

Ethical review of a multicentre study in Scotland: a weighty problem

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ABSTRACT - Objective: To assess the current working practices of local research ethics committees (LRECs) in their review of a multicentre study approved by the new multicentre research ethics committee in Scotland.

■ **Design:** Observational data collected from correspondence with LRECs.

■ **Subjects:** All LRECs within the geographical area of the study in Scotland.

■ **Interventions:** None.

■ **Outcome measures:** Delay from application to calling an LREC meeting, to an initial LREC decision, to final LREC approval, and the number of A4 pages required.

■ **Results** The median delay to review of an application at an LREC meeting was 28 days (range 14-97), the median delay from application to the time of LREC final approval was 39 days (range 21-109) and a total of 5,789 A4 pages (26.9 kg) were required to complete the application process.

■ **Conclusions:** Despite recent standardisation of ethical review of multicentre research, elimination of unnecessary delay, cost and variation in LREC operating procedures is still necessary.

In 1991 the Department of Health delegated responsibility for ethical review of research in the NHS to local research ethics committees (LRECs) of the health authorities¹. A rapidly expanding workload² and few further guidelines led to LRECs developing varying levels of autonomy and a diversity of working practices³⁻⁸. This system posed particular problems for multicentre research, which required approval from many different ethics committees⁹.

In 1997 a long-awaited, standardised method for the review of multicentre research^{10,11} began with the creation of several multicentre research ethics committees (MRECs) across Britain¹². Under this new system, multicentre research was defined as taking place over five or more LREC geographical boundaries. Nowadays, a multicentre application must be submitted by its principal investigator to a single MREC somewhere in the geographical region of the study for an independent opinion on all the ethical and scientific aspects of the research proposal. Once the application is approved by the MREC, it must then be

distributed to every LREC in the geographical location of the study, whose executive subcommittee considers the suitability of the local site, researcher(s) and/or facilities.

The new system is designed both to minimise the burden of ethical review for LRECs and to reduce the unsatisfactory delays that LRECs caused for researchers in the past¹³. The procedure is expedited by centralising the process of ethical review with MRECs, and by providing clear guidelines to LREC executive subcommittees on what aspects of an MREC-approved multicentre application they may review and how long this should take¹⁴.

The first year of the new MREC procedure is being evaluated by the Research Ethics Committee Project at the Centre of Medical Law and Ethics, King's College, London¹⁵, but the main focus of the evaluation is on the MRECs themselves. There are no published data on the working practices of LRECs in the new era of MRECs. We took the opportunity to collect data on LREC endorsement of an MREC-approved, multicentre study during the course of a recent application in Scotland.

Methods

The Scottish Intracranial Vascular Malformation Study (SIVMS) is a prospective, observational, population-based study of all patients in Scotland diagnosed with any type of intracranial vascular malformation after 1st January 1999. The primary aims of the study are to:

- establish a national disease register of all incident cases.
- collect demographic and prognostic data by case note review.
- follow up the patients using annual postal questionnaires modelled on generic outcome measures.

We had to apply to 15 LRECs for local review and endorsement of the application for SIVMS that had been approved by the MREC for Scotland in July 1998. Each LREC application required a variable number of copies of:

- the MREC application form (23 pages)
- the supplementary form covering local investigator experience plus his or her curriculum vitae (8 pages)
- all correspondence with the MREC (6 pages)
- the research protocol, consent form and patient information leaflet (7 pages).

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Recommendations for the expected time-scale of LREC executive subcommittee review of MREC-approved applications have been published¹⁴ and circulated to all LREC chairmen and administrators in Scotland, providing a 'gold standard' with which to compare our data. A meeting should be called within two weeks of receipt of an application, and a decision be communicated to the applicant within five working days of a subcommittee meeting. The whole process, therefore, should take three weeks.

Results

In our analysis, the date of receipt of an application by an LREC was assumed to be the next working day after its postage by first-class mail; all other dates were taken from LREC correspondence. LREC identities have been anonymised. Figure 1 shows the delay experienced at the outset, from assumed receipt of an application to calling an LREC meeting (only eight of the 15 LRECs had established executive subcommittees). The median delay to review of an application at an LREC meeting was 28 days (range 14-97), twice the recommendation of two weeks.

Of particular relevance to researchers is the delay from application to final LREC approval (Fig 2). The difference between the time to the initial LREC decision (light bars) and the time to the final decision (dark bars) indicates the length of time taken to resolve any LREC amendments. The median delay from application to the time of LREC final approval was 39 days (range 21-109). In fact, only three LRECs raised objections, all of them on different grounds. One LREC disputed elements of study design (which is strictly in the jurisdiction of the MREC) the second requested additional study materials, and the third changes to the content of the patient information sheet.

The process of LREC application was time-consuming and labour-intensive, although we did not have to attend any LREC meetings in person and no application forms specific to any of the LRECs were requested. There was considerable variation between LRECs in the number of copies of each application required (Fig 3). The median number of copies was 10 (range 1-18), amounting to a total of 5,789 A4 pages, weighing 26.9 kg. Photocopying and printing the applications cost £231.56 and postage by Royal Mail cost £77.15. The total of £308.71 does not include the cost of the person-hours invested by a salaried secretary, research fellow and research projects' coordinator.

Conclusions

The original Department of Health directive to LRECs¹ encouraged them to promote good research, and it has been suggested that unnecessarily delaying research of potential benefit to the public is itself unethical¹⁶. Applicants for ethical approval of multicentre research were previously frustrated by the delays incurred by the LREC system, the costs of application, and unnecessary duplication of effort^{3,6,13,17,18}.

MRECs have recently attempted to expedite and standardise the process of gaining ethical approval for multicentre research, thereby making the process more transparent and quantifiable. In our case, delays of up to 16 weeks in gaining LREC approval, using 5,789 pages of A4 paper at a cost of over £300 for materials alone, have been a large price to pay for just three different LREC amendments. Comparing our 26.9 kg of paperwork with an average person weighing 70 kg, gaining ethical approval for multicentre research in Scotland has cost us 'more than an arm and a leg'.

Fig 1. Delay between receipt of an application by a local research ethics committee (LREC) and an LREC meeting.

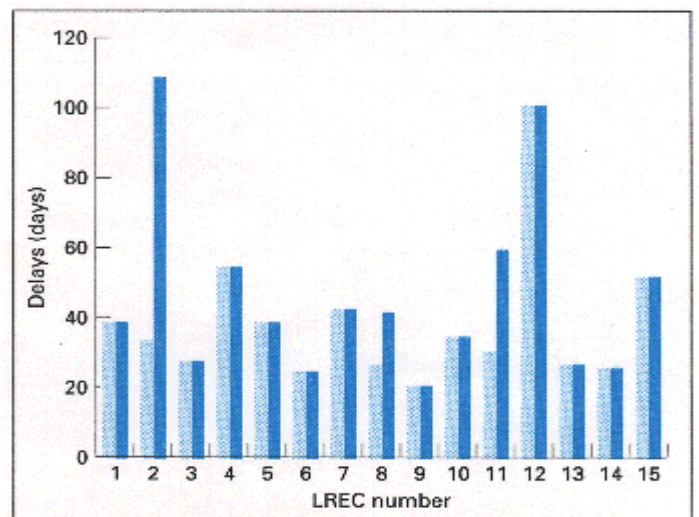
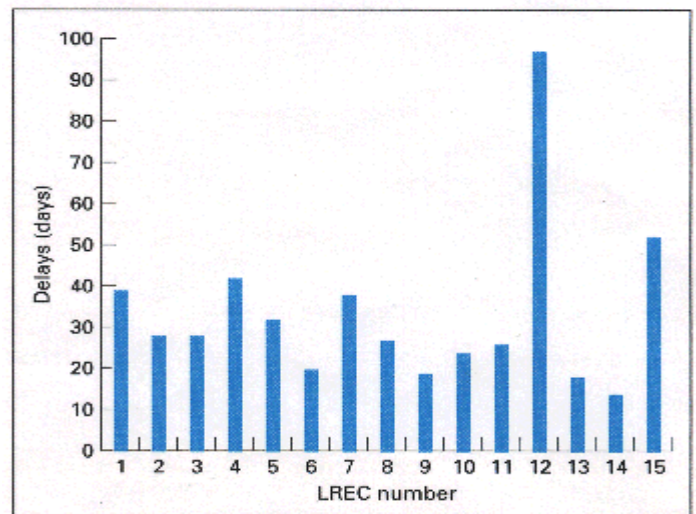


Fig 2. Delay between application to a local research ethics committee (LREC) and the initial LREC decision (light bars) and final LREC approval (dark bars).

Observation of the practices of LRECs in Scotland has demonstrated that many of the old impediments still delay multicentre research, and that elimination of unnecessary variation in LREC operating procedures is still necessary to encourage timely medical research. LRECs are certainly overburdened by a large volume of lengthy applications for approval of multicentre projects. We did not seek to address the demands imposed upon LRECs, but they are undoubtedly great. This unsatisfactory situation for researchers and ethics committees alike calls for further improvement to the process of ethical committee review of multicentre research. Constructive solutions include greater use of electronic communication by e-mail to reduce the cost and time delay of postage and the cost of reproduction of paper forms. Only a small proportion of the bulky MREC application form is required by LRECs for their review; the form could be redesigned further to minimise the amount of paperwork relayed to the LRECs. Further guidance is being prepared by a working party on the extent to which observational, epidemiological research involving minimal contact with patients needs to be subject to the same process of rigorous ethical review as clinical trials of novel treatments¹⁹.

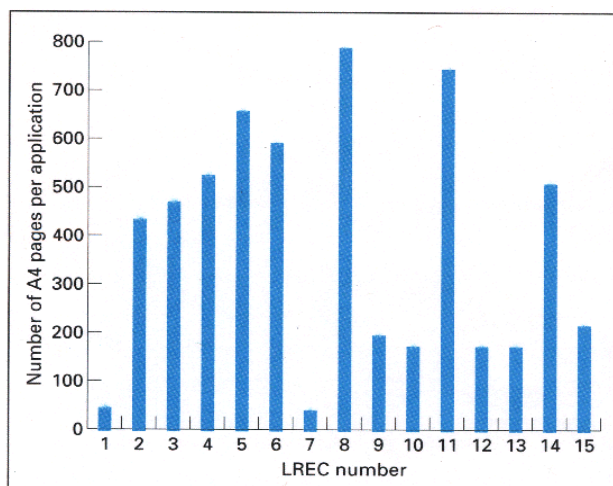
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Competing interests

None declared.

Fig 3. Number of A4 pages required for application to each local research ethics committee (LREC).



Key Points

In the past, reliance upon local research ethics committees (LRECs) for ethical approval of multicentre research led to considerable diversity in their practice and an expanding workload for both researchers and LRECs

A procedure for the review of multicentre research was standardised in 1997 with the creation of multicentre research ethics committees (MRECs) across Britain

Under the new system in Scotland, LRECs still cause potentially avoidable delay, duplication of effort and expense for multicentre researchers

Disclaimer

We did not seek ethical approval for this observational study of the process of LREC review. The views expressed in this article are those of the authors and do not necessarily represent those of either the MRC or the Chief Scientist office of the Scottish Office.

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Genital chlamydia infection

CLINICAL GUIDELINES AND STANDARDS

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Produced by the Health Education Authority with funding from the, NHS Executive**

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