Microelimination or not? The changing epidemiology of HIV-HCV coinfection in France 2012-2018

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Summary: A major shift in HCV epidemiology was observed in French HIV-infected patients from 2012 to 2018 with MSM being today the major group of HCV transmission. Three WHO targets for HCV elimination are already reached in HIV-HCV patients in France.

Abstract

Background: The arrival of highly effective, well tolerated direct-acting antiviral agents (DAA) led to a dramatic decrease in HCV prevalence. HIV-HCV coinfected patients are deemed a priority population for HCV elimination, while a rise of recently acquired HCV infections in MSM has been described. We describe the variations in HIV-HCV epidemiology in the French Dat'AIDS cohort.

Methods: Retrospective analysis of a prospective HIV-infected cohort from 2012 to 2018. Determination of HCV prevalence, incidence, proportion of viremic patients, treatment uptake and mortality rate in the full cohort and by HIV risk factors.

Results: From 2012 to 2018, 50861 HIV-infected patients with a known HCV status were followed-up. During the period, HCV prevalence decreased from 15.4% to 13.5%. HCV prevalence among new HIV cases increased from 1.9% to 3.5% in MSM but remained stable in other groups. Recently acquired HCV incidence increased from 0.36/100PY to 1.25/100PY in MSM. The proportion of viremic patients decreased from 67.0% to 8.9%. MSM became the first group of viremic patients in 2018 (37.9%). Recently acquired hepatitis represented 59.2% of viremic MSM in 2018. DAA treatment uptake increased from 11.4% to 61.5%. More treatments were initiated in MSM in 2018 (41.2%) than in IVDU (35.6%). In MSM, treatment at acute phase represented 30.0% of treatments in 2018.

Conclusions: A major shift in HCV epidemiology was observed in HIV-infected patients in France from 2012 to 2018, leading to a unique situation in which the major group of HCV transmission in 2018 was MSM.

Keywords

Hepatitis C virus, Human Immunodeficiency virus, coinfection, epidemiology, men having sex with men, microelimination

Introduction

The arrival in 2012-2013 of new, highly-effective, well-tolerated, direct-acting antiviral agents (DAA), combined with progresses in injection and blood safety resulted in a worldwide drastic decrease in Hepatitis C virus (HCV) prevalence [1,2], leading the WHO to target "HCV elimination" by 2030. WHO objectives included the diagnosis of 90% of patients with viral hepatitis infections, a 90% reduction in new chronic HCV infection, 80% of chronic HCV infections treated and a 65% reduction in mortality [3]. HCV infection is frequent among persons living with HIV (PLWH) and is usually associated with pejorative outcomes [4,5]. DAA treatment efficacy appears similar in HIV-HCV coinfected and in HCV monoinfected patients [6], and regular follow-up for antiretroviral treatment may favor DAA treatment uptake in coinfected patients [7]. As a result, the HIV-HCV population was deemed a priority population for HCV elimination. In France, harm reduction interventions and a facilitated access to opioid substitution treatment (OST) have resulted over the past decades in a dramatic decline in HIV transmission in intravenous drug users (IVDU) [8,9], which accounted for only 2% of new HIV infections in 2018 [9]. On the other hand, new ways of HCV transmission recently arose in populations previously moderately affected, such as men having sex with men (MSM), leading to an increased incidence and prevalence in this population [10–12]. Additionally, international transmission networks of HCV in MSM [13–15] and transmission in both HIV-negative and HIV-infected MSM have been described [16,17] which could fuel an otherwise relatively closed population.

Therefore, describing the HIV-HCV epidemiology with a focus on trends over time appears essential to grasp the epidemic at the global level and better target preventive measures. The objective of this study was to analyze the changing epidemiology of the HIV-HCV coinfection in France during the 2012-2018 period in a large cohort of PLWH.

Material and Methods

Source of data

Data on PLWH were extracted from the Dat'AIDS cohort based on 23 French major HIV centers. This cohort collects clinical, biological, and virological data and covers about 25% of PLWH in care in France [18,19]. The Fib4 score with a cut-off of 3.25 to estimate severe fibrosis or cirrhosis was determined yearly in HIV-HCV coinfected patients [20]. According to French recommendations, HCV screening among PLWH is performed every 12 months or more frequently in patients with high-risk practices such as intravenous or nasal drug use, unprotected sex and traumatic sex practices. Additionally, PLWH are routinely followed every 3–6 months with assessment of alanine aminotransferase (ALT) level. PLWH who have cured HCV are followed every 3-6 months with ALT and HCV-RNA assessments. In France, testing recommendations did not change during the study period. Details on the Dat'AIDS cohort and on definitions may be found as Supplementary Appendix.

Statistical analysis

Details on HCV elimination WHO targets are presented in the Supplementary appendix. Trends over time were tested using a Poisson regression model. Analyses were performed using R software (R Foundation for Statistical Computing, Vienna, Austria).

Ethical considerations

The current study was conducted in accordance with French ethics regulations. All patients gave their written inform consent, allowing the use of their clinical and biological data. The study was approved by the Hospices Civils de Lyon Ethics Committee. The Dat'AIDS cohort is registered with identifier NCT02898987 in ClinicalTrials.gov.

Results

During the 2012-2018 period, 57,339 PLWH were followed-up in the Dat'AIDS cohort of whom 50,861 had at least one HCV follow-up during the study period. Among them, 42,840 (84.2%) remained HCV negative whereas 8021 were HCV positive giving an overall HCV prevalence of 15.8% (Figure 1). Demographics and biological characteristics at last follow-up of patients with a known HCV status in the cohort are described in Table 1.

Drug use and alcohol intake

Overall, 8.3% were using drugs at last follow-up, including 9.1% of IVDU and 12.3% of MSM. Additionally, 33.3% of patients were considered as former drug users or received opioid treatment substitution, a proportion reaching 90.9% in IVDU and 26.8% in MSM. An excessive alcohol intake of more than 20g alcohol/day was reported in 11.7% of patients, a proportion reaching 26.9% in IVDU.

HCV prevalence

Overall, the HCV prevalence decreased in PLWH from 15.4% in 2012 to 13.5% in 2018 (p<0.001) (Table 2). Based on HIV risk factors, HCV prevalence remained stable over the period in IVDU (89.2% vs 89.6%; p=0.856) and in patients with other/unknown risk (17.2% vs 16.3%; p=0.336), decreased in heterosexuals (7.4% vs 6.5%; p<0.001) and increased in MSM (6.3% vs 7.6%; p<0.001).

Among new HIV cases, the HCV prevalence remained stable over time (3.6% vs 3.8%; p=0.773). The prevalence among new HIV cases remained stable in IVDU (44.4% vs 42.9%; p=0.954), in heterosexuals (3.0% vs 2.8%; p=0.849) and in patients with other/unknown HIV risk factors (7.0% vs 7.3%; p=0.940). It increased in MSM from 1.9% in 2012 to 3.5% in 2018, although this difference did not reach statistical significance (p=0.093).

Recently acquired hepatitis

The number of recently acquired HCV cases ranged from 74 in 2012 to 100 cases in 2018 with a peak of 126 in 2013. The trend over time differed according to the type of hepatitis with a regular decrease of first HCV infections from 105 cases in 2013 to 62 cases in 2018 paralleled with an increase of reinfection cases from 15 in 2012 to 38 in 2018. Overall, the incidence rate of recently acquired HCV infection increased from 0.20/100PY in 2012 to 0.73/100PY in 2018 (p<0.001), both for first infections (0.17 to 0.52/100PY; p<0.001) and for reinfections (0.91 to 1.97/100PY; p=0.011). In MSM, the incidence rate of recently acquired HCV infection increased from 0.36/100PY in 2012 to 1.25/100PY in 2018 (p<0.001). The increase was significant for first infections (0.32 to 0.84/100PY; p<0.001) but not for reinfections (2.57 to 5.79/100PY; p=0.57).

HCV viremic patients

The proportion of HCV-RNA positive patients decreased from 67.0% in 2012 to 21.4% in 2018 (p<0.001). Based on the number of DAA treatment initiated in 2018 and considering a 95% cure rate following DAA, the proportion of viremic patients was estimated to 8.9% in early 2019. IVDU represented 55.6% of viremic patients in 2012 and 37.0% in 2018 (p<0.001), while MSM represented 14.6% of viremic patients in 2012 and 37.9% in 2018 (p<0.001). HIV risk factors per calendar year among HCV-RNA positive patients are presented in Figure 2. Recently acquired hepatitis cases represented 2.2% of viremic patients in 2012. This proportion reached 26.7% in 2018 (p<0.001). Among MSM, recently acquired hepatitis represented 11.7% of viremic patients in 2012 and 59.2% in 2018 (p<0.001).

HCV genotype

HCV genotype 1 remained the most prominent genotype in viremic patients throughout the study but declined from 59.0% of patients in 2012 to 49.3% in 2018 (p=0.025). Genotype 4 fluctuated between 21.9% and 25.1% during the period (p=0.093), while genotype 3 increased from 16.0% of viremic patients in 2012 to 23.8% in 2018 (p<0.001).

In patients with recently acquired HCV infection, genotype 1 remained stable between 2012 and 2018 (40.0% vs 42.9%, p=0.894). During the same period, genotype 4 decreased from 52.0% of cases to 28.6% and genotype 3 increased from 8.0% of cases to 28.6% but these differences did not reach statistical significance (p=0.295 and 0.142, respectively).

Fibrosis stage

Overall, the median (IQR) Fib4 score fluctuated from 1.36 (1.01-1.93) to 1.46 (1.06-2.16) during the study. The proportion of patients with a Fib4 score over 3.25 decreased from 13.9% to 7.3% during the study (p<0.001).

HCV treatment uptake

The number of HCV treatments initiated each year decreased from 379 in 2012 to 265 in 2013, then increased to 604 in 2015 and decreased regularly onwards to reach 325 treatments in 2018. Overall, the HCV treatment uptake among HCV-RNA positive patients increased from 11.4% in 2012 to 61.5% in 2018 (p<0.001). Treatments in MSM represented 22.2% of all treatments initiated in 2012 and 41.2% in 2018 whereas in IVDU, this proportion decreased from 48.6% in 2012 to 35.6% in 2018 (Figure 3). Treatment at acute phase represented 4.7% of all treatments in 2012 and 13.6% in 2018. In MSM, treatment at acute phase represented 19.0% of all treatments in 2012 and 30.0% in 2018 (p=0.123)

The median time to treatment of recently acquired HCV infections was 168 days [IQR 81-1096] in 2012. This delay increased to 610 days [88-848] in 2013 and regularly decreased thereafter to 59 days [34-128] in 2018 (Figure 4).

Mortality

The overall mortality rate remained stable from 1.2/100PY in 2012 to 1.1/100PY in 2018. This rate was constantly higher in IVDU (1.6/100PY in 2012 to 1.2/100PY in 2018) than in non-IVDU (0.8 to 1.0/100PY, respectively).

The HCV-related mortality rate decreased from 0.3/100PY in 2012 to 0.0/100PY in 2018. This decrease was equally observed in IVDU (0.4 to 0.0/100PY) and in non-IVDU (0.2 to 0.0/100PY).

WHO HCV elimination targets

Overall, 3 WHO targets were fulfilled within the cohort, with indeed diagnosis of 94.9% of chronic HCV infection, treatment of 88.9% of chronic infections and 100% reduction in HCV mortality. The decline in new chronic HCV infection was less impressive (35.7%), mainly related to recently acquired HCV infections (Table 3).

Discussion

This study demonstrates both the major impact of DAA on the HIV-HCV population and the switch in HIV-HCV epidemiology during the recent years in France. The HIV-HCV coinfection shifted indeed from a chronic infection with limited ongoing transmission in former IVDU, to acute or recent infections with an increasing transmission in MSM. Indeed, while the proportion of viremic patients decreased to 8.9% in early 2019, MSM became the first group of viremic patients during the period, preceding IVDU in 2018. Additionally, the number of DAA treatments initiated in MSM exceeded that in IVDU the same year. Both phenomenon are the direct consequence of a persistently active

HCV transmission in MSM, illustrated by both the increasing HCV prevalence and incidence in this population, and by the high proportion of recently acquired hepatitis among viremic MSM, almost reaching 60% of cases at the end of the period. Even if the incidence calculation may be slightly overestimated because some patients lost-to-follow-up or with missing serological result during follow-up were censored at last HCV result, the increasing number of recently acquired hepatitis cases (with a similar cohort size) reflects an increasing incidence over the period.

The impact of a high treatment uptake on the proportion of viremic patients has been previously reported in smaller cohorts of HIV-HCV coinfected patients [21–24]. Similarly, the emerging incidence of recently acquired HCV infections in MSM has also been reported [11]. However, the epidemiological turnabout resulting in MSM currently representing the major epidemiological driver of the HCV epidemic in PLWH was never previously described.

Several factors may have contributed to these changes. First, the analysis of treatment uptake demonstrates an increase throughout the period, while the number of treatments initiated during that time peaked in 2015, then decreased. This point probably illustrates the priority treatment of the most severe cases and the treatment of the easiest to reach and easiest to treat patients. Thus, even in a semi-closed, highly motivated population, patients with erratic follow-up or reluctant to treatment can delay HCV elimination. Secondly, major modifications in HCV risk factors occurred during the period. While less than 10% of patients presumed to have been infected with HIV through IVDU were still using drugs, more than 40% of MSM were currently using drugs (12.3%) or reported a previous use (33.3%). No data was available regarding the kind of drug used and notably the use of drugs in sexual context (chemsex), as well as sexual practices associated with HCV risk such as fisting or sharing sex toys. However, this point clearly demonstrates that HIV and HCV risk factors can evolve independently in a given population, as suggested by phylogenetic analysis [25]. Thus, distinct HCV prevention strategies should be applied in these different populations. Finally, recently acquired HCV infection in MSM clearly emerged as the major driver of HIV-HCV epidemiology in France,

resulting in both an increased prevalence and incidence in this population. Such an increase in HCV incidence in HIV-infected MSM has been reported worldwide during the recent years [11]. More recently, acute HCV also emerged as a significant problem in HIV pre-exposure prophylaxis (PrEP), HIV-negative MSM [16,17,26]. The fact that HIV-infected patients under antiretroviral treatment are considered non-infectious any longer and the protective effect of PrEP regarding HIV transmission probably concurred to an increase of unprotected sex within these two populations. Several reports also highlighted the role of chemsex and mucosal traumatic practices in PrEP users [16,27,28]. HCV transmission from HIV-infected to HIV-negative MSM through sharing of HCV risk practices is probable, as illustrated by phylogenetic studies [16,17]. Considering the evolution of the HIV-HCV epidemiology, it is expected that at some point, HCV-negative MSM will fuel the HIV-HCV epidemiology in MSM as a backlash effect. Additionally, several studies have demonstrated the international diffusion of HCV strains in MSM, suggesting that prevention interventions should also include the role of travel regarding HCV transmission.

The overall mortality rate in our population remained stable, as well as the mortality rate in HIV-HCV-coinfected patients, while HCV-related mortality rate sharply declined during the study. Successful DAA treatment has been associated with a significant decrease in liver-related mortality [29,30]. The relative stability of the mortality rate in HIV-HCV coinfected patients probably relates to an increased risk of non-liver-related deaths in HIV-HCV coinfected patients, notably IVDU, as compared with HIV monoinfected patients as previously reported [31].

Regarding our results, HCV elimination in the HIV-HCV coinfected population in France seems at hand. However, the emergence of acute HCV infection in MSM could jeopardize this objective and additional efforts are needed. DAA treatment resulted in few years in a drastic decrease in the number of viremic patients, while the sustained transmission of the virus still maintains a pool of viremic patients. Reducing the delay from diagnosis to treatment of recently acquired hepatitis is probably an important point to reduce transmission. Indeed, the reproduction number (R_0) of acute

HCV in MSM has been estimated to 2.35 [32], with an infectivity period of less than 6 months, which strongly argues for the rapid treatment of recently acquired HCV infection. In our study, the median time to treatment largely evolved over time, peaking to 1.5 year in 2013, to less than 2 months in 2018. This progression relies on the absence of all oral DAA options in the 2013-2014 years, during which only combinations of pegylated interferon, ribavirin and first-generation protease inhibitors were available. Treatment of recently acquired HCV became easier in 2015, when all oral combinations became available, whereas none of these combinations is currently approved for the treatment of acute HCV infection worldwide. However, the French regulation allows prescription outside the formal approval of a treatment in the absence of any alternative, an option that was clearly used in this cohort to reduce the delay to treatment over time.

Time to treatment can be also greatly impacted by the time to diagnosis, which can be delayed by 3-6 months when based on HCV serology in HIV-infected patients. A recent study within the HIV Swiss cohort demonstrated that an aggressive strategy of HCV-RNA testing in every HIV-infected patient, followed by immediate DAA treatment could significantly reduce the viremic population in a short time and could probably decrease HCV transmission within this population [22]. However, this strategy is limited by the potential reintroduction of HCV in this population, either from HIV-negative patients or from international contacts [14]. Thus, additional efforts regarding the reduction of HCV transmission, through either harm reduction interventions in patients using drugs or through reducing the risk of condomless sex and mucosal traumatic practices are warranted, as well as continuous screening for HCV. The fact that the incidence of a first recently acquired HCV infection decreased in our study, while the incidence of reinfection remained high, probably results from a reduced transmission in naive patients, while patients who had been cleared from a previous infection pursued HCV risk practices despite prevention efforts.

Our study bears some limits. First, this is a retrospective analysis of a cohort initially designed for HIV follow-up in HIV-specialized centers. Most HIV centers in France are currently also treating viral

hepatitis, but one cannot exclude that some HCV treatments were initiated in Hepatology units without being registered in the database. Second, the study is based on regular follow-up within the cohort, based on current recommendations. However, specific considerations can hamper general recommendations. For example, systematic STI screening, including HCV, would be of limited interest in older patients who report no sexual activity. Thus, the denominator of epidemiological parameters can evolve from year to year, with less exhaustiveness over time. We chose to use only actual data to assess crude prevalence and incidence rates instead of trying to estimate these rates in patients with lacking information. Considering the relatively short period of time, only crude mortality rates were determined, without standardization.

On the other hand, our study has major strengths, including the prospective collection of data, the large number of patients and the representativeness of the cohort within the French HIV-HCV population.

In conclusion, our study demonstrates that three objectives targeted by WHO for HCV elimination were reached in the HIV-HCV coinfected population in the Dat'AIDS cohort already at the end of 2018. However, these targets did not consider a rapidly evolving epidemiology such as observed during the period. Thus, continuous efforts are needed to maintain these targets and to further reduce HCV transmission within this population. This includes identifying the most at risk patients and practices, educate these patients regarding harm reduction, an early diagnosis of acute HCV infection, reducing time-to-treatment, reaching the HIV-negative MSM population and coordinating international efforts.

Notes

Authors contributions:

All authors contributed to the design of the study.

All members of the Dat'AIDS study Group contributed to the acquisition of clinical and biological data

LC and PPr performed data-management and analyzed the data

LC and PPr drafted the article

All authors reviewed and gave approval to the final draft before submission

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Table 1: Demographics and biological characteristics at last follow-up in 50 861 PLWH in the 2012-2018 cohort

	2012-2018 cohort n=50861
Gender, n (%)	
Male	34954 (68.7%)
Female	15640 (30.8%)
Transgender women	267 (0.5%)
Age (year), median (IQR)	45 (37-52)
HIV risk factor, n (%)	
Intravenous drug use	4176 (8.2%)
Heterosexual contact	22298 (43.8%)
Men having sex with men	19945 (39.2%)
Other, unknown	4442 (8.7%)
Alcohol intake >20 g/day, n (%)	4106/35016 (11.7%)
Drug use, n (%)	n=40807
Current	3385 (8.3%)
Past / opioid substitution treatment	13197 (32.3%)
Never	24225 (59.4%)
Known duration of HIV infection (year), median (IQR)	10 (2-18)
CDC stage C, n (%)	11906 (23.4%)
Under cART, n (%)	49608 (97.5%)
Last HIV viral load <50 copies/mL, n (%)	42106/49990 (84.2%)
CD4 cell count, median (IQR)	620 (428-836)

CD4 cell count ≥500 cells/mm^3, n (%)	33104/49982 (66.2%)
Deceased, n (%)	1918 (3.8%)
HCV antibodies	
Always negative, n (%)	42840 (84.2%)
Positive <2012, n (%)	6719 (13.2%
Positive ≥2012, n (%)	1302 (2.6%)
Chronic HCV infection, n (%)	728 (1.4%)
Primary HCV infection, n (%)	574 (1.1%)
Reinfection during FU, n (%)	189 (0.4%)

Table 2: HCV prevalence rate, incidence rate, treatment uptake and mortality rate in PLWH per calendar year

	2012	2013	2014	2015	2016	2017	2018
Patients in database, n	41220	42358	43261	43904	44273	44316	42778
Unknown HCV status, n	2871	3095	3329	3537	3764	4023	4112
HCV-infected patients, n	6334	6397	6384	6379	6301	6161	5765
HCV prevalence, %	15.4	15.1	14.8	14.5	14.2	13.9	13.5
New HCV cases, n	207	224	186	199	206	152	128
Detectable HCV-RNA, n/n tested	3334/4979	3141/4888	2966/5035	2473/5152	1657/4626	898/3515	525/2452
HCV-RNA prevalence, %	67.0	64.3	58.9	48.0	35.8	25.5	21.4
First acute HCV infection, n	59	105	96	88	85	79	62
First acute HCV incidence, /100PY	0.17	0.32	0.32	0.33	0.37	0.42	0.52
All acute HCV reinfection, n	15	21	14	28	37	36	38
HCV reinfection incidence, /100 PY	0.91	1.20	0.68	1.05	1.25	1.38	1.97
All acute HCV infection, n	74	126	110	116	122	115	100
All acute HCV incidence, /100PY	0.20	0.37	0.34	0.39	0.47	0.54	0.73
HCV genotype in viremic patients, n	(n=2905)	(n=2744)	(n=2589)	(n=2122)	(n=1372)	(n=688)	(n=345)

(%)	1715 (59.0)	1587 (57.8)	1481 (57.2)	1182 (55.7)	744 (54.2)	360 (52.3)	170 (49.3)
Genotype 1	80 (2.8)	78 (2.8)	75 (2.9)	66 (3.1)	51 (3.7)	33 (4.8)	11 (3.2)
Genotype 2	464 (16.0)	430 (15.7)	398 (15.4)	334 (15.7)	231 (16.8)	133 (19.3)	82 (23.8)
Genotype 3	636 (21.9)	637 (23.2)	625 (24.1)	532 (25.1)	339 (24.7)	157 (22.8)	80 (23.2)
Genotype 4	7 (0.2)	7 (0.3)	5 (0.2)	4 (0.2)	4 (0.3)	3 (0.4)	2 (0.6)
Genotype 5	3 (0.1)	5 (0.2)	5 (0.2)	4 (0.2)	3 (0.2)	2 (0.3)	0 (0.0)
Genotype 6							
HCV genotype in acute infection, %	(n=25)	(n=57)	(n=51)	(n=53)	(n=51)	(n=39)	(n=14)
Genotype 1	10 (40.0)	28 (49.1)	23 (45.1)	25 (47.2)	20 (39.2)	22 (56.4)	6 (42.9)
Genotype 2	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	4 (7.8)	0 (0.0)	0 (0.0)
Genotype 3	2 (8.0)	2 (3.5)	3 (5.9)	7 (13.2)	7 (13.7)	9 (23.1)	4 (28.6)
Genotype 4	13 (52.0)	26 (45.6)	25 (49.0)	21 (39.6)	20 (39.2)	8 (20.5)	4 (28.6)
DAA treatment, n	379	265	604	952	827	420	323
DAA treatment uptake, %	11.4	8.4	20.4	38.5	49.9	46.8	61.5
DAA treatment at chronic phase, n	361	235	588	926	788	372	279
DAA treatment at acute phase, n	18	30	16	26	39	48	44

Fib4 score, median (IQR)	1.41 (0.97-2.22)	1.43 (1.01-2.17	1.45 (1.02-2.19)	1.46 (1.06-2.16)	1.38 (1.02-1.98)	1.38 (1.02-1.96)	1.36 (1.01-1.93)
Fib4 >3.25, %	13.9	12.8	13.0	11.5	8.9	8.2	7.3
Death, n	241	293	292	295	267	284	246
Mortality rate, %	0.6	0.7	0.7	0.7	0.6	0.6	0.6
Death in HCV-infected patients, n	78	104	86	101	63	86	64
Mortality rate in HCV-infected patients, %	1.2	1.6	1.3	1.6	1.0	1.4	1.1
HCV related death, n	21	22	16	21	4	4	0
HCV related mortality rate, %	0.3	0.3	0.3	0.3	0.1	0.1	0.0

Table 3: WHO HCV elimination targets

Targets are determined within the cohort for patients with a known HCV status, with estimates for patients within the cohort with an unknown HCV status and for patients with an undiagnosed HIV infection. For definitions of the targets, see the Supplementary appendix.

WHO target	Dat'AIDS cohort, known HCV status	Dat'AIDS cohort, with estimate of unknown HCV status	Dat'AIDS cohort with estimates of patients with undiagnosed HIV-infection
Diagnosis of chronic HCV infection (target 90%)	100%	94.9%	91.5%
Decline in new chronic HCV infections (target 90%)	35.7%	ND	ND
Treatment of chronic HCV infections (target 80%)	95.6%	88.9%	83.0%
Reduction in HCV mortality (target 65%)	100.0%	100.0%	ND

Figures legend

Figure 1: Flow chart

Figure 2: HIV risk factor among HCV-RNA positive PLWH during the 2012-2018 period

Figure 3: DAA treatment initiation in PLWH per calendar year by HIV risk factor

Figure 4: Time to treatment of acute HCV infections during the 2012-2018 period.

Figure 1

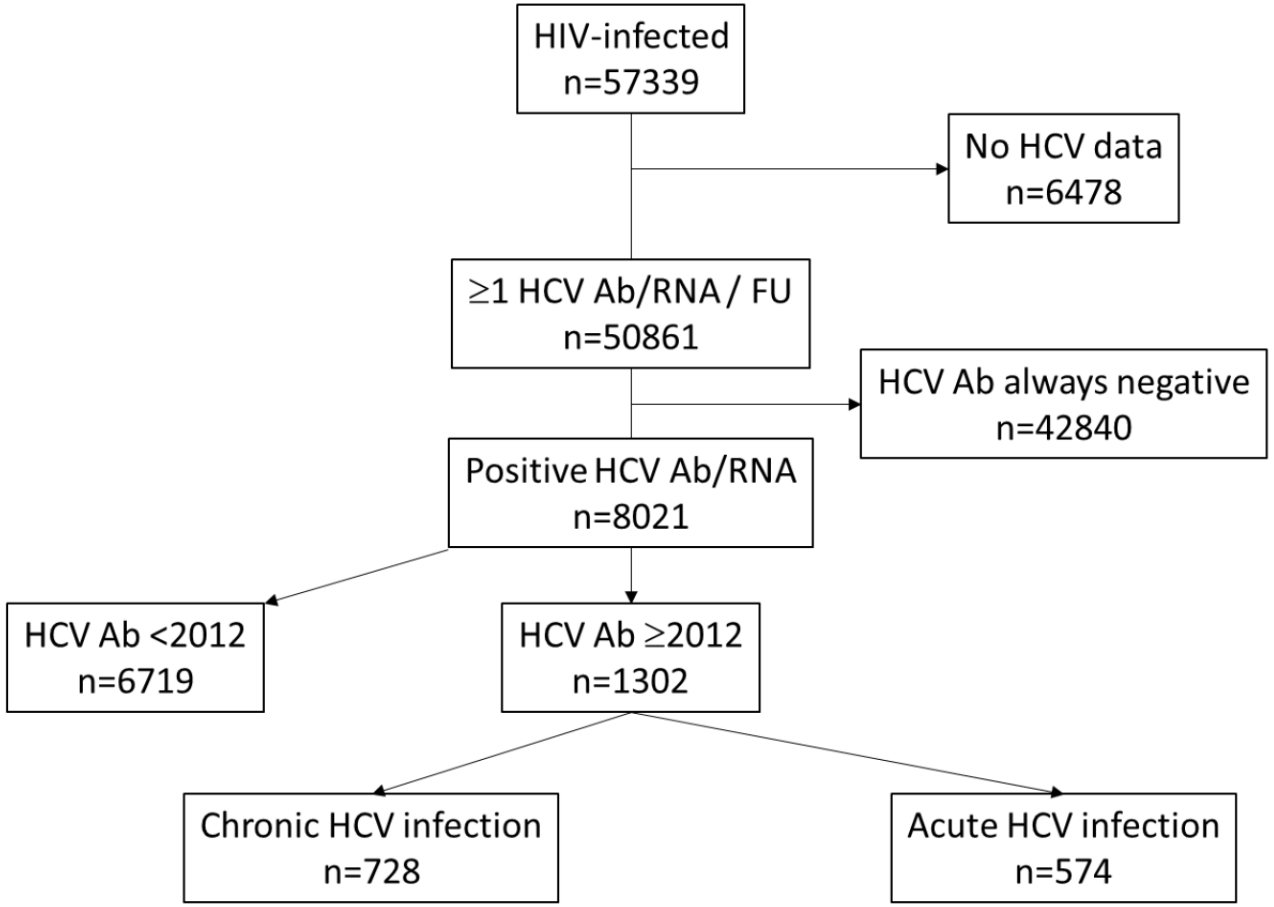

Figure 2

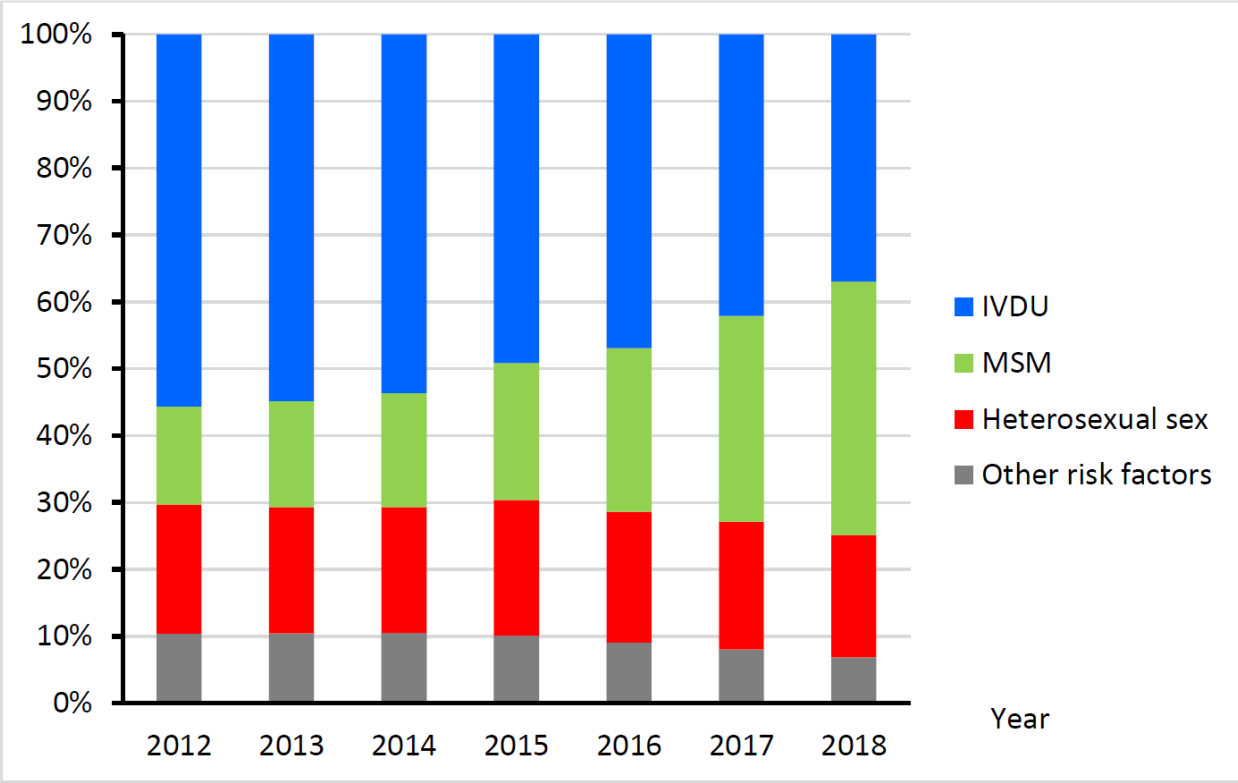

Figure 3

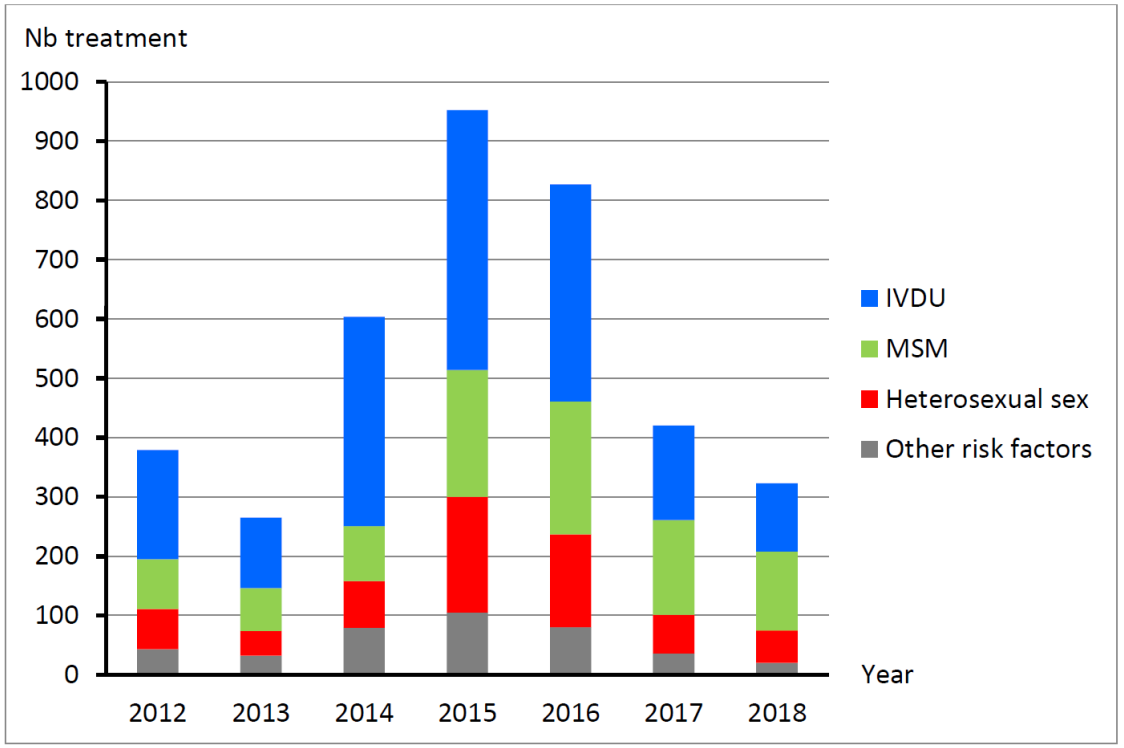

Figure 4