have been professionally top heavy, but we included representatives from the community health council and the National Childbirth Trust to ensure that someone could speak—and vote—on behalf of consumers. The point is that, because marginal analysis is explicitly based on value judgments, careful consideration of “whose values?” is a condition of its use. Contrast this with alternative methods of setting priorities used elsewhere.

The exercises in Mid Glamorgan were admittedly far from perfect, but they were judged to have been successful and to have provided a better framework for setting priorities than the alternatives. The process is under review, the aim being to achieve an improvement in the next round. But there will be a next round, and while suggestions on how to do a better job are welcome, others should not forgo the opportunity to improve priority setting in their quest for perfection.

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Interpreting results of observational research

Problem with confounders can be tackled

EDITOR,—Paul Brennan and Peter Croft argue that the application of tests of significance in observational studies is inappropriate because of the lack of randomisation and consequent likelihood of confounding.¹ The authors conclude that neither the P value nor the 95% confidence intervals should be used as evidence for the validity of findings of an observational study. We believe that this conclusion is unwarranted and unwise.

While confounding is a major problem in observational studies, statistical methods exist to test for its presence or absence. Medical statistics would be well served by the adaptation of statistical methods and tests from the discipline of econometrics. Almost all econometric data are observational, and there is no such luxury as the randomised controlled trial. Econometricians have therefore had to develop sophisticated, yet easily applied, tests for the presence of confounding factors—“omitted variables” in econometric jargon. These tests are widely accessible in standard econometric textbooks in the case of time series data² and are becoming more available for probability data.³

For example, multivariate regression analysis could be undertaken on the data in Brennan and Croft’s example of neural tube defects. In a probit model the probability of a neural tube defect occurring is estimated as a function of many independent variables, one being the treatment group to which the subject has been allocated. The coefficient on the treatment group variable gives the relative effectiveness of the placebo and active treatments, and standard statistical tests can be applied to investigate whether it is significantly different from zero. The influence of known confounders can be isolated, and, more importantly, the analysis can be tested for unknown general confounding.

The usefulness of these techniques and the dangers of forsaking statistical testing should be emphasised. To argue for the abandonment of statistical testing based on P values and confidence intervals because of possible confounding implies the loss of valid and useful information. Testing for confounding, on the other hand, affords more certainty about the usefulness of existing information and results in at least three ways. Firstly, if confounding is tested for by a general test and not found, conventional P tests and confidence intervals can be interpreted with confidence in observational studies. Secondly, if confounding is found as a consequence of a general

test the hunt for confounders can proceed. Thirdly, if there are prior suppositions to suggest what these confounders might be a specific test can be performed to investigate and isolate the influence of these factors.

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P values are still useful

EDITOR,—While we agree with Paul Brennan and Peter Croft that the greatest emphasis in reporting observational studies should be on questions of confounding and bias, we believe that their suggestion that the term “statistically significant” should be abandoned is akin to banning a useful implement such as a kitchen knife on the grounds that some people misuse it.¹ Epidemiologists accustomed to dealing with large populations are well used to ignoring statistical significance; when the sample size is measured in millions any perceived differences are bound to be statistically significant. With small samples, however, chance can play some surprising tricks, as anyone who has used simulation in teaching statistics can vouch for. For example, if one wished to see whether males were at greater risk of sudden infant death than females and found that of 2000 deaths, 1200 were of males, there would be no need for a test, but what if the figure was 120 of 200 or 12 of 20? In many situations there is no opportunity to collect more data to render chance variation unimportant compared with the variation due to bias. The P value conveys valuable information over and above that supplied by the confidence interval, and a recent paper suggested ways in which understanding of statistical inference may be improved by supplementing P values with subjective posterior probabilities.²

Useful analyses should lead to informed decisions, and surely one should not suppress any information that can help the decision making process. This includes the P value and the confidence interval.

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Diet and cancer

EDITOR,—In her review of diet and cancer Joan Austoker lists several dietary factors that may protect against cancer, but she does not mention the possible role of lower energy intake.¹ At a meeting of the US President’s Commission on Breast Cancer, summarised by Hunter and Trichopoulos,² studies on rodents were described that indicated that “energy (calorie) restriction of as little as 10% . . . had a steeper and better-fitting

dose-response relation with mammary tumours than did restriction of dietary fat.” Hunter and Trichopoulos and others have urged investigation of the effects of various energy and fat intakes in early childhood and adolescence.

Among rural Africans living traditionally, cancers related to diet—colon, prostate and breast cancers—are uncommon, although cervical, oesophageal, and liver cancers are common regionally.³ Although the pattern is altering in city dwellers, this pattern of a low prevalence of cancers related to diet prevails throughout the continent. African diets, especially among young people, are relatively low in energy and fat and high in plant foods. The habitually low energy intake of the young people is insufficiently appreciated. In the region of Johannesburg recent studies of 5 year olds showed approximate mean energy intakes to be 4.6 MJ in rural African children, 6.3 MJ in urban African children, and 8.4 MJ in white children.⁴ The rural African children were on average about 6 cm shorter (6%) and 3.5 kg lighter (20%) than white children. These dichotomies remain with increasing age, although their magnitude diminishes. In stark contrast, in the United States Afro-American girls aged 10 are now on average about 3 cm taller and 6 kg heavier than white girls.⁵ Total mortality from cancer in Afro-Americans is now higher than that in the white population.

Whether the setting be Western or urban African, any policy aimed at reducing the energy intake of young people would be hard to operate. Nevertheless, as many have emphasised, we should seek to learn more of the proneness to degenerative diseases of those who in early youth were accustomed to relatively low energy intakes.

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Persistent post-traumatic stress disorder

EDITOR,—Brigitta Bende and Robin M Philpott report on a patient with post-traumatic symptoms 50 years after the precipitating events who improved after appropriate treatment.¹ The NHS could do a great deal to treat post-traumatic symptoms in its own workers and so ensure that as few as possible develop similar syndromes.

One study found that up to 61% of clinical staff who report assaults by patients experience symptoms of post-traumatic stress disorder, and 10% meet the criteria for caseness according to the *Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised*.² A Scottish Health Management Efficiency Working Group collected all accident report forms returned by the NHS in Scotland in one week: 262 staff were injured, and the commonest cause of injury (82 cases) was assault. If this was a typical week around 4000 injuries due to assault could be expected to be reported in Scotland each year. If the American

figures hold true at least 400 staff a year may experience post-traumatic stress disorder.

Some health care settings have taken steps to reduce problems in staff after incidents,^{1,2} but in Britain the best example of an attempt at a co-ordinated programme may be that of the Scottish prison service. It has produced a structured response to assaults on staff, which is supported by a programme of management education.

Immediate care includes the opportunity for privacy followed by a one to one interview with a person in a senior management or counselling position to assess the effects of the assault and allow an opportunity for the victim to talk about it. This is followed by a psychological debriefing. The victim is provided with information on possible psychological effects of the assault and on how to seek help if symptoms persist. Longer term care, if needed, is provided by an experienced clinical psychologist. Care is supplemented by the involvement of management, with flexible allocation of duties. This type of care has gained widespread acceptance even in the previously "macho" culture of the prison service.

The NHS must do what it can to prevent its staff—its most important resource—experiencing similar problems to those experienced by Bende and Philpott's patient. This can best be done by acknowledging the frequency of violence and by learning from the example of other organisations and providing structured support for staff victims.

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Generic inhalers for asthma

EDITOR,—A major drive towards generic prescribing is occurring in the NHS on the premise that generic products deliver equally effective results while yielding an appreciable saving on costs. We have reservations about the use of generic inhalers for asthma on both counts. In November last year the NHS Supplies Authority arranged a contract for generic inhalers for asthma and at the same time wrote to the chief executives of all NHS trusts, urging them to ignore approaches from their clinicians on the grounds that they may have been influenced by the manufacturers of branded products. The letter included the statement, "there is no doubt after stringent tests by our [quality control] that the generic product is equally effective with the Allen and Hanburys products." This statement must be called into question since adequate data on therapeutic equivalence are not available to clinicians.

When the Medicines Control Agency first licensed generic salbutamol and beclomethasone inhalers it required only in vitro testing of the new

products and no in vivo testing. In vitro equivalence of two products does not, however, guarantee therapeutic equivalence. Accordingly, the Food and Drug Administration in the United States recommends that both the safety and efficacy of generic salbutamol inhalers should be evaluated clinically to show equivalence to the branded products. While new regulations in Britain also ask for such in vivo data, these requirements are not retrospective. Moreover, the principal in vitro test on which generic inhalers have been licensed—the twin impinger technique—simply divides the aerosol cloud into "respirable" and "non-respirable" fractions and cannot apparently detect differences in the quantity of the very fine particles that penetrate to peripheral airways.¹

Clinical data comparing branded and generic salbutamol products are few; we know of five published studies, none of which support bioequivalence.^{2,3} Similarly, there are good data on branded inhaled steroids but none on the bioequivalence of the generic products. Furthermore, anecdotal reports indicate confusion and concern on the part of patients when they receive a different inhaler simply because they have gone to a different chemist. This again frustrates good management: compliance is a major problem with patients with asthma, and anything that disturbs a patient's confidence will exacerbate this.

Generic substitution of calcium antagonists and long acting theophyllines has been stopped because of concern about dose equivalence, yet generic substitution of inhalers for asthma is being encouraged even though the appropriate studies have not been performed. Is this safe or desirable for patients? We are not against generic products but need to see adequate clinical data on exactly how the generic products compare with the branded products, with a placebo, and with each other before we are prepared to join the headlong rush that is the generic crusade.

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Mike Pearson has given lectures at meetings sponsored by pharmaceutical companies including Allen and Hanburys, Astra, Boehringer, and Fisons and has accepted sponsorship for travel to meetings from Astra and 3M; his unit has done pharmaceutical studies for Allen and Hanburys, Astra, Fisons, Lilly,

Boehringer Ingelheim, and 3M, for which all fees are paid into a charitable chest research fund.

Richard Lewis and Mike Pearson organised a meeting that Allen and Hanburys funded. Richard Lewis has received sponsorship from Allen and Hanburys to attend meetings, and the patent rights for a collapsible inhaler device that he developed were bought by Glaxo.

John Watson's research post is partially funded by Allen and Hanburys.

Jon Ayres has no conflict of interest.

Geoff Ibbotson has accepted fees for giving lectures at meetings sponsored by pharmaceutical companies.

Dermot Ryan has no conflict of interest.

David Flynn has done work for Allen and Hanburys and Glaxo and has accepted sponsorship from Astra, Serono, Ciba, and Glaxo to attend international meetings, and donations to his research fund have been made by Astra, Serono, and Glaxo; an associate has shares in Glaxo.

Jeff Williams has received payments for lecturing on respiratory medicine and has done clinical research that has been sponsored by several pharmaceutical companies, and his asthma specialist nurse is funded jointly by Allen and Hanburys and Astra.

Triglyceride concentration and coronary heart disease

EDITOR,—Despite the intuitive appeal of lowering the triglyceride concentration along with the cholesterol concentration when both are raised there is no evidence that this strategy is more effective than targeting treatment at cholesterol alone. Even treatments that raise triglyceride concentrations diminish the risk of coronary heart disease in hypercholesterolaemic subjects. In the Lipid Research Clinics coronary primary prevention trial, treatment with diet and cholestyramine resulted in a 19% reduction in the risk of coronary heart disease, despite an increase in serum triglyceride concentrations averaging 2.5%.¹ Oestrogen treatment is also associated with increased triglyceride concentrations and a reduced risk of coronary heart disease.² Clinical trials have not established which subgroups of hypercholesterolaemic patients, if any, benefit from a reduction in triglyceride concentrations.

A M Cruikshank notes that the rare patient with severe hypertriglyceridaemia is at risk of pancreatitis³; this association, however, is insufficient justification for universal screening of triglyceride concentrations. Certainly, screening could detect some hypertriglyceridaemic subjects who would otherwise be overlooked. But severe hypertriglyceridaemia in the range associated with pancreatitis is usually obvious from its physical manifestations and from visual inspection of a lipaemic blood specimen. Seldom will the result of a screening test be the sole clue to an extreme increase in triglyceride concentration.

The varied results in the literature make it possible to select studies that show an independent association between hypertriglyceridaemia and coronary heart disease, like the three that Peter H Winocour cites.³ But many studies support the opposite conclusion.^{4,5} Triglyceride concentrations may have a role in predicting risk when well standardised measurements of high density lipoprotein cholesterol concentration are not available, as Winocour suggests. The negative correlation between the two measurements means that the triglyceride concentration can serve as a surrogate for the high density lipoprotein cholesterol concentration, albeit a relatively imprecise one. For any lipoprotein test, and especially for one measuring triglycerides, its accuracy in predicting risk depends on the quality of the measurement in the specific laboratory, so clinicians should learn about the accuracy of lipid tests available in the laboratory they use.

Whether to measure the triglyceride concentration is largely a moot issue once hyper-