

Study Title: Smoking Cessation Intervention for Women Living with HIV
NCT NO: NCT02898597

March 31, 2018

STUDY PROTOCOL

Project Summary

I. Rationale

With the use of combined antiretroviral therapies, people with HIV infection now live longer than ever before. However, the burden of non-AIDS related health problems such as cardiovascular diseases and cancers on people living with HIV/AIDS has considerably increased, which undermines the health of those living with HIV [1-3]. Smoking is one of the major contributing factors to these health problems. Rates of cigarette smoking are substantially higher among people living with HIV than the general population: 40-75% versus 19% [2]. HIV positive women smokers have a 36% higher risk for developing AIDS and a 53% higher mortality when compared to nonsmokers with HIV/AIDS [2]. However, the rates of abstinence achieved by the existing smoking cessation interventions for this group are very modest, hovering around 6-9% [e.g., 4, 5]. These rates are substantially lower than the rates (e.g., 16-30%) obtained from the general smoker population [6]. There is thus an urgent need to develop a smoking cessation intervention that is effective for women living with HIV, which will promote and protect women's health and their wellbeing.

The HIV-related measures (instruments) used in this study identify demographic characteristics, attitudes, beliefs, and behaviors. Each of the measures is selected to collect data that affect personal health (secondary and tertiary levels). For example, stigma measures assess the degree of personalized (or self) stigma, HIV disclosure concerns, negative self-image, and concern with public attitudes toward people with HIV, which may be related to health promotion and wellness efforts, such as smoking cessation. There is empirical evidence that women perceive more HIV-related stigma than men, and those who have high perceived HIV-related stigma are less likely to disclose their HIV status to others, to seek treatment and to adhere successfully to their medication [4]. The demographics and all other instruments were chosen and reviewed by the Massachusetts Department of Public Health Office of HIV/AIDS and used successfully in a randomized controlled trial (RCT) completed by Dr. Rosanna DeMarco [7].

The smoking-related measures are chosen because they provide valuable information to tailor cessation intervention components to the specific needs of a person, based on one's smoking behavior and history of smoking cessation treatment. "Self-efficacy" has been identified as the only variable that significantly mediates the effect of smoking cessation intervention on abstinence [e.g., 8, 9]. There is ample evidence that people with depression and anxiety are less likely to succeed in smoking cessation [e.g., 10, 11]. We also include depression and anxiety measures to screen women who may have clinical depression or anxiety. They will be strongly urged to seek treatment for the condition. Of note, Dr. Kim is a licensed psychiatric advance nurse practitioner and those who earn a score of 16 or higher on the depression measure or 8 or higher on the Generalized Anxiety Disorder (GAD)-7 Scale will be interviewed for the diagnosis of depressive or anxiety disorder, respectively. If they meet the diagnostic criteria for any of the disorders based on the DSM-V, they will be excluded. All of the measures have been successfully used in previous smoking cessation studies by Dr. Sun Kim [e.g., 12, 13].

II. Background Information

Dr. Kim completed a smoking cessation intervention for Korean American women and is now preparing manuscripts for publication. She found that women with HIV and AIDS have many similarities with Korean American women in terms of their reluctance to seek smoking cessation treatment due to perceived stigma, and their preference for telephone counseling rather than in-person counseling [4, 5, 14]. Furthermore, similar to the low success rate of abstinence found among people with HIV infection, the rate of abstinence among Korean American women had been low (e.g., 5%) relative to their male counterparts (e.g., 17%) [15]. On the other hand, Dr. Kim's videoconferencing smoking cessation intervention yielded an abstinence rate (28-30%), higher than

what has been reported for this population in previous studies [16], although findings are preliminary due to the nature of a pilot study. In Dr. Kim's pilot trial, the smoking cessation interventions were tailored to the needs of Korean American women and the counseling is relatively intense (eight weekly 30-minute sessions) compared to the usual telephone counseling (four to six weekly 10-15 minute sessions). A meta-analysis of smoking cessation studies with the general US population revealed that high-intensity counseling support is more important for women than for men [17]. Thus, it is believed that if smoking cessation interventions are tailored to the specific needs of women with HIV and the cessation counseling is intense (e.g., eight weekly 30 minute sessions), women with HIV may achieve an abstinence rate that is higher than the rates reported in the literature [4, 5].

III. Methodology.

The proposed study is a 2-arm parallel-group RCT of a smoking cessation intervention with 50 English-speaking women who have been diagnosed with HIV infection. Participants will be randomized at a ratio of 1:1 to either the video arm (n = 25) or the telephone arm (n = 25). The randomization will be based on computer-generated random numbers (<http://www.randomizer.org/>). The numbers will be written in a color-coded paper (the video arm = red and the control arm = blue). These papers will be placed in an envelope in order, which will be open right after the completion of the baseline assessment. Both arms will have eight weekly individualized counseling sessions and each session will be 30 minutes long. The study is conducted to determine the acceptability and feasibility of a videoconferencing smoking cessation intervention for women with HIV. It is also being conducted to estimate the effect of the videoconferencing smoking cessation intervention on abstinence compared with telephone counseling cessation intervention for women with HIV.

Recruitment Procedures

Participants will be recruited through the Sistah Powah Group, a group of women living with HIV whose purpose is to advance HIV prevention (primary, secondary, and tertiary prevention) and assist other HIV positive women in managing their co-morbidities through care engagement (e.g., ex-smoking behaviors). We will also contact the local HIV AIDS Service Organizations (ASOs) by contacting leaders at each area personally and asking them to forward our email message (see below in Box 1) or through, explaining the study and offering fliers to be shared with clients or posted at their organizations. For example, Dimock Health Center, Boston Living Center, Multicultural AIDS Coalition, Massachusetts Department of Health Office of HIV/AIDS, Fenway Health Center, AIDS Action, AIDS Alabama, University of Mississippi Medical Center, and HOCC (Healing Our Community Collaborative).

In addition, the following will be posted in online communities of people with HIV infection (e.g., HIV/AIDS Tribe and +supportgroups).

Box 1 Online Posting Sample

Who: All Women living with HIV infection who want to quit smoking.

Study Title: **Smoking Cessation Intervention for Women with HIV**

Contact Information: Please call Dr. Sun Kim **617-287-6831** or Ms. Sabreen Darwish **781-492-7096** for more information AND eligibility.

The study is conducted at the University of Boston and the intervention is provided via phone calls. Visa gift cards (\$25-50) will be provided at each data collection point.

Anyone interested will be asked to contact the research team (Dr. Sun Kim or Ms. Sabreen Darwish). Prior to the screening interview, a verbal consent (see the verbal consent form attached) will be obtained. If the caller is determined to be ineligible or refuses to participate, all data collected will be shredded immediately and will not be used in the study. Screening data for those who agree to participate but fail to provide a written consent form within two weeks from the screening interview will also be shredded. The screening data will be transferred to baseline assessment datasheet only after the caller provide a signed consent form. Then, the paper containing screening data will be shredded.

The following screening interview script will be used:

1. Can you speak English? Yes
2. Have you been diagnosed with HIV infection? Yes
3. What kind of medications are you currently taking for HIV infection? (This question is asked as a way to verify HIV infection)
4. How old are you? 18 or older
5. How many cigarettes on average have you been smoking a day? 5 or more cigarettes per day
6. How long have you been smoking? At least for the past 6 months
7. Are you willing to quit smoking within the next four weeks? Yes
8. Are you willing to use nicotine patches? Yes
9. Do you have any active skin disease? No
10. Have you had emotional complications such as feeling anxious and depressed around quitting smoking?
No. If the caller answers “yes” to this question, we will ask whether the quit attempt was made with or without assistance. We will also ask the severity of the complication(s). If the caller answers that the complications were so distressing and required treatment, she will be excluded from the study.
11. Do you currently receive treatments (counseling and pharmacotherapy) for any of these conditions: Suicidal Ideation, Alcohol Dependence, Schizophrenia, Schizoaffective Disorder, and Bipolar Disorder?
No
12. Have you ever attempted to kill yourself? No
13. Do you currently use any illegal substances except marijuana (weed)? No
14. Are you pregnant? No
15. Are you currently using any method of birth control? Yes. We will then ask the caller to specify what type of birth control she is currently practicing. If no, we will ask whether the caller is willing to practice birth control during the intervention period (3 months). Only those who use or agree to use an approved form of birth control (e.g., oral medications, condoms, Depo Provera injection, and intrauterine devices) will be accepted into the study.
16. Are you currently breast-feeding? No
17. Do you agree to use birth control pills or devices during the study period? Yes
18. Do you have access to a telephone and an Internet-connected computer? Yes

Women who answer as above will be recruited into the study. They will be informed about the purpose and procedure of the study and then will be given time to ask questions if they have any. Once all questions being answered, Dr. Sun Kim (or Ms. Sabreen Darwish) will ask them to provide the following contact information: mailing address, e-mail address, at least two connected telephone lines (the participant’s cell phone, home phone or a third phone). Dr. Kim (or Ms. Darwish) will inform that they will be randomly selected to receive smoking cessation counseling either via a video call such as Face-time, Skype and Tango or by telephone. Individuals who are determined to be ineligible will be explained why they are not eligible for the study.

Consent Procedures

We will e-mail or mail the Consent Form along with baseline research questionnaires to prospective participants who agree to participate in the study. The consent form will be accompanied with an information letter stating that they should read the consent form carefully and call us if they have any questions before signing the form. They can e-sign and return the form via e-mail, send a scanned consent paper via e-mail, or send a picture of a signed consent form via telephone message. For individuals who do not have e-mail account or prefer the form via post office mail, we will ask them to return the signed consent form in a self-addressed stamped envelope that will be provided. Dr. Kim or Ms. Darwish will make a one-time call to remind them of returning the consent form if they have not done so within the next two weeks. Dr. Kim will be available by telephone to help them complete the form if they have any questions about it. Women who have not returned the signed consent form after the reminder call will be considered “not interested” in the study and their screening data will be shredded.

Intervention Procedure

The quit day will be determined between the second and fourth sessions based on one’s readiness for quitting. The first three sessions is focused on preparing participants for the quit day. A female therapist (Dr. Kim and Ms. Darwish) will educate neurobiological changes in the brain associated with nicotine addiction and how nicotine patches help them quit smoking. She will also train participants to learn behavioral strategies that have been found effective for dealing with symptoms of nicotine withdrawal. Post-quit sessions vary by individual needs depending on their abstinence status and severity of nicotine withdrawal symptoms. Below is the description of intervention components for each session in both videoconferencing and telephone counseling interventions.

Table 1. Intervention components of each session

| Session | Intervention Components |
|-------------------------|---|
| 1st session | <u>Assessment and Planning:</u> Assess decisional balance between pros and cons of smoking; discuss and select the target quit date; discuss how to change one’s smoking pattern for quitting; assign a homework to do an hourly smoking log sheet; provide information what has been reported in tobacco literature on people with HIV infection; and instill hope that smoking cessation is possible with guidance and support. |
| 2nd session | <u>Health Benefits of Quitting:</u> Assess the participant’s perceived health status, discuss immediate health benefits of quitting smoking; explain smoking increases bacterial and Pneumocystis pneumonia among people with HIV infection; inform women with HIV infection who smoke are more likely to develop AIDS and die from AIDS-related cancers and infections than those who don’t smoke; and encourage her to watch CDC’s Tips from Former Smokers: Smoking and HIV. |
| 3rd session | <u>Preparation for the Quit Day:</u> Explain the neurobiological change of brain associated with nicotine dependence; explain nicotine patches, effects and side effects of the medication and how to manage side effects if they occur; counsel behavior changes in preparation for the target quit day; explain possible drug-to drug interactions between nicotine patches and HIV medications; and advise to download a free smartphone quit application such as QuitPal and StayQuit Coach. |
| 4 th session | <u>Nicotine withdrawal symptoms and Medication Management:</u> Assess nicotine withdrawal symptoms, lapse/relapse, adherence to nicotine patches, and any side effects of nicotine patches; advise proper managements of any patch problems; and counsel behavioral coping strategies for the withdrawal symptoms. |
| 5th session | <u>Lapses and Relapse:</u> Assess nicotine withdrawal symptoms and lapses and relapse; discuss helpful cessation strategies including 4 Ds (delay, deep breathing, drink water, and discuss); and discuss about HIV smokers who courageously beat the deadly addiction. |
| 6th session | <u>Stress and Coping Skills:</u> Assess nicotine withdrawal symptoms and lapses and relapse; counsel to understand the effects of negative cognitions on negative moods (e.g., depression and anxiety), discuss positive coping skills; discuss any positive changes in the body; and encourage exercise and healthy living. |

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|-------------------------|--|
| 7 th Session | Medication Adherence: Assess medication adherence; explain the importance of adherence to nicotine patches; and explain about dose reduction of nicotine patches (from step 1, 21mg to step 2, 14mg). |
| 8 th session | Relapse Prevention: Discuss strategies to avoid lapses and relapse in high risk situations (e.g., meeting a friend with whom the participant used to smoke); and revisit the importance of quitting smoking and medication adherence. |

Participants in both arms will receive nicotine patches at two separate occasions: first, a 4-week supply of 21mg nicotine patches (14 mg if the participant smoke 5-9 cigarettes per day) and second, a 2-week supply of 14mg nicotine patches and a 2-week supply of 7mg nicotine patches together. All participants will also have education about the pharmacological mechanism of nicotine patches and their correct usage and management of possible side effects. Adherence to the medication will be monitored by asking participants to show used patches within the past week for the video arm and by asking participants the number of patches that have been used within the past week for the telephone arm.

Researchers

Dr. Kim has 13 years of research experience in multidisciplinary tobacco research with a focus on tailoring smoking cessation interventions for special populations such as Asian Americans, women, and people with mental illness. She recently completed a videoconferencing smoking cessation intervention study for Korean American women. She is also an advanced nurse practitioner with a specialty in mental health, and has provided cessation counseling to Asian and non-Asian smokers for the past 9 years. Dr. Sprague has 11 years of multidisciplinary research experience—focused on structural, health systems, behavioral and socio-cultural facilitators of and barriers to HIV treatment, prevention and support—primarily in Black women in South Africa and more recently in the Deep South (Alabama and Mississippi). Dr. DeMarco has 15 years of multidisciplinary research experience focused on HIV self-protective and risk factors that contribute to healthcare adherence and safe sex negotiation in low income, aging Black women.

Counselors

Dr. Kim and Ms. Darwish (a doctoral student in nursing) will provide cessation counseling. Prior to providing counseling, Ms. Darwish will have intensive trainings of tobacco dependence treatment and telephone cessation counseling. The trainings also include role-playing scenarios of common problems.

Follow-up Assessment

Women who have not returned a signed consent form will not participate in any follow-up assessment. Only participants who provide the consent form and report abstinence at 3-, and 6-month follow-ups will be asked to perform a saliva cotinine test via video calls. The tests are done only after the completion of counseling and nicotine replacement therapy and those in the telephone arm will also perform the saliva test via video calls (the video call is done for the test not as part of the intervention). For this, they will receive the saliva test kit via certified mail. Cotinine is the major proximate metabolite of nicotine. It has a long half-life approximately 15-19 hours and is widely used as a biological marker of nicotine exposure [18]. In this study, we will use the NicAlert® test that is a semi-quantitative measure of cotinine based on colorimetric immunoassay reaction. The test strip displays seven zones that represent a range of cotinine levels from 0 (0–10 ng/ml) to 6 (≥ 2000 ng/ml). Those who earn level 1 or higher will be treated as smoking irrespective of their self-report. Participants will also be assessed on the measures of self-efficacy in resisting smoking temptation, depression and anxiety to see any changes since baseline.

Participants will receive a gift card worth \$30 at baseline and \$25 at each of the three follow-up assessments (post-quit 1-, 3-, and 6-months) irrespective of their smoking status (abstinent vs. smoking). If they perform the saliva test, they will receive an additional gift card worth \$25. Thus, those who perform the test will receive a gift card worth \$50 at each time. The gift card will be mailed to the home address via a postage mail.

The study is a pilot project to obtain preliminary data for the feasibility and acceptability of a videoconferencing smoking cessation intervention for women living with HIV. Dr. Kim will identify and describe the time to recruitment and any barriers. She will also describe reasons for any refusals to study participation. She will compare abstinence and attrition rates at each follow-up. Participants will complete an Exit Survey, rating their overall satisfaction with the intervention that they have.

IV. Participant

Inclusion criteria. To participate in this study, an individual must be a woman who: (1) is able to speak English, (2) self-reports having been diagnosed with HIV infection, (3) is between the ages of 18 and 75, (4) has smoked at least 5 cigarettes per day for the past 6 months, (5) has access to smartphone and computer (a desktop or laptop) with Internet/wireless, (6) is willing to quit smoking within the next 4 weeks from the first session of counseling, and (7) agrees to use an approved form of birth control during the intervention.

Exclusion criteria. Individuals will be excluded based on any of the following criteria: (1) current involvement in other behavioral or pharmacological smoking reduction/cessation programs, (2) being pregnant or lactating, (3) active skin diseases, (4) serious alcohol use problems or current use of any illegal substances, or (5) active treatment for serious mental illness such as schizophrenia and bipolar I disorder.

V. Risks and Benefits

Reasonably foreseen risks involved in this study are symptoms of nicotine withdrawal and potential side effects of nicotine patches, although these are recognized as relatively safe. Nicotine patch is one of the FDA approved first-line cessation medications and can be purchased over the counter without a prescription [6]. The most common adverse effect of the patch is topical skin irritation, ranging from mild erythema to a more generalized skin reaction, frequently in participants with a history of eczematous dermatitis. Other potential side effects include nausea, vomiting, headache, light headedness, rapid heartbeat, and strange dreams. However, all of these side effects occur at about 10-15% and mostly are mild. They will disappear once a person stops using the medication. Another potential risk that may occur is related to the loss of privacy or breach of confidentiality. There is also a potential risk of embarrassment among those who report abstinence but their saliva cotinine test yields a positive result. False positive results are possible if participants have been exposed to secondhand smoke. In the rare event that a participant may express suicidal ideation. If this happens, Dr. Kim will evaluate the participant to assess suicidality of the participant using the Columbia-Suicide Severity Rating Scale (C-SSRS). If the counselor is Ms. Sabreen Darwish, she will immediately contact Dr. Kim at 201-388-2656 for evaluation who will evaluate the person within the next 2 hours. If the person is determined to be at immediate danger, Dr. Kim will inform that she has to break confidentiality and call 911. If the participant is not determined to be at immediate risk, Dr. Kim will strongly encourage the person to talk to her primary healthcare provider or call the Suicide Hotline if she has suicidal ideation. Dr. Kim will follow up on the person weekly for the next month and then monthly until the person completes the study.

Potential benefits. Participants may benefit because they will receive an evidence-based tobacco dependence treatment that has been developed and found effective in the general U.S. population when it is delivered via person-to-person. Their family members may also benefit if participants quit smoking because they are less likely to be exposed to secondhand smoke.

VI. Informed Consent

Dr. Kim or Ms. Darwish will initiate the consent process right after the screening interview. The screener will read the consent form to the caller. The consent form clearly states that the research study involves 8 individual

videoconferencing or telephone sessions and time at each session lasts approximately 30 minutes. The consent form also states clearly that participation in the study is absolutely voluntary and they can withdraw from the study anytime without having to justify for their action. The prospective participant will be provided time to ask questions and all questions will be fully answered. Then, the person will be asked to provide contact information so that she can receive the consent form via e-mail or post-office mail. The person will be asked to sign/e-sign and return the form via e-mail/picture message or regular mail.

Confidentiality

Personal identifying information (names, addresses, phone numbers, etc.) will be kept in a separate file from other study data. We will code their personal information and store it in a locked cabinet in Room 301-03 at the Science Building of University of Massachusetts Boston, 100 Morrissey Blvd. Boston, MA 02125. The file of personal information will be kept until the participant complete the study that is 6w-month follow-up assessment and then will promptly be destroyed. Neither the subjects' names nor any other personal identifying information will appear in the questionnaires or on audiotapes of therapy sessions. Audiotapes and transcript will be kept for one year after the completion of the study and then destroyed. Neither participants' names nor any other personal identifying information will appear on data files. Electronic files containing personal information will be password-protected. All smoking cessation materials including smoking log will be sent by postage mails.

References

1. Paudel V, Baral KP. Women living with HIV/AIDS (WLHA), battling stigma, discrimination and denial and the role of support groups as a coping strategy: a review of literature. *Paudel and Baral Reproductive Health*, 2015;12:53.
2. Goffman E. *Stigma: Notes on the management of spoiled identify*. Penguin, 1963. London UK.
3. Ho S-S, Holloway A. The impact of HIV-related stigma on the lives of HIV-positive women: an integrated literature review. *Journal of Clinical Nursing*, 2015; 25(1-2):8-19.
4. Minkoff H, Feldman JG, Strickler HD et al. Relationship between smoking and human papillomavirus infections in HIV-infected and –uninfected women. *Journal of Infectious Diseases*, 2004; 189:1821–1828.
5. Moscou-Jackson G, Commodore-Mensah Y, Farley J et al. Smoking-cessation interventions in people living with HIV infection: a systematic review. *The Journal of the Nurses Association in AIDS Care*, 2014; 25(1):32-45.
6. Fiore MC, Jaen CR, Baker TB et al. Treating tobacco use and dependence: 2008 Update. *Clinical Practice Guideline*. USDHHS, U.S. Public Health Services, 2008. Rockville, MD.
7. DeMarco RF, Chan K. Structured writing: An effective intervention for aging low income HIV positive Black women. *American Journal of Health Promotion*, 2013; 28(2):108-118.
8. Graham AL, Papandonatos GD, Cobb CO, Cobb NK, Niaura RS, Abrams DB, Tinkelman DG. Internet and telephone treatment for smoking cessation: Mediators and moderators of short-term abstinence. *Nicotine & Tobacco Research*, 2015; 17(3):299-308.
9. Vidrine DJ, Kypriotakis G, Li L, Arduino RC, Fletcher FE, Tamí-Maury I, Gritz ER. Mediators of a smoking cessation intervention for persons living with HIV/AIDS. *Drug and Alcohol Dependence*, 2015; 147:76-80.
10. McClave AK, Dube SR, Strine TW, Kroenke K, Caraballo RS, Mokdad AH. Associations between smoking cessation and anxiety and depression among U.S. adults. *Addictive Behaviors*, 2009; 34:491-497.
11. Pomerleau OF, Pomerleau CS, Mehringer AM, Snedecor SM, Ninowski R, Sen A. Nicotine dependence, depression, and gender: characterizing phenotypes based on withdrawal discomfort, response to smoking, and ability to abstain. *Nicotine & Tobacco Research*, 2005; 7:91–102.
12. Kim SS, Kim S, Fang H, Kwon S, Shelley D, Ziedonis D. A Culturally Adapted Smoking Cessation Intervention for Korean Americans: A mediating effect of perceived family norm toward quitting. *Journal of Immigrant and Minority Health*, 2015; 17(4):1120-1129.
13. Kim SS. A Culturally Adapted Smoking Cessation Intervention for Korean Americans: Preliminary Findings. *Journal of Transcultural Nursing*, in press. DOI: 10.1177/1043659615600765

14. Vidrine DJ1, Marks RM, Arduino RC et al. Efficacy of cell phone-delivered smoking cessation counseling for persons living with HIV/AIDS: 3-month outcomes. *Nicotine & Tobacco Research*, 2012; 14(1):106–110.
15. Myung SK, Seo HG, Park EC, Lim MK, Kim Y. An observational study of the Korean proactive quitline service for smoking cessation and relapse prevention. *Public Health Rep.* 2011; 126(4):583-590.
16. Kim SS, Sitthisongkram S, Bernstein K, Fang H, Choi W, Ziedonis D. A Randomized Controlled Trial of a Videoconferencing Smoking Cessation Intervention for Korean American Women: Preliminary Findings. Accepted for publication in *International Journal of Women's Health*.
17. Cepeda-Benito A, Reynoso JT, Erath S. Meta-analysis of the efficacy of nicotine replacement therapy for smoking cessation: Differences between men and women. *Journal of Counseling and Clinical Psychology*, 2004; 72:712-722.
18. Benowitz NL, Jacob P, 3rd. Metabolism of nicotine to cotinine studied by a dual stable isotope method. *Clinical Pharmacology & Therapeutics*, 1994; 56(5):483-493.