

Alcohol consumption and mortality from all causes, coronary heart disease, and stroke: results from a prospective cohort study of Scottish men with 21 years of follow up

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Abstract

Objectives To relate alcohol consumption to mortality.

Design Prospective cohort study.

Setting 27 workplaces in the west of Scotland.

Participants 5766 men aged 35-64 when screened in 1970-3 who answered questions on their usual weekly alcohol consumption.

Main outcome measures Mortality from all causes, coronary heart disease, stroke, and alcohol related causes over 21 years of follow up related to units of alcohol consumed per week.

Results Risk for all cause mortality was similar for non-drinkers and men drinking up to 14 units a week. Mortality risk then showed a graded association with alcohol consumption (relative rate compared with non-drinkers 1.34 (95% confidence interval 1.14 to 1.58) for 15-21 units a week, 1.49 (1.27 to 1.75) for 22-34 units, 1.74 (1.47 to 2.06) for 35 or more units). Adjustment for risk factors attenuated the increased relative risks, but they remained significantly above 1 for men drinking 22 or more units a week. There was no strong relation between alcohol consumption and mortality from coronary heart disease after adjustment. A strong positive relation was seen between alcohol consumption and risk of mortality from stroke, with men drinking 35 or more units having double the risk of non-drinkers, even after adjustment.

Conclusions The overall association between alcohol consumption and mortality is unfavourable for men drinking over 22 units a week, and there is no clear evidence of any protective effect for men drinking less than this.

Introduction

There have been numerous studies investigating the effects of alcohol consumption on mortality. The relation with all cause mortality is usually reported as U or J shaped, with moderate consumers having the lowest risk of mortality and high consumers the highest.¹⁻³ Non-drinkers are generally found to have a mortality between that of the moderate and high consumers. There may be problems with selection bias related to health in these studies, however, as sick people may not drink because of their illness, leading to an apparent increased risk of mortality among non-drinkers.

Moderate consumption of alcohol may protect against coronary heart disease, but whether this is true for all types of alcohol or just for wine is unclear.^{4,7} Risk of mortality from stroke has shown variable associations with alcohol consumption.

We have performed a 21 year follow up study of working men who reported their alcohol consumption, with detailed information on risk factors which might act as confounders, including socioeconomic variables, which have generally not been adequately controlled for in previous studies.^{4,8}

Methods

The analysis was based on a cohort of 5766 employed men recruited from various workplaces in Glasgow, Clydebank, and Grangemouth in Scotland between 1970 and 1973 when they were aged 35-64 years. Full details of the study have been reported elsewhere.⁹ A questionnaire was completed by each participant, followed by a screening examination. Weekly reported alcohol consumption was categorised by spirits, beer, and wine. This was converted to units of alcohol by taking one measure of spirits as 1 unit, 1 pint (about 1/2 litre) of beer as 2 units, and one bottle of wine as 6 units. Six categories of alcohol consumption were formed (none, 1-7, 8-14, 15-21, 22-34, and 35 or more units of alcohol a week). Social class was coded according to the registrar general's classification¹⁰ from the participant's father's and the participant's own occupations. Social class was defined as either non-manual or manual. Bronchitis was defined as persistent and infective phlegm and breathlessness.¹¹ Angina was considered present if the definite criteria of the Rose angina questionnaire were met.^{12,13} The adjusted forced expiratory volume in 1 second (FEV₁) was defined as the actual volume as a percentage of the expected volume.^{14,15} Ischaemia on electrocardiogram was coded according to the Minnesota system.^{16,17} Deprivation category was ascertained from the postcode of the home address at time of screening.¹⁸ In 1977 about half of the cohort (2686) returned for a repeat screening.

Deaths occurring in 21 years of follow up were identified by flagging at the NHS central register in Edinburgh. Causes of death were defined as coronary heart disease (ICD-9 (international classification of diseases, 9th revision) codes 410-414), stroke (ICD-9 codes 430-438), and alcohol related causes (ICD-9 codes 141, 143-6, 148-9, 150, 155, 161, 291, 303, 571, and 800-999).¹⁹ Insufficient information was available to classify the types of stroke.

Cox's proportional hazards models²⁰ were used to estimate proportional hazards coefficients (PHREG in SAS).²¹ Diastolic blood pressure was not initially treated as a confounder because higher alcohol consumption leads to higher blood pressure and blood pressure may mediate the relation between alcohol and mortality.²²⁻²⁴ Tests for evidence of a quadratic trend were carried out by including units per week squared as a continuous variable. Means of continuous

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Table 1 Age adjusted means and age adjusted proportions (%) of characteristics by units of alcohol consumed a week

Characteristic	None	1-7	8-14	15-21	22-34	≥35	P value for difference*	P value for trend†
No (%) of men	1833 (31.8)	1116 (19.4)	1061 (18.4)	628 (10.9)	625 (10.8)	503 (8.7)		
Age (years)	49.0	48.0	47.9	48.0	47.7	47.6	0.0001	0.26
No (%) with manual occupation	768 (41.4)	379 (34.4)	539 (51.1)	388 (62.2)	414 (66.30)	364 (72.1)	0.0001	0.0001
No (%) with fathers with manual occupation	1346 (74.8)	748 (68.4)	764 (73.1)	492 (80.3)	511 (83.2)	422 (85.1)	0.44	0.0001
No of siblings	3.2	3.0	3.5	3.7	3.9	4.3	0.0001	0.0001
No (%) who left education aged ≤14 years	901 (47.7)	419 (37.9)	517 (49.3)	385 (61.9)	397 (64.4)	318 (64.7)	0.07	0.0001
No (%) in deprivation category 6 and 7	452 (24.2)	219 (19.8)	296 (28.1)	218 (34.8)	240 (38.7)	222 (43.7)	0.0001	0.0001
No (%) of car users	991 (54.6)	716 (64.1)	587 (54.7)	288 (45.6)	257 (40.4)	149 (29.5)	0.020	0.0001
Cholesterol (mmol/l)	5.85	5.94	5.94	5.81	5.83	5.88	0.28	0.13
Systolic blood pressure (mm Hg)	133.1	131.4	133.6	135.4	135.1	140.2	0.37	0.0001
Diastolic blood pressure (mm Hg)	83.4	82.7	83.5	84.5	84.5	87.3	0.11	0.0001
Body mass index (kg/m ²)	25.2	25.0	25.1	25.1	25.3	25.5	0.32	0.0001
Triglycerides‡ (mmol/l)	1.31	1.30	1.39	1.47	1.39	1.56	0.0001	0.0001
No (%) who never smoked	490 (27.5)	193 (16.9)	169 (15.6)	50 (7.9)	59 (9.2)	55 (10.8)	0.0001	0.0001
NO (%) of current cigarette smokers	834 (45.3)	569 (51.2)	622 (58.7)	417 (66.4)	423 (67.3)	332 (65.7)	0.0001	0.0001
No of cigarettes/day§	18.0	18.5	18.6	19.6	19.4	21.4	0.0001	0.0001
No (%) with angina	115 (6.0)	64 (5.9)	53 (5.1)	48 (7.7)	45 (7.0)	33 (6.7)	0.89	0.07
No (%) with ischaemia on ECG	106 (5.5)	70 (6.3)	52 (5.0)	46 (7.4)	28 (4.6)	32 (6.4)	0.98	0.39
No (%) with bronchitis	28 (1.4)	14 (1.3)	24 (2.4)	17 (2.7)	14 (2.2)	30 (6.0)	0.017	0.0001
Adjusted FEV ₁ (%¶)	95.9	96.2	93.8	92.2	92.3	90.0	0.0001	0.0001

* Test for difference for any drinking versus none; *t* test for continuous variables, χ^2 test for discrete variables.

† Test for trend within any units of alcohol groups with continuous variable.

‡ For 5300 who fasted and were not diabetic.

§ For current smokers only.

¶ Forced expiratory volume in 1 second (%).

variables were standardised for age with PROC GLM. Proportions of categorical variables were age standardised by the direct method, with the study population as the standard. Measures of correlation (Pearson's correlation coefficient and Cronbach's coefficient α) between the initial and repeat screenings were calculated with PROC CORR.

Results

Table 1 shows that 32% of men (1833) said that they did not usually drink alcohol. This category headed "none" consists of lifetime abstainers, occasional drinkers, former drinkers, and possibly men not admitting to drinking alcohol. The non-drinkers were older, less likely to be in manual occupations or live in deprived areas, had fewer siblings, and were more likely to be car users than drinkers. There were fewer cigarette smokers among non-drinkers and the smokers used fewer cigarettes a day. Non-drinkers had lower concentrations of triglycerides, less bronchitis, and better lung function than drinkers.

Among men who consumed alcohol, higher intake was associated with worse social circumstances. Alcohol consumption showed graded associations with blood pressure, body mass index, triglyceride concentrations, bronchitis, poor lung function, proportion of smokers, and amount smoked.

Follow up

Pearson's correlation coefficient and Cronbach's α were calculated for the reported alcohol consumption of the 2686 men who were screened twice, giving 0.78 and 0.88, respectively, which suggests reliable reporting and stable consumption.

In the 21 years there were 1643 deaths, including 625 from coronary heart disease, 133 from stroke, and 108 from alcohol related causes. Men who drank over

15 units of alcohol a week had significantly higher risks of dying from all causes than the non-drinkers (table 2). Those drinking over 35 units a week had a considerably increased risk. Adjustment for other variables attenuated the risks. For the two highest categories, risks remained significantly different from those in the non-drinkers.

There was a significant overall positive association between mortality from coronary heart disease and alcohol consumption. Compared with the non-drinkers, however, there was a lower risk of mortality for the category 8-14 units a week, although this was not significant. Significantly higher rates were seen for the 15-21 category and the ≥ 35 category. Adjustment for other variables essentially removed the gradient between alcohol consumption and coronary mortality.

There was a highly significant increasing trend across the drinking categories for mortality from stroke. Drinkers of more than 15 units a week had significantly higher risks than non-drinkers. Those drinking 35 or more units had over double the risk. Adjustment for other variables reduced the risks but the trend remained. There was a strong association between mortality from alcohol related diseases and drinking. Drinkers in the heaviest category were three times more likely to die of these causes than non-drinkers.

Tests for evidence of quadratic associations found significant quadratic effects for all cause ($P=0.011$) and alcohol related mortality ($P=0.007$) when we adjusted for age. When adjustments were made for the other risk factors, the quadratic term was not significant for all cause mortality ($P=0.2$), although there were significant quadratic effects for alcohol related mortality ($P=0.021$). There were no significant quadratic effects for mortality from coronary heart disease or stroke.

Table 2 Relative rates of mortality over 21 years by units of alcohol consumed a week. Figures are relative risks (95% confidence interval) adjusted for various factors

Mortality and adjustment for relative risk	None	1-7	8-14	15-21	22-34	≥35	P value for any drinking v none*	P value for trend consumption†
All cause								
No of deaths	498	281	267	199	212	186		
Adjustment A	1	1.00 (0.87 to 1.16)	1.02 (0.88 to 1.18)	1.34 (1.14 to 1.58)	1.49 (1.27 to 1.75)	1.74 (1.47 to 2.06)	0.0003	0.0001
Adjustment B	1	1.03 (0.89 to 1.19)	0.95 (0.81 to 1.10)	1.12 (0.95 to 1.32)	1.24 (1.05 to 1.46)	1.33 (1.12 to 1.59)	0.12	0.0006
Adjustment C	1	1.03 (0.89 to 1.20)	0.93 (0.80 to 1.08)	1.10 (0.93 to 1.29)	1.22 (1.03 to 1.44)	1.25 (1.05 to 1.50)	0.22	0.006
Coronary heart disease								
No of deaths	198	122	91	79	72	63		
Adjustment A	1	1.09 (0.87 to 1.37)	0.87 (0.68 to 1.11)	1.33 (1.02 to 1.72)	1.26 (0.96 to 1.65)	1.46 (1.10 to 1.94)	0.15	0.010
Adjustment B	1	1.13 (0.90 to 1.42)	0.81 (0.63 to 1.05)	1.09 (0.83 to 1.42)	1.04 (0.79 to 1.37)	1.08 (0.80 to 1.45)	0.86	0.99
Adjustment C	1	1.13 (0.90 to 1.42)	0.79 (0.61 to 1.01)	1.06 (0.81 to 1.38)	1.01 (0.77 to 1.34)	1.00 (0.75 to 1.35)	0.91	0.69
Stroke								
No of deaths	38	20	21	19	18	17		
Adjustment A	1	0.98 (0.57 to 1.69)	1.13 (0.66 to 1.92)	1.80 (1.04 to 3.12)	1.81 (1.03 to 3.17)	2.33 (1.31 to 4.14)	0.07	0.0005
Adjustment B	1	0.98 (0.57 to 1.69)	1.08 (0.63 to 1.85)	1.53 (0.87 to 2.68)	1.59 (0.89 to 2.82)	1.98 (1.09 to 3.59)	0.19	0.006
Adjustment C	1	0.96 (0.55 to 1.65)	1.02 (0.59 to 1.75)	1.46 (0.84 to 2.57)	1.56 (0.88 to 2.79)	1.67 (0.91 to 3.06)	0.31	0.013
Alcohol related causes								
No of deaths	21	14	17	17	21	18		
Adjustment A	1	1.15 (0.58 to 2.26)	1.47 (0.78 to 2.80)	2.60 (1.37 to 4.93)	3.31 (1.81 to 6.07)	3.72 (1.98 to 7.00)	0.003	0.0001
Adjustment B	1	1.20 (0.61 to 2.37)	1.39 (0.73 to 2.64)	2.25 (1.18 to 4.31)	2.78 (1.49 to 5.17)	2.94 (1.52 to 5.68)	0.012	0.013

*With PROC PHREG with alcohol as categorical variable.

†With PROC PHREG with units per week as continuous variable.

A=adjusted for age.

B=adjusted for age, smoking, cholesterol, body mass index, adjusted FEV₁, social class (six social classes), father's social class (six social classes), education, car use, siblings, deprivation category, angina, ischaemia on electrocardiogram, and bronchitis.C=adjusted for age, smoking, cholesterol, body mass index, adjusted FEV₁, social class (six social classes), father's social class (six social classes), education, car use, siblings, deprivation category, angina, ischaemia on electrocardiogram, bronchitis, and diastolic blood pressure.

Discussion

We have shown that in this cohort there was no robust relation between consumption of alcohol and mortality from coronary heart disease, but there was a strong positive relation between consumption and mortality from stroke. Unlike other studies^{1-3 25 26} we found no strong evidence that alcohol consumption reduced all cause mortality for light and moderate drinkers. While there was a suggestion of a J shaped relation because of the slightly lower risk of mortality for men drinking 8-14 units, this was a small effect and not reflected in the risk in those who drank 1-7 units, who also fall into the "moderate drinking" category. Our study population of working men would exclude men unable to work because of ill health. Shaper has suggested that the higher risk of mortality seen in non-drinkers is caused in part by the inclusion of men with existing disease, who may have been former drinkers, into the categories of non-drinkers.²⁷ Our non-drinking category probably contained fewer men who had stopped drinking because of ill health than in general population studies and this may be why the U or J shaped relations were not evident.

Coronary heart disease mortality

Numerous studies of the relation between mortality from coronary heart disease and alcohol consumption exist, with many finding a reduction in such mortality with moderate consumption.^{1 5 6 28 29} The current study showed a non-significant lower risk of mortality from coronary heart disease for one moderate alcohol consumption group, but again the findings were inconsistent. The increased risks for drinkers of 15 units or more were attenuated by adjustments for risk factors, which shows the importance of potential confounding factors. Additional adjustment for diastolic blood pres-

sure reduced the risks further, particularly among those in the heaviest drinking category, indicating that excessive alcohol consumption may have a detrimental effect on risk of mortality from coronary heart disease through increased blood pressure.

Stroke mortality

Studies on the relation between alcohol consumption and mortality from stroke have produced contradictory findings, perhaps because the relations are different for haemorrhagic and ischaemic stroke. The risk of haemorrhagic stroke is thought to increase with alcohol consumption,^{30 31} whereas some studies have found a reduced risk of ischaemic stroke for moderate drinkers³² and either an increased risk^{31 32} or no effect³⁰ for heavy drinkers. As about 85% of strokes in adults in Great Britain are due to cerebral thrombosis and infarction most deaths from stroke in the current study are likely to have been ischaemic.^{23 33}

Studies in China,⁶ the United Kingdom,¹ and Japan³¹ have found increased risk of mortality from stroke with amount of alcohol consumed. J shaped relations have also been found.^{31 34} Conversely, the cancer prevention II study found the highest risk of mortality from stroke in non-drinkers, with a flat relation with increasing amounts of alcohol consumed.²⁹ Another study found non-drinkers to have a higher risk of stroke, but this disappeared after adjustment for obesity and exercise.³⁵ A study of fatal and non-fatal stroke found a non-significant increased risk in lifetime abstainers compared with occasional drinkers and an increased risk of stroke for the heaviest category of drinkers.²³ The current study shows a clear gradient of stroke mortality and consumption of alcohol, with a twofold risk in men in the highest drinking category. Raised blood pressure as a consequence of

drinking seems to account for much, but not all, of this association. Measurement error with respect to blood pressure may account for the residual association after adjustments for blood pressure.³⁶

Reliability of data

Questions on alcohol consumption may not be answered accurately. In this study nearly a third of the men were classified as non-drinkers. This figure was high compared with that from the Scottish heart health study, which reported 19% non-drinkers,³⁷ but similar to that in a study of Scottish drinking habits carried out in 1972, which reported 21% of men aged 41-50 years and 35% of men aged 51-65 years as non-drinkers or occasional drinkers.³⁸ Similar results were reported by the British regional heart study (2.8% non-drinkers, 6.9% former drinkers, and 29.7% occasional drinkers, totalling 39%).²³ This is comparable with the proportion of non-drinkers in our study. The lowest risk for alcohol related causes of death for men in the non-drinking category and the increased risk with amount of alcohol consumed suggests that the answers to the questionnaire are valid. Additional evidence is given by the graded association of reported alcohol consumption with blood pressure and triglyceride concentrations, which are clearly related to alcohol intake,^{22,39,40} and the high correlations between the answers to the first and second questionnaires. Given this evidence of validity of the reported alcohol data it is unlikely that our findings are due to misclassification of alcohol consumption. Therefore it is important to consider reasons for discrepancies between our results and those of some previous studies.

Differences between studies

Firstly, the inclusion of men with illnesses that lead them to be non-drinkers, and of former heavy drinkers among the non-drinking category, may be of less importance in this occupational cohort than in community based studies. Here there is an analogy with studies of the association between cholesterol concentration and mortality, where the U shaped associations are strongest in community based studies, which include individuals with low cholesterol concentrations because of illness, and weakest in healthy populations.^{41,42} Secondly, we adjusted for socioeconomic factors and other potential confounders more completely than previous studies. As socioeconomic position in early life has an important influence on mortality from cardiovascular disease,⁴³ independent of adulthood socioeconomic position, there may be important confounding by childhood social position. In this study more favourable childhood and adulthood socioeconomic profiles were seen in the low to moderate drinkers compared with the non-drinkers or heavy drinkers. Thus considerable confounding by socioeconomic position, largely uncontrolled for in previous studies, could exist. Thirdly, recent studies have suggested that binge drinking is associated with increased cardiovascular and all cause mortality.⁴⁴⁻⁴⁶ Sources suggest a more concentrated pattern of drinking in Scotland and Northern Ireland than in England and that in Britain generally drinking to intoxication periodically is more common than drinking large amounts habitually.⁴⁷ The 1972 study of Scottish drinking habits found that men who consumed 21-50 units

Key messages

- Results from a large cohort study of employed Scottish men showed different relations between alcohol consumption and mortality than previous studies
- There was no relation between mortality from coronary heart disease and alcohol consumption once adjustments were made for potential confounding factors
- There was a strong relation with mortality from stroke; drinkers of over 35 units a week had double the risk of mortality compared with non-drinkers
- Some but not all of this could be accounted for by alcohol related increases in blood pressure
- Overall, risk of all cause mortality was higher in men drinking 22 or more units a week

a week on average drank on 4 days a week, suggesting binge drinking was occurring.³⁸ Alcohol consumption may show direct associations with mortality among cohorts in which a substantial proportion of drinking consists of irregular high intake. It would thus be expected that among cohorts for whom this may not be true^{1,29} no such associations would be seen, but in cohorts in which binge drinking is relatively common (such as the current cohort) such associations would be evident.⁴⁴ This hypothesis should be tested in cohorts with detailed data on drinking patterns.

Conclusion

To conclude, we have shown that in this cohort of Scottish men there is no clear relation between alcohol consumption and mortality from coronary heart disease, but there is a strong relation with risk of mortality from stroke. The overall association between alcohol consumption and mortality is unfavourable for men drinking over 22 units a week and does not support the promotion of increased drinking for reasons of health.

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A salutary lesson Three very unwise men

Three men sharing accommodation decided to make a fresh vegetable salad, and the oldest convinced his junior flatmates that a plant growing in the back garden was Russian comfrey. Having made the salad the senior member ate three mouthfuls of the salad and then desisted because of the disagreeable taste. The second ate only one mouthful, and the junior member ate little at all because of the unpleasant taste. The two senior members started to feel ill within six hours and at this point the ringleader revised his opinion about the Russian comfrey and decided it was foxglove (*Digitalis purpurea*).

Help was sought at the accident and emergency department, where they were examined and found to be well enough to go home. However, the two men were admitted to hospital the next day, both complaining of nausea, vomiting, and irregular slow heart rates. The junior member was admitted a little later on the same day with gross anxiety and similar but less marked symptoms.

The senior diner, who had ingested the most comfrey/foxglove, had a complicated electrocardiogram featuring a high grade atrioventricular block, runs of idionodal tachycardia, and an accelerated idionodal rhythm. There was also some aberrant conduction (right bundle branch block pattern) and atrioventricular nodal escape beats. Digitalis effect was also noted.

The middle member of the group had an electrocardiogram which showed first degree and second degree sinoatrial block with occasional atrioventricular nodal escape beats and changes compatible with digitalis effect. The junior member of the group had a normal electrocardiogram with sinus bradycardia (rate 46). None of these three men were on prescribed medication at the time of their admission. All three were shown to have modest (low therapeutic range) serum digoxin concentrations; the other presumed metabolites of digitalis were unable to be measured.

The two older patients were monitored and treated with forced diuresis, potassium supplementation, and frusemide. Atropine and phenytoin were considered but not used. When their symptoms persisted they were treated by peritoneal dialysis. Both recovered slowly over the next few days, probably due to the natural excretion of the digitalis metabolites rather than the specific treatments given. The junior member of the flat required no treatment and recovered spontaneously. These three very unwise but adventurous gourmets spent 12, nine, and six days respectively in hospital, and each went home better informed about the difference between foxglove and Russian comfrey.

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