

Results of a Hepatitis C Micro-Elimination Program in Two Addiction Centers Among Subjects With Substance Use Disorder

Pablo Vega-Astudillo^{1,3} , Ignacio Basurte-Villamor^{2,3},
Inés De Ema López¹, Ruth Olmos Espinos¹, Beatriz Mesías-Pérez¹
and Nestor Szerman^{2,3,4}

¹Instituto de Adicciones, Madrid-Salud, Madrid, Spain. ²Instituto Psiquiatría y Salud Mental, Hospital General Universitario Gregorio Marañón, Madrid, Spain. ³Sociedad Española de Patología Dual, Madrid, Spain. ⁴World Association of Dual Disorders.

Substance Abuse: Research and Treatment
Volume 16: 1–12
© The Author(s) 2022
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/11782218221075058



ABSTRACT

OBJECTIVES: We aimed to evaluate a hepatitis C (HCV) micro-elimination program in 2 addiction centers among subjects with substance use disorders (SUD).

METHODS: The program was based on simplifying the diagnosis of HCV infections by avoiding referral to primary care for the diagnosis and performing the necessary tests at the point of care (ie, the addiction center) and simplifying the patient pathway by directly referring patients to the specialized care for treatment. Descriptive and multivariate analyses are presented.

RESULTS: Of the 1497 subjects included in the program, 327 reported that they were anti-HCV-positive. Among the 1170 patients who were offered the HCV rapid antibody test, 180 (15.4%) did not perform the test. Performing the HCV rapid antibody test only contributed ten patients (3%) to the 337 who were anti-HCV-positive. A high proportion (147 out of 327 [45%]) of subjects who reported being anti-HCV-positive also reported that they had not been treated for HCV. Among the 67 subjects who were HCV-RNA-positive and were referred for treatment, 53 (79%) ultimately received and completed antiviral treatment. Unfortunately, we did not find any factors associated with not performing dry blood testing, and the factors associated with not performing the HCV rapid antibody test were difficult to interpret, and the model showed low goodness of fit.

CONCLUSIONS: Our results suggest that a micro-elimination program focused on patients with SUD attending an addiction center is not effective for screening the presence of hepatitis C but is successful for linking patients with hepatitis C to antiviral treatment.

KEYWORDS: Hepatitis C, substance use disorders, dual disorders, elimination, micro-elimination

RECEIVED: October 6, 2021. **ACCEPTED:** January 5, 2022.

TYPE: Original Research

FUNDING: The author(s) received no financial support for the research, authorship, and/or publication of this article.

DECLARATION OF CONFLICTING INTERESTS: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

CORRESPONDING AUTHOR: Pablo Vega-Astudillo, Instituto de Adicciones, Madrid-Salud, C/ Pinos Alta 122, 28029 Madrid, Spain. Email: vegaap@madrid.es

Introduction

The Global Health Sector Strategy on Viral Hepatitis by the World Health Organization¹ established that the targets for 2030 are diagnosing 90% of people with HCV, get 80% of eligible persons with chronic HCV treated, and reducing the incidence of new HCV cases by 90% and mortality by 65%.

The key elements for HCV elimination are treating with new direct-acting antivirals and preventing infection and reinfection.² However, due to the complexity and cost of implementing national strategies based on those elements, a more pragmatic approach is to achieve national elimination incrementally by eliminating HCV in segments of the population, or so-called micro-elimination.^{2,3} Micro-elimination programs target high-risk populations such as migrants, people living with HIV infection, men who have sex with men, people who inject drugs (PWID), patients with dual disorders, prisoners, or patients with hemophilia.³

For the successful implementation of these micro-elimination programs, it is important to assess at what point in

the continuum of care the target population drops out.² That information and the identification of potential factors associated with dropping out of the continuum of care may inform stakeholders on how to improve micro-elimination programs. The objective of this study was to evaluate the performance of a micro-elimination program implemented in 2 addiction centers for patients with substance use disorders and to analyze the flow of those patients through the proposed continuum of care and the potential determinants of dropping out of that continuum.

Methods

Study design

This was an observational, retrospective study conducted in 2 addiction centers in Madrid (Spain), the “Centro de Adicciones de Tetúan” and the “Centro de Adicciones de Vallecas,” the patients of which participated in a hepatitis C micro-elimination program.



This study was approved by the Ethics Committee of the Hospital Gregorio Marañón (Madrid, Spain), and every subject provided written informed consent.

The micro-elimination program

The micro-elimination program was established by the public health system of the city of Madrid ("Madrid Salud," Madrid, Spain) with support from the "Fundación de Patología Dual" (Dual Pathology Foundation—FPD). The FPD provided anti-HCV antibody tests and dry blood spot tests to screen the HCV RNA-positive subjects; in addition, FPD provided support for the statistical analysis and medical writing.

The procedure was based on simplifying the diagnosis of HCV infections by avoiding referral to primary care for the diagnosis and performing the necessary tests at the point of care (ie, the addiction center) and simplifying the patient pathway by directly referring patients to the specialized care for treatment. The whole procedure is shown in Supplemental Figure 1. In brief, the patients were asked if they were anti-HCV positive, and if not or if they did not know, an OraQuick® HCV Rapid Antibody Test was performed. Patients who knew they were anti-HCV-positive and had not received treatment for HCV or had the treatment finalized more than 1 year ago and patients who were positive for a point-of-care anti-HCV antibody test underwent dry blood spot testing using a Whatman Flinders Technology Associates (FTA) card. The Whatman card was sent for analysis at the LHospital Universitari German Trias i Pujol (Badalona, Spain), which then sent the results to the addiction center. Patients who were HCV RNA-positive were directly referred for treatment at the reference hospital. Patients who were HCV RNA-negative, had a negative anti-HCV antibody test or were known to be anti-HCV-positive but had received treatment within the last year ended their participation in the micro-elimination program and continued their regular follow-up at the addiction center.

Study variables

We recorded information sociodemographic and clinical data.

The information on the micro-elimination procedure described above was also collected, including whether the tests were performed, whether the selected patients made a hospital visit and whether they finalized their treatment.

Statistical analysis

Quantitative variables are described with the mean and standard deviation, and qualitative variables are described with the absolute and relative frequency. Prevalence is presented with the corresponding 95% confidence interval (CI).

Several multiple logistic regression models were performed. To evaluate the factors associated with being anti-HCV-positive (ie, self-reported anti-HCV-positive or positive by

OraQuick® test), we included the following independent variables in the model: sex, age, cohabitation conditions, type of substance abuse disorder (SUD), disease chronicity, number of drugs of abuse, use of injectable drugs, whether the subject had shared syringes, presence of HIV infection, psychiatric diagnosis other than SUD, and number of psychiatric diagnoses. To evaluate the factors associated with having not received treatment for HCV infection, not performing the OraQuick® test, or not performing dry blood spot testing, we added the following independent variables to the abovementioned model: nationality, educational level, and working status. The goodness of fit was estimated with the pseudo R-squared, with higher values indicating a better model fit. The models were run both for the entire population or subpopulation, as well as by sex.

All analyses were performed using Stata 11.1 (Stata Corp, College Station, TX, USA).

Results

Subject characteristics

From October 2018 to October 2019, we included 1497 patients who were treated at the 2 addiction centers in the micro-elimination program. The subjects were middle-aged (60%), predominantly males (77%), Spanish (85%), individuals who lived with their parents (32%) or their own family (33%), single (56%), and predominantly unemployed (42%) (Supplementary table 1). There were no relevant differences in the patients' profiles according to sex, except for the cohabitation conditions; 35% of the men lived with their parents compared to 21% of the women, and 31% of the men lived with their own family compared to 38% of the women.

Regarding clinical characteristics (Table 1), the most frequent substance use disorders (SUDs) were alcohol (38%), opioid (29%), and cocaine (20%) use disorders, with a duration of consumption of 3 years or less in 71% of the subjects and the use of 2 or more illicit drugs (ie, polydrug abuse) in 63% of the subjects. Seventy-nine percent had never used injectable drugs, 84% had not shared a syringe, and the proportion of subjects living with HIV was 11%, with another 10% who did not know their HIV status. A psychiatric diagnosis other than SUD, and therefore a dual disorder diagnosis, was present in 81% of the subjects, the most frequent being mood disorders (22%), personality disorders (17%), and anxiety disorders (16%), mostly as a single diagnosis (74%). There were some clinical differences between males and females: alcohol abuse was less common in males (36% vs 44%), while abuse of cocaine (21% vs 16%), or opioids (30% vs 25%) was more common in males, polydrug abuse was more common in males (65% vs 46%), and a lack of a psychiatric diagnosis other than SUD was more common in males (22% vs 8%).

Subject disposition and screening for hepatitis C

The status of the subjects across the several steps of the micro-elimination program is presented in Figure 1. Of the 1497

Table 1. Clinical characteristics.

CHARACTERISTIC	TOTAL	MALES	FEMALES
Substance use disorder			
Gambling disorder	14 (0.94)	14 (1.21)	0 (0.00)
Alcohol	567 (37.88)	418 (36.19)	149 (43.57)
Amphetamines	7 (0.47)	6 (0.52)	1 (0.29)
Cannabis	166 (11.09)	119 (10.30)	47 (13.74)
Cocaine	294 (19.64)	239 (20.69)	55 (16.08)
Mephedrone	13 (0.87)	12 (1.04)	1 (0.29)
Opioids	427 (28.52)	342 (29.61)	85 (24.85)
Sedatives/hypnotics/anxiolytics	9 (0.60)	5 (0.43)	4 (1.17)
Number of drugs of abuse			
1	558 (37.27)	401 (34.72)	157 (45.91)
2	389 (25.99)	305 (26.41)	84 (24.56)
≥3	550 (36.74)	449 (38.87)	101 (29.53)
Disease chronicity			
<1 year	595 (39.75)	466 (40.35)	129 (37.72)
1-3 years	473 (31.60)	362 (31.34)	111 (32.46)
3-10 years	284 (18.97)	217 (18.79)	67 (19.59)
>10 years	145 (9.69)	110 (9.52)	35 (10.23)
Use of injectable drugs			
Never	1176 (78.56)	894 (77.40)	282 (82.46)
Past user	292 (19.51)	235 (20.35)	57 (16.67)
Current user	29 (1.94)	26 (2.25)	3 (0.88)
Heroin use			
No	1002 (66.93)	765 (66.23)	237 (69.30)
Yes	495 (33.07)	390 (33.77)	105 (30.70)
Sharing syringe			
No	1253 (83.70)	959 (83.03)	294 (85.96)
Yes	244 (16.30)	196 (16.97)	48 (14.04)
HIV infection			
No	1186 (79.23)	904 (78.27)	282 (82.46)
Yes	163 (10.89)	128 (11.08)	35 (10.23)
Unknown	148 (9.89)	123 (10.65)	25 (7.31)
Psychiatric diagnosis (other than SUDs)			
None	282 (18.84)	255 (22.08)	27 (7.89)
Schizophrenia/psychotic disorder	142 (9.49)	121 (10.48)	21 (6.14)
Adaptive disorder	153 (10.22)	124 (10.74)	29 (8.48)

(Continued)

Table 1. (Continued)

CHARACTERISTIC	TOTAL	MALES	FEMALES
Eating disorders	10 (0.67)	0 (0.00)	10 (2.92)
Personality disorder	258 (17.23)	182 (15.76)	76 (22.22)
Mood disorder	333 (22.24)	230 (19.91)	103 (30.12)
Anxiety disorder	232 (15.50)	161 (13.94)	71 (20.76)
Other disorders	87 (5.81)	82 (7.10)	5 (1.46)
Number of psychiatric disorders (other than SUDs)			
None	282 (18.84)	255 (22.08)	27 (7.89)
1	1109 (74.08)	831 (71.95)	278 (81.29)
2	103 (6.88)	69 (5.97)	34 (9.94)
≥3	3 (0.20)	0 (0.00)	3 (0.88)

Abbreviations: HIV, human immunodeficiency virus; SUD, substance use disorder.

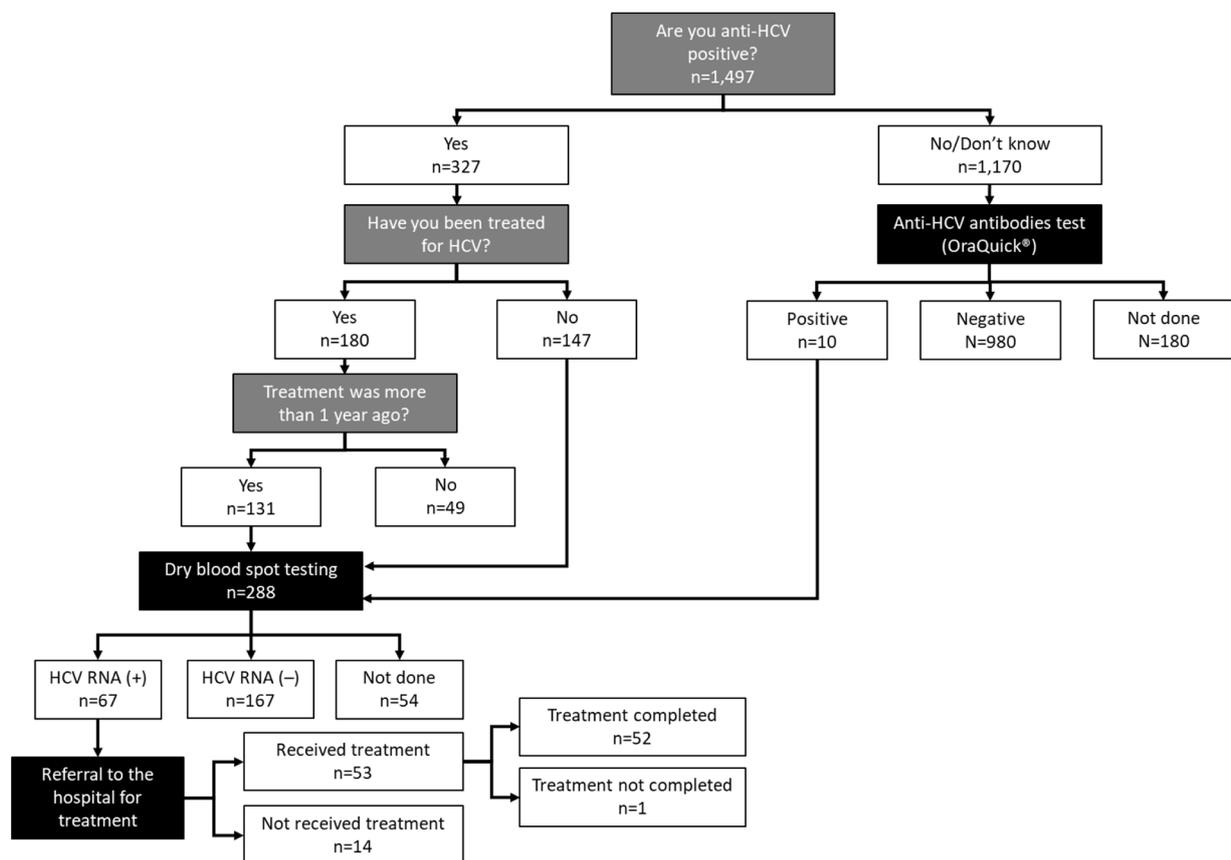


Figure 1. Subject status across the micro-elimination program.

subjects included in the program, 327 reported that they were anti-HCV-positive. Among the 1170 patients who were offered the OraQuick® test, 180 (15.4%) did not perform the test. The factors associated with an increased likelihood of not performing an OraQuick® test were being female (odds ratio [OR] 1.63, 95% CI 1.07-2.46), having a disease duration of 3-10 years compared to <1 year (OR 2.01, 95% CI 1.16-3.50),

having an unknown HIV status (OR 4.01, 95% 2.54-6.37), or being HIV-positive (OR 3.08, 95% CI 1.20-7.92) compared to being HIV-negative, and having 1 psychiatric diagnosis compared to no psychiatric diagnosis (OR 4.52, 95% 1.33- 15.39), while falling within an age range of 26-35 years compared to 18-25 years was associated with a reduced likelihood of not performing an OraQuick® test (OR 0.34, 95% 0.14-0.82)

(Table 2); however, the goodness of fit of this model was low (Pseudo R-squared 9.9%); therefore, the results by sex are not presented (with Pseudo R-squared results of 10.8% and 20.4% for the male and female models, respectively).

Of the remaining 990 subjects who performed the test, 10 (1.0%) subjects were positive by OraQuick® test. Thus, in adding up the subjects who knew their anti-HCV status and those who were positive by OraQuick® test, 337 (22.5%, 95% CI 20.5%-24.7%) subjects were anti-HCV-positive; the number of anti-HCV positive individuals was 263 among the 1,155 males (22.7%, 95% CI 20.4-25.2) and 74 among the 342 females (21.6%, 95% CI 17.6%-26.3%).

Our multivariate analysis showed that the factors associated with being anti-HCV-positive were being female (OR 2.39, 95% CI 1.35-4.22), being aged from 45 to 55 years (OR 18.18, 95% CI 1.76-187.37) or 56-65 years (OR 16.89, 1.58-180.75) compared to being aged 18-25 years, being diagnosed with opioid abuse compared to cannabis abuse (OR 10.49, 95% CI 2.97-37.07), being a current (OR 8.82, 95% CI 2.17-35.8) or past (OR 9.22, 95% CI 4.49-18.90) user of injectable drugs, having shared syringes (OR 5.23, 95% CI 2.15-12.56), and when, compared to being an abuser of 1 drug, were abusers of 2 (OR 2.13, 95% CI 1.07-4.25) or ≥ 3 drugs (OR 2.60, 95% CI 1.37-4.94) (Table 3); the pseudo R-squared was 65.3%. Neither the type of SUD disorder nor the psychiatric diagnosis was associated with being anti-HCV-positive. When splitting the multivariate analysis by sex (Supplementary Table 2), being diagnosed with opioid abuse was associated with a higher likelihood of being anti-HCV-positive, but there were some differences regarding the impact of age: in females, those aged 36-45 years old had a lower likelihood of being anti-HCV-positive compared to those aged 18-25 (OR 0.08, 95% CI 0.01-0.55), while in males, being older was a risk factor; the pseudo R-squared results were 67.4% and 66.8% for the male and female models, respectively.

Treatment of HCV infections among those with anti-HCV-positive status

Among the 327 subjects who knew that they were anti-HCV-positive, 147 (45.0%, 95% CI 39.7-50.4) reported that they had not received treatment for HCV infection (Figure 1).

Falling within a 36 to 45 year age range compared to 26 to 35 was associated with a greater likelihood of lack of treatment for HCV infection (OR 13.76, 95% CI 1.46-129.88), while having a diagnosis of HIV infection was a protective factor (OR 0.26, 0.15-0.48) and a longer-duration SUD was also a protective factor for lack of treatment. Thus, compared to those with a disease duration of <1 year, the likelihood of a lack of treatment for HCV infection was significantly reduced in subjects with an SUD duration of 1 to 3 years (OR 0.27, 95% CI 0.10-0.74) and those with a duration of 3 to 10 years (OR 0.34, 95% CI 0.12-0.97) (Table 4); the pseudo R-squared was 28.4%. When the data were analyzed by sex (Supplemental

Table 1), the only factor that was significantly associated with a lack of treatment for HCV infection was having a diagnosis of HIV, which was protective in both sexes. Working status appears to have a different role depending on sex, with permanent disability and being unemployed compared to permanent employment being significantly associated with a reduced likelihood of lack of treatment for HCV infection in males, while they were not in females (Supplemental Table 2).

Dry blood spot testing: diagnosis and treatment of subjects with HCV infection

Of the 180 subjects who had received treatment, 131 had received treatment more than 1 year ago; these patients, together with those who had not received treatment and those who were anti-HCV positive by OraQuick® test, identified 288 subjects who were subject to dry blood spot testing. Of these 288 patients, 54 (18.8%, 95% CI 14.7-23.7) did not undergo the test. We did not find any factor significantly associated with not performing dry blood spot testing (Supplemental Table 3), and the data by sex are not shown.

Sixty-seven of the subjects were HCV RNA-positive, which corresponds with 4.5% (95% CI 3.5-5.7) of the overall sample included in the program. These patients were referred to the hospital for HCV infection treatment, 53 (79.1%) received treatment, with most of them completing the treatment (Figure 1).

Discussion

Our micro-elimination program is not effective for screening the presence of hepatitis C since the vast majority of those who were anti-HCV-positive already knew their anti-HCV status. Performing the OraQuick® test only contributed ten patients to the 337 who were anti-HCV-positive (ie, 3% of the patients) and was able to detect almost 1% of cases among those attending the clinic who reported not being anti-HCV-positive or those who did not know their anti-HCV status. Therefore, in our view, in the addiction center setting, performing an HCV rapid antibody test such as the OraQuick® is not an efficient strategy. The use of the HCV rapid antibody test could be limited to those subjects who reported not being anti-HCV-positive or did not know their anti-HCV status but who have a history of those belonging to the high-risk groups, such as people who inject drugs or men who have sex with men^{4,5}; however, whether performing dry-blood testing in these high risk groups is more efficient than performing a rapid antibody testing should be further evaluated.

A high proportion (45%) of subjects who reported being anti-HCV-positive also reported that they had not been treated for HCV. Unfortunately, this figure is not far from those reported in the era before the availability of direct-acting antiviral agents. Yehia et al⁶ performed a systematic review, and they estimated that of all the patients with chronic HCV infections, 50% were diagnosed and aware, and only 16% (ie, 32% of

Table 2. Factors associated with not performing the OraQuick® test among subjects who reported not being or not knowing they are anti-HCV-positive.

VARIABLE	β	SE	Z	P-VALUE	OR	95% CI
Intercept	-2.550	1.208	-2.11	.035		
Sex (male)						
Female	0.486	0.211	2.30	.021	1.63	1.07-2.46
Age in years (18-25)						
26-35	-1.088	0.457	-2.38	.017	0.34	0.14-0.82
36-45	-0.696	0.438	-1.59	.112	0.50	0.21-1.18
46-55	-0.775	0.470	-1.65	.099	0.46	0.18-1.16
56-65	-0.350	0.495	-0.71	.480	0.71	0.27-1.86
≥ 66	-0.259	0.671	-0.39	.699	0.77	0.21-2.87
Nationality (Spain)						
Africa	-0.429	0.553	-0.78	.438	0.65	0.22-1.92
Other European	-0.617	0.564	-1.09	.274	0.54	0.18-1.63
Latin America	0.195	0.3257	0.60	.549	1.22	0.64-2.30
Other	0.371	0.459	0.81	.419	1.45	0.59-3.56
Cohabitation conditions (parents)						
Own family	-0.141	0.238	-0.59	.554	0.87	0.54-1.39
Institutionalized	0.170	0.423	0.40	.688	1.19	0.52-2.72
Alone	-0.385	0.283	-1.36	.174	0.68	0.39-1.19
Other	-0.234	0.325	-0.72	.473	0.79	0.42-1.50
International Standard Classification of Education (ISCED 5-8) ^a						
ISCED 3	-.280	0.286	-0.98	.327	0.76	0.43-1.32
ISCED 2	-.148	0.300	-0.49	.622	0.86	0.48-1.55
ISCED 1	-0.248	0.303	-0.82	.413	0.78	0.43-1.41
ISCED 0	0.462	0.349	1.32	.185	1.59	0.80-3.14
ISCED 0-illiterate	-0.006	0.738	-0.01	.993	0.99	0.23-4.22
Working status (permanent contract)						
Temporary contract	0.062	0.326	0.19	.849	1.06	0.56-2.02
Underemployed	0.266	0.322	0.83	.409	1.304	0.69-2.45
Unemployed	-0.120	0.234	-0.51	.607	0.89	0.56-1.40
Student/Preparing public exams	-0.333	0.575	-0.58	.563	0.72	0.23-2.21
Permanent disability	-0.278	0.385	-0.72	.470	0.76	0.36-1.61
Substance use disorder (Cannabis)						
Gambling disorder	-1.399	1.099	-1.27	.203	0.25	0.03-2.13
Alcohol	-0.148	0.322	-0.46	.645	0.86	0.46-1.62
Amphetamines	Omitted ^b					

(Continued)

Table 2. (Continued)

VARIABLE	β	SE	Z	P-VALUE	OR	95% CI
Cocaine	0.249	0.324	0.77	.441	1.28	0.68-2.42
Mephedrone	Omitted ^b					
Opioids	-0.307	0.443	-0.69	.489	0.74	0.31-1.75
Sedatives/hypnotics/ anxiolytics	Omitted ^b					
Number of drugs of abuse (1 drug)						
2 drugs	-0.133	0.225	-0.59	.555	0.88	0.56-1.36
≥3 drugs	-0.081	0.240	-0.34	.736	0.92	0.58-1.48
Disease chronicity (<1 year)						
1-3 years	-0.223	0.209	-1.07	.285	0.80	0.53-1.20
3-10 years	0.700	0.282	2.48	.013	2.01	1.16-3.50
>10 years	0.482	0.497	0.97	.333	1.62	0.61-4.29
Use of injectable drugs (never)						
Past user	0.013	0.623	0.02	.984	1.01	0.30-3.44
Current user	Omitted ^b					
Sharing syringe (no)						
Yes	0.084	0.834	0.10	.920	1.09	0.21-5.57
HIV infection (no)						
Yes	1.126	0.481	2.34	.019	3.08	1.20-7.92
Unknown	1.391	0.235	5.92	.000	4.02	2.54-6.37
Psychiatric diagnosis (none)						
Schizophrenia/psychotic disorder	-1.078	0.688	-1.57	.117	0.34	0.09-1.31
Adaptive disorder	-1.403	0.707	-1.98	.047	0.25	0.061-0.98
Eating disorder	Omitted ^b					
Personality disorder	-1.445	0.673	-2.15	.032	0.24	0.06-0.88
Mood disorder	-1.195	0.679	-1.76	.078	0.30	0.08-1.14
Anxiety disorder	-1.565	0.700	-2.24	.025	0.21	0.05-0.82
Other disorders	-1.430	0.759	-1.89	.059	0.24	0.05-1.06
Number of psychiatric disorders (other than SUDs) (none)						
1	1.510	0.625	2.42	.016	4.52	1.33-15.39
2	Omitted ^b					
≥3	Omitted ^b					

Abbreviations: CI, confidence interval; HIV, human immunodeficiency virus; OR, odds ratio; SE, standard error; SUD, substance use disorder.

^aISCED level 0—Early childhood education, ISCED level 1—Primary education, ISCED level 2—Lower secondary education, ISCED level 3—Upper secondary education, ISCED level 4—Post-secondary non-tertiary education, ISCED level 5—Short-cycle tertiary education; ISCED level 6—Bachelor's or equivalent level, ISCED level 7—Master's or equivalent level, and ISCED level 8—Doctoral or equivalent level.

^bNot calculated due to zero count or collinearity.

Table 3. Factors associated with the presence of hepatitis C.

VARIABLE	β	SE	Z	P-VALUE	OR	95% CI
Intercept	-0.554	1.812	-3.07	.002		
Sex (male)						
Female	0.870	0.291	2.99	.003	2.39	1.35-4.22
Age in years (18-25)						
26-35	1.641	1.211	1.36	.175	5.16	0.48-55.42
36-45	1.500	1.207	1.24	.214	4.48	0.42-47.79
46-55	2.900	1.190	2.44	.015	18.18	1.76-187.37
56-65	2.827	1.209	2.34	.019	16.89	1.58-180.75
≥ 66	0.710	1.495	0.47	.635	2.03	0.11-38.06
Cohabitation conditions (parents)						
Own family	-0.543	0.316	-1.72	.085	0.58	0.31-1.08
Institutionalized	-0.764	0.540	-1.41	.157	0.47	0.16-1.34
Alone	-0.570	0.364	-1.56	.118	0.57	0.28-1.16
Other	-0.394	0.421	-0.94	.350	0.67	0.30-1.54
Substance use disorder (Cannabis)						
Gambling disorder	Omitted ^a					
Alcohol	0.419	0.634	0.66	.508	1.52	0.44-5.27
Amphetamines	-0.386	1.578	-0.24	.807	0.68	0.03-14.99
Cocaine	-0.137	0.689	-0.20	.842	0.87	0.23-3.36
Mephedrone	1.085	1.104	0.98	.326	2.96	0.34-25.78
Opioids	2.351	0.644	3.65	.000	10.49	2.97-37.07
Sedatives/hypnotics/anxiolytics	0.724	1.429	0.51	.612	2.06	0.13-33.93
Number of drugs of abuse (1 drug)						
2 drugs	2.129	0.750	2.15	.032	2.13	1.07-4.25
≥ 3 drugs	2.602	0.852	2.92	.004	2.60	1.37-4.94
Disease chronicity (<1 year)						
1-3 years	0.840	0.269	-0.54	.586	0.84	0.45-1.57
3-10 years	0.471	0.188	-1.89	.059	0.47	0.22-1.03
>10 years	0.741	0.345	-0.64	.519	0.74	0.30-1.85
Use of injectable drugs (never)						
Past user	2.221	0.367	6.05	.000	9.22	4.49-18.9
Current user	2.177	0.715	3.05	.002	8.82	2.17-35.8
Sharing syringe (no)						
Yes	1.654	0.452	3.66	.000	5.23	2.15-12.68

(Continued)

Table 3. (Continued)

VARIABLE	β	SE	Z	P-VALUE	OR	95% CI
HIV infection (no)						
Yes	1.650	0.449	3.67	.000	5.21	2.16-12.56
Unknown	-1.828	0.917	-1.99	.046	0.16	0.03-0.97
Psychiatric diagnosis (none)						
Schizophrenia/psychotic disorder	-0.024	5.507	-0.00	.996	0.98	0.00-47544
Adaptive disorder	-0.183	5.520	-0.03	.974	0.83	0.00-41596.22
Eating disorders	Omitted ^a					
Personality disorder	-0.123	5.511	-0.02	.982	0.88	0.00-43418.25
Mood disorder	-0.516	5.516	-0.09	.925	0.60	0.00-29598.7
Anxiety disorder	-0.347	5.514	-0.06	.950	0.71	0.00-34917.63
Other disorders	-0.338	5.530	-0.06	.951	0.71	0.00-36347.35
Number of psychiatric disorders (other than SUDs)						
1	0.437	5.497	0.08	.937	1.54	0.00-73945.77
2	0.686	5.510	0.12	.901	1.98	0.00-97164.71
≥ 3	Omitted ^a					

Abbreviations: HIV, human immunodeficiency virus; SUD, substance use disorder.

^aNot calculated due to zero count or collinearity.

Table 4. Factors associated with the presence of hepatitis C and not receiving treatment.

VARIABLE	β	SE	Z	P-VALUE	OR	95% CI
Intercept	-0.433	1.397	-0.31	.756		
Sex (male)						
Female	-0.028	0.331	-0.09	.931	0.97	0.51-1.86
Age in years (26-35) ^a						
36-45	2.622	1.145	2.29	.022	13.76	1.46-129.88
46-55	1.846	1.072	1.72	.085	6.33	0.77-51.77
56-65	1.665	1.103	1.51	.131	5.28	0.61-45.91
≥ 66	2.077	1.684	1.23	.217	7.98	0.29-216.61
Nationality (Spain)						
Africa	0.393	1.559	0.25	.801	1.48	0.07-31.47
Other European	0.558	1.062	0.53	.599	1.75	0.22-14.00
Latin America	2.806	1.471	1.91	.057	16.54	0.92-295.82
Other	Omitted ^b					
Cohabitation conditions (parents)						
Own family	0.256	0.330	0.78	.438	1.29	0.68-2.47
Institutionalized	0.227	0.557	0.41	.684	1.25	0.42-3.74

(Continued)

Table 4. (Continued)

VARIABLE	β	SE	Z	P-VALUE	OR	95% CI
Alone	-0.160	0.412	-0.39	.698	0.85	0.38-1.91
Other	-0.190	0.528	-0.36	.719	0.83	0.29-2.33
International Standard Classification of Education (ISCED 5-8) ^c						
ISCED3	0.143	0.824	0.17	.862	1.15	0.23-5.80
ISCED 2	-0.126	0.796	-0.16	.875	0.88	0.19-4.19
ISCED 1	0.468	0.766	0.61	.541	1.60	0.36-7.18
ISCED 0	0.199	0.826	0.24	.810	1.22	0.24-6.16
ISCED 0-illiterate	0.811	1.121	0.72	.470	2.25	0.25-20.27
Working status (permanent contract)						
Temporary contract	-0.451	0.627	-0.72	.472	0.64	0.19-2.18
Underemployed	-0.809	0.596	-1.36	.174	0.45	0.14-1.43
Unemployed	-0.897	0.495	-1.81	.070	0.41	0.15-1.08
Student/Preparing public exams	Omitted ^b					
Permanent disability	-0.754	0.591	-1.28	.202	0.47	0.15-1.50
Substance use disorder (Cannabis)						
Alcohol	0.239	0.981	0.24	.808	1.27	0.19-8.69
Amphetamines	Omitted ^b					
Cocaine	0.626	1.157	0.54	.588	1.87	0.19-18.07
Mephedrone	Omitted ^b					
Opioids	0.547	0.929	0.59	.555	1.73	0.28-10.67
Sedatives/hypnotics/anxiolytics	Omitted ^b					
Number of drugs of abuse (1 drug)						
2 drugs	0.180	0.490	0.37	.71	1.20	0.46-3.13
≥3 drugs	-0.098	0.444	-0.22	.826	0.91	0.38-2.16
Disease chronicity (<1 year)						
1-3 years	-1.295	0.505	-2.57	.010	0.27	0.10-.74
3-10 years	-1.079	0.532	-2.03	.043	0.34	0.12-.97
>10 years	-0.972	0.580	-1.68	.094	0.38	0.12-1.18
Use of injectable drugs (never)						
Past user	0.052	0.486	0.11	.914	1.05	0.41-2.73
Current user	1.410	0.764	1.85	.065	4.10	0.92-18.30
Sharing syringe (no)						
Yes	0.295	0.424	0.70	.487	1.34	0.59-3.08
HIV infection (no)						
Yes	-1.333	0.303	-4.41	.000	0.26	0.15-0.48
Unknown	Omitted ^b					

(Continued)

Table 4. (Continued)

VARIABLE	β	SE	Z	P-VALUE	OR	95% CI
Psychiatric diagnosis (none)						
Schizophrenia/psychotic disorder	0.563	0.627	0.90	.369	1.76	0.51-6.00
Adaptive disorder	1.191	0.709	1.68	.093	3.29	0.82-13.20
Personality disorder	-0.069	0.540	-0.13	.898	0.93	0.32-2.69
Mood disorder	0.673	0.614	1.10	.273	1.96	0.59-6.53
Anxiety disorder	0.772	0.628	1.23	.218	2.17	0.63-7.41
Other disorders	0.837	0.859	0.97	.330	2.31	0.43-12.43
Number of psychiatric disorders (other than SUDs) (none)						
1	-0.837	0.448	-1.87	.062	0.43	0.18-1.04
2	Omitted ^b					
≥3	Omitted ^b					

Abbreviations: CI, confidence interval; HIV, human immunodeficiency virus; OR, odds ratio; SE, standard error; SUD, substance use disorder.

^aThere were no patients in the age category of 18 to 25 years old.

^bNot calculated due to zero count or collinearity.

^cISCED level 0—Early childhood education, ISCED level 1—Primary education, ISCED level 2—Lower secondary education, ISCED level 3—Upper secondary education, ISCED level 4—Post-secondary non-tertiary education, ISCED level 5—Short-cycle tertiary education; ISCED level 6—Bachelor's or equivalent level, ISCED level 7—Master's or equivalent level, and ISCED level 8—Doctoral or equivalent level.

those who were diagnosed) were prescribed HCV treatment. Altogether, these results suggest that despite the apparent improvement in HCV treatment access in the current era, there is room for improvement in linking treatment efforts to patients with chronic hepatitis C, reinforcing the need for specific programs such as the micro-elimination program we implemented which simplifies the patient pathway by directly referring patients to the specialized care for treatment.

The factors associated with not receiving treatment for hepatitis C in our multivariate analysis were older age as a risk factor and the presence of HIV coinfection and longer-duration SUD as protective factors. In a retrospective population-based study conducted in Canada, when analyzing the factors associated with the hepatitis C cascade of care milestones, in addition to having higher income and more advanced disease, older age was associated with a higher likelihood of receiving an antiviral prescription,⁷ and older age was also associated with a higher likelihood of linkage to care in 2 studies in specialized HCV clinics,^{8,9} which contrasts with the results of our multivariate analysis. It is important to note that our results regarding the role of age, albeit significant, were very imprecise. The protective role of HIV coinfection could be explained by the good linkage of these patients to health care. In a retrospective study on adult patients who were tested for HCV in the emergency department and were confirmed to have HCV infections, there were 2 factors associated with a lower likelihood of linkage to care failure (which was defined as not being seen by an HCV-treating provider after discharge): the presence of significant medical comorbidities (OR 0.57, 95% CI 0.41-0.78) and HIV coinfection (OR 0.11, 95% CI 0.03-0.46)¹⁰; HIV coinfection

has also been reported to be associated with a higher likelihood of linkage to care in other studies.⁹ Lastly, a longer duration of SUD showing up as a protective factor in our study probably reflects that the longer the disease duration—in this case, SUD—the higher the likelihood of being diagnosed and linked to health care; however, this is only a hypothesis. In any case, we should bear in mind that barriers to health care linkage in patients with hepatitis C are multifactorial, including not only patient-related barriers such as those included in our model but also barriers associated with the health system and the health care provider.^{11,12}

Among subjects who were HCV-RNA-positive and were referred for treatment, 79% ultimately received and completed antiviral treatment, which is consistent with the World Health Organization target and indicates that a micro-elimination program such as this one that is focused on patients with SUD could be successful for eliminating hepatitis C. These results are consistent with those reported in Italy by Messina et al¹³ on another micro-elimination program in an addiction center that specifically addressed PWID.

Despite our success regarding linkage to treatment, it is important to note that we had a failure rate of 15% regarding the screening process with the HCV rapid antibody test, a failure rate of 24% with dry blood spot testing and the above-mentioned failure rate of 21% with the initiation of antiviral treatment. Unfortunately, we did not find any factors associated with not performing dry blood testing, and the factors associated with not performing the HCV rapid antibody test were difficult to interpret, and the model showed low goodness of fit.

Our study has several limitations. This program was conducted in 2 important addiction centers, but could not be generalized to other centers or countries. Our micro-elimination program was primarily based on self-reporting of being anti-HCV positive. However, we believe that this is a valid strategy. In a study conducted among PWID subject to HCV antibody testing, self-reported anti-HCV-positive status had a predictive value of 94%, while self-reported anti-HCV-negative status had a predictive value of 72%, which is consistent with our strategy.¹⁴ Lastly, as mentioned above, our analysis of factors associated with linkage to care is incomplete since it was only focused on patient-related factors.

Conclusion

Our results suggest that a micro-elimination program focused on patients with SUD attending an addiction center is not effective for screening the presence of hepatitis C but is successful for linking patients with hepatitis C to antiviral treatment. Further follow-up is needed to ascertain whether the program could also be useful for preventing infection and reinfection.

Acknowledgements

The authors would like to thank all health care professionals from “Centro de Adicciones de Tetúan” and “Centro de Adicciones de Vallecas” (Madrid, Spain) and from the infectious disease departments of the Hospital Universitario La Paz and Hospital Universitario Infanta Leonor (Madrid, Spain) for their collaboration. The authors thank Rosa Rojo (Madrid, Spain) for the statistical analysis and Fernando Rico-Villademoros (COCIENTE SL, Madrid, Spain) for his editorial assistance in the preparation of this manuscript; their participation has been funded by Fundación de Patología Dual.

Author Contributions

PVA: Conceptualization, Methodology, Investigation, Validation, Resources, Data curation, Writing - review & editing, Supervision, Resources, Project administration and Funding acquisition. IEL, ROE and BMP: Conceptualization,

Methodology, Investigation, Data curation, Writing - review & editing, Resources, Supervision. NS and IBV: Conceptualización, Writing - review & editing, Resources, Supervision.

ORCID iD

Pablo Vega-Astudillo  <https://orcid.org/0000-0002-6085-8602>

SUPPLEMENTAL MATERIAL

Supplemental material for this article is available online.

REFERENCES

1. World Health Organization. *Global Health Sector Strategy on Viral Hepatitis 2016–2021. Towards Ending Viral Hepatitis*. World Health Organization; 2016.
2. Lazarus JV, Wiktor S, Colombo M, Thursz M. Micro-elimination - a path to global elimination of hepatitis C. *J Hepatol*. 2017;67:665-666.
3. Hollande C, Parlati L, Pol S. Micro-elimination of hepatitis C virus. *Liver Int*. 2020;40(suppl 1):67-71.
4. Hajarizadeh B, Grebely J, Dore GJ. Epidemiology and natural history of HCV infection. *Nat Rev Gastroenterol Hepatol*. 2013;10:553-562.
5. Bruggmann P, Berg T, Øvrehus ALH, et al. Historical epidemiology of hepatitis C virus (HCV) in selected countries. *J Viral Hepat*. 2014;21(suppl 1):5-33.
6. Yehia BR, Schranz AJ, Umscheid CA, Lo Re V 3rd. The treatment cascade for chronic hepatitis C virus infection in the United States: a systematic review and meta-analysis. *PLoS One*. 2014;9:e101554.
7. O'Neil CR, Buss E, Plitt S, et al. Achievement of hepatitis C cascade of care milestones: a population-level analysis in Alberta, Canada. *MOJ Public Health*. 2019;110:714-721.
8. Sherbuk JE, McManus KA, Kemp Knick T, Canan CE, Flickinger T, Dillingham R. Disparities in hepatitis C linkage to care in the direct acting antiviral era: findings from a referral clinic with an embedded nurse navigator model. *Front Public Health*. 2019;7:362.
9. Lin M, Kramer J, White D, et al. Barriers to hepatitis C treatment in the era of direct-acting anti-viral agents. *Aliment Pharmacol Ther*. 2017;46:992-1000.
10. Blackwell JA, Rodgers JB, Franco RA, et al. Predictors of linkage to care for a nontargeted emergency department hepatitis C screening program. *Am J Emerg Med*. 2020;38:1396-1401.
11. Ramers CB, Liu J, Frenette C. Barriers to treatment of hepatitis C virus in the direct-acting antiviral era. *Curr Treat Options Infect Dis*. 2019;11:92-102.
12. Madden A, Hopwood M, Neale J, Treloar C. Beyond interferon side effects: what residual barriers exist to DAA hepatitis C treatment for people who inject drugs? *PLoS One*. 2018;13:e0207226.
13. Messina V, Russo A, Parente E, et al. Innovative procedures for micro-elimination of HCV infection in persons who use drugs. *J Viral Hepat*. 2020;27:1437-1443.
14. Hagan H, Campbell J, Thiede H, et al. Self-reported hepatitis C virus antibody status and risk behavior in young injectors. *Public Health Rep*. 2006;121:710-719.