Prevalence of hepatitis C infection among general population and high-risk groups in the EU/EEA: A systematic review update

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Abstract

Background Although significant improvement in efficacy measured by sustained virological response, the high acquisition costs of direct-acting antivirals limit the access for patients and influence the costs of health care resource utilization in hepatitis C. It is important to have the latest estimates of prevalence, especially in the high risk groups, for cost of illness, cost-effectiveness and budget impact studies. Methods Original studies on the estimates of the prevalence among general and high-risk populations in the European Union/European Economic Area (EU/EEA) were retrieved from Medline and Embase for the period from 2015 to 2018. All included studies were evaluated for risk of selection bias and summarized together in narrative form. Results from previous reviews and the updated searches were compared per country among different populations, respectively. Results Among 3871 studies identified, 46 studies were included, with 20 studies used for the estimate for the general population, 3 for men who have sex with men (MSM), 6 for prisoners and 17 for people who inject drugs (PWID). Compared with the results reported in previous systematic reviews, the updated estimates were lower than previous ones in most available countries. Anti-HCV general population prevalence estimates ranges from 0.54% to 1.50% by country. The highest prevalence of anti-HCV was found among PWID (range of 7.90% - 82.00%) followed by prisoners (7.00% - 41.00%), HIV-positive MSM (1.80% - 7.10%), HIV-negative HIV status-MSM (0.20% - 1.80%), pregnant women (0.10% - 1.32%) and blood donors (0.03% - 0.09%). Conclusions Our study highlights the heterogeneity in anti-HCV prevalence across different population groups in EU/EEA. The prevalence also varies widely between European countries. There are many countries that are not represented in our results, highlighting the need for the development of robust epidemiological studies.

Introduction

Infection with hepatitis C virus (HCV) leads to an asymptomatic acute stage. However, approximately 75% of acutely infected patients face substantial risk of developing chronic HCV infection[1]. During the two decades after infection, 27% develop liver cirrhosis and 25% develop hepatocellular carcinoma (HCC) [2, 3].Worldwide, an estimated 71 million people were living with chronic HCV infection (1.0% of the global population) [4]. In the European Union/European Economic Area (EU/EEA), it was estimated that more than 14 million people were living with chronic HCV infection, suggesting a relatively higher prevalence of 1.5% in this region [4].

Given the slow rates of liver disease progression and peaks in transmission that occurred in the 1990s, many countries are yet to experience the full burden of HCV-related disease [5]. However, decades-long delay between infection and the expression of chronic liver disease or liver cancer made it difficult to link these diseases to earlier HCV infections. Reliable and timely prevalence data is therefore important to describe the current burden of disease.

Most people infected with HCV remain unaware of their infection. The hidden burden estimated based on limited data from EU/EEA shows that less than 15% of those chronically infected with HCV are aware of their diagnosis [6-8]. An anti-HCV antibodies serology test is recommended as the first-line diagnostic test by European Association for the Study of the Liver (EASL) for HCV screening, which is evidence of past or

current HCV infection [9]. If the result is positive, then current infection should be confirmed by a sensitive RNA test. Anti-HCV antibodies are detectable by enzyme immunoassay (EIA) in the vast majority of patients with HCV infection. In addition, rapid diagnostic tests (RDTs) are also recommended in settings where there is limited access to laboratory infrastructure and testing or populations where access to RDT would facilitate linkage to care [10]. The primary goal of diagnostic testing is to identify and link infected individuals to appropriate treatment. Several modelling studies suggest that scaling up HCV treatment can lead to substantial reductions in anti-HCV prevalence and reduce transmission [11-14]. The introduction of direct-acting antivirals (DAAs) has been a major breakthrough in the treatment of hepatitis C. However, the high acquisition costs of sofosbuvir-based regiments limit the access for patients and influence the costs of health care resource utilization in hepatitis C[15]. It is important to have the latest estimates of prevalence, especially in the high risk groups, for cost of illness, cost-effectiveness and budget impact studies.

We chose the most published reviews with high quality, according to an overview of systematic reviews on clinical burden of HCV infection[16]. We updated two previous systematic reviews undertaken respectively among general population [17] and high-risk groups [18] in 2015. In Europe, the high-risk groups for acquisition of HCV include people who inject drugs (PWID), men who have sex with men (MSM) and people in prison. We aim to update and expand the estimates for anti-HCV prevalence.

Objectives

The objective of the study is to update the anti-HCV prevalence (the serologic markers used as proxies for chronic infection in this study) among general population and high-risk population (MSM, prisoner, and PWID).

Methods

Date source and search strategy

Original research studies on the estimates of the prevalence among general and high-risk population in the EU/EEA were retrieved from Medline and Embase for the period from 2015 to 2018. The search strategy used was consistent with previous reviews [17, 18] and shown in additional file 1. The search terms covered the following domains: disease-related (HCV infection), outcome-related (anti-HCV/HCV RNA prevalence), and geographic-related search terms (EU/EEA). Two separate searches were conducted: to maximize the yield of the search, no population-specific search terms were included among general population, MSM and prisoners. However, PWID-specific terms were included due to two reasons: The previous reviews didn’t conduct literature database searching and the result of prevalence among PWID was only from European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) .The relevant yield among PWID was much according to our preliminary search. . To cover the whole time scope of published studies, the search for general population, MSM and prisoners were limited to records between January 2015 and December 2018 and the search for PWID was limited between January 2009 and December 2018.

Inclusion/exclusion criteria and data extraction

Inclusion/exclusion criteria included population, outcomes of interest, study designs, publication timeframe, and geographical scope. Studies were included if they: 1) reported anti-HCV seroprevalence among general population, pregnant women, first-time blood donors, PWID, MSM, or prisoners; 2) measured the actual presence of viral markers (anti-HCV antibody in this study) in bodily fluid or dried blood spot samples in human subjects; 3) reported original data; 4) were published after 2015 to present among general population, pregnant women, first-time blood donors, MSM, or prisoners and published after 2009 to present among PWID; 5) reported outcomes in one or more EU/EEA member states or any of their regions. Studies were excluded if they 1)targeted non-representative populations, e.g. homeless, migrants, patients with specific diseases etc.; 2) didn't report specified serological markers, or reported study not conducted in humans or only self-reported/unconfirmed prevalence; 3) reported modelled or extrapolated data only, or opinion papers, editorials, guidelines or recommendations, correspondence articles, systematic reviews or meta- analysis; 4) were published out the targeted timeframe; 5) reported data on non EU/EEA countries only. More details on inclusion/exclusion criteria are shown in additional file 1.

The extraction form included year, country, population of the study, the sampling method, laboratory test used, participation rate, number of participants, and anti-HCV results. For studies reporting the prevalence in MSM, data on HIV sero-status was also extracted.

Quality assessment

Each included study was evaluated for risk of selection bias using frameworks developed by Hofstraat and Hahne et [17, 18]. For studies among general population and prisoner, three domains were included: whether estimated were standardized by age and sex, the representativeness of sampling (e.g. random vs convenience sampling) and geographical coverage. For PWID and MSM studies, just one domain was included: geographical coverage. Points were awarded in each domain for a lower risk of bias, and a total score calculated by summing the values in each domain. An estimate among general population and prisoner was considered of high quality when it reached a study quality score ≥4. A high-quality estimate of prevalence in PWID and MSM was defined as a study quality score ≥1.

Data analysis

All included studies were summarized together in narrative form and in summary tables that tabulate the important description of the study population, recruiting period, results and study quality. According to the results of the systematic review previously performed, an algorithm was applied to different populations separately: If a single high quality prevalence estimate was available for a country, this was used. If a high quality estimate was not available, low quality estimates were used (these were pooled when possible). Data per country were pooled according to standard error and sample size. Then 95% confidence intervals were calculated by estimated average and pooled sample size. Results from previous reviews and the updated searches were compared per country among different populations, respectively.

Overall population were categorized into 2 groups: (1) general population, inclusive of mono-HCV infected patients with no recognized risk factors for reinfection (communities, screening participants, pregnant women, and blood donors); (2) high-risk populations, inclusive of HCV infected MSM, prisoner, and PWID.

The majority of EU/EEA countries offer antenatal HCV screening and blood donors screening. These two subgroups among general population are the most complete population prevalence source and used as a proxy population [17]. However, we conduct separate analysis between pregnant women, blood donors and other general population because previous systematic review reported that they are not representative enough. .

Some estimates among general population included exclusively multiple subgroups, overlapping with high-risk population. When pooled together, however, these subgroup data was excluded and pooled with relevant high-risk population based on the results of quality assessment.

Results

Literature search retrievals

The search for data on anti-HCV prevalence in the general population, MSM and people in prison and PWID identified 2790 and 1081 citations, respectively. After title/abstract screening, 73 articles for the general population and 2 subgroups and 26 articles for PWID were included. Following full text screening of these 99 papers, 53 publications were considered not relevant. Finally, 46 publications were included in the review of prevalence data, with 20 publications used for the estimate for the general population, 3 for MSM, 6 for prisoners and 17 for PWID (Figure 1). The results of quality assessment are shown in additional file 1.

Anti-HCV prevalence among general population in EU/EEA

General population

Anti-HCV general population prevalence estimates were found for 7 of the 34 countries in our review, ranging from 0.54% to 1.50% by country (Table 1). More than one estimate was available for 4 countries of 7 countries covered, with the most estimates for Spain (n=3). Eight high quality prevalence estimates from 5 countries (Czech Republic, Ireland, Italy, Portugal and Spain) were available. Multiple high quality estimates were available for a pooled estimate in Italy (n=2). Relatively high anti-HCV prevalence was found in Czech Republic (1.67%), Poland (1.50%) and Italy (1.37%).The estimate for Poland, however, is based one single study with low quality (score =2). The other article reporting the prevalence estimate on general female population in Poland was not pooled. Three estimates were available for Spain, of which only one was of high quality and reported an anti-HCV prevalence of 1.11%. One articles reported 1.14% in Callosa D'En Sarrià and Valencian Region. The other one reported 0.60% in general female population. Subgroup analysis was available for Italy and Poland. In Italy, the prevalence of HCV increased with age, from 0.2% in subjects born after the year 1984, to 4.2% in those born before the year 1935 ($P < 0.01$). The birth-cohort prevalence peaked (7.0%) in elderly (age > 70 years). Age > 70 years, low education level, and cohabitation with an anti-HCV positive subject predicted the HCV positivity. In Poland, a higher prevalence was found in the population of post-reproductive age (age >45 years).

Pregnant women

An estimate of antenatal anti-HCV prevalence was found for 6 of the 34 countries in our review, ranging from 0.10% to 1.32% by country (Table 2). More than one estimate was available for the UK of 6 countries covered (n=2). Five high quality prevalence estimates from 5 countries (Poland, Slovenia, Spain, Sweden and the UK) were available. Only estimate of Italy was of low quality. Relatively high anti-HCV prevalence was found in Poland (1.32%) and Spain (0.55%). Relatively low prevalence was reported in the UK (0.10%). The other article reporting the prevalence estimate on Women who attended antenatal clinics in London (0.5%) was not pooled given to the potential geographic bias. Subgroup analysis was available for the UK and Slovenia. In women born in the UK, prevalence increased with age. However, no statistically significant differences in anti-HCV prevalence between age groups (<20, 20-29 and ≥30 years) were observed in pregnant women in Slovenia.

Blood donors

An estimate of anti-HCV prevalence in first-time blood donors was available for only 2 of the 34 countries in our review, with Greece reporting 0.03% and Italy reporting 0.09% (Table 2). One low quality prevalence estimates for Greece and one high quality estimates for Italy were available. There is no subgroup analysis among blood donors available for both countries.

Anti-HCV prevalence among high-risk population in EU/EEA

MSM

An estimate of anti-HCV prevalence in MSM was found for 3 of the 34 countries in our review (Table 3). Furthermore, the MSM was divided into two categories: HIV-positive MSM and HIV-negative HIV status-MSM. The prevalence in HIV-positive MSM covered 3 countries, ranging from 1.80% (the UK) to 7.10% (Netherland). The other country, France, reported 5.10%. The prevalence in HIV-negative HIV status-MSM covered 2 countries, ranging from 0.20% (the UK) to 1.80% (France). Two high quality prevalence estimates from 2 countries (the UK and France) were available. Only estimate of Netherland was of low quality. Subgroup analysis was available for the UK and France. Higher prevalence was found in HIV-positive MSM, compared with that in HIV-negative HIV status-MSM.

Prisoner

An estimate of antenatal anti-HCV prevalence was found for 4 of the 34 countries in our review, ranging from 7.00% to 41.00% by country (Table 3). More than one estimate was available for the UK (n=2) and Portugal (n=2) of 4 countries covered. All estimates in prisoners were of low quality. All studies were single center in regional level, except the one in Portugal, which was multi center. Three studies reported ratio of sex with more males than females included. The other three studies didn’t report ratio of sex. None of these 6 studies reported data on age. The studies in Portugal and Spain used exhaustive sampling in the included prison. Sampling method for the other studies was not reported. Extremely high prevalence was found in Norway (41.00%). However, this estimate was from an single low quality study with a small sample size (n=62). There is no subgroup analysis among prisoners available for the four countries.

PWID

An estimate of antenatal anti-HCV prevalence was found for 13 of the 34 countries in our review, ranging from 7.90% to 82.00% by country (Table 4). More than one estimate was available for 4 of 13 countries covered, with the most estimates for the UK (n=3). Nine high quality prevalence estimates from 6 countries (Croatia, Hungary, Germany, France, Spain and the UK) were available. Multiple high quality estimates were available for a pooled estimate in the UK (n=3) and France (n=2). Relatively high anti-HCV prevalence was found in Sweden (82.00%) and Spain (72.00%). Relatively low prevalence was reported in the UK (36.50%) and Croatia (34.04%). However, the estimate in Spain was of low quality (score=0). One article in the UK covered the vulnerable population in London, including both PWID and prisoner. Based on the results of quality assessment (score=1), this result was also pooled into the estimate. Another article in the UK reported only subgroup prevalence based on the years when the subjects were born. However, the exact estimate of subjects who were born in the early 1990's was not available. Only estimates from the subjects born after 2000 were pooled. The article in the Croatia reported separated prevalence among PWID in the cities of Zagreb, Split and Rijeka. Data from the three cities in this article were pooled. The same situation came up in the Germany, separated prevalence estimates in native German and former Soviet Union migrants in the same article were pooled together. Subgroup analysis was available for 7 countries. In Hungary, Greece and Spain, the subgroups were based on different injection duration. Anti-HCV prevalence increased 4-fold among new injectors (injecting < 2 years) from the data in Hungary. Anti-HCV prevalence in Greece has shown a reduction over time, but increases with age and therefore the length of time of drug use. In Spain, a large proportion of PWID were new injectors.

Comparison analysis

Pooled estimates by population and by country based on the results of quality assessment was shown in Table 5. Compared with the results reported in previous systematic reviews, our results updated the prevalence in Czech Republic, Poland, Portugal among general population, Sweden and Spain among pregnant women, Netherland, the UK and France among MSM, France, Spain, Germany, Sweden and Bosnia and Herzegovina among PWID. Among general population, the updated estimates were lower than previous ones in most available countries. Significant decrease in anti-HCV prevalence was shown in Italy (1.37% vs 5.90%).

Except for Netherland (0.56% vs 0.10%) and Ireland (0.98% and 0.10%), prevalence increased. The same results were reported among high-risk populations, prevalence in most countries decreased, except for the estimates among PWID in Hungary (48.24% vs 24.10%).

Discussion

This is the first review to integrate and contrast prevalence estimates across general population and three key high-risk groups in the EU/EEA. Although gaps in evidence exist, this study reports 36 anti-HCV single study/pooled prevalence estimates from 17 of 34 EU/EEA countries, 19 of which are of high quality evidence.

Eighteen estimates are considered as intermediate/high prevalence using the WHO endemicity threshold for HCV (≥2%). This includes 2 of the 5 estimates among MSM, 4 of the 4 estimates among prisoners and 12

of the 12 estimates among PWID.

For the majority of countries, data on prevalence of HCV ware lacking. The availability of studies with relatively recent data on the prevalence is limited with data for half of the 34 countries. The prevalence of HCV varies widely across the EU/EEA countries for which estimates were available. The lack of high quality, recent, nationwide prevalence estimates and the heterogeneity of available studies makes it challenging to gain an EU/EEA overview of the current epidemiological situation. Especially in MSM and prisoners, we conducted a very broad search of the published literature, yet found many geographical gaps in the data. Significant heterogeneity in study design within and between subgroups and countries hampers the statistical comparison and pooling of prevalence across populations and countries.

In contrast with most published systematic reviews, this study updates and adds new estimates of anti-HCV prevalence for three countries in general population (Czech Republic, Poland and Portugal), for two countries in pregnant women (Spain and Sweden), for one country in MSM (Netherland), for one country in prisoners (Norway) and for five countries in PWID (Bosnia and Herzegovina, France, Germany, Spain and Sweden). Compared with previous estimates, the current estimates on prevalence among both general and high-risk populations decreased in the most available countries. The estimates of increased prevalence in Netherland and Ireland among general population and in Hungary among PWID, however, were all from single study. According to our results on quality assessment, the estimates in Ireland and Hungary were of high quality and the estimate in Ireland was from a big sample size (n=3795). Although the estimate in Netherland was also from a big sample size (n=6036), the total quality was assessed as low quality.

Another systematic review [19] reported the anti-HCV prevalence for the 20 WHO European Region countries outside the EU/EEA. The anti-HCV prevalence outside the EU/EEA was higher than inside the EU/EEA among general population (0.50% - 13.00% vs 0.54% to 1.50%), and blood donors (0.03% - 6.40% vs 0.03% - 0.09%), but lower among PWID (5.30% - 73.00% vs 7.90% - 82.00%).

Estimates of prevalence obtained from blood donor and pregnant women were found to differ from general population an estimate, which is agreed with previous result that they are not a reliable proxy population to estimate prevalence in the general population. Anti-HCV prevalence in blood donor and pregnant women were found to be considerably lower, compared with general population estimates. Within countries, the prevalence of anti-HCV among MSM, prisoners and PWID were much higher than the corresponding prevalence in the general population. Of the high risk groups considered, PWID had by far the highest prevalence. .

The strength of this review is that it covers all general population and high-risk subgroups. The previous reviews, due to pragmatic reasons, extracted prevalence estimates for PWID from the data repository from ECDDA. It is possible that this data set is not exhaustive. In our review update, however, PWID-specific search terms were used to identify potential studies. We believe that the description provided gives a sufficiently thorough review of recently published anti-HCV prevalence estimates. With latest prevalence estimates, our study aim to contribute to the analyses in cost of illness, cost-effectiveness and budget impact to optimize the health care resource utilization in hepatitis C management.

However, our study confirmed that there was an evidence gap on anti-HCV prevalence among lots of EU/EEA countries. This limitation of our study also provides idea for further research. In some countries, no national studies had been reported, thus local and reginal data were assumed to be reflective of the whole country. However, by assessing the methodological quality of the studies, this limitation can further mitigated.

Conclusion

This review emphasizes the heterogeneity in anti-HCV prevalence across different population groups in Europe. The prevalence also shows considerable diversity between EU/EEA countries. There are many countries that are not described in our results, emphasizing the existing need to develop robust epidemiological studies.

Abbreviations

EMCDDA: European Monitoring Centre for Drugs and Drug Addiction; EU/EEA: European Union/European Economic Area; HCV: Hepatitis C Virus; MSM: Men Who Have Sex with Men; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PWID: People Who Inject Drugs; HIV: Human Immuno-deficiency Virus; UK: United Kingdom

Declarations

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Availability of data and materials

The full search strategy, the inclusion/exclusion criteria and results on quality assessment of included studies are available in the Additional file 1.

Authors' contributions

HAR study concept and design, literature search, acquisition of data, analysis and interpretation of data, drafting of the manuscript. ZHJ study concept and design, literature search, acquisition of data, analysis and interpretation of data, critical revision of the manuscript for important intellectual content. FRC study concept and design, literature search, acquisition of data, interpretation of data, critical revision of the manuscript for important intellectual content, supervised the study. TOM study concept and design, literature search, analysis and interpretation of data, critical revision of the manuscript for important intellectual content, supervised the study. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Tables

Table 1. Summary of results from studies reporting anti-HCV prevalence in general population

Author, year	Country	Recruiting period	Population as reported	Sample size	Anti-HCV prevalence (%) (95% CI)	Quality assessment
Viejo, 2018[1]	Spain	February-April 2017	General adult population living in the health area of Callosa D'En Sarrià	2637	1.14 (0.73-1.55)	Low quality
Lavin, 2017[2]	Spain	2015-2016	Spanish adult population	6839	1.11 (NR)	High quality
Quesada, 2015[3]	Spain	1994-2005	Women from the general population in different geographical areas worldwide	314	0.60 (0.20-2.50)	Low quality
Andriulli, 2018[4]	Italy	2015	General population	4907	2.30 (NR)	High quality
Morisco, 2017[5]	Italy	May 14	A random 1:3 systematic sample of the adult general population of Naples	1315	3.00 (2.10-4.00)	High quality
Walewska-Zielecka, 2017[6]	Poland	2004-2014	Patients who had been tested for anti-HCV at least once in the period from 2004 to 2014	61805	1.50 (NR)	Low quality
Clifford, 2017[7]	Poland	2004-2009	General female population	909	0.80 (0.30-1.60)	Low quality
Garvey, 2017[8]	Ireland	April-June 2014 and November 2015-February 2016	Adult population in Ireland with probability proportional to the general population age-sex distribution	3759	0.98 (NR)	High quality
Chlibek, 2017[9]	Czech Republic	February 2015-September 2015	Adult general population	3000	1.67 (1.27-2.19)	Low quality
Carvalhana, 2016[10]	Portugal	April 2012-December 2014	Adults from primary care settings in mainland Portugal	1627	0.54 (0.20-0.90)	High quality
Plompen, 2015[11]	Netherland	NR	General dutch elderly population	6036	0.56 (NR)	Low quality

Table 2. Summary of results from studies reporting anti-HCV prevalence in pregnant women and blood donor

Author, year	Country	Recruiting period	Population as reported	Sample size	Anti-HCV prevalence (%) (95% CI)	Quality assessment
Pregnant women						
Orkin, 2016[12]	UK	2013	Women who attended antenatal clinics during 2013 at two London hospitals	1000	0.50 (0.06-0.94)	Low quality
Cortina-Borja, 2016[13]	UK	1 April–30 June 2012	Women delivering live-born infants in the North Thames region in England	31467	0.10 (0.07-0.14)	High quality
Kopilovic, 2015[14]	Slovenia	1999, 2003, 2009 and 2013	Pregnant women	31849	0.13 (0.09-0.17)	High quality
Lembo, 2017[15]	Italy	January 2010 - December 2015	Pregnant women consecutively admitted to the Division of Obstetrics and Gynecology of the University Hospital of Messina, Italy	5184	0.20 (NR)	Low quality
Walewska-Zielecka, 2016[16]	Poland	2004-2014	Pregnant women in Poland	42274	1.32 (NR)	High quality
Millbourn, 2017[17]	Sweden	October 2013 - March 2015 and October 2013 - February 2016	Every pregnant woman and her partner in Orebro county and in Southern part of Stockholm (288,000 and 300,000 inhabitants, respectively)	21379	0.20* (NR)	High quality
Munoz-Gamez, 2016[18]	Spain	January-October 2015	Pregnant women in Spain	NR	0.55 (0.55-0.77)	High quality
Blood donor						
Velati, 2018[19]	Italy	January 2009-December 2015	Voluntary, unpaid first-time donors	1934612	0.09 (0.08-0.09)	High quality
Politis, 2018[20]	Greece	2010-2016	Blood donor	NR	0.03 (NR)	Low quality

*calculated based on available data

Table 3. Summary of results from studies reporting anti-HCV prevalence in MSM and prisoner

Author, year	Country	Recruiting period	Population as reported	Sample size	Anti-HCV prevalence (%) (95% CI)	Quality assessment
MSM						
Ireland, 2017[21]	UK	28 February - 15 December 2014	MSM attending four genitourinary medicine clinics in Manchester	HIV+:735 HIV-:855	1.80 (NR) 0.20 (NR)	High quality
Vanhommerig, 2013[22]	Netherland	2009 -2012	HIV-infected MSM during five waves of anonymous surveys at Amsterdam STI clinic	439	7.10 (NR)	Low quality
Cotte, 2018[23]	France	January 2016 to May 2017	HIV+, HCV-negative MSM with serological follow-up in 2016	HIV+:13051 HIV-:930	5.10 (NR) 1.80 (NR)	High quality
Prisoner						
Ekeke, 2018[24]	UK	December 2015 -February 2017	Prisoners entered Pentonville prison	1324	7.00 (NR)	Low quality
Patel, 2016[25]	UK	NR	Inmates in a medium security prison	160	33.75 (NR)	Low quality
Casella, 2016[26]	Portugal	2014 and 2016	Inmates of two male prisons in the centre of Portugal (Pinheiro da Cruz and Setubal)	82	38.00 (NR)	Low quality
Liberal, 2017[27]	Portugal	January-April	Inmates from one of the largest prisons in Portugal	1208	15.70* (NR)	Low quality
Svendsen, 2017[28]	Norway	September 2015	At-risk populations in	304	41.00 (NR)	Low quality

			Trondheim, Norway			
Lerena, 2016[29]	Spain	NR	Inmates in a Northern region of Spain (Cantabria) with 600k inhabitants and focused to the regional long-stay prison of El Dueso	436	16.00 (NR)	Low quality

Table 4. Summary of results from studies reporting anti-HCV prevalence in PWID

Author, year	Country	Recruiting period	Population as reported	Sample size	Anti-HCV prevalence (%) (95% CI)	Quality assessment
Aisyah, 2018[30]	UK	May 1 2011-June 30 2013	Vulnerable populations in London	1207	11.40 (NR)	High quality
Hope, 2016[31]	UK	1992-2013	Image and performance enhancing drugs (IPEDs) injectors In England and Wales	343	7.90 (NR)	High quality
Hope, 2015[32]	UK	Since 1990	PWID from a sample of services providing needle and syringe programmes, opiate substitution therapy and addiction treatment except Scotland	123	41.70 (NR)	High quality
Valencia, 2018[33]	Spain	January 2013-December 2016	PWUD who actively consumed heroin and/or cocaine, either smoked or injected	946	33.30 (NR)	Low quality
Folch, 2016[34]	Spain	2010-2011	PWID in harm reduction centers in Catalonia	754	72.00 (68.8-75.2)	High quality
Leon, 2016[35]	France	2004 and 2011	IDU	1242	43.40 (39.00-47.90)	High quality
Weill-Barillet, 2016[36]	France	2011	Drug users having injected or snorted drugs at least once in their life	960	64.00 (59.20-68.20)	High quality
Sypasa, 2017[37]	Greece	2012-2013	During an HIV outbreak among PWID in Athens (ARISTOTLE programme)	431	49.90 (45.00-54.70)	Low quality
Sheka, 2014[38]	Greece	January 1997-December 2007	Intravenous drug users who attended the Greek	2668	72.20 (NR)	Low quality

			Organization against Drugs			
Derks, 2018[39]	Germany	2011-2014	Current injectors in eight German cities	1318	64.60 (NR)	High quality
Tarjan, 2017[40]	Hungary	2011 and 2014	PWID injecting in the last month and attending SEPs or drug treatment centres	365	65.00 (NR)	High quality
Handanagic, 2016[41]	Croatia	November 2014 - February 2015	PWID in the cities of Zagreb, Split and Rijeka	399	38.30 (31.40-44.30)	High quality
Kaberg, 2017[42]	Sweden	7 April 2013-16 October 2014	PWID in the Stockholm needle exchange program (NEP)	1386	82.00 (NR)	Low quality
Keegan, 2017[43]	Ireland	31 January 2015	Patients attending agonist opioid treatment (AOT) in a clinic in Dublin	228	63.60 (NR)	Low quality
Skocibusic, 2016[44]	Bosnia and Herzegovina	NR	PWID of both sexes included in opiate substitution treatment in the southern part of Bosnia and Herzegovina (B&H)	120	52.50 (NR)	Low quality
Svendsen, 2017[45]	Norway	September 2015-November 2016	PWID in local opioid substitution clinic, outpatient clinics and day centres in Trondheim, Norway	304	41.00 (NR)	Low quality
Nosotti, 2016[46]	Italy	NR	IDU sample in Rome	261	41.70 (NR)	Low quality

Table 5. Estimates of anti-HCV prevalence by population and by country

Country	Included references	Selected references	Sample size	Anti-HCV prevalence (%) (95% CI)	Baseline _ sample size	Baseline _prevalence (%) (95% CI)
General population						
Spain	3	Single high quality	13678	0.8 (0.65-0.95)	364	1.1(0.3-2.8)
Italy	2	Pooled high quality	12444	1.37 (1.17-1.58)	4826	5.9(5.2-6.6)
Poland	2	Single low quality	61805	1.5 (1.4-1.6)	NR	NR
Czech Republic	1	Single high quality	3000	1.67 (1.21-2.13)	NR	NR
Portugal	1	Single high quality	1627	0.54 (0.18-0.9)	NR	NR
Netherland	1	Single low quality	6036	0.56 (0.37-0.75)	4046	0.1(0.0-0.2)
Ireland	1	Single high quality	3795	0.98 (0.67-1.29)	1478	0.1(0.0-0.4)
Pregnant women						
UK	2	Single high quality	31467	0.1 (0.06-0.13)	110621	1
Slovenia	1	Single high quality	31849	0.13 (0.09-0.17)	90	4.4
Italy	1	Single low quality	5184	0.2 (0.08-0.32)	10881	1.7 (1.4-1.9)
Poland	1	Single high quality	38309	0.76 (0.67-0.85)	1534	0.1 (0.0-0.3)
Sweden	1	Single high quality	4112	0.27 (0.11-0.43)	NR	NR
Spain	1	Single high quality	21379	0.55 (0.45-0.65)	NR	NR
Blood donor						
Italy	1	Single high quality	1934612	0.09 (0.08-0.09)	NR	0·094 (0·085–0·104)
Greece	1	Single low quality	3838919	0.03 (0.03-0.03)	NR	1.202 (1.114–1.295)

MSM						
Netherland	1	Single low quality	439	7.1 (4.69-9.51)	NR	NR
UK	1	Single high quality	1140	1.8 (1.03-2.57)	NR	NR
France	1	Single high quality	13051	5.1 (4.72-5.48)	NR	NR
Prisoner						
UK	2	Pooled low quality	1484	7.9 (6.53-9.28)	5450	17.7(16.4-18.4)
Portugal	2	Pooled low quality	82	16.51 (8.42-24.6)	151	34.4(26.9-42.6)
Norway	1	Single low quality	62	51.6 (39.06-64.14)		
Spain	1	Single low quality	436	16 (12.55-19.45)	NR	22.7(18.3-27.1)
PWID						
UK	3	Pooled high quality	1818	36.5 (34.29-38.72)	3144	49.1 (47.4–50.9)
France	2	Pooled high quality	3015	57.26 (55.49-59.02)	NR	NR
Spain	2	Single high quality	754	72 (68.79-75.21)	NR	NR
Greece	2	Pooled low quality	3099	69.67 (68.05-71.29)	1309	68.1 (65.5–70.6)
Germany	1	Pooled high quality from single study	1526	66.18 (63.8-68.55)	NR	NR
Italy	1	Single low quality	261	47.1 (41.03-53.17)	743	60.5 (56.8–64.0)
Hungary	1	Single high quality	755	48.24 (44.67-51.81)	652	24.1 (20.8–27.6)
Croatia	1	Pooled high quality from single study	830	34.04 (30.81-37.26)	200	44 (37.0–51.2)
Sweden	1	Single low quality	1386	82 (79.98-84.02)	NR	NR
Ireland	1	Single low quality	228	63.6 (57.34-69.86)	200	41.5 (34.6–48.7)
Bosnia and	1	Single low quality	120	52.5 (43.53-	NR	NR

Herzegovina				61.47)		
Norway	1	Single low quality	304	41 (35.46-46.54)	6342	63.0 (61.8–64.2)

Figures

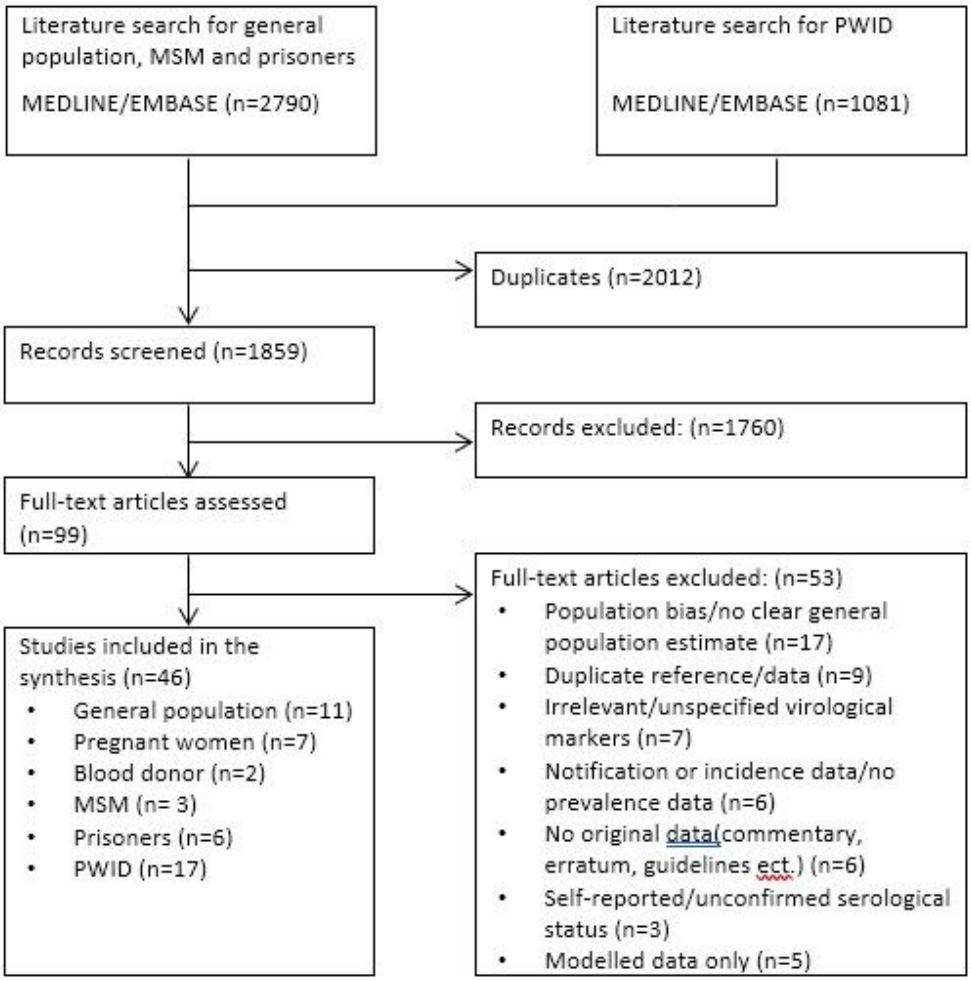

Figure 1

Flow diagram of the study selection process

Supplementary Files

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