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INVITED EDITORIAL
Genetic Tests: A Search for Economy of Scale

Bruce Hillner

Department of Medicine, Medical College of Virginia, Richmond

Driven by the growth in new therapeutic and diagnostic technologies and increasing concerns about the magnitude of medical expenditures, economic evaluations of health-care services have increased markedly over the past decade (Smith et al. 1993). In an idealized world, the adoption of a new technology would be based upon its relative cost-effectiveness in the allocation of health-care resources. The Canadians have been at the leading edge in determining how attractive a new technology has to be to warrant utilization (Laupacis et al. 1992).

Currently it is rare to have economic data collected on a new technology before their release in the marketplace or as part of the definitive phase III evaluation used in licensure. Therefore, a common approach is to develop models, most commonly by using decision analysis, to simulate the anticipated consequences of switching to the new approach. Decision analysis is an analytic modeling technique that breaks a complex problem into a series of component parts by using a decision tree to systematically consider the options, their possible outcomes, and their temporal sequence in the solution of a problem (Pauker and Kassirer 1987). When applied to a medical question, it simulates a clinical trial of an infinite number of patients. Decision analysis is an explicit, prescriptive process that "quantifies the qualifiers," that facilitates decision-making under conditions of uncertainty by making fully explicit all of the elements of the decision, so that they are open for debate and modification.

Since I have assessed a variety of medical questions by decision analysis but have minimal knowledge of contemporary controversies in medical genetics, it is a pleasure to comment on the work published, in this issue of the *Journal,* by Noorani et al. (1996) from Toronto. They describe a cost-effectiveness analysis, using a decision-analysis model to screen for retinoblastoma, that compared two different approaches, the conventional one and a molecular technique. This is an important issue to clinical geneticists, since retinoblastoma is a common primary childhood malignancy.

As is typical of most cost-effectiveness models, Noorani et al. used data derived from published reports and their local experience. The most important variables were those based on their local experience: the sensitivity of identifying the molecular mutation and their detailed tracking of the direct costs incurred by using either strategy. It is important to note the crossover design used for the molecular-screened cohort: that is, if the molecular testing were negative, then these individuals subsequently had the conventional testing performed.

The finding that the molecular approach was far more cost-effective is unlikely to surprise many readers. This efficacy is due to the high sensitivity of the molecular technique, its modest cost, the relative crudeness of the current standard approach of serial examinations under anesthesia, and the fact that >85% of tested individuals do not have the disease. Although the authors made the conservative assumption that there will be no difference between the strategies in the management of patients and at-risk family members, I think that unidentified benefits will occur with the early, molecular identification.

The proposed molecular approach is an example of an infrequent combination in which a new technique both is superior by improving clinical outcomes and has lower financial costs. Such combinations warrant wide adoption, if it can be assumed that the genetic laboratory technical skills are generalizable to other settings. Unfortunately, broad, generalized statements about the cost-effectiveness of genetic testing cannot be made. Even if the issues of insurance and universal access to health care are excluded (Ad Hoc Committee on Genetic Testing/Insurance Issues 1995; Mehlman et al. 1994), the cost-effectiveness or cost saving of genetic testing will depend on many issues. For example, prenatal testing (Cuckle et al. 1995; Lieu et al. 1994) will be very different from testing at-risk or general populations. For individuals testing positive, practitioners would be expected to alter their monitoring and treatment behavior, such that substantial induced costs will definitely occur although the benefit might be uncertain. A subtle point

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Address for correspondence and reprints: Dr. Bruce Hillner, Department of Medicine, Box 980170, Medical College of Virginia, 1101 Marshall Street, Room 7015, Richmond, VA 23298-0170. E-mail: hillner@gems.vcu.edu

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related to cost-effectiveness analysis is its intrinsic incremental nature. As Noorani et al. show, a new molecular approach, compared with a clumsy traditional approach, is a clear winner. However, for most conditions the baseline is no monitoring. In this latter situation, testing optimally should be restricted to research settings such as the National Cancer Institute's proposed genetics network (Jenks 1996), unless future decision modeling can make a compelling case for early adoption on a condition-by-condition basis.

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