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Alcohol Consumption Upon Direct-Acting Antiviral Therapy for Hepatitis C among Persons with Human Immunodeficiency Virus in the United States

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Abstract

Background: Direct-acting antivirals (DAA) are highly effective against hepatitis C virus (HCV) infection among persons with human immunodeficiency virus (PWH). However, alcohol use post-DAA treatment poses a continued threat to the liver. Whether the focus on liver health alone during HCV treatment can impact alcohol consumption is unclear. Therefore, we examined the change in alcohol use among HCV-coinfected PWH who received DAA therapy by non-addiction medical providers.

Methods: In our longitudinal clinical cohort study, we identified HCV-coinfected PWH who received interferon-free DAA therapy between January 2014 and June 2019 in the Centers for AIDS Research Network of Integrated Clinical Systems. The Alcohol Use Disorders Identification Test—Consumption (AUDIT-C) was the alcohol screening instrument. We used mixed-effects logistic regression models to estimate the longitudinal change in alcohol use upon DAA therapy.

Results: Among 738 HCV-coinfected PWH, 339 (46%) reported any alcohol use at the end of HCV treatment, including 113 (15%) with high-risk use (i.e., AUDIT-C ≥3 for women, ≥4 for men). Concurrently, 280 (38%) PWH noted active drug use, and 357 (48%) were currently smoking. We observed no changes in the odds of any alcohol or high-risk alcohol use over time with DAA therapy. Findings were similar in the PWH subgroup with a history of alcohol use before DAA treatment.

Conclusions: For PWH with HCV, alcohol use did not change following interferon-free DAA treatment by non-addiction medical providers. Thus, clinicians should consider integrating targeted alcohol use interventions into HCV care to motivate reduced alcohol consumption and safeguard future liver health.

Keywords

alcohol; drinking; addiction; direct-acting antivirals; hepatitis C; human immunodeficiency virus

1. INTRODUCTION

With over 1.1 million infected individuals 13 years and older (Centers for Disease Control and Prevention, 2021), human immunodeficiency virus (HIV) imposes a substantial health burden in the United States. Among persons with HIV (PWH), the prevalence of hepatitis C virus (HCV) coinfection ranges from 2.4% in general population cohorts to 82.4% among people with injection drug use (Platt et al., 2016). Individuals with HIV/HCV

coinfection are more likely to engage in unhealthy alcohol consumption than those with HIV mono-infection. In an urban academic center cohort study, 27.0% of HCV-coinfected PWH reported drinking ≥50 grams/day of ethanol, compared to 15.3% of PWH without HCV (Bonacini, 2011). Unfortunately, both HIV and HCV can potentiate the deleterious effects of chronic alcohol exposure. Not only do patients with HIV/HCV coinfection experience elevated alcohol-related risks for advanced liver disease and liver-related mortality (Ferguson et al., 2020; Salmon-Ceron et al., 2005), but extrahepatic sequelae from alcohol (e.g., pancreatic insufficiency) may also occur (Martin et al., 2013; Monnig et al., 2019; Pfefferbaum et al., 2018). Moreover, unhealthy drinking is a risk factor for suboptimal adherence to HIV antiretroviral therapy (Conen et al., 2013; Shuper et al., 2016), which increases the risks of subsequent virologic failure, HIV-related liver fibrosis, and death (Nachega et al., 2007; Kim et al., 2016; Wood et al., 2006).

The joint HCV Practice Guidance from the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA) recommends that all persons with active HCV infection abstain from alcohol use to attenuate the progression of liver disease. With approximately 95% effectiveness and excellent tolerability (Montes et al., 2017), interferon-free direct-acting antiviral (DAA) regimens can successfully improve treatment uptake, eliminate chronic HCV, and reduce liver disease progression among PWH (Collins et al., 2018; Ghany et al., 2020). Upon curative HCV treatment, the Practice Guidance advises patients to “avoid excess alcohol use” if there is no preexisting cirrhosis and to “abstain from alcohol” in the presence of cirrhosis (Ghany et al., 2020). Patients who engage in unhealthy alcohol use after successful HCV treatment are at risk for further liver disease progression and attenuation of DAA-related gains (Hernaez and El-Serag, 2017; Kim et al., 2020).

Despite the positive correlation between HCV infection and unhealthy drinking, other data suggest that the mere status of HCV positivity may elicit self-awareness of the need to curb alcohol use (McCusker, 2001; Oser et al., 2012). However, published literature from different eras of HCV therapy (i.e., interferon versus DAA) is conflicting on whether treating or curing HCV alone without targeted addiction interventions can modify alcohol consumption (Artenie et al., 2020; Kim et al., 2020; Knight et al., 2017; Midgard et al., 2017). Our study thus sought to assess the longitudinal change in alcohol use among HCV-coinfected PWH upon the delivery of interferon-free DAA therapy by non-addiction medical clinicians. We hypothesized that treating HCV with DAA agents, therefore highlighting liver-related health but without specific alcohol interventions, would be associated with a post-DAA reduction in alcohol consumption.

2. MATERIAL AND METHODS

We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement to report our multi-center cohort study.

2.1. Study Setting and Population

We conducted our study at six sites participating in the Centers for AIDS Research (CFAR) Network of Integrated Clinical Systems (CNICS): Johns Hopkins University, University of

Alabama at Birmingham, University of Washington, University of California San Diego, Case Western Reserve University, and Fenway Community Health Center of Harvard University. All six sites provided data on HCV treatment and had at least one PWH matching our selection criteria. CNICS is a network of academic medical center-based HIV clinical cohorts across the United States (Kitahata et al., 2008). At each center, patients engaged in routine HIV care consent to share data from their medical records. Data in the CNICS repository include patient demographics, medical diagnoses, medication prescriptions (including DAAs), and laboratory results. Each participating site's Institutional Review Boards (IRB) authorized the standard data collection protocols. The Johns Hopkins IRB approved the present study (IRB00078300).

Additionally, PWH at each CNICS site receives an invitation to participate in patient-reported outcome (PRO) assessments approximately every four-to-six months in connection with a clinical visit. Preclusions for participation include dementia, acute intoxication, or medical instability (Crane et al., 2007). PROs are collected using web-based surveys that patients access via touch screen tablet computers before their clinical visits. The structured, standardized surveys contain closed-ended questions that reduce ambiguity by allowing only one response per question and no customizable answers. Within the PRO assessments, alcohol use over the prior 12 months (i.e., the lookback period) is ascertained on the three-item Alcohol Use Disorders Identification Test—Consumption (AUDIT-C), with modified responses that referenced drinking guidelines in the United States (Babor et al., 2016; Bush et al., 1998). Recent and lifetime non-alcohol substance use are measured using the National Institute on Drug Abuse (NIDA)-modified Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST) (Newcombe et al., 2005; WHO ASSIST Working Group, 2002). The nine-item Patient Health Questionnaire (PHQ-9) from the Primary Care Evaluation of Mental Disorders (PRIME-MD) assesses the severity of depressive symptoms (Kroenke et al., 2001).

The present analysis included all patients with HIV/HCV coinfection who received interferon-free DAA therapy for HCV between January 1, 2014, and June 30, 2019. We selected the start date because the first interferon-free DAA combination became available in the United States in late 2013. Finally, we excluded PWH who did not provide any alcohol use PRO data.

2.2. Exposure

Our exposure, DAA therapy, was limited to interferon-free DAA regimens, which describe the overwhelming majority of presently available treatment strategies (Ghany et al., 2020). We did not include patients who received a first-generation DAA (i.e., telaprevir or boceprevir), which typically required concurrent interferon or peg-interferon, given the conflicting data on ethanol's potential for attenuating interferon's antiviral activities against HCV (Costentin et al., 2013; Mochida et al., 1996). All DAA prescriptions originated from a CNICS clinic. Medical providers at each site tailored the prescribed DAA therapy for an individual PWH based on patient-specific factors, including HCV genotype, presence of cirrhosis, medical comorbidities, anticipated medication interactions, and insurance formulary. While infrequent, some patients may have received more than one course of

DAA therapy depending on treatment success. We thus defined treatment duration as the total elapsed time between the start of the first treatment course and the end of the final course. The latter also marked the conclusion of DAA therapy in our analysis. Supplemental Tables S1 and S2 list the prescribed DAA agents and treatment durations observed in our study.

2.3. Outcome

Our main outcome of interest was the change in the odds of any alcohol use, represented by AUDIT-C scores >0, upon completing DAA therapy for HCV. We chose the primary outcome for its inclusiveness; current AASLD/IDSA recommendations for alcohol avoidance after curative HCV treatment differ depending on the presence of cirrhosis. Our second outcome was the change in the odds of high-risk alcohol use, defined as AUDIT-C scores ≥3 in women or ≥4 in men. For descriptive purposes, we also designated an individual's alcohol use pattern as moderate-risk for scores 1–2 in women or 1–3 in men and low-risk for a score of 0 (Frank et al., 2008). Heavy/binge drinking definitions were as per the National Institute on Alcohol Abuse and Alcoholism (NIAAA): having ≥4 drinks on one occasion for women or ≥5 drinks for men (National Institute on Alcohol Abuse and Alcoholism (NIAAA), n.d.). One standard drink contained 0.6 fluid ounce or 14 grams of pure ethanol. Pictorial illustrations placed at the start of the AUDIT-C helped demonstrate to patients the different types and quantities of alcohol beverages that contained a standard drink (e.g., 12 fluid ounces of beer or 8–9 fluid ounces of malt liquor) (National Institute on Alcohol Abuse and Alcoholism (NIAAA), n.d.). We analyzed all available alcohol PRO assessments without time restrictions.

2.4. Covariates

To standardize patients for comparison, we adjusted for HCV response to DAA therapy; assigned sex at birth; age; race; ethnicity; current (i.e., within recent three months) and past use of substances, including methamphetamines, cocaine/crack, marijuana, illicit opioids, and cigarettes; body mass index (BMI); CD4 count; and depression severity at the start of HCV treatment. We defined successful response to DAA therapy as undetectable HCV ribonucleic acid (RNA) when measured 12 weeks or later after starting treatment. Because adult heights are generally stable and thus infrequently measured, we used each PWH's median recorded height to calculate the BMI. Finally, depression severity was categorized as minimal-to-mild (PHQ-9 scores 0–9) or moderate-to-severe (PHQ-9 scores ≥10).

2.5. Statistical Analysis

To address missing covariates in our panel data, we used multiple imputation by chained equations ('mice' package, R) to create 50 imputed datasets (van Buuren and Groothuis-Oudshoorn, 2011). For every imputed dataset, we first separately imputed each time-varying covariate (i.e., substance use, BMI, CD4 count), conditional on age, birth sex, AUDIT-C score, and time (in months) from the end of DAA therapy, with a random slope for time. Next, the imputation for each remaining covariate (i.e., race, ethnicity, HCV response to DAA therapy, depression severity) was conditional on age, birth sex, AUDIT-C score, all other remaining covariates, and baseline values of the imputed time-varying covariates.

We performed mixed-effects logistic regression models using the GLIMMIX procedure in SAS to account for within-person correlations and assess whether the binary event of interest (i.e., any alcohol use or high-risk alcohol use) changed longitudinally over time with DAA therapy for HCV. The models incorporated all longitudinal outcome data within the context of the study selection criteria. All models specified a random intercept for each person and a random slope for time with an unstructured covariance matrix. In addition, we adjusted for the abovementioned patient covariates (see subsection 2.4.) and a linear term for time (in months) from the conclusion of DAA therapy. Finally, we allowed for a change in trend after the end of DAA therapy by introducing an interaction between the treatment conclusion indicator and time. In subsequent subgroup analysis, we repeated the same procedures among PWH with a history of any alcohol use before undergoing DAA treatment for HCV.

In our sensitivity analysis, we sequentially introduced lags of 3, 6, and 12 months to the conclusion of DAA therapy to assess the impact of AUDIT-C's one-year lookback period.

For each analysis, we first fitted our mixed-effects model on the 50 imputed datasets. Then we reported the pooled estimate using the MIANALYZE procedure in SAS. All statistical analyses used α=0.05 as calculated in SAS version 9.4 (SAS Institute Inc., Cary, North Carolina) or R, version 3.6.1 (R Core Team, 2021).

3. RESULTS

3.1. Descriptive Statistics

Across the six CNICS sites, 895 PWH underwent DAA therapy for HCV between January 1, 2014, and June 30, 2019. We excluded 157 PWH from our primary analysis, predominantly due to missing PRO data on alcohol use (Figure 1). The final study sample was 738 participants, most (81%) of whom were men. The median age was 54 years (interquartile range [IQR] 47, 59) (Table 1). The majority self-identified as Black (54%) or White (43%); 9% were Hispanic. The median BMI was 26.1 (IQR 23.2, 29.6). DAA regimen durations were most often from one to three months (72%) or four to six months (17%). Successful HCV response to treatment occurred for 640 (87%) PWH; 29 (4%) were unsuccessful, and 69 (9%) had missing HCV RNA data. When measured at the end of DAA treatment, the median CD4 count was 537 cells/μL (IQR 350, 775), and 76% of PWH had HIV RNA <50 copies/mL.

The 157 excluded PWH generally had similar demographic and clinical characteristics (Supplemental Table S3). However, excluded participants were somewhat less likely to be men (74%). HCV RNA data were also missing more often (21%) than in the final study sample. At the end of DAA treatment, excluded PWH had a slightly higher median CD4 count (586 cells/μL) and a proportionally larger subgroup with HIV viral load <50 copies/mL (88%).

We analyzed 4,829 total PRO assessments; each study patient participated in a median of 6 (IQR 3, 9) assessments. The final PRO survey for a PWH took place a median of 22 months (IQR 11, 34) after the end of DAA therapy, while the earliest survey was 54 months (IQR 32, 73) before the end of DAA. Substance and alcohol use were common. In PROs from

the end of DAA therapy, 38% of patients reported current drug use, 21% described past use, and 74% had a history of tobacco smoking. Concurrently, 339 (46%) patients reported any alcohol use; 113 (15%) had high-risk use as per their AUDIT-C score, and 57 (8%) noted binge drinking episodes at least once monthly (Table 1). We additionally queried PROs from 1) six months before and 2) immediately preceding the start of DAA. Substance and alcohol use patterns at these two time points were highly similar to the end of DAA therapy (Supplemental Table S4).

3.2. Multivariable Models

After adjusting for the abovementioned patient covariates (see subsection 2.4.), the odds of any alcohol use did not change over time with interferon-free DAA therapy for chronic HCV. That is, our mixed-effects model had an insignificant interaction term for the conclusion of DAA and time on the outcome of any alcohol use (adjusted odds ratio [aOR] 1.01; 95% confidence limit [CL] 0.99, 1.02). Likewise, we did not observe a change in the adjusted odds of high-risk alcohol use over time (aOR 1.02; 95% CL 1.00, 1.04) (Table 2).

In subgroup analysis, among 495 PWH with a history of any alcohol use before receiving DAA, the adjusted odds of any alcohol use did not change over time with interferon-free DAA therapy (aOR 1.01; 95% CL 0.99, 1.03). Similarly, we did not note a change in the adjusted odds of high-risk alcohol use over time (aOR 1.02; 95% CL 1.00, 1.04) (Table 3).

3.3. Sensitivity Analysis

Our sensitivity analysis comprised 12 scenarios (i.e., the three lag periods separately applied to the four full sample and subgroup regression models). Unfortunately, we were unsuccessful in obtaining estimates for the full study sample's 3- and 12-month lag scenarios on any alcohol use and the 6-month lag scenario on high-risk alcohol use: these three regression models did not converge for all imputed datasets. In all other scenarios, adding a lag period after the end of DAA therapy did not yield significantly different findings than those from the parent, without-lag model (Supplemental Tables S5 to S10).

4. DISCUSSION

In a multi-site clinical cohort study of PWH with HCV coinfection who received interferon-free DAA treatment for HCV, we observed no longitudinal change in any alcohol or high-risk alcohol use upon the completion of DAA therapy. In addition, outcomes were similar in the subgroup of PWH with a previous history of alcohol use, suggesting that prior use likely did not inform alcohol consumption practices before and after treatment for HCV. Our findings were consistent with other analyses during the DAA era, which have shown modest to no reduction in alcohol use after HCV treatment within different study populations (Artenie et al., 2020; Kim et al., 2020). Conversely, studies of the earlier interferon era indicated more substantial decreases in post-HCV treatment alcohol consumption (Knight et al., 2017; Midgard et al., 2017). One possible contributing factor may be the overall simplicity of DAA regimens relative to interferon-based strategies, leading to fewer patient-clinician engagement opportunities to address broader liver-related health issues like alcohol use (Harris and Rhodes, 2018).

Our examination of standard HCV care in the DAA era without uniform alcohol interventions contrasts with a recent trial, which tested two alcohol treatment strategies in hepatology clinics among individuals with HCV but mostly sans HIV. The Hepatitis C-Alcohol Reduction Treatment (Hep ART) study was a pragmatic, randomized controlled trial of 181 participants with chronic HCV from three health systems in North Carolina, United States (Proeschold-Bell et al., 2018). The trial's control was screening, brief intervention, and referral to treatment (SBIRT) by specially trained hepatology providers, while the intervention arm added up to six months of integrated co-located behavioral therapy by addiction therapists. Neither arm significantly outperformed the other in reducing alcohol use, but both achieved clinically meaningful metrics, including an average reduction of 70–90 grams per week of alcohol consumed and a ~15–20% gain in fully abstinent patients by the end of 12-month follow-up (Proeschold-Bell et al., 2020). Subsequently, Patel et al. performed a secondary subgroup analysis of 123 participants who received DAA therapy, showing that alcohol use reduction began during DAA therapy and persisted beyond 24 weeks post-DAA (Patel et al., 2020).

Contextual dissimilarities during care delivery likely contributed to the divergent findings between our study and Hep ART. CNICS patients receive routine HIV care outside of a clinical trial context, and the approach to alcohol may vary across clinics and providers. Unfortunately, evidence-based alcohol treatment services often are underutilized during the medical care of patients with HCV and unhealthy alcohol use (Owens et al., 2018). In contrast, due to Hep ART's standard trial protocol on training even non-addiction healthcare providers to deliver SBIRT in routine clinical practice, all trial participants received some form of alcohol use intervention (Bertholet et al., 2005), albeit not always specialized motivational, cognitive, or behavioral therapies like motivational enhancement therapy (Dieperink et al., 2014). The findings from HEP ART suggested a beneficial role for integrating alcohol therapies with standard HCV treatment to reduce the adverse sequelae from drinking after achieving HCV cure. However, future implementation research is warranted to confirm and quantify the beneficial impact.

In addition, while our analysis did not directly compare alcohol use responses after DAA therapy between HCV-coinfected PWH and persons with HCV mono-infection, we suspect that the former group may be less likely to reduce alcohol use. One possible contributor may be the higher prevalence of depressive symptoms among HCV-coinfected PWH, as demonstrated by a systematic review and meta-analysis of the published literature (Fialho et al., 2017). Furthermore, published data from Veterans Affairs facilities in the United States showed a higher proportion of HCV-coinfected PWH who consumed alcohol heavily than those with HCV mono-infection (Lim et al., 2014). Finally, two qualitative interview studies on alcohol and substance use among HCV-coinfected PWH (Howell et al., 2021) and persons with HCV mono-infection (Vega et al., 2021) provided meaningful insights. In the first study, Howell et al. noted that HCV-coinfected PWH at an HIV primary care clinic rarely described ongoing medical care as influencing their efforts toward alcohol abstinence. In contrast, Vega et al. observed a theme of the "transformative potential of HCV cure" as a motivation among persons with HCV mono-infection to engage with addiction care in general. However, the sample size limited study investigators from further examining specific substances used.

4.1. Strengths and Limitations

A notable strength of our study was the CNICS research infrastructure, which reflected real-world academic clinical practice in the United States and enhanced the generalizability of the study findings. However, we also recognize some limitations to our study. One limitation was the reliance on self-reported alcohol and other substance use measures, where underreporting was possible and could have attenuated the magnitude of change in alcohol use present in our data (Grüner Nielsen et al., 2021). However, we displayed a graphical depiction of standard drinks before administering the AUDIT-C, which might have improved participants' self-estimation of alcohol quantity consumed (Gilligan et al., 2019). Another limitation was the CNICS protocol for assessing PRO every four-to-six months at the time of a clinical visit. Since most interferon-free DAA regimens were two or three months long, the assessment schedule was not sufficiently granular to contribute robust during-therapy data toward our analysis. We thus could not rule out transient changes in alcohol consumption during DAA treatment. Nonetheless, if changes occurred, our data suggested that they did not persist beyond HCV treatment completion in the absence of concurrent alcohol harm reduction interventions. One additional methodological concern related to the typical DAA treatment durations was the study's use of the AUDIT-C, which has a one-year lookback period. Thus, early post-DAA alcohol assessments might have reflected pre-treatment drinking instead. We assessed this possibility with our sensitivity analysis that added varying lag periods up to 12 months to the end of DAA therapy, and the results were not significantly different from the without-lag models. We also acknowledge that, while evidence-based alcohol treatments are vastly underused in standard clinical practice (Grant et al., 2015; Owens et al., 2018), our observational data could not confirm whether PWH in the study received any interventions or counseling. Lastly, the PRO surveys queried specific sensitive topics (e.g., mental health), which might have been uncomfortable for some PWH to answer. Social desirability bias was therefore possible. However, surveys were both voluntary and computer-administered, which presumably helped reduce such bias (Richman et al., 1999).

4.2. Conclusions

Our analysis of a multi-center cohort of HCV-coinfected PWH did not observe an association between interferon-free DAA treatment and a longitudinal change in alcohol use. Despite published literature suggesting that a diagnosis of HCV infection may itself enhance self-awareness of the dangers of unhealthy alcohol use (McCusker, 2001; Oser et al., 2012), we found that PWH's alcohol consumption did not change significantly by merely engaging in DAA-based HCV treatment without targeted alcohol use interventions.

In 2016, the World Health Organization proposed strategies to treat 80% of eligible persons with HCV and reduce 65% of HCV-related deaths by the year 2030 (World Health Organization, 2016). The expanding availability of highly effective DAA regimens has increased HCV treatment uptake among PWH (Collins et al., 2018). Yet, focusing on HCV alone would be incomplete, as unhealthy alcohol consumption after successful HCV clearance can risk further liver disease progression (Hernaez and El-Serag, 2017; Kim et al., 2020). HCV treatment represents a central opportunity for medical providers to address broader liver-related matters, such as advising against unsafe alcohol drinking practices

according to cirrhosis status (Ghany et al., 2020). Therefore, integrating substance use screening and intervention into standard HCV care is warranted, particularly in the current DAA treatment era. Training and empowering medical clinicians to deliver evidence-based addiction interventions may be crucial for reducing unhealthy alcohol use to preserve future liver health among PWH with HCV coinfection.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Po-Hung Chen reports serving as a Medical Safety Officer for the Non-Alcoholic Steatohepatitis Clinical Research Network, a Steering Committee member for the Alcohol-associated Liver Disease Special Interest Group of the American Association for the Study of Liver Diseases (AASLD), and a Practice Guidelines Committee member of AASLD. Edward R. Cachay reports receiving Gilead Sciences Unrestricted Research Grant, Merck Sharp & Dohme Unrestricted Research Grant, and consulting for Thera Technologies. H. Nina Kim reports receiving a grant from Gilead Sciences.

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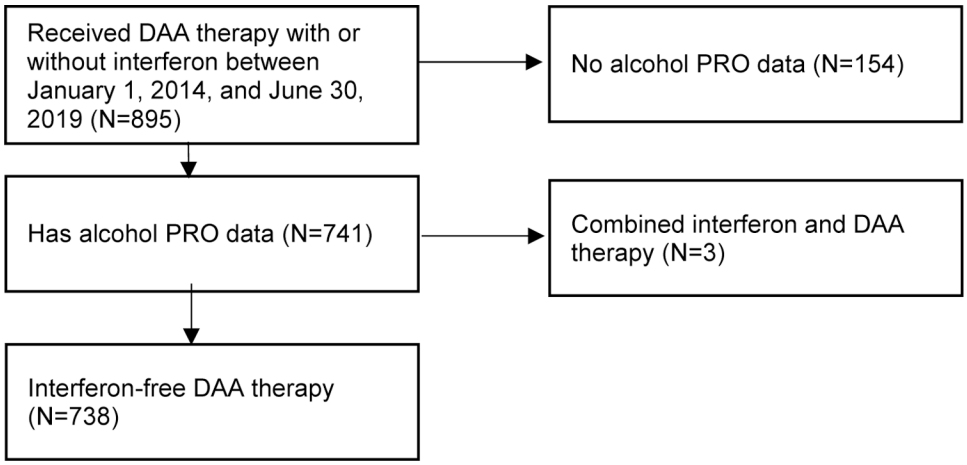

Figure 1.

Flow diagram of patient data inclusion

Abbreviations: DAA, direct-acting antiviral; PRO, patient-reported outcome

Table 1.

Demographic and clinical information of included persons with HIV/HCV coinfection who received interferon-free DAA therapy for HCV between January 1, 2014, and June 30, 2019, and participated in Patient-Reported Outcome surveys. Unless otherwise specified, data were from the survey *closest to the end* of DAA therapy (N=738).

	Summary
Age, median (IQR), y	54 (47, 59)
Birth Sex, No. (%)	
Male	598 (81)
Female	140 (19)
Race, No. (%)	
Black	398 (54)
White	315 (43)
American Indian	6 (1)
Asian	5 (1)
Multiracial	4 (1)
Other	4 (1)
Missing	6 (1)
Ethnicity, No. (%)	
Hispanic	64 (9)
Non-Hispanic	648 (88)
Missing	26 (4)
Drug use, No. (%)	
Current use	280 (38)
Past use	156 (21)
No use	261 (35)
Missing	41 (6)
Alcohol use *, No. (%)	
High-risk	113 (15)
Moderate-risk	226 (31)
Low-risk	399 (54)
Missing	0 (0)
Binge drinking **, No. (%)	
Daily/almost daily	12 (2)
Weekly	16 (2)
Monthly	29 (4)
Less than monthly	83 (11)
Never	598 (81)
Missing	0 (0)
Smoking, No. (%)	
Current smoker	357 (48)
Past smoker	191 (26)

	Summary
Never smoker	180 (24)
Missing	10 (1)
Depression[#]	
Minimal-to-Mild	598 (81)
Moderate-to-Severe	135 (18)
Missing	5 (1)
HCV response[##], No. (%)	
Successful	640 (87)
Unsuccessful	29 (4)
Missing	69 (9)
BMI, median (IQR), kg/m^2	26.1 (23.2, 29.6)
CD4, median (IQR), cells/μL	537 (350, 775)
HIV RNA copies/mL, No. (%)	
<50	560 (76)
50 to <200	62 (8)
200 to <400	7 (1)
400+	44 (6)
Missing	65 (9)

Abbreviations: HIV, human immunodeficiency virus; HCV, hepatitis C virus; DAA, direct-acting antiviral; IQR, interquartile range; BMI, body mass index; CD4, cluster of differentiation 4; RNA, ribonucleic acid

[*] High-risk defined as Alcohol Use Disorders Identification Test—Consumption score ≥3 (women) or ≥4 (men); moderate-risk defined as score 1–2 (women) or 1–3 (men); low-risk defined as score 0

[**] Having ≥4 drinks (women) or ≥5 drinks (men) on one occasion

[#] Minimal-to-mild defined as Patient Health Questionnaire-9 score 0–9; moderate-to-severe defined as score ≥10. Data were from the survey closest to the start of DAA therapy.

[##] Successful response defined as undetectable HCV RNA when measured 12 weeks or later after starting DAA therapy

Table 2.

Pooled adjusted odds ratios (aOR) and 95% confidence limits (CL) across 50 imputed datasets for the association between DAA therapy for HCV and any alcohol use or high-risk alcohol use among 738 persons living with HIV (4,829 observations)

Variable	Any Alcohol Use		High-risk Alcohol Use	
	aOR*	95% CL	aOR*	95% CL
Ended DAA	1.24	(0.89, 1.73)	0.81	(0.53, 1.24)
Time, in months	1.00	(0.99, 1.00)	1.00	(0.99, 1.00)
Ended DAA x Time	1.01	(0.99, 1.02)	1.02	(1.00, 1.04)
HCV response**				
Successful	1	Reference	1	Reference
Unsuccessful	1.43	(0.61, 3.37)	0.66	(0.25, 1.72)
Birth Sex				
Male	1	Reference	1	Reference
Female	0.53	(0.33, 0.84)	0.87	(0.54, 1.42)
Age	0.96	(0.94, 0.98)	0.96	(0.94, 0.98)
Race				
Black	1	Reference	1	Reference
White	0.90	(0.59, 1.38)	0.92	(0.59, 1.42)
Other	0.71	(0.22, 2.26)	0.61	(0.17, 2.19)
Ethnicity				
Non-Hispanic	1	Reference	1	Reference
Hispanic	1.51	(0.75, 3.05)	0.81	(0.41, 1.62)
Smoking				
None	1	Reference	1	Reference
Current	1.20	(0.86, 1.68)	1.58	(1.08, 2.33)
Past	1.08	(0.77, 1.51)	1.47	(0.99, 2.20)
Methamphetamine				
None	1	Reference	1	Reference
Current	1.78	(1.11, 2.87)	1.48	(0.91, 2.40)
Past	1.01	(0.73, 1.39)	1.03	(0.71, 1.49)
Cocaine/Crack				
None	1	Reference	1	Reference
Current	4.06	(2.62, 6.30)	3.09	(1.97, 4.84)
Past	1.44	(1.08, 1.93)	1.13	(0.80, 1.61)
Marijuana				
None	1	Reference	1	Reference
Current	2.55	(1.85, 3.50)	1.49	(1.05, 2.11)
Past	1.11	(0.85, 1.45)	0.82	(0.58, 1.15)
Illicit Opioids				
None	1	Reference	1	Reference
Current	1.04	(0.63, 1.70)	0.76	(0.45, 1.30)

Variable	Any Alcohol Use		High-risk Alcohol Use	
	aOR*	95% CL	aOR*	95% CL
Past	0.77	(0.57, 1.03)	0.87	(0.62, 1.21)
BMI	0.96	(0.93, 0.99)	0.98	(0.95, 1.01)
CD4	1.01	(0.96, 1.06)	0.98	(0.93, 1.03)
Depression***				
Minimal-to-Mild	1	Reference	1	Reference
Moderate-to-Severe	1.20	(0.74, 1.94)	1.40	(0.87, 2.25)

Abbreviations: HIV, human immunodeficiency virus; DAA, direct-acting antiviral; HCV, hepatitis C virus; BMI, body mass index; CD4, cluster of differentiation 4

*Mixed-effects logistic regression model with a random intercept for each person and a random slope for time, adjusting for patient risk factors

**Successful response defined as undetectable HCV ribonucleic acid when measured 12 weeks or later after starting DAA therapy

***Minimal-to-mild defined as Patient Health Questionnaire-9 score 0–9; moderate-to-severe defined as score ≥10. Data were from the survey closest to the start of DAA therapy.

Table 3.

Pooled adjusted odds ratios (aOR) and 95% confidence limits (CL) across 50 imputed datasets for the association between DAA therapy for HCV and any alcohol use or high-risk alcohol use among 495 persons living with HIV *with a history of any alcohol use before DAA therapy* (3,083 observations)

	Any Alcohol Use		High-risk Alcohol Use	
Variable	**aOR***	**95% CL**	**aOR***	**95% CL**
Ended DAA therapy	0.88	(0.60, 1.29)	0.72	(0.46, 1.12)
Time, in months	0.99	(0.99, 1.00)	1.00	(0.99, 1.00)
Ended DAA x Time	1.01	(0.99, 1.03)	1.02	(1.00, 1.04)
HCV response**				
Successful	1	Reference	1	Reference
Unsuccessful	1.03	(0.46, 2.31)	0.55	(0.21, 1.47)
Birth Sex				
Male	1	Reference	1	Reference
Female	0.65	(0.41, 1.04)	1.11	(0.65, 1.91)
Age	0.99	(0.97, 1.01)	0.97	(0.95, 0.99)
Race				
Black	1	Reference	1	Reference
White	0.95	(0.63, 1.43)	0.85	(0.53, 1.36)
Other	0.93	(0.27, 3.21)	0.65	(0.15, 2.81)
Ethnicity				
Non-Hispanic	1	Reference	1	Reference
Hispanic	1.29	(0.70, 2.39)	0.76	(0.38, 1.50)
Smoking				
None	1	Reference	1	Reference
Current	0.97	(0.68, 1.37)	1.53	(1.02, 2.30)
Past	1.00	(0.70, 1.44)	1.55	(1.02, 2.35)
Methamphetamine				
None	1	Reference	1	Reference
Current	1.70	(1.03, 2.79)	1.36	(0.83, 2.24)
Past	1.00	(0.71, 1.42)	1.03	(0.70, 1.52)
Cocaine/Crack				
None	1	Reference	1	Reference
Current	3.45	(2.17, 5.48)	2.80	(1.76, 4.44)
Past	1.47	(1.07, 2.03)	1.16	(0.80, 1.67)
Marijuana				
None	1	Reference	1	Reference
Current	1.99	(1.42, 2.80)	1.31	(0.91, 1.87)
Past	1.04	(0.77, 1.41)	0.81	(0.56, 1.16)
Illicit Opioids				
None	1	Reference	1	Reference
Current	0.92	(0.54, 1.56)	0.80	(0.46, 1.37)

Variable	Any Alcohol Use		High-risk Alcohol Use	
	aOR*	95% CL	aOR*	95% CL
Past	0.71	(0.51, 0.99)	0.90	(0.63, 1.28)
BMI	0.97	(0.94, 1.00)	0.99	(0.96, 1.03)
CD4	1.00	(0.95, 1.05)	0.97	(0.92, 1.02)
Depression***				
Minimal-to-Mild	1	Reference	1	Reference
Moderate-to-Severe	1.00	(0.64, 1.55)	1.20	(0.73, 1.96)

Abbreviations: HIV, human immunodeficiency virus; DAA, direct-acting antiviral; HCV, hepatitis C virus; BMI, body mass index; CD4, cluster of differentiation 4

*Mixed-effects logistic regression model with a random intercept for each person and a random slope for time, adjusting for patient risk factors

**Successful response defined as undetectable HCV ribonucleic acid when measured 12 weeks or later after starting DAA therapy

***Minimal-to-mild defined as Patient Health Questionnaire-9 score 0–9; moderate-to-severe defined as score ≥10. Data were from the survey closest to the start of DAA therapy.