

Health research in the UK: the price of success



The UK is second only to the USA in biomedical research excellence. In terms of productivity, the UK leads the world. Yet it is no exaggeration to say that the future of this remarkable national asset has entered a phase of perilous uncertainty. In March, 2006, the UK's chancellor, Gordon Brown, announced that David Cooksey—a venture capitalist who has worked closely at the interface of government and health science in various roles—would lead a study of the best institutional arrangements for a new Single Fund for medical research. Brown's aspiration is to create the UK equivalent of the US National Institutes of Health (NIH). The annual budget for Britain's new fund would be over £1 billion. Cooksey's evidence gathering ends on July 28, 2006. He is due to report by October this year.

Almost immediately after this review was launched,¹ the Medical Research Council (MRC) and the NHS Research and Development (NHS R&D) programme came under intense scrutiny. Press reports focused particularly on the futures of Colin Blakemore (the MRC's chief executive) and Sally Davies (director of research and development at the Department of Health).² Both individuals are respected by those who work with them. Davies inherited a programme foundering in a government department that displayed little appreciation for the value of research. She has worked hard to bring political credibility back to NHS R&D. Blakemore, meanwhile, is widely admired by fellow scientists. His brave stance on animal research and his international reputation as a neuroscientist are rightly praised. He is a superb ambassador for science. He too inherited an organisation that had lost its way. He has restored confidence at the MRC and set the Council on an ambitious new path, emphasising its renewed commitment to clinical research.³ He has also sought to build strong collaborations with major UK charities, such as the Wellcome Trust, Cancer Research UK, and the British Heart Foundation.

But a preoccupation with personalities threatens to overshadow the need for a careful appraisal of the merits and challenges faced by UK health research. To that end, *The Lancet* invited the MRC and NHS R&D to assess their own achievements since 1995 (the year that the NHS R&D programme began) across three areas (the same areas that Cooksey will be studying): improving patient care

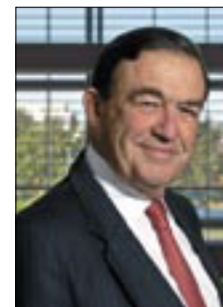
and population health, nationally and internationally; sustaining the UK science base; and delivering innovation to the UK economy (panels 1 and 2).

The MRC's scope and reach are extraordinary. Its investments are considerable: between 1995 and 2005, the MRC's total research spend was £3.76 billion (but note: the total NIH annual budget exceeds \$28 billion). It supports 32 institutes and maintains two research units in Africa. Its gross spend is divided into five areas: molecular and cellular medicine (39%, £181 million); neurosciences and mental health (17%, £82 million); infections and immunity (16%, £77 million); physiological systems and clinical sciences (15%, £73 million); and health services and public-health research (13%, £62 million). During the past 3 years, its clinical research spend has increased by 80% (compared with MRC budget increases of below 4%). The MRC has responsibilities to all four UK countries (eg, 10% of its budget goes to Scotland). As the table shows, the MRC's achievements are impressive across the full range of basic science, clinical medicine, and public health. The MRC's role in sustaining clinical trials in the UK is second to none. The MRC's report, *Clinical Trials for Tomorrow*, led to the creation, in 2004, of the James Lind Alliance, which is bringing patients and clinicians together to identify important, shared questions about the effects of treatments.

The contribution of MRC science to international medicine deserves special consideration. In 2005, the Council spent over £30 million on research relevant to global health, notably on HIV/AIDS (£7.9 million), malaria (£6.7 million), bacterial infections (£5.6 million), and other viral diseases (£4.8 million). The MRC laboratory in The Gambia is the UK's largest single investment in medical research in a low-income setting. Its work is intimately tied not only to the strategy of the MRC but also to the needs of the Gambian people (research programmes must be approved by the Gambian Government as well as by an MRC ethics committee). This partnership between the MRC and The Gambia, begun in 1948, has become a model for how a high-income country can support science for health and development in less-advantaged locations.

A further vital area of MRC activity is translational research. The success of its technology transfer arm,

Published Online
July 5, 2006
DOI:10.1016/S0140-
6736(06)68974-5



David Cooksey



Colin Blakemore



Sally Davies



Medical Research Council

MRC Technology, which manages intellectual property from MRC institutes and units, has been noteworthy (see panel 1). Translation and innovation are especially important for David Cooksey to reflect on. The notion that health research can be neatly packaged into “clinical” and “basic” science would be to misunderstand the evolving nature of scientific medicine. Translational research is the widening bridge between these more traditional clinical and basic science communities. One argument put forward by some critics of the present funding arrangements is that the MRC should be divided in two, its more clinical half going to NHS R&D, the basic half merging with the Biotechnology and Biological Sciences Research Council (BBSRC).

This simplistic dichotomising of the MRC’s role would be a disastrous error. The MRC’s success depends on its broad mandate from laboratory to clinic. To take that structure apart risks destabilising an enterprise that has demonstrably succeeded in delivering on its mission to “encourage and support high-quality research with the aim of improving human health”.

The UK’s achievements in clinical and public-health research have depended greatly on the infrastructure of the NHS. The NHS R&D programme has focused exclusively on applied research—“to promote high-quality evidence to support health and health-care policy makers, professionals and the public.” Between 1995 and 2005, NHS R&D spent £4.6 billion. By far the greatest proportion of this spending (80%) went on research support (infrastructure, training, dissemination, governance, and ethics), including support for studies funded by the MRC and other bodies. Only a relatively small proportion of the NHS R&D budget has been available for its own funding priorities. About 1500 projects have been commissioned centrally during the past decade. Nearly 4000 projects have been commissioned locally. Major national programmes are shown in panel 2. NHS R&D has become an important funding source for non-commercial clinical trials—eg, endoscopic surgery for abdominal aortic aneurysm,⁴ management of leg ischaemia,⁵ and feeding after stroke.⁶

The benefits of NHS R&D infrastructural investment to the entire UK clinical research portfolio are rarely acknowledged. Important MRC-funded trials on ovarian cancer screening, behavioural change in diabetes management, whole-body hypothermia for perinatal

asphyxial encephalopathy, and surgery for Parkinson’s disease have depended greatly on underpinning support from NHS R&D.

Notwithstanding this largely hidden contribution to primary research, NHS R&D’s investment in the

Panel 1: Selected achievements of UK’s Medical Research Council (1995–2005)*

Population and public health

- Combination drug treatment for HIV/AIDS (1995)
- Antibody-based cervical cancer screening (1997)
- Identification of agent causing vCJD (1998)
- Statins reduce risk of myocardial infarction and stroke (Heart Protection Study, 2001)
- Magnesium sulphate halves risk of pre-eclampsia (Magpie trial, 2002)
- Ropinirole slows nerve function loss in Parkinson’s disease (2003)
- Steroids increase risk of mortality after head injury (2004)
- Identifying link between red meat and bowel cancer (2005)
- Multiscreening test for common cancers developed (2005)

Clinical medicine

- DNA chip-technology developed (1997)
- First complete sequence of *Caenorhabditis elegans* (1998, contributing to understanding human genetic disease)
- First draft of complete human genome sequence (2000)
- Gene identified for asthma severity (2002)
- New technique for over-riding genetic defects in muscular dystrophy identified (2003)
- Structure of 1918 Spanish influenza virus completed (2003)
- Stem cells stimulate regrowth of spinal cord nerve fibres (2003)
- 3D tissue images with optical projection tomography (2004)
- First mouse model of Down’s syndrome (2005)

International public health

- Vaccine against *Haemophilus influenzae* proves successful (1996)
- Insecticide-treated bednets reduce childhood deaths (1998)
- Indian tuberculosis deaths linked to smoking (2003)
- Highly active antiretroviral therapy cuts death rates by 80% in people with HIV/AIDS (2003)
- WHO changed tuberculosis treatment guidelines based on MRC research (2004)
- Antipneumococcal vaccine reduces child death rate (2004)
- MRC’s presence in Uganda contributes to the country’s success in tackling HIV/AIDS (2005, acknowledged by WHO)

(Continues on next page)



(Continued from previous page)

UK science base

MRC supported publications in peer-reviewed journals from its intramural programme (half of MRC's investment in research)

Year	Number of publications
1998	1624
1999	1565
2000	1604
2001	1298
2002	..
2003	1814
2004	2011
2005	2025

Training awards

Year	Fellowships	Studentships
1995-96	97	..
1996-97	96	400 (estimate)
1997-98	96	400 (estimate)
1998-99	117	419
1999-00	135	405
2000-01	159	413
2001-02	126	492
2002-03	73	470
2003-04	102	339
2004-05	73	480
2005-06	82	473

Innovation

MRC Technology:

- Income from MRC's intellectual property rights exceeds that earned by all English universities combined
- £4.5 million gap fund supports MRC laboratories in early-stage ideas progressing towards market place
- MRC outperforms Massachusetts Institute of Technology (MIT) in knowledge-transfer revenue: revenue per pound sterling invested in research is 10.9% for MRC, 4.5% at MIT
- MRC has derived substantial revenues from its commercial transactions (eg, £152 million from buyout of Humira)
- Licensing income is rising dramatically (£27.3 million in 2004-05 compared with £14.3 million in 2003-04)

Dundee's MRC Protein Phosphorylation Unit runs the largest preclinical research collaboration between the pharmaceutical industry and a research institute

Ardana plc, a spin-off from the MRC Human Reproductive Sciences Unit in Edinburgh, develops treatments for infertility and cancer and was floated on the London Stock Exchange in 2005

*Based on a submission to *The Lancet* from the MRC.

NHS Health Technology Assessment programme, the Cochrane Collaboration, and the Centre for Reviews and Dissemination illustrate how the UK's Department of Health has become the world's most important funder of systematic reviews. Indeed, it is fair to claim that NHS R&D's most important contribution to the UK science base is through building systematic review capacity, benchmarking systematic review methods, and promulgating systematic reviews as a global public good. This remarkable achievement must not be underestimated.

NHS R&D has funded 593 time-limited programmes since 1993, publishing several hundred reports evaluating their success, across subjects as diverse as dentistry and forensic mental health, although the actual health impact of these reports remains largely unquantified. The Department of Health's support for research networks has expanded substantially the number of patients entering clinical trials. For example, the National Cancer Research Network (NCRN, established in 2001 after a successful collaboration between NHS R&D and the MRC) doubled the number of new adult cancer patients entering clinical trials after only 2 years. By 2004-05, 12% of cancer patients (24,000 individuals) in England entered NCRN trials. This number is the highest per capita rate of cancer trial participation worldwide. It has become the basis for the UK Clinical Research Network. The MRC also deserves credit here. It was the MRC's investment in childhood leukaemia trials that set the standard for patient recruitment from 1959 onwards.

Despite these respective successes, the case for a Single Fund for health research makes good sense. It will enhance strategic planning, reduce transaction costs, avoid unnecessary competition, and promote best practice in the selection and management of research. So what should David Cooksey do? The MRC and NHS R&D programme both make significant contributions to UK health, to Britain's science base, and, especially in the case of the MRC, to innovation and discovery research. Cooksey will therefore have to ask some tough questions. Here are just three.

First, does existing research spending deliver value for money? Answer: we do not know. Evidence from the USA suggests that an MRC-like model does deliver large public returns on research investments, at least for clinical trials,⁷ although others have pointed out the high

Panel 2: Selected achievements of UK's NHS R&D Programme (1995–2005)*

Health Technology Assessment

308 monographs completed (1997–2005). This work on costs, effectiveness, and impact of health technologies is used, for example, to support appraisals by the National Institute for Health and Clinical Excellence

Service Delivery and Organisation

140 projects have been commissioned since 1999 (67 have reported). Their aim is to provide an evidence base to underpin decisions on effective ways to deliver health services. Examples include how to reduce attendance and waits in casualty departments, and mental health needs of adolescents attending youth-offending teams

Research Capacity Development

Awards (over £60 million between 1999 and 2004) are designed to fast-track researchers of outstanding potential. 187 fellows are currently being supported. Since 2004, £0.5 million has been invested in 19 public-health policy areas

New and Emerging Applications of Technology (NEAT)

Since 1999, NEAT has funded 49 research projects (eg, on quantitative 3D breast imaging and screening for left ventricular dysfunction)

National Horizon Scanning Centre

This centre provides advance notice of new and emerging technologies that might require urgent evaluation or consideration

Methodology

The National Coordinating Centre for Research Methodology promotes development and application of appropriate research methods so that health and social care can be built on the best possible evidence-base

INVOLVE

A national advisory group to promote and support active public involvement in NHS research

Policy Research Programme

eg, MedLINK (technologies across a range of applications), smoking cessation, teenage pregnancy, and NHS Direct

Cochrane Collaboration

The main output is a series of Cochrane Reviews. Of 2674 full Cochrane Reviews (by 2006), 1457 (54%) received funding support from NHS R&D

Centre for Reviews and Dissemination

This centre promotes evidence-based information about effects of interventions used in health and social care (eg, National Cancer Guidance and Effective Health Care bulletins)

*Based on a submission to *The Lancet* from the NHS R&D programme.

and cost-effective value of systematic reviews.⁸ We have no idea whether the majority of non-clinical MRC spend is truly delivering value for money (largely because we have no agreed measure of what we mean by value). One measure of value is MRC Technology's success in exploiting intellectual property. Here, the MRC has delivered enormous benefits.

Second, has the MRC achieved the best balance between clinical research and basic science? Answer:

not yet. In 2004–05, the MRC's Health Services and Public Health Research Board (HSPHRB)—which has the "principal responsibility" for clinical research—was awarded only 13% of the MRC's total budget. Taking account of other MRC boards, overall MRC spend on clinical research is about 30% of its total budget. Although HSPHRB is currently funding 100% of grant applications rated at internationally competitive standards, this is sadly not the case for some other boards. The MRC therefore needs a higher total spending budget to fund all of the highest-quality research presented to it. That is the only way the MRC can fully fund the best clinical research, while not damaging the UK's biomedical science base. To complicate matters, while the MRC has steadily increased its investment in non-commercial clinical trials,⁹ the total number of those trials has declined.¹⁰ The MRC deserves greater support in its efforts to put patients at the centre of its funding priorities.

Third, has NHS R&D truly delivered on its promise to provide the public, practitioners, and policymakers with evidence to support their decision making? Answer: no. Partly for the strategic reasons already noted, its actual investments in primary research are relatively small and fail to capture important data about newly introduced technologies. The creation of large-scale national registries for new medical procedures would provide a valuable mechanism to monitor their use and effectiveness. Such registries would likely show important differences between the expectations of effect from published clinical trials or technology assessments and the realities of clinical practice.¹¹

The MRC and NHS R&D are aware of these and other objections to their work. They have ambitious plans for further strategic change to meet their critics' demands. I have discounted these promises. Instead, to ensure some measure of comparability, I have focused on one decade of demonstrable results. By doing so, it seems clear that the MRC's critical funding mass has delivered consistent success with respect to the Cooksey criteria—health impact, science base, and economic benefit. NHS R&D's achievements, while real, notably in supporting systematic reviews and several non-commercial clinical trials, are, by contrast, less consistent by Cooksey standards.

However, two important caveats should be signalled at this point. First, the spending budgets of these funders

are not directly comparable. It has been far easier for the MRC to achieve consistent success with a budget of £3.76 billion than it has been for NHS R&D with only £0.9 billion. Second, one could reasonably counter the apparent success of the MRC by arguing that, pound for pound, NHS R&D might be more efficient. Wise investments in systematic reviews by NHS R&D will have saved the MRC and other funders considerable sums by preventing wasteful use of resources on unnecessary further research. Still, most of those well acquainted with government know that a decade of lukewarm political commitment to research within the Department of Health has suffocated and debilitated NHS R&D, despite spirited efforts at resuscitation by successive directors of research, including the present incumbent. The fortunes of NHS R&D fluctuate according to the personal chemistry between its director and ministers. This is no basis for independent, stable, and high-quality science funding. Public funding for clinical research should depend neither on personalities nor on a divided system of resource allocation. Infrastructure and grant funding should be fully integrated. The question is how.

The available evidence certainly supports moving about £115 million of annual NHS R&D budget currently devoted to commissioned research into the income column of the MRC's balance sheet to create a new Single Fund. Budgets devoted to systematic reviews—the Cochrane Collaboration, the Centre for Reviews and Dissemination, and parts of the Health Technology Assessment programme—should be ring-fenced, indeed strengthened.

What should be done with the sum of about £500 million, which currently supports NHS infrastructure for research? Should that £500 million be added to the kind of Single Fund Gordon Brown envisages? While the MRC has far stronger experience as an internationally competitive scientific grant-funding body, the Department of Health seems better equipped to manage NHS infrastructure. But the fact is that a large part of this £500 million has leaked into NHS service delivery. NHS R&D wants to reclaim this lost investment in order to channel at least some of it back into grant funding. It would make more cost-effective sense to reallocate that money to the new Single Fund, specifically for clinical and public-health research. Research infrastructure spending could then be linked to grants as indirect costs.

The creation of a Single Fund should not come without strings. It should trigger further review of the UK's clinical and public-health research spending strategy and governance arrangements. It should provoke questions about value for money, monitoring and support of non-commercial clinical trials, and ways to assess new and expensive health technologies.

In some ways, the MRC and NHS R&D have been victims of their own success. As their achievements have been increasingly recognised, and as science is now seen as critical to economic development, governments will naturally seek to squeeze more out of the research pipeline. The MRC's strong international standing in the face of fierce global competition deserves to be acknowledged and supported. The NHS R&D programme has partly succeeded under often adverse political conditions. David Cooksey is fortunate to have two such world-class institutions, together with their well-recognised and respected programmes, at his fingertips. Their aspirations are more likely to be realised by fusion into a Single Fund: independent of government, combining each organisation's respective strengths, and preserving the unparalleled capacity and skill of the MRC to judge and administer research.

Richard Horton

The Lancet, London NW1 7BY, UK

I thank Colin Blakemore and Sally Davies for their help in providing information for this article.

- 1 Science and innovation investment framework 2004–2014: next steps. March, 2006.
- 2 Fazackerley A. Hotshots tipped to head new institute. *Times Higher Educ Suppl* April 28, 2006: 6.
- 3 Blakemore C, Davidson J. Putting a value on medical research. *Lancet* 2006; **367**: 1293–95.
- 4 EVAR trial participants. Endovascular aneurysm repair versus open repair in patients with abdominal aortic aneurysm (EVAR trial 1): randomised controlled trial. *Lancet* 2005; **365**: 2179–86.
- 5 Adam DJ, Beard JD, Cleveland T, for the BASIL trial participants. Bypass versus angioplasty in severe ischaemia of the leg (BASIL): multicentre, randomised controlled trial. *Lancet* 2005; **366**: 1925–34.
- 6 The FOOD Trial Collaboration. Routine oral nutritional supplementation for stroke patients in hospital (FOOD): a multicentre randomised controlled trial. *Lancet* 2005; **365**: 755–63.
- 7 Johnston SC, Rootenberg JD, Katrak S, Smith WS, Elkins JS. Effect of a US National Institutes of Health programme of clinical trials on public health and costs. *Lancet* 2006; **367**: 1319–27.
- 8 Glasziou P, Djulbegovic B, Burls A. Are systematic reviews more cost-effective than randomised trials? *Lancet* 2006; **367**: 2057–58.
- 9 Blakemore C, Chalmers I. Academic medicine: time for reinvention. *BMJ* 2004; **328**: 49.
- 10 Chalmers I, Rounding C, Lock K. Descriptive survey of non-commercial randomised controlled trials in the United Kingdom, 1980–2002. *BMJ* 2003; **327**: 1017–19.
- 11 Grilli R, Taroni F. Managing the introduction of expensive medical procedures: use of a registry. *J Health Serv Res Policy* 2006; **11**: 89–93.