“It’s Great! Oops, No It Isn’t: Why Clinical Research Can’t Guarantee The Right Medical Answers”


Review by Norman M. Goldfarb

“It’s Great! Oops, No It Isn’t: Why Clinical Research Can’t Guarantee The Right Medical Answers” is not, as the title suggests, an exposé of the failings of clinical research. It turns out to be a practical guide that pays a lot of attention to what can go wrong, to maximize the chances that things will go right. The book focuses on “seven deadly flaws”:

- The unknown population
- The imperfect sample
- The unequal treatment groups
- The uncontrolled experimental setting
- The breakdown of blinding
- The impractical result
- The insufficient sample size

The following extracts illustrate the book’s discussion of imperfect samples and impractical results:

Based on recruiting strategies, it’s tempting to describe volunteers as the “UN” people. They tend to be unemployed, uninsured, unhealthy and unselfish. If you’re not working and don’t have health insurance, a clinical trial may be quite attractive. Unfortunately, the unemployed and uninsured combination may also mean subjects are in poor health generally. On the other hand, individuals may be motivated to join a trial for commendable reasons. They believe their service will help find cures or alleviate suffering. Their unselfish, altruistic justification also means they are likely to be especially good research subjects. They may accept all protocol restrictions, and their behavior increases the chances of a positive result. However, too many subjects like this can also create a bias because such dedication is lacking in the general population. Anything that causes the sample chosen for a clinical trial to be different from the population of interest reduces study usefulness and should be considered when interpreting the findings from clinical research.

Ironically, an investigation reported in the American Journal of Geriatric Cardiology examined study volunteers and found that older people tend to be more willing than younger people to participate in clinical trials. Older people generally have fewer time constraints and a greater desire to help the next generation by advancing medical research. Nevertheless, elderly subjects usually are under-represented, especially in certain research areas. For example, trials of NSAIDs (non-steroidal anti-inflammatory drugs) often include an under-representation of elderly subjects. Yet these drugs are commonly used in older people because of the high number of arthritic disorders they have. A report in the Canadian Medical Association Journal found that, in the major drug trials evaluating NSAIDs, only about two percent of
patients were 65 years of age or over, and less than one tenth of one percent were over 75. The report pointed out that, in practice, elderly people were among the largest users of this class of drugs and had the highest incidence of serious drug-related side effects.

It’s also true that the behavior of a private patient is far less restricted than that of a subject in a trial. Researchers love subjects who are willing and able to comply with the demands placed on them by the protocol, but that behavior is atypical, and when the drug is used by the more cavalier and less compulsive patients found in a typical doctor’s practice, the clinical trial result can be quite different in the new setting. Good protocol compliers may be heroes when it comes to clinical studies, but they are saboteurs when it comes to study usefulness. If rigid compliance with a diet, taking a drug exactly on the prescribed schedule, and faithful exercising helped a new treatment become successful, all bets might be off when the drug is given to less disciplined patients treated by a family physician.

The book includes 26 chapters:

- Medical Research — Searching for Answers
- The Case-Control Method — Looking Backward
- The Cohort Study — Watchful Waiting
- The Clinical Trial — The Gold Standard
- Comparing the Methods — Qualitative Differences
- The Protocol — The Guiding Light
- The Control Group — Leveling the Playing Field
- Measurements — They’re Never Exact
- Bias Control — A Closer Look at Blinding and Randomization
- Utility — Are Clinical Trial Results Useful?
- Research Discrimination — Inadequately Tested Populations
- Seven Deadly Flaws — The Clinical Trials’ Achilles Heel
- Statistics — Was the Finding Significant?
- Analysis Issues — A Lot of Choices
- Meta Analysis — An Alternative to Large Trials
- Research Results That Clashed — What’s the Right Answer?
- Hormone Replacement Therapy — The Silver Bullet that Misfired
- Publishing — Getting the Word Out to Doctors
- The Public Forum — Sharing the News with the Public
- Protocol Development — Getting Discoveries to the Market
- Medical Innovations — Regulators, Resources and Results
- Science and Politics — A Troubling Mixture
- Research Misconduct — Irresistible Temptation
- Postmarketing Surveillance — An Imperfect System
- Regulatory Reform — Changes Needed
- Journey’s End — A Call for Action

The book is available in bookstores.
Reviewer

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