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CIGARETTE SMOKING AND HIV/AIDS: HEALTH IMPLICATIONS, SMOKER CHARACTERISTICS AND CESSATION STRATEGIES

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Abstract

Although mortality attributable to AIDS-related diseases has decreased dramatically in the current era of combination antiretroviral therapy, the proportion of deaths attributable to other diseases (e.g., cardiovascular, pulmonary, and cancer) in this population has markedly increased. Thus, efforts to reduce morbidity and mortality attributable to these non-AIDS-defining diseases represent an important public health priority. One approach to improve health outcomes for the HIV-positive population is to target health risk behaviors, such as cigarette smoking. Existing evidence indicates that smoking prevalence is significantly elevated among persons living with HIV/AIDS. In addition, smoking is associated with numerous HIV-related adverse outcomes. To date, surprisingly few efforts have been made to develop smoking cessation interventions for the HIV-positive population. However, results from the studies that have been published indicate that smoking cessation interventions, both novel and more traditional, are potentially efficacious. Moreover, existing findings support the feasibility of smoking cessation treatment within busy HIV clinics.

Dramatic improvements in survival for persons living with HIV/AIDS have been observed during the first 10 years of the highly active antiretroviral therapy (HAART) era (Lloyd-Smith et al., 2006; Palella et al., 1998; Palella et al., 2006). Recent data indicate that the life expectancy for an adult with newly diagnosed HIV can exceed 35 years (Lohse et al., 2007). Even after an AIDS diagnosis, life expectancy is estimated to be almost 15 years (Walensky et al., 2006). Thus, treatment of the disease demands a broadening of focus to include the management and prevention of both AIDS- and non-AIDS-related chronic medical conditions. In fact, patterns in causes of death have changed dramatically during the HAART era. Mortality attributable to AIDS-related causes has decreased, and the proportion of deaths attributable to non-AIDS-defining illnesses has markedly increased (Palella et al., 2006). Several of the most frequently reported non-AIDS causes of death include cardiovascular disease, pulmonary disease, and cancer (Lewden et al., 2005; Palella et al., 2006). In addition, striking racial/ethnic disparities in both the diagnosis and mortality of HIV/AIDS remain (Centers for Disease Control and Prevention [CDC, 2007b). Thus, continued effort to improve long-term outcomes associated with HIV/AIDS remains a vital public health priority.

One approach to decrease morbidity and mortality in this population is to target health risk behaviors, such as cigarette smoking. Not only are almost 440,000 deaths each year in the general U.S. population attributable to smoking (CDC, 2005), several factors indicate that this health-risk behavior is particularly problematic in the HIV-positive population. These factors include the significantly elevated prevalence of smoking, ranging from 45% to 74% (Burkhalter, Springer, Chhabra, Ostroff, & Rapkin, 2005; Gritz, Vidrine, Lazev, Amick, & Arduino, 2004; Mamary, Bahrs, & Martinez, 2002; Turner et al., 2001; Webb, Vanable, Carey, & Blair, 2007) compared with approximately 21% in the general U.S. population (CDC, 2007a) and the association of smoking with numerous HIV-related complications (e.g., cancer, cardiovascular disease, oral complications, and various pulmonary diseases) (Niaura et al., 2000). To date, surprisingly few efforts have been made to develop smoking cessation interventions for the HIV-positive population. However, results from the studies that have been published indicate that implementing smoking cessation programs in busy HIV clinics is feasible and can significantly decrease smoking rates (Cummins, Trotter, Moussa, & Turham, 2005; Elzi et al., 2006; Vidrine, Arduino, Lazev, & Gritz, 2006; Wewers, Neidig, & Kihm, 2000). The purpose of this review is to (a) provide an overview of the adverse health effects associated with smoking among persons living with HIV/AIDS; (b) describe the behavioral, psychosocial, and demographic characteristics of HIV-positive smokers; and (c) describe the results from published smoking cessation trials targeting persons living with HIV/AIDS.

EFFECTS OF SMOKING ON PERSONS LIVING WITH HIV/AIDS

The adverse health effects of cigarette smoking (e.g., various cancers, cardiovascular disease, and chronic obstructive pulmonary disease) in the general population have been well documented (American Cancer Society, 2007). Despite these health risks, recent estimates from the CDC indicate that 20.8% of Americans (45.3 million individuals) are current smokers (CDC, 2007a). Alarming, the prevalence of smoking is significantly higher in certain population subgroups, including those burdened by social inequalities. For example, individuals with low levels of education and those living below the federal poverty level are significantly more likely to be current smokers than are individuals with more education and higher income levels (CDC, 2007a).

Persons living with HIV/AIDS represent a subgroup with a significantly elevated prevalence of current cigarette smoking (Burkhalter et al., 2005; Gritz et al., 2004; Mamary et al., 2002). The reasons for this elevated prevalence are not fully understood; however, there are several characteristics that are associated with both smoking and HIV serostatus. For example, education level, income, and employment status have been identified as important independent predictors of both HIV/AIDS and smoking status (T. Diaz et al., 1994; Zierler et al., 2000). Certain behavioral and psychosocial variables (e.g., sexual orientation, heavy alcohol consumption, illicit drug use, and depressive symptoms) also appear to be associated with both smoking status and HIV/AIDS (American Medical Association, 1996; Breslau & Johnson, 2000; Degenhardt & Hall, 2001; Greenwood et al., 2005). Although smoking is a hazardous behavior for all populations, persons living with HIV/AIDS appear to be particularly susceptible to the adverse health effects of tobacco use (Niaura et al., 2000). Given the increased survival made possible by HAART, along with the relatively stable HIV

incidence rates, the number of persons living with HIV/AIDS is expected to continue to grow (CDC, 2004). Thus, behavioral treatment approaches, such as smoking cessation interventions, have the potential to significantly enhance medical management and to improve the survivorship experience for this population.

A growing body of literature provides strong evidence that smoking among persons living with HIV/AIDS is particularly harmful. In fact, results from a recent systematic review indicate that smoking may even be an independent risk factor for HIV infection (Furber, Maheswaran, Newell, & Carroll, 2007). Although this association between smoking and HIV risk requires additional research, the adverse impact of smoking on numerous HIV/AIDS-related conditions has been well documented. For example, HIV-positive smokers have an increased incidence of several pulmonary diseases, including cryptococcosis (Hajjeh et al., 1999), invasive pneumococcal disease (Nuorti, Butler, Farley et al., 2000; Nuorti, Butler, Gelling et al., 2000) and spontaneous pneumothorax (Metersky, Colt, Olson, & Shanks, 1995). Even in the absence of an AIDS-related pulmonary condition, HIV-positive smokers are significantly more likely to experience respiratory symptoms compared with HIV-negative smokers (P. T. Diaz et al., 2003). Smokers living with HIV/AIDS also have an increased risk of several HIV/AIDS-related oral diseases, such as oral hairy leukoplakia and oral candidiasis (Chattopadhyay et al., 2005; Greenspan et al., 2000; Shiboski, Neuhaus, Greenspan, & Greenspan, 1999; Slavinsky et al., 2002).

The significantly elevated risk of cancer among persons living with HIV/AIDS is well recognized (Demopoulos, Vamvakas, Ehrlich, & Demopoulos, 2003; Gallagher, Wang, Schymura, Kahn, & Fordyce, 2001; Palefsky et al., 1999; Powles et al., 2004; Spano et al., 2004). Accordingly, cancer represents a leading cause of mortality in the HIV-positive population (Lewden et al., 2005). Although HAART users have a lower risk of certain cancers (e.g., Kaposi's sarcoma), the incidence of these cancers, and many others, remains significantly higher than in non-HIV/AIDS populations (Clifford et al., 2005; Gallagher et al., 2001; Grulich, 2000). Efforts to understand the causal link between HIV and cancer risk are clearly needed. Moreover, efforts designed to decrease the risk of cancer for individuals currently living with HIV/AIDS should also be initiated.

HIV-associated malignancies, such as anal and cervical cancer, are observed significantly more frequently among persons with HIV/AIDS who smoke compared with those who do not smoke (Palefsky et al., 1999; Palefsky, Shiboski, & Moss, 1994). A possible explanation for this association is that smoking increases human papilloma virus (HPV) replication. In fact, the recent finding that HIV-positive smokers have significantly higher levels of the cancer-causing variants of HPV (i.e., HPV16 and HPV18) provides support for this hypothesis (Brockmeyer, Kreuter, Pfister, Altmeyer, & Wieland, 2007).

The incidence of other cancers commonly associated with cigarette smoking, such as lung and head and neck cancers, is significantly elevated in the HIV-positive population. The high prevalence of current smoking in the population is most likely an important factor in these increased rates, but other HIV disease-related factors may also be in play (Haigentz, 2005). Lung cancer tends to be diagnosed at a younger age and has a poorer prognosis in persons living with HIV/AIDS compared with individuals who do not have HIV (Lavole et al.,

2006). Evidence also indicates that lung cancer and head and neck cancer are observed more frequently among HIV-infected smokers compared with noninfected smokers, suggesting that a potential HIV-tobacco interaction may be present (Singh et al., 1996; Tirelli et al., 2000). Finally, Kirk and collaborators (2007) recently found that HIV serostatus is associated with an increased risk of lung cancer even after statistically controlling for the effects of smoking. The growing incidence of lung cancer among persons living with HIV/AIDS represents a significant public health problem warranting comprehensive prevention and early detection efforts (Burke et al., 2004; Spano et al., 2004).

Overall, cancer is a major cause of morbidity and mortality among persons living with HIV/AIDS. Alarming, a trend of increasing incidence of non-AIDS-defining cancers has begun to emerge during the current treatment era (Bonnet et al., 2004). Recent findings from the Data Collection on Adverse Events of Anti-HIV Drugs (DAD) study indicated that death owing to non-AIDS defining malignancies is now even more common than death owing to AIDS-defining malignancies (Monforte et al., 2007).

Cardiovascular disease (CVD) represents another medical outcome of major importance to persons living with HIV/AIDS. Similar to the trend with non-HIV/AIDS-related malignancies, the number of cases of CVD observed in this population has grown during the current era of HAART (Sax & Kumar, 2004), and CVD is now an increasingly common cause of death (Sackoff, Hanna, Pfeiffer, & Torian, 2006). Although an extended life expectancy increases the risk of CVD for individuals living with HIV/AIDS, potential antiretroviral therapy side effects are also a troubling concern. Mounting evidence suggests that important CVD risk factors, such as increased total cholesterol, increased triglycerides, reduced high-density lipoprotein cholesterol, changes in body fat distribution, increased insulin resistance, and diabetes are adverse side effects of antiretroviral therapy (Bozkurt, 2004; Mondy & Tebas, 2007). Despite the increased CVD risks associated with these side effects, compliance with antiretroviral treatment regimens remains necessary to prevent progression of HIV/AIDS. Therefore, efforts to reduce other recognized risks for CVD, such as cigarette smoking, are required.

In addition to the increased risk of numerous AIDS- and non-AIDS-related diseases, evidence indicates that cigarette smoking has an adverse impact upon the health-related quality of life (HRQOL) of persons living with HIV/AIDS. Specifically, current smokers who are HIV-positive tend to report lower levels of HRQOL compared with former and never smokers with HIV (Turner et al., 2001). There is also evidence that current smokers report greater HIV-related symptom burden compared with nonsmokers (Crothers et al., 2005). Recent findings demonstrated that among individuals attempting to quit smoking, length of smoking abstinence was significantly associated with a reduction of self-reported HIV-symptom burden (Vidrine, Arduino, & Gritz, 2007). These findings, along with the extensive evidence that symptom severity negatively affects HRQOL (Cunningham et al., 1998), indicate that smoking's adverse effects on HRQOL might be partially mediated by HIV-related symptoms. Therefore, smoking cessation efforts targeting persons living with HIV/AIDS may represent a useful behavioral approach not only to reduce HIV-related symptoms but also to ultimately improve HRQOL.

Although the true attributable risk of cigarette smoking in the HIV-positive population would be difficult to estimate due to the numerous disease- and treatment-related interrelationships, it appears highly likely that reducing smoking prevalence would result in better disease management and increased length of survival. Recently published findings from the Women's Interagency HIV Study support this view: Women who were current smokers experienced significantly poorer viral and immunologic responses to HAART and significantly higher risk of death (Feldman et al., 2006). A striking trend was also observed by Lewden and colleagues (2005). A detailed review of the causes of death among HIV/AIDS patients reported from various hospital wards in France indicated that cigarette smoking was reported in almost 75% of cancer-related deaths. This finding led the authors to conclude that the prevention of non-AIDS malignancies (especially lung cancer) ranks among the most important priorities for HIV/AIDS management (Lewden et al., 2005).

BEHAVIORAL, PSYCHOSOCIAL, AND DEMOGRAPHIC CHARACTERISTICS OF HIV-POSITIVE SMOKERS

A handful of cross-sectional studies have been conducted to gather more detailed information about HIV-positive smokers. In addition to confirming the dramatically elevated prevalence of current smoking, findings generally indicated that the majority of HIV-positive smokers (58%–66%) were planning to quit smoking (Burkhalter et al., 2005; Gritz et al., 2004; Mamary et al., 2002). Similarly, findings indicated that between two thirds and three fourths of HIV-positive smokers reported making past attempts to quit smoking (Benard et al., 2007; Burkhalter et al., 2005; Mamary et al., 2002). Despite the high level of interest in quitting and past quit attempts, findings revealed a relatively low proportion of former smokers (Burkhalter et al., 2005; Gritz et al., 2004). Together, these trends demonstrated that HIV-positive smokers may be less likely to achieve abstinence than non-HIV-positive smokers. However, the available reports also indicated that an HIV diagnosis may be associated with smoking cessation or reduction (Burkhalter et al., 2005; Collins et al., 2001). This finding suggests that an HIV diagnosis may serve as a teachable moment for smoking cessation.

Certain variables have been found to be associated with smoking status in the HIV-positive population. For example, heavy alcohol and illicit drug use were significantly associated with current smoking (Benard et al., 2007; Burkhalter et al., 2005; Gritz et al., 2004; Webb et al., 2007). In addition, differences in smoking behavior were observed among various racial/ethnic groups suggesting that interventions tailored to the specific characteristics (e.g., nicotine dependence, smoking patterns, and psychosocial variables) may be required to maximize treatment efficacy (Lloyd-Richardson et al., 2008). The role of disease progression on smoking behavior is less clear. For example, several studies indicated that CD4 cell count and viral load were not associated with smoking status (Burkhalter et al., 2005; Gritz et al., 2004; Webb et al., 2007) whereas other reports indicated that markers of disease progression were associated with an increased likelihood of smoking (Crothers et al., 2005; Turner et al., 2001). Further evidence indicated that smoking cessation interventions targeting persons living with HIV/AIDS may benefit from addressing illness-specific beliefs. In a series of focus group interviews, Reynolds and colleagues (2004) found that HIV-

positive smokers frequently discounted the health risks associated with smoking, believing that a short life expectancy would prevent them from experiencing the health conditions resulting from smoking. Together, these findings suggest that attitudes about smoking cessation may be influenced by HIV disease events/stages and/or the perceived life impact of being HIV-positive.

SMOKING CESSATION EFFORTS TARGETED TO PERSONS LIVING WITH HTV/AIDS

Despite the evidence indicating that smoking increases the risk of numerous HIV/AIDS-related and non-HIV/AIDS-related adverse outcomes, relatively few cessation trials appear in the literature. A small pilot study conducted by Wewers and colleagues (2000) compared a peer-led 8-week cessation intervention to a self-help control group. The intervention consisted of nicotine replacement therapy (NRT) along with both in-person and telephone-delivered counseling sessions. Counseling session content included cognitive behavioral components, such coping skills training and problem solving. Results indicated that the intervention was feasible and promising. Posttreatment (8-week) abstinence rates were higher for the group receiving the NRT and counseling sessions compared with the self-help control group (63% vs. 0%) (Wewers et al., 2000).

A pair of similarly designed studies provides additional support for the feasibility of delivering smoking cessation treatment consisting of counseling and NRT. The first of these pilot trials was conducted at an HIV clinic located in New South Wales, Australia. Questionnaires were used to screen patients in the general clinic population for tobacco use. Current smokers were then invited to participate in a 12-week nurse-administered intervention. NRT was dosed according to the participant's level of nicotine dependence and medical history, and a social worker conducted counseling sessions intended to increase knowledge and quit motivation. Findings indicated that at the end of treatment, 12 of the 27 participants enrolled (44%) had successfully quit smoking. The authors concluded that the provision of free NRT, which overcomes a cost barrier associated with cessation treatment, was a crucial factor for the intervention's feasibility (Cummins et al., 2005). Another pilot study conducted with participants enrolled in the Swiss HIV Cohort Study also consisted of counseling sessions and the provision of NRT. In this trial, participants in the intervention group ($n = 34$) received nurse-delivered, cognitive behavioral counseling, along with NRT. Current smokers from the Swiss HIV Cohort who did not receive the intervention ($n = 383$) served as the control group. At 12 months' post enrollment, participants who received the intervention were six times as likely to have quit smoking compared with participants in the control group (38% vs. 7%) (Elzi et al., 2006). Although these results were encouraging, the participation rate was low—only 8% of smokers consented to receive the treatment. Nevertheless, the authors concluded that administering a traditional smoking cessation intervention in an HIV clinic was feasible and could significantly reduce smoking rates.

Additional efforts, both published and under way, have been made to design more novel smoking cessation treatments for persons living with HIV/AIDS. Lazev and colleagues (2004) conducted a small ($n = 20$) study to assess the feasibility of implementing a cell

phone delivered counseling intervention. This study was conducted with a diverse sample of individuals recruited from a large inner-city HIV clinic. Participants were given cell phones and received 6 proactive phone counseling sessions delivered over a 2-week period. Results supported the feasibility of this treatment approach, with all participants completing at least 4 of the counseling sessions and an overall contact rate of 93% (Lazev, Vidrine, Arduino, & Gritz, 2004). A follow-up study was then conducted to further assess the feasibility of the cell phone approach and to provide a preliminary efficacy assessment. In this study, 95 HIV-positive smokers were recruited and randomized to either a usual care group or a cell phone intervention group. Participants in the cell phone group were asked to complete 8 proactive counseling sessions delivered via cell phone over a 2-month period. Cell phone counseling content included health education, coping skills, planning, and problem solving components. Participants randomized to the usual care condition received brief advice to quit and written materials. All participants were also offered NRT. Results indicated 3-month smoking abstinence rates of 10.3% for the usual care group and 36.8% for the cell phone group. Participants who received the cell phone intervention were 3.6 times more likely to quit smoking compared with participants who received usual care (95% confidence interval = 1.3–9.9, $p = 0.0059$). Participants in the cell phone group were also significantly more likely to have made a quit attempt and to have remained abstinent for a longer period of time compared with participants in the usual care group (Vidrine, Arduino, Lazev et al., 2006). A subsequent set of analyses revealed that reductions in depression and anxiety levels and an increase in self-efficacy were partial treatment mediators (Vidrine, Arduino, & Gritz, 2006). In sum, results of the trial indicated that cell phone delivered smoking cessation treatment targeted to individuals living with HIV/AIDS is feasible and can significantly increase smoking abstinence rates. A large, NCI funded project currently under way will provide a true long-term efficacy assessment of the cell phone treatment approach.

The Computer Retrieval of Information on Scientific Projects database indicates that several other smoking cessation intervention trials targeted to persons living with HIV/AIDS are currently being conducted. Specifically, Niaura and colleagues are currently evaluating the efficacy of a cessation intervention tailored to special needs of HIV-positive Latino smokers. In addition, Humfleet and colleagues are currently comparing a computer-based smoking cessation intervention targeting HIV-positive smokers to an individual counseling condition and a minimal contact control group.

CONCLUSIONS

The dramatic transformation of HIV/AIDS into a medically manageable condition has been a tremendous success story. As life expectancies have increased, morbidity and mortality patterns have changed. It is becoming increasingly clear that health risk behaviors, such as cigarette smoking, represent important factors affecting disease course. Cigarette smoking among persons living with HIV/AIDS is associated with an increased risk of numerous health conditions, including cancer, CVD, and reduced HRQOL. Thus, the provision of smoking cessation treatment may represent an important component of successful medical management of HIV disease. Although few efforts to assess smoking cessation interventions for persons living with HIV/AIDS appear in the literature, several reports do suggest that cessation treatments, both traditional and novel, can significantly reduce smoking rates.

However; more efforts are needed. Specifically, well-designed randomized controlled trials are required to fully assess the short-term and long-term efficacy of established cessation treatments.

Moreover, optimal treatment of smokers with HIV is likely to require tailoring of interventions to meet the special needs of this population. That is, considerable data indicate that HIV-positive smokers are more likely than the general population of smokers to suffer comorbid alcohol and substance abuse problems. Therefore, targeting smoking without also targeting these comorbid conditions may ultimately result in suboptimal smoking cessation outcomes. Future studies should examine the efficacy of interventions emphasizing smoking cessation alone versus interventions designed to facilitate multiple health behavior changes simultaneously (e.g., smoking, alcohol, illicit drug use, and medication adherence). Similarly, more tailored interventions should be designed to overcome barriers to treatment and to address additional variables known to be associated with smoking (e.g., negative affect and health beliefs). The adequacy of stand alone smoking cessation programs verses smoking cessation integration into routine HIV care should also be considered.

Research efforts to more fully explore the safety and efficacy of smoking cessation pharmacotherapy are necessary. Although previously published efforts have demonstrated that NRT can effectively be administered to smokers living with HIV/AIDS, the literature lacks reports of studies using other agents, such as bupropion and varenicline. It is possible that these agents may improve cessation rates, and research efforts should explore their usefulness in the HIV clinic. However, it will be vital to consider potential drug interactions and to monitor treatment side effects. Finally, efforts to capitalize on the potential teachable moment effect of an HIV diagnosis should be explored. A more thorough understanding of the mechanisms involved in the smoking status changes that follow an HIV diagnosis could potentially allow for development of interventions that maximize this effect.

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