

# SURVEILLANCE REPORT

Annual Epidemiological Report for 2015

# **Hepatitis B**

### **Key facts**

- In 2015, 30 EU/EEA Member States reported 24 573 cases of hepatitis B virus (HBV) infection, a crude rate of 4.7 cases per 100 000 population.
- Of these cases, 10.2% were reported as acute, 63.5% as chronic, 19.4% as unknown, and 6.9% could not be classified.
- The most affected age group for both acute and chronic infections was the group of 25–34-year-olds, accounting for 32.0% of cases; the overall male-to-female ratio was 1.6 to 1.
- There continues to be a downward trend in the rate of acute cases, which is in accordance with global trends and reflects the impact of national vaccination programmes. In contrast, the rate of newly diagnosed chronic cases continues to rise over time, and this increase is most likely to be related to changes in local testing and reporting practices.
- Data on transmission were complete for only 9.6% of cases. Among acute cases with complete information, heterosexual transmission was most commonly reported (31.1%), followed by nosocomial transmission (16.3%), transmission among men who have sex with men (11.6%) and transmission through injecting drug use (11.3%). Mother-to-child transmission was the most commonly reported route (65.3%) for those categorised as chronic cases.
- Prevention and control programmes should be maintained if the downward trend in transmission is to continue. These programmes need further scaling up if European countries are to achieve the goal of eliminating hepatitis B. Surveillance data are important in monitoring the epidemiological situation, and there is a need to improve the quality of the data.

### **Methods**

This report is based on data for 2015 retrieved from The European Surveillance System (TESSy) on 4 November 2016. TESSy is a system for the collection, analysis and dissemination of data on communicable diseases. EU Member States and EEA countries contribute to the system by uploading their infectious disease surveillance data at regular intervals [1]. An overview of the national surveillance systems is available online [2].

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A subset of the data used for this report is available through the interactive *Surveillance atlas of infectious diseases* [3].

Acute and chronic hepatitis B infections were differentiated by countries using the following definitions:

Acute stage. Detection of IgM core antigen-specific antibody (anti-HBc IgM)

OR detection of hepatitis B surface antigen (HBsAg) and previous negative HBV markers less than six months ago

OR detection of hepatitis B nucleic acid (HBV-DNA) and previous negative HBV markers less than six months ago

Any of the above with or without symptoms and signs (e.g. jaundice, elevated serum aminotransferase levels, fatigue, abdominal pain, loss of appetite, intermittent nausea, vomiting, fever)

Chronic stage. Detection of HBsAg or HBeAg or HBV-DNA AND no detection of anti-HBc IgM (negative result)

OR detection of HBsAg or HBeAg or HBV-DNA on two occasions that are six months apart. (In the event that the case was not notified the first time.)

**Unknown.** Any newly diagnosed case which cannot be classified in accordance with the above definition of acute or chronic infection

Surveillance systems across the EU/EEA countries are heterogeneous. Eighteen countries submitted national data in 2015 based on the 2012 EU case definition\_five countries used the 2008 EU case definition, and seven countries (Belgium, Denmark, Germany, Italy, Latvia, Luxembourg and Romania) used national case definitions. The 2008 EU case definition only allows for the reporting of acute hepatitis B cases whereas the 2012 case definition includes both acute and chronic cases. All reported cases were included in the analysis, regardless of which case definition was used. The data collected in accordance with the EU 2012 case definition represent confirmed cases; a few countries submitted 'probable' cases using alternative case definitions.

Annual notification rates were calculated per 100 000 population for countries with comprehensive surveillance systems using Eurostat population data (<u>http://epp.eurostat.ec.europa.eu</u>). For data reported from the United Kingdom, population data from the Office for National Statistics were used to exclude Scotland, which did not report any hepatitis B data.

In nine countries (Cyprus, the Czech Republic, Denmark, Germany, Iceland, Italy, Malta, Portugal, and Spain), historical data from the year 2006 were not included as they would not have been comparable with the subsequent enhanced data. Hepatitis B data are presented by 'date of diagnosis' or, if not available, by 'date used for statistics'. When comparing datasets in the database that used these two dates, there were only minor differences between them, and only in a few countries.

Italy reports data using two data sources. One of these sources has national coverage, but includes only a limited number of variables, and was used for the calculation of national rates and for the breakdown by age and gender. The other data source in Italy is a sentinel system covering an estimated 76% of the population; the system includes epidemiological data on a range of variables. The sentinel population is considered representative of the wider population, and the data provided were scaled up from 76% to 100%. This source was used for epidemiological analyses including the route of transmission and importation status.

The data source for Belgium is a sentinel system with unknown coverage. National rates were therefore not calculated for Belgium.

#### **Overall trends**

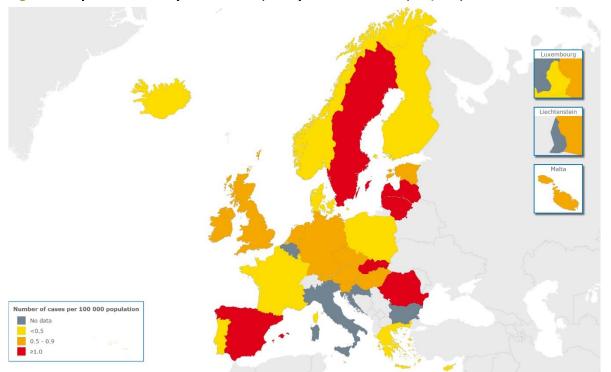
In 2015, 30 EU/EEA Member States reported 24 573 cases of hepatitis B virus (HBV) infection (no data from Liechtenstein), a crude rate of 4.7 per 100 000 population. Of these cases, 2 505 (10.2%) were reported as acute, 15 595 (63.5%) as chronic, 4 777 (19.4%) as 'unknown', and 1 696 cases (6.9%) could not be classified due to an incompatible data format.

In 2015, 24 countries were able to provide data on acute cases (Table 1). The overall rate of acute cases was 0.6 cases per 100 000 population, ranging from 0 cases in Luxembourg and Iceland to 3.4 cases in Latvia (Figure 1).

#### Table 1. Reported hepatitis B cases: number and rate per 100 000 population, EU/EEA, 2011–2015

| Country        | 2011<br>All |      | 2012<br>All |      | 2013<br>All |      | 2014<br>All |      | 2015  |      |       |      |         |      |         |      |
|----------------|-------------|------|-------------|------|-------------|------|-------------|------|-------|------|-------|------|---------|------|---------|------|
|                |             |      |             |      |             |      |             |      | All   |      | Acute |      | Chronic |      | Unknown |      |
|                | Cases       | Rate | Cases       | Rate | Cases       | Rate | Cases       | Rate | Cases | Rate | Cases | Rate | Cases   | Rate | Cases   | Rate |
| Austria        | 765         | 9.1  | 841         | 10.0 | 689         | 8.2  | 1174        | 13.8 | 1109  | 12.9 | 43    | 0.5  | 581     | 6.8  | 485     | 5.7  |
| Belgium        |             |      |             |      |             |      | 1539        |      | 1321  |      |       |      |         |      |         |      |
| Bulgaria       | 344         | 4.7  | 322         | 4.4  | 302         | 4.1  | 235         | 3.2  | 263   | 3.7  |       |      |         |      |         |      |
| Croatia        |             |      | 136         | 3.2  | 136         | 3.2  | 149         | 3.5  | 112   | 2.7  |       |      |         |      |         |      |
| Cyprus         | 10          | 1.2  | 14          | 1.6  | 9           | 1.0  | 4           | 0.5  | 2     | 0.2  |       |      |         |      | 2       | 0.2  |
| Czech Republic | 191         | 1.8  | 154         | 1.5  | 133         | 1.3  | 105         | 1.0  | 89    | 0.8  |       |      |         |      | 89      | 0.8  |
| Denmark        | 264         | 4.7  | 298         | 5.3  | 283         | 5.1  | 229         | 4.1  | 276   | 4.9  | 11    | 0.2  | 265     | 4.7  |         |      |
| Estonia        | 44          | 3.3  | 51          | 3.8  | 36          | 2.7  | 34          | 2.6  | 31    | 2.4  | 6     | 0.5  | 25      | 1.9  |         |      |
| Finland        | 247         | 4.6  | 249         | 4.6  | 268         | 4.9  | 276         | 5.1  | 397   | 7.3  | 6     | 0.1  | 391     | 7.1  |         |      |
| France         | 102         | 0.2  | 100         | 0.2  | 83          | 0.1  | 94          | 0.1  | 100   | 0.2  | 100   | 0.2  |         |      |         |      |
| Germany        | 810         | 1.0  | 686         | 0.9  | 687         | 0.9  | 764         | 0.9  | 1881  | 2.3  | 632   | 0.8  |         |      | 1249    | 1.5  |
| Greece         | 38          | 0.3  | 50          | 0.5  | 32          | 0.3  | 27          | 0.2  | 20    | 0.2  | 20    | 0.2  |         |      |         |      |
| Hungary        | 67          | 0.7  | 53          | 0.5  | 62          | 0.6  | 65          | 0.7  | 45    | 0.5  | 45    | 0.5  |         |      |         |      |
| Iceland        | 25          | 7.9  | 20          | 6.3  | 16          | 5.0  | 28          | 8.6  | 17    | 5.2  | 0     | 0    | 11      | 3.3  | 6       | 1.8  |
| Ireland        | 523         | 11.4 | 571         | 12.5 | 429         | 9.3  | 426         | 9.2  | 540   | 11.7 | 26    | 0.6  | 493     | 10.7 | 21      | 0.5  |
| Italy          | 679         | 1.1  | 561         | 0.9  | 564         | 0.9  | 500         | 0.8  | 361   | 0.6  |       |      |         |      | 361     | 0.6  |
| Latvia         | 319         | 15.4 | 329         | 16.1 | 304         | 15.0 | 303         | 15.1 | 328   | 16.5 | 67    | 3.4  | 261     | 13.1 |         |      |
| Lithuania      | 60          | 2.0  | 23          | 0.8  | 35          | 1.2  | 26          | 0.9  | 32    | 1.1  | 32    | 1.1  |         |      |         |      |
| Luxembourg     | 16          | 3.1  | 26          | 5.0  | 38          | 7.1  | 32          | 5.8  | 46    | 8.2  | 0     | 0.0  | 2       | 0.4  | 44      | 7.8  |
| Malta          | 35          | 8.4  | 18          | 4.3  | 17          | 4.0  | 22          | 5.2  | 18    | 4.2  | 3     | 0.7  | 15      | 3.5  |         |      |
| Netherlands    | 1735        | 10.4 | 1525        | 9.1  | 1305        | 7.8  | 1217        | 7.2  | 1129  | 6.7  | 108   | 0.6  | 1007    | 6.0  | 14      | 0.1  |
| Norway         | 763         | 15.5 | 706         | 14.2 | 738         | 14.6 | 695         | 13.6 | 815   | 15.8 | 19    | 0.4  | 796     | 15.4 |         |      |
| Poland         | 104         | 0.3  | 78          | 0.2  | 1541        | 4.0  | 72          | 0.2  | 51    | 0.1  | 51    | 0.1  |         |      |         |      |
| Portugal       | 26          | 0.2  | 28          | 0.3  | 24          | 0.2  | 56          | 0.5  | 120   | 1.2  | 24    | 0.2  | 59      | 0.6  | 37      | 0.4  |
| Romania        | 412         | 2.0  | 378         | 1.9  | 309         | 1.5  | 266         | 1.3  | 229   | 1.2  | 226   | 1.1  | 3       | <0.1 |         |      |
| Slovakia       | 171         | 3.2  | 159         | 2.9  | 194         | 3.6  | 191         | 3.5  | 193   | 3.6  | 67    | 1.2  | 126     | 2.3  |         |      |
| Slovenia       | 71          | 3.5  | 41          | 2.0  | 52          | 2.5  | 39          | 1.9  | 44    | 2.1  | 12    | 0.6  | 32      | 1.6  |         |      |
| Spain          | 522         | 1.1  | 525         | 1.1  | 645         | 1.4  | 633         | 1.4  | 529   | 1.1  | 529   | 1.1  |         |      |         |      |
| Sweden         | 1399        | 14.9 | 1618        | 17.1 | 1683        | 17.6 | 1957        | 20.3 | 2238  | 23.0 | 149   | 1.5  | 1963    | 20.1 | 126     | 1.3  |
| United Kingdom | 7876        | 13.6 | 8761        | 15.0 | 9149        | 15.6 | 11705       | 19.8 | 12237 | 20.5 | 329   | 0.6  | 9565    | 16.0 | 2343    | 3.9  |
| Total EU/EEA   | 17618       | 3.6  | 18321       | 3.7  | 19763       | 4.0  | 22863       | 4.3  | 24573 | 4.7  | 2505  | 0.6  | 15595   | 9.9  | 4777    | 1.8  |

Notes: Data presented by date of diagnosis; data columns for 2015 include cases reported by countries as acute, chronic or unknown using the above differentiation criteria: United Kingdom data exclude data from Scotland.



#### Figure 1. Reported acute hepatitis B cases, rate per 100 000 cases, EU/EEA, 2015

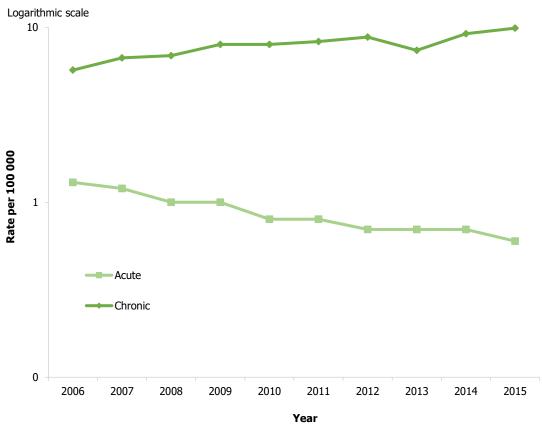
Source: Country reports from Austria, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom.

Notes: Countries were included if they were able to present data by disease status or used a case definition that includes only acute cases (e.g. EU 2008) or were known to only report acute cases, and had national coverage; under-reporting of acute hepatitis B in France was estimated at 76.5% in 2013; UK data exclude Scotland; figure includes countries that defined data by disease status or used a case definition that includes only acute cases (e.g. EU 2008) or were known to only report acute cases.

In 2015, 17 countries submitted data on chronic infections. The overall notification rate was 9.9 per 100 000, ranging from <0.1 in Romania to 20.1 in Sweden (Table 1). The United Kingdom reported 61.3% of all chronic cases reported in 2015.

In 2015, the overall reporting rate for acute cases of hepatitis B (0.6 per 100 000) was considerably lower than the rate for chronic cases diagnosed and has shown a steady decline since 2006 (1.3 per 100 000) (Figure 2). No country showed an increase in their rate of acute cases over the reporting period, and 10 of the 16 countries that reported consistently over this time period reported a steady decline in the reported number and rate of acute cases.

The rate of reported chronic infections has increased steadily over time from 5.7 per 100 000 in 2006 to 9.9 in 2015.



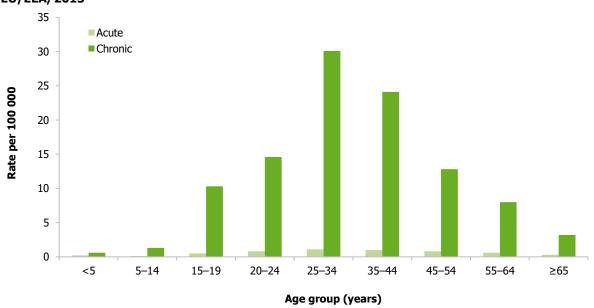
# Figure 2. Rates of acute and chronic hepatitis B per 100 000 population, EU/EEA countries, 2006–2015

Source: Country reports from: Austria, Bulgaria, Cyprus, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom.

Notes: Logarithmic scale; under-reporting of acute hepatitis B in France was estimated at 76.5% in 2013; UK data exclude Scotland.

#### Age and gender

In 2015, 14 766 cases of hepatitis B were reported in males (8.4 per 100 000) and 9 503 cases were in females (5.2 per 100 000). This represents a male-to-female ratio of 1.6 to 1. The male-to-female ratio was higher among acute cases (2.2 to 1) than among chronic cases (1.5 to 1). Just under one third of all cases (32.0%) were in the age group of 25–34-year-olds. The age distributions among reported cases of acute and chronic infections were similar (Figure 3), with 13.8% of acute cases and 13.4% of chronic cases in people under 25 years of age. Between 2006 and 2015, the proportion of acute and chronic cases in people under 25 years of age declined from 26.8% and 21.4% in 2006, respectively.

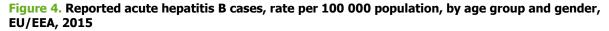


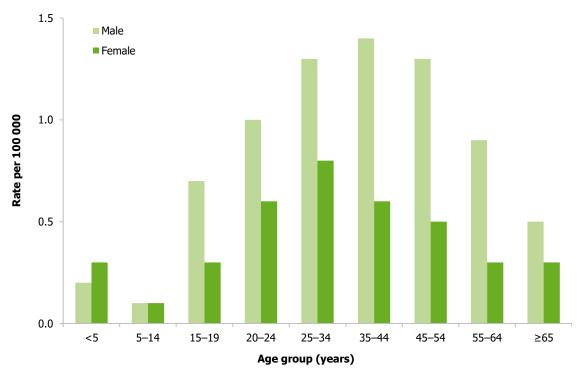
## Figure 3. Acute and chronic hepatitis B cases, rate per 100 000 population, by age group, EU/EEA, 2015

Source: Country reports from Austria, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom.

Notes: Under-reporting of acute hepatitis B in France was estimated at 76.5% in 2013; UK data exclude Scotland.

The age distribution among male and female acute cases was similar, although for all age categories above 14 years the rates were higher among males than females (Figure 4).



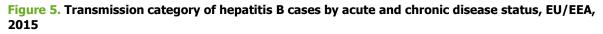


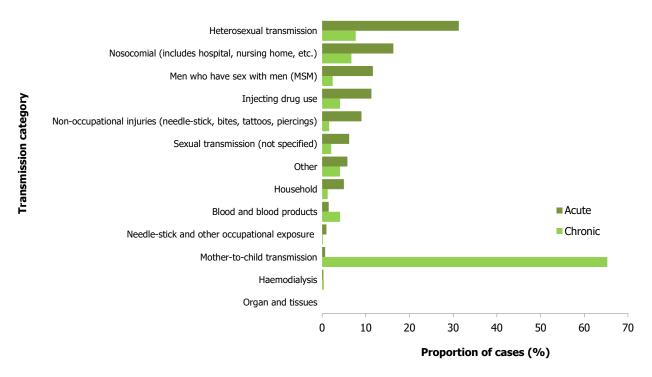
Source: Country reports from Austria, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom.

Notes: Underreporting of acute hepatitis B in France was estimated at 76.5% in 2013; UK data exclude Scotland.

#### **Route of transmission**

The data on transmission were complete for only 2 358 (9.6%) of the reported hepatitis B cases in 2015 (35.1% completeness for acute cases, 9.0% completeness or chronic cases). For the 880 acute cases with complete information, heterosexual transmission was most commonly reported (31.3%), followed by nosocomial transmission (16.3%), transmission among men who have sex with men (11.6%) and injecting drug use (11.3%) (Figure 5). Italy and Romania accounted for nearly two thirds (62.4%) of the acute cases attributed to nosocomial transmission. Mother-to-child transmission was the most common route of transmission reported for the 1 411 chronic cases with complete information (65.3%), followed by heterosexual transmission (7.7%) and nosocomial transmission (6.7%). Among chronic cases attributed to mother-to-child transmission, 96.5% were reported by three countries (Denmark, the Netherlands, and Sweden). Of the chronic cases attributed to mother-to-child transmission, 95.0% were classified as being imported. Transmission category over time showed no obvious trends among either acute or chronic cases.





Source: Country reports from: Austria, Denmark, Estonia, Finland, France, Germany, Hungary, Ireland, Italy, Latvia, Lithuania, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Sweden, and the United Kingdom.

Notes: Numbers are for cases where transmission status is known; under-reporting of acute hepatitis B in France was estimated at 76.5% in 2013; UK data exclude Scotland.

#### **Importation status**

In 2015, of 7 924 cases (32.2%) with information on importation status, 4 814 (60.8%) were reported by 24 countries as imported. The majority of these imported cases (87.7%) were chronic and 3 737 (77.6%) were reported by three countries (the Netherlands, Norway, and Sweden). The proportion of chronic cases (79.1%) reported as imported was higher than the proportion of acute cases (11.5%). The data completeness varied across countries, but among countries with complete data (>75%) on importation status, the proportion of chronic cases classified as imported ranged from 0% (Estonia, Romania, Slovakia) to over 90% (Finland, Ireland, the Netherlands, Norway, Sweden).

#### Outcome

Data on the outcome of infection were reported for 5 884 cases (23.9%) in 2015. Of these cases, 36 (0.6%) were reported to have died from causes related to hepatitis B. Although the number of reported deaths remain low, there has been a slight increase in the number and proportion of deaths since 2006 (24 deaths, 0.4%).

#### Discussion

The number of newly diagnosed hepatitis B infections reported from countries across Europe remains high, with the majority of these infections classified as chronic. There is marked variation between countries in the distribution of acute and chronic cases. This geographical variation reflects differences in local testing and reporting practices as well as underlying epidemiological differences.

For acute hepatitis B cases, there are no striking geographical trends, but four of the six countries with rates over 1.0 per 100 000 (Latvia, Lithuania, Romania, and Slovakia) are located in the eastern part of Europe where the underlying prevalence of chronic hepatitis B infection is known to be highest [4]. For the newly diagnosed cases of chronic hepatitis B reported to ECDC, the geographical trends are also unclear as data for many countries are missing. However, the highest rates are found in north European countries (Norway, Sweden, and the United Kingdom), which is contrary to what may be expected based on the results from seroprevalence surveys which indicate these countries to be of low endemicity (<1.0%). However, it is likely that prevalence surveys from north European countries with high levels of immigration may underestimate the true prevalence of hepatitis B as studies may not include migrant populations from intermediate and high (>1.0%) endemicity countries [5]. The discrepancy between reported notifications and prevalence estimates highlights the difficulty in interpreting routine surveillance data for chronic infections, which are mostly asymptomatic until late stages of the disease. Indeed, the chronic hepatitis B data reported appear to reflect the intensity of local testing policies with the highest rates reported from countries that are known to have comprehensive testing programmes [6,7]. Although chronic hepatitis B data are missing from several northern European countries, the data are dominated by the high number of cases reported from this part of the region, accounting for a substantial proportion of the cases, and this has a strong influence on the trends.

The interpretation of trends over time is hampered by the changes that have been made by countries to their surveillance systems. Indeed, the changes in the rates reported from Germany between 2014 and 2015 are known to relate to the changes in national surveillance practices. Data completeness for several variables has declined over the last two years but the number of countries using the 2012 EU case definition has remained stable. While the number of reporting countries has varied from year to year but increased over time, the number of countries reporting data over the last two years has remained stable. The overall trend for acute cases has shown a gradual but fairly steady decline between 2006 and 2015 and it is most likely that this decline is related to the impact of national hepatitis B vaccination programmes [8]. In contrast to these trends, the overall number and rate of chronic cases has continued to rise, and this increase is most likely related to changes in reporting methods and increased local testing among key populations such as migrants and prisoners [9,10].

Data on importation status of cases remain incomplete, but the impact of migration on reported cases of hepatitis B in Europe is striking for some countries, especially among chronic infections. Indeed, data from four of the north European countries with fairly complete reporting (Finland, Norway, the Netherlands and Sweden) indicate that a high proportion of newly diagnosed infections are considered to have been acquired in a different country. In recent decades, migrants to many countries in Europe, including northern Europe, come from countries with high prevalence of hepatitis B, and prevalence among some of these migrant groups is often high [5,10]. A recent study on the epidemiological burden of hepatitis among migrant populations estimated the burden of infection among migrants in relation to the overall number of chronically infected hepatitis B cases in Europe to be around 25% [10]. This study concluded that migrant populations are often disproportionately affected by hepatitis B and are a key risk group for chronic hepatitis B in certain EU/EEA countries. The influence of migration on hepatitis B highlights the need for countries to develop evidence-based screening interventions that are targeted to the most disproportionately affected migrant communities. It also highlights the importance of monitoring routine surveillance indicators of migration, such as importation status.

Transmission data are key to understanding the epidemiology of hepatitis B. While transmission data completeness was better for acute cases than chronic cases, overall incompleteness of the reported data impairs the interpretation of differences between countries, and the data are unlikely to be fully representative. The most common routes of transmission reported among acute cases include heterosexual contact, nosocomial transmission, sex between men and transmission through injecting drug use. Although nosocomial transmission is an uncommon route of transmission for acute cases in most European countries, it remains a key route of transmission in some, such as Italy and Romania, emphasising the importance of maintaining robust infection control practices across healthcare settings. Mother-to-child transmission is the most common route of transmission among reported chronic cases but is dominated by the large number of cases reported by three north European countries (Denmark, the Netherlands, Sweden), with most of these cases classified as imported. The validity of the reported route of transmission among imported cases is not known and could form a subject for future study. The changes over time in the completeness of reporting of transmission data impede any comparisons of the data over the period.

In May 2016, the World Health Assembly adopted the first global health sector strategy on viral hepatitis, which is aimed at the elimination of hepatitis B and C by 2030 [11]. The concept of elimination for these infections is based

on reducing the incidence of chronic infections by 90% and the associated mortality by 65%. Achieving these targets will require significant scaling-up of key interventions, including hepatitis B childhood vaccination, birthdose vaccination (or other means to prevent mother-to-child transmission), improved systems to assure safe blood transfusions/blood products, injection safety, interventions aimed at prevention of the transmission among people who inject drugs, and increased testing with linkage to care and treatment. To support the implementation and monitoring of this strategy, it is important that countries have a strong system of surveillance to monitor the impact of the interventions. It is particularly important in this context to improve data quality.

### **Public health implications**

Robust epidemiological information is essential to inform effective prevention and control priorities and to assess the impact of implemented strategies. The interpretation of hepatitis B data collected through routine notificationbased surveillance is a challenge due to the asymptomatic nature of chronic infections, differences in testing programmes, continued differences in surveillance practices between countries, and data quality issues. Despite such challenges, the high numbers of reported cases (especially of chronically infected persons) and diversity in reported routes of transmission across Europe suggest that countries need to maintain and strengthen local prevention and control programmes to interrupt transmission and prevent further infections. Indeed, with evidence of ongoing transmission and the importation of cases to many countries, there is a clear need for countries to improve the quality of surveillance data, especially data on the route of transmission, the country of birth and whether cases are considered to be imported, to improve the data utility. Further work is also needed to assist countries in adopting the current EU case definition to increase the standardisation of the surveillance across countries. ECDC will continue to support Member States in this area and will develop alternative epidemiological methods to complement routine surveillance, such as seroprevalence and sentinel surveys, which will help provide a more complete understanding of the epidemiology.

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