Self-reported pre-stroke alcohol consumption and smoking are not associated with initial stroke severity, disability at discharge and case fatality at 30 days and 1 year

By Klára Fekete et al

Review Summary:
The authors put a considerable effort in this manuscript, whose question is of relevance. However, because of an inherent information bias due to missing data it is not possible to draw an accurate conclusion on the impact of smoking and alcohol on outcome.

Major compulsory review:
Methods, statistical analysis:

• Please clarify “found to possess significant effects”, as the term significant effects is not clear. Do you mean those variables with a statistical relevance in univariate analysis?

• The term “and/or importance in elimination of confounding” is not appropriate. I suggest using “and/or potential confounders” and you should specify which ones.

• Please specify which alpha-level of type I error you preset as significant, i.e. which “p-value” you considered significant.

• Please specify when you used mean/SD (e.g. for normally distributed data) or median/IQR (e.g. for not normally distributed data).

Results:
• **Table 1** please specify what the percent number in parenthesis refer to. It’s “Hypertension”, not “Hypertonia”.

• **Table 2** Patients with unknown status of alcohol consumption and unknown smoking status have at least a twice as high case-fatality rate as patients with known status. This finding represents an information bias, indicating a difficulty in assessing exposure to alcohol and smoke in patients with a higher case-fatality rate, as the authors correctly point out at the end of the result section. The impact of this bias is likely relevant, as information on smoking and alcohol is missing in 10.8% and 20.8% of patients, respectively. This information bias prevents us to draw any accurate conclusion on the impact of smoking and alcohol on case-fatality after stroke (see below).

• **Table 3**: 

It is not clear which covariates were taken into account for the logistic regression analysis. Such information is not presented either in the methods section or in the table 3 legends.

• To estimate the link between information bias and case-fatality, a comparison of patients with **known vs. unknown** consumption status should be performed, rather than unknown consumption vs. non-consumer. Based on the data presented on table 2, I performed such a crude analysis for alcohol consumption and case fatality at 1 year:
“Exposed” is defined as patients with known information on alcohol consume (n=721).
“Unexposed” is defined as patients with unknown alcohol consume (n=190).
“Cases” are defined as patients dying within 1 year.
“Controls” are defined as patients alive at 1 year.
For death at 1 year, the crude OR in patients with known vs. unknown alcohol consume is 0.35 (95% CI 0.25-0.49, P<0.001), indicating that information on alcohol consume is strongly linked to 1-year case fatality. Patients with known alcohol consume are more likely to be alive at 1 year compared to patients with unknown alcohol consume (=information bias).

- Concerning smoking, the authors report that unknown status is even a significant, independent predictor of case-fatality.

- Unfortunately, the performed analysis restriction to patients with known or unknown consumption status does not suppress information bias, because in an outcome prediction study we cannot simply ignore the high proportion of patients with the highest case-fatality rates and unknown information right on the two variables of interest, smoking and drinking.

- Among patients with unavailable consumption status, we simply do not know what the smoker and drinker rates are. If those rates were high, it is possible that smoking and drinking would turn out to be predictors of bad outcome, or vice versa. Based on these data and analyses, there is no way we can figure that out. The only way to assess that would be to get information on
consumption from relatives or patients, if alive. Moreover, analysis restriction prevent us to generalize the findings to other information

**Discussion:**

- The bias the authors discuss is not selection bias, rather information bias.
- Diagnosis of ischemic stroke requires brain CT or MR.
- Please note in the limitations section that neither a CT nor MR was performed on 13% patients with ischemic stroke, who were then diagnosed only clinically.
- Please also note in the limitations section that for outcome assessment the IST-1 categories instead of the commonly accepted mRS scale were used.