Coverage and Payment Policies for Genetic Tests

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Joanne Armstrong, MD, MPH
Current Market View: Genetic Tests

Genetic medicine has arrived.

- Rapid increase in the availability of genetic tests
  - 10% increase in availability of new genetic diagnostic tests per year.\(^1\)
  - 1,000 diseases for which genetic tests are available

- Rapid increase in utilization of genetic tests
  - 20% increase in utilization of genetic diagnostic tests per year vs. 1%-3% for non-genetic diagnostic tests.\(^2\)

- Costs are modest, but trends are significant.

Aetna Genetic Test Cost Trends, by Conditions 2003-2005

- Total Medical Expenditure
- Total Genetic Tests
- Reproductive
- Oncology
- Predisposition

2X
Current Market View: Biologic Therapies

- Rapid increase in availability of new biologic/PG medications
  - 250 biologic medications on market, >300 in the pipeline\textsuperscript{1,2}
  - Biologics represent 25\% of new drugs approved by FDA since 2000\textsuperscript{1}

- Biologic cost trends significantly outpace pharmacy trends
  - 29\% vs. 9\% trend 2004 – 2005\textsuperscript{3}

- Rapid increase in per prescription cost of PG meds vs. conventional medications
  - 29\% vs. 16\% trend 2001 – 2002\textsuperscript{4}

4. The 2004 Segal Health Plan Cost Trend
DRUGS OF THE FUTURE
Amazing new medicines will be based on DNA
Find out how they will change YOUR LIFE
<table>
<thead>
<tr>
<th>Condition</th>
<th>Diagnostic Test</th>
<th>Targeted PG therapy</th>
<th>No. of Potential Cases in US</th>
<th>2004 Paid, All Products</th>
<th>Covered Benefit</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast CA</td>
<td>HER-2</td>
<td>Herceptin</td>
<td>211,000</td>
<td>$23.3M</td>
<td>Yes</td>
<td>↓Median survival ↑Avoidance of side effects</td>
</tr>
<tr>
<td></td>
<td>Oncotype Dx</td>
<td>Adjuvant chemotx</td>
<td>82,000</td>
<td>$6,200/case $3,400/test</td>
<td>Yes</td>
<td>Predict recurrence, target tx</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>Genotype</td>
<td>Interferons</td>
<td>4,000,000</td>
<td>$37.1M</td>
<td>Yes</td>
<td>Determine duration of therapy</td>
</tr>
<tr>
<td>Colorectal CA</td>
<td>EGFR</td>
<td>Erbitux</td>
<td>800,000</td>
<td>$2.5M</td>
<td>Yes</td>
<td>Shrink tumor size, no survival advantage</td>
</tr>
<tr>
<td>CML/GIST</td>
<td>BCR-ABL RT-PCR</td>
<td>Gleevec</td>
<td>328,000</td>
<td>$10.7M</td>
<td>Yes</td>
<td>Monitor recurrence</td>
</tr>
<tr>
<td></td>
<td>CYP450</td>
<td>30% of all meds on market</td>
<td>30% all meds on market³</td>
<td>No</td>
<td>Yes</td>
<td>Replaces bone marrow monitoring</td>
</tr>
</tbody>
</table>

2. Aetna Pharmacy, 2005

³30% all meds on market metabolized by 2 P450 enzymes with significant allelic variation. Warfarin, HTN, antidepressants
Clinical Coverage Policies: What evidence is needed?

- What is the purpose of testing?
- What measures are feasible?
- What outcomes matter?
- What is the role of cost & cost effectiveness?
Aetna Coverage Policy Principles for Genetic Technologies

- Services related to prevention, diagnosis, or treatment of an illness.
- Information will affect the course of treatment of the member.
- Care and/or treatment is likely to improve outcome
- Improvement must be attainable outside investigational settings.
- Services are consistent with plan design.

...same coverage policy principles for genetic technologies as for all other technologies.
Evidence Standards for Coverage of Genetic Technologies

Covered services must have:

- Final approval from the appropriate governmental regulatory bodies, when required.
- Published, peer reviewed, scientific evidence that permits conclusions concerning test performance and the effect of the technology on health outcomes:
  - Analytic validity
  - Clinical validity
  - Clinical utility
- Demonstrate improved net health outcome and be as beneficial as any established alternatives

...same evidence standards for genetic technologies as for all other technologies.
Sources of Evidence

- Peer-reviewed published literature
- Guidelines of medical professional societies and/or governmental health agencies
  - ACMG
  - ASCO
  - ACOG
  - USPSTF
- Governmental regulatory authorities, when necessary
  - FDA
- Influence of other payers, especially CMS
Case Study: APOE4 Testing

- A means to predict Alzheimer Disease (AD) risk
- Apolipoprotein E, lipid carrying protein with 3 variants: APOE2, APOE3, APOE4
- ↑ risk of AD with APOE4:
  - 2 copies: 5x higher risk, onset 10 yr earlier
  - 1 copy: 2x higher risk, onset 5 yr earlier
- No treatment available to reduce risk
- APOE testing **not covered** service for Aetna
Case Study: AmpliChip CYP450

- Amplichip tests for two common enzymes (CYP2D6 and CPY2C19) important to drug metabolism of antidepressant, cardiovascular drugs, and others drugs.
- Potential value in drug safety and efficacy
- FDA approved 2004
- Uncertain clinical utility-how do you use this in clinical practice?
  - Drivers of drug response are multi-factorial
    - Environment, diet, health status, interactions with other drugs, etc.
  - Variability of response within and across drug classes
  - Lack of evidence linking mutation to important clinical outcomes
- AmpliChip is **not covered** by Aetna
What is the Role of Cost and Cost-Effectiveness in Coverage Decisions?

- Costs of new technologies do not influence clinical policy decisions.
- Cost and cost effectiveness do influence process by which technologies are managed within plan.
  - Precertification
  - Predetermination
  - Disease management
  - Pharmacy management
Case Study: Hepatitis C

- Hepatitis C is the most common cause of chronic liver failure, liver transplant, and leading cause of death from liver disease in US. ¹
- Virus genotype predicts duration of interferon therapy and likelihood of response.

<table>
<thead>
<tr>
<th>Viral Genotype</th>
<th>Frequency in population</th>
<th>Early Viral Response Testing</th>
<th>Duration of recommended therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1,4</td>
<td>70%</td>
<td>Yes</td>
<td>48 weeks if EVR documented</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>12 weeks if EVR not documented</td>
</tr>
<tr>
<td>Type 2,3</td>
<td>30%</td>
<td>No</td>
<td>24 weeks</td>
</tr>
</tbody>
</table>

- Evidence-based therapy guidelines (NIH) exist, but not followed.²,³
  - 10% of Aetna members were on therapy >12 months
- Quality improvements and cost savings possible through guideline adherence and compliance support.

Case Study: Hepatitis C

- Aetna Hepatitis C management program-2005
  - Hepatitis C tests and pegylated interferons are covered benefits under medical plan
  - Evidence of viral genotyping required prior therapy initiation
  - Viral load required based on viral genotype
  - Compliance assessment and support built into process

- 2005 results:
  - 2,100 Hep C members on therapy managed consistent with NIH guidelines.
  - Reduction in inappropriate starts and avg. therapy duration
  - Improvements in compliance-94% vs. 49% in retail pharmacies
  - Annual cost savings-$4.3 million

Clinician Preparedness

- Shortage of trained genetics specialists
  - Fewer than 900 Board certified medical geneticists in US
    - 310 Aetna contracted
  - Fewer than 2,000 Board certified genetic counselors (GC)
    - Not independently contracted with Aetna

- PCPs, ObGyns will fill the gap, but knowledge deficit is great.
  - 72% non-genetics MDs rate their knowledge of genetics as fair to poor.
  - 69% of MD have had a genetic course in medical school but not applied genetics.

- Genetic content in nursing school curricula *declined* from 10.5 hours (1984) to 6 hours (1996).

- Lack of trained genetics clinicians employed by health plan

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Consumer Preparedness

- Poor genetics literacy
  - 82% of consumers cannot correctly answer most genetic medicine knowledge questions in national surveys.¹

- Poor scientific literacy
  - Genetic decision making requires understanding of probability and proportions.
  - Fewer than 7% of Americans are scientifically literate.²

- Consumer information is available, but content is unreliable.

- Consumers are concerned about privacy of genetic data.
  - 90% consumers believe their MDs should view genetic test results vs. 39% for health plan.³

1. Genetics and Public Policy Center Survey 2002
3. Harris Poll #26, June 2002
What is Needed to Optimize the Promise of Genetic Medicine?

- Stimulate innovation and commercialization genetic technologies
- Improve evidence basis of technologies to support coverage decisions and rational use of services
- Develop and disseminate independent technology assessments and practice guidelines
- Generate outcome data to demonstrate clinical and economic value
- Promote physicians and consumers engagement
Collaboration Opportunities:

- Stimulating innovation and commercialization of genetic technologies
  - Clear direction on level of evidence needed to cover services
  - Value pricing?
    - What end point determine value?
    - Rebates on less effective therapies?

- Improve evidence basis of existing technologies
  - Promote efforts to ensure valid and reliable tests
  - Direct contribution to the evidence basis, especially clinical utility
  - Identification of individuals for clinical trial participation
Collaboration Opportunities: Enabling Translation of Genetics into Practice

- Develop and disseminate technology assessments and practice guidelines
  - EGAP, medical professional societies

- Generate outcome data to demonstrate clinical and economic value
  - Data sharing, demonstration projects

- Promote physicians and consumers engagement/education
  - Promotion/creation of alternative vehicles for genetic counseling
  - Information “push” to providers on guidelines, best practices
Thank You!

Armstrongmj@aetna.com
281 637-3017