

How to better improve the treatment and outcomes of HCV in psychiatric patients: review of a Belgian monocentric psychiatric center

S. Chabert¹, X. Saloppe², B. Delaunoy³, G. Dupont³, P. Yengue¹

(1) Hepatogastroenterology department, Chwapi, Tournai, Belgium; (2) Research Center in Social Defense, Tournai, Belgium; (3) Psychiatric center, Les Marronniers, Tournai, Belgium.

Abstract

Introduction: Hepatitis C (HCV) is one of the major worldwide infections with 58 million infected persons in the world. HCV can lead to chronic liver disease, cirrhosis, and cancer. These past few years, clinical progress allowed a curative rate of 95% of the patients. There are still populations in which, treating the disease is more difficult, especially psychiatric patients, when substance abuse, psychiatric disorders are important risks factors for getting HCV. With the WHO organization establishing goals for clinical management and treatment of HCV, it is important to target where the difficulties lie in getting a better treatment program for those populations.

Aim: Try to highlight the challenges of treating a certain group of patients compare to the general population.

Method: This is a cross sectional monocentric study. 79 patients from a mental facility were included between 2012 and 2022. Inclusion criteria were: >18 years old, an active viral HCV infection.

Results: 34.7% of patients with a positive PCR were treated with a significant difference between the closed psychiatric unit and the open one (66.5 vs 22.6%, $p < .05$). There was an 82.4% eradication rate (Sustained Viral Response at 3 months). There were significantly more schizophrenic disorders in the closed unit and significantly more alcohol abuse in the open one.

Conclusion: Treatment of HCV in a psychiatric population is feasible with eradication rate equivalent at those in the general population. Patients with more severe mental illness are better treated in the configuration of a closed psychiatric unit. (*Acta gastroenterol. belg.*, 2024, 87, 223-228).

Keywords: hepatitis C, Sustained Viral Response, psychiatric disease, psychiatric center.

Introduction

Hepatitis C (HCV) is one of the world's leading infectious diseases, with 58 million people infected worldwide and 1.5 million new infections per year. HCV can lead to chronic liver disease, cirrhosis and cancer. Thanks to the development of diagnostics and therapeutic management and following the appearance of new molecules with direct pangenotypic action, viral eradication is now possible in 95% of patients.

The World Health Organization (WHO) (1) has set a target of complete eradication of HCV worldwide, which if achieved would prevent the deaths of 1.5 million people. In view of this objective, it is important to ask whether there are certain populations in our medicalized society where achieving it would be a challenge. We know that in certain patient groups, overall medical

care is more difficult, due to their social, medical and economic specificity.

In this group, we focused specifically on PWIDS (Patients Who Inject Drugs). These patients are at greater risk of infection with the hepatitis C virus, and their social and economic situation poses a challenge in terms of treatment. (5,6,8,11-13,15,16,19,20,22-25).

For this reason, the primary aim of our study is to evaluate HCV eradication in a specific population of drug-addicted institutionalized patients, and also to highlight the links between treatment difficulties and psychiatric illnesses, and to suggest ideas to improve the management of these patients.

Methodology

Institution

The Centre Régional de soins psychiatriques Les Marronniers is a public psychiatric hospital.

It has 3 sectors: the Secure Psychiatric Hospital (HPS) with 389 beds, the specialized hospital center (CHS) with 256 beds, and the outpatient sector (ambulatory consultations, mobile teams and residential sector).

At the HPS, forensic patients have an average length of stay of 10 years, and are hospitalized in a secure medical environment.

At the CHS, patients have stays ranging from 14 days to 40 days, depending on the unit and the patient's therapeutic project, and are hospitalized in an open, unrestricted setting.

Within the CRP Les Marronniers, a somatic polyclinic is organized, bringing together all somatic specialties and basic medical-technical equipment (radiology, ultrasound, diagnostic digestive endoscopy, dentistry, respiratory function test, electroencephalogram).

At somatic level, patients are followed up by general practitioners who visit the units (prevention and continuity

Correspondence to: Patrick Yengue, MD, Service de gastro-entérologie, Chwapi, Rue des Sports, 51, 7500, Tournai, Belgium. Tel: 003269885141, Fax: 003269331336.
Email: patrick.yengue@chwapi.be

Submission date: 11/09/2023

Acceptance date: 01/02/2024

of care) and by specialists, notably the gastroenterologist at the internal polyclinic.

Patients

Over a period from 2012 to 2022, 79 patients from two care units at Tournai's Les Marronniers psychiatric center: Hôpital Psychiatrique Sécurisé (HPS) and Hôpital Psychiatrique Générale (CHS), were included in our retrospective, monocentric study.

Inclusion criteria: over 18 years of age and HCV serology positive at screening.

Exclusion criteria: none

Participants were recruited on a voluntary basis and consented to take part in the research in accordance with the ethical principles of the Declaration of Helsinki and the right to privacy as stipulated in the Belgian law of July 30, 2018 on the processing of personal data. In addition, this study was approved by the research ethics committee of the Centre Régional Psychiatrique "Les Marronniers". All participants signed an informed consent form specifying the purpose of the study and guaranteeing anonymity and confidentiality.

HCV Diagnostic

Hepatitis C was diagnosed by performing HCV serology on all patients admitted to the Regional Psychiatric Center. If positive, infection was confirmed by determining the viral load and genotyping using the PCR (Polymerase Chain Reaction) technique.

Hepatopathy assessment

All PCR-positive patients were evaluated for underlying liver disease by fibroscan and liver ultrasound.

HCV treatment

The treatments offered to patients follow the recommendations of the EASL (European Association for the Study of Liver).

All drug interactions, particularly with psychiatric treatments, and contraindications were checked for each patient treated.

If treatment was started, we performed the PCR according to EASL recommendations at the end of treatment and three months after the end of treatment to obtain the Sustained Viral Response (SVR).

Psychiatric Diagnostic

The diagnosis of the various psychiatric illnesses is based on the DSM-V (Diagnostic and Statistical Manual of Mental Disorders Fifth Edition) (2).

Psychiatric treatments

Psychiatric treatments are tailored to the patient's pathology and symptoms.

Statistical analysis

Firstly, descriptive statistics were reported for socio-demographic, somatic, diagnostic and pharmacological variables. Then, the chideux /chisquare test (χ^2), or Fisher's exact statistical test, and Cramer's V as a measure of the strength of the association (between .10 and .20 = Weak; between .20 and .40 = Moderate; between .40 and .80 = Strong) 2 were used to compare the "HPS/CHS" groups and then the "Active/Non Active" viral load groups in terms of psychiatric disorders.

Frequency comparisons were made for psychiatric treatment and hepatitis C treatment (Treated/Not Treated) according to the "HPS/CHS" groups. Lastly, in order to understand the reason for absence of treatment at the CRP, frequency calculations were carried out on the variables "Patient discharged from care", "Patient treated outside CRP", "Patient refusing treatment", "Patient died" and "Patient spontaneously cured". Analyses were performed using SPSS 27.0 (3).

Results

Overall characteristics

The overall characteristics of the population are shown in Table 1.

94.9% were men, with an average age of 48.89 years.

40.5% of the population were in HPS and 59.5% in CHS.

Hepatological characteristics

These are shown in Table 1 and Table 2.

Of the overall population of the two units, 79 had a positive serology, 62% were confirmed by PCR.

In terms of underlying liver disease, 58.5% had F0-F1 fibrosis.

In terms of genotype, the majority were infected by genotype 1a (49%).

Of the 49 patients who meet the treatment criteria, 17 were ultimately treated (34.7%). Most hepatitis C patients were treated with Sofosbuvir/Velpatasvir, Epclusa® (47%). Response to treatment, and therefore efficacy, was assessed 3 months after discontinuation of the drug, by determining viral load (SVR). 82.4% of patients treated had an undetectable viral load at 3 months.

Of the patients treated, 62.5% were in the HPS and 37.5% in the CHS, and of those with SVR at 3 months after treatment cessation, 90% were in the HPS and 71.4% in the CHS.

Patients could not be offered hepatitis C treatment for the following reasons: "Patient out of care" (n=22; 73.3%), "Patient treated outside CRP" (n=1; 3.3%), "Patient refusing treatment" (n=4; 13.3%), "Patient deceased" (n=2; 6.7%) and "Patient in spontaneous recovery" (n=1; 3.3%).

Table 1. — Demographic, clinical and somatic characteristics of participants with hepatitis C

Demography	
Gender : male (%)	75 (94.9)
Age, year : average (E.T., extended)	48.89 (9.41, 23-74)
Status : n (%)	
HPS CHS	32 (40.5)
	47 (59.5)
Principal Diagnostic, axis : n (%)	
Mental disorders	79(100)
Disorder (D.) linked to substance (Entire life)	79(100)
D. linked to substances (Actual)	38(48.1)
D. linked to alcohol (Actual)	33(41.8)
D. of the schizophrenia spectrum	25(31.6)
D. linked to alcohol (Entire life)	23(29.1)
Depressive disorder	9(11.4)
Intellectual Disability	9(11.4)
Bipolar disorder and reated	5(6.3)
Neurocognitive impairment	5(6.3)
D. linked to traumatism	3(3.8)
Anxiety disorder	2(2.5)
Personality Disorder	34(43.0)
Cluster B "Excessiveness, emotionals, erratics"	23(29.1)
Cluster C "Anxiety or fear"	8(10.1)
Cluste A "Strangers or exentrics	1(1.3)
Comorbidity regarding mental disorders	62(78.5)
Comorbidity regarding personality disorders	4(5.1)
Comorbidity regarding all the disorders	74(93.7)
Hepatic Profil, categories n (%)	
Viral load:	75(94.9)
Active	49(62.0)
Genotypes:	
1a	24(49.0)
3a	15(30.6)
1b	4(8.2)
4a4c4d	3(6.1)
4	2(4.1)
4a	1(2.0)
Fibrosis score:	41(51.9)
F0-F1	24(58.5)
F2	5(12.5)
F4	5(12.5)
F2-F3	3(7.3)
F1-F2	2(4.9)
F3	2(4.9)

Psychiatric characteristics

Patients hospitalized at the CHS have more lifetime depressive and alcohol-related disorders than patients hospitalized at the HPS. However, patients hospitalized at the HPS have more schizophrenia spectrum disorders and intellectual disabilities (table 3).

People with positive serology but negative viral load have more schizophrenia spectrum disorders than those with active viral replication. Conversely, those for whom the virus is active have more substance- and alcohol-related disorders (table 4).

These results for substance-related disorders were found for both HPS ($p<.001$) and CHS ($p<.001$) patients. Only one trend was observed for alcohol-related disorders. HPS patients tended to have fewer alcohol-related disorders (current) than CHS patients ($p=.056$).

Discussion

HCV affects around 70 million people worldwide (1% of the global population), and is a major cause of progression to cirrhosis and HCC (hepatocellular carcinoma), with 75% of cases becoming chronic (25% spontaneous clearance spontaneous) (5,8,9,11,15,19-23).

As HCV is therefore a source of high mortality and morbidity, the WHO has decided to launch a campaign to manage HCV by 2030, with the aim of reducing infections by 80%, cutting mortality by 65%, increasing diagnosis from <20% to 90% and the number of patients receiving treatment from <10% to 80% (1).

The Hepatitis C virus is more prevalent in certain populations, such as psychiatric patients, drug addicts and alcoholics (5,6,8,11-13,15,16,19,20,22-25). We therefore decided to look at these populations in a very specific context, that of a Belgian psychiatric center, Le CRP Les Marronniers, in order to assess the effectiveness of treatments, but also to highlight the difficulties in their management and see how to improve it in order to achieve the defined objectives.

The institution has decided to implement systemic screening of all patients admitted to the center on admission. Patients with a positive serology result are all seen by the gastroenterologist. It is during this consultation that the rest of the work-up is organized. First of all, a PCR is performed on all patients, along with a fibroscan and liver ultrasound. Treatment for HCV infection is offered to all patients meeting the treatment criteria set out in the EASL guidelines. A detailed review of drug interactions is carried out to avoid side effects (4).

Table 2. — HCV Treatment Characteristics

	HPS <i>n</i> = 30-16-10		CHS <i>n</i> = 45-31-7		Test exact de Fisher	
	<i>n</i>	%	<i>n</i>	%	χ^2	V de Cramer
Charge virale positive	17	56.7	32	71.1	1.66	.15
Traité	10	62.5	7	22.6	7.28*	.39
Éradiqué	9	90.0	5	71.4	0.98	.24
Note : * $p<.05$						

Table 3. — Psychiatric disorders depending on the legal status

	HPS <i>n</i> = 32		CHS <i>n</i> = 47		Exact Fisher test	
	<i>n</i>	%	<i>n</i>	%	χ^2	V _{dc} Cramer
Tr. from the schizophrenic spectrum	16	50.0	9	19.1	8.38**	.33
Tr. depressive	0	0.0	12	19.1	6.92**	.30
Tr. linked to alcohol (Entire life)	3	9.4	20	42.6	10.2**	.36
Intellectual Handicap	7	21.9	2	4.3	5.86*	.27
Note : * <i>p</i> <.05 ; ** <i>p</i> <.01						

Table 4. — Psychiatric disorders depending on the viral load of hepatitis

	Positive <i>n</i> = 49		Negative <i>n</i> = 26		Exact Fisher test	
	<i>n</i>	%	<i>n</i>	%	χ^2	V _{dc} Cramer
Tr. from the schizophrenic spectrum	11	22.5	12	46.2	4.49*	.24
Tr. linked to substances (Actual)	38	75.6	0	0.0	40.9**	.74
Tr. linked to alcohol (Entire life)	19	38.8	3	11.5	6.1*	.28
Note : * <i>p</i> <.05 ; ** <i>p</i> <.01						

Lastly, patients treated are assessed for their response to treatment by analysing the SVR, 3 months after the end of treatment, to verify HCV eradication.

CRP les Marronniers has a closed HPS sector and an open CHS sector. In the closed HPS unit (Hôpital Psychiatrique Sécurisé), patients cannot be discharged by order of a judge. In the other unit, CHS (General Psychiatry), patients are free to enter and leave the center.

In terms of liver characteristics, the majority of patients had mild fibrosis F0-F1 on fibroscan, in terms of viral characteristics, the majority had genotype 1a, and finally, in terms of treatment characteristics, the majority of patients were treated with Epclusa®.

Since around 2010, the emergence of new antivirals has marked a turning point in patient management. Not only do they have fewer side effects than Interferon, but they also enable a greater number of patients to be treated, with broader treatment criteria. In the general population, studies have shown a treatment efficacy of over 95%. Among at-risk populations, studies have shown that the efficacy of antiviral treatments is equivalent to that of the general population. (5,6,8,9,11-15,19,24).

In our study, we found a similar eradication rate as those in the literature with, however, a significant difference between the closed unit and the open one, with more cured patients in the HPS group.

As we mentioned earlier, at-risk populations include drug addicts, alcoholics and psychiatric populations, given that the three are intertwined, as alcohol and substance abuse disorders are defined in DSM V. What's

more, many patients present with both psychiatric and substance/alcohol abuse disorders. Among substance abuse disorders, patients who inject drugs have a high prevalence of HCV (>80%) but also of severe psychiatric illness (>67%) (15).

HCV is also significantly more prevalent in psychiatric patients than in the general population (9-11x higher) (10,16,20). Patients with alcohol dependence also have higher HCV levels than the general population (4.8% vs. 1-2%) (24). Alcohol is a significant factor in the progression of liver disease. In our study, the results show (Table 4) that substance and alcohol abuse are predominantly found in patients with a positive viral load. This suggests that substance-related disorders are a risk and maintenance factor for hepatitis C.

In studies, 40% of patients with psychiatric disorders are diagnosed with an HCV infection (25). When looking at which psychiatric disorders are the most frequent, we find depression (20-50%), anxiety disorders (17-24%), schizophrenia (3.5-10%), bipolarity (9-16%) and personality disorders (30%) (25).

In our study, we find personality disorders, schizophrenia, depressive disorders and bipolar disorders (Table 1). The differences can probably be explained by the fact that most of the studies were carried out in outpatient centers, rather than in psychiatric institutions where more severe psychiatric pathologies are usually hospitalized. In our study, this is reflected by the fact that we found more schizophrenic disorders in the closed center (HPS) than in the open unit (CPS) (table 3).

Both psychiatric disorders and substance abuse disorders (alcohol and injection drug use) can lead to more risky behaviours: multiple partners, high-risk partners, failure to use protection (condoms), exchange of infected material (15,19,20,24,25). These comorbidities not only impact on quality of life, but also reduce compliance with treatment and are risk factors for treatment failure and re-infection (9,15,17,21). These are the populations we need to target if we are to achieve the WHO's objectives. This requires the development of a screening, treatment and follow-up strategy.

Before the advent of direct antivirals in 2010-2013, the reference treatment was pegylated interferon. The use of pegylated interferon was governed by strict treatment criteria, de facto excluding certain patients who are now being treated. Many practitioners were also reluctant to prescribe it to these populations, as Interferon had numerous psychiatric side-effects (depression, confusion, anxiety and psychosis). In addition, treatment duration was longer, leading to adherence problems and treatment discontinuation (6,8,11,12,14,15,19,24,25).

There are obviously risk factors linked to precariousness among these populations: poverty, a high-risk environment, poor overall health and poor access to healthcare (5,15,20).

There is also a real lack of information and knowledge of the disease among patients. In most studies, there is a majority of patients that assert having received no education about HCV (5,6,12,15,17,20). Overall, there is also a lack of information in the general population concerning not only the routes of transmission, but also the risks to the liver. As HCV is a disease with a specific symptoms, most often appearing with the severity of liver disease, many patients do not undergo screening despite their high-risk behaviours (20,25). We also know that the degree of education correlates with acceptance and adherence to treatment (18).

There are also concerns among caregivers: that patients will not adhere to treatment, that they will reinfect themselves and/or transmit the disease, ... which can lead to a reluctance to assume responsibility for referral and treatment. There is also a lack of knowledge about the disease, available treatments and a false presumption of treatment failure in this population among practitioners (5,6,12,13,16,19).

Finally, at institutional level, there is a lack of screening centers and structures adapted to the care of these patients.

We can see that there are multiple obstacles at every step of the patient care. We therefore need to act on each step to avoid any hardship with the patient.

Better communication with both patients and the doctors caring for them is needed, to educate them about the disease, its consequences, the treatments available and how to take them, and of course the introduction of follow-up care. This can be achieved through public information campaigns.

With patients who are used to be discriminated for their psychiatric disability or their history of substance abuse, the use of non-stigmatizing language is essential to improve therapeutic relationship. (5,8,12,15,23)

Stabilization of psychiatric illness is also essential, as it is known to improve HCV management (unstabilized patients are at greater risk of non-adherence and treatment failure) (5,9,15,17,21,24,25).

Regarding substance abuse disorders, substitution and withdrawal therapies should not be overlooked and different medical strategies to prevent transmission can be implemented, such as a sterile syringe/needle access program, notably in drug consumption rooms (salles de shoot). Studies have shown that the combination of substitution therapy and sterile needle access programs reduces infection (substitution therapy alone reduces infection by 50%, the two together by 74%). (8)

Institutional policies of systematic screening need to be put in place in the centres taking care of these patients, whether being general hospitals, psychiatric centres, detoxification centres or other existing structures (shooting galleries, prisons, etc.). It is clear that closed structures with easier access to a healthcare team enable greater detection, but also more treatment and better follow-up (6,8,11,23).

At the CRP Les Maronniers, a number of strategies have been put in place: systematic screening of patients, access to a gastroenterologist at the centre and liver ultrasound. The presence of a closed centre means better patient care, as evidenced by the higher number of patients treated and cured at HPS. However, there are still difficulties, with a high number of patients in CHS lost to follow-up. We therefore need to think about implementing other strategies to improve patient care. For example, the decentralization of a mobile unit in the shooting galleries, comprising a psychologist, a social worker, a nurse and a gastroenterologist, for immediate rapid diagnosis (rapid PCR test, Fibroscan) and initiation of treatment.

In conclusion, improving HCV screening and treatment in order to achieve the goals set by the WHO, requires above all comprehensive integrated care strategies, and better communication of disease-related information among both patients and caregivers, in order to reduce the stigma attached to these populations.

References

1. Global Health Sector Strategies on, respectively, HIV, viral hepatitis and sexually transmitted infections for the period 2022-2030 (no date) World Health Organization. Available at: <https://www.who.int/publications/i/item/9789240053779> (Accessed: 09 August 2023).
2. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5®). (American Psychiatric Pub, 2013).
3. IBM Corp. IBM SPSS statistics for Windows, version 27.0. Armonk, NY: IBM Corp (2020).
4. Drug-Drug Interaction Resources (no date) Liverpool University HIV/HEP/ Cancer Drug Interactions. Available at: <https://www.druginteractions.org/> (Accessed: 09 August 2023).
5. CHASSER, Y., KIM, A.Y. AND FREUDENREICH, O. (2017) 'Hepatitis C treatment: Clinical issues for psychiatrists in the Post-Interferon Era', *Psychosomatics*, 58(1), pp. 1-10. doi:10.1016/j.psych.2016.09.004.

6. CHILDS, E. et al. (2019) 'Evidence-based and guideline-concurrent responses to narratives deferring HCV treatment among people who inject drugs', *Harm Reduction Journal*, 16(1). doi:10.1186/s12954-019-0286-6.
7. COHEN, J. A power Primer. in *Methodological issues & strategies in clinical research* (3rd ed.) (ed. Kazdin, A. E.) 427-436 (American Psychological Association, 2003).
8. DAY, E. et al. (2018) 'Hepatitis C elimination among people who inject drugs: Challenges and recommendations for action within a Health Systems Framework', *Liver International*, 39(1), pp. 20-30. doi:10.1111/liv.13949.
9. DE GENNARO, N. et al. (2020) 'Efficacy and tolerability of Daas in HCV-monoinfected and HCV/HIV-coinfected patients with psychiatric disorders', *BMC Infectious Diseases*, 20(1). doi:10.1186/s12879-020-4922-2.
10. DINWIDDIE, S.H., SHICKER, L., NEWMAN, T. (2003) 'Prevalence of hepatitis C among psychiatric patients in the public sector', *American Journal of Psychiatry*, 160(1), pp. 172-174. doi:10.1176/appi.ajp.160.1.172.
11. FADNES, L.T. et al. (2021) 'Integrated treatment of hepatitis C virus infection among people who inject drugs: A multicenter randomized controlled trial (Intro-hcv)', *PLOS Medicine*, 18(6). doi:10.1371/journal.pmed.1003653.
12. FALADE-NWULIA, O. et al. (2020) 'Hepatitis C treatment uptake among people who inject drugs in the oral direct-acting antiviral era', *Liver International*, 40(10), pp. 2407-2416. doi:10.1111/liv.14634.
13. FRANKOVA, S. et al. (2021) 'Therapy of chronic hepatitis C in people who inject drugs: Focus on adherence', *Harm Reduction Journal*, 18(1). doi:10.1186/s12954-02100519-y.
14. GIRARDIN, F. et al. (2021) 'Hepatitis C prevalences in the psychiatric setting: Costeffectiveness of scaling-up screening and direct-acting antiviral therapy', *JHEP Reports*, 3(3), p. 100279. doi:10.1016/j.jhepr.2021.100279.
15. GUTIÉRREZ-ROJAS, L. et al. (2023) 'Patients with severe mental illness and hepatitis C virus infection benefit from new PANGENOTYPIC direct-acting antivirals: Results of a literature review', *Gastroenterología y Hepatología*, 46(5), pp. 382-396. doi:10.1016/j.gastrohep.2022.06.001.
16. LOFTIS, J.M., MATTHEWS, A.M., HAUSER, P. (2006) 'Psychiatric and substance use disorders in individuals with hepatitis C', *Drugs*, 66(2), pp. 155-174. doi:10.2165/00003495-200666020-00003.
17. MCGOWAN, C.E., FRIED, M.W. (2011) 'Barriers to hepatitis C treatment', *Liver International*, 32, pp. 151-156. doi:10.1111/j.1478-3231.2011.02706.x.
18. PARTIDA, D. et al. (2022) 'Formal hepatitis C education increases willingness to receive therapy in an on-site shelter-based HCV model of care in persons experiencing homelessness', *Open Forum Infectious Diseases*, 9(4). doi:10.1093/ofid/ofac103.
19. ROLLAND, B. et al. (2021) 'Hépatite c en milieu psychiatrique : UN Réservoir Oublié ?', *L'Encéphale*, 47(2), pp. 181-184. doi:10.1016/j.encep.2020.03.003.
20. ROSENBERG, S.D. et al. (2001) 'Prevalence of HIV, hepatitis B, and hepatitis C in people with severe mental illness', *American Journal of Public Health*, 91(1), pp. 31-37. doi:10.2105/ajph.91.1.31.
21. SCHAEFER, M. et al. (2012) 'Hepatitis C infection, antiviral treatment and mental health: A European expert consensus statement', *Journal of Hepatology*, 57(6), pp. 1379-1390. doi:10.1016/j.jhep.2012.07.037.
22. SYLVESTRE, D.L. (2004) 'Co-occurring hepatitis C, substance use, and psychiatric illness: Treatment issues and developing integrated models of care', *Journal of Urban Health: Bulletin of the New York Academy of Medicine*, 81(4), pp. 719-734. doi:10.1093/jurban/jth153.
23. VON DEN HOF, D.W. et al. (2022) 'Against all odds? addiction history associated with
24. Better Viral Hepatitis Care: A Dutch nationwide claims data study', *Journal of Clinical Medicine*, 11(4), p. 1146. doi:10.3390/jcm11041146.
25. YOVTICHEVA, S.P. et al. (2001) 'Psychiatric comorbidity among hepatitis C-positive patients', *Psychosomatics*, 42(5), pp. 411-415. doi:10.1176/appi.psy.42.5.411.
26. WIĘDŁOCHA, M. et al. (2017) 'The neuropsychiatric aspect of the HCV infection', *Advances in Clinical and Experimental Medicine*, 26(1), pp. 167-175. doi:10.17219/acem/37787.