From IAN WHITE

Sir—Duffy\(^1\) presents an analysis of the relationship between alcohol consumption and all-cause mortality for middle-aged men and estimates that all-cause mortality is minimized at 26 units of alcohol per week. However, there are problems with the nature of the data analysed, and problems with the analysis used: the latter cause Duffy’s estimate of the level at which all-cause mortality is minimized to be too high.

PROBLEMS WITH THE NATURE OF THE DATA
Age and smoking are important confounders of the relationship between alcohol and mortality.\(^2\) However, Duffy’s data are crude and not adjusted for any confounder. Further, it is not clear how Duffy selected the seven studies he analysed. Each of these problems could yield substantial bias in any estimates produced.

PROBLEMS WITH THE ANALYSIS

Figure 1 shows the crude data used by Duffy. Each solid line represents the results of one study (the British studies being represented by heavier lines) and shows the odds ratio at each level of alcohol consumption relative to the abstainers. The eye suggests that mortality is minimized somewhere in the range from 5 to 15 units per week. In contrast, the dotted line represents Duffy’s fit to these data from his Table 4: it gives a minimum at 26 units per week. There are two major reasons for this discrepancy.

Firstly, Duffy has assumed that a quadratic model describes the U-shaped relationship between mortality and alcohol consumption for each study. It is important to check this model empirically. For example, the quadratic model assumes that the mortality-alcohol relationship is symmetrical about its minimum, but the Figure suggests that the right-hand arm is less steep.

To allow a wider range of U-shaped models, I repeated Duffy’s analysis of the British data after first applying various power transformations (powers from 0.2 to 3) to the alcohol consumption. The model thus contained study and transformed alcohol consumption together with its square. The deviance of this model was minimized when the square root transformation was used: the deviance on 5 degrees of freedom was 3.48 compared with 9.56 for Duffy’s model (difference = 6.08, \(P = 0.01\)), showing significant lack of fit for Duffy’s model. The square-root model estimates the minimum all-cause mortality at 16 units per week (95% confidence interval by Fieller’s theorem: 12–23), which is much more consistent with the data shown in Figure 1.

The second reason for the discrepancy between the graphed data and Duffy’s result is that the non-British studies have been ignored. Figure 1 shows the effect of this: the British studies (shown with thicker lines), and especially the British Regional Heart Study which dominates this analysis, tend to show greater protective effects than the other studies, and so the protective effect of alcohol is being further exaggerated. Duffy argues that it is reasonable to ignore the non-British studies because heterogeneity has been found between all the studies. However, the existence of statistical heterogeneity does not in itself preclude meaningful estimation—indeed the minima for the different studies...
could be the same despite the heterogeneity. Nor is it safe to assume that the British studies are homogeneous merely because their heterogeneity was not significant.

In addition, Duffy's use of an abstainer factor (which amounts to excluding abstainers from the analysis) is an adequate way to allow for the possibility that sick people tend to give up drinking, but it does not allow for the possibility that sick people tend to reduce their drinking.

**CONCLUSION**

The level of alcohol consumption at which crude all-cause mortality is minimized lies well below 26 units per week. Using a quadratic model and ignoring non-British data both lead to this level being overestimated. Failure to control for confounders is likely to cause additional bias.

**REFERENCES**


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**Author's Response**

From JOHN C DUFFY

Sir—The subject matter of my paper, the protective effect of alcohol consumption against certain forms of cardiovascular mortality and hence mortality from all causes, is undoubtedly controversial, to the extent that some activities in this area almost invite interpretation as attempts to deny the putative existence of this phenomenon or to minimize its potential importance on the basis of less than objective selection of evidence. A suitable example is afforded by the joint policy statement (notably, not a consensus statement) produced following a conference on the subject in Toronto, but the literature provides many others.

Traditional versions of alcohol control policy, heavily influenced by research and thinking in State Alcohol Monopolies, as in Canada and the Nordic countries, have stressed the importance of reducing per capita consumption, on the basis of a supposed influence of per capita consumption on the proportion of heavy drinkers, or, from a perspective closer to the public health ideas of Rose, the prevention paradox. The insistence that for drinkers at all levels 'less is better' cannot be sustained in the face of evidence of beneficial health effects of light and moderate alcohol consumption.

The comments of Rehm derive from an analysis of age as a confounder in a study in the US. The point of my analysis of the seven studies referred to was precisely to show that differences between countries make it inadvisable to generalize from studies in one particular country to the population of another country. As noted in my paper, some of these differences may be due to differential patterns of confounding between populations.

Rehm claims that my conclusions concerning potential protective effects associated with various levels of consumption 'mainly interpret the confounding effects of age'. Rather than refer to the two original studies analysed by me, Rehm attempts to justify this statement on the basis of a comparison of age-adjusted and unadjusted relative risk estimates from the NHEFS study. There can be little doubt from the evidence presented that age is an important confounder in that study. But the relevance of this to the analysis of two British studies is obscure—the naive assumption that since age is a confounder in a particular study in a particular country it will be so in other studies and other countries is precisely the type of error which the first set of analyses in my paper attempted to illustrate and correct.

Had Rehm consulted reports of the two British studies providing the published data analysed in my paper, he would have seen that his assertion was incorrect. Published data from the Whitehall Study provide sufficient information to adjust for age in three groups—40-49, 50-59 and 60-64 years of age. The results of logistic-linear modelling shown in Table 1 demonstrate that adjustment for age scarcely affects the estimates (linear and quadratic) of the association between alcohol and mortality. It should also be noted that there is no evidence of significant interaction.