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Overcoming the Reimbursement Barriers for Clinical Sequencing

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Genomic tests using next generation sequencing (NGS) technologies are increasingly being offered in a range of clinical settings. However, tests based on NGS may only transform clinical practice if patients and clinicians have access to them. This requires both favorable coverage decisions by public and private payers (e.g., Medicare, Medicaid, commercial insurers and adequate reimbursement levels to reward the development of innovative tests. Given that the hallmark of NGS technologies is the production of large amounts of data that require a bioinformatics infrastructure, sophisticated computational tools and professional interpretation of the results, the current reimbursement and coding environment is not structured to necessarily recognize the value of NGS tests.

Payers typically base coverage decisions for genomic tests on an evaluation of the clinical validity of the test (accuracy with which a test can predict the presence or absence of a phenotype), as well as evidence of clinical utility (the effects of testing on net patient health outcomes). Some new NGS technologies have rapidly generate the requisite evidence. For example, non-invasive prenatal testing for fetal aneuploidies is widely reimbursed by private health insurers, based on positive reviews of evidence supporting both clinical validity and utility of the test compared to traditional screening methods in high risk women.¹ However, for other technologies, like whole exome sequencing (WES) for diagnosis of suspected Mendelian conditions, generating evidence of clinical utility is more complex, and payment less assured.

Although some payers cover such testing, others have not authorized coverage for this entire category of testing.² In our experience at one clinical laboratory, about half (49%) of the WES tests ordered cannot be performed because of denial of coverage. Of those, approximately 20% were denied because the health plan does not cover genetic testing and 80% are denied because WES is considered experimental or investigational.³ Evidence-

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based coverage decisions allow payers to provide access to interventions with demonstrated effectiveness and provide transparency for their determinations. Yet, payers are concerned that the level of promotion of NGS-based tests currently exceeds evidence of their clinical utility for many indications. This clinical utility evidence “gap” has been a long-standing issue for many established molecular diagnostic tests that only evaluate single genes or mutations and is accentuated by methods that test for millions of variations simultaneously.

To help close this gap and ensure access to tests that are likely to benefit patients, while avoiding the clinical and economic harms of potentially ineffective tests, a four-pronged approach may be useful. As a first step, test developers should invest in robust validation studies to determine analytic and clinical validity. Analytic validity refers to the ability of a test to accurately and reliably measure the genotype of interest, while clinical validity focuses on the relationship between genotype and phenotype. Both are preconditions for clinical utility studies, which payers emphasize in their coverage determinations. In this early adoption period, payers are still developing experience with the evaluation of NGS tests, and there is evidence that clinical validity can be difficult to establish in tests done on different platforms, without standards for professional interpretation of variant pathogenicity.⁴ While experts are working to develop cross-platform performance standards for NGS,⁵ test developers should conduct well-designed peer-reviewed validation studies on their own platforms. Reports of validation studies should be made readily available to payers, as well as the technology assessment groups that produce reports used by payers for coverage determinations.

Second, there should be a system for prioritizing research to assess clinical utility. To start, there needs to be a clear understanding of the quality of existing evidence of utility for different clinical applications. Priority should be given to studies of NGS-based tests that have demonstrated analytic and clinical validity, some existing evidence of utility, and for which it is feasible to conduct additional utility studies. Priority may be given to FDA approved tests because they have demonstrated validity. For example, one NGS-based platform recently received FDA approval for targeted sequencing for cystic fibrosis.⁶ Currently, this testing platform is being evaluated for utility as a companion diagnostic in oncology.

Third, whenever possible, existing evidentiary frameworks such as those recommended by technology assessment groups and large payers⁷ should be used for assessing clinical utility; there have been problems obtaining coverage and reimbursement established molecular diagnostic tests when this was not done. However, the methodologies used to generate evidence of clinical utility need to be refined in order to evaluate NGS tests where hundreds to thousands of genes are evaluated for potential pathogenicity, there are variable levels of evidence supporting each variant’s clinical interpretation, and analysis depends on the clinical context and patient’s phenotype. For example, the Roundtable on Consensus Standards for Multiplex Cancer Genomic Testing convened by the American Society of Clinical Oncology, the Association for Molecular Pathology, and the College of American Pathologists⁸

Fourth, there needs to be an evolution in the evidence review process to account for the full range of benefits that are theoretically possible with NGS-based testing. For example, while discussions of the importance of personal utility (the value of the information to the patient and/or family beyond its intended clinical use) have been prominent in the genetic counseling literature, payers typically do not cover testing that is not clinically actionable. In addition, there may be a compound utility of NGS that represents the unique potential value of this type of testing to patients and the healthcare system that are likely to occur over the long term. This would include the potential downstream benefits of knowledge and mitigation of genetic risks, incidental findings, test efficiencies and health care cost offsets. Given issues related to prevalence and penetrance of germ-line mutations in various populations and health plan membership turnover rates, individual payers are extremely unlikely to recover the purported cost savings of such genetic risk reduction strategies. For patients, the healthcare system, and society to fully benefit from NGS testing, the evidence review process must take into account this notion of utility that compounds over time, which is unlikely to affect near-term coverage and reimbursement decision-making. Incentives could even be provided to accountable care organizations to invest in testing of asymptomatic persons if the evidentiary framework supports the compound utility of such testing.

While there are frequent calls to improve our current understanding of the clinical utility of NGS tests, payers control the level of evidence necessary for coverage and reimbursement decisions, which directly impacts patient and physician access. Clinical utility studies require resources and planning. It is therefore critical to ensure that tests have established analytic and clinical validity prior to investing in these studies. Priority-setting by focusing on validated tests with the greatest evidence gaps for specific indications can help ensure that scarce resources are allocated to tests with the highest clinical potential. While some new methodological approaches will be needed, it is important to recognize that most payers are unlikely to adopt new evidentiary frameworks to evaluate NGS tests, therefore an incremental approach will likely gain the most traction. Finally, the most transformational aspects of NGS testing, which occur over the lifetime of the individual (compound utility) will require stakeholder input to define the costs, benefits and harms from a societal perspective, and policy changes will be required to incentivize behavior change if the evidence suggests that testing is cost-effective or even cost-saving. Adopting this four-pronged approach could help increase the quantity and quality of information payers need to make evidence-based coverage decisions and help to ensure that payment decisions for NGS tests are based on the evidence that best supports their clinical use and value to the health care system.

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