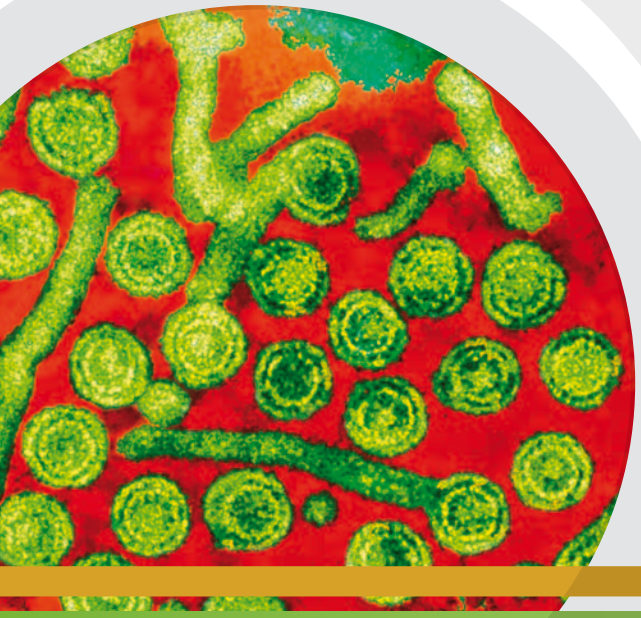

TECHNICAL REPORT

Hepatitis B and C in the EU neighbourhood: prevalence, burden of disease and screening policies

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ECDC TECHNICAL REPORT

Hepatitis B and C in the EU neighbourhood: prevalence, burden of disease and screening policies

Literature review

This review was commissioned by the European Centre for Disease Prevention and Control, coordinated by Marita van de Laar and Mika Salminen, and produced by Irene Veldhuijzen (Municipal Public Health Service Rotterdam-Rijnmond, the Netherlands) and Susan Hahné (National Institute of Public Health and the Environment, Bilthoven, the Netherlands).

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Contents

Abbreviations

DU	Drug user
HBV	Infection with hepatitis B virus
HCC	Hepatocellular carcinoma
HCV	Infection with hepatitis C virus
ICER	Incremental cost-effectiveness ratio
IDU	Injecting drug user
LYG	Life years gained
MSM	Men having sex with men
QALY	Quality-adjusted life year
STD	Sexually transmitted disease

1 Introduction

1.1 Background

Infection with hepatitis B and C virus (HBV and HCV, respectively) affects the liver and results in a broad spectrum of disease outcomes. An infection with HBV can spontaneously resolve and lead to protective immunity, result in a chronic infection and, in rare cases, cause acute liver failure with a high risk of dying. In contrast to HBV, an infection with HCV becomes chronic in most cases[1]. People with chronic hepatitis B and/or C virus infection remain infectious to others and are at risk of serious liver disease such as liver cirrhosis or hepatocellular cancer (HCC) later in life[2, 3]. HBV infection is widely present: approximately one third of the world's population has been exposed to the virus, and an estimated 350 million people are chronically infected[4, 5]. More than 500 000 people die each year of hepatitis-B-related diseases[4, 6]. The World Health Organization estimates that two to three percent of the world's population are infected with HCV, resulting in a total number of 120 to 170 million people[7, 8] .There is a distinct geographical variation in both HBV and HCV prevalence and incidence in the European Union and neighbouring countries.

1.2 Rationale for the study

Over the past decade, the possibilities for antiviral treatment of chronic HBV and HCV infection have greatly improved, e.g. there are now six registered drug therapies for chronic HBV, and several new registrations are expected in the near future. This offers the possibility of secondary prevention of HBV- and HCV-related diseases, as antiviral treatment can improve disease outcome[9, 11], even though concerns regarding the effectiveness of treatment on clinical outcomes and resistance exist and combination therapy may be warranted[12, 13]. Evidence is accumulating that recently developed antiviral therapies may provide a cost-effective intervention to reduce morbidity and mortality in patients with HBV[14-18].

However, as hepatitis B and C are largely asymptomatic, many patients who might benefit from treatment remain undetected. This raises the question whether an active effort should be undertaken to identify chronic HBV and HCV carriers so that they can be offered treatment. This would benefit patients and reduce the burden of illness and costs for the healthcare system, as costly sequelae and deaths could be prevented among a large proportion of those infected[19, 20]. In addition, this may reduce transmission of HBV and HCV through a reduction of the infected pool (by curing a proportion of cases through treatment), by reducing the viral load and therefore the infectivity of chronic carriers, and by offering increased opportunities to vaccinate susceptible contacts of identified HBV carriers.

The improved options for antiviral treatment now offer the possibility of successful secondary prevention of HBV and HCV. This raises the question whether there is a need to extend screening for chronic HBV and HCV infection to those population subgroups with the highest prevalence.

In order to promote national and European policies on secondary prevention of HBV and HCV, a systematic assessment of the need for HBV and HCV screening is required. This consists of at least two initial steps: an estimation of HBV and HCV prevalence (including the burden of disease in European countries), and an assessment of the effectiveness of current national screening policies. Subsequent steps include an assessment of stakeholder perceptions, and the identification of possible interventions and resource implications, together with required monitoring programmes[21].

The goal of this literature review is to obtain insight into HBV and HCV prevalence, burden of disease, and national screening policies and their effectiveness in EU countries.

2 Literature review

A systematic literature review was carried out by first framing the study questions. Second, a search strategy for each question was specified. Subsequently, the searches were carried out and publications of interest were selected, based on titles and abstracts. The full text of all selected publications was assessed for relevance. This was followed by extracting the relevant data from the identified publications according to the steps described in detail below. Thirty-four countries are included in the literature review: 27 EU Member States, Norway, Iceland, Liechtenstein, Switzerland and the three EU candidate countries (Croatia, the former Yugoslav Republic of Macedonia, and Turkey). The methodology used for the analysis of the literature is described separately (see review questions in Annex 2).

2.1 Research questions

The burden of disease of HBV and HCV due to chronic infection and screening effectiveness was elaborated in five research questions.

1. What is the prevalence of chronic HBV and HCV infection in the general population and in the following sub-populations?

- Blood donors
- Pregnant women
- Drug users (DUs)
- Men having sex with men (MSM)
- Migrants

Chronic HBV and HCV infection is defined by the detection of HBsAg and anti-HCV antibodies, respectively. The assessment of the prevalence of HBV and HCV among blood donors is restricted to first-time donors. Blood donors are generally selected to have a low prevalence of blood-borne infections. This can be regarded as the lower limit of the prevalence estimate in the general population. The prevalence in repeat donors is considered to be less relevant for the assessment of the burden of HBV and HCV in Europe and was therefore not included in this review.

2. What is the number of individuals with chronic HBV or HCV infection?

- Calculations are based on general population prevalence (the number of chronic infections is the prevalence of chronic infection times the population size).
- The number of chronic infections in the three largest nationality groups of first generation migrants (a foreign-born person that has migrated to the country of current residence, excluding expatriate children). The number of chronic HBV and HCV infections in these groups will be estimated for each country, if data are available, by multiplying the number of individuals in the three largest first-generation migrant groups born in medium or high endemic countries[22, 23] with the median prevalence in mid- and high endemic countries, respectively. Data on global prevalence of chronic HBV and HCV infection will be used, if available, from Marschall et al.[24] and from WHO and Perz et al.[7, 8], respectively.

3. What is the burden of HBV- and HCV-related cirrhosis and hepatocellular carcinoma (HCC)?

- What is the burden of disease, defined as morbidity and mortality due to cirrhosis and HCC?
- What is the proportion of the burden of cirrhosis and HCC that is attributable to chronic HBV and HCV infection?

4. What is the current national practice regarding screening for chronic HBV and HCV infection in:

- pregnant women;
- blood donors;
- migrants;
- IDUs; and
- MSM?

5. What is the effectiveness of these screening programmes in terms of:

- process (coverage of the programme and the proportion of the risk group screened);
- outcome (proportion of screened individuals which are HBsAg or anti-HCV positive);
- outcome (proportion of positive individuals who are receiving care);

- prevention of secondary cases (what proportion of contacts of HBsAg-positive individuals detected through screening is vaccinated?); and
- cost-effectiveness: what is the cost effectiveness of these screening programmes?

2.2 Literature research

A selection of relevant studies was performed. Following the identification of studies in literature databases using specific search strategies and inclusion criteria, a list of search terms (free and MeSH terms of each database) and a specific search-term combination was defined, including all 34 EU/EFTA country names (see Annex 1–3).

The three databases that were searched using these search-term combinations were MEDLINE (Ovid), EMBASE, and SciSearch. The reference lists of all included publications were reviewed as well. The latter could also include public health reports. The search was performed in two phases: first MEDLINE was searched using the Ovid interface, followed by a search of EMBASE and SciSearch.

Inclusion and exclusion criteria for this review were:

- Only English-language publications were included.
- Publications published between 1 January 2000 up to the date of the search (August 2009) were included.
- Only publications published in peer-reviewed journals and public health reports cited in these journals were included.
- Public health reports were included if published in English and downloadable or obtainable by other means within ten days.

Each study that met the above inclusion criteria was judged as to whether it was expected to contain data relevant to each of the research questions. This was done based on title and abstract. To check consistency between both reviewers, a selection of publications was judged by both reviewers and discrepancies were discussed. As consistency was high, the publications were divided between both reviewers. In case of doubt, a decision was made after consulting the other reviewer. Publications were only included it they were expected to contain primary data or systematic reviews.

Complete publications were obtained from available information sources. For each publication, basic data were recorded on page one and two of the data extraction form, up to question 12 (Annex 3). When a study was not considered relevant and therefore excluded, the reason for exclusion was recorded on the data extraction form. For example, publications on the prevalence of infection in blood donors were excluded if it was not specified whether the study population contained first-time donors.

Data for each publication were extracted using data collection forms (Annex 3), specific to each of the detailed questions. The form included criteria to judge the quality of the study, such as study design, sampling method, and description of the study population. Reviews were kept separate as these could not be summarised by using the data extraction form.

The data extraction forms were then entered in a Microsoft Access database.

Data were summarised for each country and region (where appropriate). Information from review publications was used for example for countries for which our search did not yield relevant studies.

2.3 Analysis of data

Prevalence of HBV and HCV infection

Among the included subpopulations, pregnant women and blood donors are to some extent representative for the general population, whereas IDUs, MSM and migrants are specific groups at a higher risk of hepatitis B and C.

The number of prevalence estimates found for HBC and HCV are summarised by country and presented in maps. The prevalence of HBV and HCV in the general population, pregnant women and blood donors are presented in six separate maps displaying 34 countries. To derive prevalence estimates per country the following algorithm was applied:

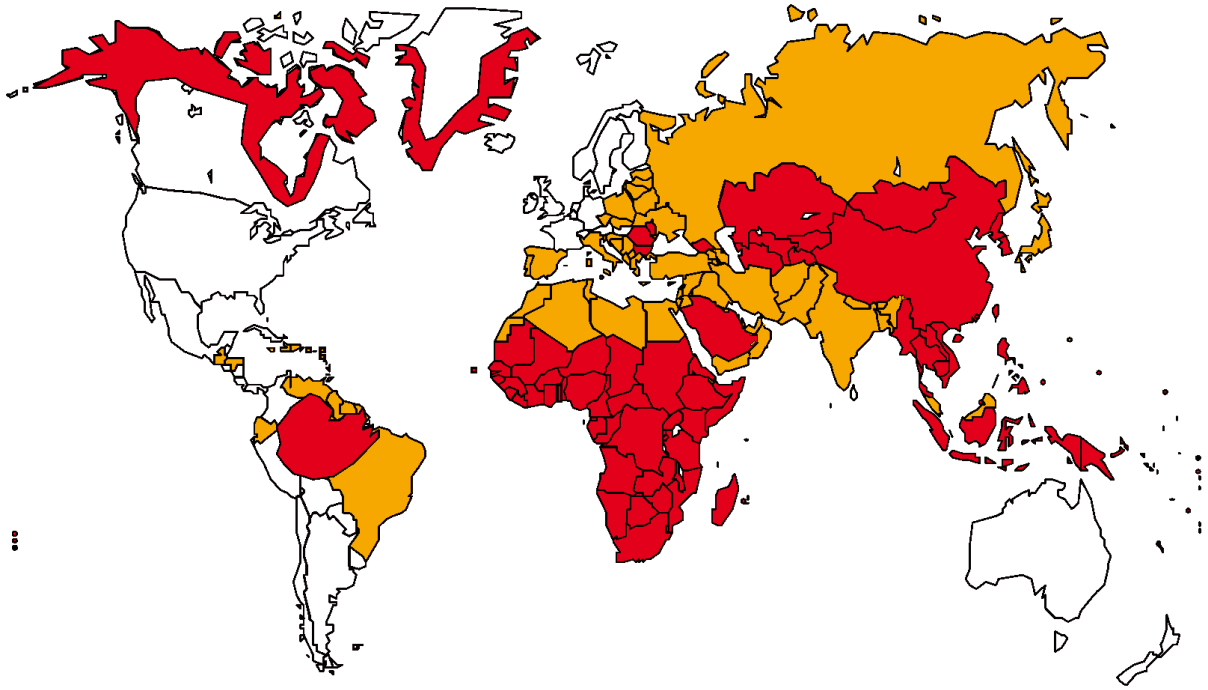
- For the prevalence in the general population, studies that are only based on children are not taken into account.
- If multiple prevalence estimates are available for a country, estimates based on studies that are representative for the whole country are preferred.
- In case of multiple estimates from comparable studies, the average prevalence is calculated and weighted by study size.
- When estimates for three or more regions in a country are available, the estimates are shown per region if the difference between regions is more than 0.5%.

To assess the HBV prevalence in IDUs, we used data from the 2009 Statistical Bulletin from the European Monitoring Centre for Drugs and Drugs Addiction (EMCDDA) [25]. The prevalence of HCV among IDUs in the EU was taken from two recent literature reviews[26, 27]. Regarding blood donors, our literature search was complemented by a report for the Council of Europe.[28]

Number of individuals with chronic HBV and HCV infection

In order to estimate the number of individuals with chronic HBV and/or HCV the estimate for the general population prevalence must be multiplied by the population size obtained from Eurostat (as of January 1, 2009) [22]. To obtain further insight in the number of individuals with chronic HBV and HCV, the number of individuals in the three largest first-generation migrant (FGM) groups born in medium- and high-HBV-endemic countries were multiplied by the median HBV and HCV prevalence of mid- and high-endemic countries, respectively. The three largest groups of FGMs from mid- and high-HBV-endemic countries in each country was obtained from the Organisation for Economic Co-operation and Development (OECD) [23] and from Eurostat[22] if there was no information available from OECD. For each country, the most recent population size estimates were used. Each FGM group was classified as mid- or high-endemic for HBV, according to the WHO classification for HBV (Figure 1)[29]. The associated prevalence was then multiplied by the number of individuals in each group to obtain the estimated number of infected individuals.

Figure 1. Geographical distribution of HBV endemicity



Red: High (HBsAg prevalence ≥8%
Orange: Intermediate (HBsAg prevalence 2%–7%)
White: Low (HBsAg prevalence <2%)

Source: World Health Organization. Introduction of hepatitis B vaccine into childhood immunization services. Management guidelines, including information for health workers and parents. Geneva: WHO; 2001.

The burden of HBV- and HCV-related cirrhosis and hepatocellular carcinoma

The assessment of the burden of HBV- and HCV-related disease was limited to mortality. The rationale for this is that reliable data on the incidence of cirrhosis are not available due to the lack of a consensus on case definitions and registrations. For HCC, mortality is a close proxy of incidence as the survival period is limited. To assess the mortality of HBV- and HCV-related cirrhosis and HCC, the method described by Perz was used[30]. Firstly, data on the overall mortality due to cirrhosis and HCC for males and females were estimated by country. Subsequently, the prevalence of anti-HCV and HBsAg was estimated among these patient groups in each country (not estimated separately for males and females). These anti-HCV and HBsAg prevalences were multiplied with the mortality estimates to assess the HBV- and HCV-attributable burden of cirrhosis and HCC mortality.

Screening practices for chronic HBV and HCV infection

All selected publications were grouped according the target population: screening recommendations for blood donors, migrants, pregnant women, drug users, and the general population. In addition to the published literature two further publications were reviewed: C. van der Poel's report for the Council of Europe (September 2009) on screening policies for blood donors, and a conference presentation by G. Loeber (Dutch Conference on pre- and neonatal screening, April 2009) regarding antenatal screening policies.

Effectiveness of screening programmes for chronic HBV and HCV infection

The following indicators were used to provide an overview of the effectiveness of screening programmes, where data were available:

- Proportion of the screened target population (coverage).
- The proportion of centres offering screening.
- The prevalence of HBV and/or HCV.
- The proportion of HBV-susceptible people that are vaccinated and the proportion of contacts of vaccinated HBV carriers.

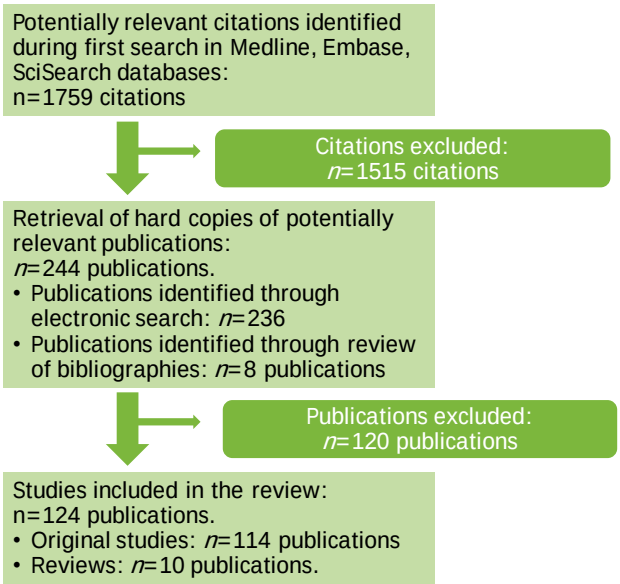
2.4 Identified citations

The prevalence of chronic HBV and HCV infection

The search identified 1759 citations, 984 through MEDLINE, and an additional 775 through EMBASE and SciSearch. Of the 984 citations from MEDLINE, 227 (23%) were selected based on title and abstract. For the 775 citations from additional databases only the titles were available, on the basis of which 47 (6%) were selected. From the reference lists of included studies, another 16 potentially relevant citations were identified based on their titles. For items that were selected based on the title alone, abstracts were retrieved and 17 were considered relevant. Finally, for a total of 244 citations the full text publication was retrieved and reviewed using the data extraction form. Based on the full text, 53 publications were considered not relevant and excluded. Furthermore, 67 publications on drug users were excluded since information on the prevalence in this group was obtained from the EMCDDA 2009 Statistical Bulletin and literature reviews (Figure 2).

77 estimates for the prevalence of hepatitis B and 68 for the prevalence of hepatitis C were found. Some publications reported both HBV and HCV prevalence, and one publication reported results from multiple countries.

Figure 2. Flowchart: number of publications included in the review of the prevalence of chronic HBV and HCV infection in Europe



Note: A similar strategy for identifying relevant publications was used for the other study questions (see text for details).

The burden of HBV- and HCV-related cirrhosis and hepatocellular carcinoma

The search identified 2130 publications, 778 through MEDLINE, and an additional 1352 through EMBASE and SciSearch. Of the 778 citations from MEDLINE, 64 (8%) were selected based on title and abstract. For the 1352 citations from additional databases only titles were available, on the basis of which 23 (2%) were selected. For these 23 selected citations, 10 relevant abstracts were retrieved. From the reference lists of included studies, another 12 potentially relevant citations were identified. Finally, for a total of 56 citations the full text publication was retrieved and reviewed using the data extraction form. Based on the full text, 10 publications were considered not relevant and excluded.

Regarding the overall burden of mortality due to HCC and cirrhosis, the search found an estimate for only four countries, and three recent reviews for Europe[49-51]. These publications were used to extract HCC and cirrhosis mortality data. The recent reviews for Europe were based on data from the World Health Organisation Statistical Information System database (http://www.who.int/whosis/en/).

Screening for HBV and HCV infection

The search on HBV and HCV screening in Europe, its effectiveness and related policies identified 310 citations, 237 through MEDLINE, and an additional 73 through EMBASE and SciSearch. Of the 237 citations from MEDLINE, 47 (20%) were selected based on title and abstract. For the 73 citations from additional databases only titles were available, on the basis of which 8 (11%) were selected. From the reference lists of included studies, another 2 potentially relevant citations were identified. For the 10 citations that were selected based on only the title, 5 relevant abstracts were retrieved. Finally, for a total of 52 citations the full text publication was retrieved and reviewed using the data extraction form. Based on the full text, 12 publications were considered not relevant and excluded. The 40 included studies reporting on screening practices and/or effectiveness represented only 10 of the 34 included countries, and were distributed unevenly. Seventeen studies originated from the United Kingdom, six from Italy, six from France, three from the Netherlands, two from Ireland and one each from Belgium, Denmark, Greece, Hungary and Switzerland.

3 Results

3.1 Prevalence of chronic HBV and HCV infections

The number of estimates per country for HBV and HCV are presented in Table 1. No recent estimates for the HBV and HCV prevalence were available for 13 and 14 countries, respectively. For Italy, a relatively high number of estimates were available. Estimates derived from EMCDDA data (HBV in drug users) and from the report for the Council of Europe (HBV and HCV in first-time blood donors) are not included in Table 1.

Table 1. Number of estimates for the prevalence of hepatitis B (HBsAg) and hepatitis C (anti-HCV)

HBsAg		anti-HCV	
Country*	**Number**	**Country****	**Number**
Belgium	2	Belgium	2
Bulgaria	1	Bulgaria	1
Cyprus	2	Croatia	1
Czech Republic	1	Cyprus	1
Denmark	4	Czech Republic	1
Finland	1	France	1
France	1	Germany	5
Germany	6	Greece	6
Greece	9	Hungary	1
Ireland	2	Italy	24
Italy	20	Netherlands	3
Lithuania	1	Norway	1
Netherlands	4	Poland	2
Poland	1	Romania	1
Romania	1	Slovakia	1
Slovakia	2	Spain	4
Spain	3	Sweden	1
Sweden	1	Switzerland	1
Switzerland	1	Turkey	4
Turkey	10	United Kingdom	7
United Kingdom	4		

** HBV: No recent data for Austria, Croatia, Estonia, the former Yugoslav Republic of Macedonia, Hungary, Iceland, Latvia, Liechtenstein, Luxembourg, Malta, Norway, Portugal, Slovenia.*
*** HCV: No recent data for Austria, Denmark, Estonia, Finland, the former Yugoslav Republic of Macedonia, Iceland, Ireland, Latvia, Liechtenstein, Lithuania, Luxembourg, Malta, Portugal, Slovenia.*

The prevalence of HBV and HCV in the general population

For the prevalence of hepatitis B and hepatitis C in the general population, 38 and 35 estimates were found, respectively. A summary of these estimates with information on the methods and population is given in Tables A1 and A2 (Annex). For HBV, the prevalence in the general population ranged from 0.1% to 7% by country (Figure 3a). Prevalence estimates that could be considered representative for the entire country were available for ten countries: Belgium, Czech Republic, Denmark, Finland, Germany, Greece, Ireland, Italy, Netherlands, Romania, Slovakia, and Turkey. Six of these estimates were derived from one study describing the prevalence of chronic HBV in several European countries[31]. For Italy and Turkey regional prevalence estimates could be presented separately. The references that were used for calculating the prevalence per country in Figures 3a/3b are marked with an asterisk in Table A1.

Figure 3a. Hepatitis B prevalence in the general population: HBsAg

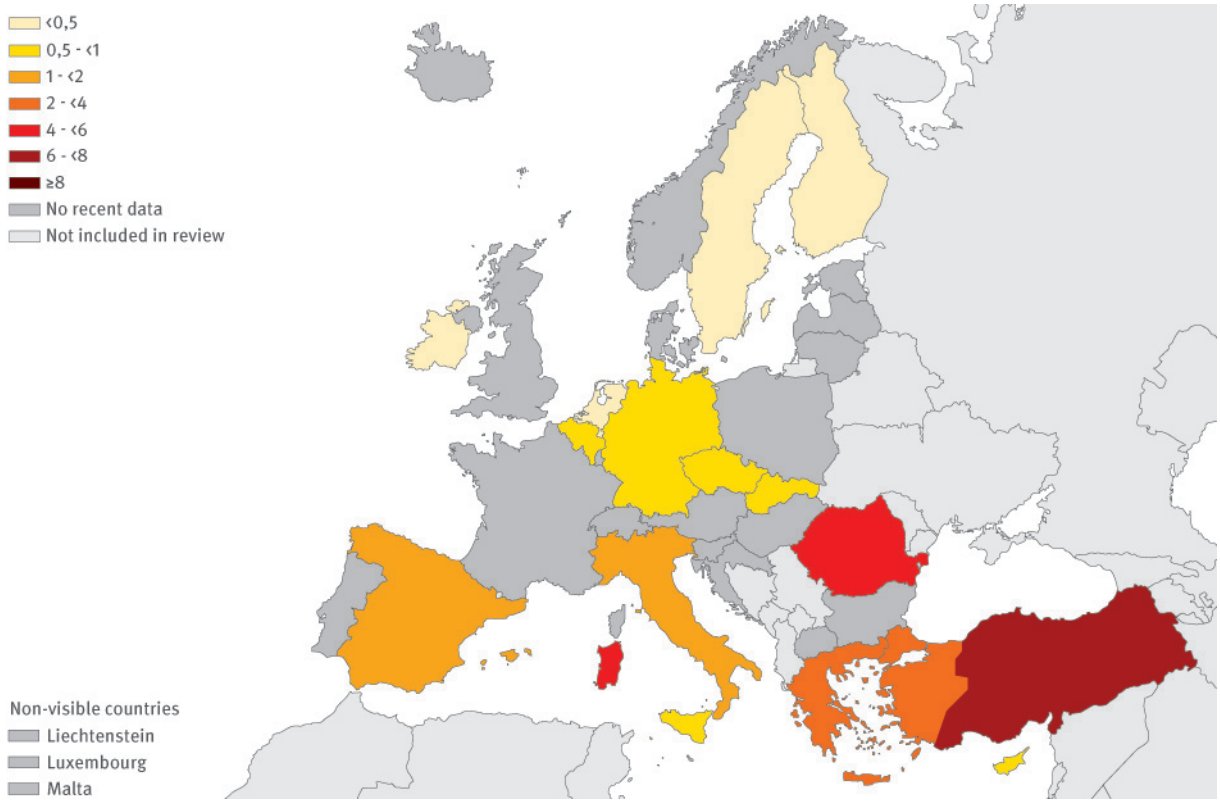
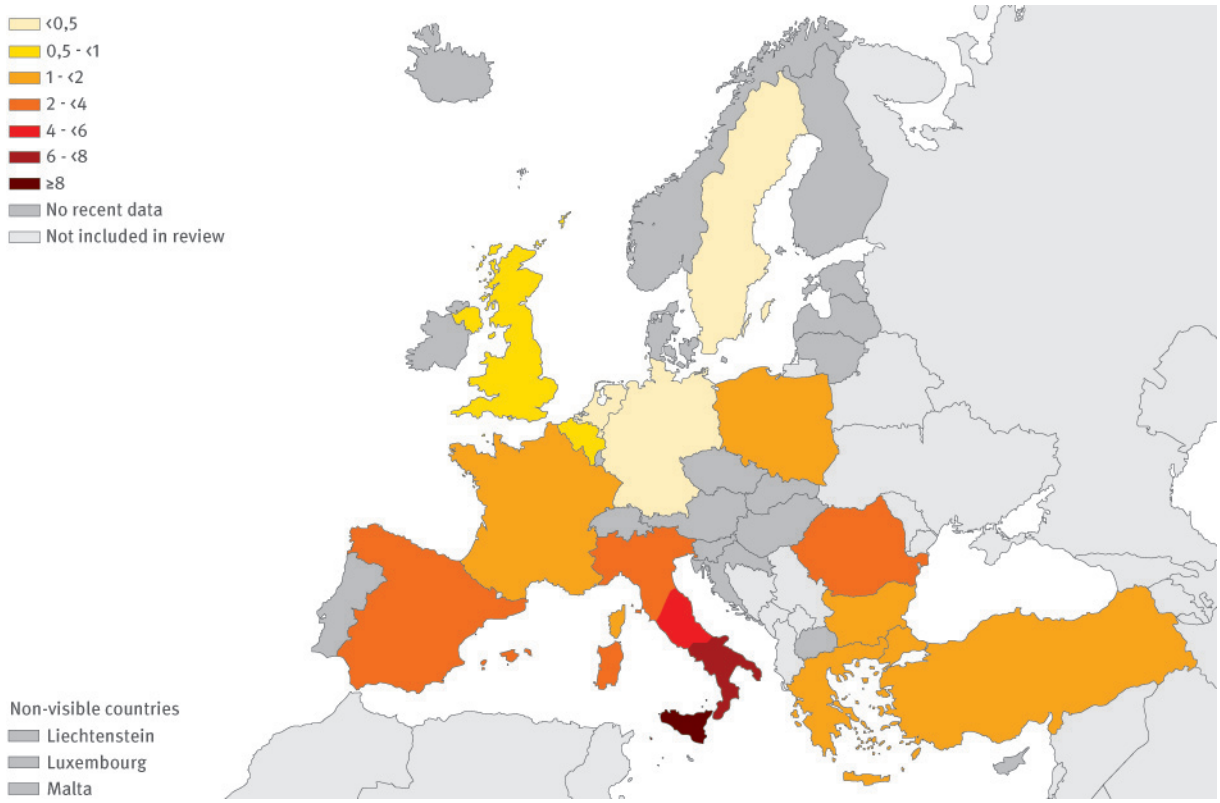


Figure3b. Hepatitis C prevalence in the general population: anti-HCV



For HCV, the prevalence ranged from 0.4% to 3.5% by country and from 0.2% to 10.4% by region within countries (Figure 3b). Prevalence estimates that could be considered representative for the entire country were available for only three countries: the Czech Republic, Germany and Romania. For Italy, regional prevalence estimates could be presented separately. The references that were used for calculating the prevalence per country in Figures 3a/3b are marked with an asterisk in Table A2.

The prevalence of HBV and HCV among blood donors

Seven estimates on the prevalence of HBV and five HCV were found among first-time blood donors. From a recent report for the Council of Europe we obtained estimates for an additional 17 countries for HBV and 18 countries for HCV[28]. All estimates are summarised in Tables A3 and A4. The references that were used for calculating the prevalence per country in the map are marked with an asterisk in Tables A3 and A4.

For HBV, the prevalence in first-time blood donors ranged from 0.0% to 5.2% by country (Figure 4a). In almost all countries with prevalence estimates available for both groups, the prevalence in first-time blood donors was lower than for the general population, with the exception of Cyprus. Cyprus reported a relatively high prevalence in first-time blood donors of 3.0%, and a low prevalence of 0.9% in the general population[32, 33]. However, the general population study only included participants aged 0–30 years and may thus not be representative for the general population including middle-aged and older adults. For Greece, a large difference was observed between the 0.9% prevalence in the study by Zervou[34], and the prevalence of 3% reported in the report for the Council of Europe[28]. A possible explanation for this discrepancy might be the proportion of voluntary, non-remunerated donations, which was 46% in the Council of Europe report, and 100% in the study by Zervou.

For HCV, the prevalence in first-time blood donors ranged from 0.02% to 3.3% by country (Figure 4b). The prevalence in first-time donors was lower than the prevalence estimate for the general population in all countries that had both estimates available.

Figure 4a. Hepatitis B prevalence in first-time blood donors: HBsAg

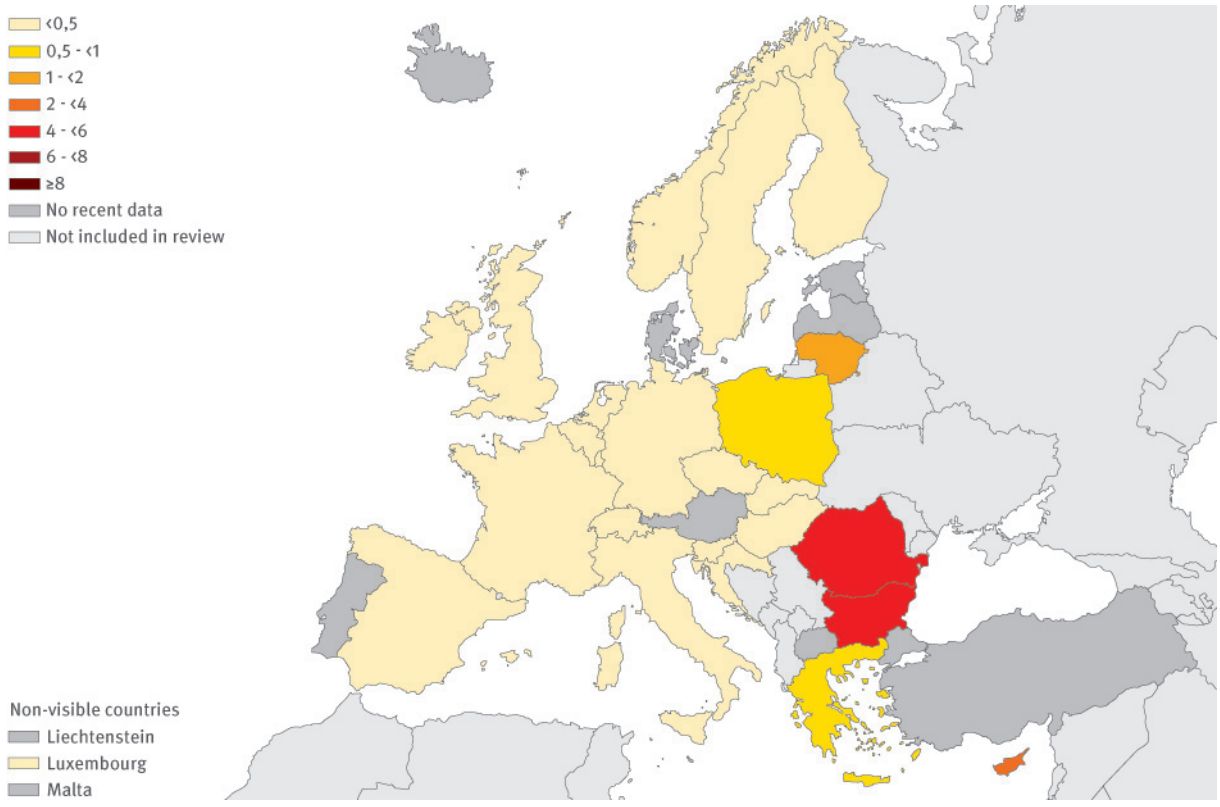
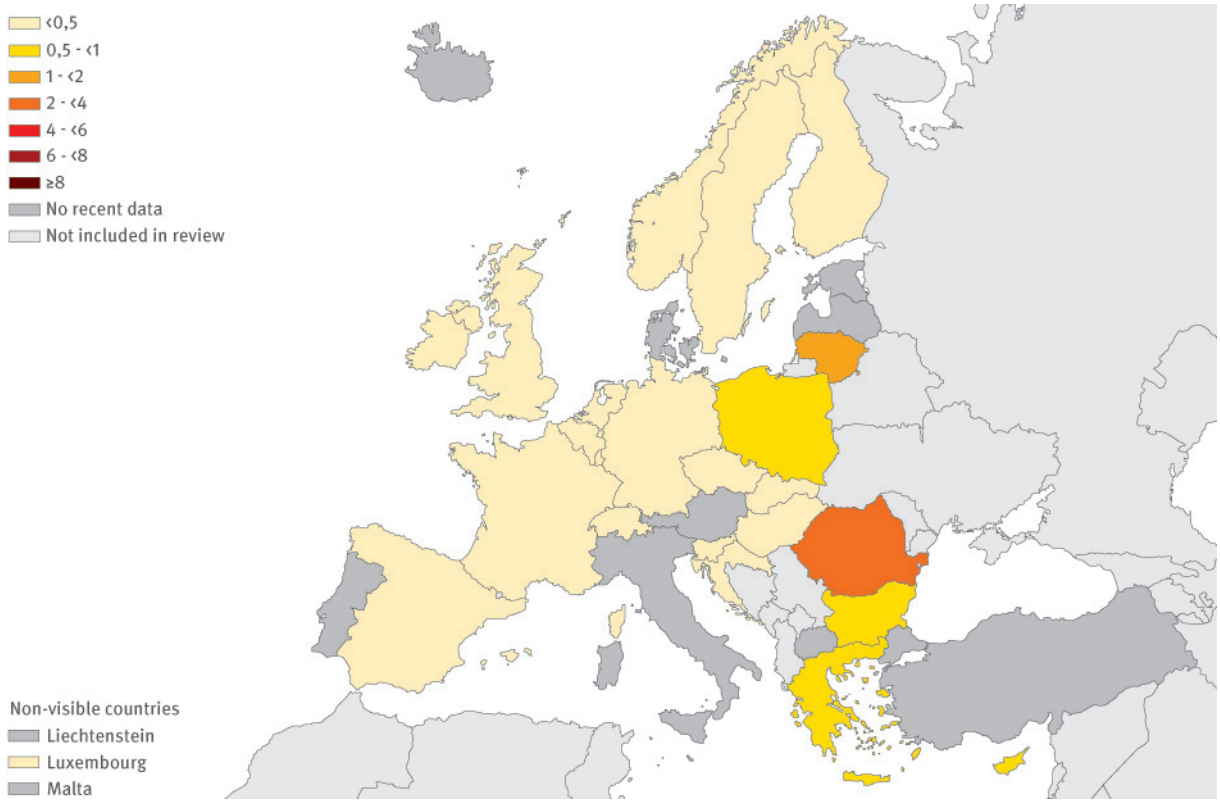


Figure 4b. Hepatitis C prevalence in first-time blood donors: anti-HCV



The prevalence of HBV and HCV among pregnant women

Sixteen estimates on the prevalence of HBV and 15 of HCV prevalence were found among pregnant women (Tables A5 and A6). The references that were used for calculating of the prevalence per country in the map are marked with an asterisk in Tables A5 and A6.

For HBV, the antenatal prevalence ranged from 0.1% to 4.4% by country (Figure 5a). The prevalence in pregnant women was generally higher than in the general population, provided that both estimates were available. This applies to Germany, Greece, Ireland, Italy, the Netherlands and Slovakia. This difference in prevalence might be connected to the fact that migrant women, which have a relatively high HBV prevalence, are better represented in studies among pregnant women than in general population studies. Spain reports the lowest prevalence in pregnant women tested in Catalonia in 2004 (0.1%)[35], which is lower than the prevalence in the general population in the same region in 2002 (0.7%)[36]. The authors attribute the low prevalence in pregnant women to the higher vaccination rate: 16% of pregnant women had serologic markers of vaccination, compared with 8% in the general population study.

For HCV, the prevalence in pregnant women ranged from 0% to 1.7% by country (Figure 5b). The 15 prevalence estimates relate to only six countries, and the prevalence estimate for pregnant women in Greece was similar to that of the general population (1.2% and 1.0%, respectively). In the UK, the prevalence estimate for pregnant women was similar to the prevalence in women in the general population, 0.3% and 0.4% respectively[37]. The prevalence in pregnant women in the north of Italy was estimated at 1.7%, which is lower than the estimated prevalence in the general population for that region (3.2%). This might be related to age, since general population studies report that HCV prevalence increases with age, with the highest prevalence rates observed in people over 55 years[38,39, 40].

Figure 5a. Hepatitis B prevalence in pregnant women: HBsAg

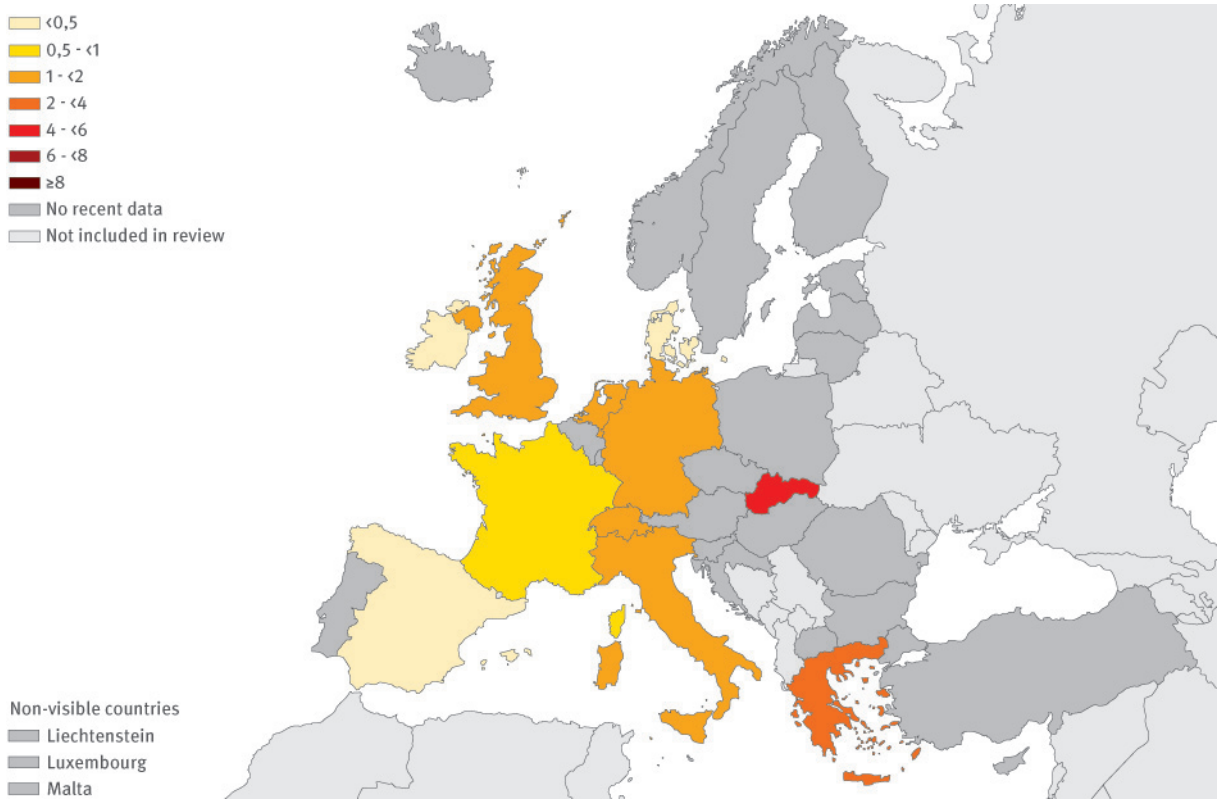
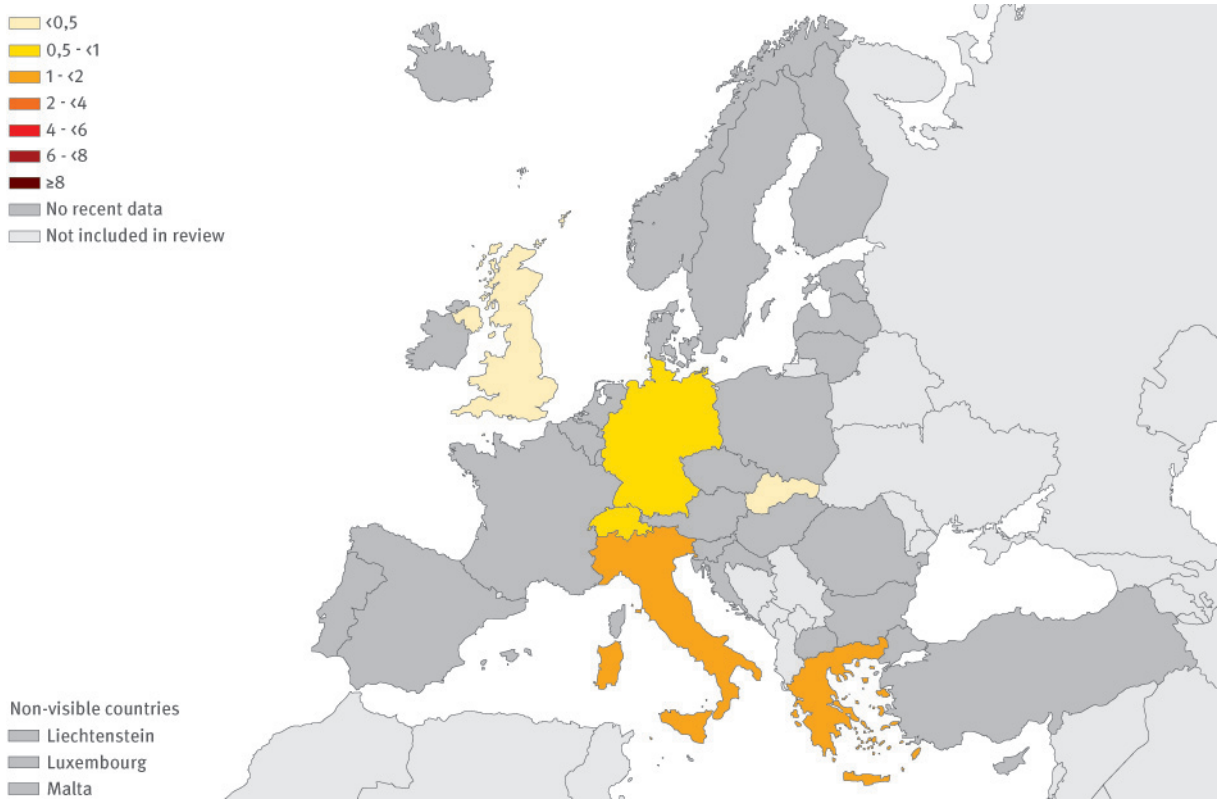


Figure 5b. Hepatitis C prevalence in pregnant women: anti-HCV



The prevalence of HBV and HCV among migrants and minority groups

Primary information on the prevalence of HBsAg among migrants and minority populations was published in 12 publications, seven of which from Italy. One of these publications reported on two migrant groups[46]. There was a wide variation in the HBsAg prevalence, ranging from 1.0% in resident first generation migrants in the Netherlands to 15.4% in Albanian refugees in Greece (Table A7). A review by Clark and Mytton regarding infectious diseases in UK asylum seekers and refugees found HBsAg prevalences ranging from 5.7 to 9.3%[47]. The authors conclude that the observed variation in prevalence is likely to reflect sampling difficulties. For all countries, the estimated HBsAg prevalence among migrants was compared to the prevalence among the general population. The results show that for all migrant groups and all countries*, HBsAg prevalence among migrants was higher than in the general population (Tables A1 and A7).

Prevalence of anti-HCV among migrants and minority populations was described in ten publications, four of which from Italy. One of these publications reported on two migrant groups[46]. The anti-HCV prevalence ranged widely from 0 to 23.4% (Table A8). The latter percentage refers to a Roma population in Hungary with a large proportion of IDUs[48]. Comparing the estimated anti-HCV prevalence among migrants in a specific country with that of the general population in that country, it was shown that for all migrant groups and all countries except Italy, the anti-HCV prevalence among migrants was higher than that in the general population (Tables A2 and A8).

The prevalence of HBV and HCV among injecting drug users (IDUs)

For the prevalence of HBsAg in IDUs, data from the EMCDDA is summarised in Table A9 (http://www.emcdda.europa.eu/stats09/inftab114) [25] . For this table, national estimates were included where available. When multiple estimates were available, the most recent estimate was included. The reported HBsAg prevalence in IDUs varied widely, ranging from 0.0% in Belgium to 11.6% in Bulgaria in 2006. Generally, the HBsAg prevalence among IDUs is higher in countries in Central and Eastern Europe, compared with those in Western Europe.

For HCV, 98 studies on HCV prevalence in IDUs in all EU countries except Luxembourg were published between 1990 and 2000[26, 27]. The review by Mathei et al. identified 66 HCV seroprevalence studies in IDUs published between 1989 and 2000[26, 27]. As for the general population estimates, Italy was overrepresented in the number of published studies.

The overall prevalence of anti-HCV and/or RNA positivity among IDUs reported in Roy's publication was 71% (21574/30359), much higher than the prevalence of HBsAg among IDUs. The ranges in the anti-HCV prevalence found by Roy and Mathei were very similar: 30% to 98% and 33% to 95%, respectively. Both reviews found that prevalence estimates varied widely within countries and concluded that this was mainly due to lack of representativeness of sampling methods. Often convenience sampling is used, whereby participants are not representative of all current, or past, IDUs. Increasing age, increasing duration of injecting drug use and imprisonment were identified as risk factors. However, neither these factors nor temporal trends could explain the heterogeneity observed in the anti-HCV prevalence rates. Both studies conclude that HCV is highly prevalent among IDUs in Europe.

The prevalence of HBV and HCV among men who have sex with men (MSM)

The estimated HBsAg prevalence was 4% in MSM studied in an sexually transmitted diseases (STD) clinic in Gothenburg, Sweden in 1993–1997[41], and lower than 1% in MSM in Scotland, studied in 1993–2003[42, 43]. The estimated anti-HCV prevalence was 1.3% among MSM in Amsterdam in 2003[44], and 2.9% among MSM in seven cities in Croatia between 2003–2006[45].

3.2 The number of individuals with chronic HBV or HCV infection

The estimated number of persons with chronic HBV and the number of persons with chronic HCV infection based on general population prevalence estimates are presented in Table A10; also the numbers in the main migrant groups are presented for countries where data were available. Figures 6 and 7 present the number of HBsAg- and anti-HCV-positive individuals, respectively, based on general population prevalence estimates. These estimates show that Turkey has the largest number of HBsAg-positive individuals; Italy has the largest number of anti-HCV-positive individuals (Figures 6, 7). Germany has the largest number of infected migrants both for HBsAg and anti-HCV (Figure 8).

* Excluding the relatively high HBsAg prevalence found in Sardinia.

Figure 6. Estimated number of HBsAg-positive individuals by country, based on general population prevalence estimates

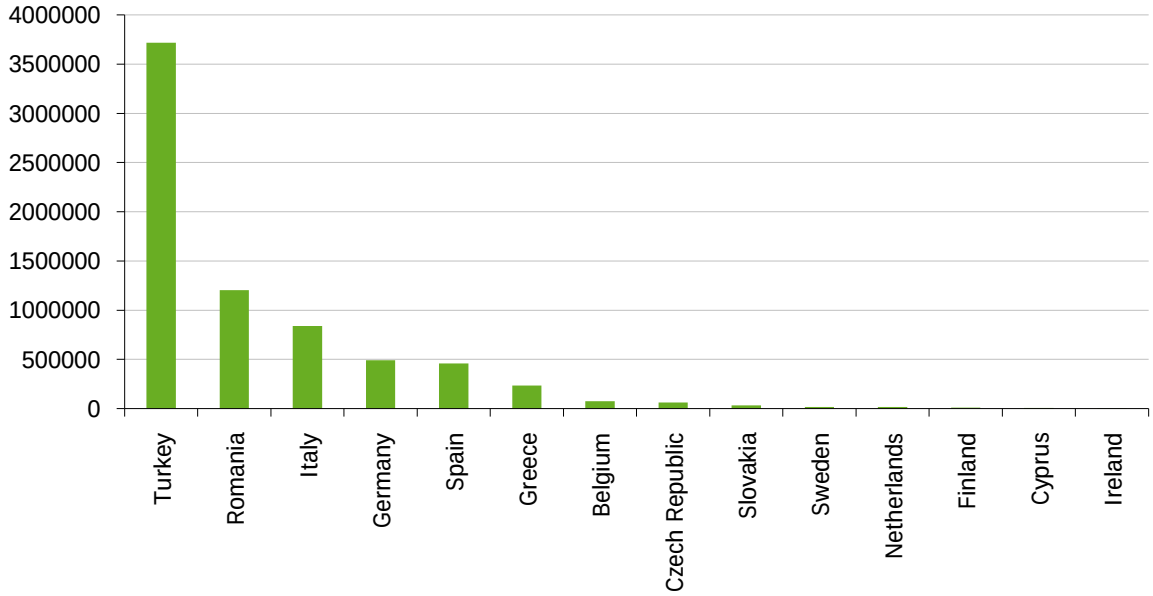


Figure 7. Estimated number of anti-HCV-positive individuals by country, based on general population prevalence estimates

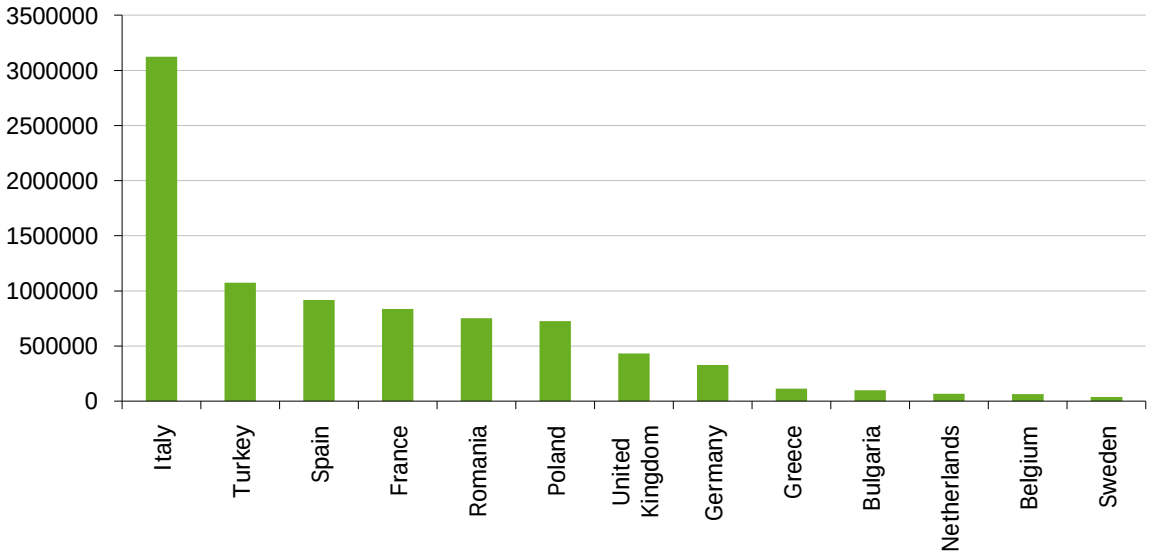
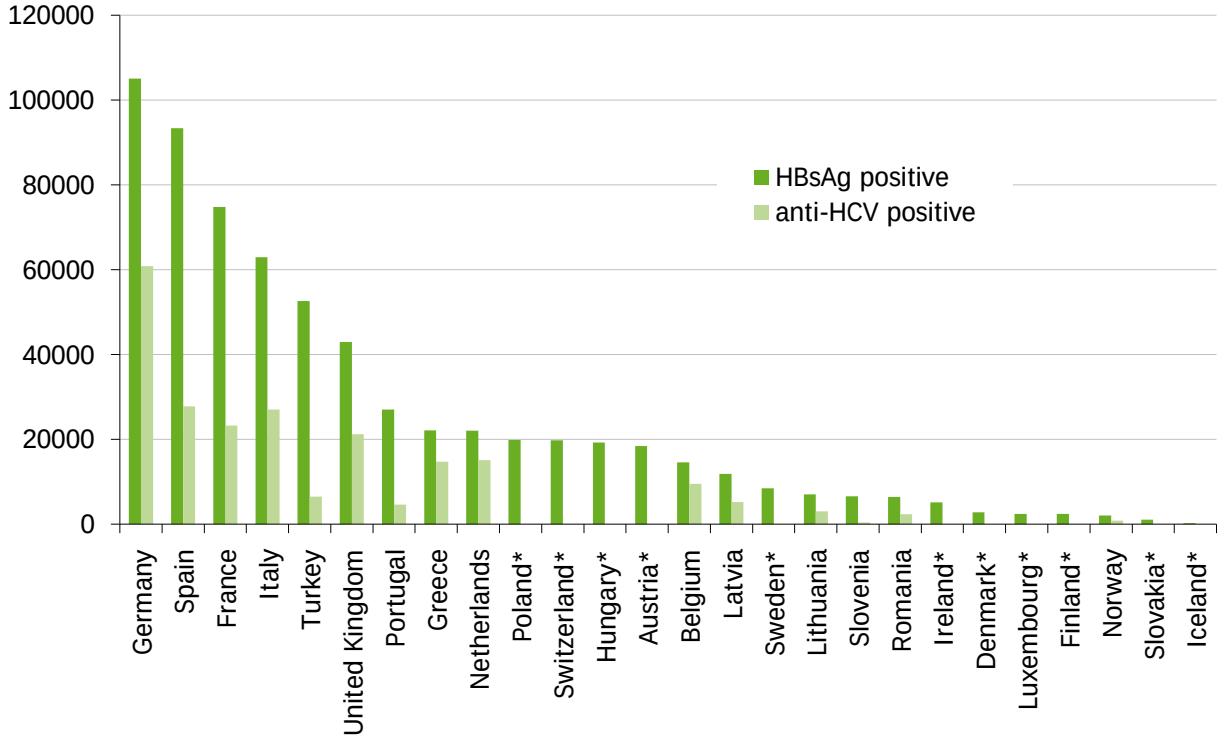


Figure 8. Estimated number of HBsAg- and anti-HCV-positive individuals in the three largest migrants groups, by country



** No data on anti-HCV prevalence*

3.3 The burden of HBV- and HCV-related cirrhosis and hepatocellular carcinoma

Table A11 and Figure 9 show the estimated HCC mortality rate for males and females by country. Annual HCC mortality ranged for women from 0.27 per 100 000 in Sweden to 5.35 per 100 000 in Bulgaria, and for men from 0.68 per 100 000 in Sweden to 8.03 per 100 000 in Bulgaria. HCC mortality for both males and females is generally lower in countries in the north-west of Europe, compared with the south-east. This can be partially attributed to the fact that data for some of the countries in Eastern Europe did not distinguish primary and metastatic liver cancer (see footnote for Figure 9). The main causes of HCC are HBV and HCV infection, alcohol consumption and, to a lesser extent, smoking.

Table A12 and Figure 10 show the estimated cirrhosis mortality rate for males and females by country. Annual cirrhosis mortality ranged for women from 1.02 per 100 000 in Malta to 20.91 per 100 000 in Hungary, and for men from 4.4 per 100 000 in the Netherlands to 68.27 per 100 000 in Hungary. Both for males and females, the mortality due to cirrhosis is relatively high in some Eastern European countries. However, similar to HCC, some of the variation may be due to validity of cirrhosis certification.

Figure 9a. Hepatocellular carcinoma related mortality per 100 000 population: men*

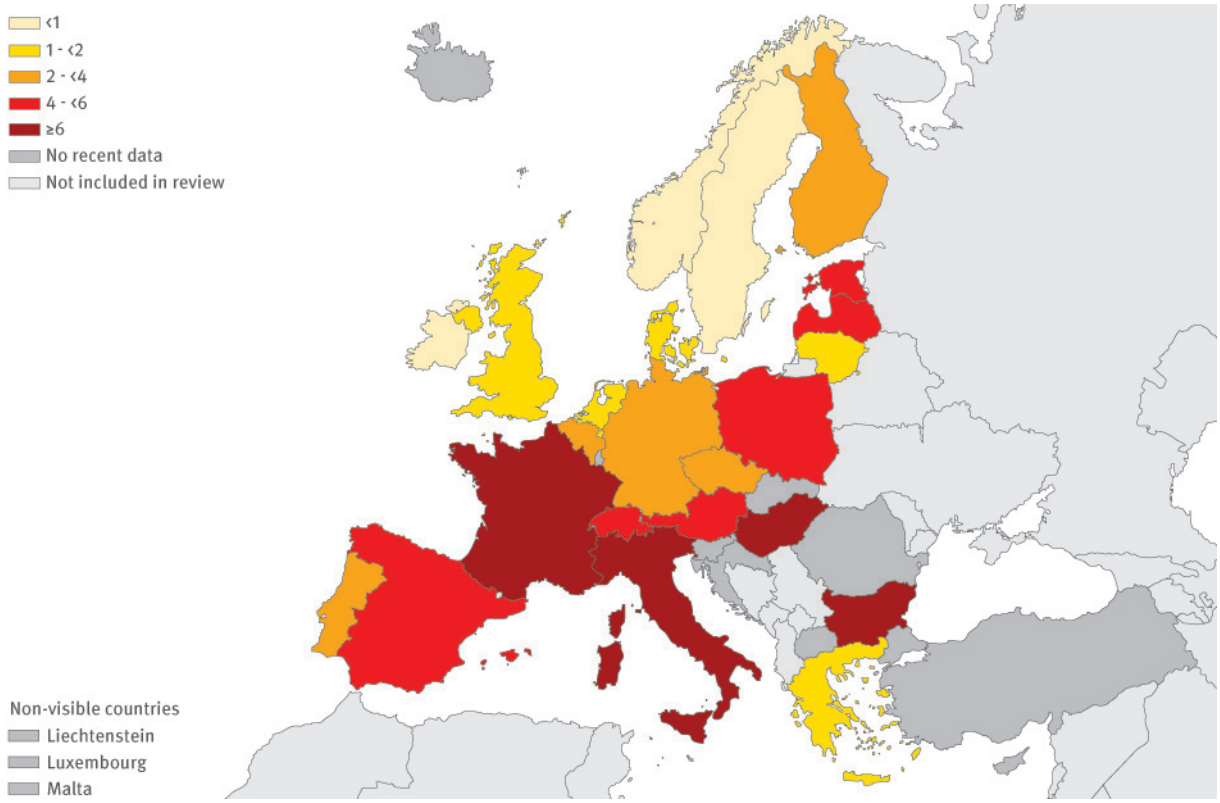
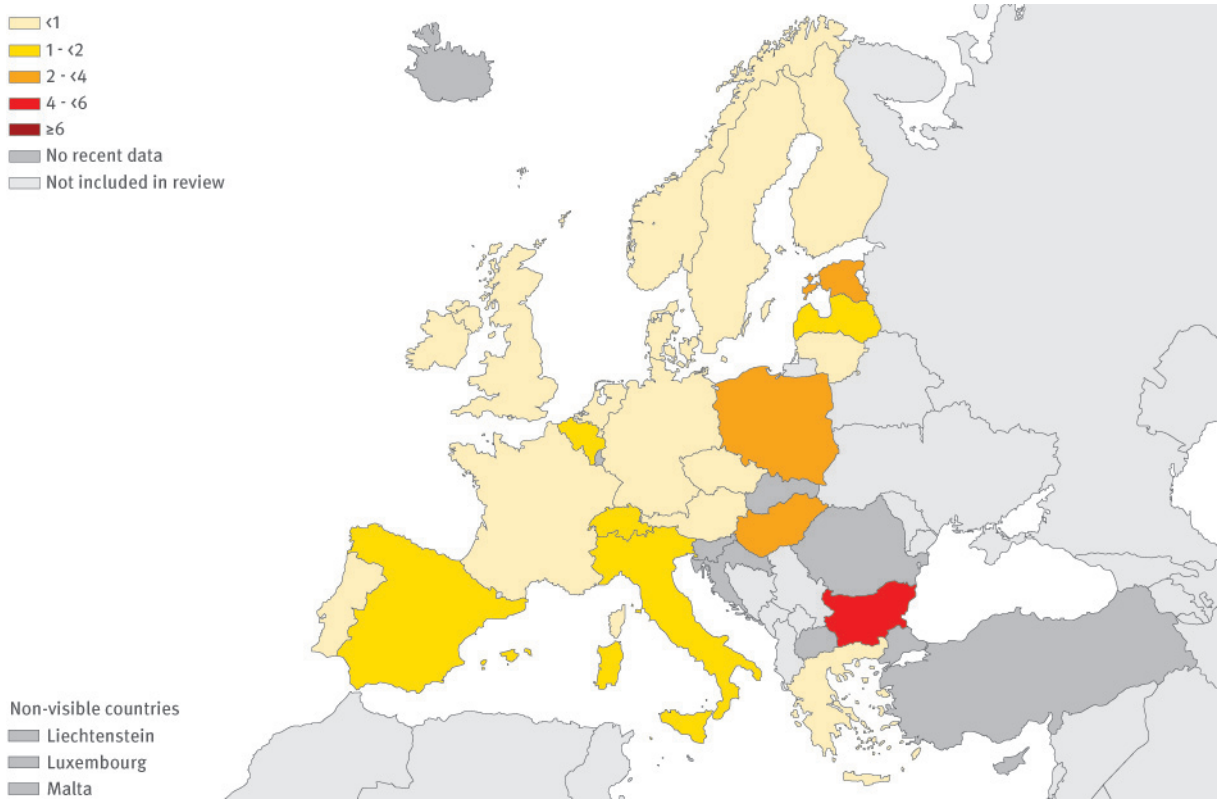


Figure 9b. Hepatocellular carcinoma related mortality per 100 000 population: women*



** Note: Data for Belgium, Bulgaria, Estonia, Hungary, Latvia, Poland, and Switzerland did not distinguish between HCC and other liver cancers.*

Figure 10a. Cirrhosis-related mortality per 100 000 population: men

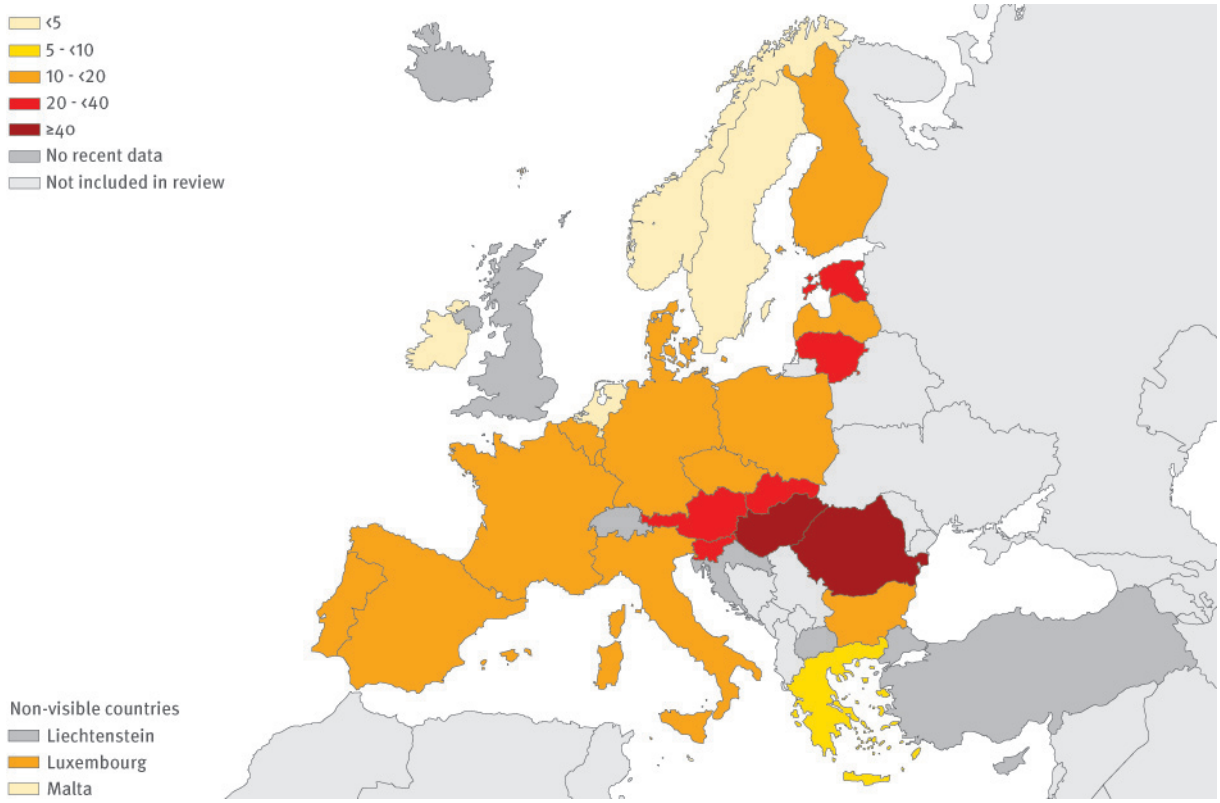


Figure 10b. Cirrhosis-related mortality per 100 000 population: women

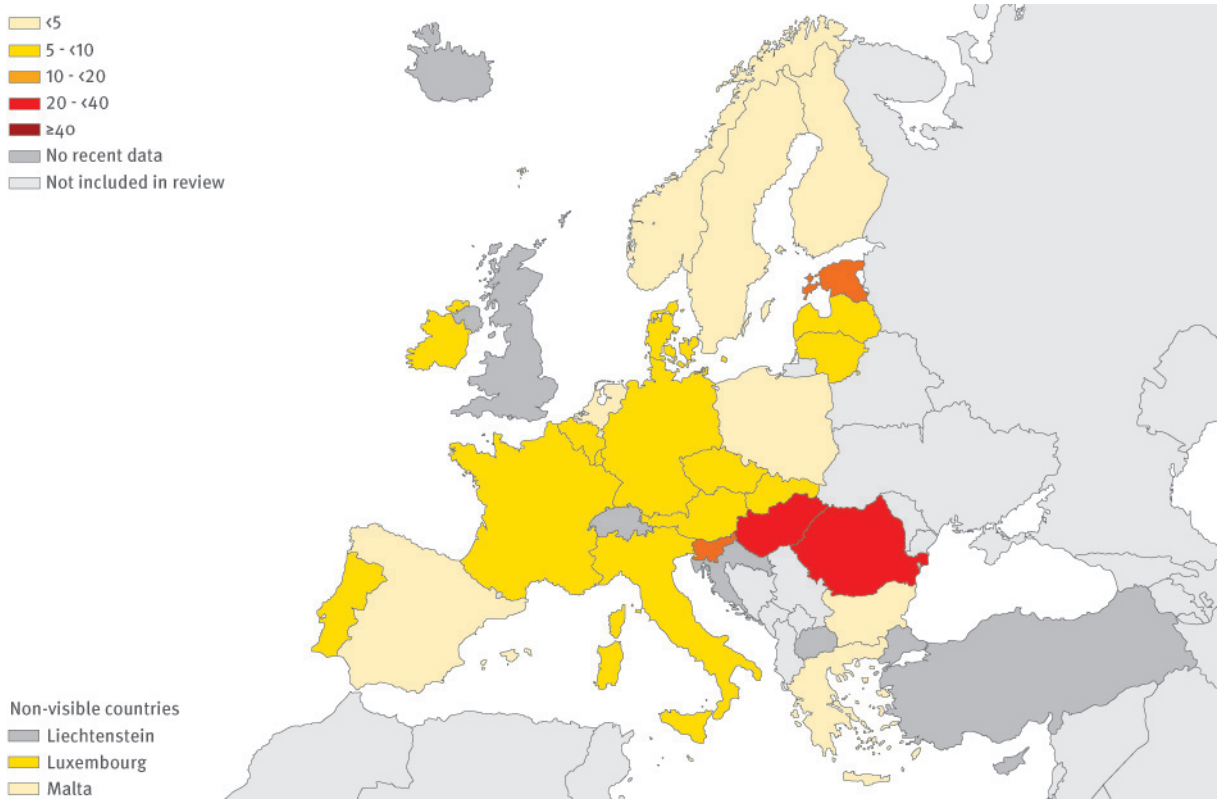


Table 2 and Figure 11 list the estimated HBsAg- and anti-HCV prevalence in cases of HCC by country. Data was available for only a quarter of countries included in this review (8 of 34, 24%). There is large variation in HBV and HCV prevalence among HCC patients in Europe. For HBV, Turkey and Greece have the highest prevalence, while Italy ranks first in HCV with an estimated 64% of HCC patients positive for HCV. This pattern is consistent with the one observed for HBV and HCV prevalence in the general population.

Table 3 combines the data on the prevalence of HBV and HCV among patients with HCC with the mortality estimates for this condition (Table A11) in order to estimate the HCV- and HBV-related HCC mortality rate for HCC in men and women by country (Table 3 and Figure 12). The same is done for cirrhosis in Tables 4 and 5 (Table A12). Among the countries where information was available, Italy has the highest HCV- and HBV-related HCC mortality rate for both men and women. For HBV/HCV-related cirrhosis mortality, available data was even more limited, covering only two countries (Italy and Spain, Table 5).

Table 2. Estimated anti-HCV- and HBsAg-prevalence in HCC patients by country

Country	Anti-HCV prevalence			HBsAg prevalence		
	%	N	References	%	N	References
Italy	64%	1268	52-57	18%	1,701	58, 52-56, 59
Spain	52%	576	60, 61	17%	576	60, 61
Austria	38%	245	62	11%	245	62
Belgium	35%	54	63, 64	23%	500	63, 64
Turkey	25%	463	65-67	54%	463	65-67
Germany	21%	386	68, 69	25%	471	68-70
Sweden	20%	95	71	4%	95	71
Greece	18%	639	72, 73	57%	639	72, 73

Figure 11. Estimated HBsAg and anti-HCV prevalence in HCC patients by country

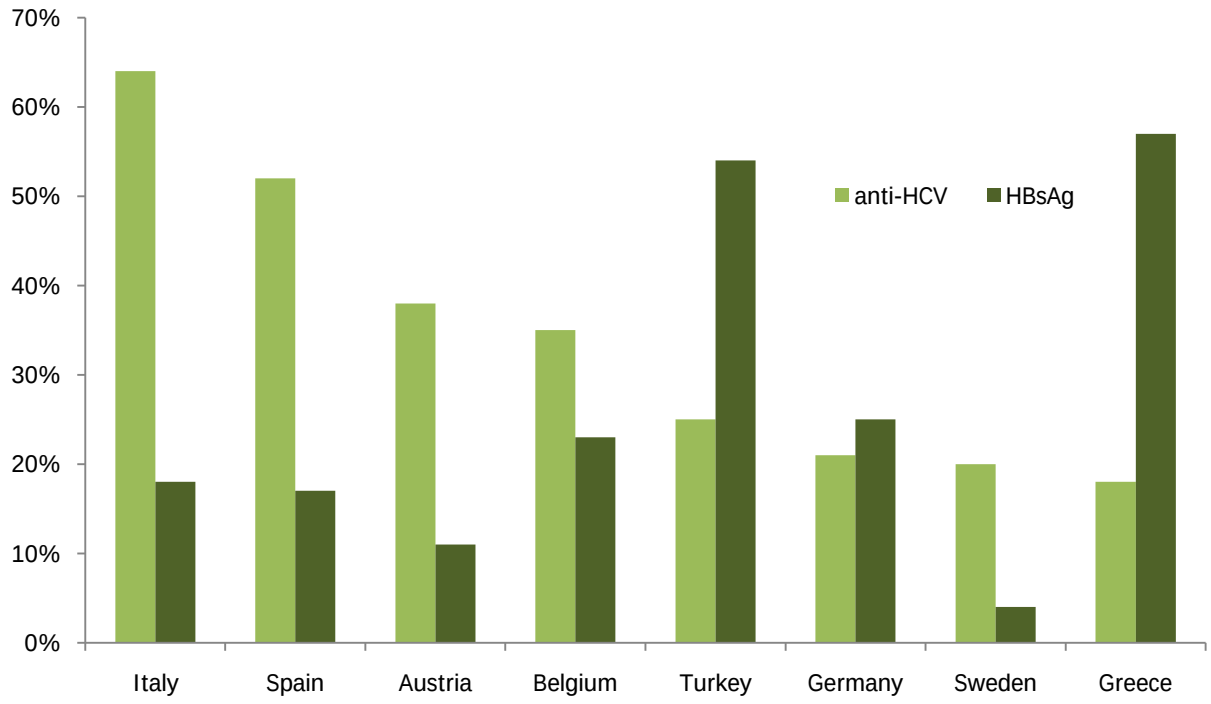


Table 3. Estimated HCV- and HBV-related HCC mortality rate by country

Country	HCV-related HCC mortality (rate per 100 000 per year)		HBV-related HCC mortality (rate per 100 000 per year)	
	Men	Women	Men	Women
Italy	4.28	1.22	1.20	0.34
Spain	2.54	0.79	0.86	0.27
Austria	1.59	0.35	0.45	0.10
Belgium	0.83	0.60	0.54	0.39
Germany	0.59	0.15	0.71	0.19
Greece	0.27	0.05	0.88	0.17
Sweden	0.14	0.05	0.03	0.01

Figure 12. Estimated HCV- and HBV-related HCC mortality rate per 100 000 men and women by country

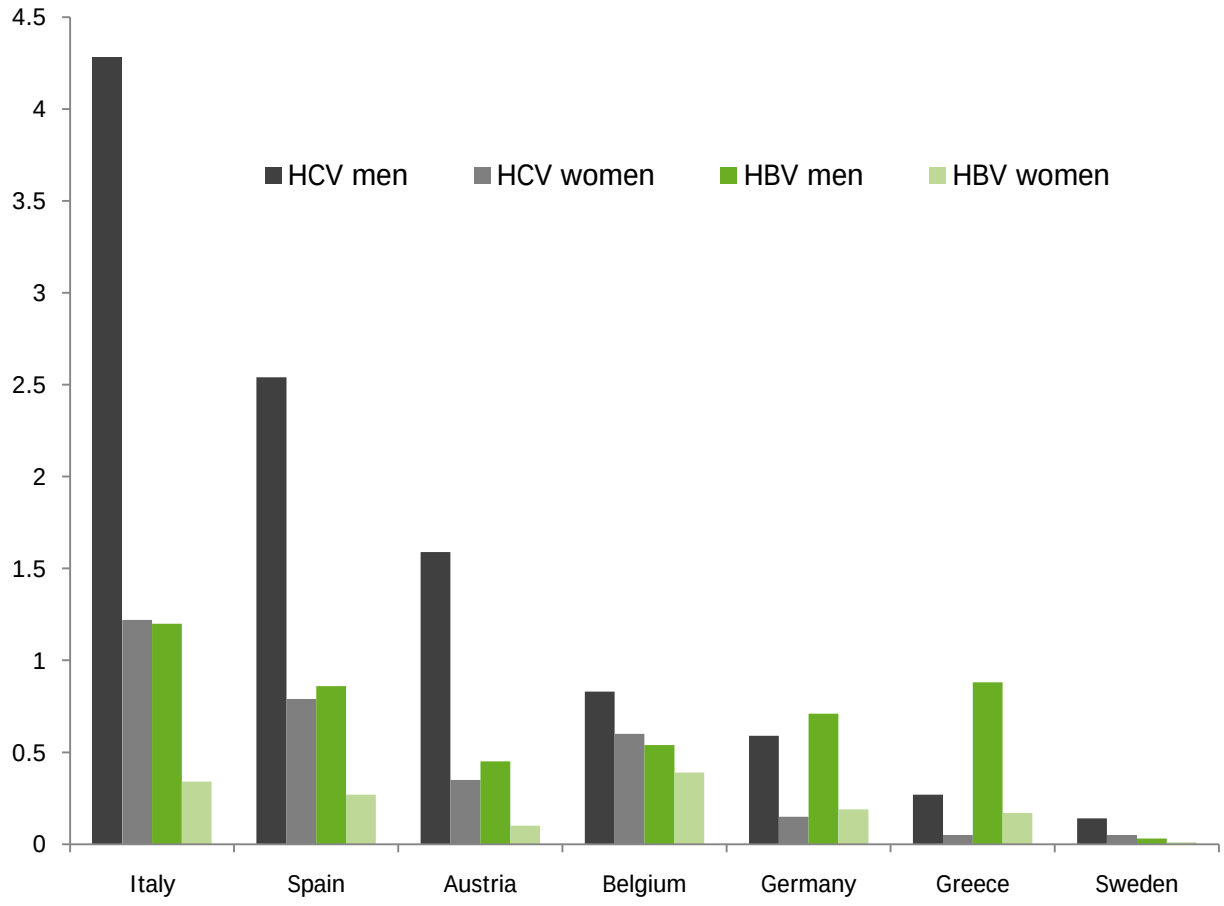


Table 4. Estimated HBsAg- and anti-HCV prevalence in cirrhosis patients by country

Country	Anti-HCV prevalence			HBsAg prevalence		
	%	N	References	%	N	References
Italy	61%	4125	56, 74	11%	4125	56, 74
Spain	32%	451	75	10%	451	75
Turkey	11%	505	66, 76	64%	731	66, 76

Table 5. Estimated HCV- and HBV-related cirrhosis mortality rate by country

Country	HCV-related cirrhosis mortality (rate per 100 000 per year)		HBV-related cirrhosis mortality (rate per 100 000 per year)	
	Men	Women	Men	Women
Italy	8.0	3.7	1.4	0.7
Spain	3.7	1.1	1.1	0.3

3.4 Screening for HBV and HCV infection

Screening recommendations

The information on national screening policies for HBV and HCV available from publications included in this study is limited. However, some policies were published and are generally similar in content, although some details differ significantly.

General population. In France, two consensus conferences in 1997 and 1999 issued recommendations that urged healthcare professionals to systematically offer hepatitis C screening to the following patient groups: haemodialysis patients, patients with history of blood transfusion before 1991, drug users who either inject or sniff drugs, persons with history of incarceration, and healthcare professionals after occupational exposure to potentially infected blood, persons having unprotected sex with multiple partners, and persons living with an HCV-positive individual[82,86]. In Italy, a consensus conference in 2005 concluded that the following risk groups should be targeted for HCV screening: haemodialysis patients, subjects who received blood coagulation factors before 1987, subjects who received blood transfusions or an organ transplant before 1992, persons living with HCV-infected individuals, subjects with multiple sexual partners who have or have had a sexually transmitted disease[87].

Pregnant women. A recent conference showed that among a sample of seven countries, all had antenatal screening for HBsAg (G. Loeber, Dutch Conference on pre- and neonatal screening, April 2009). Only Ireland and Spain were reported to also screen for HCV. In the published literature, information was found on antenatal screening policies for four countries. Denmark introduced a policy of universal screening of pregnant women for HBsAg in 2005[77]. In the United Kingdom, the Department of Health issued directives in 1987 and 1998 that all pregnant women should be offered HBsAg and HIV testing as an integral part of their antenatal care, by April 2000 and January 2001, respectively[78, 79]. One review summarised the reasons for not screening for HCV during pregnancy in the United Kingdom[80]. Italy started antenatal screening for HBsAg in 1984[81]. In France, pregnant women are not screened for HCV[82].

Blood donors. No publications were identified on national screening policies regarding screening for HBV or HCV in blood donors. However, information was obtained from a report for the Council of Europe (September 2009)[28]. This report states that in all 33 reporting member states, each donation is tested for HBsAg and anti-HCV. Anti-HBc testing is performed on all donations in 4 out of 33 (12%) reporting member states, and another five perform anti-HBc testing for donations from first-time donors. EU Member States must follow the directives on blood safety given by the European Parliament and Council[1]

Migrants. No publications were identified on national screening policies regarding screening for HBV or HCV in migrants.

[1] Directive 2002/98/EC of the European Parliament and of the Council of 27 January 2003 setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components and amending Directive 2001/83/EC.

Drug users. In 1999, the United Kingdom recommended to increase the provision of testing for HBV among drug users[83]. Screening for HCV in IDUs has been supported by a range of professional consensus statements[84]. In the Netherlands, IDUs are targeted in an HBV screening and vaccination programme[85].

MSM. In the Netherlands, MSM (and other high-risk groups) are targeted for HBV screening as part of a vaccination programme for risk groups[85].

Effectiveness of screening

Several studies reported process indicators of screening programmes such as coverage and the proportion of susceptible people which were vaccinated. These studies are listed below by target group of the screening. Similarly to information on screening policies, the numbers of studies captured was relatively limited.

IDUs. The proportion of IDUs screened for HCV varied between 5% in the United Kingdom and 88% in Ireland[88,89]. One study from Hungary reported in 2004 that testing for HIV, HBV or HCV was not routinely offered at drug treatment centres. Where testing was provided, it was often unregulated and inconsistent. Furthermore, the same study suggested that results were not always communicated to the infected individual[90]. The proportion of susceptible IDUs that were completely vaccinated ranged from 56% in Ireland to 58% in the Netherlands (Table 6).

Table 6. Overview of effectiveness studies of IDU screening for HBV and/or HCV

Country	Year of publication	Condition	Indicator	Result	Reference
Hungary	2004	HBV and HCV	Proportion of drug treatment centres offering screening	See text	90
Ireland	2005	HCV	Proportion screened	88%	89
		HBV	Proportion screened	68%	
		HBV	Proportion of susceptibles vaccinated	56%	
The Netherlands	2002	HBV	Proportion screened	19%	85
			Proportion of susceptibles vaccinated	58%	
United Kingdom	2000	HBV	Proportion of drug agencies offering testing	27%	83
		HCV	Proportion of drug agencies offering testing	24%	
United Kingdom	2008	HCV	Proportion screened	5%	88

MSM. One study described the results of HBV screening of MSM in a genitourinary medicine (GUM) clinic in London, United Kingdom[91]. In this setting, 60% of MSM were screened for HBV and 47% of susceptibles completed vaccination. In an Amsterdam study, 64% of MSM were screened for HBV, and 74% of the susceptibles were vaccinated[85].

Contacts of HBsAg-positive individuals. A total of three studies on the screening of contacts of HBsAg positive individuals were published in Wales (United Kingdom), Naples (Italy) and Amsterdam (The Netherlands) [92,93,94]. The Dutch study concerned contacts of HBsAg-positive women identified during antenatal screening. This study – the only one on the proportion of screened contacts – reported that 90% of all contacts were screened (1000 of 1219). Of susceptible household contacts, 25%, 27% and 94% were vaccinated in Naples, Wales and the Netherlands, respectively.

Pregnant women. Ten studies were published in 1990 on the screening of pregnant women for HBsAg (Table 7). The proportion of pregnant women screened for HBsAg ranged from 71% in a study from Italy to 100% in 2005. The proportion of vaccinated infants of HBV-infected mothers ranged from 85% in Italy to 100% (also in Italy; Table 7).

High-risk individuals in the general population. One study was published on the uptake of the targeted HCV screening in the general population. This concerned a study from a region in France (Poitou-Charentes), where 3.7% of the population was tested in 2003[102].

Table 7. Effectiveness studies of antenatal screening for HBsAg

Country	Year of publication	Proportion screened (%)	Proportion of infants completely vaccinated (%)	Reference
Denmark	2006	97%	Not reported	77
Greece	2006	91.3%	Not reported	95
Italy	1990	71%	85%	81
Italy	1998	91.6%	100%	96
Italy	2003	91.8%	95%	97
Italy	2005	100%	Not reported	98
Switzerland	2004	99.3%	95%	99
The Netherlands	2001	97%	99.7%	100
United Kingdom	2002	93%	Not reported	78
United Kingdom	2004	99.9%	93%	101

Economic analyses of screening for HBV and HCV

A recent study details the cost-effectiveness of screening of migrants for chronic hepatitis B[103]. The study estimates that in the Netherlands, where no active screening is performed, only 4% of the eligible migrant population receives treatment. If case detection was improved through a screening programme targeted at migrants, approximately 15% of the population with active chronic hepatitis B would receive treatment, resulting in a 10% reduction in mortality. The estimated incremental cost-effectiveness ratio (ICER) of screening is around EUR 9 000 per quality-adjusted life year (QALY) gained, well below the value of EUR 20 000 per QALY gained that is commonly accepted as a threshold for considering the introduction of screening in the Netherlands.

Seven economic analyses on screening of IDUs for HCV infection were identified[104, 105, 106, 107, 108, 84, 82]. However, two publications reported on the same economic analysis[84, 108]. Four of the six analyses were carried out in the UK and two in France (Table 8). All studies on screening IDUs, mostly conducted in the context of general practitioner practices, concluded that screening was likely to be cost-effective in terms of costs per QALY gained.

Table 8. Economic analyses of screening IDUs in general practice

Country	ICER (year)	Conclusion	Comment	Reference
UK		Cost-effective	Uncertainties regarding for example the uptake of screening remain.	104
UK	GBP 28 120/QALY (2001)	Cost-effective		108, 84
UK	GBP 20 084/ LY (2004) GBP 16 514/QALY (2004)	Cost-effective	Case finding is most cost-effective in people with longstanding infection	105
UK	GBP 10 177/QALY (1997)	Cost-effective		107
France	Not reported	Screening IDUs and transfusion recipients was the most cost-effective		106
France	ICER compared to baseline is EUR 3 825 (1998)	Cost-effective		82

HCV screening of GUM clinic attendees. The cost-effectiveness of universal HCV screening of GUM-clinic attendees was assessed in the United Kingdom[108]. This policy would probably not be cost effective, with a cost-effectiveness ratio of GBP 84 570 per QALY (estimated with considerable uncertainty).

HCV screening of prisoners. One economic analysis of screening and treatment for HCV in prisons was performed in England and Wales[109]. Screening would probably not be cost-effective, with an estimated cost per QALY of GBP 54 852. The authors concluded that the intervention would become more cost-effective if case-finding costs were reduced and treatment acceptance and adherence enhanced.

HBV screening of pregnant women. Three economic analyses were published on the screening of pregnant women for HBV[110, 111, 112]. Even though all studies were carried out in very low prevalence settings (United Kingdom and Belgium), they concluded that screening all women during pregnancy to prevent perinatal

transmission is highly cost-effective. The ICERs were GBP 2 437 and GBP 2 500 per life year gained (LYG) in the UK, and BEF 583 581 per LYG in Belgium[112,110, 111].

One study compared the cost-effectiveness of HBV NAT testing of blood donors to assay testing[113]. The authors concluded that HBV NAT testing of blood donors was not cost-effective when compared to testing with assays.

4 Discussion and conclusion

This literature review aims to provide facts and evidence that can be used to inform policy making on primary and secondary prevention of HBV and HCV. It attempts to achieve this goal by assessing published information on the burden of HBV- and HCV-related infection and disease in EU/EEA countries, and by summarising existing HBV and HCV screening policies and their effectiveness. This review is not intended to draw a complete picture of the situation in Europe, nor is it intended to form the single basis for decisions on prevention efforts. Rather, it is part of a series of ECDC-produced reports that each provide concise information on a specific area, for the benefit of decision-makers at both the EU and national levels.

The conclusions presented in the report should be seen in the context of the collected data.

4.1 The prevalence of HBV and HCV in the general population

Based on an analysis of the data extracted from the literature we reviewed for this study, the prevalence of HBV infection in the general population varies widely between EU/EFTA/EU candidate countries, ranging from 0.1% in Ireland and the Netherlands to more than 7% in the eastern part of Turkey. Countries in the central or southern part of the EU and its associated and candidate countries (e.g. Turkey, Romania, Bulgaria and Greece) have a higher prevalence than countries in the northern or western part of the EU. Unfortunately, data on the HBV-related burden of disease and mortality was not available for the countries with the highest prevalence.

Based on prevalence surveys, the prevalence of HBV in the general population is likely to be considerably underestimated in low-prevalence countries, as high-risk groups are often not adequately represented in the studies. As an illustration of this, data from the Netherlands and Ireland show that the estimated number of infected migrants is higher than the estimated total number of infected individuals in the general population, probably because migrants are underrepresented in the final population samples for HBV prevalence surveys. Although the prevalence in blood donors can be used as a proxy for the prevalence in the general population, blood donors are not a representative sample of the general population, due to their pre-selection. The prevalence in first-time blood donors can generally be regarded as the lower limit of the prevalence in the general population, except for countries where donors are remunerated. This is consistent with the finding that the prevalence estimates in first-time blood donors for both HBV and HCV were lower than those for the general population (with the exception of Cyprus for HBV). By contrast, in nearly all countries where data was available, pregnant women had a considerably higher prevalence when compared with the general population. The only exception is Spain, where the HBV prevalence estimate for pregnant women (only available for Catalonia) showed a lower prevalence than estimated for the general population (0.1 and 1.0%, respectively). Most likely this reflects the impact of the adolescent HBV vaccination programme implemented in this region since 1990.

The prevalence of HCV in the general population varies widely across countries, with ranges from 0.4% in Sweden, Germany and the Netherlands to over 20% in one region of Italy. In general, countries in the southern part have a higher HCV prevalence compared to countries in the north or west of the EU. Italy in particular has a high general population prevalence of HCV, much higher than the country's estimated HBV prevalence. Epidemiologic and phylogenetic assessments suggest this is caused by a period of increased iatrogenic transmission that took place around the 1950s[39, 40, 114].

Five groups of countries can be distinguished (Table 9) when comparing the prevalence estimates for HBV and HCV in the general population (or in pregnant women if no general population estimate was available). Table 9 assigns countries with available data in one of three prevalence groups – low (≤1%), medium (>1% and ≤2%) and high (>2%)[2].

- Romania has a high prevalence of both HBV and HCV.
- Greece and Turkey have a high HBV prevalence and a medium HCV prevalence.
- Italy has a high HCV prevalence and a medium HBV prevalence.

[2] Arbitrary classification only used for the purpose of illustration.

- France and Spain have a medium HCV prevalence and a low HBV prevalence.
- Seven countries (Belgium, Germany, Netherlands, Slovakia, Sweden, Switzerland** and the United Kingdom) have a low prevalence for both HBV and HCV.

The remaining 21 countries have insufficient data for HBV (Bulgaria, Poland), HCV (Cyprus, Czech Republic, Denmark, Finland, Ireland) or both HBV and HCV (Austria, Croatia, Estonia, the former Yugoslav Republic of Macedonia, Hungary, Iceland, Latvia, Liechtenstein, Lithuania, Luxembourg, Malta, Norway, Portugal, Slovenia).

Among countries with available data, Italy has by far the largest number of HCV infected individuals; Turkey has the largest number of HBV-infected individuals.

Table 9. Classification of countries according to prevalence estimates and availability of data

HBsAg / HCV Ab	Low (≤1%)	Medium (>1% and ≤2%)	High (>2%)	Insufficient data
Low (≤1%)	BE, CH, DE, NL, SK, SE, UK			
(>1% and ≤2%)	FR, ES		GR, TR	BU, PL
High (>2%)		IT	RO	
Insufficient data	CY, CZ, DK, FI, IE			AT, CR, EE, FYROM, HU, IS, LV, LI, LT, LU, MT, NO, PT, SL

4.2 The prevalence of HBV and HCV in high-risk groups

The number of HBV and/or HCV prevalence studies on migrants is limited. Available data show that in nearly all countries and ethnic groups the estimated prevalence of both HBV and HCV is higher among migrants compared to the general population. The only exception is HCV in Italy, where the estimated general population prevalence is higher than that estimated in migrant groups. The estimates of the number of migrants infected with HBV and HCV show that some countries (including Germany, Spain, France, Italy, and the United Kingdom) have large numbers of migrants with HBV and/or HCV infection.

A large number of studies is available on estimated HCV prevalence in IDUs. Even though the representativeness of studied populations is variable, most studies suggest that HCV infection is highly prevalent among IDUs in Europe. In the literature reviewed for this study, the prevalence of HBV among IDUs was in most cases reported to be much lower than that of HCV.

4.3 Screening policies and effectiveness

There is surprisingly little data on HBV and/or HCV screening policies for high-risk groups or the general population. Where recommendations were found, e.g. on general population screening for HCV in France and Italy, these were based on consensus conferences. It is likely that more written policies or guidance documents exist in national languages in the format of reports and other national documentation. However, a review of such literature was outside the scope and capacity of this study.

Antenatal screening for HBV with subsequent vaccination of infants born to HBsAg-positive mothers is an important intervention to control HBV, as perinatal transmission of HBV is efficient and usually leads to chronic infection in the infant. This is supported by an economic analysis which shows that universal antenatal HBV screening is highly cost-effective. Nevertheless, data or formal assessments on the effectiveness of antenatal HBV screening were lacking for most countries. It is likely that evaluations of programmes for prevention of perinatal HBV infection are generally not published in the scientific literature. For those countries where data were available, screening appears to be well implemented, with participation rates of 90% and more in all countries. Reported vaccination coverage of infants born to HBsAg-positive mothers was more than 95%. (ECDC comment: more information on this can be found in a series of reports produced by the ECDC-commissioned VENICE project.) No study was available on the follow-up, e.g. whether HBsAg-positive mothers were referred to healthcare. As new treatment options are available for HBV and HCV, access and attachment to treatment is an important indicator for the evaluation of screening programmes.

** The HBV general population prevalence for Switzerland was considered low, based on the prevalence of 1.2% in pregnant women and the prevalence of 0.14% in blood donors.

The review shows that in many countries in Europe migrants have a higher prevalence of HBV and HCV than the rest of the general population. This implies that they will also be disproportionally affected by the burden of disease due to HBV and HCV. Screening with subsequent access to treatment could prevent some of the disease burden[115]. However, this review shows that the evidence base for this cannot be completely evaluated as almost no studies exist on the effectiveness or cost-effectiveness of migrant screening for HBV and/or HCV in Europe. Evidence from the US suggests that screening migrants for chronic HBV is cost-effective[20]. The first study in Europe, conducted in the Netherlands, suggests that screening and early treatment of migrants for chronic HBV is cost-effective[103].

Limited data were available on the effectiveness of screening for MSM. The only two available studies were carried out during an HBV vaccination campaign for MSM. Considering the recently reported increase in HCV among MSM, more information on the effectiveness of screening is needed[44].

The evidence base for the screening of IDUs is somewhat better developed. Economic analyses of drug user screening for HCV in France and the United Kingdom suggest that this is a cost-effective intervention. Despite this, limited data suggest that the implementation of this policy is highly variable, with uptake ranging from 88% in Ireland to 5% in the UK. Low uptake can be explained by the fact that in several countries HCV screening is not routinely offered in drug treatment centres. No economic analyses of screening of IDUs for HBV were available in the publications reviewed for this study.

The information captured in this review shows that screening of blood donors for signs of HBV- and HCV-infection is common practice in all countries of the region.

4.4 Limitations

While a serious attempt was made to design the study in order to capture the most relevant information, it still has several limitations. To better reflect recent developments, this review was limited to studies published since 2000, which potentially excludes relevant data published earlier. This might partly explain the limited number of publications identified on antenatal screening policies. As antenatal screening programmes were uniformly implemented in the countries of the region during the last decades of the 20th century, studies reporting on this topic were probably published before 2000.

Also, a search of literature databases containing mainly scientific studies is probably not adequate when it comes to identify existing screening policies. To compensate for these shortcomings, this aspect has been included in various surveys in Member States on surveillance and prevention with respect to hepatitis B and C, conducted by ECDC or through the EUVACNET and VENICE networks.

The different ranges covered by the various studies, in combination with the differences in mean age of study participants, make it difficult to compare the prevalence estimates across countries. Although studies that covered only children were excluded, the difference in age of the participants still limits the validity of comparisons between prevalence estimates. For many prevalence estimates, the mean age of the population was not included, which made it impossible to calculate prevalence by birth cohort.

Trends over time in the burden of HBV and/or HCV infection were not covered, nor was the impact of vaccination.

Another major limitation of the study was its sole concentration on publications issued in English. This leads to a bias in favour of inclusion of studies from countries where English is the native language or where there is a strong tradition of publishing in English. It is almost inevitable that this results in major omissions of both data and bodies of evidence from several large countries/language groups.

4.5 Conclusions

Our review demonstrated the diversity in the burden of infection and disease due to HBV and HCV, but also in the availability of data across 34 countries in Europe. Data on general population prevalence of these infections were lacking for most of the countries studied. Of those countries with information based on general population studies, some have evidence of low general population prevalence of both HBV and HCV, but with a high burden in high-risk groups, the most numerous of which may be migrants. Other countries have mixed patterns of HBV and HCV endemicity. Especially for HCV infection, IDUs are still a significant group at risk, with high prevalence rates reported from most countries. Even though the information available is far from complete, neither in detail nor in coverage, some general patterns and conclusions can be drawn. The most significant finding is that there is evidence for significant disease burden caused by both HBV and HCV infection in many, if not most, countries in the EU and its neighbourhood.

It is likely that considerable health gain can be achieved by secondary prevention of HBV and HCV, including early detection through screening and treatment of identified chronically infected patients when indicated. We found indeed evidence that HCV screening of IDUs is cost-effective. The evidence-base for HBV screening of migrants is

insufficiently studied, but the one study published on this topic suggests that this intervention is cost-effective. Formally collected evidence for HBV and/or HCV screening of other high-risk groups or the general population is still lacking, as such studies or evaluations have not been performed. As part of a comprehensive prevention and control policy – including other effective measures and direct links to guaranteed access to effective treatment – wider screening could provide opportunities for significant future savings in both healthcare costs and productivity gains.

Better surveillance and monitoring activities, further research, and realistic studies on costs are needed to provide the information basis for rational policy making on future secondary prevention of HBV and HCV infection in the EU and its neighbourhood.

Annex 1. Tables

Table A1. Prevalence of HBsAg in the general population

Reference	Country	Period	Area	Region	Sampling	N	%	(95% CI)	Remarks
[31]	Belgium	2002-2003	nationwide		residual	1 496	0.7		Children only
[116]*	Belgium	2003	regional	Flanders	random	1 834	0.7	(0.5-0.8)	Oral fluid
[33]*	Cyprus	2006	regional	North	random	585	0.9	(0.2-2.0)	Age range 1-30 years
[117]*	Czech Republic	2001	nationwide		random	2 658	0.6		Standardised prevalence
[118]	Denmark	1994-1995	nationwide		convenience	2 428	0.1		Children only
[31]*	Finland	1997-1998	nationwide		residual	3 083	0.2		
[119]*	Germany	1993-1996	nationwide		random	5 305	0.6	(0.4-0.8)	
[120]	Germany	1997-2001	regional	North East	random	4 310	0.4		
[121]*	Germany	1998	nationwide		random	6 748	0.6	(0.4-0.8)	
[122]*	Greece	1997-1998	regional	Peloponnesus	random	1 500	2.1	(1.5-3.0)	
[123]	Greece	2002	regional	Athens	convenience	98	0.0		Children only
[124]	Greece	2003-2004	nationwide		random	1 286	0.6	(0.3-1.3)	Children only
[31]*	Ireland	2003	nationwide		residual	2 535	0.1		
[31]*	Italy	1996	nationwide		residual	3 522	0.6		
[38]*	Italy	2002	regional	North	convenience	956	1.0		
[125]*	Italy	1997	regional	Central	random	250	1.2		
[126]*	Italy		regional	South	random	488	0.2		
[127]*	Italy	2002-2003	regional	South	random	1 645	1.8	(0.4-1.2)	
[128]	Italy	2003-2006	regional	South	random	4 496	2.5		Standardised prevalence
[129]*	Italy	1994-1994	regional	Sardinia	convenience	3 324	4.3		
[130]*	Italy	1999-2000	regional	Sicily	random	721	0.7		
[31]*	Netherlands	1995-1996	nationwide		random	6 750	0.1		
[131]	Netherlands	2004	regional	Amsterdam	random	1 364	0.4	(0.1-0.7)	Standardised prevalence
[31]*	Romania	2002	nationwide		residual	1 259	5.6		
[31]*	Slovakia	2002	nationwide		random	3 569	0.6		
[132]*	Spain	1996	regional	Catalonia	random	2 142	1.2	(0.7-1.7)	Standardised prevalence
[36]*	Spain	2002	regional	Catalonia	random	2 620	0.7	(0.4-1.0)	
[133]*	Sweden	1991-1994	regional	Malmö	random	5 533	0.2		
[134]	Turkey	1998	nationwide		random	2 683	5.4		Age range 0-30 years
[135]*	Turkey	2006-2007	regional	West	random	2 852	2.5		
[136]	Turkey	1998	regional	West	random	717	1.7		Children only
[137]*	Turkey	2002-2004	regional	Central	convenience	1 320	6.6		
[138]*	Turkey	1996	regional	Central	convenience	571	6.7		
[139]*	Turkey		regional	Central	random	1 095	5.5		
[140]*	Turkey	1997-1999	regional	East	convenience	400	9.0		32 year olds
[141]	Turkey		regional	East	random	802	2.7		Children only
[142]	Turkey		regional	East	random	1 091	1.8		Children only
[143]*	Turkey	2003	regional	East	random	2 888	7.0		

** Included in general population prevalence estimate presented in Figure 3.*

Table A2. Prevalence of anti-HCV in the general population

Refer-ence	Country	Period	Area	Region	Sampling	N	%	(95% CI)	Remarks
[116]*	Belgium	2003	regional	Flanders	random	1 834	0.1	(0.1-0.4)	Oral fluid
[144]*	Belgium	1993-1994	regional	Flanders	random	4 055	0.9	(0.5-1.1)	
[145]*	Bulgaria	1999-2000	regional	South Central	convenience	2 211	1.3	(1.2-1.4)	Standardised prevalence
[117]*	Czech Republic	2001	nationwide		random	2 658	0.2		
[146]*	France	1997	regional	South	convenience	11 804	1.3	(1.1-1.5)	
[121]*	Germany	1998	nationwide		random	6 748	0.4	(0.2-0.5)	
[120]	Germany	1997-2001	regional	North East	random	4 310	0.5		
[123]	Greece	2002	regional	Athens	convenience	216	0.0		Children only
[122]*	Greece	1997-1998	regional	Peloponnesus	random	1 500	0.5	(0.2-1.1)	
[147]*	Greece	1997	regional	Zakinthos (Island)	random	718	1.3		
[148]	Italy	1996-1997	nationwide		residual	3 577	2.7	(2.2-3.2)	
[38]*	Italy	2002	regional	North	convenience	956	2.6		
[40]*	Italy	1994-1995	regional	North	convenience	2 154	3.3	(2.6-4.1)	
[149]*	Italy		regional	North	convenience	4 820	2.4	(2.0-2.8)	
[39]*	Italy		regional	North	random	496	11.5		Elderly >65 years
[150]	Italy	1983-1987	regional	Central	random	3 884	1.8		
[151]*	Italy		regional	Central	convenience	300	16.3	(12.0-20.6)	
[125]*	Italy	1997	regional	Central	random	250	22.4	(20.8-24.1)	
[126]*	Italy		regional	South	random	488	16.2		
[152]*	Italy	2000-2002	regional	South	convenience	2 753	7.9		
[127]*	Italy	2002-2003	regional	South	random	1 645	6.5	(5.3-7.7)	
[128]	Italy	2003-2006	regional	South	random	4 496	6.7		Standardised prevalence
[129]*	Italy	1994-1995	regional	Sardinia	convenience	3 324	3.2		
[130]*	Italy	1999-2000	regional	Sicily	random	721	10.4		
[131]*	Netherlands	2004	regional	Amsterdam	random	1 364	0.6	(0.1-1.1)	Standardised prevalence
[153]*	Netherlands	2006	regional	East	convenience	2 200	0.2		
[154]*	Poland	1999	regional	North	convenience	2 561	1.9		
[155]*	Romania	2006-2008	nationwide		random	8 039	3.5	(3.1-3.9)	
[156]*	Spain	1996	regional	Catalonia	random	2 142	2.5	(1.8-3.2)	Standardised prevalence
[157]*	Spain	1997-1998	regional	North	random	1 170	1.6	(1.0-2.6)	
[133]*	Sweden	1991-1994	regional	Malmö	random	5 533	0.4		
[135]*	Turkey	2006-2007	regional	South West	random	2 852	1.0		
[137]*	Turkey	2002-2004	regional	Central	convenience	1 320	2.2		
[139]*	Turkey		regional	Central	random	1 095	2.1		
[37]*	United Kingdom	1996	regional	England and Wales	residual	6 401	0.7		

** Included in general population prevalence estimate presented in Figure 4.*

Table A3. Prevalence of HBsAg in first-time blood donors

Reference	Country	Period		Area	Region	N	%	95% CI
[28]*	Belgium	2005					0.06	
[28]*	Bulgaria	2005					5.2	
[28]*	Croatia	2005					0.2	
[32]*	Cyprus			regional	North	5 057	3.0	
[28]*	Czech Republic	2005					0.07	
[28]*	Finland	2005					0.04	
[28]*	France	2005					0.1	
[28]	Germany	2005					0.1	
[158]*	Germany	1997	2002	nationwide		2 919 442	0.2	
[159]	Germany			not specified		14 251	0.1	
[28]	Greece	2005					3.0	
[34]*	Greece	1995	1997	regional	North West, Epirus	6 696	0.9	0.6-1.1
[28]*	Hungary	2005					0.00	
[28]*	Ireland	2005					0.02	
[160]*	Italy	2005		regional	North West, Piedmont	6 313	0.4	
[161]*	Lithuania	2005	2006	regional	Vilnius	24 880	1.7	
[28]*	Luxembourg	2005					0.1	
[28]*	Netherlands	2005					0.09	
[28]*	Norway	2005					0.02	
[162]*	Poland	1998	2000	regional	North East	22 618	0.9	
[28]*	Romania	2005					4.3	
[28]*	Slovakia	2005					0.2	
[28]*	Slovenia	2005					0.09	
[28]*	Spain	2005					0.1	
[28]*	Sweden	2005					0.06	
[28]*	Switzerland	2005					0.1	
[28]*	United Kingdom	2005					0.04	

** Included in first-time blood donor population prevalence estimate presented in Figure 4.*

Table A4. Prevalence of anti-HCV in first-time blood donors

Reference	Country	Period		Area	Region	N	%	95% CI
[28]*	Belgium	2005					0.06	
[28]*	Bulgaria	2005					0.9	
[28]*	Croatia	2005					0.06	
[32]*	Cyprus	2005		regional	North	5 057	0.5	
[28]*	Czech Republic	2005					0.1	
[28]*	Finland	2005					0.04	
[28]*	France	2005					0.06	
[28]	Germany	2005					0.08	
[158]*	Germany	1997	2002	nationwide		2 919 442	0.1	
[28]*	Greece	2005					0.6	
[28]*	Hungary	2005					0.3	
[28]*	Ireland	2005					0.02	
[161]*	Lithuania	2005	2006	regional	Vilnius	24 894	1.7	
[28]*	Luxembourg	2005					0.06	
[28]*	Netherlands	2005					0.03	
[28]*	Norway	2005					0.06	
[162]*	Poland	1998	2000	regional	north east	22 618	0.6	
[28]*	Romania	2005					3.3	
[28]*	Slovakia	2005					0.06	
[28]*	Slovenia	2005					0.02	
[28]	Spain	2005					0.1	
[163]*	Spain	1999	2001	nationwide		216 590	0.2	
[28]*	Sweden	2005					0.1	
[28]*	Switzerland	2005					0.08	
[28]*	United Kingdom	2005					0.04	

** Included in blood donor population prevalence estimate presented in Figure 4.*

Table A5. Prevalence of HBsAg in pregnant women

Reference	country	Period		Area	Region	N	%	95% CI
[77]*	Denmark	2005	2006	nationwide		29 708	0.3	
[164]	Denmark	2000	2001	regional	Copenhagen	4 094	0.4	0.3-0.7
[165]*	France	1984	1998	regional	Limoges	22 859	0.7	
[166]*	Germany	1996	2005	regional	Heidelberg	5 518	1.6	
[167]	Greece	2008	2008	regional	Athens	749	4.1	
[168]	Greece	1994	2002	regional	Athens (Piraeus)	5 497	3.9	
[95]*	Greece	2003		nationwide		3 384	2.9	2.3-3.4
[169]*	Ireland	1998	2000	regional	Dublin	16 222	0.4	
[97]*	Italy	2001		nationwide		10 881	1.7	1.4-1.9
[170]	Italy	1996		regional	North, Padua	2 059	1.0	
[98]	Italy	2001	2003	regional	Sicily, Palermo	3 318	1.1	
[100]*	Netherlands	1993	1998	regional	Amsterdam	56 756	1.2	
[171]*	Slovakia	2000	2004	regional	Bratislava	90	4.4	
[35]*	Spain	2004		regional	Catalonia	1 534	0.1	0.0-0.3
[99]*	Switzerland	2001		regional	Basel	1 503	1.2	0.7-1.8
[172]*	United Kingdom	2002		regional	London	110 621	1.0	

** Included in antenatal population prevalence estimate presented in Figure 5.*

Table A6. Prevalence of anti-HCV in pregnant women

Reference	country	Period		Area	Region	N	%	95% CI	remarks
[173]*	Germany	1992	1996	regional	Munich	3 712	0.9		
[168]*	Greece	1994	2002	regional	Athens (Piraeus)	5 497	0.8		
[174]*	Greece	1996	1997	regional	North	2 408	2.0		
[175]	Italy	1996	1999	regional	North	5 840	1.8		
[170]*	Italy	1996		regional	North	2 059	1.9		
[176]*	Italy	1995	1998	regional	North	15 250	2.4		
[177]*	Italy	1996	2001	regional	North	13 025	0.8		
[171]*	Slovakia	2000	2004	regional	Bratislava	90	0.0		
[178]*	Switzerland	1990	1991	nationwide		9 057	0.7		
[179]*	United Kingdom	1997	1998	nationwide *		126 009	0.2	0.1-0.3	neonatal dried blood spots, prevalence extrapolated to UK
[180]*	United Kingdom	1996		regional	Northern and Yorkshire	16 675	0.2	0.1-0.3	adjusted for sampling procedure
[180]*	United Kingdom	1996		regional	London	25 940	0.4	0.3-0.5	adjusted for sampling procedure
[181]*	United Kingdom	1997	1999	regional	London	4 729	0.8	0.6-1.0	
[182]*	United Kingdom	1997		regional	Scotland	3 548	0.6	0.4-1.0	
[183]*	United Kingdom	2000		regional	Scotland	30 259	0.3		neonatal dried blood spots

** Included in antenatal population prevalence estimate presented in Figure 5.*

Table A7. Prevalence of HBsAg in migrants ethnic minorities, Europe

Reference	Country	Study period	Country of birth/ ethnicity	Status	N	HBsAg prevalence (%)	Remark
[184]	Greece	not reported	Albania	Refugees	130	15.4	
[185]	Italy	1997	Albania	Refugees	670	13.6	
[186]	Italy	2005-2006	South America	Refugees	130	10.7	
[187]	Italy	2005	Africa, Asia	Refugees	556	10.7	
[188]	Italy	2005	Sub-Sahara Africa	Illegal immigrants	182	9.3	
[189]	Italy	2003-2004	Several countries	Refugees	890	9.3	
[190]	Spain	2001-2004	Several countries	Residents	1 905	7.7	
[46]	Italy*	2000	Turkey (Kurds)	Refugees	368	6.8	
[191]	United Kingdom	2000	Somalia	Residents	448	5.7	
[123]	Greece	2002	Roma	Residents	118	4.2	Children only
[192]	Italy	1999	Kosovo	Refugees	526	2.9	
[46]	Italy*	2000	Iraq (Kurds)	Refugees	637	2.2	
[193]	Netherlands	2004	Several countries	Residents	205	1.0	

** One publication on two migrant groups*

Table A8. Prevalence of anti-HCV in migrants/ethnic minorities, Europe

Reference	Country	Study period	Country of birth/ ethnicity	Status	N	anti-HCV prevalence (%)	Remark
48	Hungary	2004	Roma	Residents	64	23.4	
190	Spain	2001-2004	Several countries	Residents	1 848	3.1	
184	Greece	not reported	Albania	Refugees	130	2.3	
188	Italy	2004-2005	Sub-Saharan Africa	Illegal immigrants	182	2.2	
193	Netherlands	2004	Several countries	Residents	205	1.5	
194	Italy	2002-2006	Several countries	Residents	120	0.8	Children only
192	Italy	1999	Kosovo	Refugees	526	0.7	
185	Italy	1997	Albania	Refugees	670	0.3	
46	Italy*	2000	Turkey (Kurds)	Refugees	368	0.1	
123	Greece	2002	Roma	Residents	216	0.0	Children only
46	Italy*	2000	Iraq (Kurds)	Refugees	637	0.0	

Table A9. Prevalence of HBsAg in IDUs, 1991-2006. Adapted from table INF 114, EMCDDA

Country	Period	Area	Region	N	HBsAg prevalence (%)
Belgium	2007	regional	Antwerp	307	2.6
Belgium	2007	regional	Flanders	45	0
Bulgaria	2006	national		614	11.6
Bulgaria	2007	regional	Sofia	656	5.6
Germany	1999	regional	Munich	140	2
Ireland	2003	regional	Dublin	63	0
Greece	2006	national		1 293	3.6
Greece	2006	national		757	1.7
Cyprus	2007	national		102	7.8
Lithuania	2006	regional	Vilnius	246	8.9
Lithuania	2006	regional	Vilnius	422	3.3
Luxembourg	2005	national		255	3.9
Hungary	2007	national		564	0.4
Netherlands	2000	regional	The Hague	199	3
Poland	2005	regional	Lubelski	87	1.2
Poland	2005	regional	Warminsko-mazurskie	82	8.5
Poland	2005	regional	Warsaw	178	7.3
Portugal	2007	national		1 395	2.9
Portugal	2007	national		877	3.2
Portugal	2007	national		4 267	6.9
Romania	2007	regional	Bucharest	113	11.5
Slovenia	2002	national		564	3.4
Croatia	2007	national		200	0.5
Norway	2007	regional	Oslo	222	0.5

Table A10. Estimated number of individuals in the general population and in the largest three migrant groups who are positive for HBsAg and/or anti-HCV, by country

Country	Total population size (number)	HBsAg prevalence in the general population (%)	anti-HCV prevalence in the general population (%)	HBsAg positive individuals (number)	Anti-HCV positive individuals (number)	Migrants, three largest groups (number)	HBsAg positive migrants (number)	Anti-HCV positive migrants (number)
Austria	8 355 260					461 100	18 444	
Belgium	10 754 528	0.7%	0.6%	75 282	64 527	365 126	14 605	9 512
Bulgaria	7 606 551		1.3%		98 885			
Croatia	4 435 056							
Cyprus	793 963	0.9%		7 146				
Czech Republic	10 467 542	0.6%		62 805				
Denmark	5 511 451					69 342	2 774	
Estonia	1 340 415							
Finland	5 326 314	0.2%		10 653		52 397	2 412	
France	64 351 000		1.3%		836 563	1 871 000	74 840	23 290
Germany	82 050 000	0.6%	0.4%	492 300	328 200	2 626 700	105 068	60 839
Greece	11 257 285	2.1%	1.0%	236 403	112 573	553 093	22 124	14 718
Hungary	10 031 208					226 436	19 283	
Iceland	319 368					3 580	241	
Ireland	4 465 540	0.1%		4 466		103 394	5 115	
Italy	60 053 442	1.4%	5.2%	840 748	3 122 779	1 061 375	62 987	27 031
Latvia	2 261 294					296 816	11 873	5 199
Liechtenstein	35 590							
Lithuania	3 349 872					174 879	6 995	2 993
Luxembourg	493 500					60 412	2 416	
Macedonia	2 048 620							
Malta	413 627							
Netherlands	16 486 587	0.1%	0.4%	16 487	65 946	551 155	22 046	15 106
Norway	4 799 252					51 166	2 047	808
Poland	38 135 876		1.9%		724 582	497 353	19 894	
Portugal	10 627 250					300 118	27 018	4 636
Romania	21 498 616	5.6%	3.5%	1 203 922	752 452	72 179	6 423	2 310
Slovakia	5 412 254	0.6%		32 474		26 285	1 051	
Slovenia	2 032 362					164 222	6 569	412
Spain	45 828 172	1.0%	2.0%	458 282	916 563	1 566 951	93 337	27 761
Sweden	9 256 347	0.2%	0.4%	18 513	37 025	212 245	8 490	
Switzerland	7 700 202					493 718	19 749	
Turkey	71 517 100	5.2%	1.5%	3 718 889	1 072 757	593 999	52 609	6 535
United Kingdom	61 634 599		0.7%		431 442	1 073 000	42 920	21 187

Table A11. Estimated HCC mortality rate for males and females by country

Country	Year	Rate per 100 000 men	Rate per 100 000 women	Reference
Austria	2000-2004	4.24	0.92	50
Belgium	1990-1996	2.35	1.69	51
Bulgaria	1990	8.03	5.35	51
Czech Republic	1989	2.76	0.99	50
Denmark	2001	1.49	0.41	50
Estonia	1999	5.36	2.26	50
Finland	2000-2004	2.69	0.91	50
France	2003	6.79	0.96	50
Germany	2000-2004	2.89	0.75	50
Greece	2000-2004	1.55	0.3	50
Hungary	2003	7.72	2.92	50
Ireland	2000-2004	0.78	0.3	50
Italy	2002	6.72	1.92	50
Latvia	1999	5.09	1.87	50
Lithuania	1999	1.40	0.39	50
Netherlands	2000-2004	1.05	0.33	50
Poland	2000-2004	4.15	2.65	50
Portugal	2003	2.71	0.68	50
Spain	2000-2004	4.92	1.53	50
Sweden	2000-2002	0.68	0.27	50
United Kingdom	2000-2004	1.38	0.36	50
Norway	1986-1989	0.96	0.43	50
Switzerland	2000-2004	5.93	1.75	50

Reference 50: Bosseti, 2008
Reference 51: La Vecchia, 2000

Table A12. Estimated cirrhosis mortality rate for males and females by country

Country	Year	Rate per 100 000 men	Rate per 100 000 women
Austria	2000-2002	20.72	7.13
Belgium	1995-1996	10.44	5.42
Bulgaria	2000-2002	19.44	4.57
Czech Republic	2000-2002	18.02	9.28
Denmark	2000-2001	14.96	6.04
Estonia	2000-2002	22.4	10.55
Finland	2000-2002	13.58	4.93
France	2000-2002	14.45	5.4
Germany	2000-2002	18.2	7.38
Greece	2000-2002	5.45	1.48
Hungary	2000-2002	68.27	20.91
Ireland	2000-2002	4.77	5.64
Italy	2000-2002	13.01	5.97
Latvia	2000-2002	15.07	6.87
Lithuania	2000-2002	20.14	8.15
Luxembourg	2000-2002	17.45	7.51
Malta	2000-2002	4.87	1.02
Netherlands	2000-2002	4.4	2.33
Poland	2000-2002	15.86	4.91
Portugal	2000-2002	18.39	5.48
Romania	2000-2002	48.47	22.55
Slovakia	2000-2002	31.01	9.72
Slovenia	2000-2002	35.03	13.26
Spain	2000-2002	11.75	3.55
Sweden	2000-2002	4.99	2.46
Norway	2000-2002	4.52	2.22

Source: Bosetti, 2007 (reference 49)

Annex 2. Search strategies

1 Search strategy review question 1

What is the prevalence of chronic HBV and HCV infection* in each of the 34** countries

- in the general population?
- in the following groups:
  - blood donors;
  - pregnant women;
  - drug users (DUs);
  - men having sex with men (MSM);
  - migrants?

* Defined as HBsAg- and HCV-RNA-positive or anti-HCV-positive individuals, respectively.

** All 27 EU Member States, EEA/EFTA (Norway, Iceland, Liechtenstein and Switzerland) and candidate countries (Croatia, the former Yugoslav Republic of Macedonia and Turkey) (n=34).

Search strategy Q1a

The infection: hepatitis B or hepatitis C

1 hepatitis B
2 Hepatitis B, chronic (MeSH)
3 Hepatitis C (MeSH)
4 HBV
5 HCV
6 or 1–5

The outcome: prevalence

7 Prevalence (MeSH)
8 seroprevalence
9 Seroepidemiologic Studies (MeSH)
10 Seroepidemiolog$
11 Serologic$ markers
12 Serology
13 HBsAg
14 HBs Ag
15 Hepatitis B Surface Antigens (MeSH)
16 Hepatitis B Surface Antigen$
17 Anti-HCV
18 Hepatitis C Antibodies (MeSH)
19 HCV-RNA
20 Carrier state (MeSH)
21 Carrier
22 or 7–21

The population: general population

23 population
24 community
25 child$
26 adolesc$
27 adults$
28 elder$
29 residual sera
30 Population Surveillance (MeSH)
31 survey
32 surveillance
33 or 23-32

The population: countries

34 see country list
35 EU
36 European Union
37 Europe
38 or 34–37

39 and 6, 22, 33, 38

Search strategy Q1b

The infection: hepatitis B or hepatitis C
40 = Question 1: row 6

The outcome: prevalence
41 = Question 1: row 22

The Population: specific groups
42 Blood donors (MeSH)
43 blood-donor population
44 IDU
45 Drug users (MeSH)
46 Substance Abuse, Intravenous (MeSH)
47 Substance abuse$
48 MSM
49 men adj2 sex adj1 men (men having sex with men/men who have sex with men)
50 Homosexuality, Male (MeSH)
51 homosex$
52 homo adj3 $sexual
53 Gay men
54 Migrant$
55 Transients and Migrants (MeSH)
56 Immigrant$
57 Emigrants and Immigrants (MeSH)
58 Minorit$
59 Minority Groups (MeSH)
60 Pregnan$
61 Pregnancy (MeSH)
62 Antenatal
63 Prenatal
64 or 42-63

The population: countries
65 = Question 1: row 38

66 **and 40, 41, 64, 65**

2 Search strategy review question 3

What is the burden of HBV and HCV related cirrhosis and hepatocellular carcinoma (HCC) in each of the 34 countries*?

- What is the burden (morbidity and mortality) due to cirrhosis and HCC in each of the 34 countries*?
- What is the proportion of the burden of cirrhosis and HCC that is attributable to chronic HBV and HCV infection in each of the 34 countries*? This will be assessed by estimating the prevalence of HBsAg and HCV-RNA in cases of cirrhosis and HCC, a method that has recently been used by Perz et al.[30].

* All 27 EU Member States, EEA/EFTA (Norway, Iceland, Liechtenstein and Switzerland) and candidate countries (Croatia, the former Yugoslav Republic of Macedonia, and Turkey) (n=34).

Search strategy Q3a

Disease: cirrhosis and HCC

1 Cirrho$
2 liver cirrhosis (MeSH)
3 hepatocellular carcinoma (MeSH)
4 HCC
5 liver cancer
6 or 1-5

Outcome: burden of disease

7 morbidity (MeSH)
8 prevalence (MeSH) → under MeSH 'morbidity'
9 incidence (MeSH) → under MeSH 'morbidity'
10 burden of disease
11 QALY
12 DALY
13 mortality
14 death
15 or 7-14

Population: countries

16 = Question 1: row 38

17 and6, 15, 16

Search strategy Q3b

The infection: hepatitis B or hepatitis C

18 = Question 1: row 6

The outcome: prevalence

19 = Question 1: row 22

The population: patients with cirrhosis or HCC

20 = Question 3a: row 6

The population: countries

21 = Question 1: row 38

22 and 18, 19, 20, 21

3 Search strategy review questions 4 and 5

4. What is the current national practice regarding screening for chronic HBV and HCV infection in each of the 34 countries* in

- pregnant women;
- blood donors;
- migrants;
- IDUs;
- MSM?

5. What is the effectiveness of these screening programmes in terms of

- process: coverage of the programme and the proportion of the risk group screened;
- outcome: proportion of screened individuals found HBsAg- or HCV-RNA-positive;
- outcome: proportion of positive individuals who are receiving care;
- prevention of secondary cases: what proportion of contacts of HBsAg-positive individuals detected through screening is vaccinated?

What is the cost-effectiveness of these screening programmes?

Search strategy Q4 and Q5

Infection: hepatitis B or hepatitis C

1 = Question 1: row 6

Outcome: screening

2 Screening
3 Mass screening (MeSH)
4 Testing
5 or 2-4

Outcome: national practice

6 nation$ (national, nationwide)
7 practice
8 program$ (bv program, programme of programmatic)
9 policy
10 guidelines
11 or 6-10

Population: specific groups

12 = Question 1: row 64

Population: countries

13 = Question 1: row 38

14 and 1, 5, 11, 12, 13

Annex 3. Data extraction form

First author: _____
☐ Excluded Reason: .....
Publication year: _____

1. Date extracted: ... - ... – 2009

2. Extracted by:
1 ☐ Susan
2 ☐ Irene

3. Type of publication
1 ☐ Peer-reviewed publication
2 ☐ Public health report
3 ☐ Letter
4 ☐ Other: .....

4. Relevant for review question:
1 ☐ Q1: Prevalence
2 ☐ Q3: Burden of cirrhosis/HCC
3 ☐ Q4: National screening practice
4 ☐ Q5: Screening effectiveness

5. Subject of the study:
5a 1 □ HBV 2 □ HCV 3 □ HBV and HCV
5b 1 □ cirrhosis 2 □ HCC 3 □ cirrhosis and HCC
5c 1 □ screening

6. Period of data collection: _____ – _____

6b. Country:		
1 □ Austria	13 □ Ireland	25 □ Spain
2 □ Belgium	14 □ Italy	26 □ Sweden
3 □ Bulgaria	15 □ Latvia	27 □ United Kingdom
4 □ Cyprus	16 □ Lithuania	28 □ Norway
5 □ Czech Republic	17 □ Luxembourg	29 □ Iceland
6 □ Denmark	18 □ Malta	30 □ Liechtenstein
7 □ Estonia	19 □ Netherlands	31 □ Switzerland
8 □ Finland	20 □ Poland	32 □ Croatia
9 □ France	21 □ Portugal	33 □ the former Yugoslav Republic of Macedonia
10 □ Germany	22 □ Romania	34 □ Turkey
11 □ Greece	23 □ Slovakia	
12 □ Hungary	24 □ Slovenia	35 □ multiple countries: .....

7. Area in country:
1 □ whole country
2 □ region: .....
3 □ city: .....
4 □ not specified

8. Geographical area:
1 □ urban
2 □ rural
3 □ both
4 □ not specified

9. Study population:
1 □ general population: _____
2 □ blood donors
3 □ pregnant women
4 □ drug users
5 □ MSM: _____
6 □ migrants → proceed to 10 and 11
7 □ other: ……..

(10 and 11 only for migrant study population)

10. Country of origin:
……. …….
……. …….

11. Generation:
1 □ First generation migrants
2 □ Second generation migrants
3 □ First and second generation migrants
4 □ Not specified

12. Age groups included:
1 □ children (0–17 years)
2 □ adults (18 and older)
3 □ both children and adults
4 □ pregnant women
5 □ not specified

Quality criteria, external validity (representativeness of the sample for the target population)

13. Study design:
1 □ cross-sectional
2 □ meta-analysis
3 □ modelling
4 □ other: ……

14. Sampling method:
1 □ exhaustive (total population)
□ probabilistic sample (random sample)
2 □ high quality
3 □ medium quality
4 □ low quality
5 □ no info on quality
6 □ non-probabilistic sample (convenience sample)
7 □ other: ……
8 □ not specified

15. Type of sample:
1 □ serum
2 □ dried blood spots
3 □ neonatal dried blood spots for pregnant women
4 □ oral fluid
5 □ other: ……

16. Type of test :
1 □ HBsAg (EIA)
2 □ HBV DNA
3 □ HBV rapid test
4 □ Anti-HCV EIA
5 □ Anti-HCV Immunoblot (RIBA)
6 □ HCV-RNA
7 □ HCV rapid test

17. Outcome liver disease:
1 □ Cirrhosis 2 □ HCC 3 □ both

18. Outcome burden:
1 □ morbidity – prevalence
2 □ morbidity – incidence

3 □ mortality
4 □ prevalence in patients

(Only for review question 4 and 5: National screening practice and effectiveness)

19. Type of screening program:
1 □ universal screening
2 □ screening of risk groups

20. Condition screened for: 1 □ HBV 2 □ HCV 3 □ both

21. Coverage: 1 □ Nationwide 2 □ Regional

22. Targeted (risk) groups:
1 □ general population
2 □ blood donors
3 □ pregnant women
4 □ drug users
5 □ MSM
6 □ migrants; specify ……
7 □ other: ……

23. Outcome measures (effectiveness):
1 □ coverage
2 □ prevalence
3 □ proportion of positives receiving care
4 □ proportion of susceptibles vaccinated
5 □ proportion of contacts vaccinated
6 □ cost-effectiveness

Results

24. For cross-sectional studies: What was the participation rate? …… %

25. Number of participants: ……

26. Age of participants (not for pregnant women)
Range: ____ – _____ median:_____ mean: _____

27. Age-specific results reported:
1 □ Yes
2 □ No

Table 1a

	Standardised	n	N	% pos	95%CI	Result text
HBsAg	☐					
HBV DNA	☐					
Anti-HCV	☐					
HCV-RNA	☐					
Cirrhosis	☐					
Cirrhosis: incidence	☐					
HCC	☐					
HCC: incidence	☐					

Table 1b

	Standardised	n	N	% pos	95% CI	Result text
HBsAg	☐					
HBV DNA	☐					
Anti-HCV	☐					
HCV-RNA	☐					
Cirrhosis	☐					
Cirrhosis: incidence	☐					
HCC	☐					
HCC: incidence	☐					

Table 1c

	Standardised	n	N	% pos	95% CI	Result text
HBsAg	☐					
HBV DNA	☐					
Anti-HCV	☐					
HCV-RNA	☐					
Cirrhosis	☐					
Cirrhosis: incidence	☐					
HCC	☐					
HCC: incidence	☐					

Table 2a

(risk) group:	n	N	%	95% CI	Result text
Coverage: % screened					
% susceptibles vaccinated					
% contacts vaccinated					
Cost-effectiveness					

Table 2b

(risk) group:	n	N	%	95% CI	Result text
Coverage: % screened					
% susceptibles vaccinated					
% contacts vaccinated					
Cost-effectiveness					

Table 2c

(risk) group:	n	N	%	95% CI	Result text
Coverage: % screened					
% susceptibles vaccinated					
% contacts vaccinated					
Cost-effectiveness					

28. Special interest:
1 □ Yes
2 □ No

29. References:

30. Remarks:

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