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Cigarette smoking and antiretroviral therapy (ART) adherence in a sample of heavy drinking HIV-infected Men who have Sex with Men (MSM)

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Abstract

Cigarette smoking and heavy alcohol use is prevalent among HIV-infected men who sex with men (MSM) and have been linked to imperfect antiretroviral therapy (ART) adherence. Our study examined the correlates of smoking and whether smoking was independently associated with imperfect adherence in heavy-drinking HIV-infected MSM. Of the 185 participants, approximately half ($n = 91$, 49.2%) reported having smoked cigarettes in the past 30 days. Current smokers were more likely to have reported imperfect adherence compared to non-smokers (37.4.2% vs. 22.3%, $p < 0.05$). In multivariable regression analyses, only lower education was significantly associated with imperfect adherence. This study demonstrated that the greatest risk factor for smoking and imperfect ART adherence was low socioeconomic status, in which MSM of color were over-represented. As the first study to examine smoking and ART adherence in this population, our study has the potential to inform the clinical care provided to heavy-drinking MSM.

INTRODUCTION

Despite significant advances in antiretroviral therapy (ART), notably improved efficacy, reduced pill burden, and the development of the single tablet regimen, sustained adherence

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COMPLIANCE WITH ETHICAL STANDARDS:

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

to ART remains critical to the long-term management of HIV infection (1). For persons living with HIV (PLWH), adherence to ART is key to the prevention of drug resistance (2), the emergence of opportunistic infections, disease progression, and death (3). From a public health perspective, HIV viral suppression is important not only to reduce morbidity and mortality in PLWH, but also to reduce the likelihood of transmission. Multiple studies have demonstrated that viral suppression significantly reduces the risk of transmission and, in fact, a recent study concluded that 77% of new infections were due to transmission from previously diagnosed HIV-infected partners, further emphasizing the importance of viral suppression among those living with HIV (4–6). Gay, bisexual, and other men who have sex with men (MSM) remain the group with the highest incidence and prevalence of HIV in the U.S. (7) and understanding barriers to ART adherence in this population is critical.

Active substance use has been associated with imperfect ART adherence. For example, a meta-analysis found that those who used alcohol were 50–60% less likely to be ART adherent (OR = 0.548, 95% CI: 0.490–0.612) compared with non-alcohol users, and the largest effect was seen for those who met criteria for at-risk drinking or alcohol use disorder (OR = 0.474, 95% CI = 0.408, 0.550; (8). Heavy alcohol use has been associated with self-discontinuation of ART as well (9). Polysubstance use (cocaine or other stimulants, along with heroin) has been particularly associated with suboptimal medication adherence (10–12).

In addition to alcohol and other substance use, cigarette smoking is highly prevalent among PLWH (13, 14) and, in particular among MSM (15, 16). Smoking has been associated with increased health risks among PLWH, including increased cardiac disease, pulmonary infections, and bacterial pneumonias. Further, smoking may be related to increased viral load and progression of HIV disease, due to nicotine's effect on the metabolism of certain antiretroviral medications (17). While some studies have shown that smokers have a higher prevalence of detectable HIV viral load (14, 18–20), overall, research in this area has provided mixed results with regard to the association between cigarette smoking and ART adherence. For example, two studies found no association between smoking status and ART adherence (21, 22), while another found that nicotine dependence (measured by the Fagerstrom Test for Nicotine Dependence [FTND]) was significantly related to suboptimal adherence (23). Thus, there remain open questions about the associations between smoking and HIV medication adherence.

Given the high prevalence of smoking among HIV-infected MSM (15) and the strong association between smoking and heavy alcohol use (24), we sought to examine: (1) the socio-demographic characteristics of cigarette smokers in a sample of heavy episodic drinking HIV-infected MSM participating in a randomized clinical trial, (2) the correlates of current smoking, and, (3) whether cigarette smoking was independently associated with less than perfect adherence among MSM.

METHODS

The data in this manuscript were baseline (pre-randomization) measures from participants who enrolled in a randomized clinical trial that tested a brief motivational intervention to

reduce alcohol use among heavy drinking MSM receiving HIV treatment. The study has been described previously (25). Our sample included the 185 participants who were recruited and enrolled between 2011 and 2015 from an urban community health center.

Participants—To be eligible, participants had to: (1) be at least 18 years of age; (2) drink heavily at least once per month (5 drinks on one occasion) or drink more than 14 drinks per week; (3) have a confirmed HIV diagnosis; (4) be born as and currently self-identify as a male; (5) report having sex (oral or anal) with a male partner in the past 12 months, and, (6) be a currently enrolled patient receiving HIV primary care from the community health center. Participants prescribed ART at the time of study enrollment had to be stable on their current regimen, defined as no change in ART regimen over the three months prior to study enrollment. Participants were excluded if they reported current intravenous drug use (to limit secondary HIV transmission risk outcomes to sexual behavior), or were currently psychotic, suicidal, or manic based on clinical interview. They were also excluded if they were currently being treated, or had been treated in the past three months, for an HIV-related opportunistic infection (i.e., they were medically stable so that the effects of the intervention could be more readily observed), or if they were currently receiving treatment for an alcohol or drug problem. The institutional review boards at the appropriate institutions approved the study.

Procedures—Participants were recruited through flyers posted at the clinic or through active recruitment via study staff during scheduled visits with their HIV care providers. Potential participants completed a brief eligibility screener with a study staff member either in-person or by phone. Those who appeared eligible and interested in participating were invited to participate in an in-person baseline visit. At the baseline visit, participants completed the informed consent process, confirmation screening for eligibility, and the remainder of the baseline interview that consisted of a series of computer-assisted and interviewer-administered questionnaires.

Measures

Sociodemographic variables—Participants self-reported their age, race/ethnicity, income, education, sexual identity, relationship status, and time living with HIV. Race/ethnicity data were examined individually as reported; for analyses, we collapsed non-White participants (those reported as Black, Asian, and/or Hispanic) into a single “MSM of color” variable (with White as the reference group) due to small cell sizes of specific racial/ethnic groups. Blood specimens were obtained at baseline to assess HIV viral load and CD4 T-cell count. A threshold of undetectable viral load was set at 75 copies/mL, and CD4 was categorized into a 3-level variable: less than 200; 200 to 500; and 501 or higher.

ART adherence—A Timeline Follow-back Interview (TLFB) assessed ART adherence over the past 30 days (26). The TLFB has previously demonstrated good test-retest reliability, convergent validity, and agreement with collateral reports for drug abuse (27) and has been widely utilized with substance-using gay, bisexual, and other MSM (28–31). In addition, the TLFB has been previously used to measure HIV medication adherence in

substance-using populations (32, 33), and adherence data collected with TLFB interviews correlates well with HIV biological markers (34).

Consistent with prior studies, interviewers received extensive training in the administration of the TLFB, and demonstrated skills (as evidenced by ongoing quality assurance of audiotapes of the TLFB interviews) in the development of rapport with participants and remaining non-judgmental in order to facilitate honest self-reports and to respect the values and behaviors of all participants. An interviewer asked participants to reflect back on the past 30 days, mark memorable events (e.g., vacations, birthdays, paycheck days, parties) on the calendar as anchor points, and then recall day by day whether or not they had missed any doses of their HIV medications. We dichotomized 30-day ART adherence at greater than (perfect/near perfect) or less than (imperfect) 95% adherence (35).

Smoking variables—Participants were asked whether they smoked cigarettes in the past 30 days, the age at which they smoked their first cigarette, and the age at which they began smoking regularly. Participants were categorized as current smokers if they smoked at least one cigarette in the past 30 days, or non-smokers (those who reported no smoking in the past 30 days).

Substance use variables—The TLFB was used to assess alcohol and illicit drug use in the past 30 days. Using a calendar, interviewers asked participants to report any alcohol or illicit drug use (including marijuana, cocaine, methamphetamine, and nitrates [“poppers”]) on each day for the preceding 30 days. We created a series of aggregate variables for alcohol use: (1) average number of drinking days per week, and (2) average number of drinks per week. We dichotomized the illicit drug use variables as (1) having used in the past 30 days, versus (0) no use in the past 30 days.

Depressive symptoms—Depressive symptoms were assessed with the Center for Epidemiological Studies Depression Scale (CES-D; (36). A sum score was calculated for each participant (Cronbach’s $\alpha = 0.92$), and sum scores of 16 or greater indicated clinically significant depressive symptoms.

Data analysis

Analyses were performed using SPSS version 21. Chi-square tests and t-tests were used to assess statistical significance between socio-demographic, substance use, depressive symptoms, and ART adherence with smoking status. Next, we fit a series of binary logistic regression models to examine associations between relevant covariates and imperfect ART adherence outcome. Finally, we fit a multivariate logistic regression model to examine the associations between smoking and imperfect ART adherence, adjusting for the relevant covariates. Results of regression models are reported as Odds Ratios (ORs) and Adjusted Odds Ratios (aORs) with 95% Confidence Intervals (CIs). The alpha level for significance was set to .05 (two-tailed) for each analysis.

RESULTS

The socio-demographic characteristics of the full sample ($N=185$) and by smoking status are shown in Table 1. In the total sample, 171 (93.4%) participants identified as gay, while 11 (5.9%) identified as bisexual, and 3 (1.6%) responded “other.” Participants ranged in age from 20 to 66 years ($M = 42.2$, $SD = 10.5$) and over one-third identified as a man of color (36.2%, $n = 67$). Nearly one-third of the sample earned less than \$20,000 annually (32.6%, $n = 60$) and more than half of the sample earned less than a Bachelor’s degree (54.1%, $n = 100$). Of the 185 participants, 91 (49.2%) reported having smoked cigarettes in the past 30 days. The age at which participants reported that they smoked their first cigarette ranged from age 4 to 53 ($M=16.4$, $SD=5.9$). Of the 91 participants who reported smoking in the past 30 days, the number of years that participants had smoked regularly ranged from 1 to 40 years ($M = 16.8$, $SD = 11.7$).

At the time of enrollment, 72 participants reported taking tenofovir/emtricitabine/efavirenz and 13 participants were taking tenofovir/emtricitabine/rilpivirine. Thus, in total, 85 (45.9%) participants were taking a single-tablet regimen (STR). Less than one-third of the sample ($n = 55$, 29.7%) reported missing more than two days of ART doses in the past 30 days. Days of missed doses ranged from 0 to 26 ($M = 1.85$, $Mdn = 0.00$, $SD = 3.48$), with 77.3% of participants reporting 0 to 2 days in the last 30 days, indicating perfect/near perfect adherence versus imperfect adherence (more than 2 days of missed doses in the last 30 days). There were no significant differences in level of adherence between those taking a STR and those taking a non-STR regimen. We found that there were no significant associations between level of adherence and CD4 T-cell count, $\chi^2(2, N = 185) = 2.68$, $p = .806$, or adherence and HIV viral load, $\chi^2(2, N = 185) = 0.66$, $p = 0.717$. Among participants who reported imperfect adherence, 10.9% had a detectable viral load (>75 copies/mL) compared with only 7.4% of those who reported perfect/near perfect adherence.

In bivariate analyses comparing smokers to non-smokers, current smokers were significantly more likely to identify as a man of color (45.1% vs. 27.7%), earn less than \$20,000 annually (42.2% vs. 23.4%), have less than a Bachelor’s degree (69.2% vs. 39.4%), report their relationship status as single (71.4% vs. 51.5%), report any illicit drug use in the past 30 days (72.5% vs. 54.3%), report marijuana use in the past 30 days (57.1% vs. 33.0%), and report imperfect ART adherence (37.4.2% vs. 22.3%). Current smokers had significantly higher average number of drinks per week ($M = 27.6$, $SD = 26.0$) compared with non-smokers ($M = 19.2$, $SD = 12.8$). There were no significant differences between current smokers and non-smokers in HIV viral load or CD4 T-cell count.

Correlates of imperfect ART adherence

Table 2 presents bivariate logistic regression models predicting imperfect ART adherence. In bivariate analyses, being a current smoker versus a non-smoker (Odds Ratio [OR] = 2.07, 95% CI: 1.09, 3.95) was associated with imperfect ART adherence. Additionally, identifying as a man of color, earning less than \$20,000 annually, having less than a Bachelor’s degree, reporting any marijuana use, screening positive for depressive symptoms, and reporting a greater average number of drinks per week were also associated with imperfect ART adherence.

Table 2 (column 2) presents the results of the multivariate logistic regression model examining associations between smoking and imperfect ART adherence, adjusting for relevant covariates. In multivariate analyses, there was no significant association between current smoking and imperfect adherence; however, earning less than a Bachelor's degree (Adjusted Odds Ratio [aOR] = 2.51, 95% CI: 1.17, 5.35) was significantly associated with imperfect ART adherence.

DISCUSSION

In this study, we examined the correlates of smoking and whether there was an association between current smoking and ART adherence in a sample of urban heavy drinking HIV-infected MSM engaged in medical care. Consistent with prior studies in PLWH, we found a high prevalence of smoking in this sample. Interestingly, current smoking was significantly associated with imperfect ART adherence in bivariate analyses. However, in multivariable models after adjusting for covariates, no significant associations were found between current smoking and imperfect ART adherence. Others (21, 22) have examined medication adherence and smoking in PLWH, and also have not found an association with ART adherence. It is possible that smoking and imperfect ART adherence share similar risk factors and, perhaps, smoking may be acting as a surrogate marker for these other factors. Many people living with HIV who have access to care may be very adherent with ART (a health promoting behavior), yet engage in other unhealthy behaviors (i.e., smoking, heavy drinking, drug use). As such, people living with HIV may have a hierarchy of health priorities, which is of important clinical relevance and requires further investigation.

We found a greater likelihood of cigarette smoking among men of color, those who were single, and had lower levels of education and annual income. The smokers in our sample tended to engage in more illicit drug use and have heavier weekly alcohol intake. Prior research indicates that structural and socioeconomic conditions, as well as psychosocial factors, that were associated with smoking behavior in our sample are also predictive of imperfect ART adherence. For example, in the SUN study, a large prospective contemporary cohort study of PLWH in the U.S., imperfect adherence was associated with identifying as a person of color, unemployment, recent alcohol or drug use, and being unpartnered (37). Blashill and colleagues examined multiple demographic and clinical indicators related to adherence and concluded that a syndemic of ART non-adherence exists, in that persons with a greater number of poor prognostic indicators, such as substance abuse, mood disorders, and psychiatric illness, had higher odds of suboptimal adherence (38). In fact, those participants with 3–4 syndemic indicators were five times more likely to be non-adherent, while those with five syndemic indicators were 8.5 times more likely to be non-adherent to ART (38). Our data may provide preliminary support that a syndemic related to smoking in HIV-infected MSM exists, in that smokers, compared with nonsmokers, tended to have multiple, inter-related risk factors that could put them at risk for imperfect ART adherence. Improved understanding of the ways in which these factors co-occur and affect health-related behaviors may improve our efforts to reach this group when integrating adherence interventions into clinical settings.

Fewer years of education was the only significant predictor of suboptimal ART adherence in multivariate analyses. Low socioeconomic status has consistently been associated with imperfect ART adherence and detectable HIV viral load (39). Numerous co-morbidities are enhanced by cigarette smoking, substance use, and other poor health behaviors, which are over-represented among those of low socioeconomic status (40). As such, integrated treatment approaches to address co-occurring health conditions, which also attend to social and structural barriers to health care, are warranted to improve the HIV disease trajectories of HIV-infected MSM as well as their overall health status (41).

Previous work has suggested that depressive symptoms are often associated with non-adherence, and evidence illustrates that depressive symptoms may mediate the association between smoking and non-adherence among PLWH (42). Webb and colleagues found, in HIV-infected men and women (in which fewer than one-third of the smokers identified as MSM), that smoking negatively correlated with ART adherence and positively correlated with depressive symptoms; in addition, the relation between smoking and adherence was mediated by depressive symptoms. We did not find a significant association between smoking, imperfect adherence, and depressive symptoms in our sample of heavy drinking MSM, further emphasizing the unique characteristics and issues related to HIV care of MSM.

This study has several limitations. The findings are based on participants who enrolled in an alcohol intervention trial and may not generalize to ART adherence in other populations. Similarly, these data were from an urban sample of heavy drinking HIV-infected MSM recruited from one outpatient clinic in the Northeast U.S. and the findings may not be generalizable geographically. The study sample was relatively small ($N = 185$), which may have limited our ability to detect significant associations. Our sample was two-thirds White and thus may not generalize to other groups with a higher representation of racial/ethnic minorities. We lacked biochemical verification of current smoking status (relying instead on self-report of smoking status); we did not collect carbon monoxide (CO) levels on participants to confirm current smoking. Additionally, we relied on TLFB self-report of ART adherence, which may have been influenced by recall and social desirability biases. The majority of our sample reported near perfect adherence; thus, additional research in MSM is warranted employing objective measures of adherence (e.g., electronic monitoring, dried blood spots [43]).

CONCLUSIONS

Despite these limitations, our findings are novel in that this is the first study to examine smoking and ART adherence in heavy drinking MSM living with HIV. Thus, our findings have the potential to inform the clinical care provided to heavy drinking HIV-infected MSM who smoke cigarettes. Although smoking was not significantly associated with imperfect adherence in multivariable analyses, the smokers in this sample had several prognostic indicators for imperfect adherence. Identifying smokers in HIV clinical practice may be one method of targeting patients who may be at risk for imperfect adherence. Finally, the greatest risk factor for smoking and imperfect ART adherence was low socioeconomic status, in which MSM of color were over-represented. Thus, addressing social and structural

factors, including universal access to ART and substance use/mental health treatment, are necessary to reduce smoking and other health care disparities to improve the health condition of all persons living with HIV.

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Table 1

Characteristics of Study Sample and by Smoking Status (N = 185)

	Total (N = 185)	Current Smoker (n = 91, 49.2%)	Non-Smoker (n = 94, 50.8%)	
	N (%)	N (%)	N (%)	Test Statistic
Race/Ethnicity				$\chi^2(3)=9.46^*$
Latino	32 (17.3)	16 (17.6)	16 (17.0)	
White	118 (63.8)	50 (54.9)	68 (72.3)	
Black	34 (18.4)	24 (26.4)	10 (10.6)	
Asian	1 (0.5)	1 (1.1)	0	
MSM of color	67 (36.2)	41 (45.1)	26 (27.7)	$\chi^2(1)=7.82^{**}$
Annual Income				$\chi^2(1)=7.41^{**}$
Less than \$20,000	60 (32.6)	38 (42.2)	22 (23.4)	
\$20,000 or more	124 (67.4)	52 (57.8)	72 (76.6)	
Educational Attainment				$\chi^2(1)=16.61^{***}$
Less than Bachelor's degree	100 (54.1)	63 (69.2)	37 (39.4)	
Bachelor's degree or higher	85 (45.9)	28 (30.8)	57 (60.6)	
Relationship Status				$\chi^2(1)=8.07^{**}$
Partnered	72 (38.9)	26 (28.6)	46 (48.9)	
Single	113 (61.1)	65 (71.4)	48 (51.1)	
Any Drug Use	117 (63.2)	66 (72.5)	51 (54.3)	$\chi^2(1)=6.64^*$
Any Cocaine Use	36 (19.5)	22 (24.2)	14 (14.9)	n.s.
Any Methamphetamine Use	13 (7.0)	8 (8.8)	5 (5.3)	n.s.
Any Popper Use	31 (16.8)	12 (13.2)	19 (20.2)	n.s.
Any Marijuana Use	83 (44.9)	52 (57.1)	31 (33.0)	$\chi^2(1)=10.92^{**}$
Depressive Symptoms (CES-D 16)	95 (51.4)	52 (57.1)	43 (45.7)	n.s.
Less than 95% ART Adherence	55 (29.7)	34 (37.4)	21 (22.3)	$\chi^2(1)=4.99^*$
Detectable HIV Viral Load	21 (11.4)	10 (11.0)	11 (11.7)	n.s.
CD4 T-cell Count				n.s.
Less than 200	41 (22.2)	22 (24.2)	19 (20.2)	
200–500	103 (55.7)	53 (58.2)	50 (53.2)	
500 and higher	41 (22.2)	16 (17.6)	25 (26.6)	
	M (SD)	M (SD)	M (SD)	Test Statistic
Age	42.2 (10.5)	41.6 (10.3)	42.7 (10.6)	n.s.
Time Living with HIV (months)	88.1 (76.9)	86.7 (74.4)	89.2 (79.3)	n.s.
Age of Smoking Initiation	16.4 (5.9)	16.1 (6.7)	16.9 (4.5)	n.s.
Average number of drinks per week	23.3 (20.8)	27.6 (26.0)	19.2 (12.8)	$t(130.25)=2.76^{**}$
Number of drinking days per week	4.1 (2.1)	4.1 (2.4)	4.1 (1.9)	n.s.

Note: MSM of color refers to Black, Asian, and/or Hispanic participants.

 $p < 0.001$;

**

 $p < 0.01$;

*

 $p < 0.05$; n.s.= nonsignificant

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Table 2

Correlates of imperfect adherence among a sample of heavy drinking HIV-infected MSM (N = 185)

	OR	95% CI	aOR	95% CI
<i>MSM of color</i>	2.36 [*]	1.18, 4.70	1.69	0.79, 3.60
<i>Less than \$20,000 annually</i>	2.00 [*]	1.04, 3.96	--	--
<i>Less than a Bachelor' degree</i>	3.11 ^{**}	1.57, 6.18	2.51 [*]	1.17, 5.35
<i>In a Relationship</i>	0.96	0.50, 1.83	--	--
<i>Current Cigarette Smoking</i>	2.07 [*]	1.09, 3.95	1.36	0.66, 2.80
<i>Any Drug Use</i>	1.02	0.53, 1.97	--	--
<i>Any Cocaine Use</i>	1.68	0.78, 3.59	--	--
<i>Any Methamphetamine Use</i>	2.15	0.69, 6.73	--	--
<i>Any Popper Use</i>	1.11	0.50, 2.45	--	--
<i>Any Marijuana Use</i>	1.27 [*]	1.01, 2.40	0.77	0.37, 1.58
<i>Age</i>	1.01	0.98, 1.04	1.02	0.99, 1.05
<i>Time living with HIV (months)</i>	1.00	0.99, 1.01	--	--
<i>Age of Smoking Initiation</i>	0.94	0.88, 1.01	--	--
<i>Depressive Symptoms</i>	2.94 [*]	1.07, 3.91	1.85	0.92, 3.70
<i>Average number of drinks per week</i>	1.02 [*]	1.01, 1.04	1.02	0.99, 1.03
<i>Number of drinking days per week</i>	1.01	0.87, 1.17	--	--

Note: MSM of color refers to Black, Asian, and/or Hispanic participants OR=Odds Ratio from a logistic regression with only one independent variable in the model. aOR=Adjusted Odds Ratio from a multiple logistic regression model including the seven variables that showed significant associations with adherence in the bivariate models;

p<0.001;

**
p<0.01;

*
p<0.05