Hepatitis C in Austria

Description and Evaluation of the Hepatitis C Virus infection surveillance, Austria, 2017

A mandate from

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to the

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Table of contents

ABBREVIATIONS

AGES	Agency for Health and Food Safety
Anti-HAV	Antibody against hepatitis A virus
Anti-HBc	Antibody against hepatitis B virus
Anti-HCV	Antibody against hepatitis C virus
CD	Case definition
CI	Confidence interval
ECDC	European Centre for Disease Prevention and Control
EEA	European Economic Area
EIA	Enzyme immunoassay
ELISA	Enzyme linked immunosorbent assay
EMS	epidemiologisches Meldesystem/ electronic case recording web-based "reporting" system
EU	European Union
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
HCV	Hepatitis C virus
MoH	Ministry of Health (MoH)
MSM	Men who have sex with men
NAT	Nucleic acid test
PH	Public health
PHOs	Public health officers
PLWH	People living with HIV
PPV	Positive predictive value
PWID	People who inject drugs
TESSy	The European Surveillance System
WHO	World Health Organisation

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EXECUTIVE SUMMARY

The infection with Hepatitis C virus (HCV) poses a major global public health problem, with 71 million people estimated to live with chronic HCV infection globally. With the advent of novel treatments for HCV infection, reliable measures of the prevalence of infection are required in order to estimate costs of treatment at the national level. The prevalence of HCV infection in Austria is unknown as biomarker surveys have not been performed so far. Since 2009 a web-based case reporting-recording system (EMS) for the surveillance of all notifiable infectious diseases in Austria, the viral hepatitis included, has been in place. The number of HCV infection cases reported annually has varied considerably. Recognising these challenges, the Ministry of Health (MoH) in Austria mandated the Agency for Health and Food Safety (AGES) to perform an evaluation of the national hepatitis C surveillance system in order to assess data quality and provide recommendations to improve the HCV surveillance system, in order to obtain a more reliable estimate of the burden of HCV infection in Austria.

The Austrian HCV surveillance system is compulsory, comprehensive and passive. Cases of HCV infection are defined according to EU Commission Decision 2012/506/EC. Clinicians are mandated to notify any newly diagnosed case of HCV infection (acute, chronic) to the local public health authorities via case report; local public health authorities subsequently report the individual case data to the EMS. Since 2014, also laboratories are required to notify to the EMS of any test positive for HCV antibodies, HCV core antigen or RNA. At the national level, monthly and annual counts of cases of HCV infection are produced and published.

The description of the HCV infection surveillance system was based on interviews with representatives of the Department of Infectious Disease Epidemiology and Surveillance at AGES, with the head of the National Reference Laboratory of viral hepatitis, and by consulting the national Infectious Disease Control/Prevention legislation (i.e. Epidemiegesetz) including Austrian communicable disease reporting regulations and preventive public health activities.

We evaluated the HCV infection surveillance system by assessing the system attributes, **case validity, data completeness, acceptability, simplicity and completeness of case ascertainment** in HCV infection risk groups. The selected indicators were applied to the HCV infection case-based surveillance data extracted from the EMS, which comprised 14360 case records for surveillance years 2009-2016.

In assessing **case validity**, we found that 16% (2035/12454) of reported cases were falsely recorded as "newly diagnosed" relative to their reporting year. In 2009, 66% (658/1002) of cases had a laboratory report; this increased to 99% (1654/1676) in 2016. However, only 33% (333/1002) of cases had useful data on the laboratory test method recorded in 2009, compared to 97% (1625/1676) in 2016. We also found that information on laboratory test methods and test results were discordant in 8% of the 7689 case records with laboratory data. The proportion of cases that were compliant with the EU 2012 case definition ranged

from 27-32% in 2009-2012, improving to 61%-78% in 2013-2016. **Data completeness** for risk factor information was poor: 2% of cases over the study period (270/10843) included information on all risk factors requested. **Acceptability** of the surveillance system among clinicians improved over the study period: among cases with a laboratory report, the mandatory reporting by clinicians increased from 36% (235/658) in 2009 to 71% (1172/1676) in 2016. In assessing **simplicity** of the web-based case reporting-recording system (EMS), we found that the differentiation between active and resolved cases, and between suspected and confirmed cases, was difficult due to ambiguous laboratory data entry options. **Concerning case ascertainment** only one national screening program for HCV infection in population groups at HCV infection risk was identified, namely for federal prisoners, suggesting that cases in risk groups may be under-ascertained, and are more likely to be detected first in the phase of chronic liver disease.

In conclusion, this evaluation identified significant weaknesses in all attributes (case validity, data completeness, simplicity, acceptability and completeness of case ascertainment) assessed, which limit the ability of the HCV infection surveillance system to meet its objectives, even though some improvements over the study period were recognized.

We recommend that that all laboratories for viral hepatitis share their case-based datasets of laboratory confirmed HCV infection, to be consolidated by AGES with the HCV infection case-based surveillance data set. The expected benefits will be to maximise the case validity, the laboratory data completeness and the completeness of case reporting/recording in the national HCV surveillance dataset. We further recommend simplification of the laboratory data entry mask, which is planned by AGES. With the support of the MoH, it is recommended that clinicians support the PH authorities by collecting sensitive information such as on route of transmission/source of infection and risk factors from cases. Considering the high proportion (> 80%) of asymptomatic HCV infections among cases, we also recommend that the MoH and relevant stakeholders implement a national HCV control/prevention strategic plan including the performance of biomarker surveys to identify at-risk groups in which subsequently national biomarker screening programs should be implemented (e.g. people who inject drugs). This will improve case ascertainment and representativeness considerably.

These improvements, taken together, should provide the conditions necessary to reliably estimate the number of people currently living with HCV, and to monitor trends of new infections in the Austrian general and at-risk-populations, which is urgently required to inform decisions on treatment provision and disease prevention.

HCV INFECTION - INTRODUCTION

HCV infection - Global burden

Viral hepatitides pose major public health problems: approximately 1.46 million people die each year as a result of infection, with the majority of deaths due to hepatocellular carcinoma and cirrhosis arising from chronic hepatitis B and C infection (1–3). 71 million people are estimated to live with chronic hepatitis C globally, with Africa and Central and East Asia identified as the most highly affected regions (4,5). Hepatitis C virus (HCV), discovered in 1989, is a hepatotropic virus that is primarily transmitted parenterally, through injection drug use, blood transfusions or other nosocomial or healthcare related exposures, as well as contact with infected bodily fluids such as blood or semen (5,6). HCV infection can cause acute or chronic infection, with the vast majority of hepatitis C cases developing chronic hepatitis C (approximately 75%) and roughly a quarter of cases clearing the virus (7).

HCV infection and its surveillance in the European Union/European Economic Area (EU/EEA)

In EU/EEA, a total of 30,607, 31,513, and 35,321 newly diagnosed cases were reported for the years 2012, 2013 and 2014 according to the European Surveillance System (TESSy).

Surveillance of hepatitis C poses serious challenges for the following reasons: 1) the majority of new and chronic infections in adults are asymptomatic and may go undetected until liver disease has been manifested; 2) symptomatic infections often present with non-specific illnesses, with few clearly meeting the clinical case definition (CD) of acute hepatitis; 3) cases of HCV infection among people who inject drugs (PWID), men who have sex with men (MSM), and people living with HIV (PLWH) may be under-ascertained due to barriers they face when accessing healthcare (8).

In a critical examination of hepatitis B and C surveillance data in the EU/EEA, Duffell *et al* discussed the reliability of the European surveillance data on these notifiable diseases, reported to TESSy between 2006 and 2012 (7). A total of 206,332 hepatitis C cases were reported across 29 EU/EEA countries across these seven years. The overall crude notification rate of hepatitis C cases declined from 9.3 cases in 2006 to 7.9 cases per 100,000 population in 2012. The variation in notification rates across the EU/EEA in 2012, ranging from 0.4-1.6 per 100,000 population for acute hepatitis C, and 0.3-60.2 per 100,000 population for the chronic HCV infection, was considerable. The authors highlighted the following surveillance issues: use of outdated case definitions (2008 instead of the 2012 EU case definition), variable screening practices for

HCV infection, and the lack of a standard operating procedure to differentiate between acute hepatitis C and chronic HCV infection across EU/EEA (7).

While no hepatitis C vaccine exists, direct antiviral agents provide effective treatment; these have been available since 2011 and have a high cure rate (9,10). The current high cost of these drugs limits their availability for all HCV infected patients, which makes it even more important to prevent new infections among individuals and populations at risk, and to have reliable estimates on the number of people living with HCV, and the number of new infections (5).

HCV infection in Austria

Table 1 summarises the number of cases of HCV infection in Austria reported annually to TESSy between 2009 and 2015. In 2009, a web-based case reporting-recording system**, the EMS ("epidemiologisches Meldesystem")** was established for all 60 notifiable diseases in Austria. In 2014, the Department of Infectious Disease Epidemiology & Surveillance at the Austrian Agency for Health and Food Safety (AGES) became responsible for monitoring surveillance data of all notifiable diseases recorded in the EMS since 2009. From 2014, all laboratories offering diagnostic tests for any of the 60 notifiable diseases are legally obligated to report laboratory data (including test method, specimen and test result) for any positive test results through web-based or electronic interface mediated data entry tools to the EMS (11).

Table 1: Annual number of cases of HCV infection in Austria reported to TESSy, 2009-2015

Year	Reported cases of HCV infection (n)
2009	860
2010	855
2011	1116
2012	1119
2013	1040
2014	2149
2015	1809

Rationale for evaluating the surveillance of HCV infection in Austria

The Ministry of Health (MoH) in Austria mandated AGES to perform an evaluation of the hepatitis C surveillance system for several reasons: the annual number of hepatitis C cases over the past five years is variable; surveillance data do not allow for reliability concerning the validity of a case in terms of newly diagnosed and laboratory confirmed; and the positive predictive value of serological screening for HCV infection among the general population has been questioned by clinical stakeholders including hepatologists. It is currently difficult to estimate reliably the burden of HCV infection in Austria, to make informed policy decisions on infection prevention and treatment funding.

Recent evaluations of acute hepatitis C surveillance in Italy and the United States highlighted data quality and timeliness as two key surveillance system attributes, where weaknesses were identified (12,13). In addition, an evaluation of chronic hepatitis C surveillance system in Michigan, USA highlighted issues with data completeness (14). Finally, in 2016, the World Health Organisation produced a technical document on viral hepatitis surveillance and identified the following key attributes for evaluations of hepatitis surveillance systems: timeliness, positive predictive value, representativeness and sensitivity (8).

OBJECTIVE OF THIS EVALUATION

The objective of this evaluation was to assess the HCV infection surveillance data in Austria from 2009-2016 inclusive, to determine whether the HCV infection surveillance is performing well enough in terms of key system attributes to meet its objectives, in order to recommend necessary improvements to the MoH.

METHODS

Description of the surveillance system of HCV infection

We described the hepatitis C surveillance system in terms of its objectives, case definitions, case finding, population under surveillance, data structure, case reporting and surveillance indicators. Methods used involved interviews with representatives of the Department of the Infectious Disease Epidemiology/Surveillance at AGES, with the head of the National Reference Laboratory of viral hepatitis and virologists of former reference laboratories, consultation of a report on an overview of available data sources of Hepatitis C in Austria and a review of the national epidemic law (15,16).

In order to describe the representativeness of the surveillance system we ascertained the existence of regional, national or institutional HCV screening programs for chronic HCV infection or results of biomarker surveys in population groups at increased risk (i.e. PWID, sex workers, prisoners, HIV-positives, blood recipients, dialysis patients). For this reason, we interviewed representatives of the Austrian society of hepatologists and national public health authorities.

Evaluation of the surveillance system of HCV infection

For this system, the following surveillance attributes have been identified as those most critical to allow this system to meet its objectives: data quality (defined as completeness and validity of case information), acceptability, and simplicity.

Case-records included in the assessment analyses: Case-records were extracted from a recent download of the HCV surveillance data base (part of the EMS database) in form of a case-line list, which covered the years 2009-2016. Case records were included in the attribute specific analyses, as appropriate for the attributes under study.

Data quality: Case validity I

Objective: to determine the proportion of cases incorrectly recorded as “newly diagnosed” by reporting year from 2009 to 2016.

Analysis: A case was deemed to be incorrectly recorded as **newly diagnosed** if the first diagnosis of HCV infection had already occurred in a previous surveillance year. The quality indicator is the proportion of cases incorrectly recorded as “newly diagnosed” by reporting year, among all cases reported to the hepatitis C surveillance system, from 2009 to 2016. The case records of 2009-2016 extracted from the EMS data base were included in the analysis after exclusion of records of cases labeled as contacts, as discarded (reported to the system as suspected case and subsequently labeled as discarded when being falsified by laboratory results) or identified as duplicates based on initials, sex and date of birth.

Data quality: Case validity II

Objective: to determine the proportion of cases that met the 2012 EU case definition.

Analysis: The quality indicator is the proportion of cases that met the 2012 EU case definition; defined as the number of cases per year that corresponded to the 2012 EU case definition (assessed by laboratory data)), out of the total number of hepatitis C cases with laboratory notification including laboratory test results reported to the hepatitis C surveillance system, from 2009 to 2016. The case records of 2009-2016 extracted from the EMS data base were included in the analysis after exclusion of records of cases labeled as contacts, as discarded (definition see above), or identified as duplicates. Cases misclassified as newly diagnosed (based on an assessment of free-text data) or lacking the laboratory notification were also excluded**.**

Completeness

Objective: to assess the completeness of selected variables for cases reported in the hepatitis C surveillance system, 2009-2016.

Analysis: The quality indicator used was the proportion of cases per year, with complete data for laboratory method, transmission status, HIV status, IV drug use, and healthcare worker status out of the total number of hepatitis C cases reported from 2009 to 2016. Cases labeled as contacts, as discarded, identified as duplicates or misclassified as newly diagnosed, were excluded from the analysis.

Acceptability

Objective: to determine the compliance of clinicians with mandatory case notification

Analysis: The quality indicator used was the proportion of laboratory-confirmed cases with a clinician case report available in the EMS; calculated as the number of cases notified via clinical case report, out of the total number of laboratory-reported hepatitis C cases in the hepatitis C surveillance system by year, from 2009 to 2016.

Simplicity

Objective: to determine whether the laboratory data entry mask is sufficiently simple to permit accurate reporting of a laboratory confirmed case, compliant with the EU case definition (see Table 12).

Analysis: Data captured by a closed-ended question on the diagnostic laboratory tests was compared with an open text question on laboratory test results for Hepatitis C cases recorded in the EMS, by year, from 2009-2016. The quality indicator for simplicity was defined as the proportion of cases where these entries were discordant. Case-records that had information neither on the lab test conducted nor on the results obtained were excluded from the analysis.

RESULTS

Description of the surveillance of HCV infection

Objectives of the surveillance

From the Austrian Epidemic law (1950) (17), amended to the goals of the European Surveillance of Communicable Diseases, the following objectives for the hepatitis C surveillance system were identified:

To monitor trends in the incidence and prevalence of hepatitis C
To detect outbreaks of hepatitis C
To monitor changes in the distribution of hepatitis C in the general population and risk group
To report Austrian hepatitis C data to TESSy according to Decision No. 2119/98/EC (18)
in order to evaluate and plan treatment control measures and programs.

Population under surveillance

The population under surveillance is the entire Austrian population, an estimated 8,576,261 in 2015 (19). Austria consists of 9 provinces: Burgenland, Carinthia, Lower Austria, Salzburg, Styria, Tyrol, Upper Austria, Vienna and Vorarlberg. These provinces are further divided into a total of 95 districts.

Type of surveillance

The Austrian hepatitis C surveillance system is compulsory, comprehensive and passive. It has more active components, such as when public health officials contact physicians and hospital staff to obtain data, which are incomplete in the clinical case report. The notification of hepatitis C cases by detecting laboratories has been mandatory since 2014.

Case definitions

In Austria, the current case definition for hepatitis C infection is based on the EU Commission Decision 2012/506/EU (20). The case definitions applied are as following

A case of **acute hepatitis C** is defined as a patient with signs of hepatitis such as fever, malaise, fatigue, anorexia, nausea and jaundice in whom HCV RNA or HCV specific antigen (HCV core) is detected; it should be notified as a newly diagnosed case of acute hepatitis C (i.e. **acute stage**). A recent HCV infection may be indicated by seroconversion in an individual who is regularly tested for anti-HCV because they are at increased risk (individuals with high risk behaviors, and contacts of persons with HCV-infection); this may occur in the absence of acute hepatitis symptoms and is notified as a **confirmed case of HCV infection**, with **stage unknown;** An individual who tested positive for the first time for HCV ribonucleic acid (RNA) or for HCV core antigen following a positive HCV serological test (anti-HCV antibody ELISA), but who do not meet the clinical criteria of an acute hepatitis case, are considered to have **chronic HCV infection** and are notified as newly diagnosed case of a confirmed chronic HCV infection (i.e. **chronic stage**)

Resolved HCV infection is not notifiable: resolved HCV infection is defined as an individual who tests anti-HCV positive, negative for HCV RNA and positive for specific antibodies (core2-, NS3-, NS4-antibodies) against HCV antigens by immunoblot (see Table 2)

Table 2: Testing strategy for hepatitis C infection; differentiation between acute hepatitis C, chronic hepatitis C infection and resolved HCV infection (8)

	Biomarker criteria			
Laboratory test/ biomarker criteria	**Acute hepatitis C**	**Chronic HCV infection**	**Resolved HCV infection**	**Unspecific reaction**
anti-HCV by enzyme immunoassay (EIA)	-***/+**	+	+	+
HCV RNA by nucleic acid test (NAT)	+	+	-	-
HCV coreAg by EIA	+	+	-	-
anti-HCV by immunoblot	ns	ns	+	-

*individuals who are regularly tested for HCV and seroconvert to anti-HCV positivity would also be identified as being a case of acute hepatitis C

Specification of the information to be reported by the clinician and laboratory

By the Austrian PH regulations, **clinicians** are mandated to notify a "suspected case of Hepatitis C" (i.e. "Verdachtsfall"; no national definition available), a "newly diagnosed confirmed case of HCV infection" (including acute hepatitis C, chronic HCV infection/acute and chronic stage, chronic liver disease due to HCV infection) and a "case of death due to confirmed HCV infection" to the local public health authority. The information to be reported includes variables required by TESSy and additional variables as given in detail in Appendix (Table 13). Laboratory data includes specimen tested, tests applied, test results, patient identifiers and lab entry date and have to be reported within 24 hours of result availability by the responsible laboratories, as specified by an amendment to the Epidemic Law in 2014.

Reporting format and data entry

The clinician notifies a suspected or confirmed case of HCV infection via **a standard paper clinician case report** form to the relevant district public health (PH) office via fax or email;
Data from the paper case report form are entered into the "epidemiologisches Meldesystem" (EMS, a web-based case reporting-recording system) by the relevant district PH officer (PHO), through a web-based case data entry generating **the electronic clinician case report in the EMS**.
Primary and reference laboratories notify anti HCV positives, HCV RNA positives and HCV core antigen positives through the web-based case data entry or the interface mediated case data entry using the international standard such as Health Level Seven International (HL7) in to the EMS – creating an **electronic laboratory case report in the EMS**. The laboratory notification triggers an automatic alert email to the district PH authorities.

Data sources and data flow

Data sources

Table 3 describes the current data sources of the Austrian hepatitis C surveillance system.

Table 3: Data sources of the Austrian Surveillance System of acute hepatitis C and chronic HCV infection

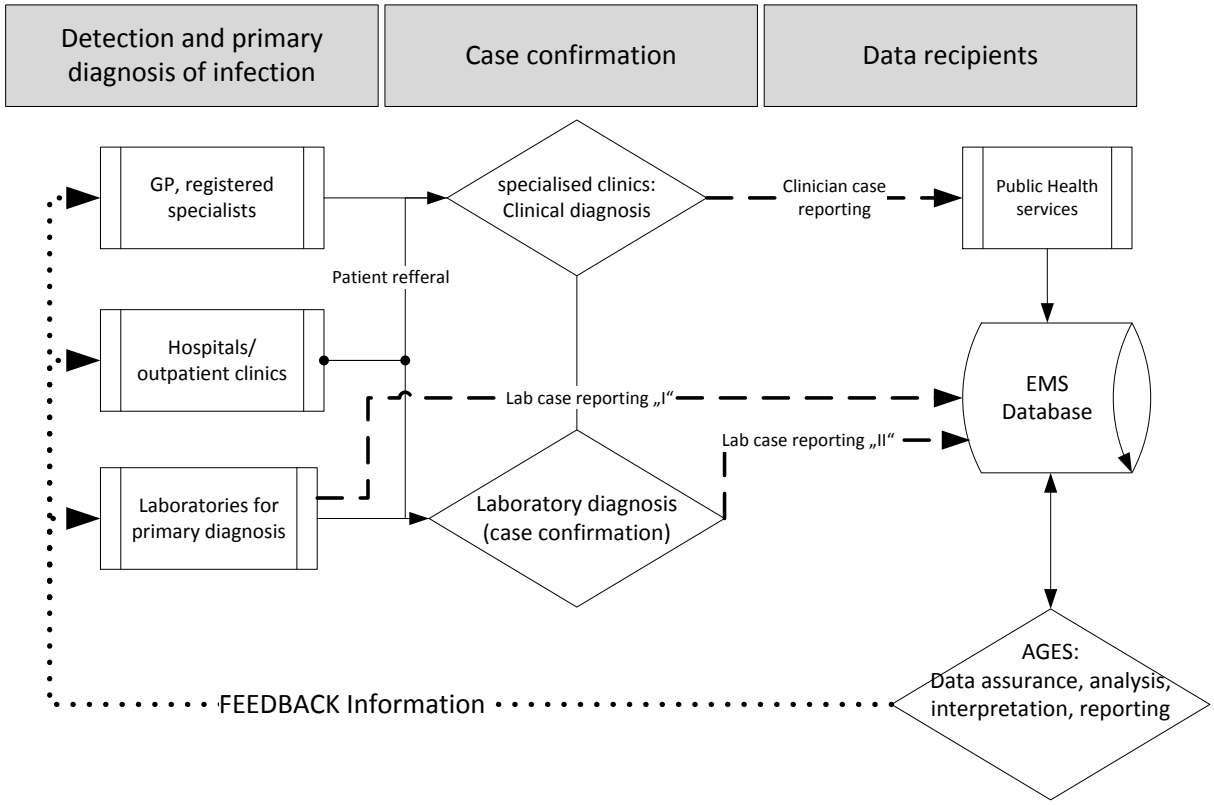
Data source	Description
Laboratories	All laboratories have been required by law since 2014 to report a case with laboratory findings indicating HCV infection to the EMS, generating the electronic laboratory case report in the EMS Primary laboratories report findings of the primary diagnosis (anti-HCV EILISA positive) to EMS Reference laboratories report findings of the confirmatory diagnosis to EMS
GPs / registered specialists (e.g. hepatologist, gastroenterologist)	All health care providers are required by law to notify a suspected case and a confirmed case of acute hepatitis C and chronic HCV infection (according to EU case definition) within 24 h of detection to the relevant district PH office by using a standard unspecific clinician case report, eligible for all notifiable disease in Austria in paper format
Hospitals/ outpatient clinics/ specialised clinics: viral hepatitis treatment centres, HIV treatment centres, drug substitution centres and prison clinics	

Case ascertainment occurs via testing in patients, who present with signs of hepatitis (such as fever, malaise, fatigue, anorexia, nausea and jaundice) or chronic liver disease at any health care facility; these patients are usually offered testing for the biomarker criteria of all viral hepatitis using a HAV-, HBV-, HCV-, HEV-serology panel followed by HCV-RNA testing in case of HAV-, HBV-, HEV-seronegativity.

Currently, only inmates of federal prisons in Austria are systematically screened for HCV infection; there is no other national program for screening of high-risk population-groups (e.g. people who inject drugs [PWID], people living with HIV/AIDS, sex workers) to detect cases of asymptomatic HCV infection in place. Since June 2016, all inmates of the Austrian federal correctional institutions are offered HBV and HCV testing at entry and discharge. Opportunistic and ad-hoc screening for asymptomatic HCV infection is occasionally offered to patients prior to surgery, in patients initiating immunosuppressive treatment, in patients with HIV infection and in patients regularly receiving blood/blood products or dialysis and in blood donors.

Data Flow

Figure 1: Data flow in the HCV infection surveillance from case detection and primary diagnosis to case confirmation and data recipients and feedback to the data providers



Case detection and primary diagnosis of infection occurs usually at general practitioners, registered specialists, hospitals and laboratories offering serology testing for hepatitis virus infection.

Case confirmation occurs at the reference lab or specialized virology laboratories (HCV RNA by nucleic acid test, HCV coreAg by EIA) and specialized clinics for hepatology (i.e. hepatology centers).

Primary laboratories report findings of the serology testing for HCV and the reference or virology laboratories report findings of the confirmatory tests to the EMS through web-based case data entry or interface mediated case data entry – generating the “electronic laboratory case report I” and “II” in the EMS database. The majority of asymptomatic cases of HCV infection undergo this two-lab, two-stage diagnosis; clinically suspected cases may be directly confirmed by the reference lab or specialized virology laboratories.

The data recipients are the district and provincial PH authorities. They receive an automatic alert from the EMS as soon as an electronic laboratory case report is generated in the EMS. The relevant district PH authority also receives a paper-based clinician case report on acute hepatitis C and chronic HCV infection by the case detecting health care provider. Subsequently, the PH authority enters the data of the clinician case report into the EMS, and the electronic clinical case report generated is then consolidated with the electronic laboratory case report (I and II) to create a single case record. Province PH authorities have access to case records of residents of their particular province.

The MoH has access to all case records. AGES, with full access to the case records and permission for database download, is responsible for data assurance, data analyses and interpretation.

ECDC receives the annual Austrian case-based dataset on Hepatitis C from AGES, following completion of data quality assurance steps.

AGES also provides feedback information to participants of the case reporting process, public health professionals, and the general public (see also surveillance output). A more detailed flow including test algorithms and case-based data flow can be seen in the Appendix.

Surveillance output

On the MoH website, available to the public, AGES publishes quarterly tables on quarterly aggregated number of all notifiable infectious diseases in Austria, stratified by the nine Austrian provinces, including cases of HCV infection (21). There is no annual report from the National Reference Laboratory for viral hepatitis.

Public health action taken

As soon as a case (suspected or confirmed) of HCV infection is reported to the district public health authorities, PH authorities' actions include collection of information on transmission modes/source of infection. Activities for contact tracing will be ascertained soon by use of a KAP survey among hepatology centres, STI clinics and PH officers. Few district PH authorities do provide the service of counseling, contact tracing associated with contact referral to HCV testing. The majority of case-detecting hepatologist also perform counselling on transmission risk reducing behavior.

Challenges of the current surveillance system of HCV infection according to findings of the description

Table 4: Challenges of the hepatitis C surveillance system

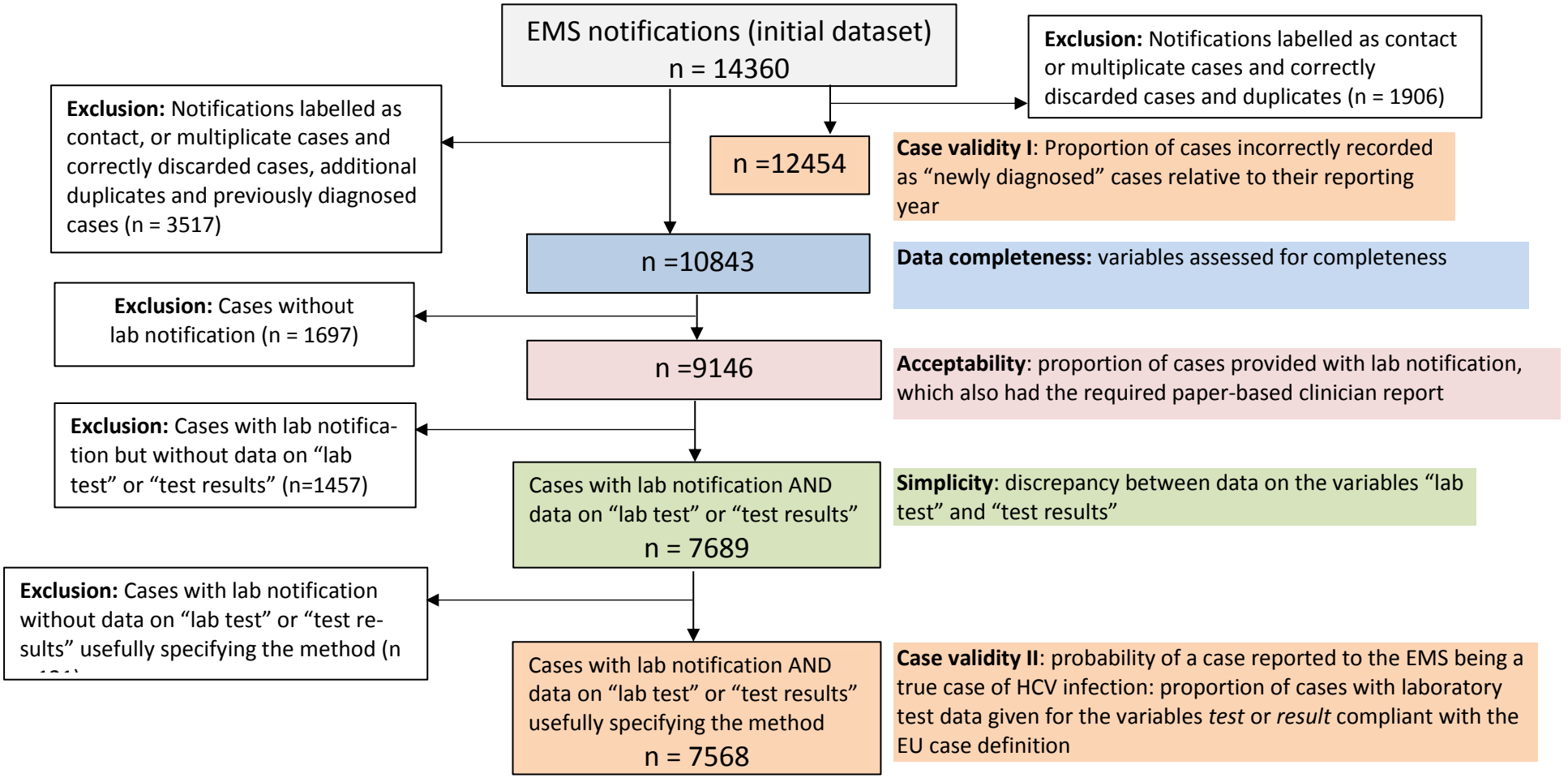
Surveillance activity	Challenges	Surveillance system attributes
Laboratory notification of any HCV test results	Testing for HCV infection in low-risk individuals without signs of hepatitis in a low-prevalence population is not recommended. Nevertheless, testing for HCV infection happens in low-risk patients: for example, in pre-surgery screening, using an anti HCV ELISA test (low positive predictive value in a low-prevalence population) within a viral hepatitis test panel; Confirmatory diagnostics such as HCV antigen or HCV RNA tests rarely occur in such diagnostic setting. Evidence-based national guidelines on diagnostics for HCV infection in order to differentiate between false positive cases (see above), cases of acute hepatitis C, chronic HCV infection and cases of resolved HCV infection are still lacking **Hypothesis**: the current HCV infection case-based surveillance data in the EMS includes cases that do not meet the EU case definition	Case validity in terms of compliance with EU CD
Screening programs/ biomarker surveys/ standardized contact tracing	There are no regional, national or institutional screening programs for or biomarker surveys of chronic HCV infection in population groups at risk (people who inject drugs [PWID], people living with HIV/AIDS, sex workers) except for inmates of Austrian federal correctional institutions; there are no standard operating procedures (SOPs) for contact tracing/investigation **Hypothesis**: due to absence of systematic screening activities or SOPs for contact tracing/contact investigation, the surveillance data based annual incidence of HCV infection likely underestimate the true burden of hepatitis C infection in the Austrian population	Completeness of case ascertainment in specific population subgroups
Incident diagnosis of HCV infection	Due to mandatory laboratory notification of any positive test results, follow-up tests and their results in HCV+ patients may be reported to the EMS **Hypothesis**: previously diagnosed cases are misclassified as newly diagnosed cases in the EMS database, when they have not been appropriately reported at the time of first diagnosis	Case validity in terms of newly diagnosed
Clinicians case reporting behaviour	Perception of hepatologists that reporting to the public health authorities negatively affects the patient-doctor relationship **Hypothesis**: Concerns over stigma experienced by patients may lead to underreporting by Austrian physicians	Acceptability by clinicians
Laboratory-based case reporting	Data entry mask for laboratory data does not clearly reflect the laboratory criteria of the EU case definition **Hypothesis**: case-based surveillance data in the EMS may include inconsistent information on laboratory tests and results	Simplicity

Evaluation of the surveillance of HCV infection

Based on the challenges identified through the description of the hepatitis C surveillance system and from previously published hepatitis C surveillance evaluations, the following attributes were selected for assessment: case validity, data completeness, acceptability, simplicity and completeness of case ascertainment as a proxy for representativeness.

Case records were excluded from the original case-based surveillance data of 2009-2016 according to the assessment of the attributes, as illustrated in the flow in Figure 2.

Figure 2: flow chart of case records excluded from the original case-based surveillance data downloaded from the EMS, 2009 to 2016



Case validity I

Quality Indicator: Proportion of cases falsely recorded as "newly diagnosed" cases relative to their reporting year

12454 case records were included for analysis (see Fig. 2). Sixteen percent of all cases (2035/12454) were incorrectly recorded as "newly diagnosed", based on the additional information found in free-text variables giving the likely year of initial diagnosis (Table 5). The proportion of cases incorrectly reported as "newly diagnosed" increased from 2009 to 2014, and decreased in 2015-2016.

Table 5: Proportion of previously-diagnosed cases of HCV infection reported as "newly diagnosed", Austria 2009-2016

Year	Case records total[1]	Cases incorrectly recorded as "newly diagnosed"	
	N	n	%
2009	943	36	4
2010	1062	110	10
2011	1283	187	15
2012	1349	239	18
2013	1177	213	18
2014	2516	548	22
2015	2179	430	20
2016	1945	272	14
2009-2016	**12454**	**2035**	**16**

[1]excluding duplicate case records, and those labelled as "discarded"

Data completeness

Indicator: proportion of cases per year with complete data on selected variables

10843 case records were included for analysis (see Fig. 2). There are currently six compulsory variables for hepatitis C case notifications to the hepatitis C surveillance system: name, surname, and sex, date of birth, national ID and hepatitis C status (acute, chronic or unknown). Table 6 summarizes the completeness of seven non-compulsory hepatitis C surveillance variables including laboratory report, laboratory test methods, date of diagnosis, and mode of transmission, HIV status, IV drug use and healthcare worker status, from 2009 to 2016.

Completeness of the **laboratory report** variable increased over the period. 66% (658/1002) of cases had a laboratory report in 2009, which increased to 99% (1654/1676) of cases by 2016. Out of all cases records in 2009, 333/1002 (33%) had useful data on the **laboratory test method** in their laboratory report. The completeness on the **laboratory test methods** increased to 97% (1625/1676) in 2016. Completeness of the **date of diagnosis** variable decreased over time, from 93% in 2009 to 55% (928/1676) in 2016. Overall, 71% (7667/10843) of cases had a date of diagnosis over the evaluation period. Completeness of the **transmission** variable ranged from 1 to 9% and of **HIV status** from 1% to 8%, with completeness of both variables increasing over the study period. Completeness of the **IV drug use** variable ranged from 4-23%. Overall, 17% (1808/10843) of cases over the evaluation period had a complete IV drug use status. Completeness of the **healthcare worker status** variable ranged from 4% in 2009 to a peak of 34% (349/1013) in 2013. Two percent (270/10843) of cases from 2009 to 2016 had complete information on all three of HIV status, IV drug use and healthcare worker status.

Table 6: Data completeness: Completeness of selected variables of the hepatitis C surveillance case-based data, Austria 2009-2016

	Case records total	Lab report		Lab test method		Date of diagnosis		Route of transmis-sion		HIV status		IV drug use		Healthcare worker status		All three risk factors	
Year	N	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
2009	1002	658	66	333	33	932	93	11	1	14	1	39	4	40	4	8	1
2010	1037	754	73	394	38	907	87	23	2	17	2	132	13	62	6	8	1
2011	1160	831	72	459	40	1075	93	16	1	18	2	189	16	46	4	7	1
2012	1164	736	63	451	39	1019	88	60	5	43	4	203	17	212	18	22	2
2013	1013	853	84	780	77	745	74	89	9	84	8	236	23	349	34	51	5
2014	2006	1917	96	1827	92	1109	55	133	7	127	6	397	20	442	22	71	4
2015	1785	1743	98	1699	95	952	53	117	7	115	6	329	18	400	22	73	4
2016	1676	1654	99	1625	97	928	55	104	6	70	4	283	17	347	21	30	2
2009-2016	**10843**	**9146**	**84**	**7568**	**70**	**7667**	**71**	**553**	**5**	**488**	**5**	**1808**	**17**	**1898**	**18**	**270**	**2**

[1] excluding duplicates, non-newly diagnosed cases from the year of report and case records labelled as “discarded”

Acceptability

Indicator: proportion (%) of laboratory notified cases with a clinician case report

9146 case records were included for analysis (see Fig. 2). The proportion of laboratory notified cases with an associated clinician report ranged between 36-85 % during the period of 2009 to 2016 (see Table 7). Overall, 67% of cases recorded in the hepatitis C surveillance system had both a laboratory notification (6136/10843) and a clinician report during this period. Since 2011, there has been an increase in the compliance of clinicians with the mandatory notification of cases of HCV infection.

Table 7: Acceptability: Annual number of case records by notification, Austria 2009-2016

Year	Case records total[1]	Case records with clinician report only		Case records with lab notification		Case records with lab + clinician report	
	N	n	%	n	%	n	%
2009	1002	342	34	658	66	235	36
2010	1037	277	27	754	73	289	38
2011	1160	325	28	831	72	351	42
2012	1164	428	37	736	63	603	82
2013	1013	160	16	853	84	727	85
2014	2006	89	4	1917	96	1488	78
2015	1785	42	2	1743	98	1271	73
2016	1676	22	1	1654	99	1172	71
2009-2016	**10843**	**1685**	**16**	**9146**	**84**	**6136**	**67**

[1] excluding duplicated, non-newly diagnosed from the year of report and correctly “discarded” cases

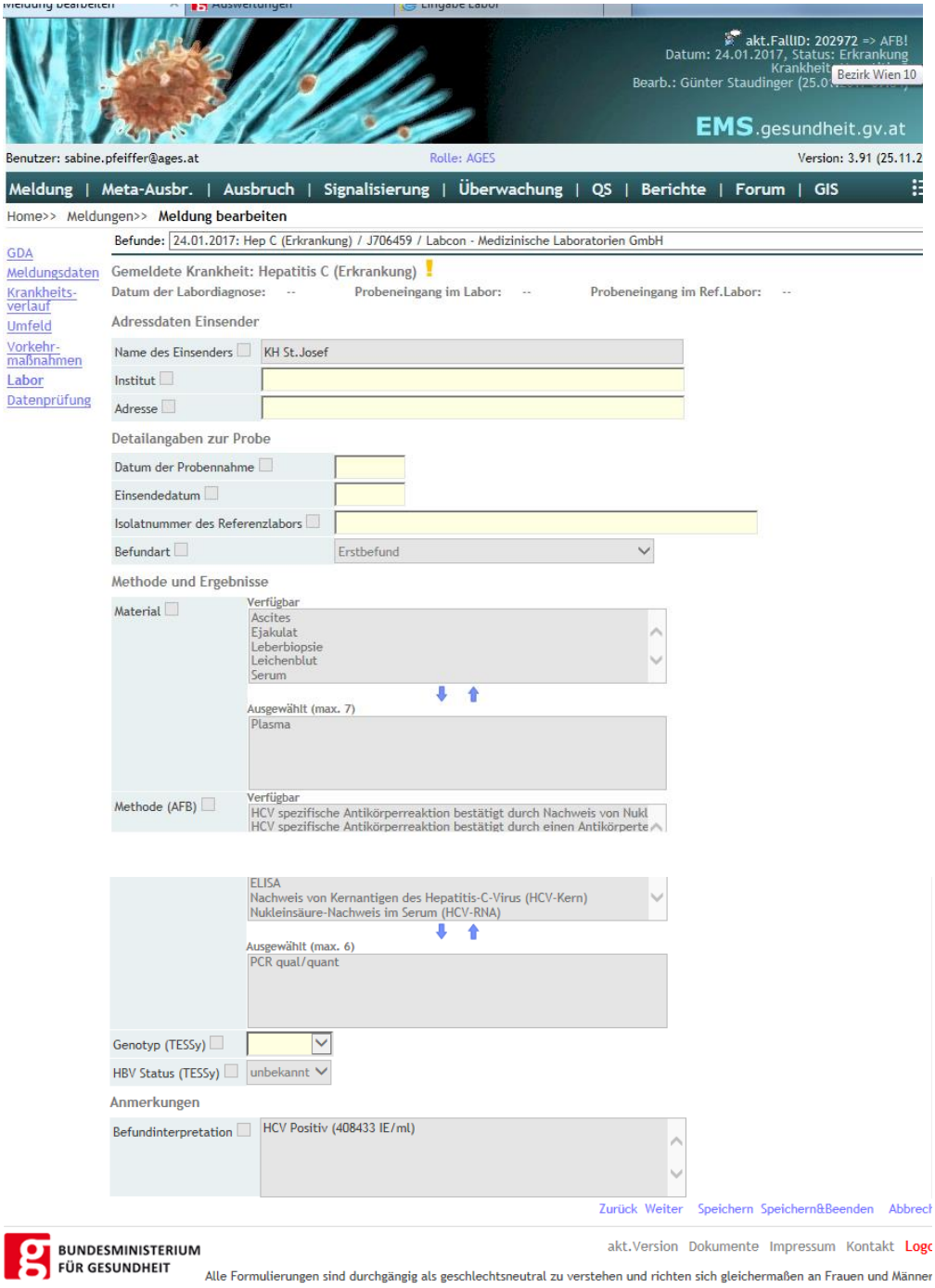
Simplicity

Description of the laboratory data entry mask

Currently, the laboratory data entry mask includes the following elements: name and address of the laboratory, date the sample was taken, the type of sample taken, laboratory test performed ("Methode" in Figure 3), genotype, HBV status and test result ("Befundinterpretation" in Figure 3).

The variable 'laboratory test' has fixed categories, and multiple choices are possible: (1) HCV RNA detected in serum sample; (2) HCV-specific antibody reaction confirmed by another antibody test; (3) Sequencing/Genotyping; (4) ELISA; (5) PCR qualitative/quantitative; (6) Detection of HCV core antigen and (7) HCV-specific antibody reaction confirmed by detection of nucleic acid of HCV in serum in person >18 months without detection of a recovered infection. The wording of the fixed categories is ambiguous. The variable "test result" is an optional, free text variable. The current data entry format of this variable does not allow laboratory personnel to separately enter each of the lab tests performed with the corresponding results of each test. These issues create barriers to accurately capturing variables required for compliance with laboratory criteria of the EU case definition.

Figure 3: Laboratory data entry mask of the EMS



Indicator: proportion of cases with discordant information between laboratory test and test results

7689 case records were included for analysis (see Fig. 2). As a measure of simplicity, we calculated the proportion of cases with discordant information on the categorical variable “laboratory test” and the free-text variable “test result” .If additional information on “test result” was found in the free-text variable but not in the “laboratory test” variable, the data were considered to be discordant, e.g., a case could have ELISA selected as “laboratory test” but also a PCR result described in the free-text variable on “test result”. Table 8 shows the proportion of discordance by year 2009-2016. The proportion of discordance ranged from 4-12 % across the study years.

Table 8: Simplicity: Number of EMS recorded hepatitis C cases with discordant information for the laboratory test and result variables per year, Austria, 2009-2016

Year	Case records with data on 'laboratory test'/'test result'	Case records with discordant information on 'laboratory test' and 'test result'	
	N	N	%
2009	336	37	11
2010	414	37	9
2011	412	51	12
2012	450	44	10
2013	799	28	4
2014	1897	123	6
2015	1734	145	8
2016	1647	169	10
2009-2016	**7689**	**634**	**8**

Case validity II

Indicator: proportion of cases compliant with the 2012 EU case definition

The proportion of the included 10843 case records (duplicates, non-newly diagnosed cases, discarded cases excluded see Fig. 2) that complied with the 2012 EU case definition was 56.1% (n=6083) and ranged from 26.2-78.5%.

Of the 7568 case records with **lab notification and information on the method available** (see Fig. 2) an average of 80.4% (range 78.7-83.6) across the study period were compliant with the EU case definition.

Table 9: Case validity II Proportion of reported cases compliant with the 2012 EU case definition, Austria 2009-2016

Year	Case records total[1]	Case records with lab notification		Case records with lab notification specifying the method		Case records with lab notification specifying the method and meeting CD		Case records total meeting CD
	N	**n1**	**n1/N, %**	**n2**	**n2/n1, %**	**n3**	**n3/n2, %**	**n3/N, %**
2009	1002	658	65.7	333	50.6	268	80.5	26.7
2010	1037	754	72.7	394	52.3	310	78.7	29.9
2011	1160	831	71.6	459	55.2	377	82.1	32.5
2012	1164	736	63.2	451	61.3	377	83.6	32.4
2013	1013	853	84.2	780	91.4	621	79.6	61.3
2014	2006	1917	95.6	1827	95.3	1474	80.7	73.5
2015	1785	1743	97.6	1699	97.5	1342	79.0	75.2
2016	1676	1654	98.7	1625	98.2	1314	80.9	78.4
09-16	**10843**	**9146**	**84.3**	**7568**	**82.7**	**6083**	**80.4**	**56.1**

[1] excluding duplicates, non-newly diagnosed from the year of report and “discarded” cases

DISCUSSION AND RECOMMENDATIONS

We evaluated the surveillance of HCV infection in the Austrian population by assessing the attributes of case validity, data completeness, acceptability and simplicity.

Case validity I: Previously- diagnosed cases incorrectly reported as newly-diagnosed in a certain surveillance year due to delayed case reporting accounted for 16% of all cases over the 7-year period. This weakness in the surveillance system is mostly explained by low case reporting through clinicians; since 2009, when EMS became operational, cases of HCV infection initially diagnosed already before 2009 became reported and recorded in the EMS with the date of the first electronically reported laboratory result.

Limitation of our analyses: One limitation of this assessment is that it depends entirely on additional information on the date of diagnosis provided in free-text variables. Differences in completion of free-text variables with information on date of diagnosis may exist between public health authorities and/or have changed over time, and thus lead to an underestimation of the true number of previously diagnosed cases. This may explain why the proportion of previously-diagnosed cases identified is low in the first year of the EMS operation, (2009) and more stable in subsequent years. A second limitation of identifying the true date of initial diagnosis was the automatic process, which considered any date in the free text variables as the diagnosis date. This may have misclassified the true year of initial diagnosis if the date in this field was not the initial diagnosis date.

Recommendations:

- AGES to support clinicians' case reporting by providing a simple clinician case report form, newly developed specifically for HCV infection, which also includes date of initial diagnosis,
- MOH to disseminate information on Hepatitis C burden in order to increase awareness among and promote case reporting compliance among clinicians
- AGES to identify previously-diagnosed cases, incorrectly reported as newly-diagnosed cases in a certain surveillance year by merging case-based datasets of laboratory-confirmed HCV infection from current and former reference laboratories for viral hepatitis with the EMS dataset, and to reassign cases to the appropriate surveillance year in the EMS

Data completeness: The proportion of cases with useful lab data improved greatly after 2012 (from 63% in 2012 to 99% in 2016), which is explained mostly by the shift to mandatory reporting of laboratory data from 2014 onwards.

Only 2% of cases had data on all risk factors assessed, which despite improvement in completeness of individual risk factors over time, is still unacceptably low in order to inform preventive actions. While our findings on risk factor (RF) completeness among reported HCV cases were comparable to some published hepatitis C surveillance system evaluations (14), the Austrian system demonstrated significantly poorer completeness for RF information compared to other systems(12). The completeness of data on transmission mode (6% of all cases) showed little improvement, and is below the proportion of notified EU cases with transmission data in the TESSy case-based data set in 2015 (15.8%); for comparison, Austria's completeness on this field was far below that of Norway in 2015 (62%) (22, 23). Eliciting this risk factor information from patients is sensitive, and few clinicians and public health officials have expertise and training in this practice for (see also acceptability, below).

Limitation of our analyses: There were no major limitations in the analysis of the completeness of the variables selected.

Recommendations:

- AGES to support routine reporting of data on source of infection/vehicle of transmission by developing a simple but complete clinician case report
- MoH to support and monitor contact tracing, partner notification through the patient-clinician interaction

Acceptability: Acceptability of the surveillance system by clinicians, as measured by their willingness to submit a clinician case report, greatly improved over the study period. However, it remains less than ideal, with only 67% of all laboratory-notified cases linked to a clinician case report. Based on personal communication with hepatologists, the main reluctance around mandatory case notification arises from their observations that patients experience stigmatization and discriminatory questioning from the responsible public health authorities, which also impacts upon patient treatment compliance.

Limitation of our analyses: A key limitation of this analysis is that we did not directly obtain the views of clinicians on the acceptability of the system, and instead used a proxy indicator of acceptability for our analyses. Furthermore, the analysis required distinguishing case reports by clinicians from those by the public health doctors/ authorities in order to create a clinical case record in the EMS. The list of public health doctors involved may be incomplete and may have changed over the study period, so all reports made by public health authorities could not be excluded from our calculations. Therefore, the proportion of cases with a clinician case report may have been overestimated.

Recommendations:

- AGES to change the laboratory data entry mask (see recommendation for simplicity) of the EMS to align with the laboratory criteria of the EU case definition: this will ensure that only confirmed cases of newly-diagnosed HCV infection (including acute hepatitis C, asymptomatic chronic HCV-infection) will generate an electronic alert to public health authorities
- MoH to request from case detecting clinicians to collect sensitive data, such as on risk factors, source of infection/route of transmission (e.g. needle) and on partner notifications', and to transfer this information to public health authorities via a clinician case report newly developed specifically for HCV infection by AGES;
- MoH to enable clinicians to report directly to the EMS via the web-based data entry or through a hospital patient information management system (HPIMS) interface with the EMS

Simplicity: Firstly, the ambiguous laboratory data entry option makes differentiation between acute hepatitis C, chronic HCV infection and resolved cases, and between suspected (anti-HCV+) and confirmed cases (HCV-RNA+, HCV-core Antigen +), difficult. In addition, laboratory data entry in a free-text variable is unnecessarily resource consuming and renders the case validity check very difficult. The discordance between data entered in the "laboratory test" and "test results" variables represented 8% of all cases over the 7-year period.

Limitation of our analyses: The identification of discrepancies between data entered in the "laboratory test (closed question)" and "test results (free-text entry)" variables was done manually and therefore, some random errors could have occurred.

Recommendations:

- AGES to simplify the laboratory data entry mask by including unambiguous data entry options on "laboratory test" and "test results" (e.g. HCV RNA PCR positive, negative, test not performed) compliant with the 2012 EU case definition, and removing free-text entry options (see figure 7 in appendix)

Case validity II: The proportion of HCV-infection cases that complied with the 2012 EU case definition greatly improved over time, from 26.7% of total cases in 2009 to 78.4% of total cases in 2016. This improvement is mostly due to the rise in the number of cases with a laboratory notification including the laboratory test applied/ test-results.

Limitation of our analyses: The case validity II assessment was limited by the completeness of the information on "laboratory test" and "test results", which were used to assess the compliance with the 2012 EU case definition. Differences in the manner of completing the "test results" variable, e.g. writing "positive" or "+", rather than specifying the result of the test performed, likely led to an underestimation of the true proportion of cases compliant with the case definition.

Recommendations:

- AGES, with support of MoH, to merge case-based laboratory-confirmed HCV infection datasets at the current and former reference laboratories for viral hepatitis, with the surveillance (EMS) case-based dataset, to improve the case validity by completion of the EU case definition laboratory criteria. This may allow also for identification of other previously-unreported cases of confirmed HCV infection

Completeness of case ascertainment in specific population subgroups: The only national screening program for HCV infection among populations at high risk exists among federal prisoners (24). Bi-

omarker surveys in the general population and /or population groups predefined as at-risk groups in the Austrian population would allow a targeted introduction of national screening programs among at-risk populations, e.g. PWID, as recommended by the WHO in order to determine reliably prevalence estimates in these specific subgroups. The lack of such systematic programs suggests that cases in at-risk groups are under-ascertained in Austria, and are more likely to be first detected at the onset of chronic liver disease. Furthermore, it results in an underestimation of the true burden of HCV infection in the Austrian population.

Recommendations: Based on a recent systematic review on cost-effectiveness studies of targeted screening programs for the control of HCV infection and the current WHO guidelines (10,25), we recommend to the MoH to implement a national strategic plan on systematic screening for HCV infection. Such programs should be based on findings of previous biomarker surveys in the general population, or specific population subgroups, which may be hard to reach and therefore not well represented in general population surveys. Targeted screening programs would increase the detection of cases of asymptomatic chronic HCV infection and reduce the delay between infection and detection.

CONCLUSIONS

In conclusion, this report highlights significant weaknesses in all attributes assessed (case validity, data completeness, simplicity, acceptability and completeness of case ascertainment in risk groups) that limit the ability of the HCV surveillance system to meet its objectives, even though some improvements over the study period were recognized. However, interventions to merge case-based laboratory data from the current and former HCV reference laboratories with the existing case-based surveillance data as recorded in the EMS will readily improve the case validity and completeness of the surveillance data. We further recommend simplification of the lab data entry mask of the web-based case reporting-recording system (EMS), and assistance in collection of case data on sensitive risk factors by clinicians using a newly developed HCV specific clinician case report. Finally, implementation of screening programs for HCV infection in predefined groups previously identified by biomarker surveys, as the at-risk groups in the Austrian population as recommended by the WHO, would increase the rate of detection of asymptomatic HCV cases and subsequently improve estimates of prevalence in the Austrian population. Together, these actions promise to strengthen the ability of the HCV surveillance system to meet its objectives and provide evidence to inform and prioritize public health interventions.

Table 10: Overview of key results, conclusions and recommendations

Table No.	Attribute	Indicator	Findings	Conclusions	Recommendations to be implemented by whom
5	Case validity I	Proportion of cases falsely recorded as newly diagnosed relative to their reporting year	16% (2035/12454) were falsely recorded as newly diagnosed cases relative to their reporting year (prevalent cases of chronic infection)	The current system does not provide reliable estimates of the prevalence of HCV infection and number of newly diagnosed infections	- Consolidate the case-based dataset of lab-confirmed HCV infection from reference laboratories with the EMS HCV case records - Identify and reassign "previously diagnosed cases" to the appropriate surveillance year; - To be done by AGES
6	Data completeness	Proportion of cases per year with complete data on selected variables	Completeness of laboratory reports has improved over time but completeness of variables of high public health value remains low	Targeting prevention efforts is limited due to lack of information on risk factors and route of transmission	- Sensitise clinicians on importance of collecting data on source of infection, vehicle of transmission, contact tracing, partner notification - Promote collection of these data by clinicians by simplifying the clinician case report - To be done by the MoH with the help of AGES
7	Acceptability of system by clinicians	Proportion of laboratory notified cases with a clinician report available	Only 67% of EMS recorded cases with a laboratory notification had a clinician report during the period	Acceptability by clinicians has improved over time but less than ideal	- Changing the EMS laboratory data entry mask should ensure that only confirmed cases of newly diagnosed HCV infection will result in an electronic alert at public health authority level - To be done by AGES - Promotion of clinicians to collect and report the data on source of infection, vehicle of transmission, contact tracing, partner notification could avoid unpleasant situations with the affected person through the PH authority activities on that issue - Technically enable clinicians to report to the EMS, done by MoH
8	Simplicity of data entry	Proportion of EMS recorded cases with	4-12 % discordance between "laboratory test"	The current laboratory data entry mask is not simple to use	- Simplify the laboratory data entry mask to allow unambiguous data entry options on "la-

	mask	discordant information between laboratory test and results variables	and “test result” variables across the study years.		boratory test” and “test results” according to the laboratory criteria of the EU case definition - The record of a case of anti-HCV positivity alone should no longer produce an electronic alert to public health authorities - To be done by AGES approved by the MoH
9	Case validity II	Proportion of EMS recorded cases that complied with the 2012 EU case definition	53.6% of EMS recorded cases between 2009-2016 complied with the 2012 EU case definition	Case validity of true hepatitis C cases has improved over time but remains unsatisfactory	- Merge historical case-based datasets of lab-confirmed HCV infection from current and former reference laboratories with the EMS case-based data - Simplify the laboratory data entry mask to allow unambiguous data entry options on “laboratory test” and “test results” according to the laboratory criteria of the EU case definition - To be performed by AGES
10	Case ascertainment in population groups at high risk	Availability of targeted biomarker screening activities	The only national targeted screening programme in place for such population groups is among prisoners at entry and discharge	The absence of biomarker surveys conducted in the Austrian general population and the lack of targeted nation-wide biomarker screening activities based on the findings of these biomarker surveys suggest that cases in such groups may be considerably under-ascertained	- Implementation of national biomarker screening programs at-risk groups identified using biomarker survey - To be applied by MOH with help of experts

APPENDIX (1):

Intervention to improve the surveillance case data on HCV infection

During the period of evaluation, the dataset of laboratory confirmed cases of the years 1998-2017 was provided by the hepatitis C reference laboratory at the Medical University of Vienna (head: Prof. Heidemarie Holzmann (MD), Head of Division of Applied Medical Virology, Centre for Virology, Medical University of Vienna). Based on the findings and recommendations of our evaluation as described above (table 10), it was decided that DI Lukas Richter, statistician at the Infectious Disease Epidemiology Department, would merge this data with the HCV infection case-based surveillance dataset , which had been extracted from the EMS (web-based case reporting/recording system).

The following steps were thus performed:

- Merge of case-based dataset of laboratory confirmed HCV infection cases of the years 1998-2017 ("reference laboratory Hepatitis C-dataset", source as given above) with the national case-based surveillance dataset newly downloaded from the EMS with date of diagnoses 1940-2016 (date of download: 10/7/2016) in form of a case line list; case merging occurred by initials, date of birth and sex
- creation of a new diagnosis date variable taking into consideration information provided in free text comment variables
- removal of case records labelled as contacts or "multiplicates"
- removal of discarded cases after validation
- removal of cases without a laboratory notification
- merging of information on laboratory test performed from the two datasets
- removal of duplicates based on an ID composed of date of birth, sex and initials
- creation of a final date of diagnosis variable by taking the earliest date present in either the EMS or the reference laboratory dataset
- re-ordering of the cases based on the final date of diagnosis i.e. reassignment of cases to the appropriate surveillance year as incidence cases

Evaluating our intervention "integration of the reference laboratory Hepatitis C-dataset"

We compared the proportion of cases compliant with the EU case definition and the annual number of cases before and after intervention.

Table 11 compares the proportion of cases compliant with the 2012 EU case definition and the number of newly recoded cases after intervention. Our intervention increased the total number of cases of HCV infection recorded for the years 2009, 2010, 2011, 2012 and 2013 and reduced the number of recorded cases for the surveillance years 2014, 2015 and 2016 (table 11 and figure 4) in the case-based 2009-2016- surveillance dataset. This led to a considerable improvement of the attribute case validity by identifying previously known cases and reassigning those to the appropriate surveillance year of initial diagnosis (now true newly diagnosed cases of confirmed HCV infection). It also resulted in an improvement of case validity II (figure 4). The proportion of cases compliant with the EU case definition increased considerably in 2009 to 2012, for example in 2009 41% versus 70%, and less in 2014 to 2016, for example in 2015 77% versus 78% after intervention (table 11 and figure 5). This intervention identified previously unreported cases (improving completeness of case reporting) (table 11 and figure 6). The proportion of additional cases of the total after intervention was 30% and 26% in 2009 and 2010, respectively, and decreased to 4% in 2016.

Conclusion and recommendations

Our intervention was effective in improving the case-based surveillance data from 2009 to 2016 in terms of completeness of case reporting and case validity. We recommend that the other three former reference laboratories for viral hepatitis provide case-based datasets of laboratory confirmed HCV infection cases for merging with the currently updated surveillance case-based dataset. The expected benefits will be to maximise case validity, laboratory data completeness and the completeness of case reporting (internal and external completeness) in the national surveillance dataset. More reliable estimates of the burden of HCV infection in the Austrian population could be produced, which are highly required for decision making on extending treatment funding.

Table 11: Proportion of cases compliant with the EU case definition and the changes of the annual number of cases after intervention before and after the intervention, Austria 2009-2016[1] (date of EMS data download: 10/7/2016)

Year	Intervention	Total	Cases compliant with EU case definition		Newly recorded cases[2]	
		N	n	%	n	%
2009	No	658	268	41		
	Yes	964	673	70	291	30
2010	No	754	310	41		
	Yes	969	658	68	250	26
2011	No	831	377	45		
	Yes	982	628	64	176	18
2012	No	736	377	51		
	Yes	853	590	69	132	15
2013	No	853	621	73		
	Yes	886	711	80	125	14
2014	No	1917	1474	77		
	Yes	1823	1450	80	111	6
2015	No	1743	1342	77		
	Yes	1524	1194	78	84	6
2016	No	1654	1314	79		
	Yes	1424	1137	80	60	4

[1] excluding duplicated, non-newly diagnosed from the year of report, correctly “discarded” cases and cases without a laboratory notification

[2] newly recorded to the national HCV surveillance system

Figure 4: Annual number of hepatitis C cases with a laboratory notification before and after the intervention, 2009-2016

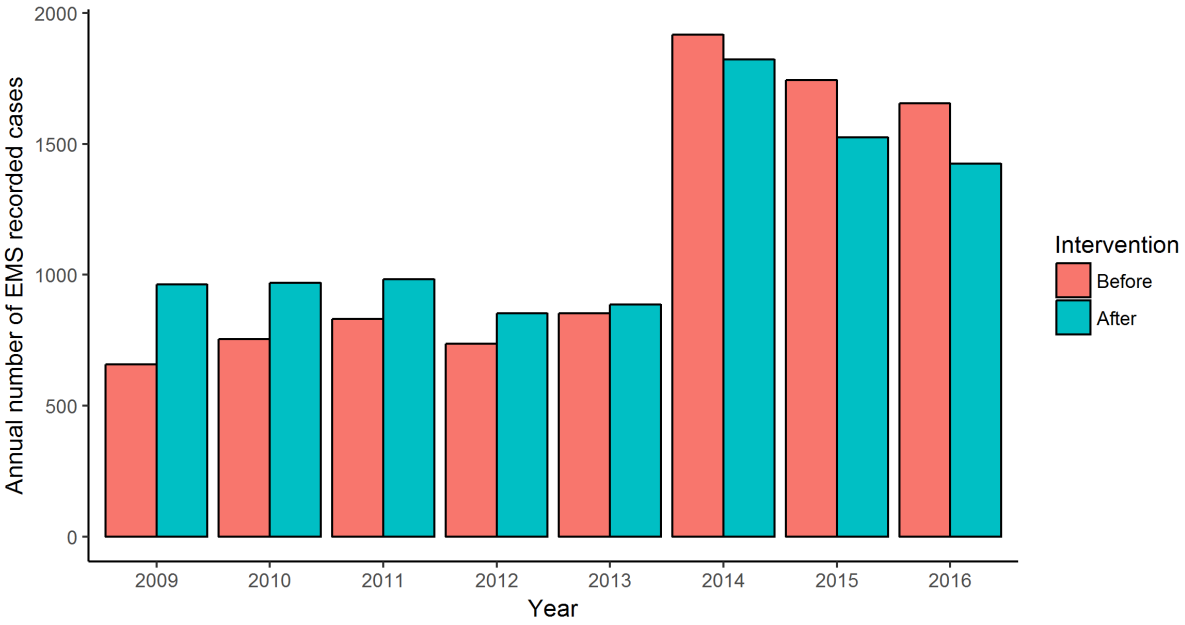


Figure 5: Percentage of cases compliant with the EU Hepatitis C case definition before and after the intervention

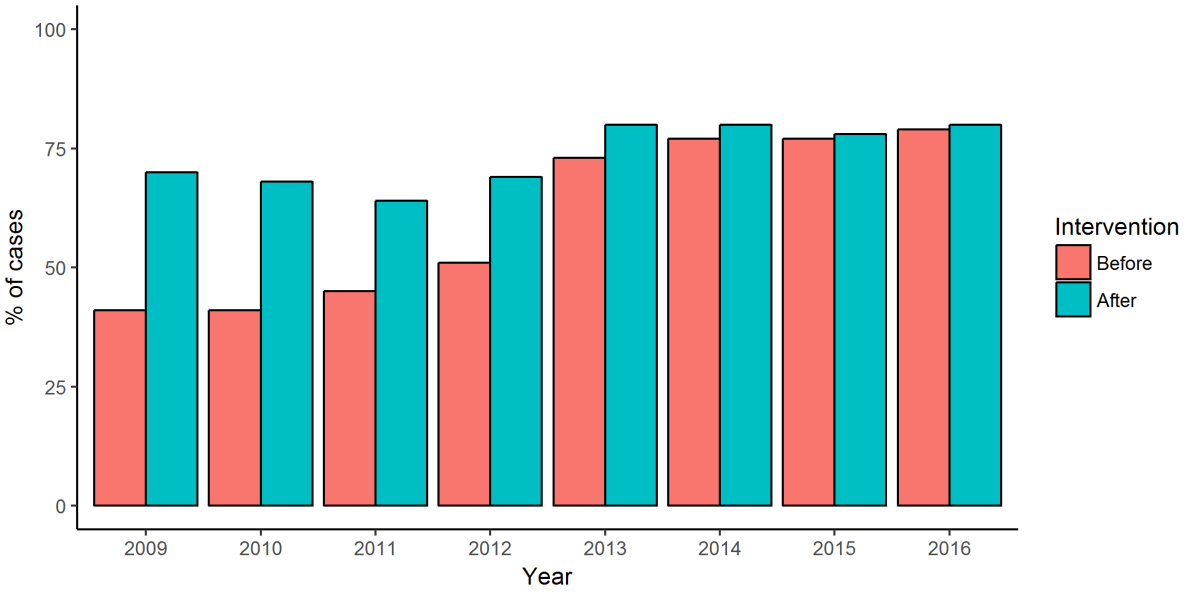
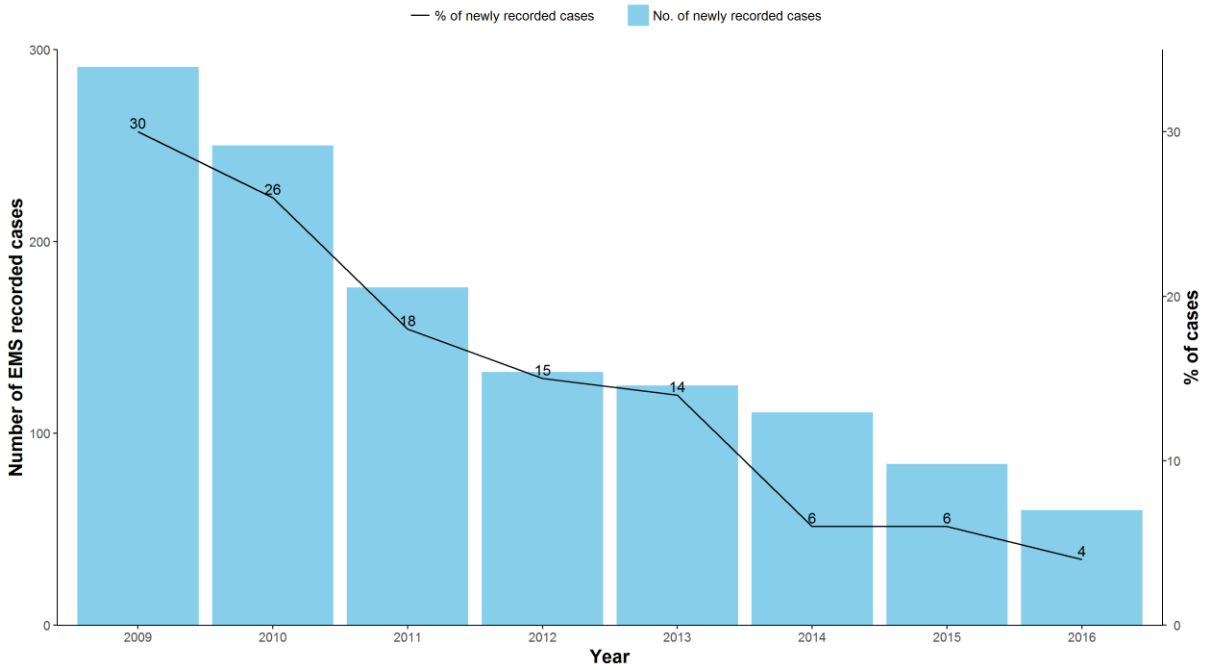


Figure 6: Number and percent of newly recorded cases in the EMS after implementation of the intervention



APPENDIX (2):

Table 12: Case definitions applied in Austria since 2008

Case definition 2012 according to EU Commission Decision 2012/506/EU		
Clinical description	NA	
Laboratory criteria for diagnosis	At least one of the following three: A. Detection of hepatitis C virus nucleic acid (HCV RNA) B. Detection of hepatitis C virus specific antigen (HCV core) C. 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	
Case classification	A. Possible case	NA
	B. Probably case	NA
	C. Confirmed case	Any person meeting the laboratory criteria
Case definition 2008 according to EU Commission Decision of 28/IV/2008		
Clinical description	NA	
Laboratory criteria for diagnosis	At least one of the following two: A. Detection of hepatitis C virus nucleic acid in serum B. Hepatitis C virus specific antibody (anti-HCV) response confirmed by a confirmatory by a different antibody test	
Case classification	D. Possible case	NA
	E. Probably case	NA
	F. Confirmed case	Any person meeting the laboratory criteria

Figure 7: Proposed new hepatitis C laboratory data entry mask of the EMS

Method and Results

Material [Single option]

- Ascites
- Ejaculate
- Liver biopsy
- Cadaver blood
- Plasma
- Serum
- Syringe contents

Result [Multiple options]
Genotype: [Textfield]
Subtype: [Textfield]
Anti-HCV Immunoassay [Single option]:

- positive
- negative
- borderline
- not performed

Anti-HCV Immunoblot [Single option]:

- positive
- negative
- inconclusive
- not performed

HCV-RNA [Single option]:

- detectable
- quantitative value [Textfield]: Number /scientific unit in IU/ml /Copy/ml
- quantitative value [Textfield]: Indication of the method-specific detection limit in IU/ml (e.g. <20 IU/ml)
- not detectable
- invalid or inconclusive
- not performed

HBV-Status [Single option]:

- positive
- negative
- unknown

Table 13: List of TESSy and additional EMS variables for hepatitis C surveillance

TESSy var	Additional EMS Var
RecordId	Ill
RecordType	Dead
RecordTypeVersion	Death due to illness
Subject	Reason for discarding case
DataSource	Date of illness
ReportingCountry	Date of death
DateUsedForStatistics	Clinician report
Age	Laboratory report
Case Classification	Symptoms
Complications	Hospitalised
Country of birth of patient	Additional comments
Country of nationality of patient	Laboratory material
Date of Diagnosis	Laboratory method
Date of Notification	Interpretation
Date of Onset of Disease	
Gender	
Genotype	
HBV Status	
Hepatitis C RNA or antigen	
Health care worker	
HIV Status	
Imported	
Outcome of case	
Place of notification	
Place of residence	
Probable Country Of Infection	
Recent injector status	
SexWorker	
StageHEP	
Testing Location	
Transmission	

Case detection (see Figure 8 for detailed data flows)

- **Patients without signs of hepatitis from the general population** presenting at health care facilities are tested for hepatitis virus infection as part of the pre-operative preparation procedure, prior to treatment with immunosuppressive drugs, within a check-up,
- **Blood recipients and dialysis patients** presenting at health care facility at a regular basis for disease specific reasons are routinely tested for blood borne infections
- Persons presenting as **blood donors** are tested for any blood borne infection
- **IV drug users**, as part of drug substitution treatment or needle exchange programs, **might** also be regularly tested for HBV-, HCV- and HIV infection at health care facilities/laboratories
- **Prisoners** are tested for HBV-, HCV- and HIV infection at admission and discharge, since mid-2016 in all Austrian federal prions
- **Patients presenting with signs of acute hepatitis** or chronic leaver disease at health care facilities are tested for hepatitis virus infection (HAV, HBV, HCV and HEV)

Testing Algorithm

1a Primary laboratories send results (positive/negative) of the HAV, HEV, HBV and HCV serology tests back to the requester (hospital physician, physician of ambulatory care in hospitals, outpatient clinics)

1b Consulting hospital physicians, physicians of ambulatory care in hospitals or physicians in outpatient clinics send blood samples from those who tested positive by anti-HCV assay to secondary/reference laboratories, or blood samples are sent directly from primary laboratories to secondary/reference laboratories for confirmatory testing and genotyping

2 Secondary laboratories/the reference laboratory send results (positive/negative) of HCV RNA test back to the requesters (consulting hospital physicians, physicians of ambulatory care in hospitals, outpatient clinics)

3 Secondary laboratories/the reference laboratory send results of HCV immunoblots back to the requesters (consulting hospital physicians, physicians of ambulatory care in hospitals, outpatient clinics)

Data sources – EMS and Data sources – district public health authorities

a Primary laboratories notify the anti-HCV positive through the web-based case data entry or the interface mediated case data entry to the EMS - the **electronic laboratory case report**

b Hospital physicians, physicians of ambulatory care in hospitals, outpatient clinics report a case of acute hepatitis C/chronic HCV infection mainly through a **clinician case report** in paper-format to the relevant district PH authority, who then enters the case data into the EMS, rarely the **clinician case report** goes directly to the **epidemiological web-based case recording (reporting)-system, the EMS**

c Secondary laboratories/reference laboratory notify HCV immunoblot positives, HCV RNA positives, HCV antigen positives through the web-based case data entry or interface mediated case data entry to the EMS - the **electronic laboratory case report**

Data recipients/users: from EMS to public health authorities, to AGES and to TESSy/ECDC

EMS: the **epidemiological web-based case recording (reporting)-system, the EMS** is the primary data base for hepatitis C cases and cases of all other notifiable infectious diseases in Austria

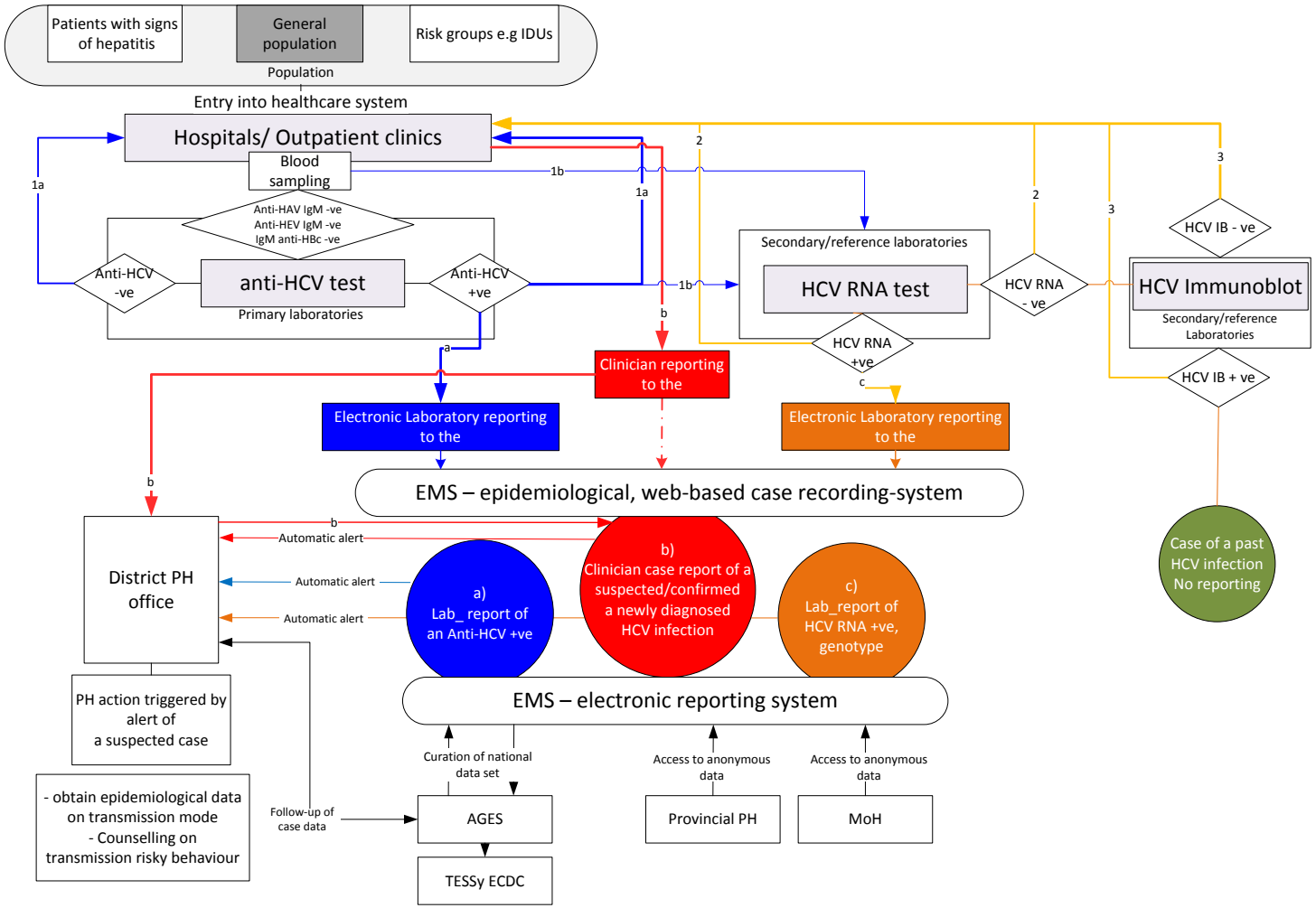
District PH authorities: Receive automatic alerts of suspected cases of Hepatitis C and have access to any EMS-Hepatitis C case report, arising from residents in the particular district

Province PH authorities: Have access to any EMS-Hepatitis C case report, arising from residents in the particular province

AGES: Acts as the curator of the dataset, and members of the department of infectious disease epidemiology conduct data quality assessments and data clean. AGES sends quality-checked data to TESSy/ECDC

ECDC: Receives the annual case-based dataset on Hepatitis C by AGES in the second quarter of the subsequent year

Figure 8: Data flow in the hepatitis C surveillance system from patient introduction, primary laboratory detection, laboratory confirmation, surveillance data collection, surveillance data recording in the EMS entry and public health action



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