

HCV Screening in Italy: Why and How

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Q. What is the burden of HCV in Italy?

In Europe, Italy is one of the countries with the greatest burden of hepatitis C virus (HCV) infection among the general population and has one of the highest mortality rates from HCV-related cirrhosis and hepatocellular carcinoma. The prevalence of infection is approximately 1%, though a rate as high as 7% has been reported among persons born between 1935 and 1944, whereas prevalence is lowest among persons 30 years of age and younger without apparent risk factors. The highest prevalence rates have been reported in Southern Italy. ⁽¹⁻⁴⁾

A large number of infections occurred in the 1950s and 1960s via iatrogenic transmission due to the use of unsterilized tools/materials (e.g., glass syringes used for vaccinations and injecting antibiotics and vitamins and dental tools). This was followed by a second wave of infection in the period 1980-1990 associated with injecting drug use. Diagnosed individuals in Italy are most likely to be older patients previously linked to care due to a manifestation of liver disease^(5,6). With more than 200,000 patients treated from 2015 to 2019, Italy has made substantial strides in managing its HCV disease burden ⁽⁷⁾. However, unless something is done to decrease underdiagnosis, the burden is expected to remain high. In particular, only an estimated 40-60% of infected individuals are diagnosed and treated (i.e., those linked to care), and although all of these individuals are expected to receive treatment by 2025, a high number of persons actually infected will remain undiagnosed and untreated, if further attempts to identify them are not made ⁽⁸⁾.

Q. Is Italy on the right track for reaching the target of HCV elimination by 2030?

The extensive use of direct acting antivirals (DAA) in the treatment of progressive liver disease in 2015-2016 in Italy led researchers to predict that the World Health Organization's (WHO) goal of reducing liver-related mortality by 65% would be reached much earlier than the target year of 2030 ^(8,9). In light of continued increases in DAA use, it was also predicted that as long as 40,000 persons continued to be treated every year, Italy would reach all WHO's goals of eliminating viral hepatitis as a public-health threat by 2030. However, in 2019, the number of treated patients started to decrease, and given that Italy does not promote active screening, the proportion of infected persons, who are diagnosed and treated, is expected to decrease even further. If this trend continues, Italy will not be able to reach WHO's goals ^(10,11).

Q. Would mass screening for HCV help to reach WHO's goals?

In Italy, both universal screening and the graduated screening of high-prevalence birth cohorts would allow Italy to reach WHO's elimination goals, and both strategies have been found to be cost-effective when compared to the status quo (i.e., treating linked to care individuals regardless of fibrosis stage). In fact, the incremental cost-effectiveness ratios of 3.552 - 6.758 per quality-adjusted life year (QALY) are far lower than the threshold of Willingness to Pay of 25,000 Euro/QALY. However, when compared to graduated birth cohort screening, universal screening requires a higher initial investment and is not cost-effective ⁽¹²⁾.

Q. What specific screening strategy should be used?

To achieve WHO's elimination goals, it is necessary to perform targeted screening among high-prevalence birth cohorts belonging to the general population, as well as among high-risk groups, independently of birth cohort. In Italy, the high-prevalence cohorts consist of individuals born in the period 1948-1988; prevalence is lower both among younger persons (i.e., born after 1988) and, because of the natural depletion of the virus, individuals born before 1948^(1,3). Graduated screening, starting with younger populations (1968-1988 birth cohorts), who are considered to be at risk of transmitting HCV, and then expanding to older individuals (1948-1967 birth cohorts) before their disease advances, has been shown to have the highest cost-effectiveness in Italy⁽¹²⁾. With specific regard to the 1968-1988 cohort, the phenomenon of transmission through injecting drug use needs to be mentioned. In Italy, injecting drug use has been a less important mode of transmission when compared to other European countries, although it was mainly responsible for the 1980-1990 wave of infections. Most individuals who have acquired HCV through injecting use belong to the 1968-1988 birth cohorts. Because these individuals are younger than those who acquired infection through iatrogenic means, a higher proportion of them are in the F0-F3 fibrosis stage and thus more likely to have gone undiagnosed⁽¹³⁾. Screening in this younger cohort would likely result in the detection of individuals at higher risk of transmitting infection, as opposed to older infected individuals who are more likely to have already been identified and less likely to contribute to increasing the disease burden⁽¹²⁾. Therefore, a graduated screening strategy in the general population, which captures both groups, is recommended, as it is immediately cost-effective without high initial costs, like the universal screening strategy. It has both clinical and economic benefits to the population and could sustain Italy's momentum towards achieving the HCV elimination goals.

An additional consideration regarding the screening of specific birth cohorts is that this strategy could reasonably be adopted by other countries, particularly those that do not have the economic or structural resources needed to implement universal screening, taking into consideration a birth-cohort approach based on the specific epidemiological data and real-life treatment rates in the given country.

Q. How do the national health policies address achieving WHO's targets in Italy?

In light of the demonstrated effectiveness and public-health benefits of screening, policy makers have recently taken important steps towards achieving the goal of elimination. In particular, the Milleproroghe Decree, through an amendment approved in March 2020, has allocated 71.5 million euros for the period 2020-2021 to introduce free-of-charge screening. In this period, the screening will focus on persons from the general population born between 1969 and 1989. Screening at public facilities for drug addiction and prisons will also remain a priority⁽¹⁴⁾. However, providing HCV treatment to the individuals diagnosed through screening will be a challenge. In particular, the "Innovative Drugs Fund", through which the State guarantees the necessary funds for DAAs, expired in April 2020. This means that Italy's 20 individual Regions will be faced with the challenge of finding a way to pay for the drugs. Yet to date, no Regional plans for eliminating HCV infection exist. In other words, if Italy is to achieve WHO's HCV elimination target, screening alone will obviously not be sufficient. It is of fundamental importance that a national plan for providing treatment for HCV infection be an integral part of Regional elimination plans.

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