Reviewer's report

Title: Trends in all cause and liver-related hospitalizations in people with hepatitis B or C: a population-based linkage study

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Reviewer: Robert Myers

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In this population-based study, Gidding et al. describe trends in hospitalizations of patients with HBV and HCV in New South Wales (NSW), Australia between 2000 and 2006. The study is well written and designed and confirms existing data that supports a rising burden of HCV-related morbidity. On the contrary, HBV-related morbidity is on the decline, perhaps due to broader use of effective antiviral therapies. As expected, coinfections (e.g. with HIV) were associated with increased hospitalization rates. The study is novel in that it compares hospitalization rates with the general population of NSW, which has not been done in other studies. I enjoyed reading the study and think it will make a valuable contribution to the literature.

Major Compulsory Revisions

1) Growth rates: Some of the growth rates for admissions are alarming (e.g. for liver-related admissions in HCV/HIV, the mean annual growth is 255%). Please compare and contrast these figures to others reported (e.g. Grant Hepatology 2005; Myers Can J Gastro 2008). Although these differences may relate to different definitions between studies (see below), it should be discussed. For example, in my study of Canadian data, the average annual growth rate of liver-related admissions in HIV/HCV coinfected patients was only 40% (1/6th of yours) between 1994 and 2004.

2) Figure 3: The curve for HBV-SHR is unexpected to say the least, specifically the very high SHRs for patients under 39 years of age. Please discuss.

Minor Essential Revisions

1) Study Cohort: In the Methods, please provide the number of exclusions for the various reasons (e.g. dialysis admissions). Also, if possible, please confirm the success of your probabilistic linkage methods under 'Linkage Process'.

2) Table 2: Under all cause admissions for HCV/HBV/HIV, the 95% CI of the SHR seems to be missing some digits (3.5 to .7) Also in Table 2, I am unclear regarding the column '% Liver disease admissions'. The footnote states that these include nonalcoholic liver disease and liver cancer admissions yet the numbers don't add to 100% (e.g. for HCV, they are 27.3% and 10.4%, respectively). Please clarify this since I may be misunderstanding the data.
Discretionary Revisions

1) Outcome Measures: You have described 3 types of hospitalizations - all cause, nonalcoholic liver disease-related, and liver cancer-related (i.e. HCC and cholangiocarcinoma) - based on the principal diagnosis field. I would recommend that the data on all cause admissions be de-emphasized because the majority of these admissions are completely unrelated to viral hepatitis (e.g. previous studies have excluded obstetric admissions).

More importantly, I would recommend that you reconsider your definitions of liver-related and liver cancer-related admissions to include all of the diagnosis fields. For example, if a patient with HCV was admitted for management of an HCC (e.g. for a TACE), they could very well have HCV coded as the primary diagnosis and HCC coded in a secondary field because HCV is the underlying cause of the HCC. As it stands, this admission would be coded as an 'all cause' admission even though it is in fact HCC-related (correct me if I'm wrong). How would the HCC data look if you considered codes for HCC within any of the diagnosis fields? On a side note, please provide a reference that confirms the validity of the diagnosis codes for primary liver cancer.

In a similar manner, I would recommend that you reconsider your definitions of liver-related admissions to include complications of cirrhosis (e.g. encephalopathy, variceal hemorrhage, SBP, etc.) rather than the frequently unrelated diagnoses with ICD-10 codes 71.0-77.8 (e.g. autoimmune hepatitis, PBC, etc.). Previous studies (e.g. Kim, Hepatology 2001; Grant, Hepatology 2005; and Myers, Can J Gastro 2008) have considered an alternative definition in which a hospitalization was considered liver-related if the principal diagnosis was HCV (or HBV); there was any diagnosis of cirrhosis, portal hypertension, or other sequelae of liver disease including primary liver cancer; or the patient had undergone a liver transplant.

**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.