International Journal of Drug Policy 72 (2019) 61–68

Contents lists available at ScienceDirect

International Journal of Drug Policy

journal homepage: www.elsevier.com/locate/drugpo

Lower HCV treatment uptake in women who have received opioid agonist therapy before and during the DAA era: The ANRS FANTASIO project

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ARTICLE INFO

Keywords:
Barrier to care
Direct acting antivirals
Hepatitis C virus
Pegylated interferon
Opioid agonist therapy
Women

ABSTRACT

Background: In the era of direct-acting antivirals (DAA) for the treatment of hepatitis C virus (HCV) infection, HCV treatment uptake remains insufficiently documented in key populations such as people with opioid dependence. Access to opioid agonist therapy (OAT) is facilitated in France through delivery in primary care, and individuals with opioid dependence can be identified as those receiving OAT. Women with opioid dependence are especially vulnerable because of associated sex-related stigma, discrimination, and marginalization, all of which negatively interfere with access to HCV prevention and care. This study, based on data collected between 2012 and 2016 in France, aimed to assess whether (i) chronically HCV-infected women with opioid dependence had lower rates of HCV treatment uptake than their male counterparts during the same period (i.e., study period), and (ii) the advent of DAA resulted in increased treatment uptake rates in these women.

Methods: Individuals with opioid dependence were identified as those receiving OAT at least once during the study period. Analyses were based on exhaustive anonymous care delivery data from the French national healthcare reimbursement database. We used multinomial logistic regression to estimate sex-based disparities in HCV treatment uptake (DAA or pegylated-interferon (Peg-IFN)-based treatment *versus* no treatment) while accounting for potential confounders.

Results: The study sample comprised 27,127 individuals, including 5640 (20.8%) women. Median [interquartile range] age was 45 [40–49] years. Between 2012 and 2016, 70.9 (women: 77.2; men: 69.3), 17.3 (14.2; 18.2) and 11.7% (8.6%; 12.5%) of the study sample received, respectively, no HCV treatment, DAA and Peg-IFN-based treatment only. After multiple adjustment for potential confounders, women were 41% (adjusted odds-ratio (AOR) [95% confidence interval (CI]): 0.59[0.53 – 0.65]) and 28% (0.72[0.66 – 0.78]) less likely than men to have had Peg-IFN-based and DAA treatment, respectively.

Conclusion: Despite increased HCV treatment uptake in women with opioid dependence in the DAA era, rates remain lower than for men. In the coming years, access to DAA treatment will continue to increase in France thanks to a forthcoming simplified model of HCV care which includes primary care as an entry point. Nevertheless, a greater understanding of sex-specific barriers to HCV care and the implementation of appropriate sex-specific measures remain a priority.

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https://doi.org/10.1016/j.drugpo.2019.05.013

Introduction

In most industrialized countries, the prevalence of hepatitis C virus (HCV) infection in people who inject drugs (PWID) is very high (Degenhardt et al., 2017; Grebely et al., 2019; Inserm, 2010) and consequently, this sub-population constitute a key population (Nelson et al., 2011) in its elimination (WHO, 2016).

Women who inject drugs, and, more generally, women with opioid dependence, are especially vulnerable because of multiple associated vulnerabilities, including mental health problems, physical and sexual violence, sex work, stigma and discrimination (Beck et al., 2017; Des Jarlais, Feelemyer, Modi, Arasteh, & Hagan, 2012; Iversen, Page, Madden, & Maher, 2015; Khuat, Morrow, Nguyen, & Armstrong, 2015; Mackesy-Amiti et al., 2018; Miller et al., 2011; NDARC, 2010). They also have a higher burden of psychiatric comorbidities (including anxiety/panic attacks, bipolar disorder, attempted suicide and major depression (Back et al., 2011; Campbell et al., 2018)), poor physical health, and stronger craving for psychoactive substances (Back et al., 2011). In addition, the risk of their acquiring HIV, HCV and other blood-borne and sexually transmitted infections (Acheampong, Striley, & Cottler, 2017), as well as engaging in certain risky practices such as sharing injection equipment or being injected by a peer (Evans et al., 2003; Morris et al., 2014, 2015; Tracy et al., 2014), is higher than for their male counterparts. Similarly, biological factors as well as factors linked to social network or differences in access to care (Esmaeili et al., 2018) lead to higher incidences of HCV infection in these women (Esmaeili et al., 2017). However, in a context where universal access to HCV treatment is now recommended as a key step towards the WHO public health goal of eliminating the disease by 2030 (Deuffic-Burban et al., 2017; WHO, 2016), the insufficient documentation regarding access for this sub-population of women is a major concern.

The FANTASIO (Factors of Access to New Therapy with Antiviral drugs for Subjects Infected with hepatitis C receiving Opioid agonist therapy) project aims to document individual and structural levers and barriers to access to HCV treatment in people treated with, or previously exposed to opioid agonist therapy (OAT). It uses data from the French national Social Insurance System database on healthcare reimbursements (SNIIRAM), which covers 98.8% of the country's population (Bezin et al., 2017), and records all treatment deliveries.

The present study, based on reimbursement data collected between 2012 and 2016, aimed to assess whether (i) chronically HCV-infected women with opioid dependence have lower rates of HCV treatment uptake than their male counterparts in France and (ii) the availability of direct-acting antivirals (DAA) has increased rates of HCV treatment uptake for these women in the country.

Materials and methods

Data source

We used anonymous individual data from the SNIIRAM for the 2012–2016 period, which enabled us to cover different phases of HCV treatment availability and initiation criteria. The SNIIRAM was set up in 1999, and is the main healthcare database in France (Tuppin et al., 2017). It gathers exhaustive individual data regarding all reimbursements for medical services from the country's different health coverage schemes and covers 98.8% of the total population living in France (Bezin et al., 2017). More specifically, it comprises data on billing and reimbursement of outpatient healthcare consumption as well as medical data regarding hospitalizations from the national hospital discharge database, which includes public and private hospitals (Bezin et al., 2017; Tuppin et al., 2017). The SNIIRAM enables population-based monitoring of drug delivery, including OAT and DAA. Individuals' data are recorded using a dedicated, unique and permanent social security number (Bezin et al., 2017). Data quality is guaranteed through multi-level data processing control and daily, monthly and annual data processing (Tuppin et al., 2017).

Data selection

OAT is delivered through primary care in France (Des Jarlais, Kerr, Carrieri, Feelemyer, & Arasteh, 2016), which considerably facilitates access. Indeed, the large majority of people with opioid dependence have access to OAT. More specifically, almost 80% of high-risk opioid users (i.e., individuals with recurrent opioid use that is causing actual harms to them - including dependence, and other health, psychological or social problems - or is placing them at a high risk of suffering such harms) in France receive regular OAT prescriptions (i.e. methadone or buprenorphine) (European Monitoring Centre for Drugs & Drug Addiction, 2018). Accordingly, we used the following two criteria to define chronic HCV infection linked to opioid dependence: (i) receiving at least one delivery of OAT during the study period (2012–2016), (ii) being classified as chronically HCV-infected at least once during the study period according to the standardized definition developed by the experts from the French national healthcare system. The latter definition identifies patients with chronic HCV infection if they i) have official long-term disease status for hepatitis C (ICD-10 (WHO, 2018) code B.18.2), ii) are hospitalized for a HCV-related condition (ICD-10 code B.18.2), or iii) have at least one delivery of HCV treatment. In France, long-term disease status is an administrative measure which provides free treatment and care for people with any chronic disease which has been pre-approved for such benefits by the French Ministry of Health.

Study outcome

Our study outcome was HCV treatment uptake, defined as having been delivered HCV treatment (pegylated interferon (Peg-IFN), ribavirin, boceprevir, telaprevir, sofosbuvir, daclatasvir, dasabuvir, simeprevir, ombitasvir, or paritaprevir) at least once during the study period. We first used a binary variable to define HCV treatment uptake globally (yes/no), then a three-category variable to define HCV treatment uptake while differentiating between treatment types as follows: 1) no HCV treatment (reference group); 2) Peg-IFN-based treatment and 3) DAA treatment. The latter included all individuals who received DAA at least once during the study period, irrespective of previous Peg-IFN-based treatment.

Explanatory variables

The following variables were tested when modelling HCV treatment uptake: sex, age at the beginning of the study period, complementary universal health coverage (in French *Couverture Maladie Universelle Complémentaire*), type of OAT received (buprenorphine, methadone, or both (i.e., when both treatments had been delivered during the study period)), being classified as chronically HCV-infected before *versus* after 2014 (labelled "HCV diagnosis period"), and liver disease severity. We distinguished between buprenorphine and methadone as, in France, they may be delivered to people with opioid dependence who have very different profiles. Complementary universal health coverage ensures extra medical care fees for people on low income who are resident in France for more than three months. We therefore used complementary universal health coverage as a proxy of financial insecurity. As DAA arrived in France in 2014, the HCV diagnosis period was dichotomized into before and after 2014 (HAS, 2016). Liver disease severity during the study period was categorized according to the presence of cirrhosis (ICD-10 codes K74.3 to K74.6) and/or liver cancer (ICD-10 codes C22.0 to C22.4, C22.7, and C22.9) using a three-category variable: 1) no cirrhosis or liver cancer, 2) cirrhosis without liver cancer and 3) liver cancer (with or without cirrhosis).

Statistical analysis

Study variables were described and then compared between men and women using a chi-square test (categorical variables) or a Mann-Whitney test (continuous variables). All tests were two-sided. The rates of HCV treatment uptake were described for both sexes for each year between 2012 and 2016. We used multinomial logistic regression for the three-category outcome variable in order to identify factors associated with HCV treatment uptake separately for Peg-IFN and DAA.

Analyses were adjusted for sex, age, complementary universal health coverage, type of OAT received, HCV diagnosis period, and liver disease severity. For sex and age, we used values recorded at the beginning of the study period. For all other variables, we used the maximum value recorded during the period starting from 1st January 2012 to the first event, defined as i) first delivery of HCV treatment, ii) 31st December 2016 or iii) death. For example, individuals who benefited from complementary universal health coverage at some time during this period were classified as having complementary universal health coverage. Analyses stratified by sex were also performed. The threshold for statistical significance was set at $\alpha = 0.05$. All analyses were performed with SAS statistical software (SAS Institute Inc, Cary NC, version 9.4).

Ethical aspects

The use of SNIIRAM data in the FANTASIO project was approved by the National Institute of Health Data (IDS – n°176 issued on 02/03/2016) and the CNIL (n°1946535 issued on 04/08/2016).

Results

Characteristics of the study sample

The study sample's main characteristics are presented in Table 1. A total of 27,127 individuals classified with chronic HCV infection and receiving OAT at least once, were included in the analysis. Among them, 70.9% did not receive any HCV treatment between 2012 and 2016, 17.3% received DAA and 11.7% received only Peg-IFN-based treatment.

Median age was 45 years (interquartile range (IQR): 40–49 years) and most individuals were men (79.2%). Twenty-eight percent of the study sample had complementary universal health coverage. Most of the population (91%) did not suffer from cirrhosis or liver cancer during the study period, and were classified with chronic HCV infection before 2014 (75.6%). Buprenorphine (without methadone prescription) was the most delivered OAT during the study period (60.8%). The comparison of characteristics between sexes showed significant differences: women were younger and more likely to have complementary universal health coverage, to be treated with methadone alone, and to have less severe liver disease (Table 1). Moreover, they had lower rates of HCV treatment uptake during the study period (22.8% *versus* 30.7% in men, $p < 0.0001$. Fig. 1 presents the rates of HCV treatment uptake by year and sex.

Univariate analyses

The results of the univariate multinomial regression analyses are presented in Table 2. Being a woman was significantly associated with lower odds of HCV treatment uptake for both Peg-IFN-based treatment (odds-ratio (OR) [95% confidence interval (CI)]: 0.62[0.56 − 0.68]; $p < 0.0001$) and DAA treatment (0.70[0.65 − 0.77]; $p < 0.0001$).

Having cirrhosis without liver cancer was associated with greater odds of HCV treatment uptake (both types). Older age and having been classified with chronic HCV infection after 2014 were both associated with greater odds of DAA treatment uptake and lower odds of Peg-IFN-based treatment uptake. Complementary universal health coverage was associated with lower odds of DAA treatment uptake. All comparisons between DAA and Peg-IFN treatments were statistically significant, except for receiving buprenorphine only (Table 2).

Multivariable analysis

The results of the multivariable multinomial logistic regression analysis are presented in Table 3. The multivariable model confirmed the associations observed in the univariate analyses. Women were 41% (adjusted odds-ratio (AOR) [95% CI]: 0.59[0.53 − 0.65]) and 28% (0.72

Table 1
Main characteristics of the study sample (n = 27,127 HCV-infected individuals with at least one delivery of OAT between 2012 and 2016; FANTASIO project; data from the French social insurance database).

	All patients (n = 27,127) no. of individuals (%) or median [IQR]	Women (n = 5640) (20.8%)	Men (n = 21,487) (79.2%)	*p-value*[1]
Type of HCV treatment				
No treatment	19245 (70.9)	4353 (77.2)	14,892 (69.3)	*< 0.0001*
Peg-IFN-based treatment	3177 (11.7)	484 (8.6)	2693 (12.5)	
DAA treatment	4705 (17.3)	803 (14.2)	3902 (18.2)	
Age in 2012 (years)	45 [40-49]	44 [39-49]	45 [40-49]	*< 0.0001*
Complementary universal health coverage				*< 0.0001*
No	19372 (71.4)	3790 (67.2)	15,582 (72.5)	
Yes	7755 (28.6)	1850 (32.8)	5905 (27.5)	
HCV diagnosis period				*0.0578*
Before 2014	20511 (75.6)	4210 (74.7)	16,301 (75.9)	
After 2014	6616 (24.4)	1430 (25.4)	5186 (24.1)	
Opioid Agonist therapy				*< 0.0001*
Buprenorphine	16,486 (60.8)	3283 (58.2)	13,203 (61.5)	
Methadone	8236 (30.4)	1895 (33.6)	6341 (29.5)	
Both treatments	2405 (8.9)	462 (8.2)	1943 (90)	
Liver disease severity				*< 0.0001*
No cirrhosis or liver cancer	24691 (91.0)	5221 (92.6)	19,470 (90.6)	
Cirrhosis without liver cancer	1966 (7.3)	362 (6.4)	1604 (7.5)	
Liver cancer [a]	470 (1.7)	57 (1.0)	427 (1.9)	

[a] Chi-square test (for categorical variables) or Mann-Whitney test (for continuous variables); DAA = direct-acting antivirals; HCV= hepatitis C virus; IQR = interquartile range; OAT =opioid agonist therapy; Peg-IFN = pegylated interferon.

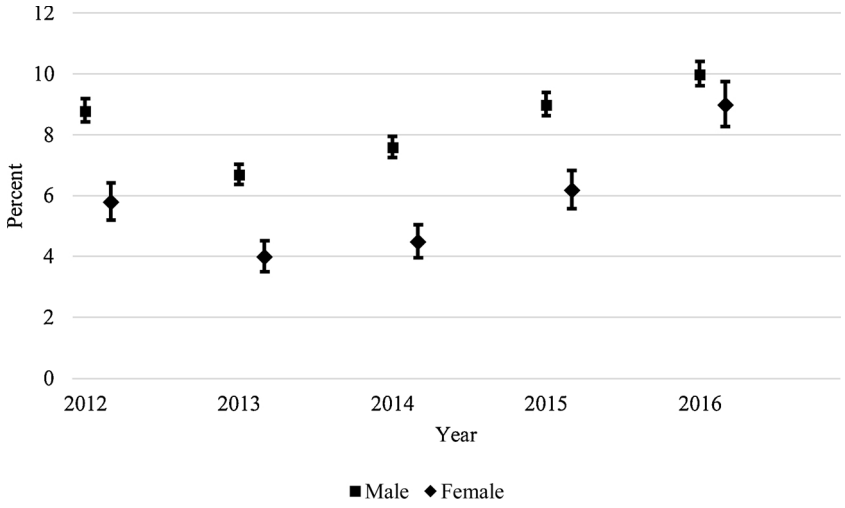

Fig. 1. Rates of HCV treatment uptake by year and sex.

Table 2
Variables associated with HCV treatment uptake in the study sample – univariate analyses (multinomial logistic regression; FANTASIO project; data from the French social insurance database).

AOR [95% CI]		Type of HCV treatment received (ref: no treatment)				Type of HCV treatment received (ref: Peg-IFN-based)	
		Peg-IFN-based	*p-value*	DAA treatment	*p-value*	DAA treatment	*p-value*
Sex	Male	1		1		1	
	Female	0.62 [0.56-0.68]	*< 0.0001*	0.70 [0.65-0.77]	*< 0.0001*	1.14 [1.01-1.29]	*0.0316*
Age	Per one-year increase	0.98 [0.97-0.98]	*< 0.0001*	1.03 [1.03-1.04]	*< 0.0001*	1.06 [1.05-1.06]	*< 0.0001*
Complementary universal health coverage	No	1		1		1	
	Yes	1.07 [0.99-1.16]	*0.0954*	0.79 [0.73-0.85]	*< 0.0001*	0.73 [0.66-0.81]	*< 0.0001*
HCV diagnosis period	Before 2014	1		1		1	
	After 2014	0.37 [0.33-0.41]	*< 0.0001*	1.91 [1.79-2.05]	*< 0.0001*	5.22 [4.59-5.94]	*< 0.0001*
Type of OAT received	Methadone only	1		1		1	
	Buprenorphine only	1.06 [0.98-1.15]	*0.1643*	1.01 [0.94-1.09]	*0.7700*	0.95 [0.86-1.05]	*0.3426*
	Buprenorphine and methadone	0.45 [0.37-0.54]	*< 0.0001*	0.81 [0.72-0.92]	*0.0009*	1.81 [1.47-2.23]	*< 0.0001*
Liver disease severity	No cirrhosis or liver cancer	1		1		1	
	Cirrhosis without liver cancer	1.29 [1.11-1.50]	*0.0009*	2.99 [2.70-3.31]	*< 0.0001*	2.32 [1.98-2.72]	*< 0.0001*
	Liver cancer[a]	0.46 [0.30-0.69]	*0.0002*	1.54 [1.24-1.91]	*< 0.0001*	3.36 [2.17-5.20]	*< 0.0001*

[a] With or without cirrhosis OR = odds-ratio; CI = confidence interval; DAA = direct-acting antivirals; HCV = hepatitis C virus; OAT = opioid agonist therapy; Peg-IFN = Pegylated interferon.

[0.66 − 0.78]) less likely than men to have been treated with Peg-IFN-based and DAA, respectively. Furthermore, women had significantly greater odds of being treated with DAA than Peg-IFN (Table 3). In the analyses stratified by sex, the association between age and HCV treatment uptake did not differ between men and women. By contrast, complementary universal health coverage was associated with increased odds of Peg-IFN treatment for men only (Supplementary Table).

Discussion

This study is the first to compare potential sex-related disparities in HCV treatment uptake in individuals with opioid dependence in France before and after the arrival of DAA (Ministère des Solidarités et de la Santé, 2017).

The main result is that HCV treatment uptake in women with opioid dependence is still lower than in men, despite increased access after the arrival of DAA. This suggests that, despite the rapid and large-scale implementation of DAA treatments at the whole HCV population level (Brouard et al., 2017), there is a need to better understand sex-specific barriers to HCV care in key populations such as people with opioid dependence, and to develop sex-specific interventions targeting these populations. It must to be noted that, in this study, people with opioid dependence were very likely to have been infected with HCV through injecting opioids, and therefore most of them were probably people who inject drugs (PWID).

Although few studies have explored sex-specific barriers to HCV care, our results are in line with previous research which also highlighted less access to Peg-IFN based regimens or DAA for women

Table 3
Variables associated with HCV treatment uptake in the study sample – multivariable analysis (multinomial logistic regression; FANTASIO project; data from the French social insurance database).

AOR [95% CI]		Type of HCV treatment received (ref: no treatment)				Type of HCV treatment received (ref: Peg-IFN-based)	
		Peg-IFN-based	*p-value*	DAA treatment	*p-value*	DAA treatment	*p-value*
Sex	Male	1		1		1	
	Female	0.59 [0.53-0.65]	*< 0.0001*	0.72 [0.66-0.78]	*< 0.0001*	1.22 [1.08-1.39]	*0.0018*
Age	Per one-year increase	0.96 [0.96-0.97]	*< 0.0001*	1.03 [1.03-1.04]	*< 0.0001*	1.07 [1.06-1.08]	*< 0.0001*
Complementary universal health coverage	No	1		1		1	
	Yes	1.08 [0.99-1.18]	*0.0587*	0.83 [0.77-0.90]	*< 0.0001*	0.77 [0.69-0.85]	*< 0.0001*
HCV diagnosis period	Before 2014	1		1		1	
	After 2014	0.33 [0.29-0.37]	*< 0.0001*	2.22 [2.07-2.38]	*< 0.0001*	6.72 [5.88-7.68]	*< 0.0001*
Type of OAT received	Methadone only	1		1		1	
	Buprenorphine only	1.12 [1.03-1.21]	*0.0101*	0.95 [0.88-1.02]	*0.1690*	0.85 [0.77-0.94]	*0.0020*
	Buprenorphine and methadone	0.42 [0.34-0.50]	*< 0.0001*	0.88 [0.78-1.01]	*0.0575*	2.13 [1.72-2.64]	*< 0.0001*
Liver disease severity	No cirrhosis or liver cancer	1		1		1	
	Cirrhosis without liver cancer	1.31 [1.12-1.52]	*0.0005*	2.92 [2.63-3.24]	*< 0.0001*	2.23 [1.89-2.62]	*< 0.0001*
	Liver cancer [a]	0.53 [0.35-0.80]	*0.0024*	1.26 [1.01-1.57]	*0.0422*	2.38 [1.53-3.71]	*0.0001*

[a] With or without cirrhosis OR = odds-ratio; CI = confidence interval; DAA = direct-acting antivirals; HCV = hepatitis C virus; OAT = opioid agonist therapy; Peg-IFN = Pegylated interferon.

(Iversen et al., 2014) especially in specifically socially vulnerable subpopulations such as indigenous people in Canada (Saeed et al., 2017). A general trend was also observed in female non-opioid users (Kanwal et al., 2016). In contrast, two recent observational studies - one based on data from both the Norwegian Prescription Database and The Norwegian Surveillance System for Communicable Diseases on people who have been treated with OAT (Midgard, Bramness, Skurtveit, Haukeland, & Dalgard, 2016), and the other on three Canadian cohorts of PWID (Socías et al., 2019) – found no association between sex and HCV treatment uptake. Findings from the latter study suggest that in recent PWID, engagement in OAT is a predictor of HCV treatment initiation.

Women who inject drugs that attend low-threshold facilities and are less engaged in OAT tend to have economic, social, emotional and psychological vulnerabilities, and experience severe addiction problems (Mutatayi, 2014), which suggests that these facilities could constitute an important entry point for HCV screening and care for the most vulnerable women.

Several studies analysing access to HCV treatment in PWID have identified a number of barriers to HCV treatment both at the individual (e.g., the difficulty to reach healthcare services, treatment refusal and/or premature interruptions, lack of financial resources) and healthcare provider (e.g., stigmatization and discrimination) levels (Broers et al., 2005; Bruggmann, 2012; Grebely et al., 2008; Lally, Montstream-Quas, Tanaka, Tedeschi, & Morrow, 2008; Lazarus, Sperle, Maticic, & Wiessing, 2014; Liakina et al., 2015; Swan et al., 2010; Treloar, Hull, Dore, & Grebely, 2012).

The lower rates of Peg-IFN based treatment uptake in OAT-treated women compared with men, may be attributable to concerns about the teratogenicity of ribavirin, which has been reported to be a significant barrier to initiating HCV treatment in women of childbearing age (Baden, Rockstroh, & Buti, 2014). In addition, as women also have slower liver disease progression, especially in the premenopausal period thanks to the protective effects of oestrogens (Baden et al., 2014), they may have been disadvantaged in the past, given that previous regulations in France only reimbursed treatment costs for people with the most severe stages of liver disease (Marshall et al., 2018).

Studies conducted during the Peg-IFN era among women with opioid dependence found sex-based differences in access to HCV treatment (Temple-Smith et al., 2007), and highlighted that women face individual and structural barriers when trying to access services. Individual barriers include increased stigmatization and discrimination because of their drug use and sex, limited knowledge about hepatitis C, and a greater likelihood of mental illness (e.g., depression) (Back et al., 2011; The European Monitoring Centre fro Drugs & Drug Addiction, 2009). Structural barriers include barriers linked to accessibility of care services and their adaptation to women's specific needs (e.g. indiscreet locations, lack of child care, etc.). These were found to significantly negatively influence access to OAT (NDARC, 2010). In France too, more interventions are still needed to ensure that specialized care centres for addiction meet the specific needs of women (Mutatayi, 2014) and to increase their access to treatment and harm reduction programs (Des Jarlais et al., 2012; El-Bassel, Wechsberg, & Shaw, 2012; NDARC, 2010).

Our results show that the HCV treatment gap between men and women was smaller with DAA treatments. It has to be noted that, in France, despite several changes in HCV treatment guidelines since the arrival of DAA in 2014, from the outset, treatment has been systematically recommended for PWID and women of childbearing age (HAS, 2017). This has certainly contributed to increased rates of treatment initiation in these specific subpopulations. The findings of our study are also in line with available data from open-access HCV treatment programs in other countries such as Canada (Prince Edwards's island), Australia, and Iceland (Grebely et al., 2017; Kwon et al., 2019; Scott et al., 2018; Smyth et al., 2017)

In addition, in our study, benefiting from the complementary health insurance coverage (complementary universal health coverage) was associated with lower odds of DAA treatment uptake for both men and

women. One possible explanation is that their high cost impacts social insurance budget constraints (Assefa, Hill, & Williams, 2018) of DAA treatment. Moreover, it is important to underline that the proportion of female complementary universal health coverage beneficiaries was higher than that for men in our study population, which is in line with recent national data (Carré & Perronnin, 2018). This would suggest that women with opioid dependence are more likely to be in a situation of financial insecurity (Carré & Perronnin, 2018) something which is known to be associated with delayed access to healthcare (Lazar & Davenport, 2018). Added to this is the higher prevalence of other diseases in the complementary universal health coverage beneficiary population, due to more exposure risks and less frequent use of preventive care services (Assurance Maladie, 2007). With respect to the high cost of new HCV therapies, the first DAA treatment to become available in France was Sofosbuvir in 2014, with a baseline price of 14 000 euros for one week of treatment (Prescrire, 2018). Furthermore, it is probable that women with opioid dependence with complementary universal health coverage face specific difficulties with administrative procedures (e.g., filling out complementary universal health coverage forms), which may act as an obstacle to their applying for and therefore accessing HCV treatment (Geeraert & Rivollier, 2014; Ministère des solidarités et de la Santé, 2018)

With regard to OAT, we found that buprenorphine delivery was associated with greater odds of Peg-IFN-based treatment uptake. By contrast, the type of OAT was not significantly associated with DAA treatment uptake. This is particularly interesting as, in France, people treated with methadone and people treated with buprenorphine may have very different profiles. The latter tend to be older users (OFDT, 2015) and receive OAT most often in urban medical practice (Delile et al., 2018). Instead, methadone remains mostly delivered in specialized care centres for addiction (Delile et al., 2018), although methadone induction in primary care has been shown to be feasible and acceptable to both physicians and patients (Carrieri et al., 2014).

In our study, both DAA and Peg-IFN based treatment uptake were more likely in patients with cirrhosis. DAA treatment uptake was also more likely in patients diagnosed with liver cancer. This may be explained by the fact that individuals with a more advanced disease stage continue to be prioritized for HCV treatment in the DAA era (HAS, 2016).

The main strength of our study is that the analyses were based on information from the French national healthcare reimbursement database, which covers 98.8% of the entire population living in France. Consequently, we were able to identify all individuals delivered OAT at least once between 2012 and 2016. With respect to limitations, first, the study sample did not include people who have no access to the French health insurance system. However, this concerns only 1.2% of the population, the majority being recent arrivals to the country (as health insurance is guaranteed after three months of stable residence). Second, our findings, based on data collected among people with opioid dependence who had chronic HCV infection, is not representative of the whole chronically HCV infected population who inject drugs. Indeed, as individuals in our study population had received OAT at some point, they were probably more engaged in care and our results cannot be considered valid for the broader population of PWID. Having said that, in France, OAT coverage is estimated at 75–80% (European Monitoring Centre for Drugs & Drug Addiction, 2018; Roux et al., 2016), thanks to facilitated access to these treatments via primary care and specialized centres, as well as a comprehensive harm reduction policy initially set up to control HIV in people who inject drugs (Des Jarlais et al., 2016). Third, the database is limited as many potential predictors are lacking (e.g., living in a couple, children, history of imprisonment, attendance of harm reduction services). Nevertheless, we had access to exhaustive data on long-term disease classification, HCV-related hospitalizations, and HCV treatment delivery.

In 2018, the French Association for the Study of the Liver recommended the implementation of a simplified HCV care management model including the prescription of HCV treatment by general practitioners, the extension of HCV treatment delivery to all pharmacies (not only hospital pharmacies), the direct provision of HCV treatment to patients for the whole treatment period, and the possibility for non-medical caregivers to follow HCV-treated patients (AFEF, 2018). We believe that when implemented, this simplified HCV care management system will decrease disparities in access to HCV treatment in France, including gender-related disparities. For women of childbearing age, this new model will have the additional benefit of lowering the risk of vertical HCV transmission. In the meantime, it will be necessary to upskill healthcare providers in drug treatment settings in order to enhance both HCV testing and treatment among people with opioid dependence.

Conclusion

Although rates of HCV treatment uptake have increased for women with opioid dependence in the DAA era, they remain lower than those of their male counterparts. In the coming years, access to DAA treatment will continue to increase in France thanks to a forthcoming simplified model of HCV care which includes primary care as an entry point. Nevertheless, a greater understanding of sex-specific barriers to HCV care and the implementation of appropriate sex-specific measures remain a priority.

Funding

This work was supported by the French National Agency for Research on Aids and Viral Hepatitis (ANRS), with the participation of MSD France. The funding source was not involved in the study's design or in the data analysis. Neither was it involved in the writing and submission of this manuscript.

Conflicts of interest

Benjamin Rolland and Amir Guidoum received grants from MSD. The other authors declare no conflict of interest.

CRediT authorship contribution statement

Teresa Rojas Rojas: Investigation, Methodology, Project administration, Validation, Writing - original draft, Writing - review & editing. **Vincent Di Beo:** Formal analysis, Investigation, Validation. **Jessica Delorme:** Validation. **Tangui Barre:** Investigation, Validation, Writing - original draft, Writing - review & editing. **Philippe Mathurin:** Validation, Writing - review & editing. **Camelia Protopopescu:** Methodology, Project administration, Validation, Writing - review & editing. **François Bailly:** Validation, Writing - review & editing. **Marion Coste:** Validation, Writing - review & editing. **Nicolas Authier:** Funding acquisition, Resources, Methodology, Project administration, Validation. **Maria Patrizia Carrieri:** Conceptualization, Funding acquisition, Resources, Investigation, Methodology, Project administration, Software, Supervision, Validation, Writing - original draft, Writing - review & editing. **Benjamin Rolland:** Conceptualization, Funding acquisition, Resources, Investigation, Methodology, Project administration, Software, Supervision, Validation, Writing - original draft, Writing - review & editing. **Fabienne Marcellin:** Conceptualization, Investigation, Methodology, Project administration, Software, Supervision, Validation, Writing - original draft, Writing - review & editing.

Acknowledgements

Scientific committee of the FANTASIO project:

Benjamin Rolland, Patrizia Carrieri, Philippe Mathurin, François Bailly, Marc Bourlière, Daniel Dhumeaux, Amir Guidoum, Jessica

Delorme, Nicolas Authier, Fabienne Marcellin, Camelia Protopopescu, Tangui Barré, Teresa Rojas Rojas, Marion Coste, Vincent Di Beo, Véronique Doré, Ventzislava Petrov-Sanchez.

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Benjamin Rolland, Jessica Delorme, Nicolas Authier, Maria Patrizia Carrieri, Fabienne Marcellin, Camelia Protopopescu, Tangui Barré, Teresa Rojas Rojas, Marion Coste, Vincent Di Beo.

Finally, our thanks to Jude Sweeney for the English revision and editing of our manuscript.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.drugpo.2019.05.013.

References

Acheampong, A. B., Striley, C. W., & Cottler, L. B. (2017). Prescription opioid use, illicit drug use, and sexually transmitted infections among participants from a community engagement program in North Central Florida. *Journal of Substance Use, 22*(1), 90–95.

AFEF (2018). *Recommandations AFEF pour l'élimination de l'infection par le virus de l'hépatite C en France.* https://afef.asso.fr/wp-content/uploads/2018/06/VF-INTERACTIF-RECO-VHC-AFEF-v2103.pdf.

Assefa, Y., Hill, P. S., & Williams, O. D. (2018). Access to hepatitis C virus treatment: Lessons from implementation of strategies for increasing access to antiretroviral treatment. *International Journal of Infectious Diseases: IJID, 70*, 65–68.

Assurance Maladie (2007). *LES ALD des bénéficiaires de la CMU-C. Points de repère.* 8. https://www.ameli.fr/fileadmin/user_upload/documents/Points_de_repere_n_8.pdf.

Back, S. E., Payne, R. L., Wahlquist, A. H., Carter, R. E., Stroud, Z., Haynes, L., et al. (2011). Comparative profiles of men and women with opioid dependence: Results from a national multisite effectiveness trial. *The American Journal of Drug and Alcohol Abuse, 37*(5), 313–323.

Baden, R., Rockstroh, J. K., & Buti, M. (2014). Natural history and management of hepatitis C: Does sex play a role? *The Journal of Infectious Diseases, 209*(Suppl 3), S81–85.

Beck, F., Obradovic, I., Palle, C., Brisacier, A.-C., Cadet-Taïrou, A., Diaz-Gomez, C., et al. (2017). Usage de drogues et conséquences: quelles spécificités féminines? *Tendances, 117*https://www.ofdt.fr/BDD/publications/docs/eftxfbx3.pdf.

Bezin, J., Duong, M., Lassalle, R., Droz, C., Pariente, A., Blin, P., et al. (2017). The national healthcare system claims databases in France, SNIIRAM and EGB: Powerful tools for pharmacoepidemiology. *Pharmacoepidemiology and Drug Safety, 26*(8), 954–962.

Broers, B., Helbling, B., François, A., Schmid, P., Chuard, C., Hadengue, A., et al. (2005). Barriers to interferon-alpha therapy are higher in intravenous drug users than in other patients with acute hepatitis C. *Journal of Hepatology, 42*(3), 323–328.

Brouard, C., Boussac-Zarebska, M., Silvain, C., Durand, J., de Lédinghen, V., Pillonel, J., et al. (2017). Rapid and large-scale implementation of HCV treatment advances in France, 2007-2015. *BMC Infectious Diseases, 17*(1), 784.

Bruggmann, P. (2012). Accessing hepatitis C patients who are difficult to reach: It is time to overcome barriers. *Journal of Viral Hepatitis, 19*(12), 829–835.

Campbell, A. N. C., Barbosa-Leiker, C., Hatch-Maillette, M., Mennenga, S. E., Pavlicova, M., Scodes, J., et al. (2018). Gender differences in demographic and clinical characteristics of patients with opioid use disorder entering a comparative effectiveness medication trial. *The American Journal on Addictions, 27*(6), 465–470.

Carré, B., & Perronnin, M. (2018). *Evolution de la dépense en part de complémentaire santé des bénéficiaires de la CMU-c analyse et prévision.* France: Les rapports de l'IRDES (Irdes/Fonds CMU-c).

Carrieri, P. M., Michel, L., Lions, C., Cohen, J., Vray, M., Mora, M., et al. (2014). Methadone induction in primary care for opioid dependence: A pragmatic randomized trial (ANRS Methaville). *PLoS One, 9*(11), e112328.

Degenhardt, L., Peacock, A., Colledge, S., Leung, J., Grebely, J., Vickerman, P., et al. (2017). Global prevalence of injecting drug use and sociodemographic characteristics and prevalence of HIV, HBV, and HCV in people who inject drugs: A multistage systematic review. *The Lancet Global Health, 5*(12), e1192–e1207.

Delile, J.-M., de Ledinghen, V., Jauffret-Roustide, M., Roux, P., Reiller, B., Foucher, J., et al. (2018). Hepatitis C virus prevention and care for drug injectors: The French approach. *Hepatology, Medicine and Policy, 3*. Retrieved March 26, 2019, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5987624/.

Des Jarlais, D. C., Feelemyer, J. P., Modi, S. N., Arasteh, K., & Hagan, H. (2012). Are females who inject drugs at higher risk for HIV infection than males who inject drugs: An international systematic review of high seroprevalence areas. *Drug and Alcohol Dependence, 124*(1–2), 95–107.

Des Jarlais, D. C., Kerr, T., Carrieri, P., Feelemyer, J., & Arasteh, K. (2016). HIV infection among persons who inject drugs: Ending old epidemics and addressing new outbreaks. *AIDS (London, England), 30*(6), 815–826.

Deuffic-Burban, S., Boursier, J., Leroy, V., Yazdanpanah, Y., Castera, L., & Mathurin, P. (2017). Are targeted treatment recommendations in chronic hepatitis C tailored to diagnostic methods of fibrosis? *Journal of Hepatology, 66*(2), 304–312.

El-Bassel, N., Wechsberg, W. M., & Shaw, S. A. (2012). Dual HIV risk and vulnerabilities among women who use or inject drugs: No single prevention strategy is the answer. *Current Opinion in HIV and AIDS, 7*(4), 326–331.

Esmaeili, A., Mirzazadeh, A., Carter, G. M., Esmaeili, A., Hajarizadeh, B., Sacks, H. S., et al. (2017). Higher incidence of HCV in females compared to males who inject drugs: A systematic review and meta-analysis. *Journal of Viral Hepatitis, 24*(2), 117–127.

Esmaeili, A., Mirzazadeh, A., Morris, M. D., Hajarizadeh, B., Sacks, H. S., Maher, L., et al. (2018). The effect of female sex on hepatitis C incidence among people who inject drugs: Results from the international multicohort InC3 collaborative. *Clinical Infectious Diseases, 66*(1), 20–28.

European Monitoring Centre for Drugs and Drug Addiction (2018). *France country drug report 2018*http://www.emcdda.europa.eu/countries/drug-reports/2018/france_en.

Evans, J. L., Hahn, J. A., Page-Shafer, K., Lum, P. J., Stein, E. S., Davidson, P. J., et al. (2003). Gender differences in sexual and injection risk behavior among active young injection drug users in San Francisco (the UFO Study). *Journal of Urban Health: Bulletin of the New York Academy of Medicine, 80*(1), 137–146.

Geeraert, J., & Rivollier, E. (2014). Access to care for vulnerable populations. *Soins – La revue de référence infirmière, 790*, 14–18.

Grebely, J., Bruneau, J., Bruggmann, P., Harris, M., Hickman, M., Rhodes, T., et al. (2017). Elimination of hepatitis C virus infection among PWID: The beginning of a new era of interferon-free DAA therapy. *The International Journal of Drug Policy, 47*, 26–33.

Grebely, J., Genoway, K. A., Raffa, J. D., Dhadwal, G., Rajan, T., Showler, G., et al. (2008). Barriers associated with the treatment of hepatitis C virus infection among illicit drug users. *Drug and Alcohol Dependence, 93*(1–2), 141–147.

Grebely, J., Larney, S., Peacock, A., Colledge, S., Leung, J., Hickman, M., et al. (2019). Global, regional, and country-level estimates of hepatitis C infection among people who have recently injected drugs. *Addiction (Abingdon, England), 114*(1), 150–166.

HAS (2016). *Prise en charge de l'hépatite C par les médicaments antiviraux à action directe (AAD).* https://www.has-sante.fr/portail/upload/docs/application/pdf/2016-12/recommandation_college_hepatite_c.pdf.

HAS (2017). *HAS – Commission de la Transparence – Rapport d'évaluation des antiviraux d'action directe dans le traitement de l'hépatite C. Actualisation 2017.* https://www.has-sante.fr/portail/upload/docs/application/pdf/2016-12/rapport_reev_aad_avis2_19102016.pdf.

Inserm (2010). *Réduction des risques chez les usagers de drogues.* http://www.ipubli.inserm.fr/handle/10608/86.

Iversen, J., Grebely, J., Topp, L., Wand, H., Dore, G., & Maher, L. (2014). Uptake of hepatitis C treatment among people who inject drugs attending Needle and Syringe Programs in Australia, 1999–2011. *Journal of Viral Hepatitis, 21*(3), 198–207.

Iversen, J., Page, K., Madden, A., & Maher, L. (2015). HIV, HCV, and health-related harms among women who inject drugs: Implications for prevention and treatment. *Journal of Acquired Immune Deficiency Syndromes (1999), 69*(Suppl 2), S176–181.

Kanwal, F., Kramer, J. R., El-Serag, H. B., Frayne, S., Clark, J., Cao, Y., et al. (2016). Race and gender differences in the use of direct acting antiviral agents for hepatitis C virus. *Clinical Infectious Diseases, 63*(3), 291–299.

Khuat, O. T. H., Morrow, M., Nguyen, T. N. N., & Armstrong, G. (2015). Social context, diversity and risk among women who inject drugs in Vietnam: Descriptive findings from a cross-sectional survey. *Harm Reduction Journal, 12*, 35.

Kwon, J. A., Dore, G. J., Grebely, J., Hajarizadeh, B., Guy, R., Cunningham, E. B., et al. (2019). Australia on track to achieve WHO HCV elimination targets following rapid initial DAA treatment uptake: A modelling study. *Journal of Viral Hepatitis, 26*(1), 83–92.

Lally, M. A., Montstream-Quas, S. A., Tanaka, S., Tedeschi, S. K., & Morrow, K. M. (2008). A qualitative study among injection drug using women in Rhode island: Attitudes toward testing, treatment, and vaccination for hepatitis and HIV. *AIDS Patient Care and STDs, 22*(1), 53–64.

Lazar, M., & Davenport, L. (2018). Barriers to health care access for low income families: A review of literature. *Journal of Community Health Nursing, 35*(1), 28–37.

Lazarus, J. V., Sperle, I., Maticic, M., & Wiessing, L. (2014). A systematic review of hepatitis C virus treatment uptake among people who inject drugs in the European Region. *BMC Infectious Diseases, 14*(Suppl 6), S16.

Liakina, V., Hamid, S., Tanaka, J., Olafsson, S., Sharara, A. I., Alavian, S. M., et al. (2015). Historical epidemiology of hepatitis C virus (HCV) in select countries – volume 3. *Journal of Viral Hepatitis, 22*(Suppl 4), 4–20.

Mackesy-Amiti, M. E., Boodram, B., Handanagic, S., Paz-Bailey, G., Prachand, N. G., Broz, D., et al. (2018). Latent classes of sexual risk behavior and engagement in outreach, intervention and prevention services among women who inject drugs across 20 US cities. *Journal of Acquired Immune Deficiency Syndromes (1999), 79*(3), 305–314.

Marshall, A. D., Cunningham, E. B., Nielsen, S., Aghemo, A., Alho, H., Backmund, M., et al. (2018). Restrictions for reimbursement of interferon-free direct-acting antiviral drugs for HCV infection in Europe. *The Lancet Gastroenterology & Hepatology, 3*(2), 125–133.

Midgard, H., Bramness, J. G., Skurtveit, S., Haukeland, J. W., & Dalgard, O. (2016). Hepatitis C treatment uptake among patients who have received opioid substitution treatment: A population-based study. *PLoS One, 11*(11), e0166451.

Miller, C. L., Fielden, S. J., Tyndall, M. W., Zhang, R., Gibson, K., & Shannon, K. (2011). Individual and structural vulnerability among female youth who exchange sex for survival. *The Journal of Adolescent Health, 49*(1), 36–41.

Ministère des solidarités et de la Santé (2018). *Précarité: accès aux soins.* https://solidarites-sante.gouv.fr/affaires-sociales/lutte-contre-l-exclusion/acces-aux-soins-des-personnes-en-situation-de-precarite/article/precarite-acces-aux-soins.

Ministère des Solidarités et de la Santé (2017). *Accès universel aux traitements innovants contre l'hépatite C.* https://solidarites-sante.gouv.fr/IMG/pdf/17_03_31_-_cp_concretisation_acces_universel_hepatite_c.pdf.

Morris, M. D., Bates, A., Andrew, E., Hahn, J., Page, K., & Maher, L. (2015). More than just someone to inject drugs with: Injecting within primary injection partnerships.

Drug and Alcohol Dependence, 156, 275–281.
Morris, M. D., Evans, J., Montgomery, M., Yu, M., Briceno, A., Page, K., et al. (2014). Intimate injection partnerships are at elevated risk of high-risk injecting: a multi-level longitudinal study of HCV-serodiscordant injection partnerships in San Francisco, CA. *PLoS One, 9*(10), e109282.
Mutatayi, C. (2014). *OFDT. Accueil addictologique et médicosocial de femmes toxicodépendantes.* 2010–2011. https://www.ofdt.fr/BDD/publications/docs/eisxcmu3.pdf.
NDARC (2010). *Women who inject drugs: A review of their risks, experiences and needs.* Sidney, Australia: National Drug and Alcohol Research Centre (NDARC). https://ndarc.med.unsw.edu.au/sites/default/files/ndarc/resources/Women%20who%20inject%20drugs.pdf.
Nelson, P. K., Mathers, B. M., Cowie, B., Hagan, H., Des Jarlais, D., Horyniak, D., et al. (2011). Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: Results of systematic reviews. *Lancet, 378*(9791), 571–583.
OFDT (2015). *Tableau de bord TSO 2015.* Junehttps://www.ofdt.fr/BDD/publications/docs/TabTSO150625.pdf.
Prescrire (2018). Antiviraux dits à action directe dans l'hépatite C: en ville aussi. *Prescrire, 38*(416), 420–421.
Roux, P., Rojas Castro, D., Ndiaye, K., Debrus, M., Protopopescu, C., Le Gall, J.-M., et al. (2016). Increased uptake of HCV testing through a community-based educational intervention in difficult-to-reach people who inject drugs: Results from the ANRS-AERLI study. *PLoS One, 11*(6), e0157062.
Saeed, S., Strumpf, E. C., Moodie, E. E., Young, J., Nitulescu, R., Cox, J., et al. (2017). Disparities in direct acting antivirals uptake in HIV-hepatitis C co-infected populations in Canada. *Journal of the International AIDS Society, 20*(3).
Scott, N., Ólafsson, S., Gottfreðsson, M., Tyrfingsson, T., Rúnarsdóttir, V., Hansdottir, I., et al. (2018). Modelling the elimination of hepatitis C as a public health threat in Iceland: A goal attainable by 2020. *Journal of Hepatology, 68*(5), 932–939.
Smyth, D., Francheville, J. W., Rankin, R., Beck, J., Hoare, C., Materniak, S., et al. (2017). Early successes in an open access, provincially funded hepatitis C treatment program in Prince Edward Island. *Annals of Hepatology, 16*(5), 749–758.
Socías, M. E., Ti, L., Wood, E., Nosova, E., Hull, M., Hayashi, K., et al. (2019). Disparities in uptake of direct-acting antiviral therapy for hepatitis C among people who inject drugs in a Canadian setting. *Liver International*.
Swan, D., Long, J., Carr, O., Flanagan, J., Irish, H., Keating, S., et al. (2010). Barriers to and facilitators of hepatitis C testing, management, and treatment among current and former injecting drug users: A qualitative exploration. *AIDS Patient Care and STDs, 24*(12), 753–762.
Temple-Smith, M., Stoové, M., Smith, A., O'Brien, M., Mitchell, D., Banwell, C., et al. (2007). Gender differences in seeking care for hepatitis C in Australia. *Journal of Substance Use, 12*(1), 59–70.
The European Monitoring Centre fro Drugs and Drug Addiction (2009). *Women's voices experiences and perceptions of women who face drug-related problems in Europe.* http://www.emcdda.europa.eu/system/files/publications/549/EMCDDA-TP_women%27s_voices_133363.pdf.
Tracy, D., Hahn, J. A., Fuller Lewis, C., Evans, J., Briceño, A., Morris, M. D., et al. (2014). Higher risk of incident hepatitis C virus among young women who inject drugs compared with young men in association with sexual relationships: A prospective analysis from the UFO Study cohort. *BMJ Open, 4*(5), e004988.
Treloar, C., Hull, P., Dore, G. J., & Grebely, J. (2012). Knowledge and barriers associated with assessment and treatment for hepatitis C virus infection among people who inject drugs. *Drug and Alcohol Review, 31*(7), 918–924.
Tuppin, P., Rudant, J., Constantinou, P., Gastaldi-Ménager, C., Rachas, A., de Roquefeuil, L., et al. (2017). Value of a national administrative database to guide public decisions: From the système national d'information interrégimes de l'Assurance Maladie (SNIIRAM) to the système national des données de santé (SNDS) in France. *Revue D'epidemiologie Et De Sante Publique, 65*(Suppl 4), S149–S167.
WHO (2016). *Combating hepatitis B and C to reach elimination by 2030.* Advocacy Brief. May 2016.
WHO (2018). *WHO International classification of diseases (ICD).* https://www.who.int/classifications/icd/en/.