Alkohol og hjertesykdom - litteratursøk etter systematiske oversikter

Rapport fra Kunnskapssenteret nr 7–2009

Litteratursøk med sortering

kunnskapssenteret

Bakgrunn: Kunnskapssenteret har, i samarbeid med forskere fra Folkehelseinstituttet, gjort et omfattende litteratursøk etter systematiske oversikter som kan belyse følgende problemstillinger: • Hva er sammenhengen mellom bruk av alkohol (sprit, vin, øl) og risikoen for å få hjerte- og karsykdom eller dø? • Hva er sammenhengen mellom bruk av alkohol og kjente risikofaktorer for hjerte- og karsykdom (som hypertensjon)? • Hvilke potensielle skeivheter (bias) er viktige å ta hensyn til i studier av slike sammenhenger? **Metode:** Aktuelle artikler ble innhentet og vurdert i fulltekst med tanke på om de oppfylte inklusjonskriteriene som var satt opp: • Formålet med oversikten skal være klart definert • Dette formålet skal gjelde sammenhengen mellom alkohol (sprit, vin, øl) og hjerte- og karsykdom eller dødelighet, eller kjent risikofaktor for hjerte- og karsykdom (hypertensjon), eller skeivheter (bias) i studier av sammenhengen mellom alkohol (sprit, vin, øl) og hjerte- og karsykdom eller dødelighet, eller kjent risikofaktor for hjerte- og karsykdom • Det skal gå fram i metodedelen av artikkelen/rapporten hvilke databaser som det er søkt i, og for hvilken tidsperiode.

(fortsetter på baksiden)

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(fortsettelsen fra forsiden) **Resultat:** Vi identifiserte i alt 34 artikler eller rapporter fra 1998 og seinere, som oppfylte våre inklusjonskriterier. Vi har ikke vurdert kvaliteten på disse og har heller ikke forsøkt å oppsummere funnene utover å gjengi sammendrag av hver oversikt.

Tittel	Alkohol og hjertesykdom – litteratursøk etter systematiske oversikter
Institusjon	Nasjonalt kunnskapssenter for helsetjenesten
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Nasjonalt kunnskapssenter for helsetjenesten fremskaffer og formidler kunnskap om effekt av metoder, virkemidler og tiltak og om kvalitet innen alle deler av helsetjenesten. Målet er å bidra til gode beslutninger slik at brukerne får best mulig helsetjenester. Senteret er formelt et forvaltningsorgan under Helsedirektoratet, uten myndighetsfunksjoner. Kunnskapssenteret kan ikke instrueres i faglige spørsmål.

Nasjonalt kunnskapssenter for helsetjenesten
Oslo, 29.04.2009

1-side oppsummering

Kunnskapssenteret har, i samarbeid med forskere fra Folkehelseinstituttet, gjort et omfattende litteratursøk etter systematiske oversikter som kan belyse følgende problemstillinger:

- Hva er sammenhengen mellom bruk av alkohol (sprit, vin, øl) og risikoen for å få hjerte- og karsykdom eller dø?
- Hva er sammenhengen mellom bruk av alkohol og kjente risikofaktorer for hjerte- og karsykdom (som hypertensjon)?
- Hvilke potensielle skeivheter (bias) er viktige å ta hensyn til i studier av slike sammenhenger?

Aktuelle artikler ble innhentet og vurdert i fulltekst med tanke på om de oppfylte inklusjonskriteriene som var satt opp:

1. Formålet med oversikten skal være klart definert
2. Dette formålet skal gjelde sammenhengen mellom alkohol (sprit, vin, øl) og hjerte- og karsykdom eller dødelighet, eller kjent risikofaktor for hjerte- og karsykdom (hypertensjon), eller skeivheter (bias) i studier av sammenhengen mellom alkohol (sprit, vin, øl) og hjerte- og karsykdom eller dødelighet, eller kjent risikofaktor for hjerte- og karsykdom
3. Det skal gå fram i metodedelen av artikkelen/rapporten hvilke databaser som det er søkt i, og for hvilken tidsperiode

Vi identifiserte i alt 34 artikler eller rapporter fra 1998 og seinere, som oppfylte våre inklusjonskriterier. Vi har ikke vurdert kvaliteten på disse og har heller ikke forsøkt å oppsummere funnene utover å gjengi sammendrag av hver oversikt.

Innhold

Forord

Nasjonalt kunnskapssenter for helsetjenesten fikk høsten 2008 i oppdrag fra Helsedirektoratet å identifisere eksisterende systematiske oversikter over forskning som belyser sammenhenger mellom bruk av alkohol og risiko for hjerte- og karsykdom.

Forskningsbibliotekar Ingvild Kirkehei (Kunnskapssenteret) utførte det elektroniske litteratursøket. Vurdering av titler, sammendrag og artikler i fulltekst ble gjort av forsker Eva Denison (Kunnskapssenteret), kst. overlege Eirin Bakke (Folkehelseinstituttet) og professor Jørg Mørland (Folkehelseinstituttet). Prosjektet ble administrert av forskningsleder Atle Fretheim (Kunnskapssenteret).

Anne Karin Lindahl	Atle Fretheim	Eva Denison
Avdelingsdirektør	*Forskningsleder*	*Forsker*

Problemstilling

Finnes det oppdatert, oppsummert kunnskap som kan besvare de følgende spørsmålene?

1. Hva er sammenhengen mellom bruk av alkohol (sprit, vin, øl) og risikoen for å få hjerte- og karsykdom eller dø?

2. Hva er sammenhengen mellom bruk av alkohol og kjente risikofaktorer for hjerte- og karsykdom (hypertensjon)?

3. Hvilke potensielle skeivheter (bias) er viktige å ta hensyn til i studier av slike sammenhenger?

Innledning

Massemediene formidler jevnlig budskapet om at alkohol er vist å ha helsefremmende effekter, og en rekke forskningsrapporter har vist at en slik sammenheng kan påvises (1, 2). Det er særlig med tanke på forebygging av hjertesykdom at alkohol hevdes å ha en gunstig effekt.

For 10 år siden nedsatte Rusmiddeldirektoratet ei ekspertgruppe som gjennomgikk forskningslitteraturen på feltet. Konklusjonen den gang var:

"Samlet må vi kunne hevde at det er mer som taler for enn i mot en kausal biologisk sammenheng mellom jevnt moderat alkoholbruk og redusert risiko for koronar hjertesykdom. Det er sannsynlig at det også er en viss beskyttende virkning overfor hjerneslag, men her øker risikoen for sykdom når eksposisjonen øker utover det som er kalt et moderat inntak." (3)

Siden er det kommet nye studier og nye oppslag i massemediene. Det er derfor aktuelt å gjennomgå den aktuelle forskningslitteraturen på nytt.

I første omgang er det hensiktsmessig å kartlegge hva som finnes av nyere oppsummert forskning, for å unngå unødig dobbeltarbeid. Vi har derfor gjort et systematisk litteratursøk for å finne fram til eksisterende systematiske oversikter som belyser problemstillinger knyttet til sammenhengen mellom bruk av alkohol og risiko for hjerte- og karsykdom eller dødelighet. Vi har ikke vurdert kvaliteten på oversiktene vi har identifisert og har heller ikke forsøkt å oppsummere resultatene fra dem.

Resultatene av vår gjennomgang vil bidra til å avklare om det bør utarbeides en ny systematisk kunnskapsoppsummering på dette feltet.

Metode

LITTERATURSØK

Vi utførte et systematisk litteratursøk i følgende databaser: Ovid MEDLINE, Ovid EMBASE, SveMed+, DARE og HTA. Søkedato: 15. januar 2009.

Litteratursøket ble utarbeidet i henhold til forhåndsdefinerte inklusjons- og eksklusjonskriter.Søket inneholdt relevante søkeord for å fange opp systematiske oversikter over studier som omhandlet alkohol og hjerte- og karsykdom eller dødelighet. Søket ble avgrenset til publikasjoner utgitt f.o.m. 1998 og med søkefiltre for relevante studiedesign. Detaljert søkestrategi er gjengitt i vedlegg 1.

INKLUSJONSKRITERIER

Publikasjoner som oppfylte følgende kriterier ble inkludert:

1. Formålet med oversikten skal være klart definert
2. Dette formålet skal gjelde
    - sammenhengen mellom alkohol (sprit, vin, øl) og hjerte- og karsykdom eller dødelighet, eller kjent risikofaktor for hjerte- og karsykdom (hypertensjon), eller
    - skeivheter (bias) i studier av sammenhengen mellom alkohol (sprit, vin, øl) og hjerte- og karsykdom eller dødelighet, eller kjent risikofaktor for hjerte- og karsykdom
3. Det skal gå fram i metodedelen av artikkelen/rapporten hvilke databaser som det er søkt i, og for hvilken tidsperiode

UTVELGELSE OG SORTERING

Referanselista som fulgte av litteratursøket ble gjennomgått av tre personer uavhengig av hverandre (ED, EB og JM). Lista innholdt stort sett både tittel og sammendrag for hver referanse. Alle referanser som ble vurdert å være potensielt relevante ble innhentet i fulltekst for nærmere vurdering. Der hvor det var uenighet om hvorvidt en referanse kunne være relevant eller ei, ble fulltekstversjon innhentet. Alle artikler i fulltekst ble også vurdert av tre personer uavhengig av hverandre (ED, EB og JM). Vi kom til enighet om hvilke

oversiktsartikler som oppfylte inklusjonskriteriene våre. Sammendragene fra oversiktene presenterer vi under ”Resultater”.

Resultat

I søket identifiserte vi 1032 unike referanser (etter dublettkontroll) – se tabell 1.

Tabell 1 Søketreff fordelt på kilder

Ovid MEDLINE	634
Ovid EMBASE	666
SveMed+	32
DARE	33
HTA	7

Av disse ble 105 titler eller sammendrag vurdert som potensielt relevante og innhentet i fulltekstversjon. Etter gjennomlesning satt vi igjen med 34 artikler eller rapporter som vi mener er relevante for den aktuelle problemstillingen (4-37).

RELEVANTE SYSTEMATISKE OVERSIKTER

1. **Ariesen MJ, Claus SP, Rinkel GJE, Algra A. Risk factors for intracerebral hemorrhage in the general population: a systematic review. Stroke 2003;34(8):2060-5.**
   Sammendrag: BACKGROUND AND PURPOSE: Although data on some risk factors for intracerebral hemorrhage (ICH) already are beyond doubt, for other factors, the evidence is less clear. We performed a systematic overview of case-control and cohort studies on risk factors for ICH. METHODS: We searched MEDLINE, LILACS, EXTRAMED, and Pascal from 1966 to 2001 to identify studies. Studies were included if they met predefined methodological criteria. When possible, 2x2 tables were extracted and combined with the Mantel-Haenszel method. Summary odds ratios (ORs) were calculated for case-control studies, and summary relative risks (RRs) were found for cohort studies and for case-control and cohort studies combined. RESULTS: Fourteen case-control and 11 cohort studies were identified. We could not always combine the results of case-control and cohort studies. In cohort studies, the crude RR for age (every 10-year increase) was 1.97 (95% confidence interval [CI], 1.79 to 2.16). In case-control studies, the crude OR for high alcohol intake was 3.36 (95% CI, 2.21 to 5.12) and for hypertension was 3.68 (95% CI, 2.52 to 5.38). Two cohort studies showed an increasing risk of ICH with increasing degree

of hypertension. In cohort and case-control studies combined, the crude RR for sex (male versus female) was 3.73 (95% CI, 3.28 to 4.25); for current smoking, 1.31 (95% CI, 1.09 to 1.58); and for diabetes, 1.30 (95% CI, 1.02 to 1.67). CONCLUSIONS: Risk factors for ICH appeared to be age, male sex, hypertension, and high alcohol intake. High cholesterol tends to be associated with a lower risk of ICH. We could not assess whether these risk factors are independent.

2. **Bagnardi V, Zambon A, Quatto P, Corrao G. Flexible meta-regression functions for modeling aggregate dose-response data, with an application to alcohol and mortality. Am J Epidemiol 2004;159(11):1077-86.**
Sammendrag: In this paper, the authors describe fractional polynomials and cubic splines with which to represent smooth dose-response relations in summarizing meta-analytical aggregate data. Use of these two curve-fitting families can help prevent the problems arising from inappropriate linearity assumptions. These methods are illustrated in the problem of estimating the shape of the dose-response curve between alcohol consumption and all-cause mortality risk. The authors considered aggregate data from 29 cohort studies investigating this issue (1966-2000). J-shaped curves with a nadir at approximately 5-7 g/day of alcohol consumption and a last protective dose of 47-60 g/day were consistently obtained from fractional polynomials and cubic splines. The authors conclude that both of the curve-fitting families are useful tools with which to explore dose-response epidemiologic questions by means of meta-analytical approaches, especially when important nonlinearity is anticipated

3. **Bagnardi V, Zatonski W, Scotti L, La Vecchia C, Corrao G. Does drinking pattern modify the effect of alcohol on the risk of coronary heart disease? Evidence from a meta-analysis. J Epidemiol Community Health 2008;62(7):615-9.**
Sammendrag: OBJECTIVE: To evaluate the strength of the evidence provided by epidemiological literature investigating drinking pattern as effect modifier of alcohol intake on the risk of coronary heart disease (CHD). DESIGN: Meta-analysis of observational studies. DATA SOURCES: Medline, citation tracking, from 1966 to 2006. Review methods: Original studies investigating the amount of alcohol intake, combined with the frequency of alcohol consumption and/or pattern of alcohol drinking affecting the risk of CHD were extracted. Among them, cohort and case-control studies reporting sufficient data to perform statistical analyses and using people who abstained from alcohol as the reference were included. RESULTS: Six (4 cohort and 2 case-control) out of 118 studies reviewed met the inclusion criteria. Compared with those who abstained from alcohol, regular heavy drinkers and heavy irregular or binge drinkers showed significantly different pooled relative risks of 0.75 (95% confidence interval 0.64 to 0.89) and 1.10 (1.03 to 1.17) respectively. The dose-response relation between the amount of alcohol intake and CHD risk was significantly different in regular and irregular drinkers. A J-shaped curve, with nadir around 28 grams of alcohol per week, and last protective dose of

131 grams per week, was obtained including drinkers who consumed alcohol for 2 days a week or less. Conversely, in people who consumed alcohol for more than 2 days a week a significant protective effect was seen even when drinking high amounts of alcohol. CONCLUSION: This meta-analysis suggests that binge and heavy irregular drinking modify the favourable effect of alcohol intake on the CHD risk. However, this conclusion should be taken with caution because of the small number of studies considered

4. **Barnett AG, Dobson AJ. Excess in cardiovascular events on Mondays: a meta-analysis and prospective study. J Epidemiol Community Health 2005;59(2):109-14.**
   Sammendrag: The aim of this paper was to summarise the reported excess in coronary events on Mondays, and examine the evidence for three competing explanations: stress, alcohol consumption, or registration errors. A review of the literature found 28 studies covering 16 countries and over 1.6 million coronary events. The overall Monday excess was small; in a population experiencing 100 coronary events per week there was one more event on Monday than other days. The excess was larger in men and in studies including sudden cardiac death or cardiac arrests. In a prospective study an increase in events on Mondays was associated with greater alcohol consumption, lower rainfall, and the month of January. The excess in coronary events on Mondays is a persistent phenomenon. The size of the effect varies widely between populations. There is some evidence of an association with alcohol consumption, but a definitive explanation remains elusive and is likely to remain so because of the smallness of the effect and the paucity of high quality data.

5. **Bradley KA, Badrinath S, Bush K, Boyd-Wickizer J, Anawalt B. Medical risks for women who drink alcohol. J Gen Intern Med 1998;13(9):627-39.**
   Sammendrag: OBJECTIVE: To summarize for clinicians recent epidemiologic evidence regarding medical risks of alcohol use for women. METHODS: MEDLINE and PsychINFO, 1990 through 1996, were searched using key words "women" or "woman," and "alcohol." MEDLINE was also searched for other specific topics and authors from 1980 through 1996. Data were extracted and reviewed regarding levels of alcohol consumption associated with mortality, cardiovascular disease, alcohol-related liver disease, injury, osteoporosis, neurologic symptoms, psychiatric comorbidity, fetal alcohol syndrome, spontaneous abortion, infertility, menstrual symptoms, breast cancer, and gynecologic malignancies. Gender-specific data from cohort studies of general population or large clinical samples are primarily reviewed. MAIN RESULTS: Women develop many alcohol-related medical problems at lower levels of consumption than men, probably reflecting women's lower total body water, gender differences in alcohol metabolism, and effects of alcohol on postmenopausal estrogen levels. Mortality and breast cancer are increased in women who report drinking more than two drinks daily. Higher levels of alcohol consumption by women are associated with increased menstrual symptoms, hypertension, and stroke. Women who drink heavily also appear to have increased

infertility and spontaneous abortion. Adverse fetal effects occur after variable amounts of alcohol consumption, making any alcohol use during pregnancy potentially harmful. CONCLUSIONS: In general, advising nonpregnant women who drink alcohol to have fewer than two drinks daily is strongly supported by the epidemiologic literature, although specific recommendations for a particular woman should depend on her medical history and risk factors.

6. **Britton A, McKee M. The relation between alcohol and cardiovascular disease in Eastern Europe: explaining the paradox. J Epidemiol Community Health 2000;54(5):328-32.**
   Sammendrag: BACKGROUND: Recent evidence from Eastern Europe of a positive association between alcohol and cardiovascular disease has challenged the prevailing view that drinking is cardioprotective. Consuming amounts of alcohol comparable to those consumed in France has been linked to detrimental cardiovascular effects. One possibility is that this could be related to the particular consequences of binge drinking, which is common in Russia. METHODS: A systematic review of literature on the relation between cardiovascular disease and heavy drinking and irregular (binge) drinking. RESULTS: Most existing reviews of the relation between alcohol and cardiovascular disease have examined the amount drunk per week or month and have not looked at the pattern of drinking. These have consistently shown that alcohol has a cardioprotective effect, even at high levels of consumption. In contrast, studies that have looked at pattern of drinking, either directly, or indirectly, using indicators such as frequency of hangovers or reports of the consequences of drunkenness, have consistently found an increased risk of cardiovascular death, particularly sudden death. A separate review of the physiological basis for a difference between regular heavy drinking and heavy binge drinking demonstrates that the two types of drinking have quite different effects. CONCLUSION: An association between binge drinking and cardiovascular death meets the standard criteria for causality. It is important that future studies of alcohol related harm examine the pattern of drinking as well as the amount drunk.

7. **Burger M, Bronstrup A, Pietrzik K. Derivation of tolerable upper alcohol intake levels in Germany: a systematic review of risks and benefits of moderate alcohol consumption. Prev Med 2004;39(1):111-27.**
   Sammendrag: BACKGROUND: The objective of this study is to weigh the risks of moderate alcohol consumption against its benefits and, as a result, to derive tolerable upper alcohol intake levels (TUALs) for the German adult population. METHODS: Human studies assessing the effects of moderate alcohol consumption (< or = 40 g/day) on coronary heart disease, stroke, blood pressure, diseases of the liver, gallbladder, bile duct, and pancreas, cancer of the mouth/pharynx/larynx/oesophagus, stomach, colon/rectum, and breast, foetal alcohol syndrome/foetal alcohol effects, as well as all-cause mortality, published in the 10-15 years before 1999, have been systematically reviewed. The quality of studies has been evaluated using a self-constructed evaluation

scheme. As a result of comparing the critical endpoints of alcohol intake related to morbidity and mortality, the TUALs have been derived. RESULTS: The TUALs have been set at 10-12 g/day for healthy women and 20-24 g/day for healthy men of the adult population (18 years and older). Additional guidelines on alcohol use have been defined, taking into account further important aspects like alcohol consumption patterns and high-risk groups. CONCLUSIONS: The TUALs are not intended to be recommended intake levels. However, if the TUALs and the additional guidelines are followed, a relation of alcohol consumption to an increased risk of alcohol-associated diseases is unlikely for the majority of the population.

8. **Campbell NRC, Ashley MJ, Carruthers SG, Lacourciere Y, McKay DW. Recommendations on alcohol consumption. Canadian Medical Association Journal 1999;160(9 SUPPL.):S13-S20.**
Sammendrag: Objective: To provide updated, evidence-based recommendations concerning the effects of alcohol consumption on the prevention and control of hypertension in otherwise healthy adults (except pregnant women). Options: There are 2 main options for those at risk for hypertension: avert the condition by limiting alcohol consumption or by using other nonpharmacologic methods, or maintain or increase the risk of hypertension by making no change in alcohol consumption. The options for those who already have hypertension include decreasing alcohol consumption or using another nonpharmacologic method to reduce hypertension; commencing, continuing or intensifying antihypertensive medication; or taking no action and remaining at increased risk of cardiovascular disease. Outcomes: The health outcomes considered were changes in blood pressure and in morbidity and mortality rates. Because of insufficient evidence, no economic outcomes were considered. Evidence: A MEDLINE search was conducted for the period 1966-1996 with the terms ethyl alcohol and hypertension. Other relevant evidence was obtained from the reference lists of articles identified, from the personal files of the authors and through contacts with experts. The articles were reviewed, classified according to study design, and graded according to the level of evidence. Values: A high value was placed on the avoidance of cardiovascular morbidity and premature death caused by untreated hypertension. Benefits, harms and costs: A reduction in alcohol consumption from more than 2 standard drinks per day reduces the blood pressure of both hypertensive and normotensive people. The lowest overall mortality rates in observational studies were associated with drinking habits that were within these guidelines. Side effects and costs were not measured in any of the studies. Recommendations: (1) It is recommended that health care professionals determine how much alcohol their patients consume. (2) To reduce blood pressure in the population at large, it is recommended that alcohol consumption be in accordance with Canadian low-risk drinking guidelines (i.e., healthy adults who choose to drink should limit alcohol consumption to 2 or fewer standard drinks per day, with consumption not exceeding 14 standard drinks per week for men and 9 standard drinks per week for women). (3) Hypertensive patients should also be advised to limit alcohol consumption to the levels

set out in the Canadian low-risk drinking guidelines. Validation: These recommendations are similar to those of the World Hypertension League, the National High Blood Pressure Education Program Working Group on Primary Prevention of Hypertension and the previous recommendations of the Canadian Coalition for High Blood Pressure Prevention and Control and the Canadian Hypertension Society. They have not been clinically tested. The low-risk drinking guidelines are those of the Addiction Research Foundation of Ontario and the Canadian Centre on Substance Abuse

9. **Chen L, Smith GD, Harbord RM, Lewis SJ. Alcohol intake and blood pressure: A systematic review implementing a mendelian randomization approach. PLoS Medicine 2008;5(3):0461-71.**
Sammendrag: Background: Alcohol has been reported to be a common and modifiable risk factor for hypertension. However, observational studies are subject to confounding by other behavioural and sociodemographic factors, while clinical trials are difficult to implement and have limited follow-up time. Mendelian randomization can provide robust evidence on the nature of this association by use of a common polymorphism in aldehyde dehydrogenase 2 (ALDH2) as a surrogate for measuring alcohol consumption. ALDH2 encodes a major enzyme involved in alcohol metabolism. Individuals homozygous for the null variant (*2*2) experience adverse symptoms when drinking alcohol and consequently drink considerably less alcohol than wild-type homozygotes (*1*1) or heterozygotes. We hypothesise that this polymorphism may influence the risk of hypertension by affecting alcohol drinking behaviour. Methods and Findings: We carried out fixed effect meta-analyses of the ALDH2 genotype with blood pressure (five studies, n = 7,658) and hypertension (three studies, n = 4,219) using studies identified via systematic review. In males, we obtained an overall odds ratio of 2.42 (95% confidence interval [CI] 1.66-3.55, p=4.8x10⁻⁶) for hypertension comparing *1*1 with *2*2 homozygotes and an odds ratio of 1.72 (95% CI 1.17-2.52, p = 0.006) comparing heterozygotes (surrogate for moderate drinkers) with *2*2 homozygotes. Systolic blood pressure was 7.44 mmHg (95% CI 5.39-9.49, p=1.13x10⁻¹²) greater among *1*1 than among *2*2 homozygotes, and 4.24 mmHg (95% CI 2.18-6.31, p=0.00005) greater among heterozygotes than among *2*2 homozygotes. Conclusions: These findings support the hypothesis that alcohol intake has a marked effect on blood pressure and the risk of hypertension.

10. **Cleophas TJ. Wine, beer and spirits and the risk of myocardial infarction: A systematic review. Biomed Pharmacother 1999;53(9):417-23.**
Sammendrag: Background: Alcohol has beneficial and harmful effects on health at the same time. Wine may be more beneficial for the heart than other types of alcoholic beverages. Objectives: 1. To assess the current status of knowledge regarding the relationship between death and alcohol consumption. 2. To assess the relationship between myocardial infarction (MI) and consumption of different types of alcoholic beverages, both low doses (1-4 drinks a day), and high doses (> 4 drinks a day). Methods:

meta-analysis of major cohort and case-control studies. For the assessment of death and alcohol consumption eight cohort studies were used; for the assessment of MI and different types of alcoholic beverages, 12 cohort and two case-control studies were used. Results and conclusions: 1. Small doses of alcohol (1-4 drinks a day) are associated with a slightly reduced risk of mortality and coronary heart disease (CHD). 2. Small doses (1-4 drinks a day) of wine, beer, and spirits are equally beneficial. 3. Apart from a direct beneficial effect of low doses of alcohol on mortality and CHD, some psychological factors may contribute to its beneficial effect. 4. High doses of alcohol ([greater-than or equal to] 5 drinks a day) are not associated with a reduced risk of death and CHD. 5. Apart from a direct effect of alcohol, confounding factors, particularly those of a psychological nature, may very well again contribute to the loss of benefits.

11. **Corrao G, Bagnardi V, Zambon A, Arico S. Exploring the dose-response relationship between alcohol consumption and the risk of several alcohol-related conditions: a meta-analysis. Addiction 1999;94(10):1551-73.**
Sammendrag: OBJECTIVE: To compare the strength of the evidence provided by the epidemiological literature on the association between alcohol consumption and the risk of six cancers (oral cavity, oesophagus, colorectum, liver, larynx, breast), hypertension, cerebrovascular diseases, gastric and duodenal ulcer, liver cirrhosis and other chronic liver diseases, pancreatitis and injures and adverse effects. METHODS: A search of the epidemiological literature from 1966 to 1998 was performed by several bibliographic databases. Meta-regression models were fitted considering fixed and random models and linear and non-linear effects of alcohol intake on the risk of each condition. The effects of some characteristics of the studies including an index of their quality were considered as putative sources of heterogeneity of the estimates. Publication bias was also investigated by asymmetry of funnel plots. RESULTS: Of the 397 initially reviewed studies, 200 were selected for meta-analysis. Since qualitative characteristics of the studies were often significant sources of heterogeneity among them, the estimates of the pooled dose-response slopes were based only on the 123 studies with higher quality score and/or reporting adjusted estimates of relative risks. Higher alcohol-related risks were found for liver cirrhosis, neoplasms of the upper respiratory and digestive tracts, haemorrhagic stroke and injuries and adverse effects. Weaker but significant associations were found for colorectum, liver and breast cancers, essential hypertension and chronic pancreatitis. For all these conditions, low intakes, corresponding to daily consumption of two drinks or two glasses of wine (25 g/day), have shown significant risks. Ischaemic stroke and gastric and duodenal ulcer seem independent of alcohol intake. The area in which the study was performed, the study's design and the outcome variable differently affected the slopes. CONCLUSIONS: The small number of sufficiently reliable studies, the strong indications of heterogeneity across them and the suspicion of publication bias suggest that there is a great need for well-conducted epidemiological studies performed in several countries, to examine the dose-response relationship between alcohol intake and the risk of several

alcohol-related conditions, as well as the role of drinking pattern in determining the risk.

12. **Corrao G, Rubbiati L, Bagnardi V, Zambon A, Poikolainen K. Alcohol and coronary heart disease: a meta-analysis. Addiction 2000;95(10):1505-23.** **Sammendrag:** OBJECTIVE: To estimate parameters of the function relating alcohol consumption with the risk of coronary heart disease and to identify the sources of heterogeneity in the parameter estimates. METHODS: A search of the epidemiological literature from 1966 to 1998 was performed using several bibliographic databases. Meta-regression models were fitted to evaluate non-linear effects of alcohol intake on the relative risk. The effects of some characteristics of the studies, including an index of their quality, were considered as putative sources of heterogeneity of the estimates. Publication bias was also investigated. FINDINGS: Among the 196 initially reviewed articles, 51 were selected. Since qualitative characteristics of the studies were significant sources of heterogeneity, the pooled dose-response functions were based on the 28 cohort studies with higher quality. Risk decreased from 0 to 20 g/day (RR = 0.80; 95% CI: 0.78, 0.83); there was evidence of a protective effect up to 72 g/day (RR = 0.96; 95% CI: 0.92, 1.00) and increased risk above > or = 89 g/day (RR = 1.05; 95% CI: 1.00, 1.11). Lower protective effects and harmful effects were found in women, in men living in countries outside the Mediterranean area and in studies where fatal events were used as the outcome. Evidence of publication bias for moderate intakes and of heterogeneity of the estimates across studies for higher intakes were found. CONCLUSIONS: The degree of protection from moderate doses of alcohol should be reconsidered. Further research investigating the effect of drinking patterns on the risk of coronary heart disease should be performed. Caution in making general recommendations is needed.

13. **Corrao G, Bagnardi V, Zambon A, La Vecchia C. A meta-analysis of alcohol consumption and the risk of 15 diseases. Prev Med 2004;38(5):613-9.** **Sammendrag:** BACKGROUND: To compare the strength of evidence provided by the epidemiological literature on the association between alcohol consumption and the risk of 14 major alcohol-related neoplasms and non-neoplastic diseases, plus injuries. METHODS: A search of the epidemiological literature from 1966 to 1998 was performed by several bibliographic databases. Meta-regression models were fitted considering fixed and random effect models and linear and nonlinear effects of alcohol intake. The effects of some characteristics of the studies, including an index of their quality, were considered. RESULTS: Of the 561 initially reviewed studies, 156 were selected for meta-analysis because of their a priori defined higher quality, including a total of 116,702 subjects. Strong trends in risk were observed for cancers of the oral cavity, esophagus and larynx, hypertension, liver cirrhosis, chronic pancreatitis, and injuries and violence. Less strong direct relations were observed for cancers of the colon, rectum, liver, and breast. For all these conditions, significant increased risks were also found for ethanol intake of 25 g per day. Threshold values were observed for ischemic and hemorrhagic strokes. For coronary heart disease, a J-shaped relation was observed with a minimum relative risk of

0.80 at 20 g/day, a significant protective effect up to 72 g/day, and a significant increased risk at 89 g/day. No clear relation was observed for gastroduodenal ulcer.
CONCLUSIONS: This meta-analysis shows no evidence of a threshold effect for both neoplasms and several non-neoplastic diseases. J-shaped relations were observed only for coronary heart disease.

14. **Daniel S, Bereczki D. Alcohol as a risk factor for hemorrhagic stroke. Ideggyogy Sz 2004;57(7-8):247-56.**
Sammendrag: PURPOSE: Whereas the protective effect of mild-to-moderate alcohol consumption against ischemic stroke has been well recognized, there is conflicting evidence regarding the link between alcohol consumption and hemorrhagic strokes. The aim of the present study is to summarize the results of case-control and cohort studies published on this issue. METHODS: Recent epidemiologic articles on the relationship between alcohol consumption and hemorrhagic stroke were identified by Medline searches limited to title words using the following search terms: "alcohol AND cerebrovascular dis*", "alcohol AND stroke", "alcohol AND cerebral hemorrhage" and "alcohol AND hemorrhagic stroke". RESULTS: Most case-control and cohort studies either reported only on total strokes or on a combined group of hemorrhagic strokes including intracerebral as well as subarachnoid hemorrhages. There was a consensus among reports that heavy alcohol consumption was associated with a higher risk of hemorrhagic strokes. Controversy remains regarding the effect of mild-to-moderate alcohol consumption: while some studies reported a protective effect, others found a dose-dependent linear relationship between the amount of alcohol consumed and the risk of hemorrhagic stroke. The differential effect of moderate alcohol consumption on hemorrhagic compared to ischemic strokes is mostly attributed to alcohol- and withdrawal-induced sudden elevations of blood pressure, and coagulation disorders. CONCLUSIONS: Heavy drinking should be considered as one of the risk factors for hemorrhagic stroke. In contrast to the protective effect of mild-to-moderate alcohol use against ischemic strokes, moderate drinking might result in an increased risk of hemorrhagic strokes.

15. **Di Castelnuovo A, Rotondo S, Iacoviello L, Donati MB, de Gaetano G. Meta-analysis of wine and beer consumption in relation to vascular risk. Circulation 2002;105(24):2836-44.**
Sammendrag: BACKGROUND: Many epidemiological studies have evaluated whether different alcoholic beverages protect against cardiovascular disease. We performed a meta-analysis of 26 studies on the relationship between wine or beer consumption and vascular risk. Methods and Results- General variance-based method and fitting models were applied to pooled data derived from 26 studies that gave a quantitative estimation of the vascular risk associated with either beverage consumption. From 13 studies involving 209 418 persons, the relative risk of vascular disease associated with wine intake was 0.68 (95% confidence interval, 0.59 to 0.77) relative to nondrinkers. There was strong

evidence from 10 studies involving 176 042 persons to support a J-shaped relationship between different amounts of wine intake and vascular risk. A statistically significant inverse association was found up to a daily intake of 150 mL of wine. The overall relative risk of moderate beer consumption, which was measured in 15 studies involving 208 036 persons, was 0.78 (95% confidence interval, 0.70 to 0.86). However, no significant relationship between different amounts of beer intake and vascular risk was found after meta-analyzing 7 studies involving 136 382 persons. CONCLUSIONS: These findings show evidence of a significant inverse association between light-to-moderate wine consumption and vascular risk. A similar, although smaller association was also apparent in beer consumption studies. The latter finding, however, is difficult to interpret because no meaningful relationship could be found between different amounts of beer intake and vascular risk.

16. **Di Castelnuovo A, Costanzo S, Bagnardi V, Donati MB, Iacoviello L, de Gaetano G. Alcohol dosing and total mortality in men and women: an updated meta-analysis of 34 prospective studies. Arch Intern Med 2006;166(22):2437-45.**
Sammendrag: BACKGROUND: Moderate consumption of alcohol is inversely related with coronary disease, but its association with mortality is controversial. We performed a meta-analysis of prospective studies on alcohol dosing and total mortality. METHODS: We searched PubMed for articles available until December 2005, supplemented by references from the selected articles. Thirty-four studies on men and women, for a total of 1 015 835 subjects and 94 533 deaths, were selected. Data were pooled with a weighed regression analysis of fractional polynomials. RESULTS: A J-shaped relationship between alcohol and total mortality was confirmed in adjusted studies, in both men and women. Consumption of alcohol, up to 4 drinks per day in men and 2 drinks per day in women, was inversely associated with total mortality, maximum protection being 18% in women (99% confidence interval, 13%-22%) and 17% in men (99% confidence interval, 15%-19%). Higher doses of alcohol were associated with increased mortality. The inverse association in women disappeared at doses lower than in men. When adjusted and unadjusted data were compared, the maximum protection was only reduced from 19% to 16%. The degree of association in men was lower in the United States than in Europe. CONCLUSIONS: Low levels of alcohol intake (1-2 drinks per day for women and 2-4 drinks per day for men) are inversely associated with total mortality in both men and women. Our findings, while confirming the hazards of excess drinking, indicate potential windows of alcohol intake that may confer a net beneficial effect of moderate drinking, at least in terms of survival.

17. **Ebrahim S, Smith GD. Lowering blood pressure: a systematic review of sustained effects of non-pharmacological interventions. J Public Health Med 1998;20(4):441-8.**
Sammendrag: BACKGROUND: Risk factors for raised blood pressure include obesity,

physical inactivity, high dietary salt intake, stress, and high alcohol consumption. Much less is known about the effects on blood pressure of modification of these risk factors for the purposes of disease prevention. A systematic review and meta-analysis of randomized controlled trials (RCTs) was conducted to estimate the effects of various non-pharmacological interventions on blood pressure. METHODS: RCTs of single interventions aimed at altering these risk factors among adults aged 45 or older with and without hypertension, and with at least six months follow-up were included. MEDLINE was the primary source and the boundaries of the study were from 1966 to April 1995. RESULTS: The majority of RCTs were of short duration and did not provide guidance on the sustainability of effects and were excluded. Totals of eight RCTs of salt restriction, eight RCTs of weight reduction, eight of stress management, eight of exercise, and one of alcohol reduction of longer than six months duration were found. Net (i.e. intervention - control group) systolic blood pressure changes, mean mm Hg (with 95 per cent confidence intervals in parentheses), in hypertensives were as follows: salt restriction -2.9 (-5.8,0.0), weight loss -5.2 (-8.3,-2.0), stress control -1.0 (-2.3,+0.3), and exercise -0.8 (-5.9,+4.2). Smaller changes were found in normotensive participants: salt restriction -1.3 (-2.7,+0.1), weight loss -2.8 (-3.9,-1.8), exercise -0.2 (-2.8,+2.4), and alcohol reduction -2.1 (-4.1,-0.1). Some interventions (e.g. stress control in normotensives) were not examined in either hypertensives or normotensives. The majority of RCTs were of low methodological quality and bias often tended to increase the changes observed. Few of the trials controlled for the confounding effects of concurrent changes in other blood pressure risk factors. CONCLUSION: These net changes are probably overestimates of the effects that might be achieved by non-pharmacological interventions. There is a need for large-scale, long duration trials of these non-pharmacological interventions in both hypertensive patients and normotensive people to determine effect sizes more accurately.

18. **Fillmore KM, Stockwell T, Chikritzhs T, Bostrom A, Kerr W. Moderate alcohol use and reduced mortality risk: systematic error in prospective studies and new hypotheses. Ann Epidemiol 2007;17(5 Suppl):S16-S23.**
Sammendrag: We have provided recent evidence suggesting that a systematic error may be operating in prospective epidemiological mortality studies that have reported "light" or "moderate" regular use of alcohol to be "protective" against coronary heart disease. Using meta-analysis as a research tool, a hypothesis first suggested by Shaper and colleagues was tested. Shaper et al suggested that people decrease their alcohol consumption as they age and become ill or frail or increase use of medications, some people abstaining from alcohol altogether. If these people are included in the abstainer category in prospective studies, it is reasoned that it is not the absence of alcohol elevating their risk for coronary heart disease (CHD) but, rather, their ill health. Our meta-analytic results indicate that the few studies without this error (i.e., those that did not contaminate the abstainer category with occasional or former drinkers) show abstainers and "light" or "moderate" drinkers to be at equal risk for all-cause and CHD

mortality. We explore the history of this hypothesis, examine challenges to our meta-analysis, and discuss options for future research.

19. **Gmel G, Gutjahr E, Rehm J. How stable is the risk curve between alcohol and all-cause mortality and what factors influence the shape? A precision-weighted hierarchical meta-analysis. Eur J Epidemiol 2003;18(7):631-42.**
Sammendrag: OBJECTIVE: To determine the influence of six determining variables on the shape of the risk curve between alcohol and all-cause mortality. METHODS: DATA: Based on a systematic search with clear inclusion criteria, all articles on alcohol and all-cause mortality until 2000 were included. STATISTICAL METHODS: Precision-weighted pooling of relative risks (RRs); precision-weighted hierarchical analysis. VARIABLES: For pooling: RRs for different categories of average volume of drinking, lifetime abstainers and ex-drinkers. For hierarchical analysis: on first level: consumption in grams of pure alcohol per day; on second level: length of follow-up time in months; per capita consumption; average age, proportion of abstainers, average volume of drinking, and variability of average volume of drinking at baseline. OUTCOMES MEASURES: RR of former and current drinkers for all-cause mortality compared to abstainers. RESULTS: The main hypotheses could be confirmed for males: Ex-drinkers had a higher mortality risk than lifetime abstainers; the higher and the more diverse the average volume of alcohol consumption, the wider the dip of the curve; the older the persons at baseline, the more pronounced the protective effect; and the longer the follow-up time, the less pronounced the protective effect. Except for average volume of drinking effects for females went in the same direction but with one exception did not reach significance. CONCLUSIONS: There are systematic influences on the shape of the risk curve between alcohol and all-cause mortality. The overall beneficial effect of light to moderate drinking remained under all scenarios, indicating a high validity of the overall shape despite the heterogeneity between studies.

20. **Iestra JA, Kromhout D, van der Schouw YT, Grobbee DE, Boshuizen HC, van Staveren WA. Effect size estimates of lifestyle and dietary changes on all-cause mortality in coronary artery disease patients: a systematic review. Circulation 2005;112(6):924-34.**
Sammendrag: BACKGROUND: Guidelines for lifestyle and dietary modification in patients with coronary artery disease (CAD) are mainly supported by evidence from general population studies. CAD patients, however, differ from the general population in age (older) and treatment with preventive drugs. This review seeks to provide evidence for a prognostic benefit of lifestyle and dietary recommendations from studies in CAD patients. METHODS AND RESULTS: A literature search was performed on the effect of lifestyle and dietary changes on mortality in CAD patients. Prospective cohort studies and randomized controlled trials of patients with established CAD were included if they reported all-causes mortality and had at least 6 months of follow-up. The effect estimates of smoking cessation (relative risk [RR], 0.64; 95% CI, 0.58 to 0.71), increased physical

activity (RR, 0.76; 95% CI, 0.59 to 0.98), and moderate alcohol use (RR, 0.80; 95% CI, 0.78 to 0.83) were studied most extensively. For the 6 dietary goals, data were too limited to provide reliable effect size estimates. Combinations of dietary changes were associated with reduced mortality (RR, 0.56; 95% CI, 0.42 to 0.74). CONCLUSIONS: Available studies show convincingly the health benefits of lifestyle changes in CAD patients. Effect estimates of combined dietary changes look promising. Future studies should confirm these findings and assess the contribution of the individual dietary factors.

21. **Koppes LLJ, Dekker JM, Hendriks HFJ, Bouter LM, Heine RJ. Meta-analysis of the relationship between alcohol consumption and coronary heart disease and mortality in type 2 diabetic patients. Diabetologia 2006;49(4):648-52.**
Sammendrag: AIMS/HYPOTHESIS: This systematic review examines the relationship between alcohol consumption and long-term complications of type 2 diabetes. Meta-analyses could only be performed for total mortality, mortality from CHD, and CHD incidence, because the availability of articles on other complications was too limited. MATERIALS AND METHODS: A PubMed search through to September 2005 was performed and the reference lists of relevant articles examined. Among the relevant articles there were six cohort studies reporting on the risk of total mortality and/or fatal and/or incident CHD in alcohol non-consumers and in at least two groups of alcohol consumers. RESULTS: Statistical pooling showed lower risks in alcohol consumers than in non-consumers (the reference category). The relative risk (RR) of total mortality was 0.64 (95% CI 0.49-0.82) in the <6 g/day category. In the higher alcohol consumption categories (6 to <18, and > or =18 g/day), the RRs of total mortality were not significant. Risks of fatal and total CHD were significantly lower in all three categories of alcohol consumers (<6, 6 to <18 and > or =18 g/day) than in non-consumers, with RRs ranging from 0.34 to 0.75. CONCLUSIONS/INTERPRETATION: This meta-analysis shows that, as with findings in the general population, moderate alcohol consumption is associated with a lower risk of mortality and CHD in type 2 diabetic populations.

22. **Krishna V, Kim DH. Ethnic differences in risk factors for subarachnoid hemorrhage. J Neurosurg 2007;107(3):522-9.**
Sammendrag: OBJECT: Studies on risk factors for subarachnoid hemorrhage (SAH) show heterogeneity. For example, hypertension has been found to be a significant risk factor in some studies but not in others. The authors hypothesized that differences in the ethnicity of the populations studied could account for these findings. METHODS: A metaanalysis was performed using 17 case-control and 10 cohort studies that met specified inclusion criteria. The authors used a random-effect model to calculate the pooled effect estimates for current smoking, hypertension, and alcohol consumption. A meta-regression analysis was performed using the ethnic composition of the study populations as a covariate. Studies were classified as multiethnic or monoethnic, and the pooled effect estimates were compared. RESULTS: Analysis of the cohort studies yielded a pooled effect estimate or risk ratio of 3.18 (95% confidence interval [CI] 2.37-4.26) for

current smoking, 3.05 (95% CI 2.09-4.44) for hypertension, and 2.46 (95% CI 1.42-4.24) for alcohol consumption at a rate of 150 g/week or more. The results were similar for the case-control studies. For current smoking, the ethnic composition of the study population was a statistically significant predictor of heterogeneity among case-control studies ($p < 0.001$, even after application of the Bonferroni correction). The risk for SAH among current smokers was higher in multiethnic populations (odds ratio 3.832) than in monoethnic populations (odds ratio 2.487). CONCLUSIONS: The results of this metaanalysis suggest that differences in susceptibility to the harmful health effects of smoking may be one cause of the observed differences in SAH incidence for different ethnic groups. The role of ethnicity in risk factors for SAH should be considered in future studies.

23. **Masters JA. Moderate drinking and cardiovascular disease. Annu Rev Nurs Res 2005;23:65-97.**
Sammendrag: The adverse consequences of heavy alcohol use are well known. However, recent media reports of a possible cardiovascular benefit associated with moderate drinking have revived public interest in the use of alcohol for "medicinal purposes." Knowledge development regarding guidelines for moderate alcohol use has lagged behind public interest in the possible health benefits of moderate alcohol use. At this time, evidence-based primary health promotion interventions related to the risks and benefits of moderate alcohol use are lacking in the health care literature. This chapter reviews 22 reports describing the relationship between moderate drinking and cardiovascular disease. The reports are classified by the level of evidence and critiqued on seven aspects of method. Conclusions related to the strength of the evidence that moderate drinking is a useful primary health promotion intervention are presented.

24. **Mazzaglia G, Britton AR, Altmann DR, Chenet L. Exploring the relationship between alcohol consumption and non-fatal or fatal stroke: a systematic review. Addiction 2001;96(12):1743-56.**
Sammendrag: OBJECTIVE: Alcohol consumption has been reported to have both beneficial and harmful effects on stroke occurrence. Several studies have demonstrated a significant association with heavy drinking, but the evidence linking light-to-moderate alcohol consumption still remains unclear. This study, using a systematic review of the published literature, aimed to explore the dose-response relationship between alcohol and stroke, the effect of irregular drinking and the effect of beverage types on the risk of stroke. METHODS: A structured search for English-language published literature since 1966 was made using several electronic databases. This was supplemented using a hand search of references in review articles and additional searches on key authors. From the 153 eligible articles, 41 studies were selected according to study design, categorization of the exposure and outcome measures. FINDINGS: An association between recent alcohol use and stroke was consistently reported. There was also some evidence for a linear positive association for haemorrhagic stroke and alcohol consumption. Inconsistent

results emerged on the J-shaped relationship between alcohol and ischaemic stroke, and the association between alcohol and non-fatal or fatal stroke combined. The importance of the pattern of drinking was also demonstrated, indicating a higher risk for irregular drinkers. CONCLUSIONS: There is insufficient evidence to conclude that light-to-moderate alcohol drinking and wine intake have beneficial effects on stroke occurrence. On the contrary, findings from this review suggest the opportunity for a primary prevention regarding heavy drinking and binge drinking. More information regarding the risk of stroke associated with irregular alcohol drinking, and the joint effects of alcohol with other risk factors, would clarify the complex interaction between alcohol and stroke.

25. **McFadden CB, Brensinger CM, Berlin JA, Townsend RR. Systematic review of the effect of daily alcohol intake on blood pressure. Am J Hypertens 2005;18(2 Pt 1):276-86.**
Sammendrag: Numerous epidemiologic investigations have found an association between moderate intake of alcohol and increased blood pressure (BP). However, in controlled clinical studies that directly tested the effects of alcohol intake on BP, findings are inconsistent, perhaps because of differences in duration of alcohol use and the timing of BP measurements. In this setting, we performed a systematic review of trials that measured BP after a period of sustained alcohol intake (defined as daily intake of at least one alcoholic drink daily) in one group and that also had a control group of individuals who consumed no alcohol. Nine studies met the entrance criteria. The review demonstrated a significant rise in systolic blood pressure (SBP) and diastolic BP (DBP) of 2.7 mm and 1.4 mm Hg, respectively, after alcohol intake. An early effect of alcohol leading to a reduction BP (in the hours after exposure) and a later effect (next day) of raising BP led to smaller differences in the net effect of alcohol on BP when ambulatory BP monitoring measurements were compared with casual office- or clinic-based measurements. Our findings may have important implications for interpreting studies measuring the effect of alcohol on BP as well as for regular clinical care. These findings indicate that the timing of BP measurements after alcohol intake has a substantial effect on the magnitude and perhaps even the direction of BP change.

26. **Rehm J, Room R, Graham K, Monteiro M, Gmel G, Sempos CT. The relationship of average volume of alcohol consumption and patterns of drinking to burden of disease: an overview. Addiction 2003;98(9):1209-28.**
Sammendrag: AIMS: As part of a larger study to estimate the global burden of disease attributable to alcohol: to quantify the relationships between average volume of alcohol consumption, patterns of drinking and disease and injury outcomes, and to combine exposure and risk estimates to determine regional and global alcohol-attributable fractions (AAFs) for major disease and injury categories. DESIGN, METHODS, SETTING: Systematic literature reviews were used to select diseases related to alcohol consumption. Meta-analyses of the relationship between alcohol consumption and disease and multi-level analyses of aggregate data to fill alcohol-disease relationships not

currently covered by individual-level data were used to determine the risk relationships between alcohol and disease. AAFs were estimated as a function of prevalence of exposure and relative risk, or from combining the aggregate multi-level analyses with prevalence data. FINDINGS: Average volume of alcohol consumption was found to increase risk for the following major chronic diseases: mouth and oropharyngeal cancer; oesophageal cancer; liver cancer; breast cancer; unipolar major depression; epilepsy; alcohol use disorders; hypertensive disease; hemorrhagic stroke; and cirrhosis of the liver. Coronary heart disease (CHD), unintentional and intentional injuries were found to depend on patterns of drinking in addition to average volume of alcohol consumption. Most effects of alcohol on disease were detrimental, but for certain patterns of drinking, a beneficial influence on CHD, stroke and diabetes mellitus was observed. CONCLUSIONS: Alcohol is related to many major disease outcomes, mainly in a detrimental fashion. While average volume of consumption was related to all disease and injury categories under consideration, pattern of drinking was found to be an additional influencing factor for CHD and injury. The influence of patterns of drinking may be underestimated because pattern measures have not been included in many epidemiologic studies. Generalizability of the results is limited by methodological problems of the underlying studies used in the present analyses. Future studies need to address these methodological issues in order to obtain more accurate risk estimates.

27. **Rehm J, Sulkowska U, Manczuk M, Boffetta P, Powles J, Popova S, et al. Alcohol accounts for a high proportion of premature mortality in central and eastern Europe. Int J Epidemiol 2007;36(2):458-67.**
Sammendrag: BACKGROUND: There is a west-east mortality gradient in Europe, more pronounced in men. The objective of this article was to quantify the contribution of alcohol use to the gap in premature adult mortality between three old (France, Sweden and United Kingdom) and four new (Czech Republic, Hungary, Lithuania and Poland) European Union (EU) member states for the year 2002. Russia was added as an external comparator. METHODS: Exposure data were taken from surveys and per capita consumption records from the World Health Organization (WHO) Global Alcohol Database. Mortality data were taken from the WHO databank. The risk relationships were taken from published meta-analyses and from the WHO Comparative Risk Assessment project. Alcohol exposure and relative risk information was combined to derive alcohol-attributable fractions for relevant causes of premature mortality. RESULTS: Alcohol consumption was responsible for 14.6% of all premature adult mortality in the eight countries, 17.3% in men and 8.0% in women. This proportion was clearly higher in the new EU member states and Russia compared with the comparison countries from the old EU. For men, Russia with 29.0 alcohol-attributable premature deaths per 10,000 population had a more than 10-fold higher rate compared with Sweden (2.7 deaths/10,000). For women, the ratio between Hungary (5.0 alcohol-attributable deaths/10,000) and Russia (4.7 deaths/10,000) compared with Sweden (0.5 deaths/10,000) was almost as high, but the rates were much lower. The Czech Republic

and Poland showed proportionally less alcohol-attributable premature mortality than the other new EU member states or Russia for both genders, which, however, was still higher than in any of the old EU member states. CONCLUSIONS: Alcohol is a strong contributor to the health gap between western and central and eastern Europe, with both average volume of consumption and patterns of drinking contributing to burden of disease and injury. Alcohol also contributes substantially to male-female differences in mortality and life expectancy. However, there are feasible and cost-effective measures to reduce alcohol-related burden that should be implemented in central and eastern Europe.

28. **Reid MC, Boutros NN, O'Connor PG, Cadariu A, Concato J. The health-related effects of alcohol use in older persons: a systematic review. Subst Abus 2002;23(3):149-64.**
Sammendrag: Increased alcohol consumption is associated with substantial morbidity and mortality in young and middle-aged adult populations, but its effects on the health of older adults have received less attention. The objective of the study was to review published studies that assessed the effects of alcohol on falls or fall injuries, functional impairment, cognitive impairment, and all-cause mortality among older adults. MEDLINE database and bibliographies of selected citations were searched for English language studies published between 1966 and 1998 that examined the relationship between alcohol and one or more of the above outcomes. Also a study was analyzed if it included participants 60 years of age or older, or a broader age range of participants and reported results for older subgroups, or predominantly older participants as evidenced by a mean age of 65 years of age or above. Information on studies' sample sizes, exposure and outcome measures, and risk estimates were extracted, and articles were evaluated for methodologic quality using predetermined criteria. Eighty-four studies were identified that examined 91 potential exposure-outcome associations including falls or fall injuries (n = 26); functional impairment (n = 13); cognitive impairment (n = 32); and all-cause mortality (n = 20). The percentage of studies demonstrating harm, no association, or benefit by outcome included falls (15% vs. 81% vs. 4%); functional disability (38% vs. 46% vs. 16%); cognitive impairment (31% vs. 66% vs. 3%); and all-cause mortality (15% vs. 65% vs. 20%). Studies (n = 84) inconsistently adhered to methodologic standards. Although 90% provided eligibility criteria; 61% cited participation rates; and 73% described the methods used to measure alcohol exposure; only 44% adjusted for potentially important confounding factors; and 26% distinguished former drinkers from nondrinkers. Of the cohort studies (n = 47), 30% assessed for change in participants' exposure status over time, and 17% determined whether losses to follow-up varied by exposure status. The magnitude of risk posed by alcohol use for falls or fall injuries, functional disability, cognitive impairment, and all-cause mortality among older adults remains uncertain. Prospective studies are needed to better define the health-related effects of alcohol use in older populations.

29. **Reynolds K, Lewis B, Nolen JD, Kinney GL, Sathya B, He J. Alcohol consumption and risk of stroke: a meta-analysis. JAMA 2003;289(5):579-88.**
Sammendrag: CONTEXT: Observational studies suggest that heavy alcohol consumption may increase the risk of stroke while moderate consumption may decrease the risk. OBJECTIVE: To examine the association between alcohol consumption and relative risk of stroke. DATA SOURCES: Studies published in English-language journals were retrieved by searching MEDLINE (1966-April 2002) using Medical Subject Headings alcohol drinking, ethanol, cerebrovascular accident, cerebrovascular disorders, and intracranial embolism and thrombosis and the key word stroke; Dissertation Abstracts Online using the keywords stroke and alcohol; and bibliographies of retrieved articles. STUDY SELECTION: From 122 relevant retrieved reports, 35 observational studies (cohort or case control) in which total stroke, ischemic stroke, or hemorrhagic (intracerebral or total) stroke was an end point; the relative risk or relative odds and their variance (or data to calculate them) of stroke associated with alcohol consumption were reported; alcohol consumption was quantified; and abstainers served as the reference group. DATA EXTRACTION: Information on study design, participant characteristics, level of alcohol consumption, stroke outcome, control for potential confounding factors, and risk estimates was abstracted independently by 3 investigators using a standardized protocol. DATA SYNTHESIS: A random-effects model and meta-regression analysis were used to pool data from individual studies. Compared with abstainers, consumption of more than 60 g of alcohol per day was associated with an increased relative risk of total stroke, 1.64 (95% confidence interval [CI], 1.39-1.93); ischemic stroke, 1.69 (95% CI, 1.34-2.15); and hemorrhagic stroke, 2.18 (95% CI, 1.48-3.20), while consumption of less than 12 g/d was associated with a reduced relative risk of total stroke, 0.83 (95%, CI, 0.75-0.91) and ischemic stroke, 0.80 (95% CI, 0.67-0.96), and consumption of 12 to 24 g/d was associated with a reduced relative risk of ischemic stroke, 0.72 (95%, CI, 0.57-0.91). The meta-regression analysis revealed a significant nonlinear relationship between alcohol consumption and total and ischemic stroke and a linear relationship between alcohol consumption and hemorrhagic stroke. CONCLUSIONS: These results indicate that heavy alcohol consumption increases the relative risk of stroke while light or moderate alcohol consumption may be protective against total and ischemic stroke.

30. **Rimm EB, Williams P, Fosher K, Criqui M, Stampfer MJ. Moderate alcohol intake and lower risk of coronary heart disease: meta-analysis of effects on lipids and haemostatic factors. BMJ 1999;319(7224):1523-8.**
Sammendrag: OBJECTIVE: To summarise quantitatively the association between moderate alcohol intake and biological markers of risk of coronary heart disease and to predict how these changes would lower the risk. DESIGN: Meta-analysis of all experimental studies that assessed the effects of moderate alcohol intake on concentrations of high density lipoprotein cholesterol, apolipoprotein A I, fibrinogen, triglycerides, and other biological markers previously found to be associated with risk of coronary heart disease. PARTICIPANTS: Men and women free of previous chronic

disease and who were not dependent on alcohol. Studies were included in which biomarkers were assessed before and after participants consumed up to 100 g of alcohol a day. INTERVENTIONS: Alcohol as ethanol, beer, wine, or spirits. MAIN OUTCOME MEASURES: Changes in concentrations of high density lipoprotein cholesterol, apolipoprotein A I, Lp(a) lipoprotein, triglycerides, tissue type plasminogen activator activity, tissue type plasminogen activator antigen, insulin, and glucose after consuming an experimental dose of alcohol for 1 to 9 weeks; a shorter period was accepted for studies of change in concentrations of fibrinogen, factor VII, von Willebrand factor, tissue type plasminogen activator activity, and tissue type plasminogen activator antigen. RESULTS: 61 data records were abstracted from 42 eligible studies with information on change in biological markers of risk of coronary heart disease. An experimental dose of 30 g of ethanol a day increased concentrations of high density lipoprotein cholesterol by 3.99 mg/dl (95% confidence interval 3.25 to 4.73), apolipoprotein A I by 8.82 mg/dl (7.79 to 9.86), and triglyceride by 5.69 mg/dl (2.49 to 8.89). Several haemostatic factors related to a thrombolytic profile were modestly affected by alcohol. On the basis of published associations between these biomarkers and risk of coronary heart disease 30 g of alcohol a day would cause an estimated reduction of 24.7% in risk of coronary heart disease. CONCLUSIONS: Alcohol intake is causally related to lower risk of coronary heart disease through changes in lipids and haemostatic factors.

31. **Stockwell T, Chikritzhs T, Bostrom A, Fillmore K, Kerr W, Rehm J, et al. Alcohol-caused mortality in australia and Canada: scenario analyses using different assumptions about cardiac benefit. J Stud Alcohol 2007;68(3):345-52.**

Sammendrag: OBJECTIVE: The purpose of this study was to examine how definitions of "abstainers" in prospective studies of alcohol and mortality influence estimates of the extent of coronary heart disease (CHD) protection due to low-risk alcohol consumption. METHOD: Meta-analyses were conducted on 35 prospective studies categorized according to the presence of up to two postulated errors for men and women regarding the classification of abstainers. Risk of death from CHD was estimated to calculate age-gender specific etiological fractions for application to mortality data for Australia and Canada in 2002. Controls for study characteristics were age, history of illness, and smoking status. Abstainers were classified as (1) lifelong abstainers, exdrinkers, and occasional drinkers--both classification errors present; (2) lifelong abstainers and exdrinkers--one error; and (3) lifelong abstainers only. "Low-risk consumption" was defined as up to 24 g, on average, per day for women and 44 g for men; "elevated risk consumption" was defined as more than 24 g on an average day for women and more than 44 g for men. Higher daily alcohol consumption was classified as "high risk." RESULTS: Significant CHD protection was found for both men (odds ratio [OR] = .79) and women (OR = .89) only in studies committing both errors; it was found for women only in studies with "occasional drinker" error (OR = .75) and for neither gender in the few available error-free studies. Estimates of net alcohol-caused deaths in 2002 varied

accordingly, from -1,405 to 2,479 for Australia and from 4,321 to 7,319 for Canada. CONCLUSIONS: There is a need for CHD mortality studies that use lifelong abstinence as the reference point for estimating CHD protection. There may be gender differences in CHD protection. Separate estimates for the effects of low- and elevated-risk alcohol consumption on mortality should be made and communicated.

32. **Svardsudd K. Moderate alcohol consumption and cardiovascular disease: is there evidence for a preventive effect? Alcohol Clin Exp Res 1998;22(7 Suppl):307S-14S.**
Sammendrag: It is well-known that the intake of large quantities of alcohol is hazardous to the health. During the last few decades, moderate alcohol consumption has been claimed to have a protective effect in the cardiovascular system. For this study, literature search and review on moderate alcohol consumption and cardiovascular disease was performed. Data from ecological studies indicate that the consumption of wine, but not hard liquor or beer, are associated with a reduced mortality from cardiovascular diseases. Data from case-referent studies indicate no beneficial effect at all, whereas data from prospective cohort studies indicate a beneficial effect from all types of alcohol. There are several interpretational problems involved in this issue. No results from interventional studies are available. In the absence of such data, less valid conclusions are drawn from other types of studies. The soundness of conclusions based on comparisons of moderate drinkers and abstainers in case-referent and cohort studies has been questioned, because abstainers may have a higher than normal incidence of cardiovascular disease due to self-selection. Several possible modes of action have been proposed. However, provided that there is a protective effect of moderate alcohol consumption, there is no hard evidence that any of the proposed modes of action would be the sole one. Probably more than one mechanism is involved.

33. **Taylor B, Rehm J. When risk factors combine: the interaction between alcohol and smoking for aerodigestive cancer, coronary heart disease, and traffic and fire injury. Addict Behav 2006;31(9):1522-35.**
Sammendrag: BACKGROUND: Alcohol and tobacco are responsible for a significant amount of burden of disease, but some diseases may be a result of the interaction between these two risk factors. METHODS: Systematic literature review identified articles on the interaction of alcohol and smoking on a number of outcomes related to both risk behaviours. RESULTS: The interaction of smoking and alcohol significantly increases risk for aerodigestive cancers, and may increase risk for traffic injury and fire injury, but there were very few quality studies on injury. The indication that the cardioprotective effect of alcohol on coronary heart disease is only valid for smokers, but this result is inconclusive because of small evidence base. CONCLUSIONS: The interaction between smoking and alcohol consumption seems to be responsible for a significant amount of disease. Unfortunately, little is known on the mechanisms and

details of this interaction on disease outcomes. Future studies, especially for coronary heart disease and injury outcomes, are warranted.

34. **White IR. The level of alcohol consumption at which all-cause mortality is least. J Clin Epidemiol 1999;52(10):967-75.**
Sammendrag: Moderate consumers of alcohol have lower mortality than either nondrinkers or heavy drinkers. This systematic review aimed to quantify the level of alcohol consumption (termed the nadir) at which the lowest mortality occurs. Twenty cohort studies reported analyses of all-cause mortality for at least three categories of alcohol consumption, giving a total of 60,224 deaths among men and 74,824 deaths among women. The nadir in each study was estimated for men and women separately in units per week, where 1 unit is 9 g of alcohol. The estimated nadirs varied substantially between countries. Combined nadirs were estimated for U.S. men (overall nadir 7.7 units per week, 95% confidence interval [CI] 6.4-9.1), U.K. men (12.9 units per week, 95% CI 10.8-15.1), and U.S. women (2.9 units per week, 95% CI 2.0-4.0). The nadirs were not found to be increased in studies of older persons and apply for ages 50 to 80 years.

Diskusjon

Vi har utført et grundig søk i flere databaser med forskningsresultater og identifisert 34 systematiske oversikter fra det siste tiåret som belyser problemstillinger om sammenhenger mellom alkoholbruk og hjerte- og karsykdom og/eller dødelighet. Vi har ikke vurdert kvaliteten på disse og har heller ikke forsøkt å oppsummere funnene utover å gjengi sammendrag av hver oversikt.

Kombinasjonen av en omfattende elektroniske søkestrategi og at alle aktuelle titler, sammendrag og fulltekstartikler har vært vurdert av tre forskere uavhengig av hverandre, gjør at vi regner det som lite sannsynlig at vi har oversett vesentlige relevante systematiske oversikter.

Lista over de systematiske oversiktene vi har identifisert bør være et godt utgangspunkt for å vurdere om det er behov for å utarbeide nye systematiske oversikter innen dette feltet, eller om de eksisterende oversikter er tilstrekkelige for å belyse de problemstillingene som er aktuelle for norske helsemyndigheter i dag.

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34. Stockwell T, Chikritzhs T, Bostrom A et al. Alcohol-caused mortality in australia and Canada: scenario analyses using different assumptions about cardiac benefit. J Stud Alcohol 2007; 68: 345-52.

35. Svardsudd K. Moderate alcohol consumption and cardiovascular disease: is there evidence for a preventive effect? Alcohol Clin Exp Res 1998; 22: 307S-14S.

36. Taylor B, Rehm J. When risk factors combine: the interaction between alcohol and smoking for aerodigestive cancer, coronary heart disease, and traffic and fire injury. Addict Behav 2006; 31: 1522-35.

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Vedlegg

VEDLEGG 1 SØKESTRATEGI

Bibliotekar: Ingvild Kirkehei, Nasjonalt kunnskapssenter for helsetjenesten

Databaser: Ovid MEDLINE, Ovid EMBASE, DARE, HTA, SveMed+

Første søk, 6. november 2008

Treff totalt inkl. dubletter: 918
Treff totalt etter dublettkontroll: 674

SØKESTRATEGI SØK 1: Alkohol og hjerte-karsykdommer

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1950 to Present
Dato: 6.11.2008
Treff: 397

	Searches
1	cardiovascular diseases/ or exp heart diseases/ or exp vascular diseases/
2	(((cardiac or heart) adj (dis* or attack* or failure* or aneurysm* or arrest* or rupture* or event*)) or cardiovascular).tw.
3	myocardial.tw.
4	(arterial adj2 disease*).tw.
5	arterioscleros*.tw.
6	carotid stenos*.tw.
7	((vascular adj (dis* or occlusion* or accident* or event*)) or cerebrovascular).tw.
8	(ischemia* or stroke* or embolism* or thrombos* or thrombus or thromboembol* or carotid artery disease* or angina* or stenocardia* or hypertension* or blood pressure).tw.

9	(coronary adj (dis* or artery disease* or occlusion* or stenos* or thrombos* or vasospasm* or event*)).tw.
10	exp Blood Pressure/
11	or/1-10
12	Alcohol Drinking/
13	(alcohol or beer or wine or liquor or spirits).tw.
14	12 or 13
15	Meta-analysis/ or exp Controlled Clinical Trials as Topic/
16	meta analy$.tw.
17	metaanaly$.tw.
18	meta analysis.pt.
19	((systematic* or comprehensive or literature or quantitative or critical or integrative or evidence$) adj4 (review$1 or overview*)).tw.
20	literature study.tw.
21	critical appraisal.tw.
22	critical analysis.tw.
23	((database* adj search*) or (literatur* adj search*) or databases).ab.
24	(medline or pubmed or cochrane).ab.
25	embase.ab.
26	(psychlit or psyclit).ab.
27	(psychinfo or psycinfo).ab.
28	(cinahl or cinhal).ab.
29	science citation index.ab.
30	bids.ab.
31	cancerlit.ab.
32	reference list$.ab.
33	bibliograph$.ab.
34	hand-search$.ab.
35	relevant journals.ab.
36	manual search$.ab.
37	selection criteria.ab.
38	data extraction.ab.
39	37 or 38
40	review.pt.
41	39 and 40
42	or/15-36,41
43	comment.pt.

44	letter.pt.
45	editorial.pt.
46	animal/
47	human/
48	46 not (46 and 47)
49	or/43-45,48
50	42 not 49
51	11 and 14 and 50
52	limit 51 to yr="1998 - 2008"

EMBASE 1980 to 2008 Week 44
Dato: 6.11.2008
Treff: 460

	Searches
1	cardiovascular disease/ or cardiovascular symptom/ or exp cardiovascular inflammation/ or exp cardiovascular system tumor/ or exp heart disease/ or exp hypertension/ or exp hypotension/ or exp vascular disease/
2	(((cardiac or heart) adj (disease* or attack* or failure* or aneurysm* or arrest* or rupture* or event*)) or cardiovascular).tw.
3	myocardial.tw.
4	(arterial adj2 disease*).tw.
5	arterioscleros*.tw.
6	carotid stenos*.tw.
7	((vascular adj (diseas* or disorder* or occlusion* or accident* or event*)) or cerebrovascular).tw.
8	(ischemia* or stroke* or embolism* or thrombos* or thrombus or thromboembol* or carotid artery disease* or angina* or stenocardia* or hypertension* or blood pressure).tw.
9	(coronary adj (disease* or artery disease* or occlusion* or stenos* or thrombos* or vasospasm* or event*)).tw.
10	exp blood pressure/
11	or/1-10
12	alcohol consumption/

13	(alcohol or beer or wine or liquor or spirits).tw.
14	or/12-13
15	11 and 14
16	Systematic Review/
17	meta analysis/
18	metaanaly$.tw.
19	meta analy$.tw.
20	((systematic or comprehensive or literature or quantitative or critical or integrative or evidence$) adj2 (review$1 or overview$1)).tw.
21	literature study.tw.
22	(critical adj (appraisal or analysis)).tw.
23	((database* adj search*) or (literature adj search*) or databases).tw.
24	(medline or pubmed or cochrane).ab.
25	embase.ab.
26	(psychlit or psyclit).ab.
27	(psychinfo or psycinfo).ab.
28	(cinahl or cinhal).ab.
29	science citation index.ab.
30	bids.ab.
31	cancerlit.ab.
32	reference list$.ab.
33	bibliograph$.ab.
34	hand-search$.ab.
35	relevant journals.ab.
36	manual search$.ab.
37	selection criteria.ab.
38	data extraction.ab.
39	37 or 38
40	review.pt.
41	39 and 40
42	or/16-36,41
43	editorial.pt.
44	letter.pt.
45	Animal/
46	Nonhuman/
47	45 or 46
48	Human/

49	47 not (47 and 48)
50	or/43-44,49
51	42 not 50
52	51 and 15
53	limit 52 to yr="1998 - 2008"

Cochrane Library (Databaser: DARE, HTA) 2008, issue 4
Dato: 6.11.2008
Treff: DARE 3, HTA 2

ID	Search
#1	MeSH descriptor Cardiovascular Diseases, this term only
#2	MeSH descriptor Heart Diseases explode all trees
#3	MeSH descriptor Vascular Diseases explode all trees
#4	(((cardiac or heart) next (dis* or attack* or failure* or aneurysm* or arrest* or rupture* or event*)) or cardiovascular):ti,ab,kw
#5	(myocardial or (arterial adj2 disease*)):ti,ab,kw
#6	(arterioscleros* or carotid stenos*):ti,ab,kw
#7	((vascular next (dis* or occlusion* or accident* or event*)) or cerebrovascular):ti,ab,kw
#8	(ischemia* or stroke* or embolism* or thrombos* or thrombus or thromboembol* or carotid artery disease* or angina* or stenocardia* or hypertension* or blood pressure):ti,ab,kw
#9	(coronary next (dis* or artery disease* or occlusion* or stenos* or thrombos* or vasospasm* or event*)):ti,ab,kw
#10	MeSH descriptor Blood Pressure explode all trees
#11	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10)
#12	MeSH descriptor Alcohol Drinking explode all trees
#13	(alcohol or beer or wine or liquor or spirits):ti,ab,kw
#14	(#12 OR #13)
#15	(#11 AND #14)
#16	(#15), from 1998 to 2008

CRD Databases (Databaser: DARE, HTA)
Dato: 6.11.2008
Treff: DARE 43, HTA 7

# 1	MeSH Cardiovascular Diseases
# 2	MeSH Heart Diseases EXPLODE 1
# 3	MeSH Vascular Diseases EXPLODE 1
# 4	"Cardiac AND arrest*" OR "heart AND disease*" OR cardiovascular OR "heart AND failure*" OR aneurysm* OR "cardiac AND rupture*" OR myocardial OR "arterial AND occlusive AND disease*" OR "arterial AND obstructive AND disease*" OR arterioscleros* OR "carotid AND stenos*" OR cerebrovascular OR "vascular AND disorder*" OR "vascular AND disease*" OR "vascular AND occlusion*"
# 5	ischemia* OR stroke* OR embolism* OR thrombos* OR thrombus OR thromboembol* OR "carotid AND artery AND disease*" OR angina* OR stenocardia* OR hypertension* OR "blood AND pressure" OR "coronary AND disease* OR "coronary AND artery AND disease*" OR "coronary AND stenos*" OR "coronary AND occlusion*" OR "coronary AND thrombosis*" OR "coronary AND vasospasm"
# 6	MeSH Blood Pressure EXPLODE 1
# 7	#1 or #2 or #3 or #4 or #5 or #6
# 8	MeSH Alcohol Drinking EXPLODE 1
# 9	alcohol OR beer OR wine OR liquor OR spirits
# 10	#8 or #9
# 11	#7 and #10
# 12	#11 RESTRICT YR 1998 2008

Svemed+
Dato: 6.11.2008
Treff: 6 (publisert f.o.m. 1998)

Sökmängd	Sökvillkor
S1	*Explodesökning på Alcohol-Drinking*
S2	öl OR vin OR sprit OR sprut OR rödvin
S3	*Explodesökning på Cardiovascular-Diseases*
S4	hjärt$ OR hjerte$ OR slag$ OR kardiovaskul$
S5	S1 OR S2

S6	S3 OR S4
S7	S5 AND S6
S9	*Explodesökning på Review*
S10	*Explodesökning på Review-Literature as Topic*
S11	*Explodesökning på Controlled-Clinical Trials as Topic*
S12	oversikts$ OR oversigts$ OR review$ OR översikts$ OR kunnskapsoppsummering$ OR litteraturoversikt$ OR litteraturöversikt$ OR literaturoversigt$ OR litteraturoversigt$
S13	S9 OR S10 OR S11 OR S12
S14	S7 AND S13
S15	S7 [översikter]
S17	S14 OR S15

Oppdatert søk 15.1.2009

Søket ble oppdatert for å identifisere systematiske oversikter over sammenhengen mellom alkohol og dødelighet generelt. Referanser identifisert i søk 1 ble trukket fra.

Databaser: MEDLINE, EMBASE, DARE, HTA, SveMed+
Treff totalt inkl. dubletter: 511
Treff totalt etter dublettkontroll: 358

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R)

1950 to Present
Dato: 15.1.2009
Treff: 237
Opprinnelig søk linje 1-52, oppdateringssøk linje 53-66

1	cardiovascular diseases/ or exp heart diseases/ or exp vascular diseases/
2	(((cardiac or heart) adj (dis* or attack* or failure* or aneurysm* or arrest* or rupture* or event*)) or cardiovascular).tw.
3	Myocardial.tw.
4	(arterial adj2 disease*).tw.
5	arterioscleros*.tw.

6	carotid stenos*.tw.
7	((vascular adj (dis* or occlusion* or accident* or event*)) or cerebrovascular).tw.
8	(ischemia* or stroke* or embolism* or thrombos* or thrombus or thromboembol* or carotid artery disease* or angina* or stenocardia* or hypertension* or blood pressure).tw.
9	(coronary adj (dis* or artery disease* or occlusion* or stenos* or thrombos* or vasospasm* or event*)).tw.
10	exp Blood Pressure/
11	or/1-10
12	Alcohol Drinking/
13	(alcohol or beer or wine or liquor or spirits).tw.
14	12 or 13
15	Meta-analysis/ or exp Controlled Clinical Trials as Topic/
16	meta analy$.tw.
17	metaanaly$.tw.
18	meta analysis.pt.
19	((systematic* or comprehensive or literature or quantitative or critical or integrative or evidence$) adj4 (review$1 or overview*)).tw.
20	literature study.tw.
21	critical appraisal.tw.
22	critical analysis.tw.
23	((database* adj search*) or (literatur* adj search*) or databases).ab.
24	(medline or pubmed or cochrane).ab.
25	embase.ab.
26	(psychlit or psyclit).ab.
27	(psychinfo or psycinfo).ab.
28	(cinahl or cinhal).ab.
29	science citation index.ab.
30	bids.ab.
31	cancerlit.ab.
32	reference list$.ab.
33	Bibliograph$.ab.
34	hand-search$.ab.
35	relevant journals.ab.
36	manual search$.ab.
37	selection criteria.ab.
38	data extraction.ab.

39	37 or 38
40	review.pt.
41	39 and 40
42	or/15-36,41
43	comment.pt.
44	letter.pt.
45	editorial.pt.
46	animal/
47	human/
48	46 not (46 and 47)
49	or/43-45,48
50	42 not 49
51	11 and 14 and 50
52	limit 51 to yr="1998 - 2008"
53	exp mortality/ exp death/
54	(mortalit* or death rate* or cause* of death* or death cause*).tw.
55	mortality.fs.
56	53 or 55 or 54
57	14 and 56
58	Alcohol Drinking/mo [Mortality]
59	57 or 58
60	59 and 50
61	limit 60 to yr="1998 - 2009"
62	61 not 52
63	limit 51 to yr="1998 - 2009"
64	(200811* or 200812*).ep,ed.
65	2009*.ep,ed.
66	64 or 65
65	63 and 66
66	62 or 65

EMBASE 1980 to 2009 Week 02
Dato: 15.1.2009
Treff: 206
Opprinnelig søk linje 1-53, oppdateringssøk linje 54-65

1	cardiovascular disease/ or cardiovascular symptom/ or exp cardiovascular inflammation/ or exp cardiovascular system tumor/ or exp heart disease/ or exp hypertension/ or exp hypotension/ or exp vascular disease/
2	(((cardiac or heart) adj (disease* or attack* or failure* or aneurysm* or arrest* or rupture* or event*)) or cardiovascular).tw.
3	myocardial.tw.
4	(arterial adj2 disease*).tw.
5	arteriosclerosis*.tw.
6	carotid stenos*.tw.
7	((vascular adj (diseas* or disorder* or occlusion* or accident* or event*)) or cerebrovascular).tw.
8	(ischemia* or stroke* or embolism* or thrombos* or thrombus or thromboembol* or carotid artery disease* or angina* or stenocardia* or hypertension* or blood pressure).tw.
9	(coronary adj (disease* or artery disease* or occlusion* or stenos* or thrombos* or vasospasm* or event*)).tw.
10	exp blood pressure/
11	or/1-10
12	alcohol consumption/
13	(alcohol or beer or wine or liquor or spirits).tw.
14	or/12-13
15	11 and 14
16	Systematic Review/
17	meta analysis/
18	metaanaly$.tw.
19	meta analy$.tw.
20	((systematic or comprehensive or literature or quantitative or critical or integrative or evidence$) adj2 (review$1 or overview$1)).tw.
21	literature study.tw.
22	(critical adj (appraisal or analysis)).tw.
23	((database* adj search*) or (literature adj search*) or databases).tw.

24	(medline or pubmed or cochrane).ab.
25	embase.ab.
26	(psychlit or psyclit).ab.
27	(psychinfo or psycinfo).ab.
28	(cinahl or cinhal).ab.
29	science citation index.ab.
30	bids.ab.
31	cancerlit.ab.
32	reference list$.ab.
33	bibliograph$.ab.
34	hand-search$.ab.
35	relevant journals.ab.
36	manual search$.ab.
37	selection criteria.ab.
38	data extraction.ab.
39	37 or 38
40	review.pt.
41	39 and 40
42	or/16-36,41
43	editorial.pt.
44	letter.pt.
45	Animal/
46	Nonhuman/
47	45 or 46
48	Human/
49	47 not (47 and 48)
50	or/43-44,49
51	42 not 50
52	51 and 15
53	limit 52 to yr="1998 - 2008"
54	exp mortality/ or exp Death/
55	(mortalit* or death rate* or cause* of death* or death cause*).tw.
56	55 or 54
57	56 and 51 and 14
58	limit 57 to yr="1998 - 2009"
59	58 not 53
60	(20084* or 20085*).em.

61	20090*.em.
62	60 or 61
63	limit 52 to yr="1998 - 2009"
64	63 and 62
65	59 or 64

Cochrane Library (Databaser: DARE, HTA) 2008 issue 4

Dato: 15.1.2009

Treff: DARE 5, HTA 2

Opprinnelig søk linje 1-16, oppdateringssøk linje 17-22

#1	MeSH descriptor **Cardiovascular Diseases**, this term only
#2	MeSH descriptor **Heart Diseases** explode all trees
#3	MeSH descriptor **Vascular Diseases** explode all trees
#4	(((cardiac or heart) next (dis* or attack* or failure* or aneurysm* or arrest* or rupture* or event*)) or cardiovascular):ti,ab,kw
#5	(myocardial or (arterial adj2 disease*)):ti,ab,kw
#6	(arterioscleros* or carotid stenos*):ti,ab,kw
#7	((vascular next (dis* or occlusion* or accident* or event*)) or cerebrovascular):ti,ab,kw
#8	(ischemia* or stroke* or embolism* or thrombos* or thrombus or thromboembol* or carotid artery disease* or angina* or stenocardia* or hypertension* or blood pressure):ti,ab,kw
#9	(coronary next (dis* or artery disease* or occlusion* or stenos* or thrombos* or vasospasm* or event*)):ti,ab,kw
#10	MeSH descriptor **Blood Pressure** explode all trees
#11	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10)
#12	MeSH descriptor **Alcohol Drinking** explode all trees
#13	(alcohol or beer or wine or liquor or spirits):ti,ab,kw
#14	(#12 OR #13)
#15	(#11 AND #14)
#16	(#15), from 1998 to 2008
#17	MeSH descriptor **Mortality** explode all trees or MeSH descriptor **Death** explode all trees
#18	(mortalit* or death rate* or cause of death* or death cause*)
#19	(#17 OR #18)
#20	(#14 AND #19)
#21	MeSH descriptor **Alcohol Drinking** explode all trees with qualifier: **MO**
#22	#20 or #21

#23	(#22), from 1998 to 2009
#24	(#23 AND NOT #16)

CRD (databaser: DARE, HTA)

Dato: 15.1.2009

Treff: DARE 30, HTA 5

Opprinnelig søk linje 1-12, oppdateringssøk linje 13-18

# 1	MeSH Cardiovascular Diseases
# 2	MeSH Heart Diseases EXPLODE 1
# 3	MeSH Vascular Diseases EXPLODE 1
# 4	MeSH Alcohol Drinking EXPLODE 1
# 5	alcohol OR beer OR wine OR liquor OR spirits
# 6	#4 or #5
# 7	MeSH Blood Pressure EXPLODE 1
# 8	Cardiac AND arrest* OR heart AND disease* OR cardiovascular AND disease* OR heart AND failure* OR aneurysm* OR cardiac AND rupture* OR myocardial AND infarct* OR myocardial AND ischemia* OR myocardial AND stunning OR arterial AND occlusive AND disease* OR arterial AND obstructive AND disease* OR arterioscleros* OR carotid AND stenos* OR renal AND artery AND obstruction* OR retinal AND artery AND occlusion* OR cerebrovascular AND disORder* OR cerebrovascular AND disease* OR cerebrovascular AND occlusion* OR cerebrovascular AND accident OR vascular AND disORder* OR vascular AND disease* OR vascular AND occlusion*
# 9	ischemia* OR stroke* OR embolism* OR thrombos* OR thrombus OR thromboembolism* OR carotid AND artery AND disease* OR angina* OR stenocardia* OR hypertension* OR blood AND pressure OR coronary AND disease* OR coronary AND aneurysm* OR coronary AND artery AND disease* OR coronary AND stenos* OR coronary AND occlusion* OR coronary AND thrombosis* OR coronary AND vasospasm OR fibromuscular AND dysplasia
# 10	#1 or #2 or #3 or #7 or #8 or #9
# 11	#10 and #6
# 12	#11 RESTRICT YR 1998 2008
# 13	MeSH Mortality EXPLODE 1 2 3 4 5 or MeSH Death EXPLODE 1
# 14	mortalit* OR "death rate*" OR "cause of death*" OR "death cause*"

15 #13 or #14

16 #15 and #6

17 MeSH Alcohol Drinking QUALIFIERS MO EXPLODE 1

18 #16 or #17

19 #19 RESTRICT YR 1998 2009

20 #20 not #12

SveMed+
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Sökmängd	Sökvillkor
S1	*Explodesökning på Alcohol-Drinking*
S2	öl OR vin OR sprit OR sprut OR rödvin
S3	*Explodesökning på Mortality*
S4	*Explodesökning på Death*
S6	mortalit$ or death rate$ or cause of death$ or death cause$
S8	dödelighet or dödsfall or dödsårsak
S9	S1 OR S2
S10	S3 or S4 or S6 or S8
S11	S9 AND S10