Letters

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Reforms to the health sector must retain vertical programmes like those for tuberculosis

EDITOR—Health sector reform has become the policy urged on poor countries in the developing world. Basically it entails transferring responsibility for health services and health budgets to local communities. I am sympathetic to this approach. But its uncritical application by governments has a dangerous obverse.

Vertical programmes—for instance, central coordination and monitoring of the World Health Organization's DOTS (directly observed treatment short course) programme for control of tuberculosis—may be discouraged. The programme may be suddenly abolished. The economy of scale resulting from national bulk buying of antituberculous drugs disappears. The tuberculosis experts in the Ministry of Health, who provide leadership and coordination and who monitor the programme, are dispersed to other jobs. Suddenly there are no drugs for tuberculosis, either centrally or at the periphery, and no control programme.

I am told that this has already occurred in Zambia and Ethiopia. It almost occurred in Bangladesh. It is threatening to occur in many other countries.

With HIV infection and multidrug resistance, the World Health Organization has declared tuberculosis to be a global emergency. It is a desperate race against time to establish good national tuberculosis control programmes, especially in the 22 countries that contain four fifths of the world's cases. National control programmes would prevent the development of multidrug resistance—always the result of bad doctoring—before the alliance of multidrug resistance with HIV infection creates an almost untreatable pandemic (tuberculosis is no respecter of frontiers).

It is essential to retain the economies of scale offered by the central purchase of drugs and basic diagnostic equipment. It is essential to retain control of central monitoring and coordination and gradually to hand over the major responsibility of the service to local communities as their skill develops. Just as in community development projects in the United Kingdom, professionals continue to be needed in the background to pick up the bits when a local administration fails.

When I raised this problem at a recent symposium on global health the representative of Save the Children supported me. He said that the child immunisation programme in Uganda had almost collapsed for the same reasons. I have just visited the School of Tropical Medicine in Liverpool and had discussions with people working on tropical disease problems in poor countries. Although sympathetic with the concept of health service reform, many are disturbed by the possibility of the sudden abolition of vertical programmes with no real provision for their effective replacement.

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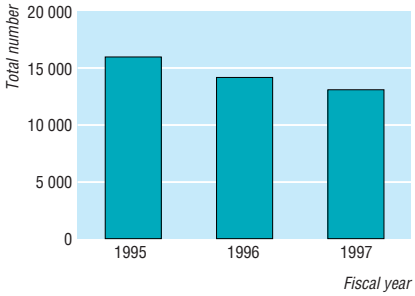
Misconceptions about tuberculosis among immigrants to the United States

EDITOR—Charatan's story in news extra about tuberculosis among foreign born people in the United States requires clarification.[1] The term immigrant is not used accurately. An immigrant to the United States is a person who is admitted as a lawful permanent resident or who becomes a permanent resident while living there. About 400 000 people qualify in each category annually; about 70 000 refugees enter annually.[2]

Within the Public Health Service, the Division of Quarantine of the Centers for Disease Control and Prevention writes the guidelines for the medical examination required for all immigrants and refugees and notifies receiving health departments of those who may have tuberculosis (figure).



Arriving immigrants and refugees with chest radiographs suggesting possible current or old healed tuberculosis, fiscal years 1995-7, United States

Potential immigrants and refugees who have infectious tuberculosis must be treated until they are not infectious. They are then allowed into the country on condition that they are followed up by the local health department. Those with possible non-infectious tuberculosis are also referred to local health departments; over 90% are evaluated.[3]

The United States Immigration and Naturalization Service has estimated that five million people born outside the United States were living in the country unlawfully in October 1996.[3] It has responded to this with increased screening of those who are apprehended and detained. Roughly 155 000 people were placed in Immigration and Naturalization Service detention during fiscal year 1999. The Public Health Service's Division of Immigration Health provides healthcare support to the immigration service by screening detainees for tuberculosis. In the last fiscal year the division screened over 52 000 detainees who were held for at least 48 hours or had symptoms of tuberculosis (G Migliaccio, personal communication, 1999). Other detainees might have been screened for tuberculosis while in correctional systems not covered by the division.

The total number of people born outside the United States who had tuberculosis in the country fell from 7930 in 1995 to 7591 in 1998. During the same period the rates of tuberculosis in people born in the United States and people born outside the United States fell to 4.4/100 000 and 28/100 000, respectively.[4]

The Centers for Disease Control and Prevention has made it a priority for state and local health departments to follow up and treat immigrants and refugees identified as possibly having tuberculosis and for the Division of Quarantine to continue forwarding their medical documentation to relevant health departments.[5] The recent decline in tuberculosis among people born outside the United States probably reflects successes in tuberculosis screening and follow up. More effort is needed to address the problem of tuberculosis among the roughly five million undocumented people living in the United States to ensure that all segments of the population receive screening and treatment.

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1 Charatan F. US alarmed over rise in tuberculosis among immigrants. bmj.com 2000;320: www.bmj.com/cgi/content/full/320/7228/140/d.
2 US Immigration and Naturalization Service. *Statistical yearbook of the Immigration and Naturalization Service, 1997.* Washington, DC: Government Printing Office, 1999.
3 Binkin NJ, Zuber PLF, Wells CD, Tipple MA, Castro KG. Overseas screening for tuberculosis in immigrants and refugees to the United States: current status. *Clinical Infect Dis* 1996;23:1226-32.
4 Centers for Disease Control and Prevention. *Reported tuberculosis in the United States, 1998.* Atlanta: US Department of Health and Human Services, 1999.
5 Centers for Disease Control and Prevention. Recommendations for prevention and control of tuberculosis among foreign-born persons. Report of the working group on tuberculosis among foreign-born persons. *MMWR Morb Mortal Wkly Rep 1998;47:1-26.*

GMC's advice in *Serious Communicable Diseases*

Is consent to testing necessary for tuberculosis in same way as for HIV infection?

EDITOR—The General Medical Council recently sent all medical practitioners in the United Kingdom its booklet *Serious Communicable Diseases*,[1] which replaces the earlier *HIV Infection and AIDS*.[2] In this the council broadens its earlier advice on consent to testing to include investigation of tuberculosis and hepatitis as well as HIV infection. We completely agree that tuberculosis should be regarded as a serious communicable disease, but treating it in the same way as HIV infection in the context of obtaining consent to investigation and treatment potentially presents major problems, which we wish to draw to the attention of readers of the *BMJ*.

Clearly, when the suspicion of tuberculosis is high it is appropriate to explain this to patients at the time of collecting sputum or other specimens for investigation. However, sputum is commonly tested for tuberculosis in patients being investigated for common respiratory symptoms, when the likelihood of having the disease is low. In our view, obtaining consent to specific testing for tuberculosis in such patients may create needless anxiety. Alternatively, it may even mean that appropriate specimens are not examined because of the concerns this might raise. We suggest that asking for general permission to test samples to exclude infection is appropriate without necessarily specifically naming tuberculosis when the probability of the patient having the disease is comparatively low.

We have raised our concerns about this advice with the GMC but it sees no need to modify its guidance.

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1 General Medical Council. *Serious communicable diseases.* London: GMC, 1997.
2 General Medical Council. *HIV infection and AIDS.* London: GMC, 1993.

GMC's reply

EDITOR—The British Thoracic Society argues that we set a single, overdemanding standard for obtaining consent to testing for serious communicable diseases. In fact, our guidance states that when obtaining consent to testing for a serious condition, doctors should provide information "appropriate to the circumstances and to the nature of the condition or conditions being tested for" (paragraph 4).[1]

In correspondence with the British Thoracic Society I have explained that doctors must use their judgment and common sense in considering what is appropriate. If one undertakes an investigation such as a chest *x* ray examination, which is comparatively non-specific and may reveal a number of different pathologies, then deciding whether to advise the patient about the possibility of tuberculosis would depend on the likelihood of it being found and whether the investigation was being undertaken specifically to exclude it. On the other hand, if one carried out a test which is specifically designed to detect tuberculous infection, the reason why the test is being undertaken needs to be explained beforehand. On this analysis, requesting a sputum sample for examination for acid fast bacillus to exclude or diagnose tuberculosis would merit an explanation to the patient beforehand, except in special circumstances.

The Standards Committee of the General Medical Council revisited the issue last year after correspondence with the society. The overwhelming view of the committee was that it was no longer acceptable to advise doctors that, as a matter of principle, they may undertake testing for serious conditions without the patient's knowledge or agreement. The whole thrust of our advice both in this guidance and in our booklet *Seeking Patients' Consent* is that it is for patients to decide, in most cases, what should be done.[2] As in other parts of medicine, we as doctors cannot hope to maintain the trust and respect of our patients unless we share information with them, respect their right to autonomy, and treat them as partners in the decision making process.

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1 General Medical Council. *Serious communicable diseases.* London: GMC, 1997.
2 General Medical Council. *Seeking patients' consent.* London: GMC, 1998.

Tracker trials

Introduction of resistance testing might be an inappropriate use of resources

EDITOR—Lilford et al argue for starting randomised studies of new health technologies as early as possible, even if the technology is in a phase of rapid development.[1] Many of the points discussed are highly relevant to assays measuring drug resistance in patients with HIV infection.

These assays are currently primarily used as research tools, but recent articles and clinical guidelines have recommended that they should be routinely performed to guide the selection of antiretroviral drugs in the management of patients with HIV infection.[2] The basis for these recommendations is not clear: the arguments are more complex than they first seem, and the empirical evidence that resistance testing improves clinical outcome is limited.[3]

The most commonly used form of resistance testing entails DNA sequencing of the reverse transcriptase and protease genes. But quality assurance studies have found that current methods frequently fail to identify key mutations associated with resistance.[4] Moreover, it is often difficult to decide how to use the result of the resistance assay, since the influence of viral polymorphisms on in vivo response to the many combination drug regimens available is poorly understood. It is likely that resistance testing will ultimately improve the selection of drug regimens and become cost effective as the accuracy and interpretation of assays improve. There is no certainty, however, that this point has been crossed, and the widespread introduction of resistance testing at this time could be an inappropriate use of scarce health resources.

Lilford et al propose flexible randomised trials—where duration is not predetermined and frequent interim analyses are conducted explicitly—and recognise that the effectiveness of a health intervention may change over time and they aim to monitor such changes.[1] Testing for resistance of HIV may be appropriately evaluated by this type of study, although, as in other areas, convincing the medical community of the merits of this approach and securing funding may be problematic.[5]

A randomised trial would collect the information required for analyses to elucidate the clinical significance of viral mutations. These analyses could be performed during the trial without compromising the main comparison of resistance testing versus no testing. In principle, the findings from these analyses could influence the interpretation of resistance assays performed later in the study. This would be a strength, not a weakness.

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Competing interests: The MRC Clinical Trials Unit is currently coordinating a (conventional) randomised controlled trial of HIV resistance testing.

1 Lilford RJ, Braunholtz DA, Greenhalgh R, Edwards SJL. Trials and fast changing technologies: the case for tracker studies. *BMJ* 2000;230:43-6. (1 January.)
2 Rodriguez-Rosado R, Briones C, Soriano V. Introduction of HIV drug resistance testing in clinical practice. *AIDS* 1999;13:1007-14.
3 Loveday C, Dunn D, McCormack S, Babiker A. The use of HIV resistance assays—random or randomised? *Sex Transm Infect* 1999;75:140-1.
4 Schuurman R, Brambilla D, de Groot T, Boucher C. Second worldwide evaluation of HIV-1 drug resistance genotyping quality using the ENVA 2 panel. *Antiviral Ther* 1999;4(supplement 1):41.
5 Support for non-competitive trials [editorial]. *Lancet* 1999;353:855.

Continuous process of trial and review is needed

EDITOR—With reference to the paper by Lilford et al, successful implementation of tracker trials would require development of a more flexible approach to research not only by the medical profession but also by prospective participants and the commercial sector.[1] The public could well be attracted to the proposition of methodically evaluated introduction of new technologies as well as skill in their use, particularly during the learning curve, following growing awareness of such problems through media coverage of, for example, the Bristol case cited by Lilford et al.

This proposal for overlap of audit and trial may be an ideal opportunity not just for flexible research but for flexible consent procedures where the current notion of trial participants being guinea pigs could be turned on its head. The public is coming to appreciate that it is those patients who are the subject of poorly monitored interventions who, in retrospect, are the guinea pigs. The medical profession acknowledges that patients in trials do better—for whatever reasons. A rigorous, standard continuous process of trial and review, discarding the inferior intervention and identifying the poor performer, would be a demonstration of the constant striving for improvement through research (rather than "breakthroughs") that would surely serve to create a new attitude and a more positive general understanding of the striving for clinical excellence.

If any notion of imposition is to be avoided it is essential to involve potential participants, namely the general public, in consideration of this new approach at an early stage. As stakeholders in the NHS, patients have a vested interest in such methods that weed out ineffective treatments by continuous evaluation. Their contribution as active partners on steering committees providing the users' viewpoint is essential in the constant iterative learning process that a tracker trial would constitute.

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Are generalists still needed in a specialised world?

Role of accident and emergency doctors should be expanded

EDITOR—Turnberg in his article on the survival of the general physician rightly highlights the potential problems posed when an undifferentiated emergency patient is cared for by medical subspecialists.[1] Four models of care are proposed as possible solutions, including the development of specialised emergency physicians, calling for a new breed of doctor and a specific training programme, although its success would depend on having enough doctors who are sufficiently motivated to take on this type of work.

The specialty of emergency medicine already exists, but its potential for contributing to a solution to the problem remains unfulfilled because of historical, cultural, and resource factors as well as perhaps the stubborn retention of the UK-specific name "accident and emergency medicine."

Turnberg alludes to the difficulties medical subspecialists have in maintaining their general skills and knowledge. Accident and emergency physicians now undergo a five year specialist training programme whose exit examination requires the demonstration of knowledge and skills in all aspects of clinical emergency medicine as well as evidence based critical appraisal and management skills. No such objective final assessment exists for trainees in general (internal) medicine. An expansion in the numbers of accident and emergency consultants, combined with a sociopolitical climate in which senior doctors' participation in all aspects of patient care will be demanded, suggests that the time is right to expand the role of accident and emergency doctors.

I therefore propose a fifth model: the undifferentiated emergency patient is cared for on an admissions or observation unit integral to the hospital's emergency department, under the supervision of the accident and emergency consultant on duty. Medical subspecialists provide advice and ongoing care when indicated. Patients no longer acutely ill who require further investigation and diagnostic expertise are referred to the general (internal) medicine specialists. This way acutely ill patients remain under the care of physicians motivated and trained to provide that care. The current system of separate medical assessment units and emergency departments, with its consequent duplication of precious resources, would end, and a single point of hospital entry would exist for emergency patients regardless of whether they dialled 999 or were referred by their general practitioner.

To create a new emergency specialty would perpetuate this duplication and thinning of resources for the patients who most need them. Far better to invest in those specialties we already have, since Turnberg's "new breed" is already breeding.

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1 Turnberg L. Survival of the general physician. *BMJ* 2000;320:436. (12 February.)

General practice enables doctors to maintain general medical skills

EDITOR—Turnberg asks if there is any room left for the general physician in today's world of increasing specialisation.[1] I am surprised that he has not realised that the hospital general physician of old is alive and well in the guise of the modern general practitioner.

The role of the secondary care physician is increasingly that of the technical engineer, practising narrowly focused medicine based on mechanical interventions and algorithms. By contrast, improvements in training for general practice, the advent of accessible evidence based medicine, and the development of primary care groups and clinical governance are bringing about a renaissance in primary care.

General practitioners now have, or are developing, the skills and knowledge that were once the preserve of the hospital doctor. Our increasing access to previously "hospital only" investigations and treatments and the abandonment of the management of many chronic diseases in secondary care have further rendered the hospital generalist redundant.

Despite the general practitioner's changing role, our close relationships with our patients ensure that we retain the holistic person centred approach that marks the physician from the technician. Graduates wishing to maintain their general medical skills should be encouraged into primary care, the last refuge of the true general physician.

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1 Turnberg L. Survival of the general physician. *BMJ* 2000;320:438-40. (12 February.)

Additional issues need to be addressed

EDITOR—Turnberg covers of many of the issues surrounding general and specialty medicine.[1] There are, however, other factors that should be considered.

Specialism is not without problems. Increased specialism goes hand in hand with decreased flexibility in bed use. "General" patients can usually be admitted to any of a number of wards, even after taking into account their sex (and sometimes age). A bed is likely to be available sooner from this larger pool than if the patient can go only to the ward of one specialty. More beds (and therefore staff) are required in a specialist system than in a general system to avoid longer trolley waits. Specialism must therefore be justified not only on grounds of clinical benefit but also on grounds of cost effectiveness.

"Specialty systems" must bring patients and the appropriate specialty together. Delayed access to specialty care is likely to reduce its benefits. Sometimes it may be impossible to get to the ward of the "correct" specialty. A system based on patients' needs as well as their geographical location is required. The patient being looked after by the "wrong" specialist is likely to be more disadvantaged the greater the degree of specialism within the system; staff will see fewer patients from "alien" specialties and run the risk of atrophied generalist expertise. It would be wrong to rely on trainees to protect patients in these circumstances.

It is not always possible to identify the relevant specialty straight away (in general practice or in accident and emergency). Some facility is therefore needed for patients whose problem cannot immediately be categorised. This facility must contain not

only beds but also clinicians whose area of expertise (and interest) lies in the initial care of patients admitted as emergency cases. Unless every specialty can maintain a service for 24 hours a day, staff are needed who are able to deal with acute problems arising from any system. We have specialties based on systems and age of patients.

There will be a need for a specialty defined in terms of the stage of patients' illnesses rather than system(s) affected ("acutism") if generalism is to go.

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Needs of patients should be considered

EDITOR—Turnberg looks primarily at the problem from the view of the physician, rather than the needs of the referring general practitioner or the patient.[1] I will deal firstly with the questions of emergency admissions, and secondly with the question of outpatient referrals.

Patients admitted to medical emergency wards can be dealt with competently by a general physician.[2] This may be desirable for several reasons. Only a physician with an interest and training in general medicine can handle the scale and scope of medical emergencies.[3] It is important that an experienced physician fully assesses these patients promptly to reduce the risk of harm to them.[4] No one seems to ask the crucial question of how, in the absence of a general physician, emergency patients are allocated to each specialty. Clearly, there will be an element of risk if the wrong specialty is chosen by the referring general practitioner or even the triage nurse.

Outpatient opinions often include patients who do not fit into a specific diagnostic category—hence the referral. Without general physicians, how can this group of patients be best served? If the referring general practitioner chooses the wrong specialty in a complicated case, does the patient get shunted from department to department while doctors hope to make a diagnosis?[5] General practitioners may recognise diagnoses in secondary care such as "abdominal pain—endoscopy normal" as the price to pay for specialisation.

Turnberg in his opening sentences by implication suggests that specialist physicians may be able to know everything. This is, of course, impossible and will always be so. It does, however, prompt the question why specialisation is becoming more popular. Perhaps physicians feel safer if they confine their activity to a narrow spectrum of medicine?

We all need general physicians. So let us attempt to build a framework for the general physician of the future, rather than waste such a valuable resource for patients and general practitioners alike.

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1 Turnberg L. Survival of the general physician. *BMJ* 2000;320:438-40. (12 February.)
2 Rhodes JM, Harrison B, Black D, Spiro S, Almond S, Moore S. General internal medicine and specialty medicine—time to rethink the relationship. *J R Coll Physicians Lond* 1999;33:341-7.
3 Hampton JR, Gray A. The future of general medicine: lessons from an admission ward *J R Coll Physicians Lond* 1998;32:39-43.
4 Neale G. Risk management in the care of medical emergencies after referral to hospital. *J R Coll Physicians Lond* 1998;32:125-9.
5 Fleetcroft R. The general physician—extinction or evolution? *J R Soc Med* 1998;91:613.

Qualitative research in health care

Good communication is essential part of educational process

EDITOR—The first Education and debate section of the new millennium was very educational in a way that was almost certainly not anticipated or intended by either the staff of the journal (unless they were being very mischievous) or the authors of the papers concerned.[1 2] In the paper by Lilford et al[1] the study under discussion was clearly defined, but unfortunately in the paper by Mays et al[2] I was not able, after reading the paper three times, to find a definition of the type of research being discussed anywhere.

The style of the paper by Lilford et al allowed an easy understanding of the thesis being developed, but the same could not be said of the paper by Mays et al, which seemed to lack a clearly discernible logic in relation to the case being made. The paper was replete with jargon and many strangely unscientific terms, which made it difficult to read—such as "epistemological," "extreme relativists," "antirealist," "reflexivity," "inductive inquiries," and "subtle realism." No such problem seemed to exist in relation to the paper by Lilford et al. As one of the "researchers from other traditions," I was appalled to read of research trying to "derive … unequivocal insights." I thought in my "naive realism" that we sought facts. Should not all research "be concerned to develop theory?" The need to develop a hypothesis to be tested is surely not "arguable." I was taught by my research mentors that the truth, rather than subtle realism, was what we were trying to attain. It would have been unthinkable to omit a clear account of the process of data collection and analysis.

In this double blind (I had no idea prior to publication of the content or style), randomised (by chance I chose to read the "unintelligible paper" first) controlled (the papers were controls for each other) trial, not intended by the journal (?), I found a significant difference (I could not even understand one of the papers) in favour of tracker studies. Perhaps this was because of my only admitted bias or conflict of interest, that of being a surgeon and an educator. I am not really sure what all of this means except that if the journal does publish papers for education and debate it follows that they should be understandable to all of the readers of the journal, including such lowly students as surgeons, and that it has to be remembered by educators that an essential part of the educational process is good communication. Quality in qualitative research is a mystery to many health services researchers, and, sadly, it is an even greater mystery to me now. I am left pondering the simple question "Who should be responsible for educating the educators?"

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1 Lilford RJ, Braunholtz AB, Greenhalgh R, Edwards SJL. Trials and fast changing technologies: the case for tracker studies. *BMJ* 2000;320:43-6. (1 January.)
2 Mays N, Pope C. Qualitative research in health care: assessing quality in qualitative research. *BMJ* 2000;320:50-2. (1 January.)

Antirealism is an excuse for sloppy work

EDITOR—We were struck by Mays and Pope's indulgent treatment of the antirealist position.[1] Antirealist qualitative researchers contend that there is no "social" reality or truth that is independent of the observer. Antirealists, a species of postmodernists, scoff at those naive enough to believe in the physical reality of social world: "what the parochial view in the social, behavioral, and service sciences has touted as 'science' is historical and practical myth."[2] Presumably "social" reality consists of the interactions of human beings—that is, spoken or written words, and all human actions that relate to other humans. Thus the antirealists apparently would contend that this letter has no reality. Antirealists thus fall headlong into self contradiction. If no utterances (presumably including their own) have reality, why should we read what they write? Furthermore, why should we pay any attention to the work of supposedly "scientific" researchers who deny the independent reality of what they research?

The antirealist view seems to be at best an excuse for sloppy work. Antirealists have argued that bias in research is good—"not something to be eliminated, but is a productive element, a foundation for formulating questions and understanding answers in the process of research."[3] They have asserted that the traditional notions of methodological rigour, "the classical canons of reliability, validity, and objectivity," are irrelevant to their kind of qualitative research, to the point that a "powerful case can be made for methodological anarchy."[4] In retreating to ancient subjectivist attitudes, antirealists have renounced qualities that are part of the scientific attitude: rigour, self discipline, humility in the face of evidence, and willingness to risk failure and blind alleys.

Alan Sokal, the physicist whose parody of postmodernism in science received wide attention, made the point well. First he decried "a particular kind of nonsense and sloppy thinking: one that denies the existence of objective reality."[5] Then he wrote, "Intellectually, the problem with such doctrines is that they are false. There is a real world; its properties are not merely social constructions; facts and evidence do matter. What sane person would contend otherwise?"

We applaud the efforts of Pope and May to bring more rigour to the design,

execution, and review of qualitative research. We fear, however, that responsible qualitative researchers will have trouble convincing others of the value of their field until they disavow the pseudo-philosophical nonsense of antirealism.

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1 Mays N, Pope C. Qualitative research in health care: assessing quality in qualitative research. *BMJ* 2000;320:50-2. (1 January.)
2 Gubrium JF. Qualitative research comes of age in gerontology. *Gerontologist* 1992;32:581-2.
3 Berkwits M, Aronowitz R. Different questions beg different methods. *J Gen Intern Med* 1995;10:409-10.
4 Henwood KL, Pidgeon NF. Qualitative research and psychological theorizing. *Br J Psychol* 1992;83:97-111.
5 Sokal A. A physicist experiments with cultural studies. *Lingua Franca* 1996;6:62-4.

Open access follow up for inflammatory bowel disease

Would have been better to use t test than Mann-Whitney U test

EDITOR—Williams et al undertook a randomised trial to evaluate whether follow up of patients with inflammatory bowel disease is better with open access than with routine appointments.[1] They compared primary and secondary care resource use and costs and concluded that open access follow up saves secondary care resources. This conclusion, however, is mistaken because they used inappropriate statistical methods.

Resource use and cost data tend to have highly skewed distributions. As a result, the authors decided that standard parametric statistical methods were not appropriate and assessed significance by using a Mann-Whitney U test. Although this is consistent with conventional statistical guidelines,[2] it does not address the question of interest in economic evaluations. As the authors themselves state, "economic analysis is mainly concerned with a comparison of means." Use of a Mann-Whitney U test, however, makes an overall comparison of distributions in the two groups, in terms of both shape and location,[3] and does not specifically test for a difference in means.

The most appropriate simple method for comparing mean costs is the ordinary *t* test. By using the means and standard deviations in each group reported by the authors, we have calculated P values from *t* tests (table). The conclusions are dramatically different from the authors'. In particular, one of the authors' main conclusions—that open access follow up used fewer resources in secondary care—is not supported: the P value from the *t* test is 0.79. Other related conclusions are also misleading (table).

Although *t* test methods are only strictly valid for data that are normally distributed, they are fairly robust and give a reliable comparison of means, provided that skewness is not too extreme and sample sizes are moderately large.[4] Using the raw data (unavailable to us), the *t* test results can be checked by non-parametric bootstrapping, an approach to compare means without the need for assumptions of normality.[4]

Use of inappropriate methods for the analysis of cost data is all too common.[5] As this example shows, inappropriate analysis can lead to seriously misleading conclusions, which could influence important policy decisions in health care. Health service researchers, health economists, statisticians, and others concerned with analysis and interpretation in economic evaluations need to be aware of this important issue.

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1 Williams JG, Cheung WY, Russell IT, Cohen DR, Longo M, Lervy B. Open access follow up for inflammatory bowel disease: pragmatic randomised trial and cost effectiveness study. *BMJ* 2000;320:544-8. (26 February.)
2 A ltman DG, Gore SM, Gardner MJ, Pocock SJ. Statistical guidelines for contributors to medical journals. *BMJ* 1983;286:1489-93.
3 Bradley JV. *Distribution-free statistical tests.* Paramus, NJ: Prentice-Hall, 1968.
4 Barber JA, Thompson SG. Analysis of cost data in randomised controlled trials: an application of the non parametric bootstrap. *Stat Med* (in press).
5 Barber JA, Thompson SG. Analysis and interpretation of cost data in randomised controlled trials: review of published studies. *BMJ* 1998;317:1195-200.

Ability of any method of follow up to detect cancer must be stated

EDITOR—Williams et al did not address an important clinical outcome—the risk of cancer developing—in their paper on inflammatory bowel disease.[1] The sample size would have had to be much larger and the study conducted for much longer for it to have the power to pick up such a rare event.

Without knowing whether detection of cancer would be adversely affected by the open access policy, it would not be prudent to recommend this strategy wholeheartedly. The authors suggest that nurse practitioners should call patients regularly for assessment if necessary to reduce the risk of gastrointestinal malignancy, but they should have included the cost of hiring, training, housing, and sustaining such staff in the cost considerations.[2] In an economic analysis it is important to consider all the costs as well as the outcomes.

We were puzzled by the statement that semistructured interviews were undertaken by general practitioners during audit visits to minimise bias. An independent blinded interviewer would eliminate or reduce bias; a general practitioner is unlikely to.

We were disappointed that sensitivity analysis was not performed as this is an important part of any cost effectiveness analysis.

As the disease specific questionnaire was not validated, drawing any conclusion from it would not be valid. Yet the table comparing quality of life (table 1 in the paper) was interesting: although the results of all results were not significant, there was a clear trend with negative numbers predominating, indicating a "better change" in the routine follow up patients compared with the open access patients. This raises the question of whether the non-significance was due to lack of power of the study to pick up a true difference when one existed.

Given these weaknesses, we do not think that an open access strategy should be recommended other than in a more powerful and longer study to answer these important issues.

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1 Williams JG, Cheung WY, Russell IT, Cohen DR, Longo M, Lervy B. Open access follow up for inflammatory bowel disease: pragmatic randomised trial and cost effectiveness study. *BMJ* 2000;320:544-8. (26 February.)
2 Lockett T. *Evidence-based and cost-effective medicine.* Oxford: Radcliffe Medical, 1997.

Authors' reply

EDITOR—We agree with Barber and Thompson that highly skewed cost data are best analysed by non-parametric bootstrapping. However, the *BMJ* set a deadline for papers submitted for its issue on managing chronic diseases. As our bootstrapping was not complete we followed conventional statistical guidelines and used the Mann-Whitney U test. Because economic analysis focuses on means we also reported these. As expected, our completed bootstrapping, to be published elsewhere, confirms the findings reported in the *BMJ*. In particular, open access greatly reduces secondary care costs.

We regret that Barber and Thompson, frustrated by our interim analysis, ignored the conventional statistical guidelines they cited by applying the *t* test to our data. The substantial differences between their findings and those achieved with the U test confirm that the data are highly skewed. Thus the findings of the *t* test are misleading.

We agree with Coomarasamy and Van Der Berg about the need to screen patients at high risk of developing malignancy. A gastrointestinal nurse practitioner could do this screening. As we do not yet have such a

Mean (SD) costs (£) per patient in hospitals over 24 months

	Open access (n=77)	Routine visit (n=78)	P value from Mann-Whitney U test (as given by authors)	P value from *t* test
Cost of investigations	198 (279)	257 (276)	0.032	0.19
Total cost of secondary care	582 (808)	611 (475)	0.012	0.79
Patient borne costs	74 (62)	87 (48)	0.002	0.14
Total	656 (860)	699 (516)	0.011	0.71

post it was not appropriate to include the costs in our study. We intend to evaluate this role in a further randomised trial.

General practitioners who were familiar with the principles of open access follow up but independent of the service at both hospitals undertook the semistructured interviews with study practitioners. Since the study practitioners had patients in both arms of the trial, however, the suggestion that the interviewers should have been blind is meaningless.

Although there was no disease specific quality of life questionnaire valid for the United Kingdom when the trial was designed, we have since developed and validated such a questionnaire.[1] The trend towards a greater improvement in quality of life with routine care was balanced by a trend towards greater improvements in other variables with open access. It would indeed have required a very large sample to classify as significant differences as small as those observed. Furthermore, we judge that they are not clinically significant.

In short, we believe that our published conclusions stand in the face of the comments from the authors of these letters.

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1 Cheung WY, Garratt AM, Russell IT, Williams JG. The UK IBDQ: development and validation of a British version of the inflammatory bowel disease questionnaire. *J Clin Epidemiol* 2000;53:41-50.

Burns after photodynamic therapy

Drug point gives misleading impression of incidence of burns with temoporfin (Foscan)

Editor—Hettiaratchy et al report partial thickness skin burns in six out of 14 healthy volunteers injected with temoporfin (Foscan) as part of a phase I pharmacokinetic study carried out on behalf of Scotia Pharmaceuticals at a contract clinical research unit.[1] However, their report creates a misleading impression of the true incidence, severity, and overall risk of burns and other photosensitivity reactions with this drug and has led to inaccurate media comment and speculation.

The total number of subjects exposed to Foscan is 957 healthy volunteers and patients, many of whom have been treated with Foscan photodynamic therapy on two or more occasions in clinical studies for a range of different indications. In total, 22 serious adverse drug reactions attributable to photosensitivity including burns have been reported (2.3% of all subjects); this includes the six burns described in the drug point. In clinical studies 15 serious adverse drug reactions involving burns or photosensitivity reactions have been reported in 931 patients injected with Foscan (1.6%). This rate is about half the commonly reported rate of drug related mortality (3-7%) in patients treated with chemotherapy for advanced head and neck cancers.[2–6]

The table shows the much greater incidence of severe photosensitivity reactions in the volunteers participating in the study referred to by Hettiaratchy et al than in patients with cancer. Furthermore, all 14 of these volunteers reported localised photosensitivity reactions in their infusion arm. The separate pharmacokinetic study in the 23 patients with head and neck cancer, which had an identical study design, reported no serious adverse drug reactions, no burns or localised photosensitivity reactions, and only three generalised photosensitivity reactions of mild or moderate severity (13%); this is similar to the overall rate observed in clinical trials. The pharmacokinetic profile of Foscan in healthy subjects and cancer patients is similar (unpublished data on file).

We conclude that the unusually high incidence and severity of the reactions reported by Hettiaratchy et al are most likely to have been caused by the method of drug administration resulting in photosensitiser being extravasated at the time of infusion. It is well documented that this can lead to delayed and prolonged photosensitivity reactions in the affected tissues. A contributing factor to the severity of the reactions may also have been the extent of volunteer compliance with instructions to avoid prolonged exposure to direct sunlight on discharge from the phase I unit.

In addition, all volunteers participating in the study signed consent forms conforming to the guidelines of the Association of the British Pharmaceutical Industry. No "disclaimers" were sought or obtained. [See correction, 17 June, p 1641.]

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1 Hettiaratchy S, Clarke J, Taubel J, Besa C. Burns after photodynamic therapy. *BMJ* 2000:320;1245. (6 May.)
2 Forastiere AA, Metch B, Schuller DE, Ensley JF, Hutchins LF, Triozzi, P, et al. Randomized comparison of cisplatin plus fluorouracil and carboplatin plus flourouracil versus methotrexate in advanced squamous cell carcinoma of the head and neck: a Southwest Oncology study group. *J Clin Oncol* 1992;10:1245-51.
3 Jacobs C, Lyman G, Velez-Garcia E, Sridhar KS, Knight W, Hochster H, et al. A phase III randomized study comparing cisplatin and fluorouracil as single agents and in combination for advanced squamous cell carcinoma of the head and neck. *J Clin Oncol* 1992;10:257-63.
4 Clavel M, Vermorken JB, Cognetti F, Cappelaere P, de Mulder PH, Schornagel JH, et al. Randomized comparison of cisplatin, methotrexate, bleomycin and vincristine (CABO) versus cisplatin and 5-fluorouracil (CF) versus cisplatin (C) in recurrent or metastatic squamous cell carcinoma of the head and neck. *Ann Oncol* 1994;5:521-6.
5 Williams SD, Velez-Garcia E, Essessee I, Ratkin G, Birch R, Einhorn LH. Chemotherapy for head and neck cancer. Comparison of cisplatin + vinblastine + bleomycin versus methotrexate. *Cancer* 1986;57:18-23.
6 Vogl SE, Schoenfeld DA, Kaplan BH, Lerner HJ, Engstrom PF and Horton J. A randomized prospective comparison of methotrexate with a combination of methotrexate, bleomycin and cisplatin in head and neck cancer. *Cancer* 1985;56:432-42.

Incidence of burns associated with temoporfin (Foscan)

	Phase I pharmokinetic study		Current Foscan safety database	
	Volunteers (n=14)[1]	Patients with cancer (n=23)	All patients (n=931)	All subjects (n=957)
No of burns	6	0	15	22
Incidence	43%		1.6%	2.3%

Authors' reply (Hettiaratchy and Clarke)

Editor—We were not suggesting that the true incidence of burns with temoporfin (Foscan) is 43%—this was just the incidence in the group of patients referred to us. As Bryce reports, the correct figure is probably around 2%. What we were trying to highlight was that photodynamic agents can cause serious burns and that these may be more severe than conventional burns. This is an unusual occurrence and we state that, to our knowledge, this is the first group of patients given photodynamic therapy ever reported to have burns after exposure to environmental light.

We agree that the incidence of complications in this group was particularly high. This may well have been due to a problem during the administration of the drug. We discussed this directly with Bryce at the time, during Scotia's initial collaboration on the paper. However, this was not a pure extravasation injury. The burns occurred only on exposure to sunlight and photoactivation, two weeks after the drug was given. In addition, other body areas away from the infusion site were also affected, though less severely. This implies that the patients were generally photosensitive because of Foscan. We suspect that there was some leaking out of the drug on administration, leading to high tissue concentrations around the infusion site. On photoactivation the most severe reaction occurred here, resulting in the worst burns.

Irrespective of whether there was some problem with the administration of the drug, these patients had serious burns and we believe that the causative agent was Foscan. This is a rare but serious complication that the medical community needs to be aware of. It is important for clinicians using photosensitisers to know that complications can occur and for burns surgeons to know that burns induced by photodynamic therapy may behave differently from conventional thermal injuries.

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Competing interests: Mr Clarke has provided medical reports on the injuries and the initial management of the six patients reported on in the drug point. No fee was charged.

Authors' reply (Täubel and Besa)

EDITOR—We have until now been cautious to enter into the debate which has arisen concerning the article of 6 May.[1] In view, however, of the legitimate interest doctors and the public have in the issues raised, and in view of the criticism of ourselves and Charterhouse Clinical Research Unit which has arisen as a result of the contents and comments on the *BMJ* article, it is important that we now set out the facts and answer some of the criticisms that have been made.

Notwithstanding that we were named as coauthors, the final form of the article published in the *BMJ* had not been approved or seen by us. Amendments which we had made were apparently rejected at some stage and an addition was made which was simply incorrect—namely, that the volunteers had signed disclaimers and were therefore not entitled to compensation. In fact, no fault compensation insurance was put in place by both ourselves and the drug company in accordance with our standard practice.

The formulation of Foscan (temoporfin) used in the trial reported in the *BMJ* article of 6 May was, we were given to understand by the drug company, different from that used in previous trials. Specifically, a new solvent was added to the drug so that it would be more soluble and less painful to administer. This factor is relevant to an evaluation of the results of the trial and any comparison of the results with those in previous trials.

While seven of the volunteers were treated by Mr Clarke at Chelsea and Westminster Hospital Burns Unit, they were the only volunteers it was appropriate to refer for specialist treatment. In fact, of the 14 volunteers on whom the new formulation of the drug was tested, all 14 suffered some form of burn on the forearm into which the drug was infused. In 13 cases the burn tracked the vein into which the drug was injected and was long and oval in shape, starting close to the site of infusion and extending along the forearm (although in one instance this was obscured by the extent of the burns to the forearm). In the other case, although there was a burn which appeared to follow the infusion vein, the burn only started to occur towards the elbow, away from the site of injection.

Charterhouse was especially careful to ensure that the drug was correctly injected into the vein of each volunteer. None of the infusions was given perivenally, and no drug was spilt on the skin as suggested in one press article. Charterhouse is very experienced at carrying out infusions which demand that there is no accidental injection into surrounding tissues and performs them on a regular basis. We applied an appropriate standard technique of administering the drug into a vein of the forearm. We did not attempt to inject into veins in the antecubital fossa as they are best avoided because of the risk of interarterial injection (aberant ulnar artery) and the possibility of median nerve damage, particularly as the drug had the potential to cause local damage. Numerous safeguards in our routine procedures prevent us from accidentally injecting any drug into surrounding tissue. These include (*a*) injecting into superficial veins in the forearm to provide a visual control as to whether or not the canula is correctly placed; (*b*) the use of pumps with an inbuilt pressure sensor that immediately stops the pump if there is an increase in pressure, which would occur if a canula slipped out of a vein and into the surrounding tissue (which would cause increased resistance); (*c*) the flushing of canulas with water for injection before starting the infusion to provide a visual and sensual check as to whether there is any resistance as a result of either a blood clot forming at the tip of the canula or the tip being displaced into tissue; and (*d*) personal supervision of each infusion by staff with the requisite expertise and experience.

Each safeguard detailed above was followed in respect of every injection given in the Foscan trial reported in the *BMJ*. Each infusion was personally supervised by one of us. In each and every case, there was no evidence or indication that the drug was administered perivenally to any of the 14 volunteers. If a perivenal injection had been given, one would expect the resultant burn to be approximately circular in shape around the site of infusion and not a long oval burn tracking the line of the vein.

We consider that the most probable cause of the burn to the infusion forearm suffered by each of the volunteers was that the drug, having being injected into the vein, then leaked from the vein by an unknown mechanism (a hypothesis supported by the number of volunteers on whom the burn was observed). We do not know whether there is any connection between the leakage and the new solvent used in the trial we performed, but so far as we are aware the characteristic shape of the burns we recorded were not recorded in previous trials of the drug.

It is unfortunate that the *BMJ* did not send us a copy of its standard form on competing interests since we would not have hesitated to provide the information requested. That said, we accept that it would nevertheless have been appropriate for us to ensure that the nature of our involvement in the relevant trial was made explicit, and the version of the article which we had approved did not do so. We are employed by Charterhouse Clinical Research Unit Limited, which conducted the drug trial on behalf of the relevant drug company, and personally supervised the trial. Charterhouse entered into a contract with the sponsoring drug company relating to the performance of the Foscan trial and received remuneration for conducting the study.

We are convinced that Foscan is a very promising drug candidate which will be valuable for the treatment of certain cancers. We have simply carried out a trial which, as is often the case, raised certain queries which may require further investigation. The primary purpose of carrying out a drug trial is to advance medical knowledge about the side effects of a particular drug formulation where this is not already known. As doctors we would not wish the continued development of Foscan to be in any way impaired by the *BMJ* article of 6 May and the debate which followed.

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1 Hettiaratchy S, Clarke J, Taubel J, Besa C. Burns after photodynamic therapy. *BMJ* 2000:320;1245. (6 May.)

Editor's reply

EDITOR—We, the *BMJ*, did not do as well as we would have liked in publishing this drug point. I must make clear, however, that we did send a proof to the corresponding author and did not make any changes to the corrected proof.

Our policy is to ask authors reporting an adverse event associated with a drug to contact the manufacturers and ask for data on whether they have had reports on similar events. We did that, but we did not take the next step of including the data in the paper. That was a mistake, and we have taken steps to avoid it happening again.

We should have sent the authors a copy of our standard form on competing interests and published their answers. Mr Clarke and Drs Täubel and Besa have now declared their competing interests. Although many journals ask authors to declare competing interests, our own experience is that virtually nobody volunteers a competing interest unless presented with a set of explicit questions. That is why we now have a form that includes explicit questions on financial competing interests (available at http://www.bmj.com/advice/5.html), and our experience is that authors do respond to this form. I am sorry that we failed to send the form to the authors on this occasion.

The letter from Drs Täubel and Besa is considerably longer than we normally allow. We apologise to readers for this, but we wanted to publish these letters and explain our part in the story promptly. When it became clear that the authors had not been communicating well among themselves we postponed publication to allow Drs Täubel and Besa to respond separately. Their letter arrived, via their lawyers, at this length at the last possible moment for inclusion in this week's journal, allowing no time for negotiation over editing. We thought that it was better to publish their letter at this length together with the other letters than to publish it separately next week.

Richard Smith *editor, BMJ*