Letters to the Editor

Are cardiovascular disease trends driven by gadflies?

From SUSANA SANS and ALUN EVANS

Sir—In the review of Epidemiology in the IJE in February the increasing obesity in the United States over the 1990s across, apparently, all subgroups of the population\(^1\) was mentioned. What is even more perplexing is that all this is happening while there is an inexorable decline in cardiovascular disease in that country. Hypotheses abound to explain the decline in cardiovascular disease observed in many countries. Ingster and Feinleib have made\(^2\) a coherent argument for salicylates in the food chain contributing to the decline in cardiovascular disease in the USA. The authors admit that there are ‘many gaps in this syllogism’ which must be addressed. One such gap which needs to be filled is provided by the meta-analysis of 61 studies which supports\(^3\) the case for a significant decline in human sperm densities in the USA and Europe. There are considerable data suggesting that this may be caused by other substances entering the food chain, i.e. pollutants, e.g. xenoestrogens (environmental hormones), pollutants with oestrogen mimicking effects (phenolics such as bisphenol A, phthalates, polychlorinated biphenyls, and diverse organo-chlorine pesticides) and naturally occurring dietary oestrogens, including flavonoids and other phytoestrogens.\(^4\) How might oestrogens protect against cardiovascular disease? Among other actions, it has been shown that they inhibit vascular smooth muscle proliferation which is a central feature of atherosclerosis.\(^5,6\)

A fairly recent report\(^7\) from the Worldwide Fund for Nature catalogues the presence of more than 350 chemicals from substances such as perfume, sun-tan lotion and pesticides, in human breast milk samples, including 87 dioxin and dioxin-like compounds. After the Seveso incident in 1976, in which large amounts of tetrachlorodibenzo-p-dioxin were liberated, a preponderance of female births was noted over the half life of the toxin. The authors felt this observation might support the hypothesis that dioxin modified hormonal balance\(^8\) but offered other explanations as well. A fair proportion of these have oestrogen mimicking effects. Even more contaminants are likely to be present because other toxic chemicals found in human body fat can potentially transfer to the newborn infant during breastfeeding. Indeed, exposure to them in utero and through breastfeeding might be acting in tandem with those postulated in the fetal/infant origins of adult cardiovascular disease hypothesis.\(^9\)

Alcoholic beverages, particularly red wine, are a source of exogenous oestrogenic substances. Indeed alcoholic males are well known to exhibit signs of feminization, but not until cirrhosis ensues.\(^10\) If this is proven, increases in moderate alcohol consumption, especially in the form of wine, could explain the decline in heart disease in both sexes: men becoming more like women and women becoming even more like women in terms of arterial disease. In addition, Ingster and Feinleib suggest\(^2\) that their hypothesis might also ‘contribute to an understanding of why the decline in mortality has continued despite a steady increase in the prevalence of obesity in the USA’. This increase has been particularly marked between NHANES II and NHANES III.\(^11\) It is well known that adipose tissue produces oestrogen\(^12\) and this might also be contributing to the decline. Indeed, it has been observed\(^12\) that ‘Morbidly obese patients possess an unlimited reservoir for peripheral estrogen synthesis’.

The decline in cardiovascular disease and increase in obesity has also been accompanied by a fall in blood pressure\(^13\) and total cholesterol,\(^14\) while evidence for high density lipoprotein (HDL) cholesterol change is more controversial.\(^15,16\) This pattern of risk factor change has also been observed in other countries.\(^17\) There is emerging evidence that some genetic polymorphisms which have been shown to add to cardiovascular risk seem to depend upon increased body weight for their expressions.\(^18\) Although the overall level of alcohol consumption in the USA has remained fairly constant over the period of the decline in cardiovascular disease, the per capita consumption of wine is reported,\(^19\) albeit by the wine industry, to have doubled. Thus, the situation is highly perplexing and the hypothesis for an oestrogen-driven decline deserves exploration.

Lastly, perhaps the title needs some explanation: oestrogens induce ‘oestrus’ which is derived from the Greek for ‘gadfly’.\(^20\)

References

\(^1\) Davey-Smith G, Ebrahim S. Epidemiology—Is it time to call it a day? Int J Epidemiol 2001;30:1–11.


of the discipline. Yet, epidemiology is social by definition. The origin of a scientific and political fight that can be traced to the origins of a social epidemiology? No Way Sir—Zielhuis and Kiemeney (Lombard Street, Baltimore, MD 21201, USA. E-mail: cmunt001@umaryland.edu)

From CARLES MUNTANER

Sir—Zielhuis and Kiemeyer (Social Epidemiology? No Way) inaccurately represent my position in the recent debate with Cooper and Kaufman. Contrary to the authors’ claim, I stated that the criticism of social epidemiology’s ‘lack of explanations’ could have been directed to other sub-specialties as well (e.g., psychiatric epidemiology). I also stated that ‘despite its current increase in recognition (e.g. Lynch et al.’s notable study on the long-term effects of economic hardship), social epidemiology is a contested discipline, as the relevance of studying social facts within epidemiology is still being intensely debated. Epidemiologists still clash over their discipline’s status as a socionatural science.’

Social Epidemiology? No Way seems to be the most recent round of a scientific and political fight that can be traced to the origins of the discipline. Yet, epidemiology is social by definition. The death of an organism is a biological fact, but dying from drinking contaminated water or from a gunshot wound is a social fact as well, making the study of population health a biosocial (or socionatural) science. The problem does not reside, then, in the adequacy of social (economic, political, cultural) explanations in epidemiology. Rather, it is the systematic shunning of social science that is surprising and alarming.

During the 20th century, such an eminent epidemiologist as Milton Terris always considered epidemiology ‘social’ and thus found the term ‘social epidemiology’ redundant. However, growth in the substantive knowledge of academic departments (Michigan, Harvard), and number of scholars devoted to the study of social determinants of health justifies today’s separate term ‘social epidemiology’. Similarly, ‘mind’ has been an intrinsic part of psychology since its origins (Weber, Fechner, James), but not until the 1960s did ‘cognitive psychology’ blossom as a distinctive subspecialty within psychology, following the efforts of psychologists and non-psychologists alike (e.g., Simon, Newell, Tversky, Neisser, Chomsky).

Why, then, attack a central part of one’s discipline? Let me suggest an externalist explanation. Public health is a public good, and in societies dominated by private economic interests there is little incentive to promote it. On the other hand, clinical medicine is easily marketable (insurance, medical technology, hospital industry, pharmaceutical companies; just to highlight a few). On the other hand, clinical medicine is easily marketable (insurance, medical technology, hospital industry, pharmaceutical companies; just to highlight a few). On the other hand, clinical medicine is easily marketable (insurance, medical technology, hospital industry, pharmaceutical companies; just to highlight a few). On the other hand, clinical medicine is easily marketable (insurance, medical technology, hospital industry, pharmaceutical companies; just to highlight a few). On the other hand, clinical medicine is easily marketable (insurance, medical technology, hospital industry, pharmaceutical companies; just to highlight a few). On the other hand, clinical medicine is easily marketable (insurance, medical technology, hospital industry, pharmaceutical companies; just to highlight a few).

Zielhuis and Kiemeyer are also incorrect when they imply that I attribute the failure of identifying underlying mechanisms exclusively to social epidemiology. It is precisely the authors’ recommendation that ‘epidemiologists can use social determinants of health (income, stress)’ without further justification that I find most questionable. My criticism was extended to epidemiology as a whole and even to medical sociology. In the area of medical sociology, I mentioned a study that considered ‘education’ a perfectly exogenous variable. Almost as disturbing as the continuous use of ‘race’ as an implicit biological category, is (as I commented) the commonsense belief among US ‘baby boomer’ academics that social inequalities in health would be
eliminated if everyone had the ‘talent’ or ‘will power’ to obtain a PhD.\textsuperscript{11} This assumption is common in epidemiological studies of drug use among minorities, welfare recipients and the homeless. Rather than looking into the social mechanisms underlying the associations with ‘race’ and ‘education,’ some epidemiologists persist in the pragmatic use of indicators that reinforce lay myths (i.e. that race is a biological category; that those who cannot make ends meet have some intrinsic deficiency such as ‘low intelligence’ or ‘laziness’). If any MD behaved with similar ethics towards a patient, she could be sued on the spot. But in a few areas of epidemiology, research with poorly conceptualized indicators that either justify health inequalities or promote the removal of health benefits in oppressed populations (welfare recipients) is rewarded with funding, publication and prestige.

Not surprisingly, epidemiology’s official philosophers seem to care only about interpersonal micro ethics of interest to clinicians, such as clinical trials, euthanasia, and genetic counselling, while macro-ethical issues such as the health effects of racism, class, war, or exploitation are seen as ‘off limits’.\textsuperscript{4} Thus, social epidemiologists often double as philosophers and historians to defend their discipline (e.g. Krieger, Kaufman).

As would happen in any other field of study, it is difficult to disagree with the criticism of some of what passes as social epidemiology—for example, the exaggerated aetiological claims that often accompany findings based on psychosocial constructs measured with self-reports (‘control’, ‘sense of coherence’, ‘hostility’, ‘perceptions of inequality’ and the like\textsuperscript{12}). However, rather than scorning social epidemiology as a field, we should recognize the contribution of the many epidemiologists who devote their careers to the study of social determinants of health. Among them we find sociologists such as Amick, Williams, Eaton, House, Link, Dohrenwend and Schwartz; epidemiologists such as Susser, Syme, Rose, Cassel and Tyrolean (the fathers of the discipline); and others that have contributed decisively to the advancement of such studies (Szkel, Comstock, Shy, Terris). In addition, social epidemiologists advanced our knowledge in the hard days of late 1970s and 1980s, when everything ‘social’ was under attack (Davey Smith, Kaplan, Marmot, Sorlie, Stansfeld, Morris, Arber, Blaxter, Macintyre, Wing, Berkman, Wilkinson and Johnson, among others).

The sharp separation between disciplines recommended by Zielhuis and Kiemene is untenable. A scientific discipline that cannot find closely related disciplines is most likely non-scientific (e.g. astrology, parapsychology). Thus epidemiologists in the last decade have successfully incorporated concepts (income inequality; e.g. Lynch, Wilkinson, Kennedy, Kawachi), measures (social class, area socioeconomic position, racism, work organization; e.g. Krieger, Lynch, Landsbergis), and statistical methods (multilevel analysis; e.g. O’Campo, Diez-Roux, Yen) from the social sciences.

Finally, let me disagree with the authors’ own characterization of their article as ‘controversial.’ In order to be controversial one needs to go against the grain. The authors’ views are in fact consistent with epidemiology’s conservative leadership.\textsuperscript{10} Luckily, social epidemiology is too developed and its substantive topic too important to retreat into oblivion.

\textbf{References}


\textbf{Alcohol consumption and plasma homocysteine: What’s brewing?}

\textbf{From ANGELIKA DE BREE, WM MONIQUE VERSCHUREN, HENK J. BLOM AND DAAN KROMHOUT}

Sir—We would like to complement recent publications\textsuperscript{1,2} on a potential beneficial health effect of moderate alcohol consumption on the cardiovascular system with data on the relation between alcohol consumption and the plasma total homocysteine concentration (tHcy). A high tHcy is associated with an increased risk of cardiovascular diseases, therefore, it is important to know how lifestyle factors might influence tHcy.

Observational studies indicate that alcohol consumption might be related to tHcy in a J-shaped fashion;\textsuperscript{3} alcoholics have a very high tHcy\textsuperscript{4} and moderate alcohol consumers (\leqslant 4 glasses/
day) have a lower tHcy as compared to non-drinkers. The study population, a random sample of a population-based cohort of Dutch men and women (20–65 years), we cross-sectionally observed a lower tHcy at higher levels of alcohol consumption (assessed with a food frequency questionnaire). This trend was statistically significant in men (P < 0.001); non-drinkers (n = 132) had a geometric mean tHcy of 14.2 μmol/L, compared to 13.9 μmol/L in drinkers of ≤2 glasses/day (n = 838), 12.5 μmol/L in drinkers of >2 to <4 glasses/day (n = 306) and 13.1 μmol/L in drinkers of ≥4 glasses/day (n = 214). An overall statistically significant inverse trend (P < 0.05) remained after correction for age, smoking, physical activity, coffee and tea consumption, dietary folate intake and vitamin B supplements use.

An intriguing question is whether the inverse relation can be ascribed to ethanol intake or that the type of alcoholic beverages consumed is important, as the recent intervention trial of Van der Gaag suggests. They showed, in a 3-week randomized cross-over trial, that despite the equally administered amount of ethanol (4 glasses/day = 40 g/day) beer does not affect tHcy, whereas wine and spirits induce an increase. Motivated by these results, we studied whether different types of alcoholic beverage were differently related to tHcy in males (Table 1) we found that higher beer consumption was inversely associated to tHcy, whereas wine (red and white) and spirits showed no relation to tHcy. Thus, like Van der Gaag et al., we showed that beer drinking does not have an adverse effect on tHcy. In fact, we observed a favourable effect, which may seem inconsistent. However, the relation between alcohol consumption and tHcy might be J-shaped and our study contained few heavy drinkers (16% of the male drinkers drank >4 glasses/day) we were probably measuring an effect in the descending part of the J-curve. The intervention trial provided relatively high alcohol doses and might have measured an effect at or beyond the nadir of the curve.

The beneficial effect of beer drinking on tHcy could be due to its folate, riboflavin and vitamin B6 content, all important for the enzymatic homocysteine conversion. Nevertheless, the inverse relation with beer was independent of these nutrients (Table 1), which might indicate a dose effect of ethanol. This is further suggested by the absence of a significant association with alcohol consumption in female drinkers, who on average drink less than men, and the fact that the amount of ethanol consumed in the third tertile (T3) of beer consumption exceeds that of T3 in the wine and spirit drinkers by far. Intervention studies with moderate amounts of ethanol (<40 g/day), or observational studies in populations where beer is not the predominant alcoholic drink, may clarify whether our result is due to residual confounding by B vitamins in beer, or show that ethanol is responsible for the beneficial effect of moderate ethanol consumption on tHcy.

Acknowledgements

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References


Table 1 Mean plasma homocysteine concentration (tHcy) in male alcohol drinkers by tertiles of beer, wine and spirits

<table>
<thead>
<tr>
<th>Tertile</th>
<th>Beer (n = 1179)</th>
<th>Wine (n = 1179)</th>
<th>Spirits (n = 1179)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intake (g/day)</td>
<td>Glasses/day</td>
<td>tHcy</td>
</tr>
<tr>
<td>1</td>
<td>423</td>
<td>20</td>
<td>0.1</td>
</tr>
<tr>
<td>2</td>
<td>387</td>
<td>177</td>
<td>0.9</td>
</tr>
<tr>
<td>3</td>
<td>369</td>
<td>747</td>
<td>3.7</td>
</tr>
</tbody>
</table>

Beta (g (95% CI)) = 0.007 (0.011, 0.003)%–0.003 (0.022, 0.016)%–0.026 (0.021, 0.074)%

a Geometric means: anti-log of the logarithmically transformed tHcy values, to normalize the distribution.

b Each glass contains about 10 g of ethanol.

c,d,e tHcy adjusted for age, coffee and tea consumption, smoking, physical activity, dietary folate intake and B vitamin supplement, other alcoholic drinks, alcohol free beer and: dietary vitamin B6 and B2 intake, wine and spirits, *beer and spirits, **beer and wine.

f Due to missing values in covariables, the multivariate analyses (analyses of covariance) were based on data of 1174 male alcohol drinkers. The betas of the regression analysis express a proportional change in tHcy, due to the logarithmic transformation. For example, an increase of 200 g of beer (1 normal glass) is associated with a decrease in tHcy of 1.4%.

g CI = confidence interval.