Letters

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Children poisoned with illegal drugs in Glasgow

EDITOR—Harkin et al reported the death of a young child in Dublin caused by methadone stored in a baby's bottle.[1] They rightly encourage the routine supply of measuring devices with methadone prescriptions, although perhaps a more appropriate arrangement in families with young children might be ongoing supervised administration within a pharmacy, which may also reduce the opportunity for resale of the drug among drug misusers.

Such tragedies are not new.[2] During 1998, among 315 children admitted for observation and treatment for poisoning to the Royal Hospital for Sick Children in Glasgow, 22 had been poisoned with illicit drugs or methadone (table). All came from the local area. They included 11 preschool children who had accidentally ingested drugs, usually within the home. Methadone played a part in three of these 11 cases, although none was related to storage in feeding bottles.

Children poisoned with illegal drugs in Glasgow (No)

Drug	Preschool (n=11)	School age (n=11)
Methadone	3	0
Amphetamine	5	3
Ecstasy	1	2
Cannabis	1	1
LSD	1	2
Heroin	0	1
Unknown stimulant	0	2

Some of these children were seriously ill, and one required intensive care. A further 11 children of school age were admitted over the same period, primarily poisoned by illicit drugs during experimental use or in the context of major psychosocial problems.

These events, together with comparatively common accidental needlestick injuries seen after exposure to discarded injecting equipment, highlight the risks run by young children living in households or environments where illegal drugs or their substitutes are used. They represent an additional issue to be considered in supervising and protecting children in such families.

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1 Harkin K, Quinn C, Bradley F. Storing methadone in babies' bottles puts young children at risk [letter]. *BMJ* 1999;318:329. (30 January.)
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Safety and effectiveness of nurse telephone consultation in out of hours primary care

Two interventions were combined as one

EDITOR—Lattimer et al report a randomised controlled trial to show the safety and effectiveness of nurse telephone consultations in out of hours primary care.[1] I accept that the results showed a reduced workload for general practitioners from the nurse intervention, probably at an increased cost. For methodological reasons, however, I am less certain whether the results show safety.

Lattimer et al report that during intervention periods, 49.8% of the calls could be managed by the nurse alone without referral to a doctor. This implies that 50.2% of the calls were assessed twice: once by an experienced and specially trained nurse using a systematic assessment with the aid of decision support software and then by the general practitioner in attendance. I would expect that the improved diagnosis and management in this subgroup would lead to much better clinical outcomes than in the control group, which had only one assessment by the general practitioner. This improved outcome could mask the potentially poorer outcomes in the 49.8% of calls handled by the nurse alone. By combining the outcomes for essentially two interventions (nurse alone and nurse and general practitioner) into a single intervention group, the issue has been clouded. I therefore question the conclusion that nurse telephone consultation is at least as safe as existing out of hours care.

To convince a sceptic of the safety of nurse telephone consultations, the outcomes for patients managed by the nurse alone should be compared with the outcomes for matched patients in the control group. I wonder whether the authors can extract this information from their data. It may be that the trial would have to run for longer than one year to fulfil sample size criteria for such a comparison.

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1 Lattimer V, George S, Thompson F, Thomas E, Mullee M, Turnbull J, et al. Safety and effectiveness of nurse telephone consultation in out of hours primary care: randomised controlled trial. *BMJ* 1998:317:1054-9. (17 October.)

Tolerance limits were too wide

EDITOR—Lattimer et al have provided some valuable evidence for the effectiveness of nurse telephone consultations as part of the NHS direct service due to be implemented by 2000.[1]

The equivalence limits of 80-125% chosen for analysis of the outcome measure of death within 7 days of call seem rather arbitrary. We question whether a tolerance level of 25% excess of deaths is acceptable for an intended nationwide scheme.

A more reasonable approach might have been to estimate the difference in rates of death between the two arms of the study. This would have allowed readers to make their own decisions about acceptable limits.

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Authors' reply

EDITOR—Tanna is correct when he states that questions remain pertaining to differences between those patients who accepted nurse advice in our trial and those who experienced the usual on-call system. We noted this in the discussion section of our paper and gave a brief explanation of the methodological difficulties associated with conducting a comparison such as Tanna proposes.[1] The trial does not answer the question of whether there were patients who should have been referred to the general practitioner on call or who should have been admitted to hospital and were not, but we have no evidence that it did happen, and it is clear that if it did it did not lead to an excess of deaths. Further work remains, however, on establishing criteria for continuous quality improvement for telephone consultation services.

Blackmore et al are also correct when they call our equivalence limits arbitrary. It is perfectly possible to estimate the difference in rates between the two arms of the study, as we have provided the number of events, the denominator population, and the period of time over which the study took place. Since we planned an equivalence trial, however, we will not be making this comparison, as we did not make a prior hypothesis about any

such difference. It is then possible to compare the significance of the difference between the rates at, say, the 5% level. It is important to realise, however, that 5%, 1%, or 0.1% are all themselves arbitrary levels of significance, and that it is just as impossible to prove difference as it is to prove equivalence. It is also important to realise that the equivalence limits set around an expected number of deaths must encompass not only the point estimate of the observed number of deaths but also the confidence intervals surrounding it. For a rare event such as death, these confidence intervals can be wide unless large numbers of cases are used. The narrowing of these limits would have increased the already large numbers of cases required in our study, and thus its costs, beyond the budgets of potential funding bodies.

Our trial provides only the first evidence for the safety and effectiveness of nurse telephone consultation. Work now remains to establish the safety and effectiveness of variations to the system including software, training, and overall organisational structure of telephone consultation services.

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Clinical trials

Simple megatrials are not sufficient

EDITOR—No one should argue with Peto and Baigent about the dangers of basing clinical practice on flawed "outcomes research" or isolated, undersized, randomised trials,[1] but the simple megatrial may not be the ideal model for the next 50 years. Although such trials have taught us not to expect a predictable physiological response from our treatments but merely an improvement in the odds of successful outcome, the homogenising effect of large numbers may still disguise important variations in response. Attempts to explore these variations through subgroup analysis are widely condemned because of the perceived association with retrospective data dredging, so that the theoretical knowledge of clinicians and the individuality of patients are seen as increasingly less relevant to decisions about treatment.

The trials that Peto and Baigent advocate focus on hard end points, such as deaths, which may be rare in some patient groups and of limited relevance in others. The ageing of the world's population may be the greatest global challenge to be faced in the next 50 years, and we will become less concerned with the length of survival in old age than with its quality. Many treatments will be evaluated in terms of their effects on "healthy active life expectancy" or on the duration and severity of "terminal dependency" rather than on mere survival. Comparatively simple measures of dependency are available for this purpose, but trial follow up will mean more than just a body count.

Older people are physiologically diverse, and we will need to look for qualitative as well as quantitative differences in treatment response in different subgroups. Trials will need to estimate not just the average effect of treatments but the benefits and risks in all important subgroups, so, despite high event rates, even large trials will be unlikely to answer all the relevant questions about a particular treatment.

Over the next 50 years the monolithic megatrial should therefore be replaced by planned collaborations between smaller studies, addressing different aspects of the same broad research question and using an agreed system for classifying patient subgroups, interventions and outcomes.[2 3] This would overcome the limitations of retrospective meta-analysis, and clinicians would participate to a greater extent in defining the research questions and agreeing on classifications. The risks and benefits of treatment would become clear, and the focus of uncertainty would gradually change. Clinicians could then use their clinical skills, as well as the latest accumulated research evidence, to select the best treatment for individual patients.

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1 Peto R, Baigent C. Trials: the next 50 years. Large scale randomised evidence of moderate benefits. *BMJ* 1998; 317:1170-1. (31 October.)
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Randomised database studies could serve as new strategy

EDITOR—The issue of the *BMJ* on 50 years of randomised controlled trials[1] clarifies future challenges to clinical trials—for example, the need to find ways of increasing the size of randomised studies,[2] the increasing demand for high quality research in primary care, and the need to translate evidence into practice. The main limitation of randomised clinical trials is the fact that while they do show whether new drugs work (efficacy) they do not show if they really work in clinical practice (effectiveness).

Although the need to conduct "naturalistic" studies was postulated 20 years ago,[3] an adequate methodology to conduct them has not been developed yet. Pragmatic clinical trials and database analyses have been the two main methods proposed to assess the effectiveness of treatments. Their inherent limitations—problems of external and internal validity, respectively—have, however, not been completely resolved. For Peto and Baigent, the key question is how a really large number of patients can be randomised in practice.[2] We believe that the main challenge is in the development of a new strategy capable of maintaining the main advantages of clinical trials (randomisation) and database analyses (capturing the full range of treatments and outcomes that occur in the normal course of medical practice). Our group has recently suggested including randomisation modules in computer based patient records, if possible.[4] This would help to conduct "randomised database studies" that can simultaneously use experimental as well as observational methods to assess the effectiveness of drugs.

Randomised database studies could be used to conduct large, long term studies and investigate outcomes of importance to clinicians and patients. We agree with Peto and Baigent that simplicity and flexibility should be two of the main aspects influencing the design of these studies. The progressive implementation of clinical practice guidelines and new computer support systems for prescribing might help to identify the best diagnostic and therapeutic options in every clinical situation. The application of randomisation using computer based clinical reports (the integration of research into daily clinical practice) could contribute to studying the problems where they come up. This would help to improve the quality of health care and enable quicker acceptance and incorporation of research results into clinical practice.

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Prescribing antibiotics for sore throats

Rapid tests are invaluable tools

EDITOR—I found Butler et al's article interesting.[1] In Norway problems with resistant bacteria are few and have been stable for 10 years. Important reasons for this may be the low total prescriptions for antibiotics and the high proportion of penicillin V prescribed. Prescriptions for antibiotics have decreased by 10% since 1993. One of the reasons for this may be the use of rapid tests in general practice.

A rapid test for detection of group A streptococci (sensitivity and specificity $>90\%$) provides results within 5 minutes. As group A streptococci are the only cause of sore throat that should be treated with penicillin V,[2] this can potentially reduce prescriptions. As test results are known quickly, the patient can be told why penicillin V would or would not be prescribed.

In a recent study we showed that a rapid test for C reactive protein performed in general practice and giving results within 10 minutes can be used to identify patients with respiratory tract infections who need antibiotics.[3] The test reduced antibiotic intake by one quarter. We believe that this test is one of the best tools to exclude bacterial causes of acute bronchitis and is also a good pedagogic tool.

After 15 years in general practice I perceive that attitudes towards antibiotics have changed. Often parents, knowing from the results of rapid tests that their child probably has a viral infection, are pleased that antibiotics will not be required.

I look forward to more research on this important topic: perhaps the effect of use of a rapid test and how this would affect the rate of prescribing and patients' attitudes?

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Prophylaxis against malaria

Preventing mosquito bites is also effective

Editor—Berger's list of measures for protecting travellers against malaria is extremely useful.[1] The particular emphasis on compliance with drug regimens should not, however, detract from the importance of strict adherence to effective measures for preventing contact with mosquitoes and bites. No drug is totally effective, and in areas of low transmission the risk of adverse events attributed to chemoprophylaxis may well exceed the benefit of avoided infections.[2]

Although the World Health Organisation advocates protection against mosquito bites as the first line of defence against malaria, the basis for this recommendation has until recently been questionable.[3] Evidence for a protective effect of insect repellants applied to the skin, air conditioners, fans, coils, vaporising mats, and long sleeved clothing has been largely speculative; use of these measures has been shown to result in decreased feeding by mosquito vectors, but direct evidence of a protective effect against malaria infection has not been gathered. Use of personal protection measures may have been compromised by widely publicised reports of encephalopathic reactions in children associated with the most widely used insect repellant, diethyltoluamide (DEET), and the nonchalance of many travellers.

This is exemplified by the results of a postal survey of visitors to the Kruger National Park, South Africa, during the seasonal high risk period. Over 95% (7034/7387) of tourists provided responses to the section investigating use of personal protection measures. Altogether 912 (13%) of these travellers used no personal protection measures and only 1209 (17.1%) used four or more. Neglect of these measures was positively associated with non-use of chemoprophylaxis, with 17.3% of tourists who were not taking chemoprophylaxis neglecting to use personal protection measures compared with 11.9% of those who were ($\chi^2 = 28.24$, df = 1; or Fisher's exact $P < 0.001$).

The most commonly used personal protection measures were insect repellants applied to the skin (by 5525 people), long sleeved clothing (by 2815), socks and shoes (by 2374), coils (by 1651), and vaporising mats (by 1076). Specific effective protection measures were little used, particularly aerosolised insecticides, usually synthetic pyrethroids, administered by spraying under pressure by a handled canister, much like a large deodorant can (by 548), bed nets (by 49) and impregnation of clothing with insecticide (by 12). Some travellers relied on ineffective measures, including ultrasonic buzzers (12 people), alcohol consumption (9), and ingestion of garlic (4).

Two recent papers are enlightening. A review of the toxicity of diethyltoluamide showed only two case reports of systemic toxicity after topical application in adults and 13 of encephalopathic toxicity in children despite 40 years of extensive use.[4] A questionnaire survey of over 100 000 European tourists to east Africa found that air conditioned rooms ($\chi^2 = 4.01$, $P = 0.05$) and clothing that covered arms and legs ($\chi^2 = 5.25$, $P = 0.02$) effectively reduced the risk of malaria.[5] Regular use of all or some of the four most important personal protection measures (air conditioned room and/or bed net, adequate clothing, insecticides and/or coils, repellants) reduced the risk of malaria to about half compared with that of other travellers using no such precautions ($\chi^2 = 8.47$, $P = 0.04$).

Geographic knowledge of the distribution, drug resistance, and prevalence of malaria should be used to determine the type and necessity of chemoprophylaxis. Travellers should also be aware of the best personal protection measures against mosquito bites.

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1 Reid AJC, Whitty CJM, Ayles HM, Jennings RM, Bovill BA, Felton JM, et al. Malaria at Christmas: risks of prophylaxis versus risks of malaria. [With science commentary by A Berger.] *BMJ* 1998;317:1506-8. (28 November.)
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Preferred prophylaxis varies by region

Editor—Reid et al's lesson of the week on prophylaxis against malaria, and Berger's science commentary on it, made me think yet again how regional preferences affect the choice of prophylaxis against malaria.[1]

British travellers are currently in the invidious position of choosing between mefloquine, which in most people's minds has a terrifying reputation, and the relatively ineffective combination of chloroquine and proguanil. Passing reference is made to pyrimethamine with dapsone (Maloprim), which is indicated for few destinations. Why is doxycycline—a drug that is deemed important for malaria prophylaxis by the rest of the world—not even mentioned? There is good clinical evidence that it is effective,[2–4] and it has the advantage of not being tainted by media reports. Interestingly, North America steadfastly continues to ignore the existence of proguanil—further perpetuating another anachronistic regional idiosyncrasy.

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More studies of mefloquine prophylaxis must be done in tourists

Editor—In their paper on the risks of malaria to travellers Reid et al state categorically that mefloquine is the most effective antimalarial agent.[1] Unfortunately, they adduce only one study in general travellers in support of this view.[2]

The much cited study by Steffen et al was an uncontrolled, questionnaire based survey of non-immune tourists visiting east Africa.[2] The tourists were taking either mefloquine (once a week) or one of the other antimalarial drug regimens commonly prescribed at that time. Because of the limitations of its design this survey does not show conclusively that mefloquine is any more or less effective than the other compounds assessed.

Steffen et al's survey was funded wholly by the manufacturers of mefloquine (Roche), but Reid et al do not mention this potential for bias; one of Reid's coauthors recently declared elsewhere in the *BMJ* that he has received research funds from Roche.[3] Reid et al cite no evidence that mefloquine is more effective than other more recent

antimalarials that are available for travellers, such as doxycycline and atovaquone-proguanil (now licensed for prophylaxis in Denmark).

It was pointed out a decade ago that the effectiveness of prophylactic mefloquine needs to be evaluated rigorously by means of a randomised controlled trial in appropriately characterised travellers.[4] Such a trial has still not taken place.[5] Reid et al castigate the media for spreading confusion about mefloquine's adverse effects, but we believe that the media have performed a valuable service to travellers by highlighting an area of clinical practice that is governed by opinion rather than sound scientific evidence.

Members of the public who seek medical advice before travelling expect a clear and unambiguous exposition of the benefits and harms of any prophylactic drugs that they may be advised to take. Such advice needs to be informed by evidence from randomised controlled field trials carried out recently in tourists and business travellers. Studies carried out on soldiers undergoing training, prisoners, and non-travelling occupational groups (such as Peace Corps volunteers) are not an adequate substitute for well designed field trials in an appropriate travelling population.[5] Instead of criticising the media we should devote our energies to ensuring that this research now takes place.

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National code of marketing of formula milks is not properly enforced in Sri Lanka

Editor—Gunasekera and Gunasekera, in their letter, state that advertising and promoting the use of formula milk as a substitute for breast feeding are prohibited in Sri Lanka.[1] This may lead us to believe that the enforcement of the national code of marketing of breastmilk substitutes is being properly carried out in Sri Lanka. I am afraid that this is not the case. Advertisements for formula milk not in keeping with the spirit and principles of the code continue to appear—even in some of the medical journals in Sri Lanka.

As one of the respondents to the national questionnaire survey on breast feeding referred to in the letter, I made the point then (in 1996), and I make it now, that the national surveillance and monitoring mechanism to ensure compliance with the national code is ineffective. Without an effective mechanism for monitoring and proper implementation of the code, the power of advertising of breastmilk substitutes, rather than scientific knowledge about breast feeding, will influence healthcare professionals' attitudes to the promotion and protection of breast feeding.

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Cholesterol screening and management guidelines

Having several guidelines is confusing

Editor—Unwin et al highlight the fact that several widely available guidelines for the management of hyperlipidaemia give conflicting advice for the primary prevention of cardiovascular disease.[1] Some of the issues deserve further scrutiny.

The New Zealand guidelines are based entirely on the ratio of total to high density lipoprotein cholesterol concentrations for calculation of the absolute risk of cardiovascular disease over five years.[2] The American national cholesterol education program, however, clearly says that it does not recommend use of the ratio of either total or low density lipoprotein cholesterol to high density lipoprotein cholesterol[3]; instead it recommends use of the absolute high and low density lipoprotein cholesterol concentrations. The rationale behind this is that these concentrations are independent risk factors with different determinants; combining them into a single number conceals information about either or both, which might be important for making clinical decisions. A patient with raised total, high density lipoprotein, and low density lipoprotein cholesterol concentrations (a common clinical problem) falls into either the low risk category or the high risk category depending on whether the ratio or absolute values are used.

The New Zealand guidelines,[2] guidelines of the European Atherosclerosis Association,[4] and Sheffield tables[5] are based largely on age and sex, unlike the guidelines of the American programme,[3] which are not; the American guidelines mention, however, that the risk is higher in men than in women. Use of these guidelines would therefore be associated with the highest number of patients requiring antilipid treatment.

Only the American guidelines give clear guidance on when measurement of high density lipoprotein cholesterol is indicated in patients with hyperlipidaemia. Measurement of this concentration is labour intensive and expensive and therefore has major implications for laboratories. The New Zealand guidelines necessitate measurement of high density lipoprotein cholesterol in all patients, which would increase the cost substantially. Financial implications may be an important factor for NHS trusts deciding on their policy for managing hyperlipidaemia.

Patients are often bewildered when different doctors give them conflicting advice about antilipid treatment. Just as too much of anything is undesirable, too many guidelines end up confusing both patients and doctors.

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Policy based on Sheffield table fully satisfies authors' criteria

Editor—One important point is incorrect in the discussion in Unwin et al's paper comparing guidelines for screening for and treating raised cholesterol concentrations.[1] The guidelines examined were not all based on consensus development without the evidence or the economic and service implications being considered.

The Sheffield table,[2] which forms the basis of the guidance in the *Drugs and Therapeutics Bulletin* and the guidance from the Standing Medical Advisory Committee, was developed after we considered the clinical trial evidence; we set out the number needed to treat, cost effectiveness, population implications, and total cost of statin treatment at different levels of absolute risk of coronary heart disease. At the risk of a coronary heart disease event proposed for primary prevention (3% a year) the number needed to treat for five years is 20[2 3]; the cost effectiveness is about £6700 per life year gained[4]; and the total cost of full implementation would be about one quarter of the drugs bill at current prices of statins.[3 4] At this threshold of risk we predicted that statin treatment would be needed by 8.2% of British adults,[2 3] a figure close to the 8.6% observed by Unwin et al.

We have also examined formally the accuracy of the Sheffield table for targeting treatment appropriately.[5] A policy based on the Sheffield table satisfies fully the criteria set out by Unwin et al and should not be bracketed with other guidelines that do indeed have the important shortcomings which they highlight. It is simple, accurate, and evidence based and takes costs and

resources into account; it is unfortunate that these authors and others have failed to recognise this.

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Effects of NSAIDs on bone healing have been widely reported in maxillofacial journals

EDITOR—Stone and Richards imply in their letter that a well designed trial in humans is required to study the possible detrimental effects of non-steroidal anti-inflammatory drugs on bone healing.[1] This is not necessary. Maxillofacial journals have published an abundance of reports studying the effects of various non-steroidal anti-inflammatory drugs on pain relief after the surgical removal of third molars.[2–4] The healing dental socket replicates the biology of fracture healing. These various studies randomised patients to placebo or non-steroidal anti-inflammatory drug; they did not specifically study bone healing, but the authors would have been obliged to report any adverse effects and they did not report any delay in bone healing.

Varghese et al's work on rodents should not be extrapolated to the clinical situation and seems to be of only academic or veterinary interest.[5] Not only would a trial be unnecessary but it would also be of questionable ethics if it deprived patients of these valuable and effective drugs.

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People are "participants" in research

Further suggestions for other terms to describe "participants" are needed

EDITOR—Congratulations to Boynton for suggesting that the word "subject" should be banned from reports of research on humans.[1] It was Curt Meinert, formerly editor of *Controlled Clinical Trials*, who first pointed out to me that the word "subject" is demeaning. Although I changed my terminology from that moment on, I found it difficult to persuade others. I was particularly disappointed that I failed in 1989 to persuade a lay group—Consumers for Ethics in Research—to purge the organisation's literature of the word.

In an article published in 1995[3] I suggested that medical researchers would do well to follow the example set by the British Psychological Society.[4] After noting that psychologists owe a debt to those who agree to take part in their studies, who therefore deserve to be treated with the highest standards of consideration and respect, the society recommended that the term "subject" should be abandoned and replaced by "participant."

I applaud the *BMJ*'s prompt and positive response to Boynton's suggestion. The journal will find that the term "participants" works well for those types of research (such as controlled trials) in which active involvement of the people being studied is required, although some may prefer the word "volunteers" to describe participants in non-therapeutic research. Choosing appropriate terms to describe people who were not actively involved in the research being reported (for example, because they were dead) presents a greater challenge. "Patients" may be appropriate in some circumstances, but not all. Maybe organisations like Consumers for Ethics in Research could help researchers and medical journals by suggesting appropriate terminology across the whole spectrum of research designs.

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Many people are not "participants" in sense that this term was initially defined

EDITOR—The *BMJ*'s decision to use the term "participant" instead of "subject" for a patient taking part in a clinical trial is well intentioned but may cause confusion.[1] I am currently writing about a multinational trial involving over 7000 patients, 800 clinical investigators, 40 clinical monitors, 6 regional coordinators, 6 members of the steering committee, and many other staff in local and regional centres and at the trial headquarters. All these people are "participants" in the trial. The issue is to find a term that separates those who are randomised from those who care for them and handle the resulting data. This applies to all trials, whether or not those who are being studied have played any part in their design.

As most clinicians will testify, the term "patient" no longer implies passivity. Is either "subject" or "participant" really a better alternative to the use of this long established term in most clinical research reports? In some studies "patient" is inappropriate, as those under investigation are not unwell. In this case, although I do not like the term "subject" (with its implications of subservience), it does have a clarity that is lacking from the term "participants." An alternative for use in many circumstances might be "volunteers."

In truth, many of the implications of the term "subject" remain accurate for most clinical trials in which most subjects (and, indeed, many other participants) are not, and never can be, "active participants in the process of deciding what research should take place, commissioning research, interpreting the results, and disseminating the findings."[1] It is laudable to suggest that every trial should be designed with consumers in mind but unrealistic to suggest that every patient or volunteer can be a full participant in that sense. Authors must not be encouraged to claim that such participation has taken place when it has not. The *BMJ*'s new policy may do this.

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Pharmaceutical companies should follow medical profession's lead

EDITOR—We live in an increasingly accountable and politically correct age. Everything we write or say has to be quantified and qualified, particularly in the medical press. When the ABC of Sexual Health was recently published in the *BMJ* the journal occasionally warned on its front cover that it contained sexually explicit material. Minerva for some time now has required submissions to her page to "include signed consent to publication from the patient." This even applied apparently when the subject was a 3500 year old Egyptian mummy with aspergillosis.[1] "Subjects" are now to be called "participants."[2] In addition, authors have to declare competing interests and to state sources of funding. Admirable requirements indeed.

To maintain these high standards of accountability I propose that the pharma-

ceutical industry should come into line with the medical profession. This could be achieved by requiring all pharmaceutical advertisements that contain photographs of "patients" to carry a declaration that the subject (or participant) indeed did, or does, have the stated disease or ailment; is not an actor or actress; and has benefited from using the stated product. Furthermore, the person in the photograph should have agreed to be depicted in the given context, and financial incentives should be declared.

Adverts often show happy faces (often, curiously, of young and attractive people) and some show "before and after" photographs. Perhaps pharmaceutical companies are aware of the current discrepancy between their and medical literature's accountability; cartoons are increasingly being used, and one company has a long association with a clown (the ultimate anonymisation?).

If the pharmaceutical industry came into line with the medical profession the discrepancy between the scientific evidence of a product's efficacy and the image or photograph displayed might remain. The image, however, would be authentic and more credible; most of all, the drug company would be more accountable.

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1 Minerva. *BMJ* 1996;313:240.
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Reporting on quality of life in RCTs

CONSORT guidelines should be expanded

Editor—Sanders et al's bibliographic study on the frequency and detail of reporting on quality of life data in randomised controlled trials listed in the Cochrane Controlled Trials Register is disturbing.[1] Despite increasing emphasis on patient centred outcomes in all aspects of clinical practice and research, less than 5% of trials reported on quality of life and even fewer comprehensively reported the quality of data using well validated, familiar instruments.

Deyo and Patrick discussed methodological, attitudinal, and conceptual barriers to the use of quality of life assessments in research in 1989.[2] They noted the paucity of information regarding the responsiveness, reliability, validity, and psychometric characteristics of most instruments. In the 1980s many authors noted the problem of a confusing array of instruments, including scales with the same purpose.[2 3] Feinstein et al noted 43 scales measuring activities of daily living.[3]

Deyo and Patrick suggested increased reporting of studies that compared different quality of life instruments in the same population and comparing the use of generic instruments in different diagnostic groups. They also advocated testing any newly developed instruments against well established scales and the development of a "quality of life research laboratory" to aid researchers with the analysis and standardisation of data on quality of life.[2]

In the light of Sanders et al's study, all trialists need to think again about the suggestions above. The CONSORT guidelines could be expanded to include recommendations on which tested, well validated quality of life instruments should be selected for use in different situations. This would aid researchers' choice and improve standardisation and generalisability.

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Authors are creating database of quality of life questionnaires

Editor—Sanders et al reported that the presentation of quality of life data in clinical trials was often flawed.[1] We are creating a database of quality of life questionnaires used in clinical trials and are assessing the quality of the trials with a checklist that we have drawn up. We have encountered 10 main biases:

(1) The trial is not comparative.[2]

(2) No justification is given of the number of patients included—the number may be too small to achieve enough power to detect a difference between two treatments or too large, leading to a difference that is significant but not clinically relevant.[3]

(3) The quality of life questionnaire is not validated, and its responsiveness has not been tested.

(4) No description is provided of the follow up of patients during the study.

(5) No description is given of withdrawals and the handling of missing data.

(6) Analysis of quality of life data is performed on a per protocol basis instead of on an intention to treat basis—for example, <530 patients are analysed instead of the 812 randomised in a trial comparing ranitidine with placebo in gastro-oesophageal reflux.[3]

(7) The presentation of quality of life results is flawed—for example, only graphs are presented and no actual value is given, and standard deviations of scores in the different domains of quality of life are missing.

(8) Ideally, the confidence intervals of the differences between treatment groups or the size effect, or both, should be given.

(9) The level of significance is not adapted to the number of statistical comparisons, leading to an increased α error.

(10) The clinical relevance of the results relating to quality of life is not discussed—for example, when only two or three among eight or nine domains of the quality of life questionnaire improve significantly in one group compared with the other[3 4] or when the differences in quality of life scores between groups seem slight.[3] In Liard et al's study, in which a specific questionnaire was used as a primary end point, only two of the nine domains had improved significantly with naftidrofuryl at six months. These two domains were pain and daily life, the minimum goals for a treatment claiming to alleviate symptoms of arteriopathy.[4]

Assessment of quality of life requires rigorous methodology, follow up of patients, and statistical analysis. Thus reporting on quality of life should be considerably improved and should follow the CONSORT guidelines.

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Drug misuse stems from a person's autonomy to choose

Editor—Robertson's critique of prison medical care of drug misusers would be valid if his fundamental proposition that drug misuse is a disease was held by all.[1] If this were the case then clearly medical practitioners would have a duty both to prevent the disease and to mitigate its sequelae.

Drug misuse is not a disease in the sense of an unfortunate assault on one's health. Rather, it stems from an individual's autonomy to choose whether or not to misuse drugs. Any medical input at this causal stage of choice could be viewed as beneficent paternalism and, from an ethical point of view, no more than that.

Drug misusers in custody do not always wish to seek medical help, so Robertson's inference that drug problems in prisons are "unacknowledged" itself needs rehabilitation. Even when prisoners are discharged, community practitioners rarely seek custodial medical information, which is always available on request. As I was drafting this letter, however, a medical practitioner did phone up regarding the treatment of a recently discharged drug misuser. He wanted to know if his patient had been receiving dihydrocodeine, zopiclone, and diazepam. The patient's record in fact showed that he had been taking tar based

shampoo, and an antibiotic and an analgesic for a dental problem. Caution is needed in dealing with drug misusers; I wonder how this vignette supports or disproves Robertson's thesis.

Discharged patients rarely consent to their community practitioners having access to their custodial medical history—save where litigation is an issue. The prevalence of mental disorders in prisoners is well documented, so practitioners must explore fully the possibility of mental illness before opting for the more nebulous clinical option of post-traumatic stress syndrome.

Perhaps the Alcoholics Anonymous method of dealing with alcohol misuse should be applied, for here the autonomy of the patient to change his or her lifestyle is paramount. Using a medical model upholds the myth that addicts are the passive agent in a disease process over which they have no control.

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1 Robertson R. Unacceptable practices: Prison to the community in one, totally unprepared, step. *BMJ* 1998; 317:757. (12 September.)

Dutch system of peer review is different and effective

EDITOR—Much has been written in the past two years about continuing medical education (see the series that began in January last year[1]), peer review,[2] and revalidation.[3] Despite this I have not seen any mention of the Dutch system of peer review, which has been running for five years (S van der Baan, conference of the Dutch Ear-Nose-Throat Society, March 1998).

Each specialist is required to belong to a group of four to eight like-minded specialists,which is reviewed every five years. The specialists need not be working in the same hospital. Before the review the group members complete a questionnaire about facilities, workload, audits undertaken, etc. The visiting team consists of three doctors from the same specialty: a member of the board of the specialist society, someone who has been reviewed in the past three months, and someone who is to be reviewed in the next three months.

One of the reviews lasts six hours. As well as discussing the questionnaire and the audit material with the group the review team meets representatives of local management, of the nursing staff, and of the local general practitioners. Before the final meeting with the group it inspects the facilities and a sample of the case notes. It sends the group a draft report of the visit for comment. The final report may include a recommendation that a further visit should take place in two years. The group decides whether or not to show the report to management. An appeal mechanism exists.

The system has three advantages. Firstly, group peer review is much less threatening than individual peer review. Secondly, as the individuals are to be reviewed as a group they are likely to meet together and support each other. This in itself often raises the quality of care. In addition, group members can be mentors for each other in the preparation of personal development plans. Thirdly, everyone in the specialty is involved as each group can visit two other centres every five years; the educational value of such visits is well established.

A visit rarely fails to identify a doctor whose performance is giving cause for concern. Even if the members of the group support each other when meeting the review team, the discussions with management, the nursing staff, and general practitioners identify any doctor who seems to be performing poorly.

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South African government's response to AIDS crisis is sound

EDITOR—Sidley reports that the South African government is refusing to provide money for giving zidovudine to pregnant women who are HIV positive.[1] It is time to come out in defence of the government. The South African health minister and her colleagues in regional governments have made an ethically responsible decision about resource allocation. They decided not to fund zidovudine for HIV positive pregnant women for two reasons: funding this programme would cripple other HIV health education efforts, and zidovudine at the price that the manufacturer demands is not a cost effective means of preventing HIV infection in South Africa.

The United Nations AIDS programme has done much to promote zidovudine to HIV positive pregnant women in developing countries, regardless of the cost implications for local health budgets. It is reassuring that not every government in the region has caved in to the market pressures that the UN organisation has created on behalf of Glaxo-Wellcome. The manufacturer demands a price for this drug that effectively puts it out of reach for HIV positive women not only in South Africa but also in other developing countries. Governments of developing countries must take a stance on this matter and not allow themselves to be held hostage by Western multinationals. The only people to blame for the excess deaths in countries such as South Africa are those in the boardrooms of Glaxo-Wellcome and its shareholders.[2]

Locals frustrated with their government's decision must make their anger known at the right address. Don't blame the South African government—applaud it for its decision.

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1 Sidley P. South African AIDS plan criticised. *BMJ* 1998; 317:1032. (17 October.)
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ECT was never used indiscriminately in early treatment of shell shock

EDITOR—Summerfield is mistaken in his review of a television programme about patients with shell shock.[1] Dr W Sargant (not Sergeant) did not use insulin comas in war neuroses. "Modified insulin," with small doses to stimulate appetite, was used in anxiety states with weight loss; patients were fed large quantities of mashed potato. This, together with extra nursing care, helped some. Small doses of intravenous amytal were used to facilitate the abreaction of the emotions associated with battle trauma.

Sargant was one of the first to use anaesthetics and muscle relaxants with electroconvulsive therapy. Electroconvulsive therapy was never used by Sargant and those working with him in an "increasingly indiscriminate fashion." This myth should not be perpetuated.

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1 Summerfield D. Shell shock victims: from cowards to victims. *BMJ* 1998;317:1396. (14 November.)

Value of educational visits in obstetrics

Randomised controlled trial was unsuitable evaluation

EDITOR—We are not surprised by the conclusions drawn by Wyatt et al that educational visits added little to the uptake of evidence into practice.[1] We question whether randomised controlled trials can be applied to studies evaluating education, which may use qualitative as well as quantitative methods.

A controlled trial may not be the appropriate tool to reflect changes of interventions in childbirth over time. It is not possible to isolate clinicians to one educational intervention (in this case an educational visit). Practice may also change as a result of experience as well as more formal learning such as reading journals and continuing medical education. Even if a change in practice had been shown by this study, a more qualitative approach would be required to determine if the change was due to the intervention being investigated.

The practice of evidence based medicine is the integration of individual expertise with the best available external clinical evidence from systematic research.[2] Research, whether

primary or review, needs to be appraised critically. Only four interventions from the 600 reviews contained in the Cochrane Database of Systematic Reviews were studied. This included a systematic review on forceps versus ventouse delivery by one of the main researchers. This review is open to criticism since many of the papers selected were written by the author of the review.[3] It would be disappointing if the practice of educational visits were to be discontinued solely on the evidence of this study.

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Staff changes will have affected ventouse rates

Editor—Wyatt et al assessed the benefits of educational visits to enhance the use of systematic reviews in 25 obstetric units.[1] Both the authors and the accompanying editorial[2] comment on the wide variation in ventouse delivery rates. There is wide variety within and between the study and control groups, with 22 of the 25 units having a baseline ventouse rate at or outside the 95% confidence interval for the average. This must cast doubt on the significance of the finding that the use of the ventouse increased in the study group.

The authors overlooked one possible reason for the variation in ventouse delivery rates and the subsequent change over nine months. Most instrumental deliveries are performed by registrars (52%) and senior house officers (45%).[3] Their preference for the ventouse versus forceps is unlikely to be affected by unit policy as much as by their education and previous experience. More significantly, most junior staff rotate between units annually. Wyatt et al do not specify at what time of year their study was performed, but it is possible that the junior medical staff had entirely changed between their baseline and follow up observations. New staff would have imported their instrumental delivery rates and preferences from their previous units.

The same argument can be extrapolated, although less convincingly, to the other markers identified. Many, although certainly not all, perineal repairs are performed by junior medical staff, who are also responsible for prescribing steroids in threatened preterm labour, often without input from senior colleagues.

Perhaps a greater effect would have been shown if, instead of using obstetric units as subjects, junior staff, such as registrars, had been chosen as subjects for randomisation and their personal practices studied.

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Good clinical audit is needed for interpreting systematic reviews

Editor—Many factors influence a change in clinical practice, and Wyatt et al cannot conclude that educational visits are any more influential than other forms of guideline or recommendation.[1] Half the 25 obstetric units already had access to the Cochrane database at the start of the study, presumably implying a willingness to consider change. That 10/13 of the non-intervention units had the Cochrane database within the 9 month trial demonstrates a progressive background change, thus questioning the validity of conclusions about the educational intervention.

It is not surprising that wide variations occurred in baseline rates from the randomisation of such small numbers. This variation has been shown before, both between hospitals and from year to year.[2]

The use of the ventouse is particularly dependent on the operator. The paper provides no data on any changes in the non-consultant grade staff, who perform the majority of such interventions, over the study period. Statistical power is implied by the use of the statement that this was a "rigorous randomised trial" and by the eminence of the statistician author, but there are several question marks about the methods and results, which were emphasised by Keirse.[3]

One of the most rapid changes in clinical practice seen recently was the immediate withdrawal of albumin from clinical practice in our hospital after publication of a paper in the *BMJ* in July.[4] This has since lead to much comment about the use and abuse of such "powerful" evidence.[5] Systematic reviews are just one part of the assessment of clinical effectiveness. We must know how they apply to our patients and be able to respond to innovations and new data. We must implement more thorough clinical audit and start allocating real time, staff, and resources to this process. This should be an ongoing exercise, with constant reviewing of the appropriateness of the standard, however set. This is costly, but allows clinicians to know how applicable a standard or recommendation is to their patients. After all, one person's proof will always be another person's conjecture.

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Having non-medical readers of papers on internet will enhance peer review

Editor—Eysenbach and Diepgen have summarised clearly the problems of quality control on the internet, but their interpretation of the current situation and likely future developments is inadequate.[1] Electronic communication is the future and is increasing the availability of information in many areas, of which medicine is only one.

The authors have underestimated the discriminatory abilities of those accessing the information. Patients have heard reports of magical cures and cancer healers for hundreds of years and have given these the short shrift that they deserve. The internet increases access to this misinformation[2] but will not change people's interpretation of it. There is a seam of arrogance running through the arguments on medical publication on the internet that assumes that only doctors can qualitatively assess and interpret the information.

The authors' suggestion that source filtering will confirm the origin of information implies a naivety similar to that of the subscribers to some of the magical cures offered online. It is easy to disguise and falsify one's origin on the internet; how many readers have received junk email that seems to be from an entirely reputable source but actually originates from somewhere untraceable? Where money is involved, website authors will not be averse to falsifying certificates of authenticity.

Our role as responsible medical practitioners has to be one of leading by example, developing authoritative websites with formal and open peer review of the material published there. We must not dismiss the input that non-medical readers may provide—not only constructive criticism of methodology but also the different interpretations of end users. Perhaps more free and open publication of data, which can then be openly assessed and criticised without the inordinate delays inherent in paper publishing, will reduce publication bias,[3] will encourage clinicians to develop their research in more relevant ways, and lead to enhanced discussion of those results.

The ultimate aim must be to bring medical research to the forefront of public awareness, to increase understanding, and subsequently to increase funding. The internet is an open market, and additional regulation and red tape will strangle online presenta-

tion of scientific and medical research and sideline it in favour of the exciting sites run by the quacks of this world.

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Population figures for capitation formulas need to be designed differently

EDITOR—The organisation of health care through primary care groups with unified cash limited budgets raises several questions concerning the methods of resource allocation that will be used. The presumption is that there will be some form of weighted capitation, and this will obviously generate considerable agonising—and eventual compromise—among the doyens of resource allocations formulas[1 2]; but there is one basic point which has to be resolved even before those discussions can start: what is the correct population base?

The formulas in the hospital and community health services sector are based on the resident population,[3] based on estimates from the Office for National Statistics. Weighted capitation formulas in the primary sector are also based on these figures, but are adjusted to reflect patients registered with the general practitioners responsible to the health authority in question.

However, allocation to sub-health authority units such as primary care commissioning groups—and eventually to practices—have to take into account the registered list sizes compiled for each practice by the responsible health authority. These lists are on average 6% higher than the estimates by the Office for National Statistics; comparison with data provided by the General Medical Services—Statistics branch of the NHS Executive shows that this varied in 1997 between −8% in Morecambe and 23% in Ealing, Hammersmith, and Hounslow.

It has been assumed that there are "reasonable" explanations of this "inflation": for example, mobility, mostly of young adults (ages 15-24), and delay in removing patients who have died or emigrated from practice lists.

Not unsurprisingly, health authorities have been attempting to "rationalise" the lists and "resolve" the conflicts between the two estimates. Notwithstanding these efforts, the values of list inflation have remained about the same and have been differentiated in the same way between age groups and between authorities over several years.

We are currently investigating the differences between the two population figures, and early results indicate that counting errors by health authorities account for only a minority of the differences. The two figures are defined, collected, and administered very differently. It is essential that, whatever the decision finally made as to which is the most appropriate and practical to be used in designing weighted capitation formulas, both the Office for National Statistics and the health authorities ensure that both sets of figures are accurate and that they are based on the most up to date information possible. Whichever is chosen, there will be substantial shifts in the target budgets for some authorities and practices.

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Reviews have to be fair and unbiased

EDITOR—As the editors of the *Textbook of Clinical Medicine of Asia* we believe that we have to respond to the unnecessarily rude and offensive review of our book in the *BMJ*.[1] Gilks has misunderstood the purpose of our textbook and also shows his ignorance of the nature of medicine in Southeast Asia.

The difference in the standard and practice of medicine between Asia and the West (North America and Europe) is considerably smaller than that between the West and Africa or South America. Most Asians live in large cities, and in some of these cities the standard of medicine and type of practice is similar to, or even better than, that found in Liverpool. In most of Asia, the incidence of infectious diseases (presumably the main interest of Gilks) has declined, and today we deal predominantly with the so-called Western diseases. Our purpose in writing this book was to provide a standard textbook that students can use, not to write a book that just highlights the differences between Western and Asian medicine. We were hoping to combine the usefulness of a standard student textbook with some emphasis on those areas where prevalence or practice are slightly different in Asia. To say that we have just provided a smattering of local data and anecdote is untrue. There is a shortage of good epidemiological data from Asia, but what there is we have quoted. Nearly every chapter has a section on the epidemiology of the subject in question in Asia and China. This includes information on hypertension, coronary artery disease, asthma, pneumonia, hepatitis (a particular problem), IgA glomerulonephritis, clinical endocrinology in Asia, diabetes in Chinese people, systemic lupus erythematosus, rheumatoid arthritis in elderly people in Asia, dermatology, etc. In addition, we have a chapter on Chinese herbal medicines.

The fact that Gilks says that "no references from Chinese sources are cited" makes us wonder if he has actually read the book. Instead, he seems to have taken the opportunity to express his bias and preference towards traditional tropical medicine, particularly as practised in Africa and South America. His disparaging and dismissive remarks about expatriate and local consultants are unfair and unworthy of a professional book review.

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1 Gilks C. Textbook of clinical medicine for Asia [review]. *BMJ* 1999;318:337. (30 January.)

Medical student electives and infectious diseases

Zidovudine alone is not recommended prophylaxis

EDITOR—Gamester et al found that only 34% of students visiting a country with a high prevalence of HIV purchased zidovudine, probably because of the cost (£40). They recommended that medical schools should consider paying for the drug.[1]

However, zidovudine alone is no longer the standard postexposure prophylaxis. United Kingdom guidelines now state that healthcare workers with high risk exposure to HIV should be advised to take a combination of zidovudine 200 mg three times a day or 250 mg twice daily plus lamivudine 150 mg twice daily plus indinavir 800 mg three times a day.[2]

Indinavir should be taken 1 hour before or 2 hours after a meal.[3] Nephrolithiasis may occur with indinavir, and manufacturers recommend drinking 1.5-2 litres of fluid daily during treatment. Reports suggest that more nephrolithiasis occurs in warm weather and that the volume should be increased in warm climates,[4] which would be relevant to many students travelling to hot countries. Advice must be given to anyone who may take treatment which includes indinavir.

Today's doctors expect adequate advice and nationally recommended treatment. We should offer no less to the doctors of tomorrow.

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Risk of hepatitis C is greater than HIV

EDITOR—Wilkinson and Symon's editorial[1] and the two associated papers[2 3] deal with extremely important issues surrounding the safety of medical students during electives spent in countries where there is a high likelihood of encountering HIV and transmissible tropical diseases professionally.

Another important issue arises out of these papers. With regard to blood-borne viruses, the emphasis was entirely on HIV. However, hepatitis C (170 million cases) is much commoner worldwide than HIV (less than 40 million cases) and is more easily acquired through needlestick injury.[4] Furthermore, it cannot be vaccinated against and must also, with the current state of knowledge, be considered incurable. Unlike for HIV, no postexposure prophylactic regimen is currently available. It would therefore be advisable to link information given to medical students about HIV prevention to advice about hepatitis C and its prevention. Such advice would also be valuable to students when they qualify—it may even save their life.

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Early discharge after surgery for breast cancer

Self selection probably occurred among patients studied

EDITOR—We are pleased that psychological implications of early discharge after surgery for breast cancer are being examined[1] but think that some important aspects of the policy have been inappropriately or inadequately researched and warrant further investigation.

There is a drawback to applying randomised controlled trial methodology in situations such as this, where patients are making choices about their care. A self selecting process operates and must be taken into account in the research design; if it is not, a randomised controlled trial will study a biased sample—it will include some patients who might not otherwise have considered earlier discharge and exclude those who are most committed to the idea and do not want to risk being randomised to the control condition. This is not a peripheral issue. The policy framework for commissioning cancer services has emphasised the need to involve both patients and their carers in decisions about their treatment. This involvement should extend to the decision regarding the timing of the patient's discharge from hospital.

We agree with Fallowfield that the impact of early discharge on a woman's carers must be examined in more detail.[2] As she emphasises, the earlier discharge of patients who are frail after surgery will simply transfer the burden of care. Earlier discharge might well appeal to patients but might place unreasonable demands on their carers. Furthermore, while early discharge from hospital may be an efficiency saving on hospital bed use, primary care may be left with increased demands to provide back up but no additional resources.

We recently audited the psychological implications of earlier discharge and found that psychological adjustment, levels of satisfaction, and involvement in the decision regarding timing of discharge were high among both patients and carers. Early discharge after surgery for breast cancer may offer important economic savings, but our findings support the view that it is not appropriate for all women. Working to a formal protocol, we found that just over a quarter of patients were eligible for early discharge, and in most cases this proceeded successfully.

The wider implications of this practice still need to be considered further.

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The introduction of walk in health centres—the end of general practice?

EDITOR—The prime minister's announcement that walk in health centres are to be set up beggars belief.[1] One of the crucial strengths of British general practice is the ability to register with a general practitioner. That doctor is able get to know patients and their families, such knowledge contributing enormously to the quality of advice that can be given. It saves a lot of expense in terms of time, unnecessary investigations, and treatment if the doctor knows the patient.

Abandoning such a fundamental component of the system has hit the first nail into the coffin of traditional, cost effective general practice. The promise of instant and late night access panders to the selfishness of consumerism. It is a foolish, expensive way of disregarding a system that would work well if it were adequately funded. Inappropriate demand will be inappropriately met by staff who do not know patients and may never see them again. Such staff will have little responsibility for their ongoing care or the consequences of their actions for patients' health or local health budgets. Of course many patients will welcome the immediacy of this innovation, the apparently virtuous staff who run the centres, but they will be unaware of the effect it will have on the NHS as a whole or even on themselves.

Inadequacies in the current service should be tackled at their roots and not sidestepped. Late night opening could be a regular feature of general practice if there are incentives. Spending £30m on 20 new centres duplicates the investment the NHS has already made in surgeries across the country. A salaried service is only appropriate where new general practitioners decline to work. Even then they should have a list.

Maybe we were wrong to scoff when Margaret Thatcher famously said, "The NHS is safe in our hands." Did we ever think things would come to this? It seems that the time is up for independent contractors if we take this lying down.

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