

Gender and racial differences in enrollment and follow-up in a smoking clinical trial targeting people living with HIV: Implementation and preliminary outcomes

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OBJECTIVES: The identification of key protocol elements and implementation challenges critical to achieve: 1) high enrollment rates of a gender and racially diverse sample and 2) retention rates over 80%, in a smoking cessation clinical trial among people living with HIV.

METHODS: Analyses of recruitment, retention and adherence of an ongoing clinical trial with 5 times points. Seven blocks of candidate risk adjusters were included: 1) Type of recruitment, 2) Education, 3) Smoking history, 4) Attitudes toward nicotine replacement therapy (NRT), 5) Type of retention strategy 6) HIV status, and 7) Socio-demographics

RESULTS: Positive outcomes include timely recruitment of 200 participants over 18 months, with a large proportion of women and minorities. Word-of-

mouth referral (53%) was the most effective recruitment strategy. Hispanics and males were more responsive to flyers ($p=0.04$). Females were more likely to be recruited from target clinics or by participating in prior studies ($p=0.004$). The expectation set forth for the behavioral intervention attendance was a 100% and 99% completed it. However, adherence to pharmacotherapy was 65% instead of 85%. We achieved 88% retention rates in a population characterized by rates as low as 42%. Analyses revealed that Non-Hispanic Whites were less likely to believe in nicotine replacement being effective, and consequently, were often lost to follow-up.

CONCLUSION: Recruitment and retention of a diverse population of smokers living with HIV can be successful using a combination of methods. However, adherence and attitudes toward pharmacotherapy should be addressed to reach the full therapeutic potential of treatments

Key Words: Enrollment; Smoking cessation; Follow-up; Race; Gender; Clinical trials; HIV

Cigarette smoking is a leading cause of morbidity and mortality in the world (1). Yet the burden is not equally distributed between men and women, where smoking prevalence in men exceeds their counterparts (22.8% versus 18.3%) (1,2). Furthermore, men and women do not benefit equally from prevention programs and treatments. Participant recruitment to clinical trials has been called “the most difficult and challenging aspect of clinical trials,” with recruitment problems representing one of the main reasons for the failure of clinical studies (3).

In the setting of HIV, appropriate recruitment of women is critical, since thus far national data suggests that gender differences in smoking rates are slim (42.9% vs. 41.5%) (4,5). Unfortunately, the published clinical trials targeting people living with HIV have presented very limited, gender-specific data with only a single study reporting gender differences in outcomes (6).

Both the Food and Drug Administration (FDA) and the Regulatory Affairs Professional Society (RAPS) have also raised concerns because many clinical studies do not have diverse demographic information (7). According to their analyses, only a quarter of the reports included a race or ethnicity subgroup analysis. Furthermore, they recognized that it is critical for clinical trials to reflect representative proportions of intended use populations. Prior pharmacological smoking cessation studies have been characterized for the limited enrollment of minorities. Clinical trials in general have an inadequate representation of African Americans. For example, large-scale trials establishing efficacy of the FDA-approved medications bupropion and varenicline included only 2-11% African Americans in their samples (8-12). Shiffman's studies with nicotine replacement therapy included between 3-10% of African Americans in their sample (13). Hispanic enrollment in research is also low. Recruiting minorities in clinical trials is important because studies should reflect the representative proportions of intended use populations. Several studies and analyses of the literature have examined successful recruitment and retention strategies. However, little is known about the logistics of successful strategies specific to people living with HIV (PLWH) (14-16). The demographics of smokers living with HIV differ substantially from the U.S. general adult population by age group, sex, race

or ethnicity, education, and poverty level (17). Poor abstinence rates among underserved groups, such as ethnic minorities and persons living with HIV (PLWH), may reflect limited referral to and/or use of effective smoking cessation treatments. In addition, people living with HIV often belong to less affluent socioeconomic classes and have multiple comorbidities (18). Monitoring of recruitment and follow-up activities is vital to a randomized clinical trial's success and should be performed regularly. Therefore, instead of reporting data when the study is finished, we decided to analyze and share this data in the middle of the trial. Analysis of the current sample size will provide information about the strengths and weaknesses of these strategies, and will help set performance standards for investigators.

Specific questions in this first analysis focus on determining whether differences exist above and beyond sociodemographics between Hispanics, African Americans, and Caucasians. There were racial differences in: (a) enrollment, (b) eligibility rates, and (c) attendance. This information has important implications for future research aimed at increasing access to, and participation in, clinical trial research for PLWH and minorities.

METHODS

Design and Setting

The PATCH Study is an ongoing randomized clinical trial study of HIV+ smokers in Miami, Florida that began in 2016 with a target sample size of 500 (Figure 1). The initial 3 months focused on IRB, training, and administrative procedures. Current analyses spanned from June 2016 until December 2017, for a total of 18 months of enrollment and follow-up. Adults were eligible if HIV status, smoking status, and willingness to quit were confirmed. For safety reasons, subjects were excluded if they had any contraindication to nicotine patches or gums, were involved in other smoking and/or drug cessation or weight control programs, or had comorbid conditions that limited their safe participation, such as presence of psychotic or disabling psychiatric disorders.

Although many clinical trials are now resorting to internet and media

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recruitment approaches, our team relies on traditional methods of enrollment. We have found that personal interactions and close assessment are necessary to ensure the provision of adequate care in this hard-to-reach population. Three general types of recruitment approaches were used: clinic-based recruitment and both active/passive community outreach methods. To increase enrollment of underserved minority smokers, clinics around the downtown area that have high concentrations of low-to-middle income African American and Hispanic smokers were specifically targeted. Recruitment sources were classified into the following categories: physician or health care professional referral, flyers left in the clinics, public transportation advertisement, and word of mouth.

Interested smokers called a central research office where they completed a telephone pre-screening with a research team member to determine eligibility. During the call, the team member inquired about the participant's referral source for the study. If eligible, potential participants were given an appointment for the baseline visit which included a more detailed in-person screening. After giving informed consent, participants provided an exhaled breath carbon monoxide sample (Vitalograph; Lenexa, KS) for biochemical verification of smoking status. Study personnel also assess the readiness to quit as measured by Readiness to Quit Ladder and Prochaska and DiClemente's TTM (1-10 scale) (19,20). Written study materials, informed consent forms, and the study protocol were approved by Western IRB (WIRB). All procedures occurred at the University of Miami Clinical Translational Research Site.

Smoking Surveys

Subjects completed several standardized surveys to profile smoking history, including number of cigarettes smoked per day and history of tobacco use (cigarettes and cigars). These data, along with age of initiation and total number of years of smoking, enables estimation of cumulative exposure. To measure nicotine dependence, we selected the Fagerström Test for Nicotine Dependence (FTND) due to strong literature evidencing validity, reliability and its availability in English and Spanish (21). Participants were also asked about exposure to second-hand smoke (SHS), symptoms of lung disease, and personal/family history of respiratory conditions. Upon completion of the baseline visit, participants were scheduled for their behavioral intervention within the next 7 to 10 days.

Follow-up

After completing the behavioral intervention, participants were scheduled to return to the clinic at 1, 3, 6 and 12 months. Retention rates of 80% in longitudinal studies with over 200 participants are considered excellent, but the investigators milestone was set at 85% (22). The study uses several retention strategies to achieve this goal, including:

- 1) **Financial incentives that are not coercive:** Participants received compensation upon completion of study procedures (\$75 for visits lasting approximately 2 ½ hours, and \$30 for shorter visits).
- 2) **Team:** A study personnel composed of a full-time study coordinator and two research assistants who are bilingual, culturally competent, specialized in the target population, well organized, and experienced running large cohorts.
- 3) **Contact:** To aid in retention efforts, the team collects contact information (phone and address of the participant) along with one or two additional contacts (e.g. friends or family members). This information was updated at each visit and/or telephone communication.
- 4) **Reminders:** A well-built data management system using Microsoft Access alerted the study coordinator of which participants needed to be contacted for follow-up interviews. The program automatically assigned each team member a number of calls on the days they were not recruiting. Phone calls and letters were used to remind participants about upcoming visits or to schedule a new appointment for those that missed visits.
- 5) Beyond routine strategies, a welcoming and respectful staff that cares for the participant is the most critical piece. The team assures friendly and personalized treatment at every encounter. Making sure that each participant feels comfortable is of great importance (e.g. water, coffee, room temperature).
- 6) According to the literature, long waiting times associated with clinic visits are a common cause of retention problems, so we will always assure that the team member is ready when the participant arrives.
- 7) **Trust:** Information about the study was given, both in writing and verbally, in a simple language. Additionally, we clearly explained the goal of the study (why were doing it) and encouraged them to ask questions or voice concerns.
- 8) The study was designed so that both arms have the best treatment available, as the literature clearly indicates that participants dislike the uncertainty associated with the trials using placebo (23). In our experience, many participants often see the placebo arm as a reason to mistrust science.
- 8) Other methods included frequent and respectful contact, and flexibility in scheduling their visits.
- 9) **Monitoring:** Finally, rigorous bi-weekly monitoring was in place for early detection of problems. Monitoring was done by the study coordinator who tabulated weekly recruitment rates.
- 10) **Results:** Participants were informed that they can have access to study results once available. They were also asked for their authorization, as well as the name of their primary physician, to release information in case of finding abnormal results.

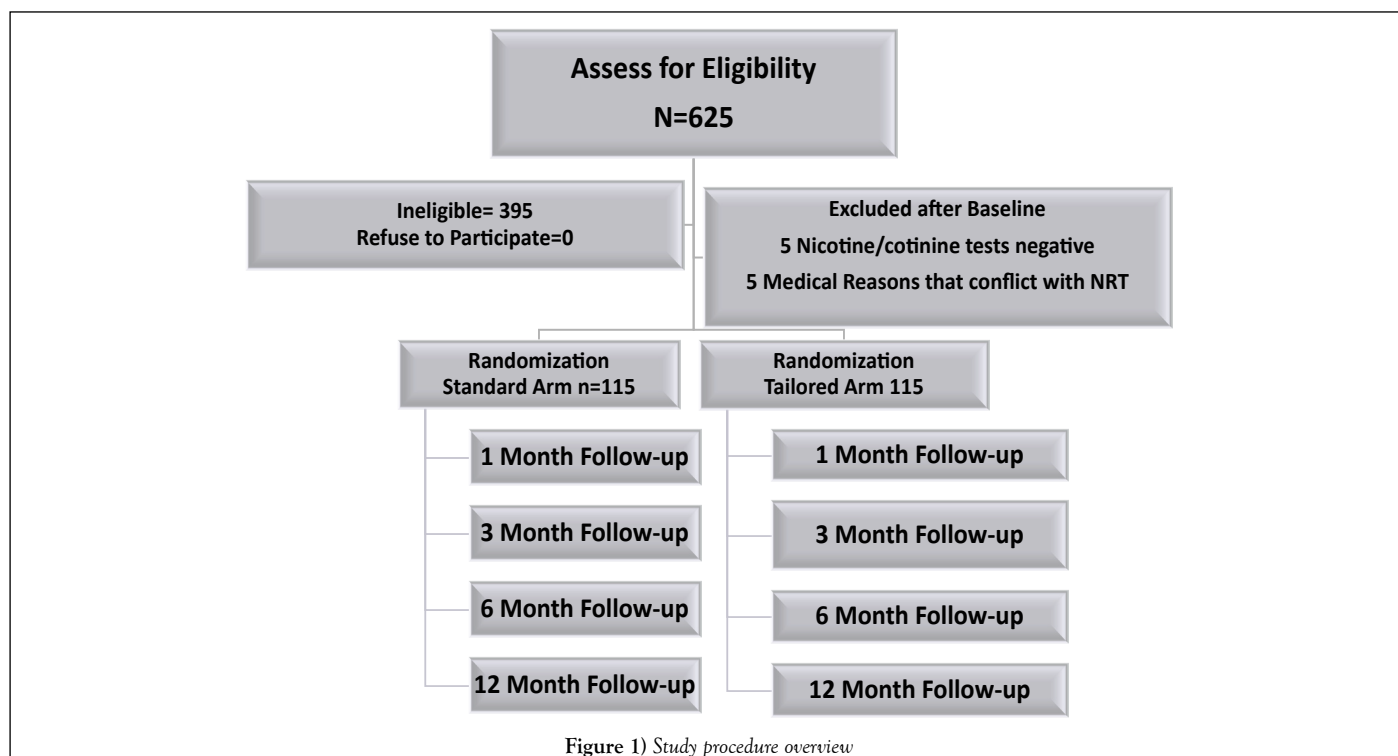


Figure 1) Study procedure overview

Data Analysis

SPSS version 23.0 (SPSS, IBM Inc., Armonk, NY) was used for analysis. Descriptive analyses were conducted to describe demographic data and to report recruitment and retention rates at 3, 6 and 12 months post-intervention. Differences among groups (e.g. types of recruitment, follow-ups, or adherence) were analyzed with chi square tests for categorical variables, and one-way analysis of variance (ANOVA) for continuous variables. Univariate analyses were used to contrast differences among the groups or strategies.

RESULTS

Recruitment

Participants in these analyses included 200 smokers living with HIV. In terms of referral sources, 52% of the sample cited referral by someone already enrolled in the study (word of mouth referrals) as the main source for their awareness of the study, the second most common source of recruitment was our other ongoing studies. Traditional flyers available at the clinics only represented 19% of the cited sources. Referral source did not significantly differ by race. African Americans, the largest segment of our sample, were more likely to be recruited by word-of-mouth referral (53%) or from our own resources. On the contrary, Caucasians were largely recruited from our other ongoing studies (53%). Hispanics were slightly more responsive to flyers (22% vs. 19%) than the other groups.

Gender was highly associated with the recruitment methods. Males were twice as likely to be recruited using flyers [OR = 1.8 (95% CI: 0.9-3.7), p=0.04]. On the other hand, females were primarily recruited from our target clinics and participation in prior studies [OR = 3.61 (95% CI: 1.3-2), p=0.004].

A total of 230 HIV infected smokers were eligible and are currently being followed in a smoking cessation and health outcomes study conducted in Miami, Florida. As a reflection of current trends of the HIV epidemic, the mean age was above 50 years (51.7 years) in both groups, however the extremes of the age distribution were 23 and 69 years old. The total sample includes 6% Caucasian, 83% African-American, and 11% identifying as Hispanic, so we have a large representation of minorities. The male to female ratio was nearly one to one. Income levels were not significantly different, and as expected, a sizable proportion reported an annual income below \$10,000. Findings are in line with prior reports indicating that smoking rates are significantly higher for persons living below the poverty line (24).

Analyses confirmed that Arm 1 and 2 are very well-balanced with regards to the above characteristics. There were approximately equal numbers of male and female participants in each arm (Table 1).

Intervention attendance and adherence to the therapy

Session attendance was used as an “early warning sign” of non-adherence. The expectation set forth by the study investigators was a 100% completeness rate for the behavioral intervention. Ninety-nine percent of the participants enrolled attended the behavioral intervention and received their first pharmacotherapy on time. As depicted in Figures 2 and 3 the overall rates of recruitment and attendance to the behavioral intervention suggests that the population is motivated to quit, that the protocol is feasible, and is producing encouraging results.

However, only 65% of the sample was fully adherent to the pharmacotherapy. A higher proportion of males were adherent to Nicotine replacement therapy (71% versus 57%, p=0.05). Males also reported missing less number of doses (6.2 ± 0.9 vs. 9.3 ± 1 doses p=0.4)

Follow-up

The final set of analyses pertained to participants “lost to follow-up” (LTFU), which was defined as a participant who misses a main protocol visit (3, 6, or 12 months visit) and cannot be found for the purposes of obtaining information related to outcomes. Incidence rate of LTFU was calculated as the number of LTFU divided by total person-years of follow-up.

The overall lost to follow-up rate was 5.7 per 100 person-years. Completion rates for the 3, 6, and 12-month post-intervention were 90%, 86%, and 88% respectively, and exceeded target rates. Retention rates did not vary by study arm. Subjects were lost to follow-up mostly as a result of relocation, use of detox clinics, or loss of interest in quitting because they believed “the medication does not work” or they were too overwhelmed with personal issues to try to quit.

Demographic factors examined included age (in years) at enrollment, sex, race/ethnicity, and years of education. Behavioral factors included history

TABLE 1

Socio-demographic and clinical characteristics of participants in both arms of the clinical trial

Variables	Arm 1	Arm 2	P-value
Age	50.6 ± 8	50.6 ± 8	0.06
Male	52%	48%	0.3
Female	48%	52%	
African American	81%	85%	0.4
Hispanic	12%	5%	
Caucasian	5%	10%	
Other	2%	0%	
Income			
<10K	77%	72%	0.7
10-29K	19%	23%	
>30K	4%	5%	

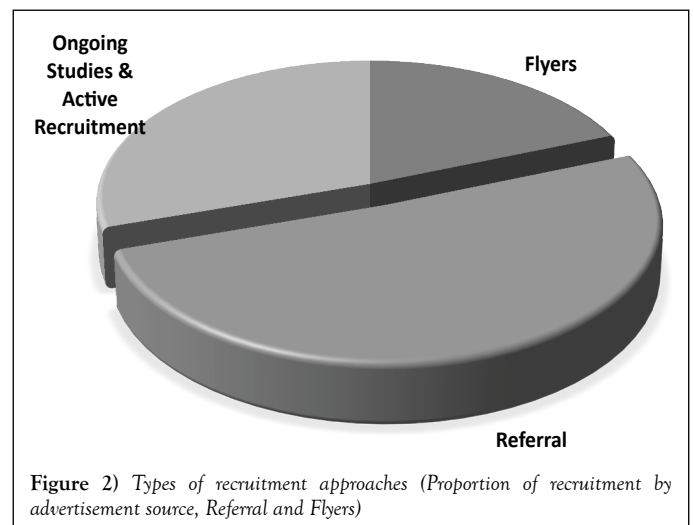


Figure 2) Types of recruitment approaches (Proportion of recruitment by advertisement source, Referral and Flyers)

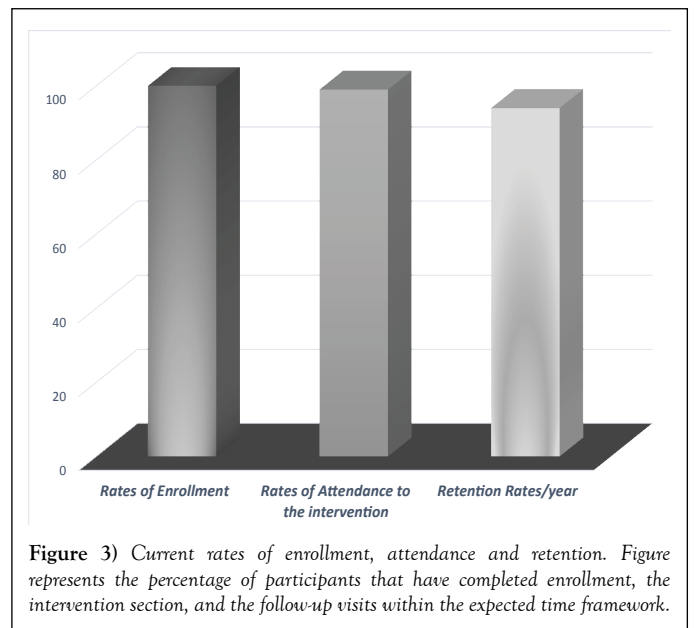


Figure 3) Current rates of enrollment, attendance and retention. Figure represents the percentage of participants that have completed enrollment, the intervention section, and the follow-up visits within the expected time framework.

of drug/alcohol use. Clinical characteristics included CD4+ T-cell count, HIV-1 RNA, anti-retroviral (ARV) therapy status, body mass index (BMI, kg/m²), and diagnosis of AIDS-defining events.

No differences in age (p = 0.88), sex (p = 0.46), income (p = 0.71), CD4 (p = 0.70), or viral load (p = 0.76) were found among those lost to follow-up. However, they tended to significantly differ in the following parameters: nicotine dependence was higher (Fagerström 6.5 ± 1.7 vs. 5.2 ± 2 p=0.001), and their scores were lower on the readiness to quit ladder (6.15 ± 0.8 vs. 6.7 ± 1.0 p=0.002).

Results indicated a significant association between race and being lost to follow-up ($X^2(16) = 54.09, p < 0.001$); a greater percentage of White, non-Hispanics (27%) were lost to follow-up compared to African Americans (10%) and Hispanics (0%). Notably, White non-Hispanics were more likely to believe that nicotine replacement was not an effective method as a reason for not quitting, resulting in a loss of interest in the study.

Safety

No serious or important adverse events related to treatment occurred during the study period. We only had two unrelated hospitalizations and neither the hospitalizations, nor the adverse events, were more prevalent by gender or race.

DISCUSSION

The evolution of effective treatments for HIV infection has enabled PLWH and other substance dependent populations to participate in more tobacco clinical trials and treatment programs. As such, it is necessary to learn how best to engage and retain populations with traditionally high lost to follow-up rates such as PLWH (25). Equally important is to analyze the rates of enrollment, retention, and success by race and gender. To date, few clinical trials targeting PLWH have addressed factors at these levels (26). Our analyses add to the literature with key findings of racial and gender differences, cited referral source. It also informed about key procedures helping to achieve an outstanding retention rate—86% completing 3, 6 and 12 months follow-up interviews after completing the biobehavioral intervention.

Socio-demographic differences in the prevalence of HIV/AIDS are well-established, often with African Americans and Hispanics bearing the greatest burden. Accordingly, efforts are especially needed to recruit these minorities who have lower rates of engagement. Recruiting these groups is critical to further current knowledge of smoking and nicotine replacement treatments, and to help ensure equity in their delivery. This study demonstrates that smokers living with HIV from these target groups can be effectively recruited into clinical trials. However, we have not been as successful in enrolling Non-Hispanic Whites. Disparities probably are reflecting the demographics of the population surrounding our clinics. Data also revealed that Non-Hispanic Whites were less likely to believe that nicotine replacement were effective than other groups. So, it is possible that this less favorable attitude toward pharmacotherapy impacted retention.

Analyses indicate that success in recruitment for clinical research requires a mix of trust and confidentiality. The repercussions of past unethical studies conducted with minorities continue to create a distrust about medical research impact. As many as 30% of participants had been enrolled in our prior studies, and 51% were referred by participants or health care professionals. These findings indicate that successful recruitment often is associated with earning the trust of the communities from which participants will be recruited. This is particularly important for groups requiring attention to subjects' respect and confidentiality, such as people living with HIV (PLWH).

Our study is unique in ensuring participation of low income individuals that may be homeless and discriminated against in other studies based on their physical appearance, level of personal hygiene, or life situation (18). Research teams without prior experience recruiting these groups may also have difficulties retaining these participants. On the other hand, by providing respectful treatment we have ensured higher rates of participation. Nevertheless, we have to deal with an unstable population, often without a permanent phone number. Many do not secure living arrangements, or move to new locations looking for job opportunities. Moving out of the area is an increasing potential barrier to subjects completing trial protocols that has not been widely reported in the literature.

The success of a randomized clinical trial is contingent upon adequate retention rates. Analyses confirmed that the strategies designed and implemented by our research center are efficient to increase retention rates, and should be used for studies focused on initially establishing feasibility. Similar to prior recommendations we use a combination of strategies. Our results indicate that with a user-friendly environment and a culturally competent and experienced team, it is possible to retain special populations such as PLWH, minorities, and those with substance use disorders. Our overall 88% follow-up rate is excellent when considering that we were following a cohort with multiple complicating factors such as lower socioeconomic status, lack of social support, high distress, distrust, or immigration status. According to the National Academies Press (NAP), the average dropout rate across all clinical trials is an alarming 30% (27).

Our analyses reflect the importance of non-routine strategies such as respect and care for an individual as a human being and not just a subject number. This is clearly reflected in the number of participants being referred by an individual previously or currently enrolled in our study.

Despite educating patients on the critical importance of using the nicotine replacement as directed, and assuring their understanding of how to use the patches and the gums, participants' adherence remains a critical problem in clinical trials (28). A similar problem has been observed in other smoking cessation trials with PLWH (28). Some patients may simply forget, and that seems to be a reasonable problem given HIV-associated cognitive disorders, but also because this population is aging, and at rapid pace. Nevertheless, this nation spends billions of dollars in prescription costs and thus the waste of funds generated from non-adherence it is distressing (29). Although protocol adherence is critical our data highlights that personal beliefs can be a significant road block that needs to be addressed.

CONCLUSION AND LIMITATIONS

Certain limitations inherent to the design of the study need to be acknowledged. The study population is limited to those in South Florida and only are aimed at smokers motivated and ready to quit. We have a lower participation of White non-Hispanics, which limits the representative capacity of our sample. On the other hand, since recruitment and retention rates are outstanding, we shared our delineated strategies to help other research groups to assure success

CONFLICT OF INTEREST

None.

REFERENCES

1. Syamlal G, Mazurek JM, Dube SR. Gender differences in smoking among U.S. working adults. *American j preventive med* 2014;47(4):467-475.
2. United States Public Health Service. Current cigarette smoking among adults—United States, 2005-2012. Atlanta, GA: MMWR; 2014;63:29-34.
3. Kadam RA, Borde SU, Madas SA, Salvi SS, Limaye SS. Challenges in recruitment and retention of clinical trial subjects. *Perspectives in Clinical Res* 2016;7:137-143.
4. Shuter J, Pearlman BK, Stanton CA, et al. Gender differences among smokers living with HIV. *Journal of the International Association of Providers of AIDS Care (JIAPAC)*. 2016;15:412-7.
5. Weinberger AH, Smith PH, Funk AP, et al. Sex differences in tobacco use among persons living with HIV/AIDS: A systematic review and meta-analysis. *JAIDS J Acquired Immune Deficiency Syndromes* 2017;74:439-53.
6. Scharf D, Shiffman S. Are there gender differences in smoking cessation, with and without bupropion? Pooled and meta-analyses of clinical trials of Bupropion SR. *Addiction* 2004;99:1462-9.
7. Food and Drug Administration. Collection of race and ethnicity data in clinical trials. Guidance for industry—collection of race and ethnicity data in clinical trials. 2013. (<https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm126396.pdf>)
8. Hurt RD, Sachs DP, Glover ED, et al. A comparison of sustained-release bupropion and placebo for smoking cessation. *New England J Med*. 1997;23:1195-202.
9. Jorenby DE, Leischow SJ, Nides MA, et al. A controlled trial of sustained-release bupropion, a nicotine patch, or both for smoking cessation. *New England Journal of Medicine*. 1999;4:685-91.
10. Gonzales D, Rennard SI, Nides M, et al. Varenicline Phase 3 Study Group. Varenicline, an $\alpha 4\beta 2$ nicotinic acetylcholine receptor partial agonist, vs sustained-release bupropion and placebo for smoking cessation: a randomized controlled trial. *Jama* 2006;5:47-55.
11. Jorenby DE, Hays JT, Rigotti NA, et al. Varenicline Phase 3 Study Group. Efficacy of varenicline, an $\alpha 4\beta 2$ nicotinic acetylcholine receptor partial agonist, vs. placebo or sustained-release bupropion for smoking cessation: a randomized controlled trial. *Jama*. 2006;5:56-63.
12. Tonstad S, Tønnesen P, Hajek P, et al. Varenicline phase 3 study Group. Effect of maintenance therapy with varenicline on smoking cessation: A randomized controlled trial. *Jama* 2006;296:64-71.

13. Shiffman S, Hughes JR, Ferguson SG, et al. Smokers' interest in using nicotine replacement to aid smoking reduction. *Nicotine & Tobacco Research*. 2007;9:1177-82.
 14. Gul RB, Ali PA. Clinical trials: The challenge of recruitment and retention of participants. *J Clinical Nur* 2010;1:227-33.
 15. Treweek S, Lockhart P, Pitkethly M, et al. Methods to improve recruitment to randomised controlled trials: Cochrane systematic review and meta-analysis. *BMJ open*. 2013;3:e002360.
 16. Probstfield JL, Frye RL. Strategies for recruitment and retention of participants in clinical trials. *Jama*. 2011;26:1798-9.
 17. 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* 2015;162:335-344.
 18. Pellowski JA, Kalichman SC, Matthews KA, et al. A pandemic of the poor: social disadvantage and the U.S. HIV epidemic. *The American psychologist*. 2013;68:197-209.
 19. Biener L, Abrams DB. The contemplation ladder: Validation of a measure of readiness to consider smoking cessation. *Health Psychology*. 1991;10:360.
 20. DiClemente CC, Prochaska JO. Toward a comprehensive, transtheoretical model of change: Stages of change and addictive behaviors.
 21. Heatherton TF, Kozlowski LT, Frecker RC, et al. The Fagerström test for nicotine dependence: A revision of the Fagerstrom Tolerance Questionnaire. *Addiction*. 1991;86:1119-27.
 22. Abshire M, Dinglas VD, Cajita MI, et al. Participant retention practices in longitudinal clinical research studies with high retention rates. *BMC medical research methodology*. 2017;17:30.
 23. Jenkins V, Fallowfield L. Reasons for accepting or declining to participate in randomized clinical trials for cancer therapy. *British journal of cancer*. 2000;82:1783.
 24. Centers for Disease Control and Prevention. Current Cigarette Smoking Among Adults—United States, 2005–2015. *Morbidity and Mortality Weekly Report* 2016;65:1205-11.
 25. Meyer JP, Althoff AL, Altice FL. Optimizing care for HIV-infected people who use drugs: evidence-based approaches to overcoming healthcare disparities. *Clinical Infectious Diseases*. 2013;57:1309-17.
 26. Colasanti J, Kelly J, Pennisi E, et al. Continuous retention and viral suppression provide further insights into the HIV care continuum compared to the cross-sectional HIV care cascade. *Clinical infectious diseases: An Official Publication of the Infectious Diseases Society of America*. 2016;62:648-654.
 27. Alexander W. The uphill path to successful clinical trials: Keeping patients enrolled. *Pharmacy and Therapeutics*. 2013;38:225-227.
 28. Tucker JS, Shadel WG, Galvan FH, et al. Pilot evaluation of a brief intervention to improve nicotine patch adherence among smokers living with HIV/AIDS. *Psychology of Addictive Behaviors*. 2017;31:148.
 29. Iuga AO, McGuire MJ. Adherence and health care costs. *Risk Management and Healthcare Policy*. 2014;7:35-44.
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