When to proceed with multivessel PCI

Ciudad de México, SOLACI Fellows Course 2012

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- History
- Guidelines
- Newer trials
- Newest retrospective study
- Conclusion

Over past 20 years
12 trials compared PCI to CABG

- BARI
- ERACI II
- RITA
- GABI
- MASS 2
- SoS
- EAST
- CABRI
- AWESOME
- ARTS 1 & ARTS 2
- SYNTAX

Many historical: POBA vs CABG

Randomized Trials of PTCA vs CABG for Treatment of Multivessel Coronary Artery Disease

Study	Randomized Patients, n	Follow-up Duration, y	In-Hospital Additional Nonrandomized CABG (PTCA Group Only)	Repeat Revascularization at Follow-up		Cumulative Mortality	
				PTCA Group	CABG Group	PTCA Group	CABG Group
RITA[7]	1011	2	5.9% (emergency, 4.3%)	38% (CABG, 22.5%)	11%	3.9%	2.7%
GABI[8]	359	1	8.2% (emergency, 2.7%)	44% (CABG, 17.6%)	6%	2.2%	5.1%
EAST[9]	392	3	10.1% (emergency, 9.6%)	54% (CABG, 18.2%)	13%	3.5%	2.1%
CABRI[10]	1054	1	5% (emergency, 3.9%)	37% (CABG, 16%)	6.5%	3.9%	2.7%
BARI[11]	1792	5	6.3% (emergency, 6.3%)	54.5% (CABG, 31.3%)	8%	13.7%	10.7%

Background (II)

SYNTAX

Long-Term Safety and Efficacy of Percutaneous Coronary Intervention With Stenting and Coronary Artery Bypass Surgery for Multivessel Coronary Artery Disease

A Meta-Analysis With 5-Year Patient-Level Data From the ARTS, ERACI-II, MASS-II, and SoS Trials

Joost Daemen, MD; Eric Boersma, PhD; Marcus Flather, MBBS; Jean Booth, MSc; Rod Stables, MA, DM, FRCP; Alfredo Rodriguez, MD; Gaston Rodriguez-Granillo, MD, PhD; Whady A. Hueb, MD; Pedro A. Lemos, MD, PhD; Patrick W. Serruys, MD, PhD

- A patient level meta-analysis of CABG vs BMS trials (ARTS, SoS, ERACI-II and MASS-II) demonstrated:
  - PCI with stenting had similar rates of death and combined safety (death/stroke/MI) to that of CABG
  - Repeat revascularization rates were increased in PCI patients leading to increased overall MACCE rates at 5 years

Circulation 2008; 118: 1146-1154

ARTS II

5 year results: JACC March 2010

Outcome	Sirolimus-eluting stent in ARTS II (n=607)	CABG in ARTS I (n=602)	Bare-metal stent in ARTS I (n=600)	p
Death	5.4	7.1	7.8	NA
Cerebrovascular accident	2.8	2.7	3.2	NA
MI	4.4	4.0	6.8	NA
Death/CVA/MI	12.7	13.8	17.8	0.1[a], 0.007[b]
Revascularization	14.5	7.0	23.3	NA
Any MACCE	27.2	20.8	41.2	0.02[a], 0.001[b]

Indications for CABG in Asymptomatic or Mild Angina

- Class I evidence
- 1. Significant left main coronary artery stenosis.
- 2. Left main equivalent: significant (>=70%) stenosis of proximal LAD and proximal left circumflex artery.
- 3. Three-vessel disease. (Survival benefit is greater in patients with abnormal LV function; eg, with an EF <0.50.)

Indications for CABG in Stable Angina

- Class I evidence
- 1. Significant left main coronary artery stenosis.
- 2. Left main equivalent: significant (>=70%) stenosis of proximal LAD and proximal left circumflex artery.
- 3. Three-vessel disease. (Survival benefit is greater when LVEF is <0.50.)
- 4. Two-vessel disease with significant proximal LAD stenosis and either EF <0.50 or demonstrable ischemia on noninvasive testing.
- 5. One- or 2-vessel coronary artery disease without significant proximal LAD stenosis, but with a large area of viable myocardium and high-risk criteria on noninvasive testing.
- 6. Disabling angina despite maximal medical therapy, when surgery can be performed with acceptable risk. If angina is not typical, objective evidence of ischemia should be obtained.

Indications for CABG in Unstable Angina

- Class I evidence
- 1. Significant left main coronary artery stenosis.
- 2. Left main equivalent: significant (>=70%) stenosis of proximal LAD and proximal left circumflex artery.
- 3. Ongoing ischemia not responsive to maximal non surgical therapy.
- Class IIa evidence
- 1. Proximal LAD stenosis with 1- or 2-vessel disease.
- Class IIb evidence
- 1. One- or 2-vessel disease not involving the proximal LAD.

New guidelines: ESC

3VD simple lesions, full functional revascularisation achievable with PCI, SYNTAX SCORE ≤22	**I A**	**IIa B**
3VD complex lesions, incomplete revascularisation achievable with PCI, SYNTAX SCORE >22	**I A**	**III A**
Left Main (Isolated or 1VD, ostium/shaft)	**I A**	**IIa B**
Left Main (Isolated or 1VD, distal bifurcation)	**I A**	**IIb B**
Left Main + 2/3VD SYNTAX SCORE ≤32	**I A**	**IIb B**
Left Main + 2/3VD SYNTAX SCORE ≥33	**I A**	**III B**

SYNTAX Trial Design

SYNTAX

62 EU Sites + 23 US Sites

Heart Team (surgeon & interventionalist)

Amenable for both treatment options

Amenable for only one treatment approach

Stratification: LM and Diabetes

Randomized Arms N=1800

CABG N=897 *vs* TAXUS* N=903

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

Two Registry Arms N=1275

CABG N=1077 | PCI N=198

*TAXUS Express

Patient Characteristics (II)

Randomized Cohort

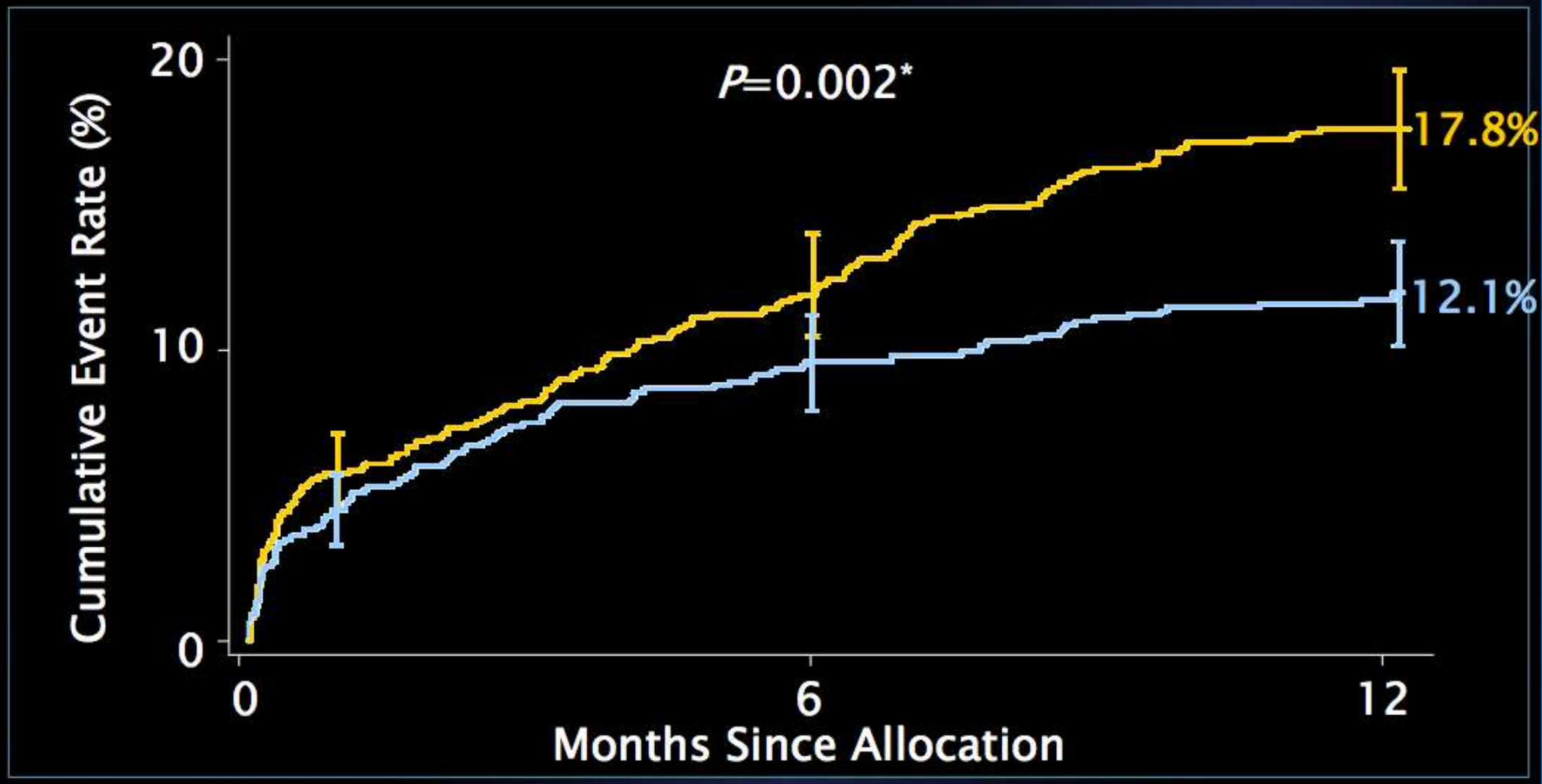
SYNTAX

Patient-based	CABG N=897	TAXUS N=903	*P* value
Total SYNTAX Score	29.1 ± 11.4	28.4 ± 11.5	0.19
Diffuse disease or small vessels, %	10.7	11.3	0.69
No. lesions, mean ± SD	4.4 ± 1.8	4.3 ± 1.8	0.44
3VD only, %	66.3	65.4	0.70
Left main, any, %	33.7	34.6	0.70
Left Main only	3.1	3.8	0.46
Left Main + 1 vessel	5.1	5.4	0.78
Left Main + 2 vessel	12.0	11.5	0.72
Left Main + 3 vessel	13.5	13.9	0.78
Total occlusion, %	22.2	24.2	0.33
Bifurcation, %	73.3	72.4	0.67
Trifurcation, %	10.6	10.7	0.92

MACCE† to 12 Months (Primary endpoint)

SYNTAX

CABG (N=897) TAXUS (N=903)



Event rate ± 1.5 SE. *Fisher exact test

†MACCE: Death, CVA, MI and Repeat Revascularization; ITT population

Combined Safety (Death/CVA/MI) to 2 Years

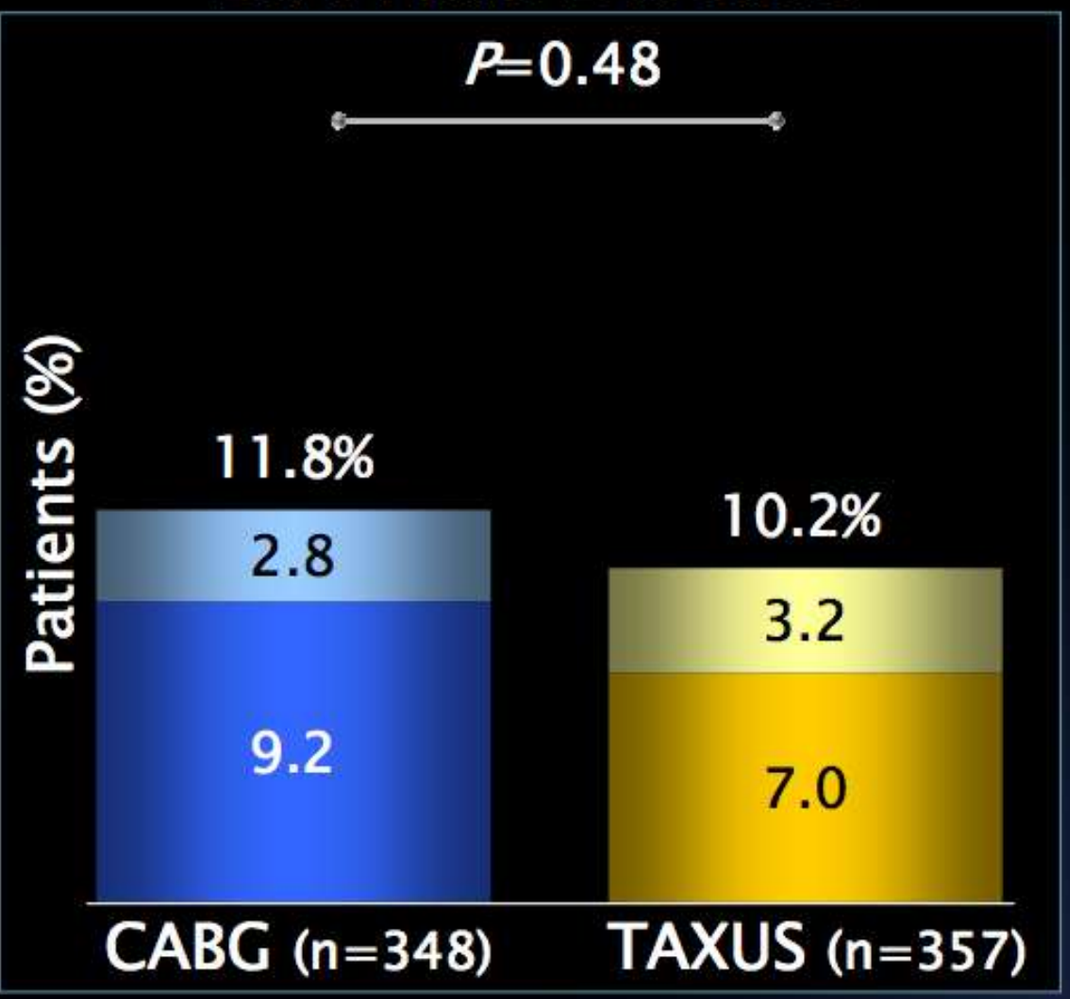
3VD & LM

SYNTAX

0–1 years 1–2 years

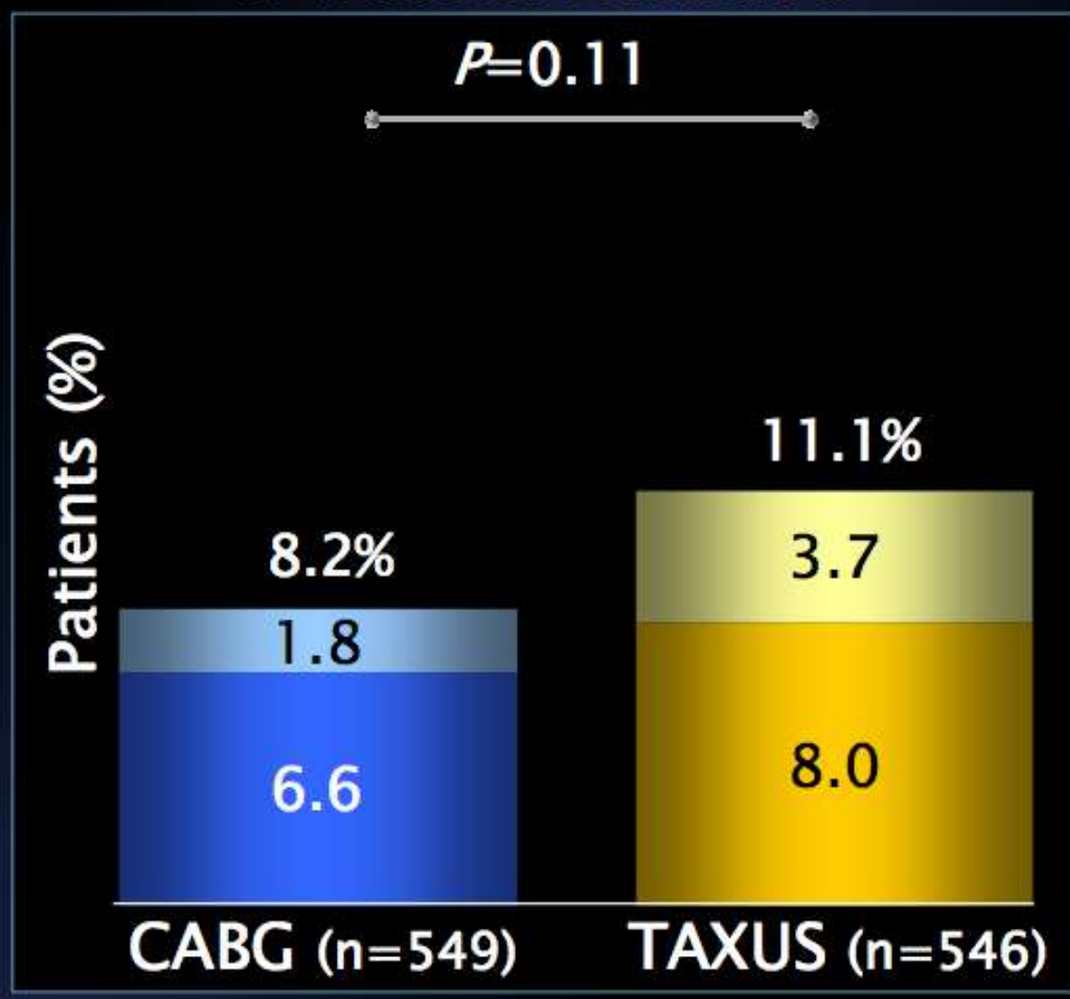
Left Main Disease

P=0.48



3 Vessel Disease

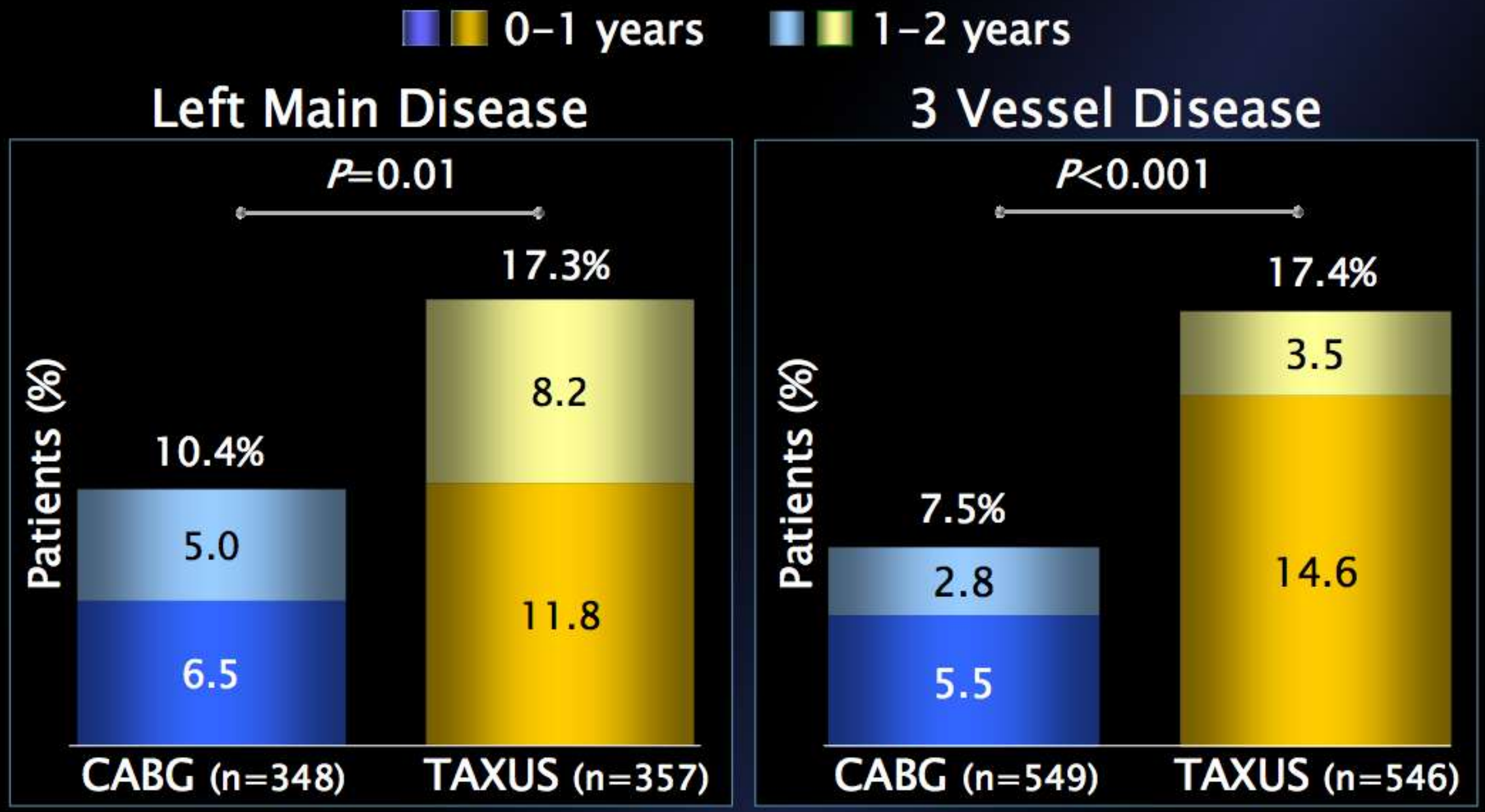
P=0.11



Total rates calculated as time-to-event; interval rates calculated as binary rates

Repeat Revascularization to 2 Years
3VD & LM

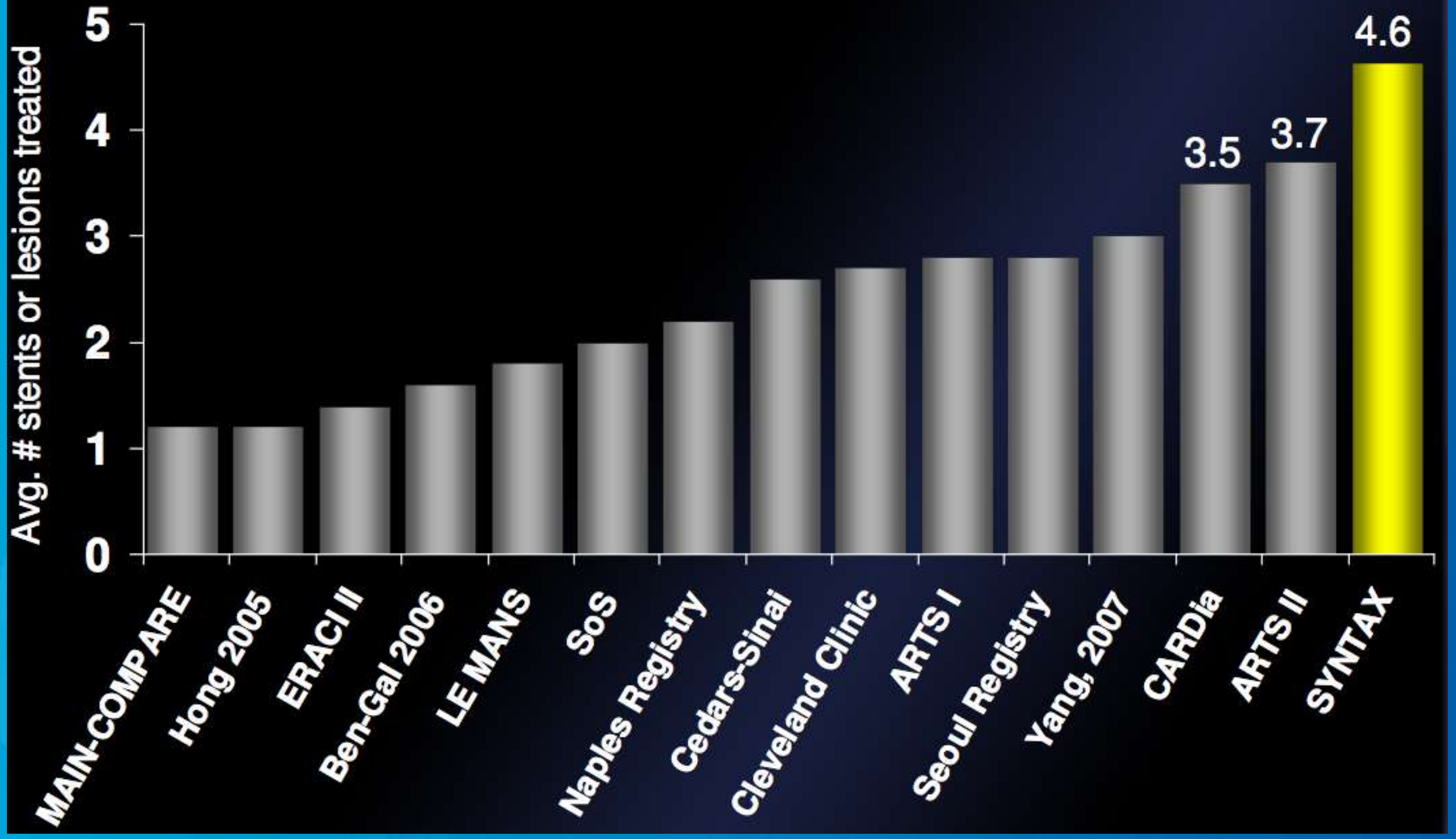
SYNTAX



Total rates calculated as time-to-event; interval rates calculated as binary rates

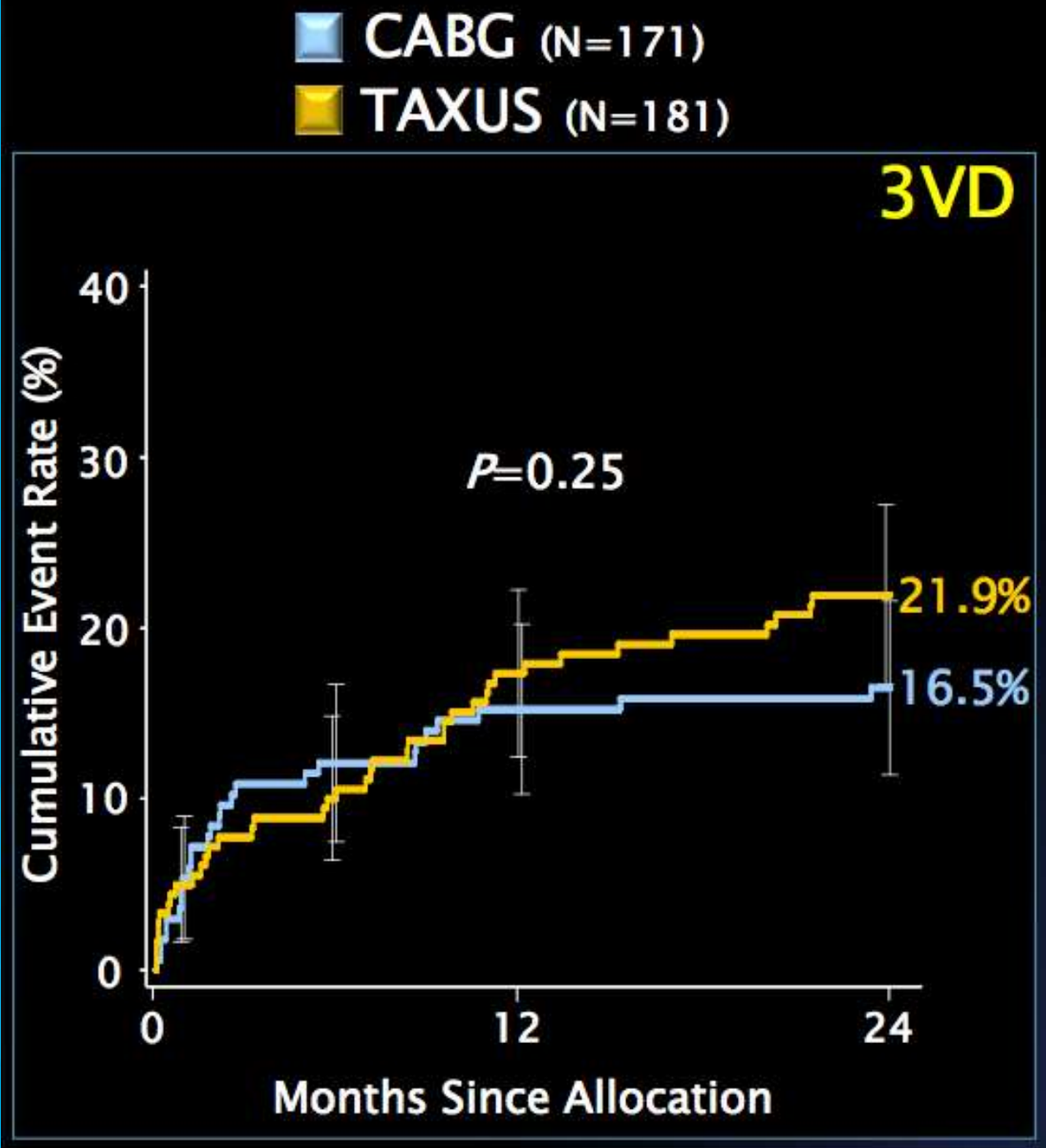
Average Number of Stents Implanted per Patient

SYNTAX



MACCE to 2 Years by SYNTAX Score Tercile 3VD *Low Scores (0–22)*

SYNTAX



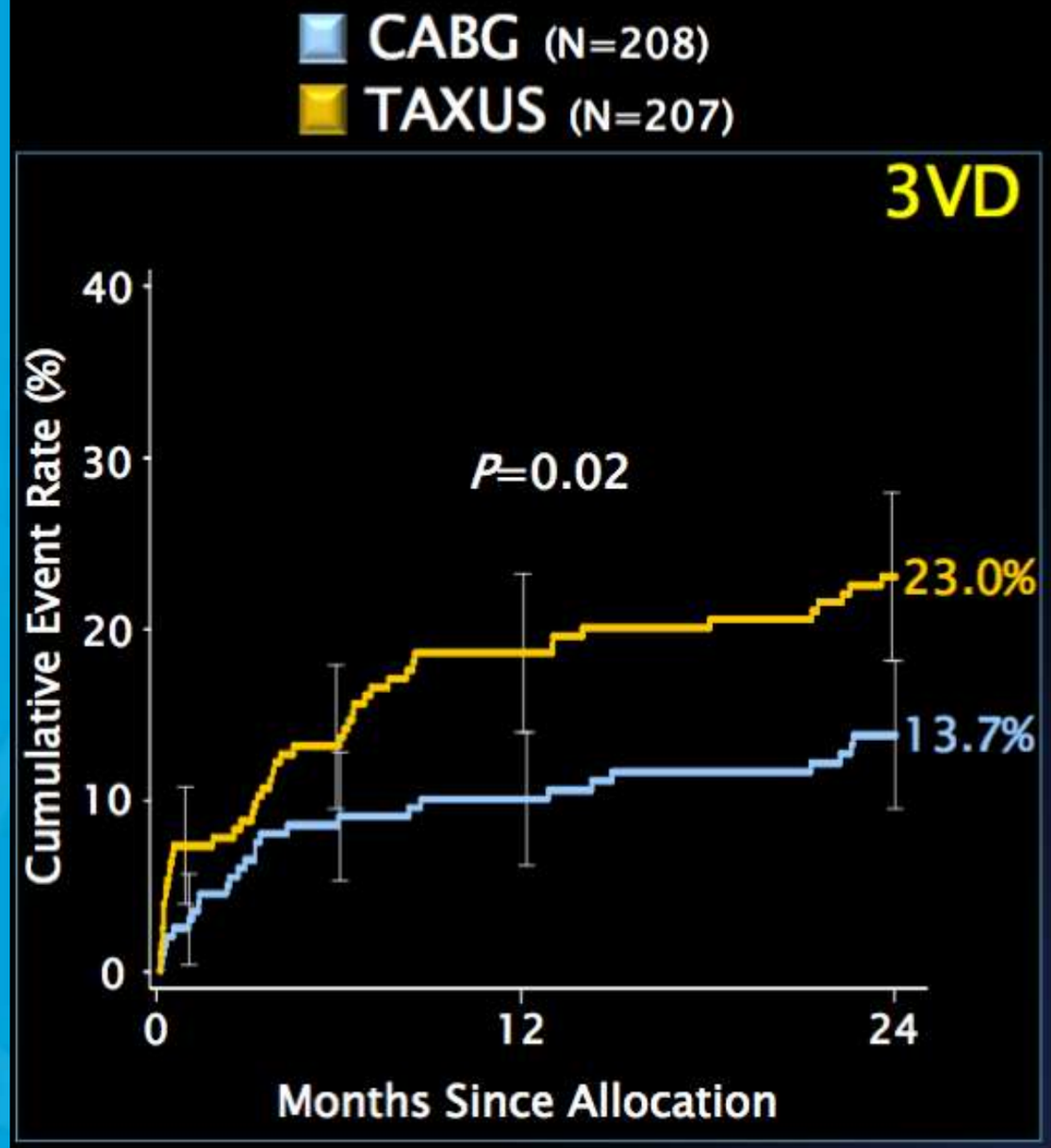
	CABG	PCI	*P* value
Death	5.5%	5.1%	0.85
CVA	1.9%	1.2%	0.57
MI	4.2%	3.9%	0.90
Death, CVA or MI	9.7%	8.4%	0.67
Revasc.	7.6%	17.1%	0.01

Cumulative KM Event Rate ± 1.5 SE; log-rank *P* value

Site-reported Data; ITT population

MACCE to 2 Years by SYNTAX Score Tercile 3VD *Intermediate Scores (23–32)*

SYNTAX



	CABG	PCI	*P* value
Death	4.1%	6.4%	0.30
CVA	3.1%	2.0%	0.50
MI	2.6%	7.4%	0.03
Death, CVA or MI	8.6%	11.7%	0.29
Revasc.	7.3%	16.1%	0.006

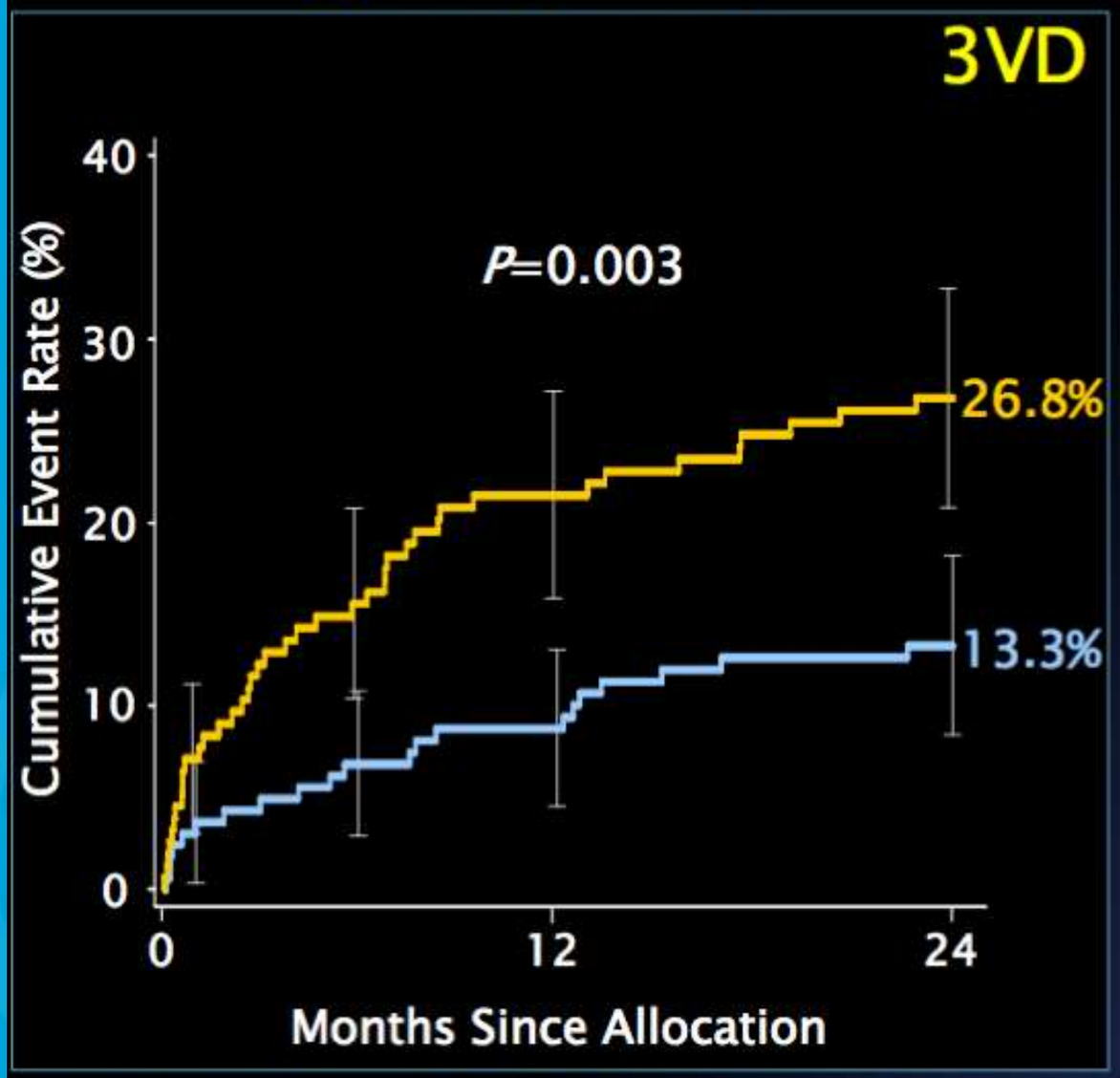
Cumulative KM Event Rate ± 1.5 SE; log-rank *P* value

Site-reported Data; ITT population

MACCE to 2 Years by SYNTAX Score Tercile 3VD *High Scores (≥33)*

SYNTAX

CABG (N=166)
TAXUS (N=155)



Cumulative KM Event Rate ± 1.5 SE; log-rank *P* value

	CABG	PCI	*P* value
Death	2.5%	8.5%	0.02
CVA	1.9%	2.1%	0.95
MI	1.9%	7.2%	0.02
Death, CVA or MI	6.3%	13.7%	0.03
Revasc.	7.7%	19.3%	0.002

Site-reported data; ITT population

Review: CABG and percutaneous coronary intervention do not differ for long-term mortality in multivessel coronary artery disease

Laura Rees Willett, MD

Coronary artery bypass graft (CABG) vs percutaneous coronary intervention (PCI) in patients with multivessel coronary artery disease*

Subgroups	5-y mortality		At median 5.9 y	
	CABG	PCI	RRR (95% CI)	NNT (CI)
All	8.4%	10%	8.6% (–2 to 17)	Not significant
Diabetes	12%	20%	28% (12 to 41)	19 (13 to 43)
No diabetes	7.6%	8.1%	2% (–11 to 13)	Not significant
Age ≥ 65 y	11%	15%	17% (3 to 28)	41 (24 to 246)
Age 55 to 64 y	8.0%	9.4%	10% (–9 to 24)	Not significant
			RRI (CI)	NNH
Age < 55 y	5.5%	5.0%	24% (–6 to 63)	Not significant

Ann Intern Med. 21 July 2009;151(2):JC1-8

ASCERT

INTERVENTIONAL/SURGERY

ASCERT CABG, PCI analysis: Lower mortality with surgery

1. Weintraub WS, Grau-Sepulveda MV, Weiss JM, et al. Comparative effectiveness of revascularization strategies. *N Engl J Med* 2012; DOI: 10.1056/NEJMoa1110717. Available at: http://www.nejm.org.
2. Mauri L. Why we still need randomized trials to compare effectiveness. *N Engl J Med* 2012; DOI:10.1056/nejme1202866. Available at: http://www.nejm.org.

Interval	HR (95% CI)
30 d	1.72 (1.52–1.89)
1 y	0.95 (0.90–1.00)
2 y	0.79 (0.76–0.83)
4 y	0.79 (0.76–0.82)

"One of the major messages to take away from the study is that cardiologists and surgeons need to be talking to each other more," according to Edwards. If CABG provides better long-term survival than PCI, "that information should be presented to the patient and be used in a dialog between the surgeon and the cardiologist."

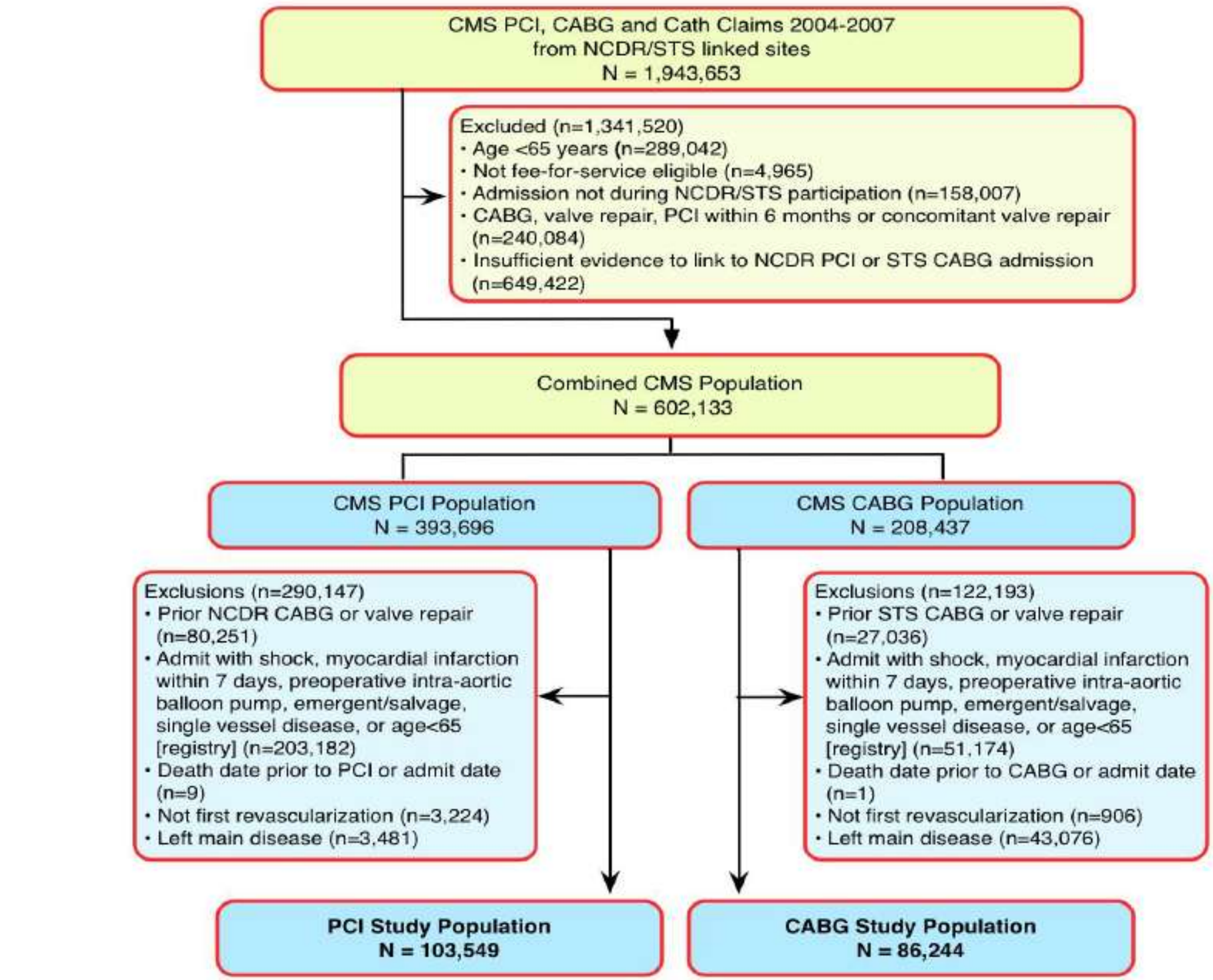
RESULTS

Among patients 65 years of age or older who had two-vessel or three-vessel coronary artery disease without acute myocardial infarction, 86,244 underwent CABG and 103,549 underwent PCI. The median follow-up period was 2.67 years. At 1 year, there was no significant difference in adjusted mortality between the groups (6.24% in the CABG group as compared with 6.55% in the PCI group; risk ratio, 0.95; 95% confidence interval [CI], 0.90 to 1.00). At 4 years, there was lower mortality with CABG than with PCI (16.4% vs. 20.8%; risk ratio, 0.79; 95% CI, 0.76 to 0.82). Similar results were noted in multiple subgroups and with the use of several different analytic methods. Residual confounding was assessed by means of a sensitivity analysis.

Data from 644 Sites

NCDR Sites

STS Sites


CMS PCI, CABG and Cath Claims 2004-2007
from NCDR/STS linked sites
N = 1,943,653
Excluded (n=1,341,520)
• Age <65 years (n=289,042)
• Not fee-for-service eligible (n=4,965)
• Admission not during NCDR/STS participation (n=158,007)
• CABG, valve repair, PCI within 6 months or concomitant valve repair (n=240,084)
• Insufficient evidence to link to NCDR PCI or STS CABG admission (n=649,422)
Combined CMS Population
N = 602,133
CMS PCI Population
N = 393,696
CMS CABG Population
N = 208,437
Exclusions (n=290,147)
• Prior NCDR CABG or valve repair (n=80,251)
• Admit with shock, myocardial infarction within 7 days, preoperative intra-aortic balloon pump, emergent/salvage, single vessel disease, or age<65 [registry] (n=203,182)
• Death date prior to PCI or admit date (n=9)
• Not first revascularization (n=3,224)
• Left main disease (n=3,481)
Exclusions (n=122,193)
• Prior STS CABG or valve repair (n=27,036)
• Admit with shock, myocardial infarction within 7 days, preoperative intra-aortic balloon pump, emergent/salvage, single vessel disease, or age<65 [registry] (n=51,174)
• Death date prior to CABG or admit date (n=1)
• Not first revascularization (n=906)
• Left main disease (n=43,076)
PCI Study Population
N = 103,549
CABG Study Population
N = 86,244

Baseline Data

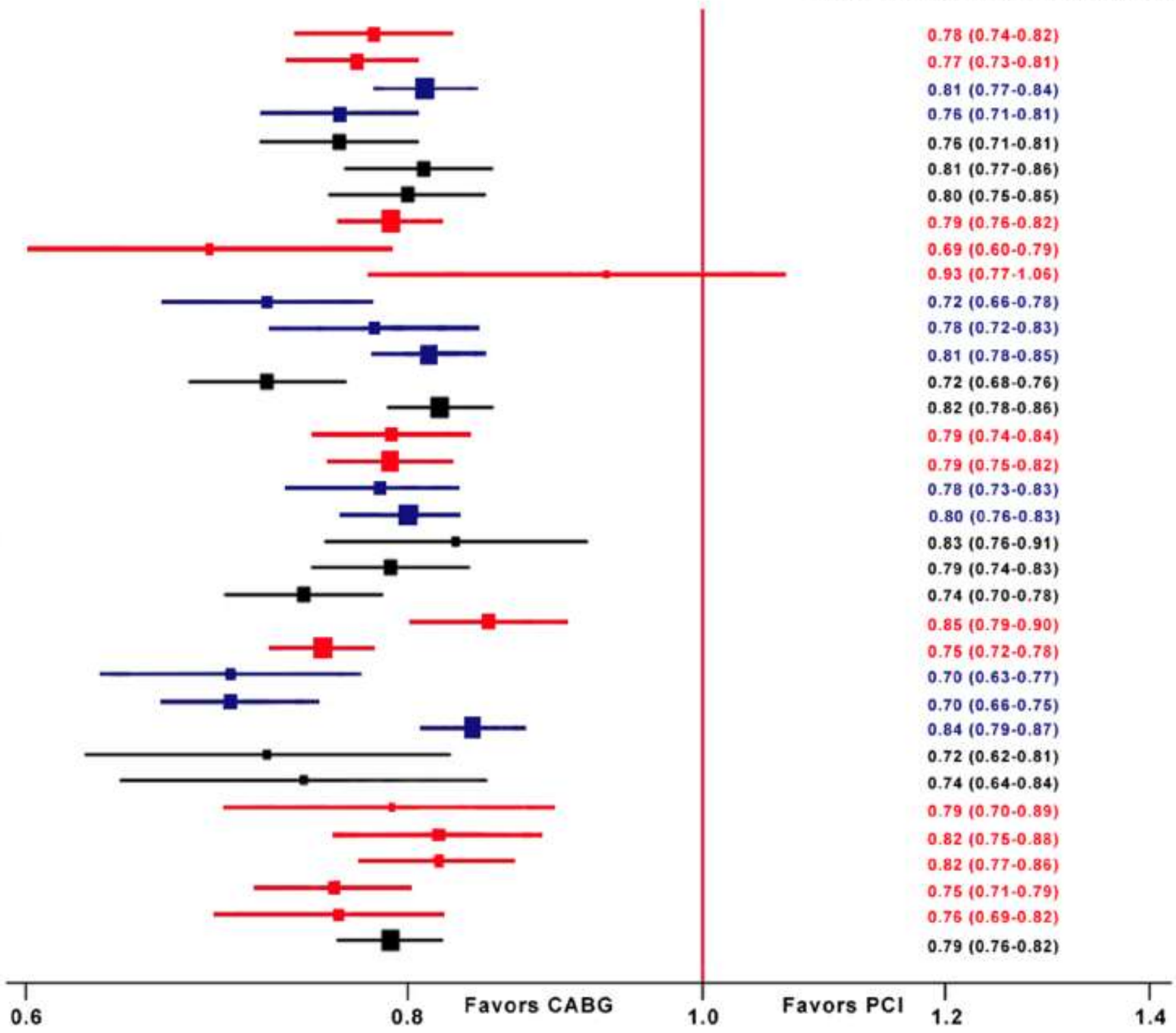
	Unadjusted			IPW Adjusted		
	CABG (n=86,244)	PCI (n=103,549)	P Value	CABG (n=86,244)	PCI (n=103,549)	P Value
Age	73.1 ± 5.6	74.7 ± 6.5	<0.0001	74.0 ± 9.2	74.0 ± 8.3	0.49
Male	68.6	57.8	<0.0001	62.3	62.8	0.17
History of CHF	11.5	10.2	<0.0001	11.2	10.8	0.067
History of MI	25.3	24.6	0.0001	24.5	24.7	0.51
Diabetes	38.6	34.4	<0.0001	35.8	35.8	0.97
Insulin Requiring	10.2	9.8	0.0069	9.7	9.9	0.35
Hypertension	84.8	83.4	<0.0001	83.9	83.8	0.58
Renal Failure	6.1	6.2	0.57	6.1	6.1	0.80
CKD	20.7	18.9	<0.0001	19.4	19.6	0.50
CVD	17.6	15.8	<0.0001	16.6	16.6	0.86
PAD	17.9	15.3	<0.0001	16.4	16.4	0.97
BMI	28.7 ± 5.8	28.7 ± 5.9	0.78	28.8 ± 8.6	28.7 ± 7.9	0.97
Former Smoker	44.0	42.5	<0.0001	43.0	43.3	0.45
Current Smoker	12.9	11.6	<0.0001	11.9	12.0	0.74
No Angina	21.8	30.8	<0.0001	26.4	26.8	0.23
Stable Angina	49.6	22.6	<0.0001	34.6	34.9	0.46
Unstable Angina	28.6	46.6	<0.0001	39.0	38.3	0.066
Ejection Fraction	52.9± 12.2	55.5 ± 11.4	<0.0001	54.4 ± 17.6	54.4 ± 16.2	0.58
3 Vessel Disease	80.3	32.1	<0.0001	53.2	53.8	0.043
Status Urgent	68.6	57.8	<0.0001	62.3	62.8	0.17

Ascert

Conclusions

- Survival was similar in the two arms at 1 years
- Survival was higher in the CABG than PCI arm at 4 years
- The results were largely consistent across subgroups
- This is largely consistent with both clinical trial and observational studies
- Causal inference requires considering the totality of the data, of which ASCERT is a critical part
- ASCERT offers critical experience in comparative effectiveness research using observational data

Subgroups	Adjusted RR at 4 Years (95% CI)
Age ≥75	0.78 (0.74-0.82)
Age <75	0.77 (0.73-0.81)
Male	0.81 (0.77-0.84)
Female	0.76 (0.71-0.81)
BMI ≤25	0.76 (0.71-0.81)
BMI 26-30	0.81 (0.77-0.86)
BMI >30	0.80 (0.75-0.85)
White	0.79 (0.76-0.82)
African American	0.69 (0.60-0.79)
Other	0.93 (0.77-1.06)
Diabetes: Insulin	0.72 (0.66-0.78)
Diabetes: No Insulin	0.78 (0.72-0.83)
No Diabetes	0.81 (0.78-0.85)
Chronic Lung Disease	0.72 (0.68-0.76)
No Chronic Lung Disease	0.82 (0.78-0.86)
Peripheral Arterial Disease	0.79 (0.74-0.84)
No Peripheral Arterial Disease	0.79 (0.75-0.82)
Prior Myocardial Infarction	0.78 (0.73-0.83)
No Prior Myocardial Infarction	0.80 (0.76-0.83)
Glomerular Filtration Rate ≤30	0.83 (0.76-0.91)
Glomerular Filtration Rate 31-60	0.79 (0.74-0.83)
Glomerular Filtration Rate >60	0.74 (0.70-0.78)
Number of Diseased Vessels = 2	0.85 (0.79-0.90)
Number of Diseased Vessels = 3	0.75 (0.72-0.78)
Ejection Fraction <30	0.70 (0.63-0.77)
Ejection Fraction 30-<50	0.70 (0.66-0.75)
Ejection Fraction ≥50	0.84 (0.79-0.87)
High Risk	0.72 (0.62-0.81)
Low Risk	0.74 (0.64-0.84)
Propensity Score, Quintile 1	0.79 (0.70-0.89)
Propensity Score, Quintile 2	0.82 (0.75-0.88)
Propensity Score, Quintile 3	0.82 (0.77-0.86)
Propensity Score, Quintile 4	0.75 (0.71-0.79)
Propensity Score, Quintile 5	0.76 (0.69-0.82)
Overall	0.79 (0.76-0.82)



Limitations

- All observational studies have possible treatment selection bias.
- This can be approached, but not fully resolved, by careful database design, statistical analysis and sensitivity analysis.
- Several variables were not available (e.g. frailty) or of limited quality (e.g. angiographic details) in the ASCERT data.
- There was missing data for several variables (e.g. GFR and EF)
- ASCERT outcomes are limited to patients age 65 and older.
- This presentation concerns mortality only (composite endpoints, angiographic analyses, economic analysis will follow)

FAME

Fractional flow reserve–guided PCI reduced major adverse cardiac outcomes compared with angiography-guided PCI in multivessel CAD

Fractional flow reserve (FFR)- vs angiography-guided percutaneous coronary intervention in patients with multivessel coronary artery disease‡

Outcomes	FFR	Angiography	At 1 y	
			RRR (95% CI)	NNT (CI)
Major adverse cardiac event	13%	18%	28% (4 to 46)	20 (12 to 137)
Death	1.8%	3.0%	42% (–32 to 74)	Not significant
Myocardial infarction	5.7%	8.7%	34% (–4 to 58)	Not significant
Repeated revascularization	6.5%	9.5%	32% (–5 to 55)	Not significant

Appropriateness

JANUARY 30, 2012

Appropriate Use Criteria for Revascularization Updated

Reply

by Larry Husten • Interventional Cardiology & Surgery • Tags: appropriate use criteria, CABG, cardiac surgeons, left main disease, multivessel disease, PCI

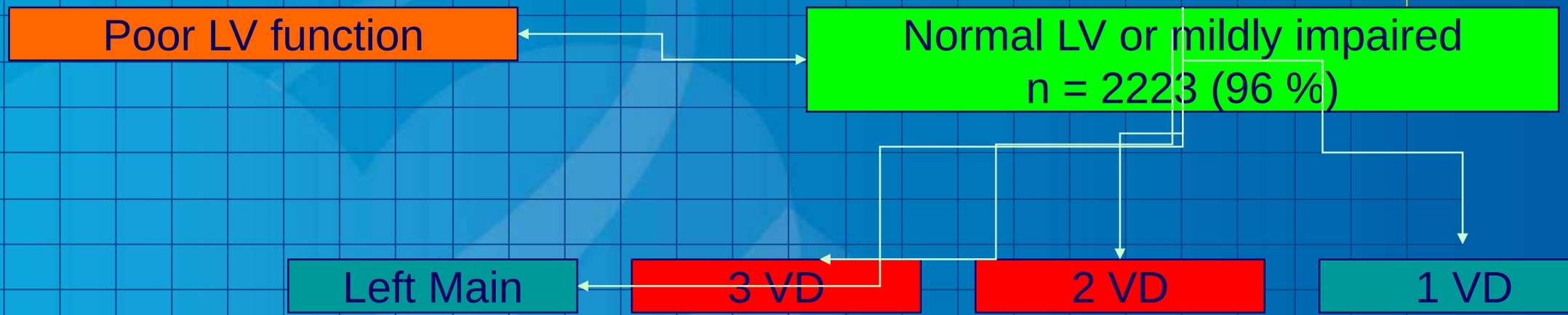
The ACC, AHA, and other organizations have released updated appropriate use criterial for coronary revascularization. The 2012 Appropriate Use Criteria for Coronary Revascularization Focused Update incorporates data from the SYNTAX trial on the indications for PCI and CABG in patients with symptomatic, multivessel disease, as well as data from the CathPCI registry.

Here are some of the key ratings:

- PCI for **low burden left main disease alone or with blockages in other arteries with a low disease burden**: *uncertain*
- PCI for **intermediate or high burden left main disease:** *inappropriate*
- PCI for **low burden three-vessel disease**: *appropriate*
- PCI for **intermediate or high burden three-vessel disease**: *uncertain*
- CABG remains *appropriate* for patients with **two vessel disease including the proximal LAD** and **all three vessel and left main disease.**

Euro Heart Survey on Coronary Revascularization

N. Mercado, on behalf of the Investigators and Expert Committee



	7.4 %	32 %	32 %	36 %
Medical R	18 %	21 %	20 %	27 %
PCR	18 %	**26 %**	**56 %**	66 %
CABG	64 %	**53 %**	**24 %**	7 %

No difference in treatment options between diabetics and non diabetics

Treatment Strategy for Stable Angina n = 2316

Conclusion 1

- Patient selection is primordial
- Scores are useful to select patients
- Age of 65 and more may be important
- Patient comorbidity is important
- Patient choice is important but often modifiable by open discussion
- Heart team and discussion of patients with surgeon is essential

Conclusion 2

- Good strategy is essential
- Right material
- Use of prior FFR is useful
- Knowing when to refer patient for surgery
- Recognizing our own limits

Thank you for your attention