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Prevalence of HCV Infection Among People Experiencing Homelessness in Madrid, Spain

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Abstract

IMPORTANCE Hepatitis C virus (HCV) microelimination aims to detect and treat hidden infections, especially in at-risk groups, like people experiencing homelessness (PEH) with alcohol or drug use disorders. Point-of-care HCV RNA testing and peer support workers are crucial for identifying and preventing HCV infection among marginalized populations, contributing to overall elimination goals.

OBJECTIVE To assess risk factors, prevalence, and trends of active HCV infection among PEH in Madrid, Spain (2019-2023).

DESIGN, SETTING, AND PARTICIPANTS This cross-sectional study was conducted between 2019 and 2023 in PEH, defined as people who lacked a fixed, regular, and adequate night residence, screened on the street or in homeless shelters via mobile unit using rapid HCV antibody testing, followed by HCV-RNA testing in Madrid, Spain. Data were analyzed from January to June 2024.

MAIN OUTCOMES AND MEASURES Active HCV infection among PEH was the main outcome. Risk factors analyzed included being born outside of Spain, alcohol misuse, lacking financial income, benzodiazepine use, injection drug use (IDU; including nonactive IDU and active IDU within the last year), opioid substitution therapy participation, and sexual behavior patterns. Data were analyzed using logistic regression. *P* values were adjusted for multiple testing using the false discovery rate (*q*-values).

RESULTS A total of 4741 individuals were screened for HCV infection, of whom 2709 (mean [SD] age, 42.2 [12.7]; 1953 [72.2%] men) were PEH and included in analysis. A total of 363 PEH (13.4%) had test results positive for HCV antibodies, of whom 172 (47.4%) had test results positive for HCV-RNA, and 148 of these (91.9%) started HCV treatment. Overall, active HCV infection prevalence was 6.3%, and the main risk factors associated with active HCV infection included IDU, encompassing both nonactive IDU (adjusted odds ratio [aOR], 10.9; 95% CI, 6.1-19.4; $q < .001$) and active IDU in the last year (aOR, 27.0; 95% CI, 15.2-48.0; $q < .001$); a lack of financial income (aOR, 1.8; 95% CI, 1.1-2.9; $q = .03$); and alcohol misuse (aOR, 1.8; 95% CI, 1.3-2.6; $q = .008$). There was a significant decrease between 2019 and 2023 in active HCV infection prevalence across the entire population, from 7.2% to 3.4% ($P = .04$).

CONCLUSIONS AND RELEVANCE In this cross-sectional study of PEH in Madrid, IDU, lack of income, and alcohol misuse were primary risk factors associated with HCV infection. The significant decline in HCV rates observed across all risk groups during the study period suggests preventive policies were effective in reducing HCV prevalence among the homeless population.

Key Points

Question What are the risk factors associated with, prevalence of, and trends in active hepatitis C virus (HCV) infection in people experiencing homelessness (PEH) in Madrid, Spain, from 2019 to 2023?

Findings In this cross-sectional study of 2709 PEH, injection drug use (IDU), lack of financial income, and alcohol misuse were the main risk factors associated with active HCV infection. The prevalence of active HCV infection decreased significantly over the study period, from 7.2% to 3.4%.

Meaning These findings suggest that a more specific focus on risk groups (people with IDU, lack of financial income, and alcohol misuse) is necessary.

+ Supplemental content

Author affiliations and article information are listed at the end of this article.

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Introduction

Hepatitis C virus (HCV) spreads through blood contact, with 70% of acute infections becoming chronic. Chronic HCV infection can lead to cirrhosis, liver cancer, and death.[1] Currently, no HCV vaccine exists, but direct-acting antivirals (DAAs) cure more than 95% of people with HCV.[2,3] This advancement has drastically improved the management of disease globally.[4] To eliminate HCV by 2030, the World Health Organization (WHO) aims to increase prevention, screening, and treatment.[2] However, only 13% of people with HCV received treatment in 2020,[5] with low engagement among high-risk groups, like people with injection drug use (IDU), being a major challenge.[6]

Global HCV prevalence was 0.7% in 2020 (56.8 million people living with HCV), with only 5% of people with HCV initiating treatment.[7] While improved from 0.9% in 2015, current efforts may miss the WHO's 2030 elimination goal. Among 45 high-income countries, only 11 are on track, including Spain.[8] The prevalence of HCV infection decreased from 1.2% in 2013[9] to 0.22% in 2017 to 2018,[10] associated with a national hepatitis strategy since 2015,[11] unrestricted DAA access since 2017,[12] and microelimination efforts.[13-16]

People experiencing homelessness (PEH) are at high risk for HCV infection due to risky behaviors, such as IDU,[17-19] and barriers to health care, including discrimination and stigmatization.[5,20] Targeting HCV microelimination strategies to this population can contribute to WHO objectives.[6,21,22] While studies have examined HCV prevalence and risk factors among PEH in other countries,[23-26] there is a significant knowledge gap in Spain. Understanding these factors is crucial to improve HCV management and achieve elimination goals.[5] Point-of-care HCV testing and peer support workers can enhance screening, linkage to care, and prevention among PEH.[6,27-29] This study aimed to assess the associated risk factors, prevalence, and temporal trends associated with active HCV infection among PEH in Madrid, Spain, between 2019 and 2023.

Methods

This cross-sectional study was approved by the Research Ethics Committee of Hospital General Universitario Gregorio Marañón in 2018. Written informed consent was obtained from all participants, and the investigation adhered to the principles stated in the 1975 Declaration of Helsinki. This report was prepared following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

Study Population

This cross-sectional study was conducted retrospectively using data from an HCV screening intervention targeting PEH through a mobile unit and support vehicle. The intervention focused on hotspots, defined as locations frequented by individuals at high risk for contracting HCV infection, between February 1, 2019, and April 3, 2023, in Madrid, following a predefined schedule. The PEH eligible for inclusion in the study were those who lacked a fixed, regular, and adequate night residence, generally people who lived on the streets or in shelters in the last 6 months.

The mobile unit visited these hotspots systematically and periodically, including homeless shelters, social assistance institutions, public areas where PEH congregate, harm reduction, and migrant centers. HCV screening was offered to all individuals considered at high risk (eg, PEH with alcohol misuse, people with IDU, people who engage in sex work, and migrants), with participant recruitment conducted consecutively on a first-come, first-served basis. Only data related to adult PEH (aged ≥18 years), whether living on the street or in shelters, were analyzed for this study.

HCV Screening

As previously described,[28] epidemiological data collection and point-of-care HCV screening tasks were performed by a peer navigator/educator and a nurse. Capillary blood samples were collected from participants for screening purposes. Initially, samples were tested for HCV antibodies using the

OraQuick HCV Rapid Antibody Test (OraSure Technologies) to detect active HCV infection. Subsequently, participants with test results positive for HCV antibodies underwent HCV-RNA testing using the Xpert HCV Viral Load Fingerstick assay, processed within the GeneXpert System (Cepheid).

Data Collection

Participant data were collected through 10-minute interviews conducted in a private setting within the mobile unit. Electronic tablets were used for data collection, which management facilitated through REDCap software.[30] The collected data encompassed various sociodemographic characteristics (ie, age, gender identity, country of birth, education level, annual financial income [derived from personal means or government financial aid], migratory and housing status, and sexual orientation), IDU status (never and inactive or active within the last year), alcohol misuse (consumption of >50 g per day, equivalent to 3-4 cans of beer), details on sexual habits, benzodiazepine or opioid substitution therapy (OST) use, and study intervention date, time, and location. The interviews and HCV screening were conducted concurrently, followed by providing fundamental harm reduction information to prevent HCV infection acquisition.

Primary Outcome

The primary outcome of this study was the presence of an active HCV infection among PEH. The active HCV infection rate was calculated by considering all PEH who underwent HCV-RNA testing.

Risk Factors

Potential risk factors (patient characteristics) associated with active HCV infection included age older than 50 years, gender (women or men), calendar year in which HCV screening was performed, birth country (Spain or other [eg, Georgia, Morocco, Romania, Venezuela]), income, undocumented residency status (defined as residing in the country without the corresponding authorization from Spanish authorities), benzodiazepines, alcohol misuse, IDU (never, nonactive IDU, and active IDU within the last year), OST, and sexual intercourse behavior (never, condom use, and no condom use) over the last year. Participants self-reported all these risk factors during the interview process.

Statistical Analysis

Statistical analyses were performed using SPSS software version 24 (IBM) and Stata software version 17 (StataCorp), with graphical representations generated using Prism software version 9 (GraphPad). A multivariable logistic regression analysis was performed to evaluate risk factors associated with having an active HCV infection, providing adjusted odds ratios (aORs), 95% CIs, and *P* values. We forced all variables into the regression model and evaluated collinearity between risk factors, and those with a variance inflation factor less than 5 or Spearman correlation (*r*) less than 0.5 were kept in the model. This multivariable logistic regression estimated the prevalence of active HCV infection during the study period based on identified main risk factors. Pairwise comparisons between levels of risk factors were conducted using the *pwcompare* command in Stata. Moreover, univariate logistic regression was used to calculate the prevalence of active HCV infection by calendar year in which HCV screening was performed (independent variable) and its temporal linear trend throughout the study period (2019-2023). In all these analyses, when a participant was examined more than once, only 1 test per calendar year was included to provide information; that is, the unit of study was the tests performed.

All regression analysis tests were performed using 1000 bootstrap replications. Finally, a multiple testing correction was performed using the false discovery rate with the Benjamini and Hochberg procedure (*q*-value).[31] *P* and *q*-values less than .05 (2-tailed) were considered statistically significant. Data were analyzed from January to June 2024.

Results

Care Cascade

Of 4741 participants screened for HCV infection, 2726 (57.5%) were PEH, but only 2709 (99.4%) underwent HCV antibody testing (mean [SD] age, 42.2 [12.7]; 1953 [72.2%] men), and 175 of these individuals were studied more than once in different years. Among 2709 participants who underwent HCV antibody testing, 363 (13.4%) had positive test results, of whom 172 (47.4%) had test results positive for HCV-RNA (**Figure 1**). Among individuals with positive test results for HCV-RNA, 167 individuals (97.1%) received their test results and were offered linkage to treatment, of whom 161 (96.4%) accepted the linkage and attended an appointment at a hospital to initiate therapy. Of these 161 individuals, 148 (91.9%) started DAA treatment.

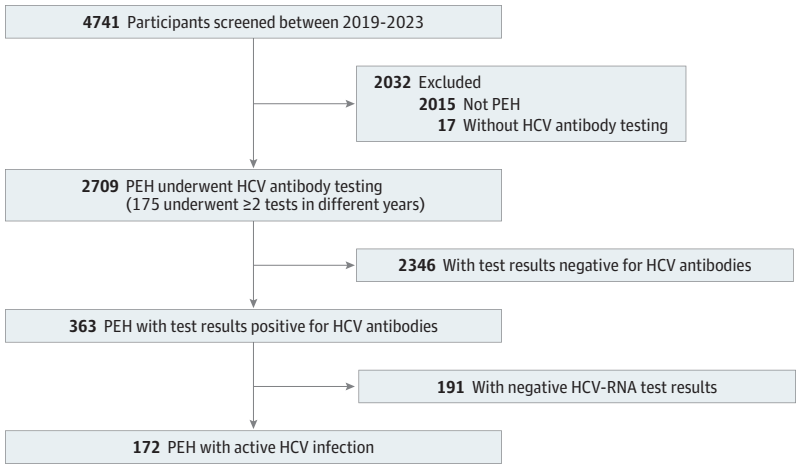
Participant Characteristics

The characteristics of the 2709 PEH screened for HCV infection are summarized in the **Table**. A total of 1660 participants (61.3%) were born outside of Spain, 632 participants (23.3%) were receiving some form of income, and 918 participants (33.9%) had alcohol misuse. Regarding drug use, 593 participants (21.9%) had any history of IDU, of whom 356 participants (60.0%) were not active in their IDU and 237 participants (40.0%) were active in their IDU in the past year. Additionally, 814 participants (30.0%) used benzodiazepine, and 365 participants (13.5%) were undergoing OST. In terms of sexual habits, 1391 participants (51.3%) reported having sexual intercourse in the past year, with 408 participants (29.3%) reporting intercourse without using a condom.

Risk Factors Associated With Active HCV Infection

We conducted a multivariable logistic regression analysis to assess the risk factors associated with active HCV infection; the calendar year when HCV screening was performed (variance inflation factor = 11.6) and OST (r = 0.73 with IDU) were excluded from the model due to collinearity. Three main risk factors were identified (**Figure 2**): IDU (nonactive IDU: aOR, 10.8; 95% CI, 6.1-19.4; q < .001; active IDU: aOR, 27.0; 95% CI, 15.2-48.0; q < .001), lack of financial income (aOR, 1.8; 95% CI, 1.1-2.9; q = .03), and alcohol misuse (aOR, 1.8; 95% CI, 1.3-2.6; q = .004). Active HCV infection prevalence was estimated according to these risk factors separately, with findings showing significantly higher rates among participants who engaged in IDU (nonactive IDU: prevalence, 12.9%; P < .001 active IDU: prevalence, 26.2%; P < .001) (**Figure 3**A), lacked any financial income (prevalence, 7.0%; P = .01) (Figure 3B), and misused alcohol (prevalence, 8.0%; P = .001) (Figure 3C). Active HCV infection prevalence was also estimated by combining these risk factors (eFigure 1 in Supplement 1),

Figure 1. Flowchart of the Study Population and Results of Diagnostic Tests



HCV indicates hepatitis C virus; PEH, people experiencing homelessness.

highlighting the highest rates among participants who had active IDU, had no income, and misused alcohol, at 37.1%, and among participants without IDU, with no economic income, and with alcohol misuse, at 19.6% (q <.05).

Temporal Trend of HCV Infection Prevalence

The mean prevalence of active HCV infection during the study period was 6.3%. Overall, active HCV infection rates showed a significant downward trend during the study period, from 7.2% in 2019 to 3.4% in 2023 (P = .04) (**Figure 4**). An analysis done according to the 3 main risk factors (eFigure 2 in Supplement 1) found a significant downward trend in active HCV infection rates from 2019 to 2023 among participants actively engaging in IDU (from 25.5% to 10.9%; P = .04), who misused alcohol (from 10.8% to 4.4%; P < .001), and who had no financial income (from 7.2% to 3.4%; P = .03). The rates of these risk factors did not decrease during the period; rather, the rate of IDU remained constant, while the rates of alcohol misuse and lack of financial income increased slightly (eFigure 3 in Supplement 1).

Table. Epidemiological Characteristics of the Study Population

Characteristics	Participants, No. (%) (N = 2709)
Gender identity	
Women	756 (27.8)
Men	1953 (72.2)
Age, y	
Mean (SD)	42.2 (12.7)
>50	772 (28.8)
Birth country	
Spain	1049 (38.7)
Other	
Any	1660 (61.3)
Europe	348 (21.0)
Africa	473 (28.5)
North and South America	714 (43.0)
Asia	105 (6.3)
NA	20 (1.2)
Receiving any financial income	632 (23.3)
Undocumented residency status	457 (16.9)
Alcohol misuse	918 (33.9)
Benzodiazepine use	814 (30.0)
Drug consumption	
Cocaine	860 (31.7)
Heroin	583 (21.5)
Marijuana	296 (10.9)
History of IDU	
Any	593 (21.9)
Nonactive IDU in the last year	356 (60.0)
Active IDU in the last year	237 (40.0)
Opioid substitution therapy	365 (13.5)
Sexual intercourse behavior in the last year	
Any	1391 (51.3)
Condom use	983 (70.7)
No condom use	408 (29.3)

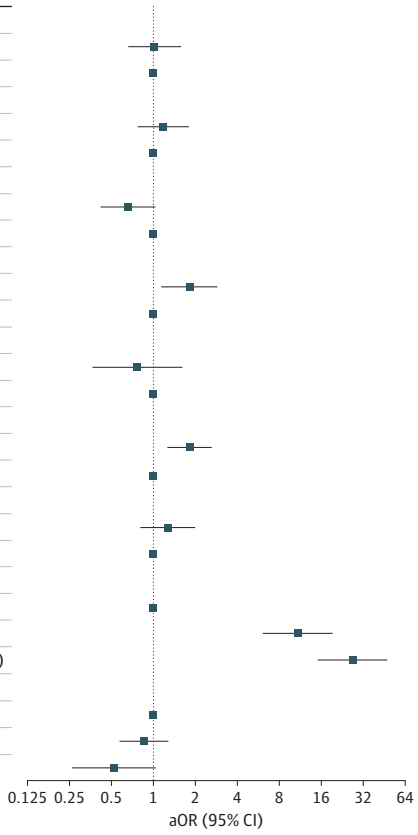
Abbreviations: IDU, injecting drug use; NA, not available.

Discussion

This cross-sectional study assessing a substantial sample of PEH in Madrid between 2019 and 2023 found that the main factors associated with active HCV infection were IDU, lack of financial income, and alcohol misuse. Moreover, an assessment of active HCV infection prevalence and its temporal trend in this population found that the rates decreased significantly over the study period overall, from 7.2% in 2019 to 3.4% in 2023.

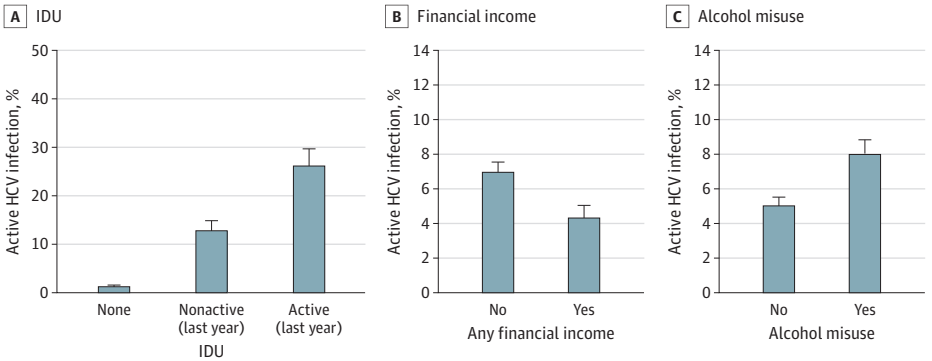
Figure 2. Risk Factors Associated With Active Hepatitis C Virus Infection Among the People Experiencing Homelessness

Characteristic	aOR (95% CI)	*P* value	*q* value
Age ≥50 y			
Yes	1.0 (0.7-1.6)	.91	.91
No	1 [Reference]		
Sex			
Male	1.2 (0.8-1.8)	.44	.54
Female	1 [Reference]		
Born in Spain			
No	0.7 (0.4-1.0)	.07	.14
Yes	1 [Reference]		
Any financial income			
Yes	1.8 (1.1-2.9)	.01	.03
No	1 [Reference]		
Undocumented residency status			
Yes	0.8 (0.4-1.6)	.49	.54
No	1 [Reference]		
Alcohol misuse			
Yes	1.8 (1.3-2.6)	.001	.004
No	1 [Reference]		
Benzodiazepine use			
Yes	1.3 (0.8-2.0)	.23	.47
No	1 [Reference]		
Injecting drug use			
Never	1 [Reference]	NA	NA
Nonactive (last year)	10.9 (6.1-19.4)	<.001	<.001
Active (last year)	27.0 (15.2-48.0)	<.001	<.001
Sexual intercourse behavior (last year)			
Never	1 [Reference]	NA	NA
Condom use	0.9 (0.6-1.3)	.46	.54
No condom use	0.5 (0.3-1.0)	.06	.14



Association analysis was performed using logistic regression adjusted by patient characteristics and 1000 bootstrap repetitions. Multiple testing corrections through the Benjamini and Hochberg procedure (*q*-value) were performed to exclude spurious associations using the false discovery rate. aOR indicates adjusted odds ratio; NA, not applicable.

Figure 3. Estimation of the Prevalence of Active Hepatitis C Virus (HCV) Infection in People Experiencing Homelessness Based on Key Risk Factors



Data were calculated using logistic regression adjusted by patient characteristics and 1000 bootstrap repetitions. IDU indicates injecting drug use.

A decline in HCV infections has been reported globally, decreasing from 0.9% in 2015 to 0.7% in 2020.[7] However, reaching the WHO's ambitious goal of eliminating HCV infection as a public health threat by 2030 faces significant challenges, such as the fact that in 2020, only 21% of people living with HCV were diagnosed and only 13% were treated.[32] The current reality underscores the barriers to HCV elimination, with only 24% of 45 high-income countries analyzed being on track to achieve the WHO's goal.[8] Thus, ensuring universal access to affordable diagnostics and treatment is crucial to meet the WHO's HCV elimination targets by 2030.[4]

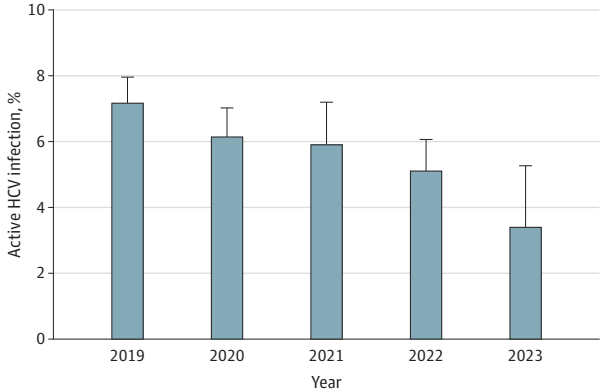
The COVID-19 pandemic also substantially hampered HCV elimination by hindering screening and treatment efforts.[33,34] Additionally, the impact of the COVID-19 pandemic on HCV elimination goals among PEH may have been affected by disruptions in health care services, changes in social services, and varied public health responses. However, other factors may have contributed to the decreased trend of active HCV infection, including increased housing stability due to emergency measures, intensified overdose prevention efforts, and reduced high-risk behaviors owing to pandemic-related lockdowns and social distancing. In summary, COVID-19 may have impacted screening for active HCV infection in our study, but we found a progressive decline. Further research is needed to evaluate the longer-term impact of the COVID-19 pandemic on the trend of active HCV infection among PEH.

PEH represent a population with limited access to HCV diagnosis and treatment, resulting in scarce and likely underestimated prevalence data.[35] Studies on this population have reported an active HCV infection prevalence rate of 10.8% in the US between 2013 and 2016[35] and 10.5% in England in 2020,[36] but reliable published data for Spain are lacking. In this study, we found an overall prevalence of 6.3% over the entire study period, with a significant decline of 52.8% between 2019 and 2023. Despite this reduction, the prevalence of active HCV infection found in this PEH population in 2023 (3.4%) remains more than 15 times higher than the estimate for the general population of Spain in the last serosurvey, conducted between 2017 and 2018, which reported a prevalence of 0.22%.[10] This highlights the persistent challenge of reducing the HCV infection burden in this high-risk group.

Homelessness is commonly associated with comorbidities (eg, mental health disorders) and risk factors (eg, alcohol misuse and illicit drug use)[37] that can impact health and increase the risk of contracting HCV infection. This study identified 3 significant risk factors associated with having an active HCV infection among PEH: IDU, lack of financial income, and alcohol misuse.

First, IDU was the most relevant risk factor associated with having an active HCV infection in our population, with participants actively engaged in IDU exhibiting the highest prevalence rate, at 28%, while those without a history of IDU had the lowest prevalence, at 1.4%. Other studies have also found that IDU is a key risk factor associated with HCV infection in PEH.[26,38,39] However, most of

Figure 4. Estimation of Active Hepatitis C Virus (HCV) Infection Prevalence and Temporal Trend by Calendar Year Throughout the Study Period Among All Included Individuals Experiencing Homelessness



Data were calculated using logistic regression using 1000 bootstrap repetitions. The unit of study was the tests performed.

those studies used HCV antibody testing, which is not useful for detecting active HCV infections. Therefore, HCV screening in PEH with a history of IDU should be a priority strategy to eliminate the virus. However, there is also the question of whether it would be more practical to focus only on people with IDU, regardless of their housing situation, since they stand out as a main intervention target for HCV elimination in PEH.[18,22] Moreover, our analysis found that even the 1.4% prevalence rate among individuals without IDU was much higher than the 0.22% prevalence for the general population in Spain, suggesting that there is a need for specific strategies targeted to PEH, regardless of their history of IDU.

Second, a lack of financial income emerged as another significant risk factor associated with having an active HCV infection among PEH. Despite the possibility that PEH who use drugs may reduce their drug consumption due to financial constraints, the lack of income may paradoxically lead to an increase in IDU behaviors.[40] Our results indicate that the lack of financial income among active drug users is a determining factor associated with increased active HCV infection prevalence among PEH. This emphasizes the importance of implementing harm reduction practices among PEH and other strategies aimed at connecting this population with social services to facilitate their integration into society and/or allow them to obtain noncontributory benefits.

Third, alcohol misuse was identified as the third main risk factor associated with having an active HCV infection in this study. Previous studies have yielded inconclusive results on the association of alcohol misuse with HCV infection. While one study also reported alcohol misuse as a significant risk factor,[39] another did not find a significant association.[41] Access to DAA treatment is often restricted based on ongoing alcohol use in many settings,[42,43] potentially impacting treatment programs, particularly in WHO regions with higher alcohol consumption rates.[44] Although HCV treatment is free in Spain and there are no restrictions based on alcohol misuse, the requirement for exclusive hospital-based administration poses challenges for microelimination strategies among PEH. Eliminating prescription restrictions for DAAs and decentralizing treatment could enhance acceptance and adherence, particularly among marginalized populations, such as PEH.[4,28,45]

The significant downward trend in active HCV infection rates found overall during the study period cannot be attributed to reductions in these risk factors. Instead, it may be attributed to improved diagnosis and enhanced care linkage through decentralized, non-hospital–based approaches, similar to the methods used by the study on which this investigation is based[28] and others.[46,47] This reduction in active HCV infection rates among participants could be primarily associated with a decrease in active HCV infection prevalence among individuals engaging in IDU between 2019 and 2023, particularly the large decrease from 2022 to 2023. This remarkable decline in active HCV infection prevalence is likely a consequence of implementing and prioritizing targeted screening and treatment programs within people with IDU, similar to the approach used by our study and others. These programs include expanded access to HCV testing at the point of care, facilitating earlier identification and treatment of individuals with HCV infection; expansion of harm reduction programs, like needle and syringe exchange, providing access to safe drug use materials; increased awareness about HCV, its risks, and available treatment options through targeted campaigns; and improved coordination across sectors to offer comprehensive care for people with HCV infection, encompassing diagnosis, follow-up, and social support.[28,46,47]

This decrease in active HCV infection is a positive finding, given that PEH have the highest incidence of active HCV infection,[48] thereby shedding light on the regional epidemiology of HCV infection. Despite the decrease in active HCV infection prevalence, our study underscores the ongoing need for prevention and risk reduction efforts. Integrating HCV services into shelter settings[49] and implementing harm reduction programs, such as safe needle provision and OST, are crucial for minimizing bloodborne disease risks.[50] Promoting safer drug consumption methods, like using clean pipes for smoking, could significantly reduce HCV transmission and improve overall well-being among vulnerable populations, such as PEH.[51]

A comprehensive understanding of the barriers impairing HCV screening, treatment uptake, and adherence among PEH is crucial for developing effective health programs tailored to this

population.[49] Societal factors, such as stigma; logistical challenges; and individual factors, including precarious living conditions, competing priorities, limited knowledge, and misconceptions about HCV, play significant roles in the burden of HCV infection among PEH.[49] Peer education is crucial in addressing knowledge gaps and enhancing engagement among PEH.[52,53] Furthermore, rapid HCV testing is essential in this context, contributing to both reducing disease transmission and improving health outcomes.[54] Mobile HCV screening units have proven to be effective, easy to implement, and cost-efficient in addressing these needs.[28,46]

We also want to highlight that in this study, the mobile screening unit played a pivotal role in reaching participants at critical locations where PEH gather, using adapted HCV screening methods suited to populationwide screening efforts. The mobile unit performed HCV screening in systematically selected locations frequented by PEH in Madrid, in coordination with the city council agency in charge of management of PEH, to make the sample as representative as possible. This system has not been modified over the years, and it has been able to identify most of the PEH in Madrid. Moreover, the mobile unit included trained peer support workers, whose participation has improved the prevention and diagnosis of HCV infection among underserved populations in Madrid.[28,29] Despite this, it should not be ruled out that our screening strategy may have included biases.

Limitations

This study has several limitations. First, there is a potential for selection bias, as some PEH may have declined study participation due to the lack of financial incentives, particularly those without financial income. Conversely, certain high-risk groups, like people with IDU, may have been more motivated to participate to receive a diagnosis. Second, data on risk behaviors and factors may have been susceptible to biases or incompleteness despite being collected by trained personnel, which likely minimized errors. This could have introduced recall bias, potentially underestimating the associations related to the frequency and route of factors, such as drug use, and overlooking other risk factors that could be associated with an active HCV infection. Third, we use a standard definition of homelessness; however, we recognize that some studies may differ in their criteria regarding the duration of homelessness, although most studies used having experienced homelessness in the past 6 to 12 months. Consequently, comparisons of HCV prevalence among studies should be interpreted with caution.

Conclusions

This cross-sectional study found that IDU, lack of financial income, and alcohol misuse were primary risk factors associated with active HCV infection among PEH in Madrid from 2019 to 2023. Active HCV infection rates decreased significantly over the study period, which may be attributed to the effectiveness of targeted approaches for HCV management among this population.

ARTICLE INFORMATION

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Author Contributions: Dr Resino had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Drs Ryan, Valencia, and Sepúlveda-Crespo contributed equally as co–first author. Drs Pérez-García, Martínez, and Resino contributed equally as co–senior authors senior authors contributed equally.

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Critical review of the manuscript for important intellectual content: Ryan, Valencia, Amigot-Sánchez, Cuevas, Lazarus, Martinez.

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REFERENCES

1. Martinello M, Solomon SS, Terrault NA, Dore GJ. Hepatitis C. *Lancet*. 2023;402(10407):1085-1096. doi:10.1016/S0140-6736(23)01320-X

2. Bhattacharya D, Aronsohn A, Price J, Lo Re V; AASLD-IDSA HCV Guidance Panel. Hepatitis C Guidance 2023 Update: AASLD-IDSA Recommendations for Testing, Managing, and Treating Hepatitis C Virus Infection. *Clin Infect Dis*. Published online May 25, 2023. doi:10.1093/cid/ciad319

3. Ji F, Yeo YH, Wei MT, et al. Sustained virologic response to direct-acting antiviral therapy in patients with chronic hepatitis C and hepatocellular carcinoma: a systematic review and meta-analysis. *J Hepatol*. 2019;71(3):473-485. doi:10.1016/j.jhep.2019.04.017

4. Lazarus JV, Pericàs JM, Picchio C, et al. We know DAAs work, so now what: simplifying models of care to enhance the hepatitis C cascade. *J Intern Med*. 2019;286(5):503-525. doi:10.1111/joim.12972

5. World Health Organization GHHaSPH. Global health sector strategies on, respectively, HIV, viral hepatitis and sexually transmitted infections for the period 2022-2030. Accessed September 5, 2024. https://www.who.int/publications/i/item/9789240053779

6. Huang CF, Chen GJ, Hung CC, Yu ML. HCV Microelimination for high-risk special populations. *J Infect Dis*. 2023;228(suppl 3):S168-S179. doi:10.1093/infdis/jiac446

7. Polaris Observatory HCV Collaborators. Global change in hepatitis C virus prevalence and cascade of care between 2015 and 2020: a modelling study. *Lancet Gastroenterol Hepatol*. 2022;7(5):396-415. doi:10.1016/S2468-1253(21)00472-6

8. Gamkrelidze I, Pawlotsky JM, Lazarus JV, et al. Progress towards hepatitis C virus elimination in high-income countries: an updated analysis. *Liver Int*. 2021;41(3):456-463. doi:10.1111/liv.14779

9. Gower E, Estes C, Blach S, Razavi-Shearer K, Razavi H. Global epidemiology and genotype distribution of the hepatitis C virus infection. *J Hepatol*. 2014;61(1)(suppl):S45-S57. doi:10.1016/j.jhep.2014.07.027

10. Estirado Gómez A, Justo Gil S, Limia A, et al; Working group of the HCV prevalence study in Spain in 2017–2018. Prevalence and undiagnosed fraction of hepatitis C infection in 2018 in Spain: results from a national population-based survey. *Eur J Public Health*. 2021;31(6):1117-1122. doi:10.1093/eurpub/ckab069

11. Ministry of Health, Social Services and Equality. Strategic plan for tackling hepatitis C in the Spanish National Health System. Accessed September 5, 2024. https://www.sanidad.gob.es/ciudadanos/enfLesiones/enfTransmisibles/hepatitisC/PlanEstrategicoHEPATITISC/docs/PEAHC_eng.pdf

12. Marshall AD, Pawlotsky JM, Lazarus JV, Aghemo A, Dore GJ, Grebely J. The removal of DAA restrictions in Europe—one step closer to eliminating HCV as a major public health threat. *J Hepatol*. 2018;69(5):1188-1196. doi:10.1016/j.jhep.2018.06.016

13. Lens S, Miralpeix A, Gálvez M, et al. HCV microelimination in harm reduction centres has benefits beyond HCV cure but is hampered by high reinfection rates. *JHEP Rep*. 2022;4(12):100580. doi:10.1016/j.jhepr.2022.100580

14. Cabezas J, Llerena S, Mateo M, et al. Hepatitis C micro-elimination beyond prison walls: navigator-assisted test-and-treat strategy for subjects serving non-custodial sentences. *Diagnostics (Basel)*. 2021;11(5):877. doi:10.3390/diagnostics11050877

15. Pérez Castaño Y, Chouza Pérez JM, Sanz Largo V, et al. Linkage to care strategy for the micro-elimination of hepatitis C among parenteral drug users on methadone replacement therapy in Gipuzkoa. *Rev Esp Enferm Dig*. 2020;112(7):545-549. doi:10.17235/reed.2020.7194/2020

16. Cuadrado A, Llerena S, Cobo C, et al. Microenvironment eradication of hepatitis C: A novel treatment paradigm. *Am J Gastroenterol*. 2018;113(11):1639-1648. doi:10.1038/s41395-018-0157-x

17. Beijer U, Wolf A, Fazel S. Prevalence of tuberculosis, hepatitis C virus, and HIV in homeless people: a systematic review and meta-analysis. *Lancet Infect Dis*. 2012;12(11):859-870. doi:10.1016/S1473-3099(12)70177-9

18. Arum C, Fraser H, Artenie AA, et al; Homelessness, HIV, and HCV Review Collaborative Group. Homelessness, unstable housing, and risk of HIV and hepatitis C virus acquisition among people who inject drugs: a systematic review and meta-analysis. *Lancet Public Health*. 2021;6(5):e309-e323. doi:10.1016/S2468-2667(21)00013-X

19. Stone J, Artenie A, Hickman M, et al. The contribution of unstable housing to HIV and hepatitis C virus transmission among people who inject drugs globally, regionally, and at country level: a modelling study. *Lancet Public Health*. 2022;7(2):e136-e145. doi:10.1016/S2468-2667(21)00258-9

20. Paisi M, Crombag N, Burns L, et al. Barriers and facilitators to hepatitis C screening and treatment for people with lived experience of homelessness: a mixed-methods systematic review. *Health Expect*. 2022;25(1):48-60. doi:10.1111/hex.13400

21. Lazarus JV, Safreed-Harmon K, Thursz MR, et al. The micro-elimination approach to eliminating hepatitis C: strategic and operational considerations. *Semin Liver Dis*. 2018;38(3):181-192. doi:10.1055/s-0038-1666841

22. Cooke GS, Andrieux-Meyer I, Applegate TL, et al; Lancet Gastroenterology & Hepatology Commissioners. Accelerating the elimination of viral hepatitis: a Lancet Gastroenterology & Hepatology Commission. *Lancet Gastroenterol Hepatol*. 2019;4(2):135-184. doi:10.1016/S2468-1253(18)30270-X

23. Guerra-Veloz MF, Han K, Oakes K, et al. Results of a model of delivering hepatitis C care in a homeless metropolitan population in England. *Am J Gastroenterol*. 2023;118(6):991-1000. doi:10.14309/ajg.0000000000002041

24. Lasmanovich R, Shaked O, Sivan A, et al. Hepatitis C virus prevalence, medical status awareness and treatment engagement among homeless people who use drugs: results of a street outreach study. *Subst Abuse*. Published online May 26, 2022. doi:10.1177/11782218221095871

25. Khalili M, Powell J, Park HH, et al. Shelter-based integrated model is effective in scaling up hepatitis C testing and treatment in persons experiencing homelessness. *Hepatol Commun*. 2022;6(1):50-64. doi:10.1002/hep4.1791

26. Leach M, Chapin S, Porges I, et al. Evaluation of risk factors for hepatitis c virus infection among Philadelphia's shelter-bound, homeless population: data from a student-run hepatitis C virus screening initiative. *Popul Health Manag*. 2021;24(4):448-453. doi:10.1089/pop.2020.0143

27. Ivanova Reipold E, Shilton S, Donolato M, Fernandez Suarez M. Molecular point-of-care testing for hepatitis C: available technologies, pipeline, and promising future directions. *J Infect Dis*. 2024;229(suppl 3):S342-S349. doi:10.1093/infdis/jiad463

28. Ryan P, Valencia J, Cuevas G, et al. Detection of active hepatitis C in a single visit and linkage to care among marginalized people using a mobile unit in Madrid, Spain. *Int J Drug Policy*. 2021;96:103424. doi:10.1016/j.drugpo.2021.103424

29. Ryan P, Valencia J, Cuevas G, et al. Decrease in active hepatitis C infection among people who use drugs in Madrid, Spain, 2017 to 2023: a retrospective study. *Euro Surveill*. 2024;29(29):2300712. doi:10.2807/1560-7917.ES.2024.29.29.2300712

30. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)–a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377-381. doi:10.1016/j.jbi.2008.08.010

31. Benjamini Y, Hochberg Y. Controlling the False Discovery Rate: A Practical and Powerful Approach to Multiple Testing. *J R Stat Soc B*. 1995;57:289-300. doi:10.1111/j.2517-6161.1995.tb02031.x

32. Feld JJ, Ward JW. Key elements on the pathway to hcv elimination: lessons learned from the AASLD HCV Special Interest Group 2020. *Hepatol Commun*. 2021;5(6):911-922. doi:10.1002/hep4.1731

33. Wingrove C, Ferrier L, James C, Wang S. The impact of COVID-19 on hepatitis elimination. *Lancet Gastroenterol Hepatol*. 2020;5(9):792-794. doi:10.1016/S2468-1253(20)30238-7

34. Kondili LA, Buti M, Riveiro-Barciela M, et al. Impact of the COVID-19 pandemic on hepatitis B and C elimination: an EASL survey. *JHEP Rep*. 2022;4(9):100531. doi:10.1016/j.jhepr.2022.100531

35. Hofmeister MG, Rosenthal EM, Barker LK, et al. Estimating prevalence of hepatitis C virus infection in the United States, 2013-2016. *Hepatology*. 2019;69(3):1020-1031. doi:10.1002/hep.30297

36. Wilkinson R, Mandal S, Phipps E. Evaluation of hepatitis C test and treat interventions targeted at homeless populations (outside London) in England during the COVID-19 pandemic. *Clin Liver Dis (Hoboken)*. 2021;17(2):90-94. doi:10.1002/cld.1098

37. Subedi K, Ghimire S. Comorbidity profiles of patients experiencing homelessness: a latent class analysis. *PLoS One*. 2022;17(5):e0268841. doi:10.1371/journal.pone.0268841

38. Nikoo N, Javidanbardan S, Akm M, et al. Hepatitis C prevalence and associated risk factors among individuals who are homeless and diagnosed with mental illness: at Home/Chez Soi Study, Vancouver, BC. *Eur J Public Health*. 2019;29(2):242-247. doi:10.1093/eurpub/cky142

39. Nyamathi AM, Dixon EL, Robbins W, et al. Risk factors for hepatitis C virus infection among homeless adults. *J Gen Intern Med*. 2002;17(2):134-143. doi:10.1046/j.1525-1497.2002.10415.x

40. Linton SL, Celentano DD, Kirk GD, Mehta SH. The longitudinal association between homelessness, injection drug use, and injection-related risk behavior among persons with a history of injection drug use in Baltimore, MD. *Drug Alcohol Depend*. 2013;132(3):457-465. doi:10.1016/j.drugalcdep.2013.03.009

41. Gelberg L, Robertson MJ, Arangua L, et al. Prevalence, distribution, and correlates of hepatitis C virus infection among homeless adults in Los Angeles. *Public Health Rep*. 2012;127(4):407-421. doi:10.1177/003335491212700409

42. Grebely J, Haire B, Taylor LE, et al; International Network for Hepatitis in Substance Users. Excluding people who use drugs or alcohol from access to hepatitis C treatments—is this fair, given the available data? *J Hepatol*. 2015;63(4):779-782. doi:10.1016/j.jhep.2015.06.014

43. Lazarus JV, Safreed-Harmon K, Stumo SR, et al; Hep-CORE Study Group. Restrictions on access to direct-acting antivirals for people who inject drugs: the European Hep-CORE study and the role of patient groups in monitoring national HCV responses. *Int J Drug Policy*. 2017;47:47-50. doi:10.1016/j.drugpo.2017.05.054

44. Rehm J, Samokhvalov AV, Shield KD. Global burden of alcoholic liver diseases. *J Hepatol*. 2013;59(1):160-168. doi:10.1016/j.jhep.2013.03.007

45. Lazarus JV, Øvrehus A, Demant J, Krohn-Dehli L, Weis N. The Copenhagen test and treat hepatitis C in a mobile clinic study: a protocol for an intervention study to enhance the HCV cascade of care for people who inject drugs (T'N'T HepC). *BMJ Open*. 2020;10(11):e039724. doi:10.1136/bmjopen-2020-039724

46. Ryan P, Valencia J, Cuevas G, et al. HCV screening based on dried blood samples and linkage to care in people who use drugs: a prospective study. *Int J Drug Policy*. 2021;92:103134. doi:10.1016/j.drugpo.2021.103134

47. Lazarus JV, Villota-Rivas M, Ryan P, et al. Combined COVID-19 vaccination and hepatitis C virus screening intervention in marginalised populations in Spain. *Commun Med (Lond)*. 2023;3(1):66. doi:10.1038/s43856-023-00292-y

48. Artenie A, Stone J, Fraser H, et al; HIV and HCV Incidence Review Collaborative Group. Incidence of HIV and hepatitis C virus among people who inject drugs, and associations with age and sex or gender: a global systematic review and meta-analysis. *Lancet Gastroenterol Hepatol*. 2023;8(6):533-552. doi:10.1016/S2468-1253(23)00018-3

49. Fokuo JK, Masson CL, Anderson A, et al. Recommendations for implementing hepatitis C virus care in homeless shelters: the stakeholder perspective. *Hepatol Commun*. 2020;4(5):646-656. doi:10.1002/hep4.1492

50. Platt L, Minozzi S, Reed J, et al. Needle syringe programmes and opioid substitution therapy for preventing hepatitis C transmission in people who inject drugs. *Cochrane Database Syst Rev*. 2017;9(9):CD012021. doi:10.1002/14651858.CD012021.pub2

51. Degenhardt L, Peacock A, Colledge S, et al. Global prevalence of injecting drug use and sociodemographic characteristics and prevalence of HIV, HBV, and HCV in people who inject drugs: a multistage systematic review. *Lancet Glob Health*. 2017;5(12):e1192-e1207. doi:10.1016/S2214-109X(17)30375-3

52. Mah A, Hull MW, DeBeck K, et al. Knowledge of hepatitis C and treatment willingness amongst people who inject drugs in an era of direct acting antivirals. *Int J Drug Policy*. 2017;47:137-143. doi:10.1016/j.drugpo.2017.02.006

53. Stagg HR, Surey J, Francis M, et al. Improving engagement with healthcare in hepatitis C: a randomised controlled trial of a peer support intervention. *BMC Med*. 2019;17(1):71. doi:10.1186/s12916-019-1300-2

54. Noska AJ, Belperio PS, Loomis TP, O'Toole TP, Backus LI. Engagement in the hepatitis C care cascade among homeless veterans, 2015. *Public Health Rep*. 2017;132(2):136-139. doi:10.1177/0033354916689610

SUPPLEMENT 1.

eFigure 1. Estimation of the Prevalence of HCV Active Infection in the Homeless Population Based on Key Risk Factors

eFigure 2. Estimation of HCV Active Infection Prevalence and Temporal Trend by Calendar Year Throughout the Study Period (2019-2023) Stratified by Risk Factors

eFigure 3. Prevalence of IDU (Active and Inactive [A]), Alcohol Intake (B), and Economic Income (C) in the Homeless Population During the Study Period (2019-2023)

SUPPLEMENT 2.

Data Sharing Statement