Title: SMOKING CESSATION INTERVENTIONS in PERSONS LIVING WITH HIV or AIDS: A SYSTEMATIC REVIEW

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Abstract
Tobacco smoking remains a prevalent behavior in people living with HIV infection (PLWH) and is associated with impaired immune functioning, increased cardiovascular risk, and decreased response to antiretroviral therapy. This review presents a critique and synthesis of evidence on effective smoking cessation interventions for PLWH. A comprehensive search identified 9 peer-reviewed intervention studies, published between 1989 and 2012. The highest odds of smoking cessation (OR 4.33-5.6) were in 2 randomized controlled trial interventions using cell phone technology. Clinically significant reductions in systolic blood pressure, weight gain, and increased CD4+ T cell count were reported for participants who ceased smoking in 3 of the 9 studies. Overall, multi-strategy smoking cessation interventions, delivered over multiple sessions, were effective. However, the most effective interventions were tailored to the unique individual needs of PLWH, including assessment and intervention of poly-substance abuse and mental health issues as well as the inclusion of access-promoting elements.

Keywords: AIDS, HIV, smoking, smoking cessation intervention, tobacco
Smoking cessation interventions in people living with HIV infection:  
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Compared to the current general U.S. smoking rate of 19%, the rate of cigarette smoking in people living with HIV infection (PLWH) is substantially greater with estimates ranging between 40% and 75% (Lifson et al., 2010; Lifson & Lando, 2012; Webb, Vanable, Carey, & Blair, 2007), suggesting that smoking is 2 to 3 times greater in PLWH (Burkhalter, Springer, Chhabra, Ostroff, & Rapkin, 2005; Minkoff et al., 2004; Niaura et al., 2000). Smoking is the most important modifiable risk factor for cardiovascular disease (CVD) and, given the high prevalence of cigarette smoking noted in PLWH (van Wijk & Cabezas, 2012), smoking cessation should be a priority for HIV care providers. Several patient-related and social factors contribute to the high prevalence of smoking in PLWH, including low education level, low socioeconomic status, illicit drug and alcohol use, age, concurrent depressive symptoms (Benard et al., 2007; Vidrine, Arduino, & Gritz, 2007), and lack of access to health services, housing, employment, and transportation (Krause, May, & Butler, 2012).

Considering the complexity of HIV management, smoking cessation may assume low priority for PLWH despite reported detrimental effects on the immune system, response to antiretroviral therapy (ART; Miguez-Burbano et al., 2003), and risk of mortality (Helleberg et al., 2013; Niaura et al., 2000). Setting PLWH apart from the general population, long-term smoking has been shown to increase risk of developing active tuberculosis (Bates et al., 2007; Jee et al., 2009; Ramin, Kam, Feleke, Jacob, & Jha, 2008), and daily tobacco use significantly attenuates the immune and virological response to antiretroviral therapies (Miguez-Burbano et al., 2003). Other detrimental effects of cigarette smoking in PLWH include cancer, dental diseases, pulmonary disease, and cardiovascular disease (CVD; Niaura et al., 2000). One study
of 5,472 PLWH showed that current smokers had a two-fold increase in the risk of a major cardiovascular event (congestive heart failure, coronary artery disease, and/or peripheral vascular disease) than never-smokers (Lifson et al., 2010), which was also noted in another recent large population-based cohort study (Helleberg et al., 2013). While these risks are similar to tobacco users in the general population, the authors also found an increased risk of AIDS-related deaths among HIV-infected smokers compared to HIV-infected non-smokers (Helleberg et al., 2013). Further, the average years of life lost by HIV-infected smokers compared to HIV-infected non-smokers was 12.3 years, which was more than a two-fold increase in the number of years lost by HIV infection alone (Helleberg et al., 2013).

Given the high prevalence of smoking by PLWH and the magnitude of the effect of smoking on CVD, response to ART, and mortality, designing and implementing effective smoking cessation strategies for this population is paramount. However, to date, no systematic literature reviews have focused on identifying smoking cessation interventions that are effective in PLWH. The purpose of our systematic review was to (a) summarize and critique current evidence on effective smoking cessation interventions for PLWH, (b) highlight gaps in the literature and suggest recommendations for future research, (c) identify effective cessation intervention components clinicians can implement, and (d) present policy recommendations to facilitate smoking cessation.

Methods

Search Strategy

A systematic review of peer-reviewed literature on smoking cessation in PLWH was undertaken. In consultation with a health librarian, the following databases and search engines were used: PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL),
PsychINFO, Cochrane, and Google Scholar. Medical Subject Headings (MeSH) and non-MeSH search terms used included: tobacco use cessation, smoking cessation, Bupropion, Varenicline, nicotine replacement therapy (NRT), smok*, quit*, ceas*, cessat, hiv infections, hiv*, human immune*, and acquired immun*. A hand search of reference lists in selected articles was also undertaken.

Inclusion and Exclusion Criteria

Only peer-reviewed journal articles, written in English, which described a smoking cessation intervention with PLWH, were included. The search was conducted in August 2012, and spanned literature published since 1989. Intervention studies that were not experimental or quasi-experimental, or were delivered to participants without HIV infection were excluded. One longitudinal descriptive study (Fuster et al., 2009) was included because it contained an embedded quasi-experimental cessation intervention.

Procedure

Two reviewers (GMJ and YCM) independently reviewed titles and abstracts of articles retrieved. Differences in inclusion articles were resolved through discussion. Both reviewers independently extracted data from included articles using a standardized extraction form developed by the reviewers. The primary outcomes of interest in this review were rates of cessation or smoking abstinence; however, additional outcomes were also extracted.

Results

The literature search yielded 535 potentially relevant articles. After duplicates were removed, 410 potentially relevant articles remained. Of these articles, only nine (Cui et al., 2012; Cummins, Trotter, Moussa, & Turham, 2005; Elzi et al., 2006; Fuster et al., 2009; Ingersoll, Cropsey, & Heckman, 2009; Lloyd-Richardson et al., 2009; Moadel et al., 2012; Vidrine,
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Arduino, Lazev, & Gritz, 2006; Vidrine, Marks, Arduino, & Gritz, 2012) met our inclusion criteria and were relevant to the question addressed in this systematic review (Figure 1).

**Study Characteristics**

Five randomized controlled trials (RCT) were included, all conducted in the United States (Table 1). Study sample sizes ranged from 33 to 474. Participants were middle age (mean ages ranged from 42-48 years) and male (49-82%). Overall, the nine studies were concentrated among participants with high unemployment (41-93%; Cummins et al., 2005; Elzi et al., 2006; Ingersoll et al., 2009; Lloyd-Richardson et al., 2009; Moadel et al., 2012; Vidrine et al., 2012) and lower education level (43%-77% with less than a high school education; Elzi et al., 2006; Ingersoll et al., 2009; Lloyd-Richardson et al., 2009; Vidrine et al., 2012).

Among the studies conducted in the United States, more than half of the participants were ethnic minorities (Ingersoll et al., 2009; Lloyd-Richardson et al., 2009; Moadel et al., 2012; Vidrine et al., 2006; Vidrine et al., 2012). Cigarette dependence was variable across studies with mean cigarettes smoked per day (CPD) ranging from 17 to 28. Additionally, mean Fagerström Test for Nicotine Dependence (FTND) scores ranged from 4.98 to 5.82, where FTND scores of 4 to 6 denote moderate nicotine dependence (Heatherton, Kozlowski, Frecker, & Fagerström, 1991). While all studies included PLWH, data on HIV severity were only reported in three studies (Cui et al., 2012; Elzi et al., 2006; Moadel et al., 2012). Furthermore, information about baseline CVD risk profile characteristics was only provided in two studies (Elzi et al., 2006; Fuster et al., 2009).

**Intervention Characteristics**

In spite of the heterogeneity of interventions, some commonalities were noted. All studies implemented multifaceted interventions and utilized a combination of motivational
interviewing/counseling techniques and pharmacotherapy, usually NRT with varying degrees of intensity. Most studies included varying degrees of tailoring or individualization, motivational interviewing, and the distribution of smoking cessation self-help materials (Cui et al., 2012; Elzi et al., 2006; Fuster et al., 2009; Ingersoll et al., 2009; Lloyd-Richardson et al., 2009; Moadel et al., 2012; Vidrine et al., 2006; Vidrine et al., 2012). The use of theory to develop smoking cessation interventions was limited and used in only four of the studies (Elzi et al., 2006; Fuster et al., 2009; Ingersoll et al., 2009; Moadel et al., 2012).

Differences across interventions were also noted. Four studies tailored smoking cessation materials and information to the benefits of smoking cessation for PLWH (Ingersoll et al., 2009; Lloyd-Richardson et al., 2009; Moadel et al., 2012; Vidrine et al., 2006). Although some studies reported brief interventions, all studies included a follow-up component after the intervention period. Intervention setting and delivery personnel differed across studies. Some interventions were delivered in HIV clinics and community-based clinics, while two studies implemented primarily technology-based interventions with counseling sessions delivered via a cell phone (Vidrine et al., 2006; Vidrine et al., 2012). Between these two cell phone interventions studies, 8 and 11 counseling sessions were delivered over a 2-3 month period with front-loaded counseling sessions delivered close to the participant’s pre-determined quit-date. Additional support between calls was obtained through access to a quit-line staffed by cessation counselors (Vidrine et al., 2006; Vidrine et al., 2012).

Interventionists also varied from health professionals (nurses or physicians) to trained counselors and research assistants. Moadel and colleagues (2012) was the only study to use a peer counselor who was an ex-smoker infected with HIV to deliver the intervention.

Effectiveness of Interventions on Primary Outcome: Smoking Cessation
Randomized control trials (RCT). Of the five RCTs, three reported significantly increased smoking cessation rates among participants in the intervention compared to control group (Odds Ratio [OR] range 1.97-5.6; Moadel et al., 2012; Vidrine et al., 2006; Vidrine et al., 2012). Interventions using cell phone technology produced the greatest odds of smoking cessation (OR range 4.33-5.6; Vidrine et al., 2006; Vidrine et al., 2012). Finally, two interventions significantly reduced smoking cessation rates utilizing motivational interviewing techniques (Ingersoll et al., 2009; Lloyd-Richardson et al., 2009); however, Lloyd-Richardson and colleagues (2009) only found significantly higher odds of abstinence at 6 months among Hispanic Americans compared to Caucasians (OR 2.53, 95% Confidence Interval [CI] 1.33-5.67).

Quasi-experimental studies (QE). All quasi-experimental studies (Cui et al., 2012; Cummins et al., 2005; Elzi et al., 2006; Fuster et al., 2009) found smoking cessation rates of 39% to 50% among intervention participants after the intervention phase and one study also found that participants in the intervention group were 6.2 times (95% CI 2.8 -14.3) more likely to remain abstinent from smoking 12 months after the intervention compared to the control group (Elzi et al., 2006). Across all QE studies, smoking cessation rates were lower at the end of the follow-up period than at the end of the intervention period.

Effectiveness of Intervention on Secondary Outcomes

In addition to smoking cessation, secondary outcomes such as reduction in CVD risk (Cui et al., 2012; Elzi et al., 2006; Fuster et al., 2009), HIV severity (Cui et al., 2012), psychosocial co-morbidities (Fuster et al., 2009), and adverse events of the pharmacotherapy (Cui et al., 2012) were examined. Clinically significant reductions in systolic blood pressure (Fuster et al., 2009) and weight gain (Cui et al., 2012) were reported among participants who ceased smoking. A
significant increase in CD4+ T cell count was also noted in one study (Cui et al., 2012). Significantly lower anxiety scale scores were noted among participants who stopped smoking (Fuster et al., 2009), and the most common adverse events experienced by participants while taking varenicline were nausea (33%), abnormal dreams (31%), affect labiality (19%), and insomnia (19%; Cui et al., 2012).

With respect to psychosocial outcomes, statistically significant increases in self-re-evaluation, emotions about smoking behavior, use of social support, substitution of alternatives to smoking, and re-engineering of the smoking environment (all \( p < .05 \)) were noted (Ingersoll et al., 2009). These psychosocial processes are theoretically related to behavior change.

**Discussion**

Interventions to reduce smoking rates in PLWH can be effective, but this review suggests that interventions may be more effective when components are tailored to the unique needs of the target population. Similar to previous smoking cessation studies in PLWH (Kwong & Bouchard-Miller, 2010), this review highlighted the need for interventions utilizing multiple strategies and delivering interventions at multiple sessions (Cummins et al., 2005; Elzi et al., 2006; Moadel et al., 2012; Vidrine et al., 2006; Vidrine et al., 2012). Notably, the high rate of recidivism among smokers highlights the importance of follow-up to ensure continuous smoking cessation in PLWH. Incorporating cell phone technology into smoking cessation interventions for PLWH may decrease socio-economic barriers associated with face-to-face interventions and also reduce fears of stigma or discrimination that often plague this population.

**Implications for Practice, Research, and Policy**

**Practice.** The success of a smoking cessation intervention is partly dependent on a patient’s readiness to quit smoking. Clinicians should become familiar with behavior change
theories/frameworks and tailor smoking cessation interventions to each individual’s stage of change. As noted in smoking cessation literature and supported in this review, effective interventions should follow the 5-As of smoking cessation counseling (ask, advise, assess, assist, and arrange; U.S. Preventive Services Task Force, 2009).

A successful intervention should also tailor cessation information to the specific needs of PLWH. In this review, most studies tailored interventions to PLWH by educating patients about the health benefits of smoking cessation with an emphasis on specific benefits for PLWH (i.e., improved immune function and decreased cardiovascular event risk). Furthermore, interventions that were most successful also asked patients about previous or current drug use and history of mental illness (e.g., depression and anxiety; Moadel et al., 2012) and tailored interventions to those needs. Studies have suggested that a history of intravenous drug addiction is associated with a higher rate of smoking addiction (Hershberger, Fisher, Reynolds, Klahn, & Wood, 2004); therefore, addressing cigarette smoking in isolation without considering other addictive behaviors may result in suboptimal outcomes. Successful interventions in this review also provided an individualized smoking cessation plan that included a support buddy, addressed social issues, and offered feasible smoking cessation programs (i.e., choice of attending a day or night program or cell phone delivery; Moadel et al., 2012; Vidrine et al., 2006). It is important for PLWH to live in a supportive environment that empowers them to quit smoking.

Although not addressed in any of the interventions identified in this review, one potential barrier to effective smoking cessation counseling strategies, may involve health professionals. Recent research has reported that HIV care providers failed to identify patients who were current smokers during the history-taking and physical exam (Crothers et al., 2007) or lacked training and confidence to initiate smoking cessation therapy (Shuter et al., 2012). One recent study
addressed this barrier by training HIV care providers on smoking cessation counseling, including identifying smokers, nicotine dependence, behavior change frameworks, counseling methods, and pharmacotherapy support (Huber et al., 2012). The intervention led to significantly increased smoking cessation rates (OR 1.23, \( p = .004 \)) and fewer relapses (OR .75, \( p = .007 \)) in PLWHs seeing trained providers compared to untrained providers (Huber et al., 2012). This finding suggests that the success of a smoking cessation intervention may also depend on provider knowledge and confidence to deliver the intervention and as such, should be evaluated.

Research. Despite the effectiveness of some interventions, the nine studies in this review highlighted the need for additional research on smoking cessation interventions for PLWH and specific interventions that (a) are uniform with respect to the interventions implemented and reporting of intervention components, (b) discuss how interventions are tailored to PLWH, and (c) contain consistent reporting of primary and secondary outcomes. This will enable providers to better identify and determine which intervention components are most effective.

According to Michie, Hyder, Walia, and West (2011), uniform taxonomy in behavior change interventions is the first step toward determining which specific intervention components (individual or in combination) will make up the most effective smoking cessation interventions. Michie et al. (2011) identified 43 behavior change techniques and developed a taxonomy for smoking cessation intervention components, which could be a starting point for standardizing future smoking cessation interventions for PLWH.

In addition to a uniform taxonomy, there is a need for additional studies that tailor interventions to the needs of PLWH, and researchers should discuss which specific intervention components were tailored to this population. Of the nine studies in this review, only two specifically discussed how information was tailored to the individual patient’s needs and
circumstances beyond providing information on the health benefits of smoking cessation for PLWH (Moadel et al., 2012; Vidrine et al., 2006). Researchers should address and highlight how techniques, resources, and considerations for PLWH have been tailored from smoking cessation interventions for the general smoking population. Furthermore, with high rates of recidivism and intervention drop-out rates, additional intervention studies should also address strategies and techniques for keeping this population engaged in treatment.

Finally, despite education about the health benefits of smoking cessation in PLWH (Ingersoll et al., 2009; Lloyd-Richardson et al., 2009; Moadel et al., 2012; Vidrine et al., 2006), only 2 studies reported changes in health status indicators and cardiovascular risk factors as an outcome (Elzi et al., 2006; Fuster et al., 2009). Additional studies, specifically longitudinal studies, should investigate the medium- and long-term impact of smoking cessation on cardiovascular risk factors considering the documented impact of smoking on years of life lost in persons with HIV (Helleberg et al., 2013). These studies should also monitor adverse effects of pharmacological smoking cessation therapies in this population.

**Policy.** Smoking cessation for patients with HIV is a public health problem as it is associated with excess mortality above HIV infection alone (Helleberg et al., 2013). None of the studies included in this review addressed the cost-effectiveness of the interventions; however, older studies have shown that in the general population, compared to other common CVD prevention interventions including hypertension and hyperlipidemia control, tobacco-cessation is more cost-effective (Cummings, Rubin, & Oster, 1989; Wasley, McNagny, Phillips, & Ahluwalia, 1997). Future smoking cessation intervention studies should incorporate a cost-effectiveness evaluation given that PLWH are a unique population with needs that are different from the general smoking population. In the meantime, strategies that build financial
 infrastructure for promoting smoking cessation in PLWH should be promoted. These strategies include promoting access to smoking cessation interventions by including smoking cessation counseling in health benefit plans, providing reimbursement for delivered smoking cessation interventions and policies to ensure the affordability of smoking cessation aids. Considering the high rates of unemployment and low levels of education of PLWH noted in this review, comprehensive social services should also be made available to PLWH to address social factors that may increase stress and hamper attempts at smoking cessation.

**Strengths and Limitations of Reviewed Studies**

Study design limitations included the use of convenience sampling, small sample sizes, few RCTs, and the use of self-reported smoking cessation measures. While each included study contained similar intervention components, each smoking cessation intervention was different with respect to counseling techniques and length of follow-up period post-intervention. Most of the studies included a short follow-up period. The inclusion of PLWH with high unemployment rates and low educational attainment across studies may limit our ability to generalize findings to other socio-economic groups; however, low education levels and lack of access to employment have been cited as patient-related and social factors contributing to the high rates of smoking in PLWH (Krause et al., 2012; Vidrine et al., 2007). Access-promoting elements noted in the interventions, including transportation, financial assistance, cultural considerations, literacy levels, compensation of participants, and other ethical issues were not disclosed and, across studies, reporting of intervention components and primary outcomes were insufficient and inconsistent. Finally, non-significant findings for the primary outcome, smoking cessation, in two RCT studies (Ingersoll et al., 2009; Lloyd-Richardson et al., 2009) were potentially related to contamination of the control group, a study effect caused by asking participants about their
smoking habits at baseline or an unknown effect of history. Nevertheless, non-significant findings in both studies supported the benefit of any versus no smoking cessation counseling by HIV care providers.

There were a few strengths in the included studies. Five of the nine studies used an RCT design. Six of the nine studies also used biochemically (carbon monoxide [CO] and serum cotinine) verified smoking status to enhance the validity of the results. In addition, two of the studies used a technology-based intervention as an access-promoting element. Technology-based interventions for PLWH can overcome traditional barriers to interventions including interventionist-related issues such as discomfort with discussing topics, incomplete implementation of the intervention, and participant-related obstacles including transportation, insurance, physical limitations, and the need for child care.

**Strengths and Limitations of this Review**

Our ability to make generalizations about effective smoking cessation strategies for PLWH depends on both the quality and quantity of studies reviewed. The main limitations of this review were the inclusion of only accessible peer-reviewed literature and exclusion of gray literature not published in English. These limitations led to a small number of smoking cessation intervention studies and possible exclusion of potentially relevant studies.

Despite these limitations, this review had multiple strengths. Peer-reviewed articles were systematically identified through a comprehensive search strategy and relevant data were extracted using a standardized extraction checklist with discussion of findings between authors. Furthermore the results of all studies were equally considered in the synthesis of findings across studies. Finally, secondary outcomes such as the impact of smoking cessation on cardiovascular health and risk factors for major cardiovascular events as well as psychosocial and behavioral
outcomes were explored and reported.

**Conclusion**

Our review presents information to guide clinical practice in regard to smoking cessation counseling for PLWH, but it also highlights the need for additional research. Overall, our review supports counseling that focuses on the 5-As of smoking cessation counseling but is tailored to the unique needs of PLWH. Tailoring should include not only discussions of the specific health benefits of smoking cessation for PLWH but also assessment and inclusion of strategies to address other drug use and mental health issues, promotion of social support and a healthy smoking cessation environment, and access promoting elements such as day and night sessions or use of telehealth technology (e.g., cell phones). Despite these findings, the limited number of studies supported the need for additional research. Future research should include similar intervention components, which can be facilitated by using the taxonomy for behavior change interventions developed by Michie et al. (2011) as well as consistent reporting of both primary and secondary outcomes.
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