

## The Value of Systematic Reviews

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In 2013, a workshop was held in Kathmandu that explored systematic reviews – what they are, how they are developed, how they are used in evidence-based clinical guidelines, and how they can inform the clinical research agenda. The workshop was funded by the Gates Foundation through FIGO, and organised by the Nepal Society of Obstetricians and Gynaecologists.

### What are Systematic Reviews?

Reviews are important because busy clinicians rarely have time to read primary research reports and therefore rely on review articles, written by experts, to keep them up-to-date with the latest developments in their chosen field. However, review articles can be unreliable if the account is biased. A review author might, for example, have strong views about something - let's say, the advantages of surgical treatment of endometriosis compared to medical (drug) treatment. S/he might then selectively cite research papers that support surgery, and ignore those that support drug treatment, to strengthen the author's prior conviction that surgery is best.

'Systematic' reviews seek to avoid this problem by using scientific principles to minimize bias. Thus the systematic review is based around a clearly articulated question-to-be-addressed: such as 'what are the advantages and disadvantages of surgery versus medical treatment for endometriosis?'

The methods of the review are then structured around the PICO approach – (P)opulation, (I)ntervention, (C)ontrol, (O)utcomes. The population here might be all women with endometriosis, or a sub-population with mild disease or with severe disease, or those with associated problems, e.g. infertility. The intervention would be surgical treatment; it could be all surgical

methods or just laparoscopic procedures or just open operations. Control treatments (drugs here) could include all drugs or specific sub-groups of drugs. The outcomes require careful consideration. These should include important symptoms: such as pelvic pain but a decision needs to be made about how pain would be measured, and when: 6 or 12 months after treatment, or later? Input by patients and other lay people can be extremely valuable in identifying clinically important outcome measures. Economic outcomes can also be important: surgery may be much more expensive (to both the health system and the patient) than simple drug treatment.

There is currently much interest in standardizing the outcomes used in clinical trials through the COMET Initiative (core outcome measures in effectiveness trials: <http://www.comet-initiative.org>) and the CROWN Initiative (involving obstetrics and gynaecology journals).<sup>1</sup>

The PICO structure is laid out in advance of analyzing any data. Also set in advance are (1) the types of studies to be used in the systematic review, and (2) the way in which these will be identified.

The types of studies are most often randomized controlled trials (RCTs) although systematic reviews can also be done on other types of study e.g. observational or case control studies. RCTs are the gold standard studies to assess the effectiveness of healthcare interventions. They are so powerful because the act of randomly allocating patients (as long as it is done properly) produces two groups of patients which should be similar in most important respects, other than exposure to experimental treatment or control treatment. It is essential to avoid so-called 'selection bias' by ensuring that randomization uses a method such as sealed envelopes or, better still, computers, which means that the clinician cannot know in advance to which treatment group his/her patient will be allocated.

Studies (in this case RCTs) are identified through a pre-set electronic search strategy. This may include papers in any language or be restricted (e.g. English

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language only). The important point is that ALL studies that meet the pre-set criteria for inclusion, are included. In this way, the review author cannot influence the conclusion of his/her article by selective citation of research papers.

The objectives of the review, the PICO, and the search strategy and methods of analysis are laid down in advance as a 'protocol'. Only when this is finished are the papers identified, the data extracted and the analyses performed. Most often, data from a number of similar RCTs are pooled together to give a composite result ('meta-analysis'). More robust results are obtained by increasing the total number of patients in the analyses through pooling.

### **The Cochrane Collaboration**

The Cochrane Collaboration produces more systematic reviews than any other organization. Cochrane reviews are also recognized as of very high quality. The Cochrane Collaboration celebrated its 20<sup>th</sup> anniversary in 2013, coincidentally the year of the Kathmandu workshop. The Cochrane Collaboration is a complex, international network of people and organizations whose core objective is to produce systematic reviews of RCTs. There are a number of Cochrane Review Groups whose work is of relevance to obstetricians and gynaecologists, e.g. pregnancy & childbirth based in Liverpool, UK; menstrual disorders and infertility based in Auckland, New Zealand; incontinence based in Aberdeen, Scotland; and fertility regulation based in Holland. All systematic reviews from all groups are published

in the Cochrane Library (<http://www.cochranelibrary.com/>).

The Cochrane Collaboration emerged from the perinatal field through work by Sir Iain Chalmers and colleagues in the 1980's. The logo of the Cochrane Collaboration's shows a so-called 'forest plot' – a graphical depiction of a meta-analysis. This shows what a particular meta-analysis would have looked like in 1981 had it been done, which it wasn't. The intervention is corticosteroid administration to pregnant women before anticipated preterm birth. The outcome is neonatal death. The pooled estimate of effect size shows a hugely significant decrease. The first meta-analysis of prenatal corticosteroids was not in fact published until 1989. Although it showed clear evidence of effectiveness in reducing neonatal mortality and morbidity, it took until around 1995 before corticosteroids were much used, for this purpose, in obstetric practice. The use of corticosteroids in low income settings is still a topical issue.<sup>2</sup>

A gap of almost 15 years between the availability of evidence to show a particular treatment is highly effective, and its uptake into clinical practice, is manifestly not good enough. There are many reasons for slow acceptance of innovations by clinicians, and by health systems. One method of speeding adoption of research into practice is through the development of evidence-based clinical guidelines, which rely heavily on systematic reviews. The World Health Organisation has produced a very helpful handbook on guideline development.

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