiable

data? If yes, describe how, by whom and when identifiers will be destroyed. If no, describe how the data and/or identifiers will be secured. The data will be stored in a locked room for 7 years after the final data is collected. After this point, the Data Manager and Principal Investigator will oversee the process in which data is destroyed or de-identified.

5. If appropriate, has a Certificate of Confidentiality been obtained? A certificate will not be requested.

SECTION V: POTENTIAL

Potential Benefits: Identify any benefits that may be reasonably expected to result from the research, either to the subject(s) or to society at large. (Payment of subjects is not considered a benefit in this context of the risk benefit assessment.)

All participants in this study will receive standard care evidence-based treatment for smoking cessation. Half of the participants will also receive real-time feedback about smoking behavior while quitting that may increase awareness of smoking behavior and help promote abstinence during their smoking quit attempt. All participants will be provided compensation for their participation in research procedures. This research has the potential to benefit other smokers who are trying to quit in the future. There is a need to improve smoking treatment because most quit attempts are unsuccessful. The purpose of this study is to test an innovative smoking intervention that may help improve cessation success. Improving smoking cessation outcomes could reduce the substantial harms and healthcare costs associated with smoking.

Importance of knowledge to be gained: Cigarette smoking is the leading cause of preventable death. Promoting smoking cessation could greatly improve public health. Most quit attempts are unsuccessful, suggesting innovations are needed in the way we deliver treatment. This study is designed to test whether a novel technology-based intervention that delivers real-time notifications when smoking is detected promotes cessation success above and beyond standard tobacco treatment. Identifying effective technology-based interventions could provide a novel way to enhance the reach of tobacco treatment and provide additional support to patients flexibly, conveniently, and remotely.

SECTION VI: RESEARCH ALTERNATIVES AND ECONOMIC CONSIDERATIONS

1. Alternatives: What other alternatives are available to the study subjects outside of the research?
   All participants will be receiving tobacco treatment from TTS at YNHH or the Winchester chest clinic. Alternatives to study participation include continuing standard TTS treatment or seeking alternative smoking treatment through an external program.

2. Payments for Participation (Economic Considerations): Describe any payments that will be made to subjects, the amount and schedule of payments, and the conditions for receiving this compensation.
   Participants will receive financial compensation for their time spent completing research activities: $20 for each appointment (week 0,4,8) for a total of $60. Participants will earn a $20 bonus for completing the last visit (week 8) and returning the smartband and charger. Participants will be paid using a Bank of America pre-paid debit card. We will have to share participant name, address, and telephone number with Bank of America for ePayments and this information is communicated in the consent form. The participant will receive a card in the mail with the first payment. Each additional payment will be automatically added to the card.
3. Costs for Participation (Economic Considerations): Clearly describe the subject's costs associated with participation in the research, and the interventions or procedures of the study that will be provided at no cost to subjects.

There are no costs for participating in the research study.

4. In Case of Injury: This section is required for any research involving more than minimal risk, and for minimal risk research that presents the potential for physical harm (e.g., research involving blood draws).
   N/A
   a. Will medical treatment be available if research-related injury occurs? *Write here*
   b. Where and from whom may treatment be obtained? *Write here*
   c. Are there any limits to the treatment being provided? *Write here*
   d. Who will pay for this treatment? *Write here*
   e. How will the medical treatment be accessed by subjects? *Write here*

IMPORTANT REMINDERS

Will this study have a billable service? Yes ☐ No☒

A billable service is defined as any service rendered to a study subject that, if he/she was not on a study, would normally generate a bill from either Yale-New Haven Hospital or Yale Medical Group to the patient or the patient's insurer. The service may or may not be performed by the research staff on your study, but may be provided by professionals within either Yale-New Haven Hospital or Yale Medical Group (examples include x-rays, MRIs, CT scans, specimens sent to central labs, or specimens sent to pathology). Notes: 1. There is no distinction made whether the service is paid for by the subject or their insurance (Standard of Care) or by the study's funding mechanism (Research Sponsored). 2. This generally includes new services or orders placed in EPIC for research subjects.

If answered, "yes", this study will need to be set up in OnCore, Yale's clinical research management system, for Epic to appropriately route research related charges. Please contact oncore.support@yale.edu

Are there any procedures involved in this protocol that will be performed at YNHH or one of its affiliated entities?
Yes ☐ No ☒

If Yes, please answer questions a through c and note instructions below.
a. Does your YNHH privilege delineation currently include the specific procedure that you will perform? Yes ☐ No ☐

b. Will you be using any new equipment or equipment that you have not used in the past for this procedure? Yes ☐ No ☐

c. Will a novel approach using existing equipment be applied? Yes ☐ No ☐

If you answered “no” to question 4a, or "yes" to question 4b or c, please contact the YNHH Department of Physician Services (688-2615) for prior approval before commencing with your research protocol.

IMPORTANT REMINDER ABOUT RESEARCH AT YNHH

Please note that if this protocol includes Yale-New Haven Hospital patients, including patients at the HRU, the Principal Investigator and any co-investigators who are physicians or mid-level practitioners (includes PAs, APRNs, psychologists and speech pathologists) who may have direct patient contact with patients on YNHH premises must have medical staff appointment and appropriate clinical privileges at YNHH. If you are uncertain whether the study personnel meet the criteria, please telephone the Physician Services Department at 203-688-2615. By submitting this protocol as a PI, you attest that you and any co-investigator who may have patient contact has a medical staff appointment and appropriate clinical privileges at YNHH.

References

1. USDHHS. The health consequences of smoking—50 years of progress: a report of the Surgeon General. Atlanta, GA: US 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;17.

2. CDC. Quitting Smoking Among Adults—United States, 2000–2015. MMWR. Morbidity and mortality weekly report. 2017;65(52):1457-1464.

3. Hughes J, Keely J, Naud S. Shape of the relapse curve and long-term abstinence among untreated smokers. Addiction. 2004;99:29 - 38.

4. Borland R, Partos TR, Yong HH, Cummings KM, Hyland A. How much unsuccessful quitting activity is going on among adult smokers? Data from the International Tobacco Control Four Country cohort survey. Addiction. 2012;107(3):673-682.

5. Whittaker R, McRobbie H, Bullen C, Borland R, Rodgers A, Gu Y. Mobile phone-based interventions for smoking cessation. Cochrane Database of Systematic Reviews. 2016;4.

6. Ybarra ML, Jiang Y, Free C, Abroms LC, Whittaker R. Participant-level meta-analysis of mobile phone-based interventions for smoking cessation across different countries. Prev Med. 2016;89:90-97.

7. Naughton F. Delivering "Just-In-Time" smoking cessation support via mobile phones: Current knowledge and future directions. Nic Tob Res. 2017;19(3):379-383.

8. Dar R. Effect of real-time monitoring and notification of smoking episodes on smoking reduction: A pilot study of a novel smoking cessation app. Nic Tob Res. 2017.

9. Tiffany ST. A cognitive model of drug urges and drug-use behavior: role of automatic and nonautomatic processes. Psychological review. 1990;97(2):147.

10. Orbell S, Verplanken B. The automatic component of habit in health behavior: Habit as cue-contingent automaticity. Health Psychol. 2010;29(4):374.

11. Hunt WA, Matarazzo JD, Weiss SM, Gentry WD. Associative learning, habit, and health behavior. Journal of Behavioral Medicine. 1979;2(2):111-124.

12. Borrelli B, Bartlett YK, Tooley E, Armitage CJ, Wearden A. Prevalence and frequency of mHealth and eHealth use among US and UK smokers and differences by motivation to quit. Journal of medical Internet research. 2015;17(7).

13. Fiore MC, Jaen CR, Baker TB, et al. Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline. Rockville, MD: U.S. Department of Health and Human Services. Public Health Service; 2008.

14. Biener L, Abrams DB. The Contemplation Ladder: validation of a measure of readiness to consider smoking cessation. Health Psychol. 1991;10(5):360-365.

15. Koffarnus MN, Bickel WK. A 5-trial adjusting delay discounting task: Accurate discount rates in less than one minute. Exp Clin Psychopharmacol. 2014;22(3):222.

16. Bickel WK, Johnson MW, Koffarnus MN, MacKillop J, Murphy JG. The behavioral economics of substance use disorders: reinforcement pathologies and their repair. Annual review of clinical psychology. 2014;10:641-677.

17. Sobell L, Sobell M. Alcohol consumption measures. In: Allen J, Columbus M. Assessing alcohol problems: A guide for clinicians and researcher. Bethesda, MD: National Institute on Alcohol Abuse & Alcoholism; 1995.

18. Sobell L, Sobell M. Alcohol consumption measures. In: B. JPAaV, Wilson. Assessing alcohol problems: A guide for clinicians and researchers. Bethesda, MD: National Institute on Alcohol Abuse & Alcoholism; 2003.

19. Heatherton TF, Kozlowski LT, Frecker RC, Fagerstrom KO. The Fagerstrom Test for Nicotine Dependence: a revision of the Fagerstrom Tolerance Questionnaire. Br J Addict. 1991;86(9):1119-1127.

20. Shadel WG, Edelen MO, Tucker JS, Stucky BD, Hansen M, Cai L. Development of the PrOMis® nicotine Dependence item Banks. Nic Tob Res. 2014;16(Suppl3):S190-S201.

21. Cox LS, Tiffany ST, Christen AG. Evaluation of the brief questionnaire of smoking urges (QSU-brief) in laboratory and clinical settings. Nicotine Tob Res. 2001;3(1):7-16.

22. Verplanken B, Orbell S. Reflections on Past Behavior: A Self-Report Index of Habit Strength1. Journal of Applied Social Psychology. 2003;33(6):1313-1330.

23. Morean ME, DeMartini KS, Foster D, et al. The self-report habit index: Assessing habitual marijuana, alcohol, e-cigarette, and cigarette use. Drug Alcohol Depend. 2018.

24. Ajzen I. Perceived behavioral control, self-efficacy, locus of control, and the theory of planned behavior. Journal of applied social psychology. 2002;32(4):665-683.

25. Godin G, Valois P, Lepage L, Desharnais R. Predictors of smoking behaviour: an application of Ajzen's theory of planned behaviour. Addiction. 1992;87(9):1335-1343.

26. Norman P, Conner M, Bell R. The theory of planned behavior and smoking cessation. Health Psychol. 1999;18(1):89.

27. Wiers R, Rinck M, Dictus M, Van den Wildenberg E. Relatively strong automatic appetitive action-tendencies in male carriers of the OPRM1 G-allele. Genes, Brain and Behavior. 2009;8(1):101-106.

28. Kong G, Larsen H, Cavallo DA, et al. Re-training automatic action tendencies to approach cigarettes among adolescent smokers: a pilot study. The American journal of drug and alcohol abuse. 2015;41(5):425-432.

29. Larsen H, Kong G, Becker D, et al. Implicit motivational processes underlying smoking in American and Dutch adolescents. Frontiers in psychiatry. 2014;5.

30. Weckler H, Kong G, Larsen H, Cousijn J, Wiers RW, Krishnan-Sarin S. Impulsivity and approach tendencies towards cigarette stimuli: Implications for cigarette smoking and cessation behaviors among youth. Exp Clin Psychopharmacol. 2017;25(5):363.

31. Wiers CE, Kühn S, Javadi AH, et al. Automatic approach bias towards smoking cues is present in smokers but not in ex-smokers. Psychopharmacology. 2013;229(1):187-197.

32. Cousijn J, Goudriaan AE, Wiers RW. Reaching out towards cannabis: approach-bias in heavy cannabis users predicts changes in cannabis use. Addiction. 2011;106(9):1667-1674.

33. Wittekind CE, Feist A, Schneider BC, Moritz S, Fritzsche A. The approach-avoidance task as an online intervention in cigarette smoking: a pilot study. Journal of behavior therapy and experimental psychiatry. 2015;46:115-120.

34. Wiers RW, Eberl C, Rinck M, Becker ES, Lindenmeyer J. Retraining automatic action tendencies changes alcoholic patients' approach bias for alcohol and improves treatment outcome. Psychological science. 2011;22(4):490-497.

35. Eberl C, Wiers RW, Pawelczack S, Rinck M, Becker ES, Lindenmeyer J. Approach bias modification in alcohol dependence: do clinical effects replicate and for whom does it work best? Developmental cognitive neuroscience. 2013;4:38-51.

36. West R, Hajek P, Stead L, Stapleton J. Outcome criteria in smoking cessation trials: proposal for a common standard. Addiction. 2005;100(3):299-303.

37. Rounsaville BJ, Carroll KM, Onken LS. A stage model of behavioral therapies research: Getting started and moving on from stage I. Clinical Psychology: Science and Practice. 2001;8(2):133-142.