Pyorala *et al*[4] suggested the possibility that this decreased anticoagulant tolerance was not due to a retardation of the metabolism of the anticoagulant drugs. Their results suggested that C_{17}-alkylated steroids affect the turnover of vitamin-K-dependent clotting factors, an impairment of synthesis being a likely mechanism. It was thought possible that C_{17}-alkylated steroids might diminish the stores of this vitamin available for metabolic competition with anticoagulant agents.

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[2] Pyorala, K, and Kekki, M, *Lancet*, 1963, **2**, 360.
[3] Murakami, M, *et al*, *Japanese Circulation Journal*, 1965, **29**, 243.
[4] Pyorala, K, Myllyla, G, and Kekki, M, *Annales Medicinae Experimentalis Fenniae*, 1965, **43**, 95.

Tuberculosis among immigrants in Glasgow

SIR,—We take your correspondents' point on the subject of tuberculosis notifications (Dr W Ducat and his colleagues (21 May, p 1346)). We did not in fact have the figures for the immigrant children population in Glasgow and were more concerned to discover the actual number of cases in the two schools selected for this investigation.

As far as the incidence of BCG vaccination is concerned, this was determined by questioning the parents and by observing the BCG scars on the children's arms. This is presumably a matter either of sampling or perhaps the accuracy of central records. On the question of overcrowding we should perhaps have made it clear that the figures for the number of people per room were obtained by health visitors who visited each home and questioned the householders. We have no hesitation in accepting their findings in preference to census reports for the whole of Glasgow in 1971.[1]

Finally, we were very concerned to think that our survey would give the impression that the incidence of tuberculosis no longer warranted further action in Glasgow. It is indeed difficult to see how the finding of the same incidence or primary tuberculosis in Scottish as in Asian children and three times as many in Chinese children could give rise to such an idea. We yield to no one in our desire for an intensive and concerted effort to eradicate tuberculosis from Glasgow. Indeed we consider such a project considerably overdue.

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[1] Registrar General, *Scotland 1971 Census*. Edinburgh, HMSO.

Diet and coronary heart disease

SIR,—As chairman of the committee which organised the Bromley Area Health Authority campaign I feel I must reply to Sir John McMichael's letter (4 June, p 1467). The leaflet we produced contained only advice given by the Joint Working Party of the Royal College of Physicians and the British Cardiac Society. It was written by a senior dietitian with great experience in the paediatric field. Apart from advice aimed at reducing the total family fat intake it dealt with many other aspects of diet such as reducing sugar and spending the family food budget more wisely. The leaflet was only given to mothers by health visitors after discussion, and I strongly resent the statement that it could be a cruel and terrifying imposition.

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Risk of coronary heart disease in different populations

SIR,—We were greatly interested in the recent contribution by Dr T Khosla and others (5 February, p 341) on attempts to measure the risk of developing coronary heart disease (CHD). In South Africa we live in juxtaposition with populations having contrasting pronenesses to CHD. Accordingly, we have wondered to what extent the variables cited by the above workers (age, serum cholesterol, blood pressure, tobacco usage) have different connotations of risk in different populations.

In their comparisons of CHD incidence and mortality rates in the United States and countries in Europe Keys *et al*[1] stated: "Rules for clinical judgments and ECG criteria and the details of the examinations and their spacing were identical, yet the US men had an incidence rate of hard CHD roughly double that of European men of the same age, blood pressure, serum cholesterol and smoking habit. Even consideration of relative body weight and of physical activity does not change the discrepancy. The conclusion seems inescapable that the incidence of CHD is strongly influenced by one or more variables unrelated to any considered in these studies." In the study on CHD in seven countries,[2] in the case of Greece the observed CHD mortality rate was only 30% of the expected rate.

The CHD position in Third World countries is especially interesting. In India CHD is reported to be common in large centres of population. The great majority of patients are under 60 years[3]; moreover, their serum cholesterol levels are low.[4] It would therefore seem that in Indians the factors of age and cholesterol level have noxious significance greater than those obtaining in Western populations.

Among South African Blacks in big urban centres, for example, Johannesburg, all orthodox CHD risk factors are present in large proportions of adults.[5] Actually, prevalence of hypertension is much higher than that prevailing in local Whites. Yet CHD is extremely uncommon in urban Blacks. In 1976 there were only 14 deaths from CHD at Baragwanath Hospital, which draws patients from a surrounding population of over a million. Obviously these people suffer far less from CHD than would be predicted from known prevalences and intensities of risk factors.

It is interesting that regarding another variable, serum $\alpha 2$ globulin, it has been reported that CHD patients in Western countries have significantly higher values than controls.[6] Yet we found mean values for elderly rural South African Blacks, among whom CHD is virtually absent, to be significantly higher (for a variety of reasons) than values on White CHD patients.[7]

Thus the risk factors mentioned either have different connotations in different populations, or influential factors, whose identity is not known, are in operation which either favour or inhibit CHD development.

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[2] Coronary Heart Disease in Seven Countries, *Circulation*, 1970, **Suppl 41, No 1**, 186.
[3] Lal, H B, and Caroli, R K, *Indian Heart Journal*, 1967, **19**, 12.
[4] Banerjea, J C, and Mukkerjee, S K, *Indian Heart Journal*, 1970, **22**, 288.
[5] Walker, A R P, *American Heart Journal*, 1975, **89**, 133.
[6] Ducimetiere, P, Warnet, J M, and Richard, J L, *Journal of Chronic Diseases*, 1976, **29**, 423.
[7] Walker, A R P, and Walker, B F, submitted for publication.

Hazards of the sauna

SIR,—Dr Sandra Dean and others give a report (4 June, p 1449) relating to the hazards of the sauna in which it was stated that the temperature of 43°C was that of the average sauna bath. This is somewhat on the low side as the usual range of temperature of the sauna room is 80° to 100°C. A novice bather should be able to tolerate a sauna temperature of around 80°, though an experienced bather can tolerate 100°C. The usual period of time exposed to those temperatures is some 10 to 15 minutes, however, and not the five hours quoted in the paper, admittedly at an apparently lower temperature.

I speak with some experience as a sauna was installed in our new surgery during construction, and I consider it one of the finest investments we ever made.

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Suppression of intractable cough

SIR,—The suppression of intractable cough without impairment of other body functions and faculties is a desirable objective rarely achieved by the commonly used cough suppressants. Three patients under our care have been so relieved with lignocaine aerosol (28 May, p 1374).[1]

One patient with a rapidly progressing oat cell carcinoma of the lung with considerable mediastinal involvement suffered uncontrollable distressing cough by day and night. This cough, which was distressing not only to himself but to the whole family, was almost completely relieved after two lignocaine aerosol treatments. He subsequently died peacefully without further medication. The second patient had an alveolar cell carcinoma of four years' standing. Her increasing breathlessness was greatly aggravated by constant cough causing retching and vomiting. After two treatments five days apart her condition was greatly improved and the cough was suppressed. It has, however, been found necessary to repeat these inhalations at varying intervals during two months. By this means her life has been made tolerable. A third patient with bronchial carcinoma developed a distressing

persistent cough following radiotherapy. An inhalation of lignocaine relieved the cough within two hours and the effect continued for a week when a further inhalation was given. Since that time there has been no recurrence of the severe coughing fits.

Each of these patients obtained relief with lignocaine 400 mg in saline administered via a Bird Micronebulizer. Salbutamol 2-5 mg was given by wet inhalation immediately before each treatment. It is our impression that mucus clearance was not impaired in these three patients. From this very limited experience we would not withhold lignocaine aerosol treatment in any patient who had distressing and otherwise uncontrollable cough and was suffering a fatal illness. We would agree with you that further evaluation of this technique is necessary in other types of illness giving rise to severe cough, particularly until the possible effects on mucus clearance is better understood.

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[1] Howard, P, *et al*, *British Journal of Diseases of the Chest*, 1977, **71**, 19.

Randomised clinical trials

SIR,—Your leading article (14 May, p 1238) presents a good case for randomised clinical trials (RCTs). Alas, I feel that many investigators will still be unconvinced, arguing that non-randomised trials are justified if no sources of bias can be identified. Thus, I would like to present some evidence that bias can exist without any apparent explanation.

In the United States cancer chemotherapy co-operative groups it is common practice to include the same control treatment in consecutive RCTs. At the statistical laboratory in Buffalo, New York, I identified 19 such pairs of trials, mostly in advanced lung cancer, and compared the annual death rates of the two groups of patients on the same treatment:

The trials were fairly large, most having over 100 patients per treatment, and there were no known sources of bias. One would have expected little change in death rates on the same treatment from one trial to the next, whereas, in fact, the changes ranged from −46% to +24%. In four instances the change was statistically significant at the 5% level (using a two-sided F-test for comparing two exponential death rates) and a further six changes were significant at the 20% level. Such marked evidence of differences between trials indicates that any comparison of treatments not within an RCT must be deemed highly suspect.

Regarding the failure to achieve sufficient patients, a current survey on the size of RCTs conducted by P Armitage, D A G Galton, and myself provides some interesting evidence. From a random sample of 50 cancer trials registered with UICC during 1972-5 our preliminary results based on 30 replies to a questionnaire indicate a median accrual rate of 34 per annum (total on all treatments) and a median of 5 years' accrual to achieve the prespecified number of patients. Evidently many will not achieve their accrual targets, so that although the design and execution of these trials were on the whole satisfactory a substantial number will prove inconclusive owing to the failure to make a realistic assessment of patient accrual.

This survey also showed that nearly all trials have repeated analyses of results, the most common interval between analyses being 6 months. Neither fixed nor sequential designs cope satisfactorily with such periodic assessments, but some recent developments in "group sequential" designs do provide a proper statistical basis for this approach.[1-3] A further point from the survey was that two-thirds of trials incorporated stratification for prognostic factors in the randomisation. Thus your leading article's declaration that stratification is unnecessary is not being followed, and I think this is sensible in view of the fact that retrospective adjustment in analysis requires rather sophisticated statistical methods and even these are useless in cases of severe imbalance.

Also, I think the suggestion of an unequal randomisation (say, a 2:1 ratio), whereby a greater proportion of patients receive the new treatment, is to be encouraged. This is especially true if there are suitable historical data on the old treatment, since there exist statistical methods for incorporating such extra information into the trial's design and analysis.[4] Lastly, I think the conversion of investigators to RCTs would be enhanced considerably if medical journals took a firmer stance in refusing to publish the results of non-randomised studies when an RCT was appropriate.

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[2] Pocock, S J, *Biometrika*, 1977 (in press).
[3] Canner, P, *Biometrics*, 1977 (in press).
[4] Pocock, S J, *Journal of Chronic Diseases*, 1976, **29**, 175.

Delivery of postgraduate education

SIR,—Professor A H Crisp (28 May, p 1397) has illustrated admirably the dilemma that faces many university departments in trying to strike a balance between undergraduate and postgraduate teaching responsibilities. In Wessex we were more fortunate than Professor Crisp in that a well-established postgraduate teaching programme existed long before the medical school at Southampton was opened, and to maintain the high quality of this programme academic sessions were specifically allocated for this purpose. Nevertheless, problems still persist, and in addition to the salaried sessional commitments by clinical tutors, suggested by Professor Crisp, a reappraisal of the teaching responsibilities of academic staff is necessary.

Although for historical and administrative reasons university clinical departments are funded according to their undergraduate teaching commitments) it is impossible (and inappropriate) for them not to be associated with postgraduate training. This should be recognised as a formal commitment to maintaining academic standards through their region. This commitment can to some extent be balanced by greater involvement of clinical teachers in undergraduate teaching. In our undergraduate teaching course in psychiatry we involve many consultants throughout the region, who devote considerable time and effort but who receive no recognition apart from the title of honorary clinical teacher. Formal recognition is needed of these changes in the job descriptions of both academic and clinical staff in addition to the extra funding that Professor Crisp suggests if we are to maintain a healthy integration between academic and clinical teaching responsibilities.

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Management of elderly demented patients

SIR,—Your leading article (21 May, p 1301) on the management of elderly demented patients is aptly coloured in pessimistic lines familiar to those who have dealt with such patients and families. Having referred to a recent conference[1] you lapse immediately into an attitude of *caring* for what seems to be assumed to be an a priori irreversible state. I wish to make two points.

(1) Although you mention "accurate diagnosis," this is quickly passed over. Recent work[2 3] indicates that a reversible cause for dementia is present in between 10 and 20% of patients referred to both specialist units and district general hospitals provided that investigation is adequate. Age alone is no guarantee that dementia is caused by irrevocable cerebral degenerative pathology. Such facts are politically unpalatable in times of stringency, because the tests necessary to the proper study of demented patients include time-consuming and expensive metabolic and neuroradiological investigations, not least the EMI scan. It is, however, our professional duty to patients to indicate clearly that unless these methods are applied to the vast numbers involved (at least 5% of the over-65s, who number several million in the UK) many will be thrown on to the scrap heap and will require unnecessarily the expensive facilities of hospitals, hostels, and day centres your article describes so well.

(2) In discussing management you fall back on the trendy euphemism of the caring team (*sic*). You say, "the doctor's role is as a member of the caring team, *not necessarily as its leader* . . ." (my italics). Is it not time we dispelled this currently fashionable notion so widely advocated by the radical chic on TV and radio? The exclusion of the doctor from leading the team, assuming that a team is needed in all cases, leads to the omission of proper diagnostic methods, the consequent prognosis, and to the pitiful retreat implicit in the practice of subsequent care. The properly trained doctor is the only person capable of initiating the correct sorting out and selection of patients for investigation. And he is the only person capable of talking to relatives in a manner based on the full understanding of the patients' disease in its complex pathological,