Strategy and Statistics in Clinical Trials
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On those fleeting occasions when I regain my sense of wonder, I marvel at the complexity of things in general. During my own short lifetime we have put a man on the moon and observed ancient organisms on deep ocean floors. Computers and cell phones have become near necessities, and even inexpensive cars do not often break down (a minor miracle to my reminiscing mind). Being adaptable, we have become accustomed to the most elaborate of devices. And we take them for granted as one might have a kitchen knife some hundreds of years ago.

Life sciences have not lagged behind. We have mapped the basic structures of life and increasingly have come to understand the human body and the substances circulating in it. Using this knowledge, we have developed products that can alter and regulate both mind and body. To be sure, there is still much to be done, and hopefully there always will be. But we have achieved a great deal already.

Now and again I talk with people outside my field and find it both fascinating and frustrating. Fascinating because there are so many incredible developments out there, and frustrating because it is nary impossible for me to know enough to truly appreciate them. Our world has become so complex that it is difficult for any one individual to have little more than a single area of expertise. And even this can only be had with a great deal of effort. While I might wish it otherwise—and I do—this is the way it is. But more disconcerting is that specialization often impedes the work of people who should be working together: professionals from disparate fields who must team up to get things done.

My own area is statistics. Within it, I specialize in biostatistics. Specializing even further, I have gained some expertise in my discipline's methods in clinical trials. And when I return to Earth from my contemplative heights, I find there is often great disorder in these trials. At times it seems to me a wonder they even work at all. Clinical studies are planned and executed by dozens of people both within and without the organization. In great measure their success depends on
the good graces of harried physicians and volunteering subjects who are often very infirm. A single trial may be conducted across many centers, countries, and even continents, making its management that much more difficult. And studies often take years to complete, during which time anything can happen and generally does.

So like most complicated ventures, success depends on numerous processes and professionals with varied expertise. A partial list of specialties includes finance, clinical, regulatory, marketing, toxicology, biology, physics, materials engineering, software engineering, medical monitoring, analytic chemistry, and information technology. And yes, statistics. If we cannot coordinate effectively between these specialties, our trials will be suboptimal at best.

Paradoxically, our complex products demand both added specialization within fields and ever more dialogue between them. So while we ask our people to know more about less, we increasingly require that they communicate with others in the same predicament. And as specialization deepens, interactions between experts become more difficult.

Simply put, for a clinical trial to work people must talk to one another. And while it is impossible for any to fully understand all others, each must know enough for the dialogue to be useful. This then brings me to my book's objective.

Statistics—be they more complex or less—are involved in virtually every clinical trial. The discipline provides essential input in the planning stage on issues like trial design, choice of endpoints, and sample size. And it supplies the language for communicating outcomes using simple statistics like mean and median, and more sophisticated tests for inferring conclusions. This is my work, and I like it. And in medical research, statistics is important work. But just because it is, I do not expect others to take year-long courses in it. Indeed, among those who already have, many are perfectly happy to leave this year behind them.

For a large number of clinical trial professionals my discipline is a black box they are content to leave as is. But this must not be if we are to design, conduct, and report trials effectively. In the chapters that follow I aim to cast some light into this box.

This book explains clinical trial statistics in the simplest language I can manage. There is very little formal mathematics in it and almost no formulas. More importantly, I place the discipline in the wider context of clinical trials—the inevitable constraints of time and money, and limitations associated with clinical practice. I also relate trial design and analysis to its intended audience—to those needing the information it provides, such as regulators, scientists, physicians, corporate managers, investors, and others.
The book is a practical guide. It is based on years of applied experience, much of it my own. In it I present numerous examples from pharmaceuticals, devices, and other products. Crucially, I describe how statisticians must consider a trial's overall needs and reconcile to them. And I show how at times it must be the other way around. Be that as it may, a clinical trial cannot maximize any one discipline's preferences. But it can optimize—and it must.

For nonstatisticians this book provides strategies for productive dialogue with those who are; it describes the statistician's approach to clinical trials and the basic tools at the statistician's disposal. For statistical professionals this is a "how-to" guide for interacting with the many others working on clinical studies. In this book I describe—for the benefit of statisticians and nonstatisticians alike—the numerous considerations involved in clinical studies and their effect on a trial's statistics.

Competence and native intelligence will get you a long way in most every field. But little apart from experience can give you experience. Well, I present here what I believe to be the next best thing: other people's experience. I describe the central topics of clinical trial statistics with real-world examples, recounting clinical tales and their morals. I have to the best of my ability written a book to facilitate communication between the field I have chosen and those I have not.