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Review: The need for smoking cessation among HIV-positive smokers

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Abstract

Most HIV-positive persons in the U.S. smoke cigarettes. Despite substantial clinical advances in HIV care in the era of highly active antiretroviral therapy (HAART), HIV-positive persons are at high risk of tobacco-related disease and death. HIV-positive persons have complex social, economic, psychiatric, and medical needs which may impact smoking behavior and response to smoking cessation interventions, but there is a dearth of research on smoking cessation interventions tailored to HIV-positive persons. HIV care providers should treat tobacco use with the array of evidence-based smoking cessation treatments available, updating their clinical practice as new data emerge. This paper reviews the literature on the health consequences of tobacco use in HIV-positive persons, the treatment of tobacco dependence, and the research to date on smoking cessation interventions in HIV-positive persons, and presents recommendations for future research and intervention.

Keywords

HIV; Tobacco; Smoking cessation

Tobacco use is the leading preventable cause of morbidity and mortality in the United States (McGinnis & Foege, 1993), but the health consequences of cigarette smoking are not borne equally among all populations. The prevalence of current tobacco use in HIV-positive smokers is estimated at between 50 and 70% (Burkhalter, Springer, Chhabra, Ostroff, & Rapkin, 2005; Cooperman, Schoenbaum, Klein, & Arnsten, 2007; Gritz, Vidrine, Lazev, Amick, & Arduino, 2004; Niaura et al., 2000), markedly higher than the 20% prevalence in the U.S. general population (Centers for Disease Control and Prevention, 2007). The significant clinical gains made in the control of HIV in the HAART era may be threatened by the cardiovascular, pulmonary, neoplastic and infectious complications of tobacco use in HIV-positive persons. Despite a call for research in the NIH State-of-the-Science statement on tobacco use to evaluate tobacco control interventions in people with co-occurring conditions (NIH State-of-the-Science Panel, 2006), few studies have investigated smoking cessation interventions in HIV-positive persons, and smoking cessation treatment has not been a priority in HIV treatment programs. The objectives of this review are to 1) examine the burden of tobacco use and tobacco-related disease in HIV-positive persons; 2) discuss evidence-based tobacco dependence treatment; 3) describe issues unique to HIV-positive smokers; 4) review the research to date on smoking cessation interventions for HIV-positive smokers; and 5) identify priorities for future research and intervention.

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The burden of tobacco use in HIV-positive persons

Over 85% of HIV-infected individuals in the U.S. have a lifetime history of smoking (Burkhalter et al., 2005), and current cigarette smoking is highly prevalent among HIV-positive persons. Among those with a lifetime history of cigarette smoking, HIV-positive persons are approximately half as likely to be currently abstinent from tobacco use as compared to HIV-negative individuals (Gritz et al., 2004). On average, HIV-positive smokers have been smoking for 22.8 years (Burkhalter et al., 2005) and smoke 16 to 23 cigarettes per day (Benard et al., 2007; Lloyd-Richardson et al., 2008). Among HIV-positive current smokers, most are moderately to highly nicotine dependent (Benard et al., 2007; Lloyd-Richardson et al., 2008).

The marked prevalence of tobacco use in HIV-positive persons has a corresponding health cost. With the decline in AIDS-related death in the HAART era (Palella et al., 1998; Walensky et al., 2006), the proportion of deaths due to tobacco-associated disease, including cardiovascular disease, pulmonary disease and non-HIV related malignancy has increased in HIV-positive persons (Palella et al., 2006). Tobacco use has been found to be independently associated with mortality in HIV-positive smokers (Crothers et al., 2005; Feldman et al., 2006). Despite the marked reductions in HIV-associated illness and mortality, HIV-positive persons have increased mortality rates compared to the general population (Lohse et al., 2007); addressing the disproportionate burden of tobacco use in HIV-positive persons may help to close that gap.

Cigarette smoking is of particular concern among HIV-positive persons given the prevalence of insulin resistance, dyslipidemia, hypertension, abdominal obesity and cardiovascular disease among HIV-positive persons in the HAART era (Carr et al., 1998; Thiebaut et al., 2000; Triant, Lee, Hadigan, & Grinspoon, 2007). Antiretroviral therapy may confer cardiovascular risk; the incidence of myocardial infarction has been shown to increase with increased exposure to antiretroviral therapy in a large prospective cohort (The DAD Study Group, 2007; The Data Collection on Adverse Events of Anti-HIV Drugs (DAD) Study Group, 2003). Of note, data from this cohort suggest that current smoking confers greater risk of myocardial infarction (RR= 2.83, 95% CI 2.04, 3.93) than protease inhibitor therapy (RR= 1.16, 95% CI 1.10, 1.23) (The DAD Study Group, 2007). HIV-positive persons also have higher rates of acute myocardial infarction and cardiovascular risk factors including hypertension, diabetes and dyslipidemia than HIV-negative patients (Triant et al., 2007). In addition, the estimated risk of cardiovascular mortality is higher in HIV-positive patients compared to the general population (De Socio et al., 2007); the main contributor to the increased risk is the high proportion of HIV-positive smokers.

HIV infection may increase susceptibility to chronic obstructive pulmonary disease (COPD) (Crothers, 2007; Crothers et al., 2006). In an observational study of HIV-positive and HIV-negative men, HIV infection was found to be an independent risk factor for COPD, adjusting for age and pack-years of smoking (Crothers et al., 2006). HIV-positive persons were 50-60% more likely to have COPD than HIV-negative persons. The increased risk of COPD in HIV-positive persons is exacerbated by tobacco use. Among a cohort of HIV-positive veterans, cigarette smoking was found to be strongly associated with respiratory symptoms and non-infectious pulmonary disease; COPD was five times more likely in current and former smokers than in never smokers (Crothers et al., 2005).

The association of cigarette smoking and cancer risk is well-established. Among HIV-positive persons, large cohort (Clifford et al., 2005; Engels et al., 2006; Kirk et al., 2007) and population-based studies (Chaturvedi et al., 2007) have demonstrated a three to four-fold increased incidence of lung cancer compared to HIV-negative persons. Though the association between HIV disease and lung cancer persists after adjustment for tobacco use in a number of studies

(Chaturvedi et al., 2007; Engels et al., 2006; Kirk et al., 2007), this increased risk partially reflects the high prevalence of tobacco use among HIV-positive persons. This is of particular concern because lung cancer is the leading cause of non-AIDS-defining malignancy in HIV-positive persons (Frisch, Biggar, Engels, & Goedert, 2001), and the prognosis is poor (Biggar et al., 2005).

Tobacco use also increases the risk of opportunistic and non-opportunistic infections in persons with HIV. Cigarette smoking is independently associated with increased risk of oral candidiasis, oral hairy leukoplakia and oral warts, after adjustment for CD4 count (Chattopadhyay et al., 2005a,2005b;Palacio, Hilton, Canchola, & Greenspan, 1997). Adjusting for antiretroviral therapy, cigarette smoking increases the risk of *pneumocystis carinii* pneumonia (Miguez-Burbano et al., 2005;Miguez-Burbano et al., 2003). Multiple studies have described the association between cigarette smoking and risk of bacterial pneumonia; cigarette smoking is associated with a 1.5 to 3-fold increased risk of bacterial pneumonia in HIV-positive persons (Crothers et al., 2005;Kohli et al., 2006;Le Moing et al., 2006;Miguez-Burbano et al., 2005).

Several studies have investigated the relationship between cigarette smoking and quality of life in HIV-positive persons (Crothers et al., 2005; Reynolds, Neidig, & Wewers, 2004; J. Turner et al., 2001; Vidrine, Arduino, & Gritz, 2007). Among HIV-positive individuals, current cigarette smoking was independently related to a decrease in general health perception, physical functioning, energy, role functioning, and cognitive functioning and an increase in physical pain, adjusting for age, immunologic function and other covariates (J. Turner et al., 2001). Another study found that HIV-positive current smokers experience greater physical symptoms and decreased quality of life compared to former and never smokers (Crothers et al., 2005). Alternatively, among HIV-positive smokers who engaged in a smoking cessation intervention, smoking abstinence was significantly related to a decrease in HIV-related symptom burden but not improved health related quality of life (Vidrine et al., 2007). In sum, HIV-positive smokers have a poorer quality of life than HIV-positive non-smokers. While quitting smoking may improve HIV symptoms, it may not be enough to improve overall health-related quality of life.

Smoking cessation interventions

Evidence-based smoking cessation treatment

Ample clinical evidence exists to support the use of a range of smoking cessation interventions in the general population. However there are no clinical practice guidelines to guide the provision of smoking cessation treatment in HIV-positive persons. Evidence-based treatments with demonstrated efficacy in the general population should thus be incorporated into the care of HIV-positive smokers. Such interventions are outlined below.

Smokers have misperceptions about the risks of smoking and the value, safety and efficacy of using evidence-based cessation methods (Bonnie, Stratton, Wallace, & Committee on Reducing Tobacco Use: Strategies Barriers and Consequences, 2007). Fewer than 20% of quitters use proven treatments, leading to lower cessation and higher relapse rates (S. Zhu, Melcer, Sun, Rosbrook, & Pierce, 2000). It is common for smokers to make multiple quit attempts prior to successful smoking cessation, and multiple courses of treatment or extended treatment may be necessary (Fiore et al., 2008).

Behavioral interventions—U.S. Public Health Service guidelines recommend brief individual smoking cessation counseling with five components (known as the "5 *A's*") at each clinical encounter. Providers are advised to systematically *ask* about tobacco use, *advise* smokers to quit, *assess* willingness to quit, *assist* with quitting, and *arrange* follow up (Fiore

et al., 2008). Brief advice has been shown to increase the likelihood that a smoker will successfully quit and remain a nonsmoker 12 months later (Lancaster & Stead, 2004) and is easily generalizable to complex clinical settings.

Smokers' telephone quitlines are a cost-effective intervention with broad reach and demonstrated efficacy for long-term smoking cessation (Abrams et al., 2003; Fiore et al., 2008; Stead, Perera, & Lancaster, 2006). They offer telephone counseling, smoking cessation educational materials, and some offer nicotine replacement therapy (NRT). Quitlines have been shown to be effective in reaching racial and ethnic minorities (S. H. Zhu et al., 2002), however in low income HIV-positive persons, lack of access to continuous telephone service may be a barrier to their utilization. Despite this potential barrier, HIV-positive persons report interest in telephone-based smoking cessation counseling (Lazev, Vidrine, Arduino, & Gritz, 2004).

Various individual and group smoking cessation counseling approaches have been used in the general population. Motivational interviewing (MI) is a patient-centered approach utilized to amplify an individual's ambivalence about a health-related behavior and enhance readiness to change (Miller & Rollnick, 2002). MI is based on four general principles: 1) express empathy, 2) develop discrepancy, 3) roll with resistance and 4) support self-efficacy. Motivational interviewing is effective in increasing quit attempts, however its efficacy in promoting cessation in motivated smokers is unclear (Fiore et al., 2008).

Cognitive behavioral interventions are another form of counseling known to help smokers quit or reduce cigarette smoking (Niaura, 2008; Simon, Carmody, Hudes, Snyder, & Murray, 2003). Interventions are designed to modify critical cognitions and actions that maintain behaviors such as smoking by promoting the thoughts and skills necessary to create behavioral change. Cognitive-behavioral interventions help a person identify thoughts, feelings and events that are associated with a behavior and subsequently teach skills to cope with those thoughts and events.

Pharmacotherapy—Smoking cessation medications have been demonstrated to increase quit rates 1.5 to 2 fold (Gonzales et al., 2006; Hurt et al., 1997; Jorenby et al., 2006; Silagy, Lancaster, Stead, Mant, & Fowler, 2004). Medications approved by the FDA for smoking cessation include nicotine replacement therapy (patch, lozenges, inhalers, gum and nasal spray), bupropion and varenicline. Selection of individual agents may be guided by patient preference, patients' prior experience with medications, patient characteristics, medical contraindications and cost considerations (Fiore et al., 2008).

All formulations of nicotine replacement therapy have similar efficacy for smoking cessation (Stead, Perera, Bullen, Mant, & Lancaster, 2008). The combination of nicotine replacement therapies is more efficacious than a single agent alone (Stead et al., 2008). Initial dosing is determined by the number of cigarettes smoked per day, and the dose is tapered over the course of treatment. The optimal duration of treatment is not known, but a standard course of treatment is generally 10-12 weeks. Nicotine replacement therapy is safe in stable cardiovascular disease, and should be used with caution in patients with myocardial infarction in the last two weeks, serious arrhythmia, unstable angina, and uncontrolled hypertension (Fiore et al., 2008). There are no known interactions between nicotine replacement therapy and HAART.

Bupropion SR (sustained release) approximately doubles quit rates (Hurt et al., 1997). Bupropion SR alone, or in combination with nicotine replacement therapy, has been shown to be more efficacious than nicotine replacement therapy or placebo (Jorenby et al., 1999). Side effects include insomnia and dry mouth. Because bupropion may lower the seizure threshold, it is contraindicated in people with a history of seizures and should be used with caution in people with a risk of seizures. Bupropion is metabolized by the hepatic cytochrome P450

CYP2B6 system, and its metabolism has been shown to be inhibited by the antiretroviral medications nelfinavir, ritonavir and efavirenz in vitro (Hesse, von Moltke, Shader, & Greenblatt, 2001). Short-term ritonavir administration does not significantly alter bupropion pharmacokinetics in healthy volunteers (Hesse, Greenblatt, von Moltke, & Court, 2006) and no medication-associated adverse events were observed in a case series of ten HIV-positive persons using either ritonavir, nelfinavir or efaverinz with bupropion (Park-Wyllie & Antoniou, 2003).

Varenicline is a partial agonist of the α4β2 nicotinic acetylcholine receptor, which mediates nicotine dependence. Varenicline, which relieves nicotine withdrawal symptoms and reduces the rewarding properties of nicotine, has been shown to be more efficacious than bupropion or placebo for smoking cessation (Gonzales et al., 2006; Jorenby et al., 2006). Side effects include nausea, insomnia, headache and abnormal dreams. Given adverse neuropsychiatric events observed in post marketing surveillance, including drowsiness, agitation, depressed mood, suicidal ideation and attempted and completed suicide, providers should monitor patients for the development or exacerbation of neuropsychiatric symptoms (U.S. Food and Drug Administration). No drug-drug interactions have been described to date with antiretroviral therapy and varenicline.

The unique needs of HIV-positive smokers

HIV-positive persons have a complex range of social, economic, psychiatric, and medical needs which may impact smoking behavior and response to smoking cessation interventions. Psychiatric comorbidity, substance use, motivational level, health risk perception and medication adherence issues are important considerations in the development and dissemination of smoking cessation interventions for HIV-positive smokers.

Social and economic issues—The consequences of tobacco use are not borne equally among all populations--African Americans, Latinos, and Native Americans face well-documented disparities in chronic disease risk, access to appropriate treatment, and cardiovascular mortality (Smedley, Stith, & Nelson, 2002). Socioeconomic status is a major determinant of both smoking prevalence (Centers for Disease Control and Prevention, 2007) and AIDS incidence (Zierler et al., 2000). There is also a higher prevalence of tobacco use among gay and bisexual men than among the general population (Stall, Greenwood, Acree, Paul, & Coates, 1999). Racial and ethnic minorities and socioeconomically disadvantaged persons may also be less likely to receive smoking cessation advice and treatment (Browning, Ferketich, Salsberry, & Wewers, 2008; Houston, Scarinci, Person, & Greene, 2005; Lopez-Quintero, Crum, & Neumark, 2006). Community-specific interventions may be necessary to effectively reduce tobacco use among HIV-positive smokers, but there is a dearth of clinical research to guide the provision of effective tailored interventions. Barriers to access to smoking cessation and HIV treatment will also need to be addressed to optimize provision of smoking cessation services to HIV-positive persons.

Co-morbid psychiatric illness and drug abuse—The high prevalence of cigarette smoking among HIV-infected individuals may be a reflection of the high prevalence of psychiatric illness and substance abuse among HIV-positive persons. Between 50 and 90% of those with psychiatric illness or substance use disorders smoke cigarettes (Nahvi, Richter, Li, Modali, & Arnsten, 2006; Richter & Arnsten, 2006; Richter, Gibson, Ahluwalia, & Schmelzle, 2001; Williams & Ziedonis, 2004) and those with mental illness (including substance use disorders) consume over 40% of the cigarettes smoked in the U.S. (Lasser et al., 2000). Although prevalence estimates for psychiatric and substance use disorders among those with HIV vary by study and disorder, studies have reported that, among those with HIV, 21-28% report current illicit drug use (Cofrancesco et al., 2008; Pence, Miller, Whetten, Eron, &

Gaynes, 2006) and the prevalence of mental illness may be as high as 63% (Tegger et al., 2008).

Among those with HIV, individuals who use drugs or alcohol are more likely to be current cigarette smokers (Burkhalter et al., 2005; Gritz et al., 2004; Webb, Vanable, Carey, & Blair, 2007). In qualitative analyses, shared psychological and physical cues and withdrawal symptoms have been reported to be associated with opiate and nicotine dependence (McCool & Richter, 2003), which may make smoking cessation more difficult for drug users. Some may smoke cigarettes to help improve psychiatric symptoms; research has shown that cigarette smoking may improve symptoms of conditions such as attention deficit disorder and schizophrenia, and quitting smoking is associated with symptoms of depression (Williams & Ziedonis, 2004). Furthermore, depressive symptoms are associated with increased nicotine dependence (Benard et al., 2007) and decreased readiness to quit smoking (Burkhalter et al., 2005) in HIV-positive smokers. Co-morbid psychiatric illness and substance abuse are thus important considerations when helping HIV-positive smokers to quit.

Risk perception and coping—HIV-positive smokers may not be aware of or concerned about the health risks of smoking, and may use cigarette smoking as a coping mechanism. In focus groups with 13 HIV-positive men who were current and former cigarette smokers, although the men acknowledged that smoking can be expensive, addictive, and cause health problems, they minimized the health risks and believed that there were benefits to smoking (Reynolds et al., 2004). The men found smoking to be soothing and helpful with social interaction. Some stated that smoking was a useful coping tool and were reluctant to quit. The study participants also felt that they would probably not live long enough to suffer the serious health problems associated with smoking.

Motivation to quit and quit attempts—Despite the high prevalence of smoking and significant barriers to quitting among those with HIV, many are interested in quitting and have made quit attempts. Studies have reported that 40% to 63% HIV-positive smokers are contemplating quitting or preparing to quit smoking (Benard et al., 2007; Burkhalter et al., 2005; Mamary, Bahrs, & Martinez, 2002), similar to smokers in the general population (Velicer et al., 1995). Approximately 70% of HIV-positive smokers have made a previous quit attempt (Benard et al., 2007; Mamary et al., 2002), with an average of 2.8 quit attempts since their HIV diagnosis (Burkhalter et al., 2005). Studies have reported that between 69% and 84% of HIV-positive smokers are interested in smoking cessation programs or nicotine replacement therapy (Burkhalter et al., 2005; Mamary et al., 2002).

Adherence to pharmacotherapy—Poor adherence to smoking cessation pharmacotherapy could prevent HIV-positive smokers from successfully quitting. The effect of smoking cessation treatment is significantly reduced among individuals who are not adherent to their pharmacotherapy regimen (Stein, Anderson, & Niaura, 2006), and medication adherence is an important clinical issue among those with HIV. Many HIV-positive individuals need to take multiple medications and manage different medication schedules. Issues such as drug abuse, psychiatric illness, and other life stressors are known to impact medication adherence among those with HIV (Arnsten et al., 2002; Arnsten et al., 2007; Leserman, Ironson, O'Cleirigh, Fordiani, & Balbin, 2008) and are likely to impact their ability to adhere to smoking cessation pharmacotherapy as well. Research has shown that cigarette smoking is associated with deceased adherence to HAART (Peretti-Watel, Spire, Lert, & Obadia, 2006; Shuter & Bernstein, 2008; Yuan, L'Italien, Mukherjee, & Iloeje, 2006), suggesting that adherence to smoking cessation pharmacotherapy could be difficult for some HIV-positive smokers.

Provider-level barriers—For smoking cessation interventions to reach smokers, health care providers must recognize and address tobacco use. In a survey of Veterans Affairs HIV and

non-HIV providers and HIV-positive and HIV-negative patients (Crothers et al., 2007), HIV providers failed to recognize current smoking status more often than non-HIV providers. Patients' HIV status was an independent predictor of a provider's failure to recognize current smoking. Recognition of smoking status was not impacted by comorbid illness, cough, dyspnea, degree of immune competence or HIV viral suppression. Furthermore, only a minority (39%) of HIV providers reported confidence in their ability to influence smoking cessation. To increase access to evidence-based smoking cessation treatment, HIV provider-level barriers must be addressed. Provider training, particularly when coupled with systems changes such as reminder systems, has been shown to increase the provision of tobacco cessation interventions (Fiore et al., 2008), however such research has not been conducted in HIV care settings to date.

HIV clinics and providers are uniquely positioned to provide smoking cessation interventions. Smoking cessation interventions delivered by different clinicians increase abstinence rates in the general population (Fiore et al., 2008). The interdisciplinary treatment model of HIV care programs, in which case management, counseling, nursing and medical treatment are co-located, is thus an ideal setting for the delivery of smoking cessation interventions. Routine HIV follow up may enhance the provision of smoking cessation advice; repeated counseling has been shown to increase smoking abstinence rates (Fiore et al., 2008). HIV providers are skilled at addressing and supporting medication adherence and troubleshooting medication adverse effects. HIV providers have also developed skills in addressing addictive disorders and integrating addiction treatment with HIV care (Basu, Smith-Rohrberg, Bruce, & Altice, 2006; B. Turner, Laine, Lin, & Lynch, 2005) that could be utilized to provide smoking cessation services. These strengths must be leveraged to systematically integrate smoking cessation treatment into HIV care.

Smoking cessation interventions for HIV-positive smokers

A review published in 2000 outlined a research agenda to facilitate expansion of smoking cessation services to HIV-positive persons. The authors called for research that 1) tests the efficacy and generalizability of proven smoking cessation interventions; and 2) understands the special concerns that may surround cessation among HIV-positive smokers (Niaura et al., 2000). Despite these recommendations, there continues to be a dearth of clinical research to help elucidate and disseminate effective interventions for HIV-positive smokers.

Persons with HIV were likely to be excluded from participation in the clinical trials that demonstrated the efficacy of nicotine replacement therapy, bupropion, or varenicline for smoking cessation (Ahluwalia, Harris, Catley, Okuyemi, & Mayo, 2002; Gonzales et al., 2006; Hurt et al., 1997; Jorenby et al., 2006; Jorenby et al., 1999). A number of studies (reviewed below) have evaluated the feasibility and effectiveness of smoking cessation treatment in HIV-positive smokers using nicotine replacement therapy; no trials to our knowledge have evaluated the efficacy of bupropion or varenicline for smoking cessation in HIV-positive smokers. Differences in smoking patterns, nicotine dependence and psychosocial factors decrease the generalizability of results of clinical trials conducted in the general population.

Pilot research suggests that smoking cessation interventions are feasible in HIV care settings. Three small studies evaluating standard smoking cessation interventions in HIV-positive smokers are summarized in Table 1. Results suggest that nicotine replacement therapy, in combination with counseling, may increase smoking cessation and decrease tobacco use in HIV-positive smokers (Cummins, Trotter, Moussa, & Turham, 2005;Elzi et al., 2006;Wewers, Neidig, & Kihm, 2000). Further research is necessary to confirm these findings in controlled trials.

Tailored interventions—HIV-positive persons have a complex range of psychiatric, social, economic and medical needs, but research on smoking cessation interventions specifically tailored to HIV-positive persons is in its infancy. To address motivational issues of HIV-positive smokers, including low interest, confidence or readiness to quit smoking, Ingersoll et al. evaluated a motivational smoking cessation intervention among 40 HIV-positive smokers reporting interest in smoking cessation (Ingersoll, Cropsey, & Heckman, 2007). All participants received nicotine patches and were randomly assigned to receive a single session of motivational counseling or written self-help material. There was no difference in smoking cessation outcomes by treatment arm, however both groups significantly reduced cigarettes smoked per day and mean Carbon Monoxide level.

The largest trial to date randomized 95 HIV-positive smokers to receive usual care (brief physician counseling, self-help written materials and nicotine replacement therapy) or a cellular telephone intervention (including eight telephone counseling contacts and usual care components) (Vidrine, Arduino, Lazev, & Gritz, 2006). The cellular phone counseling was tailored to HIV-positive smokers, addressing benefits of smoking cessation such as preventing HIV-related diseases and reducing HIV treatment-associated side effects. Biochemically verified point prevalence abstinence was 36.8% in the cellular telephone group, 3.6× higher than the usual care group, at three month follow up. These data suggest that tailored, intensive interventions are feasible and may be effective for short-term smoking cessation in HIV-positive persons.

Future directions

Much remains to be learned about effective tobacco control measures in HIV-positive persons. Further research is necessary to elucidate and expand the provision of effective smoking cessation interventions in 1) clinical, 2) behavioral, and 3) systems-based domains:

1. *Clinical research.* The efficacy, safety and tolerability of smoking cessation medications in HIV-positive persons warrants further evaluation in controlled clinical trials with long-term follow up. Medication interactions with antiretroviral therapy and effects of medication adherence must be further explored.
2. *Behavioral research.* Smoking cessation interventions with demonstrated efficacy in the general population may be less effective among HIV-positive smokers. Tailoring interventions to address the complex social, economic, psychiatric and medical needs of HIV-positive smokers may be necessary, and must be rigorously evaluated.
3. *Systems-based research.* Multiple barriers to the provision of smoking cessation treatment exist. Systems-based interventions effective in expanding routine screening for tobacco use and provision of cessation services must be developed and disseminated.

As HIV-positive persons live longer in the HAART era, the burden of tobacco-related disease and mortality must be addressed through the development and dissemination of effective smoking cessation treatment. The disproportionate prevalence of tobacco use in HIV-positive persons contributes to the increasing incidence of cardiovascular, pulmonary and non-HIV associated neoplastic disease in HIV-positive persons. Despite the marked prevalence of tobacco use and tobacco-related disease, data suggest that HIV-positive smokers are interested in smoking cessation treatment and can successfully quit. The strengths of HIV care systems and providers should be leveraged to systematically integrate tobacco cessation treatment into HIV care. In the absence of clear guidelines, HIV providers should treat tobacco use with the array of evidence-based smoking cessation treatments available, updating their clinical practice as new data emerge. Without smoking cessation treatment, thousands will benefit from antiretroviral therapy only to suffer the consequences of tobacco-related disease and death.

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Table 1

Studies of standard smoking-cessation interventions among HIV-positive smokers

Source	Setting	Participants	Interventions	Outcomes
Cummins et al., 2005	Outpatient clinic and primary care community service in New South Wales	HIV+ outpatients I: Current smokers interested in quitting (sex, age NR) C: no comparison group	I (N=27): 8-12 weeks NRT Single counseling session Smoking diary Educational materials C: no comparison group	Completion of treatment: N= 16 (59%) Self-reported abstinence: 44% at end of NRT course 15% at 5 month follow up
Elzi et al., 2006	Swiss HIV Cohort Study (SHCS) clinics in Basel, Switzerland	HIV+ SHCS participants I: Current smokers interested in quitting 82% male, age *M* = 43 C: Current smokers 67% male, age *M* = 40	I (N=34): NRT (course NR) Fifteen 30 minute counseling sessions C (N=383): usual care	Completion of treatment NR Self-reported abstinence: I: 50% at 3 months 38% at 12 months* C:15% at 3 months 7% at 12 months* *OR=6.2 (95% CI 2.8, 14.3)
Wewers et al., 2000	AIDS Clinical Trials Unit in Ohio providing primary and research care	Male, HIV+ smokers interested in quitting I: age *M* = 42 27 cigarettes/day C: age *M* = 37 28 cigarettes/day	I (N=8): Nicotine patch × 8 wks Weekly peer-led telephone counseling and smoking cessation skills training C (N=7): Written self-help materials	Completion of treatment: I: N= 7 (87.5%) C: NR Biochemically-confirmed continuous abstinence: I: 62.5% at 8 weeks 50% at 8 months C: 0% at 8 weeks 0% at 8 months

I = intervention arm C = comparison arm NR = not reported