“Principles of Research Methodology: A Guide for Clinical Investigators”
Phyllis G. Supino and Jeffrey S. Borer, 2012, 276 pages, Springer, $149.95
Review by Norman M. Goldfarb

“Principles of Research Methodology: A Guide for Clinical Investigators” is not a comprehensive guide to clinical research but, for the topics it does address, it does so exceptionally well, assuming that the reader is most interested in the how and why. The rather generic chapter headings below do not do justice to the authors’ practical insights.

As the following excerpt demonstrates, the book provides clear, detailed and practical explanations of topics not always addressed in such books:

**Run-In Periods**

It is common to have patients enter a run-in period between the time that they qualify for a clinical trial and the time that they begin active involvement, i.e., are started on the actual study intervention. There are several reasons for using a run-in period. Common reasons include establishing final patient eligibility, demonstrating stability, and assessing compliance. Not all inclusion/exclusion criteria may be completely available for assessment at the time of screening, especially if there is a requirement for recent laboratory or diagnostic information. A run-in period just before starting a new drug or a special procedure may be used to allow for obtaining any assessments that must be current (e.g., an echocardiogram to document presence of abnormal cardiac function) to confirm that the patient actually has the medical condition required for study participation. A run-in period also may be used to demonstrate that a patient has the required status of the condition being studied. For example, it may be required that a patient have stable symptoms while taking all standard treatment for the condition in order to minimize difficulty in interpreting changes in the patient’s condition after starting active treatment. If the patient was not stable or if other treatments were started after the study intervention, it would be extremely difficult to assess the cause of a change in the patient’s condition. Another common reason for using a run-in is to assess the tolerability of the study intervention. A patient may have difficulty complying with an intervention if it produces significant side effects or is difficult to administer. Furthermore, patient compliance may be influenced by other patient conditions or behaviors, e.g., substance abuse or alcoholism. A run-in period may be useful to assess the patient’s likelihood of complying with and completing all study requirements.

Treatment during run-in periods may vary. If the purpose is only to acquire final inclusion/exclusion information, no treatment may be needed. Obviously, if the purpose is to assess stability and/or compliance with an intervention, such as a study drug, it would be necessary that it be given according to the same regimen that would be used in the active phase of the study.

This phase usually involves either active study, intervention in all patients if its purpose is primarily to assess tolerability, or placebo in all patients to assess patient
compliance for reasons other than tolerability of the intervention. Clearly, the patient is kept blinded to treatment if the active phase is to be double-blinded.

Finally, the duration of the run-in period should be as short as possible, typically not more than 2-3 weeks. In general, less time is needed to obtain laboratory tests, and more time would be needed to assess tolerability or compliance. The problem with excessively long run-in periods is that patients may change during this time. In cases where a run-in period has had to be extended, it is common practice to terminate that patient from the study at that point and restart him/her as a “new patient” in the screening phase. Another potential risk and criticism of run-in periods is that they may introduce bias by selecting the better responders to the active study intervention.

The book includes 12 chapters:
- Overview of the Research Process
- Developing a Research Problem
- The Research Hypothesis: Role and Construction
- Design and Interpretation of Observational Studies: Fundamental Issues in Evaluating the Impact
- Protocol Development and Preparation
- Data Collection and Management in Clinical Research
- Constructing and Evaluating Self-Report Measures
- Selecting and Evaluating Secondary Data: The Role
- Sampling Methodology: Implications for Drawing
- Introductory Statistics in Medical Research
- Ethical Issues in Clinical Research
- How to Prepare a Scientific Paper

The book is available in bookstores.

Reviewer
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