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Ushering in a New Era of Open Science Through Data Sharing

The Wall Must Come Down

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IT MAY APPEAR THAT THE CLINICAL RESEARCH ENTERPRISE is functioning well, even thriving. Nearly 30 000 trials globally are recruiting patients,[1] and results from 75 trials are published daily in biomedical journals.[2] However, there is a crisis, with an attendant opportunity, that requires change. A wall surrounds much of these clinical research data, sequestering knowledge, impeding the free flow of information, and obscuring a clear view of the totality of evidence relevant to many research questions and clinical decisions.

Nearly half of clinical research trials are never published.[3,4] Moreover, publications are often incomplete, selectively reporting favorable outcomes and infrequently reporting relevant safety findings.[3,5] Motivations and explanations for this phenomenon vary, but whether intended or not, selective publication distorts the medical evidence and inhibits the flow of information that is vital to decision making by patients and their clinicians.

The Importance of Data Sharing

To ensure that patients and clinicians are able to make fully informed decisions about pharmaceutical agents, biological products, and medical devices tested through clinical trial research, an era of open science through data sharing is necessary. This step to establish a more transparent scientific process has already been taken by other fields, including genetics, physics, molecular biology, and the social sciences. Sharing maximizes the value of collected data and promotes follow-up studies of secondary research questions using existing data. Sharing also minimizes duplicative data collection, which in turn reduces research costs and lowers the burden on human research participants while positioning clinical trial data as a public good. Importantly, sharing maximizes the value of collected data, promoting follow-up studies of secondary research questions. Sharing also respects the contributions of the patients who consented to participate. Data management and analytic decisions have critical implications for interpretation and should be evaluable. If science is to be progressive and self-correcting, then data, not just summary conclusions, must be open to independent scrutiny. In addition, multiple examinations of clinical trial data are often necessary, particularly when pharmaceutical, biologic, and medical device sales depend so substantially on the results of only a few large clinical trials.

Clinical trial investigators and funders have raised several concerns about data sharing. Some investigators are hesitant to share data because of associated financial costs, and the possibility of inappropriate data uses—including misleading secondary analyses—and because sharing may foster competition that they consider unwelcome.[6] Trial funders, particularly industry—the largest funder of clinical trial research—have argued that clinical trial data are proprietary and that data sharing "could not only lead to misinterpretation of the risks and benefits of medicines, and potentially interfere with patient confidentiality, but would also deter future medical innovation if would-be competitors could access confidential commercial information."[7]

These concerns, while understandable, should not stand in the way of compelling societal interests. Because of their role in generating the data, trialists will necessarily have first access to the data for analysis and publication. However, the ultimate goal should be to share data and knowledge. To reward the trialists' contributions to work done by others, protocols for sharing and methods to acknowledge and cite trialists' contributions need to be developed so that the more data are used, the more credit trialists receive. Moreover, transparency of data and protocols, including details about the interventions, recruitment, and other technical issues related to trial conduct, as well as the complete results, should allay the concern that only those who conducted a study can understand the data. As for the interest of funders, the privilege of selling a medical product should be accompanied by a responsibility to share all clinical research data relevant to evaluating the product's risks and benefits.

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Recent Steps Forward

Although more work is required to bring down the wall around the clinical trial research enterprise, progress has been made. In 1997, the Food and Drug Administration Modernization Act required that the public be provided access to information about ongoing clinical trials, leading to the creation of ClinicalTrials.gov, an online registry maintained by the National Library of Medicine. However, it was not until 2005, when the International Committee of Medical Journal Editors began requiring trial registration as a condition of publication, that ClinicalTrials.gov became a prominent source of information. In 2007, the Food and Drug Administration Amendments Act broadly expanded the scope of ClinicalTrials.gov. The act required registration of all non−phase 1 trials at inception (before patient enrollment) and a report of results, including basic results such as primary and secondary outcomes and adverse events, within 12 months of study completion.

These efforts have improved the information available to patients and clinicians, helping to mitigate the problems with selective publication and outcome reporting. However, these efforts have not solved the problem. Compliance with ClinicalTrials.gov is inconsistent among investigators, including those who are federally funded.[8] Control of information resides with those who generate it. Independent evaluation of analyses reported on ClinicalTrials.gov is often impossible, as sharing of raw data is not legally required, and investigators are allowed considerable discretion regarding what they choose to report. There have been too many prominent examples in which independent analyses of trial data, often made available through litigation but sometimes through public release by the National Institutes of Health, revealed important insights about medical products' relative balances of benefit and harm that were neither identified nor reported by those who generated the data. Examples include well-known medications such as digoxin, rofecoxib, rosiglitazone, and oseltamivir.

Fortunately, further changes continue to occur. Some funders, such as the Gates Foundation and the National Institutes of Health, have policies to promote data sharing. In addition, Medtronic and GlaxoSmithKline—large, for-profit industry leaders—have taken different but promising paths toward data sharing during the past year. However, details of the GlaxoSmithKline effort are pending, and the Medtronic effort, which entailed full release of data, involved only 1 of its products. Last October, the Institute of Medicine held a 2-day workshop that brought together diverse stakeholders including funders, journal editors, investigators, and patients, not to discuss whether clinical trial data should be shared, but to explore how it can best be shared to benefit patients.

Clinical trial funders, in particular drug manufacturers, may soon have no choice but to share. While the European Medicines Agency has been releasing clinical trial reports on request since 2010 as part of its access-to-documents policy, the agency recently announced that it will provide full access to complete clinical trial data sets to outside investigators beginning in 2014.

A New Future for Clinical Research

The possibility of a new era of research is within reach. The wall is crumbling, albeit slowly, and momentum is gaining toward open science through data sharing. The imperative is to find successful pathways to share data that are attentive to all stakeholder needs, yet serve the best interests of society. The full potential of the clinical research enterprise can be realized by creating a culture that promotes sharing and provides credit to those who do—and consequences for those who do not.

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