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Editorial

The Case for Establishing a Register of Randomised Controlled Trials of Mental Health Care

A widely accessible register will minimise bias for those reviewing care

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Which psychiatric treatments are effective? In the past, this question could be answered only by referring to personal experience of treating patients or to the opinions of experts. Then, between 1930 and 1940, Bradford Hill introduced the principles of experimental methods into medical research (Doll, 1990). With the formal introduction of the randomised controlled trial (RCT), these experiments began to provide answers to important clinical questions (Medical Research Council Streptomycin in Tuberculosis Trials Committee, 1948). The RCT is now generally held to be the most powerful research design available to assess the effects of mental health care (World Health Organization, 1991). At first, there were few trials, and they were easy to summarise. However, as they have grown in number it has become difficult to evaluate them together, although it is highly desirable to do so because any one RCT is often too small to provide estimates of treatment differences of acceptable precision (*Drug and Therapeutics Bulletin*, 1992). Indeed, frequently, a single RCT can provide only very limited guidance for clinical practice.

The usual method for evaluating the results of a group of clinical trials of a single treatment is a review article, and increasingly journals are publishing these reviews as well as articles describing original findings. At first glance, the procedure for a review appears straightforward; the authors collect reports that they can identify on the chosen subject, they evaluate and summarise their contents, and then they write a report. A review restricted to RCTs might seem to be particularly reliable.

Unfortunately, important biases may affect this process of review. Reviewers may not have knowledge of all the RCTs done in the field, they may pay more attention to findings that support their views, and they may use procedures that are not quantitative (Sackett *et al*, 1991). Such unsystematic reviews are often influential, but they can result in misleading recommendations for clinical practice. For example, Antman *et al* (1992) illustrated how, years after systematic reviews would have shown otherwise, subjective reviews continued to recommend treatments for myocardial infarction that were positively harmful, and failed to recommend treatments that are beneficial.

These problems of subjective reviews can be overcome by taking a more systematic approach. Whether to include or exclude a trial in a systematic review is decided using objective, reproducible criteria that relate to both the subject matter and the quality of the RCT. Issues such as the quality of randomisation, whether the trial could have been biased because raters were not properly blinded, and what type of comparison group was used, all need to be carefully considered by systematic reviewers. If trials tackle similar issues, are of appropriate quality, and are statistically suitable, the systematic overviews may combine the results of the individual trials, using meta-analysis (Glass, 1977). In any event, the data of trials both included and excluded from the meta-analysis should be available to the reader to reanalyse if he/she so wishes. In these ways, systematic reviews endeavour to minimise bias and combine the results of similar trials in objective, explicit and reproducible ways.

Although systematic reviews and meta-analyses have been used to evaluate psychiatric treatments (Balestrieri *et al*, 1988; Song et al, 1993), two problems can lead to serious bias: failure to identify all the clinical trials that should be included in the analysis, and the inclusion of data of variable quality.

Experience from perinatal care

To understand how the problems can be tackled, it may be helpful to consider work carried out by Chalmers (1989) with trials of care during pregnancy and childbirth. In the late 1970s, Chalmers *et al* (1986) began the process of collecting all RCTs of perinatal care. This involved searches undertaken on MEDLINE as well as methodical hand-searching of journals for prospective controlled trials in which the allocation of treatments was by a random or quasi-random method. About twice as many RCTs were identified using this technique than would have been possible using MEDLINE alone (Dickersin *et al*, 1985). Once the hand-searching of the backlog of

journals, from 1950 to the present, was covered, searching of current publications was organised. From this work Chalmers *et al* produced a register that contained approximately 6000 RCTs (Oxford Database of Perinatal Trials, 1992). A network of reviewers has been established and has resulted in over 500 systematic reviews on many aspects of perinatal care. These systematic reviews were incorporated in an electronic publication and an updated version made available every six months to reflect new evidence.

These systematic reviews provide information to guide clinical practice. For example, confusion existed about the effects of corticosteroid given before pre-term delivery. A systematic review of the 12 relevant trials showed statistically and clinically significant reductions in mortality of 40–60% (Crowley *et al*, 1990). The delay between the availability of this strong scientific evidence and the changing of official recommendations for management has, unfortunately, been over three years, a length of time that is difficult to justify (Chalmers, 1993).

The advantages of perinatal medicine's system for overviewing the effects of health care was recently underlined by the House of Commons All-Party Health Committee (1992) on maternity services who, in their report state:

> "The work which [the perinatal register of RCTs and systematic reviews] has done in pointing the way towards evaluating the effects of different ways of organising maternity care cannot, we believe, be too highly praised. Their work has shown that many procedures and technologies have been introduced into intrapartum care over the last 30 years without adequate testing to ensure their efficacy and cost–benefit ratio."

In addition, such a register of trials allows investigation of the epidemiology of the RCT within that field.

The case for a psychiatric register

With a comprehensive register of RCTs of mental health care, it would be possible to show that in some areas of investigation further trials could not be justified because the hypotheses proposed in any new trial had already been answered. On the other hand, the register will identify under-researched interventions, such as rehousing on the grounds of mental ill-health (Elton & Packer, 1986). Follow-up, cohort, studies of RCTs first published as abstracts undertaken by those working with registers of trials can investigate publication bias (Easterbrook *et al*, 1991) and a register also serves as a sampling frame for investigations of quality of method within RCTs. Studies investigating whether the results of methodologically rigorous RCTs differ, in a systematic way, from the outcomes of less exacting trials have been undertaken in other fields of medicine (Schultz *et al*, 1993). Some, but not much, work has been done in this area for mental health studies. Shapiro & Shapiro (1983) have looked at the generalisability and methodological rigor of trials included in their meta-analysis (Shapiro & Shapiro, 1982) and the implications of those issues on the outcomes of their study. For mental health researchers, however, as well as issues of randomisation and generalisability, the quality of blinding within trials is in need of investigation (Oxtoby *et al*, 1989). From the vantage point of a systematically constructed register, investigators could study how methodological rigor in mental health RCTs relates to the findings of trials.

We believe that a register, similar to the database of perinatal trials, is necessary in psychiatry. Over two decades ago it was said that,

> "it is surely a great criticism of our [medical] profession that we have not organised a critical summary, by speciality or subspeciality, updated periodically, of all relevant randomised controlled trials." (Cochrane, 1972)

Cochrane's challenge has been taken up by perinatal medicine and is to be taken up by other specialities. The UK Cochrane Centre has recently been funded as part of the Information Systems Strategy being developed to support the National Health Service Research and Development Programme. It has been established specifically to facilitate systematic reviews of RCTs of health care conducted by specialists. The first challenge is to assemble as comprehensive as possible a register of RCTs. The Centre is to foster collaborative links between subspecialities to allow ease of transfer of data, for example between a mental health register and one dealing with RCTs of interventions in primary care. Those working in the latter field have already found that 18% of the RCTs identified in the primary care journals concern the management of mental illness (Silagy, 1993).

Should an initiative, systematically reviewing all RCTs of care, be taken in psychiatry? For those interested in the preparation of objective reviews of care, the answer must surely be 'yes'. Systematic reviews may be able to help resolve many dilemmas and difficulties that exist in everyday clinical practice of psychiatry. Goodwin (1989), in a review concerned with the management of depressed people who do not respond to tricyclic antidepressants, highlighted a dilemma:

"At present, the choice of what to do cannot be decided on a fully scientific basis and does not command a practical consensus. We enjoy a certain freedom to indulge our impulses for either dogma or disputation. The recommendations that follow are offered, and should be examined, with due scepticism."

Striving to command a practical consensus in treatment guidelines for several psychiatric conditions, the Quality Assurance Project (1982) of the Royal Australian and New Zealand College of Psychiatrists sought research information, the opinion of a practice sample, and the advice of elected experts. The American Psychiatric Association (APA) is formulating practical guidelines for patient care strategies to assist doctors in clinical decision-making, and these guidelines are to be updated every three to five years (Zarin *et al*, 1993). Still, however, the choice of what to do in both the Quality Assurance Project and APA's practical guidelines could not be decided on a fully scientific basis, and great efforts have gone into seeking consensus from experts. In an important effort to implement objective review techniques, the Agency for Health Care Policy and Research, in the USA, is undertaking meta-analyses of many mental health care interventions (Depression Guideline Panel, 1993). Great trouble has been taken in producing these meta-analyses; however, even if the systematic reviews were methodologically flawless, such paper publications are disadvantaged when compared to those published electronically. Paper publications of systematic reviews are out of date as soon as a relevant new RCT is completed. Systematic reviews published electronically, however, are relatively easily kept up to date, and new work or valid criticism can be quickly taken into account in revised versions.

Despite the real difficulties of generalising the findings from RCTs to everyday clinical work, up-to-date, systematic reviews of RCTs will increasingly be required to justify initiation or continuation of service provision. Although there may always be differences in the population in an RCT and the person in a clinical setting, systematic reviews, with the combination of findings from several different RCTs undertaken on slightly different clientele, may well describe a more generalisable outcome than the result of any one trial. If the services which manage psychiatric patients are to be protected, the providers will increasingly have to supply clear, objective evidence for their defence, and will need to implement systems of evaluation as thorough as those medical disciplines which are already part of the Cochrane Collaboration. Ideally, to avoid the need for hand/full-text searching, RCTs should be registered at inception. In any event, the subsequent articles should be given titles that mention how, exactly, interventions were allocated, abstracts that report methodology, and additional labels of 'RCT'. This would be invaluable to indexers and so lead to better retrieval from existing databases. Because this system does not yet exist for all publications, hand-searching of the backlog of journals is needed to form the basis of a credible register.

The mental health register of RCTs

Hand-searching the *British Journal of Psychiatry* from 1950 to the present day has identified 670 articles where an intervention was allocated by a random or quasi-random method. The number of controlled, prospective trials that concern physical, psychological or social interventions in mental health is likely to be very great indeed, running into the tens of thousands. Results from an ongoing study in Oxford shows how computer retrieval of mental health RCTs fails to find 30–50% of RCTs contained in MEDLINE, whereas a single hand-searcher identifies 95% of the trials (Adams *et al*, 1994).

The Oxford University Department of Psychiatry is collaborating with the UK Cochrane Centre (Chalmers *et al*, 1992) and others to assemble a register of RCTs of mental health care from which trials can be identified more completely and easily than at present. The register of RCTs of mental health care, part of the international register of RCTs of the Cochrane Collaboration, will be widely available to clinicians, researchers, and consumers of mental health services. This task requires joint working between centres in the UK and internationally. Psychiatry was one of the first specialities of medicine to adopt the randomised controlled trial (Ewing & Mendenhall, 1953; Baker & Thorpe, 1959), and it is important that it does not fall behind the others in setting up the continually revised register of RCTs and systematic reviews.

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