

Dear Editors

We thank to the reviewers for the insightful comments. We answered all the comments, and the modifications are tracked in the text.

We hope this meets the reviewer's expectations in regards to the questions, and appreciate your time in reading the document again.

Sincerely, the authors

Reviewer 00145542

1. Title: Please add "Brazil" to the title

Answer: "Brazil" was added to the title (lines 1 and 2).

2. Abstract and throughout: please report percentages with one decimal only.

Answer: the correction has been made in all the text.

3. Abstract and throughout: the stigmatizing word "alcoholism" should be avoided at any cost. Please use politically correct wording such as "heavy use of alcohol".

Answer: the politically correct wording was used (lines 49, 105 and 233).

4. Materials section: how was alcohol use measured? Did you use a validated questionnaire such as AUDIT?

Answer: The establishment of alcohol consumption was made through self-report of regular drinking, in a daily basis, and was included in the text (lines 144 and 145). AUDIT questionnaire was not used.

5. Results and table 1: Please state what level of alcohol intake (g/day) is considered as alcohol characteristic. It would be interesting to classify the data according to alcohol intake. Did you observe a dose-response

relationship? Was moderate drinking also associated with increased levels of HCC?

Answer: Heavy use of alcohol was considered when alcohol consumption was greater than 40 grams per day for men and women – this information was included in the text (lines 145 and 146). Considering the retrospective design of the study, the purpose of the analysis and the small number of patients with heavy use of alcohol, deeper considerations regarding to alcohol intake and dose-response relationships were not done.

- 6. Discussion: please expand the discussion on the geographic and/or racial heterogeneity in the South of Brazil. This is not known to the international reader.**

Answer: The South region of Brazil is composed predominantly by European descendants (this was added in the text – line 220).

- 7. Are ALDH2-deficient genotypes predominant?**

Answer: ALDH2 genotypes are not known in our population.

- 8. Do you have information on drinking behaviour in the south of Brazil? Is there more heavy episodic drinking or unrecorded alcohol drinking?**

Answer: A recent National Inquiry showed that the drinking behaviour of 50% of the population from the South of Brazil was characterized as “binge drinking” (“II National Inquiry for Alcohol and Drugs” (LENAD). Ronaldo Laranjeira (Supervisão) [et al.], São Paulo: Instituto Nacional de Ciência e Tecnologia para Políticas Públicas de Álcool e Outras Drogas (INPAD), UNIFESP. 2014).

- 9. Are there any specific beverages drunken, such as cachaça high in ethyl carbamate, which is associated with liver cancer?**

Answer: The same National Inquiry showed that beer (61%) and wine (29%) were the main types of alcoholic drinks consumed by the population in the

South of Brazil, followed by distilled beverages such as cachaça and vodka (9%). However, this was not evaluated in the presente study.

10. **Discussion/conclusion:** in discussing the health care services, it remains unclear what measures (if any?) have been conducted to reduce the HCC risk of the patients. Were, for example, interventions against heavy use of alcohol implemented? Or against obesity or any other potential risk factors? This should be clarified and also can be used to substantiate the differences to other countries, which probably did introduce some interventions.

Answer: All patients received specialized treatment according to the etiology of liver disease and risk factors identified. Obese and/or NAFLD patients were refered to a Clinical Nutrition outpatient clinic. Those with alcohol dependency were headed for a public specialized psychiatric service and encouraged to attend support groups to stop drinking (lines 147 to 151).

Reviewer 00068107

No comments were made to the authors.

Reviewer 00069297

No comments were made to the authors