Letters

Effectiveness of regional trauma systems

**Longer versions of three of these letters appear on the BMJ's website (www.bmj.com)*

Improvements have occurred since study*

Editor—Nicholl and Turner's attempt to perform a definitive before and after study on regionalised trauma care was beset by logistical problems.[1] Firstly, ambulance workers were not empowered to bypass the surrounding hospitals, who in turn were reluctant to be bypassed during the vulnerable period of health service reforms. Secondly, similar systems were compared. The central hospitals in Stoke, Hull, and Preston are all large hospitals with neurosurgical units on site. Thirdly, data were not collected prospectively. The researchers trawled the patients' case records often years after admission. Notes from 1990 were not requested for initial examination until 1993, by which time many had been reduced and put on to microfiche.

Fourthly, the local researcher was not trained on the nationally recognised injury scaling course. There were no intra-observer variability checks to confirm consistent application of scoring methods over the four years. Lastly, significant discrepancies in data accuracy were evident. When the number of direct admissions with severe trauma in 1993 were compared with those counted by the Trauma Research Group at Keele University there was a 25% difference. An outside expert scored the same patients independently and concurred with the Keele findings to within 3%.

Since 1994 we have adopted a strategy to enhance data accuracy. Details on every major trauma patient are checked weekly by a senior clinician and circulated to medical and nursing staff involved in the patient's care. Data shared freely in the clinical domain acts as a two way feedback system to promote accuracy and militate against entry bias in the trauma database. The problem of data validation must be addressed nationally, especially if audit information is to be released to purchasers of health care.

Nicholl and Turner's study represents at best a snapshot at the start of the development of the trauma system. Since then much progress has been made. Last year, our crude mortality in patients with severe trauma was 20%, compared with 38% in 1989-90.[2,3] The pattern of trauma deaths with many cases of potentially salvageable major haemorrhage, referred to in the Royal College of Surgeons' report,[4,5] is no longer evident: 88% of deaths after major trauma were in patients with a critical head injury or aged over 70 years.

Nicholl and Turner raise important issues but further careful studies are required to serve as evidence on which to base national policy.

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1 Nicholl J, Turner J. Effectiveness of a regional trauma system in reducing mortality from major trauma: before and after study. *BMJ* 1997;315:1349-54. (22 November.)
2 Trauma Research Group. *An incidence study of trauma in the North Staffordshire Health District.* Stoke on Trent: Keele University, 1991.
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Wrong comparisons were made*

Editor—Nicholl and Turner's study of the North Staffordshire trauma system adds further confusion to the debate on trauma management in the United Kingdom.[1] The title "effectiveness of a regional trauma system" is misleading. A trauma system is much more than a trauma centre. The trauma system was never fully established; during the study only 36% of the seriously injured patients in the experimental region were taken directly to the trauma centre. Instead of comparing the outcome of these patients with that of those taken to district general hospitals in the experimental region, the authors chose two comparison regions; both had single central hospitals with good accident and emergency departments and neurosurgical facilities on site. The central hospitals in the comparison areas received a greater proportion of the major trauma patients in their respective regions than did the experimental trauma centre. Thus, to some extent, the comparison regions were closer to functioning as trauma systems than the experimental region.

Most severely injured patients in Britain will be taken to an average district general hospital which will have an accident and emergency department of variable size and which will not have neurosurgical facilities on site. Only half the accident and emergency departments admitting more than 30 000 patients a year operate a trauma team system.[2] In Britain what we need to know first is whether outcome for severely injured patients is improved if we compare the average district general hospital with a hospital that has all acute specialties, including neurosurgery, on the same site. Outcome measurements should include morbidity; mortality alone is too insensitive. If the perceived benefit of a single site trauma hospital is confirmed the political levers are in place to introduce and study the effect of the wider concept of a regionalised trauma system. Under this system severely injured patients would be taken directly to the trauma centre, bypassing the nearest district general hospital.

The study does perhaps provide us with a clue to the most effective means of reducing deaths from trauma. The 20% fall in the number of major trauma patients seen in the experimental region over the four years was said to reflect a 28% reduction in the number of road traffic accidents and serious injuries recorded by the police. When it comes to reducing trauma deaths, the

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Advice to authors

We receive more letters than we can publish: we can currently accept only about one third. We prefer short letters that relate to articles published within the past four weeks. We also publish some "out of the blue" letters, which usually relate to matters of public policy.

When deciding which letters to publish we favour originality, assertions supported by data or by citation, and a clear prose style. Letters should have fewer than 400 words (please give a word count) and no more than five references (including one to the BMJ article to which they relate); references should be in the Vancouver style. We welcome pictures.

Letters, whether typed or sent by email, should give each author's current appointment and full address. Letters sent by email should give a telephone and fax number when possible. We encourage you to declare any conflict of interest. Please send a stamped addressed envelope if you would like to know whether your letter has been accepted or rejected.

We may post some letters submitted to us on the world wide web before we decide on publication in the paper version. We will assume that correspondents consent to this unless they specifically say no.

Letters will be edited and may be shortened.

"biggest bang for the buck" must surely come from accident prevention.

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1 Nicholl J, Turner J. Effectiveness of a regional trauma system in reducing mortality from major trauma: before and after study. *BMJ* 1997:315:1349-54. (22 November.)
2 Kazemi AR, Nayeem N. The existence and composition of trauma teams in the UK. *Injury* 1997;28:119-21.

Data do not support conclusions

EDITOR—Nicholl and Turner conclude that "any reduction in mortality from regionalising major trauma care in shire areas of England would probably be modest compared with reports from the United States." This conclusion is difficult to make from the experiment carried out in the North West Midlands region and certainly cannot be extrapolated to other regions of the United Kingdom.

The study compared an experimental region with two control regions, but during the study the proportion of patients with major trauma in the experimental region taken to the trauma centre increased only from 34% to 39%. Over 60% of major trauma victims were taken to other hospitals in the region, and these patients were included in the comparison with the control regions. The authors admit that there were only "small changes in the processes of care" and they also go on to say that the "trauma system did not develop into a comprehensive regionalised system" and the primary objective of "getting the right patient to the right hospital at the right time" was not achieved. The trauma centre had all key specialties on one site and 24 hour attendance by accident and emergency consultants, but it is not clear if there was also 24 hour attendance by experienced surgeons, radiologists, and anaesthetists.

It is impossible to conclude from this study that trauma centres anywhere in the United Kingdom would not improve survival—and in areas such as the West of Scotland there is a good argument for a trauma centre. In Glasgow during 1992-7, 16% of all major trauma was penetrating wounds (Scottish Trauma Audit Group, unpublished data), which is closer to the American figure of over 20% than the overall British figure of less than 5%.[1] In fact, the stabbing rate per capita in Glasgow is greater than that of inner city America.[2] The Glasgow hospitals serve a large urban population and receive tertiary referrals from a vast rural area, including Hebridean islands, Argyll (and its mountains), Dumfries, and Galloway.

Scotland has a single ambulance service and this could help integrate a land based and helicopter retrieval service, which could use 24 hour accident and emergency doctor cover. Perhaps the Department of Health should consider funding a new experiment into the development of a trauma service in the West of Scotland?

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1 Nicholl J, Turner J. The effectiveness of a regional trauma system in reducing mortality from major trauma: before and after study. *BMJ* 1997;315:1349-54. (22 November.)
2 Wright J. Public health aspects of assault: a Scottish accident and emergency department perspective [MPH project]. Glasgow: Glasgow University, 1997:23-6.

Authors' reply*

EDITOR—Oakley and colleagues and Parr and Nolan pick up on several points to which attention was drawn in our article. Firstly, it is true that a regional system never really developed in the North West Midlands during the four years we studied (1990-3), but this is better viewed as a significant result of the study rather than a criticism.

Secondly, the comparison regions were similar to the experimental region, but as we stressed, this was deliberate. This is an essential part of the design of controlled before and after studies (or community intervention trials). The similarities between areas in 1990 allowed us to observe what the effect of spending over £1 million per year on trauma care in one of the areas achieved relative to the other areas. The fact that the areas were still similar in process and outcome in 1993 was precisely the point of our paper.

Thirdly, with regard to the accuracy of the data collection and injury scoring, we did have a period of prospective data collection (1993), and the injury coders were trained together to achieve internal consistency, which is the key issue in the validity of the study.

The discrepancy in the number of major trauma patients recorded in 1993 (98 in our study *v* 123 collected by the Trauma Research Group) was discovered after a check instigated by us. That check also revealed that while we had found 108 cases in 1990, the Trauma Research Group had recorded only 67.[1] Our data suggest that the numbers of major trauma cases may have fallen slightly during the study; the research group data that they had nearly doubled. Since the number of fatal and serious road traffic accident casualties, which make up 57% of the Trauma Research Group's major trauma caseload, fell by 28% over the study period according to police statistics we are confident in our data.

Finally, we agree wholeheartedly with all the correspondents and especially Dr Wright that in other environments with other arrangements or in the longer term, a regionalised system based on a trauma centre could still produce improvements in outcome. However, we believe that even in the West of Scotland these benefits will be modest compared with those reported in the United States and that even these modest benefits did not fully materialise in the north west midlands between 1990 and 1993.

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1 Nicholl J P, Turner J, Dixon S. The cost-effectiveness of the regional trauma system in the North West Midlands. Sheffield: Medical Care Research Unit, University of Sheffield, 1995.

Has the *BMJ* discovered an end to ageing?

EDITOR—Having deliberated over using the word "ageing" or "aging" in a manuscript,[1] I was interested to see that the *BMJ* preferred to use the spelling without the "e" in their "aging issue" (25 October 1997). Given that the *Concise Oxford Dictionary*[2] gives credence to both spellings, I wished to establish if a consensus existed within the medical literature. A Medline search of the years from 1967 to 1996 showed that of the 14 039 titles in English that included the word, 11 774 (84%) used "aging." However, marked regional differences existed. For example, 98% (7646/7777) of papers published in the United States used "aging," while 51% (1116/2178) of the papers cited in journals published in England preferred the spelling "ageing." Nevertheless, these figures hide the fact that in the past 30 years fewer journals from England appear to be putting the "e" in "ageing": from 1967 to 1976 the word "ageing" accounted for 72% (303/422) of spellings, from 1977 to 1986 it was used 49% (339/688) of the time, and by 1987 to 1996 only 44% (474/1068) used this spelling. With the addition of your "aging issue" it would seem that the United Kingdom, like the rest of the world, is seeing an end to "ageing."

So why did I choose to use the word "ageing" in my manuscript? Because it looked right.

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1 Kilpatrick ES, Dominiczak MH, Small M. The effects of ageing on glycation and the interpretation of glycaemic control in Type 2 diabetes. *Q J Med* 1996,89:307-12.
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*Our house style is based on *Chambers English Dictionary*. When two or more options are given for spelling, as a rule we use the first. The new edition of *Chambers, Chambers 21st Century Dictionary* (1996), gives the spelling "ageing" first. Times change and so does our house style. From publication of this letter we will spell ageing with an "e."—EDITOR

Elder abuse should have been discussed in issue on ageing

EDITOR—The *BMJ* should be complimented for devoting an entire issue to healthy ageing (25 October 1997). We were, however, surprised to find that the problem of elder abuse was not discussed. Elder abuse has attracted widespread attention in recent years.[1 2] Elder abuse may be defined as psychological (verbal), financial, sexual, or violent physical abuse that causes distress to a person who is past retirement age[1]; it may occur in a variety of settings.

Elderly people in Britain are subjected to verbal, physical, and financial abuse.[2]

Elder abuse is not a problem that occurs only in the developed world. A medical and social survey of a rural geriatric population in south India found that elderly people were being abused both physically and verbally.[3] As life expectancy increases societies in the developing world will have to support more people. The problem of elder abuse will get worse because of increasing pressure on carers, traditionally the children and younger siblings of elderly people.

Though there is a lack of epidemiological studies on the abuse of elderly people a recent cohort study identified some of the risk factors found in the United States.[4] An established cohort of older adults was linked with records from the protective services during a nine year follow up period. In pooled logistic regression age, race, poverty, functional disability, and cognitive impairment were identified as risk factors for elder abuse.

We believe that more research is needed to elucidate this problem in different societies throughout the world; the *BMJ*, which took a lead by publishing an editorial[1] four years ago, should have included this subject in its agenda when formulating the issue on healthy ageing.

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1 Pitt B. Abusing old people: elder abuse needs to be looked for, quantified, and treated. *BMJ* 1992;305:968-9.
2 Ogg J, Bennett G. Elder abuse in Britain. *BMJ* 1992;305:998-9.
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Recombinant factor VIII may not abolish risk of new variant CJD from factor VIII

Editor—Barbara and Flanagan report the precautionary measures against new variant Creutzfeldt-Jakob disease that have been announced by the UK Department of Health.[1] Unfortunately, the secretary of state announced the outcome of the NHS review of the provision of factor VIII for patients with haemophilia at the same time. The rationale for endorsing the use of recombinant factor VIII in children has thus become linked to concerns over new variant Creutzfeldt-Jakob.

Recombinant factor VIII is a biologically derived product produced by cell culture, not a synthetic product as stated in the announcement from the Department of Health. This is an important distinction because the word synthetic may be taken to imply that recombinant products do not carry a risk of transmitting infectious agents.

Recombinant factor VIII typically has a total protein content that is greater than or equivalent to that contained in some high purity plasma-derived factor VIII. This protein has the potential to be a source of infection—a recognised problem for all recombinant products.[2] Seroconversion for virus has been reported in haemophilic patients receiving recombinant factor VIII.[3] All currently available recombinant and most commercial plasma-derived factor VIII products contain human plasma protein (often as stabiliser) obtained from donors in the United States. To date, new variant Creutzfeldt-Jakob has not occurred in this population. It is therefore difficult to differentiate between recombinant factor VIII and factor VIII derived from US plasma in terms of the risk of transmission of the disease from human protein. The risk is different, however, when the content of other animal protein is considered. The final product specifications for recombinant products restrict the amout of hamster, murine, and (in one case) bovine protein as well as potentially oncogenic DNA residues. The presence of these contaminants may carry its own risk.

There is strong concern that the aetiological agent of transmissible spongiform encephalopathies can jump between animal species.[4] Transmission of contamination from animal-derived starting materials is possible. Fragments of retrovirus-like particles, presumably derived from hamster culture cells, have been detected in one recombinant factor VIII.[5] Finally, the complexity of the manufacturing process for recombinant products has periodically interfered with their availability, and total reliance on them may be inappropriate for many patients.

The statement from the Department of Health is misleading, and the advice given to clinicians regarding prescribing of such products is suspect in the context of new variant Creutzfeldt-Jakob disease. Yet again, political expediency has precipitated the reaction to this threat, this time to appease vocal and perhaps misinformed groups calling for recombinant factor VIII products.

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1 Barbara J, Flanagan P. Blood transfusion risk: protecting against the unknown. *BMJ* 1998;316:717-8. (7 March.)
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Who should be liable for funding recombinant factor VIII?

Editor—On 26 February the Department of Health announced that, acting on advice from the Committee on the Safety of Medicines, it will inform health authorities of "arrangements to ensure that recombinant factor VIII is made available to those [haemophiliac] children under the age of 16 who are not already receiving it, and to new patients."[1] This policy is a response to the perceived threat from blood products contaminated with the new variant Creutzfeldt-Jakob disease prion. This threat is largely theoretical,[1–3] although many haemophiliac patients did become infected with hepatitis C virus and HIV from contaminated plasma derived factor VIII.

The average cost of haemophilia treatment for each patient is about £17 000 a year; recombinant factor VIII would increase average costs by about £13 000 each year,[3] with the additional benefits being unknown. Whatever values lie behind these decisions, the policy will at least be a national one. No "postcode rationing" will occur for recombinant factor VIII.

Haemophiliac patients tend to move to be close to haemophilia centres so are unevenly distributed. If health authorities are to pay for the treatment the costs will be unevenly borne, with some health authorities needing to divert more resources from other healthcare sectors. That is postcode rationing.

Central funding would deal with that problem but changes the rationing debate for competing disease groups: are other patients afforded similar levels of risk containment or offered such prodigious resources for equal need? The influences that have led to this policy are almost certainly those related to factors that frighten patients and trigger media interest[4]; priority setting is thus hostage to the flaws and frailties of human psychology, media interests, and the resulting political expediency.

There is an environmental principle that the polluter pays: the pollution of animal feeds that is presumed to have resulted in new variant Creutzfeldt-Jakob disease is a shared responsibility of the animal feed industry and farmers along with a past government that ignored warnings about the feeding of animal protein to ruminants. In a just world the costs should fall on the profits of the food industry and the tax payer—the consequences of the democratic right to vote for a government that is averse to regulations.

The public inquiry into bovine spongiform encephalopathy opened on 9 March: should Lord Justice Phillips apply his legal mind to this question of liability? If we are not careful a small number of unidentified patients, the embodiment of opportunity costs, will pay the price of treating haemophilia with recombinant factor VIII.

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1 Metters J. Further precautionary measures on blood products announced. Public Health Link Cascade, Feb 1998.
2 Barbara J, Flanagan P. Blood transfusion risk: protecting against the unknown. *BMJ* 1998:316:717-8. (7 March.)
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4 Department of Health. *Communicating about risks to public health; pointers to good practice.* London: DoH, 1997.

A Martian view of the Hardinian taboo

Eugenics is flourishing among population control groups and intellectual elites

EDITOR—Ideologically driven movements are rarely equipped or eager to examine their own presuppositions. The population control lobby and its apologists in the *BMJ*[1] are examples.

King and Elliott, for instance, extol the ideas of Garrett Hardin. Hardin is a eugenicist, being a former director of the American Eugenics Society. He was an active member at the same time as the Nazi eugenicist Otmar Von Verschuer, who became a foreign member in 1956.[2] Verschuer, who was a teacher of Josef Mengele and similarly interested in research on twins, helped finance Mengele's grotesque experiments at Auschwitz. "My assistant Dr Mengele has joined me in this branch of research. He is presently employed as Hauptsturmfuhrer and camp physician in the concentration camp at Auschwitz . . . the blood samples are being sent to my laboratory for analysis."[3] The activities of Verschuer were well known, but, far from being treated as an outcast, he was given honour and academic favours by the eugenics establishment.

That Hardin would associate with those who trampled on human rights is not surprising. In 1969 he wrote, "Coercion is a dirty word to most liberals now but it need not forever be so. As with the four letter words, its dirtiness can be cleansed away by exposure to the light, by saying it over and over, without apology or embarrassment."[4]

The links between eugenics and population control are not difficult to discover. The International Planned Parenthood Federation was a member of the Eugenics Society in 1977. It still financially supports China's brutal coercive population policy, under which women have undergone forced abortion and sterilisation and untold numbers of baby girls have been killed. The Chinese law promotes these atrocities on eugenic grounds.

King and Elliott claim that the genocide in Rwanda was due to population pressures. The real cause was eugenic racism. "All manner of humiliating folly was employed in the name of proving this theory of innate Tutsi superiority. Skulls and noses were measured. . . . The effect of this injustice and of the stereotyping of the Hutu as lesser beings was to create murderous feelings of inferiority and resentment."[5]

Eugenics did not die out in 1945. It is flourishing among population control groups and intellectual elites, and now it is on the pages of the *BMJ*.

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1 King M, Elliot C. To the point of farce: a Martian view of the Hardinian taboo—the silence that surrounds population control. *BMJ* 1997;315:1441-3. (29 November.)
2 www.africa2000.com/eugenics.
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4 Hardin G. *Population, evolution and birth control. A challenge of controversial ideas.* San Francisco: W H Freeman, 1969:378.
5 Keane F. "Letter from Rwanda," BBC Radio 4, 25 Nov 1996.

Author's reply

EDITOR—Our only presupposition was that there is something to be done other than casting a taboo over the whole problem when a community proceeds to starvation and slaughter as the result of exceeding the carrying capacity of its ecosystem, *and* its opportunities for migration, *and* the ability of its economy to produce necessary exports which it can exchange for essential imports, especially food—that is, it is demographically trapped. If tribal tensions are already acute, slaughter is inevitable. We argued that the level of slaughter normally endemic in the region would not have escalated in quite the way it did had not Rwanda been severely trapped.

Here is the definitive report on the genocide: "the decision to kill was made by politicians. But at least part of the reason why it was carried out so thoroughly by the ordinary … peasants was the feeling that there were too many people on too little land, and with a few less there would be more for the survivors."[1] That would be tempting indeed if each person has only 34 m^2 of some eroding hillside, as in Ruhondo.

Demeny named this taboo, as he applied it to the discussion of entrapment by his fellow demographers in his own journal, the *Population and Development Review*. He named it by virtue of the fact that, as an ecologist, Garrett Hardin has over many years described the taboos that we humans apply to our population problems, of which demographic entrapment is merely the gravest.

Whatever else Hardin may or may not have done is irrelevant to this issue. As an ecologist he considers us humans to be constrained by the limitations of food, territory, and migration and not somehow above them (the humanist exemption). Consequently, he has studied the taboos we use to avoid facing them. For this work he has had them named after him.

Gardner muddles eugenics ("controlled breeding for desirable inherited characteristics" (*Oxford English Dictionary*)) with "population control," a term inserted in the title of our paper by the editor and one that we avoid, since it is often used emotively. We argue that the legitimate incentives and disincentives for fertility control may be better than for a community, of whatever ethnic group, to proceed to starvation or slaughter. This issue needs to be debated globally in the context of a United Nations programme for a one-child world; it continues at http://www.leeds.ac.uk/demographic_entrapment.

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1 Millwood D, ed. *International response to conflict and genocide. Lessons from the Rwanda experience.* Copenhagen: Steering Committee of the Joint Evaluation of Emergency Assistance to Rwanda, 1996.

GMC must not recommend abolition of United Examining Board's examination

EDITOR—The education committee of the General Medical Council is considering recommending to the Privy Council that the United Examining Board's examination should no longer be recognised as a route to full medical registration in the United Kingdom. The United Examining Board's examination is the single examination that has recently superseded the three separate examinations for the Scottish triple qualification, the conjoint qualification, and the licence in medicine and surgery of the Society of Apothecaries (LMSSA). The General Medical Council's education committee has the power to make references to the Privy Council without consulting the full council.

The United Examining Board's examination is the only route to full registration in the United Kingdom for asylum seekers and others from abroad who for political or other reasons have been unable to complete their university training and examinations. It is also taken by overseas doctors not qualified to practise in the United Kingdom. Before taking the examination the candidates have to spend a period of structured tuition in a UK medical school and the school has to certify that they have been adequately trained

The General Medical Council has its own assessment for overseas non-European doctors, the Professional and Linguistic Assessment, which can lead via limited registration to full registration. Doctors who take this assessment do not have to have tuition in the United Kingdom beforehand. The Professional and Linguistic Assessment is not supervised by the education committee, nor has it been scrutinised by that committee. The General Medical Council also grants exemption from the Professional and Linguistic Assessment to many doctors—2039 in 1996.

As a member of both the United Examining Board and the Professional and Linguistic Assessment Board, I am aware that the route to full registration via the United Examining Board's examination is more rigorous and appropriate than that via the Professional and Linguistic Assessment. The wider public interest would not be served if recognition of the United Examining Board's examination was ended while the Professional and Linguistic Assessment, with its lower standard, was maintained. The

General Medical Council should not misuse its powers to place doctors on the full register via the Professional and Linguistic Assessment—a route unsupervised by the education committee—and at the same time recommend the end of a good and needed route to registration, the United Examining Board's examination. Should the General Medical Council be both an unsupervised examining body and at the same time a supervisor of the examinations of others?

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Prevalence study of carcinoma in situ of testis in oligozoospermic men

Study was too small to show potential benefits of screening

EDITOR—Giwercman et al evaluated the need for screening for carcinoma in situ of the testis in oligozoospermic men from infertile couples.[1] They concluded that these men do not have an increased risk of carcinoma in situ, therefore implying that screening is not justified.

Their study fails to provide the information required to form a proper judgment on the potential benefits of screening. Although no cases of carcinoma in situ of the testis were detected among the 207 men studied, the confidence intervals reported are compatible with a prevalence of almost 18 in every 1000 men and a relative risk 4.6 times that in the general population. This represents a significantly increased risk. To put this in context, the detection rate for breast cancer in the first wave of the NHS breast screening programme was 6.2/1000 women screened.[2]

No consideration was given to the suitability of testicular biopsy as a screening test. While the uptake rate in the study was 94%, the acceptability of such a highly invasive technique should be addressed.

The study population comprised men referred to Danish infertility clinics. The authors claim that this population represents the target group for screening. They admit, however, that not all oligozoospermic men are currently referred. If screening were implemented, referral rates would probably change; therefore the study group may not be representative of the target population for screening.

The basis for evaluating possible screening tests is well established.[3] In this instance we believe that the study group was too small for the true prevalence of carcinoma in situ of the testis to be accurately established. Any future evaluation should be carried out in a more representative population and should more fully assess the acceptability of testicular biopsy.

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1 Giwercman A, Thomsen JK, Hertz J, Berthelsen JG, Jensen V, Meinecke B, et al. Prevalence of carcinoma in situ of the testis in 207 oligozoospermic men from infertile couples: prospective study of testicular biopsies. *BMJ* 1997;315: 989-91.
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Author's reply

EDITOR—Although I agree with some of the theoretical considerations in Rajentheran et al's criticism, our study also needs to be seen from a practical point of view. It would be desirable to investigate more than the 207 men who were included in our study. Performing large scale screening studies in which testicular biopsy is used as a diagnostic tool is not, however, feasible, particularly if the patients cannot be informed beforehand about the magnitude of the risk of testicular malignancy. Although we could not exclude some increase in the risk of carcinoma in situ among men with moderate oligozoospermia, our study showed that this group of men is not, as has been suggested,[1] a target group for screening. On the other hand, as we also indicated in our paper, our preliminary data and other reports suggest that men with severe oligozoospermia and an irregular ultrasonic echo pattern may be a more appropriate target group for screening.[2]

I agree that men from couples referred to an infertility clinic are a highly selected group. On the other hand, if the magnitude of the risk of malignancy and the available diagnostic procedures are taken into consideration it is evident that screening for carcinoma in situ of the testis cannot be offered to a broader group of infertile men.

Finally, the authors question the suitability of testicular biopsy as a screening test. The sensitivity of the procedure in diagnosing carcinoma in situ is discussed in our paper; the complications are few and not significant.[3] Both in the current study and in previous screening studies a fairly high proportion of men who were offered a biopsy accepted it once the benefits of early diagnosis were explained to them.[4] Undoubtedly, however, a non-invasive screening procedure—for example, one based on semen analysis—must be developed. Screening for carcinoma in situ of the testis might then be offered to a broader population.

Our study is, to my knowledge, the first prospective study assessing the risk of carcinoma in situ of the testis in men attending an infertility clinic. A study of a larger group of men from infertile couples, not limited to those referred to infertility clinics, would be desirable, but I do not think that it is feasible.

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Care for the growing number of elderly people in developing countries needs to be addressed

EDITOR—I strongly agree with Black and Bowman's call for more attention to be paid to the care of elderly people[1]; the same need exists in developing countries, not just in Britain. As life expectancy increases so too does the number of elderly people living in developing countries. The World Health Organisation estimates that 200 million of the 355 million people older than 65 years are in the developing world.[2]

In addition to the health issues, which are the same as elsewhere, elderly people in developing countries have become especially vulnerable because of the rapid social changes occurring in many of these countries. Until recently, elderly people in developing countries enjoyed considerable status, respect, care, and social and psychological support from their families. Migration, urbanisation, changes in value systems and aspirations, changes in the role of women, and the breakdown of the family system have eroded traditional familial support,[3] and elderly people suddenly find themselves poor, uncared for, and without power or influence.[4]

There is almost no social support for elderly people outside the family. Except for a tiny minority who have worked in the organised sector and so receive pensions, economic support does not exist. The focus for most developing countries is on maternal and child health; health care for elderly people is neglected. Both facilities and trained personnel are lacking. Health workers that are the first point of contact for elderly people are inadequately trained and equipped to care for them. Few secondary and tertiary care institutions have separate services for elderly people. General outpatient departments and departments of general medicine provide care[5] but there are long waiting times, the care is often inadequate, and minimal attention is paid to personal care and counselling. Separate inpatient facilities are rarely designated for elderly patients. Gerontology is not a popular specialty.

The changing demographic profile in developing countries requires recognition. Systems need to be devised to engage elderly people in suitable vocations so that their wisdom and experience can be effectively utilised; this would also help them to retain their sense of self worth. Social security systems need to be developed for their general welfare. Healthcare support

services need improvement. All health personnel should have additional training in caring for elderly people. A three tier health system needs to be developed so that auxiliary health personnel can provide ambulatory care in the community and be supported by a separate referral system for specialised care.

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Management of dyspepsia in primary care

GPs are already choosing eradication therapy over endoscopy

EDITOR—Agréus and Talley's recommendations for the use of *Helicobacter pylori* testing in the management of patients with newly appeared dyspepsia[1] differ from published guidelines.[2 3] They consider eradication therapy an acceptable alternative to endoscopy for patients with a positive test result when access to this investigation is difficult. This alternative option is probably a fait accompli in primary care.

In June 1995 I sent a questionnaire to all 298 general practitioners in north and east Devon asking how they would use *H pylori* testing for the management of patients with dyspepsia. After a reminder questionnaire, 271 general practitioners (91%) responded. The table shows the results.

Only 73 (27%) said they would limit the use of this test to younger patients (under 50 years of age) as recommended by published guidelines at the time.[2] Eighty five did not know when to use the test but many of these said how they would manage patients with a positive result. Most general practitioners (73%) would use eradication therapy rather than endoscopy in younger patients with a positive test result. Seventy eight (29%) said they would also attempt eradication therapy in older patients.

At the time of the survey patients referred for endoscopy had to be placed on a waiting list. General practitioners might have preferred to prescribe antibiotics for dyspeptic patients with a positive *H pylori* result, which is likely to cure a possible peptic ulcer, rather than wait too long for the diagnosis to be confirmed by endoscopy.

General practitioners' response to questionnaire on how they would use *H pylori* testing

	No (%) of general practitioners (n=271)
Use of *H pylori* testing:	
In dyspeptic patients <50 years	73 (27)
In dyspeptic patients ⩾50 years	12 (4)
In all dyspeptic patients	101 (37)
Do not know	85 (31)
Management after positive result in a patient <50:	
Referral for endoscopy	38 (14)
Eradication therapy	198 (73)
Both	8 (3)
Do not know	27 (10)
Management after positive result in patient ⩾50:	
Referral for endoscopy	127 (47)
Eradication therapy	78 (29)
Both	35 (13)
Do not know	31 (11)

I thank all general practitioners in north and east Devon district for their cooperation and Dr I Morrel for his help in designing the questionnaire.

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1 Agréus L, Talley N. Challenges in managing dyspepsia in general practice. *BMJ* 1997;315:1284-8. (15 November.)
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Antibiotic resistance is a problem

EDITOR—Agréus and Talley advocate empirical treatment of *Helicobacter pylori* infection in selected patients with dyspepsia if a reliable non-invasive screening test confirms active infection.[1] Although we agree with their main recommendations, we want to highlight an important concern regarding empirical treatment of *H pylori* infection.

Any test and treat policy will be effective only if the treatment achieves adequate (>90%) eradication rates. A recent consensus report recommended that the first line treatment of *H pylori* infection should consist of a one week course of a proton pump inhibitor plus clarithromycin and either a nitroimidazole or amoxycillin.[2] The presence of resistance in *H pylori* to nitroimidazoles or clarithromycin significantly reduces eradication rates and may prohibit successful treatment of the infection in patients in whom eradication has been shown to be of benefit.[3] Unsuccessful treatment of the infection with a regimen containing either of those antibiotics results in high rates (up to 60%) of secondary acquisition of resistance. The use of inappropriate treatment combinations leads to low eradication rates and selection of resistant *H pylori* strains. The prevalence of antibiotic resistance in *H pylori* seems to have increased in recent years, possibly reflecting the widespread use of inadequate treatment regimens.[4]

Antibiotic resistance in *H pylori* can be assessed only after endoscopy and culture of the organism. If a course of treatment aimed at eradicating *H pylori* infection is, or is suspected of being, unsuccessful, the choice of second treatment should be guided by the results of tests for antibiotic susceptibility.

Before non-invasive testing for and treatment of *H pylori* infection is advocated for managing dyspepsia, prescribing doctors need to be educated about the hazards of inappropriate prescribing and the importance of requesting antibiotic susceptibility testing when appropriate. Awareness of the problems may prevent the emergence of strains of *H pylori* with multiple resistance. This, we believe, is the "major challenge in managing dyspepsia" in the coming years.

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1 Agréus L, Talley N. Challenges in managing dyspepsia in general practice. *BMJ* 1997;315:1284-8. (15 November.)
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Dyspepsia subgroups are useful in determining treatment

EDITOR—We agree with Agréus and Talley that patients in general practice with upper gastrointestinal symptoms should be investigated to identify peptic ulcers that can be healed after a short course of antibiotics and that *Helicobacter pylori* infection can be non-invasively investigated and possibly treated without endoscopic confirmation in young patients who do not present alarming features and are not worried about having cancer.[1]

However, some aspects of their article need further discussion. General practitioners must be aware that eradication of *H pylori* fails to control upper gastrointestinal symptoms in over half of patients with peptic ulcer [2] and in even higher proportions of patients with "non-ulcer" dyspepsia. The proposed plan will not stop most of their patients seeking medical help because of the severity of their symptoms after the frustrating experience of an ineffective treatment.

The authors state that use of predominant symptoms as predictors of distinct underlying pathophysiological symptoms is "not clinically useful," but an erroneous interpretation of this concept is applied. In fact, the severities (and not frequencies) of individual symptoms should be analysed to identify the symptom which dominates the clinical picture.[3] Preliminary results from our laboratory suggest that analysis of demographic features, predominant symptoms, and overlapping digestive syndromes can help to identify dyspepsia subgroups with different underlying pathophysiological features. Men with body weight higher than ideal and predominant epigastric pain generally have normal gastrointestinal motility, whereas women with body weight lower than ideal, predominant non-painful discomfort,

and overlapping irritable bowel syndrome often have gastrointestinal motor disorders[4] Recent studies have suggested that subgrouping based on predominant complaints and overlapping syndromes can be of therapeutic value. For instance, Gilvarry et al showed that after effective eradication of *H pylori* a significant improvement of dyspeptic symptoms is detectable in patients with predominant epigastric pain but not in those with different presenting symptoms.[5]

The concept of dyspepsia subgroups requires thorough re-evaluation since it is likely that correct history taking will be essential in the management strategies for most dyspeptic patients in the near future.

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Breath test is better than near patient blood tests

EDITOR—Agréus and Talley raise the important issue of the accuracy of near patient ("office") blood tests for *Helicobacter pylori* infection.[1] We conducted a feasibility study using laboratory staff to run ^{14}C-urea breath test clinics in general practice as part of a "test and treat" strategy for *H pylori*. The table compares data from our study with published data on sensitivity and specificity of near patient blood tests.[2-5] Up to 16% of patients with *H pylori* infection would not have received treatment if near patient blood tests had been used in the study rather than the breath test and up to 28% of those receiving eradication therapy would not have been infected with *H pylori*.

The table supports the view of Agréus and Talley that the breath test is superior to a blood test both in documenting *H pylori* infection and in guiding the management of dyspepsia in general practice. We would encourage laboratory colleagues to ensure that the breath test is made more widely available.

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1 Agréus L, Talley N. Challenges in managing dyspepsia in general practice. *BMJ* 1997;315:1284-8. (15 November.)
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Prion science is not cold fusion

EDITOR—In her news item describing the award of the 1997 Nobel prize to Stan Prusiner, Deborah Josefson stated correctly that some people are still sceptical about the prion hypothesis.[1] However, Robert Rohwer is quoted as calling prions the "cold fusion of infectious diseases." Having studied both cold fusion[2-4] and prions,[5] I believe that this comment is completely inappropriate and unfair.

When Fleischmann and Pons claimed that cold fusion could solve the world's energy problems with a simple table top experiment, many thousands of people all over the world tried to repeat it. The United States government set up a panel of 22 top scientists to investigate, and they concluded that there was no evidence. (Interestingly, each time the scientists announced a visit to a laboratory claiming cold fusion the cells stopped working and they never saw a working apparatus.) There were some dubious incidents.[2] Quickly, almost all scientists abandoned cold fusion as they recognised it required too many miracles, with various claims being wrong by enormous factors of 10^{-40} and 10^{-12}. A few true believers continue to have meetings, and some ask investors for support.

The question of prions is quite different as there are many serious experimental results consistent with the prion hypothesis, and these results are reproducible and can be seen on visiting laboratories. Also, predictions based on the prion hypothesis are fulfilled—for example, injecting scrapie prions into a transgenic mouse that has no prions should not and does not cause any disease. People who suggest that some form of virus (or virino, or light virus on the analogy of the neutrino) is the real cause of transmissible spongiform encephalopathies have been unable to identify it. A more appropriate comparison[5] with the prion hypothesis is the equally daring quark hypothesis proposed in 1964 by Zweig and Gell-Mann. Many predictions from the quark hypothesis were verified experimentally, but a determined group of physicists refused to accept it and were able to later make the same prediction without using quarks. However, in 1974 the charm quark was discovered and all opposition to quarks collapsed.

The prion hypothesis has so much evidence in its favour that it is reasonable to accept it. It does not resemble the cold fusion story in any way.

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1 Josefson D. The prion disease is finally accepted by the establishment. *BMJ* 1997;315:972. (18 October.)
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Tolerability of alendronate

Comparison group taking placebo should have been included

EDITOR—The extent of gastrointestinal side effects attributed by Kelly and Taggart to treatment with alendronate is misleading.[1] Their study of 77 patients taking alendronate did not include a comparison group taking placebo, and results have not been adjusted for the underlying prevalence of adverse experiences among the study group. In addition, an appreciable number of their patients had failed to comply with dosing instructions.

The extent of gastrointestinal disturbances among the elderly general population is high. The fracture intervention trial studied 2027 women with a mean age of 71 and at least one vertebral fracture; it found that 40% of patients taking placebo had an upper gastrointestinal adverse event.[2] The number of gastrointestinal events in women taking alendronate was not significantly higher than this.

I am concerned that exaggerated reports of intolerability of alendronate will lead to reduced prescribing in patients who could gain considerable clinical benefit from this drug. My experience is that careful prescribing in suitable patients, combined with education on compliance, results in minimal problems of intolerance. I will continue to

Diagnostic accuracy and appropriateness of eradication therapy with breath test and near patient blood tests

	Diagnostic accuracy					
	% True positive results	% False positive results	% True negative results	% False negative results	% of *H Pylori* positive subjects not treated	Patients inappropriately treated (% of all those treated)
^{14}C-Urea breath test	32	2	66	0	0	6
Helisal[2]	27	5	63	5	16	16
Flex-Sure[3]	28	8	60	5	13	22
Quick-Vue[4]	29	11	57	3	9	28
Helisal one step[5]	28	11	57	4	13	28

use this drug, which has proved efficacy in preventing fractures, but I agree that compliance with dosing instructions is an important issue and needs to be addressed with every patient taking a bisphosphonate.

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1 Kelly R, Taggart H. Incidence of gastrointestinal side effects due to alendronate is high in clinical practice. *BMJ* 1997;315:1235. (8 November.)
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Manufacturer's comment

EDITOR—Kelly and Taggart present their experience of using alendronate, which Merck Sharp & Dohme manufactures.[1] Their experience should not be viewed in isolation, but rather in the context of the wealth of data now available on alendronate. In well designed randomised double blind, placebo controlled trials in over 10 000 patients treated for up to four years, alendronate was well tolerated; the overall incidence of upper gastrointestinal adverse events was comparable to that seen with placebo.[2–4] Discontinuation rates overall, and those due to upper gastrointestinal adverse events in particular, were similar in the alendronate and control groups.

Rates of gastrointestinal adverse events in control groups can be substantial. For example, in the fracture intervention trial a fifth of patients treated with placebo (and an equal proportion of those given alendronate) reported an upper gastrointestinal adverse event within the first six months of the study (data on file). If there had not been a control group one could have concluded (erroneously) that alendronate induced upper gastrointestinal adverse events in a substantial proportion of the treated population.

Therefore, without further details of the patients' histories, and in the absence of a control group or dechallenge-rechallenge data in Kelly and Taggart's population, it is impossible to judge the background incidence of gastrointestinal symptoms or the number of cases attributable to alendronate. Indeed, our extensive controlled experience indicates that many of the gastrointestinal symptoms described are no more common in patients treated with alendronate than in those taking placebo. Alendronate has now been used to treat osteoporosis in over two million patients worldwide. Although there have been rare reports of oesophageal adverse effects,[4] in many cases these seemed to be related to inadequate adherence to the dosing instructions. Thus the available data indicate that alendronate is safe and well tolerated when taken as indicated.

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Figures given in letter were prevalences, not incidences

EDITOR—Kelly and Taggart report on 77 women treated with alendronate.[1] We are conducting a safety study of this drug, which is based in general practice and in which we use prescription event monitoring.[2] We have data for 5846 patients dispensed alendronate in England (mean age 69 (range 15-97)). Patients were observed for roughly six months, and all events reported during and after treatment were recorded by patients' general practitioners. We had 573 reports of dyspeptic symptoms in 539 patients.

We calculated incidences for events per 1000 patient months of treatment (exposure). Dyspeptic symptoms were the most frequently reported events in the first month of treatment (incidence 30.7/1000 patient months). Not all upper gastrointestinal symptoms will have been caused by alendronate, and one would expect a reasonably high background rate of such symptoms in an elderly population. Over 50 studies have been completed by prescription event monitoring; the mean cohort size has been 11 215.[2] The incidence of dyspeptic symptoms in the first month of treatment in women aged over 60 prescribed one of 10 non-gastrointestinal drugs recently studied by prescription event monitoring is 6.0 per 1000 patient months.

The probability of developing most (type A) drug side effects is related (along with other factors) to dose, accumulated dose, and duration of exposure. Kelly and Taggart discuss the incidence of side effects, but this is misleading. The percentage figures given are overall prevalences, not incidences. Some of their patients had been treated for 66 weeks, and this alone could explain why their prevalence figures are higher than those for studies conducted for six months or less. The authors also report that 21 patients had a history of gastrointestinal disease. Further symptoms in these patients are not necessarily drug related and should not be classed as drug side effects without comprehensive assessment. One needs to be cautious when causally attributing to a drug gastrointestinal symptoms occurring for the first time 50 weeks after the start of treatment.

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1 Kelly R, Taggart H. Incidence of gastrointestinal side effects due to alendronate is high in clinical practice. *BMJ* 1997;315:1235. (8 November.)
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Authors' reply

EDITOR—Our letter described an observational study of our experience with alendronate in clinical practice, not a controlled clinical trial. Thus a formal control group was not practical. However, two thirds (51) of our patients had previously been treated with cyclical etidronate for a minimum of two years and had tolerated this regimen well. Eighteen (35%) of the women developed significant side effects while taking alendronate, compared with six (23%) not previously treated with cyclical etidronate. This points to a clear difference in gastrointestinal tolerability between these two osteoporotic regimens.

While we accept that there may be a relatively high background prevalence of gastrointestinal events in a population like ours, the severity of the symptoms experienced by these women was striking. Although well motivated, nearly all the patients had to stop treatment, and their symptoms resolved when this occurred. It is now our practice to rechallenge patients with alendronate to establish more clearly whether the drug is causing the problem. In most patients the symptoms have returned, so that treatment has had to be stopped.

We accept Mackay and Mann's point that our figures refer to prevalence rather than incidence but doubt whether this would affect the conclusions significantly. The mean duration of treatment with alendronate was 39 weeks in those without side effects and 20 weeks in those with side effects, which is less than the six month observation period in their study. Nevertheless, some side effects are delayed, and we advise prolonged vigilance with alendronate treatment. One of our patients developed an oesophageal stricture after seven months' treatment.

We agree that alendronate is a valuable drug in treating osteoporosis, but attention to detail in prescribing is required, as is careful prolonged follow up. It does not serve patients well to imply that the likelihood of side effects is minimal.

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Non-steroidal anti-inflammatories should not be used after orthopaedic surgery

EDITOR—We read with interest the article by Rochon and Gurwitz[1] particularly about the association between non-steroidal anti-inflammatory drugs and blood pressure in elderly people. There is another potential problem with the use of these drugs both in elderly and younger patients for pain relief after orthopaedic surgery.

Non-steroidal anti-inflammatory drugs are a large class of compounds that inhibit cyclo-oxygenase and thus the formation of prostaglandins, which are involved in bone metabolism. However, the effect of these drugs on bone metabolism is often over-

looked. They inhibit osteoblasts at the endosteal bone surface and also reduce both the immune response and the inflammatory response.[2] Despite animal studies which have highlighted the harmful effects of these drugs on the healing of fractures[3 4] and spinal fusion,[2] they continue to be used commonly for the relief of postoperative pain in the absence of well designed human trials. Furthermore, with the advent of joint prostheses coated with hydroxyapatite, which work by promoting primary bone formation to fill the gap between the prosthesis and the host bone, the use of non-steroidal anti-inflammatory drugs may be counterproductive.

A random survey of the type of analgesia received by patients undergoing hip arthroplasties on our elective orthopaedic ward showed that 95% (18/19) were being treated with these drugs; this treatment had been started immediately after surgery and then had simply continued. Diclofenac sodium or ibuprofen were the most commonly prescribed drugs. Ibuprofen has been shown to have an irreversible effect on the healing of fractures.[3] Also the inhibitory effect of these drugs on fracture healing is greater the longer the duration of use.[2–4]

On the basis of the evidence we should ask if the use of non-steroidal anti-inflammatory drugs can be justified in the management of pain following fractures, joint replacements, and spinal fusions. If they are used, they should be prescribed in the lowest possible dose for the shortest time,[3] or an agent such as indomethacin might be a better choice, since it has been shown to have a reversible inhibitory effect on bone healing.[3]

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1 Rochon PA, Gurwitz JH. Optimising drug treatment for elderly people: the prescribing cascade. *BMJ* 1997; 315:1096-99. (25 October.)
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Patients in east London seem happy to give GPs consent for training

Editor—O'Flynn et al report a qualitative study of patients' concerns about consent and confidentiality when students are present in consultations.[1] They conclude their discussion by suggesting that patients should be given a "real choice about whether they see a student" and suggesting that explanations concerning student access to their records and discussion of their case "require further discussion." Commenting on this conclusion in an editorial, Williamson and Wilkie recommend a move "away from a position where the patient is observed by the student and discussed afterwards to an active mode where the patient joins in discussion during the consultations."[2]

General practitioners in east London, teaching small groups on junior clinical firms, have developed several strategies for seeking patients' informed consent to and involvement in teaching. Patients were contacted before the teaching session and invited to attend at a specific time, to provide a history, and to be examined (a different style of teaching from that of the individual student "sitting in" on a surgery). Immediately before teaching, general practitioners invited patients to reiterate their consent: patients have been willing to reattend teaching sessions, which suggests active consent.

In some practices general practitioners involved patients in discussion with students after the history taking and examination but took care to address any patient concerns about the content of the discussion both immediately and on their own after the teaching. Our evaluation showed that students valued the active involvement of patients in this process.

We believe that attention to the nature of the relationship between general practitioners and patients is especially important in the light of the increasing range and volume of teaching undertaken in primary care settings. As general practitioners actively seek the help of patients their relationship shifts. The patient, in being asked to cooperate in teaching but given the explicit right to refuse, gains power. Some, when asked for their views on participating in teaching, spoke of being able to "do something" for the general practitioner or the practice; this is a rather different emphasis from that of helping with "medical education" suggested by Williamson and Wilkie. In some instances, this has been uncomfortable, presenting the possibility of patients feeling that the general practitioner is indebted to them in some way. When appropriately managed, however, such interactions can lead to a deeper, more mutually satisfactory relationship.

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High cost, low volume care in haemophilia

Editor—I contest the statement of Lee et al that "there is no hard information on the benefits of using recombinant factors over plasma derived concentrate."[1] An independent review of haemophilia commissioned by the directors of public health in South Thames last year endorsed the recommendations of the United Kingdom Haemophilia Centre Directors Organisation about choosing recombinant factor VIII on the grounds of viral safety.[2]

The reason for this recommendation is the possibility of unknown viruses. At least one virus affecting humans, parvovirus B19, survives the purification processes for making factor VIII from plasma, even in the most purified products. Parvovirus itself rarely has clinical significance, but it is important as a marker for another as yet undetected virus.

Two main strategies are used to inactivate viruses in plasma products: heat treatment and solvent or detergent treatment to inactivate viruses with lipid envelopes—for example, hepatitis A virus. However, recent outbreaks of hepatitis A indicate that these methods are not always successful,[3] particularly if a starting pool of plasma is infected by a unit of plasma containing high concentrations of virus.

Hard evidence also exists of the transmission of parvovirus B19 by factor VIII treated by both methods.[4] One study traces the progression of acute parvovirus infection in haemophilic patients treated with plasma derived factor VIII through to seroconversion to IgM and later IgG antibodies.[5]

I think that the evidence adds up to more than biological plausibility and that the marginal increase in cost is justified, particularly in children.

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Correction

Patients offered treatment for CHD need full information to make decision

An editorial error occurred in this letter (28 March, pp 1021-2). The letter was attributed to P McCormack et al, but in fact the first author was James P McCormack.