

Enhanced surveillance of hepatitis C in the EU, 2006 – 2012

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Received May 2014; accepted for publication October 2014

SUMMARY. Hepatitis C is a major public health issue across Europe, and with rapidly evolving developments in the therapeutic field, it is essential that countries have access to epidemiological information. In 2011, The European Centre for Disease Prevention and Control (ECDC) introduced enhanced surveillance of hepatitis C across EU/EEA countries collecting routine data from national notification systems using standardized case definitions. Data collected from 2006 to 2012 indicate a high burden of disease with great variation in reported cases between countries. Most cases occurred among young adult males, and although injecting drug use dominated across all cases, there were increasing numbers of acute cases reported among men who have sex with men. Geographically, the reported data were the inverse of what may be expected based on findings from recent prevalence surveys in a number of EU/EEA countries. Unexpectedly, low figures were reported

through notification systems in some southern and eastern European countries where prevalence is known from surveys to be high. This discrepancy highlights the limitation of surveillance data for a disease such as hepatitis C which is largely asymptomatic until a late stage, so that notifications reflect testing practices rather than real occurrence of disease. Further improvements to the quality of the data are important to increase data utility. Improved understanding of national testing practices is necessary to allow a better interpretation of surveillance results. Additional epidemiological studies alongside routine case-based reporting in notification systems should also be considered to better estimate the true disease burden across Europe.

Keywords: epidemiology, Europe, hepatitis C, surveillance.

INTRODUCTION

Hepatitis C virus (HCV) is a major cause of cirrhosis and liver cancer around the world and with rapidly evolving developments in the therapeutic field is the focus of much attention [1]. Most individuals infected with HCV have no acute clinical symptoms and up to 25% resolve the infection spontaneously. The remainder become chronically infected with a subsequent risk for developing serious liver disease [2]. Recent estimates suggest that between 120 and 170 million people are infected with HCV globally [3,4]. Across Europe, the incidence and prevalence of HCV infections vary between countries [5]. HCV is most commonly transmitted through percutaneous exposure. In most European countries, where routine blood screening takes place, the majority of new infections occur through injecting drug use (IDU) with a small proportion of infections occurring iatrogenically and to a lesser extent in individuals exposed through unhygienic body piercing or

tattooing [6,7]. In Europe, sexual and perinatal transmissions of HCV are less commonly reported routes of transmission [8].

With increasing attention focused upon hepatitis C on account of the developments in the therapeutic arena, it is more important than ever that health planners have access to robust epidemiological information. A survey by the European Centre for Disease Prevention and Control (ECDC) in 2010 described the hepatitis surveillance systems in all European Union (EU) and European Economic Area (EEA) countries [9]. However, this survey found substantial differences in these systems, and the results confirmed the findings of a previous review of the published literature which found an inability for many countries to distinguish between acute and chronic cases [10].

Subsequent to this survey, a network of national experts from each EU/EEA country for the enhanced surveillance of hepatitis was established by ECDC. ECDC facilitates the surveillance of communicable diseases under EU surveillance through the European Surveillance System (TESSy), a web-based platform for data submission, warehousing and retrieval. The results presented in this paper are from the first collections of HCV data reported through this surveillance system.

Abbreviations: HCV, hepatitis C virus; IDU, injecting drug use.

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MATERIALS AND METHODS

The methods for data collection and analysis have been described previously in the paper Enhanced surveillance of hepatitis B in the EU, 2006 – 2012 in this edition.

Countries were formally requested to follow the 2012 EU hepatitis C case definitions for reporting at the European level [11] (text box), but data were still accepted if defined using other case definitions.

EU 2012 case definition for hepatitis C

Hepatitis C:

Clinical criteria: Not relevant for surveillance purposes

Laboratory criteria:

At least one of the following three:

- Detection of hepatitis C virus nucleic acid (HCV RNA)
- Detection of hepatitis C virus specific antigen (HCV core)
- Hepatitis C virus specific antibody (anti-HCV) response confirmed by a confirmatory (e.g. immunoblot) antibody test in persons older than 18 months without evidence of resolved infection

Epidemiological criteria: Not relevant for surveillance purposes

Case classification:

Possible case – N/A

Probable case – N/A

Confirmed case – Any person meeting the laboratory criteria

NOTE: The following combination of laboratory tests shall not be included or reported:

Resolved infection: Detection of hepatitis C virus antibody and no detection of hepatitis C virus nucleic acid (HCV RNA negative result) or hepatitis C virus core antigen (HCV core negative result) in serum/plasma.

Acute and chronic hepatitis C infections were distinguished using the following criteria (see text box below).

The map included in the results shows the overall notification rates of hepatitis C cases across EU/EEA countries. Countries were included in the data analysis, if their surveillance system were known to capture data on both acute and chronic cases, even if a large proportion of cases were classified as 'unknown'. Whilst there are limitations to this approach, it provides more complete data for comparison across countries.

RESULTS

From 2006 to 2012, 206 332 cases of hepatitis C were reported from 29 EU/EEA countries. No data were avail-

Stage	Definition
Acute	Recent HCV seroconversion (prior negative test for hepatitis C in last 12 months) or Detection of hepatitis C virus nucleic acid (HCV RNA) or hepatitis C virus core antigen (HCV core) in serum/plasma and no detection of hepatitis C virus antibody (negative result)
Chronic	Detection of hepatitis C virus nucleic acid (HCV RNA) or hepatitis C core antigen (HCV core) in serum/plasma in two samples taken at least 12 months apart*
Unknown	Any newly diagnosed case which cannot be classified according to the above definition of acute or chronic infection

*In the event that the case was not notified the first time

able from Liechtenstein or France, and only 19 countries were able to provide data for every year. The data provided had varying degrees of completeness across countries and over time. Overall, there was an increase in data completeness across most variables from 2006 to 2012. The completeness in 2012 was highest for the age and gender variables at over 96%. The completeness of the 'StageHEP' variable, which defines the cases as acute or chronic, was only 10.8%.

Sixteen countries were able to provide data in 2012 using the 2012 revised EU case definition. Three of these countries (Hungary, Malta, Lithuania) just submitted data on acute cases as only acute hepatitis C is notifiable on a national basis. Seven countries provided data according to the previous EU case definition (EU 2008) which is similar to the EU 2012 case definition as it also captures data on both acute and chronic infections and is based on laboratory criteria.

EPIDEMIOLOGICAL DATA

30 606 cases of hepatitis C were reported from 27 countries in 2012 (no data from Belgium, France, Liechtenstein and Spain). The overall crude notification rate was 7.9 cases per 100 000 population. In 2012, the number of cases reported by countries ranged from 24 in Malta (5.7 cases per 100 000) to 13 474 (21.8 cases per 100 000) in the United Kingdom. Reported rates in the north European countries were higher than in southern and east European countries (Fig. 1).

In 2012, 508 cases (1.7%) were reported as 'acute', 3905 (12.8%) as 'chronic', 23 712 (77.5%) as 'unknown' and 2481 cases (8.1%) could not be classified due to the format of the data provided. Twelve countries reported data

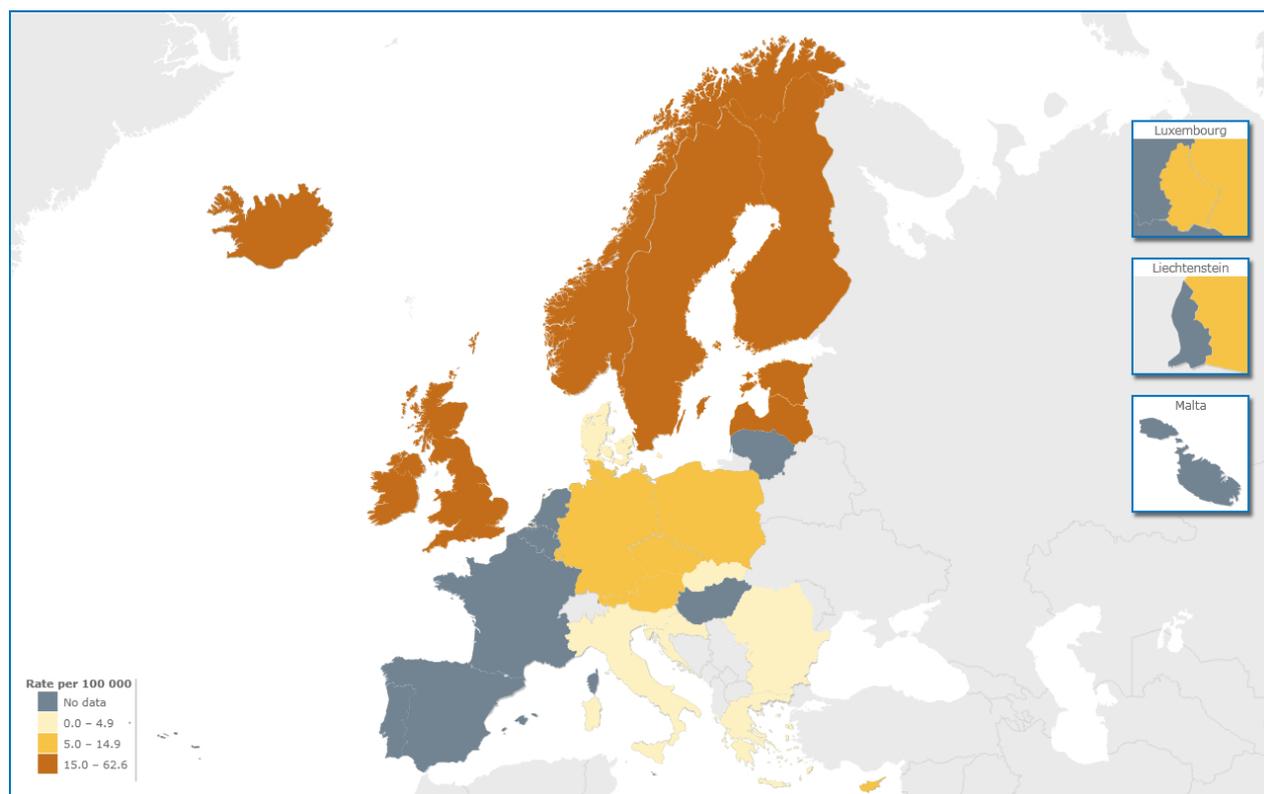


Fig. 1 Rate of reported hepatitis C cases per 100 000 population in selected EU/EEA countries, 2012. Country reports – Austria, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, Germany, Greece, Iceland, Ireland, Italy, Latvia, Luxembourg, Norway, Poland, Romania, Slovakia, Slovenia, Spain, Sweden, United Kingdom.

on acute cases of hepatitis C in 2012, with numbers ranging from nine cases in Slovenia (0.4 cases per 100 000) to 139 cases in Austria (1.6 cases per 100 000). Ten countries reported chronic cases in 2012. The numbers of chronic cases showed great variation across countries from 40 cases in Greece (0.3 cases per 100 000) to 1230 cases in Latvia (60.2 cases per 100 000). Fifteen countries provided data on 'unknown' cases with the number of 'unknown' ranging from 2 cases in Denmark (<0.1 cases per 100 000) to 12 127 cases in the United Kingdom (19.6 cases per 100 000).

The number of reported cases increased from 27 354 cases in 2006 to 30 606 cases in 2012. There was a generalized increase in the number of reported cases across all disease categories, but this was greatest among acute cases, with an increase from 164 cases in 2006 to 508 cases in 2012. The overall rate fell from 9.3 cases per 100 000 in 2006 to 6.8 in 2007 and has remained fairly stable at just over seven cases per 100 000 since.

In 2012, 19 395 of all reported cases for whom gender was reported were males (10.8 cases per 100 000) and 10 774 cases were females (5.5 cases per 100 000). This represents a male-to-female rate ratio of 2. The male to

female rate ratio remained stable over the reporting period. The number of males was mostly greater than the number of females for acute, chronic and unknown cases across all countries.

Just over a half (54.0% of cases) of all the hepatitis C cases reported in 2012 were aged between 25 and 44, and 9.5% of cases were aged under 25 years. The notification rate was highest for both males and females in the 25–34 age group at 22.3 per 100 000 in males and 13.3 per 10 000 in females (see Fig. 2).

The age distribution by disease status shows that reported cases of acute infection were younger than reported cases of chronic infection, with 17.2% of acute cases aged under 25 years compared to 7.8% of chronic cases. The notification rates by age category showed little change over time.

Data regarding transmission of hepatitis C were complete for only 25.2% of cases in 2012 and are therefore not presented by country. Overall, the most commonly reported route of transmission was injecting drug use accounting for 66.8% of all cases with known transmission route in 2012 (Table 1). The next most commonly reported transmission routes were nosocomial transmission, nonoccupational injuries and blood and blood products which

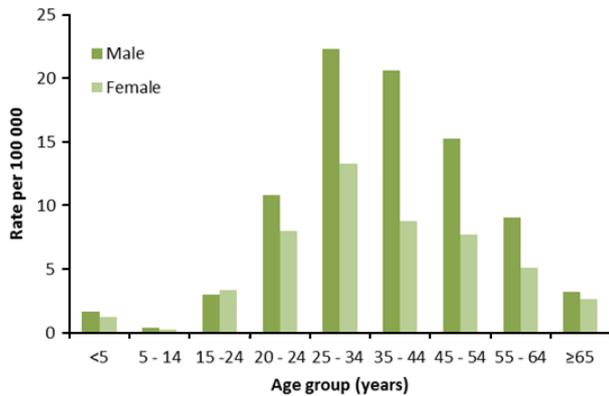


Fig. 2 Rate of reported hepatitis C cases (acute, chronic and unknown) per 100 000 by age group and gender, EU and EEA countries, 2012. Country reports: Austria, Cyprus, Czech Republic, Denmark, Estonia, Finland, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Portugal, Romania, Slovakia, Slovenia, Sweden, United Kingdom.

accounted for 8.0%, 5.8% and 4.6% of all cases, respectively. Of cases reported as having been transmitted through blood and blood products, 99.3% were classified as chronic or 'unknown'.

Across all disease status groups, injecting drug use was the most common route of transmission, although this proportion was lower among acute cases than among those classified as chronic or 'unknown'. Among acute cases, the other main routes of transmission included nosocomial

transmission (26.5%) and men who have sex with men (14.6%). However, the number of acute cases with complete information on transmission was low, so these figures may be subject to random fluctuation.

Between 2006 and 2012, a few changes in the reported transmission category were noted. The proportion of acute cases reported as male-to-male transmission increased from 0.8% in 2006 to 14.6% in 2012. There was also a rise in acute and chronic cases reported as due to unspecified sexual transmission from 1.9% of acute cases and 0.1% of chronic cases to 5.3% and 8.2% of cases, respectively.

DISCUSSION

This paper presents the first analysis of the enhanced hepatitis C surveillance data in the EU/EEA [12,13]. The findings indicate a high number of hepatitis C cases reported from countries across Europe with considerable variation between countries. The majority of all the reported cases are classified as either 'chronic' or 'unknown'. As acute hepatitis C is difficult to diagnose clinically or serologically, it is likely that most 'unknown' cases represent chronic infections. Indeed, countries able to define cases as acute or chronic report considerably more chronic cases than acute cases.

The variation between countries in the distribution of reported acute, chronic and unknown cases is likely to be related to a number of factors including differences in the ability to determine disease status as well as the quantity of diagnostic testing. Among countries able to report all categories of hepatitis C, the highest overall notification

Table 1 Transmission category of hepatitis C cases by disease status in EU/EEA countries, 2012*

Transmission category	Acute (n = 369) %	Chronic (n = 1699) %	Unknown (n = 1165) %	Total (n = 3233) %
Injecting drug use	29.9	58.6	90.5	66.8
Nosocomial (includes hospital, nursing home, etc.)	26.5	9.5	0.0	8.0
Men who have sex with men	14.6	0.1	0.1	1.8
Heterosexual transmission	10.3	3.3	0.0	2.9
Sexual transmission (not specified)	5.6	4.9	0.3	3.4
Nonoccupational injuries (needle stick, bites, tattoos, piercings)	5.3	8.2	2.6	5.8
Other [†]	4.0	4.2	3.9	4.0
Household	1.5	0.8	0.0	0.6
Haemodialysis	0.8	0.5	0.0	0.3
Blood and blood products	0.6	7.4	1.9	4.6
Mother-to-child transmission	0.5	1.4	0.8	1.1
Needle stick and other occupational exposure	0.3	1.2	0.0	0.7
Organ and tissues	0.0	0.0	0.0	0.0
Total	100.0	100.0	100.0	100.0

Country reports: Austria, Czech Republic, Denmark, Estonia, Finland, Germany, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Portugal, Romania, Slovakia, Sweden and United Kingdom. *Analyses undertaken by disease status category for all cases where transmission category is not classified as 'unknown'. [†]The route of transmission is known, but cannot be attributed to any of the specified transmission categories.

rates are in the north European countries and the lowest rates in southern and east European countries. In countries able to report all categories of hepatitis, most of these infections are likely to be chronic, as noted previously, and the overall geographical trends in infections are the opposite of findings from prevalence surveys. Indeed, the results of prevalence surveys show that countries in the south and east of the EU/EEA have a much higher prevalence of chronic HCV infection than those in the northwest [14–18].

The observed discrepancy between the reported cases of hepatitis C collected through surveillance systems, and the results from prevalence surveys highlight the challenge of interpreting hepatitis C surveillance data. Because hepatitis C is a largely asymptomatic disease, most cases are identified through screening initiatives targeting 'at risk' populations, and this explains why routine surveillance data are so strongly influenced by local testing. Surveillance data do not provide a clear epidemiological picture and therefore need to be examined carefully in the light of local screening practices and population denominator testing data, where available. ECDC is committed towards improving the quality of epidemiological data and is currently working with key Member States to explore the many differences in testing and surveillance at the local level to try and explain the observed discrepancies in detail. It is hoped that this work will inform future improvements in the surveillance of hepatitis C.

Trends in the overall numbers and notification rates across countries over time are influenced by the changes in the number of countries reporting data over time. Differences in the age and gender distribution between acute and chronic cases are most likely related to the differences between risk groups. Reported data indicate that hepatitis C predominantly affects young adult males. This reflects the demographic profile of the main risk group of people who inject drugs. Men who have sex with men (MSM) infected with HCV tend to be younger than those infected through injecting drug use.

Injecting drug use dominates as the main route of transmission across all categories of cases. The next most commonly reported routes were nosocomial transmission, nonoccupational injuries and through blood and blood products. Most of the cases reported as the latter transmission route were chronic cases probably reflecting transmission prior to routine screening of blood and blood products. There were clear changes in the reported transmission categories over time, most strikingly a steadily increasing proportion of cases among MSM. There have been reports of an increase in acute hepatitis C infections among HIV-infected MSM in several European countries [19], and routine screening of HIV-positive MSM is undertaken in these countries. This screening may have artificially elevated the number of acute cases reported as occurring among MSM.

The data presented in this paper originate from routine national surveillance with cases defined according to the

latest EU case definition based on laboratory criteria. The implementation of enhanced surveillance with this new case definition is an important step towards the standardisation of hepatitis C surveillance data across European countries. However, there are many challenges that hamper a clear interpretation of the data.

Firstly, less than two-thirds of the countries reporting in 2012 were able to provide data using the revised EU case definition. However, 23 countries used either the revised or previous EU case definition which both capture acute and chronic cases and are based on laboratory criteria. A greater problem is the legislation in a few of the countries which supports the notification of acute viral hepatitis only. The classification of cases by disease status was also a particular issue, with the majority of reported cases classified as 'unknown'. This problem with the criteria reflects the widely recognized difficulties in diagnosing hepatitis C, especially acute hepatitis C [15,20–22].

Differences in case definitions and reporting practices between countries are expected to improve as more countries are expected to adapt their surveillance systems to incorporate the new EU case definitions. However, this heterogeneity does highlight the need to have a better understanding of national surveillance systems. Although information on surveillance practices across European countries [10] was collated prior to the implementation of enhanced surveillance, more detailed and up-to-date information would help to better interpret the data.

The incomplete reporting of disease status limits the presentation of the data and the identification of geographical and temporal trends for acute and chronic cases.

In addition, many of the epidemiological variables were incomplete, and this further restricted the analysis of the data. Although data completeness improved over the reporting period, further work is necessary to address this issue.

In conclusion, the importance of better epidemiological information on hepatitis C to help tailor local public health responses is increasingly recognized with the advent of an exciting therapeutic era. The implementation of enhanced surveillance of hepatitis C across EU/EEA countries using a standardized methodology is an important step in the right direction. The results from the first data collections indicate a significant burden of disease and great variation between countries. Differences between national surveillance systems remain, which pose a major challenge in interpreting the results. The strong geographical trend in reported cases, which is divergent to what may be expected from prevalence surveys, indicates that reported data largely reflect local testing policies and practice, and this highlights the weakness of the data analysed on its own. The data should be further considered alongside other epidemiological data sources such as morbidity and mortality data and prevalence surveys, as well as information on national surveillance, screening/testing and prevention programmes. ECDC and the Member States need to review

which methods are best for providing robust epidemiological data on hepatitis C to support Member States in their efforts to tackle the public health challenges posed by this infection.

ACKNOWLEDGEMENTS

The authors would like to thank all the European Hepatitis B and C Network members and national hepatitis and

surveillance contact points for their contributions with respect to reporting national hepatitis data and for commenting on the analysis of the data. Thanks also to Phillip Zucs, Denis Coulombier and Johan Giesecke for their considered and valued comments on drafts of the paper. A special thanks to Gaetano Marrone for his support with the data analyses.

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