



## Invited Commentary—Alcohol Consumption and Coronary Heart Disease: Good Habits May Be More Important Than Just Good Wine

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More than 20 years ago, Klatsky et al. (1) published the first large-scale epidemiologic study showing an inverse association between alcohol and coronary heart disease. Since then, evidence for a causal interpretation has come from over 60 ecologic, case-control, and cohort studies using populations from across the world and measuring many different types of alcohol-containing beverages. All of the available evidence (2–5) indicates that, in general, men and women who consume 1–2 alcoholic drinks per day have the lowest risk of coronary disease. In a recent meta-analysis of cohort studies, Maclure (3) found a summary relative risk of 0.83 (95 percent confidence interval 0.77–0.89) for moderate drinkers (2–3 drinks per day) in comparison with never drinkers.

Several reports, including the article by Marques-Vidal et al. (6) in this issue of the *American Journal of Epidemiology*, have published individual relative risks attributable to consumption of beer, wine, and spirits (liquor). Although the possible additional benefits of wine—especially red wine—have received considerable attention in the lay media (7, 8) and in scientific communications (9, 10), whether any specific type of alcoholic beverage has a particular benefit has not been established. Recently, this author and colleagues (11) examined the relation between specific alcoholic beverages and the reduction in coronary heart disease by summarizing published reports from ecologic, case-control, and cohort studies. In general, we found that results from observational studies, where individual consumption can be assessed in detail and linked directly to coronary disease, provide strong evidence that a substantial proportion of the benefit of wine, beer, or spirits is attributable to ethanol. Differences in findings regarding specific beverage types may be due to differences in beverage-specific drinking patterns or to confounding by other risk factors related to beverage

type that are unique to each population under study. The current article by Marques-Vidal et al. (6) provides an excellent example of how cultural differences could explain why a specific beverage may appear more beneficial: Wine consumption was more beneficial in France and non-wine consumption was more beneficial in Northern Ireland. These differences may reflect only cultural differences in drinking patterns rather than differences in the biochemical actions of wine and non-wine alcoholic beverages.

### ECOLOGIC STUDIES

Ecologic studies of alcohol consumption and coronary heart disease are based on existing data that typically are collected by government agencies or international surveillance programs. Ecologic analyses provide investigators with a unique opportunity to study associations across a wide variation of intake. In a recent ecologic study of 18 developed countries (12), intake ranged from 2 liters of wine per person per year in Norway to over 70 liters of wine per person in France.

In 1979, St. Leger et al. (12) published the first ecologic analysis showing a strong inverse association between average per capita wine consumption and ischemic heart disease mortality. The inverse association was pronounced for wine consumption in both men and women, was less strong for spirits, and was nonexistent for beer. Other analyses of ecologic data have reported similar results. Can we conclude from these results that wine is the main (or only) alcohol-containing beverage which reduces the risk of coronary disease? Because overall per capita alcohol consumption or beverage-specific consumption may be related to other important correlates of coronary heart disease (e.g., obesity, socioeconomic status, or physical activity), a crude comparison of consumption with disease rates may be confounded and thus produce misleading results.

Even in those ecologic studies that adjust for potential confounders (13, 14), the interpretation of each confounder (and therefore of the alcohol association)

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Abbreviation: HDL, high density lipoprotein.

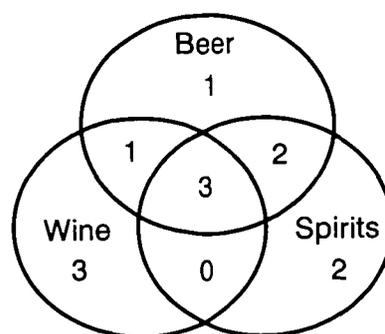
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may differ by country. For example, Artaud-Wild et al. (14) reported that an index of saturated fat and cholesterol intake was a strong modifier of the association between alcohol and coronary disease mortality. Wine (and total alcohol) was only significantly inversely associated with coronary disease mortality among countries with the higher fat and cholesterol intakes. The interpretation of per capita saturated fat and cholesterol intakes may differ between countries, because per capita consumption is based on “disappearance” statistics which do not account for losses due to wastage. To the extent that wastage of fat is greater in the wealthy, industrialized countries, controlling for fat or cholesterol intake on a population basis could introduce bias (15), since the meaning of per capita fat and cholesterol intake will differ by level of industrialization.

Ecologic studies have further important limitations that severely limit their utility in drawing direct conclusions about specific alcoholic beverages and coronary disease. In some countries, a small proportion of the population may consume a large percentage of a specific type of beverage, whereas in other countries, such as France, average per capita wine consumption may be a more accurate representation of typical consumption, since wine is drunk by much of the population. Furthermore, if beverage type is associated with drinking patterns, the ill effects of binge drinking (16) may counter the established inverse association between moderate alcohol consumption and coronary disease. For example, what may appear to be a moderate (or even low) level of spirits consumption on a per capita per day basis might mask excessive consumption by a small proportion of the population and little or none by the rest.

### CASE-CONTROL AND COHORT STUDIES

The best evidence with which to judge the association between alcoholic beverage type and coronary disease may come from observational data, where individual intake can be linked directly to coronary disease. In addition, depending on the study design, both coronary morbidity and mortality can be examined. Previously, we discussed in detail each observational study that reported beverage-specific relative risks (11). Figure 1 summarizes the results of the 12 case-control and cohort studies (including the French and Irish populations from the Marques-Vidal et al. (6) study) that have reported a significant reduction in coronary heart disease due to at least one specific type of alcoholic beverage. Three studies did not find any of the three beverage types to be inversely associated with coronary disease (17–19). The same number of studies (seven) found an inverse association between



**FIGURE 1.** Numbers of observational studies that have reported beverage-specific relative risks for the relation between moderate consumption of beer, wine, or spirits (liquor) and lower risk of coronary heart disease (4, 6, 17–21, 23, 31–39).

alcohol and coronary disease for each type of alcoholic beverage. Three of the studies (6, 19, 36) reported that only wine consumption was inversely associated with coronary disease. However, two (6, 19) of these three studies were carried out in populations whose alcohol intake was almost exclusively due to wine consumption. In many of the other instances where only one beverage type was significantly inversely associated with coronary disease, the other alcoholic beverages also showed trends toward protection even though the relative risk did not reach statistical significance. From all of the observational data collected from more than 305,000 men and women, the available evidence suggests that no particular type of beverage provides substantial additional cardiovascular benefit apart from its ethanol content.

If no single beverage type provides all or most of the cardiovascular benefit, why do results from several individual cohort studies suggest a stronger association for one type of beverage or another? The differences between studies may be due to chance, or they could be due to differences in drinking patterns or lifestyle correlates of beverage choice between populations. In those studies that have found only one type of alcoholic beverage to be significantly inversely associated with coronary disease, that beverage is consumed by much of the population, typically at levels of one or two drinks per day. This widespread pattern of “healthy” drinking is more likely to reflect drinking during meals rather than heavy or episodic drinking by a small percentage of the population. In the Marques-Vidal et al. (6) study, this seems to have been the case for wine consumption in France, where 79 percent of the alcohol consumed among controls was from wine, and for non-wine consumption in Northern Ireland, where 95 percent of alcohol consumption was not from wine.

In the Health Professionals Follow-up Study (20), spirits were most strongly inversely associated with

coronary heart disease, and alcohol from spirits was strongly correlated with total numbers of days on which alcohol was consumed. This suggests that consumption of spirits took place on most days of the week and was not restricted only to heavy weekend consumption. Conversely, in the Copenhagen City Heart Study (21), where spirits consumption did not reduce coronary disease, only 8.5 percent of the men and 4 percent of the women reported drinking spirits an average of once per day or more often. Because this small sample of spirits drinkers may have had different drinking patterns (and other lifestyle characteristics) than the rest of the Copenhagen population, such differences may explain the absence of an inverse association for spirits in this population.

In a unique analysis of data from the Kaiser Permanente Study, Klatsky et al. (22) reported that wine drinkers were least likely to develop coronary heart disease, followed by drinkers of spirits and beer. However, these differences were almost completely eliminated after further control for sex, race, number of drinks per day, cigarette smoking, coffee consumption, and education. This is strong evidence that correlates of beverage choice may explain the different beverage-specific relative risks between populations.

Observational studies that examine alcohol use in populations whose alcohol consumption is limited to one or two types of beverages provide a unique opportunity to rule out the possibility that only one type of beverage is largely responsible for the reduction in coronary disease. In the rural Italian cohorts of the Seven Countries Study (19) and the two populations from France (6), the lowest rates of cardiovascular disease were found among moderate drinkers of wine, almost exclusively. Conversely, the Honolulu Heart Study found a significant inverse association for beer and coronary disease (23) but not for wine. However, in that population, only 15 percent of the people drank wine, with a median intake of half a glass per month. These studies suggest that ethanol per se rather than a specific type of beverage is responsible for the reduction in coronary disease.

#### **ALCOHOL AND HIGH DENSITY LIPOPROTEIN CHOLESTEROL**

Several short-term experimental studies have shown that alcohol (in general) increases levels of high density lipoprotein (HDL) cholesterol (24, 25). This mechanism provides a possible biologic basis for a causal relation between alcohol and lower rates of coronary disease (26). In epidemiologic studies of total alcohol consumption and coronary disease, inclu-

sion of a measure of HDL cholesterol in a statistical model predicting risk of coronary heart disease may provide some insight into the percentage of the inverse association that can be explained by this mechanism. From previous studies (27–30), it is estimated that perhaps half of the beneficial effect of alcohol is due to its effect on HDL cholesterol. The results from the present study (6) are compatible with this hypothesis. However, this calculation does not take into account laboratory and biologic variability in HDL cholesterol levels or error in the assessment of alcohol intake. In addition, most studies do not account for other factors that may alter HDL cholesterol levels (e.g., diet, exercise, obesity, etc.) and that may also be associated with alcohol consumption.

In the Health Professionals Follow-up Study, men with moderate alcohol consumption had a healthier diet and exercised more (11, 20), both of which increase HDL cholesterol levels. Criqui et al. (29) were not able to account for diet or exercise in their study of alcohol, lipids, and coronary disease in the Lipid Research Clinics population. They reported that approximately 50 percent of the inverse association between moderate alcohol drinking and total cardiovascular disease (70 percent for coronary heart disease) in men could be explained by the positive association between alcohol and HDL cholesterol. A similar study by Langer et al. (28) using data from the Honolulu Heart Program reported that 50 percent of the coronary disease risk reduction could be explained by alcohol, even though diet and exercise were not included in the statistical models.

In a case-control study of men and women from the Boston, Massachusetts, area (27), the positive link between alcohol and HDL cholesterol explained about 70 percent of the risk reduction after diet, obesity, and exercise (and other risk factors for cardiovascular disease) were accounted for. Because these factors were not strongly associated with alcohol in the Boston-area men, the risk reduction attributable to the alcohol-HDL cholesterol link is not appreciably different from that of the previously discussed studies which did not include these potential confounders. However, in the current study by Marquis-Vidal et al. (6), where 57 percent of the risk reduction can be explained by HDL cholesterol, we can only speculate on the influence that physical activity or diet (especially the disparate diets of Northern Ireland and France) may have had on the statistical model, which included both alcohol and HDL cholesterol. The true proportion of the effect attributable to HDL cholesterol is likely to be greater, especially if one were able to consider error in the measurement of alcohol and lipids.

## CONCLUSION

When all of the available evidence from observational studies on alcohol, lipids, and coronary heart disease is considered, results from ecologic studies which support the hypothesis that wine is most beneficial in lowering heart disease rates need to be weighed against the overwhelming evidence from observational studies which suggests that the ethanol itself is the key beneficial component. Differences in findings across observational studies regarding specific beverage types may be due to differences in beverage-specific patterns of drinking or to other unaccountable correlates of beverage choice. Results from observational studies, where individual consumption can be assessed in detail and linked directly to coronary disease, provide strong evidence that a substantial proportion of the benefit of wine, beer, or spirits is attributable primarily to the ethanol content rather than to other components of each beverage.

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