Advancing the Development of Clinically Useful Genomics-Based Diagnostic Tests

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CMTP
Center for Medical Technology Policy

The Fundamental Trade-off

- There is an inherent tension between level of certainty about risk-benefit and early access to new technologies (innovation)
- Health care cost pressures also in tension with economic growth and jobs
- Not intuitively obvious what is the optimal balance to maximize long-term public health
- Clarify and predictability of regulatory and reimbursement policy are essential to all

Key Barriers and Solutions

- Regulatory and reimbursement decision making use binary model of approval
  - Need for progressive / adaptive regulatory and reimbursement framework
- Poorly defined evidentiary thresholds for regulatory and reimbursement decisions
  - Collaborative process to define evidentiary thresholds for decision making
- Can be done with existing authorities and institutions

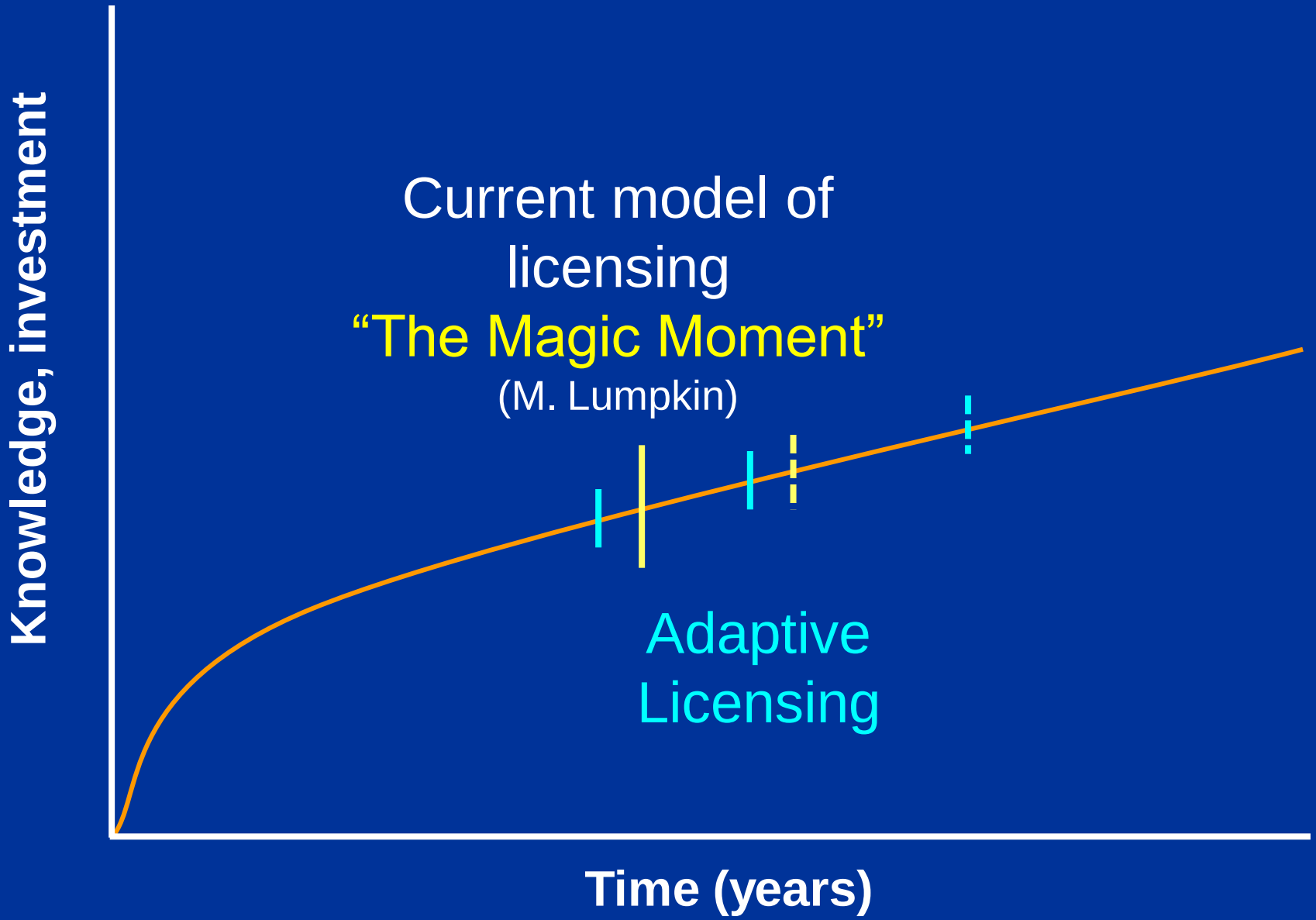
FDA Regulation of IVD

- reasonable assurance that the probable benefits outweigh any probable risks
  - 21CFR860.7(d)(1)
- reasonable assurance that the use of the device will provide clinically significant results
  - 21CFR860.7(e)(1)

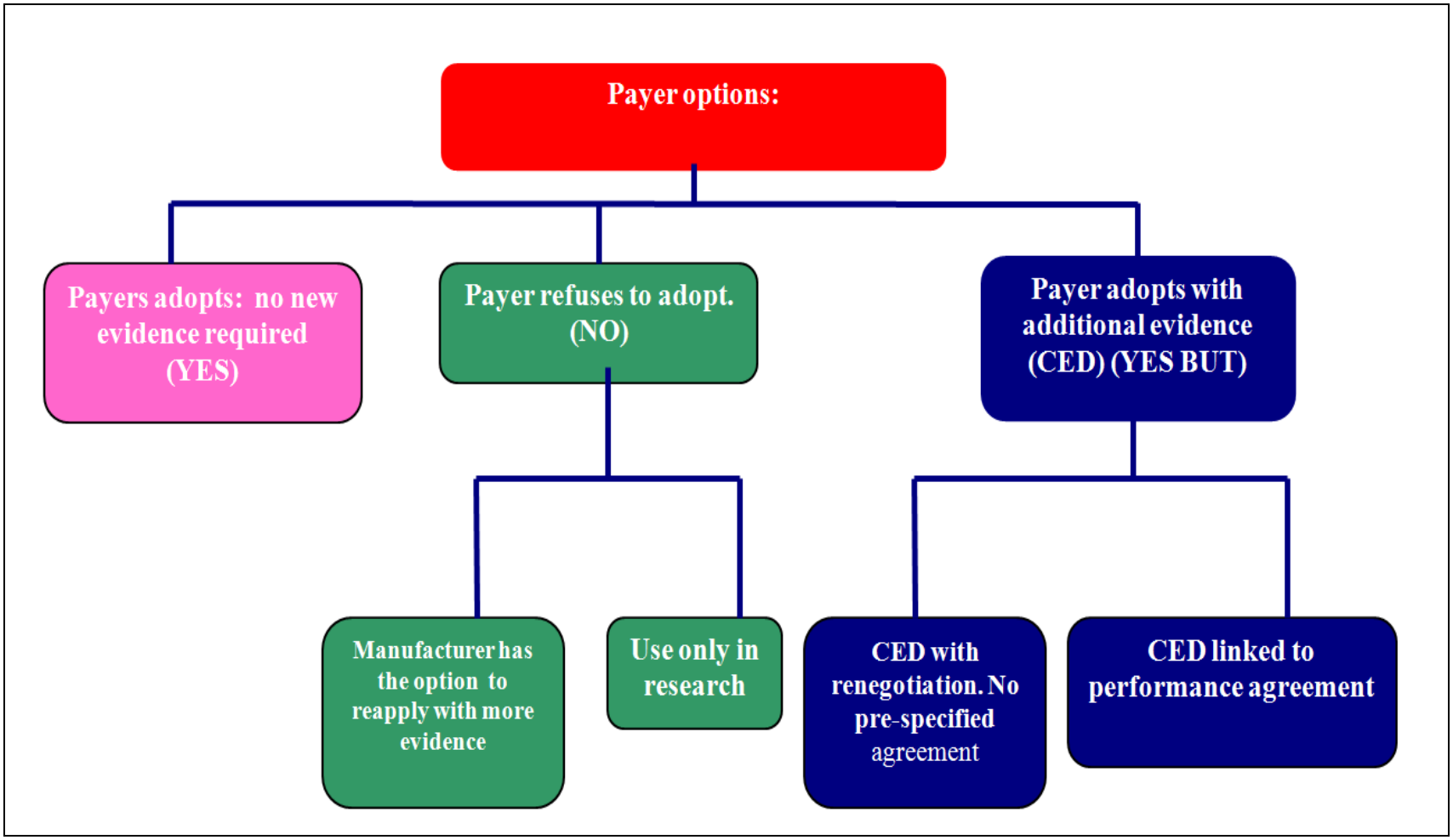
Reimbursement Standard

- Reasonable and Necessary (Medicare)
  - "Adequate evidence to conclude that the item or service improves health outcomes"
- Medically Necessary (private payers)
  - The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes

A better model for drug-licensing?



Managed Entry Schemes



Source: Good Research Practices for Designing, Implementing, and Evaluating Performance-Based Risk-Sharing Arrangements. Working Paper. *ISPOR Task Force, 2011.*

SACGHS recommendation

- "Information on clinical utility is critical for managing patients, developing professional guidelines, and making coverage decisions."
- "HHS should create a public private entity of stakeholders to….establish evidentiary standards and levels of certainty required for different situations"

Guidance for Studies of Clinical Utility

- "Effectiveness Guidance Documents"
- Analogous to FDA-guidance
- Recommendations for study design reflecting information needs of patients, clinicians, payers
- Targeted to product developers, clinical researchers
- Objective is to provide "reasonable confidence of improved health outcomes"
- Balance validity with relevance, feasibility, timeliness

EGD Development Process

- Begin with systematic reviews, HTA, etc
- Content experts generate initial draft recommendations
- Technical working group refines draft recs
- Mutely-disciplinary methods symposium to discuss draft recommendations
- Revised recs circulated for public comment
- Final methods recommendations posted

Multi-Stakeholder Working Group

- **Technical Working Group**

TWG Member Name	Stakeholder Category	Affiliation
Linda Bradley	Geneticist/Lab Director	Women & Children's Hospital of Rhode Island
Louis Jacques	Payer	Center for Medicare & Medicaid Services
Gary Lyman	Clinician	Duke University
Howard McLeod	Researcher	UNC Institute PGx & Individualized Therapy
David Nelson	Industry	Epic Sciences
David Parkinson	Industry	Nodality
TBD	FDA	FDA Representative
Margaret Piper	Payer	Blue Cross Blue Shield Tech Assessment
Richard Simon	Methodologist	National Cancer Institute
Mary Lou Smith	Patients & Consumers	Research Advocacy Network
Plus 2-4 Additional Members		

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Review Methods vs Guidance

- EGAPP methods: "What was the relative importance of outcomes measured; which were pre-specified primary outcomes and which were secondary"
- CMTP EGD: "Valid outcomes or surrogates for breast cancer prognosis include distant recurrence at 5 or 10 years, disease free survival, disease specific mortality, and overall survival"

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