Association of alcohol consumption with morbidity and mortality in patients with cardiovascular disease: original data and meta-analysis of 48423 men and women

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Background

Light-to-moderate alcohol consumption has been reported to be cardio-protective among apparently healthy individuals, however, it is unclear whether this association is also present in those with disease.

To examine the association between alcohol consumption and prognosis in individuals with pre-existing cardiovascular disease (CVD), we conducted a series of meta-analyses of new findings from three large-scale cohorts and existing published studies.
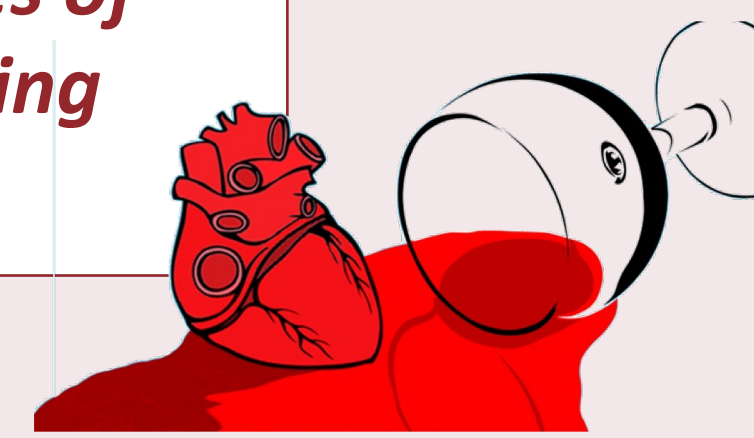
Methods

De novo cohort analyses

We assessed alcohol consumption in relation to all-cause mortality, cardiovascular mortality, and subsequent cardiovascular events via *de novo* analyses of

- 14386 patients with a previous myocardial infarction (MI), angina, or stroke in UK Biobank (median follow-up 8.7 years, IQR 8.0–9.5), involving 1640 deaths and 2950 subsequent events, and

- 2802 patients and 1257 deaths in 15 waves of the Health Survey for England (HSE) 1994–2008 and three waves of the Scottish Health Survey (SHeSs) 1995, 1998, and 2003 (median follow-up 9.5 years, IQR 5.7–13.0).

Systematic review and meta-analysis

This was augmented with findings from

- 12 published studies identified through a systematic review, providing data on 31235 patients, 5095 deaths, and 1414 subsequent events.

To determine the best-fitting dose-response association between alcohol consumption and each outcome examined in the combined sample of 48423 patients, models were constructed using fractional polynomial regression, adjusting at least for age, sex, and smoking status.

Results

De novo cohort analyses (Figure 1)

- Maximally-adjusted models of UK Biobank dataset revealed a J-shaped association for both all-cause and cardiovascular mortality; although similar J-shaped trends were observed for HSE/SHeSs, none of the associations were statistically significant.

- A lower risk of cardiovascular events was observed across all categories of current drinkers.
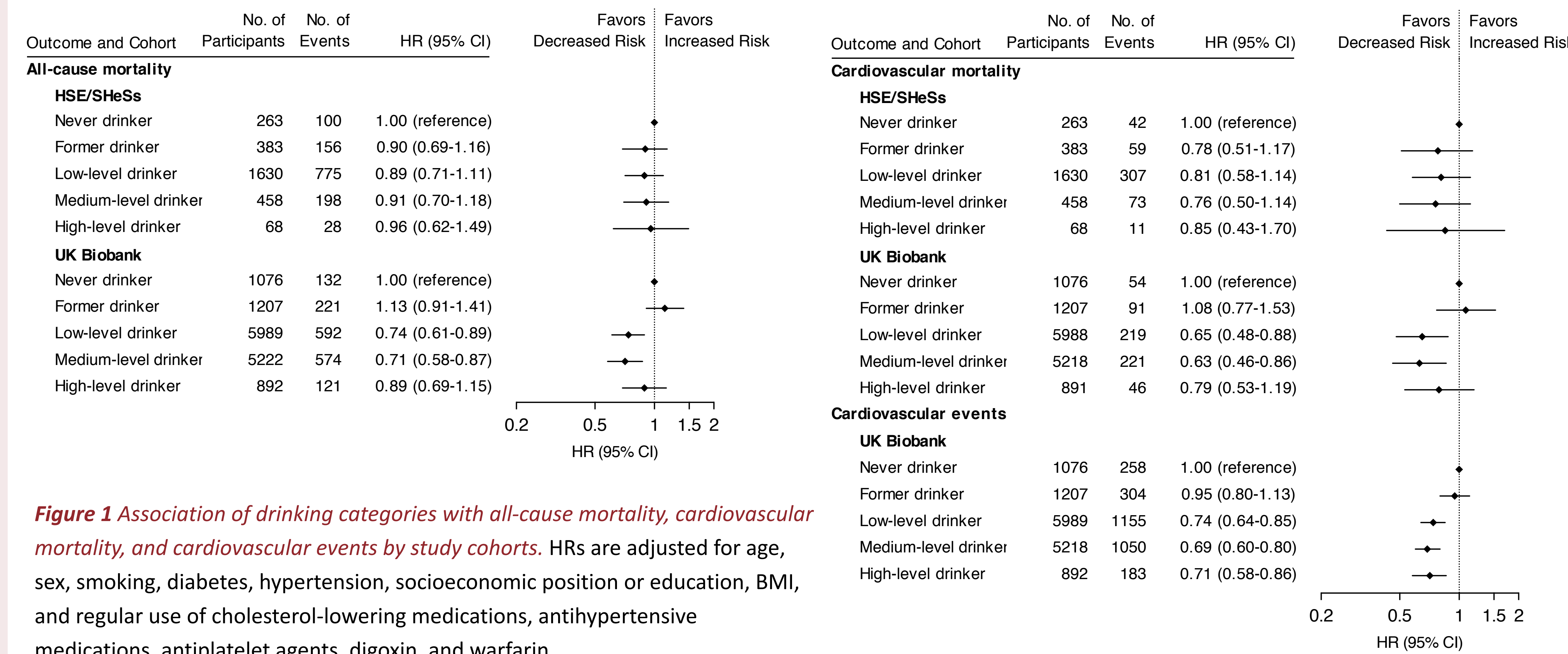
Results

Figure 1 *Association of drinking categories with all-cause mortality, cardiovascular mortality, and cardiovascular events by study cohorts.* HRs are adjusted for age, sex, smoking, diabetes, hypertension, socioeconomic position or education, BMI, and regular use of cholesterol-lowering medications, antihypertensive medications, antiplatelet agents, digoxin, and warfarin.
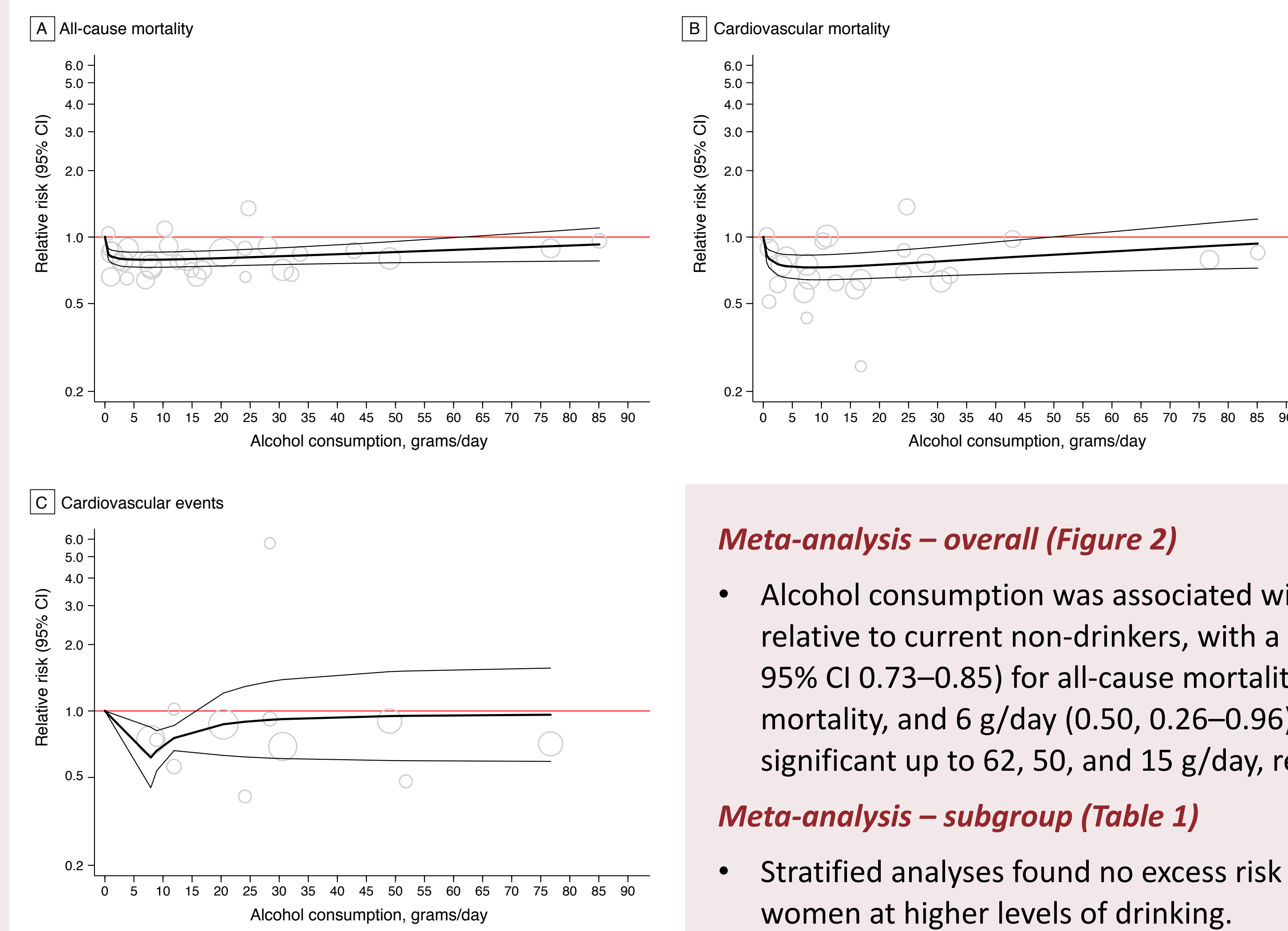

Figure 2 Overall dose-response relationship between alcohol consumption and risk of mortality and subsequent cardiovascular events, using maximally-adjusted estimates. Best-fitting second-degree fractional polynomial models (with 95% CIs) are shown in solid curves with each data point overlaid as circles. Circle size indicates the weighting of each data point and is inversely proportional to the variance of the log-transformed relative risk.

Meta-analysis – overall (Figure 2)

- Alcohol consumption was associated with all assessed outcomes in a J-shaped manner relative to current non-drinkers, with a risk reduction that peaked at 7 g/day (RR 0.79, 95% CI 0.73–0.85) for all-cause mortality, 8 g/day (0.73, 0.64–0.83) for cardiovascular mortality, and 6 g/day (0.50, 0.26–0.96) for cardiovascular events, and remained significant up to 62, 50, and 15 g/day, respectively.

Meta-analysis – subgroup (Table 1)

- Stratified analyses found no excess risk of mortality or subsequent events among women at higher levels of drinking.

Results

Meta-analysis – subgroup (Table 1)

- In the few studies that excluded former drinkers from the non-drinking reference group, reductions in risk among light-to-moderate drinkers were attenuated.

Table 1 Results of meta-analysis on alcohol consumption and risk of mortality and subsequent cardiovascular events

Outcome and subgroup		No. of studies	No. of patients	Maximal effect size [a]		Reversion point, g/day [b]
				RR (95% CI)	g/day	
All-cause mortality						
Overall		11	41743	0.79 (0.73–0.85)	7	62
Sex	Male	6	19897	0.82 (0.72–0.93)	9	39
	Female	3	6046	0.64 (0.36–1.14)	54	49
Primary event	MI	9	29554	0.82 (0.68–0.99)	2	7
	Angina	2	8938	0.79 (0.63–0.99)	39	46
	Stroke	3	3618	0.71 (0.42–1.20)	12	NA
Excluding former drinkers		4	17526	0.85 (0.71–1.00)	3	3
Cardiovascular mortality						
Overall		9	24770	0.73 (0.64–0.83)	8	50
Sex	Male	5	14536	0.72 (0.62–0.85)	9	32
	Female	2	4790	0.29 (0.09–1.01)	54	54
Primary event	MI	6	12422	0.76 (0.64–0.91)	3	25
	Angina	2	8934	0.72 (0.42–1.23)	56	NA
	Stroke	3	3617	0.63 (0.37–1.08)	26	NA
Excluding former drinkers		5	17683	0.71 (0.55–0.90)	7	29
Cardiovascular events						
Overall		4	28621	0.50 (0.26–0.96)	6	15
Sex	Male	3	13598	0.56 (0.23–1.34)	8	NA
	Female	1	3775	0.67 (0.43–1.05)	54	49
Primary event	MI	4	20361	0.79 (0.66–0.94)	11	35
	Angina	1	8747	0.69 (0.59–0.81)	35	n.a.
	Stroke	1	1855	0.49 (0.26–0.92)	72	n.a.
Excluding former drinkers		2	17020	0.78 (0.46–1.31)	17	NA

[a] Defined as the lowest point of the dose-response curve within the range of dose reported by the studies
[b] Defined as the dose of alcohol at which protection against the outcome is no longer statistically significant at the 95% confidence level; not applicable (NA) if non-significant association was found at any level of consumption; not available (n.a.) if the association remained significant within the range of dose reported by the studies

Summary and impact

- Among CVD patients, the drinking limit associated with the lowest risk of mortality and cardiovascular morbidity was up to approximately 105 g/week.

- Our findings therefore support that, for secondary prevention of CVD, current drinkers may not need to stop drinking but should drink within lower risk limits than is recommended in most current guidelines.

- Non-drinking patients should not be encouraged to take up light drinking because of well-known adverse effects on other health outcomes.

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