Symposium on ethics and clinical trials

Clinical trials: two neglected ethical issues

Andrew Herxheimer  UK Cochrane Centre, University of Oxford

Author’s abstract

Ethical reasons are presented for requiring 1) that a proposal for a clinical trial should be accompanied by a thorough review of all previous trials that have examined the same and closely related questions, and 2) that a trial should be approved by a research ethics committee only if the investigator undertakes to register it in an appropriate register of clinical trials as soon as one exists.

Introduction

Important questions to be asked about a clinical trial include: 1) Why is the trial necessary, or worth doing? 2) Will the findings of the trial be made public? Both questions raise ethical issues, discussed below, which have implications for the work of ethics committees.

1) The need for systematic review

A trial may be necessary to answer an important unanswered question. It may be that the question has been examined in previous trials, with inconclusive or conflicting results; or it may not have been addressed before. However, if the question has been clearly answered by previous trials, the gain from doing another may be negligible, and it would not be justified. A well known example is the use of a placebo in a condition for which a treatment of proven effectiveness exists. In such a case the use of a placebo is unacceptable, unless the condition is a trivial one.

It follows that a proposal for a trial should be accompanied by a thorough review of all previous trials that have examined the same and closely related questions. Only in the light of such a review can a sound opinion be given on whether the proposal is ethical.

2) Publication of the results

It is important that the evidence generated in well performed clinical trials is published, but much of it remains inaccessible. This under-reporting of research must be regarded as a form of scientific misconduct, because it creates a distortion in the publicly available evidence. It represents not only a waste of the resources used in the unreported work (patients’ co-operation, investigators’ skill, health facilities, time, money), but impedes the use of effective treatment or the abandonment of ineffective treatment; it also requires otherwise avoidable subsequent research to correct the distortions. It is mainly investigators and commercial sponsors, rather than referees or journal editors, who appear to be responsible for the under-reporting (1). Investigators, research ethics committees and funding agencies should all take steps to ensure that this form of scientific misconduct is minimised.

It may be unrealistic to expect all trials to be published, but their findings must be made accessible to anyone wishing to make a systematic review of the trials concerned with a particular problem. The first step towards this goal is to ensure that it is possible to obtain a complete listing of these trials, and the names and addresses of the people who have information about them. A simple way of achieving this would be to register all clinical trials at inception in a register (2). Such registers already exist for trials in some areas of medicine. However, more systematic development of such registers is needed, both in Britain and in other countries. Ethics committees have important opportunities to foster these developments and to ensure that the necessary information is assembled efficiently.

Implications for ethics committees

Ethics committees should routinely require that a proposal to undertake a clinical trial be accompanied by a systematic review of previous work concerned with the same and closely related questions, so that the proposal can be put into its proper context.

Approval by an ethics committee of a proposal to do a trial should be conditional on it being registered

Key words

Clinical trials; systematic review of clinical trials; publication of clinical trials; registration of clinical trials.

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in an appropriate register of clinical trials as soon as one exists.

Andrew Herxheimer, FRCP, is a Consultant at the UK Cochrane Centre, Oxford, part of the international Cochrane collaboration, which prepares and maintains systematic, up-to-date reviews of randomized controlled trials of health care. UK Cochrane Centre, University of Oxford, NHS Research and Development Programme, Summertown Pavilion, Middle Way, Oxford, OX2 7LG.

References


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A Herxheimer

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