Combined effect of alcohol consumption and lifestyle behaviors on risk of type 2 diabetes

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ABSTRACT

Background: It has been suggested that the inverse association between alcohol and type 2 diabetes could be explained by moderate drinkers’ healthier lifestyles.

Objective: We studied whether moderate alcohol consumption is associated with a lower risk of type 2 diabetes in adults with combined low-risk lifestyle behaviors.

Design: We prospectively examined 35,625 adults of the Dutch European Prospective Investigation into Cancer and Nutrition (EPIC-NL) cohort aged 20–70 y, who were free of diabetes, cardiovascular disease, and cancer at baseline (1993–1997). In addition to moderate alcohol consumption (women: 5.0–14.9 g/d; men: 5.0–29.9 g/d), we defined low-risk categories of 4 lifestyle behaviors: optimal weight [body mass index (in kg/m²) <25], physically active (>30 min of physical activity/d), current nonsmoker, and a healthy diet [upper 2 quintiles of the Dietary Approaches to Stop Hypertension (DASH) diet].

Results: During a median of 10.3 y, we identified 796 incident cases of type 2 diabetes. Compared with teetotalers, hazard ratios of moderate alcohol consumers for risk of type 2 diabetes in low-risk lifestyle strata after multivariable adjustments were 0.35 (95% CI: 0.17, 0.72) when of a normal weight, 0.65 (95% CI: 0.46, 0.91) when physically active, 0.54 (95% CI: 0.41, 0.71) when nonsmoking, and 0.57 (95% CI: 0.39, 0.84) when consuming a healthy diet. When ≥3 low-risk lifestyle behaviors were combined, the hazard ratio for incidence of type 2 diabetes in moderate alcohol consumers after multivariable adjustments was 0.56 (95% CI: 0.32, 1.00).

Conclusion: In subjects already at lower risk of type 2 diabetes on the basis of multiple low-risk lifestyle behaviors, moderate alcohol consumption was associated with an ≈40% lower risk compared with abstention. Am J Clin Nutr 2010;91:1777–83.

INTRODUCTION

Several studies have shown that type 2 diabetes can largely be prevented through a healthy lifestyle (1, 2). Components of such a lifestyle include maintaining a normal body weight (1), being physically active (3), refraining from smoking (4), and eating a healthy diet (5). Moderate alcohol consumption has consistently been associated with a decreased risk of type 2 diabetes in prospective cohort studies compared with abstention or excessive consumption (6, 7). Much of this association is thought to be attributable to an improved insulin sensitivity due to moderate alcohol consumption (8, 9). Therefore, moderate alcohol consumption could be considered a fifth favorable behavioral lifestyle factor that lowers the risk of type 2 diabetes. Despite this evidence, some have suggested that the observed inverse association between alcohol and disease such as type 2 diabetes can be explained by the fact that moderate drinkers have a healthier lifestyle in general (10). Previous studies on the relation between alcohol consumption, lifestyle, and type 2 diabetes have only considered individual lifestyle behaviors (11–13), but low-risk lifestyle habits are often intercorrelated and may be most effective when present in combination.

Little is known about the association between type 2 diabetes risk and alcohol consumption in the context of healthy lifestyle behaviors, especially when multiple low-risk lifestyle habits are combined. We therefore examined the association of alcohol intake with risk of type 2 diabetes in strata of separate lifestyle behaviors based on body mass index (BMI; in kg/m²), physical activity level, smoking, and adherence to the Dietary Approaches to Stop Hypertension (DASH) diet and in strata of combined low-risk lifestyle behaviors in a prospective population-based study of men and women (of which almost half were postmenopausal at baseline).

SUBJECTS AND METHODS

Study population

The EPIC-NL cohort is the Dutch contribution to the European Prospective Investigation into Cancer and Nutrition (EPIC) and...
general assessments

At baseline, participants filled in a general questionnaire on demographic characteristics and risk behaviors for the presence of chronic diseases. The general questionnaires from both cohorts were largely similar. Coding of this information was standardized and merged into one uniform database. Body weight, height, and waist and hip circumferences were measured. Physical activity was assessed by using a questionnaire that had been validated in an elderly population (15). The Cambridge Physical Activity Index (CPAI) was used to allocate individuals to 4 ordered categories: inactive, moderately inactive, moderately active, and active, as previously described (16). Because we could not calculate a total physical activity score for 14% of all participants, we imputed missing scores by single imputation using linear regression modeling (SPSS MVA procedure; SPSS Inc, Chicago, IL) with other lifestyle factors (eg, smoking and BMI) and the outcome (type 2 diabetes). Smoking was defined as never, past, or current. Daily nutritional intake was obtained from a food-frequency questionnaire (FFQ) containing questions on the usual frequency of consumption of 79 main food items during the year preceding enrollment. This questionnaire allows the estimation of the average daily consumption of 178 foods. The FFQ was validated against 12 monthly 24-h recalls (17). Through the general questionnaire, subjects were asked whether they had ever consumed alcohol. If so, they were asked the number of units of alcohol-free beer, beer, white wine, red wine, port/sherry/vermouth, and spirits consumed. Subjects indicated that their consumption frequency on a daily, weekly, monthly, or yearly scale or as “never consumed.” Alcohol consumption at baseline was determined by multiplying the percentage of alcohol in each beverage by the standard ethanol weight content (5% for beer, 18.5% for fortified wine, 12.5% for red wine, 12% for white wine, and 40% for liquor; means from the average sorts of beverages).

Assessment of type 2 diabetes

The method for ascertaining type 2 diabetes was described in more detail elsewhere (20). The incidence of type 2 diabetes was first assessed by self-report in follow-up questionnaires and with a urine dipstick test in the Prospect cohort only. Also, data on diagnosis of type 2 diabetes were obtained from the Dutch Centre for Health Care Information, which holds a standardized computerized register of hospital discharge diagnoses [all diagnosis were coded according to the International Classification of Diseases, Ninth Revision (ICD-9, ICD codes 250)] (22). The records from this database were linked to the EPIC-NL cohort with a validated probabilistic method (21). All potential cases of type 2 diabetes were verified against medical records of the general practitioners and pharmacists. Verification information was available for 89% of all potential diabetes cases. Of these potential diabetes cases, 72% were verified as having type 2 diabetes and were used as such in the analysis. The remaining 28% was verified as not having type 2 diabetes or having another type of diabetes, such as gestational diabetes, and were therefore included in our analysis as noncases.
Definition of low-risk lifestyle behaviors and alcohol categories

We used the World Health Organization cutoff for healthy weight (BMI < 25). Results were essentially the same when we defined low risk of BMI as 18.5 to < 25 (data not shown). We used waist circumference as a surrogate measure for healthy weight. Low risk was defined as a waist circumference < 88 cm in women or 92 cm in men (Adult Treatment Panel III criteria) (23). We dichotomized the population based on the 4 categories of CPAI into physically active (≥ 30 min of combined recreational, household, and occupational physical activity daily; CPAI categories: moderately active and active) and physically inactive (< 30 min of combined daily recreational, household, and occupational physical activity daily; CPAI categories: inactive and moderately inactive). In terms of cigarette smoking, participants were categorized as current nonsmokers (never or former) or current smokers. The DASH diet score categories were as follows: low adherence (lower 3 quintiles; composite score range: 8–25) or high adherence (upper 2 quintiles; composite score range: 26–40). Alcohol categories were divided in 4 alcohol groups in line with the 2005 US Department of Agriculture Dietary Guidelines (24) as follows: teetotalers (lifelong abstainers), light (0–4.9 g/d for both women and men; includes former drinkers), moderate (5.0–14.9 g/d for women; 5.0–29.9 g/d for men), and heavier (≥ 15.0 g/d for women; ≥ 30.0 g/d for men) consumers.

Statistical analysis

Follow-up time was calculated from the date of enrollment into the study to the date of diabetes diagnosis or date of death; all other participants were censored at the end of follow-up (January 2006). We used a Cox proportional hazards model to calculate the relative risk for each alcohol consumption category using teetotalers as a reference and 95% CIs, adjusted for age (continuous), BMI (continuous), physical activity (inactive, moderately inactive, moderately active, and active), smoking (never, former, and current), adherence to the DASH diet (quintiles), parental history of type 2 diabetes (present or not), education (high, middle, and low), postmenopausal status (premenopausal, postmenopausal, perimenopausal, and surgical postmenopausal), cohort (Prospect-EPIC-NL or MORGEN-EPIC-NL), and daily energy intake (continuous) and stratified by sex. To determine the effects of alcohol consumption and individual lifestyle behaviors,

### TABLE 1
Distribution of variables by alcohol consumption of 26,243 Dutch women and 9382 men of the Dutch European Prospective Investigation into Cancer and Nutrition (EPIC-NL) cohort at baseline

<table>
<thead>
<tr>
<th>Alcohol-consumption category (g/d)</th>
<th>Women</th>
<th></th>
<th>Men</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Teetotaler</td>
<td>Light</td>
<td>Moderate</td>
<td>Heavier</td>
</tr>
<tr>
<td>Participants (n)</td>
<td>3370</td>
<td>11,461</td>
<td>6176</td>
<td>5236</td>
</tr>
<tr>
<td>Age (y)</td>
<td>50 ± 13</td>
<td>51 ± 12</td>
<td>50 ± 11</td>
<td>52 ± 9</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>84 ± 12</td>
<td>83 ± 11</td>
<td>81 ± 10</td>
<td>82 ± 10</td>
</tr>
<tr>
<td>Physically active (%)</td>
<td>55.0</td>
<td>63.6</td>
<td>69.0</td>
<td>64.2</td>
</tr>
<tr>
<td>Physically inactive (%)</td>
<td>45.1</td>
<td>47.0</td>
<td>42.9</td>
<td>47.3</td>
</tr>
<tr>
<td>High educational level (%)</td>
<td>13.2</td>
<td>22.7</td>
<td>37.1</td>
<td>41.7</td>
</tr>
<tr>
<td>Total energy intake (kcal/d)²</td>
<td>1840 ± 539</td>
<td>1838 ± 481</td>
<td>1908 ± 466</td>
<td>1955 ± 470</td>
</tr>
<tr>
<td>Alcohol intake (g/d)²</td>
<td>0 (0–0)⁶</td>
<td>1 (0–3)</td>
<td>9.1 (7–12)</td>
<td>24 (20–33)</td>
</tr>
<tr>
<td>Components of DASH diet²</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fruit (g/d)²</td>
<td>280 ± 182</td>
<td>297 ± 174</td>
<td>291 ± 167</td>
<td>269 ± 164</td>
</tr>
<tr>
<td>Vegetables (g/d)²</td>
<td>141 ± 59</td>
<td>146 ± 56</td>
<td>149 ± 55</td>
<td>152 ± 56</td>
</tr>
<tr>
<td>Nuts and legumes (g/d)²</td>
<td>16 ± 16</td>
<td>17 ± 15</td>
<td>19 ± 16</td>
<td>19 ± 16</td>
</tr>
<tr>
<td>Whole grains (g/d)²</td>
<td>53 ± 60</td>
<td>63 ± 59</td>
<td>69 ± 57</td>
<td>66 ± 53</td>
</tr>
<tr>
<td>Low-fat dairy intake (g/d)²</td>
<td>269 ± 223</td>
<td>290 ± 220</td>
<td>289 ± 213</td>
<td>263 ± 212</td>
</tr>
<tr>
<td>Red and processed meat (g/d)²</td>
<td>78 ± 46</td>
<td>77 ± 43</td>
<td>78 ± 42</td>
<td>84 ± 44</td>
</tr>
<tr>
<td>Sweetened beverages (g/d)²</td>
<td>62 ± 93</td>
<td>55 ± 84</td>
<td>50 ± 76</td>
<td>45 ± 72</td>
</tr>
<tr>
<td>Sodium intake (mg/d)²</td>
<td>2161 ± 749</td>
<td>2171 ± 656</td>
<td>2234 ± 646</td>
<td>2201 ± 698</td>
</tr>
</tbody>
</table>

1 DASH, Dietary Approaches to Stop Hypertension.
2 P < 0.05 between alcohol categories within sex based on ANOVA (continuous variables) or chi-square (categorical variables).
3 Mean ± SD (all such values).
4 Physical activity was based on an index of combined recreational, household, and occupational physical activity (physically active: ≥ 30 min of combined recreational, household, and occupational physical activity/d).
5 High educational level: higher vocational education and university.
6 Median; 25th–75th percentiles in parentheses (all such values).
7 The DASH diet focuses on 8 components: high intake of fruit, vegetables, nuts and legumes, low-fat dairy products, and whole grains and low intake of sodium, sweetened beverages, and red and processed meats.
the association of alcohol consumption with type 2 diabetes was first estimated stratified by each lifestyle factor separately. Second, to determine the effects of alcohol consumption and combined low-risk lifestyle factors on type 2 diabetes incidence, participants could score one point for each low-risk lifestyle: BMI < 25, physically active, current nonsmoker, and upper 2 quintiles of the DASH diet. They could have a score ranging from 0 (no low-risk behaviors) to 4 (all low-risk behaviors). Statistical interaction of alcohol consumption with sex and with lifestyle behaviors was assessed based on likelihood ratio tests in models with and without the cross-product terms in the multivariable model. Statistical analyses were performed by using the SAS statistical software package (SAS version 9; SAS Institute, Cary, NC).

RESULTS

In both men and women, teetotalers smoked less and were less highly educated compared with alcohol consumers (Table 1). Less than 2.0% of the women reported drinking >45 g/d (>3 drinks/d), and 2.2% of the men reported drinking >75 g/d (>5 drinks/d). To validate the self-reported alcohol intake, we determined the relation between alcohol intake and HDL cholesterol in a 6.5% subcohort. This analysis showed a linear association ($P < 0.001$) between alcohol intake and HDL-cholesterol concentrations in both men ($n = 604$) and women ($n = 1719$) ($\beta \pm SD: 0.062 \pm 0.005$ mmol/L per 5 g alcohol/d in women and $0.043 \pm 0.007$ mmol/L per 10 g alcohol/d in men) adjusted for all confounders from the multivariable model.

During a median follow-up of 10.3 person-years (360,661 person-years), we verified incident cases of type 2 diabetes in 618 women and 178 men. Compared with female teetotalers, hazard ratios (HRs) for type 2 diabetes were 0.75 (95% CI: 0.61, 0.91) for light, 0.48 (95% CI: 0.36, 0.63) for moderate, and 0.54 (95% CI: 0.40, 0.73) for heavier drinkers after multivariable adjustment. Among men, HRs were 0.98 (95% CI: 0.53, 1.80) for light, 0.79 (95% CI: 0.43, 1.44) for moderate, and 0.71 (95% CI: 0.37, 1.38) for heavier drinkers compared with male teetotalers after multivariable adjustment. Because we did not find a sex-based difference ($P$ for interaction = 0.50) between alcohol consumption and type 2 diabetes, we combined men and women in further analyses. In the entire population, HRs for type 2 diabetes were 0.78 (95% CI: 0.64, 0.95) for light, 0.55 (95% CI: 0.43, 0.69) for moderate, and 0.57 (95% CI: 0.44, 0.74) for heavier alcohol consumers compared with teetotalers after multivariable adjustment.

The prevalence of low-risk lifestyle behaviors was 47.1% for having an optimal weight, 68.7% for having an optimal waist circumference, 62.3% for being physically active, 69.3 for not smoking, and 38.5% for having a high diet quality. After multivariable adjustments, HRs for risk of type 2 diabetes in high-risk strata of lifestyle behaviors were 6.11 (95% CI: 4.74, 7.83) for BMI, 5.96 (95% CI: 5.02, 7.08) for waist circumference, 1.06 (95% CI: 0.92, 1.22) for physical activity, 1.19 (95% CI: 1.01, 1.40) for smoking, and 1.18 (95% CI: 1.01, 1.37) for the DASH diet compared with the low-risk levels of each lifestyle behavior. When analyzing physical activity over the 4 categories in the multivariable-adjusted model, more pronounced associations were observed: Each increase in physical activity category was significantly associated with a 7% lower risk of type 2 diabetes after multivariable adjustments ($P < 0.05$ for trend). The results were essentially the same when we excluded imputed values for physical activity.

Compared with teetotalers, HRs of moderate alcohol consumers for risk of type 2 diabetes in low-risk lifestyle strata after multivariable adjustments were 0.35 (95% CI: 0.17, 0.72) when having an optimal weight or 0.45 (95% CI: 0.28, 0.72) when having an optimal waist circumference, 0.65 (95% CI: 0.46, 0.91) when being physical active, 0.54 (95% CI: 0.41, 0.71) when being a nonsmoker, and 0.57 (95% CI: 0.39, 0.84) when consuming a healthy diet (Table 2). The results were essentially the same when we excluded imputed values for physical activity: 0.67 (95% CI: 0.46, 0.98). Comparable results were found for moderate alcohol consumers in subgroups reporting less healthy lifestyle behaviors. There were significant interactions between alcohol-consumption categories and physical activity and between alcohol-consumption categories and smoking, but these were mainly due to the lower risks of heavier drinkers who smoke or are physically inactive. Interactions between alcohol-consumption categories and other dichotomous lifestyle behaviors were not significant (Table 2).

To have adequate power to investigate the effect of combined low-risk lifestyle factors across categories of alcohol consumption, we grouped participants with 3 or all 4 (38.2%), 2 (35.5%), and 1 or none (26.3%) low-risk lifestyle behaviors together. When ≥3 low-risk lifestyle behaviors were combined, the HR for incidence of type 2 diabetes among moderate alcohol consumers after multivariable adjustments was 0.56 (95% CI: 0.32, 1.00). The results were essentially the same but more precise when we used the low-risk category for waist circumference instead of the low-risk category of BMI with the combined lifestyles analysis: 0.60 (95% CI: 0.37, 0.97). Similar associations were found among moderate alcohol consumers reporting fewer low-risk lifestyle habits (Table 3). We observed no effect modification of the association of sex with combined low-risk lifestyle behaviors ($P$ for interaction = 0.23) or alcohol and combined low-risk lifestyle behaviors ($P$ for interaction = 0.17) after multivariable adjustment.

When the data for each cohort were analyzed separately, almost identical HRs, although less precise, were observed among moderate alcohol consumers with ≥3 low-risk lifestyle behaviors combined. The HR for the Prospect cohort was 0.54 (95% CI: 0.27, 1.08), whereas the HR for the MORGEN cohort was 0.59 (95% CI: 0.22, 1.57) after multivariable adjustment. Again, when the low-risk category of BMI was replaced with the low-risk category of waist circumference in the combined score, virtually the same HRs were observed among moderate alcohol consumers with ≥3 low-risk lifestyle behaviors combined when results from the multivariate model were split up according to cohort: Prospect cohort (0.55; 95% CI: 0.30, 1.00) and MORGEN cohort (0.61; 95% CI: 0.28, 1.32).

DISCUSSION

This prospective study showed that moderate alcohol consumption is associated with a reduced risk of developing type 2 diabetes, regardless of other favorable behavioral lifestyles. Among participants already at lower risk of developing type 2 diabetes based on the combined effect of body weight, physical activity level, smoking habits, and diet quality, moderate alcohol
consumption was associated with a lower risk of the incidence of type 2 diabetes.

Our results confirm that moderate alcohol consumption reduces the risk of type 2 diabetes in the presence of individual low-risk lifestyle behaviors, such as BMI, physical activity, and smoking, which is in line with 3 previous observational studies (11–13). In addition, they show that moderate alcohol consumption remains to be associated with a lower risk of type 2 diabetes among those with multiple low-risk lifestyle behaviors combined. These findings indicate that the relation between alcohol consumption and type 2 diabetes is not likely to be explained by a healthier lifestyle of moderate drinkers in general.

Our findings of joint moderate alcohol consumption and healthy lifestyle behaviors are comparable with the findings of Mukamal et al for risk of coronary heart disease (25). In their study, men with 4 healthy lifestyle behaviors, who drank alcohol in moderation (5.0–29.9 g/d), remained to have a significant lower risk of myocardial infarction as compared with abstainers. Therefore, the associations of alcohol consumption with both type 2 diabetes and coronary heart disease do not seem to be confounded by healthier lifestyles of moderate drinkers.

In our cohort, heavier drinkers had lower risks of developing type 2 diabetes than did teetotalers. Even heavier drinkers with a less favorable lifestyle behavior (based on smoking status, physical activity, and diet), had lower risks of developing type 2 diabetes than did teetotalers with the favorable lifestyle behavior (Table 2). These findings warrant clarification. A reduction in the risk of developing type 2 diabetes was observed for an alcohol intake up to 50 g/d (6, 7). However, the upper limit for moderate drinking in the current study was based on the 2005 US

Table 2: Hazard ratios (and 95% CIs) for the risk of type 2 diabetes in 35,625 Dutch women and men according to alcohol consumption stratified by BMI, waist circumference, physical activity, smoking, and Dietary Approaches to Stop Hypertension (DASH) diet score

<table>
<thead>
<tr>
<th>Alcohol-consumption category (g/d)</th>
<th>Teetotaler (0 for men and women)</th>
<th>Light (0.0–4.9 for men and women)</th>
<th>Moderate (5.0–14.9 for men; 5.0–29.9 for men)</th>
<th>Heavier (≥15.0 for men; ≥30.0 for men)</th>
<th>P for trend</th>
<th>P for interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BMI</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25 kg/m²</td>
<td>1.00 (referent)</td>
<td>0.44 (0.23, 0.84)</td>
<td>0.35 (0.17, 0.72)</td>
<td>0.43 (0.21, 0.89)</td>
<td>0.23</td>
<td></td>
</tr>
<tr>
<td>≥25 kg/m²</td>
<td>4.36 (2.56, 7.44)</td>
<td>3.38 (2.01, 5.67)</td>
<td>2.22 (1.30, 3.80)</td>
<td>2.22 (1.28, 3.84)</td>
<td>&lt;0.001</td>
<td>0.38</td>
</tr>
<tr>
<td><strong>Waist circumference (cm)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;88 for women, &lt;92 for men</td>
<td>1.00 (referent)</td>
<td>0.61 (0.41, 0.92)</td>
<td>0.45 (0.28, 0.72)</td>
<td>0.48 (0.29, 0.79)</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>≥88 for women, ≥92 for men</td>
<td>5.02 (3.42, 7.36)</td>
<td>4.04 (2.83, 5.78)</td>
<td>2.65 (1.80, 3.92)</td>
<td>2.59 (1.73, 3.90)</td>
<td>&lt;0.001</td>
<td>0.65</td>
</tr>
<tr>
<td><strong>Physical activity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physically active</td>
<td>1.00 (referent)</td>
<td>1.07 (0.80, 1.42)</td>
<td>0.65 (0.46, 0.91)</td>
<td>0.80 (0.56, 1.15)</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>Physically inactive</td>
<td>1.63 (1.18, 2.26)</td>
<td>0.94 (0.69, 1.27)</td>
<td>0.79 (0.55, 1.12)</td>
<td>0.67 (0.45, 1.00)</td>
<td>&lt;0.001</td>
<td>0.01</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Currently nonsmoking</td>
<td>1.00 (referent)</td>
<td>0.78 (0.62, 0.96)</td>
<td>0.54 (0.41, 0.71)</td>
<td>0.73 (0.54, 0.98)</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>1.21 (0.82, 1.80)</td>
<td>1.03 (0.78, 1.36)</td>
<td>0.75 (0.53, 1.04)</td>
<td>0.51 (0.35, 0.74)</td>
<td>&lt;0.001</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>DASH diet</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High adherence</td>
<td>1.00 (referent)</td>
<td>0.81 (0.59, 1.13)</td>
<td>0.57 (0.39, 0.84)</td>
<td>0.45 (0.28, 0.73)</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Low adherence</td>
<td>1.18 (0.84, 1.67)</td>
<td>0.89 (0.65, 1.22)</td>
<td>0.63 (0.44, 0.90)</td>
<td>0.74 (0.51, 1.07)</td>
<td>&lt;0.001</td>
<td>0.38</td>
</tr>
</tbody>
</table>

1 Hazard ratios were derived by using Cox proportional hazard models and were adjusted for age (continuous), parental history of diabetes (present or not), menopausal status (premenopausal, surgical postmenopausal, perimenopausal, and postmenopausal), education (high, middle, and low), cohort [Prospect or Monitoring Project on Risk Factors for Chronic Diseases (MORGEN)], and daily energy intake (continuous) and were stratified by sex. Furthermore, models were adjusted for each of the other 3 lifestyle behaviors not stratified on BMI (continuous); physical activity (inactive, moderately inactive, moderately active, and active); smoking (never, former, and current), and adherence to the DASH diet (quintiles).

2 Derived by using linear trend test across ordinal categories of alcohol consumption (teetotaler, light, moderate, and heavier).

3 Derived by using likelihood ratio tests with and without the cross-product term of alcohol category (teetotaler, light, moderate, and heavier) and each lifestyle behavior (low-risk and high-risk) in the multivariable model.

4 Physical activity was based on an index of combined recreational, household, and occupational physical activity (physically active: ≥30 min of combined recreational, household, and occupational physical activity daily; physically inactive: <30 min of combined recreational, household, and occupational physical activity daily).

5 The DASH diet focuses on 8 components: high intake of fruit, vegetables, nuts and legumes, low-fat dairy products, and whole grains and low intake of sodium, sweetened beverages, and red and processed meats [high adherence: upper 2 quintiles (composite score range of 26 to 40); low adherence: lower 3 quintiles (composite score range of 8 to 25)].
Department of Agriculture Dietary Guidelines (24), directed at prevention of all chronic diseases rather than on the maximum risk reduction of type 2 diabetes. These relatively low cutoffs, particularly for women, could explain the low risks observed among the heavier drinkers.

Clearly, the observations for heavier drinkers must be considered in light of the potential harmful effects of excessive alcohol intake and greater risk of certain cancers, such as breast and rectum (26). Heavy or excessive drinking should always be discouraged, whereas moderate alcohol consumption could be regarded as a complement, rather than an alternative, to other low-risk lifestyle habits. Guidelines and personal advice on alcohol consumption should consider the full range of benefits and risks to the individual.

The association between alcohol consumption and type 2 diabetes tended to be stronger in women than in men, which is consistent with previous meta-analyses (6, 7). However, studies in these meta-analyses that reported results for both men and women did not find this trend. Men in this cohort were substantially younger than women, and only about one-fourth of the entire cohort consisted of men. Subsequently, there were fewer incident cases of type 2 diabetes in men than in women, which may explain the weaker association between alcohol intake and incidence type 2 diabetes in men.

There are several biologically plausible mechanisms to explain an inverse association between moderate alcohol consumption and type 2 diabetes. In 2 short-term randomized controlled crossover trials of women without diabetes, alcohol consumption of 30 and 25 g/d decreased insulin resistance and triglyceride concentrations (8, 9). Besides these effects, moderate alcohol consumption increases both gene expression and circulating protein concentrations of adiponectin (9). Adiponectin is positively associated with insulin sensitivity and inversely associated with inflammation and type 2 diabetes (27). Recently, it was suggested that adiponectin may explain ~25–30% of the inverse association between alcohol consumption and type 2 diabetes in women (28).

Some limitations of our study warrant consideration. First, an FFQ was used for nutritional assessment, including alcohol intake. Self-reported alcohol intake is generally being underestimated (29). However, there was a high correlation between alcohol consumption from the FFQ and the twelve 24-h recalls reported (29). However, there was a high correlation between alcohol consumption and serum HDL-cholesterol concentrations. This suggests sufficient validity for ranking participants on alcohol consumption. Also, we could not take drinking pattern (regular compared with episodic/binge drinking) into account. However, among moderately drinking middle-aged and older women, binge drinking does not occur frequently (30). It is therefore unlikely that this influenced the results in this cohort of predominantly middle-aged and older women. Furthermore, we did not take into account beverage type in the association between alcohol and type 2 diabetes. However, a previous study in one of the cohorts presented here showed that beverage type did not influence this association (20).

Second, we used only baseline measurements to characterize individuals and did not take into account possible changes in alcohol consumption or other lifestyle behaviors over follow-up. Persons who are already ill or have poor health might be more likely to change their diet and could therefore drink less or even quit drinking as a result of this. However, we repeated the analyses excluding persons with type 2 diabetes within the first 2 y of follow-up, and the association persisted (data not shown). We excluded those with prevalent cardiovascular diseases and cancer at baseline. In addition, we used lifetime abstainers as a reference category without occasional or former drinkers to rule out “the sick quitter” hypothesis (31). Therefore, our results are unlikely to be confounded by such reverse causality.

Third, although we adjusted for several known potential confounders, we cannot completely rule out the possibility of residual confounding. Finally, the presence of type 2 diabetes...
often goes undetected and may be preclinical for up to 9 to 12 y (32). Undetected diabetes cases in our cohort may have been misclassified as nondiabetic individuals, which resulted in the attenuation of associations.

In summary, this study supports the presence of an inverse association between moderate alcohol consumption and incidence of type 2 diabetes in a mixed population and extends this association to subjects already at low-risk on the basis of their multiple low-risk lifestyle behaviors. Moderate alcohol consumption (=0.5–1 drink/d for women and 0.5–2 drinks/d for men) appears to reduce the risk of type 2 diabetes, independently of other lifestyle behaviors.

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