

# Study Protocol and Statistical Analysis Plan

Title	Randomized Pilot Study of a mHealth App for Ambivalent Smokers Living With HIV
Principal Investigator	Jennifer McClure, PhD Director of Investigative Science Kaiser Permanente Washington Health Research Institute Seattle, WA
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## **LIST OF ABBREVIATIONS**

ADL	Activities of Daily Living
AE	Adverse Event/Adverse Experience
AIDS	Acquired Immunodeficiency Syndrome
CFR	Code of Federal Regulations
DSMB	Data and Safety Monitoring Board
HIPAA	Health Insurance Portability and Accountability Act
HIV	Human Immunodeficiency Virus
ICH	International Conference on Harmonization
IRB	Institutional Review Board
KPWA	Kaiser Permanente Washington
KPWHRI	Kaiser Permanente Washington Health Research Institute
MOP	Manual of Procedures
NCI	National Cancer Institute
NIH	National Institutes of Health
NRT	Nicotine Replacement Therapy
OHRP	Office for Human Research Protections
OTC	Over the Counter
PAQS	People Ambivalent About Quitting Smoking
PAQS-HIV	Smokers Living with HIV who are Ambivalent About Quitting
PHS	Division of Public Health Services
SAE	Serious Adverse Event/Serious Adverse Experience
SLWH	Smokers Living with HIV
UP	Unanticipated Problem

### PROTOCOL SUMMARY

<b>Title</b>	<i>Randomized Pilot Study of a mHealth App for Ambivalent Smokers Living With HIV</i>
<b>Objective</b>	Conduct a randomized pilot to assess the feasibility and acceptability of a novel mHealth app designed for smokers who are ambivalent about quitting smoking and have been diagnosed with HIV.
<b>Outcomes of Interest</b>	Our primary outcome of interest is app utilization. Secondary outcomes include a range of measures to evaluate the program's feasibility (e.g., ability to recruit participants), acceptability (e.g., utilization of component features, indices of satisfaction and helpfulness), impact on cognitive mediators of change (e.g., self-efficacy, motivation), impact on smoking behavior change (quit attempts, smoking reduction, and abstinence), and use of provided smoking cessation treatments.
<b>Population</b>	Adult smokers living with HIV who are not interested in quitting smoking in the next month and meet other eligibility criteria. Up to 50 participants will be enrolled.
<b>Number of Sites</b>	This pilot study includes 1 site (KPWHRI).
<b>Description of Intervention</b>	The experimental app blends sound scientific theory, evidence-based treatment, and best practice treatment for nicotine dependence with additional content designed for people ambivalent about quitting smoking (PAQS) and people living with HIV.
<b>Subject Participation Duration</b>	Each participant will be enrolled for a period of ~3 months.

## **1 INTRODUCTION: BACKGROUND INFORMATION AND SCIENTIFIC RATIONALE**

### **1.1 Background Information**

Smoking is a leading cause of death and illness, but it has particularly deleterious health effects among smokers living with HIV (SLWH). More people living with HIV who smoke will die from tobacco related disease than from HIV. While many SLWH want to quit someday, the majority are not ready to quit in the near term. Therefore, interventions are needed that can motivate and support smoking cessation among SLWH.

The proposed research builds on our programmatic work developing motivational interventions for ambivalent smokers—including SLWH—and developing motivational and action-oriented smoking cessation apps.

### **1.2 Rationale**

We recently demonstrated the feasibility and acceptability of a novel mHealth app targeted to people who are ambivalent about quitting smoking (PAQS).<sup>1,2</sup> The current study seeks to adapt this intervention for use with smokers living with HIV who are ambivalent about quitting (PAQS-HIV) and evaluate the feasibility and acceptability of the intervention. Findings will inform plans for a future large-scale RCT. If the intervention ultimately proves to be effective, it could be widely offered to PAQS-HIV through health care systems, tobacco quitlines, AIDS service organizations, or other public health sponsors.

### **1.3 Potential Risks and Benefits**

#### **1.3.1 Potential Risks**

- breach of confidentiality
- emotional upset or embarrassment due to assessment and intervention
- nicotine withdrawal symptoms (such as irritability, cravings to smoke, difficulty concentrating, headache, constipation, trouble sleeping), if one quits smoking
- side-effects associated with nicotine replacement therapy (NRT) if people elect and elect to use this treatment. (most common symptoms include: rash/skin irritation at patch site, headache, nausea, and indigestion)

#### **2.3.2 Potential Benefits**

- All participants may receive some satisfaction or indirect benefit from contributing to this research.
- People who quit smoking may experience positive gains such as improved health and well-being.
- Receipt of free smoking cessation treatment via the mHealth app.

## **2 OBJECTIVES**

### **2.1 Study Objectives**

The objectives of this study are to:

- Design and develop a scalable mHealth app targeted to PAQS-HIV.
- Conduct a randomized pilot trial to evaluate the program's feasibility, acceptability, and potential effectiveness compared to a similar app without the experimental content targeted to PAQS-HIV.
- Plan for a future randomized efficacy trial to test the program.

### **2.2 Study Outcome Measures**

#### **2.2.1 Primary**

The primary outcome of interest that will be explored *at 3-month follow-up* is:

- Utilization of intervention (i.e., number of user sessions)

#### **2.2.2 Secondary**

Secondary outcomes to be explored at both the 1- and 3-month follow ups are:

- Overall satisfaction with app content and advice
- Number of cigarettes smoked per day
- Motivation for quitting smoking
- Self-efficacy for quitting smoking

Secondary outcomes that will be explored at the 3-month follow up only include:

- App installation status
- Number of user sessions
- Utilization metrics for each key component feature, including features common to both apps and those unique to the experimental intervention
- Self-reported 24-hour quit attempt
- Number of cigarettes smoked per day
- Proportion making a 50% reduction in smoking
- Self-reported no smoking in the last 7 days (7 day point prevalence abstinence)
- Proportion who earned free NRT and the proportion who requested it

#### **2.2.3 Exploratory**

- Utilization of individual program content and, in experimental arm, personal experiments

### **3 STUDY ENROLLMENT AND WITHDRAWAL**

#### **3.1 Subject Inclusion Criteria**

Participants will be eligible if they:

- Are 18 years of age or older;
- Can comfortably speak and read in English;
- Have smoked at least 100 cigarettes in their lifetime;
- Have smoked, even a puff, in the past 7 days;
- Have smoked at least 5 cigarettes a day;
- Are interested in quitting smoking someday, but not in the next month;
- Have an iOS or Android smartphone which they use at least weekly;
- Agree to download and try the app;
- Do not use a VPN on their smartphone;
- Live in the United States and have a US-based mailing address and phone number;
- Have been diagnosed with HIV

#### **3.2 Subject Exclusion Criteria**

Individuals will be excluded if they:

- Refuse to answer all screening questions or fail to meet any of the inclusion criteria above
- Self-report a lifetime history of dementia, manic disorder, bipolar disorder, or schizophrenia
- Have medical contraindications for NRT use (i.e., recent heart attack, an arrhythmia, or currently pregnant)
- Have visual impairments that preclude their ability to view content on their smartphone and lack adaptive devices to view content
- Have a household member who is already enrolled in the study (based on self-report or mailing addresses on file for participants)
- Have previously participated in related formative or evaluative research of the mHealth app
- Have unverifiable contact information (i.e., incorrect or suspicious phone number, email address, or mailing address) or otherwise fail to pass the fraud detection protocol.

#### **3.3 Strategies for Recruitment and Retention**

##### **Recruitment:**

We will utilize several recruitment methods to maximize enrollment and evaluate the potential of each for reaching/recruiting people living with HIV:

- Online advertising using social media platforms (e.g., Facebook, Instagram, Twitter) and on sites highly utilized by HIV populations (e.g., Grindr, Poz).
- Direct outreach via ResearchMatch.org
- Partnering with HIV service organizations
- Proactive contact with Kaiser Permanente Washington (KPWA) patients



- Flyers distributed through local community health clinics

#### Retention:

Steps taken to ensure participant retention include:

- Participants will be compensated a \$25 e-gift card for completing the baseline and each follow-up survey, for \$75 total compensation.
- Participants will receive an additional \$20 e-gift card for providing timely biochemical confirmation of their smoking status via saliva testing following the 3-month survey.
- Assessments will be kept brief and will be available for completion online. If not completed online within 2 weeks, they will be offered by phone.
- We will collect multiple forms of contact information in order to track participants, including: mailing address, email address, and phone number(s).

### **3.4 Treatment Assignment Procedures**

#### **3.4.1 Randomization Procedures**

Randomization will use a stratified block randomization scheme to stratify by cigarettes per day ( $\geq 15$  vs.  $< 15$ ) and frequency of smartphone use (daily vs. non-daily). Half will be randomized to each of the two study arms (control vs. experimental).

#### **3.4.2 Masking Procedures**

Participants will be blinded to their study arm.

Staff completing follow-up surveys by phone will be blinded to participants' treatment arm until the last section of the survey, which will contain additional satisfaction questions for participants in the experimental arm.

Staff who interpret the saliva test results will be blinded to participants' study arm.

### **3.5 Subject Withdrawal**

#### **3.5.1 Reasons for Withdrawal**

Participants may withdraw from participation at any time upon request.

Participants could also be withdrawn without their consent (i.e., investigator-initiated) if we learn post-randomization that they did not meet eligibility criteria (e.g., they are not smoking or another enrolled subject is found to be living at the same address, etc.), or if they cannot participate in study activities due to outside factors (e.g., hospitalization, incarceration, etc.).

We will also administratively withdraw participants if we have reason to believe they may have provided false information (e.g., fraudulent identity or contact information) when they enrolled in the study. If an enrolled participant is flagged for suspicious activity, we will attempt to contact them and clarify their information/verify their identity. If we are unable to verify their identity, we will administratively withdraw the participant and discontinue any further study-related outreach.

### **3.5.2 *Handling of Subject Withdrawals or Subject Discontinuation of Study Intervention***

Participants who request to drop out will be given the option to withdraw from the intervention, but still participate in the follow-up evaluations. Participants who refuse this offer and request to withdraw from the study will no longer be contacted. However, previously obtained data will be retained with subject consent.

Budget permitting, we may attempt to recruit replacement participants for drop-outs. Persons who withdraw as a result of an adverse event will be referred for appropriate care.

## **3.6 Premature Termination or Suspension of Study**

This study may be prematurely terminated if, in the opinion of the investigator, the sponsor, or the IRB, there is sufficient reasonable cause. Written notification documenting the reason for study termination will be provided to the investigator and/or sponsor by the terminating party. Circumstances that may warrant termination include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to subjects.

If the study is prematurely terminated or suspended, the sponsor will promptly inform the investigators/institutions, and the regulatory authority(ies) of the termination or suspension and the reason(s) for the termination or suspension. The IRB will also be informed promptly and provided the reason(s) for the termination or suspension by the sponsor or by the investigator/institution, as specified by the applicable regulatory requirement(s).

## **4 STUDY INTERVENTION**

### **4.1 Description**

Participants will be randomized to a control or experimental arm. Both arms will receive an mHealth intervention consisting of:

- Best-practice self-help guidance for quitting based on the US PHS's Clinical Practice Guidelines for treating nicotine dependence and best-practice treatment recommendations (aka, Quit Guide)
- App-based tools which allows users to track how many cigarettes they smoke a day, calculate what they would save if they stopped smoking, read motivational testimonials from others, and take notes within the app on things they've learned.
- A referral to a free tobacco cessation quitline counseling
- The ability to earn utilization "badges" in the app. Once the requisite number of badges are earned, participants can request a free 2-week starter kit of nicotine replacement patches.

Experimental arm participants will receive the same as above plus:

- A series of 10 exercises, each designed to help people clarify their values, build/strengthen their motivation for quitting, or teach specific skills needed to resist cravings to smoke
- Additional HIV-specific risk and benefit information
- Differential graphics (e.g., models chosen to appeal to people living with HIV based on user-centered design testing)
- Messaging acknowledging their ambivalence for quitting smoking
- Periodic text reminder prompts to encourage continued engagement with the app and timely completion of each experiment. Messages will not contain any sensitive information.

### **4.2 Administration of Intervention**

Subjects will download the app to their phone and have access to the intervention for the full study period.

Experimental participants will earn badges for each experiment they attempt (whether they succeed or not).

Participants in both arms can earn badges for viewing/using other program content.

### **4.3 Assessment of Subject Compliance with Study Intervention**

System-generated program utilization data will be tracked to confirm participants' use of the assigned intervention.

Participant self-reported program use will also be collected.

## **5 STUDY SCHEDULE**

### **5.1 Screening and Enrollment**

Individuals who are interested in participating will call a study toll free number to learn more or request screening. Potentially eligible patients from KPWA will either call a toll-free number or be contacted by study staff to assess interest and eligibility.

Eligibility screening will be conducted by phone. Those who screen eligible will provide consent and staff will verify their cell phone number and email address during the screening call.

Once an individual's contact information is confirmed, staff will be sent a link to the online consent form. After providing documented consent online, they will be invited to complete a baseline survey online.

### **5.2 Baseline and Randomization**

Participants will complete an online baseline survey. At completion, they will be automatically randomized to receive one of two versions of the app (control versus experimental).

### **5.3 Intervention Access**

Following randomization, participants will be sent instructions how to download and install their assigned study app. If the app has not been installed and activated after 3 days, staff will contact them to offer assistance.

As participants use the program, they will earn utilization badges. After earning 6 badges, participants will be able to request a free 2-week trial of over-the-counter nicotine patches or nicotine gum.

Participants who wish to enroll in free stop-smoking counseling through their local tobacco quitline can do so using an in-app call feature.

### **5.4 1 and 3-month Follow-up Assessments**

Participants will be invited to complete an online survey at one- and three-months post-randomization. If the survey is not completed after 10 days, study staff will begin phone outreach to administer the survey over the phone.

Participants will receive a \$25 electronic gift card after each follow-up survey is completed.

### **5.5 Biochemical Verification – In-Home Cotinine Saliva Test**

Participants who report not smoking (7 day point prevalent abstinence) at 3-month follow up will be asked to complete a saliva test to biochemically confirm abstinence. Kits will be mailed to participants and completion of the tests will be monitored over telehealth video software.

After completion of the test, the study staff will email a final \$20 gift card.

## **6 STUDY PROCEDURES /EVALUATIONS**

Standard operating procedures for the study will be detailed in the Manual of Procedures (MOP), which will be provided to study staff prior to study start-up. Overviews of the procedures are provided here. Data collected will be directly entered into our electronic data collection system.

## 7 STUDY OVERSIGHT

According to NCI's Policy for Data and Safety Monitoring of Clinical Trials (<http://deainfo.nci.nih.gov/grantspolicies/datasafety.pdf>), the method for monitoring patient safety should be commensurate with the level of risk. For Phase I and II trials, a DSMB is not required and data safety can be monitored by the study PI and/or project manager.

For the current low risk pilot study, the PI will be responsible for monitoring the data integrity and patient safety as outlined above.

## **8 ASSESSMENT OF SAFETY**

### **8.1 Specification of Safety Parameters**

This is a minimal risk behavioral intervention. Nevertheless, adverse events (AEs) and serious adverse events (SAEs) will be recorded and reported over the course of the study.

An adverse event is any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research.

Project staff with participant contact will be trained to identify potential AEs and SAEs and instructed to report them immediately to the study PI and the project manager.

#### **8.1.1 Severity of Event**

The following scale will be used to grade the severity of adverse events:

- 1) Asymptomatic or mild symptoms; no intervention needed (non-serious);
- 2) Moderate: minimal, local, or non-invasive intervention indicated; limiting on ADL (non-serious);
- 3) Severe or medically significant but not immediately life threatening; hospitalization or prolonged hospitalization needed; disabling; limited self-care ADL (serious);
- 4) Life-threatening; urgent intervention required (serious);
- 5) Death related to AE (serious).

#### **8.1.2 Non-serious Adverse Event Reporting**

Non-serious AEs will be reported annually to the IRB.

#### **8.1.3 Serious Adverse Event Reporting**

All serious AEs will be reported within 48 hours, consistent with KPWHRI IRB policy and NIH guidelines. All participants learned to be deceased, regardless of the cause of death or relatedness to the program, will be reported to the IRB. The IRB will work with the PI to ensure additional agencies (e.g., NIH, etc.) are notified as required. All SAEs will be followed until satisfactory resolution or until the PI deems the event to be chronic or the patient to be stable.

#### **8.1.4 Expected Adverse Reactions**

Expected, associated adverse events include:

- Upset due to participation in research assessments. Such reactions are expected to be mild and transient.
- Nicotine withdrawal. Participants who chose to quit smoking may experience nicotine withdrawal symptoms such as irritability, cravings to smoke, difficulty concentrating, headache, constipation, and trouble sleeping.

- NRT side-effects. Participants who chose to use the optional OTC NRT patches may experience side-effects such as rash/skin irritation at patch site, headache, nausea, and indigestion. These adverse events are expected, transient, and generally mild to moderate intensity. While NRT use is considered safer than smoking, female participants will be advised to use birth control while using NRT.

## **8.2 Time Period and Frequency for Event Assessment and Follow-Up**

Reportable events will be recorded in the data collection system throughout the study. Events will be followed for outcome information until resolution or stabilization.

The PI will record all reportable events with start dates occurring any time after informed consent is obtained until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation.

## **8.3 Characteristics of an Adverse Event**

### **8.3.1 Relationship to Study Intervention**

The Study PI will determine if AE's are deemed possibly related to the individual's study involvement. The following guidelines will be used.

- Associated – The event is temporally related to the study participation and no other etiology explains the event.
- Not Associated – The event is temporally independent of study participation and/or the event appears to be explained by another etiology

### **8.3.2 Expectedness of SAEs**

The Study PI will be responsible for determining whether an SAE is expected or unexpected. An adverse event will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the intervention.

## **8.4 Unanticipated Problem**

### **8.4.1 Definition**

The Office for Human Research Protections (OHRP) considers unanticipated problems (UP) involving risks to subjects or others to include, in general, any incident, experience, or outcome that meets all of the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
- Related or possibly related to participation in the research ("possibly related" means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and



- Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

#### **8.4.2     *Unanticipated Problems Reporting to IRB and NCI***

Incidents or events that meet the OHRP criteria for unanticipated problems will be reported to the IRB within 48 hours of when the team is made aware of the event.

Unanticipated problem reports will include:

- Appropriate identifying information for the research protocol, such as the title, investigator's name, and the IRB project number;
- A detailed description of the adverse event, incident, experience, or outcome;
- An explanation of the basis for determining that the adverse event, incident, experience, or outcome represents an unanticipated problem;
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the unanticipated problem

The IRB will determine if other immediate action is required (e.g., suspension of recruitment, protocol closure, etc.). Temporary or permanent suspension of an NIH-funded protocol will be reported to the NCI Program Official responsible for the grant.

#### **8.5        *Halting Rules***

Study halting may occur as required by the IRB or NCI. The study PI may temporarily suspend enrollment pending review by these authorities if warranted based on the presence, type, or frequency of SAE's or other changes in the study protocol which may place participants at greater than anticipated risk.

## **9 CLINICAL SITE MONITORING**

Clinical site monitoring will not be done for this study; however, the NCI reserves the right to conduct independent audits or clinical monitoring as necessary.

## **10 STATISTICAL CONSIDERATIONS**

### **10.1 Study Hypotheses**

As a formative, pilot study, we are not testing specific a priori hypotheses. Nevertheless, we anticipate PAQS-HIV will find the experimental content engaging and, as a result, they will be more likely to use the provided app compared to those assigned to the control app.

We will also assess differences in use of the best practice treatment provided (i.e., self-help quit guidance, NRT, and 1-800-QUIT NOW referral) and other indices of behavior change (quit attempts, smoking reduction, and abstinence) at 3-month follow-up. We will also explore differential change in motivation for quitting and self-efficacy for quitting at 1-month follow-up, as each represents a potential mediator of behavior change at 3-month follow-up.

### **10.2 Sample Size Considerations**

The primary analytic goals of this pilot study are to assess feasibility and acceptability of the intervention. A secondary goal is to assess the potential magnitude of the intervention effects on study outcomes. The target sample size ( $n = 50$ ) is larger than required for feasibility and acceptability outcomes, but is based on recommended guidelines for estimating effect sizes in behavioral treatment development research. However, by design, this pilot is not powered to evaluate efficacy or to test for statistically significant differences between intervention groups.

### **10.3 Statistical Analysis Plan**

We will conduct a modified intent-to-treat analysis, limiting the analytic sample to participants who download the app before the end of the study, retaining assignment to their randomization arm for analyses regardless of actual app usage.

For continuous outcomes (e.g., scores on Likert scale for self-efficacy to quit smoking or change in cigarettes smoked per day), we will fit linear regression models to estimate expected differences in outcomes between randomization groups, accompanied by p-values from t-tests and compatible 95% confidence intervals. For precision, we will adjust for the number of cigarettes smoked per day at baseline, and when applicable, baseline values of the outcome. We will fit separate regression models for outcomes collected at each of 1- and 3-month post-enrollment surveys.

Due to the small sample size and potent rarity of many binary outcomes, we will estimate risk differences (RDs) using observed arithmetic differences in rates between randomization groups, accompanied by p-values from Barnard's exact test.<sup>3,4</sup> We will calculate exact 95% confidence intervals following Wang's inductive method.<sup>5,6</sup>

While automated app utilization data (e.g., number of user sessions) are collected on everyone, self-reported outcomes from the 1- and 3-month surveys (e.g. quit attempt lasting at least 24 hours or app satisfaction ratings) are subject to missingness. Per convention, missing smoking outcomes will be conservatively imputed as smoking<sup>7</sup>. For consistency, we will use a similar

approach when analyzing 24-hour quit attempts (i.e., missing data imputed as not making a quit attempt). For all other outcomes, analyses will use complete cases without imputation.

Analyses of average helpfulness ratings across eight app features will be further restricted to participants who self-report use of each feature, which is then substantiated by automated app data. Participants will be included in comparisons of app satisfaction ratings only if they have earned at least one badge by the time of the survey. Self-efficacy to *stay* quit will be compared only among participants who report not smoking (even a puff) in the last seven days.

## **11 SOURCE DOCUMENTS AND ACCESS TO SOURCE DATA/DOCUMENTS**

Study staff will maintain appropriate treatment and research records for this study, in compliance with ICH E6, Section 4.9 and regulatory and institutional requirements for the protection of confidentiality of subjects. Study staff will permit authorized representatives of NCI and regulatory agencies to examine (and when required by applicable law, to copy) research records for the purposes of quality assurance reviews, audits, and evaluation of the study safety, progress and data validity.

## **12 ETHICS/PROTECTION OF HUMAN SUBJECTS**

### **12.1 Ethical Standard**

The investigator will ensure that this study is conducted in full conformity with the principles set forth in The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, as drafted by the US National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (April 18, 1979) and codified in 45 CFR Part 46 and/or the ICH E6.

### **12.2 Institutional Review Board**

The protocol, informed consent form(s), recruitment materials, and all subject materials will be submitted to the IRB for review and approval. IRB approval of the protocol and consent processes must be obtained before any subject is enrolled. Any amendment to approved study materials will require re-review and approval by the IRB before the changes are implemented in the study.

### **12.3 Informed Consent Process**

Each person will provide consent to be screened for eligibility by phone. If screened eligible, they will provide verbal consent and be emailed a link to a study information sheet for their records. The study team may email a PDF as a back-up method if a participant is unable to open the study information sheet using the link.

Informed consent will include permission for contacting participants by push notification/mail/email/text to remind them of follow-up surveys and other study events and permission to collect all study data and track their use of the program. It will also include permission to order a 2-weekly supply of NRT patches from an online pharmacy and have it sent to participants' homes, for those participants meet the study requirements to receive the NRT and also specifically request for it to be mailed to them. (Note: receipt of the NRT is optional for participants.)

Participants are free to refuse to answer any survey questions or drop out of the study at any time. Participants will be instructed how to discontinue involvement in the intervention or drop out of the study as part of the consent process.

### **12.4 Exclusion of Women, Minorities, and Children (Special Populations)**

Individuals of any gender or racial/ethnic group may participate. Children under the age of 18 years will be excluded.

### **12.5 Subject Confidentiality**

Appropriate steps will be taken to safeguard participant confidentiality. This includes the following:

- KPWA is a HIPAA covered entity and complies with all HIPAA regulations regarding data security. All study files will be maintained in a centralized location on the KPWHRI departmental server. Access to this data is password protected and subject to the same security protections as other confidential health plan data. Access will be limited to staff

working on this study and require access to these files. All staff are trained in appropriate security protections, computer passwords are changed on a regular basis, and all staff sign annual confidentiality agreements.

- Participants' identities will not be shared with anyone other than relevant team members at KPWHRI as needed to perform their study roles.
- Electronic communications we send will not contain personal health information (PHI) other than references to smoking and participant first names.
- Biochemical confirmation of smoking abstinence will be remotely monitored using a secure video conference software for Apple and Android devices. The software does not store or access PHI, uses encrypted video streaming to protect confidentiality, and does not allow video sessions to be recorded, to further protect patient confidentiality.
- Participant information will not be stored on their phones. Data generated by the GEMS app will be encrypted when transmitted and then securely stored in a back-end database behind the KP firewall. Access will be limited to staff who need it, who will log-in using their NUID or other secure password (as recommended by KP).
- Data exported from the GEMS backend database will be stripped of identifiers before being stored or analyzed.
- Data from study surveys (collected in REDCap) will not be tied to personal identifiers.

#### **12.6 Future Use of Identifiable Data**

Identifiable information will be destroyed within 5 years of the end of the study, consistent with HIPAA and our IRB requirements.

We have no plans to retain identifiable information beyond this period. If this plan changes, we will obtain appropriate IRB approval and participant consent.

## **13 DATA HANDLING AND RECORD KEEPING**

### **13.1 Data Management Responsibilities**

Data collected will be captured in electronic records.

Final datasets will be saved electronically, clearly labeled and stored in a secure project folder on the KPWHRI server accessible only to study staff.

No electronic participant data shall be overwritten by study staff. As necessary, variables may be recoded into new variables for analyses, but will be done in a way to preserve the original record. All changes will be documented.

### **13.2 Types of Data**

Data for this study will include eligibility screening, baseline and follow-up assessments, web analytics monitoring the program use, confirmation of smoking abstinence, and safety data.

### **13.3 Data Capture Methods**

- Eligibility screening and consent will be completed by telephone and documented in REDCap.
- The baseline assessment will be completed by participants online in REDCap.
- Participants will be sent a link to complete the 1 and 3-month follow-up surveys online in REDCap. If unresponsive to the online survey, study staff may attempt to administer the assessment by phone.
- Video-based confirmation of smoking abstinence will be conducted using a secure telemedicine program. Participants will use saliva test kits mailed to them by the study. Results of biochemical confirmation of abstinence will be recorded in REDCap by study staff and a photo of the de-identified saliva test securely saved to the study files.
- Adverse events may be self-reported to study staff via email or by phone. Events will be documented in study records and followed up for resolution and stabilization, as appropriate. Adverse events will not be reported or tracked through the GEMS+ intervention/app.
- All electronic records will be kept in a 21 CFR Part-11 compliant data capture system, which includes password protection.

### **13.4 Study Records Retention**

All study data will be maintained for at least 5 years after the conclusion of the study. At that time, consistent with HIPAA guidelines, identifying information and linking files will be destroyed unless consent to retain these files is granted by study participants or the IRB.

### **13.5 Protocol Deviations and Violations**

All staff will immediately report protocol deviations and violations to the KPWHRI Project Manager, who will inform the PI. Deviations will be considered any noncompliance with this clinical trial protocol, Good Clinical Practice, or the Manual of Procedures.



Protocol deviations will be reported annually to the IRB. Protocol violations will be reported to the IRB in a timely manner.

## 14. REFERENCES

1. Heffner JL, Catz SL, Klasnja P, Tiffany B, McClure JB. Development of a Mobile Health Intervention with Personal Experiments for Smokers Who Are Ambivalent About Quitting: Formative Design and Testing. *JMIR Form Res*. Aug 27 2020;4(8):e21784. doi:10.2196/21784
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4. Signorell A, Aho K, Alfons A, et al. DescTools: Tools for Descriptive Statistics, R Package Version 0.99-50. 2023; <<https://CRAN.R-project.org/package=DescTools>>.
5. Wang W. On construction of the smallest one-sided confidence interval for the difference of two proportions. *The Annals of Statistics*. 2010;38(2):1227-1243, 17.
6. Shan G, Wang W, Shan MG. \_ExactCldiff: Inductive Confidence Intervals for the Difference Between Two Proportions. 2022; <<https://CRAN.R-project.org/package=ExactCldiff>>.
7. West R, Hajek P, Stead L, Stapleton J. Outcome criteria in smoking cessation trials: proposal for a common standard. *Addiction*. Mar 2005;100(3):299-303. doi:10.1111/j.1360-0443.2004.00995.x



**Human Subjects Review Office**  
Kaiser Permanente Washington  
Health Research Institute  
1730 Minor Ave, Suite 1600  
Seattle, WA 98101

206-287-2919

DATE: May 12, 2022

PRINCIPAL INVESTIGATOR: Jennifer McClure

STUDY TITLE: [1842460-3] Design and Testing of a mHealth App for Ambivalent Smokers Living with HIV: A Randomized Pilot Study

REFERENCE #: 2021

SUBMISSION TYPE: Amendment/Modification

ACTION: APPROVED

STATUS DATE: February 3, 2022

EXPIRATION DATE: December 14, 2022

REVIEW TYPE: Expedited Review

REVIEW CATEGORY: Expedited review category # 5 & 7

Thank you for your submission of Amendment/Modification materials for this research study. The Kaiser Permanente Washington Region IRB has reviewed your response to the modifications required letter and has APPROVED the study.

**Determinations:**

The Committee agreed that the overall study design is reasonable, the risk/benefit ratio is reasonable, and the confidentiality protections are adequate.

All research must be conducted in accordance with this approved submission.

The IRB has approved one or more consent waivers and a waiver of authorization per HIPAA. Please see the additional waiver approval document(s) for details.

You will be required to submit a progress report prior to the following date: December 14, 2022. Prior to this date, you will be prompted to submit the Continuing Review Report, available in the IRBNet library. You are required to submit an annual progress report because this project is actively interacting with participants to obtain consent.

This letter is documentation of an IRB review. The IRB reviews only the issues related to the protection of human subjects in research. There may be approvals needed by other departments at Kaiser Permanente Washington.

Any revisions to approved research (**screening, recruitment, mailings, phone calls and data pulls, etc.**) may not be initiated without IRB review and approval unless they are necessary to eliminate apparent immediate hazards to subjects. Please use the IRBNet modification form to request revisions.

Investigators are required to promptly report to the IRB for the following: 1) any modifications in procedures, particularly those affecting risks and benefits to subjects, and 2) any serious and/or unanticipated events or other problems involving risks to subjects or others.

The Principal Investigator is responsible for disseminating this information to project staff.

If you have any questions, please contact the HSRC office at (206)-287-2919 or [hsrcoffice@kp.org](mailto:hsrcoffice@kp.org). Please include your study title and reference number in all correspondence with this office.

FW00002344 · All relevant regulations and policies are available upon request