Reviewer's report

Title: HCV-Related Burden of Disease in Europe: A Systematic Assessment of Incidence, Prevalence, Morbidity, and Mortality

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Reviewer: Mary E Ramsay

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General comments

The authors have aimed to review information on the incidence, prevalence and burden of hepatitis C in 22 European countries. The objective is important and admirable, given the difficulty of studying hepatitis C and the inconsistent methods of surveillance in use. The subject of the paper is of interest to the readership of BMC Public Health. The methods the authors have used are appropriate and include formal literature review and obtaining “grey” literature from national and international agencies. The article is very well written and clear.

The main weakness of this paper is the quality of the information available. The authors have acknowledged the limitations of the data and have chosen therefore to use the most consistent and comparable data sources available (such as data submitted to WHO). Because of this some of the more valid data sources are rejected and most of the extrapolations and conclusions are based upon these globally available data sources. This naturally weakens the conclusions and interpretation of the information.

The authors discuss the weaknesses of the data but do choose to make general conclusions (such as geographical trends, overall burden etc). I suspect that some of these conclusions cannot be justified given the weakness of the data sources and I wonder if they would be better acknowledging these weaknesses and refusing to comment (other than in terms of what it says about the data) on the potential differences between countries. It would be helpful to make more comments on how surveillance and data sources could be improved.

There are three areas where I think that minor essential revisions are required:

The first is the nature of the population affected. There is only one reference to injecting drug use in the paper and I think the fact that most recent infections in the region are likely to be in injectors deserves more acknowledgement and discussion – this has implications for the validity of incidence and prevalence estimates as they are largely a marginalised group. I wonder if some of the lessons learnt from the HIV epidemic in Eastern Europe – about second-generation surveillance for example – could be discussed with respect to HCV.
The second area that deserves more attention is the incidence data. Despite the statement that this data is acute hepatitis C I suspect in many cases, and know in some, that these diagnoses are not acute infections. I am not sure if the HFA database is clear but recent WHO joint reporting forms do specify acute and chronic infection separately, and when I looked today the on-line Euro database does not have hepatitis C incidence displayed. This may not have been the case in the past and may have mislead the authors of this manuscript. I understand that many countries feel obliged to report something even if they are not able to work out whether cases are acute or chronic. In addition, doctors often report chronic cases to schemes where acute infections are requested and national surveillance leads feel unable to contradict an incorrect report. This has been a long-standing issue for other forms of hepatitis and other authors have misinterpreted hepatitis B data from northern European countries in the past (eg. Zuckerman J, van Hattum J, Cafferkey M, et al. Should hepatitis B vaccination be introduced into childhood immunisation programmes in northern Europe? Lancet Infect Dis 2007; 7: 410–19.). I feel strongly that trends in numbers of reports probably reflect trends in testing – this is certainly the case for the UK and may well be more general.

The third issue refers to the use of attributable fractions where specific data is not available. Although the authors discuss this and mention that it does not allow inter-country comparisons, they do then make conclusions about trends across Europe using these fractions. I cannot see that it is internally consistent to compare prevalence between countries and then use a broad regional AF to compare burden in the same countries – this makes the discussion of trends across the continent rather self-fulfilling. Surely burden must vary according to past and current prevalence and a more appropriate analysis might have been to estimate attributable fraction from a constant relative risk and the prevalence of infection. If the data does not support this more valid approach I would suggest that discussion of inter-country comparisons is limited and interpretation simplified to estimate overall burden.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests