

# Cognitive decline and alcohol consumption adjusting for functional status over a 3-year period in French speaking community living older adults

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## ABSTRACT

**Background** The effect of alcohol consumption on cognitive decline is not clear. We aimed to study the association between alcohol consumption and cognitive functioning controlling for functional health status.

**Methods** A total of 1610 older adults with a score  $\geq 26$  on the Mini-Mental State Examination (MMSE) were followed to assess the change in scores at the 3-year follow-up. Information on alcohol consumption as well as socio-demographic, lifestyle, psychosocial and clinical factors, as well as health service use were assessed at baseline and 3-year follow-up interviews. Linear mixed models with repeated measures were used stratifying by functional status.

**Results** Close to 73% reported consuming alcohol in the past 6 months, of which 11% were heavy drinkers ( $\geq 11$  and  $\geq 16$  drinks for women and men). A significant decrease in MMSE scores was observed in low functioning non-drinkers ( $-1.48$ ; 95% CI:  $-2.06$ ,  $-0.89$ ) and light to moderate drinkers ( $-0.99$ ; 95% CI:  $-1.54$ ,  $-0.44$ ) and high functioning non-drinkers ( $-0.51$ ; 95% CI:  $-0.91$ ,  $-0.10$ ).

**Conclusions** Alcohol consumption did not contribute to cognitive decline. Cognitive decline was greater in individuals reporting low functional status. Research should focus on the interaction between changing patterns of alcohol consumption and social participation in individuals with low and high functioning status.

**Keywords** alcohol consumption, dementia, older people

## Introduction

Dementia has become a global public health issue<sup>1</sup> affecting close to 50 million people worldwide with societal costs reaching US\$ 600 billion.<sup>2</sup> Recent meta-analyses focusing on modifiable risk factors of cognitive decline have identified education, physical inactivity<sup>3,4</sup> and smoking.<sup>4</sup> There is less clear evidence on the effect of alcohol.<sup>5,6</sup>

Antsey *et al.*'s<sup>7</sup> meta-analysis and Ilomaki *et al.*'s<sup>8</sup> review of systematic reviews showed that, compared to non-drinkers, those reporting light to moderate drinking (up to 28 drinks/week) had up to a 40% decreased risk of dementia, whereas

heavy to excessive drinking did not affect the risk.<sup>8</sup> In Neafsy and Collins<sup>9</sup> systematic review moderate drinking (up to 3 drinks/day) reduced up to 30% the risk of cognitive impairment but not cognitive decline. The results observed may in part be explained by a cohort selection effect where

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lifetime abstainers are grouped together with past alcohol drinkers more likely to develop disease thus rendering this reference group sicker.<sup>7–9</sup> This has been called the ‘sick quitter’ bias.<sup>10</sup> Ng Fat *et al.*<sup>11</sup> showed that having limitations due to a chronic illness was associated with the cessation or reduction of alcohol consumption.

More recently, Topiwala *et al.*<sup>12</sup> showed that alcohol consumption was associated with brain atrophy in men, but not in women. The authors also reported that as opposed to abstainers, higher alcohol consumption (>7 drinks a week) was associated with a faster decline on lexical fluency but not on word recall or semantic fluency. There was no association between alcohol consumption and cognitive performance. Differences in baseline cognitive scores among abstainers and alcohol users may have influenced the results.

In Canada, the prevalence of alcohol abstainers among older adults has decreased from 31% in 2001 to 24% in 2014.<sup>13</sup> An increasing trend of drinking between 1997 and 2014 among older adults was also recently observed in the USA where the prevalence of heavy episodic drinking increased yearly by 3.7%.<sup>14</sup> The fact that more than 80% of those aged  $\geq 65$  years are prescribed at least one drug, with an average reaching 5.5 drugs per senior,<sup>15</sup> the interaction with alcohol increases the potential for side effects.

The objective of this study was to assess, in a sample of community living older adults recruited in primary care practices, the association between alcohol consumption and cognitive decline over a 3-year period. This study will contribute to the present literature by considering both quantity and frequency of alcohol consumption, as well as assessing the effect of a change in alcohol consumption on cognitive status while controlling for a number of important confounders including self-rated functional status. This variable, not previously controlled for in the literature, will allow to control for the possible effect that non-drinkers stopped drinking due to functional limitations associated with illness and in part control for the ‘sick quitter’ bias.

## Methods

### Data source and study population

The sample consisted of older adults aged  $\geq 65$  years ( $n = 1811$ ) recruited in the ESA-Services study (2011–13) while waiting for medical services in a general practice clinic located in one of the most populated administrative health regions of the province of Quebec representative of metropolitan, urban and rural areas. Participating clinics were recruited via general practitioners practicing in the region full time (>4 days/week). Among eligible physicians, 60%

participated. Detailed information on the methodology has been previously published.<sup>16</sup>

Briefly, patients were contacted within 30 days of the visit to schedule an at home interview. In order to minimize bias associated with cognitive impairment, individuals in the 10th percentile of the Mini-Mental State Examination (MMSE)<sup>17</sup> at baseline (MMSE < 26) were excluded from the analyses.<sup>18</sup> Among the 1627 eligible individuals, we were able to contact and re-interview at home 1061 of these individuals, 3 years later. Study variables were ascertained at both interviews. Losses to follow-up did not differ with respect to baseline MMSE scores (28.5 versus 28.6,  $P = 0.27$ ); past or current smoking status (62 versus 61%,  $P = 0.76$ ); and alcohol consumption group (non-drinkers: 27 versus 31%, light to moderate: 68 versus 66%, heavy drinkers: 4 versus 5%,  $P = 0.06$ ); low income (97 versus 98%,  $P = 0.05$ ); the presence of minor (1.9 versus 1.2%,  $P = 0.20$ ) and major (2.6 versus 1.6%,  $P = 0.17$ ) depression; reporting 3 or more chronic physical disorders (70 versus 67%,  $P = 0.18$ ), female gender (62 versus 57%,  $P = 0.05$ ); completed primary level of education and less (14 versus 11%,  $P = 0.05$ ). Those lost to follow-up were however younger (65–74 years) (40 versus 47%,  $P < 0.01$ ), exercised on average fewer times a week (3.2 versus 4.0,  $P < 0.001$ ) and more likely to have reported an anxiety disorder (12.0 versus 6.4%,  $P < 0.0001$ ). Reasons given for not participating at follow-up ( $n = 18$ ) included cognitive impairment. These participants were included in the analyses and given a MMSE median score of 16. Finally, subjects were compensated \$15CDN for their participation at each interview. The study was approved by the University of Sherbrooke Institute of Geriatrics ethics committee.

### Measures

Cognitive functioning was measured at both baseline (year 1) and follow-up interviews (year 4) with the MMSE with possible scores ranging between 0 and 30.<sup>17</sup> The MMSE has been shown to have good psychometric properties in assessing general cognitive functioning, in community living older adults consulting in primary care practices, with sensitivity and specificity estimates reaching 80 and 98%.<sup>19,20</sup> In our study sample, the intra-class correlation coefficient was 0.82 ( $P < 0.001$ ) when examining MMSE scores at baseline by interviewer. Further, we assessed the change in MMSE over an interval that was over 3 years which is recommended when using the MMSE to assess cognitive change.<sup>21</sup>

Self-reported alcohol consumption was assessed at both interviews with three questions. The first question ‘have you consumed alcohol in the past 6 months’, was categorized as yes/no. Those responding yes were then asked, ‘what has

been the usual frequency, with which you have consumed alcohol in the past 6 months. There were six possible answers to this last question: less than once a month; more than once a month but less than once a week; once a week; two to four times a week; five to seven times a week; and never'. The interviewer then proceeded with the question 'how many alcoholic drinks (where one glass of white wine or red equals to one beer, equals to a shot of spirit or strong alcohol) do you usually consume on average during a 24-h period' and 'were you ever drunk or in an inebriated state, in the past 6 months'.

Alcohol consumption was based on the product between the number of drinks ordinarily consumed in one occasion (24 h period) and the weekly frequency of drinking alcohol<sup>10</sup> and categorized according to Canadian guidelines on alcohol consumption<sup>11</sup> as follows: non-drinkers (0 drinks), light to moderate drinkers ( $\leq 10$  drinks/week for women and  $\leq 15$  drinks/week for men) and heavy drinkers ( $> 10$  drinks/week for women and  $> 15$  drinks/week for men). In Canada a standard drink contains 13.6 g of alcohol.<sup>11</sup>

Smoking status was also measured at both interviews using the following question: 'Do you smoke cigarettes' and the possible answers included never smoked, former smoker and current smoker. Physical activity was assessed at baseline and follow-up with the following question: 'How many times a week do you exercise for more than 20 min (e.g. walking at a rapid pace)'. Similar single self-reported items are just as valid as other questionnaire-based measures of physical activity.<sup>22,23</sup>

The past 6-month presence of an anxiety disorder (agoraphobia, social or specific phobia, panic disorder, generalized anxiety disorder) and major and minor depression were assessed by trained interviewers using the ESA-Q diagnostic computer-assisted questionnaire based on DSM-5 criteria and similar to the CIDI.<sup>24</sup> The questionnaire has reported consistent results<sup>25</sup> and was recently included in a large meta-analysis.<sup>26</sup>

Functional status was also assessed at both interviews and was based on 29 questions relating to the presence of difficulties, ranging from no problem to extreme problem, in activities and instrumental activities of daily living, relating to mobility, self-care and usual activities, pain and the presence of generalised anxiety disorder and psychological distress. As detailed elsewhere,<sup>27</sup> responses to these questions were summarised into an index ranging from 0 (worst health) to 1 (perfect health). The calculated functional status index was dichotomized at the lowest quintile (yes/no).

The self-reported presence of a chronic disorder, as diagnosed by a physician, was assessed with a list of 20 disorders

(WHO, 2004) and included arthritis, heart and cardiovascular diseases, diabetes and endocrine system disorders, digestive system, and kidney, liver and eye disorders was also measured and categorized as 0–2 versus 3 and over conditions.

The number of ambulatory visits (i.e. emergency department, outpatient clinic) in the year prior to baseline interview was also retained from the 'Régie de l'assurance maladie du Québec' (RAMQ), Quebec's public health insurance plan, where residents are covered for practically all medical consultations with physicians.

Other study variables considered in the analyses as possible confounding factors included age, gender, education (primary and less versus some high school and above) and income ( $< \$55\,000$  versus  $\geq \$55\,000$ ). Social and material deprivation of area of residence was also characterized by the validated Pampalon indices, which are summarized into one index on a scale of 1–5, representing the most advantaged to the most disadvantaged quintiles (highest socioeconomic status, medium high, medium, medium-low, low).<sup>28,29</sup> This variable was dichotomized at quintiles 4 and 5, to identify area of residence with high social or material deprivation, versus quintiles 1–3, for low to medium deprivation (quintiles 1–3).

Social support was assessed during the interviews with the three following questions: (i) In your environment, is there someone you can confide in or talk to freely about your problems? (ii) Is there someone in your family or circle of friends who could assist you in time of need? (iii) Is there someone you feel close to, a family member or friend, who shows affection towards you? Social support was then categorized as the presence of all three sources (yes/no).

The number of daily hassles was also assessed and measured using the French version of Daily Hassle scale.<sup>30</sup> This French version produced a Cronbach alpha of 0.90 and test-retest reliability coefficients of 0.79 for the frequency of hassles.<sup>31</sup> The 30-item questionnaire included seven domains relevant to older people (family, health, money, security and transportation) and experienced during the last month. Possible scores ranged from 0 to 30, with higher scores indicating a higher number of daily hassles.

### Statistical analyses

Linear mixed models with SAS PROC MIXED for repeated measures were used.<sup>32,33</sup> This allowed for people with missing follow-up data to be included in the analyses as well as to consider the change in study variables at both data collection interviews. The change in MMSE scores was predicted by fitting six dummy time  $\times$  alcohol groups (non-drinkers,

**Table 1** Sample characteristics at baseline interview as a function of alcohol consumption defined by Canadian guidelines

	<i>Non-drinkers</i> N = 435 (27%)	<i>Light to moderate drinkers (≤10 for women and ≤15 drinks/week for men)</i> N = 1111 (68%)	<i>Heavy drinkers (≥11 for women and ≥16 drinks/week for men)</i> N = 82 (5%)	<i>Chi-square</i> df = 2 <i>P-value</i>
Age				
65–74 years	252 (58%)	745 (67%)	56 (68%)	0.003
≥75 years	183 (42%)	366 (33%)	26 (32%)	
Gender				
Men	139 (32%)	505 (45%)	38 (46%)	<0.001
Women	296 (68%)	606 (55%)	44 (54%)	
Education				
Primary	61 (15%)	100 (9%)	4 (9%)	0.002
High school/College/University	350 (85%)	1052 (91)	43 (91%)	
Income				
<\$55 000	422 (97%)	1091 (98%)	81 (99%)	0.29
≥\$55 000	13 (3%)	20 (2%)	1 (1%)	
Married				
Yes	249 (57%)	734 (66%)	56 (68%)	0.004
No	186 (43%)	377 (34%)	26 (32%)	
Area of residence				
High deprivation	261 (60%)	642 (58%)	43 (52%)	0.41
Low/Medium deprivation	174 (40%)	469 (42%)	39 (48%)	
Social support				
0–2	84 (19%)	992 (89%)	15 (18%)	<0.0001
3	351 (81%)	119 (11%)	67 (82%)	
Daily hassles				
0–2	246 (57%)	603 (54%)	48 (59%)	0.59
3+	189 (43%)	508 (46%)	34 (41%)	
# of chronic physical disorders				
0–2	109 (25%)	381 (35%)	30 (37%)	0.001
≥3	326 (75%)	730 (65%)	52 (63%)	
Functional status index				
Lowest quintile	125 (29%)	195 (18%)	14 (17%)	<0.0001
Higher quintiles	310 (71%)	916 (82%)	68 (83%)	
Depression				
Yes	33 (8%)	49 (4%)	3 (4%)	0.03
No	402 (92%)	1062 (96%)	79 (96%)	
Anxiety				
Yes	67 (15%)	130 (12%)	7 (9%)	0.08
No	3468(85%)	981 (88%)	75 (91%)	
Psychotropic drug use				
Yes	123 (28%)	183 (16%)	18 (22%)	<0.0001
No	312 (72%)	928 (84%)	64 (78%)	
Smoking status				
Never smoker	199 (46%)	411 (37%)	19 (23%)	<0.0001
Past or current smoker	236 (54%)	700 (63%)	63 (77%)	
		Mean (95% CI)		Pr > F
Cognitive functioning (MMSE)	28.5 (28.4, 28.6)	28.7 (28.6, 28.8)	28.7 (28.4, 29.0)	0.04
Exercise (# of time per week)	3.5 (3.1, 3.9)	3.6 (3.4, 3.9)	3.7 (3.0, 4.4)	0.78
# of ambulatory visits in past year	9.7 (8.6, 10.8)	7.9 (7.4, 8.4)	7.9 (6.3, 9.6)	0.004

light to moderate and heavy drinkers) controlling for study variables. Linear mixed model analyses with a maximum likelihood method and unstructured correlation structure, with random intercept, were used to examine the correlates of cognitive functioning, as measured with MMSE scores, accounting for within-subject correlation over repeated measures. We also accounted for individuals nested within type of primary care practice recruited in (family medicine group, local community health centres, private practice with ≤3 physicians, and private practice with >3 physicians). We also stratified the analyses by functional status at the lowest quintile. Analyses were carried out with SAS version 9.4.

**Results**

The characteristics of the study sample with respect to alcohol consumption groups are presented in Table 1. As seen, close to 27% of participants reported no alcohol consumption in the past 6 months whereas 68% were light to moderate and 5% heavy drinkers. There was a significant association between cognitive functioning (MMSE scores) and alcohol consumption at baseline ( $P < 0.04$ ).

The results also showed significant decline in MMSE scores in the overall sample (mean change: -0.43; 95% CI: -0.22, -0.64) as well as in the sample restricted to those with low functioning (mean change: -0.93; 95% CI: -1.65, -0.20) and high functioning status (mean change: -0.34; 95% CI: -0.12, -0.55) (Fig. 1). The multivariate analysis

(Table 2) showed a significant time × alcohol consumption interaction ( $X^2_{(2)} = 6.32, P < 0.002$ ) in predicting change in MMSE scores between baseline and follow-up.

The results showed cognitive decline in non-drinkers and light to moderate drinkers in the overall sample and in each functional status group (Table 3).

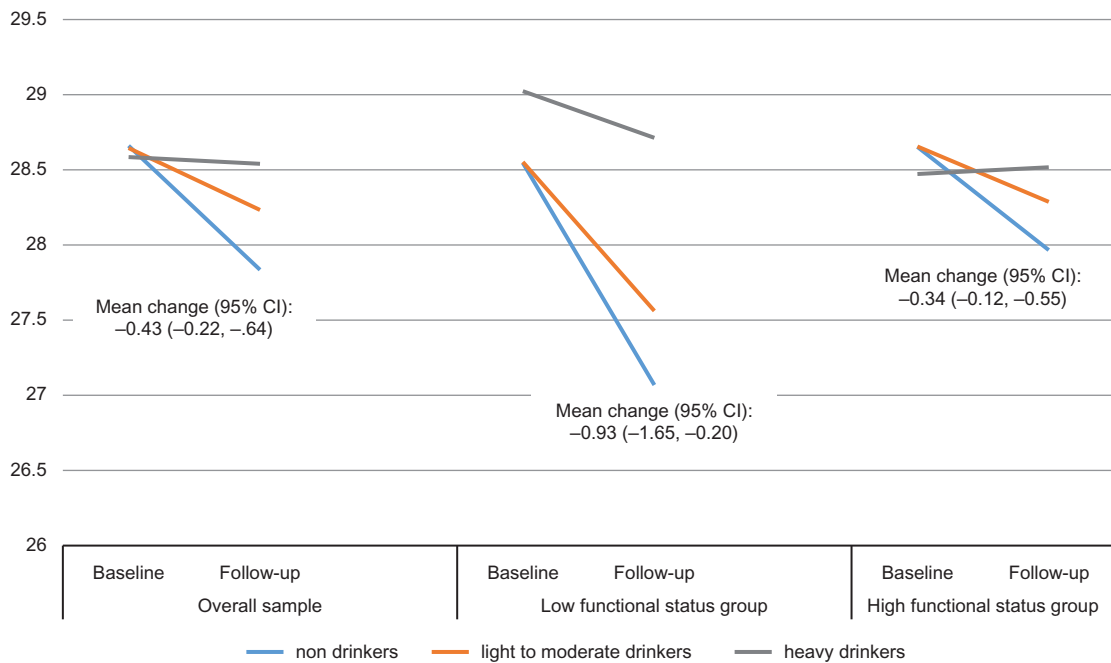
**Discussion**

**Main finding of this study**

There is no evidence in this study that alcohol contributes to cognitive decline. In this study, the 6-month prevalence of alcohol use was 73%, of which 7% was heavy drinking.<sup>13</sup> Within this observation period, the results showed cognitive decline in non-drinkers and light to moderate drinkers in the overall sample as well as in each of the functional status subsamples. We did not observe a change in MMSE scores in heavy drinkers. When looking at individuals in the low functioning group, prior heavy drinkers reporting no alcohol consumption and light to moderate drinking at follow-up had a 2 and 1.5 point decrease in MMSE scores.

**What is already known on this topic**

In a Spanish cohort study of adults aged ≥55 years there was no association between low to moderate alcohol consumption and cognitive decline with the MMSE over 4.5 years.<sup>34</sup> In a US cohort study of older adults participating in



**Fig. 1** Cognitive functioning (MMSE scores) at baseline and 3-year follow-up by alcohol consumption group.

**Table 2** Multivariate model assessing change in MMSE scores as a function of study variables in repeated analysis from baseline to follow-up

	<i>Estimate (95% CI)</i>
Time × alcohol consumption	
Baseline—non-drinkers	0.12 (−0.38, 0.62)
Baseline—light to moderate drinker	0.10 (−0.38, 0.59)
Baseline—heavy drinker	0.05 (−0.52, 0.61)
Follow-up—non-drinkers	−0.71 (−1.21, −0.20)
Follow-up—light to moderate drinker	−0.31 (−0.80, 0.18)
Follow-up—heavy drinker	Reference
Age (≥75 years versus 65–74 years)	−0.58 (−0.72, −0.45)
Gender (women versus men)	0.33 (0.19, 0.48)
Education (primary versus high school/college/university)	−0.74 (−0.94, −0.54)
Income (≥\$55 000 versus < \$55 000)	−1.41 (−1.81, −1.01)
Married (yes versus no)	0.06 (−0.08, 0.20)
Area of residence (high versus low/medium deprivation)	−0.15 (−0.28, −0.02)
Social support (3 versus 0–2)	0.49 (0.31, 0.67)
Daily hassles (3+ versus 0–2)	0.03 (0.02, 0.05)
# of chronic physical disorders (≥3 versus 0–2)	0.001 (−0.14, 0.14)
Functional status index (lowest quintile versus higher quintiles)	−0.24 (−0.41, −0.08)
Depression (yes versus no)	−0.17 (−0.47, 0.13)
Anxiety (yes versus no)	−0.26 (−0.47, −0.10)
Psychotropic drug use (yes versus no)	−0.11 (−0.31, 0.09)
Smoking status (never smoker versus past or current smoker)	−0.06 (−0.19, 0.08)
Exercise (# of time per week)	0.01 (−0.003, 0.03)
# of ambulatory visits in past year	−0.004 (−0.01, 0.004)
Nested for type of primary care practice individuals were recruited in	

the Rancho Bernardo Study,<sup>35</sup> moderate and heavy drinkers, compared to non-drinkers, were more likely to survive up to age 85 without cognitive impairment on the MMSE.

### What this study adds

The sample consisted of older adults not presenting signs of cognitive impairment at baseline to control for the possibility for reverse causation that is if patients with cognitive problems had already altered their exposure to alcohol in response to their impairment. The repeated measures during the two at home interviews 3 years apart also allowed to account for the change in alcohol consumption in the analyses minimizing the potential misclassification of alcohol status. The protective effect of light to moderate drinking observed by some may be confounded by what has been called the ‘sick quitter’ bias where current non-drinkers,

have health disabilities leading them to quit.<sup>7–11,34</sup> This was the case in this study sample where non-drinkers reported lower functional status. In order to control for this potential confounding, this study adds to prior research by stratifying the analyses by functional status and showing on average cognitive decline among non-drinkers and light to moderate drinkers in those with and without disabilities. Further to this, we also controlled for lifestyle factors such as smoking status, exercise as well as the presence of physical and psychiatric disorders but also characteristics of the patient’s living environment,<sup>21</sup> such as socio-demographic and economic factors, health service use, daily stressors and social support, previously not accounted for systematically in the literature.

### Limitations of this study

This study also includes a number of limitations. First, although losses to follow-up did not differ with respect to baseline cognitive scores and alcohol consumption, they were more likely younger. When looking at the characteristics of the sample at baseline, younger participants were more likely at risk alcohol consumers. A more detailed look into the MMSE scores of younger participants, those lost to follow-up did not differ with respect to baseline scores than those who persisted in the study ( $P = 0.77$ ). Given that there was no difference in the baseline MMSE scores, the effect of losing these younger participants at follow-up, which may have other lifestyle factors, is difficult to predict.

Second, one may argue that excluding from the analyses those with MMSE scores < 26 and potentially eliminating individuals with mild and major neurocognitive disorders due to alcohol consumption, as mentioned in the DSM-5, may have underestimated the damages related to alcohol abuse. However excluding these individuals may limit the selection bias in the study of cognitive decline and alcohol consumption at follow-up. Others have also chosen a similar methodology.<sup>36</sup> Additional analysis including these individuals however showed similar results.

Third, participants having more than three chronic conditions were less likely to consume alcohol. If these participants were more likely to have changed their alcohol consumption habits because of their chronic diseases, it is possible that this group also included past at risk drinkers which may have limited our ability to detect an increased risk of cognitive decline with at risk alcohol consumption, which has been previously hypothesized.<sup>37</sup>

Fourth, alcohol consumption in this study was measured over a 6-month period to better represent individual

**Table 3** Estimated mean cognitive change (95% CI) from baseline to 3-year follow-up in each alcohol consumption group

	<i>Non-drinkers</i>	<i>Light to moderate drinkers (≤10 for women and ≤15 drinks/week for men)</i>	<i>Heavy drinkers (≥11 for women and ≥16 drinks/week for men)</i>
Overall sample	−0.83 (−1.05, −0.60)	−0.41 (−0.56, −0.27)	−0.05 (−0.61, 0.52)
Low functional status	−1.48 (−2.06, −0.89)	−0.99 (−1.54, −0.44)	−0.31 (−2.26, 1.65)
High functional status	−0.69 (−0.93, −0.44)	−0.37 (−0.52, −0.22)	0.04 (−0.53, 0.62)
Comparing heavy drinkers at baseline to all other groups			
Overall sample			
Baseline	ns	ns	Reference
Follow-up	−0.75 (−1.14, −0.37)	−0.35 (−0.71, 0.0)	ns
Low functional status			
Baseline	ns	ns	Reference
Follow-up	−1.96 (−3.06, −0.85)	−1.46 (−2.56, −0.36)	ns
High functional status			
Baseline	ns	ns	Reference
Follow-up	−0.51 (−0.91, −0.10)	ns	ns

Estimates are adjusted for age, gender, education, marital status, income, area of residence deprivation, social support, number of daily hassles, number of chronic conditions, the presence of depression and anxiety, psychotropic drug use, ambulatory visits in previous year of interview and smoking status, exercise, and functional status, and type of primary care practice subjects were recruited in.

\*NS: not significantly different from reference group,  $P > 0.05$ .

drinking patterns over a longer period of time. Alcohol consumption was based on both frequency and quantity. The latter may be subject to misclassification bias as this was not based on a number of standard drinks but on the number of reported drinks where respondents were asked to consider that one glass of wine equals to one beer equals to one shot of spirit or strong alcohol. Measures are also usually larger when drinking at home. Participants may have therefore underestimated the average quantity consumed. This would have a greater effect on those reporting a higher number of drinks and this may have led to underestimating the effect of heavy drinking on cognitive decline.

Finally, the participants were recruited in primary care settings and therefore may exhibit more health problems than those from the general older adult population and also receive more recommendations from physicians on healthier lifestyle habits, which may limit the generalizability of results. Further, the majority of the sample consisted of white French-speaking Canadians in the province of Quebec, limiting extrapolation of results to other populations with different lifestyle factors.

## Funding

This study was supported in part by a CIHR operating (Grant # 201403) and by a Fonds de Recherche du Québec - Santé (FRQ-S) operating (Grant # 22251).

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