Why Evidence Matters in Innovation

The importance of clinical evidence in today's medical practice.

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It is axiomatic that health care costs are escalating at an unsustainable rate that, until recently, exceeded that of the economy as a whole.[1] The growth is, in large part, a result of inpatient procedure-based hospital care. Appropriately, focus has been centered on those interventions with undefined or marginal long-term clinical benefit. Third-party payors are placing increasing scrutiny on these procedures. Objective evidence of clinical benefit and cost-effectiveness is becoming a prerequisite to payment for many interventions.

In their 2006 book *Redefining Health Care: Creating Value-Based Competition on Results*, Michael E. Porter and Elizabeth Olmstead Teisberg advanced the concept of value-driven health care.[2] Simplistically, value was defined as the ratio of quality to cost. In a pure market-driven model, consumers (patients) would be able to accurately assess quality. Costs (price) would be well-defined a priori and also borne directly by the consumer.

VALUE-DRIVEN HEALTH CARE?

Current health care paradigms in the United States and elsewhere are far from value-driven. Patients and even health care providers are often unable to accurately judge quality. There exist few readily accessible and objective quality indices.[3] What few outcome measures do exist are highly dependent on the severity of illness and thus of marginal utility when applied to a specific patient or a unique clinical scenario. Price, a driver of non–health care decisions, has not been a major factor in health care. A patient's choice of treatment is usually made at a time when the ultimate cost of care cannot be accurately estimated by his or her providers because the complexity of the treatment is often impossible to predict prospectively. Of possibly greater importance is the isolation of the consumer from the economic burden of treatment. Absent a high-deductible insurance plan, economic issues play a marginal role in a patient's decision-making process.[4]

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Pricing issues are neither the subject of this article nor likely to be soluble in the foreseeable future. By contrast, the objectification of quality is not only attainable but is rapidly becoming a prerequisite for payors and patients alike. Quality must be assessed in the context of at least three criteria to ensure comparability among different physicians, hospitals, and patients.

First, outcome measures must be standardized—that is, evaluated and reported in a consistent manner. As one example, comparing the risk of major adverse events after endovascular and open surgical aneurysm repair is only meaningful when similar definitions and time frames are used for both treatment groups. Second, outcome measures must be considered in the context of the baseline illness severity of the patients. For example, the risk of perioperative death in a New York Heart Association functional class III patient about to undergo aneurysm repair should not be estimated from a study of healthier patients. Last, outcome measures should be easily accessible to and understandable by physicians and the lay public. Only then are such data useful for guiding treatment decisions.

MEDTRONIC INITIATIVES FOR LONG-TERM EVIDENCE

The quest for evidence begins with the acquisition of useful clinical data from clinical trials performed before regulatory approval of a product. The design and execution of well-designed trials are based upon the reporting of standard, relevant outcome measures and specification of the baseline characteristics of the population being studied. Ideally, the sample size should be large enough to allow robust multivariable analyses that can identify individual predictors of outcomes. After product approval, postmarket studies should be performed to confirm the findings of the premarket trials in a real-world setting. These studies should be rigorously monitored and adjudicated in order to guarantee and maintain the quality and consistency of the collected data. Finally, clinicians should be cognizant of their own results, benchmarking against registries such as the Society for Vascular Surgery Quality Initiative.[5] Such societal registries offer a means for collecting enough baseline patient characteristics to allow severity-based outcome assessments.

The Medtronic Endurant® program (Medtronic, Inc., Minneapolis, MN) is a good example of an initiative designed to provide the outcome evidence necessary for the acceptance of a new innovation. The initial Endurant® clinical trials were designed with well-defined, standard definitions for outcome measures.[6] The study populations were well-characterized with respect to baseline comorbidities and anatomic measures, with a total of 274 patients studied in the European and United States premarket approval trials.

After regulatory approval in Europe and the United States, the Endurant device was evaluated in a large global prospective study, the ENGAGE registry.[7] ENGAGE was designed to assess long-term clinical outcomes within the context of contemporary, real-world use of Endurant in 1,263 patients. Such large sample sizes allow for subgroup analyses highly relevant to the risks that an individual patient might expect after aneurysm repair with the Endurant device.

The midterm results from the US IDE trial were presented in 2013, with an absence of aneurysm-related mortality, postimplantation rupture, migration, or open surgical conversion in 107 patients followed to 3 years.[8] Contemporaneous with this report, over 100,000 Endurant® II Stent Grafts have been implanted by now, approximately 5 years after the initial introduction of the device in Europe. The Endurant paradigm is being repeated by Medtronic's IN.PACT® program of drug-eluting balloons for lower extremity occlusive disease.[9] Outcomes of drug-eluting balloon therapy were evaluated with well-designed and monitored clinical trials followed by large registries similar in size to ENGAGE, enrolling a globally diverse, real-world series of patients.

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Medtronic's Endurant and IN.PACT programs serve as models for the evidence-based approach to any new medical device. In combination with continued data acquisition through participation in clinically rigorous registries along with the eventual incorporation of economic data, the ultimate "value" of these innovative devices will be defined in a manner consistent with that espoused by Porter and Teisberg. This is precisely the level of evidence that will be required if novel technologies are to be introduced into the armamentarium of the practicing clinician at this juncture, when intense scrutiny of quality and cost is becoming the norm. The bar for evidence-based medicine has been raised, and companies such as Medtronic are leading the way. ■

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