This Section of *Epidemiology and Psychiatric Sciences* regularly appears in each issue of the Journal to cover methodological aspects related to the design, conduct, reporting and interpretation of clinical and epidemiological studies. The aim of these Editorials is to help developing a more critical attitude towards research findings published in international literature, promoting original research projects with higher methodological standards, and implementing the most relevant results of research in every-day clinical practice.

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What are evidence-based treatment recommendations?

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In recent years new methodologies for developing treatment recommendations that give consideration to evidence, values, preferences and feasibility issues have been developed. One of the most well-developed approaches is the *Grading of Recommendations Assessment, Development and Evaluation* (GRADE) methodology. This article briefly presents how this methodology may be employed to develop treatment recommendations that might constitute a permanent infrastructure between primary research and everyday clinical practice.

According to the principles of evidence-based medicine, research findings should guide doctors when taking decisions in daily clinical practice. However, not all research findings are attributed the same value, as randomized evidence is considered more reliable than observational evidence (Cipriani & Geddes, 2009), and systematic reviews of randomized controlled trials are nowadays at the pinnacle of the evidence hierarchy.

In such a system, a crucial issue is how the results of systematic reviews may effectively be translated into evidence-based practice, considering that access and use of systematic reviews may not be straightforward for most doctors in most countries of the world. Moreover, professionals and the public may want that treatment recommendations are informed by other aspects, including values, preferences and any other feasibility and practical issues.

In recent years, in order to tackle this global issue, new methodologies for aggregating, synthesizing and grading the quality of evidence extracted from systematic reviews have progressively been developed, and approaches for creating treatment recommendations based on explicit assessments of the evidence base are nowadays commonly employed in several fields of medicine, including mental healthcare. These approaches may be used to develop treatment recommendations that give similar consideration to evidence, value, preferences and feasibility issues. One of the best-developed approaches is the *Grading of Recommendations Assessment, Development and Evaluation* (GRADE) methodology (Guyatt *et al.* 2008*a, b, c*). This methodology, developed by an international network of methodologists with an interest for grading quality of evidence and strength of recommendations, may be employed not only to develop specific treatment recommendations for professionals working in a single mental health service or department but also to develop recommendations for a wide range of interventions and disorders to be adopted at a district or regional level or at a national level.

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Fig. 1. The four aspects that inform treatment recommendations according to the GRADE methodology.

According to the GRADE methodology, treatment recommendations are informed by four aspects (Fig. 1). The first is the evidence base supporting a specific intervention. The approach works in such a way that initially a specific controversial question should be agreed upon by the group of professionals developing the guideline, say, for example, the efficacy and tolerability of antipsychotic polypharmacy *v.* monotherapy. Then the best available evidence base on this specific issue is retrieved, typically in the form of a systematic review of randomized trials. A further step is to extract from the systematic review the summary data and statistics for each pre-defined outcome of interest (e.g. psychotic symptoms, treatment acceptability, adverse events, mortality, etc.), and these summary data are reported in a table that is called GRADE table. GRADE tables can be produced automatically by using software developed by the GRADE working group called GRADEPro (freely available from the GRADE web site at http://www.gradeworkinggroup.org/). The merit of GRADE tables is that the magnitude of effect is presented in a simple tabular format for each included outcome, and it is therefore very easy to get an overview of the evidence base.

The second step is the assessment of the quality of the evidence summarized in the GRADE table. This aspect is rated for each included outcome because it is possible that high-quality evidence is available for one outcome (say, psychotic symptoms), while low quality or almost no evidence might be available for other outcomes (for instance, mortality). According to the GRADE methodology, five factors should be considered when assessing quality: *limitations in the design* of the studies included in the selected systematic review, *inconsistency* (which refers to similarities of estimates of effect across studies), *indirectness* (which refers to the applicability of the evidence to real-world patient populations), *imprecision of the summary effect size* and *publication bias*. The software GRADEPro provides raters with instructions on how to rate these aspects, and once the rating has been completed it automatically produces a summary measure of the overall quality of the evidence for each included outcome, ranging from high quality to moderate, low and very low quality.

The third aspect is the assessment of values and preferences. It is possible that professionals who develop the guideline want to check how the evidence base in favor or against a specific intervention matches with some *a priori* values that are considered key reference aspects. In mental healthcare, examples of values include promotion of social inclusion, prevention of discrimination and stigma, prevention of medicalization of social problems. So, for example, we may have evidence supporting the use of antidepressants in minor depression, but we may argue that in situations where people are exposed to severe ongoing social stressors minor depression may be difficult to differentiate from a transient reaction, with a risk of medicalization of a social problem that needs a social solution. This value may be taken into account when a recommendation is drafted, and it is possible, for example, to have a negative recommendation even in the presence of a positive evidence base (Barbui *et al.* 2010).

The fourth aspect refers to feasibility issues. Often there is high-quality evidence in favor of interventions that are not feasible in specific settings of care. Some psychological interventions, for example, require extensive training, supervision and time to deliver the treatment, and this may be feasible in some settings (specialized mental healthcare) but not in others (primary healthcare or rural or low-income settings). Similarly, assertive community treatment may not be feasible in low-resource settings, and lithium may not be a feasible treatment if regular blood checks cannot be performed.

Evidence-based treatment guidelines may be a valuable link between primary research and everyday clinical practice. Useful technical frameworks for synthesizing and presenting evidence on the effectiveness of clinical interventions may be employed by professionals who want to promote evidence-based practice. These technical frameworks attribute value not only to the evidence base but also to other issues, such as value judgments, resource use and feasibility, which are major considerations in mental healthcare.

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