Clinical research

Malcolm Green

The Tomlinson inquiry into London's health care was published last week (p 975). Ministers have promised to consult widely on its proposals before making decisions early next year. This week we begin a series looking at the issues highlighted by Tomlinson, in the belief that they are not unique to London but are shared by many other large cities both in the United Kingdom and abroad. An editorial is published on p 1039.

Summary

Sir Bernard Tomlinson's report focuses on London's health services, but his proposals have major implications for the future of clinical research—not just in London but in the United Kingdom as a whole. They must be seen in the context of a widely perceived decline in British research and development which also threatens clinical research.^{1,2} This article examines the implications of Tomlinson's proposals and related strategies and recommends the construction of a research market for the patient costs of clinical research to complement the NHS market for patient services introduced in 1991. These arrangements would help sustain the clinical research base and guarantee excellence.

Research is the lifeblood of medical advance. The United Kingdom has a long tradition of contributing to research and today is one of the handful of countries with a major commitment to the interface between science and clinical medicine, taking research "from the molecule to man." This not only benefits the health of the nation but is also important economically.

Clinical research needs patients. The internal market for patient services is having a major effect on patient flows. The imbalance between supply and demand is particularly acute in London, and if patient flows to research based institutions are not protected the impact could be serious. Such hospitals should not have to compete primarily in the patient market, but rather in a market appropriate to them, a clinical research market, for the service costs of research. Should the reorganisation of London medicine (table I) after Tomlinson result, at the extreme, in the dismantling of London's clinical research activity the effect would be a body blow to Britain's medical research (table I). Neither is this just a London problem. Difficulties in funding research patients are

surfacing in other cities in Britain and around the world: as far apart as Sydney, Vancouver, and New York.

What is clinical research?

Clinical research implies medical research which is patient or disease oriented.¹ It requires the participation of patients. Increasingly, medical research is based on the dramatic advances in cellular and molecular biology, knowledge of genetic mechanisms, and advanced techniques developed by basic scientists. Clinical research therefore requires close collaboration between clinicians, clinical scientists, and basic scientists. At a practical level it requires close proximity of a critical mass of scientists, who need to be at the forefront of their own scientific discipline. They act as intellectual and practical bridges between large basic science institutions and patient related research, which has to be carried out in hospitals or other medical establishments.

Is clinical research necessary?

Clinical research is difficult and expensive. Can we and should we afford clinical research? Many other countries, including most developing countries, manage without major clinical research programmes, basing their medical activities on recommended practice elsewhere.

All research is expensive. It needs the commitment of time by experienced and well trained people, and by its very nature the outcomes are uncertain. Many avenues pursued turn out to be unproductive, or unforeseen problems lie in the path of progress. Clinical research is more expensive still, as in addition a secure supply of appropriate patients is necessary, with the additional costs of their clinical care and supplementary tests, investigations, and studies.

Abolition of clinical research would rapidly result in relegation of Britain from the league of first world medical countries. Britain's major universities have for centuries been seats of medical learning to which others have come. It would be sad if this process were reversed. Researchers are at the forefront of their specialties. They attend international meetings where they contribute to the scientific debate. They are up to date with the world literature. Their skills mean that they can translate the latest evidence into the highest quality care for patients in Britain as soon as it is scientifically secure. Today's research is tomorrow's development and thereafter medical best practice. Without a major base in clinical research our doctors would have to attend postgraduate courses in other countries and bring home the condensed views of experts from abroad which may not be relevant to the problems and practice of medicine in Britain.

There are clear economic benefits from clinical research. London is internationally renowned as a centre of medical experience, closely linked to its reputation for research. Patients come from all over the world to be treated in London, generating invisible exports which have been calculated as over £1bn annually (about 3% of the NHS budget), and in excess

TABLE I—London's medical schools and their main affiliated hospitals

Medical school	Main affiliated hospital(s)
Undergraduate	
Charing Cross and Westminster	Charing Cross Westminster
Imperial College—St Mary's	St Mary's
King's College	King's College
Royal Free	Royal Free
London Hospital	Royal London
St Bartholomew's	St Bartholomew's
St George's	St George's
University College and Middlesex	University College Middlesex
United Medical and Dental Schools	Guy's St Thomas's
Postgraduate	
British Postgraduate Medical Federation	
Institute of Child Health	Hospital for Sick Children (Great Ormond Street)
Institute of Cancer Research	Royal Marsden
Institute of Dental Surgery	Eastman Dental
National Heart and Lung Institute	Royal Brompton
Institute of Neurology	National Hospital for Neurology and Neurosurgery (Queen Square)
Institute of Ophthalmology	Moorfields
Institute of Psychiatry	Bethlem Royal and Maudsley
London School of Hygiene and Tropical Medicine	Hospital for Tropical Diseases
Royal Postgraduate Medical School	Hammersmith

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TABLE II—United Kingdom medical schools: research grants and contracts income, 1989-90 (see box)

School	Income (£m)	Universities Funding Council quality rating
British Postgraduate Medical Federation	28.3	4
Oxford	15.8	5
United Medical and Dental Schools	12.5	3
Glasgow	12.1	4
Royal Postgraduate Medical School	12.1	5
University College and Middlesex	11.9	4
St Bartholomew's	8.1	3
Edinburgh	7.6	4
London School of Hygiene and Tropical Medicine	7.2	4
Wales	7.0	4
King's	6.5	3
Newcastle upon Tyne	6.4	4
Manchester	5.5	3
Charing Cross	5.3	3
London Hospital	5.2	3
Birmingham	4.9	3
Royal Free	4.9	3
St Mary's	4.8	3
St George's	4.7	3
Cambridge	4.4	5
Southampton	4.2	3
Liverpool	3.8	3
Bristol	3.5	3
Leeds	3.4	2
Dundee	2.9	2
Belfast	2.8	2
Sheffield	2.8	2
Nottingham	2.4	3
Aberdeen	2.4	3
Leicester	2.1	2
	205.5	3.27

of the total NHS expenditure on research.¹ The United Kingdom is also home to several major international pharmaceutical companies, which are estimated to spend more than £1.6bn annually on research in Britain. This expenditure is crucially dependent on a viable and thriving national medical research base.²

Is medical research now too difficult for a small, relatively poor, nation such as Britain to play on the world stage? It may indeed be increasingly hard for Britain to compete with the huge basic science institutions of the United States and now, increasingly, of Japan. By contrast, the interaction between basic science and clinical medicine is not so well established in these countries as in Britain; and in the United States and clinical research is said to be "in crisis."³

How should clinical research be organised?

As with research generally, clinical research should be focused, selective, and accountable. It should be carried out in institutions with an adequate critical mass of skills in basic research, clinical research, and clinical care. These goals are easy to enunciate but hard to fulfil. It is easy to envisage a substantial critical mass of basic scientists and clinicians focusing on one specialty, say mental health, or one approach to disease, say molecular medicine. To imagine an institution which had adequate critical mass in every medical specialty and every investigative approach, or even a substantial number of them, would be to imagine an institution larger than the United States National Institutes of Health in Bethesda. A massive venture in the United Kingdom of this type is unrealistic for logistical and financial reasons, even if it were considered desirable. The Medical Research Council's Clinical Research Centre at Northwick Park was an attempt to achieve this, but now it is being dismantled.⁶

The alternative, therefore, is smaller pockets of adequate critical mass, with appropriate focus. Since clinical research involves patients there has to be a hospital or other clinical activity in close association. Because of the importance of close communication and collaboration between clinicians and scientists, it is

essential that they should be located on integrated sites. The larger the campus, or even the higher the building, the less this integration occurs. In a review of the relatively small Australian research institutes Smith noted the tension between critical mass and the tendency for large research organisations to become unproductive and bureaucratic.⁷ Similar conclusions have been reached in the United States.⁸ There is a trade off between size and integration.⁸ The ideal is probably a relatively compact site, with critical mass focused on strategically selected research subjects and combining clinical activities with closely integrated science.

Clinical research under threat

Clinical research is under threat nationally and internationally. To this in London is added the threats from the post-Tomlinson rationalisation of services. London makes a large contribution to clinical research (tables II and III), so reductions across the board in London would have a major national impact. General threats to medical research in the United Kingdom include uncertainty of career prospects, and reducing numbers of securely funded academic posts.⁹⁻¹¹ There are major uncertainties in funding research, and the struggle for research grants and contracts is becoming more and more of a marathon with the odds stacked against winning. Many of these problems are magnified in London.¹²

These difficulties are compounded for clinical research by the problems of funding the related patient costs, which can be divided into two parts (figure). The core clinical cost of a research patient would be the costs of treating a similar patient in a non-research hospital by "reasonable" but cost effective treatment. The excess costs of research arise from the costs of additional investigations, the extra time spent by staff,

Research grants and contracts income

Table II shows the research income generated by medical schools from research councils, grant giving bodies, charities, etc in open competition as reported in annual returns to the Universities Funding Council (UFC). The quality ratings were allocated by the UFC in 1989, after the research assessment exercise, which evaluated research quality in all departments in British universities. A further research assessment exercise is in progress.

The British Postgraduate Medical Federation includes the income from the Institute of Cancer Research (£9.9m), which does not make returns to the UFC.

London contributes substantially to British clinical research. In a survey of Europe's universities the French journal *Libération* voted London Europe's top centre for medical training and research, citing its unique diversity and concentration as the reason for its excellence.¹ This view is qualitative whereas table II shows a more quantitative approach. London's medical schools gained 54% by value of the total United Kingdom research grants and contracts income in open competition from funding bodies, of which London's postgraduate institutions received £47.6m.

The overall research income averaged over each member of the medical academic staff in London in 1990-1 was £106 000 compared with £80 000 for the United Kingdom as a whole. The highest UFC rating (5) was awarded to the Royal Postgraduate Medical School and the Institute of Neurology in London and to Oxford and Cambridge outside London, with an average rating for medical schools in London of 3.42 and for the rest of the country of 3.17.

TABLE III—Medical Research Council grants expenditure in universities 1990-1 (over £1m)

University/medical school	Grants £'000
British Postgraduate Medical Federation	6048
Oxford	5669
University College London	4455
Cambridge	4303
Imperial (St Mary's)	2974
Edinburgh	2504
Royal Postgraduate Medical School	1641
Bristol	1613
Glasgow	1297
London School of Hygiene and Tropical Medicine	1261
Birmingham	1214
Nottingham	1107
Dundee	1053
Manchester	1038

Grants are fiercely peer reviewed and are generally considered most difficult and prestigious to achieve. London gained 44% of the United Kingdom total.

Breakdown of costs of clinical research. Funding for the research projects and programmes of an institution comes from a variety of sources including the Medical Research Council, medical research charities, the European Community, other grants, and contracts (A). The clinical costs of the patients necessary to underpin this research can be subdivided into the core patient costs (C), which are the costs of treating a similar patient in a non-research hospital, and the excess patient costs (B). These include the increased overheads of a research institution, the research time of senior staff, and the extra costs associated with the care of patients who are part of research protocols

and the overall extra costs of running a research institution.

These costs are not new. Previously, however, they were absorbed into the general budgets of teaching and other hospitals where the research was carried out. They were not identified separately, nor was it necessary to fund them separately. The advent of the internal market for patient services means that this loose but workable knock for knock system is coming to an end. Hospitals' income is increasingly defined by the money they raise in winning contracts from district and general practitioner purchasers of health care. Research based hospitals, with their higher costs due to their research, are at a severe disadvantage in selling their beds. Where such hospitals can provide complex treatments as a result of their special skills they may be able to compete in the patient market, but this is not likely to cover most patients needed for clinical research.

This position would represent a challenge even in a stable market, where supply and demand for clinical services were roughly in equilibrium. Weatherall has pointed out the importance of protecting clinical research due to its vulnerability in the service market.¹³ In London there is a substantial excess of supply over demand and the position facing research based institutions is correspondingly grave. It is difficult enough for non-research based institutions to sell their beds in London but those carrying out research would face an impossible task if they had to pass the full excess costs of research on to the purchaser. Many would reach terminal decline within a short period. Fortunately for research the teaching hospitals still benefit from an undefined research component of the funds given as a service increment for teaching and research (SIFTR). The special health authorities continue to be centrally supported and thus do not take part in the market for patient services, but this will change in 1994 and effective new arrangements are crucial if clinical research is to be maintained. It would be easy for clinical research to become the first and indeed greatest casualty of reductions in size in London.

NHS research and development strategy

Despite the uncertainties of funding the patient costs of research, there has been encouraging progress in developing a research and development strategy for the NHS. The government does seem to have committed itself in principle to the continuing support of clinical research recognising that "research is an essential part of the NHS"^{14 15} and the Medical

Research Council has given the strengthening of clinical research as one of its objectives.¹⁶

Following the House of Lords report on the priorities in medical research,¹ the Directorate of Research and Development was set up in the Department of Health with Professor Michael Peckham, a member of the NHS Management Executive, as director. He in turn has set up a review of NHS funded research and is establishing priorities with the help of an advisory committee. The funds currently being spent diffusely will be more focused under the regional directors of research and development.¹⁷

The recent concordat between the Medical Research Council and the health departments indicates commitment by the NHS to funding the service support for research, although the mechanisms for this are not spelt out and the concordat is limited to research sponsored by the Medical Research Council.¹⁸ It is vital for the government to extend this commitment to other funding bodies, particularly the medical research charities, of which the Wellcome Trust alone will next year be spending £220 million on medical research.

A market for clinical research

Clinical researchers need not fear the marketplace as they already work in a highly competitive environment. The danger is that research institutions will be damaged by competition in an inappropriate market for patient services. The patient market is focused on high turnover, low price, an annual timescale, and clinical need. Clinical research needs a secure supply of patients, often with specific diseases or conditions, whose associated costs may be substantial. The flow of these patients may need to continue over three to five years, as stability of the research environment is an indispensable condition for clinical research.¹⁹

Rather than force it into the patient market, clinical research should compete in its own market, a clinical research market. In some ways this is no more than giving word to the notion that clinical research should be fully accountable and should be judged on its success in achieving research goals rather than its success in achieving patient throughputs. This implies

**"Science is central to wealth
creation in an advanced industrial
nation"²²** THE ROYAL SOCIETY

a bidding process against a pool of funds and subsequent review and audit of the use of such funds. Such mechanisms have been developed and widely accepted for many decades for funding by the Medical Research Council, medical research charities, and others for the direct costs of research. There is no reason why similar criteria should not apply to the patient and hospital costs associated with clinical research.

Where would the money come from?

There are already funds in the system which underwrite the patient costs of clinical research and development. These are not specified and are certainly not ringfenced:

- The service increment for teaching and research goes partly to support the clinical costs of research in teaching hospitals but is distributed on the basis of student numbers rather than on research quantity or quality. Efforts to disaggregate the components of SIFTR in the past have had limited success²⁰
- The London postgraduate special health authority

ULRIKE PREUSS

This doesn't come cheap

hospitals are still centrally funded until April 1994. Finding appropriate mechanisms for funding the clinical consequences of their research was seen to be difficult at the time of the 1991 reforms, and it was agreed to develop mechanisms later. The nature of these is still to be decided, but most of the moneys currently going to the special health authorities are used to fund the patient costs of clinical research

- Funding for supraregional services is given centrally for the clinical costs of expensive treatments or techniques whose scientific basis has been established but which are not yet appropriate for widespread introduction because of their rarity. Some of these costs relate to the introduction of developments into NHS practice

- There are other sources: commercial contracts from pharmaceutical companies may cover excess patient costs and some of the wealthier charities have also supported the patient costs of research.²¹ There are, however, few charities which have the funds or the will to do this.

The research component of SIFTR, the special health authority funding, and perhaps some of the supraregional funds could reasonably be included in a research pot, against which bids could be made by suitable institutions with adequate research critical mass for the service costs associated with clinical research.

How would a research market work?

There are already well developed research markets for the direct costs of research. The patient research market proposed here is to address specifically the problem of the patient costs of clinical research. It is envisaged that the research itself will continue to be sponsored as at present by the Medical Research Council, Wellcome Trust, other charities, the NHS projects, commercial contracts, endowments, and other sources. The patient research market would provide a "dual funding" system to cover the patient costs necessary to carry out clinical research programmes. If an institution were approved for funding of this type there are two main ways in which patient flows could be supported. These would not be exclusive, and different combinations might be appropriate for different institutions.

Under the first model funds would be allocated to cover the excess patient costs attributable to the research. The core costs of the patients would be raised in the patient market by the institution bidding for patients under the normal purchaser-provider relation-

ships. This mechanism is analogous to SIFTR and would cover the excess clinical costs, but the funding would be based on the research programme rather than on student numbers as for SIFTR. The level of support would enable the institution to compete on equal terms with other providers in the patient services market. This model has considerable attractions in fairness but not in simplicity. Identifying the excess costs due to research might not be easy. Furthermore, the patient market might still not provide a secure supply of patients even at equal cost. Because research needs a number of complex cases the geographical catchment area could be large and individual purchasers might supply only a few cases. This might not justify the complexities of the contracting process. Extra-contractual referrals are not providing patients in the numbers expected or necessary for clinical research. The unpredictable nature of the patient market might create the danger that a steady patient flow would not be maintained over the long period necessary for a research project.

Under the second model the entire clinical costs of patients judged necessary for the research programmes could be covered by central contracts. This is analogous to the funding of clinical research by the National Institutes of Health, both in its central hospital in Bethesda and in its outlying general clinical research centres. The system has the advantage of simplicity, but the disadvantage that it is separate from the patient market.

In practice it would seem plausible that both mechanisms could work at once, with partial support

"The association [ABPI] is deeply concerned that the government does not appear to appreciate the relationship between expenditure on research and development and the national economic performance. The successful performance of the pharmaceutical industry has long been based on this relationship"²³

for the patient costs of some research activities and full funding for others. Full support could be provided for those cases where partial support was not a sufficient incentive to purchasers to send patients to the research based institutions. Under both models institutions could be free to win extra patient contracts in the market over and above those needed for research, although care would have to be taken that these contracts were not won with the aid of moneys paid to support the research and that the overall balance of priorities was not distorted.

Since research grants have been won in tough competition, there is a good case for the clinical costs automatically following the research, as agreed for research sponsored by the Medical Research Council in the concordat.¹⁸ Nevertheless, the sums of NHS money are substantial, and it may be appropriate for judgments as to the quantity and quality of the research portfolios to be made by the NHS directorate of research and development, with the help of expert peer review. This would allow audit of performance and accountability for outcomes. It is important, however, that this process does not act as a difficult double hurdle for clinical research and also does not inhibit or diminish curiosity driven and basic medical research.

There needs to be recognition that the clinical costs of research departments and hospitals represent more than the sum of individual patients entered into protocols—there has to be ongoing clinical activity to underpin the agreed research portfolio.

There are indications that Professor Michael Peckham is planning academic review for the post-graduate hospitals, and this could be a prelude to funding mechanisms along the lines outlined above. Such funding could and should be available for other institutions both within and outside London. If the mechanisms are fair and the funding is adequate to ensure survival of excellent research then the clinical research community may have cause to cheer. If, on the other hand, they result in lip service commitment to clinical research, but inadequate funding for its clinical consequences and a blind commitment to push research into the patient market, then the outlook is indeed bleak.

Conclusions

Clinical research is under threat internationally and nationally. The problem is urgent in London. It is vital that secure mechanisms be found for funding the patient costs of clinical research, before the service rationalisations cause destruction of London's clinical research programme. These mechanisms need to be robust, peer reviewed, and fully accountable. They should become a national framework, so that institutions in London compete on an equal basis with others across the country. In this way, clinical research throughout Britain could benefit and be strengthened by the current reorganisations.

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For public or profession?—the new GMC performance procedures

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Summary

The upheaval in the General Medical Council two decades ago came from doctors not the consumers the council was set up to protect. Since then there have been repeated calls for doctors to improve their self regulation by amending the disciplinary procedures. Private member's bills have failed and the GMC has now proposed performance procedures to deal with doctors who exhibit a "pattern of poor performance." After months of wide consultation in and outside the medical profession the GMC will decide next week whether to endorse the procedures, which unlike the conduct hearings will be inquiries by peers. Professor Margaret Stacey suggests that the procedures lack clarity, smacking of that "trust me" principle whose subtext is "but I'm not telling you what I'm up to."

When in the 1970s Merrison reviewed the regulation of the medical profession¹ there was little challenge to its sanctity. In the course of my research on the General Medical Council (GMC)² I interviewed a retired, senior civil servant who had had some responsibility in relation to the council. When I asked why there had been no discussion of the merits of professional self regulation his rather nonplussed reply was that in those days it would have been unthinkable. Rudolf Klein's voice³ calling for a council to oversee all the professions—which he felt got away with a good deal too much—had few echoes and nothing was done.

The upheaval in the GMC in the 1970s came not

from consumers but from medical practitioners who felt it was out of date, unrepresentative, and too expensive. The resultant Medical Act, 1978, produced a greatly enlarged council with, for the first time in its 120 years, a majority of elected members. However, no sooner was the reformed council getting into its stride than the radicalism of the new right released the iconoclasm of the 1980s, leaving no profession unscathed and giving new heart to many consumer movements, in health care as elsewhere.

Among challenges to the GMC came Nigel Spearing's 1983 bill proposing two levels of disciplinary charge, adding unacceptable professional conduct to serious professional misconduct. This flowed from the sad and well documented case of Alfie Winn, which I need not repeat here. Parliamentary interference in the GMC's affairs was unusual (and unwelcome), but this and other signals led the council to conclude that it must pay more attention to the area of competence.

The doctrine of clinical autonomy

The statutory duty of the GMC is to protect the public (unlike the BMA, whose duty is to protect the profession). As Merrison pointed out, the main way the council does this is by maintaining a "register of the competent."⁴ Yet, when I sat on the old discipline committee as a lay member in the second half of the 1970s, only the most severe cases of incompetence ever came to that committee, no doubt as a result of the doctrine of clinical autonomy. Apart from those convicted by the courts, doctors were charged with

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