

**Journal title: World Journal of Gastroenterology**

**Manuscript NO: 64184**

Dear Editor,

We would like to submit the revised manuscript: "Planning the Hepatitis C virus elimination in Cyprus. A modeling study" for consideration in World Journal of Gastroenterology. We thank the reviewers for their points, which have been addressed in our point by point response below. We believe these revisions have significantly strengthened and clarified the manuscript.

Sincerely,

Dr Ilias Gountas, on behalf of the authors

**Reviewer 1**

**Comment 1:** At the end of the Introduction is not clear which are the innovative aspects of the research.

**Response:** We thank the reviewer for this point. Please see comment 3

**Comment 2:** There were too many tables and figures in this paper

**Response:** In the manuscript, we tried to present only the most essential outputs of the model. This is the reason for the extensive supplementary document. However, we think that the model's outputs regarding prevalence, incidence, deaths, and estimated treatments per scenario are vital information for the readers of the study.

**Comment 3:** Authors need to emphasize the novel insights obtained from their study.

**Response:** We thank the reviewer for this point. Two are the novel insights obtained from our study. The first is that HCV elimination in Cyprus is an achievable target. The second one is the combined use of a relative and an absolute target regarding the mortality part of the elimination. This has been done because the WHO's relative mortality target (65% reduction in mortality in 2030 compared to 2015) is not suitable in a country where the baseline mortality was very low (~2 HCV-related deaths per year). Although the WHO's relative targets have been extensively used since their introduction, the absolute HCV elimination targets have recently been put on the agenda.

In response to the reviewer's comment, we have added the following on page 10 "Our study is the first analysis that estimated the required interventions to achieve HCV elimination in the Republic of Cyprus".

Additionally, we added an "Added value of the study" section on page 13 of the discussion: "Our study contributes to the discussion regarding the feasibility of HCV elimination by 2030. First, the analysis underlined that HCV elimination in Cyprus is achievable and computed the required interventions. Second, due to the very low baseline HCV-related mortality (~2 per year), we have used both an absolute (i.e. preventing the cumulative number of deaths by 2034 from surpassing the limit of 5 per 100,000 people) and a relative target (i.e. reduce CHC prevalence among the general population by over 80% in 2034 compared to 2020) regarding the mortality part of the elimination. Although the relative targets have been extensively used since their introduction, the absolute HCV elimination targets have recently been put on the agenda (20, 26)."

## **Reviewer 2**

**Comment 1:** Page 5 – "...advanced disease (i.e., beyond the F3 liver fibrosis stage)": the latest Baveno consensus introduced the term "chronic advanced liver disease", encompassing fibrosis stages 3 and 4. Therefore, not only F4 is considered advanced disease.

**Response:** We thank the reviewer for this point. In our whole analysis, the advanced disease was defined as  $\geq$ F3 liver fibrosis stage. In response to the reviewer's comment, we have rephrased the sentence on page 5: "(i.e., F3 liver fibrosis stage and beyond ~~the F3 liver fibrosis stage~~)"

**Comment 2:** All figures – please correct typographical errors in the legends ("scenario")

**Response:** We thank the reviewer for noting this typo. We have corrected all figure legends.

**Comment 3:** Pages 5 and 29 – please explain by which tools were the fibrosis stages prevalences estimated in the population.

**Response:** The stage of fibrosis was evaluated by FibroScan. In response to the reviewer's comment, we have added the following on page 32 of the updated manuscript "The stage of fibrosis was evaluated by FibroScan".