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## Prospective study of alcohol drinking patterns and coronary heart disease in women and men

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### Abstract

**Objective** To determine the association between alcohol drinking patterns and risk of coronary heart disease in women and men.

**Design** Population based cohort study.

**Setting** Denmark, 1993-2002.

**Participants** 28 448 women and 25 052 men aged 50-65 years, who were free of cardiovascular disease at entry to the study.

**Main outcome measures** Incidence of coronary heart disease occurring during a median follow-up period of 5.7 years.

**Results** 749 and 1283 coronary heart disease events occurred among women and men. Women who drank alcohol on at least one day a week had a lower risk of coronary heart disease than women who drank alcohol on less than one day a week. Little difference was found, however, between drinking frequency: one day a week (hazard ratio 0.64, 95% confidence interval 0.51 to 0.81), 2-4 days a week (0.63, 0.52 to 0.77), five or six days a week (0.79, 0.61 to 1.03), and seven days a week (0.65, 0.51 to 0.84). For men an inverse association was found between drinking frequency and risk of coronary heart disease across the entire range of drinking frequencies. The lowest risk was observed among men who drank daily (0.59, 0.48 to 0.71) compared with men who drank alcohol on less than one day a week.

**Conclusions** Among women alcohol intake may be the primary determinant of the inverse association between drinking alcohol and risk of coronary heart disease whereas among men, drinking frequency, not alcohol intake, seems more important.

### Introduction

Prospective studies have reported a lower risk of coronary heart disease among consumers of moderate amounts of alcohol compared with abstainers.<sup>1</sup> A few studies have investigated this association by including measures of alcohol drinking patterns. Results consistently imply that the pattern of drinking is important and that steady drinking is more beneficial than drinking in binges.<sup>2-6</sup> In a recent study among men, drinking frequency was found to be the primary determinant of the inverse association between alcohol intake and coronary heart disease, and alcohol intake was of minor importance.<sup>6</sup> Data on the importance of drinking patterns among women are limited and results for men may not apply to women for various reasons.

We determined the association between alcohol drinking patterns and coronary heart disease among middle aged Danish men and women.

### Methods

From December 1993 to May 1997, 160 725 Danish men and women were invited to participate in the diet, cancer, and health study.<sup>7</sup> Eligible cohort members were born in Denmark and had no previous cancers. Overall, 27 178 men and 29 875 women agreed to participate (response rate 35%). A food frequency questionnaire was enclosed with the invitation.<sup>8,9</sup> This



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**Table 1** Hazard ratios (95% confidence intervals) of coronary heart disease according to drinking frequency among women and men

Variable	Frequency of drinking alcohol (days/week)						P for trend*
	Never	<1	1	2-4	5 or 6	7	
Women:							
No of cases	24	276	95	187	77	90	
Adjusted for age	1.01 (0.66 to 1.53)	1.00	0.60 (0.47 to 0.76)	0.56 (0.47 to 0.68)	0.69 (0.54 to 0.89)	0.62 (0.49 to 0.79)	0.0004
Adjusted for multiple factors†	0.92 (0.61 to 1.41)	1.00	0.64 (0.51 to 0.81)	0.63 (0.52 to 0.77)	0.79 (0.61 to 1.03)	0.65 (0.51 to 0.84)	0.007‡
Men:							
No of cases	39	180	140	424	195	305	
Adjusted for age	1.38 (0.98 to 1.95)	1.00	0.86 (0.69 to 1.07)	0.69 (0.58 to 0.83)	0.65 (0.53 to 0.79)	0.60 (0.50 to 0.73)	<0.0001
Adjusted for multiple factors†	1.44 (1.02 to 2.04)	1.00	0.93 (0.75 to 1.16)	0.78 (0.66 to 0.94)	0.71 (0.57 to 0.87)	0.59 (0.48 to 0.71)	<0.0001

\*Never drinkers not included in analyses for trend.

†Age, smoking, education, physical activity, body mass index, total intake of fruit, vegetables, fish, and saturated fat.

‡P for trend was 0.49 when women were excluded who never drink or drink on less than one day a week.

questionnaire was checked during a clinic visit, when another questionnaire on lifestyle and background factors was completed.

Alcohol intake was reported as the average amount over the preceding year. Total intake was converted into number of standard drinks, containing 12 g of ethanol. Drinking frequency was recorded in predefined categories (never, less than once a month, 1-3 times monthly, once a week, 2-4 times weekly, five or six times weekly, and daily). We defined abstainers as those who reported no alcohol intake and no drinking occasions. (See [bmj.com](http://bmj.com) for exclusions.)

#### Follow-up

We obtained information on coronary heart disease from the Danish Hospital Discharge Register and from the Danish Register of Causes of Death. The hospital register is updated to 2002, whereas the causes of death register, with information on fatal coronary heart disease events, is updated to 2000. We decided to end follow-up at January 2002, being aware that information on some fatal cases would be missed from January 2000 to January 2002.

Vital status of the participants came from the National Central Person Register. We excluded 2367 participants who were registered with any cardiovascular disease at baseline.

We observed participants from enrolment until date of coronary heart event (n=2113), death from other causes (n=1483), emigration (n=183), loss to

follow-up (n=3), or 1 January 2002, whichever came first.

#### Statistical analysis

We calculated risk estimates using Cox proportional hazard regression models. These estimates were adjusted for known risk factors for coronary heart disease: length of school education; smoking; physical activity during leisure time; body mass index; total intake of fruit, vegetables, and fish; and percentage of total energy intake from saturated fat (all as continuous variables). Using linear splines with knots set at quintiles of the covariate in question we evaluated the assumed linearity of quantitative risk factors.

To test for linear trends we treated the median value within categories continuously. We did not include abstainers when testing for trend because they may have different trait and health status than people who consume alcohol lightly to moderately.<sup>10</sup>

To examine the magnitude of rank correlation between drinking frequency and amount of alcohol, we calculated Spearman's correlation coefficient. We tested the interaction between sex and drinking frequency using a nested log likelihood test where we compared a model containing the variables as single terms with a model including the interaction terms.

To tackle the external validity of our results, we compared the observed with the expected number of cases, on the basis of age and calendar year specific incidence rates in the general Danish population.

**Table 2** Hazard ratios (95% confidence intervals) of coronary heart disease according to drinking frequency and amount of alcohol intake among women and men

Alcohol intake (drinks/week)	Frequency of drinking alcohol (days/week)				P for trend
	Never	≤1	2-4	5-7	
Women:					
0	1.03 (0.68 to 1.56) (n=24)	—	—	—	
1-6	—	1.00 (n=360)	0.78 (0.63 to 0.97) (n=114)	1.32 (0.84 to 2.07) (n=20)	0.57
7-13	—	0.67 (0.35 to 1.31) (n=9)	0.74 (0.57 to 0.96) (n=66)	0.82 (0.61 to 1.10) (n=52)	0.12
≥14	—	0.65 (0.16 to 2.61) (n=2)	0.27 (0.13 to 0.58) (n=7)	0.72 (0.57 to 0.92) (n=95)	0.01
P for trend	—	0.002	<0.0001	0.0003	—
Men:					
0	1.47 (1.05 to 2.06) (n=39)	—	—	—	
1-6	—	1.00 (n=278)	0.80 (0.65 to 0.98) (n=141)	0.70 (0.41 to 1.17) (n=15)	0.02
7-13	—	0.89 (0.62 to 1.29) (n=31)	0.81 (0.67 to 0.98) (n=190)	0.66 (0.52 to 0.83) (n=90)	0.0001
14-20	—	1.10 (0.54 to 2.23) (n=8)	0.91 (0.68 to 1.23) (n=52)	0.68 (0.54 to 0.87) (n=90)	0.001
≥21	—	1.00 (0.32 to 3.13) (n=3)	0.67 (0.48 to 0.93) (n=41)	0.63 (0.53 to 0.74) (n=305)	<0.0001
P for trend	—	0.25	0.22	<0.0001	—

Hazard ratios are adjusted for age, education, smoking, physical activity, body mass index, and total intake of vegetables, fruit, fish, and saturated fat. Number of cases in parentheses.

## Results

Overall, 28 448 women and 25 052 men were eligible for our study. Women consumed a median of 5.5 alcoholic drinks a week (fifth to 95th centiles, 0.3-24) and men 11.3 (1.1-47). Drinking frequency was highly correlated with amount of alcohol intake among both women and men ( $r=0.86$  and  $r=0.78$ ).

Infrequent drinkers (less than one day a week) and daily drinkers were more likely to be smokers, to have a lower intake of fruit and vegetables, and to be less educated than participants in the in between drinking frequencies (see [bmj.com](http://bmj.com)). Body mass index was inversely associated with drinking frequency and frequent drinkers had the lowest body mass index. These trends applied to both sexes. Generally, fewer women than men were current and heavy smokers (>25 g of tobacco daily) and women had more hours of physical activity a week and consumed more fruit and vegetables.

During a median 5.7 years (range 0.01-8.10) of follow-up 749 women and 1283 men developed coronary heart disease. Based on incidence rates from the general population the expected number of cases from this register was 716 women (737 observed) and 1217 men (1196 observed). The observed number did not differ significantly from the expected ( $P>0.10$ ).

Amount of alcohol intake was inversely associated with coronary heart disease among women and men (see [bmj.com](http://bmj.com)).

Among women, drinking on at least one day a week was associated with a lower risk of coronary heart disease than drinking more rarely (table 1). Hazard ratios were similar for drinking on one day a week (0.64, 95% confidence interval 0.51 to 0.81), 2-4 days a week (0.63, 0.52 to 0.77), five or six days a week (0.79, 0.61 to 1.03), and seven days a week (0.65, 0.51 to 0.84).

Among men, drinking frequency was inversely associated with risk of coronary heart disease over the whole range of drinking frequencies (table 1). Hazard ratios were 0.93 (0.75 to 1.16) for drinking on one day a week, 0.78 (0.66 to 0.94) for 2-4 days a week, 0.71 (0.57 to 0.87) for five or six days a week, and 0.59 (0.48 to 0.71) for seven days a week ( $P$  for trend  $<0.0001$ ). A statistically significant interaction was found between sex and drinking frequency on the risk of coronary heart disease ( $P=0.02$ ).

Within similar categories of drinking frequency, women drinking the largest amounts generally had the lowest risk (table 2). For men, hazard ratios were generally lowest for the most frequent intake within similar categories of amount (table 2). Within categories of drinking frequency, hazard ratios tended to be similar.

## Discussion

The frequency of drinking alcohol is inversely associated with risk of coronary heart disease among men, independent of alcohol intake. Among women, intake, not frequency, was inversely associated with coronary heart disease.

A limitation of our study is that only 35% of the invited people participated. People who choose to participate may have a different risk profile and be in better health than those who decline. However, the

### What is already known on this topic

Alcohol intake is inversely associated with risk of coronary heart disease

In men, for the same weekly amount of alcohol intake, frequent drinkers have a lower risk of coronary heart disease than less frequent drinkers

Little is known about drinking pattern and the risk of coronary heart disease among women

### What this study adds

Intake may be more important than frequency for the inverse association between alcohol drinking and risk of coronary heart disease among women

In men, frequency is more important than alcohol intake

observed incidence of coronary heart disease did not differ from that of the general population.

We cannot exclude the possibility that participants with early symptoms of coronary heart disease at baseline had reduced their drinking frequency, explaining the inverse association. This association persisted when we analysed early cases separately.

Some unhealthy traits such as smoking were common at both extremes of drinking frequency. For the most rare drinkers, the unhealthy lifestyle may be explained by the fact that they were the poorest educated, which probably correlates with low social status. Also this category may include former alcoholics. Together, results for the extremes of drinking frequency are more likely to be residually confounded than results for the in between drinking frequencies and should be interpreted with caution. However, at least among men, we found an inverse association between drinking frequency and coronary heart disease over the entire range of drinking frequencies.

Several explanations may account for a possible interaction between sex and drinking frequency. We cannot exclude that men who drink frequently are more likely to drink with meals, which may contribute to a greater risk reduction compared with men with a less frequent alcohol intake. It is unlikely that wine drinking, which may be more beneficial than drinking beer or spirits,<sup>11</sup> is responsible for our results because it has been shown that wine drinkers in this cohort drink less often than beer drinkers.<sup>12</sup> Differences in alcohol pharmacokinetics between sexes may be another explanation.<sup>13</sup>

The association between alcohol and coronary heart disease among women may be modified by menopausal status. Oestrogens have beneficial effects on the cardiovascular system, protecting women until menopause.<sup>14</sup> Moderate alcohol drinking is thought to increase oestrogen levels.<sup>15</sup> Few women in this study (17%) were premenopausal and our findings may be limited to postmenopausal women.

The inverse association between alcohol and coronary heart disease can be explained by several biologically plausible mechanisms, including dose dependent effects on high density lipoprotein levels, lower plasma

fibrinogen levels, and reduced platelet aggregation.<sup>16</sup> The question is if the balance between beneficial and harmful effects is affected by drinking pattern.

Heavy alcohol drinking is positively associated with many problems such as liver diseases, cancers, and road crashes, and overall mortality is higher among individuals with a high alcohol intake compared with light consumers. Also, the beneficial effect of alcohol is probably confined to middle aged or older people.<sup>17</sup> Therefore the inverse association between alcohol intake and coronary heart disease should be viewed in this context when giving public health advice.

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## Effective control of dengue vectors with curtains and water container covers treated with insecticide in Mexico and Venezuela: cluster randomised trials

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### Abstract

**Objectives** To measure the impact on the dengue vector population (*Aedes aegypti*) and disease transmission of window curtains and water container covers treated with insecticide.

**Design** Cluster randomised controlled trial based on entomological surveys and, for Trujillo only, serological survey. In addition, each site had a non-randomised external control.

**Setting** 18 urban sectors in Veracruz (Mexico) and 18 in Trujillo (Venezuela).

**Participants** 4743 inhabitants (1095 houses) in Veracruz and 5306 inhabitants (1122 houses) in Trujillo.

**Intervention** Sectors were paired according to entomological indices, and one sector in each pair was randomly allocated to receive treatment. In Veracruz, the intervention comprised curtains treated with lambda-cyhalothrin and water treatment with pyriproxyfen chips (an insect growth regulator). In Trujillo, the intervention comprised curtains treated

with longlasting deltamethrin (PermaNet) plus water jar covers of the same material. Follow-up surveys were conducted at intervals, with the final survey after 12 months in Veracruz and nine months in Trujillo.

**Main outcome measures** Reduction in entomological indices, specifically the Breteau and house indices.

**Results** In both study sites, indices at the end of the trial were significantly lower than those at baseline, though with no significant differences between control and intervention arms. The mean Breteau index dropped from 60% (intervention clusters) and 113% (control) to 7% (intervention) and 12% (control) in Veracruz and from 38% to 11% (intervention) and from 34% to 17% (control) in Trujillo. The pupae per person and container indices showed similar patterns. In contrast, in nearby communities not in the trial the entomological indices followed the rainfall pattern. The intervention reduced mosquito populations in

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