Survey of surveillance systems and select prevention activities for hepatitis B and C, European Union/ European Economic Area, 2009

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Citation style for this article:
Duffell EF, van de Laar MJ. Survey of surveillance systems and select prevention activities for hepatitis B and C, European Union/European Economic Area, 2009. Euro Surveill. 2015;20(13):pii=21080. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=21080

Article submitted on 05 March 2014 / published on 02 April 2015

Hepatitis B and C viral infections are leading causes of hepatic cirrhosis and cancer. The incidence and prevalence of both hepatitis B and C varies across European countries. European wide surveillance data help to understand the dynamic epidemiology of hepatitis B and C, which is important for the implementation and effectiveness of prevention and control activities. Comparison of surveillance data between countries in Europe is hampered by the differences in national healthcare and reporting systems. This report presents the results of a survey in 2009 which was undertaken to collect baseline information on surveillance systems and core prevention programmes for hepatitis B and C in individual European Union/ European Economic Area countries. The results provide key information to aid the interpretation of surveillance data, and while indicating heterogeneity in national surveillance systems and programmes, they highlight the potential of these systems. This resource has supported the implementation of a standardised European enhanced surveillance programme.

Introduction

Infections with hepatitis B (HBV) and C (HCV) viruses can result in acute and chronic hepatitis and are leading causes of hepatic cirrhosis and cancer. Both infections are globally prevalent. According to the World Health Organization (WHO), one third of the world's population has been infected with HBV and around 240 million people have chronic infection [1,2]. The WHO additionally estimates that 2.8% of the global population have been infected with HCV, resulting in 185 million people with antibodies to HCV [3,4]. Across Europe, HBV and HCV are prevalent, but the incidence and prevalence vary between countries [5], with some specific subpopulations within countries particularly affected, such as people who inject drugs (PWIDs) and men who have sex with men (MSM) [6-8].

The modes of transmission of HBV and HCV differ and vary considerably around the world [6-10]. In areas where the prevalence of HBV is high (defined as prevalence of hepatitis B specific antigen (HBsAg) ≥ 2%), transmission is mostly perinatal or during childhood through horizontal transmission to close household contacts. In areas of lower prevalence, HBV transmission usually occurs later in life mostly through injecting drug use (IDU) and sexual exposure [11]. HCV is most commonly transmitted through percutaneous exposure. In countries that have introduced blood screening and have good systems of infection control, most infections appear to have occurred through IDU. Some infections however, occur among renal dialysis patients, patients who have undergone surgical procedures and individuals exposed through body piercing or tattooing [12]. Sexual and perinatal transmission of HCV is uncommon [13].

Because transmission of HBV and HCV varies between countries, the most effective prevention strategy depends on the underlying epidemiology or its drivers. Prevention strategies tackling HBV in all European countries include either a universal or targeted vaccination programme. The prevention of HCV infection, however, is more problematic, as there is currently no effective vaccine. Reducing the HCV disease burden is achieved through early diagnosis and effective prevention strategies to reduce or eliminate the risk for transmission from nosocomial exposures (e.g. blood transfusion, unsafe injection practices) and high-risk practices (e.g. IDU) [9,14].

Harmonisation of the surveillance of viral hepatitis in the European Union (EU) was identified by the European Parliament in 2006 as one of the priorities for the European Centre for Disease Prevention and Control (ECDC) [15,16]. Robust surveillance information is important for effective public health action. Comparison of surveillance data between countries is nevertheless hampered by differences in healthcare, screening practices and surveillance systems [15]. Detailed information on national surveillance and

prevention programmes is important for a clear interpretation of epidemiological data at the international level. There is known to be variation in the case definitions used and no clear distinction in the reporting between acute and chronic hepatitis B and C cases in many countries [15].

In order to provide a foundation for the development of enhanced surveillance of hepatitis B and C across Europe, ECDC undertook a survey in 2009 to describe existing national surveillance systems and core prevention programmes among EU/European Economic Area (EEA) countries. The survey aimed to build upon the findings of Rantala and van de Laar in 2008 whereby a preliminary review of programmes in a select number of European countries was undertaken [15].

Box

European Union 2002 and 2008 case definitions for hepatitis B and C[a]

EU 2002/253/EC Hepatitis B (acute) case definition:

Clinical criteria – In symptomatic cases, clinical picture compatible with hepatitis e.g. discrete onset of symptoms and jaundice or elevated serum aminotransferase levels.

Laboratory criteria – IgM antibody to hepatitis B core antigen (anti-HBc) positive. Detection of hepatitis B virus (HBV) nucleic acid in serum.

EU 2002/253/EC Hepatitis C case definition:

Clinical criteria – in symptomatic cases, clinical picture compatible with hepatitis, e.g. discrete onset of symptoms and jaundice or elevated serum aminotransferase levels.

Laboratory criteria – Detection of hepatitis C virus (HCV) specific antibodies. Detection of HCV nucleic acid from clinical samples.

EU 2008/426/EC Hepatitis B (acute) case definition:

Clinical criteria - Any person with a discrete onset of symptoms (e.g. fatigue, abdominal pain, loss of appetite, intermittent nausea and vomiting) AND at least one of the following three: fever; jaundice; and elevated serum aminotransferase levels.

Laboratory criteria – Hepatitis B virus core IgM antigen specific antibody response. Laboratory results need to be interpreted according to the vaccination status.

Epidemiological criteria -An epidemiological link by human to human transmission (e.g. sexual contact, vertical transmission or blood transmission).

EU 2008/426/EC Hepatitis C (acute) case definition:

Clinical criteria – not relevant for surveillance purposes.

Laboratory criteria – at least one of the following two: Detection of HCV specific antibodies; detection of HCV nucleic acid in serum OR HCV specific antibody response confirmed by a different antibody test.

[a] Replaced in 2012 by new case definitions, European Commission 2012/506/EU, which capture data on acute and chronic cases of hepatitis B and C.

Methods

All 27 EU Member States as well as Iceland, Liechtenstein and Norway were invited to participate in a web-based survey on surveillance and prevention of HBV and HCV. Nominations of technical experts for hepatitis B and C surveillance were requested from the formal ECDC contact point at each of the national organisations for surveillance. The link to the questionnaire, along with a cover letter, was sent to these nominated contacts or to the general ECDC contact person if no nomination was received in September 2008. All non-responder countries were followed up with a reminder email and countries were able to upload their data until October 2009.

The survey was divided into separate parts for hepatitis B and C and further sub-divided into four sections covering: (i) general aspects of hepatitis surveillance (including case definitions and objectives); (ii) key sources and the type of data collected; (iii) other questions related to surveillance e.g. linkage to other data sources; and (iv) local provision of screening and vaccination services.

Survey data were analysed in Excel version 2007 (Microsoft, Redmond/Washington, United States). The results were collated into a report and the participants were asked to validate their country-specific information to check that it had been correctly analysed and interpreted.

Data collected on vaccination programmes were validated and completed with data from the Vaccine European New Integrated Collaboration Effort (VENICE) project (http://venice.cineca.org/) and data from the European surveillance network for selected vaccine-preventable diseases (EUVAC.NET) (http://www.euvac.net/).

Results

All 30 countries participated in the survey, the Czech Republic only completed the hepatitis C section and Liechtenstein completed only the hepatitis B section. The overall response rate was high at 29 of 30 for each disease.

Surveillance systems

A detailed summary of the information on national surveillance systems for hepatitis B and C is shown in Table 1. All countries reported having a system in place for the surveillance of hepatitis B and C and this system is mandatory for most of these countries for both hepatitis B (27/29) and hepatitis C (26/29). The survey asked if the surveillance system could be defined as active, which meant that the surveillance system was based on the initiative of public health officials to actively contact physicians, laboratory, hospital staff or other relevant sources to report data. Only four countries reported having an 'active' surveillance system for hepatitis B and five countries for hepatitis C. Around half the countries (15/29 for hepatitis B and 14/29 for

Table 1

Summary, by disease, of information obtained on national surveillance systems for hepatitis B and C, European Union/ European Economic Area countries, 2009 (n=30)[a]

Properties	Number of countries	
	Hepatitis B	Hepatitis C
Type of surveillance		
Mandatory	27	26
Voluntary	2	3
Passive[b]	25	24
Active[c]	4	5
Case-based data (individual anonymised patient data)	26	26
Aggregate data (data aggregated at regional or national level)	8	9
Type of surveillance system		
A hepatitis specific surveillance system	15	14
Several different hepatitis specific surveillance systems, one of which is the most comprehensive	3	3
Several different hepatitis specific surveillance systems, none is the most comprehensive	1	2
Syndromic surveillance[d] of viral hepatitis	5	5
Other	5	5
Objectives		
Monitor trends	29	29
Detect outbreaks	26	25
Monitor changes in disease distribution	28	27
Evaluate and plan control measures	28	28
Improve knowledge of epidemiology	27	28
Other	5	2
Case definitions		
EU 2002/253/EC[e]	3	4
EU 2008/426/EC[e]	8	11
Possibly European Union (lack of information)	5	5
Extended European Union	5	4
No case definition	3	2
Other	5	3
Case classification[f]		
Possible	1	1
Probable	15	6
Confirmed	28	28
Acute	29	27
Chronic	17	18
Asymptomatic	9	12
Suspected	1	1
Duplicates		
Including duplicates	4	9
Under-reporting		
No	3	2
Exists	26	27

[a] Of the 30 countries, all but Liechtenstein completed the survey for hepatitis B, and all but the Czech Republic completed the survey for hepatitis C.

[b] A surveillance system based on healthcare providers reporting notification data on their own initiative without being reminded.

[c] A surveillance system based on a public health officials initiative to actively contact physicians, laboratory or hospital staff or other relevant sources to report data.

[d] A surveillance system where public health officials monitor disease indicators in real-time or near real-time to detect outbreaks of disease earlier than would otherwise be possible with traditional public health methods.

[e] See text box.

[f] As defined by country.

Table 2

Set of variables in national surveillance systems for hepatitis B and C, European Union/European Economic Area countries, 2009 (n=30)[a]

Characteristics		Number of countries	
		Hepatitis B	Hepatitis C
Basic data	Patient ID	24	22
	Date of birth or age	29	29
	Sex	29	29
	Country of birth	16	16
	Place of residence	28	27
	Date of onset of the disease	26	23
	Date of diagnosis	21	21
	Date of reporting/notification	27	28
	Date used for statistics	19	18
	Country where infection has most likely been acquired	19	19
	Immunisation status	24	11
	Outcome	18	15
Clinical and case classification information	Clinical symptoms	16	13
	Laboratory results	23	24
	Epidemiological information	21	22
Transmission route/risk factors	Homosexual contact	16	14
	Heterosexual contact	16	13
	Injecting drug use	21	21
	Mother HBsAg/HCV-positive	19	15
	Close family member HBsAg/HCV- positive	20	17
	Sex partner HBsAg-positive	17	17
	Blood or blood product transfusion	21	21
	Invasive healthcare procedure/dental treatment	18	20
	Organ transplantation	16	17
	Haemodialysis	18	19
	Needle injury or other occupational exposure	18	19
	Tattooing/body piercing	18	19
	Other	8	8
Other factors	Hospitalisation	19	17
	Length of hospitalisation	8	8
	Genotype information	1	3

HCV: hepatitis C virus; HBsAg: hepatitis B specific antigen; ID: identity.

[a] Of the 30 countries, all but Liechtenstein completed the survey for hepatitis B, and all but the Czech Republic completed the survey for hepatitis C.

hepatitis C) reported that they had a specific hepatitis surveillance system in place and several countries (4 for hepatitis B and 5 for hepatitis C) reported more than one surveillance system for hepatitis B or C. In five countries (Hungary, Italy, Latvia, Romania and Slovakia), the reporting systems for hepatitis B and C are part of a syndromic surveillance system.

Most countries accorded with the specific objectives for surveillance listed in the questionnaire with only a few countries identifying 'other' objectives (Table 1). These 'other' objectives included 'the resource allocation and healthcare planning' identified by Ireland and the 'monthly publication of statistics required by law' noted by Luxembourg.

There were differences in the case definitions between countries (Table 1). A total of 11 of 29 countries confirmed that they used one of the standardised EU case definitions (textbox) for hepatitis B and 15 of 29 reported they did so for hepatitis C. Three countries reported there being no case definition in use for hepatitis B and two countries reported no case definition for hepatitis C.

Of the 29 countries participating in the hepatitis B questionnaire, 28 reported that confirmed cases were included in surveillance and 15 reported that probable cases were also included. All 29 countries included acute hepatitis B cases and 17 countries included chronic cases. Thirteen of the 17 countries that include

both acute and chronic cases reported that they could differentiate between acute and chronic infection. In relation to hepatitis C surveillance, 28 countries included confirmed cases in their national systems and five countries included probable cases. Twenty-seven of the 29 countries included acute hepatitis C cases. Eighteen countries included both acute and chronic cases and half of these countries reported that they were able to differentiate between these cases.

Data sources were very similar for both diseases with physicians being cited as the main source. In addition, nine countries reported sexually transmitted infection (STI) clinics as a source of data for hepatitis B and six countries reported these clinics as a source for hepatitis C. Seven countries also collect data for these infections through laboratory networks, four countries collect the data through sentinel surveillance and five countries collect it through serosurveys in the general population.

Electronic data collection was the most common route reported (23/29 for hepatitis B; 25/29 for hepatitis C). Four countries (Bulgaria, Norway, Poland and Romania) collect hepatitis C data using a paper-based system and three countries use this system for hepatitis B (Poland, France and Liechtenstein). Some countries reported using both paper and electronic data collection.

Twenty-six of the countries had case-based data available for both hepatitis B and C while three countries (Bulgaria, Poland and Romania) reported the availability of only aggregated data at the time of the survey. Several countries reported that duplicates may be included in the national surveillance system (4/29 for hepatitis B; 9/29 for hepatitis C). Twenty-six countries reported that under-reporting exists for hepatitis B and 27 countries reported this for hepatitis C.

Countries collected data on a number of different variables (Table 2). Over two-thirds of the countries collected a broad set of data covering demographic and clinical data as well as information on transmission routes. Other countries, such as Belgium, Luxembourg and Spain, collected a much more select dataset focused on basic demographic data. Few countries collected data on genotype information or length of hospitalisation.

Ten of the countries reported that they can link their hepatitis data to local registers on liver transplants, liver cancer, mortality and/or hospital admissions. Five countries (Denmark, Finland, Iceland, Slovakia and the United Kingdom (UK)) reported links to all these registers.

Prevention programmes

Screening

All countries (except Luxembourg) reported at least one national screening programme in place for HBV or HCV (Table 3). The most commonly reported screening programmes included antenatal screening of pregnant women for HBV (24/29) and the screening of blood and organ donors for HBV (26/29) and HCV (28/29). Many of the countries had hepatitis screening programmes in place for specific risk groups including PWIDs (15/29 for HBV; 15/29 for HCV), prisoners (11/29 for HBV; 11/29 for HCV) and attendees of STI clinics (10/29 for HBV; 8/29 for HCV). Very few countries reported national screening programmes for military recruits, people with multiple sexual partners or residents of long-term health facilities.

Table 3

Screening programmes for hepatitis B and C, European Union/European Economic Area countries, 2009 (n=30)[a]

Screening programme	Number of countries	
	Hepatitis B	Hepatitis C
Pregnant women	24	3
Military recruits	3	1
People who inject drugs	15	15
STI clinic patients	10	8
Multiple sex partners	2	1
Prisoners	11	11
Haemodialysis patients	21	22
Long-term healthcare facilities	2	0
Healthcare workers	7	7
Workers who are occupationally exposed to the virus	11	10
Blood and organ donors	26	28
Other groups	4	4

STI: sexually transmitted infection.

[a] Of the 30 countries, all but Liechtenstein completed the survey for hepatitis B, and all but the Czech Republic completed the survey for hepatitis C.

Four of 30 countries reported 'other' types of national screening programmes for HBV and HCV. Where specified, these included all people with human immunodeficiency virus (HIV) infection or HIV-infected MSM.

Immunisation

Twenty-two countries reported that they have a universal hepatitis B vaccination programme in place. The other seven countries (Denmark, Finland, Iceland, the Netherlands, Norway, Sweden and the UK) reported that they have opted for selective vaccination programmes targeting specific risk groups at the time of the survey. In addition to the routine childhood vaccination programmes in place, 11 countries reported catch-up programmes for older children and adolescents. Four countries reported 'other' universal vaccination programmes, which included a programme targeting children before entry to primary school in Slovenia.

Over half of the countries with a universal vaccination programme provided information on coverage and ten countries reported coverage rates in infants younger than two years of over 95%. The reported coverage did vary between countries and age groups ranging from between 30% and 99% for coverage among infants to between 31% and 98% for coverage among adolescents.

In addition to universal programmes, most countries have implemented selective vaccination programmes for key groups. The main risk groups targeted for vaccination included 'individuals at risk for HBV due to occupation' (27/29 countries), household contacts of HBsAg positive patients (23/29 countries), haemodialysis patients (23/29 countries), and neonates born to HBsAg positive mothers (22/29 countries). Two countries with universal vaccination programmes in place (Austria and Liechtenstein) reported no targeted vaccination programme for specific risk groups. Each of the seven countries with no universal vaccination programme in place reported at least five targeted vaccination programmes for risk groups. Many countries reported vaccinating a range of 'other' risk groups such as HIV and chronic liver disease patients, MSM, prisoners, PWIDs sex workers, and travellers to countries with a high prevalence of HBV.

Discussion

The results of the survey conducted in this study provide an overview of national surveillance systems and key aspects of prevention programmes for hepatitis B and C across Europe. The survey aimed to pull together detailed information particularly on the existing surveillance systems at country level to better understand the European landscape before embarking upon the implementation of an EU/EEA wide surveillance system. There are some key limitations to this survey. Firstly, although the overall response rate from countries was high there were gaps in the completeness of data provided with countries not completing all questions, especially those on vaccine coverage. Secondly, although additional explanatory information was provided to countries to help clarify terms used in the survey, respondents may have understood and interpreted terms differently. For example, there were differences in the interpretation of the ECDC definition of an active surveillance system that was provided in the questionnaire (Table 1) with some countries describing active surveillance as a system which stipulates that physicians or laboratories report cases directly to public health authorities. Thirdly, the questionnaire was quite broad in its scope, covering both hepatitis B and C prevention and surveillance activities and it is possible that this contributed to the incompleteness of the data collected as the questionnaire was quite lengthy. Also in terms of prevention, the questionnaire collected basic information on screening programmes and HBV vaccination so only provides a limited overview. Programmes have continued to evolve since the survey was undertaken and Romania, for example, started to implement case-based data collection. A further and more comprehensive survey would therefore provide a more accurate picture of current prevention activities across EU/EEA countries.

All countries participating in the survey undertook surveillance of both hepatitis B and C. However, there is considerable variation in surveillance systems across Europe and earlier surveys have also found differences between countries in terms of surveillance system structures, reporting practices, data collection methods and case definitions [15]. In this survey, the main objectives for hepatitis surveillance were found to be similar across countries and included the monitoring of trends, detecting outbreaks, and the evaluation and planning of control measures. The consensus across countries around these core objectives was obviously important during the development and implementation of the enhanced surveillance programme.

Most countries included acute cases of HBV and HCV in their systems which may reflect the fact that most national systems historically focused on newly acquired infections in patients with clinical symptoms of hepatitis [16] Some countries reported that they were unable to differentiate between acute and chronic cases of HBV and HCV. This inability to differentiate data and the lack of chronic hepatitis data from some countries has obvious implications for the comparison of data between countries and for a clear interpretation of the data.

Case definitions varied between countries, although most countries used an EU-related case definition. It should be noted that this survey took place during 2008 and 2009 in a period of transition as the EU 2008 case definitions (2008/426/EC) replaced previous case definitions (2002/253/EC) for hepatitis and this may explain some of the variation. Indeed, subsequent to the initial survey, there was a validation process for countries and a number of countries changed their information on case definitions at this time. Since the survey was undertaken, the EU case definitions were further revised in 2012 to incorporate acute and chronic cases of both infections based on laboratory criteria only [17]. Countries demonstrated flexibility in being able to adapt their data, as in the first data collections most countries were able to provide data defined by these new case definitions, although the differentiation of hepatitis C cases as acute or chronic was problematic [18].

In the survey, deviation from the EU case definitions was observed. Some countries who reportedly used the EU 2008 case definition for hepatitis B included chronic and asymptomatic cases, even though these are not covered by this case definition. There was similar variation for hepatitis C. The heterogeneity around case definitions, data collected and the possibility of duplicate records and under-reporting have all been

hurdles for the harmonisation of surveillance activities at EU level. These potential difficulties were also previously identified and highlighted by the former EUROHEPNET team [16]. This team, established in 2002 by the European Commission to develop a European network on suveillance and prevention of vaccine preventable hepatitis, undertook a similar scoping survey and identified similar issues. The information collected in this current survey however, undoubtedly helped in addressing these differences during the implementation phase of the enhanced surveillance programme at the EU level. While this programme aims to harmonise surveillance, differences in surveillance systems inevitably exist between countries and a clear understanding of local systems therefore aids the interpretation of data and of any differences in these data between countries.

The survey highlighted that most countries have case-based hepatitis B and C data available at the national level which is mostly in an electronic format. The existence of these national surveillance systems across Europe provided an essential platform for building the EU-wide enhanced surveillance system. The collection of a vast body of data from countries and the possibility in some countries to link these data to other registers of morbidity and mortality offer exciting prospects for taking forward surveillance data of hepatitis B and C at EU level.

In relation to prevention activities, the survey was restricted to screening and HBV immunisation programmes and these programmes may have changed since the survey was undertaken. For example, subsequent to the undertaking of survey, universal hepatitis B vaccination began to be implemented in the Netherlands. Nevertheless, the information collected provides a valuable resource to facilitate the interpretation of data. Comparison of vaccination coverage figures between countries is somewhat challenged by the differences in the denominators and dates for the data provided. The results however highlight that while some countries reported low coverage, many countries reported high coverage, particularly among infants, confirming the findings of the VENICE project [19]. This project, conducted in 2009, included 27 EU Member States and two EEA countries (Norway and Iceland) and found routine vaccination programmes in 74% of countries, with reported coverage ranging from 29% to 99%. Further evaluation of vaccination strategies across Europe is important and would benefit from greater harmonisation around coverage and surveillance data. The targeted screening of risk groups also showed considerable variation. Further cost-effectiveness studies of screening different risk groups would help countries target their resources more efficiently.

Following this survey, a working group was established consisting of national experts from a number of EU/EEA countries to assist the ECDC in preparing the protocol for European-wide hepatitis surveillance. By evaluating the common denominators in national surveillance systems and by establishing the core values and objectives of European surveillance, a protocol was developed and discussed at the first European network meeting on hepatitis in 2011. It was recognised that not all countries would be able to comply with the new EU case definitions and not all countries would be able to collect data on the defined set of variables (of which only a few were compulsory such as age, data source, date of diagnosis, date used for statistics, classification, record type, reporting country, sex, stage of hepatitis, transmission and subject). However, it was agreed that implementation should start in 2011 with a retrospective data collection of five years. Indeed, the first data collections were challenging in terms of data comparability and completeness, as described in the report published by ECDC in 2013 [18]. Future analysis will aim to improve the interpretation of the surveillance results by directly linking the surveillance data with current screening and vaccination programmes.

In conclusion, the epidemics of HBV and HCV infections in Europe have emerged over recent decades to pose major challenges to public health and both epidemics continue to evolve [7,20-23]. The strengthening and standardisation of national surveillance systems is widely recognised as important to assess the burden of diseases, evaluate prevention and control strategies and identify epidemiological trends [16,24]. While standardisation across countries is considered a huge challenge [25], the results of this survey provided a foundation which assisted in the development of a common enhanced European surveillance system. Although harmonising systems across Europe will take time, as demonstrated by the experience with HIV, there is great potential to improve surveillance of hepatitis B and C at the European level with interesting possibilities for data linkage which may maximise the utility of this information.

Acknowledgements

We would like to thank the hepatitis contact points in EU/EEA for providing the information for this survey; to Merja Rantala for her input in constructing and conducting the survey. To Anastasia Pharris for her thoughts on a very early draft. We would also like to thank Philip Zucs, Denis Coulombier and Johan Giesecke for their reviews of the paper.

Conflict of interest

None declared.

Authors' contributions

Marita van de Laar commissioned the original survey and contributed to the production of the survey report. Erika Duffell wrote the paper for publication and undertook revisions through close collaboration with Marita van de Laar.

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