The Cost-Effectiveness of Clinical Sequencing

David L. Veenstra and P. J. Brooks*

February 12, 2015

*The authors are participants in the activities of the IOM Roundtable on Translating Genomic-Based Research for Health.

The views expressed in this discussion paper are those of the authors and not necessarily of the authors’ organizations or of the Institute of Medicine. The paper is intended to help inform and stimulate discussion. It has not been subjected to the review procedures of the Institute of Medicine and is not a report of the Institute of Medicine or of the National Research Council.
The types of evidence needed to support the use of genome sequencing in the clinic varies by stakeholder and circumstance. In this IOM series, seven individually authored commentaries explore this important issue, discussing the challenges involved in and opportunities for moving clinical sequencing forward appropriately and effectively.

The Cost-Effectiveness of Clinical Sequencing

David L. Veenstra, University of Washington; and P. J. Brooks,1 National Center for Advancing Translational Sciences, National Institutes of Health2,3

TOPIC DEFINITION

The IOM’s Roundtable on Translating Genomic-Based Research for Health has held several meetings over the past year and a half at which experts from diverse fields have discussed the challenges and opportunities of implementing sequencing using next-generation sequencing (NGS) technologies in clinical practice. These meetings have focused on issues related to analytic validity, variant validation, clinical utility, implementation, and, specifically, economics (IOM, 2013).

In our view, an overarching theme has been the need to define what is meant by the cost-effectiveness of NGS-driven genomic medicine. “Cost-effective” does not necessarily imply “cost saving.” If an intervention improves patient outcomes yet increases overall health care cost, it can quite easily be cost-effective if, for example, the cost per life-year gained or quality-adjusted life-year gained is commensurate with other commonly reimbursed health care technologies (Neumann et al., 2014). In other words, cost-effectiveness is about value—improving patients’ lives as efficiently as or more so than current clinical practice.

KEY CHALLENGES AND EVIDENCE NEEDS

A key challenge is to understand what evidence is needed to assess the value of clinical sequencing. Three major components to the economic value of clinical sequencing need to be better understood. First, what are the patient and economic impacts of improvements in clinical diagnosis, prognosis, and prediction with clinical use of clinical sequencing? In other words, if we improve diagnostic yield, for example, what is the clinical benefit (reduction in morbidity and mortality)? What are the consequent impacts on health care costs to payers, providers, and patients? Do these represent good economic value?

Second, what are the near- and long-term impacts of returning incidental findings to patients? Questions arise similar to those for intended findings. However, there are two crucial differences. First, a wide variety of incidental findings could be returned. What are the clinical and economic impacts of different return policies and practices, and which ones present greater economic value?

---

1 On detail from the National Institute on Alcohol Abuse and Alcoholism.
2 The authors are participants in the activities of the IOM Roundtable on Translating Genomic-Based Research for Health.
Second, incidental findings, at least for currently known clinically actionable findings, are fairly rare—in the ballpark of 1–3 percent. Gathering data on the value of incidental findings will require very large studies—most likely observational and implemented in real-world practice settings for efficiency. Furthermore, novel approaches to modeling long-term impacts will be needed, given the potential lifetime impacts of some incidental findings.

Third, what value do patients place on both intended and incidental findings from clinical sequencing that is not captured by clinical measures? Are novel patient-centered measures needed? How will and should patient-centered value drive use and inform guideline and reimbursement policies? For example, the families of patients with a rare genetic disease can spend years seeing different specialists in search of a diagnosis. In addition to the psychosocial impact, the financial burden of the so-called diagnostic odyssey can be substantial for both the family and the medical care system when one considers time missed from work, as well as the costs of clinician time and diagnostic testing. In some cases, patients undergo unnecessary medical procedures resulting from an incorrect diagnosis and/or experience complications, all of which could have been avoided by an accurate diagnosis from clinical sequencing. As the cost of clinical sequencing continues to drop, understanding the financial impact of not having a diagnosis is important for evaluating cost-effectiveness.

**RECOMMENDATIONS**

The evidence needs described above drive our recommendations for future research and policy development:

1. A conceptual framework for measuring and interpreting the economic value of clinical sequencing that is acceptable to technology developers, providers, and health care payers.
2. Controlled clinical trials to measure the short-term attributable impact of clinical sequencing on patients and health care systems.
3. Very large observational studies of the direct and indirect costs of clinical sequencing implementation in the near and intermediate term, coupled with modeling studies of the long-term clinical and economic impacts of clinical sequencing for both intended and incidental findings.
4. Data sharing across both controlled and observational studies to reduce uncertainty and better understand heterogeneity of rare outcomes.
5. A better understanding of the value patients place on findings from clinical sequencing and its relationship with patients’ health care decisions and their experience with the diagnostic odyssey.

**References**
