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Reinfection in a large cohort of prison inmates with sustained virological response after treatment of chronic hepatitis C in Catalonia (Spain), 2002–2016

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ABSTRACT

Background: Prisoners and other high-risk patients who show a sustained virological response (SVR) after treatment for hepatitis C virus (HCV) can become reinfected. We aimed to calculate the rate of HCV reinfection in a large cohort of inmates with SVR and to determine factors that predict reinfection.

Methods: We included all inmates treated for hepatitis C in Catalonia (Spain) from January 2002 to December 2016 who achieved SVR and in whom viral load was subsequently determined. The incidence rate was calculated per 100 person-years (100 py) of follow up. Risk factors associated with reinfection were evaluated by bivariate log-rank test and multivariate Cox regression. Hazard ratio (HR) and their 95% confidence intervals (CI) were calculated.

Results: 602 patients were included, with a mean age of 37.9 years: 95% were men, 74.1% had a history of intravenous drug use (IDU) and 28.7% were HIV-infected. Patients were followed for a total of 2154.9 years (average 3.58 ± 3.1 years). 63 (10.5%) had HCV reinfection. 41 (65.1%) presented different genotype/subgenotype, 8 the initial genotype/subgenotype, and in 14 (22.2%) the genotype could not be determined. Of the 21 reinfected patients who were interviewed, 20 (95.2%) reported IDU after antiviral treatment, and 7 (33.3%) during treatment. The overall incidence of reinfection was 2.9 cases per 100 py. All reinfections occurred in patients with IDU history. At multivariate level, HIV infection was associated with reinfection (HR = 3.03; CI:1.82-5.04).

Conclusion: In HIV-infected inmates with IDU history, the rate of reinfection of HCV post-SVR is very high. Prisons play a key role in the detection and treatment of infection and reinfection by HCV and in the post-treatment monitoring in these patients, which should be combined with counseling and the optimization of the harm reduction programs. Effective control of these vulnerable groups favours the elimination of the HCV infection.

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Introduction

In recent years, the emergence and development of direct-acting antivirals (DAA), which act at various steps of the viral replication cycle, has revolutionized the treatment of chronic hepatitis C. Currently, the probability of achieving cure with the available DAA combinations is 95–100% in most scenarios. These drugs are characterized by their high efficacy, their good safety profile and their short period of administration, and are therefore enormously attractive for clinicians and patients. If their economic cost continues to fall, the use of DAA may spread to countries with more limited economic resources, and the challenge of eliminating HCV infection in the short or medium term may no longer seem unattainable. However, this goal may be difficult to achieve in certain patients with high risk of reinfection such as people who inject drugs (PWID), patients coinfected with HIV, men who have sex with men, and prison inmates.

In general, the studies which have tried to establish the true incidence of HCV reinfection have been limited by the sample size, the short follow-up time, and by the low number of cases of reinfection detected. An exception is the study of Islam et al. (2017), from the British Columbia Center for Disease Control Public Health Laboratory, which included more than 5000 patients with an incidence rate of 1.27 per 100 person/years. However, studies of prison inmates are few and far between (Bate, Colman, Frost, Shaw, & Harley, 2010; Marco et al., 2013), probably due to the difficulty of accessing treatment in some countries (Beckman et al., 2016; Webster, 2015) and also due to the loss of follow-up caused by transfers between prisons, release from prison, and so on.

Catalonia (an autonomous community in Spain) has 11 prisons with a total of 13,868 inmates/year. Prison policy, including the provision of health resources, is the responsibility of the autonomous government. Among prison inmates in Catalonia the prevalence of HCV infection is 8.2% (Direcció General de Serveis Penitenciaris, 2018) and most infected patients have a history of intravenous drug use (IDU) and/or HIV infection. In a study carried out by the Centre for Epidemiological Studies on HIV/AIDS and STIs in Catalonia, some 70% of PWID had been in prison at some point, and 35.3% of Spanish PWID and 16.5% of foreign PWID reported injecting drugs in prison (Folch et al., 2016). Besides, the persistence of high-risk behaviors among PWID during leave from prison or after release is well known, and favours HCV infection and transmission both inside the prison and in the community. All inmates have the same access to treatment as the general population, and the same efficacy is obtained (Marco et al., 2018). The majority of inmates are still in prison after sustained virological response (SVR) or have re-entered prison: for example, in 2017, 54.8% of inmates were serving at least their second term. In Catalonia, universal screening for HCV infection is performed upon prison admission. All these circumstances argue in favour of periodically determining HCV-RNA in inmates at risk of reinfection such as patients with a history of IDU, and also when they re-enter prison. The **objective** of our study is to determine the incidence rate and predictive factors of HCV reinfection in a large cohort of inmates with SVR after antiviral treatment.

Patients, materials and methods

Study design

Multicenter, retrospective cohort study in inmates from all 11 Catalan prisons treated for hepatitis C between January 2002 and December 2016.

Patients

Patients treated in prison who had obtained SVR, and in whom at least one HCV-RNA measurement had been carried out after SVR, were selected.

Methods

At each follow up visit post-SVR (annually if the patient was in prison, or upon reincarceration) a blood sample was obtained and tested for HCV RNA. Reinfections were considered when the viremia was detectable and the presence of HCV RNA was confirmed with at least one second measurement. In cases of reinfection, we also checked whether the patient remained incarcerated during the entire follow-up period. The reinfection date was defined as the midpoint between the last negative and first positive HCV-RNA test dates.

Patients who achieved SVR and were then reinfected, and were then treated for the second time and again achieved SVR, were included twice in the analysis.

Inmates who were in prison at the time of the statistical analysis (February 2018) were asked to answer an *ad hoc* questionnaire on their drug use during and after hepatitis C treatment, and on the route of administration.

The following variables were collected from electronic clinical records: birth date, gender, country of origin (Spanish vs foreign-born), lifetime history of IDU (yes vs no), HIV co-infection (yes vs no), HCV genotype, baseline HCV-RNA viral load, date and type of HCV treatment, and subsequent HCV-RNA viral load values (usually measured annually after SVR).

The data were obtained from the prison clinical histories, which have been computerized since 2002. Any changes in the genotype/viral subtype were recorded. If this result was not available in prison medical records, it was checked in the shared clinical history of the Catalan Health Institute, which collects data on more than 90% of health centres in Catalonia. No other extra-penitentiary medical records were used.

Study follow-up was closed on 12-31-2017, at which time the final result was established (reinfection vs no reinfection).

Ethical considerations

Subjects did not receive monetary compensation or any benefit for their collaboration, nor did their responses affect their healthcare or status within the prison. Inmates who were still in prison at the end of the follow-up period of the study received an informative handout regarding the nature of the study and signed an informed consent document prior to answering the questionnaire and taking part in the interview. The study was performed in accordance with international ethical recommendations (Helsinki Declaration and Oviedo Convention), the Spanish government's good clinical practice recommendations (Royal Decree 711/2002), and the legislation currently in force (Spanish Agency of Medicines and Health Products, Circular 15/2002). Likewise, confidentiality was ensured in compliance with the 1999 Spanish legislation regarding the protection of personal data. The study was approved by the Catalan Government's Institute of Health.

Statistical analysis

Descriptive data were expressed as absolute numbers, percentages and means with standard deviation (SD). The rate of infection was calculated for the entire population and by characteristic per 100 person-years of follow-up (100 py). Variables showing potential associations with reinfection (p-value < 0.10), or considered epidemiologically relevant at the bivariate, were included in the multivariate analysis using a backward stepwise approach, sequentially eliminated and subjected to a likelihood ratio test.

Reinfection curves were estimated using the Kaplan–Meier method and different groups of interest were compared using the log rank test. Multivariate analysis was performed using Cox's proportional hazards model. The proportionality of the risk was tested over time using the Schoenfeld residuals (Schoenfeld, 1980). Hazard Ratios (HR) were used as the measure of association, and their 95% confidence intervals (CI)

were calculated. A p-value < 0.05 was considered statistically significant.

All the analyses were performed using the SPSS 22.0 statistical package.

Results

Descriptive results

Between 2002 and 2016, a total of 1265 treatments (872 with peginterferon plus ribavirin; 44 with boceprevir or telaprevir and peginterferon plus ribavirin; and 349 with interferon-free therapy) were prescribed in 1151 prisoners. Of these, 1039 inmates were treated once, 110 twice and two patients were treated three times.

Eight hundred and seventy patients (75.6%) achieved SVR. In the cases treated with DAAs the SVR rate was 93.6%. HCV-RNA determinations were available after SVR in 602 cases (69.2%), and these were the patients who were definitively included in the study (Fig. 1). Of these patients, 95% were men, 74.1% patients had IDU history and 28.7% were infected with HIV. The prevalence of HIV infection among patients with IDU history was 35.7%. The mean age was 37.9 +/- 9.9 years (range: 21–64 years). Patients were followed for a total of 786,536 days (mean 1306.54 days or 3.58 ± 3.1 years). In 163 patients (27.1%), follow-up lasted longer than five years and in 40 (6.6%) longer than 10 years.

Reinfection analysis

Sixty-three of the 602 subjects (10.5%) had HCV reinfection. Eight of the reinfected individuals were incarcerated throughout the follow-up period and therefore the reinfection was known to have occurred in prison, but the rest (n = 55, 87.3%) had been granted prison leave on one or more occasions and so in these cases reinfection may have occurred either inside or outside prison.

The overall incidence rate of reinfection was 2.9 cases per 100 py (CI: 2.25–3.74) (Fig. 2). In eight cases (12.7%), reinfection was detected within a year of SVR, in 40 (63.5%) within five years and in 62 (98.4%) within ten years. In the cases treated with DAAs the incidence rate of reinfection was 3.62 per 100 py, (95%CI: 1.28–7.74) while in those not treated with DAAs it was 2.87 per 100 py (CI: 2.44-3.72**).** Mean time of follow up in reinfected patients was 4.35 ± 2.7 years, and 3.49 ± 3.1 years in non-reinfected patients (p < 0.001).

In 49 reinfected patients (77.8%) the genotype/subgenotype of the new infection was detected. Forty-one patients (83.7%) presented a different genotype, and the other eight (12.7%) were infected by the same genotype; in 14 cases (22.2%) the new genotype/subtype could not be identified.

Risk factors for reinfection

Twenty-one reinfected inmates in prison were interviewed. Of these, 20 (95.2%) reported using intravenous illicit drugs after finishing the treatment and seven (33.3%) during treatment. In addition, seven (33.3%) reported having inhaled illicit drugs during the treatment and 18 (85.7%) after finishing treatment. Consumption took place either inside or outside prison, during leave from prison or after release.

All 63 reinfected patients had IDU-history. The reinfection rate in this group was 3.9 per 100 py. Furthermore, the reinfection rate was 2.5-fold higher among subjects co-infected with HIV than in HIV-negative subjects (5.6 per 100 py vs. 2.2 per 100 py respectively; p < 0.001). The distributions of reinfection according to category are shown in Table 1. The incidence rate by categories and risk factors for HCV reinfection after treatment-induced SVR is presented in Fig. 5.

In the bivariate analysis, two variables (lifetime history of IDU and HIV infection) were significantly associated with reinfection (Table 1). At multivariate level, only HIV infection was associated with HCV reinfection (HR = 3.03; CI:1.82-5.04) (Fig. 3).

Discussion

In patients who had been treated for HCV in prison and had achieved SVR, we found a reinfection rate of 2.92/100 py (CI95: 2.25–3.74). As expected, the main risk of reinfection was drug use, aggravated by the presence of HIV infection. The cohort includes a broad range of patients with a “high risk of reinfection” as defined by Simmons, Saleem, Hill, Ryley, and Cooke (2016)): i.e., patients treated in prison, 74.9% of whom had a history of IDU and 28.7% of whom were HIV-infected.

All patients reinfected post-SVR had a history of IDU. Individuals with this history sometimes continues to use drugs and engage in behaviors that raise the risk of infection (Martinello et al., 2017). Although injectable drug consumption may fall during and after hepatitis C treatment (Midgard et al., 2017), it is estimated that at least 10–46% of treated PWIDs continue consumption after treatment (Backmund, Meyer, & Edlin, 2004; Bruggmann et al., 2008; Dalgard, 2005; Grebely et al., 2007, 2010; Grebely et al., 2012; Martinello et al., 2017). In our

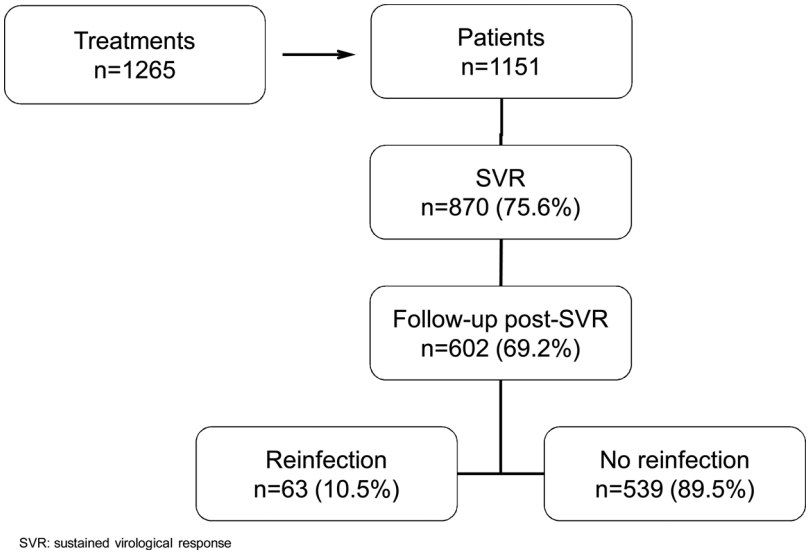

Fig. 1. Distribution of chronic hepatitis C treatments in 2002–2016 according to Sustained Virological Response and reinfection.

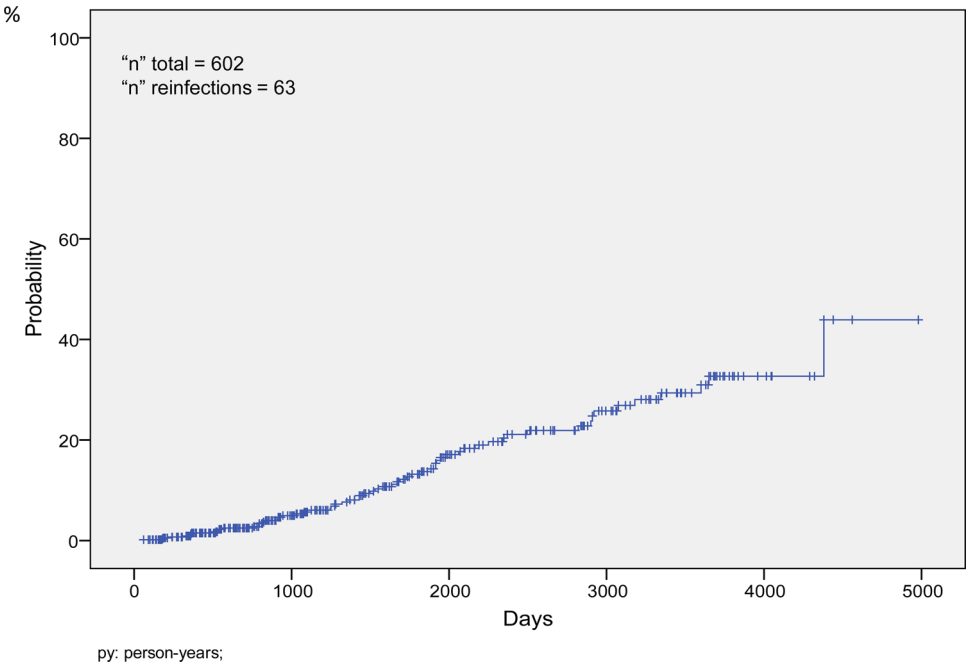

Fig. 2. Probability of HCV reinfection after treatments-induced Sustained Virological Response for the entire cohort.

study, almost all subjects with reinfection who could be interviewed engaged in intravenous illicit drug consumption; in fact, only one of them did not report post-SVR intravenous drug use. Nonetheless, the proportion of recurrent HCV infection cases caused by reinfection in patients with a history of IDU was 14.1%; that is to say, 85.9% were not reinfected after a mean follow-up of 3.6 years. Drug consumption, therefore, is a possibility that should be evaluated regularly in treated patients who present a history of IDU, but it should not be used to stigmatize this population group. PWIDs should not be discriminated against in treatment, not just for ethical reasons but for strategic reasons as well: due to their high risk of transmitting infection they must be treated rapidly (Grebely, Hajarizadeh, & Dore, 2017; Hickman, De Angelis, Vickerman, Hutchinson, & Martin, 2015; Martin et al., 2015; Martinello et al., 2017; Pineda et al., 2015).

The overall reinfection rate found in this cohort is very similar to other studies (Backmund, Meyer, Von Zielonka, & Eichenlaub, 2001; Grady et al., 2012; Grebely et al., 2007; Hilsden, Macphail, Grebely, Conway, & Lee, 2013; Midgard, Bjøro et al., 2016; Pineda et al., 2015). Indeed, a recent meta-analysis (Aspinall et al., 2013) reported a confidence interval of reinfection (0.9–6.1 per 100 py) that closely matches our results. Our rate of reinfection is lower than the two other studies previously published in prison inmates (Bate et al., 2010; Marco et al., 2013). However, comparing our results with those obtained in the study carried out in four prisons in Catalonia prior to the use of DAAs, with a much smaller prison population and a much shorter follow-up period, the reinfection rate observed in the present study is much lower (5.27 cases/100 p/y vs 2.92 cases / 100 p/y). This is probably due to the fact that the risk of reinfection is associated with the risk of relapsing into drug use; this risk is greater in the first months of abstinence, but decreases proportionally with the passing of time (Clark et al., 2015).

In agreement with previous studies (Midgard, Bjøro et al., 2016; Simmons et al., 2016), we found a higher incidence rate of reinfection in the patients infected with HIV. This may be because these patients are less prone to spontaneous clearance of HCV (Grebely et al., 2006)

Table 1
Recurrence and incidence by categories and risk factors for HCV reinfection after treatments-induced Sustained Virological Response.

Variable	Bivariate Analysis							Multivariate Analysis	
	"n"	Reinfection n (%)	Recurrence (%)	Follow-up (years)	Incidence rate (x100py)	95% CI	p-value	p-value	HR (95% CI)
Sex									
• Male	572	61 (96.8)	10.7	3.6	2.9	2.26-4.69	0.84		
• Female	30	2 (3.2)	6.7	2.9	2.3	0.21-8.35			
Age ≤30 old									
• Yes	121	21 (33.3)	17.4	4.9	3.5	2.17-7.20	0.63		
• No	481	42 (66.6)	8.7	3.2	2.7	1.94-4.60			
Spanish-born									
• Yes	530	60 (95.2)	11.3	3.7	3.1	2.34-3.94	0.42		
• No	72	3 (4.8)	4.2	2.7	1.5	0.29-4.62			
History of IDU ever									
• Yes	446	63 (100)	14.1	3.6	3.9	3.04-5.06	< 0.001		0.91 (0.00-9.11)
• No	156	0 (0)	0	3.6	0	0.00-0.09			
HIV infection									
• Yes	173	26 (41.3)	15	2.7	5.6	3.62-8.14	< 0.001	0.002	3.03 (1.82-5.04)
• No	429	37 (58.7)	8.6	3.9	2.2	1.54-3.02			
All patients	602	63 (100)	10.5	3.6	2.9	2.25-3.74			

95% CI: 95% Confidence Interval; py: patients/year; IDU: injecting drug use; **HR: Hazard ratio.**

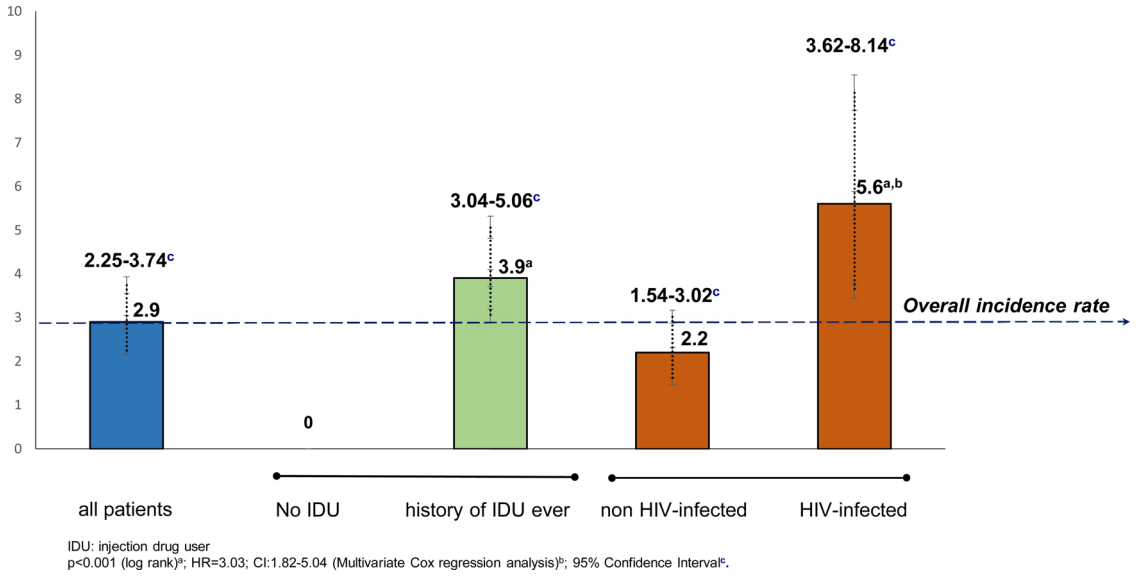

Fig. 3. Incidence by categories and risk factors for HCV reinfection after treatments-induced Sustained Virological Response.

due to the involvement of the immune system (Pineda et al., 2015). It is also possible that HIV-infected patients generally engage in more risk behaviors (associated either with sex or with drug consumption) than their non-HIV-infected counterparts. Usually, reinfection has been studied in subgroups with a predominant and continuous type of risk behavior (PWIDs or men who have sex with men, MSM), but the risk behaviors may vary, may coincide in time or may be more frequent in certain population groups. For example, in a recent study, Martinello et al. (2017) found a reinfection incidence of 7.4 per 100 person years (95% CI 4.0–13.8), mainly in HIV-infected MSM who are also injecting drug users.

The results reported so far with respect to age are contradictory. The fact that younger individuals are more likely to be reinfected has been cited in some studies, associated with the fact that it is young PWID who most often relapse (Midgard, Bjøro et al., 2016). Other authors, however, have found that reinfection is more frequent in older people, at least in cases with continued consumption (Martinello et al., 2017). In our study, with a long-term follow-up of a high number of patients with SVR, age was not associated with the risk of reinfection.

Our study could not evaluate the importance of opioid substitution therapy (OST) in the prevention of HCV reinfection since in most cases it was difficult to establish adherence to OST due to release from prison. However, this strategy is very effective in reducing reinfection if combined with other interventions designed to reduce damage (Martinello, Dore, Matthews, & Grebely, 2018), such as harm-reduction, mental health assessment, peer-based injecting and sexual education, post-treatment surveillance and early retreatment of reinfection (Islam et al., 2017; Martinello et al., 2017).

It was not possible to determine the change of genotype/subgenotype in all patients. Although we cannot entirely rule out the possibility that the eight cases that were not studied might be late relapses, since the reappearance of HCV-RNA years after an SVR may be due to the relapse of the initial viral infection rather than to reinfection by a different virus, this is in fact highly unlikely (Hara et al., 2014; Simmons et al., 2016). Probably, these cases are indeed reinfections, but the possibility of late relapse cannot be ruled out in patients who do not have evidence of genotype change. This limitation should be acknowledged.

Another limitation of the study is its retrospective design. The disadvantage is that the variables analysed are inevitably the data that are available from the databases. Potential bias due to physicians' criteria or the presence of missing data resulting from incomplete patient records or data entry errors cannot be ruled out, although it was not considered relevant. Another limitation due to the retrospective nature of the study is that not all reinfected patients could be interviewed, because many had been released. Fortunately, all the reinfected prisoners who remained in prison were willing to collaborate in the interview, but some of these interviews were made many years later and there may be considerable recall bias. Further, our interview did not include details on drug equipment sharing and other high-risk injecting practices, or on high-risk sexual practices among non-IDU men who have sex with men. Nonetheless, it is unlikely that factors other than those related to drug-injecting practices would significantly affect the risk of reinfection, as already observed in a previous study of HCV reinfection in Spanish prisoners (Marco et al., 2013).

This study also has some notable strengths. To our knowledge, only two studies to date (Bate et al., 2010; Marco et al., 2013) have assessed the incidence of HCV reinfection in prisoners treated for hepatitis C. In those studies, the number of subjects investigated and the number of reinfections observed were much smaller and the follow-up time much shorter. Specifically, in the study by Marco et al. (2013) conducted at four prisons in Catalonia (Spain) in the period prior to the use of DAAs, the population was six times smaller (109 vs 602), the follow-up time 2.3 times shorter (1.4 years vs 3.53 years) and the number of reinfections seven times lower (9 vs 63). Thus, the data reported in the present study are more substantial.

In conclusion, our study shows that HCV reinfection in our large cohort of inmates with an initial SVR occurs only in PWID, especially among those with HIV infection. These results emphasize the need to maintain close post-treatment monitoring in these patients, which should be combined with counseling, education and the optimization and improvement of the harm reduction programs currently in use. Finally, we stress the importance of prisons programs for the control of HCV and also for the control of HIV because HIV infection favours infection and reinfection by HCV. Prisons play an important role in the detection and treatment of HCV, and without thorough control of these vulnerable groups in the prison setting the elimination of HCV in the general population is likely to remain an unattainable goal.

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Conflict of interest statement

Andrés Marco has given lectures for Abbvie, Gilead, Janssen Cylag and MSD. Mercedes Vergara has received fees as an advisory board member from Gilead and has given lectures for Abbvie, MSD, Janssen Gylag and Gilead. The rest of the authors have no conflicts of interest to declare.

References

Aspinall, E. J., Corson, S., Doyle, J. S., Grebely, J., Hutchinson, S. J., Dore, G. J., ... Hellard, M. E. (2013). Treatment of hepatitis C virus infection among people who are actively injecting drugs: A systematic review and meta-analysis. *Clinical Infectious Diseases, 57*(Suppl 2), S80–S89.

Backmund, M., Meyer, K., Von Zielonka, M., & Eichenlaub, D. (2001). Treatment of hepatitis C infection in injection drug users. *Hepatology, 34*(1), 188–193.

Backmund, M., Meyer, K., & Edlin, B. R. (2004). Infrequent reinfection after successful treatment for hepatitis C virus infection in injection drug users. *Clinical Infectious Diseases, 39*(10), 1540–1543.

Bate, J. P., Colman, A. J., Frost, P. J., Shaw, D. R., & Harley, H. A. (2010). High prevalence of late relapse and reinfection in prisoners treated for chronic hepatitis C. *Journal of Gastroenterology and Hepatology, 25*(7), 1276–1280.

Beckman, A. L., Bilinski, A., Boyko, R., Camp, G. M., Wall, A. T., Lim, J. K., ... Gonsalves, G. S. (2016). New hepatitis C drugs are very costly and unavailable to many state prisoners. *Health Affairs (Millwood), 35*(10), 1893–1901.

Bruggmann, P., Falcato, L., Dober, S., Helbling, B., Keiser, O., Negro, F., ... Swiss Hepatitis C Cohort Study (2008). Active intravenous drug use during chronic hepatitis C therapy does not reduce sustained virological response rates in adherent patients. *Journal of Viral Hepatitis, 15*(10), 747–752.

Clark, R. E., Baxter, J. D., Aweh, G., O'Connell, E., Fisher, W. H., & Barton, B. A. (2015). Risk factors for relapse and higher costs among medicaid members with opioid dependence or abuse: Opioid agonists, comorbidities, and treatment history. *Journal of Substance Abuse Treatment, 57*, 75–80.

Dalgard, O. (2005). Follow-up studies of treatment for hepatitis C virus infection among injection drug users. *Clinical Infectious Diseases, 40*(suppl 5), S336–S338.

Direcció General de Serveis Penitenciaris (2018). *Descriptors estadístics serveis penitenciaris.* Barcelona, Spainhttp://www.gencat.cat/justicia/estadistiques_serveis_penitenciaris/3_pob.html.

Folch, C., Casabona, J., Espelt, A., Majó, X., Meroño, M., Gonzalez, V., ... REDAN Group (2016). High prevalence and Incidence of HIV and HCV among new injecting drug users with a large proportion of migrants–Is prevention failing? *Substance Use & Misuse, 51*(2), 250–260.

Grady, B. P., Vanhommerig, J. W., Schinkel, J., Weegink, C. J., Bruisten, S. M., Lindenburg, C. E., ... Prins, M. (2012). Low incidence of reinfection with the hepatitis C virus following treatment in active drug users in Amsterdam. *European Journal of Gastroenterology & Hepatology, 24*(11), 1302–1307.

Grebely, J., Conway, B., Raffa, J. D., Lai, C., Krajden, M., & Tyndall, M. W. (2006). Hepatitis C virus reinfection in injection drug users. *Hepatology, 44*(5), 1139–1145.

Grebely, J., Raffa, J. D., Meagher, C., Duncan, F., Genoway, K. A., Khara, M., ... …Conway, B. (2007). Directly observed therapy for the treatment of hepatitis C virus infection in current and former injection drug users. *Journal of Gastroenterology and Hepatology, 22*(9), 1519–1525.

Grebely, J., Knight, E., Ngai, T., Genoway, K. A., Raffa, J. D., ... Conway, B. (2010). Reinfection with hepatitis C virus following sustained virological response in injection drug users. *Journal of Gastroenterology and Hepatology, 25*(7), 1281–1284.

Grebely, J., Pham, S. T., Matthews, G. V., Petoumenos, K., Bull, R. A., Yeung, B., ... ATAHC Study Group (2012). Hepatitis C virus reinfection and superinfection among treated and untreated participants with recent infection. *Hepatology, 55*(4), 1058–1069.

Grebely, J., Hajarizadeh, B., & Dore, G. J. (2017). Direct-acting antiviral agents for HCV infection affecting people who inject drugs. *Nature Reviews Gastroenterology & Hepatology, 14*(11), 641–651.

Hara, K., Rivera, M. M., Koh, C., Demino, M., Page, S., Nagabhyru, P. R., ... …Heller, T. (2014). Sequence analysis of hepatitis C virus from patients with relapse after a sustained virological response: relapse or reinfection? *The Journal of Infectious Diseases, 209*(1), 38–45.

Hickman, M., De Angelis, D., Vickerman, P., Hutchinson, S., & Martin, N. K. (2015). Hepatitis C virus treatment as prevention in people who inject drugs: Testing the evidence. *Current Opinion in Infectious Diseases, 28*(6), 576–582.

Hilsden, R. J., Macphail, G., Grebely, J., Conway, B., & Lee, S. S. (2013). Directly observed pegylated interferon plus self-administered ribavirin for the treatment of hepatitis C virus infection in people actively using drugs: A randomized controlled trial. *Clinical Infectious Diseases, 57*(suppl 2), S90–S96.

Islam, N., Krajden, M., Shoveller, J., Gustafson, P., Gilbert, M., Buxton, J. A., ... Janjua, N. Z. (2017). Incidence, risk factors, and prevention of hepatitis C reinfection: A population-based cohort study. *The Lancet Gastroenterology & Hepatology, 2*(3), 200–210.

Marco, A., Esteban, J. I., Sole, C., da Silva, A., Ortiz, J., Roget, M., ... Caylà, J. A. (2013). Hepatitis C virus reinfection among prisoners with sustained virological response after treatment for chronic hepatitis C. *Journal of Hepatology, 59*(1), 45–51.

Marco, A., Roget, M., Cervantes, M., Forné, M., Planella, R., Miquel, M., ... In and Out of Prison Study Group (2018). Comparison of effectiveness and discontinuation of interferon-free therapy for hepatitis C in prison inmates and non-inmates. *Journal of Viral Hepatitis, 25*(11), 1280–1286.

Martin, N. K., Foster, G. R., Vilar, J., Ryder, S., Cramp, M. E., Gordon, F., ... Hickman, M. (2015). HCV treatment rates and sustained viral response among people who inject drugs in seven UK sites: Real world results and modelling of treatment impact. *Journal of Viral Hepatitis, 22*(4), 399–408.

Martinello, M., Grebely, J., Petoumenos, K., Gane, E., Hellard, M., Shaw, D., ... Matthews, G. V. (2017). HCV reinfection incidence among individuals treated for recent infection. *Journal of Viral Hepatitis, 24*(5), 359–370.

Martinello, M., Dore, G. J., Matthews, G. V., & Grebely, J. (2018). Strategies to reduce hepatitis C virus reinfection in people who inject drugs. *Infectious Disease Clinics of North America, 32*(2), 371–393.

Midgard, H., Hajarizadeh, B., Cunningham, E. B., Conway, B., Backmund, M., Bruggmann, P., ... ACTIVATE Study Group (2017). Changes in risk behaviours during and following treatment for hepatitis C virus infection among people who inject drugs: The ACTIVATE study. *The International Journal of Drug Policy, 47*, 230–238.

Midgard, H., Bjøro, B., Mæland, A., Konopski, Z., Kileng, H., Damås, J. K., ... Dalgard, O. (2016). Hepatitis C reinfection after sustained virological response. *Journal of Hepatology, 64*(5), 1020–1026.

Pineda, J. A., Núñez-Torres, R., Tellez, F., Mancebo, M., García, F., Merchante, N., ... HEPAVIR Group of The Andalusian Society of Infectious Diseases (SAEI) (2015). Hepatitis C virus reinfection after sustained virological response in HIV-infected patients with chronic hepatitis C. *The Journal of Infection, 71*(5), 571–577.

Schoenfeld, D. (1980). Chi-squared goodness-of-fit tests for the proportional hazards regression model. *Biometrika, 67*(1), 145–153.

Simmons, B., Saleem, J., Hill, A., Ryley, R. D., & Cooke, G. S. (2016). Risk of late relapse or reinfection with hepatitis C virus after achieving a sustained virological response: a systematic review and meta-analysis. *Clinical Infectious Diseases, 62*(6), 683–694.

Webster, P. C. (2015). Federal inmates treated for hep C drop 29%. *Canadan Medical Association Journal, 187*(18), 1345–1346.