Effect of Alcohol Consumption on Diabetes Mellitus

A Systematic Review

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Background: **Both diabetes mellitus and alcohol consumption are prevalent in the United States, yet physicians are poorly informed about how alcohol use affects risk for or management of diabetes.**

Purpose: **To conduct a systematic review assessing the effect of alcohol use on the incidence, management, and complications of diabetes mellitus in adults.**

Data Sources: **English-language studies in persons 19 years of age or older that were identified by searching the MEDLINE database from 1966 to the third week of August 2003 and the reference lists of key articles.**

Study Selection: **Two independent assessors reviewed 974 retrieved citations to identify all experimental, cohort, or case–control studies that assessed the effect of alcohol use on diabetes risk, control, self-management, adverse drug events, or complications.**

Data Extraction: **Two independent reviewers extracted data and evaluated study quality on the basis of established criteria.**

Data Synthesis: **Thirty-two studies that met inclusion criteria were reviewed. Compared with no alcohol use, moderate consumption (one to 3 drinks/d) is associated with a 33% to 56% lower incidence of diabetes and a 34% to 55% lower incidence of diabetes-related coronary heart disease. Compared with moderate consumption, heavy consumption (>3 drinks/d) may be associated with up to a 43% increased incidence of diabetes. Moderate alcohol consumption does not acutely impair glycemic control in persons with diabetes.**

Conclusions: **Moderate alcohol consumption is associated with a decreased incidence of diabetes mellitus and a decreased incidence of heart disease in persons with diabetes. Further studies are needed to assess the long-term effects of alcohol consumption on glycemic control and noncardiac complications in persons with diabetes.**

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Diabetes mellitus is one of the most common chronic diseases in the United States, affecting 7.8% of adults 20 years of age or older (1). The microvascular and macrovascular complications of diabetes make it the 6th leading cause of death and a leading cause of blindness in the United States (2). Successful long-term control of hyperglycemia decreases the risk for diabetic complications (3). Although a family history of diabetes is an established risk factor for type 2 diabetes, lifestyle factors also play an important role in its cause (4). For example, the incidence of diabetes has been associated with physical inactivity and obesity, both of which can be modified to decrease the risk for diabetes (5).

Alcohol consumption is also prevalent in the United States: An estimated 109 million Americans 12 years of age or older currently drink alcohol (6). Practicing physicians are thus likely to encounter patients who use alcohol in addition to having or being at risk for diabetes. Yet, physicians are poorly informed about how their patients' alcohol use affects risk for or management of diabetes.

We performed a systematic review of the medical literature to assess the effects of alcohol consumption on 5 aspects of the epidemiology and treatment of diabetes: incidence, glycemic control, adherence to therapy and self-care behaviors, medication-associated complications, and disease complications.

METHODS

Search Strategies

We searched the MEDLINE database for reports published from 1966 to the third week of August 2003 by using a search strategy developed in collaboration with a medical librarian. The search was limited to English-language studies of persons 19 years of age or older. We conducted separate searches for the Medical Subject Headings *diabetes mellitus, hypoglycemic agents, and receptors, angiotensin/antagonists & inhibitors*, combined with each of the following Medical Subject Headings: *ethanol, alcoholism, alcoholic beverages, alcohol-related disorders,* or *alcohol drinking*. In addition, we manually searched the reference lists of retrieved articles and relevant reviews.

Study Collection

Two reviewers independently assessed each MEDLINE citation by using predefined inclusion and exclusion criteria. To be included, a study had to be an experimental, cohort, or case–control study; include persons who had been administered or were current users of alcohol; include persons who had not been administered or were not users of alcohol; and have a relevant primary outcome. For analyses of the incidence of diabetes, the outcome was diabetes. For glycemic control, outcomes were glucose and hemoglobin A_{1c} levels. For self-management behaviors, outcomes were adherence to therapy, home glucose monitoring, diet, and exercise. For medication complications, outcomes were drug levels or adverse drug events. For diabetic complications, outcomes were acute complications, including diabetic ketoacidosis, hyperosmolar coma, infection, and amputation; chronic microvascular complications, including retinopathy, peripheral neuropathy, nephropathy, and erectile dysfunction; and chronic macrovascular complications, including coronary heart disease, cerebral vascular

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Key Summary Points

Best evidence suggests that moderate alcohol consumption is associated with a reduced incidence of diabetes mellitus.

Some evidence suggests that heavy alcohol use may be associated with an increased incidence of diabetes mellitus.

There is no evidence of an acute effect of moderate alcohol ingestion on glycemic control.

The effect of alcohol use on diabetes self-care behaviors has not been well studied.

Limited evidence suggests that ingestion of alcohol while using a sulfonylurea or thiazolidinedione does not result in an adverse event.

Strong evidence shows that moderate alcohol consumption is associated with a decreased incidence of coronary heart disease in persons with diabetes.

Evidence is insufficient to establish the effect of alcohol consumption on noncardiac complications in persons with diabetes.

disease, and peripheral vascular disease. Experimental studies in which alcohol was administered to healthy volunteers were considered beyond the scope of this review and were excluded. We used SPSS software, version 10.1 (SPSS, Inc., Chicago, Illinois) to calculate κ agreement coefficients. Ratings between reviewers had 95% agreement ($\kappa = 0.75$). Reviewer disagreements were resolved by discussion after review of the citation and the review protocol.

Assessment of Study Quality

Two reviewers independently rated the quality of each study by using the criteria of the U.S. Preventive Services Task Force for determining internal validity (7). For cohort studies, these criteria include consideration of and adjustment for potential confounders, maintenance of comparable groups, a low rate of and nondifferential loss to follow-up, use of valid measurements, use of clearly defined interventions, and consideration of important outcomes. For experimental trials, these specifications also include adequate randomization and intention-to-treat analysis. On the basis of these criteria, we assigned each study one of the following ratings: "good" (study meets all criteria well), "fair" (study does not meet at least 1 criterion but has no limitations that could invalidate its results), or "poor" (study does not meet at least 1 criterion and has important limitations). Studies that were found to be of poor quality were excluded. Ratings between reviewers had 89% agreement ($\kappa = 0.76$). Reviewer disagreements were resolved by consensus after review of the article and the review protocol.

Data Extraction

From each included study, 2 investigators abstracted data on the study sample, study duration, alcohol dose or definition of alcohol exposure, definition and method of measuring outcome, confounders for which the investigators controlled, and measure of association.

To aid in comparing results across studies, we converted the measures of alcohol consumption to a single scale whenever possible, in which one drink was equivalent to 12.6 g of ethanol. This conversion was based on the U.S. Department of Agriculture definition of a standard drink (8).

Role of the Funding Source

The funding source had no role in the collection, analysis, or interpretation of the data or in the decision to submit the manuscript for publication.

DATA SYNTHESIS

Search Results

We identified 974 studies. Of these, 942 were excluded because they did not meet the predefined selection criteria (**Figure**). Of the 32 included studies, 27 were studies of type 2 diabetes only (8–34), 2 were studies of both type 1 and type 2 diabetes (35, 36), and 3 did not specify the type of diabetes (37–39). No included study assessed the effects of alcohol consumption on diabetes self-care behaviors or on diabetic complications other than coronary heart disease and retinopathy.

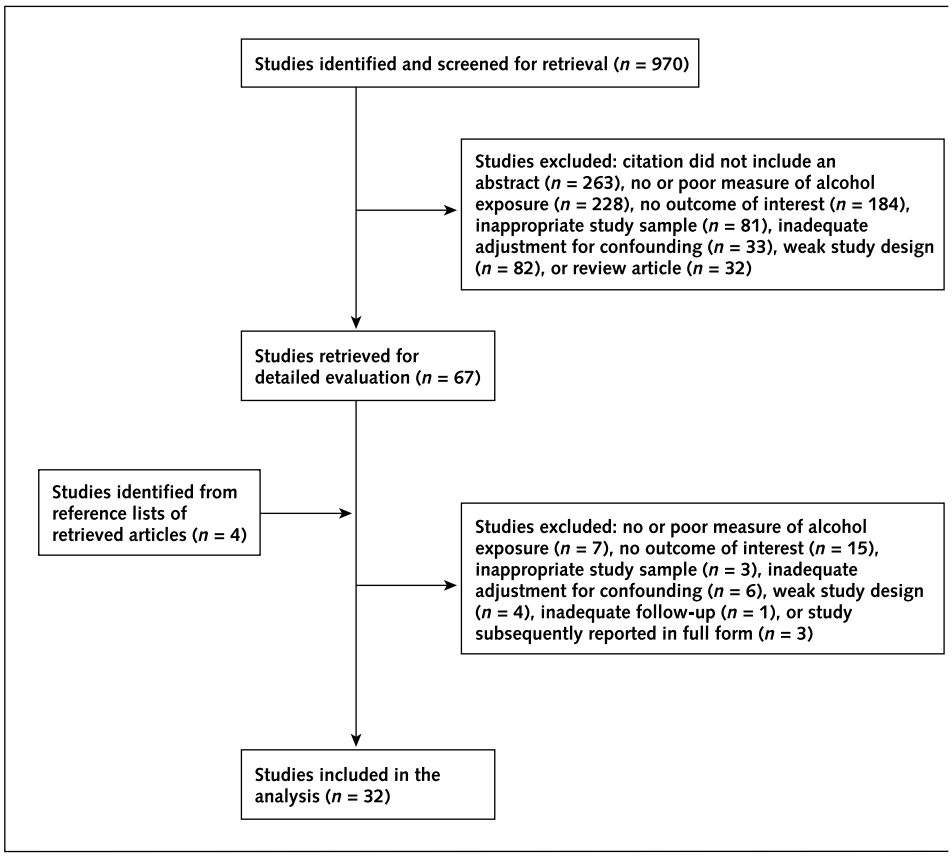
Association of Alcohol Consumption and Diabetes Incidence

Eighteen prospective cohort studies assessed the association between alcohol consumption and the incidence of diabetes (**Appendix Table**, available at www.annals.org). Alcohol consumption was categorized in numerous ways, including times per week, grams per week or per day, drinks or units per week, and milliliters or ounces per day. The method by which diabetes was measured also varied, in part because of the change in American Diabetes Association criteria for the diagnosis of diabetes in 1997 (40). Six studies used oral glucose tolerance tests (10, 13, 14, 17, 18, 21), 11 used fasting glucose levels (10, 13, 14, 16–21, 24, 25), and one used random glucose levels (16). Seven studies used self-report of diabetes (8, 9, 11, 15, 22, 23) or use of hypoglycemic medication (12) as the only measure of diabetes incidence. In 2 studies, the outcome included impaired fasting glucose and diabetes (19, 20), and in one study, the outcome was worsening glucose tolerance (progression from normal glucose tolerance to impaired glucose tolerance or diabetes, or progression from impaired glucose tolerance to diabetes) (17).

All studies were rated "fair." A limitation of many studies was that a standard screening test was not used to diagnose diabetes (8, 9, 11, 12, 15, 22, 23). Another common limitation was that alcohol intake was assessed at baseline only (9–11, 13, 14, 16–19, 21, 22, 25). Several studies dichotomized alcohol consumption and did not distinguish moderate from heavy alcohol use (11, 13, 20, 24). In addition, many studies failed to control for important confounders, including waist-to-hip ratio, family history of diabetes, and race.

Six studies used both an objective measure of diabetes

Figure. **Study selection.**



incidence and a nondichotomous categorical measure of alcohol consumption (10, 16, 17, 19, 21, 25). Five of these studies (10, 16, 19, 21, 25) and 3 additional studies (12, 22, 23) found a U-shaped relationship between alcohol consumption and incidence of diabetes, with moderate drinkers having the lowest risk for diabetes and nondrinkers and heavy drinkers having a higher risk. Compared with nondrinkers, persons who consumed approximately one to 3 drinks daily had a 33% to 56% reduction in the risk for diabetes. Compared with moderate drinkers, persons who consumed more than 3 drinks daily had up to a 43% greater risk for diabetes; however, this difference was statistically significant in only 2 studies (19, 25). The study that assessed impaired glucose tolerance and diabetes found no association between alcohol use and worsening glucose tolerance (17).

Three studies found an inverse relationship between alcohol consumption and diabetes incidence, with moderate drinkers having a 43% to 46% reduction in risk for diabetes compared with nondrinkers (8, 9, 15). In each of these studies, the prevalence of heavy drinking was low (1% to 3%), and power may have thus been insufficient to detect a relationship between heavy alcohol use and diabetes. The quantity of alcohol associated with the lowest risk for diabetes in these studies ranged from about one drink daily in women (15) to about 3 drinks daily in men (8). These studies are consistent with those reporting a U-shaped relationship between alcohol consumption and diabetes incidence.

Alcohol consumption was treated as a dichotomous variable in 4 studies. Two of these studies found no association between alcohol use and risk for diabetes (11, 13). One study reported an increased risk in persons who drank alcohol more than 2 to 3 times weekly (20). Another study found an increased risk for diabetes with current alcohol use in persons with a low body mass index ($\leq$22 kg/m^2) and a decreased risk in those with a normal body mass index (22.1 to 24.9 kg/m^2) (24). Two studies treated alcohol consumption as a continuous variable and found a positive association with a risk for diabetes in men but no association in women (14, 18).

Effect of Alcohol Consumption on Glycemic Control

Six experimental studies assessed the effect of alcohol consumption on glycemic control in persons with type 1 (35) or type 2 (26–29, 35, 37) diabetes. All of these studies included only 5 to 20 adults, and all were rated "fair." The ethanol dose ranged from approximately 1 to 2 drinks (27–29, 37) to 5 to 6 drinks (26, 35). Three studies were conducted after fasting (27–29). Ethanol was ingested with

Table. **Studies of the Association between Alcohol Consumption and Risk for Diabetic Complications***

Study, Year (Reference)	Sample	Study Quality	Duration of Follow-up	Measurement of Alcohol Consumption
Ajani et al. (Physicians' Health Study), 2000 (38)	2790 men with self-reported diabetes (enrollment cohort)	Good	5.5 y (480 876 person-years)	Baseline
	510 men with self-reported diabetes (randomized cohort)		12 y (1187 person-years)	Baseline
Solomon et al. (Nurses' Health Study), 2000 (32)	5103 women with self-reported diabetes	Fair	39 092 person-years	Baseline and years 4, 6, and 10
Tanasescu et al. (Health Professionals' Follow-up Study), 2001 (33)	2419 men with self-reported diabetes	Good	11 411 person-years	Baseline and 2 follow-up interviews
Valmadrid et al. (Wisconsin Epidemiologic Study of Diabetic Retinopathy), 1999 (34)	983 adults with older-onset diabetes recruited from primary care	Fair	12.3 y (7004 person-years)	Baseline
Moss et al. (Wisconsin Epidemiologic Study of Diabetic Retinopathy), 1994 (36)	436 adults with younger-onset and 193 adults with older-onset diabetes	Good	6 y	Baseline
	439 adults with younger-onset diabetes and 478 adults with older-onset diabetes			
Young et al., 1984 (39)	296 men from a diabetes clinic	Fair	4.7 y (mean)	Baseline

* BMI = body mass index; CABG = coronary artery bypass grafting; PTCA = percutaneous transluminal coronary angioplasty.

(26, 28, 35) or without food (27, 37) in 5 studies and was administered intravenously in one study (29). In all studies, participants served as their own controls by completing both the experimental arm and the control arm in random order. One study was double blinded (29).

Two studies found a decrease in plasma glucose concentration after alcohol consumption with (35) or without (37) a meal; in one study (35), this decrease was statistically (but not clinically) significant in persons with type 2 diabetes but not in those with type 1 diabetes. Another study found a statistically significant decrease in plasma glucose after ethanol infusion during a fast (29). Three other studies found that ingesting small to moderate amounts of alcohol with (26, 28) or without (27) food had no acute effect on glycemic control. Whether these negative studies were adequately powered to detect an effect was not stated.

Effect of Alcohol Consumption on Medication-Related Complications

Two experimental studies assessed the effect of alcohol consumption on medication-related complications. One study (rated "good") assessed the effect on troglitazone-related complications (30), and one study (rated "fair") on sulfonylurea-related complications (31). No study that met

Table—**Continued**

Outcome Measure	Events, *n*	Confounders for Which the Investigators Controlled	Categories of Alcohol Consumption	Measure of Association (95% CI)
Coronary heart disease mortality (confirmed by death certificates)	133	Age, aspirin use, smoking, physical activity, BMI, history of angina, hypertension, high cholesterol level	Rarely Monthly Weekly Daily	Relative risk: 1.00 1.11 (0.66–1.89) 0.67 (0.42–1.07) 0.42 (0.23–0.77)
Incident coronary heart disease (myocardial infarction, CABG, or PTCA) (confirmed by medical records)	120	Age, randomized treatment assignment (aspirin, β-carotene), smoking, physical activity, BMI, parental history of myocardial infarction, angina, hypertension, high cholesterol	Rarely Monthly Weekly Daily	Relative risk: 1.00 0.84 (0.46–1.54) 0.75 (0.45–1.26) 0.66 (0.38–1.16)
Self-reported myocardial infarction (majority confirmed by medical records)	204	Age, time period, aspirin use, smoking, physical activity, BMI, parental history of myocardial infarction, hypertension, hypercholesterolemia, menopausal status/postmenopausal hormone use, vitamin E use	None <0.4 drink/d ≥0.4 drink/d	Relative risk: 1.00 0.72 (0.54–0.96) 0.45 (0.29–0.68)
Fatal myocardial infarction (confirmed by medical records or autopsy reports)	72		None <0.4 drink/d ≥0.4 drink/d	Relative risk: 1.00 0.60 (0.36–1.01) 0.43 (0.21–0.88)
Myocardial infarction by self-report (majority confirmed by medical records)	71	Smoking, physical activity, BMI, family history of myocardial infarction, hypertension, high cholesterol level, diabetes duration, vitamin E use, intake of fiber, folate, energy intake, percent calories from polyunsaturated fat and trans fat	None 0–0.5 drink/d 0.5–2.0 drinks/d >2.0 drinks/d	Relative risk: 1.00 0.78 (0.52–1.15) 0.62 (0.38–1.00) 0.48 (0.25–0.94)
Fatal coronary heart disease (confirmed by medical records or autopsy reports)	32		None 0–0.5 drink/d 0.5–2.0 drinks/d >2.0 drinks/d	Relative risk: 1.00 0.79 (0.44–1.41) 0.59 (0.29–1.21) 0.45 (0.17–1.14)
Coronary heart disease mortality (confirmed by death certificates)	198	Age, sex, smoking, history of angina or myocardial infarction, insulin use, glycosylated hemoglobin level, C-peptide level, digoxin use, presence and severity of retinopathy	Never Former <0.2 drink/d 0.2–1.0 drink/d ≥1.1 drinks/d	Relative risk: 1.00 0.69 (0.43–1.12) 0.54 (0.33–0.90) 0.44 (0.23–0.84) 0.21 (0.09–0.48)
Incident retinopathy assessed by stereoscopic fundus photography	32 (younger onset), 98 (older onset)	Age, sex, glycemia	Per 0.5 drink/d	Odds ratio: 2.09 (0.04–1.07) for younger onset, 0.75 (0.40–1.42) for older onset
Progression of retinopathy assessed by stereoscopic fundus photography	246 (younger onset), 227 (older onset)			Odds ratio: 1.25 (0.75–2.08) for younger onset, 0.73 (0.44–1.20) for older onset
Incident retinopathy assessed by direct ophthalmoscopy	66	Duration of diabetes, glycemic control, impotence	≤1.9 drinks/d >1.9 drinks/d	Relative risk: 1.00 2.25 (1.15–4.42)

our inclusion criteria assessed the interaction of alcohol and angiotensin-converting enzyme inhibitors in persons with diabetes.

In a double-blind, placebo-controlled, parallel-group study in 23 patients with diet-controlled diabetes, participants were randomized to receive 200 mg of troglitazone or placebo daily for 45 days (30). On days 42 and 45, participants underwent a single-blind, crossover, placebo-controlled alcohol challenge test (0.6 g/kg ethanol [equivalent to 3 drinks] in orange juice, or orange juice alone) with a meal. The glycemic response to alcohol over 4 hours did not significantly differ between the 2 groups, and no serious adverse events were noted.

In a crossover study, 0.5 g of ethanol per kg of body weight (about 2.5 drinks) was administered to 5 groups of 10 persons with type 2 diabetes before and after 10 days of treatment with a sulfonylurea derivative (31). Chlorpropamide was found to decrease the rate of ethanol elimination from the blood. However, no significant difference was found in the glycemic response to ethanol over 6 hours. Neither study discussed the adequacy of the sample size.

Alcohol Consumption and Incidence of Diabetic Complications

Coronary Heart Disease

Four prospective cohort studies assessed the relationship between alcohol consumption and the incidence of coronary heart disease (32, 33, 38) or death (32–34, 38) in diabetic persons (**Table**). One of these studies was nested within a randomized clinical trial (38). The diagnosis of diabetes was determined by self-report in 3 studies (32, 33, 38) and by medical chart review in one study (34).

Ascertainment of alcohol consumption varied among studies. Alcohol consumption was expressed as grams per day (32, 34), drinks per day (33), or frequency of consumption (38). In classifying nondrinkers, one study distinguished former drinkers from lifetime abstainers (34).

The method of outcome assessment also varied. Death due to coronary heart disease was confirmed by death certificates (34, 38) or medical records and autopsy reports (32, 33). Incident coronary heart disease was defined as cases of myocardial infarction only (32, 33) or included patients who underwent coronary artery bypass graft or percutaneous transluminal coronary angioplasty (38).

Two studies were rated "good" (33, 38), and 2 were rated "fair" (32, 34). A common limitation was that alcohol consumption was assessed only at baseline (34, 38). In some studies, coronary heart disease was inconsistently measured; although most cases were confirmed by medical records, some were ascertained only through self-report and verification of hospitalization (32, 33).

Each study reported a decreased risk for death due to coronary heart disease in association with alcohol use; in 3 of the studies, the results were statistically significant (32, 34, 38). All 3 studies that assessed the incidence of coronary heart disease demonstrated an inverse association between alcohol consumption and risk for coronary heart disease; in 2 of the studies, the results were statistically significant (32, 33). Compared with nondrinkers, moderate drinkers had a 34% to 55% decrease in the incidence of coronary heart disease and a 55% to 79% decrease in the rate of death from coronary heart disease.

Diabetic Retinopathy

Two prospective cohort studies assessed the association between alcohol consumption and risk for retinopathy (**Table**). One study comprised men recruited from a diabetes clinic (39), and one included a population-based sample of men and women with diabetes (36). Both studies assessed alcohol consumption at baseline only. One study defined "heavy drinking" as consumption of more than 10 pints of beer or the equivalent weekly (39), and one expressed the odds of retinopathy per ounce of alcohol consumed daily (36). The prevalence of heavy drinking differed between the studies, as did the method of outcome assessment (direct ophthalmoscopy [39] or stereoscopic fundus photography [36]).

One study (rated "good") found no association between alcohol consumption and incidence or progression of diabetic retinopathy (36), whereas the other study (rated "fair") found an increased risk for diabetic retinopathy with heavy alcohol use (39).

DISCUSSION

We performed a systematic review of the literature to assess the effect of alcohol consumption on risk for and management and complications of diabetes mellitus. The best evidence suggests that moderate alcohol consumption is associated with a decreased risk for diabetes, whereas heavy alcohol consumption may be associated with an increased risk. Furthermore, ingestion of moderate amounts of alcohol appears to have no acute effect on glycemic control in persons with diabetes. We found no studies that assessed the effects of alcohol use on diabetes self-care behaviors. Limited data suggest that alcohol ingestion along with use of a sulfonylurea or thiazolidinedione does not increase the risk for an adverse drug event. Our analysis demonstrates that mild to moderate alcohol consumption in persons with diabetes is associated with a decrease in cardiovascular events. However, the effect of alcohol use on other diabetic complications, including retinopathy, nephropathy, and neuropathy, remains uncertain.

Although the results of the included studies did not all agree, the balance of evidence suggests that there is a U-shaped relationship between alcohol consumption and risk for diabetes. Compared with nondrinkers, moderate drinkers (those who consume one to 3 drinks daily) have a 33% to 56% lower risk for diabetes. In addition, some evidence suggests that compared with moderate drinkers, persons who consume more than 3 drinks daily have up to a 43% greater risk for diabetes. An association between light to moderate alcohol consumption and lower risk for diabetes is biologically plausible. Development of insulin resistance is a key factor in the pathogenesis of type 2 diabetes (41), and light to moderate drinking has been associated with enhanced insulin sensitivity in several observational studies (42–44). However, moderate alcohol consumption may be a marker for a healthy lifestyle that investigators did not entirely account for by adjusting for physical activity and diet. The association between heavy alcohol use and increased risk for diabetes in some studies may have been mediated by an increase in obesity, and particularly in truncal adiposity, which is a strong risk factor for type 2 diabetes (45). Although many studies controlled for body mass index, most did not control for anthropometric indices more closely correlated with intra-abdominal obesity, such as waist-to-hip ratio.

The epidemiologic studies included in our review had several important limitations. The methods of diagnosing diabetes were inconsistent among studies, and many studies used self-report of a diabetes diagnosis or use of a hypoglycemic medication rather than a standard screening

test. Even if self-report were reliable for detecting diagnosed cases in these samples, misclassification of undiagnosed cases is still likely to have occurred, because as many as 44% of Americans with type 2 diabetes have undiagnosed disease (1). If heavy drinkers were more likely than more moderate drinkers or nondrinkers to be screened for diabetes by using an objective test, differential misclassification may have contributed to the observed increase in risk for diabetes associated with heavy drinking in some studies.

Methods of measuring alcohol consumption were also inconsistent among studies. Lack of a standardized measure of alcohol use complicates the interpretation of findings across studies, especially since some investigators used frequency of consumption rather than quantity consumed. In addition, many longitudinal studies assessed alcohol consumption only at baseline, whereas some repeated measures of alcohol consumption. Most studies combined lifetime abstainers and former drinkers into one "nondrinker" referent group rather than analyzing the risk for diabetes in these 2 groups separately. Combining these groups could introduce bias because if many of the former drinkers stopped using alcohol for health reasons, an artifactual protective effect of alcohol use would result (46). Finally, the distribution of alcohol consumption differed among the study samples. For example, several studies contained few heavy drinkers and were thus underpowered to detect a relationship between heavy drinking and the incidence of diabetes.

Our review suggests that consumption of a moderate amount of alcohol does not acutely impair glycemic control in persons with diabetes. In fact, the data suggest that alcohol consumption may result in a small decrease in plasma glucose concentration in persons with type 1 or type 2 diabetes. This decrease may be the result of enhanced insulin secretion, or reduced hepatic gluconeogenesis (35). However, data on the long-term effects of alcohol consumption on glycemic control are lacking, and further research is needed.

We found no studies that addressed the effects of alcohol use on diabetes self-care behaviors, including medication adherence, home glucose monitoring, diet, or exercise. Heavy alcohol use may adversely affect diabetes self-care behaviors because it is associated with nonadherence to medical therapy in other chronic disease states, such as HIV infection (47). Given the importance of adherence in decreasing diabetes-associated morbidity and mortality, research is needed to assess the effect of alcohol use on self-care behaviors in persons with diabetes.

Few studies have assessed the effect of alcohol consumption on complications of medical therapy. However, the available data suggest that consumption of 2 to 3 drinks while taking a sulfonylurea or thiazolidinedione does not result in adverse events. Of note, chlorpropamide decreases the rate of ethanol clearance (31). Although we found no well-conducted studies of the effect of alcohol on complications of biguanide therapy, clinicians should be aware of the black-box warning that cautions against excessive alcohol intake while taking metformin, because alcohol use potentiates the risk for lactic acidosis (48).

Our review demonstrates that among persons with diabetes, mild to moderate alcohol consumption is associated with a 34% to 55% decrease in risk for coronary heart disease and a 55% to 79% decrease in risk for death from coronary heart disease. This finding is in concordance with epidemiologic studies conducted in general populations that have consistently demonstrated an inverse association between moderate alcohol consumption and coronary heart disease (49). The apparent protective effect of alcohol may result from the increase in high-density lipoprotein cholesterol level (50), decrease in platelet aggregation (51), or increase in fibrinolytic activity (52) associated with alcohol consumption. These beneficial effects of alcohol are particularly relevant in diabetic persons, in whom coronary risk factors (such as dyslipidemia) and a predilection to thrombosis are highly prevalent. The effect of alcohol use on the risk for noncardiac diabetic complications, including retinopathy, remains uncertain. Although polyneuropathy is a common complication of alcoholism (53), good-quality studies that assess the effect of alcohol use on diabetic neuropathy are lacking.

In summary, moderate alcohol consumption appears to be associated with a reduced risk for diabetes, whereas some evidence suggests that heavy alcohol consumption may be associated with an increased risk. Among persons with diabetes, ingestion of moderate amounts of alcohol appears to have no acute effect on glycemic control. The effect of alcohol use on diabetes self-care behaviors has not been studied. Limited data suggest that alcohol consumption in persons with diabetes is not associated with complications of medical therapy. Furthermore, among persons with diabetes, mild to moderate alcohol consumption is associated with a decreased risk for cardiovascular events. On the basis of these data, it is reasonable for physicians to inform patients with diabetes who already drink alcohol that moderate alcohol consumption (one to 3 drinks daily) does not appear to be associated with adverse outcomes. However, because most of the available evidence is observational, these data cannot support recommendation of alcohol consumption to persons with or at risk for diabetes who do not currently drink. Given the high prevalence of both diabetes and alcohol consumption in the United States, further research is needed to determine the long-term effects of alcohol consumption on glycemic control, self-management behaviors, and noncardiac complications of diabetes mellitus.

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Appendix Table. **Studies of the Association between Alcohol Consumption and Risk for Diabetes***

Study, Year (Reference)	Sample	Study Quality	Duration of Follow-up	Measurement of Alcohol Consumption
Ajani et al. (Physicians' Health Study), 2000 (9)	20 951 men age ≥ 40 y without cardiovascular disease or cancer	Fair	12.1 y (mean)	Baseline
Conigrave et al. (Health Professionals Follow-up Study), 2001 (8)	46 892 men	Fair	12 y (508 901 person-years)	Baseline and every 2 y
de Vegt et al. (Hoorn Study), 2002 (10)	1322 adults	Fair	6 y	Baseline
Feskens and Krumhout (Zutphen Study), 1989 (11)	841 men	Fair	25 y	Baseline
Gurwitz et al. (East Boston Senior Health Project), 1994 (12)	2737 adults age ≥ 65 y	Fair	6 y	Baseline and year 4
Hodge et al., 1993 (13)	574 Nauruan adults	Fair	5 y	Baseline
Holbrook et al. (Rancho Bernardo Study), 1990 (14)	604 adults	Fair	14 y	Baseline
Hu et al. (Nurses' Health Study), 2001 (15)	84 941 women	Fair	16 y (1 301 055 person-years)	Year 4, 8, 10, 14
Kao et al. (Atherosclerosis Risk in Communities Study), 2001 (16)	12 261 adults	Fair	6 y	Baseline
Lu et al. (Strong Heart Study), 2003 (17)	2601 American Indians	Fair	4 y (mean)	Baseline
Monterrosa et al. (San Antonio Heart Study), 1995 (18)	844 Mexican-American adults	Fair	8 y	Baseline
Nakanishi et al., 2003 (19)	2953 Japanese men without impaired fasting glucose, coronary heart disease, stroke, or antihypertensive medication	Fair	7 y (17 871 person-years)	Baseline
Sugimori et al., 1998 (20)	2573 Japanese adults	Fair	16 y	Entire observation period (16 y)

Appendix Table—**Continued**

Outcome Measure	Confounders for Which the Investigators Controlled	Categories of Alcohol Consumption	Measure of Association (95% CI)
Self-report of diabetes	Age, BMI, physical activity, smoking		Relative risk:
		Rarely/never	1.00
		1–3 drinks/mo	0.89 (0.68–1.18)
		1 drink/wk	0.86 (0.67–1.12)
		2–4 drinks/wk	0.70 (0.55–0.90)
		5–6 drinks/wk	0.69 (0.52–0.92)
		≥1 drink/d	0.54 (0.42–0.70)
Self-report of diabetes	Age, profession, family history of diabetes, BMI, physical activity, dietary glycemic load, fiber, trans fats and polyunsaturated fats (energy adjusted), smoking, hypertension, hypercholesterolemia, coronary heart disease, cancer		Relative risk:
		None	1.00
		<0.4 drink/d	1.05 (0.92–1.20)
		0.4–0.8 drink/d	0.80 (0.68–0.95)
		0.8–1.2 drinks/d	0.71 (0.59–0.86)
		1.2–2.4 drinks/d	0.64 (0.53–0.78)
		2.4–4.0 drinks/d	0.57 (0.45–0.71)
		≥4.0 drinks/d	0.61 (0.43–0.86)
Fasting glucose concentration ≥ 7.0 mmol/L (≥126 mg/dL), or 2-hour glucose concentration ≥ 11.1 mmol/L (≥200 mg/dL) during OGTT	Age, sex		Relative risk:
		None	1.56 (0.99–2.48)
		<0.8 drink/d	1.0
		≥0.8 drink/d	1.29 (0.80–2.06)
Self-report of diabetes verified by general practitioner	Age, energy intake, subscapular skin fold, smoking, heart rate		Hazard ratio:
		None	1.0
		≥0.8 drink/d	1.1 (0.6–2.3)
New use of hypoglycemic medication	Age, sex, BMI, physical activity level, blood pressure, high blood sugar by self-report		Odds ratio:
		None	1.2 (0.85–1.8)
		<0.8 drink/d	1.0
		0.8–1.6 drinks/d	0.41 (0.17–0.99)
		≥1.7 drinks/d	0.98 (0.53–1.50)
Fasting glucose concentration ≥7.8 mmol/L (≥140 mg/dL), or 2-hour glucose concentration ≥ 11.1 mmol/L (≥200 mg/dL) during OGTT, or taking hypoglycemic medication	Age, sex, family history of diabetes, BMI, 2-hour glucose level at baseline, 2-hour insulin level at baseline	Alcohol intake	Odds ratio: 0.649 (0.332–1.309)
Fasting glucose concentration ≥ 7.8 mmol/L (≥140 mg/dL), or 2-hour glucose concentration ≥ 11.1 mmol/L (≥200 mg/dL) during OGTT, or self-report of physician-diagnosed diabetes	Age, family history of diabetes, BMI, smoking, systolic blood pressure		Relative risk:
		Per 1.9 drinks/d	Men: 1.5 (1.01–4.48) Women: no association
Self-report of diabetes	Age, time, family history of diabetes, exercise, dietary score (intake of trans fat, fiber, glycemic load, polyunsaturated fat/saturated fat ratio), smoking, menopausal status, hormone replacement therapy		Relative risk: BMI <25.0 kg/m^2:
		0 drink/d	1.0
		<0.4 drink/d	0.85 (0.65–1.11)
		0.4–0.8 drink/d	0.64 (0.42–0.98)
		>0.8 drink/d	0.85 (0.63–1.14)
			BMI 25.0–29.9 kg/m^2:
		0 drink/d	1.0
		<0.4 drink/d	0.70 (0.60–0.82)
		0.4–0.8 drink/d	0.62 (0.48–0.81)
		>0.8 drink/d	0.57 (0.46–0.71)
			BMI ≥ 30.0 kg/m^2:
		0 drink/d	1.0
		<0.4 drink/d	0.81 (0.72–0.90)
		0.4–0.8 drink/d	0.60 (0.48–0.76)
		>0.8 drink/d	0.61 (0.50–0.74)
Fasting glucose concentration ≥ 7.0 mmol/L (≥126 mg/dL), or random glucose concentration ≥ 11.1 mmol/L (≥200 mg/dL), or current use of hypoglycemic medication, or self-report	Age, race, education, family history of diabetes, BMI, waist-to-hip ratio, physical activity, energy intake, smoking, hypertension		Relative odds
			Men:
		Abstainer	1.14 (0.79–1.65)
		Former user	1.06 (0.77–1.47)
		≤0.1 drink/d	1.00
		0.2–1.0 drink/d	1.12 (0.82–1.52)
		1.0–1.9 drinks/d	0.80 (0.55–1.17)
		1.9–2.9 drinks/d	1.07 (0.68–1.69)
		>2.9 drinks/d	1.50 (1.02–2.20)
			Women:
		Abstainer	1.10 (0.84–1.43)
		Former user	1.10 (0.81–1.49)
		≤0.1 drink/d	1.00
		0.2–1.0 drink/d	1.09 (0.80–1.49)
		1.0–1.9 drinks/d	0.81 (0.47–1.37)
		1.9–2.9 drinks/d	0.64 (0.25–1.64)
		>2.9 drinks/d	0.41 (0.10–1.77)
Impaired glucose tolerance or diabetes (fasting glucose concentration ≥ 7.0 mmol/L (≥126 mg/dL) or 2-hour glucose concentration ≥ 7.8 mmol/L (≥140 mg/dL) during OGTT)	Age, sex, BMI, smoking, physical activity, study center, waist circumference, hypertension, insulin, high-density lipoprotein cholesterol, triglycerides		Odds ratio:
		Abstainer	1.0
		Former user	0.90 (0.63–1.30)
		<0.6 drink/d	0.90 (0.59–1.37)
		0.6–1.7 drinks/d	1.28 (0.73–2.27)
		>1.7 drinks/d	1.18 (0.61–2.28)
Fasting glucose concentration ≥ 7.8 mmol/L (≥140 mg/dL), or 2-hour glucose concentration ≥ 11.1 mmol/L (≥200 mg/dL) during OGTT, or taking hypoglycemic medication	Age, socioeconomic status, structural assimilation, dieting, physical activity, BMI		Odds ratio:
		Per 0.1 drink/d	Men: 2.31 (1.03–5.15) Women: no association
Impaired fasting glucose or diabetes (fasting glucose concentration ≥ 6.1 mmol/L [≥110 mg/dL], or taking hypoglycemic medication)	Age, family history of diabetes, BMI, smoking, physical activity		Relative risk:
		0 drink/d	1.51 (1.07–2.13)
		<1.8 drinks/d	1.31 (0.93–1.84)
		1.8–3.6 drinks/d	1.00
		3.7–5.5 drinks/d	1.18 (0.87–1.61)
		>5.5 drinks/d	1.43 (1.01–2.02)
Fasting glucose concentration ≥ 6.1 mmol/L (≥110 mg/dL), or initiated therapy with hypoglycemic medication	Age, family history of diabetes, BMI, eating breakfast, dairy intake, smoking, hypertension, hyperlipidemia, hyperuricemia, fasting blood glucose		Hazard ratio:
		Never–sometimes	1.00
		2–3 times/wk–daily	1.80 (1.34–2.42)

Appendix Table—**Bottom**

Study, Year (Reference)	Sample	Study Quality	Duration of Follow-up	Measurement of Alcohol Consumption
Tsumura et al. (Osaka Health Study), 1999 (21)	6362 men without impaired fasting glucose, hypertension, or cirrhosis	Fair	4–16 y (62 016 person-years)	Baseline
Wannamethee, et al. (British Regional Heart Study), 2002 (22)	5221 men	Fair	16.8 y (mean)	Baseline
Wannamethee, et al. (Nurses' Health Study II), 2003 (23)	109 690 women age 25–42 y without gestational diabetes, heart attack, angina, or cancer	Fair	10 y	Baseline, year 3 and year 7
Watanabe et al., 2002 (24)	5636 Japanese adults without chronic pancreatitis	Fair	5.7 y (mean)	Baseline and annually
Wei et al., 2000 (25)	8633 men with a normal electrocardiogram and no history of myocardial infarction, stroke, or cancer	Fair	6 y (mean)	Baseline

* BMI = body mass index; OGTT = oral glucose tolerance test.

Appendix Table—**Bottom, Continued**

Outcome Measure	Confounders for Which the Investigators Controlled	Categories of Alcohol Consumption	Measure of Association (95% CI)
Fasting glucose concentration ≥ 7.8 mmol/L (≥140 mg/dL), or 2-hour glucose concentration ≥ 11.1 mmol/L (≥200 mg/dL) during OGTT; or fasting glucose concentration ≥ 7.0 mmol/L (≥126 mg/dL) if OGTT not performed	Age, parental history of diabetes, BMI, physical activity, smoking, fasting plasma glucose	Nondrinker <1.3 drinks/d 1.3–2.0 drinks/d 2.0–3.5 drinks/d >3.5 drinks/d	Relative risk: 1.0 0.99 (0.73–1.36) 1.0 (0.74–1.34) 0.67 (0.47–0.94) 1.10 (0.81–1.51)
Self-report of diabetes confirmed by medical record review	Age, social class, BMI, physical activity, smoking, prevalent coronary heart disease	None <0.1 drink/d 0.1–1.5 drinks/d 1.6–4.3 drinks/d >4.3 drinks/d	Relative risk: 1.1 (0.61–2.00) 1.0 0.81 (0.55–1.20) 0.66 (0.44–0.99) 0.96 (0.60–1.52)
Self-report of diabetes mellitus	Age, smoking, physical activity, BMI, family history of diabetes, oral contraceptive use, hypertension, antihypertensive drug use, cholesterol level, infertility	Lifelong abstainer Former drinker 0.4–1.2 drinks/d <0.4 drink/d 1.2–2.4 drinks/d >2.4 drinks/d	1.00 1.04 (0.86–1.24) 0.75 (0.62–0.91) 0.52 (0.38–0.72) 0.55 (0.29–1.05) 0.71 (0.33–1.52)
Fasting glucose concentration ≥ 7.8 mmol/L (≥140 mg/dL), or self-report of diabetes	Age, sex, current tobacco use, baseline fasting plasma glucose	 None Current None Current None Current	Relative risk: BMI ≤22 kg/m^2: 1.0 3.19 (1.09–9.37) BMI 22.1–24.9 kg/m^2: 1.0 0.41 (0.23–0.73) BMI ≥25 kg/m^2: 1.0 0.74 (0.44–1.25)
Fasting glucose concentration ≥ 7.0 mmol/L (≥126 mg/dL), or current insulin use	Age, parental diabetes, years of follow-up	Nondrinker <0.7 drink/d 0.7–1.4 drinks/d 1.4–3.1 drinks/d >3.1 drinks/d	Odds ratio: 1.8 (1.0–3.3) 1.4 (0.7–2.6) 1.0 2.2 (1.2–3.9) 2.4 (1.4–4.4)