Increasing Statistical Power in Breast Cancer Clinical Trials

The recently reported decline in breast cancer mortality in the United States and United Kingdom has been attributed to multiple factors, including the increased use of screening mammography, adjuvant chemotherapy and endocrine therapy with tamoxifen. These advances are directly attributable to practice standards that have been shaped by data from randomized clinical trials. The human impact of these reductions in breast cancer mortality has led to larger cooperative studies with the statistical power to detect modest, but important, improvements in outcomes. A fascinating footnote is the ATAC adjuvant trial — now with 47 months of follow-up — that has about 10 times as many patients as initial adjuvant studies launched in the 1970s.

HISTORICAL PERSPECTIVE

“Arguably one of the most important advances during the last 50 years has been the introduction of prospectively randomized controlled trials to clinical medicine. Such trials provide information about the natural history of a disease and evaluate the worth of a particular therapy. Moreover, they allow for testing of biological hypotheses and, therefore, provide a mechanism whereby the scientific method can be applied to clinical problem-solving. By replacing anecdotal information (which has influenced therapeutic decision-making in the past) with more credible and substantive data, clinical trials play a major role in transforming the practice of medicine from an art to a science. As a vital component of the “research chain,” clinical trials are an essential link between the laboratory and the clinic, providing means for determining whether the use of laboratory findings in the treatment of patients is justified. Without trials, much of the scientific information currently being reported could not be evaluated for its therapeutic worth.”

—Bernard Fisher, MD

News from the Commission on Cancer of the American College of Surgeons 1991;2(2).

TRIALS AND CLINICAL DECISIONS

“The randomized controlled trial has become the gold standard for evidence-based medicine: through the unbiased comparison of competing treatments it is possible to accurately quantify the cost-benefits and harm of individual treatments. This allows clinicians to offer patients an informed choice and provides the data on which purchasing authorities can make financial decisions. We, of course, subscribe to this view but also recognize this as a gross over-simplification of the power of the randomized controlled trial. The randomized controlled trial is the expression of deductive science in clinical medicine. Not only is it the most powerful tool we have for subjecting therapeutic hypotheses to the hazard of refutation, but also the biological fallout from such trials should allow clinical scientists to refine biological hypotheses. Trials of treatments for breast cancer have, at least twice, contributed substantially to a paradigm shift in our understanding of the disease.”

—Michael Baum, CMB, FRCS; Joan Houghton, BSc

INTERNATIONAL META-ANALYSIS

There are thousands of randomized trials in the world, which will lead to “zigs and zags” in the data. And, the “zags” are probably the ones that are going to be the most noteworthy and the most emphasized in meetings, because they look odd. So if you take lots of trials and then pick out the ones where the results look out of line with the other trials together, you get reliable knowledge. If you take lots of trials and then pick out the ones where the results look odd, you’ve got to systematically bring where the results look out of line with the other trials together, you get reliable knowledge. If you take lots of trials and then pick out the ones where the results look out of line with the other trials together, you get reliable knowledge. If you take lots of trials and then pick out the ones where the results look odd, you’ve got to systematically bring where the results look out of line with the other trials together, you get reliable knowledge. 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