Although pharmacologic treatment remains a critical element in the short- and long-term management of schizophrenia, the past decade has been a challenging time in terms of real progress. Despite the introduction of several new medications as well as the conduct of larger and more diverse clinical trials, there remains considerable debate as to how far we have progressed in addressing some of the fundamental unmet needs in treating this disorder. A theme in this issue of Schizophrenia Bulletin addresses a number of topics in this context.

Although the notion of careful, systematic, and critical summaries of all relevant randomized controlled trials is not a new one, the Cochrane Schizophrenia Group is relatively young. Clive Adams, one of its founders, and colleagues provide the rationale and history of the group as well as reviewing its methods and contributions. The Bulletin also carries a “Cochrane Corner” in each issue to alert the field to schizophrenia-related reviews. Systematic meta-analyses are playing an increasingly important role in informing both the research agenda and clinical practice. The work of the Cochrane collaboration has been enormously valuable in this process.

In recent years, the field of schizophrenia research has benefited from the application of various clinical trial methodologies to enhance the study of treatment outcomes and determine generalizability. Large effectiveness trials have provided data to expand our knowledge base beyond that which is provided by traditional efficacy trials. Stroup and Geddes provide examples of each type of trial to illustrate their relative advantages and disadvantages. Within the context of different trial designs, Leucht et al provide an overview addressing critical aspects of trial design, potential population sampling bias, endpoint choices and definitions, quality of assessments, data analysis and reporting, as well as, other potential sources of bias or confounds relevant to the interpretation of clinical trials data in schizophrenia.

One of the most difficult challenges in the design, conduct, analysis, and interpretation of clinical trials is the problem of dropouts—those individuals who do not complete the trial, often for unknown reasons. A variety of statistical techniques have been developed and applied in order to address this issue; however, none is entirely satisfactory. Rabinowitz and Davidov discuss the association of dropout and outcome in trials of antipsychotic medication and its implications for strategies to address missing data.

Another strategy to minimize dropouts in acute treatment trials would be to shorten the length of the trial, particularly when placebo control groups are included. Addressing this issue and drawing on recent meta-analysis suggesting that a substantial proportion of antipsychotic drug response occurs within the first 2 weeks, McMahon and colleagues present an exploratory analysis from short-term placebo controlled clinical trial data suggesting the potential feasibility of reducing the duration of such trials. Much more work needs to be done to determine the benefits and risks of such an approach, but this is a very valuable first step.

In the final article, we provide a review of unanswered questions in the pharmacologic treatment of schizophrenia. Despite numerous trials being conducted with antipsychotic medication, there are many clinical decisions that must be made on a day-to-day basis for which sufficient data are not available to provide an adequate evidence base.

We hope that these articles will provide a snapshot of current challenges and opportunities for further progress in the design, conduct, and interpretation of psychopharmacologic trials in schizophrenia.