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Optimization of hepatitis C virus screening strategies by birth cohort in Italy

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Abbreviations: HCV: hepatitis C virus

DAA: direct-acting antiviral

WHO: World Health Organization

GHSS: Global Health Sector Strategy

AIFA: Agenzia Italiana del Farmaco (The Italian Medicines Agency)

PWID: persons who inject drugs

ICER: incremental cost-effectiveness ratio

UI: uncertainty interval

QALY: quality-adjusted life year

LRD: liver-related death

WTP: willingness to pay

US: United States

RNA: ribonucleic acid

PCR: polymerase chain reaction

Comp. cirrhosis: compensated cirrhosis

DCC: decompensated cirrhosis

HCC: hepatocellular carcinoma

LTx: liver transplant

LTx, subs years: liver transplant, subsequent years

SVR: sustained virologic response

EUR: euros

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Abstract

Background and Aims: Cost-effective screening strategies are needed to make hepatitis C virus (HCV) elimination a reality. We determined if birth cohort screening is cost-effective in Italy.

Methods: A model was developed to quantify screening and healthcare costs associated with HCV. The model-estimated prevalence of undiagnosed HCV was used to calculate the antibody screens needed annually, with a €25,000 cost-effectiveness threshold. Outcomes were assessed

under the status quo and a scenario that met the World Health Organization's targets for elimination of HCV. The elimination scenario was assessed under five screening strategies.

Results: A graduated birth cohort strategy (screening 1: 1968–1987 birth cohorts then expanding to 1948–1967 cohorts) was the least costly. This strategy would gain 143,929 quality adjusted life years (QALYs) by 2031 and result in an 89.3% reduction in HCV cases, compared to an 89.6%, 89.0%, 89.7%, and 88.7% reduction for inversed graduated screening, 1948–77 birth cohort, 1958–77 birth cohort, and universal screening, respectively. Graduated screening 1 yielded the lowest incremental cost-effectiveness ratio (ICER) of €3,552 per QALY gained.

Conclusions: In Italy, a graduated screening scenario is the most cost-effective strategy. Other countries could consider a similar birth-cohort approach when developing HCV screening strategies.

Keywords: cost-effectiveness, HCV, screening, WHO targets

Word Count: 199

Lay Summary

In 2016, the World Health Assembly passed a resolution to eliminate hepatitis infection by 2030 and the World Health Organization (WHO) introduced global targets for the care and management of HCV infection, known as the Global Health Sector Strategy Goals (GHSS) for hepatitis. The lack of available patients linked to care and available to treat, however, remain the key bottlenecks for several countries aiming to achieve HCV elimination. The data reported in this study are of importance in that they demonstrate the cost-effective profiles of several screening strategies in the general population of a high-endemic country. Differentiated screening strategies based on epidemiological peculiarities of HCV infection can support increases in diagnosis and subsequent treatment of infected patients necessary for realizing elimination.

Introduction

Hepatitis C virus (HCV) is a leading cause of liver-related morbidity and mortality, causing an estimated 71 million infections globally¹. The size of the infected population and the risk of severe complications make HCV a serious public health problem². However, the use of direct-acting antiviral (DAA) therapy regardless of fibrosis stage is the current standard of care in many high-income countries. Thus, the limitation of HCV therapy is no longer treatment efficacy or adherence, but the identification of available patients to treat. Achieving the World Health

Organization (WHO)'s Global Health Sector Strategy Goals (GHSS) for the elimination of HCV by 2030³ has reinvigorated public health initiatives aimed at identifying patients with the disease. Studies originally suggested finding and diagnosing populations at risk for the acquisition and transmission of HCV. While targeted screening programmes for high-risk populations such as injection drug users are necessary for the elimination of HCV^{4,5}, more is needed to identify what increases in diagnosis are necessary in the general population of high-endemic countries for achieving elimination.

Italy has been considered the European country with one of the largest burdens of HCV in the general population, with the highest prevalence in the older-aged population and decreasing risk in younger populations^{1,6,7}. The HCV prevalence in the country is approximately 1%, though previous studies have estimated rates as high as 7% in those born between 1935 and 1944, while those aged 30 years and younger are at less risk of acquiring HCV⁷. A large number of infections occurred from the 1950s to the 1960s via iatrogenic transmission due to the use of unsterilized materials^{4,7}. More so, there are geographical differences in prevalence distribution. The highest rates of HCV have been reported in Southern Italy, where the HCV prevalence in younger cohorts is quite limited⁸. Considering the natural history of chronic HCV infection and the wide use of antiviral therapy in Italy, total HCV cases still remain higher than in other European countries, such as Spain and France¹. With more than 56,000 patients treated in 2018, Italy has taken substantial strides in managing its HCV disease burden. However, the number of HCV-infected individuals available to treat is estimated to run out by 2025 given the current treatment rates, leaving a large proportion of individuals with the potential to progress to later-stage liver disease⁸. Thus, cost-effective screening strategies are needed to make elimination a reality in Italy. We aimed to determine the cost-effectiveness of expanded HCV screening strategies among different population cohorts in Italy.

Materials and Methods

Study design

An Excel-based Markov disease burden model¹ was populated with Italian data to quantify the annual HCV-infected population by liver disease stage, sex, and age⁸. The model simulates the natural history of the disease and forecasts disease burden, medical costs, and health effects of HCV, assessed under the status quo and a scenario to achieve the WHO's GHSS targets (80%

reduction in incidence of chronic HCV infections between 2015 and 2030, 65% reduction in HCV-related deaths due to chronic HCV infection between 2015 and 2030, 90% diagnosis coverage of the HCV-infected population in 2015, and 80% treatment coverage of the eligible HCV-infected population in 2015)³ considering five screening strategies:

1. Status quo: only at-risk populations screened in Italy²,
2. Targeted general population screening for the 1948–77 birth cohort[†],
3. Targeted general population screening for the 1958–77 birth cohort[†],
4. Graduated birth cohort screening 1 (birth cohorts 1968–1987 beginning in 2020 to identify young populations at risk for transmitting HCV, expanding to the 1948–1967 birth cohort beginning in 2023 to identify older populations before their disease advances)[‡],
5. Graduated birth cohort screening 2 (birth cohorts 1948–1967 beginning in 2020 to identify older populations before their disease advances, and the younger birth cohort 1968–1987 at risk for transmitting HCV beginning in 2023)[‡],
6. Universal screening. The entire Italian population was considered to be screened.

[†]These two screening strategies are based on a previous modelling study⁸, which estimated more than 70% of infected (F0–F3) individuals were within the 1948–1978 birth cohorts by 2020.

[‡]These two screening strategies are based on a previous modelling study that estimated the proportion of undiagnosed HCV cases by ten-year age cohorts⁸.

Input parameters

The Italian HCV-infected population, with or without a prior HCV diagnosis⁷, disease burden⁸, cost (in euros)^{10,11}, and health-related quality of life measures¹² were obtained from recently published literature (Table 1). The number of patients treated with DAAs from 2015–2018 was available through the Agenzia Italiana del Farmaco (AIFA, The Italian Medicines Agency)^{13,14}.

The per-patient cost associated with implementing each screening strategy was calculated, considering the proportion of persons who inject drugs (PWID) in each cohort. Higher implementation costs were assumed for identifying cases among PWID (€55 per person screened) relative to the general population (€15 per person screened). The estimated proportion of PWID in each cohort is calculated and summarized in Appendix 2. Briefly, a standardized mortality ratio was applied to the 15–44-year-old HCV-infected population, considering the proportion of the HCV-infected population that is actively injecting. Using this estimated proportion, the average screening cost per person, per scenario, was calculated (Appendix 2). Prevalence of asymptomatic

HCV infections not yet linked to care was used to calculate the number of HCV antibody screens needed annually to diagnose one case, as described in Appendix 1.

Sensitivity Analysis

Deterministic and probabilistic sensitivity analyses were conducted for each scenario to identify the drivers in the model that accounted for the greatest variation in the incremental cost-effectiveness ratio (ICER) and to generate 95% uncertainty intervals (UIs) around the ICER, given uncertainties in model parameters, using Crystal Ball, a Microsoft Excel (Microsoft Corporation, Redmond, WA, United States) add-in by Oracle (Oracle Corporation, Redwood City, CA, United States). In accordance with the International Society of Pharmacoeconomics and Outcomes Research¹⁵, costs were assumed to be gamma-distributed and quality-adjusted life year (QALY) utilities were assumed to be beta-distributed (Table 1). Uncertainty in starting prevalence was not considered, since the ICER was calculated relative to the status quo, and the starting prevalence under the status quo would be the same as the prevalence under a screening scenario. Finally, to determine the impact of the uncertainty in the cost of screening on the variation in ICER, a deterministic and probabilistic sensitivity analysis was conducted for the scenario found to be the most cost-effective, assuming a beta-PERT-distributed cost of screening among both low- and high-risk groups, with a minimum of half the base-case price and a maximum of double the base-case price (Table 1).

Role of the funding source

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Results

Under the status quo, 290,400 persons would be diagnosed and linked to care, corresponding to 11.3 million screening tests (Figure 1, Table 2). Additionally, 309,200 patients would be initiated on treatment between 2018 and 2031. Total viremic infections and liver-related deaths (LRDs) would decline 65% by 2031 (Figure 1). Although this meets the WHO target for a reduction in LRDs, Italy would not achieve the incidence and diagnosis targets.

A WHO targets scenario (Table 2) was assessed under five different screening strategies. Under these scenarios, between 15.0 million and 55.4 million screening tests would be performed, to diagnose between 340,400 and 385,300 persons (Figure 1). Under all screening scenarios, 548,500 persons would start treatment between 2018 and 2031, resulting in an accelerated drop in the number of viremic cases and LRDs (11,100–15,300 LRDs averted) by 2031, relative to the status quo.

The results of the cost-effectiveness analysis are presented in Table 3 and shown in Figure 2. Under the status quo, annual screening costs would increase 55%, from €3.4 million in 2018 to €5.3 million by 2031. Annual direct medical costs would show a 70% reduction, from €783.5 million in 2018 to €214.1 million by 2031, cumulating to €5.5 billion over the study period.

Compared to the status quo, all screening scenarios were found to be highly cost-effective, with an ICER of €3,552/QALY (95% UI 1,486–6,114) for graduated screening 1, €4,349/QALY (95% UI 2,265–7,014) for screening the 1948–77 birth cohort, €4,532/QALY (95% UI 2,102–7,610) for graduated screening 2, €4,831/QALY (95% UI 2,470–7,973) for screening the 1958–1977 birth cohort, and €6,758/QALY (95% UI 4,589–9,481) for universal screening. The graduated screening 1 scenario was the least costly, with €6.0 billion in total direct medical costs by 2031. This was €54.3 million less than graduated screening 2, €107.4 million less than screening in the 1948–77 birth cohort, €109.1 million less than screening in the 1958–1977 birth cohort, and €467.1 million less than universal screening. Relative to the status quo, graduated screening 1 would gain approximately 144,000 QALYs by 2031, compared to 125,000, 145,000, 142,000, and 128,000 QALYs for graduated screening 2, universal, 1948–1977 birth cohort, and 1958–77 birth cohort screening, respectively. Excluding the three scenarios that were costlier and less effective than graduated screening 1, universal screening yielded an ICER of €562,855 per QALY relative to graduated screening 1.

One-way sensitivity analysis showed that more than 90% of the variation in the 2018–2031 ICER was due to the annual follow-up costs of cirrhosis, decompensated cirrhosis, hepatocellular carcinoma, the QALY utility for cirrhosis, and the cost of liver transplantation (Figure 3). Since the choice of scenario does not make a difference in the ranking of uncertain parameters by

explained variation in the ICER, only results for the graduated screening scenario 1 were reported. The probabilistic sensitivity analysis revealed that, at a willingness to pay (WTP) threshold of €25,000 per QALY gained, all scenarios were cost-effective 100% of the time (Figure 4).

Allowing for uncertainty (i.e., varying the price from half to up to double the assumed base price of screening) in the cost of screening among both low- and high-risk groups, graduated screening 1, which was the most cost-effective scenario relative to the status quo, had an ICER of €3,552/QALY (95% UI 1,570–6,359). One-way sensitivity analysis revealed that more than 90% of variation in the ICER was mainly due to the annual follow-up costs of cirrhosis, decompensated cirrhosis, hepatocellular carcinoma, followed by the cost of screening among low-risk groups, the QALY utility for cirrhosis, and the cost of liver transplantation (Figure 5a). The probabilistic sensitivity analysis showed that at a WTP of €25,000, graduated screening 1 remained cost-effective 100% of the time (Figure 5b).

Discussion

This study aimed to evaluate the cost-effectiveness of five potential HCV screening strategies in Italy. The universal screening and birth cohort screening scenarios, which achieve all targets of the HCV elimination goals, were found to be cost-effective when compared to the status quo scenario, suggesting a coordinated screening program may be beneficial in moving Italy towards elimination of HCV.

Birth Cohort Screening

We evaluated the cost-effectiveness of screening in the birth cohorts 1948–1988, as they were previously identified as having the highest prevalence of undiagnosed HCV infection⁸. Screening the 1948–77 birth cohort would result in fewer QALYs gained compared to the universal and graduated screening 1 scenario and cost less than the universal screening scenario, but more than the graduated screening strategies. Other studies also found that targeted screening among sub-populations with high HCV prevalence is cost-effective²¹⁻²². In a previous meta-analysis of all available cost-effectiveness studies before the availability of DAAs, the cost per QALY gained of screening programs among asymptomatic cohorts at general risk for HCV ranged between US \$4,200 and \$50,000. This was much lower than focusing on specific risk groups, which had an estimated ICER of between \$848 and \$128,424 per QALY gained²³. In the study, age of the target population to be screened and prevalence were the main drivers of cost-effectiveness²³. These are

also important drivers for developing screening strategies in Italy. Despite the lower rates of drug use across Italy compared to other countries, this risk group represents the most recent wave of new infections²⁴ and are mainly distributed amongst the 1968–1988 birth cohorts²³⁻²⁷, who are asymptomatic. Without including these groups in specific screening policies, continued disease burden is expected. Additionally, results of the sensitivity analysis, which examined the cost-effectiveness of each strategy using a €25,000/QALY WTP threshold, remained high ($p>99\%$) once the uncertainty in parameters was considered. Parameters relating to the disease state costs and health outcome utilities were found to have the highest impact on the cost-effectiveness results.

Graduated Screening

Consequently, the graduated screening strategies aim to capture individuals who may be at a higher risk for HCV but are currently asymptomatic. The graduated screening 1 scenario, which identifies young populations at risk for transmitting HCV before expanding to identify older populations before their disease advances, was the least costly screening strategy, with €6.0 billion in direct medical costs by 2031. Relative to the status quo, graduated screening 1 would gain approximately 144,000 QALYs by 2031, which was more than the birth cohort strategies and also produced a lower ICER. The graduated screening 2 scenario, which first identifies older populations before their disease advances and then screens younger cohorts at risk for transmitting HCV, was also less costly (€6.0 billion), but had fewer QALYs gained (125,000) compared to graduated screening 1 scenario. From a disease burden perspective, both graduated screening strategies have significant impact on overall reduction in total viremic infections and liver-related mortality by 2031 (Figure 1), though graduated screening scenario 1 results in more QALYs gained because it is more likely to identify asymptomatic individuals early and prevent the progression of liver disease. Additionally, both graduated scenarios were found to be highly cost-effective (as seen in Table 3). Even upon allowing for a wide variation in the cost of screening among both low- and high-risk groups, the graduated screening 1 scenario remained highly likely ($p>99\%$) to be cost-effective at the €25,000/QALY WTP threshold (Figure 5b). Screening in this younger cohort would likely detect individuals at higher risk of infectiousness, decreasing the potential to transmit new infections compared to screening older patients who are more likely already identified and less likely to contribute to further disease burden.

Programmatic Considerations

It is important for policymakers to consider not only the cost-effectiveness of such strategies, but also their implementation and sustainability. Though the universal screening strategy is recently recommended^{9,28}, it requires higher initial up-front investment, while the graduated strategy 1 would result in a similar number of QALYs gained and have the largest decline in liver-related deaths and associated mortality, limiting the initial cost of the investment. Other high-income countries have reported the opposite, where the epidemiology of chronic HCV infection differs from the situation in Italy^{6,7,18}. In the United States, for example, a larger proportion of new HCV transmission is driven by injection drug use among younger populations^{27,29-30}, meaning universal screening would capture these individuals who are likely asymptomatic²⁸. In Italy, risk-based HCV testing should be implemented independently by birth cohort. Those aged 30 years and younger without high-risk behaviors however, are at less risk of acquiring HCV infection⁷. 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.

Limitations

This study has several limitations that could affect the robustness of the model and the impact of the results. This model does not dynamically estimate new infections and reinfections, nor does it focus on treatment as prevention. However, the current treatment rate in Italy and the need to expand such treatment levels in order to achieve the GHSS Targets exceeds the proportion required for treatment when compared to other transmission-based models³¹. Next, the cost-effectiveness of a screening strategy is strongly linked to the patient's disease stage at the time of treatment initiation. If treatment is delayed and only patients with severe fibrosis are screened, those with more severe liver disease will accrue higher costs, reducing the impact on QALYs. Additionally, the true cost of DAA treatment in Italy is unknown. A previous analysis estimated that at €4,000, treating all patients compared to treating symptomatic individuals would be both cost-effective and produce a cost-benefit¹². Subsequently, this was assumed a reasonable estimate for the cost of therapy. As discussed in a recent systematic review, analyses should consider this rapidly varying cost of DAAs²⁰, however, drug price was not found to be an important factor in the sensitivity analysis. Further, this study partially considered the related costs of healthcare management and reliability of screening tests²⁰. In particular, the adequate organizational, health

system-level, and operational costs regarding screening of HCV are only partially considered in this study. While diagnosed and immediate initiation of DAA therapy would be the most efficient strategy, screening strategies which further consider the cost for general practitioners to screen and diagnosis HCV-patients, though included empirically here, have not yet been fully evaluated. Thus, this modelling work requires real life validation in different Italian regions. One such validation study has been carried out in another high-income, European country. Recent findings from a population-based, cross-sectional study in Spain found that a stepwise screening strategy, similar to the graduated screening 1 scenario described here, was cost saving³², supporting that this type of strategy may be feasible. Though graduated or birth cohort screening is less costly than universal screening, further examinations of each scenario's associated programmatic costs should be evaluated in terms of their impact on the Italian Health Sanitary budget and their sustainability.

Conclusions

Holistic screening strategies for hepatitis C should be implemented, considering the prevalence, the reliability of diagnostic assays, the natural history of infection, the benefits and risks of therapeutic intervention, and the potential benefits to society. Universal screening and birth cohort screening scenarios, which achieve all targets of the HCV elimination goals, were found to be cost-effective when compared to the status quo scenario in Italy, suggesting a coordinated screening program may be beneficial in moving Italy towards elimination of HCV. A graduated screening strategy has both clinical and economic benefits to the population and could sustain Italy's momentum towards achieving the HCV elimination goals. Other countries, particularly those whom may not have the economic or structural means to implement universal screening, but are interested in developing screening strategies based on specific HCV epidemiology, could consider a birth cohort approach based on specific epidemiological data and real-life treatment rates.

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Table 1. Direct medical cost and health effect input parameters

	Parameter	Base	Distribution	First parameter (α for beta, shape for gamma, minimum for beta-PERT)	Second parameter (β for beta, scale for gamma, maximum for beta-PERT)	Reference
Diagnostic and treatment costs (€)	Total screening cost, low-risk groups [†]	15.00	Beta-PERT	7.50	30.00	Sum of price of HCV antibody test [‡] and per-screen implementation cost [§] , assuming half the total cost as minimum and double the total cost as maximum
	Total screening cost, high-risk groups [†]	55.00	Beta-PERT	27.50	110.00	Sum of price of HCV antibody test [‡] and per-screen implementation cost [§] , assuming half the total cost as minimum and double the total cost as maximum
	RNA test/PCR	63.01	–	–	–	Ministero della Salute 2013 (code 91.19.3)
	Genotyping	77.47	–	–	–	Ministero della Salute 2013 (code 91.20.2)
	Fibroscan	50.00	–	–	–	[10, 11]
	Lab costs	50.00	–	–	–	[10, 11]
	Antiviral treatment	4,000.00	–	–	–	[10, 11]
Healthcare costs (€)	Fibrotic (F0–F3)	–	Gamma	100.00	2.77	[10, 11]
	Comp. cirrhosis	–	Gamma	100.00	8.76	[10, 11]
	DCC	–	Gamma	100.00	66.26	[10, 11]
	HCC	–	Gamma	100.00	128.96	[10, 11]
	LTx, first year	–	Gamma	100.00	737.74	[10, 11]
	LTx, subs years	–	Gamma	100.00	23.65	[10]
	Death	–	–	–	–	[11]
	Post-SVR monitoring for cirrhotic patients	50.00	–	–	–	Cost of one ultrasound
QALY utilities, pre-SVR	Fibrotic (F0–F3)	–	Beta	11.12	1.52	[12]
	Comp. cirrhosis	–	Beta	16.17	3.31	[12]
	DCC	–	Beta	26.27	9.72	[12]
	HCC	–	Beta	46.47	41.21	[12]
	LTx, first year	–	Beta	26.27	9.72	[12]
	LTx, subs years	–	Beta	26.27	9.72	[12]
	Healthy	1	–	–	–	[12]
QALY utilities, post-SVR	Fibrotic (F0–F3)	1	–	–	–	[12]
	Comp. cirrhosis	Same as pre-SVR				
	DCC	Same as pre-SVR				
	HCC	Same as pre-SVR				
	LTx, first year	Same as pre-SVR				
	LTx, subs years	Same as pre-SVR				

HCV: hepatitis C virus; RNA: ribonucleic acid; PCR: polymerase chain reaction; comp. cirrhosis: compensated cirrhosis; DCC: decompensated cirrhosis; HCC: hepatocellular carcinoma; LTx: liver transplant; LTx, subs years: liver transplant, subsequent years; QALY: quality-adjusted life year; SVR: sustained virologic response

[†] Uncertainty in input considered in the most cost-effective scenario

[‡] Assumption and [22]

[§] Assumption

Table 2. Scenario inputs, 2017–2031

Status quo	2017	2018	2019	2020	2021	2022	2025+
Treated	45,000	56,400	44,600	33,700	23,200	15,100	15,100
Newly diagnosed/newly linked to care	30,400	30,400	20,000	20,000	20,000	20,000	20,000
Fibrosis score restriction	≥F0						
New infections	8,200	7,500	6,700	6,100	5,600	5,200	5,200
Treated ages	15+	15+	15+	15+	15+	15+	15+
SVR	95%	95%	98%	98%	98%	98%	98%
GHSS elimination	2017	2018	2019	2020	2021	2022	2025+
Treated	45,000	56,400	44,600	35,700	35,700	36,700	38,000
Incremental newly diagnosed/newly linked to care	–	–	10,400	13,400	13,400	15,400	16,400
Fibrosis score restriction	≥F0						
New infections	8,200	7,500	6,700	5,500	5,000	4,100	2,600
Treated ages	15+	15+	15+	15+	15+	15+	15+
SVR	95%	95%	98%	98%	98%	98%	98%

SVR: sustained virologic response; GHSS: Global Health Sector Strategy

Table 3. Direct medical costs and health effects, by scenario, 2018–2031

Scenario	Cost (€ millions), 2018–2031	QALYs gained, 2018–2031	ICER relative to status quo (€/QALY)	ICER relative to previous least costly scenario (€/QALY)	
Status quo	5,463	–	–		
GHSS Targets	Graduated screening 1	5,974	144,000	3,552	3,552
	Graduated screening 2	6,028	125,000	4,532	†
	Screening 1948–1977	6,081	142,000	4,349	†
	Screening 1958–1977	6,083	128,000	4,831	†
	Universal screening	6,441	145,000	6,758	562,855

Values have been rounded, so ICERs may not be reproducible using table values

ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life year; GHSS: Global Health Sector Strategy

† Strongly dominated scenario (costlier and less effective than another scenario)

Figure 1. Cumulative diagnosed patients and screens, as well as modelled viremic cases and liver-related deaths, by scenario, 2018–2031

GHSS: Global Health Sector Strategy; HCV: hepatitis C virus

Figure 2. Economic impact of scenarios as measured by screening costs, direct medical costs, QALYs gained relative to the status quo, and 13-year ICER, by scenario, 2018–2031

QALYs: quality-adjusted life year; ICER: incremental cost-effectiveness ratio; EUR: euros

Figure 3. One-way sensitivity analysis for the 2018–2031 incremental cost-effectiveness ratio, Graduated screening 1 scenario

DCC: decompensated cirrhosis, HCC: hepatocellular carcinoma; QALY: quality-adjusted life year

The central vertical line in the tornado diagram represents all parameters at base values and the base 2018–2031 cost-effectiveness ratio for the graduated screening 1 scenario. The horizontal bars represent the variation in the incremental cost-effectiveness ratio given the variations in the parameters of the scenario. The variables are arranged by explained variation in the incremental cost-effectiveness ratio, with “Annual follow-up cost, Cirrhosis” being the most impactful.

Figure 4. Cost-effectiveness acceptability curve, by scenario

QALY: quality-adjusted life year

The cost-effectiveness acceptability curve shows the proportion of Monte Carlo simulations resulting from varying cost and QALY (quality-adjusted life year) parameters that are cost-effective given a willingness-to-pay threshold.

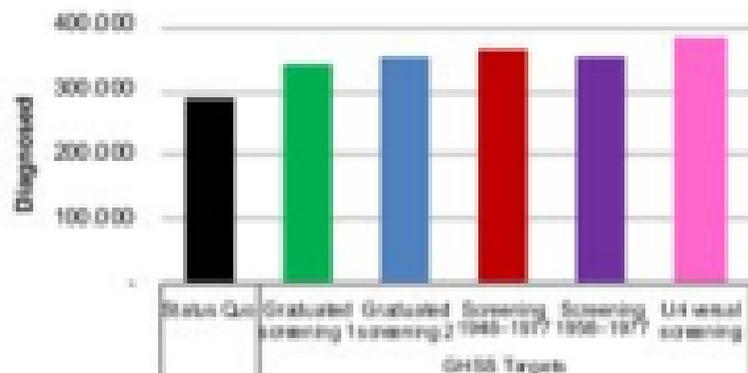
Figure 5a. One-way sensitivity analysis for the 2018–2031 incremental cost-effectiveness ratio, including uncertainty in cost of screening, Graduated screening 1 scenario

DCC: decompensated cirrhosis, HCC: hepatocellular carcinoma; QALY: quality-adjusted life year

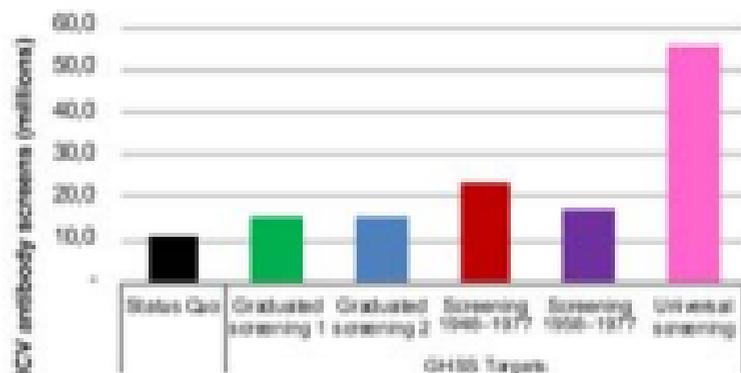
Figure 5b. Cost-effectiveness acceptability curve, including uncertainty in cost of screening, Graduated screening 1 scenario

QALY: quality-adjusted life year

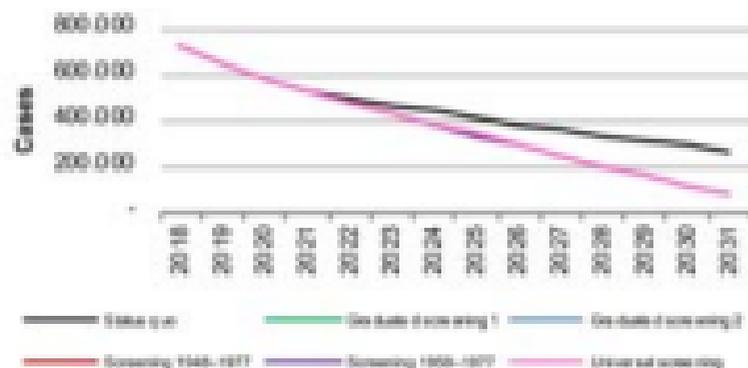
Cumulative diagnosed, 2018–2031



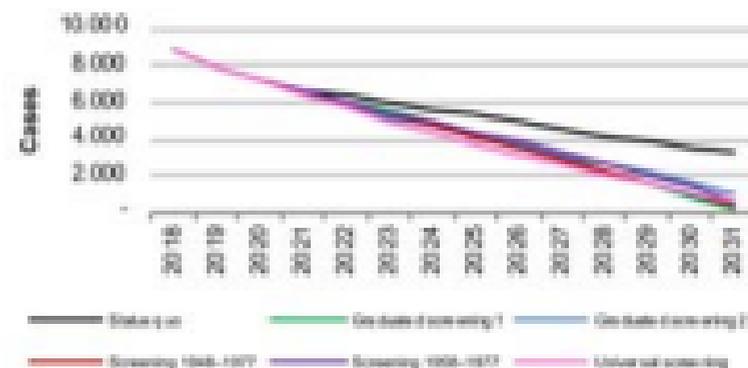
Cumulative screened, 2018–2031



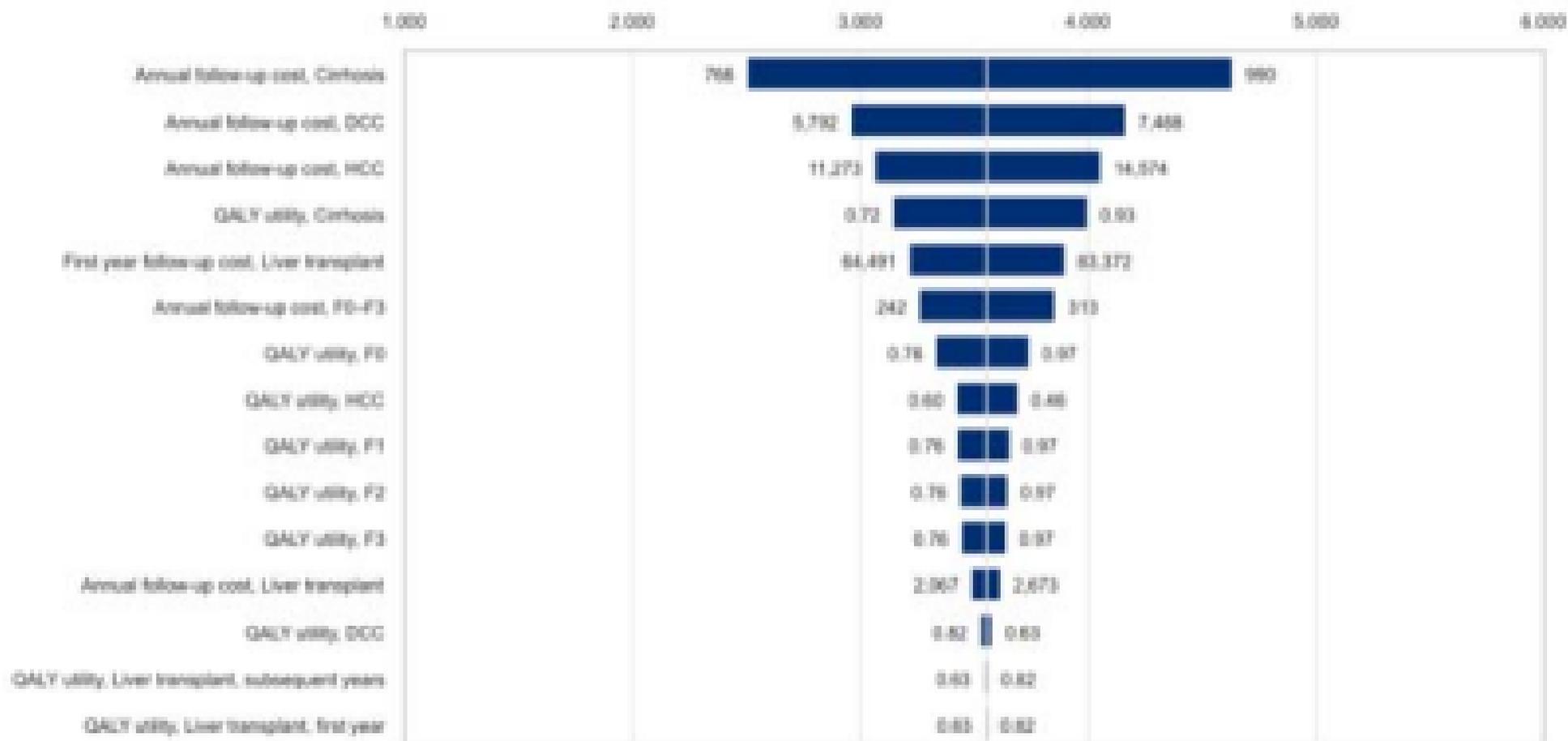
Total infected cases (viremic), 2018–2031

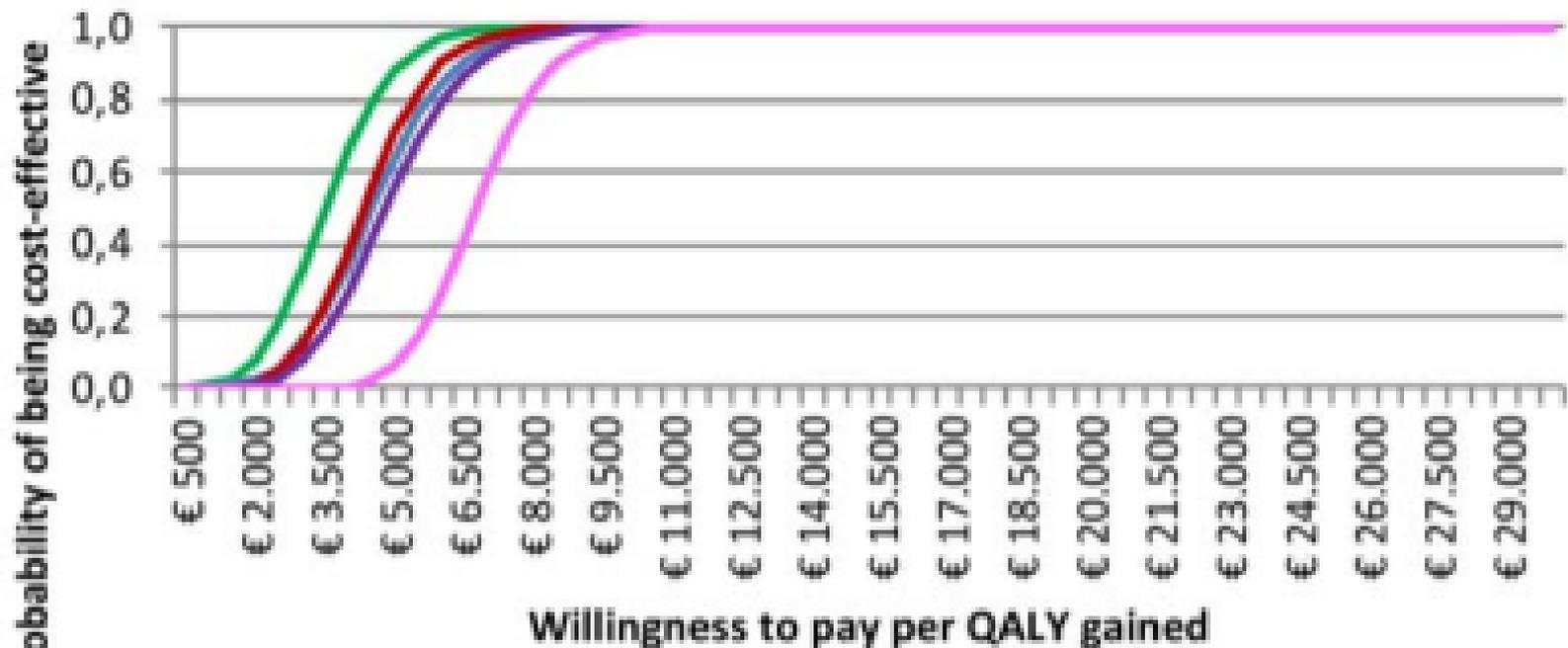


Liver-related deaths, per year, 2018–2031



Incremental cost-effectiveness ratio (2018–2031), Graduated screening





- Graduated screening 1
- Graduated screening 2
- Screening 1948-77
- Screening the 1958-77
- Universal screening

Incremental cost-effectiveness ratio (2018–2031), Graduated screening

1,000 2,000 3,000 4,000 5,000 6,000

