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Descriptive survey of non-commercial randomised controlled trials in the United Kingdom, 1980-2002

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Abstract

Objectives To describe the characteristics of randomised controlled trials supported by the main non-commercial sources of funding in the United Kingdom between 1980 and 2002.

Design Descriptive survey.

Setting Randomised controlled trials funded by the Medical Research Council, NHS research and development programme, Department of Health, Chief Scientist Office in Scotland, and medical research charities.

Participants 1464 randomised controlled trials supported by the main non-commercial sources of funding.

Results Support for randomised controlled trials by the main sources of non-commercial funding in the United Kingdom has fallen in recent years, without any concomitant increase in the sample sizes of these studies. Drug trials in a limited range of health problems have dominated among the studies supported by the Medical Research Council and medical research charities. Until recently, the NHS research and development programme supported randomised controlled trials of various healthcare interventions, in a wide range of health problems, but between 1999 and 2002 many of the subprogrammes that had commissioned trials were discontinued.

Conclusions The future of non-commercial randomised controlled trials in the United Kingdom has been threatened by the discontinuation or demise of national and regional NHS research and development programmes. Support also seems to be declining from the Medical Research Council and the medical research charities. It is unclear what the future holds for randomised controlled trials that address issues of no interest to industry but are of great importance to patients and practitioners.

Introduction

During 2002 the UK Medical Research Council conducted a major review of its approach to supporting randomised controlled trials.¹ Data were collected for the review on the characteristics of randomised controlled trials funded between 1980 and 2002 through three main sources of non-commercial support in the United Kingdom: the Medical Research Council; the NHS research and development programme, Department of Health, and Chief Scientist Office in Scotland (NHS randomised controlled trials); and medical research charities. We conducted a descriptive survey to describe trends in the number and characteristics of randomised controlled trials funded by non-commercial sources between 1980 and 2002.

Methods

A randomised controlled trial was defined as a study in which formal randomisation or alternation had been used to create the groups compared. Our principal sources for identifying trials were the main providers of funds for randomised controlled trials (see bmj.com).

We coded the health problems and interventions studied. Each study was assigned to at least one health problem and at least one intervention category.

Results

Overall, we identified 1464 randomised controlled trials supported by the main non-commercial sources between 1980 and 2002. The Medical Research Council was the principal source of funding for 323 (22.1%) trials, the NHS for 770 (52.6%) trials, and medical research charities for 371 (25.3%) trials.

Figure 1 shows trends in the number of randomised controlled trials funded over this period. Of 615 randomised controlled trials funded between 1991 and 2002 by the NHS research and development programme or Department of Health, 514 (83.6%) were funded through programmes that stopped commissioning between 1999 and 2002. No evidence was detected that the recent decline in the number of trials in all three sectors had been accompanied by an increase in the size of trials or any trend towards multi-centre collaboration.

A wider variety of health and other problems were studied in trials funded by the NHS than in those funded by either the Medical Research Council or medical research charities, among which cancer predominated (see bmj.com). Similarly, a wider variety of healthcare interventions were studied in trials

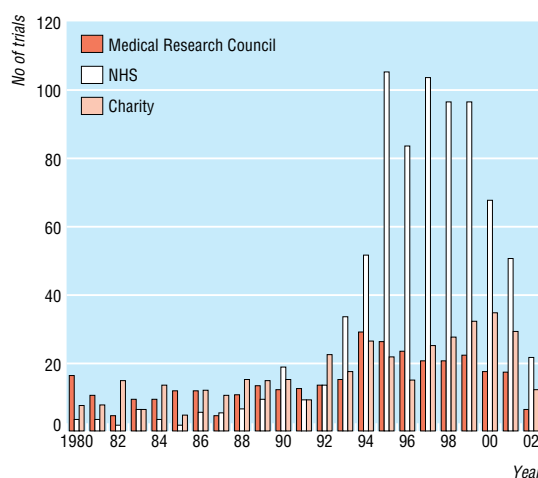


Fig 1 Number of randomised controlled trials in United Kingdom supported by the main non-commercial sources between 1980 and 2002, by funding body



Acknowledgments appear on bmj.com

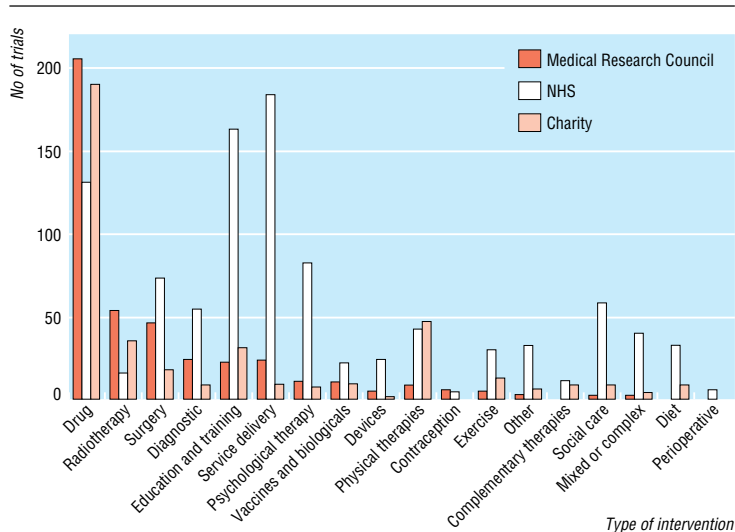


Fig 2 Number of randomised controlled trials in United Kingdom supported by the main non-commercial sources between 1980 and 2002, by type of intervention

funded by the NHS (fig 2). Contrasts are evident in education and training, service delivery, psychological therapy, and social and complex care. Such methodologically challenging trials featured in the NHS trials' portfolio, but infrequently among trials funded by the Medical Research Council and medical research charities, where drug trials dominated.

Discussion

It is unclear what the future holds for randomised controlled trials that address issues of no interest to industry but are of great importance to patients and practitioners. We believe that we have identified most trials funded by the Medical Research Council that began between 1980 and 2002. The capture of data on NHS trials before the mid-1990s is likely to be incomplete as systematic information on randomised controlled trials funded before this time was unobtainable. The increase in the number of trials funded by the NHS between 1992 and 1995 is thus likely to be less dramatic than it seems in figure 1.

By contrast, the noticeable decline in the number of trials funded by the NHS between 1998 and 2002 is likely to be real and to reflect the conclusion of the series of time limited national NHS research and development programmes (for example, those in mental illness and asthma) and the fact that regional NHS research and development programmes were brought to an abrupt end during another unanticipated reorganisation of the NHS. These programmes gave substantial visibility to the NHS research and development programme in high impact journals such as the *BMJ* and the *Lancet*.

In addition, the regional NHS research and development programmes also provided a mechanism through which new ideas could be piloted on a limited scale before a substantive study. The demise of these programmes is therefore particularly regrettable.

Contrasts were apparent in the range of health problems and interventions addressed by the studies. These patterns seem likely to reflect the fact that the NHS research and development programme actively

commissioned studies in under-researched areas, whereas the funding patterns of the Medical Research Council and the medical research charities reflect their responses to the interests of investigators.

The dominance of trials in cancer reflects not only support from wealthy research charities in this discipline but also the Medical Research Council budget for cancer trials that existed until the late 1990s. The important infrastructure for cancer trials established over previous decades has provided an excellent foundation for the work of the recently established National Cancer Research Network.

The dominance of drug trials among studies funded by the Medical Research Council and the medical research charities is all the more remarkable since most commercially funded trials are studies on drugs. Some of the most important drug trials supported by the Medical Research Council tend to be large studies that have yielded strong evidence on the effects of drugs on outcomes that matter to patients, which have not been studied in prelicensing studies funded by industry. Furthermore, industry has shown little or no interest in evaluating the effects of inexpensive but important drugs (such as aspirin in cardiovascular and other diseases) in "head-to-head" studies comparing the relative merits of alternative drug regimens, or in the long term follow up studies that are needed to obtain a more complete view of the effects of drugs.

The information that has emerged from our survey influenced the Medical Research Council's review.¹ It recommended that the council should be more proactive in fostering trials testing some of the more methodologically challenging interventions (psychological therapies and service organisation, for example) and in evaluating healthcare interventions in areas of morbidity that have tended to be neglected, such as mental ill health.¹

It cannot be assumed that the things that get studied in trials, or the way that they are studied, necessarily reflect the priorities of patients and health professionals.^{2,3} Patients may be engaged to a greater extent in prioritising and designing randomised controlled trials and might also be helped further if a patient led guide could be established.^{4,5} At a time when industry's clinical research agenda seems likely to compromise the future of non-commercial trials, it is important to consider how best to foster randomised controlled trials that address questions relevant to the needs of people using and working in the health services.^{6,7}

Given the Department of Health's response to the European Clinical Trials Directive, a new Department of Health and Medical Research Council Task Force has been established to find solutions to some of the concerns that demand immediate attention.⁷ But the greatly reduced capacity of the NHS to commission randomised controlled trials relevant to its work is a serious threat to the organisation's ability to generate information relevant to serving patients and the public effectively.¹ This is surprising and regrettable given the implicit desire in *The NHS Plan* to increase the proportion of patients treated within the context of randomised controlled trials.⁸

What should be the contribution of the medical research charities in supporting randomised con-

trolled trials relevant to the needs of patients? Although some have a longstanding commitment to supporting randomised controlled trials, there is overall modest investment in such trials by medical research charities.⁹ Through the Pharmaceutical Industry Competitiveness Task Force, the government has made clear its commitment to facilitate the conduct of commercial drug trials in the NHS.¹⁰ We believe that a coherent strategy is also needed to ensure support for the many randomised controlled trials that are of no interest to industry but are nevertheless of importance to patients and practitioners. Given the responses to the Medical Research Council's consultation, factors that will have to be taken into account include the increased administrative burden that now faces anyone contemplating involvement in clinical research of this kind.¹

The views expressed in this article are those of the authors and are not necessarily the views or the policies of the Cochrane Collaboration.

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What is already known on this topic

No data have been published on the number and characteristics of randomised controlled trials supported by the main non-commercial sources in the United Kingdom

What this study adds

The number of non-commercial randomised controlled trials has declined without a concomitant increase in the sample sizes of these studies

The future of these trials is threatened by the discontinuation of the time limited NHS research and development programmes and by the demise of the regional programmes

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Decline in mortality, AIDS, and hospital admissions in perinatally HIV-1 infected children in the United Kingdom and Ireland

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Abstract

Objective To describe changes in demographic factors, disease progression, hospital admissions, and use of antiretroviral therapy in children with HIV.

Design Active surveillance through the national study of HIV in pregnancy and childhood (NSHPC) and additional data from a subset of children in the collaborative HIV paediatric study (CHIPS).

Setting United Kingdom and Ireland.

Participants 944 children with perinatally acquired HIV-1 under clinical care.

Main outcome measures Changes over time in progression to AIDS and death, hospital admission rates, and use of antiretroviral therapy.

Results 944 children with perinatally acquired HIV were reported in the United Kingdom and Ireland by October 2002; 628 (67%) were black African, 205

(22%) were aged ≥ 10 years at last follow up, 193 (20%) are known to have died. The proportion of children presenting who were born abroad increased from 20% in 1994-5 to 60% during 2000-2. Mortality was stable before 1997 at 9.3 per 100 child years at risk but fell to 2.0 in 2001-2 (trend $P < 0.001$). Progression to AIDS also declined ($P < 0.001$). From 1997 onwards the proportion of children on three or four drug antiretroviral therapy increased. Hospital admission rates declined by 80%, but with more children in follow up the absolute number of admissions fell by only 26%.

Conclusion In children with HIV infection, mortality, AIDS, and hospital admission rates have declined substantially since the introduction of three or four drug antiretroviral therapy in 1997. As infected children in the United Kingdom and Ireland are



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