

TIMACS – An Early Invasive Versus Delayed Invasive Strategy

Deepak L. Bhatt MD, MPH, FACC, FAHA

Chief of Cardiology, VA Boston Healthcare System

**Director, Integrated Interventional Cardiovascular Program at Brigham
and Women's Hospital and the VA Boston Healthcare System**

Senior Investigator, TIMI Study Group

Harvard Medical School

Disclosure for Dr. Bhatt

Dr. Bhatt has served as a consultant to: Arena, Astra Zeneca, Bristol-Myers Squibb, Cardax, Cogentus, Daiichi Sankyo, Eli Lilly, Eisai, Glaxo Smith Kline, Johnson & Johnson, Medtronic, Millennium, Otsuka, Paringenix, PDL, Philips, Portola, sanofi aventis, Schering Plough, Takeda, The Medicines Company, Vertex. Honoraria are waived or donated to NPOs.

Principal Investigator for several potentially related studies. His institution has received funding from Bristol Myers Squibb, Eisai, Ethicon, HeartScape, Sanofi Aventis, The Medicines Company.

This presentation discusses off-label and/or investigational uses of various drugs and devices.

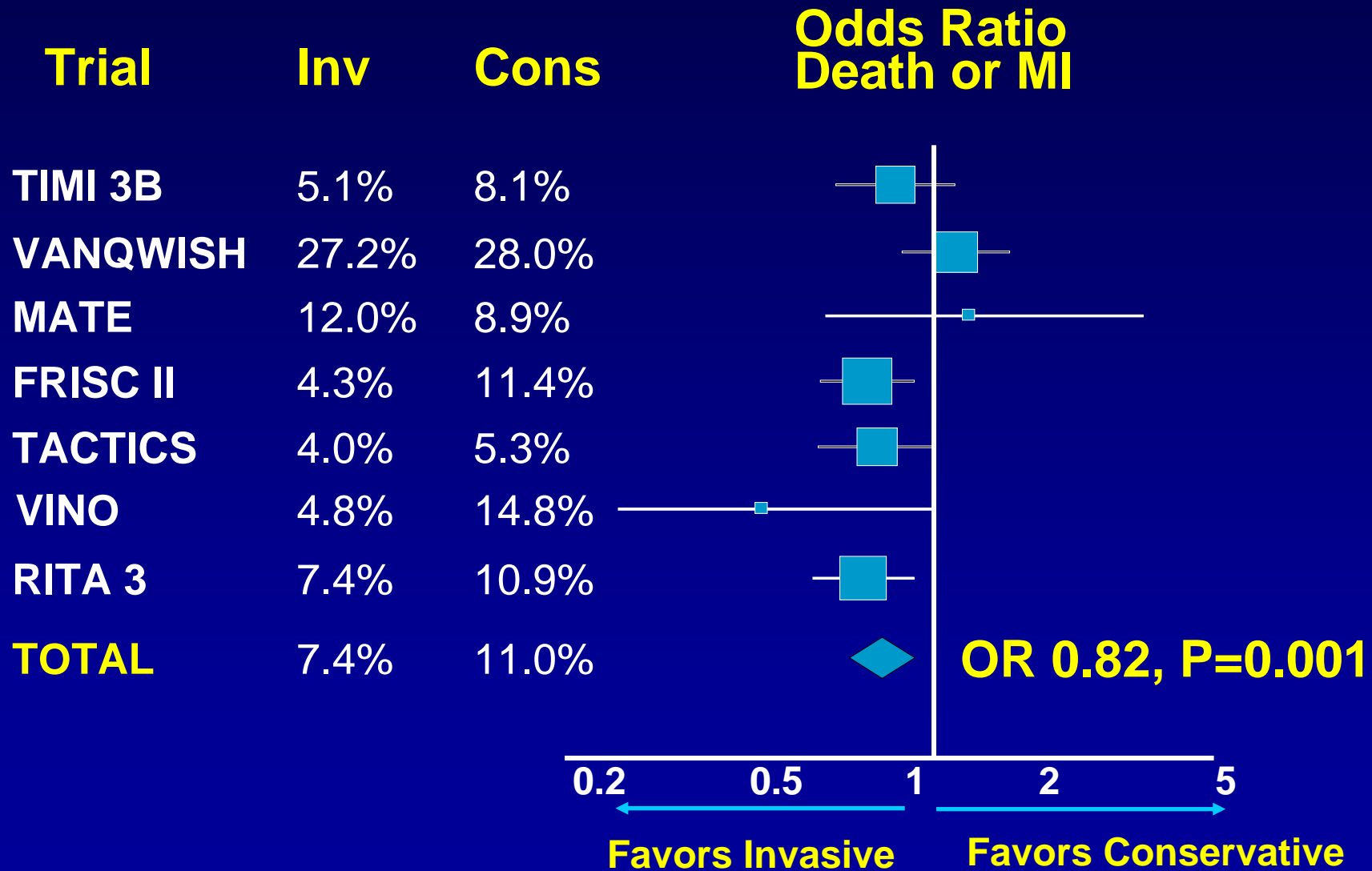
Routine vs Selective Invasive Strategies in ACS

To Cath or Not to Cath

That Is No Longer the Question

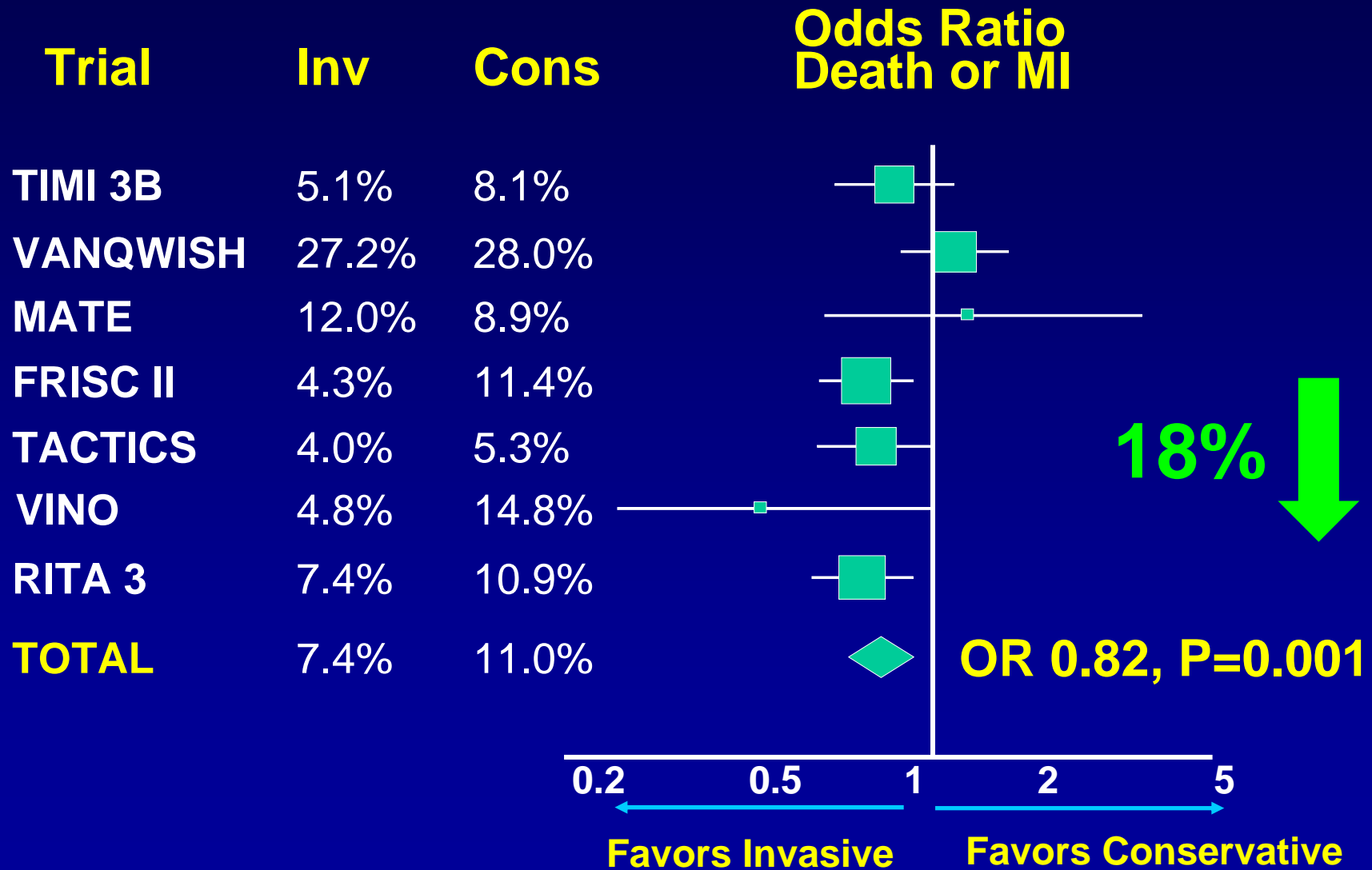
Invasive Management of UA/NSTEMI

Meta-analysis: ↓ Death/MI at 17 mo. F/U

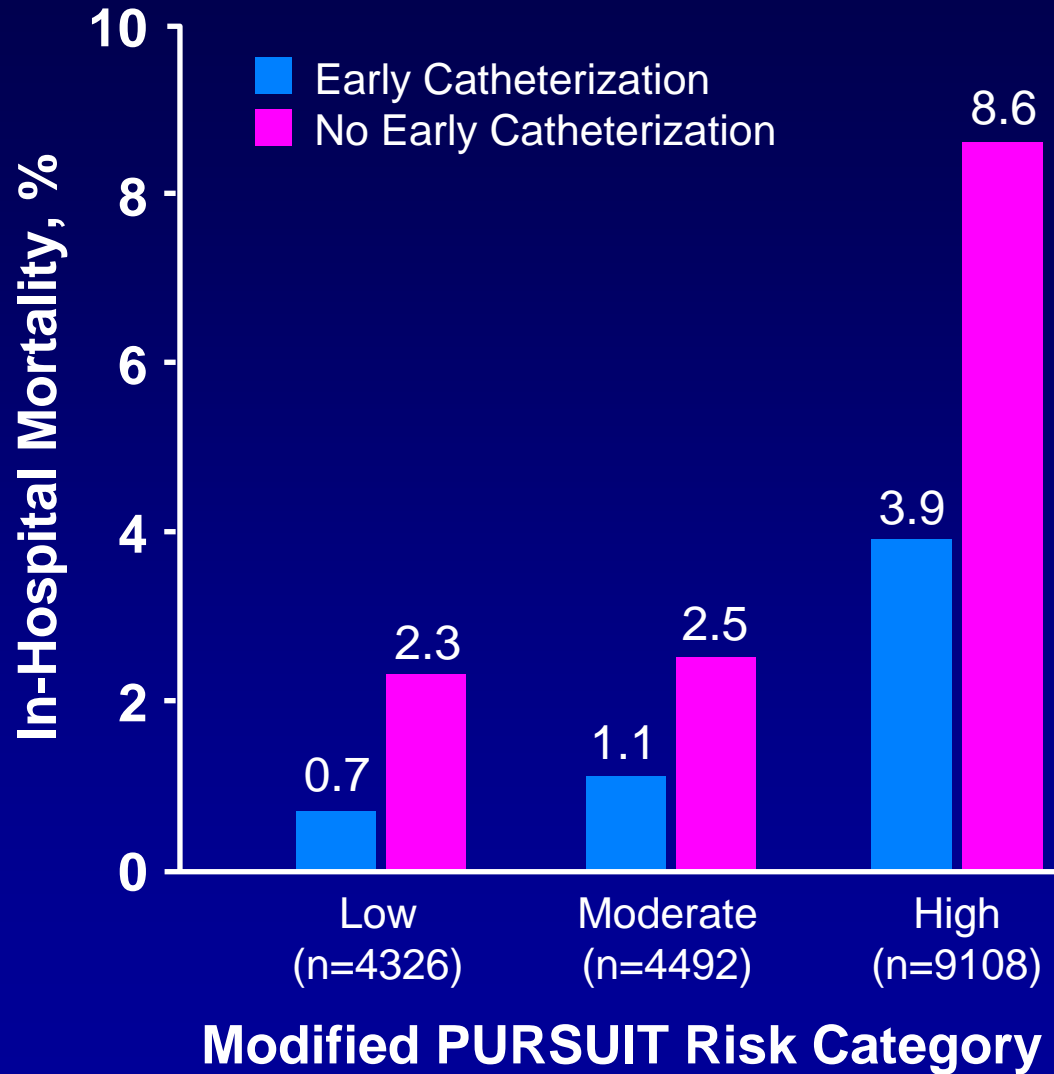


Invasive Management of UA/NSTEMI

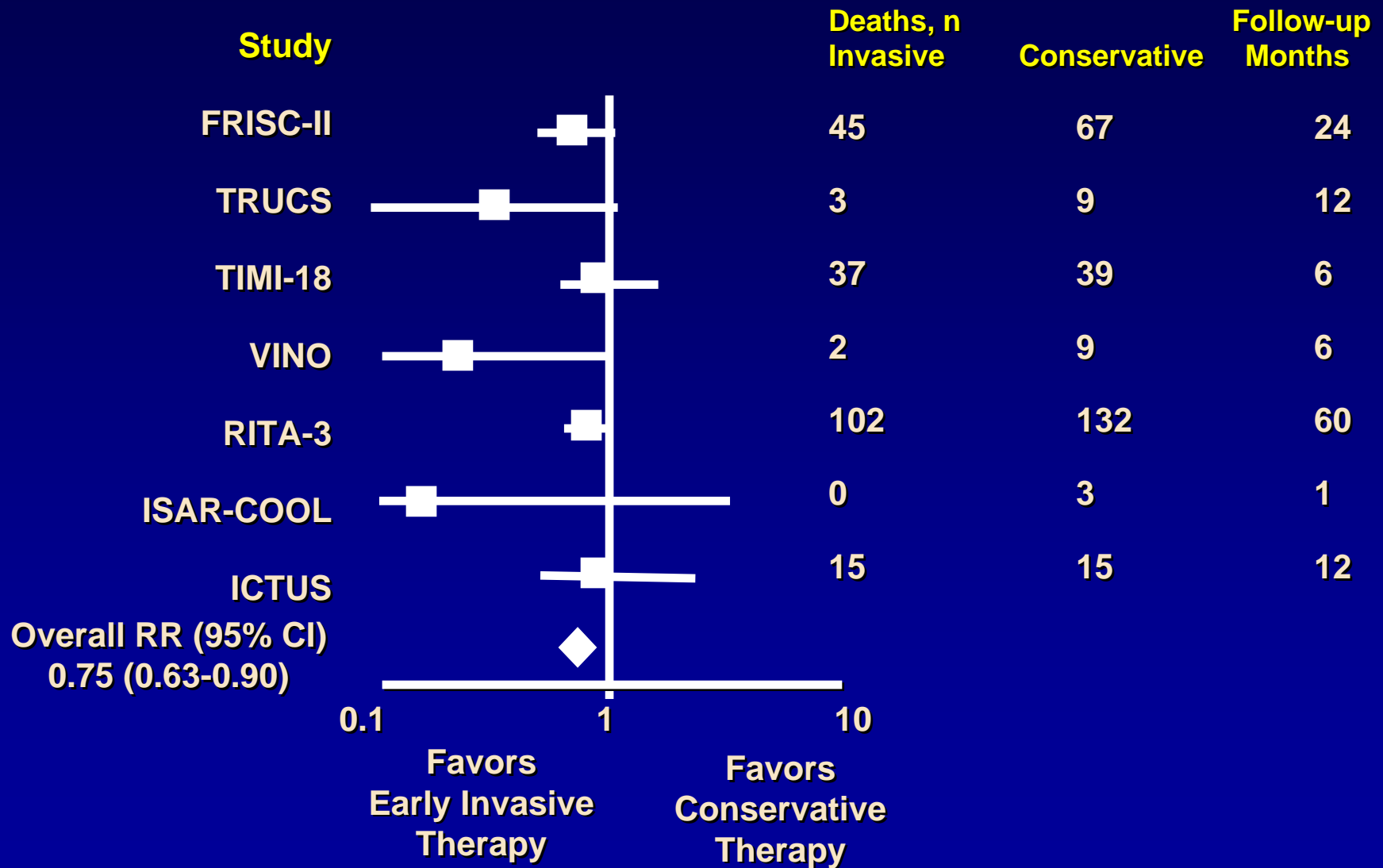
Meta-analysis: ↓ Death/MI at 17 mo. F/U



Mortality Rates by Early Catheterization



Updated Meta-Analysis: Mortality



Bavry, Kumbhani, Rassi, Bhatt, Askari. *JACC* 2006.

Primary and Secondary Outcomes

| | Early N=1,593 | Delayed N=1,438 | HR | 95% CI | P |
|--|-------------------------|---------------------------|-------------|------------------|--------------------|
| Death, MI, Stroke | 9.7% | 11.4% | 0.85 | 0.68-1.06 | 0.15 |
| Death, MI, refractory ischemia | 9.6 | 13.1 | 0.72 | 0.58-0.89 | 0.002 |
| Death, MI, Stroke, refractory ischemia + repeat intervention | 16.7 | 19.7 | 0.84 | 0.71-0.99 | 0.039 |
| Death | 4.9 | 6.0 | 0.81 | 0.60-1.11 | 0.19 |
| MI | 4.8 | 5.8 | 0.83 | 0.61-1.14 | 0.25 |
| Stroke | 1.3 | 1.4 | 0.90 | 0.48-1.68 | 0.74 |
| Ref. Ischemia | 1.0 | 3.3 | 0.30 | 0.17-0.53 | <0.00001 |
| Rep. Intervention | 8.8 | 8.6 | 1.04 | 0.82-1.34 | 0.73 |

Primary and Secondary Outcomes

| | Early N=1,593 | Delayed N=1,438 | HR | 95% CI | P |
|--|------------------|--------------------|------|-----------|----------|
| Death, MI, Stroke | 9.7% | 11.4% | 0.85 | 0.68-1.06 | 0.15 |
| Death, MI, refractory ischemia | 9.6 | 13.1 | 0.72 | 0.58-0.89 | 0.002 |
| Death, MI, Stroke, refractory ischemia + repeat intervention | 16.7 | 19.7 | 0.84 | 0.71-0.99 | 0.039 |
| Death | 4.9 | 6.0 | 0.81 | 0.60-1.11 | 0.19 |
| MI | 4.8 | 5.8 | 0.83 | 0.61-1.14 | 0.25 |
| Stroke | 1.3 | 1.4 | 0.90 | 0.48-1.68 | 0.74 |
| Ref. Ischemia | 1.0 | 3.3 | 0.30 | 0.17-0.53 | <0.00001 |
| Rep. Intervention | 8.8 | 8.6 | 1.04 | 0.82-1.34 | 0.73 |

Primary and Secondary Outcomes

| | Early N=1,593 | Delayed N=1,438 | HR | 95% CI | P |
|--|------------------|--------------------|------|-----------|----------|
| Death, MI, Stroke | 9.7% | 11.4% | 0.85 | 0.68-1.06 | 0.15 |
| Death, MI, refractory ischemia | 9.6 | 13.1 | 0.72 | 0.58-0.89 | 0.002 |
| Death, MI, Stroke, refractory ischemia + repeat intervention | 16.7 | 19.7 | 0.84 | 0.71-0.99 | 0.039 |
| Death | 4.9 | 6.0 | 0.81 | 0.60-1.11 | 0.19 |
| MI | 4.8 | 5.8 | 0.83 | 0.61-1.14 | 0.25 |
| Stroke | 1.3 | 1.4 | 0.90 | 0.48-1.68 | 0.74 |
| Ref. Ischemia | 1.0 | 3.3 | 0.30 | 0.17-0.53 | <0.00001 |
| Rep. Intervention | 8.8 | 8.6 | 1.04 | 0.82-1.34 | 0.73 |

Caveats

- **Large and very well-done trial, but underpowered**
 - ~30% RRR unlikely, since inv vs conservative is ~20% RRR
 - ~10-25% crossover further diminishes power in intent to treat
- **Numerical trend in hard endpts leaves open possibility of benefit**
- **Only 6 month follow up – may take longer for mortality reduction**
- **Important to examine subgroups – occluded LCx should = STEMI**
- **Definitely no evidence of harm with early strategy – no need to “cool off”**
 - **Hard endpoints each numerically lower**
 - **Bleeding rates numerically lower**

Conclusions

- **No statistically significant difference in primary endpoint**
- **Therefore, hospitals that cath within first few days of index hospitalization can continue to do so and if recurrent ischemia cath right away – still consistent with evidence based medicine**
- **Strong suggestion, though, that earlier is better – esp if high risk**
- **In addition, shorter length of stay, presumably lower cost as well**
- **From a patient's perspective better to go to cath earlier – nothing to lose, potential to gain – so if it were me, take me early!**