Epidemiological burden estimates for pathologies with a nonconstant risk: an application to HCV in Italy according to age, Metavir score, and genotype

A systematic review and meta-analysis

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Abstract

Between western European countries, the hepatitis C virus (HCV) endemic is highest in Italy. The main objective of this paper is to estimate the endemic diffusion of hepatitis C at the national level and by geographical area, with an extrapolation at the regional level and by uniform cohorts of subjects (by sex and year of birth). The secondary objective is a stratification by gravity of the estimated statistical figures to provide an overview of possible targets of the new anti-HCV treatments.

PubMed and the Cochrane Library were searched for relevant Italian populations studies regarding HCV prevalence. Random and fixed effect models were used for pooling data. To develop the epidemiological model, a meta-analysis of studies of Italian populations and the explicit consideration of the changes in the situation of the disease in different cohorts (by year of birth) of populations and the impact of effective treatments that have been introduced since the 1990s. A Markovian transition model, which is based on the distribution of HCV+ and HCV Ribonucleic Acid (RNA)+ subjects, provides a plausible assessment of the Italian situation. The Meta-analysis of Observational Studies in Epidemiology recommendations/statements were followed.

In 2014, 1569,215 HCV+ subjects (95% credible interval [CrI]: 1202,630–2021,261) were estimated in Italy, with a 2.58% prevalence (95% CrI: 1.98%–3.33%). A total of 828,884 HCV RNA+ subjects (95% CrI: 615,892–1081,123), which is equal to a 1.36% prevalence (95% CrI: 1.01%–1.78%), is higher in southern Italy and the islands (1.9%) than in central–northern Italy (1.1%). The predominance of adult and elderly subjects, with an old or very old infection, inevitably entails a significant number of HCV RNA+ subjects in the advanced stages of the illness. According to our estimates, approximately 400,000 subjects have cirrhosis, decompensated cirrhosis, and hepatocarcinoma, with a median age of 70 years.

The model aims to support policymakers to define action plans by providing an estimate of both the emerged infected population and nonemerged infected population by age, gender, gravity, genotype, and geographical area. In the future, the model may contribute to simulation of the costs and outcome of different action strategies that can be adopted by health authorities.

Abbreviations: \textsuperscript{a} CrI = credible interval, HCV = hepatitis C virus, NHS = National Health Service, PegIFN = pegylated interferon, RBV = ribavirin, SVR = sustained viral response.

Keywords: HCV genotype prevalence, HCV Metavir score prevalence, HCV prevalence, HCV RNA+ prevalence, hepatitis C epidemiology, Italy, meta-prevalence
1. Introduction

Hepatitis C virus (HCV) infection is currently the most frequent or concomitant cause of chronic liver disease, cirrhosis, and liver cancer in the world.

Based on a current estimate of 150 to 180 million chronic carriers of HCV worldwide, a significant increase in liver complications (decompensated cirrhosis and liver cancer) is predicted within the next 10 to 20 years if effective therapeutic measures are not implemented.

In recent years, the gradual introduction of new treatments against the HCV that are capable of producing a persistently negative viremia, which is tantamount to biological healing from the infection, has introduced possible epidemiological scenarios, including the possible eradication of this disease.

The high costs associated with these treatments, however, oblige healthcare systems to define action plans and strategies that are grounded in an in-depth knowledge of the phenomenon, with regard to both quantity (prevalence) and quality, namely, its distribution in terms of age and level of liver damage (Metavir score).

As highlighted in the paper by Esteban et al., a distinct north–south gradient has been observed in Europe, with endemic peaks in the Mediterranean countries, in particular Spain, southern France, Italy, and Greece, with a total prevalence between 2.5% and 3.5%. In northern and central Europe, these values range between 0.1% and 1.2%.

Considering the fact that the virus was identified in 1989 and that a gradual adoption of protection and prevention measures in at-risk groups have considerably reduced the number of new cases, especially in the western European countries, the greater prevalence of infected persons in southern Europe is likely related to a greater circulation of the virus in these regions, especially in the 1950s and 1960s. In these countries, surveys detected a consistent presence of cohorts of elderly subjects who were infected in a preserological era during transfusions or unsafe medical procedures, such as the use of nondisposable syringes. We must add cohorts of subjects who were infected in the 1980s and 1990s as a result of an epidemic that was related to endovenous drug abuse; this epidemic remains problematic.

These diverse epidemiological models, which entail different genotype compositions between the older cohorts and the more recent infected cohorts, require more complex treatment strategies that must consider non-neutral consequences on public health.

Against this scenario, the situation of Italy—where the HCV virus is endemic—is particularly significant. A predominance of subjects in Italy who were born prior to the 1950s and were infected many years ago has generated the assumption that the number of cases of cirrhosis and its complications peaked in 2008.

Various mathematical models have been employed to estimate the Italian prevalence. Although these models produced significantly different estimates, they highlight the alarming diffusion of the infection in the country and rank Italy as the European country with the highest number of infected people. The estimated prevalence over the general population ranges from 5.1%, as estimated by the European Centre for Disease Prevention and Control, which has calculated over 3 million HCV-positive subjects, to 3.0%, 2.0% as estimated by Gower et al. and 1.42%,

National surveys do not provide a stratification of the phenomenon by age group or level of gravity.

The main objective of this paper, which is based on all epidemiological surveys of the general population that have been conducted in Italy since the identification of the virus, is to estimate the endemic diffusion of hepatitis at the national level and by geographical area, with an extrapolation to the regional level and by uniform cohorts of subjects (by sex and year of birth). Based on these results, the secondary objective is a stratification by level of gravity (according to the Metavir score) of the estimated statistical figures to provide an overview of the possible targets of new anti-HCV treatments—by age and gravity of the disease, that highlights a particularly high level of sustained viral response (SVR), which will enable the planning of healthcare policies and treatment strategies that are aimed at the (possible) eradication of the disease.

2. Materials and methods

This systematic review and meta-analysis of available nationally and internationally published literature and gray literature was performed according to the Meta-analysis of Observational Studies in Epidemiology Guidelines 13. Ethical approval was not required considering the nature of the study.

With regard to the published literature, the following databases were consulted:

1. MEDLINE;
2. Cochrane Library.

The research strategy was consistent with the terminology of the National Library of Medicine’s Medical Subject Headings and specific keywords. The main research concepts were as follows: hepatitis C, hepacivirus, hepatitis C antibodies, epidemiology, incidence, prevalence, and Italy, including all Italian regions.

The research was limited to studies in English and Italian that were published after 1989 (excluding conference abstracts).

To obtain unpublished records, such as guidelines and reviews, which can provide useful information, the following websites and databases were consulted:

1. the websites of the major regulatory agencies (Food and Drug Administration, Canadian Agency for Drugs and Technologies in Health, and National Institute for Health and Clinical Excellence);
2. the websites of the major Health Technology Assessment agencies;
3. the database of the University of York Centre for Reviews and Dissemination.

The research was completed on October 25, 2014 (refer to Supplementary materials SM1, http://links.lww.com/MD/B355). A total of 358 records were identified (343 published literature publications and 15 gray publications). The diagram in Fig. 1 shows the literature review and selection process.

With regard to the 17 applicable records, the following records were discarded:

1. Epidemiological surveys of populations in specific areas that featured high rates of HCV prevalence;
2. Epidemiological surveys of hospitalized subjects and/or healthcare facilities;
3. Epidemiological surveys of specific population subgroups, in particular drug addicts and the prison population;
4. Surveys that did not specifically report the distribution of the prevalence by age group.
For prevalence estimation purposes, therefore, 9 records were selected, which refer to a total population of 20,654 subjects who were screened for HCV, the principal characteristics of which are listed in Table 1.

To define a strategy for estimating the prevalence of HCV in the Italian population, 2 main factors of the dynamics of diffusion of the virus were considered: time and geographical location. Regarding the former, the infection risk has significantly changed over the years. From 1989 to 1990, the HCV virus was identified and the first ad hoc virological tests were developed. This period may be considered as a watershed period between 2 eras that features vastly different methods of transmission and intensity of infection. In the preserological era, the risk of infection was much more widespread in terms of population, primarily due to the use of nondisposable syringes, which highlights a greater diffusion in earlier periods. In addition, the inability to identify the virus has also prompted widespread medical practices, such as blood transfusions and dialysis, which can have grave outcomes. Although the implementation of adequate prevention and protection measures since the early 1990s had the initial effect of limiting and deleting these methods of infection and substantially restricting new infections to specific population groups, such as drug addicts and the prison population. For prevalence estimation purposes, the risk of mother–child or sexual infection is considered to be minimal. A higher prevalence of HCV is observed in the southern regions of Italy and the islands probably due to the delayed subsequent scrapping of nondisposable syringes. As a result, the population samples of the selected studies have not been analyzed by age but separately by year of birth for 2 macroareas (north and central

### Table 1
Principal characteristics of the studies included in the analysis.

| Reference          | Geographical area | Type of survey | Cohort sample no., responders no. | Year of survey               |
|--------------------|-------------------|----------------|-----------------------------------|-------------------------------|
| Osella et al[17]   | Puglia Castellana (BA) | General population (30 y e +) | 3,500; 2,079                        | 1985–1986 (test carried out on frozen serum) |
| Mazzeo et al[18]   | Emilia Romagna Loiano e Monghidoro (BO) | General population (18–69 y) | 3,572; 1,842                        | 1986 (test carried out on frozen serum) |
| Bellentani et al[19] | Emilia Romagna Campogalliano (MO) Friuli Venezia Giulia Cormons (GO) | General population (12–65 y) | 10,151; 6,917                       | 1991–1993 |
| Guadagnino et al[20] | Calabria Senzale (CZ) | General population (all ages) | 1,400 (1:4 on birth registry records); 1,382 | 1996 |
| Maio et al[21]     | Campania Buonlabergo (NA) | General population (all ages) | 532; 488                              | 1997 |
| Maggi et al[22]    | Lombardia Albavilla (CO) | General population (18–65 y) | 3,997; 2,403                        | 1997 |
| Di Stefano et al[23] | Sicilia Camporeale (PA) | General population (all ages) | 800; 721                             | 1999–2000 |
| Cozzolongo et al[24] | Puglia Putignano (BA) | General population (18 y e +) | 2,550 (1:5 on birth registry records); 2,195 | 2005–2007 |
| Guadagnino et al[25] | Calabria Sersale (CZ) | General population (all ages) | 1,100 (1:4 on birth registry records); 1,012 | 2010 |
Italy and southern Italy and the islands). Regarding the years of birth, we have identified 5 cohorts that are characterized by uniform risk factors.

With regard to the 9 selected studies, Fig. 2 shows the population sample ranges by year of birth; the vertical bars indicate the 5 cohorts of the population.

Supplementary materials provide the distribution of the cases by uniform cohort in each of the 9 studies (refer to Supplementary materials SM2, http://links.lww.com/MD/B355).

The percentage of HCV RNA positivity was separately estimated by macroarea with reference to the same studies. The meta-prevalences were estimated with the MetaXL ver. 2.0 package (© EpiGear International Pty Ltd ABN 51 134 897 411 Brisbane, Australia, 2011-2014)[26] (refer to Supplementary materials SM3, http://links.lww.com/MD/B355).

A Markovian transition model, which is based on the distribution of HCV+ and HCV RNA+ subjects and provides a plausible assessment of the Italian situation (Fig. 3), was constructed. Table 2 lists the clinical parameters and sources.

As the majority of the epidemiological surveys of the surveyed populations were conducted in the 1990s, the projection of the meta-prevalences on the resident population on January 1, 2014 may overestimate the phenomenon, especially in the case of the elderly population. Although the risk of new infections among the elderly is considered to be minimal, we can presume that the endemic diffusion has been reduced due to the new specific treatments that have been introduced over the years and with regard to the specific mortality for decompensated cirrhosis and liver cancer. Therefore, we have proceeded as follows:

(1) We have considered the basic population as the resident population on January 1, 1995 by sex, age, and region of residence (we have assumed that the proportion of adult/elderly subjects who were infected as a result of transfusions and dialysis since 1995 is negligible, and therefore, significantly stable with regard to the endemic diffusion among the adult population).

(2) We projected the model to 10 years (2005) based on the following assumptions:
(a) Likelihood of transition, per the model (Table 2).
(b) Likelihood of specific death, 5.3% (Table 2).
(c) Likelihood of transplant has not been considered.
HCV: likelihood of annual transition.

| From          | To               | Prob.          | (95% CI)         | Source                                |
|---------------|------------------|----------------|------------------|---------------------------------------|
| HCV—          | HCV+ (18–34 y)   | 0.000035       | (0.000027–0.000043) | CADTH, 2007[27]                        |
| HCV—          | HCV+ (35–69 y)   | 0.000001       |                   |                                        |
| HCV—          | HCV+ (>70 y)     | 0.000001       |                   |                                        |
| HCV+          | HCV RNA+ (northern + central Italy) | 0.7358   | (0.6437–0.8188) | Our assessment                        |
| HCV+          | HCV RNA+ (southern Italy + islands) | 0.6884   | (0.5389–0.8226) | Our processing (meta-prevalence)      |
| HCV RNA+      | F0               | 0.82           | (0.55–0.85)      | Razavi et al[28]                      |
| F0            | F1               | 0.079          | (0.076–0.083)    | Razavi et al[28]                      |
| F1            | F2               | 0.06           | (0.056–0.063)    | Razavi et al[28]                      |
| F2            | F3               | 0.109          | (0.099–0.119)    | Razavi et al[28]                      |
| F3            | F4               | 0.112          | (0.097–0.129)    | Razavi et al[28]                      |
| F4            | F4s              | 0.039          | (0.016–0.085)    | Razavi et al[28]                      |
| F4s + F4s     | Trap             | 0.033          | (0.025–0.040)    | CADTH, 2007[27]                        |
| F4s + Trap    | Dec              | 0.053          | (0.0415–0.0647)  | Razavi et al[28]                      |

CADTH = Canadian Agency for Drugs and Technologies in Health, CI = confidence interval, Trap = transplant, Dec = HCV-related death, HCV = hepatitis C virus, Prob = transition probability, RNA = Ribonucleic Acid.
† CI not reported defined as ±22% of the effect.
* The likelihood of infection in the adult and elderly population has been deemed insignificant.

3. Results

Based on the studies that are deemed eligible for the purposes of the survey (refer to Table 3 and the supporting materials for details) to determine the relevant meta-analysis of prevalence and considering that the analyzed studies predominantly date to the period from 1991 to 2000 (some were previous studies were conducted using frozen serum), these estimates can be considered to be valid for the mid-1990s.

In 1995, 3166,393 HCV+ subjects (95% credible interval [CrI]: 2527,484–3887,328)—1428,674 males and 1737,719 females—were estimated in Italy, with a prevalence of 5.57% (95% CrI: 4.45%–6.84%); this prevalence is considerably higher in southern Italy and the islands (8.1%) than in central—northern Italy (4.1%). In the same year, 2284,286 million HCV RNA+ subjects (95% CrI: 1829,944–2807,443)—1030,175 million men and 1254,110 million women—were estimated, with a prevalence of 4.02% (95% CrI: 3.22%–4.94%); this prevalence is considerably higher in southern Italy and the islands (5.7%) than in central—northern Italy (3.1%).

Due to the lack of recent populations, a Markovian model has been employed, as described in Section 2. We have estimated the effect of the introduction of infection contrast policies in the 1990s and the gradual appearance of increasingly effective treatments.

The endemic load of HCV in the Italian population considerably decreased in 2014: the number of HCV+ subjects decreased to 1569,215 (95% CrI: 1202,630–2021,261) with a 2.58% prevalence (95% CrI: 1.98%–3.33%). The contraction of RNA+ subjects over the years is significant: it decreased to 828,884 (95% CrI: 615,892–1081,123) with a 1.36% prevalence (95% CrI: 1.01%–1.78%) (refer to Table 4).
Table 3
Estimated prevalence for HCV+ and HCV RNA+ pooling analysis by cohort.

| Age cohorts, by year of birth | Northern and central Italy | Southern Italy and Islands |
|------------------------------|----------------------------|---------------------------|
|                              | Males prevalence (95% CrI) | Female prevalence (95% CrI) | Males prevalence (95% CrI) | Female prevalence (95% CrI) |
| <1935                        | 0.1003 (0.0612–0.1474)     | 0.1003 (0.0612–0.1474)     | 0.2729 (0.1884–0.3664)     | 0.2212 (0.3243–0.4366)     |
| 1936–1949                    | 0.0601 (0.0167–0.124)      | 0.0601 (0.0167–0.124)      | 0.1171 (0.0579–0.1924)     | 0.1914 (0.1181–0.2771)     |
| 1950–1960                    | 0.0222 (0.0161–0.0293)     | 0.0222 (0.0161–0.0293)     | 0.04116 (0.0142–0.071)     | 0.0491 (0.0141–0.1000)     |
| 1961–1970                    | 0.0150 (0.01–0.021)        | 0.0150 (0.01–0.021)        | 0.0356 (0.0205–0.0547)     | 0.0152 (0.0066–0.0270)     |
| >1970                        | 0.007 (0.0038–0.0112)      | 0.007 (0.0038–0.0112)      | 0.0121 (0.0057–0.0206)     | 0.0057 (0.0021–0.0111)     |
| Total HCV RNA+ prevalence    | 0.7398 (0.6437–0.8100)     | 0.6894 (0.5369–0.8226)     |                           |                           |

CrI = credible interval. HCV = hepatitis C virus, RNA = Ribonucleic Acid. Source: figures processed by authors.

Table 4 also enables an analysis of the different impacts of the effectiveness of the treatments before and after 2005.

The total distribution by sex remains approximately constant over time, with a higher female component (54.4% of cases). If we consider the population aged below 35 years, a prevalence in the specific population of 0.9% is observed for both sexes. In contrast from the 1990s to the principal methods of infection of the epidemic, a significant alteration in composition by age of the infected population is evident: 70+ year old HCV+ subjects increased from 28.1% in 1995 to 45% in 2014. The median age in 1995 was 61 years, which increased to 68 years in 2014. Therefore, the distribution of HCV+ subjects by age group highlights a large imbalance toward the older groups; only 6.4% of positive subjects are aged between 18 and 34 years, with a prevalence of 0.9%; 48.3% of positive subjects are aged between 35 and 69 years, with a prevalence of 2.6%; and 45.3% of positive subjects are aged over 70 years, with a specific prevalence of 7.5%.

Therefore, the peak of the epidemic with the greater number of serious consequences has been overcome.¹ By 2014, the cases of cirrhosis and its complications were less than approximately 56% compared with the case studies in 1995. The dynamics of cirrhosis and its complications were less than approximately 14.9% of the subjects belong to genotype 3, and 7.7% (95% CrI: 1.4%–14.0%) of the subjects belong to genotype 4 (refer to Table 5).

In the case of formulated emersion, the NHS should be aware and engaged in the treatment of 385,553 (95% CrI: 275,351–520,819) subjects, which accounts for 47% of the HCV RNA+ subjects. The assumed cases of emersion are strictly related to the gravity of the illness and inevitably entail an even greater percentage of elderly subjects. Among the emerged subjects, the 70+ year-olds account for 47.32% (95% CrI: 38.56%–54.71%) compared with only 2.78% (95% CrI: 1.60%–4.53%) of subjects aged below 34 years.

### 4. Discussion

In methodological terms, the estimated prevalence in Italy poses a number of challenges, which primarily derive from changes in the etiology of the infection over time.

Therefore, the model that we have adopted employs the meta-prevalences that are estimated based on epidemiological studies

Table 4
Estimated endemic load of HCV infection (1995–2005–2014).

| Year | Resident population | HCV+ | RNA+ | F0 | F1 | F2 | F3 | F4 | F4s |
|------|---------------------|------|------|----|----|----|----|----|-----|
| 1995 | 56,844,408          | 3166,393 (5.57) | 2284,286 (4.02) | 169,505 (0.30) | 416,520 (0.73) | 276,993 (0.49) | 293,602 (0.52) | 612,177 (1.08) | 515,491 (0.91) |
| 2005 | 57,874,753          | 2230,562 (4.01) | 1338,737 (2.31) | 100,517 (0.17) | 244,175 (0.42) | 161,948 (0.28) | 171,145 (0.30) | 359,633 (0.62) | 301,318 (0.52) |
| 2014 | 60,782,668          | 1569,215 (2.58) | 828,884 (1.36) | 69,985 (0.12) | 147,960 (0.24) | 97,033 (0.16) | 103,014 (0.17) | 230,188 (0.36) | 190,714 (0.31) |

Crl = credible interval. HCV = hepatitis C virus, SVR = sustained viral response. Source: figures processed by authors.

¹ 1995–2005 transition weighting for general and specific mortality, serum versions, treatments (SVR=30%).
² 1995–2005 transition weighting for general and specific mortality, serum versions, treatments (SVR=62.5%).
of Italian populations that are applied by cohorts with the risk of uniform infection. We incorporated the estimates using a Markovian model and a correction based on the supermortality caused by the large percentage of subjects that became infected a long time ago.

Regarding HCV infection, Italy is undoubtedly a peculiar case among Western countries. The Italian endemic load is unquestionably higher than the endemic load in other countries. However, the struggle against the transmission of the epidemic with the greatest impact and the introduction of increasingly effective specific treatments has curbed the spread of HCV since the 1990s. The model confirms a significant reduction in prevalence over the last 20 years, which is estimated at 2.6%, and the predominance of the percentage of elderly subjects in advanced stages of the disease: cirrhosis, decompensated cirrhosis, and hepatocarcinoma, of which 70+-year-olds account for 53% of the total number of these subjects.

The main peculiarity of the infection in Italy, therefore, is the vast difference in the epidemiological structure of the cases, with a predominance in Italy, of cases in the preserological period compared with recent cases, which are primarily related to drug abuse.

Our studies have confirmed that the prevalence of HCV among youth and adults in Italy is comparable to the prevalence of other developed countries: for west European countries, Gower et al[1] has estimated a prevalence of 0.9% (95% confidence interval: 0.7%–1.5%). Therefore, the difference can be interpreted as the result of the high prevalence of elderly and very elderly subjects.

### Table 5

| Age group | Genotype | HCV+ | RNA+ | F0 | F1 | F2 | F3 | F4 | F4s |
|-----------|----------|------|------|----|----|----|----|----|-----|
| Young (18–34 y) | GT1ab | 53.589 | 38.318 | 20.833 | 12.570 | 3.251 | 1.193 | 428 | 44 |
| GT2ab | 28.039 | 20.049 | 10.900 | 6.577 | 1.701 | 624 | 224 | 23 |
| GT3 | 11.971 | 8.560 | 4.654 | 2.808 | 726 | 266 | 96 | 10 |
| GT4 | 7.837 | 5.604 | 3.047 | 1.838 | 475 | 174 | 63 | 6 |
| Total | 101.436 | 72.531 | 39.434 | 23.793 | 6.153 | 2.257 | 811 | 84 |
| Adults (35–69 y) | GT1ab | 401.037 | 237.465 | 14.173 | 52.059 | 35.827 | 36.340 | 61.677 | 37.389 |
| GT2ab | 209.833 | 124.248 | 7.416 | 27.239 | 18.745 | 19.014 | 32.271 | 19.566 |
| GT3 | 89.590 | 53.049 | 3.166 | 11.630 | 8.003 | 8.118 | 13.778 | 8.353 |
| GT4 | 58.649 | 34.728 | 2.073 | 7.613 | 5.293 | 5.314 | 9.020 | 5.468 |
| Total | 759.109 | 449.489 | 26.828 | 98.540 | 67.815 | 68.787 | 116.746 | 70.772 |
| Elderly (70+) | GT1ab | 376.504 | 163.254 | 1.449 | 13.126 | 12.131 | 17.049 | 55.176 | 64.323 |
| GT2ab | 196.996 | 85.419 | 758 | 6.868 | 6.347 | 8.921 | 28.869 | 33.655 |
| GT3 | 84.109 | 36.470 | 324 | 2.932 | 2.710 | 3.809 | 12.326 | 14.369 |
| GT4 | 55.061 | 23.875 | 212 | 1.920 | 1.774 | 2.493 | 8.069 | 9.407 |
| Total | 712.671 | 309.017 | 2.742 | 24.846 | 22.962 | 32.272 | 104.441 | 121.755 |
| Total | GT1ab | 831.130 | 439.037 | 36.455 | 77.755 | 51.208 | 54.562 | 117.282 | 101.756 |
| GT2ab | 434.868 | 229.716 | 19.074 | 40.683 | 26.793 | 28.559 | 61.365 | 53.241 |
| GT3 | 185.671 | 85.419 | 758 | 6.868 | 6.347 | 8.921 | 28.869 | 33.655 |
| GT4 | 121.547 | 64.260 | 5.331 | 7.689 | 7.982 | 17.152 | 14.881 |
| Total | 1,573.216 | 831.038 | 69.004 | 147.179 | 96.930 | 103.316 | 221.998 | 192.611 |

HCV = hepatitis C virus.

* Deterministic estimates.
However, the model highlights that the most serious effects of the disease (cirrhosis, decompensated cirrhosis, and hepatocarcinoma) have peaked, and a further gradual and significant reduction over the coming years is projected due to new treatments that ensure very high percentages of SVR.

The change of the infection’s etiology over time has also determined the considerable diversity in prevalence across the country, with a higher prevalence in southern Italy by 1.8% compared with central-northern Italy (3.8% vs 2.0%). With regard to conditions of seropositivity, the higher prevalence decreases to 0.8% for subjects with a viral load (1.9% vs 1.1%).

Although they generate the hope of eradicating this disease, at least locally, the introduction of new and highly effective antiretroviral treatments on the market poses a problem of sustainability due to the high cost of these treatments.

These financial constraints are probably directing Italian health authorities toward priority treatment of more serious cases—cases that have already emerged or will emerge in the forthcoming years as a result of occasional specimens or the evolution of the disease.

This type of strategy inevitably entails the treatment of elderly or very elderly subjects, which does not bode well for the rapid eradication of the disease.

The assumptions that are adopted with respect to emergence have produced an estimated percentage of 47% of HCV RNA+ subjects, who are unknown to the health services.

Therefore, we hope that proactive strategies and policies may be assessed to enable the emergence of unknown cases, especially among the younger members of the population at risk.

5. Conclusion

The proposed model elaborates estimates of the endemic load of HCV in Italy by adopting a meta-analysis of the studies of Italian populations and explicitly considering the changes in the etiology of the disease in the different cohorts (by year of birth) of the population and the impact of effective treatments since the 1990s.

A significant limitation of the proposed model is its lack of consideration of the endemic load of HCV in the immigrant population, which is undoubtedly increasing and originates in consideration of the endemic load of HCV in the immigrant population and the impact of effective treatments since the 1990s.

Another limitation is the adoption of emergence estimates based on clinical experience, of which the impact has been assessed by a Probability Sensitivity Analysis.

The proposed model aims to support policymakers in the determination of rational action plans by providing estimates of the emerged and nonemerged infected population by age, gender, gravity, and genotype, as well as by geographical area. In the future, the model may contribute to simulations of the costs and outcomes of the different action strategies that are adopted by the health authorities.

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