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Tobacco Use and HIV Symptom Severity in Chinese People Living with HIV

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Abstract

Exposure to nicotine among people living with HIV (PLWH) may impact physical health as indicated by experienced symptoms. Yet, the empirical evidence documenting the relations between tobacco use and symptom experiences among PLWH remains limited. This study aims to assess the relationships between tobacco use and HIV symptoms through a cross-sectional survey conducted in Beijing and Shanghai. The WHO ASSIST screening test was used for frequency of tobacco use. Sixty-four items from the revised signs and symptoms checklist for persons with HIV disease (SSC-HIVrev) were used. “Total number of symptoms” was created by summing all the binary coded and “Maximal symptom severity” was created by taking the maximal severity level across all symptoms for each participant. After controlling for confounding variables, tobacco use was not associated with the total number of symptom, yet was associated with the maximal symptom severity. This study documents the link between tobacco use and experienced symptoms among PLWH by demonstrating that higher frequency of tobacco use is associated with greater odds of reporting more severe symptoms. Smoking cessation strategies should be integrated into symptom management interventions for PLWH to optimize their effectiveness.

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Conflict of Interest Statement

No conflicts of interest have been declared by the authors.

INTRODUCTION

People living with HIV (PLWH) present with two to three times the tobacco use of the general population (Chang, Lim, Lau, & Alicata, 2017), and tobacco-using PLWH experience greater levels of HIV-related symptoms, lower social support, and increased nicotine reliance (Savin, Frank-Pearce, Pulvers, & Vidrine, 2018). Moreover, use of these substances is associated with more chronic pain, insomnia, constipation, depression, anxiety, and other substance use among PLWH (Perry et al., 2013).

Globally, over 33% of the world's tobacco smokers are located in China (Eriksen, Mackay, Schluger, Islami, & Drope, 2015) where there are an estimated 300 million tobacco users with 52.9% of men and 2.4% of women being smokers (Schwartlander & Pratt, 2015), and a 52% smoking rate among PLWH (Wang et al., 2016). Among men who have sex with men in China, one study suggested that nearly two thirds are smokers (Berg et al., 2011).

As HIV has become a chronic disease with the advent of antiretroviral therapy (ART), chronic disease symptoms associated with aging are increasingly reported (Frain et al., 2014; Iribarren et al., 2018). Symptoms including pain, sleep disturbance and low quality of life have been reported (de Souza et al., 2018; Scott et al., 2018), along with frequent presentation of chronic respiratory diseases including asthma (Kirenga et al., 2018), lung cancer, COPD, and TB, which causes spirometric restriction (Meghji et al., 2016).

Literature investigating impact of smoking on PLWH's wellbeing is emerging, such as reports of depression, anxiety and stress in HIV-positive smokers (Berg et al., 2014; Kee et al., 2015). Recent studies show that PLWH smokers have more and worse neurocognitive disorders compared to non-smoking PLWH (Benevides, Filho, Debona, Bergamaschi, & Nunes, 2017; Chang et al., 2017) along with common reports of peripheral neuropathy (Saylor et al., 2017). Paradoxically, to cope with experienced symptoms, especially pain, PLWH often turn to using tobacco and other substances (Gardner et al., 2016; Newshan & Staats, 2013). However, existing studies mainly focus on individual symptoms rather than evaluating symptomology of PLWH as a whole. Therefore, this study aims to assess the relationships between tobacco use and broad symptom experience and severity among Chinese PLWH.

METHODS

Sample, Settings, and Procedures

169 HIV-positive individuals were recruited from two leading infectious disease hospitals in China in two waves, from 2009–2010 and 2014–2016. Participants completed Audio Computer-Assisted Self-Interview questionnaires, and met inclusion criteria of (a) being 18 years or older, (b) HIV seropositive, and (c) receiving care at the hospitals. Study procedures were approved by ethics review boards of institutions involved.

Measures

Demographic and Clinical Factors—Demographics included sex, age, education, and income. Clinical factors included years living with HIV, AIDS diagnosis, most recent CD4 levels, and ART status.

Tobacco, alcohol, and drug use were captured by a 10-item scale adapted from the WHO ASSIST screening (Lightfoot et al., 2005). Participants rate use over the past week from 0 (never) to 8 (more than once a day). We dichotomized all substances other than tobacco and alcohol to 0 (never) and 1 (any use in the previous week), and summarized across the eight drugs.

Symptom Checklist—Sixty-four items that can be experienced by either gender were selected from the Revised Sign and Symptom Checklist (Holzemer, Henry, Portillo, & Miramontes, 2000; Holzemer, Hudson, Kirksey, Hamilton, & Bakken, 2001). SSC-HIVrev (Cronbach's alpha=0.97) asks respondents to rate intensity of each symptom experienced that day (no/not at all: 0; mild: 1; moderate: 2; or severe: 3). Two variables were derived: "total number of symptoms" sums up the binary coded symptoms (0: not at all/no experience; 1: any severity) resulting in a range of 0 to 64, and "maximal symptom severity" is taken across all symptoms for each participant (no/not at all: 0; mild: 1; moderate: 2; or severe: 3).

Analysis

Univariate statistics were computed to obtain overall characteristics of the sample and distributions of all variables. Negative binomial models and ordered logit models were used for count and ordinal outcomes respectively. We adopted a step-wise approach to demonstrate how the relationships between tobacco use and outcomes change after additional variables (alcohol and drug use, demographic, and clinical factors) were entered into the model. The likelihood-ratio test for negative binomial models and the Brant test for ordered logit models were conducted to test violation of model assumptions. Model-adjusted marginal probabilities of outcomes with regard to tobacco use were calculated for data visualization. Finally, the cluster-robust estimator was used for statistical inference to handle the data structure. Study sites were also entered into the model as fixed effects. Statistical procedures were conducted in Stata15.

RESULTS

Table 1 summarizes the sample's demographic and clinical characteristics. During the past week, 51% of this sample of PLWH had used tobacco at least once, and on average they used tobacco for nearly two days a week. In contrast, this sample used alcohol only 0.5 times per day, and 0.38 types of drugs. On average, participants complained of more than 17 unpleasant symptoms (SD = 16.35) and 42 (25%) stated that these symptoms were severe enough to affect them in daily living.

For descriptive analyses, we present the 20 most frequent and severe symptoms in Table 2. Tables 3 and 4 summarize the model-fitting results for the two outcomes: total number of symptoms and maximal severity of symptoms, respectively. Table 3 shows that tobacco use

was not associated with the number of reported symptoms, even in Model 1 (a.IRR = 1.043, 95% CI: 0.975–1.116, $p > 0.1$) where only study sites were controlled for. In contrast, Table 4 shows that the significant relationship between tobacco use and maximal severity of symptoms remained similar across all three models regardless of which confounding factors were controlled for. In fact, in Model 3 (the full model) it was tobacco use (a.OR=1.072; 95% CI: 1.053–1.092; $p < 0.01$) but not the use of alcohol (a.OR=1.038; 95% CI: 0.865–1.246; $p > 0.10$) or drugs (a.OR=1.055; 95% CI: 0.874–1.274; $p > 0.10$) that was significantly associated with maximal severity of symptoms. A one-unit increase in tobacco use (smoking one more day during the previous week) increased odds of going up one severity category by 7.2%. Other associated variables included income (just enough vs. not enough: a.OR=0.336; 95% CI: 0.238–0.475; $p < 0.01$; more than enough vs. not enough: a.OR=0.380; 95% CI: 0.208–0.696; $p < 0.01$) and CD4 levels (a.OR=0.950; 95% CI: 0.933–0.967; $p < 0.01$).

Given model-fitting results, we plotted model-adjusted, marginal relations between tobacco use and probabilities of maximal symptom severity. As illustrated in Figure 1, while probability of reporting moderate symptoms remained stable across levels of tobacco use, with increasing tobacco use, probability of reporting severe symptoms increased and probabilities of reporting no or mild symptoms decreased.

DISCUSSION

We examined relations between tobacco use and experience of HIV-related symptom among Chinese PLWH and found that use of tobacco in the previous week was not related to current numbers of symptoms but was associated with the maximal severity symptoms. Moreover, this association appeared to have dosage-effect: when PLWH smoked one more day per week, the odds of reporting greater symptom severity increased by 7.2%.

Although a study of a large sample of PLWH in France identified three groups of PLWH with varying numbers of “bothersome symptoms” and found that those PLWH who smoked were significantly less likely to belong to the “low number of bothersome symptoms” group (Mary-Krause et al., 2014), the present study did not replicate an association between tobacco use and total number of symptoms. This discrepancy may be due to the fact that we aggregated all the symptoms together regardless of their severity, which may have attenuated true relations as there were many reported mild symptoms as well as symptoms that might arise from diverse mechanisms.

On the other hand, we found a dosage effect of tobacco use on participants’ reported maximal severity of symptoms, suggesting that greater frequency of tobacco use was associated with higher probability of reporting more severe symptoms. One possible attribution is the shared mechanisms through which tobacco use impacts pain experiences which has been well documented, including evidence that tobacco use is a risk factor for onset and progression of chronic pain, which in turn often further motivates individuals to use tobacco for pain management (Jakobsson, 2008). Therefore, it is possible that tobacco use may sensitize PLWH to pain and magnify their painful experiences associated with HIV symptoms.

Limitations

Limitations of the study include its cross-sectional nature limiting casual inference, and data collection from two major cities, potentially limiting generalizability. Additionally, we did not divide the study sample by gender. As we know, women may have different symptom experiences than men including a much lower tobacco using rate. Therefore, future studies should conduct stratified analysis to evaluate relationships between tobacco use and symptom experience by gender.

Despite these limitations, our findings demonstrate a relationship between tobacco use and symptom severity among PLWH in China, suggesting potential utility of future research to examine utility of healthcare providers offering smoking cessation resources to HIV-positive tobacco users in order to increase efficacy of HIV symptom management.

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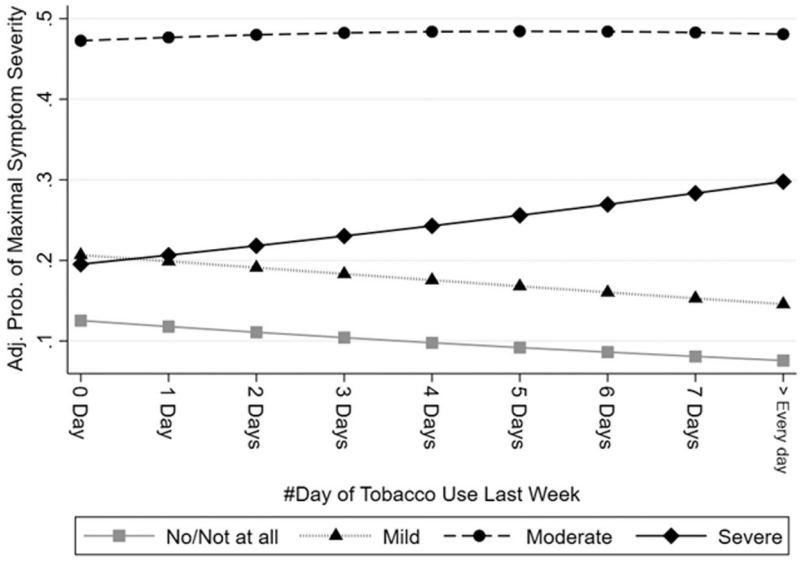

Figure 1:
Number of Days of the Tobacco Use and Maximal Symptom Severity

Table 1:

Sample Characteristics and Univariate Analysis

Variables	Mean or N	SD or %
Tobacco Use (mean, SD)	1.95	3.19
Alcohol Use (mean, SD)	0.50	1.63
Drug Use (mean, SD)	0.38	1.02
# of total symptoms (mean, SD)	17.27	16.35
Maximal symptom severity (n, %)		
No/Not at all	24	14.20
Mild	31	18.34
Moderate	72	42.60
Severe	42	24.85
Demographic Factors		
Birth Sex (n, %)		
Male	111	65.68
Female	58	34.32
Age (mean, SD)	39.48	10.31
Education (n, %)		
< College	111	65.68
≥ College	58	34.32
Income (n, %)		
Not enough	68	40.24
Just enough	75	44.38
More than enough	26	15.38
Clinical Factors		
Year with HIV (mean, SD)	5.31	3.97
AIDS Diagnosis (n, %)		
Ever	27	15.98
Never	142	84.02
CD4 Level[a] (mean, SD)	3.70	7.82
HIV Medication (n, %)		
Currently on	140	82.84
Not currently on	29	17.16
Study sites[b]		
2012 Study	107	63.31
2015 Study	62	36.69

[a] CD4 value was divided by 100;

[b] 2012 study was conducted in Shanghai SPHCC and 2015 study was conducted at SPHCC and Ditan Hospital in Beijing.

Table 2:

Top 20 of the Most Reported Symptoms and the Most Severe Symptoms Among Reported

	Most Reported Symptoms		Most Severe Symptoms Among Reported		
	Symptoms	**% of Sample Reported**	**Symptoms**	**% of Sample Reported**	**Average Severity[a]**
1	Fatigue	65.09%	Rash	20.12%	1.588
2	Dry mouth	53.25%	Skinny arms	20.12%	1.559
3	Thirstiness	53.25%	Concern over weight loss	32.54%	1.545
4	Weakness	52.66%	Thirstiness	53.25%	1.522
5	Fear/Worry	49.11%	Difficulty concentrating	46.15%	1.513
6	Difficulty concentrating	46.15%	Insomnia	43.20%	1.493
7	Muscle ache	43.20%	Weakness	52.66%	1.483
8	Insomnia	43.20%	Fear/worry	49.11%	1.482
9	Anxiety	43.20%	Depression	36.09%	1.475
10	Gas/bloating	40.83%	Fatigue	65.09%	1.473
11	Painful join	39.64%	Dry mouth	53.25%	1.467
12	Memory loss	39.64%	Swollen glands	21.89%	1.459
13	Dizziness	39.64%	Anxiety	43.20%	1.411
14	Itchy skin	39.05%	Tingling of arms	26.04%	1.409
15	Loose stool	37.28%	Tingling of legs	21.89%	1.405
16	Depression	36.09%	Flushing	19.53%	1.394
17	Coughing	34.32%	Tingling of feet	21.30%	1.389
18	Lack of appetite	33.73%	Lack of appetite	33.73%	1.386
19	Blurred vision	33.14%	Swollen feet	12.43%	1.381
20	Concern over weight loss	32.54%	Itchy skin	39.05%	1.379

[a]. 1: Mild; 2: Moderate; 3: Severe

Table 3:

Results of Multivariable Negative Binomial Regression Models With Total Number of Symptoms as the Outcome (N = 169)

	Total Number of Symptoms (Negative Binomial Regression)					
	Model 1		Model 2		Model 3	
	a.IRR[a]	95% CI	a.IRR[a]	95% CI	a.IRR[a]	95% CI
Tobacco Use	1.043	(0.975-1.116)	1.026	(0.954-1.103)	1.032	(0.939-1.133)
Alcohol Use			1.034	(0.934-1.144)	1.024	(0.915-1.147)
Stimulant Use			1.163**	(1.105-1.223)	1.113†	(0.980-1.264)
Demographic Factors						
Female (vs. Male)					0.977	(0.729-1.309)
Age					1.007	(0.998-1.016)
≥ College (vs. < College)					1.566	(0.781-3.139)
Income						
Just enough (vs. not enough)					0.645**	(0.586-0.709)
More than enough (vs. not enough)					0.601**	(0.468-0.772)
Clinical Factors						
Years with HIV					0.998**	(0.997-0.999)
AIDS Diagnosis					1.018	(0.928-1.116)
CD4 Levels					0.943**	(0.925-0.961)
On HIV Medication (vs. not on med)					0.798	(0.363-1.754)
Study waves	5.416**	(5.117-5.731)	5.036**	(4.81-5.273)	4.640**	(4.151-5.187)
Constant	4.140**	(3.748-4.573)	4.096**	(3.533-4.75)	5.334**	(3.103-9.168)

Model 1: Simple regression with control of study site; Model 2: Regression with control of alcohol and drug use and study site; Model 3: Regression with full control;

[a]IRR: model-adjusted Incident Rate Ratio;

†< 0.1;

*< 0.05;

**< 0.01

Table 4:

Results of Multivariable Ordinal Logistic Regression Models with Maximal Symptom Severity as the Outcome (N = 169)

	Maximal Severity of Symptoms (Ordinal Logistic Regression)					
	Model 1		Model 2		Model 3	
	a.OR[a]	95% CI	a.OR[a]	95% CI	a.OR[a]	95% CI
Tobacco Use	1.083**	(1.078-1.087)	1.071**	(1.07-1.072)	1.072**	(1.053-1.092)
Alcohol Use			1.024	(0.917-1.145)	1.038	(0.865-1.246)
Drug Use			1.139*	(1.004-1.293)	1.055	(0.874-1.274)
Demographic Factors						
Female (vs. Male)					1.000	(0.463-2.16)
Age					1.004	(0.992-1.017)
≥ College (vs. < College)					1.733†	(0.949-3.165)
Income						
Just enough (vs. not enough)					0.336**	(0.238-0.475)
More than enough (vs. not enough)					0.380**	(0.208-0.696)
Clinical Factors						
Year with HIV					1.016	(0.966-1.068)
AIDS Diagnosis					0.770	(0.558-1.062)
CD4 Level					0.950**	(0.933-0.967)
On HIV Medication (vs. not on med)					0.509	(0.166-1.562)
Study waves	2.78**	(1.966-3.931)	2.663**	(1.917-3.7)	2.610**	(2.219-3.069)

Model 1: Simple regression with control of study site; Model 2: Regression with control of alcohol and drug use and study site; Model 3: Regression with full control;

[a]. a.OR: model-adjusted Odds Ratio;

† < 0.1;

* < 0.05;

** < 0.01