scientific reports

OPEN

Meta-analytic evidence for a sex-diverging association between alcohol use and body mass index

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Alcohol use is an important health issue and has been suggested to contribute to the burden produced by obesity. Both alcohol use and obesity are subject to sex differences. The available studies on the relationship between alcohol use and body mass index (BMI) report inconsistent results with positive, negative, and null findings which requests a meta-analytic approach. Therefore, we conducted a meta-analysis of case–control, cohort, and cross-sectional studies. The systematic literature search and data extraction was performed by 3 independent raters. We conducted sex-separated meta-analyses and -regressions to investigate how alcohol consumption associates with BMI. Our systematic literature search resulted in 36 studies with 48 data sets (N_{men} = 172,254; k_{men} = 30; N_{women} = 24,164; k_{women} = 18; $N_{unknown\ sex}$ = 672,344; $k_{unknown\ sex}$ = 24). Alcohol use was associated with higher BMI in men (g = 0.08 [0.07; 0.09]) and lower BMI in women (g = − 0.26 [− 0.29; − 0.22]). Moreover, we found the amount of daily alcohol intake in men (β = 0.001 [0.0008; 0.0014]) and ethnicity in women (g[Caucasians] = − 0.45 versus g[Asians] = − 0.05; z = 11.5, p < 0.0001) to moderate these effects. We here identified sex-diverging relationships between alcohol use and BMI, found daily alcohol intake and ethnicity to sex-specifically moderate these effects, and argue that sex-specific choice of beverage type and higher amount of daily alcohol use in men than in women account for these observations. Future research is needed to provide empirical evidence for the underlying mechanisms.

For 2016, the World Health Organization (WHO)[1] estimates a total alcohol per capita consumption of 6.4 L. Harmful use of alcohol accounted for approximately 3 million deaths (= 5.3% of all deaths) and 132.6 million disability-adjusted life years (DALYs) (= 5.1% of all DALYs). Moreover, high prevalence rates for harmful alcohol use and dependence of 8.8% and 8.2% are estimated in the WHO European Region and the WHO Region of the Americas. Women vary from men in their alcohol use patterns and risk of alcohol use disorder (AUD); also, sex differences in mechanisms underlying alcohol use and AUD have been reported[2–16].

Obesity is a health concern, particularly in the Western world. As alcohol contains much energy (29 kJ per gram alcohol) and most people in Europe (59.9%) and the Americas (54.1%) drink alcohol[1], it is speculated that alcohol contributes to the obesity problem. However, the association between alcohol intake and body mass index (BMI) is not that simple. Ethanol intake inhibits different insulin actions in the body[17] with the possible long-term consequence of a generalized insulin resistance[17,18] contributing to overweight. Furthermore, obesity and AUD share common etiopathogenetic mechanisms such as mesolimbic dysfunction[19–22] with lower dopamine D2 receptor availability[23], increased cue-reactivity[24,25], and genetics[26,27]. Similar to alcohol use, BMI and obesity vary significantly between women and men with higher rates of obesity in the female group[28].

A systematic review published in 2011 addressed the association between alcohol intake and gain of weight[29]. The authors' evaluation of large cross-sectional and well-powered prospective studies with long follow-up periods revealed contradictory results. However, they assumed a positive association to be more likely in men (vs.

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women) and in heavy drinkers, whereas there were negative or no associations in moderate consumers. Indeed, also studies that were published more recently demonstrate positive and negative relationships as well as null findings[30–32]. Negative associations might be explained by the greater thermogenic effect of alcohol than carbohydrates or fat with a lower net efficiency[33]. Initial evidence also indicates that sex differences (e.g., in choice of beverage type and drinking patterns, which influence the energy intake) might account for the ambiguous relationship between alcohol intake and BMI[29]. A more recent systematic review and meta-analysis published in 2022 showed that alcohol consumption increased the risk of obesity in adults 2.05 times compared to non-drinkers[34], but did not distinguish between moderate vs. heavy drinkers or men vs. women. Another recent meta-analysis that focused on overweight, obese, or abdominally obese subjects again reports higher odds of obesity and overweight in heavy drinkers, but did not include normal weight samples[35].

Thus, we here present a systematic review and meta-analysis to investigate how alcohol consumption is related to BMI while also exploring the moderating influence of sex, the amount of alcohol consumed, the percentage of smokers, and differences between ethnicities. Since the existing literature is inconclusive, we decided to follow an exploratory approach.

Materials and methods

Search strategy and study selection. We conducted a two-step literature search from study inception until February 4th, 2021, using PubMed and Google Scholar including case–control, cohort, and cross-sectional studies. In the course of the review process, we updated this literature search from study inception until September 9th, 2022. Due to the enormous number of results when applying a full-text search strategy (> 1,150,000 hits), we limited our search strategy exclusively to titles. The search terms *alcohol dependence, alcohol use disorder, binge drinking, alcohol, social consumption, social drinking, withdrawal, alcohol intoxication, seizure, delirium, AUDIT, CAGE, beer, wine, liquor* were used to represent alcohol intake and were combined with the search terms *BMI* and *body mass index.* In a second step, the reference lists of retrieved articles were searched manually for further eligible titles. All abstracts were screened applying the selection criteria that are detailed in our coding protocol (Supplementary Table S1). The remaining articles were checked for eligibility according to the Preferred Reporting Items for Systemic Reviews and Meta-analyses (PRISMA) statement[36] on the basis of a full-text review and the entire literature search was summarized according to these PRISMA guidelines[37].

Data extraction. The data extraction process strictly followed our approach described in Siegmann et al.[11] and Siegmann et al.[38] and was performed by two out of three investigators (C. M., E. S., M. M.) for different portions of the publications each. All recorded variables can be found in the previously defined coding protocol (Supplementary Table S1). Disagreement was resolved by discussion and compromise on the eventually extracted values. We assessed the risk of bias with either the Newcastle–Ottawa Scale for case–control studies[39] or an adaptation of the Newcastle–Ottawa Scale for cohort studies[39], which was specifically designed for cross-sectional studies by Herzog et al.[40] in their systematic review. The final risk of bias values were obtained by averaging the extractors' values.

Statistical analysis. All analyses were conducted and all figures were made using the metafor package[41] within the open-source software environment R, version 4.1.1[42] and GraphPad Prism 8.4.3 (Graph Pad Software Inc., San Diego, CA, USA).

We estimated the standardized mean difference (Hedges' g) in BMI among drinking subjects and control subjects and, in a second step, explored the influence of sex. Following our coding protocol (Supplementary Table S1) we distinguished between data from males, data from females, and data from studies not reporting sex-separated measures ("unknown group").

In order to combine studies reporting different measures of effect, correlative and odds ratio data were transformed into Hedges' g using common transformation formulas[43]. The drinking group was characterized by various measures: (1) alcohol consumption levels in grams per day, (2) blood alcohol levels, (3) frequency of alcohol drinking, (4) score in the AUDIT questionnaire[44], (5) being diagnosed with AUD by a psychiatrist, (6) score in the Obsessive–Compulsive Drinking Scale, German version (OCDS-G)[45], (7) frequency of hospital readmissions following withdrawal treatment, and (8) being classified as binge drinkers according to a definition by Patrick et al.[46]. The control group either consisted of never-drinkers and non-binge-drinkers or was defined as consuming < 1 drink per week, drinking < 1 day per week, or scoring below the cut-off value of the AUDIT questionnaire[44].

Owing to our study design which compared more than one variation of drinking status (e.g., light, moderate, and heavy drinking) against a single control group, the meta-analytic effect size estimates are correlated and non-independent, respectively. To account for this repeated usage of one common control group, we performed a multivariate random-effects meta-analysis recommended for the analysis of multiple-treatment studies[47,48]. The Q-statistic is reported as a measure for heterogeneity. We decided against conventional ad-hoc approaches, e.g., averaging multiple reported effects, since these would have resulted in loss of useful information for moderator analyses[47]. We ran prespecified multivariate meta-regressions for the moderators drinking amount in grams per day, percentage of smokers in the drinking group, and study quality (i.e., the risk of bias in these studies). We also tested whether drinking amount is suited as a quadratic predictor. All meta-regressions were Bonferroni-corrected for multiple testing. Since ethnicity is a variable that influences both alcohol-related behavior[49,50] as well as BMI or body fat[51], we investigated the difference in the outcome measure among the ethnicities Caucasian, Asian, African, and Hispanic in a prespecified subgroup analysis. Based on the aforementioned results by Sayon-Orea et al.[29] concerning the influence of different beverage types, we planned to run another prespecified subgroup analysis distinguishing between beer, wine, liquor, and mixed alcohol consumption.
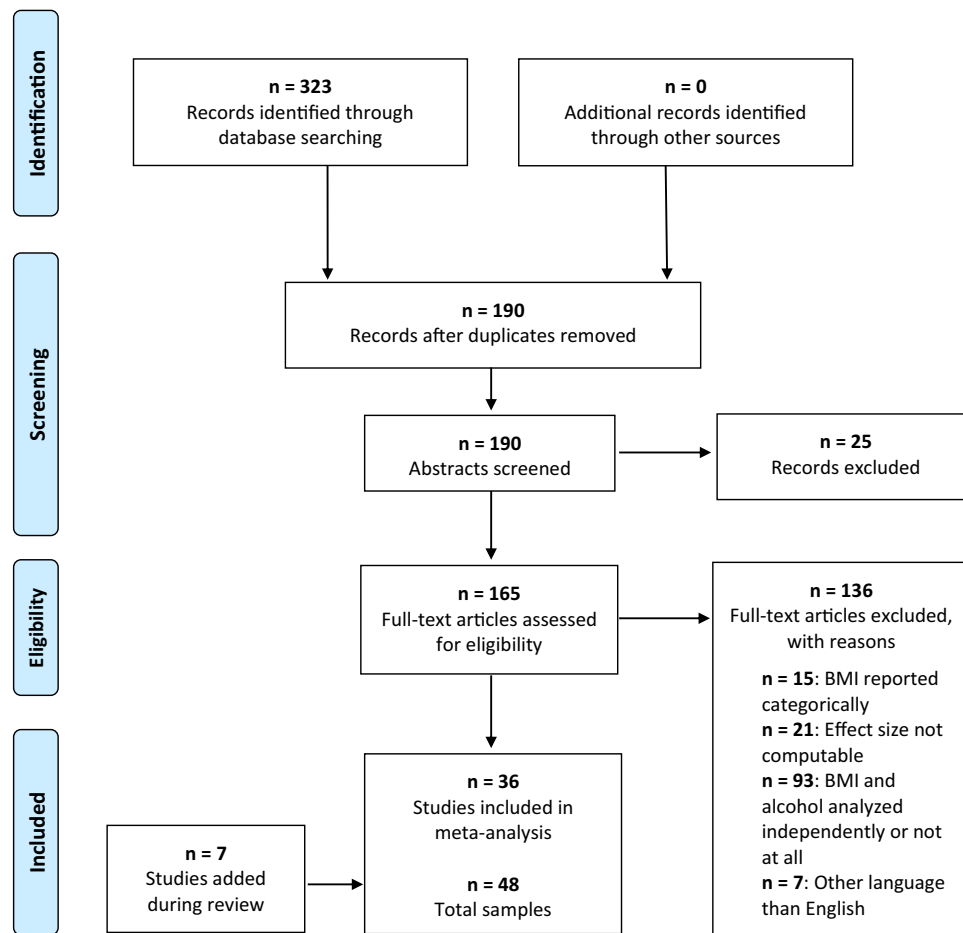
Figure 1. The PRISMA flow chart. This flow diagram visualizes the systematic literature search for eligible studies as well as reasons for exclusion of uneligible studies.

Small study effects were assessed by visual detection of asymmetries in a contour-enhanced funnel plot[52,53]. The sensitivity of our analysis was evaluated by comparing models with and without effect sizes which we assume to be influential outliers[54]. They were detected following an exploratory data analysis[55]. $p < 0.05$ (2-sided) was considered statistically significant.

Results

Eligible studies. The literature search is summarized in the PRISMA flow chart (Fig. 1). We identified 36 articles[13,31,56–89] comprising 48 independent samples. The characteristics of all included studies are detailed in Table 1.

Meta-analytic results and moderator analyses. Since sensitivity analyses revealed one substantially influential outlier[78], we conducted our analysis without this study. When analyzing all of the studies together we found a very small positive association between alcohol use and BMI ($g = 0.01$, 95% CI [0.01; 0.02]) with a high heterogeneity index ($Q = 1139.74$, $p < 0.0001$). Including the factor sex as a moderator revealed a significant moderating effect for male ($z = 0.08$, $p < 0.0001$) and female sex ($z = -0.26$, $p < 0.0001$) while the group of studies with unknown sex distribution remained non-significant ($z = 0.004$, $p = 0.27$). This indicates that sex substantially influences the effect size and we therefore conducted sex-separated analyses: while in men the association was slightly positive ($g = 0.08$, 95% CI [0.07; 0.09]), we found a negative effect in women ($g = -0.26$, 95% CI [-0.29; -0.22]). In both samples, heterogeneity was rather high ($Q = 237.90$ for women, $Q = 106.21$ for men, $p < 0.0001$ for both) indicating that these models are not yet of adequate fit for the data and require further moderator analyses. The sex-separated results in comparison to the overall results are shown in Figs. 2 and 3.

Bearing this sex-diverging result in mind, we first analyzed the interaction of sex and ethnicity before conducting a subgroup analysis for this moderator. It revealed a significant interaction of Asian ethnicity with female sex ($z = 0.39$, $p < 0.0001$) again suggesting that analyses concerning ethnicity should be performed sex-separately. No African and only one Hispanic study provided sex-separated data; therefore, sex-separated subgroup analyses were limited to Asian vs. Caucasian participants. In men, these ethnic groups did not differ significantly

First author, year of publication	Country	Sex	Sample's mean age (in years)	Study design	Mean amount of alcohol consumed (in g per day)	Drinking group n	Drinking group BMI (M±SD)	Control group n	Control group BMI (M±SD)
				Case–control data					
						Drinking group		**Control group**	
Roggi et al. 1992[74]	Italy	Male	51.8	Cross-sectional	59.5	210	26.04 ± 3.7	20	26.63 ± 4.0
Roggi et al. 1992[74]	Italy	Female	55.0	Cross-sectional	23.7	162	25.44 ± 4.6	122	26.63 ± 4.7
Männistö et al. 1996[63] a,d	Finland	Male	NA	Cross-sectional	7.5	12,850	26.17 ± NA	3045	26.03 ± NA
Männistö et al. 1996[63] a,d	Finland	Male	NA	Cross-sectional	22.5	6019	26.45 ± NA	3045	26.03 ± NA
Männistö et al. 1996[63] a,d	Finland	Male	NA	Cross-sectional	45.0	4031	26.52 ± NA	3045	26.03 ± NA
Männistö et al. 1996[63] a,d	Finland	Male	NA	Cross-sectional	90.0	1270	26.44 ± NA	3045	26.03 ± NA
Männistö et al. 1997[64] e	Finland	Male	45.8	Cross-sectional	14.4	367	26.10 ± NA	70	28.00 ± NA
Männistö et al. 1997[64] e	Finland	Male	45.8	Cross-sectional	14.4	75	26.50 ± NA	70	28.00 ± NA
Männistö et al. 1997[64] e	Finland	Male	45.8	Cross-sectional	14.4	228	26.90 ± NA	70	28.00 ± NA
Männistö et al. 1997[64] e	Finland	Male	45.8	Cross-sectional	14.4	122	26.10 ± NA	70	28.00 ± NA
Männistö et al. 1997[64] e	Finland	Female	45.8	Cross-sectional	3.6	248	25.10 ± NA	174	26.60 ± NA
Männistö et al. 1997[64] e	Finland	Female	45.8	Cross-sectional	3.6	255	24.90 ± NA	174	26.60 ± NA
Männistö et al. 1997[64] e	Finland	Female	45.8	Cross-sectional	3.6	162	26.70 ± NA	174	26.60 ± NA
Männistö et al. 1997[64] e	Finland	Female	45.8	Cross-sectional	3.6	146	25.30 ± NA	174	26.60 ± NA
Skrzypczak et al. 2008[61]	Poland	Female	56.3	Cross-sectional	NA	1579	25.26 ± 3.9	8675	27.92 ± 4.83
Kawamoto et al. 2009[83]	Japan	Male	NA	Cross-sectional	11.5	205	23.60 ± 3.1	80	23.40 ± 3.6
Kawamoto et al. 2009[83]	Japan	Male	NA	Cross-sectional	34.4	234	23.40 ± 2.8	80	23.40 ± 3.6
Kawamoto et al. 2009[83]	Japan	Male	NA	Cross-sectional	68.7	159	23.90 ± 3.0	80	23.40 ± 3.6
Loomba et al. 2009[82]	US	Mixed	70.0	Cross-sectional	6.0	739	25.00 ± 4.0	869	25.00 ± 4.0
Loomba et al. 2009[82]	US	Mixed	70.0	Cross-sectional	18.0	414	25.00 ± 3.0	869	25.00 ± 4.0
Loomba et al. 2009[82]	US	Mixed	70.0	Cross-sectional	30.0	233	25.00 ± 3.0	869	25.00 ± 4.0
Loomba et al. 2009[82]	US	Mixed	70.0	Cross-sectional	54.0	109	26.00 ± 4.0	869	25.00 ± 4.0
Yue et al. 2012[81]	China	Male	NA	Cross-sectional	9.9	213	25.64 ± 3.2	243	25.50 ± 3.9
Yue et al. 2012[81]	China	Male	NA	Cross-sectional	30.0	123	26.48 ± 3.1	243	25.50 ± 3.9
Yue et al. 2012[81]	China	Male	NA	Cross-sectional	60.0	61	25.43 ± 3.2	243	25.50 ± 3.9
Ahaneku et al. 2014[57]	Nigeria	Mixed	43.8	Cross-sectional	NA	70	25.64 ± 5.9	121	24.75 ± 4.7
Shaikh et al. 2015[80] f	US	Mixed	NA	Cohort	2.6	7288	27.40 ± NA	4710	27.20 ± NA
Shaikh et al. 2015 f	US	Mixed	NA	Cohort	14.6	3679	26.80 ± NA	4710	27.20 ± NA
Shaikh et al. 2015[80] f	US	Mixed	NA	Cohort	36.0	1219	26.60 ± NA	4710	27.20 ± NA
Yi et al. 2016[79]	Republic of Korea	Male	58.8	Cohort	6.7	46,503	23.70 ± 2.6	34,435	23.50 ± 2.8
Yi et al. 2016[79]	Republic of Korea	Male	58.8	Cohort	41.1	26,797	23.80 ± 2.7	34,435	23.50 ± 2.8
Rask-Andersen et al. 2017[78] a,c	Great Britain	Mixed	NA	Genome-wide association study (GWAS)	NA	12,966	28.09 ± 0.1	7944	28.31 ± 0.1
Rask-Andersen et al. 2017[78] a,c	Great Britain	Mixed	NA	Genome-wide association study (GWAS)	NA	30,412	27.57 ± 0.1	7944	28.31 ± 0.1
Rask-Andersen et al. 2017[78] a,c	Great Britain	Mixed	NA	Genome-wide association study (GWAS)	NA	27,250	27.08 ± 0.1	7944	28.31 ± 0.1
Rask-Andersen et al. 2017[78] a,c	Great Britain	Mixed	NA	Genome-wide association study (GWAS)	NA	24,424	26.84 ± 0.1	7944	28.31 ± 0.1
Cho et al. 2018 e	Republic of Korea	Mixed	15.2	Cross-sectional	NA	15	22.32 ± NA	520	21.18 ± NA
Booranasuksakul et al. 2019[77]	Thailand	Male	NA	Cross-sectional	6.1	69	21.43 ± 3.5	44	20.78 ± 4.12
Booranasuksakul et al. 2019[77]	Thailand	Male	NA	Cross-sectional	29.9	12	21.76 ± 4.1	44	20.78 ± 4.12
Booranasuksakul et al. 2019[77]	Thailand	Male	NA	Cross-sectional	208.7	19	23.11 ± 3.1	44	20.78 ± 4.12
Booranasuksakul et al. 2019[77]	Thailand	Female	NA	Cross-sectional	6.2	98	21.34 ± 3.7	123	20.74 ± 3.9
Booranasuksakul et al. 2019[77]	Thailand	Female	NA	Cross-sectional	29.9	12	23.34 ± 3.7	123	20.74 ± 3.9
Booranasuksakul et al. 2019[77]	Thailand	Female	NA	Cross-sectional	199.8	19	22.49 ± 3.5	123	20.74 ± 3.9
Nishigaki et al. 2020[76]	Japan	Male	NA	Cohort	NA	1565	22.90 ± 2.9	2298	22.80 ± 3.2
Nishigaki et al. 2020[76]	Japan	Male	NA	Cohort	NA	530	23.20 ± 2.9	2298	22.80 ± 3.2
Nishigaki et al. 2020[76]	Japan	Male	NA	Cohort	NA	723	22.90 ± 2.7	2298	22.80 ± 3.2
Nishigaki et al. 2020[76]	Japan	Female	NA	Cohort	NA	1592	20.40 ± 2.5	3871	20.60 ± 2.9
Nishigaki et al. 2020[76]	Japan	Female	NA	Cohort	NA	281	20.60 ± 2.4	3871	20.60 ± 2.9
Nishigaki et al. 2020[76]	Japan	Female	NA	Cohort	NA	333	20.40 ± 2.4	3871	20.60 ± 2.9
Agarwal et al. 2021[84]	US	Mixed	29.5	Case–control	NA	24	33.35 ± 2.9	85	35.45 ± 4.2
Agarwal et al. 2021[84]	US	Mixed	28.6	Case–control	NA	86	23.46 ± 2.0	223	22.81 ± 2.7
Bouna-Pyrrou et al. 2021[31]	Germany	Male	NA	Cross-sectional	NA	55	23.67 ± 3.5	38	22.08 ± 2.4
Bouna-Pyrrou et al. 2021[31]	Germany	Male	NA	Cross-sectional	NA	84	23.27 ± 2.9	9	21.43 ± 1.4
Continued									

First author, year of publication	Case–control data								
						Drinking group		Control group	
	Country	Sex	Sample's mean age (in years)	Study design	Mean amount of alcohol consumed (in g per day)	n	BMI (M ± SD)	n	BMI (M ± SD)
Bouna-Pyrrou et al. 2021[31]		Female	NA		NA	45	22.41 ± 2.9	54	21.60 ± 2.8
Bouna-Pyrrou et al. 2021[31]					NA	75	22.15 ± 3.2	24	22.27 ± 2.3
Gao et al. 2021[86]	China	Mixed	50.1	Cross-sectional	55.3	1016	23.50 ± 3.3	8430	23.30 ± 3.5
Hashimoto et al. 2021[87]	Japan	Mixed	62.0	Cross-sectional	15.0	3157	22.40 ± 2.9	6199	22.20 ± 3.2
Hashimoto et al. 2021[87]					29.5	1162	22.70 ± 2.9		
Hashimoto et al. 2021[87]					50.0	657	22.60 ± 2.9		
Innes et al. 2021	Great Britain	Mixed	57.0	Cohort	NA	96,388	27.30 ± 4.3	374,303	27.40 ± 4.9
Innes et al. 2021					NA	18,755	27.90 ± 4.6		
Crovetto et al. 2022[85]	Chile	Male	NA	Cross-sectional	NA	111	23.40 ± 3.1	207	23.40 ± 3.2
Crovetto et al. 2022[85]		Female			NA	266	23.10 ± 3.0	864	23.20 ± 3.1

	Correlative data						
	Country	Sex	Sample's mean age (in years)	Study design	Mean amount of alcohol consumed (in grams per day)	n	Correlation coefficient
Kauffmann et al. 1989[66] g	France	Male	NA	Cross-sectional	NA	384	0.14
Ishizaki et al. 1994[65] g	Japan	Male	47.1	Cross-sectional	176.0	83	-0.01
Kleiner et al. 2004[62] g	US	Female	40.6	Cross-sectional	NA	298	-0.12
Gearhardt et al. 2009g	US	Mixed	46.6	Cohort	9.8	37,259	-0.07
Gearhardt et al. 2009g						23,928	-0.16
Gazdzinski et al. 2010[59] b,h	US	Male	50.8	Cross-sectional	NA	55	-0.07
Gazdzinski et al. 2010[59] b,h					NA		0.17
Gazdzinski et al. 2010[59] b,h					NA		-0.05
Amorim et al. 2012[69] g	Brazil	Mixed	NA	Cross-sectional	NA	203	0.40
Hooper et al. 2012[67] g	US	Mixed	13.8	Cross-sectional	NA	51	-0.04
Hooper et al. 2012[67] g			41.8		NA	51	-0.11
Sebelien et al. 2013[71] g	Norway	Mixed	61.0	Cross-sectional	NA	26	-0.22
Remus et al. 2014[70] g	Romania	Mixed	20.8	Cross-sectional	NA	319	0.14
Ventus and Jern 2016[72] g	Finland	Male	33.1	Case–control	NA	863	0.02
Ventus and Jern 2016[72] g			43.8		NA	69	0.08
Cronce et al. 2017[56] g	US	Female	21.3	Cross-sectional	16.2	313	0.01
Cronce et al. 2017[56] g			20.8		13.0	425	-0.07
Weinland et al. 2019[13] h	Germany	Male	48.0	Case–control	155.0	101	0.11
Weinland et al. 2019[13] h		Female			60.0	72	0.10
Kokubun et al. 2021[89] g	Japan	Mixed	49.7	Cross-sectional	NA	142	0.12

	Odds ratio data								
	Country	Sex	Sample's mean age (in years)	Study design	Mean amount of alcohol consumed (in grams per day)	Drinking subjects with high BMI	Drinking subjects with normal BMI	Control subjects with high BMI	Control subjects with normal BMI
						n or %	n or %	n or %	n or %
Janssens et al. 2001[75] i	Belgium	Male	45.1	Cohort	9.4	11%	89%	10%	90%
Janssens et al. 2001[75] i					27.4	13%	87%		
Janssens et al. 2001[75] i					54.0	12%	88%		
Janssens et al. 2001[75] i		Female	45.9		6.8	9%	91%	13%	87%
Janssens et al. 2001[75] i					18.8	4%	96%		
Janssens et al. 2001[75] i					36.0	9%	91%		
Wakabayashi 2012[58] i	Japan	Male	48.1	Cross-sectional	11.0	10.7%	12.4%	35.6%	27.1%
Wakabayashi 2012[58] i					33.0	32.8%	37.4%		
Wakabayashi 2012[58] i					66.0	20.9%	23.0%		
Santangelo et al. 2019[73]	Italy	Mixed	22.1	Cross-sectional	NA	27	104	183	673
Weinland et al. 2019[13] j	Germany	Male	48.0	Case–control	155.0	NA	NA	NA	NA
Weinland et al. 2019[13] j		Female			60.0	NA	NA	NA	NA

Table 1. Characteristics of all included studies. [a]Data obtained from graphs. [b]Data obtained by contacting the authors. [c]Excluded as outlier in sensitivity analyses. [d]Standard deviations derived from confidence intervals. [e]Standard deviations derived from standard errors of the mean. [f]Standard deviations derived from p-values. [g]Pearson correlation coefficient r. [h]Spearman's ρ. [i]No absolute numbers reported. [j]Data only reported as odds ratios.
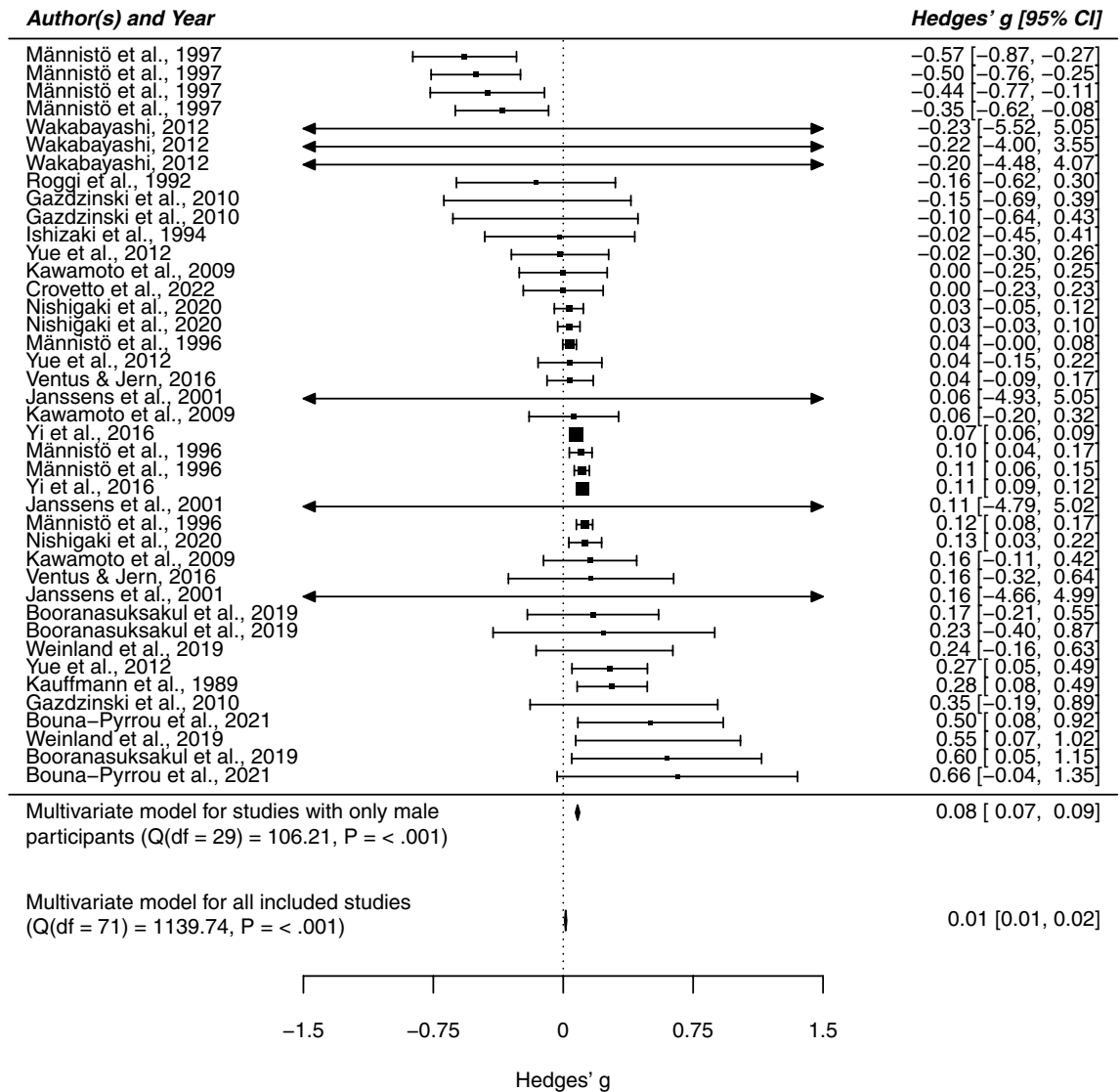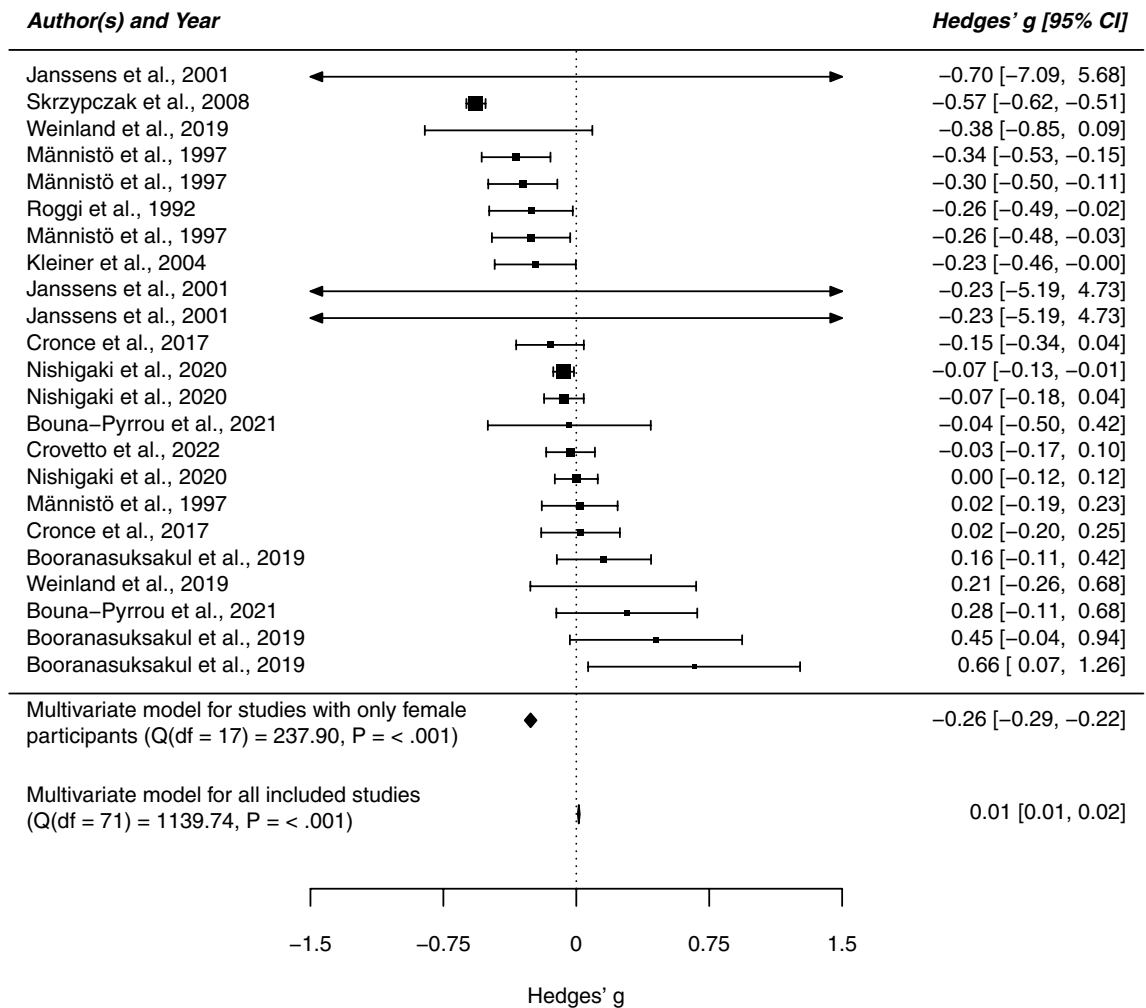
Figure 2. Forest plot of the standardized mean difference in BMI among male drinking and non-drinking subjects. This plot shows the results of the individual studies examining males together with their 95% confidence interval (CI). The weight of each study contributing to the overall effect is illustrated by the size of the square. The summary polygons at the bottom of the plot show the results from the multivariate meta-analytic model for (1) the subgroup of males and for (2) all included studies.

(z = 1.35, p = 0.51), whereas in women, the negative association between alcohol consumption and BMI was more pronounced in Caucasian than in Asian participants (g = −0.45 compared to g = −0.05; z = 11.5, p < 0.0001).

Due to insufficient data, it was not possible to compute the moderator analysis distinguishing between different beverage types: only one study[64] reported separate BMI data for beer, wine, and liquor drinkers.

Meta-regression analyses. Since all our meta-analytic results revealed a strong influence of sex, we also performed sex-separated meta-regression analyses. The threshold for significant results was Bonferroni-corrected at p = 0.006.

The meta-regression analysis concerning the amount of alcohol in gram per day revealed a significant moderating influence on the effect sizes of the overall sample (β = 0.0009, p < 0.0001) and of men (β = 0.001, p < 0.0001). This result suggests that in men with every additional gram of alcohol per day the association of alcohol use and BMI increases by 0.001. In women, the meta-regression was not significant (β = 0.002, p = 0.07). The addition of a quadratic term did not explain for more variance than the linear term (no U-shaped association detectable) (data not shown). In our sample, the mean alcohol consumption was 23.14 g/day for men and 13.82 g/day for women.

Ethanol intake and smoking was correlated in our sample, insofar that the amount of alcohol (g/day) and the percentage of smokers in the drinking group was moderately associated for males (r = 0.39, p = 0.097) and highly associated for females (r = 0.92, p = 0.003). The meta-regression regarding the percentage of smokers revealed a non-significant influence on the effect size (males: β = 0.06, p = 0.05; females: β = −0.52, p = 0.09).

Figure 3. Forest plot of the standardized mean difference in BMI among female drinking and non-drinking subjects. This plot shows the results of the individual studies examining females together with their 95% confidence interval (CI). The weight of each study contributing to the overall effect is illustrated by the size of the square. The summary polygons at the bottom of the plot show the results from the multivariate meta-analytic model for (1) the subgroup of females and for (2) all included studies.

The mean study quality assessed via the Newcastle–Ottawa-Scale[39,40] was 5.37 ± 0.79. The meta-regression analyses regarding study quality remained non-significant for the male sample (β = − 0.019, p = 0.11), but suggest an influence of the studies' risk of bias on the female (β = 0.350, p < 0.0001) and overall effect size (β = − 0.038, p < 0.0001).

Small study effects and sensitivity analyses. When visually examining the funnel plot (Supplementary Fig. S1), no evidence of small study effects or publication bias was detectable. Sensitivity analyses revealed one influential outlier[78] whose inclusion biased the results substantially, especially in terms of heterogeneity (result before exclusion: g = − 0.04, 95% CI [− 0.05, − 0.04], Q = 115,516.38; after exclusion: g = 0.01, 95% CI [0.01; 0.02], Q = 1139.74). Therefore, this study was excluded from all analyses.

Discussion

To our knowledge, this is the first systematic literature search and meta-analysis to investigate how alcohol use associates with BMI in normal to overweight individuals while focusing on possible sex differences. We found a sex-diverging relationship of small size: whereas alcohol use was slightly related to higher BMI in men, it was more strongly linked to lower BMI in women. Thus, our meta-analytic findings provide empirical evidence to confirm the previous assumption of a systematic review[29] that alcohol use is to a small extent, but positively associated with BMI in men; to this state of knowledge, we also add that alcohol use in women is related to a lower BMI. This also matches data of a recent study indicating that higher BMI is related to an increased risk for hospital readmissions in male in-patients with AUD, while it tends to be protective in female in-patients[90]. When analyzing both sexes together, our results match previous meta-analyses suggesting that higher alcohol intake associates with higher BMI[34,35]. In terms of practical relevance, the small effect sizes of up to Hedges' g = − 0.26 mean that the BMI of approximately 60% of female drinkers is below the average BMI of non-drinking women[91].

One has to bear in mind that with a non-overlap of approximately 15% between drinkers and non-drinkers the practical impact of these findings is small[91]. Nevertheless, these effects raise the question which mechanisms underlie the sex-diverging relationships between alcohol use and BMI. In moderator analyses, we found significant and sex-separated effects of the amount of daily ethanol intake and ethnicity.

The amount of alcohol consumed daily influenced the BMI in men. This supports the assumption that caloric intake due to alcohol consumption leads to higher BMI in men. Sayon-Orea et al.[29] suggest in their review that the caloric impact of alcohol use (represented by a positive association of BMI and alcohol use) is only evident in subjects who drink more often and in larger quantity. On average, males consume more alcohol than females[1] which also holds true for the here analyzed sample (mean[males] = 23.14 g/day; mean[females] = 13.82 g/day). It is possible that a part of the sex-diverging effect found here is attributable to the differences in the mean ethanol intake between men and women. Accordingly, we did not observe such a significant moderating effect in the female samples, which suggests that either their drinking quantity was too low or that mechanisms other than calorie supply are relevant in women. A further explanation of the positive association found in men might be the toxic effect of alcohol on different body functions. Regular alcohol consumption can lead to a state of generalized insulin resistance by inhibiting, for example, glucose disposal or insulin release in men[17]. This resistance is commonly paralleled by higher body weight[18,92].

We aimed at testing whether sex differences in choice of beverage type account for the sex diverging relationships of alcohol use and BMI. However, we were not able to provide meta-analytic support of this association here, as our systematic literature search identified only one early paper that provided beverage type-specific data[64]. This study indicates higher BMI in liquor than in wine drinkers of both sexes. Similarly, Sayon-Orea et al.[29] found that beer and liquor consumption (≥ 7 drinks/week) are associated with weight gain, whereas no such effect was found for wine consumption. We also analyzed correlations between beverage-type specific alcohol drinking and BMI in an additional data set[7] and found a positive correlation between liquor intake and BMI in male patients with AUD (see Supplementary Fig. S2). As men prefer liquor[7,93], the higher caloric intake associated with liquor consumption (which is more often found in men vs. women) might account for our observation of higher BMI in men with alcohol use vs. men who deny alcohol consumption. Furthermore, the sex-specific choice of beverage type might also help to explain why our meta-analysis demonstrates lower BMI in women with alcohol use. Consumption of wine, but not use of beer or liquor, is related to more frequent exercising in both sexes[94] and to a more healthy dietary behavior[95,96]. Choice of beverage type was also suggested to associate with intake of fat, carbohydrate, and vitamins[64]. Women more often choose wine[7,93] and thus the alcohol intake in women is expected to be related to more frequent exercising and possibly to a more healthy life-style which might account for the here observed lower BMI in alcohol-using women. However, future research is needed to study the mechanisms underlying the identified sex-diverging association between alcohol use and BMI.

A higher percentage of smokers in the drinking group amplified the sex-diverging association of alcohol use and BMI but remained non-significant. Usually, smoking is associated with weight loss and lower BMI[80,97] as in our female sample. However, more recent studies with large sample sizes suggest that this relationship is less clear, especially in obese persons[98,99], corresponding to the results in our male sample. Weinland et al.[13] also reported an amplifying effect of active smoking status which might be due to a positive association of smoking and alcohol consumption in general[61,80]. In our study, these two variables were highly correlated, as well. It is possible that the results of this meta-regression reflect the results for subjects drinking in higher quantity since subgroups comprising more smokers consumed more alcohol here.

We here also provide first meta-analytic evidence that ethnicity modulates the sex-separated relationship between alcohol use and BMI. The effect size of the lower BMI values in alcohol-drinking vs. control women was stronger in the Caucasian than in the Asian subsample. It is well-established that genetics influences the response to alcohol and the vulnerability to develop AUD[100,101], and this might explain the here observed inter-ethnic variation of the relationship between alcohol use and BMI.

Limitations and strengths.   There are some limitations to this study. First, the literature search was restricted to titles resulting in a smaller number of eligible studies. We tried to extend the literature search to abstracts or a full-text search, but the number of results was too high to be economically screened for eligibility. Additionally, the literature search only identified two studies addressing patients with AUD[13,59]; thus, it remains to be shown whether the here reported associations could be generalized to AUD. Third, we could not properly test for an inverted U-shaped relationship between the amount of alcohol consumption and BMI since we lacked studies with highly consuming participants. Even if there was an inverted U-shaped association between these two variables, our dataset with light to moderate drinkers would only be able to detect the ascending slope up to the point of inflection. Fourth, all effect sizes computed in this study are small following Cohen[102]. Consequently, they do not reach the extent of the minimal clinically relevant difference defined by Sayon-Orea et al.[29]. Fifth, the usage of a multivariate meta-analytic model might also involve some limitations[103]. It assumes, for example, that missing values are missing at random which is not always true, especially when they are missing due to non-significance. Furthermore, additional modeling assumptions are required and harder to verify than in univariate meta-analyses. Applying the multivariate model also entails numerous strengths. It uses more information improving statistical properties such as smaller mean-square error and greater precision[104]. It also allows for accounting for covariances between pooled estimates and for reducing reporting bias when some outcomes are selectively missing. A detailed summary of advantages and disadvantages of multivariate meta-analysis can be found in Jackson et al.[103]. Further strengths of this study are the strict adherence to the standardized PRISMA guidelines[36,37] (see Supplementary Table S2), the probable absence of small study effects, the reasonably robust results revealed by our sensitivity analyses and by the stability of our results after updating the literature search, and the rather representative control group. In case–control studies, a control group is usually defined by the

strict absence of the variable of interest[105]. Concerning the variable alcohol use, this is not typical for the average population where, for example, only 23.5% are lifetime abstainers in the European region[1]. Our control subjects are defined by different measures (see section "Statistical analyses") and therefore, are not classed among "super healthy" controls. Thus, our results can more easily be generalized to the general population[105]. This also holds true for our drinking group with especially women being comparable to the general population in terms of their mean ethanol intake (14 g/day here compared to 15 g/day among females worldwide[1]). Additionally, this is, up to our knowledge, the first meta-analysis specifically examining the association of alcohol consumption and BMI for different ethnicities.

Conclusion

As far as we know, this is the first meta-analysis to show that alcohol use associates with higher BMI in men and lower BMI in women. The effect size is lower in female Asians than Caucasians and it is influenced by the amount of alcohol consumption per day. However, our effect sizes did not reach the extent of the minimal clinically relevant difference defined by a previous review[29]. The differences in average daily alcohol consumption between men and women as well as sex-specific choice of beverage linked to life style factors such as exercise and intake of fat and carbohydrates might account for these sex-diverging effects. This interpretation requests validation by future studies. Our findings lay the foundation of further studies investigating mechanisms underlying alcohol use.

Data availability

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

References

1. World Health Organization. *Global Status Report on Alcohol and Health 2018* (World Health Organization, 2019).
2. Hansson, A. C. *et al.* Oxytocin reduces alcohol cue-reactivity in alcohol-dependent rats and humans. *Neuropsychopharmacology* **43**, 1235–1246. https://doi.org/10.1038/npp.2017.257 (2018).
3. Hansson, A. C. & Spanagel, R. No changes in the oxytocin system in alcohol-dependent female rodents and humans: Towards a sex-specific psychopharmacology in alcoholism. *Addict. Biol.* **26**, e12945. https://doi.org/10.1111/adb.12945 (2021).
4. Lenz, B. *et al.* Prenatal and adult androgen activities in alcohol dependence. *Acta Psychiatr. Scand.* **136**, 96–107. https://doi.org/10.1111/acps.12725 (2017).
5. Lenz, B., Köllner, M. G., Mühle, C., Weinland, C. & Kornhuber, J. Basic human body dimensions relate to alcohol dependence and predict hospital readmission. *J. Clin. Med.* **8**, 2076. https://doi.org/10.3390/jcm8122076 (2019).
6. Lenz, B. *et al.* Sex hormone activity in alcohol addiction: Integrating organizational and activational effects. *Progress Neurobiol.* **96**, 136–163. https://doi.org/10.1016/j.pneurobio.2011.11.001 (2012).
7. Lenz, B. *et al.* Oxytocin blood concentrations in alcohol use disorder: A cross-sectional, longitudinal, and sex-separated study. *Eur. Neuropsychopharmacol.* **51**, 55–67. https://doi.org/10.1016/j.euroneuro.2021.04.015 (2021).
8. Mühle, C., Barry, B., Weinland, C., Kornhuber, J. & Lenz, B. Estrogen receptor 1 gene variants and estradiol activities in alcohol dependence. *Progress Neuro-psychopharmacol. Biol. Psychiatry.* **92**, 301–307. https://doi.org/10.1016/j.pnpbp.2019.01.008 (2019).
9. Mühle, C., Weinland, C., Gulbins, E., Lenz, B. & Kornhuber, J. Peripheral acid sphingomyelinase activity is associated with biomarkers and phenotypes of alcohol use and dependence in patients and healthy controls. *Int. J. Mol. Sci.* **19**, 4028. https://doi.org/10.3390/ijms19124028 (2018).
10. Müller, C. P., Mühle, C., Kornhuber, J. & Lenz, B. Sex-dependent alcohol instrumentalization goals in non-addicted alcohol consumers versus patients with alcohol use disorder: Longitudinal change and outcome prediction. *Alcoholism* **45**, 577–586. https://doi.org/10.1111/acer.14550 (2021).
11. Siegmann, E.-M., Bouna-Pyrrou, P., Lenz, B. & Kornhuber, J. Digit ratio (2D:4D) in relation to substance and computer use: A meta-analysis. *J. Neural Transmission.* **126**, 623–636. https://doi.org/10.1007/s00702-019-02002-2 (2019).
12. Weinland, C., Braun, B., Mühle, C., Kornhuber, J. & Lenz, B. Cloninger type 2 score and Lesch typology predict hospital readmission of female and male alcohol-dependent inpatients during a 24-month follow-up. *Alcoholism* **41**, 1760–1767. https://doi.org/10.1111/acer.13468 (2017).
13. Weinland, C., Mühle, C., Kornhuber, J. & Lenz, B. Body mass index and craving predict 24-month hospital readmissions of alcohol-dependent in-patients following withdrawal. *Progress Neuro-psychopharmacol. Biol. Psychiatry.* **90**, 300–307. https://doi.org/10.1016/j.pnpbp.2018.11.019 (2019).
14. Weinland, C., Mühle, C., Kornhuber, J. & Lenz, B. Crossed eye/hand laterality and left-eyedness predict a positive 24-month outcome in alcohol-dependent patients. *Alcoholism* **43**, 1308–1317. https://doi.org/10.1111/acer.14051 (2019).
15. Weinland, C., Mühle, C., Kornhuber, J. & Lenz, B. Progesterone serum levels correlate negatively with craving in female postmenopausal in-patients with alcohol use disorder: A sex- and menopausal status-separated study. *Progress Neuro-psychopharmacol. Biol. Psychiatry.* **110**, 110278. https://doi.org/10.1016/j.pnpbp.2021.110278 (2021).
16. Weinland, C., Mühle, C., von Zimmermann, C., Kornhuber, J. & Lenz, B. Sulphated dehydroepiandrosterone serum levels are reduced in women with alcohol use disorder and correlate negatively with craving: A sex-separated cross-sectional and longitudinal study. *Addict. Biol.* **27**, e13135. https://doi.org/10.1111/adb.13135 (2022).
17. Boden, G., Chen, X., DeSantis, R. A. & Kendrick, Z. Ethanol inhibits insulin action on lipolysis and on insulin release in elderly men. *Am. J. Physiol.* **265**, 197–202. https://doi.org/10.1152/ajpendo.1993.265.2.E197 (1993).
18. de La Monte, S., Derdak, Z. & Wands, J. R. Alcohol, insulin resistance and the liver–brain axis. *J. Gastroenterol. Hepatol.* **27**(Suppl 2), 33–41. https://doi.org/10.1111/j.1440-1746.2011.07023.x (2012).
19. Volkow, N. D. & Wise, R. A. How can drug addiction help us understand obesity?. *Nat. Neurosci.* **8**, 555–560. https://doi.org/10.1038/nn1452 (2005).
20. Bowirrat, A. & Oscar-Berman, M. Relationship between dopaminergic neurotransmission, alcoholism, and Reward Deficiency syndrome. *Am. J. Med. Genet. Part B Neuropsychiatr. Genet.* **132B**, 29–37. https://doi.org/10.1002/ajmg.b.30080 (2005).
21. Volkow, N. D., Fowler, J. S., Wang, G.-J. & Goldstein, R. Z. Role of dopamine, the frontal cortex and memory circuits in drug addiction: Insight from imaging studies. *Neurobiol. Learn. Memory.* **78**, 610–624. https://doi.org/10.1006/nlme.2002.4099 (2002).
22. Verdejo-Román, J., Vilar-López, R., Navas, J. F., Soriano-Mas, C. & Verdejo-García, A. Brain reward system's alterations in response to food and monetary stimuli in overweight and obese individuals. *Hum. Brain Mapping.* **38**, 666–677. https://doi.org/10.1002/hbm.23407 (2017).

23. Martinez, D. *et al.* Alcohol dependence is associated with blunted dopamine transmission in the ventral striatum. *Biol. Psychiatry.* **58**, 779–786. https://doi.org/10.1016/j.biopsych.2005.04.044 (2005).
24. Filbey, F. M., Myers, U. S. & DeWitt, S. Reward circuit function in high BMI individuals with compulsive overeating: Similarities with addiction. *Neuroimage* **63**, 1800–1806. https://doi.org/10.1016/j.neuroimage.2012.08.073 (2012).
25. Garcia-Garcia, I. *et al.* Reward processing in obesity, substance addiction and non-substance addiction. *Obes. Rev.* **15**, 853–869. https://doi.org/10.1111/obr.12221 (2014).
26. Lichenstein, S. D. *et al.* Familial risk for alcohol dependence and developmental changes in BMI: The moderating influence of addiction and obesity genes. *Pharmacogenomics* **15**, 1311–1321. https://doi.org/10.2217/pgs.14.86 (2014).
27. Ehlers, C. L. & Wilhelmsen, K. C. Genomic screen for substance dependence and body mass index in southwest California Indians. *Genes Brain Behav.* **6**, 184–191. https://doi.org/10.1111/j.1601-183X.2006.00246.x (2007).
28. Flegal, K. M., Kruszon-Moran, D., Carroll, M. D., Fryar, C. D. & Ogden, C. L. Trends in obesity among adults in the United States, 2005 to 2014. *JAMA* **315**, 2284–2291. https://doi.org/10.1001/jama.2016.6458 (2016).
29. Sayon-Orea, C., Martinez-Gonzalez, M. A. & Bes-Rastrollo, M. Alcohol consumption and body weight: A systematic review. *Nutr. Rev.* **69**, 419–431. https://doi.org/10.1111/j.1753-4887.2011.00403.x (2011).
30. Nies, M. A., Sun, L., Kazemi, D., Carriker, A. & Dmochowski, J. Relationship of body mass index to alcohol consumption in college freshmen. *TheScientificWorldJOURNAL* **2012**, 849018. https://doi.org/10.1100/2012/849018 (2012).
31. Bouna-Pyrrou, P., Mühle, C., Kornhuber, J., Weinland, C. & Lenz, B. Body mass index and serum levels of soluble leptin receptor are sex-specifically related to alcohol binge drinking behavior. *Psychoneuroendocrinology* **127**, 105179. https://doi.org/10.1016/j.psyneuen.2021.105179 (2021).
32. Wills, A. G., Evans, L. M. & Hopfer, C. Phenotypic and genetic relationship between BMI and drinking in a sample of UK adults. *Behav. Genet.* **47**, 290–297. https://doi.org/10.1007/s10519-017-9838-2 (2017).
33. Schutz, Y. Role of substrate utilization and thermogenesis on body-weight control with particular reference to alcohol. *Proc. Nutr. Soc.* **59**, 511–517. https://doi.org/10.1017/s0029665100000744 (2000).
34. Wulandari, A. N. & Hanida, A. N. Meta-analysis: Relationship between alcohol consumption and age on obesity in adults. *J. Epidemiol. Public Health.* **7**, 153–166. https://doi.org/10.26911/jepublichealth.2022.07.02.01 (2022).
35. Golzarand, M., Salari-Moghaddam, A. & Mirmiran, P. Association between alcohol intake and overweight and obesity: A systematic review and dose–response meta-analysis of 127 observational studies. *Crit. Rev. Food Sci. Nutr.* **62**, 8078–8098. https://doi.org/10.1080/10408398.2021.1925221 (2022).
36. Liberati, A. *et al.* The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. *BMJ* **339**, b2700. https://doi.org/10.1016/j.jclin (2009).
37. Moher, D., Liberati, A., Tetzlaff, J. & Altman, D. G. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Med.* **6**, e100097. https://doi.org/10.1016/j.ijsu.2010.02.007 (2010).
38. Siegmann, E.-M. *et al.* Digit ratio (2D:4D) and transgender identity: New original data and a meta-analysis. *Sci. Rep.* **10**, 19326. https://doi.org/10.1038/s41598-020-72486-6 (2020).
39. Wells, G. A. *et al.* The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.Accessed 3 November 2018.
40. Herzog, R. *et al.* Are healthcare workers' intentions to vaccinate related to their knowledge, beliefs and attitudes? A systematic review. *BMC Public Health* **13**, 1–17. https://doi.org/10.1186/1471-2458-13-154 (2013).
41. Viechtbauer, W. Conducting meta-analyses in R with the metafor package. *J. Stat. Softw.* **36**, 1–48. https://doi.org/10.18637/jss.v036.i03 (2010).
42. R Core Team. R: A Language and Environment for Statistical Computing}. https://www.R-project.org/ (2021). Accessed 4 January 2019.
43. Borenstein, M., Hedges, L. V., Higgins, J. P. & Rothstein, H. R. *Introduction to Meta-analysis* 45–49 (Wiley, 2009).
44. Saunders, J. B., Aasland, O. G., Babor, T. F., La Fuente, J. R. de & Grant, M. Development of the alcohol use disorders identification test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption—II. *Addiction (Abingdon, England).* **88**, 791–804. https://doi.org/10.1111/j.1360-0443.1993.tb02093.x (1993).
45. Mann, K. & Ackermann, K. Die OCDS-G: Psychometrische Kennwerte der deutschen Version der Obsessive Compulsive Drinking Scale. *SUCHT* **46**, 90–100. https://doi.org/10.1024/suc.2000.46.2.90 (2000).
46. Patrick, M. E. *et al.* Extreme binge drinking among 12th-grade students in the United States: Prevalence and predictors. *JAMA Pediatr.* **167**, 1019–1025. https://doi.org/10.1001/jamapediatrics.2013.2392 (2013).
47. Cheung, M.W.-L. A guide to conducting a meta-analysis with non-independent effect sizes. *Neuropsychol. Rev.* **29**, 387–396. https://doi.org/10.1007/s11065-019-09415-6 (2019).
48. Gleser, L. J. & Olkin, I. Stochastically dependent effect sizes. in *The Handbook of Research Synthesis and Meta-analysis* (ed. Cooper), 2nd ed. (Russell Sage Foundation, 2009), pp. 357–376.
49. Agarwal, D. P. & Goedde, H. W. Medicobiological and genetic studies on alcoholism. Role of metabolic variation and ethnicity on drinking habits, alcohol abuse and alcohol-related mortality. *Clin. Investigator* **70**, 465–477. https://doi.org/10.1007/BF00210227 (1992).
50. Wall, T. L., Luczak, S. E. & Hiller-Sturmhöfel, S. Biology, genetics, and environment: Underlying factors influencing alcohol metabolism. *Alcohol Res.* **38**, 59–68 (2016).
51. WHO expert consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet* **363**, 157–163. https://doi.org/10.1016/S0140-6736(03)15268-3 (2004).
52. Peters, J. L., Sutton, A. J., Jones, D. R., Abrams, K. R. & Rushton, L. Contour-enhanced meta-analysis funnel plots help distinguish publication bias from other causes of asymmetry. *J. Clin. Epidemiol.* **61**, 991–996. https://doi.org/10.1016/j.jclinepi.2007.11.010 (2008).
53. Sterne, J. A. & Egger, M. Funnel plots for detecting bias in meta-analysis. *J. Clin. Epidemiol.* **54**, 1046–1055. https://doi.org/10.1016/S0895-4356(01)00377-8 (2001).
54. Viechtbauer, W. & Cheung, M. W. Outlier and influence diagnostics for meta-analysis. *Res. Synthesis Methods* **1**, 112–125. https://doi.org/10.1002/jrsm.11 (2010).
55. Greenhouse, J. B. & Iyengar, S. Sensitivity analysis and diagnostics. in *The Handbook of Research Synthesis and Meta-analysis* (ed. Cooper), 2nd ed. (Russell Sage Foundation, 2009), pp. 417–433.
56. Cronce, J. M., Bedard-Gilligan, M. A., Zimmerman, L., Hodge, K. A. & Kaysen, D. Alcohol and binge eating as mediators between posttraumatic stress disorder symptom severity and body mass index. *Obesity (Silver Spring, Md.)* **25**, 801–806. https://doi.org/10.1002/oby.21809 (2017).
57. Ahaneku, G. I., Ahaneku, J. E., Osuji, C. U., Oguejiofor, C. O. & Opara, P. C. (2014) Lipid patterns, alcohol intake and BMI of adult Nigerians in a sub-urban slum in Enugu, Nigeria. *Pan Afr. Med. J.* **18**, 37. https://doi.org/10.11604/pamj.2014.18.37.1926.
58. Wakabayashi, I. Increased body mass index modifies associations between alcohol intake and blood cholesterol profile. *Eur. J. Clin. Investig.* **42**, 179–185. https://doi.org/10.1111/j.1365-2362.2011.02568.x (2012).
59. Gazdzinski, S., Durazzo, T. C., Mon, A. & Meyerhoff, D. J. Body mass index is associated with brain metabolite levels in alcohol dependence—A multimodal magnetic resonance study. *Alcoholism Clin. Exp. Res.* **34**, 2089–2096. https://doi.org/10.1111/j.1530-0277.2010.01305.x (2010).

60. Gearhardt, A. N. & Corbin, W. R. Body mass index and alcohol consumption: Family history of alcoholism as a moderator. *Psychol. Addictive Behav.* **23**, 216–225. https://doi.org/10.1037/a0015011 (2009).
61. Skrzypczak, M., Szwed, A., Pawlińska-Chmara, R. & Skrzypulec, V. Body mass index, waist to hip ratio and waist/height in adult Polish women in relation to their education, place of residence, smoking and alcohol consumption. *Homo* **59**, 329–342. https://doi.org/10.1016/j.jchb.2008.06.003 (2008).
62. Kleiner, K. D. *et al.* Body mass index and alcohol use. *J. Addictive Diseases* **23**, 105–118. https://doi.org/10.1300/J069v23n03_08 (2004).
63. Männistö, S. *et al.* Reported alcohol intake, diet and body mass index in male smokers. *Eur. J. Clin. Nutr.* **50**, 239–245 (1996).
64. Männistö, S., Uusitalo, K., Roos, E., Fogelholm, M. & Pietinen, P. Alcohol beverage drinking, diet and body mass index in a cross-sectional survey. *Eur. J. Clin. Nutr.* **51**, 326–332. https://doi.org/10.1038/sj.ejcn.1600406 (1997).
65. Ishizaki, M. *et al.* Erythrocyte Na+/K(+)-ATPase and membrane and serum lipid profiles: As related to alcohol, body mass index and blood pressure. *Clin. Exp. Hypertension (New York, NY" 1993)* **16**, 741–759. https://doi.org/10.3109/10641969409078023 (1994).
66. Kauffmann, F., Annesi, I., Neukirch, F., Oryszczyn, M. P. & Alperovitch, A. The relation between snoring and smoking, body mass index, age, alcohol consumption and respiratory symptoms. *Eur. Respir. J.* **2**, 599–603 (1989).
67. Hooper, L. M., Doehler, K., Jankowski, P. J. & Tomek, S. E. Patterns of self-reported alcohol use, depressive symptoms, and body mass index in a family sample: The buffering effects of parentification. *Family J.* **20**, 164–178. https://doi.org/10.1177/1066480711435320 (2012).
68. Cho, M.-K. & Kim, M. Y. Differences in SBP, BMI, and stress with AUDIT score in adolescents. *TONURSJ* **12**, 228–237. https://doi.org/10.2174/1874434601812010228 (2018).
69. Amorim, T. C., Amorim, M. E., Guedes, L. A. & Lima, S. Evaluation of alcohol addiction among Brazilian Northeast medical students through the alcohol use disorders identification test and the relation with body mass index and smoking. *Rev. Bras. Clin. Med.* **10**, 398–401 (2012).
70. Remus, D. Body mass index and alcohol consumption influences (physical education). *Int. J. Sci. Res.* **3**, 484–485 (2014).
71. Sebelien, M. B. BMI status and intake of red meat, dietary fiber and alcohol in colorectal cancer patients prior to diagnosis. An interim analysis. Master thesis. University of Oslo, 2013.
72. Ventus, D. & Jern, P. Lifestyle factors and premature ejaculation: Are physical exercise, alcohol consumption, and body mass index associated with premature ejaculation and comorbid erectile problems?. *J. Sexual Med.* **13**, 1482–1487. https://doi.org/10.1016/j.jsxm.2016.08.007 (2016).
73. Santangelo, O. E. *et al.* Is there a link between BMI and depressive symptomatology, risky consumption of alcohol and anxious symptomatology? Study in a sample of university students. *Minerva Psichiatr.* https://doi.org/10.23736/S0391-1772.19.02011-9 (2019).
74. Roggi, C., Silva, S., Maccarini, L., Mazzei, B. & Meloni, C. Alcohol, smoking and body mass index in a sample of adults from the general population. *Ann. Ig.* **4**, 359–367 (1992).
75. Janssens, J. P. *et al.* Overweight, obesity and beer consumption—Alcohol drinking habits in Belgium and body mass index. *Arch Public Health* **59**, 223–238 (2001).
76. Nishigaki, D. *et al.* Body mass index modifies the association between frequency of alcohol consumption and incidence of hypertension in men but not in women: A retrospective cohort study. *Hypertension Res.* **43**, 322–330. https://doi.org/10.1038/s41440-019-0382-8 (2020).
77. Booranasuksakul, U., Singhato, A., Rueangsri, N. & Prasertsri, P. (2019) Association between Alcohol Consumption and Body Mass Index in University Students. *Asian/Pacific Island Nursing J.* **4**, 57–65. https://doi.org/10.31372/20190401.1035.
78. Rask-Andersen, M., Karlsson, T., Ek, W. E. & Johansson, Å. Gene-environment interaction study for BMI reveals interactions between genetic factors and physical activity, alcohol consumption and socioeconomic status. *PLoS Genet.* **13**, e1006977. https://doi.org/10.1371/journal.pgen.1006977 (2017).
79. Yi, S.-W., Hong, J.-S., Yi, J.-J. & Ohrr, H. Impact of alcohol consumption and body mass index on mortality from nonneoplastic liver diseases, upper aerodigestive tract cancers, and alcohol use disorders in Korean older middle-aged men: Prospective cohort study. *Medicine* **95**, e4876. https://doi.org/10.1097/md.0000000000004876 (2016).
80. Shaikh, R. A., Siahpush, M., Singh, G. K. & Tibbits, M. Socioeconomic status, smoking, alcohol use, physical activity, and dietary behavior as determinants of obesity and body mass index in the United States: Findings from the National Health Interview Survey. *Int. J. MCH AIDS.* **4**, 22–34. https://doi.org/10.21106/ijma.53 (2015).
81. Yue, F. *et al.* Association of alcohol consumption with the impaired β-cell function independent of body mass index among Chinese men. *Endocrine J.* **59**, 425–433. https://doi.org/10.1507/endocrj.ej12-0003 (2012).
82. Loomba, R., Bettencourt, R. & Barrett-Connor, E. Synergistic association between alcohol intake and body mass index with serum alanine and aspartate aminotransferase levels in older adults: The Rancho Bernardo Study. *Alimentary Pharmacol. Therapeutics* **30**, 1137–1149. https://doi.org/10.1111/j.1365-2036.2009.04141.x (2009).
83. Kawamoto, R. *et al.* Alcohol consumption is associated with decreased insulin resistance independent of body mass index in Japanese community-dwelling men. *Tohoku J. Exp. Med.* **218**, 331–337. https://doi.org/10.1620/tjem.218.331 (2009).
84. Agarwal, K., Demiral, S. B., Manza, P., Volkow, N. D. & Joseph, P. V. Relationship between BMI and alcohol consumption levels in decision making. *Int. J. Obesity.* **45**, 2455–2463. https://doi.org/10.1038/s41366-021-00919-x (2021).
85. Crovetto, M. *et al.* Association of weekend alcohol consumption with diet variables, body mass index, cardiovascular risk and sleep. *Human Nutr. Metab.* **27**, 200140. https://doi.org/10.1016/j.hnm.2022.200140 (2022).
86. Gao, C. *et al.* Four-way decomposition of effect of alcohol consumption and body mass index on lipid profile. *Int. J. Environ. Res. Public Health.* https://doi.org/10.3390/ijerph182143211 (2021).
87. Hashimoto, Y. *et al.* Effect of body mass index on the association between alcohol consumption and the development of chronic kidney disease. *Sci. Rep.* **11**, 20440. https://doi.org/10.1038/s41598-021-99222-y (2021).
88. Innes, H. *et al.* Characterizing the risk interplay between alcohol intake and body mass index on cirrhosis morbidity. *Hepatology (Baltimore, MD)* **75**, 369–378. https://doi.org/10.1002/hep.32123 (2022).
89. Kokubun, K., Pineda, J. C. D. & Yamakawa, Y. Unhealthy lifestyles and brain condition: Examining the relations of BMI, living alone, alcohol intake, short sleep, smoking, and lack of exercise with gray matter volume. *PLoS ONE* **16**, e0255285. https://doi.org/10.1371/journal.pone.0255285 (2021).
90. Hoffmann, S. *et al.* Body mass index interacts with sex to predict readmission in in-patients with alcohol use disorder. *Addiction Biol.* **28**, e13239. https://doi.org/10.1111/adb.13239 (2023).
91. Kim, H.-Y. Statistical notes for clinical researchers: Effect size. *Restorative Dentistry Endodontics* **40**, 328–331. https://doi.org/10.5395/rde.2015.40.4.328 (2015).
92. Schindler, T. H. *et al.* Relationship between increasing body weight, insulin resistance, inflammation, adipocytokine leptin, and coronary circulatory function. *J. Am. College Cardiol.* **47**, 1188–1195. https://doi.org/10.1016/j.jacc.2005.10.062 (2006).
93. Klatsky, A. L., Armstrong, M. A. & Kipp, H. Correlates of alcoholic beverage preference: Traits of persons who choose wine, liquor or beer. *Br. J. Addiction* **85**, 1279–1289. https://doi.org/10.1111/j.1360-0443.1990.tb01604.x (1990).
94. Watten, R. G. Sports, physical exercise and use of alcohol. *Scand. J. Med. Sci. Sports* **5**, 364–368. https://doi.org/10.1111/j.1600-0838.1995.tb00060.x (1995).

95. Hansel, B. *et al.* Relationships between consumption of alcoholic beverages and healthy foods: The French supermarket cohort of 196,000 subjects. *Eur. J. Prevent. Cardiol.* **22**, 215–222. https://doi.org/10.1177/2047487313506829 (2015).
96. Johansen, D., Friis, K., Skovenborg, E. & Grønbaek, M. Food buying habits of people who buy wine or beer: Cross sectional study. *BMJ* **332**, 519–522. https://doi.org/10.1136/bmj.38694.568981.80 (2006).
97. Seeley, R. J. & Sandoval, D. A. Weight loss through smoking. *Nature* **475**, 176–177. https://doi.org/10.1038/475176a (2011).
98. Wang, Q. Smoking and body weight: Evidence from China health and nutrition survey. *BMC Public Health* **15**, 1238. https://doi.org/10.1186/s12889-015-2549-9 (2015).
99. Courtemanche, C., Tchernis, R. & Ukert, B. The effect of smoking on obesity: Evidence from a randomized trial. *J. Health Econ.* **57**, 31–44. https://doi.org/10.1016/j.jhealeco.2017.10.006 (2018).
100. Enoch, M.-A. Genetic influences on the development of alcoholism. *Curr. Psychiatry Rep.* **15**, 412. https://doi.org/10.1007/s11920-013-0412-1 (2013).
101. Enoch, M.-A. Genetic influences on response to alcohol and response to pharmacotherapies for alcoholism. *Pharmacol. Biochem. Behav.* **123**, 17–24. https://doi.org/10.1016/j.pbb.2013.11.001 (2014).
102. Cohen, J. *Statistical Power Analysis for the Behavioral Sciences* 2nd edn. (Routledge, 1988).
103. Jackson, D., White, I. R. & Riley, R. D. Multivariate Meta-Analysis. In *Handbook of Meta-Analysis,* edited by C. H. Schmid, T. Stijnen & I. R. White (Chapman and Hall/CRC, First edition. | Boca Raton : Taylor and Francis, [2020] | Series: Chapman & Hall/CRC handbooks of modern statistical methods, 2020), pp. 163–186.
104. Jackson, D., Riley, R. & White, I. R. Multivariate meta-analysis: Potential and promise. *Stat. Med.* **30**, 2481–2498. https://doi.org/10.1002/sim.4172 (2011).
105. Jablensky, A. Research methods in psychiatric epidemiology: An overview. *Aust. New Zealand J. Psychiatry* **36**, 297–310. https://doi.org/10.1046/j.1440-1614.2002.01035.x (2002).
106. Heinz, A. *et al.* Addiction Research Consortium: Losing and regaining control over drug intake (ReCoDe)-From trajectories to mechanisms and interventions. *Addiction Biol.* **25**, e12866. https://doi.org/10.1111/adb.12866 (2020).

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Funding

Competing interests

The authors declare no competing interests.

Additional information

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1038/s41598-022-25653-w.

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