Emerging Trends in Drugs, Addictions, and Health 1 (2021) 100003

Contents lists available at ScienceDirect

Emerging Trends in Drugs, Addictions, and Health

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

Systematic review of hepatitis C virus prevalence and incidence among HIV-positive men who have sex with men (MSM) in England

Sarah Savić-Kallesøe[a], David Palma Díaz[b], Andres Roman-Urrestarazu[a,c,*]

[a] Cambridge Institute of Public Health, University of Cambridge, Cambridge, United Kingdom
[b] Consorcio de Investigación Biomédica en Red de Epidemiología y Salud Pública – CIBERESP, Spain
[c] Faculty of Health, Medicine and Life Sciences, Department of International Health, University of Maastricht, Maastricht, the Netherlands

ARTICLE INFO

Handling Editor: Dr. Francesco Saverio Bersani

Keywords:
Hepatitis C
Chem sex
Infectology
England
MSM

ABSTRACT

Background: Hepatitis C virus (HCV) infection is a leading cause of hepatitis C, liver cancer, and cirrhosis. It is treatable with directing acting antivrials (DAAs), yet still accounts for over 580,000 global deaths annually. Due to the nature of transmission and particular risk factors, men living with HIV who have sex with other men (HIV+ MSM) are disportionately burdened. Whilst HCV is a statutorily notifiable disaease in England and a virtually complete registry exists, data specific to MSM are not captured, leaving gaps in our knowledge of HCV trends among HIV+ MSM.

Methods: This paper aims to investigate the HCV prevalence and incidence among HIV+ MSM in England through a systematic review of academic literature.

Results: The systematic review resulted in six articles. Evidence suggests that incidence has generally risen between 2002-2015 and declined between 2015-2018, which may be attributed to the introduction of DAAs. The range of reported prevalences varied from 2.2%-9.9% , the most recent estimate being 4.24% in 2018.

Conclusions: This review's deficiency is the non-existent record of behavioural risk factors across the studies. Most studies recruited HIV+ MSM from HIV clinics, an arguably robust sampling method considering that 90% of those living with HIV in England are engaged in care at an HIV clinic. The gaps in the academic literature and national surveillance for HCV among HIV+ MSM demonstrate this group to be disproportionately under-studied. National surveillance ought to record HCV cases and risk factors specific to HIV+ MSM to better inform interventions.

1. Introduction

The hepatitis C virus (HCV) is a small (55–65 nm), enveloped, positive-sense single-stranded RNA virus of the family Flaviviridae (Harris et al., 2019). Left untreated, HCV infection can lead to chronic hepatitis C, cirrhosis, and liver cancer (Harris et al., 2019). In 2013, HCV had a global burden of 580,000 deaths and 7.05 million disability-adjusted life years (Roth et al., 2018) and currently, an estimated 71 million people are living with chronic HCV infection (World Health Organization, 2017). While treatments are available, HCV infection is a slow progressing and usually asymptomatic disease, often causing severe liver damage by the time of diagnosis (Harris et al., 2019). Delayed diagnosis contributes to an underestimation of HCV prevalence, which partly explains the global incline of preventable HCV-related deaths, especially in vulnerable populations that may be a threat to the global strategy of hepatitis C elimination by 2030 (Roth et al., 2018). In England, an estimated 143,000 people live with chronic HCV (Harris et al., 2019), representing 75% of cases within the UK (Jones et al., 2012) and a majority of the £82.7 million of UK healthcare costs associated with diagnosis and treatment (Jones et al., 2012).

The World Health Organization recommends rapid diagnostic tests, laboratory-based immunoassays, or nucleic acid testing for confirming HCV infection (World Health Organization, 2017). Rapid diagnostic tests (RDTs) are single-use and provide a result in under 30 minutes (World Health Organization, 2017). Nucleic acid testing (NAT) is laboratory-based and detects the presence of HCV RNA (World Health Organization, 2017). Laboratory-based serological immunoassays detect HCV antibodies, antigens, or a combination of both (World Health Organization 2017). According to the National Institute for Health and Care Excellence (NICE), the standard method of diagnosing HCV infection in England is with an antibody test to detect if the patient has even been infected and a ribonucleic acid (RNA) test to identify active infection (National Institute for Health and Care Excellence, 2021). With the introduction of publicly-funded directly acting antiviral (DAA) therapy by the National Health Services England (NHSE) in 2016 (Garvey et al., 2019), curative treatment for HCV in-

* Corresponding author.
E-mail address: aer56@medschl.cam.ac.uk (A. Roman-Urrestarazu).

https://doi.org/10.1016/j.etdah.2021.100003
Received 28 October 2020; Received in revised form 28 January 2021; Accepted 3 February 2021
Available online 13 February 2021

fection is becoming universally accessible. Between 2015 and 2017, HCV-related mortality decreased by 16% in England (Harris et al., 2019). As case presentation can vary across acute to chronic, both incidence and prevalence are needed to capture infection pattern and frequency.

Given the risk profile of HCV transmission, namely through parenteral and sexual routes, the burden is disproportionately borne by subpopulations that are exposed to a major vulnerability, particularly men who have sex with men (MSM) (Harris et al., 2019). According to the World Health Organisation (WHO), MSM are "males who have sex with other males, regardless of whether or not they have sex with women or have a personal or social identity associated with that behaviour, such as being gay or bisexual" (UNAIDS, 2010). Recent outbreaks of sexually transmitted HCV among MSM living with HIV (HIV+ MSM) have been reported (American Association for the Study of Liver Diseases, Infectious Diseases Society of America, 2019), and while the trend is not fully understood, risk factors have been identified. Certain high-risk practices, such as condomless sex, group sex, and slamming/chemsex (the recreational use of drugs in sexual settings, usually specific to the MSM community), increase the risk of HCV transmission. The rising trend of condomless sex can partly be attributed to the success of pre-exposure prophylaxis (PrEP) and antiretroviral therapy (ART), which drastically reduced the risk of HIV transmission (Rodger et al., 2016; Donnell et al., 2014). This reduced risk of HIV de-incentivizes condom use, raising the risk of HCV transmission (Hess et al., 2017). Group sex practices among MSM can also increase the risk of HCV infection, specifically practices that result in tearing of mucous membranes, such as condomless receptive anal sex and fisting (American Association for the Study of Liver Diseases, Infectious Diseases Society of America, 2019). The recent trend of chemsex parties has also been associated with an increased risk of HCV transmission (American Association for the Study of Liver Diseases, Infectious Diseases Society of America, 2019).

Substance use, especially injection drug use, is a well-documented risk factor for HCV infection due to the transmission through the sharing of contaminated equipment, specifically needles. However, other forms of substance use, such as chemsex and slamming, have been related to elevated risks of HCV infection. The risk of HCV infection associated with these practices is exemplified in a study carried in Manchester, 2017, which found that MSM newly diagnosed with HCV had significantly higher prevalence of ever slamming and using recreational drugs ($p<0.002$) (Ireland et al., 2017). Whilst this review focuses on the general MSM community and excludes studies which selectively focuses on MSM who participate in chemsex (which will be discussed in the methods section), the sexualized use of drugs is prevalent among MSM and carries a high risk of acquisition and reinfection of hepatitis C. In a European survey carried on 2,646 MSM, HCV diagnosis was associated with slammingw in the last 12 months (Odds Ratio = 13.37; 95% confidence interval: 3.26-54.81) (Trouiller et al., 2020).

Practices like these increase the risk of HCV for MSM. With approximately 12,000 HIV-positive MSM aged 16 to 44 accessing HIV care in London alone, there is a substantial population at risk (Johnson et al., 2001; Health Protection Agency, 2019). Moreover, while HCV is a statutorily notifiable disease in England and a virtually complete registry exists, it does not include data specific to MSM. There are gaps in our understanding of HCV transmission among HIV+ MSM which ought to be bridged to develop evidence-informed interventions. This paper aims to approach this knowledge gap by investigating HCV prevalence and incidence among HIV+ MSM in England through a systematic review of academic literature.

2. Methods

2.1. Literature search strategy

A systematic review was conducted between October 28th, 2019 and May 6th, 2020 using Embase, Web of Science, Medline, and PubMed to capture literature relating to HCV among HIV+ MSM in England. Considering the decentralized healthcare system structure within the UK, the acquisition of studies was limited to within England, where populations across the region would have comparable access to care. This is especially pertinent considering that the introduction of DAAs as treatment became available at different times across the UK. For example, DAAs became available in 2016 in England (Garvey et al., 2019) and in 2014 in Scotland (The Scottish Government, 2018). Table 1 outlines the keyword, exploded, and Medical Subject Heading (MeSH) terms used. The articles were screened following the inclusion/exclusion criteria outlined. The review process is summarised in Table 1 according to PRISMA guidelines (Moher et al., 2009).

Three levels of screening by three independent researchers were used on all citations. Our electronic search yielded 178 articles. We reviewed the titles and abstracts and eliminated any articles that clearly fell outside our inclusion/exclusion criteria. If there was any doubt, the article was retained for the next level of scrutiny. This process yielded 106 articles. Three authors examined each article's title and abstract more closely and, if needed, examined the full text of each article and made independent judgments as to whether the article met inclusion and exclusion criteria. Disagreements were resolved by discussion, leading to a consensus judgement. Six articles met our inclusion and exclusion criteria.

2.2. Quality assessment of included studies and literature bias analysis

The Effective Public Health Practice Project Tool (EPHPP) was used to assess and compare the quality of included studies. The tool generates a total quality score between one (strong) and three (weak) based on six sub-scores, assessing components of internal and external validity. Five studies receive a weak score, while one article receive a moderate score (2 points), assessing components of internal and external validity (Table 3). These results were mainly due to the study design (cross-sectional or retrospective cohort), as well to the lack of control of confounders. Overall, the evidence base was rated as low. However, the applied tool might not be ideal for rating the quality of studies on secondary data such as insurance claims data and medical records since some of the assessed components seem to be inappropriate (e.g. study design, data collection methods, or blinding).

3. Results

3.1. Methodology

This paper reviews six articles, with summary characteristics outlined in Table 2. The studies took place between 2002 and 2018, except for one in 1987. Four were of cohort design and two cross-sectional. All six studies confirmed HCV cases with laboratory-based testing, either HCV antibody or nucleic acid testing, except for one which employed both (Tedder et al., 1991). Four of the studies ranged from 168 to 17,574 participants. However, three studies did not explicitly report a sample size (Garvey et al., 2019; Giraudon et al., 2008; Ruf et al., 2008). The principal investigators of these three studies were contacted via email on November 19th 2019, and one response was received (Garvey et al., 2019).

All four cohort studies reported incidence, two of which also reported prevalence. The four cohort studies recruited their sample from HIV clinics across London, East Sussex, and the South East Region. MSM accessing care at participating clinics were routinely screened for HCV and incident cases were recorded.

Both cross-sectional studies reported prevalence. One study recruited participants from gay clubs, bars, and saunas in London (Price et al., 2013), the other from a London genitourinary clinic (Tedder et al., 1991). HCV and HIV status for both studies were confirmed with antibody testing.

Table 1
Search strategy and criteria.

A: Search terms
(exp hepatitis C/ or Hepatitis C.mp.) OR (HCV.mp. or Hepatitis C virus/)
AND (prevalence.mp. or exp prevalence/) OR (incidence.mp. or exp incidence/)
AND (England.mp. or England/)
AND ("men who have sex with men".mp.) OR (MSM.mp.) OR (exp men who have sex with men/)
B: Inclusion and exclusion criteria
Inclusion criteria:

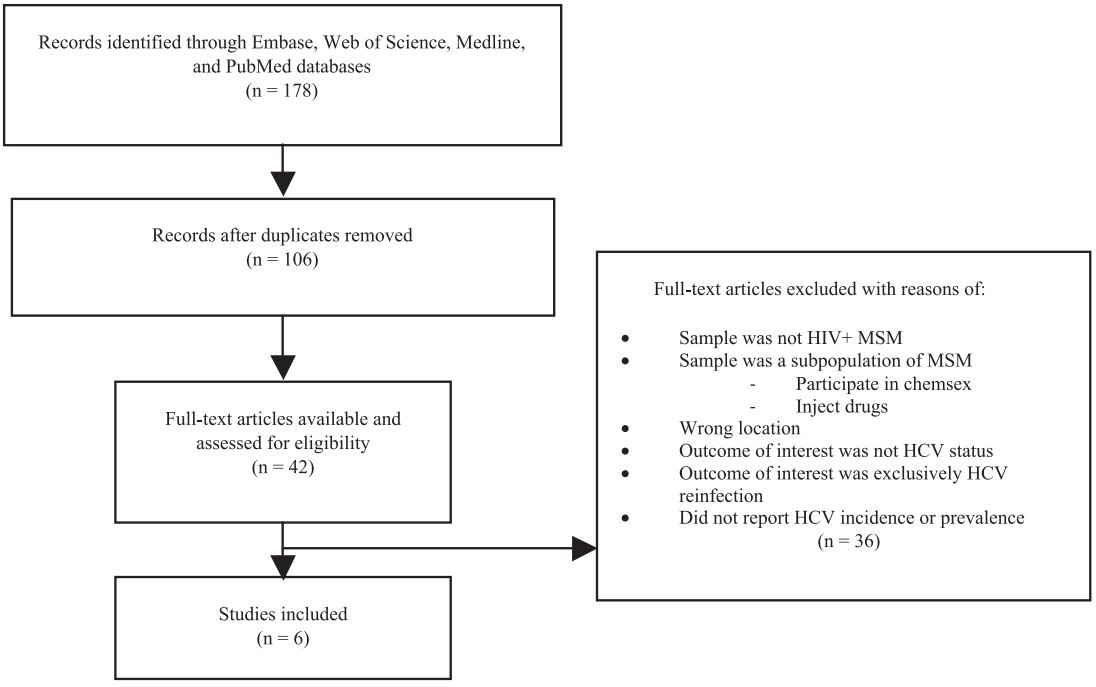
- Published in English
- Study population are MSM living with HIV
- Study population living in England
- HCV status as outcome of interest
- Specifies incidence and or prevalence of HCV
- Diagnosis of hepatitis C by a standard diagnostic criteria

Exclusion criteria:

- Outcome of interest is exclusively HCV reinfection
- Recruited sample is a subpopulation of the HIV+ MSM community

- (Ex: MSM who inject drugs, who participate in chemsex, etc)

C. Review process



3.2. Descriptive epidemiology

The range of reported prevalence of HCV among HIV+ MSM varied from 2.2% (n=270) in 1987 (Tedder et al., 1991) to 9.9% (n=17,574) in 2011 (Martin et al., 2016), the most recent estimate being 4.24% in 2018 (Garvey et al., 2019) (Fig. 2). Incidence ranged from 7.8 cases per 1,000 patient-years (sample size not stated) in 2007 (Ruf et al., 2008) to 10.7 cases per 1,000 patient-years (95% CI: 8.5 - 13.3) in 2011 (Martin et al., 2016) (Fig. 1).

3.2.1. Time

Collectively, the cohort studies span from 2002 to 2018, which may provide insight on temporal trends. Considering that DAAs were made available under public funding in 2016, the trends observed by these cohort studies may reflect the intervention's efficacy. From 2002 to 2004, the incidence of HCV increased by 69% (from 6.9 to 9.0 cases per 1,000 patient-years) (Giraudon et al., 2008). Two studies overlapped in the years 2004 to 2006 (Giraudon et al., 2008; Martin et al., 2016) and may suggest a slight increase of incidence. One study found little change of incidence (10.3 to 10.2 cases per 1,000 patient-years) (Martin et al., 2016), while the other observed an increase of 29% (9.0 to 11.58 cases per 1,000 patient-years) (Giraudon et al., 2008). Two studies overlapped in the years 2006 to 2007 (Martin et al., 2016; Ruf et al., 2008) and found conflicting trends. One observed a slight increase in incidence by 11% (7.4 to 8.2 cases per 1,000 patient-years) (Ruf et al., 2008) while the other saw a decrease of incidence by 22% (13.8 to 10.7 cases per 1,000 patient-years) (Martin et al., 2016). From 2007 to 2011, incidence steadily decreased by 22% from 13.8 to 10.7 cases per

Table 2
Summary statistics of the literature.

First Author	Study Design	HCV Prevalence	HCV Incidence	Consideration For Age	HCV Cases Stratified?	Sample Source	HCV Case Confirmation	Sample Size (HIV+ MSM)
Garvey et al.	Cohort	4.24%	17 cases per 1,000 PY (95% CI 13-22)	No	Incidence of first and all infections compared. "17 overall cases per 1,000 PY 17 overall cases per 1,000 PY 15 first infection cases per 1,000 PY"	HCV cases among HIV+ MSM were identified from three HIV clinics in London.	HCV antibody test or HCV NAT test	6,040
Martin et al.	Cohort	9.90% (95% CI 7.26 -10.12)	10.7 cases per 1,000 PY (95% CI 8.5–13.3)	No	No	Data collected from the UK Collaborative HIV Cohort (UK CHIC), which follows patients from 16 HIV treatment centres.	HCV antibody test or HCV NAT test	17,574
Price et al.	Cross-sectional	7.7% (95% CI 4.2-12.9%)	N/A	Yes. No evidence for an association between HCV infection and age (p-value = 0.24, no CI reported).	No	Survey participants were recruited from gay bars, clubs, and saunas across London. Oral fluid sample collected and test for antibodies to HIV and HCV.	HCV antibody test	168
Ruf et al.	Cohort	200 cases (but sample size not stated)	7.8 cases per 1,000 PY	No	No	HCV cases among HIV+ MSM were identified from 25 HIV clinics in London and the South East region.	HCV antibody test or HCV NAT test	Not explicitly stated
Giraudon et al.	Cohort	389 cases (but sample size not stated)	9.05 cases per 1,000 PY	No	No	HCV cases among HIV+ MSM were identified from 19 HIV clinics in London and three in East Sussex were recruited.	HCV antibody test or HCV NAT test	Not explicitly stated
Tedder et al.	Cross-sectional	2.2% (95% CI 0.5-4.0%)	N/A	Yes, but not specifically for HCV infection.	No	HCV cases among HIV+ MSM were identified from patients attending a genitourinary clinic in London for routine syphilis testing.	Both HCV antibody test and HCV NAT test	270

Table 3
Quality scores.

Citation	L. Garvey	N. Martin	H. Price	M. Ruf	I. Giraudon	R. Tedder
Study design	Cohort	Cohort	CSS	Cohort	Cohort	CSS
Sample source	HCV cases among HIV+ MSM were identified from three HIV clinics in London.	Data collected from the UK Collaborative HIV Cohort (UK CHIC), which follows patients from 16 HIV treatment centres.	Survey participants were recruited from gay bars, clubs, and saunas across London. Oral fluid sample collected and test for antibodies to HIV and HCV.	HCV cases among HIV+ MSM were identified from 25 HIV clinics in London and the South East region.	HCV cases among HIV+ MSM were identified from 19 HIV clinics in London and three in East Sussex were recruited.	HCV cases among HIV+ MSM were identified from patients attending a genitourinary clinic in London for routine syphilis testing.
Number of subjects	6,040	17,574	168	Not explicitly stated	Not explicitly stated	270
A. Selection Bias	1	1	1	1	1	2
B. Design	2	2	2	2	2	2
C. Confounders	3	3	3	3	3	3
D. Blinding	3	3	1	3	3	2
E. Data collection methods	1	1	1	1	1	1
F. Withdrawals & Dropouts	1	1	1	3	1	1
Overall score	3	3	3	3	3	2

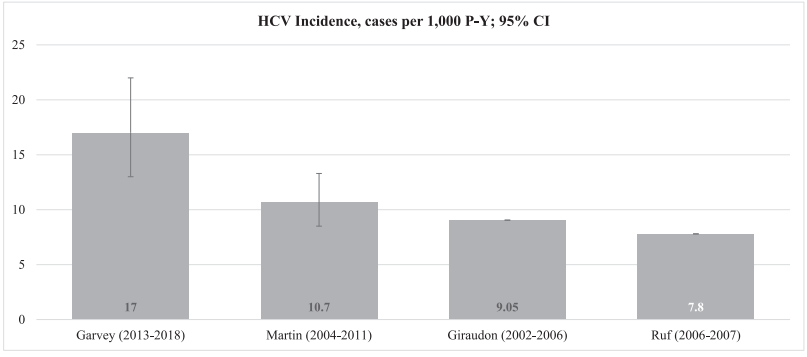


Fig. 1. HCV incidence.

1,000 patient-years (Martin et al., 2016). Literature was not available for the years 2011 through 2013. From 2013 to 2015, incidence sharply inclined from 8 cases per 1,000 patient-years to 17 cases per 1,000 patient-years in 2015 (Garvey et al., 2019). From 2015 to 2018, incidence dropped by 65%, falling to less than the study's baseline observed in 2013 (17 to 6 cases per 1,000 patient-years) (Garvey et al., 2019).

In summary, the literature suggests a general increase of HCV incidence among HIV+ MSM from 2002 to 2015, with a rapid increase leading up to 2015 and a sharp decrease of incidence from 2015 to 2018. No data were available for the years 2012 to 2013. The sharpest decline in HCV incidence was observed between 2015 and 2018, which may be partly accounted for by the introduction of DAAs in 2016.

3.2.2. Person

Of the cohort studies, none collected participant behavioural or demographic information, except for one study which stratified incidence rates between first acute HCV infections and re-infections (Garvey et al., 2019). This is likely a product of the study design, as these studies recruited clinics rather than individuals. As HCV cases were identified among HIV+ MSM patients during routine screening, clinics would report incident cases to the study investigators. However, additional information, such as high-risk practices, age, and ethnicity, were not collected by the clinics.

The two cross-sectional studies did collect demographic information, such as age, ethnicity, history of drug use, sexual practices, and history of sexually transmitted infections. However, the samples of these studies captured MSM in general and HIV+ MSM were a subset. The prevalence of HCV was calculated for the two sample strata, MSM living with and without HIV, which provides insight for prevalence of HCV among HIV+ MSM. However, the other demographic statistics were reported at the sample level and not at the strata level within the sample. Thus, these reports are reflective of the collective MSM sample, both those living with and without HIV, and cannot be interpolated to just those living with HIV.

3.2.3. Location

Due to the study design of the four cohort studies, sample participants were recruited through HIV clinics. As such, access to participants was constrained by clinic location and due to population density of cities, the majority of HIV clinics in England are located in London, which is where all four cohort studies recruited their samples from (Garvey et al., 2019; Giraudon et al., 2008; Ruf et al., 2008; Martin et al., 2016). Three studies also engaged with clinics from the South East Region (Giraudon et al., 2008; Ruf et al., 2008; Martin et al., 2016). Collectively, these studies identified London and Brighton to be regional hotspots for HCV cases. Considering that HIV+ MSM are a difficult population to access, recruiting them through HIV clinics is the most efficient method. However, this limits the geographic generalisability of the study, as clinics where participants access care may not reflect where cases occur. It would be reasonable to expect that cases occurring in rural areas would be under-represented as they would not be as well served with HIV clinics as major cities.

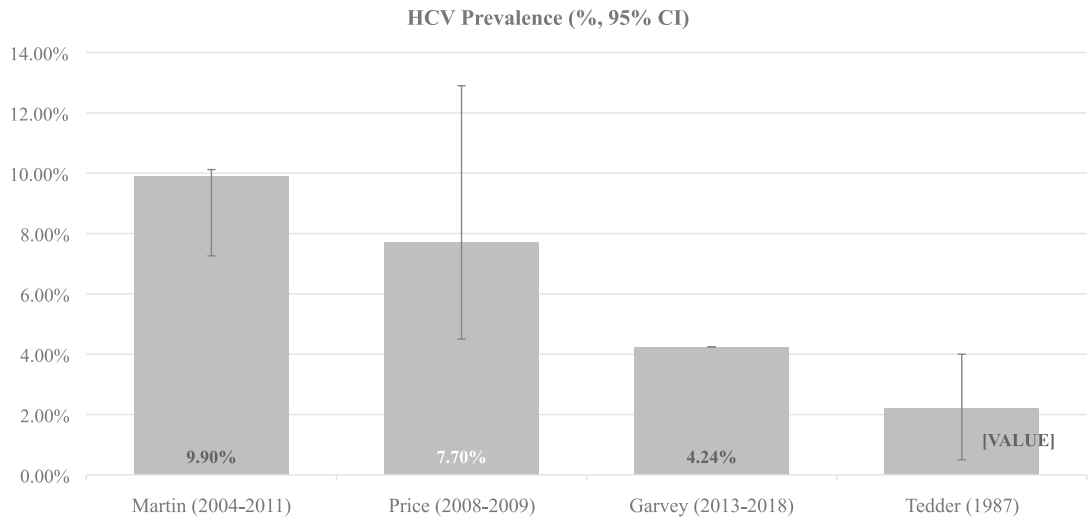


Fig. 2. HCV prevalence.

4. Discussion

4.1. Evidence: limitations

Sampling a population as specific as HIV+ MSM is a balance between prioritising the feasibility of gathering participants and sample representativeness. The cohort studies in this literature review favoured feasibility at the cost of the generalisability by recruiting participants from HIV clinics. As HIV clinics tend to be clustered in major cities, the study results are limited in their potential to provide insight on nationwide HCV trends.

The sampling methods of the two cross-sectional were less systematic than that of the cohort studies. One cross-sectional study recruited participants from gay bars, saunas, and clubs across London (Price et al., 2013) and the other recruited participants attending a London-based genitourinary clinic for routine syphilis testing. Both sampling methods would have failed to include those who participate in sex with other men and are living with HIV but were not actively pursuing syphilis testing or frequenting establishments designed to facilitate partner-seeking. Therefore, these sampling methods may have increased selection bias and likely overestimated the prevalence of HCV, as individuals who are engaging in partner-seeking activities or testing for syphilis may be at a higher risk for HCV transmission than those who do not.

While 90% of those living with HIV in England are engaged with care and on treatment (Nash et al., 2018) there are MSM living with HIV who are undiagnosed or who choose to not interact with care. Though this proportion may be small, they would not have been captured by the cohort studies and this could increase selection bias.

Participants in all the studies included in this review were self-identified MSM, which does not capture the entire MSM population. Some men who engage in sex with other men may not be willing to participate in studies focusing on MSM in avoidance of being identified as a man who has sex with other men. We would expect that the literature to underreport the magnitude of the MSM community, and especially underreport those who self-identify as heterosexual and those who seldomly or only once ever participated in sex with other men.

Other limitations of the evidence have to do with the outcome of interest. While hepatitis C is a statutory notifiable disease and all known cases are registered, this registry does not include those who are undiagnosed. Considering that HCV infection can often be asymptomatic for years before suspecting infection, the proportion of undiagnosed cases may be significant. Current research approximates that almost two thirds of the estimated HCV cases in the United Kingdom are undiagnosed (Merkinaite et al., 2008), indicating that a significant diagnosis gap may be present in the HIV+ MSM community. These undiagnosed cases were not captured by the studies, which may colour the results, depending on the ratio of undiagnosed cases to known cases. It is anticipated that a greater the ratio of undiagnosed to known cases would bias the results towards the null, dampening whatever association may be apparent between HIV+ MSM and HCV transmission.

Considering that HCV infection can be asymptomatic, as well as fatal if undiagnosed and untreated, survivor bias may be influential. Survivor bias would affect the reported prevalence of HCV of the cross-sectional studies, as they would only capture cases who are still alive at one point in time rather than tracking them from baseline to diagnosis. As such, survivor bias may have underrepresented the prevalence of HCV in the cross-sectional studies. Moreover, the most marginalised and deprived members of society tend to have the poorest survival rates (Newton et al., 2015). Therefore, they are also less likely to be represented in the study sample.

In terms of the study design, the studies had generally low power, given by the small sample size, except for one study which recruited over 17,000 participants (Martin et al., 2016). However, two studies did not explicitly state their sample sizes and their investigators could not be reached to clarify the study sample size (Giraudon et al., 2008; Ruf et al., 2008), which poses questions about the studies' robustness. Moreover, two studies did not report confidence intervals for the prevalence or incidence estimates (Giraudon et al., 2008; Ruf et al., 2008).

Additionally, the four cohort studies were not of true cohort design. Rather than assessing the baseline group of HIV+ MSM without HCV, the investigators were notified of incident cases as patients at participating HIV clinics were routinely screened. While subtly different, the case notification design of these studies did not capture the behaviours of the participants at baseline or at follow up as a cohort study would. Consequently, this limits the studies' abilities to describe the risk factors of HCV infection as they were not evaluated.

This review does not include grey literature that can provide more information, however, gaps in epidemiological research of HCV among HIV+ MSM exist beyond academic literature. Even at the national surveillance level, there is a poor recording of risk factors of HCV. Less than one third of HCV laboratory reports contain any information on the patient's risk factors and many reports are left incomplete, especially in London clinics, which serve the largest population of HIV+ MSM (Hurrelle et al., 2006). Without national surveillance data, it is difficult

to precisely estimate the burden of HCV and to evaluate the strength of associations of risk factors and HCV transmission among HIV+ MSM. Consequently, there is no sound national surveillance data to compare the academic literature with.

4.2. Evidence: strengths

The sampling methods of the cohort studies ought to be granted merit. While recruiting participants from HIV clinics predominantly clustered in London and Brighton may not allow for national generalisation, it does capture a large portion of the population. Two cohort studies determined the proportion of HIV+ MSM attending HIV care represented in the participating clinics using data from the Survey of Prevalent HIV Infections Diagnosed (SOPHID). One study determined that 91% of HIV+ MSM attending HIV care in London and 57% in the South East Region were cared for by participating clinics (Ruf et al., 2008). Similarly, the second study had recruited clinics which provided care for 84% of HIV+ MSM attending HIV care in London and 100% in Brighton (Giraudon et al., 2008). This indicates that recruiting HIV clinics is likely a robust option for capturing a sample representative of the HIV+ MSM in the area surrounding the clinics.

Since hepatitis C is a statutory notifiable disease in England and is routinely screened for at HIV clinics, it is likely that a high proportion of HCV cases that actually occur are detected. This rigorous method of HCV case detection was employed by the cohort studies. All the reviewed studies also used standardised laboratory-based diagnostic methods to identify HCV cases.

4.3. Literature review: limitations

One of the limitations of this review is its inability to compare trends identified in the literature to national surveillance data. While there is a national HCV registry, these data are not specific to the MSM community, let alone to HIV+ MSM. This review excluded studies which only focused re-infection cases. Ideally, there would be enough literature to compare trends of first and repeated infections. Finally, the search terms used to specify males who engage in sex with other males did not include the “gay”, “bisexual”, or “homosexual”, which were traditionally used in older studies. These terms were not used as they describe identities rather than behaviours and exclude those who engage in sex with other men but do not identify as gay or bisexual. Including these terms would yield studies with incomparable populations.

4.4. Literature review: strengths

The primary strength of this review is the use of multiple databases and lack of limits on year or sample size, maximising the literature captured. While the search was only limited to publications in English, this is likely redundant as the study population is based in England. This review also limited to those that used standardised HCV diagnostic criteria to ensure comparability. Lastly, the investigators of the three studies which did not disclose a sample size were contacted, one of whom responded (Garvey et al., 2019).

4.5. Future directions

Considering that the current literature does not provide information on high-risk behaviours, there is a need for prospective cohort research focusing on the risk factors of HCV among HIV+ MSM. Key risk factors should include condom usage, group sex practices, and drug use within the context of group sex (reflective of the chemsex scene).

5. Conclusion

Available academic literature indicates a general increase of HCV incidence among HIV+ MSM between 2002 until 2015, partly accountable to the efficacy of ART and corresponding decline in condom usage. The sharp decline of incidence following 2015 until 2018 may be attributed to the introduction of DAAs in 2016. However, the risk factors facilitating HCV transmission among HIV+ MSM are not yet fully understood, evidenced by the gaps in the literature and lack of national surveillance HCV infection data specific to MSM. Further evidence is needed on behavioural risk factors to identify potential leverage points for primary prevention to reduce the risk of transmission. Gaps in national HCV surveillance result in no systematic record of HCV infection trends or risk factors specific to MSM, which needs to be addressed. A unified surveillance program with the focus of identifying individual-level risk factors among MSM ought to be promoted to inform specialised prevention programs.

Declaration of Competing Interest

Declares no conflict of interest.

CRediT authorship contribution statement

Sarah Savić-Kallesøe: Conceptualization, Methodology, Writing – review & editing, Software. **David Palma Díaz:** Data curtion, Writing – original draft. **Andres Roman-Urrestarazu:** Writing – review & editing, Supervision.

References

American Association for the Study of Liver Diseases, Infectious Diseases Society of America, 2019. HCV in Key Populations: Men Who Have Sex With Men, HCV Guidance. https://www.hcvguidelines.org/unique-populations/msm. Accessed December 2, 2019.

Donnell, D., Baeten, J.M., Bumpus, N.N., et al., 2014. HIV protective efficacy and correlates of tenofovir blood concentrations in a clinical trial of PrEP for HIV prevention. J. Acquir. Immune Defic. Syndr. 66 (3), 340–348. doi:10.1097/QAI.0000000000000172.

Garvey, L., Smith, C., Stingone, C., et al., 2019. Fall in HCV incidence in HIV+ MSM in London following expansion of access to DAA therapy. HIV Med. 20 (Supplement 5), 12 http://dx.doi.org/10.1111/hiv.127388.

Giraudon, I., Ruf, M., Maguire, H., et al., 2008. 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. 84 (2), 111–115. doi:10.1136/sti.2007.027334.

Harris, H., Costella, A., Harris, R., Mandal, S. Hepatitis C in England, 2019 report: working to eliminate hepatitis C as a major public health threat.; 2019. www.gov.uk/pheTwitter:@PHE_ukFacebook:www.facebook.com/PublicHealthEngland. Accessed December 2, 2019.

Health Protection Agency, 2019. Survey of Prevalent HIV Infections Diagnosed (SOPHID) https://www.gov.uk/guidance/hiv-surveillance-systems#survey-of-prevalent-hiv-infections-diagnosed-sophid.

Hess, K.L., Crepaz, N., Rose, C., Purcell, D., Paz-Bailey, G., 2017. Trends in sexual behavior among men who have sex with men (MSM) in high-income countries, 1990–2013: a systematic review. AIDS Behav. 21 (10), 2811–2834. doi:10.1007/s10461-017-1799-1.

Hurrelle, M., Balogun, M.A., Klapper, P., et al. Sentinel laboratory surveillance of hepatitis C antibody testing in England: understanding the epidemiology of HCV infection. 2006. doi:10.1017/S0950268806006832

Ireland, G., Higgins, S., Goorney, B., Ward, C., Ahmad, S., Stewart, C., Simmons, R., Lattimore, S., Lee, V., 2017. Evaluation of hepatitis C testing in men who have sex with men, and associated risk behaviours. In: Manchester, UK. Sexually Transmitted Infections, 93, pp. 404–409 Sep 1.

Johnson, A.M., Mercer, C.H., Erens, B., et al., 2001. Sexual behaviour in Britain: partnerships, practices, and HIV risk behaviours. Lancet 358 (9296), 1835–1842. doi:10.1016/S0140-6736(01)06883-0.

Jones, L., Bates, G., McCoy, E., et al., 2012. A Systematic Review of the Effectiveness & Cost-Effectiveness of Interventions Aimed at Raising Awareness and Engaging with Groups Who Are at an Increased Risk of Hepatitis B and C Infection Final Report. Liverpool John Moores University, Liverpool, UK.

Martin, N.K., Thornton, A., Hickman, M., et al., 2016. Can hepatitis C virus (HCV) direct-acting antiviral treatment as prevention reverse the HCV epidemic among men who have sex with men in the United Kingdom? Epidemiological and modeling insights. Clin. Infect. Dis. 62 (9), 1072–1080. doi:10.1093/cid/ciw075.

Merkinaite, S., Lazarus, J.V., Gore, C., 2008. Addressing HCV infection in Europe: reported, estimated and undiagnosed cases. Cent. Eur. J. Public Health 16 (3), 106. http://www.afl. Accessed December 2, 2019.

Moher, D., Liberati, A., Tetzlaff, J., Altman, D.G., 2009. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 6 (7), e1000097. doi:10.1371/journal.pmed.1000097.

Nash, S., Desai, S., Croxford, S., et al. Public health England: progress towards ending the HIV epidemic in the United Kingdom 2018 report.; 2018. www.facebook.com/PublicHealthEngland. Accessed December 2, 2019.

National Institute for Health and Care Excellence. Hepatitis C diagnosis [Internet]. NICE guidelines. [cited 2021 Jan 14]. Available from: https://cks.nice.org.uk/topics/hepatitis-c/diagnosis/how-to-test/

Newton, J.N., Briggs, A.D.M., Murray, C.J.L., et al., 2015. Changes in health in England, with analysis by English regions and areas of deprivation, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 386 (10010), 2257–2274. doi:10.1016/S0140-6736(15)00195-6.

Price, H., Gilson, R., Mercey, D., et al., 2013. Hepatitis C in men who have sex with men in London - a community survey. HIV Med. 14 (9), 578–580. doi:10.1111/hiv.12050.

Rodger, A.J., Cambiano, V., Bruun, T., et al., 2016. Sexual activity without condoms and risk of HIV transmission in serodifferent couples when the HIV-positive partner is using suppressive antiretroviral therapy. JAMA - J. Am. Med. Assoc. 316 (2), 171–181. doi:10.1001/jama.2016.5148.

Roth, G.A., Abate, D., Hassen Abate, K., et al., 2018. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: a systematic analysis for the global burden of disease study 2017 GBD 2017. Causes of Death Collaborators* doi:10.1016/S0140-6736(18)32203-7.

Ruf, M., Cohuet, S., Maguire, H., Brant, L.J., Ramsay, M., Lattimore, S., Delpech, V., 2008. Setting up an enhanced surveillance of newly acquired hepatitis C infection in men who have sex with men: a pilot in London and South East region of England. Euro Surveill. 13 (47). http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed10&NEWS=N&AN=550110610.

Tedder, R.S., Gilson, R.J., Briggs, M., et al., 1991. Hepatitis C virus: evidence for sexual transmission. BMJ 302 (6788), 1299–1302. doi:10.1136/bmj.302.6788.1299.

The Scottish Government. Clinical review of the impacts of hepatitis C: short life working group report for the Scottish government [Internet]. 2018 [cited 2021 Jan 14]. 51 p. Available from: https://www.gov.scot/binaries/content/documents/govscot/publications/independent-report/2018/07/clinical-review-impacts-hepatitis-c-short-life-working-group-report/documents/00538235-pdf/00538235-pdf/govscot%3Adocument/00538235.pdf

Trouiller, P., Velter, A., Saboni, L., Sommen, C., Sauvage, C., Vaux, S., Barin, F., Chevaliez, S., Lot, F., Jauffret-Roustide, M., 2020. Injecting drug use during sex (known as “slamming”) among men who have sex with men: Results from a time-location sampling survey conducted in five cities, France. Int. J. Drug Policy 79, 102703 May 1.

UNAIDS. A hidden epidemic: HIV, men who have sex with men and transgender people.; 2010. http://www.unaids.org/en/media/unaids/contentassets/dataimport/pub/report/2009/jc1720_action_framework_msm_en.pdf. Accessed December 2, 2019.

World Health Organization. WHO guidelines on hepatitis B and C testing.; 2017.

World Health Organization, 2017. Global Hepatitis Report 2017. World Health Organization doi:10.1149/2.030203jes.