Revascularization for Stable Coronary Artery Disease

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Dallas CARDIOVASCULAR INNOVATIONS 2013

Disclosures

Speaker

AstraZeneca

Gore

Abbott Vascular

Consultant

St Jude Medical

Why is this topic important????

- ❑ Increased emphasis on cost containment
- ❑ Growing evidence of limitations of PCI for stable disease
- ❑ Increasing public and press focus on the “overuse” of PCI

HEART | AUGUST 15, 2013, 6:00 AM | 84 Comments

Heart Stents Still Overused, Experts Say

By ANAHAD O'CONNOR

FACEBOOK

DECEMBER 6, 2010

Senate Report

30 Stents in 1

by Larry Husten • Uncategoriz

[Updated] Mark Midei, the interventional cardiologist who has been accused of implanting hundreds of unnecessary stents at St. Joseph Medical Center in Maryland, was congratulated by Abbott Labs for implanting 30 stents in one day. "I heard thru the grapevine that you had a truly outstanding day with Xience in the labs on Friday, perhaps setting the single day implant record," wrote an Abbott official. Two days later, Abbott spent $2,159 for a barbecue at Midei's house that included a whole smoked pig and other fixings.

The Daily Briefing

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Behind bars: The downfall of the nation's busiest cardiologist

Colleagues say Patel brought modern heart medicine to a Louisiana town

Topics: Finance, Mortality, Quality, Performance Improvement, Safety, Patient Satisfaction, Workforce, Recruitment and Retention

October 31, 2013

Writing in *Bloomberg* this month, David Armstrong chronicles how Mehmood Patel—who once bragged of being the nation's busiest cardiologist—ended up behind bars after being convicted of 51 counts of billing for placing unnecessary stents in patients.

According to the attorneys who argued the case, Patel's case marked the first time a cardiologist was convicted in the United States based only on charges of billing for medical unnecessary procedures. It was a watershed case for the federal government and was followed by convictions for two other cardiologists and investigations in at least six states.

LIFE | HEALTH | OPINION

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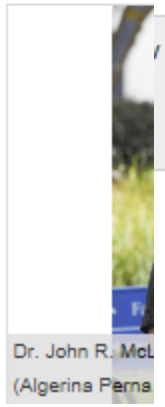
York



Dr. John R. McL
(Algerina Perna

There are many ways to interact with this map. Zoom in to see localities & move your cursor over the map for more details. Switch map views in the menu below to see additional data, and search for your city, state or ZIP code.

Click below to see other data layers

Rate of stent-related procedures
The number of PCIs for every 1,000 Medicare enrollees.

Procedures per angiographies

Procedures per ischemia cases

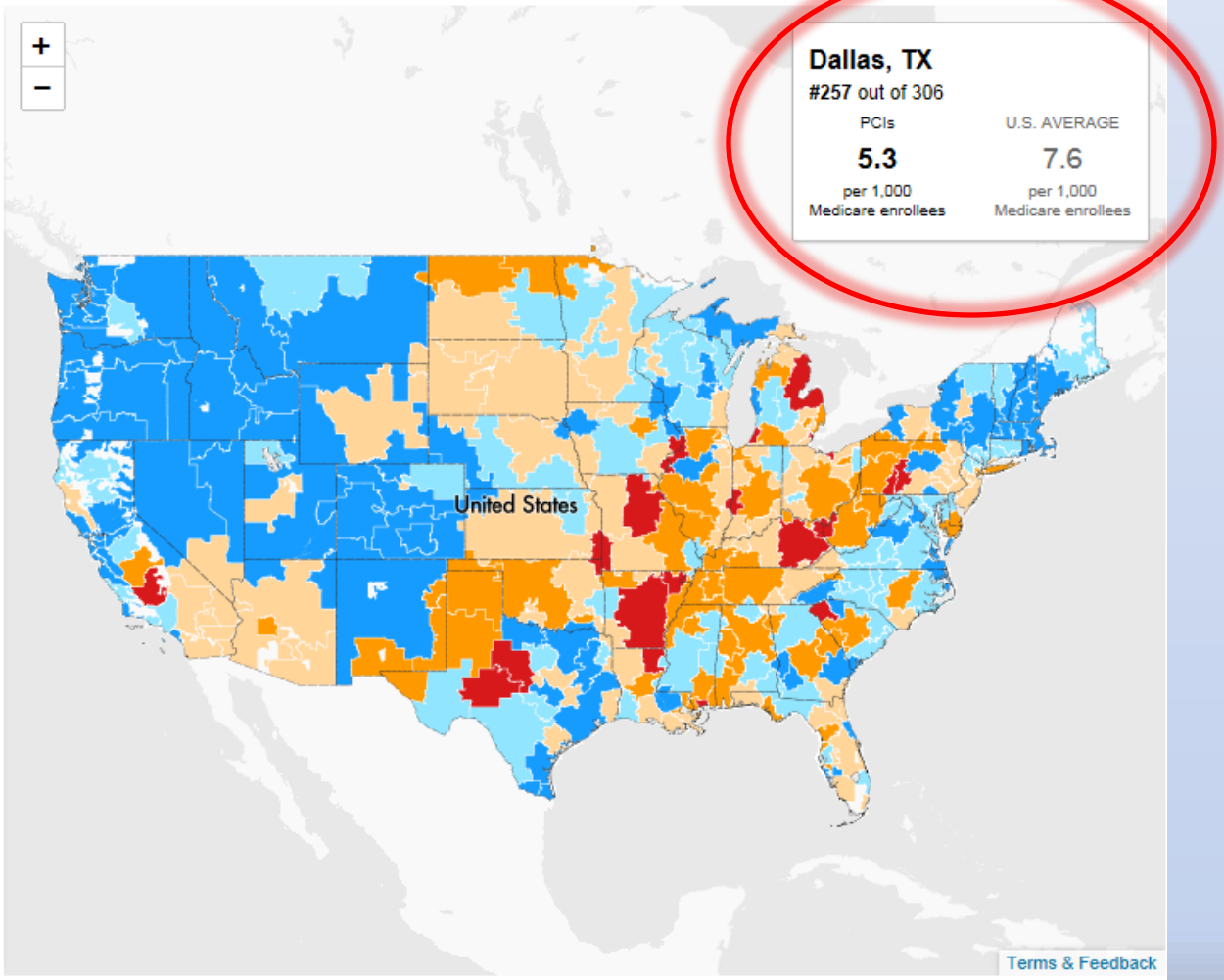
Search by city, state or ZIP

Locate

Indicated Stent Usage

- 20 hospital regions with highest usage
- High usage
- Above average usage
- Below average usage
- Low usage
- Insufficient data

Note: 2010 data. Orange, tan, light blue and dark blue areas divided by quartiles. Areas colored red are included in the top quartile.



Sources: Dartmouth Atlas of Health Care, U.S. Centers for Medicare & Medicaid Services. Data on Medicare beneficiaries excludes those in Medicare Health Maintenance Organizations and patients under 65 years of age.

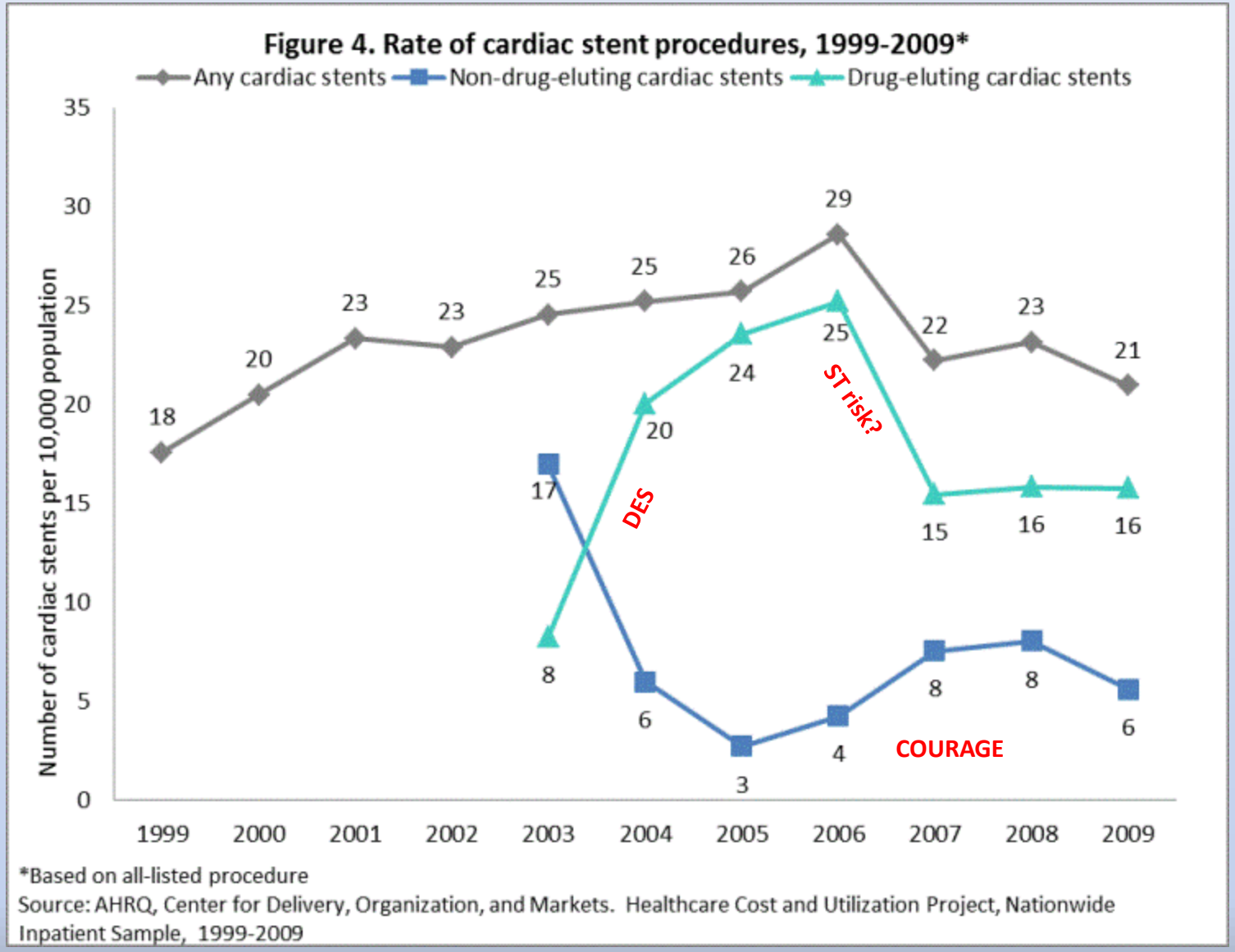
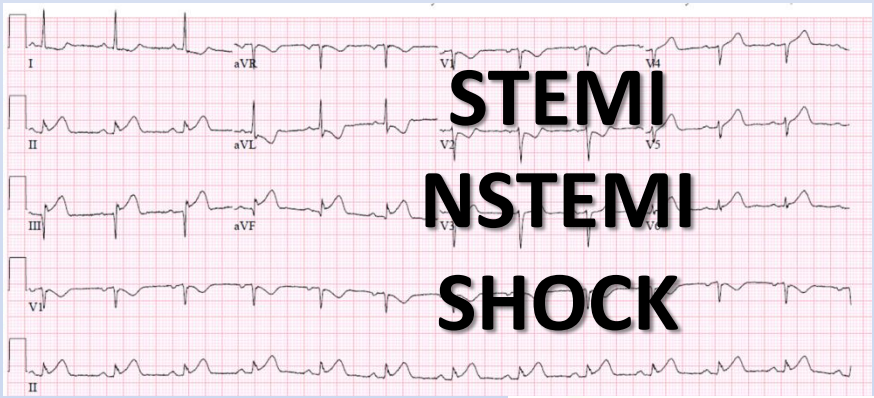


Figure 4. Rate of cardiac stent procedures, 1999-2009*
Any cardiac stents
Non-drug-eluting cardiac stents
Drug-eluting cardiac stents
Number of cardiac stents per 10,000 population
35
30
25
20
15
10
5
0
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
18
20
23
23
25
25
26
29
22
23
21
17
6
3
4
8
8
6
8
20
24
25
15
16
16
DES
ST risk?
COURAGE
*Based on all-listed procedure
Source: AHRQ, Center for Delivery, Organization, and Markets. Healthcare Cost and Utilization Project, Nationwide Inpatient Sample, 1999-2009

Stents save lives and reduce morbidity!!



STEMI
NSTEMI
SHOCK

SCAI SecondsCount
When Seconds Count, We Give Second Chances.

secondscount.org

“PCI overuse”?……

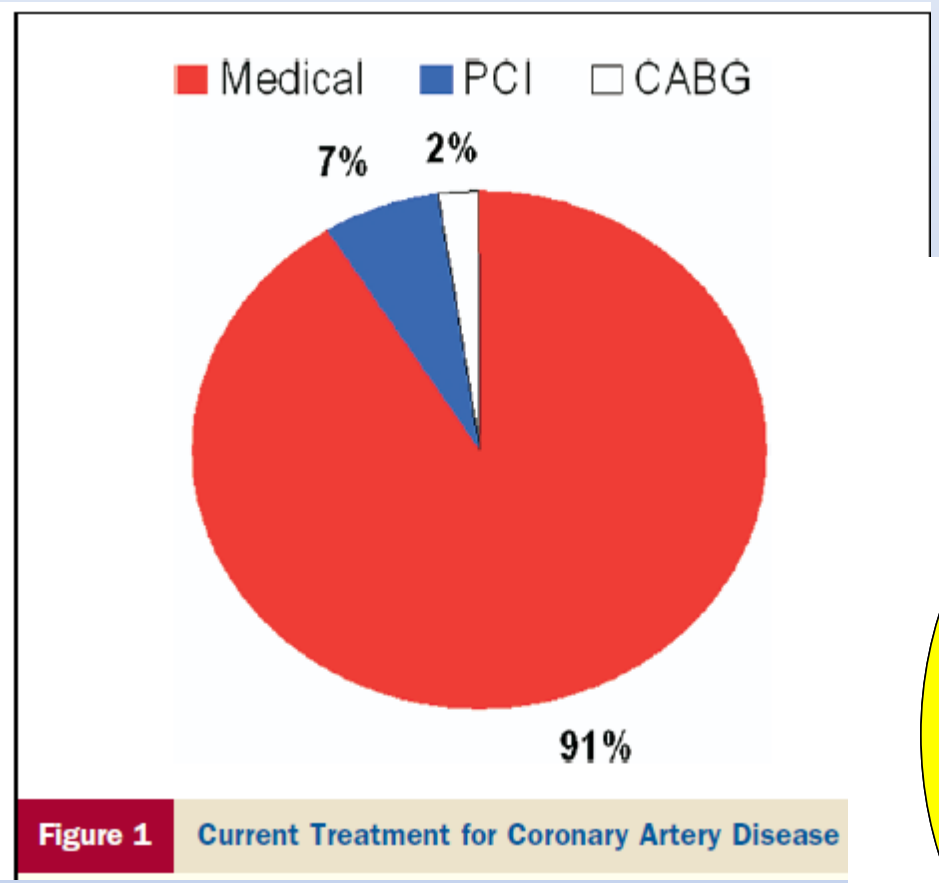
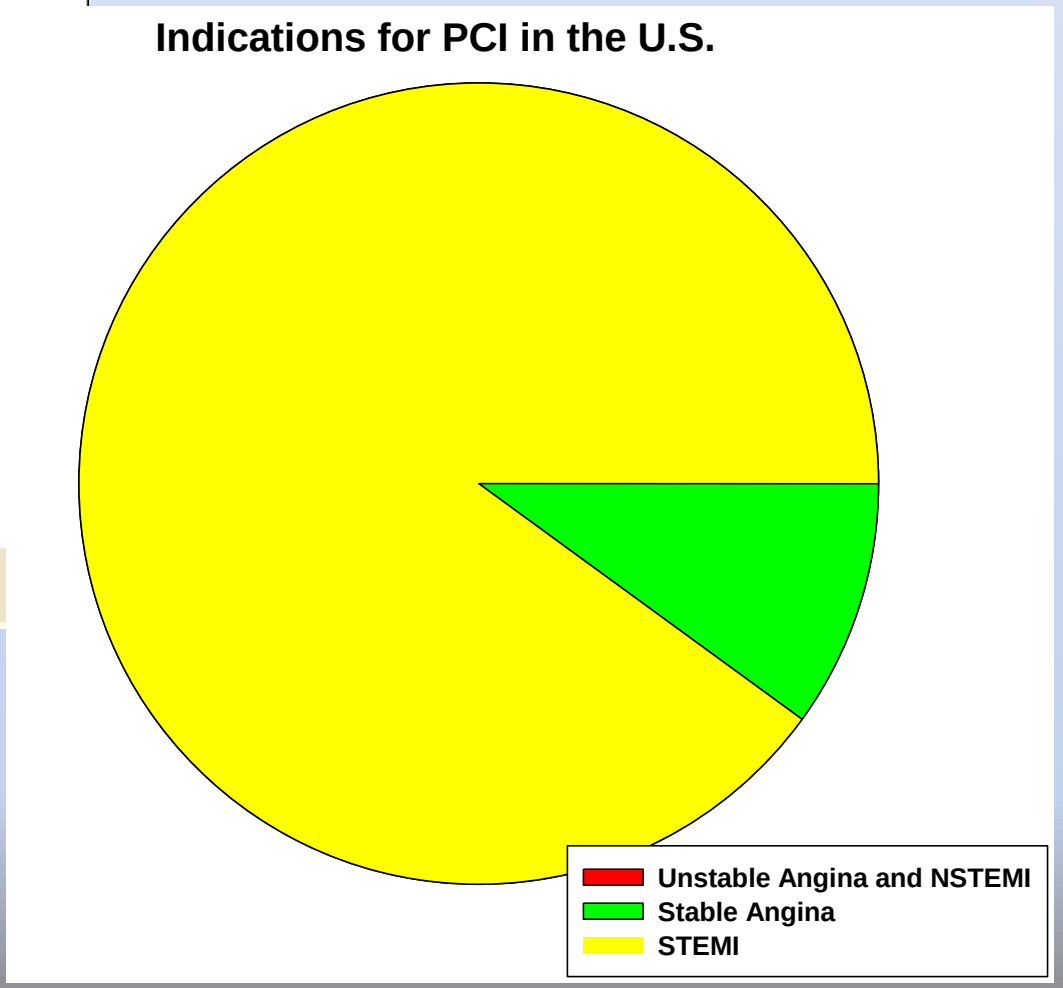


Figure 1 Current Treatment for Coronary Artery Disease



Kereiakes et al. J Am Coll Cardiol 2007;50:1598–603

Appropriateness Guidelines?

Intermediate Risk Findings on Noninvasive Study					
Symptoms Med. Rx					
Class III or IV Max Rx	A	A	A	A	A
Class I or II Max Rx	U	A	A	A	A
Asymptomatic Max Rx	U	U	U	U	A
Class III or IV No/min Rx	U	U	A	A	A
Class I or II No/min Rx	U	U	U	A	A
Asymptomatic No/min Rx	I	I	U	U	A
Coronary Anatomy	CTO of 1 vz.; no other disease	1-2 vz. disease; no Prox. LAD	1 vz. disease of Prox. LAD	2 vz. disease with Prox. LAD	3 vz. disease; no Left Main

CCS Class I or II Angina					
Stress Test Med. Rx					
High Risk Max Rx	A	A	A	A	A
High Risk No/min Rx	U	A	A	A	A
Int. Risk Max Rx	U	A	A	A	A
Int. Risk No/min Rx	U	U	U	A	A
Low Risk Max Rx	U	U	A	A	A
Low Risk No/min Rx	I	I	U	U	U
Coronary Anatomy	CTO of 1 vz.; no other disease	1-2 vz. disease; no Prox. LAD	1 vz. disease of Prox. LAD	2 vz. disease with Prox. LAD	3 vz. disease; no Left Main

Patel et al. JACC Vol. 59, No. 9, 2012

“Inappropriate” is a strong word!

ACC: "Inappropriate" Now "Rarely Appropriate"

Given the negative connotations of "inappropriate" and the judgment of clinicians it implies, the societies now use "rarely appropriate" to define PCI cases that don't meet the AUC. In a statement, ACC past president **Dr Ralph Brindis** (University of California, San Francisco) said, "The new terminology acknowledges that in certain rare cases when the patient's individual circumstances are considered as part of a shared decision-making process, stents in this category would be considered 'appropriate.'"

In his statement, Brindis goes on to say that the ACC is very concerned about racial and socioeconomic disparities in care, noting that the "overuse of tests and procedures puts our patients at risk for adverse outcomes and potential complications."

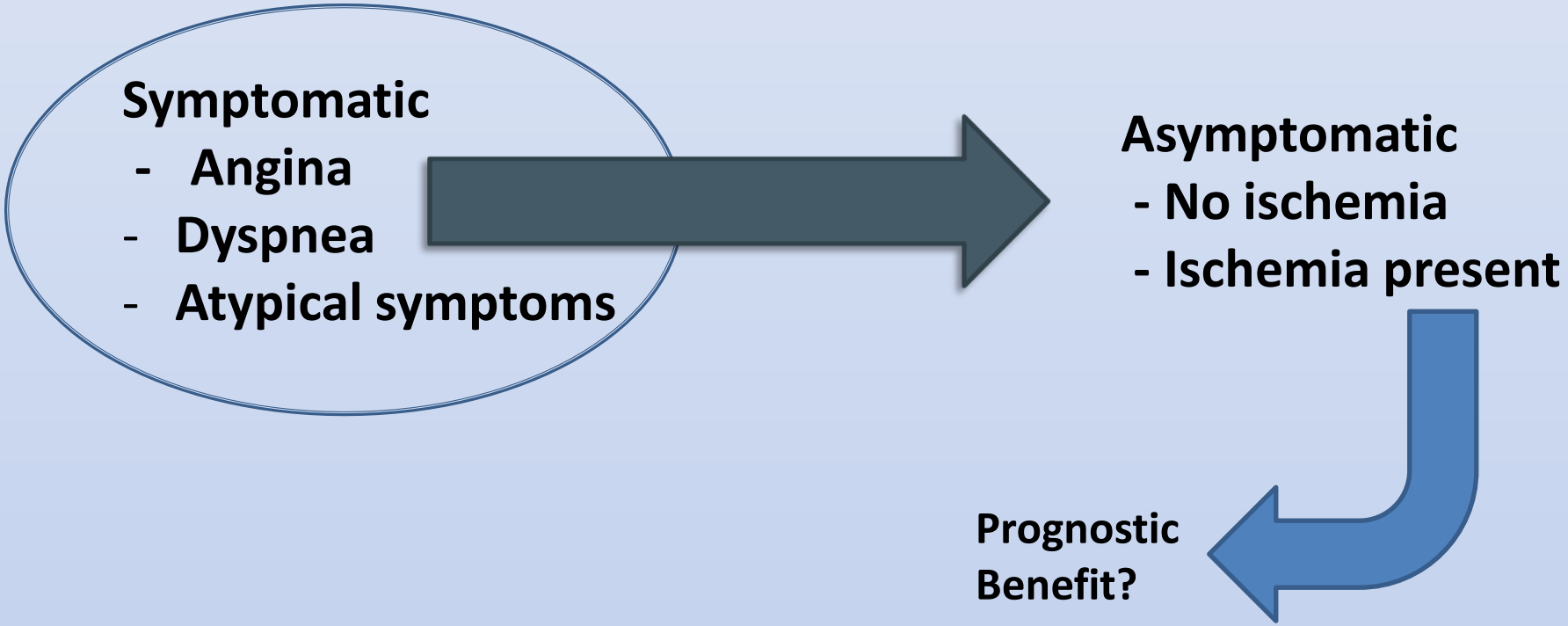
Table 32 Indications for revascularization of stable coronary artery disease patients on optimal medical therapy (adapted from ESC/EACTS 2010 Guidelines)[172]

Indication [a]	To improve prognosis:		To improve symptoms persistent on OMT:		
	Class [d]	Level [e]	Class [d]	Level [e]	Ref. [f]
A Heart Team approach to revascularization is recommended in patients with unprotected left main, 2–3 vessel disease, diabetes or comorbidities.	I	C	I	C	172, 426–428
Left main >50% diameter stenosis[b].	I	A	I	A	172
Any proximal LAD >50% diameter stenosis[b].	I	A	I	A	172
2–3 vessel disease with impaired LV function / CHF.	I	B	IIa	B	172
Single remaining vessel (>50% diameter stenosis[b]).	I	C	I	A	172
Proven large area of ischaemia (>10% LV[c])	I	B	I	B	172
Any significant stenosis with limiting symptoms or symptoms non responsive/intolerant to OMT.	NA	NA	I	A	172
Dyspnoea/cardiac heart failure with >10% ischaemia/viability[c] supplied by stenosis >50%.	IIb	B [429, 430]	IIa	B	172
No limiting symptoms with OMT in vessel other than left main or proximal LAD or single remaining vessel or vessel subtending area of ischaemia <10% of myocardium or with FFR ≥0.80.	III	A	III	C	23, 25, 172, 400

References attached to these recommendations can be found in Table 8 of the original ESC guidelines for myocardial revascularization.[172]
CCS = Canadian Cardiovascular Society; CHF: congestive heart failure; FFR = fractional fow reserve; LAD = left anterior descending; LV = left ventricle; NA: not available; OMT = optimal medical treatment; SCAD = stable coronary artery disease.
[a] In asymptomatic patients, the decision will be guided by the extent of ischaemia on stress testing.
[b] With documented ischaemia or FFR < 0.80 for angiographic diameter stenoses 50–90%.
[c] As assessed by non-invasive test (SPECT, MRI, stress echocardiography).
[d] Class of recommendation.
[e] Level of evidence.
[f] Reference(s) supporting levels of evidence.

ESC 2013 Guidelines European Heart Journal (2013) 34, 2949–3003

Goal of revascularization in stable CAD….



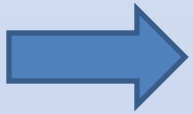
Key questions….

- When do we favor optimal medical therapy as an initial strategy over PCI?
- When should we consider revascularization with PCI?
- When is CABG the preferred strategy over PCI?

Stable CAD…Management Algorithms

<u>Low risk patients</u>
(mortality < 1%/year)

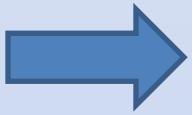
- **Mild anginal sx**
- **Low risk features on non-invasive stress testing**
- **Low risk clinical features**



Can begin with trial of medical therapy

Stable CAD…Management Algorithms

<u>Intermediate risk patients</u>
(mortality 1 to <3%/year)
- Moderate anginal sx
- Moderate risk features on non-invasive stress testing
- Presence of clinical risk factors (diabetes, smoking, HTN)



Can begin with trial of medical therapy

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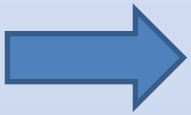
Coronary Angiography

Dangers of not knowing coronary anatomy….

Stable CAD…Management Algorithms

<u>High risk patients</u>
(mortality ≥ 3%/year)
- Severe anginal sx
- High risk features on non-invasive stress testing (early positive, large ischemic burden)
- Presence of multiple clinical risk factors (diabetes, smoking, HTN, LVEF depression)



medical therapy
+
along with coronary angiography

COURAGE trial

The NEW ENGLAND JOURNAL of MEDICINE

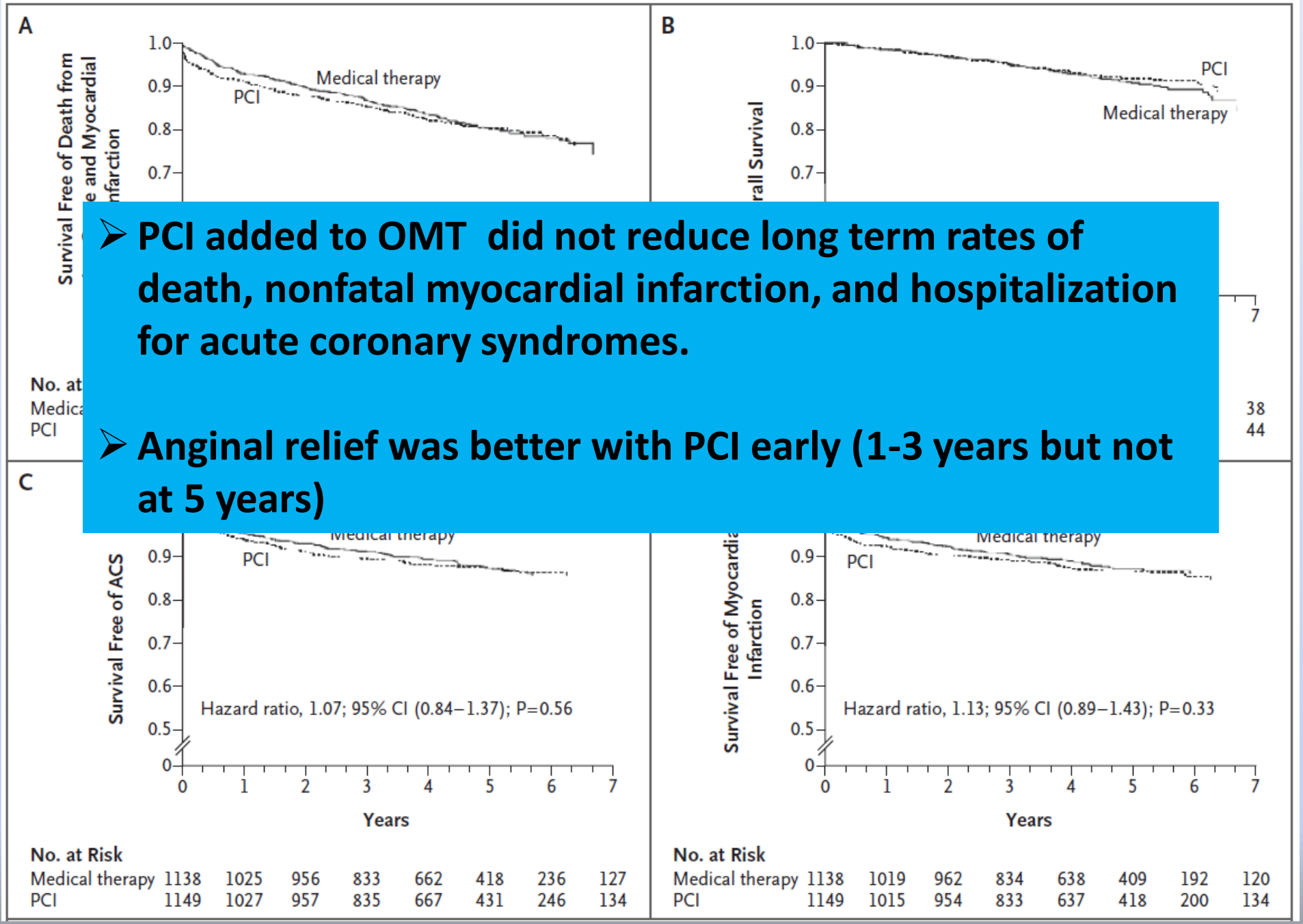
ESTABLISHED IN 1812 APRIL 12, 2007 VOL. 356 NO. 15

Optimal Medical Therapy with or without PCI for Stable Coronary Disease

William E. Boden, M.D., Robert A. O'Rourke, M.D., Koon K. Teo, M.B., B.Ch., Ph.D., Pamela M. Hartigan, Ph.D., David J. Maron, M.D., William J. Kostuk, M.D., Merril Knudtson, M.D., Marcin Dada, M.D., Paul Casperson, Ph.D., Crystal L. Harris, Pharm.D., Bernard R. Chaitman, M.D., Leslee Shaw, Ph.D., Gilbert Gosselin, M.D., Shah Nawaz, M.D., Lawrence M. Title, M.D., Gerald Gau, M.D., Alvin S. Blaustein, M.D., David C. Booth, M.D., Eric R. Bates, M.D., John A. Spertus, M.D., M.P.H., Daniel S. Berman, M.D., G.B. John Mancini, M.D., and William S. Weintraub, M.D., for the COURAGE Trial Research Group*

- In patients with stable CAD, is a strategy of initial optimal medical therapy better than OMT + PCI (with BMS) at reducing cardiovascular events?
- The primary outcome measure was a composite of death from any cause and nonfatal myocardial infarction.
- Secondary outcomes included a composite of death, myocardial infarction, and stroke and hospitalization for unstable angina with negative biomarkers.

Boden et al. N Engl J Med 2007;356:1503-16.



- **PCI added to OMT did not reduce long term rates of death, nonfatal myocardial infarction, and hospitalization for acute coronary syndromes.**
- **Anginal relief was better with PCI early (1-3 years but not at 5 years)**

How COURAGEOUS was COURAGE?

Table 1 Summaries of Trials Comparing Medical Therapy Versus PCI for Stable Coronary Artery Disease Patients

Trial (Ref. #)	Mortality and MI	Angina Relief	QOL	Repeat Revascularization
RITA-2 (7)	No difference	PCI	PCI	PCI
ACME (8)	No difference	PCI	PCI	PCI
ACME-2 (16)	No difference	PCI	PCI	NA
MASS (9)	No difference	PCI	NA	No difference
MASS-II (11)	No difference	PCI	PCI	No difference
AVERT (10)	No difference	PCI	PCI	No difference
TIME*	No difference	PCI	PCI	PCI
COURAGE (12)	No difference	No difference	PCI	PCI

*TIME Investigators. Lancet 2001;358:951–7.
MI = myocardial infarction; NA = not available; PCI = percutaneous coronary intervention; QOL = quality of life.

Boden et al. N Engl J Med 2007;356:1503-16.

Potential caveats and criticisms…

- Optimal medical therapy in COURAGE may be difficult to achieve in "real life"
- Knowing coronary anatomy may have led to selection bias
- The population studied in COURAGE was relatively low risk for events
- The liberal definition of peri-procedural MI may have biased the study against PCI
- Only 31 patients (2.7%) in the study received DES
- Concerns over crossover rate to PCI in the medical arm (32%)

Reality of COURAGE…not really all that "COURAGEOUS"…

1. **Confirms the finding that PCI for stable patients is unlikely to reduce mortality**

2. **Reaffirms the importance of medical therapy in stable patients**

Boden et al. N Engl J Med 2007;356:1503-16.

BARI 2D

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 11, 2009 VOL. 360 NO. 24

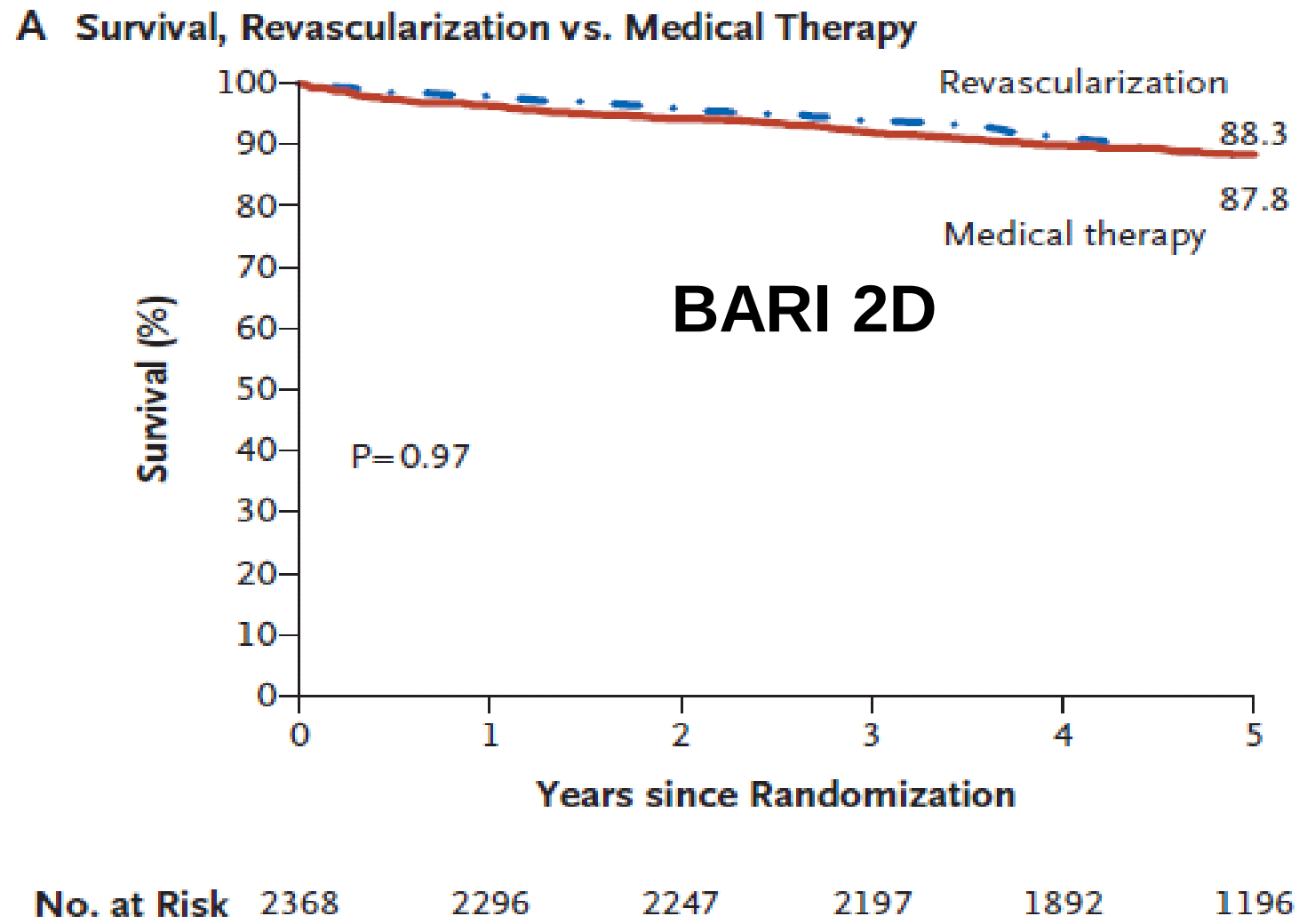
A Randomized Trial of Therapies for Type 2 Diabetes and Coronary Artery Disease

The BARI 2D Study Group*

- 2368 patients with type 2 diabetes and SIHD randomized to prompt revascularization + OMT or OMT alone
- Primary endpoint: all-cause death

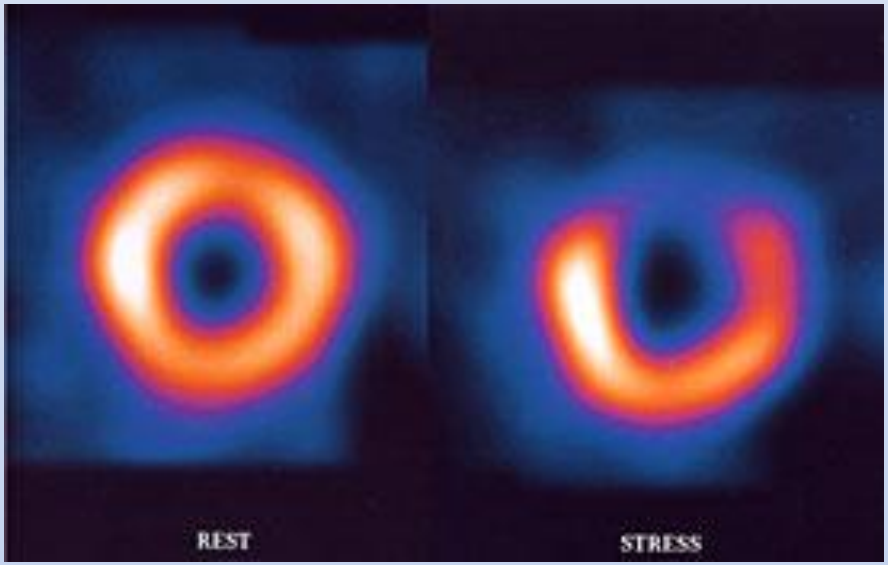
BARI 2D Study Group. *N Engl J Med* 2009;360:2503-2515.

Revascularization Did Not Improve Survival in SIHD Patients with Diabetes



BARI 2D Study Group. *N Engl J Med* 2009;360:2503-2512.

Perhaps the presence of ischemia is the key to deriving benefit from revascularization….



How Does Ischemia Confer Risk?

- Moderate-to-severe ischemia is a marker for high risk of death
- Unclear whether increased risk of death related to. . .
    - Adverse effects of ischemia
    - Subsequent complete occlusion of a severe stenosis
    - Arrhythmias
    - More severe ischemia as a marker of atherosclerotic burden with more vulnerable plaques

ACIP trial (n=558)

- **The target population was clinically stable patients with angiographically documented coronary disease (≥50% stenosis in ≥1 major vessel or branch) suitable for revascularization.**

- **To be eligible, patients also had to have ischemia during exercise or pharmacological stress testing and at least one episode of asymptomatic ischemia during 48-hour AECG monitoring. Patients either were free of angina or had symptoms that could be well controlled by medical therapy.**

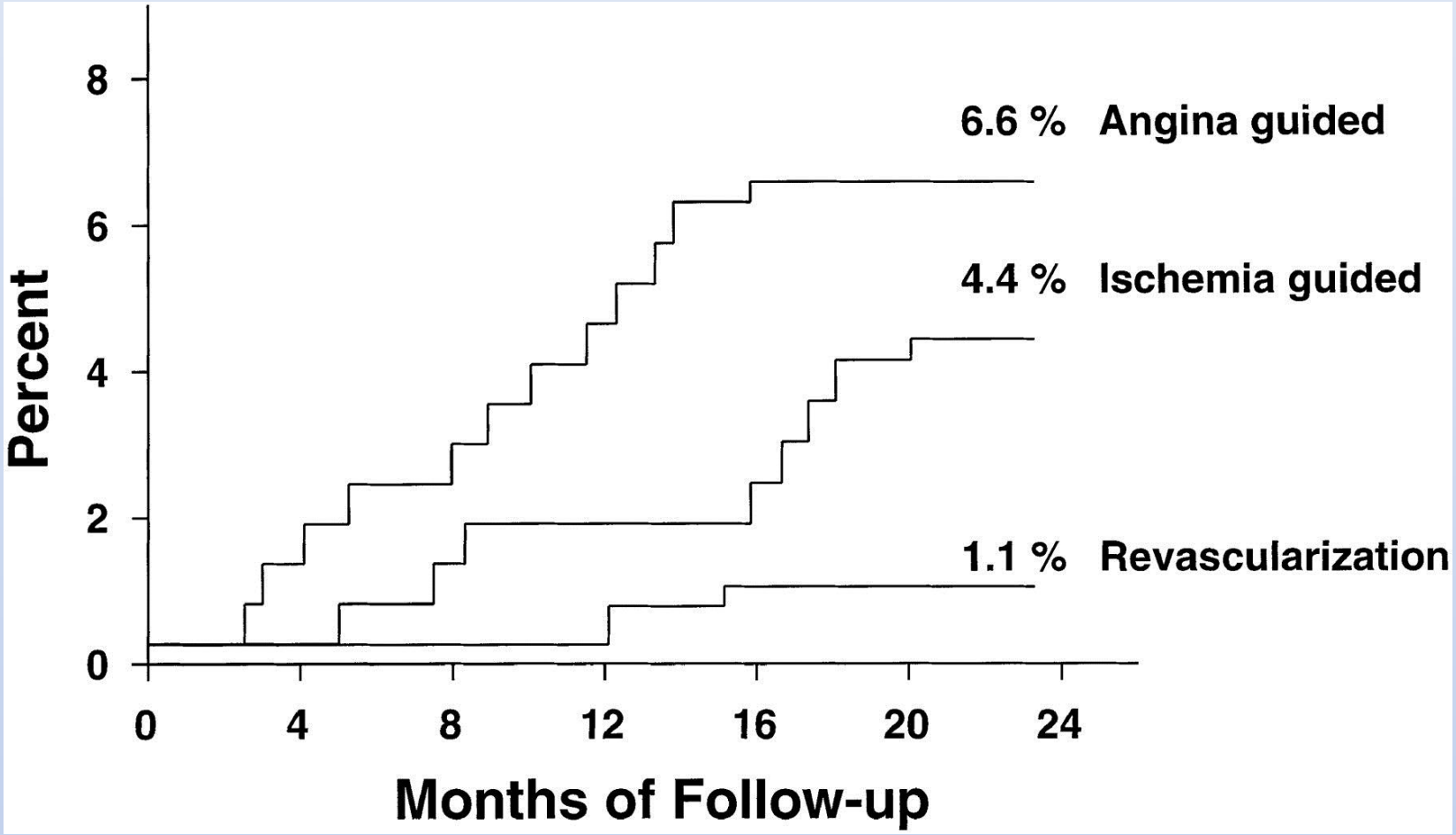
Patients were randomized to one of three initial treatment strategies:

- **angina-guided medical treatment**
- **ischemia-guided medical treatment**
- **or revascularization**

Circulation 1997; 95: 2037-2043

ACIP trial

Two-year cumulative mortality rates for three treatment strategies.



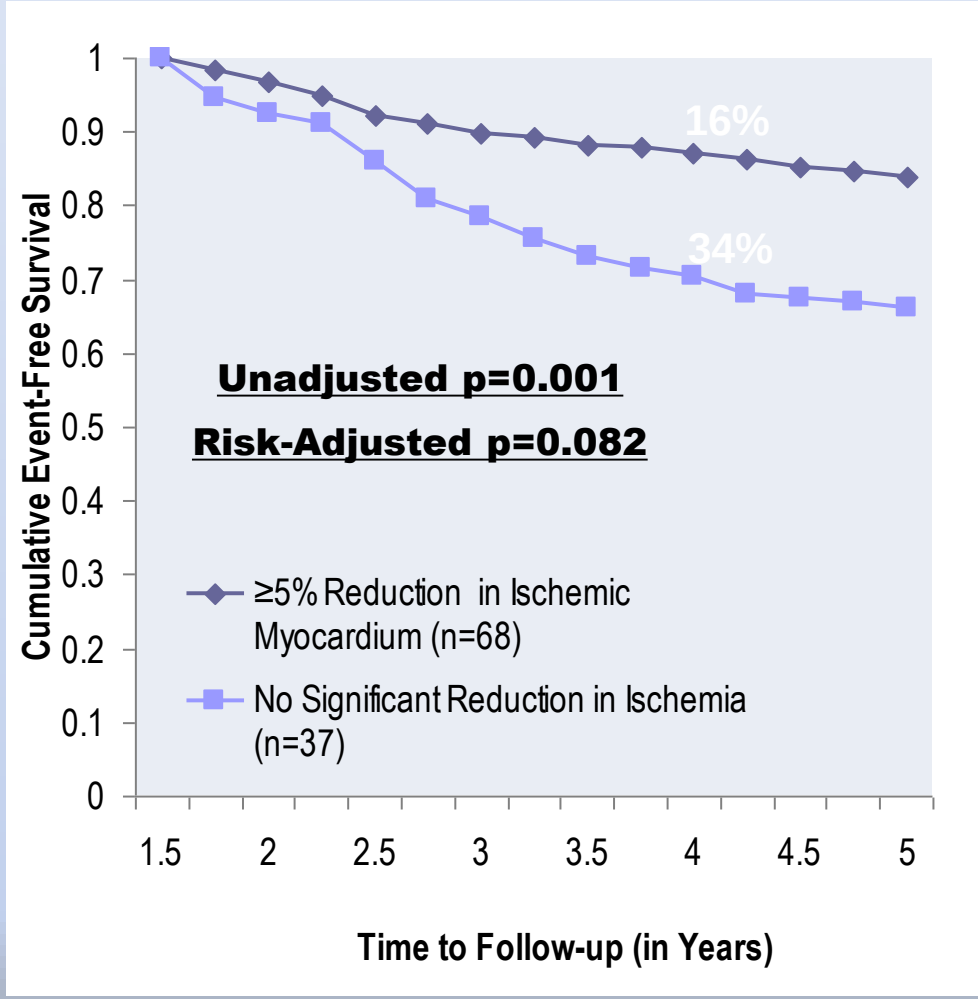
Davies R et al. Circulation 1997;95:2037-2043

COURAGE Serial Nuclear Substudy: Outcomes in 105 Patients with Moderate-to-Severe Baseline Ischemia Who Returned for 2nd Study @ 6-18 months

A: PCI reduces ischemia better than OMT alone

B: For both groups combined, ischemia reduction is associated with fewer events

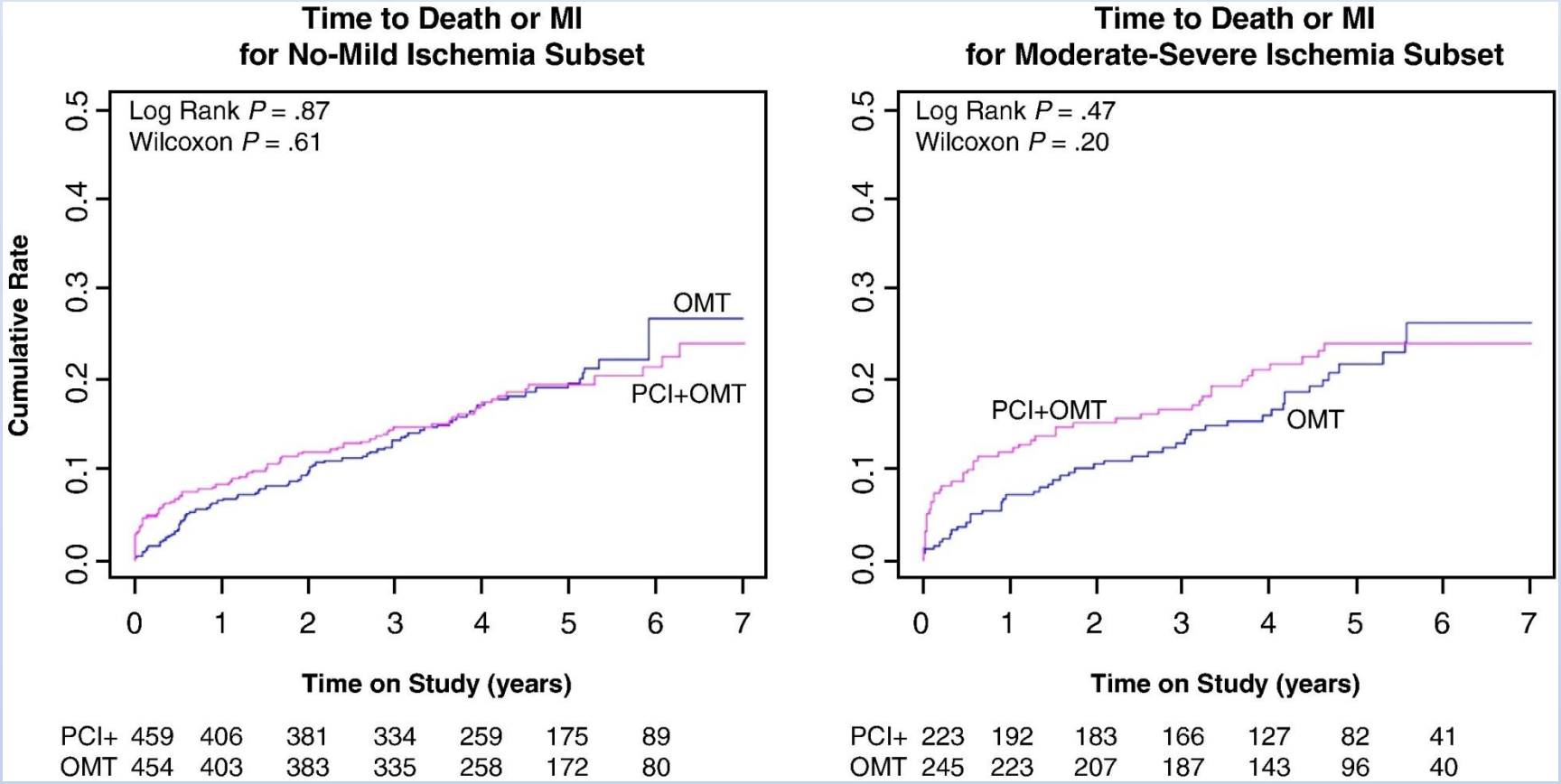
C: Does PCI Reduce Events?



Shaw et al. *Circulation*. 2008;117:1283-1291.

PCI did not Reduce Events

Subset with Moderate-to-Severe Ischemia at Baseline, with or without a 2nd scan during follow up



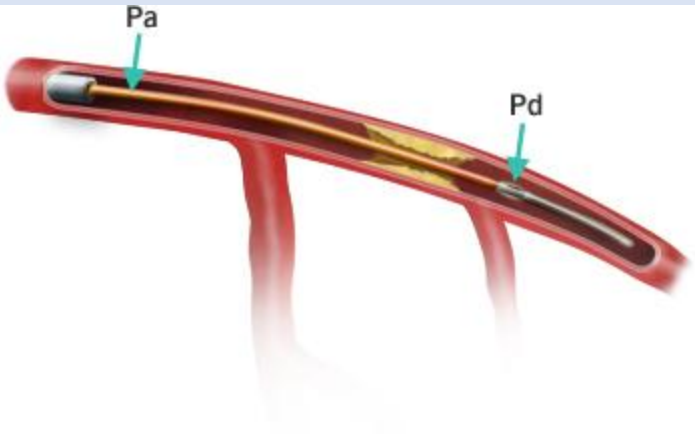
For 189 pts with core lab-interpreted moderate-severe ischemia, PCI vs. OMT 24% vs. 21%, HR 1.19 (95% CI 0.65-2.18)

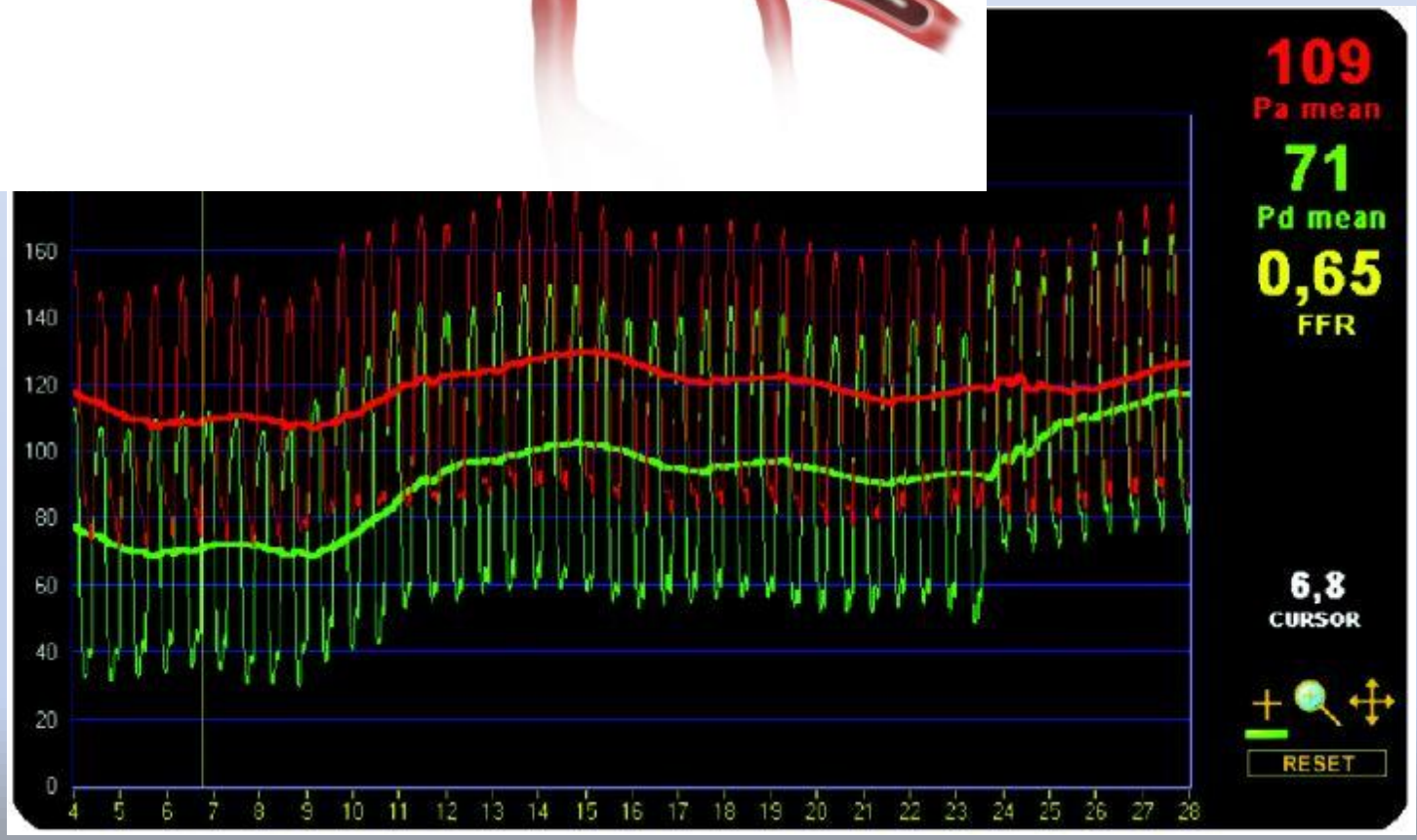
Shaw et al. AHJ 2012

Fractional Flow Reserve: Emerging gold standard for ischemia assessment…

$$FFR = \frac{\text{Distal Coronary Pressure (Pd)}}{\text{Proximal Coronary Pressure (Pa)}}$$

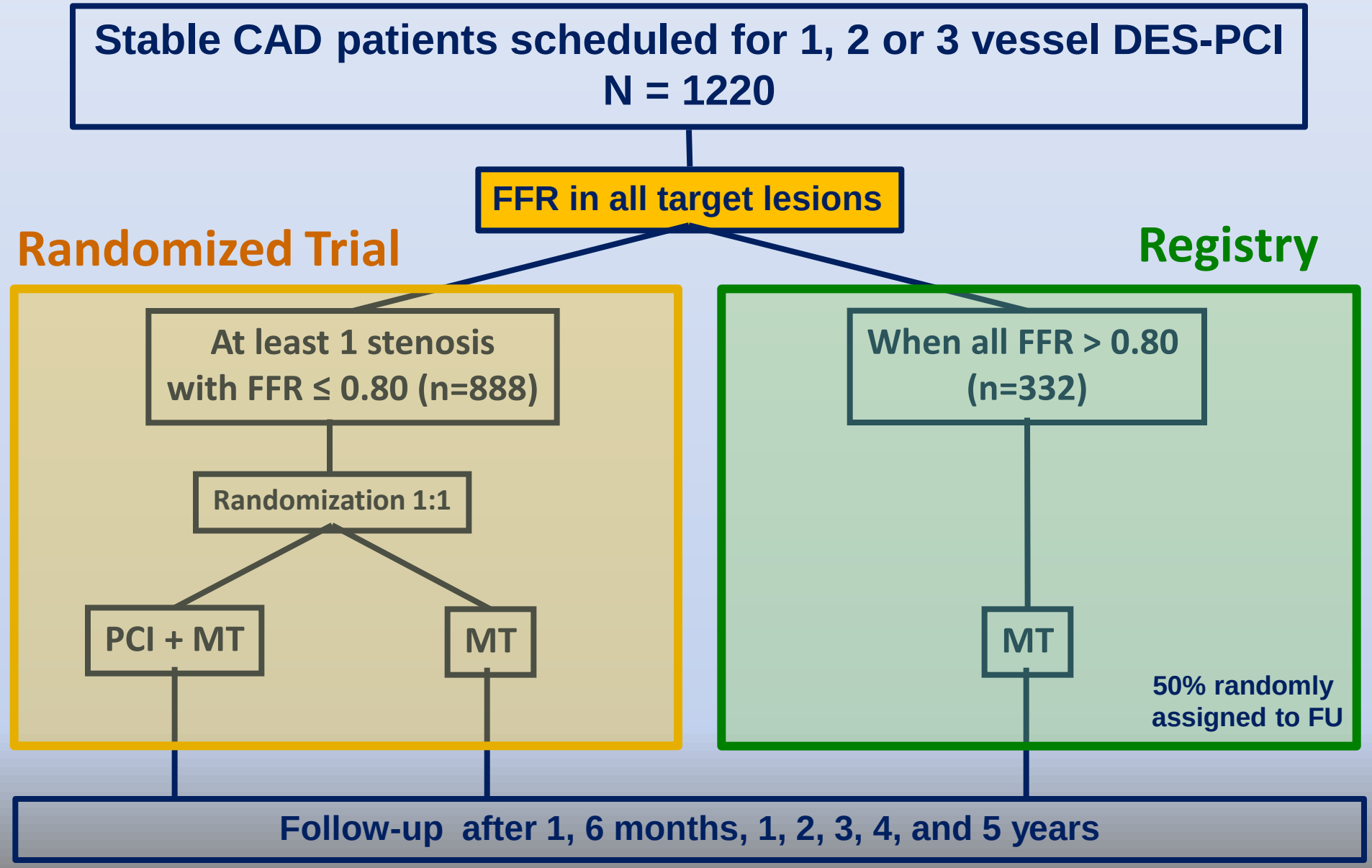
(During Maximum Hyperemia)





FAME 2

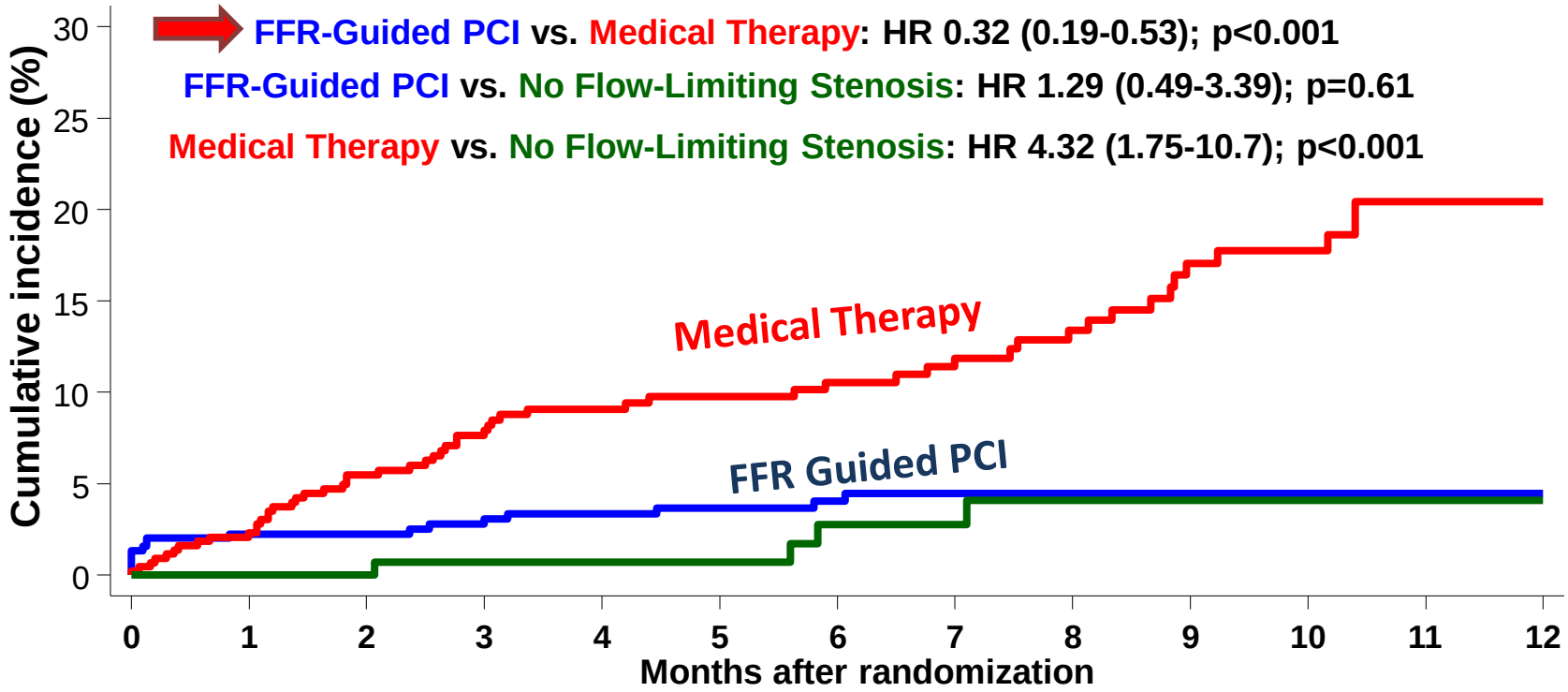
NEJM 2012;367:991-1001.



FAME 2: FFR-Guided PCI vs. Medical Therapy in Stable CAD

Primary Outcome

All-cause death, MI, or urgent revascularization



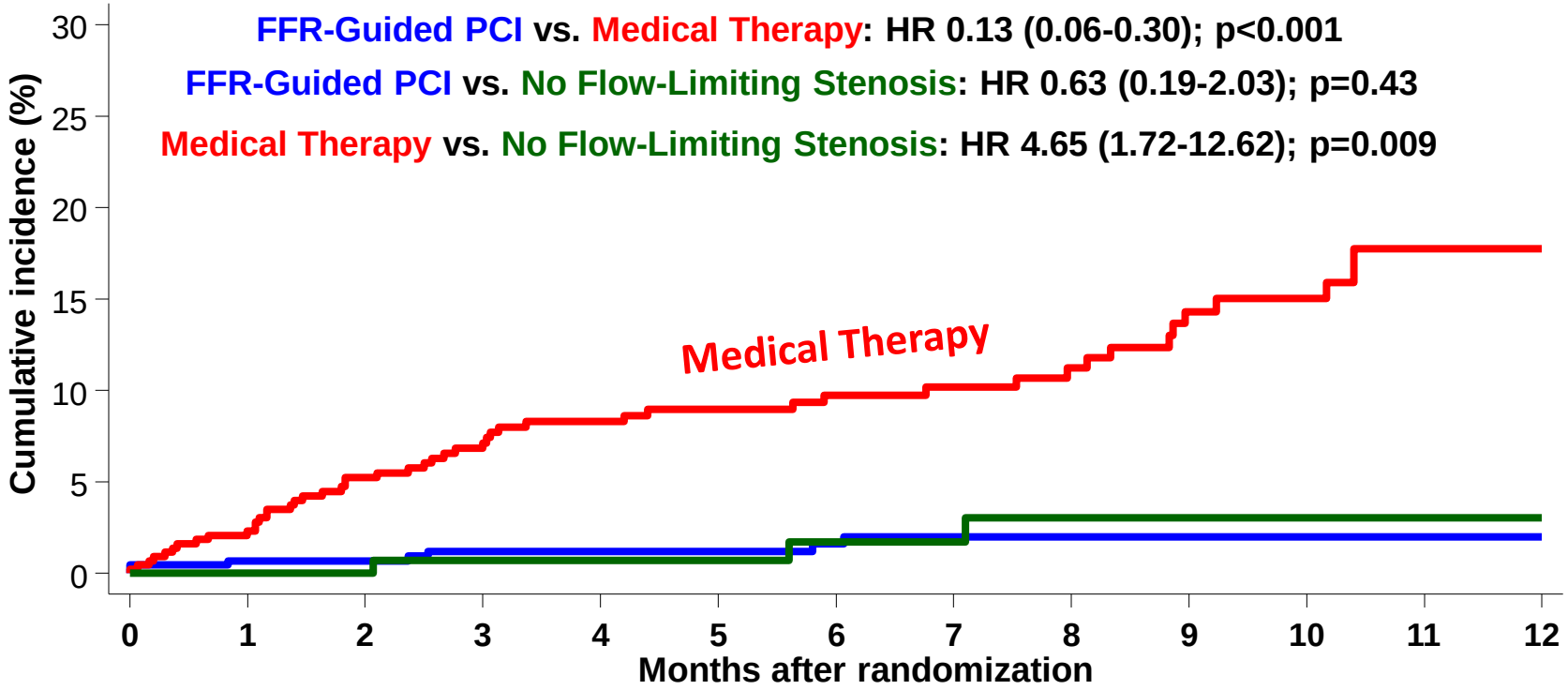
No. at risk

MED	441	414	370	322	283	253	220	192	162	127	100	70	37
FFR-PCI	447	414	388	351	308	277	243	212	175	155	117	92	53
Registry	166	156	145	133	117	106	93	74	64	52	41	25	13

De Bruyne et al. NEJM 2012;367:991-1001.

FAME 2: FFR-Guided PCI vs. Medical Therapy in Stable CAD

Primary Endpoint Driven by Urgent Revascularization



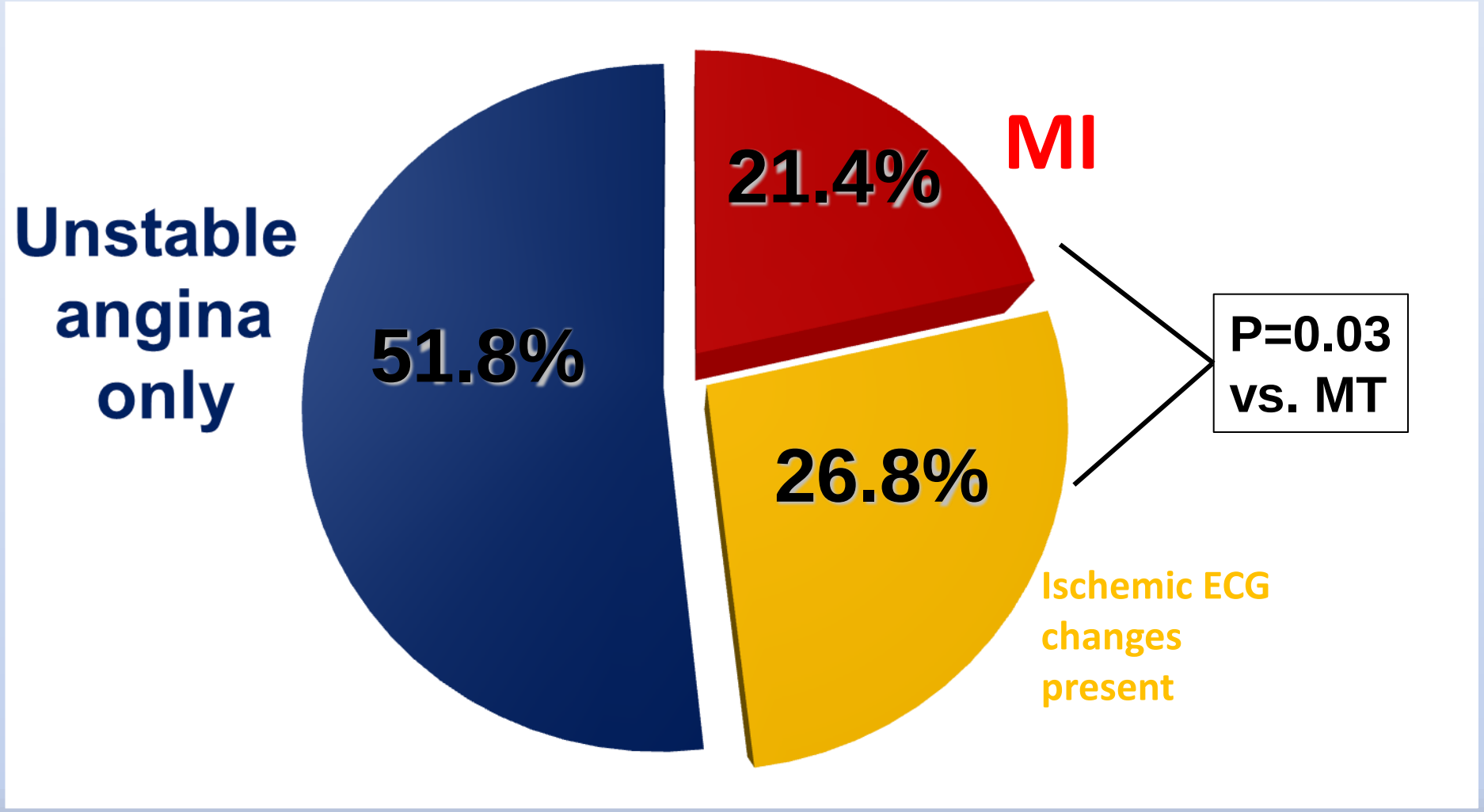
No. at risk

MED	441	414	371	325	286	256	223	195	164	129	101	71	38
FFR-PCI	447	421	395	356	315	285	248	217	180	160	119	93	53
Registry	166	156	145	133	117	106	94	75	65	53	42	26	13

De Bruyne et al. NEJM 2012;367:991-1001.

FAME 2: FFR-Guided PCI vs. Medical Therapy in Stable CAD

Reasons for Urgent Revascularization



De Bruyne et al. NEJM 2012;367:991-1001.

FAME 2 Perspective

- FAME 2 randomized patients *after* cath; physicians treating OMT-assigned patients knew the anatomy and FFR results
- If primary endpoint of COURAGE and BARI 2D included revascularization procedures, there would have been significant Δ between arms
- No difference in death or MI
- Success of medical therapy/risk factor control not reported

A Fundamental Question

- If clinical trials in the OMT era show no clear death or MI benefit from an initial strategy of revascularization, do we need to cath and revascularize patients prior to a trial of OMT?

ISCHEMIA Overview

International Study of Comparative Health Effectiveness with Medical and Invasive Approaches

Chair - Judith Hochman, Co-Chair/PI - David Maron
Co-PIs William Boden, Bruce Ferguson, Robert Harrington, Gregg Stone, David Williams

- Patients: stable, at least moderate ischemia (core lab)
- Hypothesis: an initial invasive strategy of cath and revascularization (PCI or CABG) + OMT is superior to a conservative strategy of OMT alone, with cath reserved for OMT failure
- Composite Primary Endpoint: CV death or MI
- Major Secondary Endpoint: angina-related QOL
- Sample Size: 8,000
- Follow-up: average~ 4 years

National Heart Lung and Blood Institute

Attempt to Avoid Prior Design Limitations

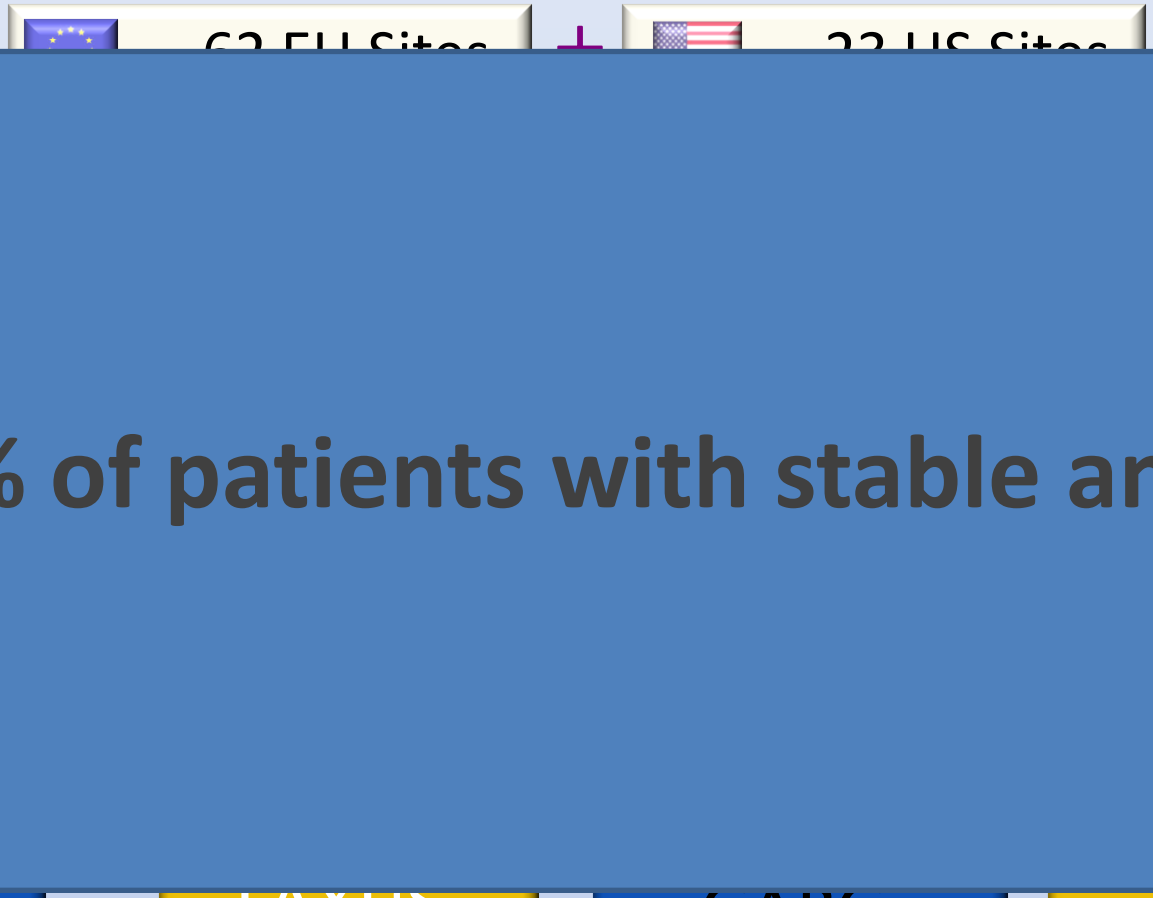
- Exclude low risk patients
- Reduce referral bias by randomizing prior to cath
- Optimize revascularization procedures (DES, FFR, Heart Team)
- Have sufficient power to detect a difference between treatment strategies

Invasive Strategy

- Cath and revascularize all INV patients
- Revascularization method based on highest likelihood to safely and effectively relieve significant ischemia in viable myocardial territories
- FFR required per algorithm

CABG versus PCI for stable CAD

SYNTAX Trial Design



CABG N=897 vs TAXUS N=903

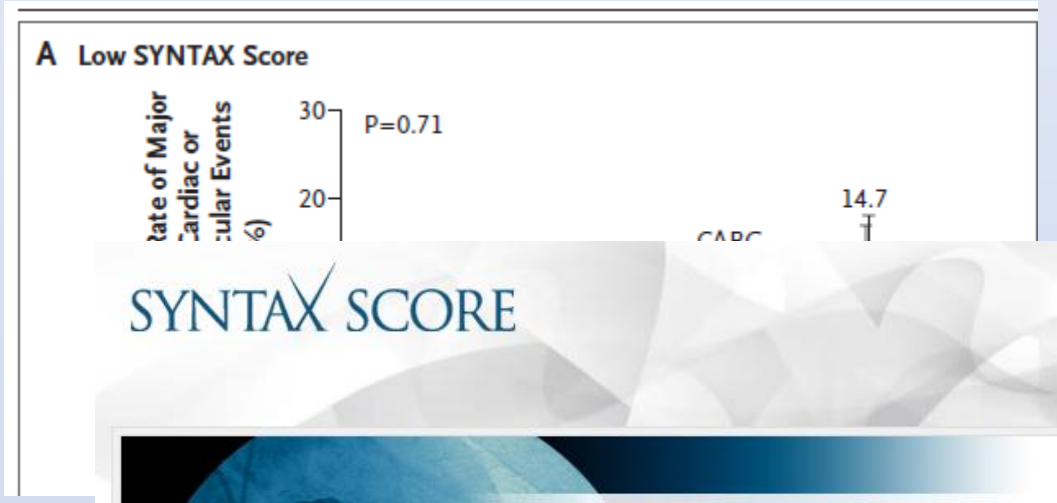
DM 28.5% | Non DM 71.5% | DM 28.2% | NonDM 71.8%

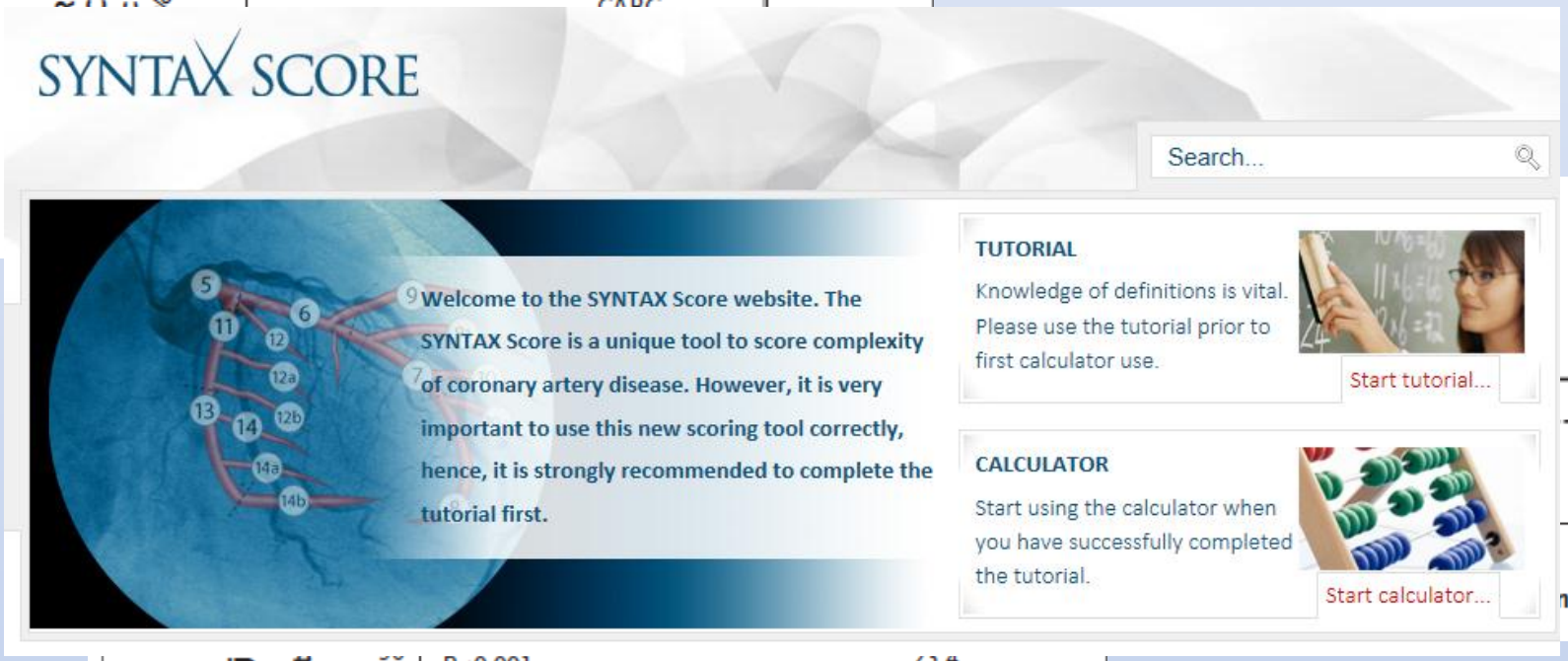
CABG N=1077 | PCI N=198

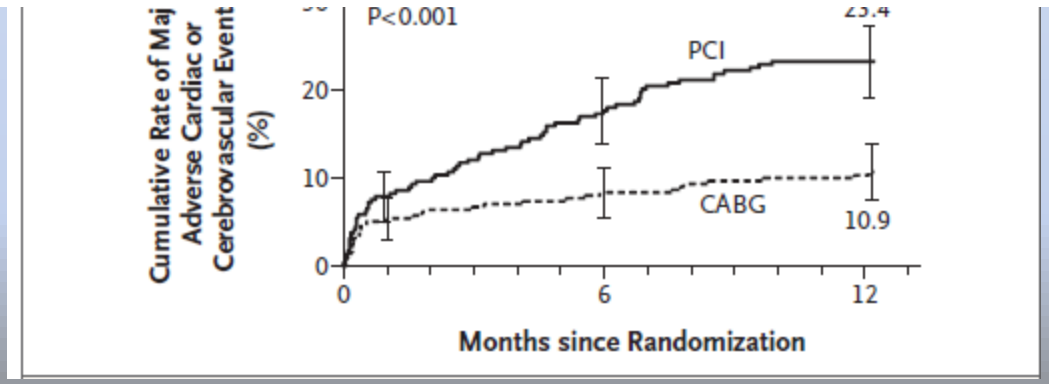
*TAXUS Express

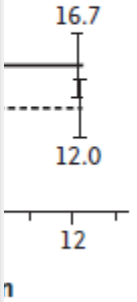
Serruys et al. N Engl J Med 2009;360:961-72

SYNTAX Key findings



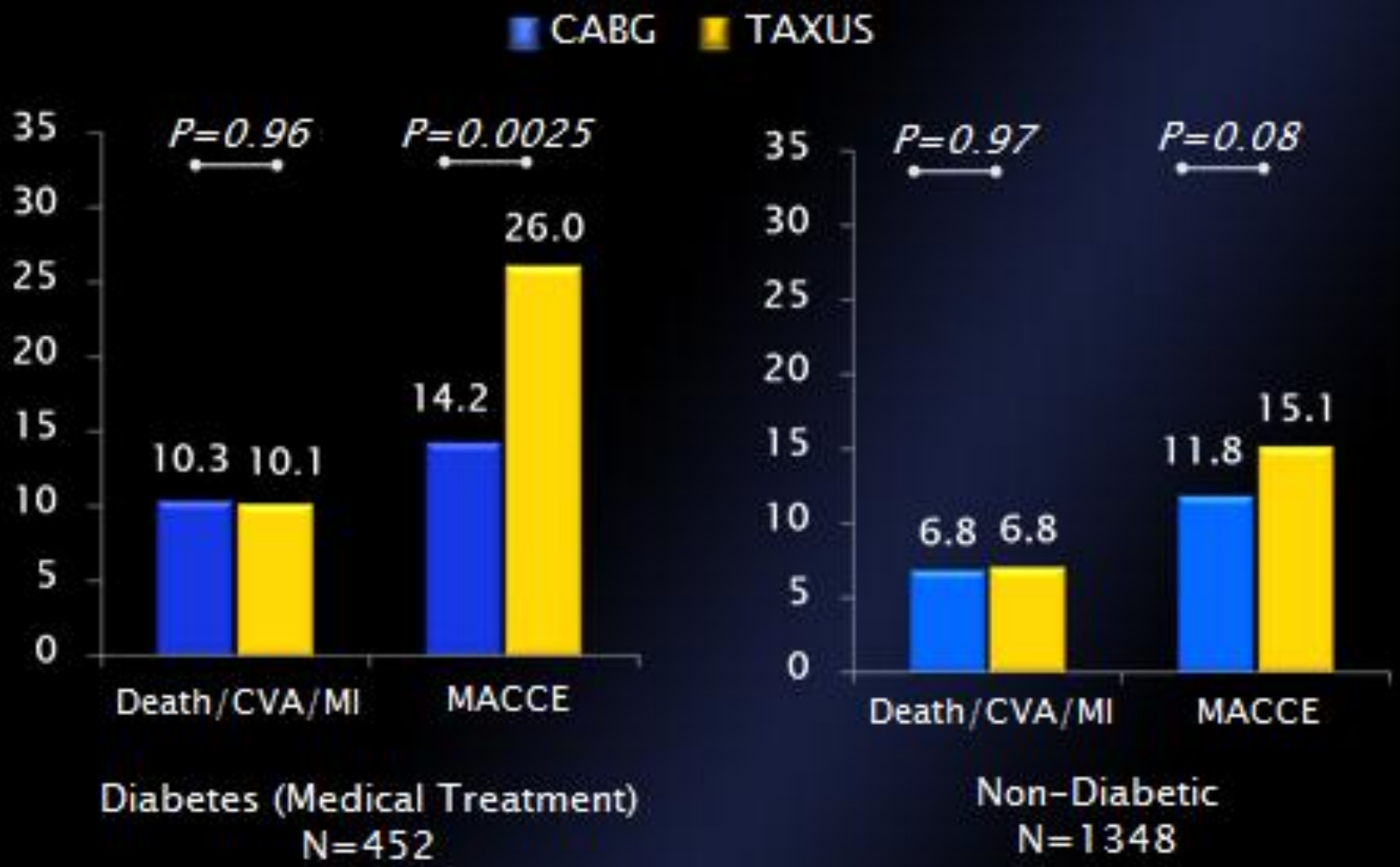






Outcome according to Diabetic Status

SYNTAX



Serruys et al. N Engl J Med 2009;360:961-72

FREEDOM TRIAL

Eligibility: DM patients with MV-CAD eligible for stent or surgery
Exclude: Patients with acute STEMI

Randomized 1:1

- **MV-Stenting** With Drug-eluting
- **CABG** With or Without CPB

All concomitant Meds shown to be beneficial were encouraged, including: clopidogrel, ACE inhib., ARBs, b-blockers, statins

Farkouh et al. N Engl J Med 2012;367:2375-84

Conclusion

- In patients with diabetes and advanced coronary disease, **CABG was of significant benefit as compared to PCI.** MI & all cause mortality were independently decreased, while stroke was slightly increased

- There was **no significant interaction** between the treatment effect of CABG on the primary endpoint according to **SYNTAX score or any other prespecified subgroup.**

- **CABG surgery is the preferred method** of revascularization for patients with diabetes & multi-vessel CAD.

Farkouh et al. N Engl J Med 2012;367:2375-84

Take home messages for revascularization for stable CAD…

- ✓ Optimal medical therapy remains the cornerstone for management.
- ✓ Reasonable to refer to coronary angiography for intermediate and high risk patients
- ✓ PCI for stable angina primarily driven by symptoms despite OMT
- ✓ Role of ischemia in guiding PCI unclear but FFR may be helpful
- ✓ For complex disease (SYNTAX score >32) CABG is preferable to PCI
- ✓ In diabetics with complex multivessel disease CABG is preferable to PCI

Thank you……

CME Questions

57 year old male, mild HTN, former smoker presents with chest discomfort when walking up 3 flights of stairs – relieved with rest. The symptoms have been present for the past 4 months.

An exercise stress test (mod BRUCE) demonstrates 1 mm inferior lateral ST segment depression at a work load of 9.5 METs associated with dyspnea and typical chest pain. Symptoms and ECG changes resolve <1.5 minutes into recovery.

Which is the next best step:

A.

A. Begin aspirin, beta blocker, SLNTG, statin and observe patient in clinic
B. Begin above medical therapy and refer for coronary angiography
C. Proceed with coronary angiography and PCI if lesion amenable
D. Reassurance and observation

Revascularization in stable CAD….PCI versus CABG

64 y/o with HTN, HLD, DM, presents with CCS 3 angina on medical therapy.

Coronary angiography reveals a chronic total occlusion of the RCA, bifurcation disease involving the mid LAD and first diagonal (both involved) and long diffuse calcified disease of OM1.

Which is the best revascularization strategy in this patient?

A. PCI
B. Attempt PCI of RCA first then consider CABG if PCI fails
C. CABG

C.

In comparison to OMT alone, PCI + OMT for stable CAD has been shown in clinical trials to be superior in all of the following outcomes EXCEPT…..

A. Reduction of anginal symptoms to a greater degree in the first year after therapy.
B. Greater reduction in the presence of ischemia by non-invasive testing
C. Greater reduction in the occurrence of future myocardial infarction
D. Reduction in future need for urgent revascularization

C.

EXTRA SLIDES

Stable plaque or stable patient? or Both?

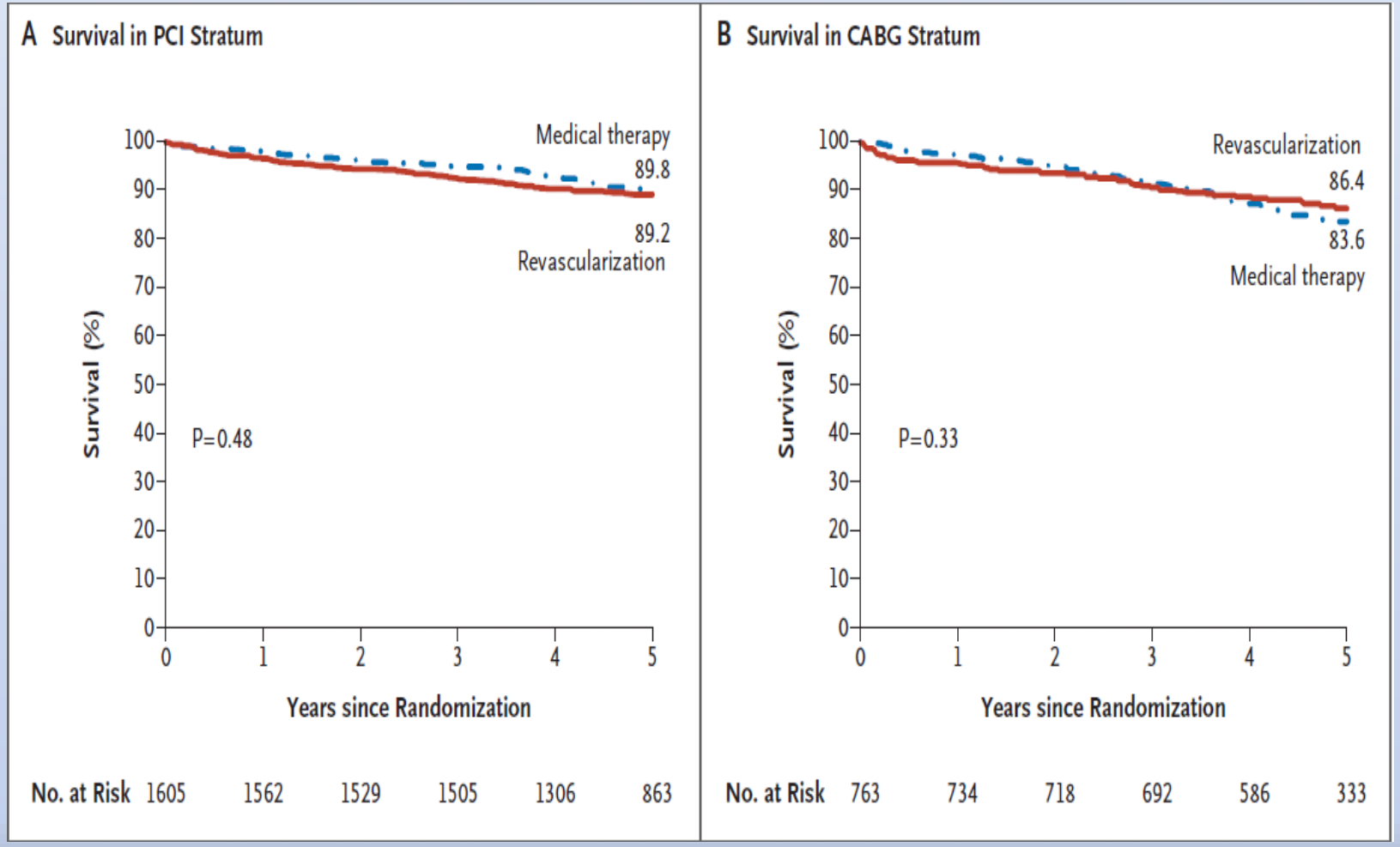
Table 3 Main features of stable coronary artery disease

Pathogenesis
Stable anatomical atherosclerotic and/or functional alterations of epicardial vessels and/or microcirculation
Natural history
Stable symptomatic or asymptomatic phases which may be interrupted by ACS
Mechanisms of myocardial ischaemia
Fixed or dynamic stenoses of epicardial coronary arteries;
Microvascular dysfunction;
Focal or diffuse epicardial coronary spasm;
The above mechanisms may overlap in the same patient and change over time.

ESC 2013 Guidelines European Heart Journal (2013) 34, 2949–3003

BARI 2D Survival by Revascularization Mode

PCI vs. CABG Selected by Treating Physicians

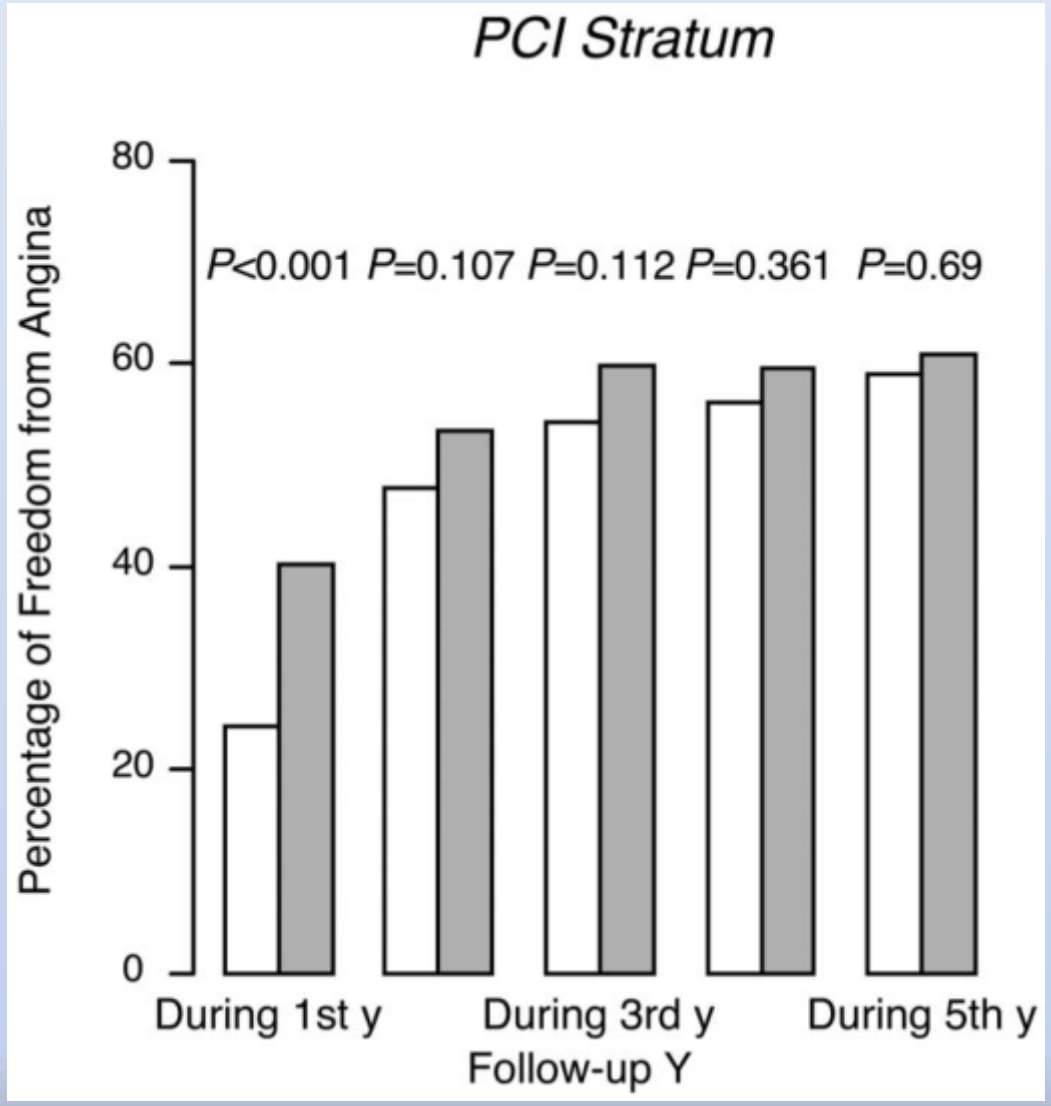


35% DES (after April 2003, 61% DES)

84% IMA grafts

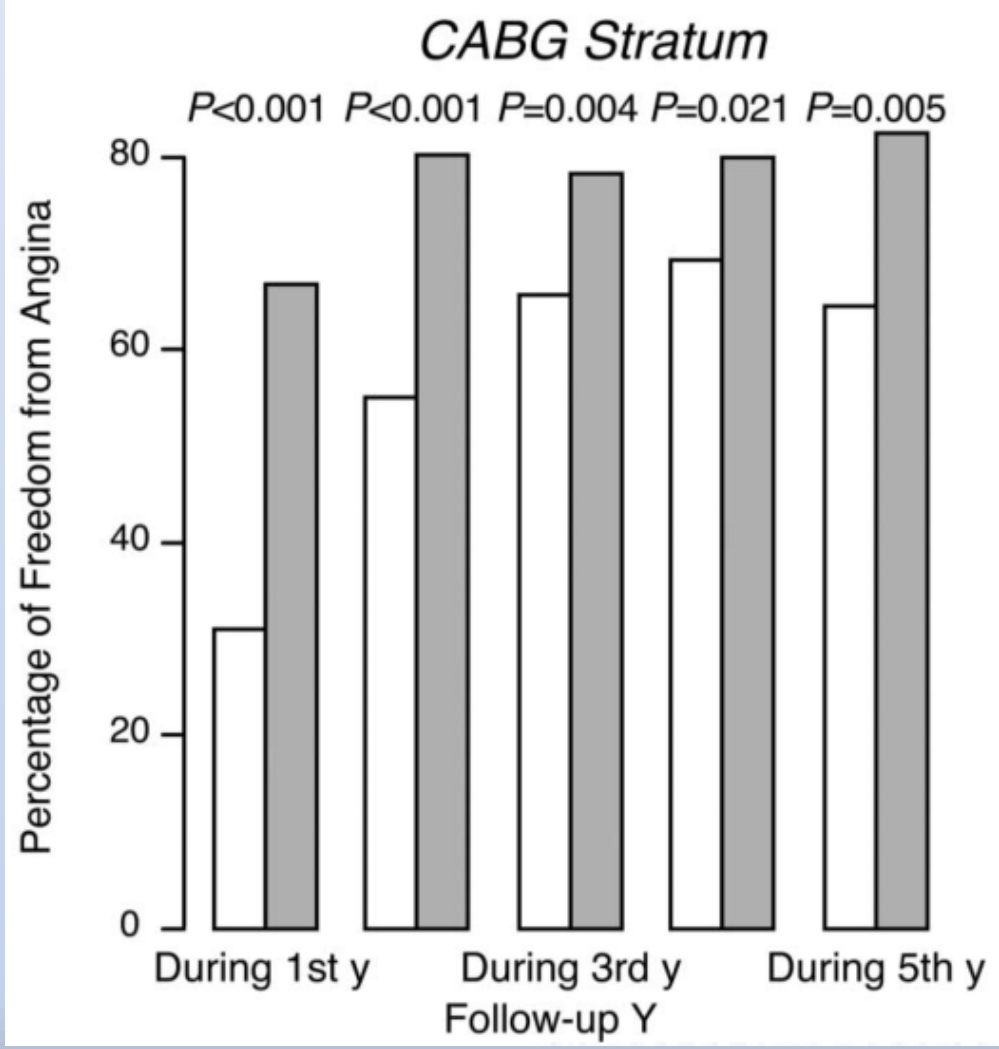
BARI 2D Study Group. *N Engl J Med* 2009;360:2503-2512.

Freedom from Angina in BARI 2D: PCI



Dagenais et al. Circulation 2011;123:1492-1500

Freedom from Angina in BARI 2D: CABG



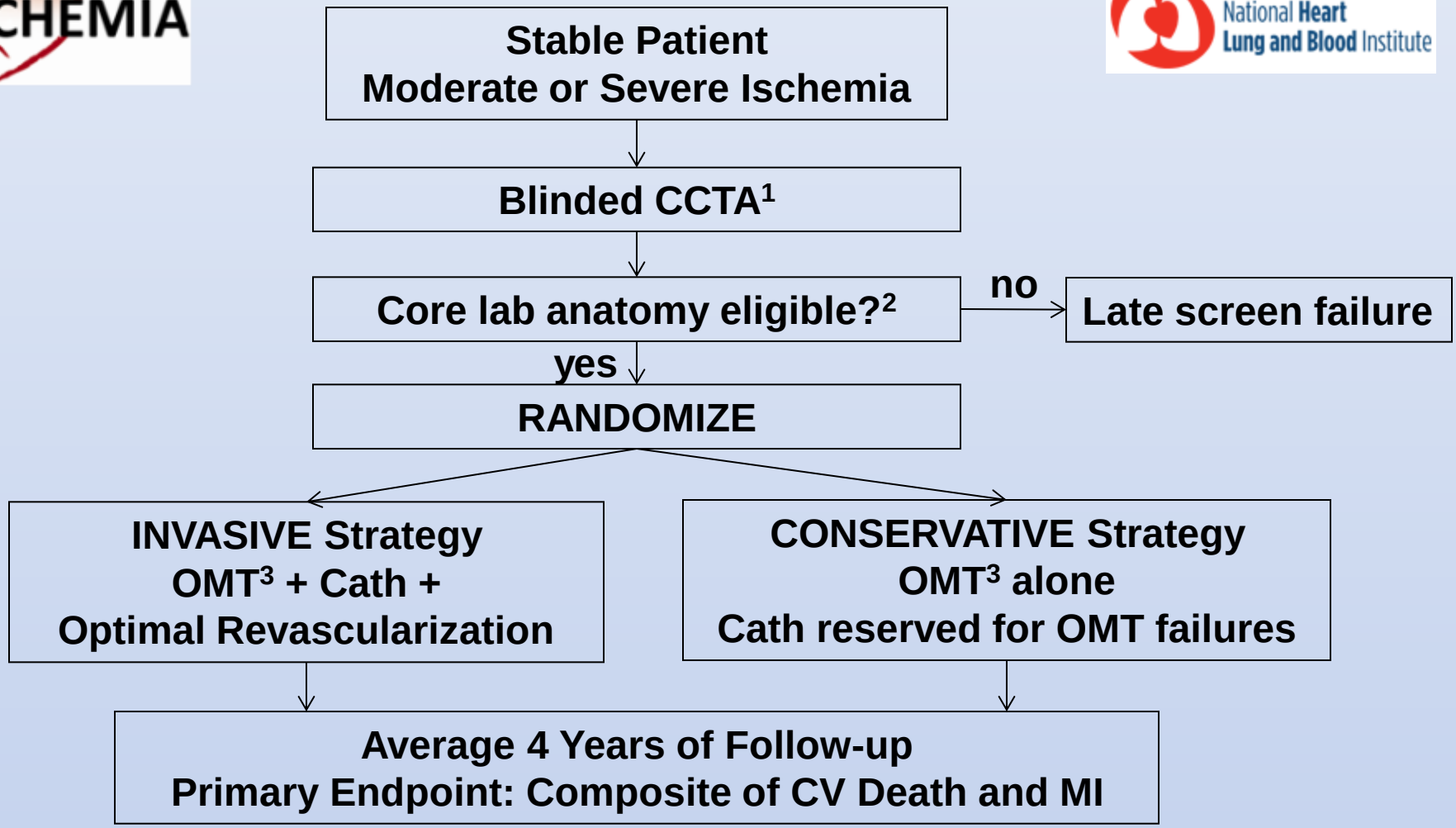
Dagenais et al. Circulation 2011;123:1492-1500

Ischemia Eligibility Criteria

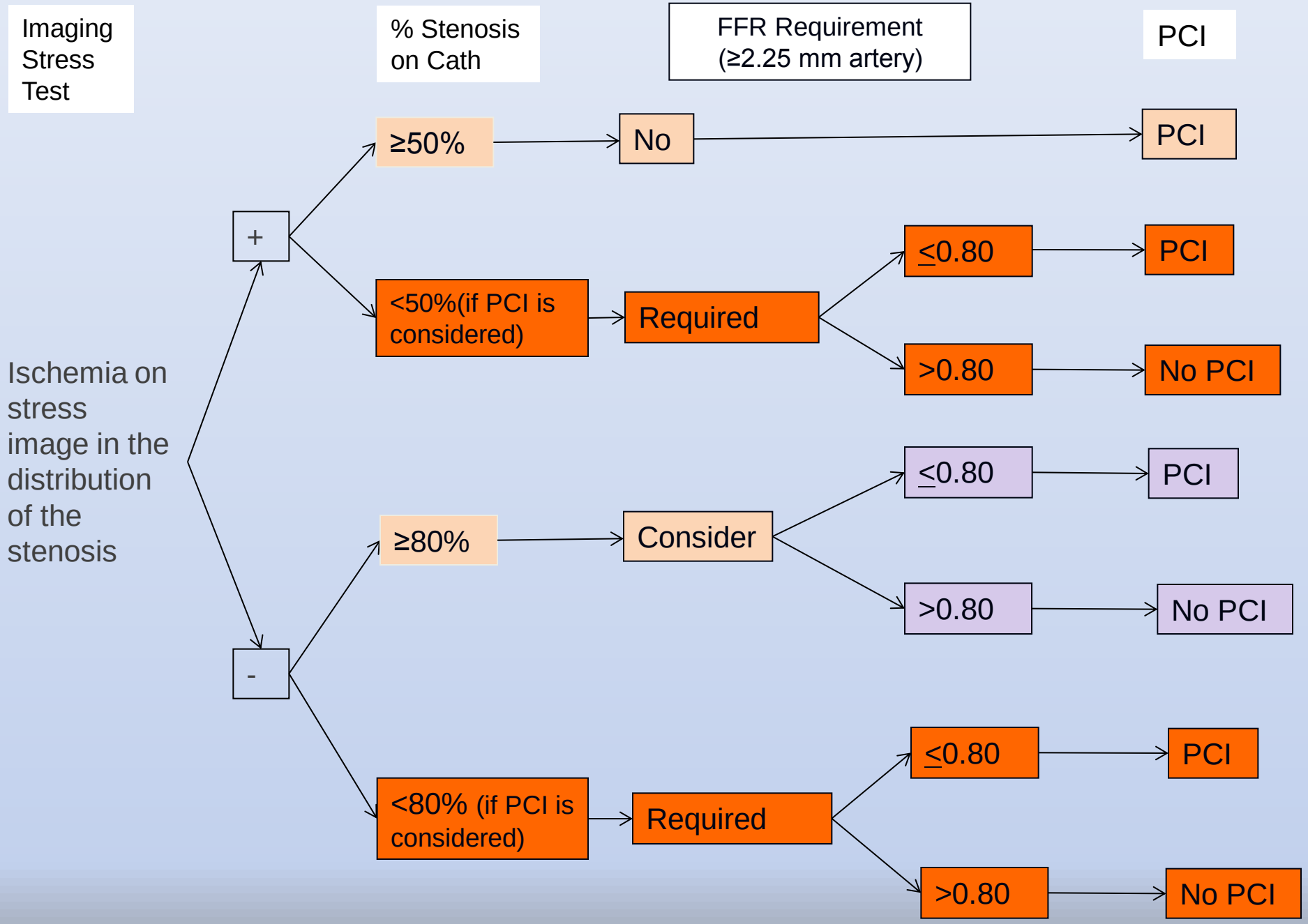
Fulfillment of one of the following ischemia eligibility criteria, reviewed by core lab:

Nuclear Perfusion	**Echo/CMR Wall Motion**	**CMR Perfusion**
≥10% myocardium	≥3/16 segments with stress-induced severe hypokinesis or akinesis	≥12.5% myocardium

Projected annual CV death/MI rate across modalities = 5%



[1]CCTA will be performed in all patients with eGFR ≥60 mL/min
[2]Exclude patients with LM disease or no obstructive disease
[3]OMT=Optimal medical therapy



PCI based on anatomic feasibility and clinical considerations