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## HCV infection status and care seeking among people living with HIV who use drugs in Vietnam

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### Abstract

HCV co-infection is widespread among people living with HIV who use drugs (PLHWUD). However, HCV testing was inconsistently implemented among PLHWUD. The low infection awareness and mental health challenges together impede PLHWUD's treatment-seeking. The study used baseline data of a randomized controlled trial conducted in Vietnam. HCV infection status was collected through self-report and medical record review. A linear mixed-effects regression model was used to examine the relationships between PLHWUD's perceived barriers to seeking healthcare, their depressive symptoms, and the consistencies in HCV status reports. Among the 181 PLHWUD in the study, one-third (64; 35.4%) had inconsistent self-reports and medical records of HIV infection status. The agreement between the two records was fair (Kappa statistics = 0.43). PLHWUD with consistent HCV infection confirmed by both medical records and self-reports perceived lower levels of healthcare-seeking barriers than those with discrepant HCV reports (estimated difference =  $-1.59$ , SE = 0.71,  $P = 0.027$ ). Depressive symptoms were significantly correlated with healthcare-seeking barriers among those with discrepant HCV results (estimate = 0.17, SE = 0.06,  $P = 0.007$ ). There is an urgent need to extend HCV screening efforts and increase HCV awareness among PLHWUD. Explicit HCV result notification and integrated mental health support are recommended to facilitate patients' access to needed care.

### Keywords

HCV; HIV comorbidity; access to care; people who use drugs; Vietnam

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Disclosure statement

No potential conflict of interest was reported by the author(s).

Ethical Approval

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

Informed consent

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

## Introduction

HCV infection is one of the most common comorbidities of HIV due to the shared transmission route of HIV and HCV (Platt et al., 2016; Pouget et al., 2012; Sulkowski, 2008). Among people living with HIV who use drugs (PLHWUD), HCV co-infection rate can be as high as 82% is (Platt et al., 2016). HCV infection can persist for decades, and it increases the risk of hospitalization and death for HIV-infected population because it contributes to liver cirrhosis and liver failure (Collins et al., 2006; Hernando et al., 2012; Sulkowski et al., 2002; Thein et al., 2008). Direct-acting antivirals can mitigate the progression of liver fibrosis and reduce the risk of liver-related mortality in HCV/HIV co-infected patients (Schlabe & Rockstroh, 2018). Given the adverse health effects of HCV infection and the availability of highly effective treatment (Bruno & Saracino, 2017; Doyle et al., 2013; Poordad & Dieterich, 2012; WHO, 2016), PLHWUD with HCV co-infection should be given priorities to receive medical attention.

Despite the urgent healthcare needs, PLHWUD face significant challenges in seeking medical services (Bruggmann & Grebely, 2015; Oramasionwu et al., 2014). Testing and diagnosis of HCV infection is the gateway to necessary hepatitis treatment and care services; however, only a tiny fraction of the patients is aware of their HIV infection because of the high cost and low availability of virological testing (Easterbrook et al., 2017). As a result, they tend to delay medical care until the disease has progressed to an advanced stage (Easterbrook et al., 2016). HCV-infected patients who use drugs frequently experience refusal of treatment by service providers, as their drug use status is often perceived as an impediment to treatment readiness (Osilla et al., 2011). Last but not least, the layered stigma and discrimination towards HIV and drug use to a large extent hinders PLHWUD's access to healthcare (Lekas et al., 2011; Treloar et al., 2013).

Mental health challenges, which are common among PLHWUD (Baum et al., 2008; Fialho et al., 2017), further complicate the aforementioned barriers to treatment access (Beaulieu et al., 2018; Mojtabai et al., 2014; Souliotis et al., 2017). Mental health conditions were found to be consistently associated with increased barriers to access among PLHWUD, with or without HCV-coinfection (Wang et al., 2016). One explanation is that substance use disorders and mental illnesses are considered as contraindications to HCV therapy, due to the potential neuropsychiatric effects of interferon (Hepworth et al., 2013). Secondly, the coexistence of emotional or psychosocial problems in HCV-infected patients contribute to the level of difficulties in communicating with healthcare providers, which lead to the misdiagnoses or inadequate treatment in patients (Zickmund et al., 2004). Third, the presence of multiple psychiatric comorbidities often jeopardizes the patients' ability to adhere to treatment regimens and retain in care (Kamarulzaman & Altice, 2015).

In order to effectively prevent and control HCV/HIV co-infection, further investigation on barriers to healthcare seeking among PLHWUD population is warranted. We conducted this study in Vietnam because it is one of the countries that is substantially affected by drug use and its correlated HCV/HIV co-infection. Among the 271,000 estimated people who injected drugs in Vietnam, approximately 40,000 are living with HIV (WHO, 2014). HCV/HIV co-infection among people who use drugs was estimated to be as high as 95%

(Berto et al., 2017; Nadol et al., 2015). The burden of mental health challenges among PLHWUD in Vietnam is also comparable to that in Western countries (Pham et al., 2018). Although HCV testing and direct-acting antivirals are available and recommended for people living with HIV and people who use drugs (VMOH, 2010, 2016, 2017), access to these services is generally complicated and expensive even with health insurance coverage (VMOH, 2018). In this study, we explore PLHWUD's HCV diagnosis and awareness and its impact on patients' perceived barriers to seeking healthcare, taking into account the patients' mental health status. The understanding generated from the study is crucial to facilitate HCV-related service provision in the context of HIV/drug use control efforts.

## Methods

### Study participants

This study used the baseline data of a randomized controlled trial conducted in Northern Vietnam. The data were collected in 2018. PLHWUD participants were recruited through study flyers mounted in local commune health centers, HIV testing sites, needle exchange sites, and other addiction treatment clinics. Eligibility criteria included: (1) age 18 and above; (2) being HIV seropositive based on self-report; (3) currently using opiates or having a history of opiate use, and (4) either not receiving antiretroviral therapy (ART) or not receiving methadone maintenance therapy (MMT) at the time of the data collection. All participants have been informed of the study purpose, procedures, confidentiality, voluntary participation, and potential risk and benefits of the study. They were assured that their decision to participate in the study and their responses to the assessment questions would not affect their health services in any way. Written informed consent was obtained from all participants before data collection. A total of 181 PLHWUD were included in this study. Among the participants, 133 were on ART (73.5%), 19 were on MMT (10.5%) and the rest were naïve to both treatments at the time of the data collection.

### Data collection

After enrollment, participants completed the questionnaire in a private office at the commune health center using a computer-assisted personal-interview method. The interviewers administered the assessment to the respondents and keyed in their answers directly to computers. The assessment took approximately 45–60 min to complete, and each participant received 200,000 VND (8 USD) as compensation for their time and effort. The study procedures and assessment materials were approved by the Institutional Review Boards of the participating institutes in the U.S. and Vietnam.

### Measures

*Barriers to seeking healthcare* were measured by a 10-items scale adapted from Clement and colleagues' study (2012). The original scale consists of 36 questions. We selected ten questions that are most relevant to our research purpose and study population. Participants were asked to indicate the level of barriers they had experienced when seeking healthcare (ranging from 1= "not at all" to 4= "a lot"). The sample questions included "being unsure about where to get professional care," "being unable to afford the financial costs involved," and "having experience of unfair treatment previously." A score of barriers to seeking

healthcare was generated by summing up the responses of all questions (ranging from 10–40). A higher score indicated a higher level of perceived barriers to seeking healthcare (Cronbach’s alpha = 0.71).

As an indicator of mental health status, participants’ *depressive symptoms* were assessed by a short version of the Zung Self-Rating Depression Scale, which is a ten-item scale adapted from the original 20-item instrument (Zung, 1965). The PLHWUD were asked to report how often they felt the ten situations. The sample questions included “I feel hopeful about the future,” “I feel downhearted and blue,” and “I get tired for no reason.” Responses were categorized on a five-point Likert scale (from 1= “none of the time” to 5= “all of the time”). The overall score was generated by summing the responses to all items, with the positively worded ones being reversely coded (ranging from 10–50). A higher score indicated a higher level of depressive symptoms (Cronbach’s alpha = 0.82).

*HCV infection status* was measured by both medical record and self-report. Self-reported HCV infection status was documented by asking the question, “have you ever been told by a health professional that you have HCV?” At the same time, the study team members searched the participants’ medical records located in local hospitals, commune health centers, ART clinics, and MMT clinic. The earliest HCV-positive testing results and the corresponding date of testing were recorded. These data were merged with the survey data using a unique participant identification number. The review of medical records was conducted upon the study participants’ written informed consent.

Other collected information included participants’ *demographic characteristics* (gender, age, marital status, years of education, employment status, annual family income, and years of heroin use) and *HIV confirmation date* (verified by HIV testing records located in the Provincial AIDS offices).

### Statistical analysis

Descriptive statistics and frequencies were used to summarize demographic characteristics as well as years of drug use and years since HIV diagnosis. Agreement (Cohen’s Kappa) between the self-reported and medical record of HCV status was calculated to report consistency. To examine whether perceived barriers to seeking healthcare were associated with depressive symptoms and variation in HCV reports, we used a linear mixed-effects regression model with a commune-level random effect to account for multiple participants within the same commune. The fixed-effects included in the model were HCV status based on the medical record (yes vs. no), HCV status based on the self-report (yes vs. no), 2-way interaction of these two main factors, depressive symptoms, and the pre-selected background characteristics. An exploratory analysis was conducted to further explore whether the association between perceived barriers and depressive symptoms differed by PLHWUD’s variations of HCV reports using a 3-way interaction model (i.e., Extended the above model to a 3-way model). All statistical analyses were conducted using the SAS System for Windows version 9.4 (SAS Institute Inc., Cary, North Carolina), and graphs were generated using R (R core team, 2019).

## Results

Table 1 presents the sample characteristics of PLHWUD. The average age was 40.6 years old ( $SD = 5.2$ ), and more than half of them were married or living with partners (52.5%). The majority of the participants (71.3%) had between seven and 12 years of education (completed some junior/senior high school education). Approximately three-quarters (75.7%) reported having a part-time or full-time job, and 66.8% reported an annual family income of 100 million VND (equivalent to 4,294 USD) or less. The average years of heroin use were about eight years, with 26.5% of more than ten years of heroin use. Twenty percent of PLHWUD had been diagnosed with HIV infection for more than ten years.

Regarding HCV-infection status, 82 PLHWUD (45.3%) self-reported having been informed of HCV infection by health professionals. Fifty-two percent of the participants had positive HCV testing results on their medical records. The estimated Kappa statistics was 0.43 (95% CI: 0.31, 0.55), indicating a fair level of agreement between the self-report and medical record of HCV status (Fleiss, 1981). Fifty-six PLHWUD (30.9%) had both medical record-verified and self-reported HCV-positive status. Among the 64 (35.4%) PLHWUD who had discrepant self-report and medical record results, 38 (21.0%) had HCV infection indicated in the medical records but they self-reported to be HCV-uninfected, and 26 (14.4%) self-reported to have HCV infection but no positive testing result was found in the medical records. The remaining 61 PLHWUD (33.7%) had no positive testing results and self-reported to have no HCV infection.

Results from the mixed-effects regression analysis (Table 2) indicated that the level of depressive symptoms was positively associated with the perceived level of barriers to seeking healthcare (estimate = 0.17,  $SE = 0.04$ ,  $P < .0001$ ). PLHWUD with an HCV infection confirmed by both medical records and self-report had a significantly lower level of barriers to seeking healthcare than those with discrepant results on HCV infection (estimated difference =  $-1.59$ ,  $SE = 0.71$ ,  $P = 0.027$ ). Figure 1 shows the estimated associations between barriers to seeking healthcare and depressive symptoms for (a) PLHWUD with consistent medical records and self-reports and (b) PLHWUD with discrepant reporting of HCV status. The relationship between depressive symptom and barriers to seeking healthcare was only significant among those with discrepant HCV results (estimate = 0.17,  $SE = 0.06$ ,  $P = 0.007$ ).

## Discussion

This study showed that a considerable proportion of the participants had inconsistent self-reported and medical record-verified HCV status. The finding could be interpreted at the patient-, provider- and healthcare system- levels. At the patient-level, self-reported HCV status may not be accurate due to lack of HCV knowledge and awareness. WHO estimated that only a small fraction of people infected with chronic hepatitis were aware of their disease status (Singh, 2018). In the context of HIV, PLHWUD's attention to HCV and other comorbidities is likely to be diverted by HIV due to the tremendous burden of HIV poses on health and quality of life (Edlin, 2004). From the service providers' perspective, it was well-documented that patient-provider communication plays a critical role in HCV treatment

initiation, medication adherence, and clinical outcomes (Rogal et al., 2016; Salmon-Ceron et al., 2012). Without a clear and adequate explanation from the service provider, the patients may not be able to distinguish the type of laboratory testing they have received or understand the meaning and consequences of positive results (Lin et al., 2019). Fear of stigma and discrimination from providers have driven PLHWUD to seek HCV testing in private sectors using pseudo names, which explains the absence of HCV diagnosis in the medical records. At the system-level, the HCV testing and treatment services in Vietnam are centralized in high-level hospitals in major cities (VMOH, 2010, 2016, 2017), and patients sometimes have to pay out-of-pocket for HCV testing because of the shortages in health insurance coverage. Our findings point to a clear need for more secured government funding and resources to scale-up HCV screening programs. Service providers should be trained to inform patients of their HCV status more explicitly. Integrated harm reduction, HIV, and HCV care have also been recommended as an actionable measure to upturn HCV testing and care for PLWHUD (Broeckeaert & Challacombe, 2015).

We observed that PLHWUD with inconsistent self-reported and medical recorded HCV status reported a higher level of barriers to seeking healthcare. The finding suggests that the group with HCV infection confirmed by both self-report and medical record are perhaps the patients who have successfully gained access to local health services. At the same time, they might have higher health literacy to apprehend various diseases. These factors justify the lower level of perceived barriers to seeking healthcare among this group. The healthcare gap, however, is wider among those who have inconsistent medical record and self-report. As discussed earlier, the unawareness of HCV infection in spite of documented positive result requires enhanced patient education and communication efforts from service providers. For those who had self-awareness of HCV infection but no medical record, we speculate that their HCV infection could have been detected in other locations where they reside as migrant workers, or they were not tested or engaged in treatment in local facilities. These issues could be addressed by strengthening the referral system and medical data consolidation across the country so that PLHWUD and other hard-to-reach could be linked to needed services in a timely manner.

Consistent with previous studies, this study found that mental health plays a role in PLHWUD's perceived barriers to seeking healthcare (Iversen et al., 2015; Souliotis et al., 2017). This association might be explained patients' psychological stressors and inability to receive care, as well as providers' entrenched beliefs about mental illness as a clinical contraindication to treatment commencement (Hepworth et al., 2013). Taking one step further, we observed that the association between depressive symptoms and barriers to seeking healthcare was particularly significant among the group with inconsistent reports. Future studies addressing PLHWUD's healthcare-seeking challenges should pay attention to the role of mental health in HCV diagnosis and service utilization. We echo other researchers in the integration of psychological support services within the existing HIV care and infectious disease treatment systems to facilitate healthcare access and utilization for PLHWUD (Chu et al., 2016; Wang et al., 2016).

Findings of this study should be interpreted within the context of limitations. First, the study findings may not be generalizable to other areas with different HCV screening and treatment



policies. Secondly, the study participants were recruited from local healthcare agencies that provide HIV or harm reduction services. We expect the level of healthcare-seeking barriers would be underestimated among this study sample as compared to the PLHWUD in general. Third, the cross-sectional design limited our ability to make any causal inferences. Despite the limitations, the findings in this study provided several recommendations for HCV prevention and care among PLHWUD. Regular HCV testing and consistent result notification are the vital first steps to improve access to care. HCV awareness campaign and education programs should be offered to the population at risk. Training programs on the frequencies of HCV testing, result notification, and referral mechanisms should be provided to service providers in primary care, harm reduction, and HIV treatment settings. Integration of HCV and mental health services, as well as decentralization of these services to community-based healthcare settings, are also recommended to narrow the service gap for PLHWUD.

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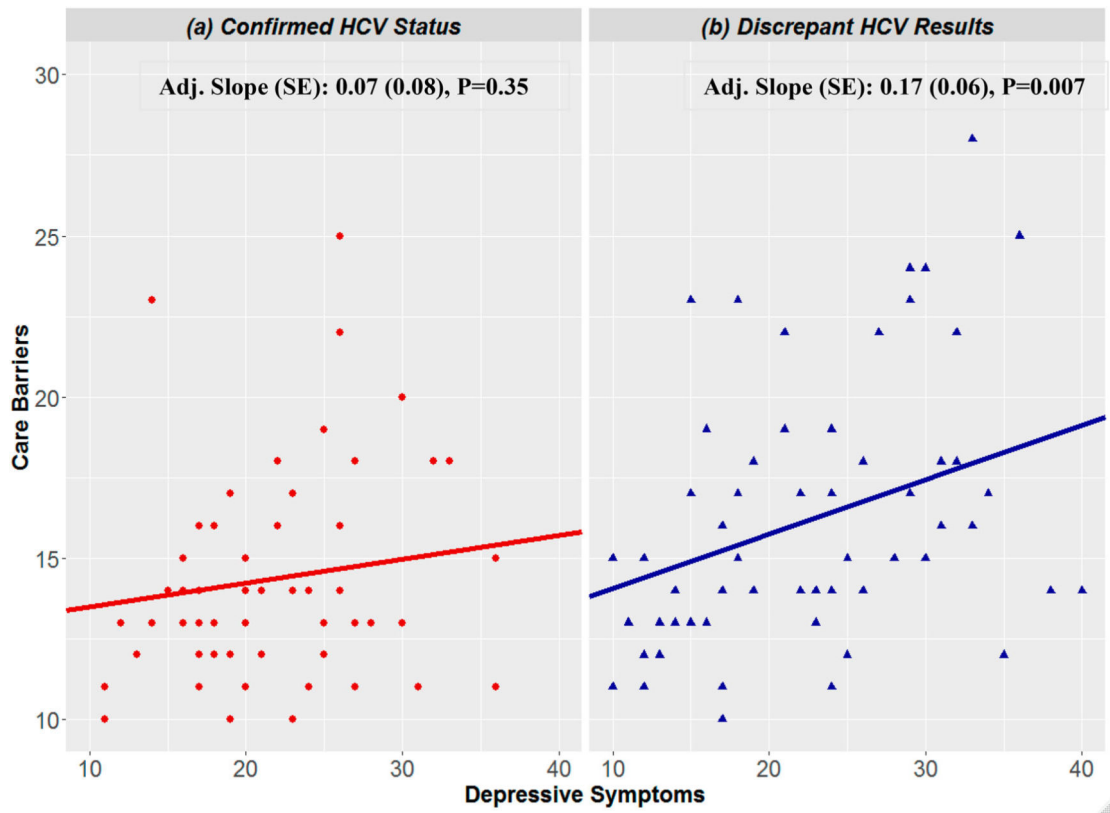


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**Figure 1.** Adjusted associations between barriers to seeking healthcare and depressive symptoms by PLHWUD’s HCV reports: (a) consistent HCV results and (b) discrepant HCV results between their self-reported and medical records.

**Table 1.**

Sample characteristics of people living with HIV who use drugs.

	N (%)
Age (years)	
35	26 (14.4)
36–45	125 (69.1)
46	30 (16.5)
Mean±SD	40.6 ± 5.2
Married/living with partners	95 (52.5)
Education (years)	
6	39 (21.5)
7–12	129 (71.3)
13	13 (7.2)
Mean ± SD	8.6 ± 3.3
Currently working	137 (75.7)
Annual family income (million VND)	
50	47 (26.0)
>50–100	74 (40.9)
> 100	60 (33.2)
Years of heroin use	
5	78 (43.1)
6–10	55 (30.4)
>10	48 (26.5)
Mean ± SD	8.4 ± 6.5
Years since HIV diagnosis	
5	77 (45.5)
6–10	67 (37.0)
>10	37 (20.4)
Mean ± SD	6.8 ± 4.3
Positive HCV Results	
Medical record	94 (52.2)
Self-report	82 (45.3)
Barriers to seeking healthcare, Mean ± SD	15.2 (3.7)

Note. Total sample size = 181, with only one female participant.

SD: Standard deviation.

**Table 2.**

Mixed-Effects Regression Results on Barriers to Seeking Healthcare.

	Estimate (SE)	P-value
Age (years)		
35	1.290 (0.986)	0.193
36–45	0.486 (0.726)	0.505
46	REF	
Married/living with partners	−0.014 (0.600)	0.982
Education (years)		
6	−0.456 (1.146)	0.692
7–12	−0.012 (1.004)	0.991
13	REF	
Currently working	−0.093 (0.657)	0.888
Annual family income (million VND)		
50	0.357 (0.803)	0.657
>50–100	−0.141 (0.649)	0.829
> 100	REF	
Years of heroin use		
5	−0.814 (0.716)	0.257
6–10	−0.932 (0.712)	0.193
>10	REF	
Years since HIV diagnosis		
5	−0.131 (0.727)	0.857
6–10	−0.249 (0.736)	0.736
>10	REF	
Depressive Symptoms	0.173 (0.041)	<.0001
Comparisons of Interest		
Confirmed HCV vs. discrepant HCV results	−1.591 (0.711)	0.027
Confirmed HCV vs. no HCV report	−0.743 (0.685)	0.281