IJID Regions 8 (2023) 95–104

Contents lists available at ScienceDirect

IJID Regions

journal homepage: www.elsevier.com/locate/ijregi

# Hepatitis C antibody prevalence and active hepatitis C infection in HIV-negative gay, bisexual, and other men who have sex with men in Barcelona and Madrid, Spain (March 2018-March 2021)

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ARTICLE INFO

*Keywords:*
Hepatitis C
Sexually transmitted diseases
GBMSM
Men who have sex with men
Sexual health
Epidemiology

ABSTRACT

*Objectives:* Hepatitis C virus (HCV) has been recognized as a sexually transmitted infection (STI) in HIV-positive men who have sex with men (MSM), with an increased notification in HIV-negative MSM. The aim of this study was to determine the prevalence of HCV antibody and active HCV infection in HIV-negative gay, bisexual, and other MSM (GBMSM), and their characteristics, in Barcelona and Madrid, from March 2018 to March 2021.
*Methods:* Cross-sectional study conducted on 3548 HIV-undiagnosed GBMSM, across four HIV/STI testing centers. Respondents submitted an online, self-administered questionnaire after consultation, which collected information on sociodemographics, sexual health history, HCV knowledge, and substance consumption. Prevalence of HCV antibodies was determined by a reactive result in a rapid anti-HCV test or enzyme-linked immunosorbent assay (ELISA), while active HCV infection was determined by participants who were also positive on an HCV-RNA test. Crude and adjusted Poisson analyses with robust variance are presented for both prevalence and active infection.
*Results:* In total, 97.6% of participants (n = 3463) were HIV-negative. Of those, 18 were found to have HCV antibodies (0.52%), of which nine (0.26%) were also HCV-RNA positive. Those with HCV antibodies were associated to have lived with an HCV (+) person (adjusted prevalence ratio [APR]: 7.84, [95% confidence interval: 2.50-24.53]), using injectable drugs for sex (APR: 6.92, [1.20-39.79]) and testing positive for an STI in the previous year (APR: 4.06, [1.09-15.12]). Presenting an active infection was strongly associated with a previous HCV diagnosis (APR: 100.82 [22.16-458.76]), sexualized injectable drug use (APR: 17.53 [2.70-113.76]), and sharing douching material (APR: 7.45, [2.12-25.95]).
*Conclusion:* Sexual practices with a higher risk of bleeding and sexualized drug use, particularly sexualized injectable drug use, were associated with higher rates of HCV diagnosis in GBMSM. Identifying these practices during consultation, contact tracing new cases and regularly testing those with a previous history of HCV, will facilitate HCV eradication.

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https://doi.org/10.1016/j.ijregi.2023.07.001
Received 5 May 2023; Received in revised form 4 July 2023; Accepted 4 July 2023

## Introduction

Untreated hepatitis C virus (HCV) is a leading cause of hepatitis C-related liver disease, cirrhosis, and hepatocellular carcinoma [1,2]. With an estimated 71 million chronically infected patients worldwide, HCV epidemics affect all World Health Organization (WHO) regions, although prevalence is higher in region European and the Eastern Mediterranean [2], partly due to testing practices [3]. In 2019, there were an estimated 1.5 million new cases of HCV and an additional 290,000 deaths related to HCV infection [4].

In recent years, the implementation of direct-acting antivirals (DAA) has transformed the prognosis of the infection into a completely curable disease, favorably reducing HCV mortality [4–6]. In 2016, the WHO adopted the first global health sector strategy on viral hepatitis, setting targets for HCV eradication by 2030 [7]. As one of the few countries on track to reach the WHO goals by 2030 [2,6], Spain developed its 2015 Strategic Plan for the Approach to Hepatitis [8], which includes the widespread use of DAAs.

Since early 2000, HCV has been considered a sexually transmitted infection (STI), particularly in gay, bisexual, and other men who have sex with men (GBMSM) [2,5,7,9,10]. Within this key population, those with an HIV diagnosis have an increased risk of HCV acquisition [7,9,11]. Some proposed explanation includes serosorting practices during the widespread initiation of combined antiretroviral therapy in the US and Western Europe ever since the 1990s, which may lead to condomless anal sex [9]. Furthermore, the rise of sexualized drug use or chemsex [11], especially the increase in sexualized injection drug use (slam-sex or slamming) [9,12,13] has been associated with an increase in HCV cases. Additional blood-sharing risk practices include having multiple sexual partners, sharing douching materials, and/or sexual practices which may damage anal mucosa (fisting) [9].

In HIV-negative GBMSM, the observed risk has been lower than their HIV-positive peers; although their incidence is reported to be higher than general population and rising in some occidental countries [9,10,12]. Some explanations include chemsex and increased condomless serosorting practices due to HIV pre-exposure prophylaxis (PrEP) [5], overlapping the sexual networks between HIV-positive and negative GBMSM [14]. A systematic review described that, in HIV-negative GBMSM who do not use PrEP, the pooled HCV incidence was 0.12 per 1000 person-years (95% confidence interval [CI] 0.00-0.72) while in PrEP users this pooled incidence was 14.80 per 1000 person-years (9.65-20.95) [7]. Moreover, few studies have specifically looked at how social and structural factors facilitate HCV transmission, what is missing in HCV information and support for GBMSM, or the efficacy of specific HCV interventions in GBMSM [9,15].

In Spain, according to the second National Study of HCV seroprevalence (2017-2018) [16], the prevalence of HCV antibodies among 20-80s is an estimated 0.85% (95% CI: 0.64-1.08%) and the prevalence of active HCV infection is 0.22% (0.12-0.32%). According to the National Centre of Epidemiology [1], by 2020, 819 cases were notified across Spain (incidence rate of 2.36 per 100.000 citizens) but of those only 7.8% (n = 64) were confirmed as active cases. Among Spain's HIV-negative GBMSM, the data remains unclear. In order to provide clinical recommendations for HCV screening key populations, the aim of this study is to estimate the HCV antibodies prevalence and active HCV infection in HIV-negative GBMSM of Barcelona and Madrid, from March 2018 to March 2021, and their characteristics.

## Methodology

### *Study design*

This cross-sectional study was carried out using a structured, virtual, and self-administered questionnaire, from March 2018 to March 2021 in the two most populated cities of Spain. The study took place in two STI-specific clinics, references in each city (Drassanes Express in Barcelona, and Sandoval Clinic in Madrid), and two community programs for rapid HIV testing: the Rapid Test Program of the Epidemiologic Service of Barcelona's Public Health Agency, and Madrid's Pink Peace Program. The STI clinics primarily offer on-demand services, PrEP delivery, and conduct standard testing for all STIs in accordance with Spain's guidelines [17]. In contrast, community programs provide rapid testing for HIV (Determine™ HIV-1/2), syphilis (Determine™ Syphilis TP), and during this study, for HCV (OraQuick® HCV Rapid Antibody Test [OraSure Technologies, Inc]). Additionally, they employ various methods of active recruitment, including creating profiles on popular dating apps targeting GBMSM.

### *Population and sample selection*

All cisgender males voluntarily attending STI clinics were approached in the waiting room by researchers, commenting on the aim of the study and the inclusion criteria. HIV-negative individuals, who reported sex with partners of the same gender, were asked to participate before or after the consultation. If agreed, a researcher provided them with a digital tablet with the online survey to be answered in the waiting room. Attenders to community programs, when identified as GBMSM by the community worker, were asked to complete the online survey using a tablet provided by the same worker while awaiting results. If a reactive HCV test was detected in a community program, the participant was referred to the local specialized STI center for HCV-RNA detection and viral load determination.

### *Questionnaire and data collection*

Researchers developed an anonymous, self-administered questionnaire in the SurveyMonkey platform, to be administered via tablet during or after the consultation. Depending on the participant's responses, it could take a minimum of 20 minutes, with the potential for additional time when answering questions related to sexualized drug consumption. The questionnaire covered various topics, including sociodemographic information, history of HIV and HCV testing, HCV knowledge, sexual behaviors, and both recreational and sexualized drug use history. The data obtained from participants were coded and kept anonymous. Later, the research team linked this anonymized data to the HIV and HCV results. The team also verified previous diagnoses and RNA negativization before categorizing cases as reinfection.

### *Variables*

Prevalence of HCV antibodies (AB) was defined as having a reactive HCV rapid test in the community centers or a positive ELISA in STI centers. A reactive HCV rapid test with presence of HCV-RNA was defined as active HCV infection (AC). Sociodemographic data included age, country of birth, employment status, educational level, economic welfare, and disclosure of sexual orientation. HCV history includes previous HCV diagnosis and treatment, previous hepatitis A and B vaccination, previous tattoos or piercings, and knowledge about hepatitis. Sexual health history included previous STI diagnosis, previous HIV/STI testing, and sexual behavior practices, such as lifetime and last year receptive penetrative sex, unprotected receptive sex, and sex with women; receiving fingering or fisting; sharing douching material, sex toys or lubricant; group sex, or visible bleeding after sex. Also includes consuming or practicing male sex work and venues to find sexual partners. To evaluate sexualized drug use, different drugs, including erectile medication, opioids, and sedatives were listed. For each one it was quantified general and sexualized use. Moreover, the questionnaire evaluated the proportion of sex under influence of drugs in the last year, mixing drugs and alcohol, injecting drugs for sex, and sharing injectable or snorting material, quantifying total times and time of last practices. Previous analysis of this database in relation to drug surveillance have been published [13,18].

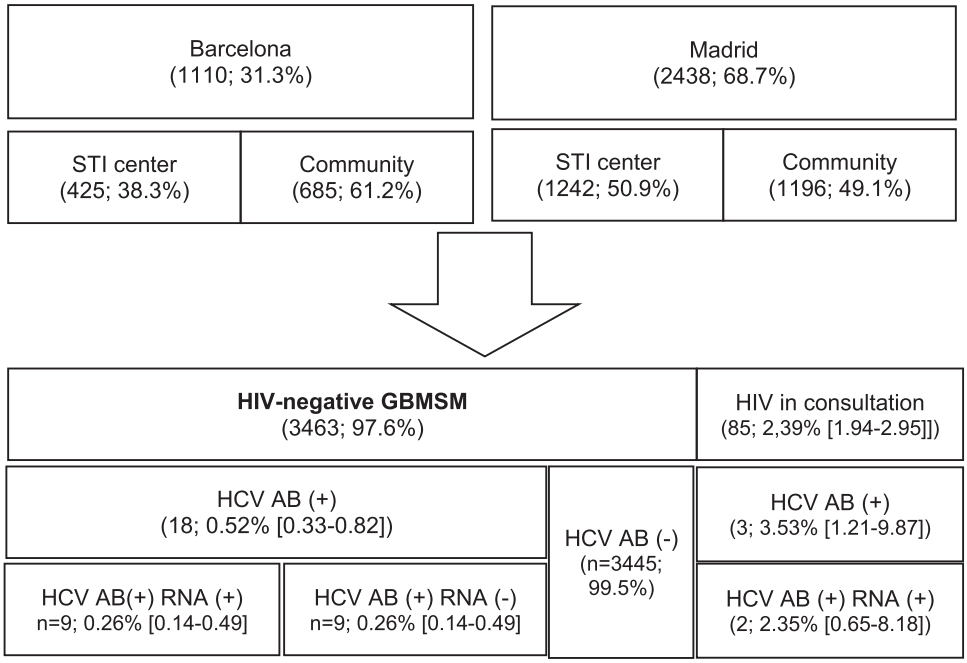


**Figure 1.** Flowchart according to city of testing and type of facility. Results are presented in absolute frequency and prevalence with 95% confidence interval, according to their HIV status. AB, antibody; GBMSM, gay, bisexual, and other men who have sex with men; HCV, hepatitis C virus; STI, sexually transmitted infection.

*Analysis*

The prevalence for both HCV antibodies and active infection was calculated according to those with a negative HIV test during consultation. Results are presented in a flowchart in percentages and 95% CIs, with percentages regarding city and type of program of testing. Then, a descriptive analysis of those HCV (+) was performed according to presence or absence of HCV-RNA, and the rest of HIV-negative cases. HIV-positive and total sample are presented in Supplementary material 1. Poisson regression models with robust variations were made for both the presence of antibodies and for active infection, compared with being HCV/HIV-negative. Models were presented in crude prevalence ratios, and adjusted by age, country of birth, study level, economic welfare, and sexual orientation disclosure (adjusted prevalence ratio 1 [APR1]). Those significant (<0.05) were explored to create a single adjusted Poisson model for each dependent variable (APR2). Non-significant variables, and crude prevalence ratio/APR for those with presence of HCV antibodies, but RNA negative, are presented in the Supplementary material 2. All the analyses were carried out in STATA 15 and 16.

*Ethical considerations*

Each participant signed an informed consent accepting to participate voluntarily, after being explained the aim of the study and the confidentiality of the obtained data. To guarantee confidentiality of the data and records, we adhered to the regulations established by the Organic Law on the Protection of Personal Data 15/1999 in Spain and the successive updates. The project was approved by Research Ethics Committee of Parc de Salut Mar, on June 25, 2019, and by the Research Ethics Committee of the Instituto de Salud Carlos III (CEI PI 44_2018_subproyecto1-v2 and CEI PI 44_2018_subproyecto2).

## Results

From March 2018 to March 2021, 3548 participants attended any of the services in Barcelona or Madrid, where 97.6% (n = 3463) were HIV-negative. Of them, 18 participants (0.52%, 95% CI: 0.33-0.82) tested positive for HCV AB, of which nine participants (0.26% 95% CI: 0.14-0.49) were diagnosed later with an active HCV (AC). Of the 2.4% (n = 85) participants who tested positive for HIV, some 3.5% (n = 3) tested also positive for HCV AB, with 2.4% (n = 2) presenting an active HCV (Figure 1).

Most HIV-negative cases with a reactive HCV test (AB/AC) had attended university education, had a subjective comfortable economic welfare, and lived an openly sexual orientation between their peers. Most of the cases had sex exclusively with men and had been tested for HIV in the last 6 months. In total, 77.8% of the cases (AB/AC) have had some STI in their lifetime, mostly syphilis and gonorrhea, and mostly had their last STI during the last year. Two of the nine diagnosed with an AC-HCV have had a previous HCV diagnosis. Between the participants, the best-known statement was the existence of several types of hepatitis named by letters of the alphabet, and the worst known was that healthcare providers recommend that GBMSM gets vaccinated against viral hepatitis A and B. Some 66.7% of AC-HCV had ever shared douching material and some 77.8% had ever participated in group sex. All AC-HCV cases reported use of drugs related to sex (AB: 77.8%). Injectable drug use was described by 83.3% of HCV AB and 66.7% of HCV-AC (Table 1).

In the single Poisson model, those with HCV antibodies were associated to have ever lived with an HCV (+) person (APR: 7.84, [95% CI: 2.50-24.53]), ever using injectable drugs for sex (APR: 6.92, [1.20-39.79]) and referring an STI in the previous year (4.06, [1.09-15.12]). The adjusted models found associations with previous STIs (syphilis and chlamydia), higher amount of condomless encounters with different sexual partners, group sex, and sex work. Furthermore, presenting an active infection was strongly associated with a previous HCV diagnosis (APR: 100.82 [22.16-458.76]), also to sexualized injectable drug use (APR: 17.53 [2.70-113.76]) and to ever have shared douching material (APR: 7.45, [2.12-25.95]). Similar to AB-HCV, associations were found with a higher amount of condomless sexual partners, previous syphilis, and sharing shaving material with HCV partners, but also for sharing sniffing material for sex, and the use of gamma-hydroxybutyrate/gamma-hydroxybutirolactone (GHB/GBL) (Table 2).

**Table 1a**
Descriptive of the sample. Only those HIV (-) are presented. Sociodemographic and HCV practices and knowledge.

| | HCV AB (+) HIV (−) (a) | | | | HCV (−) HIV (−) (n = 3445) | | Total HIV (−) (n = 3463) | |
|---|---|---|---|---|---|---|---|---|
| | RNA (+) (n = 9) | | RNA (−)(n = 9) | | | | | |
| | N | % | N | % | N | % | N | % |
| Age in three groups | | | | | | | | |
| Under 30 years old | 2 | 22.2 | 3 | 33.3 | 1348 | 39.1 | 1353 | 39.07 |
| Between 30-39 years | 6 | 66.7 | 3 | 33.3 | 1182 | 34.3 | 1191 | 34.39 |
| 40 years or more | 1 | 11.1 | 3 | 33.3 | 915 | 26.6 | 919 | 26.54 |
| Country of birth | | | | | | | | |
| Spain | 4 | 44.4 | 5 | 55.6 | 2164 | 62.8 | 2173 | 62.75 |
| Latin-America | 3 | 33.3 | 4 | 44.4 | 914 | 26.5 | 921 | 26.59 |
| Others | 2 | 22.2 | 0 | 0 | 367 | 10.7 | 369 | 10.66 |
| Study level | | | | | | | | |
| None or primary | 1 | 11.1 | 0 | 0 | 234 | 6.8 | 235 | 6.79 |
| Secondary | 1 | 11.1 | 1 | 11.1 | 1143 | 33.2 | 1145 | 33.06 |
| University or more | 7 | 77.8 | 8 | 88.9 | 2056 | 59.7 | 2071 | 59.80 |
| Missing values | 0 | 0 | 0 | 0 | 12 | 0.3 | 12 | 0.35 |
| Economic welfare last year | | | | | | | | |
| Comfortable | 7 | 77.8 | 6 | 66.7 | 2055 | 59.7 | 2068 | 59.72 |
| Thigh, hard or very hard | 2 | 22.2 | 3 | 33.3 | 1343 | 39 | 1348 | 38.93 |
| Missing values | 0 | 0 | 0 | 0 | 47 | 1.4 | 47 | 1.36 |
| Orientation disclosure with others | | | | | | | | |
| Openly | 6 | 66.7 | 6 | 66.7 | 2093 | 60.8 | 2105 | 60.79 |
| Not openly | 3 | 33.3 | 3 | 33.3 | 1299 | 37.7 | 1305 | 37.68 |
| Missing values | 0 | 0 | 0 | 0 | 53 | 1.5 | 53 | 1.53 |
| Employment status | | | | | | | | |
| Employed | 4 | 44.4 | 5 | 55.6 | 1723 | 50.0 | 1732 | 50.01 |
| Unemployed | 1 | 11.1 | 0 | 0 | 168 | 4.9 | 169 | 4.88 |
| Others | 0 | 0 | 0 | 0 | 421 | 12.2 | 421 | 12.16 |
| Missing values | 4 | 44.4 | 4 | 44.4 | 1133 | 32.9 | 1141 | 32.95 |
| Sex also with women | | | | | | | | |
| Exclusively with men | 5 | 55.6 | 6 | 66.7 | 2154 | 62.5 | 2165 | 62.52 |
| Occasionally | 2 | 22.2 | 3 | 33.3 | 1044 | 30.3 | 1049 | 30.29 |
| Frequently | 2 | 22.2 | 0 | 0 | 247 | 7.2 | 249 | 7.19 |
| Vaccinated against hepatitis A | | | | | | | | |
| Yes | 3 | 33.3 | 7 | 77.8 | 1876 | 54.5 | 1886 | 54.46 |
| No | 2 | 22.2 | 0 | 0 | 484 | 14 | 486 | 14.03 |
| Unknown | 4 | 44.4 | 2 | 22.2 | 1085 | 31.4 | 1091 | 31.50 |
| Vaccinated against hepatitis B | | | | | | | | |
| Yes | 4 | 44.4 | 8 | 88.9 | 1842 | 53.5 | 1854 | 53.54 |
| No | 1 | 11.1 | 0 | 0 | 387 | 11.2 | 388 | 11.20 |
| Unknown | 4 | 44.4 | 1 | 11.1 | 1216 | 35.3 | 1221 | 35.26 |
| Ever being tested for HCV | | | | | | | | |
| Yes | 5 | 55.6 | 8 | 88.9 | 1536 | 44.6 | 1549 | 44.73 |
| No | 1 | 11.1 | 0 | 0 | 836 | 24.3 | 837 | 24.17 |
| Unknown | 3 | 33.3 | 1 | 11.1 | 1073 | 31.2 | 1077 | 31.10 |
| Ever being diagnosed HCV | | | | | | | | |
| No | 7 | 77.8 | 1 | 11.1 | 3408 | 98.9 | 3416 | 98.64 |
| Yes | 2 | 22.2 | 8 | 88.9 | 24 | 0.7 | 34 | 0.98 |
| Missing values | 0 | 0 | 0 | 0 | 13 | 0.4 | 13 | 0.38 |
| Knowing that viruses cause most hepatitis | | | | | | | | |
| knows it | 6 | 66.7 | 6 | 66.7 | 1996 | 57.9 | 2008 | 57.98 |
| US/UK/DU/DB(b) | 3 | 33.3 | 2 | 22.2 | 1425 | 41.4 | 1430 | 41.29 |
| Missing values | 0 | 0 | 1 | 11.1 | 24 | 0.7 | 25 | 0.72 |
| Knowing that there are several types of viral hepatitis, named by the letters of the alphabet | | | | | | | | |
| knows it | 7 | 77.8 | 9 | 100 | 3049 | 88.5 | 3065 | 88.51 |
| US/UK/DU/DB(b) | 2 | 22.2 | 0 | 0 | 360 | 10.4 | 362 | 10.45 |
| Missing values | 0 | 0 | 0 | 0 | 36 | 1.0 | 36 | 1.04 |
| Knowing that there are only vaccines for hepatitis A and hepatitis B, but not for hepatitis C. | | | | | | | | |
| knows it | 4 | 44.4 | 7 | 77.8 | 1700 | 49.3 | 1711 | 49.41 |
| US/UK/DU/DB(b) | 5 | 55.6 | 2 | 22.2 | 1710 | 49.6 | 1717 | 49.58 |
| Missing values | 0 | 0 | 0 | 0 | 35 | 1.0 | 35 | 1.01 |
| Knowing that health care providers recommend that men who have sex with men get vaccinated | | | | | | | | |
| knows it | 4 | 44.4 | 5 | 55.6 | 1843 | 53.5 | 1852 | 53.48 |
| US/UK/DU/DB(b) | 5 | 55.6 | 4 | 44.4 | 1566 | 45.5 | 1575 | 45.48 |
| Missing values | 0 | 0 | 0 | 0 | 36 | 1.0 | 36 | 1.04 |
| Knowing that people who have HIV are more likely to be infected with hepatitis. | | | | | | | | |
| knows it | 4 | 44.4 | 6 | 66.7 | 1399 | 40.6 | 1409 | 40.69 |
| US/UK/DU/DB(b) | 5 | 55.6 | 3 | 33.3 | 2009 | 58.3 | 2017 | 58.24 |
| Missing values | 0 | 0 | 0 | 0 | 37 | 1.1 | 37 | 1.07 |

(a) HCV: Hepatitis C virus; AB: antibodies. (b) US, UK, DU, DB: Unsure, unknown, don't understand it or don't believe it

**Table 1b**
Descriptive of the sample. Sexual health and sexual behaviors.

| | HCV AB (+) HIV (−) (a) | | | | HCV (−) HIV (−) (n = 3445) | | Total HIV (−) (n = 3463) | |
|---|---|---|---|---|---|---|---|---|
| | RNA (+) (n = 9) | | RNA (−)(n = 9) | | | | | |
| | N | % | N | % | N | % | N | % |
| Last HIV testing | | | | | | | | |
| In the last 6 months | 8 | 88.9 | 7 | 77.8 | 1691 | 49.1 | 1706 | 49.26 |
| More than 6 months ago | 0 | 0 | 2 | 22.2 | 1532 | 44.5 | 1534 | 44.29 |
| Never tested before | 1 | 11.1 | 0 | 0 | 222 | 6.5 | 223 | 6.44 |
| Lifetime STI (a) (multiple options) | | | | | | | | |
| Syphilis | 6 | 66.7 | 4 | 44.4 | 803 | 23.3 | 813 | 23.48 |
| Gonorrhea | 5 | 55.6 | 5 | 55.6 | 1121 | 32.5 | 1131 | 32.66 |
| Chlamydia | 4 | 44.4 | 5 | 55.6 | 613 | 17.8 | 622 | 17.96 |
| Lymphogranuloma | 0 | 0 | 0 | 0 | 20 | 0.6 | 20 | 0.58 |
| Last diagnosed STI | | | | | | | | |
| More than 1 year ago | 2 | 22.2 | 1 | 11.1 | 941 | 27.3 | 944 | 27.26 |
| During the last year | 5 | 55.6 | 6 | 66.7 | 1010 | 29.3 | 1021 | 29.48 |
| Missing values | 2 | 22.2 | 2 | 22.2 | 1494 | 43.4 | 1498 | 43.26 |
| Lifetime condomless received penetration | | | | | | | | |
| None | 0 | 0 | 0 | 0 | 554 | 16.1 | 554 | 15.99 |
| Less than five people | 2 | 22.2 | 1 | 11.1 | 1790 | 52.0 | 1793 | 51.78 |
| More than five people | 7 | 77.8 | 8 | 88.9 | 1087 | 31.6 | 1102 | 31.82 |
| Missing values | 0 | 0 | 0 | 0 | 14 | 0.4 | 14 | 0.40 |
| Lifetime HIV (+) condomless received penetrations | | | | | | | | |
| None | 5 | 55.6 | 6 | 66.7 | 2507 | 72.8 | 2518 | 72.71 |
| Some | 4 | 44.4 | 3 | 33.3 | 566 | 16.4 | 573 | 16.55 |
| Missing values | 0 | 0 | 0 | 0 | 372 | 10.8 | 372 | 10.74 |
| Last year condomless received penetrations | | | | | | | | |
| None | 1 | 11.1 | 0 | 0 | 819 | 23.8 | 820 | 23.68 |
| Less than five people | 5 | 55.6 | 7 | 77.8 | 1767 | 51.3 | 1779 | 51.37 |
| More than five people | 2 | 22.2 | 2 | 22.2 | 326 | 9.5 | 330 | 9.53 |
| Missing values | 1 | 11.1 | 0 | 0 | 533 | 15.5 | 534 | 15.42 |
| Lifetime unprotected anal fingering | | | | | | | | |
| None | 3 | 33.3 | 4 | 44.4 | 1338 | 38.8 | 1345 | 38.84 |
| Some | 6 | 66.7 | 5 | 55.6 | 2097 | 60.9 | 2108 | 60.87 |
| Missing values | 0 | 0 | 0 | 0 | 10 | 0.3 | 10 | 0.29 |
| Lifetime fisting | | | | | | | | |
| None | 7 | 77.8 | 8 | 88.9 | 3239 | 94.0 | 3254 | 93.96 |
| Some | 2 | 22.2 | 1 | 11.1 | 202 | 5.9 | 205 | 5.92 |
| Missing values | 0 | 0 | 0 | 0 | 4 | 0.1 | 4 | 0.12 |
| Ever having visible bleeding after unprotected anal penetration | | | | | | | | |
| None | 5 | 55.6 | 5 | 55.6 | 2436 | 70.7 | 2446 | 70.63 |
| Some | 4 | 44.4 | 4 | 44.4 | 1008 | 29.3 | 1016 | 29.34 |
| Missing values | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0.03 |
| Ever sharing unprotected sex toys | | | | | | | | |
| None | 8 | 88.9 | 9 | 100 | 3005 | 87.2 | 3022 | 87.27 |
| Some | 1 | 11.1 | 0 | 0 | 434 | 12.6 | 435 | 12.56 |
| Missing values | 0 | 0 | 0 | 0 | 6 | 0.2 | 6 | 0.17 |
| Ever sharing lubricant from the same pot | | | | | | | | |
| None | 3 | 33.3 | 3 | 33.3 | 1340 | 38.9 | 1346 | 38.87 |
| Some | 6 | 66.7 | 6 | 66.7 | 2088 | 60.6 | 2100 | 60.64 |
| Missing values | 0 | 0 | 0 | 0 | 17 | 0.5 | 17 | 0.49 |
| Ever sharing douching material | | | | | | | | |
| None | 3 | 33.3 | 7 | 77.8 | 2751 | 79.9 | 2761 | 79.73 |
| Some | 6 | 66.7 | 2 | 22.2 | 689 | 20.0 | 697 | 20.13 |
| Missing values | 0 | 0 | 0 | 0 | 5 | 0.1 | 5 | 0.14 |
| Participating in group sex (being penetrated by two or more men in one session) | | | | | | | | |
| None | 2 | 22.2 | 4 | 44.4 | 2267 | 65.8 | 2273 | 65.64 |
| Some | 7 | 77.8 | 5 | 55.6 | 1170 | 34.0 | 1182 | 34.13 |
| Missing values | 0 | 0 | 0 | 0 | 8 | 0.2 | 8 | 0.23 |
| Ever pay a man for sex | | | | | | | | |
| None | 7 | 77.8 | 8 | 88.9 | 2842 | 82.5 | 2857 | 82.50 |
| Some | 2 | 22.2 | 1 | 11.1 | 603 | 17.5 | 606 | 17.49 |
| Ever been paid for sex | | | | | | | | |
| None | 4 | 44.4 | 6 | 66.7 | 2705 | 78.5 | 2715 | 78.40 |
| Some | 5 | 55.6 | 3 | 33.3 | 739 | 21.5 | 747 | 21.57 |
| Missing values | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0.03 |
| Lifetime sexualized use of drugs (multiple options) | | | | | | | | |
| Poppers | 6 | 66.7 | 4 | 44.4 | 1456 | 42.3 | 1466 | 42.33 |
| Erectile medication | 4 | 44.4 | 2 | 22.2 | 695 | 20.2 | 701 | 20.24 |
| Sedatives or tranquilizers | 0 | 0 | 1 | 11.1 | 58 | 1.7 | 59 | 1.70 |
| Cannabis or synthetic cannabinoids | 1 | 11.1 | 3 | 33.3 | 727 | 21.1 | 731 | 21.11 |
| Powder or crack cocaine | 4 | 44.4 | 2 | 22.2 | 534 | 15.5 | 540 | 15.59 |
| Heroin or other opium derivatives | 1 | 11.1 | 0 | 0 | 11 | 0.3 | 12 | 0.35 |
| Amphetamine | 3 | 33.3 | 1 | 11.1 | 222 | 6.4 | 226 | 6.53 |

(*continued on next page*)

**Table 1b** (*continued*)

| | HCV AB (+) HIV (−) (a) | | | | HCV (−) HIV (−) (n = 3445) | | Total HIV (−) (n = 3463) | |
|---|---|---|---|---|---|---|---|---|
| | RNA (+) (n = 9) | | RNA (−)(n = 9) | | | | | |
| | N | % | N | % | N | % | N | % |
| Ecstasy or MDMA (b) in its pill or crystal form | 1 | 11.1 | 2 | 22.2 | 430 | 12.5 | 433 | 12.50 |
| Methamphetamine | 3 | 33.3 | 1 | 11.1 | 268 | 7.8 | 272 | 7.85 |
| Mephedrone | 3 | 33.3 | 0 | 0 | 267 | 7.8 | 270 | 7.79 |
| Gamma-hydroxybutyrate/ gamma-hydroxybutirolactone | 4 | 44.4 | 1 | 11.1 | 459 | 13.3 | 464 | 13.39 |
| Ketamine | 2 | 22.2 | 0 | 0 | 245 | 7.1 | 247 | 7.13 |
| LSD (c) | 0 | 0 | 0 | 0 | 58 | 1.7 | 58 | 1.67 |
| Lifetime use of alcohol during sex | | | | | | | | |
| None | 2 | 22.2 | 4 | 44.4 | 1108 | 32.2 | 1114 | 32.17 |
| Less than 10 times | 2 | 22.2 | 2 | 22.2 | 1367 | 39.7 | 1371 | 39.58 |
| More than 10 times | 5 | 55.6 | 3 | 33.3 | 942 | 27.3 | 950 | 27.43 |
| Missing values | 0 | 0 | 0 | 0 | 28 | 0.8 | 28 | 0.81 |
| Injectable drug use, for sex | | | | | | | | |
| Yes | 6 | 66.7 | 9 | 100 | 3352 | 97.3 | 3367 | 97.23 |
| No | 3 | 33.3 | 0 | 0 | 51 | 1.5 | 54 | 1.56 |
| Missing values | 0 | 0 | 0 | 0 | 42 | 1.2 | 42 | 1.21 |
| Sharing sniffing material, for sex | | | | | | | | |
| None | 3 | 33.3 | 8 | 88.9 | 2813 | 81.7 | 2824 | 81.55 |
| Some | 5 | 55.6 | 1 | 11.1 | 589 | 17.1 | 595 | 17.18 |
| Missing values | 1 | 11.1 | 0 | 0 | 43 | 1.2 | 44 | 1.27 |

(a) STI: sexually transmitted infection.(b) MDMA: 3,4-metilendioximetanfetamina (c) LSD: Lysergic acid diethylamide.

## Discussion

Our study results estimate that HCV seroprevalence and active infection in HIV-negative GBMSM from Barcelona and Madrid are similar to the prevalence among the general population. However, individuals with a history of HCV were positively associated with a range of sexual behaviors epidemiologically linked to an increased risk of bleeding, particularly condomless anal sex, an elevated number of penetrations in a given sexual encounter, and sexualized drug consumption. Other practices with risk of blood-sharing observed with this population include group sex participation and sharing douching, sniffing, or injection materials.

Our HCV antibody prevalence seem a bit lower than what has been observed in previous reports on HIV-negative GBMSM [7,12], although they correlate very well with previous analysis of this population conducted in community centers in Barcelona [19,20]. Systematic review from Jin et al. [7] described a general HCV seroprevalence in GBMSM of 3.4% (2.5-10.4%), independent of their HIV status, and 1.5% (1.0-2.1%) in HIV-negative GBMSM. Zheng et al. [12]'s review pooled an HCV prevalence of 5.9% (5.1-6.8%) in general GBMSM and 2.8% (1.9-4.0%) in the HIV-negative group. In Spain's GBMSM, While earlier studies reported a general prevalence of 4.2% (2.2-6.7%) [7]; they found no cases of HCV in HIV-negative GBMSM (0% [0-0.9%]); Zheng et al. [12]'s study reported a general GBMSM seroprevalence of 6.3% (3.7-9.4%), with a seroprevalence of 3.0% (0.7-6.6%) in HIV-undiagnosed GBMSM, being correlated with our results. Many factors could explain these differences, like the study's region, the sample selection method, or the inclusion of specific populations, such as people who inject drugs (PWID). In Barcelona, Saludes et al. [19] reported an HCV seroprevalence of 0.75% (0.1-1.6%) in 617 HIV-negative GBMSM recruited voluntarily from a community center, while Coll et al. [20] followed 258 HIV-undiagnosed GBMSM from 2009-2012, recruited as well from community centers, finding an HCV seroprevalence of 2.0% (0.7-4.8%), both similar with our results. Furthermore, Jin et al. [7]'s results describe that HCV seroprevalence was higher in low and lower-middle-income economies, independent of their HIV status, unlike Spain, which is close to HCV eradication [2], and other countries that have adopted DAA strategies [21]. Other studies evaluating HCV seroprevalence in GBMSM in Spain begin by recruiting HIV-positive individuals and assessing the coinfection risk. In our sample, those who received an HIV diagnosis presented an HCV antibody prevalence of 3.53% (1.21-9.87) and a prevalence of active infection of 2.35% (0.65-8.18), supporting the correlation between these two infections [7,9,11].

Both antibodies and presenting an active HCV were strongly associated with ever being in close contact with an HCV partner diagnosed, especially if they have previously shared shaving material. Moreover, presenting an active infection was strongly associated with a previous HCV diagnosis, supporting previous evidence of reinfection risk [22]. Ever being paid for sex presented significant associations in both adjusted models but may have interacted with other variables in the final models, like slamming or sharing douching material. It is important, for screening and surveillance implications, the correct identification of key populations, contact tracing when a diagnosis is made, and the linkage for regular testing in an HCV-diagnosed patient. Adu et al. [23] found that in reinfected HCV HIV (+) GBMSM, mental health counseling could reduce the risk of reinfection, so targeted interventions could be beneficial also in those HIV-negative.

PWID, in general, has been targeted as a key population for HCV eradication [2,24], with reported seroprevalence in European PWID ranging from 7-95% and national PWID's seroprevalence estimated at 66.6% [25]. Due to this previous assumption, we expected the high association of seroprevalence observed with ever using heroin or using injectable drugs, for any purpose. PWID who also identifies as GBMSM may constitute a unique group with an increased risk of HCV acquisition. Moreover, high rates of injecting drug use appear to be one of the main drivers of the HCV epidemic in this population. In our sample, the association of using injectable drugs for sex was higher than using them for any purpose. Previous analyses on this sample have been published on this subject [13], describing associations with an increased number of sex partners and meeting them in private parties. Slamming sex is a practice reported to be rising among individuals practicing chemsex [7,13,26], so screening and preventive interventions during sexual health consultation should be mandatory [27]. Previous data published in this sample observed a significant increase compared with previous Spanish reports, where 81.9% of first injectors were in a sexual context, 62.7% started with mephedrone, and 32.2% with methamphetamine [13].

Mephedrone and Crystal Methamphetamine have been recognized as two of the drugs in "4-Chem", along with GHB/GBL and ketamine [18], with an increasing amount of research focused on their sexualized use within GBMSM communities, and their effects [28]. Although a single definition for chemsex does not yet exist [29,30], the

**Table 2**
Crude and adjusted Poisson regression with robust variance for HCV antibodies prevalence and active infection. APR is adjusted by age, country of origin, study level, economic welfare, and orientation disclosure (APR1), while APR2 is a single model with adjusted and significant variables. Only significant variables are presented. For more information refer to Supplementary material 2.

| | HCV antibodies prevalence | | | | | | Active HCV infection | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | HCV AB (+) HIV(−), (n = 18) | | | | | | HCV AB (+) RNA (+) HIV(−), (n = 9) | | | | | |
| | CPR | 95% CI | APR (1) | 95% CI | APR (2) | 95% CI | CPR | 95% CI | APR (1) | 95% CI | APR (2) | 95% CI |
| Age (three groups) | | | | | | | | | | | | |
| Under 30 years old | 1 | | 1 | | 1 | | 1 | | 1 | | 1 | |
| Between 30-39 years | 2.07 | 0.69-6.16 | 1.75 | 0.61-5.05 | 2.62 | 0.68-10.14 | 3.45 | 0.69-17.08 | 2.84 | 0.59-13.60 | 2.93 | 0.70-12.18 |
| 40 years or more | 1.21 | 0.32-4.48 | 1.11 | 0.28-4.34 | 1.63 | 0.32-8.22 | 0.75 | 0.06-8.31 | 0.64 | 0.05-8.63 | 0.6 | 0.10-3.61 |
| Country of birth | | | | | | | | | | | | |
| Spain | 1 | | 1 | | 1 | | 1 | | 1 | | 1 | |
| Latin-America | 1.77 | 0.66-4.73 | 2.22 | 0.82-5.98 | 2.07 | 0.65-6.59 | 1.71 | 0.38-7.61 | 2.04 | 0.45-9.13 | 1.75 | 0.38-8.13 |
| Others | 1.30 | 0.28-6.00 | 1.19 | 0.26-5.45 | 0.74 | 0.09-5.84 | 2.93 | 0.54-15.94 | 2.59 | 0.47-14.06 | 5.06 | 0.94-27.16 |
| Study level | | | | | | | | | | | | |
| None or primary | 1 | | 1 | | | | 1 | | 1 | | 1 | |
| Mandatory secondary | 0.41 | 0.04-4.54 | 0.38 | 0.03-4.52 | [a] | | 0.21 | 0.01-3.29 | 0.18 | 0.01-3.29 | 0.11 | 0.01-1.96 |
| University or more | 1.74 | 0.23-13.18 | 1.55 | 0.19-12.89 | [a] | | 0.82 | 0.10-6.60 | 0.59 | 0.06-5.91 | 0.98 | 0.14-6.87 |
| Economic welfare last year | | | | | | | | | | | | |
| Comfortable | 1 | | 1 | | 1 | | 1 | | 1 | | 1 | |
| Thigh. hard/very hard | 0.58 | 0.21-1.62 | 0.62 | 0.21-1.82 | 0.55 | 0.16-1.81 | 0.43 | 0.09-2.06 | 0.43 | 0.08-2.23 | 0.46 | 0.09-2.21 |
| Employment status | | | | | | | | | | | | |
| Employed | 1 | | 1 | | | | 1 | | 1 | | | |
| Unemployed | 1.04 | 0.13-8.15 | 1.64 | 0.14-19.48 | | | 2.33 | 0.26-20.81 | 4.78 | 0.27-86.29 | | |
| Orientation disclosure | | | | | | | | | | | | |
| Openly | 1 | | 1 | | 1 | | 1 | | 1 | | 1 | |
| Not openly | 0.79 | 0.30-2.13 | 0.79 | 0.27-2.31 | 0.89 | 0.27-3.02 | 0.79 | 0.20-3.19 | 0.9 | 0.22-3.67 | 1.51 | 0.30-7.59 |
| Sex also with women | | | | | | | | | | | | |
| Exclusively with men | 1 | | 1 | | | | 1 | | 1 | | | |
| Occasionally | 0.94 | 0.33-2.69 | 0.95 | 0.33-2.72 | | | 0.82 | 0.16-4.24 | 0.86 | 0.17-4.32 | | |
| Frequently | 1.59 | 0.35-7.12 | 2.38 | 0.54-1043 | | | 3.49 | 0.67-17.92 | **6.37** | **1.74-23.26** | | |
| Last HIV testing | | | | | | | | | | | | |
| In the last 6 months | 1 | | 1 | | | | 1 | | 1 | | | |
| More than 6 months ago | 0.15 | 0.03-0.64 | **0.15** | **0.03-0.67** | | | [a] | | [a] | | | |
| Never tested before | 0.51 | 0.07-3.89 | 0.84 | 0.09-7.79 | | | 0.96 | 0.12-7.66 | 1.75 | 0.15-19.86 | | |
| Lifetime STI (multiple option) | | | | | | | | | | | | |
| Syphilis | 4.06 | 1.61-10.26 | **4.09** | **1.51-11.11** | | | 6.49 | 1.63-25.93 | **6.33** | **1.52-26.35** | | |
| Gonorrhea | 2.61 | 1.03-6.59 | 2.45 | 0.89-6.69 | | | 2.61 | 0.70-9.69 | 2.33 | 0.62-8.88 | | |
| Chlamydia | 4.66 | 1.86-11.71 | **4.61** | **1.67-12.70** | | | 3.73 | 1.00-13.91 | 3.42 | 0.86-13.61 | | |
| Last diagnosed STI | | | | | | | | | | | | |
| More than 1 year ago | 1 | | 1 | | 1 | | 1 | | 1 | | | |
| During the last year | 3.38 | 0.94-12.06 | **3.79** | **1.06-13.63** | **4.06** | **1.09-15.12** | 2.30 | 0.44-11.84 | 2.36 | 0.44-12.74 | | |
| Lifetime received penetrations | | | | | | | | | | | | |
| Less than 50 people | 1 | | 1 | | | | 1 | | 1 | | | |
| More than 50 people | 4.22 | 1.64-10.85 | **4.32** | **1.64-12.00** | | | 1.34 | 0.34-5.36 | 1.21 | 0.27-5.33 | | |
| Lifetime condomless received penetration | | | | | | | | | | | | |
| Less than five people | 1 | | 1 | | | | 1 | | 1 | | | |
| More than five people | 8.01 | 2.32-27.66 | **8.86** | **2.52-31.14** | | | 5.60 | 1.17-26.94 | **5.83** | **1.18-28.73** | | |
| Lifetime HIV (+) condomless received penetrations | | | | | | | | | | | | |
| None | 1 | | 1 | | | | 1 | | 1 | | | |
| Some | 2.79 | 1.08-7.20 | **2.89** | **1.09-7.69** | | | 3.51 | 0.94-13.03 | 3.39 | 0.70-16.43 | | |
| Last year condomless received penetrations | | | | | | | | | | | | |
| None | 1 | | 1 | | | | 1 | | 1 | | | |
| Less than five people | 5.44 | 0.71-41.78 | 5.58 | 0.69-44.71 | | | 2.27 | 0.27-19.38 | 2.32 | 0.25-21.22 | | |
| More than five people | 9.58 | 1.07-85.43 | **10.19** | **1.00-103.95** | | | 4.79 | 0.43-52.66 | 4.51 | 0.31-66.48 | | |

(*continued on next page*)

**Table 2** (*continued*)

| | HCV antibodies prevalence | | | | | | Active HCV infection | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | HCV AB (+) HIV(−), (n = 18) | | | | | | HCV AB (+) RNA (+) HIV(−), (n = 9) | | | | | |
| | CPR | 95% CI | APR (1) | 95% CI | APR (2) | 95% CI | CPR | 95% CI | APR (1) | 95% CI | APR (2) | 95% CI |
| Sharing douching material | | | | | | | | | | | | |
| No | 1 | | 1 | | | | 1 | | 1 | | 1 | |
| Yes | 3.17 | 1.26-8.00 | **3.38** | **1.29-8.82** | | | 7.92 | 1.98-31.69 | **8.45** | **2.08-34.41** | **7.45** | **2.12-25.95** |
| Group sex (penetrated by two or more men in one session) | | | | | | | | | | | | |
| No | 1 | | 1 | | | | 1 | | 1 | | | |
| Yes | 3.78 | 1.42-10.05 | **3.61** | **1.21-10.76** | | | 6.62 | 1.38-31.81 | **6.03** | **1.01-35.91** | | |
| Ever been paid for sex | | | | | | | | | | | | |
| No | 1 | | 1 | | | | 1 | | 1 | | | |
| Yes | 2.89 | 1.14-7.29 | **3.50** | **1.42-8.60** | | | 4.51 | 1.21-16.78 | **5.44** | **1.41-21.04** | | |
| Ever being diagnosed HCV | | | | | | | | | | | | |
| No | 1 | | 1 | | | | 1 | | 1 | | 1 | |
| [b]Yes | 128.68 | 54.1-306.0 | **175.57** | **63.65-476.12** | | | 29.41 | 6.11-141.58 | **37.29** | **7.10-195.86** | **100.82** | **22.16-458.76** |
| Have lived with an HCV(+) person | | | | | | | | | | | | |
| No | 1 | | 1 | | 1 | | 1 | | 1 | | | |
| Yes | 6.67 | 2.40-18.53 | **6.99** | **2.42-20.21** | **7.84** | **2.50-24.53** | 4.96 | 1.04-23.71 | **5.81** | **0.99-33.87** | | |
| Shared razors or shaving brushes with an HCV(+) person | | | | | | | | | | | | |
| No | 1 | | 1 | | | | 1 | | 1 | | | |
| Yes | 27.56 | 6.89-110.19 | **28.54** | **6.48-125.68** | | | 27.56 | 3.66-207.83 | **33.21** | **4.24-259.99** | | |
| Lifetime sexualized use of drugs (multiple option) | | | | | | | | | | | | |
| Poppers | 1.71 | 0.68-4.32 | 1.59 | 0.62-4.11 | | | 2.73 | 0.69-10.93 | 2.47 | 0.59-10.31 | | |
| Erectile medication | 1.97 | 0.74-5.23 | 1.80 | 0.59-5.45 | | | 3.15 | 0.85-11.71 | 3.05 | 0.75-12.51 | | |
| Cannabis or synthetic cannabinoids | 1.07 | 0.35-3.25 | 1.04 | 0.35-3.06 | | | 0.47 | 0.06-3.74 | 0.44 | 0.06-3.08 | | |
| Powder or crack cocaine | 2.71 | 1.02-7.20 | 2.81 | 0.88-8.97 | | | 4.34 | 1.17-16.12 | 4.21 | 0.76-23.27 | | |
| Heroin or other opium derivatives | 17.33 | 2.50-120.11 | **16.45** | **1.99-135.97** | | | 36.83 | 4.98-272.27 | **39.15** | **4.39-349.15** | | |
| Ecstasy or MDMA in its pill or crystal form | 1.41 | 0.41-4.84 | 1.31 | 0.34-5.01 | | | 0.88 | 0.11-7.02 | 0.77 | 0.08-7.91 | | |
| Amphetamine | 4.12 | 1.36-12.42 | **4.31** | **1.42-13.13** | | | 7.21 | 1.82-28.66 | **6.83** | **1.78-26.12** | | |
| Methamphetamine | 3.35 | 1.11-10.10 | **3.43** | **1.02-11.51** | | | 5.86 | 1.47-23.30 | **5.61** | **1.20-26.15** | | |
| Mephedrone | 2.31 | 0.67-7.92 | 2.22 | 0.62-7.97 | | | 5.77 | 1.45-22.94 | **5.33** | **1.17-24.11** | | |
| Gamma-hydroxybutyrate/ gamma-hydroxybutirolactone | 2.46 | 0.88-6.88 | 2.36 | 0.77-7.20 | | | 5.12 | 1.38-19.02 | **4.68** | **1.18-18.54** | | |
| Ketamine | 1.57 | 0.36-6.78 | 1.54 | 0.33-7.19 | | | 3.58 | 0.75-17.17 | 3.29 | 0.58-18.64 | | |
| Injectable drug use. for sex | | | | | | | | | | | | |
| Yes | 1 | | 1 | | 1 | | 1 | | 1 | | 1 | |
| No | 12.55 | 3.74-42.10 | **12.26** | **3.26-46.13** | **6.92** | **1.20-39.79** | 31.36 | 7.84-125.41 | **33.36** | **7.63-145.74** | **17.53** | **2.70-113.76** |
| Sharing sniffing material. for sex | | | | | | | | | | | | |
| No | 1 | | 1 | | | | 1 | | 1 | | | |
| Yes | 2.59 | 0.96-6.98 | 2.65 | 0.91-7.69 | | | 7.92 | 1.89-33.05 | **8.34** | **1.74-39.90** | | |

AB, antibody; APR, adjusted prevalence ratio; CI, confidence interval; CPR, crude prevalence ratio; HCV, hepatitis C virus; STI, sexually transmitted infection.

[a] Excluded due to no cases.

[b] Probably related to previous diagnosis.

practices associated with consuming these substances present a pathway for HCV acquisition, such as participating in group sex or the association with GHB/GBL using, besides the other chem drugs. Unlike others with a clear correlation due to the sniffed or injected pathway of administration, GHB/GBL is orally administrated. This could be explained due to the sexual context where the substances are consumed, where they could facilitate the occurrence of known risk of bleeding practices. Furthermore, social determinant variables such as peer pressure, mental health-related variables, or hegemonic masculinity could increase those related risks [28,30].

Rectal douching, or the use of enemas before sex, has been reported as a risk factor for HIV and other STIs, including HCV [31]. Sharing douching material may be a regular practice in those who practice receptive anal sex (bottoming), especially those who attend saunas or private sex parties. It is important to discuss the normative expectations of an anal sexual encounter, balancing the risk and benefits of a regular douching practice, as well as risk reduction strategies, like utilizing their own instruments and attending regular anal checkups in higher-risk populations [31].

Sexual health services are cost-effective and critical points to addressing sexual behaviors with risk of HCV acquisition [32,33]. Personalized risk reduction strategies should be recommended according to their practices, the number of sexual partners, and the preventive strategies of choice, independent of their gender or sexual orientation. Targeting recommendations in sexually active and non-monogamous individuals, with early detection of bleeding risk practices and sexualized substance use, are key elements to an effective response for current needs as well as future outbreaks and epidemics related to sex [34].

Spain's 2017 guidelines for STI management include a yearly HCV screening, with recommendations on 3-6 months of screening in those of "higher risk", not specifying what indeed defines a "riskier" GBMSM [17]. However, although 6.4% of our total sample was tested for the first time for HIV, only 44.7% of the sample referred to being previously tested for HCV. As the 2022 mpox (monkeypox) outbreak demonstrated, there is a need for homogeneous, integrated, and articulated sexual health-related services, with sanitary, surveillance, and community entities developing effective risk communication strategies, clear and informed, but free of stigma. Considering globalized culture and patterns of human movements, it is possible that practices associated with a higher risk of HCV transmission have also increased in countries where HCV testing policies are less expanded, especially in sexual health context.

## Limitations

This study has an important limitation of not including PrEP usage as a variable since the beginning of the study, which was difficult due to the particular political environment around the start of the study. PrEP in Spain was included in the sanitary system in November of 2019, and since then, the number of users has been growing, especially in Barcelona and Madrid. PrEP users who engage in condomless sex are identified as a key population for STI prevention [5,7,14], and between this group, the observed risk of acquiring HCV is reported to be higher than their nonusers' peers, for different causes previously discussed [7,14]. Spanish current guidelines in PrEP management indicates HCV screening at the first visit, without recommendations for further control [35], so better recommendations are needed. Nevertheless, PrEP use should not be seen as a causal correlation of acquiring HCV, but as a tool to improve their sexual health. Regular HCV testing in PrEP users, especially in those with practices with risk of bleeding, among counseling interventions, could impact this increased risk.

Other limitations of this study include the selection bias as a result of recruiting individuals from sexual health centers, which may overrepresent higher-risk GBMSM. However, some compensation may be achieved by designing the recruitment from health care centers and community centers in different cities, which may encompass the different profiles of users in the most populated areas of Spain, who attract GBMSM from other parts of Spain and abroad. The COVID-19 pandemic may have affected the access to sexual health services during a good part of our recruitment, as well as restrictions in mobility, which translated into fewer screening checkups, however, most of the sample was recruited before the confinement period. The cross-sectional design does not allow to define causality, so further research is encouraged. The strengths of this study include the power of the sample, the diversity of recruitment sites in highly concentrated GBMSM cities, and the deep research in bleeding risk practices, hepatitis knowledge, and substance use consumption. Our results reinforce the need to develop clear and updated indications on HCV screening, and better interventions in key populations, understanding the specific characteristics of this population in preparation for stronger services.

## Conclusion

During 2018-2021, the risk of HCV infection among Barcelona and Madrid's HIV-negative GBMSM was similar to the general population, but higher in those who engage in sexual practices with bleeding risk, such as slamming, chemsex, and sharing rectal douching material. With the increase of PrEP users, HCV diagnosis between HIV-negative GBMSM may rise, due to regular testing but also to the incorporation of new sexual practices. The increased risk for HIV and STIs in GBMSM responds to multiple factors yet to be better understood. Future research is needed to elucidate the contextual, behavioral, and cultural differences of this group allowing to improve the quality of the continuum of care and strengthen the response to potential outbreaks or epidemics related to sex. Sexual health services should identify these practices early during consultation, promoting targeted risk reduction strategies, such as hepatitis A and B vaccination and regular testing. Frequent testing should be recommended in non-monogamous individuals, according to their individual needs and epidemiological context. When a diagnosis is made, contact tracing is highly recommended for cohabitants and sex partners. Further preventive interventions that address mental health and social determinants of health should be promoted, integrating community entities with healthcare and surveillance systems.

## Declarations of competing interest

The authors have no competing interests to declare.

## Funding

Both a Health Research Grant (Fondo de Investigación en Salud, FIS P117/02077) and an Intramural Strategy Action Grant (PI17CIII/00037), From the Carlos III Institute, at the Science and Innovation Ministry of the Spain Government, supported this study.

## Ethical approval

Each participant signed an informed consent accepting to participate voluntarily, after being explained about the aim of the study and the confidentiality of the obtained data. To guarantee confidentiality of the data and records, we adhered to the regulations established by the Organic Law on the Protection of Personal Data 15/1999 in Spain and the successive updates. The project was approved by Research Ethics Committee of Parc de Salut Mar, on June 25, 2019 and by the Research Ethics Committee of the Instituto de Salud Carlos III (CEI PI 44_2018_subproyecto1-v2 and CEI PI 44_2018_subproyecto2).

## Author contributions

Patricia García de Olalla (PGO), María José Belza (MJB), Juan-Miguel Guerras (JMG), and María Jesús Barberá (MJB) worked on the conceptualization and first methodology design of the proposed work and trial design. Cristina Rius (CR), PGO, and MJB were in charge

of funding acquisition and project administration, including resources. JMG developed the survey, supervised by MJB and PGO. Then, David Palma (DP), Miguel Alarcón (MA), Jorge García (JG), Oscar Ayerdi (OA), and Mar Vera García (MVG) were in charge of the patient recruitment and acquisition of the data in both cities. JMG and DP independently worked in the data curation, organization of the database and performed the statistical analysis. DP performed the formal analysis for this manuscript, literature search, and wrote the first draft of the manuscript, tables, and figures. PGO, CR, and Andrés Román-Urrestarazu (ARU) have supervised the PhD of DP. PGO, MA, JMG, MJB, ARU, Carles Pericas (CP), and CR worked in the validation and interpretation of data for the work, and supervised DP work in data visualization. All the authors provided editing to the manuscript and their final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. MJB and CR have contributed equally to the senior authorship.

## Role of funding source

Both FIS P117/02077 and PI17CIII/00037 allowed the development of the research project and data dissemination in congress. None of the funders has any inference in the interpretation of results and recommendations obtained from the conclusions.

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijregi.2023.07.001.

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