Authors’ reply

In our analysis, we estimated the theoretical minimum risk exposure level (TMREL) and the non-drinker equivalence of alcohol use, using a new approach to weight relative risk (RR) curves by estimated disability-adjusted life-years (DALYs) in every region, age, sex, and year. This differed from our previous research where we used global DALYs to estimate alcohol risk. Our current analysis showed that the TMREL increases with age and varies across regions, ranging from zero to two standard drinks per day. However, we found minimal differences in TMREL by sex. This variation is driven primarily by differences across background rates of disease rather than differences in the estimation of relative risks.

In response to Mika Kivimäki and G D Batty, we did not treat non-drinkers as a single group within our meta-analyses. Similar to our approach in 2018, we adjusted all estimates for the choice of a reference category, by either recalculating RRs on the basis of non-drinkers exclusively (rather than former drinkers) or by including a study-level covariate for the reference category. We chose this approach to minimise the risk of including people who quit drinking for health reasons within the estimates of RRs.

As noted by both Kivimäki and Batty, and by Jakob Manthey, Kevin Shield, and Jürgen Rehm, we did not adjust RRs for heavy episodic drinking. This limitation of our approach highlights a data gap in the field: most cohort studies of our approach highlights a data gap in the field: most cohort studies on the risk of alcohol use do not contain measures for heavy episodic drinking or interactions between heavy episodic drinking and drinking volumes. As such, there is an absence of sufficient high-quality and reliable data to assess how heavy episodic drinking might modify risk of alcohol use across the range of health outcomes included in our study.

We encourage future researchers to design cohort studies with this important relationship in mind.

Manthey, Shield, and Rehm suggest our RR results do not incorporate known age-effects and regional effects modifying the relationship between alcohol use and disease outcomes, and C Mary Schooling and Gabriel M Leung note that our RR estimates could reflect survival bias in participant recruitment. Many of the available cohort studies recruit older participants as part of trials on cardiovascular disease or cancers. To properly account for this limitation within a meta-analysis, there need to be studies that recruit across a wider age range with longer study periods.

We hope that future cohort studies incorporate a life-course perspective when estimating the health risks of alcohol use, which would mitigate the risk of survivor bias and could increase estimated RRs.

We hope that improved study designs that recruit people across broader age groups, include more representative populations, and incorporate heavy episodic drinking into risk estimation will yield stronger and more precise evidence on the health risks of alcohol use. Our results show that the TMREL of alcohol use is sensitive to differences in background rates of disease. As such, we hope policy makers consider local background rates of disease when developing alcohol consumption guidelines.

We declare no competing interests.

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1 GBD 2020 Alcohol Collaborators. Population-level risks of alcohol consumption by amount, geography, age, sex, and year: a systematic analysis for the Global Burden of Disease Study 2020. Lancet 2022; 400: 185–235.