Chronic Heavy Drinking and Ischaemic Heart Disease: A Systematic Review and Meta-Analysis

SUPPLEMENTARY MATERIAL

Supplementary Methods

Systematic Review Protocol

Supplementary Figures

Supplementary Tables

Supplementary Methods

Systematic Review Protocol

Title: Systematic review and meta-analysis of heavy drinking and ischaemic heart disease

Protocol Information
Dates
All searches were conducted in week 4 of March 2014.

Stage
Review completed in April 2014.
Current stage: Meta-analysis completed.

Collaborators
None.

Review Methods

Review questions
What is the relative risk for ischaemic heart disease among heavy drinkers?

Context
Specific risk of chronic heavy drinking for ischaemic heart disease (IHD) in comparison to lifetime abstainers has not been systematically examined before and it is currently unclear whether chronic heavy drinking has a protective, neutral, or detrimental association with IHD.
Population studies often miss many chronic heavy drinkers in order to maximize follow-up or because of other sampling issues [1]. Inadvertently, these samples mostly contain more favorable drinking behavior, such as low and regular alcohol consumption within a certain stratum of the socioeconomic continuum in high income countries. However, as is increasingly evident in middle income countries, this is not the drinking pattern observed globally [2]. Among participants missed in typical cohort studies is a sub-group of chronic heavy drinkers, namely people with alcohol use disorders (AUD), who drink on average considerably more than our threshold for heavy drinking [3 4].

Condition or domain
Ischaemic heart disease (morbidity or mortality).

Primary outcomes
Incidence of IHD events.

Secondary outcomes
Fatal and non-fatal IHD events.

Intervention/exposure

Chronic heavy drinking is the exposure of interest.

Comparators/controls
Standardized mortality rates compared to the general population or measure of relative risk in comparison to abstainers (current or lifetime).

Types of studies to be included initially
Observational studies (historical or prospective cohort and case-control studies).

Literature searches
Using PRISMA and MOOSE guidelines [5 6], we conducted two systematic searches using electronic databases from their inception (clinical samples) or 1980 (population samples) to fourth week of March 2014 for original articles, excluding letters, editorials, conference abstracts, reviews, and comments for variations of search terms for the exposure (alcohol consumption), outcome (IHD), and study design. Additionally, we hand searched references of identified papers and relevant reviews and meta-analyses.

Participants/population
Inclusion criteria: Adults (≥15 years) from population samples or clinical samples (patients with AUD in treatment), IHD was analyzed as a separate outcome (ICD-9: 410-414, ICD-10: I20-25), a measure of risk and its corresponding measure of variability was reported (or sufficient data to calculate these), and English-, German-, or Spanish-language.
Exclusion criteria: Adolescents (<15 years), population samples from people with IHD-related conditions. We excluded self-reported IHD outcomes, as well as studies reporting estimates on cardiovascular outcomes combined rather than IHD separately and studies with precursors as outcome.
Further inclusion criteria for population studies:
Case-control or prospective or historical cohort study design, exposure measurement had to cover a reference period of more than 2 weeks for average alcohol consumption at baseline.
Further inclusion criteria for clinical studies:
Prospective or historical cohort study design, mortality risk for diagnosed participants currently in AUD treatment (in- or out-patient, this includes DSM-III and IV ‘alcohol abuse and dependence’ and International Classification of Diseases [ICD-9 and 10] ‘harmful use’ or ‘non-dependent alcohol abuse’ and ‘alcohol dependence’) compared with the general population.

Searches
Population samples
Databases searched: MEDLINE, EMBASE, Web of Science (Science Citation Index Expanded, Social Sciences Citation Index, Arts & Humanities Citation Index), and ETOH (Alcohol and Alcohol Problems Science Database, National Institute on Alcohol Abuse and Alcoholism, January 1980–December 2003).
Search strategy in Medline (through OVID):

1	human/
2	(comment or editorial or letter or meta-analysis or review).pt.
3	1 not 2
4	(alcohol drinking or alcoholic beverages or heavy drinking occasion* or heavy episodic drinking or binge drinking or alcoholic intoxication or problem drinking or hangover* or irregular drinking or drinking pattern or inebriation).mp.
5	exp drinking behavior/ or exp alcohol drinking/ or exp binge drinking/
6	4 or 5
7	(myocardial ischemia or myocardial infarction or myocardial infarct$ or coronary disease or heart diseases or coronary artery disease or coronary heart disease or angina or cardiac death$ or ischaemic heart disease or ischemic heart disease or cardiac event$ or coronary event$).mp.
8	exp myocardial ischemia/ or exp coronary artery disease/
9	7 or 8
10	exp Case-Control Studies/
11	exp cohort studies/ or exp follow-up studies/ or exp longitudinal studies/ or exp prospective studies/ or exp retrospective studies/
12	exp risk/
13	10 or 11 or 12
14	3 and 6 and 9 and 13
15	limit 14 to yr="1980 - 2014"

Clinical samples

Databases searched: MEDLINE, EMBASE, Web of Science (Science Citation Index Expanded, Social Sciences Citation Index, Arts & Humanities Citation Index), and ETOH (Alcohol and Alcohol Problems Science Database, National Institute on Alcohol Abuse and Alcoholism, January 1980–December 2003).

Search strategy in Medline (through OVID):

1	(alcohol dependence or alcohol abuse).mp.
2	exp Alcoholism/
3	exp Mortality, Premature/ or exp Mortality/
4	cohort studies.mp. or exp Cohort Studies/
5	1 or 2
6	3 and 4 and 5

URL to search strategy

None.

Data extraction

From all relevant articles we extracted authors' names, year of publication, country, calendar year(s) of baseline examination, follow-up period, setting, assessment of IHD and alcohol consumption or AUD diagnosis, mean and range of age at baseline, sex, number of observed IHD cases or deaths among participants by drinking group, number of total participants by drinking group, adjustment for potential confounders, and RR and its standard error. We used the most adjusted RR reported, and gave priority to estimates comparing heavy drinking to lifetime abstainers were abstracted by one reviewer. Full-text articles with uncertain eligibility were discussed by both authors until consensus was reached. To control for subjectivity, 10 papers were randomly selected and extracted by another author. No changes in abstraction were recorded. Primary

authors were not contacted by the authors in case there was not enough information presented in the article.

Risk of bias
Most quality scores are tailored for meta-analyses of randomized trials of interventions [7-10] and many criteria do not apply to epidemiological studies like the ones examined here. Also, their use in meta-analyses remains controversial [10 11]. Thus, quality assessment was incorporated differently by including quality components such as study design and alcohol measurement into the inclusion and exclusion criteria (please see also Data abstraction and Supplementary Table 1 for details). Quality checklists therefore would not have been able to distinguish the quality of selected studies in our analysis.

Strategy for data synthesis
Standardized mortality ratios (i.e. comparisons of mortality risks of patients in AUD treatment with the sex- and age-specific general population; see [12]), hazard ratios, odds ratios, and relative risks were treated as equivalent measures of risk. Analyses were stratified by sex where possible. If necessary, relative risks within studies were re-calculated based on the method described by Hamling et al. [13] and pooled across studies using inverse-variance weighted DerSimonian-Laird random-effect models to allow for between-study heterogeneity [14]. We quantified between-study heterogeneity using Cochran's Q [15] and the I^2 statistic [16]. I^2 can be interpreted as the proportion of the total variation other than chance that is due to heterogeneity between studies. We tested for potential publication bias using Egger's test [17]. Sensitivity analyses for the influence of single studies on the pooled relative risks were conducted omitting one study at a time and re-estimating the pooled relative risk. No change in conclusions was observed. All meta-analytical procedures were conducted on the natural log scale in Stata statistical software, version 12.1 (Stata Corp, College Station, Texas), and $p<0{\cdot}05$ (two-sided) was considered statistically significant.

Analysis of subgroups or subsets
Subgroup analyses were completed for different classification of alcohol exposure (chronic heavy drinking based on average alcohol consumption and AUD patients in treatment), and for incidence, mortality,morbidity, and adjustment for confounders. Meta-regression was conducted to identify study characteristics (study design) that might influence the association between heavy drinking and IHD in all subgroups considered when more than 10 studies were available.

Type of review
Prognostic.

Language
English, Spanish, German.

Country
Canada.

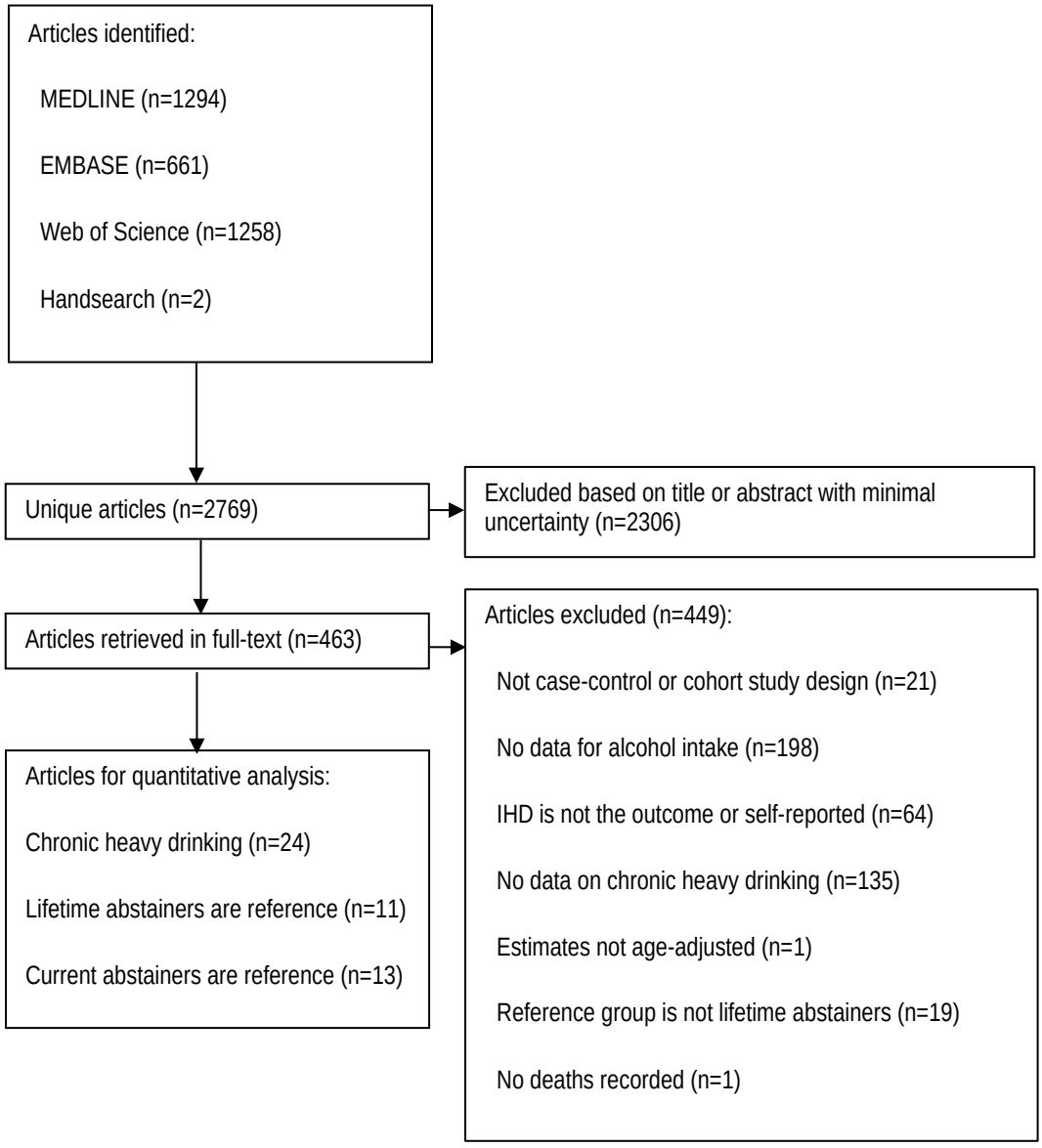
Dissemination plans
Publication in peer-review journal.

Keywords
Heavy drinking, alcohol use disorder, heart disease, incidence, mortality, systematic review, meta-analysis

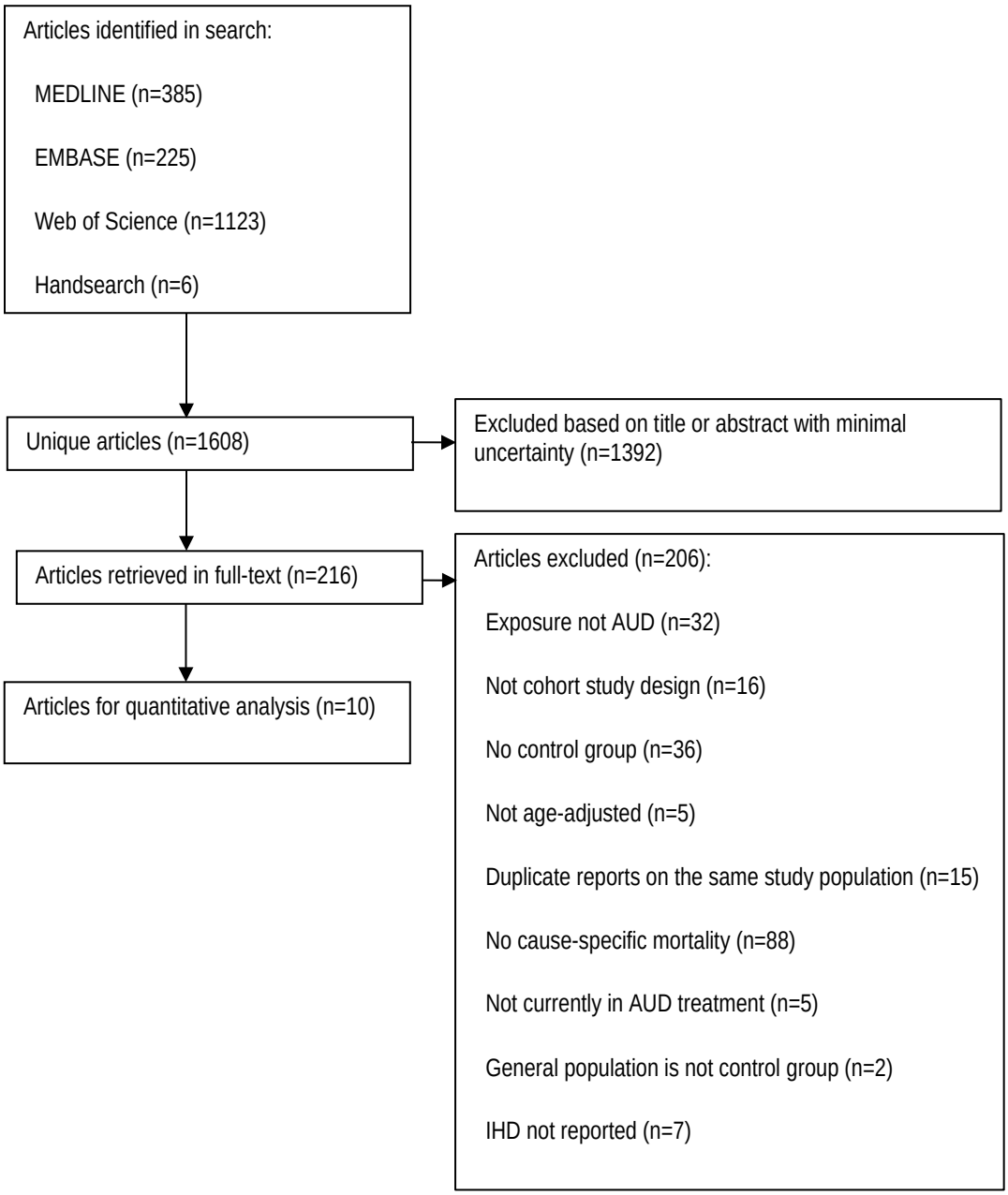
Details of any existing review of the same topic by the same authors
None.

Review status
Completed, but not published.

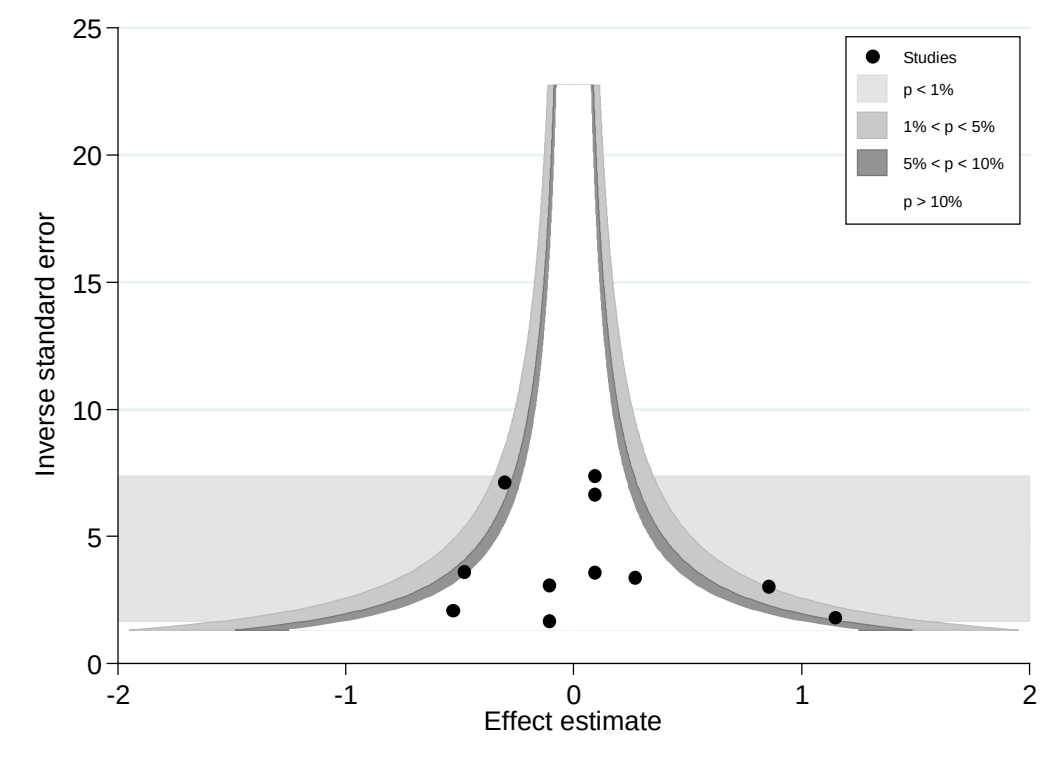
Supplementary Figure 1. Search Results for Population Studies on Chronic Heavy Alcohol Consumption and Ischaemic Heart Disease Risk



Supplementary Figure 2. Search Results for Patients with Alcohol Use Disorder (AUD, Clinical Samples) and Ischaemic Heart Diseases Mortality

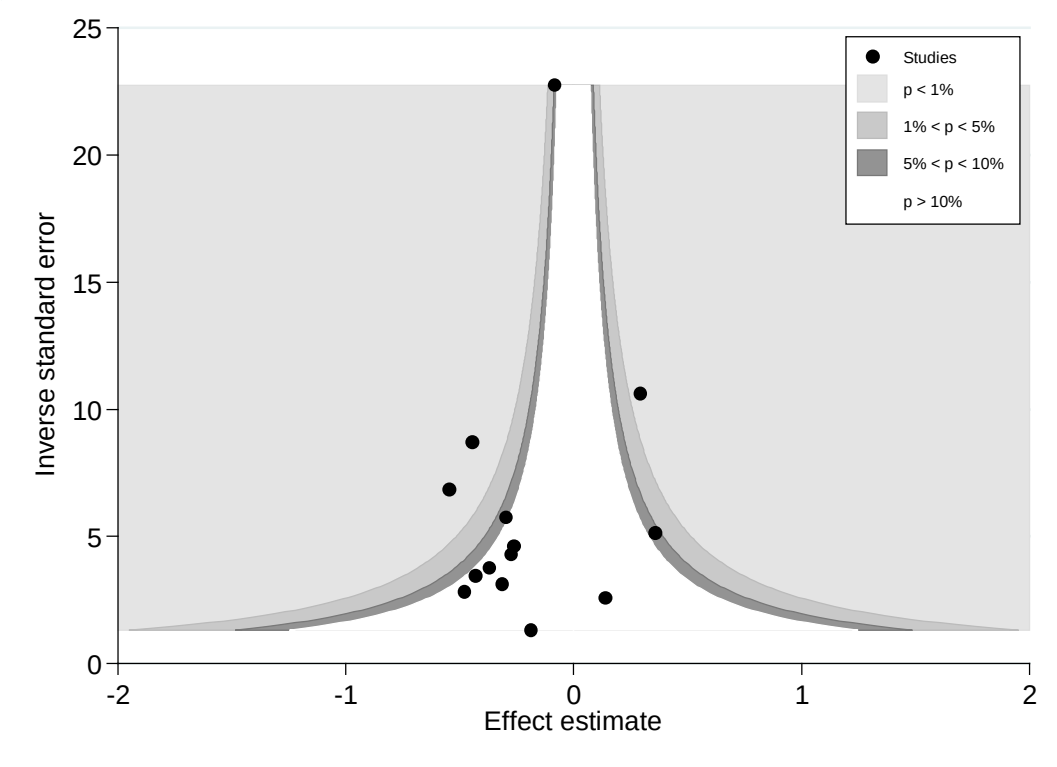


Supplementary Figure 3. Funnel Plot for Ischaemic Heart Disease Incidence among Chronic Heavy Drinkers with Lifetime Abstainers as the Reference Group



Effect size is log(RR)

Supplementary Figure 4. Funnel Plot for Ischaemic Heart Disease Incidence among Chronic Heavy Drinkers with Current Abstainers as the Reference Group



Effect size is log(RR)

Supplementary Table 1. Characteristics of 34 Studies for Ischaemic Heart Disease Risk in Chronic Heavy Drinkers, 1967-2012

Source	Sex, Age at baseline	Location, baseline period	Setting	No. of heavy drinkers (IHD events/ total participants)	IHD assessment	Heavy drinking definition	Reference category	Adjustment
Population samples								
Lifetime abstainers are the reference group								
Dyer et al., 1981[18]	M, 40-55	US, 1957-74	Chicago Western Electric Company Study	12/78	Mortality, ischaemic heart disease (not defined)	≥77 g/day average (based on total intake per month)	Lifetime abstainers	Age (participants free of definite ischaemic heart disease)
Kaufman et al., 1985[19]	M, 30-55	US, 1980-83	Hospital-based, North eastern US (78 hospitals)	209/299	Morbidity, first MI (WHO criteria)	≥67 g/day average (based on typical frequency and amount)	Lifetime abstainers	Age (no history of MI or angina pectoris among controls)
Jackson et al., 1991[20]	M, 25-64	New Zealand, 1986	Auckland	33/68	Incidence (fatal and non-fatal events mortality and morbidity were reported separately), MONICA criteria	>81 g/day (based on typical frequency and amount last 3 months)	Lifetime abstainers	Age, smoking, hypertension, social class, exercise, recent (12 months) change in drinking
Iso et al., 1995[21]	M, 40-69	Japan, 1975-87	Ikawa, Honjo and Kyowa	4[a]/439	Incidence (fatal + non-fatal events), WHO criteria for ischaemic heart disease (definite or suspected MI, angina pectoris, sudden death)	≥70 g/day average (based on usual weekly intake)	Lifetime abstainers	Age, hypertension, serum total cholesterol, smoking, diabetes (history of ischaemic heart disease or stroke were excluded)
McElduff & Dobson 1997[22]	M, 35-69	Australia, 1983	New South Wales (MONICA)	89/103	Incidence (fatal + non-fatal events), definite MI, possible MI, or coronary	≥90 g/day typical amount per drinking day on 5-6 days per week or daily	Lifetime abstainers	Age, smoking, BP, cholesterol, angina, stroke, MI, diabetes

					death			
Rehm et al., 1997[23]	M, 40-75	US, 1971-87	NHANES I	15/61	Incidence (fatal + non-fatal events), ICD-9: 410-414 based on death certificate or hospital discharge diagnosis	≥72 g/day (based on typical frequency and amount)	Lifetime abstainers	Age
Kitamura et al., 1998[24]	M, 40-59	Japan, 1975-93	Osaka	6/580	Incidence (fatal + non-fatal events) based on death certificates, absenteeism reports, insurance claims, and annual risk factor surveys; for all cases medical records were reviewed), ischaemic heart disease (WHO criteria)	≥69 g/day (based on usual weekly intake)	Lifetime abstainers	Age, serum total cholesterol, smoking, BMI, left ventricular hypertrophy, history of diabetes
Klatsky et al., 2003[25]	M, W, 18+	US, 1978-98	Kaiser Permanente, California	88 [a] /2004	Mortality, ICD-9: 410-414 from death certificates	≥6 drinks daily (FFQ)	Lifetime abstainers	Age, race, BMI, education, marital status, smoking, IHD symptoms at baseline
Romelsjö et al., 2003[26]	M, 45-70	Sweden, 1992-94	Stockholm Heart Epidemiology Program (SHEEP)	81/153	Incidence (fatal + non-fatal events), morbidity was reported separately, (all first MI, based on death certificate, autopsy findings, or medical records)	≥70 g/day average (based on frequency in previous year and typical amount)	Lifetime abstainers	Age, hospital, marital status, SES, smoking, physical activity, cardioatheriosclerotic disease, job strain, social anchorage, life control
Inoue et al., 2012[27]	M, 35-101	Japan, 1988-2006	Pooled analysis of 6 large cohort studies in Japan	228/12 393	Mortality based on death certificates, ICD-10: I20-25	≥69 g/day average (based on frequency and amount)	Lifetime abstainers	Age, area, smoking, BMI, hypertension, diabetes, leisure time physical activity
Bergmann et al., 2013 [28]	M, 25-70	Europe (23 centres in 10	EPIC	302/20 228	Mortality (record linkage with death	>60 g/day (based on amount per week	Lifetime abstainers	Stratified by age and centre; adjusted for BMI, height,

		countries), 1992-2000			and municipality registries), ICD-10: I20-25	during the previous 12 months or in lifetime)		waist circumference, intake of fruits, vegetables, red meat, and meat products, dietary fibre, physical activity, education, and smoking
Current abstainers are the reference group								
Friedman & Kimball 1986[29]	M, 30-59	US, 1948-72	Framingham Heart Study, Massachusetts	15/138	Mortality, ischaemic heart disease (not defined)	≥67 g/day average (based on total intake per month)	Current abstainer	Age (all participants free of ischaemic heart disease at baseline)
Shaper et al., 1987[30]	M, 40-59	UK, 1978-85	British Regional Heart study	22/631	Incidence (fatal + non-fatal events), ICD-9: 410-414, based on death certificates, non-fatal MI: 2 of 3 criteria (severe prolonged chest pain, changes detectable by ECG or enzyme changes)	>70 g/day daily or on most days	Current abstainer	Age, smoking years, social class(participants free of ischaemic heart disease at baseline)
Boffetta et al., 1990[31]	M, 40-59	US, 1959-72	CPS II	551/7698	Mortality (based on death certificates), ICD-7: 420-422	≥6 drinks/day (FFQ)	Current abstainer	Age, smoking
Renaud et al., 1998 [32]	M, 40-60	France, 1978-1993	Health examination at the Centre de Medicine Preventive de Nancy	86/9385	Mortality (based on death information from physicians) ICD-9: 410-414	≥77 g/day (based on daily consumption)	Current abstainer	Age, education, smoking, serum total cholesterol, systolic blood pressure, BMI
Maskarinec et al., 1998[33]	M, W, 30+	US, 1975-94	Multiethnic cohort study, Hawaii	12/308	Mortality (based on mortality files), ICD-9: 410-414	≥43 drinks per week (based on usual amount and frequency)	Current abstainer	Age, ethnicity, smoking, BMI, education,
Gun et al., 2006[34]	M, not reported	Australia, 1980-2001	Health Watch (Petroleum-industry workers)	30/1226[a]	Mortality (based on death register), ischaemic heart disease (death records provided by	≥7 drinks per day (based on typical frequency and amount)	Current abstainer	Age, calendar year, smoking

					NDI)			
Bazzano et al., 2009[35]	M, 40+	China, 1991-2000	China National Hypertension Survey Epidemiology Follow-up Study	52/6389	Incidence (fatal + non-fatal events), mortality reported separately, (determined by endpoint committee based on medical records, death certificates)	≥63 g/day (based on number of drinks per month)	Current abstainer	Age, BMI, BP, physical activity, smoking, diabetes, education, urban vs rural, living in North China (history of IHD excluded)
Sull et al., 2009[36]	M, 55+	South Korea, 1985-2005	Kangwha Cohort Study	2/182	Mortality (based on death certificate), ICD-10: I20-I25	≥72 g/day daily (based on frequency per year and typical amount)	Current abstainer	Age, history of chronic disease, smoking, BMI, BP, education
Oliveira et al., 2009[37]	M, 18+	Portugal, 1999-2003	Cardiology Department of 4 hospitals, Porto	186/284	Morbidity, first AMI patients who survived four days after diagnosis	≥60 g/day (FFQ)	Current abstainer	Age, education, family history of MI, waist-to-hip ratio, smoking, total energy intake, leisure time physical activity
Ruidavets et al., 2010 (Northern Ireland)[38]	M, 50-59	Northern Ireland, 1991-2004	Prospective Epidemiological Study of Myocardial Infarction (PRIME)	9/240	Incidence (fatal + non-fatal events), defined as coronary death and non-fatal MI (established by medical committee based on detailed clinical information from hospital or GPs)	≥75 g/day average (based on usual weekly total intake)	Current abstainer	Restricted age range, previous IHD (medically diagnosed or Rose questionnaire) excluded
Ruidavets et al., 2010 (France)[38]	M, 50-59	France, 1991-2004	Prospective Epidemiological Study of Myocardial Infarction (PRIME)	33/1134	Incidence (fatal + non-fatal events), defined as coronary death and non-fatal MI (established by medical committee based on detailed clinical information from hospital or GPs)	≥75 g/day average (based on usual weekly total intake)	Current abstainer	Restricted age range, previous IHD (medically diagnosed or Rose questionnaire) excluded

Hvidtfeldt et al., 2010[39]	M, W, 30-80	North America and Europe, 1974-1996	Pooled analysis of 8 cohort studies	105/2972	Incidence (fatal + non-fatal events), ischaemic heart disease (standard criteria met in all individual studies)	≥60 g/day (FFQ)	Current abstainer	Age, year of baseline, smoking, BMI, education, physical activity, energy intake, polysaturated fat, monosaturated fat, saturated fat, fiber, cholesterol intake, study origin (participants free of CVD, diabetes, cancers)
Yang et al., 2012[40]	M, 40-79	China, 1990-2005	Nationwide cohort study	123/20 586	Mortality (based on death certificate), ICD-9: 410-414	≥60 g/day (based on typical weekly intake)	Current abstainer	Age, geographical area(participants with prior diseases at baseline were excluded)
Romelsjö et al., 2012[41]	M, 18-20	Sweden, 1969-2004	Swedish conscripts	12/600[a]	Incidence (fatal + non-fatal events) mortality (based on National Death Register and National Swedish inpatient register), , ICD-9: 410 (MI)	>60 g/day (based on frequency and amount)	Current abstainer	Smoking, father (blue collar worker), divorced parents, runaway from home, truancy, low emotional control, low social maturity, IQ, health status, BMI
AUD treatment patients (clinical samples)								
Sundby 1967 [42]	M, 15+	Norway, 1925-62	Ulleval Hospital, Psychiatric Department, Oslo	97/1716	National Central Bureau of Statistics comparison to Oslo mortality statistics, ICD-7: ischaemic heart disease	Diagnosis of alcoholism	General population	Age- and sex-standardized
Schmidt & de Lint 1972 [43]	W, M, 15+	Canada, 1951-1964	Clinic of the Addiction Research Foundation, Toronto	258/6478	Death records in Ontario, other provinces, and some foreign countries, ICD-7: 420 ischaemic heart disease (253 cases), 422 myocardial degeneration (5 cases)	All patients with physical examination at entry for alcoholism treatment at specialized clinic	Ontario general population	Age- and sex-standardized

Adelstein & White1976 [44]	W, M, 15+	UK, 1953, 1974	4 London Mental Hospitals, Mental Health Enquiry	137/2070	ICD-8: 410-414	Inpatient treatment for alcoholism	General population	Age- and sex-standardization
Thorarinsson 1979 [45]	M, 15+	Iceland, 1951-1974	National Psychiatric Register	125/2863	Death certificate, underlying cause, ICD-7: 420	First admission to in- or out-patient institution	General population	Age-standardized
Polich et al., 1981 [46]	M, 18+	US, 1973-77	8 of 44 NIAAA Alcoholism Treatment Centers	24/755	Underlying cause, ICDA-8: 410-414	Admission to specialized program for alcoholism	General population	Age-, sex-, and race-standardized
Lindberg & Agren 1988 [47]	W, M, 15+	Sweden, 1969-1983	Magnus Huss Clinic, Karolinska Hospital	126/4543	National Central Bureau of Statistics, underlying cause, ICD-8: 410-414	First admission for alcoholism to specialized clinic	General population	Age-and sex-standardized
Denison et al., 1997 [48]	M, 20+	Sweden, 1986-1991	University Psychiatric Clinic, Lillhagen Hospital, Goeteborg	25/1049	Death certificate, underlying cause, ICD-9: 410-414	Inpatients for detoxification, DSM-III-R criteria for alcohol dependence	General population	Age, calendar year, and length of follow-up
Noda et al., 2001 [49]	M, 21-77	Japan, 1972-92	All in or out-patient treatment facilities, Takatsuki City	4/306	Death certificate, underlying cause, ICD-9: 410-414	Diagnosis of alcohol dependence/psychosis	General population	Age- and time period standardization
Haver et al., 2009 [50]	W, 18+	Sweden, 1981-2007	Early Treatment for Women with Alcohol Addiction (EWA) Unit, Karolinska Hospital	10/420	Swedish Causes of Death Register, ICD-8, ICD-9, and ICD-10: ischaemic heart disease	First admission for alcohol treatment (second sample 96% met DSM-III-R criteria for alcohol dependence)	General population	Matched on year of birth, marital status, SES, education
Saieva et al., 2012 [51]	W, M, 16-94	Italy, 1985-2006	Alcohol Centre treatment	30/2272	Regional Mortality Register, ICD-9: 410-414	Physician diagnosis alcohol dependence (ICD-9)	General population	Age- and sex-standardized

Abbreviations: AMI, acute myocardial infarction; AUD, Alcohol use disorder; BMI, body mass index; BP, blood pressure; CVD, cardiovascular disease; DSM, Diagnostic and Statistical Manual of Mental Disorders; ICD, International Classification of Diseases; EPIC, European Prospective Investigation into Cancer and Nutrition; FFQ, food frequency questionnaire; ICDA, International Classification of Diseases, Adapted for Use in the United States ; IHD, ischaemic heart disease; M, men only; MI, myocardial infarction; MONICA, Monitoring Trends and Determinants in Cardiovascular Disease; NHANES, National Health and Nutrition Examination Survey; PRIME, Prospective Epidemiological Study of Myocardial Infarction; SES, socio-economic status; SHEEP, Stockholm Heart Epidemiology Program; W, women only; WHO, World Health organization. ICD codes were included were reported.

[a] Estimated.

Reference List

1. Rothman KJ, Greenland S, Lash TL. *Modern Epidemiology, 3rd ed*. Philadelphia, PA: Lippincott Williams & Wilkins, 2008.
2. World Health Organization. *Global status report on alcohol and health*. Geneva, Switzerland: World Health Organization, 2011.
3. Rehm J, Anderson P, Gual A, Kraus L, Marmet S, Room R, et al. The tangible common denominator of substance use disorders: a reply to commentaries to Rehm et al.(2013). Alcohol Alcohol 2014;49:118-22
4. Rivas I, Sanvisens A, Bolao F, Fuster D, Tor J, Pujol R, et al. Impact of medical comorbidity and risk of death in 680 patients with alcohol use disorders. Alcohol Clin Exp Res 2012;37:E221-E27
5. Moher D, Liberati A, Tetzlaff J, Altman DG, The Prisma Group. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA Statement. PLoS Med 2009;6:e1000097
6. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D. Meta-analysis of observational studies in epidemiology: a proposal for reporting. JAMA 2000;283:2008-12
7. Moher D, Pham B, Jones A, Cook DJ, Jadad AR, Moher M, et al. Does quality of reports of randomised trials affect estimates of intervention efficacy reported in meta-analyses? Lancet 1998;352:609-13
8. Chalmers TC, Smith HJ, Blackburn B, Silverman B, Schroeder B, Reitman D, et al. A method for assessing the quality of a randomized control trial. Control Clin Trials 1981;2:31-49
9. Detsky AS, Naylor CD, O'Rourke K, McGreer AJ, L'Abbé KA. Incorporating variations in the quality of individual randomized trials into meta-analysis. J Clin Epidemiol 1992;45:255-65
10. Greenland S, O'Rourke K. On the bias produced by quality scores in meta-analysis, and a hierarchical view of proposed solutions. Biostatistics 2001;2:463-71
11. Herbison P, Hay-Smith J, Gillespie WJ. Adjustment of meta-analyses on the basis of quality scores should be abandoned. J Clin Epidemiol 2006;59:1249-56
12. Rothman K, Greenland S. *Modern epidemiology*. Philadelphia, PA: Lippincott-Raven Publishers, 1998.
13. Hamling J, Lee P, Weitkunat R, Ambühl M. Facilitating meta-analyses by deriving relative effect and precision estimates for alternative comparisons from a set of estimates presented by exposure level or disease category. Stat Med 2008;27:954-70
14. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986;7:177-88
15. Cochran WG. The combination of estimates from different experiments. Biometrics 1954;10:101-29
16. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med 2002;21:1539-58
17. Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315:629-34
18. Dyer AR, Stamler J, Paul O, Berkson DM, Shekelle RB, Lepper MH, et al. Alcohol, cardiovascular risk factors and mortality: the Chicago experience. Circulation 1981;64:III 20-27
19. Kaufman DW, Rosenberg L, Helmrich SP, Shapiro S. Alcoholic beverages and myocardial infarction in young men. Am J Epidemiol 1985;121:548-54
20. Jackson R, Scragg R, Beaglehole R. Alcohol consumption and risk of coronary heart disease. BMJ 1991;303:211-16
21. Iso H, Kitamura A, Shimamoto T, Sankai T, Naito Y, Sato S, et al. Alcohol intake and the risk of cardiovascular disease in middle-aged Japanese men. Stroke 1995;26:767-73
22. McElduff P, Dobson AJ. How much alcohol and how often? Population based case-control study of alcohol consumption and risk of a major coronary event. BMJ 1997;314:1159-64
23. Rehm J, Bondy S, Sempos CT, Vuong CV. Alcohol consumption and coronary heart disease morbidity and mortality. Am J Epidemiol 1997;146:495-501

24. Kitamura A, Iso H, Sankai T, Naito Y, Sato S, Kiyama M, et al. Alcohol intake and premature coronary heart disease in urban Japanese men. Am J Epidemiol 1998;147:59-65
25. Klatsky AL, Friedman GD, Armstrong MA, Kipp H. Wine, liquor, beer, and mortality. Am J Epidemiol 2003;158:585-95
26. Romelsjö A, Branting M, Hallqvist J, Alfredsson L, Hammar N, Leifman A, et al. Abstention, alcohol use and risk of myocardial infarction in men and women taking account of social support and working conditions: the SHEEP case-control study. Addiction 2003;98:1453-62
27. Inoue M, Nagata C, Tsuji I, Sugawara Y, Wakai K, Tamakoshi A, et al. Impact of alcohol intake on total mortality and mortality from major causes in Japan: a pooled analysis of six large-scale cohort studies. J Epidemiol Community Health 2012;66:448-56
28. Bergmann MM, Rehm J, Klipstein-Grobusch K, Boeing H, Schutze M, Drogan D, et al. The association of pattern of lifetime alcohol use and cause of death in the European Prospective Investigation into Cancer and Nutrition (EPIC) study Int J Epidemiol 2013;42:1772-90
29. Friedman LA, Kimball AW. Coronary heart disease mortality and alcohol consumption in Framingham. Am J Epidemiol 1986;124:481-89
30. Shaper AG, Phillips AN, Pocock SJ, Walker M. Alcohol and Ischemic heart disease in middle-aged British men. BMJ 1987;294:733-37
31. Boffetta P, Garfinkel L. Alcohol drinking and mortality among men enrolled in an American Cancer Society prospective study. Epidemiology 1990;1:342-48
32. Renaud SC, Gueguen R, Schenker J, d'Houtaud A. Alcohol and mortality in middle-aged men from Eastern France. Epidemiology 1998;9:184-88
33. Maskarinec G, Meng L, Kolonel L. Alcohol intake, body weight, and mortality in a multiethnic prospective cohort. Epidemiology 1998;9:654-61
34. Gun RT, Pratt N, Ryan P, Gordon I, Roder D. Tobacco and alcohol-related mortality in men: estimates from the Australian cohort of petroleum industry workers. Aust N Z J Public Health. 2006;30:318-24
35. Bazzano LA, Gu DF, Reynolds K, Chen J, Wu XQ, Chen CS, et al. Alcohol consumption and risk of coronary heart disease among Chinese men. Int J Cardiol. 2009;135:78-85
36. Sull JW, Yi SW, Nam CM, Ohrr H. Binge drinking and mortality from all causes and cerebrovascular diseases in korean men and women: a Kangwha cohort study. Stroke 2009;40:2953-58
37. Oliveira A, Barros H, Azevedo A, Bastos J, Lopes C. Impact of risk factors for non-fatal acute myocardial infarction. Eur J Epidemiol 2009;24:425-32
38. Ruidavets JB, Ducimetière P, vans A, Montaye M, Haas B, Bingham A, et al. Patterns of alcohol consumption and ischaemic heart disease in culturally divergent countries: the Prospective Epidemiological Study of Myocardial Infarction (PRIME). BMJ 2010;341:c6077
39. Hvidtfeldt UA, Tostrup JS, Jakobsen MU, Heitmann BL, Grønbaek M, O'Reilly E, et al. Alcohol intake and risk of coronary heart disease in younger, middle-aged, and older adults. Circulation 2010;121:1589-97
40. Yang L, Zhou M, Sherliker P, Cai Y, Peto R, Wang L, et al. Alcohol drinking and overall and cause-specific mortality in China: nationally representative prospective study of 220,000 men with 15 years of follow-up. Int J Epidemiol 2012;41:1101-13
41. Romelsjö A, Allebeck P, Andréasson S, Leifman A. Alcohol, mortality and cardiovascular events in a 35 year follow-up of a nationwide representative cohort of 50,000 Swedish conscripts up to age 55. Alcohol Alcohol 2012;47:322-27
42. Sundby P. Alcoholism and mortality. Oslo, 1967.
43. Schmidt W, de Lint J. Causes of death of alcoholics. Q J Stud Alcohol 1972;33:171-85
44. Adelstein A, White G. Alcoholism and mortality. Popul Trends 1976;6:7-13
45. Thorarinsson AA. Mortality among men alcoholics in Iceland, 1951-74. J Stud Alcohol 1979;40:704-18

46. Polich JM, Armor DJ, Braiker HB. *The Course of Alcoholism: Four Years After Treatment*. New York: John Wiley & Sons, 1981.
47. Lindberg S, Agren G. Mortality among male and female hospitalized alcoholics in Stockholm 1962-1983. Br J Addict 1988;83:1193-200
48. Denison H, Berkowicz A, Oden A, Wendestam C. The significance of coronary death for the excess mortality in alcohol-dependent men. Alcohol Alcohol 1997;32:517-26
49. Noda T, Imamichi H, Tanaka H. Cause-specific mortality risk among male alcoholics residing in the Osaka metropolitan area. Psychiatry Clin Neurosci 2001;55:465-72
50. Haver B, Gjestad R, Lindberg S. Mortality risk up to 25 years after initiation of treatment among 420 Swedish women with alcohol addiction. Addiction 2009;104:413-19
51. Saieva C, Bardazzi G, Masala G, Quartini A, Ceroti M, Iozzi A, et al. General and cancer mortality in a large cohort of Italian alcoholics. Alcohol Clin Exp Res 2012;36:342-50