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Title

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Permalink

<https://escholarship.org/uc/item/966177fb>

Journal

Value in Health, 21(9)

ISSN

1098-3015

Author

Phillips, Kathryn A

Publication Date

2018-09-01

DOI

10.1016/j.jval.2018.06.012

Peer reviewed

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/jval

Themed Section: Assessing the Value of Next-Generation Sequencing

Assessing the Value of Next-Generation Sequencing Technologies: An Introduction



Themed sections in *Value in Health* provide readers an opportunity to learn more about a specific contemporary issue in health care, research, or policy from several perspectives. This issue of *Value in Health* includes a themed section on assessing the value of precision or personalized medicine—the use of genomics to target health care interventions. We focus specifically on next-generation sequencing (NGS) technologies, which are the fastest growing type of precision medicine technology [1]. Genetic testing is evolving from the use of single-gene tests toward the use of more complex tests that measure multiple genes using high-speed deoxyribonucleic acid sequencing technologies (i.e., “next-generation sequencing”). NGS includes panels that test multiple genes for a single indication, whole exome sequencing tests that evaluate the entire exome (coding regions of the genome), and whole genome sequencing tests that evaluate the entire genome.

It is critical to assess the value of NGS, but there are many methodological challenges to doing so. This theme section adds to the literature by going beyond just identifying challenges to identifying potential solutions, using both systematic reviews and case studies. All of the included articles “push the envelope” by delving into solutions to move the agenda forward. The articles incorporate a wide range of perspectives and topics, but they all focus on the overarching issue of how to appropriately consider and assess the value of NGS technologies. Our findings will be useful not only to researchers but also to other stakeholders, including payers and industry.

The article by Phillips et al. [2] sets the stage by addressing the methodological issues in assessing the economic value of NGS tests. Although several articles have described many of the methodological challenges in assessing the economic value of NGS, there has not been a systematic review of these challenges and solutions that have been applied to them. This article examines key methodological challenges for conducting economic evaluations of NGS, prioritizes these challenges for future research, and systematically identifies how studies have attempted solutions to address these challenges. The results can be used to guide future research and inform decision makers on how to prioritize research on the economic assessment of NGS tests.

The article by Regier et al. [3] addresses the valuation of health and nonhealth benefits from NGS. NGS tests provide large amounts of genomic information with a multitude of implications on patients’ and families’ preference-based utility and on the health care system. In addition, the information provided has an impact not only on health outcomes but also on nonhealth outcomes (e.g., false-positive rate) and process outcomes (e.g., time waiting for results). This article conducts a structured

review of studies valuing patients’ preference-based utility for NGS outcomes, highlights identified methodological challenges, and considers how studies addressed the identified challenges. The article concludes that failing to account for the utility or disutility of NGS-related nonhealth outcomes may lead to over- or underinvestment in NGS, and thus there is a need for research addressing unresolved challenges.

The article by Wordsworth et al. [4] is a commentary titled, “Using ‘Big Data’ in the Cost-Effectiveness Analysis of Next-Generation Sequencing Technologies: Challenges and Potential Solutions.” NGS has been described as a prominent example of a “big data” technology because of the massive amount and complexity of data it produces, but the question is whether big data can be used to support cost-effectiveness analyses of NGS. The creation of large national sequencing initiatives such as the United Kingdom’s 100,000 Genomes Project, the All of Us Research Program in the United States, and the Cancer 2015 Study in Australia have brought this question into sharp focus. This article summarizes the main methodological and practical challenges to using big data as an input into cost-effectiveness analyses of NGS technologies and describes potential solutions based on input from a group of global experts. It concludes that big data could be a rich source of evidence for cost-effectiveness analyses of NGS, but analysts must be cognizant of methodological and practical challenges before big data can be confidently used to produce evidence on the cost-effectiveness of NGS.

The article by Christensen et al. [5] outlines a real-world example of lessons learned in a cost analysis. Improvements in NGS are making it feasible to integrate whole genome sequencing into patient care at a population level, raising the need for well-designed studies of its cost and budgetary impact. This case study describes key methodological and data challenges that were encountered or are likely to emerge in future work, describes the pros and cons of approaches considered by the study team, and summarizes the solutions that were implemented, using the example of MedSeq, the first randomized controlled trial of whole genome sequencing in general and specialty medicine. Findings provide guidance for researchers to consider when conducting or analyzing economic analyses of whole genome sequencing and other NGS tests, particularly regarding costs.

The final article by Trosman et al. [6] addresses insurer coverage frameworks for next-generation tumor sequencing (NGTS). NGTS promises advancements in precision oncology but faces insurance coverage challenges. A key challenge is that NGTS features do not fit payers’ coverage framework, and thus various proposals to adapt the coverage framework have

been published. Nevertheless, no comparative analyses of these proposals have been conducted to date and the recent Medicare National Coverage Determination for NGTS [7,8] raises the need to examine it in the context of past proposals to determine whether and how it addressed challenges. This article uses a literature review to evaluate three previously proposed approaches for adaptation of the NGTS coverage framework, highlight their innovations, and outline remaining gaps in their ability to assess the features of NGTS. These three approaches are then compared with Medicare's National Coverage Determination and its implications for US private payers, as well as for other technologies and clinical areas. This article will inform future policymaking by private and public payers, as well as further efforts to adapt the coverage framework for NGTS and other genomic sequencing technologies.

Acknowledgments

This study was funded by a grant from the National Human Genome Research Institute (R01 HG007063) and consulting agreement with Illumina.

Kathryn A. Phillips, PhD*

Department of Clinical Pharmacy

UCSF Center for Translational and Policy Research on Personalized Medicine (TRANSPERS)

UCSF Philip R. Lee Institute for Health Policy

UCSF Helen Diller Family Comprehensive Cancer Center

University of California San Francisco

San Francisco, CA, USA

E-mail: kathryn.phillips@ucsf.edu

* Address correspondence to: Kathryn A. Phillips, 3333 California St, Room 420, Box 0613, San Francisco, CA 94143.

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<https://doi.org/10.1016/j.jval.2018.06.012>

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