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Original Article

Risky sexual practices and hepatitis C viremia among HIV-positive men who have sex with men in Taiwan



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Introduction

After the introduction of highly effective direct-acting antivirals (DAAs) against hepatitis C virus (HCV), the World Health Organization (WHO) announced its first global target of combating viral hepatitis in 2016.¹ The goal was to eliminate viral hepatitis as a major public health threat by 2030, aiming to reduce the new diagnoses of viral hepatitis by 90% and hepatitis-related deaths by 65%.²

Since 2000, increasing incidences of HCV infection have been observed in the Europe, the United States, Australia and several Asian-Pacific countries.^{3,4} However, rather than parenteral exposures to infected blood through injection drug use, use of contaminated medical equipment, or transfusion. HCV infection during this emerging epidemic has been demonstrated to transmit through sexual contacts, especially among men who have sex with men (MSM).^{3,5} The detection of a high amount of HCV in the rectal fluid, semen and nasal fluid from HCV-viremic patients, particularly those with HIV coinfection, implies that unprotected, traumatic sexual contacts may increase the risk of HCV acquisition.^{6,7} Several studies among people living with HIV (PLWH) who were MSM with HCV coinfection also found strong association between recent HCV acquisition and concomitant diagnosis of other sexually transmitted infections (STIs) such as syphilis.^{8–10}

With the expanding access to DAA treatment, studies in Australia, Europe, Egypt and Taiwan have demonstrated significant declines of HCV incidence and prevalence among different key populations.^{11–18} However, sexually-transmitted HCV reinfections after successful treatment with DAAs might hinder our progress toward HCV

elimination, especially among high-risk key populations. While the significance of HCV reinfections may vary in different regions and populations, $^{19-27}$ recent studies have revealed a high annual rate of HCV reinfection of around 4.0–9.8% among PLWH in Taiwan; $^{25-28}$ moreover, a recent study in Taiwan revealed that HCV reinfections accounted for 82.8% of new HCV infections in 2021, despite a significant reduction of HCV infection with the implementation of DAA treatment program. 18 Of note, certain risky sexual behaviors were found to be independently associated with HCV reinfections. 27

The increases of sexually-transmitted HCV infections, and possibly reinfections, might become an important obstacle when it comes to tackling the HCV epidemics, which warrant more efforts on risk reduction and public health interventions. Many studies in the United States, Switzerland, France and the Netherlands have linked chemsex, slamming, unprotected anal intercourse, fisting, sharing sex toy, or having multiple sex partners to HCV infections among MSM.²⁹⁻³⁴ Recently, the expansion of the users receiving pre-exposure prophylaxis (PrEP) against HIV transmission and the campaigns of "undetectable equals untransmissible" also raise concerns about behavioral risk compensation.³⁵ However, the risk behaviors associated with sexually-transmitted HCV infections were seldomly investigated systemically in Asian-Pacific region. Understanding the modifiable behaviors associated with HCV viremia might help mitigate the risks among key populations in the region. In this study, we conducted face-to-face questionnaire interviews aiming to identify risky behavioral factors among PLWH who were MSM and underwent regular follow-up for occurrences of HCV viremia in Taiwan.

Materials and methods

Study design and population

In this single-center study, we performed a cross-sectional survey with face-to-face questionnaire interviews to obtain information on the sexual practices among PLWH who participated in a follow-up study to detect HCV viremia. In this study, PLWH who were aged 20 years or older and at high risk of acquiring HCV infection were enrolled for monitoring of HCV viremia every 12 weeks with the use of three-stage pooled-plasma HCV RNA testing.³⁶ The study included PLWH who met at least one of the following criteria: (1) any elevation of liver aminotransferases in the past 6 months; (2) acquisition of STIs in the past 6 months; or (3) having achieved sustained virologic response 12 weeks off-therapy (SVR12) with DAA or spontaneous clearance of HCV viremia. A case record form was used to collect information from electronic medical records on the clinical characteristics of the participants. including previous HCV viremia and treatments, plasma HIV RNA load (PVL), CD4 cell count, and use of combination antiretroviral therapy.

All eligible PLWH who self-identified themselves as MSM underwent face-to face questionnaire interviews by a trained study nurse at enrolment. During the interviews, information regarding the demographics of participants, sexual history, sexual preferences, medical history of STI in the past 12 months, personal experience with using recreational drugs or sexualized drugs was collected. The details of the questionnaire used, courtesy of Professor Jürgen K. Rockstroh, Department of Medicine I, University of Bonn, Bonn, Germany, are attached in the supplementary material. The information obtained in the interviews was analyzed and linked to the results of HCV RNA testing to determine potential association between high-risk behaviors and HCV viremia. The study was approved by the Research Ethics Committee of National Taiwan University Hospital (registration number, 201904086RIPB), and all participants who participated in the questionnaire interview gave additional written informed consents.

Definition and detection of HCV viremia

The participants in the study underwent HCV RNA testing at the beginning of follow-up to determine their HCV status. Those who were HCV RNA-negative in the initial tests would be followed every 12 weeks with the use of three-stage pooled-plasma HCV RNA testing.³⁶ In brief, plasma samples from 20 PLWH were pooled together for HCV RNA testing, and subsequent testing of mini-pools consisting of 5 samples would be performed if the initial test was positive; testing of individual samples would be performed for the mini-pooled samples tested positive for HCV RNA. The detection of HCV RNA was performed using Roche Cobas® 6800 system (AmpliPrep HCV Test, v2.0, Roche, USA), with a detection limit of 15 IU/ml. The designated follow-up duration for each participant in the pooled-plasma study for occurrence of HCV viremia was 48 weeks. Although repeat enrolment was allowed in the pooled-plasma HCV RNA testing, we only included the participants who

participated in the study for the first time and completed the questionnaire interview.

In this study, the participants who tested positive for HCV RNA at enrolment and those who developed HCV viremia during follow-up were classified into the "HCV viremia" group, as compared to those who remained free of HCV viremia ("HCV aviremia" group) during follow-up. The clinical characteristics and risk behaviors were compared between these two groups, and the association between high-risk behaviors and presence of HCV viremia was analyzed using multivariate regression models.

Statistical analysis

The demographics, clinical characteristics, and the practice of risk behaviors were compared between those who acquired HCV during follow-up and those who remained free of HCV viremia during follow-up. Non-categorical variables were compared using Student's t test or Mann-Whitney U test, and categorical variables were compared using chi-square test or Fisher's exact test. In order to identify potential factors associated with HCV infections, we constructed a multivariable logistic regression model with different demographics, clinical characteristics and risky behaviors. To avoid potential multicollinearity between risk behaviors, we performed pair-wised analyses of all variables to identify possible correlations using Pearson or Spearman's correlation coefficients. A correlation coefficient greater than 0.4 were considered to have significant collinearity and only one of the two variables will be included in the model. After excluding variables with significant collinearity, a backward elimination process was used during the multivariable analyses, in which all possible demographic and clinical factors were included in the model initially and factors were removed from the model starting with factors with the largest p value. The process was repeated until all factors in the model had a p value of <0.2. All statistical analyses were performed using STATA software v.14.0 S/E (StataCorp LP, College Station, TX). All p values were two-sided.

Results

Characteristics of the participants

After excluding non-MSM participants and those who were not willing to participate in the questionnaire interview, 781 PLWH who were MSM underwent questionnaire interviews (Fig. 1). Twenty-six of these 781 (3.3%) PLWH tested positive for HCV RNA at baseline. During the followup, 755 PLWH who were HCV RNA-negative at baseline contributed to 604.12 person-years of follow-up (PYFU) and incident HCV viremia was diagnosed in 31 (4.1%) PLWH, resulting in an incidence rate of HCV viremia of 5.1 per 100 PYFU (95% confidence interval [CI], 3.3-6.9). If stratified by previous history of HCV viremia, the incidence of HCV viremia was 7.3 per 100 PYFU among those with previous HCV viremia, as compared to 4.5 per 100 PYFU among those without previous HCV viremia (p = 0.10). A total of 57 PLWH who tested positive for HCV RNA at enrolment or during follow-up were classified in the "HCV viremia" group



Figure 1. Study flow and inclusion criteria.

Abbreviations: PLWH, people living with HIV; MSM, men who have sex with men.

to compare with 724 PLWH in the "HCV aviremia" group (Fig. 1). In the HCV-viremic group, 20 (35.1%) PLWH had HCV reinfections and 37 (64.9%) had the first episodes of HCV infection.

The baseline clinical characteristics of all participants are shown in Table 1. Most participants enrolled in the study were young MSM receiving combination antiretroviral therapy and having achieved good control of HIV. As compared to HCV-aviremic participants, HCV-viremic participants were significantly younger (33 vs 36 years, p = 0.01) and were more likely to have elevated aminotransferases in the past 6 months (22.8% vs 8.3%, p < 0.001).

Comparisons of high-risk behaviors between HCVviremic and HCV-aviremic groups

The self-reported risk behaviors for the two groups in the past 12 months are shown in Table 2. Both groups reported high rates of having engaged in high-risk sexual behaviors. Compared with HCV-aviremic participants, HCV-viremic participants had more sex partners (having more than 5 sex partners in past 12 months, 34.6% vs. 21.4%, p = 0.02), were more likely to participate in group sex (40% vs. 17.6%, p < 0.001), and were more likely to have condomless receptive anal sex (67.9% vs. 52.5%, p = 0.03), as well as condomless insertive anal sex (66.0% vs. 49.0%, p = 0.02).

Overall, 38.9% (303/778) of the participants reported having had use of recreational drugs in the past 12 months; however, HCV-viremic participants were significantly more likely than HCV-aviremic participants to have used recreational drugs (68.4% vs 36.6%, p < 0.001). Of note, 91.4% of

the participants who had used recreational drugs reported having "chemsex" (86.8% in the HCV-viremic group vs. 92.1% in the HCV-aviremic group, p = 0.28). In terms of the route of administration, 34.4% (104/302) of MSM who used recreational drugs reported ever having injected the illicit drugs, but the difference between HCV-viremic and the HCV-aviremic groups was not statistically significant (52.8% vs. 33.5%, p = 0.18). Only 5 of these 104 (4.8%) participants who injected drugs reported ever sharing their injection equipment, and the proportion was significantly higher in HCV-viremic group than HCV-aviremic group (18.8% vs. 2.3%, p = 0.03). We also compared the risky behaviors among different subgroups of HCV-viremic patients, but no statistically significant differences were identified (Supplementary Table S1).

Multivariate analysis

After excluding factors with significant collinearity, univariate and multivariate analysis were performed to identify potential factors associated with HCV viremia and the results are shown in Table 3. In univariate logistic regression, younger age (odds ratio [OR] per 1-year increase, 0.96; 95% CI 0.92–0.99), having used recreational drugs (OR, 2.92; 95% CI 1.67–5.11), having participated in group sex (OR, 3.12; 95% CI, 1.76–5.53), and having had condomless receptive anal intercourse (OR, 1.92; 95% CI, 1.06–3.49) were significantly associated with HCV viremia. After adjustments made in multivariable logistic model, use of recreational drugs (adjusted OR [aOR], 2.14; 95% CI, 1.16–3.96), having participated in group sex (aOR, 2.35; 95% CI 1.24–4.40) and having had condomless receptive

Baseline characteristics	All participants	HCV-viremic	HCV-aviremic	<i>p</i> -value
	N = 781	N = 57	N = 724	
Age, median (IQR), years	36 (31-43)	33 (29–39)	36 (31–43)	0.01
Highest education level				
University or above, n (%)	626 (80.2)	49 (85.7)	577 (79.7)	0.25
Inclusion criteria for				
pooled-plasma HCV RNA testing				
Recent STIs \leq 6 months, n (%)	603 (77.2)	38 (66.7)	565 (78.0)	0.05
Prior HCV infections, n (%)	205 (26.3)	20 (35.1)	185 (25.6)	0.11
Elevated aminotransferases, n (%)	73 (9.4)	13 (22.8)	60 (8.3)	<0.001
Ongoing ART, n (%)	781 (100)	57 (100)	724 (100)	_
Plasma HIV RNA load, median (IQR),	1.3 (1.3–1.3)	1.3 (1.3–1.3)	1.3 (1.3–1.3)	0.26
log ₁₀ copies/ml				
Plasma HIV RNA <50 copies/mL, n (%)	717 (91.8)	50 (87.7)	667 (92.1)	0.56
CD4 counts before enrolment,	614 (452–794)	582 (403-721)	622 (460-795)	0.12
median (IQR), cells/mm ³				
Any STIs 12 months prior to enrolment, n (%)	494 (63.3)	32 (56.1)	462 (63.8)	0.25
Syphilis	453 (58.0)	28 (49.1)	425 (58.7)	0.16
Gonorrhea	50 (6.4)	7 (12.3)	43 (5.9)	0.06
Chlamydia	38 (4.8)	2 (3.5)	36 (5.0)	0.71
Genital or anal herpes	5 (0.6)	0 (0)	5 (0.7)	0.86
Genital or anal warts	38 (4.8)	3 (5.3)	35 (4.8)	0.89
HCV genotypes, n (%)				
Genotype 1a	NA	12 (21.1)	NA	
Genotype 1b	NA	14 (24.6)	NA	
Genotype 2	NA	7 (12.3)	NA	
Genotype 6	NA	23 (40.4)	NA	

Table 1	Baseline characteristics of HI	/-positive men who h	have sex with men	participated in the	questionnaire interview.
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Abbreviations: ART, antiretroviral therapy; HCV, hepatitis C virus; IQR, interquartile range; STI, sexually transmitted infection.

anal intercourse (aOR, 1.97; 95% CI 1.07–3.62) remained significantly associated with HCV viremia.

To further investigate the potential difference of behavioral risk factors among PLWH with and those without previous HCV viremia, we also attempted to split the multivariate model according to the previous history of HCV viremia among our participants. Interestingly, HCV viremia was associated with recreational drug use (aOR, 3.62; 95% CI, 1.20–10.9) and receptive condomless anal sex (aOR 3.65; 95% CI, 1.003–13.3) among PLWH with previous HCV viremia. On the other hand, participation in group sex was associated with HCV viremia among those without prior HCV viremia (aOR, 3.74; 95% CI, 1.75–7.97), but not among those who had previous HCV viremia.

Discussion

In this cross-sectional survey of high-risk sexual practices and the use of recreational drugs among 781 Taiwanese PLWH who were MSM, we found that 57 (7.3%) were HCV viremic at baseline or during the observation with the use of three-stage pooled-plasma HCV RNA testing every 12 weeks. Participants in the study reported a high rate of having used recreational drugs and engaged in high-risk sexual practices. In multivariable analyses, high-risk behaviors, including use of recreational drugs, group sex and condomless receptive anal intercourse, were linked to the presence of HCV viremia among our participants.

Since 2000, viral hepatitis C have emerged as an STI among MSM in the Europe, the United States, Australia and several Asian-Pacific countries.^{3,4} However, behavioral risk factors related to HCV acquisition in this key population were seldomly investigated in Asia-Pacific region. Some of the behavioral risk factors identified in our study were similarly reported in previous studies in Western countries. For example, having had condomless receptive anal intercourse and use of recreational drugs have been repeatedly linked with HCV infection in studies from Switzerland, the United States, and France.^{29,30,33,34,37} Having had group sex was strongly associated with HCV viremia in both our study and another report in Spain.³⁷ However, other risk factors identified in our study were slightly different from those in previous studies. Survey in France and Spain identified being fisted and sharing sex toys in the past 12 months as potential risk factors, which were not demonstrated in our study.^{33,37} The discrepancies observed might be partly explained by how different sexual acts were preferred by MSM in different regions. For example, only 1.6% of MSM in our study had reported being fisted as compared to 16.7% in the French survey.³³ Furthermore, our study included only MSM who were at high risk for HCV acquisition. The purpose was to identify the risk behaviors among this key population for future interventions, and therefore the results might be different from other studies enrolling all HIV-positive MSM.

Our study reported a high rate of recreational drug use (38.9% of all participants). Although this proportion was

Table 2	Reported high-risk	behaviors by the	participants in the	past 12 months.
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Baseline characteristics	All participants N = 781	HCV-viremic N = 57	HCV-aviremic $N = 724$	<i>p</i> -value
Sexual practices or behaviors in the past 12 mor	oths			
Number of male sex partners				0.02
0, n (%)	89/755 (11.8)	2/55 (3.6)	87/700 (12.4)	
1–5	497/755 (65.8)	34/55 (61.8)	463/700 (66.1)	
>5	169/755 (22.4)	19/55 (34.6)	150/700 (21.4)	
Ever having had group sex, n (%)	146/759 (19.2)	22/55 (40.0)	124/704 (17.6)	<0.001
Ever having had condomless insertive anal sex, n (%)	346/689 (50.2)	33/50 (66.0)	313/639 (49.0)	0.02
Ever having had condomless receptive anal sex, n (%)	379/707 (53.6)	36/53 (67.9)	343/654 (52.5)	0.03
Anal bleeding after receptive anal sex, n (%)	151/754 (20.0)	12/55 (21.8)	139/699 (19.9)	0.73
Anal douching before anal sex, n (%)	469/739 (63.5)	36/52 (69.2)	433/687 (63.0)	0.37
Ever having performed rimming, n (%)	260/756 (34.4)	22/54 (40.7)	238/702 (33.9)	0.31
Ever having been fisted, n (%)	12/761 (1.6)	0/54 (0)	12/707 (1.7)	0.34
Ever having had anorectal problems, n (%)	238/750 (31.7)	16/55 (29.1)	222/695 (31.9)	0.66
Ever having shared dildo or anal sex toy, n (%)	86/743 (11.6)	10/54 (11.6)	76/689 (11.0)	0.10
Having ≥ 1 HIV-positive sex partners, n (%)	529/743 (71.2)	43/53 (81.1)	486/690 (71.2)	0.10
Recreational drug use in the past 12 months				
Reported recreational drug use, n (%)	303/778 (38.9)	39/57 (68.4)	264/721 (36.6)	<0.001
Ever having had "chemsex" ^a , n (%)	256/280 (91.4)	33/38 (86.8)	223/242 (92.1)	0.28
Ever having shared snorting equipment, n (%)	220/291 (75.6)	28/37 (75.7)	192/254 (75.6)	0.99
Ever having Injected recreational drugs ("Slamming"), n (%)	104/302 (34.4)	16/39 (52.8)	88/263 (33.5)	0.15
Ever having shared injection equipment, n (%)	5/104 (4.8)	3/16 (18.8)	2/88 (2.3)	0.03

^a "Chemsex" is defined as having sexual contact while using recreational drug simultaneously. Abbreviations: MSM, men who have sex with mem.

likely overestimated as our study included MSM who were at higher risk for HCV infection, we believed the high rate of recreational drug use still reflected the growing epidemic of sexualized drug use among Taiwanese MSM. Overall, 91.4% of MSM who had used recreational drug reported having chemsex. Using sexualized drugs during intercourse or parties may result in impaired judgement and reduce the adherence to condom use; or it could increase the threshold of pain, which may result in more trauma or injuries during sexual intercourse, and therefore facilitate transmission of various STIs, including viral hepatitis C. In our survey, among MSM who used recreational drugs, a significant proportion (34.4%) reported ever having slamming during the questionnaire interview. However, unlike the results from other European studies, slamming was not associated with HCV viremia in our study, which might be explained by fact that a low rate of sharing needles (4.8%) among our participants who injected recreational drugs. However, it is worth noting that, despite this low rate of needle sharing in our cohort, we still observed a high incidence rate of HCV infection (5.1 cases per 100 PYFU). Moreover, sharing needles or diluent were still more frequent among with HCV-viremic group than HCV-aviremic group in our study. While our findings suggested that unprotected mucosal contact during highrisk sexual intercourse might be a new driving factor of the HCV epidemics among young MSM in Taiwan, vigilant surveillance of parenteral route of HCV transmission remained important for HCV prevention.

Our study has important clinical and public health implications when Taiwan has committed to HCV elimination by 2025.³⁸ MSM, particularly PLWH, continue to have higher rates of HCV infection and reinfection despite the implementation of free-of-charge access to HCV testing and DAA treatment program in Taiwan.^{18,25,27,28} Recent published studies suggesting the annual incidence of HCV reinfection among Taiwanese PLWH ranged from 4.0 to 9.8%, depending on the observed populations.^{18,25,27,28} Similar studies in North America and Europe also suggested high-risk MSM being the most affected subpopulation in the era of DAA.^{37,39-41} The findings of our study suggest that this subpopulation is unlikely to benefit from traditional harm reduction programs for people who inject drugs, in which clean injection equipment is provided; instead, information, education and communication for HCV are needed to promote the awareness of HCV being a sexually-transmitted as well as parenterallytransmitted viral hepatitis among MSM. Our study also suggested the risk behaviors associated with HCV acquisition might be different among PLWH with or those without previous HCV infection in Taiwan. However, further studies are warranted to confirm or explain these findings.

Our study had several limitations and the results should be interpreted with necessary caution. First, our questionnaire interview only included those who were at highrisk for HCV transmission. In this study, the incidence rate of HCV viremia among these high-risk MSM was 5.1 per 100 PYFU. Our previous survey suggested that the risk for HCV

Risk factors	Univariate analysis	Multivariate analysis
Age, per 1-year increase	0.96 (0.92–0.99) ^a	0.96 (0.93–1.003)
Being bisexual	1.86 (0.54-6.43)	
Having bachelor's degree of above	1.56 (0.72-3.37)	
History of STIs within 6 months	0.56 (0.32-1.00)	
Prior HCV infection	1.57 (0.89–2.78)	
Recreational drug u se within past 12 months	2.92 (1.67–5.11) ^a	2.14 (1.16-3.96) ^a
Group sex within past 12 months	3.12 (1.76–5.53) ^a	2.35 (1.26-4.40) ^a
Receptive condomless anal intercourse within past 12 months	1.92 (1.06–3.49) ^a	1.97 (1.07–3.62) ^a
Rimming within past 12 months	1.34 (0.76–2.36)	
Sharing sex toys during intercourse within past 12 months	1.83 (0.89–3.79)	
Anal bleeding after anal intercourse within past 12 months	1.12 (0.58–2.19)	
Having HIV-positive sex partners	1.80 (0.89-3.66)	

Table	3	Univariate	and	multivariable	logistic	regression
model	for	risk factors	asso	ciated with H	CV virem	nia.

^a Statistically significant.

Abbreviations: HCV, hepatitis C virus; STI, sexually transmitted infections.

viremia was low to negligible (0 per 100 PYFU) among MSM who did not meet the three inclusion criteria for pooledplasma HCV RNA testing.³⁶ Therefore, the AOR for each risky behavior in our study might be smaller as compared with those of other studies including all HIV-positive MSM regardless of risky behaviors. Second, we interviewed the participants regarding their high-risk behaviors in the past 12 months at the enrolment of study; however, it was not clear whether these behaviors remained unchanged and affected the risk for contracting HCV similarly during the follow-up. Third, the self-reported estimations of various risk behaviors were also subjected to recall bias and the participants might be reluctant to answer some questions that were deemed sensitive. Moreover, some of the risky sexual behaviors might be intercorrelated in this survey. For example, those who participated in group sex were likely to have more sexual partners. Therefore, including all behavioral variables in the multivariable analysis would create significant multicollinearity and affect the interpretation of model. We performed a pair-wised analyses of all behavioral variables to identify possible correlations using Pearson or Spearman's correlation coefficients. In the

event of significant correlation, only one of the intercorrelated variables will be used in the model. Therefore, some of the behavioral variables were excluded in this step and were not evaluated in the logistic regression models (see Figure S1 for the results of pair-wised correlation coefficients).

In conclusion, our study found that use of recreational drugs, group sex and condomless receptive anal intercourse were associated with occurrences of HCV viremia among high-risk HIV-positive MSM in Taiwan. While a high proportion of participants reported having used recreational drugs and slamming, sharing needles was an infrequent behavior among our participants. These findings further underline the importance of preventing unprotected sexual encounters as the key to HCV harm reduction among MSM in Taiwan.

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Declaration of competing interest

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References

- 1. Schlabe S, Rockstroh JK. Advances in the treatment of HIV/HCV coinfection in adults. *Expet Opin Pharmacother* 2018;**19**(1): 49–64.
- 2. World Health Organization. Global health sector strategy on viral hepatitis, 2016–2021: towards ending viral hepatitis. 2016.
- 3. Bradshaw D, Matthews G, Danta M. Sexually transmitted hepatitis C infection: the new epidemic in MSM? *Curr Opin Infect Dis* 2013;26(1):66–72.
- 4. Ho SY, Su LH, Sun HY, Huang YS, Chuang YC, Huang MH, et al. Trends of recent hepatitis C virus infection among HIV-positive men who have sex with men in Taiwan, 2011–2018. *EClinicalMedicine* 2020;24:100441.
- Danta M, Brown D, Bhagani S, Pybus OG, Sabin CA, Nelson M, et al. Recent epidemic of acute hepatitis C virus in HIV-positive men who have sex with men linked to high-risk sexual behaviours. *AIDS* 2007;21(8):983–91.
- 6. Chromy D, Schmidt R, Mandorfer M, Lang GF, Bauer D, Schwabl P, et al. Hepatitis C virus RNA is commonly detectable

in rectal and nasal fluids of patients with high viremia. *Clin Infect Dis* 2020;**71**(5):1292–9.

- 7. Turner SS, Gianella S, Yip MJS, van Seggelen WO, Gillies RD, Foster AL, et al. Shedding of hepatitis C virus in semen of human immunodeficiency virus-infected men. *Open Forum Infect Dis* 2016;3(2):ofw057.
- Sun HY, Chang SY, Yang ZY, Lu CL, Wu H, Yeh CC, et al. Recent hepatitis C virus infections in HIV-infected patients in Taiwan: incidence and risk factors. J Clin Microbiol 2012;50(3):781–7.
- 9. Gambotti L, Acute Hepatitis C Collaborating Group C. Acute hepatitis C infection in HIV positive men who have sex with men in Paris, France, 2001-2004. *Euro Surveill* 2005;10(5):3–4.
- 10. Götz HM, van Doornum G, Niesters HG, den Hollander JG, Thio HB, de Zwart O. A cluster of acute hepatitis C virus infection among men who have sex with men – results from contact tracing and public health implications. *AIDS* 2005; 19(9):969–74.
- Hajarizadeh B, Grebely J, Byrne M, Marks P, Amin J, McManus H, et al. Evaluation of hepatitis C treatment-asprevention within Australian prisons (STOP-C): a prospective cohort study. *Lancet Gastroenterol Hepatol* 2021;6(7):533-46.
- Shiha G, Soliman R, Mikhail NNH, Easterbrook P. Reduced incidence of hepatitis C in 9 villages in rural Egypt: progress towards national elimination goals. J Hepatol 2021;74(2): 303–11.
- Averhoff F, Shadaker S, Gamkrelidze A, Kuchuloria T, Gvinjilia L, Getia V, et al. Progress and challenges of a pioneering hepatitis C elimination program in the country of Georgia. J Hepatol 2020;72(4):680–7.
- 14. Garvey LJ, Cooke GS, Smith C, Stingone C, Ghosh I, Dakshina S, et al. Decline in hepatitis C virus (HCV) incidence in men who have sex with men living with human immunodeficiency virus: progress to HCV microelimination in the United Kingdom. *Clin Infect Dis* 2021;72(2):233–8.
- 15. Boerekamps A, van den Berk GE, Lauw FN, Leyten EM, van Kasteren ME, van Eeden A, et al. Declining hepatitis C virus (HCV) incidence in Dutch human immunodeficiency viruspositive men who have sex with men after unrestricted access to HCV therapy. *Clin Infect Dis* 2018;66(9):1360–5.
- 16. Doyle JS, van Santen DK, Iser D, Sasadeusz J, O'Reilly M, Harney B, et al. Microelimination of hepatitis C among people with human immunodeficiency virus coinfection: declining incidence and prevalence accompanying a multicenter treatment scale-up trial. *Clin Infect Dis* 2021;73(7):e2164–72.
- 17. Braun DL, Hampel B, Ledergerber B, Grube C, Nguyen H, Künzler-Heule P, et al. A treatment-as-prevention trial to eliminate hepatitis C among men who have sex with men living with human immunodeficiency virus (HIV) in the Swiss HIV cohort study. *Clin Infect Dis* 2021;73(7):e2194–202.
- **18.** Chen GJ, Ho SY, Su LH, Chang SY, Hsieh SM, Sheng WH. Hepatitis C microelimination among people living with HIV in Taiwan. *Emerg Microb Infect* 2022;**11**(1):1664–71.
- Lambers FAE, Prins M, Thomas X, Molenkamp R, Kwa D, Brinkman K, et al. Alarming incidence of hepatitis C virus reinfection after treatment of sexually acquired acute hepatitis C virus infection in HIV-infected MSM. *AIDS* 2011;25(17):F21–7.
- **20.** Martin TCS, Rauch A, Salazar-Vizcaya L, Martin NK. Understanding and addressing hepatitis C virus reinfection among men who have sex with men. *Infect Dis Clin* 2018;**32**(2):395–405.
- Ingiliz P, Martin TC, Rodger A, Stellbrink HJ, Mauss S, Boesecke C, et al. HCV reinfection incidence and spontaneous clearance rates in HIV-positive men who have sex with men in Western Europe. J Hepatol 2017;66(2):282-7.
- Martin TCS, Martin NK, Hickman M, Vickerman P, Page EE, Everett R, et al. Hepatitis C virus reinfection incidence and treatment outcome among HIV-positive MSM. *AIDS* 2013; 27(16):2551-7.

- 23. Ingiliz P, Wehmeyer MH, Boesecke C, zur Wiesch JS, Schewe K, Lutz T, et al. Reinfection with the hepatitis C virus in men who have sex with men after successful treatment with directacting antivirals in Germany: current incidence rates, compared with rates during the interferon era. *Clin Infect Dis* 2020;71(5):1248–54.
- 24. Hagan H, Jordan AE, Neurer J, Cleland CM. Incidence of sexually transmitted hepatitis C virus infection in HIV-positive men who have sex with men. AIDS 2015;29(17):2335–45.
- 25. Huang MH, Chang SY, Liu CH, Cheng A, Su LH, Liu WC, et al. HCV reinfections after viral clearance among HIV-positive patients with recent HCV infection in Taiwan. *Liver Int* 2019; 39(10):1860-7.
- **26.** Cheng CY, Ku SY, Lin YC, Chen CP, Cheng SH, Lin IF. Incidence and risk factors of reinfection with HCV after treatment in people living with HIV. *Viruses* 2022;14(2):439.
- 27. Chen GJ, Sun HY, Chang SY, Su LH, Chen YT, Hsieh SM, et al. Sexually-transmitted hepatitis C virus reinfections among people living with HIV in Taiwan: the emerging role of genotype 6. *Emerg Microb Infect* 2022;11(1):1227–35.
- 28. Liu CH, Sun HY, Peng CY, Hsieh SM, Yang SS, Kao WY, et al. Hepatitis C virus reinfection in people with HIV in taiwan after achieving sustained virologic response with antiviral treatment: the RECUR study. Open Forum Infect Dis 2022;9(8):ofac348.
- 29. Wandeler G, Gsponer T, Bregenzer A, Günthard HF, Clerc O, Calmy A, et al. Hepatitis C virus infections in the Swiss HIV Cohort Study: a rapidly evolving epidemic. *Clin Infect Dis* 2012; 55(10):1408–16.
- **30.** Witt MD, Seaberg EC, Darilay A, Young S, Badri S, Rinaldo CR, et al. Incident hepatitis C virus infection in men who have sex with men: a prospective cohort analysis, 1984–2011. *Clin Infect Dis* 2013;**57**(1):77–84.
- Tieu H Van, Laeyendecker O, Nandi V, Rose R, Fernandez R, Lynch B, et al. Prevalence and mapping of hepatitis C infections among men who have sex with men in New York City. *PLoS One* 2018;13(7):e0200269.
- 32. Schmidt AJ, Falcato L, Zahno B, Burri A, Regenass S, Müllhaupt B, et al. Prevalence of hepatitis C in a Swiss sample of men who have sex with men: whom to screen for HCV infection? BMC Publ Health 2014;14:3.
- 33. Vaux S, Chevaliez S, Saboni L, Sauvage C, Sommen C, Barin F, et al. Prevalence of hepatitis C infection, screening and associated factors among men who have sex with men attending gay venues: a cross-sectional survey (PREVAGAY), France, 2015. BMC Infect Dis 2019;19(1):315.
- 34. Vanhommerig JW, Lambers FAE, Schinkel J, Geskus RB, Arends JE, van de Laar TJW, et al. Risk factors for sexual transmission of hepatitis C virus among human immunodeficiency virus-infected men who have sex with men: a casecontrol study. Open Forum Infect Dis 2015;2(3):ofv115.
- 35. Hoornenborg E, Coyer L, Achterbergh RCA, Matser A, Schim van der Loeff MF, Boyd A, et al. Sexual behaviour and incidence of HIV and sexually transmitted infections among men who have sex with men using daily and event-driven pre-exposure prophylaxis in AMPrEP: 2 year results from a demonstration study. *Lancet HIV* 2019;6(7):e447–55.
- **36.** Sun HY, Chiang C, Huang SH, Guo WJ, Chuang YC, Huang YC, et al. Three-stage pooled plasma hepatitis C virus RNA testing for the identification of acute HCV infections in at-risk populations. *Microbiol Spectr* 2022;**10**(3):e0243721.
- 37. Martínez-Rebollar M, De La Mora L, Campistol M, Cabrera B, Bagué A, De Lazzari E, et al. Impact of sexualized substance use and other risk practices on HCV microelimination in GBMSM living with HIV: urgent need for targeted strategies. Results of a retrospective cohort study. *Infect Dis Ther* 2021;10(3):1253–66.
- **38.** Chen DS. Taiwan commits to eliminating hepatitis C in 2025. *Lancet Infect Dis* 2019;**19**(5):466–7.

- **39.** Newsum AM, Matser A, Schinkel J, Van Der Valk M, Brinkman K, Van Eeden A, et al. Incidence of HCV reinfection among HIV-positive MSM and its association with sexual risk behavior: a longitudinal analysis. *Clin Infect Dis* 2021;**73**(3): 460–7.
- 40. Young J, Rossi C, Gill J, Walmsley S, Cooper C, Cox J, et al. Risk factors for hepatitis C virus reinfection after sustained virologic response in patients coinfected with HIV. *Clin Infect Dis* 2017;64(9):1154–62.
- 41. Huang CF, Chen GJ, Hung CC, Yu ML. HCV micro-elimination for high-risk special populations. J Infect Dis 2023. https: //doi.org/10.1093/infdis/jiac446.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jmii.2023.01.006.