

# A Prospective Study of Drinking Patterns in Relation to Risk of Type 2 Diabetes Among Men

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Using data from a 12-year prospective study, we determined the importance of the pattern of alcohol consumption as a risk factor for type 2 diabetes in a cohort of 46,892 U.S. male health professionals who completed biennial postal questionnaires. Overall, 1,571 new cases of type 2 diabetes were documented. Compared with zero alcohol consumption, consumption of 15–29 g/day of alcohol was associated with a 36% lower risk of diabetes (RR = 0.64; 95% CI 0.53–0.77). This inverse association between moderate consumption and diabetes remained if light drinkers rather than abstainers were used as the reference group (RR = 0.60, CI 0.50–0.73). There were few heavy drinkers, but the inverse association persisted to those drinking  $\geq 50$  g/day of alcohol (RR = 0.60, CI 0.43–0.84). Frequency of consumption was inversely associated with diabetes. Consumption of alcohol on at least 5 days/week provided the greatest protection, even when less than one drink per drinking day was consumed (RR = 0.48, CI 0.27–0.86). Compared with infrequent drinkers, for each additional day per week that alcohol was consumed, risk was reduced by 7% (95% CI 3–10%) after controlling for average daily consumption. There were similar and independent inverse associations for beer, liquor, and white wine. Our findings suggested that frequent alcohol consumption conveys the greatest protection against type 2 diabetes, even if the level of consumption per drinking day is low. Beverage choice did not alter risk. *Diabetes* 50:2390–2395, 2001

**A** reduced incidence of type 2 diabetes has been observed among moderate drinkers in several large prospective studies (1–5). This inverse association has been demonstrated in both women (2) and men (1,3). In contrast, other studies have shown an increased risk of diabetes among a proportion of

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subjects in the top alcohol consumption category (4,6). No association between alcohol consumption and incidence of diabetes has been seen in several other studies (7–9). Possible explanations for inconsistencies in findings include differences in drinking patterns and type of alcoholic beverage in the populations studied.

The effect of alcohol being consumed with or without a meal has not been examined in prospective studies. In the experimental setting, peak alcohol concentration is reduced if alcohol is consumed with meals (10). Alcohol can lead to hypoglycemia resulting from reduced gluconeogenesis during fasting, but in the postprandial state, alcohol can result in reduced glucose disposal and increased blood glucose levels (11,12). Although the tannic acid content of red wine might improve insulin sensitivity (13), the influence of beverage choice in relation to risk of diabetes has not been addressed in prospective studies.

In 1995, Rimm et al. (1) reported a reduced incidence of type 2 diabetes in drinkers as compared with abstainers in a cohort of >40,000 male health professionals followed for 6 years. In the current analysis, we re-examined the association between alcohol consumption and incidence of type 2 diabetes in the same cohort after 12 years of follow-up. We extended the analysis to examine the impact of frequency of alcohol consumption, relationship of consumption to meals, and beverage choice on the incidence of diabetes.

## RESEARCH DESIGN AND METHODS

In 1986, 51,529 men aged 40–75 years were recruited for the Health Professionals Follow-Up Study (14). At that time, these men, who were dentists (58%), veterinarians (20%), pharmacists (8%), optometrists (7%), osteopaths (4%), and podiatrists (3%), completed a postal questionnaire about alcohol and cigarette use, diet and lifestyle factors, medical history, and medications. Follow-up questionnaires were sent every 2 years to update exposures of interest and ascertain newly diagnosed illnesses. After repeated mailings, an average of 94% of the cohort responded to each questionnaire cycle during the first 12 years of follow-up.

We assessed the average use of beer, white wine, red wine, and liquor during the previous year as part of the baseline 131-item semiquantitative food frequency questionnaire. Use of one drink of each beverage type was recorded separately using nine intake categories, ranging from “never” or “less than monthly” to “six or more times per day.” Consumption for each beverage type was multiplied by the ethanol content—one can/bottle/glass of beer = 12.8 g, one glass of white or red wine = 11.0 g, and one glass of liquor = 14.0 g (15)—to give grams of alcohol per day for that beverage. Beverage-specific intake was then summed to give total average grams of alcohol per day. Alcohol consumption was reassessed in 1990 and 1994 using similar procedures. In a detailed study designed to assess the validity and reproducibility of this method of assessment, we found self-reported alcohol consumption correlated highly with independent measures of alcohol intake from 14 days of diet records (Spearman correlation coefficient = 0.86) (16,17). Alcohol consumption, as measured by the food frequency questionnaire, also showed

TABLE 1  
Baseline characteristics by alcohol consumption in 46,936 U.S. men: the Health Professionals Follow-Up Study, 1986

	Alcohol consumption (g/day)						
	0	0.1–4.9	5.0–9.9	10.0–14.9	15.0–29.9	30.0–49.9	≥50.0
Participants ( <i>n</i> )	10,770	11,339	6,888	6,022	6,249	4,184	1,440
Mean age (years)	54.7	53.8	53.8	54.9	54.3	56.1	55.8
Mean BMI (kg/m <sup>2</sup> )	25.6	25.5	25.4	25.3	25.3	25.4	25.7
Mean number of days/week alcohol was consumed	0.04	0.9	2.3	3.9	5.0	6.2	6.6
Beer (g/day)	0	0.6	2.4	4.2	5.7	12.6	25.9
Red wine (g/day)	0	0.4	0.8	1.3	2.5	2.4	5.6
White wine (g/day)	0	0.7	1.5	2.4	4.0	3.8	7.0
Liquor (g/day)	0	0.6	2.5	4.4	7.5	19.3	31.6
Current smoker (%)	10.2	12.4	14.6	16.4	17.0	28.1	31.3
Past smoker (%)	30.4	38.1	43.4	47.3	51.6	52.5	51.0
Physical activity (METs/week)	17.8	19.5	21.7	22.0	22.8	20.3	18.9
Hypertension (%)	21.4	19.6	20.9	19.8	21.9	25.9	28.8
Family history of diabetes (%)*	13.6	14.2	14.1	12.4	12.3	11.4	11.8
Mean daily intakes							
Total energy (kcal/day)	1,926	1,921	1,955	1,961	2,074	2,151	2,436
Energy consumed as alcohol (kcal/day)	0	3	10	17	29	66	113
Glycemic load (units/day)†	13,595	13,204	12,617	12,081	11,547	10,353	9,246
Trans-fats (g/day)†	3.0	2.9	2.9	2.8	2.7	2.5	2.2
Polyunsaturated fats (g/day)†	13.4	13.3	13.4	13.3	13.3	12.3	10.8
Dietary fiber (g/day)	22.4	22.1	21.4	20.8	20.2	17.5	15.3

Data are *n*. Except for age, all variables are adjusted by direct standardization to the age distributions of the study population. \*History of diabetes with onset at age ≥30 years in immediate family; †adjusted for total calories in diet. MET, metabolic equivalent.

the expected linear association with blood levels of HDL cholesterol ( $r = 0.35$ ) (16).

In addition to assessing the amount of alcohol consumption, in 1986 we also asked the following question: "In a typical week, on how many days do you have any form of alcoholic beverage?" Responses were recorded as 0, 1–2, 3–4, 5–6, or 7 days per week. This frequency measure correlated highly with frequency of consumption on dietary records ( $r = 0.79$ ) (16). Subsequently, in 1992, a question was included to identify subjects who were lifelong abstainers or very light drinkers: "Apart from Communion or Passover, have you drunk 50 or more drinks in your life?"

In 1994, subjects, if they were drinkers, were asked to record the percentage of alcohol consumed with meals, with choices ranging from "<25%" to "75% or more." Data on alcohol consumption with meals were limited to 33,750 men who responded to the long form of the questionnaire.

We considered a participant to have a family history of type 2 diabetes (in mother, father, or siblings) if the diagnosis was made after 30 years of age.

When subjects reported a new diagnosis of diabetes on a biennial follow-up questionnaire, they were sent a supplementary questionnaire and asked to provide information on the date of diagnosis, symptoms at time of diagnosis (polyuria, weight loss, hunger, thirst, visual changes, or coma), blood glucose levels, glycosuria, history of ketoacidosis at the time of diagnosis, and hypoglycemic medication. Before 1996, type 2 diabetes was diagnosed according to any one of the following criteria (18): 1) one or more classic symptoms of diabetes with an elevated plasma glucose (i.e., fasting glucose of ≥7.8 mmol/l [140 mg/dl], nonfasting glucose of ≥11.1 mmol/l [200 mg/dl], or 2-h glucose levels ≥11.1 mmol/l on glucose tolerance test; 2) elevated plasma glucose levels on two different occasions; or 3) hypoglycemic treatment; as long as the subject did not fulfill criteria for type 1 diabetes (i.e., two or more of the following: repeated ketonuria, not obese, and onset at age <30 years). These type 2 diabetes criteria are similar to those of the National Diabetes Data Group (19). From 1996 onward, in keeping with the new guidelines for definition of type 2 diabetes, we used a lower threshold for fasting plasma glucose (≥7 mmol/l [126 mg/dl]) (20). The validity of self-report of diabetes was tested in a subsample of 71 subjects who reported newly diagnosed diabetes between 1996 and 1998. A physician blinded to the information reported on the supplementary questionnaire reviewed the records according to the revised diagnostic criteria. Of the 71 patients, 12 had incomplete records, but each case was strongly suggestive of diabetes. Among the remaining 59 cases, the diagnosis of type 2 diabetes was confirmed in 57 subjects (97%).

We excluded from the analysis men missing data on alcohol consumption, age, BMI, or diet at baseline or who had previously diagnosed diabetes. In total, 4,637 men were excluded, leaving a cohort of 46,892.

**Analysis.** Person-months analysis was used to assess the rate of type 2 diabetes for each alcohol consumption level standardized for age. Men

contributed person-months from the date of the return of the baseline questionnaire until diagnosis of diabetes, death, or the end of the 12-year follow-up period (31 January 1998), whichever came first. Pooled logistic regression with biennial updating of exposure variables was used to calculate multivariate relative risks. This method has been shown to approximate Cox's proportional hazard models when the time period was short and disease incidence was low within each time period (21). The model included age (7 categories), BMI (10 categories), pack-years of cigarette use (6 categories), average daily exercise in metabolic equivalents (quintiles), profession, family history of type 2 diabetes (as recorded in 1987), and history of diagnosed hypertension, coronary heart disease, cancer, or hypercholesterolemia. Quantity and frequency of alcohol consumption were also modeled as quasi-continuous variables, using the midpoint of each response category. If alcohol consumption or BMI data were missing for any one follow-up period, data from the previous follow-up was used in its place. Dietary information was also included in the model, and was updated every 4 years; variables included quintiles of energy-adjusted glycemic load, dietary fiber, trans-fatty acids, and polyunsaturated fats.

## RESULTS

During 508,901 person-years of follow-up among 46,892 men, we documented 1,571 cases of newly diagnosed type 2 diabetes. As expected, men with higher alcohol consumption were more likely to be smokers at baseline and at the highest levels of consumption had a higher prevalence of hypertension (Table 1). Men with higher alcohol consumption had a lower prevalence of family history of type 2 diabetes.

**Baseline alcohol consumption of the cohort.** The median daily alcohol consumption was 6 g (less than half a U.S. standard drink). The majority (75%) of the sample drank ≤15 g/day, and 95% drank <43 g/day; 13% of the sample reported daily drinking at baseline. Of the 46,795 (99.8%) men who responded to the questions on frequency of consumption, a third (33.4%) reported not drinking at all in a typical week, 26.5% drank 1–2 days per week, and 39.9% drank 3–7 days per week. Among drinkers, the correlation between average daily grams of alcohol and frequency of consumption was 0.69.

TABLE 2  
RR of type 2 diabetes in relation to average daily alcohol intake: the Health Professionals Follow-Up Study, 1986–1998

Alcohol intake (g/day)	Cases (n)	Person-years	RR*		
			Age and BMI adjusted	Multivariate analysis 1	Multivariate analysis 2
0	416	115,646	Reference group	Reference group	—
0.1–4.9	450	123,237	1.09 (0.95–1.24)	1.05 (0.92–1.20)	Reference group
5.0–9.9	214	75,331	0.88 (0.74–1.04)	0.80 (0.68–0.95)	0.75 (0.63–0.89)
10.0–14.9	163	65,657	0.77 (0.64–0.92)	0.71 (0.59–0.86)	0.65 (0.54–0.79)
15.0–29.9	174	68,598	0.80 (0.67–0.96)	0.64 (0.53–0.78)	0.61 (0.50–0.74)
30.0–49.9	116	45,030	0.72 (0.58–0.88)	0.57 (0.45–0.71)	0.53 (0.42–0.67)
≥50.0	38	15,403	0.64 (0.46–0.89)	0.61 (0.43–0.86)	0.55 (0.39–0.79)
P			<0.0001	<0.0001	<0.0001

\*Data are RR (95% CI). In multivariate analysis 1, abstainers used as reference group. RR controlled for age and BMI (seven categories each); smoking (pack-years: six categories); physical activity level; quintiles of dietary glycemic load, fiber, *trans*-fats and polyunsaturated fats, all energy adjusted; profession; history of diagnosed hypertension, hypercholesterolemia, coronary heart disease, or cancer; and family history of type 2 diabetes. In multivariate analysis 2, only current drinkers included, with light drinkers (0.1–4.9 g/day) used as reference group. RR adjusted for all covariates in analysis 1.

**Average daily consumption as a predictor of type 2 diabetes.** Average daily alcohol consumption was inversely associated with a risk of developing type 2 diabetes (Table 2). Compared with abstainers, men drinking 15.0–29.9 g/day of alcohol had a RR of 0.80 (CI 0.67–0.96), after adjusting for age and BMI. The lowest RR was in the group drinking ≥50 g/day of alcohol (RR 0.64; 95% CI 0.46–0.89). After further adjustment for smoking, physical activity, dietary factors (glycemic load, fiber, *trans*-fatty acids, and polyunsaturated fat), profession, history of hypertension, hypercholesterolemia, history of coronary heart disease or cancer, and family history of type 2 diabetes, the inverse association between alcohol and diabetes was slightly augmented. Compared with zero alcohol, the RR was 0.64 (CI 0.53–0.78) for 15–29.9 g/day, 0.57 (0.45–0.71) for 30.0–49.9 g/day, and 0.61 (0.43–0.86) for ≥50 g/day. In a separate model with alcohol as a continuous variable, the reduction in risk associated with a 15-g increment in alcohol consumption was 19% (RR 0.81, CI 0.76–0.87). Removal of hypertension from the model did not alter the results.

To determine whether the inverse association between alcohol and type 2 diabetes was exaggerated by the inclusion of “sick quitters” (i.e., persons who ceased drinking because of ill health) in the nondrinking control group, the analysis was repeated using low level drinkers (0.1–4.9 g/day) as the reference category and excluding nondrinkers (Table 2). This strengthened the inverse association slightly. In those drinking 15–29.9 g/day, the RR was 0.61 (CI 0.50–0.74). If lifelong abstainers or very light drinkers (those who had consumed <50 drinks across their life) were used as the referent group, the findings were unchanged, with those drinking 15–29.9 g/day having a RR of 0.58 (CI 0.47–0.72). Because men who routinely seek medical screening are more likely to have asymptomatic diabetes detected, the analysis was repeated considering only the 1,046 diabetes cases who were symptomatic at the time of diagnosis. This had little effect on the inverse association (data not shown).

The inverse association between average daily consumption and risk of diabetes did not vary appreciably by BMI. For those drinking 15–29.9 g/day, the RR was 0.64 (CI 0.52–0.79) in men with a BMI ≥25 kg/m<sup>2</sup> and 0.63 (0.39–1.00) in slimmer men. The association in men aged <65

years (RR 0.64, CI 0.51–0.82) was similar to that in older men (0.65, 0.48–0.89).

**Pattern of consumption.** Men who consumed alcohol two or fewer times per week did not have a lower risk of type 2 diabetes (Table 3), regardless of whether they drank less than one or three or more drinks (per drinking day) on these occasions. Men who drank three to four times per week had only marginally significant reduction in risks, whereas those drinking ≥5 days per week had the lowest risks, even when consuming less than one drink per drinking day. When grams of consumption and frequency of consumption were modeled as quasi-continuous variables, using the midpoint of each response category, along with confounders, frequency was a significant predictor of diabetes ( $P = 0.0007$ ), and total grams of alcohol consumed became nonsignificant ( $P = 0.44$ ). Compared with less frequent drinkers, for every extra drinking day per week, risk of diabetes was 7% lower (RR 0.93, CI 0.90–0.97) after controlling for average daily grams of alcohol consumed and confounders.

**Beverage choice.** Beer, white wine, red wine, and liquor were all inversely associated with risk of type 2 diabetes when controlling for other alcoholic beverage use; however, the association for red wine was not statistically significant (Table 4). The apparent reduction in risk was similar for beer, white wine, and liquor; the multivariate relative risks for a 15-g increment were 0.70 (CI 0.60–0.81) for beer, 0.74 (0.62–0.88) for white wine, and 0.75 (0.66–0.84) for liquor. After controlling for frequency of any alcohol consumption, the beverage-specific association became nonsignificant.

**Drinking with meals.** Data on alcohol consumption with meals, collected in 1994, were available for 21,511 drinkers. During 4 years of follow-up, 283 cases of type 2 diabetes were diagnosed in this subcohort. Just under half (49.2%) of the men reported drinking <25% of their alcohol with meals in 1994, whereas 26.8% drank ≥75% with meals. The average total amount of alcohol consumed per day was only modestly correlated with the percentage alcohol consumed with meals ( $r = 0.15$ ).

The proportion of alcohol consumed with meals was not a significant predictor of type 2 diabetes over 4 years of follow-up after adjusting for confounding variables. For example, compared with men who consumed <25% of

TABLE 3

RR of type 2 diabetes in relation to pattern of alcohol use among drinkers: the Health Professionals Follow-Up Study, 1986–1998

Quantity of consumption divided into groups by frequency	Cases	Person-years	RR	
			Age and BMI adjusted	Multivariate†
1–2 drinking days per week				
<1 drink per drinking day	135	37,542	Reference group	Reference group
1–1.9 drinks per drinking day	85	27,000	0.91 (0.71–1.18)	0.84 (0.63–1.12)
2–2.9 drinks per drinking day	125	40,218	0.85 (0.67–1.09)	0.80 (0.62–1.03)
>3 drinks per drinking day	88	28,083	0.81 (0.62–1.05)	0.84 (0.64–1.10)
3–4 drinking days per week				
<1 drink per drinking day	23	10,024	0.68 (0.48–0.96)	0.67 (0.43–1.04)
1–1.9 drinks per drinking day	86	30,167	0.89 (0.69–1.16)	0.82 (0.62–1.08)
2–2.9 drinks per drinking day	47	21,410	0.66 (0.48–0.91)	0.67 (0.48–0.94)
≥3 drinks per drinking day	33	12,137	0.73 (0.53–1.00)	0.67 (0.45–0.98)
≥5 drinking days per week				
<1 drinks per drinking day	11	7,093	0.46 (0.30–0.72)	0.48 (0.27–0.85)
1–1.9 drinks per drinking day	122	50,711	0.74 (0.58–0.94)	0.70 (0.54–0.90)
2–2.9 drinks per drinking day	69	31,986	0.63 (0.47–0.83)	0.56 (0.42–0.76)
≥3 drinks per drinking day	102	39,569	0.66 (0.51–0.86)	0.59 (0.44–0.78)

Data are *n* or RR (95% CI). Quantity of consumption derived by dividing total grams of alcohol per week by the number of days alcohol is consumed each week. †RR controlled for age and BMI (seven categories each); smoking (pack-years: six categories); physical activity level; quintiles of dietary glycemic load, fiber, *trans*-fats and polyunsaturated fats, all energy adjusted; profession; history of diagnosed hypertension, hypercholesterolemia, coronary heart disease, or cancer; and family history of type 2 diabetes.

their alcohol intake with meals, the multivariate relative risk of diabetes was 0.89 (CI 0.66–1.19) among men consuming ≥75% of alcohol with meals. However, because of the smaller number of cases in this analysis, a modest association could not be excluded.

## DISCUSSION

In the current analysis, we found that frequent moderate alcohol consumption is inversely associated with risk of type 2 diabetes. Other aspects of consumption patterns, such as beverage choice, consumption with meals, or even overall amount consumed, did not substantially affect risk after taking frequency into account. Even low levels of alcohol, when taken regularly (five or more times per week), were associated with a lower risk of diabetes. Consumption of less than one standard drink per day, or less than seven standard drinks per week, when consumed on a regular basis, was associated with a significant reduction in risk of diabetes. However, when the same

weekly consumption was consumed over 1–2 drinking days in a week, there was no apparent benefit.

Our calculation of alcohol consumption relied on self-report, so frequency of alcohol consumption may have acted in part as a proxy measure for total alcohol consumption. It also may be more difficult to obtain accurate information on episodic consumption than regular consumption, and when asked to average their alcohol use, subjects may have tended to recall the modal amount of alcohol consumed (22). However, our assessment of average intake and frequency of consumption has previously been shown to correlate well with 2 weeks of dietary records (16,17). Furthermore, the data on consumption patterns were collected prospectively; thus, any error was likely to be nondifferential and bias our results toward the null. Despite some potential error, frequency was significantly inversely associated with incidence of type 2 diabetes, even after controlling for quantity.

In previous cross-sectional and prospective studies of

TABLE 4

RR of type 2 diabetes in relation to beverage choice among drinkers: the Health Professionals Follow-Up Study, 1986–1998

Beverage	RR for a 15-g increment in alcohol consumption		
	Age & BMI adjusted	Multivariate analysis 1	Multivariate analysis 2
Beer	0.80 (0.70–0.91)	0.70 (0.60–0.81)	0.91 (0.78–1.05)
<i>P</i>	0.0010	<0.0001	0.19
White wine	0.77 (0.65–0.90)	0.74 (0.62–0.88)	0.89 (0.74–1.07)
<i>P</i>	0.0014	0.0010	0.22
Red wine	0.91 (0.78–1.08)	0.92 (0.77–1.09)	1.01 (0.84–1.20)
<i>P</i>	0.28	0.33	0.87
Liquor	0.85 (0.76–0.94)	0.75 (0.66–0.84)	1.02 (0.89–1.16)
<i>P</i>	0.0017	<0.0001	0.80

Data are RR (95% CI). In multivariate analysis 1, RR controlled for age and BMI (seven categories each); smoking (pack-years: six categories); physical activity level; quintiles of dietary glycemic load, fiber, *trans*-fats and polyunsaturated fats, all energy adjusted; profession; history of diagnosed hypertension, hypercholesterolemia, coronary heart disease, or cancer; and family history of type 2 diabetes. In multivariate analysis 2, RR adjusted for frequency of total alcohol consumption as well as all covariates controlled for in model 1.

the association between alcohol consumption and glucose intolerance or diabetes, data on frequency of consumption have not been presented. In studies on ischemic stroke (23) and coronary disease (24,25), moderate alcohol consumption spread throughout the week has been found to be more beneficial than episodic consumption. On the other hand, alcohol's adverse health effects, such as hypertension, may also be increased with frequency of consumption (26–28). In the case of stroke and myocardial infarction, alcohol's short-term effects on platelet aggregation and fibrinolysis may be responsible for the greater benefit of regular consumption (29). Changes in other biological parameters are more likely to explain the benefits of frequent alcohol consumption in relation to type 2 diabetes.

In cross-sectional studies, usual moderate alcohol consumption has been found to be associated with improved insulin sensitivity (30–35), though this has not been a universal finding (36). In contrast, alcohol dependence and heavy drinking have been associated with impaired glucose tolerance (37–39). Experimental studies of the effect of acute moderate alcohol consumption on carbohydrate metabolism have also produced conflicting results, and at times have suggested reduced insulin sensitivity. In hyperinsulinemic-euglycemic clamp studies using doses of  $\leq 60$  g ethanol, alcohol acted as a preferred fuel, reducing glucose disposal (40,41). Administration of this amount of alcohol has been associated with enhanced insulin release and either reduced (12,40,41) or unchanged (42) glucose tolerance. The metabolism of alcohol produces a variety of effects on carbohydrate metabolism, including reduced gluconeogenesis and fat oxidation (11,43,44). Moderate doses of alcohol have also been reported to affect levels of the counter-regulatory hormones, growth hormone, and glucagon, particularly in response to hypoglycemia (45,46). The duration of many of the effects of alcohol on carbohydrate metabolism is not clear, but the results of this study suggest that at least some may be of relatively short duration. It is also possible that carbohydrate metabolism adapts over time to the presence of alcohol, so that the effects of chronic or regular alcohol use may be different to the effects of acute or episodic use.

In the current study, the inverse association between average daily consumption and risk of type 2 diabetes persisted in the highest category of alcohol consumption ( $\geq 50$  g/day), though the maximum risk reduction was reached among those drinking 30–49 g/day. The cohort had few heavy drinkers, so the results cannot be extrapolated to heavy drinking populations. Two community-based studies have shown increased risk of diabetes in subpopulations of heavy drinkers. In a study of Japanese employees, there was an increased risk of diabetes in lean men drinking  $>50$  g/day of ethanol (4). Similarly, in a 12-year follow-up of 524 U.S. adults from the general community, there was a significantly increased incidence of diabetes in men (but not women) with the highest tertile of alcohol consumption ( $>25$  g/day) (6). In keeping with these findings, two large prospective studies have reported a nonlinear association between alcohol consumption and risk of diabetes, with risk lowest in moderate drinkers and higher in both heavier drinkers and lower level drinkers or nondrinkers (3,47).

In heavy drinkers, diabetes may be secondary to reduced insulin secretion associated with chronic pancreatitis (48) or insulin resistance associated with alcohol-induced liver changes (49). Repeated large doses of alcohol alone have been shown to be capable of producing reversible insulin resistance (50,51). Heavy alcohol consumption may affect cortisol and adrenaline levels (11), and, in vitro, high concentrations of ethanol may lead to reduced insulin binding (42) and inhibition of intracellular signaling related to insulin (52).

Some of the apparent conflict in the results of past epidemiological studies may have arisen because of differences in drinking patterns and in the prevalence of heavy drinking between samples. Furthermore, often only linear associations appear to have been sought (7–9).

The current study finds no benefit of red wine over other beverage types. In contrast, the group with the greatest risk reduction (men drinking 30–49 g/day ethanol) consumed considerably more alcohol as beer or liquor than wine. Accordingly, frequency and quantity of ethanol consumption, rather than consumption of red wine's congeners, are inversely associated with incidence of diabetes. Although we found no benefit of drinking with meals over consumption at other times, the number of person-years of follow-up was lower for this analysis, and we cannot exclude a modest effect.

Critics in the past have expressed concerns that apparent benefits of moderate alcohol consumption may merely reflect lower alcohol consumption in sick people. In the current study, we found the reduced incidence of diabetes in moderate drinkers persisted when light drinkers, rather than nondrinkers, were used as a reference group. The same was true when lifelong abstainers or very light drinkers (rather than current nondrinkers or light drinkers) were used as a reference group.

In summary, frequent low-to-moderate alcohol consumption appears to offer the greatest protection against type 2 diabetes, regardless of the type of alcoholic beverage chosen or the total amount of alcohol consumed per week. The evidence from the literature of a possible U- or J-shaped association between alcohol consumption and incidence of diabetes is further illustration of the delicate balance between beneficial and harmful effects of alcohol. Decisions about alcohol consumption should consider the full range of benefits and risks to an individual; our data suggest that a reduction in type 2 diabetes may be among the benefits of regular moderate consumption.

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