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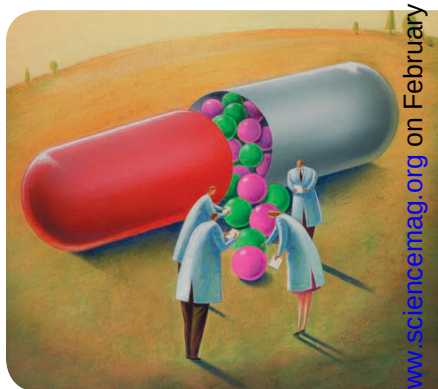
Rethinking Clinical Trials

THE BIOMEDICAL INDUSTRY SPENDS OVER $50 BILLION PER YEAR ON RESEARCH AND DEVELOPMENT and produces some 20 new drugs. One reason for this disappointing output is the byzantine U.S. clinical trial system that requires large numbers of patients. Half of all trials are delayed, 80 to 90% of them because of a shortage of trial participants. Patient limitations also cause large and unpredicted expenses to pharmaceutical and biotech companies as they are forced to tread water. As the industry moves toward biologics and personalized medicine, this limitation will become even greater. A breakthrough in regulation is needed to create a system that does more with fewer patients.

The current clinical trial system in the United States is more than 50 years old. Its architecture was conceived when electronic manipulation of data was limited, slow, and expensive. Since then, network and connectivity costs have declined ten thousand–fold, data storage costs over a million-fold, and computation costs by an even larger factor. Today, complex and powerful applications like electronic commerce are deployed on a large scale. Amazon.com is a good example. A large database of customers and products form the kernel of its operation. A customer's characteristics (like buying history and preferences) are observed and stored. Customers can be grouped and the buying behavior of any individual or group can be compared with corresponding behavior of others. Amazon can also track how a group or an individual responds to an outside action (such as advertising).



We might conceptualize an "e-trial" system along similar lines. Drug safety would continue to be ensured by the U.S. Food and Drug Administration. While safety-focused Phase I trials would continue under their jurisdiction, establishing efficacy would no longer be under their purview. Once safety is proven, patients could access the medicine in question through qualified physicians. Patients' responses to a drug would be stored in a database, along with their medical histories. Patient identity would be protected by biometric identifiers, and the database would be open to qualified medical researchers as a "commons." The response of any patient or group of patients to a drug or treatment would be tracked and compared to those of others in the database who were treated in a different manner or not at all. These comparisons would provide insights into the factors that determine real-life efficacy: how individuals or subgroups respond to the drug. This would liberate drugs from the tyranny of the averages that characterize trial information today. The technology would facilitate such comparisons at incredible speeds and could quickly highlight negative results. As the patient population in the database grows and time passes, analysis of the data would also provide the information needed to conduct postmarketing studies and comparative effectiveness research.

Today's e-commerce systems started small and took nearly 20 years to develop. Adapting this kind of capability to medical information would be a monumental undertaking. Initiating and overseeing it would be an appropriate task for the professional societies. There are encouraging signs, including a call in 2004 by the American Medical Association for public registries of drugs, as well as a proposal for trials that incorporate feed-forward mechanisms.* Another proposal would allow patients to choose between medicines whose efficacy has been determined in different manners.† There is also a suggestion to use control of pricing to encourage drug developers to move forward in a "progressive" trial design.‡ Ideas, however, are not enough. We need the professions to mobilize and take advantage of this enormous opportunity.

– Andrew Grove

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*H. Hvitfeldt *et al.*, *Qual. Manag. Health Care* **18**, 247 (2009). †B. J. Madden, *Free to Choose Medicine* (Heartland Institute, Chicago, IL, 2010). ‡M. Boldrin, S. J. Swamidass, "A New Bargain for Drug Approvals," *Wall Street Journal*, 25 July 2011.

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