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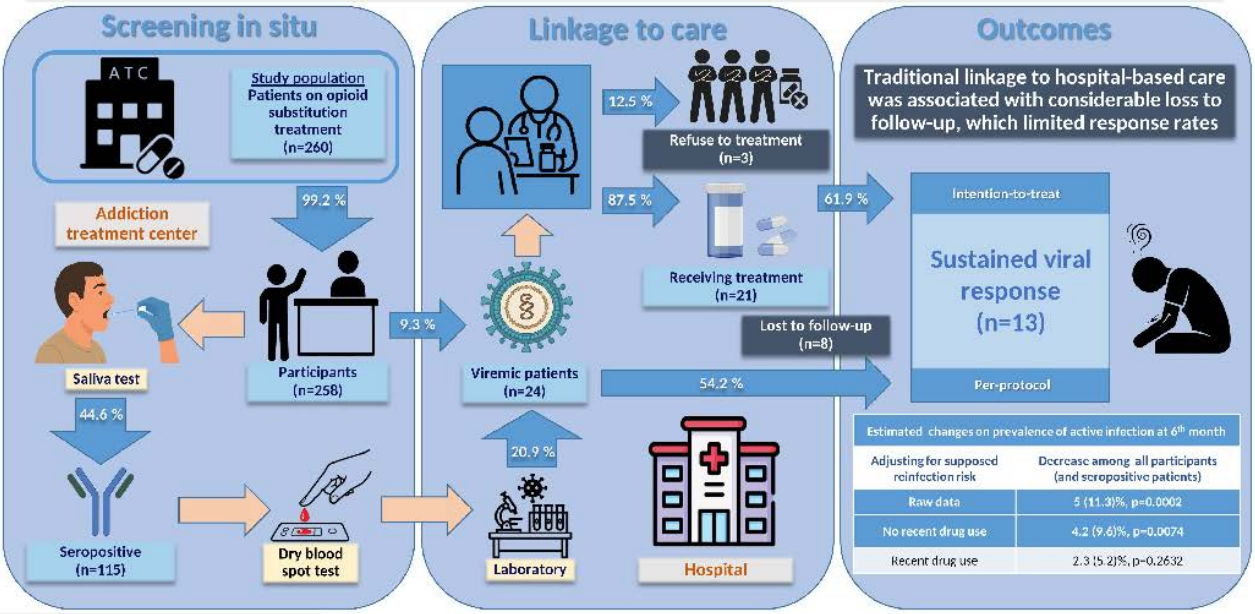

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RESULTS OF A HEPATITIS C MICROELIMINATION PROJECT IN AN ADDICTION TREATMENT CENTER

Short tittle: hepatitis C microelimination in an addiction treatment center

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Keywords: Hepatitis C, Microelimination, People who inject drugs, Opioid substitution therapy, Addiction treatment center, Saliva serological screening, Dry blood spot test, Direct-acting antivirals

Abbreviations (in the order of appearance in the text):

HCV	hepatitis C virus
WHO	World Health Organization
SMH	Spanish Ministry of Health

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PWID	people who inject drugs
OST	opioid substitution therapy
ATC	addiction treatment center
DBST	dry blood spot test
VRUH	Virgen del Rocío University Hospital
RT-qPCR	real time quantitative polymerase chain reaction
SVC	spontaneous viral clearance
FIB4	fibrosis-4 index for liver fibrosis
APRI	aspartate aminotransferase-to-platelet ratio index
DAAs	direct-acting antivirals
SVR	sustained viral response
ITT	intention-to-treat
PP	per-protocol
HIV	human immunodeficiency virus
HBV	hepatitis B virus
HAV	hepatitis A virus

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ABSTRACT

Background: Patients on opioid substitution therapy constitute a collective with a high burden of hepatitis C and candidate to interventions aimed to microelimination.

Aims: To analyze the baseline prevalence of both previous contact and/or active infection patients, measure the response to current treatment provided through a simplified circuit and estimate the impact of this intervention on reduction of proportion of viremic population.

Methods: People affiliated in an addiction treatment center was subjected to an *in situ* diagnostic sequence using a saliva serological screening and viremia quantification with dry blood spot test. Viremic patients were linked to care and treatment was administered in the first single appointment with pan-genotypic direct-acting antivirals. The McNemar test was used to compare proportions of active infection before and after intervention.

Results: With a participation of 99.2%, seroprevalence for hepatitis C was 44.6% (115/258) while active infection was present in a 20.9% of seropositive people (24/115). The response rate to treatment was 54.2% by intention-to-treat and 61.9% by per-protocol analysis. Successfully treating of 13 patients allowed to estimate a global reduction of active infection rate from 9.3% to 4.3% (p=0.0002), for a theorical scenario with no reinfections. By adjusting for the known reinfection rates, the prevalence of active infection also decreased a 4.2% for people with assumed no recent drug use (p=0.0074), but no changes were found for estimates in patients with supposed recent drug use (p=0.2632).

Conclussions: Focused efforts targeted to this high-risk group, including both screening and treatment initiatives, can potentially reduce the prevalence of active hepatitis C infections.

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Key points

1. The current seroprevalence of hepatitis C virus is close to 50% among patients on opioid substitution therapy, while active infection affects only 1 in 5 cases of previous contact patients.

2. Simplifying the diagnostic cascade, using saliva test and dry blood spot samples, is an essential tool for enabling access to rapid treatment initiation.

3. Despite insufficient follow-up, achieved response rate were acceptable after just a single course of treatment.

4. Future effort should scale these microelimination projects to other vulnerable communities with high prevalence and/or probability of reinfection.

Lay summary

Microelimination of hepatitis C in vulnerable populations constitutes a challenging public health topic. This pragmatic initiative, designed for patients on opioid substitution therapy, provides valuable operational information on the current rate of viremic patients, close to 10%. Screening conducted using the addiction treatment center as the point of care, by simple tools, led to almost universal participation. This sequential diagnostic model (saliva test and dry blood spot samples), which did not involve venipuncture sampling, is feasible and potentially adaptable to similar populations. However, traditional linkage to hospital-based care was associated with considerable loss to follow-up, which limited response rates by intention to treat, only slightly more than half of cases. The potential reinfections described in this population could also compromise the project's impact, especially in recent drug use patients. Decentralizing treatment and further efforts to extend the observation period could

provide more robust empirical support for these strategies.

INTRODUCTION

Hepatitis C virus (HCV) infection affects more than 71 million people worldwide (**1**). If left untreated, it becomes a relevant cause of advanced liver diseases, cirrhosis and/or hepatocellular carcinoma, and represents a notable indication for liver transplant. In Europe, patients with active HCV infections not only experience reduced a remarkable quality of their life, but also contribute to substantially increased direct and indirect health, social and economic burden (**2**).

The World Health Organization (WHO) has set the ambitious goal of global HCV elimination by 2030. In line with this objective, the Spanish Ministry of Health (SMH) has implemented since May 2015 a strategic plan for addressing and monitoring HCV within the National Health Service (**3**). Several strategies have been designed to overcome the barriers that prevented progress in the elimination of HCV (**4**), such as one-step (automatic-reflex) diagnosis (**5**). The global prevalence of HCV was estimated to be around 1% (**6**). In Spain, HCV affects over 300,000 people, with a historical prevalence of active infection around 0.3-0.5% (**7,8**), although with a very asymmetric distribution according to the presence of certain risk factors. In fact, there are same groups where the prevalence of HCV is higher and one is the namely people who inject drugs (PWID), currently considered a previous risk factor, usually remote in time (**9**), because many of them have already quit this habit and are now enrolled in harm reduction programs by opioid substitution therapy (OST) as the main strategy for managing the consequences of addiction. Globally, it has been estimated that 8.5% of all HCV infections occurs in previous PWID (**10**). Indeed, this is one of the most significant collectives where projects are being conducted to achieve HCV elimination. Reinfection following successful treatment can compromise outcomes among people receiving OST, especially with recent injecting (even non-injecting) drug use (**11**).

To this end, we have implemented an intervention project aimed to achieving the microelimination of HCV in OST patients affiliated with an addiction treatment

center (ATC), focused on actively seek viremic people, to identify those candidates to treat, in accordance with the guidelines of the SMH and the WHO. Our objectives were: 1) prospectively analyze the baseline prevalence of both previous contact and/or viremic patients, by a diagnostic sequence using a saliva serological screening and viremia quantification with dry blood spot test (DBST), 2) measure the real-life impact on the accessibility and outcome of antiviral treatment provided by this route in this population, and; 3) estimate the effect of this intervention in terms of reducing the percentage of viremic patients, adjusting treatment successes to the reinfection rate described in this scenario.

METHODS

The Investigation and Ethics Committee of Virgen del Rocío University Hospital (VRUH) of Seville approved our protocol. All patients included received oral and written information and voluntarily accepted to participate through the signing of the corresponding informed consent.

Phase I: Screening *in situ*.

Our study was conducted at an ATC located in the city of Seville, named Torreblanca, a public center that provides attendance for different types of addiction disorders, including those patients with substance dependence (**Figure 1**). The simultaneous quota of this ATC is of 900 people, of which 450 are patients in OST. They serve about new 15 people weekly. All patients who agreed to participate in screening constituted the complete population.

Patient screening process took place between January 2020 and July 2022 and include an initial saliva test OraQuick ADVANCE® supplied by OraSure Technologies (Bethlehem, Pensilvania, USA) detecting anti-HCV antibodies (**12**), that remain positive for life. Only those patients who tested positive in the saliva test (previous contact population) underwent a following DBST supplied by Ahlstrom-Munksjö (Helsinki, Finland) for HCV viremia (**13**), in an automatically-conducted sequential-one step diagnostic schedule. Samples for the DBST were collected at the ATC and transported to the Microbiology-Serology Laboratory belonging VRUH, where

viremia quantification was carried out using real time quantitative polymerase chain reaction (RT-qPCR) with the Roche Cobas® HCV reagent on the Roche 6800 autoanalyzer.

Patients with negative results in the screening were considered as having not prior contact with HCV. In those patients positive for anti-HCV antibodies but with negative viremia, we investigate in their clinical histories data about any previous treatments against HCV or spontaneous viral clearance (SVC), in an attempt to understand these results. Both non-immune or non-viremic patients were informed in writing about the meaning of their results and, at the same time, advised on appropriate preventive measures to avoid future exposure to HCV.

Phase 2: Linkage to care.

The viremic patients were linked to our health system (VRUH, Hepatology Unit) and, in one single appointment, with a previously agreed date handled according to personal preferences, they underwent a clinical history and physical examination. Additionally, a venipuncture was offered to obtain blood samples for other viral infections screening (within the comprehensive process recommended by current guidelines) and to systematically estimate liver fibrosis by using indirect methods (**14-16**). The fibrosis-4 index for liver fibrosis (FIB4) score were used with their clasical cut-offs for no fibrosis (<1.45) and for advanced fibrosis (>3.25), while values between 1.45-3.25 were considered as significant fibrosis. For aspartate aminotransferase-to-platelet ratio index (APRI) score the cut-off for absence of fibrosis was below 0.5 and for advanced fibrosis was above 0.5, while significat fibrosis was establised for values between 0.5-1.5. Whenever possible, these same blood samples were used for HCV genotyping, for academical purposes at the discretion of the researcher.

Interestingly, we dispensed the complete treatment in the first single appointment, prior evaluation for possible drug-to-drug interactions. In this same act, a comprehensive review was also carried out about any previous treatments for HCV. The treatment was administered at the Hospital Pharmacy with pan-genotypic direct-acting antivirals (DAAs), used over eight (Glecaprevir/Pibrentasvir) or 12 weeks (Sofosbuvir/Velpatasvir). After treatment patients were followed according to usual

recommendations. Undetectable viremia by RT-qPCR after 12 weeks of treatment ending (sustained viral response -SVR12-) was used as an indicator of cure. To describe the response rate, we considered the number of patients successfully cured relative to the complete viremic population at baseline (intention-to-treat -ITT- analysis) and, within these, to those who accessed the intervention (per-protocol -PP- analysis). With this same purpose, refuse to treatment was considered as a failure to ITT response rate while any type of post-treatment lost to follow-up interfering SVR was taken into account a failure to PP response rate. Data collected on genotype, degree of fibrosis, and prior treatment experience were in detail compared between patients with and without SVR, using the Fisher's exact test. For pragmatic reasons, this statistical analysis was simplified comparing patients with 1 *vs.* non-1 genotype, significant or advanced *vs.* no fibrosis, advanced *vs.* significant or no fibrosis, and previous treatment *vs. naive*.

Considering that the maximum duration of treatment with DAAs was 12 weeks, and that SVR was also measured at week 12 post-treatment, the effect of successful treatment on decrease of prevalence of active infection was obtained at 24 weeks. Changes in prevalence of active infection were firstly inferred based on the assumption that the population remained constant in terms of its proportion of viremic patients, with no differences occurring for any reason other than the study intervention itself (Model 1, “raw data”), that is, considering that there were no reinfections in the group of patients who were non-viremic at baseline on the total sample (complete population), and again on the seropositive sample (previous contact population). Secondly, the effect of successful treatment on decrease of prevalence of active infection was adjusted for an estimated reinfection rate. Thus, two theoretical models were created attempting to simulate two real scenarios with different risk of reinfection (Model 2, “no recent drug use”; Model 3, “recent drug use”). Thus, a number of cases were attributable to reinfection, for that same period of approximately six months, for each one of these models. The estimates were made according to the data reported among people receiving OST from a recent meta-analysis, showing reinfection rates ranged from 1.4-5.9/100 person-years, without and with recent drug use (injecting or non-injecting), respectively (**11**). To compare the

paired proportions of patients with or without active infection before and after the intervention, the non-parametric McNemar test was used. The absolute difference was expressed as a percentage, with its corresponding 95% confidence interval. A two-sided P-value of less than 0.05 was considered statistically significant.

For all patient's linkage to care, a possible co-infection status for hepatitis A and/or B viruses, and for human immunodeficiency virus (HIV) was identified. To those with advanced fibrosis, we offered both a complete evaluation and follow-up to screen liver diseases complications over the time.

RESULTS

Continues variables are reported as median and interquartile range and categorical variables are reported as absolute and relative frequencies.

Phase I:

Of the full baseline population (n=260) at the ATC, 231 (88.8%) were males with a median age of 51 (46-56) years (**Figure 2**). The majority of patients (n=210, 80.8%), were in OST. After the refuse of two patients to participate in the study, HCV screening was carried out in 258 patients (complete population), of which 115 (44.6%) had antibodies against HCV detected with the saliva test (seropositive population), and of these, only 24 (20.9%) patients were viremic (by DBST). Demonstrated non-viremic patients (91/115) were the majority of patients screened (79.1%) and in them, we were able to find, in their clinical records, evidence of SVC (14.3%) or SVR (82.4%), but no data were found for three patients (3.3%). Treatment experienced for patients with documented SVR was mainly based on Interferon-free regimens with DAAs (74.7%).

Phase 2:

Regarding the treatment of HCV viremic patients, 87.5% (21/24) of them were immediately treated with pan-genotypic DAAs (**Figure 2**). The ITT response rate was 54.2% (13/24). Of the 21 treated patients, 13 patients (61.9%) achieved SVR12 (PP response rate), two patients (9.5%) are pending evaluation of response, and six patients (28.6%) were lost to follow-up. Hence, we did not find non-responders for

virological reasons or intolerance to the treatment. In fact, failures were due to refuse to treatment (n=3) and/or to anyway post-treatment lost to follow-up (n=8). Comparative analysis of SVR according to different potentially predictive baseline factors did not reveal any relevant patterns that would allow for improved clinical interpretation of the results (**Table 1**). Considering only the 14 cases with available data, SVR rates were 40% in 1 (4/10) *vs.* 75% in non-1 genotype (3/4); p=0.559. For all treated patients (n=21), SVR rate was 50% in significant or advanced (6/12) *vs.* 77.8% in no fibrosis (7/9), and 100% in advanced (4/4) *vs.* 52.9% in significant or no fibrosis (9/17); p=0.367, and p=0.131, respectively. For treatment experienced patients, SVR rate was 80% (4/5) *vs.* 56.3% in *naive* (9/16); p=0.606.

In Model 1, changes in the number of viremic patients before and after treatment were attributed exclusively to the impact of the intervention, that is, to the 13 cases who achieved SVR after treatment, immediately administered. Hence, the absolute number for non-viremic patients before intervention in contingency tables remained constant six months after, assuming a zero-reinfection rate. Consequently, the active infection rate was reduced from 9.3% (24/258) before to 4.3% (11/258) after intervention (p=0.0002). Considering only seropositive participants, the rate of viremic patients was reduced from 20.9% (24/115) before to 9.6% (11/115) after intervention (p=0.0002). Throughout the 6-month period, of the susceptible patients (non-viremic at baseline), two new cases were imputed as a result of reinfections according to Model 2 [(1.4*234/100)/2=1.6], while seven cases could become viremic due to reinfections, for Model 3 [(5.9*234/100)/2=6.9]. Therefore, for Model 2, the percentage of viremic patients during the observation window could have reached 5% (13/258) and 11.3% (13/115), in the complete and seropositive populations, respectively. However, even assuming a certain risk of reinfection as possible, despite no recent drug use, the prevalence of active infection was also reduced, maintaining statistical significance (p=0.0074) in both groups. Instead, under the unverified assumption of recent drug use (Model 3), the new viremic cases attributed to reinfections caused the estimated prevalence of active infection to only show a downward trend, without this decrease reaching statistical significance. All these data are shown in **Table 2.**

Of the 21 treated individuals, we do not found evidence of neither co-infection with HIV or active hepatitis B virus (HBV) infection in any case. However, and regarding HBV, nine patients (42.9%) showed serological markers of previous natural exposure, while only other nine patients (42.9%) had protective any way-obtained immunity. Similarly, eight patients (38.1%) presented protective antibodies against the hepatitis A virus (HAV), either by vaccination or naturally obtained. These data are in more detail shown in **Table 3**. Both FIB4 and APRI scores correlated to each other, showing an almost complete correspondence for their three strata.

DISCUSSION

Screening effort, majorly focused on vulnerable communities with high prevalence of active HCV infection, are the first approach for microelimination projects, a proven and reliable strategy to the primary purpose to achieving total HCV elimination in the coming years, as demanded by WHO. In our project, we addressed the population in OST, as the main harm reduction program focused in previous PWID, a particularly high-risk group for infection.

To reach this key community, it is crucial to work closely in coordination with every corresponding ATC. People in OST accounts for a significant proportion of global HCV infections, and constitute a challenging population due to its precarious and sometimes marginal condition. In fact, many of these people do not participate in the generic follow-up for health-care imposed by physicians. The ideal situation for the implementation of microelimination projects in this scenario, would be the belonging of the ATC to the SMH, which would improve the communication with hospitals, allowing targeted interventions. Unfortunately, many of these centers in Spain do not yet depend on the SMH, instead on their local/council institutions. On the other hand, some Spanish policies promote certification of ATC by a proposed guide with 22 important criteria, mainly focused on achieving the goal of HCV elimination (**17**).

The introduction of one-step diagnosis and the ability to use dried blood samples instead of venipuncture, has made it possible to obtain a high number of patients evaluated in this project. The DBST has proven to be a highly sensitive and specific method for quantifying HCV viremia compared to classical tests in

venipuncture samples and appears to be a highly accurate diagnostic alternative for communities with high prevalence. Additionally, DBST is noteworthy for its efficiency, and useful for diagnosis even three months later, when samples were at room temperature (**18**,**19**)**.** By offering a seamless diagnostic approach, the adopted screening scheme mitigated barriers such as delays in diagnosis and lack of follow-up care, which are often seen in vulnerable populations.

With a percentage for participation close to 100%, seroprevalence for HCV was close to 50%, while previous unrecognized active infection was identified in only a 20.9% of anti-HCV positive people. While Spain is not the country with the highest prevalence in this community, the percentage is not negligible, suggesting that this population is an important target for elimination (**20**). Interestingly, most of data about VHC prevalence in Spain corresponds to a previous period, whose analyses were prior to the widespread application of the new treatments for HCV, and consequently, its full impact could not be accurately evaluated. Our results show a recent figure in this specific group and we believe it is more representative of the current reality. In fact, more than 80% of non-viremic anti-HCV positive patients were any-drug ultimately effective treatment experienced. This group probably included those patients who were sufficiently motivated to have been treated even within a traditional, non-outsourced care process, fraught with barriers at various levels.

However, the study also reveals areas for improvement. Despite the immediate treatment provided to viremic patients using pan-genotypic DAAs, only a modest number of cases achieved SVR after just a single course of treatment. The seemingly poor results in terms of success rate may again be due to a pre-selection of those patients who were less suitable for whatever reason. The authors explicitly acknowledge that our results are below the SVR rates typically observed in OST populations with integrated care (**21**). However, our study sheds light on the effectiveness (on real-life conditions) of DAAs in a group historically challenging to treat due to both social and medical factors. A notable limitation was the loss to follow-up, with a high rate of treated patients not completing the required post-treatment monitoring. In fact, dropouts were the predominant reason for non-response to treatment, not virological failures. This could be attributed to the

challenges of maintaining engagement with a vulnerable population that may face instability in housing, employment, and healthcare access. However, similar studies show the same problem even in different countries (**22**,**23**). Our project design outsourced the diagnostic process and improved access to treatment for this population, but without eliminating the barrier that the hospital itself usually represents for OST people. This, highlights the need for comprehensive, patient-centered care that extends beyond treatment to include robust follow-up systems to ensure the highest possible rates of cure. Hence the importance of patient re-engagement programs, called "re-link" which aim to find patients lost in microelimination projects during the follow-up, to re-treat them if necessary (**24**).

The estimated changes in the prevalence of viremic patients should be interpreted with caution. First, the observation period in our study was short (six months). Furthermore, the estimates made after a single intervention were based on unproven assumptions (patients with unverified SVR were classified as non-responders, and the reinfection rate was derived from the literature). Regarding this topic, reinfection in this population still not completely solved to date, just as shown studies evaluating the HCV reinfection in actively PWID after DAAs treatment but not in OST non-HIV people who not maintains that risk factor (**20**,**25**). In fact, in studies in similar settings, despite an injection drug use rate of approximately 20%, the reported reinfection rate was as low as 0-3.1/100 person-years (**26**-**30**). In our study, we assumed in Model 1 a zero-reinfection rate, considering the participants' adequate adherence to the OST program and the widespread abandonment of intravenous drug use in Spain for almost decades. Hence, we could speculate that the real reinfection rate in patients who were non-viremic at baseline was probably zero, which made the population itself the same before and after the intervention. Nevertheless, it will be necessary more accurate revision in persistent PWID and also education programs to avoid HCV reinfection.

Additionally, it should be noted that screening for other viral infections were only offered to patients linked to care, and that this is another limitation of our study. While the study found no instances of co-infection with HIV or active HBV in the treated patients, the prevalence of prior exposure to HBV and HAV in the cohort is an

important consideration. The high rates of protective antibodies against HAV and the evidence of immunity to HBV may indicate prior exposure or vaccination, which should be taken into account when planning for future vaccine programs and screening efforts in this group. In fact, more than half of the patients tested benefit from specific vaccination programs. The fibrosis assessment through indirect methods also provided valuable insight into the liver health of patients. The correlation between these scores suggests that they can serve as reliable, cost-effective tools for identifying individuals at risk of advanced liver disease, helping to prioritize patients for more intensive care. Although it is encouraging that patients with advanced fibrosis were successfully treated, we must not forget further highlighting the importance of early detection and treatment. In any case, the benefit of antiviral treatment in this scenario is sustained more in terms of public than individual health.

In conclusion, this study provides a compelling case for the effectiveness of targeted interventions aimed in reducing HCV prevalence at vulnerable populations. While the results are promising, the challenges related to follow-up care, and the complexity of managing emphasize the need for a multifaceted approach to HCV elimination. By combining efficient screening, timely treatment, and comprehensive follow-up care, the healthcare systems can make significant strides toward meeting the ambitious goal of HCV eradication by 2030 (**31**).

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Table 1: Comparative analysis of the baseline characteristics of viremic patients receiving treatment and their relationship with response.

	Total, n=21	SVR, n=13	Non-SVR, n=8	P-value
Genotype*	n (%)			0.559†
Unknown	7 (33.3)	6 (46.1)	1 (12.5)	
1	10 (47.6)	4 (30.8)	6 (75)	

2	1 (4.8)	0 (0)	1 (12.5)	
3	2 (9.5)	2 (15.4)	0 (0)	
4	1 (4.8)	1 (7.7)	0 (0)	
Fibrosis	n (%)			0.367‡
No	9 (42.9)	7 (53.8)	2 (25)	
Significant	8 (38.1)	2 (15.4)	6 (75)	
Advanced§	4 (19)	4 (30.8)	0 (0)	
Previous treatment	n (%)			0.606‖
Naïve	16 (76.2)	9 (69.2)	7 (87.5)	
Interferon-based¶	3 (14.3)	2 (15.4)	1 (12.5)	
DAAs**	2 (9.5)	2 (15.4)	0 (0)	

Non-SVR were due to anyway post-treatment lost to follow-up. Only for 14 patients with available data*. Genotype 1 *vs.* others†. Any grade *vs.* no fibrosis‡. For advanced *vs.* non-advanced fibrosis, p=0.131§. Experienced *vs. naive* patients‖. Two patients with Pegylated Interferon/Ribavirin and the other one with Interferon alone¶. Both patients with Sofosbuvir/Velpatasvir**. Abbreviations: SVR, sustained viral response; DAAs, direct-acting antivirals.

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Table 2: Estimation of the effect achieved with the intervention on prevalence of active infection in percentages (A) and of absolute number of patients with and without viremia before and after the intervention (B).

A	Before intervention, n (%)	After intervention, n (%)	% Difference (95% confidence interval)	P-value

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Model 1	Complete population, n=258			
Viremic	24 (9.3)	11 (4.3)	-5.0 (-7.7 to -2.4)	0.0002
Non-viremic	234 (90.7)	247 (95.7)		
	Seropositive population, n=115			
Viremic	24 (20.9)	11 (9.6)	-11.3 (-17.1 to -5.5)	0.0002
Non-viremic	91 (79.1)	104 (90.4)		
Model 2	Complete population, n=258			
Viremic	24 (9.3)	13 (5)	-4.2 (-7.2 to -1.4)	0.0074
Non-viremic	234 (90.7)	245 (95)		
	Seropositive population, n=115			
Viremic	24 (20.9)	13 (11.3)	-9.6 (-15.9 to -3.2)	0.0074
Non-viremic	91 (79.1)	102 (88.7)		
Model 3	Complete population, n=258			
Viremic	24 (9.3)	18 (7)	-2.3 (-5.7 to +1.1)	0.2632
Non-viremic	234 (90.7)	240 (93)		
	Seropositive population, n=115			
Viremic	24 (20.9)	18 (15.7)	-5.2 (-12-8 to +2.3)	0.2632
Non-viremic	91 (79.1)	97 (84.3)		

B	Viremic after	Non-viremic after	Total
Model 1	Complete population		
Viremic before	11	**13**	24
Non viremic before	**0**	234	234

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Total	11	247	258
	Seropositive population		
Viremic before	11	**13**	24
Non viremic before	**0**	91	91
Total	11	104	115
Model 2	Complete population		
Viremic before	11	**13**	24
Non viremic before	**2**	232	234
Total	13	245	258
	Seropositive population		
Viremic before	11	**13**	24
Non viremic before	**2**	89	91
Total	13	102	115
Model 3	Complete population		
Viremic before	11	**13**	24
Non viremic before	**7**	227	234
Total	18	240	258
	Seropositive population		
Viremic before	11	**13**	24
Non viremic before	**7**	84	91
Total	18	97	115

Discordant entries are highlighted in bold. Persistent viremic patients were due to refuse to treatment (n=3) and/or to anyway post-treatment lost to follow-up (n=8).

Table 3: Infection status for hepatitis B and A viruses in patients receiving treatment.

	Of 21 patients treated, n (%)
HBV status	

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antiHBc -/antiHBs -	8 (38)
antiHBc -/antiHBs +	4 (19)
antiHBc +/antiHBs -	4 (19)
antiHBc +/antiHBs +	5 (24)
HAV status	
Anti-HAV (Ig G) +	8 (38)

Abbreviations: HBV, hepatitis B virus; antiHBc, hepatitis B core antibody; antiHBs, hepatitis B surface antibody; HAV, hepatitis A virus; Ig, immunoglobulin.