
**STRESS ⇒ SIRIUS ⇒
TAXUS ⇒ ENDEAVOR**

We've come a long way with respect
to methodology and data quality

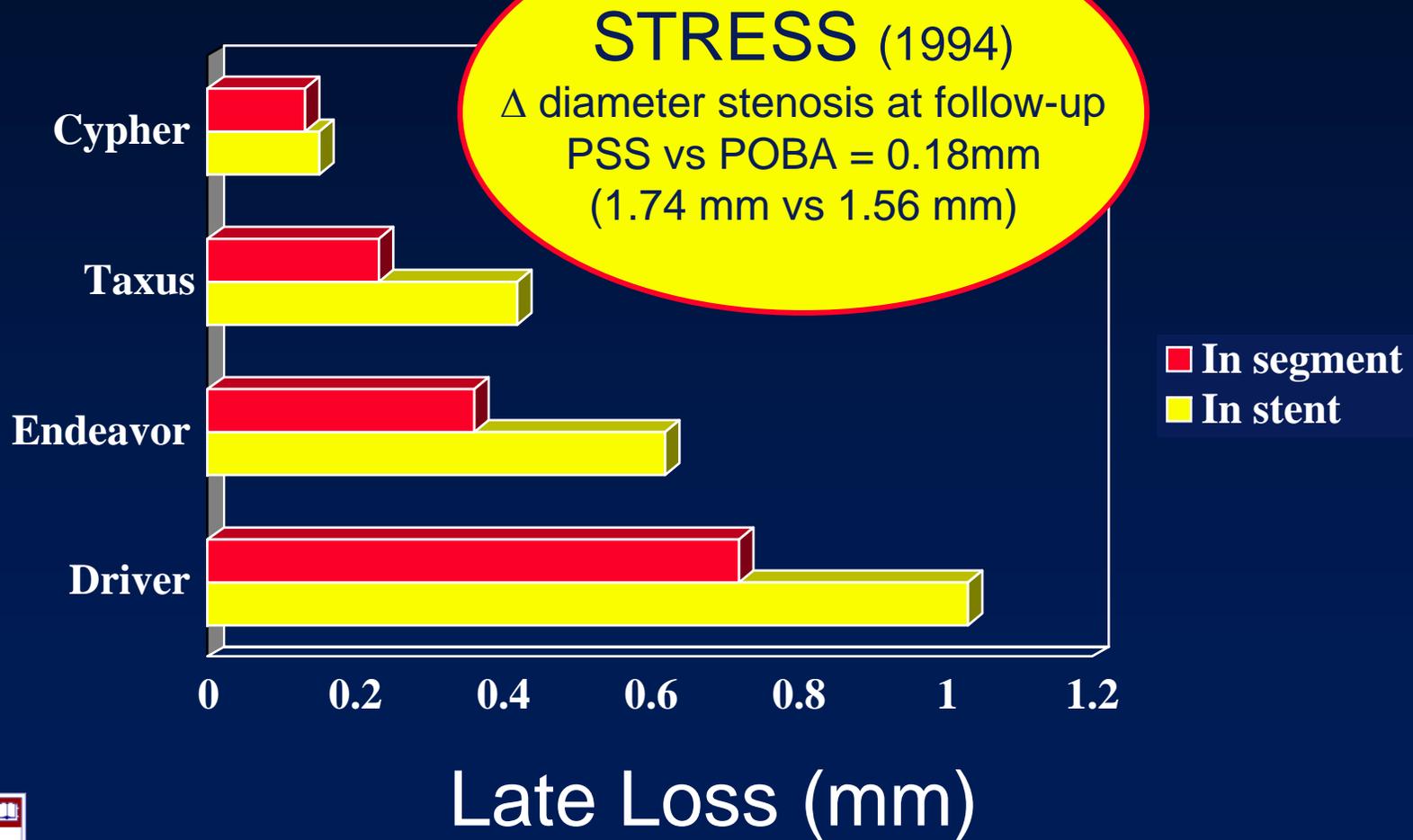


Safety and Effectiveness

- Completely safe - no adverse events (ever!)
- Completely effective - no restenoses
- What about incompletely safe and/or effective?
 - What is the appropriate comparator?
 - POBA?
 - BMS?
 - Currently approved DES?
 - How do we set the bar?
 - How do you adjudicate a tradeoff between safety and effectiveness?
 - How must a candidate device compare to a currently approved similar device?



Instant Late Loss - Four Stents



Late Loss

- Is there an “optimal” amount of late loss?
- How does late loss relate to safety and effectiveness?
- Is there a late loss “effectiveness” range?
 - Too much late loss \Rightarrow excessive restenosis
 - Does too little late loss mean too much late/very late stent thrombosis?
 - Optimal late loss \Rightarrow acceptable balance of restenosis and late/very late stent thrombosis



A Paradigm for Arriving at an Approval Recommendation

EFFECTIVENESS

SAFETY

	Better	Similar	Worse
Better	++++	+++	+/-?
Similar	+++	++	--
Worse	+/-?	--?	-----



Endeavor - Driver Comparison

EFFECTIVENESS

SAFETY

	Better	Similar	Worse
Better	++ ++	+++	+/-?
Similar	+++	++	--
Worse	+/-?	--?	-----



Endeavor - Taxus Comparison

EFFECTIVENESS

SAFETY

	Better	Similar	Worse
Better	++++	+++	+/-?
Similar	+++	++	--
Worse	+/-?	--?	-----



Approval Recommendation Basis

- Ultimately must be based on clinical performance rather than theoretical performance characteristics
 - Balance of safety and effectiveness
 - Safety
 - Adverse event rate
 - Effectiveness
 - Restenosis rate
 - Late loss
 - Binary restenosis
 - Target vessel revascularization
 - Target vessel failure
- Safety cannot be fully judged until long-term real world experience is tabulated

