Evidence-based nephrology: The Cochrane Renal Review Group

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«it is surely a great criticism of our profession that we have not organised a critical summary, by specialty or subspecialty, adapted periodically, of all relevant randomised controlled trials».
ARCHIE COCHRANE, 1979

This statement was part of an essay by the Welsh Epidemiologist, Archie Cochrane (1909-1988). Archibald Leman Cochrane was born in Scotland, studied at Cambridge and did his medical training at the University College Hospital in London. In 1936 he was part of the international brigade during the Spanish Civil war and in 1939 became a captain in the Royal Army Medical Corps. He was taken prisoner of war in 1941 in Crete and was the prisoner of war medical officer in Salonica and then at three prisoner of war camps in Germany. His great interest was tuberculosis and he studied its epidemiology in the USA before taking up a post in Wales. In 1960 he was appointed the David Davies Professor of Tuberculosis and Chest Diseases at the Welsh National School of Medicine in Cardiff. During his long and distinguished career he completed 20 and 30 year follow-up studies of Welsh mining communities and in 1972 wrote the book *Effectiveness and efficiency - Random reflections on Health Sciences*[1]. In 1987, the year before he died, he referred to a systematic review (SR) of randomised controlled trials (RCTs) of care during pregnancy and childbirth as «a real milestone in the history of randomized trials and in the evaluation of care», and suggested that other specialties should copy the methods used.

This challenge was taken up by a small team led by Sir Iain Chalmers who gathered together 3,500 reports of controlled trials in perinatal medicine published between 1940 and 1984 and published this bibliography in 1985.

From 1985 to 1992 there was international collaboration to prepare systematic reviews of controlled trials in pregnancy and childbirth and the neonatal period. This led to four publications, *Effective Care in Pregnancy and Childbirth, A Guide to Effective Care of Pregnancy and Childbirth (GECPG), The Oxford Database or Perinatal Trials (ODPT),* and *Effective Care of the Newborn Infant (ECNI)*[2-5]. A six-monthly electronic journal was developed from the ODPT. These SRs were well received and the first Director of Research & Development in the British Health Service approved funding for a Cochrane Centre 'to facilitate the preparation of systematic reviews of randomised controlled trials in health care'[6]. The Cochrane Centre was opened in 1992. In March 1993 the concept of the Cochrane Collaboration was presented at a conference *(«Doing more Good than Harm»)* at the New York Academy of Science and in October 1993 the Cochrane Collaboration was officially launched.

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The Cochrane Collaboration

The Cochrane Collaboration is an international network of health care professionals, researchers, and consumers who are interested in developing and maintaining comprehensive, regularly updated critical reviews of evidence from randomised clinical trials relevant to their speciality and interests. There are over 19,000 people currently involved from over 120 countries.

The Cochrane Collaboration has 10 guiding principles:

1. Collaboration
2. Building on the enthusiasm of individuals
3. Avoiding duplication
4. Minimising bias
5. Keeping up to date
6. Striving for relevance
7. Promoting access
8. Ensuring quality
9. Continuity
10. Enabling wide participation

The Cochrane Logo

The Cochrane Collaboration logo demonstrates why Cochrane reviews matter. It shows how one review saved tens of thousands of babies' lives, and how delay in assessing health care can cost lives. The diamond shows the summary estimate of the results of a systematic review of the findings of individual randomised trials —the horizontal lines— comparing one treatment with a placebo.

This systematic review evaluated the effectiveness of a short, inexpensive course of a corticosteroid given to women at risk of giving birth too early. The first trial was reported in 1972, and another seven were reported by 1981. The logo summarises the evidence that would have been revealed had all these trials been reviewed systematically. It indicates strongly that the drug reduces the risk by 30 to 50 per cent of babies dying from the complications of immaturity.

Structure of The Cochrane Collaboration

The Cochrane Collaboration has a unique structure and assesses most areas of health care. To do this, it is divided into Collaborative Review Groups (CRGs), each of which concentrates on a specific health care area; Fields, that draw together health care issues impacting on many CRGs (such as child health and vaccines); a Consumer Network, that represents the interests of health care consumers; Methods Groups which develop methodological techniques; Centres, which support the members of The Cochrane Collaboration within their geographical sphere and are responsible for liaising with national government; and a Steering Group, which is the policy and decision making body of the Collaboration, and this, in turn, is supported by the Secretariat.

Collaborative Review Groups

The main work of the Collaboration is done by fifty CRGs, within which Cochrane reviews are prepared and maintained. The members of these groups —researchers, health care professionals, people using the health services (consumers), and others— have come together because they share an interest in generating reliable, up-to-date evidence relevant to the prevention, treatment and rehabilitation of particular health problems or groups of problems.

Fields

There are currently 16 fields. The role of fields is to ensure that the CRGs reflect their areas of interest and are in general focused on areas of health care rather than health conditions (e.g. setting of care – prehospital and emergency health; type of consumer – elderly; type of intervention – complimentary medicine). They assist by providing bursaries, compiling registers and assisting with the peer review process.

Consumer Network

The Cochrane Consumer Network provides information and a forum for networking among consumers involved in the Collaboration. It assists with the writing of plain language summaries for all Cochrane reviews, provides training and assistance for consumers who are involved in the peer-review process, and provides stipends for active consumers to attend the annual Cochrane Colloquium.

Methods Groups

Methods Groups have been established to develop methodology and advise the Collaboration on how the validity and precision of systematic reviews can be improved. There are 11 methods groups that cover areas from information retrieval to reporting bias and individual patient data meta-analysis. For example, the Screening and Diagnostic Tests Methods Group is currently preparing guidelines and methods for the next phase of Cochrane Reviews-diagnostic test systematic reviews.

Centres

There are 12 Centres around the world (Australia, Brazil, Canada, China, Denmark, Germany, Italy, the Netherlands, South Africa, Spain, UK, and the USA) funded by both government and charitable sources. They share responsibility for helping to co-ordinate and support members of the Collaboration in areas such as training, and they promote the objectives of the Collaboration at a national level. Each Centre is responsible for a number of different countries in the world, and some Centres have branches within those countries.

Cochrane Collaboration Steering Group and Secretariat

The Cochrane Collaboration is overseen by a steering group comprised of elected members representing the various entities within The Cochrane Collaboration. The Steering Group meets face-to-face twice a year with the various working groups communicating via regular teleconferences. The work of the steering group is supported by the Secretariat.

The Cochrane Library

The Cochrane Collaboration and its output have grown rapidly since the organisation was established in 1993. The first issue of the *Cochrane Database of Systematic Reviews (CDSR)*, the main product of the Collabo-

ration, was published at the beginning of 1995, and included 36 Cochrane reviews. There were 500 Cochrane reviews in 1999, and *CDSR* now contains the full text of more than 3,000 Cochrane reviews, each of which is kept up-to-date as new evidence accumulates. Protocols (reviews in progress) are also published on the *CDSR* and there are currently over 1,700. In 2004 *CDSR* was listed with the Institute for Scientific Information (ISI) and its first impact factor should appear in 2008.

The Cochrane Library also contains several other important databases and registers. These are:

- *The Cochrane Central Register of Controlled Trials (CENTRAL):* bibliographic information on over 500,000 reports of studies, including those published in conference proceedings and many other sources not currently listed in other bibliographic databases.
- *The Cochrane Methodology Register:* bibliographic information on articles and books on the science of reviewing research, and a prospective register of methodological studies. *The Cochrane Library* also contains links to a handbook on how to conduct a Cochrane review, and a glossary of terms.
- *The Database of Abstracts of Reviews of Effects (DARE):* critical assessments and structured abstracts of other systematic reviews, conforming to explicit quality criteria, assembled and maintained by the Centre for Reviews and Dissemination in York (UK).
- *Heath Technology Assessment Database (HTA; Technology Assessments):* details of completed and ongoing health technology assessments from around the world. The aim of the database is to improve the quality and cost-effectiveness of health care.
- *NHS Economic Evaluation Database (NHSEED; Economic Evaluations):* systematically identifies economic evaluations from around the world, appraising their quality and highlighting their relative strengths and weaknesses.

The Cochrane Library is an online publication available at *http://www.thecochranelibrary.com.* Many countries have national licensing agreements with our publisher John Wiley and Sons Limited, which provides free access to *The Cochrane Library*. In addition to the English version, the Iberoamerican Cochrane Centre translates *The Cochrane Library* into Spanish (La Bilbioteca Cochrane Plus –*http://www.cochrane.es/clibplus/).* This is freely available in Spain and in several South American countries.

The Cochrane Renal Review Group

The Cochrane Renal Review Group *(http://www.cochrane-renal.org)* was officially registered on 1st March 1997 with its editorial base, headed by Prof Denis Fouque, in Lyon (France). In May 2000 the editorial base was relocated to Sydney (Australia) and is located in the Centre for Kidney Research at The Children's Hospital at Westmead.

Located at the editorial base are:

- the Coordinating Editor,
- the Review Group Coordinator (RGC),
- the Trial Search Coordinator (TSC), and
- the Administration Officer.

The editorial team also includes a group of international editors from Australia, France, Germany, Italy, UK and USA.

Other members of the group include authors, handsearchers, peer referees, consumer referees and other interested parties (e.g. government, not-for-profit organisations, medical and consumer groups).

The main role of the editorial base is to support authors through the review process. This includes:

- Assisting authors in the preparation of their protocols, reviews and updates.
- Assembling an edited module of systematic reviews prepared by the authors.
- Disseminating information about the group via the module (scope, trial search strategy, members etc.).

The module is then disseminated through *The Cochrane Library*. This use of electronic media allows reviews to be regularly updated as new evidence becomes available.

Other roles of the Editorial team are:

- Organising peer and consumer referees.
- Identifying all trials concerning renal disease and create a specialised registry.
- Coordinating handsearching of conference proceedings and journals not cited in the electronic databases.

Author support

As can be seen the role of Cochrane Renal Review Group is more than publishing reviews –we take the author through the whole review process. The assistance that we offer includes:

- Selecting and registering a title with the Cochrane Collaboration.
- Providing handbooks and training in the relevant software and Cochrane methodology, either by face-to-face or online training.
- Assistance with defining the search terms required to identify relevant studies for electronic searching.
- Access to our specialised register of controlled trials identified through electronic searching and handsearching of non-indexed journals and conference proceedings.
- Retrieval of relevant trials.
- Copies of data extraction forms and quality checklists.
- Writing of the protocol and the review.
- Statistical assistance for all types of data sets.
- Amending the protocol and review in response to editorial input.
- Preparation of manuscripts for publication (copy editing, technical and statistical input.

- Assisting with the mandatory updating required for all Cochrane Reviews (which is a condition for publication in *The Cochrane Library*).

We are therefore more akin to a research office that also publishes.

Topic area

The Cochrane Renal Review Group's scope covers the major areas of kidney disease including:

- Acute renal failure
- Chronic renal failure
- Renal transplantation
- Drugs and the kidney
- Renovascular hypertension
- Glomerular diseases
- Urinary tract infections
- Nephrolithiasis

The review process

There are three stages to any Cochrane review:

1. The protocol or plan of the review
2. The review
3. Future updates

Protocol

The protocol is the plan of the proposed review and must include:

1. The specific purpose (question to be answered) of the review.
2. The comparison groups (as the stated comparisons are central to each review, particular care should be taken with their development).
3. The sources and search methods used to find evidence (primary studies).
4. Explicit criteria for deciding which studies to include in the review. This includes the population, who or what will be included and/or excluded.
5. Avoidance of bias in the selection of articles.
6. Reasons for excluding studies from the review.
7. Appropriate criteria for assessing the quality of the studies.
8. Appropriate methods (whether qualitative or quantitative) for combining the findings.

These equate to the background, objectives and methods section of any research paper.

Review

Upon completion and publication of the protocol the review is then undertaken. The protocol acts as the template for completing the review and the steps involved in completing the review are:

1. The location of trials with the help of the Trials Search Coordinator who sends to the authors a list of potential studies identified from our specialised register and from electronic searching of MEDLINE, EMBASE and CENTRAL.
2. The application of inclusion and exclusion criteria for identified studies.
3. For all included studies the quality is assessed, data extracted and entered into the review manager programme RevMan (ref).
4. Results are interpreted and discussed.
5. As for all published articles, an abstract, tables and additional figures, as well as a consumer plain language summary must be prepared.
6. The completed review is again submitted for peer refereeing.
7. An additional step here is that now the review will also be refereed by a statistical editor.
8. Once the review is amended in response to peer refereeing and approved by the editorial office, it undergoes technical and copy editing, changes are approved by the authors, a permission to publish form signed and it is published in *The Cochrane Library.*

Updating a Cochrane review

Cochrane reviews are regularly updated and The Cochrane Collaboration policy is that all reviews should be reassessed every two years.

There are two types of updates:

1. New trials sought but not found or excluded –this is classified as an up-to-date review.
2. New trials sought and included –this is an updated review.

To assist in the updating the TSC reruns the electronic search strategies every 12 months. The results are screened and if any potential new trials are identified, these are sent to the authors. The author is then responsible for determining whether these trials should be included or excluded, amending the relevant sections of the review and returning the review to the editorial office. If new trials are included the review once again undergoes peer refereeing, the review is amended to reflect any comments by the referees and the review is republished.

Updated reviews are listed again on MEDLINE as a second publication and will be included in the impact factor score for *CDSR*.

The editorial process

All CRG reviews undergo an editorial process similar to that of other journals. One additional step however is the peer review of the protocol.

When a protocol or review is submitted it is reviewed at an editorial meeting for suitability for peer refereeing. Once

it is approved, the assigned editor and external referees are contacted, and the protocol or review is sent with a checklist for assessment. Comments are collated and reviewed at a second editorial meeting and sent to both the authors and the peer referees. The Cochrane Renal Review Group has an open editorial process and this process has been adopted by some of the major medical journals (e.g. BMJ). Authors are advised which points we feel should be addressed and are asked for a covering letter to explain both the changes made and those that have not been changed.

An important difference between our editorial process and that of a paper journal is that we also have a consumer referee. This is to ensure that the outcomes are patient focused. Consumers today get their information from a wide variety of resources and as Cochrane reviews are available on the internet we must ensure that the information is also in a format that they can understand. This is one of The Cochrane Collaboration's guiding principles. This is also the reason why all Cochrane reviews contain a consumer plain language summary.

Prospective trials register

The 2004 decision by the International Committee of Medical Journal Editors (ICMJE) to only publish trials that have been registered before commencement of recruitment was a significant step forward in avoiding publication bias when undertaking a review. The ICMJE definition of what trials should be registered is «Any research project that prospectively assigns human subjects to intervention and comparison groups to study the cause and effect relationship between a medical intervention and a health outcome». Trials can be registered on any publicly available website and there is WHO-defined data that must be entered. All trials submitted for publication must quote the unique registration number. The Cochrane Renal Review Group has such a database on its website and this initiative has been supported by the major nephrology journals. The trial submission form can be found at *http://www.cochrane-renal.org/trialsubmissionform.php.*

From a review author point of view, prospective registration should ensure that all trials can now be identified and included in systematic reviews.

Renal Health Library

Another important initiative of the Cochrane Renal Review Group is the annual production of the Renal Health Library, supported by an unrestricted educational grant from AMGEN Australia. This first began as a bibliography of 2000 RCTs in kidney disease and the first edition was released in 2001. It has since grown and in 2005 the Renal Health Library contains the full text of 80 Cochrane systematic reviews related to kidney disease, our trials register of 8,854 published and ongoing trials, 176 reports of non-Cochrane meta-analyses and 201 reports of diagnostic test accuracy studies.

The Renal Health Library is available on CD-ROM.

Why are Cochrane reviews different?

Many people produce systematic reviews. Nobody produces as many as The Cochrane Collaboration, across such a wide range of healthcare topics, with such rigorous research methods. What makes Cochrane reviews different is that they are updated regularly, ensuring that treatment decisions can be based on the most up-to-date and reliable evidence.

The latest estimate is that at least 10,000 Cochrane reviews are needed to cover all healthcare interventions that have already been investigated in controlled trials, and these reviews will need to be updated at the rate of 5,000 per year.

In nephrology we have approximately 190 reviews being undertaken. A third of these are completed reviews. We feel that there are at least another 200 reviews that could be undertaken based on the trials in our specialised register.

The next challenge for the Cochrane Collaboration is diagnostic test reviews. The methods and software are now finalised and the trials register is currently being developed. We hope to see the first review in 2008.

Become involved

We are always looking for new contributors. You can become involved in many ways:

- Conducting a systematic review.
- As a referee of systematic reviews.
- Notifying the editorial base of any randomised controlled trials in renal diseases ongoing or not published.
- Carrying out handsearching of journals particularly those that are not listed in MEDLINE, and those published in languages other than English.
- Sending abstract books of conference proceedings to us.
- Providing Consumer input.

References

1. Effectiveness and efficiency –Random reflections on Health Sciences.
2. Effective Care in Pregnancy and Childbirth.
3. A Guide to Effective Care of Pregnancy and Childbirth (GECPG).
4. The Oxford Database or Perinatal Trials (ODPT).
5. Effective Care of the Newborn Infant (ECNI).
6. Chronology of the Cochrane Collaboration. http://www.cochrane.org/docs/cchronol.htm Accessed September 2007.