# A Cross-Sectional Analysis of Tobacco Use and Concurrent Alcohol and Substance Use Among Patients Living with HIV/HCV Co-infection: Findings from a Large Urban Tertiary Center

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## Abstract

This study aimed to assess the prevalence of and factors associated with tobacco use among patients living with HIV/HCV co-infection. Patient reported outcomes (PROs) were analyzed of patients living with HIV/HCV co-infection ($n = 313$) who presented for clinical evaluation and treatment of HCV between 2013 and 2017 at a university-affiliated HIV/HCV Co-infection Clinic. The prevalence of tobacco use in patients living with HIV/HCV co-infection was 48%. Compared to non-smokers, a higher proportion of tobacco smokers had substance use disorders and concurrent alcohol and substance use. In the multivariate analysis, concurrent alcohol and substance use was positively associated with tobacco use. The findings suggest clinical interventions are urgently needed to reduce tobacco use among patients living with HIV/HCV co-infection—a doubly-vulnerable immunocompromised population. Otherwise, failed efforts to dedicate resources and targeted behavioral interventions for this respective population will inhibit survival—especially considering the recent and evolving COVID-19 pandemic.

**Keywords** HIV · HCV · Tobacco · Smoking · Alcohol use · Substance use

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# Introduction

Although tobacco use has declined over the past 50 years (National Center for Chronic Disease Prevention and Health Promotion (US), 2014), it continues to be the leading preventable cause of morbidity and mortality in the United States (U.S.), accounting for over 480,000 annual deaths. The existing evidence indicates that tobacco use has adverse health effects on almost all parts of the human body (National Center for Chronic Disease Prevention and Health Promotion (US), 2010, 2014), yet 14% (34.2 million) of adults ≥ 18 years old (16% males; 12% females) were current cigarette smokers in 2018 (Creamer et al., 2019). Thus, while it has been established that tobacco use causes chronic diseases such as cardiovascular diseases (CVD), cancer, and chronic obstructive pulmonary disease (COPD) (National Center for Chronic Disease Prevention and Health Promotion (US), 2010, 2014), increasing evidence indicates that it worsens disease progression of several infectious diseases—in particular human immunodeficiency virus (HIV) and hepatitis C virus (HCV) (Bean, Richey, Williams, Wahlquist, & Kilby, 2016; Helleberg et al., 2013; Nahvi & Cooperman, 2009; Tesoriero, Gieryic, Carrascal, & Lavigne, 2010).

Tobacco use in patients living with HIV exacerbates the natural history of HIV by negatively affecting both innate and adaptive immune responses (e.g. T helper cells, CD4 regulatory T cells, dendritic cells, macrophages, and natural killer cells) (Arnson, Shoenfeld, & Amital, 2010; Calvo, Laguno, Martínez, & Martínez, 2015; Feldman & Anderson, 2013; Steel et al., 2018; Strzelak, Ratajczak, Adamiec, & Feleszko, 2018). Not only does tobacco use alter and hinder immune and virological responses in patients living with HIV, it increases susceptibility to acquisition and development of opportunistic infections and medical conditions—including *among* patients living with HIV who are actively receiving antiretroviral therapy (ART) (Petrosillo & Cicalini, 2013; Rahmanian et al., 2011). In particular, tobacco use in patients living with HIV increases the risk for lower respiratory tract infections, bacterial pneumonia, chronic obstructive pulmonary disease COPD, cardiovascular disease, and various types of malignancies (Petrosillo & Cicalini, 2013; Rahmanian et al., 2011). Consequently, tobacco use has emerged as a leading cause of death in patients living with HIV (Shuter, Kim, An, & Abroms, 2018). It is estimated that patients living with HIV who are actively receiving ART will lose more years of life due to smoking than due to HIV (5.1 years lost to HIV; whereas, 12.3 years lost to smoking) (Cropsey et al., 2016; Helleberg et al., 2013). Despite the synergistic effects of tobacco use and HIV infection, prevalence estimates of tobacco use in the U.S.

in patients living with HIV are three times higher than the general population (50–70% vs. 15–20%) (Bhatta, Subedi, & Sharma, 2018; Rahmanian et al., 2011).

Similarly, the most recent epidemiologic study estimated that the prevalence of tobacco use in those living with *HCV* (62%) is three times higher than the general population (Kim et al., 2018). Although literature that characterizes the negative effects of tobacco use in patients living with HCV is not as well established as HIV literature, tobacco use also worsens the natural history of HCV (Zhao, Li, & Taylor, 2013). Tobacco use in patients living with HCV is associated with a heightened risk for pulmonary disease, elevated liver enzymes (i.e. ALT), and acceleration of disease progression to advanced stages of liver fibrosis and liver cancer (Gartner, Miller, & Bonevski, 2017; Hézode et al., 2003; Pessione et al., 2001; Shuter et al., 2016; Zhao et al., 2013).

More than a third of patients living HIV in the U.S. are living with HCV co-infection (HIV/HCV) (Easterbrook, Sands, & Harmanci, 2012; Koziel & Peters, 2007; Taylor, Swan, & Mayer, 2012). Due to the synergistic effects of HIV and HCV, patients living with HIV/HCV co-infection have greater risks of both HCV and HIV-associated morbidity and mortality compared to patients with HIV or HCV mono-infection (Bosh et al., 2018; Konopnicki et al., 2005; Re et al., 2014; Teira & VACH Study Group, 2013; Thein, Yi, Dore, & Krahn, 2008). Tobacco use further amplifies pathophysiological synergistic effects of HIV/HCV co-infection, and tobacco use compromises HIV-associated wellness and liver wellness, and survival. Surprisingly and to date, no study has estimated the prevalence of tobacco use in patients living with HIV/HCV co-infection. Empirical data that fills this respective knowledge gap would be advantageous for behavioral health (i.e. clinical psychologists, clinical social workers, psychiatrists, addiction specialists) and public health professionals and liver and infectious disease specialists who provide public health and clinical services to patients living with HIV/HCV co-infection. Therefore, this study aimed to assess the prevalence of and factors associated with tobacco use among patients living with HCV/HIV co-infection.

# Methods

## Study Design

This study retrospectively collected and analyzed patient-reported outcomes (PROs) and electronic medical record data of patients living with HIV/HCV co-infection ($n = 313$) who were receiving ART and in clinical care at the University of Alabama at Birmingham's HIV Clinic from 2015 to 2017. The HIV Clinic provides primary and sub-speciality care to patients living with HIV. When ready for or

considering HCV treatment, patients living with HIV/HCV co-infection who received primary care at the HIV Clinic are referred to the HIV/HCV Co-infection Clinic (located within the HIV Clinic). At each clinic visit, patients complete computerized PROs (i.e. validated psychometric scales) on touch-screen tablets. For this study, PROs and electronic medical records data from patients' first visit with the HIV/HCV Co-infection Clinic were collected and analyzed. The psychometric scales used by the clinic and included in this study are from the Patient-Reported Outcomes Measurement Information System (PROMIS) (National Institutes of Health, 2019). This study was approved by the institutional review board at University of Alabama at Birmingham.

## Outcomes

The main outcomes of interest were prevalence of tobacco use and factors independently associated with tobacco use among patients living with HIV/HCV co-infection. Two questions from a smoking questionnaire were used (1) to dichotomize patients with and without tobacco use: "Do you currently smoke cigarettes?", and (2) to assess the number of cigarettes smoked per day: "How many packs of cigarettes do you smoke a day?" (e.g. less than a pack a day, half a pack to 1 a day, between 1 and 2 packs a day, more than 2 packs a day).

## Variables

### Demographics, Medical Conditions, and Laboratory Values

Data on age, self-reported sex and racial *identity*, insurance status, HCV and liver-related characteristics, HIV-related characteristics, other medical conditions, and laboratory values were extracted from electronic medical records.

### Psychiatric, Alcohol, and Substance Use Disorders

Psychiatric, alcohol, and substance use disorders were extracted from electronic medical records.

### Alcohol and Substance Use

Two questions from the Alcohol Use Disorders Identification Test (AUDIT-C) (Bradley et al., 1998; Bush, Kivlahan, McDonell, Fihn, & Bradley, 1998) were used to identify patients with current alcohol use and their amount of use. The following question was used to dichotomize patients who were current users of alcohol and those who were abstainers: "How often do you have a drink containing alcohol (during the past 12 months)?" Patients who endorsed "never" were defined as abstainers of alcohol and those who endorsed "any usage" (e.g. monthly or less,

2–4 times a month, 2–3 times a week, 4–5 times a week, or 6–7 times a week) were defined as current users of alcohol. The Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) (Newcombe, Humeniuk, & Ali, 2005) was used to identify patients with current substance use. Specifically, the ASSIST assesses current usage of the following illicit substances in the past 3 months: cocaine, amphetamines, street opiates, hallucinogens, inhalants, and non-medical use of cannabis, sedatives or sleeping pills, and prescription stimulants. Patients who endorsed any substance use in the past 3 months were defined as current substance users. Patients who simultaneously endorsed alcohol and substance use on both the AUDIT-C and ASSIST were defined as concurrent users of alcohol and substances.

### Depression

Depression was assessed with a 9-item, 4-point Likert scale—The Patient Health Questionnaire (PHQ-9) (Kroenke, Spitzer, & Williams, 2001). The PHQ-9 assesses severity of symptoms of depression. Total scores of 5–9, 10–14, 15–19, and $\geq 20$ represent mild, moderate, moderately severe, and severe depression, respectively.

### Anxiety

Anxiety was assessed with a 4-item, 4-point Likert scale—The Patients Health Questionnaire-4 (PHQ-4) (Kroenke et al., 2001). Total scores of 0–2, 3–5, 6–8, and 9–12 represent normal, mild, moderate, and severe anxiety, respectively.

### Health-Related Quality of Life

The European Quality of Life Five Dimensions (EQ-5D-3L) (Rabin & de Charro, 2001) instrument was used to measure patients' health-related quality of life. The EQ-5D-3L is composed of two sections: a set of five questions and a visual analogue scale. This study only analyzed the five health-related quality of life questions. The scale assesses health-related quality of life in five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each question uses a 3-point scale: no problems, some or moderate problems, extreme problems. The US population-based EQ-5D index scoring algorithm (U.S. Department of Health & Human Services, 2015) was used to calculate each patients' EQ index score (i.e. quality of life score). For EQ index scores ranging from 0 to 1, 0 represents worst imaginable health and 1 represents best imaginable health.

## Statistical Analysis

Measures of central tendency were used to characterize the sample. Chi-square and the independent samples *t*-test were used to compare patients with and without tobacco use on dichotomous and continuous variables. Binomial logistic regression was used to identify factors that were independently associated with tobacco use. Analyses were run to avoid multicollinearity in the binomial logistic regression model. Statistical analyses were conducted using IBM Corp. Released 2016. SPSS Statistics for Windows, Version 24.0 Armonk, NY: IBM Corp.

## Results

The mean age of the sample was $53 \pm 11.1$ years, and the majority of patients were African American (56%) and insured (88%) (Table 1). Patients were aware of their HCV diagnosis for $7 \pm 7.3$ years, the majority were HCV treatment naïve (i.e. had not ever received treatment for HCV) (88%), and a minority of patients had cirrhosis (13%) and hepatitis B virus (HBV) (3%). Patients were aware of their HIV diagnosis for $14 \pm 9.3$ years. All patients were actively receiving ART, and patients were on an ART regimen for $11 \pm 7.2$ years.

**Table 1** Sample characteristics

| Variables | Frequency/M, (SD) |
| --- | --- |
| $N = 313$ | |
| Demographics | |
| Age | $52.5 \pm 11.06$ |
| Sex | |
| Female | 77 (25%) |
| Male | 234 (75%) |
| Self-reported race | |
| African American | 174 (56)% |
| White American | 139 (44%) |
| Insured | 273 (87%) |
| HCV characteristics | |
| Number of years aware of HCV diagnosis | $7.42 \pm 7.31$ |
| HCV treatment naïve | 274 (88%) |
| Cirrhosis | 41 (13%) |
| Hepatitis B virus (HBV) | 9 (3%) |
| HIV characteristics | |
| Number of years aware of HIV diagnosis | $13.77 \pm 9.32$ |
| Currently on ART | 313 (100%) |
| Number of years on ART | $11.26 \pm 7.18$ |
| Tobacco use | |
| Smoked cigarettes | 160 (49%) |

The prevalence of tobacco use in patients living with HIV/HCV co-infection was 48%. Of those who reported the number of cigarettes smoked per day, 47% and 36% smoked $\frac{1}{2} - 1$ and 1–2 packs of cigarettes per day, respectively. Compared to those without tobacco use, a higher proportion of those with tobacco use had substance use disorders (29% vs. 44%, $p = 0.00$), and concurrent alcohol and substance use (21% vs. 40%, $p = 0.000$) (Table 2). Patients with and without tobacco use did not differ in any other clinical characteristic.

In the multivariate analysis, concurrent alcohol and substance use (OR 3.059, $p = 0.011$) was positively associated with tobacco use (Table 3).

## Discussion

This study utilized outpatient electronic medical record data obtained from a large urban tertiary center to assess prevalence of and factors associated with tobacco use in patients living with HIV/HCV co-infection. Several notable findings emerged from this study. First, the prevalence of tobacco use in patients with HIV/HCV co-infection was 48%, and this rate is significantly higher than the national rate (14%) (Creamer et al., 2019). This finding is quite alarming considering the many ways in which tobacco use further amplifies pathophysiological effects of both HIV and HCV. Tobacco use alone in those without HIV or HCV shortens life expectancy by 10 years (Jha et al., 2013), and it is probable that tobacco use in patients with HIV/HCV co-infection further reduces life expectancy. The findings suggest that there is a need for clinical and public health efforts to reduce tobacco use among this doubly-vulnerable immunocompromised population. Otherwise, failed efforts to dedicate resources and targeted interventions for this respective population will inhibit patient survival and achievement of the U.S. Department of Health and Human Services' national public health goal of reducing and eliminating health disparities and improving the health of all groups as outlined in *Healthy People 2020* (Promotion, 2020).

Second, those with concurrent alcohol and substance use were 3.06 times more likely to use tobacco. It has been previously demonstrated that alcohol and substance use in general facilitates uptake of tobacco use (Barrett, Darredeau, & Pihl, 2006; Cohn et al., 2018) and use is positively associated with tobacco use in patients living with HIV mono-infection (Humfleet et al., 2009). Though not well-established in the HIV/HCV co-infection literature, findings from the present study suggest concurrent alcohol and substance use considerably increases the odds of tobacco use in patients living with HIV/HCV co-infection. This finding is alarming as well because these multiple agents working in concert (e.g. HIV, HCV, ethanol, and nicotine) exponentially increases the

**Table 2** Bivariate comparisons of patients living with HIV/HCV co-infection with and without tobacco use

| Variables | Sample | With tobacco use | Without tobacco use | *p*-value |
|---|---|---|---|---|
| *N* = 313 | | 160 (49%) | 167 (51%) | |
| Demographics | | | | ns |
| Age | 52.5 ± 11.06 | 51.68 ± 10.99 | 53.29 ± 11.10 | ns |
| Sex | | | | ns |
| Female | 77 (25%) | 42 (27%) | 35 (22%) | |
| Male | 234 (75%) | 113 (73%) | 121 (78%) | |
| Self-reported race | | | | ns |
| African American | 174 (56%) | 82 (53%) | 92 (58%) | |
| White American | 139 (44%) | 73 (47%) | 66 (42%) | |
| Insured | 273 (87)% | 138 (95%) | 135 (94%) | ns |
| HCV/liver-related characteristics | | | | |
| HCV treatment naïve | 274 (88%) | 137 (88)% | 137 (87%) | ns |
| Years aware of HCV diagnosis | 7.42 ± 7.31 | 7.31 ± 7.57 | 7.53 ± 7.07 | ns |
| Alanine transaminase (ALT) | 38.27 ± 33.53 | 39.19 ± 36.10 | 37.35 ± 30.86 | ns |
| Hepatitis B virus (HBV) | 9 (3%) | 5 (3%) | 4 (3%) | ns |
| Cirrhosis | 41 (13)% | 21 (14%) | 20 (13%) | ns |
| End stage liver disease | 6 (2%) | 4, (3%) | 2 (1%) | ns |
| HIV characteristics | | | | |
| Years aware of HIV diagnosis | 13.77 ± 9.32 | 12.85 ± 9.22 | 14.67 ± 9.36 | ns |
| Years on ART | 11.26 ± 7.18 | 10.51 ± 6.75 | 12.00 ± 7.53 | ns |
| HIV viral load | | | | ns |
| Detectable | 97 (32%) | 44 (29%) | 53 (34%) | |
| Undetectable | 210 (68%) | 107 (71%) | 103 (66%) | |
| Other medical conditions | | | | |
| Diabetes | 19 (6%) | 7 (5%) | 12 (8%) | ns |
| Renal disease | 29 (9%) | 15 (10%) | 14 (9%) | ns |
| Renal impairment | 60 (19%) | 23 (15%) | 37 (23%) | ns |
| Psychiatric disorder | | | | |
| Psychiatric disorder | 154 (49%) | 82 (53%) | 72 (46%) | ns |
| Alcohol and substance use disorder | | | | |
| Alcohol use disorder | 41 (13%) | 22 (14)% | 19 (12%) | ns |
| Substance use disorder | 114 (36%) | 68 (44%) | 46 (29%) | 0.00 |
| Alcohol and substance use | | | | |
| Used both alcohol and substances | 81 (26%) | 62 (40%) | 19 (21%) | 0.00 |
| Used alcohol or substances—not both | 108 (35%) | 66 (43%) | 42 (47%) | |
| Did not use alcohol or substances | 55 (17%) | 26 (17%) | 29 (32%) | |
| Psychometric scale scores | | | | |
| Depression | 6.42 ± 6.62 | 6.83 ± 6.88 | 5.61 ± 6.03 | ns |
| Anxiety baseline | 1.44 ± 2.45 | 1.50 ± 2.49 | 1.32 ± 2.40 | ns |
| Quality of life index | 0.77 ± 0.21 | 0.75 ± 0.22 | 0.80 ± 0.18 | ns |

*ns* not statistically significant

risk for advanced disease complications and death. Equally important, these factors working in concert increases the complexity of patient care for health care practitioners and professionals. As such, an interdisciplinary approach of care (e.g. health care teams made up of liver or infectious disease specialists, clinical social workers, psychiatrists, psychologists, and other behavioral health specialists, and nurses) for patients living with HIV/HCV co-infection may be more

ideal than a traditional approach of care (e.g. a single provider or referrals from a single provider to *several* individual specialists) (Sims, Melton, & Ji, 2018).

To the authors' knowledge, studies that have investigated effective smoking cessation treatments in patients living with HIV/HCV co-infection are limited. However, effective interventions that have been published for use with patients living with HIV include but are not limited to hospital-initiated

**Table 3** Binomial logistic regression assessing factors associated with tobacco use in patients living with HIV/HCV co-infection

| Variables | Categories | OR | *p*-values |
|---|---|---|---|
| Age | | 1.028 | 0.066 |
| Sex | Male | 1 | |
| | Female | 0.890 | 0.752 |
| Self-reported race | White American | 1 | |
| | African-American | 0.671 | 0.223 |
| Psychiatric disorder | No | 1 | |
| | Yes | 1.053 | 0.875 |
| Alcohol and substance use | Did not use alcohol or substances | 1 | |
| | Used alcohol or substances but not both | 1.974 | 0.091 |
| | Used both alcohol and substances | 3.059 | 0.011* |
| Depression score | | 1.034 | 0.337 |
| Anxiety score | | 0.989 | 0.882 |
| Quality of life score | | 0.406 | 0.327 |

*OR* odd ratio

*$p < 0.05$

smoking cessation interventions, pharmacologic agents (e.g. nicotine replacement therapy, bupropion, varenicline), smartphone-delivered proactive counselling, motivational interviewing alone and in combination with pharmacologic agents (Calvo-Sanchez & Martinez, 2015; Gritz et al., 2013; Keith, Dong, Shuter, & Himelhoch, 2016; Mercie et al., 2018; Pool, Dogar, Lindsay, Weatherburn, & Siddiqi, 2016; Shuter et al., 2018; Triant et al., 2019; Vidrine, Marks, Arduino, & Gritz, 2012). It is plausible that adaptation and implementation of these respective approaches may also be effective for patients living with HIV/HCV co-infection, but caution must be taken because motivators and factors that drive or facilitate tobacco use in patients living with HIV/HCV co-infection have not been fully characterized. Deductive and inductive investigative approaches are needed to acquire a more in-depth understanding of tobacco use in this respective population to identify the most optimal intervention approaches for adaptation and implementation or to develop novel or specialized intervention approaches that may be needed.

Clinical research largely focuses on frequency of alcohol and substance use, harmful effects of alcohol and substance use, and use reduction and cessation among patients living with HIV or HCV. Undoubtedly, attention to both alcohol and substance use are warranted. Alcohol use accelerates HIV and HCV viral replication and worsens liver damage (Lim et al., 2014; Szabo et al., 2010), and both alcohol and substance use reduces medication adherence and increases the risk of transmission to those living without infection (Massa & Rosen, 2012; Sims et al., 2019) Despite tobacco use also expediting HCV and HIV disease progression and other negative health outcomes, tobacco use in patients living with HIV/HCV co-infection is rarely addressed in HIV clinical settings and in research. Health professionals

and researchers are encouraged to consider intervention approaches that target concurrent alcohol and substance use as a method of reducing the likelihood of tobacco use or intervention approaches that collectively target alcohol, substance, and tobacco use. Intervention approaches that only target tobacco use without regard to alcohol and substance use may be suboptimal.

The study had some noteworthy limitations and strengths. The study was cross-sectional. The study was limited to an analysis of baseline data (e.g. only PRO and electronic medical records data from patients' first clinic visit) and did not track or collect data on patients' uptake of HCV treatment. Potentially there are other variables outside of those included in this study that could be associated with tobacco use. The study was limited to a single site and a single state. Multiple racial groups were without representation. Nevertheless, the study sample was comprised of a large number of African American patients. The study used questionnaires with validated psychometric properties. The study sample consisted of patients who had been living with both HIV and HCV for a significant number of years (i.e. were not newly diagnosed patients), were largely insured, were on ART, and actively involved in their HIV care.

Given the recent and evolving COVID-19 pandemic (Huang, Wei, Hu, Wen, & Chen, 2020), efforts are urgently needed—more so now than ever—to identify interventions to assist patients living with HIV/HCV co-infection with smoking cessation. COVID-19 is an opportunistic infection for patients living with weakened immune systems such as HIV and HCV (Felsenstein, Herbert, McNamara, & Hedrich, 2020; Jiang, Zhou, & Tang, 2020), and COVID-19 is quite virulent in patients living with smoking-related respiratory illnesses (Berlin, Thomas, Le Faou, & Cornuz, 2020; Emami, Javanmardi, Pirbonyeh, & Akbari, 2020; Zhao

et al., 2020). Smoking cessation has the potential to reduce COVID-19-related morbidity and mortality in patients living with HIV/HCV co-infection.

## Compliance with Ethical Standards

**Conflict of interest** Omar T. Sims, Asti Jackson, Yuqi Guo, Duong N. Truong, Emmanuel A. Odame and Hadii M. Mamudu declare that they have no conflict of interest.

**Research Involving Human Participants and/or Animals** This research study was conducted retrospectively from data obtained for clinical purposes. We consulted extensively with the IRB of the University of Alabama at Birmingham who determined that our study did not need ethical approval. An IRB official waiver of ethical approval was granted from the IRB of the University of Alabama at Birmingham.

**Informed Consent** The study was a retrospective analysis of de-identified secondary data. The IRB at the University of Alabama at Birmingham deemed the study exempt from informed consent.

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