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RESEARCH ARTICLE

TEST AND CURE Towards hepatitis C Micro Elimination by Increase Outreach Linkage to Care by use of HCV Viral Load Real Time Measure and Same Day Treatment

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Highlights

- Access to HCV treatment was insufficient in vulnerable people
- Mobil unit could propose one day test to cure (TTC) session
- TTC was efficient to improve access to treatment for vulnerable people.

ABSTRACT

Introduction and objective: HCV treatment for all was effective in France since 2017. HCV testing, diagnosis and treatment of drugs users and precarious people remain low. Lost follow-up was too important since several stages are necessary. Pangenotypic direct antiviral agents were available. Point-of-care HCV RNA testing offers advantage over antibody testing, enabling diagnosis of active infection with real time measure in a single visit. It is missing link between HCV RDT, liver fibrosis evaluation by FIBROSCAN and treatment. Validated Xpert HCV Viral Load assay CEPHEID, fast training technique, allow developing projects of diagnosis to treatment session. Our objective was to evaluate test to cure session allowing the access in 5 hours to an antiviral treatment to vulnerable and precarious populations (drug users, migrants, psychiatric patients).

Materials and methods: Eligible patients had to have known positive serology or risk behavior, an unknown or unchecked viral load after antiviral treatment; 5 to 7 patients were recruited per each session by social or nursing interview. Between 9 am and 2 pm these patients had access to measure of the hepatic fibrosis by FIBROSCAN, HCV viral load in real time by CEPHEID Xpert HCV Viral load finger-stick samples, social interview, shared educational evaluation, collective workshops, especially harm reduction, depiction of results by hepatologist and prescription of DAA (sofosbuvir velpastasvir combination) allowed delivery of 1st month of treatment. Specific social and nursing follow-up was made during and after treatment. Compliance and sustained virological rate were determinate at week 12.

Results: From October 2019 to December 2021, 223 sessions were realized on 27 sites: 9 drug units, one prison, 17 social units; 1602 patients with drug using history were screened; 427 patients had HCV positive serology and 24 patients did not come; 403 FIBROSCAN measures and 403 measures of viral load in real time were realized. Mean value of liver stiffness was 8.2 and 29% of patients were F3 or F4: 229 patients were HCV RNA positive (56.8%), 57 declared knew their HCV status; 228 treatments began same day, only 1 was delayed due to default social rights; 120 patients had a negative viral load spontaneously and 54 following prior treatment; 399 social interviews and 405 collective workshops were realized. On 31st January 2022, 207 antiviral treatments were completed and 199 patients were cured; 12 patients interrupted treatment; 3 patients relapsed and 5 reinfections; 89% of patients were satisfied with this program.

Conclusions: Despite 3 months interruption by COVID 19 pandemic lockdown and sanitary restrictions, 94% of positive participants were linked to care and cure with this mobile clinic model, by screening and RNA real time measure in unity of place adapted to precarious public, patients distant from system of care had access immediately to treatment.

Keywords: hepatitis C; screening; test to cure

Abbreviations

- DAA Direct Antiviral acting Agents
- HVC Hepatitis Virus C
- MHT Mobile Hepatitis Team
- OST Opioid Substitution Treatment
- POCT point-of-care testing
- PWID People Who Inject Drugs
- RDT Rapid Diagnosis Test

Introduction

In 2016, the World Health Organization (WHO) set an ambitious goal to eliminate hepatitis C as a major public health threat by 2030 (1). Specific targets include increasing sterile needles/syringes distributed from 20 to 200 per person per year for PWID, reducing new hepatitis C infections by 80% and hepatitis C-related deaths by 65%, increasing hepatitis C diagnoses from <20% to 90% and the number of people receiving hepatitis C treatment from less 10% to 80%. Drug injection was main contamination route of hepatitis C virus (HCV) in France and western Europe since 1990 (2). Although highest European HCV screening rate in France, 33% of patients didn't take care of hepatitis C because there were no diagnosed (3). On 2018, the International Network of Hepatitis in Substance Users (INHSU) published recommendations for good practices about HCV pathway on drug users (4). There were detailed on table 1.

Table 1: recommendations INHSU for Hepatitis C elimination among people who inject drugs (3)

Epidemiology and prevention of HCV 1) PWID should be provided with appropriate access to OST and sterile drug injecting equipment as part of widespread comprehensive harm reduction programs (Class I, Level B). (2) PWID should be offered HCV treatment, given they are at elevated risk of HCV transmission and successful treatment may yield transmission reduction benefits (Class IIa, Level C).
Natural history of HCV and effects of drugs on the liver (1) PWID should be counselled to moderate alcohol intake, or abstain if evidence of advanced liver disease (Class I, Level A). (2) Cessation of injecting is not required to limit HCV disease progression (Class IIa, Level C).
Testing of HCV infection (1) An anti-HCV test is recommended for HCV testing among PWID, and if the result is positive, current infection should be confirmed by a sensitive RNA test (Class I, Level B). (2) PWID who are anti-HCV negative should be routinely and voluntarily tested for HCV antibodies/RNA and if negative, every 12 months. Testing should also be offered following a high risk injecting episode (Class IIa, Level B). (3) PWID who are anti-HCV antibody positive and HCV RNA negative (through spontaneous or treatment-induced clear- ance) should receive regular HCV RNA testing, every 12 months or following a high risk injecting episode (Class IIa, Level B).
Non-invasive liver fibrosis assessment (1) Non-invasive assessments have a reduced risk and greater acceptance than liver biopsy, may enhance HCV screening and disease assessment among PWID, and should be offered, if available (Class I, Level B). (2) Combining multiple non-invasive assessments is recom- mended, when possible (Class I, Level B).
Pre-therapeutic assessment (1) Pre-therapeutic education should include discussions of HCV transmission, risk factors for fibrosis progression, treatment, reinfection risk and harm reduction strategies (Class I, Level B). (2) Pre-therapeutic assessment should include an evaluation of housing, education, cultural issues, social functioning and support, finances, nutrition and drug and alcohol use. PWID should be linked into social support services, and peer support if available (Class I, Level B). (3) Models of HCV care integrated within addiction treatment and primary care health centers, as well as prisons, allow successful pre-therapeutic assessment (Class I, Level B). (4) Peer-driven interventions delivered within OST settings may lead to higher rates of treatment initiation and should be offered, if available (Class IIa, Level C). (5) Care coordination in conjunction with behavioural interven- tions can increase likelihood of PWIDs being evaluated and initiating treatment and should be offered, if available (Class I, Level B).
Indications for treatment (1) PWID should receive HCV assessment, with treatment deci- sions based on an individualised evaluation of social, lifestyle, and clinical factors (Class I, Level B).

(2) Treatment is recommended for PWID with chronic HCV infection (Class I, Level A).

PEG-IFN and DAA-based treatment: treatment recommendations

(1) Evaluation of safety and efficacy of interferon-free DAA regimens is required in PWID (Class I, Level C).
(2) Sofosbuvir, sofosbuvir/ledipasvir, paritaprevir/ritonavir/ombi- tasvir/dasabuvir, daclatasvir, and simeprevir can be used in PWID on OST (Class I, Level B).
(3) The decision to institute therapy in PWID should be based on the availability of agents locally and individual disease characteristics of infected persons. For regions without access to interferon-free DAA therapy, PWID with early liver disease should generally be advised to await access to interferon-free DAA regimens. For those with access to highly effective interferon-free DAA therapy, anyone with chronic HCV infection should be considered for therapy, taking into account social circumstances, adherence and medical and social co- morbidities (Class I, Level B).
(4) DAA therapy does not require specific methadone and buprenorphine dose adjustment, but monitoring for signs of opioid toxicity or withdrawal should be undertaken (Class I, Level B).

Impact of drug use on adherence and SVR

(1) Adherence assessments should consider missed doses and treatment discontinuation (Class I, Level B).
(2) PWID should be counselled on the importance of adherence in attaining an SVR (Class I, Level A).
(3) A history of IDU and recent drug use at treatment initiation are not associated with reduced SVR and decisions to treat should be made on a case-by-case basis (Class I, Level B).
(4) PWID with ongoing social issues, history of psychiatric disease and those with more frequent drug use during therapy are at risk of lower adherence and SVR and need to be monitored closely during therapy (Class I, Level B).

Impact of mental health on adherence and SVR

(1) Pre-treatment assessment should include an evaluation of previous or current psychiatric illness, engagement with a drug and alcohol counselor or psychiatrist and discussions around potential treatment options (Class I, Level A).
(2) In cases of acute major and uncontrolled psychiatric disorders, a pre-treatment psychiatric assessment is recommended (Class IIa, Level C).
(3) In case of relevant psychiatric co-morbidities with an increased risk for interferon-associated psychiatric side effects interfer- on-free DAA therapy should be considered (Class IIb, Level C).

Treatment management

(1) HCV treatment for PWID should be considered on an individualized basis and delivered within a multidisciplinary team setting (Class I, Level A).
(2) Access to harm reduction programs, social work and social support services should be a component of HCV clinical management (Class I, Level A).
(3) Peer-based support should be evaluated as a means to improve HCV clinical management (Class I, Level B).

HCV treatment in prisons

(1) Screening and assessment for HCV should be offered to PWID in custody (Class IIa, Level C).
(2) Antiviral treatment for PWID in custody is feasible and clinically effective and should be offered to PWID in custody (Class IIa, Level B).

Reinfection following successful HCV treatment

(1) PWID should not be excluded from HCV treatment on the basis of perceived risk of reinfection (Class I, Level B).
(2) Harm reduction education and counselling should be provided for PWID in the context of HCV treatment to prevent HCV reinfection following successful treatment (Class I, Level B).
(3) Following SVR, monitoring for HCV reinfection through annual HCV RNA assessment should be undertaken on PWID with ongoing risk behaviour (Class I, Level B).

Treatment of acute HCV

(1) PWID with acute HCV symptoms should be monitored for 12– 16 weeks (including HCV RNA levels) to allow potential spontaneous clearance (Class I, Level B).
(2) PEG-IFN mono-therapy for 24 weeks may be considered for PWID with acute HCV (Class I, Level B).
(3) Strategies to optimize adherence should be used in the setting of acute HCV, with consideration of directly observed PEG-IFN therapy (Class I, Level B).

HIV/HCV co-infection

(1) HCV-infected PWID should be screened for HIV (Class I, Level C).
(2) The accelerated HCV disease progression in HIV/HCV should be considered in treatment decision-making; HCV treatment should be prioritized in HIV/HCV patients regardless of fibrosis stage (Class I, Level B).

(3) HIV/HCV-coinfected PWID should be treated and retreated with the same DAA regimens as HCV-monoinfected persons, after recognizing and managing interactions with antiretrovi- ral medications (Class I, Level B).
(4) Early introduction of cART should be offered to all people with HIV infection (Class I, Level A).
(5) Potential drug–drug interactions between HIV, HCV and OST need to be considered. Consultation with a frequently updated database/prescribing information is indicated (Class I, Level A).

Management of hepatitis B virus (HBV) co-infection
(1) PWID should be vaccinated for hepatitis A virus and HBV (Class I, Level B).
(2) HBV DNA testing should be performed on all patients with evidence of chronic HBV infection (hepatitis B surface antigen positive) (Class I, Level A).
(3) PWID with active HBV/HCV co-infection should be treated according to guidelines for monoinfection (for both infections) (Class IIb, Level C).

From 2016 French Health Ministry guidelines (5) were to treat all inmates and drug users, even fibrosis level with direct antiviral agents (DAA). Also, HCV treatment for all was effective in France since 2017. Success rate of DAA, one or two pills per day for 8- or 12-weeks therapy, was 95 to 97%. Before that, access of HCV screening, care and treatment in drugs users, prisoners and homeless was low in France. They were considered as difficult to treat populations. All these patients need support especially psycho-educative interventions. The Mobile Hepatitis Team (MHT was set up in 2013, following the publication of a scientific report on reducing risks of infection amongst drugs users in 2011 (2), which recommends screening all drug users for HCV and establishing multidisciplinary clinics with 'all-in-one' screening to treatment and providing medical and social care. MHT was composed of 1 hepatologist, 3 nurses (coordinating nurse, screening nurse and educative nurse) 1 secretary, 1 social worker, 2 health care workers, for a cross-disciplinary approach. Resources include two specific cars, on van, serology point-of-care testing (POCT), and two mobile FIBROSCAN®. Forty-two different medical and social units were partners: low and high threshold drug units, retention and detention center medical units, outside psychiatric units, emergency, and homeless food/hosting units. We proposed part or all our services to our medical and social partners. There were 19 services to cover six hundred thousand people area in south of France near Spain border. All services were free for patients and for partners. Services were organized in 4 successive steps (6):

<u>For early detection and primary prevention</u>

1. On-sites screening by serology Rapid Diagnostic Tests (RDT) for HIV HBV HCV
2. Green thread: outside RDT and FIBROSCAN® in specific converted truck in outdoor sites.
3. COMPASS, an outreach open center 5 days a week for reception, orientation information and support of vulnerable people
4. Prevention information sessions toward drug users in day-care or housing structures
5. Free blood tests in primary care for patients without social insurance
6. Training of socio-medical institutions staff with trimestral days of exchange or on-demand and on-premises.

<u>For linkage to care and fibrosis assessment:</u>

7. Social screening and diagnosis (by using EPICES, specific social score)
8. On-premises mobile FIBROSCAN® for indirect measurement of liver fibrosis in site
9. Advanced on-site liver specialist consultations

10. TEST TO TREAT ONE DAY sessions

11. Hospital zero hepatitis program
12. Prison zero hepatitis program

<u>For access to treatment:</u>

13. Easy and rapid access to pre-treatment commission with hepatologists, nurses, pharmacist, social worker, GP, psychiatric and/or addictologist.
14. Low-cost mobile phones lending to patients to keep in touch with MHT

<u>For follow up during and after treatment</u>

15. Individual sessions of therapeutic education inside an Regional Health Agency authorized program.
16. Collective educative workshops (nurse, psychologist, nutritionist, pharmacist)
17. e-therapeutic education with specific website
18. Expert patient support with peer-to-peer educational program
19. Dedicated one day hospitalizations

FIBROSCAN was a technic using liver stiffness for measurement of hepatic elasticity to detect liver fibrosis and liver cirrhosis. It was uninvasive testing with rapid results, combined with RDT/POCT. It was performed outreach with mobile FIBROSCAN 402 (Echosens, Paris, France) to assess liver fibrosis stage. Results of liver stiffness measurement (LSM) were expressed in kilopascals (kPa). 10 consecutive inter-costal measurements were required to validate the examination. It was performed by

nurse trained in the framework of a Memorandum of Cooperation (Public Health Law Article 51).
RDT HCV / HIV / HBV were an alternative to serology blood test, but in case of positive test, blood test confirmation was necessary. Nurse could do it in 15 minutes on digital puncture for immediate results and could repeat to know HCV status as soon as necessary.
Social no specific score EPICES included 11 questions. The answer to each question is assigned a coefficient, the sum of the 11 answers gives the EPICES score. The score is continuous, it varies from 0 (absence of precariousness) to 100 (maximum precariousness).
Every social or medical MHT partner could choose and access to part or all our services. They choose only services what they need. Our services did not replace existing services but only completed them.
Specific follow-up of drugs users and other HCV high-risk patients including screening, early detection, diagnosis, and treatment increase rate of treated and cured patients, with low rate of relapse and new infections. MHT offers 'all-in-one' care for drug users and vulnerable people with HCV, using outside social and medical teams. MHT was partnered with organizations including hospital services, psychiatric units, non-hospital organizations such as drug services, and the associative section such as patient associations and a hepatitis network.
The current availability of exceptionally effective new direct antiviral acting agents (DAA) has led to a paradigm shift in hepatitis C management. Chronic Hepatitis C is a silent epidemic, a major cause of cirrhosis and hepatocarcinoma can now be cured in more than 95% of the cases through pangenotypic drugs courses of 8 to 12 weeks, pretty much free from side effects. The United Nation resolution on 2030 Goals for a Sustainable Development and the WHO's Global health sector strategy on viral hepatitis, 2016-2021 (1) consider HCV elimination as their major objective and estimate that 90% of HCV positive patients should be diagnosed and 80% of the viremic population should be treated within this timeframe. According to the French recommendations eliminating hepatitis C virus by 2025 could be a realistic public health goal (7). HCV treatment for all was effective in France since 2017. HCV testing, diagnosis and treatment of drugs users and precarious people remain low. Lost follow-up was too important since several stages are necessary. In France, 100 000 people are undiagnosed and 60 000 are not still treated. PWIDs represent a large proportion of patients to be screened and treated (45,000 estimated). Drug users sharing needles and syringes have poor access to treatment. Dealing with PWIDs in addiction care centers, shelters and food distribution associations is one way to promote HCV testing and to keep them in the care pathway. To meet this ambitious objectives, effective screening policies should be intensified and access to treatment promoted through a new care strategy for patients who escape the usual care pathways i.e. people who inject drugs (PWIDs), prisoners and migrants. DAA were available and HCV genotype determination was not necessary anymore. Point-of-care HCV RNA testing offers advantage over antibody testing, enabling diagnosis of active infection with real time measure in a single visit. It is missing link between HCV RDT, liver fibrosis evaluation by FIBROSCAN and treatment. Validated Xpert HCV Viral Load assay CEPHEID, fast training technique, allow developing projects of diagnosis to treatment session.

Objective and methods

The screening strategy used a dual screening RDT method and FIBROSCAN® and from 2019, Gene Xpert® to directly detect HCV RNA and treat and cure patients in on day session, to reduce the temporality. Diagnostic testing and treatments can be brought directly to patients at point of care. Our immediate goal in France is the widespread use of GeneXpert in addiction care centers and its formalization with the help of virology departments, with task delegation to trained nurses already practicing RDT. The Xpert HCV Viral Load Test (Cepheid) detects active infection from fingerstick capillary whole blood sample in a decentralized setting. This new tool is promising in the diagnostic of HCV requiring treatment and allows its immediate prescription when patients meet the criteria of the simplified pathway (no comorbidities, no potential drug interactions).
Our main objective was to increase outreach screening care treatment access and cure of our target population by completing all steps from screening to treatment in one day session. Target population was drugs users, prisoners, homeless, precarious people, migrants, and psychiatric patients. It has been authorized by Southwest people protection committee (CPP) and declared to health authorities with number IRB 2019-A00989-48. Anonymized data including demographic characteristics, medical history and addiction behaviors were collected on a secure database in accordance with European General Data Protection Regulation » and the MR004 procedure of the French National Comity for Data Protection (CNIL). Study has been carried out in accordance with the code of ethics of the World Medical Association

(declaration of Helsinki) for experiments involving humans. Informed consent was obtained for all participating patients;

We conducted a prospective study in addiction care centers, shelters, social associations, and food distribution centers. On these sessions, all key project actors could be gathered : hepatologist, screening nurse, educational nurses, health care worker and social worker. Each session was prepared in advance and the information disseminated by multiple means: multidisciplinary network associating psychiatrists / addictologists, general practitioners, pharmacists, and social workers aimed to identify and refer patients to the site. The sessions were announced by social networks, posters and flyers distributed in general practice, pharmacies, to recruit as many sensitized patients as possible. Word of mouth also played a significant role in patient communities. Patients were included after information and consent if they had HCV known or discovered positive serology during MHT screening. We proposed to them to participate to test to cure sessions. There were 2 sessions per week, including liver fibrosis measure by FIBROSCAN, HCV RNA real time, social and educational evaluation, collective workshops from 9am to 2 pm session. All RNA results were given by a hepatologist by telemedicine. If RNA was positive, DAA was started same day by a pangenotypic DAAs regimen on site, sofosbuvir/velpatasvir for 12 weeks. We projected to include 270 RNA positive patients in 2 years.

Results

From October 2019 to December 2021, 223 test to cure sessions were realized on 27 sites: 9 drug units, one prison, 17 social units. Study was interrupted during first COVID lockdown in March to May 2020; 1602 patients with drug using history were screened. We presented in table 1 the three groups of patients: 1/ HCV serology negative patients, HCV serology positive and RNA negative 3/ HCV serology and RNA positive. Differences between 3 groups are detailed in table 2. There were statistic difference between HCV RNA positive patients and 2 others groups for history of incarceration, FIBROSCAN value, included F3F4 level.

Table 2: characteristics of 3 different patients groups

item	HCV antibody negative	HCV RNA negative	HCV RNA positive	p
number of patients	1175	174	229	ns
median age	45.2	54.8	52.5	ns
male sex	78	75	76	ns
born in France (%)	70	72	78	ns
born in European Union (%)	18	18	15	ns
born outside the European Union (%)	12	10	7	ns
IVDU or former IVDU (%)	79	82	88	ns
history of incarceration (%)	66	75	78	0.01
piercing and tatoos (%)	81	84	85	ns
EPICES social score	55.3	48.1	51.2	ns
homeless (%)	36	29	31	ns
alcohol (g per day)	75	72	70	ns
median FIBROSCAN value (Kpa)	nd	6.7	8.3	0.05
F3F4 (%)	nd	15	29	0.01

Among group 3, 76% were male 24% female; median age was 52.5 years (extremes 18-68 years); 88% of people are drugs users or former drug users; 97% are precarious (EPICES social score above 30); 427 patients (26.7%) had HCV positive serology, even 57 declared knew their HCV status; 24 patients did not come to test to cure sessions.

All patients (100%) accepted FIBROSCAN and real time HCV RAN measure; 403 FIBROSCAN measures and 403 measures of viral load in real time were realized. Mean value of liver stiffness was 8.2 and 29% of patients were F3 or F4: 229 patients were RNA HCV positive (56.8%); HCV genotype has not been determined according to pangenotypic treatment; 228 treatments began same day, only 1 was delayed due to default social rights. All could be taken care of on the site as part of the simplified course offered by the French association for the study of the liver (5). The comorbidities were consistent with the course and the potential drug interactions were checked; 120 patients had a negative viral load spontaneously and 54 following prior treatment; 399 social interviews and 405 collective works shops were realized.

On 31st January 2022, 207 antiviral treatments were completed, and 199 patients were cured; 12 patients interrupted treatment but 4 were cured with only 1 or 2 months DAA treatment. After treatment, there were only 3 relapsers and 5 reinfections by drug injection. Our cured rate was 94%. Cascade of care of HCV patients was detailed on figure 1.

Sociological evaluation by of our project showed that 4 program main qualities for patients were free access, closeness (outside hospital), speed (of the results) and availability (of nurse and social workers); 89% of patients were satisfied or very satisfied with this one-day program (figure 2).

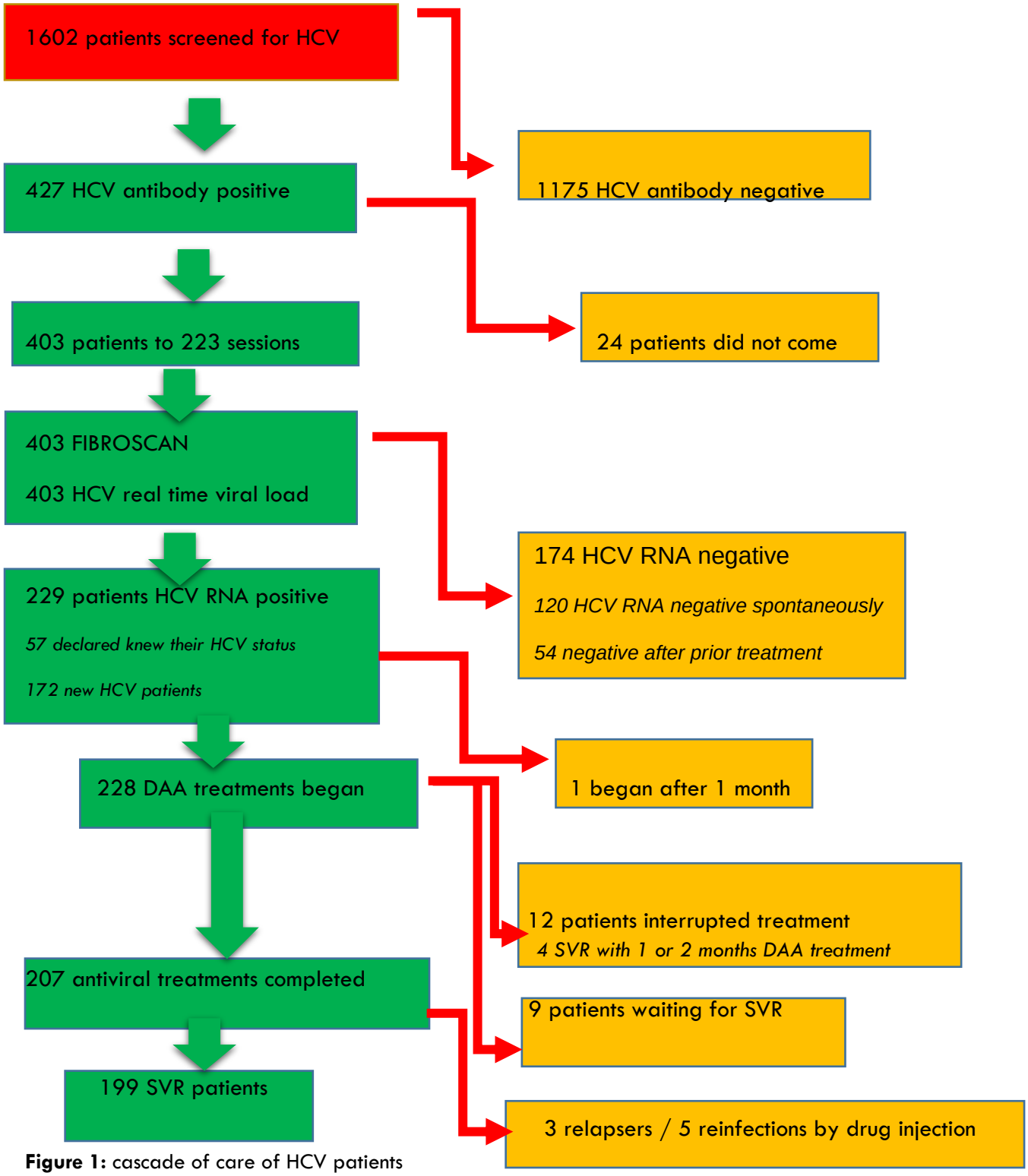


Figure 1: cascade of care of HCV patients

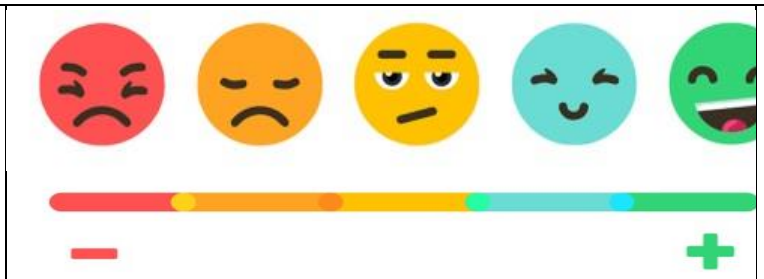
Satisfaction rating scale (5 levels) 3 questions						ND*
1.How do you rate your support?	0 %	0 %	0 %	7,3 %	81,8 %	10.9%
2. What do you think about the length of the session?	0 %	0 %	3,6 %	10.9 %	74,5 %	10.9%
3. Would you advise the session to those around you?	0 %	0 %	0 %	5,5 %	83,6 %	10.9 %

Figure 2: Rate of satisfaction to sessions "Test to cure "by patients
***ND=** not realized

Discussion

Highlights of MHT model included rapid DAA initiation of diagnostic procedures after first contact rapid specialist consultation as needed, within 72 hours, an easy link between outside structures and hospital (with a date of appointment and orientation hospital partners) coverage over a wide geographical and socially disadvantaged area with a territory of almost 600,000 people. Specific screening, follow up and support of these difficult to treat populations are essential for increase medical management and cure of HCV patients. MHT offered complement services, not substitution of existing services and was a new useful tool to screening, diagnosis and treatment of these patients by outside pathway of care. MHT was a cost-efficient program to treat every HCV patient. The reasons of our success were combination of simple ideas:

- go with and for HCV vulnerable people,
- cross-disciplinary approach and share practices,
- committed financiers: state credits, executive management of our hospital / pharmaceutical companies and private foundations
- team of motivated men and women
- new manners to work and\or new approaches of the relation users-professionals

Specific follow-up of drugs users and other HCV high-risk patients included screening, early detection, diagnosis and treatment increase rate of treated and cured patients, with low rate of relapse and new infections. MHT offers 'all-in-one' care for drug users and vulnerable people with HCV, using outside social and medical teams. MHT was partnered with 88 different organizations including hospital services, psychiatric units, non-hospital organizations such as drug services, and the associative section such as patient associations and a hepatitis network. Treatment with pangenotypic 8 or 12 weeks regimens, including sofosbuvir/velpatasvir or glecaprevir/pibrentasvir, led to a new paradigm in the management of chronic hepatitis C patients particularly in difficult to treat populations such as drug users, requiring a minimum of pre-treatment data, presenting an excellent tolerance, a high success rate of response, greater than 95% and very few drug-to-drug interaction with OST.

One day test to cure session was new approach to efficient model of HCV pathway care, according to INSHU recommendations. Although COVID lockdown, we included 229 patients up from the 270 expected, which is close to 85%. Our test to cure session was an innovative and potential cost-effective approach. It has proven its effectiveness in making the screening for hepatitis C virus profitable

(26,7% of HCV serology positivity), treating patients immediately on site (99% of HCV RNA positive patients) and keeping them in the care pathway with an excellent therapeutic compliance (94% were cured, 10.5% lost to follow-up, 3% relapsers and reinfections). Moreover, the multidisciplinary care is essential to reduce risky behaviors. Finally, the strategy saves human care resources.

There was no other French experience of test to cure sessions like our project for effective interventions to improve HCV care for people who use drugs. It was a novel testing pathway for rapid hep C treatment after a unique, opt-out dried blood spot testing approach. Numerous initiatives have been developed in France to achieve the goal of hepatitis C elimination but a lot at effective interventions does not improve HCV testing and treatment among people who use drugs. Grebely and al (8) proposed same model of one day session from diagnosis to treatment without mobile unit and drugs centers association in same project.

Hepatitis C treatment in this population is essential not only to prevent the hepatic or extra-hepatic complications but also to prevent onward transmission of HCV through "treatment as prevention". Test to cure is not only an original efficient strategy to screen and cure the PWID population but also proposes a global territorial structuration of the prevention of chronic liver diseases via the liver fibrosis evaluation including chronic alcoholism, liver toxicity of psychotropic drugs. It also benefits from a systematic multidisciplinary approach only made possible by dedicated days with the participation of hepatologists, educational nurses and social workers to keep the patients in the care pathway. With invested teams and adherence to the project, use of a MHT could increase the number of drug users and vulnerable people with HCV who are supported, treated and cured. In 2021, there was too many under diagnosed HCV patients, especially in homeless, prisoners and drugs users (9). The model MHT aimed to achieve the barriers to HCV screening and treating in marginalized patients and to be applicable to other populations and other territories in order to effectively improve health outcomes. Patients with no advanced fibrosis screened by FibroScan and without uncontrolled severe comorbidities could be managed in the simplified care pathway recommended by the French Association for the study of Liver disease (AFEF) and received their treatment at most within one week or immediately when we began to use real time PCR on site. DAA prescribed in this study i.e. grazoprevir/elbasvir or sofosbuvir/velpatasvir offered an excellent safety and tolerability and high cure rates (87% in ITT analysis and 100% in per protocol analysis) and except patients completely lost to follow-up, all our IWDUs who received a brief treatment course of 8 to 12 months remained adherent.

Multidisciplinary care possible thanks to test to cure sessions played an essential role. it is critical that HCV care in PWIDs be integrated within a framework that addresses drug-related harms, prevents overdose mortality, addresses social inequalities, and improves drug user health. Injecting drug use and risk behaviors appear to remain stable or decrease during and following DAA-based HCV treatment. Successful models have been multidisciplinary and often peer-supported in community-based clinics, drug treatment clinics, correctional facilities, needle-syringe programs, supervised consumption rooms, specialized hospital-based clinics and primary care. Pre-therapeutic education should include discussion and counselling about HCV transmission, risk factors for fibrosis progression, treatment, reinfection risk and harm reduction strategies.

Reflex testing, i.e. testing for HCV RNA in the sample obtained for anti-HCV antibody testing was systematically proposed as an important step for shorter treatment pathway in the "test and treat" and "all inclusive" strategy. It was accepted by about quasi totality of patients This strategy is part of the most recent EASL recommendations (10). In the same way, Heffernan showed that global strategy offering treatment by DAAs at diagnosis without delay can reduce of 75% the risk of infection in PWID population (11). Another elegant but still expensive solution and therefore not accessible to all structures is the cartridge-based point-of-care HCV RNA assay. This assay can be used with fingerstick capillary whole blood, with a great performance and in a short time of 60 minutes. The device (Xpert® HCV VL Fingerstick) was systematically carried out as a second-line screening in case of positive HCV RDT in our partners centers from beginning of 2018. GeneXpert has been considered too expensive to be used instead of anti-HCV antibody testing for first-line screening.

In our process for PWIDs, we were able in the same temporality to screen HCV, evaluate liver fibrosis by FIBROSCAN, to screen liver and addictive comorbidities with interviews or consultations performed by an hepatologist, to propose risk prevention education with an educational nurse, the use of clean drug injecting equipment. Alcohol consumption and substance abuse were assessed and quantified, with specific counselling given. A

non-delayed prescription of hepatitis C treatment. Finally, a key aspect of this management was also the psycho-social evaluation by a social care worker which often remained an essential prerequisite to the entry in the care process.

FIBROSCAN was always accepted among our drug users (100%). Of course, assessment of liver disease severity is necessary prior to therapy. Diagnosing clinically unapparent cirrhosis (METAVIR score F4) or advanced (bridging) fibrosis (METAVIR score F3) is required, as the choice of treatment regimen and the post-treatment prognosis and surveillance for hepatocarcinoma every 6 months or esophageal varices screening may depend on the stage of fibrosis. One third of our patients had advanced fibrosis and were referred to a specialized hepatologic course.

Treatment monitoring could be carried out by training nurse. Healing was checked by one RNA testing within 3 to 6 months after stopping treatment by blood test or GeneXpert occasionally. GeneXpert HCV could be used in the next future to confirm SVR as soon as the device will be permanently available on site. This would simplify the whole strategy in the goal of HCV elimination and would prevent the lost to follow-up of patients who have completed their treatment. Our study was a real success for HCV treatment access. Lost follow up between patients screening and test to cure sessions was very low. Almost all HCV viral positive patients acceded to DAA treatment. It needed coordination of all actors of project. We proposed a new clinic model (Figure 3), by screening and real time measure in unity of place, adapted to precarious people with fewer steps between screening and treatment. Patients distant from system of care had access immediately to treatment. Using of mobile real time viral load system was real progress for patients. Benefits of test to cure sessions were multiple: rapid screening to rapid access to treatment in one day session, reduced role for hepatologist and greater role for nurses. Nurses followed up monthly HCV patients. It permitted reduced healthcare personnel hours (e.g. social worker, nursing staff) with one-session model. It was an illustration of original solution to improve linkage to care for HCV vulnerable patients like other teams described (12-14).

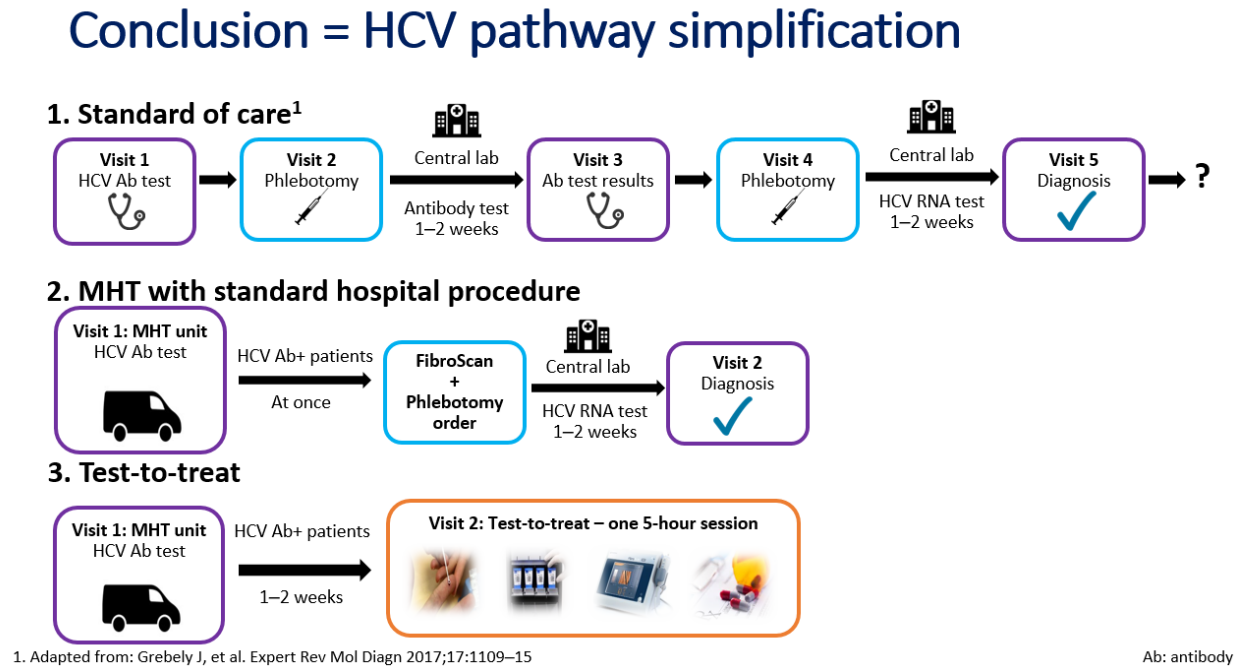


Figure 3: HCV pathway simplification

Conclusions

Our project is the first effective process, organized on one-day session to create the event "treat and cure HCV" in vulnerable patients and contribute to the elimination of this virus with a great benefice for public health. Moreover, the objective is even more global aiming to screen together HCV, HBV, HIV, excessive alcohol consumption or other drug use in PWID and former PWID populations by bringing caregivers to these difficult to approach patients. This model offers harm reduction services for reducing transmissible infections, proposes addiction management and finally makes these vulnerable populations aware of the care pathway

(figure 3). FIBROSCAN remains a pedagogic partner of value. New devices like the GeneXpert HCV Viral Load Test allow the decrease of temporality in the test, treat and cure strategy and show promising results. This innovative concept bringing together on one day a multidisciplinary team with medical practitioners, nurses and social workers entirely dedicated to the patients remains the key to efficacy, rentability, and of a comprehensive care of the patients. Our project was unique by an all-inclusive strategy. Ours results were integrated in European Union project OPTIMISE et we are selected to participate on future project IMPLEMENTE.

With invested teams and adherence to the project, use of a MHT could increase the number of drug users and vulnerable people with HCV who are supported, treated and cured. Next step was to develop test to cure sessions like in Australia (7-8) to create HCV pathway simplification (Figure 3) and going to the way of microelimination in our territory. In 2022, there was too many under diagnosed HCV patients, especially in homeless, prisoners and drugs users (13).

Our projects for 2023-2025 were to develop and to increase the number of people taken care at the time of treatment (almost) for all to find missing patients, cure to decrease reluctance of patients and medical and social professionals, go towards "forgotten" populations: psychiatric and alcoholic patients and help in reintegration after cure and to prevent reinfection.

Declaration of interest

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REMY AJ consulting, conferences and meeting invitations by ABBVIE and GILEAD,
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