



Review

Employment Status and Alcohol-Attributable Mortality Risk— A Systematic Review and Meta-Analysis

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Table S1. PRISMA 2009 checklist [1].

| Section/topic | # | Checklist item | Reported on page # |
|---------------------------|----|---|--------------------|
| TITLE | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | Title page |
| ABSTRACT | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | Title page |
| INTRODUCTION | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 1-2 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 2 |
| METHODS | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | 2 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 2-3 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 2 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | Text S1 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 2-3, Figure 1 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 3 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 3 |

| Section/topic | # | Checklist item | Reported on page # |
|------------------------------------|----|--|---------------------------------|
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 3 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 3 |
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | 3 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis. | 3 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | n.a. |
| RESULTS | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 3, Figure 1 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 4, Table 1 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | 6, Figure 2 |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | Figure 2, Table 1 as applicable |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | 6, Figure 2 |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | 6 |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | 6 |

| Section/topic | # | Checklist item | Reported on page # |
|---------------------|----|--|--------------------|
| DISCUSSION | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 7 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 8 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 8 |
| FUNDING | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 8 |

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

Text S1. Search terms.

The searches included a set of keywords, wildcards, truncation and medical subject headings (where applicable). The search terms used are shown below.

OvidSP (Embase, MEDLINE, and PsycINFO)

(alcohol *abuse/ OR (alcohol abuse).ti,ab. OR exp *Drinking Behavior/ OR exp *Alcohol Drinking/ OR exp *Drinking/ OR *Binge Drinking/ OR (alcoholic beverages).ti,ab. OR (alcohol and (drinking or intake or consumption)).ti,ab.)

AND

(exp *socioeconomic factors/ OR exp *social class/ OR socio?economic status.ti,ab. OR Educational status/ OR income/ OR Employment/ OR (education* ADJ (level OR attain*)).ti,ab. OR (socio?economic OR SES OR SEP OR asset? score OR income).ti,ab.)

AND

(exp Mortality/ OR exp Mortality, Premature/ OR exp *excess mortality/ OR *differential mortality/ OR (mortality).ti,ab. OR *cause of death/)

AND

(exp Case?Control Studies/ OR exp Cohort studies/ OR (case OR cohort OR control group* OR ratio OR risk* OR prospective* OR follow* OR longitudinal OR retrospective OR effect modifi*).ti,ab.)

Limit 1 to yr="2013-Current"

Web of Science

TS=(alcoholic beverages OR alcohol AND (drinking OR intake OR consumption)) OR TS=(Alcohol abuse)

AND

TS=(mortality OR death* OR cause of death)

AND

TS=(ses OR socioe\$economic status OR social class OR socio\$economic variable* OR (education* AND (attain* OR status OR level)) OR income OR employment)

AND

TS=(case?control stud* OR cohort?stud* OR ratio OR risk* OR prospective* OR follow* OR longitudinal OR retrospective OR effect modifi*)

Table S2. Diagnoses and ICD-10 codes of 100% alcohol-attributable conditions [2].

| Diagnosis | ICD-10 code |
|---|-------------|
| Alcohol-induced pseudo-Cushing's syndrome | E24.4 |
| Mental and behavioural disorders due to use of alcohol | F10 |
| Acute intoxication | F10.0 |
| Harmful use | F10.1 |
| Dependence syndrome | F10.2 |
| Withdrawal state | F10.3 |
| Withdrawal state with delirium | F10.4 |
| Psychotic disorder | F10.5 |
| Amnesic syndrome | F10.6 |
| Residual and late-onset psychotic disorder | F10.7 |
| Other mental and behavioural disorders | F10.8 |
| Unspecified mental and behavioural disorder | F10.9 |
| Degeneration of nervous system due to alcohol | G31.2 |
| Alcoholic polyneuropathy | G62.1 |
| Alcoholic myopathy | G72.1 |
| Alcoholic cardiomyopathy | I42.6 |
| Alcoholic gastritis | K29.2 |
| Alcoholic liver disease | K70 |
| Alcoholic fatty liver | K70.0 |
| Alcoholic hepatitis | K70.1 |
| Alcoholic fibrosis and sclerosis of liver | K70.2 |
| Alcoholic cirrhosis of liver | K70.3 |
| Alcoholic hepatic failure | K70.4 |
| Alcoholic liver disease, unspecified | K70.9 |
| Alcohol-induced pancreatitis | K85.2 |
| Alcohol-induced chronic pancreatitis | K86.0 |
| Finding of alcohol in blood | R78.0 |
| Toxic effect of alcohol | T51 |
| Toxic effect of ethanol | T51.0 |
| Toxic effect of methanol | T51.1 |
| Toxic effect of other alcohols | T51.8 |
| Toxic effect of alcohol, unspecified | T51.9 |
| Accidental poisoning by and exposure to alcohol | X45 |
| Intentional self-poisoning by and exposure to alcohol | X65 |
| Poisoning by and exposure to alcohol, undetermined intent | Y15 |
| Evidence of alcohol involvement determined by blood alcohol level | Y90 |

Table S3. Diagnoses and ICD-10 codes of conditions with an alcohol-attributable fraction >10% for mortality globally [3].

| Category | Sub-category | Cause of death | ICD-10 code | AAF |
|--------------------------|---|-------------------------------|--|-----|
| Communicable diseases | Respiratory infections and tuberculosis | Tuberculosis | A15-A19, B90 | 20% |
| Injuries | Intentional injuries | Self-harm | X60-64, X66-X69, X65, X70-X84 | 18% |
| | | Interpersonal violence | X85-Y09, Y871 | 18% |
| | Unintentional injuries | Road injury | V01-V04, V06, V09-V80, V87, V89, V99 | 27% |
| | | Poisonings | X40, X43, X46-X48, X49 | 12% |
| | | Falls | W00-W19 | 11% |
| | | Drowning | W65-W74 | 12% |
| | | Exposure to mechanical forces | W20-W38, W40-W43, W45, W46, W49-W52, W75, W76 | 14% |
| | | Other unintentional injuries | V2*, W39, W44, W53-W64, W77-W99, X20-X29, X50-X59, Y40-Y86, Y88, Y89 | 14% |
| | Digestive diseases | Cirrhosis of the liver | K70, K74 | 48% |
| | | Pancreatitis | K85-K86 | 26% |
| Noncommunicable diseases | Malignant neoplasms | Lip and oral cavity | C00-C08 | 26% |
| | | Other pharyngeal cancers | C09-C10, C12-C14 | 31% |
| | | Oesophagus cancer | C15 | 17% |
| | | Colon and rectum cancers | C18-C21 | 11% |
| | | Larynx cancer | C32 | 22% |
| | Neurological disorders | Epilepsy | G40-G41 | 13% |

* V-series not included in road injuries

AAF alcohol-attributable fraction.

Note. 100% alcohol-attributable conditions are excluded from this table and shown in Table S2.

Table S4. Inclusion criteria.

| Criterion | Inclusion | Exclusion |
|-----------|---|---|
| Outcome | The outcome is mortality measured at the individual level | Indirectly affected people are investigated (e.g., sober victims of car drivers under the influence of alcohol) |
| | The outcome is attributable to alcohol use | |
| SES | SES is measured via occupation or employment | SES is measured only via income, or education |
| | SES is measured at the individual, parental, or household level | SES is measured on the neighborhood-level |
| Design | The study is empirical and quantitative | The study is an intervention study |
| | The study employed a case-control, cohort/prospective/longitudinal, data-linkage, or retrospective design | The study is using exclusively cross-sectional data |
| Sample | The sample is population-based | A clinical sample is investigated |
| | Participants are at least 15 years of age | |
| Results | The outcome (including N) is reported by SES of the deceased | |
| | One point estimate measure of relative risk (RR, odds ratio (OR), hazard ratio (HR), standardized mortality ratio (SMR) etc.) comparing risk in different SES strata and its confidence interval, standard error, or sufficient raw data for calculation (N total and n cases) are reported | |
| Language | No restrictions | |
| Time | Studies published since February 2013 | |

Table S5. Quality rating.

| Criterion | Categories | Evaluation | Code |
|--|--|--------------|------|
| Sample representativeness | Nationally representative sample | Satisfactory | 0 |
| | Fraction of the target population | Insufficient | 1 |
| Assessment of SES | Assigned based on most recent census | Satisfactory | 0a |
| | Assigned through family or household member | Satisfactory | 0b |
| | Use of an own or 'other' category | Satisfactory | 0c |
| | One or more pairwise comparisons are not reported | Satisfactory | 0d |
| | Exclusion of meaningful parts of the population | Insufficient | 1 |
| Definition of alcohol-attributable mortality | 100% alcohol-attributable mortality exclusively | Satisfactory | 0 |
| | Inclusion of diseases of the liver and/or pancreatitis | Insufficient | 1a |
| | Inclusion of neoplasms in the upper gastrointestinal tract | Insufficient | 1b |
| | Inclusion of all types of injuries | Insufficient | 1c |
| | Inclusion of two or more of the above categories | Flawed | 2 |
| Data linkage | Individual linkage | Satisfactory | 0 |
| | No linkage | Insufficient | 1 |
| Age adjustment | Age-adjusted | Satisfactory | 0 |
| | Not age-adjusted | Insufficient | 1 |

SES, socioeconomic status.

Table S6. Quality checklist. Ratings on population representativeness of the sample, measurement of socioeconomic status (SES), operationalization of alcohol-attributable mortality, data linkage, and age-adjustment for each study included in the meta-analysis.

| Study | Population representativeness of the sample | Measurement of SES | Operationalization of alcohol-attributable mortality | Data linkage | Age adjustment |
|-----------------------------|---|--------------------|--|--------------|----------------|
| Agren et al., 1992 [4] | 0 | 0 | 0 | 0 | 0 |
| Connolly et al., 2010 [5] | 0 | 0 | 1 | 0 | 0 |
| Grigoriev et al., 2017 [6] | 0 | 0 | 0 | 0 | 0 |
| Herttua et al., 2008 [7] | 0 | 0 | 0 | 0 | 0 |
| Mäki et al., 2008 [8] | 0 | 1 | 1 | 0 | 0 |
| Mäki et al., 2009 [9] | 0 | 1 | 1 | 0 | 0 |
| Mustard et al., 2013 [10] | 0 | 0 | 0 | 0 | 0 |
| Pulido et al., 2017 [11] | 0 | 0 | 0 | 0 | 0 |
| Vågerö & Garcey, 2016 [12] | 0 | 0 | 0 | 0 | 0 |
| Zagozdzon et al., 2009 [13] | 0 | 0 | 1 | 1 | 0 |

0=Satisfactory, criterion is met (e.g., sample is representative; data were linked etc.)

1=Not satisfactory, criterion is not met

Table S7. Causes of death included in each of the studies.

| Study | Includes deaths with an AAF <100% | ICD version(s) | Causes included |
|----------------------------|-----------------------------------|----------------|--|
| Agren et al., 1992 [4] | No | ICD-8 | Alcohol-related liver cirrhosis; high alcohol consumption; alcohol intoxication; alcohol psychosis |
| Connolly et al., 2010 [5] | Yes | ICD-10 | Mental and behavioural disorders due to use of alcohol (F10); degeneration of nervous system due to alcohol (G31.2); alcoholic polyneuropathy (G62.1); alcoholic cardiomyopathy (I42.6); alcoholic gastritis (K29.2); alcoholic liver disease (K70); chronic hepatitis, not elsewhere classified (K73); fibrosis and cirrhosis of liver (K74; excluding K74.3-K74.5 biliary cirrhosis); alcohol-induced chronic pancreatitis (K86.0); accidental poisoning by and exposure to alcohol (X45); intentional self-poisoning by and exposure to alcohol (X65); and poisoning by and exposure to alcohol (Y15) |
| Grigoriev et al., 2017 [6] | No | ICD-10 | Cirrhosis of the liver (K70, K74); accidental poisonings by alcohol (X45) |
| Herttua et al., 2008 [7] | No | ICD-10 | Alcohol dependence syndrome (F10.2), other mental and behavioural disorders due to alcohol use (F10.1 and F10.3-10.9), alcoholic cardiomyopathy (I42.6), alcoholic liver disease (K70), and alcoholic diseases of the pancreas (K86.0), as well as a few rarely occurring additional categories (K29.2, G31.2, G40.51, G62.1, and G72.1) |
| Mäki et al., 2008 [8] | Yes* | ICD-9/ICD-10 | Alcohol-related suicides (ICD9: E95.0-E95.9; ICD10: X60-X84 and Y87.0) Defined as alcohol-attributable as follows: “alcoholic intoxication was stated as one of the three contributory causes,” |
| Mäki et al., 2009 [9] | Yes* | ICD-9/ICD-10 | Alcohol-related suicides (ICD9: E95.0-E95.9; ICD10: X60-X84 and Y87.0) Defined as alcohol-attributable as follows: “in order for alcohol to be classified as a contributory cause the pathologist must determine that intoxication indeed played a role in the process that ended in suicide” |
| Mustard et al., 2013 [10] | No | ICD-9/ICD-10 | Mental and behavioural disorders due to use of alcohol (ICD-9: 291, 303, 305.0; ICD-10: F10); alcoholic cardiomyopathy (ICD-9: 425.5; ICD-10: I42.6); alcoholic liver disease (ICD-9: 5710-5713; ICD-10: K70); alcoholic diseases of the pancreas (ICD-9: 5770, 5771; ICD-10: K85, K86.0) Accidental poisoning by and exposure to alcohol (ICD-9: 860; ICD-10: X45) |
| Pulido et al., 2017 [11] | No | ICD-10 | Alcohol-use disorders (F10); alcoholic cardiomyopathy (I42.6); alcoholic liver disease (K70); alcohol-induced pancreatitis (K85.2, K86.0); alcohol poisoning (X45, X65, Y15); other pathologies due to alcohol (E24.4, G31.2, G62.1, G72.1, K29.2, R78.0) |
| Vågerö & Garcy, 2016 [12] | No | ICD-10 | Mental and behavioural disorders due to use of alcohol (F10); degeneration of nervous system due to alcohol (G31.2); alcoholic polyneuropathy (G62.1); alcoholic cardiomyopathy (I42.6); alcoholic gastritis (K29.2); alcoholic liver disease (K70); alcohol-induced chronic pancreatitis (K86.0); toxic effect of alcohol (T51); alcoholic |

| | | | |
|--------------------------------|-----|--------|---|
| Zagozdzon et al., 2009 [13] | Yes | ICD-10 | myopathy (G72.1), other pathologies due to alcohol (E52, E24.4, P04.3, O35.4, Q86.0, Z50.2, Z71.4, Z72.1, R78.0) Cancers (C01-C06, C09, C10, C12-C15, C22, C32); mental and behavioural disorders due to use of alcohol (F10); alcoholic liver disease (K70) |
|--------------------------------|-----|--------|---|

AAF alcohol-attributable fraction.

* Even though all deaths were defined as alcohol-attributable by the pathologies, we did not code this as 100% attributable only based on to the included ICD codes.

References

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