ORIGINAL ARTICLE

Specific types of alcoholic beverage consumption and risk of type 2 diabetes: A systematic review and meta-analysis

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ABSTRACT

Aims/Introduction: Previous meta-analyses identified an inverse association of total alcohol consumption with the risk of type 2 diabetes. The current study further explored the relationship between specific types of alcoholic beverage and the incidence of type 2 diabetes.

Materials and Methods: A search of PubMed, Embase and Cochrane Library databases from January 1966 to February 2016 was carried out for prospective cohort studies that assessed the effects of specific types of alcoholic beverage on the risk of type 2 diabetes. The pooled relative risks with 95% confidence interval were calculated using random- or fixed-effect models when appropriate.

Results: A total of 13 prospective studies were included in this meta-analysis, with 397,296 study participants and 20,641 cases of type 2 diabetes. Relative to no or rare alcohol consumption, wine consumption was associated with a significant reduction of the risk of type 2 diabetes, with the pooled relative risks of 0.85, whereas beer or spirits consumption led to a slight trend of decreasing risk of type 2 diabetes (relative risk 0.96, 0.95, respectively). Further dose–response analysis showed a U-shaped relationship between all three alcohol types and type 2 diabetes. Additionally, the peak risk reduction emerged at 20–30 g/day for wine and beer, and at 7–15 g/day for spirits, with a decrease of 20, 9 and 5%, respectively.

Conclusions: Compared with beer or spirits, wine was associated with a more significant decreased risk of type 2 diabetes. The present study showed that wine might be more helpful for protection against type 2 diabetes than beer or spirits.

INTRODUCTION

Diabetes is a chronic metabolic disease characterized by hyperglycemia. Approximately 439 million people around the world are estimated to develop diabetes by the year 2030, and 12% of global health expenditure was spent on diabetes in 2010, estimated to rise to US$490 billion over the next two decades.[1] Type 2 diabetes, accounting for approximately 90% of diabetes, has become a global public health concern as a result of population aging, urbanization and associated lifestyle changes.[2,3] Given the rapid increased prevalence worldwide and substantial economic burden, identifying the risk factors is of importance for the prevention of type 2 diabetes.

Diverse risk factors, such as sugar-sweetened beverages, smoking and coffee consumption, have been investigated to be associated with the incidence of type 2 diabetes.[4–6] A number of recent prospective studies have also attracted attention to the role of alcohol consumption in the development of type 2 diabetes.[7,8] A previous meta-analysis had considered alcohol consumption as a risk factor for type 2 diabetes,[9] and showed that moderate alcohol consumption lowered the risk of type 2 diabetes, with a U-shaped dose–response between them.[10,11] In addition, in view of the misclassification bias, a more recent meta-analysis undertaken by Knott *et al.*[12] in 2015 had further

revised the relationship and dose–response between alcohol consumption and type 2 diabetes.

Alcoholic beverages are mainly categorized as wine, beer and spirits (liquor). Different effects of specific alcoholic beverages on diseases have been shown. A recent study reported that spirits or liquor drinkers seemed to have higher risk for mortality, stroke, cancer, injury, admission to hospital, and the composite outcome than wine and beer drinkers.[13] In addition, wine consumption was associated with the lowest risk for cardiovascular disease.[13] Similar observations are also shown in the relationship between specific alcoholic beverages and type 2 diabetes. A prospective study showed that wine was the only alcoholic beverage that decreased the risk of type 2 diabetes in the male population. In contrast, there were no significant associations for beer and spirits consumption.[14] These findings suggest the potential differential associations of specific alcohol types and the risk of type 2 diabetes.

Several studies have explored the issue of whether the consumption of wine, beer or spirits (liquor) had a differential association with the risk of type 2 diabetes.[15,16] However, to our knowledge, the existing meta-analyses have not systematically assessed the association of specific types of alcoholic beverage with the risk of type 2 diabetes. Hence, in the present article we included 13 prospective studies, and carried out a systematic review and meta-analysis of the association of specific types of alcoholic beverages with the risk of type 2 diabetes.

MATERIALS AND METHODS

Search strategy

We did not prospectively register this meta-analysis, but carried it out in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. We searched the PubMed (MEDLINE), Embase and Cochrane Library databases for prospective cohort studies that evaluated the association of the consumption of wine, beer or spirits with the risk of type 2 diabetes between January 1966 and February 2016. The search terms included an alcohol-related term ("alcohol" "ethanol," "wine," "beer," "spirits," "liquor" or "drink"), plus a diabetes-related term ("type 2 diabetes," "T2DM" or "diabetes"), plus a term indicative of prospective data ("prospective," "cohort," "incidence," "case"). A typical electronic search strategy was shown as follows: "(alcohol or ethanol or drink or wine or beer or liquor or spirits) and (type 2 diabetes or T2DM or diabetes) and (cohort or prospective or case)". Titles and abstracts of the resulting publications were screened for articles that are possibly of interest for our meta-analysis. In addition, reference lists of retrieved papers and recent reviews were manually scanned for identifying other potentially eligible studies. No language restriction was applied. Unpublished literatures, including conference abstracts and working papers, were not included.

Study selection

Two reviewers (JH and XW) identified articles eligible for further meta-analysis according to the following criteria: (i) the study design was a prospective cohort or case–cohort; (ii) the exposures were reported as specific alcoholic beverages including wine, beer or spirits (liquor) consumption; (iii) the outcome was the risk of type 2 diabetes; and (iv) adequate data of the association of specific types of alcoholic beverage with the risk of type 2 diabetes were reported. Studies were excluded if they: (i) were review articles, meta-analyses or case reports, and retrospective cohort, cross-sectional or case–control in design; (ii) did not use the incidence of type 2 diabetes as the outcome; (iii) had inadequate relevant information; or (iv) were duplicate publications.

Data extraction and quality assessment

One author (JH) extracted the data, and another (XW) independently double-checked the available data. The following information was extracted from each included article: first author's name, publication year, country, sex, age, length of follow up, sample size, number of type 2 diabetes events, type of alcoholic beverage, confounder adjustment and risk estimates for each exposure category.

The relative risks (RRs) were used as the common measure of association across studies. The odds ratios (ORs) and hazard ratios (HRs) used in the original publications were interpreted to reflect RRs. When more than one RR, OR or HR were shown, the one adjusted with the most potential confounders was extracted.

We used the Newcastle–Ottawa Scale (NOS) to assess the methodological quality of included studies.[17,18] For cohort studies, the NOS is divided into three categories: (i) selection (0–4 points); (ii) comparability (0–2 points); and (iii) outcome (0–3 points). The scale ranges from 0 to 9 points, with higher points indicating the higher study quality.

Statistical analysis

For analyzing the effects of different alcoholic dosages, grams per day was used to evaluate alcohol consumption. If studies were not originally reported as expected, the daily alcohol intake was converted to grams per day according to the amount of pure alcohol equivalent described in the articles. For studies that only reported ranges of alcohol consumption for the categories, the midpoint of the upper and lower limits in each category was assigned as the average consumption. If the upper limit of a category was not reported, we assigned 25% higher than the lower limit of that category as the mean consumption. Correspondingly, if the lower limit was not provided, we assigned one-half of the upper limit of the category as the mean consumption. In this meta-analysis, alcohol consumption was categorized into three groups: low (0–10 g/day), moderate (10–20 g/day) and high (>20 g/day). The alcohol consumption categories in each study were assigned into the aforementioned three groups according its average consumption. If a study reported more than one RR within one of the aforementioned three groups, a pooled RR was calculated for the study.

For the dose–response meta-analysis, a spline model was used, and the studies were included when they had at least three quantitative categories. We extracted the data of cases and person-years for every category. If these data were not reported, we estimated them according to the provided total numbers of cases or person-years.

We calculated the natural logarithms of the RR estimates from the individual studies to normalize the data, and used the natural logarithms of the reported 95% confidence interval (CI) limits to calculate the standard errors of the log RR estimates. The RRs reported separately by alcohol dosage category in a study were pooled by a fixed effects model before combining it with the overall meta-analysis. Considering that the risk estimates differed across studies, we used a random effects model to combine the reported RRs in these studies.

The heterogeneity was tested using a standard Cochran Q statistic ($P < 0.1$), and an I^2 statistic with I^2 values of 50% or more indicated a high heterogeneity.[19–21] Stratified analysis was carried out for sex, study quality and the length of follow up. Egger's test and Begg's test were used to assess the potential publication bias.[22,23] A P-value <0.1 was considered to be statistically significant. To assess the influence of individual studies on the pooled results, a sensitivity analysis was carried out by excluding each study one by one and recalculating the combined RRs on the remaining studies. All analysis was carried out with STATA 12.SE statistical software (StataCorp, College Station, TX, USA).

RESULTS
Characteristics of studies
In terms of study selection, the initial search retrieved 10,722 citations from PubMed, Embase and Cochrane Library database, plus 105 additional articles identified from the conference lists of relevant papers. After removing the duplicates, the unique 8,672 articles remained. Of these, 8,434 articles were excluded after the first screening based on the abstracts or titles. The remaining 238 articles were screened for further full-text review. In the second screening, we excluded a total 225 articles that did not fulfill the inclusion criteria (161 articles for not providing adequate data of the association of specific types of alcoholic beverage with the risk of type 2 diabetes; 6 articles for animal studies; 47 review articles, letters or meta-analyses; and 11 articles for cross-sectional design), ultimately leaving 13 articles for inclusion in the systematic review and meta-analysis (Figure 1).[14,24–35]

The included 13 prospective cohort studies comprised total 397,296 study participants and 20,641 cases of type 2 diabetes. The main characteristics of these 13 studies are shown in Table 1. As shown, four studies were carried out in the USA, seven in Europe, one in Asia and one in Oceania. Eight studies included both men and women, four studies included only women and one study only men. The duration of follow up in these studies ranged from 2 to 32 years, with an average of 9.3 years. All studies reported risk estimates between specific alcoholic beverages (wine, beer or spirits) and the incidence of type 2 diabetes, with associated 95% CIs. Type 2 diabetes was
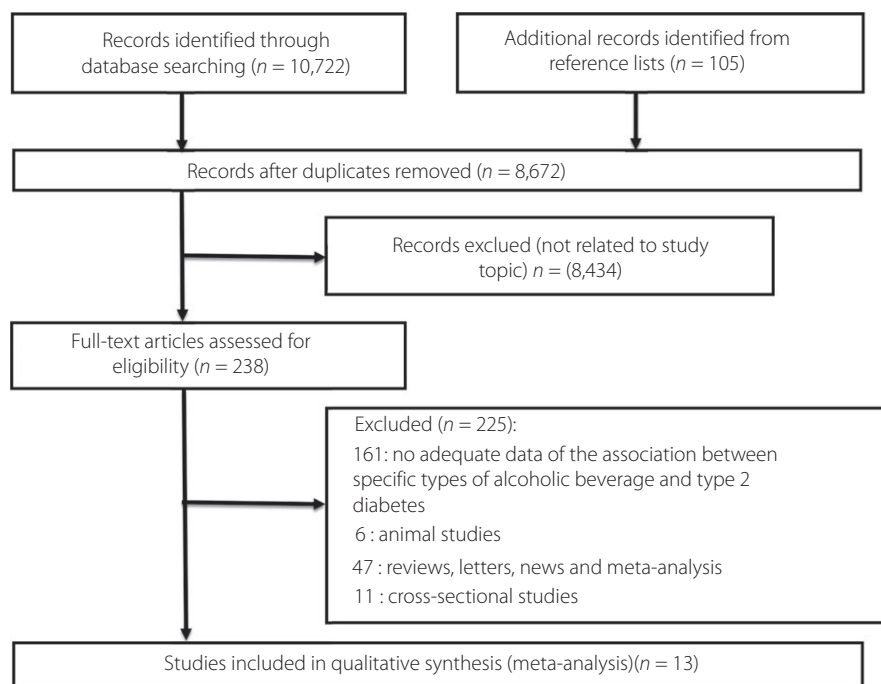

Figure 1 | Flow diagram for selection of studies.

Table 1 | Basic characteristics of the included studies

Study ID	Country	Sex	Age (years)	Follow-up (years)	Total n	n	Type 2 diabetes assessment	Type of alcoholic beverage	Confounding adjustments	Study quality (nos)
Adjemian et al. 2015[24]	USA	M & W	Mean 55	2	24,784	1,487	Self-reported	Wine, beer, liquor	Race, region, marital status	5
Marques-Vidal et al. 2015[25]	Sweden	M & W	Mean 51.7 ± 10.5	5.5	4,765	284	Serum fasting glucose ≥7 mmol/L or receiving treatment for diabetes	Wine, beer, spirits	Age, sex, BMI categories, waist circumference, maternal and paternal diabetes, hypertension, heart rate, smoking status, educational level and physical activity	8
Fagherazzi et al. 2014[26]	French	W	Mean 52.7 ± 6.6	14	66,485	1,372	Self-reported	Wine, beer, spirits	Age, years of education, smoking status, physical activity, hypertension, hypercholesterolemia, family history of diabetes, omega 3 fatty acid intake, carbohydrate intake, energy from fat and protein, coffee, dietary patterns, fruit and vegetables, processed meat consumption, and PRAL score and BMI	6
Shi et al. 2013[27]	China	M	40–74	5.4	51,464	1,304	Self-reported	Wine, beer, liquor	Age, energy intake, physical activity, METs, smoking, education level, occupation, income level, hypertension, family history of diabetes, BMI, WHR	8
Rasouli et al. 2013[28]	Norway	M & W	≥20	11	42033	940	Fasting blood glucose measurement and analysis with regard to levels of C-peptide and anti-GAD	Wine, beer, spirits	Age, lifestyle, family history and intake of the other types of beverage	7

Table 1 (*Continued*)

Study ID	Country	Sex	Age (years)	Follow-up (years)	Total *n*	*n*	Type 2 diabetes assessment	Type of alcoholic beverage	Confounding adjustments	Study quality (nos)
Beulens *et al.* 2012[29]	European	M & W	35–70	9.9	26,817	11,559	Self-reported diabetes from follow-up questionnaires and linkage to primary or secondary care registers, medication use, hospital admissions and mortality data	Wine, beer, spirits	Age, BMI, education level, smoking status, physical activity index, energy intake, and intake of fruit, vegetables, red meat, processed meat and coffee	7
Cullmann *et al.* 2012[30]	Sweden	M & W	35–56	8–10.0	5,128	162	OGTT	Wine, beer, spirits	Age, BMI, tobacco use, physical activity, family history of diabetes and education	6
Djousse *et al.* 2007[31]	USA	M & W	Mean 73.2 ± 5.2 for men, mean 72.4 ± 5.3 for women	6.3	4,655	234	Fasting blood glucose ≥7 mmol/L or using insulin or oral hypoglycemic agents	Wine, beer, liquor	Age, sex, BMI, education and smoking	7
Hodge *et al.* 2006[14]	Australia	M & W	40–69	4	31,422	362	Self-reported	Wine, beer, spirits	Age, country of birth, dietary glycemic index, dietary energy intake and alcohol intake from other beverage types	5
Beulens *et al.* 2005[32]	European	W	49–70	6.2	16,330	760	Self-reported	Wine, beer, liquor	Age, BMI, smoking status, education, systolic blood pressure, menopause, physical activity, family history of type 2 diabetes, daily energy intake and hypertension	7
Lapidus *et al.* 2005[33]	Sweden	W	38–60	32	1,462	126	Fasting blood glucose ≥7 mmol/l, or taking therapy against diabetes, or diagnosis of diabetes made by physician, or diagnosis written on the death certificate	Wine, beer, liquor	Age, BMI	7

Table 1 (*Continued*)

Study ID	Country	Sex	Age (years)	Follow-up (years)	Total n	n	Type 2 diabetes assessment	Type of alcoholic beverage	Confounding adjustments	Study quality (nos)
Wannamethee *et al.* 2003[34]	USA	W	25–42	10	109,690	935	Self-reported	Wine, beer, liquor	Age, smoking status, physical activity, BMI, family history of diabetes mellitus, use of an oral contraceptive, history of hypertension, use of hypertensive drugs, elevated cholesterol level, infertility and other alcohol beverage	5
Kao *et al.* 2001[35]	USA	M & W	45–64	3–6	12,261	1,116	Blood glucose measurements and self-reported	Wine, beer, spirits	Age, race, education, family history of diabetes, BMI, waist/hip ratio, physical activity score, total energy intake, smoking history, history of hypertension and other types of alcohol beverage	7

BMI, body mass index; GAD, glutamic acid decarboxylase; M, men; *n*, number of type 2 diabetes events; NOS, Newcastle–Ottawa Scale; OGTT, oral glucose tolerance test; PRAL, potential renal acid load; W, women; WHR, waist-to-hip ratio.

diagnosed by self-report in seven studies, and by oral glucose tolerance test or blood glucose measurements in other studies. The risk estimates in all studies were adjusted for a number of confounders, ranging from 2 to 15. A median score of included studies was 6.5 according to the nine-star NOS, suggesting a good quality of studies.
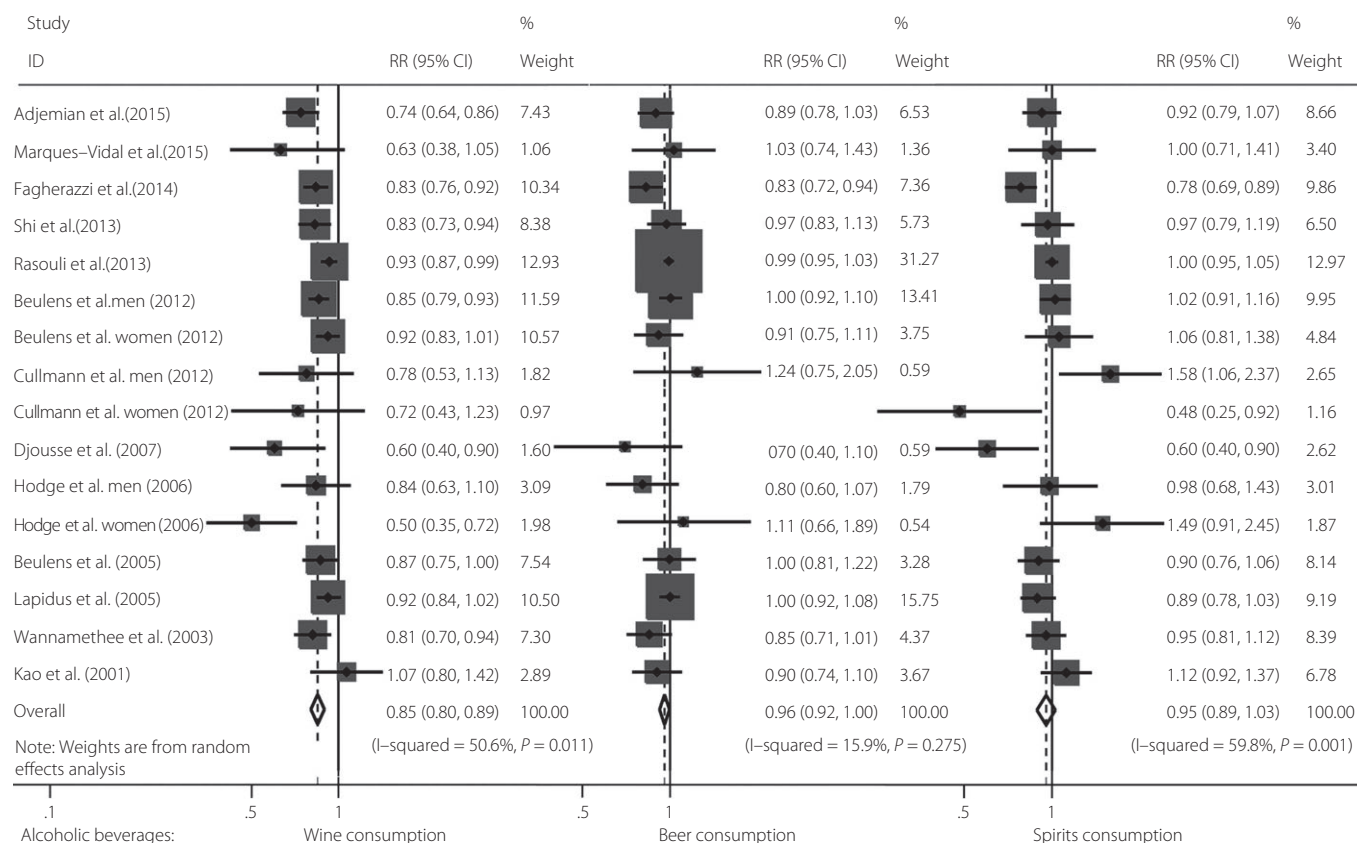
Wine consumption and risk of type 2 diabetes

All 13 included studies had reported the risk estimates of the incidence of type 2 diabetes for specific alcoholic beverages. To assess the specific association of wine consumption with type 2 diabetes, the relative risk estimates from these studies were extracted, and pooled by a fixed effects model before combining it with the overall meta-analysis if they were reported separately by alcohol dosage category in a study. As shown in Figure 2, all but one study showed an inverse association between wine consumption and type 2 diabetes. We pooled the RRs using a random effects model, with a result that wine consumption produced a 15% reduced risk of type 2 diabetes (RR 0.85, 95% CI 0.80–0.89; Figure 2). There was evidence of moderate heterogeneity of RRs across studies, as suggested by the I^2 statistic ($I^2 = 50.6\%$).

As for the estimation of publication bias, the Egger's test and Begg's test were carried out. Visual inspection of Begg's funnel plot is shown as Figure S1a. The *P*-values of the Begg's and Egger's test were 0.065 and 0.012, respectively, raising a possibility of publication bias. To explore the influence of publication bias, we carried out a sensitivity analysis by excluding each study one by one and recalculating the combined RRs on the remaining studies. The RRs were not impacted in the sensitivity analysis, ranging from 0.836 to 0.862, indicative of a good stability of results (Table S1 and Figure S1b).

Beer consumption and risk of type 2 diabetes

For analyzing the relationship between beer consumption and type 2 diabetes, the relative data from the included 13 studies were extracted and evaluated as previously mentioned. The pooled RRs in this meta-analysis showed that beer consumption led to a slightly decreased risk of type 2 diabetes (RR 0.96, 95% CI 0.92–1.0), with a low heterogeneity ($I^2 = 15.9\%$; Figure 2). The Begg's test ($P = 0.843$) and Egger's test ($P = 0.118$) showed no evidence of publication bias, with a visual inspection of the Begg's funnel plots shown in Figure S2a. An additional

Study ID	RR (95% CI)	% Weight	RR (95% CI)	% Weight	RR (95% CI)	% Weight
Adjemian et al.(2015)	0.74 (0.64, 0.86)	7.43	0.89 (0.78, 1.03)	6.53	0.92 (0.79, 1.07)	8.66
Marques–Vidal et al.(2015)	0.63 (0.38, 1.05)	1.06	1.03 (0.74, 1.43)	1.36	1.00 (0.71, 1.41)	3.40
Fagherazzi et al.(2014)	0.83 (0.76, 0.92)	10.34	0.83 (0.72, 0.94)	7.36	0.78 (0.69, 0.89)	9.86
Shi et al.(2013)	0.83 (0.73, 0.94)	8.38	0.97 (0.83, 1.13)	5.73	0.97 (0.79, 1.19)	6.50
Rasouli et al.(2013)	0.93 (0.87, 0.99)	12.93	0.99 (0.95, 1.03)	31.27	1.00 (0.95, 1.05)	12.97
Beulens et al.men (2012)	0.85 (0.79, 0.93)	11.59	1.00 (0.92, 1.10)	13.41	1.02 (0.91, 1.16)	9.95
Beulens et al. women (2012)	0.92 (0.83, 1.01)	10.57	0.91 (0.75, 1.11)	3.75	1.06 (0.81, 1.38)	4.84
Cullmann et al. men (2012)	0.78 (0.53, 1.13)	1.82	1.24 (0.75, 2.05)	0.59	1.58 (1.06, 2.37)	2.65
Cullmann et al. women (2012)	0.72 (0.43, 1.23)	0.97			0.48 (0.25, 0.92)	1.16
Djousse et al. (2007)	0.60 (0.40, 0.90)	1.60	070 (0.40, 1.10)	0.59	0.60 (0.40, 0.90)	2.62
Hodge et al. men (2006)	0.84 (0.63, 1.10)	3.09	0.80 (0.60, 1.07)	1.79	0.98 (0.68, 1.43)	3.01
Hodge et al. women (2006)	0.50 (0.35, 0.72)	1.98	1.11 (0.66, 1.89)	0.54	1.49 (0.91, 2.45)	1.87
Beulens et al. (2005)	0.87 (0.75, 1.00)	7.54	1.00 (0.81, 1.22)	3.28	0.90 (0.76, 1.06)	8.14
Lapidus et al. (2005)	0.92 (0.84, 1.02)	10.50	1.00 (0.92, 1.08)	15.75	0.89 (0.78, 1.03)	9.19
Wannamethee et al. (2003)	0.81 (0.70, 0.94)	7.30	0.85 (0.71, 1.01)	4.37	0.95 (0.81, 1.12)	8.39
Kao et al. (2001)	1.07 (0.80, 1.42)	2.89	0.90 (0.74, 1.10)	3.67	1.12 (0.92, 1.37)	6.78
Overall	0.85 (0.80, 0.89)	100.00	0.96 (0.92, 1.00)	100.00	0.95 (0.89, 1.03)	100.00

Note: Weights are from random effects analysis

(I–squared = 50.6%, *P* = 0.011)   (I–squared = 15.9%, *P* = 0.275)   (I–squared = 59.8%, *P* = 0.001)

Alcoholic beverages: Wine consumption   Beer consumption   Spirits consumption

Figure 2 | Forest plot of the association between wine, beer or spirits consumption and the risk of type 2 diabetes. CI, confidence interval; RR, relative risk.

sensitivity analysis had no impact on RRs, with a range of 0.942–0.977 (Table S2 and Figure S2b).

Spirits consumption and risk of type 2 diabetes

For spirits, we extracted the relevant data from the 13 studies that reported the risk estimates for "spirits" or "liquor" consumption, and assessed its association with type 2 diabetes, like wine and beer. The pooled RR was 0.95 (95% CI 0.89–1.03), suggesting that spirits consumption had a slight, but not significant, effect on reducing the risk of the incidence of type 2 diabetes (Figure 2). There was an evident heterogeneity, with I^2 statistic (I^2 = 59.8%; Figure 2). The Begg's test (P = 0.753) and Egger's test (P = 0.662) showed no evidence of publication bias, with a visual inspection of the Begg's funnel plots shown in Figure S3a. The followed sensitivity analysis had no impact on RRs, with a range of 0.942–0.975 (Table S3 and Figure S3b).

Stratified analysis

To explore the potential study heterogeneity, we further carried out stratified analysis by sex, study quality, the length of follow up, body mass index (BMI) and other alcoholic beverages (Table 2). For wine consumption, high heterogeneity was found in studies of women (I^2 = 55.7%), studies with shorter follow up (I^2 = 61.6%), studies not adjusted for BMI (I^2 = 83.3%) and

studies adjusted for other alcoholic beverages (I^2 = 72.7%). The inverse associations between wine consumption and the risk of type 2 diabetes were similar in all subgroup analysis. No sex difference was shown, while studies of lower quality and shorter follow up, studies not adjusted for BMI, and studies adjusted for other alcoholic beverages showed a stronger inverse association between wine consumption and type 2 diabetes. For beer consumption, no obvious high heterogeneity was found in all subgroup analysis. In studies of women, lower quality and shorter follow up, and studies adjusted for BMI and other alcoholic beverages, there was a slightly stronger association of beer consumption with type 2 diabetes. For spirits consumption, high heterogeneity was found in studies of women (I^2 = 57.2%), low quality studies (I^2 = 71.2%), studies with longer follow up (I^2 = 64.7%), studies adjusted for BMI (I^2 = 63.5%) and studies not adjusted for other alcoholic beverages (I^2 = 62.0%). The association of spirits consumption with type 2 diabetes was slightly stronger in studies of women, lower quality and shorter follow up, studies adjusted for BMI, and studies not adjusted for other alcoholic beverages.

Additional meta-analysis

To detect whether the different dosages of a specific alcoholic beverage had a similar effect on the incidence of type 2

Table 2 | Stratified analysis of the association between specific types of alcoholic beverage and type 2 diabetes

Stratified analysis	Total no. studies	RR	95% CI	I^2 (%)	P-value
Adjustment for sex					
Wine					
Men	5	0.85	0.80–0.91	0.0	0.000
Women	7	0.85	0.78–0.92	55.7	0.000
Beer					
Men	5	0.97	0.91–1.04	0.0	0.470
Women	6	0.92	0.85–1.01	37.1	0.070
Spirits					
Men	5	1.06	0.95–1.19	24.1	0.300
Women	7	0.90	0.80–1.01	57.2	0.087
Adjustment for study quality (nos)					
Wine					
<7	5	0.78	0.71–0.85	30.5	0.000
≥7	8	0.89	0.85–0.93	32.0	0.000
Beer					
<7	5	0.86	0.80–0.94	0.0	0.000
≥7	8	0.99	0.96–1.02	0.0	0.414
Spirits					
<7	5	0.96	0.81–1.14	71.2	0.635
≥7	8	0.97	0.91–1.04	30.9	0.419
Adjustment for the length of follow up					
Wine					
<5	2	0.70	0.55–0.88	61.6	0.003
≥5	11	0.88	0.84–0.91	23.5	0.000
Beer					
<5	2	0.89	0.78–1.00	0.0	0.057
≥5	11	0.96	0.93–1.00	17.7	0.080
Spirits					
<5	2	1.02	0.81–1.28	39.3	0.895
≥5	11	0.95	0.87–1.03	64.7	0.192
Adjustment for BMI					
Wine					
No	3	0.77	0.62–0.94	83.3	0.013
Yes	10	0.86	0.83–0.90	4.5	0.000
Beer					
No	3	0.96	0.88–1.03	23.4	0.262
Yes	10	0.95	0.90–1.0	17.4	0.053
Spirits					
No	3	0.99	0.92–1.07	15.4	0.837
Yes	10	0.94	0.85–1.04	63.5	0.214
Adjustment for the other alcoholic beverages					
Wine					
No	9	0.85	0.81–0.89	26.6	0.000
Yes	4	0.84	0.71–0.98	72.7	0.030
Beer					
No	9	0.95	0.90–1.01	17.0	0.086
Yes	4	0.94	0.86–1.02	27.3	0.143
Spirits					
No	9	0.92	0.83–1.02	62.0	0.100
Yes	4	1.01	0.96–1.05	0.4	0.826

BMI, body mass index; CI, confidence interval; NOS, Newcastle–Ottawa Scale; RR, relative risk.

diabetes, we carried out an additional meta-analysis based on three categories: low (0–10 g/day), moderate (10–20 g/day) and high (>20 g/day). For wine consumption, the results showed that all three categories were associated with a significantly decreased risk of type 2 diabetes. The pooled RRs in the moderate and high category were 0.83 (95% CI 0.76–0.91), with the peak reduction risk of type 2 diabetes (Figure 3). For beer consumption, though the association was slight, the moderate category (RR 0.93, 95% CI 0.87–1.0) still had a better effect on reducing the risk of type 2 diabetes than the low category (RR 0.95, 95% CI 0.89–1.01). When exposed to high-level consumption of beer, there was no decreased risk of type 2 diabetes (RR 1.01, 95% CI 0.88–1.16; Figure 4). For spirits consumption, low- and moderate-level consumption led to a mildly decreased risk of type 2 diabetes (low: RR 0.94, 95% CI 0.84–1.05; moderate: RR 0.95, 95% CI 0.84–1.08), whereas high-level consumption of spirits was associated with an increased risk of type 2 diabetes (RR 1.24, 95% CI 0.87–1.77; Figure 5).

Dose–response meta-analysis

Several studies had investigated the dose–response of total alcohol consumption and type 2 diabetes, showing that moderate alcohol consumption lowered the risk of type 2 diabetes.[10,11] We further carried out a dose–response analysis between specific alcoholic beverages and the risk of type 2 diabetes. The results showed a U-shaped relationship between all three types of alcoholic beverage and type 2 diabetes, indicative of the non-linear dose–response relationship (Figure 6). For wine, all levels of wine consumption <80 g/day were associated with reductions in the risk of type 2 diabetes. The lowest risk of type 2 diabetes was present between the 20–30 g/day level, with a decrease of 20% (Figure 6a). For beer, the lowest risk of type 2 diabetes was also present between the 20–30 g/day level, with a decrease of 9%. However, there was an increased risk of type 2 diabetes when the level of beer intake was >80 g/day (Figure 6b). Similarly, the peak risk reduction of type 2 diabetes emerged at the levels of spirits consumption between 7–15 g/day, with a decrease of 5%. Meanwhile, spirits consumption remained protective until an intake of 23 g/day (Figure 6c).

DISSCUSION

To the best of our knowledge, the present study is the first meta-analysis to explore the relationship between the specific types of alcoholic beverages and the incidence of type 2 diabetes. Here we included 13 prospective studies, enrolling 397,296 participants and 20,641 cases of type 2 diabetes. The results suggested that wine consumption was associated with a robust significantly decreased risk of type 2 diabetes, whereas beer or spirits consumption showed a slight trend of decreasing the risk of type 2 diabetes.

A number of studies have investigated the association between total alcohol consumption and the risk of type 2 diabetes.[36–38] Previous meta-analyses had systematically shown that total alcohol consumption was associated with a decreased risk
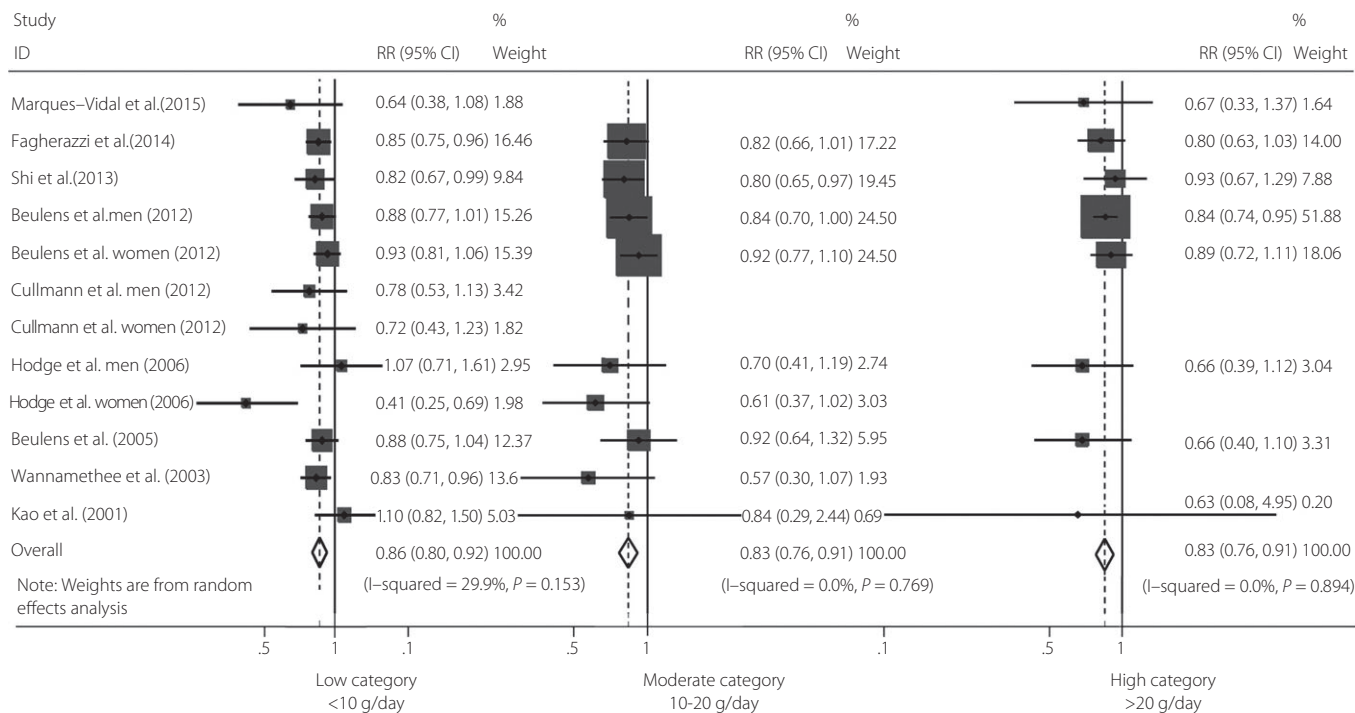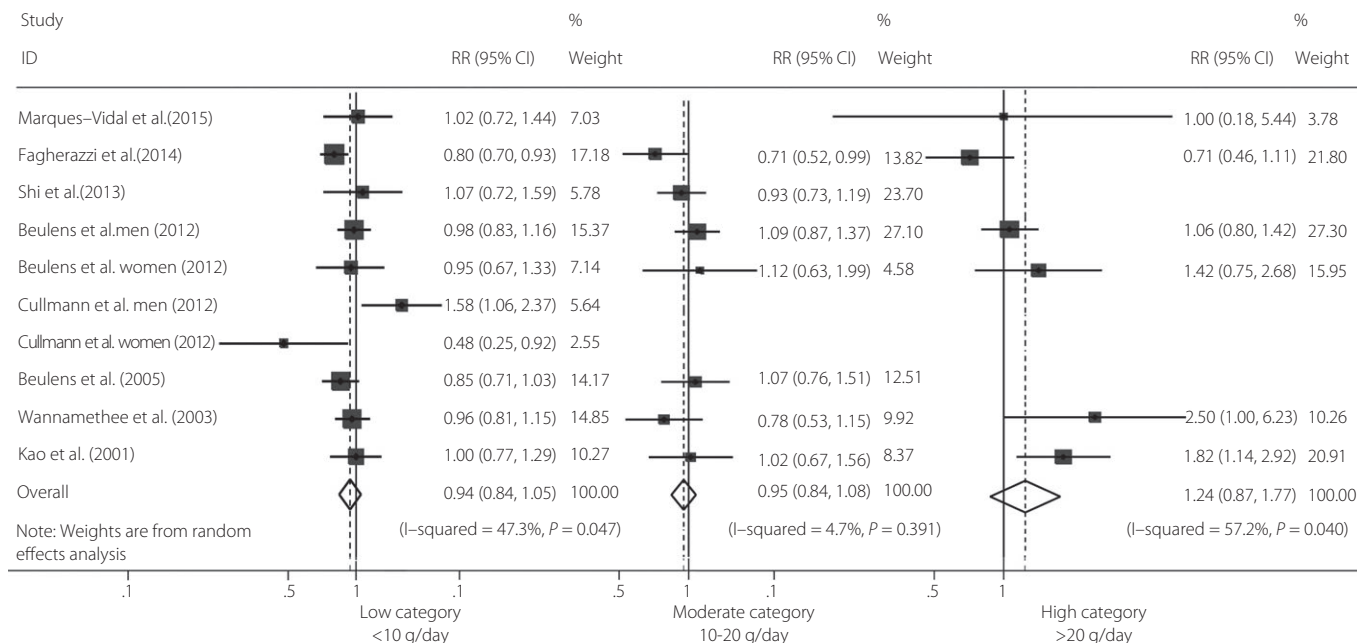
Figure 3 | Forest plot of the associations between different categories of wine consumption and the risk of type 2 diabetes. Low category (<10 g/day); moderate category (10–20 g/day); high category (>20 g/day). CI, confidence interval; RR, relative risk.
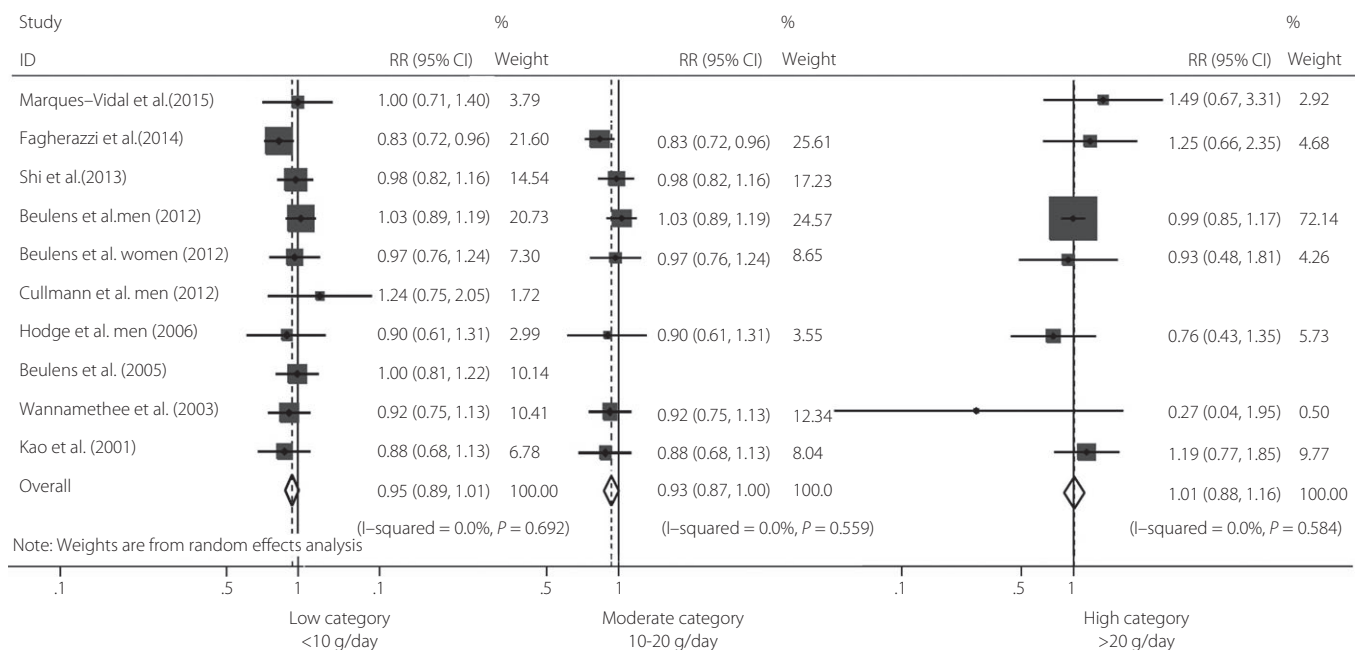
Figure 4 | Forest plot of the associations between different categories of beer consumption and the risk of type 2 diabetes. Low category (<10 g/day); moderate category (10–20 g/day); high category (>20 g/day). CI, confidence interval; RR, relative risk.

of type 2 diabetes,[10,11] although the most recent meta-analysis carried out by Knott *et al.*[12] considered that the reduction in the risk of type 2 diabetes might be specific to women rather than men. In the current meta-analysis, we further explored whether the specific types of alcoholic beverages had different effects on decreasing the risk of type 2 diabetes. In line with

Figure 5 | Forest plot of the associations between different categories of spirits consumption and the risk of type 2 diabetes. Low category (<10 g/day); moderate category (10–20 g/day); high category (>20 g/day). CI, confidence interval; RR, relative risk.

the conclusion that total alcohol consumption decreased the risk of type 2 diabetes, the pooled RRs for different alcoholic beverages showed that all of wine, beer or spirits consumption were associated with a decreased risk of type 2 diabetes. Despite the similarity, there were still diversities among the different types of alcoholic beverages. Wine consumption, rather than beer or spirits consumption, had a better significant reduction in the risk of type 2 diabetes (RR 0.85, 95% CI 0.80–0.89), whereas beer or spirits consumption was associated with a slight trend of decreasing the risk of type 2 diabetes (beer: RR 0.96, 95% CI 0.92–1.0; spirits: RR 0.95, 95% CI 0.89–1.03). Thus, in contrast to beer or spirits, wine consumption as the most prevalent alcoholic beverage worldwide appeared to be more beneficial for decreasing the risk of type 2 diabetes. Accordingly, several studies have realized the potential protective role of wine consumption in type 2 diabetes.[39,40] A plausible biological mechanism is that resveratrol, the polyphenols extracts in wine, might contribute to a more effective reduction in the risk of type 2 diabetes. In response to this issue, one recent study carried out by Lam et al.[41] in 2015 showed a potential molecular mechanism of resveratrol controlling the level of blood glucose in rats with diabetes through sirtuin 1. The resveratrol activated sirtuin 1 in the small intestine, which subsequently triggered a series of neural networks involved in gut, liver and brain, ultimately leading to a decrease of blood glucose. Additionally, resveratrol as a powerful anti-oxidant fought against the oxidative stress caused by the ingestion of a meal or environmental toxins.[42,43]

With respect to the dose–response between alcohol consumption and the risk of type 2 diabetes, a number of studies

have reported that moderate alcohol consumption lowered the risk of type 2 diabetes.[10,11] For instance, Baliunas et al.[9] reported a U-shape relationship between total alcohol consumption and type 2 diabetes, with a peak risk reduction at 22 g/day for men (RR 0.87, 95% CI 0.76–1.0) and at 24 g/day for women (RR 0.60, 95% CI 0.52–0.69). Similarly, Knott et al.[12] found a peak risk reduction of 18% between 10 and 14 g/day. The present results strengthened the aforementioned opinion. Despite the presence of the different effects of specific alcoholic beverages on decreasing the risk of type 2 diabetes, all three types of alcoholic beverages showed a U-shaped relationship with the risk of type 2 diabetes. Moderate doses, such as 20–30 g/day for wine and beer, 7–15 g/day for spirits, led to the peak risk reduction of type 2 diabetes, with the decrease of 20%, 9% and 5% respectively. It was apparent that wine had a better protective effect than beer and spirits. All levels of wine consumption were associated with a decreased risk of type 2 diabetes. In contrast, high beer and spirits consumption increased the risk. To account for this phenomenon, the content of wine, such as polyphenols, which were reported to reduce the risk of type 2 diabetes, was a possible reason. In addition, given that the robust protective effect of wine consumption was associated with the incidence of type 2 diabetes, it might be reasonable to believe that high wine consumption was still helpful for type 2 diabetes. Alternatively, high wine consumption might mean a better economic income or social status, which was considered to be associated with a decreased risk of type 2 diabetes in recent studies.[44,45]

There are several strengths in the present meta-analysis. First, in contrast to the previous meta-analysis focusing on the
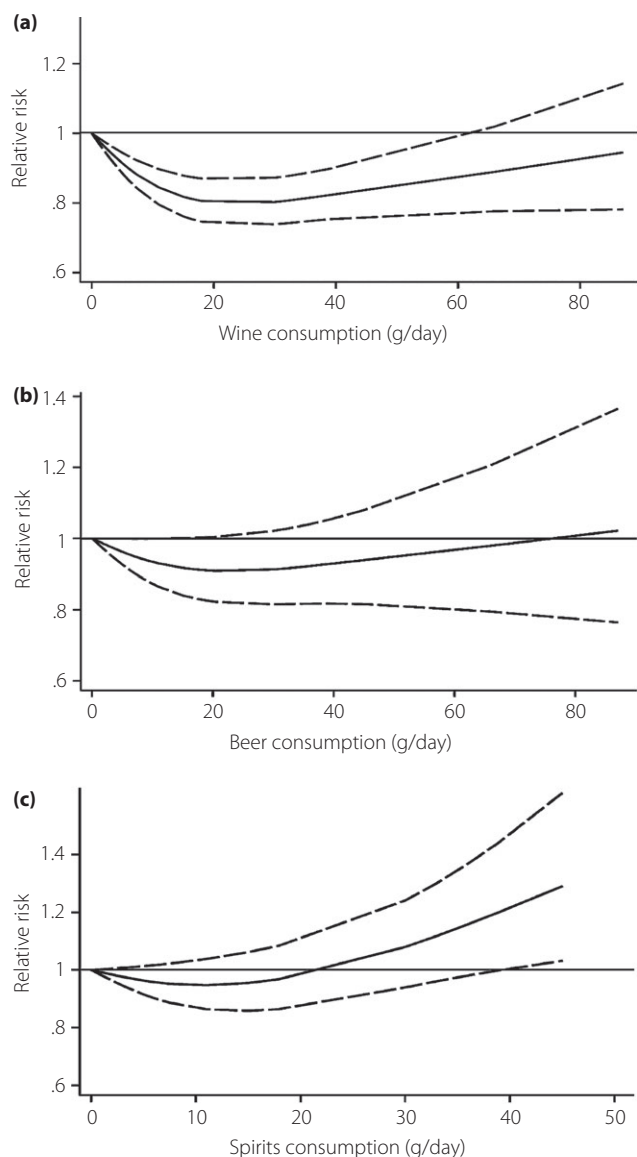
Figure 6 | Dose–response analysis of the association between specific types of alcoholic beverages and type 2 diabetes. (a) The dose–response relationship between wine and type 2 diabetes. (b) The dose–response relationship between beer and type 2 diabetes. (c) The dose–response relationship between spirits and type 2 diabetes.

relationship between total alcohol consumption and the risk of type 2 diabetes, we retrieved and pooled a substantial number of studies to systematically assess the association between specific alcoholic beverages and type 2 diabetes. Second, all 13 included studies were prospective cohort in design, and high quality with an average NOS score of 6.5. Thus, the recall bias among studies was minimized. Third, sensitivity analysis was carried out to assess the influence of individual studies and reduce the publication bias. The similarity of results in sensitivity analysis also strengthened the conclusions in this meta-analysis.

The present meta-analysis also has several limitations. First of all, moderate heterogeneity was detected in the analysis of wine and spirits consumption. Although stratified analysis showed the potential sources of high heterogeneity, the presence of heterogeneity might still influence the reliability of our results. Furthermore, not all studies had adjusted the main confounders, such as age, BMI and sex, and the direct conversion of ORs or HRs to RRs in some studies could have underestimated the variance of the RRs. Moreover, the included studies contained two types of reference groups: alcohol abstainers and occasional drinkers, which could also impact the reliability of the present results. Additionally, the Egger's test and Begg's test suggested that publication bias might exist. The sensitivity analysis did not change the general results, showing the stability of our results. Nevertheless, the influence of publication bias was not fully excluded by this method. Finally, because of the observational nature of the studies, a causal relationship could not be established in this meta-analysis.

In conclusion, the present meta-analysis shows strong evidence that specific alcoholic beverages had different effects on reducing the risk of type 2 diabetes. Wine consumption was associated with a significant reduction in the risk of type 2 diabetes, whereas beer or spirits consumption showed a slight decrease in the risk of type 2 diabetes. The present study provides a new perspective to explore the association between alcohol consumption and type 2 diabetes. However, long-term randomized controlled trials in the future are required to establish causality and to elucidate the underlying mechanisms.

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DISCLOSURE
The authors declare no conflict of interest.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Figure S1 | Begg's funnel plot and sensitivity analysis of the association between wine consumption and risk of type 2 diabetes.
Figure S2 | Begg funnel plot and sensitivity analysis of the association between beer consumption and risk of type 2 diabetes.
Figure S3 | Begg's funnel plot and sensitivity analysis of the association between spirits consumption and risk of type 2 diabetes.
Table S1 | Sensitivity analysis of the association between wine consumption and type 2 diabetes.
Table S2 | Sensitivity analysis of the association between beer consumption and type 2 diabetes.
Table S3 | Sensitivity analysis of the association between spirits consumption and type 2 diabetes.