Excess mortality associated with alcohol consumption

Peter Anderson

Abstract

To estimate the excess mortality due to alcohol in England and Wales death rates specific to alcohol consumption that had been derived from five longitudinal studies were applied to the current population divided into categories of alcohol consumption. Because of the J shaped relation between alcohol consumption and death the excess mortality used as a baseline was an alcohol consumption of 1-10 units/week and an adjustment was made for the slight excess mortality of abstainers. The number of excess deaths was obtained by subtracting the number of deaths expected if all the population had the consumption of the lowest risk group; correction for the total observed mortality in the population was made. This resulted in an estimate of 28 000 deaths each year in England and Wales as the excess mortality among people aged 15-74 associated with alcohol consumption.

Introduction

Consumption of alcohol is associated with many types of physical harm,¹ but death certificates rarely mention alcohol as a primary or secondary cause of death. Only two to three thousand death certificates a year in England and Wales refer to alcohol. Thus little is known about the excess mortality associated with alcohol consumption. This paper reviews current estimates of excess mortality associated with alcohol consumption and offers a means of calculating this estimate based on the methods used for the relation between cigarette smoking and death.

Current estimates

Current estimates for the excess mortality associated with alcohol consumption in England and Wales range between 5000 and 40 000 deaths a year.¹⁻⁴ McDonnell and Maynard reported a yearly excess mortality of 5000-8000 associated with use of alcohol in England and Wales in the age group 25-84.⁴ This estimate was based on work by Holtermann and Birchell, who calculated the proportion of disease attributable to "alcoholism" as

$$\frac{(X_1 - X_2)/(X_2 \times Y_2)}{Y_1} \times 100$$

where X_1 is the prevalence of disease among alcoholics, X_2 is the prevalence of disease among the whole population, Y_1 is the number of alcoholics, and Y_2 is the total population. They used a low and a high estimate for the number of alcoholics: the low estimate (350 700) was taken from data on the prevalence of alcoholism in general practice,⁶ and the high estimate (600 000) was taken from a study by Donnan and Haskey on alcoholism and cirrhosis of the liver⁷ that was based on the method of Schmidt and de Lint.⁸ The prevalence of disease among alcoholics was taken from a follow up study of people with a diagnosis of alcoholism discharged from mental hospitals.⁹

McDonnell and Maynard used these estimates to calculate the proportion of deaths that are related to alcohol within selected diagnoses. The resulting numbers were summed to give the estimate of 5000-8000 premature deaths related to alcohol. The range is based on the low and high estimates of the number of alcoholics used by Holtermann and Birchell. As it is based on an "alcoholic" population

determined in the early 1970s it is likely to be an underestimate.

A report of the Royal College of Physicians gives a figure of 25 000 deaths a year related to alcohol,¹ based on a Swedish study of 8000 men in Malmö aged 46-48 who were followed up for three and a half to eight years.¹⁰ During the follow up 218 died; 83% of these underwent necropsy, and one quarter of the deaths were found to be related to alcohol. If this rate is applied to men aged 35-64 in England and Wales the estimated number of deaths associated with alcohol is 17 000.

The Royal College of General Practitioners gives a figure of 40 000 excess deaths for adults (age 15 or over) in England and Wales.³ The figure was calculated by attributing a proportion of deaths within selected diagnoses to alcohol and then summing these deaths. The proportions of deaths were taken from several different studies.

An alternative method

I devised an alternative method for calculating excess mortality due to alcohol consumption based on that used by the Royal College of Physicians in calculating the excess mortality associated with cigarette smoking.¹¹ Four types of information are used: the population of England and Wales by age and sex (table I)¹²; the distribution of alcohol consumption in England and Wales by age and sex (table II)¹³; the total number of deaths in England and Wales by age and sex (table III)¹⁴; and data from follow up studies. Five follow up studies were used.

TABLE II—Distribution of alcohol consumption by age in men and women. Numbers are percentages; data are for England and Wales in 1978

Units of alcohol consumed per week	Men			Women		
	18-34	35-64	≥65	18-34	35-64	≥65
0	4	6	9	4	42	24
1-10	37	53	67	74	45	70
11-35	38	28	21	19	12	6
≥36	21	13	3	3	1	

The Honolulu heart study was a study of cardiovascular disease in men of Japanese descent living in Hawaii: 8006 men aged 45-65 were recruited during 1965-8 and followed up for eight years.¹⁵ The quantity and frequency of alcohol consumption were measured and validated by 24 hour dietary recall. Death rates were adjusted by the direct method to represent the age structure (in five year groups) of the entire population. Multivariate analysis controlled for cigarette smoking, weight, systolic blood pressure, and serum cholesterol concentration; these factors made little difference to the association of alcohol intake with mortality.

The United Kingdom study of male civil servants recruited 1422 men aged 40-64 in London in 1967-9 and followed them up for 10 years.¹⁶ Their alcohol consumption was obtained from a three day dietary record. Death rates were standardised for age of the total population by the direct method. Adjustment of these rates for smoking habit, diastolic blood pressure, plasma cholesterol concentration, and grade of employment made little difference to the relative risk of death according to alcohol consumption.

The Kaiser-Permanente study divided 8060 people

TABLE I—Population of England and Wales by age and sex in 1984 (millions)

Age (years)	Men	Women
15-34	6.48	6.22
35-64	8.05	8.24
65-74	1.74	2.32

TABLE III—Number of deaths in England and Wales in 1985

Age (years)	Men	Women
15-34	6245	2872
35-64	67529	40765
65-74	83728	57813

Oxfordshire Health Authority, Oxford
OX3 9DZ

Peter Anderson, MRCPG,
senior registrar in community
medicine

(aged 15-79) according to alcohol consumption into four groups matched for age, sex, race, and cigarette smoking.¹⁷ They had been recruited from multiphasic health examinations in California and were followed up for 10 years. Alcohol consumption was measured by the number of drinks of specific beverages per day over the previous year. Data were reported separately by sex, age, and smoking habit.

The *Chicago Western electric study* was a study of coronary heart disease in 1832 men employed by the Western Electric Company.¹⁸ They were aged 40-55 and free of coronary heart disease and were followed up for 17 years. The number of drinks of specific beverages per month was determined. Death rates

TABLE VIII—Estimates of excess deaths due to alcohol consumption among women aged 35-64 in England and Wales

	Duration of follow up period (years)	Sample size	Estimate of excess deaths	95% Confidence interval
Kaiser-Permanente study	10	1724	3375	2801 to 4852
Framingham study	22	2641	393	0 to 761

were adjusted for the age of the total population. Adjustment for diastolic blood pressure, smoking habit and pulse rate made little difference to the relative risk of death according to alcohol consumption.

The *Framingham study* was a study of cardiovascular disease in 5209 men and women aged 29-62 in Framingham, Massachusetts.¹⁹ They were first examined in 1948 and were followed up for 17 years. Alcohol consumption was obtained by estimating the average number of drinks of specific beverages per month. Death rates were adjusted for the age of the total population by the direct method. Adjustment for systolic blood pressure, cigarette consumption, relative weight, and serum lipoprotein concentrations made little difference to the relative risk of death according to alcohol consumption. Data were reported separately for men and women.

I converted the alcohol consumption of the different groups in the five studies to units of alcohol consumed per week (one unit contains 8 g of absolute alcohol) and calculated the death rates for men (table IV) and women (table V). As all five studies showed a J shaped relation between alcohol consumption and death (abstainers have higher death rates than those drinking 1-10 units per week) I used a consumption of 1-10 units per week as the baseline measurement and subtracted the excess deaths for abstainers from this figure. For example, to calculate the excess deaths associated with alcohol consumption among men aged 35-64 from the death rates in the study of civil servants I applied the proportions of drinkers found in Wilson's study¹³ (table II) to the total population to give the number of men in England and Wales consuming specified amounts of alcohol. These population figures were multiplied by the death rates calculated from the study of civil servants.¹⁶ The total number of estimated deaths was 57 809 (table VI). The baseline, deaths in the consumption band 1-10 units, was 50 220 (death rate multiplied by total population: in this example $6.2/1000 \times 8.1$ million). The excess deaths for abstainers were 1568 (excess rate of $(9.4-6.2)/1000 = 3.2/1000$ applied to 0.49 million abstainers); thus the excess mortality was 6021 ($57\,809 - 50\,220 - 1568$). As the actual number of deaths in 1985 among men aged 35-64 in England and Wales was 67 529 applying a correction factor of 1.16 ($67\,529/57\,809$) gave a total number of excess deaths of 7033 ($67\,529 - (50\,220 \times 1.168) - (1568 \times 1.168)$).

This calculation was made for all five studies. Tables VII and VIII give the estimates of excess deaths derived from the different studies for men and for women, respectively, in the age range 35-64. The 95% confidence intervals for the estimated excess deaths were based on the 95% confidence intervals for the rates given in tables IV and V. The data from the Kaiser-Permanente study gave a total number of excess deaths of 28 178—say 28 000—in England and Wales among people aged 15-74 (table IX).

Discussion

The estimates of the excess mortality associated with alcohol consumption provided in previous studies present several problems. The estimate of McDonnell

TABLE IV—Mortality and alcohol consumption among men

	Units of alcohol consumed/week			
	0	1-10	11-35	≥36
Civil servant study:				
Population at risk	477	390	367	188
No of deaths	45	24	24	20
Annual average death rate/1000 over 10 years	9.4	6.2	6.5	10.6
95% Confidence interval	6.8 to 12.1	3.8 to 8.5	4.0 to 9.1	6.2 to 15.1
Kaiser-Permanente study:				
Population at risk	1584	1584	1584	1584
No of deaths	157	109	158	227
Annual average death rate/1000 over 10 years	9.9	6.9	10.0	14.3
95% Confidence interval	8.4 to 11.4	5.6 to 8.1	8.5 to 11.5	12.6 to 16.1
Chicago Western Electric study:				
Population at risk	632	542	580	78
No of deaths	96	77	91	32
Annual average death rate/1000 over 17 years	8.9	8.5	9.2	24.1
95% Confidence interval	7.3 to 10.6	6.7 to 10.2	7.5 to 11.0	17.7 to 30.6
Honolulu Heart study:				
Population at risk	3747	1316	1593	1232
No of deaths	264	68	86	93
Annual average death rate/1000 over 8 years	8.8	6.5	6.7	9.4
95% Confidence interval	7.8 to 9.8	5.0 to 8.0	5.4 to 8.1	7.6 to 11.3
Framingham study:				
Population at risk	402	668	783	253
No of deaths	155	179	215	97
Annual average death rate/1000 over 22 years	17.5	12.2	12.5	17.3
95% Confidence interval	15.4 to 19.7	10.7 to 13.7	11.1 to 13.9	14.6 to 20.0

TABLE V—Mortality and alcohol consumption among women

	Units of alcohol consumed/week			
	0	1-10	11-35	≥36
Kaiser-Permanente study:				
Population at risk	431	431	431	431
No of deaths	19	16	28	28
Annual average death rate/1000 over 10 years	4.4	3.7	6.5	6.5
95% Confidence intervals	2.5 to 6.4	1.9 to 5.5	4.2 to 8.8	4.2 to 8.8
Framingham study:				
Population at risk	1079	1041	456	65
No of deaths	240	182	86	13
Annual average death rate/1000 over 22 years	10.1	7.9	8.6	9.1
95% Confidence interval	9.0 to 11.2	6.9 to 9.0	6.9 to 10.2	4.7 to 13.5

TABLE VI—Deaths of men aged 35-64 in England and Wales related to alcohol consumption and calculated from death rates in civil servants¹⁶

Consumption band (units/week)	No of men (millions)	Deaths/1000	No of deaths
0	0.49	9.4	4606
1-10	4.29	6.2	26598
11-35	2.27	6.5	14755
≥36	1.05	10.6	11130
Total population	8.1		57803

TABLE VII—Estimates of excess deaths due to alcohol consumption among men aged 35-64 in England and Wales

	Duration of follow up (years)	Sample size	Estimate of excess deaths	95% Confidence interval
Honolulu heart study	8	8006	4462	3807 to 5463
Civil servant study	10	1422	6645	6019 to 6875
Kaiser-Permanente study	10	6336	13909	12863 to 15341
Chicago Western Electric study	17	1832	14117	13164 to 14729
Framingham study	22	2106	3806	3640 to 3934

TABLE IX—Estimate of excess deaths due to alcohol consumption in England and Wales by age group (based on Kaiser-Permanente study)

Age range (years)	Estimate of excess deaths	95% Confidence interval
15-34	3 716	3 281 to 4 525
35-64	17 284	15 664 to 20 193
65-74	7 178	6 232 to 8 680
Total population	28 178	25 177 to 33 398

and Maynard was based on data from the early 1970s and on a select group of the population; "alcoholics" discharged from mental hospitals. Alcoholics are likely to contribute only a small proportion of the total excess mortality due to alcohol consumption.²⁰ The Royal College of Physicians based its estimate on a Swedish population that is unlikely to be representative of the English and Welsh populations, and data were provided only for middle aged men. The estimate of the Royal College of General Practitioners was based on the total population aged over 15, whereas most deaths occur in those aged over 75, when there is great uncertainty over whether death is associated with alcohol consumption.

The estimate presented in this paper is based on methods previously applied to ascertain the association between death and cigarette smoking.¹¹ Unfortunately there is no single basic study of the association of death with alcohol consumption so estimates were based on results from one British and four American studies.

The five studies used in my calculations have drawbacks. Firstly, four of the studies were carried out in the United States on populations differing in ethnic origin, social class, and employment state, all of which have independent effects on alcohol consumption and mortality. Data on mortality from these North American studies may not apply to populations in the United Kingdom. Secondly, a cohort phenomenon may limit the applicability of these studies. The risk related to alcohol consumption in populations derived 25 or so years ago may be different from that in current populations with the same alcohol consumption. Thirdly, four of the studies were studies of coronary heart disease; although they included an estimate of

alcohol consumption, they were not designed to relate alcohol consumption to mortality. Finally, four of the five studies give little detail about risk for different age groups, providing data only for the range 35-64 years. Only the Kaiser-Permanente study provided adequate data for different age ranges.

An estimate of total excess deaths based on one study should increase the validity of this calculation. Based on the Kaiser-Permanente study the total excess mortality came to 28 000 deaths. This is an estimate of the association between alcohol consumption and mortality, not between alcohol consumption and specific diseases. Further longitudinal studies are needed to investigate the association of alcohol consumption with morbidity and mortality.

- 1 Royal College of Physicians. *A great and growing evil*. London: Tavistock, 1987.
- 2 Royal College of Psychiatrists. *Alcohol, our favourite drug*. London: Tavistock, 1986:x.
- 3 Royal College of General Practitioners. *Alcohol: a balanced view*. London: RCGP, 1986:45.
- 4 McDonnell R, Maynard A. Estimation of life years lost from alcohol-related premature death. *Alcohol Alcohol* 1985;20:435-43.
- 5 Holtermann S, Burchell A. *The costs of alcohol misuse*. London: Department of Health and Social Security, 1981.
- 6 Wilkins R. *The hidden alcoholic in general practice*. London: Elek Science, 1974.
- 7 Donnan SPB, Haskey J. Alcoholism and cirrhosis of the liver. *Population Trends* 1977;7:18-24.
- 8 Schmidt W, de Lint J. Estimating the prevalence of alcoholism from alcohol consumption and mortality data. *Q J Stud Alcohol* 1970;31:957-64.
- 9 Adelstein A, White G. Alcoholism and morbidity. *Population Trends* 1976;6:7-13.
- 10 Petersson B, Trell E, Henningsen N-C, Hood B. Risk factors for premature death in middle aged men. *Br Med J* 1984;288:1264-8.
- 11 Royal College of Physicians. *Smoking and health now*. London: Pitman Medical, 1971.
- 12 Central Statistical Office. *Social trends*. London: HMSO, 1987;16:19-21.
- 13 Wilson P. *Drinking in England and Wales*. London: HMSO, 1980:10.
- 14 Office of Population Censuses and Surveys. Deaths by cause, 1984. *OPCS Monitor* 1985;No 3. (DH2 85/3.)
- 15 Blackwelder WC, Yano K, Rhodes GG, Kogan A, Gordon T, Palesch Y. Alcohol and mortality: the Honolulu heart study. *Am J Med* 1980;60:164-9.
- 16 Marmot MG, Rose G, Shipley NJ, Thomas BJ. Alcohol and mortality: a U-shaped curve. *Lancet* 1981;i:580-2.
- 17 Klatsky AL, Friedman GD, Siegelaub AB. Alcohol and mortality: a ten-year Kaiser-Permanente experience. *Ann Intern Med* 1981;95:139-45.
- 18 Dyer AR, Stamler J, Paul O, et al. Alcohol consumption and 17-year mortality in the Chicago Western Electric Company study. *Prev Med* 1980;9:78-90.
- 19 Gordon T, Kannel WB. Drinking and mortality. *Am J Epidemiol* 1984;120:97-107.
- 20 Kreitman N. Alcohol consumption and the preventive paradox. *Br J Addict* 1986;81:353-63.

(Accepted 3 June 1988)

Postmarketing surveillance of enalapril. I: Results of prescription-event monitoring

William H W Inman, Nigel S B Rawson, Lynda V Wilton, Gillian L Pearce, Christopher J Speirs

Abstract

To identify and measure the incidence of adverse effects of the angiotensin converting enzyme inhibitor enalapril 13 713 patients were studied for one year by prescription-event monitoring. Precise information about the duration of treatment was available for 12 543 patients. The frequency of many events was calculated, including dizziness (483 patients; 3.9%), persistent dry cough (360; 2.9%), headache (310; 2.5%) hypotension (218; 1.7%), and syncope (155; 1.2%). Less common reactions included angioedema, urticaria, and muscle cramps. Altogether 1098 (8%) patients died and the notes of 913 of them (83%) were obtained for detailed scrutiny. With the exception of a few patients with renal failure who deteriorated during treatment (reported on separately), no death was attributed to enalapril. Enalapril was considered to be effective, even in patients with advanced cardiac failure.

These results for enalapril are reassuring and

provide further evidence of the value of prescription-event monitoring.

Introduction

The angiotensin-converting enzyme inhibitor enalapril maleate was first marketed in general practice in the United Kingdom in April 1985. Arrangements were made immediately to conduct postmarketing surveillance by prescription-event monitoring, which has been developed by the Drug Safety Research Unit. The purpose of prescription-event monitoring is to identify and measure adverse effects of new drugs soon after their introduction into general practice.

Patients and methods

The method has been described elsewhere.¹ Briefly, prescription-event monitoring uses copies of NHS prescriptions as a means of identifying a patient, a

Drug Safety Research Unit,
Botley, Southampton
William H W Inman, FRCP,
director and professor of
pharmacoepidemiology
Nigel S B Rawson, PHD,
principal research officer
Lynda V Wilton, PHD, senior
research officer
Gillian L Pearce, BSC,
senior technical officer

Department of Clinical
Pharmacology, Royal
Postgraduate Medical
School, London W12 0NN
Christopher J Speirs, MRCP,
lecturer in clinical toxicology

Correspondence and
requests for reprints to:
Professor W H W Inman,
Drug Safety Research Unit,
North Croft House,
Winchester Road, Botley,
Southampton SO3 2BX.