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Commentary: Alcohol, coronary heart disease and public health: which evidence-based policy?

Pascal Bovet and Fred Paccaud

In a comprehensive review of the evidence available in 1984, Marmot concluded that moderate alcohol intake was associated with decreased coronary heart disease (CHD) mortality while heavy drinking resulted in higher mortality compared to non-drinkers.[1] The consistency of the findings across ecological, case-control and prospective studies and the availability of convincing data on plausible mechanisms suggested a cardio-protective effect of moderate alcohol consumption. However, Marmot warned that increased intake was not recommended in view of the social and medical consequences of an increase of alcohol consumption in the population. Epidemiological data published since this review support the original conclusions by Marmot and have provided further information to fine tune our understanding of the relation of alcohol to CHD and their relevance to policy.

Large prospective cohort studies have provided further solid data since 1984. Cohorts among middle-aged or elderly people included, for example, 51 529 American male health professionals with information on alcohol consumption studied for 12 years,[2] 87 526 American female nurses followed for 4 years,[3] 276 802 men enrolled by the American Cancer Society followed for 12 years,[4] 490 000 American men and women from the American Cancer Study II followed for 9 years,[5] 123 840 American adults from a prepaid health plan followed for 8 years,[6] 12 321 British male doctors followed for 13 years,[7] 36 250 middle-aged French men followed 12–18 years[8] or 13 285 Danish men and women followed for an average of 13.5 years.[9] These and most other studies and reviews[10–14] have consistently found that consumption of 1–6 drinks a day was associated with a 20–50% lower risk of CHD. (One 120–150 ml glass of wine, one 280–360 ml bottle/can of light beer or one 20–30 ml measure of spirit each typically correspond to one 'unit' or 'drink' and contain 10–17 ml alcohol or 8–15 g of alcohol). Moderate alcohol intake has also been associated with a 20–30% reduced risk of stroke and other cardiovascular diseases[5,7] and a 20% reduced risk of sudden death.[15] Consistency of results among various populations and analytical control for several potential confounders in many of these studies makes it very unlikely that the apparent inverse relation between alcohol intake and CHD results from selection biases or confounding factors. In particular, results were generally not substantially altered in analyses excluding people with illnesses or abnormal risk factor levels at baseline. This argues against the view that higher mortality in non-drinkers relates to the inclusion of sick people (including former drinkers) into the categories of non-drinkers.[16] Although ethical and feasibility issues preclude the conduct of clinical trials of alcohol consumption, current epidemiological evidence supports, virtually irrefutably, that light-to-moderate drinking substantially reduces the risk of CHD.

The effects of moderate alcohol consumption on all-cause mortality depends on a person's underlying (or absolute) risk

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of disease that can be improved or worsened by alcohol.[17] Moderate alcohol intake reduces the relative risk of CHD and ischaemic stroke but alcohol consumption has a linear relationship with mortality from hepatic cirrhosis, injury from external causes, haemorrhagic stroke,[3,6,18] upper digestive tract cancers and probably breast cancer[19] and large-bowel cancer.[20] Hence, the reduction in all-cause mortality among middle-aged and elderly people associated with light to moderate alcohol intake (15–50 g, typically 1–3 drinks) is related to the distribution of deaths from cardiovascular disease and from conditions potentially worsened by alcohol. For example, among the 226 871 men aged 56 years on average and free of cancer and cirrhosis at baseline (among whom one drink per day was associated with a 20% reduction in all-cause mortality), 47% of the 25 424 deaths occurring during 9-year follow-up were due to cardiovascular conditions while only 10% were due to conditions potentially worsened by alcohol.[5] In a recent cohort of 1536 Italian middle-aged men followed for 30 years, age-adjusted life expectancy was 2 years longer for men drinking 49–84 g alcohol per day (typically 3–6 drinks) than for men drinking 0–12 g per day (a similar 2-year longer life expectancy was found for non-smokers compared to smokers).[21]

In contrast to the situation in the middle-aged, moderate drinking is generally associated with increased all-cause mortality in young adults as mortality in this age group results mainly from violent deaths (accidents, suicide, homicide) which are all worsened by alcohol. For example, moderate drinking was associated with a 30–50% increase in all-cause mortality in a cohort study of 49 618 young Swedish military conscripts in which there were only 38 fatalities from myocardial infarction among a total of 1473 deaths over a 25-year follow-up.[22] This and other studies[17] suggest that benefits of moderate alcohol intake may outweigh harm among men in their 40s and women in their 50s.

Irrespective of age, more benefit (in terms of absolute risk) will result from moderate alcohol intake in people with multiple cardiovascular risk factors. Conversely, more harm will result from moderate alcohol consumption in populations with high rates of deaths from external causes or alcohol-related diseases. Also worthy of consideration is the fact that populations with low CHD mortality (which relates inversely with alcohol intake) tend to have high death rates from haemorrhagic stroke (which relates directly with alcohol intake). Hence, it is no surprise that alcohol consumption results in a heavier burden of disease in developing countries (low CHD mortality, high mortality from haemorrhagic stroke and injury, demographically young populations) than in western countries (where opposite characteristics are found).[23]

A causal interpretation of the inverse relation between moderate alcohol consumption and CHD is supported by consistent evidence linking alcohol intake with several factors associated with CHD, particularly high density lipoprotein (HDL) cholesterol and apolipoprotein AI. A recent meta-analysis of 42 experimental studies demonstrates that moderate alcohol drinking substantially reduces HDL cholesterol, apo A lipoprotein, lipoprotein(a), fibrinogen, plasminogen and tissue type plasminogen activator antigen.[24] On the basis of published studies (considering that no single study has simultaneously calculated the risk of CHD associated with all biological factors), the authors calculated that an intake of 30 g alcohol a day would cause a 25% reduction in risk of CHD. However, it has been suggested that alcohol preferentially increases a type of HDL particles (LpAI:AII) that are less clearly associated with cardioprotection.[25,26] This issue is not yet fully clarified and needs further research. Cardioprotection from moderate alcohol consumption has also been challenged on the grounds that alcohol intake increases blood pressure. However, while heavy alcohol intake (e.g. >4 drinks/day) is known to induce hypertension,[27,28] the response is less clear at levels of light-to-moderate intake.

An inverse relationship between alcohol intake and CHD has been described in populations with widely different traditional consumption patterns of alcoholic beverages, suggesting a common effect of ethanol. However, several studies have suggested a larger effect of grape or rice wine over other beverages,[8,9,29] although a reduced risk of CHD has also been demonstrated for beer[30,31] or spirit.[2] The issue is complicated because, in several countries, wine drinkers tend to be better educated, earn more, have a healthier diet, and get more medical care; thus, they tend to have different risks of diseases and different drinking patterns compared to other drinkers. Wine, unlike most other alcoholic beverages, contains phenolic substances that are known to inhibit oxidation of low-density lipoprotein,[32] affect platelet functions[33] and inhibit stages of carcinogenesis.[34] The different effects of alcoholic beverages could also relate to nitrosamine, a potentially carcinogenic substance, which is found in beer and spirits but insignificantly in wine.[35] A recent large Danish cohort study found that upper digestive tract cancers were strongly associated with beer and even more so with spirits while no consistent relation was found for wine intake.[36] Violent deaths were found to be less frequent in wine drinkers than in beer drinkers.[37] Further research should clarify the role of substances other than ethanol in different beverage types and characteristics of drinkers of specific beverages. Such factors could explain part of the variation in mortality from alcohol-related diseases between populations.

Drinking pattern has specific health consequences irrespective of total alcohol intake. A Finnish population-based prospective study showed, for example, that beer bingeing was associated with increased all-cause mortality, deaths from external causes, and fatal myocardial infarctions regardless of the total average consumption of beer, wine and spirits.[38] Binge drinking may also partly explain the lack of reduced CHD mortality in a cohort of Scottish middle-aged men[39] and may be a key factor in the current rise in mortality in Eastern European countries.[40] In contrast to binge drinking, regular alcohol consumption with meals might result, for example, in slowed alcohol absorption, lower blood alcohol, less alcohol-related damage and more sustained stimulation of high-density lipoproteins. The relationship between alcohol intake and CHD and all-cause mortality is therefore likely to differ among populations where binge drinking and spirit consumption are common as compared to populations where regular moderate drinking of wine is predominant.

Societies largely rely on historical, cultural and religious attitudes for their stances toward alcohol consumption. There are 'temperance' cultures (e.g. UK, Scandinavia) and 'non-temperance' cultures (e.g. France, Italy, Belgium). Alcohol consumption per capita is twice as high in the latter but Alcoholics Anonymous groups are four times higher in the former.[41] An average of 21 drinks per week may appear as quite ordinary

drinking in the latter but define a 'problem drinker' in the former. Religious beliefs may acquiesce with moderate drinking (Saint Paul advised to 'use a little wine for thy stomach's sake') while others (typically Protestant and Islamic religions) favour abstinence. More subtle influences are also likely. Authors of publications demonstrating substantial benefits from moderate alcohol intake have often refrained, unusually, from generalizing their findings, while moderate alcohol consumption was an explicit criterion for a healthy lifestyle in a recent large American primary prevention study using diet and lifestyle.[42] It is therefore important to acknowledge that interpretation of data and subsequent recommendations related to alcohol consumption can be influenced to various extents by societal and cultural preferences.

However, from an epidemiological point of view, the evidence currently available is large enough to guide recommendations on alcohol consumption. A net health benefit can be expected in people aged at least 40 and drinking no more than 2–3 drinks a day. How long moderate alcohol consumption must continue for these benefits to occur is however unknown. Benefits are accrued in people who are at high risk of CHD; conversely, the health risk of individuals at low risk of CHD is potentially worsened by alcohol intake. In that sense, the available evidence does not point to a universal threshold for a safe (less so preventive) alcohol intake that would apply to all adults, as is often suggested. In addition, old prescriptions still hold: one should abstain from drinking in case of pregnancy, personal or family history of alcoholism, when taking a medication that interacts with alcohol or when planning to drive or engage in other activities that require one to be alert. Therefore no simple recommendations can be advised for alcohol consumption. Because the risk reduction in CHD mortality associated with moderate alcohol intake can be as large as that associated with cardioprotective drugs (e.g. aspirin, beta-blockers or cholesterol-lowering drugs), individual advice for moderate consumption of alcohol, and preferably wine, should be considered for patients at high risk of CHD and without contraindications. This includes in particular patients who have had myocardial infarction.[43] An approach based on absolute risk has similarly influenced the rationale of recent guidelines for the clinical management of raised blood pressure, dyslipidaemia and, generally, CHD.[44,45]

Possible strategies in this field include the provision of clear information on the benefits and harms of alcohol consumption, which should be an integral part of health education programmes for health professionals, the general public and children. At the same time, innovative approaches to strengthen social norms protecting against alcohol problems should be developed. Knowledge-based orientation to prevention may be of particular importance in young adults to clarify the ambivalence found in many societies about alcohol and drinking, e.g. institutional perspectives encouraging abstinence in teenagers but experimentation in young adults.[46] These strategies would be better than the current propagation of mixed messages or simplistic views, including the misleading claim that 'a small amount of alcohol is safe' (achieved through skilful marketing by the industry), and the numerous and many-sided information channels currently available.

Any strategy in this field should be carefully monitored and evaluated. Although promotion of regular drinking of small amounts of alcohol restricted to specific population segments seems attractive, it is hardly feasible. Noticeably, no trial has yet assessed whether increased problem drinking would outweigh the benefit of reduced CHD mortality if regular drinking of small amounts of alcohol were to be advocated for specific population subgroups. Specifically, longitudinal studies should gather more information on who would start drinking, who would maintain light-to-moderate drinking and who would progress to heavier or hazardous drinking.

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