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Adherence to clinical follow-up recommendations for liver function tests: A cross-sectional study of patients with HCV and their associated risk behaviors

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ABSTRACT

This study examined whether patients with Hepatitis C virus (HCV) infection adhered to their physicians' recommendation and HCV clinical guidelines for obtaining a regular liver function test (LFT), and whether high-risk behaviors are associated with behavioral adherence. A cross-sectional survey was administered to 101 eligible patients with HCV who were recruited from health centers in New Jersey and Washington, DC. Adherence outcomes were defined as the patients' self-report of two consecutive receipts of LFTs in accordance with their physicians' recommended interval or the clinical guidelines for a LFT within 3–6 months. 67.4% of patients (66/98) reported a receipt of their physicians' recommendation for a LFT. The rate of adherence to physician recommendation was about 70% (46/66), however over 50% (52/101) of patients with HCV did not obtain regular LFTs. 15.8% (16/101) of patients continued to use injection drugs. Patients who used injection drugs had 0.87 (adjusted odds ratio (aOR) = 0.13, 95% confidence interval 0.03–0.59) times lower odds adhering to their physician recommendation, relative to non-users. Patients with HIV co-infection had increased odds of adhering to the clinical guidelines (odds ratio 3.41, 95% confidence interval 1.34–8.70) vs. patients who did not report HIV co-infection. Additionally, patients who had received a physician's recommendation had 7.21 times (95% confidence interval of 2.36–22.2) greater odds adhering to the clinical guidelines than those who had not. Overall, promoting HCV patient-provider communication regarding regular LFTs and reduction of risk behaviors is essential for preventing patients from HCV-related liver disease progression.

1. Introduction

Hepatitis C virus (HCV) infection is a significant public health concern nationally and globally, with HCV-infection rates increasing every year, over the last 10 years (National Progress Report 2020 Goal, 2020). The Center for Disease Control and Prevention (CDC) estimated that 3.5 million people are infected with HCV in the United States (Commentary | U.S., 2016; Denniston et al., 2014) and the World Health Organization (WHO) has reported 185 million people are infected with HCV, globally (Jefferies et al., 2018). Population-based research has demonstrated that patients with HCV are at an increased risk of hepatocellular carcinoma (HCC) and advanced liver disease (Kanwal et al., 2011). The slow progression from acute to chronic HCV can go unnoticed, as acute HCV infection is asymptomatic in about 60–70% of patients, the vast majority of whom come to clinical attention years later as a result of screening tests, signs of cirrhosis, HCC, or liver failure (Viner et al., 2015; Skolnik et al., 2019; Alter et al., 1992). The asymptomatic progression of the disease contributes to the high mortality of persons

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with HCV (Toshikuni et al., 2014). Promoting awareness and prevention of high-risk behaviors that further contribute to chronic liver disease progression, together with clinical monitoring of liver injury and function, are critical elements of managing the disease.

HCV infection is associated with several risk behaviors. Specifically, alcohol consumption and drug use have been associated with the accelerated progression of chronic liver disease for patients with HCV. Research has shown the prevalence of chronic HCV infection was significantly associated with both former and current excessive alcohol consumption, after controlling for covariates (Taylor et al., 2016). Additional studies revealed an association between HCV and HCC in patients with alcoholic cirrhosis (Bruix et al., 1989; Fuster et al., 2016). Two thirds of new HCV infections in western countries was associated with injection drug use (IDU) (Fuster et al., 2016). Among individuals 17–59 years of age, drug use and high-risk sexual behaviors are additional risk factors for acquiring HCV infection (Alter et al., 1999).

The American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society for America (IDSA) guidelines for HCV management have recommended that patients with HCV should follow a continuum of care that includes monitoring before, during, and after antiviral therapy. The AASLD-IDSA guidelines recommend comprehensive cirrhosis management for patients with HCV, such as receipt of regular liver function tests (LFTs) every three to six months to reduce risks of further liver damage (Monitoring Patients Who Are Starting HCV Treatment, Are on Treatment, or Have Completed Therapy | HCV Guidance, 2019). The AASLD-IDSA guidelines recommend the use of LFTs, as their clinical utility is widely supported in the literature to check liver function, liver diseases, and complications (Wai et al., 2003; Sterling et al., 2006; Chou and Wasson, 2013). Few research studies have examined whether patients with HCV receive follow-up care recommendations from physicians and obtain regular LFTs consistent with the AASLD-IDSA guidelines (Mathes et al., 2014).

To address these gaps in knowledge, we conducted an exploratory, cross-sectional survey in a racially diverse sample of patients with HCV to examine: 1) whether patients with HCV self-reported receiving and adhering to their physician recommendations for regular liver function tests (LFTs), and 2) whether these patients adhered to those recommendations for a continuum of care (e.g. timely LFTs) as recommended by the AASLD-IDSA guidelines, and 3) what risk behavior factors, if any, were associated with non-adherence. Results will inform clinical practice and guide development of strategies to increase adherence to post-treatment liver testing in an effort to prevent HCV-related liver disease progression.

2. Methods

2.1. Study population and recruitment

This study was approved by the Institutional Review Boards at Georgetown University Medical Center (GUMC) and Hackensack University Medical Center (HUMC). To ensure a diverse sample, we enrolled eligible patients from health centers in both New Jersey (NJ) and Metropolitan Washington, DC area. Eligible patients were: 1) patients with HCV regardless of treatment status, 2) ages 18 years and older, and 3) English or Spanish speaking.

Eligible patients were recruited, consented, and surveyed by trained bilingual research assistants either by telephone or in-person recruitment between January 2017 to April 2019 (Fig. 1). In the DC area, we collaborated with the Practice-Based Research Network (PBRN) Capital Area Primary Care Research Network (CAPRICORN). The HUMC research team extended the patient enrollment with in-person recruitment from three community-based healthcare centers in northern New Jersey and New York metropolitan areas. All of the healthcare centers in the NJ sites served patients that were uninsured or underinsured, and enrolled in Medicaid or Medicare. In contrast, the Georgetown sites were primarily insured patients.

Each participant who completed the one-time survey received a $25 gift card as an incentive to compensate for their time and effort. Trained research assistants administered the survey over the phone for both sites, which took approximately 30–40 min to complete.

2.2. Data collection instrument

Trained bilingual interviewers administered the cross-sectional, self-reported survey by telephone to all participants.

2.2.1. Outcome variables

We assessed two study outcomes: 1) whether patients with HCV reported receiving and adhering to their physician's recommendation concerning LFT, and 2) whether patients adhered to the 2015 clinical AASLD-IDSA guidelines, which recommend patients with HCV should obtain a LFT every three to six months (Monitoring Patients Who Are Starting HCV Treatment, Are on Treatment, or Have Completed Therapy | HCV Guidance, 2019). Since this study was patient-focused, it did not assess which clinical guidelines were used for follow-up care recommendations by our patients' physicians. It is possible that physicians may adopt different guidelines, however AASLD-IDSA guidelines are widely recognized national guidelines for HCV treatment, monitoring, and care – curated by a panel of hepatology and infectious disease

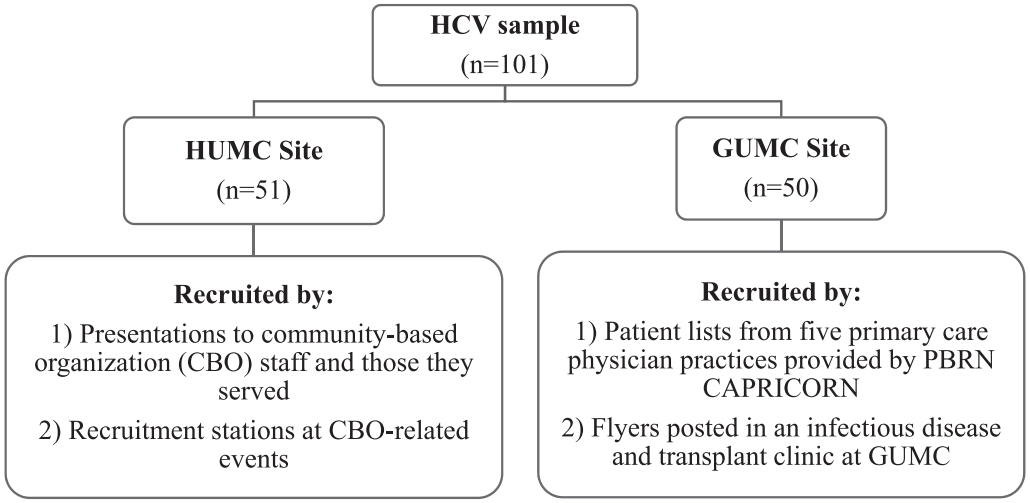

Fig. 1. Patient sample and recruitment methods.

clinicians (Hepatitis C Guidance 2019 Update, 2019). As such, we developed the following questionnaire to assess HCV patients' adherence.

We asked patients to self-report: 1) whether they had received a physician's recommendation to obtain LFTs, 2) how often their physician recommended them to obtain a LFT, 3) when was the most recent time they had a LFT (e.g., 1–2 months, 3–6 moths, 7–12 months, or over 12 months), and 4) how many months ago they received a LFT, since their most recent LFT. Patients were labeled as "adherent" to the timing of follow-up testing when their LFTs were obtained either more frequently or equal to the physician's recommended interval. If the patients were not able to answer the first two questions above, then the patient was labeled as not receiving a physician's recommendation. If patients' self-reported follow up LFTs were consistent to AASLD-IDSA recommended frequency for LFTs of 3–6 months, then they were labeled as "adherent" to the guidelines.

2.2.2. Independent variables

Alcohol use behavior score was assessed using the validated WHO Alcohol Use Disorder Identification Test (AUDIT) (WHO | AUDIT: The Alcohol Use Disorders Identification Test, 2019; Saunders et al., 1993) which is used to identify harmful patterns of alcohol consumption through a 5-point Likert-type survey. Responses to the 10 alcohol behavior questions were summed for each participant, and the mean was taken. The total score ranged from 0 to 40, in which zero indicated "no risk" and anything above 20 was considered to be "addiction likely." Alcohol use was measured using the question: "During the past 12 months, how often did you have a drink containing alcohol?" Alcohol use was defined as having at least 1 drink in the past 12 months and no alcohol use was defined as having zero drinks in the past 12 months.

Drug use questions were taken from the CDC's National HIV Behavioral Surveillance (NHBS) of 2014–2016 (CDC's Nation HIV Behavioral Surveillence (NHBS), 2015). Example questions include: "Have you ever in your life shot up or injected drugs other than those prescribed for you? (yes/no)"; "When was the last time you injected any drug? (e.g., 30 days ago)"; and "How many times have you injected any drug in the last month?". Ever used injection drugs was defined using the last question and respondents were characterized into: 1) ever used injection drugs (including patients who had ever injected or injected in the last month); and 2) never used injection drugs.

Sexual history questions were from the CDC's A Guide to Taking a Sexual History (U.S. Department of Health and Human Services, 2011). We assessed the number of sexual partners by asking about their sexual history. Responses to the question, "In the past 12 months, how many sexual partners have you had?" were categorized at "none to one partner" or "more than one partner".

Other risky behavior questions were adapted from 2008 Blood Donor History Questionnaire (BDHQ), (Blood Donor History Questionnaires, 2019). BDHQ survey questions measured other risky behaviors in the past 12 months such as blood transfusion, transplant, come into contact with someone else's blood, accidental needle-stick, tattoo, ear/body piercing, lived with someone with HCV or HBC, sexual contact with anyone who has used needles for unprescribed drugs, been incarcerated, or had hemodialysis. The total number of "yes" responses to each of these questions for each participant was summed to calculate the *risky behavior score.* Each yes to a question received 1 point and the total score ranged from 0 to 10.

Demographic variables included age, gender, birthplace, education, ethnicity, and race. Patient-reported comorbidity was based on the Charlson Comorbidity Index (CCI) assessing the presence of 12 chronic diseases (e.g., diabetics, hypertension, and arthritis). These comorbid diseases were coded as present versus not present.

Hepatitis C Knowledge was assessed using a Hepatitis C questionnaire, taken from HCV knowledge surveys developed by Sinclair and Trelor (Sinclair, 2012; Treloar et al., 2012). Knowledge questions included risk factors associated with HCV and how it spreads. The total number of correct responses was summed to create the Hepatitis C knowledge score in a 29-item survey, in which each correct item was scored 1 point. A higher score demonstrated higher HCV knowledge.

2.3. Statistical analysis

Descriptive analysis was performed to calculate frequency, percentage, mean, and standard deviation for all categorical or continuous variables. Chi-square tests and Pearson correlations were used to examine bivariate associations of demographic and other sample characteristics with risk behaviors and adherence outcomes. Independent variables were considered potential predictors for the multivariate model when their bivariate associations with the outcomes resulted in a p-value of 0.20 or less. Next, we produced two logistic regression models for each of the adherence outcomes: whether or not the patient reported receiving their physician's recommendations for LFTs, and whether or not they received a follow-up LFT within the AASLD-IDSA guideline of 3–6 months. The final multivariate logistic regression models were determined by using a backwards selection method in which the predictor with the highest p-value was removed until all remaining predictors' p-values were 0.20 or less. All statistical analyses were performed using SAS version 9.4.

3. Results

3.1. Sample characteristics

The age of patients with HCV (N = 101) ranged between the ages of 18 and 80 (mean 56.75, SD: 11.0). Of the 101 patients, about 9% reported currently undergoing HCV treatment, 58% have completed treatment, and 33% had not started treatment. The participant pool was 54.6% male and 45.5% female. In terms of education completion, 55.5% completed less than high school, and 44.6% completed high school and above. The majority of patients identified their race as Non-Hispanic Black (63.4%), followed by 17.8% White, 10.9% Hispanic and 7.9% identified as other.

Among all respondents, 55.5% were current smokers and 83.2% had never injected drugs. Approximately 38% of patients had engaged in at least one of the other risky behaviors (e.g., tattoo, blood transfusion, unprotected sex with someone with HBV or HIV). Alcohol behavior score was about 2.5, which demonstrated that on average patients indicate no risk of having alcohol addiction (see Table 1).

3.2. Adherence rates

As shown in Table 2, 67.4% (66/98) of respondents reported that their physicians recommended a future liver function testing regimen. Among those who received a recommendation, 69.7% (46/66) received a LFT consistent with their physician's recommended interval. Among those who did not report receiving a recommendation for a follow up LFT by their physician (n = 32), about 13% received a LFT within 3–6 months, consistent with the AASLD-IDSA clinical guidelines. There were no differences in the above outcomes by study site (data not shown).

3.3. Multivariate regression results

The multivariate logistic regression demonstrated that patients who were persons who inject drugs (PWID), compared to non-users, had an 87% (adjusted odds ratio (aOR) = 0.13, 95% confidence interval (CI): 0.03–0.59) reduced odds for adhering to the physician recommendations. In a subgroup analysis, PWID had 93% (aOR = 0.07, 95% CI: 0.02–0.26) lower odds to be currently on or have already completed HCV treatment vs. those who did report ever using injection drugs (data not shown). For adherence to AASLD guidelines, patients who reported having HIV had an adjusted odds 3.41 (95% CI; 1.34–8.70) times greater to receive a LFT within 3–6 months. Likewise, if the patient received a

Table 1
Demographic and Behavioral Differences by Adherence Outcomes.

Variable	Adherence to physician recommendation[+]			Adherence to guidelines			
	Not Adherent (n = 20) n (%)	Adherent (n = 46) n (%)	*p*-value	Not Adherent (n = 52) n (%)	Adherent (n = 49) n (%)	*p*-value	Total (N = 101) n (%)
Physician Recommendation							
No				26 (50.0)	6 (13.0)	<0.001*	32 (32.7)
Yes				26 (50.0)	40 (87.0)		66 (67.4)
Gender							
Female	10 (50.0)	19 (43.2)	0.49	23 (44.2)	22 (45.8)	0.94	45 (45.0)
Male	9 (45.0)	25 (56.8)		28 (53.9)	26 (54.8)		54 (54.0)
Transgender	1 (5.0)	0		1 (1.9)	0		1 (1.0)
Education							
<High School	10 (50.0)	25 (55.6)	0.44	30 (57.70)	26 (53.1)	0.64	56 (55.5)
≥High School	10 (50.0)	20 (44.4)		22 (42.3)	23 (46.9)		45 (44.6)
Race/Ethnicity							
Non-Hispanic White	5 (25.0)	8 (17.8)	0.76	10 (19.2)	8 (16.3)	0.87	18 (17.8)
Non-Hispanic Black	12 (60.0)	29 (64.4)		32 (61.5)	32 (65.3)		64 (63.4)
Hispanic	1 (5.0)	5 (11.1)		5 (9.6)	6 (12.2)		11 (10.9)
Other	2 (10.0)	3 (6.7)		5 (9.6)	3 (6.1)		8 (7.9)
HIV-Coinfection							
No	13 (65.0)	24 (53.3)	0.38	39 (75.0)	25 (51.0)	<0.001*	64 (63.4)
Yes	7 (35.0)	21 (46.7)		13 (25.0)	24 (49.0)		37 (36.6)
Hep A Vaccination							
No	8 (44.4)	19 (46.3)	0.89	32 (65.3)	21 (47.7)	0.09	53 (57.0)
Yes	10 (55.6)	22 (53.7)		17 (34.7)	23 (52.3)		40 (43.0)
Hep B Vaccination							
No	8 (47.1)	20 (45.5)	0.98	28 (59.6)	20 (42.6)	0.10	48 (51.1)
Yes	9 (52.9)	24 (54.6)		19 (40.4)	27 (57.5)		46 (48.9)
HCV Treatment							
No	6 (31.6)	10 (22.7)	0.46	19 (38.0)	11 (23.4)	0.12	30 (30.9)
Yes	13 (68.4)	34 (77.3)		31 (62.0)	36 (76.6)		67 (69.1)
HCV Education							
No	3 (15.8)	3 (6.8)	0.28	13 (25.5)	4 (8.5)	0.03*	17 (17.4)
Yes	16 (84.2)	40 (93.2)		38 (74.5)	43 (91.5)		81 (82.7)
Alcohol use							
None	9 (45.0)	25 (55.6)	0.43	27 (51.9)	26 (53.1)	0.91	53 (52.5)
≥1 in the last 12 months	11 (55.0)	20 (44.4)		25 (48.1)	23 (46.9)		48 (47.5)
Ever used injection drugs							
No	13 (65.0)	42 (93.3)	<0.001*	38 (73.1)	46 (93.9)	0.01*	84 (83.2)
Yes	7 (35.0)	3 (6.6)		14 (26.9)	3 (6.1)		17 (16.8)
Sexual partners							
None to one	12 (60.0)	39 (86.7)	0.02*	36 (69.2)	43 (89.6)	0.01*	79 (79.0)
More than one	8 (40.0)	6 (13.3)		16 (30.8)	5 (10.4)		21 (21.0)
Smoker							
Not Currently	8 (40.0)	23 (51.1)	0.41	23 (44.2)	22 (44.9)	0.95	45 (44.6)
Currently	12 (60.0)	22 (48.9)		29 (55.8)	27 (55.1)		56 (55.5)
Age[++]	58.5 (11.3)	57.5 (10.8)	0.75	57.2 (10.6)	56.3 (11.5)	0.68	56.8 (11.0)
Alcohol Use Behavior score[++]	2.4 (4.2)	1.7 (3.4)	0.64	3.5 (4.9)	1.5 (3.2)	0.11	2.5 (4.3)
Risky Behavior score[++]	1.1 (1.3)	1.0 (1.4)	0.65	0.7 (1.1)	0.9 (1.4)	0.55	0.8 (1.3)
Hepatitis C Knowledge score[++]	19.3 (3.3)	19.6 (3.2)	0.63	18.5 (4.0)	19.7 (3.3)	0.09	19.1 (3.7)

[*] *p*-value < 0.05;
[+] Sample size is smaller since only 66 out of 98 patients reported the receipt of a recommendation from their physician (yes/no), physician recommended time period to get a LFT, and their last two completed LFTs;
[++] For continuous variables, Mean (*SD*) was shown.

Table 2
Adjusted Odds Ratios for Adherence Outcomes (vs. Non-Adherence).

Outcomes	Variable	Adjusted OR	95% CI
Physician Adherence	Ever Used Injection Drugs (yes vs no)	0.13	[0.03–0.59] *
Guideline Adherence	HIV-Coinfection (yes vs no)	3.41	[1.34–8.70] *
	Alcohol Use Behavior score	0.91	[0.74–1.12]
	Receiving Physician Recommendation	7.21	[2.36–22.2] *

[*] $p < 0.05$.

physician's recommendation, they had an adjusted odds about 7 (95% CI: 2.36–22.2) times greater to adhere to the clinical guidelines. Lastly, alcohol use behavior score was not statistically significant after controlling for HIV co-infection and receipt of a physician's recommendation (Table 2). The number of sexual partners was no longer significant after controlling for injection drug use and alcohol use behavior score. As such, the number of sexual partners was removed from the final model during backward selection.

4. Discussion

The findings indicated that 67.4% of patients with HCV reported receiving their physicians' recommendation for obtaining regular LFTs. Overall, 69.7% of patients with HCV, who received a physician recommendation, obtained regular LFTs. However, only 49% of the overall sample obtained regular LFTs in adherence to the AASLD-IDSA follow-up care guidelines of 3–6 months. Those who ever used injection drugs were less likely to adhere to physician recommendation to obtain LFTs within the recommended interval. Patients with HIV/HCV co-infection

were more likely to adhere to the AASLD-IDSA guidelines. It is notable that 36.6% of the sample were co-infected with HIV and about 16.8% ever used injection drugs. While alcohol abstinence and Hepatitis A and B vaccinations were not predictors of the adherence outcomes, they are recommended practices for patients with HCV, according to the AASLD-IDSA guidelines (Monitoring Patients Who Are Starting HCV Treatment, Are on Treatment, or Have Completed Therapy | HCV Guidance, 2019). However, 47.5% of the sample were alcohol users during the time of the interviews and only about 43–48.9% of the sample reported receipt of the vaccinations.

Our results suggest that routine inquiring of patients with HCV about their receipt of LFTs and their involvement in risky behaviors, through patient self-reports, may help monitor their risk of HCV re-infection and receipt of recommended follow-up care. While most of our patients were enrolled from primary care clinics and community health services, this study did not adequately examine how patients with HCV communicate with providers, nor did it examine factors affecting physician's ability to provide follow-up care recommendations for patients with HCV, including HCV treatment. This is the first study that we are aware of investigating adherence to follow-up recommendations for patients with HCV in the U.S. and is largely exploratory in nature. Prior research has mainly focused on screening and treatment (Skolnik et al., 2019; Mathes et al., 2014; Edlin et al., 2005; Larrey et al., 2014). Further research is needed on patients with HCV adherence to LFTs and the recommended follow-up care.

Our study indicated that injection drug use was a key risky behavior related to patients with HCV adherence to receipt of LFTs. 16.8% of our patients reported the use of injection drugs. PWIDs oftentimes lack stable housing, access to primary care services, and may have concurrent psychiatric comorbidities (Edlin et al., 2005), making them less able to receive routine care or manage psychiatric comorbid conditions in order to follow recommended healthcare practices (i.e. making it to appointments or following medical advice). Our findings showed the PWIDs were less likely to comply with their physician recommendations for regular LFTs (i.e. lower adherence) and AASLD-IDSA guidelines, and engage in HCV treatment. The AASLD-IDSA guidelines recommend a multidisciplinary setting to decrease future reinfection risks and manage various social and psychiatric comorbidities (Monitoring Patients Who Are Starting HCV Treatment, Are on Treatment, or Have Completed Therapy | HCV Guidance, 2019). Several studies reported ways to facilitate management of care such as using patient navigators to reduce barriers in linkage and retention in care, providing on-site testing and treatment (Ford et al., 2018; Coyle et al., 2019), or enhancing patients' knowledge about HCV transmission (Jost et al., 2019). Patients' adherence to testing - consistent with AASLD-IDSA guidelines - may also be largely attributed to their health provider's awareness of up-to-date guidelines and routine testing procedures; but patient recall of testing may also be variable. Addressing barriers to care and patient education is critical to ensure effective treatment and management of HCV by providers (Ford et al., 2018; Jost et al., 2019).

Among the variables examined as possible predictors for adherence to AASLD-IDSA guidelines, HIV-coinfection and receiving a physician's recommendation demonstrated strong associations with adherence to the guidelines. Patients with HIV/HCV co-infection had 2.36 times increased odds of adhering to the guidelines. Nationally, about 21–25% of HIV individuals tested positive for HCV (Garg et al., 2014; Maier and Wu, 2002), which is similar to the proportion of our study participants (26.7%). Liver disease progresses more rapidly in patients with HIV/HCV coinfection (Maier and Wu, 2002; Solà et al., 2006) and they experience more liver-related morbidity and overall mortality, compared to patients mono-infected with HCV (Re et al., 2014; Meta-analysis: Increased Mortality Associated With Hepatitis C in HIV-infected Persons Is Unrelated to HIV Disease Progression - PubMed, 2020). As a unique population, established in the AASLD-IDSA guidelines, follow-up testing may be a routine part of their HIV-associated medical care, which necessitates routine lab testing that often includes blood panels containing LFTs. This may explain why they get LFTs more frequently compared to those who were not co-infected with HIV. It is unknown whether those infected with only HCV perceive lower risk for re-infection or other liver-related diseases, which may deter them from following their physician recommendation. Investigating and strengthening patient-provider communication on injection drug use among patients with HCV are particularly needed, as it was the only significant predictor found in this study to reduce adherence to physician recommendations.

4.1. Limitations

This study was limited to the selected DC and NJ clinics and may not represent persons with HCV in those regions as a whole, nor in other cities or states. Second, the sample size was relatively modest. The observed associations will need to be confirmed in larger population-based research. In addition, we did not look at outcomes related to the development of HCC or cirrhosis, and it is unclear whether adherence to the recommended follow-up care will prevent persons with HCV from developing cirrhosis or liver cancer. This study was also solely based on patient recall, which may largely affect whether patients accurately reported physician recommendations, and subsequent liver function testing and time of completion; although, patients' self-report has previously been used to understand health care utilization and a patient's health behaviors (Short et al., 2009). This study also did not record which clinical guidelines were utilized by our patients' physicians. Therefore, we do not have data from physicians to support whether they follow AASLD-IDSA guidelines. Future prospective, longitudinal research will be needed to examine the effects of adherence to clinical recommendations and liver-related morbidity and mortality, as well as the use of patient medical records to record physician liver function testing referrals and test dates for accuracy.

4.2. Clinical implications and recommendations

Primary care providers (PCPs) are essential partners in delivering evidence-based care and services for patients with HCV, particularly for at risk patients involved in risky behavior (i.e. injection drug use), as well as monitor important disease markers such as liver function tests (Artenie et al., 2014). As a first point of contact for patients with HCV, PCPs can provide additional information on how to avoid high-risk behaviors, especially among people who inject drugs (PWID) and those with HIV/HCV coinfection. Those that continue to be involved in high-risk behaviors, despite their HCV diagnosis, may benefit from physician education and recommendations. Our findings showed that a substantial number of patients (32.7%, 22/98) did not report receiving a physician recommendation for LFT, but physician recommendation was a strong predictor of patient adherence to regular LFTs. Other research also showed that PWIDs with access to a PCP are more likely to receive referrals to a liver clinic (Artenie et al., 2014). Additionally, our study indicated that the rates of Hep B and A vaccination were moderate, despite being among the recommended vaccinations in the AASLD-IDSA guidelines. Being regularly tested with LFTs can provide important surveillance for serious complications such as HCC and cirrhosis (Viner et al., 2015; Skolnik et al., 2019; Alter et al., 1992). Disseminating HCV care guidelines and increasing PCPs awareness of AASLD-IDSA's recommended vaccinations can help facilitate adherence to follow-up appointments for LFTs and prescription of Hep A/B vaccinations.

5. Conclusions

HCV-infections are increasing in the U.S. (National Progress Report 2020 Goal, 2020), largely due to the rise in injection drug use as a result of the opioid epidemic (Commentary | U.S., 2016; Jost et al., 2019; Zibbell et al., 2018). These cross-sectional study findings are preliminary but shed light on the relationship between continued use of injection

drugs and adherence to recommended practice in risk monitoring. This study suggests that prioritizing patient education about HCV and risk behaviors, and PCP recommendations will need to be strengthened in public health interventions (e.g., educational campaigns), as well as patient-provider communication regarding follow-up care guidelines. Additional research is needed to understand the long-term health outcomes associated with such adherence, which may be helpful in reducing advanced liver disease.

CRediT authorship contribution statement

Allison Dormanesh: Data curation, Formal analysis, Writing - original draft, Writing - review & editing. **Judy Huei-yu Wang:** Conceptualization, Supervision, Funding acquisition, Methodology, Investigation, Resources, Data curation, Formal analysis, Writing - original draft, Writing - review & editing. **Ranit Mishori:** Conceptualization, Supervision, Investigation, Resources, Writing - review & editing. **Paula Cupertino:** Supervision, Investigation, Resources, Writing - review & editing. **Joshua Longcoy:** Data curation, Formal analysis, Writing - original draft, Writing - review & editing. **Seble Kassaye:** Investigation, Resources, Writing - review & editing. **Linda Kaljee:** Investigation, Resources, Writing - review & editing. **Coleman Smith:** Investigation, Resources, Writing - review & editing. **Christopher A. Loffredo:** Conceptualization, Supervision, Funding acquisition, Methodology, Investigation, Resources, Data curation, Formal analysis, Writing - original draft, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Author contributions

JW and CL conceived of, and designed, the study. RM, PC, CS, LK, JW, CL and SK were responsible for patient enrollment and data collection. JL, AD, JW, and CL were responsible for data analysis. AD, JW, CL, and JL drafted the initial manuscript. AD, JW, RM, PC, JL, SK, LK, CS, and CL revised it critically for important intellectual content. All authors approved the final manuscript.

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Patient consent

Not required.

Ethics approval

Georgetown University and Hackensack University Institutional Review Boards approved all study procedures.

Data sharing statement

Data are available upon reasonable request.

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