Evidence-Based Medicine Case Studies

PROLOGUE: Clinical trials for evidence-based medicine (EBM) can stop traditional therapies dead in their tracks; likewise, they can introduce new drugs and procedures to medical practice. In the 1990s clinical trials disproved the benefits of anti-arrhythmic drugs to prevent heart attacks in patients with a history of prior heart attack. It was only from the findings of clinical trials that these therapies were found to do more harm than good. These findings have spurred the EBM community to promote clinical trials, particularly randomized controlled trials (RCTs), for the introduction of new drugs, techniques, and devices. Papers in this section look at the history and conduct of RCTs. Collectively, they reveal that even the best-intentioned, most rigorously conducted RCTs are not immune from politics, economics, or the ambiguities of science.

At the end of September 2004, the Centers for Medicare and Medicaid Services (CMS) extended the coverage for implantable cardioverter defibrillators (ICDs), one of the interventions analyzed here. Many questions remain about ICDs, mainly which group of patients benefit and who bears the cost of finding out. Mark Hlatky, a professor and cardiologist at Stanford Medical School, and his co-authors, Gillian Sanders and Douglas Owens, analyze the evidence available to the CMS in making its decision. The costs of ICDs, their life-saving potential, their cost-effectiveness compared with other therapies, and other considerations had to be acknowledged in the decision-making process. Marshall Stanton of Medtronic, one of the makers of ICDs, offers a critical perspective, particularly regarding the decision allowing cost-effectiveness to be used as a tool in decisions about coverage for ICDs and other technologies.

Next, Scott Ramsey and Sean Sullivan of the University of Washington offer a case study of the RCT for lung volume reduction surgery (LVRS), a treatment for severe emphysema. Ramsey and Sullivan describe the raucous political atmosphere that surrounded the establishment of the RCT, the objections to holding a trial, the rigor with which the trial was conducted, and ultimately the factors that led the CMS to extend coverage to a subset of emphysema patients.

Thomas Fleming then discusses the difficulties inherent in determining what are useful measurements. Clinical trials often must use a measurement that is not the final outcome but a marker—a surrogate endpoint—along the way to the final outcome or endpoint. Fleming, a professor of biostatistics at the University of Washington, evaluates the pros and cons of the surrogate approach and casts a critical eye on the U.S. Food and Drug Administration's adoption of accelerated approval for interventions that are “reasonably likely to predict clinical benefit” but may not have any long-term benefit or effect on the disease process itself.