

# Toward Evidence-based Assessment for Coverage and Reimbursement of Laboratory-based Diagnostic and Genetic Tests

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Despite the pervasiveness of laboratory tests and their importance to medicine, evidence for their appropriate use often is very limited. In this article, we argue for a fundamental restructuring of the process by which laboratory tests are evaluated and reimbursed. We present an approach that would promote more evidence-based appraisals for laboratory tests. In addition, we urge that coverage and reimbursement for laboratory tests move toward an evidence- and value-based approach, using the tools that largely have been adopted for pharmaceuticals by many US healthcare payers. To address this information gap for laboratory tests, we note several potential strategies to encourage manufacturers, laboratory service providers, and payers to collect outcome and cost data that will better support effective use of new laboratory tests. Integral to increasing appropriate use and reimbursement will be the development of a common language and format for dialogue—facilitating the development, review, and delivery of evidence-based tests by manufacturers, clinical laboratories, and healthcare payers.

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Laboratory tests are an important yet often underappreciated component of healthcare and the health economy.<sup>1</sup> It is estimated that as much as \$56 billion will have been spent on laboratory diagnostic services in 2005.<sup>2</sup> More important, laboratory tests by their very nature are designed to initiate a cascade of decisions regarding further testing, prevention, or treatment—decisions that ultimately determine the course of illness and cost of healthcare for patients who receive them. A recent report estimated that although diagnostics account for 1.6% of the Medicare total costs, they influence 60% to 70% of downstream treatment decisions.<sup>3</sup>

Despite their pervasiveness and importance to medicine, the evidence for the application and utility of laboratory tests often is limited.<sup>4,6</sup> Tests being brought to market do not require the same data as therapeutics do, and technology assessments of laboratory tests have not undergone the revolutionary changes in evidence review that have occurred for drugs.<sup>7</sup> Instead, payment

for tests is linked to an antiquated coding system.<sup>8</sup> Finally, innovative insurance coverage and payment policies that are common for drugs are rare for laboratory tests.<sup>9</sup>

In this article, we argue for a fundamental restructuring of the way laboratory tests are evaluated and reimbursed. We propose that coverage and reimbursement for laboratory tests should move toward an evidence- and value-based approach, using some of the tools that have been adopted for pharmaceutical assessment by many US healthcare payers. Furthermore, reevaluating the methods used to assess and pay for tests is a timely endeavor, as diagnostic tests are on the forefront of the trend toward personalized medicine.<sup>10,11</sup>

## CHALLENGES FOR THE CURRENT PROCESS OF ADOPTING LABORATORY TESTS

Public and private health insurers pay for tests performed in laboratories that meet standards certified under the Clinical Laboratory Improvement Amendments (CLIA) of 1988, according to *Current Procedural Terminology (CPT)* codes.<sup>12</sup> In cases where a CPT code does not exist, health insurers sometimes reimburse the new test by using a CPT code for an existing test, a process known as “mapping.”<sup>13,14</sup>

Once a CPT code is established, test payments are established by “cross-walking” or “gap-filling.” In cross-

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walking, a new test is determined to be similar to an existing test, multiple existing test codes, or a portion of an existing test code. Payment is set at an “appropriate” percentage of the payment for the existing test.<sup>15</sup> In gap-filling, insurers are left to determine an appropriate payment amount for the new code. The Centers for Medicare & Medicaid Services uses local carrier decisions as a basis for the next year’s clinical laboratory fee schedule.<sup>15</sup>

A recent report by the Institute of Medicine suggested that the process of establishing reimbursement levels for novel laboratory tests is out-of-date and not equipped to handle emerging diagnostic and genomic tests:

[Medicare] payments for some individual tests likely do not reflect the cost of providing services, and anticipated advances in laboratory technology will exacerbate the flaws in the current system. Problems with the outdated payment system could threaten beneficiary access to care and the use of enhanced testing methodologies in the future.<sup>16</sup>

More broadly, some argue that reimbursement must more accurately reflect clinical and economic value.<sup>3,14</sup>

Public and private payers have not developed uniform methods for requesting information from laboratory test service providers about novel tests. There are several likely reasons. The first reason is historical: most health plans do not have standing test evaluation groups similar to pharmacy and therapeutics (P&T) committees, possibly because laboratory tests have not been viewed as clinically or economically significant enough to justify the expense associated with these groups. Second, in contrast to pharmaceutical manufacturers, neither test manufacturers nor laboratory service providers generally have large, sophisticated marketing teams targeting physicians, health plans, and patients. (A relevant exception may be the marketing of the ThinPrep test.<sup>17</sup>) Third, as noted above, federal regulatory requirements do not compel manufacturers or distributors to provide the type of evidence (eg, randomized clinical trials) that lends itself to systematic review.<sup>18</sup> Finally, the way laboratory tests are used in practice makes it difficult to apply the pharmaceutical evaluation model. Unlike most pharmaceuticals, laboratory tests are used in a wide range of clinical settings. For example, a complete blood count is used in hundreds of clinical situations, while antihypertensive drugs are used in a limited number of conditions.

In lieu of an evidence-driven, value-based approach, the process of adopting new laboratory tests is essentially what economists call an “administering pricing” system. Pricing is set through a negotiation process that may be based on historical comparators in the case of

cross-walking or perceived levels of analytic complexity in the case of gap-filling. As a result, there is little reward for creating additional value (either in a clinical or an economic sense) and hence little incentive to create the evidence to support value creation (L. P. Garrison, PhD, and M. J. F. Austin, PhD. *The economics of personalized medicine: a model of incentives for value creation and capture*. Unpublished observations, January 2006). We describe a process that is designed (1) to improve the quality of the evidence that is available when an insurance coverage decision is being made and (2) to increase the transparency and uniformity of the process by which payers request information from test manufacturers or laboratory service providers.

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### FRAMEWORK FOR PRESENTING EVIDENCE ON LABORATORY TESTS

#### **Developing a Language for Describing Benefit**

Test manufacturers, laboratory service providers, and health insurance plans will benefit from standardizing the way evidence supporting new laboratory tests is presented. Methodological standards for the evaluation of diagnostic tests have been published.<sup>5</sup> In addition, several domains relevant to health insurers, clinicians, and patients are considered in a published framework to evaluate diagnostic technologies (Table).<sup>19</sup> Although many agree about the value of using these domains to evaluate tests, there is less agreement on how much evidence is necessary for an insurance coverage decision.

In addition to considering the relevant domains from the Table, it is important to evaluate the incremental impact of a test; that is, the improvement that the new test provides over current diagnostic strategies (L. P. Garrison, PhD, and M. J. F. Austin, PhD. *The economics of personalized medicine: a model of incentives for value creation and capture*. Unpublished observations, January 2006). Because prospective trials directly comparing new laboratory tests with established diagnostic strategies are uncommon (particularly those evaluating the impact of the tests on patient outcomes), decision-analytic modeling techniques often are necessary to conduct quantitative evaluations.<sup>20</sup> Modeling is an underappreciated approach to evaluating new tests. Models help frame questions, provide transparent mechanisms for stating hypotheses about cause and effect, highlight deficiencies in clinical data, and force decision makers to make explicit judgments about values for data that are used to inform the model. Although some clinicians and health insurance plan executives remain skeptical of decision models, quality standards for models have been published and are readily accessible to

decision makers who wish to assess their quality.<sup>21</sup>

**Definition of Value for Laboratory Tests**

We define value for laboratory tests as it is defined for other health technologies: The intervention provides an overall benefit to the patient at an acceptable cost (ie, it is cost-effective). Petitti notes that there are 4 well-recognized criteria for identifying an intervention as cost-effective<sup>22</sup>:

- Less costly and at least as effective.
- More effective and more costly, with the added benefit worth the added cost.
- Less effective and less costly, with the added benefit of the alternative not worth the added cost.
- Cost saving with an outcome equal to or better than that of the alternative.

Assessing value for tests can be difficult because tests are intermediate steps in the treatment pathway. The advantage of Petitti's framework<sup>22</sup> is that it allows flexibility, because value for tests can be defined narrowly (eg, the least expensive way to make a diagnosis) or broadly (improvement in survival at an acceptable added cost).

**Format for Dialogue Among Test Manufacturers, Providers, and Payers**

Manufacturers and laboratory service providers cannot expect, and payers cannot promise, coverage of and appropriate reimbursement for every new test that comes to market. Similarly, payers cannot expect, and manufacturers and their delivery partners cannot promise, the same level of evidence for all tests. Nevertheless, the process should be transparent, and adopting a standard format would help clarify expectations and improve the decision-making process. We propose a process for information content and interaction that is intentionally similar to the format developed by the Academy of Managed Care Pharmacy (AMCP) for the evidence-based evaluation of drugs. More than 50 public and private health insurers covering more than 100 million lives have adopted the AMCP format.<sup>7,23</sup> The Appendix provides a template for manufacturers' reporting of clinical and economic information regarding laboratory tests. This template takes into account differences in

**Table.** Hierarchy of Diagnostic Evaluation When Determining Test Benefit\*

| Level | Characteristic                         | Description  |
|-------|--|--|
| 1     | Technical feasibility and optimization | Ability to produce consistent results  |
| 2     | Diagnostic accuracy                    | Sensitivity, specificity, positive predictive value, negative predictive value                         |
| 3     | Impact on diagnostic thinking          | Percentage of time that physicians' estimated probability of a diagnosis changes after the test result |
| 4     | Impact on therapeutic choice           | Percentage of time that the planned therapeutic strategy changes after the test result                 |
| 5     | Impact on patient outcome              | Percentage of patients who improve with the test versus the percentage who improve without the test    |
| 6     | Impact on society                      | Cost-effectiveness   |

\*Adapted from reference 19.

evidence that are typically available for new laboratory tests compared with new pharmaceuticals.

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**IMPLEMENTATION**

Some health plans might have a designated organizational unit that evaluates laboratory tests, providing a structure for soliciting and reviewing manufacturers' products. In the case of pharmaceutical products, that unit is the P&T committee. Health plan staff working with P&T committees usually are receptive to receiving information from manufacturers or service laboratories about new products. Indeed, the "unsolicited request" process pioneered by AMCP was designed to create a structure for dialogue between manufacturers and payers. A similar scheme would improve transparency and the flow of information for new laboratory tests.

P&T committee members often are not health plan employees. Having such a quasi-independent group evaluate novel laboratory tests may improve the credibility of the decision process in the eyes of manufacturers, clinical laboratories, physicians, and patients. Still, maintaining committees is costly, and such maintenance may not be justified given the relatively low volume of tests that are introduced annually. One option is to fold the test evaluation process into the existing P&T structure. Alternatively, payers could hire consultants to evaluate select novel tests and make recommendations regarding coverage and reimbursement.

Payers should be timely both in coverage decisions and in setting reimbursement levels, and when decisions are made, they should be supported with a rationale. In cases where requests for coverage are denied,

such information allows manufacturers to design studies or collect other data that address concerns regarding the quality or content of the information supporting the product.

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**OPTIONS FOR IMPROVING THE LEVEL  
OF EVIDENCE SUPPORTING NOVEL  
LABORATORY TESTS**

To address known methodological weaknesses in studies evaluating diagnostic tests,<sup>24-26</sup> we describe in this section options for improving the quality of information. Some focus on market incentives; others are more regulatory in nature. At this early stage, we do not advocate one approach over another. Rather, we hope to foster a dialogue among stakeholders.

**Enhancing Regulation in Evaluating  
Laboratory Tests**

Testing services in the United States are regulated by both federal and state laws and agencies, and are further reviewed by accrediting professional entities. All laboratory tests that meet the legal definition of in vitro diagnostic devices (IVDs; generally, diagnostic assays made for distribution outside a single provider laboratory) are evaluated by the US Food and Drug Administration's (FDA's) Center for Devices and Radiological Health. However, most tests offered by laboratory service providers are not IVDs; the manufacture of analytes or other components of such tests (called analyte-specific reagents) may need to meet FDA specifications for legal distribution. IVD approval, which typically is based on analytical performance, does not require other types of evidence that the FDA often mandates for devices that carry significant risk (eg, prospective controlled trials for implantable defibrillators). Although laboratory tests usually pose little direct risk of injury or death, they often lead to a cascade of clinical decisions, sometimes involving procedures that do carry significant risk for patients. For example, a positive prostate-specific antigen test often leads to prostate biopsy, which carries risk of bleeding and infection. As an extreme example, women whose genetic tests show BRCA mutations often choose to have prophylactic mastectomies and oophorectomies.<sup>27</sup> Genomic tests that are used to guide therapy choices also could represent a class of laboratory assays that pose unique patient risks.

To address potential downstream indirect risk, the FDA could require test manufacturers or service providers distributing IVDs to submit clinical algorithms with recommended follow-up plans based on test results. In cases where the downstream consequences

are significant, the FDA could require specific postmarketing studies. Another area of concern is laboratory-developed or "home brew" tests—those that are supplied by a single laboratory or laboratory company and therefore are not subject to federal regulatory review beyond CLIA. Many tests, including genetic assays, are brought to market as home brew tests.<sup>28</sup> Strengthening regulatory requirements for some of these tests might enhance the ability of payers and clinicians to gauge their value. With a goal of more uniform quality standards for testing, federal, state, and professional oversight measures should be considered in toto.

**Levies to Support Clinical Research**

To increase funding of high-quality clinical studies focused on patient outcomes,<sup>29-32</sup> some advocate levies on medical services to fund prospective and retrospective clinical and economic studies for new and existing technologies.<sup>33</sup> Such research could be directed through existing agencies within the National Institutes of Health, the Agency for Healthcare Research and Quality, or freestanding private clinical research facilities. Such a system would be expensive and difficult to administer and manage only for laboratory tests, however, given the inconsistencies in reimbursement for tests across the settings where they are ordered. Levies also may create a significant disincentive for test development. In this context, levies could not be directed solely at laboratory testing; rather, they should include all reimbursable health services.

**Improved CPT Coding and Risk Pooling**

Under current *CPT*-based reimbursement, if novel tests are not promptly and specifically assigned codes, reimbursement and hence use are hindered. And because *CPT* codes are updated only annually, opportunities for gathering clinical information are lost. To avoid these problems, novel tests could be assigned unique temporary *CPT* codes that would allow billing and tracking of the test's use in delivery systems, and its effect on clinical decision making and patient outcomes.

These unique codes would allow manufacturers or service laboratories to obtain reimbursement for novel tests, but such a strategy would shift a large part of the cost of test development and evaluation to payers. To address this problem, a risk-sharing approach could be implemented: payers could agree to preliminarily cover new tests on the contingency that manufacturers and service laboratory providers have a certain amount of time to establish clinical utility and value. Although these types of agreements are just beginning to be used for pharmaceuticals, they may offer promise for laboratory tests, given the fact that the evidence available at

the time of market launch is different from the evidence that will be available after clinical use.<sup>34</sup>

**Value-based Reimbursement**

Finally, and perhaps most important, consideration should be given to rewarding innovative and novel tests with greater reimbursement based on an explicit measure of the additional value they create. Health economists have developed techniques for measuring the incremental value of new technologies in terms of cost savings, morbidity reduction, and life extension, and for integrating these impacts into models that provide a measure of overall incremental value. Furthermore, higher expected levels of reimbursement can be used to justify greater investments in measuring and demonstrating ultimate clinical utility and economic value.

CONCLUSION

Laboratory tests are developed under a different regulatory structure than pharmaceuticals and have a unique and complex function in medical care. Novel tests may come to market with little information supporting their role in clinical decision making or evidence regarding their impact on patient outcomes. To address these issues and to improve patient care and outcomes, we have outlined a structure and process for information sharing among laboratory test manufacturers, clinical laboratories that provide tests, and payers that make coverage and reimbursement decisions about these tests. Although it is unlikely and perhaps unnecessary that the evaluation process for laboratory tests will equal that required for drugs, we can move much further toward a system that supports better gathering and sharing of high-quality evidence. Test manufacturers, clinical laboratories, payers, and clinicians all must play a role in this process.

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See Appendix on following page.

**Appendix.** Evidence and Transparency Standard to Support Coverage and Reimbursement for Diagnostic, Therapeutic, and Genetic Testing

**1. Product Information**

- 1.1. Product description.
  - 1.1.1. Place of the product in therapy.
  - 1.1.2. Disease description. The disease description should include the disease and characteristics of the patients in the target population.

**2. Supporting Clinical and Economic Information**

- 2.1. Evidence-table spreadsheets of all published and unpublished clinical trials.
- 2.2. Outcome studies and supporting data for economic evaluation (3-4 pages maximum per study).
  - 2.2.1. Evidence-table spreadsheets (noted above) of all published and unpublished outcomes studies.

**3. Cost-effectiveness Modeling Report**

- 3.1. Model overview. We recommend that producers and users of modeling studies subscribe to the sound guidance provided by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Good Practice Modeling Principle.

**4. Product Value and Overall Cost**

**5. Supporting Information**

- 5.1. References contained in dossiers.
- 5.2. References for economic models.