

Dear Editor

Thank you for reviewing our manuscript *The rising incidence, progression and changing patterns of liver disease in Wales 1999-2019 (Manuscript number 79531)*. We were very pleased that this manuscript has been provisionally accepted in World Journal of Hepatology. In particular we were pleased that Reviewer 2 scored the scientific and language quality excellent and that we have met our aim of novel insights to liver disease. We note that reviewer 2 did not make any suggestions to alter the manuscript. In addition the science editor scored the scientific quality as very good.

Reviewer 1 noted that the percentage distribution of liver different diagnosis was done well. They have made several suggestions which we have addressed below and have included in the tracked manuscript.

Incidence rates are needed (number of new cases / estimated population) – not just the number of new cases per year.

The population of Wales is described in the data sources section (paragraph 1 page 10). The Welsh population has remained reasonable static over this time period. We have included the European age standardised rates per 100,000 for liver diseases in Wales (method description page 10) Figure 2 B.

In addition, a clear explanation of the novel system is missing. For example, how is it novel/different from what is currently being done in Wales and in other parts of the UK/world?

As described in the introduction page 8 para 1 previous studies have only used mortality data, specific cohorts by aetiology or disease stage. The novel methodology specifically pseudonymising individuals and defining stages and aetiological diagnoses the is described in detailed in pages 11-14 with clinical example in the supplementary data.

The first paragraph of the discussion page 20 has been altered to further highlight this approach has not previously been used.

Specific suggestions: Please use hyphens consistently (ICD-10) and make word plural in Abbreviations (Diseases); capitalize Office of National Statistics; alcohol-related, liver-related (with a hyphen) Reviewed and corrected

The authors refer to 20 years of data, but 1999-2019 is equivalent to 21 years. Reviewed and corrected

Figure 1 needs to be revised so that the different diagnoses are on the same level. Currently, they are vertical, which is misleading.

Each of the progressive boxes are demonstrating a subset of preceding box which is why they have been arranged vertically in the manner of a modified CONSORT flow diagram. The figure title and legend have been altered to describe in more detail.

Cut back on the number of tables and figures. Please shorten the manuscript – it is too long.

We have aimed to give a thorough and detailed description of the Wales Liver Registry's methodology and initial findings. We note your observation on the length of the paper, and the number of figures and tables. However, we have kept to within the guidelines of the journal. Certainly, if the editor also objected to the length, the option to move some figures etc. into the supplementary data is possible, but we will leave the final decision to the editor.

The editor-in-chief's comments are noted and the figure legends have been altered and the decomposable figures attached as a power point slide.

Many thanks for provisionally accepting this manuscript.

Yours sincerely

Tom Pembroke