

Title: **Smoking Cessation Pilot for People Living With HIV (PLWH)**

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Stand Alone Protocol: SMOKING CESSATION PILOT – IRB-AAAS6990

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Background:

Of the approximately one million persons living with HIV (PLWH) in the United States (U.S.), it is estimated that between 40-70% smoke cigarettes, at least three times the prevalence (14%) observed in the general U.S. adult population. Consequently, PLWH experience substantial tobacco-related morbidity and mortality. In PLWH, after achieving and maintaining a suppressed viral load, smoking cessation is the next most important health behavior to maximize both quality of life and life expectancy. Indeed, PLWH who quit smoking upon entering HIV care gain greater than 5 years of life expectancy as compared to those who enter HIV care and continue smoking.^{1,2}

Given the high prevalence of cigarette smoking among PLWH and the benefit of smoking cessation, there is an urgent need for swift action to intervene to reduce tobacco use rates. However, evidence to improve tobacco cessation among PLWH is inadequate. Few tobacco cessation interventions have been tested among PLWH, and of those which have, there is 'very low' quality evidence that tobacco cessation interventions were effective in the short-term, and 'moderate' quality evidence indicating similar outcomes to controls in the long-term.³ Given the few randomized controlled trials (RCTs) examining smoking cessation interventions for PLWH, and the major methodological limitations of many of these studies (e.g., lack of randomization, comparison conditions, treatment fidelity assessments, abstinence verification tests), it is critical to develop evidence-based tobacco cessation interventions to address the complex and unique needs of PLWH (e.g., risk factors, treatment needs). Tailored cessation studies designed for dissemination and implementation are necessary to focus efforts on PLWH who use tobacco products.

Pharmacotherapy Offered to All Participants. Current treatment guidelines recommend pharmacotherapy be offered to all smokers making a quit attempt.⁴ Pharmacotherapy doubles quit rates when compared to placebo,⁵ and the highest abstinence rates are achieved when pharmacotherapy is combined with a behavioral intervention.⁶ There are also ethical concerns about offering a placebo treatment only in a historically mistreated group;⁷⁻⁹ therefore, the interventions would likely be less acceptable or feasible if a placebo was part of the study design. As part of this intervention, we will provide all participants with NicoDerm CQ Patch as a form of Nicotine Replacement Therapy. As all forms of nicotine replacement therapy are over-the-counter medications, participants are not required to obtain physician clearance to take them.

Mobile health (mHealth) is an ideal platform for implementation and dissemination of evidence-based strategies.¹⁰ mHealth can provide mechanisms for improving the efficiency and effectiveness of care provided while reducing administrative burden. mHealth technology can be used for achieving health equity in vulnerable groups because it is a widely available and relatively inexpensive tool for health behavior change and can be ¹¹ adapted to meet the needs of its end-users.¹²⁻¹⁵ The emerging evidence base on mHealth delivered behavioral interventions supports their promise to improve health disparity outcomes.¹⁶ Therefore, mHealth interventions such as Lumme proposed through this study is timely, relevant, scalable and likely to improve health outcomes in our health disparate study population -- PLWH who smoke.

Aim: To conduct a pilot study on the Lumme mobile app in a population of PLWH as a tobacco cessation intervention (N=40) *Hypothesis 1:*

Overview of Study Aims, Design and Methods

Purpose: The purpose of the research study is to find out more about smoking behaviors in people living with HIV and the subsequent efficacy of tobacco cessation strategies.

Study Design: A pilot study will be conducted with 40 PLWH randomized to 2 arms. Participants will be randomly assigned to receive Lumme (active) or a control condition (standard smoking cessation counseling session). Participants will also receive a survey at baseline and at 12-weeks post-baseline.

Recruitment: We will recruit PLWH by posting flyers at local clinics and community-based organizations throughout New York City. Potential participants will be pre-screened for eligibility over the phone by study staff. We will also provide enrolled participants with a study flyer to share with potentially eligible individuals.

Study Populations: Our study participants will consist of 40 individuals who smoke tobacco. Inclusion criteria. (1) PLWH; (2) ≥ 18 years of age; (3) own an Android smartphone; (4) understand and read English; (5) not pregnant or breastfeeding; (6) permanent contact information; (7) smokes ≥ 5 cigarettes per day for the past 30 days; (8) interested in quitting smoking within 30 days; and (9) blow >5 CO into a breath analyzer at baseline. Exclusion criteria. (1) self-report being HIV-negative or unknown status; (2) pregnant, breastfeeding, or planning to become pregnant during the study period; (3) planning to move within 3 months of enrollment; (4) a positive history of a medical condition that precludes use of the nicotine patch; (5) current use of nicotine replacement therapy or other smoking cessation medications (e.g., Chantix or Zyban); (6) current enrollment in another smoking cessation program; and (7) blows ≤ 5 CO into a breath analyzer at baseline.

Screening: Potential study participants will provide verbal informed consent to complete a phone screening that assesses eligibility. If eligible, participants will attend a baseline session described below. Those who do not screen eligible will be informed and thanked for their time.

Procedures: Eligible participants up to this point will be scheduled to attend a baseline visit at the Columbia University School of Nursing. Prior to arriving, participants will be asked to complete the Fagerstrom Test for Nicotine Dependence (FTND) and identify their cigarette type (menthol vs regular). Upon arrival to the study site, scheduled participants will be asked to blow into a breath analyzer to complete determining study eligibility. Breath samples will be analyzed for exhaled carbon monoxide (CO) levels (in ppm) using a breathalyzer (Micro ^{+TM basic} Smokerlyzer®). Those identified as ineligible will be given a Metrocard to thank them for their time. Those identified as eligible will be given an informed consent form and the study staff will read the form to them. Before a participant signs the informed consent form, staff will answer any questions. Participants will be given a copy of the informed consent form for their records.

After providing written consent, study participants will complete a timeline follow back to track their cigarette use for the last 30 days. Afterwards, they will complete a baseline questionnaire that includes demographic characteristics, tobacco use history, substance use history, alcohol use history, psychosocial factors, pharmacotherapy use, and more (See Table 1). Survey instruments will be collected through Qualtrics, a secure, Web-based application designed to support data capture for research studies, providing an intuitive interface, audit trails, and automated export. Qualtrics is a free service offered through Columbia University Irving Medical Center.

Following the completion of the baseline study instruments, study participants be randomized (1:1) to the Lumme arm or the control arm. Participants in both arms will undergo a smoking cessation counseling session and be provided with nicotine replacement therapy (NRT) in the form of the NicoDerm CQ Patch, under the supervision of a nurse. They will be provided

NRT sufficient for an 8-week supply in order to follow the three-step program. However, they will be encouraged not to begin NRT until 2-weeks after the baseline visit. This will be the quit date set for participants in both arms.

Participants who smoke more than 10 cigarettes per day will receive the following dosage: one 21 milligram patch per day for 4 weeks; one 14 milligram patch per day for 2 weeks; and one 7 milligram patch per day for 2 weeks. Participants who smoke 10 or less cigarettes per day will receive the following dosage: one 14 milligram patch per day for 6 weeks; and one 7 milligram patch per day for 2 weeks. This is considered the standard clinical treatment and participants will receive additional instructions on usage of the patch. Subjects will be told the risks of using the patch, which include skin irritation, itching, dizziness, headache, rapid heartbeat, and nausea. Participants will also be advised that they can curb additional cravings with their choice of gum or lozenge available for purchase over-the-counter.

For those in the intervention arm, study staff will provide participants with a Misfit Vapor 2 or Skagen Falster 2 smartwatch and initiate the Lumme app on the participant's mobile phone. Both smartwatches are compatible with the Lumme app. Participants will be asked to wear the smartwatch and use the app for 12 weeks to collect baseline data and improve detection of smoking. Study staff will help users create an account with the Lumme app which will passively collect smoking data during the first 2 weeks, such as when the user smokes (time of day, day of week, before/after eating, after waking up/before going to sleep, before driving to/from work, while driving), where the user smokes, and who is nearby when the user smokes (based on the seeing the same Bluetooth static address as Lumme does not collect identities). Once created, the Lumme app will be paired with the smartwatch so that smoking will be detected by the smartwatch and be sent directly to the Lumme app. The smartwatch will detect cigarettes smoked throughout the time the user wears the smartwatch, or users can manually enter a smoking session. The Lumme app will then be able to reliably predict cravings, target users with notifications to prevent individuals from smoking, refine the notifications for each user, and display their change in smoking behavior and money saved in a smoking diary. Users will also be able to see their quit plan with their assigned quit date 2 weeks after baseline, along with smoking trends, supporting tips, and earn badges from the amount of money saved. Data related to participants' smoking behaviors and patterns will be shared with Lumme. The study coordinator will also be able to access smoking behaviors and subject information through Lumme's anonymized online dashboard. At the end of the baseline visit, all enrolled participants will be compensated \$40 for their participation in the form of a pay card.

On the day before their quit date, study staff under the supervision of a nurse will call participants in both arms to remind them of their quit date and to start using their NRT NicoDerm CQ patches the morning of their quit date. This phone call will consist of the staff reassuring and encouraging the participant to stick to their quit date. Specific details for the call will be provided to staff via a phone script.

Upon reaching their quit date, participants in the intervention arm will receive personalized feedback in the Lumme app. Also, participants in both the control and intervention arm will receive biweekly checkin calls from study staff members. Staff will complete these calls in order to 1) track participants reported NRT fidelity, 2) provide technology assistance to those in the intervention arm who might experience difficulties with the smartwatch or app, and 3) keep participants engaged in the study.

Table 1. Study Measures

Construct	Measures (if applicable)	Measurement Time Points
Demographics	Gender, age, education, income, employment, health insurance, housing, time since diagnosis with HIV, tobacco, alcohol, substance use, health literacy (measured by Short Test of Functional Health Literacy in Adults [S-TOFHLA]), ¹⁷ and co-morbid conditions	Baseline
Tobacco Use History	Age of initiation, current smoking, daily smoking, types of products used (e.g., menthol cigarettes, e-cigarettes), history of quit attempts, prior use of quitline/telephone counseling services	Baseline
Tobacco Cessation	CO lung/blood concentration, 7-day point prevalence abstinence –Timeline follow-back (TLFB) ^{18,19} ; number of quit attempts; days of continuous abstinence	Baseline, 12 weeks
Illicit Substance and Alcohol Use	NIDA ASSIST ^{20,21} , Short Michigan Alcoholism Screening Test (SMAST), Drug Abuse Screening Test (DAST)	Baseline
Health-Related Quality of Life	PROMIS-29 ²²	Baseline, 12 weeks
Predictors of Tobacco Cessation	Fagerstrom Test for Cigarette Dependence, ²³ Readiness to quit ²⁴	Baseline, 12 weeks
Cravings and Withdrawal	Minnesota Withdrawal Scale, ²⁵	Baseline, 12 weeks
Marker of HIV/AIDS immune status/ ART Adherence	Case Adherence Index (self-report) ²⁶	Baseline, 12 weeks
Intervention Quality	Health Information Technology (IT) Usability Evaluation Scale (Health-ITUES) ²⁷ ; Post-System Study Usability Questionnaire (PSSUQ) ²⁸ , Intervention ratings	12 weeks
Psychosocial Factors	Stress: Perceived Stress Scale (PSS) ^{29,30} , Depression: Center for Epidemiological Studies Depression scale (CESD score) ³¹ , Anxiety: State-Trait Anxiety Inventory (STAI score) ³² , Social support ³³	Baseline, 12 weeks
Pharmacotherapy use	Nicotine replacement therapy, Bupropion, Varenicline Use and Self-Reported Adherence	Baseline, 12 weeks

At 12 weeks after the baseline visit, participants will attend a 12-week follow-up visit at the study site. Or if requested, participants can complete a remote study visit, where they will be mailed a CO monitor (by the study team and complete study tasks via video call on Zoom Health with a study team member. Study participants will be asked to report a 7-day point prevalence abstinence of smoking cigarettes and provide a breath sample using Micro +™ basic Smokerlyzer®. They will also be given a follow-up survey that includes questions asked at baseline and process questions dictated by the primary outcomes that assess the usability and acceptability of Lumme (see Table 1).

At the 12-week follow-up visit, semi-structured in-depth interviews will take place with participants. The in-depth interviews will be approximately 10-30 minutes in length and no additional compensation will be provided. The in-depth interviews will be conducted by the study coordinator and research assistants, the members responsible for conducting follow-up visits. These interviews aim to fill gaps in the literature by taking a qualitative approach to understanding the acceptability of the

Lumme app as a smoking cessation tool in the intervention arm and learn more about all participants' opinions on the recruitment and enrollment process. Both groups will answer questions including: 1) How would you modify the outreach and recruitment process to improve it or make it easier? 2) How comfortable were you with the recruitment, screening and enrollment process? 3) How can we improve the current screening process? Some of the questions the questionnaire will include for the intervention group are: 1) Please describe your general perceptions and expectations of the app, 2) How often did you use the app? 3) How helpful was the app for tobacco cessation?

The team will adhere to qualitative research processes to ensure the credibility, confirmability, dependability, and transferability of the qualitative data from these analyses.³⁴ To support the credibility of the data, we will conduct peer debriefing and triangulate findings across multiple data sources (surveys). In addition, we will use "member checks," i.e., sharing of initial data interpretations with participants to ensure accurate interpretations. Triangulation of findings, along with reflexivity, will enhance the confirmability of the interpretations. The investigators will carefully record an audit trail and keep extensive field notes to facilitate transferability of study findings into other contexts. At the end of the 12-week follow-up visit, participants will be compensated \$60 for their participation. Compensation will be provided in the form of pay cards or Amazon gift codes. All participants will also receive a Metrocard at each in-person visit.

Operationalization of Outcome Measures: The primary outcome for determining preliminary efficacy will be biochemically validated 7-day point prevalence abstinence.

Analysis: This is a pilot study meant to assess preliminary feasibility, acceptability, and efficacy. Given the small sample size, the purpose of the arms is simply to monitor for unexpected, gross differences between arms.

To determine acceptability, we will ask participants in both arms how useful each of the intervention components are (1 = *Not at all useful* to 7 = *Extremely useful*) and whether they would recommend the program to a friend (1 = *Definitely would not recommend* to 7 = *Definitely would recommend*). For the intervention to be deemed acceptable, the mean level for each of these measures would have to be five or higher.

All in-depth interviews will be transcribed verbatim and then coded. The development and application of a coding scheme is an integral component of the data analysis process. It enables the systematic examination and interpretation of the data related to the primary analytic foci. The coding scheme is conceptualized as a multilevel structure. At the highest level are the primary analytic foci coded as headings. Specific aspects or dimensions of the headings are assigned core codes. Specific aspects or dimensions of the core codes are assigned sub codes. We use ATLAS.ti, a software program for qualitative analysis, to facilitate the analysis.

The following 7 steps will be used to develop the coding scheme:

Step 1: Identify the principal issues discussed by interviewees.

Step 2: Construct definitions of the primary analytic themes.

Step 3: Develop and apply core codes and sub-codes to the initial set of interviews.

Step 4: Develop a provisional coding scheme.

Step 5: Test and refine the provisional coding scheme.

Step 6: Reconcile coding differences and construct an updated and final coding scheme. Step 7: Apply the coding scheme to the full data set and assess inter-coder reliability.

After all transcripts have been coded, we will extract and examine the content of text segments linked to core codes and sub-codes relevant to understanding the technology acceptance of the Lumme app and barriers and facilitators to its use. Based on the coded data, we will propose ways in which certain themes are analytically related. A careful examination of the coded text will reveal the associations among these themes, and may lead to more refined data searches. Once we establish patterns of relationships among themes and issues, we will identify participants' accounts that support or refute these patterns. Identifying and accounting for cases that deviate from an interpretative pattern enable us to test and confirm the pattern's validity and robustness. Schnall has done extensive work understanding technology acceptance with particular emphasis on end-users' needs. 35-38

Efficacy of the intervention will be based on self-reported 7-day point prevalence abstinence at the follow-up survey. Lost-to-follow-up participants will be included as smokers. The abstinence rate will be calculated.

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