Alcohol Consumption and the Risk of Type 2 Diabetes Mellitus

Atherosclerosis Risk in Communities Study

W. H. Linda Kao,1 Ian B. Puddey,2 Lori L. Boland,3 Robert L. Watson,4 and Frederick L. Brancati1,5

Evidence regarding the association between alcohol consumption and type 2 diabetes risk remains inconsistent, particularly with regard to male-female differences. The authors conducted a prospective study of type 2 diabetes risk associated with alcohol consumption in a cohort of 12,261 middle-aged participants of the Atherosclerosis Risk in Communities Study (1990–1998), who were followed between 3 and 6 years. Alcohol consumption at baseline was characterized into lifetime abstainers, former drinkers, and current drinkers of various levels. Incident diabetes was determined by blood glucose measurements and self-report. After adjustment for potential confounders, an increased risk of diabetes was found in men who drank >21 drinks/week when compared with men who drank ≤1 drink/week (odds ratio = 1.50, 95% confidence interval: 1.02, 2.20) while no significant association was found in women. This increased diabetes risk among men who drank >21 drinks/week was predominantly related to spirits rather than to beer or wine consumption. The relative odds of incident diabetes in a comparison of men who drank >14 drinks of spirits per week with men who were current drinkers but reported no regular use of spirits, beer, or wine were 1.82 (95% confidence interval: 1.14, 2.92). Results of this study support the hypothesis that high alcohol intake increases diabetes risk among middle-aged men. However, more moderate levels of alcohol consumption do not increase risk of type 2 diabetes in either middle-aged men or women.


Type 2 diabetes mellitus affects over 15 million Americans and leads to excess risk of cardiovascular diseases and other morbidities (1–3). Aside from obesity and physical inactivity, there are few other well-established modifiable risk factors for type 2 diabetes. Alcohol consumption represents a potentially important, modifiable risk factor of type 2 diabetes, especially given that more than half of the adults in the United States are current drinkers (4).

The hypothesized diabetogenic effects of alcohol include its contribution to excess caloric intake and obesity, induction of pancreatitis, disturbance of carbohydrate and glucose metabolism, and impairment of liver function (5–7). However, the association between alcohol and diabetes or other diabetes-related physiologic endpoints has been inconsistent in previous small clinical studies (8–16), animal studies (17, 18), and larger cross-sectional epidemiologic studies (5, 19–24).

Prospective epidemiologic studies have yielded similarly equivocal results; furthermore, results of these studies suggest a potential difference in the association of alcohol and incident type 2 diabetes between women and men (25–32). The Atherosclerosis Risk in Communities (ARIC) Study offers a unique opportunity to examine the association between alcohol consumption and the risk of type 2 diabetes mellitus in a large community-based cohort of middle-aged women and men.

MATERIALS AND METHODS

Study population

The ARIC Study is an ongoing prospective study that examines clinical and subclinical atherosclerotic diseases in a cohort of 15,792 persons, aged 45–64 years at baseline examination, selected by probability sampling from four US communities. The sampling procedure and methods used in the ARIC Study have been described in detail elsewhere (33). This analysis was based on information obtained over 6 years of follow-up, which included two clinic visits sched-
uled at 3 (visit 2) and 6 (visit 3) years after baseline. We excluded participants who reported ethnicity other than Black or White (n = 48), had diabetes at visit 1 (n = 1,867), had missing exposure information (n = 89), had missing diabetes information at visit 1 or were lost to follow-up before visit 2 of the study took place (n = 1,022), and had missing information on the potential confounders (n = 315), as well as persons in whom total caloric intake was within the top 1 percent or bottom 1 percent of the entire cohort due to probable reporting error (n = 190). After these exclusions, 12,261 participants (6,838 women and 5,423 men) remained.

Exposure assessment

Alcohol consumption was assessed using five questions. The following two questions were used to determine the current drinking status of the persons: “Do you presently drink alcoholic beverages?” and “Have you ever consumed alcoholic beverages?” Persons were classified as lifetime abstainers if they answered “no” to both questions. Persons who answered “no” to the first question and “yes” to the second question were classified as former drinkers. Persons who answered “yes” to both questions were considered current drinkers. Among current drinkers, the following three questions were used to determine the amount and type of alcoholic beverage consumed: “How many glasses of wine do you usually have per week (4-ounce glasses)?”; “How many bottles or cans of beer do you usually have per week (12-ounce bottles or cans)?”; and “How many drinks of hard liquor do you usually have per week (1.5-ounce shots)?” (One ounce = 29.57 ml.) For the primary analyses, ethanol, rather than a specific beverage, was the main independent variable. Weekly ethanol consumption was derived from the responses to the three beverage questions using the following conversion factors: 4 ounces of wine = 10.8 g of ethanol, 12 ounces of beer = 13.2 g of ethanol, and 1.5 ounces of spirits = 15.1 g of ethanol. To reclassify current drinkers by the number of drinks (nonspecific to type of alcohol) consumed per week, we assumed one generic drink to be equal to 12 g of ethanol. Seven consumption groups were created: lifetime abstainers, former drinkers, current drinkers who consume <1 drink/week (reference group), current drinkers who consume 1–7 drinks/week, current drinkers who consume 7.1–14 drinks/week, current drinkers who consume 14.1–21 drinks/week, and current drinkers who consume more than 21 drinks/week.

For alcohol-specific analyses, derivation of weekly ethanol consumption from the three beverages was not used (method described in the previous paragraph). Instead, the original number of glasses, bottles, and drinks was used to categorize wine, beer, and spirit consumption, respectively. For each beverage type, persons who identified themselves as current drinkers but reported an average weekly consumption of zero servings of that beverage were used as the reference group.

Information on age, gender, race, family history of diabetes, and education was obtained from home and clinic interviews conducted at the baseline visit. A positive family history of diabetes was defined as having either biologic parent with diabetes. Body mass index (weight (kg)/height (m)²) and waist/hip ratio were determined by the anthropometric measurements taken at the baseline clinic visit. Measurements were made with the participants wearing light-weight, nonconstricting underwear and no shoes. Waist and hip measurements were taken at the level of the umbilicus and the level of maximal protrusion of the gluteal muscles, respectively. Intrareader and interreader correlations between repeated waist/hip ratio measures were 0.94 and 0.91, respectively (34). Physical activity was assessed using a modified interviewer-administered version of the questionnaire developed by Baecke et al. (35). Results from the questionnaire concerning physical activity were further condensed to a sport-related physical activity index with scores ranging from 1 to 5, with 1 indicating the lowest level of activity and 5 the highest level. Total caloric intake was derived from an interviewer-administered, modified version of the 61-item food frequency questionnaire developed by Willett et al. (36). Smoking status was categorized into never, former, and current smokers. Hypertension was defined by the presence of any of the following: 1) systolic blood pressure of ≥140 mmHg, 2) diastolic blood pressure of ≥90 mmHg, or 3) current use of antihypertensive medication.

Outcome assessment

Diabetes mellitus was defined as the presence of any one of the following: 1) fasting glucose of ≥7.0 mmol, 2) non-fasting glucose of ≥11.1 mmol, 3) current use of diabetic medication, or 4) a positive response to the question, “Has a doctor ever told you that you had diabetes (sugar in the blood)?” Persons with diabetes or who had unknown diabetes status at baseline were excluded from the prospective analyses. Persons without diabetes at baseline who met any of the these conditions at visit 2 or visit 3 were considered incident cases of diabetes (n = 239). Persons who met the criteria for diabetes at visit 2 but not at visit 3 were nonetheless considered to have incident type 2 diabetes.

Statistical analysis

All analyses were stratified by gender. The means and frequencies of potential confounders assessed at baseline were calculated for each group of alcohol consumption, and analysis of variance and chi-square analysis were used to assess the statistical significance of the differences across consumption groups. For continuous variables, p values for test for trend among current drinkers were also reported. Incidence rates were calculated for each consumption group with the use of a person-years approach, and a Poisson regression model was fitted to determine if the incidence rates for the seven consumption groups differed significantly. Because the outcome was assessed only at 3-year intervals, the time of follow-up for incident cases was assigned to the midpoints between visits, that is, 1.5 and 4.5 years. For example, persons who were nondiabetic at baseline but became diabetic at visit 3 were considered to have followed for 4.5 years. Nondiabetic persons at both

Am J Epidemiol  Vol. 154, No. 8, 2001
visit 1 and visit 2 who were lost to follow-up after visit 2 were censored at 3 years after the baseline visit.

The independent association between baseline alcohol consumption and subsequent incident diabetes was examined using logistic regression models. Alcohol consumption was treated both nominally and continuously (for trend among current drinkers). Multiple linear regression analysis was also performed to examine the association between baseline alcohol consumption and fasting glucose levels at visit 2 or visit 3 among persons who did not have diagnosed diabetes by the time of the visit. All statistical analyses were performed using a SAS statistical package (Cary, North Carolina) (37).

RESULTS
Baseline characteristics

As shown in table 1, among the 6,838 female ARIC Study participants, almost one third reported that they were lifetime abstainers, and roughly half identified themselves as current drinkers, of whom roughly half reported an average weekly consumption of ≤1 drink/week. Both lifetime abstainers and former drinkers tended to be older, less physically active, and more obese; they were more similar to each other than to current drinkers. There was also a greater proportion of Blacks, positive family history of diabetes, and hypertension among lifetime abstainers and former drinkers. Among current drinkers, total caloric intake and prevalence of hypertension were positively associated with alcohol consumption, while educational level, family history of diabetes, and body mass index were inversely associated with alcohol consumption. Persons who drank more than 21 drinks per week had a noticeably higher waist/hip ratio and total caloric intake and less physical activity. As expected, smoking and alcohol consumption were highly associated. Although the fasting serum glucose level was slightly positively associated with alcohol consumption among current drinkers, the fasting serum insulin level was inversely associated with alcohol consumption in this group.

Only about 10 percent of the 5,423 male ARIC Study participants were lifetime abstainers, and approximately 70 percent were current drinkers (table 2). Among current drinkers, men were drinking more drinks per week than were women, with the amount consumed by men slightly higher for each consumption group. The most striking male-female difference was among the heavier drinkers: 8 percent of men drank >21 drinks/week with a mean intake of 402 g of alcohol per week, whereas less than 1 percent of women drank >21 drinks/week with a mean intake of 347 g/week. Despite the disparity in ethanol intake, the associations between alcohol consumption and most potential confounders were similar in men and women. Men who drank >21 drinks/week had the highest waist/hip ratio and energy intake and the lowest physical activity score. The proportions of current smokers and persons with hypertension were also highest in this group of men.

**Table 1. Means (SDs) and frequencies of selected baseline characteristics of 6,838 female ARIC Study participants by alcohol consumption group, 1990–1998**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Current drinkers (drinks/week)</th>
<th>Former drinkers</th>
<th>Never drinkers</th>
<th>Abstainers</th>
<th>( p ) overall</th>
<th>( p ) trend for overall group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethanol consumed (g/week)</td>
<td>1,346 (14.2)</td>
<td>1,223 (13.7)</td>
<td>765 (10.9)</td>
<td>402 (12.5)</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Age (years)</td>
<td>54.5 (5.8)</td>
<td>53.9 (5.5)</td>
<td>53.2 (5.5)</td>
<td>53.2 (5.6)</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Black (%)</td>
<td>31.3 (5.8)</td>
<td>35.5 (5.7)</td>
<td>39.5 (5.7)</td>
<td>44.8 (5.7)</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Education (%)</td>
<td>51.5 (6.1)</td>
<td>50.0 (6.3)</td>
<td>53.3 (6.3)</td>
<td>53.3 (6.3)</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Family history of diabetes (%)</td>
<td>24.7 (5.7)</td>
<td>25.9 (5.7)</td>
<td>25.9 (5.7)</td>
<td>25.9 (5.7)</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>59.5 (5.7)</td>
<td>60.3 (5.7)</td>
<td>59.5 (5.7)</td>
<td>59.5 (5.7)</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Serum glucose‡ (mmol)</td>
<td>36.2 (4.7)</td>
<td>31.3 (4.7)</td>
<td>31.3 (4.7)</td>
<td>31.3 (4.7)</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Serum insulin‡ (pmol)</td>
<td>5.40 (0.51)</td>
<td>6.40 (0.51)</td>
<td>5.40 (0.51)</td>
<td>5.40 (0.51)</td>
<td>0.001</td>
<td>0.001</td>
</tr>
</tbody>
</table>

* SD, standard deviation; ARIC, Atherosclerosis Risk in Communities; BMI, body mass index (kg/height² m²).

† Limited to trend among current drinkers.
TABLE 2. Means (SDs*) and frequencies of selected baseline characteristics of 5,423 male ARIC Study participants by alcohol consumption group, 1990–1998

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Lifetime abstainers</th>
<th>Former drinkers</th>
<th>Current drinkers by alcohol consumption group (drinks/week)</th>
<th>p overall</th>
<th>p trend†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td></td>
<td>≤1</td>
<td>1.1–7</td>
<td>7.1–14</td>
</tr>
<tr>
<td>No. (%)</td>
<td>669 (12.3)</td>
<td>1,096 (20.2)</td>
<td>815 (15.0)</td>
<td>1,366 (25.2)</td>
<td>725 (13.4)</td>
</tr>
<tr>
<td>Alcohol consumed (g/week)</td>
<td></td>
<td></td>
<td>1</td>
<td>1</td>
<td>7.1–14</td>
</tr>
<tr>
<td>Age (years)</td>
<td>55.1 (5.5)</td>
<td>54.8 (5.6)</td>
<td>54.2 (5.8)</td>
<td>53.9 (5.8)</td>
<td>54.3 (5.7)</td>
</tr>
<tr>
<td>Black (%)</td>
<td>32.4</td>
<td>23.9</td>
<td>7.7</td>
<td>15.8</td>
<td>15.6</td>
</tr>
<tr>
<td>Education (%)</td>
<td></td>
<td></td>
<td>11 years or less</td>
<td>23.9</td>
<td>15.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High school graduate</td>
<td>54.0 (5.7)</td>
<td>19.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Attended college</td>
<td>54.4 (5.6)</td>
<td>15.0</td>
</tr>
<tr>
<td>Family history of diabetes (%)</td>
<td></td>
<td></td>
<td>0.96 (0.052)</td>
<td>0.96 (0.050)</td>
<td>0.95 (0.052)</td>
</tr>
<tr>
<td>BMI* (kg/m²)</td>
<td>27.26 (4.10)</td>
<td>27.38 (4.37)</td>
<td>27.29 (3.84)</td>
<td>27.24 (3.67)</td>
<td>27.00 (3.69)</td>
</tr>
<tr>
<td>Waist ratio</td>
<td>1.706 (580)</td>
<td>1.749 (661)</td>
<td>1.719 (583)</td>
<td>1.723 (589)</td>
<td>1.795 (585)</td>
</tr>
<tr>
<td>Physical activity score</td>
<td>2.47 (0.78)</td>
<td>2.52 (0.81)</td>
<td>2.67 (0.82)</td>
<td>2.58 (0.83)</td>
<td>2.46 (0.85)</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td></td>
<td></td>
<td>12.7</td>
<td>28.7</td>
<td>20.0</td>
</tr>
<tr>
<td>Former</td>
<td></td>
<td></td>
<td>27.6</td>
<td>50.8</td>
<td>43.4</td>
</tr>
<tr>
<td>Never</td>
<td></td>
<td></td>
<td>59.6</td>
<td>20.5</td>
<td>36.6</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td></td>
<td></td>
<td>34.8</td>
<td>30.5</td>
<td>27.2</td>
</tr>
<tr>
<td>Serum glucose‡ (mmol)</td>
<td></td>
<td></td>
<td>5.52 (0.49)</td>
<td>5.57 (0.51)</td>
<td>5.55 (0.48)</td>
</tr>
<tr>
<td>Serum insulin‡ (pmol)</td>
<td>85.63 (82.52)</td>
<td>84.19 (58.82)</td>
<td>82.43 (56.88)</td>
<td>77.73 (55.58)</td>
<td>72.79 (47.58)</td>
</tr>
</tbody>
</table>

* SD, standard deviation; ARIC, Atherosclerosis Risk in Communities; BMI, body mass index (weight (kg)/height (m)²).
† Limited to trend among current drinkers.
‡ Based on 5,281 fasting participants.

To test the robustness of our results, three subsidiary analyses were conducted. The first set of analyses included adjustment for fasting serum insulin and glucose levels at baseline because both variables were associated with the fasting serum insulin level at baseline (table 4). Adjustment for fasting serum insulin and glucose levels at baseline slightly strengthened the association between alcohol consumption and diabetes risk. In both men and women, the risk of diabetes among lifetime abstainers and former drinkers was similar to that of current male drinkers. Among current drinkers, the incidence rates were found in lifetime abstainers and former drinkers (19.16 and 20.69 per 1,000 person-years, respectively). Among current drinkers, the incidence rates were found in lifetime abstainers and former drinkers (19.16 and 20.69 per 1,000 person-years, respectively). Among current drinkers, the incidence rates were found in lifetime abstainers and former drinkers (19.16 and 20.69 per 1,000 person-years, respectively).
group at baseline). In contrast, adjustment for the fasting serum glucose level at baseline weakened the association between alcohol consumption and the risk of diabetes in men but strengthened the association in women. Because the baseline fasting insulin level is hypothesized to be in the causal pathway and the baseline glucose level is part of the outcome, models 2 and 3 of table 4 likely represent overadjusted models.

The second set of analyses examined the association between alcohol consumption at baseline and incident diabetes at visit 2 or at visit 3 separately. This set of analyses was performed to determine if the association between alcohol consumption and diabetes risk was dependent on follow-up time. The increased risk of diabetes for men who consumed >21 drinks/week at baseline was present at both visits 2 and 3; however, neither association was statistically significant at the 0.05 level.

The last set of analyses was conducted using continuous serum glucose at either visit 2 or visit 3 as the outcome among current drinkers who did not have diagnosed diabetes, who were not taking antidiabetic medication at the time of the visit, and who were nondiabetic at the previous visit. The fully adjusted mean fasting glucose levels at either visit 2 or visit 3 were similar among the five consumption groups in women; however, the adjusted mean fasting glucose levels were different among the five consumption groups in men. At visit 2, the mean glucose levels (mg/dl) for the five consumption groups in men were 104.8 (≤1 drinks/week), 104.3 (1.1–7 drinks/week), 104.3 (1.1–14 drinks/week), 105.8 (14.1–21 drinks/week), and 106.5 (>21 drinks/week) (p = 0.02 for

### TABLE 4. Adjusted relative odds (95% confidence intervals) of incident type 2 diabetes mellitus in a comparison of alcohol consumption groups in 12,261 ARIC* Study participants by sex, 1990–1998

<table>
<thead>
<tr>
<th>Alcohol consumption (drinks/week)</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Model 1†</td>
<td>Model 2‡</td>
</tr>
<tr>
<td>≥1</td>
<td>1.00 (reference)</td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>1.1–7</td>
<td>1.19 (0.89, 1.59)</td>
<td>1.20 (0.87, 1.65)</td>
</tr>
<tr>
<td>7.1–14</td>
<td>0.88 (0.67, 1.17)</td>
<td>0.90 (0.67, 1.23)</td>
</tr>
<tr>
<td>&gt;21</td>
<td>0.52 (0.36, 0.75)</td>
<td>0.53 (0.37, 0.77)</td>
</tr>
</tbody>
</table>

* ARIC, Atherosclerosis Risk in Communities.
† Model 1 adjusted for age (<49 vs. 49.1–53.9 vs. 54–58.9 vs. ≥59), race (binary), education (11 years or less vs. high school graduate vs. attended college), family history of diabetes (binary), body mass index (quartiles), waist/hip ratio (quartiles), physical activity score (continuous), total energy intake (quartiles), smoking history (never vs. former vs. current), and history of hypertension (binary) using logistic regression.
‡ Model 2 = model 1 + fasting serum insulin level (quartiles) at baseline.
§ Model 3 = model 2 + fasting serum glucose level (quartiles) at baseline.
| p for overall‡ | 0.53 | 0.82 | 0.10 | 0.13 | 0.13 | 0.56 |
| p for trend§ | 0.11 | 0.35 | 0.02 | 0.16 | 0.04 | 0.65 |
overall difference). The corresponding numbers from visit 3 were 100.0, 101.2, 101.2, 101.2, and 102.8 (p = 0.06 for overall difference). At both visits 2 and 3, men who drank >21 drinks/week at baseline had the highest fasting serum glucose level at subsequent visits.

**Consumption of specific alcoholic beverages and the risk of type 2 diabetes**

To assess whether the discrepancy between women and men might have been explained by differences in alcoholic beverage preference, we characterized the beverage preference of current drinkers. Figure 1 shows the mean percentage of ethanol contributed by specific alcoholic beverages for each consumption group (total alcohol intake) in women and men. In the reference groups (≤1 drink/week), although all persons identified themselves as current drinkers, only 11 percent of the women and 8 percent of the men reported regular weekly alcohol consumption (the remaining persons in the reference group identified themselves as current alcohol drinkers but reported no regular weekly alcohol consumption), and in those persons who reported regular use of alcohol, wine accounted for 100 percent of ethanol consumed. In general, the contribution to total alcohol intake from wine was roughly two times higher in women than in men, the contribution from beer was about two times higher in men than in women, and the contribution from spirits was similar between women and men.

Next, we examined the association between incident type 2 diabetes and each of the three alcoholic beverages, spirits, beer, and wine, separately. Since the amount of alcohol consumed by female ARIC Study participants was relatively small, analysis by alcohol type was limited to the male participants. In each beverage analysis, the reference group was composed of male participants who identified themselves as current drinkers but reported no regular weekly consumption of wine, beer, or spirits. Table 5 shows the adjusted relative odds of diabetes from multiple logistic regression, which adjusted for intakes of other types of alcoholic beverages; that is, nine dummy variables were included in the regression to adjust for intake of other alcoholic beverages, in addition to the potential confounders mentioned previously. In the fully adjusted model, persons who drank >14 drinks of spirits per week were still at higher risk for developing diabetes (odds ratio = 1.82, 95 percent confidence interval: 1.14, 2.92). There was no statistically significant association between wine intake and the risk of diabetes at the conventional 0.05 level.

One possible explanation for the excess risk associated with spirits might be differences in underlying health behaviors as compared with wine drinkers, particularly with regard to diet. To investigate this possibility, we examined the correlation between the percentage of ethanol contributed by each alcoholic beverage and measures that were thought to indicate healthy behavior. In general, the increased percentage of ethanol from wine was associated with healthier behaviors, such as increased physical activity and total intake of dietary fiber and decreased total fat intake. Although these associations were statistically significant, the magnitude of the correlations was small (|r| < 0.2). Additional adjustment for dietary intakes of carbohydrate, total fat, and protein did not alter the association between a high intake of spirits (>14 drinks/week) and the risk of diabetes in men (results not shown).

**DISCUSSION**

These data support the following conclusions. First, after adjustment for potential confounders, middle-aged women...
and men who consumed a moderate amount of alcohol (1–14 drinks/week) were not at higher risk of developing type 2 diabetes compared with their counterparts who drank little alcohol (≤1 drink/week). Second, after adjustment for potential confounders and established diabetes risk factors, middle-aged men who consumed a substantial amount of alcohol (>21 drinks/week) were about 50 percent more likely to develop type 2 diabetes compared with their counterparts who drank ≤1 drink/week. Third, this increased risk of diabetes among men who drank >21 drinks/week was predominantly related to spirits consumption. The risk of diabetes among middle-aged men who drank >14 drinks of spirits per week was about 80 percent higher than the risk of men who were current drinkers but did not drink any spirits.

There are two major limitations to this study. First, our analyses of heavy consumption and alcohol beverage types were limited to men only. This study did not have sufficient power to estimate the relative odds of diabetes at higher levels of alcohol intake in women, specifically consumption of ≥14 drinks/week. Second, like most previous studies in this field, our assessment of alcohol was likely suboptimal for several reasons. The assessment was done at a single time point and did not evaluate drinking pattern. Participants, especially those in the heavier drinking groups, may have underreported their consumption level because the questions regarding alcohol use were administered by an interviewer.

Nevertheless, this study had several strengths. First, this is the only community-based, prospective study of the association between alcohol and the risk of type 2 diabetes with the baseline fasting serum glucose level and incident diabetes during follow-up was observed.

The divergent results from epidemiologic studies of alcohol consumption and the risk of diabetes are reflected in nonepidemiologic studies, which have also reported both diabetogenic and nondiabetogenic effects of ethanol on physiologic endpoints associated with diabetes. In vitro studies indicate that exposure of beta cells to alcohol is associated with decreased insulin secretion (40, 41). On the other hand, hepatic oxidation of ethanol results in an increased ratio of reduced nicotinamide adenine dinucleotide to nicotinamide adenine dinucleotide, which can lead to impairment in gluconeogenesis (42). In physiologic studies, acute ethanol ingestion has been shown to improve glucose tolerance in normal subjects and insulin sensitivity in diabetic subjects (11, 16); however, acute ethanol administration has been shown to cause a reduction in the glucose disposal rate, cause acute insulin resistance in nondiabetic

### Table 5. Adjusted relative odds (95% confidence intervals) of incident type 2 diabetes mellitus in 5,423 male ARIC† Study participants by alcoholic beverage type and alcohol consumption groups, 1990–1998

<table>
<thead>
<tr>
<th>Servings of alcohol per week†</th>
<th>Spirits (none vs. 1–7 servings/week, 8–14 servings/week, &gt;14 servings/week)</th>
<th>Beer (none vs. 1–7 servings/week, 8–14 servings/week, &gt;14 servings/week)</th>
<th>Wine (none vs. 1–7 servings/week, 8–14 servings/week, &gt;14 servings/week)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;14 servings/week</td>
<td>1.82 (1.14, 2.92)</td>
<td>1.19 (0.77, 1.85)</td>
<td>0.63 (0.08, 4.95)</td>
</tr>
<tr>
<td>8–14 servings/week</td>
<td>1.02 (0.67, 1.56)</td>
<td>0.74 (0.48, 1.14)</td>
<td>0.84 (0.29, 2.44)</td>
</tr>
<tr>
<td>1–7 servings/week</td>
<td>1.00 (0.77, 1.29)</td>
<td>0.88 (0.68, 1.13)</td>
<td>1.10 (0.82, 1.50)</td>
</tr>
<tr>
<td>None</td>
<td>1.00 (reference)</td>
<td>1.00 (reference)</td>
<td>1.00 (reference)</td>
</tr>
</tbody>
</table>

* Adjusted for age (<49 vs. 49.1–53.9 vs. 54–58.9 vs. ≥59), race (binary), education (11 years or less vs. high school graduate vs. attended college), family history of diabetes (binary), body mass index (quartiles), waist/hip ratio (quartiles), physical activity score (continuous), total energy intake (quartiles), smoking history (never vs. former vs. current), history of hypertension (binary), spirits consumption (none vs. 1–7 servings/week, 8–14 servings/week, >14 servings/week), wine consumption (none vs. 1–7 servings/week, 8–14 servings/week, >14 servings/week), and beer consumption (none vs. 1–7 servings/week, 8–14 servings/week, >14 servings/week) using logistic regression.

† ARIC, Atherosclerosis Risk in Communities.

‡ One serving of spirits is one 1.5-ounce glass, one serving of beer is one 12-ounce can, and one serving of wine is one 4-ounce glass. One ounce = 29.57 ml.
subjects, and worsen insulin resistance in diabetic patients, while chronic alcohol consumption has also been implicated to induce beta-cell dysfunction (10, 14, 15). Similarly contradictory results arise from animal studies. In rats, acute alcohol administration can attenuate basal and hormone-induced glucose utilization by skeletal muscles while, in obese mice, chronic ethanol consumption can lower blood glucose and insulin (17, 18). The exact relation between alcohol and diabetes-related endpoints may depend on the nature of alcohol exposure, that is, acute versus chronic and alcohol administration versus alcohol ingestion.

Since 1965, eight prospective studies have examined the association between alcohol consumption and the risk of type 2 diabetes (25, 26, 28–32, 43, 44). Five are comparable with the present study, while significant differences in the study methodology and study population exist between the other three studies and the present study. Of these three, two showed no association between alcohol intake and the risk of diabetes in men even at >21 drinks/week (29, 43). We believe that two methodological issues could explain the discrepancy between our study and these two studies. First, both previous studies lacked information on potential confounders, such as the waist/hip ratio, education, and hypertension, all of which were significantly associated with both alcohol and diabetes in our study. Second, these studies had data on current drinking status only and so had to combine former drinkers, lifetime abstainers, and occasional drinkers into a single reference group. In the present study, former drinkers and lifetime abstainers had the highest unadjusted risk of diabetes; thus, such misclassification of exposure status may lead to an overestimation of the risk of diabetes in the reference group and produce a bias toward the null. The last of these three studies found a protective association of moderate alcohol among the elderly (44). Differences in the age distribution of the two populations and, hence, in the inherent risks for developing diabetes and differences in the characterization of alcohol use (moderate use was defined as 0.5–<1 ounce/day) may explain the discrepancy with our results.

Of the five studies that were comparable with the present study regarding methodology and population, three studies presented results regarding women (25, 28, 31, 32), and in these studies, either an inverse or no association between alcohol intake and diabetes risk was reported. The Nurses’ Health Study demonstrated a significant inverse association between light-to-moderate alcohol consumption, irrespective of beverage type, and the risk of type 2 diabetes (28, 32). The remaining two smaller studies showed that increased alcohol intake was not associated with diabetes risk but was strongly associated with a decreased body mass index (25, 31). This strong inverse association, as indicated by previous ARIC studies (34), may account for the lack of association between alcohol and the risk of diabetes. In our study, women with moderate alcohol consumption were not more likely to develop diabetes than were their counterparts who drank occasionally, even after adjustment for body mass index and the waist/hip ratio.

Of the five studies that were comparable with the present study regarding methodology and population, four presented results regarding men (25, 26, 30, 31). The increased risk of diabetes seen in ARIC Study male participants who drank >21 drinks/week is consistent with results reported by two of these studies, the Rancho Bernardo Study and the San Antonio Heart Study (25, 31). However, an inverse association was found in the other two studies, the Health Professionals’ Follow-up Study and the British Regional Heart Study (26, 30). Given the unique nature of the Health Professionals’ cohort, it is conceivable that these persons had different beverage preference and drinking patterns from those of ARIC Study men or that they had healthier behaviors, which were not measured and were associated with increased consumption of alcohol. Furthermore, the association between the waist/hip ratio and alcohol consumption, which was positive in the ARIC Study, was unknown in the Health Professionals’ Study and therefore was not included in their multivariate analyses. The main difference between the present study and the British Regional Heart Study may lie in the populations studied. The prevalence of coronary heart disease was reported to be 24 percent in the British Regional Heart Study but only about 8 percent in male ARIC Study participants at baseline. Because the lower risk of diabetes seen in moderate drinkers was more apparent and significant only in men with preexisting coronary heart disease versus men without evidence of coronary heart disease in the British Regional Heart Study, one cannot exclude the possibility that the reference group in the British Regional Heart Study (current occasional drinkers) was contaminated with persons with prevalent coronary heart disease who may have been advised to reduce their alcohol consumption.

Several reasons can possibly explain the differences in risk noted between women and men in this study. First, women and men may have differing responses to dietary questionnaires. Previous studies have shown differences between men and women in their attitudes toward alcohol use (45). If women who consumed high amounts of alcohol were more likely to develop diabetes but were also more likely to underreport the amount of alcohol they consumed, then this could result in an apparent protective effect of alcohol on diabetes risk. We have no knowledge of previous studies’ using questionnaires similar to ours that indicated that such underreporting occurs; however, it has been reported that the sensitivity of instruments designed to detect problem drinking, such as the CAGE questionnaire (a four-item test with questions on Cutting down, Annoyance at criticism, Guilty feelings, and use of Eye openers), is lower in college women than men (46). Second, a different beverage preference between women and men may explain some of the observed interaction. Our data showed that the increased diabetes risk in men in the highest alcohol intake group was related to the consumption of spirits. In this study, women were about as likely to consume spirits as men, but women were also more likely to consume wine and less likely to consume beer. Alcoholic beverage preference is associated with demographic and health behavior-related characteristics. Persons who prefer wine are likely to be women, temperate, nonsmokers, better educated, and free of symptoms or risk of illness while persons who prefer spirits are likely to be men, heavier drinkers, less educated, and
afflicted with symptoms or risk factors of major illnesses, and persons who prefer beer had intermediate traits (24). In addition, we demonstrated in our study that wine consumption was statistically associated with healthier behaviors while spirits and beer consumption were not. Therefore, we cannot exclude the possibility that the differences in beverage preference may simply represent differences in lifestyles, which we were not able to adequately measure and adjust in our regression model. Third, this difference could simply be a type II error due to the small number of women who drank >14 drinks/week.

The results of the present study support the hypothesis that high alcohol intake (≥21 drinks/week) predicts type 2 diabetes mellitus among middle-aged men, specifically men who drink more than 14 drinks of spirits per week. However, more moderate levels of consumption (<21 drinks/week) do not appear to increase the risk of type 2 diabetes in middle-aged men and women. Our results, along with those of previous studies, suggest that strategies for the prevention of type 2 diabetes need not target moderate alcohol consumption. In contrast, men who drink >14 drinks of spirits per week should be advised of the increased risk of diabetes associated with heavy alcohol consumption. Further research should investigate the potential effect modification by sex and alcoholic beverages in the association between alcohol and the risk of type 2 diabetes.

ACKNOWLEDGMENTS

The ARIC Study is carried out as a collaborative study supported by contracts N01-HC-55015, N01-HC-55016, N01-HC-55018, N01-HC-55019, N01-HC-55020, N01-HC-55021, and N01-HC-55022 from the National Heart, Lung, and Blood Institute. F. L. B. was supported by an Established Investigator Grant from the American Heart Association (Dallas, Texas). W. H. L. K. was supported by NIH training grant T32HL07024-23. The authors thank the staff and participants in the ARIC Study for their important contributions.

REFERENCES