

RESEARCH

Open Access



Association between non-injection drug use and hepatitis C infection among HIV-negative men who have sex with men

Jing Zhao^{1*}, Charles Green², Christine Markham³, Kayo Fujimoto³, Alan G. Nyitray⁴ and Lu-Yu Hwang⁵

Abstract

Background Prior research predominantly examined the association between HIV-positive men who have sex with men (MSM) or those using injection drugs and hepatitis C virus (HCV) infection. However, limited attention has been given to understanding the association among HIV-negative MSM who do not inject drugs. This gap leaves a portion of the population unexamined, potentially overlooking an important factor that may contribute to the transmission and prevalence of HCV. This study aims to investigate the relationship between non-injection drug use and HCV infection in this population.

Methods In this cross-sectional study, we analyzed data on 118 MSM who reported use of non-injection drugs. The participants were recruited from two inner-city communities in Houston, TX, between 2004 and 2007 and were negative for both HIV and hepatitis B virus infection. Latent class analysis (LCA) was used to identify drug use latent classes. Multinomial logistic regression analysis was used to evaluate the association between drug use latent class and HCV infection.

Results Four distinct latent classes of drug use were identified: class 1, persons ≥ 42 years of age who used only crack cocaine; class 2, persons approximately 42 years of age who used > 2 drugs; class 3, persons < 42 years of age who used > 5 drugs; and class 4, persons ≥ 42 years of age who used > 6 drugs. Class 4 was significantly associated with HCV infection. The odds of HCV infection in members of class 4 was 17 times higher than in class 2 members (adjusted odds ratio [aOR] = 16.9, 95% confidence interval [CI]: 1.4–205.4) and almost 22 times higher than in class 3 members (aOR = 21.8, 95% CI: 1.5–322.8).

Conclusions Among MSM with non-injection drug use, the subgroup of individuals who were ≥ 42 years of age and used multiple drugs (including heroin, speedball, methamphetamine, crack cocaine, and marijuana) had a high probability of HCV infection. Public health and education programs, as well as drug treatment and rehabilitation programs, should be developed for this high-risk subgroup of individuals to prevent HCV acquisition and transmission.

Keywords Hepatitis C virus, Non-injection drug use, Men who have sex with men, Latent class analysis, Multinomial logistic regression, HIV-negative MSM

*Correspondence:

Jing Zhao

jzhao11@mdanderson.org

Full list of author information is available at the end of the article



© The Author(s) 2024. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc-nd/4.0/>.

Background

Compared to the general population, men who have sex with men (MSM) are disproportionately affected by various infectious diseases, including HIV, syphilis, and other sexually transmitted infections (STIs) [9]. Additionally, there is evidence suggesting that hepatitis C virus (HCV) infections may also affect MSM disproportionately. Reports of an HCV epidemic or outbreaks among MSM have been emerging since 2000 [6, 16, 41, 42, 44, 45]. Most of these studies have focused on MSM who were HIV positive, used injection drugs, or were HIV positive and used injection drugs. However, there have been fewer studies specifically targeting HIV-negative MSM who do not use injection drugs [14].

Although overall HCV prevalence rates are comparable in HIV-negative MSM and the general United States (U.S.) population [4, 36], individuals who use non-injection drugs have a higher rate of HCV infection (2.3% to 35.3%) than the general population (1%) [37]. Furthermore, non-injection drug use is higher in MSM than in heterosexual men, with past-month prevalence rates of 16.3% versus 9.9% [11]. These results therefore suggest that HIV-negative MSM with non-injection drug use may have a higher rate of HCV infection than the general population.

People who use drugs are typically heterogeneous with regard to the type of drug, as a number of different drug types are available, and a person may choose multiple drug types at the same or different times. Studying the isolated effects of individual drugs may not fully capture the complexity of using multiple drugs concurrently, which could potentially limit its relevance to real-world scenarios. To simultaneously analyze drug use variables, latent class analysis (LCA) [8, 25, 30, 38, 47] is a widely applied and highly effective approach. The authors of one U.S. internet-based MSM sample used LCA to identify a distinct multiple drug use group [27]. Another study recruited a similar sample of MSM and found that individuals in the “high polydrug” subgroup (identified using LCA) were more likely to report unprotected anal intercourse and STIs [48]. In a Malaysian internet-based MSM sample, LCA identified an “amphetamine-type stimulant use” latent class, which was associated with a higher likelihood of high-risk sexual behavior, HIV infection, and STIs, compared with a low-risk drug use group [26].

Furthermore, previous research has highlighted specific factors that may facilitate HCV transmission among individuals who use non-injection drugs, including the sharing of pipes when smoking drugs and having cracked lips [21]. These findings underscore the need to investigate the potential mechanisms behind HCV transmission in this context.

While there have been some studies on HCV infection among MSM, Fitzpatrick et al. [14] conducted a study on acute hepatitis C in HIV-uninfected men who have sex with men and do not report injecting drug use. However, their study did not specifically focus on latent class analysis or the identification of latent classes among this population. To address this gap and provide a more comprehensive understanding, we employed LCA to identify latent classes among HIV-negative MSM reporting non-injection drug use in our study and examined the association between these latent classes and HCV infection in this population. Subsequently, we examined the association between these latent classes and HCV infection in this specific group of men. The results of this study may provide important insights for HCV prevention and health education programs targeting HIV-negative MSM who use non-injection drugs.

Methods

Study design and participants

Data for this study were collected from the Drugs, AIDS, STDs, and Hepatitis (DASH) project, a community-based intervention study focused on preventing HIV, HBV, and HCV infections [23]. Participants were untreated drug users recruited from two highly endemic drug-using urban neighborhoods in Houston, Texas, USA, from February 2004 to October 2007. Participants were recruited by outreach workers using a chain referral approach. Eligibility criteria included being 18 years or older, residing locally, self-reported use of illegal or non-medically prescribed drugs (including cocaine or heroin) in the past 48 h, and the presence of drug metabolites confirmed by urinalysis (OnTrak Varian Testik, Palo Alto, CA). Individuals who tested negative for HIV and HBV were enrolled in the baseline study.

Data collection

Enrollment interviews were conducted using verbally administered questionnaires via computer-assisted personal interview (CAPI, QDS, Bethesda, MD). Baseline data were obtained from the enrollment interview. All data collection procedures and laboratory protocols were approved by the Committee for the Protection of Human Subjects at the University of Texas Health Science Center at Houston.

Variables and measurements

Information was collected on the following sociodemographic characteristics age, race/ethnicity, sexual orientation, education level, marital status, working status, income level, living arrangement, previous incarceration for more than 24 h, and drug treatment history.

Sexual behavior variables included number of male sexual partners in the past 30 days, frequency of condom use, trading sex for money or drugs in the past 30 days, and trading money or drugs for sex in the past 30 days.

Disease-related data included self-reported histories of sexually transmitted infections (STIs) such as gonorrhea, herpes, chlamydia, and trichomoniasis, as well as the participants' HIV, HBV, and HCV infection statuses. Screening tests for HIV1/2 antibodies, hepatitis B surface antigen (HBsAg), and antibodies to HCV (anti-HCV) were conducted using the Combo test (Core Combo HIV-HBsAg-HCV, Core Diagnostics, United Kingdom). Confirmatory tests for HIV were performed using the Microparticle Enzyme Immunoassay test (Abbott Laboratories, Chicago, IL) [23]. HCV infection was defined as a positive HCV antibody test.

For the collection of drug use variables, participants were asked if they had ever used the following drugs: crack cocaine, methamphetamine, marijuana, alcohol, fry (embalming fluid and phencyclidine [PCP]-laced cigarettes or marijuana sticks), powder cocaine, heroin, speedball (mixture of heroin and cocaine), and codeine syrup. Drug use indicators were recorded as “never used” (0) or “have ever used” (1). Age was also considered an indicator variable, as it is associated with the type of drug use [5, 17]. Based on the median age of 42 years, participants were categorized as “<42 years old” (0) or “≥42 years old” (1).

Statistical analysis

Latent Class Analysis (LCA) was used to identify subgroups of drug use. LCA models use a maximum likelihood approach to identify subgroups or classes of individuals with similar patterns of responses to a set of indicator variables [28, 46]. Drug use variables and age were used as indicator variables. We began with a 1-class model and increased the number of classes up to 6-class models, using 5,000 random starts to obtain global maxima for each model. Model selection was based on the Bayesian Information Criterion (BIC), parametric bootstrap likelihood ratio test (BLRT), and Lo-Mendell-Rubin adjusted likelihood ratio test (LMR). We also used entropy, a measure of classification accuracy, with higher values indicating better classification.

The final latent class solution was based on statistical significance and epidemiological interpretation of drug use patterns. After identifying latent classes, multinomial logistic regression models were conducted to examine associations between class membership and HCV status, sociodemographic characteristics, sexual behaviors, and STI history. We used the AUXILIARY (r) option [31] for multinomial logistic regression estimation, which incorporates posterior probabilities of membership into

the estimation procedure [34]. Bivariate associations between latent class and each independent variable were analyzed. Variables with a p -value < 0.25 were included in the joint model to evaluate the adjusted relationships between class membership and HCV infection. LCA model building, and logistic regression analysis were conducted using Mplus 6.1 (Muthén & Muthén, CA), and data management was performed using SAS 9.4 (Cary, NC).

Results

In the DASH parental project study, the prevalence of HCV was 36.1% (1011 out of 2800) among 2,800 drug users contacted for HIV/HBV/HCV screening. [22]. Among 273 MSM who reported non-injection drug use, 40 individuals tested HCV positive, resulting in an HCV prevalence of 14.7%. In these individuals, only age was significantly associated with HCV infection. The odds of HCV infection was 2.1 (95% confidence interval [CI]: 1.4–3.0) times higher in participants ≥ 42 years of age than in those < 42 years old (Supplementary Table 1).

The final analysis included 118 HIV and HBV negative participants who reported male-to-male sex and used only non-injection drugs. Of these, 21 (17.8%) were infected with HCV. Table 1 presents the sociodemographic characteristics and behavioral variables of the analytical sample. The age of these participants ranged from 19 to 61 years (mean: 39.6 years, interquartile range: 35–46 years), 83% were African American, 83% reported sexual orientation as bisexual or homosexual, 76% completed only high school or had less than a high school education, 65% were single, 50% worked < 14 days in the past month, 50% had an income < \$400 dollars in the past month, 46% were homeless at least once in the past, 76% had been arrested and spent > 24 h in jail, and 35% never received drug treatment. Regarding sexual risk behaviors, 41% of participants had 0 or 1 male sexual partners in the past month, approximately two-thirds used condoms < 50% of the time while having sex, approximately two-thirds traded sex for money or drugs in the past month, and > 50% traded money for drugs or sex in the past month. Regarding disease history, 45% were previously diagnosed with STI(s). The majority of participants had used multiple drugs (defined as ever using > 2 drugs); the most prevalent drug types were crack cocaine (98%), marijuana (89%), and alcohol (86%). The prevalence rates for other types of drugs were 57% for powder cocaine, 22% for codeine, 21% for fry, 14% for methamphetamine, 6.8% for heroin, and 3.4% for speedball.

Table 2 presents the results of statistics and entropy for LCA models ranging from 1-class to 6-class solutions. While the 2-class model had the lowest Bayesian Information Criterion (BIC), other statistical criteria favored

Table 1 Characteristics of 118 HIV-negative MSM who reported only non-injection drug use in two inner-city communities in Houston, TX (2004–2007)

Characteristics	N	%
All	118	100
Latent class indicators ^a		
Crack cocaine	116	98.3
Methamphetamine	17	14.4
Marijuana	105	89.0
Alcohol	101	85.6
Fry	25	21.2
Powder cocaine	67	56.8
Heroin	8	6.8
Speedball	4	3.4
Codeine	26	22.0
≥ 42 years of age	59	50
Sociodemographic characteristics		
African American	98	83.1
Self-reported homosexual or bisexual	98	83.1
Education ≤ high school	90	76.3
Single marital status	77	65.3
Worked < 14 days in the past 30 days	58	49.2
Income < \$400 in the past month	70	59.3
Homeless at some time in the past	54	45.8
Previously in jail for > 24 h	90	76.3
Never received drug treatment	41	34.7
Sexual behaviors		
0 or 1 male sexual partner in the past month	48	40.7
Condom use frequency ≤ 50%	71	60.7
Traded sex for money or drugs in the past month	74	62.7
Traded money or drugs for sex in the past month	68	57.6
Disease history		
Sexual transmitted infection in the past	53	44.9
Blood exposure		
Previous blood transfusion	4	3.4
History of occupational blood exposure	7	5.9

^a Except for age, these variables refer to the response to the question, "Have you ever used the following drugs ...?"

the 3-class and 4-class models. Specifically, the Lo-Mendell-Rubin (LMR) test showed significance for the 2-class, 3-class, 4-class, and 5-class models ($P < 0.05$), and the Bootstrapped Likelihood Ratio Test (BLRT) supported the use of the 2-class through 4-class models ($P < 0.05$). Notably, all models from 3-class to 6-class demonstrated satisfactory precision with entropy values exceeding 0.8. Considering statistical significance and practical utility, we opted for the 4-class model as the best-fit model. This decision was substantiated by the comprehensive evaluation of statistical criteria, where the 4-class model exhibited the significant LMR and BLRT values, and an Entropy value closer to 1, collectively affirming its suitability for our analytical framework.

Figure 1 shows the estimated probabilities for each indicator variable in our 4-class model. Participants in class 1 (accounting for 6.5% of the sample) had a high probability (> 95%) of using only crack cocaine, the lowest probability of using all other types of drugs, and 75% probability of being ≥ 42 years of age. We thus referred to class 1 as "persons ≥ 42 years of age who used only crack cocaine". Class 2 members accounted for 70.3% of the sample and had a high probability (> 90%) of using crack cocaine and marijuana, moderate probability (50%) of using powder cocaine, and 50% probability of being ≥ 42 years of age. We therefore referred to class 2 as "persons approximately 42 years of age who used > 2 drugs". Class 3 members accounted for 20.1% of the participants; had a high probability (> 90%) of using crack cocaine, marijuana, and powder cocaine; had the highest probability of using fry and codeine, compared to other groups; and had an only 35% probability of being ≥ 42 years of age. We thus referred to class 3 as "persons < 42 years of age who used > 5 drugs". Individuals in class 4 accounted for 3.2% of the sample; had a high probability of using all types of drugs except fry and codeine, with the probability of using methamphetamine, heroin, and speedball being the highest of all classes; and had a very high probability (> 99%) of being ≥ 42 years of age. We referred to class 4 as "persons ≥ 42 years of age who used > 6 drugs".

Table 3 presents the results of our bivariate multinomial logistic regression analysis. We found that only

Table 2 Model fit statistics and entropy values for LCA models with 1 to 6 latent classes

No. of Classes	LL	Free parameters	BIC	LMR (P-value)	BLRT (P-value)	Entropy
1	-462.630	10	972.966	NA	NA	NA
2	-430.427	21	961.039	0.0001	< 0.0001	0.731
3	-418.644	32	989.950	0.0177	0.0100	0.957
4	-406.801	43	1018.742	0.0424	0.0400	0.963
5	-400.104	54	1057.826	0.0115	0.4000	0.957
6	-394.546	65	1099.186	0.1469	0.6200	0.978

BIC, Bayesian Information Criteria; BLRT, bootstrapped likelihood ratio test; LL, log-likelihood; LMR, Lo-Mendell-Rubin adjusted likelihood ratio test; NA, not applicable

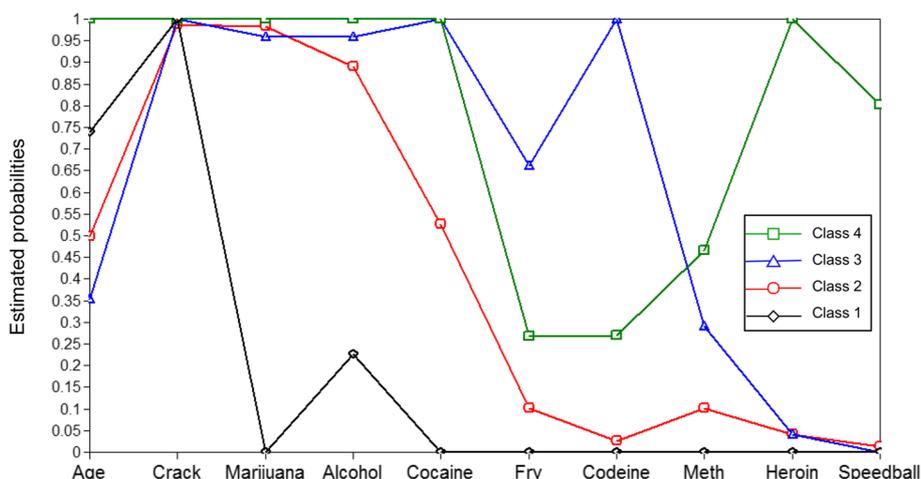


Fig. 1 Estimated probability for each indicator variable in each drug use class in the 4-latent class model (Meth represents methamphetamine). Class 1 (6.5%): persons ≥ 42 years of age who used only crack cocaine. Class 2 (70.3%): persons approximately 42 years of age who used > 2 drugs. Class 3 (20.1%): persons < 42 years of age who used > 5 drugs. Class 4 (3.2%): persons ≥ 42 years of age who used > 6 drugs

Table 3 Bivariate associations between latent class membership and characteristics of 118 HIV-negative MSM with non-injection drug use

Characteristics	Class 4 vs 1 cOR (95% CI)	Class 4 vs 2 cOR (95% CI)	Class 4 vs 3 cOR (95% CI)	Class 1 vs 2 cOR (95% CI)	Class 1 vs 3 cOR (95% CI)	Class 3 vs 2 cOR (95% CI)
Never received drug treatment vs Received drug treatment	0.7 (0.0–12.0)	0.6 (0.1–6.2)	1.2 (0.1–15.6)	0.8 (0.1–4.6)	1.8 (0.3–12.1)	0.5 (0.2–1.5)
Traded money or drugs for sex in the past month: Yes vs No	2.5 (0.2–39.1)	2.3 (0.2–24.6)	1.2 (0.1–14.9)	0.9 (0.2–4.5)	0.5 (0.1–2.9)	1.9 (0.7–5.2)
Previous sexually transmitted infection(s): Yes vs No	1.6 (0.1–25.4)	4.4 (0.4–46.4)	2.1 (0.2–25.0)	2.8 (0.5–14.0)	1.4 (0.2–7.9)	2.1 (0.8–5.4)
HCV infection: Yes vs No	7.8 (0.5–134.7)	14.2*(1.3–157.4)	20.5*(1.4–291.7)	1.8 (0.3–10.6)	2.6 (0.3–21.8)	0.7 (0.2–3.0)

CI, confidence interval; cOR: crude odds ratio; HCV, hepatitis C virus

* $P < 0.05$

HCV status was significantly associated with the drug use latent class. Compared with members of the other classes, class 4 members had the highest odds of HCV infection. The odds of HCV infection in class 4 members was 14 times higher (crude odds ratio [cOR]=14.2, 95% CI: 1.3–157.4) than the odds of having HCV infection among individuals in class 2 and 20 times higher (cOR=20.5, 95% CI: 1.4–291.7) than the odds of HCV infection among MSM in class 3. The probability of HCV was also higher in class 4 members than in class 1 members, although the difference was not statistically significant (cOR=7.8, 95% CI: 0.5–134.7). Associations between drug use classes and other variables, such as sociodemographic characteristics, sexual behaviors, self-reported STI history, blood transfusion history, and

occupational blood exposure history, were not statistically significant.

Table 4 presents the results of our multivariable regression model. We entered drug treatment history, self-reported STI history, and trading money or drugs for sex in the past month (variables with p-values < 0.25 in bivariate analysis) into the model to adjust for these factors when examining the association between drug use class and HCV infection. The results showed that HCV infection was significantly associated with drug use class. The odds of HCV infection in class 4 members was almost 17 times higher than in class 2 members (adjusted OR=16.9, 95% CI: 1.4–205.4) and almost 22 times higher than in class 3 members (adjusted OR=21.8, 95% CI: 1.5–322.8), when controlling for drug treatment history,

Table 4 Multivariable association between latent class membership and characteristics of 118 HIV-negative MSM with non-injection drug use

Characteristics	Class 4 vs 1 aOR (95% CI)	Class 4 vs 2 aOR (95% CI)	Class 4 vs 3 aOR (95% CI)	Class 1 vs 2 aOR (95% CI)	Class 1 vs 3 aOR (95% CI)	Class 3 vs 2 aOR (95% CI)
Never received drug treatment vs Received drug treatment	0.8 (0.0–17.0)	0.7 (0.1–9.8)	1.2 (0.1–19.7)	0.9 (0.1–5.1)	1.5 (0.2–11.0)	0.6 (0.2–1.9)
Previous STI(s) vs Never had STI	1.9 (0.1–33.5)	5.3 (0.4–65.3)	2.7 (0.2–36.6)	2.8 (0.5–14.6)	1.4 (0.2–8.6)	2.0 (0.7–5.3)
Traded money or drugs for sex in the past month vs Did not trade money or drugs for sex in the past month	2.5 (0.1–48.4)	2.4 (0.2–33.2)	1.4 (0.1–21.6)	1.0 (0.2–4.8)	0.6 (0.1–3.4)	1.7 (0.6–5.0)
HCV infection: Yes vs No	8.5 (0.5–154.0)	16.9* (1.4–205.4)	21.8* (1.5–322.8)	2.0 (0.3–12.2)	2.6 (0.3–22.2)	0.8 (0.2–3.5)

aOR: adjusted odds ratio; CI, confidence interval; HCV, hepatitis C virus; STI: sexually transmitted infection

* $P < 0.05$

self-reported STI history, and trading money or drugs for sex in the past month.

Discussion

In this study, we applied LCA to identify latent classes among HIV-negative MSM who used non-injection drugs. We found four distinct latent classes: class 1, persons ≥ 42 years of age who used only crack cocaine; class 2, persons approximately 42 years of age who used > 2 drugs; class 3, persons < 42 years of age who used > 5 drugs; and class 4, persons ≥ 42 years of age who used > 6 drugs. We also found associations between certain latent classes of drug use and HCV infection. After adjusting for drug treatment history, self-reported STI history, and the behavior of trading money or drugs for sex in the past month, we found that persons ≥ 42 years of age who used > 6 drugs had an almost 17 times higher odds of HCV infection, compared with persons approximately 42 years old who used > 2 drugs, and an almost 22 times higher odds of HCV infection, compared with persons < 42 years of age who used > 5 drugs.

Among participants aged 42 years or older, drug use latent class membership was polarized. Members in one class (class 1) used only crack cocaine, whereas members in the other class (class 4) used multiple drugs, including crack cocaine, marijuana, powder cocaine, methamphetamine, heroin, and speedball. Individuals in class 4 had a higher probability of HCV infection than those in class 1, although the difference did not reach statistical significance. The lack of significance may have resulted from the relatively small number of individuals in these classes: they accounted for only 3.2% and 6.5% of the sample, respectively, thus limiting the statistical power of the study to detect differences between these two classes.

The mean age of class 3 members was slightly lower than that of class 2 members. Class 3 members had a higher probability of using fry and codeine than class 2 members, which is consistent with the results of previous reports of fry [29, 33] and codeine abuse [13, 32] in the 1990s, especially among teenagers. Nevertheless, in the current study, using fry and codeine in addition to crack cocaine and marijuana did not increase the likely of HCV infection, compared with using crack cocaine and marijuana alone. One explanation for this finding may relate to their modes of use. Fry is generally smoked, and codeine is usually consumed orally in the form of syrup, pills, or drinks (mixed with soda); both routes of administration have a low likelihood of blood exposure. Although studies have reported increased high-risk sexual behavior among fry or codeine drug users [32], these studies were not restricted to MSM. In the present study, which involved only MSM, use of fry or codeine was not associated with sexual risk behaviors.

By comparing latent classes of drug use with different ages, we found an interaction between age and drug use types on the probability of HCV infection. This indicates that both age and drug use types were associated with HCV infection, and that differences in age were linked to different preferences for type of drug use. Participants who used multiple types of drugs (heroin, speedball, and methamphetamine, in addition to the commonly used crack cocaine and marijuana) were all ≥ 42 years of age and formed a latent class with a much higher HCV infection probability than that of other latent classes. Some studies have reported that people born between 1945 and 1965 have a higher HCV infection rate than other individuals, suggesting that age alone contributes to the higher probability of HCV infection in people 42 years

or older. However, other studies have indicated that use of heroin, speedball, and methamphetamine may increase the risk of HCV infection for several reasons. First, repeated intranasal use of heroin, cocaine (speedball is heroin mixed with cocaine), and methamphetamine may cause mucosal trauma and hyperemia [2, 3, 35, 40], and HCV has been detected in the nasal secretions [1] of people with HCV infection. Second, drug use paraphernalia are often shared among people who use drugs, and HCV RNA may remain in the paraphernalia for up to 16 h [24]. Third, people who use heroin, speedball, and methamphetamine may be exposed to social networks with a higher HCV infection rate than those who use other drugs because a proportion of people who use heroin, speedball, and methamphetamine inject these drugs, and 40%-90% of people who use injection drugs are infected with HCV [15, 19]. Nevertheless, some studies have found no increased risk of HCV infection in people who share straws or dollar bills when snorting drugs but do not use injection drugs [18, 20]. More research is required to determine whether sharing equipment for non-injection drug use is a transmission route for HCV.

We cannot directly compare the present LCA findings with the results of previous studies using LCA because of differences in recruitment strategies, indicator variables, and disease of interest between studies. However, our findings are consistent with the results of previous studies demonstrating high rates of infectious diseases, including HIV, among multiple drug users [7, 10, 12, 43]. Previous LCA studies in MSM have also demonstrated that multiple drug use is associated with increased transmission of STIs by promoting disinhibition and subsequent high-risk sexual behavior [26, 48], however, we found no association between multiple drug use and STIs in the current study. One reason for this lack of association may be that individuals with HIV and/or HBV infection were excluded from the baseline data collection in the DASH project. This may have resulted in the exclusion of individuals also coinfecting with STIs and thus led to an underestimation of the effects of multiple drug use on STIs and high-risk sexual behavior in our sample of MSM.

This study had several limitations. First, the limited sample size within certain drug use classes raises concerns about the precision of our results. The small number of HCV-infected individuals, particularly within latent classes, necessitates extreme caution in interpreting the results. Wide confidence intervals further underscore variability. Future studies should include larger sample sizes within specific non-injection drug use groups. Second, there is potential for misclassification of drug use behaviors, especially past injection drug use, which may not be accurately recalled or reported. This could affect the association between non-injection drug use and HCV

infection. Third, the unspecified timeframe for reporting non-injection drug use may lead to variability in reports, complicating the distinction between lifetime and recent behaviors. Fourth, self-report and injection mark identification used to confirm injection drug use are imperfect. Some individuals hide injection marks, and those who stopped injecting long ago might no longer display them. Participants concealing their injection drug use could lead us to overestimate the risk of HCV infection in the target population. Fifth, information on drug use routes and equipment sharing was not collected, which could provide crucial insights into HCV transmission [39]. Sixth, drug use types and sexual risk behaviors were self-reported, potentially leading to underreporting despite lab verification of drug use. Seventh, the study's age categories were based on a median age of 42 years, potentially introducing bias and it may not fully capture the complexity of age-related factors. Future research should use predefined age categories. Eighth, the cross-sectional design does not permit conclusions about the temporality of risk behaviors and HCV infection. Ninth, data from 2004 to 2007 do not account for newer drugs like MDMA and LSD. An updated study is needed for more current and comprehensive evidence. Lastly, the study did not collect information on drug administration routes, equipment sharing, or specific sexual behaviors related to HCV transmission. Future studies should include these aspects, and a longitudinal design could clarify the temporality of risk behaviors and HCV infection.

Despite these limitations, this study has several strengths. To our knowledge, this is the first study to evaluate the association between latent class of non-injection drug use and HCV infection among HIV-negative MSM using LCA. LCA provided a valuable tool for categorizing participants based on their age and patterns of drug usage, allowing us to uncover nuanced association between these factors and HCV infection. By reducing the dimension of drug use types, LCA enabled us to explore the interaction between age and multiple drug use types on the likelihood of HCV infection. This approach, which has been relatively underutilized in previous studies, allowed us to gain deeper insights into the complex relationship between drug use behavior and HCV infection risk within this specific population. In addition, we excluded individuals with HIV and/or HBV infection from this study. Although it led to a smaller sample size, it allowed us to demonstrate that even in the absence of HIV and HBV infection, the interaction of age and multiple drug use types was associated with HCV infection.

Additionally, it is crucial to emphasize the broader implications of our findings in the context of HCV infection among MSM populations. Hepatitis C virus (HCV) infection represents a significant public health concern,

and our study sheds light on a specific at-risk subgroup within the MSM community. The identification of latent classes of drug use and their association with HCV infection provides valuable insights for targeted intervention strategies. Understanding the intersecting factors of age and drug use in driving HCV transmission is not only relevant for this specific study population but also contributes to the broader understanding of infectious disease dynamics among marginalized communities. This knowledge can inform public health efforts aimed at reducing the prevalence of HCV and improving the overall health and well-being of MSM individuals.

Conclusion

In conclusion, our study reveals essential insights into drug use patterns among MSM, identifying four distinct latent classes and emphasizing the heightened risk of HCV infection among individuals aged 42 years or older who use multiple drugs. Tailored interventions, including health education, promotion, and drug treatment programs, are imperative for this specific subgroup to raise awareness, increase testing, and reduce the transmission of HCV. Our research contributes to the understanding of the intricate interplay between age, drug use, and infectious diseases within the MSM community, providing a foundation for targeted public health strategies. Future research should further investigate transmission mechanisms and social networks. This study underscores the urgency of addressing HCV infection within the MSM population and offers valuable insights for effective public health interventions.

Abbreviations

HCV	Hepatitis C virus
MSM	Men who have sex with men
LCA	Latent class analysis
STI	Sexually transmitted infection

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12879-024-09685-3>.

Supplementary Material 1.

Acknowledgements

We thank the participants who volunteered biological specimens and data, the DASH staff who collected the data, and Dr. Dimpy Shah, who managed the data. I would like to thank my previous affiliations, UTHealth and Baylor College of Medicine, for their support and resources during the research for this article. I especially appreciate the guidance and assistance of the faculty and staff at these institutions.

Authors' contributions

JZ analyzed the data and wrote the manuscript, with support from CM and AGN. CG and KF verified the analytical methods. LYH helped supervise the project. All authors read and approved the final manuscript.

Funding

This study was funded by The National Institute on Drug Abuse (NIDA# 1R01DA017505). This work was funded (in part) by a Research Training Award for Cancer Prevention Post-Graduate Training Program in Integrative Epidemiology from the Cancer Prevention & Research Institute of Texas, grant number RP160097 (PI: M. Spitz) and the Systems Epidemiology of Cancer Training (SECT) Program (RP210037; PI: A. Thrift).

Availability of data and materials

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

We confirm that this study was performed in accordance with the relevant guidelines and regulations. All data collection procedures and laboratory protocols were approved by the Committee for the Protection of Human Subjects at the University of Texas Health Science Center at Houston (HSC-SPH-03-082). Informed consent was obtained from all of the subjects and/or their legal guardian(s).

Consent for publication

NA.

Competing interests

The authors declare no competing interests.

Author details

¹Department of Epidemiology, MD Anderson Cancer Center, Houston, TX, USA. ²Department of Pediatrics, McGovern Medical School, The University of Texas Health Science Center at Houston, Houston, TX, USA. ³Department of Health Promotion and Behavioral Sciences, The University of Texas Health Science Center at Houston, Houston, TX, USA. ⁴Department of Psychiatry and Behavioral Medicine, Medical College of Wisconsin, Milwaukee, WI, USA. ⁵Department of Epidemiology, Human Genetics, and Environmental Sciences, The University of Texas Health Science Center at Houston, Houston, TX, USA.

Received: 16 February 2023 Accepted: 29 July 2024

Published online: 17 September 2024

References

- Aaron S, McMahon JM, Milano D, Torres L, Clatts M, Tortu S, Simm M. Intranasal transmission of hepatitis C virus: virological and clinical evidence. *Clinical Infectious Diseases*. 2008;47(7):931–4.
- Bakhshaei M, Khadivi E, Sadr MN, Esmatinia F. Nasal septum perforation due to methamphetamine abuse. *Iranian journal of otorhinolaryngology*. 2013;25(70):53.
- Blaise G, Vanhootehem O, De La Brassinne M. Cocaine sniffing-induced lesions. *J Eur Acad Dermatol Venereol*. 2007;21(9):1262–3.
- Blaxhult A, Samuelson A, Ask R, Hökeberg I. Limited spread of hepatitis C among HIV-negative men who have sex with men in Stockholm, Sweden. *Int J STD AIDS*. 2014;25(7):493–5.
- Bluthenthal RN, Wenger L, Chu D, Bourgois P, Kral AH. Drug use generations and patterns of injection drug use: Birth cohort differences among people who inject drugs in Los Angeles and San Francisco, California. *Drug Alcohol Depend*. 2017;175:210–8.
- Bottieau, E., Apers, L., Van Esbroeck, M., Vandenbruaene, M., & Florence, E. (2010). Hepatitis C virus infection in HIV-infected men who have sex with men: sustained rising incidence in Antwerp, Belgium, 2001–2009. *Euro Surveill*, 15(39), 19673. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/20929655>.
- Buchacz K, McFarland W, Hernandez M, Klausner JD, Page-Shafer K, Padian N, Morrow S. Prevalence and correlates of herpes simplex virus type 2 infection in a population-based survey of young women in low-income neighborhoods of Northern California. *Sexually transmitted diseases*. 2000;27(7):393–400.

8. Carlson RG, Wang J, Falck RS, Siegal HA. Drug use practices among MDMA/ecstasy users in Ohio: a latent class analysis. *Drug Alcohol Depend.* 2005;79(2):167–79.
9. CDC. (2017). STDs in Men Who Have Sex with Men. Retrieved from <https://www.cdc.gov/std/stats17/msm.htm>.
10. Chitwood DD, Comerford M, Sanchez J. Prevalence and risk factors for HIV among sniffers, short-term injectors, and long-term injectors of heroin. *J Psychoactive Drugs.* 2003;35(4):445–53.
11. Cochran SD, Ackerman D, Mays VM, Ross MW. Prevalence of non-medical drug use and dependence among homosexually active men and women in the US population. *Addiction.* 2004;99(8):989–98. <https://doi.org/10.1111/j.1360-0443.2004.00759.x>.
12. Drumright LN, Colfax GN. HIV risk and prevention for non-injection substance users. In *HIV Prevention*. Elsevier; 2009. p. 340–75.
13. Elwood WN. Sticky business: patterns of procurement and misuse of prescription cough syrup in Houston. *J Psychoactive Drugs.* 2001;33(2):121–33.
14. Fitzpatrick C, Pinto-Sander N, Williams D, Richardson D. Acute hepatitis C in HIV-uninfected men who have sex with men who do not report injecting drug use. *Int J STD AIDS.* 2017;28(11):1158–1158.
15. Gerberding JL. Incidence and prevalence of human immunodeficiency virus, hepatitis B virus, hepatitis C virus, and cytomegalovirus among health care personnel at risk for blood exposure: final report from a longitudinal study. *J Infect Dis.* 1994;170(6):1410–7.
16. Giraudon I, Ruf M, Maguire H, Charlett A, Ncube F, Turner J, Barton S. Increase in diagnosed newly acquired hepatitis C in HIV-positive men who have sex with men across London and Brighton, 2002–2006: is this an outbreak? *Sex Transm Infect.* 2008;84(2):111–5. <https://doi.org/10.1136/sti.2007.027334>.
17. Golub A, Johnson BD, Dunlap E. Subcultural evolution and illicit drug use. *Addiction research & theory.* 2005;13(3):217–29.
18. Gyarmathy VA, Neaigus A, Miller M, Friedman SR, Jarlais DD. Risk correlates of prevalent HIV, hepatitis B virus, and hepatitis C virus infections among noninjecting heroin users. *JAIDS-HAGERSTOWN MD.* 2002;30(4):448–56.
19. Hagan H, Pouget ER, Des Jarlais DC, Lelutiu-Weinberger C. Meta-regression of hepatitis C virus infection in relation to time since onset of illicit drug injection: the influence of time and place. *Am J Epidemiol.* 2008;168(10):1099–109.
20. Howe CJ, Fuller CM, Ompad DC, Galea S, Koblin B, Thomas D, Vlahov D. Association of sex, hygiene and drug equipment sharing with hepatitis C virus infection among non-injecting drug users in New York City. *Drug Alcohol Depend.* 2005;79(3):389–95.
21. Hunter C, Strike C, Barnaby L, Busch A, Marshall C, Shepherd S, Hopkins S. Reducing widespread pipe sharing and risky sex among crystal methamphetamine smokers in Toronto: do safer smoking kits have a potential role to play? *Harm Reduct J.* 2012;9:9. <https://doi.org/10.1186/1477-7517-9-9>.
22. Hwang LY, Grimes CZ. Human immunodeficiency virus, hepatitis B and Hepatitis C virus infections among injecting and non-injecting drug users in inner city neighborhoods. In *Insight and control of infectious disease in global scenario.* 2012.
23. Hwang LY, Grimes CZ, Tran TQ, Clark A, Xia R, Lai D, Williams M. Accelerated hepatitis B vaccination schedule among drug users: a randomized controlled trial. *J Infect Dis.* 2010;202(10):1500–9. <https://doi.org/10.1086/656776>.
24. Kamili S, Krawczynski K, McCaustland K, Li X, Alter MJ. Infectivity of hepatitis C virus in plasma after drying and storing at room temperature. *Infect Control Hosp Epidemiol.* 2007;28(5):519–24.
25. Kuramoto S, Bohnert A, Latkin C. Understanding subtypes of inner-city drug users with a latent class approach. *Drug Alcohol Depend.* 2011;118(2–3):237–43.
26. Lim SH, Cheung DH, Guadamuz TE, Wei C, Koe S, Altice FL. Latent class analysis of substance use among men who have sex with men in Malaysia: Findings from the Asian Internet MSM Sex Survey. *Drug Alcohol Depend.* 2015;151:31–7.
27. McCarty-Caplan D, Jantz I, Swartz J. MSM and drug use: a latent class analysis of drug use and related sexual risk behaviors. *AIDS Behav.* 2014;18(7):1339–51.
28. McCutcheon AL. *Latent class analysis*: Sage Publications, CA: Thousand Oaks; 1987.
29. Modesto-Lowe V, Petry NM. Recognizing and managing "illy" intoxication. *Psychiatr Serv.* 2001;52(12):1660–1660.
30. Monga N, Rehm J, Fischer B, Brissette S, Bruneau J, El-Guebaly N, Leri F. Using latent class analysis (LCA) to analyze patterns of drug use in a population of illegal opioid users. *Drug Alcohol Depend.* 2007;88(1):1–8.
31. Muth n L, Muth n B. *Mplus user's guide. Seventh.* Los Angeles, CA: Muth n & Muth n; 2012.
32. Peters RJ Jr, Amos C Jr, Meshack A, Savage C, Sinclair MM, Williams LT, Markham C. Codeine cough syrup use among sexually active, African-American high school youths: Why southern males are down to have sex. *Am J Addic.* 2007;16(2):144–5.
33. Peters RJ Jr, Kelder SH, Meshack A, Yacoubian GS Jr, McCrimmon D, Ellis A. Pilot Study, Beliefs and Social Norms about Cigarettes or Marijuana Sticks Laced with Embalming Fluid and Phencyclidine (PCP): Why Youth Use "Fry." *Subst Use Misuse.* 2005;40(4):563–71.
34. Petras H, Masyn K. General growth mixture analysis with antecedents and consequences of change. In *Handbook of quantitative criminology.* Springer; 2010. p. 69–100.
35. Peyri re H, L glise Y, Rousseau A, Cartier C, Gibaja V, Galland P. Necrosis of the intranasal structures and soft palate as a result of heroin snorting: a case series. *Substance abuse.* 2013;34(4):409–14.
36. Price H, Gilson R, Mercey D, Copas A, Parry J, Nardone A, Hart G. Hepatitis C in men who have sex with men in London—a community survey. *HIV medicine.* 2013;14(9):578–80.
37. Scheinmann R, Hagan H, Lelutiu-Weinberger C, Stern R, Des Jarlais DC, Flom PL, Strauss S. Non-injection drug use and Hepatitis C Virus: a systematic review. *Drug Alcohol Depend.* 2007;89(1):1–12. <https://doi.org/10.1016/j.drugalcdep.2006.11.014>.
38. Sherman SG, Sutcliffe CG, German D, Sirojbn B, Aramrattana A, Celen-tano DD. Patterns of risky behaviors associated with methamphetamine use among young Thai adults: a latent class analysis. *J Adolesc Health.* 2009;44(2):169–75.
39. Tortu S, McMahon JM, Pouget ER, Hamid R. Sharing of noninjection drug-use implements as a risk factor for hepatitis C. *Subst Use Misuse.* 2004;39(2):211–24.
40. Trimarchi M, Miluzio A, Nicolai P, Morassi ML, Bussi M, Marchisio PC. Massive apoptosis erodes nasal mucosa of cocaine abusers. *Am J Rhinol.* 2006;20(2):160–4.
41. Urbanus AT, van de Laar TJ, Stolte IG, Schinkel J, Heijman T, Coutinho RA, Prins M. Hepatitis C virus infections among HIV-infected men who have sex with men: an expanding epidemic. *AIDS.* 2009;23(12):F1–7. <https://doi.org/10.1097/QAD.0b013e32832e5631>.
42. Urbanus, A. T., van Houdt, R., van de Laar, T. J., & Coutinho, R. A. Viral hepatitis among men who have sex with men, epidemiology and public health consequences. *Euro Surveill.* 2009;14(47). Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/19941800>.
43. Vallejo F, Toro C, De la Fuente L, Brugal MT, Soriano V, Silva TC, Barrio G. Prevalence of and risk factors for hepatitis B virus infection among street-recruited young injection and non-injection heroin users in Barcelona Madrid and Seville. *Eur Addict Res.* 2008;14(3):116–24.
44. van de Laar TJ, van der Bij AK, Prins M, Bruisten SM, Brinkman K, Ruys TA, Coutinho RA. Increase in HCV incidence among men who have sex with men in Amsterdam most likely caused by sexual transmission. *J Infect Dis.* 2007;196(2):230–8. <https://doi.org/10.1086/518796>.
45. Wandeler G, Gsponer T, Bregenzer A, Gunthard HF, Clerc O, Calmy A, Swiss HIVCS. Hepatitis C virus infections in the Swiss HIV Cohort Study: a rapidly evolving epidemic. *Clin Infect Dis.* 2012;55(10):1408–16. <https://doi.org/10.1093/cid/cis694>.
46. Whitesell, N. R., Beals, J., Mitchell, C. M., Novins, D. K., Spicer, P., Manson, S. M., & Team, A.-S. Latent class analysis of substance use: comparison of two American Indian reservation populations and a national sample. *J Stud Alcohol.* 2006;67(1), 32–43. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/16536127>.
47. Wittchen H-U, Behrendt S, H fler M, Perkonig A, Rehm J, Lieb R, Beesdo K. A typology of cannabis-related problems among individuals with repeated illegal drug use in the first three decades of life: evidence for heterogeneity and different treatment needs. *Drug Alcohol Depend.* 2009;102(1–3):151–7.
48. Yu G, Wall MM, Chiasson MA, Hirschfield S. Complex drug use patterns and associated HIV transmission risk behaviors in an Internet sample of US men who have sex with men. *Arch Sex Behav.* 2015;44(2):421–8.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.