Papers

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

Iain Chalmers, Cath Rounding, Kate Lock

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] The review aimed "to pave the way for better controlled trials for the future—trials that have the best possible prospects for delivering reliable, high quality answers to the healthcare questions of the 21st century."[1] After extensive consultation during 2002, a report was finalised and accepted by the council early in 2003.[2]

The UK Randomised Controlled Trial Registration Project provided data 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 the 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

We defined a randomised controlled trial as a study in which formal randomisation or alternation had been used to create the groups compared. Our search strategies for identifying eligible studies are available elsewhere.[3] In brief, our principal sources for identifying trials were the main providers of funds for randomised controlled trials (box).

Missing core data items for each trial identified were sought directly from the trialists, if possible, or extracted from publications associated with the studies. Health problems and interventions studied were coded by using a scheme developed during the project.[3] Each study was assigned to at least one health problem and at least one intervention category.

Information was assembled in an Access database, with trials (rather than reports of trials) as the units of analysis. The registers of randomised controlled trials assembled in the UK Randomised Controlled Trial Registration Project have now been transferred to the Medical Research Council Clinical Trials Unit for maintenance and updating, with the intention that they will be made publicly accessible.

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.

UK Randomised Controlled Trial Registration Project, UK Cochrane Centre, Oxford OX2 7LG
Iain Chalmers
coordinator

Medical Research Council and Medical Research Charities Subproject, UK Randomised Controlled Trial Registration Project
Cath Rounding
coordinator

Department of Health and NHS Subproject, UK Randomised Controlled Trial Registration Project
Kate Lock
coordinator

Correspondence to:
I Chalmers
ichalmers@jameslindlibrary.org

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Main sources of non-commercial support for randomised controlled trials

Medical Research Council
Medical Research Council Trials Directory
National Research Register
The trials' register maintained by the UK Coordinating Committee on Cancer Research
Cochrane Central Register of Controlled Trials

NHS
Staff responsible for elements of the NHS research and development programme, including:
- Ten time limited national programmes (such as those in mental illness and asthma) that had funded randomised controlled trials
- Eight NHS regional research programmes
  The ongoing national health technology assessment programme
- Staff responsible for the national programme funded by the Chief Scientist Office in Scotland

Medical research charities
The trials' register maintained by the UK Coordinating Committee on Cancer Research
The metaregister of controlled trials maintained by Current Controlled Trials
Charities deemed likely by the director of research at the Association of Medical Research Charities to fund randomised controlled trials
Charities that stated they supported randomised controlled trials in response to a survey conducted by the University of Exeter[4]

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. We were unable to detect any evidence 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 multicentre collaboration (data not shown).

Figure 2 shows the categories of health problem studied in the trials, for each source of funds. Symptoms and general pathology covered problems such as pain and insomnia. The category for not applicable generally referred to randomised controlled trials of service organisation. 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.

Figure 3 shows the categories of intervention studied in the trials for each source of funds. A wider variety of healthcare interventions were studied in trials funded by the NHS than in those funded by either the Medical Research Council or medical research charities. 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. Our identification of NHS trials before the mid-1990s is likely to be incomplete, as systematic information on randomised controlled trials funded before this time was unobtainable, either through the NHS research and development programme or through the locally organised research schemes run by regions before the inception of the programme. This was due to repeated changes in regional boundaries over this period, the abolition of regional research and development offices during the course of our data collection, and computer systems that were not fully functional in regional NHS research and development offices until the mid-1990s. 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 time limited national and regional 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 being scaled up for substantive study. For example, regional funding supported a pilot randomised comparison of endovascular coiling with neurosurgical clipping for ruptured intracranial aneurysms. The results of this study provided the justification for proceeding to a large multicentre randomised

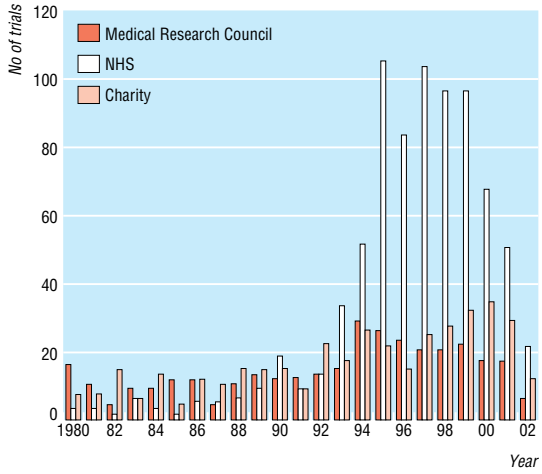

Fig 1 Number of randomised controlled trials in United Kingdom supported by main non-commercial sources between 1980 and 2002, by funding body

controlled trial, funded by the Medical Research Council, which showed that the new endovascular technology offered a substantial advantage over surgery.[5] Because the regional NHS research and development programmes were particularly well suited to supporting exploratory and pilot studies, the demise of these programmes is 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, shown by its support of the Medical Research Council Cancer Trials Office in Cambridge, and coordination of the leukaemia trials by the Clinical Trial Service Unit in Oxford. 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 when it is taken into account that 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 and magnesium sulphate in pre-eclampsia) 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 of its strategy for clinical trials, *Clinical Trials for Tomorrow*.[2] The review 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.[2]

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.[6 7] It may be possible to reduce these mismatches by engaging patients to a greater extent in prioritising and designing randomised controlled trials.[8] Potential participants might also be helped to choose among studies of potential relevance to their needs if a patient led guide could be established.[9] At a time when the pursuit of industry's clinical research agenda seems likely to compromise the future of non-commercial trials, it is important to consider how best

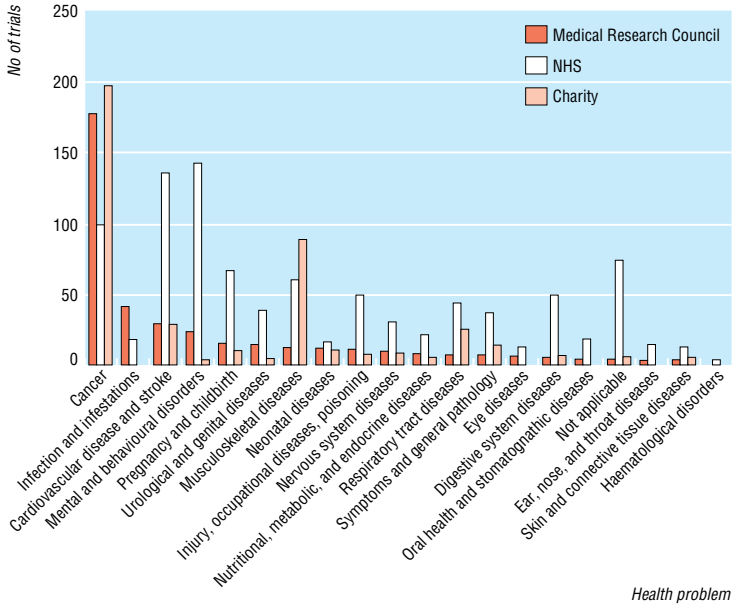

Fig 2 Number of randomised controlled trials in United Kingdom supported by main non-commercial sources between 1980 and 2002, by funding body and health problem

to foster randomised controlled trials that address questions relevant to the needs of people using and working in the health services.[10 11]

Given the Department of Health's response to the Medical Research Council led impact assessment on the implementation of 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.[11] The *Clinical Trials for Tomorrow* report addresses some of the more longstanding problems identified, 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.[2] This is par-

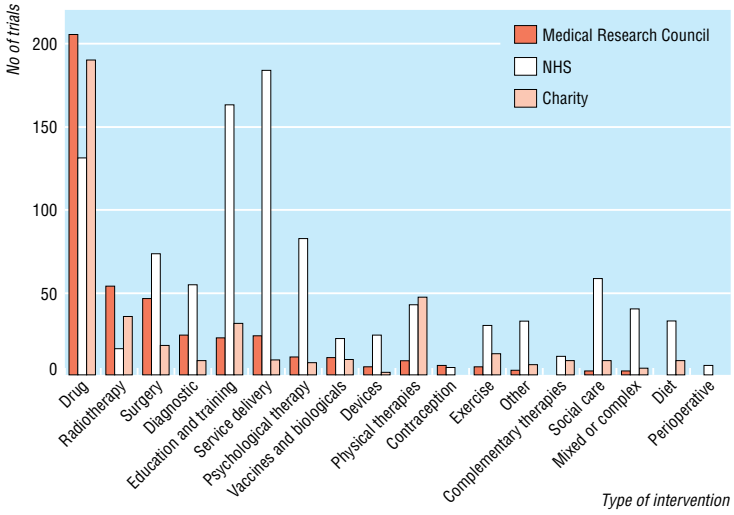

Fig 3 Number of randomised controlled trials in United Kingdom supported by main non-commercial sources between 1980 and 2002, by type of intervention

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

ticularly 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.[12]

What should be the contribution of the medical research charities in supporting randomised controlled trials relevant to the needs of patients? Although some charities such as Cancer Research UK, the British Heart Foundation, and the Arthritis Research Campaign have a longstanding commitment to supporting randomised controlled trials, other researchers have already drawn attention to the overall modest investment in such trials by medical research charities.[4]

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.[13] 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.[2]

Contributors: IC conceived the project, sought funding, supervised the data collection and processing, and wrote the report. CR was principally responsible for the data collection, management, and analysis of trials funded by the Medical Research Council and medical research charities. KL was principally responsible for the data collection, management, and analysis of trials funded by the NHS, the Department of Health, and the Chief Scientist Office in Scotland. IC and CR will act as guarantors for the paper. 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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Competing interests: IC is employed on a part-time basis to help promote some of the objectives arising from the *Clinical Trials for Tomorrow* review. He is funded for this purpose by the Medical Research Council and the Department of Health.

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