Multi-centre clinical respiratory research: a new approach?

ABSTRACT  — Background: Recruitment to clinical trials organised by the research committee of the British Thoracic Society (BTS) has declined. We suspected that this was due to increasing workloads for consultant physicians in the National Health Service (NHS). We investigated possible causes in study 1 and a possible solution in study 2.

Methods: Study 1 — a questionnaire was sent to BTS members listing possible factors that might deter them from entering patients into trials. These were scored on a 0–5 scale. Study 2 – we set up 13 panels of experts to cover all major fields of respiratory medicine. They were asked to design projects that would address the most important research questions that could be answered by multi-centre clinical trials. We sent 11 projects for scoring to consultant members of the BTS who were asked to score them on scientific merit and on their ability to contribute patients to the study.

Results: Study 1 – of the 59% of consultants who responded, 77% said that competition with increasing demands on their time was the major reason for not participating. Study 2 – 40% of consultants returned project scores. Three projects were subsequently selected for grant application.

Conclusions: Clinical research in the UK is under threat from increasing workloads on consultants. One solution to this problem is a national approach to commission major projects. The most important clinical research questions might then still be answered in the limited time available to consultants.

This paper describes how the research committee of the British Thoracic Society (BTS) has attempted to identify and quantify the problem of lack of time for clinical research in respiratory medicine in the UK, and to maximise limited clinical research resources through an experimental research prioritisation exercise. These studies were carried out on a national scale.

The research committee of the BTS was originally set up over 30 years ago to coordinate clinical trials in treatment of tuberculosis and was highly successful in this role. In more recent years, it has set up multiple projects in all aspects of respiratory disease that required the participation of many clinicians in order to answer research questions; for example in sarcoidosis\(^1\), cryptogenic fibrosing alveolitis\(^2\) and pneumonia\(^3\). In the past, these projects met with considerable enthusiasm and support. However, in 1994 we became concerned that recruitment rates to our portfolio of projects were apparently falling. In discussion with other colleagues, and from our own experience as a committee predominantly composed of clinicians, we suspected that a major factor in this decline in participation in multi-centre research projects might be lack of time due to increasing clinical workloads and the constraints of the ‘purchaser–provider’ management system in the NHS.

To test the hypothesis that NHS reforms were a major factor in declining recruitment to our multi-centre studies (and to evaluate other possible reasons), we sent a questionnaire to members of the BTS in September 1994 (study 1). The results of this strengthened our concerns, and led us to conduct a further study (study 2) in 1995–6. This constituted a research prioritisation exercise in which all consultant members of the BTS were invited to participate.

Here we describe these two studies and their possible contribution towards a new approach to sustaining high quality clinical research despite the diminishing resources that all national health care programmes now face.

Methods

Study 1 – Questionnaire to BTS members

A questionnaire sent to members of the BTS asked for their views, on a scale of 0–5, on how much of a deterrent to participation in clinical trials various factors constituted (0 no deterrent, 5 definite deterrent). At the end of the questionnaire respondents were also invited to make free text personal comments on why they might now be less likely to participate in clinical trials than they had been in the past.

Study 2 – Research prioritisation exercise

To identify the most important research questions in respiratory medicine that might be answerable by clinical studies (as opposed to priorities in laboratory-based respiratory science), we divided respiratory medicine into 13 categories (Table 1). In each of these wide fields we identified small groups of colleagues who we felt would be generally recognised as experts by respiratory physicians in the UK and abroad. These groups were then asked to put forward brief outlines of one or two projects, designed to address the most important research questions in their field,

M R HETZEL MD FRCP, Consultant Physician, Bristol Royal Infirmary, Bristol
T LEE MD MD, FRCP, Professor of Allergy and Respiratory Medicine, Guy’s Hospital, London
R J PRESCOTT PhD, Director, Medical Statistics Unit, University of Edinburgh Medical School, Edinburgh
M WOODHEAD MD FRCP, Consultant Physician, Manchester Royal Infirmary, Manchester
A B MILLAR MD FRCP, Consultant Senior Lecturer, University of Bristol, Bristol
M PEAKE MB CHB FRCP, Consultant Physician, Pontefract General Infirmary, Pontefract
B STACK MB FRCP, Consultant Physician, Western Infirmary and Gartnavel Hospital, Glasgow

for the research committee of the British Thoracic Society

412 Journal of the Royal College of Physicians of London Vol. 32 No. 5 September/October 1998
that could be answered by a multi-centre clinical trial. All the colleagues whom we approached were willing to undertake this task and agreed a deadline for submission.

The research committee reviewed the proposals in November 1995. Three working parties, viz. those looking at lung cancer, asthma and sleep apnoea, had decided that existing projects were already addressing the most important issues and did not feel that they could be improved upon. The others all offered one or more projects, from which the research committee decided to proceed with 10 topics. By this time a further project on pulmonary embolism had been independently proposed to us. We realised that this should have been a further category for major project proposals and therefore decided to include it.

Thus, the consultant members of the BTS were presented with the outlines of 11 projects and were asked to score them in two categories: first, to score them from 1 to 10 on scientific merit, the score being based on their overall knowledge of respiratory medicine, the importance of the research question(s) involved and the design of the study. The projects might be outside their own area of expertise or ability to participate but they were asked not to let these personal factors influence their score. They were then asked to indicate the probability that they would be able and willing to enter patients if the trial were subsequently set up.

Each project was also submitted to three referees, one of whom was from outside the UK. These referees were chosen as internationally recognised experts in the field. They were asked to score each outline project on an ‘alpha–gamma’ system (as used by many grant-giving bodies in assessing projects submitted to them for funding).

Results

Study 1 – Questionnaire to BTS members

Although we were also interested in the views of junior members of the BTS, only data from consultant members will be discussed in this paper. We sent questionnaires to 440 consultants and received 261 replies. The response rate (59%) was somewhat disappointing but, because of the anonymity of the questionnaires, we were unable to attempt to improve the response through a second mailing to non-responders. Moreover, the BTS membership list at that time did not identify retired or non-clinical members. This is therefore an underestimate of the effective response rate. Forty-seven per cent of respondents worked in teaching hospitals, and 96% of them were working for NHS Trusts. Thirty-two per cent had entered patients into a BTS

Table 1. Fields of clinical respiratory research for projects by working parties.

| Field of clinical respiratory research |
|----------------------------------|
| Asthma                           |
| Cancer                           |
| Chronic obstructive pulmonary disease (COPD; including cystic fibrosis) |
| Environment and pulmonary disease (excluding atmospheric pollution) |
| HIV infections and the lung      |
| Infections (excluding TB), community/hospital acquired |
| Immunological/interstitial lung disease |
| Pollution and lung disease       |
| Pulmonary embolism               |
| Respiratory disease in children  |
| Respiratory disease in the elderly |
| Respiratory disease in general practice |
| Sleep                            |
| Tuberculosis                     |

*Added later; see text for details.

Table 2. Impact of determining factors on entering patients into BTS multi-centre studies.

| Deterring factor | Mean deterrent score (0–5 scale*) | Percentage no deterrent | Percentage definite deterrent |
|------------------|---------------------------------|-------------------------|-------------------------------|
| The projects     |                                 |                         |                               |
| – Inadequately described | 1.6 | 42 | 7 |
| – Forms too complicated/time consuming | 2.7 | 17 | 16 |
| – Lack of suitable patients | 2.4 | 20 | 16 |
| – Difficulty in obtaining patients’ consent | 1.4 | 35 | 1 |
| – Lack of interest in project | 1.5 | 34 | 5 |
| NHS administrative difficulties |                             |                         |                               |
| – Ethical Committee | 1.8 | 38 | 11 |
| – Hospital unwilling to fund | 1.8 | 42 | 13 |
| – GP unwilling to fund | 1.4 | 48 | 9 |
| – Recent NHS reforms | 1.9 | 36 | 13 |
| Other factors    |                                 |                         |                               |
| – Nothing in it for me | 1.2 | 48 | 4 |
| – Competition with other unit or personal research | 1.8 | 39 | 13 |
| – Competition with other multi-centre studies | 1.3 | 43 | 4 |
| – Competition with all other demands on my time | 4.0 | 6 | 55 |

* 0 = no deterrent; 5 = definite deterrent.
research study within the previous year. The ages of responders were distributed symmetrically around the 40–49 years age group, which contained half of the respondents.

Three broad categories of potential deterrent were assessed: factors in the projects themselves, NHS administrative difficulties, and other miscellaneous issues. Table 2 gives the mean scores allocated to potential deterrent factors, together with percentages in the two most extreme categories.

By far the largest deterrent was the competition with other demands on time, with 77% reporting one of the top two grades. Respondents in teaching hospitals found lack of suitable patients and competition with unit or personal research to be problems, with scores 0.5 units higher on average than those in district general hospitals. Consultants in district general hospitals found that more competition with other demands on their time was a greater deterrent, with a mean score 0.4 units higher than for consultants in teaching hospitals.

Among other principal deterrents in the projects were overcomplicated forms, which were time consuming, and, for some respondents, lack of eligible patients; NHS administrative problems were a definite deterrent for some 10% of respondents in each field assessed.

Some respondents took up the invitation to make personal comments at the end of the questionnaire. These further emphasised the main message from this survey, which was the lack of time for research which had been overtaken by increasing clinical and administrative workloads. This especially affected consultants in district general hospitals. It was also clear, however, that most consultants remained committed in principle to participating in clinical research and still wanted to be involved if they could find the time.

Study 2 – Research prioritisation

Consultant members of the BTS received the portfolio of proposed projects in January 1996. By this time an improved manpower database was available which included recent new consultant appointments, from which 483 consultant members could be circulated, and 196 (40%) responded. Figure 1 shows the results as a histogram of total scores and potential numbers of participating consultants for each project.

The research committee met to discuss these results in March 1996. Figure 1 shows that substantial numbers of consultants considered all the projects to be good in terms of scientific merit. Interestingly, we found a wide range of scoring by individual clinicians for every project. The top possible score for any project (with 196 respondents able to award a maximum 10 points) would have been 1,960 points. The highest scoring project (pulmonary embolism) achieved 67% of this maximum possible score. Three projects scored less that 50% of the maximum possible score, but even the least favoured attracted 42%, and all received high points from some individual respondents.

It was not logical on this evidence to try to select one ‘outright winner’ project. In particular, the wide range of points (1–10) awarded by individual consultants for the

Fig 1. Consultant scores for proposed projects. Shaded bars show total points awarded to each project (divided by 10 for convenience of scale). Unshaded bars show numbers of consultants willing to participate in each project. This is substantially lower for the two paediatric projects because there are many more respiratory consultants for adults than for children. The projects are listed in the order shown in Table 1: no projects were submitted by the panels for asthma, cancer or sleep; two projects were submitted in the category respiratory disease in children. COPD = Assessment of continuous oxygen for patients with COPD falling outside current recommendations; Environment = Is prognosis of occupational asthma different when mechanism is known to be immunological, when hypersensitivity without IgE is present, or when the mechanism is likely to be irritant?; HIV = Evaluation of chemoprophylaxis in HIV-infected patients considered at high risk for tuberculosis; Infections = Are antibiotics of benefit in previously fit adults presenting to GP with acute lower respiratory tract illness and cough?; Interstitial = Strategy to establish incidence and factors predictive of outcome in diffuse lung disease; Pollution = Five-year study of patients with COPD or ischaemic heart disease to assess effects of air pollution; Embolism = Thrombolysis in pulmonary venous thromboembolism and optimum duration of anticoagulation; Children 1 = Prospective descriptive study of natural history of prolonged cough in childhood; Children 2 = Early origins of respiratory disease; Elderly = Randomised controlled trial of nutritional care in patients hospitalised for community-acquired pneumonia; Tuberculosis = Investigation of usefulness of molecular techniques in diagnosis and management of tuberculosis.)
projects, in contrast to the relatively narrow range of maximum possible score awarded (42–67%), deterred us from putting too much emphasis on which project had received the highest score for scientific merit. The number of clinicians likely to participate in each project was clearly very relevant. The scores of the referees were considered to be probably the best predictors of the subsequent response from grant-giving bodies. Taking all these factors into consideration, we put projects into three categories:

1. Suitable for immediate development into a full project application to an appropriate grant-giving body.
2. Projects likely to be successful after referees’ criticisms had been addressed. These projects should be further developed and submitted for grant application at a later date.
3. Projects which, although good in principle, appeared impracticable. We did not feel that it would be appropriate to develop them further in the UK at the present time.

Three projects (on infection, atmospheric pollution and pulmonary thromboembolism) were put into category 1 and are currently under submission to grant-giving bodies for funding as major multi-centre clinical studies.

Discussion

Are increasing consultant workloads really putting pressure on clinical research? Not much information can be found in peer reviewed journals to answer this question, but a survey in 1994 by the United Kingdom Co-ordinating Committee on Cancer Research of contributors to its clinical trials showed a picture similar to that in our study. Moreover, work by the management consultants KPMG for the Review Body on Doctors’ and Dentists’ Pay and a substantial correspondence in other sectors of the medical press suggest that we are not alone in holding this view. More objective data are currently being obtained from a MORI survey, commissioned by the Office of Manpower Economics, of a diary week completed by consultants in May 1998. These pressures (even if only perceived) are predicted to increase. Initial data from investigations currently in progress at the Royal College of Physicians suggest a need for 80% more consultants to implement the Calman recommendations on hours of work for junior medical staff and the government’s White Paper proposals of December 1997.

Study 1 has increased our fears that the present organisation of the NHS is an important deterrent to clinical research. The response rate was poor but this may well reflect the pressures under which many clinicians are working. Consultants in district general hospitals were experiencing the greatest problems with their clinical and administrative workload. While these consultants may not have enough time to run their own research projects, they have traditionally been the backbone of BTS multi-centre clinical research and often have better access than those in teaching hospitals to suitable patients for participation in trials of this type. Other factors, such as protocol forms which are not user friendly, were also identified as problems which should be overcome by better project design.

The results of study 1 led us to examine the concept of research prioritisation at a national level in study 2. If clinical time is scarce and research funds limited, it follows that these precious resources have to be used as effectively as possible. If we could identify the most important research questions that could be answered by multi-centre clinical trials, clinicians might feel that it was worth finding time for one major project. Moreover, funding bodies might feel that such a project, widely supported by BTS membership, would be a particularly good investment of their limited resources. These agreed projects could also secure recruitment of patients from appropriate populations already well classified by experienced clinicians.

Although the response rates were only 59% for study 1 and 40% for study 2, two important points need to be borne in mind. First, the circulation list contained all members of the BTS who have consultant status and includes some non-clinical members such as respiratory pathologists who could not participate in a project on clinical research. More importantly, responding to study 2 involved reading the outline proposals of 11 research projects and then assessing their relative merits. Even clinicians with a wide background knowledge of all the research fields considered would take at least an hour to do so, and many probably took considerably longer. Those who responded to the questionnaire thus showed considerable commitment in taking part in the study. Moreover, any project backed by 40% of the UK consultant body in respiratory medicine should be capable of recruiting substantial numbers of patients and producing a powerful study. We therefore consider a 40% response to study 2 to be encouraging for a new concept in organising research.

At the time of writing, projects in category 1 have been submitted for grant application and the outcome is not yet known. Because they are currently sub judice with various grant-giving bodies, it is clearly not appropriate at present to give details of these projects, of others that were considered less attractive, or of our referees’ scores. However, we have shown that an increase in workload for clinicians, whether actual or perceived, creates a problem for sustaining clinical research; this needs to be addressed. Moreover, we have demonstrated that a specialist society can develop a method for allocating priorities for research projects so that limited resources can be allocated in a more cost-effective way.

All the projects considered were conceived on a large scale, with some lasting up to five years. It will probably take at least that long to determine whether projects that develop out of this commissioning approach can prove their worth by attracting large grants and give clear answers to important questions. It could be argued, even if its true value may not be known for perhaps five years, that this exercise should be repeated in a shorter time (two to three years). Having a constantly updated portfolio of major
projects developed and supported by the BTS could enable us to realise funding opportunities as soon as they arise.

If the exercise were repeated, several important improvements should be made in its execution. In particular, many respondents regretted that only outline proposals for projects were submitted to them for review as they found that this made their choices harder. We had adopted this approach because we did not want to put too much of a burden on either our panels who devised the outline projects, or on those who had to read them. It seems, however, that more detailed project proposals would have been well received and justified.

The Culyer report\textsuperscript{11} has recommended a central source of ‘ring fenced’ NHS money for clinical research. NHS Trusts, in theory at least, will be reimbursed for the expenses that they have to underwrite for research projects carried out on their premises. The mechanisms for funding research centrally from this dedicated money are still in their infancy. Our research prioritisation approach could be an appropriate way of allocating at least a proportion of NHS research and development monies, since it offers expert advice from the whole of a specialist society and a willingness to study important clinical problems on a national scale.

As it seems unlikely that pressures of time and money will get any easier in the UK or elsewhere in the world, failure to allocate priorities and to think ahead now might be deeply regretted in the new millennium. We therefore publish our methodology at the present time so that other specialties, both in the UK and abroad, have the opportunity to consider it. To the best of our knowledge, no other specialist society has previously adopted this approach.

Acknowledgements

We would like to thank the following members of the working parties: R Agius, R Anderson, J Ayres, P Barnes, D Bellamy, R Bettle, P S Burge, P Burney, P Calverley, I Campbell, K de Cock, J Collins, J Couriel, J Darbyshire, P Davies, R Davies, D Geddes, N Douglas, L Dow, R M Du Bois, G J Gibson, D Girling, P Helms, W Holmes, P A Jenkins, M Johnson, I Johnston, K Jones, A G Leitch, M Levy, J Macfarlane, R Millar, D Mitchell, R Neville, A J Newman-Taylor, P Ormerod, L Poulter, J Poulsford, A Pozniac, R Read, R Rudd, R Shaw, M Silverman, S Spiro, R Stockley, J Stradling, N Thomson, J O Warner, J Watson, A Williams, A Woodcock, M Woodhead.

We also thank our panels of referees and all BTS members who responded to the questionnaires for their help and enthusiasm in making this project possible, and the anonymous referee for help in clarifying this article. The project was funded by the British Thoracic Society.

References

1. Gibson JG, Prescott RJ, Muers MF, Middleton WG, \textit{et al}. British Thoracic Society sarcoidosis study: effects of long term corticosteroid treatment. \textit{Thorax} 1996;51:238–47.

2. Johnston IDA, Prescott RJ, Chalmers JC, Rudd RM for the Fibrosing Alveolitis Sub-committee of the Research Committee of the British Thoracic Society. British Thoracic Society study of cryptogenic fibrosing alveolitis: current presentation and initial management. \textit{Thorax} 1997;52:38–44.

3. Research Committee of the British Thoracic Society and the Public Health Laboratory Service. Community-acquired pneumonia in adults in British hospitals in 1982–1983: a survey of aetiology, mortality, prognostic factors and outcome. \textit{QJM} 1987;62:195–220.

4. Manpower Sub Committee of BTS. Data base of consultants. Prepared by Dr Warren Perks, Chairman Manpower Committee, British Thoracic Society, 1995.

5. Smyth JF, Mossman J, Hall R, Hepburn S, \textit{et al}. Conducting clinical research in the new NHS: the model of cancer. \textit{Br Med J} 1994;309:457–61.

6. Study confirms work increase. \textit{Hospital Doctor} 5 February 1998:8.

7. Figures expose rising burden (Health and Personal Social Services Statistics for England). \textit{Hospital Doctor} 12 February 1998:4.

8. Concern over toll on seniors. \textit{Hospital Doctor} 19 March 1998:5.

9. Alberti KGMM. \textit{The White Paper and its implications. College Commentary}. London: The Royal College of Physicians, January/February 1998:1–2.

10. The new NHS: modern, dependable. London: HMSO, December 1997.

11. Culyer A. Supporting research and development in the National Health Service. London: HMSO, 1994.

Address for correspondence: Dr M R Hetzel, Respiratory Medicine Department, Bristol Royal Infirmary, Bristol BS2 8HW.