Author's response to reviews

Title: Potential for alcohol and drug interactions in older adults: Evidence from the Irish Longitudinal Study on Ageing

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Author's response to reviews:

Thank you for the opportunity to resubmit our paper “Potential for alcohol and drug interactions in older adults: Evidence from the Irish Longitudinal Study on Ageing” (Ms. Ref. No. MS: 1534361811117207). As requested we have addressed each of the reviewer’s suggestions in this letter, point-by-point.

Response to suggestions from reviewer 1

Major Compulsory Revisions:

1) This study includes participants aged 60 years and older. According to Table 1 nearly 1/3 of the study population is younger than 65 years old. In most (if not all) of the other studies sited in the discussion the population included in those studies were 65 years and older. It should be noted somewhere in the text that you are comparing two different populations.

Response: We have amended the discussion to acknowledge this point, however given the high prevalence of alcohol consumption among the older age groups, it is unlikely that this accounts for differences in our study and suggests that our cohort overall have a higher prevalence of alcohol consumption. To support this we have included an additional analysis showing the proportion of patients reporting alcohol consumption by age group.

[Results additional text: 3,815 adults over 60 years (mean age 69.7 ±7.3, range 60-99 years) responded to alcohol items in the self-completed questionnaire, with 2,490 (62.8%) reporting alcohol consumption in the past 6 months. The prevalence of alcohol consumption declined with age, ranging from 78% (60-64 years), 70% (65-69 years), 59% (70-74 years), 55% (75-79 years) and 47% (80+ years).] Page:10
[Discussion additional text: Some of these differences may be explained by our younger cohort (60 years and older), however this is unlikely to account for the total variation as, although the prevalence of alcohol consumption declined with age, it remained relatively high among our older age-groups.] Page: 13

2) In the conclusions it should state that the findings indicate that many Irish older adults (not many older adults as it currently states)

Response: The conclusion has been amended accordingly. Page: 16

Discretionary Revisions

1) Other limitations to the study include the inaccuracy of patients report of their own medical conditions and medications.

Response: We have acknowledged this limitation in relation to self-report of medical conditions in the discussion. However, in relation to medication, they were not self-reported, rather based on an in-home medication inventory, whereby all medication packages were presented to interviewers, reducing any recall bias. Therefore we did not feel this needed to be commented on as a limitation of this study. We did however amend the methods section to clarify this point. See amendments below)

[Methods section amendment to address this point: Home interviews were conducted by trained professional social interviewers using Computer Assisted Personal Interviewing (CAPI). Interviewers asked participants in their homes “to record all medications that you take on a regular basis, like every day or every week”, and to provide medication packages to copy down the correct medication names. Assistance from relatives was permitted. Medications were coded using the World Health Organization Anatomical Therapeutic Chemical (ATC) classification system.] Page: 7

[Discussion: When interpreting our findings, the following limitations should be considered. A number of medical conditions, and drinking frequency and quantity were based on self-report, which may result in misclassification bias.] Page: 15

Response to suggestions from reviewer 2

Major Compulsory Revisions:

1) According to the Measures of alcohol consumption in the Method section, the study subjects were divided into three groups based on their alcohol consumption: non-drinkers, light/moderate drinkers, or heavier drinkers. However, the authors lumped them altogether in Table 1. The authors should divided all study subjects based on their definitions and provide more details regarding potential differences in sociodemographic and health factors across these groups.

Response: Table 1 has been amended, dividing the sample according to their level of alcohol consumption as suggested by the reviewer, providing details
regarding potential differences in sociodemographic and health factors across these groups.[Page 24-25]

2) No data regarding study subjects with problem drinking has been provided
Response: We have addressed this point, and have provided the following detail in relation to problem drinking.

[Problem drinking, defined by CAGE, was identified in 8% of the total sample (12.7% of current drinkers). The proportion of older adults with problem drinking declined with age, ranging from 12% (60-64 years), 9% (65-69 years), 7% (70-74 years), 4% (75-79 years) and 2% (80+ years). The prevalence of problem drinking was higher among men (12.2% vs 4%), living in an urban setting (10% vs 6%). Approximately, one in ten adults with third level education reported problem drinking (11%) compared to 7% of those with primary or secondary education. The prevalence of problem drinking was highest among participants who reported being separated or divorced (17.5%). This compares to approximately 9% among those who were married or never married and 5% of those widowed. A higher proportion of adults with depression (13% vs 8%), were identified as problem drinkers.] Page:10-11

3) Table 2 should be modified accordingly based on their alcohol consumption as well, not just yes/no categorisation
Response: We appreciate the reviewers comment in relation to Table 2, however the purpose of table 2 is to consider the prevalence of exposure to AI medications, and whether exposure to AI medications influences whether or not a person drinks alcohol. This allows us to determine whether there is a difference in whether a person drinks by exposure to a particular class of AI drug. We feel that this is important to examine and report in its current format. However, we appreciate the need to address the reviewers comments and have also presented a further analysis by drinking status using a bar chart to display the proportion of people within each of the classes of AI drugs and conditions by the 3 drinking categories, and have discussed. [Page 12]

[Further analysis of drinking status among AI drug users also showed variability by therapeutic class (Figure 1). More than a quarter of those reporting antihistamine use were identified as heavier drinkers. Similarly, almost one in five older adults combined heavy drinking with cardiovascular agents, blood (anti-coagulant or anti-platelet) and antidiabetic agents, with 16% combining heavy drinking with CNS agents. Thirteen per cent of people taking anti-epileptics, antipsychotics or hypnotics reported heavy drinking, with 18% of those taking antidepressants also reporting heavy drinking. Furthermore, approximately one in five older adults with diabetes, hypertension, peptic ulcer, or depression, were identified as heavy drinkers. Individuals with breast cancer were least likely to report heavy drinking (9.6%). In contrast, almost 43% of older adults with gout reported heavy drinking. (Figure 1)]

4) The discussions should be based on the results presented in the results section. Some data were firstly seen in the Discussion section.
Response: We have amended the manuscript to ensure that any results discussed in the discussion, are reported in the results section first. This was an oversight on our part, where we discussed details of psychotropics in the discussion without prior reference in results section. They are now referenced in the results prior to discussion.

[Results: Thirteen per cent of people taking anti-epileptics, antipsychotics or hypnotics reported heavy drinking, with 18% of those taking antidepressants also reporting heavy drinking] [Page 12]

5) Currently, there are very few discussions or explanations regarding the potential association between alcohol and AI medications in different therapeutic classes.

Response: We have addressed this comment, by commenting on prevalence of concurrent alcohol use across therapeutic class, and then focusing on psychotropics as they have the greatest potential for alcohol related adverse drug reactions. [page 13-14]

[72% were exposed to at least one AI medication, with exposure varying by therapeutic class....... Although exposure to AI medications varied by therapeutic class, an examination of concurrent alcohol use suggests consistency across therapeutic classes. Concurrent alcohol use ranged between approximately 50-60% for most therapeutic classes, with the exception of muscle relaxants (80%). Similarly, heavy drinking was identified in approximately one in five older adults reporting concurrent use of cardiovascular, blood and anti-diabetic agents. The concurrent use of psychotropics with heavy alcohol consumption is of particular concern, as they may cause the most dangerous alcohol related adverse drug reactions. [8] Sixteen percent of older adults taking CNS agents were identified as heavy drinkers; 14.8% of people taking opioid analgesics reported heavy drinking. Similarly, 13% of people taking anti-epileptics, antipsychotics or hypnotics reported heavy drinking, with almost one in five of those taking antidepressants also reporting heavy drinking. This is consistent with other studies, which suggest that concurrent use of psychotropic drugs and alcohol has become more prevalent in older adults. [33, 34] However, this may be an artefact of increased use of psychotropic medications with age. We also found a high prevalence of alcohol consumption among people with conditions known to be exacerbated by alcohol consumption.]

Yours Sincerely,
Gráinne