Reviewer's report

**Title:** The epidemiology of hepatitis C virus in Egypt: A systematic review and data synthesis

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**Reviewer:** Joan Robinson

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This study attempts to solve the mystery of why the incidence of HCV infection is so high in Egypt. The systematic review appears to be done appropriately – I agree with not combining the results of studies with such heterogeneous populations. It is not possible to look at risk of bias for studies that for the most part did not have an experimental design. The paper is fairly well written and very concise considering the large number of relevant studies.

**Major compulsory revisions:**

1. Change in incidence of HCV over time is clearly the crux of the paper. It is not clear how the authors decided which patient groups to use in the time trend analysis as this is not mentioned in the methods. How does “general population” differ from “healthy population”? Why were army recruits included? The results section mentions 8 different groups but I did not see these groups clearly outlined in the methods. Are any of the changes statistically significant? There certainly is a downward trend in blood donors and in children.

2. It is not at all clear how the multiple logistic regression was done. How was it determined what percentage of the population fell into each of the 8 groups (and what were the 8 groups?) over the years of the study? Did these 8 groups include everyone in the country? Did they overlap at all? It might be more accurate to just report the prevalence in groups of interest over time and not imply that you can estimate rates in the whole population from the biased data that you have.

3. One of the limitations of interpreting the time trend analysis is that if most cases of HCV are due to anti-schistosomiasis therapy, it could still take a very long time to see a downward trend in a group like blood donors, most of whom will still were likely born before this therapy ended in the 1980s. Furthermore, one would predict that about 5% of children born to infected women will have HCV, so the incidence could remain high for a very long time even if there is no transmission in health care facilities or other postulated means of transmission. This should be mentioned as a limitation of the study.

**Minor compulsory revisions:**

3. The seroprevalence ranges in the results are all rounded off to the nearest 5%. I usually complain that people go to too many decimal points but here I would prefer that they be rounded to the nearest 1%.
4. The first line of the paper states that the prevalence of HCV in Egypt is 14.7%. It needs to be clarified that this is an estimate.

5. What is the Egyptian demographic health survey database? Most readers will not know.

6. On Page 7, the authors mention “Special clinical population groups such as Hodgkin’s lymphoma (HL) patients, lichen planus (LP), and liver disease patients who because of their respective diseases are at variable risk levels to be classified with any of the afore mentioned population groups.” This is confusing. It might be clearer to say “patients with specific diseases or findings not known to be associated with HCV”

7. We all know that it often takes years from the end of a study until it is published. Using the date of publication for studies that did not specify the years of data collection introduces significant bias and should be mentioned as a limitation of the study.

8. Near the end of the manuscript, two sentences are not totally clear: “Therefore, it seems plausible that HCV incidence rate has declined drastically in the last two decades since the discovery of the epidemic in 1991-1992 [76, 77]. Nevertheless, our study could not identify a signature for a drastic reduction in incidence, and the totality of evidence points towards substantial ongoing HCV transmission though the precise scale of which is not yet known.” I think that you are trying to say that one would have expected the incidence to have fallen dramatically but your study suggests that this may not be the case.

9. Figure 4 is the most interesting part of the paper. I would make the graphs larger and add in more numbers on the y axis and provide p values and confidence intervals on the figure or in the text.

Level of interest: An article of importance in its field

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' below