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Prevalence of potentially serious alcohol-medication interactions in older adults in community pharmacy setting: A cross-sectional study

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Abstract

Objective: Previous prevalence estimates of POSAMINO are based on in-home inventories of medications, however this method has been shown to be associated with under-reporting of medications when compared to dispensing records. This study aims to estimate the prevalence of POSAMINO among community dwelling older adults using drug dispensing data from the community pharmacy setting.

Design: Cross-sectional study.

Setting: Irish Community Pharmacy.

Participants: 1599 consecutive older adults presenting with a prescription to one of 120 community pharmacies nationwide; community-dwelling, aged ≥65 years, able to speak and understand English, with no evidence of cognitive impairment. The mean age of sample was 75.5 years (SD 6.5); 55% (n=884) female.

Measures: 38 POSAMINO criteria were identified using participants’ pharmacy dispensing records linked to their self-reported alcohol consumption (beverage specific quantity and frequency measures) over the last 12 months.

Results: The overall prevalence of POSAMINO in the study population was 28%, with 10% at risk of at least one POSAMINO criteria and 18% at risk of two or more. Exposure to POSAMINO most commonly involved cardiovascular agents (19%) and central nervous system agents (15%). Heavy alcohol consumption with low dose aspirin was the most common POSAMINO (13%), followed by heavy alcohol consumption with multiple anti-hypertensive combinations (12%); benzodiazepines (5.5%); and opioids (4.6%). Any POSAMINO and number of POSAMINO were associated with younger age, male sex, and increasing co-morbidities.
Conclusions: This study adds to the growing body of evidence which suggests that older adults are vulnerable to potentially serious alcohol-medication interactions, particularly those involving cardiovascular and CNS agents, increasing their risk of orthostatic hypotension, gastrointestinal bleeds and increased sedation. Application of the POSAMINO criteria at the point of prescribing may facilitate the risk stratification of older adults, and prioritise alcohol screening and brief alcohol interventions in those at greatest risk of harm.

Keywords: POSAMINO, alcohol-medication interaction, older adults, alcohol, geriatric medicine

Article Summary

Strengths and limitations

- This study examined the prevalence of potentially serious alcohol-medication interactions in community-dwelling older adults using POSAMINO criteria, which avoids overestimating risk by excluding interactions which are of limited clinical significance
- Objective evaluation of medication exposures, using pharmacy dispensing records, reduces risk of bias in recall and reporting of medications
- Although alcohol consumption involved self-report measures, the use of beverage-specific quantity and frequency alcohol measures, with flash cards, reduce the risk of under-reporting alcohol consumption
- We cannot exclude potential selection bias, as we excluded participants who did not routinely attend the same pharmacy during the observation period
Introduction

Alcohol is estimated to be the seventh-leading risk factor for the global burden of mortality and disability adjusted life-years, with older adults experiencing a heightened susceptibility for alcohol-related harm. Even at relatively low levels of alcohol consumption, older adults are vulnerable to alcohol-related harms due to age-related physiological and anatomical changes. While alcohol consumption changes over the life-course, with a reduction in consumption with age, evidence from UK and Irish prospective cohort studies has shown that the number of drinking occasions tend to become more frequent among older adults. The use of multiple medications also increases with age, making older adults particularly susceptible to harm arising from alcohol-medication interactions, such as increased sedation, hypoglycaemia, enhanced orthostatic hypotension, increased risk of gastrointestinal bleeds and liver damage. A recent systematic review estimated that between one-in-five and one-in-three older adults are potentially susceptible to alcohol-medication interactions. However, these estimates may be biased as there was a lack of consensus regarding what constitutes an alcohol interactive medication across studies, and many of the proposed interactions were theoretical with trivial clinical significance. Furthermore, most studies failed to acknowledge that certain interactions may occur with any alcohol, whereas others may follow a dose response, with severity and risk of the interaction increasing with increasing levels of alcohol consumption.

To address these limitations we developed the POSAMINO criteria (POtentially Serious Alcohol-Medication Interactions in Older Adults), an explicit set of 38 potentially serious alcohol-medication interactions in older adults, using a two-step process involving a systematic review and a two-round Delphi process. The POSAMINO criteria are organised according to BNF physiological classification:
central nervous system (CNS) (n=15), cardiovascular system (CVS) (n=9), endocrine system (n=5),
musculoskeletal system (n=3), infections (n=3), malignant disease & immunosuppression (n=2) and
respiratory system (n=1). In our initial validation of the POSAMINO criteria using the first three waves of
the Irish Longitudinal Study of Ageing (TILDA), we estimated that 18% of older adults are at risk, with 8%
at risk of one potentially serious alcohol-medication interaction, and 10% at risk of two or more.\textsuperscript{10} These
estimates were observed using an in-home inventory of regular medications, which, when compared
with pharmacy dispensing records is associated with an under-reporting of psychotropics, analgesics,
anti-inflammatory and anti-rheumatics.\textsuperscript{11,12} Consequently, our previous estimates of POSAMINO
exposure may represent an underestimate, particularly for CNS agents, which have been shown to be
associated with adverse outcomes. We found that exposure to CNS POSAMINO criteria, was associated
with a 19% increase in risk for falling and an 8% increase in injurious falls at four years follow-up among
older community-dwelling adults.\textsuperscript{13} Therefore, the aim of this study was to estimate the prevalence of
POSAMINO among community dwelling older adults using drug dispensing data from the community
pharmacy setting.

Methods

Study setting and design

We conducted a cross-sectional study, recruiting participants from 120 community pharmacies across
the Republic of Ireland between May and August 2017. Community pharmacies were selected on the
basis of participating in the National Pharmacy Internship Programme. Consecutive participants were
invited to take part if they met the following inclusion criteria: presenting to a participating pharmacy to
fill their own prescription (for any prescribed medication), aged 65 years or older, community dwelling,
able to speak and understand English, and no evidence of cognitive impairment. After obtaining
informed consent, participants completed a structured face-to-face interview conducted by trained pharmacy interns. Each interview was subsequently linked to participants’ dispensing records from that pharmacy for the 12 months preceding interview. Ethical approval was obtained from the Royal College of Surgeons in Ireland, with all participants providing written informed consent (REC1365). The STROBE standardised reporting guidelines for cross-sectional studies have been adhered to for the reporting of this research.\textsuperscript{14}

\textit{Patient and public involvement}

Patients were not involved in the design, conduct or reporting of this study.

\textit{Application of the POSAMINO Criteria}

Potentially serious alcohol-medication interactions according to the POSAMINO criteria were identified using participants’ pharmacy dispensing records and self-reported alcohol consumption over the last 12 months. Medications were coded using the World Health Organization Anatomical Therapeutic Chemical (ATC) classification system. Participants, who reported drinking alcohol in the past 12 months, completed beverage-specific quantity and frequency measures for beer/cider, wine and spirits, as recommended by international guidelines for alcohol measurement in general population surveys.\textsuperscript{15} Quantity was measured by asking participants to think of a typical day in the last 12 months on which they drank wine, for example, and how many standards drinks of wine they drank. In Ireland a standard drink contains 10 grams of pure alcohol and is equivalent to half a pint of beer or cider, a single pub measure of spirits, a small (100 ml) glass of wine or bottle of alcopops. Participants were provided with beverage-specific flash cards so they could accurately report how many standard drinks they consumed
for each drink type. The trained interviewer facilitated the conversion of number of drinks to standard
drinks for each beverage. Average weekly alcohol consumption was calculated as total grams of alcohol
consumed per week. As the POSAMINO criteria specify “any alcohol consumption” or “heavy alcohol
consumption” depending on the medication, we categorised participants as current drinkers (drank
alcohol in the past 12 months), or heavy drinkers if they reported drinking in excess of 60 grams alcohol
per drinking occasion or > 110 grams alcohol/week for women or > 170 grams alcohol/week for men.

Statistical analysis
Statistical analyses were performed using STATA version 15.0. The overall prevalence of POSAMINO and
the prevalence per individual POSAMINO criterion were calculated as a proportion of all eligible
participants. The prevalence of each criterion was also calculated as a proportion of participants taking
the medicine of interest. Logistic regression and negative binomial regression models were used to
identify factors associated with experiencing any POSAMINO and the number of POSAMINO,
respectively. Models were adjusted for age, gender, area of residence, education status, polypharmacy,
self-rated health, smoking status and number of co-morbidities. Polypharmacy was defined as the use of
five or more medications.\textsuperscript{16-18} Medicines dispensed during the observation period were also used to
identify medical conditions using the validated Rx-Risk tool.\textsuperscript{19} We mapped the Rx-Risk tool to the
International Classification of Diseases, Tenth Revision (ICD-10), by matching the disease categories to
ICD-10 chapter groupings.\textsuperscript{20}

Results

Description of study population

7
In total, 2704 consecutive patients were invited to participate, 1780 (65.8%) consented to complete the interview and have it linked to their pharmacy dispensing records. Subsequently, we excluded participants attending other pharmacies as their pharmacy records were incomplete (n=125), and those with incomplete alcohol data (n=47) and missing data on age (n=9), leaving a final sample of 1599 participants. Figure 1 outlines the flow of participants through the study.

The mean age of this sample was 75.5 years (SD 6.5) and 55% were female (n=884). Two-thirds (67%; n=1065) of participants were identified as current drinkers, with 27% identified as heavy drinkers. Men were significantly more likely to be heavy drinkers, relative to women (40% vs 17%, p<0.001). Alcohol consumption declined with age, 72% of adults aged 65–69 years were identified as current drinkers, compared to 61% of adults aged ≥ 80 years. Polypharmacy was identified in 70% of the sample. Using the Rx-Risk tool participants were found to have an average of 6 conditions (SD 2.9). The most common co-morbidities included diseases of the circulatory system (90%), the digestive system (57%) and mental and behavioural disorders (35%). Further characteristics of the study sample are presented in Table 1.

INSERT TABLE 1

Prevalence of potentially serious alcohol medication interactions

The overall prevalence of POSAMINO was 28%, with 10% of participants at risk of one potentially serious alcohol-medication interaction and 18% at risk of two or more serious interactions. Table 2 shows the prevalence of the POSAMINO criteria according to physiological system. An estimated 19% of participants were identified as being at risk of a serious alcohol-medication interaction due to their
concurrent use of alcohol with cardiovascular agents. Heavy alcohol consumption with low dose Aspirin was the most common potentially serious interaction, with an estimated 13% of participants at risk. This was followed by heavy alcohol consumption with multiple anti-hypertensive combinations (12%). An estimated 15% of participants were identified as at risk due to their concurrent use of alcohol with CNS agents, particularly in relation to concurrent alcohol use with long term paracetamol (7.3%), benzodiazepines and benzodiazepine related medications (5.5%) and opioids (4.6%). Further analysis found that of those meeting the criteria for benzodiazepines and benzodiazepine related medications, 90% (n=79) had a prescription for 84 days or over. In addition, approximately one-in-four older adults who were dispensed benzodiazepines reported concurrent heavy drinking. A similar estimate was observed among those dispensed opioids (25.6%), with almost two-thirds of participants dispensed tricyclic antidepressants reporting concurrent alcohol use.

**INSERT TABLE 2**

The regression analyses (Table 3) showed that increasing age (AOR: 0.95; 95% CI: 0.93-0.97) and female gender (AOR: 0.42; 95% CI: 0.33-0.53) were associated with reduced odds of any POSAMINO; whilst urban dwellers (AOR: 1.40; 95% CI: 1.05-1.86) and higher number of co-morbidities (AOR: 1.09; 95% CI: 1.03-1.14) were associated with increased odds of any POSAMINO exposure. A similar pattern was observed from the negative binomial regression analysis which also showed that increasing age (AIRR: 0.97; 95% CI: 0.95-0.98) and female gender (IRR: 0.55; 95% CI: 0.45-0.67) were associated with a reduction in the number of POSAMINO criteria. Increasing number of co-morbidities (AIRR: 1.05; 95% CI: 1.01-1.13) were associated with an increase in the number of POSAMINO criteria.

**INSERT TABLE 3**
Discussion

In this cohort of 1599 community dwelling older adults, we observed that more than one-in-four were at risk of a potentially serious alcohol-medications interaction according to the POSAMINO criteria, with almost one-in-five at risk of two or more potentially serious interactions. Risk of exposure to multiple POSAMINO criteria was associated with younger age, male sex and increasing co-morbidities. This is the first study to investigate the prevalence of potentially serious alcohol-medications interactions in community-dwelling older adults using drug dispensing records from the participants’ community pharmacy. When we compare our estimates from this study to our previous study of older adults in TILDA, using an in-home inventory for ascertainment of medications, we note a higher risk of exposure to any potentially serious alcohol-medications interactions using POSAMINO (28% v’s 18% in TILDA) and to number of POSAMINO criteria (18% with ≥ 2 POSAMINO criteria v’s 8% in TILDA). Both studies suggest that older adults are at greatest risk of potentially serious alcohol-medications interactions due to their concurrent use of alcohol with cardiovascular agents, with almost 19% of the current sample exposed to POSAMINO criteria involving cardiovascular agents compared to 15% in TILDA. The second most common criteria involve CNS agents. However, in TILDA we estimated exposure to POSAMINO criteria involving CNS agents at 4%, compared to our current estimate of 15%. This difference is not accounted for by exposure to alcohol consumption, as estimates of current drinkers (67% v’s 64% in TILDA) and heavy drinking (27% v’s 27% in TILDA) were comparable across cohorts. The observed difference may arise from the different methods of ascertaining exposure to medications, in-home inventory compared to pharmacy dispensing records, particularly in relation to CNS agents. As previously noted, self-reports or in-home inventories of medications such as analgesics and psychotropics are lower when compared to dispensing records. It has been suggested that medications stored by the bedside maybe forgotten during in-home inventory, and stigmatization bias potentially affects self-reporting of psychotropic medications.
While the estimates observed here are higher than our previous validation of POSAMINO criteria, they are lower than a number of previous studies examining the concurrent use of alcohol with medications, which estimated that between 31 and 39% of older adults are at risk of drug alcohol interactions. The POSAMINO criteria represent potentially serious alcohol-medication interactions, with specific alcohol consumption patterns specified for each individual criteria. In contrast, considerable heterogeneity was observed in the inclusion of medications in previous studies and estimates related to the concurrent use of any alcohol consumption, which may overestimate the potential risk when interactions are likely to occur with concurrent heavy alcohol consumption.

The strengths of this study include the recruitment of community-dwelling older adults from a national sample of pharmacies in Ireland, using a consecutive recruitment process. Although consecutive recruitment involves non-probabilistic sampling, it provides structured recruitment ensuring all participants can be enrolled thus, producing a more representative sample of the target population than convenience sampling. Furthermore, the use of POSAMINO criteria, which focus on potentially serious alcohol-medication interactions, avoids overestimating risk by excluding those interactions which are of limited clinical significance. In addition, medication use was evaluated objectively using pharmacy dispensing records. However, dispensing of medications from the pharmacy does not necessarily guarantee adherence. A further limitation was the use of self-report measures for alcohol consumption, which may have introduced potential biases in recall and reporting. This may have led to the misclassification of participants, especially for POSAMINO criteria involving heavy alcohol consumption, as older adults are more likely to under-report heavy consumption. However, the use of beverage specific quantity and frequency measures, using flash cards, may have facilitated more
accurate responses. In addition, levels of alcohol consumption observed in this study are similar to those reported in previous population studies of older adults. Finally, we cannot exclude selection bias as we excluded participants who reported attending other pharmacies.

This study adds to the growing body of evidence which suggests that older adults are vulnerable to potentially serious alcohol-medication interactions, particularly those involving cardiovascular and CNS agents, increasing their risk of orthostatic hypotension, gastrointestinal bleeds and increased sedation. Furthermore, the absolute number at risk of potentially serious alcohol-medication interactions involving CNS agents is likely to be higher than previously estimated. The POSAMINO criteria may be useful in a clinical setting to risk stratify patients at the point of prescribing, particularly among younger older adults, men and those with multiple co-morbidities, allowing for the identification of patients whose alcohol consumption places them at increased risk of harm. POSAMINO criteria could also be integrated into pharmacy dispensing systems to flag patients who should be advised against consuming alcohol. Discussing the risk of alcohol more broadly and alcohol-medication interactions more specifically at the point of prescribing or dispensing may reduce the risk of harm arising from the concurrent use of alcohol and medications, many patients may simply be unaware of the potential risk, and once informed may reduce their alcohol consumption. A recent systematic review found that older adults considered themselves as responsible drinkers, often not recognizing the risks associated with their alcohol consumption. Others may benefit from a brief intervention or referral to specialist services. Finally, the association between POSAMINO criteria and adverse outcomes in terms of morbidity and mortality requires further investigation to inform the development of targeted interventions aimed at reducing alcohol-related harm in older adults.
In conclusion, our study confirms previous findings which indicate that there is a high propensity for alcohol-medication interactions among older adults, particularly in relation to cardiovascular and CNS agents. Application of the POSAMINO criteria at the point of prescribing or dispensing medications, may facilitate the risk stratification of older adults, and prioritise alcohol screening and brief alcohol interventions in those at greatest risk of harm.

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Table 1: Characteristics of sample by POSAMINO exposure

|                        | No POSAMINO (n=1156; 72%) | One or more POSAMINO (n=443; 28%) | Total (%) (n=1599) | P-value |
|------------------------|---------------------------|-----------------------------------|---------------------|---------|
| **Gender**             |                           |                                   |                     |         |
| Male                   | 445 (39%)                 | 270 (61%)                         | 715 (45%)           | <0.001  |
| Female                 | 711 (61%)                 | 173 (39%)                         | 884 (55%)           |         |
| **Age**                |                           |                                   |                     |         |
| 65-69                  | 217 (19%)                 | 111 (25%)                         | 328 (21%)           | <0.001  |
| 70-74                  | 301 (26%)                 | 135 (30%)                         | 436 (27%)           |         |
| 75-79                  | 305 (26%)                 | 105 (24%)                         | 410 (26%)           |         |
| 80+                    | 333 (29%)                 | 92 (21%)                          | 425 (27%)           |         |
| **Area**               |                           |                                   |                     |         |
| Rural                  | 283 (25%)                 | 87 (20%)                          | 370 (23%)           | 0.03    |
| Urban                  | 857 (75%)                 | 355 (80%)                         | 1212 (77%)          |         |
| **Relationship status**|                           |                                   |                     |         |
| Married/Partner        | 619 (54%)                 | 271 (62%)                         | 890 (56%)           | 0.02    |
| Single/Separated/Divorced | 211 (19%)           | 75 (17%)                          | 286 (18%)           |         |
| Widowed                | 311 (27%)                 | 93 (21%)                          | 404 (26%)           |         |
| **Education status**   |                           |                                   |                     |         |
| None/Primary           | 354 (31%)                 | 152 (35%)                         | 506 (32%)           | 0.17    |
| Secondary School       | 482 (43%)                 | 164 (38%)                         | 646 (41%)           |         |
| Third Level            | 299 (26%)                 | 123 (28%)                         | 422 (27%)           |         |
| **Self-rated health**  |                           |                                   |                     |         |
| Excellent to very good | 370 (32%)                 | 108 (24%)                         | 478 (30%)           | 0.01    |
| Smoking status          | Good            | Fair to poor | Poor | Total |
|-------------------------|-----------------|--------------|------|-------|
| Current Smoker          | 458 (40%)       | 186 (42%)    | 644  | <0.001|
| Past Smoker             | 325 (28%)       | 148 (33%)    | 473  |       |
| Never Smoked            | 111 (10%)       | 45 (10%)     | 156  |       |

| Polypharmacy            | Yes             | No            | Total |
|-------------------------|-----------------|---------------|-------|
| 779 (67%)               | 344 (78%)       | 1123 (70%)    | <0.001|
| 377 (33%)               | 99 (22%)        | 476 (30%)     |       |

| Co-morbidities‡ (ICD-10 classification) | Good | Fair to poor | Poor | Total |
|-----------------------------------------|------|--------------|------|-------|
| Diseases of the circulatory system      | 1019 (88%) | 415 (94%) | 1434 (90%) | <0.001|
| Diseases of the digestive system        | 621 (54%) | 286 (64%) | 907 (57%) | <0.001|
| Diseases of the genitourinary system    | 107 (9%) | 64 (14%) | 171 (11%) | 0.003 |
| Mental and behavioural disorders        | 379 (33%) | 173 (39%) | 552 (35%) | 0.02  |
| Endocrine, nutritional and metabolic dis| 346 (30%) | 117 (29%) | 463 (29%) | 0.17  |
| disorders                               |      |             |      |       |
| Disease of the musculoskeletal system   | 234 (20%) | 90 (20%) | 324 (20%) | 0.97  |
| and connective tissue                   |      |             |      |       |
| Neoplasms                               | 25 (2%) | 4 (1%) | 29 (2%) | 0.09  |
| Diseases of the nervous system          | 130 (11%) | 71 (16%) | 201 (13%) | 0.01  |
| Diseases of the respiratory system      | 324 (28%) | 121 (27%) | 19 (2%) | 0.02  |

‡ Determined by the RxRisk-V tool
Table 2: POSAMINO prevalence by drug class

| Criteria Description                                                                 | n  | % of sample | % on drug |
|--------------------------------------------------------------------------------------|----|-------------|-----------|
| **Cardiovascular System**                                                           |    |             |           |
| Heavy alcohol consumption with multiple anti-hypertensive combinations               | 188| 11.8        | 28.0      |
| Heavy alcohol consumption with warfarin (and phenindione)                           | 27 | 1.7         | 26.2      |
| Heavy alcohol consumption with regular use of low dose aspirin (75mg)               | 204| 12.8        | 30.4      |
| Heavy alcohol consumption with both regular and as required nitrates (e.g. glyceryl trinitrate, isosorbide dinitrate and isosorbide mononitrate) | 21 | 1.3         | 30.9      |
| Heavy alcohol consumption with the vasodilatory medication nicorandil               | 0  | 0           | 0         |
| Heavy alcohol consumption with the combined use of both nitrates and vasodilator (e.g. nicorandil) | 0  | 0           | 0         |
| Heavy alcohol consumption with diuretics (e.g. loop diuretics (furosemide), thiazide diuretics (bendroflumethiazide) & potassium sparing diuretics (amiloride) | 77 | 4.8         | 25.2      |
| Heavy alcohol consumption with alpha blockers (e.g. terazosin)                      | 20 | 1.3         | 27.0      |
| Condition                                                                 | Rating | Incidence | Risk Factor |
|---------------------------------------------------------------------------|--------|-----------|-------------|
| Heavy alcohol consumption with centrally acting anti-hypertensives (e.g. clonidine or methyldopa) | 0      | 0         | 0           |
| **Respiratory System**                                                    |        |           |             |
| Any alcohol consumption with first generation anti-histamines (e.g. promethazine) | 10     | 0.6       | 52.6        |
| **Central Nervous System**                                               | 241    | 15%       | 30.4        |
| Heavy alcohol consumption combined with opioids                           | 73     | 4.6       | 25.6        |
| Heavy alcohol consumption with duloxetine                                | 5      | 0.3       | 27.8        |
| Heavy alcohol consumption with all anti-psychotics                        | 7      | 0.4       | 14.6        |
| Any alcohol consumption with barbiturates                                 | 3      | 0.2       | 60.0        |
| Heavy alcohol consumption with anti-epileptic drugs (AEDs)               | 35     | 2.2       | 23.6        |
| Any alcohol consumption with tricyclic anti-depressants (TCAs)           | 45     | 2.8       | 66.7        |
| Any alcohol with tetracyclic antidepressants                              | 3      | 0.19      | 0           |
| Any alcohol consumption with mirtazapine | 19 | 1.2 | 55.9 |
|------------------------------------------|----|-----|------|
| Any alcohol consumption with monoamine oxidase inhibitors (MAOIs) | 0  | 0   | 0    |
| Heavy alcohol consumption with long term regular paracetamol use (e.g. 1g four times a day) | 118 | 7.3 | 23.7 |
| Heavy alcohol consumption with gabapentin (when used for neuropathic pain) | 0  | 0   | 0    |
| Heavy alcohol consumption with pramipexole or amantadine | 1  | 0.1 | 16.7 |
| Heavy alcohol consumption with apomorphine | 0  | 0   | 0    |
| Heavy alcohol consumption with levodopa (alone or in combination with carbidopa) | 1  | 0.1 | 10.0 |

**Endocrine System**

| Heavy alcohol consumption with insulin | 15 | 0.9 | 25.4 |
|--------------------------------------|----|-----|------|
| Heavy alcohol consumption with metformin | 53 | 3.3 | 26.8 |
| Heavy alcohol consumption with sulphonylureas | 14 | 0.9 | 17.3 |
| Heavy alcohol consumption with meglitinides (e.g. nateglinide) | 0  | 0   | 0    |
| Heavy alcohol consumption with thiazolidinediones (e.g. pioglitazone) | 0  | 0   | 0    |
| Condition                                                                 | Count | Percent | Adjusted Percent |
|---------------------------------------------------------------------------|-------|---------|------------------|
| **Musculoskeletal and joint diseases**                                    | 71    | 4.4     | 30.6             |
| Heavy alcohol consumption with any nonsteroidal anti-inflammatory drugs (NSAIDs) (including COX-2 inhibitors) | 63    | 3.9     | 29.9             |
| Heavy alcohol consumption combined with methotrexate or leflunomide       | 7     | 0.4     | 25.0             |
| Heavy alcohol consumption with oral muscle relaxants (e.g. baclofen)      | 3     | 0.2     | 100.0            |
| **Malignant disease and immunosuppression**                               | 0     | 0       | 0                |
| Any alcohol consumption with procarbazine                                  | 0     | 0       | 0                |
| Heavy alcohol consumption with interferon alpha or interferon beta        | 0     | 0       | 0                |
| **Infection**                                                              | 49    | 3.1     | 75.4             |
| Heavy alcohol consumption with anti-mycobacterial medications such as isoniazid, pyrazinamide, ethionamide and rifampicin (alone or in combination) | 0     | 0       | 0                |
| Any alcohol consumption with cycloserine                                   | 0     | 0       | 0                |
| Any alcohol consumption with metronidazole or tinidazole                  | 49    | 3.1     | 75.4             |
Table 3. Logistic regression and negative binomial regression models for any and number of POSAMINO

|                                        | Adjusted OR (95% CI) | Adjusted IRR (95% CI) |
|----------------------------------------|----------------------|-----------------------|
|                                        | Any POSAMINO^a       | Number of POSAMINO^b  |
| Age (years)                            | 0.95 (0.93-0.97)^*   | 0.97 (0.95-0.98)^*    |
| Women (vs. men)                        | 0.42 (0.33-0.53)^*   | 0.55 (0.45-0.67)^*    |
| Urban (vs. rural)                      | 1.40 (1.05-1.86)^*   | 1.25 (0.99-1.58)      |
| Education                              |                      |                       |
| Secondary School (vs. none/primary)    | 0.86 (0.65-1.13)     | 0.90 (0.72-1.13)      |
| Third level (vs. none/primary)         | 1.07 (0.78-1.43)     | 1.03 (0.81-1.31)      |
| Polypharmacy                           | 1.28 (0.92-1.79)     | 1.21 (0.91-1.59)      |
| Self-reported health status            |                      |                       |
| Good (vs. Excellent)                   | 1.27 (0.94-1.70)     | 1.18 (0.92-1.50)      |
| Fair to poor (vs. Excellent)           | 1.21 (0.87-1.68)     | 1.14 (0.87-1.48)      |
| Smoking status                         |                      |                       |
| Past smoker (vs. current smoker)       | 1.43 (0.95-2.17)     | 1.25 (0.90-1.75)      |
| Never smoker (vs. current smoker)      | 1.02 (0.67-1.54)     | 1.00 (0.71-1.41)      |
| Number of comorbidities (using Rx-Risk Comorbidity Index) | 1.09 (1.03-1.14)^* | 1.05 (1.01-1.13)^* |
Logistic regression model of any POSAMINO; OR Odds Ratio and 95% Confidence Interval; Negative binomial regression model of number of POSAMINO Criteria; IRR Incident Rate Ratio and 95% Confidence Interval
Figure 1: Flow diagram of study participants

Total number of patients invited (n=2704)

≥ 65 years with complete alcohol and medicines data (n=1599)

Declined to complete interview (n=924)

Missing alcohol data (n=47)

Did not always attend pharmacy with linking data (n=125)

Missing age data (n=9)
STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

| Item No | Recommendation |
|---------|----------------|
| **Title and abstract** | 1 |
| (a) Indicate the study’s design with a commonly used term in the title or the abstract | 1 |
| (b) Provide in the abstract an informative and balanced summary of what was done and what was found | 2 |
| **Introduction** | |
| Background/rationale | 2 |
| Explain the scientific background and rationale for the investigation being reported | 4-5 |
| Objectives | 3 |
| State specific objectives, including any pre-specified hypotheses | 5 |
| **Methods** | |
| Study design | 4 |
| Present key elements of study design early in the paper | 5-6 |
| Setting | 5 |
| Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 5-6 |
| Participants | 6 |
| (a) Give the eligibility criteria, and the sources and methods of selection of participants | 5-6 |
| Variables | 7 |
| Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 5-7 |
| Data sources/measurement | 8* |
| For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 5-7 |
| Bias | 9 |
| Describe any efforts to address potential sources of bias | 5-7 |
| Study size | 10 |
| Explain how the study size was arrived at | Figure 1 |
| Quantitative variables | 11 |
| Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 7 |
| Statistical methods | 12 |
| (a) Describe all statistical methods, including those used to control for confounding | 7 |
| (b) Describe any methods used to examine subgroups and interactions | 7 |
| (c) Explain how missing data were addressed | n/a |
| (d) If applicable, describe analytical methods taking account of sampling strategy | n/a |
| (e) Describe any sensitivity analyses | n/a |
| **Results** | |
| Participants | 13* |
| (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | Figure 1 |
| (b) Give reasons for non-participation at each stage | Figure 1 |
| (c) Consider use of a flow diagram | Figure 1 |
| Descriptive data | 14* |
| (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | 8 & Table 1 |
| (b) Indicate number of participants with missing data for each variable of interest | n/a |
| Outcome data | 15* |
| Report numbers of outcome events or summary measures | 8-9 & Table 2 |
| Main results | 16 |
| (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | 8-9 & Table 3 |
| (b) Report category boundaries when continuous variables were categorized | |

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(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | n/a |

**Discussion**

| Key results | 18 | Summarise key results with reference to study objectives | 9-10 |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 11 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 12 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | 11-12 |

**Other information**

| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | n/a |

*Give information separately for exposed and unexposed groups.*
# Prevalence of potentially serious alcohol-medication interactions in older adults in community pharmacy setting: A cross-sectional study

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Prevalence of potentially serious alcohol-medication interactions in older adults in community pharmacy setting: A cross-sectional study

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Word Count: 2,744
Abstract

Objective: Previous prevalence estimates of Potentially Serious Alcohol-Medication Interactions in Older adults (POSAMINO) are based on in-home inventories of medications, however this method is associated with under-reporting of medications when compared to dispensing records. This study aims to estimate the prevalence of POSAMINO among community dwelling older adults using drug dispensing data from the community pharmacy setting.

Design: Cross-sectional study.

Setting: Irish Community Pharmacy.

Participants: 1599 consecutive older adults presenting with a prescription to one of 120 community pharmacies nationwide; community-dwelling, aged ≥65 years, able to speak and understand English, with no evidence of cognitive impairment. The mean age of sample was 75.5 years (SD 6.5); 55% (n=884) female.

Measures: 38 POSAMINO criteria were identified using participants’ pharmacy dispensing records linked to self-reported alcohol consumption (beverage specific quantity and frequency measures) over the last 12 months.

Results: The overall prevalence of POSAMINO in the study population was 28%, with 10% at risk of at least one POSAMINO criteria and 18% at risk of two or more. Exposure to POSAMINO most commonly involved cardiovascular agents (19%) and central nervous system agents (15%). Exposure to a higher number of POSAMINO criteria was associated with younger age (Adjusted Incident Rate Ratio (AIRR) 0.97, 95% CI 0.95-0.98), male sex (AIRR 0.55, 95% CI 0.45-0.67), and a higher number of co-morbidities (AIRR 1.05, 95% CI 1.01-1.13).
Conclusions: This study adds to the growing body of evidence which suggests that older adults are vulnerable to potentially serious alcohol-medication interactions, particularly those involving cardiovascular and CNS agents, increasing their risk of orthostatic hypotension, gastrointestinal bleeds and increased sedation. Application of the POSAMINO criteria at the point of prescribing may facilitate the risk stratification of older adults, and prioritise alcohol screening and brief alcohol interventions in those at greatest risk of harm.

Keywords: POSAMINO, alcohol-medication interaction, older adults, alcohol, geriatric medicine

Article Summary

Strengths and limitations

- This study examined the prevalence of potentially serious alcohol-medication interactions in community-dwelling older adults using POSAMINO criteria, which avoids overestimating risk by excluding interactions which are of limited clinical significance
- Objective evaluation of medication exposures, using pharmacy dispensing records, reduces risk of bias in recall and reporting of medications
- Although alcohol consumption involved self-report measures, the use of beverage-specific quantity and frequency alcohol measures, with flash cards, reduce the risk of under-reporting alcohol consumption
- We cannot exclude potential selection bias, as we excluded participants who did not routinely attend the same pharmacy during the observation period
**Introduction**

Alcohol is estimated to be the seventh-leading risk factor for the global burden of mortality and disability adjusted life-years, with older adults experiencing a heightened susceptibility for alcohol-related harm.\(^1\)\(^2\) Even at relatively low levels of alcohol consumption, older adults are vulnerable to alcohol-related harms due to age-related physiological and anatomical changes.\(^3\) While alcohol consumption changes over the life-course, with a reduction in consumption with age, evidence from UK and Irish prospective cohort studies has shown that the number of drinking occasions tend to become more frequent among older adults.\(^4\)\(^5\) The use of multiple medications also increases with age, making older adults particularly susceptible to harm arising from alcohol-medication interactions, such as increased sedation, hypoglycaemia, enhanced orthostatic hypotension, increased risk of gastrointestinal bleeds and liver damage.\(^6\)\(^7\) A recent systematic review estimated that between one-in-five and one-in-three older adults are potentially susceptible to alcohol-medication interactions.\(^8\) However, these estimates may be biased as there was a lack of consensus regarding what constitutes an alcohol interactive medication across studies, and many of the proposed interactions were theoretical with trivial clinical significance. Furthermore, most studies failed to acknowledge that certain interactions may occur with any alcohol, whereas others may follow a dose response, with severity and risk of the interaction increasing with increasing levels of alcohol consumption.\(^7\)\(^8\)

To address these limitations we developed the POSAMINO criteria (POtentially Serious Alcohol-Medication Interactions in Older Adults), an explicit set of 38 potentially serious alcohol-medication interactions in older adults, using a two-step process involving a systematic review and a two-round Delphi process.\(^8\)\(^9\) The POSAMINO criteria are organised according to BNF physiological classification: central nervous system (CNS) (n=15), cardiovascular system (CVS) (n=9), endocrine system (n=5), musculoskeletal system (n=3), infections (n=3), malignant disease & immunosuppression (n=2) and
respiratory system (n=1). In our initial validation of the POSAMINO criteria using the first three waves of the Irish Longitudinal Study of Ageing (TILDA), we estimated that 18% of older adults are at risk of any potentially serious alcohol medication interactions, with 8% at risk of one potentially serious alcohol-medication interaction and 10% at risk of two or more. These estimates were observed using an in-home inventory of regular medications, which, when compared with pharmacy dispensing records is associated with an under-reporting of psychotropics, analgesics, anti-inflammatories and anti-rheumatics. Consequently, our previous estimates of POSAMINO exposure may represent an underestimate, particularly for CNS agents, which have been shown to be associated with adverse outcomes. We found that exposure to CNS POSAMINO criteria, was associated with a 19% increase in risk for falling and an 8% increase in injurious falls at four years follow-up among older community-dwelling adults. Therefore, the aim of this study was to estimate the prevalence of POSAMINO among community dwelling older adults using drug dispensing data from the community pharmacy setting.

Methods

Study setting and design

We conducted a cross-sectional study, recruiting participants from 120 community pharmacies across the Republic of Ireland between May and August 2017. Community pharmacies were selected on the basis of participating in the National Pharmacy Internship Programme. Consecutive participants were invited to take part if they met the following inclusion criteria: presenting to a participating pharmacy to fill their own prescription (for any prescribed medication), aged 65 years or older, community dwelling, able to speak and understand English, and no evidence of cognitive impairment. After obtaining informed consent, participants completed a structured face-to-face interview conducted by trained pharmacy interns. Each interview was subsequently linked to participants’ dispensing records from that
pharmacy for the 12 months preceding interview. Ethical approval was obtained from the Royal College of Surgeons in Ireland, with all participants providing written informed consent (REC1365). The STROBE standardised reporting guidelines for cross-sectional studies have been adhered to for the reporting of this research.¹⁴

Patient and public involvement

Patients were not involved in the design, conduct or reporting of this study.

Application of the POSAMINO Criteria

Potentially serious alcohol-medication interactions according to the POSAMINO criteria were identified using participants’ pharmacy dispensing records and self-reported alcohol consumption over the last 12 months. Medications were coded using the World Health Organization Anatomical Therapeutic Chemical (ATC) classification system. Participants, who reported drinking alcohol in the past 12 months, completed beverage-specific quantity and frequency measures for beer/cider, wine and spirits, as recommended by international guidelines for alcohol measurement in general population surveys.¹⁵ Quantity was measured by asking participants to think of a typical day in the last 12 months on which they drank wine, for example, and how many standards drinks of wine they drank. In Ireland a standard drink contains 10 grams of pure alcohol and is equivalent to half a pint of beer or cider, a single pub measure of spirits, a small (100 ml) glass of wine or bottle of alcopops. Participants were provided with beverage-specific flash cards so they could accurately report how many standard drinks they consumed for each drink type. The trained interviewer facilitated the conversion of number of drinks to standard drinks for each beverage. Average weekly alcohol consumption was calculated as total grams of alcohol
consumed per week. As the POSAMINO criteria specify “any alcohol consumption” or “heavy alcohol consumption” depending on the medication, we categorised participants as current drinkers (drank alcohol in the past 12 months), or heavy drinkers if they reported drinking in excess of 60 grams alcohol per drinking occasion or > 110 grams alcohol/week for women or > 170 grams alcohol/week for men.

Statistical analysis
Statistical analyses were performed using STATA version 15.0. The overall prevalence of POSAMINO and the prevalence per individual POSAMINO criterion were calculated as a proportion of all eligible participants. The prevalence of each criterion was also calculated as a proportion of current drinkers and those participants taking the medicine of interest. Logistic regression and negative binomial regression models were used to identify factors associated with experiencing any POSAMINO and the number of POSAMINO, respectively. Models were adjusted for age, gender, area of residence, education status, polypharmacy, self-rated health, smoking status and number of co-morbidities. Polypharmacy was defined as the use of five or more medications.\textsuperscript{16-18} Medicines dispensed during the observation period were also used to identify medical conditions using the validated Rx-Risk tool.\textsuperscript{19} We mapped the Rx-Risk tool to the International Classification of Diseases, Tenth Revision (ICD-10), by matching the disease categories to ICD-10 chapter groupings.\textsuperscript{20}

Results

Description of study population

In total, 2704 consecutive patients were invited to participate, 1780 (65.8%) consented to complete the interview and have it linked to their pharmacy dispensing records. Subsequently, we excluded participants attending other pharmacies as their pharmacy records were incomplete (n=125), and those...
with incomplete alcohol data (n=47) and missing data on age (n=9), leaving a final sample of 1599 participants. Figure 1 outlines the flow of participants through the study.

**INSERT FIGURE 1 HERE**

The mean age of this sample was 75.5 years (SD 6.5) and 55% were female (n=884). Two-thirds (67%; n=1065) of participants were identified as current drinkers, with 27% identified as heavy drinkers. Men were significantly more likely to be heavy drinkers, relative to women (40% vs 17%, p<0.001). Alcohol consumption declined with age, 72% of adults aged 65–69 years were identified as current drinkers, compared to 61% of adults aged ≥ 80 years. Polypharmacy was identified in 70% of the sample. Using the Rx-Risk tool participants were found to have an average of 6 conditions (SD 2.9). The most common co-morbidities included diseases of the circulatory system (90%), the digestive system (57%) and mental and behavioural disorders (35%). Further characteristics of the study sample are presented in Table 1.

**INSERT TABLE 1**

*Prevalence of potentially serious alcohol medication interactions*

The overall prevalence of POSAMINO among the total sample was 28%, with 10% of participants at risk of one potentially serious alcohol-medication interaction and 18% at risk of two or more serious interactions. Among current drinkers, 42% were at risk of any POSAMINO, with 15% at risk of one POSAMINO and 27% at risk of 2 or more. Table 2 shows the prevalence of the POSAMINO criteria according to physiological system. An estimated 19% of participants were identified as being at risk of a serious alcohol-medication interaction due to their concurrent use of alcohol with cardiovascular agents. Heavy alcohol consumption with low dose Aspirin was the most common potentially serious interaction, with an estimated 13% of participants at risk. This was followed by heavy alcohol consumption with
multiple anti-hypertensive combinations (12%). An estimated 15% of participants were identified as at risk due to their concurrent use of alcohol with CNS agents, particularly in relation to concurrent alcohol use with long term paracetamol (7.3%), benzodiazepines and benzodiazepine related medications (5.5%) and opioids (4.6%). Further analysis found that of those meeting the criteria for benzodiazepines and benzodiazepine related medications, 90% (n=79) had a prescription for 84 days or over. In addition, approximately one-in-four older adults who were dispensed benzodiazepines reported concurrent heavy drinking. A similar estimate was observed among those dispensed opioids (25.6%), with almost two-thirds of participants dispensed tricyclic antidepressants reporting concurrent alcohol use.

**INSERT TABLE 2**

The regression analyses (Table 3) showed that older age (AOR: 0.95; 95% CI: 0.93-0.97) and female gender (AOR: 0.42; 95% CI: 0.33-0.53) were associated with lower odds of any POSAMINO; whilst urban dwellers (AOR: 1.40; 95% CI: 1.05-1.86) and higher number of co-morbidities (AOR: 1.09; 95% CI: 1.03-1.14) were associated with a higher odds of any POSAMINO exposure. A similar pattern was observed from the negative binomial regression analysis which also showed that older age (AIRR: 0.97; 95% CI: 0.95-0.98) and female gender (IRR: 0.55; 95% CI: 0.45-0.67) were associated with a lower number of POSAMINO criteria. While, a higher number of co-morbidities (AIRR: 1.05; 95% CI: 1.01-1.13) were associated with a greater number of POSAMINO criteria.

**INSERT TABLE 3**
Discussion

In this cohort of 1599 community dwelling older adults, we observed that more than one-in-four were at risk of a potentially serious alcohol-medication interaction according to the POSAMINO criteria, with almost one-in-five at risk of two or more potentially serious interactions. Risk of exposure to multiple POSAMINO criteria was associated with younger age, male sex and a higher number of co-morbidities. This is the first study to investigate the prevalence of potentially serious alcohol-medication interactions in community-dwelling older adults using drug dispensing records from the participants’ community pharmacy. When we compare our estimates from this study to our previous study of older adults in TILDA, using an in-home inventory for ascertainment of medications, we note a higher risk of exposure to any potentially serious alcohol-mediation interactions using POSAMINO (28% v’s 18% in TILDA) and to number of POSAMINO criteria (18% with ≥ 2 POSAMINO criteria v’s 8% in TILDA). Both studies suggest that older adults are at greatest risk of potentially serious alcohol-medication interactions due to their concurrent use of alcohol with cardiovascular agents, with almost 19% of the current sample exposed to POSAMINO criteria involving cardiovascular agents compared to 15% in TILDA. The second most common criteria involve CNS agents. However, in TILDA we estimated exposure to POSAMINO criteria involving CNS agents at 4%, compared to our current estimate of 15%. This difference is not accounted for by exposure to alcohol consumption, as estimates of current drinkers (67% v’s 64% in TILDA) and heavy drinking (27% v’s 27% in TILDA) were comparable across cohorts. The observed difference may arise from the different methods of ascertaining exposure to medications, in-home inventory compared to pharmacy dispensing records, particularly in relation to CNS agents. As previously noted, self-reports or in-home inventories of medications such as analgesics and psychotropics are lower when compared to dispensing records. It has been suggested that medications stored by the bedside maybe forgotten during in-home inventory, and stigmatization bias potentially affects self-reporting of psychotropic medications.
While the estimates observed here are higher than our previous validation of POSAMINO criteria, they are lower than a number of previous studies examining the concurrent use of alcohol with medications, which estimated that between 31 and 39% of older adults are at risk of drug alcohol interactions.\textsuperscript{21-25} The POSAMINO criteria represent potentially serious alcohol-medication interactions, with specific alcohol consumption patterns specified for each individual criteria.\textsuperscript{10} In contrast, considerable heterogeneity was observed in the inclusion of medications in previous studies and estimates related to the concurrent use of any alcohol consumption,\textsuperscript{21-25} which may overestimate the potential risk when interactions are likely to occur with concurrent heavy alcohol consumption.\textsuperscript{8}

The strengths of this study include the recruitment of community-dwelling older adults from a national sample of pharmacies in Ireland, using a consecutive recruitment process. Although consecutive recruitment involves non-probabilistic sampling, it provides structured recruitment ensuring all participants can be enrolled, thus producing a more representative sample of the target population than convenience sampling.\textsuperscript{26,27} Furthermore, the use of POSAMINO criteria, which focus on potentially serious alcohol-medication interactions, avoids overestimating risk by excluding those interactions which are of limited clinical significance. In addition, medication use was evaluated objectively using pharmacy dispensing records. However, dispensing of medications from the pharmacy does not necessarily guarantee adherence.\textsuperscript{28} A further limitation was the use of self-report measures for alcohol consumption, which may have introduced potential biases in recall and reporting. This may have led to the misclassification of participants, especially for POSAMINO criteria involving heavy alcohol consumption, as older adults are more likely to under-report heavy consumption.\textsuperscript{29,30,31} However, the use of beverage specific quantity and frequency measures, using flash cards, may have facilitated more
accurate responses. In addition, levels of alcohol consumption observed in this study are similar to those reported in previous population studies of older adults. Future studies of POSAMINO could further reduce the potential risk of under-reporting of alcohol consumption by asking participants to pour a simulated drink, particularly for beverages which often involve free pouring such as wine and spirits. A study of 844 current drinkers aged 65-74 years in Australia found that older men poured drinks that were 32% larger than a standard drink of 10 grams alcohol, with older women pouring drinks that were 16% larger. Furthermore, in the absence of internationally agreed age-specific drinking guidelines, we used national Irish recommendations to define heavy alcohol consumption in the development of the POSAMINO criteria and in this study to classify participants as heavy drinkers. Given that older adults are more vulnerable to harm even at low levels of alcohol consumption, our estimates of POSAMINO may reflect an underestimate of the true prevalence among older adults particularly for those criteria involving heavy alcohol consumption. Finally, we cannot exclude selection bias as we excluded participants who reported attending other pharmacies.

This study adds to the growing body of evidence which suggests that older adults are vulnerable to potentially serious alcohol-medication interactions, particularly those involving cardiovascular and CNS agents, increasing their risk of orthostatic hypotension, gastrointestinal bleeds and increased sedation. Furthermore, the absolute number at risk of potentially serious alcohol-medication interactions involving CNS agents is likely to be higher than previously estimated. The POSAMINO criteria may be useful in a clinical setting to risk stratify patients at the point of prescribing, particularly among younger older adults, men and those with multiple co-morbidities, allowing for the identification of patients whose alcohol consumption places them at increased risk of harm. POSAMINO criteria could also be integrated into pharmacy dispensing systems, as part of a Screening, Brief Intervention and Referral to
Treatment (SBIRIT) intervention. Discussing the risk of alcohol more broadly and alcohol-medication interactions more specifically at the point of prescribing or dispensing may reduce the risk of harm arising from the concurrent use of alcohol and medications, since many patients may simply be unaware of the potential risk, and once informed may reduce their alcohol consumption. A recent systematic review found that older adults considered themselves as responsible drinkers, often not recognizing the risks associated with their alcohol consumption. Others may benefit from a brief intervention or referral to specialist services. Finally, the association between POSAMINO criteria and adverse outcomes in terms of morbidity and mortality requires further investigation to inform the development of targeted interventions aimed at reducing alcohol-related harm in older adults.

In conclusion, our study confirms previous findings which indicate that there is a high propensity for alcohol-medication interactions among older adults, particularly in relation to cardiovascular and CNS agents. Application of the POSAMINO criteria at the point of prescribing or dispensing medications, may facilitate the risk stratification of older adults, and prioritise alcohol screening and brief alcohol interventions in those at greatest risk of harm.

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be published; agreed to be accountable for all aspects of the work, ensuring that questions related to
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Table 1: Characteristics of sample by POSAMINO exposure

| POSAMINO Exposure | Total (%) | P-value |
|-------------------|-----------|---------|
| (n=1156; 72%)     | (n=1599)  |         |
| **Gender**        |           |         |
| Male              | 445 (39%) | 715 (45%) | <0.001 |
| Female            | 711 (61%) | 884 (55%) |         |
| **Age**           |           |         |
| 65-69             | 217 (19%) | 328 (21%) | <0.001 |
| 70-74             | 301 (26%) | 436 (27%) |         |
| 75-79             | 305 (26%) | 410 (26%) |         |
| 80+               | 333 (29%) | 425 (27%) |         |
| **Area**          |           |         |
| Rural             | 283 (25%) | 370 (23%) | 0.03   |
| Urban             | 857 (75%) | 1212 (77%)|         |
| **Relationship status** | | |
| Married/Partner   | 619 (54%) | 890 (56%) | 0.02   |
| Single/Separated/Divorced | 211 (19%) | 286 (18%) |         |
| Widowed           | 311 (27%) | 404 (26%) |         |
| **Education status** | | |
| None/Primary      | 354 (31%) | 506 (32%) | 0.17   |
| Secondary School  | 482 (43%) | 646 (41%) |         |
| Third Level       | 299 (26%) | 422 (27%) |         |
### Self-rated health

| Level                | N     | Proportion (%) |
|----------------------|-------|----------------|
| Excellent to very good| 370   | 32%            |
| Good                 | 458   | 40%            |
| Fair to poor         | 325   | 28%            |

### Alcohol consumption‡

| Category                                           | N     | Proportion (%) |
|----------------------------------------------------|-------|----------------|
| Non-drinker                                        | 534   | 46%            |
| Current drinker (but not heavy drinker)            | 556   | 48%            |
| Heavy drinker                                      | 66    | 6%             |

### Smoking status

| Status       | N     | Proportion (%) |
|--------------|-------|----------------|
| Current Smoker| 111   | 10%            |
| Past Smoker  | 444   | 38%            |
| Never Smoked | 600   | 52%            |

### Polypharmacy

| Category | N     | Proportion (%) |
|----------|-------|----------------|
| Yes      | 779   | 67%            |
| No       | 377   | 33%            |

### Co-morbidities† (ICD-10 classification)

#### Diseases of the circulatory system

| Category | N     | Proportion (%) |
|----------|-------|----------------|
| 1019 (88%) | 415   | 94%            |
| 1434 (90%) |       |                |

#### Diseases of the digestive system

| Category | N     | Proportion (%) |
|----------|-------|----------------|
| 621 (54%) | 286   | 64%            |
| 907 (57%) |       |                |

#### Diseases of the genitourinary system

| Category | N     | Proportion (%) |
|----------|-------|----------------|
| 107 (9%)  | 64    | 14%            |
| 171 (11%) |       |                |

#### Mental and behavioural disorders

| Category | N     | Proportion (%) |
|----------|-------|----------------|
| 379 (33%) | 173   | 39%            |
| 552 (35%) |       |                |

#### Endocrine, nutritional and metabolic disorders

| Category | N     | Proportion (%) |
|----------|-------|----------------|
| 346 (30%) | 117   | 29%            |
| 463 (29%) |       |                |

#### Disease of the musculoskeletal system and connective tissue

| Category | N     | Proportion (%) |
|----------|-------|----------------|
| 234 (20%) | 90    | 20%            |
| 324 (20%) |       |                |

#### Diseases of the nervous system

| Category | N     | Proportion (%) |
|----------|-------|----------------|
| 130 (11%) | 71    | 16%            |
| 201 (13%) |       |                |

#### Diseases of the respiratory system

| Category | N     | Proportion (%) |
|----------|-------|----------------|
| 324 (28%) | 121   | 27%            |
| 445 (28%) |       |                |

‡ Alcohol consumption was based on self-reported alcohol consumption in the past 12 months: non-drinkers reported not drinking in the past 12 months;
Current drinkers (drank alcohol in the past 12 months); Heavy drinkers (reported drinking >60 grams alcohol per drinking occasion or drinking >110 grams alcohol/week for women or >170 grams alcohol/week for men; † Determined by the Rx Risk-V tool
Table 2: Number and prevalence of POSAMINO criteria among total sample, current drinkers and those using medications included in POSAMINO

| Criteria Description                                                                 | Number of people fitting POSAMINO criteria | % of total sample (n=1599) | % of current drinkers (n=1065) | % taking medication class† |
|-------------------------------------------------------------------------------------|-------------------------------------------|---------------------------|-------------------------------|---------------------------|
| **Cardiovascular System**                                                           |                                           |                           |                               |                           |
| Heavy alcohol consumption with multiple anti-hypertensive combinations               | 188                                        | 12%                       | 17.7%                         | 28.0%                     |
| Heavy alcohol consumption with warfarin (and phenindione)                           | 27                                         | 2%                        | 2.5%                          | 26.7%                     |
| Heavy alcohol consumption with regular use of low dose aspirin (75mg)                | 204                                        | 13%                       | 19.2%                         | 30.4%                     |
| Heavy alcohol consumption with both regular and as required nitrates (e.g. glyceryl trinitrate, isosorbide dinitrate and isosorbide mononitrate) | 21                                         | 1%                        | 2.0%                          | 31.3%                     |
| Heavy alcohol consumption with the vasodilatory medication nicorandil                | 0                                          | 0                         | 0                             | 0                         |
| Heavy alcohol consumption with the combined use of both nitrates and vasodilator medication (e.g. nicorandil) | 0                                          | 0                         | 0                             | 0                         |
| Heavy alcohol consumption with diuretics (e.g. loop diuretics (furosemide), thiazide diuretics (bendroflumethiazide) & potassium sparing diuretics (amiloride) | 77                                         | 4.8%                      | 7.2%                          | 25.2%                     |
| Condition                                                                 | Count | 1.3% | 1.9% | 27.0% |
|--------------------------------------------------------------------------|-------|------|------|-------|
| Heavy alcohol consumption with alpha blockers (e.g. terazosin)          | 20    |      |      |       |
| Heavy alcohol consumption with centrally acting anti-hypertensives      | 0     | 0    | 0    | 0     |
| (e.g. clonidine or methyldopa)                                          |       |      |      |       |
| **Respiratory System**                                                   | **10**| 0.6% | 0.9% | 52.6% |
| Any alcohol consumption with first generation anti-histamines (e.g.     | 10    | 0.6  | 0.9  | 52.6% |
| promethazine)                                                            |       |      |      |       |
| **Central Nervous System**                                               | **241**| 15%  | 22.6%| 30.4% |
| Heavy alcohol consumption with benzodiazepines (e.g. diazepam)          | 88    | 5.5% | 8.3% | 24.3% |
| and benzodiazepine related medications (e.g. zopiclone)                 |       |      |      |       |
| Heavy alcohol consumption combined with opioids                          | 73    | 4.6% | 6.9% | 25.6% |
| Heavy alcohol consumption with all anti-psychotics                       | 7     | 0.4% | 0.7% | 14.6% |
| Heavy alcohol consumption with anti-epileptic drugs (AEDs)              | 35    | 2.2% | 3.3% | 23.6% |
| Any alcohol consumption with tricyclic anti-depressants (TCAs)          | 45    | 2.8% | 4.2% | 66.7% |
| Any alcohol consumption with mirtazapine                                 | 19    | 1.2% | 1.8% | 55.9% |
| Any alcohol consumption with monoamine oxidase inhibitors (MAOIs)       | 0     | 0    | 0    | 0     |
| Heavy alcohol consumption with long term regular paracetamol use         | 118   | 7.3% | 11.1%| 23.7% |
| (e.g. 1g four times a day)                                               |       |      |      |       |
| Condition                                                                 | Count | Percentage | Male     | Female   | Others |
|---------------------------------------------------------------------------|-------|------------|----------|----------|--------|
| Heavy alcohol consumption with gabapentin (when used for neuropathic pain)| 0     | 0          | 0        | 0        | 0      |
| Heavy alcohol consumption with apomorphine                                 | 0     | 0          | 0        | 0        | 0      |
| **Endocrine System**                                                       | 60    | 3.8%       | 5.6%     | 24.8%    |
| Heavy alcohol consumption with insulin                                     | 15    | 0.9%       | 1.4%     | 25.4%    |
| Heavy alcohol consumption with metformin                                   | 53    | 3.3%       | 5.0%     | 26.8%    |
| Heavy alcohol consumption with sulphonylureas                              | 14    | 0.9%       | 1.31%    | 17.3%    |
| Heavy alcohol consumption with meglitinides (e.g. nateglinide)             | 0     | 0          | 0        | 0        |
| Heavy alcohol consumption with thiazolidinediones (e.g. pioglitazone)      | 0     | 0          | 0        | 0        |
| **Musculoskeletal and joint diseases**                                     | 71    | 4.4%       | 6.7%     | 30.6%    |
| Heavy alcohol consumption with any nonsteroidal anti-inflammatory drugs (NSAIDs) (including COX-2 inhibitors) | 63    | 3.9%       | 5.9%     | 29.9%    |
| Heavy alcohol consumption combined with methotrexate or leflunomide       | 7     | 0.4%       | 0.7%     | 25.0%    |
| **Malignant disease and immunosuppression**                               | 0     | 0          | 0        | 0        |
| Any alcohol consumption with procarbazine                                  | 0     | 0          | 0        | 0        |
| Heavy alcohol consumption with interferon alpha or interferon beta        | 0     | 0          | 0        | 0        |
| Infection                                           | Users | 3.1% | 4.6% | 75.4% |
|----------------------------------------------------|-------|------|------|-------|
| Heavy alcohol consumption with anti-mycobacterial medications such as isoniazid, pyrazinamide, ethionamide and rifampicin (alone or in combination) | 0     | 0    | 0    | 0     |
| Any alcohol consumption with cycloserine           | 0     | 0    | 0    | 0     |
| Any alcohol consumption with metronidazole or tinidazole | 49    | 3.1% | 4.6% | 75.4% |

Any individual POSAMINO criteria with less than five individuals are not reported in this table to ensure anonymity of respondents. †The denominator for medication users varied across drug classes; Cardiovascular System (n=1066); Respiratory System (n=19); Central Nervous System (n= 791); Endocrine System (n=241); Musculoskeletal and joint diseases (n= 231); Malignant disease and immunosuppression (n=0); Infection (n=65)
Table 3. Logistic regression and negative binomial regression models for any and number of POSAMINO among total sample (N=1599)

|                                      | Adjusted OR (95% CI) | Adjusted IRR (95% CI) |
|--------------------------------------|----------------------|-----------------------|
|                                      | Any POSAMINO<sup>a</sup> | Number of POSAMINO<sup>b</sup> |
| Age (years)                          | 0.95 (0.93-0.97)*    | 0.97 (0.95-0.98)*     |
| Women (vs. men)                      | 0.42 (0.33-0.53)*    | 0.55 (0.45-0.67)*     |
| Urban (vs. rural)                    | 1.40 (1.05-1.86)*    | 1.25 (0.99-1.58)      |
| Education                            |                      |                       |
| Secondary School (vs. none/primary)  | 0.86 (0.65-1.13)     | 0.90 (0.72-1.13)      |
| Third level (vs. none/primary)       | 1.07 (0.78-1.43)     | 1.03 (0.81-1.31)      |
| Polypharmacy                         | 1.28 (0.92-1.79)     | 1.21 (0.91-1.59)      |
| Self-reported health status          |                      |                       |
| Good (vs. Excellent)                 | 1.27 (0.94-1.70)     | 1.18 (0.92-1.50)      |
| Fair to poor (vs. Excellent)         | 1.21 (0.87-1.68)     | 1.14 (0.87-1.48)      |
| Smoking status                       |                      |                       |
| Past smoker (vs. current smoker)     | 1.43 (0.95-2.17)     | 1.25 (0.90-1.75)      |
| Never smoker (vs. current smoker)    | 1.02 (0.67-1.54)     | 1.00 (0.71-1.41)      |
| Number of comorbidities (using Rx-Risk Comorbidity Index) | 1.09 (1.03-1.14)* | 1.05 (1.01-1.13)* |
aLogistic regression model of any POSAMINO; OR Odds Ratio and 95% Confidence Interval; bNegative binomial regression model of number of POSAMINO Criteria; IRR Incident Rate Ratio and 95% Confidence Interval
Figure 1: Flow diagram of study participants
Figure 1: Flow diagram of study participants

Total number of patients invited (n=2704)

≥ 65 years with complete alcohol and medicines data (n=1599)

Declined to complete interview (n=924)

Missing alcohol data (n=47)

Did not always attend pharmacy with linking data (n=125)

Missing age data (n=9)
STROBE Statement—Checklist of items that should be included in reports of cross-sectional studies

| Item No | Recommendation |
|---------|----------------|
| **Title and abstract** | 1. *(a)* Indicate the study’s design with a commonly used term in the title or the abstract  
*(b)* Provide in the abstract an informative and balanced summary of what was done and what was found |
| **Introduction** | 2. Explain the scientific background and rationale for the investigation being reported |
| **Objectives** | 3. State specific objectives, including any pre-specified hypotheses |
| **Methods** | 4. Present key elements of study design early in the paper |
| **Setting** | 5. Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection |
| **Participants** | 6. *(a)* Give the eligibility criteria, and the sources and methods of selection of participants |
| **Variables** | 7. Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable |
| **Data sources/measurement** | 8*. For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group |
| **Bias** | 9. Describe any efforts to address potential sources of bias |
| **Study size** | 10. Explain how the study size was arrived at |
| **Quantitative variables** | 11. Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why |
| **Statistical methods** | 12. *(a)* Describe all statistical methods, including those used to control for confounding  
*(b)* Describe any methods used to examine subgroups and interactions  
*(c)* Explain how missing data were addressed  
*(d)* If applicable, describe analytical methods taking account of sampling strategy  
*(e)* Describe any sensitivity analyses |
| **Results** | 13*. *(a)* Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed  
*(b)* Give reasons for non-participation at each stage  
*(c)* Consider use of a flow diagram |
| **Descriptive data** | 14*. *(a)* Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders  
*(b)* Indicate number of participants with missing data for each variable of interest |
| **Outcome data** | 15*. Report numbers of outcome events or summary measures  
*(a)* Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included  
*(b)* Report category boundaries when continuous variables were categorized  
*(c)* Describe analytical methods taking account of sampling strategy |
| **Main results** | 16. *(a)* Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included  
*(b)* Report category boundaries when continuous variables were categorized  
*(c)* Describe analytical methods taking account of sampling strategy |
(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | n/a |

### Discussion

| **Key results** | **18** | Summarise key results with reference to study objectives | 9-10 |
| **Limitations** | **19** | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 11 |
| **Interpretation** | **20** | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 12 |
| **Generalisability** | **21** | Discuss the generalisability (external validity) of the study results | 11-12 |

### Other information

| **Funding** | **22** | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | n/a |

*Give information separately for exposed and unexposed groups.*