



# HCV infection in Europe

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(formerly the Central and Eastern European Harm Reduction Network - CEEHRN)  
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#### **1. Introduction**

The hepatitis C virus (HCV) is a major public health problem due to its high prevalence, high rates of ongoing transmission and health complications. As many as 80% of people infected with HCV may go on to develop chronic infection. It is a leading cause of cirrhosis and already the most common cause of chronic liver disease and reason for liver transplantation in a number of countries.<sup>1,2</sup> It is estimated that delays in preventing new HCV infections in the 15 western European countries of the EU alone will lead to an increase in treatment costs of an additional €1.4 billion annually.<sup>3</sup>

The scale and urgency of the HCV problem is made alarmingly clear in mortality statistics. The most recent available estimates by the World Health Organization (WHO) on global numbers of deaths (2002) show an estimated 53,700 deaths annually are directly attributable to HCV. However, WHO mortality estimates also indicate that more than 308,000 deaths annually are likely to be due to liver cancer caused by HCV, alongside a significant proportion of the 785,000 deaths due to cirrhosis.<sup>4</sup> Together, these data suggest that as many as 500,000 deaths a year, and possibly even more, could be caused by HCV. Worryingly, morbidity and mortality rates from HCV infection are predicted to continue to rise in the near future.

According to WHO, an estimated 180 million people globally are infected with HCV, with 130 million of these being chronic HCV carriers, which is often asymptomatic but may lead to chronic liver diseases, such as cirrhosis, hepatocellular carcinoma or liver cancer.<sup>5</sup> The prevalence of HCV in the general population varies substantially, from 0.5% in northern Europe to 2% in Mediterranean countries,<sup>6</sup> and reaching over 13% in Egypt.<sup>7</sup>

Due to the nature of the virus, which is about 10 times more infectious than the human immunodeficiency virus (HIV), and therefore requires less exposure to reach high prevalence, there are a large number of undiagnosed individuals. This report

summarizes the known data on HCV prevalence and the extent of reported and undiagnosed cases in selected European countries. It aims to raise awareness about the issue and encourage countries to implement policies that ensure early diagnosis of HCV and effective measures to prevent infection and treat those with HCV infection.

## **2. HCV – reported, estimated and undiagnosed cases in selected European countries**

The following section summarizes the available data from 17 European countries. The key objective of the section is to provide an overview of the HCV burden in different countries and attract attention to the issue that regardless of the country, many people are living with the virus without knowing it. This in part can indicate lack of commitment to the issue on national level, lack of awareness about HCV on state and society level, or lack of accessible testing, adequate reporting and surveillance.

Overall data on HCV is limited for most of the countries – therefore, we calculated the number of undiagnosed cases as a difference between reported cases and estimated cases, if not indicated otherwise. Due to differences in HCV case definition and reporting systems existing across the European countries, the number reported cases and diagnosed cases can differ, since not all diagnosed cases are reported to national surveillance systems.

<b>Country</b>	<b>Reported number of cases</b>	<b>Estimated number of cases in general population</b>	<b>Undiagnosed</b>
Armenia	71 cases reported in 2006 <sup>8</sup>	–	–
Belarus	4,775 <sup>9</sup>	–	–
Bulgaria	–	83,160 <sup>10, 11</sup>	–
Czech Republic	7,372 <sup>12</sup> (1993–2006)	20,440 <sup>13</sup>	~13,068
France		365,055 <sup>14</sup>	Around 56% of cases are identified,

			corresponding to about 44% undiagnosed in 2005 <sup>15</sup>
Georgia	2005–961 cases, 2006–791 <sup>16</sup>	301,500 <sup>17</sup>	–
Germany	47,235 <sup>18</sup>	400,000–500,000 <sup>19</sup>	~352,765–452,765
Hungary	–	60,600 <sup>20</sup>	–
Italy	–	1,800,000 <sup>21</sup>	500,000 – 700,000 <sup>22</sup>
Lithuania	3,000–3,500 <sup>23</sup>	50,000–70,000 <sup>24</sup>	~47,000–67,000
The Netherlands	–	16,250–66,250 <sup>25</sup>	~50,000–55,000
Poland	20,000 <sup>26</sup>	750,000 <sup>27</sup>	~730,000
Romania	–	1,058,000 <sup>28</sup>	–
Russian Federation	2,000,000 <sup>29</sup>	~6,000,000 <sup>30</sup>	–
Spain	–	800,000–1,000,000 <sup>31</sup>	–
Ukraine	1,115 in 2004, 1,212 in 2005 and 1,027 in 2006. <sup>32</sup>	~310,000 –700,000 <sup>33</sup>	–
United Kingdom England and Wales	66,264 <sup>34</sup>	231,000 [144,000–381,000] <sup>36,37 *</sup> About 200,000 chronic infections <sup>38</sup> 466,000–900,000 chronic infections <sup>39</sup>	164,736 [194,736–204,736] 399,736–833,736
Scotland	22,073 <sup>35</sup>	50,000 <sup>40</sup>	27,927

### **Armenia**

Cumulative number of cases or estimate of total number of people living with HCV is not available.

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\* It is estimated that only 12% (95% CI 3-23) of infections are attributable to the non-IDU sub-group, with 57% (95% CI 39-72) occurring in ex-IDUs. The number corresponds to prevalence in people aged 15 – 59, additionally estimated 30,000 – 40,000 under 15 and over 60 can be anti-HCV positive.

### ***Belarus***

Cumulative number of cases not available. Out of all cases reported in 2006, 2026 (20.94/10,000 people) were chronic hepatitis C cases, indicating lack of early detection of HCV cases.<sup>41</sup>

### ***Bulgaria***

Early statistics report data on hepatitis A, B, C and D together. According to the National Centre on Health Information for 2005, the total registered number of acute viral hepatitis infections (hepatitis A, B, C, D) was 85.2/100,000 population.<sup>42</sup>

### ***The Czech Republic***

Number of undiagnosed cases in Prague: 330 HCV cases were identified in 2006, while according to experts there are believed to be about three times more people with HCV who remain undiagnosed.<sup>43</sup>

### ***France***

In France, surveillance of HCV is carried out through population-based seroprevalence surveys every ten years; national surveillance of HCV testing by laboratories; and national surveillance of HCV by voluntary hepatology reference centers.<sup>44</sup>

The availability of testing and tests done increased between 10% to 20% annually between 1998 and 2002.<sup>45</sup>

### ***Georgia***

In 2005, the majority of reported cases were chronic (more than 80% of all cases reported), indicating possible lack of timely diagnosis before the chronic stage of the infection.

### ***Germany***

The number of diagnosed HCV cases is increasing; however chronic cases make up the majority of newly diagnosed cases, indicating lack of early diagnosis.<sup>46</sup>

### ***Hungary***

Only the number of acute hepatitis C cases detected annually is reported via the national communicable disease reporting system. The incidence of the reported cases in 2001-2005 varied between 0.2-0.4/100,000 people.<sup>47</sup>

### ***Italy***

The estimated number of people living with HCV should be interpreted with caution, since prevalence in different regions varies substantially from 3% to over 20% in southern Italy.<sup>48</sup> Moreover, acute HCV cases account for only 10% of total newly identified HCV cases.

### ***Lithuania***

Acute HCV cases are reported; however, there is no registry of chronic hepatitis C cases. According to the population-based study in 2001 anti-HCV prevalence was about 1.7% (in adult population) and 0.5% (among children).<sup>49</sup>

### ***The Netherlands***

According to the National Hepatitis Center in the Netherlands there are about 60,000 people with chronic hepatitis C (0.37% of total population), with around 5,000 to 10,000 knowing their status.<sup>50</sup>

The Working Group for Clinical Virology reported 739 newly diagnosed HCV infections for 2006 (which also includes the chronic hepatitis C cases); however, this number represents likely underreporting, since not all laboratories report their results.<sup>51</sup>

### ***Poland***

The prevalence of HCV in different regions ranges substantially – from 1.2% to over 15%.<sup>52</sup>

### ***Romania***

No number of total reported cases could be obtained. According to the First National Campaign for Hepatitis C, HCV incidence in Romania is the highest in the European Union, with about 44.5 mortalities per 10,000 inhabitants being related to HCV.

### ***The Russian Federation***

No estimation of the total number of people living with HCV has ever been made.

### ***Spain***

HCV is not part of the mandatory notification system in Spain. Official data is collected via the microbiological information system – which covers only 25% of Spain.

Prevalence differs depending on the region, varying from 0.7% (Zamora, 2001) to 2.64% (Catalonia, 2002).<sup>53</sup>

### ***Ukraine***

Case reporting system for HCV infection was introduced in 2004. However, only cases of acute HCV are subject of notification. Since the introduction of the reporting system, the number of cases reported remained stable – 1,115 in 2004, 1,212 in 2005 and 1,027 in 2006.<sup>54</sup>

### ***United Kingdom***

UK Government statistics state that the UK has detected only 19% of these estimated cases and treated less than 5% (these figures are based on the government estimates of 200,000 people with chronic hepatitis C). The treatment figure drops even further taking into account the suggested prevalence of 466,000 – 900,000 people infected.<sup>55</sup>

In Scotland, a review of all country-specific data on incidence and prevalence of HCV among different populations showed that out of an estimated 50,000 people with HCV (about 1% of Scotland population) only 33% were diagnosed. A separate modeling by the authors estimated that 5,500 current and 16,600 former IDUs, in addition to 3,000 individuals that have never injected, were unaware of their chronic hepatitis C status.<sup>56</sup>

## **3. Transmission patterns and risk factors**

In most of the countries assessed, the infection primarily affects men and is concentrated in individuals under the age of 44. Increasing numbers of cases are occurring in young adults (from 15 to 30 years old) as reported from the Belarus, Czech Republic, Germany, Poland, Russia, Spain and United Kingdom.

In countries with a high prevalence in older age groups such as Italy - where 60% of estimated HCV cases are in people older than 65 years<sup>57</sup> - therapeutic injections 30–50 years ago probably had a substantial role in HCV transmission. A review of data for 1997 also showed that diagnostic or treatment procedures in hospitals were among key transmission routes in the countries of central and eastern Europe in the late 1990s (approximately 59–65% of cases in Poland, 59% in Latvia and 46% in Lithuania<sup>58</sup>).

However, after the introduction of blood- and blood-product-screening in most countries, the predominant source of new HCV infections in the past few decades is injecting drug use. This is particularly the case in countries where most newly identified cases occur in young adults. The percentage of newly diagnosed cases attributed to either active injecting drug users (IDUs) or people with a history of injecting varies from 20% to 89%.<sup>59,60,61,62,63,64</sup> In Italy, where the infection is concentrated in older people, about 60% of cases among young people (aged 15-24) occur among IDUs.<sup>65</sup>

Due to the particular efficacy of transmission of HCV through sharing of infected injecting equipment, it is estimated that after 5 years of exposure, the majority of IDUs may acquire infection with HCV<sup>66</sup>. Therefore, the prevalence of HCV among IDUs is extremely high: ranging from 10% to 40% in samples in the Czech Republic and Hungary, to 40–70% in samples in Bulgaria, Georgia, Germany, France, the Netherlands, Italy, Poland and Ukraine, reaching up to 80–90% in Germany, France, Italy, Poland, Romania and Spain.<sup>67, 68, 69</sup>

HCV co-infection with HIV is also common among active and former IDUs, who acquire both viruses from injecting. Such co-infection reduces the chance of recovery from acute HCV, compromises the effectiveness of existing HCV treatment, and accelerates the progression of HCV infection to cirrhosis and liver failure.<sup>70</sup> Liver disease is also becoming one of the lead causes of death in people living with HIV and AIDS<sup>71</sup>

In European countries, high HCV prevalence among IDUs living with HIV has been reported from Russia - 93% among HIV-positive IDUs in Togliatty, and Poland - 90% among HIV positive IDUs in Bialystok. In Spain, three estimates varied from 48% to 95%.<sup>72</sup>

#### **4. Undiagnosed HCV infection – issues and recommendations**

Determining the prevalence of HCV infection is difficult because most acute infections are asymptomatic. Moreover, most countries do not systematically collect data on HCV prevalence or chronic infection, and in a number of the countries assessed HCV is not a mandatory notifiable disease. Even in countries where it is notifiable by law the number of newly diagnosed cases remains underreported. Further, a number of countries (Hungary, Italy, Lithuania, and Ukraine) do not report chronic hepatitis C cases, which means that there is lack of information about how many people are at risk of developing chronic liver diseases and how many people will eventually need hepatitis C treatment.

More data on the estimated prevalence of HCV infection is available from population-based studies performed in Western Europe than Central and Eastern Europe and most of them indicate that most people with HCV remain undiagnosed. In countries where data on acute cases is divided from chronic cases, most newly reported HCV cases are chronic hepatitis C cases (Georgia, Germany, Italy), indicating a lack of early diagnosis.

A number of studies also indicate that the awareness of HCV in the general population is low. According to surveillance data in France (from 2003–2004), 57% of people showing antibodies to HCV (a marker of HCV infection, whether cured or not) knew their status; furthermore, 74% of those who had been infected but had no history of drug use or transfusion were unaware of their infection<sup>73</sup>. During a screening campaign in Lyon, nearly 80% of positive cases were unknown prior to the campaign.<sup>74</sup> At the same time, due to government led campaigns, patient awareness in France has increased substantially – it is estimated that about 56% of those infected now know that they have the infection, compared to 24% in 1994<sup>75</sup>. In comparison, in northern Spain, of 1,170 people who tested positive for HCV antibodies, only 16% were aware of their status.<sup>76</sup>

Data from European countries also suggest that some groups in the population are not currently sufficiently reached by testing, such as drug users<sup>77</sup>, residents of rural areas<sup>78</sup><sup>79</sup> and homeless people, with only limited attention given to HCV status among prisoners.

## **Recommendations**

- Data from across European countries show that there are a large number of people who remain undiagnosed and are at risk of developing chronic hepatitis C. Moreover, most newly diagnosed cases are of chronic hepatitis C, which indicates a lack of early diagnosis. Therefore, greater commitment from policy-makers, health care officials and health care providers is needed to raise awareness about HCV and to facilitate and improve early diagnosis among the general population as well as among risk groups, such as IDUs and prisoners;
- Improving diagnostic services for HCV and making testing and counseling accessible and affordable through anonymous, free-of-charge testing is crucial to prevent further infections, and to limit the burden of HCV through timely diagnosis, treatment and care of people with HCV;
- Available data from across European countries show that HCV is a major and increasing health issue among IDUs, suggesting that scaling-up of harm reduction interventions is a priority, especially in settings with high HCV prevalence among people injecting drugs. Further, increasing the coverage of IDUs by HCV testing requires linkage of HCV testing and counselling to already established harm reduction services;
- Different reporting systems and reporting practices exist in European countries, with most of the available surveillance data coming from western European countries (France, Germany, the Netherlands or United Kingdom). A hepatitis C case definition needs to be adopted on the European level;

This analysis highlights the ongoing need to improve the availability and quality of national, regional and global estimates of HCV infection for evaluation of the burden of the infection as well as crucial for forming effective HCV prevention strategies, taking into account current risk factors and transmission patterns. Collaboration between researchers, scientists and healthcare officials as well as service providers is crucial in conducting population-based studies (especially for central and eastern Europe) with the goal of evaluating the current dynamic of HCV transmission as well as evaluating the burden of the problem, with the goal of forming effective reporting

systems, prevention and management strategies, ensuring further prevention and timely treatment and care services for those already infected.

## **Appendix 1: Methodology**

The information was collected in three stages:

- Assessment of existing secondary data from international agencies and organizations: Centers for Disease Prevention and Control (CDC), European Association for the Study of the Liver (EASL), European Center for Disease Prevention and Control (ECDC), European Liver Patient Association (ELPA), European Monitoring Center for Drugs and Drug Addiction (EMCDDA), Viral Hepatitis Prevention Board (VHPB), and WHO Europe were contacted and/or information available on-line assessed;
- Literature review: A search was conducted through the on-line versions of Journal of Hepatology, Journal of Gastroenterology & Hepatology, European Journal of Gastroenterology & Hepatology, Hepatology International, Gut – An International Journal of Gastroenterology & Hepatology, and Comparative Hepatology. Additionally, a search was carried out through PubMed as well as official reports of national healthcare agencies available in English or Russian;
- Questionnaire: A standardized questionnaire was developed and sent to experts in countries; WHO country offices, national health protection agencies, hepatology and patient associations/organizations, NGOs and harm reduction programmes, with the goal of collecting data on HCV prevalence in selected countries.

The primary geographical scope was 15 European countries – Armenia, the Czech Republic, Denmark, Egypt, France, Georgia, Germany, Hungary, Italy, Poland, Romania, Russia, Spain, Ukraine, and United Kingdom. However, the information request was sent out to experts in 25 countries of Europe with the goal of collecting as much data as possible. As a result, after follow-up, information was obtained from 17 countries – Armenia, Belarus, Bulgaria, the Czech Republic, France, Georgia, Germany, Hungary, Italy, Netherlands, Lithuania, Poland, Romania, Russia, Spain, Ukraine and United Kingdom.

The focus of the information search was reported HCV cases, estimated prevalence in general population and different risk groups and estimated number of undiagnosed cases. The undiagnosed cases were identified by the difference between reported and estimated number of cases if not indicated otherwise in section 2 of this report.

## Appendix 2: Limitations

Access to health care, availability of tests and diagnostics policies as well as patient advocacy may significantly affect the number of people being diagnosed with the virus; however, the analysis of these factors was not within the remit of this study and must still be evaluated to form effective policies that will ensure early diagnosis and efficient treatment and care for people living with the virus.

Due to the diverse surveillance and reporting systems existing in countries and the fact that HCV is not a mandatory notifiable disease in a number of countries, the number of reported cases in some cases may not always correspond to diagnosed number of cases. This should be taken into account when interpreting the number of undiagnosed cases.

Most of the data were obtained from population-based surveys and surveys of high risk populations available through either experts or on-line scientific journals. Based on the available studies, it is difficult to ascertain the incidence (new onset of infection) of HCV accurately, because acute infection in most cases is asymptomatic. Thus, most epidemiological data available to date describe the prevalence (current presence) of the infection, which does not necessarily reflect current transmission trends.

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