Randomised controlled trials in general practice

Are preferable to observational studies

EDITOR,—Mike Pringle and Richard Churchill rightly emphasise that a randomised controlled trial should be used in general practice only when it is the appropriate method for the research question that is being posed.[1] However, they refer to the potential biases in randomised controlled trials without paying due regard to the advantages of such trials over observational methods.

Observational studies do not provide definitive answers to questions about therapeutic effectiveness.[2] This is because bias and confounding are much harder to control for with observational methods than with experimental designs. Without randomisation, decisions about treatment will depend on patients' characteristics, and thus treatment and control groups will differ in ways other than the treatment they receive. Differences in outcome may then be due to these other factors rather than to the treatment.[2] Even in experimental studies the adequacy of randomisation has an important bearing on the assessment of a treatment effect.[3] For this reason, when appropriate and when possible, randomised controlled trials should be performed in preference to observational studies.

Failure to recruit all eligible patients in a randomised controlled trial does not imperil that trial's subsequent generalisability as much as the authors suggest. Once effectiveness has been established by a randomised controlled trial the application of the results to individual patients is not limited by the eligibility criteria of that trial.[4] Extrapolation to individual patients relies on the assessment of their likely risk. Each patient's risk and benefit are calculated from large cohort studies, from which the outcome of multiple risks in a population can be seen and applied. Guidelines on the treatment of hypertension have taken this approach, basing the assessment of individual risk and benefit on data from the Framingham study and the results of randomised controlled trials.[5]

There is a paucity of evidence from randomised controlled trials and systematic reviews of such trials in general practice; by contrast, an entire database is devoted to such trials in pregnancy and childbirth. Without randomised controlled trials in general practice we will not be able to distinguish harmful from beneficial treatment. Such trials should continue to be performed in general practice for the same reason as in any other clinical setting—that is, when doubt exists about the efficacy of a treatment.

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Internal validity of trials is more important than generalisability

EDITOR,—Mike Pringle and Richard Churchill raise important issues relating to the practicalities of performing and interpreting the results of randomised controlled trials in general practice.[1] They suggest that observational studies are acceptable when a randomised study is too difficult to perform or when its results will be clinically meaningless, reminding us of the complementary (rather than competing) roles that experimental and observational methods should have in the evaluation of health care interventions.[2] We are concerned, however, that they overstate the problems of conducting randomised controlled trials in general practice. By so doing they may discourage practitioners from participating in research that can provide important evidence that can be used to inform clinical decision making.

Firstly, many of the methodological problems that the authors raise apply to randomised controlled trials in general, not just to those in primary care settings. Patients should never be treated as experimental animals. It is important in any trial that patients' autonomy is respected, that patients are not coerced into taking part, that confidentiality is maintained, and that the potential risks and benefits of the treatments are explained. It is one of the shortcomings of modern medicine that more attention is paid to obtaining informed consent in most randomised controlled trials than in everyday clinical practice.[3]

Secondly, we disagree with the assertion that failure to recruit consecutive patients (which is bound to occur if genuine informed consent is obtained) introduces selection bias. Selection bias occurs when allocation to treatment is influenced by factors that might affect outcome. This is an inevitable consequence of non-random allocation of treatment, as occurs in any observational design; it is eliminated by randomisation. Pringle and Churchill raise the issue of generalisability. This is always a potential problem with randomised controlled trials but is more so when studies are performed in secondary care and then results are applied to primary care.[4] The solution to problems such as this is to perform more trials in primary care settings, not fewer.

It is a basic principle of epidemiology that the internal validity of a study is always more important than its generalisability, since it is never appropriate to generalise an invalid finding.[5] This principle should not be forgotten when the practical difficulties of carrying out randomised trials in primary care settings are being considered.

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General practice research framework carries out such trials

EDITOR,—Allowing that "randomised controlled trials are not impossible to perform in general practice," Mike Pringle and Richard Churchill ask if they are really the gold standard long advocated by the *BMJ* or fool's gold.[1] They conclude that "it would be wrong to stick blindly to a gold standard which is likely to produce the wrong findings—methodologically pure but clinically meaningless."

They seem to have overlooked the Medical Research Council's general practice research framework.[2] This now includes almost a tenth of the British population; in addition, about 400 general practitioners attend its annual meetings to discuss the opportunities presented by high quality networked randomised controlled trials as well as the authors' long list of problems and obstacles, which all of us know only too well. Since it was set up in 1977 for the Medical Research Council's study of treatment for mild hypertension[3] the general practice research framework has published studies on many clinical topics, involving many millions of person years of observation. All were methodologically sound, and I cannot recall one that was clinically meaningless.

Instead of giving up before we try, why not pay some attention to ways in which these obstacles to good work have been overcome?

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Neonatal circumcision does not protect against penile cancer

EDITOR,—Although Morten Frisch and colleagues have made a valuable contribution to the study of penile cancer, they mistakenly repeat the myth that neonatal circumcision renders the subject immune to penile cancer.[1] The reference given for this statement is not an epidemiological study but an opinion article by the American circumcisionist Abraham L Wolbarst in 1932.[2] Wolbarst invented this myth and was directly responsible for its proliferation; he based it on unverifiable anecdotes, ethnocentric stereotypes, a faulty understanding of human anatomy and physiology, a misunderstanding of the distinction between association and cause, and an unbridled missionary zeal. It was not based on valid scientific and epidemiological research.

All subsequent repetitions of this myth are traceable to Wolbarst's article, though Wolbarst himself advocated universal neonatal circumcision principally as a preventive for epilepsy, paralysis, and masturbation. Circumcisionists such as Wolbarst do not seem to have promoted the myth because they have a genuine interest in reducing the rate of penile cancer; they have used it instead as a scare tactic to increase the rate of neonatal circumcision. It is surprising that sober scientists such as Frisch and colleagues could have relied on such a reference in their research.

Epidemiological studies disproved Wolbarst's myth long ago. In North America the rate of penile cancer has been estimated to be 1 in 100 000[3]—somewhat higher than the rate of 0·82 per 100 000 found by Frisch and colleagues. Maden *et al* reported penile cancer among a fifth of elderly patients from rural areas who had been circumcised neonatally and had been born at a time when the rate of neonatal circumcision was about 20% in rural populations.[4] Their study also shows that the rate of penile cancer among men circumcised neonatally has risen in the United States relative to the rise in the rate of neonatal circumcision.

Science must look beyond normal human anatomy to discover the true risk factors for penile cancer. Current investigations into risks posed by infection with human papillomavirus (circumcised males have been shown to have an increased risk of such infection) and use of tobacco have been instructive.[5] Frisch and colleagues have otherwise injected a welcome note of scientific rationalism into the debate over circumcision, which, despite the active participation of medical staff, is in

essence an issue not of medical science but of human rights.

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Brachial plexus neuropathy after radiotherapy can be treated by specialist surgeons

EDITOR,—Neuritis is an unfortunate complication of radiotherapy,[1] for which patients may be denied treatment. I have been told by several patients that their oncologist told them that the pain was untreatable. I have also been told by oncologists that the pain is due to tumour infiltration and is a sign of untreatable recurrence. Both these statements are untrue.

Treatment of neuritis after radiotherapy has been extensively documented.[2-5] It consists of exploration of the plexus, an extensive neurolysis of all affected nerves, and placement of free vascularised tissue on top of the scarred area in an attempt to revascularise the scarred tissues and to prevent further scarring. Le Quang used this technique and followed up 60 cases for a minimum of two years, reporting good results in 84%.[2] In the remaining 16% there was partial loss of sensation or motor power. In all the patients, however, the pain was ameliorated. After the preoperative investigations metastases were found at the time of surgery in only three cases. Le Quang was still willing to perform surgery to relieve pain in cases of tumour involvement, although the prognosis is necessarily more guarded.

In conclusion, although brachial plexus neuropathy after radiotherapy is an unfortunate complication, the outlook is not totally bleak and these patients should be referred for consideration of surgery. The surgery is extremely specialised, and patients should be referred to a specialist surgeon. These surgeons have a major interest in brachial plexus surgery and can transfer free tissue with a high success rate.

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Benefits of fetal surgery must be carefully evaluated

EDITOR,—The expanding role of intrauterine fetal surgery is creating much interest.[1] At the fetal medicine centre in Birmingham we have performed an intrauterine angioplasty for critical pulmonary stenosis, which led to the birth of a viable baby (J Wright *et al*, meeting of Fetal Medicine and Surgery Society, Belgium, 1994).

Fetal surgery should be used only in properly evaluated cases and when the prognosis of postnatal correction is poor. In his editorial on fetal surgery François I Luks uses intrauterine treatment of congenital diaphragmatic hernia as an illustration. At our regional fetal therapy unit we reviewed 48 consecutive cases of congenital diaphragmatic hernia referred between 1988 and 1995 and found that, once babies with coexistent anomalies and karyotypic abnormalities had been excluded, half of the babies survived (unpublished findings). Thus the benefits of prenatal surgery may not be that much greater than those of traditional management in appropriately selected cases. Any intrauterine surgery should be assessed by randomisation of cases to traditional or prenatal surgery and by the establishment of a register noting both perinatal and maternal mortality and morbidity.

Disappointingly, the editorial makes no mention of the need to improve our understanding of the natural course of congenital anomalies. Surely greater emphasis should be placed on this if real progress in fetal survival is to be made.

We look forward to participating in the acquisition and analysis of potentially exciting data.

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NHS will be left with high risk, low profit services under private finance initiative

EDITOR,—Chris Ham's editorial highlights genuine concerns about the government's private finance initiative in the NHS.[1] In Carlisle, where a single consortium has tendered to build and manage a major development of the hospital, we already have experience of private finance in the form of a contracted dialysis service. Under the terms of the contract (which is usually described as a "partnership" by the company), equipment, disposables, and nursing cover are provided for a fixed fee per treatment.

Several consequences arise from the contractual relationship between the private dialysis company and the publicly funded health service. In the first place, the company has been able to increase its charges substantially because any increase in the number of dialysis treatments is fully funded under the contract, in addition to the cost per dialysis session being linked to inflation. Our NHS trust, on the other hand, has been required to find annual cost improvements of the order of 5% a year. Secondly, the financial risk taken on by the company in providing a dialysis service has been minimal, as evidenced by the unit, quite predictably, reaching full capacity within three years. In contrast, the health service retains the risk of increasing numbers of patients and the responsibility for preparing patients for dialysis, including providing vascular access, and for complications arising from dialysis, which often necessitate admission to hospital. This has to be achieved on a fixed budget. The NHS also has the expense of monitoring the performance of the contracting company in respect of not only the number of dialysis treatments performed but also the varieties of treatment, the quality of service delivery, and the training and performance of the company's nursing staff.

The financial risk of building, equipping, and staffing any medical facility is trivial compared with the risk of providing potentially open ended clinical services with their attendant medicolegal obligations, which remains with the NHS. Our experience of private finance partnership in Carlisle is that the private sector adopts the low risk, high profit element of the service. Increased financial returns, which can be generated through operational efficiencies possibly at the expense of quality, go to private shareholders. Meanwhile the NHS is left with high risk and low or non-existent "profits."

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Advertisement's selective quotation from old article misrepresents current situation

EDITOR,—Readers of the *BMJ* may have noticed that a private health care insurance company is currently running an advertising campaign that selectively quotes from articles on waiting lists that were published in the journal in 1993 and 1994.[1,2] I am currently corresponding with the marketing director of the insurance company and with the Advertising Standards Authority in an attempt to prevent further use of the first of these articles, an editorial that I wrote.

I am concerned that the use of my name in this advertisement may be taken to imply that I endorse or recommend private medical insurance. This is not my personal view, nor is it a view expressed in my editorial. As a health services researcher I have not been uncritical of many of the changes associated with this government's reforms of the NHS. However, the use of a small part of my editorial, which is now rather dated, misrepresents the current situation with regard to inpatient waiting times: the Department of Health's latest figures indicate that 85% of people wait less than six months for elective admission.

As well as presenting out of date information the advertisement perpetuates misunderstandings about waiting lists. It confuses the size of the waiting list and waiting time, and it makes no distinction between urgent and non-urgent cases, life threatening conditions, and elective admission and thus implies that immediate admission is always necessary or desirable.

Evidence from countries such as the United States suggests that one of the first casualties of systems funded by private health care insurance is equity: people who are uninsured (for example, poor and unemployed people) or uninsurable (for example, chronically ill people) do not get health care. For all the problems with the NHS, I feel obliged to defend waiting lists rather than see the 1948 vision of a health service free at the point of delivery destroyed.

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