

Pediatric Clinical Trial Registration and Trial Results: An Urgent Need for Improvement

Performing research studies in children to evaluate drugs and other therapies is critical to providing proper pediatric medical care. For too long, medication use in children has been limited to extrapolation from adult studies or off-label use for indications that have not been properly evaluated in children. It has been less than 20 years since practical measures have been put in place to ensure that the necessary research evaluating therapies is more consistently carried out in children. Prompted by the American Academy of Pediatrics and other pediatric organizations, the Food and Drug Administration (FDA) in 1997 and the National Institutes of Health (NIH) in 1998 initiated policies designed to increase the number of children in research studies, including drug trials.^{1,2} Along with subsequent legislation, including the Best Pharmaceuticals for Children Act (2002), and the Pediatric Research Equity Act (2007), the initiatives by the FDA and NIH have succeeded in better including children in pharmaceutical trials.

To ensure that clinical drug trials in children are not unnecessarily repeated, the importance of a clinical trial registry has long been recognized.³ It is the policy of the American Academy of Pediatrics that “all clinical trials should be registered before initiation, and any results (including negative findings) should be published or otherwise made available to all researchers and the public.”⁴ This policy is consistent with the requirements of FDA and NIH, and an online database, ClinicalTrials.gov, was created for this purpose.

In this issue of *Pediatrics*, Shamliyan and Kane have provided an important first look at how well clinical research registration is working for studies involving children.⁵ Significant concerns were identified with regard to registration, completion rates, and posting of results. Although more than 20 000 studies involving children have been registered on ClinicalTrials.gov since 2000, it appears that a substantial proportion of NIH-sponsored studies have not registered. Although 70% of closed studies involving children have been completed, the proportion of noncompleted studies seems to be rapidly increasing. Perhaps most troubling, 95% of completed studies involving children have not posted results to ClinicalTrials.gov, and fewer than one-third of these completed studies have been published. At present, the results of most clinical studies of children are unavailable to the pediatric research community and the public. As a consequence, trials may be unnecessarily repeated, and the information cannot be used to guide therapy.

Also in this issue of *Pediatrics*, Carrasco and Bloch have provided a specific example of how the unavailability of trial results can disadvantage children and their physicians.⁶ The efficacy of serotonin receptor inhibitors (SRI) for treating repetitive behaviors in autism spectrum disorders was examined by searching the published literature and

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KEY WORDS

pediatric research, trial registries

ABBREVIATIONS

FDA—Food and Drug Administration

NIH—National Institutes of Health

SRI—serotonin receptor inhibitors

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ClinicalTrials.gov. Meta-analysis of the published literature suggested a small but significant effect of SRI in the treatment of repetitive behaviors. There was substantial evidence of publication bias, however; and adjusting for this extinguished the significant effect of SRI treatment. Of particular note, there were 5 completed trials identified on ClinicalTrials.gov without posted results. This lack of timely and complete disclosure of trial findings results in physicians being unable to make rational informed

decisions about the efficacy and risks of SRI treatment of children with autism spectrum disorders. It is especially ironic that problems in making research data available about the use of this class of drugs in children created a firestorm almost 10 years ago.⁷ Unfortunately, this problem has not been resolved.

We have made great progress toward including children in research, and thousands of children have participated in clinical investigations. One of the most important obligations to the

children and families who have willingly enrolled in trials is to ensure that their participation can benefit all children. Only timely, complete, and readily available clinical trial results can meet this obligation. We have a viable mechanism (ClinicalTrials.gov) to post trial results, but have fallen far short of the goal. Addressing this deficiency will require a renewed commitment by clinical investigators, the NIH, the pharmaceutical industry, and the FDA. It is time for urgent action.

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