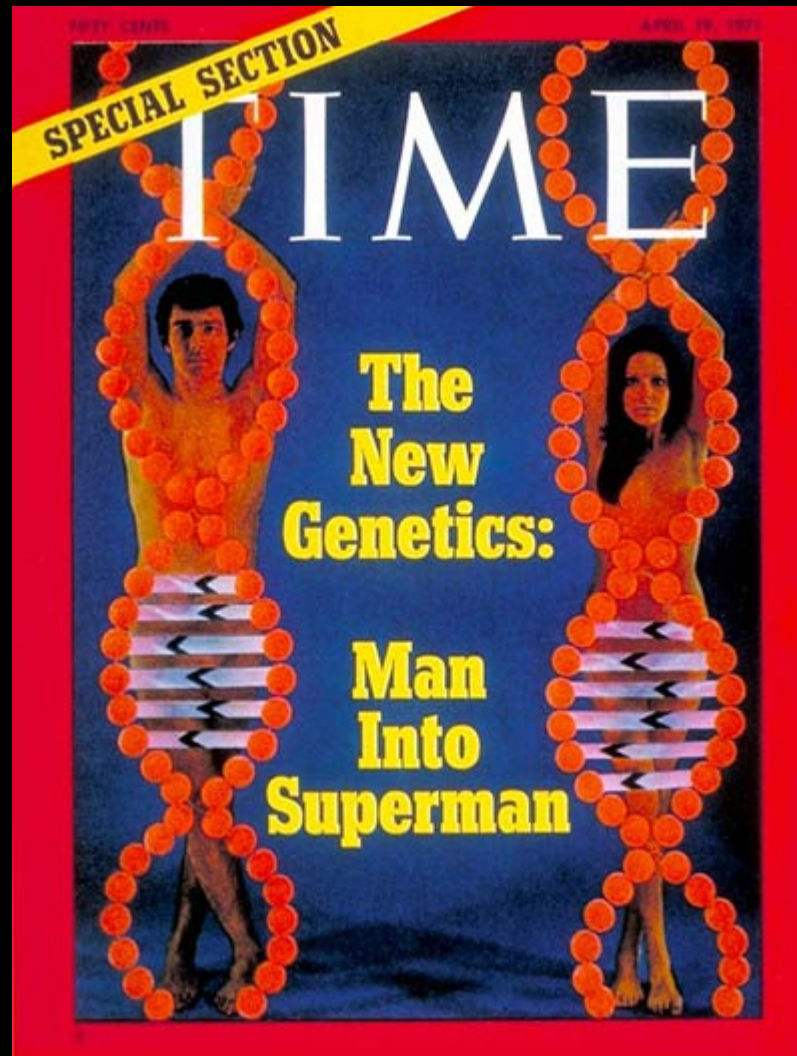


Coverage and Payment Policies for Genetic Tests

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Current Market View: Genetic Tests

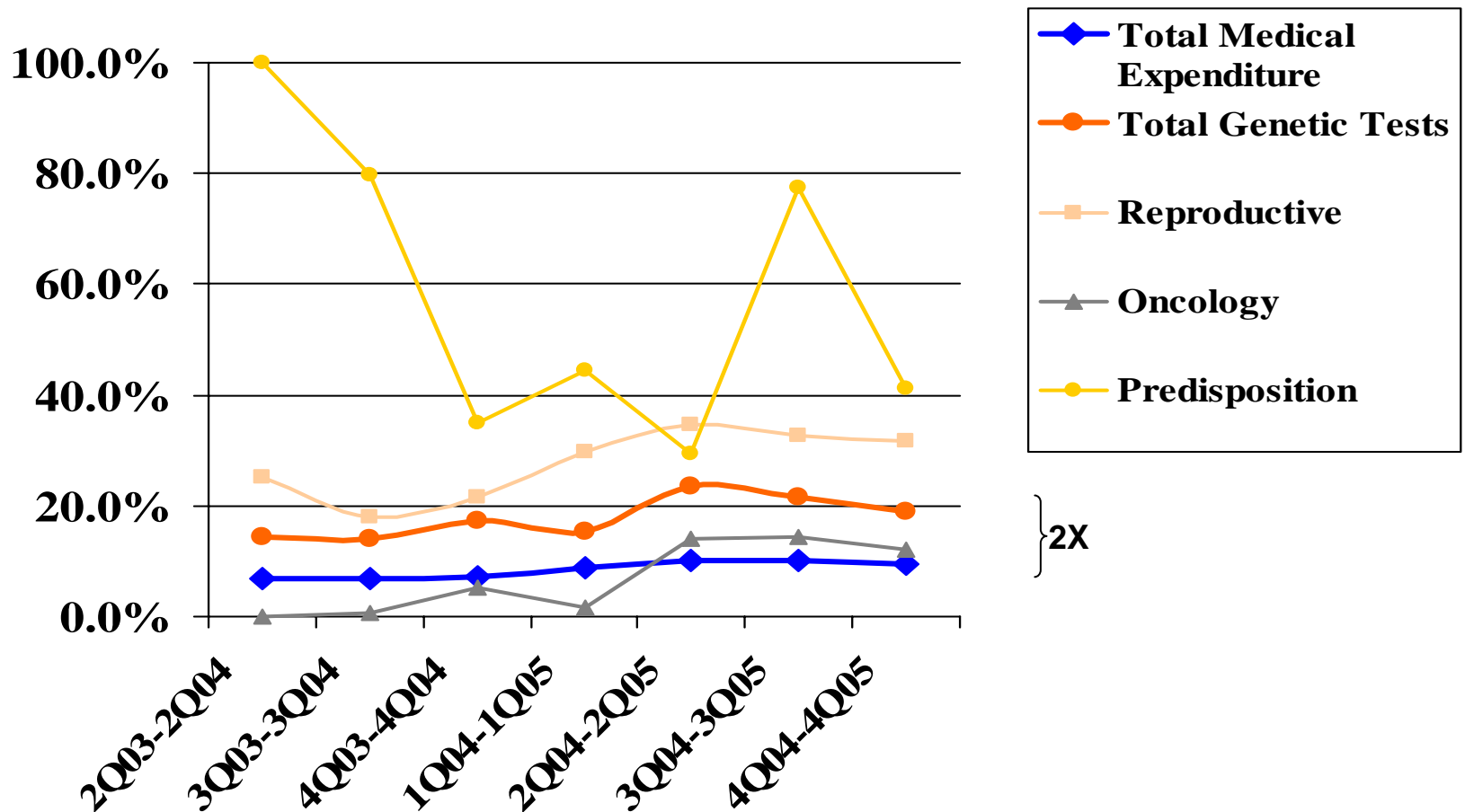
Genetic medicine has arrived.

- 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.

1. GeneTests, 2006

2. SunTrust Robinson Humphrey, March 2002.

Aetna Genetic Test Cost Trends, by Conditions 2003-2005



Current Market View: Biologic Therapies

- Rapid increase in availability of new biologic/PG medications
 - 250 biologic medications on market, >300 in the pipeline^{1,2}
 - Biologics represent 25% of new drugs approved by FDA since 2000¹
- Biologic cost trends significantly outpace pharmacy trends
 - 29% vs. 9% trend 2004 – 2005³
- Rapid increase in per prescription cost of PG meds vs. conventional medications
 - 29% vs. 16% trend 2001 – 2002⁴

1. K Phillips. Health Affairs 25, no.5 (2006):1271-1280
2. Advance PCS's Benefit Source Book, 2004.

3. Aetna Pharmacy data, 2006 Survey.
4. The 2004 Segal Health Plan Cost Trend

JANUARY 15, 2001 \$3.50

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Targeted Therapies Candidate Conditions

	Condition	Diagnostic Test	Targeted PG therapy	No. of Potential Cases in US ¹	2004 Paid, All Products ²	Covered Benefit		Value
						DX	TX	
Current Clinical Applications	Breast CA	HER-2	Herceptin	211,000	\$23.3M	Yes	Yes	↑Median survival ↓Avoidance of side effects
	Breast CA	Oncotype Dx	Adjuvant chemotx	82,000	\$6,200/case \$3,400/test	Yes	Yes	Predict recurrence, target tx
	Hepatitis C	Genotype	Interferons	4,000,000	\$37.1M	Yes	Yes	Determine duration of therapy
	Colorectal CA	EGFR	Erbitux	800,000	\$2.5M	Yes	Yes	Shrink tumor size, no survival advantage
	CML/GIST	BCR-ABL RT-PCR	Gleevec	328,000	\$10.7M	Yes	Yes	Monitor recurrence Replaces bone marrow monitoring
Future Clinical Applications	Drug Metabolism	CYP450	30% of all meds on market ¹			No	Yes	30% 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 CYP2C19) important to drug metabolism of antidepressants, cardiovascular drugs, and other 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.

Viral Genotype	Frequency in population	Early Viral Response Testing	Duration of recommended therapy
Type 1,4	70%	Yes	48 weeks if EVR documented 12 weeks if EVR not documented
Type 2,3	30%	No	24 weeks

- 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.

1. Alter, NEJM 1999;341:556.
2. AASLD, 2004.
3. NIH Consensus, 2002.

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-\$4.3million

Clinician Preparedness

- Shortage of trained genetics specialists
 - Fewer than 900 Board certified medical geneticists in US¹
 - 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.²
 - 69% of MD have had a genetic course in medical school but not applied genetics.²
- Genetic content in nursing school curricula *declined* from 10.5 hours (1984) to 6 hours (1996).⁴
- Lack of trained genetics clinicians employed by health plan

1. Judith Cooksey, MD, SACGHS Testimony, Oct 22, 2003
2. Menasha. The Mt. Sinai J of Med 67(2):144-51,2000
3. Hunter, A. Clinical Genetics 53:447-55, 1998
4. Monsen R. J Continuing Ed in Nursing 30(1):20-24,1999

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
[p://www.dnapolicy.org/research/index.html](http://www.dnapolicy.org/research/index.html).
2. Miller, Jon. 1998. *Public Understanding of Science* 7:203-223.
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!

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