Biomarker Tests for Molecularly Targeted Therapies: Key to Unlocking Precision Medicine

Every patient is unique, and the evolving field of precision medicine aims to ensure that the right treatment is delivered to the right patient at the right time. To achieve this, health care providers are increasingly turning to advanced technologies known as biomarker tests for molecularly targeted therapies. These tests can identify molecular variations specific to an individual patient and help determine the most effective therapy for a patient's disease or avoid treatments that may be ineffective or harmful. Given rapid developments in this field, how can health care providers, regulators, payers, and test developers ensure that patients have timely access to tests that can accurately direct targeted treatments, while at the same time protect them from potential harm caused by the use of poorly validated or inappropriate tests?

The Institute of Medicine of the National Academies of Sciences, Engineering, and Medicine appointed a committee of experts to examine this question. In its report, *Biomarker Tests for Molecularly Targeted Therapies: Key to Unlocking Precision Medicine,* the committee recommends an integrated set of actions aimed at addressing clinical practice, regulatory and reimbursement policy, and data challenges through the framework of a rapid learning system (see Figure on the next page).

To enhance patient care and clinical outcomes, a rapid learning system is needed that can integrate research with clinical practice.

THE NEED FOR A RAPID LEARNING SYSTEM

Biomarker tests for molecularly targeted therapies represent a crucial area of focus for achieving the full potential of precision medicine. Appropriate regulatory oversight of these tests is needed to ensure they are accurate, reliable, properly validated, and appropriately implemented in clinical practice. To enhance patient care and clinical outcomes, a rapid learning system is needed that can integrate research with clinical practice. This would enable health care providers to continuously collect and assess real-world patient data for continuous learning and rapidly apply new knowledge to a wide variety of clinical practice settings, while also enabling regulators and payers to make more informed decisions.

In addition to addressing regulatory and reimbursement policy issues, developing this rapid learning system will require the collection of structured patient data in electronic health records (EHRs) and laboratory information systems (LIS)
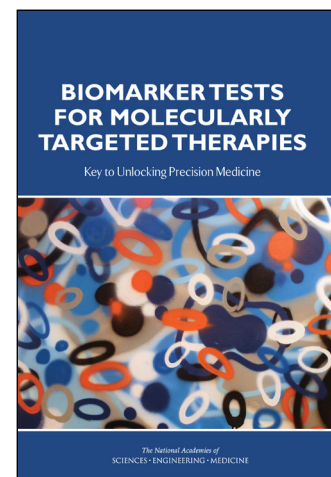
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to understand the potential benefits and risks of biomarker tests and associated therapies. Currently, data on biomarker tests and patient outcomes are not collected or structured in a way that can inform clinical practice. The development of one or more large clinical databases to gather these data will be critical to accelerate progress in this area of precision medicine.

GOALS FOR ADVANCING APPROPRIATE USE OF BIOMARKER TESTS

The IOM committee identified ten goals to further advance the development and appropriate clinical use of biomarker tests for molecularly targeted therapies.

1) Establish common evidentiary standards of clinical utility—using evidence generated both within and outside the context of clinical trials—across all stakeholders.

Common 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, health care providers, test developers, regulators, and payers.
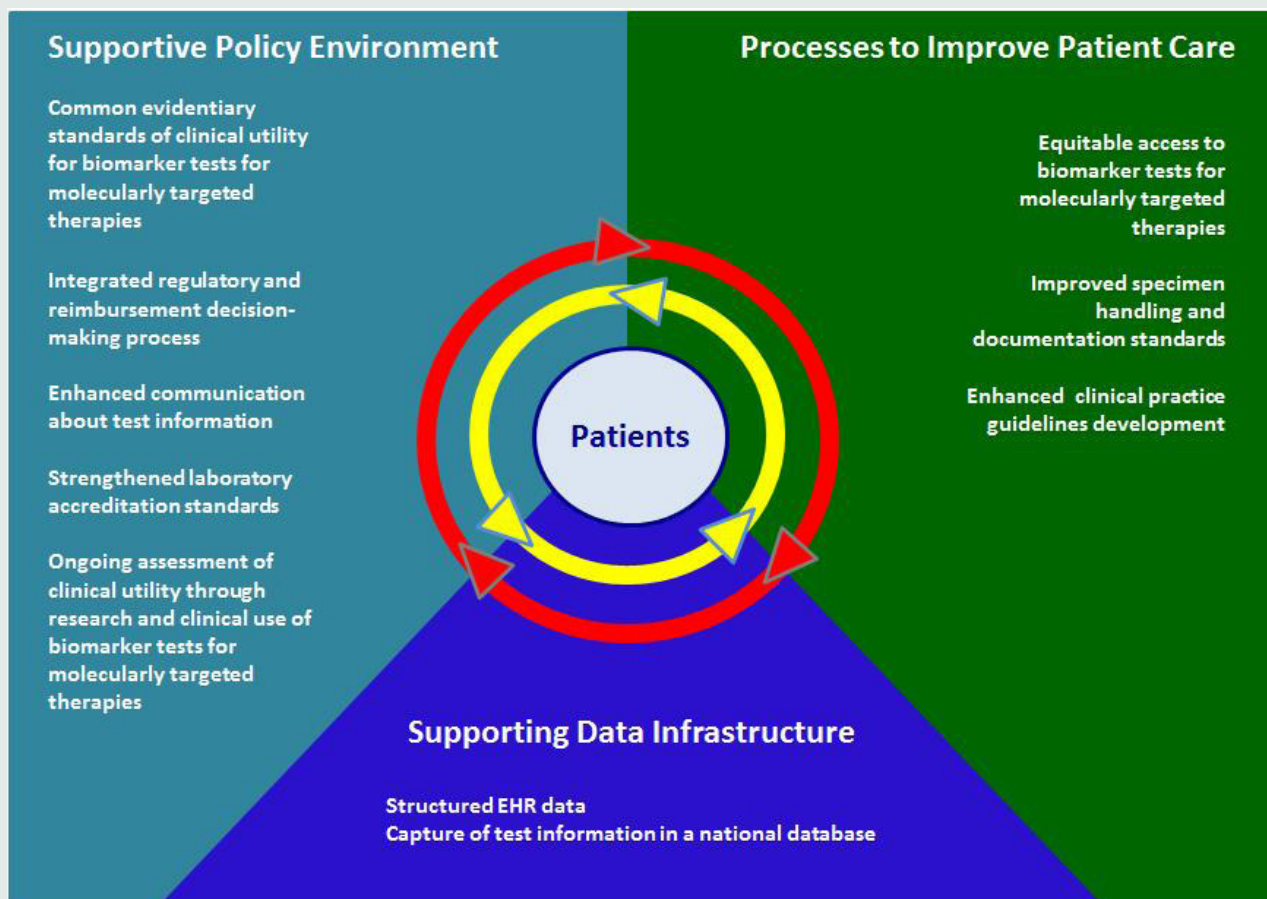
FIGURE
Rapid Learning System for Biomarker Tests for Molecularly Targeted Therapies

Supportive Policy Environment

Common evidentiary standards of clinical utility for biomarker tests for molecularly targeted therapies

Integrated regulatory and reimbursement decision-making process

Enhanced communication about test information

Strengthened laboratory accreditation standards

Ongoing assessment of clinical utility through research and clinical use of biomarker tests for molecularly targeted therapies

Processes to Improve Patient Care

Equitable access to biomarker tests for molecularly targeted therapies

Improved specimen handling and documentation standards

Enhanced clinical practice guidelines development

Patients

Supporting Data Infrastructure

Structured EHR data
Capture of test information in a national database

> The committee's proposed rapid learning system is expressly designed to promote the proper development, effective and ongoing assessment, and appropriate use of biomarker tests for molecularly targeted therapies.

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.

Health care 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 health care 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 EHRs and related biomedical informatics tools and assessments that support the effective clinical use of biomarker tests for molecularly targeted therapies.

EHR and LIS developers need to facilitate the collection of real-time patient data that includes information about tests, treatments, and outcomes. These data should be structured to provide support for health care 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 silos at individual institutions. A national repository for such data needs to be developed, and incentives should be used to encourage all health care systems and providers to submit their data to the repository, which should have appropriate de-identification, security, and patient consent measures.

8) Promote equity in access to biomarker tests for molecularly targeted therapies and the

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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 health care 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.

CONCLUSION

The committee's proposed rapid learning system is expressly designed to promote the proper development, effective and ongoing assessment, and appropriate use of biomarker tests for molecularly targeted therapies. Such a supportive framework would enable precision medicine's promising treatment-tailoring technologies to realize their full potential to improve patient outcomes.♦♦♦

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