# Health gains and costs of HCV treatment: a cost effectiveness analysis of two different health policies scenarios simulated in PITER (Piattaforma Italiana per lo studio della Terapia delle Epatiti viRali) real life cohort.

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## ABSTRACT

**Background and aims:** New DAA treatments for HCV infection are highly efficacious, yet costly. Nevertheless, it is time to move from treating selected prioritized patients to strategies that include treatment of all HCV infected patients. To this end a lifetime multi-cohort model of 8125 real life HCV infected patients, enrolled in the PITER cohort was used to compare two IFN free treatment's policies. Policy 1:Treat all patients of the cohort in any fibrosis stage(F0-F4). Policy 2: Treat first: patients who are prioritized by the EASL HCV CPG 2015; Wait and treat: the remaining patients when they would reach the F3 stage. Dynamic lifetime HCV disease progression and the related costs were evaluated adapting a Markov model in a lifetime horizon from a health care system perspective.

Each real life patient entered the model at the proper age and fibrosis stage and was followed in the model over a lifetime. Total medical costs, quality-adjusted life-years (QALYs), and incremental cost-effectiveness ratios (ICERs) were evaluated. Probabilistic and scenario analyses were performed. **Results:** In the base-case analysis (base price of HCV regimen: € 15,000), treating all fibrosis stages vs treating first the prioritized patients, adds: € 31,083,475 (incremental costs) and 3,497 incremental QALYs, for an ICER of € 8,893 per QALY gained. The Monte Carlo scenarios (10,000 simulations) were arranged on a cost-effectiveness plot and then reported on a cost-effectiveness acceptability curve (CEAC). ICERs (incremental costs by the incremental QALYs between Policy 1 vs Policy 2 remain cost effective (below € 40,000/QALY) in 91 % of the simulations assumed. In the scenario analysis, different ICERs were calculated for fourteen prices' combinations, differentiated by fibrosis staging and the discount rate. The base price of IFN-free treatment regimen (€ 15,000), remained unvaried on time for patients with moderate to severe liver disease stage, whereas decreasing combinations of discount prices in patients with F1/F2 and F0 stage were applied. ICER was very sensitive at price variations for patients at F0 stage. For the price levels lower than 60% and 70% of the base price, applied in patients with F1/F2 and F0 respectively, the Policy 1 resulted to be dominant (less costs and greater benefits than Policy 2; policy 1 become cost effective in 97% of the simulations and dominant in 40% of them by the sensitivity analysis. **Conclusion:** Treating HCV infection at any fibrosis stage appeared to improve health outcomes and to be cost-effective. Cost effectiveness increases significantly lowering the treatment's prices in early fibrosis stages.

## OBJECTIVES

We conducted an evaluation of scenario treatment policies evaluation through cost effectiveness analysis of two treatment strategies based on different start times of DAA IFN free regimens for treatment of HCV chronic infection. A lifetime multi-cohort model of 8125 real life patients with chronic HCV infection consecutively enrolled in Italian Platform for the study of Viral hepatitis therapies (PITER) framework was used for the treatment stimulations scenarios with the final goal to design strategies of health policy first then to consider pricing.

## PATIENTS AND METHODS

A real life ongoing cohort of 8,125 patients from 93 public general hospitals and university medical centers in various Italian regions, who are consecutively enrolled in PITER HCV framework from May 2014- to December 2015 was used for scenario analyses . Sociodemografic and clinical data, related to the stage of liver disease are captured using the PITER electronic data-collection system which covers all clinical and therapeutic aspects of chronic HCV infection.

Treatment was firstly defined overall as: "prioritized", "justified " and "deferred" according to the EASL 2015 CPG treatment prioritization algorithm. Two HCV treatment policies were stimulated :

1.Policy 2. Treat with DAA s of second generation regimens, (IFN-free treatment) all patients of the cohort in any stage of fibrosis stage (F0-F4)

2.Policy 2. Treat patients that are at F3/F4 of fibrosis stage and those who are prioritized by the scientific guidelines first; wait and treat the remaining patients they would reach the F3 fibrosis stage.

Dynamic lifetime HCV disease progression during the natural history of chronic infection and the related costs are evaluated adapting a Markov model that use empirical and published data on the HCV disease progression and previously reported modeling.

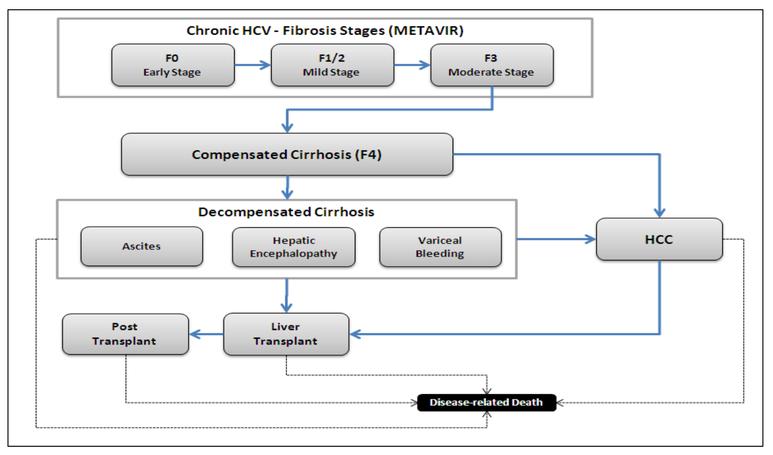


Fig. 1. Markov model structure

**Resource consumption and costs.** The use of health care resources are based on the real disease status of each real life patient entered the model and annual health care costs are associated with their respective disease status. The cost of the resources used for the implementation of the model was calculated from the perspective of the Italian National Health Service (INHS).

**Health state Utility values.** The model uses health state utility values by fibrosis stage. The quality of life values related to the complications of the liver disease and to the patients that undergo treatment, have been deduced from literature

**Model Outcomes.** The outcomes of the model are expressed in terms of quality adjusted life years (QALYs). The rationale to choose the cost utility in terms of cost effectiveness analysis is that the design of this analysis is not to evaluate the effectiveness of two treatment regimens between rather than two scenarios of the same treatment which strongly impact life quality in addition to years of life gained. The model used produces discounted lifetime QALYs and direct medical costs for each strategy of treatment. The incremental cos-effectivness ratios (ICERs) is than calculated as the ratio of the difference in costs between treatment strategies divided by the difference in QALYs.

A policy producing an ICER inferior of €40.000 per QUALY was considered cost-effective.

## RESULTS

Median age was 58 years (range 20-95 years); of whom 3797 (56%) were male. Of the enrolled patients, 48% were IFN based treatment-experienced. HCV RNA genotype distributions is as follows: genotype 1 in 58% of patients, genotype 2 in 15%, genotype 3 in 10%, genotype 4 in 7% and in 10% of patients.

**Base case analysis**

The results of the base case analysis are reported in Table2. At the IFN-free price level of € 15,000, treating all patients regardless of the fibrosis stage (Policy1) costs € 271,366,854 and produce a QALY of 90,926. On the other hand, treating prioritized patients first and the remaing patients once they reach the F3 fibrosis stage costs € 240,283,379 and produce 87,430 QALYs. Treating all stages of fibrosis compared with treating only the "prioritized" patients increases drug costs by € 31,083,475 whereas the incremental QALYs are 3,495. The ICER obtained using Policy 1 is € 8,893 per QALY. The incremental cost-effectiveness ratio therefore is cost effective compared to the threshold value generally taken into account by National Institute for Clinical Excellence (UK agency) which ranges to € 20,000–40,000/QALY.

| | Costs | QALYs | Incremental Costs | Incremental QALYs |
|---|---|---|---|---|
| Strategy 1 | € 271.366.854 | 90.926 | € 31.083.475 | 3.495 |
| Strategy 2 | € 240.283.379 | 87.430 | | |
| **ICER** | | | **€ 8.893** | |

The Monte Carlo scenarios (10,000 simulations) were arranged on a cost-effectiveness plot and then reported on a cost-effectiveness acceptability curve (CEAC).

The CEAC curve in Figure 2 displays how in treating all stages of liver disease, ICERs remain below € 40,000/QALY in 91 % of the scenarios assumed

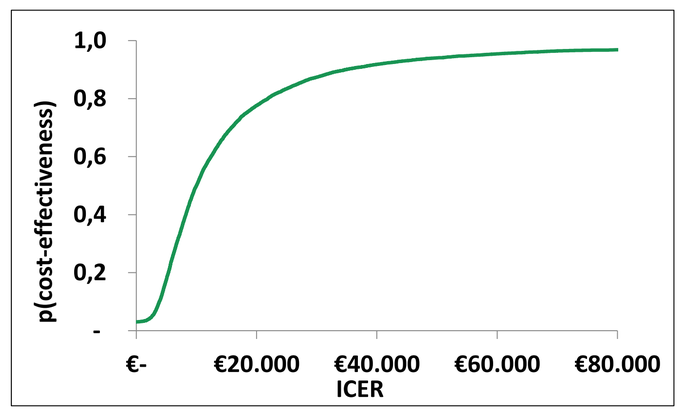


Fig. 2. Cost- Effectiveness Acceptability Curve

**Scenario analysis**

We also conducted a scenario analysis, in which we calculated different ICERs for fourteen different combination of level price differentiated by fibrosis staging and discount rate. Figure 3 shows the results of these scenario analysis. We considered base price fixed unvaried (no discounts) on time for patients with moderate to severe stage of liver disease (F3-F4-Decompensated cirrhosis) and discount prices for treatments regimens applied in patients with fibrosis levels lower than F3. Applying a discount of 30% of base price in patients with F1/F2 fibrosis stage and of 40% in those with F0, the ICER produced is € 4,148,32. ( which is the half of base case value). As it is observed in Figure 2 the ICER is very sensitive at price variations for patients with no sign of liver damage ( F0 fibrosis stage). The ICERs continue to decrease with the decreasing of the price levels of the treatment regimens in patients with F0 fibrosis. Different ICERs obtained considering each price combinations are ordered in a graph in which in the discount prices of the base price applied are shown.

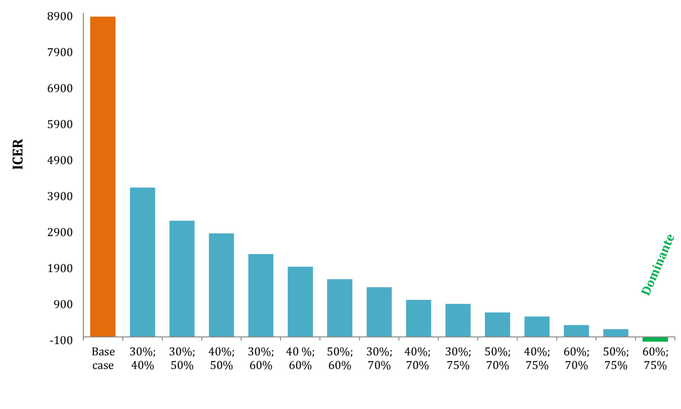


Fig 3.Results of the Scenario Analysis

## CONCLUSIONS

We evaluated the benefits and costs of two scenarios of health policies for DAA access, adopting a real-life cohort of patients to populate the Markov model. Because the cohort is a representative sample of patients in care, the only assumptions reflected in the results are those made for the model, and not assumptions made on a hypothetical population.

Treating HCV infection at early stages of fibrosis appeared to improve health outcomes and to be cost-effective. Cost-effectiveness increased significantly when varying the price of treatment regimens in early stages of fibrosis. For the price levels less than 75% of the base price applied in patients with F0-F2 fibrosis stage, Policy 1 become dominant (less costs and greater benefits in terms of QALYs, compared to Policy 2).