sources outside the systematic review, such as relevant cohort studies.[1]

Senn's concerns arise from what he calls the principle of "label invariance." We agree that many analyses of data from clinical trials are unaffected by which group is called the treated group and which the control group. The distinction does, however, need to be made in analyses of underlying risk, when this term usually refers to the risk in the placebo, control, standard, or reference treatment group. In a withdrawal trial the "standard treatment" group would comprise those patients receiving the active treatment, because then the question of interest is whether the effect of withdrawing this treatment is the same for patients who are at different levels of risk while they are receiving it. In a trial comparing two active treatments, A and B, the definition of underlying risk would depend on the precise question being addressed, which might be the effect of changing from A to B given the risk associated with A or, alternatively, the effect of changing from B to A given the risk associated with B.

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1 Glasziou P, Irwig L. An evidence based approach to individualising treatment. *BMJ* 1995;311:1356-9.

Britain was healthier than Germany in 1914

EDITOR,—In his review of my book *The Economic Laws of Scientific Research* Tom Wilkie writes that its thesis has been disproved by a historical experiment.[1] Since, however, I believe that it is he who has got the experiment wrong, and since it concerns matters of medicine, I should like to correct his statement.

Wilkie says that "when called up for service in the first world war those German peasants [were] taller, healthier, and stronger than the British proletariat." The standard authors in this field are Mitchell[2] and Winter.[3 4] Their studies show that the British were much healthier than the Germans in 1914. Thus infant mortality was 160/1000 births in Germany but only 100 in England and Wales and 110 in Scotland. Between 1901 and 1914 life expectancy at birth was between one and three years greater in Britain than in Germany. None of this is surprising, as the British gross domestic product per capita was 125% of Germany's.[5] Yet that increased wealth also threatened health as it was associated with urbanisation, so it is remarkable that British rates of tuberculosis were lower and that the British were taller, particularly when similar populations are compared. This error is widely believed, and this letter provides a useful opportunity of correcting it.

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1 Wilkie T. The economic laws of scientific research [book review]. *BMJ* 1996;313:697. (14 September.)
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Influences of practice characteristics on prescribing in practices

Multiple regression models depend on explanatory variables included

EDITOR,—Although Robert P H Wilson and colleagues acknowledge that demographics and morbidity are important influences on variations in prescribing costs at the level of health authorities, they proceed to consider multiple regression models for variation in prescribing at the level of practices that do not allow for either of these as explanatory variables.[1]

Analysis of patient linked prescribing data has shown that, within practices, the prescribing rate for those aged 55-64 is about six times that for children and young male adults, and for those aged over 65 the factor is 10 or more.[2] The authors' use of rates per prescribing unit rather than per patient as the dependent variable (1 prescribing unit for those under 65; 3 prescribing units for those ≥ 65) may give some preliminary adjustment for age but makes no allowance for the wide variation between the age bands under age 65. Both the effect size and the significance of explanatory variables in regression models may depend heavily on the presence or omission of other explanatory variables.[3] Furthermore, the authors' model for $\log_e$ (1993-4 costs), which includes historical costs as an additional explanatory variable, explains 67% of the variation, compared with 7% without this variable, and yet they quote only the estimated coefficients from this latter worse fit model.

On a more positive note, the use of log (prescribing rate) as the dependent variable is intuitively more plausible than the common practice of using the rate itself.[4 5] The linear regression model for log (rates) transforms to a multiplicative model for effects of explanatory variables on the prescribing rate, which accords far better with reality. (Effects are then in terms of percentage change rather than absolute change.) Having embarked on using the multiplicative model for prescribing rates, however, the authors then consider the absolute difference in rates between the two years studied rather than the difference in log (rates), thus reverting to the additive case. Increases of £15 in practices with initial (1990-1) rates of £30 and £45 per prescribing unit are very different in percentage terms and should not be interpreted as equivalent.

The validity of results and conclusions drawn from multiple regression models depends heavily on the goodness of fit of the models, yet appropriate assessments, such as analysis of residuals,[3] are rarely satisfactorily reported and probably never conducted in many cases.

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1 Wilson RPH, Hatcher J, Barton S, Walley T. Influences of practice characteristics on prescribing in fundholding and non-fundholding general practices: an observational study. *BMJ* 1996;313:595-9. (7 September.)
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Authors' reply

EDITOR,—We agree with Sarah J Roberts that an ideal analysis would reflect all morbidity and demographic factors that may influence prescribing. However, breakdowns by age and sex were not available to us for all the practices in the former Mersey region for the period of our study. Thus we used the best available information for our analyses.

It is well known that prescribing in any year is strongly related to historical patterns of prescribing. In our paper, however, we aimed "to investigate the variation in prescribing among general practices by examining the contribution to this variation of fundholding, training status, partnership status, and the level of deprivation." The determinants that we were investigating would also have influenced historical costs. We therefore emphasised those analyses that did not include historical costs.

Goodness of fit was investigated for all models by examination of the percentage of variation explained and the distribution of the residuals (as stated in the methods). We used the log transformation of all the dependent variables, except the changes between years, to normalise the residuals from the regression and thus to improve the fit of the model. We did not transform the data for the changes between years because in these instances transformation did not change the fit of the model. We thought that interpretation of the analyses was easier in the natural scale.

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Postal surveys in general practice

More analytical studies should be carried out

EDITOR,—Having received many questionnaires (as a single handed general practitioner) and having produced many (as a trainee in public health medicine), I share Brian R McAvoy and Eileen F S Kaner's desire to see changes in both the quality and quantity of questionnaire surveys.[1] I believe, however, that the time has now come to move on from the emphasis on questionnaire studies if general practice is to develop a credible research base. Randomised controlled trials may often be inappropriate, but analytical studies (especially the case-control design) seem to have been largely ignored as a research method in primary care.[2] Analytical studies seem ideally suited to the examination of many issues in general practice and, if undertaken rigorously, provide stronger epidemiological evidence than a questionnaire survey does.[3]

Table 1 shows the results of a Medline search from 1992 to 1996 with three MeSH subject headings: case-control studies, questionnaires, and family practice. The overall ratio of

Table 1—*Result of Medline search for "case-control studies," "questionnaires," and "family practice" 1992-6*

MeSH heading	No of citations
1 Case-control studies	9172
2 Questionnaires	14 786
3 Family practice	6863
1+3	21
2+3	548

questionnaire studies to case-control studies was 1.6:1, whereas for family practice the ratio was 26:1.

The time has come to redress the balance and move on from placing too much emphasis on questionnaire surveys as a quantitative method of research in general practice.

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1 McAvoy BR, Kaner EFS. General practice postal surveys: a questionnaire too far? *BMJ* 1996;313:732-4. [With commentaries by S Lydeard and by M P Springer and H W J van Marwijk.] (21 September.)
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3 Hennekens CH, Buring JE. *Epidemiology in medicine*. Boston: Little, Brown, 1987.

Surveys demand too much time

EDITOR,—I suppose that I identify myself as one of the general practitioners who do not respond to postal surveys as defined by Brian R McAvoy and Eileen F S Kaner—older, more experienced, and possibly under stress.[1] But there is another reason for the failure to complete and return questionnaires.

Over the past few months I have been collecting (not returning) questionnaires and now have a total of 19. Eight of these are "national" surveys, nine are from my family health services authority or health authority, and the remaining two I am unable to classify. One offered to advise me of the results; five had "threatening" deadlines (this must be completed and returned by ...). The only incentive to completion was the chance to win a weekend in Amsterdam. Given that each questionnaire would take some 10-15 minutes to complete, filling them all in would take 3-4 hours of my time. I recollect that in my first 10 years in general practice I completed perhaps one survey a year.

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Scotland's new chief medical officer welcomes reforms of training

EDITOR,—A recent item in Medicopolitical Digest implied that I (now the chief medical officer in Scotland) was critical of the current reform of postgraduate training.[1] This is not the case. I welcome the reforms, and during my chairmanship of the Scottish Council for Postgraduate Medical and Dental Education I helped to alter the funding and delivery of postgraduate training. My purpose at the BMA's clinical meeting in Istanbul was to highlight several unresolved issues that could adversely affect implementation of the reforms and compromise moves towards a health service delivered by consultants.

I did indeed emphasise the problems posed by a reduction in the hours of training, and, while I subscribe totally to the view that specialist training can be condensed if training programmes are structured, we must be careful to ensure that the consultants who emerge are sufficiently experienced to fulfil the demands expected of them. Junior doctors in some acute specialties are aware that a reduction in working hours may adversely affect their training if carried too far, and there have been heartening moves to define and monitor the quality of training offered to them. I strongly oppose any return to the prolonged unstructured apprenticeships of the past, but I suspect that some doctors pursuing careers in highly specialised areas may elect to gain additional experience after completing conventional specialist training.

I am not enthusiastic about the suggestion that consultants produced by the new training programmes will be identified as junior consultants, and I suspect that most of them would find this offensive. We all, however, need to accrete experience throughout our professional life, and many newly appointed consultants will find the help of senior colleagues particularly welcome at the start of their consultant career. In surgery there is a growing acceptance that the nature of a consultant's working week may change as his or her career progresses, and this could be beneficial as far as support for new colleagues and an increased role in teaching are concerned.

It would be tragic if the potential benefits of the reforms of training were lost because of failure to make the necessary adjustments elsewhere in the system. The successful development of all aspects of our NHS will depend on the continued commitment of a motivated and sufficiently numerous consultant workforce. Postgraduate training is no exception.

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1 Beecham L. New Scottish CMO criticises training reforms. *BMJ* 1996;313:947. (12 October.)

Adverse events associated with mefloquine

Study in returned travellers confirms authors' findings

EDITOR,—The excess of disabling neuropsychiatric side effects of mefloquine reported by P J Barrett and colleagues has attracted attention.[1] Focus on disabling reactions has detracted from milder disturbances, which may be sufficiently common to reduce compliance and increase the risk of malaria.[2] We conducted a questionnaire based survey among recently returned travellers to assess the impact of adverse reactions on compliance.

Altogether 347 questionnaires were returned (response rate 60.5%), 255 of which were from respondents who had been born in malaria free areas, were based in Britain, and were attending our hospital for reasons not involving malaria. The median age of these 255 patients was 30.5 years and their median length of travel 3.2 months. One hundred and thirteen respondents had taken mefloquine, 81 had taken chloroquine plus proguanil, and 61 had used alternative regimens or no prophylaxis. The rates of reported side effects were high: 80 (71%) respondents who had taken mefloquine and 52 (64%) who had taken chloroquine plus proguanil reported one or more side effects. Depression and anxiety were more common in those who had taken mefloquine, with 23 (20%) of this group and 8 (10%) of those who had taken chloroquine plus proguanil reporting symptoms ($\chi^2 = 3.86$, $P<0.05$). Only 16 (14%) of those who had taken mefloquine and 11 (14%) of those who had taken chloroquine plus proguanil, however, reported having stopped their prophylaxis because of side effects.

Forty five (30%) travellers to Africa and eight (8%) travellers to other destinations had been treated for symptoms of malaria at least once. Among the travellers to Africa 24 (26%) of the 94 who had taken mefloquine and 17 (40%) of the 43 who had taken chloroquine plus proguanil had been treated for symptoms of malaria, and seven had stopped using prophylaxis as a result. The drugs used for treatment varied and in some instances were potentially ineffective or dangerous.

Although people attending hospital are not representative of travellers as a whole, our survey supports Barrett and colleagues' findings of an increased frequency of neuropsychiatric side effects in people taking mefloquine. Side effects severe enough to necessitate discontinuation of prophylaxis were, however, similar in people taking mefloquine and those taking chloroquine plus proguanil. A high proportion of the cohort had received treatment for symptoms of malaria while abroad. Travellers need advice on drugs' side effects before they travel and should ideally be provided with emergency treatment for use if malaria is diagnosed abroad. They should be warned of the risk of breakthrough infections and advised not to stop their prophylaxis without seeking medical advice.

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1 Barrett PJ, Emmins PD, Clarke PD, Bradley DJ. Comparison of adverse events associated with use of mefloquine and combination of chloroquine and proguanil as antimalarial prophylaxis: postal and telephone survey of travellers. *BMJ* 1996;313:525-8. (31 August.)
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Women may be more susceptible to adverse events

EDITOR,—The methodology that P J Barrett and colleagues used in their study comparing adverse events associated with mefloquine with those associated with chloroquine plus proguanil for antimalarial prophylaxis[1] is similar to that used in a study that Kass and I carried out.[2] We, however, compared mefloquine with doxycycline, which is widely used by Australians and North Americans as the alternative to mefloquine for travellers to chloroquine resistant areas.[3] Our subjects were enrolled in the study prospectively, at the time that their drug was chosen, and received a postal questionnaire after returning from their trip. It is reassuring that, with respect to the tolerability of mefloquine, our results were so similar to those of Barrett and colleagues (table 1)

Barrett and colleagues detail the cases of 10 people who used mefloquine and suffered disabling neuropsychiatric adverse events. They do not, however, comment in their discussion on the fact that eight of these subjects were women. This would represent a rate of disabling neuropsychiatric events in women taking mefloquine of 8/698 (1.1%). In our study all disabling adverse events occurred in women taking mefloquine, with a rate of major neuropsychiatric events of 3/171 (1.8%). Two of the three women