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Abstract:	Background: HCV infection among vulnerable populations is currently a major issue for HCV elimination program. Incarcerated people and people who inject drugs (PWIDs) are key population groups potentially at high risk for HCV infection. Our aim was to evaluate an extended program of screening, staging and treatment in Italian prison settings. Methods: Patients from eight prisons in five different Italian Regions were enrolled. HCV saliva test (QuickOral Test ®) was offered. Data on infection awareness and illicit drug use were also collected. Positive patients underwent early HCV RNA evaluation, staging and prescription on DAAs treatment. The definition of PWID was based on self-reported injecting drug use extracted from medical records (injecting drug use during the previous six months). Results: A total of 2,376 out of 2,687 individuals (88%) was tested. The median (IQR) age was 42 (32-50) years. PWIDs were 537out of 2,376 (23%). Prevalence of HCV antibodies was 10.4% (248/2,376). PWIDs had a lower awareness of their HCV-Ab positivity than non-PWIDs (p -value <0.001). Furthermore, PWIDs were less likely to be previously treated than non-PWIDs (78% vs 96%, p -value= 0.017). Active infection was found in 41% of patients (101/248). Overall, 61% HCV-positive were PWIDs, with 44% HCV RNA positive. HCV therapy was prescribed to 83% (84/101) of patients with active HCV infection and 67% of these (56/84) were PWIDs. Prescription for HCV treatment in PWIDs accounted for 84% (56/67) (while for non-PWIDs was 82% (28/34) p -value: 0.88. Seventeen patients were referred to a Specialist in other prisons because they were going to be transferred soon to another prison. EOT, as well as SVR12 were achieved in 98% (82/84) treated patients. Conclusions: Among patients, PWIDs had a lower awareness of their HCV-Ab positivity and had previously received less treatments. Saliva test allowed to achieve a more rapid result, stage, and treatment approach. More than 80% of patients underwent treatment, without differences between PWIDs and non-PWIDs. Linkage to care during prison transfer allowed to avoid unplanned interruptions and offered more chances to reach the end of treatment.

Ethical Issues

This study was conducted in accordance with the Declaration of Helsinki. All patients signed an informed consent before participating, although data collection was anonymous. All studies regarding the Italian Penitentiary System are approved by Istituto Superiore di Sanità, Roma, Italy – PRE BIO CE n. 38762, req. 27/11/2018.

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Declaration of Competing Interest

The authors have no conflict of interest to declare.

HCV testing and treatment initiation in an Italian prison setting:

A step-by-step model to micro-eliminate hepatitis C

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Abstract

Background: HCV infection among vulnerable populations is currently a major issue for HCV elimination program. Incarcerated people and people who inject drugs (PWIDs) are key population groups potentially at high risk for HCV infection. Our aim was to evaluate an extended program of screening, staging and treatment in Italian prison settings.

Methods: Patients from eight prisons in five different Italian Regions were enrolled. HCV saliva test (QuickOral Test®) was offered. Data on infection awareness and illicit drug use were also collected. Positive patients underwent early HCV RNA evaluation, staging and prescription on DAAs treatment. The definition of PWID was based on self-reported injecting drug use extracted from medical records (injecting drug use during the previous six months).

Results: A total of 2,376 out of 2,687 individuals (88%) was tested. The median (IQR) age was 42 (32-50) years. PWIDs were 537out of 2,376 (23%). Prevalence of HCV antibodies was 10.4% (248/2,376). PWIDs had a lower awareness of their HCV-Ab positivity than non-PWIDs (*p*-value <0.001). Furthermore, PWIDs were less likely to be previously treated than non-PWIDs (78% vs 96%, *p*-value= 0.017). Active infection was found in 41% of patients (101/248). Overall, 61% HCV-positive were PWIDs, with 44% HCV RNA positive. HCV therapy was prescribed to 83% (84/101) of patients with active HCV infection and 67% of these (56/84) were PWIDs. Prescription for HCV treatment in PWIDs accounted for 84% (56/67) (while for non-PWIDs was 82% (28/34) *p*-value: 0.88. Seventeen patients were referred to a Specialist in other prisons because they were going to be transferred soon to another prison. EOT, as well as SVR12 were achieved in 98% (82/84) treated patients.

Conclusions: Among patients, PWIDs had a lower awareness of their HCV-Ab positivity and had previously received less treatments. Saliva test allowed to achieve a more rapid result, stage, and treatment approach. More than 80% of patients underwent treatment, without differences between PWIDs and non-PWIDs. Linkage to care during prison transfer allowed to avoid unplanned interruptions and offered more chances to reach the end of treatment.

Keywords: HCV; penitentiary settings; micro-elimination; PWIDs.

Introduction

Hepatitis C virus (HCV) infection is more prevalent in inmates than in the general population (Larney et al., 2013). High risk behaviors (e.g., people who inject drugs, PWIDs) and the probability of HCV transmission in the community after their release, makes inmates one of the target populations for HCV elimination (Rich et al., 2014).

In the direct acting antivirals (DAAs) era, shorter treatments with low adverse reaction rates increased the number of infected patients under therapy. Several scientific articles have been published on the feasibility and effectiveness of HCV therapy in prison, without updating the information about the epidemiological burden.

HCV prevalence among incarcerated patients was reported to be up to 38% in Italy in 2005 (Babudieri et al., 2005), with active HCV infection in ~90% anti-HCV positive patients. More recent data suggest a reduction to around 14% (Masarone et al., 2020). However, prevalence data on HCV among prisoners in Italy are based on old or monocentric cross-sectional studies, and characteristics of incarcerated people have probably changed a lot over the years. As of January 2019, data from Italian Ministry of Justice showed 60,125 daily inmates, and 50,000 new entries per year estimated, for a global annual population above 100,000 people (Italian Ministry of Justice, 2019). This brings the need to a reassessment, both for global prevalence and hepatitis staging and treatment. Furthermore, previous studies highlighted the close relationship between incarceration and injection drug use, with a substantial risk of HCV transmission in such settings. Italian Ministry of Justice official data highlighted that 21,213 imprisonments were due to drug offenses in 2019 (Italian Ministry of Justice, 2019). This condition may also lead to the possibility of non-sterile injection equipment use among people in prisons, with high HCV spread related to PWIDs (Italian Ministry of Justice, 2019; Larney et al., 2013; Stone et al., 2018). In the DAA era, the availability of a highly effective therapy

characterized by short treatment duration with few side effects could more easily lead to HCV micro-elimination in penitentiary settings, as well as among PWIDs. As previously discussed in literature, projects of micro-elimination are easier, cost-effective, and can lead to new models of care for different specific populations (Lazarus et al., 2018). As a consequence, HCV therapy in vulnerable populations has been proposed as one of the key strategies for HCV elimination. This is also in line with the priority of the European Association for the Study of Liver Disease (European Association for the Study of the Liver, 2018).

The aim of our study was to describe the current HCV prevalence, active infection rate, clinical features, and the efficacy of viral elimination strategy in Italian prisons proposed by Doctors and Nurses of the Italian Society of Penitentiary Healthcare (SIMSPe), with a focused insight on PWIDs.

Patients and methods

HCV micro-elimination in prison is a project promoted by SIMSPe with the aim to maximally increase the acceptance and the provision of HCV screening among inmates, the identification of unaware HCV positive prisoners, and the promotion of the linkage to care for HCV viremic patients. The goal of the project can be achieved through specific micro-elimination paths.

Eight penitentiary institutes located in five Italian Regions (Campania, Lazio, Liguria, Lombardia, Sardegna) were involved in a survey conducted between January and June 2019, whose focus was to assess differences on infection awareness between PWIDs and other patients, on previous treatment and therapy prescription during the incarceration. The only inclusion criterion for the study was being adult (>18 years old) and presently incarcerated.

Before offering HCV screening, a dedicated pre-testing phase was conducted. This was based on meetings including peer-to-peer education, and information provided by health-care providers on blood-borne viruses (BBV) transmission. Clinical history, serological status awareness, previous HCV treatment, and being PWID, were defined by medical records, compiled at prison admission, based on dependencies service evaluation, which are available in every Italian prison. PWID

definition by dependency service is based on the history of illicit substances injection during the last six months. Two or three penitentiary wards with around 50-60 patients were involved per meeting. At the end of the meetings, HCV saliva test (QuickOral Test®) was offered. Subsequently, patients with a positive test underwent staging with HCV RNA load, genotype, and FIB-4, the non-invasive estimate of liver scarring in HCV and HBV patients (Sterling et al., 2006), and therapy prescription in a maximum of one week, telematically. Venous blood samples were immediately collected from individuals with a positive saliva test. Viremic patients were prescribed DAAs, regardless of liver stage of fibrosis (AISF, 2019). Screening for other blood-borne viruses (i.e., HIV and HBsAg positive patients) were carried out. Drug choice depended on patient's characteristics and drug-drug interactions with chronic therapy. Available first-line treatments during the period of this study were glecaprevir/pibrentasvir, sofosbuvir/velpatasvir, and grazoprevir/elbasvir. Saliva tests and blood samples collection were conducted by the Specialists with dedicated nurses. Nurses were in charge of blood samples transport to the laboratories. The flow-chart showing our test, staging and treat model approach has been reported in figure 1.

Outcomes

Seroprevalence was based on the detection of HCV antibodies in screened inmates. HCV active infection was defined by the detection of HCV RNA. End of treatment (EOT) was defined as treatment completion, and sustained virological response (SVR 12) as HCV RNA undetectability after 12 weeks from the EOT. Virological failure was defined as positive HCV RNA at EOT. Breakthrough was defined as a new rise of viral load after an undetectability during treatment. Drop-outs were considered as unplanned interruptions during treatment.

Sample size and statistical analysis

Basing on prison population, a prevalence up to 38% (Sabbatani et al., 2004; Babudieri et al., 2005), a 0.05 precision and a confidence interval (CI) of 95%, the sample size needed was of 360 patients (confidence interval specified limits 33%-43%). Qualitative variables were summarized with absolute and relative (percentage) frequencies, whereas quantitative variables were described with means (standard deviations, SD) or medians (interquartile ranges, IQR), depending on their parametric and non-parametric distribution, respectively. Data were elaborated as numbers on total (percentages), means ± standard deviations and median (IQR). Categorical variables were evaluated with Chi-squared test or Fischer exact test, when appropriate.

Logistic regression analyses were carried out to assess the relationship between HCV-positivity or active HCV infection and epidemiological, clinical, and demographic variables.

A two-tailed *p*-value less than 0.05 was considered statistically significant. All statistical computations were carried out with the statistical software STATA version 16 (StatsCorp, Texas, USA).

Ethical issues

This study was conducted in accordance with the Declaration of Helsinki. All patients signed an informed consent before participating, although data collection was anonymous. Our HCV micro-elimination protocol into the Italian Penitentiary System was approved by Istituto Superiore di Sanità, Roma, Italy – PRE BIO CE n. 38762, req. 27/11/2018.

Results

HCV antibody prevalence, active infection and clinical features

A total of 2,687 persons were incarcerated in the recruited centers, accounting for 4.5% of the Italian penitentiary population.

Overall, 93% (2,498/2,687) incarcerated patients were involved in pre-testing phase; as 5% (122/2,687) refused to participate, and 7% (189/2,687) were counselled but released before the execution of the screening, a total of 88% (2,376/2,687) participants were tested. Of them, 98% (2,325/2,376) were male, 61% (1,448/2,376) were Italian, and the median (IQR) age was 42 (32-50) years. 23% (537/2,376) were PWIDs. HCV antibody prevalence was 10% (248/2,376). Active infection was found in 41% (101/248). When considering only the PWIDs subgroup, they represented 61% (152/248) of patients with positive HCV antibodies (HCV-Ab), and HCV RNA positive in 44% (67/152). It follows that PWIDs represented the 66% of the identified active HCV infections. Among patients with positive HCV antibodies, HCV active infection was found in 35% (78/223) and 92% (23/25) in those with and without Italian nationality, respectively. Male and female incarcerated patients showed active infection in 41% (97/239) and 44% (4/9) of the cases, respectively. Among PWIDs with or without opioid substitution therapy (OST), HCV active infection was detected in 17% (8/48) and 57% (59/104) individuals. HIV co-infected patients were HCV RNA positive in 100% (3/3) of cases.

The most frequent HCV genotype was 3a, found in 45% (45/101) of chronic infections. The majority had low FIB-4 values, showing a negative predictive value of 90% for advanced liver fibrosis (Table 1). When evaluating the relationship between patients who tested HCV-Ab positive, epidemiological and clinical variables, logistic regression showed that having Italian nationality, PWID, and being on OST were significantly associated with serological status (p-value <0.001), as reported in table 2.

Level of awareness among individuals who tested HCV antibody positive

Overall, 15% (38/248) of incarcerated patients who tested HCV antibody positive were unaware of their serological status, with 32% (12/38) showing an active HCV infection, and 75% (9/12) were PWIDs. Furthermore, when comparing serological status level of awareness, PWIDs had a lower awareness of their HCV antibody positive status.

In fact, PWIDs were aware in 78% (118/152), and non-PWIDs in 96% (92/96) of cases (*p- value* <0.001). In adjusted analyses, people with Italian nationality and those currently receiving OST had a lower odds of having active HCV infection (p-value <0.001). Evaluation of the relationship between active HCV-infection and epidemiological and clinical variables is reported in table 3.

Reasons of HCV RNA negativity and previous HCV treatment

Overall, 59% (147/248) incarcerated patients who tested HCV antibody positive were HCV RNA negative: 18% (26/147) had spontaneous clearance, and 82% (121/147) were treated: 21% (25/121) received interferon-based therapies, and 79% (96/121) were treated with DAAs. Among previously treated patients, 50% (60/121) were PWIDs. When comparing previous HCV treatment in PWIDs vs non-PWIDs, they were 47% (60/127) vs 64% (61/95) of cases, respectively (*p*-value= 0.017).

Treatment prescription, start and outcome

Overall, 83% (84/101) with viremic HCV infection were prescribed for HCV therapy, and 67% (56/84) were PWIDs. HCV treatment was prescribed to 84% (56/67) of PWIDs and to 82% (28/34) of non-PWIDs, *p*-value= 0.88. The remaining seventeen patients were near to prison transfer or release and were linked to the Specialist in the new correctional institute or outside to a referral center, to start antiviral therapy.

The used combinations were: 8-week therapy with glecaprevir/pibrentasvir (55/84, 66%), sofosbuvir/velpatasvir (26/84, 31%), and grazoprevir/elbasvir (3/84; 4%). EOT was achieved in 98% (82/84) patients. SVR12 rates were 100% (55/55) and 92% (22/24) for glecaprevir/pibrentasvir and sofosbuvir/velpatasvir, respectively. All patients who reached the EOT achieved SVR12. Two dropouts occurred following unexpected release from prison, and one was PWID; dropout rate in PWIDs vs non-PWIDs was 2% (1/56) vs 4% (1/28), *p*-value: 1.00. No breakthroughs were observed. The full cascade of care among incarcerated patients included in our study is shown in figure 2.

Discussion

High participation during the educational programs, acceptance of screening, rapid staging of antibody positive patients, were achieved in our cohort, as well as SVR12 rates, and no statistically significant differences occurred between PWIDs and non-PWIDs in HCV care.

The approach based on a step-by-step screening, with fast-track staging and treatment in prison micro-environments, as well as the possibility of linkage to care both in other correctional facilities and on territorial services, allows to guarantee maximum access to HCV treatment. We believe that a widespread extension of these procedures to all the 190 Italian penitentiary institutions can favor reduction of HCV spread.

As highlighted by previous data, HCV is the cause of chronic disease in more than 50% of patients admitted to hospital for liver problems (Sagnelli et al., 2016). Furthermore, it spreads among incarcerated people more than in the general population (Larney et al., 2013), thus inmates should be provided with counseling and have immediate access to HCV screening and treatment (Almasio et al., 2011).

Even if barriers to treatment initiation have not been clearly reported in studies on DAA-based therapies, the high cost of DAAs and doubts about being able to reach the EOT linked to the time spent in prison might influence the choice to start treatment by clinicians (Vroling et al., 2018).

Our study showed a high participation to educational meetings and acceptance to screening execution among incarcerated people. In fact, as previously discussed in the literature, HCV screening acceptance among inmates was at least doubled when information and educational programs were available, but there is still a lack of data about interventions for HCV cascade of care increase in prison settings (Kronfli et al., 2018).

For what concerns screening methods, saliva quick test allowed a rapid approach in staging without any therapeutic delays, in accordance with available literature. In fact, HCV point-of-care testing with rapid tests has been well described as a feasible and acceptable screening method among people in

prison, as well as a possible way to increase test and diagnosis among hard to reach populations (Beckwith et al., 2016; Bottero et al., 2015; Candfield et al., 2017).

Previous studies reported HCV antibody prevalence of 38%, with HCV RNA positivity in ~90% of cases (Babudieri et al., 2005). Our data found a lower prevalence (fourfold), and an unexpectedly lower viremic HCV infection levels (<50% of cases). HCV epidemiology is probably changing, including the epidemiological scenario in prison. Furthermore, active infection rate seems to be reduced due to wide DAAs use. The majority of people who tested HCV antibody positive and HCV RNA negative, had been previously treated with the new antiviral agents. However, some critical issues can be found, such as the level of awareness of infection among PWIDs. This represents a big challenge in some hard to reach populations. In fact, HCV screening is reported to be offered among PWIDs in no more than 60%–70% of cases, also when considering territorial assistance in methadone clinics (Litwin et al., 2009; Bachhuber et al., 2013). As reported by literature, there is a lack of PWIDs linkage to HCV care and <10% of PWIDs evaluated for HCV infection start antiviral therapy (Metha et al., 2008; Hellard et al., 2009, Norton et al., 2018). Furthermore, sometimes PWIDs seem to be excluded from treatment for perception of poor eligibility, compliance problems, and in treatment outcomes, as well as the possibility of re-infection (Norton et al., 2018).

Our study is concordant with the previous literature. In fact, PWIDs had been less frequently treated before incarceration with DAAs, when compared to non-PWIDs. Therefore, treating PWIDs during detention represents an optimal time for access to DAAs, with consequent benefits for public health and HCV elimination programs. Reaching vulnerable populations is one of the fundamental steps towards HCV elimination, as discussed in literature (Grebely et al., 2019).

When considering HCV-antibody positivity and epidemiological and clinical variables, having Italian nationality, being PWID and on OST were significantly associated with serological status.

Regarding HCV RNA, being on OST was highlighted as a factor associated to negative viremia. Also, Italian nationality appeared as a protective factor. However, the majority of the cohort was Italian, and this may represent a bias in our logistic regression analysis. In addition, a major administrative

problem must be pointed out, linked to the fact that foreigners in Italian prisons are frequently irregular migrants. For this reason, the Italian healthcare system does not allow any prescriptions when they are in freedom. Instead, incarceration allows foreigners to have a temporary access to healthcare system. This paradox makes treatment more accessible to incarcerated foreigners.

The majority of patients had a low level of liver fibrosis, according to FIB-4 values, datum concordant with the low median age of incarcerated population.

Previous data has demonstrated that prison release or transfer during therapy can influence retention and attainment of SVR in prison settings (Aspinall et al., 2016). Among prison-based studies where the SVR12 was 90% among people who remained in follow-up, the proportion of people with SVR by intent to treat is <70% as a result of loss to follow=up (Pontali et al., 2018; Overton et al., 2019; Papaluca et al., 2019). In the current study, patients near to transfer or release to freedom did not immediately start treatment, but were staged and linked to care in the new penitentiary institute or in the referral center, both guaranteeing treatment and avoiding unplanned interruption, resulting in a higher treatment coverage. As such, our cohort demonstrated higher retention in care, minimizing loss to follow-up which was associated with higher intent to treatment SVR compared to previous studies (Pontali et al., 2018; Overton et al., 2019; Papaluca et al., 2019).

Although BBV infections are higher among incarcerated patients and PWIDs than in the general population, there is a lack of interventions to prevent, quickly diagnose, and treat these hard to reach populations. Focused programs should be implemented, given the challenge of reaching prospective patients in community settings, thus for these vulnerable groups the prison setting represents a big opportunity for BBV prevention and treatment as discussed in the literature (Dolan et al., 2016).

Surely, the approach of fast-track treatment and linkage to care represent a major advantage in reaching WHO targets (WHO, 2016).

Our experience highlights the high level of acceptance for both tests and treatment by incarcerated patients. When information is clear and correctly provided, together with appropriate communication

methods, there is no limitation in health care provision and use regarding HCV infection control in prisons.

In conclusion, extended programs of education with subsequent tests, staging, and treatment for HCV, seem to be highly feasible in prison settings, independently of patient's risk factors. Furthermore, linkage to care in other centers allows to reduce the possibility of unplanned interruptions. The current incarcerated society is the future outside community, and extended programs of HCV healthcare provision should be implemented without delays. Currently, point of care testing, HCV RNA rapid test, and pangenotypic DAAs are available, so a widespread use of these interventions could be the next step towards an even faster diagnostic and therapeutic path. This would allow to easily reach WHO targets, reducing possibilities of advanced liver disease development, as well as extending benefits to the entire community after prison release.

Limitations of the study

Some limitations should be addressed regarding our study. Specifically, no data regarding treatment and SVR12 rates among patients linked to care in other centers were collected.

Regarding the gender of population, only 2.1% (51/2,376) were female. In Italian penitentiary settings the 4.4% of incarcerated people are female. Instead, women recruited during our study with active HCV infection were only 3.9% (4); although they were all treated and reached the SVR12, the sample was too small. It follows that this is an even more difficult population to reach.

When defining PWIDs, data were carried out from patient's medical records at admission. This might lead to an underestimation of people injecting illicit drugs and there might be a bias towards identifying some people as non-injectors. However, given the fact that SVR rates were similar between those identified as injecting drug users and those who were not, and SVR was high across all participants, this would have had low impact on our results. Generally, it is very difficult to evaluate active drug users during detention as needle and syringe programmes are not available in Italy, and this also makes more difficult to assess potential illicit drug use among incarcerated people.

As far as clinical information on liver comorbidities are concerned, data on ethanol consumption, metabolic, and psychiatric disorders were not collected, even though such information would be useful to better define patients with higher FIB-4 values.

When considering nationality, being Italian had a positive association with HCV-Ab positivity. Instead, it appeared to be a protective factor for active HCV infection. As discussed, the majority of the cohort was Italian while foreign inmates were irregular migrants. This may have affected our analysis. It should also be taken into consideration that in our system it is easier to follow-up Italian individuals as they also tend to access more easily to methadone clinics.

Moreover, as our data come from 4.5% of all Italian penitentiary Institutes, we were unable to compare participating and non-participating centers. As a result, our survey may not completely reflect the national situation.

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Declaration of Competing Interest

The authors have no conflict of interest to declare.

References

AISF (2019) Documento di indirizzo dell'Associazione Italiana per lo Studio del Fegato per l'uso razionale dei farmaci anti-HCV disponibili in Italia. Retrieved 3rd June 2019 from https://www.webaisf.org/wp-content/uploads/2019/01/documento_hcv_200618.pdf.

Almasio, P.L., Babudieri, S., Barbarini, G., Brunetto, M., Conte, D., Dentico, P., et al (2011). Recommendations for the prevention, diagnosis, and treatment of chronic hepatitis B and C in special population groups (migrants, intravenous drug users and prison inmates). *Digestive and Liver Disease*, 43, 589- 595.

Aspinall, E.J., Mitchell, W., Schofield, J., Cairns, A., Lamond, S., Bramley, P., et al. (2016). A matched comparison study of hepatitis C treatment outcomes in the prison and community setting, and an analysis of the impact of prison release or transfer during therapy. *Journal of Viral Hepatitis*, 23, 1009-1016.

Babudieri, S., Longo, B., Sarmati, L., Starnini, G., Dori, L., Suligoi, B., et al. (2005) Correlates of HIV, HBV, and HCV infections in a prison inmate population: results from a multicentre study in Italy. *Journal of Medical Virology*,76, 311–317.

Bachhuber, M.A., & Cunningham, C.O. (2013). Changes in testing for human immunodeficiency virus, sexually transmitted infections, and hepatitis C virus in opioid treatment programs. *JAMA*, 310, 2671-2672.

Beckwith, C. G., Kurth, A. E., Bazerman, L., Solomon, L., Patry, E., Rich, J. D., et al. (2015). Survey of US correctional institutions for routine HCV testing. *American Journal of Public Health*, 105, 68–71.

Bottero, J., Boyd, A., Gozlan, J., Carrat, F., Nau, J., Pauti, M.-D., et al. (2015). Simultaneous human immunodeficiency virus-hepatitis B-hepatitis C point-of-care tests improve outcomes in linkage-to-care: Results of a randomised control trial in persons without healthcare coverage. *Open Forum Infectious Diseases*, 2, ofv162-fv162.

Candfield, S., Samuel, M. I., Ritchie, D., McDonald, C., Brady, M., et al. (2017). Use and acceptability of salivary hepatitis C virus testing in an English Young Offender Institution. *International Journal of STD & AIDS*, 28, 1234-1238.

Dolan, K., Wirtz, A.L., Moazen, B., Ndeffo-Mbah, M., Galvani, A., Kinner, S.A. et al. (2016). Dolan K, Wirtz AL, Moazen B, et al. Global burden of HIV, viral hepatitis, and tuberculosis in prisoners and detainees. *Lancet*, 388, 1089-1102.

European Association for the Study of the Liver (2018). EASL Recommendations on Treatment of Hepatitis C. *Journal of Hepatology*, 69, 461-511.

Grebely, J., Hajarizadeh, B., Lazarus, J.V., Bruneau, J., & Treloar, C. International Network on Hepatitis in Substance Users. (2019). Elimination of hepatitis C virus infection among people who use drugs: Ensuring equitable access to prevention, treatment, and care for all. *International Journal of Drug Policy*, 72, 1-10.

Hellard, M., Sacks-Davis, R., Gold, J. (2009). Hepatitis C treatment for injection drug users: a review of the available evidence. *Clinical Infectious Diseases*, 49, 561-573.

Italian Ministry of Justice statistics. Retrieved 2nd December 2019 from https://www.giustizia.it/giustizia/it/mg_1_14.page.

Kronfli, N., Linthwaitea, B., Kouyoumdjianb, F., Kleina, M.B., Lebouchéa, B., Sebastiani, G. et al. (2018). Interventions to increase testing, linkage to care and treatment of hepatitis C virus (HCV) infection among people in prisons: A systematic review. *International Journal of Drug Policy*, 57:95-103.

Larney, S., Kopinski, H., Beckwith, C.G., Zaller, N.D., Jarlais, D.D., Hagan, H., et al. (2013). Incidence and prevalence of hepatitis C in prisons and other closed settings: results of a systematic review and meta-analysis. *Hepatology*, 58, 1215–1224.

Lazarus, J.V., Safreed-Harmon, K., Thursz, M.R. 2, Dillon, J.F., El-Sayed, M.H., Elsharkawy, A.M., et al. (2018). The Micro-Elimination Approach to Eliminating Hepatitis C: Strategic and Operational Considerations. S*eminars in Liver Disease*, 38, 181-192.

Litwin, A.H., Harris, K.A. Jr., Nahvi, S., Zamor P.J., Soloway I.J., Tenore, P.L., et al. (2009). Successful treatment of chronic hepatitis C with pegylated interferon in combination with ribavirin in a methadone maintenance treatment program. *Journal of Substance Abuse Treatment*, 37, 32–40.

Masarone, M., Caruso, R., Aglitti, A., Izzo, C., De Matteis, G., Attianese, M.R., et al. (2020). Hepatitis C virus infection in jail: Difficult to reach, not to treat. Results of a point-of-care screening and treatment program. *Digestive and Liver Disease*, 52, 541-546.

Mehta, S.H., Genberg, B.L., Astemborski, J., Kavasery, R., Kirk, G.D., Vlahov, D., et al. (2008). Limited uptake of hepatitis C treatment among injection drug users. *Journal of Community Health*, 33, 126-133.

Norton, B.L., Akiyama, M.J., Zamor, P.J., & Litwin, A.H. (2018). Treatment of Chronic Hepatitis C in Patients Receiving Opioid Agonist Therapy: A Review of Best Practice. *Infectious Disease Clinics of North America*, 32, 347- 370.

Overton, K., Clegg, J., Pekin, F., Wood, J., McGrath, C., Lloyd, A. (2019). Outcomes of a nurse-led model of care for hepatitis C assessment and treatment with direct-acting antivirals in the custodial setting. *International Journal of Drug Policy*, 72, 123-128.

Papaluca, T., McDonald, L., Craigie, A., Gibson, A., Desmond, P., Wong, D., et al. Outcomes of treatment for hepatitis C in prisoners using a nurse-led, statewide model of care. *Journal of Hepatology*, 2019, 70, 839-846.

Pontali, E., Fiore, V., Ialungo, A.M., Ranieri, R., Mollaretti, O., Barbarini, G., et al. (2018). Treatment with direct-acting antivirals in a multicenter cohort of HCV-infected inmates in Italy. *International Journal of Drug Policy*, 59, 50-53.

Rich, J.D., Allen, S.A., & Williams, B.A. (2014). Responding to hepatitis C through the criminal justice system. *New England Journal of Medicine*, 370, 1871- 1874.

Sabbatani, S., Giuliani, R., Fulgaro, C., Paolillo, P., Baldi, E., & Chiodo, F. (2004). HIVAb, HCVAb and HBsAg seroprevalence among inmates of the prison of Bologna and the effect of counselling on the compliance of proposed tests. *Epidemiologia e prevenzione*, 28, 163–168.

Sagnelli, E., Stroffolini, T., Sagnelli, C., Smedile, A., Morisco, F., Furlan, C., et al. (2016). Epidemiological and clinical scenario of chronic liver diseases in Italy: Data from a multicenter nationwide survey. *Digestive and Liver Disease,* 48,1066- 1071.

Sterling, R.K., Lissen, E., Clumeck, N., Sola, R., Correa, M.C., Montaner, J., et al. (2006). Development of a simple noninvasive index to predict significant fibrosis patients with HIV/HCV co-infection. *Hepatology*, 43, 1317-1325.

Stone, J., Fraser, H., Lim, A.G., Walker, J.G., Ward, Z., Louis MacGregor Stone J, Fraser H, Lim AG, et al. (2018). Incarceration history and risk of HIV and hepatitis C virus acquisition among people who inject drugs: a systematic review and meta-analysis. *Lancet Infectious Diseases*,18, 1397-1409.

Vroling, H, Oordt-Speets, A.M., Madeddu, G., Babudieri, S., Monarca, M., O'Moore, E., et al. (2018). A systematic review on models of care effectiveness and barriers to Hepatitis C treatment in prison settings in the EU/EEA. *Journal of Viral Hepatitis*, 25, 1406-1422.

WHO (2016). Combating hepatitis B and C to reach elimination by 2030. Geneva, Switzerland.

Figure 1. Flow-chart approach: test, staging and treatment model

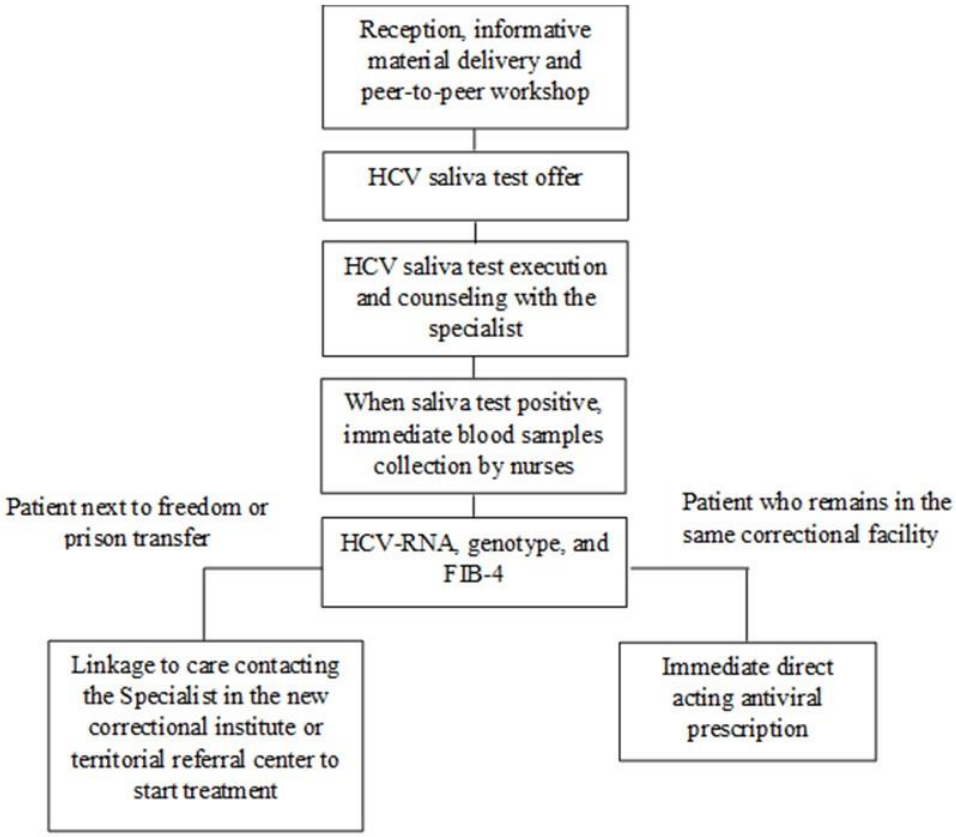

Table 1. Demographics and clinical characteristics of HCV infected prisoners enrolled in our study.

Variable		Treated (n=84)	Untreated (n=17)
Italian nationality, n (%)		61 (60.4)	17 (100)
Mean (SD) age, years		42.3 (10.7)	40 (10.7)
Males, n (%)		80 (95.2)	17 (100)
PWIDs, n (%)		56 (66.6)	11 (64.7)
On OST, n (%)		8/56 (14.3)	-
HBsAg n (%)		-	-
HIV, n (%)		3 (3.6)	-
On ART, n (%)		3/3 (100)	-
Median (IQR) HCV RNA value		432,300 (97,475-997,500)	280,000 (97,950-4,570,000)
Genotype distribution, n (%)	1a	28 (33.3)	8 (47)
	1b	6 (7.1)	1 (5.9)
	2	-	1 (5.9)
	3a	38 (45.2)	7 (41.2)
	4	12 (14.3)	-
FIB-4 value, n (%)	Low (<1.45)	56 (66.6)	16 (94.1)
	Intermediate (1.45-3.25)	25 (29.8)	-
	Advanced (>3.25)	3 (3.6)	1 (5.9)

IQR: Interquartile range; PWIDs: people who inject drugs; OST: opioid substitution therapy; ART: anti-retroviral therapy.

Table 2. Logistic regression analysis aimed at evaluating the relationship between HCV-antibody positivity and epidemiological and clinical variables.

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	***p*-value**	**OR (95% CI)**	***p*-value**
Italian nationality	6.6 (4.3-10.0)	<0.001	4.3 (2.7-6.7)	<0.001
Age, years	1.0 (1.0-1.0)	0.07	1.0 (1.0-1.0)	0.32
Male	0.5 (0.3-1.1)	0.09	0.6 (0.3-1.4)	0.23
PWIDs	7.2 (5.4-9.5)	<0.001	3.6 (2.6-5.0)	<0.001
On OST	15.2 (9.6-24.3)	<0.001	5.5 (3.3-9.1)	<0.001
HIV-positivity	26.1 (2.7-251.4)	0.005	8.8 (0.7-120.7)	0.10

PWIDs: people who inject drugs; OST: opioid substitution therapy

Table 3. Logistic regression analysis aimed at evaluating the relationship between active HCV-infection and epidemiological and clinical variables.

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	***p*-value**	**OR (95% CI)**	***p*-value**
Italian nationality	0.05 (0.01-0.20)	<0.001	0.03 (0.01-0.13)	<0.001
Age, years	1.0 (1.0-1.0)	0.29	1.0 (1.0-1.1)	0.05
Male	0.9 (0.2-3.3)	0.82	1.2 (0.3-5.3)	0.82
PWIDs	1.4 (0.9-2.4)	0.18	-	-
On OST	0.2 (0.1-0.5)	<0.001	0.2 (0.1-0.39)	<0.001
Previous awareness	1.6 (0.8-3.3)	0.21	-	-

PWIDs: people who inject drugs; OST: opioid substitution therapy

Figure 2. Cascade of care among incarcerated people enrolled in a multicentric Italian survey.