

Considerations in Determining Effectiveness for Clinical and Payment Considerations



Health Industry Forum
April 4, 2006



Important Factors

- Source of evidence/basis for decision: what counts/should count?
 - Registry data (new potential CMS goal): OHRP* concerns
 - One study only even if RCT?
 - Opinions, abstracts
- Types of endpoints; what if contradictory?
- Breadth of indications
- Political intrusions

*Office of Human Research Protections, HHS

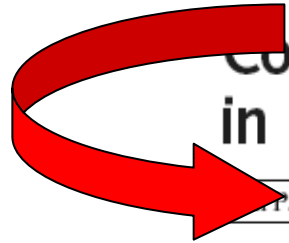


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Why Worry?

More than 1000 times



Contradicted and Initially Stronger Effects in Highly Cited Clinical Research

P. A. Ioannidis, MD

CLINICAL RESEARCH ON IMPORTANT questions about the efficacy of medical interventions is sometimes followed by subsequent studies that either reach opposite conclusions or suggest that the original claims were too strong. Such disagreements may upset clinical practice and acquire publicity in both scientific circles and in the lay press. Several empirical investigations have tried to address whether specific types of studies are

Context Controversy and uncertainty ensue when the results of clinical research on the effectiveness of interventions are subsequently contradicted. Controversies are most prominent when high-impact research is involved.

Objectives To understand how frequently highly cited studies are contradicted or find effects that are stronger than in other similar studies and to discern whether specific characteristics are associated with such refutation over time.

Design All original clinical research studies published in 3 major general clinical journals or high-impact-factor specialty journals in 1990-2003 and cited more than 1000 times in the literature were examined.

Main Outcome Measure The results of highly cited articles were compared against subsequent studies of comparable or larger sample size and similar or better controlled designs. The same analysis was also performed comparatively for matched studies that were not so highly cited.

Results Of 49 highly cited original clinical research studies, 45 claimed that the inter-

JAMA, July 13, 2005; 294: 218 - 228.



Of 49 highly cited studies

- 45 said to be effective. Of these,
 - 7 contradicted
 - 7 had effects stronger than shown subsequently
 - 20 replicated
 - 11 unchallenged so far
- 32%*

*5 of 6 observational studies and 9 of 39 RCTs




Use of Evidence by Decision Makers

- Blue Cross
 - Journal articles only
- CMS: local decisions
 - Journal articles: 26-27%
 - Medical texts: 12-17%
 - “Other” professional sources (e.g., registries, opinions): 36-40%
- CMS: national decisions – usually published, some patient input
- Others – a mix



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Registries: the Coming Issue

- **Background:** CMS wants to promulgate registries as a way to expedite coverage decisions and to find out what happens in real world. Lots of controversy.
- **Possible cases:** AICD, **PET**
- **Current issue:** OHRP* objects to registry because of human subject concerns

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Grid Evaluation? Do Different Sources Disagree?

Yes

	Hayes	ECRI	BC TEC	CMS MCAC
PET/AD				
AMD				
Bariatric Surgery				



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- Endpoints; what ones? Relevance? Statistical correlations?
- Expanded indications
- Political intrusions

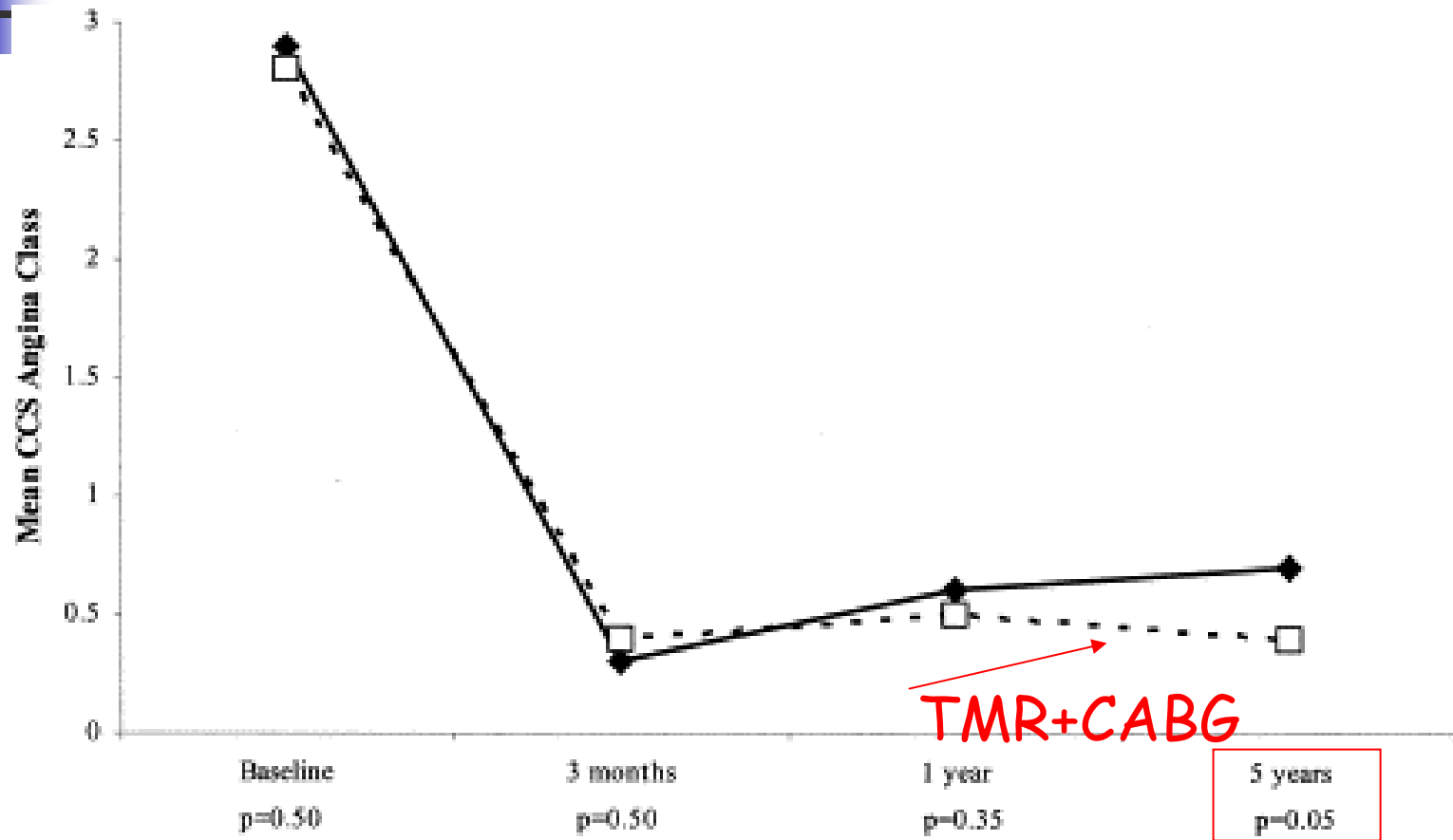


“One Study Issue”

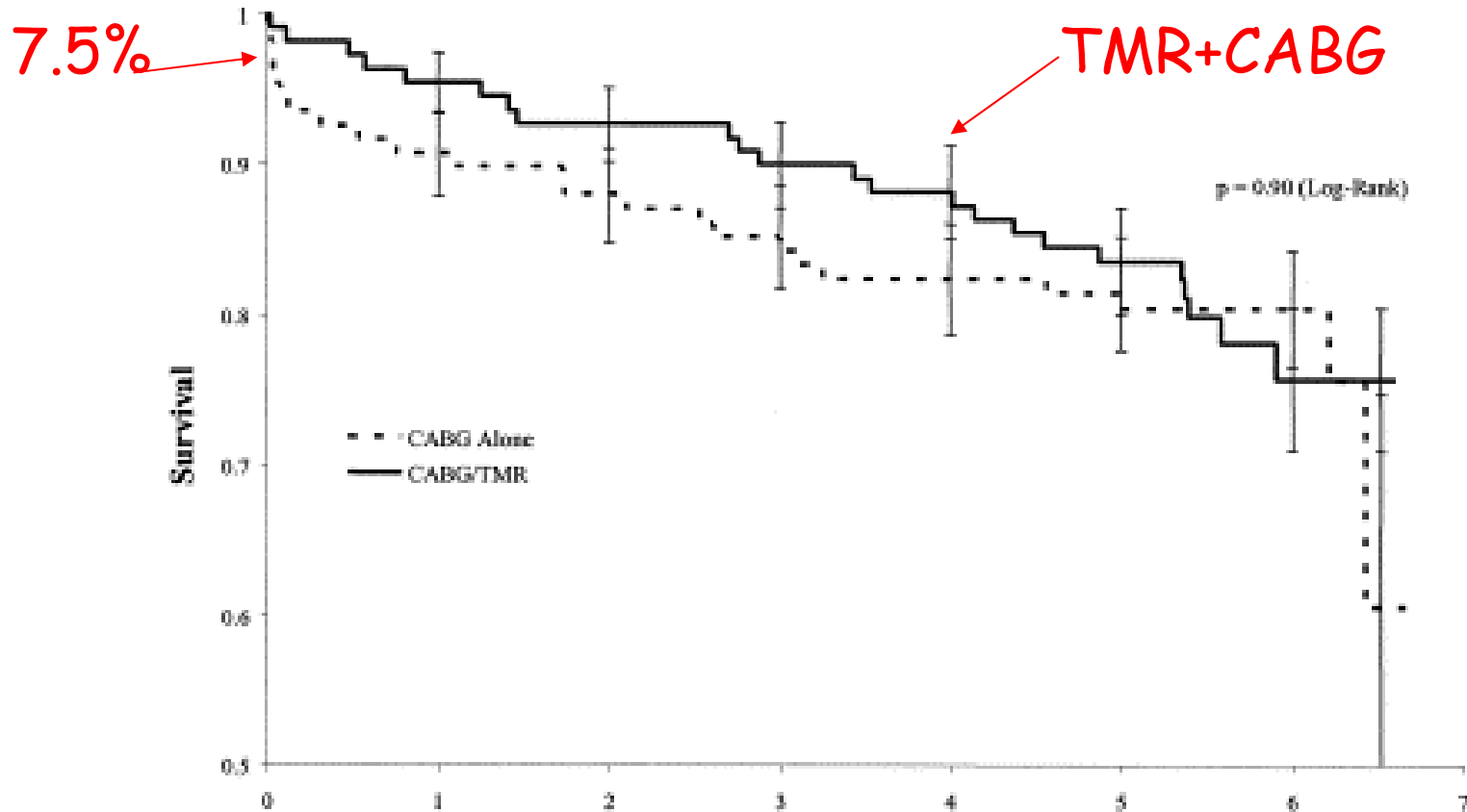
- TMR

- Extracorporeal Shock Wave Rx
for Chronic Shoulder Tendinitis

Symptom Scores for TMR+ CABG (---) vs. CABG Alone (-)



Survival for TMR+ CABG (-) vs. CABG Alone (---)



263 patients in 13 centers (1996-8)



Choice of Endpoints

- What ones?
 - TMR as auxiliary to CABG: mild relief of chest pain or survival
 - AMD and Verteporfin: Is it visual acuity or function?
- What weighting?



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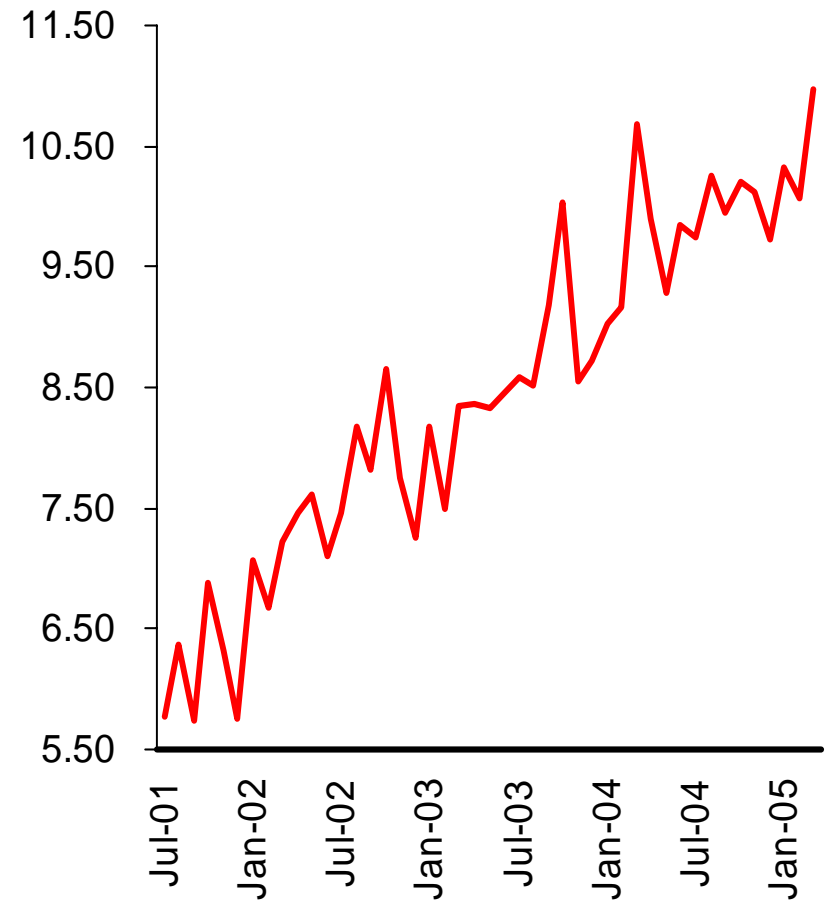
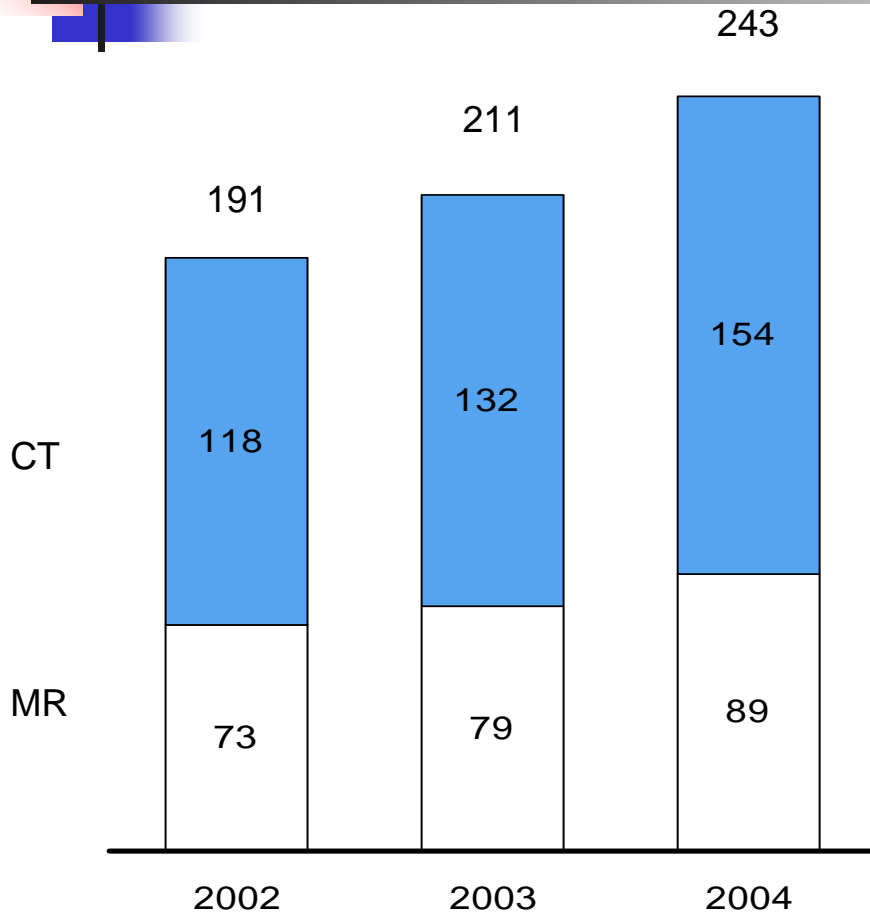


Breadth of Indications

- If AICDs work for selected patients, how many other clinical trials are necessary? Who will do these?
- Is cancer cancer as far as PET is concerned?

*Growth of Technology and
Expanded Indications—
Radiology as Prototype*

Likely expanded indications for CT and MRI





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Political Intrusions for PET and AD

- Key decision pending by MCAC
 - Lobbying by Capitol Health Group to “soften” negative stand of Alzheimer’s Association
 - Intervention by member of Congress and a friend of PET’s inventor, who says: “We drink together, we suffer together, we celebrate together, we fish together.” *
- Pressure on then Secretary Thompson
- Conditional coverage approved

*Washington Post: Tale of Politics: PET Scans’ Change in Medicare Coverage. October 14, 2001 page A1



Two Final Thoughts Regarding

- C/E

- Will their inclusion imply “skimping” on part of the provider?
- Will providers always use “societal perspective” in their analyses?

- Timeliness

- Will analyses ever keep up with biomedical advances?
- What can we do about “moving target” argument in terms of new devices?