

The COCHRANE Collaboration - Making the results of controlled trials properly accessible

Dr. Andrew Herxheimer

UK COCHRANE Centre, Oxford

Clinicians and clinical scientists have often felt frustrated by the difficulties of finding out what randomised controlled trials (RCTs) have been done, and of interpreting their results critically. The COCHRANE Collaboration will help to register, assemble, and disseminate evidence derived from systematic reviews of RCTs.

The COCHRANE Centre in Oxford was officially opened in November 1992, and is perhaps the most visible part so far of the recently launched *NHS Research and Development Programme*. Its task is to facilitate and extend the creation of systematic reviews of *randomised controlled trials (RCTs)* evaluating health care. It is named after ARCHIE COCHRANE (1909 - 1988), the epidemiologist who first emphasised that reliable information from RCTs, together with other essential information, is vital for making sound decisions in health care and research. Most clinicians and clinical scientists who have tried to review the evidence for a particular procedure or treatment have felt frustrated by the difficulties of finding out what RCTs have been done, and of interpreting their results critically.

The UK COCHRANE Centre is just one element of the rapidly evolving COCHRANE Collaboration. Together with COCHRANE Centres in Canada, Australia, Denmark (for the Nordic countries), the United States, Italy and the Netherlands the COCHRANE Collaboration will help to assemble and disseminate evidence derived from systematic reviews of RCTs. These differ from traditional reviews in that they are prepared as methodically and as meticulously as a piece of primary research, and they include a detailed description of the way in which the trials were identified, selected and evaluated. Specifically, the COCHRANE Collaboration is working to build and maintain a database of systematic, up-to-date reviews of RCTs of health care, and to make them readily accessible through electronic media.

How the COCHRANE Centres are supporting the Collaboration

The time needed to prepare valid reviews of RCTs tends to be grossly underestimated. Lack of experience and time often force good scientists to produce scientifically inadequate reviews. The COCHRANE Centres will give

practical support to those preparing and updating reviews within the COCHRANE Collaboration in several ways.

Systematic reviews of RCTs must be based on as high a proportion of eligible studies as possible. In addition to a register and library of published reviews of RCTs, therefore, the *Baltimore COCHRANE Centre* is helping to coordinate the creation of as comprehensive as possible a register of RCTs, in collaboration with the *US National Library of Medicine*. Because bibliographic databases like MEDLINE identify only around 50% of RCTs, selected journals are being searched by hand. Efforts are meanwhile being made to improve the rate of RCT retrieval from bibliographic databases in future. The Register of RCTs will also aim to include references to unpublished, ongoing and planned controlled trials, so that people preparing systematic reviews can consider them.

In addition to containing completed reviews of RCTs, the *COCHRANE Database of Systematic Reviews* will include details of reviews which are being prepared or planned. This information will help participants in the *COCHRANE Collaboration* to avoid unnecessary duplication of effort, and others to know about forthcoming systematic reviews.

The *Centres* are developing protocols and software to help people preparing systematic reviews, and they collaborate to develop policies and set standards for this work, based when possible on relevant methodological research. For example every review must include a brief section summarising its implications for practice, so that readers can quickly see whether it has messages relevant to them. It must also include a section on its implications for future research, perhaps suggesting what work is most urgently needed, and what requires no further work. The *COCHRANE Collaboration Tool Kit* is now available to participants in the *Collaboration*, offering detailed help on all aspects of the preparation, presentation and publication of systematic reviews.

Adverse effects and risks

It is helpful if a review attempts to assess the disadvantages and risks of an intervention as well as its benefits. If trials have been designed to look for specific adverse effects, then the findings must clearly be included in the review. If however adverse effects have been observed incidentally, their weight as evidence is more anecdotal, and much less than that of observations which the study was designed to obtain. To include such incidental observations in a systematic review might falsely imply that they were as reliable as those concerned with the end points specified in the protocol. The asymmetry of the weight of the evidence on the positive and the negative side of the balance sheet is inevitable: knowledge

of adverse effects almost always accrues later than evidence of benefit, and tends to be less precise. For now, it may be best to leave individual authors or editors of reviews to decide how to handle the issue, pointing out that it will often fit well under the headings on implications for practice and for research.

Economic evaluations

The economic assessment of interventions in health care may also have to be considered in systematic reviews when clinical trials have included data on economic costs and benefits - whether expressed in monetary or other terms. The COCHRANE Collaboration aims to assist the development of methods for systematic evaluation of these aspects.

An editorial system based on collaborative review groups

Those contributing reviews to the COCHRANE Database do so as members of collaborative review groups, each coordinated by an editorial team which oversees a group of related reviews. Most collaborative review groups focus on specific health problems, e.g. stroke, diabetes mellitus, schizophrenia. Reviewers considering whether to form such a review group can attend workshops to discuss some of the likely implications with already established groups. That group responsible for reviewing RCTs in pregnancy and childbirth now maintains about 600 systematic reviews of RCTs, prepared by over 30 reviewers in seven countries; it has to deal with 200-300 new reports of trials every year. The editorial team of this review group consists of four editors, an administrator and a data clerk.

The *module of reviews of RCTs in pregnancy and childbirth* is being used as a pilot to explore how best to build, update and disseminate the COCHRANE Database of Systematic Reviews. For example, it must be possible to criticise and amend the reviews whenever necessary. The use of electronic publications makes this easy and offers obvious advantages for disseminating the reviews. In the first half of 1995 the database of systematic reviews so far completed, together with information about the COCHRANE COLLABORATION, will be available for use on personal computers both on *disk and on CD-ROM*. Specialty databases for particular groups of users will be compiled and published on disk. Subscribers can obtain the first of these, the *COCHRANE Pregnancy and Childbirth Database*, on a single 3 1/2" disk. It is replaced by an update twice a year.

Many collaborative review groups are evolving within the COCHRANE Collaboration. In over 40 topic areas a systematic search for RCTs has been started or an exploratory meeting convened (*see Table 1*). In many of the areas

Malaria	Trauma
Cancer	Pain
Musculo-skeletal disease	Anxiety disorders
Back pain	Depression
Functional bowel disease	Schizophrenia
Hepato-biliary disease	Intensive care
Inflammatory bowel disease	Surgery
Peptic ulcer disease	Anaesthesia
Oral health	Physical therapy
Dementia	Children
Neuromuscular disorders	Elderly
Visual disability	Developing countries
Stroke	Primary health care
Subfertility	Nursing
Pregnancy & childbirth	Behaviour change
Neonatal diseases	Effective professional practice
Wound healing	Health education
Obesity	Social interventions
Fractures	Complementary medicine

Tab. 1: Some of the topic areas

drug trials are prominent. The *Collaboration* will ensure that overlaps do not lead to duplication of work.

The up-to-date systematic reviews of *RCTs* being prepared and maintained by the *COCHRANE Collaboration* can help clinicians to keep their practice up to date and should facilitate the development of soundly based clinical guidelines. Of course reliable information from sources other than *RCTs* must also be given due weight in this process, and that will include information on risks and safety. Systematic reviews are also essential for ensuring that the lessons from previous studies are applied in the design of new clinical trials. Because reviews are contributed to the *COCHRANE Database* on the understanding that copyright will not be assigned exclusively to any publisher, all journals, as well as various electronic media, can play their part in disseminating the results of these reviews, and thus help to ensure that the findings can be widely applied in practice.

Further reading

CHALMERS I, DICKERSIN K, CHALMERS TC. Getting to grips with Archie Cochrane's agenda. *British Medical Journal* 1992; 305: 786 - 788.