COVERAGE WITH EVIDENCE DEVELOPMENT

OVERVIEW AND USE TO PROMOTE BIOMARKER DEVELOPMENT

IOM National Cancer Policy Forum

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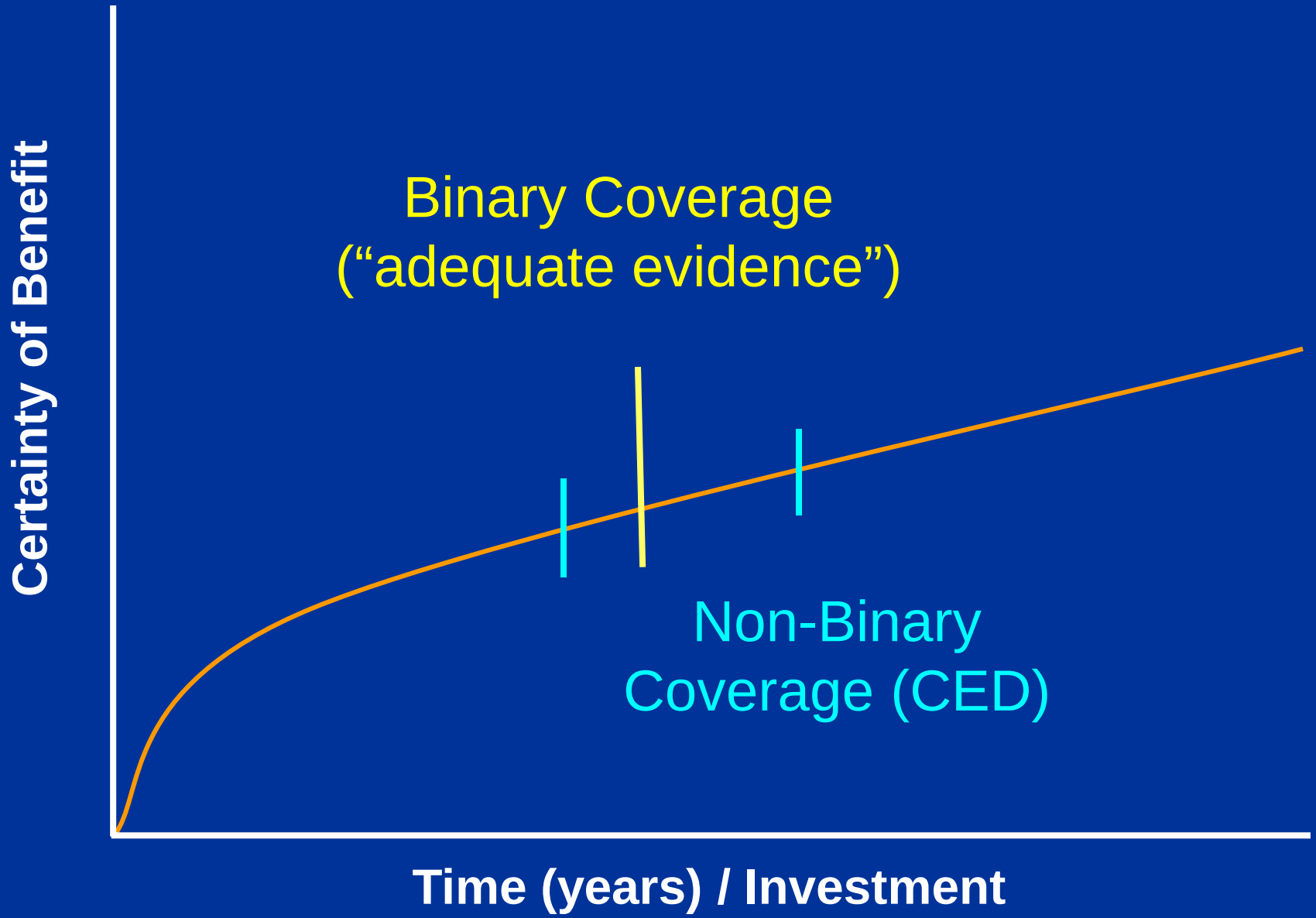
CENTER FOR MEDICAL TECHNOLOGY POLICY

CED DEFINITION AND PURPOSE

- Reimbursement that is linked to patient participation in clinical studies
- Payer approves choice of technologies, research questions and study design
- Intent is to allow early access to promising technologies while promoting studies that confirm real world safety and effectiveness

Yes/No Coverage vs. CED



EXAMPLES OF MEDICARE CED

- Lung volume reduction surgery (pre-CED)
- FDG-PET for suspected dementia
- Implantable defibrillator for primary prevention of SCD
- FDG-PET for oncology
- Genetic testing for warfarin sensitivity
- Transcatheter aortic value replacement
- Molecular dx tests for prostate cancer (Palmetto LCDs)

CORE ELEMENTS OF CED FRAMEWORK

- Technology addresses an important health need and/or specific payer priority
- Existing evidence is adequate to conclude that the technology is “promising”
- Proposed study will generate valid and relevant evidence to inform future clinical/policy decisions
- Study is reasonably likely to be feasible
- Credible process exists to assess all above elements

CED AND EVIDENTIARY STANDARDS

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MEDICARE GUIDELINES FOR EVALUATION OF DX TESTS

- **Question 1:** ***Is the evidence adequate to determine whether the test provides more accurate diagnostic information?***

- **Question 2:** ***If the test changes accuracy, is the evidence adequate to determine how the changed accuracy affects health outcomes?***

FACTORS CITED IN MDX COVERAGE DECISIONS

- “Published prospective or prospective-retrospective trials”; retrospective data is inadequate to demonstrate clinical utility
- Included in “widely accepted” treatment guidelines, such as ASCO, NCCN
- Service delivered by providers with specific training who maintain registry on all testing patients
- Data collected and reported on metastases or death in low risk patients
- MD surveys demonstrate impact of test on patient management
- Non-coverage because “perceived level of oncologist enthusiasm is relatively low”

SACGHS RECOMMENDATION (2008)

- “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”

THE NEED FOR "REIMBURSEMENT SCIENCE"

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REGULATORY SCIENCE – FDA DEFINITION AND GOALS

"Regulatory Science is the science of developing new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of all FDA-regulated products."

"FDA will advance regulatory science to speed innovation, improve regulatory decision-making, and get products to people in need….(and) to protect and promote the health of our nation and the global community."

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WHY REGULATORY SCIENCE IS IMPORTANT

- Several legitimate social objectives related to medical products:
  - Ensure that marketed products are safe and effective
  - Promote rapid patient access to promising new products
  - Promote life sciences innovation
  - Minimize burdens on product developers
- These objective can create tension with respect to evidence standards
- Regulatory science provides an opportunity to develop a scientific framework that reflects multiple legitimate competing views
- Process must be inclusive, sustained, transparent, iterative
- FDA provides the natural platform to support this process

MARKET ACCESS AND REIMBURSEMENT

- Access to new products no longer ensured by FDA approval
- Increasing demands from payers for evidence of effectiveness and value
- Many different payers with many different implicit standards
- Multiple legitimate social objectives impacted by reimbursement decisions and the evidence standards used to make them
  - Access to new therapy
  - Innovation
  - Safety, efficacy, effectiveness
  - Value for money, cost-effectiveness, efficiency
- No single platform analogous to FDA to support the sustained dialogue

REIMBURSEMENT SCIENCE – DEFINITION AND GOALS

"Reimbursement Science is the science of developing new tools, standards, and approaches to assess the comparative effectiveness, value of products covered by public and private health plan.

??? will advance reimbursement science to speed innovation, improve reimbursement decision-making, and get products to people in need….(and) to improve population health outcomes and efficient use of resources."

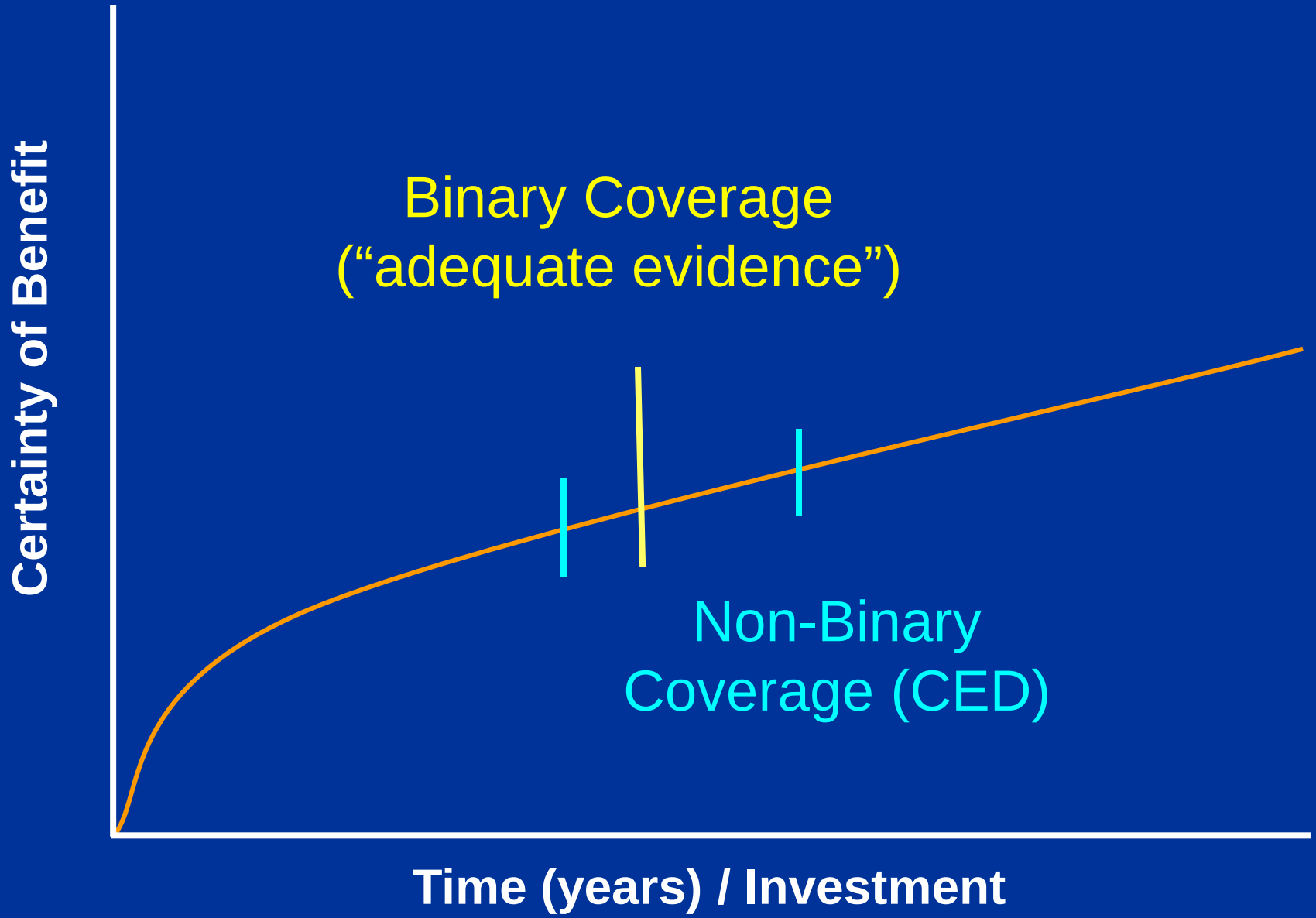
GREEN PARK COLLABORATIVE - USA

- A multi-stakeholder forum to clarify the evidence expectations of public and private payers
- Informed by views of patients and clinicians,
- With participation of regulators, methods experts, life sciences, others
- Focus on “comparative effectiveness and value
- Produce recommendations for study designs for specific clinical condition, class of interventions or methods
- Essentially a forum to advance reimbursement science

PAYERS INVOLVED IN GPC - USA

- America's Health Insurance Plan
- BCBSA
- CMS central office
- MACs (Palmetto, Novitas, others)
- Humana
- Aetna
- United
- Kaiser
- Wellpoint
- Many regional payers (e.g. Johns Hopkins Health Plan)

Yes/No Coverage vs. CED



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EXTRA SLIDES

COMMON FOCUS OF CED STUDIES

- Impact on broader patient population
- Comparison to current alternative standard(s) of care
- More meaningful outcomes (longer duration, QoL / functional, patient-reported)
- Services provided by non-expert clinicians in community settings
- Results achieved outside of rigidly controlled study protocol context

SELECTING TECHNOLOGIES

- Technology intended to diagnose or treat a serious disease, important unmet health need
- Intervention can be plausibly anticipated to:
  - substantially improve health outcomes with modest increase in or similar net health spending
  - Produce comparable health outcomes at substantially reduced aggregate spending
- Other compelling scientific, clinical or institutional justification

EVIDENCE THRESHOLD FOR "PROMISING"

- No formal definition exists
- Variably applied in Medicare CEDs to date
- One option: a moderate level of confidence based on available evidence that the item or service will improve health outcomes.
  - "preponderance of evidence"
  - Benefits considered more likely than not to exceed risks ("preponderance of evidence")

CED STUDY DESIGN

- Should provide an “adequate level of confidence that the technology improves health outcomes”
  - Medicare’s reasonable and necessary standard
- Registries and RCTs have been approved
- RCTs have included active controls and shams
- Choice of primary outcomes and duration usually determined through dialogue with CMS
- Study feasibility is usually an implicit factor, though not “officially” considered.

LOCAL CED CASE STUDIES

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MEDICARE LOCAL COVERAGE UNDER CED

- Palmetto GBA has issued one final and two draft LCD with “CED”
  - 1862(a)(1)(E) authority not available to MACs
  - Statutory issues may be clarified in new guidance
- Final LCD issued for ConfirmDx
  - Epigenetic assay for patients with suspected prostate cancer, negative bx, to inform repeat biopsy decision
  - Substantial evidence of clinical validity and retrospective evidence of clinical utility considered “promising”
  - Prospective, randomized study proposed to be conducted under CED

PROs IN ONCOLOGY TRIALS

- In all oncology trials for advanced disease, report the following symptoms
  - Anorexia , anxiety, constipation, depression, diarrhea, dyspnea, fatigue, insomnia, mucositis, nausea, pain, sensory neuropathy, psychological distress, rash, vomiting

- Select measures from one of the following:
  - EORTC QLQ-C30; FACT; MDASI; PROMIS; PRO-CTCAE

ONCOLOGY PRO GUIDANCE

www.cmtpnet.org/wp-content/uploads/downloads/2012

JOURNAL OF CLINICAL ONCOLOGY REVIEW ARTICLE

Recommendations for Incorporating Patient-Reported Outcomes Into Clinical Comparative Effectiveness Research in Adult Oncology

Ethan Basch, Amy P. Abernethy, C. Daniel Mullins, Bryce B. Reeve, Mary Lou Smith, Stephen Joel Coons, Jeff Sloan, Keith Wenzel, Cynthia Chauhan, Wayland Eppard, Elizabeth S. Frank, Joseph Lipscomb, Stephen A. Raymond, Marianne Spencer, and Sean Tunis

A B S T R A C T

Examining the patient's subjective experience in prospective clinical comparative effectiveness research (CER) of oncology treatments or process interventions is essential for informing decision making. Patient-reported outcome (PRO) measures are the standard tools for directly eliciting the patient experience. There are currently no widely accepted standards for developing or implementing PRO measures in CER. Recommendations for the design and implementation of PRO measures in CER were developed via a standardized process including multistakeholder interviews, a technical working group, and public comments. Key recommendations are to include assessment of patient-reported symptoms as well as health-related quality of life in all prospective clinical CER studies in adult oncology; to identify symptoms relevant to a particular study population and context based on literature review and/or qualitative and quantitative methods; to assure that PRO measures used are valid, reliable, and sensitive in a comparable population (measures particularly recommended include EORTC QLQ-C30, FACT, MDASI, PRO-CTCAE, and PROMIS); to collect PRO data electronically whenever possible; to employ methods that minimize missing patient reports and include a plan for analyzing and reporting missing PRO data; to report the proportion of responders and cumulative distribution of responses in addition to mean changes in scores; and to publish results of PRO analyses simultaneously with other clinical outcomes. Twelve core symptoms are recommended for consideration in studies in advanced or metastatic cancers. Adherence to methodologic standards for the selection, implementation, and analysis/reporting of PRO measures will lead to an understanding of the patient experience that informs better decisions by patients, providers, regulators, and payers.

J Clin Oncol 30.