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Innovation/Changing Times

1977 First PTCA by Andreas Gruentzig

1986 First Stent Implanted by Ulrich Sigwart

1994 STRESS & BENESTENT Results Released

2000 “First in Man Results” – Patrick Surreys

2001 RAVEL Results – Marie-Claude Morice

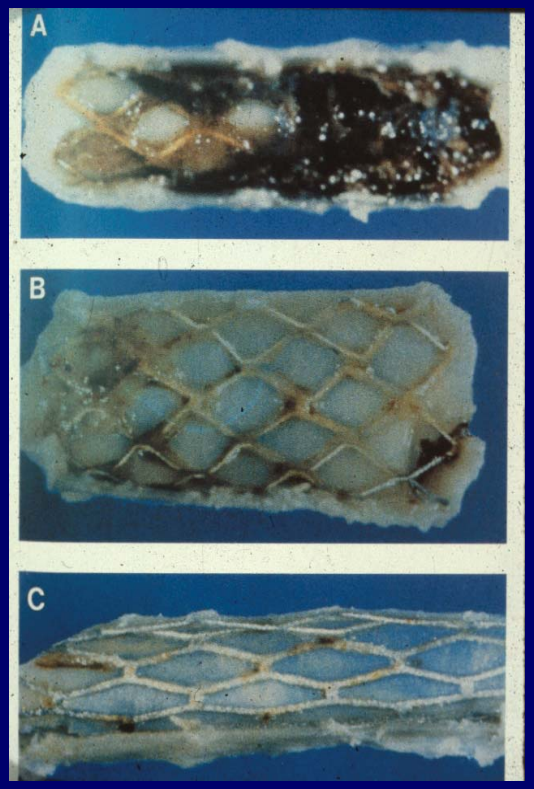
2002 The DES Era with the First Generations DES Stents

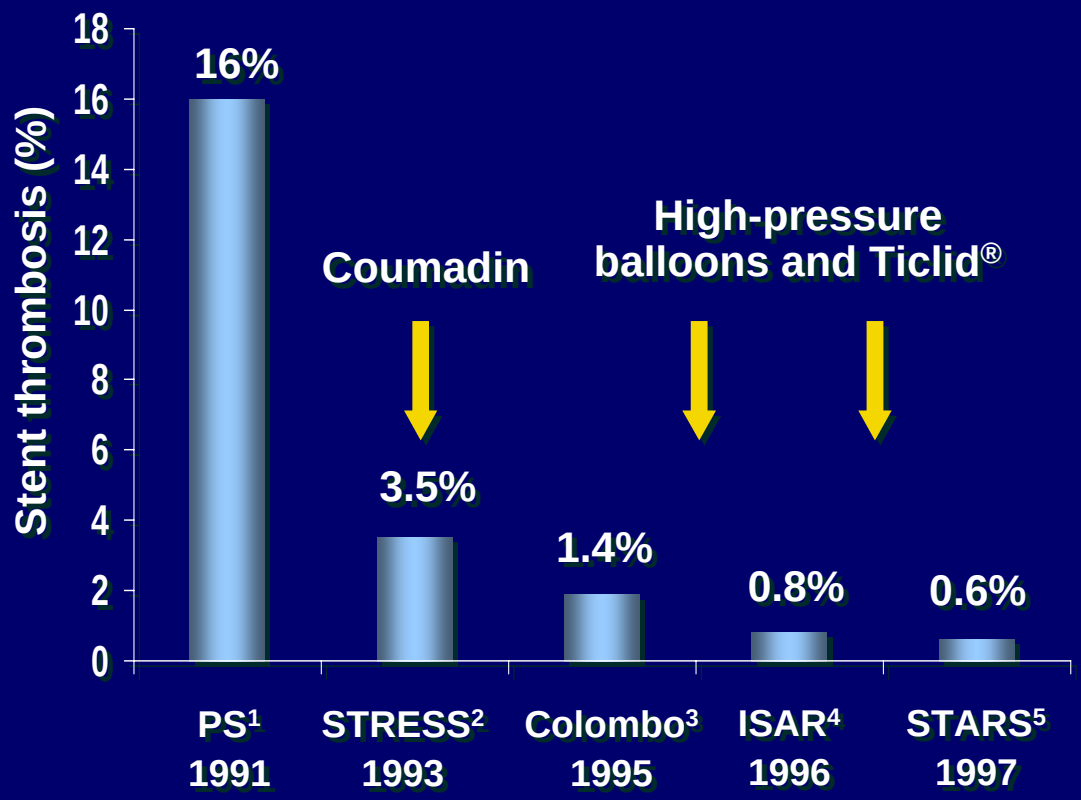
2003 Cypher: US

2004 TAXUS: US

2005 and Beyond: New Generation DES stents

History of Stent Thrombosis





Stent Thrombosis - clot formation inside a stent - has been an important complication since the earliest stent implants, but fortunately has progressively decreased in incidence due to the use of high-pressure stent deployment and current dual anti-platelet (aspirin and either ticlopidine or clopidogrel) therapy

1. Schatz et al. *Circulation*.1991;83:148; 2. Fischman et al. *N Engl J Med.* 1994;331496; 3. Colombo et al. *Circulation*.1995;91:1676;
4. Schömig et al.*Circulation.*1994,90:2716; 5. Leon et al. *N Engl J Med*. 1998;339:1665; 6. Joner et al. *J Am Coll Cardiol*. 2006;48:193.

DES Use Considerations

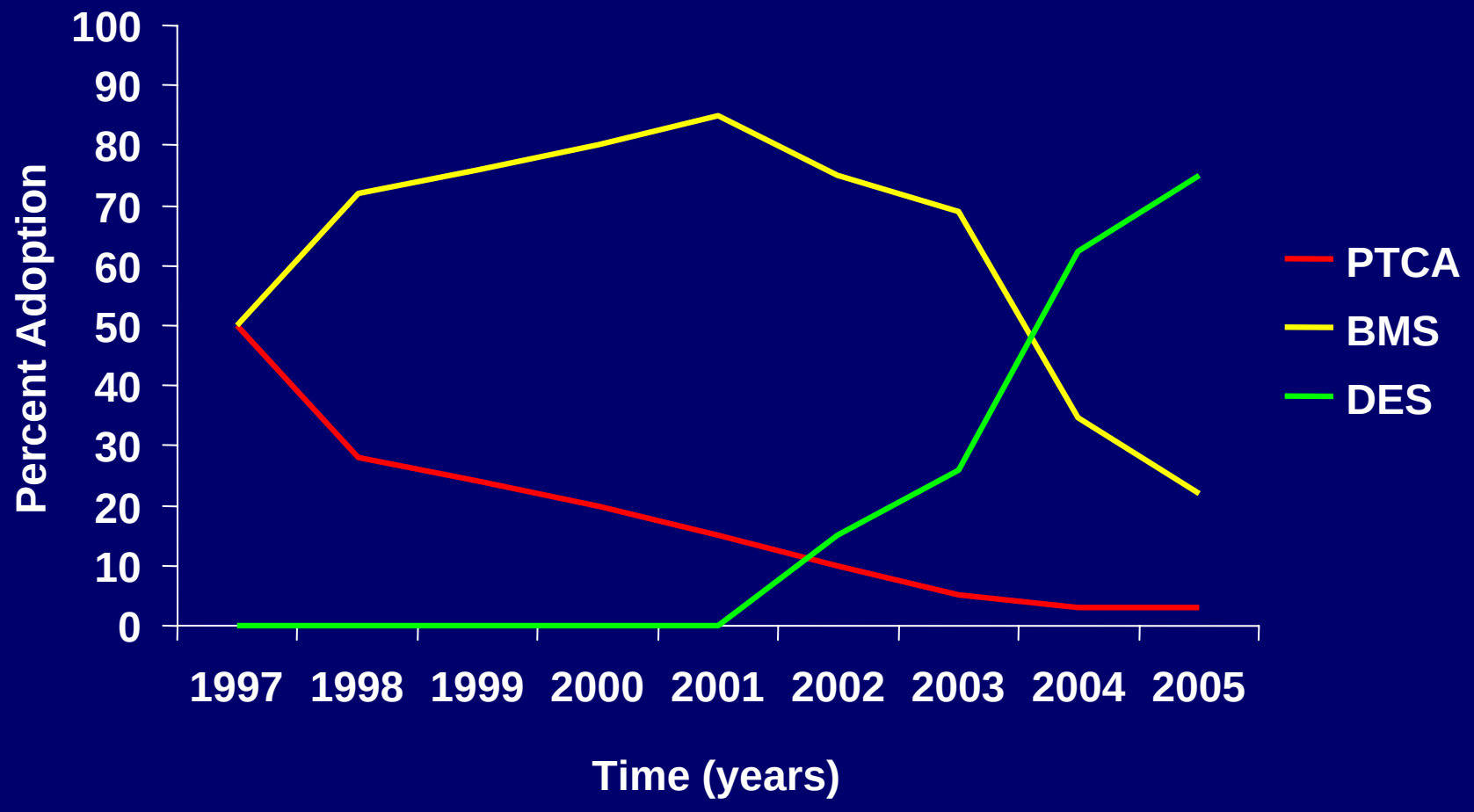
- Safety (death, MI, and stent thrombosis)
- Efficacy
  - ✓ biologic activity (suppression of in-stent intimal hyperplasia)
  - ✓ clinical benefit (prevention of repeat revascularization events)
- Deliverability (user-friendly features)
- Durability (sustained efficacy over time)
- Indications/Patient selection
- Deployment techniques

DES Use Considerations

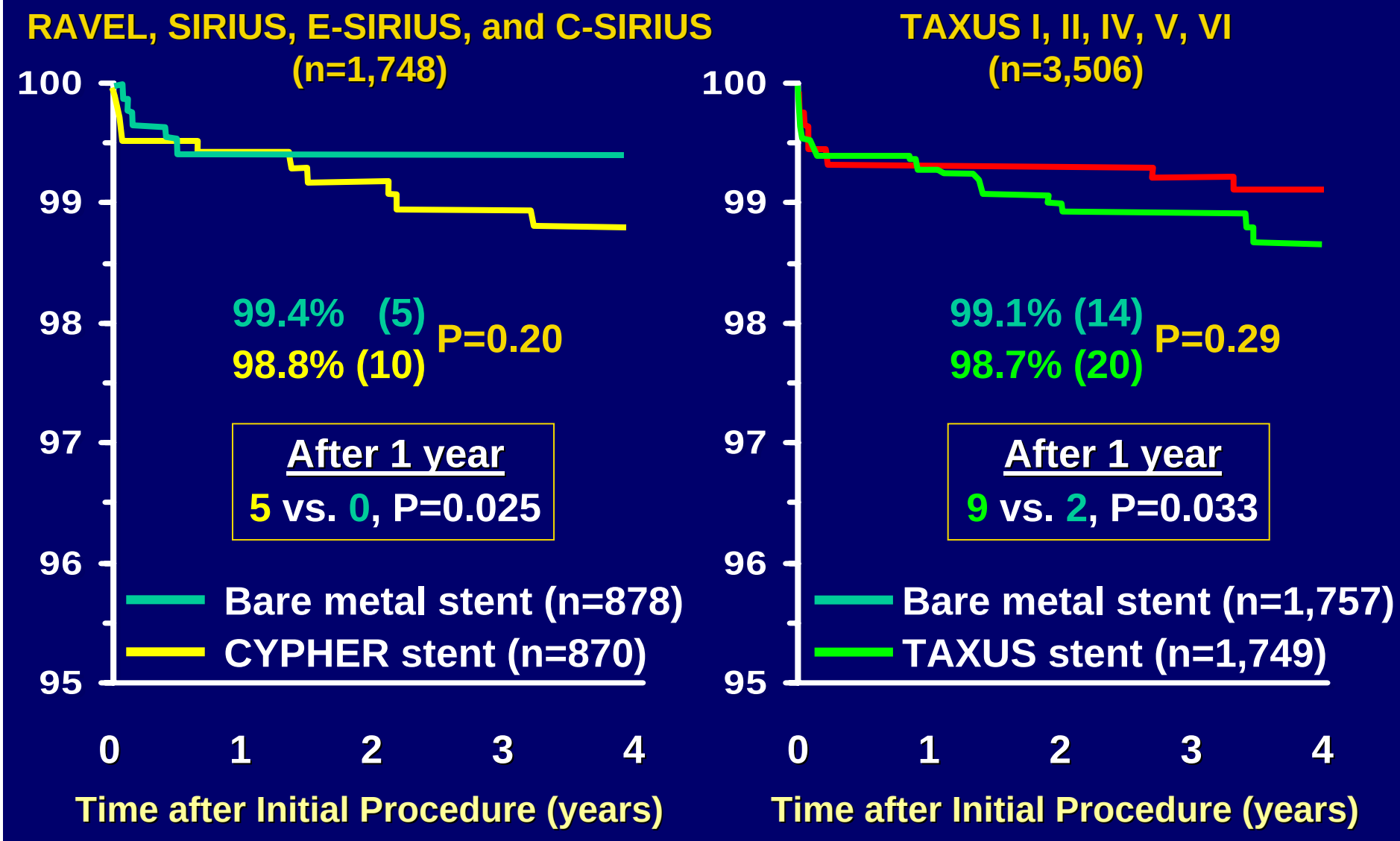
Attribute	Bare Metal Stents	1st Generation DES
Efficay	++	++++
Safety	+++	++
Deliverability	++++	++
Durability	++++	+++

Potential Areas for Improvement

Ravenous DES Penetration

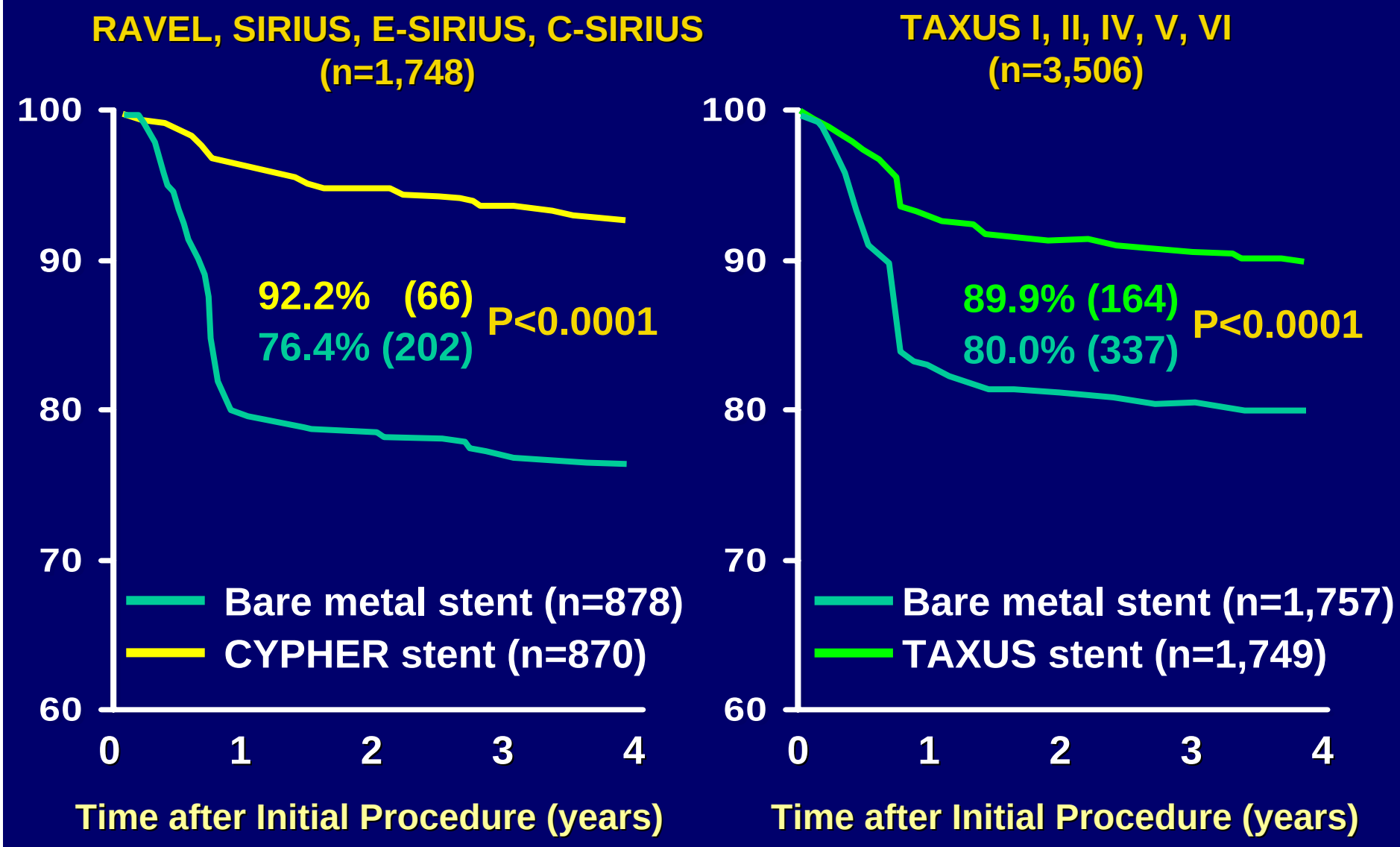


9 Prospective, Double-Blind, Randomized Trials
Freedom From (Protocol) Stent Thrombosis



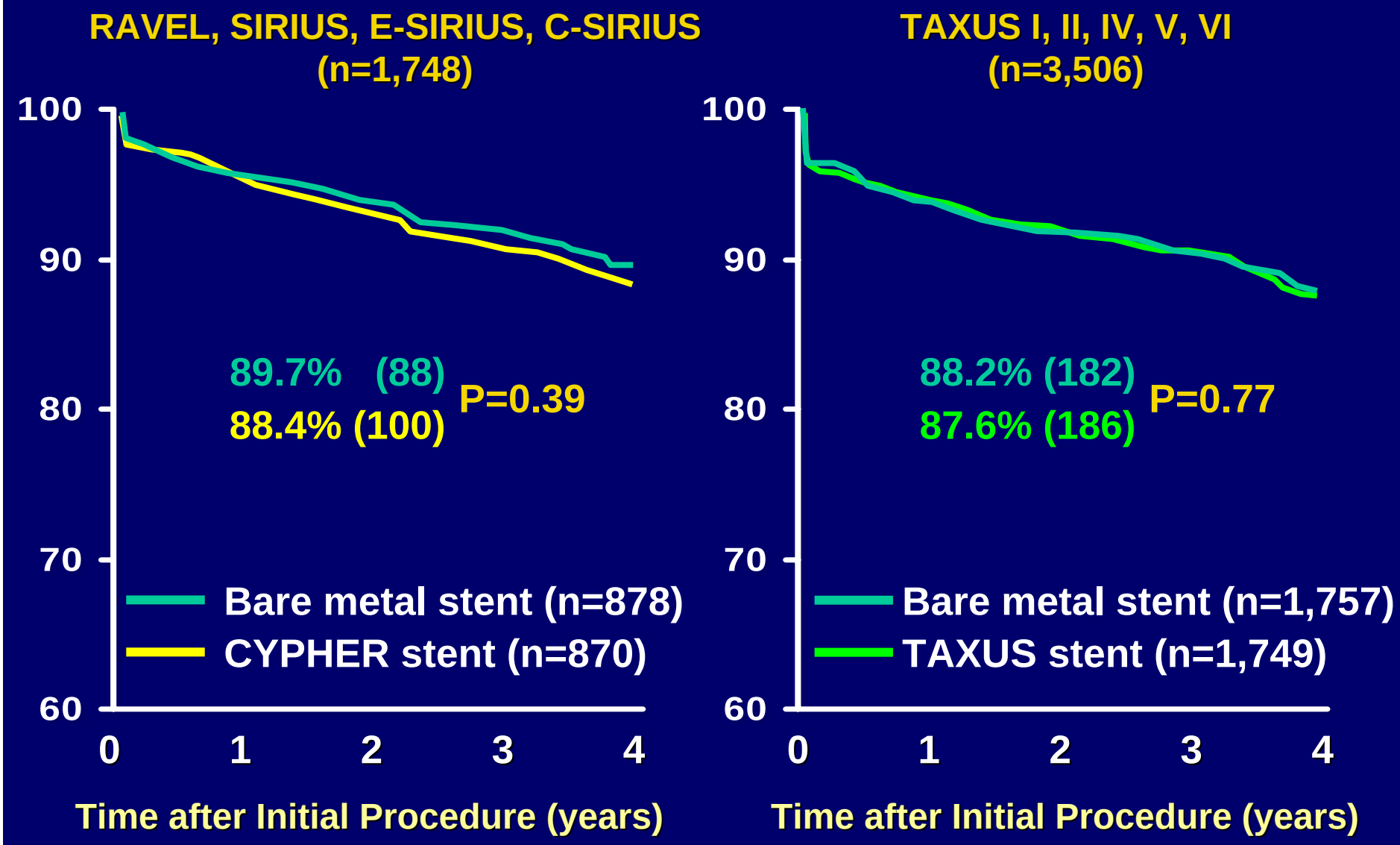
Independent CRF patient-level meta-analysis from TCT 2006

9 Prospective, Double-Blind, Randomized Trials
Freedom From Ischemic TLR



Independent CRF patient-level meta-analysis

9 Prospective, Double-Blind, Randomized Trials
Freedom From Death or Myocardial Infarction



Independent CRF patient-level meta-analysis TCT2006

DES in high risk patient and lesions subsets

- Diabetics
- Ostial lesions
- Long lesions
- Small vessels
- Treatment of in-stent restenosis
- Drug-eluting stent failures
- SVGs
- LM
- Bifurcation lesions
- Acute MI

Stent Thrombosis

Complex interactions

Procedure

- Post Dilation
- Flush apposition

Stent Thrombosis

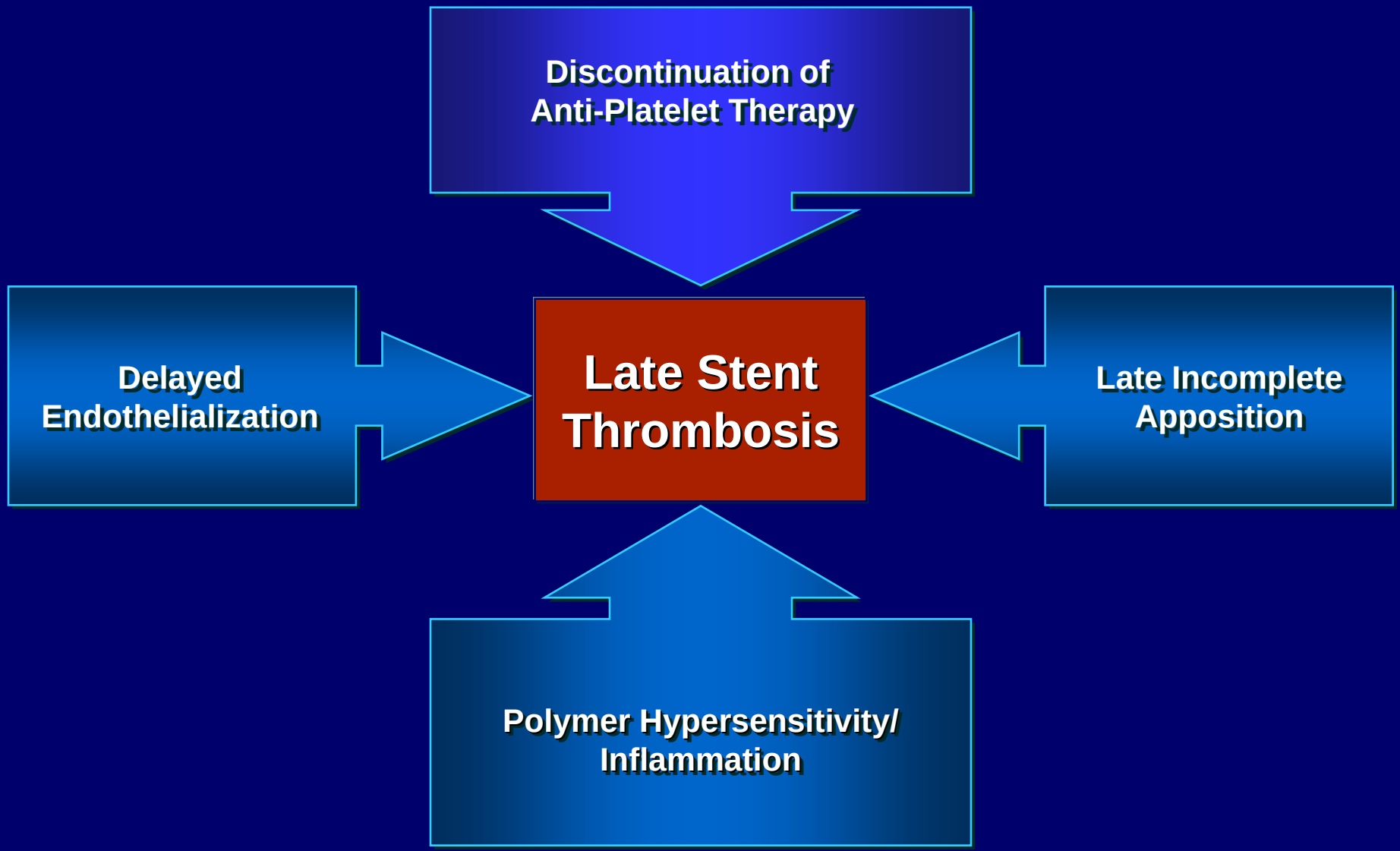
Device

- *Polymer integrity and reactions*
- Drug effects

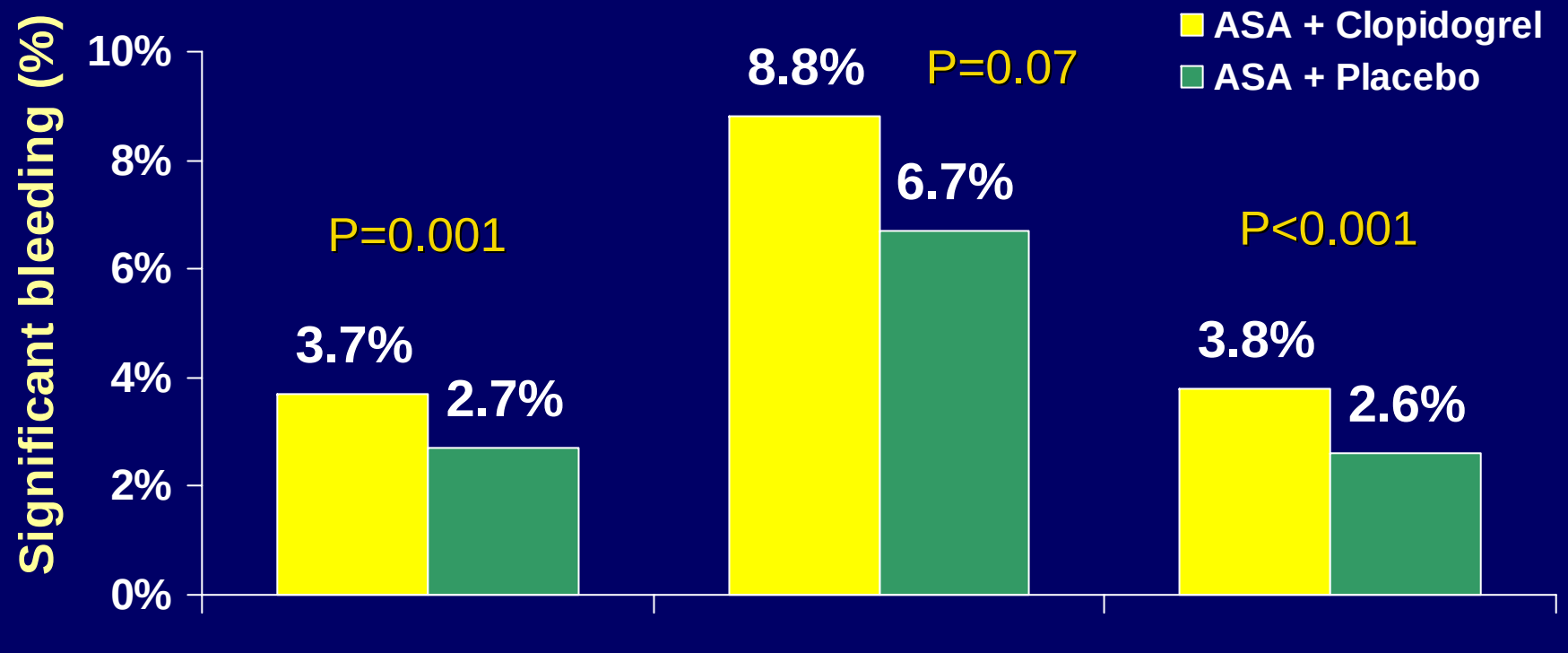
Patient

- Higher Risk
- AP Compliance and Resistance

Late Stent Thrombosis— Factors to Consider



Safety of Long-Term Clopidogrel
3 Placebo Controlled Trials

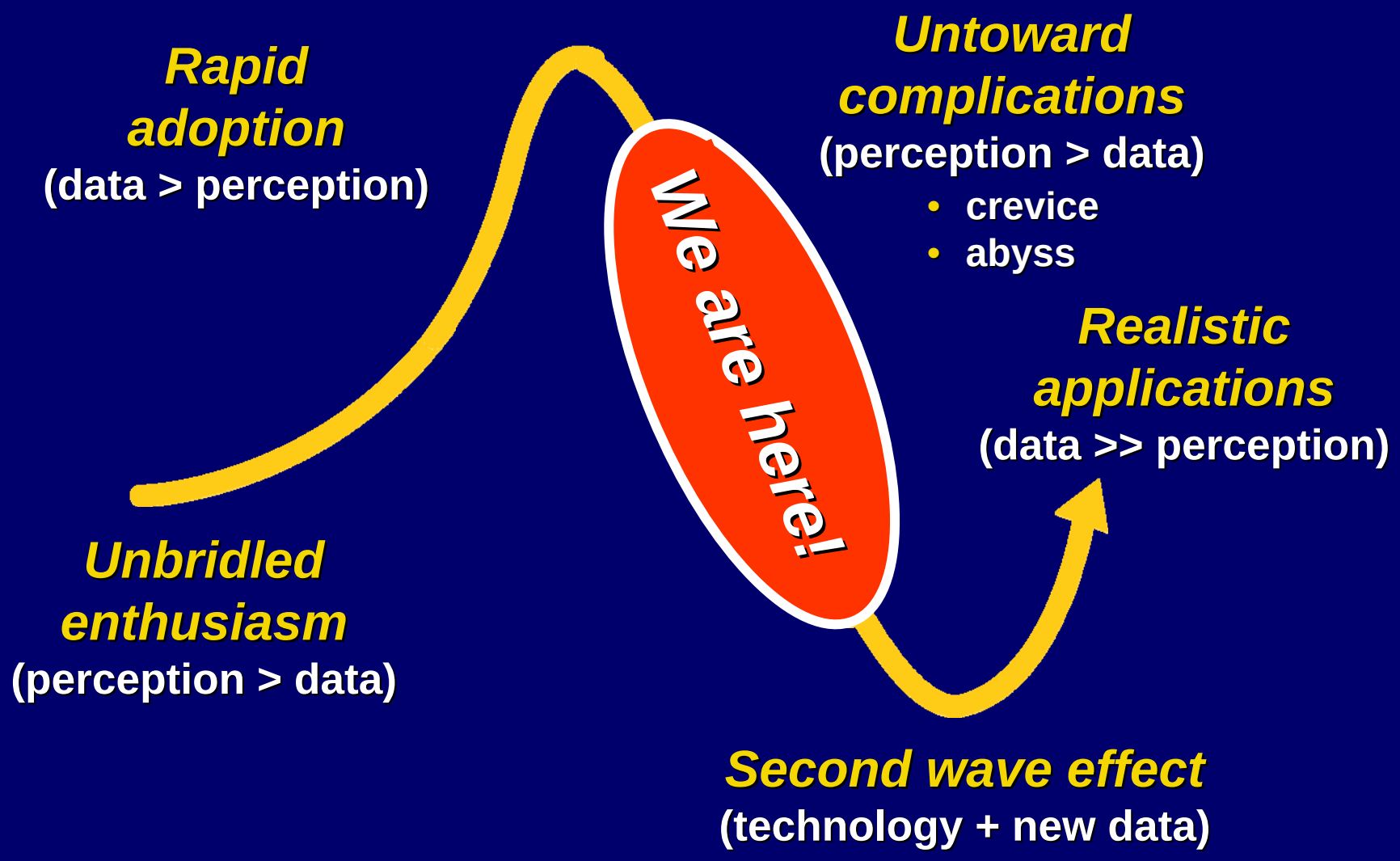


CURE
N=12,563
1 year FU
CURE major bleed
NEJM 2001;345;494-502

CREDO
N=2,116
1 year FU
TIMI major bleed
JAMA 2002;288:2411-20

CHARISMA
N=15,603
2.5 year FU
GUSTO major
+ moderate bleed
NEJM 2006;354:1706-17

Innovative Technology Lifecycle



Unmet Clinical Needs in DES Era

- Diabetic vascular disease
- Diffuse/Multi vessel disease
- Bifurcation
- Chronic Total Occlusions
- Left Main/Ostial disease

Future Post Market Data

STENT Thrombosis Registry: 10,000 patients

E-Select : 30,0000 patients

PROTECT Trial: 8,000 patients

Conclusion

- Weigh risks and benefits
- The DES device-related contributions to LST are poorly understood but need to be determined.
- We must focus on safety first and solve any dilemma of LST associated with DES, while preserving clinical efficacy.
- New drug carrier systems need to be appropriately and aggressively evaluated.
- If we do not continue to push forward and add to the advances of DES we will be left with need that have not been met.