

## REVIEW

# ALCOHOL, HEALTH, AND THE HEART: IMPLICATIONS FOR CLINICIANS

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**Abstract** — The association between light drinking and reduced mortality compared to lifetime abstinence is robust. Confounders, such as unhealthy diet, social class, and social isolation, which are associated both with abstaining and with poorer health, have made it difficult for doctors to assess the meaning of the association, and to know how to respond to individual patients seeking advice on 'drinking for health'. This paper attempts to bring up to date the evidence concerning the confounders. The evidence for a preventive effect is reviewed according to pattern of alcohol use and type of patient. The balance of risk to benefit appears to favour giving medical advice to some patients in middle life with uncontrollable risk factors for coronary heart disease (and probably of ischaemic stroke), who are very infrequent drinkers, to increase slightly the frequency of drinking (not the per session amount) and for some abstainers to consider starting to take alcohol. However, caveats render quite small the number of patients to whom physicians will give this advice. There is also the theoretical risk of a ripple in the population such that more people may move into harmful drinking.

## INTRODUCTION

The epidemiological association between light/moderate drinking and better health, compared to abstaining, is now robust. Reviewers have tended to concentrate on the implications for public health policy and government strategy (for recent reviews, see Holman and English, 1996; Edwards, 1996; Chenet *et al.*, 1997; Casswell, 1997; Doll, 1997; White and McKee, 1997). In many populations, the benefits to overall health from alcohol are outstripped by harm. For example, the reduction of 400 Finnish deaths per year due to coronary heart disease (CHD) estimated to be due to alcohol (Makela *et al.*, 1997b) is small compared to the 3000 deaths per year in that country certified as attributed to alcohol (Makela *et al.*, 1997a). In countries where there is less heavy session drinking, such as Canada, the

number of deaths estimated to be prevented by alcohol use is greater than the number deemed attributable to alcohol (Single *et al.*, 1998).

Reviewers have seldom attempted to extrapolate to the clinical situation — doctors have not been given information on how to advise individual patients. This paper will attempt to do so, and will pay particular attention to the potential confounders in the published data. The chief confounders are: (a) that some people are non-drinkers because their physical or mental health is already poor; (b) that non-drinkers are psychologically, or in their way of life, different in some way which predisposes to poor health; and (c) [(the converse of (b))] namely that moderate drinking is associated with a healthier lifestyle because it is a part of a subcultural constellation including privileged work relationships, career opportunities, exercise, diet, and freedom from the harmful results (Davey Smith, 1996) of being at the wrong end of the ferule of income disparity.

Of these, (a) has been well answered in recent reviews (e.g. Doll, 1997) and will only be touched on here. There is relatively recent evidence related

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to confounders (b) and (c), and this will be discussed in more detail. This will be followed by a résumé of the possible mechanisms by which alcohol may be prophylactic. Then an attempt will be made to define how, today, doctors should advise individual patients. This review does not propose a message for the whole population.

'Light drinking' will refer here to consumption at least once a week, but less than five drinks (45 g of ethanol) per week, and 'moderate drinking' six to 28 drinks (50 to 250 g) per week without heavy sessions (8 drinks in a session). These are definitions for men; for women moderate drinking will refer to six to 21 drinks per week, and a heavy session is defined as six drinks. These are the commonest definitions used in the literature, although a few studies have used slightly varying definitions.

An article on the controversy of whether mental health can benefit from light drinking has been submitted for publication.

#### ALCOHOL, MORTALITY, AND PHYSICAL MORBIDITY

Longitudinal ('cohort') studies showing that light or light/moderate drinkers live longer than abstainers already amounted to over 5 million patient-years in 12 countries, when the *British Heart Journal* published a review in 1995 (Griffith, 1995). Poikolainen (1995) in a systematic review of all the relevant papers located up to 1993 found that none of the 29 studies showed a lower mortality rate in abstainers compared to light drinkers. Ecological studies (comparisons across different countries or communities) and case-control studies had shown the same association. Since then, more data supporting the association have emerged. A recent meta-analysis of data pooled from 16 cohort studies and 132 other epidemiological studies concluded that drinking 1–1.9 drinks per day (10–20 g/day) reduced the risk of male death relative to abstainers to 0.84. In females, the lowest relative risk was at 0.1–0.9 drinks per day (Holman *et al.*, 1996). The benefits come from reductions in CHD and ischaemic strokes. These are such common causes of premature death that these benefits outweigh the risk due to light/moderate drinking of death from liver cirrhosis, injury, haemorrhagic stroke, breast cancer, and perhaps large bowel

cancer (Jackson and Beaglehole, 1995). The relation of consumption to mortality has come to be known as the J-shaped curve, where the high points for mortality are abstainers on the left point of the J and heavy drinkers on the right point of the J.

However, there are still some data emerging which have not found a J-shaped curve for mortality, as seen in the Swedish 19-year twin follow-up study (Andreasson and Brandt, 1997). (The study, however, showed the J-shape for hospital admissions.)

Survey researchers specializing in measuring alcohol use in populations have criticized the clumsy questions on which drinking data are based in some of the mortality studies. However, there is no reason why clumsy questioning about consumption should be the reason why, selectively, sick people more than healthy people appear in the abstainer category.

#### CONFOUNDERS OF THE ASSOCIATION

##### *Abstainers were already ill*

An objection to much early work, that abstainers included people already sick, was illustrated in the review of his own and others' data by Shaper (1990). However, when these 'sick quitters' had already been excluded, for example, in the Honolulu heart study (Klatsky *et al.*, 1986) the same increased rate of CHD among abstainers had been found. Our Scottish case-control study found the J-shaped curve for CHD admissions persisting after excluding those who had given up alcohol for medical reasons, but not those who had been chronically ill (Chick *et al.*, 1986).

Attempts were made to deal with this in most later studies, usually by excluding from the sample (e.g. Camargo *et al.*, 1997) or from the analysis, those already sick at the time of recruitment or who reported stopping drinking for health reasons, and the association has held up. In the British male doctors' study (Doll *et al.*, 1994), the original questionnaire did not differentiate life-time abstainers from former drinkers, but the authors made a post-hoc adjustment.

From the earliest studies, adjustments have been made for obesity and smoking.

## Diet

When Moore and Pearson (1986) reviewed the J-shaped curve, they cited 163 references. They concluded that there was 'persuasive' evidence for the protective effect of alcohol, but specified the need for further study of the influence of personality, diet and lifestyle. Few of the earlier reports of longitudinal studies included details of diet. Doll *et al.* (1994) discussed diet, but tended to discount it as a confounder, because apparently non-drinkers if anything had reported more than drinkers that they had reduced their saturated fat intake during the study. Among American health professionals, it was the moderate consumers who had a healthier diet than non-drinkers (Rimm *et al.*, 1991).

Rimm (1996) and Rimm *et al.* (1996) reviewed cohort and ecological studies which had controlled for fat content of diet, and, on the whole, the protective effect of moderate drinking tended to hold. Not included in their review but supporting its conclusions was the US Nurses' Health Study of 85 708 women (Fuchs *et al.*, 1995a,b), in which fibre and fat content of diet was independent of amount of drinking. In Scottish men, regularity of drinking is not associated with unhealthy diet, but heavier quantity per session most definitely is (though this relationship was not seen in the Scottish women studied) (Abel *et al.*, 1992). Even within a country with the healthier Mediterranean diet, the apparent protective effect of alcohol still appears: for example, La Vecchia *et al.* (1995) found that Italians who abstained from alcohol were at increased risk of diabetes, hypertension, heart attacks, and peptic ulcers (associations consistent across age, area of residence, education, and smoking; however, they did not make the crucial distinction between never- and ex-drinkers).

On the other hand, there is some evidence that light/moderate drinkers have a healthier diet. Shaper *et al.* (1987) found that British men who drank lightly and regularly (8–16 g per day) tended to have more favourable blood lipid concentrations than abstainers. Furthermore, a study started in 1958 in Japan, Finland, Italy, Greece, the former Yugoslavia, the USA, and The Netherlands demonstrated the relationship between moderate drinking and healthy eating (Kromhout *et al.*, 1996). Nearly 13 000 men were

enrolled, and their diet, smoking, and drinking patterns were recorded. In the next 25 years, over 6000 died. Drinking alcohol, as expected from all the other work, was associated with lower risk of death from heart disease. However, this association disappeared when the confounding effects of dietary saturated fatty acids and flavonoids and smoking were taken into account. There was a negative correlation (–0.058) amongst these communities between average alcohol consumption and saturated fat in the diet.

The Copenhagen study (Grønbaek *et al.*, 1995), showing that wine consumers lived longer than abstainers (and longer than spirits and beer drinkers), did not include dietary data. Wine is known to be consumed preferentially by higher social class groups in Denmark, but the authors did not show their data controlling for social class. We know that wine drinking countries have healthier diets (e.g. Evans *et al.*, 1995) and it is likely that wine drinking northern Europeans have tended to adopt the diet that goes with their new taste for wine. More data are needed before the importance of diet as a confounder can be fully understood.

## Social class

(a) *Social class effect on health.* Social class has a strong effect on mortality and ill health, even when obesity and smoking are controlled. Fathers having manual occupations increase mortality from cardiovascular disease by a relative ratio of 1.41 (confidence interval 1.15 to 1.72) and the risk of death from all major causes increases with the amount of time spent in manual, rather than non-manual, occupations (Blane *et al.*, 1996; Davey Smith *et al.*, 1997). The accumulation of social disadvantage over the course of life is linked to poorer adult health (Mann *et al.*, 1992). The relationship is linear, that is, even people with safe prestigious jobs have poorer health than those with safer, more prestigious jobs (Marmot *et al.*, 1984). Certain biological effects of social inequality have been discovered in primates, which contribute to the higher mortality of the lower social classes (Brunner, 1997).

(b) *Social class predicts drinking pattern.* In many countries, higher social class is associated with light/moderate drinking.

In Scotland, professional classes contain higher rates of 'regular' drinkers than other social class

groups, but among semi-skilled and unskilled manual workers those who did drink regularly consumed an above average number of alcoholic units per week (Dight, 1976).

In English civil servants, daily drinking was commonest among the highest grade staff but amount per session was higher among middle and lower grades (Marmot *et al.*, 1993).

In the US National Health Interview Survey (Williams and DeBakey, 1992), there was a higher rate of abstainers and heavy drinkers in those with lower incomes than in middle to high income groups, where rates for light and moderate drinking were higher. Lower educational level was associated with higher rates of both abstainers and heavy drinkers, while higher educational levels were associated with higher levels of light and moderate drinking. In the national US study of drinking in the general population (Hilton, 1991), the higher the social class the higher the numbers who drank above 60 drinks per month. But for heavy session drinking (8+ drinks per day or weekly intoxication) the class differences tended to disappear or reverse. In the residents of Alameda County, California, USA, abstinence was strongly associated with low income and low education (Camacho *et al.*, 1987).

The link between low social class (by education and job) and abstaining did not appear in one Copenhagen sample, but data were not given on whether daily drinking rather than heavy session drinking was, as in the UK, commoner in higher social classes (Hein *et al.*, 1996). In France, the proportion of male drinkers in the lowest socio-professional class who consume an average of over 80 g per day is double that in the superior class for each age group, as is the proportion who are total abstainers (data from 1978/9: D'Houtaud and Taleghani, 1995). The combined data of the Collaborative Alcohol-Related Longitudinal Project (Fillmore *et al.*, 1998a) showed this link for several US studies.

Thus, these findings of both more abstaining and more very heavy drinking and/or heavy session drinking in lower social classes could confound, at least for some communities, the J-shaped curve of drinking vs ill health.

(c) *Adjusting for social class in mortality studies.* Some of the cohort studies made adjustments for social class when reporting association between drinking and mortality, and found that the

J-shape disappeared. Camacho *et al.* (1987), in 6928 men and women aged over 35 years and followed for 15 years (1093 deaths), adjusted for covariates including social class and found only a non-significantly greater mortality in abstainers than light drinkers, while the sample was large enough to show a significantly raised mortality (relative risk 2.5) in those drinking over 90 drinks per month. In the British Regional Heart Disease Study (Shaper *et al.*, 1988, 1994), the J-shaped curve for coronary heart disease mortality disappeared when only non-manual workers were analysed [adjusted for age and body mass index (BMI: the weight in kg divided by the square of the height in m)], but in the total population, with adjustments for social class, age, smoking, and BMI, it was still present with a relative risk of 0.85 for light drinkers compared to abstainers. Their data for stroke events showed a worse relative risk for non-drinkers, but this was reduced to a non-significant level ( $P = 0.08$ ) when adjustments were made for age, smoking, social class, diabetes, and pre-existing ischaemic heart disease (Wannamethee and Shaper, 1996). For women, there also remains doubt. Fillmore *et al.* (1998b) combined data from three USA general population follow-up studies and found that the J-shape disappeared when psychosocial variables were included in the model. This is important, because both consumption data and social class data were collected more carefully than in most of the follow-up studies in the heart-disease mortality literature.

On the other hand, in the Whitehall I study (Marmot *et al.*, 1981), the J-shape remained when adjustment was made for grade of employment. In New Zealand men, adjustments for age, smoking, socioeconomic status and BMI left the J-shaped curve for drinking and all-cause mortality intact (Norrish *et al.*, 1995). In the NHANES I data (Rehm and Sempos, 1995), adjustments were made for educational level, which is a proxy for social class. The data were analysed in two age groups, and in the group over 60 years, the J-shape remained. (A J-shape had not been found in the under 60s.)

In the Shanghai longitudinal study (Yuan *et al.*, 1997), higher levels of education were associated with less drinking (patterns of drinking by educational group were not shown), but the J-shaped relationship of mortality to alcohol consumption remained after adjustment for educa-

tion plus diet (data not shown), smoking, and age.

The social class confounder is partly disposed of when the cohort consists of a relatively homogeneous social class group, as in the doctors' and nurses' studies. The British male doctors' study (Doll *et al.*, 1994), the American male physicians' study (Camargo *et al.*, 1997), and the US Nurses' Health Study (Fuchs *et al.*, 1995a) all revealed the J-shape.

The Japanese physicians' study is one of the few studies which did not find the J-shape. Neither at 13 years (Kono *et al.*, 1983) nor at 19 years (Kono *et al.*, 1986) did the data support a protective effect of drinking, once ex-drinkers had been excluded. Thus the weight of the evidence is that the J-shape exists in many cultures despite social class, but there may be some settings where this is not the case and at least ought to be tested.

### Exercise

Regular exercise, which helps prevent vascular disease, has only recently been included as a co-variate in epidemiological studies of mortality. Claiming 'to do something to keep you fit' correlated, even after correction for education, BMI, smoking, alcohol, marital status, and other co-variables, with survival in the coming 7 years among 40 000 American women aged 55–69 years (Kushi *et al.*, 1997). The authors did not report whether light drinking 'protected' when exercise was controlled. Shinton *et al.* (1993) compared 125 first-time stroke patients with 198 matched controls. The apparent protective effect of light and moderate drinking disappeared when obesity and exercise were taken into account. However, some of the same researchers (Palmer *et al.*, 1995) in a longitudinal study of 6369 treated hypertensive patients found that reduced mortality associated with light drinking persisted after controlling for BMI (though adjustments were not made for social class). It is conceivable that 'couch potatoes' (no exercise, a lot of television) contain a disproportionate number of abstainers (socially isolated who go out little, do not take part in sports where people go for a drink, do not drink while watching the video) but this has yet to be shown across the cultures where the J-shaped curve has been found. Data on this are therefore needed.

### Social isolation and psychological factors

Socially isolated people die at two to three times the rate of people who have a network of relationships and sources of emotional support. Berkman and Syme (1979) demonstrated this clearly and evidence continues to accumulate (Kawachi and Kennedy, 1997). The reason why these variables are potential confounders of the link between abstaining and ill-health is that, in a number of western societies, socially isolated or psychologically vulnerable people tend disproportionately to be abstainers (reviewed by J. Chick, submitted). In a longitudinal study in drinkers and former drinkers attending a health centre for any reason, Mertens *et al.* (1996) found that mortality, which was greatest in abstainers, was predicted independently by the following psychosocial measures: less participation in activities with friends, and different strategies for coping with stress such as greater use of resigned acceptance and less use of cognitive avoidance and emotional discharge.

Psychological measures showed a potential confounding effect in the data of the Whitehall II study of British Civil Servants (6900 males, 3414 females, age 35–55 years: Roberts *et al.*, 1995). Compared to both abstainers and heavy drinkers, light drinkers of both genders showed better psychological well-being in terms of hostility, and among men, but not women, light drinkers showed better psychological well-being in terms of the General Health Questionnaire (GHQ: a measure of psychiatric symptoms), 'positive affect', and 'level of upset'. For men only, psychological health correlated with healthier scores on the risk factors apolipoprotein B, fibrinogen, and factor 7. This raises the possibility that psychologically healthy men might have better physiology and they also happen to drink lightly/moderately because they are psychologically healthy. Mortality data are not yet available.

Rehm *et al.* (1993) examined personal relationships, alcohol consumption, and mortality in a prospective study of Bavarians, but unfortunately for our discussion did not present data separately for abstainers.

A finding which refutes psychological frailty as an explanation of the excessive mortality of abstainers is that the J-shaped curve is seen in populations where abstaining is the norm or

almost the norm. Among the female samples in North America, e.g. in the Nurses' Health Study (Fuchs *et al.*, 1995a) one-third were abstainers. Among male Japanese Americans 47% were abstainers (Yano *et al.*, 1977), among the men of Shanghai 57% 'had never drunk alcoholic beverages regularly' (Yuan *et al.*, 1997). It goes beyond belief that such large proportions of populations can be psychologically unhealthy.

### *Ethnicity*

Adjustments were made for ethnic background in most US studies, but few of the European ones. The obituary columns of the *British Medical Journal* reveal that deaths of British doctors born in the Indian subcontinent occur at a mean age of 61.8 years, compared to 75.2 years for doctors born in the UK (Wright and Roberts, 1996). The former are from a group with a higher proportion of abstainers, from a different gene pool, have a different diet, as well as perhaps being subjected to greater levels of stress. The British doctors' study (Doll *et al.*, 1994) did not examine ethnicity as a confounder, nor did the American doctors' study (Camargo *et al.*, 1997), and it is likely that both populations contained a significant number of such doctors. However, specific studies must answer the question of how much the increased risk of heart disease in the British residents born in the Indian subcontinent compared to native British (Balarajan, 1996) is contributed to by different use of alcohol. We can only speculate that this is at most a minor confounder.

### THE ABSENCE OF THE RELATIONSHIP IN YOUNG PEOPLE

The longitudinal studies quoted above were mostly commenced in people well over the age of 30 years. Cohort studies of younger people have often not found a protective effect of alcohol. When Swedish conscripts were followed from age 18 years to their 30s, Andreasson *et al.* (1988) found that mortality increased linearly with drinking recorded at age 18 years. A case-control study of men under age 55 years admitted to hospital in north-eastern USA with a first non-fatal myocardial infarction (median age 47 years) was conducted by Kaufman *et al.* (1985). Controls were men in hospital for other, non-alcohol related conditions. Adjustments were made for smoking,

age, and a number of social variables and no reduced risk was found in light drinkers. However, there was a high rate of abstaining in the controls and in cases which may have masked the J-shaped relationship. Or, the effect is not so strong in younger men. When the same method was applied in the same hospitals to young women with a first myocardial infarction, the J-shaped curve was observed (Rosenberg *et al.*, 1981).

Leino *et al.* (1998) combined five studies for adult men from USA general population surveys. Compared to most alcohol-and-mortality studies published to date, these studies used more detailed alcohol consumption data and psychosocial data, although data on diet and obesity were not available. In 487 deaths in a sample of 3540, no J-shaped curve was found, even before adjusting for psychosocial variables. These studies can be criticized for absence of follow-up data in 20% or more of the subjects. But it is important that the samples were relatively youthful at time 1 (from age 21 years in three studies, from age 23 in one study, and from age 28 in the only study where a suggestion of a J-shape was found). Also, these studies had used a relatively short length of follow-up (less than 10 years in three studies).

The few other reports of drinking in the young and later morbidity tend to support a protective effect. Vaillant (1995) found that among a cohort of Harvard University men followed from college days, lifelong heavy drinkers had better health at age 50 years than moderate drinkers (there were almost no abstainers in this cohort). Gillman *et al.* (1995) studied drinking and cardiovascular health in working class Bostoners age 18–26 years. At that age, there were no subjects who had stopped drinking because of CHD. Adjustments were made for age, sex, smoking, and BMI. Those drinking one to two drinks (12–24 g) per day had lower blood pressure than abstainers. This suggested that light drinking from young adulthood onwards could offer some protection in those predisposed to cardiovascular disease. Palmer *et al.* (1995) followed for an average of 11 years 6369 attenders (age 18 to 90 years) at English hypertension clinics. Lowest total mortality, adjusted for age, smoking, and untreated systolic blood pressure (BMI not a confounder in males) was lowest in men and women drinking 9–90 g of alcohol per week. The safety window is narrow, however: Hillbom *et al.* (1995) found that a first ischaemic

stroke in patients aged 16–40 years was associated with admitting to consuming over, not under, 40 g ethanol in the preceding 24 h, when a comparison was made with other hospitalized controls.

Rehm and Sempos (1995) reported a J-shaped relationship between alcohol consumption and all cause mortality in the US National Health and Nutrition Study (NHANES) but found this was not present when separately examining the subgroup aged 25–69 years, where the relationship was linear. Duffy (1995) criticized this type of subgroup analysis, recommending that multivariate analysis with age as an interactive factor should be the correct method. By contrast, when Grønbaek *et al.* (1995) specifically tested whether age interacted in the relationship between mortality and alcohol consumption, they reported that it did not.

### *Conclusions concerning confounders*

Social class and social support are the potential confounders of the J-shaped curve which are most in need of further understanding. There is one refutation of their role which has not yet been mentioned. To paraphrase Jackson (1997): ‘Yes, abstaining could be a proxy in the mortality studies for low social class or social isolation. But many causes of death — suicide, accidents, cancer — are also strongly associated with these social factors. Why, then, is the J only seen for cardiac disease and ischaemic strokes, and not for these other conditions?’ This is a convincing argument.

Despite their unequivocal potential as confounders, and the absence of appropriate adjustments in some studies, the balance of the argument seems to be that social class, diet, exercise, obesity, smoking, and social and psychological contributors to mortality have not so far proved *sufficient* to explain away the J-shaped curve. Some formerly sceptical social scientists now appear more accepting of the evidence (Rehm *et al.*, 1997). The roles of social factors and diet should, however, continue to be studied.

## WOMEN

In women as well as in men, light drinking is associated with reduced all-cause mortality (reviewed by Engs, 1996). The window of safety appears narrower than in men, because of the association of breast cancer death with drinking

above two drinks (20 g) per day or three drinks per day, to quote a report not reviewed by Engs, which also failed to find any link between breast cancer and wine drinking (Longnecker *et al.*, 1995). Pooled analysis of six cohort studies by Smith-Warner *et al.* (1998) showed a linear relationship between breast cancer and alcohol consumption in women.

## MODERATE DRINKING AND NON-FATAL ILLNESSES

Longnecker and MacMahon (1988) found a U-shaped relationship between alcohol consumption and hospital utilization in both men and women in the US 1983 National Health Service Survey. This held up after adjusting for income, race, smoking, and age. Adjustment was not, however, made for health status, and the chronically disabled or seriously ill may, of course, be unfit to go out for a drink or are on medication. In the Swedish twin follow-up study (Andreasson and Brandt, 1997), light consumption of alcohol recorded in 1973 was associated in both sexes with fewer hospitalizations in the next 19 years than abstinence, after adjustment for significant background factors of region, age, smoking, psychological stability, unemployment, body weight, and (for men only) serious illness.

In the Canadian National Health Survey, time off work, days in bed, and visits to the doctor (adjusted for age, sex and income) were least in regular beer drinkers (especially low quantity per session) (Richman and Warren, 1985). Perhaps the Canadian tavern may promote health through sociability. The authors also speculate that, in Canada, beer has been so frequently promoted with a sporting image that beer drinkers may have taken up sport and thereby improved their health! Subsequent North American surveys have found that, even controlling for health status, light and moderate drinkers make fewer visits to health professionals than ex-drinkers or abstainers (Rice and Duncan, 1995; Kunz, 1997), though only in the study by Kunz (1997) was adjustment made for age, gender, health problems, psychological well-being, income, and education.

When 391 subjects were intentionally exposed to the common cold virus and their reaction observed for the next 7 days while they remained in quarantine, those non-smokers who at intake

had reported drinking more than one drink per day (8 g/day) developed less clinical evidence of colds, and this effect was greater at more than two drinks per day. (The apparent benefit was not present in smokers.) The researchers were not able to state whether this was due to drinking during the experiment or prior to the experiment (Cohen *et al.*, 1993). Engs and Aldo-Benson (1995) did not, however, find that, among university students, abstainers had more colds and upper respiratory infections than light/moderate drinkers.

Osteoporosis and fracture is a serious cause of disability in the elderly. Although alcoholics have an increased rate of osteoporosis, the association between improved bone density and light/moderate drinking after middle age is fairly well established (e.g. Holbrook and Barrett-Connor, 1993; Felson *et al.*, 1995), though age, diet, and social class could confound this relationship.

Another orthopaedic finding is that amongst older women, light drinkers [1–13 drinks (9–150 g) per week] perform better than non-drinkers (whether former or never) on grip, hip, and step-up movement tests (controlling for age, history of stroke, BMI, and smoking) (Nelson *et al.*, 1994).

Ankle brachial arterial pressure index (ABPI) is a marker of peripheral vascular disease, a condition which is difficult to treat and leads to difficulty walking and sometimes even to leg amputation to prevent gangrene. For men in the general population, independent of smoking and a number of protective nutrients such as fibre and vitamin E, alcohol intake was associated with better ABPI (Donnan *et al.*, 1993). The finding was suggestive, but not statistically significant, for women. Exercise was not controlled for.

In summary, regarding non-fatal illnesses, the medical literature more easily finds positive than negative health associations for light drinking. However, the direction of causality has not always been clear.

#### THE MOST IMPORTANT BENEFITS ARE FOR THOSE AT HIGH RISK OF CHD

Fuchs *et al.* (1995a,b), in the American women nurses prospective study, found the J-shaped curve, but demonstrated that there was no benefit of light to moderate drinking in women without cardiac risk factors (defined as a history of

hypertension or diabetes, smoking, a high cholesterol level, a myocardial infarction in a parent  $\leq 60$  years of age, or a BMI  $> 29.0$ ).

The Copenhagen male study (Hein *et al.*, 1996) also found that alcohol did not modify the risk of ischaemic heart disease in men with low risk defined as having low concentration of serum low-density lipoprotein cholesterol. On the other hand, among men with a high concentration of low-density lipoprotein cholesterol, there was a five times greater risk of ischaemic heart disease in men who did not drink alcohol compared with men who drank three drinks a day or more. This was a post-hoc analysis and is a finding which requires replication. (Low-density lipoprotein level is partly determined by diet.)

The analysis of the American Cancer Society 9-year follow-up study of middle-aged and elderly US adults (Thun *et al.*, 1997), excluding subjects who at outset were former drinkers, found that the reduction in cardiovascular mortality associated with one or more drinks per day was greater in those who at intake to the study reported heart disease, hypertension, use of medications for these, stroke or diabetes.

The correspondence on this paper is interesting. Lowenfels (1998) quoted the study of Kjaerheim *et al.* (1993) which found that members of a teetotal organization had lower than expected mortality. However, this study did not adjust for smoking or social class. He also queried whether the absence of drinking data on a proportion of subjects biased the results, especially since they noted that the reported drinking in the sample was less than US sales figures would have predicted. However, surveys always obtain lower reported totals than sales (see Chick *et al.*, 1981), and the fact that some people did not give alcohol data does not alter the results in those that did. Urbach and Bell (1998) suggest that people with bad habits may selectively be prone to lie and state they abstain from alcohol, thus associating undue illness with abstinence. This does not accord with clinical and research experience with alcoholics, where admitting minimal drinking is a commoner way of bringing a veil across a relapse than claiming abstinence. Their point that people in this study who did not give alcohol data had relatively high mortality can perhaps more easily be explained by the result presented in the paper showing that they had a lower educational level.



The putative protective action of moderate drinking for ischaemic stroke may likewise be only, or mainly, in those at risk, specifically those with hypertension. In a 26-year follow-up of healthy Japanese people in the general population, consumption of up to 34 g ethanol per day slightly reduced the risk of cerebral infarction, but over 34 g per day increased the risk, compared to abstainers (Kiyohara *et al.*, 1995).

A study of vegetarians and other health-conscious individuals with low rates of smoking, obesity and tending to be of higher social class, found only a non-significant tendency to reduced mortality in light drinkers compared to abstainers (Mann *et al.*, 1997).

Other ways of characterizing those in whom alcohol has an apparent protective effect will doubtless emerge in the coming years.

#### ACTIONS BY WHICH ALCOHOLIC BEVERAGES MIGHT PREVENT CARDIOVASCULAR DISEASE

These were reviewed by Rimm *et al.* (1996).

##### *High-density lipoprotein (HDL) cholesterol*

One of the best established physiological risk factors for vascular disease is improved by moderate drinking: low serum levels of HDL cholesterol concentrations. It was illustrated in the MONICA study, of Toulouse and Belfast, where the protective effect seen in the analysis of alcohol consumption was largely attenuated when serum HDL cholesterol was introduced into the analytic model (Marques-Vidal *et al.*, 1996). The US MRFIT study (Suh *et al.*, 1992) followed for 6 years 11 688 men at high risk for CHD but who did not present any evidence at entry of the disease. Subjects gave several interviews about drinking during the follow-up, rather than only one report at baseline. It was clear that the usual J-shaped curve of mortality vs drinking was in part mediated by HDL cholesterol levels. (These authors ventured that the protection apparently conferred by alcohol use 'may have some application when advising selected patients'.) Lipid chemists find that alcohol with dinner (wine in most studies) reduces some of the postulated harmful pathways in lipid metabolism which lead to atheroma (e.g. Van Tol *et al.*, 1995; Fuhrman *et al.*, 1995).

##### *Clotting*

Examining another aspect of thrombosis, clotting, it was found that alcohol (40 g) with dinner changes the plasminogen system towards less clotting that evening and into the next morning (Hendricks *et al.*, 1994). In a cross-sectional study in 631 healthy male physicians, moderate alcohol intake was associated with a higher plasma concentration of endogenous plasminogen activator, which is part of the clot-busting mechanism. This correlation was independent of age, BMI, family history of CHD, and blood pressure (Ridker *et al.*, 1994). There are reports suggesting that red wine lowers platelet stickiness (Renaud and de Lorgeril, 1992; Ruf *et al.*, 1995; Demrau *et al.*, 1995; Renaud and Ruf, 1996). Salicylates reduce clotting and it is of interest that they are present in wine (Muller and Fugelsang, 1994).

##### *Antioxidant activity*

The antioxidant activity of red wine has been much discussed (see e.g. Maxwell *et al.*, 1994).

##### *Diabetes*

Another risk factor is diabetes: it has now been shown that, independent of BMI, exercise, diet, smoking, and medication, low to moderate amounts of alcohol taken on a regular basis are associated with improved insulin sensitivity i.e. reduced diabetic tendency (Kiechl *et al.*, 1996; Razay and Heaton, 1997; Lazarus *et al.*, 1997). Rimm *et al.* (1995), in the Health Professionals' follow-up study, found a lower rate of newly diagnosed diabetes in moderate drinkers than abstainers, after controlling for various risk factors including diet (1810 middle-aged and elderly US males). Perry *et al.* (1995) found the same association between lower risk of diabetes and moderate drinking in 7577 British middle-aged men (exercise was also associated with lower risk, and it is theoretically possible that it was a confounder of the alcohol association).

##### *Helicobacter pylori*

Another putative mediator of the association is *Helicobacter pylori*. Ethanol consumption ( $\geq 100$  g/week) appears to reduce the rate of *H. pylori* infection (Brenner *et al.*, 1997), but the proposed evidence that *H. pylori* seropositivity is a risk factor for CHD (Brenner *et al.*, 1997; Jenkins,

1997) has not withstood the test of a recent meta-analysis (Danesh and Peto, 1998).

### *Importance of pattern*

It is likely that a major part of the protective effect of alcohol is an acute effect. In a New Zealand study, individuals who had had a myocardial infarction were less likely to have taken alcohol during the 24-h period before the attack than would their age- and sex-matched controls drawn from the general population during a randomly chosen recent 24-h period (Jackson *et al.*, 1992). This study had not excluded patients experiencing prodromal symptoms, who could for that reason have stopped drinking. However, it directs attention to the finding from a number of studies that it is regular small amounts rather than the same amount in one weekly session which is cardioprotective. When McEldruff and Dobson (1997) compared the drinking of 11 511 Australian cases of acute myocardial infarction or coronary death with 6077 general population controls, they found that drinking one to four drinks on 5 or 6 days a week (for women, 1 to 2 drinks on 3–4 days/week) had a 'protective effect'. Drinking the same weekly amount of alcohol, but on only 1 or 2 days per week, carried an increased risk. This also suggested to them that an acute factor, such as the alteration in the clotting, played a part. (Drinking on 7 days per week was *not* associated with reduced risk, an explanation for which could be that 7-day drinkers include some heavy drinkers.)

[The time-series association found in Sweden (Messner and Petersson, 1996) and the association in a prospective Danish sample (Grønbaek *et al.*, 1995) between CHD mortality and consumption of wine and not of beer or spirits, could be explained in part by pattern — wine being less likely to be consumed in the Scandinavian heavy drinking session.]

An anti-clotting action is consistent with the finding that protection is related to regular, rather than sporadic, drinking. Another, probably less important, explanation might be drinking's relationship with blood pressure. When light/moderate drinking is made up of regular small amounts rather than sporadic drinking ('low variability'), the linear increase of blood pressure with alcohol consumption found in the multinational INTER-SALT study disappears (Marmot *et al.*, 1994:

analysis was adjusted for smoking, weight, and urinary sodium and potassium excretion but not social class, diet, or beverage type; not presented for women). A slight dip with light drinking in the otherwise linear relationship between blood pressure and alcohol consumption had been found previously (e.g. Harburg *et al.*, 1980; Michigan general population, controlling for age, sex, weight) and in some studies there is a flat section of the curve up to moderate/heavy drinking rather than a dip (e.g. Jones-Webb *et al.*, 1996; US national CARDIA study: social class remains a confounder in these studies).

Torgerson *et al.* (1997) found that the onset of the menopause was later in women who drank alcohol daily and nearly daily, in both cross-sectional and longitudinal data. Social class and smoking were controlled for. This may be an additional co-factor in explaining the J-shaped curve in the female data.

### SPECIFIC BEVERAGE?

During the recent controversy, the major review by Rimm *et al.* (1996) concluded that the apparent specific benefits of wine, and red wine in particular, were probably spurious, and that the main 'protective' effects are due to ethanol itself, rather than other components. This will not be debated here. In a number of populations studied, social class and diet were clearly potential confounders of the apparent greater protective effect of wine over beer and spirits. Pattern of drinking — red wine being associated with regular drinkers, beer and spirits with heavier session drinking — is another confounding factor. [See also correspondence on the Copenhagen study of Grønbaek *et al.*, 1995 in the *British Medical Journal* (1995) **311**, 1166–1167.]

### CONCLUSIONS, ADVICE FOR PRACTICE, AND THE ETHICAL ISSUE

#### *(a) Advice for practice*

*Caveats.* (1) The following suggestions are annulled when there is pregnancy, evidence of organ damage where ethanol has a known link, personal history of breast cancer or sub-arachnoid haemorrhage, likelihood of engendering conflict within a close family holding religious beliefs of

abstinence, or past or family history of alcohol dependence or harmful drinking.

(2) The effect of advising light or moderate drinking to reduce the risk of heart disease or ischaemic stroke has never been evaluated. As Egger *et al.* (1998) showed for  $\beta$ -carotene's role in CHD, there can be a difference, even in the opposite direction, between cohort observational data (which show 'protection') and experimental data in randomized controlled trials (which show an increase in risk).

*Patients who drink and have developed CHD.* They need not stop drinking. They should moderate their drinking and avoid heavy sessions.

*Patients seeking advice on healthy lifestyle.* General practice research in the UK has found advising patients about the recognized risk factors — obesity, diet, smoking, and heavy drinking — to be fairly ineffective (Stott, 1994). Worldwide, randomized controlled trials of the efficacy of attempts in workforces and primary care to reduce individuals' conventional risk factors for CHD have not withstood the test of systematic review (Ebrahim and Davey Smith, 1997).

There has been better compliance with taking cholesterol-lowering drugs than altering lifestyle; advice to drink to reduce risk, for those who are abstainers or very infrequent drinkers, may be more acceptable to some patients, than some other healthy advice. Authorities on preventing heart disease in clinical practice tend to be conservative. Only some add 'light drinking' to their recommendations (e.g. Pearson and Terry, 1994; Simon, 1994), whereas others do not (e.g. Pyorala *et al.*, 1994). However, the weight of current evidence appears now to be that those at high risk for heart disease (as defined, for example, by Fuchs *et al.*, (1995a,b) — a history of hypertension or diabetes, smoking, a high cholesterol level, a myocardial infarction in a parent  $\leq 60$  years of age, or a BMI  $> 29.0$ ) should be invited to consider taking one or two drinks most evenings with food. Simon (1994) adds the caveat 'responsible patients': 'Responsible patients with CHD risk factors, particularly low HDL levels, should consider low-dose alcohol, but women should be advised that alcohol may increase the risk of breast cancer'. (Responsible presumably means those who will not treble the prescribed dose.) This is in addition to advice on weight control, smoking, exercise, and diet (low total fat, low saturated fats, low cholesterol,

water-soluble fibre, regular fish, foods rich in antioxidants such as vitamin E, and perhaps garlic).

In populations where drinking is the norm, most abstainers and very occasional drinkers will have a good reason for the choice which they have made (e.g. dislike of the effect, religion, family history of alcoholism). It may not be fair or safe to give them advice which conflicts with that. In a 'wet' society, the number of abstainers who are not in that category, and who also have CHD risk factors, will be small. However, the family physician who knows the patients well, may, albeit rather rarely, wish to present the medical risk-benefit equation to selected patients, allowing the patient to choose a course of action. There is no evidence that such patients would then cease attending to other risk factors, but some doctors have expressed that concern.

Early symptoms of intermittent claudication indicating peripheral vascular disease, might be another indicator for an abstainer or very infrequent drinker to consider light drinking, because this is associated with CHD and because of the evidence that regular alcohol intake aids peripheral circulation (Donnan *et al.*, 1993).

*The age group.* On the evidence to date such advice should be confined to those in the at-risk age-group for CHD, say, over 40 years old. However, the elderly on their own at home can fall and seriously injure themselves with alcohol, and this is another group who would probably be excluded.

*The prescription.* There is the risk that patients, even those not genetically predisposed to escalate their drinking, may decide that if one drink is good for them, two will be even better. Fortunately, the epidemiological underpinning of this advice is biased towards under- rather than over-estimation of the protective dose. This is because in surveys people tend to under-report rather than over-report (e.g. Dight, 1976; Chick *et al.*, 1981; Poikolainen, 1985). Nevertheless the physician should be able to monitor the patient's alcohol use in the coming years and make this a precondition to giving advice to consider taking alcohol.

*Dose.* The dose is 10–20 g. It should be taken with meals so that it is absorbed slowly, reducing the risk of intoxication, and has a more prolonged effect on, for example, blood platelets at a time when they are under the influence of the

alimentary lipids known to increase platelet reactivity (Renaud and de Lorgeril, 1992). Heavy sessional drinking is neither safe nor effective in reducing CHD.

*The risk/benefit ratio.* The doctor should be aware that a person who has never taken alcohol, and perhaps comes from a social group which does not drink, has not had training in restrained drinking at the usual age for this learned behaviour and could become a harmful drinker. Doctors have sometimes rightly been blamed for encouraging a patient to drink (to help sleep or stress) and thereby promoting dependence on alcohol. For the UK, we can posit that, in the age group above 40 years, there are about 4% who drink excessively and experience one or more medical or social associated harms. About three out of four of them would have a family history of alcohol problems and thus would not have been in the group advised to consider drinking by a doctor following the caveats given above. This leads to the estimate that the risk of experiencing harm from drinking in a patient selected by their doctor to receive advice to consider drinking for health is around 1%.

#### (b) Wider implications?

If some abstainers and light drinkers drink a little more, there might be a ripple through the population which could result in some moderate drinkers drifting into harmful drinking and some genetically predisposed drinkers drifting towards dependence (Skog, 1985; Rose and Day, 1990; Edwards *et al.*, 1994; Skog, 1995).

In a drinking society, the numbers getting a physician's advice to consider taking up drinking would be so few as to obviate this risk. But in the United States, or other countries with abstainer rates at or above 20%, the numbers could become significant. We then have an ethical dilemma: what for some patients at risk of CHD may be their right and might even save life, may not be best for community health. Antibiotic prescribing presents an analogous dilemma: should a doctor prescribe an antibiotic for a patient's upper respiratory infection but risk contributing to the community's pool of antibiotic-resistant bacteria? That dilemma is easily resolved for the doctor, if the medical condition is life-threatening. Thus, when a patient's risk for CHD or stroke is high, the doctor is justified in advising those without risk factors for alcohol dependence or medical or

social contraindications to consider the use of alcohol.

## REFERENCES

- Abel, T., McQueen, D., Backett, K. and Currie, C. (1992) Patterns of unhealthy eating behaviours in a middle aged Scottish population. *Scottish Medical Journal* **37**, 170–174.
- Andreasson, S. and Brandt, L. (1997) Mortality and morbidity related to alcohol. *Alcohol and Alcoholism* **32**, 173–178.
- Andreasson, S., Alleback, P. and Romelsjö, A. (1988) Alcohol consumption and mortality among young men: longitudinal study of Swedish conscripts. *British Medical Journal* **296**, 1021–1025.
- Balarajan, R. (1996) Ethnicity and variations in the nation's health. *Health Trends* **27**, 114–119.
- Berkman, L. F. and Syme, L. (1979) Social networks, host resistance and mortality: a nine year follow-up study of Alameda county residents. *American Journal of Epidemiology* **109**, 186–204.
- Blane, D. B., Hart, C. L., Davey-Smith, G., Gillis, C. R., Hole, D. J. and Hawthorne, W. M. (1996) The association of cardiovascular disease risk factors with socio-economic position during childhood and during adulthood. *British Medical Journal* **313**, 1434–1438.
- Brenner, H., Rothenbacher, D., Bode, G. and Adler, G. (1997) Relation of smoking and alcohol and coffee consumption to active *Helicobacter pylori* infection: cross sectional study. *British Medical Journal* **315**, 1489–1493.
- Brunner, E. (1997) Stress and the biology of inequality. *British Medical Journal* **314**, 1472–1476.
- Camacho, T. C., Kaplan, G. A. and Cohen, R. D. (1987) Alcohol consumption and mortality in Alameda County. *Journal of Chronic Diseases* **40**, 229–236.
- Camargo, C. A., Hennekens, C. H., Gaziano, M., Glynn, R. J., Manson, J. E. and Stampfer, M. J. (1997) Prospective study of moderate alcohol consumption and mortality in US male physicians. *Archives of Internal Medicine* **157**, 79–85.
- Casswell, S. (1997) Population level policies on alcohol: are they still appropriate given that 'alcohol is good for the heart'? *Addiction* **92** (Suppl. 1), S81–S90.
- Chenet, L., McKee, M., Osler, M. and Krasnik, A. (1997) Alcohol policy in the Nordic countries — why competition law must have a public health dimension. *British Medical Journal* **314**, 1142–1143.
- Chick, J., Kreitman, N. and Plant, M. (1981) Saving face? Survey respondents who claim their last week's drinking was atypical. *Drug and Alcohol Dependence* **7**, 265–272.
- Chick, J., Duffy, J., Lloyd, G. and Ritson, B. (1986) Medical admissions in men: the risk among drinkers. *Lancet* **ii**, 1380–1383.
- Cohen, S., Tyrrell, D. A., Russell, M. D., Jarvis, M. J. and Smith, A. P. (1993) Smoking, alcohol consumption and susceptibility to the common cold. *American Journal of Public Health* **83**, 1277–1283.

- Danesh, J. and Peto, R. (1998) Risk factors for coronary heart disease and infection with *Helicobacter pylori*: meta-analysis of 18 studies. *British Medical Journal* **316**, 1130–1132.
- Davey Smith, G. (1996) Income inequality and mortality: why are they related? *British Medical Journal* **312**, 987–988.
- Davey Smith, G., Hart, C. L., Balne, D., Gillis, C. and Hawthorne, V. (1997) Lifetime socio-economic position and mortality: prospective observational study. *British Medical Journal* **314**, 547–552 (correction on page 1012).
- Demrau, H. S., Slane, P. R. and Folts, J. D. (1995) Administration of wine and grape juice inhibits in vivo platelet activity and thrombosis in stenosed canine coronary arteries. *Circulation* **91**, 1182–1188.
- D'Houtaud, A. and Taleghani, M. (1995) *Sciences Sociales et Alcool*, pp. 178–184. Editions L'Harmattan, Paris.
- Dight, S. E. (1976) *Scottish Drinking Habits*. Office of Population Censuses, and Surveys, Her Majesty's Stationery Office, London.
- Doll, R. (1997) One for the heart. *British Medical Journal* **315**, 1664–1668.
- Doll, R., Peto, R., Hall, E., Wheatley, K. and Gray, R. (1994) Mortality in relation to consumption of alcohol: 13 years observations on male British physicians. *British Medical Journal* **309**, 911–918.
- Donnan, P. T., Thomson, M., Fowkes, F. G. R., Prescott, R. J. and Housley, E. (1993) Diet as a risk factor for peripheral arterial disease in the general population: The Edinburgh Artery Study. *American Journal of Clinical Nutrition* **57**, 917–921.
- Duffy, J. C. (1995) Analysing the balance of risk. *Addiction* **90**, 484–485.
- Ebrahim, S. and Davey Smith, G. (1997) Systematic review of randomised controlled trials of multiple risk factor interventions for preventing coronary heart disease. *British Medical Journal* **314**, 1666–1674.
- Edwards, G. (1996) Sensible drinking. *British Medical Journal* **312**, 1.
- Edwards, G., Anderson, P. and Babor, T. (1994) *Alcohol Policy and the Public Good*. Oxford University Press, Oxford.
- Egger, M., Schneider, M. and Davey Smith, G. (1998) Spurious precision? Meta-analysis of observational studies. *British Medical Journal* **316**, 140–144.
- Engs, R. C. (1996) Women, alcohol, and health: a drink a day keeps the heart attack away? *Current Opinion in Psychiatry* **9**, 217–220.
- Engs, R. D. and Aldo-Benson, M. (1995) The association of alcohol consumption with self-reported illness in university students. *Psychological Reports* **76**, 727–736.
- Evans, A. E., Ruidavets, J. B., McCrum, E. E. *et al.* (1995) Autres pays, autres coeurs? Dietary patterns, risk factors, and ischaemic heart disease in Belfast and Toulouse. *Quarterly Journal of Medicine* **88**, 469–477.
- Felson, D. T., Zhang, Y. and Kiel, D. P. (1995) Alcohol intake and bone mineral density in elderly men and women: the Framingham study. *American Journal of Epidemiology* **142**, 485–492.
- Fillmore, K., Golding, J. M., Graves, K. L. *et al.* (1998a) Alcohol consumption and mortality, I: Characteristics of drinking groups. *Addiction* **93**, 183–202.
- Fillmore, K., Golding, J. M., Graves, K. L. *et al.* (1998b) Alcohol consumption and mortality, III: Studies of female populations. *Addiction* **93**, 219–231.
- Fuchs, C. S., Stampfer, M. J., Colditz, G. A. *et al.* (1995a) Alcohol consumption and mortality among women. *New England Journal of Medicine* **332**, 1245–1250.
- Fuchs, C. S., Stampfer, M. and Willet, W. C. (1995b) Alcohol consumption and mortality among women. *New England Journal of Medicine* **333**, 1082.
- Fuhrman, B., Lavy, A. and Aviram, M. (1995) Consumption of red wine with meals reduces the susceptibility of human plasma and low-density lipoprotein to lipid peroxidation. *American Journal of Clinical Nutrition* **61**, 549–554.
- Gillman, M. W., Cook, N. R., Evans, D. A., Rosner, B. and Hennekens, C. E. (1995) Relationship of alcohol intake with blood pressure in young adults. *Hypertension* **25**, 1106–1110.
- Griffith, M. J. (1995) A New Year Toast... to the cardioprotective effects of alcohol. *British Heart Journal* **73**, 8–9.
- Grønbaek, M., Deis, A., Sørensen, T., Becker, U., Schnor, P. and Jensen, G. (1995) Mortality associated with moderate intakes of wine, beer or spirits. *British Medical Journal* **310**, 1165–1169.
- Harburg, E. H., Ozgoren, F., Hawthorne, V. M. and Schork, M. A. (1980) Community norms of alcohol usage and blood pressure: Tecumseh, Michigan. *American Journal of Public Health* **70**, 813–820.
- Hein, H. O., Suadicani, P. and Gynzelberg, F. (1996) Alcohol consumption, serum low density lipoprotein cholesterol concentration, and risk of ischaemic heart disease: a six year follow-up in the Copenhagen male study. *British Medical Journal* **213**, 736–741.
- Hendricks, H. F., Veenstra, J., Veltuis, T. W., Schaafsma, G. and Kluit, C. (1994) Effect of moderate dose of alcohol with evening meal on fibrinolytic factors. *British Medical Journal* **308**, 1003–1006.
- Hillbom, M., Haapaniemi, H., Juvela, S., Palomaki, H., Numminen, H. and Kaste, M. (1995) Recent alcohol consumption, cigarette smoking and cerebral infarction in young adults. *Stroke* **26**, 45–45.
- Hilton, M. E. (1991) The demographic distribution of drinking patterns in 1984. In *Alcohol in America*, Clark, W. B. and Hilton, M. E. eds, pp. 73–86. State University of New York Press, New York.
- Holbrook, T. L. and Barrett-Connor, E. (1993) A prospective study of alcohol consumption and bone mineral density. *British Medical Journal* **306**, 1506–1509.
- Holman, C. D. and English, D. R. (1996) Ought low alcohol intake to be promoted for health reasons? *Journal of the Royal Society of Medicine* **89**, 123–129.

- Holman, C. D., English, D. R., Milne, E. and Winter, M. G. (1996) Meta-analysis of alcohol and all cause mortality: a validation of NHMRC recommendations. *Medical Journal of Australia* **164**, 141–145.
- Jackson, R. (1997) Alcohol and all-cause mortality: who benefits from drinking? Paper presented at the Stockholm Meeting of the European Society for Biomedical Research on Alcoholism. *Alcohol and Alcoholism* **32**, 305 (abstract).
- Jackson, R. and Beaglehole, R. (1995) Commentary. Alcohol consumption guidelines: relative safety vs absolute risks and benefits. *Lancet* **346**, 716.
- Jackson, R., Scragg, R. and Beaglehole, R. (1992) Does recent alcohol consumption reduce the risk of acute myocardial infarction and coronary death in regular drinkers? *American Journal of Epidemiology* **136**, 819–824.
- Jenkins, D. J. A. (1997) *Helicobacter pylori* and its interaction with risk factors for chronic disease. *British Medical Journal* **315**, 1481–1482.
- Jones-Webb, R., Jacobs, D. R., Flack, J. M. and Liu, K. (1996) Relationships between depressive symptoms, anxiety, alcohol consumption and blood pressure: results from the CARDIA study. *Alcoholism: Clinical and Experimental Research* **20**, 420–427.
- Kaufman, D., Rosenberg, L., Helmrach, S. P. and Shapiro, S. (1985) Alcoholic beverages and myocardial infarction in young men. *American Journal of Epidemiology* **121**, 548–564.
- Kawachi, I. and Kennedy, B. P. (1997) Health and social cohesion: why care about income inequality? *British Medical Journal* **314**, 1037–1040.
- Kiechl, S., Willeit, W., Poewe, W., Egger, G., Oberhollenzer, F., Muggeo, M. and Bonora, E. (1996) Insulin sensitivity and regular alcohol consumption: large, prospective, cross sectional population study (Bruneck study). *British Medical Journal* **313**, 1040–1044.
- Kiyohara, Y., Kato, I., Iwamoto, H., Nakayama, K. and Fujishima, F. (1995) The impact of alcohol and hypertension on stroke incidence in a general Japanese population: the Hisyama Study. *Stroke* **26**, 368–372.
- Kjaerheim, J., Andersen, A. and Helseth, A. (1993) Alcohol abstainers: a low-risk group for cancer — a cohort study of Norwegian teetotallers. *Cancer Epidemiology, Biomarkers and Prevention* **2**, 93–97.
- Klatsky, A. L., Armstrong, M. A. and Friedman, G. D. (1986) Relationship of alcoholic beverages use to subsequent coronary artery disease hospitalisation. *American Journal of Cardiology* **58**, 170–174.
- Kono, S., Ikeda, M., Ogata, M., Tokudome, S., Nishizumi, M. and Kuratsune, M. (1983) The relationship between alcohol and mortality among Japanese physicians. *International Journal of Epidemiology* **12**, 437–441.
- Kono, S., Ikeda, M., Tokudome, S., Nishizumi, M. and Kuratsune, M. (1986) Alcohol and mortality: a cohort study of male Japanese physicians. *International Journal of Epidemiology* **15**, 527–532.
- Kromhout, D., Bloemberg, B. P. M., Feskens, E. J. M., Hertog, M. G. L. and Blackburn, H. (1996) Alcohol, fish, fibre and antioxidant vitamins do not explain population differences in coronary heart disease mortality. *International Journal of Epidemiology* **25**, 753–759.
- Kunz, J. L. (1997) Alcohol use and reported visits to health professionals — an exploratory study. *Journal of Studies on Alcohol* **58**, 474–479.
- Kushi, L. H., Fee, R. M., Folsom, A. R., Mink, P. J., Anderson, K. E. and Sellars, T. A. (1997) Physical activity and mortality in postmenopausal women. *Journal of the American Medical Association* **277**, 1287–1292.
- La Vecchia, C., Decarli, A., Franceschi, S., Ferraroni, S. F. M. and Pagano, R. (1995) Prevalence of chronic disease in alcohol abstainers. *Epidemiology* **6**, 436–438.
- Lazarus, R., Sparrow, D. and Weiss, S. T. (1997) Alcohol intake and insulin levels: the Normative Ageing Study. *American Journal of Epidemiology* **145**, 909–916.
- Leino, E. V., Romelsjo, A., Shoemaker, C. et al. (1998) Alcohol consumption and mortality, II: Studies of male populations. *Addiction* **93**, 203–218.
- Longnecker, M. P. and MacMahon, B. (1988) Associations between alcoholic beverage consumption and hospitalization, 1983 National Health Interview Survey. *American Journal of Public Health* **78**, 153–156.
- Longnecker, M. P., Newcomb, P. A., Mittendorf, R., Greenberg, E. R., Clapp, R. W., Bogdan, G. F., Baron, J., MacMahon, B. and Willett, W. C. (1995) Risk of breast cancer in relation to lifetime alcohol consumption. *Journal of the National Cancer Institute* **87**, 923–929.
- Lowenfels, A. B. (1998) Alcohol consumption and mortality in US adults. *New England Journal of Medicine* **338**, 1385.
- Makela, P., Valkonen, T. and Martelin, T. (1997a) Contribution of deaths related to alcohol use to socioeconomic variation in mortality: register based follow-up study. *British Medical Journal* **315**, 211–216.
- Makela, P., Valkonen, T. and Poikolainen, K. (1997b) Estimated numbers of deaths from coronary heart disease 'caused' and 'prevented' by alcohol: an example from Finland. *Journal of Studies on Alcohol* **58**, 455–463.
- Mann, S. J. L., Wadsworth, M. E. J. and Colley, J. R. T. (1992) Accumulation of factors influencing respiratory illness in members of a national cohort and their offspring. *Journal of Epidemiology and Community Health* **46**, 286–292.
- Mann, J. I., Appleby, P. N., Key, T. J. and Thorogood, M. (1997) Dietary determinants of ischemic heart disease in health conscious individuals. *Heart* **78**, 450–455.
- Marmot, M. G., Rose, G. and Shipley, M. J. (1981) Alcohol and mortality: a U shaped curve. *Lancet* **i**, 580–583.
- Marmot, M. G., Shipley, M. J. and Rose, G. (1984) Inequalities in death-specific explanations of a

- general pattern? *Lancet* **i**, 1003–1006.
- Marmot, M. G., North, F., Feeney, A. and Head, J. (1993) Alcohol consumption and sickness absence: from the Whitehall II study. *Addiction* **88**, 369–382.
- Marmot, M. G., Elliott, P., Shipley, M. J. *et al.* (1994) Alcohol and blood pressure: the INTERSALT study. *British Medical Journal* **308**, 1263–1267.
- Marques-Vidal, P., Cuimetiere, P., Evans, A., Cambou, J.-P. and Arvelier, D. (1996) Alcohol consumption and myocardial infarction: a case-control study in France and Northern Ireland. *American Journal of Epidemiology* **143**, 1089–1093.
- Maxwell, S., Cruickshank, A. and Thorpe, G. (1994) Red wine and antioxidant activity in serum. *Lancet* **344**, 193–194.
- McEldruff, P. and Dobson, A. J. (1997) How much alcohol and how often? Population based case-control study of alcohol consumption and risk of a major coronary event. *British Medical Journal* **314**, 1159–1164.
- Mertens J. R., Moos, R. H. and Brennan, P. L. (1996) Alcohol consumption, life context, and coping predict mortality among late-middle-aged drinkers and former drinkers. *Alcoholism: Clinical and Experimental Research* **20**, 313–319.
- Messner, T. and Petersson, B. (1996) Alcohol consumption and ischaemic heart disease mortality in Sweden. *Scandinavian Journal of Social Medicine* **24**, 107–113.
- Moore, R. D. and Pearson, T. A. (1986) Moderate alcohol consumption and coronary artery disease. *Medicine* **65**, 242–267.
- Muller, C. J. and Fugelsang, K. C. (1994) Take two glasses of wine and see me in the morning. *Lancet* **343**, 1428–1429.
- Nelson, H. D., Nevitt, M. D., Scott, J. C., Stone, K. L. and Cummings, S. R. (1994) Smoking, alcohol and neuromuscular and physical function of older women. *Journal of the American Medical Association* **272**, 1825–1831.
- Norrish, A., North, D., Yee, R. R. and Jackson, R. (1995) Do cardiovascular risk factors predict all-cause mortality? *International Journal of Epidemiology* **24**, 908–914.
- Palmer, A. J., Fletcher, A. E., Bulpitt, C. J., Beevers, D. G., Coles, E. C., Ledingham, J., Petrie, J. C., Webster, J. and Dollery, C. T. (1995) Alcohol intake and cardiovascular mortality in hypertensive patients: report from the Department of Health Hypertension Care Computing project. *Journal of Hypertension* **12**, 957–964.
- Pearson, T. A. and Terry, P. (1994) What to advise patients about drinking alcohol: the clinician's conundrum. *Journal of the American Medical Association* **272**, 967–968.
- Perry, I. J., Wannamethee, S. G., Walker, M. K., Thomson, A. G., Whincup, P. H. and Shaper, G. (1995) Prospective study of risk factors for development of non-insulin dependent diabetes in middle-aged British men. *British Medical Journal* **310**, 560–564.
- Poikolainen, K. (1985) Underestimation of recalled alcohol intake in relation to actual consumption. *British Journal of Addiction* **80**, 215–216.
- Poikolainen, K. (1995) Alcohol and mortality: a review. *Journal of Clinical Epidemiology* **48**, 455–465.
- Pyyrala, K., De Backer, G., Poole-Wilson, P. and Wood, D. (1994) Prevention of coronary heart disease in clinical practice: Recommendations of the Task Force of the European Society of Cardiology, European Atherosclerosis Society and European Society of Hypertension. *European Heart Journal* **15**, 1300–1331.
- Razay, G. and Heaton, K. W. (1997) Moderate alcohol consumption has been shown previously to improve insulin sensitivity in men. *British Medical Journal* **314**, 443–444.
- Rehm, J. and Sempos, C. T. (1995) Alcohol consumption and all-cause mortality. *Addiction* **90**, 471–480.
- Rehm, J., Fichter, M. M. and Elton, M. (1993) Effects on mortality of alcohol consumption, smoking, physical activity and close personal relationships. *Addiction* **88**, 101–112.
- Rehm, J., Ashley, M. J. and Dubois, G. (1997) Alcohol and health: individual and population perspectives. *Addiction* **92** (Suppl. 1), S109–S116.
- Renaud, S. and de Lorgeril, M. (1992) Wine, alcohol, platelets and the French paradox for coronary heart disease. *Lancet* **339**, 1523–1526.
- Renaud, S. C. and Ruf, J.-C. (1986) Effects of alcohol on platelet functions. *Clinica Chimica Acta*, **246**, 77–89.
- Rice, C. and Duncan, D. F. (1995) Alcohol use and reported physician visits in older adults. *Preventive Medicine* **24**, 229–234.
- Richman, A. and Warren, R. A. (1985) Alcohol consumption and morbidity in the Canada Health Survey: interbeverage differences. *Drug and Alcohol Dependence* **15**, 255–282.
- Ridker, P. M., Vaughan, D. E., Stampfer, M. J., Glynn, R. J. and Hennekens, C. H. (1994) Association of alcohol consumption and plasma concentration of endogenous tissue-type plasminogen activator. *Journal of the American Medical Association* **272**, 929–933.
- Rimm, E. B. (1996) Invited commentary — Alcohol consumption and coronary heart disease: good habits may be more important than just good wine. *American Journal of Epidemiology* **143**, 1094–1099.
- Rimm, E. B., Giovannucci, E. L., Willett, W. C. *et al.* (1991) Prospective study of alcohol consumption and risk of coronary disease in men. *Lancet* **338**, 464–468.
- Rimm, E. B., Chan, J., Stampfer, M. J., Colditz, G. A. and Willett, W. C. (1995) Prospective study of cigarette smoking, alcohol use and the risk of diabetes in men. *British Medical Journal* **310**, 555–559.
- Rimm, E. B., Klatsky, A., Grobbee, D. and Stampfer, M. J. (1996) Review of moderate alcohol consumption and reduced risk of coronary heart disease: is the effect due to beer, wine or spirits? *British Medical Journal* **312**, 731–736.
- Roberts, R., Brunner, E. and Marmot, M. G. (1995)

- Psychological factors in the relationship between alcohol and cardiovascular morbidity. *Social Science and Medicine* **41**, 1513–1516.
- Rose, G. and Day, S. (1990) The population mean predicts the number of deviant individuals. *British Medical Journal* **301**, 1031–1034.
- Rosenberg, L., Slone, D. and Shapiro, S. *et al.* (1981) Alcoholic beverages and myocardial infarction in young women. *American Journal of Public Health* **71**, 82–84.
- Ruf, J.-C., Berger, J.-L. and Renaud, S. (1995) Platelet rebound effect of alcohol withdrawal and wine drinking in rats: relation to tannins and lipid peroxidation. *Arteriosclerosis, Thrombosis and Vascular Research Biology* **15**, 140–144.
- Shaper, A. G. (1990) Alcohol and mortality: a review of prospective studies. *Addiction* **85**, 837–847.
- Shaper, A. G., Phillips, A. N., Pocock, S. J. and Walker, M. (1987) Alcohol and ischaemic heart disease in middle-aged British men. *British Medical Journal* **294**, 1287–1289.
- Shaper, A. G., Wannamethee, G. and Walker, M. (1988) Alcohol and mortality in British men: explaining the U-shaped curve. *Lancet* **ii**, 1267–1273.
- Shaper, A. G., Wannamethee, G. and Walker, M. (1994) Alcohol and coronary heart disease: a perspective from the British Regional Heart Study. *International Journal of Epidemiology* **23**, 482–494.
- Shinton, R., Sager, G. and Beevers, G. (1993) The relation of alcohol consumption to cardiovascular risk factors and stroke: the West Birmingham Stroke Project. *Journal of Neurology, Neurosurgery and Psychiatry* **56**, 458–462.
- Single, E., Robson, L., Xie, X. and Rehm, J. (1998) The economic costs of alcohol, tobacco and illicit drugs in Canada, 1992. *Addiction* **93**, 983–998.
- Simon, H. B. (1994) Patient-directed, nonprescription approaches to cardiovascular disease. *Archives of Internal Medicine* **154**, 2283–2296.
- Skog, O.-J. (1985) The collectivity of drinking cultures: a theory of the distribution of alcohol consumption. *British Journal of Addiction* **80**, 83–99.
- Skog, O.-J. (1995) The J-curve, causality and public health. *Addiction* **90**, 490–492.
- Smith-Warner, S. A., Spiegelman, D., Yaun, S. *et al.* (1998) Alcohol and breast cancer in women: a pooled analysis of cohort studies. *Journal of the American Medical Association* **279**, 535–540.
- Stott, N. (1994) Screening for cardiovascular risk in general practice: blanket health promotion is a waste of resources. *British Medical Journal* **308**, 285–286.
- Suh, I., Shaten, B. J., Cutler, J. A. and Kuller, L. H. (1992) Alcohol use and mortality from coronary heart disease. *Annals of Internal Medicine* **116**, 881–887.
- Thun, M. J., Peto, R., Lopez, A. D., Monaco, J. H., Henley J., Heath, C. W. and Doll, R. A. (1997) Alcohol consumption and mortality among middle-aged and elderly U.S. adults. *New England Journal of Medicine* **337**, 1705–1714.
- Torgerson, D. J., Campbell, M. K., Thomas, R. E. and Reid, D. M. (1997) Alcohol consumption may influence onset of the menopause. *British Medical Journal* **315**, 188.
- Urbach, D. R. and Bell, C. M. (1998) Alcohol consumption and mortality in U.S. adults. *New England Journal of Medicine* **338**, 1385.
- Vaillant, G. E. (1995) *The Natural History of Alcoholism Revisited*, pp. 133–137. Harvard University Press, Cambridge, MA.
- Van Tol, A., Groener, J. E. M., Scheek, L. M. *et al.* (1995) Induction of net mass lipid transfer reactions in plasma by wine consumption with dinner. *European Journal of Clinical Investigation* **25**, 390–395.
- Wannamethee, S. G. and Shaper, G. (1996) Patterns of alcoholic intake and risk of stroke in middle-aged British men. *Stroke* **27**, 1033–1039.
- White, I. R. and McKee, M. (1997) Festive cheer for all? Headaches for alcohol policy makers. *British Medical Journal* **315**, 1638–1639.
- Williams, G. D. and DeBaakey, S. F. (1992) Changes in levels of alcohol consumption: United States, 1983–1988. *British Journal of Addiction* **87**, 643–648.
- Wright, D. L. M. and Roberts, A. P. (1996) Which doctors die first? Analysis of BMJ obituary columns. *British Medical Journal* **313**, 1581–1582.
- Yano, K., Rhoads, G. G. and Kagan, A. (1977) Coffee, alcohol and risk of coronary heart disease among Japanese men living in Hawaii. *New England Journal of Medicine* **277**, 405–409.
- Yuan, J.-M., Ross, R. K., Gao, Y.-T., Henderson, B. E. and Yu, M. C. (1997) Follow-up study of moderate alcohol intake and mortality among middle-aged men in Shanghai, China. *British Medical Journal* **314**, 18–23.