Alcohol as a Risk Factor for Type 2 Diabetes

A systematic review and meta-analysis

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OBJECTIVE — To clarify the dose-response relationship between alcohol consumption and type 2 diabetes.

RESEARCH DESIGN AND METHODS — A systematic computer-assisted and hand search was conducted to identify relevant articles with longitudinal design and quantitative measurement of alcohol consumption. Adjustment was made for the sick-quitter effect. We used fractional polynomials in a meta-regression to determine the dose-response relationships by sex and end point using lifetime abstainers as the reference group.

RESULTS — The search revealed 20 cohort studies that met our inclusion criteria. A U-shaped relationship was found for both sexes. Compared with lifetime abstainers, the relative risk (RR) for type 2 diabetes among men was most protective when consuming 22 g/day alcohol (RR 0.87 [95% CI 0.76–1.00]) and became deleterious at just over 60 g/day alcohol (1.01 [0.71–1.44]). Among women, consumption of 24 g/day alcohol was most protective (0.60 [0.52–0.69]) and became deleterious at about 50 g/day alcohol (1.02 [0.83–1.26]).

CONCLUSIONS — Our analysis confirms previous research findings that moderate alcohol consumption is protective for type 2 diabetes in men and women.

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D iabetes is a major public health problem with long-term consequences including loss of vision; kidney failure; amputations; gastrointestinal, genitourinary, and cardiovascular symptoms; and sexual dysfunction (1). Several factors increase the risk of diabetes, including being overweight, lack of physical activity, and family history of diabetes (2). There is growing consensus that alcohol consumption is an influencing factor. The biological mechanism is uncertain, but there are several factors that may explain the relationship, including increases in insulin sensitivity after moderate alcohol consumption (3), changes in levels of alcohol metabolites (4), increases in HDL cholesterol concentrations (5), or via the anti-inflammatory effect of alcohol (6).

The exact nature of the dose-response relationship remains unclear (7). Several reviews have suggested a U-shaped relationship or a protective effect of moderate consumption with some question about the effect of higher levels of alcohol consumption (7–10). However, these reviews are narrative. Two quantitative reviews have been conducted. Carlsson et al. (11) categorized consumption into predetermined moderate- and high-consumption groups and used current abstainers or low consumers as the reference group. In their analysis, moderate consumption was associated with a 30% reduced risk of diabetes among men (relative risk [RR] 0.72

[95% CI 0.67–0.77]) and women (0.68 [0.61–0.75]). The risk associated with high consumption was described as being unclear. In the other meta-analysis, in which alcohol consumption was treated continuously, a U-shaped relationship was found for both men and women, with a more protective effect of moderate consumption observed for women (12). However, in both of these reviews, the reference group was composed of former drinkers and lifetime abstainers. Because former drinkers may be inspired to abstain due to health concerns, they may actually be at increased risk of developing diabetes, known as the sick-quitter effect (13). Our goal, therefore, was to examine the relationship between alcohol consumption and the risk of type 2 diabetes by conducting a meta-analysis that uses a flexible modeling approach and that, for the first time, uses lifetime abstention as the reference category.

RESEARCH DESIGN AND METHODS — Non–insulin-dependent diabetes (type 2) was the outcome. Although this outcome can be measured in various ways, the current World Health Organization (WHO) clinical diagnostic criteria were considered the gold standard for this meta-analysis. These criteria define diabetes by a fasting plasma glucose (FPG) level ≥ 7.0 mmol/l or a venous plasma concentration ≥ 11.1 mmol/l 2 h after a 75-g oral glucose challenge (14). The American Diabetes Association (ADA) also includes as sufficient criteria symptoms of hyperglycemia and a random plasma glucose concentration ≥ 11.1 mmol/l (1). The criteria, however, changed in 1996 (ADA) and 1999 (WHO) from an FPG ≥ 7.8 mmol/l.

Articles were found via a search of the following sources: Medline (via OVID and PubMed), the Cumulative Index to Nursing and Allied Health Literature (CINAHL), the Excerpta Medica Database (EMBASE), CAB Abstracts, World Health Organization Library Information System (WHOLIS), the System for Information on Grey Literature in Europe (SIGLE), the Alcohol and Alcohol Problems Science

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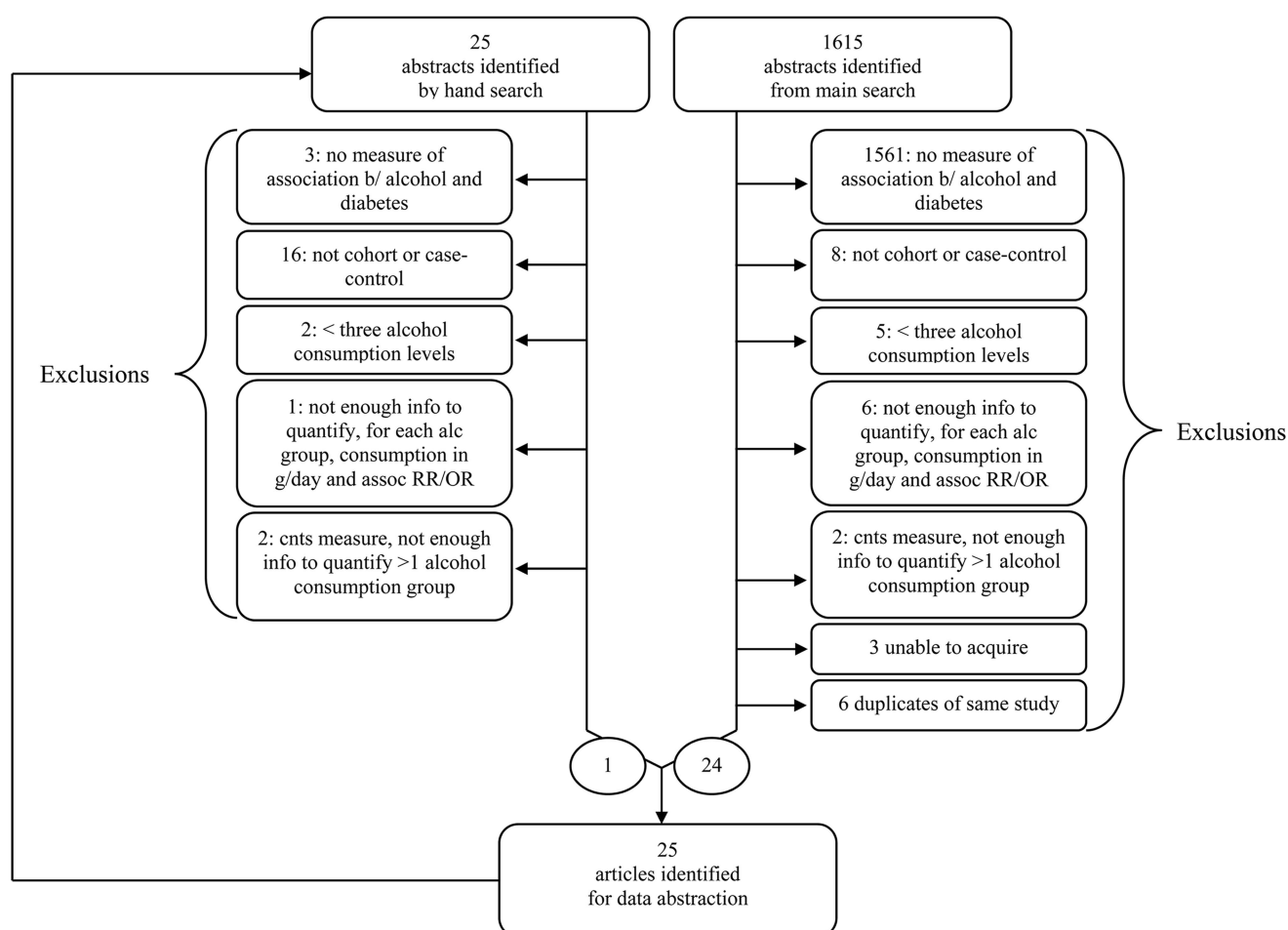
Figure 1—*Flow diagram of literature search for the relationship between alcohol consumption and risk of type 2 diabetes.*

(ETOH), Web of Science, and the Alcohol In Moderation (AIM; an alcohol industry database) databases. The databases were searched for reports published from 1 January 1980 to 31 January 2008, with the following keywords: alcohol or ethanol, diabetes, case-control or cohort or prospective, and risk. Animal studies, commentaries, editorials, letters, and review articles were excluded. No language restriction was applied. A simplified search using the terms alcohol or ethanol as well as diabetes was used for WHOLIS and SIGLE, which could not support the complex strategy. AIM is not a searchable index, but a selective list of articles was reviewed.

The results of the search are shown in Fig. 1. The strategy resulted in 1,615 hits after the removal of duplicates. The abstracts or complete publications were reviewed and excluded if they contained no indication of a measure of association between alcohol and either morbidity or mortality due to diabetes ($n = 1,561$), if the measure was cross-sectional ($n = 8$),

or if fewer than three levels of alcohol consumption (i.e., no dose-response data) were reported ($n = 5$). For all non-English articles, the authors were able to ascertain eligibility. Of the 41 publications remaining, 3 (student theses) could not be obtained and 6 did not contain enough information to quantify, for each alcohol group, consumption in grams per day and/or the measure of association. Two publications reporting consumption using continuous measures could not be revised to provide a measure of association. In cases where more than one publication was generated from a given study, the most comprehensive analysis was used. After exclusion of 6 such duplicates, 24 articles remained. The references of these and relevant review articles were checked for additional publications, and 25 articles were identified. One remained after applying the same criteria described above. Combining the database and hand searches, 25 articles were identified for data abstraction. However, four were excluded because the number of cases of

diabetes per alcohol exposure group, which was required for the analysis, was not reported. One was excluded because the measure was for a recent drinking occasion and not a typical day. Thus, 20 articles were included in the analysis (15–34).

Data abstracted included descriptors of study design in addition to measures of association. Alcohol consumption was converted to grams per day (if not originally reported as such). For studies that reported ranges of alcohol consumption for the categories, the midpoint was used. When the highest category was open ended, three-quarters the width of the previous interval was added to the lower limit. Where consumption was reported in drinks and not grams, the grams of pure alcohol equivalent described in the article, if stated, was used as a conversion factor; if not stated, conversion was based on typical drink sizes of the country (35). In one case, due to ambiguity over a suspected misprint, the authors were contacted via e-mail for clarification (16). 1.
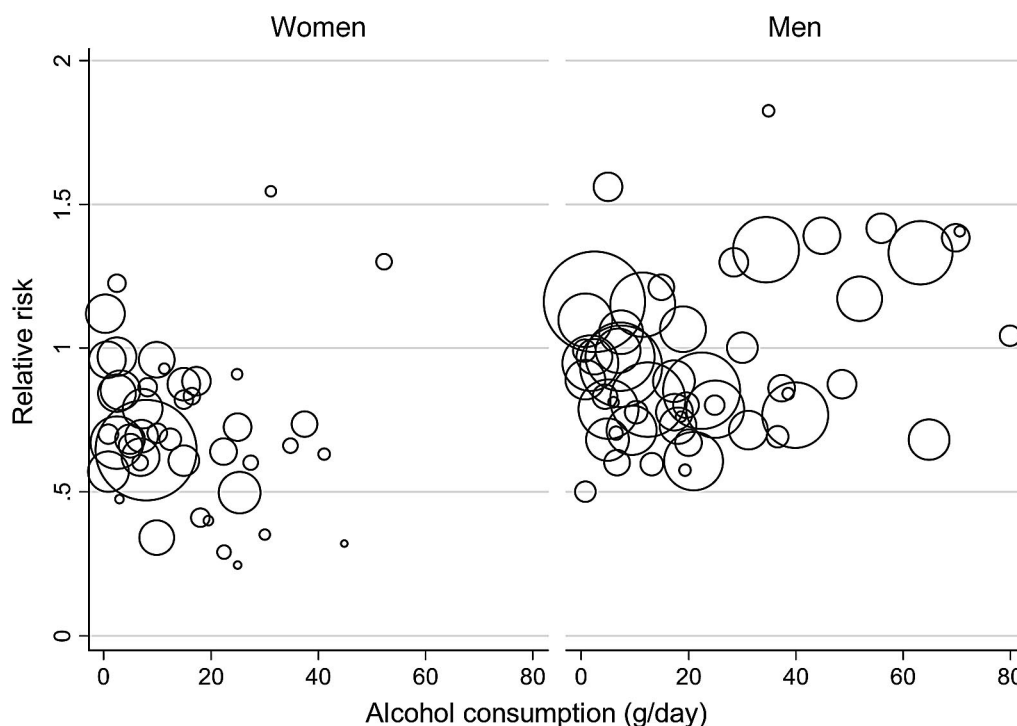
Figure 2—*Scatter plot of the RR estimates of type 2 diabetes reported in the 20 studies included in the analyses. Each study provides more than one RR estimate. The area of each circle is proportional to the precision of the RR estimate.*

The measures of effect abstracted were hazard ratios, odds ratios, and RRs but are referred to hereafter using the general term RR. Where RRs were not specifically presented but sufficient information was available, they were calculated. Where some consumption group was used as the reference, the RRs were reformulated to make abstainers the reference group. For studies for which various estimates including more or less covariates were reported, and a choice existed as to which to include, those that controlled for the most potential confounders not on the causal pathway were chosen. In five cases, crude measures were used when no other measure was available. In one study, where males and females were analyzed together, the RRs were applied to both men and women.

The studies contained two types of reference groups: lifetime and current alcohol abstainers. In order to use lifetime abstention as the reference, RRs for those studies that had current abstention as the reference were adjusted; for each sex, studies that had both current and lifetime abstainers were used to determine the overall prevalence of former drinkers among current abstainers and the RR of former drinkers relative to lifetime abstainers (weighted by precision). The RR for current abstention was then re-weighted by the overall prevalence and the RR calculated above and then multiplied by the dose-specific RRs.

The literature search, review, and abstraction were carried out by D.B. To ensure accuracy in abstraction, a limited double entry was performed by B.T. and the results compared. Both authors agreed on 5/5 articles reviewed for inclusion/exclusion and 605/664 data points abstracted over 10 articles. Where disagreements existed, both authors reviewed the materials together until a consensus was reached.

To assess potential publication bias, separate funnel plots were drawn for consumption <20 g/day and ≥20 g/day. In the absence of a known cutoff for decreasing and increasing diabetes risk, these categories were chosen because they correspond to the WHO's low-risk drinking level guidelines (36). The estimates were prepooled using the inverse variance–weighted method because funnel plot methodology assumes one overall RR per article. We assessed publication bias using the tests of Egger and Begg (37,38). The Q test was used to assess the presence of heterogeneity (39). Additionally, the I^2 statistic was used to measure inconsistency across studies and represents the proportion of variability in the estimates that is due to between-study variation (40).

We conducted the meta-regression using linear, first-order, and second-order fractional polynomial regression of the inverse variance–weighted data to estimate a best-fitting curve (41). Best-fit curves were assessed using decreased deviance compared with the reference model. Comparisons of curves to determine the best fit were made using a χ^2 distribution (41).

Two sensitivity analyses were conducted. Because the meta-analysis by Koppes et al. (12) suggested that studies that used self-report of diabetes status reported a more protective effect than those that tested for diabetes, we assessed whether the model varied by self-reported outcome. Also, we abstracted estimates that did not adjust for potential intermediates on the causal pathway to avoid over adjustment. However, this may have resulted in using estimates that were not sufficiently adjusted. Therefore, we repeated the analysis using the most-adjusted estimates available, selecting models for men and women based on fit and comparability with the main analysis. All analyses were conducted using Stata software (version 10.1; StatCorp, College Station, TX).

Table 1—Characteristics of 20 cohort studies included in the analyses

First author (year of publication)	Location	Sex	Age at baseline (years)	n	Follow-up Duration (years)	Follow-up Events (no.)	Alcohol consumption No. categories	Alcohol consumption Description	Diabetes definition	Adjustments
Ajami (2000)	U.S.	Men	40–85	20,951	12.7	766	6	No. of drinks: rarely/never, 1–3/month, 1/week, 2–4/week, 5–6/week, or ≥1/day	Self-report (physician participants)	Age, BMI, treatment assignment, smoking status, and physical activity
Beulens (2005)	The Netherlands	Women	49–70	16,330	6.2	760	7	g/week: teetotaler, 0–4.9, 5–29.9, 30–69.9, 70–139.9, 140–209.9, or ≥210	Self-report and/or urinary glucose strip and/or Dutch register of hospital discharge diagnosis	Age and BMI
Carlsson (2003)	Finland	Men	Not reported	10,970	19.4	277	4	g/day: abstainers, <5.0, 5.0–29.9, or ≥30.0	Linkage to Finnish national hospital discharge register and national drug register; patients who received only oral medication, dietary therapy, or insulin as an adjuvant treatment to hypoglycemic drugs were categorized as type 2 diabetic	Age and BMI
		Women	Not reported	11,808	19.8	297	4	g/day: abstainers, <5.0, 5.0–19.9, or ≥20.0		
Conigrave (2001)	U.S.	Men	40–75	46,892	10.9	1,571	7	g/day: 0, 0.1–4.9, 5.0–9.9, 10.0–14.9, 15.0–29.9, 30.0–49.9, or ≥50.0	Self-report; criteria: any of 1) one or more classic symptoms with FPG ≥7.8 mmol/l, nonfasting glucose ≥11.1 mmol/l, or OGTT ≥11.1 mmol/l, 2) elevated plasma glucose levels on two different occasions, 3) hypoglycemia treatment (but not type 1 diabetic)	Age and BMI
de Vegt (2002)	The Netherlands	Men and women combined	50–75	1,322	Not reported	241	3	g/day: 0, <10, or ≥10	FPG ≥7.0 mmol/l or OGTT ≥11.1 mmol/l; or subjects already being treated for diabetes	Age and sex
Djoussé (2007)	U.S.	Men	64–95	1,909	6.3	109	4	Drinks/week: never, former, <1, 1–7, or ≥7	Use of insulin or oral hypoglycemic agents; or FPG ≥7.0 mmol	Age, BMI, education, and smoking status
		Women	63–95	2,746	6.3	125	4	Drinks/week: never, former, <1, 1–7, or ≥7		

Table 1—*Continued*

First author (year of publication)	Location	Sex	Age at baseline (years)	Follow-up Duration (years)	Follow-up Events (no.)	Alcohol consumption No. categories	Alcohol consumption Description	Diabetes definition	Adjustments
Hodge (2006)	Australia	Men	40–69	4	179	5	g/day: never drinker, former drinker, <10, 10–20, 20–30, or >30	Participants mailed questionnaire covering diagnosis of diabetes, with verification from primary care physician	Age, BMI, country of birth, dietary glucose intake, dietary energy intake, and waist-to-hip ratio
		Women	40–69	4	183	4	g/day: never drinker, former drinker, <10, 10–20, or >20		
Holbrook (1990)	U.S.	Men	40–79	14	31	4	g/week: nondrinker, 0.1–84.3, 84.4–176.0, or ≥176.1	FPG ≥140 mg/dl, OGTT ≥200 mg/dl (11.1 mmol/l), or self-report of diabetes diagnosis by a physician	Age
		Women	40–79	14	44	4	g/week: nondrinker, 0.1–41.3, 41.4–117.4, or ≥117.5		
Hu (2006)	Finland	Men	35–74	13.4	517	3	g/week: none, 1–100, or >100	Linkage of info in Finnish national hospital discharge register and national drug register	Age; BMI; study year; education; systolic blood pressure; bread, vegetable; fruit, sausage, coffee, and tea consumption; smoking status; and physical activity
		Women	35–74	13.4	447	3	g/week: none, 1–100, or >100		
Kao (2001)	U.S.	Men	45–64	5.3	547	6	Drinks/week: lifetime abstainer, former drinker, ≤1, 1.1–7, 7.1–14, 14.1–21, or ≥21	Any of 1) FPG ≥7.0 mmol, 2) nonfasting glucose ≥11.1 mmol, 3) current use of diabetic medications, or 4) positive response to "Has a doctor ever told you that you had diabetes?"	None
		Women	45–64	5.4	569	6	Drinks/week: lifetime abstainer, former drinker, ≤1, 1.1–7, 7.1–14, 14.1–21, or ≥21		
Lee (2003)	Korea	Men	25–55	4	83	5	g/week: abstainer, 1–90, 91–180, 181–360 g, or >360 g	Serum fasting glucose concentration ≥126 mg/dl or taking diabetes medication	None
Lee (2004)	U.S.	Women	55–69	11	1,921	3	g/day: 0, 1–14, or ≥15	Self-report	None
Meisinger (2002)	Germany	Men	35–74	7.5	128	3	g/day: 0, 0.1–39.9, or ≥40.0	Self-report diagnosis or taking antidiabetes medications	Age, BMI, and survey
		Women	35–74	7.6	85	3	g/day: 0, 0.1–19.9, or ≥20.0		

Table 1—*Continued*

First author (year of publication)	Location	Sex	Age at baseline (years)	n	Follow-up Duration (years)	Follow-up Events (no.)	Alcohol consumption No. categories	Alcohol consumption Description	Diabetes definition	Adjustments
Stampfer (1988)	U.S.	Women	34–59	85,051	4	524	5	g/day: 0, <1.5, 1.5–4.9, 5.0–14.9, or ≥15.0	Self-report by questionnaire, then supplementary questionnaire regarding classic symptoms with FPG ≥140 mg/dll or random plasma glucose ≥200 mg/dll (or at least two elevated plasma glucose levels if no symptoms)	Age, BMI, and caloric intake
Strodl (2006)	Australia	Women	70–74	8,896	3	231	3	Drinks/day: none or rarely, 1–2, or ≥3	Asked whether a doctor had told them they had a diagnosis of diabetes	None
Tsumura (1999)	Japan	Men	35–61	6,362	9.7	456	5	ml/day: abstainer, 0.1–19.0, 19.1–29.0, 29.1–50.0, or ≥50.1	FPG ≥7.8 mmol/l, OGTT ≥11.1 mmol/l, or FPG ≥7.0 mmol/l	Age, BMI, smoking status, leisure time physical activity, parental diabetes, and FPG level
Waki (2004)	Japan	Men	40–59	12,913	Not reported	703	4	g/day: abstainer and infrequent drinker, ≤23.0, 23.1–46.0, or ≥46.1	Self-report "Has a doctor ever told you that you have diabetes?"	Age, BMI, smoking status, family history of diabetes, leisure time physical activity, and hypertension
		Women	40–59	15,980	Not reported	480	4	g/day: abstainer and infrequent drinker, ≤4.9, 5.0–11.5, or ≥11.6		
Wannamethee (2002)	U.K.	Men	40–59	5,221	16.8	198	5	Units/week: none, <1, 1–15, 15–42, or >42	Diagnosis of diabetes not accepted on basis of self-completed questionnaire unless confirmed in primary care records	Age and BMI

Table 1—*Continued*

First author (year of publication)	Location	Sex	Age at baseline (years)	n	Follow-up Duration (years)	Follow-up Events (no.)	Alcohol consumption No. categories	Alcohol consumption Description	Diabetes definition	Adjustments
Wannamethee (2003)	U.S.	Women	25–42	109,705	8.1	935	5	g/day: lifelong abstainer, former drinker, <5.0, 5.0–14.9, 15.0–29.9, or ≥30.0	Report on biennial questionnaire, then supplementary questionnaire regarding symptoms: before 1997 1) ≥1 classic symptoms and FPG ≥7.8 mmol/l or random plasma glucose ≥11.1 mmol/l, 2) ≥2 elevated plasma glucose results on different occasions (FPG ≥7.8 mmol/l, random plasma glucose ≥11.1 mmol/l, and/or OGTT ≥11.1 mmol/l in absence of symptoms), or 3) treatment with hypoglycemia medications	Age
Wei (2000)	U.S.	Men	30–79	8,633	6	149	5	g/week: abstainer, 1–61.8, 61.9–122.7, 122.8–276.6, or >276.6	FPG ≥7.0 mmol/l or history of diabetes plus current insulin therapy	Age, parental diabetes, and years of follow-up

RESULTS — Characteristics of the 20 studies included are presented in Table In total, data from 477,200 individuals, including 12,556 incident cases of diabetes, were included. Six studies included only men, five only women, eight both men and women (separately), and one men and women combined together. All were prospective cohorts. Adjustment for confounders varied. All but four adjusted for age at minimum; for these, only crude measures were available once those that adjusted for factors on the causal pathway were excluded. Diabetes ascertainment varied from self-report and data linkage to national registers to an oral glucose tolerance test (OGTT), the current clinical gold standard.

Figure 2 shows the RRs for the individual studies in the meta-analyses for women and men, respectively. Marked heterogeneity was found for both women ($Q = 69.97$, $P = 0.004$, $I^2 = 40\%$, 95% CI 13–58%) and men ($Q = 79.58$, $P = 0.008$, $I^2 = 35\%$, 95% CI 8–53%). Random-effects models were used for all subsequent analyses. No significant publication bias was detected.

Among women, the best-fitting model was the second-degree model with powers 0.5 and 3 (and function $\beta_1 x^{0.5} + \beta_2 x^3$) ($P < 0.001$). Among men, the best-fitting model was the second-degree fractional polynomial with powers 1 and 1 (and function $\beta_1 x + \beta_2 x \ln x$) ($P = 0.007$).

Figure 3 displays the relationship between the risk of alcohol consumption and type 2 diabetes among women and men. For both sexes, the relationship was U shaped. For women, the protective effect was greatest at the 24 g/day level, with a risk reduction of 40% compared with lifetime abstainers (95% CI 0.52–0.69). Alcohol consumption remained protective until just under 50 g/day. For men, the protective effect of alcohol consumption was greatest at 22 g/day, with the risk of diabetes being ~0.87 times that of lifetime abstainers (95% CI 0.76–1.00), and remained protective until consumption of ~60 g/day. Thus, for both women and men, the protective effect of alcohol consumption on incident type 2 diabetes was greatest with the consumption of about two drinks per day. Similarly, for both men and women, higher levels of consumption (above ~50 g/day for women and 60 g/day for men) were no longer protective but actually increased the risk for diabetes.

The mode of ascertainment of diabetes, self-report versus objective measure-
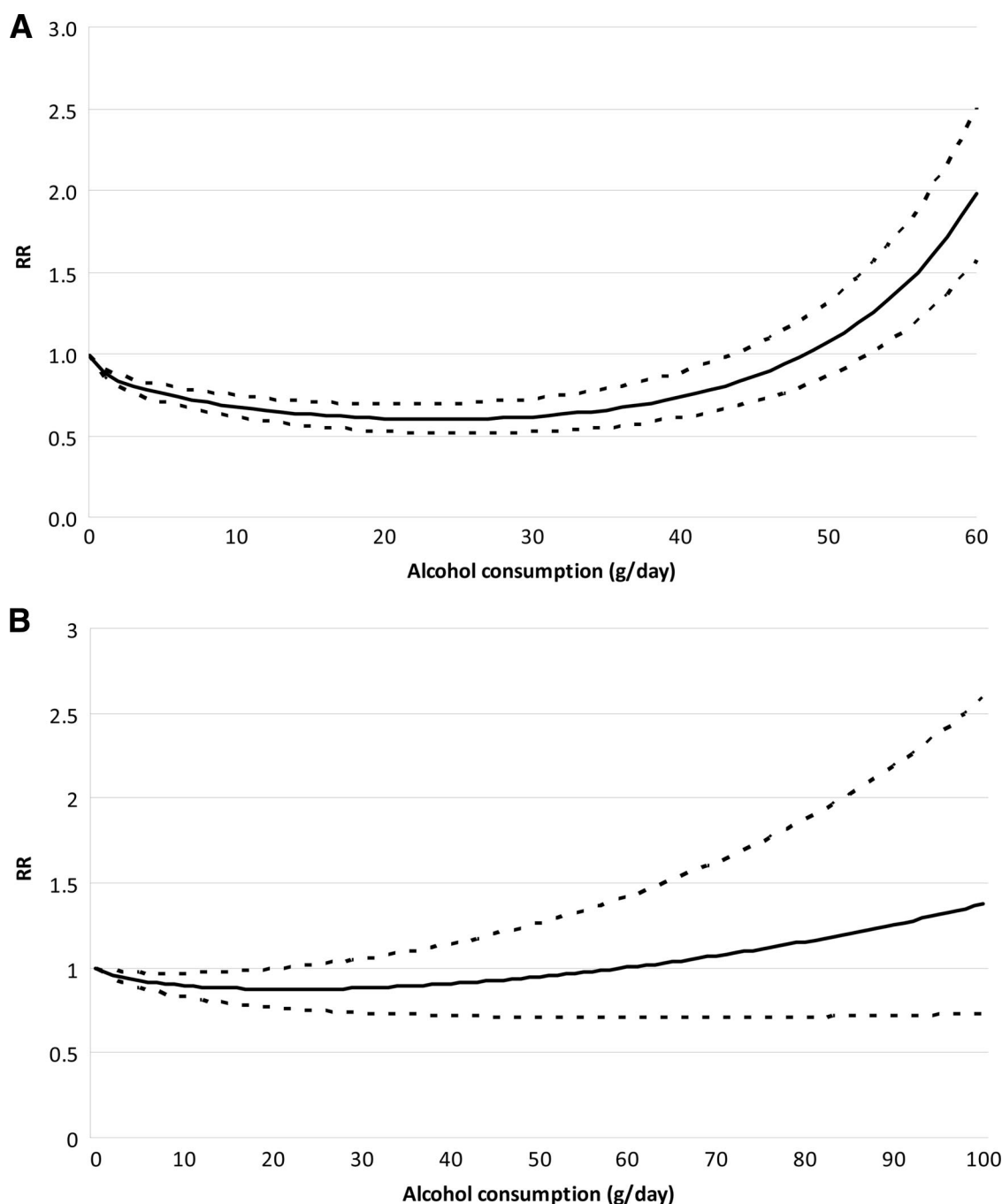
Figure 3—*Pooled and fitted RR estimates and 95% CI band. A: The highest single alcohol consumption measure for women was 52.35 g/day, thus x-axis is scaled to 60 g/day. B: Among men, the single highest alcohol consumption measure was 80.04 g/day.*

ment, did impact the risk relation with volume of alcohol exposure but only for men; there was no effect for women. Accordingly, we repeated the analyses separately for self-report versus no self-report in men and found a linearly decreasing dose-response relationship in the studies with self-report (15,18,27,31),as well as a model similar to the main analysis in the rest of the studies. The result in the group based on self report was mainly influenced by two studies (15,18) that accounted for 81% of the observations.

The second sensitivity analysis, performed using the most adjusted estimates available, resulted in models remarkably similar to those in the main analysis for both sexes. For men, the U-shaped relationship was most protective at a consumption of 22 g/day and crossed back over the RR 1 at 62 g/day. For women, the U-shaped relationship, as with the main analysis, was most protective at a consumption of 25 g/day and crossed back over to deleterious effect at 51 g/day.

CONCLUSIONS — Our meta-analysis confirms the U-shaped relationships between average amount of alcohol consumed per day and risk of incident type 2 diabetes among men and women, although a more protective effect of moder-

ate consumption was found for women. For women, the protective effect at moderate consumption and hazardous effect at higher consumption were both statistically significant. For men, the protective effect was statistically significant, but for higher consumption the CI did not exclude the RR 1.

Previous reviews found a protective effect of moderate alcohol consumption but limited evidence for a deleterious effect of heavy consumption. In comparison to the 2 previous meta-analyses, our analysis included 20 cohort studies in total: an additional 6 studies not included by Koppes et al. and an additional 10 not included by Carlsson et al. The meta-analyses by Koppes et al. used a total of 15 studies but included 2 that did not meet our inclusion criteria. That by Carlsson et al. included 13 studies, including 4 that did not meet our criteria. Thus, although there is substantial overlap in the data included in the respective analyses, our article is the most comprehensive in terms of the amount of data contributing to the summary estimates.

Meta-analyses are vulnerable to several biases. Although the gold standard in diabetes ascertainment is the OGTT, the individual studies ascertained diabetes status in various ways including self-report, linkage with national registries, and clinical tests. Additionally, because the diagnostic criteria cutoffs changed during the 1990s, even use of clinical tests was not consistent from study to study. As a result, some misclassification was likely. It is difficult to gauge the extent or type of any misclassification, although it is likely to be nondifferential and hence would attenuate any true causal association. In addition to misclassification due to testing differences, there is also potential misclassification due to the use of self-reporting of diabetes. However, we investigated the potential role of self-reported outcomes versus clinical tests and found no difference in results for women. Lastly, some misclassification of alcohol consumption may have occurred but would likely present as underreporting and not overreporting of consumption, resulting in a shift of the relationship curve to the left. That is, associations that appear to exist at a given consumption level in our analysis would, in fact, exist at some higher level.

Alcohol consumption, and the resulting health effects, is more complex than mere volume of consumption measured at one point in time. Though several studies measured alcohol more than once

(18,19,28,30,33), only one study used more than one alcohol measurement in its main analysis (17). Additional alcohol measurements would add weight to the validity and relevance to the alcohol measure because it is long-term consumption that tends to be of medical and public health concern. Additionally, the way in which alcohol is consumed (i.e., with meals or bingeing on weekends) affects various health outcomes (42). Thus, it may be the case that the risk of diabetes associated with heavy alcohol consumption is due to consumption mainly on the weekend as opposed to the same amount spread over a week. A few studies measured drinking pattern but did not present any analysis or did not present it in an analysis that combined it with volume (17,18,21).

Our meta-analysis addresses the sick quitter effect by making lifetime abstention the reference category. For diabetes, ignoring the sick quitter effect will tend to overestimate the benefit of moderate consumption and underestimate the risk of heavy consumption. However, adjusting for this required some estimate of the proportion of abstainers who are lifetime abstainers. For men, this was based on three studies (19,21,24) in which 37.6% of current abstainers were former drinkers and, for women, four studies (19,21,24,33) in which 49.6% of current abstainers were former drinkers. These estimates are a potential source of bias because the true underlying proportion of former drinkers may be higher or lower. Given the lack of a valid external estimate, we felt our data-driven approach was reasonable.

The included articles varied in adjustment for potential confounders. It was not possible to include only articles thath adjusted for the same factors. The sensitivity analysis in which the most fully adjusted estimates were used resulted in a relationship similar to that found in the main analysis. This consistency of results adds weight to the validity of our findings.

We found significant heterogeneity among men and women, which was expected because of the different methods used in the individual studies. Most studies were conducted in Western countries with the exception of three studies of Japanese and Korean populations; however, this was not a significant source of heterogeneity for men or women (analyses not shown). Study type cannot be a source of heterogeneity because only cohort studies were included, though the variable follow-up time may have contributed. The

finding of heterogeneity indicates that there are additional factors such as pattern of consumption that should be considered in future research.

Our findings confirm previous research, both individual studies and summary estimates, of the U-shaped relationship between average alcohol consumption and risk of diabetes in both men and women. Although the biological mechanism responsible for this relationship is still a matter of research, several possibilities exist including increased insulin sensitivity with low levels of alcohol consumption. These factors, together, add weight to the argument for a causal role of alcohol consumption in diabetes. Alcohol consumption in men and women should thus be limited to moderate amounts, and heavy consumption should be discouraged. Moreover, the balance of risk of alcohol consumption on other diseases and health outcomes, even at moderate levels of consumption, may outweigh the positive benefits with regard to diabetes.

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