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EDITOR'S PAGE

Unraveling the Complexities of Statistical Presentation

Why it Is Important

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Over the course of the past month in the *Journal*, we have published a 4-part series on statistics for clinical trials from Professor Stuart Pocock and his colleagues, which included "Making Sense of Statistics in Clinical Trial Reports" (1), "Statistical Controversies in Reporting of Clinical Trials" (2), "Design of Major Randomized Trials" (3), and "Challenging Issues in Clinical Trial Design" (4). I have been most impressed with the clarity with which Pocock et al. (1-4) communicated the challenges and presented recommendations on these complex topics. In my opinion, this is a must-read series for all of us who are engaged in caring for patients, reading the literature, and conducting clinical trials in the field of cardiovascular medicine. We have been so encouraged by the outcome of this statistics series that the *JACC* board and I have decided to select several additional timely topics and have those areas of interest explicated across 4 successive papers in forthcoming issues of the *Journal*.

I initially commissioned this series to appear in 4 sequential issues as a response to widespread confusion among the clinical community with regard to statistics in the design and presentation of clinical trials. We have published this series with the hope of informing and creating a dialogue for improvement among the clinical community. For instance, there has been an obsessive focus on p values in recent years. Yet, p values can be grossly misinterpreted. As an example, a p value that may be very significant in a study with a large population or a meta-analysis may not represent a clinically important effect when treating patients in our daily lives. As another example, authors often present the relative risk rather that the absolute risk difference, the latter of which has more value to patients. Thus, the decrease of an event rate from 4% to 2% is often reported as a 50% decrease, which is the relative risk reduction, but the absolute decrease is 2%. To overcome some of these challenges, it is tremendously important that the statistician, writers, and researchers of a trial maintain a close relationship throughout the process.

Some of the considerations with the presentation of statistics recently became apparent through the publication of SPRINT (Systolic Blood Pressure Intervention Trial) in the *New England Journal of Medicine* (5). This landmark trial will have a widespread effect on increasing the use of blood pressure-lowering medications in the general population. Thus, in interpreting the trial's findings, it is important to consider both relative and absolute risk differences for both efficacy and safety outcomes in a consistent manner. For instance, in the discussion section, the authors wrote: "Trial participants assigned to the lower systolic blood-pressure target (intensive-treatment group), as compared with those assigned to the higher target (standard-treatment group), had a 25% *lower relative risk* of the primary outcome" (5) (italics in quotation marks included for emphasis). In actuality, this is an absolute risk reduction of 5.2% versus 6.8% patients with a primary outcome over a median 3.26-year follow-up. However, in our charge as investigators to assess both the safety and efficacy of therapies for our patients, we need to be very clear when presenting adverse outcomes. When reporting on the serious adverse events, the authors wrote that 4.7% of the intensive-treatment group and 2.5% of the standard-treatment group had serious adverse events that were classified as possibly or definitely related to the

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intervention (5), which is a relative risk increase of 88%. Also, the authors reported an important excess risk of acute kidney injury or acute renal failure in the intensive group: 4.4% versus 2.6% patients affected, which is a relative risk increase of 71%. This trade-off between efficacy and safety (benefits and risks) is essential in achieving cautious balanced conclusions from this trial.

Importantly, the SPRINT trial's patient population deserves attention as well. The investigators excluded anyone younger than 50 years of age, as well as patients with prior stroke (5). In addition, they excluded diabetic patients—a population that comprised 29.1 million Americans in 2012, or nearly 10% of the U.S. population (6). Thus, we, as clinicians, have to be particularly cautious when interpreting these results in the overall hypertension population, because the patients included in this study are 20% of our actual hypertensive patients seen in practice (**Table 1**) (7). Nevertheless, these comments are in no way an attempt to discount the importance of the SPRINT trial that was conducted with the highest degree of standards and which will have an effect in treating hypertension. I am simply attempting to call attention to the delicacy of presenting statistics.

TABLE 1 Generalizability of U.S. Population, Including All Patients Treated or Untreated With Hypertension, Using the SPRINT Eligibility Criteria

Population	Number in Millions	Percent (95% CI) SPRINT Eligible
All U.S. adults	219.4	7.6 (7.0-8.3)
Hypertension	68.5	20.0 (18.6-21.5)
Treated hypertension	49.2	16.7 (15.2-18.3)

The percentage of U.S. adults who meet the eligibility criteria for SPRINT. Data from Bress et al. (7).

CI = confidence interval; SPRINT = Systolic Blood Pressure Intervention Trial.

In conclusion, it is our responsibility as clinicians and investigators to carefully conduct trials and communicate those data in a straightforward and precise manner. To do that, statisticians and manuscript authors need to maintain a close-knit relationship throughout the process to ensure alignment in the interpretation and presentation of the data. In addition, it is important that the cardiovascular research community develop practical standards and similar language around this process. We truly hope that the 4-part review series by Pocock et al. (1–4) has helped to contribute to the published data, and more importantly, that it becomes a useful companion to the community's paper writing and to clinicians' understanding of published reports.

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