Meeting the challenges facing research ethics committees: some practical suggestions

Jennifer Blunt, Julian Savulescu, Alastair J M Watson

Manchester
M45 7PR

Jennifer Blunt,
former chairman,
Salford Research
Ethics Committee

Oxford Radcliffe
Hospitals, Oxford
OX3 9RP

Julian Savulescu,
clinical ethicist

Department of
Medicine,
University of
Manchester, Hope
Hospital, Salford
M6 8HD

Alastair J M Watson,
senior lecturer

Correspondence to:
Mrs J Blunt,
53 Hawkstone
Avenue, Whitfield,
Manchester
M45 7PR

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The local research ethics committee is the most independent body regulating the ethical conduct of research.¹ The committee works on behalf of the subjects of research, to protect them from unacceptable risks and practices. However, the effectiveness of local research ethics committees in fulfilling their role has been challenged increasingly (see table).^{2–10}

Key challenges for research ethics committees

Volume and nature of research

Because of the volume and varied nature of the research reviewed, members of local research ethics committees have a demanding task maintaining a coherent approach.¹¹ The committee workload varies considerably, from fewer than 10 to more than 40 protocols for review at each meeting. The workload also depends on the type of research community within which the committee operates.¹² A snapshot of the work of the former Salford Local Research Ethics Committee (box) illustrates the difficulties.

Multicentre research studies

Improving the competence and uniformity of approach in relation to the increasingly complex field of multicentre research is a further challenge. Local research ethics committees have been criticised for delaying good research, particularly in multicentre studies.^{13–16} The efficiency of the committee's ethical review, the diversity of practice, and the waste of research time and funds (often from charitable sources) in seeking ethical approval have also been criticised.^{3–10} To meet these criticisms the Department of Health has created a multicentre research ethics committee system to provide independent advice on the science and general ethics of multicentre research.¹⁶

Challenges from research synthesis

The third challenge derives from failure to do research synthesis—to aggregate and integrate the results of related primary studies.¹ Some researchers have failed to undertake adequate systematic reviews of existing research at the outset and some have failed to report the results of their research subsequently; both can lead to unnecessary, sometimes harmful, research.

Detection of scientific malpractice and fraud

The fourth challenge relates to the detection of fraud in clinical research. Concern is growing over scientific fraud and misconduct in medicine.^{17–25} Husson defines fraud as an "intentional act aimed at misleading someone—in general for personal advantage," but other less deliberate acts may equally affect the quality of scientific research.²⁶ Carelessness, overcommitment, and overambition can all contribute to second rate, even unethical, practices. Each investigator has a duty to check research before accepting responsibility for it.²⁷

Summary points

Local research ethics committees face several challenges—the increasing volume, type, and complexity of research; the creation of a multicentre research ethics committee system; failure to do research synthesis; and the detection of scientific malpractice and fraud

To meet these challenges, local committees must have a trained and multiskilled membership, sufficient human and financial resources, and a system for monitoring the progress of studies they have approved

In multicentre research, ethical evaluation will be divided between multicentre committees and local committees, which will retain autonomy only for decisions on local acceptability

Effectiveness and efficiency can be promoted if local and multicentre research ethics committees adopt common standards of ethical review

Some have called for research ethics committees to have a more pivotal role in the detection and management of suspected fraud.²⁸ In 1995, the General Medical Council struck a consultant off the Medical Register for fraudulent claims.²⁷ In 1996, two general practitioners were struck off for fraudulent activities in drug trials—one had forged consents from patients; the other had repeatedly forged ethics committee approval.^{25 29–31}

Possible solutions to key challenges

Committee membership

Research ethics committees must have an appropriate membership with a diverse range of expertise and experience.^{12 16 32} Committees should include at least one member with a thorough knowledge of the scientific aspects of clinical research and of methods of research synthesis.^{1 14} Valuable contributions can be made by biostatisticians, bioethicists, lawyers, and lay people from community groups. Committees have power to co-opt members. This is especially important when dealing with new technologies such as genetic research.^{16 32 33} Bodies such as the Gene Therapy Advisory Committee and the United Kingdom Xenotransplantation Interim Regulatory Authority advise local research ethics committees and are required to approve research proposals in their areas of expertise.¹⁶ Published guidance for the evaluation of complex new research is increasingly available. One example is the *IRB: A Review of Human Subjects Research*, a journal devoted to research ethics.³⁴

Work of the Salford Local Research Ethics Committee

- The Salford committee served a district health authority with four trusts, including tertiary referral centres, a medical school, and universities with health care and social science departments
- A wide range of work was reviewed: it covered NHS patients and healthy volunteers; clinical trials in hospitals and general practice; records based research; qualitative and health services economic research; and surveys
- Studies originated from: academic departments; researchers, as part of funding applications; and prequalifying and postqualifying students on courses with a research component that required access to patients or their records
- Submissions doubled in 10 years. In 1995-6, 230 new applications were reviewed—44% were approved at first review and 46% after subsequent amendment; 3 were refused on grounds of safety, 12 were considered not to need ethical approval, and 8 were withdrawn. Applications for amendments or extensions were granted in 85 studies approved previously, and follow up reports were received for 164 of 196 studies approved in 1994-5
- Ten adverse events were noted for studies approved in the present and past years
- The committee's records were computerised. The database was managed by one part time administrator. Members spent an average of 7-8 hours a month on committee work (unpaid). Fifteen minutes on average was available at monthly meetings to review each study

Resources

Ethical review is a key function of health authorities. Authorities should ensure that local research ethics committees have adequate support and administrative help.³³ We suggest this should be from trained staff working solely for the local committee. Core material for members and continuing training for new and existing members should be budgeted for.³⁵ This support has been recognised for multicentre research ethics committees.¹⁶

Training

Documents have been developed that promote consistency in decision making among local research

ethics committees.^{11 12 36} Members need time to assimilate this material. Training courses have been organised in various ways, and should include the evaluation of systematic reviews of existing research.¹ These skills can be taught to lay people through the critical appraisal skills programme.³⁷ Administrators, who are the first points of contact for researchers, also need training alongside members.

Monitoring

Monitoring of submissions, progress, and publication can reduce fraud and malpractice. One local research ethics committee uncovered a case of fraud through monitoring. The committee was uncertain about the whereabouts of a submission from a general practitioner who was conducting many research studies. The study sponsors then asked the committee to authenticate an approval letter for this study that they had already been sent by the general practitioner. At a hearing of the General Medical Council, the general practitioner admitted forging the letter and said that he had never done this before. However, the sponsors subsequently found two more forged letters, both predating the first. The general practitioner's name was struck off the Medical Register.³¹

After approval for a study has been granted by the local research ethics committee, its subsequent responsibilities are limited to producing an annual progress report, approving amendments, and reporting any adverse events.³² More detailed monitoring has been recommended.^{33 38} In Canada, research ethics committees have an obligation to monitor research, and this is specified when ethical approval is granted.²¹

Investigators who are involved in several trials

Research ethics committees should know if an investigator is participating in concurrent trials.³⁹ Misconduct in international drug trials could be reduced by asking for these details—or even limiting participation in clinical trials.⁴⁰ Research ethics committees should be satisfied that investigators who take on several research commitments can conduct these studies adequately.

Failure to publish results

Projects approved by local and multicentre research ethics committees must be monitored to ensure scientific integrity. Both committees demand that research

Key challenges for local and multicentre research ethics committees and possible solutions

Key challenges	General solutions	Solutions in multicentre research	Solutions for local committees in relation to multicentre and student studies
Increasing volume, type, and complexity of research	Appropriate, trained membership from a diversity of backgrounds	Review the science and general ethics of multicentre research in terms of clinical trials, records based research, qualitative and health service research, surveys	Categorise student research in relation to educational value Ensure local acceptability of projects in terms of recruitment of subjects, funding, health and safety, pharmacy, confidentiality
Creation of multicentre research ethics committee system	Sufficient administrative support, computer equipment, and finance for training and members' expenses	Generate funds to cover administration, independent training for multicentre and local research ethics committees	Investigate the acceptability of the investigator: concurrent and recent involvement in studies, previous track record
Challenges deriving from research synthesis	Audit of performance against a standards framework	Ensure results of studies are made publicly accessible	
Detection of scientific malpractice and fraud	Monitoring system to ensure scientific integrity—common application form, requirement to publish results, computer based records, and vigilance		Monitor local investigator in multicentre research

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results are made available publicly.¹ In commercially sponsored studies, pressure exists to keep the findings secret, and where unsatisfactory results are suppressed, participants have been put to inconvenience and risk, and no contribution has been made to wider knowledge and future research.⁴¹ A recent report showed that one drug company, which took legal action to prevent publication, suppressed research findings for seven years.⁴² An audit by Wise and Drury showed substantial ethical concern about the process of approving multicentre pharmaceutical research in general practice and about low rates of publication.⁴³

Distribution of duties between multicentre and local research ethics committees

The creation of multicentre research ethics committees is an important development but presents new challenges for local committees.¹⁶ Multicentre committees will be able to negotiate with sponsors and investigators; modify design, including eligibility criteria; improve consent procedures; and prevent marketing studies from continuing under the guise of research.⁴³

Local committees will retain autonomy only for decisions on the local acceptability of research proposals, and will have two options—acceptance or rejection (giving reasons for the latter). However, the question of which committee ultimately has the legal responsibility to protect patients has not been addressed; in the United States, local committees have this responsibility.⁴⁴

Local committees will determine the criteria for local acceptability of projects and investigators. These could include the current disease patterns and particular social and cultural needs of the local population and the need to protect patients with rare or “fashionable” conditions from unwarranted scientific curiosity.⁴⁵ Suitability of a local investigator could be judged in relation to published guidelines on good clinical practice, the volume of current research, and the track record of researchers.^{46 47} The responsibility for monitoring individual researchers falls most appropriately on local committees; multicentre committees are responsible for ensuring that the results of multicentre research are made available. The expertise available in multicentre research ethics committees could be used to train members of local committees.

Student research: ethical criteria for educational purposes

Student projects seldom attain the scientific standards normally required by research ethics committees because of the student's inevitable lack of experience and time. As student projects are rarely published, the research results themselves bring little benefit to patients, but studies can be justified ethically if the education received results in better patient care once the student qualifies. It seems appropriate, therefore, that the usual requirement of scientific excellence be supplemented by criteria relating to educational usefulness. The committee should be satisfied that the quality of supervision is adequate and that research questions and design are evaluated critically before the project is started.

Conclusion

The changes suggested here can best be achieved if research ethics committees adopt a common approach to the problems of ethical review—meeting the standards commended in the Department of Health's standards framework, preferably using a common application form, and adopting a consistent approach to monitoring.^{11 12 16 35} Perhaps then, criticisms of the efficiency of review by local research ethics committees will be resolved.

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Meta-analysis

Bias in location and selection of studies

Matthias Egger, George Davey Smith

Meta-analysis has received a mixed reception since the outset. Some people have rejected what they see as exercises in "mega-silliness,"¹ while the purveyors of a highly distinguished series of meta-analyses of perinatal medical care² have been dismissed as "an obstetrical Baader-Meinhof gang."³ To some clinicians objecting to the findings of meta-analyses, "a tool has become a weapon."⁴ At the other end of the spectrum, the application of a technique that basically consists of calculating a weighted average has been hailed as "Newtonian,"⁵ and it has been suggested that meta-analysis has left no place for the narrative review article.⁶ The truth is likely to lie somewhere between these extreme views.

That meta-analysis holds potential problems can be illustrated by contrasting the conclusions of two meta-analyses comparing low molecular weight heparins and standard heparin in the prevention of thrombosis after surgery.^{7,8} One group concluded that "low molecular weight heparins seem to have a higher benefit to risk ratio than unfractionated heparin in preventing perioperative thrombosis,"⁷ whereas the other considered that "there is at present no convincing evidence that in general surgery patients low molecular weight heparins, compared with standard heparin, generate a clinically important improvement in the benefit to risk ratio."⁸ Various differences exist between these meta-analyses, but the main difference relates to the selection of studies for inclusion (table). Nurmohamed et al based their analysis on a subgroup of trials that they considered to possess the highest methodological strength,⁸ while Leizorovicz et al included all trials in their analysis.⁷ The table shows that many other elements—for

Summary points

Bias can be introduced in many ways into the process of locating and selecting studies for inclusion in meta-analysis

Studies with significant results are more likely to get published than studies without significant results, leading to publication bias

Among published studies, those with significant results are more likely to get published in English, more likely to be cited, and more likely to be published repeatedly, leading to English language bias, citation bias, and multiple publication bias

In less developed countries, studies with significant results may be more likely to get published in a journal indexed in a literature database, which can introduce database bias

Criteria for including studies in a meta-analysis may be influenced by knowledge of the results of the set of potential studies, leading to inclusion bias

The likely presence or absence of bias should be routinely examined in sensitivity analyses and funnel plots

example, language restrictions or use of unpublished material—could contribute to contrasting conclusions being reached.

This is the fourth in a series of six articles examining the procedures in conducting reliable meta-analysis in medical research

Department of Social Medicine, University of Bristol, Bristol BS8 2PR

Matthias Egger, reader in social medicine and epidemiology
George Davey Smith, professor of clinical epidemiology

Correspondence to: Dr Egger
m.egger@bristol.ac.uk

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