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## A Review of the Literature Concerning HIV and Cigarette Smoking: Morbidity and Mortality, Associations with Individual- and Social-Level Characteristics, and Smoking Cessation Efforts

Lauren R. Pacek<sup>1,2,\*</sup> and Rosa M. Crum<sup>1,2,3</sup>

<sup>1</sup>Johns Hopkins Bloomberg School of Medicine, Department of Psychiatry and Behavioral Sciences, Baltimore, Maryland <sup>2</sup>Johns Hopkins Bloomberg School of Public Health, Department of Mental Health, Baltimore, Maryland <sup>3</sup>Johns Hopkins Bloomberg School of Public Health, Department of Epidemiology, Baltimore, Maryland

### Abstract

Cigarette smoking is endemic among many populations, but is especially prevalent among people living with HIV, and is consequently associated with a variety of types of morbidity as well as mortality. Despite this knowledge, relatively little research has been conducted among smokers living with HIV. Extant research has focused on examining individual-level characteristics associated with smoking behaviors, to the neglect of examining social-level factors. This manuscript represents a critical literature review of the intersecting research fields of HIV and cigarette smoking. Topics considered within this review include: morbidity, mortality, as well as treatment and medication adherence outcomes; individual- and social-level characteristics associated with various smoking behaviors; evidence-based smoking cessation interventions; and findings from cessation interventions among smokers living with HIV. Additionally, gaps in the existing literature, as well as directions for future research were identified and discussed.

### Keywords

HIV; cessation; cigarette smoking; morbidity; mortality

### INTRODUCTION

The prevalence of cigarette smoking has been on the decline in the United States general population since the 1960's, and is currently approximately 20% (CDC, 2011a). Despite the public health intervention successes in reducing smoking overall, certain subgroups of the population still exhibit an unduly high prevalence of cigarette smoking. Among persons living with human immunodeficiency virus (HIV), the prevalence of cigarette smoking has been estimated to be 40–70% (Pines et al., 2011; Collins et al., 2001; Gritz et al., 2004; Mamary et al., 2002; Burkhalter et al., 2005; Crothers et al., 2005; Lifson et al., 2010). In

\*Corresponding author. Address: 5510 Nathan Shock Drive, Behavioral Biology Research Center Room 1708, Baltimore, MD 21224. Phone: 410-550-6756, Fax: 410-550-0030, lpacek@jhmi.edu.

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the past, little research attention was paid to the intersection of HIV and smoking. However, the widespread availability and use of highly active antiretroviral therapy (HAART) has resulted in increased life expectancies for persons living with HIV (Palella et al., 1998). In fact, recent estimates indicate that the life expectancy for an individual diagnosed with autoimmune deficiency syndrome (AIDS) is approximately 15 years (Walensky et al., 2006), while the life expectancy for individuals newly diagnosed with HIV can exceed 35 years (Lohse et al., 2007). Along with increased life expectancies, the causes of death have changed significantly in the HAART era: mortality due to AIDS-related conditions has decreased and deaths due to non-AIDS-defining illnesses have increased (Palella et al., 2006). Many of these conditions—such as cardiovascular disease, pulmonary conditions, and lung cancer—are associated with cigarette smoking. These aforementioned statistics suggest that targeting cigarette smoking, a modifiable risk factor for these non-AIDS-related conditions, could potentially improve the quality of life and further increase the life expectancies of individuals with HIV/AIDS. In this review, we summarize the effects of cigarette smoking on a number of health outcomes that are relevant to people living with HIV and discuss issues related to smoking behavior and smoking cessation.

## **SMOKING AND ASSOCIATED MORBIDITY, MORTALITY, MEDICAL ADHERENCE AND TREATMENT OUTCOMES**

### **Cardiovascular disease**

Cardiovascular conditions have become an important source of morbidity for HIV-positive patients. Compared to individuals without HIV, individuals living with HIV have an increased risk of developing cardiovascular disease (CVD) (Lifson et al., 2010; Lewden et al., 2005; Petoumenos et al., 2011; Barbaro et al., 2003; Friis-Møller et al., 2003; Savès et al., 2003). The high prevalence of cigarette smoking in this population may further contribute to the development of CVD. In an attempt to explain the disproportionately high risk for CVD among people living with HIV, research has indicated that the use of protease inhibitors as a part of combination antiretroviral therapy may increase the risk of cardiovascular-related events. Barbaro and colleagues (2003) conducted a study in which patients were given a HAART regimen either with or without a protease inhibitor and then monitored for the incidence of cardiovascular events. Findings indicated that the cumulative annual incidence of CVD was higher in the group receiving protease inhibitors (Barbaro et al., 2003). Additionally, although specific classes of HAART medications and cigarette smoking both contribute to the increased risk of CVD among people living with HIV, findings from one study indicate that current cigarette smoking is associated with greater risk for myocardial infarction than protease inhibitor therapy (Friis-Møller et al., 2007).

### **Respiratory conditions**

Research has shown that people living with HIV have elevated risks of numerous respiratory-related conditions, such as chronic obstructive pulmonary disease (Lewden et al., 2005; Diaz et al., 2002; Crothers et al., 2006) and bacterial pneumonia (Crothers et al., 2005; Lifson et al., 2010; Miguez-Burbano et al., 2005). In a multicenter prospective study of women living with HIV, the most prominent clinical risk factor for the development of

bacterial pneumonia in the HAART era was current cigarette smoking status (Kohli et al., 2006). Miguez-Burbano and colleagues (2003) found that, after controlling for confounders, cigarette smoking doubled the risk for developing *Pneumocystis carinii* pneumonia (PCP), and that long-term smoking increased the risk of developing tuberculosis.

## Cancer

The incidence of several types of non-AIDS-defining cancers has been found to be significantly higher among people living with HIV than among the general population, including: anal, vaginal, oropharyngeal and colorectal cancer, Hodgkin lymphoma, leukemia, melanoma, as well as cancer of the liver, kidney and lung (Patel et al., 2008). Additionally, anal and cervical cancers have a higher prevalence among people living with HIV who are smokers than among those living with HIV who do not smoke (Palefsky et al., 1994; Palefsky et al., 1999). Lung cancer is of particular interest given the clear association between this type of malignancy and cigarette smoking, as well as the fact that lung cancer is now the third most commonly diagnosed cancer among people living with HIV, behind the AIDS-defining cancers Kaposi sarcoma and non-Hodgkin lymphoma (Kirk et al., 2007). Compared to the general population, people living with HIV exhibit an elevated risk of lung cancer (Chaturvedi et al., 2007; Lifson et al., 2010). Numerous studies have explored the relationship between lung cancer and HIV infection. Though a few concluded that the increased prevalence of lung cancer among this population was attributable to heavy smoking among people living with HIV (Levine et al., 2010; Clifford et al., 2012), others have identified a potentially more complex relationship between HIV and lung cancer. For instance, in separate analyses, Engels and colleagues (2006), Kirk and colleagues (2007), and Sigel and colleagues (2012) found that the risk of developing lung cancer among people living with HIV was elevated as compared to people without HIV, even after controlling for smoking status.

## Immunosuppression

Studies have shown that cigarette smoking has immunosuppressive effects: Smoking has broad immunosuppressive effects on host cell-mediated and humoral immune responses (Arcavi & Benowitz, 2004; Huttunen et al., 2011). One study has shown that cigarette smoking is an independent risk factor for the progression to AIDS among HIV-infected patients (Nieman et al., 1993), though there have been inconsistencies in establishing a negative relationship between smoking and the course of HIV/AIDS (Galai et al., 1997; Coates et al., 1990; Furber et al., 2007). These findings regarding smoking and negative effects on the immune system are troubling, regardless of the population under investigation. However, they are of particular concern among a group of people who are facing a condition that suppresses the immune system, such as HIV.

## Medication adherence and treatment outcomes

Though only a few studies have included cigarette smoking in analyses as a potential correlate of medication adherence, among the few studies that have, findings indicate that cigarette smoking is associated with decreased adherence to highly active antiretroviral therapy (HAART). For instance, Feldman and colleagues (2006) found that smokers were significantly more likely to report noncompliance with their HAART regimens within the

past 6 months as compared to non-smokers (32.3% vs. 23%). Additionally, Yuan and colleagues (2006) showed that discontinuation of an initial HAART regimen was positively associated with current cigarette smoking. Furthermore, among females receiving HAART in the Women's Interagency HIV Study (WIHS), cigarette smoking was shown to be significantly associated with decreased HAART adherence (Lazo et al., 2007). Similarly, Shuter and Bernstein (2008) found current cigarette smoking to be an important and significant marker of inferior HIV medication adherence. However, one should bear in mind that all of the aforementioned studies were cross-sectional, and therefore could not shed light on whether smoking increased the risk for non-adherence. It is possible that both non-adherence and smoking resulted from another factor such as personality traits related to health behavior in general, or mental health symptoms. For example, an additional cross-sectional study (Webb et al., 2009) found smoking to be negatively associated with decreased HAART adherence, and proposed that the relationship may be mediated by depression.

In terms of adverse treatment outcomes, some reports suggest that cigarette smoking can decrease the response to highly active antiretroviral therapy (HAART) by 40% (Miguez-Burbano et al., 2003). In the Women's Interagency HIV Study (WIHS), a cohort study of females on HAART, findings from one study indicate that smokers are more likely than non-smokers to have poorer treatment outcomes, including poorer viral and immunologic responses, greater risks of virologic rebound, more frequent immunologic failure, and a higher risk of developing AIDS (Feldman et al., 2006).

### Quality of life

In addition to various morbidities, cigarette smoking is associated with decreased quality of life among people living with HIV. In one such analysis (Turner et al., 2001), cigarette smokers were found to have lower health-related quality of life than non-smokers. Specifically, cigarette smoking was associated with lower scores for general health perception, physical functioning, bodily pain, energy, role functioning, and cognitive functioning. After adjusting for confounders, Crothers and colleagues (2005) found that, among a sample of HIV-positive military veterans, cigarette smoking was associated with significantly lower quality of life as compared with never smokers.

### Death

Worldwide, tobacco use causes more than 5 million deaths per year (WHO, 2011). Additionally, cigarette smoking remains the leading preventable cause of death in the general United States population, resulting in approximately 443,000 deaths annually (CDC, 2011b). Correspondingly, in addition to the aforementioned morbidity, research has shown that cigarette smoking is associated with higher risk of death among people living with HIV. In a United States-based cohort of people living with HIV receiving clinical care, current cigarette smoking, in addition to a low baseline CD4 cell count and older age, was an independent predictor of mortality (Modrich et al., 2010). Additionally, Pines and colleagues (2011) showed that, compared to never smokers, current smokers were at greater risk of all-cause mortality. Crothers and colleagues (2005) examined more than 800 veterans in the United States living with HIV who were taking HAART and found that the mortality rate for

smokers was twice that of nonsmokers after adjusting for confounding factors like age, CD4 cell count, and viral load. Additionally, authors of a large cohort study estimated that 24% of deaths among people living with HIV in the modern HAART era are attributable to tobacco use (Lifson et al., 2010). Results from a population-based Danish cohort study (Helleberg et al., 2013) showed that smokers living with HIV lose more life-years to smoking than to HIV itself. Furthermore, the excess mortality of smokers is tripled and the population-attributable risk of death associated with smoking is doubled among patients with HIV as compared to population controls (Helleberg et al., 2013).

## FACTORS INFLUENCING PATTERNS OF CIGARETTE SMOKING

Several highly interactive factors prominently associated with cigarette smoking patterns and behaviors can be observed among people living with HIV, including certain sociodemographic, drug and alcohol use, psychiatric comorbidity, and access to treatment characteristics.

### Individual-level characteristics

**Sociodemographic characteristics**—Research among people living with HIV has fairly consistently identified several sociodemographic characteristics that are associated with current cigarette smoking status. For instance, men are more likely than women to be current smokers among people living with HIV (Mamary et al., 2002; Stewart et al., 2012). Findings regarding age have been mixed, with some research indicating that younger individuals were more likely to be current smokers (Gritz et al., 2004), while other research implicates older age (Tesoriero et al., 2010). Additionally, Gritz and colleagues (2004) and Chander and colleagues (2012) found that the prevalence of current cigarette smoking decreased as age increased. Gritz and colleagues (2004) also found that White participants were significantly more likely than Hispanic participants to be current smokers.

**Drug and alcohol use**—Characteristics such as heavy drinking (Gritz et al., 2004) and illegal drug use (Gritz et al., 2004; Burkhalter et al., 2005; Marshall et al., 2011) have been found to be associated with current smoking status among people living with HIV. Additionally, in a study examining people with and without HIV who are injection drug users, Marshall and colleagues (2011) found that compared to former injectors, current injectors had a higher smoking prevalence, greater daily cigarette consumption, and slightly higher scores on the Fägerstrom Test for nicotine dependence. In addition to associations with current smoking status, one study found that among HIV-positive smokers, greater current illegal drug use is associated with being less ready to quit smoking and being less interested in quitting (Burkhalter et al., 2005).

**Psychiatric comorbidity**—The prevalence of depression among people living with HIV ranges from 22–32% (Bing et al., 2001; Ferrando & Freyberg, 2008; Rabkin et al., 1997), two to three times higher than what is observed in the general population. Research has shown an association between depression and smoking behaviors among people living with HIV. Stewart and colleagues (2010) found that having depression predicted participants' current smoking status. Additionally, research has shown that higher rates of cigarette

smoking, greater nicotine dependence, and abuse of other substances are associated with a variety of mental health conditions, in addition to depression, such as schizophrenia and anxiety disorders among individuals living with HIV (Niaura & Abrams, 2002; Ziedonis et al., 2008). Greater levels of emotional stress have also been found to be associated with less readiness to quit smoking and less interest in quitting (Burkhalter et al., 2005).

**Attitudes and beliefs**—In addition to the aforementioned individual-level characteristics, the beliefs held by people living with HIV may be important in determining or sustaining smoking behaviors. For instance, self-efficacy has been found to be important in influencing cessation and dependence. Vidrine and colleagues (2006) found that self-efficacy mediated the efficacy of cessation treatment. Additionally, low-self efficacy to resist temptations and triggers to smoke has been found to be associated with nicotine dependence (Lloyd-Richardson et al., 2008). Furthermore, some research has shown that people living with HIV believe that they will not live long enough to suffer the health risks of tobacco use, or they think that they are at decreased health risk for continued smoking (Burkhalter et al., 2005; Reynolds et al., 2004). As a result, these individuals may be less concerned with smoking cessation.

### **Social-level characteristics**

To date, among people living with HIV, research examining the association between social environmental characteristics and cigarette smoking behaviors has been lacking. Research among the general population has shown that social-level characteristics influence smoking behaviors. For instance, the presence of smoking in an individuals' social network is associated with current smoking status and age of smoking initiation (Alexander et al., 2001; Unger & Chen, 1999). In terms of smoking cessation, Christakis and Fowler (2008) found that groups of interconnected smokers tend to quit in concert. Additionally, receiving high levels of support from partners, as well as perceived availability of support were associated with cessation and short-term abstinence, while the presence of smoking in one's social network was a hindrance to maintaining abstinence in the long-term (Mermelstein et al., 1986). Based on this research conducted among the general population, it is possible that social-level characteristics are associated with cigarette smoking behaviors among people living with HIV, and have the potential to serve as important points for interventions.

## **SMOKING CESSATION IN HIV**

### **Interest in quitting/readiness to quit**

In light of the high prevalence of smoking among people living with HIV, and the deleterious health concerns associated with it, it is perhaps not surprising that many smokers with HIV report being counseled to quit smoking. One study reported that 81% of current smokers recalled receiving medical advice to quit smoking within the past year (Burkhalter et al., 2005). Additionally, some studies have shown that a significant proportion of smokers living with HIV report being currently interested in quitting smoking, or are currently thinking about quitting. For instance, Marmy and colleagues (2002) and Tesoriero and colleagues (2010) reported that 63% and 75% of smokers, respectively, were interested in quitting. Additionally, among South African HIV clinic attendees, 42% reported that they



had intentions to quit smoking within the next year, and an additional 55% reported a desire to quit, but without having a concrete plan for cessation (Shapiro et al., 2011). Though interest in quitting appears to be high among HIV-positive smokers, individuals may have differing perceptions of what “quitting” means. For instance, in a sample of smokers living with HIV recruited from outpatient clinics in San Francisco, less than half (45%) of respondents chose total abstinence as a smoking cessation treatment goal (Humfleet et al., 2009). Other responses included quitting smoking with the possibility of relapse (32.2%), abstaining for a time (5.6%), smoking in a controlled manner (4.4%), while the remaining respondents indicated that they would like to smoke occasionally (2.2%), had no clear goal (4.4%), or had some other goal (6.1%) (Humfleet et al., 2009). In addition to examining interest in quitting, Burkhalter and colleagues (2005) and Gritz and colleagues (2004) found that 18% and 34% of smokers living with HIV in their respective cohorts were in the preparation or action stages of quitting cigarette smoking. These estimates can be contrasted with findings from a study conducted by Shuter and colleagues (2012a) where approximately two-thirds of participants with HIV surveyed at an infectious disease clinic in New York City indicated that they were in the preparation or action stages. Thus, though it appears that interest in quitting smoking among HIV-positive smokers is high, actual readiness to quit tends to vary.

In addition to exploring interest in smoking cessation, several studies have explored the smoking cessation modalities preferred by smokers living with HIV. In one study (Shuter et al., 2012a), more than half of smokers reported interest in each of the following types of cessation interventions: nicotine replacement therapy (NRT) (64.4%), individual counseling (64.4%), group counseling (55.9%), and using telephone quit lines (52.5%). Slightly less than half of the sample reported interest in making use of a “buddy system”-type intervention (49.2%) or oral medications for smoking cessation (40.7%) (Shuter et al., 2012a). Similar to the aforementioned findings, a study conducted by Shapiro and colleagues (2011) in South Africa found that the most highly endorsed cessation modality was free NRT (91%); much less endorsement was received for NRT that participants would have to pay for (28%). Likewise, 91% of smokers reported being interested in utilizing free prescription medications for smoking cessation, while 26% would be interested in using prescription medications if they had to pay for it (Shapiro et al., 2011). Additionally, many were interested in utilizing the following counseling-based cessation methods: talking with a doctor or nurse (83%), participating in a support group (85%), and participating in a support group for smoking cessation that is restricted to persons with HIV (87%) (Shapiro et al., 2011). Participants also reported an interest in using telephone quit lines (61%) and text message-based cessation support (65%) (Shapiro et al., 2011). Marmy and colleagues (2002) reported that, among smokers with HIV currently thinking about quitting, 69% were interested in participating in a group smoking cessation program, 82% were interested in nicotine replacement therapy, and 56% were interested in receiving both nicotine replacement therapy and group therapy for smoking cessation. HIV-positive cigarette smokers have reported interest in a variety of types of smoking cessation aids and interventions, with endorsement of the same modalities varying between studies. It is possible that the popularity of certain smoking cessation methods may vary based on the

region in which the study was conducted, or other sample characteristics such as familiarity with or prior experience with specific methods.

Some research has also documented prior quit attempts made by cigarette smokers living with HIV. In general, a significant proportion (33–82%) of smokers reported having made at least one quit attempt in the past (Benard et al., 2007; Mamary et al., 2002; Shapiro et al., 2011; Encrenaz et al., 2010). Mamary and colleagues (2002) have found that prior quit attempts among smokers with HIV may vary based on gender: twice as many men reported making past quit attempts compared to women (81% versus 40%). Some research also indicates that many smokers (42–65%) made their quit attempts following receipt of their HIV diagnosis (Benard et al., 2007; Burkhalter et al., 2005).

### Barriers to cessation

**Patient characteristics**—Despite significant interest in quitting, people living with HIV, as a group, bear numerous characteristics that may serve as barriers to smoking cessation (Moadel et al., 2012). For instance, smokers living with HIV have high rates of other substance use and comorbid psychiatric conditions (Shuter et al., 2012a). Additionally, they are often exposed to a variety of chronic stressors including poverty, racism/discrimination, stigmatization, loneliness, and health concerns (Encrenaz et al., 2010; Goldberg et al., 2010; Shuter et al., 2012a; Riley et al., 2007; Boarts et al., 2008; Bogart et al., 2008; Reynolds et al., 2004). As a result, these factors tend to decrease the likelihood that smoking cessation interventions, especially brief and “simple” interventions, will be successful among cigarette smokers living with HIV.

Beliefs held by smokers with HIV may also influence smoking cessation. For instance, Shuter and colleagues (2012a) asked smokers with HIV how much they felt that cigarette smoking helped them with a variety of factors. A majority of participants felt that smoking helped “somewhat” or “a lot” with the following activities: controlling anxiety, controlling anger, controlling depression, and relaxing. Slightly less than half of participants believed that smoking helped with weight control (44%), regulating bowel movements (39%), enhancing the high from other drugs (35.6%), increasing social contact (39%), and being accepted by other smokers (42.4%). Belief that cigarette smoking may confer positive benefits, such as those discussed above may hamper smokers' willingness to engage in smoking cessation.

Additionally, one study also identified several factors, related to low socioeconomic status, associated with difficulties in participating in a cessation program utilizing cellular telephones: lack of access to a working telephone, high number of household moves, and lack of transportation (Lazev et al., 2004). Furthermore, concerns regarding the potential for increased toxicities, side effects and drug–drug interactions between antiretroviral therapies and medications for smoking cessation may complicate care.

**Provider characteristics**—In addition to characteristics of the smokers living with HIV themselves, characteristics of healthcare providers may provide barriers to cessation as well. In general, smoking cessation among people with HIV has received less attention from practitioners as compared to smokers in the general population. This decreased emphasis



may be due to the focus on acute treatment of HIV, perceived high mortality rate related to HIV as compared with smoking, lack of cessation treatment tailored to this population, and the perceived lack of relevance of smoking to treatment outcome and survival (Gritz et al., 2007). HIV care providers may be less aware of cigarette smoking among their patients than providers in the general population (Crothers et al., 2007). This decreased awareness of the prevalence of smoking has the potential to impact the promotion of smoking cessation among people living with HIV.

Additionally, some research shows that HIV care providers were less confident in their ability to achieve smoking cessation in their patients (Shuter et al., 2012b; Horvath et al., 2012). For instance, in one study assessing HIV provider attitudes and practices regarding smoking-related services, 55% of providers surveyed reported that they were not confident in their ability to provide resources and advice regarding cessation to their patients (Horvath et al., 2012). In another study of HIV care providers, 24.9% of practitioners reported that they either agreed or strongly agreed that their efforts to get HIV-positive smokers to quit are unlikely to succeed (Shuter et al., 2012b).

This lack of confidence may stem from a variety of sources. For instance, a majority of providers (60%) believe that their patients know that smoking is a problem, but do not want to quit (Horvath et al., 2012). Additionally, approximately one-third (35.9%–38%) of practitioners report feeling as though they do not have adequate time to address smoking cessation among people living with HIV during clinic visits (Horvath et al., 2012; Shuter et al., 2012b). This diminished confidence also could be due to a lack of training in tobacco treatment and counseling methods (Shuter et al., 2012b). In a survey of providers listed in the HIV Medicine Association, only 22.9% reported that they had ever received formal training or clinical education on this topic (Shuter et al., 2012b). Furthermore, a potentially troubling statistic indicates that only 29.2% of providers from this sample (Shuter et al., 2012b) and less than one-third of physician providers from another sample (Horvath et al., 2012) would be interested in obtaining additional smoking-related training and educational opportunities.

## Cessation interventions

**Evidence-based smoking cessation interventions**—Each year, a significant proportion of smokers in the general population make quit attempts; more than half of adult smokers made a quit attempt in 2010 (CDC, 2011c). Success in these quit attempts varies, at least in part, based on whether or not an individual employs some method to aid cessation. Research has shown that, on average, smokers seeking cessation assistance have twice the success with smoking cessation at 12 months than do smokers who did not seek such assistance (Zhu et al., 2000). Evidence-based smoking cessation methods are varied, but can include counseling interventions, nicotine replacement therapy, and non-nicotine replacement therapy interventions, as described below.

Counseling interventions can include, but are not necessarily limited to, individual, group, telephone, or online counseling. Research has shown that the most successful counseling interventions tend to be those that are more intensive (i.e., longer in duration and occur over multiple visits) (Fiore et al., 2008). For instance, brief interventions lasting 3 minutes

resulted in abstinence rates of 13% compared to longer interventions lasting 10 minutes or more, which resulted in abstinence rates of 22% (Reus & Smith, 2008; Fiore et al., 2008). One advantage of utilizing counseling interventions is that they can be provided by a variety of types of providers such as physicians, nurses, social workers, and health educators (Kwong & Bouchard-Miller, 2010).

Nicotine replacement therapy (NRT) provides small doses of nicotine to the user, and is intended to replace the nicotine that one would receive from smoking cigarettes. NRT is available in several forms, including patch, gum, lozenges, inhaler, and nasal spray. The patch, gum, and lozenges are available over-the-counter, without a prescription while nicotine inhalers and nasal sprays require prescriptions. The amount of nicotine delivered by NRT varies based on the exact method used. Moreover, the method of nicotine delivery from NRT products is different than when smoking cigarettes. As a result, NRT can reduce, but not necessarily eliminate craving or withdrawal symptoms (Kwong & Bouchard-Miller, 2010). Nevertheless, a Cochrane review reported that any form of NRT was more effective than placebo in helping smokers to quit (Stead et al., 2008).

Non-nicotine replacement therapy (NNRT) includes prescription medications that do not contain nicotine for the purpose of smoking cessation. Two such NNRT medications that are often prescribed for smoking cessation include sustained-release bupropion (bupropion SR) and varenicline. Bupropion SR acts as a nicotinic acetylcholine receptor antagonist, is used to reduce the severity of nicotine cravings and withdrawal symptoms, and is recognized as a first-line pharmacotherapy for smoking cessation in the United States and Europe (Slemmer et al., 2000; Fiore, 2000; Tønnesen et al., 2007). Varenicline on the other hand, is a nicotinic receptor partial agonist (Mihalak et al., 2006), and is used to reduce cigarette cravings as well as to decrease the pleasurable effects of cigarettes and other tobacco products. Despite carrying a U.S. Food and Drug Administration mandated black box warning (Food and Drug Administration, 2009), both bupropion SR and varenicline have generally been shown to be safe, and to be more efficacious than placebo (Oncken et al., 2006; Jorenby et al., 2006; Gonzales et al., 2006) or nicotine patch (Aubin et al., 2008) in randomized controlled trials (RCT). Existing RCTs have also shown varenicline to be more effective than bupropion SR for enabling both short- and long-term cessation (Jorenby et al., 2006; Gonzales et al., 2006).

### **Smoking cessation interventions conducted among smokers living with HIV—**

Despite the high prevalence of cigarette smoking and the significant associated health-related consequences, as well as evidence that 40–63% (Mamary et al., 2002; Burkhalter et al., 2005) of cigarette smokers living with HIV are at least contemplating smoking cessation, very few studies have investigated the effectiveness of smoking cessation interventions among people living with HIV. This lack of emphasis on smoking cessation may be attributable to a variety of factors: the desire of practitioners/patients to focus on acute treatment of a life-threatening illness such as HIV, a perceived lack of relevance of smoking to treatment outcome and survival, a lack of interventions tailored to the population, or the belief that other substance use treatment issues should be addressed first. However, the somewhat limited existing research concerning smoking cessation shows promise for the use of smoking cessation strategies among smokers living with HIV.

See Table 1 for a summary of smoking cessation trials conducted among samples of people living with HIV. Several trials have been conducted to examine the effectiveness of counseling-based approaches to smoking cessation among smokers living with HIV. For instance, a feasibility study examining a cell phone-delivered counseling intervention found that, at the end of a 2-week time period, 75% of smokers were abstinent (Lazev et al., 2004). In two larger, more extensive trials of cell phone-delivered smoking cessation interventions, smokers living with HIV receiving the phone-delivered intervention were significantly more likely than individuals in the usual care group to quit smoking at 3 months (Vidrine et al., 2006: 36.8% vs. 10.3%; Vidrine et al., 2011: 8.9% vs. 2.9%). Moadel and colleagues (2012) found that HIV-positive smokers receiving a group-based smoking cessation intervention were more likely than smokers randomized to receive standard care to be abstinent from smoking at the 3-month follow-up time period (19.2% vs. 9.7%).

Additionally, studies have examined the use of NRT for smoking cessation among persons living with HIV. Findings from a pilot study, conducted by Elzi and colleagues (2006), showed that smokers living with HIV who received counseling plus NRT, as compared to the self-help control condition, were more likely to quit smoking (38% vs. 7%). Similarly, another pilot study found that smokers with HIV receiving a nurse-delivered individual cessation counseling plus NRT reported greater abstinence rates at 8 weeks (62.5% vs. 0%) than a control group of smokers (Wewers et al., 2000). Additionally, Ingersoll and colleagues (2009) randomized smokers living with HIV to receive self-guided reading plus the nicotine patch or motivational interviewing plus the nicotine patch. No significant group differences were observed, although the percentage of smoking days were reduced by 41% among both groups combined, and 22% of all participants were abstinent at follow-up, indicating that the nicotine patch is potentially a viable smoking cessation aid option for HIV-positive smokers. Furthermore, Lloyd-Richardson and colleagues (2009) randomized a group of smokers living with HIV to receive standard care plus the nicotine patch or motivationally enhanced counseling along with the nicotine patch. Again, although no group differences were observed, 6-month abstinence rates of 9–10% were observed for both groups.

Furthermore, several non-randomized studies have examined the effectiveness of pharmacological therapies for smoking cessation among cigarette smokers living with HIV. In one small study, in conjunction with physician advice participating smokers were given the choice of utilizing varenicline, bupropion, NRT, or no cessation aids. At the end of 12 months, 25% of the sample was verified to be abstinent from smoking (Fuster et al., 2009). In one study, among the 21 smokers administered bupropion, 38% self-reported abstinence from smoking at the 12-month follow-up visit (Pedro-Clotet et al., 2006). Two additional studies explored the effectiveness of varenicline among HIV-positive smokers: Tornero and Mafé (2006) found that 24% of smokers administered varenicline were biochemically verified to be abstinent at 6 months, while Cui and colleagues (2011) found 42% of smokers given varenicline to be abstinent at 3 months. Thus, though non-significant differences were observed between intervention and control groups in some of the trials, and abstinence rates in intervention groups varied (8.9%–75%), smoking cessation interventions show promise among cigarette smokers who have HIV.

## CONCLUSION

People living with HIV display a high prevalence of cigarette smoking, and are disproportionately affected by smoking-related conditions, such as cardiovascular and respiratory conditions, lung cancer, immunosuppressive effects, poor quality of life, and adverse HIV treatment outcomes. Despite the burden of cigarette smoking in this group, and the associated adverse health outcomes, relatively little research has been conducted among cigarette smokers living with HIV. Additionally, among the existing research assessing potential predictors and correlates, much of the emphasis has been placed on examining individual-level characteristics and their associations with patterns of cigarette smoking behaviors. The extant literature has identified a variety of individual-level characteristics, such as sociodemographics, substance use, psychiatric comorbidity, and supporting beliefs that are associated with current smoking status, interest in quitting, and barriers to cessation. Though these types of characteristics are undoubtedly important in helping to elucidate patterns of smoking and barriers to cessation, additional research should be conducted to examine social-level characteristics and their associations with cigarette smoking among people living with HIV. The omission of social-level characteristics in extant research is notable, given that prior research among the general population has shown such characteristics to be associated with cigarette smoking behaviors. Additionally, much of the existing research has focused on examining characteristics associated with current cigarette smoking status among people living with HIV. Again, though this is certainly a behavior of much interest, other cigarette smoking behaviors are worthy of investigation as well. Future research should include the examination of characteristics associated with additional smoking behaviors, such as quit attempts and cessation success.

Prior research has also examined and identified numerous provider-related characteristics that may serve as barriers to smoking cessation among smokers with HIV. Some of the most notable and troubling findings concern HIV care providers' lack of training in smoking cessation and counseling methods, as well as physicians' lack of interest in participating in such educational programs in an attempt to receive more training. Given the nearly ubiquitous nature of cigarette smoking among HIV-positive persons, it would seem prudent to include some form of smoking cessation-related training as part of HIV care providers' education, regardless of their level of interest in such education. Having experience with this type of training may increase providers' self-efficacy for successfully providing smoking cessation advice and therapy to their patients, and subsequently increase cessation attempts and eventual cessation among smokers living with HIV.

Few published studies and randomized controlled trials exist concerning smoking cessation interventions among people living with HIV. Additional research is needed in this area to determine which smoking cessation modalities are most effective in this population, as well as to investigate the potential for adverse drug-drug interactions when using pharmacological therapies for smoking cessation, as few studies have looked into this among people living with HIV on HAART. In addition to investigating the effectiveness of smoking cessation therapies, given the high prevalence of smoking and the deleterious associated health consequences, the feasibility and cost-effectiveness of integrating smoking cessation therapy within HIV care settings should be investigated. Furthermore, the belief that

addressing cigarette smoking is not a priority is prevalent among people living with HIV as well as among their healthcare providers. Such issues suggest the need for educational efforts to inform providers and patients about the healthcare, adherence, and treatment risks associated with cigarette smoking among people with HIV.

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**Table 1**  
Summary of studies investigating evidence-based smoking cessation modalities among samples of persons living with HIV

Study	R/NR <sup>a</sup>	Intervention(s)	n	Follow-up	Outcome - abstinence
Cui, 2011	NR	Varenicline	36	3 months (BCV) <sup>c</sup>	42% (15/36)
Elzi, 2006	NR	Counseling + NRT <sup>b</sup> ; no treatment control	34; 383	12 months (SR) <sup>e</sup>	38% (13/34); 7% (27/383)
Fuster, 2009	NR	Varenicline, bupropion, NRT, no aids	6; 12; 8; 3	12 months (BCV)	25% (8/32)
Ingersoll, 2009	R	NRT + self help; NRT + motivational interviewing	18; 22	3 months (BCV)	22% (9/40) overall; ns <sup>e</sup> group difference
Lazev, 2004	NR	Cell phone counseling	19	2 weeks (SR)	75% (15/19)
Lloyd-Richardson, 2009	R	NRT + motivational interviewing; NRT + standard care	232; 212	6 months (BCV)	9% (21/232); 10% (21/212) – ns group difference
Moadel, 2012	R	Group treatment; standard care	73; 72	3 months (BCV)	19.2% (14/73); 9.7% (7/72)
Pedro-Clotet, 2006	NR	Bupropion	21	12 months (SR)	38% (8/21)
Tomero, 2009	NR	Varenicline	22	6 months (BCV)	24% (5/21)
Vidrine, 2006	R	Cell phone counseling; standard care	48; 47	3 months (BCV)	36.8% (14/38); 10.3% (4/39)
Vidrine, 2011	R	Cell phone counseling; standard care	236; 238	3 months (BCV)	8.9% (21/236); 2.9% (7/238)
Wewers, 2000	R	Peer-led intervention + NRT; no treatment control	8; 7	8 weeks (BCV)	62.5% (5/8); 0% (0/7)

<sup>a</sup>R=randomized; NR=non-randomized

<sup>b</sup>NRT=nicotine replacement therapy

<sup>c</sup>BCV=biochemically verified

<sup>d</sup>SR=self-report

<sup>e</sup>ns=non significant