Biases inherent in all-cause mortality studies: implications for shaping the 2025–2030 dietary guidelines for Americans on alcohol consumption

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Alcohol is an addictive substance that has both detrimental and protective health outcomes at low doses.[1] The net impact of alcohol on health at low doses depends on the underlying risks of diseases and injuries causally linked to alcohol and thus varies across countries. As such, informing the public about the health risks of alcohol consumption requires country-specific information. The *Review of Evidence on Alcohol and Health* by the National Academies of Sciences, Engineering, and Medicine (NASEM) aims to inform the 2025–2030 Dietary Guidelines for Americans. The report compares the impact of consuming ≤1 drink/day (≤14 g of ethanol) for women and ≤2 drinks/day (≤28 g of ethanol) for men on all-cause mortality, relative to never consuming alcohol.[2] However, the ability of this analysis to draw conclusions is limited by several factors.

All-cause mortality risk estimates derived from cohort studies have limited relevance to the impact of alcohol on health. Cohort studies are often impacted by selection bias because their samples consist largely of middle-class, middle-aged individuals from similar cultural backgrounds whose distribution of mortality is not representative of jurisdiction they are sampled from. Furthermore, cohorts from outside the US do not reflect the distribution of deaths in the US population. This impacts the NASEM report, as only one cohort study included in the meta-analysis was from the US.[3] The remaining studies included participants from both Australia and the US,[4] Australia and Europe,[5] China,[6] Japan,[7] the Republic of Korea,[8] and Spain[9,10] (Table 1).

All-cause mortality studies include deaths from diseases not causally linked to alcohol, which increases the impact of confounding factors in observed associations. This issue is compounded by using regression models that are not disease-specific, leading to potential confounding due to the omission of disease-specific variables in all-cause models such as diet. To evaluate this limitation we examined the study that contributed the most weight to the NASEM meta-analysis, Tian et al., 2023.[3] This study found that consuming >0·4–1 drink/day for women and >0·4–2 drinks/day for men was associated with a relative risk (RR) of 0·82 (95% Confidence interval (CI): 0·80, 0·85) for all-cause mortality. When stratified by cause of death, some of the protective effects of alcohol were attributed to reductions in deaths due to accidents and injuries (RR: 0·90, 95% CI: 0·77, 1·06), and influenza and pneumonia (RR: 0·58, 95% CI: 0·46, 0·73). Given the lack of plausibility for alcohol reducing the injury and infection risk, these results are likely spurious and contribute to the overestimation of the protective effects of alcohol on health.

The operationalization of alcohol exposure poses challenges. The NASEM report meta-analysis included studies examining the impact of consuming >0–≤2 drinks/day for men and >0–≤1 drink/day for women on health. However, categorical analyses provide a weighted average risk and do not offer information about the risk at the higher end of these categories. As a result, the average risk within a category may appear protective, while the health risks at the upper end of the consumption range could be detrimental. This issue is exacerbated by two factors. First, in six of the eight studies included in the NASEM meta-analysis, the upper limits of the consumption categories were well below the thresholds of ≤2 drinks/day for men and ≤1 drink/day for women (see Table 1). Second, the distribution alcohol consumption is log-normal (i.e., left-skewed), meaning that consumption within a category will be closer to the lower limit (in this case, >0 drinks) than to the upper limit (e.g., 2 drink/day for men or 1 drink/day for women). For example, using National Health Interview Survey 2014 data (which is used in

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Study	Country	Actual consumption level associated with the RR given	
		Men	Women
Chang et al., 2020[8]	Republic of Korea (cohort)	<0·7	<0·7
Di Castelnuovo et al., 2022[5]	Australia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Italy, Lithuania, Norway, Poland, Russian Federation, Spain, Sweden, United Kingdom (cohort)	<0·7	<0·7
Martínez-González et al., 2022[9]	Spain (cohort)	<0·7	<0·4
Muraki et al., 2022[7]	Japan (cohort)	<1·6	–
Neumann et al., 2023[4]	Australia and the United States of America (randomized controlled trial healthy older adults)	0·5–1·0	0·5–1·0
Ortolá et al., 2019[10]	Spain (cohort)	<1·4	<0·7
Qui et al., 2022[6]	China (cohort)	<0·8	<0·8
Tian et al., 2023[3]	United States of America (cohort)	0·4–2·0	0·4–1·0

Table 1: **Studies included in the National Academies of Sciences, Engineering, and Medicine, committee on review of evidence on alcohol and health meta-analysis of alcohol consumption and all-cause mortality.**

Tian et al., 2023),[3] we estimate that the average consumption for the 0·4–2 drinks/day category is 0·98 drinks/day for men, and for the 0·4–1 drink/day category, it is 0·67 drinks/day for women.

An estimated 177·3 million Americans consume alcohol and 178,000 Americans die from excessive alcohol use every year.[1] The US public needs accurate information about impact of alcohol on health to make informed decisions and unfortunately, the NASEM all-cause mortality analysis provides little insight how the health of Americans is affected by alcohol consumption at or near the 2020–2025 Dietary Guidelines upper threshold of 2 drinks/day for men and 1 drink/day for women. Moreover, due to the inherent limitations of all-cause mortality analysis, such analyses should not be used to guide alcohol and health recommendations. Instead, cause-specific approaches that model the health impact of alcohol consumption based on specific causes of death should be prioritized.

Contributors

Conceptualization: KS, KK, PM, AJM, JR, TSM, Writing – original draft: KS, Writing – review & editing: KS, KK, PM, AJM, JR, TSM.

Declaration of interests

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