A SPRINT to the Finish

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When investigators enroll patients in a clinical study, they make an implicit contract with each participant. Through the data and safety monitoring board (DSMB) mechanism, they fulfill the first part of the contract — protecting the participant from avoidable harm that might result from participation in the trial. They fulfill the second part of the contract — the commitment to honor the time at risk that the participant spent in the trial — by deriving the clearest and most clinically directive information possible from the data gathered during the trial. This task takes tremendous time and energy.

The SPRINT (Systolic Blood Pressure Intervention Trial) investigators now report in the Journal the results of a National Institutes of Health (NIH)–sponsored trial studying the impact on major cardiovascular events of a lower systolic blood-pressure target in adults with hypertension. To the surprise of many, the trial was stopped on September 11, 2015, years earlier than planned. The leadership of the National Heart, Lung, and Blood Institute (NHLBI) stopped the trial on the recommendation of the DSMB, which had identified a survival benefit in patients assigned to the lower blood-pressure target.

When the study was stopped, the NIH immediately notified the participants that those in the low-target group had done better than those in the usual-care control group; the public was also notified, although a full report of the study was not yet available. The investigators, who were also taken by surprise, then hunkered down to the serious business of understanding the available data, knowing that the data set they had would change, since close-out visits are still ongoing.

Although unraveling the clinical messages buried in a data set may sound like a simple task, it is not. Rarely does a trial’s clinically important message jump out fully formed. Instead, the process requires detailed analyses that weigh the risks and benefits of the study intervention as translated into a clinical care setting.

The trial investigators are uniquely qualified to analyze the data, and their only agenda is a meticulous, fair, and informative reporting of the study results. Not only are they the ones who delineated the end points, crafted the inclusion and exclusion criteria, and collected the data, they are also the ones who best understand the adverse events. The process requires a deep knowledge of the study design and, most of all, time for scrupulous analysis and thoughtful reflection. Even in this rapid-fire information age, there is no substitute for serious thought, and that takes time.

We were therefore surprised by the call from Topol and Krumholz for immediately “placing the data on the NIH website.” We believe that it is critical to give the investigators, on behalf of the study participants, who invested years of their lives in the study, the opportunity to see what led the sponsor to stop the trial and then the opportunity to distill a clinical message from it. There are cogent reasons to follow this approach rather than put trial data in the public domain before those who gathered the data have had a chance to analyze it.

Although no one denies the importance of treating hypertension, the clinical message from SPRINT is a matter of public health urgency and not an emergency. The subtleties of the clinical
message need to be teased from the data. To put the issue in perspective, the investigators took about 8 weeks to prepare their study for publication; they had previously spent over 250 weeks conducting the trial and perhaps another 50 to 100 weeks getting the trial ready to enroll patients at all. Through their perseverance and hard work, the data were accrued and an important clinical question has been addressed. The investigators have spent the past 5 years thinking about and working on the study question, and they are the ones best qualified to undertake the first interpretation of the data. Once their interpretation is in the public domain, scientific discourse on the strengths and weaknesses of the trial design, the gathered data, and the clinical directions should follow.

The manuscript reporting on SPRINT arrived in our office 4 weeks after the trial was stopped. That manuscript was reviewed rapidly by multiple outside peer reviewers, a statistical consultant, and several editors. Their critiques and queries led to two rounds of substantial revision. After expedited editing of the manuscript and preparation of the figures, the report has been published to coincide with the investigators’ presentation at the meeting of the American Heart Association. Together with this important report, Journal readers have a pair of expert commentaries in an editorial and a Perspective article. There is also a short Quick Take video summary of the article and a Clinical Decisions article in which readers can participate in a poll and comment on the key questions and clinical concerns raised by SPRINT.

This clinical trial will change practice, and we are proud to publish it and to defend the importance of the expedited peer-review and publication process that it has undergone. The report is now in the public domain, and the investigators’ data interpretation, analysis, and clinical discussion are open to examination and comment. We understand that in the months ahead the underlying data from this taxpayer-funded trial will be put in the public domain by the NHLBI. We agree with the importance of making those data open and available to others. But with the article now published, physicians and the public have a detailed, critical, peer-reviewed report from the investigators who conducted the study and know it best.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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