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Methodological Concerns Regarding the American Heart Association Scientific Statement on Alcohol Use and Cardiovascular Disease

We read the American Heart Association scientific statement on alcohol use and cardiovascular disease with great interest. Given alcohol's substantial role in the global burden of disease, it is crucial to review what is known about alcohol and cardiovascular risk. Unfortunately, we have several concerns regarding the scientific statement and its development.

First, the statement appears to have been developed without any systematic review methodology. Systematic searches of multiple databases with pre-defined inclusion and exclusion criteria are essential, especially with respect to alcohol and cardiovascular disease research where there exists significant controversy and debate.

Furthermore, when presenting the evidence, the authors do not give differential weight to studies based on their quality, despite mentioning that observational evidence frequently suffers from abstainer bias, reverse causality and residual confounding. This results in significant discrepancies between the presented evidence and recommended patient education.

For example, for coronary artery disease (CAD), the authors cite evidence from observational studies, some of which employed a biased, non-drinker (versus occasional drinker) reference group, to state that moderate alcohol use may be cardioprotective. Importantly, the authors miss a meta-analysis which found that, collectively, higher-quality observational studies controlling for various biases do not find cardioprotective effects.[1] Furthermore, as discussed by the authors, high-quality mendelian randomization studies also have not replicated beneficial effects of moderate alcohol use. Perplexingly, the authors state that patients should be informed that consuming alcohol in moderation "may provide some risk reduction for CAD," even though the abundance of higher-quality evidence does not support this.

In addition, the summary recommendations provided in this statement appear overly compartmentalized, treating cardiovascular health as an isolated entity disconnected from overall health. It would be both concerning and confusing for patients to receive education regarding contentious cardiovascular benefits of moderate alcohol use without clear discussion of the well-documented impacts of alcohol use on other health outcomes such as cancer.[2]

Ultimately, higher quality evidence is needed to truly understand the impacts of 1-2 standard drinks per day on cardiovascular outcomes. In the absence of randomized evidence, it is premature to make claims about the purported cardiovascular benefits of moderate alcohol use, especially given the known carcinogenic effects of ethanol.

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2. Office of the Surgeon General (US). *Alcohol and Cancer Risk: The U.S. Surgeon General's Advisory*. Washington (DC): US Department of Health and Human Services; 2025.

Author Reply: the American Heart Association Scientific Statement on Alcohol and Cardiovascular Disease

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We appreciate the opportunity to address these important questions.

First, we did employ a systematic approach to our literature search, which was designed to be as complete, comprehensive, and devoid of bias as possible. We did not publish those initial approaches, but they are available upon request. Of note, we sought to highlight randomized controlled trials and recent meta-analyses, avoiding abstracts and generally focusing on studies completed in approximately the last 10 years.

Importantly, as a Scientific Statement of the American Heart Association, the purpose of the document was to review and report the most up-to-date science regarding relationships between alcohol and cardiovascular disease. This was not a clinical practice guideline and therefore was neither intended nor written to provide recommendations. Please see the last sentence of the introductory paragraph, "This document reviews, evaluates, and summarizes data on the association of alcohol use as it pertains to CVD to guide health care professionals, patients, and the lay public and highlights limitations of current studies and lingering uncertainties that warrant further scientific investigation." The patient education section similarly followed this rubric, and therefore the content communicated there was indeed intended to be in regard to the latest knowledge (rather than any specific recommendation regarding behavior or use of alcohol per se). We were very careful to avoid any language directly instructing anyone (or any patient) to engage in any particular behavior, and no language similar to what is employed in clinical practice guidelines (such as specific recommendations and levels of evidence to support those recommendations) was used.

It appears there was a misunderstanding regarding what was written under that patient education section. We disagree that our statement states (as written in the letter), "that patients should be informed that consuming alcohol in moderation 'may provide some risk reduction for CAD." Clearly this is taken out of the broader context regarding the communicated harms regarding excess alcohol consumption and the many uncertainties highlighted regarding the current evidence regarding drinking in moderation. Indeed, in that section of the Statement, we point very specifically to the potential harms of communicating benefits of alcohol and how that may inadvertently lead to heavier consumption of alcohol: from the Statement, " It is important to note that among patients surveyed in cardiology services (N=498), 66.3% were exposed to reports that indicated moderate drinking can be good for the heart.[118] It is important to deliver the right message because that study also reported that exposure to reports of healthy-heart effects or mixed messages about the cardiovascular effects of alcohol were associated with increased odds of hazardous alcohol use (odds ratio, 1.67 [95% CI, 1.02–2.74]).[118]"

Regarding the breadth of the content covered, the Scientific Statement met the prespecified criteria, which fits with the title: “Alcohol Use and Cardiovascular Disease.” Therefore, as intended prior to drafting the content, as approved by the American Heart Association, and ultimately with input from multiple levels of peer review, the Statement is in fact focused on Cardiovascular Disease. We of course understand and acknowledge that this is one outcome among many relevant to alcohol, medicine, and health: we state (italics added for emphasis here), “More research into the following areas is needed: the heterogeneous effects within individuals, potentially driven by differences in SES status, other demographics, interactions with other environmental or dietary exposures, concomitant comorbidities, *balancing overall health effects (eg, differential effects related to CVD versus cancer*), and genetics, as well as effective strategies for behavior change to influence the healthiest patterns of alcohol consumption, for which evidence in populations without alcohol use disorders is especially lacking.” We also emphasize these points in Figure 1, which states, “Any level of alcohol consumption carries health risks…” And very plainly also in Figure 1, “Drinking alcohol increases the risks of cancers of the mouth, throat, esophagus, liver, and more.” We will note here that these statements are much more definitive than any statement about potential health benefits (or neutral health effects) of alcohol related to outcomes throughout the entire manuscript. This is despite the fact that the heightened risks of cancer with alcohol are also based on observational evidence, that such evidence is mainly in regard to excess alcohol consumption (and not moderate consumption), and that there is even some evidence that drinking in moderation has been associated with lower risks of certain cancers (such as leukemia and lymphoma).

We were indeed not able to reference every manuscript published on the subject. We agree that the meta-analysis mentioned is an important contribution to the literature, but it is very important to highlight a few related points. First, we did reference a manuscript from the same group, on the same topic, but that was more up-to-date (please see reference 32, from 2024 instead of the one from 2017 as suggested here). But, just to comment on the 2017 paper: the main conclusions from the main results of that meta-analysis were that moderate alcohol consumption was associated with highly statistically significant reductions in mortality from coronary heart disease. In a separate analysis reported in the same paper in which only studies with very specific criteria were included, no statistically significant findings were observed. However, the point estimates continued to favor a lower risk of mortality due to coronary heart disease, and the substantial reduction in the number of studies not surprisingly reduced statistical power and therefore was associated with wider confidence intervals.

Importantly, ultimately we believe that we are in full agreement with Dr. Farkouh and colleagues in highlighting the need for more randomized controlled clinical trials on these

topics. Indeed, we not only acknowledge the limitations of the great majority of studies examining 1-2 drinks of alcohol per day, we deliberately emphasize those limitations in the Statement. Throughout the Statement, we call for higher quality studies, and specifically randomized trials on the subject.

This letter provides us an opportunity to distinguish between dogma, or motivated reasoning based on assumed conclusions, versus science, which is clearly a major concern related to alcohol consumption. Following dogma means there is a fixed belief, and the danger is that only evidence that fits a particular narrative will be selected. This might mean focusing on one health outcome (such as cancer, although the majority of the evidence suggests that, on the whole, 1-2 drinks a day is most reliably associated with the lowest risk of *overall* mortality) or even in selecting only results even within the same study to fit a preconceived conclusion. Whereas we are all in agreement that heavy alcohol use almost certainly only increases harm regardless of the outcome being studied, this Statement provided a comprehensive assessment of the best evidence, reported the currently available best , and concluded that uncertainty remains regarding the true effects of 1-2 drinks a day on cardiovascular health.

Conducting clinical research and especially randomized clinical trials is known to be one of the most difficult tasks in medicine. If there is a general assumption regarding an overarching conclusion that 1-2 drinks a day must be harmful and cannot possibly either have a beneficial effect or no meaningful effect on cardiovascular health, all of the challenges already faced by clinical investigators only become more arduous: convincing institutional review boards (IRBs) to approve such studies, funders to support such studies, and even patients or members of the lay public to participate in such research would all be hindered. One of the main goals of the current Statement is to shine a light on lingering uncertainties and the important limitations underlying the current evidence in order to promote the conduct of such randomized trials. We hope this official statement can reassure IRBs, funders, and potential research participants that there is indeed sufficient equipoise regarding the cardiovascular effects of 1-2 drinks per day to justify both the ethical conduct of as well as the significance of such original research.