

Citation:

Corrao G, Rubbiati L, Bagnardi V, Zambon A, Poikolainen, K. Alcohol and coronary heart disease: A meta-analysis. *Addiction*. 2000; 95: 1,505-1,523.

PubMed ID: [11070527](#)

Study Design:

Meta-analysis or Systematic Review

Class:

M - [Click here](#) for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

- To summarize estimates of the parameters describing the relationship between alcohol consumption and the risk of coronary heart disease (CHD)
- To measure the heterogeneity across studies describing the relationship between alcohol consumption and the risk of CHD
- To evaluate whether the characteristics of the studies and of the individuals may explain a part of the heterogeneity across studies describing the relationship between alcohol consumption and the risk of CHD
- To evaluate the possibility of publication bias concerning studies describing the relationship between alcohol consumption and the risk of CHD.

Inclusion Criteria:

- Case control or cohort study
- Published as a primary article
- Findings expressed as relative risk, considering three or more levels of alcohol consumption
- Reported number of cases and non-cases for each exposure level
- When results of a study were published more than once, the most recent comprehensive article was included.

Exclusion Criteria:

None explicitly stated.

Description of Study Protocol:**Search Procedures**

- Listing in MEDLINE, reference listed in article listed on MEDLINE, reference by other

bibliographic databases available at the University of Milan (Current Content from 1996, EMBASE from 1980, CAB Abstracts from 1973, and Core Biomedical Collection from 1993), hand search of general reviews and meta-analyses published on issue.

- Publication Between 1966 and 1998
- Keywords listed as disease (coronary heart disease, coronary artery disease, coronary event, coronary death, myocardial infarction, ischemic heart disease and angina pectoris), alcohol consumption (alcohol or ethanol and consumption, intake and drinking) and the association measures (relative risks, risk ratio, odds ratio and rate ratio).

Was Study Quality Assessed?

Study eligibility was assessed by readers blinded to authors' names and affiliations and to the reported results. These same blinded readers evaluated the quality of studies by scoring quality based on the pre-defined criteria of study design, data collection methods and data analysis. Points were awarded using a standard scale. Maximum scores were given when methods least likely to result in bias were used. Discrepancies between readers were resolved through discussions.

Type of Intervention and Outcomes Investigated, Population Included

- Relationship between alcohol consumption and the relative risk of CHD
- Determine if qualitative characteristics of included studies modified effect of alcohol
- Determine a more reliable function of the relationship between alcohol consumption and CHD risk by including only high-quality studies in analysis
- Identify sources of heterogeneity of the effects of alcohol intake
- Determine if publication bias affected validity of the estimates
- Population included adult males and females.

Data Collection Summary:

What Type of Information Was Abstracted from Articles?

- Study quality parameters
- Design
- Outcomes
- Diagnostic category
- Cases and non-cases
- Country of residence for subjects
- Age of subjects
- Gender of subjects
- Alcohol consumption: Amount and dose
- Association concerning each level of alcohol consumption and the corresponding confidence interval.

How Was it Combined?

- Alcohol consumption combined based on grams per day
- Alcohol consumption given in ranges was combined by assigning dose as the midpoint of the range. For the highest level of consumption, the range was assumed to be close-ended based on the width for all other dose ranges.
- Association measures and corresponding confidence intervals were translated into natural logarithm relative risks and corresponding variances.

What Analytic Methods Were Used, If Any?

- Relationship between alcohol consumption and the relative risk of CHD: Non-linear models fitted by pre-pooling the results of all included studies. Models within the fractional polynomial family were used. Specifically, a family of second-degree models was generated by power transformation of the exposure variable. The best-fitting model was chosen to summarize the relation of interest. This step was performed using all studies as well as studies gauged to be of highest quality by blinded readers.
- Determine if qualitative characteristics of included studies modified effect of alcohol: Meta-regression models were fitted. Qualitative characteristics included in analysis were quality score, three key components of quality score and study design. A significant effect of the interaction term (interaction between alcohol intake and value of covariate describing a qualitative characteristic) implies the covariate modifies the effect of alcohol intake on the relative risk. This step was performed using all studies as well as studies gauged to be of highest quality by blinded readers. However, the latter included an interaction term representing objects of interest rather than criteria for selection of studies. To perform the latter, the goodness of fit was assessed by the residual deviance and the D statistics were compared for the two models using the likelihood ratio test.
- Determine if publication bias affected validity of the estimates: Tested by a funnel-plot-based approach where a test of asymmetry of the funnel plot was conducted based on the method proposed by Egger et al.

Description of Actual Data Sample:

- Number of articles included: 51
- Number of articles identified: 196
- Number and type of studies reviewed:
 - 43 cohort studies
 - Eight case control studies
- Various geographic locations represented
- Some gender specific results reported (38 for males and 17 for females)
- Sample size of studies, and characteristics of the study participants.

Main Characteristics of the 51 Studies Included in the Meta-analysis

First Author and Year	Design	Outcome*	Diagnostic Category**	Subjects***
Klatsky, 1974	Case control	NF	MYI	298/299
Yano, 1977	Cohort	F+NF	CHD NFI ANP	294/7,705
Blackwelder, 1980	Cohort	F	CHD	132/8,006
Dyer, 1980	Cohort	F	CHD	89/1,832

Kagen, 1981	Cohort	F+NF	CHD	287/7,304
Klatsky, 1981	Cohort	F	CHD AMI	317/8,060
Gordon, 1983	Cohort	F+NF	CHD	906/4,625
Kittner, 1983	Cohort	F+NF	CHD	643/9,150
Colditz, 1985	Cohort	F	CHD	42/1,184
Kaufman, 1985	Case control	NF	MYI	981/2,170
Gordon, 1985	Cohort	F+NF	CHD	159/823
Friedman, 1986	Cohort	F	CHD	174/2,310
Klatsky, 1986	Cohort	F+NF	CAD	694/5,001
Kono, 1986	Cohort	F	CHD AMI	113/5,135
Scragg, 1987	Case control	NF	MYI	456/1,582
Suhonen, 1987	Cohort	F	CHD	140/4,532
Garfinkel, 1988	Cohort	F	CHD	18,984/581,321
Stampfer, 1988	Cohort	F NF F+NF	NFI FHD SHD	400/87,526
Boffetta, 1990	Cohort	F	CHD	18,771/276,802
Klatsky, 1990	Cohort	F	CAD	600/123,840
Miller, 1990	Cohort	F+NF	CHD	49/1,341
Kono, 1991	Case control	NF	AMI	83/271
Lazarus, 1991	Cohort	F	IHD	187/4,070

Rimm, 1991	Cohort	F NF F+NF	NFI FHD CAD	350/51,529
De Labry, 1992	Cohort	F	CHD	74/1,823
Farchi, 1992	Cohort	F	CHD	104/1,563
Jackson, 1992	Case control	F NF	MYI COD	526/1,183
Kalandidi, 1992	Case control	NF	CHD	329/570
Klatsky, 1992	Cohort	F	CHD	940/12,8934
Suh, 1992	Cohort	F	CHD	190/11,668
Wannamethee, 1992	Cohort	F	IHD	182/5,778
Bianchi, 1993	Case control	NF	AMI	298/685
Cullen, 1993	Cohort	F	CHD	325/2,171
Garg, 1993	Cohort	F+NF	IHD	475/3,718
Hein, 1993	Cohort	F+NF	IHD	86/2,563
Prineas, 1993	Cohort	F	FMI	115/32,898
Doll, 1994	Cohort	F	IHD	974/12,321
Goldberg, 1994	Cohort	F	CHD	132/3,793
Fuchs, 1995	Cohort	F	CHD	320/85,709
Iso, 1995	Cohort	F+NF	CHD	31/2,890
Serdula, 1995	Cohort	F	IHD	785/8,187
Camargo, 1997	Cohort	F NF F+NF	CHD MYI ANP	2,243/22,071
Keil, 1997	Cohort	F+NF	CHD	62/2,084

McElduff, 1997	Case control	F+NF	MCE	8,681/60,65
Rehm, 1997	Cohort	F	CHD	434/6,788
Thun, 1997	Cohort	F	CHD	2,622/489,626
Wannamethee, 1997	Cohort	F+NF	CHD	490/7,735
Yuan, 1997	Cohort	F	IHD	104/18,224
Kitamura, 1998	Cohort	F+NF	CHD MYI ANP	163/8,476
Renaud, 1998	Cohort	F	CHD	284/34,014

* Fatal (F); non-fatal (NF); fatal and non-fatal events (F+NF).

** Acute myocardial infarction (AMI); angina pectoris (ANP); coronary artery disease (CAD); coronary heart disease (CHD); coronary death (COD); fatal heart disease (FHD); fatal myocardial infarction (FMI); ischemic heart disease (IHD); major coronary event (MDE); myocardial infarction (MYI); non-fatal infarction (NFI); severe heart disease (SHD).

*** Number of cases/Number of non-cases (total number of subjects in cohort study or number of controls in a case control study).

Summary of Results:

Findings

- A total of 21 models were tested to identify the best fitting one to describe the relationship between alcohol consumption and the relative risks of coronary heart disease. All 51 included studies were considered in this analysis.
- All models left a significant residual deviance (tabulated chi square = 311.6, DF=272). The model including the linear and root-squared alcohol terms fit the data best.

Key Findings

- Studies of the highest quality (those reporting relative risks adjusted for the main risk indicators, those considering lifetime abstainers as referents, those excluding subjects with pre-existing disease at baseline and those performed with a cohort design) showed lower protective effect of alcohol.
- Pooled analysis of all 51 studies found:
 - Protective effect evident up to 90g per day (RR=0.94; 95% CI: 0.90, 1.00)
 - Harmful effect reached at 113g per day (RR=1.08; 95% CI: 1.00, 1.16)
- Pooled analysis of the 28 highest-quality studies found:
 - Protective effect evident up to 72g per day (RR=0.96; 95% CI: 0.92, 1.00)
 - Harmful effect reached at 89g per day (RR=1.05; 95% CI: 1.00, 1.11)
- Considering fatal events as outcome, it was noted that:

- Protective effect evident up to 56g per day (RR=0.96; 95% CI: 0.92, 1.00)
- Harmful effect reached at 73g per day (RR=1.06; 95% CI: 1.00, 1.12)
- Considering both fatal and non-fatal events:
 - Protective effect evident up to 114g per day (RR=0.94; 95% CI: 0.89, 1.00)
 - Harmful effect reached at 141g per day (RR=1.10; 95% CI: 1.00, 1.20)
- Considering females:
 - Protective effect evident up to 31g per day (RR=0.93; 95% CI: 0.87, 1.00)
 - Harmful effect reached at 52g per day (RR=1.12; 95% CI: 1.00, 1.26)
- Considering males:
 - Protective effect evident up to 87g per day (RR=0.94; 95% CI: 0.88, 1.00),
 - Harmful effect reached at 114g per day (RR=1.09; 95% CI: 1.00, 1.19)
- Considering the Mediterranean countries: Protective effect evident up to 145g per day (RR=0.76; 95% CI: 0.61, 1.00)
- Considering all other countries: Protective effect evident up to 80g per day (RR=0.93; 95% CI: 0.87, 1.00)
- Small studies reporting relative risks greater than one for these intakes were less likely to be published compared with small studies reporting relative risks less than one (low intake: intercept= α =-0.31, 95% CI: -0.58, -0.00; moderate intake: intercept= α =-0.23, 95% CI: -0.46, -0.00).

Author Conclusion:

- The degree of any protective effect due to moderate doses of alcohol should be reconsidered, since the degree of protection from high-quality studies are smaller than those based on all studies
- High intake levels of alcohol are related to increased risk of CHD
- When considering the combination of protective and harmful effects, a J-shaped curve best describes the relationship between alcohol intake and CHD risk
- Both gender and area in which the study is performed modify the effect
- These results strongly suggest that the higher alcohol-related susceptibility of women acts towards both protective and harmful effects.

Reviewer Comments:

This study was extremely thorough and demonstrates a strong conclusion as to the knowledge of alcohol consumption effects concerning CHD. Recommendations must take into account where the recommendations are being provided and to whom.

Research Design and Implementation Criteria Checklist: Review Articles

Relevance Questions

- | | | |
|----|---|-----|
| 1. | Will the answer if true, have a direct bearing on the health of patients? | Yes |
| 2. | Is the outcome or topic something that patients/clients/population groups would care about? | Yes |
| 3. | Is the problem addressed in the review one that is relevant to nutrition or dietetics practice? | Yes |

4. Will the information, if true, require a change in practice? Yes

Validity Questions

1. Was the question for the review clearly focused and appropriate? Yes

2. Was the search strategy used to locate relevant studies comprehensive? Were the databases searched and the search terms used described? Yes

3. Were explicit methods used to select studies to include in the review? Were inclusion/exclusion criteria specified and appropriate? Were selection methods unbiased? Yes

4. Was there an appraisal of the quality and validity of studies included in the review? Were appraisal methods specified, appropriate, and reproducible? Yes

5. Were specific treatments/interventions/exposures described? Were treatments similar enough to be combined? Yes

6. Was the outcome of interest clearly indicated? Were other potential harms and benefits considered? Yes

7. Were processes for data abstraction, synthesis, and analysis described? Were they applied consistently across studies and groups? Was there appropriate use of qualitative and/or quantitative synthesis? Was variation in findings among studies analyzed? Were heterogeneity issues considered? If data from studies were aggregated for meta-analysis, was the procedure described? Yes

8. Are the results clearly presented in narrative and/or quantitative terms? If summary statistics are used, are levels of significance and/or confidence intervals included? Yes

9. Are conclusions supported by results with biases and limitations taken into consideration? Are limitations of the review identified and discussed? Yes

10. Was bias due to the review's funding or sponsorship unlikely? Yes