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PERSPECTIVE

New Institute of Medicine Report on Molecular Biomarkers

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In recognition of the expanding field of precision medicine and the desire to give the right person the right medicine at the right time, the National Academies of Sciences, Engineering, and Medicine took up the task of making recommendations about molecular biomarkers. The consensus committee met throughout 2015 and released the report ''Biomarker Tests for Molecularly Targeted Therapies: Key to Unlocking Precision Medicine'' (National Academies of Sciences, Engineering, and Medicine, 2016) on March 4, 2016.

As a result of their consensus study, the committee stated 10 goals and associated recommendations. These address clinical practice, regulatory and reimbursement policy, and data challenges through the framework of a rapid learning system.

The 10 goals are as follows:

(1) Establish common evidentiary standards of clinical utility—using evidence generated both within and outside the context of clinical trials—across all stakeholders.
ECommon evidentiary standards, which establish the evidence needed to demonstrate that a biomarker test is useful for selecting molecularly targeted therapies and improves patient outcomes, are critical for consistent regulatory, coverage, and reimbursement decisions. Currently, lack of such standards is a significant limiting factor for patients, healthcare providers, test developers, regulators, and payers.

(2) Establish a more coordinated and transparent federal process for regulatory and reimbursement decisions for biomarker tests for molecularly targeted therapies.
Processes for making regulatory and reimbursement decisions regarding biomarker tests used in clinical care are misaligned, creating inefficiencies. The Food and Drug Administration (FDA) and the Centers for Medicare & Medicaid Services (CMS) should work closely together to enable effective coordination of these decision-making processes.

(3) Enhance communication to patients and providers about the performance characteristics and evidence for use of specific biomarker tests for molecularly targeted therapies.
Healthcare providers and patients both lack adequate information about biomarker tests for molecularly targeted therapies. New patient- and provider-friendly labeling information, including evidence to support test use in specific clinical scenarios, would increase transparency and empower patients and their healthcare providers to make more informed treatment decisions.

(4) Update and strengthen oversight and accreditation of laboratories providing biomarker tests for molecularly targeted therapies.
Currently, all clinical laboratories are regulated by CMS through the Clinical Laboratory Improvement Amendments (CLIA). However, regulatory oversight under CLIA is widely viewed as insufficient for laboratories providing increasingly complex biomarker tests.

(5) Ensure ongoing assessment of the clinical utility of biomarker tests for molecularly targeted therapies.
The generation of evidence of the clinical utility of any biomarker test should be viewed as a continuous process. CMS and other payers should develop payment models to support ongoing data collection to further assess the clinical utility of promising biomarker tests.

(6) Ensure development and use of Electronic Health Records (EHRs) and related biomedical informatics tools and assessments that support the effective clinical use of biomarker tests for molecularly targeted therapies.
EHR and laboratory information system developers need to facilitate the collection of real-time patient data that include information about tests, treatments, and outcomes. These data should be structured to provide support for healthcare providers in making decisions about test ordering and treatment, as well as to facilitate data transfer to a national data repository.

(7) Develop and maintain a sustainable national database for biomarker tests for molecularly targeted therapies through biomedical informatics technology to promote rapid learning for the improvement of patient care.
Currently, a tremendous learning opportunity is lost because biomarker test data are maintained in separate siloes at individual institutions. A national repository for such data needs to be developed, and incentives should be used to encourage all health-

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care systems and providers to submit their data to the repository, which should have appropriate deidentification, security, and patient consent measures.

(8) Promote equity in access to biomarker tests for molecularly targeted therapies and the expertise for effective use of the results in clinical decision making.
Patients of particular economic, ethnic, and cultural backgrounds and geographic locations may face challenges in obtaining access to biomarker tests and associated therapies. Research should identify existing barriers to equitable access and develop approaches to address them. Areas of focus include the potential for telemedicine to expand access to relevant clinical expertise. Licensing and specialty boards should ensure provider competency in communicating about these tests and therapies to patients.

(9) Enhance specimen handling and documentation to ensure patient safety and the accuracy of biomarker test results.
The reliability of biomarker test results depends on the quality of the patient specimens. Professional organizations and healthcare institutions should develop and implement standards for obtaining adequate specimens.

(10) Improve the processes for developing and updating clinical practice guidelines for the effective use of biomarker tests for molecularly targeted therapies.
Increasingly, a broader base of interdisciplinary expertise is needed to generate trustworthy clinical practice guidelines for biomarker tests. Such guidelines should consider the evolving nature of evidence for biomarker tests for molecularly targeted therapies.

These goals are very ambitious. I am very glad to see that they are rooted in a learning healthcare system that puts patients at the center. This system is not an easy one, and is inherently not amenable to the sort of evidence and rigor that populate the recommendations. The development of accessible, patient-centric, clinically relevant biomarkers, with the request for additional oversight and guideline development, lies in the murky interface of precision measurement and the practice of medicine. There is essentially nothing precise about human beings and their health and disease. In attempting to refine understanding of human biology to iteratively refine molecular biomarkers, and biomarkers for molecular medicine, an entire system of many actors is called on in the recommendations.

This is not new territory. The proper oversight of molecular biomarkers has been hotly debated for several decades now. What this report does is to more clearly recognize the need to be more patient centric, as well as to emphatically state that this must be conducted in a rapid learning system. Now it remains to be seen whether the various actors named in the report will rise to the occasion.

Author Disclosure Statement

No competing financial interests exist.

Reference

National Academies of Sciences, Engineering, and Medicine (2016) Biomarker Tests for Molecularly Targeted Therapies: Key to Unlocking Precision Medicine. The National Academies Press, Washington, DC.

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