Diagnostic hepatitis C testing of people in treatment for substance use disorders in Belgium between 2011 and 2014 : a cross-sectional study

L. Van Baelen, J. Antoine, K. De Ridder, G. Muyldermans, L. Gremeaux

Department of Public Health and Surveillance, Sciensano, Brussels, Belgium.

Abstract

Background **: Hepatitis C prevalence figures for people who use drugs in Belgium are scarce, and particularly for people who inject drugs. The current study refines the existing HCV estimates by focussing on diagnostic HCV testing practices for this population at risk.**

Methods **: The analysis is the result of a descriptive cross-sectional study, based on data extracted from the linkage between a database of people in treatment for substance use disorders in Belgium and a database of the Belgian health insurance companies. By using national nomenclature codes for HCV tests, the number of people in treatment for substance use disorders who were tested on HCV, were estimated.**

Results **: 18,880 out of 30,905 patients (61.1%) in treatment for substance use disorders between 2011 and 2014 have been screened at least once for HCV between 2008 and 2015. 58.0% of those who had never injected and 59.1% of those with an unknown injecting status were tested for HCV, compared to 86.5% of the patients who had recently injected and 84.5% of those who had ever injected. 36.8% of the people who had recently injected were tested for HCV RNA.**

Conclusions **: This study supports the need of a continued effort of health care providers to identify people infected with HCV. For a population at risk such as people who use drugs, regular screening is needed to reach the goal set by WHO of near viral elimination of HCV by 2030.** (Acta gastroenterol. belg., **2019**, 82, **35-42**).

Key Words : Hepatitis C, PCR, genotyping, anti-HCV, people who use drugs, people who inject drugs

Background

In 2016, the World Health Organization (WHO) has set a target of a worldwide 90% reduction of hepatitis C virus (HCV) by 2030 (1). In high-income countries like Belgium, sharing needles, syringes and paraphernalia by people who inject drugs (PWID) are considered to be the primary mode of HCV transmission (2), but also other people who use drugs are considered at higher risk of contracting HCV than the general population (3,4). Hence, it remains important to focus on a reduction of the number of HCV infected drug users, in particular PWID.

Estimates about the number of people living with HCV in Belgium are rare. Even less is known about HCV among people who use drugs, and more specifically among PWID. Particularly with the increased efficacy of new medication (i.e. the availability of direct-acting antivirals (DAA) with sustained viral response (SVR) ≥ 95%) and the changes in the Belgian reimbursement policy (where since January 2017 treatment of patients with liver fibrosis stage ≥ F2 is reimbursed within

the health care system), it is important to get reliable baseline figures.

In 2016, Matheï et al. estimated that approximately 2,970 PWID were HCV infected in Belgium (2). Based on data from 2010 and mathematical modelling, a standard has been set for the size and the nature of PWID with HCV. The aim of the current paper is to contribute to the understanding of HCV diagnostic testing prevalence figures among people with substance use disorders in Belgium and to illustrate the existing HCV estimates by focussing on HCV testing practices among PWID.

Methods

In this cross-sectional study, data from two Belgian national health and population registers were used. Data from the Belgian Treatment Demand Indicator (TDI) register (5) were linked to pharmacoepidemiological and health service use data gathered through the seven Belgian health insurance agencies and consolidated in the InterMutualistic Agency database (IMA) (6-8). The Belgian National Identification Number (NIN) was used to link both databases. This number is unique for every Belgian citizen and for other people living in Belgium with social security rights. 99% of the people living in Belgium has a NIN (6).

Case definition

As described in detail by the research protocol (9), inclusion of subjects was defined by patients' registration of the first treatment episode for substance use disorders between 2011 and 2014 in the Belgian TDI-database. An episode was defined as the period between the start of the treatment (i.e. the first face-to-face contact between a professional and the patient) and the end of activities in the context of the program prescribed. Subjects were patients who had sought treatment for substance use disorders within the reference period, without any exclusion criteria concerning nationality or age. If in that period patients had been in treatment more

than once, data from the first episode were used. All patients registered with a NIN who had been in treatment for substance use disorders between 2011 and 2014 have been confirmed eligible subjects (n=31,521). After exclusion of patients who could not be identified in the IMA-database (n=616), 30,905 subjects were included in the study. The TDI-database provided self-reported information on socio-demographic variables, substances for which treatment was sought, treatment history and injecting history at the start of the treatment episode (5).

Data collection HCV testing

For these 30,905 subjects, the IMA-database provided administrative data on the quantity and nature of the HCV-tests they had undergone in the period between 2008 and 2015. In general, screening for HCV consists of three subsequent tests, with each test being carried out in case the previous test was positive. The HCV antibody test detects the presence of antibodies and screens for past exposure or current infection. A positive antibody test is confirmed by a qualitative or quantitative PCR test to detect HCV viral RNA. A positive PCR test is followed by genotyping. The therapy choice and HCV treatment success rate will depend on the HCV genotype.

Since July 2008, all HCV tests, with the exception of the immunoblot, are reimbursed by the Belgian health insurance companies up to a limited number per year, depending on the kind of test and the reason for testing (10,11). The tests are prescribed by a variety of health professionals such as general practitioners, hepatologists or gastroenterologists working in e.g. general hospitals, private practices or health centres. Through the IMA-database, data was gathered on the history of reimbursed HCV testing between 2008 and 2015, based on national nomenclature codes for anti-HCV screening tests (i.e. codes 551154 and 551165), qualitative PCR (i.e. codes 556710 and 556721) and quantitative PCR (i.e. codes 556732 and 556743) for respectively confirmation and treatment follow-up, and genotyping (i.e. codes 556754 and 556765), performed only on HCV positive patients with an intention to treat (6,8).

Statistical analysis and reporting

Descriptive statistical analysis was performed using SAS software version 9.3 (SAS Institute Inc., Cary, NC). Numbers and proportions were used to describe the characteristics for four categories of subjects: PWID, former PWID who did not inject drugs recently, people who have never injected drugs and people with an unknown injecting status. The reporting of this study conforms to the STROBE guidelines (12).

Results

Out of 30,905 people in treatment for substance use disorders between 2011 and 2014, 3.6% (n=1,125)

reported recent injecting behaviour, 7.2% (n=2,227) had injected in the past, whereas 70.5% (n=21,796) reported that they had never injected. 18.6% (n=5757) of the subjects have an unknown injecting status (table 1). The median age category was 30-39 years. Patients were mainly men (73.7%) and the majority (55.5%) had already been in treatment for substance use disorders before. Alcohol was the main primary substance (42.4%) for which people sought treatment, but all substances combined, more than 50% of the patients had problems with opiates, cocaine or stimulants.

As shown in table 2, 18,880 out of 30,905 patients (61.1%) in treatment for substance use disorders between 2011 and 2014 have been screened at least once for HCV between 2008 and 2015. Of them, 91.2% was screened only for HCV antibodies, 4.4% was not only serologically tested but also for HCV RNA through a qualitative or quantitative PCR, and another 4.0% was tested for HCV antibodies, HCV RNA as well as HCV genotyping. 86.5% of the patients who had recently injected and 84.5% of those who had ever injected were tested for HCV at least once between 2008 and 2015, compared to 58.0% of those who had never injected and 59.1% of those with an unknown ever injecting status.

With regards to the testing procedures, for almost all of those who were tested, HCV antibodies screening tests were performed. Testing rates for hepatitis C RNA reached 36.8% for people who had recently injected and 34.2% for people who had injected in the past. In comparison, for the group who never injected or reported unknown injection history, respectively 3.0% and 7.7% were tested on hepatitis C RNA. For 19.4% of those who had recently injected and for 16.7% of those who had injected in the past, genotyping was done. In comparison, for the group who never injected or reported unknown injection history, genotyping was done for respectively 1.4% and 3.8%.

Out of 212 patients who had never injected and for whom a PCR test was done (not followed by genotyping), 43.9% was tested through PCR for the first time after their first episode in specialized treatment, with a median number of days between this first episode and the PCR test of 390 (range 0-1642 days; IQR 767). Out of 153 patients who had never injected and for whom a PCR test and genotyping was done, 48.4% was genotyped for the first time after their first treatment episode, with a median number of days between this first episode and the genotyping of 446 (range 4-1551 days; IQR 638 days).

Figure 1 gives an overview of the sequence of tests that have been conducted for patients who had ever or recently injected. Out of 3,352 patients with a history of injecting drugs 14.7% has not been screened for HCV between 2008 and 2015. The other 85.3% has been tested at least once for HCV. Detailed socio-demographic information for patients who have been tested for HCV is provided in appendix 1.

Table 1. — **Sociodemographic and substance use profile of people in treatment between 2011 and 2014 in Belgium by injecting history (recent, ever, never and unknown)**

| | Injecting history | | | | | | | | | |
| | Recent | | Ever | | Never | | Unknown | | Total | |
	N	%	N	%	N	%	N	%	N	%
Sex										
Male	903	80.3%	1,807	81.1%	15,804	72.5%	4,263	74.0%	22,777	73.7%
Female	222	19.7%	420	18.9%	5,992	27.5%	1,494	26.0%	8,128	26.3%
Unknown	1	0.1%	0	0.0%	4	0.0%	4	0.1%	9	0.0%
Age categories										
<20y	14	1.2%	27	1.2%	1,864	8.6%	129	2.2%	2,034	6.6%
20 y-29 y	339	30.1%	531	23.8%	5,456	25.0%	1,042	18.1%	7,368	23.8%
30 y-39 y	449	39.9%	845	37.9%	5,169	23.7%	1,179	20.5%	7,642	24.7%
40 y-49 y	257	22.8%	636	28.6%	4,414	20.3%	792	13.8%	6,099	19.7%
50 y-59 y	49	4.4%	160	7.2%	3,300	15.1%	423	7.3%	3,932	12.7%
≥ 60 y	3	0.3%	6	0.3%	1,320	6.1%	136	2.4%	1,465	4.7%
Unknown	14	1.2%	22	1.0%	273	1.3%	2,056	35.7%	2,365	7.7%
Main substance										
Opioids	700	62.2%	1,216	54.6%	2,088	9.6%	809	14.1%	4,813	15.6%
Cocaine	116	10.3%	195	8.8%	2,039	9.4%	463	8.0%	2,813	9.1%
Stimulants (amphetamines, MDMA…)	180	16.0%	186	8.4%	1,262	5.8%	437	7.6%	2,065	6.7%
Hypnotics and sedatives	17	1.5%	51	2.3%	829	3.8%	219	3.8%	1,116	3.6%
Cannabis	33	2.9%	226	10.1%	5,280	24.2%	1,040	18.1%	6,579	21.3%
Alcohol	69	6.1%	335	15.0%	10,022	46.0%	2,676	46.5%	13,102	42.4%
Other	10	0.9%	18	0.8%	276	1.3%	113	2.0%	417	1.3%
All substance (main + 6 other substances)										
Opioids	832	74.0%	1,421	63.8%	2,497	11.5%	942	16.4%	5,692	18.4%
Cocaine	592	52.6%	740	33.2%	3,969	18.2%	1,022	17.8%	6,323	20.5%
Stimulants (amphetamines, MDMA…)	363	32.3%	412	18.5%	2,599	11.9%	872	15.1%	4,246	13.7%
Hypnotics and sedatives	315	28.0%	564	25.3%	2,994	13.7%	677	11.8%	4,550	14.7%
Cannabis	445	39.6%	1,029	46.2%	8,600	39.5%	1,984	34.5%	12,058	39.0%
Alcohol	375	33.3%	1,022	45.9%	14,310	65.7%	3,450	59.9%	19,157	62.0%
Past treatment										
No	170	15.1%	293	13.2%	9,369	43.0%	2,140	37.2%	11,972	38.7%
Yes	871	77.4%	1,800	80.8%	11,593	53.2%	2,901	50.4%	17,165	55.5%
Unknown	84	7.5%	134	6.0%	834	3.8%	716	12.4%	1,768	5.7%
Total	1,125	3.6%	2,227	7.2%	21,796	70.5%	5,757	18.6%	30,905	100%
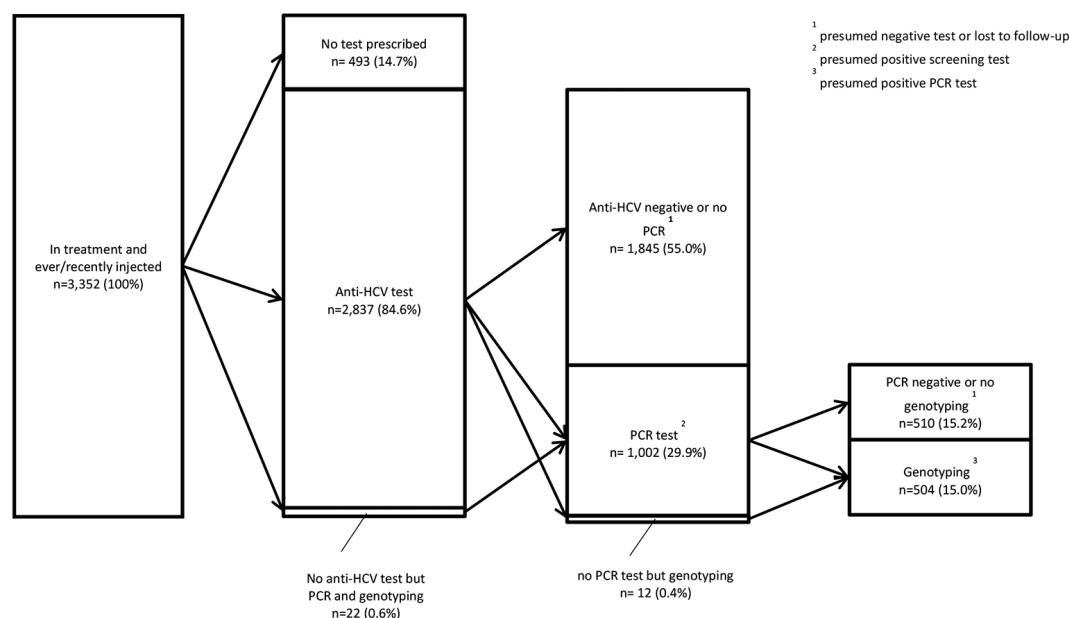
Fig. 1. — Sequence of HCV tests, conducted between 2008 and 2015, for patients in treatment between 2011 and 2014 in Belgium, who had recently or ever injected

Table 2. — **Combination analysis screening: number of patients in treatment for substance use disorders per test according to injecting history in Belgium between 2008 and 2015**

| Test | | | Injecting history | | | | | | | | | |
| | | | Recent | | Ever | | Never | | Unknown | | Total | |
Anti-HCV	PCR	Genotyping	N	%	N	%	N	%	N	%	N	%
X			609	62.6%	1236	65.5%	12,237	97.0%	3,140	92.3%	17,222	91.2%
X	X		171	17.6%	328	17.4%	212	1.7%	128	3.8%	839	4.4%
X	X	X	179	18.4%	302	16.0%	153	1.2%	122	3.6%	756	4.0%
X		X	6	0.6%	6	0.3%	7	0.1%	5	0.1%	24	0.1%
	X		4	0.4%	7	0.4%	1	0.0%	6	0.2%	18	0.1%
	X	X	4	0.4%	7	0.4%	7	0.1%	2	0.1%	20	0.1%
		X	0	0.0%	0	0.0%	1	0.0%	0	0.0%	1	0.0%
Total			973	100%	1,886	100%	12,618	100%	3,403	100%	18,880	100%
Tested for HCV			973	86.5%	1,886	84.7%	12,618	58.0%	3,403	59.1%	18,880	61.1%
Not tested for HCV			152	13.5%	341	15.3%	9,178	42.0%	2,354	40.9%	12,025	38.9%
Total in treatment			1,125	100%	2,227	100%	21,796	100%	5,757	100%	30,905	100%

Discussion

A population-based prevalence study from 1993-1994 estimated HCV prevalence in Flanders at 0.87% (13). Together with the introduction of second generation DAAs and the changed reimbursement policy in Belgium in January 2017, several other studies have been published with models and scenarios on the prevalence rate of HCV in the general population and how HCV treatment protocols could have an impact on these figures (2,14-17). For instance recent modelling has estimated viremic infections of HCV in the Belgian general population at 0.6% (95% CI 0.2%-0.7%), of which 43% were diagnosed (14). With the current study on HCV screening within a risk group of patients who have been in treatment for substance use disorders, the figures that are provided could give new input to the debate on HCV in Belgium. To this end, a clear distinction has been made between people without injecting history and others who have injected in the past or recently.

Indeed, risk behaviour among substance users is not limited to using and sharing injection material but also to sharing paraphernalia such as sniffing implements (18). It has been reported before that HCV prevalence rates among people with substance use disorders who have never injected are higher than rates in the general population (3,4). The current study showed that 58.0% of the patients who reported that they had never injected have been tested for HCV and for 1.4% of them genotyping was done, which is an indication for viremic HCV infection. However, some of them might have started injecting and might have been HCV infected after their first registration in the TDI-database. This can be illustrated by the fact that for 43.9% of the patients who had never injected and for whom a PCR test was done, the median time for the first PCR test was more than a year after the first episode in specialized treatment. For 48.4% of those who had never injected and for whom a PCR test and genotyping was done, the median time for the first genotyping was almost one year and three months after the first treatment episode for substance use disorders. Nevertheless, using and sharing injection material remains the leading cause of HCV transmission (19). In the current study, more than 85% of the 3,352 people with a history of injecting drug use have been screened at least once for HCV between 2008 and 2015. As mentioned in reports from the Belgian work field (20), PWID have several intake sessions in a treatment centre before they are offered serological or molecular testing. For instance, in a low-threshold service in Brussels with a monthly active patient flow of approximately 300 patients, this argument is given as the main reason for the fact that for 20% of the patients the HCV-status is unknown (20). Some of them drop out after registration in the system but before being tested for HCV anti-bodies. This might explain the number of patients with injecting history who have not been tested.

However, the median test frequency between 2008 and 2015 for screened patients with a history of injecting drugs was 3 per patient, i.e. once every 2.6 years. For people who had stopped injecting or who were injecting but not sharing needles, one test might have been enough, but for others with more risky drug behaviour WHO recommends repeated screening, with the possibility of reinfection after spontaneous clearance or successful treatment to be taken into consideration (19).

Testing rates for hepatitis C RNA are also lower than expected. Indeed, according to a European systematic review in 2014 (21), the level of chronic infections in

anti-HCV positive PWID ranged between 53% and 97% with a median of 72% (IQR 64%–81%). In the current study, only 37.4% of the screened patients who had recently injected were tested for HCV RNA (or immediately through viral genotyping). This could mean that 62.6% of the anti-HCV tests were negative, which would contradict existing national and international prevalence figures or, as mentioned before, it could indicate that a large group of patients who were anti-HCV positive dropped out before a PCR could be done. As reported by other research, the prescription of both anti-HCV and HCV RNA tests during a single testing event might be a solution (22), as well as a central HCV register with details of conducted tests, treatment and follow up per patient (23).

Finally, viral genotyping was done for 189 patients (19.4%) who had recently injected and for 315 patients who had ever injected (16.7%). For 115 of these 504 patients (22.8%) genotyping was done more than once, with a maximum of 4 times for 5 patients (data not shown). These percentages are an indication of the intention to treat, although up to 2017, reimbursement of treatment was restricted to patients with F3 or F4 fibrosis. In 2016, Matheï et al. developed a model for PWID in which the impact of HCV treatment on the reduction of HCV infections was estimated (2). One of the conclusions was that between 2015 and 2030 each year 30 PWID had to be treated to reach a 5% reduction in total HCV infections among PWID by 2030. In the current study 189 PWID were genotyped between 2008 and 2015, meaning an average of 24 PWID annually. Since genotyping is not necessarily followed by treatment, the actual treatment uptake rate is likely to be even lower. This would mean that the abovementioned goal regarding the reduction in HCV infections of 5% by 2030 would not be met if the same pace of screening and treatment will be maintained. One of the reasons for this low number might be that although recent studies (24,25) have shown that there is no significant difference in outcome between HCV treatment of PWID and non-PWID, the former have always been considered by clinicians as difficult to treat because of existing social and psychological barriers and concerns about adherence and reinfection (26-28). In the near future, the increased efficacy of new medication and the changes in the Belgian reimbursement policy could have a positive impact on this number.

The main strength of the current research is the national coverage of the database and the availability of longitudinal data. However, there are also several key limitations to the study, some of which are related to the linkage of the TDI- and IMA-database as discussed already before (9). Firstly, not all health care providers working with people with substance use disorders participated in TDI between 2011 and 2014. The database covers inpatient and outpatient services, but for instance general practitioners did not provide data and hence their work with people who seek treatment for substance use disorders is not reflected in the current analysis. If a general practitioner requested HCV-tests for a person with substance use disorders who was in specialized treatment between 2011 and 2014, this will appear in the database, but if the person was not in specialized treatment during that period, it will not.

Secondly, people who were subject to testing in prison were not registered in the TDI-database. A comprehensive literature search of data published between 2005 and 2015 on HCV in imprisoned PWID revealed HCV prevalence figures for Western Europe almost systematically above 30%, up to 58% for the Netherlands and 83% for Germany (29). Since 18.1% of the prisoners in Belgium have ever injected (30), this could again result in an underestimation of the number of PWID screened for HCV. At the same time previous imprisonment might be an explanation for the people in present study for whom PCR or genotyping was done without data available about prior anti-HCV tests or PCR respectively.

Thirdly, the results are based on patients who were in treatment for substance use disorders between 2011 and 2014. Almost 80% of the patients with a history of injecting drug use reported that they had been in treatment already before. This means that some of them might have been tested before 2008 and when they were HCV-positive, it is unclear whether they were tested again when they came back between 2011 and 2014. In addition, by linking cross-sectional data from TDI with longitudinal data from IMA, it might be that patient characteristics are not correctly reflecting the situation at every single moment. For instance, it might be that some people are correctly registered in TDI as not injecting whereas at the moment they were tested for HCV they were already injecting.

A fourth limitation concerns the fact that the data only reflects HCV-tests, without taking into account the impact of subsequent treatment. Indeed, the numbers reflect people with substance use disorders who have been tested between 2008 and 2015, and who were eventually HCV-positive. However, some of them might have been treated in the same period or they might have cleared spontaneously the HCV. Also, patients who were cleared or treated might have been reinfected afterwards. Even if they were tested each time they were infected, they were only counted once in the current study. Indeed, the data did not allow differentiating between people who were reinfected after treatment and people who were tested multiple times without treatment.

Conclusion

The most important information gained from this analysis is that almost 60% of the patients without and more than 85% of the patients with a history of injecting drugs were screened for HCV. Particularly for this population at risk, this screening ratio might not be sufficient to reach the goal set by WHO of near

viral elimination of HCV by 2030 (1). The results also underline the utility of a screening procedure including multiple tests during a single screening event (22), as well as the implementation of a national patient register with results of tests and treatment (23).

References

1. WHO. Combating hepatitis B and C to reach elimination by 2030. WHO, Geneva : 2016.
2. MATHEÏ C., BOURGEOIS S., BLACH S., BRIXKO C., MULKAY J.P., RAZAVI H. *et al*. Mitigating the burden of hepatitis C virus among people who inject drugs in Belgium. *Acta Gastroenterol. Belg.,* 2016, **79 :** 227-232.
3. MATHEÏ C., WOLLANTS E., VERBEECK J., VAN RANST M., ROBAEYS G., VAN DAMME P. *et al*. Molecular epidemiology of hepatitis C among drug users in Flanders, Belgium: association of genotype with clinical parameters and with sex- and drug-related risk behaviours. *Eur. J. Clin. Microbiol. Infect. Dis.* 2005, **24 :** 514-522.
4. MACÍAS J., PALACIOS R.B., CLARO E., VARGAS J., VERGARA S., MIRA J.A. *et al*. High prevalence of hepatitis C virus infection among noninjecting drug users: association with sharing the inhalation implements of crack. *Liver Int.,* 2008, **28 :** 781-786.
5. ANTOINE J., DE RIDDER K., PLETTINCKX E., BLANCKAERT P., GREMEAUX L. Treatment for substance use disorders: the Belgian Treatment Demand Indicator registration protocol. *Arch. Public Health,* 2016, **74 :** 27.
6. IMA. IMA Population Database. 2014. Retrieved from: http://www.aim-ima.be/Data-Populatie-53
7. IMA. IMA Pharmaceutical Database. 2014. Retrieved from : http://www.aim-ima.be/Data-Farmanet
8. IMA. IMA Health Service Database. 2013. Retrieved from: http://www.aim-ima.be/Data-Gezondheidszorgen
9. VAN BAELEN L., DE RIDDER K., ANTOINE J., GREMEAUX L. Protocol of the Belgian TDI-IMA linkage: a database for longitudinal pharmacoepidemiological and health services research for substance users in treatment. *Arch. Public Health,* 2018, **76** : 3
10. MUYLDERMANS G., VAN GUCHT S., VAN BAELEN L. Jaarrapport 2016 Hepatitic C Virus. WIV-ISP, Brussels : 2016.
11. AGENTSCHAP ZORG & GEZONDHEID. Richtlijnen Infectiebestrijding Vlaanderen - Hepatitis C. Agentschap Zorg & Gezondheid, Brussels : 2017.
12. VON ELM E., ALTMAN D., EGGER M., POCOCK S., GØTZSCHE P., VANDENBROUCKE J. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *BMJ,* 2007, **335 :** 806-808.
13. BEUTELS M., VAN D., AELVOET W., DESMYTER J., DONDEYNE F., GOILAV C. *et al*. Prevalence of hepatitis A, B and C in the Flemish population. *Eur. J. Epidemiol.,* 1997, **13 :** 275-280.
14. BOURGEOIS S., BLACH S., BLACH C., LALEMAN W., MATHEÏ C., MULKAY J. *et al*. Achieving WHO recommendations for Hepatitis C Virus Elimination in Belgium. *Acta Gastroenterol. Belg.,* 2016, **79 :** 227-232.

15. VAN DAMME P., LALEMAN W., STÄRKEL P., VAN VLIERBERGHE H., VANDIJCK D., HINDMAN S. *et al*. Hepatitis C Epidemiology in Belgium. *Acta Gastroenterol. Belg.,* 2016, **77 :** 277-279.
16. VANDIJCK D., MORENO C., STÄRKEL P., VAN DAMME P., VAN VLIERBERGHE H., HINDMAN S. *et al*. Current and future health and economic impact of hepatitis C in Belgium. *Acta Gastroenterol. Belg.,* 2016, **77 :** 285-290.
17. STÄRKEL P., VANDIJCK D., LALEMAN W., VAN DAMME P., MORENO C., HINDMAN S. *et al*. The disease burden of hepatitis C in Belgium: development of a realistic disease control strategy. *Acta Gastroenterol. Belg.,* 2015, **78 :** 228-232.
18. AARON S., MCMAHON J., MILANO D., TORRES L., CLATTS M., TORTU S. *et al*. Intranasal Transmission of Hepatitis C Virus: Virological and Clinical Evidence. *Clin. Infect. Dis.,* 2008, **47 :** 931-934.
19. WHO: Guidelines for the screening, care and treatment of persons with hepatitis infection. Geneva : 2014.
20. MAISON D'ACCUEIL SOCIO-SANITAIRE (MASS) DE BRUXELLES. Rapport d'activité. MASS, Brussels : 2017.
21. WIESSING L., FERRI M., GRADY B., KANTZANOU M., SPERLE I., CULLEN K. *et al*. Hepatitis C Virus Infection Epidemiology among People Who Inject Drugs in Europe: A Systematic Review of Data for Scaling Up Treatment and Prevention. *PLOS ONE* 2014, **9 :** e103345.
22. BLACKBURN N., PATEL R., ZIBBELL J. Improving Screening Methods for Hepatitis C Among People Who Inject Drugs: Findings from the HepTLC Initiative, 2012-2014. *Public Health Rep.,* 2016, **131 :** 91-97.
23. MINISTERIE VAN SOCIALE ZAKEN EN VOLKSGEZONDHEID Protocolakkoord 'HCV-plan'. Brussels : 2014. Retrieved from: http://overlegorganen.gezondheid.belgie.be/sites/default/files/documents/interministeriele_ conferentie_volksgezondheid/2014_protocolakkoord_hcv-plan.pdf
24. BIELEN R., MORENO C., VAN VLIERBERGHE H., BOURGEOIS S., MULKAY J., VANWOLLEGHEM T. *et al*. Belgian experience with direct acting antivirals in people who inject drugs. *Drug Alcohol Depend.,* 2017, **177 :** 214-220.
25. ROBAEYS G., CHRISTENSEN S., LUCIDARME D., ARAIN A., BRUGGMANN P., KUNKEL J. *et al*. Chronic Hepatitis C Treatment in Patients with Drug Injection History: Findings of the INTEGRATE Prospective, Observational Study. *Infect. Dis. Ther.,* 2017, **6 :** 265-275.
26. HIGGS P., SACKS-DAVIS R., GOLD J., HELLARD M. Barriers to receiving hepatitis C treatment for people who inject drugs: Myths and evidence. *Hepat. Mon.,* 2011, **11 :** 513-518.
27. FOSTER G. Injecting drug users with chronic hepatitis C: should they be offered antiviral therapy? *Addiction,* 2008, **103 :** 1412-1413.
28. MARTIN N., VICKERMAN P., MINERS A., FOSTER G., HUTCHINSON S., GOLDBERG D. *et al*. Cost-effectiveness of hepatitis C virus antiviral treatment for injection drug user populations. *Hepatology,* 2012, **55 :** 49-57.
29. DOLAN K., WIRTZ A., MOAZEN B., NDEFFO-MBAH M., GALVANI A., KINNER S. *et al*. Global burden of HIV, viral hepatitis, and tuberculosis in prisoners and detainees. *Lancet,* 2016, **388 :** 1089-1102.
30. TODTS S., GLIBERT P., VAN MALDEREN S., VAN HUYCK C., SALIEZ V., HOGGE M. Druggebruik in Belgische gevangenissen - Monitoring van gezondheidsrisico's. Federale Overheidsdienst Justitie, Brussels : 2008.

Appendix 1 — Socio-demographic and substance use profile of patients in treatment for substance use disorders in Belgium, who have been tested for HCV between 2008 and 2015 in Belgium, by injecting history (recent, ever, never and unknown)

	Injecting history									
	Recent		Ever		Never		Unknown		Total	
	N	%	N	%	N	%	N	%	N	%
Sex										
Male	775	79.7%	1499	79.5%	8602	79.7%	2413	70.9%	13289	70.4%
Female	198	20.3%	387	20.5%	4016	20.3%	990	29.1%	5591	29.6%
Age categories										
<20y	12	1.2%	18	1.0%	608	4.8%	63	1.9%	701	3.7%
20 y-29 y	304	31.2%	451	23.9%	2975	23.6%	673	19.8%	4403	23.3%
30 y-39 y	386	39.7%	705	37.4%	3377	26.8%	845	24.8%	5313	28.1%
40 y-49 y	220	22.6%	550	29.2%	2861	22.7%	555	16.3%	4186	22.2%
50 y-59 y	38	3.9%	137	7.3%	1938	15.4%	248	7.3%	2361	12.5%
≥ 60 y	1	0.1%	5	0.3%	665	5.3%	68	2.0%	739	3.9%
Unknown	12	1.2%	20	1.1%	194	1.5%	951	27.9%	1177	6.2%
Region of treatment for substance use disorders[1]										
Flanders	707	72.7%	1167	61.9%	7685	60.9%	2492	73.2%	12051	63.8%
Wallonia	183	18.8%	514	27.3%	3796	30.1%	591	17.4%	5084	26.9%
Brussels	83	8.5%	205	10.9%	1137	9.0%	320	9.4%	1745	9.2%
Program type										
Medical Social Care Center	249	25.6%	382	20.3%	1172	9.3%	321	9.4%	2124	11.3%
Specialized outpatient service	203	20.9%	595	31.5%	3042	24.1%	640	18.8%	4480	23.7%
Crisis center	199	20.5%	272	14.4%	749	5.9%	116	3.4%	1336	7.1%
Therapeutic community	16	1.6%	95	5.0%	693	5.5%	87	2.6%	891	4.7%
Mental health service	0	0.0%	3	0.2%	29	0.2%	836	24.6%	868	4.6%
Psychiatric hospital	211	21.7%	424	22.5%	3793	30.1%	744	21.9%	5172	27.4%
General hospital	95	9.8%	115	6.1%	3137	24.9%	652	19.2%	3999	21.2%
Unknown	0	0.0%	0	0.0%	3	0.0%	7	0.2%	10	0.1%
Past treatment										
No	130	13.4%	215	11.4%	4353	34.5%	959	28.2%	5657	30.0%
Yes	776	79.8%	1562	82.8%	7736	61.3%	1991	58.5%	12065	63.9%
Unknown/missing	67	6.9%	109	5.8%	529	4.2%	453	13.3%	1158	6.1%
Source of referral										
Own initiative	556	57.1%	1012	53.7%	5433	43.1%	1278	37.6%	8279	43.9%
Family or friends	92	9.5%	131	6.9%	1784	14.1%	352	10.3%	2359	12.5%
Outpatient center for substance use	72	7.4%	119	6.3%	295	2.3%	117	3.4%	603	3.2%
General practitioner	21	2.2%	90	4.8%	1433	11.4%	415	12.2%	1959	10.4%
Hospital or other medical service	59	6.1%	144	7.6%	1526	12.1%	490	14.4%	2219	11.8%
Social service	45	4.6%	72	3.8%	374	3.0%	161	4.7%	652	3.5%
Police or justice	86	8.8%	263	13.9%	1327	10.5%	459	13.5%	2135	11.3%
Other	17	1.7%	19	1.0%	187	1.5%	71	2.1%	294	1.6%
Unknown/missing	25	2.6%	36	1.9%	259	2.1%	60	1.8%	380	2.0%
Education										
No	19	2.0%	47	2.5%	107	0.8%	24	0.7%	197	1.0%
Primary education	334	34.3%	701	37.2%	2971	23.5%	462	13.6%	4468	23.7%
Secondary education	464	47.7%	895	47.5%	6866	54.4%	1770	52.0%	9995	52.9%
Higher education	38	3.9%	73	3.9%	1764	14.0%	386	11.3%	2261	12.0%
Unknown/missing	118	12.1%	170	9.0%	910	7.2%	761	22.4%	1959	10.4%
Main substance										
Opiates	48	4.9%	102	5.4%	148	1.2%	41	1.2%	339	1.8%
Heroin	526	54.1%	807	42.8%	1195	9.5%	483	14.2%	3011	15.9%
Methadone	27	2.8%	139	7.4%	131	1.0%	53	1.6%	350	1.9%

[1] Of all treatment programs participating in the TDI registration, 54% is located in Flanders, 32% in Wallonia and 14% in Brussels

Buprenorphine	4	0.4%	17	0.9%	17	0.1%	1	0.0%	39	0.2%
Other opiates	6	0.6%	6	0.3%	72	0.6%	19	0.6%	103	0.5%
Opioids (total)	611	62.8%	1071	56.8%	1563	12.4%	597	17.5%	3842	20.3%
Cocaine	109	11.2%	142	7.5%	1218	9.7%	309	9.1%	1778	9.4%
Cocaine (other)	2	0.2%	13	0.7%	36	0.3%	8	0.2%	59	0.3%
Cocaine (total)	111	11.4%	155	8.2%	1254	9.9%	317	9.3%	1837	9.7%
Amphetamines	139	14.3%	135	7.2%	597	4.7%	249	7.3%	1120	5.9%
Stimulants (other)	8	0.8%	7	0.4%	98	0.8%	28	0.8%	141	0.7%
Stimulants (total)	147	15.1%	142	7.5%	695	5.5%	277	8.1%	1261	6.7%
Hypnotics and sedatives	1	0.1%	5	0.3%	60	0.5%	11	0.3%	77	0.4%
Barbiturates	0	0.0%	0	0.0%	4	0.0%	9	0.3%	13	0.1%
Benzodiazepines	10	1.0%	35	1.9%	398	3.2%	93	2.7%	536	2.8%
Other hypnotics and sedatives	3	0.3%	3	0.2%	70	0.6%	24	0.7%	100	0.5%
Hypnotics and sedatives (total)	14	1.4%	43	2.3%	532	4.2%	137	4.0%	726	3.8%
Cannabis	26	2.7%	177	9.4%	2146	17.0%	468	13.8%	2817	14.9%
Alcohol	56	5.8%	282	15.0%	6259	49.6%	1536	45.1%	8133	43.1%
Other	8	0.8%	16	0.8%	169	1.3%	71	2.1%	264	1.4%
Frequency of use main substance										
Not used in the last month	45	4.6%	345	18.3%	1177	9.3%	447	13.1%	2014	10.7%
Once per week or less	64	6.6%	162	8.6%	791	6.3%	152	4.5%	1169	6.2%
Two to six times per week	176	18.1%	266	14.1%	2125	16.8%	550	16.2%	3117	16.5%
Daily	656	67.4%	1059	56.2%	8064	63.9%	1726	50.7%	11505	60.9%
Unknown/missing	32	3.3%	54	2.9%	461	3.7%	528	15.5%	1075	5.7%
Age first use main substance										
Median age first use	19.6		18.9		19.5		20.0		19.5	
(Missing age first use)	(94)	(9.7%)	(161)	(8.5%)	(2142)	(17.0%)	(2003)	(58.9%)	(4400)	(23.3%)
Year of start treatment										
2011	305	31.3%	630	33.4%	2276	18.0%	544	16.0%	3755	19.9%
2012	251	25.8%	522	27.7%	3274	25.9%	722	21.2%	4769	25.3%
2013	226	23.2%	386	20.5%	3302	26.2%	981	28.8%	4895	25.9%
2014	191	19.6%	348	18.5%	3766	29.8%	1156	34.0%	5461	28.9%
Nationality										
Belgian	887	91.2%	1669	88.5%	11680	92.6%	3090	90.8%	17326	91.8%
EU citizen but not Belgian	33	3.4%	98	5.2%	322	2.6%	74	2.2%	527	2.8%
Non-EU citizen	51	5.2%	97	5.1%	424	3.4%	87	2.6%	659	3.5%
Unknown/missing	2	0.2%	22	1.2%	192	1.5%	152	4.5%	368	1.9%
Professional situation										
Regular job	111	11.4%	260	13.8%	3026	24.0%	760	22.3%	4157	22.0%
Student	7	0.7%	22	1.2%	607	4.8%	61	1.8%	697	3.7%
Economically non-active	437	44.9%	896	47.5%	5409	42.9%	1426	41.9%	8168	43.3%
Unemployed	270	27.7%	446	23.6%	2525	20.0%	652	19.2%	3893	20.6%
Other	70	7.2%	150	8.0%	542	4.3%	266	7.8%	1028	5.4%
Unknown/missing	78	8.0%	112	5.9%	509	4.0%	238	7.0%	937	5.0%
Total tested on HCV	973	100%	1,886	100%	12,618	100%	3,403	100%	18,880	100%