Reviewer's report

Title: Regional disparities in interferon therapy for chronic hepatitis C in Japan: A nationwide, retrospective cohort study

Version: 1 Date: 3 December 2014

Reviewer: Scott McDonald

Reviewer's report:

Review: Masaki et al. 'Regional disparities in interferon therapy for chronic hepatitis C in Japan: A nationwide, retrospective cohort study'

This is a well-designed observational study of the association between HCV treatment and a number of demographic and other factors in a large clinical patient population. It would be helpful to the reader if the authors clearly stated their principal research question at the end of the Background section, and in the Abstract. Although the title, abstract, and discussion put emphasis on the reported regional disparities in outcome, these disparities are not particularly surprising. Demographic and other characteristics of treatment patients are likely to vary between regions, for almost any disease one cares to study. Given the large sample size, the Chi-squared test will be sensitive to very small differences between regions, so focusing on this 'significant' p-value is not at all insightful. The report of treatment outcomes alone is sufficient contribution to warrant publication. What would make a more substantial contribution is the explanation of what underlies these disparities; this, however, could be the focus of a follow-up paper. A start has been made, in some of the Additional files, but much more could be done. In the last sentence of the Discussion it is mentioned that information on access to medical resources was unavailable; such information might well be an extremely important factor in explaining regional disparities.

Major Compulsory Revisions

1. Abstract, conclusions: 'regional disparities ... may affect treatment performance and outcome'. This is an observational study; a causal relationship cannot be inferred.

2. Abstract, conclusions, final sentence: Which measures and how exactly should they be formulated to match the regional characteristics? This is too vague... treatment regimes are designed for individual patients, so it is not clear what was meant here.

3. Results, Treatment performance section and further throughout manuscript: sub-group analyses within strata formed by genotype and viral load appear to have been conducted without adjusting the family-wise error rate. If this has been done, by the Bonferroni method or another method, please clearly state so.

4. Results, Predictive factors for performance section: again the wording 'factors
that might affect...' implies causality; ‘factors associated with..’ is better. Adjust further uses of 'affect' and 'cause' similarly.

5. Concl.: This study does not suggest how to solve the 'problem' of across-region heterogeneity, perhaps because data on relevant factors has not not been collected. As already commented above, please explain further exactly what measures would be considered and how they could be implemented. Most of the patient factors investigated (i.e. demographic) cannot be modified to achieve better performance; if the clinical patient base is on average older in one region compared with another, elderly patients obviously cannot be refused treatment. I'd reword 'equally receive' to something like 'all receive the highest standard' (otherwise, you could also achieve equality by reducing the treatment performance of the best regions!).

Minor Essential Revisions

1. Background last paragraph: Final sentence is not grammatical/understandable.

2. Results, Predictive factors for outcome section: 'tentatively' is not the right word here. Delete.

3. Table 2: the ORs for 2008, 2009 and 2010+ are extremely lower, indicating that a better reference category should be chosen.

4. Indicate in Tables 2 and 3 the number of patients in each category (n). I would delete the p-value column as the same information is present in the 95% CI

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests