ABC of Methodology

This is a Section of *Epidemiologia e Psichiatria Sociale*, that regularly covers methodological aspects related to the design, conduct, reporting and interpretation of clinical and epidemiological studies. We hope that these articles will help develop a more critical attitude towards research findings published in the international literature and, additionally, will help promote the implementation of original research projects with higher standards in terms of design, conduct and reporting.

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Assessing risk of bias in randomized controlled trials

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Abstract. Even though randomised controlled trials are the design of choice for evaluating the efficacy of health care interventions, they are not immune to bias that may affect research process and validity of results. In the present paper we discussed how trial quality may be appraised considering both whether a clinical trial is reported in a comprehensive and complete way (consistently with what had been declared in the study protocol), and whether the characteristics of the trial itself are associated with risk of bias.

KEY WORDS: quality, randomised controlled trial, bias, outcome reporting.

Even though randomised controlled trials (RCTs) are the design of choice for evaluating the efficacy of health care interventions, they are not immune to bias that may affect research process and validity of results (Cipriani & Geddes, 2009). Trial quality may be appraised at two different levels: the *level of reporting* – that is, whether a clinical trial is reported in a comprehensive and complete way, consistently with what had been declared in the study protocol; the *level of the methodological quality* – that is, whether the characteristics of the trial itself are associated with risk of bias.

Assessing the quality of reporting. Even though potentially misleading, quality of reporting is often used as a proxy measure for overall study quality. To face this problem and help authors improve quality of study reports, the Consolidated Standard Of Reporting Trial (CONSORT) has been developed (Schulz *et al*., 2010). CONSORT encompasses various initiatives developed by the CONSORT Group to alleviate the problems arising from inadequate reporting of RCTs. The main product of CONSORT is the CONSORT Statement, (http://www.consort-statement.org/consort-statement/overview0/) which consists of a set of recommendations, that are regularly updated, for reporting RCTs. These recommendations are a tool for authors of reports of clinical trials, who aim at disseminating their findings in a transparent and complete way, and for readers of reports of clinical trials, who may want to critically appraise the research findings. The CONSORT Statement comprises a 25-item checklist and a flow diagram. The checklist items focus on how the trial design, analysis, and interpretation should be reported; the flow diagram describes the phases of patient enrollment and progress through the trial. The CONSORT Statement has been endorsed by many international journals so far and it can be freely accessed at: www.consort-statement.org. Even though CONSORT is a tool that has certainly improved quality of study reports, it is not a rating scale of trial quality with validated psychometric properties.

Assessing the methodological quality. Many tools have been proposed for assessing the quality of RCTs. Most tools are rating scales in which various components of quality are scored and combined in a summary score (Jüni *et al*., 2001). In 1995, Moher *et al*. (1995) identified

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25 scales that had been used to assess the validity or 'quality' of randomized trials. These scales included between 3 and 57 items and rating scales were likely to include criteria that did not directly relate to study validity (Cipriani *et al*., 2009). The Cochrane Collaboration recommends simple approaches for assessing methodological quality using a specific tool for evaluating the risk of bias. This tool – developed between 2005 and 2007 by a working group of methodologists – is a domain-based evaluation, in which critical assessments are made separately for the following domains: randomization, sequence generation, allocation sequence concealment, blinding, incomplete outcome data and outcome reporting.

Theoretically, it is expected high coherence between the quality of reporting and the methodological quality. In practice, it is possible to see clinical trials with a high methodological quality that are poorly reported, but also high quality study reports of clinical trials with a poor methodological quality (Figure). In A (top left) and D (bottom right), there is full coherence between reporting and methodological quality: good (or poor) quality of reporting corresponds to good (or poor) methodological quality, respectively. By contrast, in B (top right) and C (bottom left) there are contrasting situations: an apparently complete and detailed reporting is hiding a low methodological quality or (B) a scant and poor reporting is hiding a study with high methodological standards (C). So, when considering the two combined levels of quality, studies with high methodological quality (A and C) are clearly to be preferred; by contrast, results from study with low methodological quality (B and D) must be considered with caution because the high risk of bias that may undermine study results.

Instruments to assess study reporting and methodological quality like CONSORT or risk of bias are mainly used for research purposes. The CONSORT Statement is used by authors when writing a paper to be submitted to a journal and the risk of bias tool is used by researchers when carrying out a systematic review to critical appraise and weigh study quality among all studies included in the review. Journal readers need easier instruments and simpler ways to understand study quality and to judge how reliable results are. Even though to assess quality of RCTs is a complex issue, in order to have a rough idea of the quality of a RCT we recommend to have a careful look at the table reporting the baseline clinical and sociodemographic characteristics of the patients allocated to the new and reference treatment. It is possible to check how many patients were truly randomised (a small sample size generally correlates with low study quality) and whether there are imbalances in the randomization procedures that may be suggestive of high risk of bias.

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