Is elimination of HCV possible in a country with low diagnostic rate and moderate HCV prevalence? The case of Greece

Running title: ***Modeling HCV elimination in Greece***

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Abstract

Background and Aim

The treatment of hepatitis C (HCV) with interferon (IFN)-free Direct-Acting Antivirals (DAAs) is anticipated to change the future burden of disease. Aim of this study is to quantify the impact of IFN-free DAAs on HCV-related morbidity and mortality in Greece under different scenarios concerning treatment coverage and primary prevention, including the proposed by World Health Organization Global Hepatitis Strategy.

Methods

A previously described model was used to project the future disease burden up to 2030 under scenarios which includes treatment based on the combination of pegylated-IFN with ribavirin (base case) and scenarios using DAAs therapies.

Results

Under the base case scenario, an increase in HCV-related morbidity and mortality is predicted in Greece (mortality in 2030: +23.6% compared to 2015). If DAAs are used with the same treatment coverage, the number of hepatocellular carcinoma cases and of liver related deaths are predicted to be lower by 4%-7% compared to 2015. Under increased treatment coverage (from 2,000 treated/year to approximately 5,000/year in 2015-2020 and 2,500/year subsequently), morbidity and mortality will decrease by 43%-53% in 2030 compared to 2015. To achieve the WHO Global Hepatitis Strategy goals, a total number of 86,500 chronic hepatitis C patients will have to be treated during 2016-2030.

Conclusions

Elimination of HCV in Greece by 2030 necessitates great improvements in primary prevention, implementation of large screening programs and high treatment coverage.

Keywords: Disease Burden, Elimination, Hepatitis C, Modeling, Projections, Grecce

Introduction

Hepatitis C virus (HCV) infection is a major public health issue and one of the most common causes of end-stage liver disease and hepatocellular carcinoma (HCC) [1]. It is estimated that more than 185 million people are infected with HCV worldwide in 2005 [2]. The recent introduction of treatments with interferon (IFN)-free Direct-Acting Antivirals (DAAs) has the potential to change the future burden of disease of chronic hepatitis C. DAAs achieve higher rates of sustained virological response (SVR), have fewer side effects and are simpler regimens compared to IFN based therapies [3, 4]. Due to the clinical achievements, the elimination goal is being seriously considered. Recently, World Health Organization (WHO)

released an integrated strategy about HCV infection which includes both prevention and treatment strategies targeting HCV-elimination until 2030 [5].

Greece has one of the highest prevalence rates of chronic HCV infection in Europe [6, 7] and an older infected population compared to other countries. Approximately one third of chronically infected patients are at advanced fibrosis stages (F3, F4) [8, 9]. Although blood screening has resulted in elimination of HCV from blood transfusion, there has been an increase in the annual prevalence rates of HCV among People Who Inject Drugs [10] .

Modeling studies in selected countries, including Greece [8, 11, 12] have projected the future of HCV-related liver disease. However, it is vital to take into consideration the expected high coverage of DAAs and the effect of prevention for planning integrated healthcare strategies. The aim of this study is to quantify the impact of IFN-free DAAs on HCV-related morbidity and mortality under different scenarios of treatment coverage and primary prevention including the proposed by WHO global hepatitis strategy for HCV elimination.

Methods

To estimate the current number of patients in the various disease stages and to project the future burden of disease, we have used a dynamic mathematical model constructed by the Center for Disease Analysis (Colorado, USA) [13]. This model simulates the progression of HCV-infected persons through the various stages of the disease, according to the METAVIR scoring system, with appropriate transition probabilities between stages [13]. It has been used in several countries with country-specific data as input [14-19]. Appropriate input for Greece was obtained from the literature. More specifically, Greece population estimates were obtained, as 5-year age and sex cohorts, based on the United Nations population database [20]. Estimates of anti-HCV prevalence were taken from a nationally representative phone survey conducted

among Greek adults 18-70 years of age in 2012 [6]. Based on this study, anti-HCV prevalence in the adult population was 1.87%. The percentage of the anti-HCV positive population who were viremic was estimated at 80% [7]. Moreover, it is estimated that 80% of chronic HCV patients in Greece are unaware of their infection and only 48% of diagnosed chronic HCV patients have ever been treated [6]. It was estimated that about 3700 and 1970 individuals were newly infected and treated per year, respectively, in Greece [12]. The genotype distribution was approximately 45%, 7%, 34% and 14% for genotypes 1, 2,3 and 4, respectively [21].

Progression was simulated by multiplying the total number of cases at a particular stage of disease by the appropriate progression rate to the next stage. Newly infected patients can enter the model at any year, progress through the disease stages based on progression rates and exit the model on: i) spontaneous clearance of HCV; ii) achieving SVR; iii) death (all-cause or HCV-related). Thirty-six 5-year age and gender cohorts were used through 84 years of age. Individuals with age greater than 85 were treated as one cohort. Each year, one fifth of the population in each age group, except for 85 and older, was moved to the next age cohort to simulate aging after taking into consideration mortality. Annual background age and gender-specific mortality rates for Greek population were used [22]. Mortality rates were adjusted for people who inject drugs and patients with transfusion [23-26]. Furthermore, separate mortality rates have been applied for patients with decompensated cirrhosis, HCC, or liver transplantation. Treated patients with SVR were considered cured and they had the same risk of HCC and similar mortality as the general population. Summary of the inputs of the model is provided in Supplementary Table S1.

To examine the impact of different strategies for the future burden of disease, six different scenarios were considered (Table 1):

Scenario A: Base case

In the baseline scenario, patients are treated with pegylated-IFN (Peg-IFN) and ribavirin. It is assumed that there are 3700 diagnosed cases and 1970 treated patients annually. SVR rates were 70%, 90%, 75%, 65%, for genotype 1, 2, 3, 4 respectively and only patients between 30 and 69 years old, irrespective of fibrosis stage, could be treated.

Scenario B: Base case & Prevention

In this scenario, we assessed the impact of the base case scenario including expansion of primary prevention strategies. More specifically, we examined the effect of a 10% decrease per year in the number of new infections in the period 2015-2020. Under this assumption, the number of new infections at 2020 and afterwards would be 2140 per year compared to 3720 at 2015. SVR rates and patients' eligibility criteria were the same as in the base case scenario.

Scenario C: IFN-free scenario

This scenario was built to assess the effect of IFN-free DAA regimens, i.e. of higher SVR rates, under the same treatment coverage as in the base case scenario. More specifically, SVR was assumed 90% for genotypes 1, 3 and 95% for genotypes 2 and 4 in 2015. The treatment was limited to individuals with fibrosis stage ≥F2 and aged 30-69 years. In 2016 and onwards, SVR was assumed 95% for all genotypes.

Scenario D: IFN-free scenario & Targeted to F3-F4

Under this scenario, we assumed higher treatment efficacy at a slightly higher treatment coverage and targeted to patients with F3-F4. More specifically, the number of patients treated per year with IFN-free DAAs was assumed to increase to 3000 during 2016-2020 (and to return to 2000 for the subsequent years). SVR rates were modeled as in the previous scenario. Only patients with F3 or higher fibrosis stage and aged between 30 and 69

years old could be treated during 2016-2020. After 2020, patients with F2 could be treated too.

Scenario E: IFN-free scenario & increased treatment coverage

In this scenario we examined the potential effects of aggressive increase of treatment coverage under treatment with INF-free DAAs. More specifically, the number of treated patients during 2016-2020 was assumed to be 5000 patients per year and 2500 afterwards. For the purposes of this analysis, i.e. to attain this number of patients receiving treatment, the number of diagnosed patients had to increase. In particular, it was required to increase the number of diagnosed patients progressively up to 8790 at 2017. Until 2017, it was assumed that treatment would be restricted only in patients with fibrosis stage F3 of higher, aged between 30 and 69 years; after 2017 patients with fibrosis stage F2 were included in the pool of patients eligible for treatment.

Scenario F: WHO Global Hepatitis Strategy

Recently, WHO proposed strategies to achieve a major reduction in HCV burden of disease until 2030 [5]. Those strategies include both prevention and increased treatment coverage interventions. More specifically, prevention strategies aim: a) to reduce new infection by 90% and b) to increase diagnosis rate and treatment eligibility at 90% and 80% in 2030 compare to the number of new infections in 2015, respectively. Furthermore, increased treatment coverage strategies aim at 65% reduction in HCV mortality in 2030, compared to 2015. A realization of this strategy in Greece could be obtained by progressively increasing the number of diagnosed patients and treated patients up to 9000 and 6300 patients per year respectively. Initially, patients with fibrosis stage ≥F3 should be treated until 2018. After 2019 treatment coverage should gradually expand to F2/F1 patients. Age limits should be

expanded from 30-69 to 25-79 due to the fact that older chronic hepatitis C patients have more rapid fibrosis progression and higher probability of HCV-related mortality or morbidity.

Results

HCV prevalence in Greece peaked in 2005 with 138800 viremic cases and it is anticipated to decline to 106700 cases in 2030 under Peg-IFN and ribavirin treatment (Figure 1). Under the base case scenario (Scenario A), the model predicts a decline in the number of viremic cases in Greece by 2030 (Figure 1, Figure 2A). However, an increase in the numbers of compensated cirrhosis, decompensated cirrhosis, HCC and HCV-related deaths is anticipated in the following years as a result of the aging of the HCV cohort (Figure 1, Figures 2B-2E). More specifically, patients with compensated cirrhosis would be 19779 in 2030 compared to 17904 in 2015 (Table 2). Similarly, the number of individuals with decompensated cirrhosis would be 2820 in 2030 compared to 2342 in 2015 (20.4% increase), the number of patients with HCC is anticipated to reach 1222 cases in 2030 (compared to 974 cases in 2015, 25.5% increase) and the number of liver-related deaths was forecasted equal to 1026 in 2030 compared to 830 in 2015 (23.6% increase) (Table 2, Figure 2B-2E).

In the prevention scenario (Scenario B), the projected number of total infected persons would decrease by 10.4% and 32% in 2020 and 2030, respectively, compared to the number of total infected in 2015 (Table 2, Figure 2A). The model predicted that the number of individuals with compensated cirrhosis would increase by 7.1% and 9.2% in 2020 and 2030, respectively, compared to 2015 (Table 2, Figure 2B-2E). Similarly, the number of individuals with decompensated cirrhosis, HCC and liver related deaths are predicted to increase by 19.5%, 24.7%, 23.0% in 2030, respectively, compared to the number of individuals with decompensated cirrhosis, HCC or liver related deaths at 2015.

Under the scenario of increased treatment efficacy (IFN-free scenario) (Scenario C), the total number of infected persons was projected to be lower by 7.8% and 21.3% at 2020 and 2030, respectively, compared to 2015 (Table 2, Figure 2A). Regarding individuals with compensated and decompensated cirrhosis, the model projected a decrease of 22.1% and 17.7% in 2030, respectively, compared to 2015. A decline of 4.7% is predicted in the number of HCC cases in 2030 compared to 2015 (Table 2, Figure 2B-2E).

Under the scenario of increased treatment efficacy and targeted treatment (IFN-free scenario & Targeted to F3-F4) (Scenario D), the predicted decline in the number of patients with compensated and decompensated cirrhosis was approximately 30% in 2030, compared to 2015. The number of HCC cases is also forecasted to decline by 16% in 2030. As for HCC and liver related deaths, the model predicted a decrease of 16% and 20%, respectively, in 2030 compared to 2015 (Table 2, Figure 2B-2E).

Launching an intervention to increase treatment coverage (IFN-free scenario & increased treatment coverage - Scenario E), would result in a decline in the number of patients in advanced fibrosis stages. Compared to 2015, the number of cases with compensated cirrhosis and decompensated cirrhosis was projected to be lower by 31.8% and 34% in 2020 and by 52.8% and 54.3% in 2030, respectively. Moreover, HCC cases and liver related deaths would be lower by 40.5% and 43.3% in 2030, respectively, compared to 2015 (Table 2, Figure 2B-2E).

As it was anticipated under the WHO Global Hepatitis Strategy (Scenario F), the burden of morbidity and mortality would decrease substantially. Specifically, the number of patients with compensated cirrhosis, decompensated cirrhosis and HCC in 2030 would be lower by 77%, 76% and 72%, respectively, compared to 2015 (Table 2, Figure 2B-2E). Furthermore, the total number of infected individuals in 2030 would be lower by 81.5%

compared to 2015 (Table 2, Figure 2A).These targets would be reached if a total number of 86,500 patients received treatment during 2015-2030.

Discussion

Under the IFN regimens, HCV prevalence in Greece is projected to decrease, which is partly attributed to the lower HCV incidence after blood screening, whereas morbidity and mortality burden is anticipated to grow by 2030. According to our results, HCV prevalence peaked in 2005 in Greece and is anticipated to decline even under Peg-IFN and ribavirin treatment. Under this treatment scenario, advanced HCV related disease (decompensated cirrhosis, HCC and liver related deaths) would peak in Greece in 2030. Similar patterns have been observed in the majority of European countries under the interferon regimes [11].

The expansion of prevention strategies, in the absence of increased treatment efficacy or coverage, was not projected to have an impact on HCV morbidity until 2030. This is not surprising; given the slow progression of HCV infection, the time horizon of our projections is relatively short to observe the impact of primary prevention on morbidity and mortality. This result does not mean that strategies aiming at reducing HCV incidence are not important, but rather that primary prevention alone cannot lead to a notable reduction to morbidity and mortality in the short term. Moreover, the model did not predict significant changes even if treatment with high efficacy was adopted, due to the low treatment coverage existing in Greece. The impact of DAAs, under today's treatment coverage, is modest and would reduce the disease burden at levels similar to 2011.

In order to decrease the morbidity and mortality burden in Greece, strategies should focus to increase diagnostic rates and treatment coverage, through expanding HCV-testing especially in high risk groups' population, as PWIDs. If financial restrictions make it necessary to prioritize treatment in Greece, treatment strategies should focus on the

population with advanced liver disease. According to our findings, if treatment with DAAs is prioritised to F3-F4 patients, the number of patients with decompensated cirrhosis and of liver related deaths would be 30% and 20% lower in 2030 than in 2015, respectively.

As it is anticipated, under the scenario simulating the targets of WHO Global Hepatitis Strategy, a significant decline would be observed in advanced fibrosis stages and in the total infected population. The above strategy comprises two components; prevention and expansion of antiviral treatment. More specifically, in order to implement the prevention part of the strategy, the number of new infections per year should be reduced to 1820 until 2018, 1270 until 2022, 760 until 2024 and 390 until 2030. Taking into account that the primary source of HCV infection is through injecting drug use, harm reduction strategies should be expanded. However, because the majority of infected PWIDs are undiagnosed and unlinked to care, a case-finding, linkage to care intervention should be implemented to increase diagnosis rate per year about 2.5 times higher than today. Specifically, diagnosed patients per year must be increased initially to 6000 until 2019 and 9000 patients per year in the subsequent years until 2030. Updated recommendations of general population screening should be implemented in order to diagnose HCV infected individuals who do not recognize themselves as high-risk individuals.

To achieve the goal of 65% reduction in HCV mortality in 2030 [5], treatment must be prioritized to those patients who have higher probability of HCV-related mortality; those populations are patients with fibrosis stage ≥F3 or older chronic hepatitis C patients. After 2019, treatments should gradually expand to F2/F1 patients. Moreover, to implement the WHO strategy, the annual number of treated patients should be expanded to 3000 in 2015-2018, 4400 in 2018-2020, 5300 in 2020-2022 and 6370 in 2022-2030.

There are a number of limitations that could impact the outcomes of the study. Patients who achieved SVR were not tracked, so all reinfection in the model were managed as naïve cases. Another limitation of this model is that it assumes that new infections and re-infections would remain stable at 2015 levels. Thus, the model does not account for treatment as prevention and its predictions may be more conservative. A further limitation of the study is that the model assumed that new therapies, guidelines or treatment strategies are adopted immediately. In reality, medical communities and treatment strategies take time to be implemented. As an example, in one of the evaluated scenarios we assumed an increase of treatment rate. Actually, as diagnosis rate increases, it becomes more difficult to find undiagnosed patients as the latter may not have the opportunity to access to the health systems. Finally, the issue of the high cost of IFN-free treatments was not considered in our analysis.

In conclusion, our results support that the implementation of prevention strategies or the adoption of new antiviral treatments without increasing treatment coverage are not anticipated to have a significant impact on HCV-related morbidity and mortality in the next 15 years. Targeted treatment with DAAs of patients with advanced fibrosis stage could result in a more pronounced decline in morbidity and mortality compared to strategies without fibrosis stage criteria. Improved prevention strategies, large and effective screening programmes and increased treatment coverage with DAAs are necessary to reach the goal of HCV elimination in Greece by 2030.

References

1. Hatzakis A, Wait S, Bruix J, et al. The state of hepatitis B and C in Europe: report from the hepatitis B and C summit conference*. J Viral Hepat 2011;18 Suppl 1:1-16.
2. Mohd Hanafiah K, Groeger J, Flaxman AD, et al. Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence. Hepatology 2013;57:1333-42.
3. Feld JJ, Kowdley KV, Coakley E, et al. Treatment of HCV with ABT-450/r-ombitasvir and dasabuvir with ribavirin. N Engl J Med 2014;370:1594-603.
4. Sulkowski MS, Gardiner DF, Rodriguez-Torres M, et al. Daclatasvir plus sofosbuvir for previously treated or untreated chronic HCV infection. N Engl J Med 2014;370:211-21.
5. WHO. Global Health Sector Strategies for HIV / Viral Hepatitis / Sexually Transmitted Infections, 2016-2021. Volume 2015: WHO, 2015.
6. Papatheodoridis G, Sypsa V, Kantzanou M, et al. Estimating the treatment cascade of chronic hepatitis B and C in Greece using a telephone survey. J Viral Hepat 2015;22:409-15.
7. Sypsa V, Touloumi G, Tassopoulos NC, et al. Reconstructing and predicting the hepatitis C virus epidemic in Greece: increasing trends of cirrhosis and hepatocellular carcinoma despite the decline in incidence of HCV infection. J Viral Hepat 2004;11:366-74.
8. Gane E, Kershenobich D, Seguin-Devaux C, et al. Strategies to manage hepatitis C virus (HCV) infection disease burden - volume 2. J Viral Hepat 2015;22 Suppl 1:46-73.
9. Wedemeyer H, Duberg AS, Buti M, et al. Strategies to manage hepatitis C virus (HCV) disease burden. J Viral Hepat 2014;21 Suppl 1:60-89.
10. Paraskevis D, Nikolopoulos G, Fotiou A, et al. Economic recession and emergence of an HIV-1 outbreak among drug injectors in Athens metropolitan area: a longitudinal study. PLoS One 2013;8:e78941.
11. Hatzakis A, Chulanov V, Gadano AC, et al. The present and future disease burden of hepatitis C virus (HCV) infections with today's treatment paradigm - volume 2. J Viral Hepat 2015;22 Suppl 1:26-45.
12. Saraswat V, Norris S, de Knegt RJ, et al. Historical epidemiology of hepatitis C virus (HCV) in select countries - volume 2. J Viral Hepat 2015;22 Suppl 1:6-25.
13. Razavi H, Elkhoury AC, Elbasha E, et al. Chronic hepatitis C virus (HCV) disease burden and cost in the United States. Hepatology 2013;57:2164-70.
14. Vandijck D, Moreno C, Starkel P, et al. Current and future health and economic impact of hepatitis C in Belgium. Acta Gastroenterol Belg 2014;77:285-90.
15. Starkel P, Vandijck D, Laleman W, et al. The disease burden of hepatitis C in Belgium: development of a realistic disease control strategy. Acta Gastroenterol Belg 2014;77:280-4.
16. Myers RP, Krajden M, Bilodeau M, et al. Burden of disease and cost of chronic hepatitis C infection in Canada. Can J Gastroenterol Hepatol 2014;28:243-50.
17. Cramp ME, Rosenberg WM, Ryder SD, et al. Modelling the impact of improving screening and treatment of chronic hepatitis C virus infection on future hepatocellular carcinoma rates and liver-related mortality. BMC Gastroenterol 2014;14:137.
18. Duberg AS, Blach S, Falconer K, et al. The future disease burden of hepatitis C virus infection in Sweden and the impact of different treatment strategies. Scand J Gastroenterol 2015;50:233-44.
19. Waked I, Doss W, El-Sayed MH, et al. The current and future disease burden of chronic hepatitis C virus infection in Egypt. Arab J Gastroenterol 2014;15:45-52.
20. United Nations – Population Division of the Department of Economic and Social Affairs of the United Nations Secretariat, World Population Prospects: The 2010 Revision and World Urbanization Prospects: The 2010 Revision.

21. Raptopoulou M, Touloumi G, Tzourmakliotis D, et al. Significant epidemiological changes in chronic hepatitis C infection: results of the nationwide HEPNET-GREECE cohort study. Hippokratia 2011;15:26-31.
22. United Nations Statistics Division. 2013. UNSD Demographic Statistics: Deaths by age, sex and urban/rural residence.
23. Hickman M, Carnwath Z, Madden P, et al. Drug-related mortality and fatal overdose risk: pilot cohort study of heroin users recruited from specialist drug treatment sites in London. J Urban Health 2003;80:274-87.
24. Engstrom A, Adamsson C, Allebeck P, et al. Mortality in patients with substance abuse: a follow-up in Stockholm County, 1973-1984. Int J Addict 1991;26:91-106.
25. Perucci CA, Davoli M, Rapiti E, et al. Mortality of intravenous drug users in Rome: a cohort study. Am J Public Health 1991;81:1307-10.
26. Kamper-Jorgensen M, Ahlgren M, Rostgaard K, et al. Survival after blood transfusion. Transfusion 2008;48:2577-84.

Table 1: Evaluated scenarios for projections of the future burden of HCV infection in Greece

	SVR ǂ	**Treatment coverage**	**Fibrosis stage**
Scenario A Base case scenario	65%-90%	~2000/year	All
Scenario B Base case & Prevention	65%-90%	~2000/year	All
	10% decline in new infections/year (2015-2020)		
Scenario C IFN-free scenario	up to 95%	~2000/year	≥F2
Scenario D IFN-free scenario & Targeted to F3-F4	up to 95%	~3000/year in 2015-2020 ~2000/year in 2021-2030	≥F3 (≥F2 since 2020)
Scenario E IFN-free scenario & increased treatment coverage	up to 95%	~5000/year in 2015-2020 ~2500 in 2021-2030	≥F3 (≥F2 since 2017)
Scenario F WHO global hepatitis strategy	up to 95%	~3000/year in 2015-2018 ~4400/year in 2018-2020 ~5300/year in 2020-2022 ~6300/year in 2022-2030	≥F3 (≥F2 since 2019) (≥F1 since 2021)

ǂ SVR: Sustained virological response

Table 2: Estimated number of total HCV infected (viremic cases), compensated cirrhosis, decompensated cirrhosis and hepatocellular carcinoma (HCC) cases in 2020 and 2030 under different scenarios.

	2015 N	2020 N (% change compared to 2015)	2030 N (% change compared to 2015)	2030 N (% change compared to base case in 2030)
Scenario A: Base case				
Total infected	130166	122368 (-6.0)	106706 (-18.0)	-
Fibrosis Cases	108892	99504 (-8.6)	82819 (-23.9)	-
Comp. cirrhosis	17904	19158 (+7.0)	19779 (+10.5)	-
Decomp. cirrhosis	2342	2557 (+9.2)	2820 (+20.4)	-
HCC[ǂ]	974	1090 (+11.9)	1222 (+25.5)	-
Liver related deaths	830	924 (+11.3)	1026 (+23.6)	-
Scenario B: Base case & Prevention				
Total infected	130166	116594 (-10.4)	88431 (-32.0)	88431 (-17.1)
Fibrosis Cases	108892	93716 (-13.9)	64805 (-40.4)	64805 (-21.7)
Comp. cirrhosis	17904	19170 (+7.1)	19546 (+9.2)	19546 (-0.1)
Decomp. cirrhosis	2342	2559 (+9.2)	2800 (+19.5)	2800 (-0.01)
HCC[ǂ]	974	1090 (+12.0)	1215 (+24.7)	1215 (-0.06)
Liver related deaths	830	925 (+11.4)	1021 (+23.0)	1021 (-0.05)
Scenario C: IFN-free scenario				
Total infected	130166	119993 (-7.8)	102359 (-21.3)	102359 (-4.1)
Fibrosis Cases	108892	99548 (-8.5)	85515 (-21.4)	85515 (+0.3)
Comp. cirrhosis	17904	17079 (-4.6)	13944 (-22.1)	13944 (-29.5)
Decomp. cirrhosis	2342	2290 (-2.2)	1927 (-17.7)	1927 (-31.7)
HCC[ǂ]	974	1023 (+5.0)	928 (-4.7)	928 (- 24.1)
Liver related deaths	830	869 (+4.7)	765 (-7.8)	765 (-25.4)
Scenario D: IFN-free scenario & Targeted to F3-F4				
Total infected	130166	115138 (-11.5)	99232 (-23.7)	99232 (-7.0)
Fibrosis Cases	108892	98934 (-9.1)	84018 (-22.8)	84018 (+0.1)
Comp. cirrhosis	17904	13510 (-24.5)	12734 (-28.8)	12734 (-35.6)
Decomp. cirrhosis	2342	1764 (-24.6)	1626 (-30.5)	1626 (-42.3)
HCC[ǂ]	974	888 (-8.8)	818 (-16.0)	818 (-33.0)
Liver related deaths	830	754 (-9.1)	665 (-19.9)	665 (-35.2)
Scenario E: IFN-free scenario & increased treatment coverage				
Total infected	130166	102904 (-21.0)	85322 (-34.4)	85322 (-20.0)
Fibrosis Cases	108892	88310 (-18.9)	75205 (-30.9)	75205 (-9.2)
Comp. cirrhosis	17904	12196 (-31.8)	8444 (-52.8)	8444 (-57.3)
Decomp. cirrhosis	2342	1544 (-34.0)	1069 (-54.3)	1069 (-62.1)
HCC[ǂ]	974	817 (-16.1)	579 (-40.5)	579 (-52.6)
Liver related deaths	830	702 (-15.4)	470 (-43.3)	470 (-54.2)
Scenario F: WHO global hepatitis strategy				

Total infected	130166	100319 (-23.0)	24139 (-81.5)	24139 (-77.4)
Fibrosis Cases	108892	86828 (-20.2)	19193 (-82.4)	19193 (-76.8)
Comp. cirrhosis	17904	11262 (-37.1)	4098 (-77.1)	4098 (-79.3)
Decomp. cirrhosis	2342	1531 (-34.6)	563 (-76.0)	563 (-80.0)
HCC[ǂ]	974	659 (-32.3)	272 (-72.1)	272 (-77.7)
Liver related deaths	830	688 (-17.1)	293 (-64.7)	293 (-71.4)

[ǂ]HCC: hepatocellular carcinoma

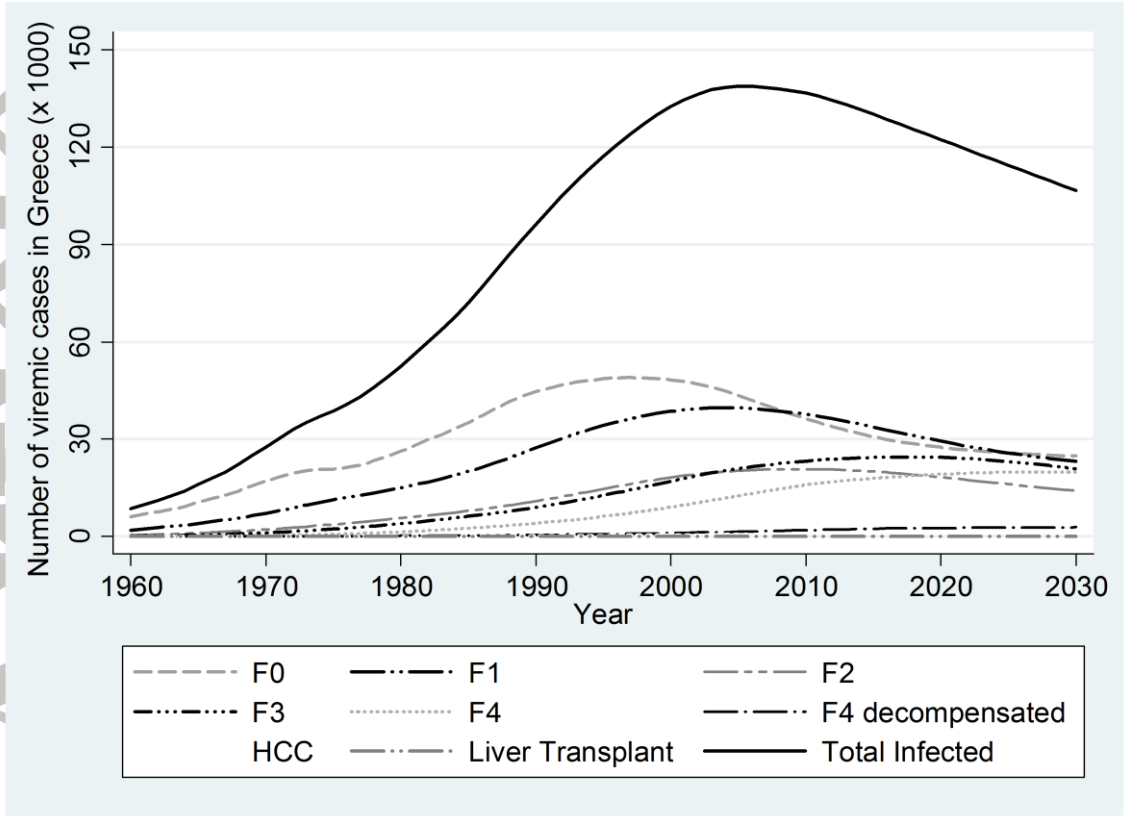

Figure 1: The number of viremic cases (total and in the various disease states) in Greece from 1950 to 2030 under the base case scenario (peg-interferon and ribavirin, approximately 2,000 patients treated per year)

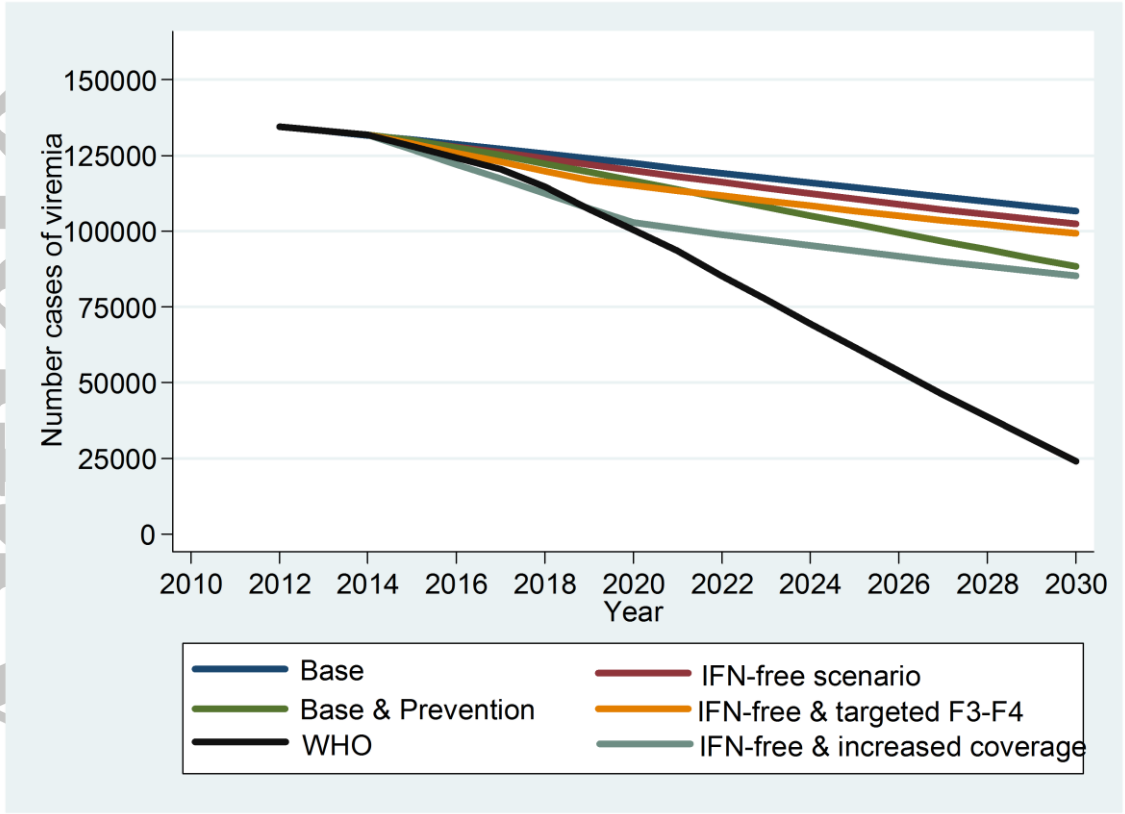

Figure 2a: Projections of future chronic HCV infection and complications under different treatment strategies (the scenario are described in detail in Table 1). Total number of viremic cases

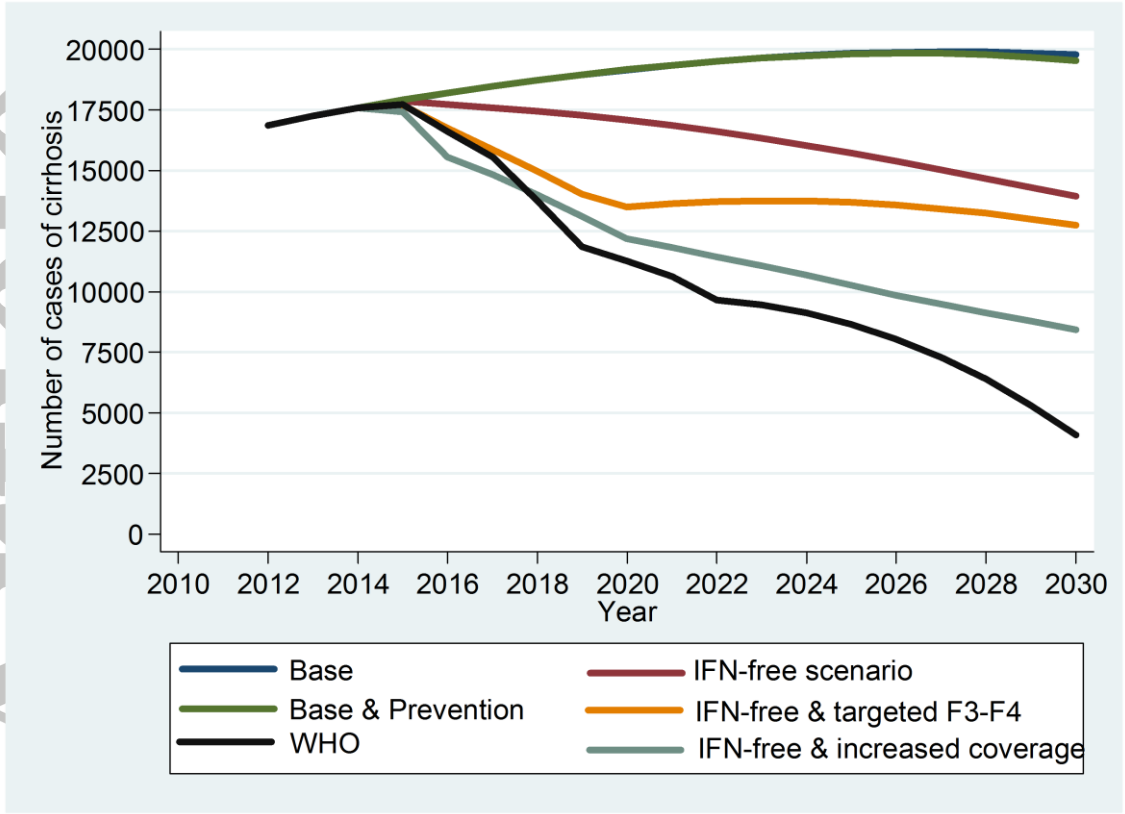

Figure 2b: Projections of future chronic HCV infection and complications under different treatment strategies (the scenario are described in detail in Table 1). Cirrhosis

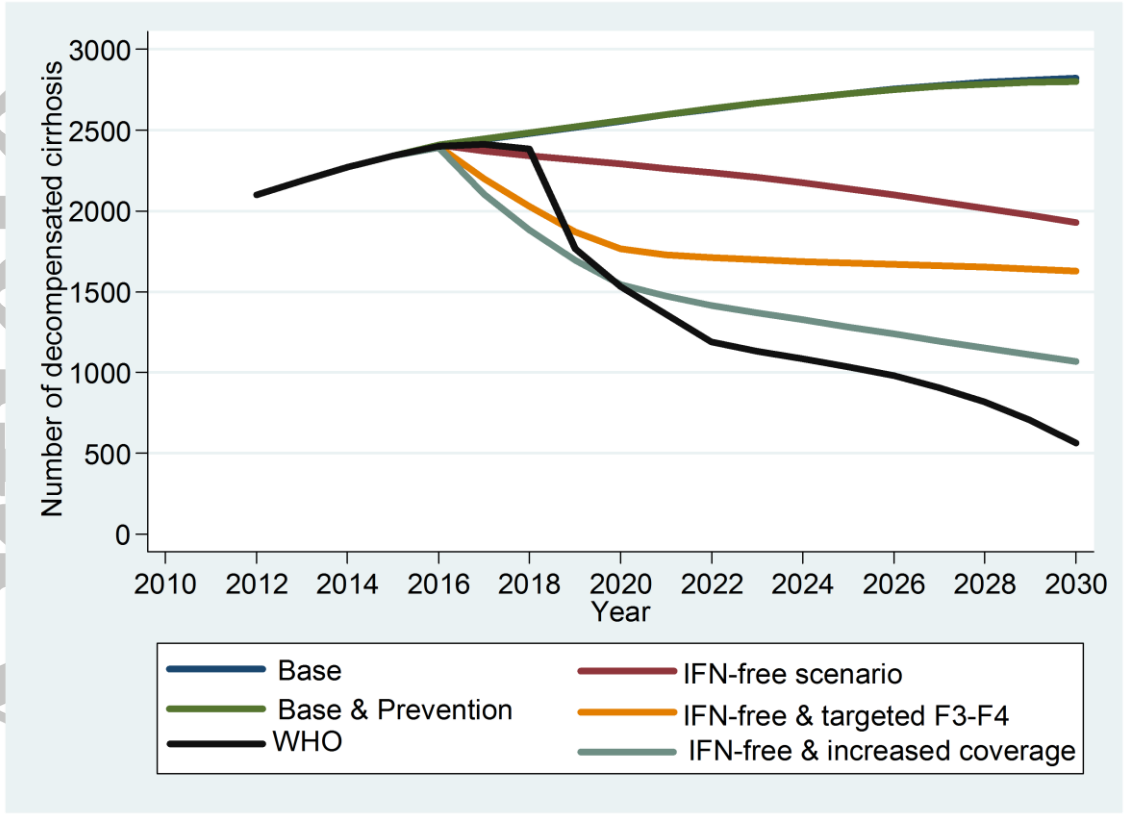

Figure 2c: Projections of future chronic HCV infection and complications under different treatment strategies (the scenario are described in detail in Table 1). Decompensated cirrhosis

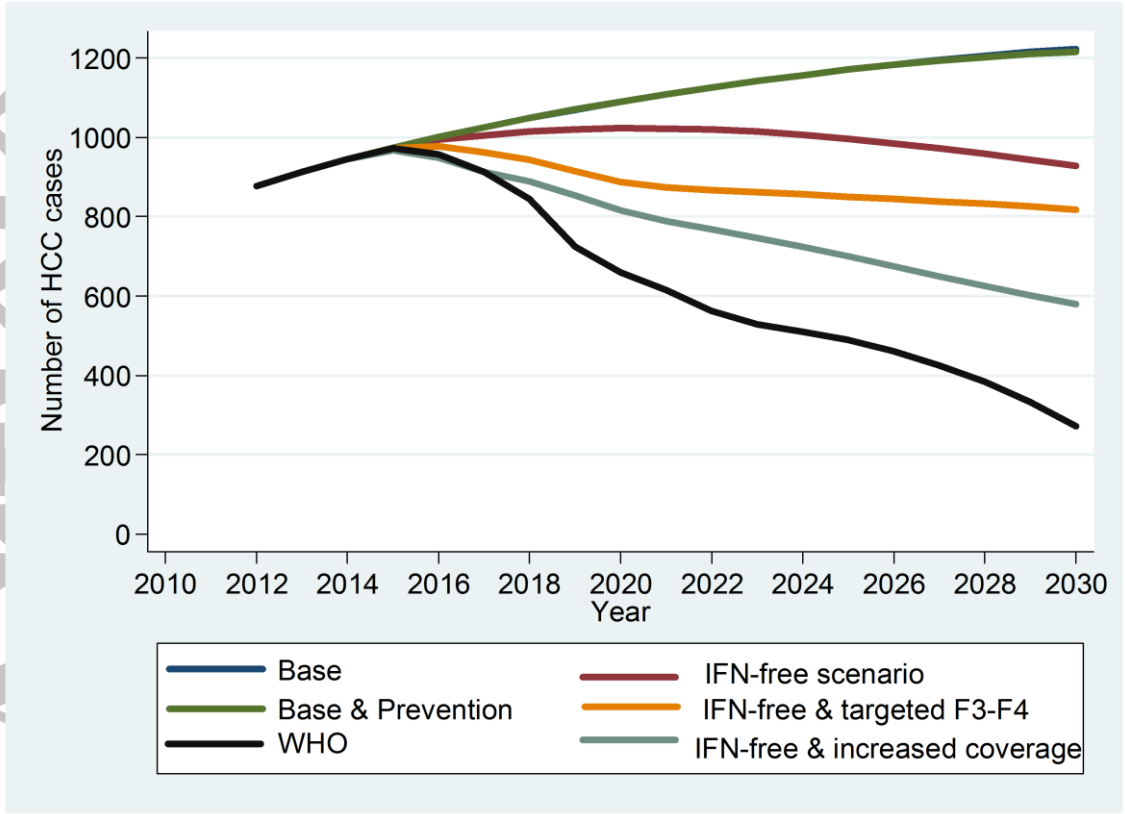

Figure 2d: Projections of future chronic HCV infection and complications under different treatment strategies (the scenario are described in detail in Table 1). HCC

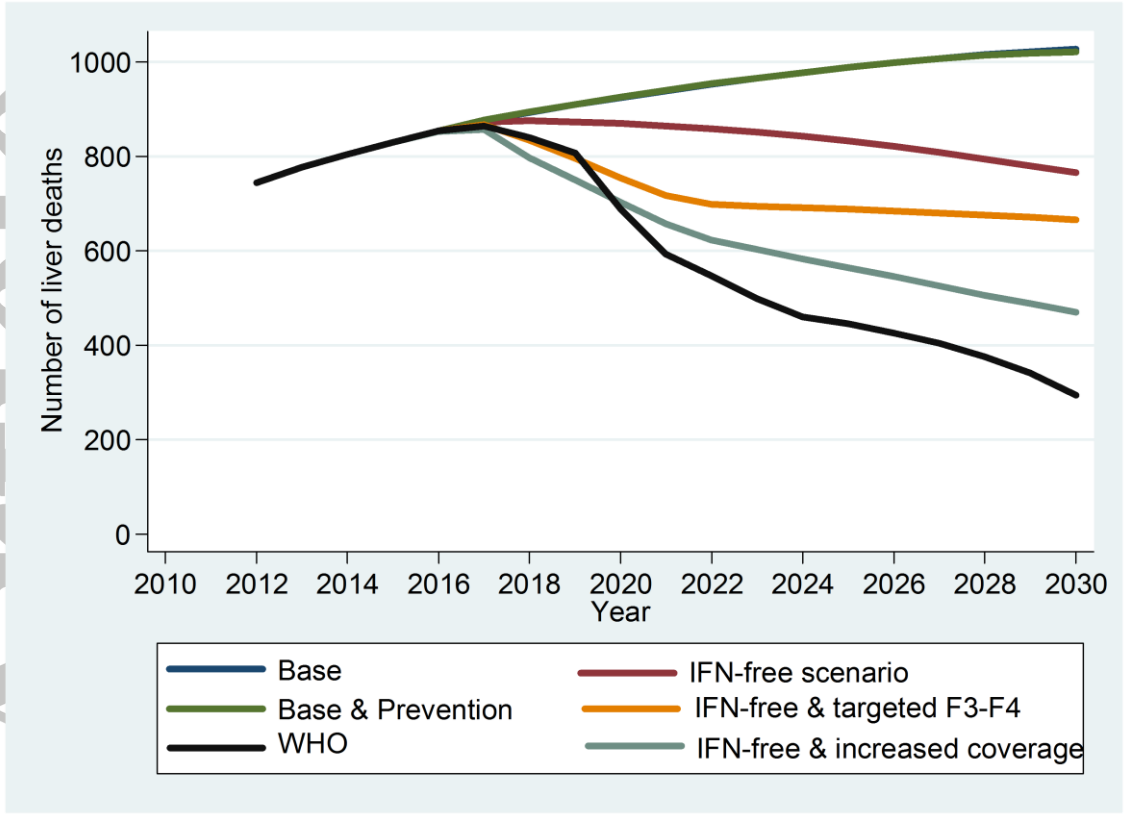

Figure 2e: Projections of future chronic HCV infection and complications under different treatment strategies (the scenario are described in detail in Table 1). Liver deaths