Alcohol Consumption and Risk for Coronary Heart Disease in Men With Healthy Lifestyles

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Background: Although moderate alcohol intake is associated with lower risk for myocardial infarction (MI), guidelines generally suggest that adults seek other lifestyle measures to reduce cardiovascular risk. We studied whether alcohol consumption is inversely associated with risk for coronary heart disease in men who report consistently favorable lifestyle behaviors.

Methods: From 51,529 male participants of the Health Professionals Follow-up Study who have reported diet and other lifestyle factors in biennial questionnaires since 1986, we defined a cohort of 8867 men free of major illness to participate in a prospective study. All participants reported 4 healthy lifestyle behaviors, including a body mass index (calculated as weight in kilograms divided by height in meters squared) of less than 25, moderate to vigorous activity for 30 minutes or more per day, abstention from smoking, and a summary diet score in the top 50% for men. High dietary scores reflected a high intake of vegetables, fruits, cereal fiber, fish, chicken, nuts, soy, and polyunsaturated fat; low consumption of trans-fat, and red and processed meats; and multivitamin use. We ascertained the incidence of nonfatal MI and fatal coronary heart disease according to reported intake of beer, wine, and liquor every 4 years.

Results: During 16 years of follow-up, we documented 106 incident cases of MI. Compared with abstention, the hazard ratios for MI were 0.98 (95% confidence interval, 0.55-1.74) for alcohol intake of 0.1 to 4.9 g/d, 0.59 (95% confidence interval, 0.33-1.07) for alcohol intake of 5.0 to 14.9 g/d, 0.38 (95% confidence interval, 0.16-0.89) for alcohol intake of 15.0 to 29.9 g/d, and 0.86 (95% confidence interval, 0.36-2.05) for alcohol intake of 30.0 g/d or more. In men who met 3 criteria, the lower risk associated with alcohol intake of 5.0 to 29.9 g/d tended to be similar to the lower risk associated with the remaining healthy lifestyle behavior.

Conclusion: Even in men already at low risk on the basis of body mass index, physical activity, smoking, and diet, moderate alcohol intake is associated with lower risk for MI.

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Moderate alcohol consumption is consistently associated with a lower risk for myocardial infarction (MI) than is abstention in prospective cohort studies. Much of this association is thought to be attributable to the higher levels of high-density lipoprotein cholesterol found in moderate drinkers, an effect confirmed in short-term randomized trials of alcohol administration. Studies of variation in MI risk linked to the alcohol dehydrogenase 1C gene, a form of mendelian randomization, also support the causal nature of this relationship. To our knowledge, alcohol consumption has not been tested in a long-term, large-scale, randomized trial with clinical end points. Alcohol consumption is not the only lifestyle factor that is supported by experimental evidence for cardiovascular risk factors and observational evidence for clinical end points, but which has only limited or conflicting evidence from large-scale clinical trials. For example, we know of no clinical trials to support weight loss or smoking cessation for primary prevention of MI, and diet has primarily been tested in patients with established coronary heart disease (CHD). Because of the risks associated with high alcohol intake, clinical guidelines generally do not recommend alcohol consumption; rather, they suggest that other lifestyle features be emphasized. For example, a recent review of alcohol and CHD stated, “We have other means of lowering cardiovascular risk that are safe and proven.” The American Heart Association has adopted a similar position. One difficulty with the approach that these guidelines adopt is that healthy behaviors are generally not considered mutually exclusive. Pursuit of exercise, for ex-
ample, does not obviate the need for a prudent diet. This issue is most clearly exemplified by the subset of adults who have healthy lifestyles. For individuals who exercise, abstain from smoking, maintain optimal weight, and adhere to an appropriate diet, there may be few other standard lifestyle interventions to lower risk. Whether alcohol intake is related to a lower risk for MI in such individuals is unknown. To determine the association of alcohol intake with risk for MI in adults with healthy lifestyles, we studied men enrolled in the Health Professionals Follow-up Study (HPFS), a prospective cohort study of male health professionals in the United States.

**STUDY METHODS**

The HPFS is a prospective investigation of 51,529 US male dentists, pharmacists, veterinarians, optometrists, osteopathic physicians, and podiatrists aged 40 to 75 years who returned a mailed questionnaire about diet and medical history in 1986. Participants subsequently have provided diet, lifestyle, and medical information on biennial questionnaires. In all analyses, we excluded men with cardiovascular disease; cancer, except for non-melanoma skin cancer; or diabetes at baseline and those with missing baseline information on diet and alcohol consumption. All analyses were approved by the Harvard School of Public Health Human Subjects Committee.

**ASSESSMENT OF ALCOHOL CONSUMPTION**

At baseline, men reported their alcohol consumption on a 131-item semiquantitative food frequency questionnaire (FFQ) that included separate items for beer, red wine, and liquor. Participants were asked how often, on average over the past year, they consumed each beverage. We calculated total alcohol intake by multiplying the average consumption of each beverage by the alcohol content of the specified portion size (12.8 g for beer, 11.0 g for wine, and 14.0 g for liquor) and summing across beverages. The FFQ was administered again every 4 years, with an item for light beer added in 1994. Participants also reported their overall drinking frequency in 1986, 1988, and 1998.

We assessed the validity of self-reported alcohol consumption by comparing estimated alcohol intake from the FFQ with the intake derived from two 7-day dietary records among 127 participants who returned questionnaires in 1986 and 1987 and resided in or near Boston, Mass. The Spearman rank correlation coefficient between alcohol intake estimated from the FFQ and corresponding intake from diet records was 0.86.

**HEALTHY LIFESTYLE BEHAVIORS**

We selected 4 domains of healthy lifestyle, as previously described, body mass index (calculated as weight in kilograms divided by height in meters squared), physical activity, smoking, and diet. For each domain, we identified a cutoff point to select men engaged in healthy lifestyle behaviors.

Men reported their height on the baseline questionnaire and their weight on each biennial questionnaire. Self-reported height was highly correlated with technician-assessed measures (Pearson r = 0.97) in a subset of this cohort. We defined optimal body mass index as less than 25, the World Health Organization definition of healthy weight.

Participants reported physical activity on biennial questionnaires as the average time engaged in specific activities during the previous year. We determined the total hours spent per week in moderate to vigorous activity (≥4 metabolic equivalents), including walking at a brisk pace (≥3 mph), jogging, running, bicycling, swimming, tennis, squash, racquetball, rowing, and calisthenics. Self-reported vigorous physical activity from the questionnaire was correlated with similar activity from the average of four 1-week activity logs (r = 0.38) within a validation subset of this cohort. We defined optimal physical activity as at least 30 minutes per day of moderate to vigorous activity based on current guidelines.

Men reported their current use of cigarettes on each biennial questionnaire in 7 categories. We considered current abstinence from smoking as optimal. Most former smokers had stopped smoking for at least 30 years, and the risk for CHD among former smokers reaches that of individuals who never smoked approximately 10 to 14 years after smoking cessation; thus, former smokers were grouped with lifetime nonsmokers.

We assessed dietary information with the FFQ using the Harvard University Food Composition Database to estimate average nutrient intake. The reproducibility and validity of the FFQ has been extensively assessed for nutrients and specific food items. We calculated a summary score for overall diet based on the Alternate Healthy Eating Index, a modification of the Healthy Eating Index proposed by the US Department of Agriculture. High values on the Alternate Healthy Eating Index-based diet score result from low intake of trans-fat; higher ratios of polyunsaturated to saturated fat and of white to dark meat (in grams); higher intake of fruits, vegetables, vegetable proteins (legumes, tofu, and soy products), and cereal fiber; and multivitamin use. The Alternate Healthy Eating Index also includes alcohol intake of 530 g/d, which we excluded for the purposes of analysis. Each component is given a score ranging from 0 to 10. Because we did not include alcohol intake, our total diet score represents the sum of scores from the 8 non-alcoholic components of the Alternate Healthy Eating Index, ranging from 2.5 (worst) to 77.5 (best). Given the generally high diet quality of these men, we defined an optimal diet as a diet score in the top 50% of the distribution of participants (score ≥ 39.95); alternate analyses using a diet score in the top 40%, a cutoff point used previously, yielded nearly identical point estimates with less precision.

**ASCERTAINMENT OF MI**

The outcome for this analysis was incident MI, defined as non-fatal MI or fatal CHD that occurred between the return of the baseline questionnaire in 1986 and January 31, 2002. We wrote to participants who reported an incident MI on the follow-up questionnaires to confirm the report and to request permission to review medical records. We also sought medical records for deceased participants, whose deaths were identified by families and postal officials and through the National Death Index. Physicians blinded to the participants’ questionnaire reports reviewed all medical records. Incident cases of MI and fatal CHD were identified primarily through review of medical records, as previously described. We included self-reported coronary revascularization as a secondary outcome; 98 of 102 such cases were confirmed in a previous validation study.

We have previously shown that alcohol consumption has similar relationships to the risk for nonfatal MI, fatal CHD, and coronary revascularization in the full HPFS cohort.

**STATISTICAL ANALYSIS**

Each individual contributed person-time from the return of the 1986 questionnaire to the date of a first coronary event, date of diagnosis of cancer or stroke, death, or January 31, 2002, which-
ever came first. We identified men who successfully met the criteria for optimal weight, diet, activity, and smoking and assessed the prospective relationship of alcohol intake with risk for MI. We used Cox proportional hazards models to calculate relative risk and 95% confidence intervals (95% CI), adjusted for age, parental history of MI before age 60 years, presence of hypertension or hypercholesterolemia at baseline (based on self-report of physician diagnoses), and aspirin use (ascertained biennially).

Our Cox analyses used alcohol intake updated every 4 years as a time-varying covariate, using an Anderson-Gill data structure.23 Thus, we used the 1986 questionnaire to determine the risk for MI during the period from 1986 to 1990, the 1990 questionnaire for the period from 1990 to 1994, and so on. In these analyses, men contributed person-time only during each 2-year period in which their questionnaires indicated that they met all 4 healthy lifestyle criteria. For individuals missing information about any low-risk behavior, we carried forward information from the previous questionnaire, when available. To represent long-term dietary information and minimize measurement error, we used the cumulative average of the diet score based on repeated dietary assessments.23 To minimize potential bias due to changes in alcohol use or diet that occurred on diagnosis of mediating conditions, we stopped updating this information after diagnosis of hypertension, diabetes, or angina during follow-up. We identified former drinkers with a time-varying covariate and examined their risk compared with that of long-term abstainers.

We also compared moderate alcohol intake with each of the other healthy lifestyle behaviors in men who had optimal levels of 3, rather than all 4, behaviors. In these analyses, we identified men who met each combination of 3 of the healthy lifestyle criteria and compared the relationship of risk for MI with alcohol use with the corresponding association with the potentially unmet criterion. For example, we compared the relative associations of alcohol intake and smoking in the subgroup of men who had optimal activity, diet, and weight, whether or not they were smokers. Results are shown from models in which alcohol intake and the final criteria were included simultaneously, but results from models that examined them separately were similar. To illustrate the joint effects of alcohol intake and healthy lifestyle, we also evaluated age-adjusted rates of MI according to alcohol intake in men meeting none or 1, or 2 or 3 criteria.

We calculated the population-attributable risk24 with its 95% CI to estimate the proportion of incidence cases that may have been prevented had all men in the population consumed at least 5.0 g/d of alcohol. We used the SAS statistical package (version 8.2; SAS Institute Inc, Cary, NC) for all analyses.

At some point during follow-up, 8867 men reported optimal levels of weight, physical activity, smoking, and diet. Table 1 lists the characteristics of these men at the first time they met all 4 criteria according to alcohol use. Within this healthy population, differences across categories of alcohol intake were generally modest.

During 16 years of follow-up, we documented 106 incident cases of MI (Table 2). Alcohol intake of 15.0 to 29.9 g/d (ie, 2 drinks per day) was associated with the lowest risk for MI, with higher intake associated with intermediate risk. Results were similar when we further adjusted our multivariable analyses for actual levels of body mass index, diet scores, and physical activity (as continuous variables), and smoking (as never smoker, former smoker, and unknown smoking history). Additional adjustment for cardiovascular medication use (lipid-lowering agents, β-blockers, calcium channel antagonists, thiazide diuretic agents, and other antihypertensive drugs) did not alter our results, with hazard ratios of 0.56 (95% CI, 0.31-1.03) associated with alcohol intake of 5.0 to 14.9 g/d and 0.40 (95% CI, 0.17-0.95) associated with intake of 15.0 to 29.9 g/d.

We explored this relationship further in several ways. The lower risk associated with moderate alcohol intake was also evident when we expanded our analyses to the

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### Table 1. Characteristics According to Alcohol Intake in 8867 Men With Healthy Levels of 4 Lifestyle Factors (Weight, Activity, Smoking, and Diet)

<table>
<thead>
<tr>
<th>Alcohol Intake, g/d</th>
<th>0</th>
<th>0.1-4.9</th>
<th>5.0-14.9</th>
<th>15.0-29.9</th>
<th>≥30.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 1889)</td>
<td>(n = 2252)</td>
<td>(n = 2730)</td>
<td>(n = 1282)</td>
<td>(n = 714)</td>
<td></td>
</tr>
<tr>
<td>Age, mean, y</td>
<td>57</td>
<td>56</td>
<td>56</td>
<td>56</td>
<td>58</td>
</tr>
<tr>
<td>Body mass index, mean*</td>
<td>22.9</td>
<td>23.1</td>
<td>23.1</td>
<td>23.2</td>
<td>23.2</td>
</tr>
<tr>
<td>Moderate to vigorous exercise ≥4 metabolic equivalents, h/wk</td>
<td>7.9</td>
<td>7.6</td>
<td>7.6</td>
<td>7.8</td>
<td>8.0</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>15</td>
<td>16</td>
<td>17</td>
<td>18</td>
<td>20</td>
</tr>
<tr>
<td>Parental history of myocardial infarction, %</td>
<td>11</td>
<td>13</td>
<td>13</td>
<td>12</td>
<td>15</td>
</tr>
<tr>
<td>Hypercholesterolemia, %</td>
<td>23</td>
<td>24</td>
<td>24</td>
<td>24</td>
<td>23</td>
</tr>
<tr>
<td>Aspirin use, %</td>
<td>27</td>
<td>29</td>
<td>31</td>
<td>37</td>
<td>40</td>
</tr>
<tr>
<td>Mean daily intake</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol, g/d</td>
<td>0</td>
<td>2.3</td>
<td>9.8</td>
<td>20.4</td>
<td>44.4</td>
</tr>
<tr>
<td>Total energy, kcal/d</td>
<td>2024</td>
<td>2019</td>
<td>2067</td>
<td>2206</td>
<td>2362</td>
</tr>
<tr>
<td>Folate, µg/d</td>
<td>589</td>
<td>589</td>
<td>588</td>
<td>567</td>
<td>553</td>
</tr>
<tr>
<td>Trans-fat, g/d</td>
<td>2.4</td>
<td>2.4</td>
<td>2.3</td>
<td>2.3</td>
<td>2.1</td>
</tr>
<tr>
<td>Saturated fats, g/d</td>
<td>20.2</td>
<td>20.7</td>
<td>20.6</td>
<td>20.7</td>
<td>18.7</td>
</tr>
<tr>
<td>Polyunsaturated fats, g/d</td>
<td>13.6</td>
<td>13.3</td>
<td>13.4</td>
<td>13.5</td>
<td>12.7</td>
</tr>
<tr>
<td>Cereal fiber, g/d</td>
<td>8.4</td>
<td>7.9</td>
<td>7.6</td>
<td>6.8</td>
<td>6.1</td>
</tr>
<tr>
<td>Vitamin E, mg/d</td>
<td>66.2</td>
<td>67.7</td>
<td>65.5</td>
<td>65.6</td>
<td>61.3</td>
</tr>
<tr>
<td>Diet score, mean</td>
<td>50.0</td>
<td>49.5</td>
<td>49.5</td>
<td>49.1</td>
<td>48.3</td>
</tr>
</tbody>
</table>

*Calculated as weight in kilograms divided by height in meters squared.

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### RESULTS

At some point during follow-up, 8867 men reported optimal levels of weight, physical activity, smoking, and diet. Table 1 lists the characteristics of these men at the first time they met all 4 criteria according to alcohol use. Within this healthy population, differences across categories of alcohol intake were generally modest.

During 16 years of follow-up, we documented 106 incident cases of MI (Table 2). Alcohol intake of 15.0 to 29.9 g/d (ie, 2 drinks per day) was associated with the lowest risk for MI, with higher intake associated with intermediate risk. Results were similar when we further adjusted our multivariable analyses for actual levels of body mass index, diet scores, and physical activity (as continuous variables), and smoking (as never smoker, former smoker, and unknown smoking history). Additional adjustment for cardiovascular medication use (lipid-lowering agents, β-blockers, calcium channel antagonists, thiazide diuretic agents, and other antihypertensive drugs) did not alter our results, with hazard ratios of 0.56 (95% CI, 0.31-1.03) associated with alcohol intake of 5.0 to 14.9 g/d and 0.40 (95% CI, 0.17-0.95) associated with intake of 15.0 to 29.9 g/d.

We explored this relationship further in several ways. The lower risk associated with moderate alcohol intake was also evident when we expanded our analyses to the
312 incidences of MI or revascularization, with a hazard ratio of 0.67 (95% CI, 0.47-0.96) associated with intake of 5.0 to 14.9 g/d and 0.69 (95% CI, 0.44-1.07) associated with intake of 15.0 to 29.9 g/d. Likewise, risks were comparable when we relaxed the criterion for optimal exercise to $\frac{1}{2}$ hours per week, with hazard ratios of 0.63 (95% CI, 0.38-1.05) associated with intake of 5.0 to 14.9 g/d and 0.51 (95% CI, 0.27-0.99) associated with intake of 15.0 to 29.9 g/d. We found no statistical evidence of higher risk in former drinkers, with a relative risk of 1.16 (95% CI, 0.55-2.43).

When we compared alcohol intake of 5.0 g/d or more vs less than 5.0 g/d, the hazard ratio was 0.58 (95% CI, 0.37-0.89). Given that 55% of person-time was contributed by consumers of 5 g/d or more of alcohol, we estimate that 25% of the incidence cases of MI in this population were attributable to consuming less than 5 g/d (95% CI, 11%-47%).

Our results were also qualitatively similar when we incorporated drinking frequency rather than average alcohol intake, even though this variable was not updated with each FFQ. For example, compared with abstention, the hazard ratios in men who drank at least 3 days per week were 0.58 (95% CI, 0.33-1.01) for risk for MI and 0.52 (95% CI, 0.31-0.87) for the combined end point of MI or revascularization.

We next compared the relationship between moderate alcohol intake and risk for MI with the corresponding relationships between healthy lifestyle behaviors and risk for MI (Table 3). In these analyses, we identified the subgroups of men with each combination of 3 healthy lifestyle behaviors and compared the associations of alcohol intake and the remaining lifestyle factor with MI risk. Abstinence from smoking was associated with the greatest magnitude of lower risk (hazard ratio, 0.26; 95% CI, 0.10-0.72). However, among nonsmoking men with 2 other healthy lifestyle factors, moderate alcohol intake tended to be associated with at least as great a risk reduction as was the final lifestyle factor, whether it was diet, activity, or weight.

Finally, we separately evaluated the association of alcohol intake with risk for MI in men meeting none or 1, 2 or 3, or all 4 criteria (Figure). As expected, men meeting more criteria had lower rates of MI, but the difference was not statistically significant.
ence between abstainers and moderate drinkers tended to be similar in all 3 groups.

**COMMENT**

In this prospective analysis of men with favorable levels of 4 healthy lifestyle factors, moderate alcohol consumption was associated with a lower risk for MI, with the lowest risk in men who drank 5 to 30 g/d (approximately one half to 2 drinks). The magnitude of this association was similar to the association previously found for the entire HPFS cohort.

An important concern related to previous studies of alcohol intake and risk for MI is the possibility that an unmeasured or poorly measured confounding factor, such as exercise or diet, could lead to a false association. In this study, we focused on a tightly restricted group of participants, that is, nonsmoking male health professionals with healthy diets, regular vigorous physical activity, and normal body weight. It is striking that in this group of men, in whom residual confounding has been minimized to the greatest degree, the inverse association between alcohol consumption and risk for MI was as strong as in more heterogeneous populations. While observational results such as these cannot prove causality, it seems unlikely, but not impossible, that an unknown confounding factor is sufficiently strongly associated with both alcohol use and risk for MI to have produced these findings.

Moderate alcohol consumption has been associated with lower risk for MI or death in population-based studies, in populations at higher risk, and in patients with known CHD. Despite this diversity in epidemiologic evidence, to our knowledge, no cohort studies have assessed alcohol intake and risk for MI in a population with lifestyle features as narrowly constrained as in this study. Because the rates for MI differ substantially in the populations studied, the absolute benefit attributable to moderate drinking also differs and is likely low in populations of adults with lifestyles as ideal as those of the men studied here. Moreover, even moderate drinking has potential health risks, such as breast cancer in women and acceleration of cirrhosis in patients with hepatitis C. As a result, physicians and patients must weigh both the absolute health risks and benefits of alcohol when discussing alcohol intake.

There is a complicated mix of risks and benefits attributed to moderate drinking in observational studies, and the individual and societal complications of heavy drinking are well known. It is easy to understand why clinical guidelines encourage physicians and patients to concentrate on seemingly more innocuous interventions, despite the relative paucity of effective, straightforward, and generalizable methods for encouraging regular physical activity, weight reduction, and abstinence from smoking in clinical practice. Our results suggest that moderate drinking could be viewed as a complement, rather than an alternative, to these other lifestyle interventions, a viewpoint espoused by some authors.

Limitations of our study warrant comment. One hundred six participants in this study had an MI during follow-up, yielding us sufficient power to demonstrate a statistically significant association with moderate alcohol intake even in this restricted cohort, but with correspondingly wide CIs. Moreover, the range of overall alcohol consumption reported by these men was truncated, limiting our ability to define the potentially detrimental effects of heavy drinking. We also could not assess the effects of specific drinking patterns, changes in alcohol intake over time, the modifying effect of drinking with meals, or differences among individual beverage types; we have previously reported on these factors in the full HPFS cohort.

Although we relied on self-reported alcohol consumption, we validated the measures of quantity and frequency of alcohol consumption used in this study, and any misclassification in our instruments is unlikely to affect the rank order of alcohol consumption. Nevertheless, the actual amount and frequency of alcohol consumed by these men may differ from that reported here.

In summary, in this population of male health professionals with otherwise healthy lifestyle behaviors, the risk for MI was lowest in men whose alcohol intake was 5 to 30 g/d (approximately one half to 2 drinks). Given our findings, future guidelines for moderate drinking need not consider healthy lifestyle behaviors as mutually exclusive and should instead focus on the strengths and limitations of the evidence about moderate alcohol intake.

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**Author Contributions:** Dr Chiuve had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Mukamal and Chiuve. Acquisition of data: Chiuve and Rimm. Analysis and interpretation of data: Mukamal, Chiuve, and Rimm. Drafting of the manuscript: Mukamal. Critical review of the manuscript for important intellectual content: Chiuve and Rimm. Statistical analysis: Chiuve. Obtained funding: Mukamal and Rimm. Administrative, technical, and material support: Chiuve and Rimm. Study supervision: Mukamal and Rimm.


