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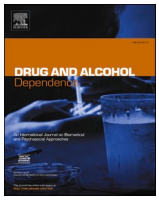

A dose-response meta-analysis on the relationship between average amount of alcohol consumed and death by suicide

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ABSTRACT

Background: To determine whether sub-clinical levels of drinking may contribute to suicide risk, and whether the risk differs by sex, we aimed to evaluate the relationship between average amount of alcohol consumed per day and death by suicide.

Methods: A systematic literature search was performed in Embase, Medline, PsycINFO, PubMed, and Web of Science from database inception up to April 27, 2022. The search strategies incorporated a combination of medical subject headings and keywords for "alcohol use" and "suicide". One-stage dose-response meta-analyses using a restricted maximum likelihood random-effect estimator were conducted to explore the relationship between average alcohol volume consumed and suicide, by sex. Three different shapes of the dose-response relationship–linear (on the log-scale), quadratic, and restrictive cubic splines–were tested.

Results: A total of eight studies were included (three studies for females (n=781,205), and eight studies for males (n=1,215,772)). A linear dose-response relationship between average alcohol volume consumed and the log-risk of suicide was identified for both males and females. For males and females, a relative risk (RR) of 1.11 (95% CI: 1.05, 1.18) and 1.64 (95% CI: 1.07, 2.51) for suicide when consuming an average of 10 g of pure alcohol per day compared to lifetime abstention, 1.38 (95% CI: 1.14, 1.66) and 4.39 (95% CI: 1.21, 15.88) for 30 g/day, and 1.71 (95% CI: 1.25, 2.33) and 11.75 (95% CI: 1.38, 100.33) for 50 g/day, respectively.

Conclusions: As consumption increases, the risk of suicide increases proportionally. The risk of suicide associated with average daily alcohol consumption may be elevated for females, compared with males. Albeit, more research is needed, particularly among females.

1. Introduction

Suicide is a global phenomenon that has received much international attention (UN General Assembly, 2015). In their Comprehensive Mental Health Action Plan, the World Health Organization (WHO) set a target of a one-third reduction in the global rate of suicide between 2013 and

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2030 (World Health Organization, 2021a). Despite numerous calls for action, suicide remains a public health concern, with over 700 thousand people dying by suicide in 2019 (World Health Organization, 2021b); highlighting the need for innovative suicide prevention strategies.

Alcohol use has been established as a risk factor for suicide (GBD 2016 Alcohol Collaborators, 2018; World Health Organization, 2018). Despite being referred to as an unmet public health crisis (Ahmed and Stanciu, 2017) and a missed opportunity (Kalk et al., 2019) in suicide prevention, alcohol consumption is a promising, and modifiable, target in suicide prevention efforts (Lange et al., 2023a). However, the relationship is nuanced, as alcohol use is a multi-dimensional exposure, having both precipitating and predisposing effects. Further, the relationship between alcohol use and suicide has been shown to differ by sex (for example, see (Kaplan et al., 2014) and (Roerecke and Rehm, 2014)), with females having an elevated risk compared to males.

Existing meta-analyses on the relationship between alcohol use and suicide have been limited to acute alcohol use (Borges et al., 2017) and alcohol use disorder (Abdul-Rahman et al., 2018; Darvishi et al., 2015; Ferrari et al., 2014; Roerecke and Rehm, 2014; Wilcox et al., 2004). However, another dimension of alcohol use expected to have a predisposing effect on suicide is average volume of alcohol consumed per day. Yet, to date, there is no evidence synthesis on the relationship between average daily consumption of alcohol and death by suicide. Gaining a better understanding of the relationship between average consumption and suicide will allow us to determine whether subclinical levels of drinking may also contribute to suicide risk (Lamis and Malone, 2012). Therefore, the aim of the current study was to synthesize all available evidence of the sex-specific relationship between average amount of alcohol consumed per day and death by suicide.

2. Material and methods

The current systematic review was reported according to the Preferred Reporting Items for Systematic Review and Meta-Analysis 2022 statement (Page et al., 2021). The protocol has been published elsewhere (Lange et al., 2022) and was registered with the International Prospective Register of Systematic Reviews (PROSPERO, registration number CRD42022320918).

2.1. Search strategy

A systematic literature search was performed in Embase, Medline (including Medline In-Process), PsycINFO, PubMed, and Web of Science from database inception up to April 27, 2022. The search strategy incorporated a combination of medical subject headings and keywords for "alcohol use" and "suicide" (Text S1). Manual reviews of citations in the articles deemed relevant and the studies included in related reviews and meta-analyses were conducted. The search results were imported into EndNote 20.3 (The EndNote Team, 2013) for deduplication.

2.2. Study selection

Two individuals (KVK and AML) were trained to screen titles and abstracts using batches of 100 randomly selected records. Training involved independent review and discussion of all discrepancies, until substantial interrater agreement was reached (McHugh, 2012). A total of eight batches of 100 were used for training; a percent agreement of 92% was achieved. Title and abstract screening of the remaining records were then screened by a single reviewer. The same process was used for full-text screening. In cases of uncertainty, a discussion was had between the two reviewers, and if necessary, third-party adjudication was used if an agreement could not be reached. Title and abstract screening was completed using EndNote 20.3 (The EndNote Team, 2013) and full-text screening was performed in Covidence (Covidence Systematic Review Software, 2023). After piloting a template created in Microsoft Excel using ten randomly selected studies (Microsoft Corporation, 2021), data extraction was completed by one reviewer and cross-checked by a second reviewer. If there was inadequate reporting of data, if data were unavailable (e.g., effect estimate values were not published), or sex-specific estimates were not reported, corresponding authors were contacted.

2.2.1. Eligibility criteria

The inclusion criteria were 1) an original, quantitative observational study, with 2) a measure of risk (or enough data to calculate a crude estimate) and its corresponding measure of variability (or sufficient data to calculate these; e.g., 95% confidence intervals), and 3) estimates of risk stratified by sex. Twin studies were not excluded, as they can provide information about the importance of specific risk factors independent of genetic confounding. There were no restrictions on setting, language of publication, geographical location, or year of publication. Beyond the inclusion criteria that the population under study be 15+ years of age (Table 1), in line with the vast literature on alcohol-attributable harm–e.g., see (GBD 2016 Alcohol Collaborators, 2018)–there were no other population restrictions applied given the suspected scarcity of studies on the relationship of interest. Studies that used qualitative labels, such as "social", "moderate", or "heavy" consumption were excluded if the quantification of volume of alcohol intake used to define these qualitative labels was not reported, as these terms lack standardization. See Table 1 for the specific inclusion and exclusion criteria.

2.2.1.1. Definitions and data transformations. Average alcohol volume consumed was operationalized as grams of pure alcohol consumed per day (g/day) on average. Among individuals who consumed alcohol, we converted reported alcohol intake categories (e.g., 0–20 g/day) into an average using the midpoints (mean) of each respective drinking category. For open-ended categories (e.g., ≥70 g/day), we added ¾ of the width of the previous category's range to the lower limit of the open-ended category of alcohol intake if the mean was not reported. Where necessary, standard drink size was used to convert all measures (e.g., number of drinks) to g/day. If standard drink size was not reported, we used the standard drink size of the country where the study was conducted. For our analyses, average alcohol volume consumed was

Table 1
PICOS criteria for study selection.

Criteria	Inclusion criteria	Exclusion criteria
Population	- Individuals ≥ 15 years of age	- None*
Intervention/ exposure	- Average amount of alcohol consumed	- Qualitative labels of alcohol use, such as "social", "moderate", or "heavy" consumption
Comparators	- Lifetime abstainers, individuals who previously consumed alcohol, or another category of average alcohol volume consumed (e.g., lowest category)	- None
Outcome	- Death by suicide - Sex-specific estimates	- Death by suicide and suicide attempt cannot be disaggregated - Individuals with an undetermined cause of death
Study design	- Quantitative observational study designs: cohort, case-control, or cross-sectional	- None
Other	- Any language, any geographical region, and any year of publication	- Overlapping sample with another study that has a more comprehensive sample or is more recent - Dissertation or conference abstract

* No further restrictions were applied given the suspected scarcity of studies on the relationship of interest.

classified as follows, given data availability: 1) lifetime abstainers; 2) individuals who previously consumed alcohol; and 3) average amount of alcohol consumed per day during the reference period. With respect to the outcome of interest, death by suicide was defined as death caused by any self-inflicted injurious behavior that was intended to kill oneself (Crosby et al., 2011), or applicable International Classification of Diseases-9, -10 or -11 codes.

2.3. Risk of bias

Risk of bias was independently assessed by two reviewers (KVK and AML) using the "Risk of bias in non-randomized studies of exposure" (ROBINS-E) tool for cohort studies (ROBINS-E Development Group et al., 2023), and Joanna Briggs Institute (JBI) critical appraisal tools for case-control studies (Moola et al., 2020). The JBI tool is a checklist of ten items used to assess the methodological quality of a study and to determine the extent to which a study has addressed the possibility of bias in its design, conduct and analysis. ROBINS-E includes seven domains of bias (i.e., risk of bias i) due to confounding, ii) arising from measurement of the exposure, iii) in selection of participants in to study (or analysis), iv) due to post-exposure interventions, v) due to missing data, vi) arising from measurement of the outcome, and vii) in selection of the reported results), each of which is addressed using a series of signaling questions. After the signaling questions are completed, the risk of bias is determined for each domain: low risk of bias–little or no concern about bias; some concerns–some concern about bias, although whether it is an important risk of bias is unclear; high risk of bias–some important concerns, with study characteristics giving rise to a high risk of bias; and very high risk of bias–very problematic, with study characteristics giving rise to a high risk of bias. Assessment of domain 1, risk of bias due to confounding, requires the assessors to 'list the important confounding factors relevant to all or most studies on this topic"; for this, it was specified that at minimum, age should be adjusted for.

2.4. Statistical analysis

In order to avoid the "sick quitter bias" (i.e., the bias of categorizing individuals who have stopped drinking alcohol due to health concerns as the reference group) (Shaper et al., 1988), we first separated lifetime abstainers from individuals who previously consumed alcohol based on a subset of studies that reported the relative risk (RR) for individuals who previously consumed alcohol (Lange et al., 2023b; Nakaya et al., 2007) and harmonized the reference category of the studies included in our analysis. Three different scenarios were encountered: a) lifetime abstainers as the reference category, b) individuals who previously consumed alcohol as the reference category, and c) some other group as reference category, such as the lowest category of alcohol consumed. Sex- and country-specific proportions of lifetime abstainers and individuals who previously consumed alcohol were retrieved for the baseline assessment year of each study using data from a global modeling study (Manthey et al., 2019) and from two reports which had historical data (Hansagi et al., 1995; Simpura, 1987). Using these data, we calculated the corresponding risk for individuals who currently consume alcohol compared to lifetime abstainers as the reference group and obtained a scaling factor which accounted for this risk. The scaling factor was then used to multiply the risk estimates of the other alcohol use categories (Orsini, 2010) (for studies using the same reasoning, see (Llamosas-Falcón et al., 2022, 2021)). For additional details on the methods used to harmonize the reference category, see Text S2.

One-stage dose-response meta-analyses using a restricted maximum likelihood (REML) random-effect estimator were conducted to explore the relationship between average alcohol volume consumed and death by suicide (Crippa et al., 2019; Crippa and Orsini, 2016). Hazard ratios, relative risks, and odds ratios were treated as equivalent measures of association. All analyzes were stratified by sex. We modeled the intercept to go through zero on the logarithmic scale. We tested three different shapes of the dose-response relationship–linear (on the log scale), quadratic, and restrictive cubic splines. The best fitting model was selected based on the Akaike information criterion (AIC) and Bayesian information criterion (BIC).

Two sensitivity analyses were performed. First, we conducted the analysis having lifetime abstainers and individuals who previously consumed alcohol, combined, as the reference category. This allowed us to investigate whether the dose-response relationship is under- or overestimated when not accounting for the "sick quitter bias". In our second sensitivity analysis, meta-analysis via a multilevel meta-regression model was used as an alternative modeling approach (Assink and Wibbelink, 2016; Viechtbauer, 2010), and we compared it with the results obtained with the methods described above.

All statistical analyses were conducted using meta (Harrer et al., 2021) and dosresmeta (Crippa and Orsini, 2016) packages for the main analysis and metafor (Viechtbauer, 2010) for the second sensitivity analysis, in R software version 4.2.3 (R Core Team, 2023).

3. Results

3.1. Study selection and characteristics

Our search strategy initially yielded 29,533 records; 16,326 after deduplication (Fig. 1). After abstract screening and full-text review, a total of eight studies were included (two studies provided risk estimates for males and females (Jee et al., 2011; Lange et al., 2023b), five studies provided risk estimates for males only (Akechi et al., 2006; Mukamal et al., 2007; Nakaya et al., 2007; Pridemore, 2013; Romelsjö et al., 2012), and one corresponding author provided sex-stratified estimates upon request (Koivumaa-Honkanen et al., 2001); Table 2). See Table 2 for the study characteristics of all included studies.

3.2. Risk of bias

Overall, based on the ROBINS-E (ROBINS-E Development Group et al., 2023), the risk of bias was considered low for five cohort studies (Akechi et al., 2006; Jee et al., 2011; Lange et al., 2023b; Mukamal et al., 2007; Nakaya et al., 2007), there was some concern about risk of bias due to confounding for one cohort study (Romelsjö et al., 2012), and the risk of bias due to confounding was considered high for another cohort study (Koivumaa-Honkanen et al., 2001) (Figure S1). Although neither of these two cohort studies controlled for age (the minimum expectation for adjustment), the age group in the study with "some concern" was restricted to 18–20 years (Romelsjö et al., 2012), while the other study included individuals aged 18–64 years (Koivumaa-Honkanen et al., 2001); accordingly, not adjusting for age was considered to be less of a concern for the former study. There were no concerns of bias for the case-control study by Pridemore (2013) (Table S1).

3.3. Dose-response relationship

For males, we identified a linear dose-response relationship between average alcohol volume consumed per day and the log-risk of death by suicide (Figure S2). We identified a RR of 1.11 (95% CI: 1.05, 1.18) when consuming an average of 10 g of pure alcohol per day compared to lifetime abstention, a RR of 1.38 (95% CI: 1.14, 1.66) for 30 g/day, and a RR of 1.71 (95% CI: 1.25, 2.33) for 50 g/day (Fig. 2 and Table 3). For females, a linear dose-response relationship between average alcohol volume consumed per day and the log-risk of death by suicide was also found (Figure S3), with a RR of 1.64 (95% CI: 1.07, 2.51) when consuming an average of 10 g of pure alcohol per day compared to lifetime abstention, a RR of 4.39 (95% CI: 1.21, 15.88) for 30 g/day, and a RR of 11.75 (95% CI: 1.38, 100.33) for 50 g/day (Fig. 2 and Table 3).

It was found that females who consumed 20 g/day, 30 g/day, 40 g/day, and 50 g/day were two-, three-, nearly five-, and nearly seven-times as likely to die by suicide, respectively, compared to males who

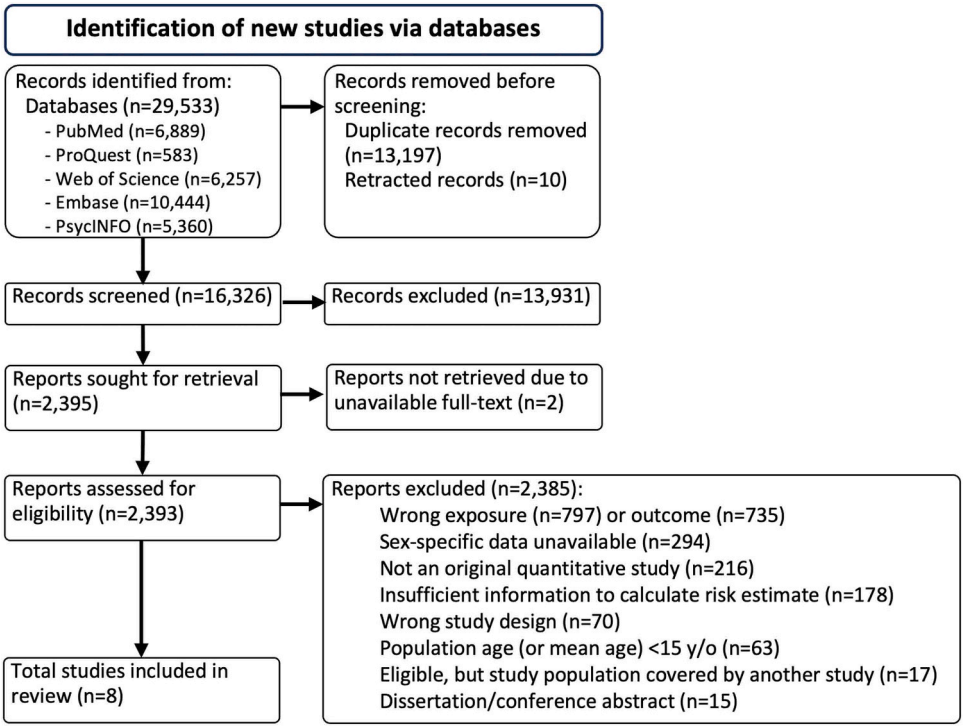

Fig. 1. Study PRISMA flowchart.

consumed the same amount of alcohol per day (Table 3).

3.3.1. *Sensitivity analyses*

In our first sensitivity analysis, using lifetime abstainers and individuals who previously consumed alcohol, combined, as the reference category, we identified a linear dose-response relationship for both males and females. Compared to our main analysis, the results obtained when using lifetime abstainers and individuals who previously consumed alcohol, combined, as the reference category appear to be underestimating the risk relationship between average alcohol volume consumed per day and death by suicide for both sexes (Figure S4 and Table S3). Finally, our results from the main models were confirmed using multilevel meta-regression model in our second sensitivity analysis, where a linear dose-response for both males and females was identified (Figure S5 and Table S4).

4. Discussion

The results of the current study provide evidence of a linear dose-response relationship between average alcohol volume consumed per day and the log-risk of death by suicide for both males and females. Based on a limited number of studies available, the risk relationship may be heightened for females, compared with males. Regardless, it appears that as average daily consumption of alcohol increases so does the risk of dying by suicide for both sexes.

The results suggest that subclinical levels of drinking may also contribute to suicide risk–i.e., it is not only alcohol use disorder that is associated with an increased risk of dying by suicide. This has prevention implications. At the clinical-level, clinicians can use the findings of the current study to educate their patients of the risk relationship between alcohol use and suicide. Additionally, screening, brief intervention and referral interventions for subclinical alcohol use would be an intervention that could impact suicide risk. Further, it is possible that the addition of a suicide prevention module in brief interventions would increase suicide prevention counseling coverage among individuals who consume heavy amounts of alcohol (Giesbrecht et al., 2022). On a population-level, it is possible that alcohol control policies (e.g., increased excise taxation or reduced availability) could be implemented to reduce the suicide mortality rate in a given country (see, for example, (Lange et al., 2023a)). Apart from the prevention implications of the current study, the findings can be used to subsequently estimate the proportion of suicides attributable to alcohol use beyond just those attributable to excessive alcohol use or alcohol use disorder.

Additionally, given the finding that the risk of suicide associated with average daily alcohol consumption may be elevated for females, compared with males, future research is needed to understand mechanisms that increase the impact of alcohol use on suicide risk among females. Such research may better inform targeted prevention interventions. However, it should be acknowledged that despite a sex difference in the association between alcohol use disorder and suicide mortality being found in some previous studies, a recent meta-analysis found that any such differences are a function of bias introduced by the study design, and do not reflect causal impact (Lange et al., 2024). Specifically, when only longitudinal studies were considered the pooled risk for males and females with alcohol use disorder were not statistically significantly different from one another. Thus, additional longitudinal studies on the sex-specific relationship between average alcohol volume consumed and suicide mortality are needed to determine whether the sex differences found are truly reflective of causal impact.

Although it is undisputable that consumption of alcohol occurs prior to suicide–a core criterion for establishing causality–disentangling the possible pathways from alcohol use to suicide is challenging, especially when mediating or moderating variables are considered (Lamis and Malone, 2012). For example, not only is alcohol use a risk factor for suicide, but alcohol use also increases the risk of developing depression, which, in turn, is risk factor for suicide (Lasserre et al., 2022). Thus, it is important to acknowledge that suicide is a complex phenomenon arising from a multitude of factors, each with a complex relationship with one another, as well as with both alcohol use and suicide (Conner and Duberstein, 2004; Lamis and Malone, 2012). That is to say, suicide does not occur because of alcohol use alone. However, alcohol use is a modifiable factor that can be targeted at both the individual and population-level.

The current study is the first to generate sex-specific, high-quality

Table 2
Study characteristics of all included studies.

Author, year	Country	Study design	Population	Age range	Study years		Controls	Total cases/ total N	Avg. alc intake (g/day)	Cases/n of intake level	Measure of risk	Effect size (95% CI)
					Start	End						
Males												
(Akechi et al., 2006)	Japan	Cohort	General[a]	40–69 years	1990, 1993	1999, 2000	Living or death by all other COD	168/ 43,383	0	52/ 10,326	RR[b]	ref
									2	10/4166	RR[b]	0.53 (0.22, 1.16)
									9.9	19/6592	RR[b]	0.64 (0.27, 1.39)
									27.9	24/7632	RR[b]	0.75 (0.32, 1.55)
									47.6	22/7041	RR[b]	0.70 (0.32, 1.55)
									76.5	41/7626	RR[b]	1.23 (0.64, 2.51)
(Jee et al., 2011)	South Korea	Cohort	General[c]	30–95 years	1992–95	2006	Living or death by all other COD	389/ 794,905	0	79/ 183,822	HR[d]	ref
									12.5	239/ 454,221	HR[d]	1.54 (1.19, 1.98)
									43.75	71/ 156,862	HR[d]	1.31 (0.95, 1.82)
(Koivumaa-Honkanen et al., 2001)	Finland	Cohort	Twin-pairs[e]	18–64 years	1976	1995	Living or death by all other COD	147/ 14,237	0	9/1364	OR	ref
									1.67	27/3768	OR	1.29 (0.60, 2.74)
									8.32	45/4457	OR	1.82 (0.89, 3.72)
									19.98	30/2706	OR	2.00 (0.94, 4.22)
									36.64	36/1942	OR	3.36 (1.61, 7.00)
(Lange et al., 2023b)	USA	Cohort	General[f]	≥25 years	1997	2018	Living or death by all other COD	370/ 242,463	0	123/ 51,946	HR[g]	ref
									10	333/ 138,954	HR[g]	0.92 (0.72, 1.17)
									30.5	50/ 18,062	HR[g]	1.05 (0.73, 1.51)
									50.5	32/5964	HR[g]	1.72 (1.14, 2.60)
									75.25	22/5487	HR[g]	1.15 (0.66, 1.99)
(Mukamal et al., 2007)	USA	Cohort	Health care workers[h]	40–75 years	1986	2002	Living or death by all other COD	136/ 47,654	0	41/ 11,226	HR[i]	ref
									5	47/ 18,458	HR[i]	1.07 (0.70, 1.64)
									20	26/ 12,312	HR[i]	0.87 (0.52, 1.44)
									45	22/5658	HR[i]	1.41 (0.81, 2.43)
(Nakaya et al., 2007)	Japan	Cohort	General[j]	40–79 years	1995	2001	Living or death by all other COD	73/ 22,804	0	8/3880	HR[k]	ref
									39.7	60/ 16,141	HR[k]	1.70 (0.80, 3.70)
									11.4	12/5164	HR[k]	1.20 (0.50, 2.70)

(continued on next page)

Table 2 (*continued*)

Author, year	Country	Study design	Population	Age range	Study years		Controls	Total cases/ total N	Avg. alc intake (g/day)	Cases/n of intake level	Measure of risk	Effect size (95% CI)
					Start	End						
									34.2	11/3751	HR[k]	1.50 (0.70, 3.40)
									62.7	37/7226	HR[k]	2.40 (1.20, 4.60)
(Pridemore, 2013)	Russia	Case-control	General	25–54 years	2003–2005		Matched living control	86/ 1610	0	4/216	OR[l]	ref
									5.48	23/609	OR[l]	2.26 (1.13, 4.52)
									16.44	15/299	OR[l]	2.71 (1.36, 5.43)
									27.4	7/155	OR[l]	2.26 (0.90, 5.66)
									38.36	7/105	OR[l]	3.62 (1.36, 8.82)
									52.05	30/241	OR[l]	6.11 (3.39, 11.31)
(Romelsjö et al., 2012)	Sweden	Cohort	General	18–20 years	1969	2004	Living or death by all other COD	454/ 48,716	0	23/3057	HR	ref
									5	264/ 30,089	HR	1.37 (0.89, 2.09)
									20	128/ 13,457	HR	1.48 (0.96, 2.31)
									45	28/1500	HR	2.95 (1.69, 5.11)
									82.5	11/613	HR	2.95 (1.44, 6.03)
Females												
(Jee et al., 2011)	South Korea	Cohort	General[c]	30–95 years	1992–95	2006	Living or death by all other COD	83/ 445,022	0	63/ 381,376	HR[d]	ref
									12.5	20/ 63,367	HR[d]	2.44 (1.47, 4.03)
(Koivumaa-Honkanen et al., 2001)	Finland	Cohort	Twin-pairs[e]	18–64 years	1976	1995	Living or death by all other COD	33/ 14,675	0	8/3589	OR	ref
									1.67	8/7317	OR	0.59 (0.22, 1.56)
									8.32	9/2890	OR	1.67 (0.64, 4.34)
									19.98	4/664	OR	3.25 (0.97, 10.81)
									36.64	4/215	OR	10.15 (3.03, 33.99)
(Lange et al., 2023b)	USA	Cohort	General[f]	≥25 years	1997	2018	Living or death by all other COD	205/ 311,508	0	46/ 119,326	HR[g]	ref
									10	128/ 164,667	HR[g]	1.18 (0.60, 2.32)
									36	12/9882	HR[g]	1.36 (0.57, 3.23)

COD, cause of death; ref, reference group.

[a] Japan Public Health Centre-Based Prospective Study

[b] Adjusted for age at baseline, public health centre area, living alone, and employment status

[c] Korean Cancer Prevention Study (KPCS)

[d] Adjusted for age

[e] Finnish Twin Cohort

[f] National Health Interview Survey 2023

[g] Adjusted for level of education, marital status, psychological distress, race and ethnicity, and survey year

[h] Health Professional Follow-up Study (HPFS)

[i] Adjusted for age, smoking, body mass index, geographical region, average daily exertion, and marital status

[j] Ohsaki National Health Insurance (NHI) cohort
[k] Adjusted for age, education, employment status, marital status, body mass index, smoking status, time spent walking, history of chronic disease, perceived mental stress, self-rated health, and sleep duration
[l] Adjusted for age group, smoking status, marital status and education

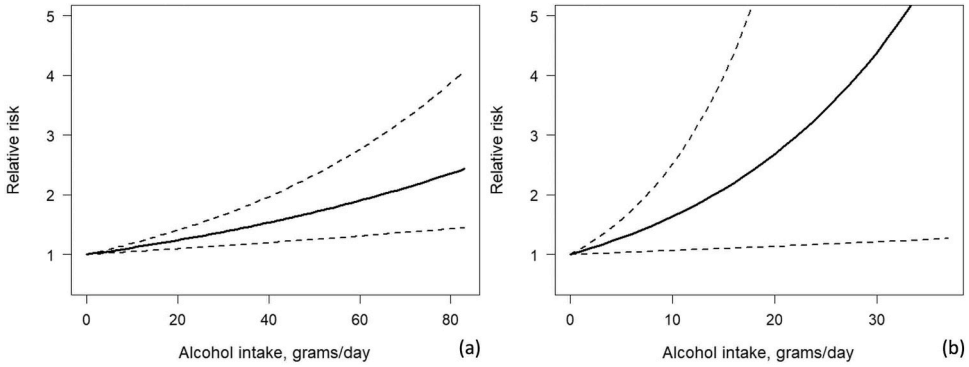

Fig. 2. Dose-response relationship between average alcohol volume consumed in grams per day and the risk of death by suicide, for a) males and b) females.

Table 3
Relative risk and risk ratio for death by suicide by sex for some levels of alcohol use, compared to lifetime abstainers.

Grams of pure alcohol per day	Males	Females	Risk ratio
	RR (95% CI)	RR (95% CI)	
10	1.11 (1.05–1.18)	1.64 (1.07–2.51)	1.48
20	1.24 (1.09–1.40)	2.68 (1.14–6.32)	2.16
30	1.38 (1.14–1.66)	4.39 (1.21 – 15.88)	3.18
40	1.54 (1.20–1.97)	7.18 (1.29 – 39.92)	4.66
50	1.71 (1.25–2.33)	11.75 (1.38 – 100.33)	6.87

RR: relative risk; CI: confidence intervals.

quantitative evidence syntheses for the relationship between average alcohol volume consumed per day and the risk of death by suicide. This study was designed to fill an identified gap in the scientific literature, providing findings with high clinical and public health importance. There are a few limitations of the current study, however, that should be acknowledged. Title and abstract screening of the majority of records was done independently by a single reviewer. Albeit, this took place following the screeners being trained using batches of 100 randomly selected records, which involved independent review and discussion of all discrepancies, until substantial interrater agreement (McHugh, 2012) was reached. Further, the data used were from various countries over a 20+ year span, as there was no restriction on geographic location or study year. Given the sociocultural aspects of both alcohol use and suicide, which can differ by culture and change over time, the risk relationship could also vary by country and over time to a certain degree. With the limited number of available studies, it was not possible to explore potential regional or temporal differences. Most notably, there were a limited number of studies available, for females in particular, and this precluded the ability to explore any other potential moderating factors, beyond sex. Lastly, the exposure–average alcohol volume consumed per day–was not only ascertained via self-reports, but is also a dynamic exposure that can change over the course of a lifetime. Thus, reporting bias, as well as potential misclassification in studies that assess consumption at a single timepoint, years prior to the outcome, must be acknowledged.

Given that the outcome of interest in the current study is a mortality outcome, typically ascertained via official statistics or death report data where biological sex is discerned and documented, the term sex has been used throughout. However, the role of gender and more specifically gender-related factors (e.g., social norms surrounding both alcohol use and suicide) should not be overlooked, nor should the terms sex and gender be conflated (as is a possibility in some on the studies included here).

5. Conclusions

Overall, the results of the current study suggest that as average alcohol consumption per day increases, the risk of death by suicide increases, and the risk may be elevated for females, compared with males. However, more research is needed, particularly with respect to the relationship among females as well as including repeated measures of average alcohol consumption over time.

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CRediT authorship contribution statement

Shannon Lange: Writing – original draft, Supervision, Funding acquisition, Conceptualization. **Laura Llamosas-Falcón:** Writing – original draft, Formal analysis. **Kawon V. Kim:** Writing – review & editing, Validation, Data curation. **Aurélie M. Lasserre:** Writing – review & editing, Validation, Data curation. **Heather Orpana:** Writing – review & editing, Funding acquisition. **Courtney L. Bagge:** Writing – review & editing, Funding acquisition. **Michael Roerecke:** Writing – review & editing, Funding acquisition. **Jürgen Rehm:** Writing – review & editing, Funding acquisition. **Charlotte Probst:** Writing – review & editing, Methodology.

Declaration of Competing Interest

Drs. Lange, Orpana, Roerecke, and Rehm report receiving grant

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Data availability

All data necessary to replicate the findings are included in the Article or Supplementary Material. The R code used to analyse these data can be requested from the corresponding author.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.drugalcdep.2024.111348.

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