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EDITORIAL

Looking beyond randomized controlled trials

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While many treatments in child and adolescent psychiatry have a well-established evidence base, there is a clear lack of studies that directly compare different treatment modalities for a particular clinical problem. Thus, unfortunately, clinicians and families are often left in the dark when it comes to looking for empirical evidence e.g., whether to choose between stimulant medication and parent management training for a child's behavioral problems, or between habit reversal training and antipsychotics for a chronic tic disorder. Families rightly ask and discuss with their clinicians the pros and cons of such highly differing treatments to reach a rational treatment decision.

As a rare example of a well conducted comparative study, the current issue of the European Journal of Child and Adolescent Psychiatry describes the results of a randomized controlled trial comparing the effects of three highly different types of treatment for children with attention-deficit/hyperactivity disorder: neurofeedback, stimulant medication, and physical activity. This is indeed a very welcome and interesting study [1]. The authors report superior effects of stimulant medication in comparison to the two non-pharmacological treatments on improving inhibition, impulsivity, and attention. Working memory, however, showed similar improvements from pre- to post-intervention across all three treatment groups. Overall, the effects of neurofeedback on neurocognitive functioning were not better than the effects of physical activity training. Although the study took 3.5 years for data collection, it managed to include only 60% of the planned number of participants.

Why is it so difficult to perform a well powered randomized controlled trial comparing different treatments and why are such studies so rarely reported despite being of such high relevance from a clinical point of view? The biggest bottle neck is recruitment. Families typically do not like major and highly personal treatment decisions for their child to be determined just by throwing the dice. They typically tend to have strong preferences for one treatment over the other. Thus, recruiting children into randomized controlled trials has become a major challenge. This is especially true for Europe where access to treatment within the field of child and adolescent psychiatry is typically being covered by universal health coverages, and not dependent on participation in a treatment trial. Even if families consent to randomization they may comply poorly if they are not being allocated to their preferred treatment.

Obviously a randomized controlled trial remains the classical and well established method to compare the efficacy of different treatments, as such a design avoids many kinds of potential bias through the randomization process. However, when so few families are willing to consider participation into randomized trials, these not only become unfeasible giving slow recruitment but also know their own bias as those who do consent to participate are hardly representative of the typical patient population. Therefore, it is good to be aware of alternative treatment evaluation designs that overcome the need to determine treatment allocation by chance, which families with strong treatment preferences tend to refuse. The so-called patient preference trial is one possible alternative [2]. Patients with treatment preferences are allowed their desired treatment; those who do not have strong views are randomized conventionally. Thus, in such a trial design, only patients who have

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no strong preferences for a particular treatment are being randomized, while those who refuse randomization may opt for their treatment of choice. Potential pre-treatment differences between the groups may be taken care with by determining propensity scores, i.e., the probability of treatment choice conditional on observed baseline characteristics. Moreover, the potential role of patient preference may be estimated by comparing the effects of treatments of the randomized patients with those receiving their preferred treatment.

Another alternative design would be to randomize patients before consent to participate has been sought and to just offer them the pre-randomized treatment. While a so-called Zelen's design completely avoids randomization, and may a suitable design in certain circumstances, there are obvious ethical concerns [3].

A last point to consider in designing a treatment trial is that randomization and blinding to treatment allocation are two separate issues. Even if randomization is not feasible it is still advisable to consider the use of independent and blinded treatment assessors, who are not aware of the treatment received by the child. It has indeed been shown that treatment effects may be substantially attenuated when using blinded assessments [4].

Treatment trials require tremendous efforts from participating families, clinicians, and researchers alike. To enlarge the current evidence base in the field of child and adolescent psychiatry, funding agencies should certainly look beyond the merits of only randomized controlled trials.

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