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The relationship between ART adherence and smoking status among HIV+ individuals

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Abstract

Smoking is highly prevalent among HIV+ individuals and studies indicate that it may be associated with poor ART adherence, though the relationship is poorly understood. In addition little is known about interest in quitting among HIV+ smokers who are having adherence difficulties. We examined smoking and ART adherence among 203 HIV+ individuals enrolled in a randomized trial of interventions to increase ART adherence. Prior analyses indicated there were no overall treatment group effects. Smoking status and motivation to quit was assessed at baseline and ART adherence was assessed at week 12, 24, 36, and 48. Longitudinal generalized estimating equation analysis that controlled for treatment group revealed that smoking status was not significantly related to adherence over time. Motivation to quit was high with 58% intending to quit in the next 6 months and 25% intending to quit in the next 30 days. Findings suggest that smoking is not associated with adherence among those with adherence difficulties. However it does not diminish importance of addressing both behaviors especially given HIV+ smokers substantial interest in changing smoking behavior.

INTRODUCTION

For HIV+ individuals, high adherence to antiretroviral (ART) medications is essential for reducing viral load, preventing drug resistance, avoiding opportunistic infections (1–4) and increasing long-term survival (5–8). In spite of its importance, studies indicate that high adherence is a significant problem among HIV+ individuals (9–11). Research indicates that many factors are related to adherence including covariates of race, such as discrimination (12, 13), psychiatric diagnoses (14,15) such as depression, alcohol or other drug use (16–18), stress (18,19), social support (20) and coping styles (21). However, there is emerging literature suggesting that tobacco smoking, which is highly prevalent among HIV+ individuals, may also be associated with poor ART adherence (22–26). An estimated 47–70% of people living with HIV/AIDS (PLWHA) smoke cigarettes (24,27,28) and smokers have been shown to be less adherent to a variety of medications (29).

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Although the few studies published to date suggest that smoking may be associated with poorer ART adherence, the nature of that relationship is not clear. It seems most plausible that the relationship would be due to smoking status and poor adherence sharing similar risk factors. Consistent with this, one study of infectious disease clinic patients found through mediational analyses that lower levels of self-reported adherence in smokers might be due to smokers having higher levels of depressive symptoms (24). Similarly, O'Cleirigh et al. (22) found that smoking was not only related to non-adherence but that smokers were more likely than non-smokers to endorse problematic alcohol, cocaine, heroin, and marijuana use. On the other hand, Shuter and Bernstein (25) found that current cigarette smoking was a predictor of non-adherence to ART among HIV+ men and women, independent of factors such as drug use history, history of psychiatric illness, and current depression (n= 64). Another study that examined adherence *within* a sample of HIV+ smokers (n=326) enrolled in a randomized controlled smoking cessation trial (23) found that nicotine dependence, illicit drug use, and alcohol use were associated with nonadherence, though depression and stress were not.

In light of the few studies that have been conducted and the limited understanding of the relationship between smoking and ART adherence, the purpose of this study was to further explore the relationship in a diverse sample of HIV-infected patients who participated in a randomized trial to increase ART adherence. Further, given that nicotine dependence has been linked to ART adherence in one study (23) and that non-daily or occasional smokers are considered to have distinct personal and smoking characteristics compared to daily smokers (30,31), we assessed differences in ART adherence by smoking level. Because of the potential importance of reducing smoking in this population with a high smoking prevalence and adherence difficulties, we also examined the motivation and confidence of participants to quit as an indicator of how receptive smokers would be to smoking cessation treatment.

METHODS

Data for this study were drawn from Project MOTIV8, a randomized controlled trial comparing three interventions to increase ART adherence: Motivational Interviewing-based cognitive behavioral therapy (MI-CBT) combined with modified directly observed therapy (MI-CBT/mDOT); MI-CBT alone; and standard care (SC). Detailed methods are provided elsewhere (32), but in brief, participants were recruited from six outpatient clinics and after completing baseline measures were randomly assigned to one of the three study groups for a period of 24 weeks. Participants receiving MI-CBT (regardless of arm) received 10 sessions over 24 weeks. Participants receiving mDOT received daily visits or verifying phone calls to observe or confirm their pill taking for 24 weeks. Adherence data was collected using medication event monitoring system (MEMS) caps, which were uploaded at follow-up assessments (12, 24, 36, and 48 weeks). Participants were incentivized up to $165 for the main study, and the study was approved by the relevant institutional review boards. Main outcome analyses for the original study indicated there was no significant difference in baseline characteristics between groups and no overall treatment group effect on adherence (32).

Participants

Eligible participants had reported adherence problems (confirmed by provider documentation and/or HIV RNA >1000 copies/mL), were starting ART for the first time or making a change to their regimen. Other eligibility criteria included being HIV+, ≥18 years of age, and English speaking. Of the 204 participants randomized to the trial, 203 were included in the analyses for the present study with one participant excluded due to missing smoking data.

Measures

Baseline and final follow-up data at week 48 were collected with audio computer-assisted self-interviews (ACASI) surveys. Measures used in the analyses for this study included demographics and HIV related sample characteristics, smoking characteristics, and medication adherence. Demographic and sample characteristic measures included age, gender, race, sexual orientation, education, income, relationship status, recent and ever drug use, alcohol use, CD4 cell count (<200), Stage of Change for adherence (33), and whether or not they were starting ART for the first time.

The reported number of days smoked in the previous 30 days at baseline was used to characterize participants as being daily smokers, occasional smokers, and non-smokers (34). Daily and occasional smokers were analyzed separately because the literature indicates that these groups of smokers are distinct with different levels of nicotine dependence, motivation to quit, and ability to achieve abstinence (35–37). We also collected the average number of cigarettes smoked per day (CPD; 34). These are established, validated, self-report measures of smoking behavior drawn from a national surveillance survey (CDC, 2004). The Fagerstrom Test of Nicotine Dependence (FTND; 38) is a 6-item scale that assesses behavioral indexes of dependence (e.g., how soon you smoke after waking, whether you find it difficult to refrain from smoking in places where it is forbidden, and the number of cigarettes smoked per day). It is the most widely used measure of nicotine dependence (39).

Motivation and confidence to quit were measured on 1–10 scales, asking participants “On a scale from 0 to 10, how motivated/confident are you to quit smoking?” These items have been shown to be sensitive to baseline levels of interest in quitting prior to treatment, and to relate to cessation outcomes in both adults and college students (40–42). We also assessed the reported number of quit attempts in the previous year and established stage of change for quitting (33) by asking participants about their intention to quit in the next 6 months and 30 days.

ART adherence was measured using electronic drug monitoring (EDM), specifically medication bottle caps (Medication Event Monitoring System; www.aardex.ch) that record the date and time of each opening. Although the necessary level of adherence for viral suppression is currently under debate and appears to vary by class of antiretroviral therapies (43,44), we used the dichotomous summary measure of 95% or greater adherence to all doses during the 30-day period before the 12-week, 24-week, 36-week and 48-week visits as the criterion because this is more commonly used in prior studies (43). Supplementary

analyses that used alternative methods of operationalizing adherence (i.e., continuous measure, 90%, 85%, and 80% dichotomous measures) did not change the conclusions.

RESULTS

Participant demographic and descriptive characteristics as well as mean differences between the smoking status groups are displayed in Table 1. The majority of participants were male (75%), African-American (57%), nearly half were heterosexual (47%), and middle-aged. As can be seen in Table 1, based on reported number of days smoked in the previous 30 days, we identified 68 (33.5%) non-smokers, 48 (23.6%) occasional smokers, and 87 (42.9%) daily smokers. Given that this sample of HIV+ individuals were randomized to adherence treatment groups, we examined whether there were any differences in the distribution of smoking status across treatment groups and found no significant differences (χ^2 (2) = .24, p = .993).

Relationships between smoking and adherence

To assess the relationship between smoking and adherence we used a longitudinal analysis with a generalized estimating equation (GEE) model in which smoking status (non-smoker, occasional, and daily, with non-smoker as the reference group) was used to predict adherence throughout the 48-week period, controlling for treatment group. Results (displayed in Table 2) revealed that smoking status measured at baseline was not significantly related to adherence over time (Wald χ^2 (2) = 5.44, p = .066). Although the overall model did not reach significance, an examination of individual effects revealed that there was significantly lower adherence in the occasional smoking group compared to the non-smoking group. Follow-up analyses examined adherence levels between groups at each of the measurement points (7-day post; 12, 24, 36, 48 weeks) using chi-square analysis. As can be seen in Table 1, although there were no significant differences at any time point, the significant effect of occasional smoking in the overall model appeared to be due to occasional smokers having lower adherence than non-smokers at the 36-week assessment and lower adherence than both non-smokers and daily smokers at the 48-week assessment.

Motivation and Confidence to quit

Smoking characteristics and motivation measures are displayed in Table 1. Daily smokers expressed moderate levels of motivation and confidence to quit smoking and made less than two quit attempts on average in the past 30 days. On the other hand, occasional smokers reported high levels of motivation and confidence to quit smoking and made over three quit attempts in the past 30-days. Forty-eight percent of daily smokers and 62% of occasional smokers made a quit attempt in the past year. With regard to stage of change for smoking, 23% of daily smokers and 36% of occasional smokers were in the preparation stage of quitting.

DISCUSSION

The primary purpose of this study was to examine the relationship between smoking and ART adherence in a group of HIV+ individuals enrolled in a randomized clinical trial to

increase adherence to ART. The parent trial found no overall effect of treatment group. Our primary findings indicated that overall smoking was not strongly related to adherence. In particular, longitudinal analyses that incorporated all time-points found no overall significant association between adherence and smoking, though examination of individual effects revealed occasional smokers to have lower adherence than non-smokers. Comparisons made at each time point were consistent with the overall longitudinal model in that there were no significant differences at any of the times points but trends were observed at 36 weeks and 48 weeks, with occasional smokers being less adherent than non-smokers.

These findings are somewhat different than prior studies that reported smoking to be significantly associated with adherence among HIV+ patients (22–26). The most likely explanation for the different results is that the majority of the participants in this study (66%) were recruited specifically because they were having adherence difficulties. If smoking is correlated with other risk factors for adherence, selecting only poorly adherent individuals could diminish any association between smoking and adherence. Our results therefore suggest that if smoking is related to adherence, it is most likely because smoking and poor adherence share similar risk factors (22, 24).

Another important difference between the present study and prior studies is that this study included and analyzed occasional smokers separately from daily smokers. Surprisingly, the only indication of any differences in adherence in the present study was between occasional smokers and non-smokers. However, examination of the participant characteristics in this study indicates that occasional smokers were younger, predominantly identified as an ethnic/racial minority, had lower levels of education and lower income, and reported higher rates of recent and ever drug use. In this study occasional smoking status may have been a marker for associated factors that can directly or indirectly negatively impact adherence. With regard to a possible link between lighter smoking and adherence it is worth noting that although Marks-King et al. (23) reported that *higher* nicotine dependence (which is typically associated with more regular, heavier smoking) was associated with poorer adherence, participants in that study were all daily smokers (at least 5 cigarettes per day). No prior studies have examined the full range of nicotine dependence or compared occasional, daily, and non-smokers. Our results might explain inconsistencies in previous research and suggest that further examination of adherence by the frequency of smoking could help clarify the relationship between smoking and HIV medication adherence.

Results regarding the motivation of HIV+ smokers to quit revealed that a sizable proportion (58%) intended to quit in the next 6 months with 27% expressing interest in quitting in the next 30 days, which is similar to what has been found in other samples of HIV+ smokers (45–47). Our sample of smokers also reported high levels of motivation and confidence to quit with occasional smokers having higher levels of motivation and confidence to quit and higher intentions to quit than daily smokers. Given that analyses showed that occasional smokers may be less adherent than daily smokers, future studies should explore the relationship between interest in quitting smoking and adherence. The overall findings suggest that HIV+ individuals with adherence difficulties would welcome interventions to assist them to quit. Integration of smoking cessation services into HIV treatment in

infectious disease clinics could reduce morbidity and mortality in these patients (28) regardless of whether it helps with adherence.

This study had several limitations deserving mention. Although this study included a large sample size with objective measures of adherence, the study findings are based on participants and associations in an adherence treatment trial and may not generalize to adherence behavior outside a treatment context. Relatedly, inclusion of more individuals without adherence problems may also have led to different conclusions. This sample was also a diverse urban sample recruited from outpatient clinics in the Midwest and findings may not generalize to other settings and populations.

Nevertheless the results suggest smoking was weakly if at all related to adherence, perhaps due to the high proportion of individuals with a history of adherence difficulties. The lack of association between ART adherence and smoking does not diminish the importance of addressing both behaviors and raising awareness of the importance of addressing smoking among HIV providers who often do not raise it with patients (48). Our results indicate that there is not only a high prevalence of smoking, but also substantial interest in changing smoking behavior among HIV+ individuals.

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Table 1

Baseline Characteristics[a]

	Non-Smokers (N=68)	Occasional Smokers (N=48)	Daily Smokers (N=87)	Total (N=203)	*p* value
Age	41.4 (10.4)	36.8 (10.2)	41.6 (7.8)	40.45 (9.5)	.011[b d]
Men, No. (%)	51 (75.0)	33 (68.8)	70 (80.5)	154 (75.9)	.308
Sexual Orientation, No. (%)					.657
Heterosexual	32 (47.1)	26 (54.2)	37 (42.5)	95 (46.8)	
Gay/Gay-Identified	28 (41.2)	14 (29.2)	35 (40.2)	77 (37.9)	
Bi-sexual/Other/Refused	8 (11.7)	8 (16.6)	15 (17.3)	31 (15.3)	
Marital Status, No. (%)					.529
In a relationship/Married	18 (26.5)	9 (18.8)	23 (27.1)	50 (24.9)	
Single/Divorced/Separated/Widowed	50 (73.5)	39 (81.2)	62 (72.9)	151 (75.1)	
Ethnicity, No. (%)					.030[b]
Black or African American	40 (59.7)	32 (66.7)	44 (50.6)	116 (57.4)	
White	19 (28.4)	9 (18.8)	35 (40.2)	63 (31.2)	
Other	8 (11.9)	7 (14.6)	8 (9.2)	23 (11.4)	
Education, No. (%)					.001[c d]
Less than HS degree	7 (10.3)	19 (39.6)	20 (23.0)	46 (22.7)	
HS degree/GED	19 (27.9)	11 (22.9)	32 (36.8)	62 (30.5)	
Post-high school education	42 (61.8)	18 (37.5)	35 (40.2)	95 (46.8)	
Monthly Household Income, No. (%)					.017[b d]
<$500	18 (29.0)	23 (54.8)	26 (32.5)	67 (36.4)	
>$500	44 (71.0)	19 (45.2)	54 (67.5)	117 (63.6)	
Ever Drug use, No. (% YES)	28 (41.2)	31 (64.6)	58 (66.7)	117 (57.6)	.003[c d]
Recent Drug use, No. (%YES)	19 (27.9)	25 (52.1)	44 (50.6)	88 (43.3)	.007[c d]
Alcohol Use, No. (% YES)	32 (47.1)	27 (56.2)	55 (63.2)	114 (56.2)	.132

	Non-Smokers (N=68)	Occasional Smokers (N=48)	Daily Smokers (N=87)	Total (N=203)	*p* value
CD4 cell count	272.2 (193.3)	246.0 (269.7)	257.9 (193.1)	259.8 (213.1)	.807
ART Experience, No. (%)					.563
Naïve	25 (36.8)	18 (37.5)	26 (29.9)	69 (34.0)	
Experienced	43 (63.2)	30 (62.5)	61 (70.1)	134 (66.0)	
Stage of Change for ART adherence, No. (%)					.355
Preparation	23 (54.8)	13 (41.9)	41 (64.1)	77 (56.2)	
Action	10 (23.8)	9 (29.0)	13 (29.0)	32 (23.4)	
Maintenance	9 (21.4)	9 (29.0)	10 (15.6)	28 (20.4)	
Fagerstrom Test for Nicotine Dependence	-	2.60 (2.0)	4.56 (2.0)	3.89 (2.2)	<.001
Cigarettes smoked per day (CPD)	-	-	14.40 (8.3)	-	-
Number of Days Smoked	-	12 (9.6)	-	-	-
Total # Cigarettes Smoked in 30 days	-	105.3 (131.8)	432.1 (250.4)	211.1 (264.2)	<.001
Intend to quit in 6 mo (% Yes)	-	32 (71.1)	45 (51.7)	77 (58.3)	.032
Intend to quit in next 30 days (% Yes)	-	16 (35.6)	20 (23.0)	36 (27.3)	.124
Motivation to quit (1–10)	-	7.5 (2.3)	5.1 (3.0)	5.9 (3.0)	<.001
Confidence to quit (1–10)	-	7.7 (2.5)	5.6 (2.9)	6.4 (2.9)	<.001
Quit attempts in past year	-	3.5 (5.4)	1.4 (2.4)	2.1 (3.8)	.003
Adherence Variables: 95% of Doses Taken, No. (%YES)					
7-day post (N=190)	38 (59.4)	26 (61.9)	51 (60.7)	115 (60.5)	.966
12 weeks (N=184)	32 (49.2)	13 (31.0)	36 (46.8)	81 (44.0)	.145
24 weeks (N=181)	27 (42.9)	11 (26.2)	30 (39.5)	68 (37.6)	.203
36 weeks (N=175)	26 (41.3)	8 (20.0)	27 (37.5)	61 (34.9)	.072[d]

	Non-Smokers (N=68)	Occasional Smokers (N=48)	Daily Smokers (N=87)	Total (N=203)	*p* value
48 weeks (N=165)	19 (32.2)	5 (13.5)	23 (33.3)	47 (28.5)	.072[b d]

[a] All values presented are means (SDs) except where noted; *p* values reported for ANOVA, t-tests, and chi-square analyses

[b] Daily versus Occasional $p < .05$;

[c] Daily versus Non-smoker $p < .05$;

[d] Occasional versus Non-smoker $p < .05$

Table 2

Results of GEE Analysis Predicting 95% ART Adherence with Smoking Status (0= Non-adherence; 1 = adherence)[a] [b]

	Estimate	SE	95% CI	Z	*p*
Intercept	−.160	0.241	−.313–.632	.439	.508
MI-CBT/mDOT	−.068	0.261	−.444–.580	.068	.794
MI-CBT	−.019	0.262	−.495–.533	.005	.941
Daily Smokers	−.045	0.246	−.437–.528	.034	.854
Occasional Smokers	−.610	0.290	.041–1.179	4.410	.036

[a] Reference groups: Non-smokers and Standard Care condition

[b] Model effects: Smoking status, Wald χ^2 (2) = 5.44, p = .066; Tx Group, Wald χ^2 (2) = 0.73, p = .964