EDITORIALS

Clinical Trials Series

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Clinical trials are our best vehicle for turning medical information that we may think is true into evidence that we know, within reasonable limits, to be true. Since the introduction of random assignments to treatment in the 1930s,[1] the clinical trial has been in continuous evolution. Among the major milestones have been the development of methods to perform randomization; the convening of data and safety monitoring committees; the formulation of stopping guidelines for safety, efficacy, and futility; and many others. Indeed, the clinical trial landscape is far different today from what it was over 80 years ago, when investigators first confronted the conundrum of how to obtain unbiased data that could be used to guide clinical practice. Today, trials range from a single person[2] to 100,000 people, from a single lab to hundreds of centers around the world, from simple two-arm randomizations to increasingly complex study designs.

In this issue, we inaugurate a series of articles called "The Changing Face of Clinical Trials," in which we examine the current challenges in the design, performance, and interpretation of clinical trials. The series will deal with contemporary challenges that affect clinical trialists today. It is not meant to be a course in clinical trial performance; rather, the articles are written by trialists for trialists about issues that face us all. We plan to cover new trial designs, current issues related to the performance of clinical trials, how to deal with unexpected events during the progress of trials, difficulties in the interpretation of trial findings, and challenges faced by specific sectors of trialists, including those working for large or small companies; the viewpoint of regulators who use trial data in their decision making will also be included. Each review article will define a specific issue of interest and illustrate it with examples from actual practice. The articles will occasionally be accompanied by Perspective pieces to bring additional history and color to the topic. We begin with an article on integrating comparative effectiveness trials into patient care,[3] accompanied by a history of clinical trials.[4] We have enjoyed putting the series together for you, and we hope that it will stimulate thought and discussion.

An audio interview with Dr. Drazen is available at NEJM.org

*Deceased.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We dedicate this series to James H. Ware, Ph.D., our colleague at the *Journal* for a quarter of a century, whose passion was to change what we think into what we know.

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1. Amberson JB Jr, McMahon BT, Pinner M. A clinical trial of sanocrysin in pulmonary tuberculosis. Am Rev Tuberc 1931;24:401-35.
2. Guyatt GH, Keller JL, Jaeschke R, Rosenbloom D, Adachi JD, Newhouse MT. The n-of-1 randomized controlled trial: clinical usefulness — our three-year experience. Ann Intern Med 1990;112:293-9.
3. Fiore LD, Lavori PW. Integrating randomized comparative effectiveness research with patient care. N Engl J Med 2016;374:2152-8.
4. Bothwell LE, Greene JA, Podolsky SH, Jones DS. Assessing the gold standard — lessons from the history of RCTs. N Engl J Med 2016;374:2175-81.

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