

Alcohol's contribution to cancer is underestimated for exactly the same reason that its contribution to cardioprotection is overestimated

Connor discusses whether it is consistent to doubt epidemiological studies that low-dose alcohol is cardioprotective while accepting similar evidence that it also causes cancer. We show that misclassification of former and occasional drinkers as abstainers is widespread in alcohol epidemiology. This practice leads to a systematic underestimation of health risks from drinking (e.g. for cancer) and overestimation of health benefits. Correction of this problem in future studies should lead to significantly larger estimates of alcohol's contribution to chronic disease.

We greatly appreciate Dr Connor's thoughtful analysis of the evidence that alcohol consumption can be considered a cause of cancer and not just a possible link or association [1]. She illustrates well how proposed causal associations can, through induction, stimulate new research questions that may help to refute or confirm a causal hypothesis. For example, many observational studies indicate a dose-response relationship between level of prior alcohol consumption and subsequent risk of different cancers. Conversely, there is evidence that cutting down on drinking or abstaining is associated later with a significantly reduced risk of these same cancers. In the same vein, we would add that confirmation of the main causal pathway for cancers of the digestive system via exposure to the alcohol metabolite acetaldehyde [2] has also been provided by genetic studies. These have shown that population subgroups with a genetic propensity to experience a build-up of acetaldehyde after drinking have a higher risk of such cancers [3].

Connor also addresses a criticism that it may be seen as inconsistent to doubt studies pointing to protection against cardiovascular disease (CVD), while accepting evidence from similar studies as the basis for alcohol causing cancer. Methodological problems with these studies have been highlighted in recent years as a basis for being sceptical of the hypothesis that moderate alcohol use reduces cardiac risk [4–7]. How can the same types of studies be considered dubious for one outcome (CVD) but acceptable for another (cancer)? We would like to add to her discussion of the significance of former and occasional drinker biases in this literature and highlight how they can cause both overestimation of cardioprotection and underestimation of cancer risks across the whole drinking continuum. The underlying theory here is that, as a population ages, a selection bias operates whereby individuals with poorer health are more likely to cut down or stop drinking completely [4].

Such individuals are often still classified as 'abstainers' and used as a reference against which all current drinkers are compared. In simple terms, they make drinkers at all levels of consumption 'look good' by comparison. This, in turn, results in both the appearance of protection at low levels of drinking and reduced risk at higher levels (assuming an underlying dose-response risk relationship applies). It is worth noting that the misclassification of former and occasional drinkers as abstainers is virtually the norm in alcohol epidemiology. In a new meta-analysis on alcohol and prostate cancer, we found that 21 of 27 included studies contained abstainer bias [8]. In a recent meta-analysis of alcohol and all-cause mortality, we reported abstainer biases in 74 of 87 studies [5].

It is thus entirely consistent to be sceptical about cardioprotection at low levels of alcohol intake while accepting evidence of a dose-response risk for cancer from the same or similar studies. What is often not spelt out, however, is how these prevalent biases lead to a substantial underestimation of alcohol's contribution to premature mortality generally, including that from cancer. It is also often overlooked that J-shape (= protective) risk relationships are not specific to CVD, but have been observed for many implausible conditions such as deafness, the common cold, hip fractures, some cancers and even liver cirrhosis [7]. In a recent meta-analysis of alcohol and prostate cancer, we reported a nearly threefold increase in risk for low-volume drinkers when studies with former drinker bias were eliminated: the risk increased from 8% when all studies were included to 23% when only bias-free studies were retained [8].

For the first time, the latest estimates of the global burden of disease from alcohol [9] factor in an increased risk of alcohol-caused mortality among former drinkers [10]. However, there is still no account of the residual underestimation among all current drinkers. The result of correcting for this underestimation is likely to be a substantial increase in the proportion of cancers attributable to alcohol consumption. It is clear that a new generation of alcohol epidemiological studies are required which avoid misclassifying former and occasional drinkers as abstainers and, further, risk estimates based on past meta-analyses need to be adjusted upwards to correct for these past errors. Along with increased understanding of biological pathways, revised estimates of the scale of alcohol's contribution to cancer may eventually cause a seismic shift in cultural attitudes to drinking.

Declaration of interests

T.S. is a recipient of research funds through the University of Victoria from Sweden's government retail alcohol monopoly for a study on the public health consequences of government controls.

Keywords Alcohol, cancer, cardiovascular disease, chronic disease, former drinkers, misclassification error.

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