# Alcohol consumption and risk of incident frailty: the English Longitudinal Study of Ageing.

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#### **ABSTRACT**

**Background**: Alcohol consumption is a common modifiable lifestyle factor. Alcohol may be a risk factor for frailty, however there is limited evidence in the literature.

**Objective**: The objectives of this study were to examine the association of alcohol consumption with the risk of incident frailty.

**Methods**: This is a prospective panel study of 2544 community-dwelling people aged 60 years and older in England. Frailty status defined by frailty phenotype criteria was measured at baseline and 4 years later. Participants free of frailty at baseline were divided into five groups based on quantity of self-reported alcohol consumption per week with cut-points at 0, 7, 14 and 21 UK units per week. Adjusted odds ratios (OR) were calculated for incident frailty according to the alcohol consumption using logistic regression models.

**Results**: Compared with the low consumption group (>0 and ≤7 units per week), incident frailty risk over 4 years was significantly higher among non-drinkers (OR=1.71, 95% confidence interval (CI)=1.12-2.60, p value=0.01), after controlling for socio-demographic confounders. In a supplementary analysis this became non-significant after further adjustment for baseline health status. Heavy drinkers (> 21 units per week) had a significantly lower incident frailty risk (unadjusted OR=0.45, 95% CI=0.27-0.75, p<0.01), which became non-significant on adjustment for socio-demographic factors (OR=0.64, 95% CI=0.37-1.13, p=0.12).

Conclusions/Implications: We found that non-drinkers were more likely than those with low alcohol consumption to develop frailty, but this appeared to be explained by poorer baseline health status. No evidence was found for an association between becoming frail and high levels of alcohol consumption. Future studies with information on life-course history of alcohol use, especially for those classified as non-drinkers in old age, is warranted.

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#### INTRODUCTION

Frailty is a common syndrome caused by the accumulation of multiple deficits and reduction in physiological reserves that occur across multiple body systems as people age.<sup>1</sup> Thus, frail individuals are vulnerable to various adverse health outcomes, including falls,<sup>2</sup> fractures,<sup>3,4</sup> disabilities,<sup>5,6</sup> emergency department visits,<sup>7</sup> hospitalisation,<sup>8</sup> nursing home placement,<sup>9,10</sup> dementia,<sup>8</sup> poor quality of life<sup>11</sup> and mortality.<sup>12-14</sup> In light of these consequences and the substantial burden on both older people and healthcare systems, frailty has been recognised as an important public health concern.<sup>15,16</sup> Furthermore, given the rapidly ageing population worldwide,<sup>17</sup> it is of great importance to identify modifiable risk factors for frailty. Knowledge of modifiable risk factors allows for the development and implementation of targeted interventions aimed at delaying the onset and slowing the progression of frailty.<sup>18</sup>

Alcohol, especially in large quantities, is known to have immediate and long term negative effects on the human body, causing a variety of diseases and conditions. <sup>19</sup> Thus, it is possible that alcohol consumption may be a risk factor for frailty. Habitual alcohol consumption is one of the most common modifiable lifestyle factors, even in older populations. <sup>19</sup> A number of observational cohort studies have examined the association between alcohol consumption and health outcomes, and many of these have shown U- or J-shaped relationships in which light-to-moderate drinkers have the lowest risk compared with non-drinkers and heavy drinkers. <sup>20</sup> Although the mechanisms underlying this potential beneficial effect of low alcohol consumption are not clear, it has been suggested that light-to-moderate alcohol intake may improve insulin sensitivity, increase high-density lipoprotein cholesterol, decrease inflammation and increase adiponectin. <sup>21</sup> However, this apparent protective effect of alcohol consumption in moderation is controversial, and it has been argued that it may be explained by biases and confounding factors. <sup>20,22</sup>

There is limited evidence in the literature on the role of alcohol consumption as a possible risk factor for frailty.<sup>23-25</sup> Findings have been contradictory. For example, a meta-analysis of three cohort studies showed that higher alcohol consumption is associated with lower incident frailty risks,<sup>23</sup> whereas a recent dose-response meta-analysis suggested heavy drinking (at least 30 grams of alcohol per day) may have a negative impact on frailty.<sup>26</sup> However, the apparent beneficial effect of alcohol may be confounded by a number of factors,<sup>23</sup> one of which is that the reference group used in these studies was non-drinkers, who are known to have a worse health profile than drinkers and may not be drinking because of ill health.<sup>27</sup>

Therefore the objectives of this study were to examine the association of alcohol consumption with the risk of incident frailty controlling for important confounders and addressing methodological limitations of an appropriate comparator group.

## **METHOD**

## Study setting and population

The English Longitudinal Study of Ageing (ELSA) is a nationally representative longitudinal cohort study including community-dwelling men and women aged ≥50 years in England who were recruited from households participating in the Health Survey for England (HSE).<sup>28</sup> The participants of ELSA have been followed up every two years since the study began in 2002. Ethical approval for ELSA was granted by the National Research and Ethics Committee, and informed consent was obtained from each participant.

The current study considered those aged  $\geq$  60 years at wave 2 in 2004 (baseline) as walking speed, one of the frailty criteria, was only measured in those aged  $\geq$ 60 years.

Of the 6183 participants aged  $\geq$ 60 years who underwent the interview at wave 2, 3450 were excluded due to missing data for frailty at wave 2 or wave 4 (in 2008, follow-up). In order to examine the risk of incident frailty, the 189 participants who were already frail at wave 2 were further excluded, leaving 2544 participants for the analysis.

## Outcome variable: incident frailty

Frailty was measured at wave 2 in 2004 and again at wave 4 in 2008 to examine incident frailty over 4 years. Frailty was defined using the frailty phenotype criteria as described in the Cardiovascular Health Study by Fried et al., <sup>29</sup> but with slight modifications according to data availability.<sup>30</sup> The five criteria components were (i) shrinking, (ii) self-reported exhaustion, (iii) weakness, (iv) slow walking speed and (v) low physical activity.<sup>29</sup> Shrinking was defined as a body mass index < 18.5 kg/m<sup>2</sup> or a 5% decrease or more in body weight since wave 0 (HSE) in 1998, 1999 or 2001 at baseline (or since wave 2 for weight loss at wave 4). Exhaustion was defined as the participant reporting that they felt that everything they did was an effort or that they could not get going, for much of the time during the past week, extracted from their responses to these items on the Center for Epidemiology Studies Depression (CES-D) eight item scale. Weakness was defined as being in the lowest 20% of handgrip strength, based on the highest measurement of three trials on each hand using Smedley hand-held dynamometer (Stoelting Co, IL, USA), stratified by gender and body mass index quartiles. Slow walking speed was defined as being in the lowest 20% of walking speed, based on the average of two attempts of walking a distance of 8 feet at a usual pace, stratified by gender and median height. Those who were in a wheelchair, bed-bound or unable to walk without assistance were considered to have the slowest walking speed. Low physical activity was defined as being in the lower two of four physical activity categories based on a combination of intensity (vigorous, moderate or mild exercise) and frequency (more than once per week; once per week; one to three times per month; hardly ever or never) of usual exercise involved. Participants were defined as robust, prefrail or frail when they met 0, 1-2 and 3-5 of the five criteria, respectively.<sup>29</sup> The outcome variable for our study was then defined as a binary indicator equal 1 if the participant was frail and 0 otherwise (prefrail or robust).

## **Explanatory variables**

## Alcohol consumption

Data on the quantity of alcohol consumption were available from wave 0 (i.e. the wave they responded to the HSE) in 1998, 1999 or 2001. The amount of alcohol consumption per week was calculated based on drinking frequency over the past 12 months and the amount of different types of alcoholic beverages on a typical occasion, including normal beer, strong beer, spirits, sherry, wine and alcopops. The amount of alcohol was converted into the number of UK units (1 UK unit = 8 g of pure alcohol). The cohort was divided into five groups with cut-points at 0, 7, 14 and 21 units. The cut-points were chosen based on the current UK alcohol guidelines recommending not drinking more than 14 units per week<sup>31</sup> and the fact that older people are more likely to be affected by alcohol than younger people.<sup>32</sup>

## **Confounders**

In addition to alcohol consumption we considered age, gender, smoking, education and wealth. Age was categorised into five groups: 60-64 years, 65-69 years, 70-74 years, 75-79 years and ≥80 years. Smoking was categorised as current smoking or non-smoking. Education was divided into higher education (national vocational qualification (NVQ) level 4, level 5, degree or equivalent), intermediate education (NVQ level 1/Certificate of Secondary Education equivalent, level 2/General Certificate of Education (GCE) O level

equivalent, level 3/ GCE A level equivalent, higher education below degree, or foreign/other qualification) and no qualification. Wealth was based on total net wealth quintiles, referring to participants' savings, investments, physical wealth and housing wealth deducting financial debt and mortgage debt, which is a widely used robust indicator in ELSA.<sup>33</sup> In a supplementary analysis we also considered cognitive function, comorbidities and self-reported general health, which may be on the causal pathway of alcohol consumption and development of frailty. Cognitive function was measured using a total score of four tests: animal naming task, letter cancellation task and immediate and delayed recall tasks, with a higher score suggestive of better cognitive function.<sup>28</sup> A comorbidity index was created as the summed number of 15 chronic diseases: hypertension, angina, heart attack, congestive heart failure, heart murmur, abnormal heart rhythm, diabetes, stroke, chronic obstructive pulmonary disease, asthma, arthritis, osteoporosis, cancer, Parkinson's disease and any emotional, nervous or psychiatric problems. Participants were asked to describe their general health by choosing either excellent, very good, good, fair or poor.

## Statistical analysis

Univariate and multivariable logistic regression models were used to examine the association between risk of incident frailty and the alcohol consumption groups. Given that the non-drinker group includes those who have never drunk or quit drinking due to health problems and may not be appropriate to be used as a reference, <sup>27,34,35</sup> the 'low consumption' group that consumed >0 - 7 units/week was used as the reference group. <sup>36</sup> Longitudinal weighting provided by the National Centre for Social Research, a co-investigator of the ELSA study, was used in all analyses to minimise any bias from sample loss due to attrition. <sup>28</sup> All statistical analyses were conducted using StataSE 14, <sup>37</sup> and were based on 2-tailed tests with significance level set at 0.05.

#### RESULTS

**Table 1** shows the baseline characteristics by alcohol consumption group of the 2544 older men and women who were considered in our study. Approximately two-thirds of the cohort consumed 7 units of alcohol or less per week (n=1225, 66.5%). A quarter (633, 24.9%) consumed more than 14 units of alcohol per week, the threshold for low-risk drinking recommended in the recently published guidelines of the UK Chief Medical Officers. At baseline non-drinkers were more likely to be prefrail rather than robust, older, women, current smokers, with no educational qualification, in the lowest wealth quintile, had poorer cognitive function and more comorbidities.

**Table 2** presents the results of our unadjusted and adjusted logistic regression models. In the unadjusted model, compared with the low consumption group (>0 - 7 units per week), non-drinkers were more likely to develop frailty (OR=1.81, 95% CI=1.20-2.74, p<0.01) and those drinking > 21 units per week were less likely to develop frailty (OR=0.45, 95%CI=0.27-0.75, p<0.01). The elevated incident frailty risk for non-drinkers remained significant after adjustment for socio-economic factors (Model 1: OR=1.88, 95%CI=1.25-2.84, p<0.01, Model 2: OR=1.71, 95%CI=1.12-2.60, p=0.01). However, in a supplementary analysis with further adjustment for cognition, comorbidities and self-reported general health the adjusted OR were attenuated and became non-significant (OR=1.39, 95%CI=0.88-2.19, p=0.15). The association between incident frailty and drinking > 21 units per week became non-significant after adjusting for confounders including age, gender, smoking, education and wealth. No significant difference in incident frailty risk was found when comparing those drinking >7 - 14 and > 14 - 21 units per week with those drinking > 0 - 7 units per week in any models.

#### DISCUSSION

This study, performed using data from a nationally representative longitudinal panel study of 2,544 English community-dwelling older people, showed that non-drinkers had a worse health profile and were associated with an increased risk of frailty compared to low-moderate drinkers. This is in line with previous studies. The non-drinkers category is likely to include those who have never consumed alcohol<sup>27</sup> or who had quit drinking due to health reasons, for example cognitive decline or ill-health due to multi-morbidity ('sick quitters'), and this may affect the alcohol-frailty association. Therefore we decided to use those drinking >0 - 7 units/week as the reference category, in order to at least partially address this concern. The non-drinkers had a significantly higher risk of incident frailty in Model 2 adjusted for age, gender, smoking, education and wealth. However this elevated risk became non-significant after further adjustment for cognition, comorbidities and self-reported general health, which supports the 'sick quitters' theory above. Increasing alcohol consumption appeared to be crudely associated with reduced frailty risk, however this association became non-significant after adjustment for socio-demographic confounding factors.

Most of the previous studies used non-drinkers as the reference group. <sup>23,24</sup> We found only one paper that did not use such a reference - a study of male businessmen in Finland with a long follow-up period of almost 30 years that examined associations between alcohol intake in midlife and frailty in old age. <sup>25</sup> In their study, heavy alcohol intake (>196g/week) in mid-life (mean age 49 years) was associated with a significantly higher risk of developing frailty and pre-frailty 26 years later, compared with light intake (1-98g/week), while heavy use in old age (mean age 74 years) was not associated with frailty risk three years later, <sup>25</sup> as in our study. It should be noted that some important factors, such as education and socioeconomic status, were not adjusted for in their study.

There is a similarity between our findings and that of alcohol and mortality. Until recently, multiple epidemiological studies have shown mortality benefit with moderate alcohol use.<sup>22</sup> However, more studies are revealing that the benefit disappeared by avoiding potential biases.<sup>22,38,39</sup> Similarly in frailty research, initial studies showed alcohol's beneficial effects against frailty.<sup>23</sup> However recent studies that took potential biases into consideration, including ours, have negated it.<sup>25</sup>

The strengths of our study include data from a large nationally representative cohort of English community-dwelling older men and women and the prospective study design. In addition, a set of socio-demographic and lifestyle covariates was used to control for potential confounders.

Limitations include alcohol consumption was self-reported, and therefore subject to recall bias, and measured only at one time point (3-7 years before the baseline). Those excluded from the analyses were likely to be older, current smokers, less educated and in the lower wealth quintiles, which could underestimate the alcohol-frailty association. However, longitudinal weighting was used for all analyses to account for this.<sup>28</sup> There were few people drinking heavily (>28 units/week) in our sample, so we were not able to therefore explore associations at the more extreme end of heavy drinking. We cannot exclude a negative association with frailty (i.e. a U-shaped pattern) in those with very heavy drinking patterns. Although we used various covariates for adjustment, there may have been other unobserved important confounders. Another limitation is that more in-depth data were not available about the non-drinker group, such as whether they had never been drinking, were past drinkers or their reasons for abstaining, as people who are not in good health decrease alcohol

intake or stop drinking.<sup>35</sup>

There are several implications for future research on alcohol-frailty in older people. The alcohol consumption pattern and frailty status changes over time, 1,40 and these associations seem complex and possibly bidirectional. They are also affected by various factors. For example, alcohol consumption patterns in old age may not be the same as in mid-life, and current non-drinkers or light drinkers may have been heavy drinkers in the past. Those who are in the process of developing frailty due to alcohol-related or other health issues may furthermore be reducing their intake or may no longer tolerate alcohol. Such changes in people's drinking behaviours are likely to mask the harmful effects of alcohol on frailty. Therefore, a longitudinal history of alcohol use, including that in mid-life, is preferred to one-time alcohol use information.

## CONCLUSION/RELEVANCE

After adjusting for socio-demographic factors, we found that non-drinkers were more likely than those with low-moderate alcohol consumption to develop frailty, however in a supplementary analysis we found that this relationship attenuated and became non-significant after accounting for baseline health status (cognition, comorbidities and self-reported general health). No evidence was found of an association between becoming frail and high levels of alcohol consumption. From a clinical point of view, the findings from our study do not currently support targeting reducing alcohol consumption in older people as a key factor aiming to reduce the development of frailty over the short-medium term (4 years). The relationship between alcohol intake and frailty is complex and may be influenced by a number of factors. Future studies with information on life-course history of alcohol use, especially for those classified as non-drinkers in old age, are warranted.

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## **Conflict of Interest**

The authors have no conflicts of interest to disclose.

#### **Author Contributions**

Study concept and design: GK, SJ, SI, MF, and KW. Acquisition of data: ELSA researchers. Analysis and interpretation of data: GK, SJ, SI, MF, AL and KW. Drafting the article: GK. Revising the article critically for important intellectual content: GK, SJ, SI, MF, AL and KW. Final approval of the version to be published: GK, SJ, SI, MF, AL and KW

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**Table 1**. Characteristics of the study population\*

	Entire sample†	Non-drinker	>0 - 7 units/week	>7 - 14 units /week	>14 - 21 units /week	>21 units /week
Number of participants (%)	2,544	219 (8.6%)	1,225 (66.5%)	467 (16.4%)	268 (5.4%)	365 (2.2%)
Incident frailty, n (%)	271 (10.7%)	43 (19.6%)	140 (11.4%)	41 (8.8%)	26 (9.7%)	21 (5.8%)
Frailty status at baseline						
Robust	1,431 (56.3%)	101 (7.1%)	686 (47.9%)	261 (18.2%)	161 (11.3%)	222 (15.5%)
Prefrail	1,113 (43.8%)	118 (10.6%)	539 (48.4%)	206 (18.5%)	107 (9.6%)	143 (12.9%)
Age group						
60-64	611 (24.0%)	40 (6.6%)	270 (44.2%)	133 (21.8%)	52 (8.5%)	116 (19.0%)
65-69	826 (32.5%)	69 (8.4%)	406 (49.2%)	132 (16.0%)	99 (12.0%)	120 (14.5%)
70-74	543 (21.3%)	54 (9.9%)	266 (49.0%)	94 (17.3%)	60 (11.1%)	69 (12.7%)
75-79	354 (13.9%)	34 (9.6%)	179 (50.6%)	66 (18.6%)	37 (10.5%)	38 (10.7%)
80+	210 (8.3%)	22 (10.5%)	104 (49.5%)	42 (20.0%)	20 (9.5%)	22 (10.5%)
Gender						
Male	1,150 (45.2%)	73 (6.4%)	412 (35.8%)	233 (20.3%)	155 (13.5%)	277 (24.1%)
Female	1,394 (54.8%)	146 (10.5%)	813 (58.3%)	234 (16.8%)	113 (8.1%)	88 (6.3%)
BMI, median (IQR)	27.1 (24.7-30.1)	27.4 (24.3-31.5)	27.1 (24.5-30.3)	26.7 (24.5-29.5)	26.8 (25.0-29.2)	27.1 (25.1-30.0)
Smoking						
Non-smoker	2,281 (89.7%)	188 (8.2%)	1,110 (48.7%)	424 (18.6%)	239 (10.5%)	320 (14.0%)
Current smoker	261 (10.3%)	31 (11.9%)	114 (43.7%)	43 (16.5%)	28 (10.7%)	45 (17.2%)
Education						
Higher education	322 (12.7%)	9 (2.8%)	113 (35.1%)	67 (20.8%)	45 (14.0%)	88 (27.3%)
Intermediate	1,314 (51.7%)	91 (6.9%)	617 (47.0%)	258 (19.6%)	159 (12.1%)	189 (14.4%)
No qualification	908 (35.7%)	119 (13.1%)	495 (54.5%)	142 (15.6%)	64 (7.1%)	88 (9.7%)
Wealth quintile						
Richest	662 (26.3%)	24 (3.6%)	267 (40.3%)	146 (22.1%)	94 (14.2%)	131 (19.8%)
2nd	570 (22.7%)	51 (9.0%)	275 (48.3%)	107 (18.8%)	69 (12.1%)	68 (11.9%)
3rd	523 (20.8%)	39 (7.5%)	284 (54.3%)	90 (17.2%)	43 (8.2%)	67 (12.8%)
4th	446 (17.7%)	56 (12.6%)	219 (49.1%)	75 (16.8%)	37 (8.3%)	59 (13.2%)
Poorest	312 (12.4%)	46 (14.7%)	168 (53.9%)	41 (13.1%)	23 (7.4%)	34 (10.9%)
Cognition, mean (SD)	13.9 (1.3)	13.3 (3.2)	13.9 (3.2)	14.2 (3.2)	13.8 (3.3)	13.9 (3.3)
Comorbidity index	1.6 (1.3)	1.8 (1.4)	1.6 (1.3)	1.6 (1.3)	1.5 (1.3)	1.5 (1.2)
Self-reported general						
health						
Excellent	366 (14.4%)	21 (5.7%)	159 (43.4%)	82 (22.4%)	39 (10.7%)	65 (17.8%)
Very good	838 (33.0%)	51 (6.1%)	436 (52.0%)	145 (17.3%)	95 (11.3%)	111 (13.3%)
Good	873 (34.3%)	92 (10.5%)	402 (46.1%)	156 (17.9%)	96 (11.0%)	127 (14.6%)
Fair	394 (15.5%)	46 (11.7%)	194 (49.2%)	74 (18.8%)	28 (7.1%)	52 (13.2%)
Poor	72 (2.8%)	9 (12.5%)	33 (45.8%)	10 (13.9%)	10 (13.9%)	10 (13.9%)

BMI: body mass index, IQR: Interquartile range, SD: standard deviation

<sup>\*</sup> Median + interquartile range, mean (standard deviation) or n (%).

<sup>†</sup> Two and 31 participants are missing for smoking status and wealth, respectively. The first column reports column percentages and the rest report row percentages. The percentages may not sum up to 100% due to rounding.

**Table 2.** Univariable and multivariable logistic models predicting 4-year incident frailty

according to alcohol consumption.

	Unadjusted model		Model 1		Model 2		Model 3	
	OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)	p
Non-drinkers	1.81 (1.20-2.74)	< 0.01	1.88 (1.25-2.84)	< 0.01	1.71 (1.12-2.60)	0.01	1.39 (0.88-2.19)	0.15
>0 - 7 units/week	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-
>7 - 14 units/week	0.83 (0.56-1.23)	0.35	0.89 (0.60-1.33)	0.57	0.97 (0.64-1.49)	0.90	0.98 (0.62-1.55)	0.92
>14 - 21 units/week	0.73 (0.46-1.16)	0.18	0.83 (0.50-1.39)	0.48	1.01 (0.60-1.70)	0.98	1.01 (0.60-1.71)	0.97
>21 units/week	0.45 (0.27-0.75)	< 0.01	0.62 (0.36-1.06)	0.08	0.64 (0.37-1.13)	0.12	0.63 (0.34-1.18)	0.15

Model 1: adjusted for age and gender.

Model 2: adjusted for age, gender, smoking, education and wealth.

Model 3: adjusted for age, gender, smoking, education, wealth, cognition, comorbidity index and self-reported general health.

CI: Confidence interval

OR: Odds ratio