Introduction Page

1 * Abbreviated Title:
Optimizing Smoking Cessation Interventions for PLWH

2 * Full Title:
Optimizing smoking cessation interventions for PLWH in Nairobi, Kenya

3

* Select Type of Submission:

- (●) **IRB Application**
- ( ) Humanitarian Use Device (for FDA approved Indication & non-research purposes ONLY)
- ( ) Single Patient Expanded Access (pre-use)
- ( ) Single Patient Emergency Use (post-use)
- ( ) Unsure if this proposal requires IRB review (Not Human Subject Research)

Note: The Type of Submission cannot be changed after this application has been submitted for review.

4 Original Version #:

Research Team Information

1 * Principal Investigator - Who is the PI for this study (person must have faculty status)? ***Faculty status is defined as being a full-time (>51% effort) faculty member holding one of the following titles at UM: Professor; Associate Professor; Assistant Professor.***
Seth Himelhoch

CITI Training: ID00008909

1.1 * Does the Principal Investigator have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

2 Point of Contact - Who is the alternative point of contact for the PI? This person can be a study coordinator or any other study team member. In case the IRB cannot contact the PI, this person is a secondary person to contact:
Wendy Potts

CITI Training: ID00008918

2.1 Does the Point of Contact have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

3 Other Team Members - list all additional members of the research team for this study. DO NOT include the PI or POC in this list:

	Name	Edit Submission	cc on Email	Research Role	Has SFI?	CITI Training
View	Melanie Bennett	no	no	Sub-Investigator	no	ID00006944
View	Jon Shuter	no	no	Sub-Investigator	no	
View	Julia Cohen	no	no	Other	no	
View	Emily Koech	no	no	Research Team Member	no	ID00011276
View	Andrea Weinberger	no	no	Other	no	
View	Patience Oduor	no	yes	Research Team Member	no	ID00010712
View	Sylvia Ojoo	no	yes	Sub-Investigator	no	ID00008762
View	Deborah Medoff	no	no	Statistician	no	ID00006254
View	Lijuan Fang	no	no	Statistician	no	ID00019454
View	LAN LI	no	no	Statistician	no	ID00019102
View	Jeanette Robinson	no	no	Technician or Assistant	no	ID00008752

IMPORTANT NOTE: All research team members (including PI) must have current CITI and HIPAA training completed.

Resources

If this study is a collaborative UM/VA study, please clarify which resources are being used at each institution.

1 * Describe the time that the Principal Investigator will devote to conducting and completing the research:
The Principal Investigator will devote a portion of his time to conduct and complete this research study. The PI will have regular team meetings and supervisions with all staff members working on this project both in Maryland and Kenya.

2 * Describe the facilities where research procedures are conducted:
This study will be carried out with patients care at a variety of heath care settings clinics. If needed, the intervention sessions may be conducted via phone.

3 * Describe the availability of medical and/or psychological resources that subjects might need as a result of anticipated consequences of the human research:
We do not anticipate that subjects will need medical and/or psychological resources following their participation in this study, however the recruitment site will provide medical/psychological resources for participants if needed. In emergent psychiatric situations Dr. Sylvia Ojoo, a Co-PI, will be available for immediate consultation.

4 * Describe the process to ensure that all persons assisting with the research are adequately informed about the protocol, the research procedures, and their duties and functions:
Study staff working on this protocol will be specially trained in working with participants with HIV and mental illness. Their assigned duties on this project will be described to them in detail. They will become very familiar with the protocol through ongoing study team meetings and trainings. All of our staff are extensively trained on obtaining informed consent and the study assessments. Study staff practice study procedures beforehand and are observed prior to meeting with a research participant alone.

Sites Where Research Activities Will Be Conducted

1 * Is this study a:

- (●) **Multi-Site**
- ( ) Single Site

2 * Are you relying on an external IRB (not UM) to be the IRB of Record for this study?

( ) Yes (●) **No**

3 * Are any other institutions/organizations relying on UM to be the IRB of Record for this study?

(●) **Yes** ( ) No

3.1 Attach the applicable regulatory documents here (i.e., IRB Authorization Agreement (IAA), FWA, local ethics approval, other IRB approvals, etc.). Final UM approval will be contingent upon final execution of all required regulatory approvals:

Name	Created	Modified Date
SKM_C654e18110815330.pdf(0.02)	10/19/2018 8:34 AM	11/9/2018 1:01 PM

4 * Is UM the Coordinating Center for this study? (Applicable for multi-site studies. A Coordinating Center is responsible for overall data management, monitoring and communication among all sites, and general oversight of conduct of the project.)

( ) Yes (●) **No**

5 Is VA the Coordinating Center for this study? (Applicable for Collaborative studies between the VA, UM and other sites. A Coordinating Center is responsible for overall data management, monitoring and communication among all sites, and general oversight of conduct of the project)

( ) Yes ( ) No

6 * Institution(s) where the research activities will be performed:

- [ ] University of Maryland, Baltimore
- [ ] University of Maryland, Upper Chesapeake Kaufman Cancer Center
- [ ] VAMHCS
- [x] **UMB School of Medicine**
- [ ] Marlene and Stewart Greenebaum Cancer Center
- [ ] University Physicians Inc.
- [ ] Shock Trauma Center
- [ ] General Clinical Research Center (GCRC)
- [ ] Maryland Psychiatric Research Center (MPRC)
- [ ] Johns Hopkins
- [ ] International Sites
- [ ] UMB Dental Clinics
- [ ] Center for Vaccine Development
- [ ] Community Mental Health Centers
- [ ] Private Practice in the State of Maryland
- [ ] Institute of Human Virology (IHV) Clinical Research Unit
- [ ] Joslin Center
- [ ] UMB Student Classrooms
- [ ] National Institute of Drug Abuse (NIDA)

- [ ] National Study Center for Trauma and EMS
- [ ] Univ of MD Cardiology Physicians at Westminster
- [ ] Nursing Homes in Maryland
- [ ] University of Maryland Biotechnology Institute
- [ ] Maryland Department of Health
- [ ] Maryland Proton Treatment Center
- [ ] Mount Washington Pediatric Hospital
- [ ] Institute of Marine and Environmental Technology (IMET)
- [x] **Other Sites**
- [ ] University of Maryland Medical System (Select below)

ID: VIEW4DF870DF2C000
Name: v2_Sites Where Research Activities Will Be Conducted

Other Sites Where Research Activities Will Be Conducted

You selected "Other Sites," "Private Practice," "Community Mental Health Centers," and/or "Nursing Homes in Maryland" as a site where research will be conducted.

3.1 * Specify the name of the site(s):
Please see additional documents

3.2 * Contact Person(s) for Other Site:
Please see additional documents

3.3 * Phone (if no phone available, input "none"):
Please see additional documents

3.4 * Email Address (if no email available, input "none"):
Please see additional documents

ID: VIEW4DF8712DB5800
Name: v2_Other Sites Where Research Activities Will Be Conducted

Funding Information

1 * Indicate who is funding the study:

- [x] **Federal**
- [ ] Industry
- [ ] Department / Division / Internal
- [ ] Foundation
- [ ] Private
- [ ] State Agency

2 * What portion of the research is being funded? (Choose all that apply)

- [x] **Drug**
- [ ] Device
- [x] **Staff**
- [x] **Participant Compensation**
- [x] **Procedures**
- [ ] Other

3 Please discuss any additional information regarding funding below:

ID: VIEW4DF85DF452400
Name: v2_Funding Information

DHHS Funded Study

You indicated that this is a Federally funded study.

1 * Is this study sponsored by a Department of Health and Human Services (DHHS) agency?

● **Yes** ○ No

2 You may upload any grant documents here:

Name	Created	Modified Date
Human_subjects_5_7_17_final.docx(0.01)	10/17/2017 11:06 AM	10/17/2017 11:06 AM
Research Plan _5_7_17_FINAL.docx(0.01)	10/17/2017 11:06 AM	10/17/2017 11:06 AM
Specific_Aims_5_7_17_FINAL.docx(0.01)	10/17/2017 11:05 AM	10/17/2017 11:05 AM
Abstract_5_7_17_FINAL.docx(0.01)	10/17/2017 11:05 AM	10/17/2017 11:05 AM

ID: VIEW4DF87B9560800
Name: v2_DHHS Funded Study

Federal Agency Sponsor Contact Information

You indicated that this is a Federally funded study.

1

* Agency Name:
NIH

* Address 1:
6701 Rockledge Drive

Address 2:
Room 1040-MSC 7710

* City:
Bethesda

* State:
MD

* Zip Code:
20892

* Contact Person:
Dr. Mark Parascandola

* Phone Number:
1-240-276-5810

* Federal Agency Email:
NCIGlobalHealth@mail.nih.gov

Grant Number 1 (if applicable):
1 RO1 CA 225 419- OR - Check here if Grant 1 is not assigned a number. ☐

If Grant 1 has no number, please provide the following information:
Title of Grant 1:

PI of Grant 1:
Seth Himelhoch

Grant Number 2 (if applicable):
- OR - Check here if Grant 2 is not assigned a number. ☐

If Grant 2 has no number, please provide the following information:
Title of Grant 2:

PI of Grant 2:

Grant Number 3 (if applicable):
- OR - Check here if Grant 3 is not assigned a number ☐

If Grant 3 has no number, please provide the following information:
Title of Grant 3:

PI of Grant 3:

Grant Number 4 (if applicable):
- OR - Check here if Grant 4 is not assigned a number. ☐

If Grant 4 has no number, please provide the following information:
Title of Grant 4:

PI of Grant 4:

Research Protocol

1 * Do you have a research protocol to upload?

- ○ Yes
- ● **No, I do not have a research protocol and will use the CICERO application to enter my study information**

2 If Yes, upload the research protocol:

Name	Created	Modified Date
There are no items to display		

ID: VIEW4E00563F8D000
Name: v2_Research Protocol

Risk Level

What is the risk level of your study? (Ultimately, the IRB will determine the appropriate risk level and your designation is subject to change.)

* Choose One:

- ○ Minimal - The probability & magnitude of harm/discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations/tests.
- ● **Greater Than Minimal - Does not meet the definition of Minimal Risk.**

ID: VIEW4E02805225800
Name: v2_Risk Level

Type of Research

1 * Indicate **ALL** of the types of research procedures involved in this study (Choose all that apply):

- [x] **Use of unapproved drug(s)/biologic(s) or approved drug(s)/biologic(s) whose use is specified in the protocol.**
- [ ] Evaluation of food(s) or dietary supplement(s) to diagnose, cure, treat, or mitigate a disease or condition.
- [ ] Use of device(s) whose use is specified in the protocol
- [x] **Psychological/Behavioral/Educational Method or Procedure (i.e., survey, questionnaires, interviews, focus groups, educational tests).**
- [ ] Sample (Specimen) Collection and/or Analysis (including genetic analysis).
- [x] **Data Collection or Record Review (i.e., chart review, datasets, secondary data analysis).**
- [ ] None of the above.

2 * Is this study a clinical trial OR will this study be registered at ClinicalTrials.gov?
A clinical trial is a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.

(●) **Yes** ( ) No

Lay Summary

1 * Provide a summary of the background and purpose of the study in language that can be understood by a person without a medical degree.

Worldwide estimates suggest that people living with HIV/AIDS (PLWH) smoke at nearly three times the rate of the general population. Smoking among PLWH living in sub-Saharan Africa is associated with gender (male>female), with living in an urban slum community, and perhaps most importantly with illicit substance use. Although precise prevalence estimates of tobacco use among PLWH in Kenya are lacking, recent data collected from a large, well established methadone maintenance program in Nairobi found the prevalence of smoking among PLWH with opiate use disorders was 100%. This compares to 7.7-9.1%10;11 Kenyan general population. Many interventions are effective in helping smokers in the general population quit. To what degree these data translate to PLWH in lower-middle income countries that may have greater challenges with health infrastructure, resources and medication access, is not clear.

Our proposed study will use a factorial design to evaluate the most promising and accessible behavioral and pharmacologic treatments aimed at achieving maximal efficacy for smoking cessation among PLWH who smoke. We propose to randomize 300 participants PLWH, who smoke and who are receiving care in a health care setting program in Nairobi, Kenya to one of the following 4 conditions: (1) bupropioin + Positively Smoke Free (an 8 session tailored behavioral intervention for PLWH smokers); (2) bupropion + Standard of Care (brief advice to quit); (3) Placebo + Positively Smoke Free; and (4) Placebo + Standard of Care. We plan to use a factorial design as it is a highly efficient method of assessing multiple treatments in a single trial with the possibility of saving both time and resources. We plan to conduct the study in a methadone maintenance clinic for several reasons. First, smoking rates are shockingly high in this setting, and the need for effective tobacco treatment is enormous. Second, there is great synergy in providing behavioral and pharmacological treatment for smoking cessation interventions to clients who are already receiving a pharmacological intervention (i.e., methadone) with concomitant substance use counseling. Third, people in methadone maintenance come regularly to receive treatment which is likely to enhance smoking cessation treatment follow-up and completion. All participants will be assessed at baseline,12 weeks and 36 weeks with the main outcome being 7-day abstinence (defined as self-reported no smoking in the past 7 days + CO<7 ppm). Additionally, we plan to conduct an implementation costs assessment to provide rigorously obtained approximations of total implementation costs of each intervention tested in this trial.

As Kenya has one of the strongest anti-tobacco legislations in sub-Saharan Africa, results of this study will provide policymakers, community leaders and clinicians with critical evidence of the most effective smoking cessation treatments for PLWH smokers in the methadone maintenance setting.

Sub Study:
In the main protocol, participants randomized to positive smoke free (PSF) interventions already receive a syllabus-driven, culturally congruent intervention that directly communicates and provides education about the cancer risk associated with tobacco use. Given the co-occurrence of alcohol use reported among tobacco users in Kenya, a logical next step is to develop, culturally adapt and incorporate educational material about the cancer risk associated with tobacco and alcohol use within the PSF syllabus.

This study aims to create culturally congruent health education materials, through conducting focus groups and in-depth interviews with key informants, to evaluate understanding and acceptance of these educational materials, and iteratively update the PSF syllabus to ensure maximal impact. The proposed work will add a previously standardized group of questions to evaluate awareness of the link between alcohol and cancer at each of the study visits. These questions evaluated comparing baseline to 12-week follow-up and 36-week follow-up, will help to determine the extent, if any, the new material added to the PSF syllabus changes awareness of the link between alcohol and tobacco use and cancer. The participants will be recruited from HIV clinics in Nairobi, Kenya. The results of this study will provide policymakers, community leaders and clinicians with critical evidence of the most effective alcohol and smoking cessation treatments for PLWH.

Justification, Objective, & Research Design

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer boxes below.

1 * Describe the purpose, specific aims, or objectives of this research. State the hypothesis to be tested:

Primary Aim 1: Compare bupropion therapy to placebo on rates of 7-day point prevalence abstinence (PPA) at 36 weeks in smokers with HIV/AIDS. We hypothesize that rates of smoking abstinence at week 36 will be higher in those treated with bupropion compared to placebo.

Primary Aim 2: Compare Positively Smoke Free to low intensity, brief counseling on rates of 7-day PPA at 36 weeks in smokers with HIV/AIDS. We hypothesize that rates of smoking abstinence at week 36 will be higher in those treated with Positively Smoke Free compared to brief counseling.

Primary Aim 3: Compare Positively Smoke Free + bupropion to the other two study conditions outlined above on rates of 7-day PPA in smokers with HIV/AIDS at 36 weeks. We hypothesize the effect of Positively Smoke Free with bupropion therapy is greater than the effect of Positively Smoke Free or bupropion therapy alone.

Secondary Aim: Estimate the organizational costs of implementing Positively Smoke Free, bupropion or both. All cost estimates will be appropriately time-discounted and inflation-adjusted13;28. The planned assessment will yield rigorously obtained approximations of total implementation costs at a new site of care.

Exploratory Aim: Explore whether the effect of PSF compared to brief counseling with bupropion is greater than the effect of PSF without bupropion.

Given the critical need for information about the up-front expenses required to implement smoking cessation services in Kenya, we plan to conduct an implementation costs assessment to provide rigorously obtained approximations of total implementation costs of each intervention tested in this trial.

Sub Study:
AIM 1: Develop, culturally adapt and update the PSF intervention in the main study to include educational material about the cancer risk associated with tobacco and alcohol use.

AIM 2: Preliminarily determine the extent the updated PSF syllabus changes awareness of the link between alcohol and tobacco use and cancer.

Alcohol consumption and tobacco use are common among PLHIV and associated with significant morbidity and mortality which is preventable13–16,40. In Kenya, tobacco use has been shown to be strongly and significantly associated with higher odds of heavy alcohol consumption33. Both alcohol and tobacco significantly impact the progression and outcome of HIV disease and increase the risk of NCD among people with HIV7–10,31,32,44,45. Kenya, with an estimated population of 1.5 m PLHIV has initiated 1.16m individuals on ART in comprehensive HIV clinics. This provides an opportunity to screen for alcohol and tobacco use routinely and provide evidence-based interventions and treatments to reduce or stop the use of these harmful substances.

The proposed work of the administrative supplement fills an important gap in the literature and addresses a key topic listed under the NCI research interests, that being, to understand how to effectively communicate the cancer-related risks of tobacco and alcohol co-use to populations at high risk for the two behaviors such as PLWH who smoke in Kenya. The proposed work is within the scope of the parent grant. In the parent grant, participants randomized to PSF already receive a syllabus-driven, culturally congruent intervention that directly communicates and provides education about the cancer risk associated with tobacco use. Given the co-occurrence of alcohol use reported among tobacco users in Kenya, a logical next step is to develop, culturally adapt and incorporate educational material about the cancer risk associated with tobacco and alcohol use within the PSF syllabus.

2 * Discuss the research design including but not limited to such issues as: probability of group assignment, potential for subject to be randomized to placebo group, use of control subjects, etc.:

We propose to randomize 300 participants to one of the following 4 conditions: (1) bupropion + Positively Smoke Free (an 8 session tailored behavioral intervention for PLWH smokers); (2) bupropion + Standard of Care (brief advice to quit); (3) Placebo + Positively Smoke Free; and (4) Placebo + Standard of Care. Given the factorial nature of the design, we will be able to assess the main effect of bupropion vs. Placebo, Positively Smoke Free vs. Standard of Care, and the additive effect of those two treatments. We chose to use a factorial design as it is a highly efficient method of assessing multiple treatments in a single trial with the possibility of saving both time and resources. All participants will be assessed at baseline, 12 weeks and 36 weeks (6 months post study completion).

Participants will be randomly assigned to one of the four conditions using permuted blocks which will randomly vary in size. The research pharmacy will be notified of the drug randomization (bupropion or placebo). All raters, investigators, and other staff will be blind to treatment assignment except for the dispensing pharmacist.

Separate emergency unblinding envelopes for each participant will be kept in a locked cabinet at the dispensing pharmacy in the case of a medical emergency. All participants who are randomized will be taught the correct use of the study medication, and assisted in setting a quit date.

Sub study:
There will be no group assignment or randomization.

3 * Describe the relevant prior experience and gaps in current knowledge. Describe any relevant preliminary data:

Although precise prevalence estimates of smoking among PLWH are lacking in the Republic of Kenya (to be referred to as Kenya from this point forward), based on data collected from several clinical sites in Nairobi, smoking among PLWH ranged from 16-100%. This is in contrast to rates 7.7%-9.1% in the general population10;11. It is important to note that among those living in sub-Saharan Africa (including Kenya), smoking among PLWH is associated with gender (male>female), with living in an impoverished, urban ("slum") community, and perhaps most importantly with illicit substance use 8.

Kenya has one of the strongest anti-tobacco legislations in sub-Saharan Africa (tobacco control measures in Kenya include a ban on advertising, no smoking in public places, mandatory cigarette warnings, and age verification)11;50, yet, smoking cessation treatment is limited by several contextual factors. First, the vast majority of healthcare providers in Kenya report insufficient training to provide basic smoking cessation treatment (i.e., 5As)51. Other barriers to providing smoking cessation treatment include lack of guidelines and lack of knowledge. Second, varenicline, currently the most effective smoking cessation pharmacological intervention, is not available in Kenya. Third, the pharmacological smoking cessation treatments available in Kenya are limited to NRT (which can be purchased over the counter (cost: $120/month) and bupropion (which requires a prescription (cost: $60/month). Of note, a pack of cigarettes costs about $2.40 (or about $72/month [one pack per day]) which makes NRT almost twice as expensive as smoking. Fourth, it is unclear if and where behavioral interventions are provided within the healthcare system and telephone quit-lines do not exist. Given the lack of clinician training, the potential lack of access to pharmacological interventions, the cost differential between prescription and non-prescription medication, and the lack of accessible behavioral interventions, there is clearly a critical need to evaluate accessible, evidence based smoking cessation treatments that can be delivered within the clinical infrastructure in Kenya.

The evidence-base relating to tobacco treatment in the methadone maintenance program setting is limited, and only two published studies have explored methadone program-based tobacco treatment in countries that are not upper income (one in Vietnam58 and one in China59). The USPHS voices its strong support for tobacco treatment in methadone programs, stating that all individuals "with substance use disorders should be offered tobacco dependence treatment, and clinicians must overcome their reluctance to treat this population13." Listed among their priorities is research to define "the effectiveness and impact of tobacco dependence treatments within the context of nontobacco chemical dependency treatments13." The great majority (76-80%) of methadone-maintained smokers wish to quit60, but they face a

range of obstacles when trying to realize this goal, including pharmacodynamic interactions between nicotine and methadone (methadone increases tobacco use and smoking increases methadone dosing requirements61, fear of substance use relapse, high rates of smoking within social networks62, and the various psychosocial disadvantage that pervade the methadone maintenance population, e.g. poverty, psychiatric illness, and stigmatization. Similar to the tobacco treatment in PLWH experience, the range of strategies tried to promote cessation in methadone-maintained individuals have met with mixed and limited success60. Particularly relevant to the current proposal, one trial combined bupropion with a behavioral intervention, and the investigator reported a respectable 6-month biochemically-confirmed abstinence rate of 14% without any evidence of bupropion toxicity63. Whereas the literature on this topic exhibits a tendency to focus on challenges, it is important to point out the advantages that the methadone maintenance setting offers in the realms of tobacco treatment and research, especially the high levels of reliable follow-up (promising favorable rates of adherence to counseling protocols and low rates of attrition) and the substance use treatment mentality that obtains in the program environment. We cannot assume that the psychobehavioral characteristics of Kenyan PLWH methadone-maintained individuals match those described in the aforementioned studies (largely from US samples), so start-up activities in Y1 will include data collection to better characterize the Kenyan participants and allow us to optimize the tailoring of the PSF intervention. We expect that the revised PSF program that we develop in Y1 will include sections on the pharmacologic interactions of nicotine and methadone, the reality that smoking cessation does not increase illicit substance relapse rates, and strategies to promote social support and decrease exposure to other smokers in one's social network, etc.

Pharmacotherapy and behavioral therapy are the two pillars of tobacco treatment, and abundant evidence supports their efficacy alone and in combination in the general population19. However, the relative values of pharmaco- and behavioral therapy for PLWH smokers, both individually and in combination, remain unknown. In the general population, bupropion is an efficacious pharmacologic agent for smoking cessation. It (unlike varenicline) is available in Kenya at about ½ the cost of NRT. No large controlled trials using bupropion have been conducted among PLWH who smoke and it is likely that, as a result, an effective tobacco treatment for PLWH smokers may be significantly underutilized 20. The evidence base for behavioral therapy is similarly unclear with several trials demonstrating efficacy 21;22 and several showing no effect 23-26. Yet, evidence from a recent meta-analysis suggests that interventions tailored to the needs of PLWH who smoke (i.e., co-occurring psychiatric disorders and substance use) and use ≥8 sessions have a large and significant effect on smoking cessation27. In the following sections we review the existing evidence base, identify gaps that remain, and propose to answer 3 critical questions using a factorial design to test best psychopharmacological and psychosocial interventions for smoking cessation among PLWH living in Kenya who smoke.

Bupropion is an efficacious pharmacologic agent for smoking cessation. It's mechanism of action is not well understood but is believed to be related to inhibition of reuptake of dopamine, noradrenaline, and serotonin in the central nervous system as well as its action as a non-competitive nicotine receptor antagonist. A meta-analysis found that bupropion doubles the odds of quitting smoking compared with placebo. The most significant side effect is insomnia which occurs in 30-40% of recipients. The FDA-approved dose for bupropion for smoking cessation is 300mg per day. Bupropion has no reported interactions with methadone. Among PLWH who smoke, there has been only one small uncontrolled pilot study that reported bupropion was safe and provided significant benefit with respect to smoking cessation interventions64.Thus, while current data show that bupropion is safe in this population, no large-scale clinical trial has evaluated the efficacy of bupropion on smoking cessation outcomes among those with HIV/AIDS20.

To our knowledge, there have been 8 randomized control trials evaluating the efficacy of behavioral interventions plus nicotine replacement targeting smoking cessation among PLWH who smoke21-26;65;66. Some trials demonstrated efficacy21;22;65;66 and several showed no effect 23-26. We recently published a systematic review and meta-analysis in JAIDS 27, representing 1822 subjects from these eight smoking cessation studies. We found a statistically significant effect of behavioral interventions compared to control in increasing abstinence in HIV-infected smokers with a moderate effect size RR 1.51 (95% CI 1.17, 1.95). Of note, those studies with interventions of ≥8 sessions (such as the intervention we will be using: Positively Smoke Free) had a large effect size for the abstinence endpoint RR 2.88 (95% CI: 1.89-4.61).

Positively Smoke Free (PSF) is a suite of tailored behavioral tobacco treatments originally developed by Dr. Shuter under the auspices of an American Legacy Foundation research grant program. The tailoring was based upon formative work exploring psychobehavioral drivers of cigarette smoking in PLWH48, and was guided by input from HIV specialists, tobacco treatment experts, and many PLWH smokers. Two NIH-funded RCTs of PSF interventions have been completed and published21;67. A recent analysis of the pooled patient cohorts proved program efficacy in achieving smoking abstinence with an adjusted odds ratio of 2.99 [1.26-7.01], P=0.01 compared to standard care 68. Based on the promise of these pilot trials, NIDA is funding Dr. Shuter to conduct a definitive trial of PSF group therapy. The PSF group treatment is a structured 8 session program based on Bandura's Social Cognitive Theory model (i.e. emphasizing observational learning through discussion of real-life scenarios, promoting abstinence self-efficacy, anticipating likely challenges and planning appropriate responses, and fostering positive outcomes expectations for cessation and negative expectation for continued smoking) with an 86 page syllabus. Although PSF was originally developed as a group therapy intervention Drs. Himelhoch and Shuter have already successfully adapted PSF to an individual counseling format. Meta-analytic data as summarized in the 2008 PHS Tobacco Treatment Guidelines support the superiority of individual counseling over group therapy in achieving abstinence (aggregated odds ratios of 1.7 vs. 1.3)13. These recommendations also indicate that the efficacy of such behavioral interventions is increased by tailoring, by increasing numbers of sessions, and by combining them with pharmacotherapy13;19;48. Based on all of the aforementioned data, we believe that the PSF adapted to an individual counseling format that we propose represents the most effective available approach to behavioral treatment. Furthermore, combined use of pharmacological and behavioral interventions may improve the chances of maintaining long-term abstinence69 thus it is likely that PSF combined with bupropion represents the maximally aggressive approach to tobacco treatment for PLWH smokers in Kenya.

Research has not identified the best intervention in terms of a sustained abstinence endpoint or examined the impact of sustained abstinence on mortality risk. This highlights the need to study longer-term abstinence outcomes among PLWH who smoke, in order to identify interventions or combinations of interventions that will yield sustained cessation over time. There is a critical need to evaluate accessible, evidence based smoking cessation treatments that can be delivered in their intended format within the clinical infrastructure in Kenya. A logical next step is to employ a factorial design to define the individual and combined effects of maximalist pharmaco- and behavioral treatments on longer term abstinence.

Sub Study:
Alcohol and HIV
Globally, an estimated 2.3 billion people aged ≥ 15 years (43% of this population; 32% in Africa) take alcohol, while harmful use of alcohol was responsible for about 3 million deaths in 201634,46. Alcohol use is prevalent among PLHIV13,16 and in sub-Saharan African the region with the highest population of PLHIV this higher prevalence of alcohol use in this population has been well documented11,12,14,15,24. Further, alcohol use has been associated with male gender, cigarette smoking, alcohol use in the family, missed ART, mental distress, low CD4+ cell count and low income12,24. Alcohol use among PLHIV interferes with adherence to ART and retention in HIV care, which negatively affects viral suppression17–19. Harmful use of alcohol has also been shown to be associated with increased toxicity from ART, lower CD4+ cell count, increased opportunistic infections due to compromised immunity and higher resistance to ART20,21,23,36.

Alcohol and Non-communicable Diseases
The global increase in morbidity and mortality from NCD in low-, middle- and high-income countries is alarming. In 2016, alcohol use caused 1.7 million deaths (4.3% of NCD deaths) and 65.5m disability adjusted life years46. Alcohol consumption is associated with increased risk of cancers including liver, oral and pharyngeal cavity, esophageal, colon, rectal, breast and gallbladder27–29 and cardiovascular diseases (CVDs)25,26,30. In 2016, 0.4 million of the 9 million cancer deaths were attributed to alcohol use46. Similarly, alcohol use caused 0.6 million of the CVD-related deaths (3.3% of CVD deaths)46. Harmful alcohol consumption amongst PLHIV may further aggravate to the increased risk of NCD even among stable virally suppressed PLHIV on ART. The need to address this emerging trend in NCDs is paramount so as not to lose the gains made in fighting the HIV scourge and providing PLHIV with quality long life.

Co-occurrence of alcohol and tobacco use among PLWH in Kenya
The concomitant use of alcohol and cigarette is high in the general population and among PLHIV12,16,24. Although precise prevalence estimates of alcohol and smoking among PLWH are lacking in Kenya, the Kenyan Ministry of Health STEPWISE Survey 2015 (a nationally representative household survey of 4203 adults aged 18-69 years conducted in Kenya between April and June 2015) reported tobacco use to be strongly and significantly associated with higher odds of heavy alcohol consumption (unadjusted OR 6.9, 95% CI 4.4-10.8—tobacco users compared to non-tobacco users).33 Yet, Kenyans generally hold positive attitudes towards consumption of substances such as cigarettes (73%), packaged liquor (72%), traditional brew (69%), and other tobacco products (68%). These positive attitudes may severely underestimate the risk of cancer associated with using alcohol and tobacco together.

Behavioral interventions for alcohol cessation
Behavioral interventions including brief interventions and cognitive behavioral therapy, have been used to help reduce alcohol use among PLHIV with promising results41,42
We published a systematic review and meta-analysis in JAIDS representing 1822 subjects from these eight smoking cessation studies. We found a statistically significant

effect of behavioral interventions compared to control in increasing abstinence in HIV-infected smokers with a moderate effect size RR 1.51 (95% CI 1.17, 1.95). Of note, those studies with interventions of ≥8 sessions (such as the intervention we will be using: Positively Smoke Free) had a large effect size for the abstinence endpoint RR 2.88 (95% CI: 1.89-4.61).

4 * Provide the scientific or scholarly background, rationale, and significance of the research and how it will add to existing knowledge:

Smoking Rates among People Living with HIV/AIDS are Alarmingly High: Smoking is the leading preventable cause of death and disease in the developed nations. Worldwide estimates, albeit largely from cohorts in the developed world, suggest that people living with HIV/AIDS (PLWH) smoke at nearly three times the rate of the general population1-7. These extraordinary smoking rates are associated with greater AIDS related morbidity29;30 31, greater non-AIDS related morbidity (including non-AIDS cancers, cardiovascular disease, and pulmonary disease)32-39 and greater mortality40-43. Smoking significantly impacts the progression and outcome of HIV disease, and has been identified as the leading contributor to premature mortality among people with HIV14. In fact, a study from Denmark estimated that HIV-positive individuals lose more years from smoking than from HIV infection in and of itself44. In our view, shared by others in the field12-18 20, effective tobacco treatment strategies in the US would be the single most impactful intervention to improve survival in PLWH. A recent modeling study completed at Harvard estimated that an intervention with 10-25% in the US efficacy would save 106,000-265,000 life years45. As the reach of antiretroviral therapy (ART) improves throughout Africa, and life expectancies of PLWH improve there, the importance of tobacco use as a proximate and leading cause of morbidity and mortality is bound to escalate as will the need for effective tobacco treatments 46-49. Most PLWH who smoke want to quit 46-49. Although many interventions are effective in helping general population smokers quit 13, research examining outcomes of smoking cessation treatments for PLWH is limited to high income countries. To what degree these data translate to lower-income countries that may have greater challenges with health care infrastructure, resources and medication access is not clear. Thus, establishing the efficacy of interventions that are accessible to PLWH who reside in lower-middle income countries is of critical importance.

sub study:

Alcohol and HIV

Globally, an estimated 2.3 billion people aged ≥ 15 years (43% of this population; 32% in Africa) take alcohol, while harmful use of alcohol was responsible for about 3 million deaths in 201634,46. Alcohol use is prevalent among PLHIV13,16 and in sub-Saharan African the region with the highest population of PLHIV this higher prevalence of alcohol use in this population has been well documented11,12,14,15,24. Further, alcohol use has been associated with male gender, cigarette smoking, alcohol use in the family, missed ART, mental distress, low CD4+ cell count and low income12,24. Alcohol use among PLHIV interferes with adherence to ART and retention in HIV care, which negatively affects viral suppression17–19. Harmful use of alcohol has also been shown to be associated with increased toxicity from ART, lower CD4+ cell count, increased opportunistic infections due to compromised immunity and higher resistance to ART20,21,23,36.

Alcohol and Non-communicable Diseases

The global increase in morbidity and mortality from NCD in low-, middle- and high-income countries is alarming. In 2016, alcohol use caused 1.7 million deaths (4.3% of NCD deaths) and 65.5m disability adjusted life years46. Alcohol consumption is associated with increased risk of cancers including liver, oral and pharyngeal cavity, esophageal, colon, rectal, breast and gallbladder27–29 and cardiovascular diseases (CVDs)25,26,30. In 2016, 0.4 million of the 9 million cancer deaths were attributed to alcohol use46. Similarly, alcohol use caused 0.6 million of the CVD-related deaths (3.3% of CVD deaths)46. Harmful alcohol consumption amongst PLHIV may further aggravate to the increased risk of NCD even among stable virally suppressed PLHIV on ART. The need to address this emerging trend in NCDs is paramount so as not to lose the gains made in fighting the HIV scourge and providing PLHIV with quality long life.

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Supporting Literature

1 * Provide a summary of current literature related to the research: ***If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer box below.***

(1) Mamary EM, Bahrs D, Martinez S. Cigarette smoking and the desire to quit among individuals living with HIV. AIDS Patient Care STDS 2002;16:39-42.
(2) Kwong J, Bouchard-Miller K. Smoking cessation for persons living with HIV: a review of currently available interventions. J Assoc Nurses AIDS Care 2010;21:3-10.
(3) Niaura R, Shadel WG, Morrow K, Tashima K, Flanigan T, Abrams DB. Human immunodeficiency virus infection, AIDS, and smoking cessation: the time is now. Clin Infect Dis 2000;31:808-812.
(4) Tesoriero JM, Gieryic SM, Carrascal A, Lavigne HE. Smoking among HIV positive New Yorkers: prevalence, frequency, and opportunities for cessation. AIDS Behav 2010;14:824-835.
(5) Burkhalter JE, Springer CM, Chhabra R, Ostroff JS, Rapkin BD. Tobacco use and readiness to quit smoking in low-income HIV-infected persons. Nicotine Tob Res 2005;7:511-522.
(6) Moscou-Jackson G, Commodore-Mensah Y, Farley J, Digiacomo M. Smoking-Cessation Interventions in People Living With HIV Infection: A Systematic Review. J Assoc Nurses AIDS Care 2013.
(7) Lifson AR, Lando HA. Smoking and HIV: prevalence, health risks, and cessation strategies. Curr HIV/AIDS Rep 2012;9:223-230.
(8) Mwiru RS, Nagu TJ, Kaduri P, Mugusi F, Fawzi W. Prevalence and patterns of cigarette smoking among patients co-infected with human immunodeficiency virus and tuberculosis in Tanzania. Drug Alcohol Depend 2017;170:128-132. doi: 10.1016/j.drugalcdep.2016.11.006. Epub;%2016 Nov 12.:128-132.
(9) Uthman OA, Ekstrom AM, Moradi TT. Influence of socioeconomic position and gender on current cigarette smoking among people living with HIV in sub-Saharan Africa: disentangling context from composition. BMC Public Health 2016;%20;16:998. doi: 10.1186/s12889-016-3637-1.:998-3637.
(10) WHO Report on the Global Tobacco Epidemic, 2015: Country Profile, Kenya. 1-13. 2015.
Ref Type: Report
(11) Nturibi EM, Akinsola AK, McCurdy SA. Smoking prevalence and tobacco control measures in Kenya, Uganda, the Gambia and Liberia: a review. Int J Tuberc Lung Dis 2009;13:165-170.
(12) Lundgren JD, Battegay M, Behrens G et al. European AIDS Clinical Society (EACS) guidelines on the prevention and management of metabolic diseases in HIV. HIV Med 2008;9:72-81.
(13) Treating tobacco use and dependence: 2008 update U.S. Public Health Service Clinical Practice Guideline executive summary. Respir Care 2008;53:1217-1222.
(14) Davies TL, Gompels M, Johnston S, Bovill B, May MT. Mind the gap: difference between Framingham heart age and real age increases with age in HIV-positive individuals-a clinical cohort study. BMJ Open 2013;3:e003245.
(15) Grinspoon SK, Grunfeld C, Kotler DP et al. State of the science conference: Initiative to decrease cardiovascular risk and increase quality of care for patients living with HIV/AIDS: executive summary. Circulation 2008;118:198-210.
(16) Hoffman AC, Starks VL, Gritz ER. The impact of cigarette smoking on HIV/AIDS: urgent need for research and cessation treatment. AIDS Educ Prev 2009;21:1-2.
(17) Nahvi S, Cooperman NA. Review: the need for smoking cessation among HIV-positive smokers. AIDS Educ Prev 2009;21:14-27.
(18) Niaura R, Chander G, Hutton H, Stanton C. Interventions to address chronic disease and HIV: strategies to promote smoking cessation among HIV-infected individuals. Curr HIV/AIDS Rep 2012;9:375-384.
(19) Hartmann-Boyce J, Stead LF, Cahill K, Lancaster T. Efficacy of interventions to combat tobacco addiction: Cochrane update of 2013 reviews. Addiction 2014;109:1414-1425.
(20) Pacek LR, Cioe PA. Tobacco Use, Use Disorders, and Smoking Cessation Interventions in Persons Living With HIV. Curr HIV /AIDS Rep 2015;12:413-420.
(21) Moadel AB, Bernstein SL, Mermelstein RJ, Arnsten JH, Dolce EH, Shuter J. A randomized controlled trial of a tailored group smoking cessation intervention for HIV-infected smokers. J Acquir Immune Defic Syndr 2012;61:208-215.
(22) Vidrine DJ, Marks RM, Arduino RC, Gritz ER. Efficacy of cell phone-delivered smoking cessation counseling for persons living with HIV/AIDS: 3-month outcomes. Nicotine Tob Res 2012;14:106-110.
(23) Humfleet GL, Hall SM, Delucchi KL, Dilley JW. A randomized clinical trial of smoking cessation treatments provided in HIV clinical care settings. Nicotine Tob Res 2013;15:1436-1445.
(24) Lloyd-Richardson EE, Stanton CA, Papandonatos GD et al. Motivation and patch treatment for HIV+ smokers: a randomized controlled trial. Addiction 2009;104:1891-1900.
(25) Manuel JK, Lum PJ, Hengl NS, Sorensen JL. Smoking cessation interventions with female smokers living with HIV/AIDS: a randomized pilot study of motivational interviewing. AIDS Care 2013;25:820-827.
(26) Ingersoll KS, Cropsey KL, Heckman CJ. A test of motivational plus nicotine replacement interventions for HIV positive smokers. AIDS Behav 2009;13:545-554.
(27) Keith A, Dong Y, Shuter J, Himelhoch S. Behavioral Interventions for Tobacco Use in HIV-infected Smokers: A Meta-analysis. J Acquir Immune Defic Syndr 2016.
(28) Drummond MF, Sculpher MJ, Claxton K, Stoddart GL, Torrance GW. Methods for the Economic Evaluation of Health Care Programmes. 4 ed. Oxford, United Kingdom: Oxford University Press, 2015.
(29) Nieman RB, Fleming J, Coker RJ, Harris JR, Mitchell DM. The effect of cigarette smoking on the development of AIDS in HIV-1-seropositive individuals. AIDS 1993;7:705-710.
(30) Feldman JG, Minkoff H, Schneider MF et al. Association of cigarette smoking with HIV prognosis among women in the HAART era: a report from the women's interagency HIV study. Am J Public Health 2006;96:1060-1065.
(31) Cropsey KL, Willig JH, Mugavero MJ et al. Cigarette Smokers are Less Likely to Have Undetectable Viral Loads: Results From Four HIV Clinics. J Addict Med 2015.
(32) Metersky ML, Colt HG, Olson LK, Shanks TG. AIDS-related spontaneous pneumothorax. Risk factors and treatment. Chest 1995;108:946-951.
(33) Saves M, Chene G, Ducimetiere P et al. Risk factors for coronary heart disease in patients treated for human immunodeficiency virus infection compared with the general population. Clin Infect Dis 2003;37:292-298.
(34) Palella FJ, Jr., Phair JP. Cardiovascular disease in HIV infection. Curr Opin HIV AIDS 2011;6:266-271.
(35) Winstone TA, Man SF, Hull M, Montaner JS, Sin DD. Epidemic of lung cancer in patients with HIV infection. Chest 2013;143:305-314.
(36) De P, Farley A, Lindson N, Aveyard P. Systematic review and meta-analysis: influence of smoking cessation on incidence of pneumonia in HIV. BMC Med 2013;11:15.
(37) Akgun KM, Gordon K, Pisani M et al. Risk factors for hospitalization and medical intensive care unit (MICU) admission among HIV-infected Veterans. J Acquir Immune Defic Syndr 2013;62:52-59.
(38) Calvo-Sanchez M, Perello R, Perez I et al. Differences between HIV-infected and uninfected adults in the contributions of smoking, diabetes and hypertension to acute coronary syndrome: two parallel case-control studies. HIV Med 2013;14:40-48.
(39) Kingsley LA, Deal J, Jacobson L et al. Incidence and progression of coronary artery calcium in HIV-infected and HIV-uninfected men. AIDS 2015;29:2427-2434.
(40) Crothers K, Goulet JL, Rodriguez-Barradas MC et al. Impact of cigarette smoking on mortality in HIV-positive and HIV-negative veterans. AIDS Educ Prev 2009;21:40-53.
(41) Lifson AR, Neuhaus J, Arribas JR, Berg-Wolf M, Labriola AM, Read TR. Smoking-related health risks among persons with HIV in the Strategies for Management of Antiretroviral Therapy clinical trial. Am J Public Health 2010;100:1896-1903.
(42) Helleberg M, May MT, Ingle SM et al. Smoking and life expectancy among HIV-infected individuals on antiretroviral therapy in Europe and North America: The ART Cohort Collaboration. AIDS 2014.
(43) Morlat P, Roussillon C, Henard S et al. Causes of death among HIV-infected patients in France in 2010 (national survey): trends since 2000. AIDS 2014;28:1181-1191.
(44) Helleberg M, Afzal S, Kronborg G et al. Mortality attributable to smoking among HIV-1-infected individuals: a nationwide, population-based cohort study. Clin Infect Dis 2013;56:727-734.
(45) Reddy KP, Parker RA, Losina E et al. Impact of Cigarette Smoking and Smoking Cessation on Life Expectancy Among People With HIV: A US-Based Modeling Study. J Infect Dis 2016;214:1672-1681.
(46) Drach L, Holbert T, Maher J, Fox V, Schubert S, Saddler LC. Integrating smoking cessation into HIV care. AIDS Patient Care STDS 2010;24:139-140.
(47) Fuster M, Estrada V, Fernandez-Pinilla MC et al. Smoking cessation in HIV patients: rate of success and associated factors. HIV Med 2009;10:614-619.
(48) Shuter J, Bernstein SL, Moadel AB. Cigarette smoking behaviors and beliefs in persons living with HIV/AIDS. Am J Health Behav 2012;36:75-85.
(49) Burkhalter JE, Springer CM, Chhabra R, Ostroff JS, Rapkin BD. Tobacco use and readiness to quit smoking in low-income HIV-infected persons. Nicotine Tob Res 2005;7:511-522.

(50) Husain MJ, English LM, Ramanandraibe N. An overview of tobacco control and prevention policy status in Africa. Prev Med 2016;91S:S16-S22. doi: 10.1016/j.ypmed.2016.02.017. Epub;%2016 Feb 12.:S16-S22.
(51) Gichuki JW, Opiyo R, Mugyenyi P, Namusisi K. Healthcare Providers' Level of Involvement in Provision of Smoking Cessation Interventions in Public Health Facilities in Kenya. J Public Health Afr 2015;6:523.
(52) United Nations Office on Drugs and Crime. The global Afghan opium trade: A threat assessment, 2011. http://www.unodc.org/documents/data-and-analysis/Studies/Global_Afghan_Opium_Trade_2011-web.pdf . 2017.
Ref Type: Online Source
(53) Guise A, Kazatchkine M, Rhodes T, Strathdee SA. Editorial commentary: successful methadone delivery in East Africa and its global implications. Clin Infect Dis 2014;59:743-744.
(54) Lambdin BH, Masao F, Chang O et al. Methadone treatment for HIV prevention-feasibility, retention, and predictors of attrition in Dar es Salaam, Tanzania: a retrospective cohort study. Clin Infect Dis 2014;59:735-742.
(55) Mathers BM, Degenhardt L, Phillips B et al. Global epidemiology of injecting drug use and HIV among people who inject drugs: a systematic review. Lancet 2008;372:1733-1745.
(56) Mathers BM, Degenhardt L, Ali H et al. HIV prevention, treatment, and care services for people who inject drugs: a systematic review of global, regional, and national coverage. Lancet 2010;%20;375:1014-1028.
(57) Uthman OA, Ekstrom AM, Moradi TT. Influence of socioeconomic position and gender on current cigarette smoking among people living with HIV in sub-Saharan Africa: disentangling context from composition. BMC Public Health 2016;%20;16:998. doi: 10.1186/s12889-016-3637-1.:998-3637.
(58) Tran BX, Nguyen LH, Phan HT, Nguyen LK, Latkin CA. Preference of methadone maintenance patients for the integrative and decentralized service delivery models in Vietnam. Harm Reduct J 2015;12:29. doi: 10.1186/s12954-015-0063-0.:29-0063.
(59) Li L, Sangthong R, Chongsuvivatwong V, McNeil E, Li J. Multiple substance use among heroin-dependent patients before and during attendance at methadone maintenance treatment program, Yunnan, China. Drug Alcohol Depend 2011;116:246-249.
(60) Zirakzadeh A, Shuman C, Stauter E, Hays JT, Ebbert JO. Cigarette smoking in methadone maintained patients: an up-to-date review. Curr Drug Abuse Rev 2013;6:77-84.
(61) Talka R, Tuominen RK, Salminen O. Methadone's effect on nAChRs--a link between methadone use and smoking? Biochem Pharmacol 2015;97:542-549.
(62) de Dios MA, Stanton CA, Caviness CM, Niaura R, Stein M. The social support and social network characteristics of smokers in methadone maintenance treatment. Am J Drug Alcohol Abuse 2013;39:50-56.
(63) Richter KP, McCool RM, Catley D, Hall M, Ahluwalia JS. Dual pharmacotherapy and motivational interviewing for tobacco dependence among drug treatment patients. J Addict Dis 2005;24:79-90.
(64) Pedrol-Clotet E, Deig-Comerma E, Ribell-Bachs M, Vidal-Castell I, Garcia-Rodriguez P, Soler A. [Bupropion use for smoking cessation in HIV-infected patients receiving antiretroviral therapy]. Enferm Infecc Microbiol Clin 2006;24:509-511.
(65) Shuter J, Morales DA, Considine-Dunn SE, An LC, Stanton CA. Feasibility and preliminary efficacy of a web-based smoking cessation intervention for HIV-infected smokers: a randomized controlled trial. J Acquir Immune Defic Syndr 2014;67:59-66.
(66) Stanton CA, Papandonatos GD, Shuter J et al. Outcomes of a Tailored Intervention for Cigarette Smoking Cessation Among Latinos Living With HIV/AIDS. Nicotine Tob Res 2015;17:975-982.
(67) Shuter J, Morales DA, Considine-Dunn SE, An LC, Stanton CA. Feasibility and Preliminary Efficacy of a Web-Based Smoking Cessation Intervention for HIV-Infected Smokers: A Randomized Controlled Trial. J Acquir Immune Defic Syndr 2014;67:59-66.
(68) Shuter J, Moadel AB, Kim RS, Weinberger AH, Stanton CA. Self-Efficacy to Quit in HIV-Infected Smokers. Nicotine Tob Res 2014;ntu136.
(69) Stead LF, Lancaster T. Combined pharmacotherapy and behavioural interventions for smoking cessation. Cochrane Database Syst Rev 2012;10:CD008286. doi: 10.1002/14651858.CD008286.pub2.:CD008286.
(70) Rounsaville BJ, Carroll KM, Onken LS. A Stage Model of Behavioral Therapies Research: Getting Started and Moving on From Stage I. Clin Psychol 2001;8:133-142.
(71) Lloyd-Richardson EE, Stanton CA, Papandonatos GD et al. Motivation and patch treatment for HIV+ smokers: a randomized controlled trial. Addiction 2009;104:1891-1900.
(72) Vidrine DJ, Marks RM, Arduino RC, Gritz ER. Efficacy of Cell Phone-Delivered Smoking Cessation Counseling for Persons Living With HIV/AIDS: 3-Month Outcomes. Nicotine Tob Res 2011.
(73) Biochemical verification of tobacco use and cessation. Nicotine Tob Res 2002;4:149-159.
(74) Bedfont Scientific U. Stopping smoking and carbon monoxide. Medford: Bedfont Scientific LtD., 1993.
(75) Abrams DB, Biener L. Motivational characteristics of smokers at the workplace: A public health challenge. Prev Med 1992;21:679-687.
(76) Sacktor NC, Wong M, Nakasujja N et al. The International HIV Dementia Scale: a new rapid screening test for HIV dementia. AIDS 2005;19:1367-1374.
(77) Stanton CA, Papandonatos GD, Shuter J. Project Aurora: A culturally tailored intervention for cigarette smoking cessation among Latinos living with HIV/AIDS. . 2013. Boston, MA.
Ref Type: Generic
(78) Roddy E, Antoniak M, Britton J, Molyneux A, Lewis S. Barriers and motivators to gaining access to smoking cessation services amongst deprived smokers--a qualitative study. BMC Health Serv Res 2006;6:147.:147.
(79) Mohr DC, Duffecy J, Jin L. Internet treatment for depression supported by brief telephone support: A feasibility trial. Journal of Medical Internet Research. In press.
(80) Pagoto SL, McDermott MM, Reed G et al. Can attention control conditions have detrimental effects on behavioral medicine randomized trials? Psychosom Med 2013;75:137-143.
(81) DHHS USDoHaHSNCfHS. The third national heatlh and nutrion examination survey 1988-1994 (NHANES III). 1998. Center for Disease Control and Prevention.
Ref Type: Report
(82) Heishman SJ, Singleton EG, Moolchan ET. Tobacco Craving Questionnaire: reliability and validity of a new multifactorial instrument. Nicotine Tob Res 2003;5:645-654.
(83) Shiffman SM, Jarvik ME. Smoking withdrawal symptoms in two weeks of abstinence. Psychopharmacology (Berl) 1976;50:35-39.
(84) Velicer WF, Fava JL, Prochaska JO, Abrams DB, Emmons KM, Pierce JP. Distribution of smokers by stage in three representative samples. Prev Med 1995;24:401-411.
(85) DiClemente CC, Prochaska JO, Fairhurst SK, Velicer WF, Velasquez MM, Rossi JS. The process of smoking cessation: an analysis of precontemplation, contemplation, and preparation stages of change. J Consult Clin Psychol 1991;59:295-304.
(86) Prochaska JO, DiClemente CC, Norcross JC. In search of how people change. Applications to addictive behaviors. Am Psychol 1992;47:1102-1114.
(87) Morera O, Johnson T, Freels S et al. the measue of stage of readiness to change: Some psychometric considerations. Psychological Assessments 1998;10:182-186.
(88) Crittenden KS, Manfredi C, Warnecke RB, Cho YI, Parsons JA. Measuring readiness and motivation to quit smoking among women in public health clinics: predictive validity. Addict Behav 1998;23:191-199.
(89) DeClemente C, Prochaska J, Gibertinin M. Self-efficacy and the stages of self-change of smoking. Cognitive Therapy Research 1985;9:181-200.
(90) Janis IL, Mann L. Decision Making: A Psychological Analysis of Conflict, Choice, and Commitment. New York: The Free Press, 1977.
(91) Russell DW. UCLA Loneliness Scale (Version 3): reliability, validity, and factor structure. J Pers Assess 1996;66:20-40.
(92) Radloff LS. The CES-D Scale: A self-report depression scale for research in the general popuation. Applied Psychological Measurement 1977;1:385-401.
(93) Cacciola JS, Alterman AI, McLellan AT, Lin YT, Lynch KG. Initial evidence for the reliability and validity of a "Lite" version of the Addiction Severity Index. Drug Alcohol Depend 2007;87:297-302.
(94) Cancer Therapy Evaluation Program NCI. Common Terminology Criteria for Adverse Events (CTCAE) and Common Toxicity Criteria (CTC). http://ctep cancer gov/protocolDevelopment/electronic_applications/ctc htm [serial online] 2010; Accessed November 20, 2013.
(95) Cinciripini PM, Robinson JD, Karam-Hage M et al. Effects of varenicline and bupropion sustained-release use plus intensive smoking cessation counseling on prolonged abstinence from smoking and on depression, negative affect, and other symptoms of nicotine withdrawal. JAMA Psychiatry 2013;70:522-533.
(96) Cohen J. A power primer. Psychological Bulletin 1992;112:155-159.
(97) Benjamini Y, Yekutieli D. The control of the false discovery rate in multiple testing under dependency. Annals of Statistics 1997;29:1165-1188.
(98) MacKinnon DP, Fairchild AJ, Fritz MS. Mediation analysis. Annu Rev Psychol 2007;58:593-614.:593-614.

Sub Study:
1. UNAIDS. Global HIV & AIDS statistics - 2020 fact sheet. End Aids Epidermics. Published online 2020.
2. Rodger AJ, Lodwick R, Schechter M, et al. Mortality in well controlled HIV in the continuous antiretroviral therapy arms of the SMART and ESPRIT trials compared with the general population. AIDS. Published online 2013. doi:10.1097/QAD.0b013e32835cae9c
3. Keiser O, Taffé P, Zwahlen M, et al. All cause mortality in the Swiss HIV cohort study from 1990 to 2001 in comparison with the Swiss population. AIDS. Published

online 2004. doi:10.1097/00002030-200409030-00013
4. Trickey A, May MT, Vehreschild JJ, et al. Survival of HIV-positive patients starting antiretroviral therapy between 1996 and 2013: a collaborative analysis of cohort studies. Lancet HIV. Published online 2017. doi:10.1016/S2352-3018(17)30066-8
5. Egger M. Mortality of HIV-infected patients starting potent antiretroviral therapy: Comparison with the general population in nine industrialized countries. Int J Epidemiol. Published online 2009. doi:10.1093/ije/dyp306
6. Brinkhof MWG, Boulle A, Weigel R, et al. Mortality of HIV-infected patients starting antiretroviral therapy in sub-Saharan Africa: Comparison with HIV-unrelated mortality. PLoS Med. Published online 2009. doi:10.1371/journal.pmed.1000066
7. Juma K, Reid M, Roy M, et al. From HIV prevention to non-communicable disease health promotion efforts in sub-Saharan Africa: A Narrative Review. AIDS. Published online 2018. doi:10.1097/QAD.0000000000001879
8. Achwoka D, Waruru A, Chen TH, et al. Noncommunicable disease burden among HIV patients in care: A national retrospective longitudinal analysis of HIV-treatment outcomes in Kenya, 2003-2013. BMC Public Health. Published online 2019. doi:10.1186/s12889-019-6716-2
9. Nguyen KA, Peer N, Mills EJ, Kengne AP. A meta-analysis of the metabolic syndrome prevalence in the global HIV-infected population. PLoS One. Published online 2016. doi:10.1371/journal.pone.0150970
10. Patel P, Rose CE, Collins PY, et al. Noncommunicable diseases among HIV-infected persons in low-income and middle-income countries: A systematic review and meta-analysis. AIDS. Published online 2018. doi:10.1097/QAD.0000000000001888
11. Duko B, Ayalew M, Ayano G. The prevalence of alcohol use disorders among people living with HIV/AIDS: a systematic review and meta-analysis. Subst Abuse Treat Prev Policy. 2019;14(1):52. doi:10.1186/s13011-019-0240-3
12. Necho M, Belete A, Getachew Y. The prevalence and factors associated with alcohol use disorder among people living with HIV/AIDS in Africa: a systematic review and meta-analysis. Subst Abuse Treat Prev Policy. 2020;15(1):63. doi:10.1186/s13011-020-00301-6
13. Chander G, Josephs J, Fleishman JA, et al. Alcohol use among HIV-infected persons in care: Results of a multi-site survey. HIV Med. Published online 2008. doi:10.1111/j.1468-1293.2008.00545.x
14. Desmond K, Milburn N, Richter L, et al. Alcohol consumption among HIV-positive pregnant women in KwaZulu-Natal, South Africa: Prevalence and correlates. Drug Alcohol Depend. Published online 2012. doi:10.1016/j.drugalcdep.2011.07.004
15. Wandera B, Tumwesigye NM, Nankabirwa JI, et al. Alcohol consumption among HIV-infected persons in a large urban HIV clinic in Kampala Uganda: A constellation of harmful behaviors. PLoS One. Published online 2015. doi:10.1371/journal.pone.0126236
16. Galvan FH, Bing EG, Fleishman JA, et al. The prevalence of alcohol consumption and heavy drinking among people with HIV in the United States: Results from the HIV cost and services utilization study. J Stud Alcohol. Published online 2002. doi:10.15288/jsa.2002.63.179
17. Monroe AK, Lau B, Mugavero MJ, et al. Heavy alcohol use is associated with worse retention in HIV care. In: Journal of Acquired Immune Deficiency Syndromes. ; 2016. doi:10.1097/QAI.0000000000001083
18. Samet JH, Horton NJ, Meli S, Freedberg KA, Palepu A. Alcohol Consumption and Antiretroviral Adherence among HIV-Infected Persons with Alcohol Problems. Alcohol Clin Exp Res. Published online 2004. doi:10.1097/01.ALC.0000122103.74491.78
19. Hendershot CS, Stoner SA, Pantalone DW, Simoni JM. Alcohol use and antiretroviral adherence: Review and meta-analysis. J Acquir Immune Defic Syndr. Published online 2009. doi:10.1097/QAI.0b013e3181b18b6e
20. Hahn JA, Samet JH. Alcohol and HIV disease progression: Weighing the evidence. Curr HIV/AIDS Rep. Published online 2010. doi:10.1007/s11904-010-0060-6
21. Baum MK, Rafie C, Lai S, Sales S, Page JB, Campa A. Alcohol use accelerates HIV disease progression. AIDS Res Hum Retroviruses. Published online 2010. doi:10.1089/aid.2009.0211
22. Fisher JC, Bang H, Kapiga SH. The association between HIV infection and alcohol use: A systematic review and meta-analysis of African studies. Sex Transm Dis. Published online 2007. doi:10.1097/OLQ.0b013e318067b4fd
23. Azar MM, Springer SA, Meyer JP, Altice FL. A systematic review of the impact of alcohol use disorders on HIV treatment outcomes, adherence to antiretroviral therapy and health care utilization. Drug Alcohol Depend. Published online 2010. doi:10.1016/j.drugalcdep.2010.06.014
24. Duko B, Toma A, Abraham Y. Alcohol use disorder and associated factors among individuals living with HIV in Hawassa City, Ethiopia: A facility based cross- sectional study. Subst Abus Treat Prev Policy. Published online 2019. doi:10.1186/s13011-019-0212-7
25. Xi B, Veeranki SP, Zhao M, Ma C, Yan Y, Mi J. Relationship of Alcohol Consumption to All-Cause, Cardiovascular, and Cancer-Related Mortality in U.S. Adults. J Am Coll Cardiol. Published online 2017. doi:10.1016/j.jacc.2017.06.054
26. Rehm J, Shield KD, Roerecke M, Gmel G. Modelling the impact of alcohol consumption on cardiovascular disease mortality for comparative risk assessments: An overview. BMC Public Health. Published online 2016. doi:10.1186/s12889-016-3026-9
27. Boffetta P, Hashibe M. Alcohol and cancer. Lancet Oncol. Published online 2006. doi:10.1016/S1470-2045(06)70577-0
28. Hamajima N, Hirose K, Tajima K, et al. Alcohol, tobacco and breast cancer - Collaborative reanalysis of individual data from 53 epidemiological studies, including 58 515 women with breast cancer and 95 067 women without the disease. Br J Cancer. Published online 2002. doi:10.1038/sj.bjc.6600596
29. Bagnardi V, Rota M, Botteri E, et al. Alcohol consumption and site-specific cancer risk: A comprehensive dose-response meta-analysis. Br J Cancer. Published online 2015. doi:10.1038/bjc.2014.579
30. Parry CD, Patra J, Rehm J. Alcohol consumption and non-communicable diseases: Epidemiology and policy implications. Addiction. Published online 2011. doi:10.1111/j.1360-0443.2011.03605.x
31. Calvo-Sánchez M, Perelló R, Pérez I, et al. Differences between HIV-infected and uninfected adults in the contributions of smoking, diabetes and hypertension to acute coronary syndrome: Two parallel case-control studies. HIV Med. Published online 2013. doi:10.1111/j.1468-1293.2012.01057.x
32. Winston TA, Man SFP, Hull M, Montaner JS, Sin DD. Epidemic of lung cancer in patients with hiv infection. Chest. Published online 2013. doi:10.1378/chest.12-1699
33. MoH-Kenya. Kenya STEPwise Survey for Non Communicable Diseases Risk Factors 2015 Report.; 2015.
34. Hammer JH, Parent MC, Spiker DA, World Health Organization. Global Status Report on Alcohol and Health 2018.; 2018. doi:10.1037/cou0000248
35. Kalichman SC, Simbayi LC, Kaufman M, Cain D, Jooste S. Alcohol use and sexual risks for HIV/AIDS in sub-saharan Africa: Systematic review of empirical findings. Prev Sci. Published online 2007. doi:10.1007/s11121-006-0061-2
36. Pandrea I, Happel KI, Amedee AM, Bagby GJ, Nelson S. Alcohol's role in HIV transmission and disease progression. Alcohol Res Heal. Published online 2010.
37. Shuper PA, Neuman M, Kanteres F, Baliunas D, Joharchi N, Rehm J. Causal considerations on alcohol and HIV/AIDS - A systematic review. Alcohol Alcohol. Published online 2010. doi:10.1093/alcalc/agp091
38. Williams EC, Hahn JA, Saitz R, Bryant K, Lira MC, Samet JH. Alcohol Use and Human Immunodeficiency Virus (HIV) Infection: Current Knowledge, Implications, and Future Directions. Alcohol Clin Exp Res. Published online 2016. doi:10.1111/acer.13204
39. Baliunas D, Rehm J, Irving H, Shuper P. Alcohol consumption and risk of incident human immunodeficiency virus infection: A meta-analysis. In: International Journal of Public Health. ; 2010. doi:10.1007/s00038-009-0095-x
40. Mdodo R, Frazier EL, Dube SR, et al. Cigarette smoking prevalence among adults with HIV compared with the general adult population in the United States: Cross-sectional surveys. Ann Intern Med. Published online 2015. doi:10.7326/M14-0954
41. Kaner EFS, Beyer FR, Muirhead C, et al. Effectiveness of brief alcohol interventions in primary care populations. Cochrane Database Syst Rev. Published online 2018. doi:10.1002/14651858.CD004148.pub4
42. Papas RK, Sidle JE, Martino S, et al. Systematic cultural adaptation of cognitive-behavioral therapy to reduce alcohol use among HIV-infected outpatients in Western Kenya. AIDS Behav. Published online 2010. doi:10.1007/s10461-009-9647-6
43. Huis in 't Veld D, Skaal L, Peltzer K, Colebunders R, Ndimande J V., Pengpid S. The efficacy of a brief intervention to reduce alcohol misuse in patients with HIV in South Africa: Study protocol for a randomized controlled trial. Trials. Published online 2012. doi:10.1186/1745-6215-13-190
44. Lake JE, Currier JS. Metabolic disease in HIV infection. Lancet Infect Dis. Published online 2013. doi:10.1016/S1473-3099(13)70271-8
45. Hemkens LG, Bucher HC. HIV infection and cardiovascular disease. Eur Heart J. Published online 2014. doi:10.1093/eurheartj/eht528
46. World Health Organization. Global Status Report on Alcohol and Health 2018.; 2018.

2 If available, upload your applicable literature search:

Name	Created	Modified Date

There are no items to display

Study Procedures

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer boxes below. (If this study is a collaborative UM/VA study please list each procedure that is being conducted and the locations where it is being conducted.)

1 * Describe all procedures being performed for research purposes only (these procedures would not be done if individuals were not in the study) and when they are performed, including procedures being performed to monitor subjects for safety or to minimize risks:

Formative Sessions:
Prior to starting the main study, we will interview a set of individuals currently attending one of the recruitment clinics. The interview will either be a focus group (of about 8-10 individuals) or a stand alone interview. The purpose of the formative sessions is to learn about the population and ensure our study intervention and study guidance is appropriate for our audience.

Screening:
Screening will consist of a chart review for medical history. Additional screening questions will include: MINI International Neuropsychiatric Interview (Sections: Alcohol, Drug, and Suicide), Readiness to Quit Ladder, and Hopkins HIV Dementia Scale. Expired air CO will be assessed with using a Smokerlyzer-Breath Carbon Monoxide Monitor.

Baseline and Evaluation Phase (EP):
Upon completion of the consent and screening process, participants will enter the evaluation phase in which they will provide a thorough medical history including documentation of all medications including antiretroviral medication (via review of medical record) and complete a physical assessment- including vital signs--blood pressure, heart and respiratory rates, height and weight.

If a potential participant has been evaluated clinically within the last month, the research clinician may choose to rely on data from that evaluation per their clinical judgement and their clinical impression of need for replication of this data for the purpose of the eligibility evaluation. This would not include vital signs.

Pregnancy Testing:
Female participants who have the potential to become pregnant will have a pregnancy test during the evaluation phase and approximately monthly during the study (while taking study medication). They will be asked to use acceptable method of contraception during the medication phase of the study (week 1-12). Participants will sign a contraception consent to confirm their agreement (In the baseline packet). Condoms will also be provided at research appointments.

Baseline Interview:
Participants will also complete a series of assessment questionnaires (baseline interview). Vital signs will also be recorded. Only those continuing to meet full inclusion criteria and do not meet exclusion criteria will proceed to randomization and remain in the study. The list of assessments to be completed are located in the study schedule in the Additional Documents section.

Randomization
Study participants who are deemed eligible for the study will complete baseline testing and will then be randomized 1:1:1:1 to four study conditions: (1) Bupropion + PSF; (2) Bupropion + SOC; (3) Placebo + PSF; (4) Placebo + SOC. Participants will be randomly assigned to one of the four conditions using permuted blocks which will randomly vary in size. The research pharmacy will be notified of the drug randomization (Bupropion or placebo). All raters, investigators, and other staff will be blind to treatment assignment except for the dispensing pharmacist. Separate emergency unblinding envelopes for each participant will be kept in a locked cabinet at the dispensing pharmacy in the case of a medical emergency. All participants who are randomized will be taught the correct use of the study medication, and assisted in setting a quit date with the instruction to quit on approximately Day 8 (beginning of Week 2) following one week of medication.

Medication Intervention:
Once randomization is complete, participants will initiate medication treatment (either Bupropion or placebo) for smoking cessation with a quit date scheduled for approximately day 8 following first study dose of the medication. All medication will be provided to participants by the study team. Participants will receive a weekly supply of medication for the first two weeks to ensure proper dosing and monitor for adverse events. For the subsequent weeks of the trial, participants will return at week 4 and week 8 receive the next month's supply of medication. No smoking cessation information will provided during those meetings. Adverse events monitoring will continue. Dosage adjustments will be permitted in an effort to control adverse effects throughout the trial. This will allow us to balance internal validity with good clinical practice.

Bupropion (FDA approved for the indicated use):
Bupropion will be dosed at 150 mg/day (approximately days 1-3), then 150 mg twice per day (approximately days 4-7). After the 7th day, varenicline will be dosed at 150 mg twice per day for weeks 2-12 of the study. This is in accordance with package labeling.
Placebo:

Those who are not randomized to Bupropion will receive placebo medication that will be dosed on the same schedule as Bupropion. All participants regardless of condition will be supplied medication in identical form.

Therapy Intervention:
In addition to being randomized to Bupropion or placebo participants will be randomized to receive either Positively Smoke Free (PSF) or the standard of care control condition (see below). Those randomized to PSF will be contacted by a PSF interventionist within approximately 48 hours of being randomized to schedule their first appointment.

Positively Smoke Free (PSF):
PSF is an intensive, tailored, social cognitive theory-driven intervention that promotes cessation in PLWH smokers. Its development was guided by previous pilot work characterizing the sociobehavioral drivers of tobacco use in PLWH 40. It is an 8-session program, with session lengths ranging from 45-60 minutes. A syllabus serves as a guide for therapists. The course content has gone through multiple rounds of revision in response to input from intra and extra-institutional experts in HIV and smoking cessation, PLWH smokers, and the ID Clinic community advisory board. Themes of particular relevance to HIV-infected smokers permeate the course content, and the heterogeneity of the PLWH community and how this relates to smoking behaviors (i.e. similarities and differences between drug users, LGBT, and depressed individuals) is highlighted. The "microtargeting" of these subsets of PLWH has received the praise of group participants. An overview of the course content, including tailoring themes, has been previously published. All treatment sessions are audiotaped. If a participant misses an intervention session, we will call him/her to reschedule. If the participant is having difficulty attending some of the sessions in person, we will offer to conduct them over the telephone.

Control Condition
Those randomized to standard of care will receive of standard of care smoking cessation treatment by a trained research assistant at the time of randomization. Participants will be given a quit smoking brochure and brief advice to quit (i.e. < five minutes)

Follow Up Assessment Interviews:
All participants will be re-assessed at approximately week 12 and approximately week 36. Vital signs will also be recorded. All assessments will be administered in a confidential and private location by experienced research assistants who are masked to the results of randomization. The list of assessments to be completed are located in the study schedule in the Additional Documents section.

Participants will also complete a brief visit when they return at week 1, 2, 4, and 8 for their medication refill. All participants will complete vital signs as well as answer a few questions about their medication side effects (if any), medication adherence, their mood and smoking status.

Expired carbon monoxide (CO):
Expired air CO provides an accurate indirect measure of carboxyhemoglobin (COHb) level and is a standard biochemical method for assessing a smoker's level of intake. According to the SRNT Subcommittee on Biochemical Classification report, measuring CO provides a sensitivity and specificity of approximately 90% for current tobacco use. Expired air CO will be assessed with using a Smokerlyzer-Breath Carbon Monoxide Monitor.
Expired CO will be monitored at each visit (Screening, Evaluation Phase, Baseline, week 1, 2, 4, 8, 12, and week 36).

Implementation Costs Assessment is to estimate the organizational costs of implementing Positively Smoke Free services, using data from the study site. Data for the implementation costs assessment component will include the amount of personnel time spent completing each step in the Positively Smoke Free implementation process, including all training and supervision activities and all meetings required to set up Positively Smoke Free services. Personnel time will be multiplied by appropriate wage rates (i.e., the salary cost per hour or per year) for each person, and then fixed percentages will be added to account for additional personnel costs 28. The time use data for this component will come from project records of training meeting attendance and meeting duration as well as from a brief time use survey of personnel involved in delivering the intervention. Provider organizational and administrative expenses associated with the implementation process, such as the time costs of managing implementation activities and any friction costs associated with having to adapt to new workflow processes, will be included in implementation costs. These organizational/administrative implementation costs will be identified from qualitative interviews conducted with key informants (i.e., senior clinic administrators) at the study site, and then estimated based on clinic accounting records or based on imputed cost estimates, using standard economic cost imputation approaches 28adapted for the Kenyan context. The qualitative interviews will allow us to gain insight into the specific workflow or administrative changes that may have been required to implement Positively Smoke Free services. Other implementation resources may include clinic space and associated utilities, software licensing fees, computer use, and supplies. We will maintain detailed project records of these expenses or, as in the case of room space, we will create imputations in the standard ways based on the notion of resource opportunity cost 28. All cost estimates will be appropriately time-discounted and inflation-adjusted 28. The planned assessment will yield rigorously obtained approximations of total implementation costs at a new site of care. We will share these estimates in an annual project report to NIH and will also share them with our partners in Kenya.

Sub Study:
Procedures:
Create culturally congruent health education materials around cancer-related risks of tobacco and alcohol co-use to populations at high risk for the two behaviors such as PLWH who smoke in Kenya.

This will be completed by conducting focus groups and in-depth interviews with key informants, to evaluate understanding and acceptance of these educational materials, and iteratively update the Positively Smoke Free (PSF) syllabus to ensure maximal impact.

The proposed work will add a previously standardized group of questions to evaluate awareness of the link between alcohol and cancer at each of the parent study visits. These questions evaluated comparing baseline to 12-week follow-up and 36-week follow-up, will help to determine the extent, if any, the new material added to the PSF syllabus changes awareness of the link between alcohol and tobacco use and cancer.

The participants will be recruited from HIV clinics in Nairobi, Kenya. This protocol will use consent forms from the University of Nairobi. Their drafted consent forms are uploaded in the Additional Documents section. The results of this study will provide policymakers, community leaders and clinicians with critical evidence of the most effective alcohol and smoking cessation treatments for PLWH.

We are looking to consent approximately 70 individuals to either:

Option 1: Participate in a one time feedback group with other individuals who use alcohol – called a focus group (Topic questions are uploaded in the focus group section)

OR

Option 2: Participate in a one time private interview where the individual will have a one on one interview with a trained interviewer in a private area. (Interview questions are uploaded into the survey section)

Each option will take approximately 1 hour plus the time for consenting procedures.

The group discussion and the one on one interview will be audio-taped. The audio-tape will be used only by the research team to ensure we captured all information provided by the participants. The audio-tape will not be used for commercial or teaching purposes and will be destroyed at the end of the project.

2 * Describe all procedures already being performed for diagnostic or treatment purposes (if not applicable to the study, enter "N/A"):
n/a

3 * Describe the duration of an individual participant's participation in the study:
Approximately 6 months

Sub Study: Approximately 2 hours.

4 * Describe the amount of time it will take to complete the entire study:
Approximately 4 years

Sub Study:
Approximately 1 year.

5 * Describe any additional participant requirements:
n/a

Sample Size and Data Analysis

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer boxes below.

1 * Provide the rationale and sample size calculations for the proposed target population:

With a total of 300 participants and an estimated 20% attrition, we will have 60 participants per cell in the factorial design. This will provide a total of 120 participants per main effect condition (Drug or Psychosocial Intervention). Meta analyses119 of bupropion vs. placebo in the general population estimate the effect as an increase in abstinence from 10% with placebo to 25% with bupropion. The effect for PSF compared to SOC without any drug intervention is estimated to be an increase from 7% to 20%. Using a logistic regression model with alpha equal to .05 (two tailed) we will have greater than 80% power to detect these main effects. We will assess whether the combination of PSF and bupropion will have a simple additive effect on smoking abstinence (no interaction) or synergistic effect on smoking cessation (interaction). We will have 80% power to detect a 10% increase in relative abstinence when PSF is compared to SOC without bupropion to PSF compared to SOC with bupropion. Power was calculated using the PASS software. (Version 13, Logistic Regression Procedure.)

Overview of Analytic Methods:
The primary study analyses will adopt an intent-to-treat strategy. Data will be screened for errors using frequency and contingency tables and univariate and bivariate plots before formal analysis. These plots and summaries will allow us to be cognizant of data distribution characteristics before building regression models. To assess indication of self-selection bias, we will compare the demographic characteristics of the participants that agreed to participate in the study to those who were approached, but were not interested in participating.

Covariate Selection:
We expect, due to randomization and sufficiently large sample size, that demographic, clinical characteristic, and outcome variables at baseline in the four conditions will not be significantly different. However, we will perform tests for differences (imbalances) on demographic (e.g. age, race, gender) and other potential confounder variables across the four groups. Imbalances may occur in spite of the randomization procedure. If by chance there are important variables significantly out of balance we will add them as covariates in the models.

Sub study:
We will interview a set of individuals currently attending one of the recruitment clinics. The study anticipates to conduct at least 3 focus group (of about 8-10 individuals) discussions (FGDs) and stand-alone interviews with 50 participants to learn about the population and ensure our study intervention and study guidance is appropriate for our audience.

Please note:
We have increased the total N from 445 to 650, an increase of about 200. This was done for 2 reasons:

1. We previously added a sub study in a prior modification and did not increase the N at that time because enrollment numbers were lower. We have since then consented several individuals to the sub study and we are close to reaching our current N.

2. In the beginning, most individuals we consented for the main smoking study were eligible, however, after consenting approximately 200 individuals, we are having more difficulty consenting individuals who meet eligibility after screening. We may Consent 5 individuals and only 1 is eligible.

We are still keeping the main study at 300 individuals, therefore we are not updating the total N in the consent form. We may need to consent 400 people in order to have 300 eligible.

2 * Provide the plan for data analysis. Include in the description the types of comparisons that are planned (e.g., comparison of means, comparison of proportions, regressions, analysis of variance, etc.), which is the primary comparison/analysis, and how the analyses proposed will relate to the primary purposes of the study:

Primary Aims: We will use generalized linear mixed models (SAS, 9.3: Proc GLIMMIX) using a contrast for each post baseline time point to assess the main effects of bupropion vs. placebo(Drug) and PSF vs. SOC (Beh) on smoking cessation. In addition we will assess the interaction of Drug*Beh and any covariates that were identified above. The test of the hypotheses will be the test of whether the coefficients for the main effects and the interaction are significantly different from 0 based on the likelihood ratio test. If the interaction is significant, we will run additional analyses to explore the simple main effects and will interpret those as opposed to the main effects.

Exploratory Analyses:
Other smoking outcomes: We will use a Generalized Linear Mixed Model (GLMM; Proc MIXED) to assess if the treatment conditions have a significant effect on other smoking outcomes (e.g number of cigarettes smoked per day) over time. Treatment conditions, time and the interaction of time with the treatment conditions will be included in the model. A random intercept will be used to account for the non-independece of the repeated measures. An unstructured covariance matrix will be employed. Significant effects will be followed up with specific contrast statements.

Mediation: We will use Proc Mixed to assess the interventions impact on possible mediating variables for bupropion (craving, withdrawal) and for PSF (self-efficacy, depression, loneliness, substance abuse). Mediators will be assessed at 12 weeks, controlling for baseline. For those variables that are significant we will conduct additional analyses to determine if change in those mediators is related to smoking cessation at 24 weeks. If all conditions are met, we will use the MacKinnon 121 approach to formally assess for mediation of smoking cessation by the targets of the interventions.

Moderators: We will assess possible clinical (e. g. depression, smoking severity at baseline, years smoked) and demographic (e.g. age, race) moderators on smoking cessation. We use the analyses described in For Aims1-3 to assess moderation by including these variables and their interaction with the treatment conditions to the models.

Sub Study:
In order to adapt PSF we will follow recommended methods from Rounsaville's Stage Model of Behavioral Therapy Research. Our group already used similar methods in developing and adapting other behavioral interventions in the context of R34 grants as well as adapting the PSF syllabus for use in Nairobi. The adaptation will allow interventionists and clients at the methadone maintenance clinic an opportunity to review and comment on the format of the manualized intervention and make recommendations regarding treatment content with an eye toward cultural relevance and meaning. All additions to the workbook will be appropriately translated into Swahili with the translation verified by performing an independent back-translation. The updated workbook will be given to a purposive sample of clients and clinicians to review and mark up. We've completed multiple focus groups in the course of our formative work in the trial and are well positioned to complete new ones quickly and well. The results of these in-depth interviews will be summarized and reviewed by Drs. Himelhoch, Shuter and Ojoo. Based on the recommendations appropriate changes will be made to the PSF workbook.

We will add a series of standardized questions regarding alcohol consumption (e.g., quantity, frequency, and craving) to better describe the pattern and utilization of alcohol in the study sample. We will also add a series of questions developed by Bukyx et al. to evaluate awareness of the link between alcohol and cancer. All additional questions will be translated into Swahili with the translation verified by performing an independent back-translation. The analysis of change in awareness of the link between alcohol and tobacco use comparing baseline to 12-week follow-up and 36-week follow-up will be conducted by Dr. Deb Medoff, our study statistician, using methods and procedures already described in the parent study. Additionally, we will track longitudinal outcomes of alcohol use over time to determine if alcohol consumption changes as a result of the information provided by the updated PSF syllabus.

Please note:
We have increased the total N from 445 to 650, an increase of about 200. This was done for 2 reasons:

1. We previously added a sub study in a prior modification and did not increase the N at that time because enrollment numbers were lower. We have since then consented several individuals to the sub study and we are close to reaching our current N.

2. In the beginning, most individuals we consented for the main smoking study were eligible, however, after consenting approximately 200 individuals, we are having more difficulty consenting individuals who meet eligibility after screening. We may Consent 5 individuals and only 1 is eligible.

We are still keeping the main study at 300 individuals, therefore we are not updating the total N in the consent form. We may need to consent 400 people in order to have 300 eligible.

Sharing of Results

1 * Describe whether results (study results or individual subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings) will be shared with subjects or others (e.g., the subject's primary care physicians) and if so, describe how it will be shared:

During the pre-screening phase if abnormalities are found , they will be shared with the participant and the participant's HIV clinician with their consent.

Sub Study:
Overall results will be shared with the University and public. No individual results will be reported to participants.

ID: VIEW4E02808CBD800
Name: v2_Sharing of Results

Research with Drugs or Biologics

You indicated on the "Type of Research" page that your study involves use of unapproved drug(s)/biologic(s) or approved drug(s)/biologic(s) whose use is specified in the protocol AND/OR evaluation of food(s) or dietary supplement(s) to diagnose, cure, treat, or mitigate a disease or condition.

1 * List all drugs/biologics to be administered in this study. Be sure to list each drug/biologic with its generic name only.

	Drug Name	FDA Approved	IND Number	PI IND Holder
View	Bupropion (Wellbutrin)	yes		no

2 * Attach the drug package insert or investigational drug brochure for the drugs being administered in this study:

Bupropion Drug Package Insert.docx(0.01) 11/8/2017 11:47 AM 11/8/2017 11:47 AM

3 If more than one drug is administered, discuss the risk implications of drug/therapy interactions:

4 * Will you be using Investigational Drug Services?

○ Yes ● **No**

ID: VIEW4E0916E6E1400
Name: v2_Research with Drugs or Biologics

Drug or Biologic Storage and Handling

4.1 * Do you have a plan regarding access controls for essential and approproate research personnel?
● **Yes** ○ No

4.2 * Will you have procedures for verifying physical access to the drugs(s)?
● **Yes** ○ No

4.3 * Will you label the drug(s) so that it is (they are) used appropriately for the study?
● **Yes** ○ No

4.4 * Will there be an establishment of a drug transfer process both into and out of the research site?
● **Yes** ○ No

4.5 * Will the storage of the drug(s) be in a secure environment and include locks on doors and controlled access?
● **Yes** ○ No

4.6 * Do you have a plan for only allowing trained personnel to administer the drug(s)?
● **Yes** ○ No

4.7 If applicable, will the storage of the drug(s) be at the appropriate temperature, with a storage and temperature log?
● **Yes** ○ No

ID: VIEW4E1D85CC57C00
Name: v2_Drug or Biologic Storage and Handling

Placebos

1

* Is this study placebo controlled?

(●) **Yes** ( ) No

ID: VIEW4E0514EECCC00
Name: v2_Placebos

Placebo Use

You indicated that this study is placebo-controlled.

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer box below.

1.1 * Justify the use of the placebo study design and how the benefit to society outweighs the risks to the participants:

Results of 3 small, uncontrolled pilot studies have evaluated the safety and tolerability of bupropion among PLWH who smoke 30-33. These uncontrolled pilot studies found that bupropion was safe and provided significant benefit with respect to smoking cessation interventions among PLWH. However, no large controlled trials using bupropion have been conducted among PLWH who smoke. While current data show that bupropion is safe for smokers, no large-scale clinical trial has evaluated the efficacy of bupropion on smoking cessation outcomes among those with HIV/AIDS. This comparison is critical as bupropion may represent a superior treatment option55.

Those who are not randomized to bupropion will receive placebo medication that will be dosed on the same schedule as bupropion. All participants regardless of condition will be supplied medication in identical form in blister packs. Rationale for not including NRT: We chose not to offer NRT as part of the trial based on conflicting evidence of its efficacy among PLWH. Specifically, 2 RCTs demonstrated efficacy of nicotine replacement therapy both alone and combined with behavioral therapy 34;98, while two RCTs showed no effect of NRT on cessation rates31;53. In addition to this uncertainty some participants prefer not to use NRT given past experience of side effects, lack of effect or strong preference not to use it 99 which may limit a subject's interest in participating in the study or following through with study procedures.

1.2 * Is the placebo being used in place of standard therapy?

○ Yes ● **No**

1.3 * Is the standard treatment considered effective?

● **Yes** ○ No

ID: VIEW4E0514D79B400
Name: v2_Placebo Use

Psychological/Behavioral/Educational Methods & Procedures

You indicated on the "Type of Research" page that your study involves a psychological/behavioral/educational method or procedure such as a survey, questionnaire, interview, or focus group.

1 * Select all behavioral methods and procedures which apply to this study:

- [x] **Surveys/questionnaires**
- [ ] Key informant or semi-structured individual interviews
- [x] **Focus groups or semi-structured group discussions**
- [x] **Audio or video recording/photographing**
- [ ] Educational tests or normal educational practices (education instructional strategies, techniques, curricula, or classroom management methods)
- [ ] Individual or group behavioral observations
- [x] **Psychosocial or behavioral interventions**
- [ ] Neuropsychological or psychophysiological testing
- [ ] Deception
- [ ] Other psychosocial or behavioral procedures

ID: VIEW4E09416F57800
Name: v2_Psychological/Behavioral/Educational Methods and Procedures

Surveys/Questionnaires

You indicated that this study involves surveys and/or questionnaires.

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer boxes below.

1 * List all questionnaires/surveys to be used in the study, including both standardized and non-standardized assessments:

Program Satisfaction Survey
Study Contamination Questionnaire
Center for Epidemiologic Studies Depression Scale (CES-D)
UCLA Loneliness Scale
Smoking Temptation Scale
Abstinence Self-Efficacy Scale
Shiffman/Jarvik Withdrawal Questionnaire (SWQ)
Addictions Severity Index Lite (ASI-Lite)
Smoking Decisional Balance Questionnaire
The Smoking History Form
Demographic and History Questionnaire
Medication Side Effects
Time line follow back
Expired CO Monitoring

Readiness to Quit Ladder
Hopkins HIV Dementia Scale
MINI International Neuropsychiatric Interview (Suicide, Drug and Alcohol Sections)

Substudy:
1. Demographics and clinical history
2. Smoking History and Dependence
3. Motivation to Quit
4. Alcohol Use and History
5. Short Interview of Problems
6. Alcohol Urge Questionnaire
7. Alcohol Outcome Expectancies Scale
8. Alcohol Abstinence Self Efficacy Scale
9. Locus of Control
10. Substance Use Questionnaire
11. Depression and Anxiety Questionnaire
12. Alcohol Use Addendum

2 * Upload a copy of all questionnaires/surveys:

Name	Created	Modified Date
Alcohol use addendum.docx(0.01)	8/1/2022 8:15 AM	8/1/2022 8:15 AM
Sub study interview.docx(0.01)	2/24/2021 12:54 PM	2/24/2021 12:54 PM
Quit ladder.pdf(0.01)	10/17/2017 11:34 AM	10/17/2017 11:34 AM
MINI_Updated1_4_17.pdf(0.01)	10/17/2017 11:34 AM	10/17/2017 11:34 AM
HIV Dementia Scale (modified).pdf(0.01)	10/17/2017 11:34 AM	10/17/2017 11:34 AM
MIRECC HIV Smoking Program Satisfaction (42418 - Activated, Traditional).pdf(0.01)	10/17/2017 11:33 AM	10/17/2017 11:33 AM
MIRECC HIV Smoking Study Contamination (42439 - Activated, Traditional).pdf(0.01)	10/17/2017 11:32 AM	10/17/2017 11:32 AM
Baseline Packet 5_24_17.pdf(0.01)	10/17/2017 11:32 AM	10/17/2017 11:32 AM
Week 12 Packet 5_24_17.pdf(0.01)	10/17/2017 11:32 AM	10/17/2017 11:32 AM
Week 36 Packet 7_25_17.pdf(0.01)	10/17/2017 11:31 AM	10/17/2017 11:31 AM

3 * What is the total length of time that each survey is expected to take?

Each individual assessment should take approximately 3-5 minutes.

4 * Are any of the questions likely to cause discomfort in participants or cause harm if their confidentiality were breached? (i.e., Illegal activities)

● **Yes** ○ No

5 * Do any questions elicit information related to the potential for harm to self or others?

● **Yes** ○ No

5.1 If Yes, what procedures are in place to assure safety?

Screening: If a potential participant scores positive for the suicide screening, he/she will be referred to psychiatric services that are on site at the clinic for further evaluation.

Baseline and other time points: During the baseline interview and all subsequent interview time points (Week 1,2,4,8, 12 and 36), we will be administering a suicide questionnaire (MINI suicide model) as well as a medication side effects check list. If, during the course of a meeting, a participant endorses HI or SI behavior, we will follow our Suicidal or Homicidal Ideation/Intent Checklist (attached in Additional Documents). The document clearly details what do to and who to contact in a situation. Dr. Ojoo is a Physician and will be the first contact in many situations. We are also recruiting at clinic sites, so there will also be several clinicians available on site if needed.
We will also hand out our study business cards at several time points for the study. The card has our contact information on the one side and crisis information and hotline numbers on the second side (attached in Additional Documents).
The CES-D evaluates depressive symptoms but does not assess suicidal ideation or intent. It is important to note that the CES-D is not a diagnostic scale. If a participant has a score of greater than 16 on the CES-D will be referred for further evaluation by a study PI.
ASI-Lite: We will be requesting a certificate of confidentiality,
For All participants: We will provide them with information regarding what to do in case of a psychiatric emergency including contacting a Crisis hotline or going to the closest emergency department for further assessment.

Focus Groups

You indicated that this study involves focus groups or semi-structured group discussions.

1 * Are any of the questions likely to cause discomfort in participants or cause harm if their confidentiality were breached? (i.e., Illegal activities)

○ Yes ● **No**

2 * Upload a copy of the interview script or guide that will be used to guide the interviews:

Name	Created	Modified Date
Focus Group Guide .docx(0.01)	2/24/2021 12:54 PM	2/24/2021 12:54 PM

3 * How much time are the groups expected to require?

Approximately 1 hour

4 * How will the data be recorded?

It will be audio taped

5 * Do any questions elicit information related to the potential for harm to self or others?

○ Yes ● **No**

5.1 If Yes, what procedures are in place to assure safety?

ID: VIEW4E094A8F91800
Name: v2_Focus Groups

Audio or Video Recording/Photographs

You indicated that this study involves audio or video recording/photographing.

1

* Indicate the type of recording (check all that apply):

- [ ] Video
- [x] **Audio**
- [ ] Still Photo
- [ ] Other

1.1

If Other, specify:

2

* What is the purpose of the recording? (i.e., for therapeutic purposes, to establish treatment fidelity, or to establish reliability of assessments)

Our procedure for ongoing monitoring/supervision of interventionists involves weekly supervision in which Dr. Bennett (co-PI) reviews digital recordings of treatment sessions (all treatment sessions are audio taped), and clinical feedback is provided.

sub study:
The audio-tape will be used only by the research team to answer our research questions. To ensure we collected all information correctly provided during the interaction.

3

* Could the recording be likely to cause discomfort in participants or cause harm if their confidentiality were breached?

- ○ Yes
- ● **No**

4

* How will individuals' identities be protected?

Only first names will be used during the sessions and participants will be reminded not to use identifiable statements during the taping.

Behavioral Intervention

You indicated that this study involves psychosocial or behavioral interventions.

1 * Describe the intervention (duration, number of sessions, focus, etc.):

Positively Smoke Free (PSF): PSF is an intensive, tailored, social cognitive theory-driven intervention that promotes cessation in PLWH smokers. Its development was guided by previous pilot work characterizing the sociobehavioral drivers of tobacco use in PLWH 40. It is an 8-session program, with session lengths ranging from 45-60 minutes. A syllabus serves as a guide for therapists. The course content has gone through multiple rounds of revision in response to input from intra and extra-institutional experts in HIV and smoking cessation, PLWH smokers, and the ID Clinic community advisory board. Themes of particular relevance to HIV-infected smokers permeate the course content, and the heterogeneity of the PLWH community and how this relates to smoking behaviors (i.e. similarities and differences between drug users, LGBT, and depressed individuals) is highlighted. The “microtargeting” of these subsets of PLWH has received the praise of group participants.

ID: VIEW4E0BC12A9F800
Name: v2_Behavioral Interventions

Data Collection/Record Review

You indicated on the "Type of Research" page that your study involves data collection or record review (i.e., chart review, not self-report).

1 * What type of data will be collected/analyzed in this study? (Check all that apply)

- [ ] Retrospective/Secondary Analysis (data has already been collected at the time of initial IRB submission)
- [x] **Prospective (data is not yet in existence and/or collected)**

2 * Will this study involve adding data to a registry or database for future use?

○ Yes ● **No**

3 * Will the data be released to anyone not listed as an investigator on the protocol?

○ Yes ● **No**

3.1 If Yes, give name(s) & affiliation(s):

ID: VIEW4E0E25A8CA400
Name: v2_Data Collection / Record Review

Prospective Data

You indicated that the study involves the collection of prospective data.

1 * Where is the data being collected from? (Check all that apply)

- [x] **Medical records**
- [ ] Medical images
- [ ] Commercial (for profit) entity
- [ ] Publicly available records
- [ ] Schools
- [ ] Other

1.1 If Other, please specify:

2 * What data fields will you have access to/collect for the study? For example, name, initials, date of birth, Social Security number, income, demographic information, family units, housing, etc.

Names
Date of Birth
demographic information
CD4 count and Viral Load
medication use
Methadone Dose
Health Outcomes and hospitalizations

You can also upload a copy of the data fields/variables to be collected for the study:

Name	Created	Modified Date
There are no items to display		

Clinical Trial Registration

You indicated on the "Type of Research" page that your study is a clinical trial.

1 * Does the UM Clinical Trials Registry policy require registration of this trial?

● **Yes** ○ No

2 * Has this trial been registered?

● **Yes** ○ No

ID: VIEW4E093BF078C00
Name: v2_Clinical Trial Registration

Clinical Trial Registration Information

You indicated that this clinical trial has been registered.

1 * Was this trial registered at www.clinicaltrials.gov?
(●) **Yes** ( ) No

2 If no, was this trial registered on a site other than clinicaltrials.gov?
( ) Yes ( ) No

2.1 If Yes, specify the name of the other site:

2.2 Provide justification for registering this trial on this site:

3 * Registration Number
NCT03342027

ID: VIEW4E093BF1D0800
Name: v2_Clinical Trial Registration Information

Participant Selection

1 * How many local potential participants (or specimens/charts) do you anticipate will be screened for this study? ***Screening includes determining potential participants' initial eligibility for and/or interest in a study.***
1100

2 * How many participants (or specimens, or charts) will be enrolled/used for this study? ***A local prospective participant is considered enrolled in the study when a UM-approved Informed Consent Document (not including separate screening consent forms) is signed.***

Local - the number being enrolled at this site:
0

Worldwide - the number being enrolled total at all sites (including local enrollment):
650

3 * Gender:

- [x] **Male**
- [x] **Female**

4 * Age(s):

- [ ] 0 to 27 days (newborn infants)
- [ ] 28 days to 12 months (Infant)
- [ ] 13 months to 23 months (Toddler)
- [ ] 2 to 5 years (Preschool)
- [ ] 6 to 11 years (Child)
- [ ] 12 to 17 (Adolescents)
- [x] **18 to 88 years (Adult)**
- [ ] 89 years and older

5 * Race/Ethnicity:

- [x] **All Races Included**
- [ ] American Indian or Alaskan Native
- [ ] Asian/Other Asian
- [ ] Asian/Vietnamese
- [ ] Black or African American
- [ ] Hispanic or Latino
- [ ] Mixed Race or Ethnicity
- [ ] Native Hawaiian or Pacific Islander
- [ ] White or Caucasian

6

* Language(s):

- [x] **English**
- [ ] Chinese
- [ ] French
- [ ] Italian
- [ ] Japanese
- [ ] Korean
- [ ] Local Dialect

- [ ] Spanish
- [ ] Vietnamese
- [x] **Other**

6.1 Specify Other:
Swahili

7 * Are you excluding a specific population, sub-group, or class?
○ Yes ● **No**

7.1 If Yes, indicate your justification for excluding a specific population, sub-group, class, etc.:

Vulnerable Populations

1 * Will you be targeting ANY of the following Vulnerable Populations for enrollment? (Select all that apply)

- [ ] Employees or Lab Personnel
- [ ] Children (Minors)
- [ ] Cognitively Impaired/ Impaired Decision Making Capacity
- [ ] Pregnant Women/Fetuses
- [ ] Wards of the State
- [ ] Students
- [ ] Prisoners
- [ ] Nonviable Neonates or Neonates of Uncertain Viability
- [ ] Economically/Educationally Disadvantaged
- [x] **None of the above**

Only select populations which you will be targeting for enrollment. Do not include populations that may be enrolled incidentally. Enrollment of a vulnerable population is considered to be "targeted" if the study team will be aware that a subject is from a vulnerable group as a result of interaction with the subject or collection of specific information about the subject, and the research team does not wish to exclude them. "Incidental" enrollment is limited to situations where a study team is unaware that a subject is from a vulnerable group.

Eligibility

1 * Do you have an existing Eligibility checklist(s) for this study?

● **Yes** ○ No

1.1 If Yes, upload here. If you need a template, you can download it by clicking **HERE**. The checklists you upload will also be available under the Documents tab of this application.

Name	Created	Modified Date
Sub Study Eligibility (1).doc(0.01)	2/26/2021 8:58 AM	2/26/2021 8:58 AM
InclusionExclusion (2).doc(0.03)	9/21/2017 3:05 PM	11/14/2018 9:31 AM
Formative Eligibililty Form.doc(0.01)	11/13/2018 9:22 AM	11/13/2018 9:22 AM

1.2 If No, create an eligibility checklist below:

List inclusion criteria (List each Inclusion Criteria individually, using the ADD button):

Number	Criteria
There are no items to display	

List exclusion criteria (List each Exclusion Criteria individually, using the ADD button):

Number	Criteria
There are no items to display	

After entering the inclusion and exclusion criteria above, click the Save link. CICERO will automatically generate a printable Eligibility Checklist for you to use in your research. To review the checklist, click on the resulting link below. This checklist is also available under the Documents tab of this application.

Eligibility Checklist for HP-00077523_6 v2-26-2021-1614347906779(0.01)

ID: VIEW4E0E5185F9000
Name: v2_Eligibility

Recruitment

1 * Describe plans for recruitment, including the identification of potential participants (or acquisition of charts/records/samples) and initial interactions with them: (If this study involves the VA please list all sites at which recruitment will take place.):

main study and sub study:
Potential participants will be referred by their treatment team or through self-referral via IRB approved flyers that will be posted in the waiting room at the clinic sites. Potential participants will be screened in the clinic on a scheduled screening visit day. During screening, the RA will briefly describe the study protocol, including potential risks and benefits and obtain written consent for completion of the screening questions. Potential participants who do not meet all inclusion criteria or meet any of the exclusion criteria will not be eligible for the study.

We will also obtain a list of current clinic participants so that we can screen the clinic for eligible participants. All eligible individuals will be reviewed with the clinic staff to ensure they are stable enough to approach for the study.

2 * Describe measures that will be implemented to avoid participant coercion or undue influence (if not applicable to the study, enter "N/A"):

Participants will be reminded at every visit that their participation is completely voluntary and neither their care will not be affected by their willingness to participate or not.

3 * Who will recruit participants (or acquire charts/records/samples) for this study? (Check all that apply)

- [ ] PI
- [x] **Study Staff**
- [ ] Third Party

3.1 If you are using a third party, specify Third Party Recruiters:

4 Upload any recruitment tools such as screening/telephone scripts and introductory letters (do not upload advertisements here):

Name	Created	Modified Date

There are no items to display

Advertising

1 * Will you be using advertisements to recruit potential participants?

● **Yes** ○ No

ID: VIEW4E0BCCF811000
Name: v2_Advertising

Advertising Detail

You indicated that you will be using advertisements to recruit potential participants.

1.1 * Select the mode(s) of advertising (check all that apply):

- [ ] Radio
- [ ] Internet
- [x] **Print**
- [ ] Television
- [ ] Other

1.1.1 If Other, specify:

1.2 * Provide exact text of all proposed advertisement(s):

Do you want to quit smoking? Are you willing to join a research study?
University of Maryland Baltimore is looking for 300 volunteers to participate in a research study on various smoking cessation treatments.

You qualify for the study if you are: HIV positive, age 18 and above, smoked at least one cigarette in the last week. willing to quite smoking, if a woman, should not be pregnant or be a nursing mother.
Qualified participants will receive: study related counseling on how to quit smoking, study related medicines, compensation for travel and study related time.
Study length: 36 weeks
Screening and evaluation visits, baseline visit and follow up visit.
Benefits: Participants will receive counseling sessions on how to quit smoking. Receiving medication that can assist with quitting smoking.

Did you know that when you smoke: people with HIV are more likely to develop harmful consequences of smoking then those without HIV.
you are more likely to get pneumonia and asthma attaches.
You are more likely to suffer from cancer. You spend money that could be used on other things.
You harm the health of your children and those around you.
The good new is that when you quit: you will be less likely to get pneumonia, asthma and cancer, You will protect your children and those around you.

For more information, please call
University of Maryland Baltimore Smoking cessation study
on: 0741935184 or 0741935186 or 0741935187
Or visit the clinic located at the Methadone clinic;
Mathari National Teaching and Referral Hospital in Muthaiga, along Thika Road.

Sub Study Flyer:
We want to hear your thoughts about HIV, cancer and Alcohol.
Are you willing to join a research study?
University of Maryland Baltimore is looking for volunteers to participate in a research study. You will either complete a one-time interview or participate in a focus group (a group of about 6-8 people responding to several questions in a group room setting).

You qualify for the study if you are: HIV positive, age 18 and above and a smoker
Study length: 1 day
Screening and an interview or screening and a focus group.
Benefits: Participants may learn more about smoking, cancer, and alcohol

For more information, please call
University of Maryland Baltimore Smoking cessation study
on: 0741935184 or 0741935186 or 0741935187
Or visit the clinic located at the Methadone clinic;
Mathari National Teaching and Referral Hospital in Muthaiga, along Thika Road.
Study leads are Dr. Seth Himelhoch (Maryland) and Dr. Emily Koech (Kenya).

1.3 * Upload advertisement(s) here:

Name	Created	Modified Date
English brochure Back - main study (2).pdf(0.01)	4/9/2021 11:39 AM	4/9/2021 11:39 AM
Substudy Flyer.docx(0.01)	3/4/2021 10:25 AM	3/4/2021 10:25 AM
English brochure_Front_Main study.jpg(0.01)	3/4/2021 10:09 AM	3/4/2021 10:09 AM

Research Related Risks

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer box below.

1 * Individually list each research-related risk, using a separate line for each. Next to each risk, delineate the likelihood/seriousness of the risk, and the provisions for minimizing the risk:

Risks associated with the use of bupropion include allergic reactions (most commonly skin rashes and itching), dry mouth (10%), insomnia (30%), dizziness, tremor, and headaches. Of these, dry mouth and insomnia are most common. These problems are generally well tolerated and transient. The risk of seizure, when using sustained-release bupropion in the dose range used in this study, is 0.1%, a rate similar to that of other antidepressants.

Risks related to participating in research interviews (Research Risk). The risk from research interviews is minimal and relatively uncommon. During assessments participants may be uncomfortable discussing their smoking habits or mental health history and treatments. Participants may become frustrated and tense when they encounter difficulty when completing these measures. Careful planning and observation of the participant's response to these sessions will allow the testing to be completed with a minimum of discomfort. Participants will take breaks when necessary to help alleviate any discomfort. All interviews are trained to recognize signs of distress or anxiety. The participant will be reminded that they can refuse to answer any question that makes them uncomfortable and may take breaks whenever they are needed. There is a slight risk of breach of confidentiality. All data will be coded with an ID number that is unique. All data including information from chart reviews, therapist reports and laboratory results will be label by ID only. Only the study team will have access to the link between the ID and participant's name. Data containing names and personal information will never be included in published materials.

Risks related to participating in Behavioral Treatment for Smoking Cessation (Therapeutic Risk). The behavioral treatment sessions may cause some temporary anxiety or distress due to discussing smoking habits and attempts to quit smoking. The interventionists are all trained mental health providers who will work with the participants to help alleviate any feelings of distress. This risk is minimal and uncommon.

The risks and discomforts for those randomized to receive placebo+standard of care may include nicotine withdrawal symptoms.

Other risks. There are additional types of risks in this study that relate to smoking cessation and its treatment. One is the stress of and symptoms associated with nicotine withdrawal. Depressed mood, insomnia, anger, anxiety, difficulty concentrating, restlessness, and decreased heart rate are all common. However, these symptoms are short-lived and uncomfortable, though well tolerated. There is no evidence in the literature of psychiatric relapse or significant psychiatric worsening in the context of nicotine withdrawal. Further, the use of nicotine replacement products may diminish the withdrawal symptoms.

The risks of experiencing weight gain, appetite change, and irritability are identified as possible long-term risks that are not well tolerated. In the absence of receiving a properly working treatment, you may also experience a possible relapse.

Sub study:
The risk from research interviews is minimal and relatively uncommon. During assessments participants may be uncomfortable discussing their smoking habits, alcohol use, or mental health history and treatments. Participants may become frustrated and tense when they encounter difficulty when completing these measures. Careful planning and observation of the participant's response to these sessions will allow the testing to be completed with a minimum of discomfort. Participants will take breaks when necessary to help alleviate any discomfort. All interviewers are trained to recognize signs of distress or anxiety. The participant will be reminded that they can refuse to answer any question that makes them uncomfortable and may take breaks whenever they are needed.
There is a slight risk of breach of confidentiality. All data will be coded with an ID number that is unique. All data including information from chart reviews, therapist reports and laboratory results will be label by ID only. Only the study team will have access to the link between the ID and participant's name. Data containing names and personal information will never be included in published materials.

ID: VIEW4E1B52509F000
Name: v2_Research Related Risks

Potential Benefits and Alternatives

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer boxes below.

1 * Describe the potential direct benefit(s) to participants:
The great benefit of smoking cessation on lowering risk of mortality, especially cardiac-related mortality, would be especially pronounced in smokers living with HIV/AIDS.

2 * Describe the importance of the knowledge expected to result from the study:
This study will allow us the opportunity to examine which of the factorial design was the most effective on smoking cessation.

3 * Describe how the potential risks to participants are reasonable in relationship to the potential benefits:
We believe that the risks to participants in this study are outweighed by the potential societal benefits described above.

4 * Describe the alternatives to participation in this study. If there are no alternatives, state that participation is voluntary and the alternative is not to participate. For intervention studies, describe appropriate alternative clinical procedures or courses of treatment available to subjects.
There are no alternatives, participation is voluntary and the alternative is not to participate. However, participants who choose not to participate in the study will have the option of receiving buporipion and regular clinical care.

Withdrawal of Participants

If the questions below are not applicable to the research (i.e., chart review), enter "N/A".

1 * Describe anticipated circumstances under which subjects will be withdrawn from the research without their agreement:

1) They have a serious reaction during the study

2) They fail to follow instructions from research staff

3) If the PI decides that the study is no longer in the best interest of the participant.

Withdrawal will take place in the case of a significant side effect or at a participant's request. At discontinuation, interviews and ratings will be performed if possible. If suicidal ideation or intent is observed, the study suicide prevention plan (SPP) will be implemented and the participant will be withdrawn. The SPP consists of immediate psychiatric evaluation, use of a suicide prevention contract, provision of 24-hour access to a physician, referral to emergency services.

2 * Describe procedures for orderly termination:

The study will conclude after the last participant completes their last assessment interview.

3 * Describe procedures that will be followed when subjects withdraw from the research, including partial withdrawal from procedures with continued data collection:

When individuals withdraw from the protocol, we will keep all data that was already collected.

Privacy of Participants

If the study does not involve interaction with participants, answer "N/A" to the questions below.

1 * Describe how you will ensure the privacy of potential participants throughout the study ***(privacy refers to persons and their interest in controlling access to themselves):***
All in person research assessments and focus groups will be conducted in private rooms

2 * Describe the location where potential participants will receive research information and detail the specific actions the study team will take to ensure adequate privacy areas:
Potential participants will receive research information in a private room for in person interviews.

3 * Describe potential environmental stressors that may be associated with the research:
We are not aware of any potential environmental stressors that may be associated with the research.

4 * Will this study have a site based in the European Union?
○ Yes ● **No**

5 * Will the study have planned recruitment or data collection from participants while they are located in the European Union?
○ Yes ● **No**

Access link below for information about the EU General Data Protection Regulations to assist in answering these questions.
https://www.umaryland.edu/oac/general-data-protection-regulation/

Confidentiality of Data

1 * Will stored research data contain identifiers or be able to be linked to and identify individual participants (either directly or through a code/research ID)?

- (●) **Yes**
- ( ) No, the data will be stored de-identified/anonymous (stripped of all identifiers, no way to identify individual participants)

2 * Where will research data be kept (address electronic and paper data as applicable)? (If this is a VA study please list specific sites that data will be kept.)

Data will be collected using the REDCap system. REDCap (Research Electronic Data Capture) data collection projects rely on a thorough study-specific data dictionary defined in an iterative self-documenting process by all members of the research team. The iterative development and testing process results in a well-planned data collection strategy for individual studies. The REDCap system provides secure, web-based applications that are flexible enough to be used for a variety of types of research, provide an intuitive interface for users to enter data and have real time validation rules (with automated data type and range checks) at the time of entry. These systems offer easy data manipulation with audit trails for reporting, monitoring and querying patient records, and an automated export mechanism to common statistical packages (SPSS, SAS, Stata, R/S-Plus). REDCap servers are housed in our local data center at the Clinical and Translational Research Informatics Center (CTRIC), a service center within the Department of Epidemiology and Public Health at the University of Maryland School of Medicine. All web-based information transmission is encrypted. REDCap was developed specifically around HIPAA-Security guidelines. REDCap has been disseminated for use locally at other institutions and currently supports 240+ academic/non-profit consortium partners on six continents and over 26,000 research end-users (www.project-redcap.org).

3 * How will such data be secured?

All consent forms will be kept in locked files in a locked research office belonging to Dr. Ojoo. Participant confidentiality will be maintained by restricting access to specified study personnel.
All research materials transferred via REDcap to the University of Maryland with participants' evaluation study materials will be identified by code only. A separate file will hold the code key. Participants will not be personally identified in any publications or reports of the study. Any data used will be re-copied to research files with the participant identified by code only. The highest standards of participant confidentiality will be kept, and no participants will have identifiable information available.
Computerized records of data will be kept in a password-only accessible computer in a locked room. Appropriate firewalls and protections of computerized data are maintained to ensure that entry by those other than research personnel is not possible. The protocol data collection schedule will be kept in a database table and will be used to monitor the progress of participants through the protocol, missing assessments, and other protocol deviations during the study. Data entry screens will incorporate range checks or lists of valid responses for each item. Forms with missing or invalid data in key identifying fields will be referred back to raters for correction before entry. Participant confidentiality will be maintained by restricting study data access to specified study personnel. Most authorized personnel will have read-only access, and write/edit access will be restricted to data entry and data management staff assigned to the study. An electronic audit trail will record all changes to the database once data have been entered. The database will reside on a central server, and all server data will be backed up several times weekly. Access to the server from outside the Division of Psychiatric Services Research will be restricted by a firewall. Norton Anti-Virus software, updated automatically whenever new virus data files are provided, is installed on the server, and all computers are linked to the server. Development of the data management system for this study will be facilitated by the existence of this database structure, which already contains tables and data entry screens for many of the assessments used in this study.
Digital audio recordings will be collected to evaluate fidelity. No names will be recorded in the audio files. Each audio file will be labeled with a unique study ID. These audio files will be transferred using encrypted software and stored securely on a server in the Division of Psychiatric Services Research.
All of the above data will be gathered specifically for research purposes only. All data and the study computers will be encrypted and backed up to a secure University server. Access to research data stored in the database will be limited to investigators who have been granted user names and passwords by the PI.

4 * Who will have access to research data?

The PI, co-investigators, and authorized research study staff will have access to the research data.

5 * Will study data or test results be recorded in the participant's medical records?

- ( ) Yes
- (●) **No**

6 * Will any data be destroyed? ***(Please note that data for FDA regulated research cannot be deleted however, VA data must be destroyed according to the VHA Records Control Schedule (RCS) 10-1)***

- (●) **Yes**
- ( ) No

6.1 If Yes, what data (e.g., all data, some recordings, interview notes), when and how?

All data will be destroyed after all research activities are completed. This includes data analysis. This will occur approximately 7 years after the last journal publication

7 Do you plan to obtain a Certificate of Confidentiality?

- (●) **Yes**
- ( ) No

7.1 If Yes, upload your Certificate of Confidentiality. If you have not yet obtained the Certificate, please note that once it is obtained, you will need to submit an amendment to attach the document, make any needed changes to the submission and make needed changes to the Informed Consent Document.

Name	Created	Modified Date

There are no items to display

8 * Discuss any other potential confidentiality issues related to this study:

n/a

Monitoring Plan Selection

1 * Type of data safety monitoring plan for the study:

- ○ Will use/defer to the external sponsor's Data Safety Monitoring Plan
- ● **Data Safety Monitoring by a Committee**
- ○ Data Safety Monitoring by an Individual
- ○ There is no data safety monitoring plan in place

ID: VIEW4E1B00E30D400
Name: v2_Monitoring Plan Selection

Monitoring Plan - Committee

You indicated that the monitoring will be done by a Committee.

1 * Will the Committee be Internal or External?

- (●) **Internal DSMB**
- ( ) External DSMB

2 * What data will be reviewed?

- [x] **Adverse Events**
- [x] **Enrollment Numbers**
- [ ] Patient Charts/Clinical Summaries
- [ ] Laboratory Tests
- [ ] Medical Compliance
- [ ] Procedure Reports
- [ ] Raw Data
- [ ] Outcomes (Primary, Secondary)
- [ ] Preliminary Analyses
- [ ] Other

2.1 If Other, specify:

3 * What will be the frequency of the review?

- (●) **Annually**
- ( ) Bi-Annually
- ( ) Other

3.1 If Other, specify:

4 * Safety monitoring results will be reported to:

- [x] **IRB**
- [ ] GCRC
- [x] **Sponsor**
- [ ] Other

4.1 If Other, specify:

Monitoring Plan - Internal DSMB

You indicated that the monitoring committee will be an internal DSMB.

1 * List Internal DSMB Members:

Name
View Dr. Deanna Kelly
View Dr. Christina Mwachari
View Dr. Craig Rush

2 * Confirm that no financial or other conflicts of interest exists for the above individuals.

● **Yes** ○ No

3 * Will there be an interim efficacy analysis?

○ Yes ● **No**

3.1 If Yes, when?

4 * Briefly describe the DSM review process itself. Will it be an open or closed review to the investigator? Blinded/unblinded data? How will confidentiality of individual participant data be maintained?

The data would remain blinded unless risks to participants justify unblinding. To safeguard confidentiality, data are presented in aggregate or are identified only by an ID number. The PI is invited to the DSMB meetings and is asked to give a review of the past year with a particular emphasis on safety, side effects and enrollment

5 * What are the criteria defined in the protocol to be used for decision making regarding continuation, modification, or termination of study?

The DSMB is comprised of a psychiatrists, a pharmacist and a statistician. The DSMB will be charged with the following responsibilities: 1) to establish a regular meeting schedule; 2) to review the protocol; 3) to review the consent form; 4) to monitor the occurrence of side effects/adverse events, and serious adverse events throughout the course of the study; and 5) to review with investigators, the study data management system; and 6) to establish stop rules for the study as a whole. The DSMB will review the project prior to study enrollment and then receive annual side effect/adverse event updates. All serious adverse events (SAEs) will be reported to the DSMB, PIs, the Kemri IRB in Nairobi, Kenya the the University of Maryland, School of Medicine IRB. The PIs will receive all SAE reports within 24 hours of their occurrence. If as a result of data monitoring or interim analysis, the DSMB determines that the study poses an unreasonable or unnecessary risk to study participants, the DSMB and the PI will determine what possible protocol modifications are required to minimize the future occurrence of such events. Unexpected adverse events will be reported in accord with NIH and Federal requirements. Non-serious and expected adverse events will be reported annually to the IRBs. The PIs will be invited to the DSMB meetings and will be asked to provide a review of the past year with a particular emphasis on safety, side effects and enrollment. The data will remain blinded unless risks to participants justify unblinding. To safeguard confidentiality, data will be presented in aggregate or will be identified only by an ID number.

Research-Related Costs

1 * Is the study's financial supporter (e.g., commercial sponsor, federal or state grant or contract, private foundation, physician-sponsor) covering any research-related costs?

- ○ No
- ● **Yes**

1.1 If Yes, check all that apply:

- ☑ **Research-Related Services (personnel costs, tests, supplies, exams, x-rays, or consultations required in the study)**
- ☐ Investigational or Study Device
- ☐ Investigational or Study Drug
- ☐ Investigational Procedure(s)

1.2 If No, who is responsible for payment?

2 * Who is responsible for the uncovered research-related costs?

- ☐ Participant
- ☐ Sponsor
- ☐ UM
- ☐ Other
- ☑ **There will be no uncovered research-related costs**

2.1 If Other, specify:

3 If the participant is responsible for any research-related costs, identify and estimate the dollar amount:

Compensation for Research-Related Injury

1 * Is this study under a master agreement that includes a provision requiring the sponsor to provide compensation to participants for research-related injury?

◯ Yes ● **No**

1.1 If Yes, please provide the date and title of the agreement and upload the portion of the contract language relevant to compensation for research-related injury:

Name	Created	Modified Date

There are no items to display

1.2 If No (the study is not under a master agreement), is there proposed contract language concerning payment to participants for treatment in the event of a research-related injury?

◯ Yes ● **No**

1.2.1 If Yes, indicate the status of the contract review/approval with the ORD and upload the proposed language relevant to compensation for research-related injury:

1.2.2

Name	Created	Modified Date

There are no items to display

Payment/Reimbursement to Participants

1 * Will participants receive payment (money, gift certificates, coupons, etc.) or reimbursement for their participation in this research?

● **Yes** ○ No

ID: VIEW4E1C52A5D7800
Name: v2_Payment to Participants

Payment/Reimbursement Detail

You indicated that participants will receive payment (money, gift certificates, coupons, etc.) or reimbursement for their participation in this research.

1 * Payment/reimbursement to participants will be for: (check all that apply)

- [ ] Travel
- [ ] Parking
- [ ] Meals
- [ ] Lodging
- [x] **Time and effort**
- [ ] Other

1.1 If Other, specify:

2 * What is the total dollar value of the payments/reimbursements over the duration of the study? ***Total payment(s) for participation in research of $600 or more in a calendar year is required to be reported on an IRS Form 1099.***

$65

3 * Describe the timing and distribution plan for the payment/reimbursement (schedule, means, etc.)?

Formative Session: Participants will be paid $5 for either of the private interview or the focus group.

Participants will be paid $5.00 for each of the following visits:

Screening, Evaluation, Baseline, Week 1, Week 2, Week 4, Week 8, Week 12 and Week 36.

We will also offer a small gift (e.g., rock with affirmation statements, water bottle, small journal) for those who attend the Positively Smoke Free Intervention sessions. The value of the trinkets will be about $5 each.

Sub study:
Individuals will be reimbursed $5.00 (Kenya shillings of Ksh.500) either for the focus group or the individual interview. All the payments will be in form of cash and they will be submitted at the end of the interview.

4 * Method(s) of payment/reimbursement to be Used:

- [x] **Cash**
- [ ] Check
- [ ] Money Order
- [ ] Gift Certificate/Gift Card
- [ ] Other

4.1 If Other, specify:

HIPAA (Health Insurance Portability and Accountability Act)

1 * Are you affiliated with, or will you be accessing data from a HIPAA-covered entity? A covered entity might be a hospital, a physician practice, or any other provider who transmits health information in electronic form.

• At UMB, this includes UMB schools designated as covered entities (School of Medicine and School of Dentistry) and entities under the University of Maryland Medical System (UMMS). The Baltimore VA Medical Center is also a covered entity.

• If you are a researcher from any school that is not a covered entity but is accessing electronic medical records from a covered entity (such as UMMC), HIPAA would be applicable. Please see a list of covered entities included under UMMS here: *executed-ace-designation-042018.pdf*

◯ Yes ● **No**

ID: VIEW4E1B0A2114400
Name: v2_HIPAA

Informed Consent Process

If the study does not involve interaction with participants or a waiver of consent is being requested , answer "N/A" to the questions below.

1 * Indicate the type(s) of consent that will be involved in this study: (check all that apply)

- [ ] Not applicable (study may qualify as exempt)
- [ ] Request to Waive Consent/Parental Permission (Consent is not being obtained)
- [ ] Request to Alter Consent (Some Elements of Consent Waived)
- [ ] Request to Waive Documentation of Consent (Verbal/Oral Consent)
- [x] **Written Consent Form**
- [ ] Electronic Consent

2 * Describe the Informed Consent process in detail:

During the consent visit for the patient participants, the RA will describe the study protocol, risks and benefits and provide information regarding informed consent. Each component of the consent form is reviewed with an emphasis on risks and benefits. We require that the potential patient participant to answer a series of questions about the study correctly in order to demonstrate that their consent is truly informed (please see the 'Additional Documents' section of the protocol application for questions). If the patient is unable to answer the questions correctly, the RAs re-review the aspects of the study that he/she did not understand. The RAs asks the questions a second time. If the patient cannot answer all questions correctly, he/she will not be enrolled in the study. Each RA will be trained in the ethical conduct of research including consent procedures according to IRB standards. RAs who obtain consent are trained to work with people with substance abuse disorders as well as those who are economically disenfranchised. After the consent process is complete the participant will sign 2 copies of the consent form. One copy will be for the research teams records and the second copy will be given to the participant to take home with them for their own personal records. A copy of the consent form will also be kept on file at the study pharmacy per pharmacy guidelines.

3 * Confirm that the consent process will explain the following:

- The activities involve research.
- The procedures to be performed.
- That participation is voluntary.
- The name and contact information for the investigator.

(●) **Yes** ( ) No

4 * Describe who will obtain Informed Consent:

The PI or study staff

5 * If obtaining consent from a legally authorized representative (LAR), describe how you will confirm that the individual is the LAR and can provide legally effective informed consent. *(Answer "N/A" if not obtaining consent from LARs)*

N/A

6 * Describe the setting for consent:

The consent visit takes place in a private room with the door closed.

7 * Describe the provisions for assessing participant understanding:

In order to ensure informed consent we require that the potential patient participant answer a series of questions about the study correctly in order to demonstrate that their consent is truly informed (please see the 'Additional Documents' section of the protocol for questions). If the patient is unable to answer the questions correctly, the RAs re-review the aspects of the study that he/she did not understand. The RAs asks the questions a second time. If the patient cannot answer all questions correctly, he/she will not be enrolled in the study. Each RA will be trained in the ethical conduct of research including consent procedures according to IRB standards. RAs who obtain consent are trained to work with people with with substance abuse disorders as well as those who are economically disenfranchised.

8 * Describe the consideration for ongoing consent:

The research staff will check in with the participants at each visit to ensure their level of understanding.

Non-English Speakers

You indicated that participants may speak languages other than English.

1 * Describe how you will explain the study and ensure that the non-English speaking subjects understand the study and their participation in research:
Participants at the recruitment clinic are fluent in English. We are adding a few Swahili translated statements in case a specific question in English is troubling for a participant to understand in English.

2 * Indicate the method of translation:

- (●) **Investigator will provide IRB with translation of approved consent form**
- ( ) Translated short form consent form will be used with an interpreter along with a study summary document (Limited Use)

3 If the research will primarily include subjects who speak a language other than English, the informed consent documents should be translated into that language. Indicate the language(s) and method of translation.
We will provide consent in English. If a participant needs translation, we will provide a consent in Swahili.

Participants at the recruitment site are fluent in English. The consent forms for this study are not getting approved and stamped by UMB. Since all of the consents are happening in Kenya, the consents are being stamped by the University of Nairobi.
After we conduct the formative interviews and get a better understanding of the population, and before the main clinical trial will start, we will review if we need to translate more participant items into Swahili.

Upload the certificate of translation:

Name	Created	Modified Date
Certificate of Translation from Kenya.pdf(0.01)	10/4/2019 8:11 AM	10/4/2019 8:11 AM

4 * Indicate whether or not an interpreter will be used. If so, how will you guarantee that the interpreter will maintain confidentiality of subjects? For whom does the interpreter work and how will the interpreter be recruited for the study?
The staff who will be working with the participants, are fluent in both English and Swahili, just like the participants. Staff are employed by the University of Maryland but live and work Kenya.

5 * Indicate who will be responsible for updating subjects about study progress or any changes, collecting complaints, etc. during the course of the study:
As with any modifications, an update consent form will be created if needed.

6 If this research will be conducted outside the United States, indicate subjects' native language and literacy level:
The clinic recruitment site participants are fluid in both English and Swahili. Both English and Swahili are the official languages of Kenya.

Consent and HIPAA Authorization Forms - Draft

1 Upload all of your Consent Forms for approval. Use only Microsoft Word.

Name	Created	Modified Date
No Consent Forms Uploaded		

IMPORTANT NOTE: the above list of consent forms (if any) are DRAFT versions. Under no circumstances should copies of these be distributed to patients/study subjects. If/when this research submission is approved by the IRB, approved consent forms will be available for download and use from the "Documents" tab of the Submission's workspace (click Exit and then look for the Documents tab - approved submissions only)

1A Archived Consent Forms:

Name	Created	Modified Date
There are no items to display		

2 Upload any HIPAA authorization forms here:

There are no items to display

Please refer to HRPO's website for specific instructions for preparing informed consent documents and to access current templates:
http://hrpo.umaryland.edu/researchers/consents.html

ID: VIEW4E1C7712D3000
Name: v2_Consent Forms - Draft

Organization Review Requirements (other than IRB)

Answer the following questions to determine additional organizational review requirements:

1 **Department/Division Review** - All research submissions are required to undergo department/division/institutional review prior to IRB review. The following entity is listed as the required department/division/institutional review:

Psych CMHSR General

If this information is incorrect, please notify the HRPO office.

2 **RSC Review Criteria** - select 'Yes' if the answer is 'Yes' for any of the following questions. Review by the Radiation Safety Committee may be required.

* 2.1 Does the research involve the use of ionizing radiation? ○ Yes ● **No**

2.2 Does the research involve the sampling of radioactive human materials for subsequent use or analysis in a laboratory?

3 **IBC Review Criteria** - select 'Yes' if the answer is 'Yes' for any of the following questions. Review by the Institutional Biosafety Committee may be required.

* 3.1 Does the research involve human gene transfer? ○ Yes ● **No**
-OR-
Does the research specifically apply to human studies in which induction or enhancement of an immune response to a vector-encoded microbial immunogen is the major goal, and such an immune response has been demonstrated in model systems, and the persistence of the vector-encoded immunogen is not expected? This type of research is often referred to as recombinant vaccine trials.

3.2 Does the research involve the exposure of human subjects to pathogenic microorganisms, or the exposure of research staff to human subjects or samples known or reasonably expected to carry infectious disease(s)?

3.3 Does the research involve the sampling of materials from persons with no known infectious disease and where the only risk to study staff is occupational exposure to bloodborne pathogens as defined by the OSHA Bloodborne Pathogen Standard?

4 **Cancer Center Criteria** - Answer the following to determine if review by the Cancer Center (Hematology-Oncology) may be required.

* Does the protocol involve in any way studies related to the prevention, treatment, diagnosis, or imaging of neoplastic diseases? ○ Yes ● **No**

5 **General Clinical Research Center Review Criteria** - the GCRC offers free and/or cost shared resources for patient-oriented research. Click Here for more information.

Answer the following to determine if review by the GCRC may be required.

* Will the General Clinical Research Center (GCRC) facility or resources be used to conduct this activity? ○ Yes ● **No**

6 **VA Review Criteria** - Answer the following questions to determine if review by the VAMHCS R&D Committee may be required.

* 6.1 - Will the research be conducted by VA Investigators including PIs, Co-PIs, and Site Investigators on VA time (serving on compensated, WOC, or IPA appointments)? ○ Yes ● **No**
* 6.2 - Will the research utilize VA resources (e.g., equipment, funds, medical records, databases, tissues, etc.)? ○ Yes ● **No**
* 6.3 - Will the research be conducted on VA property, including space leased to and used by VA? ○ Yes ● **No**

PLEASE NOTE that the research may be funded by VA, by other sponsors, or may be unfunded.

ID: VIEW4E1AF91AB2400
Name: v2_Organization Review Requirements (other than IRB)

Summary of Required Reviews (other than IRB)

1 **Additional Committee Reviews** - Based on your responses to the previous questions, you have identified the following additional reviews. To complete or view these additional committees' forms, click on the links below or exit this application and click on the appropriate button on left side of this submission's webpage.

Name of Related Submission

This protocol has no related submissions (RSC, GCRC, IBC, etc)

2 **Required Department and Specialty Reviews** - Based on the PI's organization (department, division, etc.) affiliation and answers to previous questions (use of Cancer Center, etc.), the organizations listed below are required to review this application. These reviews are conducted online and no additional forms or steps by the study team are required.

Name of Organization	**Review Status**
Psych CMHSR General	Complete

Additional Documents

1

Upload all additional documents here:

Name	Created	Modified Date
Sub Study Kenya Informed consent form (English and Swahili).docx(0.01)	2/24/2021 1:07 PM	2/24/2021 1:07 PM
Formative sessions_Swahili consent V1.0.pdf(0.01)	10/4/2019 8:21 AM	10/4/2019 8:21 AM
Formative Interview 8.14.19.pdf(0.02)	11/13/2018 12:54 PM	9/17/2019 8:53 AM
Other Sites Where Research Activities Will Be Conducted (3).docx(0.02)	10/4/2018 1:08 PM	11/14/2018 11:10 AM
Formative Focus Group.doc(0.01)	11/13/2018 12:54 PM	11/13/2018 12:54 PM
Smoking Kenya Consent - Feedback Sessions.doc(0.01)	11/13/2018 9:29 AM	11/13/2018 9:29 AM
Emily Koch certificate(0.01)	10/24/2018 8:54 AM	10/24/2018 8:54 AM
Dr. Ojoo CITI 2018.pdf(0.01)	1/16/2018 10:31 AM	1/16/2018 10:31 AM
HIV Smoking Consent Form - Kenya (1).doc(0.03)	12/20/2017 7:34 AM	1/16/2018 8:52 AM
Babatunji Oni's Certificates(0.01)	11/7/2017 11:04 AM	11/7/2017 11:04 AM
STaff Certificates.pdf(0.01)	10/18/2017 8:24 AM	10/18/2017 8:24 AM
HIV Study Schedule 2017 KENYA.docx(0.02)	10/17/2017 3:02 PM	10/18/2017 8:02 AM
SI HI Checklist Kenya.docx(0.01)	10/18/2017 7:57 AM	10/18/2017 7:57 AM
PSF.Curriculum.DSR.2015 MODIFIED.docx(0.01)	10/17/2017 2:56 PM	10/17/2017 2:56 PM
Brochure for Control Group.pub(0.01)	10/17/2017 2:54 PM	10/17/2017 2:54 PM
Questions of Understanding.docx(0.01)	10/17/2017 2:54 PM	10/17/2017 2:54 PM
Contraception Consent Form.docx(0.01)	10/17/2017 2:53 PM	10/17/2017 2:53 PM
Package Insert for Bupropion.docx(0.01)	10/17/2017 2:52 PM	10/17/2017 2:52 PM

ID: VIEW4E0962513A000
Name: v2_Additional Documents

Final Page of Application

You have reached the final page of this application. It is recommended that you click on the "Hide/Show Errors" link on the upper or lower breadcrumb row of this page. The "Hide/Show Errors" will do a search of your application, and highlight areas that are required or need to be completed prior to submitting.

By submitting this application, you are electronically routing the protocol for departmental scientific review and all other necessary reviews. According to information you have provided, this application will be routed to the following Departments for review prior to being forwarded to the IRB for review. These reviews are conducted online and no additional forms or steps by the study team are required.

Name of Organization	**Review Status**
Psych CMHSR General	Complete

Required Safety Committee Reviews - In addition to the IRB, the following committees must review this submission. Each additional committee has a separate online form that the study team will be required to fill out. All committee applications (IRB plus those listed here) must be completed properly before the 'package' of applications can be submitted. The team may complete these additional forms in any order or at any time prior to submission of the IRB Application. To complete or view these additional committees' forms, click on the links below or exit this application and click on the appropriate button on left side of this submission's Workspace.

Name of Related Submission

This protocol has no related submissions (RSC, GCRC, IBC, etc)

You may check the progress of your application at any time by returning to the Workspace of this submission. A detailed history, including notes, dates, and times of events, is provided to you for this purpose.

If a reviewer returns the application to you, you must address their concerns and resubmit the protocol for review to all designated departments. After all departments have reviewed the application, it will automatically be sent to the IRB for review. Changes made to the submission after its approval must be submitted as modifications.

Investigator Attestation
By submitting this application, I, the Principal Investigator (PI), certify that the information provided in this application is complete and correct. Research will be conducted according to the submission as described, only by the approved principal investigator and study team members.

In addition, I agree to the responsibilities of a PI, including:

- Obtaining informed consent (if applicable) from all subjects as outlined in the submission.
- Reporting new information to the IRB per the requirements of the Investigator Manual.
- If Required, obtaining renewal of the protocol prior to the expiration of the approval period or halt all study activities upon study expiration.
- Accepting ultimate responsibility for the protection of the rights and welfare of human subjects, conduct of the study and the ethical performance of the project.
- Ensuring performance of all research activities by qualified personnel according to the IRB approved submission.
- Ensuring that research personnel have or will receive appropriate training.
- Ensuring no changes will be made in the research until approved by the IRB (except when necessary to eliminate apparent immediate hazards to subjects).

Click the "Finish" button and then click "Submit Application" in the submission Workspace.

Add a Team Member

1 * Select Team Member:
Melanie Bennett

2 Research Role:
Sub-Investigator

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Dr. Bennett will be providing supervision for the smoking intervention.

Add a Team Member

1 * Select Team Member:
Jon Shuter

2 Research Role:
Sub-Investigator

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Dr. Shuter has created Positively Smoke Fee (PSF), the intervention being used in this protocol. He will adapt his current intervention to meet the needs of our Kenya population. We will also provide guidance and supervision for the intervention.

Add a Team Member

1 * Select Team Member:
Julia Cohen

2 Research Role:
Other

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Ms. Cohen will be working with de identifiable data for the purposes of publication. Here trainings have been completed.

Add a Team Member

1 * Select Team Member:
Emily Koech

2 Research Role:
Research Team Member

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Dr. Koech will act as a study physician in Kenya. She has completed all trainings.

Add a Team Member

1 * Select Team Member:
Andrea Weinberger

2 Research Role:
Other

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Dr. Weinburger will be working with de identifiable data for the purposes of publication. Her trainings have been completed. Dr. Weinburger has several years experience with tobacco and underserved populations.

Add a Team Member

1 * Select Team Member:
Patience Oduor

2 Research Role:
Research Team Member

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
● **Yes** ○ No

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Ms. Patience has several years of experience coordinating studies.

Add a Team Member

1 * Select Team Member:
Sylvia Ojoo

2 Research Role:
Sub-Investigator

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
● **Yes** ○ No

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Dr. Ojoo will be the PI in Kenya. She will oversee the day to day operations in Kenya including being the primary contact for emergency issues.

Add a Team Member

1 * Select Team Member:
Deborah Medoff

2 Research Role:
Statistician

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Dr. Medoff will oversee the data analysis.

Add a Team Member

1 * Select Team Member:
Lijuan Fang

2 Research Role:
Statistician

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Ms. Fang will assist with data analysis.

Add a Team Member

1 * Select Team Member:
LAN LI

2 Research Role:
Statistician

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Ms. Li will assist with data analysis.

Add a Team Member

1 * Select Team Member:
Jeanette Robinson

2 Research Role:
Technician or Assistant

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Ms. Robinson will assist with data analysis.

UNIVERSITY of MARYLAND
THE FOUNDING CAMPUS

RESEARCH CONSENT FORM

Protocol Title: Optimizing smoking cessation interventions for PLWH in Nairobi, Kenya

Study No.: HP-00077523

Principal Investigator: Seth Himelhoch, M.D., M.P.H. 410.706.2490

Sponsor: NIH

This is a research study. Your participation is voluntary. You can ask any questions at any time.

PURPOSE OF STUDY

The purpose of this study is to determine the best treatment to help people who have HIV quit smoking tobacco.

You will be 1 of approximately 300 individuals who will be asked to join this study. The current recruitment site is a methadone maintenance program in Nairobi, Kenya

PROCEDURES

Initial Screening

Upon completion of the consent process, you will be asked several questions to see if you are eligible to be in this study. We will be asking you questions about your smoking habits and health history. During your Evaluation appointment, you will be asked to provide a thorough medical history and complete a physical assessment. This includes procedures such as taking your vital signs and listening to your lungs with a stethoscope.

We will have you blow into our Carbon Monoxide Breath Monitor to measure the amount of carbon monoxide in your lungs. This tells us if you have been smoking. Finally, you will be asked other questions about your daily activities.

If you pass all of the screening procedures, you will be asked to complete a baseline interview. This interview will ask you several questions. The topics include: your smoking history, your mental health history and questions about your daily routine.

Female participants will be asked to take a pregnancy test during this visit and approximately monthly while taking study medication. We will also ask individuals to sign a contraception consent form. This will provide written consent that you will use an acceptable form of contraception during the 12 weeks you are taking study medication. Condoms will be available from study staff.

Only those continuing to meet full eligibility criteria will proceed to randomization and remain in the study.

Randomization:

Eligible individuals will then be randomized to one of four treatments:
(1) Bupropion + Positively Smoke Free (an 8 session tailored behavioral intervention for People Living with HIV (PLWH) smokers);

(2) Bupropion + Standard of Care (brief advice to quit -1 session);

(3) Placebo + Positively Smoke Free (PSF);

(4) Placebo + Standard of Care.

The chance that you will get picked to be in one of the 4 treatments is like pulling a number out of a hat.

Medication Intervention:
Medication will be given for approximately 12 weeks during the study. All participants will receive a pill to take each day for 12 weeks. Depending on how you are randomized, pills will either be Bupropion or they will be a placebo (a sugar pill). The study physician will provide medical clearance and sign off on prescription orders. All medication will be provided by the study team. All participants will be supplied medication in identical form.

You will receive a weekly supply of medication for the first few weeks to ensure proper dosing and monitoring. During week 1 and week 2 of the study, you will come in for a brief meeting to ensure you are doing ok with your medication and to talk to the staff if you are having any medication side effects or other concerns. We will also ask you about your mood, any side effects you may be experiencing and check you vital signs. You will also be asked about the amount you are smoking and then we will have you blow into our Carbon Monoxide Breath Monitor to measure the amount of carbon monoxide in your lungs. At the week 2 visit, you will receive medication for weeks 3-4.

During week 4 and week 8 of the study, you will return to receive a four week supply of medication. That means that you will come in for a brief 20 minute appointment on approximately week 4 and week 8 of the study. We will ask you about your mood, any side effects you may be experiencing, check you vital signs and have you take a pregnancy test if applicable. You will also be asked about the amount you are smoking and then we will have you blow into our Carbon Monoxide Breath Monitor to measure the amount of carbon monoxide in your lungs.

Bupropion:
Bupropion is a medication used to help individuals quit smoking. It will be given to you in accordance with package labeling. You will be given 150 mg/day (days 1-3), then 150 mg twice per day (days 4-7). You will be given 150 mg twice per day for weeks 2-12 of the study.

Placebo:
A placebo simply means a sugar pill that contains no medication. It will be given to you on the same schedule as Varenicline.

Therapy Intervention:
In addition to being randomized to receive either Bupropion or placebo, you will also be randomized to receive one of two treatment conditions, either Positively Smoke Free or the standard of care.

Positively Smoke Free:
Positively Smoke Free is an individual intervention that promotes smoking cessation. It is an 8-session program that takes place over a 12 week period. The session length averages about 45 minutes. You will be contacted by a PSF interventionist within about 48 hours of being randomized to schedule your first appointment.

Control Condition:
Those randomized to standard of care will receive of standard of care smoking cessation treatment by a trained research assistant at the time of randomization. Participants will be given a quit smoking brochure and a one session brief advice to quit smoking. This one time session will last approximately 5 minutes.

All treatment sessions will be audiotaped. If you miss a session, we will call you to reschedule. If you are having difficulty attending some of the sessions in person, we will offer to conduct a few of the sessions over the telephone.

Assessment Interviews:
All participants will be interviewed at baseline, at approximately week 12, and at approximately week 36. The interview topics include: your smoking history, your mental health history and questions about your daily routine. We will also record your vital signs.

There will also be a short check up on your vital signs, your medication adherence, your health and any medication side effects at weeks 1, 2, 4 and 8. This was already discussed under the medication section. All assessments will be administered in a confidential and private location by experienced staff.

WHAT ARE MY RESPONSIBILITIES IF I TAKE PART IN THIS RESEARCH?

If you take part in this research, you will be responsible to complete a physical, review your medical and HIV history with staff, complete a series of interview assessments. You will also be asked to take a medication for smoking cessation and attempt to quit smoking. You may also be asked to participate in a program on how to quit smoking.

POTENTIAL RISKS/DISCOMFORTS:

Bupropion
Risks associated with Bupropion include the following side effects: skin rashes, anxiety, dry mouth, hyperventilation, irregular heartbeats, irritability, restlessness, shaking, shortness of breath, and trouble sleeping.

You will be closely monitored for depression and suicidal feelings. If at any point during the study you endorse any concerning feelings/behaviors, a study investigator (Dr. Ojoo) will be contacted. You may need to meet with her and/or your treatment team to ensure your safety.

Assessment Interviews:
The risk from research interviews is minimal and relatively uncommon. During assessments you may be uncomfortable discussing your smoking habits or mental health history and treatments. You may become frustrated and tense if you encounter any difficulties while completing these measures. All interviewers are trained to recognize signs of distress or anxiety. You will be reminded that you can refuse to answer any question that makes you uncomfortable and may take breaks whenever you need. There is a slight risk of breach of confidentiality.

Risks related to PSF (Therapeutic Risk).
The behavioral treatment sessions may cause some temporary anxiety or distress due to discussing smoking habits and attempts to quit smoking. The interventionists are all trained mental health providers who will work with the participants to help alleviate any feelings of distress. This risk is minimal and uncommon.

Nicotine withdrawal symptoms:
There are additional types of risks in this study that relate to smoking cessation and its treatment. One is the stress of and symptoms associated with nicotine withdrawal. Depressed mood, insomnia, anger, anxiety, difficulty concentrating, restlessness, and decreased heart rate are all common. These symptoms may cause discomfort; however, they are short lived and well tolerated. There is no evidence in the literature of psychiatric relapse or significant psychiatric worsening in the context of nicotine withdrawal. Furthermore, the use of nicotine replacement products may diminish the withdrawal symptoms.

Confidentiality:
There is a risk of breach of confidentiality. To minimize this risk all data will be coded with an ID number that is unique. All data including information from chart reviews and therapist reports will be labeled by ID only. Only the study team will have access to the link between the ID and participant's name. Data will be stored in a secure location in a locked office within a locked cabinet and electronic data will be password-protected. Audio taped sessions will be transferred to a CD and stored in a locked office within the study division. The CDs will be labeled with your study ID number, never your name.

Pregnancy:
If you become pregnant at any time during this study, you will be removed from the study and will immediately stop take the medication provided. You will speak to the study physician about the best medical course of action moving forward.

There may be risks in this study which are not yet known.

POTENTIAL BENEFITS
You may or may not benefit by taking part in this study. There is no guarantee that you will receive direct benefit from your participation in this study. However, for those who quit smoking there is the benefit of lowering risk of mortality, especially cardiac-related mortality.

ALTERNATIVES TO PARTICIPATION

Your alternative is to not take part in this study and seek smoking cessation treatment at a site convenient to you. If you choose not to take part, your healthcare at University of Maryland, Baltimore will not be affected. If you choose to seek smoking cessation treatment at a site that is convenient to you please speak to the clinical team who will be providing smoking cessation treatment about the potential risks and benefits of treatment.

All participants who are excluded from the study will be provided with information regarding the benefits of smoking cessation treatment and will be counseled to discuss optimal treatment with their primary HIV provider. Participants who are excluded for medical reasons will be referred to their HIV clinician for further treatment and management. Potential participants who were screened out because of low motivation to quit smoking will receive a Positively Smoke Free smoking cessation brochure and will be encouraged to call the free smokers quit line.

COSTS TO PARTICIPANTS
It will not cost you anything to take part in this study.

PAYMENT TO PARTICIPANTS

You will receive $5 in cash for completing the screening for eligibility. If you are not eligible for the study, you will not receive any more payment.

If you are eligible for the study you will receive $5 in cash for completing the Evaluation Phase, $5 for completing the baseline assessment interview, $5 for completing the week 12 assessment interview and $5 for completing the week 36 assessment interview. We will also offer $5 for your check in visits on weeks 1, 2, 4 and 8. The total amount of money you could be paid is $45 in cash.

Small trinkets (water bottle or etc) will be provided for those who attend the PSF sessions.

If an injury should occur from the study, medical treatment is available to you through your usual treatment providers at your own expense.

CONFIDENTIALITY AND ACCESS TO RECORDS
We will be collecting personal information from you as part of this study. Only study personnel will have access to your information, which will be labeled with a non-identifying study number instead of your name. We will keep your information locked in a cabinet in a locked office, separate from any documents which have your name on them.

Electronic data files and audio recordings of will be stored in password-protected files on a secure database. Data files including confidential personal information will not include your name or other personally identifying information. Audio recordings will not be labeled with your name. They will be reviewed to make sure that the programs are being delivered correctly. We will not share your responses with your physician, your counselors, or any other staff person not directly involved in the research study.

If, during your study participation, you disclose to us that you are actively suicidal or homicidal, or you disclose to us that you are abusing a minor child, we are unable to keep that information confidential. We will disclose that information to health care providers and/or to the authorities in order to ensure the safety of everyone involved.

The data from the study may be published. However, you will not be identified by name. People designated from the institutions where the study is being conducted and people from the sponsor will be allowed to inspect sections of your medical and research records related to the study. Everyone using study information will work to keep your personal information confidential. Your personal information will not be given out unless required by law.

Efforts will be made to limit your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete secrecy. Organizations that may inspect and copy your information include the National Institute of Mental Health, the IRB and other representatives of this organization.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

The monitors, auditors, the IRB, the Food and Drug Administration will be granted direct access to your medical records for verification of the research procedures and date. By signing this document you are authorizing this access.

A Certificate of Confidentiality will be obtained from the Federal Government for this study to help insure your privacy. This Certificate means that the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative or other proceedings. But, if you request disclosure, we can release the information.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

The Certificate of Confidentiality does not prevent the researchers from disclosing voluntarily, without your consent, information that would identify you as a participant in the research project under the following circumstances: report of child abuse or threats to harm oneself or another person.

RIGHT TO WITHDRAW

Your participation in this study is voluntary. You do not have to take part in this research. You are free to withdraw your consent at anytime. Refusal to take part or to stop taking part in the study will involve no penalty or loss of benefits to which you are otherwise entitled. If you withdraw from this study, already collected data may not be removed from the study database. You will be asked whether the investigator can collect data from your routine medical care. If you agree, this data will be handled the same as research data. If you decide to stop taking part, or if you have questions, concerns, or complaints, or if you need to report a medical injury related to the research, please contact the investigator: Seth Himelhoch, MD, MPH at (410) 706-2490. There are no adverse consequences (physical, social, economic, legal, or psychological) of your decision to withdraw from the research.

CAN I BE REMOVED FROM THE RESEARCH?

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include but are not limited to failure to follow instructions of the research staff as well as the person in charge decides that the research study is no longer in your best interest.

The sponsor can also end the research study early. The study doctor will tell you about this and you will have the chance to ask questions if this were to happen.

UNIVERSITY STATEMENT CONCERNING RESEARCH RISKS

The University of Maryland, Baltimore (UMB) is committed to providing participants in its research the rights due them under State and federal law. You give up none of your legal rights by signing this consent form or by participating in the research project. This research has been reviewed and approved by the Institutional Review Board (IRB). Please call the Institutional Review Board (IRB) if you have questions about your rights as a research subject.

Participating in research may result in an injury, as explained above. If you suffer an injury directly related to your participation in this project, UMB and/or one of its affiliated institutions or health care groups will help you obtain medical treatment for the specific injury and provide referrals to other health care facilities, as appropriate. UMB and/or its affiliated institutions or health care groups will not provide you with financial compensation or reimbursement for the cost of care provided to treat a research-related injury or for other expenses arising from a research-related injury. The institution or group providing medical treatment will charge your insurance carrier, you, or any other party responsible for your treatment costs. If you incur uninsured medical costs, they are your responsibility. The HRPO will assist you in contacting the sponsor if you have an injury caused by the sponsor's drug or device under study. Uninsured medical costs to treat research related injuries not caused by the drug or device under study are your responsibility. The study staff can give you more information about this if you have a study injury.

By signing this Consent Form, you are not giving up any legal rights. If this research project is conducted in a negligent manner and you are injured as a direct result, you may be able to recover the costs of care and other damages from the individuals or organizations responsible for your injury.

If you have questions, concerns, complaints, or believe you have been harmed through participation in this research study as a result of researcher negligence, you can contact members of the IRB or the Human Research Protections Office (HRPO) to ask questions, discuss problems or concerns, obtain information, or offer input about your rights as a research participant. The contact information for the IRB and the HRPO is:

University of Maryland Baltimore
Human Research Protections Office
620 W. Lexington Street, Second Floor
Baltimore, MD 21201
410-706-5037

Signing this consent form indicates that you have read this consent form (or have had it read to you), that your questions have been answered to your satisfaction, and that you voluntarily agree to participate in this research study. You will receive a copy of this signed consent form.

If you agree to participate in this study, please sign your name below.

_____
Participant's Signature

Date:_____

_____
Investigator or Designee Obtaining Consent
Signature

Date:_____