Alcohol and cardiovascular disease: the status of the U shaped curve

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Alcohol is responsible for considerable morbidity and mortality and for considerable social problems. Excess mortality associated with alcohol consumption has been estimated at 28 000 per year in England and Wales,¹ and the annual cost of alcohol associated illness in Britain was calculated to be £167 million in 1986; this is in addition to a social cost of about £1600 million. The public health importance of limiting alcohol consumption is not questioned. This is the context within which to place the debate on the effect of moderate levels of alcohol consumption on morbidity and mortality associated with coronary heart disease.

This debate has centred on the so called U shaped curve describing the relation of alcohol consumption to risk of death from all causes. Heavy drinkers have an increased risk of death compared with moderate drinkers, but moderate drinkers have a lower mortality than abstainers. One commentator, surprisingly, labelled this U shaped curve a myth.² It is not mythical. Its existence is now not seriously in doubt. It is due largely to the lower death rate from coronary heart disease among moderate drinkers. What has been questioned is whether this is a consequence of a protective effect of alcohol. Abstainers include people who have stopped drinking because of ill health ("sick quitters") and people who are at higher risk for other reasons. Either of these groups may account for the higher risk among non-drinkers.

The only major prospective study that failed to show that moderate drinkers had a lower risk of cardiovascular disease was that from Alameda County.³ On p 553 in a follow up to this study, Lazarus *et al* have reported that among the women former drinkers had a higher risk of death than lifetime non-drinkers, but this was not true for the men. Among the men lifetime abstainers had a higher relative risk estimate than drinkers, although the confidence limits overlapped.⁴ A study from New Zealand reported recently in this journal showed that moderate drinkers had a lower incidence and mortality from coronary heart disease compared with both former drinkers and never drinkers.⁵

What then is the status of the U shaped curve? Does it represent causation? Is moderate drinking protective? Against the possible protective effect of moderate alcohol consumption on the risk of coronary heart disease has to be set the direct effect on blood pressure and the possible effect on risk of stroke.

Alcohol and coronary heart disease

A study using data from 18 countries showed a strong inverse association between average national wine consumption and mortality from coronary heart disease.⁶ This type of ecological correlation, which used a country's average value as the unit of analysis, is subject to the criticism that other factors may vary among countries. The relation may not be specific to alcohol consumption. Interestingly, a more recent

international correlation study shows that the inverse association between alcohol intake and mortality from coronary heart disease is independent of the well known association of mortality from coronary heart disease with fat intake. Indeed, adding mean alcohol intake to the multiple regression equation linking fat intake to incidences of coronary heart disease improved the correlation coefficient from 0.79 to 0.92.⁷ These ecological data have been complemented by numerous studies of individuals.

Several case-control studies, including that of Jackson *et al*,⁸ have shown that moderate drinkers of alcohol have a lower risk of coronary heart disease compared with non-drinkers (fig 1). A review of prospective studies in 1984 showed similarly that moderate drinking is associated with apparent protection from coronary heart disease.¹⁴ This has been updated to include studies published subsequently (fig 2). All of these studies, with, until now, the exception of the Alameda County study, found a lower rate of coronary heart disease in moderate drinkers than abstainers.

The studies did not show uniformly that heavy drinkers have a higher risk of cardiovascular disease than moderate drinkers. The U shaped curve describing the link of alcohol with risk of death comes from the higher rate of death from various other causes in heavy drinkers.

There is no clear evidence that one type of alcoholic beverage is more protective than another, although the international study referred to above showed a stronger correlation with wine.⁶

Interpreting the association

NATURE OF THE EVIDENCE

Each of the studies relating alcohol to cardiovascular disease has its flaws. This is neither unique nor surprising. Despite the flaws of each individual investigation, what stands out in reviews of these studies¹⁴⁻³⁰ is the consistency of the findings in populations as diverse as British civil servants, men in different regions of the United Kingdom, men and women in Framingham (Massachusetts), Yugoslavs, Puerto Ricans, Japanese Americans in Hawaii, Japanese physicians, West Australians, nurses in the north eastern United States, and others. Although consistency is often cited as one of the criteria making an observed association more likely to be causal than artefactual, studies can be wrong consistently. Nevertheless, where a large number of studies have used different methods but produced similar results artefact is less likely; where studies have been performed in diverse populations confounding is less likely.

"SICK QUITTERS"

One of the major criticisms levelled at many of the studies is that non-drinkers will include people who have given up drinking because they were unwell.¹⁷ Such people would be expected to have an increased

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BMJ 1991;303:565-8

rate of disease. The argument suggests that it is the inclusion of "sick quitters" with the non-drinkers that accounts for the high incidence of coronary heart disease in non-drinkers compared with moderate drinkers.

Many of the studies do not give data on lifetime drinking patterns, but a few are able to separate the mortality in lifetime abstainers. These are the studies of people enrolled in the Kaiser-Permanente prepaid health plan in California,^{32,33} which show never drinkers and former drinkers both to have higher incidences of coronary heart disease than moderate drinkers. Similarly, never drinkers among Japanese physicians²¹ and Japanese Americans²⁰ have higher incidences of coronary heart disease than moderate drinkers. In the Kaiser study former drinkers who stopped for medical reasons had higher mortality from non-cardiovascular causes but not cardiovascular causes.³³ The report from Alameda County in this issue looks specifically at the effect of change in alcohol consumption on mortality. Among men lifetime abstainers had a higher relative risk estimate than moderate drinkers, although the confidence intervals overlapped. The study is some-

what inconclusive among women. Women who gave up drinking had increased relative risks of death from all causes and from ischaemic heart disease, but this was not accounted for by existing chronic disease such as diabetes, cancer, and cardiovascular disease. The Auckland case-control study, in addition to showing that never drinkers were at significantly increased risk of coronary heart disease compared with drinkers, suggested that former drinkers may have a reduced risk of myocardial infarction and an identical risk of fatal coronary disease compared with never drinkers.⁵

The inclusion of sick quitters in the non-drinking group therefore did not account for the higher incidence of coronary heart disease in non-drinkers in those studies that have the data to address the question directly.

ILL HEALTH IN ABSTAINERS

A variant of the sick quitter argument is that abstainers may have a greater burden of ill health than moderate drinkers, regardless of their previous drinking status.³¹ Presumably the suggestion is that ill people may not develop the drinking habit. It is this burden of ill health that is held to account for the high rate of coronary heart disease in abstainers. Three arguments make this not the most likely explanation of the findings.

Firstly, most longitudinal studies exclude people who have evidence of illness at the time they are enrolled into the study. In studies of coronary heart disease such exclusions are often limited to people with evidence of prevalent cardiovascular disease. In the most recent report from Kaiser moderate alcohol consumption was associated with lower mortality from coronary heart disease, even in the half of the population left after excluding anyone who had one of 17 indicators of cardiovascular illness or risk factors.³² Among the 276 802 men enrolled in the American Cancer Society cohort and followed up for 12 years by using a very broad definition of ill health 33% were classified as sick at enrolment. Among the healthy remainder, the higher incidence of coronary heart disease in non-drinkers compared with moderate drinkers was clear.¹⁶

Secondly, it would be surprising if this selection of already ill people recruited into the non-drinking group resulted in a higher risk only of coronary heart disease and not of other disease.³⁰ The data show that if there is a higher risk of other diseases among abstainers, it is less pronounced than for coronary heart disease. Figure 3 comes from the American Cancer Society cohort study.¹⁶ There is a suggestion that mortality from a range of causes may be lower in men drinking one drink a day, which is consistent with "selection" of sicker men into the abstainer category. At consumption levels higher than this mortality from other causes rises; for coronary heart disease the relative risk stays at about 0.8.

Thirdly, if people with pre-existing illness are recruited into studies as non-drinkers this could account for higher rates of illness in the earlier years of follow up in a longitudinal study. This effect might be expected to wear off as the follow up extended. It does not seem to. In the Framingham study the lower mortality in moderate drinkers persisted over a 24 year follow up period.¹⁹ In the American Cancer Society study the relative risk of death from coronary heart disease associated with 1-2 drinks a day among men healthy at baseline was 0.77 for both the whole 12 year follow up and for the last six years of it.¹⁶

CONFOUNDING

It has been argued that non-drinkers are an unusual group in a society in which some alcohol intake is the norm.³¹ If non-drinkers were different from

FIG 1—Relative risk of coronary heart disease in moderate drinkers compared with non-drinkers in case-control studies. Bars show 95% confidence interval where available. (Moderate drinking= ≤ 5 units of alcohol daily; if >1 drinking category rate ratio was calculated for highest consumption category)

FIG 2—Relative risk of coronary heart disease in moderate drinkers compared with non-drinkers in prospective studies. Bars show 95% confidence interval where available. (Moderate drinking= ≤ 5 units of alcohol daily)

FIG 3—Alcohol consumption and relative risk of death over 12 years in American Cancer Society prospective study of 276 802 men aged 40–59. Mortality ratios are adjusted for age and smoking habits and for the four most common causes of death and death from all causes¹⁶

drinkers in other ways that accounted for their high risk of coronary heart disease we would have confounding. It is worth recalling that a higher risk in non-drinkers was found among Japanese Americans, in whom 47% of men were non-drinkers, as was found in British studies, in which 6% of men were non-drinkers. It is unlikely that the features that distinguish non-drinkers from drinkers are identical in the two societies, but in both cases non-drinkers seem to be at higher risk.

Most studies have controlled for smoking directly when examining the higher incidence of coronary heart disease in non-drinkers. The degree to which the effect of other risk factors has been allowed for varies greatly, but none of the studies has been able to account for the observations by confounding.

One special factor that should receive attention is social class. An apparent greater protection from wine compared with other alcoholic beverages could arise from the fact that moderate drinkers of wine tend to be of higher social class than non-drinkers. That alone is associated with lower risk. The Whitehall²⁵ and British regional heart studies¹⁷ controlled for this directly, and the apparent protection has been found in various different cultures where the factors associated with social class are likely to vary.

QUALITY OF DATA

It is widely accepted that it may be difficult to obtain accurate data on alcohol consumption. The methods of assessing alcohol consumption varied widely in the different studies. This seems to have had little effect on the results for risk of coronary heart disease. Nor has it affected the ability of these studies to show that increasing alcohol consumption is associated with increasing mortality from a range of causes (see fig 3). The authors of the American Cancer Society study argue that if alcohol histories were correct they would expect to see alcohol associated with mortality from cancer of the oral cavity and oesophagus, liver cirrhosis, suicide, and accidents. This is, in fact, what they found.¹⁶

The higher risk of coronary heart disease in non-drinkers could therefore only be due to inaccurate alcohol history if drinkers at high risk declared themselves to be non-drinkers and, in some studies, lifetime abstainers. Against this is the finding in some studies^{32,33} of an inverse association between alcohol and coronary heart disease that was not simply limited to a higher incidence of disease in non drinkers.

POSSIBLE PATHWAYS

Alcohol can increase the risk of cardiovascular disease by its effect in raising blood pressure. This is seen at intake levels above 2–3 drinks a day. The effect

may, in part, account for an increased risk of stroke. At higher intake levels alcohol is associated with cardiomyopathy.

Moderate consumption is associated with increased concentrations of high density lipoprotein cholesterol.³⁴ Numerous studies have shown that higher concentrations of high density lipoprotein cholesterol are associated with reduced risk of coronary heart disease. In the American Lipid Research Center study²⁵ and the Honolulu heart study,³⁰ about half the association between non-drinking and coronary heart disease could be accounted for, statistically, by the lower concentrations of high density lipoprotein cholesterol. Similarly, Jackson *et al* reported that controlling for low density lipoprotein cholesterol concentration had no effect on risk estimates but controlling for high density lipoprotein cholesterol concentration weakened the association between alcohol and coronary heart disease.⁵

Alcohol is also associated with lower plasma fibrinogen concentrations³⁵ and with reduced platelet activity, and hence with a lower probability of thrombosis.

Public health implications

The evidence suggests that two drinks a day are associated with no cardiovascular harm and may be protective against coronary heart disease. A public health recommendation that emphasised the positive effects of alcohol would be likely, however, to do more harm than good. Above two drinks a day there is evidence of harm, biological as well as social. Although the relation between mean alcohol consumption and the prevalence of heavy drinking has been much debated,³⁶ a recent analysis from the Intersalt study is revealing.³⁷ Among 52 populations worldwide, the correlation between mean level of consumption and the prevalence of heavy drinking (≥ 300 mg alcohol a week) was greater than 0.9. It suggested that an increase in mean consumption of only 15 g alcohol (about one drink) a week would be associated with a 10% increase in the prevalence of heavy drinkers. Hence anything that increased the mean level of consumption may well have an effect on the prevalence of heavy drinking.

In conclusion, the balance of harm and benefit does not weigh in favour of making a recommendation to the public to drink in order to prevent coronary heart disease.

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(Accepted 29 July 1991)

Observations on the NHS reforms: an American perspective

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In the waiting rooms of family practices across the US patients can pick up a prominently displayed, large, four colour, free *Special Report on Health* featuring a story of the Montagues, entitled, "Can you afford to get sick?" Their daughter contracted leukaemia, and, although this middle class family has standard health insurance, the parents have spent the past three years dealing with scores of different claim forms, deductibles, copayments, caps, exclusions, and erroneous (perhaps) denials in order to cope with the \$500 000 of bills for treating her.

The report pictures Mrs Montague before a dining table covered with seven piles of different correspondence over bills and claims; boxes full of files for each doctor, laboratory, and hospital; and even a photocopier she bought to help in the fight against constant threats of financial ruin. An accompanying article features Dr Niles, a physician on the other side of the private competitive insurance market.² He is seen coping with myriad insurance forms and hundreds of provisos, protocols, or rules that insurance companies have elaborated as the counterparts to the exclusions, deductibles, copayments, and caps for Mrs Montague. Each elaboration serves to reduce payments by the insurers or to delay what has to be paid so that the insurance companies can earn more interest on the premium income. All Mrs Montague wants is to have the bills for her daughter Jenni paid. All Dr Niles wants is to be paid for the services he renders.

With about 35 million Americans being uninsured and about 70 million more suffering from private Swiss cheese policies full of holes in coverage, at the same time that medical expenses have surged past 12% of the gross national product and the \$600bn mark, an American observer is hardly in a position to say anything critical about the NHS reforms. Yet it is perhaps just this experience with payer and provider markets over the past 10 years (during which costs rose faster than before the market reforms began) and a Yankee bred outlook on human folly that may provide a valuable perspective.

Upending an efficient system

To start at the bottom line, the vigorous effort by

Mrs Thatcher, Mr Clarke, and officers in the Treasury to wrench the NHS out of its allegedly wasteful, inefficient, and expensive ways seems strange to a student of comparative health care systems. Do they not know that they were (and are) getting better value for money than any other system in the industrialised world?³ No other system comes close in services per thousand pounds, even after taking into account the million patients waiting for elective procedures.

Do they not know that experts from other systems marvel at how hard British nurses, technicians, and physicians work for so little pay? The level of dedication measurable in services rendered per million pounds of pay provides this government with one of the greatest bargains in the world. Moreover, medical expenditures have been rising more slowly than in any comparable system. Yet the government's response has been to purchase services at marginal rather than average costs, forcing the whole NHS to become run down, while all the time complaining about how expensive the system is.

Ironically, this systemic parsimony has made the NHS steadily more inefficient: equipment breaks down, inefficient or obsolete equipment is not replaced, arrangements are not replaced, poor working conditions and pay contribute to high staff turnover, and a growing number of people opt out of the system through private insurance whenever they can. Thus the government is running down what many used to perceive as a competent, inexpensive, universal health care system. The alternative private system will be much more expensive. These private costs, however, will not show up on the bills that the government pays.

To summarise, the restructuring of a system that delivers more services per million pounds than any other on the grounds that it does not do so seems insane. Were the cost of the NHS £45bn and rising at 5% over inflation it would be understandable why the government thought it had a problem; but with NHS costs at £30bn, rising at 2% over inflation, the question is why do British leaders think they can treat the nation's ill for a third less than anyone else?

Although the government apparently intends the reforms to make the NHS more efficient, their latent function is to transfer the political heat of parsimony from politicians to managers and doctors in the guise of

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BMJ 1991;303:568-70