

RESEARCH PAPER

Alcohol consumption in later life and reaching longevity: the Netherlands Cohort Study

PIET A. VAN DEN BRANDT^{1,2}, LLOYD BRANDTS¹

¹Department of Epidemiology, Maastricht University Medical Centre, GROW- School for Oncology and Developmental Biology, Maastricht, The Netherlands

²Department of Epidemiology, Maastricht University Medical Centre, Care and Public Health Research Institute (CAPHRI), Maastricht, The Netherlands

Address correspondence to: Piet A. van den Brandt, Department of Epidemiology, Maastricht University Medical Centre, PO Box 616, 6200 MD Maastricht, The Netherlands. Tel.: +31 (0)43 3882361; Fax number: +31 (0)433884128. Email: PA.vandenBrandt@maastrichtuniversity.nl

Abstract

Background: whether light-to-moderate alcohol intake is related to reduced mortality remains a subject of intense research and controversy. There are very few studies available on alcohol and reaching longevity.

Methods: we investigated the relationship of alcohol drinking characteristics with the probability to reach 90 years of age. Analyses were conducted using data from the Netherlands Cohort Study. Participants born in 1916–1917 ($n = 7,807$) completed a questionnaire in 1986 (age 68–70 years) and were followed up for vital status until the age of 90 years (2006–07). Multivariable Cox regression analyses with fixed follow-up time were based on 5,479 participants with complete data to calculate risk ratios (RRs) of reaching longevity (age 90 years).

Results: we found statistically significant positive associations between baseline alcohol intake and the probability of reaching 90 years in both men and women. Overall, the highest probability of reaching 90 was found in those consuming 5– < 15 g/d alcohol, with $RR = 1.36$ (95% CI, 1.20–1.55) when compared with abstainers. The exposure-response relationship was significantly non-linear in women, but not in men. Wine intake was positively associated with longevity (notably in women), whereas liquor was positively associated with longevity in men and inversely in women. Binge drinking pointed towards an inverse relationship with longevity. Alcohol intake was associated with longevity in those without and with a history of selected diseases.

Conclusions: the highest probability of reaching 90 years was found for those drinking 5– < 15 g alcohol/day. Although not significant, the risk estimates also indicate to avoid binge drinking.

Keywords: alcohol, longevity, aging, dose–response relationship, mortality, cohort studies, older people

Key points

- The highest probability of reaching 90 years of age (longevity) was found for men and women drinking 5– < 15 g alcohol/day (or 0.5–1.5 glass/day); the exposure–response relationship was significantly non-linear in women.
- Usual drinking pattern and binge drinking were not significantly associated with longevity, but the risk estimates indicate to avoid binge drinking.
- The estimated modest risk ratios (RRs) should not be used as motivation to start drinking if one does not drink alcoholic beverages.

Introduction

Whether light-to-moderate alcohol intake is related to reduced mortality remains a subject of intense research and controversy, e.g. [1, 2]. Whereas alcohol consumption has been studied frequently in relation to mortality (especially CVD), the findings were inconsistent. Many studies have reported J-shaped curves relating alcohol to mortality, suggesting the lowest risk for light-moderate drinkers [2–5], while others found non-significant associations or linear associations [1, 6, 7]. Many early cohort studies may have suffered from ‘abstainer bias’ where ex-drinkers are misclassified as abstainers and related inclusion of subjects with chronic diseases (sick quitters), and limited confounder adjustment [5, 6, 8]. A recent meta-analysis addressing these issues [6] found no protective effect of low-moderate drinking in the subset of studies that controlled for these biases, but this selection was criticized [9]. While mortality studies investigate risk factors for premature death (i.e. earlier than average), longevity studies investigate determinants of attaining exceptionally high ages (exceeding life expectancy). The relationship between alcohol and longevity has been investigated rarely, with survival cut-off ages of 85 [10, 11] or younger [12] in early cohort studies, and 90 in recent studies [13, 14]. Furthermore, most studies involved men only [10, 11, 13], did not exclude ex-drinkers and results were inconsistent.

We investigated the relationship between habitual alcohol intake in later life and the probability of reaching 90 years in men and women (because alcohol affects women differently from men [15]), within the Netherlands Cohort Study (NLCS). Given the controversies surrounding light-to-moderate alcohol intake and mortality, we concentrated on this category in dose–response modelling. We also aimed to investigate beverage types, stability of drinking over time and effect of excluding ex-drinkers, and binge drinking, because these factors were important in mortality studies.

Methods

Study design and population

For this study, data from the ongoing NLCS were used. The NLCS started in September 1986 as a large population-based prospective study, with detailed information on baseline alcohol use and many confounders available from men and women [16, 17]. Eligible subjects were men and women living in 204 Dutch municipalities, aged 55–70 years at cohort baseline (1986). NLCS-participants born in 1916–1917 were selected to form the longevity cohort for the current analyses (i.e. aged 68–70 at baseline), because younger birth cohorts could not have reached age 90 at the end of follow-up [14, 18]. Vital status follow-up consisted of record linkage to the Central Bureau for Genealogy and to municipal population registries from 1986 to 2007, yielding exact dates of death. Vital status follow-up of the longevity cohort until age 90 (2006–07) was 99.9% complete; seven participants were lost to follow-up due to migration. The

resulting study population consisted of 3,646 men and 4,161 women (Appendix-Figure 1).

Exposure assessment

The 11-page baseline questionnaire measured dietary intake, detailed information on lifestyle factors and medical conditions [16]. Habitual consumption of food and (alcoholic) beverages during the year preceding baseline was assessed using a semi-quantitative food-frequency questionnaire (FFQ), which was validated against a 9-day diet record [19].

Consumption of alcoholic beverages was addressed by questions on beer, red wine, white wine, sherry and other fortified wines, liqueur types containing on average 16% ethanol, and (Dutch) gin, brandy and whiskey. Respondents who consumed alcoholic beverages less than once a month were considered non-users. Four items from the questionnaire (i.e. red wine, white wine, sherry and liqueur) were combined into one wine variable, since these items were substantially correlated [20]. Mean daily alcohol consumption was calculated using the Dutch food composition table [21]. The FFQ has been validated and tested for reproducibility [19, 22]. For mean daily ethanol intake, Spearman correlation coefficients between the 9-day diet record and the questionnaire were 0.89 for all subjects and 0.85 for alcohol users [19]. The absolute amount of ethanol reported in the questionnaire by alcohol users was, on average, 86% of that reported in the 9-day diet record [19].

The baseline questionnaire also asked about the usual pattern of drinking alcoholic beverages (parties only/weekend and parties/throughout week). To measure binge drinking, subjects were asked how often they drank more than six alcoholic drinks per occasion during the half year preceding baseline. Finally, a question provided information on the subjects’ drinking habits 5 years before baseline (Appendix Methods). Ex-drinkers were defined as participants who were not drinking alcohol at baseline, but who drank alcoholic beverages 5 years before baseline.

Statistical analyses

Subjects with missing data on alcohol and confounding variables were excluded. The associations of alcohol consumption, alcoholic beverages and drinking characteristics with the probability of reaching 90 years (longevity) were estimated in age(sex) and multivariable-adjusted analyses using Cox regression models with a fixed follow-up time [18, 23], in categorical and continuous exposure analyses, correcting for potential confounders (related to longevity and alcohol (see footnotes in Tables)). Standard errors were calculated using the Huber–White sandwich estimator [24]. Ex-drinkers were excluded from the main analyses to avoid misclassification of ex-drinkers as abstainers. Beverage-specific analyses for beer, wine and liquor were additionally mutually adjusted to evaluate the association of each beverage with longevity independently of other alcoholic beverages. Analyses of the effect of pattern of drinking, and

binge drinking, were additionally adjusted for total intake of alcoholic beverages.

Tests for trends were assessed using Wald tests, by fitting median values of intake per intake category as continuous terms. Restricted cubic spline regression analyses using four knots (at the midpoints of the categories used in categorical analyses) and Wald test were performed to test for non-linearity. We conducted sensitivity analyses, by restricting analyses to participants who reported to have had the same alcohol intake 5 years before baseline, including abstainers on both occasions (i.e. the stable subgroup). To evaluate potential residual confounding by other risk factors, and effect modification, analyses of alcohol and longevity were also conducted within strata of covariables. Interactions were tested using Wald tests and cross-product terms. Analyses were performed using Stata 14; presented P-values are two-sided.

The NLCS study was approved by the Medisch-Ethische Toetsingscommissie (METC), Maastricht University Medical Centre, Maastricht, the Netherlands.

Results

Amongst the 2,591 men, 433 (16.7%) survived until 90 years, and there were 994 survivors (34.4%) amongst the 2,888 women. In the total group, 40 men and 32 women were ex-drinkers. When excluding ex-drinkers, the proportion of alcohol abstainers was higher amongst non-survivors than survivors in both men (15.6% versus 10.6%) and women (37.4% and 30.1%). Amongst male alcohol consumers, mean intake (SD) was 16.5 (15.8) g/day in non-survivors and 15.9 (14.9) g/day in survivors. For women, these numbers were 8.0 (10.5) and 7.2 (9.0) g/day, respectively. Appendix Table 1 also shows these comparisons for beverage types (glasses/week), pattern of drinking, stable drinking and binge drinking. The proportion of binge drinkers was higher amongst non-survivors than survivors, and higher in men: 18.5% versus 14.2% in men, and 6.1% versus 4.0% in women, respectively. Alcohol consumption was positively associated with smoking, educational level and energy intake in both sexes, with physical activity in women, and with BMI and height in men (Appendix Table 2). There was no clear association with history of selected diseases. Ex-drinkers more often had a history of selected diseases than those in other drinking categories. Excluded subjects with missings had a lower likelihood of reaching 90, were less often smokers and less highly educated (Appendix Table 3).

Alcohol intake was positively associated with the probability of reaching 90 years in men and women in multivariable-adjusted analyses (Table 1). In analyses of men and women combined, those drinking 5– < 10 g alcohol/day had a RR of 1.41 (95%CI, 1.21–1.63) of reaching 90, compared to abstainers. This probability remained elevated at higher alcohol intake levels (*P*-trend = 0.014). Ex-drinkers had a decreased probability of reaching 90, when compared to abstainers. Ex-drinkers were excluded from subsequent

analyses. When alcohol was analysed as continuous variable, the RR per increment of 10 g/d was 1.05 (95%CI 1.01–1.09). In analyses limited to the stable subgroup, similar associations were seen as in the overall group. There was no statistically significant interaction between men and women (*P* = 0.168). However, the estimated associations showed differences: whereas in men the probability of reaching 90 remained elevated at higher alcohol consumption levels (e.g. RR = 1.64 (1.15–2.34) for men drinking 30+ g/day compared to abstainers), this was not seen in women with RR = 0.99 (0.69–1.44). This difference in dose–response was also noticed in restricted cubic splines analyses, where a significantly non-linear relationship was observed in women (*P* for non-linearity = 0.004), but not in men (Figure 1). We therefore continued with sex-specific analyses.

In beverage-specific analyses, we found no association with beer intake (Table 2). Wine intake was associated with higher chances of reaching 90 amongst women, with RRs of 1.43 (95%CI 1.21–1.68) and 1.35 (1.14–1.59) for women drinking 3.5– < 7 and 7+ glasses/week, respectively, when compared to non-drinkers of wine (*P*-trend < 0.001, and *P*-trend = 0.049 amongst wine drinkers). For men, the weakly positive associations with wine were non-significant. Liquor intake was significantly positively associated with longevity amongst men in several drinking categories compared to non-drinkers of liquor, but the trend test and continuous analyses were not significant. In women, however, higher liquor intake was inversely associated with longevity (*P*-trend = 0.044, and *P*-trend = 0.018 amongst liquor drinkers).

There was no significant association with pattern of drinking (Appendix Table 4). Although binge drinkers seemed to have a lower probability of reaching 90 than non-binge drinkers, especially in women, the multivariable-adjusted associations were non-significant. This may be due to the small proportion of binge drinking women. When binge drinking was further categorized according to frequency, lower chances of longevity were found in more frequently binge drinking men, but the trend test was not significant.

In subgroup analyses of alcohol and longevity, categorical (or continuous) alcohol intake showed no significant interactions with smoking status, BMI, physical activity, level of education or history of diseases at baseline (Appendix Table 5). Significant associations between alcohol and probability of reaching 90 were seen in many subgroups, including never and current smokers, and those with or without a history of selected diseases. The highest RRs were generally observed in those drinking 5– < 15 g/day.

Discussion

In this large prospective study, we found statistically significant positive associations between alcohol intake and the probability of reaching 90 years in both men and women. Overall, the highest probability was found in those consuming 5– < 15 g/d alcohol, which corresponds to 0.5–1.5 glass of alcoholic beverage per day. The exposure–response

Table 1. Age- and multivariable-adjusted^a RRs for reaching longevity according to alcohol intake in birth cohort 1916–17; Netherlands Cohort Study (1986–2007)

	Alcohol (g/day)							P for trend ^b	Continuous ^b , per 10 g/d	P for interaction ^b
	Ex, 0 g/d	Abstainers	>0–<5 g/d	5–<10 g/d	10–<15 g/d	15–<30 g/d	30+ g/d			
Men and women										
Overall										
Median intake (g/day)	0.0	0.0	1.6	7.2	12.1	21.4	39.5			
N	72	1391	1710	597	520	742	447			
Survivors(90+)	11	345	507	181	131	166	86			
Age-sex-adjusted RR	0.74	1	1.26	1.49	1.32	1.24	1.15	0.391	1.01	
(95 %CI)	(0.43–1.30)	(Ref.)	(1.13–1.42)	(1.28–1.73)	(1.11–1.56)	(1.06–1.46)	(0.93–1.43)		(0.97–1.05)	
Multivariable-adjusted RR ^a	0.84	1	1.19	1.41	1.30	1.29	1.31	0.014	1.05	0.168
(95 %CI)	(0.48–1.47)	(Ref.)	(1.07–1.33)	(1.21–1.63)	(1.10–1.55)	(1.10–1.52)	(1.06–1.63)		(1.01–1.09)	
Stable subgroup										
Median intake (g/day)	0.0	0.0	1.8	7.2	12.1	22.0	40.0			
N	1180	1180	907	364	319	467	292			
Survivors(90+)	288	288	287	114	83	109	60			
Age-sex-adjusted RR	1	1	1.37	1.52	1.34	1.28	1.18	0.364	1.01	
(95 %CI)	(Ref.)	(Ref.)	(1.20–1.57)	(1.27–1.82)	(1.09–1.64)	(1.05–1.55)	(0.92–1.52)		(0.97–1.06)	
Multivariable-adjusted RR ^a	1	1	1.25	1.42	1.30	1.31	1.36	0.024	1.05	0.468
(95 %CI)	(Ref.)	(Ref.)	(1.09–1.43)	(1.18–1.70)	(1.05–1.60)	(1.08–1.59)	(1.05–1.76)		(1.00–1.11)	
Men										
Median intake (g/day)	0.0	0.0	2.1	7.4	12.1	22.4	40.6			
N	40	383	618	335	332	527	356			
Survivors(90+)	6	46	106	75	52	84	64			
Age-adjusted RR	1.24	1	1.43	1.86	1.31	1.33	1.50	0.453	1.01	
(95 %CI)	(0.56–2.72)	(Ref.)	(1.04–1.97)	(1.33–2.61)	(0.90–1.89)	(0.95–1.86)	(1.06–2.13)		(0.96–1.07)	
Multivariable-adjusted RR ^a	1.49	1	1.39	1.81	1.37	1.43	1.64	0.100	1.04	
(95 %CI)	(0.69–3.23)	(Ref.)	(1.01–1.90)	(1.30–2.53)	(0.95–1.97)	(1.02–1.99)	(1.15–2.34)		(0.98–1.10)	
Women										
Median intake (g/day)	0.0	0.0	1.4	7.2	12.1	20.7	35.6			
N	32	1008	1092	262	188	215	91			
Survivors(90+)	5	299	401	106	79	82	22			
Age-adjusted RR	0.53	1	1.24	1.36	1.42	1.29	0.81	0.526	1.01	
(95 %CI)	(0.23–1.18)	(Ref.)	(1.09–1.40)	(1.14–1.62)	(1.17–1.72)	(1.06–1.56)	(0.56–1.19)		(0.96–1.07)	
Multivariable-adjusted RR ^a	0.62	1	1.17	1.28	1.38	1.31	0.99	0.078	1.05	
(95 %CI)	(0.27–1.38)	(Ref.)	(1.03–1.32)	(1.08–1.52)	(1.13–1.68)	(1.08–1.60)	(0.69–1.44)		(0.99–1.11)	

^aMultivariable analyses were adjusted for: age at baseline (continuous, in years), tobacco smoking status (coded as never, former, current smoker), number of cigarettes smoked per day, and years of smoking (both continuous, centered), body height (continuous, m), BMI (<18.5, 18.5–<25, 25–<30, ≥30 kg/m²), non-occupational physical activity (<30, 30–60, 61–90, ≥90 min/day), history of selected diseases at baseline (physician-diagnosed myocardial infarction, angina pectoris, stroke, cancer (excluding skin cancer), diabetes and hypertension; categorized as 0,1,2,3+ diseases), highest level of education (primary school or lower vocational, secondary or medium vocational, and higher vocational or university), energy intake (continuous, kcal/day), ^bExcluding ex-drinkers

Table 2. Age- and multivariable-adjusted RRs for reaching longevity according to intake of specific alcoholic beverages in birth cohort 1916–17; Netherlands Cohort Study (1986–2007)

Alcoholic beverage	Men				Women						
	Median (gl/wk)	N	90+	RR ^a	(95% CI)	RR ^b	(95% CI)	RR ^a	(95% CI)	RR ^b	(95% CI)
<i>Beer (glasses/week)</i>											
No	0.0	1388	221	1	(reference)	1	(reference)	1	(reference)	1	(reference)
> 0–< 3.5	1.0	764	144	1.18	(0.98–1.43)	1.03	(0.85–1.25)	1.06	(0.86–1.30)	1.00	(0.82–1.22)
3.5–< 7	5.0	198	33	1.05	(0.75–1.46)	1.00	(0.71–1.39)	1.33	(0.74–2.41)	1.22	(0.70–2.12)
7+ gl/wk	13.0	201	29	0.91	(0.63–1.29)	0.92	(0.64–1.31)	0.58	(0.10–3.32)	0.61	(0.09–4.09)
<i>P</i> for trend				0.493		0.611		0.970		0.857	
<i>P</i> trend, beer drinkers				0.140		0.545		0.768		0.913	
Continuous, per 7 gl/wk		2551	427	0.98	(0.85–1.13)	1.01	(0.86–1.18)	1.00	(0.59–1.70)	0.97	(0.55–1.73)
<i>P</i> for interaction by sex										0.739	
<i>Wine (glasses/week)</i>											
No	0.0	1149	159	1	(reference)	1	(reference)	1	(reference)	1	(reference)
> 0–< 3.5	1.0	881	167	1.37	(1.12–1.67)	1.17	(0.95–1.44)	1.25	(1.10–1.40)	1.16	(1.03–1.30)
3.5–< 7	5.0	236	49	1.50	(1.12–2.00)	1.15	(0.85–1.55)	1.50	(1.27–1.77)	1.43	(1.21–1.68)
7+ gl/wk	13.0	285	52	1.32	(0.99–1.76)	1.08	(0.81–1.46)	1.33	(1.14–1.56)	1.35	(1.14–1.59)
<i>P</i> for trend				0.087		0.880		0.001		<0.001	
<i>P</i> trend, wine drinkers				0.825		0.400		0.287		0.049	
Continuous, per 7 gl/wk		2551	427	1.08	(0.99–1.19)	1.04	(0.94–1.16)	1.09	(1.02–1.16)	1.11	(1.04–1.19)
<i>P</i> for interaction by sex										0.555	
<i>Liquor (glasses/week)</i>											
No	0.0	1011	156	1	(reference)	1	(reference)	1	(reference)	1	(reference)
> 0–< 3.5	1.2	603	120	1.29	(1.04–1.60)	1.34	(1.08–1.67)	1.08	(0.89–1.31)	1.02	(0.85–1.24)
3.5–< 7	5.0	365	55	0.98	(0.74–1.30)	1.12	(0.83–1.49)	0.67	(0.45–0.99)	0.72	(0.49–1.07)
7+ gl/wk	13.0	572	96	1.09	(0.86–1.37)	1.30	(1.02–1.66)	0.53	(0.31–0.91)	0.67	(0.40–1.15)
<i>P</i> for trend				0.956		0.172		0.003		0.044	
<i>P</i> trend, liquor drinkers				0.257		0.919		0.003		0.018	
Continuous, per 7 gl/wk		2551	427	0.97	(0.89–1.07)	1.05	(0.95–1.16)	0.69	(0.54–0.89)	0.78	(0.60–1.01)
<i>P</i> for interaction by sex										0.062	

^aAge-adjusted analyses.

^bMultivariable analyses were adjusted for: age at baseline (continuous, in years), tobacco smoking status (coded as never, former, current smoker), number of cigarettes smoked per day, and years of smoking (both continuous, centered), body height (continuous, m), BMI (<18.5, 18.5–<25, 25–<30, ≥30 kg/m²), non-occupational physical activity (<30, 30–60, 61–90, ≥90 min/day), history of selected diseases at baseline (physician-diagnosed myocardial infarction, angina pectoris, stroke, cancer (excluding skin cancer), diabetes and hypertension; categorized as 0, 1, 2, 3+ diseases), highest level of education (primary school or lower vocational, secondary or medium vocational, and higher vocational or university), energy intake (continuous, kcal/day), intake of the other two types of alcoholic beverages (each categorical).

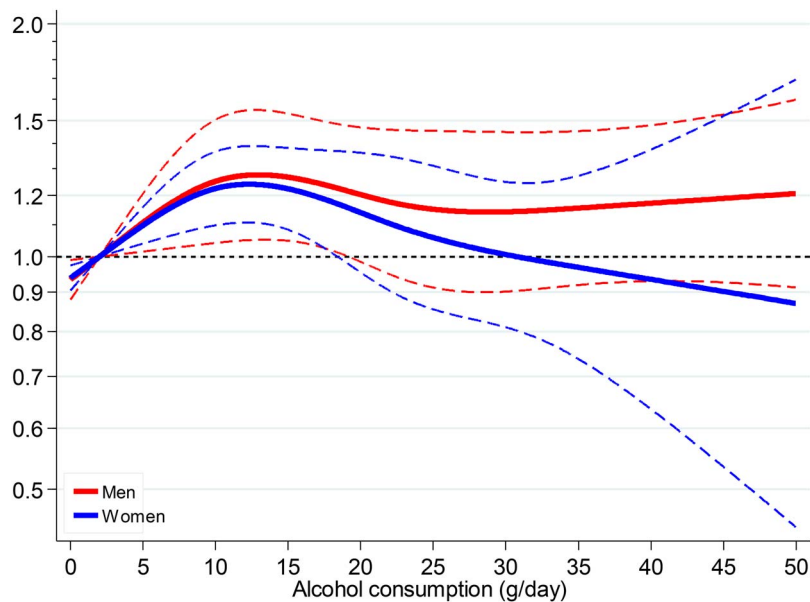


Figure 1. Spline regression curves for the association of alcohol consumption with the probability of reaching longevity in men and women separately. Red lines: men. Blue lines: women. Solid lines represent point estimates and dashed lines represent 95% confidence intervals. Multivariate HRs are calculated by restricted cubic spline regression adjusting for: age at baseline (continuous, in years), tobacco smoking status (coded as never, former, current smoker), number of cigarettes smoked per day, and years of smoking (both continuous, centered), body height (continuous, m), BMI (<18.5 , $18.5- < 25$, $25- < 30$, ≥ 30 kg/m²), non-occupational physical activity (<30 , $30-60$, $61-90$, ≥ 90 min/day), history of selected diseases at baseline (physician-diagnosed myocardial infarction, angina pectoris, stroke, cancer (excluding skin cancer), diabetes and hypertension; categorized as 0,1,2,3+ diseases), highest level of education (primary school or lower vocational, secondary or medium vocational, and higher vocational or university), energy intake (continuous, kcal/day).

relationship was significantly non-linear in women, but not in men. Whereas the probability of longevity was decreasing in women with alcohol intakes above 15 g/d, it remained elevated at higher alcohol consumption levels in men. In beverage-specific analyses, wine intake was positively associated with longevity (notably in women), whereas liquor was positively associated with longevity in men and inversely in women. Binge drinking was not significantly associated with longevity, but the risk estimates indicate to avoid binge drinking. In subgroup analyses, alcohol intake was associated with longevity in those with or without a history of selected diseases.

Previous prospective studies on longevity from the US and France that reported on alcohol were rather limited (no alcohol focus) and found no significant associations using longevity cut-offs of 75 [12] and 90 years [13, 25]. However, higher alcohol intakes were seen in survivors compared to non-survivors [25], and in subsequent analyses (85+ years) of the Framingham Heart Study [26]. The Physicians Health Study amongst US male physicians (survival cut-off 90) reported small and non-significantly increased chances of longevity for various drinking categories compared to rarely/never alcohol drinkers, with no dose-response relationship [13]. The association between alcohol drinking and longevity was studied twice in the Honolulu Heart Program (HHP) amongst Japanese-American men using 85 years as

longevity cut-off [10, 11]. Heavy alcohol intake, measured at baseline age 45–68 years, was significantly inversely related to longevity (OR = 0.63, for 3+ drinks/day versus drinking less) [10]. In the second analysis, moderate-heavy alcohol intake around 75 years was also significantly inversely related to longevity (OR = 0.66, for drinking >14.5 g/day versus less) [11]. The fact that the HHP study was conducted amongst men of Japanese ancestry may (partly) explain the more negative association of alcohol with longevity, and suggests a potential mechanism. It is known that East Asians are less efficient alcohol metabolizers due to a common loss-of-function variant of the *ALDH2*-gene, which decreases breakdown of acetaldehyde, the first, toxic alcohol metabolite [27]. It could be that those who nevertheless drink experience a higher mortality risk.

Overall, the results of previous longevity studies seem quite limited. Our detailed analyses show significantly positive associations between alcohol and longevity in both men and women, which is in agreement with the PHS [13]. Overall in men and women combined in the NLCS, the highest probability of reaching 90 was found in those consuming 5– <15 g/d alcohol, with a HR of 1.36 compared to abstainers. Women experience higher blood alcohol concentrations than men of similar weight due to lower total body water [15]. Thus, adverse effects of higher alcohol intakes may appear earlier in women. This might explain

the non-linear exposure–response relationship in women and not in men. We also found that wine intake was positively associated with longevity, whereas liquor was positively associated with longevity in men, and inversely in women. Before speculating on reasons for these beverage differences, future longevity studies are needed to replicate these sex-specific findings, with those on pattern and binge drinking. In mortality studies, there was no clear indication for sex differences [2, 5], and although beneficial associations with wine have been described for mortality, e.g. [2], this topic remains controversial.

As in observational studies on alcohol and mortality [1, 2, 8], studies on alcohol and longevity may be hampered by possible biases (selection and residual confounding biases). Here, selection bias can refer to abstainer bias (when the reference category of non-drinkers also includes sick quitters), the healthy drinker/survivor bias (when cohorts of older participants may be overrepresented by healthier drinkers who may have survived adverse effects of alcohol). Reverse causation may occur because health status may influence alcohol drinking [8], which could be addressed by restricting analyses to healthy people at baseline. Incomplete adjustment for confounding factors may lead to residual confounding. In our longevity analysis, we tried to address these possible biases by: (i) excluding ex-drinkers from the reference category; (ii) limiting analyses to stable drinkers and abstainers by taking alcohol consumption 5 years before baseline into account; (iii) restricting analyses to participants without prevalent diseases and (iv) adjusting for a large range of possible confounders with detailed information. These analysis strategies do not necessarily provide a full remedy against all possible biases [8], but these were the possibilities with the available data from our cohort. For example, we had no information on lifetime alcohol consumption or consumption on various ages during lifetime, so our analysis of past consumption was limited. After excluding ex-drinkers from the reference category, the analyses in the stable subgroup were essentially similar to what was seen overall. We also found that alcohol intake was associated with longevity in the subgroup without a history of selected diseases. Still, other diseases might have affected alcohol use or longevity. Residual confounding by socioeconomic status is also possible, because we only controlled for educational level.

It should be noted that the percentages of never drinkers were relatively high in the NLCS: 15% in men and 35% in women, making this common behaviour a logical reference category. These percentages were substantially higher than in other cohorts, e.g. 8% in male and 16% in female PLCO-participants [2], and 6% in male and 16% in female EPIC-participants [28]. Strengths of the NLCS are the prospective design and high completeness of follow-up, making information bias and selection bias due to differential follow-up unlikely. The validation study of the food frequency questionnaire has shown that it performs relatively well with respect to alcohol [19], but measurement error may still have attenuated associations. The lack of possibilities

to update alcohol intake or other lifestyle data during follow-up may have resulted in some attenuated associations too. Our study was aimed at measuring alcohol intake at 68–70 years. Therefore, our study results are limited to alcohol drinking in later life; future longevity studies preferably include lifetime consumption. The alcohol measures in our study were not aimed to get an all-encompassing indication of risky drinking, like in the Alcohol Use Disorders Identification Test/AUDIT [29]. Our cut-off for binge drinking (>6 drinks per occasion) as used in the 1980s/1990s [29, 30] is somewhat higher than current cut-offs [29]. Because we were interested in the association of late life drinking with longevity, our study likely examined a resilient population that survived already until 68 years despite possible earlier risky drinking.

While older people perceive themselves as controlled responsible drinkers, according to a recent thematic synthesis of qualitative studies, they consider alcohol use often as important part of social occasions, and report that alcohol helps creating feelings of relaxation [31]. A possible beneficial effect of light-moderate alcohol intake on longevity (with inverted J-shaped dose-response on longevity) may also be related to hormesis [32, 33]. With higher consumption in older people, medication may be negatively affected by alcohol, and there is decreased physiological tolerance [34].

In conclusion, in this prospective study of men and women aged 68–70 years at baseline, we found the highest probability of reaching 90 years of age for those drinking 5–< 15 g alcohol/day. This does not necessarily mean that light-to-moderate drinking improves health. The estimated RR of 1.36 implies a modest absolute increase in this probability and should not be used as motivation to start drinking if one does not drink alcoholic beverages. Although no significant association was found, the risk estimates also indicate to avoid binge drinking.

Supplementary data: Supplementary data mentioned in the text are available to subscribers in *Age and Ageing* online.

Declaration of conflicts of interest: None.

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