Mortality in relation to alcohol consumption: a prospective study among male British doctors

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Background	To relate alcohol consumption patterns to mortality in an elderly population.
Methods	We undertook a 23-year prospective study of 12 000 male British doctors aged 48–78 years in 1978, involving 7000 deaths. Questionnaires about drinking and smoking were completed in 1978 and once again in 1989–91. Mortality analyses are standardized for age, follow-up duration, and smoking, and (during the last decade of the study, 1991–2001) subdivide non-drinkers into never-drinkers and ex-drinkers.
Results	In this elderly population, with mean alcohol consumption per drinker of 2 to 3 units per day, the causes of death that are already known to be augmentable by alcohol accounted for only 5% of the deaths (1% liver disease, 2% cancer of the mouth, pharynx, larynx, or oesophagus, and 2% external causes of death) and were significantly elevated only among men consuming >2 units/day. Vascular disease and respiratory disease accounted for more than half of all the deaths and were both significantly less common among current than among non-drinkers; hence, overall mortality was also significantly lower (*relative risk, RR* 0.81, CI 0.76–0.87, *P* = 0.001). The non-drinkers, however, include the ex-drinkers, some of whom may have stopped recently because of illness, and during the last decade of the study (1991–2001) overall mortality was significantly higher in the few ex-drinkers who had been current drinkers in 1978 than in the never-drinkers or current drinkers. To avoid bias, these 239 ex-drinkers were considered together with the 6271 current drinkers and compared with the 750 men who had been non-drinkers in both questionnaires. Even so, ischaemic heart disease (RR 0.72, CI 0.58–0.88, *P* = 0.002), respiratory disease (RR 0.69, CI 0.52–0.92, *P* = 0.01), and all-cause (RR 0.88, CI 0.79–0.98, *P* = 0.02) mortality were significantly lower than in the non-drinkers.
Conclusions	Although some of the apparently protective effect of alcohol against disease is artefactual, some of it is real.

Much has been learnt in the last 30 years about the effects on mortality of drinking alcohol. These effects can be benefits as well as harm,[1,2] including, in certain circumstances, a reduction in some types of vascular disease. Alcohol can substantially augment the incidence of certain chronic diseases (cirrhosis and cancers of the liver, mouth, pharynx, larynx, and oesophagus), and it can increase mortality from external causes (accident, suicide, and homicide). In some populations these

'alcohol-augmentable' causes account for an appreciable fraction of all mortality, particularly in early adult life; in addition, severe intoxication can cause sudden death. There remains, however, some uncertainty about the effects of more moderate alcohol consumption on vascular and other diseases, and about its effects on total mortality, particularly in later middle age and in old age. One source of uncertainty has been the paucity of deaths in some of the prospective studies; another has been variation in the definition of 'non-drinker', which in some studies has included ex-drinkers and in others has excluded them (in part or in whole). In this article we report the findings from a 23-year prospective study of elderly men that

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recorded 7364 deaths; in the last 10 years of the study, non-drinkers were divided into ex-drinkers and never-drinkers.

Methods

Subjects

Of 34 000 male British doctors who had responded in 1951 to a questionnaire about their smoking habits, those born in or after 1900 were sent a further questionnaire in 1978 (when they were 48–78 years of age) that included questions about their drinking habits. They were asked to categorize themselves as 'never or almost never' taking alcohol, as taking alcohol 'occasionally' (that is, less than weekly), or as taking it 'regularly' (that is, in most weeks); if 'regularly', they were asked how much they customarily drank per week. In the hope of avoiding misleading answers, those who did not wish to say how much they drank were asked to say 'occasionally', but subsequent information indicated that few regular drinkers actually availed themselves of this option. Hence, those who described themselves as 'occasional' drinkers can be considered as such. Non-drinkers were not asked in 1978 whether they had drunk in the past.

In a third questionnaire sent out 11 years later (i.e., in 1989, with subsequent reminders over the next 2 years to the diminishing numbers of non-responders), those who had previously described themselves as non-drinkers were asked if they had at any time in the past drunk 'at least as often as most weeks' and, if so, when they had started and stopped and how much they used to drink when they drank most. It was consequently possible to categorize them either as never–drinkers (defined as never having drunk as often as in most weeks) or as ex-drinkers in the analyses of mortality during the last 10 years of the study (i.e., after October 1991). Those men who had in 1978 described themselves as occasional or regular drinkers were asked the same questions in the 1989 questionnaire as in the 1978 questionnaire. The high response rates and the close relationship between the replies to these two questionnaires (more than ten years apart) have been described previously:[2] briefly, for the 8190 men who answered both questionnaires and survived to November 1991, the mean consumption per drinker fell from 2.7 to 2.4 units/day, and the minority who reported consuming more than 4 units/day in either questionnaire (mean: 6 units/day) reported, on average, consuming somewhat less (only 4 or 5 units/day) in the other questionnaire, but otherwise the replies to the two questionnaires were quite consistent.

Follow-up

This article first analyses mortality in the whole 23-year period (November 1978–October 2001), relating each individual's death to the last recorded drinking habit (which was in 1978 for mortality during 1978–1991 and in 1989–91 for mortality during 1991–2001). It then examines separately mortality during the last 10-year period, as only in this period could ex-drinkers be separated from never-drinkers. Altogether, 12 325 men (4 more than reported previously[2]) completed the first questionnaire and were still alive in November 1978. Of this total, 3856 (31%) died during the first period (10 more than previously known to have done so, as all have now been traced), 279 (2%) were known to be alive but were withdrawn from the study at the end of the first period (56 at their own

request, 215 because they did not complete the second questionnaire, and 8 because they were lost to follow-up during the second period), 3508 (28%) died during the second period, and the remaining 4682 (38%) are known from personal contact to have been alive in November 2001.[3]

Statistical methods

Some analyses are of the entire 23 years of the study (periods 1 and 2: November 1978–October 1991 and November 1991–October 2001, respectively), whereas others are of just period 2. In both cases relative risks (RRs) are calculated by Cox regression, standardized for age and smoking as described previously.[2] The 'floated' variance, V, of each log RR is calculated using the methods of the Prospective Studies Collaboration[4] (and the standard error of that RR is then estimated to be $RR\sqrt{V}$). These variances are used to make the statistical comparisons among the log RR values in different alcohol categories. Finally, all these relative risks and their standard errors are multiplied by a common factor to yield standardized death rates ('floating absolute risks'[4,5]) and their standard errors. Both for the analyses of the whole study and for the analyses of just period 2, the multiplying factor is chosen so that a weighted average of the standardized death rates (with weights proportional to the number of deaths in each category divided by the RR) equals the crude death rate per 1000 man-years during the 23-year period of the study as a whole. Numerically, the rates yielded by this procedure are approximately equivalent to death rates at ages 70–74 years. This procedure means that the standardized death rates in period 2 must, on average, be the same as those in the study as a whole, even though the age-specific death rates in this population were falling, like those of the general UK population. Thus, the death rates are standardized not only for age but also for time period.

When just two categories of alcohol consumption are being compared, a relative risk (with 95% confidence interval and two-sided P-value) is given. When non-drinkers are compared with more than one category of current drinker then because any effects of mortality may not be simply proportional to the weekly amount consumed, the statistical test of the dose–response relationship involves two degrees of freedom χ_2^2. This is calculated using quadratic regression (weighted by the inverse of the floated variance) of the log death rate on the mean self-reported weekly alcohol consumption (which is zero for non-drinkers) in each category.

Results

Our findings for mortality among current drinkers, occasional drinkers, and non-drinkers (ex-drinkers and never-drinkers combined) for the whole 23-year period, standardized for age and smoking status, are shown in Tables 1 and 2. Rates are given for six categories of causes of death and for all causes combined, including only in the latter the 98 deaths (1.3%) with unknown cause. The first category involves the alcohol-augmentable causes which, from other studies, are known to be made more probable by heavy alcohol consumption (accident, violence, alcoholic psychosis, upper aerodigestive cancer, and liver disease). Perhaps because the mean consumption per current drinker in this study was only 2 to 3 units of alcohol per day, these alcohol-augmentable causes constituted only 5% of the

Table 1 Annual mortality rate during 1978–2001, by cause and drinking habit when last asked

Cause of death (and ICD 9 categories)	Age-standardized rate per 1000 men ± standard error (and numbers of deaths)			Relative risk, current drinkers vs non-drinkers (and 95% CI)	*P*-value
	Non-drinkers (ex or never)	Occasional drinkers	Current drinkers		
Alcohol-augmentable causes[a]	1.4 ± 0.3 (28)	1.6 ± 0.3 (37)	1.9 ± 0.1 (295)	1.35 (0.91–2.00)	0.14
Ischaemic heart disease (410–414)	13.7 ± 0.8 (324)	11.8 ± 0.7 (294)	9.8 ± 0.3 (1495)	0.71 (0.63–0.81)	<0.0001
Other vascular disease (other 390–459)	8.7 ± 0.6 (220)	7.1 ± 0.5 (181)	7.2 ± 0.2 (1085)	0.83 (0.71–0.96)	0.02
Cancer (other[b] 140–239)	9.6 ± 0.7 (217)	9.2 ± 0.6 (222)	8.8 ± 0.3 (1368)	0.92 (0.80–1.07)	0.26
Respiratory disease (460–519)	4.2 ± 0.4 (107)	3.7 ± 0.4 (91)	3.3 ± 0.2 (504)	0.78 (0.63–0.97)	0.03
Other known medical (other 001–796)	5.2 ± 0.4 (137)	4.1 ± 0.4 (105)	3.7 ± 0.2 (556)	0.72 (0.59–0.87)	0.001
All causes[c]	43.5 ± 1.4 (1043)	37.9 ± 1.2 (939)	35.2 ± 0.5 (5382)	0.81 (0.76–0.87)	0.001
Number of men, 1978[d]	1245	1584	9496		

[a] Causes known from other studies to be augmentable by heavy drinking: suicide, homicide, accident, or other external cause 167 deaths; alcoholic psychosis 1; cirrhosis 41; cancers of the mouth (excluding lips and salivary gland) 12, pharynx (excluding nasopharynx) 14, oesophagus 75, larynx 13, and liver 37. (ICD 9 categories 141, 143–146, 148–150, 155, 161, 291–303 and 800–999.)

[b] Other than the alcohol-augmentable types of cancer listed above.

[c] Includes 98 deaths with unknown cause.

[d] Numbers of men in 1991 are shown in Table 3.

The mortality in period 1 (1978–91) is related to the 1978 habits, and that in period 2 (1991–2001) is related to the habits reported in 1989–91.

Table 2 Annual mortality rate during 1978–2001, by cause and weekly alcohol consumption when last asked

Cause of death (as in Table 1)	Age-standardized rate per 1000 men ± standard error (and numbers of deaths)					Statistical test[a] (χ^2_2) *P*-value
	Non-drinkers (ex- or never-)	Current drinkers, by units per week (and 1978 means)				
		1–7 (4.6)	8–14 (11.3)	15–28 (21.2)	29+ (46.0)	
Alcohol-augmentable causes	1.4 ± 0.3 (28)	1.3 ± 0.2 (45)	1.6 ± 0.2 (64)	2.0 ± 0.2 (94)	2.8 ± 0.3 (92)	26.3 <0.0001
Ischaemic heart disease	13.7 ± 0.8 (324)	10.4 ± 0.5 (392)	9.5 ± 0.5 (386)	9.0 ± 0.4 (404)	10.4 ± 0.6 (313)	30.6 <0.0001
Other vascular disease	8.7 ± 0.6 (220)	7.1 ± 0.4 (270)	6.6 ± 0.4 (260)	6.9 ± 0.4 (299)	8.8 ± 0.6 (256)	15.6 0.0004
Cancer (other[b])	9.6 ± 0.7 (217)	8.3 ± 0.5 (317)	8.1 ± 0.4 (327)	9.5 ± 0.5 (428)	9.7 ± 0.6 (296)	2.9 0.23
Respiratory disease	4.2 ± 0.4 (107)	3.0 ± 0.3 (118)	2.9 ± 0.3 (114)	3.3 ± 0.3 (143)	4.4 ± 0.4 (129)	11.0 0.004
Other known medical	5.2 ± 0.4 (137)	3.7 ± 0.3 (145)	3.7 ± 0.3 (144)	3.7 ± 0.3 (156)	4.0 ± 0.4 (111)	7.2 0.03
All causes[c]	43.5 ± 1.4 (1043)	34.4 ± 0.9 (1310)	32.8 ± 0.9 (1314)	34.8 ± 0.9 (1547)	40.4 ± 1.2 (1211)	42.5 <0.0001
Number of men, 1978	1245	2130	2595	2794	1977	

[a] The statistical test is on two degrees of freedom, as the effect on the death rate may not be directly proportional to the tabulated mean alcohol intake (zero, for non-drinkers). The mean intake in each category of response was similar in both the 1978 and the 1989 questionnaires.

[b] Other than the alcohol-augmentable types of cancer.

[c] Includes 89 deaths with unknown cause.

deaths (1% liver disease, 2% upper aerodigestive cancer, 2% external causes) and were in aggregate only slightly, and not significantly, more common among current drinkers than among non-drinkers (Table 1), although there was a highly significant dose–response relationship (Table 2). For each of the other five groups of causes of death, and for the aggregate of all causes of death, the mortality rates were higher in non-drinkers than in current drinkers (Table 1), although for some conditions the rates in those drinking 29 or more units a week (mean = 46) matched those in the non-drinkers. The higher mortality in non-drinkers than in current drinkers is not significant for

cancer, but it is significant for the other four categories of cause and for the aggregate of all causes of death. When the amount drunk is taken into account (Table 2) there is a direct relationship of increasing risk with increasing dose only for the alcohol-augmentable causes of death, although the increase is significant only for those who reported drinking an average of more than 2 units of alcohol a day (14 per week). For the other causes of death, and for the aggregate of all causes, the dose–response relationships appear in general to be U-shaped, with higher risks for non-drinkers and for those reporting an average of more than 4 units a day (28 per week)

than for those reporting intermediate levels of consumption. For cancer the dose–response relationship is not significant, but for vascular disease, respiratory disease, and all-cause mortality it is highly significant.

In the foregoing analyses mortality was related to the more recent report of drinking habits, which, for period 2 of follow-up (1991–2001), was the 1989–91 questionnaire. If, instead, mortality for both periods is related only to the habits reported in 1978, then the ratio of the overall death rate among non-drinkers to that among drinkers was more favourable in period 1 than in period 2 of follow-up (data not shown).

For period 2 only, non-drinkers can be divided, on the basis of their replies to the 1989–91 questionnaire, into never-drinkers, long-term ex-drinkers (who had already stopped or were drinking only occasionally in 1978), and 'recent' ex-drinkers (who had stopped after 1978), and the mortality during 1991–2001 is subdivided accordingly in Table 3. The results in Table 3 differ quantitatively, but not for the most part qualitatively, from those

in Table 1. In Table 3 current drinkers (6271 men) continue to show the lowest death rates for ischaemic heart disease, for respiratory disease, and for the aggregate of all causes while the small number of recent ex-drinkers (only 239 men) show the highest death rates for most causes and for the aggregate of all causes. In contrast, long-term ex-drinkers (326 men) have death rates similar to those of never-drinkers (as, for ischaemic heart disease, do the occasional drinkers).

In general, the separation of ex-drinkers from never-drinkers reduces the apparent benefit associated with drinking, but it also increases the scope for random error (as it restricts analysis to only period 2 and halves the number of non-drinkers remaining for analysis). Nevertheless, the lower relative risk for current drinkers compared with never-drinkers remains conventionally significant for both ischaemic heart disease and respiratory disease, and is nearly so for the aggregate of all causes. In Table 4, the recent ex-drinkers are combined with the current drinkers to allow for the possibility of reverse causality

Table 3 Annual mortality rate during period 2 only (1991–2001), dividing non-drinkers into never-drinkers, long-term ex-drinkers, and recent ex-drinkers

Cause of death (as in Table 1)	Age-standardized rate per 1000 men ± standard error (and numbers of deaths)				
	Never-drinkers	Ex-drinkers		Occasional drinkers	Current drinkers
		Long-term	Recent		
Alcohol-augmentable causes[a]	0.3 ± 0.3 (1)	0.4 ± 0.4 (1)	1.6 ± 0.9 (3)	1.8 ± 0.5 (14)	2.0 ± 0.2 (104)
Ischaemic heart disease	13.2 ± 1.7 (62)	14.2 ± 2.0 (49)	16.1 ± 2.6 (38)	12.8 ± 1.1 (124)	9.5 ± 0.4 (597)
Other vascular disease	7.9 ± 1.2 (47)	8.4 ± 1.4 (36)	9.7 ± 1.8 (28)	6.6 ± 0.7 (78)	7.3 ± 0.3 (539)
Cancer (other[b])	8.6 ± 1.3 (44)	8.6 ± 1.5 (33)	10.7 ± 2.0 (29)	9.8 ± 0.9 (106)	8.8 ± 0.4 (659)
Respiratory disease	5.0 ± 0.8 (36)	4.5 ± 0.9 (24)	5.0 ± 1.2 (18)	3.6 ± 0.5 (53)	3.2 ± 0.2 (299)
Other known medical	3.7 ± 0.7 (27)	5.3 ± 1.0 (27)	8.2 ± 1.6 (28)	4.4 ± 0.6 (62)	3.7 ± 0.2 (303)
All causes[c]	39.5 ± 2.7 (218)	42.3 ± 3.2 (171)	52.6 ± 4.4 (146)	39.2 ± 1.9 (440)	34.9 ± 0.7 (2533)
Number of men, 1991	424	326	239	930	6271

[a] Numbers of deaths from suicide, homicide, accident, or other external cause 52; alcoholic psychosis 0; cirrhosis 17; cancers of the mouth (excluding lips and salivary gland) 5, pharynx (excluding nasopharynx) 7, oesophagus 26, larynx 5, and liver 11. The one such death in a never-drinker was due to conflagration and the one in a long-term ex-drinker was due to cancer of the oesophagus.

[b] Other than the alcohol-augmentable types of cancer.

[c] Includes 39 deaths with unknown cause.

Table 4 Annual mortality rate during period 2 only (1991–2001), comparing current drinkers in 1991 plus recent ex-drinkers (stopped <13 years before 1991) with never-drinkers plus long-term ex-drinkers

Cause of death (as in Table 1)	Age-standardized rate per 1000 men ± standard error (and number of deaths)		Relative risk (and 95% CI)	P-value
	Never-drinkers plus long-term ex-drinkers	Current drinkers plus recent ex-drinkers		
Alcohol-augmentable causes	0.3 ± 0.2 (2)	1.9 ± 0.2 (107)	—	0.01
Ischaemic heart disease	13.6 ± 1.3 (111)	9.7 ± 0.4 (635)	0.72 (0.58–0.88)	0.002
Other vascular disease	8.1 ± 0.9 (83)	7.4 ± 0.3 (567)	0.92 (0.72–1.16)	0.50
Cancer (other[a])	8.6 ± 1.0 (77)	8.9 ± 0.4 (688)	1.04 (0.82–1.32)	0.75
Respiratory disease	4.7 ± 0.6 (60)	3.3 ± 0.2 (317)	0.69 (0.52–0.92)	0.01
Other known medical	4.3 ± 0.6 (54)	3.8 ± 0.2 (331)	0.88 (0.66–1.19)	0.40
All causes[b]	40.6 ± 2.1 (389)	35.6 ± 0.7 (2679)	0.88 (0.79–0.98)	0.02

[a] Other than the alcohol-augmentable types of cancer.

[b] Includes 36 deaths with unknown cause.

Table 5 Annual mortality rate during period 2 only (1991–2001), by amount drunk per week

| Cause of death (as in Table 1) | Never-drinkers plus long-term ex-drinkers | Current drinkers plus recent ex-drinkers: range [and mean] of units of alcohol per week | | | | Trend test[a] | |
		1–7 [4.4]	8–14 [11.5]	15–28 [21.2]	29 + [41.5]	(χ^2_2)	*P*-value
Alcohol-augmentable causes	0.3 ± 0.2 (2)	1.3 ± 0.3 (22)	2.1 ± 0.4 (29)	2.3 ± 0.4 (35)	2.3 ± 0.5 (21)	8.4	0.02
Ischaemic heart disease	13.6 ± 1.3 (111)	10.2 ± 0.7 (204)	9.5 ± 0.7 (158)	9.5 ± 0.7 (172)	9.5 ± 1.0 (101)	7.4	0.03
Other vascular disease	8.1 ± 0.9 (83)	7.1 ± 0.5 (169)	7.5 ± 0.6 (146)	7.5 ± 0.6 (156)	7.8 ± 0.8 (96)	0.2	0.9
Cancer (other[b])	8.6 ± 1.0 (77)	7.8 ± 0.6 (180)	8.5 ± 0.7 (166)	9.9 ± 0.7 (211)	10.1 ± 0.9 (131)	6.5	0.04
Respiratory disease	4.7 ± 0.6 (60)	3.3 ± 0.3 (97)	3.0 ± 0.3 (72)	3.2 ± 0.3 (83)	4.0 ± 0.5 (65)	6.9	0.03
Other known medical	4.3 ± 0.6 (54)	3.7 ± 0.4 (101)	4.3 ± 0.4 (94)	3.6 ± 0.4 (83)	3.9 ± 0.5 (53)	0.2	0.9
All causes[c]	40.6 ± 2.1 (389)	34.2 ± 1.2 (789)	35.3 ± 1.4 (673)	36.3 ± 1.3 (746)	38.1 ± 1.8 (471)	2.7	0.3
Number of men	750	1989	1663	1812	1046		

The heading spanning all rate columns reads: Age-standardized rate per 1000 men ± standard error (and numbers of deaths)

[a] As in Table 2, the statistical test is on two degrees of freedom as the effect on the death rate may not be directly proportional to the tabulated mean alcohol intake.

[b] Other than the alcohol-augmentable types of cancer.

[c] Includes 33 deaths with unknown cause.
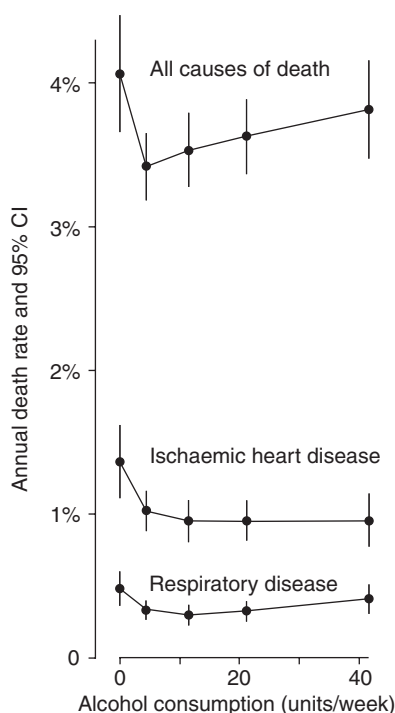
Exclusions as in Table 4.

Figure 1 Standardized annual mortality rates among British doctors, 1991–2001, by prior history of alcohol consumption (as in Table 5), for ischaemic heart disease, respiratory disease and all causes of death: floating absolute risk and 95% CI

(whereby illness could cause cessation of drinking), and the never-drinkers are combined with the long-term ex-drinkers (to increase the numbers). The reduction in mortality is then significant not only for ischaemic heart disease (*P* = 0.002) and for respiratory disease (*P* = 0.01), but also for overall mortality (*P* = 0.02).

When current drinkers are divided according to the amount reported usually to have been drunk per week, the results vary only slightly with the amount drunk, as is shown in Table 5 and in Figure 1, in both of which the relatively small number of recent ex-drinkers has been added to the current drinkers, and the long-term ex-drinkers have been added to the never-drinkers. Both for ischaemic heart disease and for respiratory disease, the rates among current drinkers appear to vary little with the usual weekly consumption of alcohol over the range ~4–42 units per week (mean 0.5–6 units per day). For neoplastic disease (after liver cancer and upper aerodigestive cancer have been excluded) there is a conventionally significant trend towards higher mortality with higher weekly consumption that is chiefly accounted for by lung cancer and, to a lesser extent, cancer of an unspecified site. This is not, however, supported by the comparison of all current drinkers with never-drinkers (Table 3) or with non-drinkers (Table 1) and may well be due chiefly to chance or to incomplete standardization for the association of alcohol with the intensity of smoking. For other medical causes (excluding cirrhosis) the differences are generally small, with no clear pattern. For the aggregate of all causes the rates among current drinkers appear to increase progressively with the amount drunk, but the trend is not significant and in each category of alcohol consumption in this population the overall mortality rate among current drinkers appears lower than the rate among never-drinkers.

Discussion

That recent ex-drinkers should have had the highest mortality rates, significantly higher than in current drinkers, whereas long-term ex-drinkers had rates very similar to the never-drinkers, can plausibly be attributed to 'reverse causality'—that is, a tendency for some drinkers who have developed a life-threatening disease to become ex-drinkers (perhaps on medical advice) because of the disease. Any such effect on the results of our study seems to wear off within about a decade, as the mortality during the period 1991–2001 of long-term ex-drinkers (that is, of men who were ex-drinkers in 1978 as well

as in 1991) was similar to that of never-drinkers. Our finding for recent ex-drinkers does, however, raise the question of the appropriate comparison to make when assessing the mortality associated with drinking. For, if the mortality of recent ex-drinkers has been raised by the inclusion of men who have stopped because of the presence of disease, then this implies that the mortality of current drinkers has been correspondingly lowered. Thus, in assessing the hazards and benefits associated with the consumption of alcohol it may sometimes be appropriate to combine recent ex-drinkers with current drinkers for comparison with never-drinkers (or with never-drinkers plus long-term ex-drinkers). When both these things are done (Table 4), the mortality of the combined group remains significantly below that of non-drinkers for ischaemic heart disease, for respiratory disease, and for the aggregate of all causes.

There is evidence from other studies that some specific causes of death that we have not considered separately may also be related positively[6] or negatively[7,8] to the amount drunk. We have not, however, shown our findings for these here, as the numbers of deaths attributed to them in this study are too small to be informative. (We also make no estimate of the extent to which alcohol-induced changes in behaviour affect the exposure to important causes of disease, such as cigarette smoking or, in other populations, HIV infection.)

For further progress on understanding the epidemiological relationship of moderate alcohol consumption to vascular, respiratory, and other particular causes of death, a meta-analysis of results from several prospective studies may be helpful. This cannot be obtained reliably from just the literature, however, partly because of publication bias (whereby striking results are particularly likely to be published) and partly because the definition of the non-drinkers with whom current drinkers are to be compared has varied from study to study and has often included some, if not all, of the recent ex-drinkers. But, for vascular disease, and perhaps also for respiratory disease, the findings from this and other studies, which take into account the possible effects of confounding,[9] do suggest that although some of the apparently protective effect of alcohol consumption is artefactual, some of it is real.

Acknowledgements

References

[1] Doll R. The benefit of alcohol in moderation. *Drug Alcohol Review* 1998;**17:**353–63.

[2] Doll R, Peto R, Hall E, Wheatley K, Gray R. Mortality in relation to consumption of alcohol: 13 years' observations on male British doctors. *Br Med J* 1994;**309:**911–18.

[3] Doll R, Peto R, Boreham J, Sutherland I. Mortality in relation to smoking: 50 years' observations on male British doctors. *Br Med J* 2004;**328:**1519–33.

[4] Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet* 2002;**360:**1903–13.

[5] Easton DF, Peto J, Babiker AGAG. Floating absolute risk: an alternative to relative risk in survival and case-control analysis avoiding an arbitrary reference group. *Stat Med* 1991;**10:**1025–35.

[6] Longnecker MP, Orza MJ, Adams ME, Vioque J, Chalmers C. A meta-analysis of alcoholic beverage consumption in relation to risk of colorectal cancer. *Cancer Causes Control* 1990;**1:**59–68.

[7] Leitzmann MF, Giovanucci EL, Stampfer MJ *et al*. Prospective study of alcohol consumption patterns in relation to symptomatic gallstone disease in men. *Alcohol Clin Exp Res* 1999;**23:**835–41.

[8] Ajani UA, Hennekens CH, Spelsberg A, Manson JE. Alcohol consumption and risk of type 2 diabetes mellitus among US male physicians. *Arch Intern Med* 2000;**160:**1025–30.

[9] Doll R, Peto R, Hall E, Wheatley K, Gray R. Alcohol and coronary heart disease reduction among British doctors: confounding or causality? *Eur Heart J* 1997;**18:**23–25.

[10] Doll R, Peto R, Wheatley K, Gray R, Sutherland I. Mortality in relation to smoking: 40 years' observations on male British doctors. *Br Med J* 1994;**309:**901–11.