

# Why has the Uptake of New Antiplatelet Agents Been Slow?

David J. Cohen, MD, MSc

Director of Cardiovascular Research  
Saint-Luke's Mid America Heart Institute

Professor of Medicine  
University of Missouri-Kansas City

# Disclosures

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## Grant Support/Drugs

- Daiichi-Sankyo
- Astra-Zeneca
- Eli Lilly

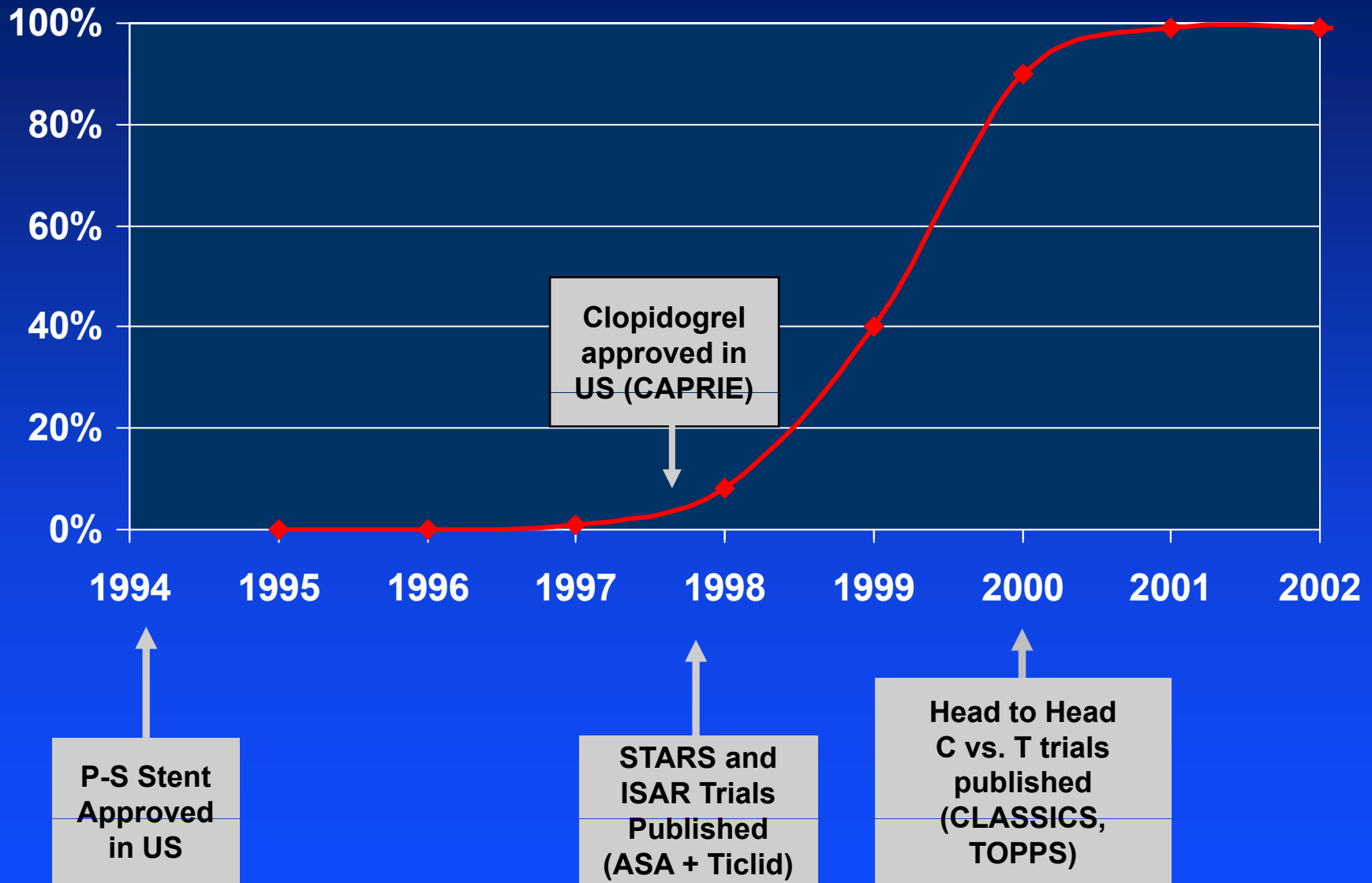
## Grant Support/Devices

- Edwards Lifesciences
- Medtronic
- St. Jude Medical
- Abbott Vascular
- Boston Scientific

## Consulting/Advisory Boards

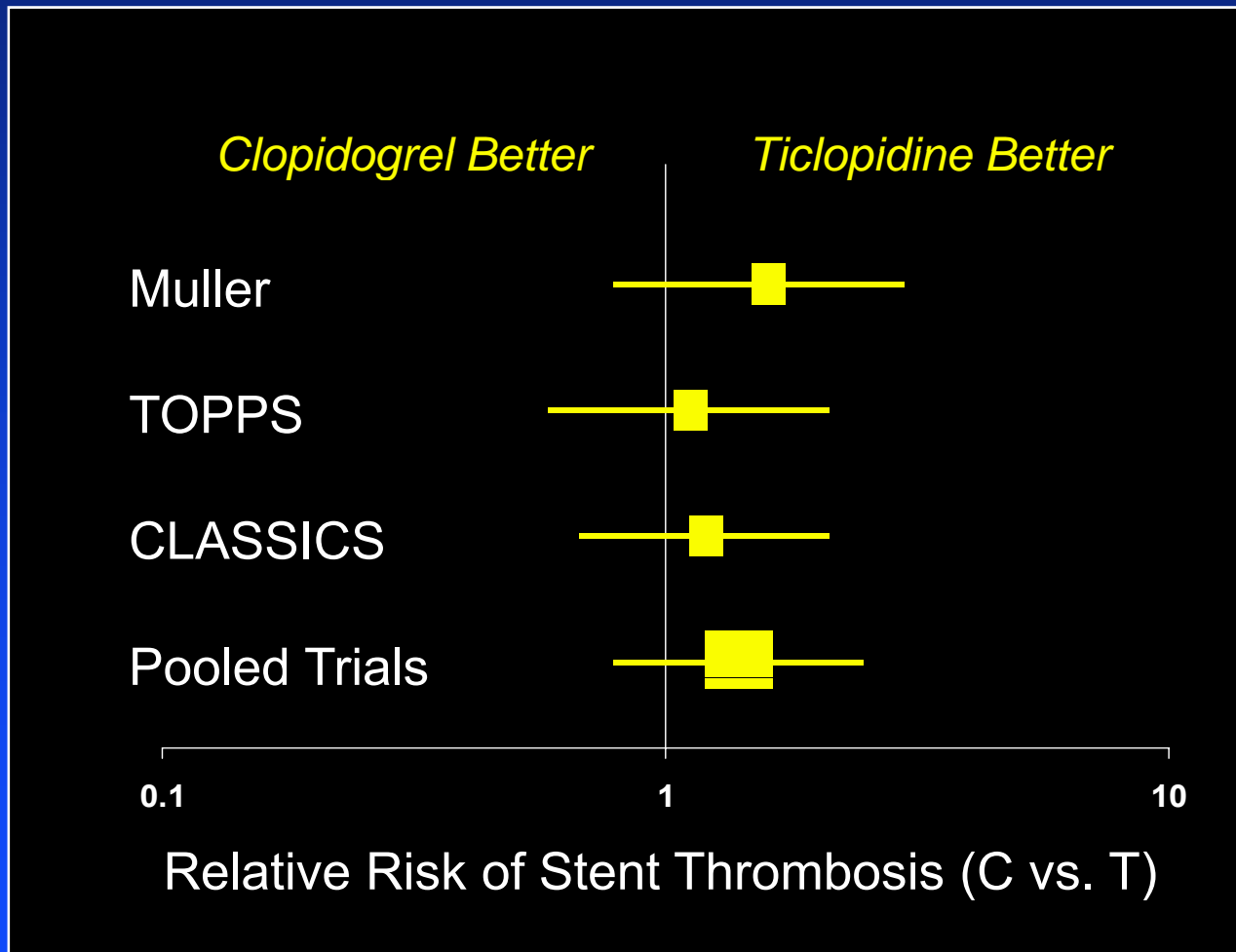
- Medtronic
- Abbott Vascular
- Boehringer-Ingelheim

# Timeline of Clopidogrel Use in PCI



# Clopidogrel vs. Ticlopidine: Stent Thrombosis

## Meta-analysis of RCTs



Stent Thrombosis		
<u>C</u>	<u>T</u>	<u>RR</u>
1.9%	0.6%	3.2
2.0%	1.9%	1.1
1.2%	0.9%	1.3
1.8%	1.2%	1.5

# Why was Clopidogrel Uptake so Rapid?

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Everyone hated ticlopidine....

- 2x/d dosing
- Frequent side effects— rash/nausea/diarrhea
- Need to monitor for neutropenia in all patients
- Non-trivial risk of TTP

Given these obvious short-comings, interventional cardiologists rapidly adopted clopidogrel with no evidence of improved ischemic outcomes

# **David Cohen's Top 3**

**Reasons why adoption of new  
antiplatelet agents has been slow**

**Reason**

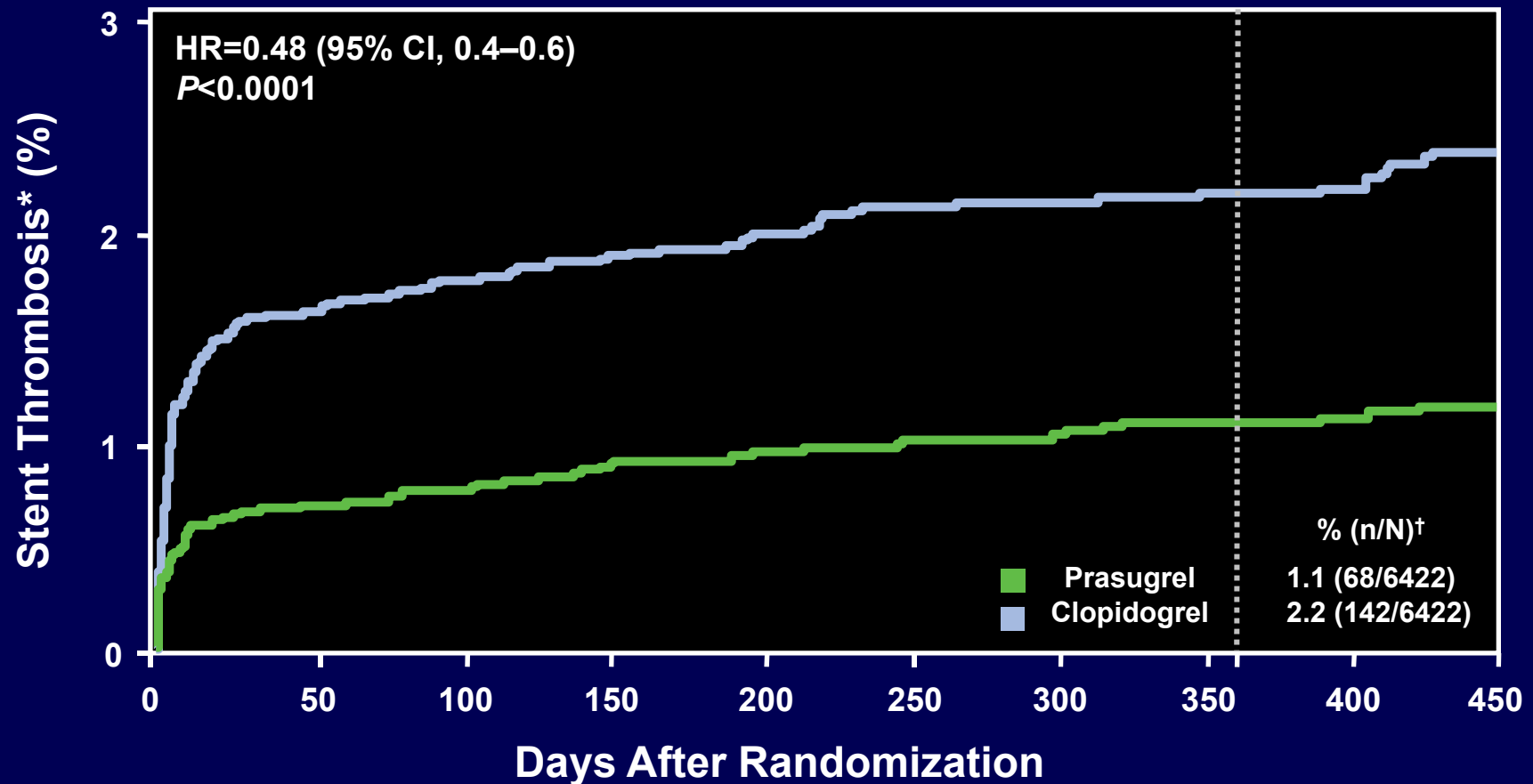
**# 1**

- Ischemic risk after PCI is often underestimated

# Stent Thrombosis: All ACS

TRITON-  
TIMI 38

## Any Stent Post-Randomization



\*Stent thrombosis defined as Academic Research Consortium definite or probable.

†Observed data.

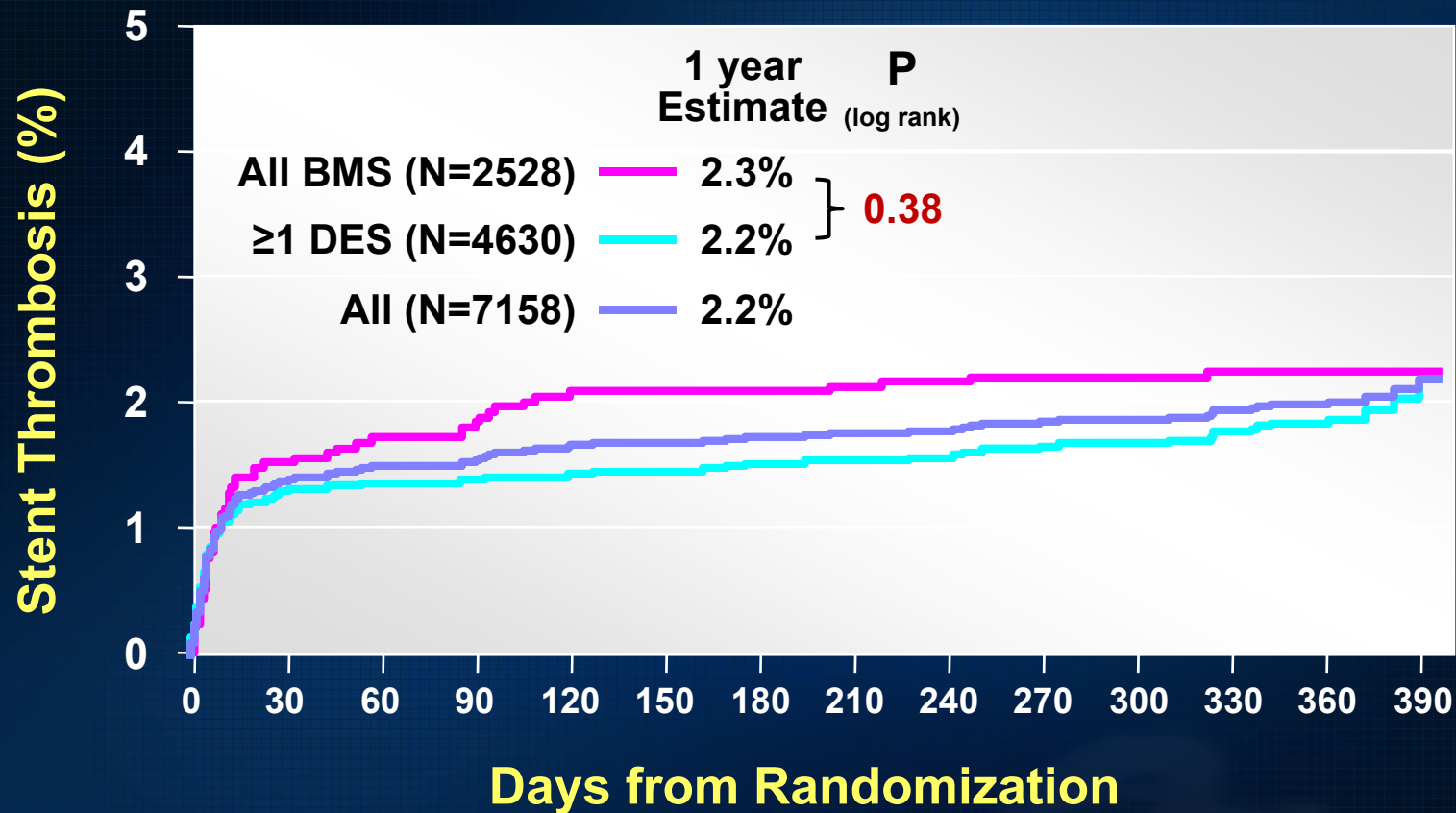
1. Wiviott et al. *Lancet*. 2008;371:1353-1363. 2. Data on file: #EFF20091204b: DSI/Lilly.





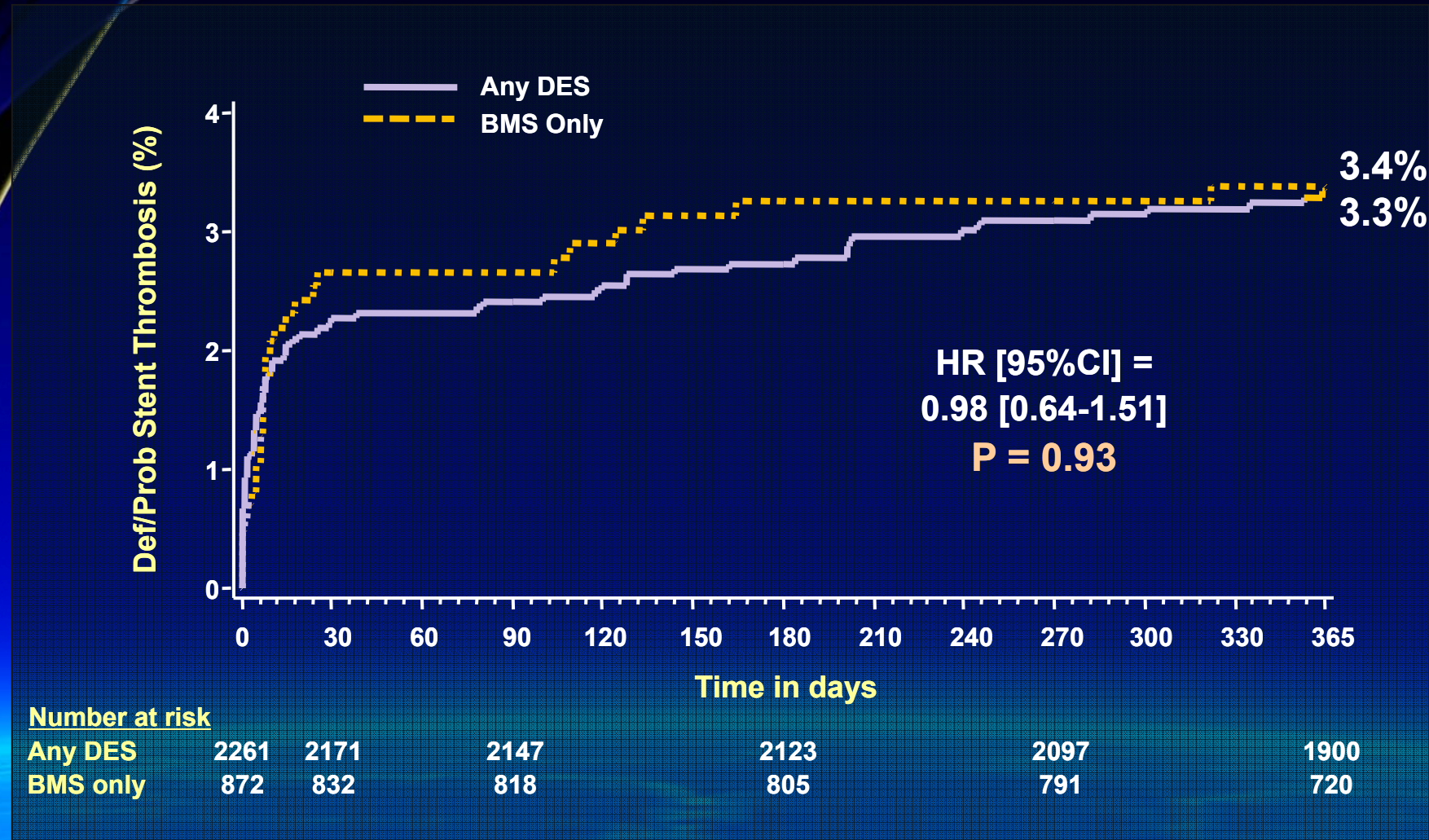
# NSTE-ACS: Stent Thrombosis

## Drug-eluting Stents (DES) vs. Bare Metal Stents (BMS)



# STEMI: Stent Thrombosis

## Impact of Implanted Stent Type



**Reason**

**# 2**

- Concordance of bleeding and ischemic risk

# Predictors of Ischemic vs. Bleeding Events

## Ischemic Complications

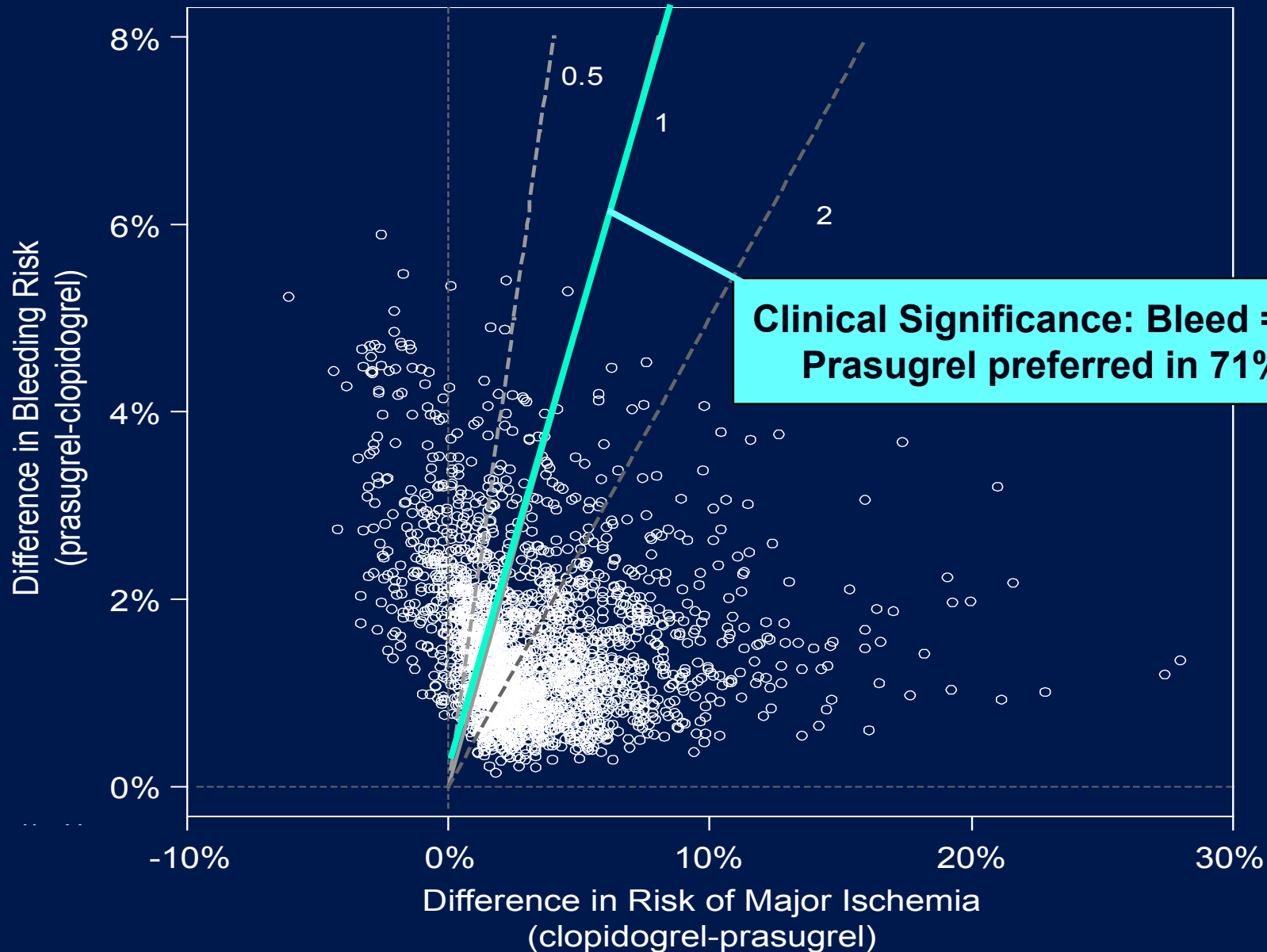
- STEMI presentation
- NSTEMI presentation
- Age
- Female Gender
- Renal Insufficiency
- PAD
- Diabetes
- Prior CAB

## Bleeding Complications

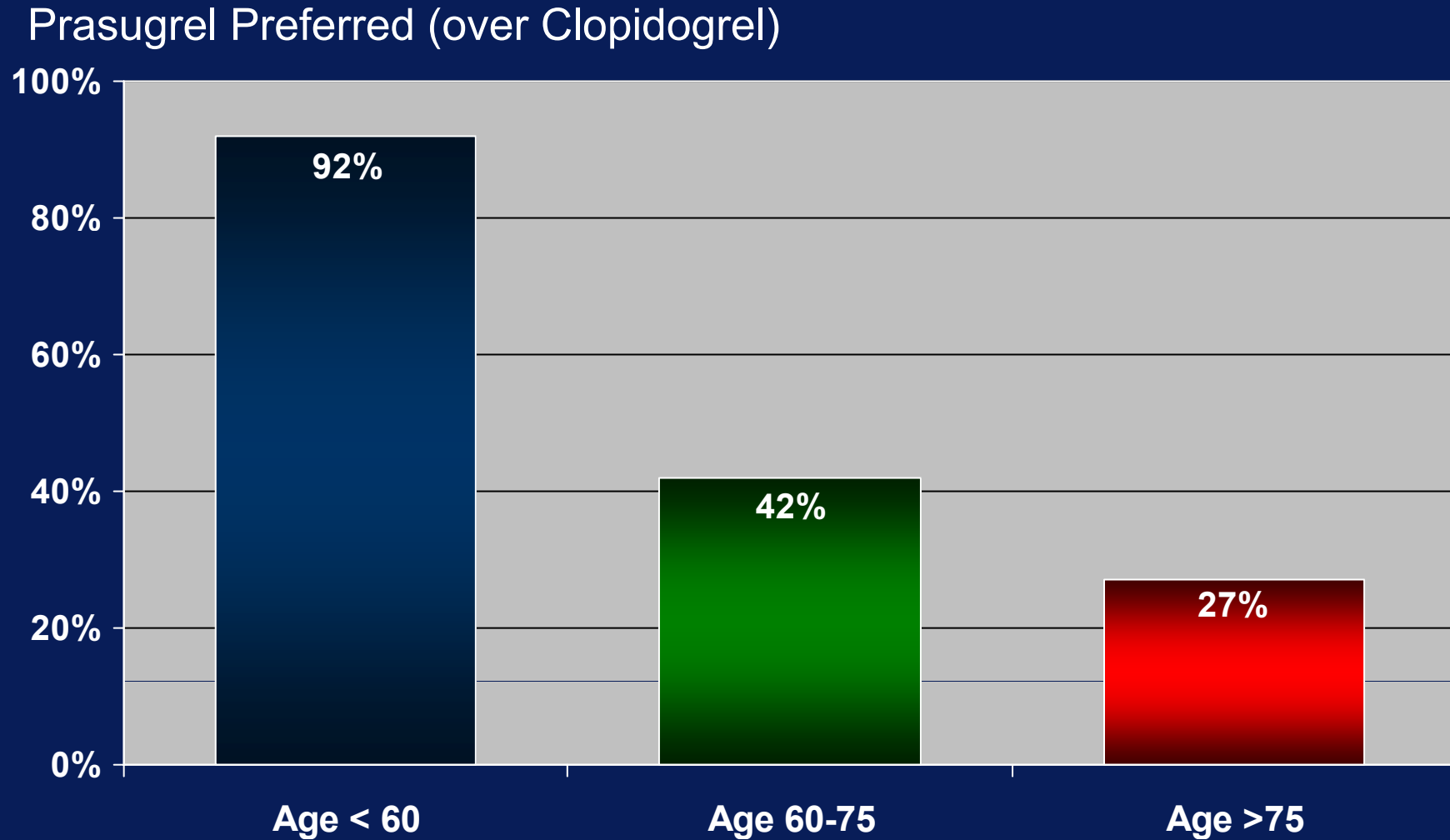
- STEMI presentation
- Low weight/BSA
- Age
- Female Gender
- Renal Insufficiency
- PAD

***Implications: Challenging to identify individual patients who are likely to derive benefit or harm***

# Prasugrel vs. Clopidogrel: Predicted Risk vs. Benefit at Individual Level



# Impact of Age on Net Benefit of Prasugrel



\* Assumes that bleeding and ischemic complications have similar clinical impact

**Reason**

**# 3**

- Physician psychology-- difference between errors of omission and commission

# Physician Psychology: Errors of Omission vs. Errors of Commission

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## Ischemic Event (Error of Omission)

- Related to underlying disease or non-compliance
- “It was the patient’s fault”

## Bleeding Event (Error of Commission)

- Related to the drug(s)
- “It was my fault”



## Additional Factors

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- **Cost/Availability**
  - *Concerns that local pharmacies may not stock the drug, or insurance plan may not cover it → vicious cycle*
- **Compliance concerns, especially with ticagrelor**
- **Care patterns firmly established**
  - *Prasugrel and ticagrelor only approved for ACS*
- **No clear guidance on how to switch from one agent to another**
  - *Is reloading safe/necessary?*
  - *Especially challenging with ticagrelor*

## The Bottom Line

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- Change is difficult
- Physician behavior not always “rational”
- As treatment options proliferate, we need help (at the bedside) to ensure that we make optimal decisions for our patients