Relationships between intake of alcoholic beverages and the risk of cardiovascular disease

This is an excerpt from the full technical report, which is written in Norwegian.

The excerpt provides the report's main messages in English.

No. 13–2013

Systematic review, overview over systematic reviews

kunnskapssenteret

Title	Relationships between intake of alcoholic beverages and the risk of cardiovascular disease
Norwegian title	Sammenhengen mellom inntak av alkoholholdige drikker og risiko for hjerte- og karsykdom
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ISBN	978-82-8121-546-7
ISSN	1890-1298
Report	No. 13 – 2013
Project number	702
Type of report	Overview of reviews
No. of pages	70 (118 incl. attachments)
Client	The Norwegian Directorate of Health, Public Health division – Knut-Inge Klepp
Subject heading (MeSH)	Alcohol; Alcohol Drinking; Cardiovascular Diseases
Keywords	Systematic review
Citation	Lidal IB, Denison E, Mathisen M. Relationships between intake of alcoholic beverages and the risk of cardiovascular disease. Report from Kunnskapssenteret no. 13–2013. Oslo: Norwegian Knowledge Centre for the Health Services, 2013.

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We would like to thank all contributers for their expertise in this project. Norwegian Knowledge Centre for the Health Services assumes final responsibility for the content of this report.

Norwegian Knowledge Centre for the Health Services
Oslo, October 2013

Executive summary (English)

Background

Media reports regularly present findings from single studies showing that consumption of alcoholic beverages may decrease the risk of cardiovascular diseases. Such reports can have an effect on individuals' attitudes towards and choices related to consumption of alcoholic beverages. Therefore, it is important that the information conveyed is based on sound scientific evidence.

In 2009, The Norwegian Knowledge Centre for the Health Services published the report *Alcohol and cardiovascular disease - a literature search for systematic reviews* in collaboration with the Norwegian Institute of Public Health, commissioned by the The Norwegian Directorate of Health. The mission was to indentify systematic reviews examining the relationship between consumption of alcoholic beverages and the risk of cardiovascular diseases. In total 34 publications were identified. The Public Health Division at the Directorate of Health has now requested an updated report. For this report we searched for litterature published after the 2009 report. We judged the methodological quality of the reviews found both before and after 2009. Results from reviews of good methodological quality (based on the checklists from Norwegian Knowledge Centre for the Health Services) are presented.

Objective

We conducted a review of high methodological quality systematic reviews that summarize the available evidence regarding the relationship between the consumption of alcoholic beverages (spirits, wine, beer) and the risk of cardiovascular diseases.

Method

Librarian Mariann Mathisen developed a search strategy based on the inclusion criteria. The search was an update of a former search from January 15th 2009. The new search covered January 15th 2009 to January 2012, but combined with the former, the search covered the period from 1998 to January 2012. We searched the following databases:

- Ovid MEDLINE (R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 2009 to present
- Ovid EMBASE 2009 to present
- Cochrane Database of Systematic Reviews (CDSR)
- Cochrane and CDSR: Database of Reviews of Effects (DARE), 2009 to present
- Cochrane and CDSR: Health Technology Assessment (HTA), 2009 to present
- ISI Web of science 2009 to present

We had no language restrictions.

Two persons independently read titles and abstracts to identify eligible reviews to be examined based on the full text versions. We considered the relevance of selected articles based on the following inclusion criteria:

Population	Persons > 18 years of age.
Exposure	Consumption of alcoholic beverages (wine, spirits, beer), where the amount of alcohol was specified.
Comparison	Consumption of another type and/or amount of alcoholic beverages or no intake of alcohol.
Outcomes	Cardiovascular related mortality and/or morbidity, such as cardiovascular death, acute myocardial infarction, re-vascularization, angina pectoris, heart failure, stroke, development of diabetes. Changes in known risk factors for cardiovascular disease (such as hypertension, composition of blood lipids, diabetes, the metabolic syndrome).
Study design	Systematic reviews of high methodological quality.
Languages	English, German and Scandinavian languages were included. Systematic reviews in other languages were considered for translation.

In cases of disagreement about whether retrieved articles were relevant, we consulted a third person for clarification. Two persons assessed the quality of each systematic review by using the Norwegian Knowledge Centre for the Health Services' checklist for systematic reviews. One person extracted data from the reviews and assessed the quality of the evidence of each outcome measure by the GRADE-method. Another colleague verified the data extraction and the GRADE assessments. Information regarding the baseline population risks for death, coronary heart disease, stroke and atrial fibrillation were gathered from the National Health Registry on cardiovascular disease, Statistics Norway, and from the Tromsø study.

According to our protocol, we were supposed to restrict the report to results from systematic reviews of high methodological quality. However, four of the included reviews lacked important information and we found it necessary to complement missing data through the primary studies. The reviews had incomplete data on the study population (age, sex, health status), exposure time, type of alcoholic beverages, and confounding variables.

Results

The literature search resulted in 903 unique references, of which 52 publications were retrieved for further review in full text. In addition, we reviewed the 34 articles identified in 2009. In total, twelve publications were assessed for their methodological quality. Five systematic reviews satisfied our quality criteria, four examined alcohol intake and the risk of cardiovascular diseases, and one examined relationships between alcohol intake and biomarkers associated with cardiovascular disease risk. Four of the systematic reviews were published in 2010/ 2011, while one was published in 1999 with more results published in 2000 and 2004. The five systematic reviews summarized in total 196 unique primary studies. Two of the included reviews also examined relationships between alcohol intake and other outcomes than cardiovascular diseases.

The main results of the systematic reviews were that among otherwise healthy persons and compared no alcohol intake:

- daily intake of 100 g alcohol considerably increased the risks of hemmoragic stroke (RR 4.7; CI 3.35 to 6.59), hypertension (RR 4.15; CI 3.13 to 5.52), and probably also the risk of ischemic stroke (RR 4.37; CI 2.28 to 8.37).

- daily intake of 50 g alcohol probably increased the risks of hemmoragic stroke (RR 1.82; CI 1.46 to 2.82) and hypertension (RR 2.04; CI 1.77 to 2.35) .
- daily intake of 25 g alcohol daily probably increased the risk of hypertension (RR 1.43; CI 1.33 to 1.53).
- daily intake of 24 g (RR 1.07; CI 1.04 to 1.10), 60 g (RR 1.42; CI 1.23 to 1.64) and 120 g (RR 2.02; CI 1.60 to 2.97) alcohol probably increased the risk of atrial fibrillation in women.
- daily intake of 24 g (RR 1.08; CI 1.04 to 1.11), 60 g (RR 1.44; CI 1.23 to 1.69) and 120 g (RR 2.02; CI 1.52 to 2.86) alcohol probably increased the risk of of atrial fibrillation in men.

The risk of hemmoragic stroke, hypertension and atrial fibrillation increased with higher alcohol intake levels.

It was not possible to identify for how long exposure to these alcohol intake levels had been ongoing, - days, months or years, nor whether the two sexes (except for atrial fibrillation) or age groups had different risks.

100 g alcohol ≈ 8 glasses of wine 12 vol% or 8 bottles of 33 cl beer 4.5 vol%. Most of the studies documented self-reported consumption of alcoholic beverages.

We have very little confidence in the effect estimates presented in the reviews of how alcohol intake may modify the risk of coronary artery disease or coronary death, death from stroke, or atrial fibrillation.

For some of the outcomes, the reviews presented sensitivity analyses to examine whether the effect of alcohol exposure on cardiovascular disease risk differed between the sexes, for former alcoholics, and lifetime abstainers. These analyses included adjustments for confounding factors, but the reviews present insufficient information about these factors. The documentation is too limited for any consideration of whether different types of alcoholic beverages may have dissimilar effects on the outcomes.

The documentation on biomarkers for cardiovascular diseases showed that among otherwise healthy persons and compared to no alcohol intake:
- daily intake of on average 33 g (10 to 75) alcohol probably posed a slight advantage (higher) on HDL-cholesterol levels (MD 0.100 mmol/l; CI 0.072 to 0.128) after on average 4 weeks of exposure.
- daily intake of on average 25 g (15 to 35) alcohol probably posed a slight advantage (lower) on fibrinogen levels (MD -0.208 g/l; CI -0.308 to -0.109) after on average of 4 weeks of exposure.
- daily intake of 12 to 75 g of alcohol probably made little or no difference to LDL-cholesterol, total cholesterol and triglycerides levels after on average 4 weeks of exposure.

The documentation found in the systematic reviews is too limited to conclude whether daily alcohol intake modifies the biomarkers apolipoprotein A1, lp(a)lipoprotein, C reactive protein (CRP), interleukin 6, tumor necrosis factor α, plasminogen activator inhibitor, tissue-plasminogen activator and/or adiponectin.

Discussion

Our purpose was to critically examine and summarize the results of systematic reviews that assess the relationship between alcohol intake and cardiovascular diseases. Based on the available research, we concluded that alcohol intake increased the risks of both haemor-

rhagic stroke and hypertension, and probably the risks of ischemic stroke and atrial fibrillation as well. However, we do not know whether these risks increased after days, months or years of alcohol exposure.

We further conclude that alcohol intake probably gave a slight advantage on HDL-cholesterol and fibrinogen levels after four weeks of exposure compared to abstention an equally long period. Higher levels of HDL-cholesterol and lower levels of fibrinogen are thought to be associated with lower risk of coronary heart disease. However, the importance of these biomarkers on cardiovascular disease risk is not fully established.

Concerning death from coronary heart disease, death from stroke, and relevant biomarkers, the research documentation was too weak to draw conclusions on whether alcohol exposure changed disease risk or mediators. Both methodological considerations and lack of documentation limit our confidence in these results. There may still be a real relationship between alcohol and these outcomes. However, based on the present research findings we cannot conclude whether alcohol modify the risks of these diseases or relevant biomarkers.

Through evaluation of the five reviews, we identified inadequate documentation that hamper interpretation of the results. Particularly there was missing information regarding the studied populations and controls (healthy or sick, age, ethnicity), time at risk (duration of alcohol exposure), type of alcoholic beverages consumed and adjustment for confounders in the analyses. We searched for this information in the primary studies and found that methodological weaknesses and lack of information were persistent from the primary studies into the systematic reviews. Moreover, the systematic reviews had to some extent merged heterogeneous studies in the analyses. With in total 196 primary studies, it should be possible to perform meta-analyses that explores heterogeneity to the results – analyses that can allow us to have greater confidence in the merged effect estimates.

The current knowledge about health benefits from alcohol intake on cardiovascular disease risk is limited, but we know about harms such as stroke, hypertension and atrial fibrillation. Experts in the field need to judge whether further investments in studies exploring these relationships are warranted. In drug trials, the researchers are required to report potentially side effects. It is important to give balanced information about both benefits and harms. The same should also be expected from studies of alcohol intake and cardiovascular disease risk. Systematic reviews on these issues should report on the whole spectrum of effects from alcohol intake – and these should be communicated so the public can make informed decisions regarding their own alcohol consumption.

Conclusion

Our main conclusion is that alcohol intake increased the risks of haemorrhagic stroke and hypertension in otherwise healthy persons, and probably the risks of ischemic stroke and atrial fibrillation, while alcohol probably mediated a modest advantage on HDL-cholesterol and fibrinogen levels after an average of four weeks of exposure compared to no alcohol intake.

We do not know if the duration of the exposure, - days, months or years, was of importance for the estimated increased risks of stroke, hypertension or atrial fibrillation. The results on biomarkers were measured after on average 4 weeks, and we know little about the long-term effects. We do not have information on the study participants' baseline drinking habits, nor their baseline levels of biomarkers. There was minimal changes in LDL-cholesterol, total-cholesterol and triglyceride levels after alcohol exposure versus no alcohol exposure. We have not summarised how these biomarkers may affect risk of cardiovascular diseases, but the research literature point to that this relationship is not fully established.

For several of the studied outcomes, we request reanalysed meta-analyses with stricter inclusion criteria to avoid problems of heterogeneity. Such analyses may contribute to more solid conclusions on how alcohol intake affects the risks of coronary heart disease and death and stroke-related death, as well as a number of relevant biomarkers. The available 196 primary studies and probably more recently published studies as well, should be well fit for this purpose.

This field of research field is burdened with methodological weaknesses and incomplete reporting, which means that we have limited or very little confidence in the effect estimates presented for many of the outcomes. To ensure thorough documentation in the future, it is crucial that both the study population and the control group are well defined, that alcohol exposure (type of beverage, quantity, exposure time etc.) is described accurately, and that important confounding variables are specified and taken into account in the analyses – both in the primary studies and further into the systematic reviews. Only then, we can describe a more complete picture of how various intakes of alcohol may affect people's risk of cardiovascular disease.

We conclude that the knowledge on benefits from alcohol exposure on cardiovascular disease is limited, however we did find that there was an association between alcohol consumption and increased risk of stroke, hypertension and atrial fibrillation. A systematic review of pros and cons from alcohol intake on cardiovascular disease should be reported along with the whole spectrum of effects from alcohol intake – and such form the basis for each one of us to take informed decisicons related to consumption of alcoholic beverages.