Drug-Eluting Stents

The Health Industry Forum

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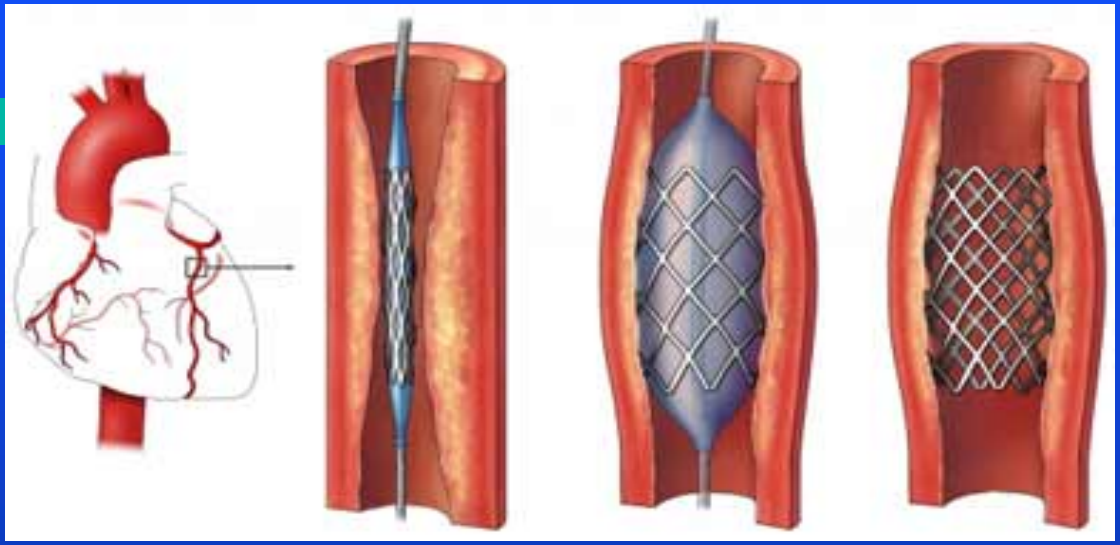
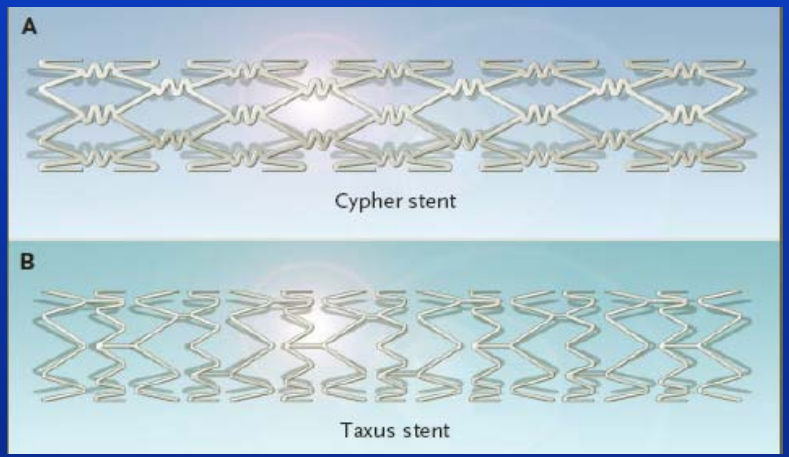
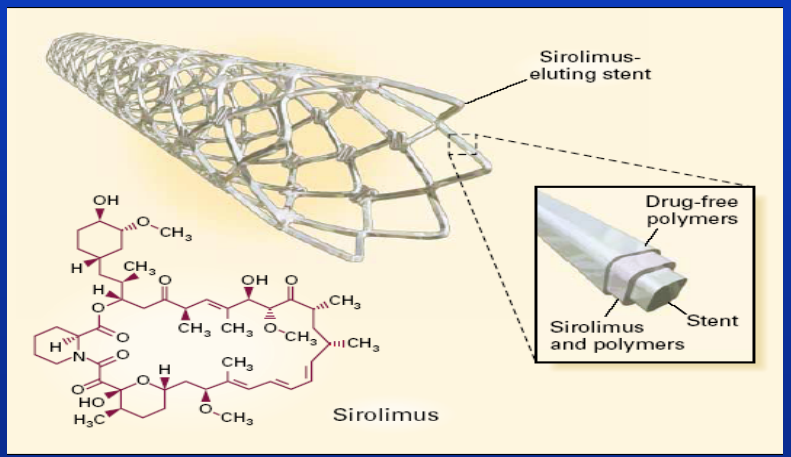
Percutaneous Coronary Intervention (PCI)

- Balloon angioplasty developed by Andreas Gruentzig in 1977
- Dilation improved blood flow, but restenosis common within 6 months
  - Many therapies tried, but none effective
- Coronary stents developed in 1986, pivotal RCTs in 1993 showed less restenosis
- Drug-eluting stents (DES) – pivotal studies in 2002-2003
- Concerns about stent thrombosis increased in 2006

Coronary artery stents







Clinical Trials in PCI

- Focus on reducing restenosis
- Outcomes in RCTs were either
  - Angiographic measures of coronary narrowing
  - Major adverse events – death, MI, or repeat revascularization procedures
- Clinical outcomes dominated by repeat procedures

Meta-Analysis

- Single trials designed to show reductions in restenosis, but not death or MI
- Meta-analyses of all trials to increase statistical power for “hard outcomes”
  - Balloon vs. BMS: 29 RCTs, 9918 patients, follow-up 6-16 months
  - BMS vs. DES: 11 RCTs, 5103 patients, follow-up 6-12 months
- Death and MI were not significantly different
- Repeat procedures: balloon > BMS > DES

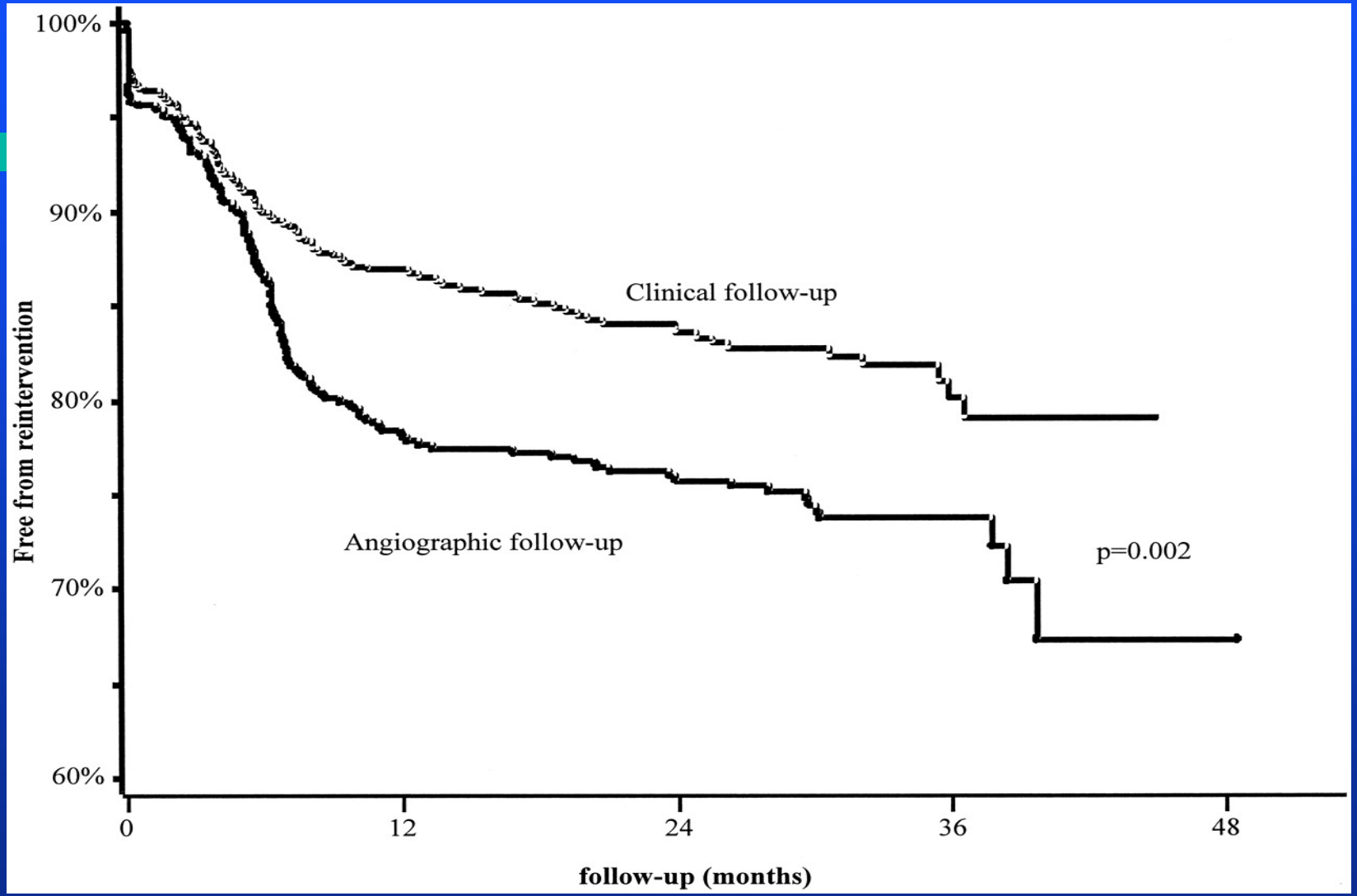
Ann Intern Med 2003;138:777-786

Lancet 2004;364:583-591

Issues with Stent Trials

- Few patients in trials compared with PCI volumes
  - 620,000 stent procedures in 2005 in US
- Patients were highly selected, and generally had less CAD and co-morbidity
- PCIs were done in high volume centers of excellence
- Length of follow-up was short compared with device lifetime
- Follow-up angiograms were routine by protocol

Freedom from revascularization after randomization to clinical follow-up versus angiographic follow-up



J Am Coll Cardiol 2001;38:1061-1069

Real World Data on Stents

- Clinical registries reflect use and outcomes in widespread practice
  - ACC, SCAI databases
  - Single referral centers (e.g., Duke)
  - NHLBI dynamic registry
  - Northern New England registry (voluntary)
  - New York State registry (mandatory)
- Value of registries is greatly increased by systematic, complete, long-term follow-up

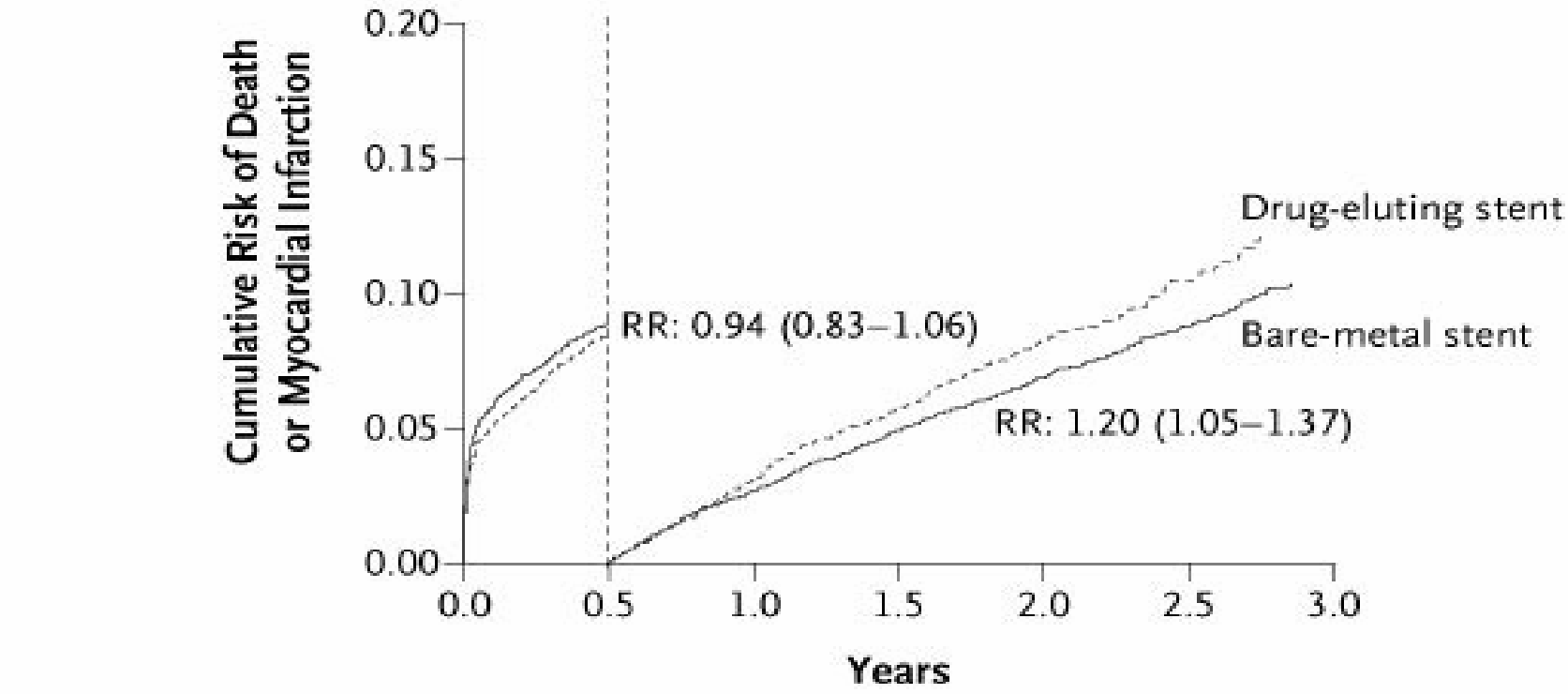
Value of Real World Data

- Patient selection for DES, BMS, balloon
  - How much “off-label” use?
  - Disparities in use by race, gender, etc.
- Short-term risks by patient, provider characteristics
  - Young vs. old vs. “old-old”, etc.
  - Hospital and MD procedure volumes
- Repeat procedure rates without distortion by protocol angiography
- Documentation of rare events
  - RCTs had <500 patients/arm
  - Short follow-up

Late Stent Thrombosis

- Stent thrombosis has been a concern from the first use
  - Cumbersome initial anticoagulation
  - Dual antiplatelet therapy made BMS use practical
  - Duration – 3 to 6 months
- Late events with DES
  - Less tissue growth reduces restenosis, but can leave stent struts exposed
  - Detection is difficult (specificity vs sensitivity)
  - 5 year RCT follow-up – FDA
  - Much evidence from registries

Landmark Analysis: Swedish Registry



N Engl J Med 2007: 356: 1009-1019.

Coverage with Evidence Development

- Pivotal RCTs led to approval, but have numerous limitations
- Large registries helpful in monitoring use and outcomes in actual practice
- Clinical data and complete follow-up are critical
  - Will HIPAA concerns interfere?
- Pro-active use of CVD registries is of value in clinical care and policy