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POLICY FORUM

BIOMEDICAL INNOVATION

Diagnostics investments and disease burden

Regulatory and payment policies could facilitate investment and innovation in diagnostics

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Screening and testing for disease using "diagnostics" (see the box) is increasingly essential across global health care systems to identify and target individuals who will most benefit from health care interventions and to address unmet disease burden. However, access to diagnostics is uneven and often inadequate, particularly in lower- and middle-income countries, with an estimated 47% of the world's population having limited or no access to diagnostics (*1*). Despite these needs, diagnostics historically have received lower investment, insurance coverage, and payment rates than drugs, creating barriers to innovation (*2*). We leverage a recent, in-depth assessment of the mismatch between drug development and disease burden in the US (*2*) to address two critical gaps: (i) policies specifically relevant to diagnostics and integrated diagnostic–drug combinations, and (ii) how findings for the US extrapolate globally. We focus on underinvestment in diagnostics and explore how regulatory and payment policies could facilitate diagnostic innovation.

With the emergence of diagnostic tests using genomic biomarkers and new drugs requiring diagnostics for targeted therapies, the importance of diagnostics in early diagnosis, targeted treatment, and outcome monitoring continues to grow (*3, 4*). The global diagnostics market, valued at $109 billion in 2023, is projected to reach $169 billion by 2030 (*5*). This growth will be accelerated by emerging diagnostic technologies that use new methods, apply existing techniques to new clinical applications, and/or are necessary to identify patients who will benefit the most from targeted drugs. Examples include multicancer detection tests; blood-based biomarker tests for Alzheimer's disease and cancer treatment selection; the application of other "omics" beyond genomics, such as nutrigenomics, to provide personalized dietary recommendations; and polygenic risk scores that aggregate an individual's risk for complex diseases such as cardiovascular disease (*5*). The application of artificial intelligence will also be critical, as it transforms diagnostic capabilities by enabling the analysis of multimodal datasets, including imaging (both radiology and digital pathology), test results, and clinical data, to identify patterns and predict outcomes. In addition, innovative, but often costly, drugs highlight the need for better diagnostics to identify patients who are good candidates for treatment, thereby improving clinical and economic outcomes.

For example, glucagon-like peptide–1 (GLP-1) receptor agonists for diabetes and obesity represent a rapidly expanding market. Despite their promise, studies on the efficacy of GLP-1s for weight loss show an 18% nonresponse rate and up to 50% discontinuation within 12 months (*6, 7*). Yet, no validated diagnostic exists to predict treatment response before initiation. Given the scale of the worldwide obesity epidemic and the substantial costs of these therapies, diagnostics that identify likely responders could prevent inappropriate treatment exposure, reduce health care expenditures, and improve patient outcomes.

Although diagnostics have not always demonstrated evidence of sufficient value to justify investment and coverage, there are many examples in which scientific and market factors have caused diagnostics to be undervalued (*1*). Thus, opportunities for innovation to address disease burden are missed. The *Lancet* Commission on diagnostics found that, although diagnostics are central and fundamental to quality health care, their value is underrecognized, leading to underinvestment and inadequate funding in the US and globally (*1*).

There are many reasons that diagnostic innovation may be hindered, some of which are the same scientific and market factors identified for drugs (*2*) and are ubiquitous across countries, such as scientific complexity, small patient populations for certain diseases, high development costs, lack of regulatory approval and/or insurance coverage, and low reimbursement rates (*2*). Additionally, regulatory approvals typically consider safety and efficacy but often do not examine the evidence on clinical utility or economic value that would inform payment decisions.

However, diagnostics also present special challenges. First, diagnostics inherently face higher evidentiary standards because it is more challenging to assess the linkage between diagnostics and patient outcomes, given that diagnostics provide information rather than direct treatment. Second, diagnostic regulatory approvals and payment policies are typically separate from those for drugs, leading to fragmentation. Third, diagnostics generally have less standardized and predictable regulatory and reimbursement pathways than drugs.

The need to measure disease burden and use this information to guide policies for both drugs and diagnostics has long been recognized globally. In the 1990s, the World Bank commissioned the Global Burden of Disease study to estimate disability and death resulting from specific causes, which is unparalleled in its scope and continuity (*8*). To examine challenges in better aligning innovations in therapeutic development with disease burden and to offer strategies and recommendations for improvement, a conceptual framework was developed by a recent committee of the National Academies of Sciences, Engineering, and Medicine (NASEM) (*2*) to address key questions: What factors facilitate the innovation pipeline, from the initial stages of investment and discovery to population health impact? Which disease areas are the current focus of innovation and investment? Where is disease burden concentrated now and expected in the future? Given current innovation and disease burden, where are misalignments contributing to unmet needs? What changes in policies, payment, investment, and incentives would address those unmet needs?

We use this framework—expanding it beyond the report's focus on drugs in the US—to examine two types of underinvestment in diagnostics globally: in the diagnostics needed to identify patients suitable for specific drugs on the basis of disease burden (*2*), and in diagnostics relative to drugs.

ALIGNING INNOVATION WITH DISEASE BURDEN

Regulatory and payment strategies represent key policy levers to remove barriers to diagnostic innovation. We apply insights from the US experience with regulatory and payment strategies for drugs (*2*) to diagnostic innovation both in the US and globally. Because most countries have different regulatory and payment mechanisms for diagnostics than for drugs (*9, 10*), efforts to enhance diagnostic innovation must consider this particular context.

To facilitate diagnostic innovation, we assess two approaches that can be considered when clinically relevant and supported by evidence: Enhance and expand pathways for expedited diagnostic regulatory ap-

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provals (*11*) and enhance and expand integrated reviews of diagnostics and drugs for regulatory and payment decisions (*10*, *12*).

Regulatory policies

In drug regulatory policy, the US Food and Drug Administration (FDA) plays a critical role in driving innovation to address unmet needs through its multiple, flexible expedited regulatory pathways. However, these pathways operate differently for drugs versus diagnostics (which are regulated as devices) (*10*).

Drug approvals are expedited more often than approvals for diagnostics. Specifically, the percentage of drugs that received accelerated approval between 2015 and 2024 (26.0%) is higher than the percentage of diagnostics that received Breakthrough Device Designation, the comparable expedited pathway, during the same timeframe (4.6%) (see supplemenatary materials). This gap suggests potential missed opportunities to accelerate diagnostics that could help address disease burden.

The relative lack of expedited approvals for diagnostics has many possible explanations, including insufficient industry incentives for developing and submitting diagnostics for regulatory approval, difficulty demonstrating clinical utility that requires evidence that the diagnostic improves patient outcomes and not just analytical performance, and barriers to accessing pharmaceutical companies' clinical trial data and biospecimens needed for validation, which limit third-party development (*13*).

These regulatory challenges are compounded by the reality that many diagnostics face uncertain or inadequate reimbursement prospects, creating a cycle in which developers are reluctant to invest in rigorous regulatory processes when coverage and payment remain unclear. Current systems exacerbate this cycle by incentivizing manufacturers to conduct minimal validation studies required for market entry, rather than partnering with health systems to collect real-world evidence on clinical utility throughout the product life cycle that could reduce development costs and facilitate coverage, potentially without delaying initial market entry. Programs such as the US Centers for Medicare and Medicaid Services' (CMS) Coverage with Evidence Development, which makes participation in evidence generation a prerequisite for coverage, demonstrate one approach to incentivizing such evidence collection. However, this approach has been used much more often for devices than diagnostics (or drugs).

Recent FDA policy changes aim to address this misalignment. In January 2024, the FDA announced that specific companion diagnostics may be approved through a faster, less costly regulatory pathway [510(k) rather than premarket approval]. Combined with existing programs, such as the FDA-CMS Parallel Review (see the box), these changes recognize that aligning drug and diagnostic timelines can improve patient access. Health care systems internationally are also developing pathways to facilitate companion diagnostic approval when the evidence supports this designation, which often enables reimbursement.

These recent reforms address one aspect of diagnostic regulation. Still, the widespread use of laboratory-developed tests, which are subject to less regulatory oversight than companion diagnostics (see the box), presents another challenge. There has been considerable controversy over whether laboratory-developed tests should be subject to FDA premarket approval and clearance, including the US's proposed Verifying Accurate Leading-edge IVCT Development (VALID) Act to regulate in vitro clinical tests (IVCTs), the 2024 FDA rule, and the European Union's (EU's) In Vitro Diagnostic Medical Device Regulation (EU-IVDR). These controversies reflect broader global tensions in how to ensure safety and efficacy while preserving pathways for innovation, particularly for rare diseases and emerging clinical needs.

Lastly, there are global efforts to harmonize regulatory requirements. One example is the International Medical Device Regulators Forum, a global coalition of medical device regulators, including the FDA, that works to accelerate international regulatory harmonization by managing regulatory challenges for new devices, including diagnostics, and creating a global regulatory model that harmonizes documentation and procedures across countries to reduce compliance costs and enable faster patient access to diagnostic innovations.

Definitions

Diagnostics

Definition: Tests used for in vitro and in vivo determination of physiological status or presence and characteristics of a disease.
Example: Blood-based biomarker tests for Alzheimer's disease to identify patients with amyloid pathology and aid in treatment selection.

Companion diagnostics

Definition: Tests that have received regulatory approval based on providing information essential for the safe and effective use of a corresponding therapeutic product and are thus required for use of the therapeutic.
Example: HER2 testing for breast cancer patients to determine eligibility for trastuzumab (Herceptin) therapy.

Complementary diagnostics

Definition: Tests that may inform benefit–risk decisions about a therapeutic product but are not required for therapeutic use.
Example: Tumor mutational burden (TMB) testing that aids in identifying cancer patients who may benefit from immunotherapy, but it is not required for prescribing.

Laboratory-developed tests

Definition: Diagnostic tests designed and performed within a single clinical laboratory under federal laboratory regulations rather than FDA-regulated tests requiring premarket approval or clearance.
Example: Hospital-developed gene sequencing assay for cancer mutations.

Expedited regulatory review and approval

Definition: Regulatory pathways that prioritize assessment of innovative medical products and devices (including diagnostics) that address serious conditions and/or unmet needs.
Example: FDA's Breakthrough Device Designation expedites the development, assessment, and review of devices (including diagnostics) that provide more effective treatment or diagnosis of severe conditions, offering benefits such as priority review and interactive communication with regulators.

Technology assessments of diagnostics and therapeutics as linked products

Definition: Evaluation processes that assess diagnostics and their associated therapies as linked combinations to determine their combined clinical and economic value.
Example: Health technology assessments that evaluate both a diagnostic and its associated targeted therapy to determine the cost-effectiveness and clinical value of the diagnostic-guided treatment strategy.

Integrated regulatory-reimbursement reviews of diagnostics and therapeutics

Definition: Programs that align regulatory approval pathways with coverage and payment determinations, enabling streamlined assessment and reduced time to patient access for innovative therapeutics and devices (including diagnostics).
Example: FDA-CMS Parallel Review is a collaborative program where the FDA and the Centers for Medicare and Medicaid Services review medical products (including diagnostics) concurrently.

Payment policies

For payment policies, we focus on one key challenge: Diagnostics and drugs are often not linked together and integrated for economic assessments and payment determinations (in addition to not being directly linked for regulatory decisions).

As with regulatory policies, payers typically manage diagnostics and drugs through separate budget line items with distinct coverage and payment policies, rather than evaluating them as linked and integrated diagnostic–therapeutic combinations (see the box). This fragmentation, combined with the lack of developer incentives to create diagnostics and disconnected regulatory and payment pathways, creates barriers to diagnostic innovation (*13*).

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The relationship between diagnostics and drugs may vary by clinical context, ranging from single diagnostics guiding multiple treatment options to multiple diagnostics informing a single therapy. However, integrated coverage assessment is essential when diagnostics are clinically necessary for appropriate therapeutic decision-making. A lack of integrated assessments, combined with complex and variable payment policies across payers, makes diagnostics undervalued even when they are essential to the drug's clinically indicated use (*13*).

To illustrate, an international review of health technology assessments across 12 agencies found that the majority of assessments did not adequately describe the value of companion diagnostics required for the targeted therapies being evaluated (*14*). Even when diagnostics were included in economic evaluations, assessments focused primarily on testing costs rather than integrated assessments of the clinical and economic value of diagnostic-guided therapy. Multiple interconnected challenges contribute to the pattern of treating diagnostics solely as cost inputs rather than as value-generating technologies, including a lack of clear evidence on the incremental benefits of diagnostics in the treatment pathway. This systematic undervaluation represents the upstream policy challenges that we aim to highlight.

Additionally, the value of diagnostics should be considered holistically—both their contribution as an essential component of linked diagnostic–drug treatment combinations and, when applicable, their lifetime benefits, such as for inherited genetic conditions. Consider, by analogy, the value of one-time therapies, such as cell and gene therapies, which can be costly but may offer lifetime benefits. Thus, it has been proposed that new payment approaches holistically reflect their benefits (*10*, *13*).

The US can gain insights from other global efforts. The NASEM report recommended that Congress reform the statutory framework regulating public reimbursement for drugs to enable the use of price negotiations to better align reimbursement rates with evidence of clinical benefit. Because many other countries have extensive experience with using price negotiations, the US could consider applying these experiences to diagnostics. Second, a major global initiative that could provide key insights as it is implemented is the EU Health Technology Assessment Regulation (HTAR) program. The long-awaited and recently implemented network marks a considerable milestone by standardizing evidence submissions across EU member states, including diagnostics (initially high-risk diagnostics and devices), through joint clinical assessments and consultations.

BETTER TESTS FOR SCREENING AND DIAGNOSIS

Alzheimer's disease is an example of a high global disease burden that would benefit from better diagnostics (*2*), as several innovative drugs to delay progression are entering the market. However, the usefulness and affordability of these drugs have been hindered by the lack of readily accessible, noninvasive, and low-cost blood-based diagnostics to accurately target them to patients (*15*). Current diagnostic approaches rely on expensive conventional diagnostics such as PET (positron emission tomography) scans or cerebrospinal fluid testing, which are not globally accessible. To meet the need for innovative diagnostics, several blood-based biomarker tests are under development or entering the market; however, the pathway for insurance coverage and reimbursement remains unclear.

One test (Lumipulse) recently received European regulatory approval and FDA Breakthrough Device Designation and is now available via LabCorp in the US. However, as of March 2026, there is no published evidence that insurers are covering these tests either in the US or globally (*15*). Newer anti-amyloid drugs cost ~$30,000 annually in the US. In comparison, blood-based biomarker tests that could identify appropriate treatment candidates and spare nonresponders the cost and risk of unnecessary treatment have a list price of ~$1000. This illustrates the broader challenge: Even when diagnostics receive regulatory approval, reimbursement remains uncertain or limited, leaving unclear whether similar tests in development will receive appropriate regulatory pathways, insurer coverage, and reimbursement if the evidence warrants.

Even if emerging drugs are ultimately shown not to provide sufficient clinical benefits to justify their risks and costs, Alzheimer's disease diagnostics can still provide value. Early and accurate diagnosis provides considerable benefits beyond directing therapeutic interventions, including enabling patients to engage in advance care planning and access support services, benefits that many individuals prioritize regardless of therapeutic options. Regulators and payers could play key roles in developing appropriate regulatory, coverage, and payment policies to facilitate innovation in this area and address this substantial disease burden.

There is no single policy change that will remedy the challenges to diagnostic innovation, but several incremental changes together could improve the situation. These policy recommendations center on the assertion that diagnostics should often be considered an essential component of the regulatory and payment pathways alongside associated therapeutics. Specific policy changes could include joint regulatory, payment, and value assessments of diagnostics combined with drugs; incentives for generating evidence on clinical utility of diagnostics through programs like Coverage with Evidence Development; standardized and coordinated regulatory and payment pathways (e.g., aligning FDA's Breakthrough Devices Program with expedited pathways for drugs); and value-based payment models that assess the combined value of diagnostic-informed therapy and use this information for payment decisions. New and dynamic regulatory and payment strategies that keep pace with technological innovations will be necessary to facilitate the appropriate development and use of diagnostics in addressing these critical issues. □

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SUPPLEMENTARY MATERIALS

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