Current Issues and Options: Coverage and Reimbursement for Complex Molecular Diagnostics

This is a policy analysis document developed to inform ongoing discussions regarding certain types of diagnostic tests.

Bruce Quinn MD PhD
Foley Hoag LLP

The Committee on Medicare Payment Methodology for Clinical Laboratory Services studied many aspects of the current payment system…From the perspective of the committee, the current system contains irrationalities, which could exacerbate current problems and jeopardize beneficiary access in the future.

Institute of Medicine (2000)
Medicare Medical Laboratory Policy

The American health care system is in need of major restructuring. This will not be an easy task, but the potential benefits are great. To cross the divide between today's system and the possibilities of tomorrow, strong leadership and clear direction will be necessary.

Institute of Medicine (2001)
Crossing the Chasm

The fields of political science, public administration, law, and policy analysis have a common mission of rescuing public policy from the irrationalities and indignities of politics, hoping to make policy instead with rational, analytical, and scientific methods…. People do not always perceive a goal first…Often, they see a problem first, which triggers a search for solutions and a statement of goals.

Deborah Stone (2002)
Policy Paradox

Skip contents

Table of Contents

Section One - INTRODUCTION

TOP

1.1 Administrative barriers should not surpass technological barriers

The Institute of Medicine monograph "Crossing the Chasm: A New Health System for the 21st Century" has been frequently cited across the broad efforts to bring transformational change to the American healthcare system. Published in 2001, the report describes a "chasm" between the circumstances of today and the possibilities of the future.

At the Department of Health and Human Services, Secretary Leavitt has emphasized the Department's interest in shifting our healthcare system toward effective, personalized healthcare. *Personalized medicine* – getting the right treatment to the right patient at the right time – will be a major pillar of efforts to bring increased effectiveness and efficiency to healthcare. At the beginning of this decade, when "Crossing the Chasm" was published, the emergence of molecular personalized medicine lay mostly in the future. Today, we know far more about the molecular heterogeneity of major diseases, including cancer. And today, it is clear that targeted and more effective medical treatments will often be unattainable unless physicians have precise molecular information about the patient's disease. In short, is a priority that our healthcare system (both private payors and Medicare) facilitates the adoption of new molecular technologies when they are shown to be efficient and effective.

Personalized medicine diagnostics will develop through clinical trials not unlike those for drugs. In this "new generation" of clinically important and cost-effective molecular diagnostics, each test will be developed in the face of substantial technological challenges and development risks. Within a set of concepts and paradigms, important molecular tests can be developed through molecular information harvested from clinical trials.

Of course, all drugs and devices emerge through such a process. But the lynchpin of this study of personalized medicine diagnostics is the discovery that, to a degree which is rarely so near to the surface, a considerable number of purely administrative and process-based challenges exist as well. These are the challenges that laboratory innovators, physicians, and private and government payors face in crafting good rules for billing and payment, and processes for sound but timely coverage decisions. Unlike scientific or

technological barriers, purely administrative or process-based barriers can be discussed objectively -- including payor goals and pro's and con's of alternatives -- with confidence that improvement is possible. Legacy administrative conventions, at least when better solutions are possible, ought never present a greater barrier to progress than do natural scientific challenges.

TOP

1.2 This survey canvasses five basic operations of payors

This background document will briefly survey current processes and models for change in five areas:

- Benefits eligibility
- Billing processes
- Coding systems (CPT-4, ICD-9/10)
- Pricing processes
- Guidelines for coverage decision-making

As much as possible, we will frame issues similarly for both private payors and Medicare. However, while we held this as a major goal, our study found that there are currently some fundamental ways in which private insurer processes and Medicare processes differ. One straightforward example is *pricing*, where federal statutes and regulation tightly channel and enumerate Medicare's administrative method for a core business process. In contrast, private payors have flexibility to negotiate and contract as they find best – they establish a "market price" based on value and competition. After surveying the five issue areas, we present alternate models which are briefly described and then framed in terms of major pro's and con's.

Scope of "Complex Molecular Tests"

A few words should also address the scope of tests we are concerned with. In general, we focus on problems facing "personalized medicine" tests for disease-specific purposes, such as gene panel tests for cancer classification. But we emphasize for the purpose of this paper, we do not limit "molecular tests" to DNA/RNA tests. The tests studied here are complex tests that may be based on tissue samples or blood samples, and the tests may measure nucleic acids, proteins, or other metabolites. As we will see, these tests often defy the historical segregation of "chemistry" tests and "pathology" tests.

We also note that the term "diagnostic laboratory tests" is interpreted broadly. The immediate use of the test may be diagnostic (does the patient have disease X, e.g. recurrent ovarian cancer?), prognostic (e.g.

what will be this patient's disease course?), or predictive (e.g. wil this patient respond to Drug X?). Just to list these factors hints at problems the tests may face with the current reimbursement system. Are the tests prognostic, or diagnostic? Are they billed by inpatient or outpatient rules? Do they have a CPT code – likely not, they are too new. Are they found on a fee schedule? Are they covered? The provider of the test will likely ask a high price, due to high development costs, while the payor may question the price and also have difficulty with coverage decisions. These questions outline the range of our report.

TOP

1.3 Concerns with the present system have been raised in diverse forums

Concerns with the present reimbursement processes (and/or options for alternative systems) have been presented in diverse forums since 2000:

Source		**Representative Examples**
Government-sponsored research		Institute of Medicine (2000) Medicare Laboratory Payment Policy, Now and in the Future. 241pp. Medicare Payment Advisory Commission. (2002) Annual Report to Congress. Secretary's Advisory Commission on Genetics, Health, and Society (2006) Coverage and Reimbursement of Genetic Tests and Services. Agency for Healthcare Research & Quality (AHRQ; 2008) Infrastructure to monitor utilization and outcomes of gene-based applications: An assessment. President's Council of Advisors on Science and Technology (expected, 2008). [Report on Personalized Medicine industry].
Industry associations		Advamed American Clinical Laboratory Association
Congress	Past Legislation	Social Security Act/Medicare: 1833(h)(2)(B) BBA (Section 531) MMA (Section 942)
	Proposed	H.R.5369 (Medicare Clinical Laboratory Fee Schedule

	Legislation	Improvement Act of 2006) H.R.1321/S.2404 (Medicare Advanced Laboratory Diagnostics Act) S.736 (Laboratory Test Improvement Act) S.976 (Genomics and Personalized Medicine Act)

The most comprehensive study of the American laboratory payment system is "Medicare Laboratory Payment Policy" (IOM, 2000, 240 pp.) Here, we will cite this report as "IOM 2000." The "IOM 2000" report focuses on Medicare billing, coding, coverage, and pricing processes across all laboratory tests. However, as a reference source its value is more broad, because IOM 2000 frequently compares Medicare's processes to the status quo for the private insurers. A few processes are found to be very similar, such as coding, where national regulations enhance uniformity of process (42 CFR 160/162 specifies the CPT-4 and the ICD-9 code sets for all U.S. payor/provider interactions.) The IOM's report, now eight years old, contains far more detail than the update we present here, and IOM 2000 explored topics outside the scope of the present document. However, in Section Two we will overview the recommendations found in the IOM 2000 report and salient changes between 2000 and 2008.

TOP

1.4 Our presentation follows two organizing premises:

(i) Legacy processes met certain needs.

(ii) Options can be presented with pro's and con's.

The first premise we used in approaching the topics is that current (legacy) processes are usually rational, insofar as they reflect a good response to some historical demand. For example, a largely fixed system of procedure codes (e.g. CPT-4 codes) are an excellent means to deal with provider/payor coding of medical services that change rarely. After seeing what good purpose legacy rules serve, we can distinguish clearly why some aspects of these processes appear irrational or dysfunctional with reference to the expected expansion in very complex molecular tests. We survey alternative processes which better address the new issues.

The second organizing premise is that pro's and con's can be laid out -- notwithstanding that different parties may hold sharply contrasting views regarding the proper weight accorded to different pro's and con's, or indeed the net feasibility of different solutions to improve the system. For example, *fixed fee schedules* (like the Medicare clinical laboratory fee schedule, set in 1984) have the *advantage* of yielding highly predictable annual expenditures for the payor. In addition, fixed fee schedules have the *advantage* of strongly encouraging innovations which drop the cost of production below the fixed and

stable price (either through technologic innovation or through economies of scale gained by industry consolidation). At the same time, the fixed fee schedule *discourages or prevents* other important types of innovation which have high healthcare value and may even be net cost-saving for the healthcare system:

> Consider a hypothetical molecular test which replaces $800 of imaging, or a $1000 biopsy, or redirects $20,000 of chemotherapy. The lab test required substantial clinical research, which can be amortized over 5 years, 10,000 tests per year. The marginal test cost cost including amortized research is $200, *but* the legacy fee schedule for the relevant CPT code is frozen at $15.
>
> *No one will ever develop or supply the test, although both net healthcare dollar savings and improved outcomes would result.*

Following our second premise, whether a frozen and fixed fee schedule is, on the whole, "good" or "bad" depends on balancing its pro's and con's. Whether at the end we favor the status quo or favor change, the pro's and con's are still there and can be articulated. The "brainstorming" effort to enunciate these pro's and con's also may lead toward new strategic options, such as a fixed fee schedule for some tests and some kind of negotiated or de novo price for others.

We note that literature citations in the present report are selective and not comprehensive.

TOP

Section Two - IOM 2000 AS A DEPARTURE POINT

2.1 IOM (2000) is the most detailed survey of the present U.S. system

The Balanced Budget Act of 1997 commissioned a report by the Institute of Medicine on the U.S. laboratory reimbursement system, and also that CMS to report on its findings to Congress, along with any recommended legislative changes. [i] As a result, in 2000, the IOM published a comprehensive 240-page report entitled "Medicare Laboratory Payment Policy: Now and in the Future."

Key features of the IOM 2000 recommendations are shown in the table below. One sees that most of the recommendations made by the IOM committee (particularly recommendations with the most radical implications, such as a *de novo* basis for the

Medicare lab fee schedule) were not implemented. This could be due to any of several factors:

- The IOM committee might have been overly concerned that the system had many problems, but such concern has not been shared by most regulators, the majority of the industry, or by Congress;
- A balance of forces has existed between
  -
  - pro's and con's of the existing systems and the pro's and con's of novel systems;
  - different parties benefiting from the existing system and/or being disadvantaged by it;
- There is a general tendency of a regulatory system to stasis in the absence of crisis;
- High barriers to disruptive change, not fully foreseen by the committee; or
- Any combination of the above.

	Recommendation for Medicare (2000)	**Interval Events (2000-2008)**
1	Single national fee schedule, eliminating variant local Medicare lab schedules.	No change.
2	Set all payments at "NLA" (National Limitation Amount)	No change.
3	Alternate basis for the fee schedule (e.g. competitive bidding	No change, but a demonstration local competitive bidding system is in development. New codes, selectively, can be priced by methods not based on the legacy schedule (gap-fill).
4	Geographic adjustments (weights) to a single national fee schedule (variant on recommendation 1)	No change. Would occur only after Recommendation 1.
5	Open, timely process, with appeal.	Substantially changed, as required by Medicare Modernization Act (2003, S. 942). CMS established procedures by regulation for determining the basis for and the amount of payments for clinical laboratory tests with new or substantially revised codes "assigned after January 1, 2005. CMS implemented a novel public meetings each summer and an appeal step. The legacy process of "cross-walk" and "gap-fill" were unchanged, but are now defined by regulation (42 CFR 414.514).

6	Process to periodically update the Clinical Laboratory Fee Schedule.	No change. The update remains depending on irregular legislative actions (e.g. update 2% in year X).
7	Review alternatives to the coding system.	No change at CMS. However, since IOM 2000, the AMA CPT has implemented a temporary code system called Category III codes.
8	Do not begin to impose a co-pay for laboratory tests.	No change requested; the status quo was recommended. However, in the interim, the introduction of much more complex and costly tests (>$1000) changes the assumptions of the IOM committee (most legacy tests range from $5-$30).
9	CMS should discontinue use of ICD-9 codes to determine medical necessity.	No change. The recommended change would require regulatory change at 45 CFR 160, 162. IOM 2000's perceived fundamental flaws in using the ICD-9 system as a basis for medical necessity decisions.
10	CMS should formulate laboratory policy after stakeholder input, increased communication with its own contractors.	No specific change. However, both annual rulemaking and ad hoc rulemaking allow considerable public comment to be reviewed.
11	CMS should consolidate the number of contractors processing laboratory claims.	Change via MMA, 2003. The IOM request in 2000 seems to be concordant with the 1997 BBA (S. 4554(a) reduces laboratory test contractors to four regional contractors.) This change did not occur. The 2003 MMA reduces national Part A/B contractors to 15 or less by 2010, however.
12	Collect data to manage the performance of the clinical laboratory payment system. Trends in the existing program, or trends following change (such as competitive bidding) to be monitored for impact on access, responsiveness (e.g. of the coding	The MMA created a Council on Technology and Innovation at CMS to evaluate and reduce any problems caused by coding and reimbursement systems, which meets this end, but is not specific to

	system), value (quality/cost.)	clinical laboratory tests. Data collection & payor databases reviewed by AHRQ (2008), "Infrastructure to Monitor…Gene Based Applications."

The full IOM 2000 report is readable online, and may be purchased as a PDF:

http://www.nap.edu/catalog.php?record_id=9997

Section 3 - FIVE BASIC OPERATIONS OF PAYORS

- Benefits categories
- Billing processes which avoid discontinuity of services
- Coding systems (CPT-4, ICD-9/10) to describe tests and diagnostic conditions
- Pricing processes
- Guidelines for coverage decision-making

The summaries below are relatively short and highlight certain aspects of particular interest. This should provide the general reader with a background and vocabulary for to understand features of several major payor business processes which are relevant this report.

TOP

3.1 Benefits Categories

Benefits: Meaning. An individual is enrolled in a health plan (either a private plan or Medicare). In return, a given type of healthcare service, such as a laboratory test, may fall within a "*benefit category*" of the plan. Health plans have "exclusions," meaning services that are never eligible for coverage. Medicare may exclude screening tests; a private plan might exclude chiropractic benefits; payors may exclude "experimental" services.

Workshop participants noted that there is direct relationship between the benefit category a tests falls into and billing issues. Billing rules such as copays can now vary based on whether a service falls into different benefit categories for "screening," "preventative," or "diagnostic" tests. Under Medicare, we will see that billing jurisdiction currently shifts drastically depending on whether a test is classified as a "clinical laboratory" (chemistry) or "pathology" test although there is no longer any simple hallmark for the difference.

Note that where "experimental" services are excluded by a contractual statement, identifying *whether* a specific service the patient encounters in the future is

"experimental" becomes a process, a medical policy or medical review function. Therefore, the "coverage" aspect of this particular categorical decision is found in section 3.5, guidelines for coverage decision-making.

Benefits: Medicare perspective. Medicare covers a broad range of healthcare, but each service must fit into a specific "statutory" category. These include physician services, hospital inpatient services, hospital outpatient services, ambulance services, diagnostic tests, and other categories. Diagnostic tests encompass all tests, from PET scans to a blood glucose test.

Diagnostic tests under Medicare must contribute to the diagnosis or the management of disease [n.b., the patient shows evidence of a disease] except for a short list of "screening tests." Some Medicare-covered screening tests span the entire Medicare population. Others are covered in an "at risk" subpopulation. A periodic stool-guaiac test to screen for colon cancer is covered for all beneficiaries, but periodic glucose tests are covered only in patients pre-defined "at risk" for the appearance of diabetes.

Dilemmas can occur. A screening test that is directed toward a new disease that is occult, that has no apparent symptoms, is *not* covered by Medicare (except for the small screening test list.) But test that screen for *secondary* occult conditions generally *are* covered: consider a hematocrit test in a cancer patient on chemotherapy, which is a test for anemia, although the patient lacks any specific symptom of anemia. But pre-test risk, in the Bayesian sense, is not determinative. If the patient has a known condition with a 5% association with a second problem, the second problem may be tested-for, but if his familial history gives him a 25% or 50% risk of an even more serious problem, that test is not covered. This highlights a Medicare principle that family history *per se* is never considered a personal "sign or symptom," although in the presence of one actual sign or symptom, family history *would* of course govern the choice of tests. [ii] Prognostic tests are also problematic; Medicare's coverage documents include examples where Medicare has specifically stated it cannot cover prognostic tests. [iii] The principles for covering occult or secondary disorders are difficult to enumerate, which creates a gray zone where some personalized medicine tests may fall.

The Medicare Improvements for Patients and Providers Act of 2008 allows CMS to offer coverage for preventive tests approved by the U.S. Preventive Services Task Force.

Benefits: Private payor perspective. Two broad categories of private payor are usually differentiated. One is subject to state benefit mandates for screning tests, the other is not.

- "Health insurers" Private payor plans may offer health insurance in exchange for premiums; the payor bears risk and is usually regulated as a state insurance entity. The state may legislate various coverage requirements include screening tests (CAHI, 2008). Outside of these requirements, benefit breadth typically starts (and may finish) with a carte of options offered by the private plan.

- "ASO organizations" Alternately, private payors may manage benefits (i.e. claims processing; "administrative services only" or ASO) for a large employer. ASO plans generally fall under ERISA and are exempt from state-based insurance mandates. In ASO plans, benefit breadth is established by contracting between the employer and the ASO plan. A large proportion of US employer-based insurance falls under ASO plans.

As mentioned earlier, private insurers may vary co-pays based on benefit categories such as screening, preventive, and diagnostic services. As to diagnostic test benefits, insurers under state regulation face state-to-state requirements. All states require private insured plans to cover mammography while only 2/3 require coverage of PSA and colorectal cancer screening. No state mandates were identified which relate directly related to any complex diagnostics for personalized medicine (e.g., internet search for BRCA + "state mandate"; 5/2008). Privacy regarding use of mutation information is now regulated by Genetic Information Nondiscrimination Act (GINA, 2008), but this law does not deal with coverage (payment) for genetic testing.

Key similarities and differences (Medicare, private payor). Assuming molecular laboratory tests are not excluded as "experimental," new molecular tests for the management of disease are medical benefits which can be covered by U.S. payors. Tests which are purely "preventive" in the absence of signs and symptoms of disease are not covered by Medicare unless they are specifically enumerated in advance by law or regulation. Private insurers may be somewhat more flexible about "preventive" services but will usually enumerate preventive services in advance, such as an annual physical or mammography.

In practice, both government and private payors may be *unable* to actually distinguish between preventive and diagnostic tests during routine claims processing.

TOP

3.2 Billing Processes.

Billing: Meaning. *Billing processes* means the pathway that leads from the medical care event to payment for that service. Although a part of the billing process, *coding systems* per se are considered separately in the next section, Section 3.3. What remains of the billing process after the exclusion of coding systems are the processes of provider enrollment, determining who will bill the service, where a claim will be submitted, and who will be paid for the service. Medicare and many states have laws requiring laboratories to direct-bill the payor (e.g. a physician may not "purchase" the lab test for $10 and "re-sell" it to a payor for $20.)

Billing: Medicare perspective. Medicare regulations for billing laboratory tests are strikingly complex, and have ramified into new categories and exceptions over time, with unusual new layers of rules added in 2006 and 2007. The rules distinguish among (a) multiple locations of specimen collection, (c) test-performing entity (hospital lab,

independent lab), (d) type of test performed ("pathology" versus "chemistry" tests), and (e) time between specimen collection and test order. These billing rules for a specimen defy condensed description.

(i) Hospital inpatient. Both "pathology" and "clinical laboratory" (chemistry) tests are "bundled" with Medicare's inpatient DRG inpatient payment. This means that molecular tests based on blood or tissue samples of inpatient origin must be paid by the hospital from its DRG reimbursement *while* the patient is an inpatient, *and* up to 14 days after discharge *or* 30 days after the biopsy, whichever comes first.

But, due to BIPA 542(c), if the test is a pathology test and performed by an *outside* lab for the inpatient, *and* fits under certain additional conditions, *and* it is billed before 12/31/2009, it *must* be billed by the non-hospital lab, *whether inside or outside* the 14 day rule. [iv]

(ii) Physician office patient. Tests are billed by the physician if his office performs the test. But if the specimen is sent to the independent lab which performs the test must bill it.

(iii) Independent laboratory. Tests taken at an independent laboratory's blood draw center: the laboratory bills Medicare directly.

(iv) Hospital outpatients. The most complex intersection of specimen, test, location, and date rules occurs for Medicare hospital outpatients. (The patient was in a hospital-based outpatient clinic at time of blood draw or biopsy, and registered as an outpatient.)

(iv-a, Test performed on-site by hospital)

The hospital has bills Medicare as a line-item for each test it performs itself.

(iv-b, Test sent to outside reference lab)

The rules here continue to shift and in some cases are poorly defined. In 1999, Medicare stated that an outpatient's lab tests, if transferred for outside lab pathology tests should be billed by the outside lab unless re-purchased by the hospital, which would then bill Medicare (64 FR 39623, 59408). In 2001, Medicare revised this position (65 FR 55285), asking the outside lab to bill the hospital rather than Medicare. But thereafter, Congress requires an outside pathology lab to bill Medicare directly for pathology tests on both hospital outpatient and inpatient specimens until 12/31/2009 (BIPA 542(c); footnote (iv)). "Chemistry" or "clinical laboratory" tests are handled differently. If the test is *ordered* during the hospital outpatient encounter, but the blood is *drawn* off the hospital grounds, the reference lab bills (65 FR 18440ff). If the test is drawn by the hospital for its outpatient and sent to a reference lab, the hospital bills. Policy statements in 2000-2003 received elevated visibility both within CMS and for hospitals/laboratories when placed in formal regulations in 2005 and 2006 (42 CFR 414.510). Corresponding

instructions to Medicare's contractors implement the chemistry test rule effective either 1/1/2007 or 1/1/2008 (interpretations vary) for clinical chemistry specimens, and 1/1/2009 for those outpatient pathology specimens not covered by BIPA 542. Rules change if the specimen is stored 14 days before the day the physician orders the test. Additional issues are discussed in an endnote. [v]

(iv-c. Hospital "non-patient" & on-site hospital lab.)

If the patient is *not* formally registered as an outpatient (CMS calls him/her a "non-patient") and the test is performed at the hospital lab, the hospital bills. For example, the specimen may be triaged to the hospital from an independent blood draw site.

(iv-d, Hospital non-patient, unrelated reference lab)

If the patient is *not* registered as a "hospital outpatient" *and* receives only a blood draw from the hospital, the test referred elsewhere for processing, the service appears to be classifiable as a non-patient service but several complexities can occur. [vi]

Billing: Private payor perspective. Generally, the performing entity (private payor, hospital, or independent laboratory) bills the insurer for the laboratory test. The plan may contract with a limited network of laboratories at preferred prices.

Key similarities and differences (Medicare, private payor). The most obvious difference is that Medicare's rules for billing jurisdiction can barely be summarized in a page, while private payors' rules fit within a sentence. This violates the spirit, if not the letter, of HIPPA legislation which required CMS to superintend nationwide consolidation and standardization of efficient billing processes between providers and *all* payors (e.g. see 45 CFR 160, 162).

The rising discrepancies between Medicare and national private payor billing processes require laboratories to make complex distinctions not only among services for non-Medicare and Medicare patients but also between subtypes of Medicare samples, location of collection date of collection, date of physician order, interval between these dates and hospital discharge, etc. A specialty molecular lab that directly bills private payors may need to establish a payment contract with each national private payor plan (circa 1000; GAO, 2005). In the case of a specialty molecular lab that bills for Medicare patients, it may need to establish one contract with its local carrier (for physician-origin or independent lab-origin specimens) and also establish contracts with each hospital in the U.S. (circa 5000 hospitals; AHA, 2008) to invoice each hospital, after which the hospital bills its fiscal intermediary. A deeper problem is that for Medicare, billing jurisdiction whipsaws among providers based on the poorly defined nature of a "covered hospital" and service under BIPA 542, and the ambiguous nature of a "pathology" versus "clinical laboratory" test, which has been badly blurred by the advent of modern complex diagnostics that intimately merge the two disciplines within one test product.

TOP

3.3 Coding systems (CPT-4, ICD-9/10)

Coding systems: Meaning. The HIPAA act required the Secretary of Health and Human Services to establish standard code sets for transmitting healthcare services data between providers and payors (HIPAA, 1996, section 1173). Regulations were finalized in 2000 [vii] and establish the AMA's CPT-4 as the U.S. code set for physician services and laboratory tests, and the ICD-9-CM code set for diseases. In choosing the code sets, HHS followed ten guiding principles including ease of use, flexibility, minimize burdens on users, and encouragement of innovation. [viii]

For procedures, CPT-4 describes thousands of physician services and some 9000 laboratory tests in a five-digit system (e.g. 12345). The CPT-4 laboratory test codes fall in the 80000 series. Molecular tests are described in three different ways. The molecular test may be identified by a single unique code (e.g. HIV RNA quantitation). Molecular tests may also be described by a series or "stack" of generic chemical test steps (e.g. DNA extraction, DNA amplification). Finally, test may be described by "not otherwise classified" codes (84999, unspecified chemistry procedure.)

For diagnoses, codes in the ICD-9-CM describe conditions such as appendicitis or acute leukemia, and symptoms such as abdominal pain or cough. The main format for ICD-9 codes is 5 digits, of which two are decimals (e.g. 555.12). Generally, providers submit a procedure code and one or more related diagnosis codes on their insurance claims. Payors may edit to "procedure + diagnosis" in order to autopay or autodeny a claim. For example, "hematocrit + anemia = pay"; and "appendectomy + schizophrenia [+ no other diagnosis] = deny."

Issuance of a new CPT code requires widespread use of the test, acceptance of the test as medically necessary by an AMA review panel, and a timeline of roughly 18 months between proposal of the test (e.g. by the manufacturer) and activation of a new code. [ix] ICD-9-CM is also updated annually, but updates are typically modest in scope. In 2005, the AMA added an Appendix "I" which lists 83 two-place modifiers for types of genetic tests (e.g. 2B, BCR/ABL genes associated with 9:22 translocation in chronic leukemia.)

Formally, all codes for items and services are HCPCS codes, of which the CPT-4 code set are "Level I" codes. In common usage, many average users call Level I codes "CPT" and Level II "HCPCS" codes. "Level II" codes begin with letters (A1234) and typically indicate disposable supplies, durable medical equipment, and injectable drugs. Medicare and private payors differ in the use of alphanumeric HCPCS Level II "G codes" for Medicare and "S codes" for private payors (see below).

Coding systems: Medicare. Medicare contractors are required to follow all rules in the AMA CPT manual plus additional rules released from time to time by Medicare. CPT requires that codes used must "precisely, not approximately, match the service rendered" and that when a precise code is not found, a not-otherwise-classified code should be used. Level II "G" codes represents services for which Medicare claims processing requires a code but no exact code is available in the CPT system. [x]

Coding systems: Private insurers. Due to HIPAA and federal regulations which apply to all provider:payor transactions for "healthcare services" CPT-4 and ICD-9-CM code sets are also used by private insurers. Private insurers may also use a set of HCPCS Level II codes beginning with "S". Nominally proposed to CMS by Blue Cross Blue Shield plans for includes in the S-code list, the S-codes can be used by other private payors as well, but are not recognized by Medicare. Of 593 "S" codes current in 2007, about 40 represented laboratory tests (ICD9data.com, 2007) about about 30 of those were molecular tests (S38nn: S3818, complete gene analysis, BRCA1; S3854, gene panel for managing breast cancer).

Key similarities and differences (Medicare, private payor). Most complex molecular tests have no specific code, although private payors have created about 30 "S" codes which do not exist in the standard CPT-4 system, including S3854, gene panel test for breast cancer management. This suggests that private payors see a need to call out these tests specifically (either for payment or for denial purposes), and the regular CPT system has not met this need, requiring them to institute S-codes on a one-off basis.

There are no clear guidelines as to the scope of existing CPT codes; only the text of the code is binding on the providers/payors under HIPAA regulations (implemented at 45 CFR 160, 162). No entity is designated as the final arbiter of CPT code ambiguities. For example, parties may differ on whether the code 83898 (amplification of nucleic acid), established in 1993, includes high-sensitivity quantitative PCR or not. Use of telegraphic CPT codes which are only a few words long requires a certain depth of content knowledge about the underlying services. For example, in the 83XXX series the adjective "molecular" refers only to nucleic acid tests -- although any protein or metabolite is also a "molecule" -- because the original authors *intended* that "molecular" referred only to nucleic acids (DNA, RNA). Otherwise, a reader could not guess whether or not:

88384 Array-based evaluation of multiple molecular probes; 11 through 50 probes

includes protein arrays as well as DNA arrays, since both proteins and DNA are "molecules."

The addition of the CPT's "Appendix I" molecular test modifiers provides some additional information ("2B" = BCR/ABL gene translocation) but is focused on gene tests of longstanding interest and it is unclear how often this Appendix will be updated to reflect novel personalized medicine molecular tests.

TOP

3.4 Pricing process

Pricing process: Meaning. Pricing refers to the payment transferred between payor and laboratory. This is usually a flat per-item reimbursement. Recently, new reimbursement models contractually encompass risk-sharing arrangements between the provider and the

payor (in the U.K.: NHS re bortezomib/Velcade; for a U.S. molecular test, United Healthcare, Genomic Health/Oncotype DX; see Pollack, 2007).

Pricing process: Medicare. Medicare prices most laboratory tests based on a clinical laboratory fee schedule set in 1983 and occasionally revised upward or downward en masse by legislation (IOM, 2000; Raab & Logue, 2001; Young, 2002).

A public and very specific Medicare pricing process is triggered when the AMA CPT panel issues a new laboratory CPT code. To add prices to new codes entering its Clinical Laboratory Fee Schedule, Medicare "crosswalks" the price from an existing, similar laboratory service, or else "gap-fills," that is, interpolates a price (e.g. 30% above Code X, 20% below Code Y). Through legislation, Congress asked CMS to refine its policy to assure appropriate pricing of new tests (BBA 531, MMA 942). CMS now holds public meetings each summer to solicit public comment on appropriate pricing for new CPT codes which will become effective on the following January 1. In brief, if most commenters recommend the same crosswalk price, CMS will assign a crosswalk price. If commentators differ, or CMS believes a crosswalk price is of low accuracy, a "gap-fill" process begins. For one year, regional carriers price the test and submit their chosen price to CMS. Carriers consider a number of disparate pricing tools (e.g. invoiced charges; prices paid by other insurers; resources required to perform the test; resources required by related services; or other data.) At the end of the gap-fill year, current regulations require CMS to then assign a price which is the median of prices submitted by its contractors (each contractor having equal weight, regardless of the number of claims reviewed; see 42 CFR 414.514.)

CMS may adjust prices by up to 15% per year based on an "inherent reasonableness" authority (Health Law Alert, 2006) or by following a similar clause in the laboratory pricing section of the Social Security Act at 1833(h)(2)(b) [xi].

Formally, the crosswalk/gapfill rules are invoked when a *new* CPT code is created by the AMA. What if a new test is released, but no new CPT code yet exists? Medicare contractors are likely to follow the crosswalk and gapfill alternatives when a new test is submitted as a not-otherwise-classified code, e.g. CPT 84999. As the regulations are written, CMS does not directly instruct carriers to follow any specific process to price a not-otherwise classified code (e.g. 84999; see CMS 2008) whereas CMS instructs carriers to follow specific gap-fill rules after CMS categorizes a *new* CPT code as a gap-fill code. In the *hospital outpatient* system, unlisted laboratory codes such as 84999 and 94920 were until recently assigned to APC 0342 at circa $10 (e.g. 72 FR 66937). Now one of these codes, 84999, is currently assigned to individualized pricing through a series of steps based on manual review and the judgment of the reviewer (see CMS, 2007).

Some of the molecular testing CPT codes are priced similarly across most but not all Medicare regions. But some of the molecular testing CPT codes are priced a great deal lower in several states, e.g. 83902-83912. In a handful of states (e.g. Massachusetts; Georgia) these codes are paid at only 20% of the levels in most other states. Similar fee schedule paradoxes apply to *proteomics tests*; there are very few historical codes for

proteomics tests and payment rates are fixed ($10-20). A new test may be ambiguously classified under 83950 (oncoprotein assay) versus 86316 (immuno assay for tumor) versus 84166 (quantitative protein assay) versus 84999 (unlisted chemistry test) or 82940 (unlisted pathology test) with 10X pricing variation depending on the coding choice and the location of service.

Pricing process: Private payors. Most private payors pay for laboratory tests in some proportion to the Medicare Clinical Laboratory Fee Schedule, although they are not required to do so (IOM, 2000). As of the IOM 2000 study, most private payors paid rates roughly similar to the Clinical Laboratory Fee Schedule (IOM, 2000, Tables C1-C11), particularly at the private payor median. No similarly comprehensive but more recent survey of private payor pricing was identified. The IOM surveyed a sampling of CPT codes but none in the "molecular diagnostics" series. As noted earlier (Section 3.3) private insurers may use "S" codes for some molecular diagnostic tests, but pricing schedules for these codes are not publicly available. One company, Genomic Health, has a single marketed test (Oncotype DX) in the $3000 range. Publicly available SEC reports indicate that this test is paid near its list price by both private payors and Medicare.

Some payors have proposed innovative risk-sharing coverage and payment for at least one complex molecular test (Pollack, 2007). Specific details of a reported contract between United Healthcare and Genomic Health for reimbursement of the Oncotype DX test have not been released. However, the cited report (Pollack, 2007) compared the arrangement to the UK NHS reimbursement of bortezomib/Velcade, in which payment is tied to the drug's observed effects in individual patients.

Key similarities and differences (Medicare, private payor). Medicare is required to follow a fixed fee schedule when pricing complex molecular diagnostics, by "code-stacking" individual steps in the test process. This is based on a principle that when CPT codes (or a combination of codes) exist to code a test, it must be so coded. And once it is so coded, the resulting price is read out from the Medicare Clinical Laboratory Fee Schedule. However, it can be ambiguous whether existing CPT codes do or do not describe proprietary steps in new-generation diagnostic tests. When "code-stacking" is not feasible, and the claim is submitted with an "unlisted" code, Medicare provides no defined pricing algorithm, although most contractors are likely to elect to apply the gap-filling guidelines they would use for a specific new, but unpriced, CPT code.

It has been questioned whether the legacy Medicare fee laboratory fee schedules covers costs in molecular tests (e.g. Raab & Logue, 2000; IOM 2000) and this problem would be accentuated if a personalized molecular medicine laboratory was located in states with very low molecular reimbursement (e.g. Georgia; Massachusetts), and its test was reimbursed through "code-stacking." Medicare's pricing guidance for "gap-filling" asks contractors to compare a range of price references (e.g. median of invoiced priced; prices paid by other payors; resources required to "perform" the test) which could span a very wide range of price benchmarks. The resulting uncertainty in test payment could discourage investment in new complex molecular tests, because of the difficulty of making reliable projections for early decision-making.

Private payors have considerably more discretion to negotiate pricing with providers, for example, to depart from the published Clinical Laboratory Fee Schedule and negotiate "value-based pricing" using pharmacoeconomic models or other reimbursement models, such as more complex risk-sharing agreements.

A note on economics of pricing

Note 1. The use of "value based pricing," usually in reference to a pharmacoeconomic or similar model, is problematic in practice. For example, a test costs $1 to run but saves $1000 in healthcare costs. If many competitors can produce the test, microeconomics suggest the price will tend toward $1. If there is one seller and one rational buyer, the price may tend toward $1000 (although behavioral economics suggests there may be a face-off until the price is near $500). Where the price settles between $1 and $500 will include factors like the availability of alternatives or work-arounds, and market segmentation of purchasers (by their available funds and/or their perceived test value), as well as uncertainty about the real value of the test (will it really save $1000? Maybe one-fourth that?). Value based pricing rarely can establish a single price without much knowledge of other market factors.

Note 2. Medicare's "crosswalk" and "gap-fill" rules lead to other complexities. Clinical laboratory fee schedule prices, as described in IOM 2000, were set for mature, commodity tests in the 1980s and thus microeconomics suggests they reflect marginal-cost pricing. If in fact they allow little room for "producer surplus" over marginal cost, it will be impossible for the producer to run clinical trials to develop new tests. On the other hand, Medicare's quirky "gap-fill" rules yield a wide but unpredictable range of solutions, from which the Medicare carrier will set one single price for the test. For example, one "gap-fill" metric is median price paid by other insurers (say, $1000) while another "gap-fill" metric is "resources to perform the test" which the Mediare carrier may estimate at $50, that is, a bare marginal cost of chemicals, tubes, minutes of technician time. While Medicare (and any other payor) will aim for the lowest price possible, attempting to reimburse a service with high development costs at marginal cost could simply yield a "null" marketplace. Both classical and recent economists have argued cogently that some market "inefficiency" – that is, prices above marginal costs – is a critical factor for technologic progress (McKenzie & Lee, 2008, and references therein). In addition, one would predict that the extremely high variance alone of the gap-fill rules would lead to general under-investment due to the wide uncertainty of returns due to pricing, beyond the uncertainty of long R&D pathways. (Variance here points to the elaborately developed concept of risk and volatility in financial valuation theory; see e.g. Boer, 1999. One set of risk-narrowing tools, real options analysis, e.g. Mun, 2006, will not be helpful here because of the volume of variability stored in the final step in product development, the Medicare gap-fill process).

TOP

3.5 Guidelines for Coverage Decision-Making.

Meaning. Both public and private payors want to pay for only medically necessary services. However, ruling whether a given procedure or service is "medically necessary" is subjective and the border between "investigational" and "medically necessary" care is difficult to define. [xii] There is an enormous amount of literature on the validation of biological and medical concepts (Schaffner, 1993; Thagard, 1999; Haack, 2007) and on what should constitute "evidence-based medicine" (EBM; CEBM, 2008; Jenicek & Hitchcock, 2005; Riegelman, 2004). There is a good deal less known about exactly how payors make coverage decisions, or better stated, exactly how individuals making coverage decisions, or how individuals or teams weigh the diverse components of the decisions. Coverage decisions rely more strongly on data from trials high in the "levels of evidence" hierarchy (e.g. U.S. Preventive Services Task Force; randomized clinical trials rank above cohort studies, etc.) The Blue Cross Blue Shield "TEC" criteria list five questions which are used to structure reviews of the evidentiary support for a new technology, although TEC reviews are labeled as not being coverage decisions (BCBS, 2008). Very specific thought capital regarding analysis of prognostic cancer gene panels is available in the academic literature (e.g. Ioannidis, 2006).

Coverage guidelines: Medicare. Medicare coverage decisions may be published National Coverage Decisions (NCDs), published Local Coverage Decisions (LCDs), or unpublished contractor coverage decisions applied during claims processing (claims are paid or are denied, but there is no published explanation). All of these decisions follow from a statutory requirement that Medicare not pay for coverage that is not reasonable and necessary to diagnose or treat disease.

Medicare has published general guidance to be used for local coverage decisions (CMS, 2008b). Medicare has published several regulatory approaches to defining medical necessity in its NCDs; the last of these was published in draft in 2000 and never finalized (65 FR 31124). National coverage decisions (NCDs) are reached in the conclusion of a national coverage analysis (NCA), which contains an extensive discussion of the published literature on the technology or service in question (CMS, 2008c). These discussions provide a comprehensive review of the relevant literature and are usually framed around a series of questions (such as, Is the evidence sufficient to establish X?). However, other than review of the "case law" of diverse decisions, exactly how different factors are weighed is uncertain (Giacomini, 2005).

Medicare's LCDs vary greatly in how (or whether) they present a reasoning process behind the coverage position. Not infrequently, Medicare LCDs may state tersely that a given service was reviewed and found to be "not reasonable and necessary." Almost no LCDs provide a critical *discussion* of the literature, although either few or many journal articles may be *cited* in an LCD (Foote & Town, 2007).

Coverage guidelines: private payors. Private payors vary in the number of coverage decisions available on their websites. Among private payors, Aetna and Cigna maintain large websites with regularly updated coverage policies, as do some Blues plans. Aetna (2008), for example, lists some 500 medical policies. Most include several pages of literature review. Like Medicare NCDs, private payor coverage policies review and

discuss the available literature. Typically, in private payor systems, non-covered devices or procedures are described as "experimental" or "investigational." This description foots to contractual statements that experimental or investigational devices and procedures are not covered in the insurance policy.

Key similarities and differences (Medicare, private payor). Both Medicare and private payors prefer to base coverage decisions on large, double-blind randomized controlled trials. However, coverage decisions must give equal weight to the internal validity and external validity of studies. Undertaking a double blinded trial may be impossible (e.g. the surgeon knows his type of surgical procedure, or the drug has distinct adverse effects compared to placebo). The more precisely the study population is defined, the greater may be its differences from the general population in whom the procedure or test may be used. It is difficult to lay out procedures in advance for balancing conflicting data or balancing conflicting clinical needs (Braddick et al., 1999), yet these clinical counter-forces may be at the heart of coverage decisions. There is a general interest in diffusing the adoption of medically useful innovation, balanced by the concern that early positive results are sometimes never replicated (Ioannidis, 2005). In some circumstances, enough may be known about a test (e.g. it categorizes high- and low-risk patients accurately) that randomized clinical trials are unethical (e.g. known low-risk patients will not be ethically randomized to chemotherapy.) This raises a dilemma if an insurer requires a prospective randomized controlled trial for its coverage decision. [xiii]

TOP

Section Four – Alternative Approaches to Key Processes

4.1 Benefit Categories

Problems to be solved:

- Health insurance would be impractical without defined benefits; for example, actuarial calculations would be disrupted.
- Services should be readily identified as part of a covered or non-covered category.
- States may require specific test benefits.
- Medicare statute excludes "screening" services which are not enumerated, but border between screening & diagnostic services is occasionally problematic.

Current Benefit Approach	Pro	Con
+ Coverage benefits are broadly (telegraphically) defined.	+ Economy of contracting. + Meaning of benefit categories have been	+ Gray zone between categories.

+ Excluded categories may contain enumerated exceptions (Medicare excludes “screening tests” as a category, then lists exceptions.) + Primary benefit category distinctions for laboratory tests are between “screening”, “preventative”, and “diagnostic” tests.	established by time and by convention. Relatively few tests raise uncertainty as to their classification. + Additional tests may be specifically excluded or included by name.	
Benefit Proposal 1:		
+ CMS, AHIP, or other entities produce reference document defining “screening”, “preventative” and “diagnostic” tests.	+ This will reduce uncertainty. + Better match contracted payments for the “screening” and “preventive” categories	+ Consensus definitions may be difficult to achieve. Even if this is so, key problems in the definitions could be better articulated.

TOP

4.2 Billing Processes

Problems to be solved:

- Billing processes are administratively efficient for payor.
- Billing processes are administratively efficient for laboratory or physician/hospital.
- Double-billing to different entities is avoided.
- All entities are properly verified (enrolled lab, enrolled patient, enrolled doctor, etc)

Current Billing Approach	Pro	Con
+ Medicare and state laws generally require direct-bill to payor by performing laboratory. + Medicare exceptions for hospital outpatients (see next row) + Labs enroll with payor.	+ States have flexibility to set regional requirements. Few lab tests fall under state mandates. + Set pathway of bill submission reduces double payments to two entities (e.g. physician office and performing lab.)	+ Multi-state insurers must vary lab test benefit plans by states.
+ Medicare has additional complex rules for the hospital outpatient setting.	+ Although complex, such rules implement the statute, through regulations and evolving agency interpretation of prior statutory language.	+ Processes change after years with no statutory update. + Hospitals newly become responsible for costs and medical necessity of lab tests ordered by distant, unaffiliated physicians and performed by distant, unaffiliated labs. + Complex rules generate additional gray zones. + Basic facts such as the “date of service” of a lab test vary depending on what payor the provider is submitting to, and the

		coverage category of the test.
Billing Proposal 1:		
+ Private plans: No change suggested.		
Billing Proposal 2:		
+ Medicare: Revisit recent billing rules for outpatient-origin specimens. Replace existing complex rules with simple rule, e.g. add modifier "HS" to indicate a hospital specimen but allow performing lab to bill.	+ Along with allowing performing laboratory to bill, responsibility for repayment on audit returns to the performing laboratory + One contractor audits and controls most of laboratory's payments. + Revenue-neutral.	+ Regulatory change required.

TOP

4.3 Coding

Problems to be solved:

- Define services performed, in uniform exchanges between provider and payor.
- Most services are well served by fixed codes which change rarely.
- Interfaces between codes may be complex and require specialty or subspecialty understanding of current & proposed codes.
- Coding system should adapt to changing technology.
- Coding system should support needs of coverage decisions, since they are specifically interchanges between provider and payor. Provider and payor exchange information primarily for reimbursement. Provider and/or payor may need to distinguish among categorical services (e.g. prostate gene panel X is acceptable; prostate gene panel Y is not.) But in general, CPT codes do not distinguish mfgr-specific services.

Current Coding Approach	**Pro**	**Con**
+ Coding system changes rarely. + New codes are carefully scrutinized for necessity & for conflicts or "interface" with existing codes. + Infinite range of genomic tests can be coded by a small number of fixed codes (e.g. "gene amplification")	+ System is stable and uniform nationally.	+ Payor need to distinguish among services (panel X, panel Y) is unmet. Recent two-places modifiers fail to meet this need. + Timeline to new code is lengthy. + Uncertainty about so-called "politics" of code creation. + Delay in new codes raises administrative costs due to manual processing of "unclassified" codes.
Coding Proposal 1:		
Increase use of Category III codes ("temporary tracking codes") for molecular tests.	Mechanism is in place; revisions annually; barrier to entry not high.	Codes are by definition temporary, so this is not a long-term solution. Reports of payor bias

		against paying Category III codes.
Coding Proposal 2:		
Increase use of Level II (HCPCS) codes for molecular tests.	Codes could be updated separately from the AMA CPT process.	Level II codes (except S codes) are managed by CMS, which has limited administrative resources. CMS issues procedure codes primarily for clear programmatic need, e.g. to edit services under an NCD.
Coding Proposal 3:		
Establish new code set, more similar to NCD codes for specific drugs.	Rapid and specific identification of new test. System works well for drugs (NCD system) and consumer products (UPC system.) Five-place codes using letters (LWXYZ) allows 12 million codes.	Would require new national process; but some Congressional proposals have proposed a national multi-stakeholder committee to issue codes (and set prices). Unless linked to some external validator, like FDA approval number, the exact process of test is uncertain.

TOP

4.4 Pricing

Problems to be solved:

- Maximize overall economic efficiency (e.g. if U.S. healthcare spending is $2T, distribute among an optimal array of services.)
- Definition of economic efficiency of healthcare services is uncertain and overall allotment of resources very difficult to control and monitor.
- Encourage value-creating innovation. *De minimus*, cost-saving to cost-neutral innovations should be promoted.
- Definition of value in healthcare is uncertain.
- Administrative efficiency.
- Transparency (particularly government payors).

Current Pricing Approach	**Pro**	**Con**
+ Private payors – free hand to contract at market prices; more often than not, payments near CMS fee schedule (IOM, 2000). + Rarely (so far), use of risk-sharing contracts (see white paper)	+ Market forces define exchange prices + Innovative pricing systems are possible	+ Complexity of services, volume of services, and relatively small charge-per-service makes negotiations cumbersome
+ Medicare – priority to price molecular diagnostics by "code-stacking" + When code-stacking is not possible, entirely different rules appear (e.g. median of invoiced charges)	+ Total costs for lab tests highly predictable across CMS + Administratively efficient	+ Fee schedules for some molecular lab steps vary sharply (5X) among states
Pricing Proposal 1:		
+ Competitive bidding	+ Natural market process for private payor (e.g. Megalab X and Y compete for Insurer X) + Some limited experience in the Medicare system + Congress requires demo	+ Coding system does not allow precise specification of molecular tests + "Competitive bidding" fails to work well for sole-source (e.g. monopoly) products

	projects in Medicare system	
Pricing Proposal 2:		
+ Medicare – price by market surveys (similar to drugs/ASP)	+ Assumes market prices are fair and competitive	+ Administratively cumbersome + Does not leverage "pricing power" of government vis a vis sole source products
Pricing Proposal 3:		
+ Medicare – set "code-stack" price and adjust upward to account for development costs	+ Avoids marginal pricing which could prevent new product development	+ Administratively cumbersome + Assumes a "fair" composite price can be established + Requires rules for choice of "add-on" value above "code-stack" price
Pricing Proposal 4:		
+ Creative contracting	+ Optimize incentives for both lab and payor	+ Little experience with this process + Administratively cumbersome

TOP

4.5 Coverage decisions

Problems to be solved:

- Pay for care that is "reasonable and necessary" and "not experimental"
- Terms not clearly defined
- Timelines are long
  -
    - Genuine uncertainty with replicability of new publications
    - Review period is long (4-8 months)
    - Concern about "Type 2 error", that is, withholding high-value services from member patients
- Developers/investors have high uncertainty about requirements and judgment processes used

Current Coverage Approach	**Pro**	**Con**
+ Primarily technology assessments which leverage principles of critical thinking in experimental design and principles of evidence-based medicine	+ Numerous US payors and tech assessment groups (govt/non-profit/commercial) "compete" for credibility and probably collate toward consensus over time	+ Less than optimal understanding of how "incommensurate" factors are weighed (blinded RCT with large effect has high internal validity, but use of restricted test population limits external validity; *versus* a study with the opposite characteristics) + Differences between "EBM" and "coverage decisions" not well articulated
Coverage Proposal 1:		
+ Use of focused guidelines, similar to FDA guidelines for narrow product categories	+ Works well for FDA + Maximizes predictability for industry	+ Difficult-to-articulate factors may play variably large role, depending on coverage decision
Coverage Proposal 2:		
+ Produce book or thorough white paper of "case studies" of natural coverage decisions	+ Raise visibility of issues for future work	+ Unclear who would ever do this

	+ Other fields, such as judicial decision-making, have enormous literature of this type (e.g. Posner, 2008) + A few examples exist (e.g. Giacommini, 2004)	

Notes to Tables

Giacomini M (2005) One of These Things Is Not Like the Others: The Idea of Precedence in Health Technology Assessment and Coverage Decisions. Milbank Quarterly 83:193-223.

Posner M (2008) How Judges Think. Harvard University Press. Writings in the field extend back a century (e.g. Holmes; Cardozo.)

BIBLIOGRAPHY

Aetna (2008) Clinical Policy Bulletins, Alphabetical List.

http://www.aetna.com/cpb/medical/data/cpb_alpha.html

AHA (2008) AHA Chartbook.

www.aha.org/aha/trendwatch/chartbook/2008/08chapter2.ppt

AHRQ (2008) Infrastructure to monitor utilization and outcomes of gene-based applications: An assessment. Online at www.ahrq.org

BCBS (2008) Blue Cross Blue Shield Technology Evaluation Center (TEC).

http://www.bcbs.com/blueresources/tec/

Boer FP (1999) The Valuation of Technology: Financial issues in R&D. Wiley.

Braddick M et al. (1999) The use of balance sheets in developing clinical guidelines. J Am Board Fam Pract 12:48-54

CAHI (2008) Health insurance mandates in the states, 2008. www.cahi.org.

http://www.cahi.org/cahi_contents/resources/pdf/HealthInsuranceMandates2008.pdf

CEBM (2008) Centre for Evidence-Based Medicine. www.cebm.net

CMS (2007) CR 5544 [rules for pricing of unlisted laboratory code in hospital outpatient claims]. http://www.cms.hhs.gov/Transmittals/downloads/R1209CP.pdf

CMS (2008) Claims Manual, Chapter 16, 100.4. [rule for pricing of unlisted laboratory code in carrier claims]. http://www.cms.hhs.gov/manuals/downloads/clm104C16.pdf

CMS (2008b) Program Integrity Manual, Chapter 11, Local Coverage Decisions.

Foote SB & Towne RJ (2007) Implementing evidence-based medicine through Medicare coverage decisions. Health Affairs 26:1634-42.

GAO (2005) Private health plans in U.S. Memo to Congresswoman Snowe. http://www.gao.gov/new.items/d06155r.pdf

Giacomini M (2005) One of These Things Is Not Like the Others: The Idea of Precedence in Health Technology Assessment and Coverage Decisions. Milbank Quarterly 83:193-223. Online at:

http://www.milbank.org/quarterly/8302feat.html

GINA (2008) Genetic Information Non-discrimination Act. Enacted, 5/2008.

Health Law Alert (2006) CMS publishes inherent reasonableness final rule. [70 FR 73623]

http://www.ober.com/shared_resources/news/newsletters/HLA/hla_fall06_14.html

ICD9data.com (2007). S-codes (private payor codes).

http://www.icd9data.com/hcpcs/2007/S/default.htm

IOM (2000) Medicare Laboratory Payment Policy: Now and in the Future.

Ioannidis JM (2005) Contradicted and initially stronger effects in highly cited clinical research. JAMA 294:218-28.

Ioannidis JM (2006) Is molecular profiling ready for use in clinical decision-making? Oncologist 12:301-11.

Jenicek M & Hitchcock D (2005) Evidence-based practice: Logic and critical thinking in medicine. AMA Press.

Lab Technologist (2007). 'Free drugs', but only if they don't work, proposes drug firm. http://www.labtechnologist.com/news/printNewsBis.asp?id=77064

McKenzie RB & Lee DR (2008) In Defense of Monopoly. Univ. Michigan.

Mun J (2006) Real Options Analysis. Wiley.

Pollack A (2007) Pollack, Pricing Pills by Results, New York Times, July 14, 2007. See also Lab Technologist (2007). http://www.nytimes.com/2007/07/14/business/14drugprice.html?_r=1&pagewanted=print&oref=slogin

Raab GG & Logue LJ (2001) Medicare coverage of new clinical diagnostic laboratory tests: the need for coding and payment reforms. Clin Leadersh Manag Rev15:376-87.

Riegelman RK (2004) Studying a Study, Testing a Test. 5th ed., Williams & Wilkins.

Young (2002) Reforming Laboratory Reimbursement. Clin Chem 48:792-5.

---

[i] The BBA is identified as PL105-33. Section 4553[c] requests the IOM to issue a comprehensive study of laboratory test reimbursement, the IOM 2000 report. Of historical interest, the subsequent section, 4554(a), created four regional carriers who would handle all laboratory test claims. Exactly this system was established for DME carriers (Regions A-D). But no "laboratory test carriers" were never created. 4554(b) required the creation of uniform national policies for laboratory tests through "negotiated rulemaking". This included a date of service rule (for example, to bill a 24-hour collection, would the claims date-of-service be: [a] the first day, when the test is ordered, [b] the second day, when the sample is taken, [c] the third day when the test is completed, or [d] the fourth day, on which the test is reported). The effort created 23 national coverage decisions for common laboratory tests, with precise coding instructions. The committee met nine times between July 1998 and August 1999. For results of 4554(b) see 65 FR 13082ff, 3/10/2000 and 66 FR 58788ff, 11/23/2001.

[ii] *Incongruous coverage* can result. For example, a regular screening test for glaucoma is covered for asymptomatic patients with a racial heritage of being African-American or Hispanics; though how far the benefit extends to multi-racial individuals is unknown. Some individuals with one or more parents with glaucoma have a *higher* risk of glaucoma than an African-American or Hispanic individual, but the "family history" does not count as a personal sign or symptom, and despite the higher risk, glaucoma testing is not covered.

[iii] In 2000, CMS stated that, in general, under some circumstances prognostic cancer tests were necessary in the care of disease: "Prognostic information, even if it did not affect a treatment decision, *could be considered* to improve health outcomes." Decision Memo CAG-00065N. However, in 2003, CMS said that it *would not undertake* a request for a prognostic clinical test in cancer patients. After receiving a request to at review published data on prognostic accuracy of PET scans for thyroid cancer patients, CMS answered concisely, " [The proposed clinical situation, cancer prognosis] is not reasonable and necessary and *was not addressed*." Decision Memo, CAG-00095N. It could be that the question was misphrased, for example, a request to test cancer prognosis "for hospice care decisions" or another enumerated decision might have been opened for consideration.

[iv] BIPA 2000, Section 242(c), requires that *only* the outside laboratory can bill for "physician pathology services" on inpatient or outpatient specimens, if the specimen is taken at a "covered hospital." A "covered hospital" is a hospital which sent some pathology tests to an outside lab before 1999. One possible interpretation of the language is that 95% of US hospitals are "covered hospitals" and any "pathology test" is covered. CMS's own manuals and transmittals have stated contradictory interpretations, and no formal rulemaking has occurred, probably because BIPA 242(c) has been renewed year by year and always appeared to be on the edge of expiration, ameliorating the need for rulemaking. The law is challenging to implement because there is no bright line between "chemistry" and "pathology" tests in the CPT manual, and many newer laboratory steps are not found in the manual at all. Like rules of Latin grammar, CMS's classifications of "chemistry" and "pathology" tests must be memorized one by one. Essentially chemical tests such as flow cytometry and gene panel (microarray) tests are classed by CMS as "pathology tests." Complex personalized medicine tests now in the marketplace torture the historical but ill-defined border between "clinical laboratory" and "pathology" tests. For example, a modern tumor analysis may use tumor tissue, even paraffin blocks, laser microdissection, and a gene panel microarray (defined as pathology tests) but be critically dependent on interwoven steps such as DNA separation and amplification (defined as chemistry tests). The classification using "unlisted" codes is particularly treacherous. For example, a hospital may code an outside complex diagnostic test as 84999 (unlisted chemistry code) but its Medicare contractor or a future Medicare claims auditor may reclassify the same test as 94920 (unlisted pathology code), which could change the hospital's payment by as much as 100X.

[v] Initially effective 1/1/2007 for clinical lab tests with effective date deferred by a CMS transmittal until 1/1/2008; and 1/2008 for pathology lab tests. These are referred to as "date of service" or "DOS" regulations because they administratively fix the "date of service" of the future laboratory test as *during* the hospital outpatient encounter (42 CFR 414.510), even if the test is performed several weeks later. Services performed *during* a hospital outpatient encounter must be billed by the hospital (42 CFR 410.42; see also 410.2).

[vi] For Medicare, a hospital outpatient is defined as one who receives services (as opposed to supplies) from the hospital, AND is not an inpatient, AND is registered as an outpatient (thus, there are three separate conditions to be an outpatient.) Many hospital-associated physicians may see some patients within "hospital outpatient clinics" where the physician charges a facility-based reduced fee to Medicare and where the outpatient clinic support staff are hospital employees. The same physician may see other patients in a "private" hospital space nearby, which may be an office tower owned wholly or in part by the hospital but in which the physician rents space and operates entirely independently (patients are not registered "outpatients," he hires his own staff, maintains his own medical records, and bills for all services.)

[vii] 65 FR 50312; creating 45 CFR 160, 162.

[viii] 65 FR 50351 (8/17/2000). The ten guiding principles were: (i) Improve efficiency and effectiveness of the health care system re: electronic transactions. (ii) Meet the needs of users, e.g. providers, health plans. (iii) Consistency with other regulatory standards. (iv) Low implementation costs. (v) Codes are updated by accredited or [reliable] private or publications; continuity and efficient updating over time. (vi) Timely implementation and updating standards. (vii) Technically platform-independent. (viii) Prcise and unambiguous and as simple as possible. (ix) Burdens on users as low as possible. (x) Incorporate flexibility to adapt to new services and information technology; encouragement of innovation.

[ix] AMA, CPT Code Process: http://www.ama-assn.org/ama/pub/category/3866.html

[x] As hypothetical examples, the CPT system might have a code 12345 for wound care, and Medicare might require use of a special Medicare code G1001 for small wounds and G1002 for large wounds. Variably, Medicare may issue a "G-code" to describe a certain service or issue instructions that a certain not-otherwise-classified CPT code be used.

[xi] SSA 1833(h)(2)(B). The Secretary may make further adjustments or exceptions to the fee schedules to assure adequate reimbursement of… (ii) certain low volume high-cost tests where highly sophisticated equipment or extremely skilled personnel are necessary to assure quality.

[xii] "Just when a scientific principle or discovery crosses the line between the experimental and demonstrable stages is difficult to define. Somewhere in this twilight zone the evidential force of the principle must be recognized…[the principle] must be sufficiently established to have gained general acceptance in the particular field in which it belongs." Frye v United States, 293 F. 1013 (DC Cir 1923)

[xiii] The general point, that strong but not definitive data may make future randomized trials unethical, has been made before, e.g. Ioannidis J et al. (2001) JAMA 286:821-30. A classic older paper on problems with RCTs is "An additional basic science for clinical medicine: The limitations of randomized clinical trials", A.R. Feinstein (1983) Ann Intern Med 99:544-50.