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Original article

Coordinated hospital-community organisation model for the prevention, monitoring and treatment of patients with addiction and HCV

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Summary. *Background:* Hepatitis C Virus (HCV) infection is a common cause of chronic liver disease, cirrhosis and hepatocellular carcinoma. Epidemiological studies have shown a prevalence amongst the general Italian population that varies between 0.4% and 16.2%, depending on the age bracket and the geographic area considered. The prevalence amongst persons who inject drugs (PWID) is approximately 70%, making this population one of the main reservoirs of the virus. The complex issues of addiction impact access to antiviral therapy, despite the presence of efficacious treatments, with considerable personal, family and social costs. According to the available literature, testing is a critical issue in Drug Addiction Services and at the current time a mere 37.3% of users are screened, which translates into delayed diagnosis and access to antiviral therapies, with a considerable risk of an exacerbation of the clinical situation and of unconscious transmission of the condition to others. *Purpose:* To describe the coordinated organisation model for the therapeutic management of patients who inject drugs with HCV, implemented by Trieste Department of Dependency (DoD); to monitor its clinical efficacy and its ability to guarantee continuing care between hospital and community medicine settings. *Methods:* The aim of the model is to promote certain activities and partnerships that are already implemented by infectious disease/ hepatology specialists as part of the coordinated HCV prevention and treatment programme and to test novel strategies for preventing post-treatment reinfection. The programme is broken down into three different specialised levels: 1. the first level consists of on-site screening, performed at the Department of Dependency outpatient clinic; 2. the second level is characterised by clinical and diagnostic investigations conducted by the infectious diseases/hepatology specialist, to whom the subject is referred when found to be positive at level one; 3. the third level consists of pharmacological treatment and follow-up, which commences when the subject starts treatment with direct-acting antivirals; three different medicinal product management methods are contemplated, depending on the individual's level of self-sufficiency. Follow-up starts at the end of treatment and lasts a year. *Conclusions:* The experience of Trieste DoD demonstrates the feasibility of a coordinated management organisation model with hospital specialists and its efficacy in the clinical management of a population of PWID with viral hepatitis C. The provision by the DoD of daily, highly organised on-site screening managed by a specially- trained medical team has proven strategic for facilitating access to and compliance with the protocol for treatment with new direct-acting antivirals (DAA). In this team, a key role is played by the nurse, as the professional who manages the fiduciary relationship that is closest to the patient. A linkage to care approach that is differentiated according to the level of self-sufficiency and the complexity of the patient's needs makes it possible to avoid drop-out and to complete all pharmacological programmes. Harm reduction activities are important for pursuing changes in at-risk behaviour and preventing reinfection and are implemented at different time points during treatment and follow-up. (www.actabiomedica.it)

Key words: Dependency Service, HCV, epidemiology, direct-acting antivirals, infectious diseases, PWID

Introduction

Hepatitis C virus (HCV) infection is a viral infection of global importance that is transmitted by blood (1,2). Approximately 160 million people, 2-3% of the world's population, have chronic hepatitis C, a condition that single-handedly accounts for one quarter of all cases of cirrhosis and hepatocellular carcinoma (HCC) (1-4). Furthermore, there is evidence that HCV infection is associated with extrahepatic sequelae, such as circulatory disorders, kidney disease and neuropsychiatric disorders (5), and it has been proven that treatment can reduce the complications associated with the infection, including all-cause mortality (6). However, although widespread, this illness is still relatively unknown in both the general population and amongst medical sector professionals (7).

Most incident and prevalent cases of HCV infection worldwide are associated with the use of drugs and substance abuse involving at-risk injection practices (8). This behaviour is concentrated in high-income countries, where there are a significant number of people who inject drugs (PWID) (1,9). In these countries, prevalence ranges from 50-80% in the PWID population, which is chronically infected (1,10).

In Europe (including Russia), it is estimated that the number of subjects with HCV infection is between 11.3 and 14.7 million. Prevalence rates (identified by HCV antibody positivity) in the population vary from 0.5% observed in southern European countries to 7% in eastern Mediterranean countries (11). This population includes both subjects who have previously injected drugs, or "recent injectors", who have injected drugs for no more than one month or one year, depending on the different definitions established in scientific literature. Those subjects with a history of injected substance abuse can also include those on replacement medication for dependence, some of whom potentially continue to inject substances (12).

Every year, worldwide over 1.75 million people contract the disease (with a global incidence rate of 23.7/100,000) and most of these become infected through unsafe use of syringes used to administer drugs (13). In Italy, the prevalence of HCV in the general population varies, depending on the age bracket and geographical area considered, between 0.4% and 16.2%. The figure amongst the PWID population is around 70%, to the extent that it can be said that this target represents one of the main "reservoirs" of the virus (14).

Worldwide, of the 71 million patients with HCV, the impact of the infection amongst PWID with a recent history of injection is particularly significant, with a prevalence of chronic infection of 50%, reflecting an estimated incidence of 5.6 million subjects (8% of all infections worldwide) (1,13). However, although it has not been calculated, there is also a high number of chronic HCV infections amongst those PWID who have stopped injecting drugs (1,15) and that could be accounted for by other at-risk behaviour, such as unprotected sex. In addition, one worrying aspect is represented by the fact that an unquantifiable part of new infections is contracted by people who previously recovered from HCV infection and who become re-infected due to a persistence of at-risk behaviour. This makes it essential to provide harm reduction and counselling initiatives. In this sense, it is important to remember that the morbidity and mortality associated with HCV infection continues to rise in both PWID with a recent history of substance use and in past users (15,16).

However, despite the strong impact of HCV infection, only 1-2% of PWID are on treatment (17-21).

There are a number of viral and subject-related factors that make the identification, diagnosis and treatment of HCV infection difficult in this target (22). Acute infection is usually asymptomatic and chronically infected subjects may not develop significant symptoms for decades after contagion (23). If the disease is not treated, chronic liver disease develops in 60-70% of cases, cirrhosis in 5-20% of cases, and 1-5% die of decompensated cirrhosis or HCC (24). It is estimated that fewer than 5% of PWID are treated for chronic HCV infection (17,25).

It is interesting to observe that in countries in which infection control procedures have been implemented (including counselling and first-level blood test screening), it has been observed that the main means of HCV transmission is at-risk injection practices (2,26). Conversely, in countries in which the adoption of healthcare procedures aimed at preventing the transmission of pathogens in blood is less well or-

ganised, the spread of HCV is extensively related also to nosocomial and iatrogenic causes (27).

Generally speaking, there is a discrepancy between the response of public health services, in terms of primary prevention, and the speed with which HCV is spread, which explains why the prevalence of the virus remains high despite the availability of efficacious and well-tolerated treatments (28,29). It is therefore of paramount importance to promote further research and to invest the resources needed to improve prevention and treatment strategies in PWID populations, also in order to control possible coinfections, in particular, human immunodeficiency virus (HIV) and hepatitis B virus (HBV).

According to the WHO's Global Hepatitis Strategy, the goal is to treat three million subjects with HCV infection by 2030, by implementing a series of resolutive measures: vaccination practices for HBV, HAV and HEV, the prevention of sexual transmission and checks on blood and blood products, long-term treatments for the management to HBV and the treatment of HCV with interferon-free (IFN-free) therapies and the administration of direct-acting antivirals (DAA). Since the achievement of the goal of the HBV and HCV eradication campaign depends above all on the implementation of schemes in "key" contexts and populations, the WHO recommends defining in each country the specific populations that are worst hit by the hepatitis virus epidemic: of these, PWID are a target at a very high risk of contracting HCV infection through blood due to the use of infected syringes or other instruments used to take substances (30).

The new treatments for HCV infection have introduced shorter pharmacological regimens that are associated with manageable side effects and that have high probabilities of healing (31). However, the cost of these treatment options is still high and could clearly orientate guidelines making active substance users ineligible for treatment (4,32-34). One example of this situation is what is happening in many public insurance schemes in the United States (with the exception of Medicaid), which restrict the coverage of the novel treatments to the subjects with the most advanced disease, leading to several years' delay in access to these treatments. These restrictions represent a severe disadvantage for PWID populations and low-income patients (35).

Initially, the guidelines on the treatment of HCV did not take PWID into consideration, justifying this decision by issues concerning compliance with treatment, the increased susceptibility to the side effects (such as depression) and to re-infection. However, there is ever-greater evidence regarding the safety and efficacy of treatment for HCV amongst PWID (36-38). In two systematic reviews evaluating treatment for PWID (one of which focussed on subjects with a recent history of injection at the start of treatment), the overall sustained virologic response (SVR) rate was 56% (37,38). These response rates are similar to those reported in large randomised controlled trials on treatment with pegylated interferon/ribavirin (PEG-IFN/RBV) (39). Therefore, at the current time, international guidelines recommend treating PWID according to an individualised approach (33,40,41). With this in mind, international recommendations have reconsidered the evidence on the relationship between substance use and treatment of HCV infection, stressing that the presence of a history of injected substance abuse does not, in itself, compromise compliance, the completion of treatment or SVR (33).

It has also been demonstrated that early intervention in the PWID population, universally recognised as the true "reservoir" of the infection, with a massive use of DAA, can generate a significant impact on the global HCV epidemic (in terms of a significant decrease) and prevent these subjects from developing cirrhosis, hepatic decompensation and HCC, thereby reducing the impact of its morbidity and mortality (42).

Strong points and limits of coordinated care schemes for the treatment of PWID populations

Therapeutic intervention in PWID, involving referral and management and subsequent HCV clearance, represents a tangible and achievable target in order to motivate the subject to abandon practices that are harmful for his/her health, but also in order to prevent him/her from constituting a universal source of contagion. This makes it possible to achieve a positive impact on the progression of the liver disease, with an improvement in the quality of life and life expectancy.

A number of experiences conducted in different countries have shown that the treatment of PWID, as subjects at a higher risk of acquiring HCV, can contribute to reducing the incidence of HCV infection and therefore prevent its transmission, especially if therapy is associated in a coordinated manner with counselling and harm reduction interventions (replacement opioid therapy and syringe distribution) (42-44). One recent study, for example, calculated that in Edinburgh (where 30% of PWID have HCV), doubling the therapy use rate to 15 per thousand could halve the prevalence and incidence of HCV in 10 years. In other countries such as the United States, on the other hand, a 68% reduction in the prevalence of HCV has been estimated over the next few years with treatment of 20 per thousand PWID/year, with a prevalence of 25% (42).

Despite the obvious usefulness of this approach, in real life the potential results of treatment with DAA would still appear to be limited compared to the benefit that these subjects could obtain from therapy. A number of factors contribute to this situation, including the variability between countries with regard to the organisation and the geographic distribution of specialised drug addiction centres, the presence and absence of screening and harm-reduction intervention, and policy that criminalises and discriminates against PWID, which impacts pleas for help and increases the submerged need (45,46).

Screening, testing and risk assessment counselling activities are important for improving the individual's awareness of his or her serological status and allowing an earlier start to therapy. Specific harm reduction and sexual education schemes are very important also for motivating the individual to adopt safer new behavioural models.

The inadequacy of testing strategies and the limited access by PWID to the new antiviral therapies, has led to the development of combined treatment models, based on cooperation between addiction service specialists and hospital specialists; The individualisation of programmes and their modulation according to the person's actual self-sufficiency have made it possible to trial new ways of managing antiviral therapy in diversified settings, such as outpatient clinics, drug dependency clinics and specialised treatments, also through the use of DOT (directly observed therapy) and peer-based models(47). At the basis of this strategy is a pragmatic, realistic and non-judgemental multidisciplinary approach, guided by public health objectives. The application of integrated models able to develop a strong synergy between specialists, through the drafting and implementation of common procedures and guidelines has facilitated the access to care in at-risk populations.

In Italy, the coordinated care model for HCV infection in PWID was implemented by the different professional figures working in the drug addiction services, namely psychiatrists, psychologists, toxicologists, social workers, nurses and educators.

The Drug Addiction Service is able to guarantee a privileged relationship with the patient: in these facilities, serological tests can be performed in order to guarantee early diagnosis and the introduction of treatment, DAAs can be administered directly and the harm reduction activities needed to eliminate at-risk behaviour and prevent virus transmission and reinfection can be performed. Operational protocols between community and hospital specialists are also useful for follow-up and the monitoring of any adverse event. The importance of a combined management of HCV infection in Addiction Services has long since been assimilated also by the National Health Council, which with its guidelines for screening and early diagnosis of the main infections associated with drug use, published in 2010, envisaged the organisation within the Drug Addiction Service of Special Units for the management of the associated infectious diseases (HIV, HBV, HCV, TB and STDs), also in cooperation with local infectious diseases departments. The aim is to facilitate access to therapy for infectious diseases, to improve treatment compliance and to reduce the dropouts associated with referral to Infectious Diseases units.

The staff working in Drug Addiction Services and dedicated to the management of drug users in 2016 amounted to 7,186 professionals, 75.6% of whom working full time. 51.9% of these professionals are doctors and nurses, 38.5% are psychologists, social workers and educators and the remainder are administrative staff and other professional figures, with an availability rate of between 8 and 24 resources per 100,000 inhabitants, a value that varies greatly from one area to another.

This situation has led to a partial collapse of the Drug Addiction Service system. According to the most recent Report to parliament on the drug addiction situation, which was published last year, in 2016, these Services managed 143,271 users (of whom 21,458 were new users, equal to 15% of the total, and the remaining 121,813 had already been managed in previous years); it is estimated that approximately double this number of users are not treated but would require treatment (Report to parliament on the drug addiction situation 2017). Furthermore, the recent general crisis in the healthcare sector has also had a hefty negative effect on the treatment of PWID and, more generally addiction prevention activities and the lack of resources available is obvious. According to the data available, in 2016 in Italy 28,197 Addition Service users were tested for HCV, a mere 25% of the total number of subjects treated and 275 of PWID. For 9% of users on treatment, i.e. 12,380 subjects, the test was positive, showing significant territorial variability: indeed, the percentage of users testing positive for HCV varies between 0.4% and 36.6%. By analysing subjects who inject heroin and/or cocaine alone, it is observed that the percentage of subjects tested for HCV is approximately 28% for heroin and 30% for cocaine (Report to Parliament on the drug addiction situation 2017). In the drug addiction services, testing therefore still involves significant problems: on average nationwide the number of users who undergo screening is equal to one third of all potentially testable and manageable users (49).

In order to deal with these critical aspects, for some time now Italy's regional authorities have adopted an organisation compatible with a coordinated hospital-community approach to providing diagnosis and care programmes for infectious diseases in PWID. One particularly significant example is that of the Friuli Venezia Giulia Regional Authority that, already in 2014 undertook the "PIT project - Substance use and related disease: Programmes, Identification and Testing", aimed at developing a regional protocol in an attempt to develop procedures in order to standardise the availability of testing and to define a shared diagnosis programme, in concert with infectious diseases experts, with test laboratories, with sexually-transmitted diseases centres and the managements of

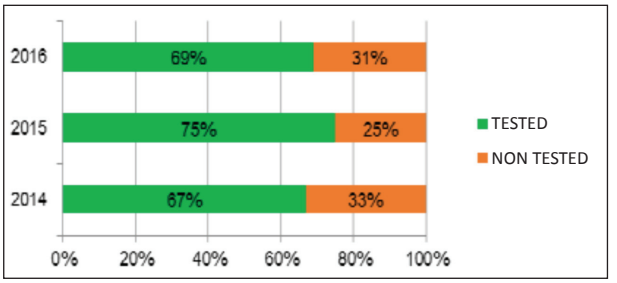

Figure 1. Percentages of users tested for HCV out of total treated by Friuli Venezia giulia Drug Addiction Services in 2014, 2015 and 2016

regional disciplinary facilities. The aim was to improve the availability of testing for HIV, HBV and HCV amongst the substance users followed by the region's addiction services, also through the analysis and reprogramming of the management models. The activity reports for the first two years of introduction of the PIT scheme have shown an improvement in the regional trend (Figure 1).

The experience of Trieste Department of Dependency

The screening work performed by Trieste Department of Dependency (DoD) started in 1985, following the AIDS emergency, with the opening of a dedicated on-site outpatient clinic managed in conjunction with the infectious diseases unit. Considered a strategical part of treatment services, over the years the organisation of this activity has developed, through a gradual increase in the interest dedicated to the impact of the hepatitis viruses (B and "non-A, non-B", then C). In the presence of a low prevalence of HIV, a high prevalence of HCV was observed.

Trieste DoD currently offers an HCV prevention, monitoring, treatment and follow-up service, based on a facilitating and proactive approach and on specific linkage to care activities to prevent drop-out and the development of viral resistance and to favour treatment compliance. Over time, the cooperation with infectious diseases specialists has had a very positive evolution; the introduction of DAAs to the clinic represented a fundamental step for optimising the continuing care pathway. Indeed, up to 2015, an-

tiviral therapy was managed directly by the Infectious Diseases Unit, with an unsatisfactory result in terms of the presence of a great many drop-outs, due to the fragmented and complex nature of the pathway and the difficulties of managing a therapeutic relationship with PWID.

The DoD's work has been reworked and reorganised over the years, with a view to obtaining an ongoing improvement in performance. The DoD headquarters is currently home to a multipurpose facility dedicated to the associated infectious diseases, which operates in close connection with Local Health Authority specialists (infectious diseases, hepatology, cardiology and dermatology specialists). The presence of an infectious diseases expert at the service once a month for scheduled clinical assessments and the availability of a dedicated medical team has allowed greater efficacy and efficiency in the use of resources and time. This activity meets the criteria of clinical appropriateness and is provided in accordance with operational agreements with specialised units, in order to simplify user programmes.

The integrated model implemented in Trieste is made efficacious by a series of organisational and functional "principles", identified on the basis of some of the peculiar characteristics of the target, with the aim of facilitating as far as is possible access to and compliance with the care protocol (Table 1). The screening outpatient service is located next to that for the management of replacement therapy and is open every morning, in order to guarantee testing to all individuals regardless of whether they have an appointment. The staff have a pro-active approach, the HCV test is offered to everyone, free of charge, without a doctor's prescription and whilst respecting the user's anonymity. The team that follows the patient is selected and formed specifically and is capable of managing complex problems that could affect compliance: psychiatric comorbidities, psychosocial unease, fear, difficult venous access, presence of deep skin lesions. In this programme, nurses play a key role in the fiduciary and confidential relationship and in the individualised support provided to patients, in concert with the specialist doctors.

The DoD diagnostic and therapeutic pathway has three different levels of specialisation, which identified in accordance with the clinical assessment. The first (screening) envisages the following activities:

- Pre-test counselling, risk assessment and acquisition of written informed consent (nurse/ doctor);
- Performance of screening serological test (nurse/ doctor);
- Delivery of the results (doctor/ nurse);
- Informative counselling (nurse);
- Support in the event of positive serology (doctor/nurse/psychologist)

The second level (in-depth diagnostic tests and procedures) commences when the subject tests positive for the first level and more detailed diagnostic assessment through clinical and laboratory tests is required. In this case, the Service's pro-active action is expressed: a) by performing the blood draw for the specific test (qualitative and quantitative HCV RNA) directly and by booking an appointment with the infectious diseases specialist at the DoD outpatient clinic; b) by guaranteeing counselling and therapeutic continuity with the Department, if the person if not self-sufficient. The third level (treatment programme) is initiated when the clinical situation requires specialist therapeutic intervention. Once again in these cases the support and counselling provided to improve compliance with the treatment programme and pre-

Table 1. The active "ingredients" of the Trieste DoD coordinated model

- Fully-equipped screening clinic, open every morning, next to the replacement therapies clinic.
- Free, unpaid and anonymous access, no doctor's prescription required.
- Dedicated, specially-trained healthcare team, able to manage complex issues that could affect compliance (psychosocial problems, prejudice/fear, venous access difficulties, presence of skin lesions, etc.).
- Pre- and post-test counseling, personal delivery of results.
- For users who test positive, start of coordinated protocol with Infectious Diseases staff (on-site management of diagnostic work-up and specialist assessment).
- Management of DAA therapy in concert with the infectious diseases specialist, depending on the individual's level of self-sufficiency.
- Specific intervention to improve access to and compliance with treatment (linkage to care), including individualised accompaniment or home visits (service car).

vent dropout involve a series of measurements such as assistance during appointments, consultations in the event of hospitalisation, home help, supervision when taking pharmacological treatment, family-relationship mediation, social support and intervention in conjunction with community services.

Results of HCV screening

Since 2012, Trieste DoD has had a certified database regarding all the activities offered to users, made possible by the implementation of a computerised platform. The data regarding HCV serological screening over the past five years are summarised in Table 2. As is shown, since 2012 there has been an increase in the percentage of users undergoing screening for HCV infection: the percentage of tested subjects out of total users remained above 70%.

The data regarding the DoD's work has shown a decrease in the prevalence of HCV infection amongst the users managed (from 70.52% in 2012 to 67.64% in 2014 and 64.01% in 2016), which may suggest that the continuous and incisive prevention and testing activities are reducing the spread of the virus (Figure 2).

The compliance of HCV+ PWID subjects for the in-depth diagnosis (second-level screening) was very good (equal to 89.2%), showing that, once the patient has been informed and responsibilised, he/she takes adequate care of him/herself. In 2016, 298 were found to have viraemia; of these subjects, almost 60%

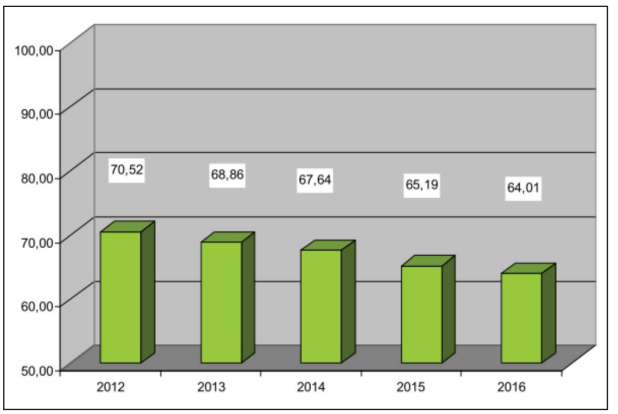

Figure 2. Percentage of users managed by Trieste DoD who tested positive on the HCV antibody test between 2012 and 2016

Table 2. Data and characteristics of users managed by Triests DoD: serology screening for HCV for the five-year period 2012 - 2016

	2012	2013	2014	2015	2016
No. of PWID managed	873	882	892	907	998
No. of users screened for HCV	648	684	717	721	728
% users screened	74,23	77,55	80,38	79,49	72,95
No. of HCV+ users	457	471	485	470	466
% of HCV+ users	70,52	68,86	67,64	65,19	64,01
No. of users HCV positive on HCV-RNA test	423	432	436	427	416
% of users positive on HCV-RNA test	92,56	91,72	89,90	90,85	89,27
No. of users with viraemia	301	311	313	305	298
% of HCV+ users with viraemia	65,86	66,03	64,54	64,89	63,95
No. of viraemic users examined by infectious diseases specialist	106	137	225	263	222
% of viraemic users examined by infectious diseases specialist	35,22	34,08	33,87	34,75	35,57

were infected with genotype 3. In 2016, 222 subjects were examined by the infectious diseases specialist; although this is a good result, it can be improved on, as all subjects with active infection should be examined.

Furthermore, the outcome of the test defines the aims of counselling: in the event of negativity, it aims to promote protective behaviour and raises the individual's awareness regarding serological status monitoring over time; in the presence of a positive result, it promotes the start of a coordinated specialised treatment programme and the modification of at-risk behaviour.

Second-level screening for -Ab+ HCV users is guaranteed on-site with qualitative and quantitative HCV-RNA testing; thanks to the linkage to care approach taken, the offer is taken up in over 90% of cases (Figure 3). Viral genotyping in HCV-RNA-positive subjects showed genotype 3 to be prevalent in the population target studied (Figure 4).

Il 2015, the DoD in concert with the Infectious diseases Unit devised a diagnostic and treatment programme addressing patients with chronic HCV, which was formalised with the protocol titled "Management of continuing care pathways between the Infectious Diseases Unit and the Drug Addiction Unit". This protocol was also stimulated by the availability of new direct-acting antivirals (DAA) and the need to manage the various stages of treatment in a more coordinated manner. The strategic objective was to achieve a standardisation of this activity and to guarantee all users facilitated access to the specialist programme and treatment. The screening clinic staff performs

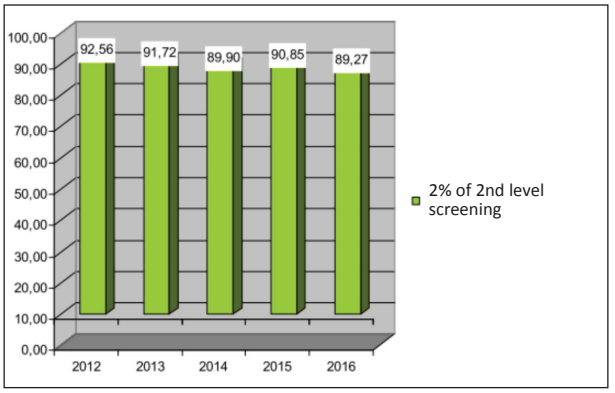

Figure 3. Percentages of subjects with HCV antibodies undergoing second-level screening with qualitative/quantitative HCV-RNA test

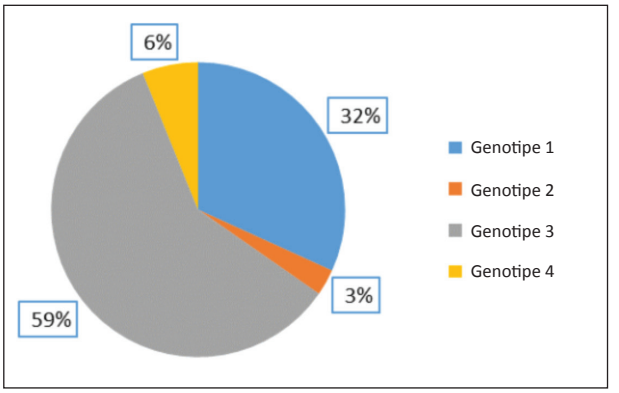

Figure 4. Percentage breakdown for viral genotyping in HCV-RNA-positive subjects managed at DoD between 2012 and 2016

the second-level tests before the appointment with the infectious diseases specialist in order to save time. Until 2015, antiviral therapy was managed directly by the Infectious Diseases Unit, which managed the individual after the diagnostic work-up performed at the DoD screening clinic. This practice was seen to be unsatisfactory given the high dropout rate due to the fragmented and complex nature of the programme and the difficulties managing the therapeutic relationship with drug users.

Until 2017, one of the protocol's critical aspects was the time patients had to wait for a liver ultrasound elastography, which was only performed in 15% of subjects. This led to a delay in the completion of the phase in preparation for the start of pharmacological treatment with DAAs. This critical aspect was overcome in 2018.

The adoption of the protocol permitted good levels of activity and a positive response by users, who did not show reluctance or fear and accepted the programme willingly.

Trials with DAAs

Treatment with DAAS is managed by the infectious diseases specialist/hepatologist, according to the addiction problem and the individual's level of self-sufficiency (the spectrum of operative options ranges from direct and supervised administration to the provision of a supply for a certain period of time). One

strong point is the linkage to care mentioned above, that involves specific intervention in order to improve treatment compliance and prevent drop-out, including individualised accompanying to treatment centres, home visits, telephone reminder activities, supervised medication taking and administration of direct-acting antivirals.

The protocol envisages three types of medication management (Table 3): self-sufficient patients are encouraged to "do it themselves" and the Service's contribution consists in overseeing the administration of the treatment, with reminder calls and communication with the infectious diseases specialist. Treatment can be assigned for a month or week, depending on the reliability of the subject. If the subject is not self-sufficient, the treatment is collected by the Addiction Service and administered, as specified in the treatment plan, daily or twice-weekly (DOT). Counselling is implemented before and during treatment in order to promote the motivation of the subject; follow-up is guaranteed for one year after the end of treatment.

In 2016, 14 people (13 males and 1 female started treatment). All the treatment programmes devised where completed, thanks to the coordinated management approach.

It should be noted that no individual was excluded from treatment for reasons associated with substance use or poor treatment compliance: in accordance with Italian Medicines Agency criteria all patients who were eligible at the time were recruited and treated. In 2016, the "cascade of care" was similar to that of other experiences (Figure 5).

In 2017, 57 people started treatment:

- 27 people, with low self-sufficiency levels and poor compliance, took the medicinal product directly at the Department of Dependency clinic (DOT);
- 20 partially self-sufficient individuals took the treatment themselves, collecting a 7-day supply of treatment from the hospital pharmacy;
- 10 self-sufficient individuals took the treatment themselves, collecting a 28-day supply of treatment from the hospital pharmacy;

Table 3. Activities managed by the Trieste DoD team at the screening clinic, in concert with infectious diseases specialists.

Pre-treatment	Joint, multidisciplinary DoD/ infectious diseases assessment before the patient is included in the pharmacological treatment protocol; during this phase, staff discuss the following with the subject: the pharmacological regimen, the commitment required, the anticipated repercussions, any side effects and the importance of regular blood chemistry monitoring during the treatment. Counselling to promote motivation regarding the treatment, compliance and regular treatment in the long term, as well as to prevent drug and alcohol use. Identification and involvement of any carers.
During therapy	Prescription of the DAA treatment programme by infectious diseases specialist with clinical examination of patient at the DoD screening clinic. Supervision of pharmacological treatment by screening service team. During the first month, the individual's ability to self-manage treatment and follow the treatment regimen is assessed every day; more specifically, depending on the subject's level of self-sufficiency, the following may options may be employed: • Treatment reminder phone calls or texts from the infectious diseases staff; • Collection of medication from the hospital pharmacy and daily of twice-weekly administration c/o the Drug Addiction Service clinic, to avoid leaving non-self-sufficient subjects to manage their therapy alone (DOT – Daily observed therapy) Scheduling and performance of blood chemistry tests c/o DoD screening clinic in accordance with national guidelines with the provision of a home visit service. The outcomes of these tests are discussed with the infectious diseases specialist, who remains in close contact with the screening team and staff of the local DoD unit at all times. Motivational counselling and toxicological and alcohol monitoring
Post-treatment	Serological follow-up (quantitative HCV-RNA test) and clinical follow-up to monitor any re-infection. This phase lasts 1 year. Counselling intended to improve protective behaviour and prevent any at-risk behaviour and re-infection.

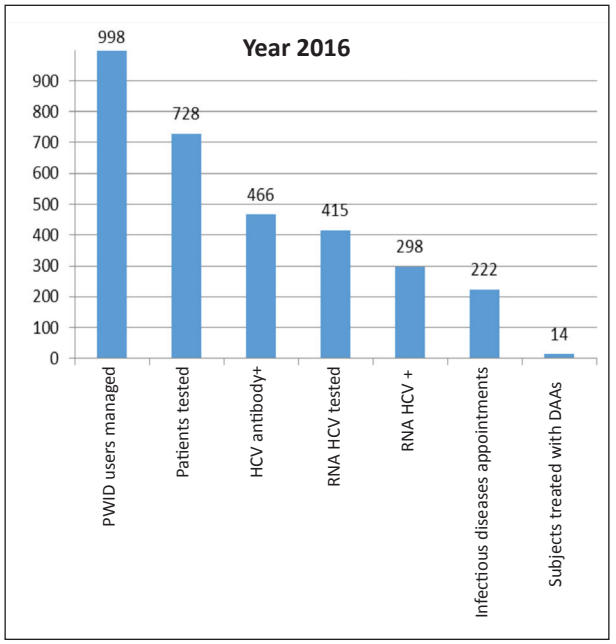

Figure 5. Cascade of care within Trieste DoD. Year 2016

Strong points of the coordinated approach

The preliminary data regarding the sustainability and the outcomes of the DAA treatment programme conducted by the Addiction Service are extremely encouraging. The adoption of a management model coordinated with infectious diseases specialists /hepatologists based on a proactive linkage to care approach that simplifies access to and retention in treatment, is able to avoid drop-outs and the risk of infection. In this approach, a key role is played by the screening clinic nursing staff, who manage the fiduciary relationship that motivates the patient.

The strong points are:

- Trained and dedicated staff (with the appointment of a specific dedicated nurse);
- On-site structured screening service, next to the treatment clinic;
- Pleasant, barrier-free, multipurpose outpatient facility environment;
- Long working hours, free, unpaid access;
- On-site management of the first and second level of the programme, in order to save time and favour an early start to treatment;
- Well-developed linkage activities that also make it possible to recruit individuals with more complex issues;
- Fiduciary partnership with infectious diseases/ hepatology specialists;
- Individualised treatment management, depending on the person's level of self-sufficiency;
- Availability of easy to take medicinal products, including single-dose pangenotypical products.

Financial resources for project consolidation

The coordinated approach proposed by Trieste Department of Dependency is based on a system envisaging dedicated human resources with special skill sets (multidisciplinary team in which a key role is played by the nurse), logistical resources (dedicated outpatient clinic), instrumental resources (medical equipment and material, hard- and software) and organisational resources (operative protocol, swift communication between partners, direction and shared programming of the various phases of activity, collection and dissemination of data, on-going innovation).

Discussion

The PWID population is more exposed to HCV viral infection than the general population. At-risk drug-taking practices, tattoos performed in unsterile conditions and unprotected sex are still the main risk factors. This target can be considered an HCV "reservoir" as prevalence in Italy amongst managed users is higher than 70%, compared to an average of 3% in the general population.

The percentage of untested users in Italian Addiction Services continues to increase and this alarming trend contributes to delaying diagnosis and access to antiviral therapies, with a considerable risk of a deterioration in the subject's clinical situation and unconscious transmission of the disease to others.

According to one study promoted by the Italian National Institute for Health (ISS), the lack of testing performed in Addiction Services would first and foremost appear to be associated with a series of factors such as restricted opening hours, no on-site blood

sample collection facility, the difficulties in identifying a peripheral venous entry portal and user fear/refusal.

The Trieste DoD approach provided a tangible response to these critical aspects by implementing an on-site, free of charge screening clinic that allows user anonymity and is open every morning from Monday to Friday. The close partnership with the local health authority's infectious diseases/hepatology specialists, which led to the preparation of a shared operational protocol, is managed by a purpose-built medical team within the drug Addiction Service. In addition to the specific infection situations, this makes it possible to deal with important health issues that complicate clinical management (psychiatric comorbidity, presence of psychosocial issues, resistance to care due to poor/inadequate information, difficult peripheral venous portals, severe skin lesions caused by "self-injection", feelings of shame and fear).

The rationale of the project is based on the assumption that implementing an HCV prevention, monitoring and treatment service characterised by an approach centring on the specific needs and characteristics of users could facilitate access to and compliance with the specialised programme, even in a high-risk, poorly-compliant population.

Despite the comforting data emerging from the application of the organisational and medical approach and the working method described, this project still has room for improvement. More specifically, the Service intends to increase the number of viraemic subjects who are assessed by the infectious diseases specialist/ hepatologist and those referred for DAA treatment and to reinforce the follow-up and harm-reduction activities, in order to prevent reinfection.

The main methodological and organisational principles of the model could be standardised and exported to other Italian Addiction Services.

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