

From Prioritization to Universal Treatment: Successes and Challenges of Hepatitis C Virus Elimination in Italy

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Italy has had the highest prevalence of hepatitis C virus (HCV) infection and mortality from HCV-related liver cancer in Europe. Although direct-acting antivirals (DAA) were initially restricted to persons with advanced fibrosis, their use has since been extended to all infected individuals; more than 244 000 persons have been treated to date. HCV liver-related mortality is expected to decline by 75% by 2030, achieving the World Health Organization target for mortality. However, Italy risks failing to meet the overall goal of eliminating HCV infection by 2030. In this light, €71.5 million have been allocated for screening initially specific target populations (persons who inject drugs, prison inmates, and the 1969–1989 birth cohort). Herein, we outline the challenges and recommendations for how to move Italy toward HCV elimination, including expanding screening programs in other populations, increasing awareness through strategic communication, sustaining DAA access, and tailoring care models to meet the needs of key populations.

Keywords. HCV; HCV model of care; PWID; WHO elimination targets; global burden of disease; inmates; linkage to care; public health; screening; viral hepatitis elimination.

In this article, we outline the challenges for eliminating infection due to the hepatitis C virus (HCV) in Italy, focusing on expanding screening programs, increasing awareness of (and access to) screening and direct-acting antivirals (DAA), and adopting treatment and care models tailored to meet the needs of the affected populations.

At the end of the second millennium, Italy had the highest prevalence of chronic HCV infection in Europe, as well as the greatest number of deaths due to HCV-related hepatocellular carcinoma (HCC) and cirrhosis [1]. Before DAAs were introduced in Italy in 2015, Italy had the highest mortality rate from viral hepatitis overall, compared to other European Union countries, with 38 deaths per 1 million inhabitants in 2016 [2]. The high prevalence of severe liver disease and

mortality can be explained by long duration of infection due to an intensive epidemic wave of HCV infection in the 1950s–1960s, which was mainly attributed to the use of glass syringes for vaccinations and for the injection of antibiotics and vitamins and poor hygiene during invasive medical procedures. In other European countries, the most intense epidemic waves occurred in the 1980s–1990s and were mainly associated with intravenous drug use; at this time, a second epidemic wave also occurred in Italy [3, 4]. The incidence of HCV infection through iatrogenic routes and blood transfusion (first epidemic wave) has decreased over time in Italy, reaching a 98% decrease in risk in 2000 [5].

Because of the high numbers of patients with advanced liver disease, when DAAs were first introduced in 2015, their high cost demanded that treatment be restricted to groups whose immediate need for treatment was deemed most urgent, specifically, persons with stages F3 and F4 liver fibrosis and cirrhosis. Despite these restrictions, between 2015 and 2017, Italy treated more people than any other country in Europe (approximately 74 000 individuals), successfully eradicating HCV in persons with advanced liver disease [6, 7]. Based on these figures, HCV-related mortality in Italy is expected to decrease by 75% by 2030, allowing Italy to meet the goal of the World

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Health Organization (WHO) for HCV mortality reduction [8, 9]. In light of this success, at the time in Italy, it was decided to continue to provide DAAs at no cost to patients, with €1.6 billion budgeted for treatment through 2019. Moreover, in 2018, DAAs were made available to all persons diagnosed with HCV infection and were no longer restricted to those with advanced fibrosis (Figure 1).

Although the impact of treatment on the incidence of new infections and the progression of chronic liver disease is not evident yet, the burden of HCV-related morbidity seems to be decreasing. This is also suggested by a recent study that reviewed all primary and secondary discharge diagnoses of HCV-related cirrhosis, and HCC from public and private Italian hospitals in the period 2012–2019. Specifically, there was a 40% reduction in new HCV-cirrhosis-related hospitalizations (from 73 cases per 100 000 inhabitants in 2012 to 44 in 2019), as well as a decrease in incident cases of HCC due to HCV (from 52 to 45 per 100 000 inhabitants). Moreover, for HCV-related cirrhosis and HCC, the reduction was more significant in the period 2016–2019 (compared to 2012–2015), suggesting that it was in large part attributable to the expanded access to DAA treatment [10].

Considering this high treatment coverage, Italy was 1 of the 12 countries in the world on track to achieve the 2030 HCV elimination goals defined by WHO, as long as 40 000 patients continued to be treated every year until 2030 [9, 11]. However, beginning in 2019, the number of individuals treated each year began to decrease [7]. Although this was mainly attributed to the fact that a large proportion of the persons identified as needed to receive treatment had already done so (and also to the limited access to health care services resulting from the coronavirus disease 2019 [COVID-19] pandemic), an estimated 398 610 infected persons in Italy had not been diagnosed [12, 13]. In fact, a study showed that without extensive screening for HCV infection, the pool of eligible persons to be treated would run out between 2025 and 2028, leaving many individuals undiagnosed and without treatment [8]. In light of this [9, 14], and based on this trajectory of the number of treated patients in the future, the Polaris Observatory Foundation predicted that Italy would not achieve the HCV elimination goals set by WHO (Figure 2, updated 22 September 2022, personal communication from S. Blach, CDA Foundation).

To address this gap in diagnoses (and ultimately achieve the goal of eliminating HCV infection), the only effective tool is mass screening [8]. However, it was necessary to convince policymakers to make the necessary resources available. To do so, additional analyses of the cost-effectiveness and the cost-benefits of screening and treatment were performed. A cost-benefit study conducted in Italy estimated that treating and eliminating HCV from a sample of 1000 patients standardized for stage of fibrosis and age would allow more than 1200 events related to HCC, decompensated cirrhosis, and liver transplant to be avoided over a 20-year period for persons treated in the

period 2015–2016 and approximately 630 events to be avoided for those treated in 2017–2019. In monetary terms, the health care system would save from €45 to €275 million, and the investment in expanding access to DAAs would be recovered in less than five and a half years [15]. Furthermore, screening the 1948–1988 birth cohorts from the general population was shown to be a cost-effective strategy, with the final goal of achieving HCV elimination by 2030. Although universal screening is actually cost-effective, the most cost-effective strategy is to screen individuals born in the period 1948–1988. However, the sustainability and feasibility of this approach are a major challenge. It was thus determined that the best approach is to perform graduated screening, first among the younger population (individuals born in 1968–1988), who are at higher risk of transmission (thus, mainly to reduce the rate of new infections) and then among the older population (to further reduce prevalence and disease progression) [16].

In June 2022, the Coalition for Global Hepatitis released the National Hepatitis Elimination Profile for Italy, in collaboration with several Italian stakeholders. The present article builds upon this profile, outlining the challenges and recommendations for how to get Italy back on track for meeting its goals for HCV elimination (Figure 3) [17].

SEEKING THE UNDIAGNOSED: HEALTH POLICIES FOR GUARANTEEING ACCESS TO TREATMENT TO ALL INFECTED PEOPLE

Programmatic Approach to Increase HCV Diagnosis and Linkage to Care

Based on evidence and recommendations provided by diverse stakeholders with a strong commitment to eliminating HCV infection (eg, the central government, the *Istituto Superiore di Sanità* [Italy's National Institute of Public Health], scientific societies, and patient association), the Ministry of Health approved specific legislation (Ministry of Health Decree of 14 May 2021), and €71.5 million were allocated for the years 2020–2021 to develop a free-of-charge HCV screening program [18] (Figure 4). This screening campaign focuses on key populations, specifically, persons who inject drugs (PWIDs) covered by the services for the territorial dependencies (SerD), prison inmates, and general population cohorts born in 1969–1989. The infection in this birth cohort belongs mainly to the second epidemic wave of HCV infection in Italy due to the widespread intravenous drug use since 1980–1990 and at-risk sexual behavior, and percutaneous exposure from beauty or medical treatments [4, 13]. To date, the estimated prevalence of active infections in this birth cohort is around 0.6%; these individuals are frequently not symptomatic and thus not yet diagnosed, although they have a high risk of transmitting the infection to others [13, 19, 20].

According to this screening campaign, primary health care providers and clinicians working in prevention services, prison

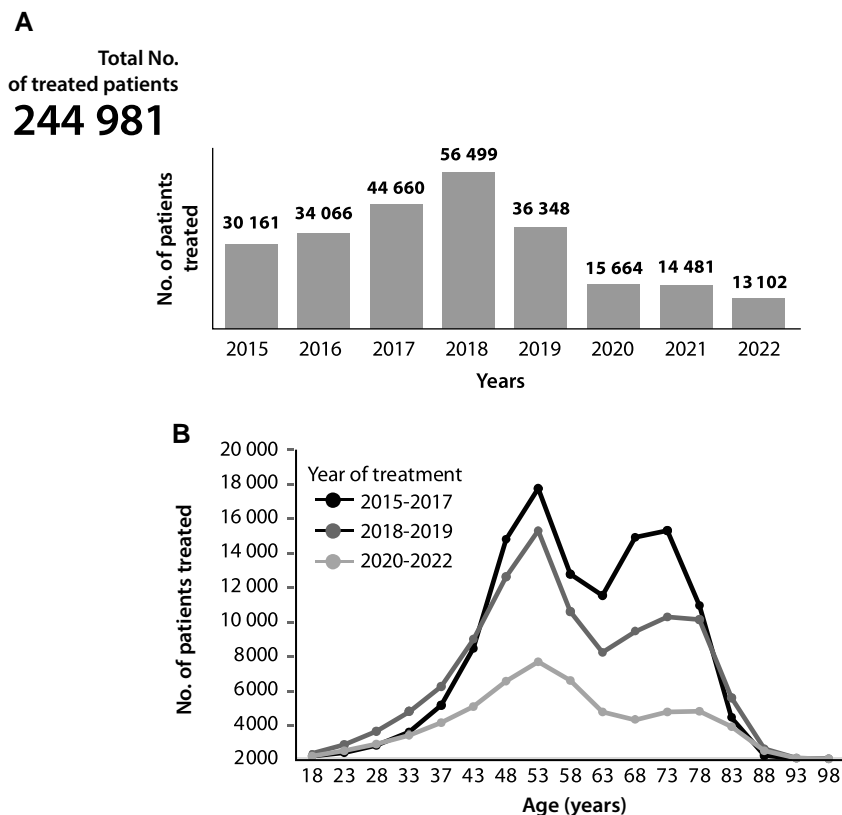


Figure 1. A, Number of patients with HCV treated per year; and (B) number of patients with HCV treated per year by age group as reported by the Italian Medicines Agency Registry for Direct Acting Antivirals (DAA) Monitoring.

health services, and SerD can reach out to individuals through various means, not only during visits but also by way of active calls. Additionally, screening could be performed on hospital patients (both inpatients and outpatients) who belong to the target population. Moreover, the above decree recommends using reflex testing to detect active HCV infection in a single-step diagnosis. In PWIDs specifically, the decree recommends using rapid HCV RNA point-of-care testing as the single step for identifying active HCV infection. Not only does this reduce the time from diagnosis to treatment in a population that has been traditionally difficult to reach, but counseling and harm reduction services could also be provided (Ministry of Health Decree of 14 May 2021) [18].

This program was initially meant to last for 2 years, but because of the COVID-19 epidemic it has been extended until 2023. There are also plans to expand the program to other birth cohorts of the general population, although this has yet to be implemented [17]. As of this writing, data from this screening program are not yet available from Italy's regions.

Challenges to Implementing and Expanding Screening

Diagnosing individuals with HCV infection, particularly those populations who have been difficult to reach, presents some unique challenges, some of which are highlighted here. A major

challenge is that Italy's health care system is largely decentralized among its 20 regions. Of course, legislation and policies exist at the national level: the National Hepatitis Prevention Plan was implemented in 2015 [21] and was transformed into the National Hepatitis Elimination Plan in 2020, not to mention the recently updated national guidelines for the diagnosis and treatment of HCV infection [22]. However, the country's individual regions have a great amount of autonomy in planning, organizing, and financing health care services within their area, resulting in inconsistencies among the regions in how screening is implemented. As of the end of 2022, fewer than half of the regions have started to conduct screening, and most screening activities have only involved prevention services and not primary health care doctors, who would be responsible for reaching the general population. Moreover, the funds allocated by the central government only cover the cost of the actual screening kit: all other costs must be covered by the regions, and no specific funding has yet been allocated for the other activities proposed for the HCV screening program.

As mentioned, a large percentage of the infected population has not been diagnosed; a related concern is late diagnosis, which continues to be an important challenge. Recent data from hospitals and primary health care doctors have shown

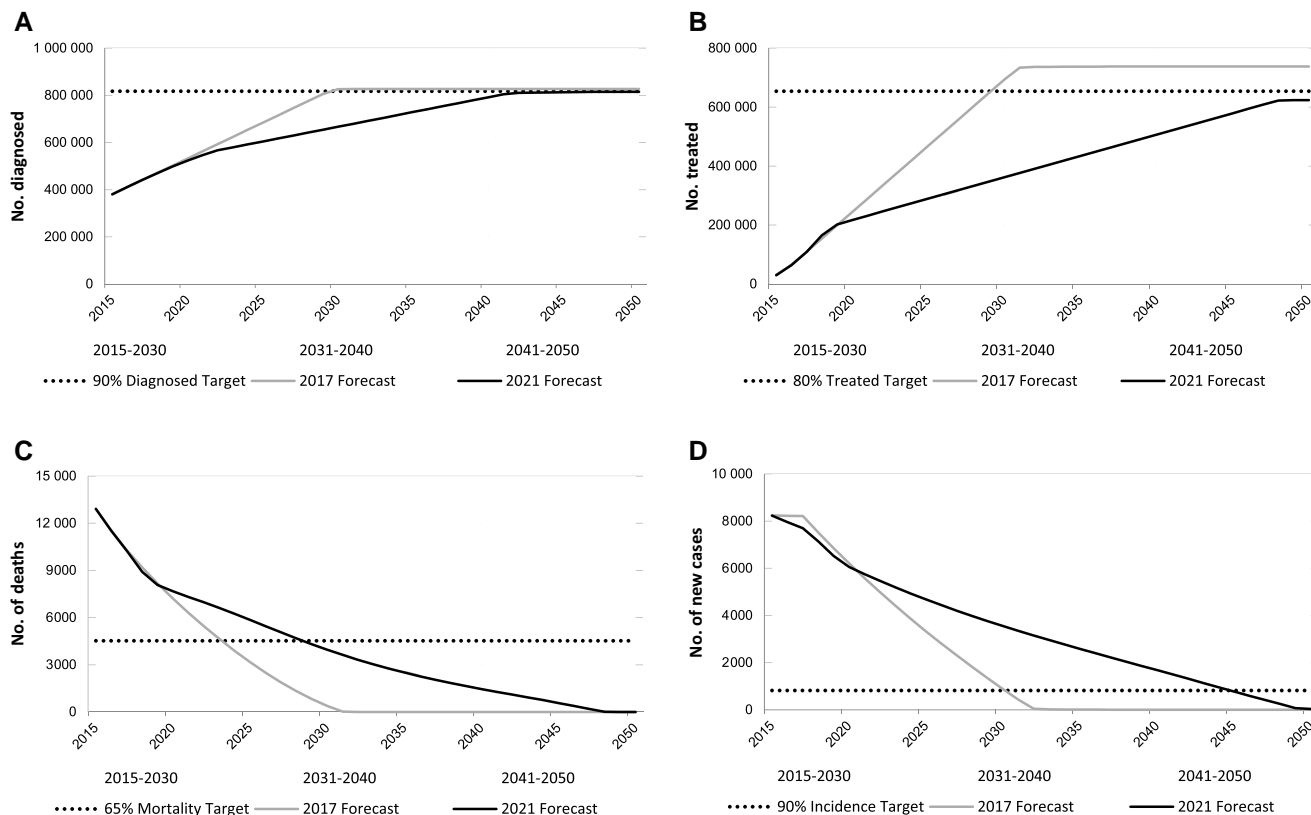


Figure 2. The number of years needed to achieve the World Health Organization (WHO) elimination goals in Italy, by scenario. Horizontal dotted lines identify the achievement of the WHO targets for diagnosis, treatment, correlated deaths, and new infections. The grey lines identify the year of achievement of WHO targets if the treatment rates remain as in 2017. The black lines identify the year of achievement of WHO targets considering the treatment rates up to 2021 declining even further without expanding screening and cure of asymptomatic hepatitis C virus (HCV) infections. *A*, Cumulative diagnosed: target, 90% diagnosed by 2030; 2017 scenario, by 2030, 90% of viremic patients will be diagnosed; 2021 scenario, by 2030, fewer than 90% of viremic patients will be diagnosed. It will take more than 12 years, given the scenario-specific diagnosis, to achieve the diagnosis target. *B*, Cumulative treated: target, 80% treated in 2030; 2017 scenario, the model estimates 80% of patients will be treated by 2030; 2021 scenario, the model estimates, given the scenario-specific diagnosis and treatment rates without expanding screening, the treatment target will be not be achieved even over 2050. *C*, Liver-related deaths: target, 65% reduction in HCV correlated deaths (this target is achievable in Italy with both scenarios); 2017 scenario, the target is achievable by 2023; 2021 scenario, the target is achievable 7 years later, by 2030. *D*, New acute infections: target, 90% reduction of new HCV infections; 2017 scenario, the 90% reduction of new infections will be achieved by 2030; 2019 scenario, the target is achievable 15 years later, in 2045.

an increased rate of active infection in patients who have never been tested or linked to care for HCV infection [23–25]. Late diagnosis in persons with severe liver damage has also been documented by the DAA Monitoring Registry of the Italian Medicine Agency: more than 20% of treated patients in the last years had liver cirrhosis, patients would have been treated since 2015 [7]. Active screening of individuals in the 1948–1968 birth cohorts in Italy, yet not addressed for free-of-charge screening, could identify an estimated 110 000 persons (mainly over 50 years of age) with active HCV infection and advanced liver disease [13, 19, 20]. The widespread phenomenon of late diagnosis also stresses the clear need to educate general practitioners and other health care professionals on the importance of HCV testing among persons seeking medical care for other conditions, particularly those associated with HCV extrahepatic manifestations such as diabetes, renal disorders, vasculitis, etc. [26].

Challenges Concerning Awareness and Engagement in the Screening Campaign

Among the challenges that Italy faces today to achieve the goal of HCV elimination, encouraging and convincing people to get tested is one of the hardest and most underrated [27]. When planning HCV screening, policymakers should consider that some population groups need to be convinced to undergo testing and treatment. Individuals may not be aware that they are at risk of infection, or they may be wary of the stigma associated with infection. They may also not be aware that effective treatment is available and thus not believe that it is even worth being tested. Furthermore, some individuals may have difficulties expressing a specific request for testing and/or treatment, or they may be discouraged by the complexity of the access to available testing and treatment [28]. These reasons can also be influenced by extraclinical factors, such as socioeconomic status, work-related issues, and geographic area (ie, there may be fewer facilities in certain areas),

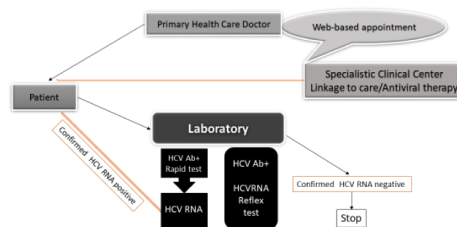
STRATEGIC INFORMATION

Mortality	Not Adopted Modelled
Incidence	Partially Adopted
Prevalence	Partially Adopted Modelled
Estimates of HCV economic burden	Adopted
Monitoring HCV diagnosis and treatment	Partially Adopted
HCV testing of pregnant women	Adopted
TESTING TO DIAGNOSE HCV INFECTION	
Risk Based	Adopted
Universal	Partially Adopted
HCV: Registration of originator DAAs	Adopted
HCV: Eligible for generic DAAs	Not Eligible
Licensed point-of-care PCR testing to detect HCV	Partially Adopted
HCV: NATIONAL TREATMENT GUIDELINES	Developed
Simplified care algorithm: Less than 2 clinic visits during treatment	Partially Adopted
Simplified care algorithm: Non specialists can prescribe treatment	Not Adopted
Simplified care algorithm: No patient treatment co-pays	Adopted
Public budget line HCV testing and treatment	Adopted
No fibrosis and No sobriety restrictions	Adopted
No genotyping	Not Adopted
National strategy addresses populations most affected	Adopted
NATIONAL POLICY FOR	Adopted
Harm reduction for persons who inject drugs (PWID)	Developed
Syringe exchange in federal prisons	No Data
Number of needles/syringes per PWID per year	No Data
Decriminalization of possession of syringes & paraphernalia	Adopted
Decriminalization of drug use	Adopted

Figure 3. HCV elimination-related health policies in Italy adopted by the National Hepatitis Elimination Plan. Abbreviations: DAA, direct-acting antiviral; HCV, hepatitis C virus; PCR, polymerase chain reaction; PWID, people who inject drugs.



- Implementation of innovative active screening strategies beyond a risk-based approach
- Approach Hepatitis C Virus Screening by **systematic opportunistic hepatitis testing** in emergency departments and for all in and outpatients admitted to the hospital.



Implement alerts to remind General Practitioner to test individuals of a targeted cohorts or whole population (e.g. electronic health records used to remind physicians through alerts that a patient who has never been screened should be tested)



- Intensify the commitment for training, information and collaboration between Primary Health Care doctor and Specialists

Figure 4. Italian Ministry of Health decree indications regarding HCV screening in the general population. Abbreviations: Ab, antibody; HCV, hepatitis C virus.

all of which can result in inequalities. These concerns have yet to be addressed at the national or regional level. In this light, communication strategies for both professionals involved in implementing screening and the general public should raise awareness of HCV infection, disease and its health risks, at-risk behavior, and the safety and effectiveness of the most up-to-date treatment. Moreover, these strategies should promote active participation and generate behavioral change, which are essential for improving adherence to treatment, adoption of harm reduction measures [29–31], and managing stigma and discrimination [28]. Thus, strategic communication campaigns, in addition to epidemiological and cost-effectiveness assessments, should be developed. An example of this type of communication strategy can be found in the region of Sicily, which is currently attempting to develop a strategy that includes social marketing (marketing based on social media) and behavior change communication (communication for a behavioral change). Social marketing translates an approach created for commercial marketing to the domain of social change, including public health interventions [32]. The main design tool, however, is behavior change communication [29].

Knowledge-sharing across regions can improve screening practices and encourage improved and innovative methods for convincing these individuals to get tested.

Challenges Due to the COVID-19 Pandemic

The COVID-19 pandemic has had a profound negative effect on endeavors to eliminate HCV infection in Italy. A survey

conducted by the Italian Association for the Study of the Liver (AISF) found that during 2020, 99% of outpatient visits for patients with viral hepatitis ceased, and only 32% of patients with decompensated cirrhosis were able to undergo regular medical care [12]. Of the existing liver units, 75% stopped treatment with DAAs, with less than 5% of these units being able to start treatment in patients without advanced fibrosis. As the COVID-19 pandemic has progressed, these figures have rebounded, with 60% of Italian liver units able to manage HCV patients and start DAA treatment. However, the number of persons treated has gone unchanged, with no increase from 2019 to the present [7, 33].

To explore the possibility of integrating HCV testing with testing for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and/or COVID-19 vaccination, a number of pilot projects were conducted. In these studies, although the prevalence of active HCV infection was found to be low, only about half of the individuals who were positive for HCV knew of their infection [34, 35]. In evaluating the suitability of integrating HCV screening with COVID-19 testing and vaccination, potential inequities need to be evaluated, in that individuals who tend to participate in vaccination and screening programs are often of higher socioeconomic status and at lower risk of having acquired HCV infection [27].

Barriers to Treatment in PWIDs and Prison Inmates: Necessary Changes in the Model of Care

This section highlights the main challenges to expanding screening to PWIDs and prison inmates, who are considered

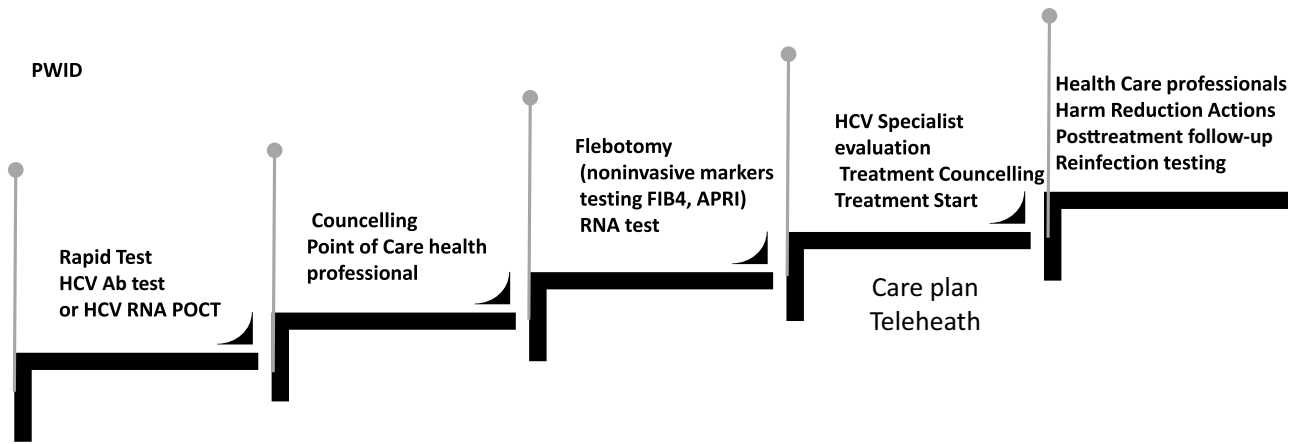


Figure 5. Point-of-care services for screening and linkage to care of PWIDs recommended by the Italian Ministry of Health decree for HCV screening. Abbreviations: Ab, antibody; APRI, aspartate aminotransferase to platelet ratio index; FIB4, Fibrosis 4 score; PWID, people who inject drugs; HCV, hepatitis C virus.

as the most at-risk populations for acquiring and transmitting HCV infection. PWIDs have been systematically underdiagnosed and undertreated in Italy, and it has been estimated that more than 150 000 current or former PWIDs have an undiagnosed/untreated active infection [13, 18, 19]. Recent data (July 2022) from the Italian Parliament Report on Drug Use indicate that only 21% of PWIDs have been screened for HCV, although the prevalence in this group is estimated to exceed 39% [36]. As mentioned, the reasons for which adherence to HCV screening and linkage to care remain low among PWIDs include: patients' lack of knowledge of the disease and of available treatment, social and economic difficulties, negative relationships with doctors and other health professionals, feelings of being stigmatized, and low motivation to seek treatment. Moreover, various health professionals may lack updated knowledge of new therapies, in addition to there being insufficient coordination and communication among professionals engaged in efforts for providing diagnosis and treatment.

The ability of SerD to provide HCV diagnosis and linkage to care and treatment is also hindered by logistical hurdles, such as excessive distance between SerDs and specialist centers that prescribe treatment, lack of specific rooms for drawing blood, and low availability of rapid screening tests [37]. Resource limitations also influence the ability of SerDs to provide harm-reduction services. Although harm reduction is not covered by funds allocated for screening, since 2017 an Essential Level of Assistance has been recognized for PWIDs. However, this level of assistance has yet to be fully applied in all of the country's regions. To address some of these issues, diverse efforts have been made. For instance, several good practices have been shown to reduce treatment drop-out in high-risk populations by shortening their care pathway, as shown with the Caserta Model of Integrated HCV Care, as well as other efficient test and treatment models [38–40].

Screening in prison populations also faces challenges, despite the fact that HCV testing is available in all of Italy's correctional facilities, as guaranteed by the Essential Level of Assistance and funded by the screening decree of the Ministry of Health. As with the SerD, the most critical impediments to systematic screening include logistical and organizational challenges such as overcrowding, difficulties in applying clinical practice standards, and lack of resources. In any case, several microelimination actions have been implemented, suggesting that, in most prisons where specific actions were undertaken, more than 80% of the inmates were tested [41–44]. However, there are several challenges to providing access to care and treatment for diagnosed individuals, and only about half of inmates diagnosed with active infection are linked to treatment. Moreover, not all prisons manage to guarantee services quickly, and interruptions in treatment can occur as a result of institutional factors, such as transfers to different prisons or the release of inmates.

Ineffective testing and linkage to care and the use of ineffective models of care are just some impediments that can hinder these key populations in accessing testing and completing HCV treatment. Currently, PWIDs in SerD and prison inmates receive a vertical model of care, where the patient's journey is based on a stepped model of care, being developed by different specialists in several places. The point of care, supported by the HCV screening decree, is a horizontal model of care consisting of a patient-centered approach where he/she is supported by multiple professionals in the same place of care closer to him or her. It is effective in reducing several barriers to treatment, expanding also the harm reduction activities [45] (Figure 5).

Microelimination programs must be provided and tailored efforts must be made to reach otherwise neglected individuals such as migrants, men who have sex with men, and sex workers, not explicitly addressed in the decree on HCV screening issued by Ministry of Health. Although migrant populations have been addressed in a few studies, tailored screening efforts are needed,

as they are the hardest group to track, especially when they are undocumented [46, 47]. Integrated screening for infectious diseases (tuberculosis, hepatitis B virus, and human immunodeficiency virus) and a dedicated approach to overcoming cultural and socioeconomic barriers to linkage to care are also required for vulnerable and potentially high-risk populations.

Italian Implementation of the WHO Recommendations on Simplified Delivery and Diagnostics for Hepatitis C Infection

To achieve the WHO elimination goal for HCV infection, the focus should be shifted to broader challenges facing the health care system. Decentralization, integration, and task sharing have also been strongly recommended by WHO with the aim of increasing screening uptake and eliminating gaps between diagnosis and treatment [48]. However, these recommendations have yet to be fully realized in Italy. Although antiviral treatment is delivered free of charge to all patients in a capillary manner in each geographical area, their prescription is still restricted to gastroenterologists and infectious disease professionals. A people-centered approach and application of a test-and-treat model have been partially adopted in the screening decree for PWIDs and inmate populations; however, not all health care centers are able to deal with the specialized needs of people who use drugs. The availability of HCV rapid diagnostic tests and of self-testing is an innovative approach that is potentially useful to decentralizing HCV diagnostics in Italy [48].

Expanding use of point of care testing to general practitioners, adapting service delivery to meet the key ‘populations’ specific and complex needs, and the screening strategies outlined in this article, need to be efficiently implemented and expanded to achieve HCV elimination in Italy.

CONCLUSIONS

HCV elimination is an achievable goal in Italy, if real action is taken now. Expanding tailored screening programs, increasing awareness through strategic communication tools, sustaining access to DAAs, and tailoring programs and care models to meet the needs of key populations are strategies that can allow Italy to eliminate HCV within the next decade. Innovative steps have already been taken, and continued commitment is needed to further the momentum to eliminate HCV as a silent public health threat in Italy.

Notes

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References

1. Associazione Italiana Per Lo Studio Del Fegato. Epidemiologia delle epatopatie acute e croniche in Italia. https://www.webaisf.org/wp-content/uploads/2019/01/epidemiologia_.pdf. Accessed October 26, 2022.
2. Eurostat. Over 6 600 deaths from hepatitis in the EU. Available from: <https://ec.europa.eu/eurostat/web/products-eurostatnews/-/edn-20190726-1>. Accessed October 26, 2022.
3. Deuffic-Burban S, Deltenre P, Buti M, et al. Predicted effects of treatment for HCV infection vary among European countries. *Gastroenterology* **2012**; 143: 974–85.e14.
4. Andreoni M, Giacometti A, Maida I, Meraviglia P, Ripamonti D, Sarmati L. HIV-HCV co-infection: epidemiology, pathogenesis and therapeutic implications. *Eur Rev Med Pharmacol Sci* **2012**; 16:1473–83.
5. Mariano A, Scalia Tomba G, Tosti ME, Spada E, Mele A. Estimating the incidence, prevalence and clinical burden of hepatitis C over time in Italy. *Scand J Infect Dis* **2009**; 41:689–99.
6. Russo P, Pani L, Staniscia T, Romano F, Marzioni M. Impact of reimbursement limits on patient access to direct-acting antivirals in Italy: analysis of data from

- national registries. *Eur Rev Med Pharmacol Sci* **2020**; 24: 5758–68.
7. Italian Medicine Agency. DAA monitoring registry. <https://www.aifa.gov.it/en/aggiornamento-epatite-c>.
 8. Kondili LA, Robbins S, Blach S, et al. Forecasting hepatitis C liver disease burden on real-life data. Does the hidden iceberg matter to reach the elimination goals? *Liver Int* **2018**; 38:2190–8.
 9. Kondili LA, Blach S, Razavi H, Craxì A. Tailored screening and dedicated funding for direct acting antiviral drugs: how to keep Italy on the road to hepatitis C virus elimination? *Ann Ist Super Sanita* **2020**; 56:325–9.
 10. Mennini FS, Sciatella P, Simonelli C, Marcellusi A, Kondili LA. The impact of treatment and health policies for Hepatitis C virus on hospitalizations in the last decade: data analysis of records of hospital discharge (SDO) at Italian national level. *J Hep* **2022**; 77 (Suppl 1):S232–3. <https://www.sciencedirect.com/science/article/pii/S0168827822008376?via%3Dihub>.
 11. Gamkrelidze I, Pawlotsky J-M, Lazarus JV, et al. Progress towards hepatitis C virus elimination in high-income countries: an updated analysis. *Liver Int* **2021**; 41:456–63.
 12. Aghemo A, Masarone M, Montagnese S, et al. Assessing the impact of COVID-19 on the management of patients with liver diseases: a national survey by the Italian association for the study of the liver. *Dig Liver Dis* **2020**; 52: 937–41.
 13. Kondili LA, Andreoni M, Aghemo A, et al. Prevalence of hepatitis C virus estimates of undiagnosed individuals in different Italian regions: a mathematical modelling approach by route of transmission and fibrosis progression with results up to January 2021. *New Microbiol* **2022**; 45: 249–59.
 14. CDA Foundation's Polaris Observatory. Country Dashboard Italy 2020. <https://cdfound.org/polaris-countries-dashboard/> Accessed September 20, 2022.
 15. Mennini FS, Marcellusi A, Robbins Scott S, et al. The impact of direct acting antivirals on hepatitis C virus disease burden and associated costs in four European countries. *Liver Int* **2021**; 41:934–48.
 16. Kondili LA, Gamkrelidze I, Blach S, et al. Optimization of hepatitis C virus screening strategies by birth cohort in Italy. *Liver Int* **2020**; 40:1545–55.
 17. Coalition for Global Hepatitis Elimination. The task force for global health. Data dashboard: Italy. <https://www.globalhep.org/country-progress/italy>. Accessed February 20, 2023.
 18. Kondili LA, Aghemo A, Andreoni M, et al. Milestones to reach hepatitis C virus (HCV) elimination in Italy: from free-of-charge screening to regional roadmaps for an HCV-free nation. *Dig Liver Dis* **2022**; 54:237–42.
 19. Kondili LA, Andreoni M, Alberti A, et al. Estimated prevalence of undiagnosed HCV infected individuals in Italy: a mathematical model by route of transmission and fibrosis progression. *Epidemics* **2021**; 34:100442.
 20. Kondili LA, Andreoni M, Alberti A, et al. A mathematical model by route of transmission and fibrosis progression to estimate undiagnosed individuals with HCV in different Italian regions. *BMC Infect Dis* **2022**; 22:58.
 21. Ministero della Salute (Italian Ministry of Health). Prevention hepatitis B and C plan. https://www.salute.gov.it/portale/documentazione/p6_2_2_1.jsp?lingua=italiano&id=2437.
 22. Ministero della Salute (Italian Ministry of Health) Linee di indirizzo nazionali sui percorsi diagnostico terapeutici assistenziali per l'infezione da virus dell'epatite C [National guidelines for diagnostic-therapeutic paths on hepatitis C infection]. <https://www.quotidianosanita.it/allegati/allegato7403086.pdf>.
 23. Minutolo R, Ravera M, Cupisti A, et al. Prevalence of hepatitis C virus infection in non-dialysis CKD patients: a multicentre study in renal clinics. *Nephrol Dial Transplant* **2021**; 36:2348–50.
 24. Rosato V, Kondili LA, Nevola R, et al. Elimination of hepatitis C in southern Italy: a model of HCV screening and linkage to care among hospitalized patients at different hospital divisions. *Viruses* **2022**; 14:1096.
 25. Citarella A, Cammarota S, Bernardi FF, et al. Screening, linkage to care and treatment of hepatitis C infection in primary care setting in the south of Italy. *Life (Basel)* **2020**; 10: E359.
 26. Ferri C, Zignego AL, Antonelli A. Extrahepatic manifestations of chronic HCV infection. *N Engl J Med* **2021**; 385: 94–6.
 27. Kondili LA, Craxì L, Andreoni M, Mennini FS, Razavi H. Opportunistic co-screening for HCV and COVID-19-related services: a creative response with a need for thoughtful reflection. *Liver Int* **2022**; 42:960–2.
 28. Manns MP, Burra P, Sargent J, Horton R, Karlsen TH. The Lancet-EASL commission on liver diseases in Europe: overcoming unmet needs, stigma, and inequities. *Lancet* **2018**; 392:621–2.
 29. European Centre for Disease Prevention and Control. Technical document. Communication strategies for the prevention of HIV, STIs and hepatitis among MSM in Europe. Stockholm, **2016**. <https://www.ecdc.europa.eu/sites/default/files/media/en/publications/Publications/Communication-strategy-prevention-HIV-STI-hepatitis-MSM.pdf>. Accessed October 16, 2022.
 30. Yeung A, Palmateer NE, Dillon JF, et al. Population-level estimates of hepatitis C reinfection post scale-up of direct-acting antivirals among people who inject drugs. *J Hepatol* **2022**; 76:549–57.

31. Marteau TM, Rutter H, Marmot M. Changing behaviour: an essential component of tackling health inequalities. *BMJ* **2021**; 372:n332.
32. European Centre for Disease Prevention and Control. Social marketing guide for public health programme managers and practitioners. <https://www.ecdc.europa.eu/en/publications-data/social-marketing-guide-public-health-programme-managers-and-practitioners>. Accessed October 16, 2022.
33. Ponziani FR, Aghemo A, Cabibbo G, et al. Management of liver disease in Italy after one year of the SARS-CoV-2 pandemic: a web-based survey. *Liver Int* **2021**; 41:2228–32.
34. Torre P, Annunziata M, Sciorio R, Coppola C, Masarone M, Persico M. Hepatitis C screening during SARS-CoV-2 testing or vaccination. Experience in an area of southern Italy in the province of Salerno. *Liver Int* **2022**; 42:1467–9.
35. D'Ambrosio R, Rizzardini G, Puoti M, et al. Implementation of HCV screening in the 1969–1989 birth-cohort undergoing COVID-19 vaccination. *Liver Int* **2022**; 42:1012–6.
36. Relazione Annuale al Parlamento sul fenomeno delle tossicodipendenze in Italia 2022. (Italian Parliament Report on drug use 2022) <https://www.politicheantidroga.gov.it/media/3402/relazione-al-parlamento-2022.pdf>. Accessed October 9, 2022.
37. Molinaro S, Resce G, Alberti A, et al. Barriers to effective management of hepatitis C virus in people who inject drugs: evidence from outpatient clinics. *Drug Alcohol Rev* **2019**; 38:644–55.
38. Rinaldi L, Messina V, Di Marco V, et al. Factors enhancing treatment of hepatitis C virus-infected Italian people who use drugs: the CLEO-GRECA experience. *Am J Gastroenterol* **2021**; 116:1248–55.
39. Messina V, Russo A, Parente E, et al. Innovative procedures for micro-elimination of HCV infection in persons who use drugs. *J Viral Hepat* **2020**; 27:1437–43.
40. Persico M, Masarone M, Aglitti A, et al. HCV point-of-care screening programme and treatment options for people who use drugs in a metropolitan area of Southern Italy. *Liver Int* **2019**; 39:1845–51.
41. Fiore V, De Matteis G, Ranieri R, et al. HCV Testing and treatment initiation in an Italian prison setting: a step-by-step model to micro-eliminate hepatitis C. *Int J Drug Policy* **2021**; 90:103055.
42. Giuliani R, Casigliani V, Fornili M, et al. HCV micro-elimination in two prisons in Milan, Italy: a model of care. *J Viral Hepat* **2020**; 27:1444–54.
43. Pontali E, Fiore V, Ialungo AM, et al. Treatment with direct-acting antivirals in a multicenter cohort of HCV-infected inmates in Italy. *Int J Drug Policy* **2018**; 59:50–3.
44. Masarone M, Caruso R, Aglitti A, et al. Hepatitis C virus infection in jail: difficult-to-reach, not to-treat. Results of a point-of-care screening and treatment program. *Dig Liver Dis* **2020**; 52:541–6.
45. Stange KC. Forces for integration. *Ann Fam Med* **2018**; 16:192–4.
46. Coppola N, Alessio L, Onorato L, et al. Epidemiology and management of hepatitis C virus infections in immigrant populations. *Infect Dis Poverty* **2019**; 8:17.
47. Prestileo T, Di Marco V, Dino O, et al. Effectiveness of a screening program for HBV, HCV, and HIV infections in African migrants to Sicily. *Dig Liver Dis* **2022**; 54:800–4.
48. World Health Organization. Updated recommendations on simplified service delivery and diagnostics for hepatitis C infection. <https://www.who.int/publications-detail-redirect/9789240052697>. Accessed October 27, 2022.