CABG & OMT Evolving Again ?

Microcirculation & OMT+Adherence

ACC - New York, Dec. 11, 2015

No Disclosures

Revascularization for Coronary Artery Disease

OMT vs PCI vs CABG

1980's. LMD, The Rule of 2 / 3 – CABG

-Moderate <LVEF

-Severe Ischemia

-3 Vessel Disease

2vd + pLAD

[1]Severe - Yes, STICH

Moderate – COURAGE OMT

ISCHEMIA

[1]2vd in DM

1990's. The Rule of 2 / 3 – PCI ?

2010's[1]. PCI <, CABG > (DM), Microc., OMT

2020,s. Anatomical, Isch.Score, Microc.: Ninv. - OMT+

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Results From the Surgical Treatment for Ischemic Heart Failure (STICH) Trial

In both STICH trials (hypotheses), 2136 patients with a left ventricular ejection fraction of ≤35% and coronary artery disease were allocated to medical therapy, CABG plus medical therapy, or CABG with surgical ventricular reconstruction. CABG can be performed with relatively low 30-day mortality in patients with left ventricular dysfunction. Serious postoperative complications occurred in nearly 1 in 4 patients and were associated with mortality.

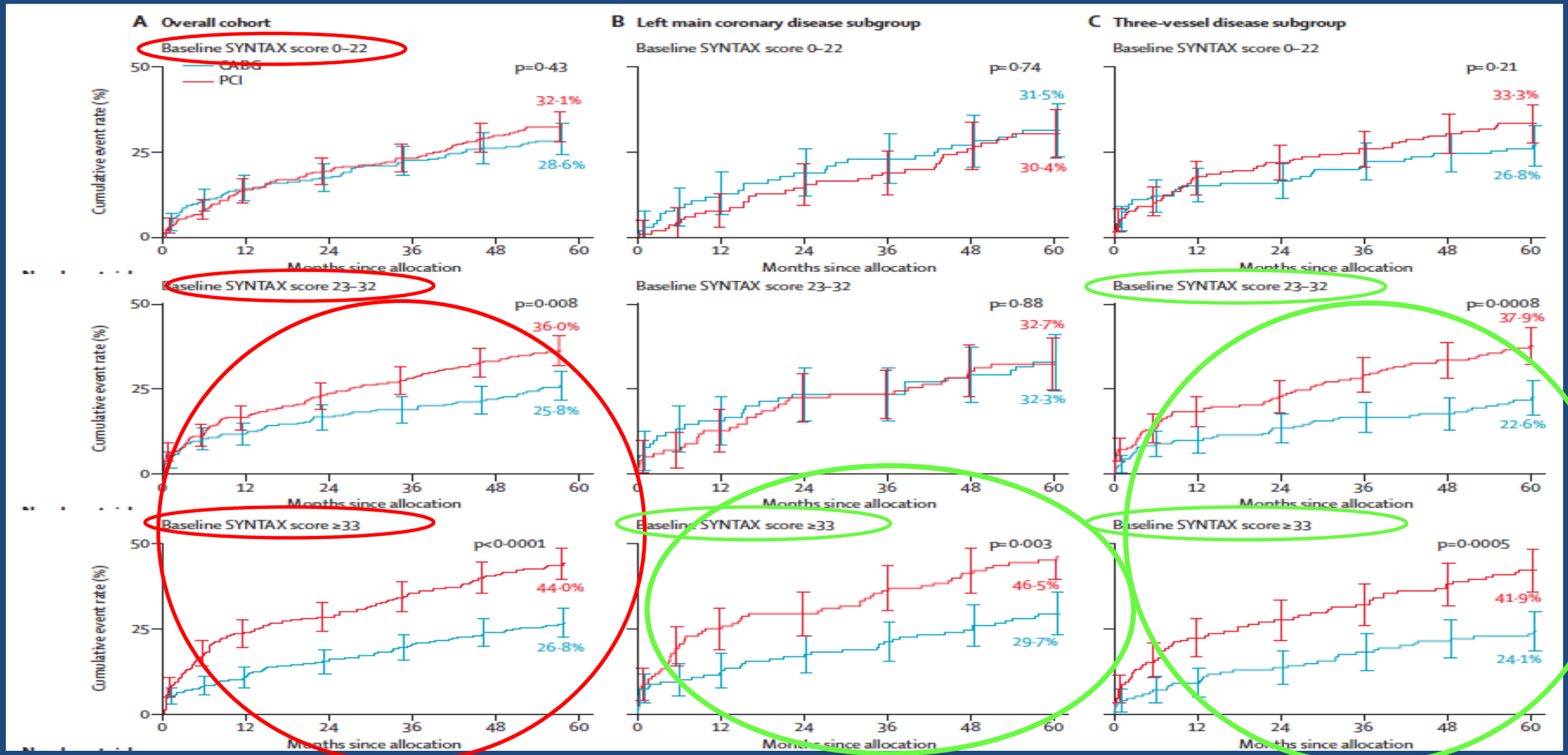
STICH (K Wrobel et al.) Circulation 2015; 132:720

COMPLEX, STABLE CORONARY DISEASE

TRIAL	MVD	DM	INTERV.	MT.	EP.-R	Data
SYNTAX	+	-	++	-	++	CABG > PCI SYNTAX Score
FAME	-	-	+	-	+	PCI "ISCHEMIA" Score
BARI	-	+	+	+	+	CABG / PCI = MT X.OV.ER 42%
COURAGE	-	-	+	+	+	PCI = MT "ISCHEMIA">10%-Events
FREEDOM	+	+	++	(+)	+	CABG > PCI No Freedom of Choice?

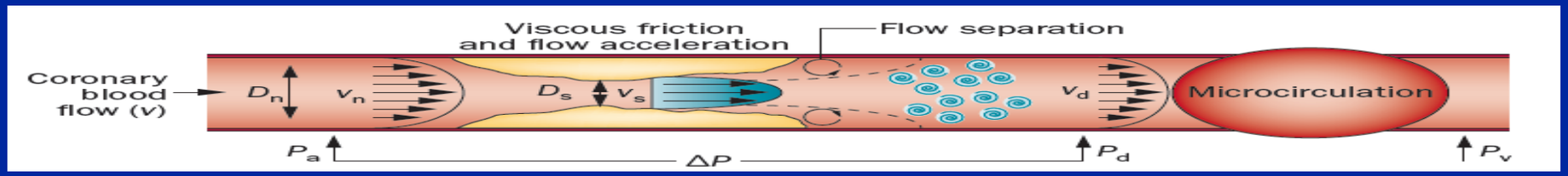
Conditions Methods-Interests Conclusions

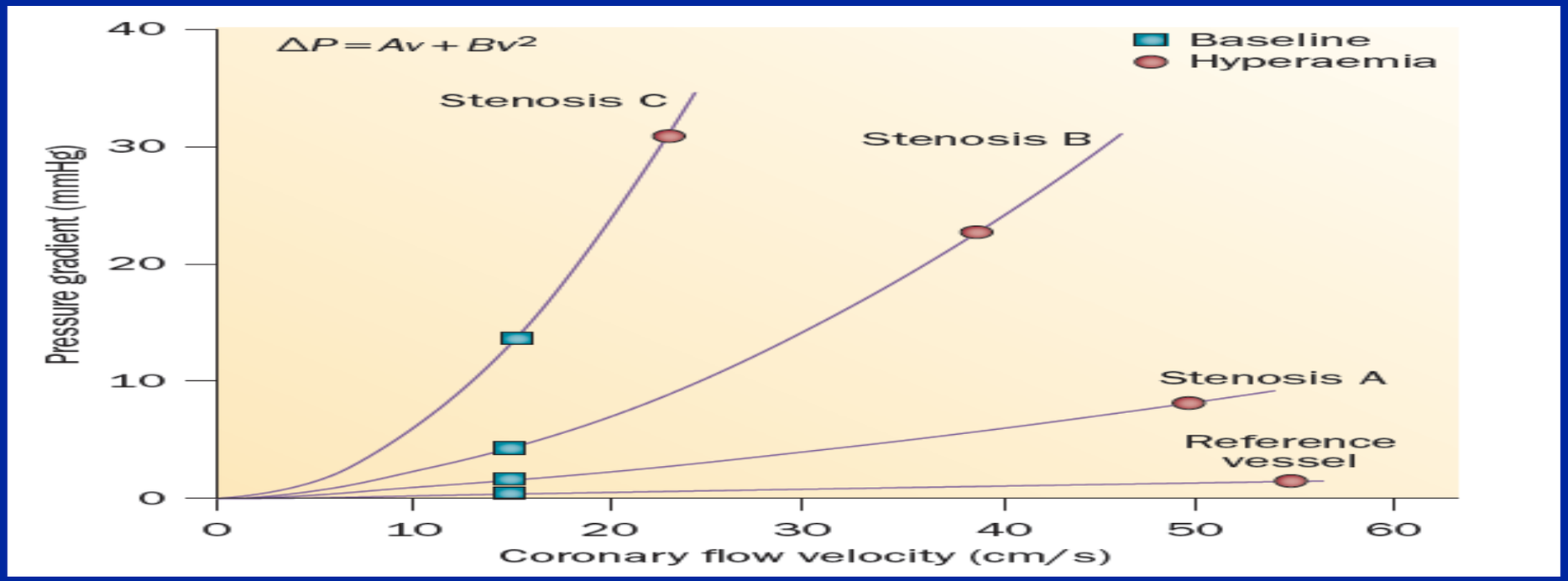
Baseline SYNTAX Score Tercile -CABG
Cumulative Event Curves For MACCE



SYNTAX (FW Mohr, PW Serruys et. al.) Lancet 2013; 381: 629

FFR As A Surrogate For Inducible Myocardial Ischaemia

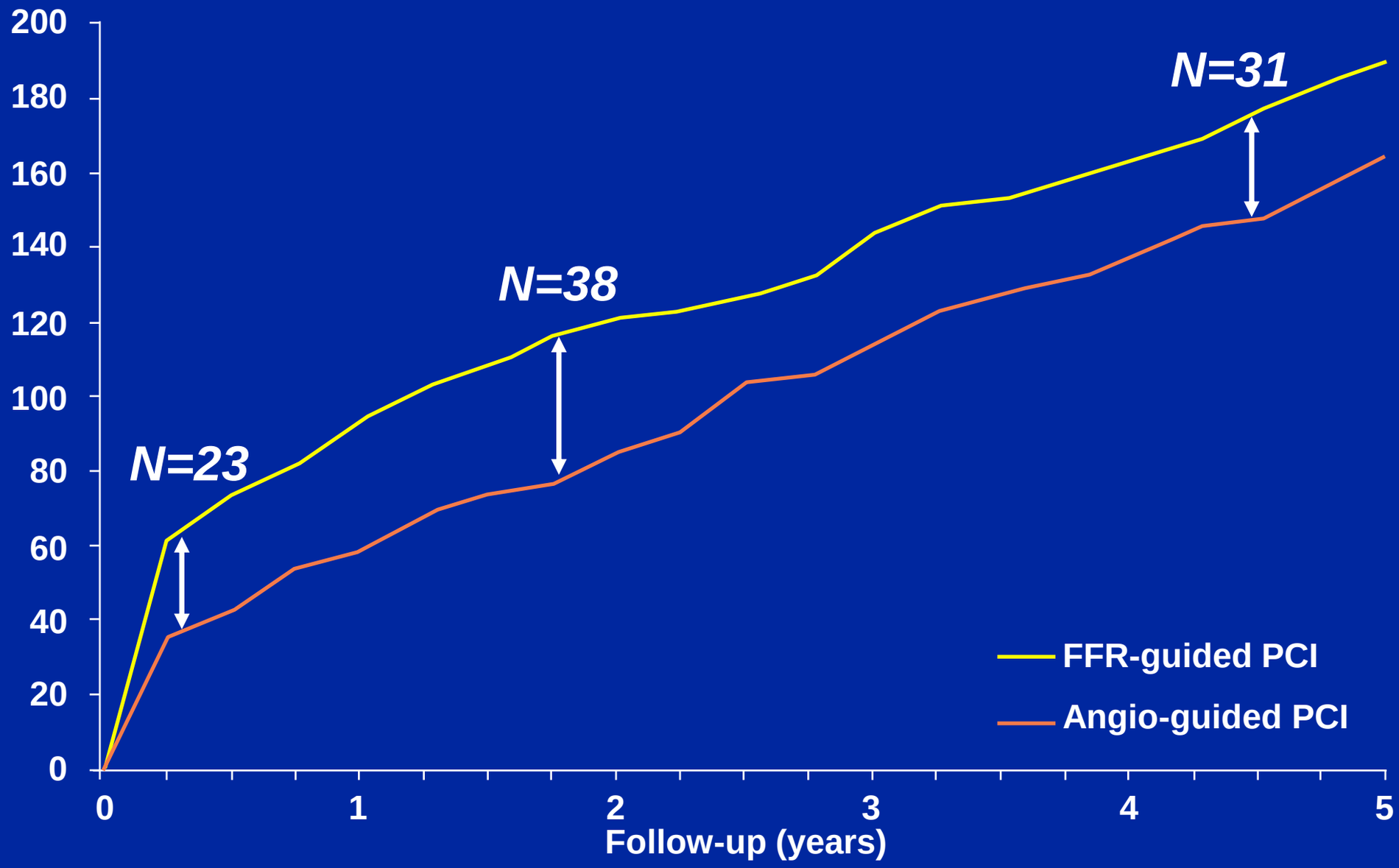




FAME I (FFR>0.8) - OMT of Non-Isch.Les.– Prevent MI/Death
FAME II (FFR<0.8) - PCI Isch. Les. – Prevent MI/Death –FAME III-CABG?

TP van de Hoef Nat. Rev. Cardiol. 2013;10:439 – FAME 2 (B De Bruyne) NEJM 2014; 371:1208

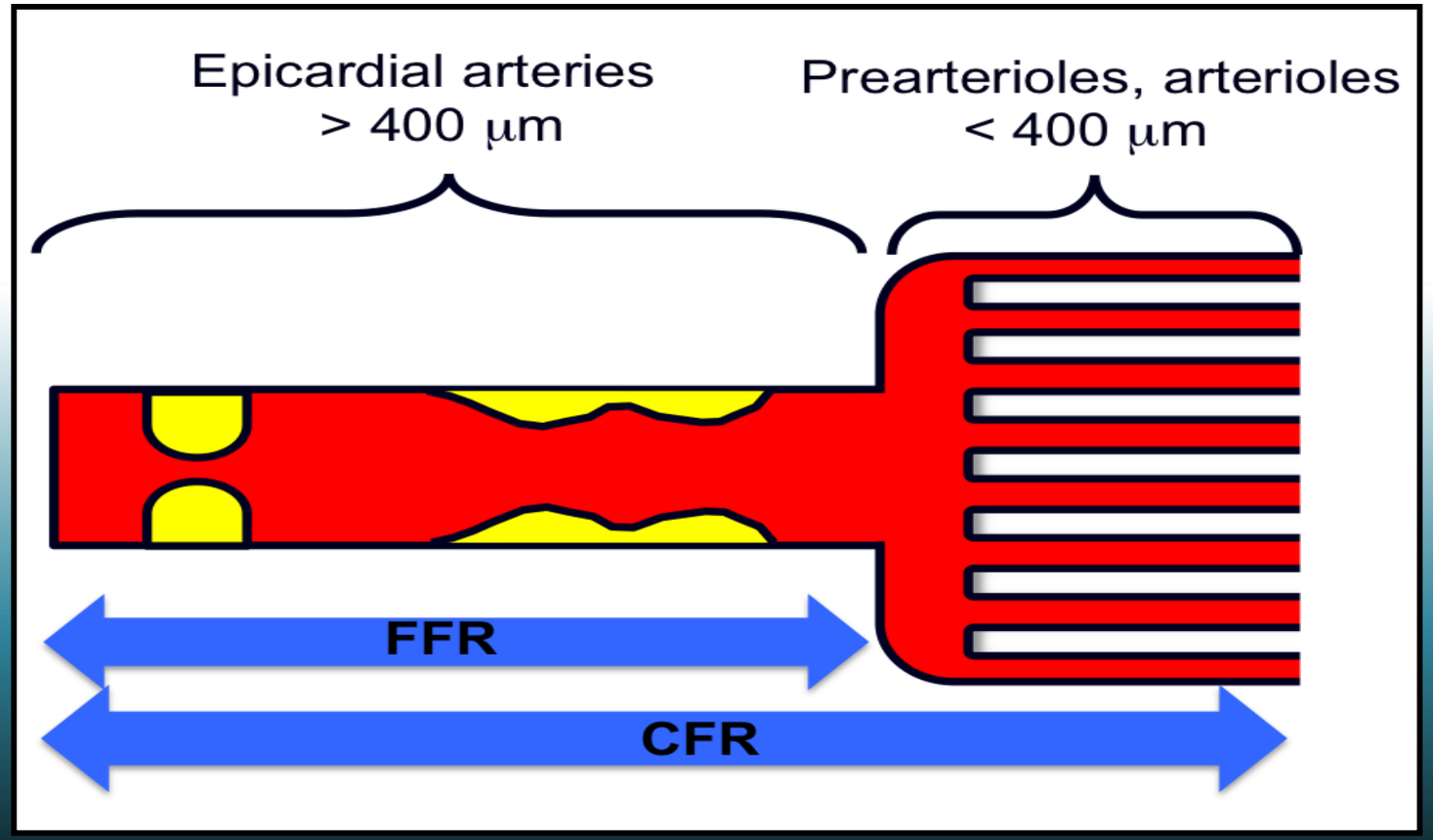
FAME STUDY: CUMULATIVE EVENTS DURING 5-YEAR FOLLOW-UP



FAME (LX van Nunen et al., The Lancet 2015; 386:1853

1. Coronary Flow Reserve (CFR)

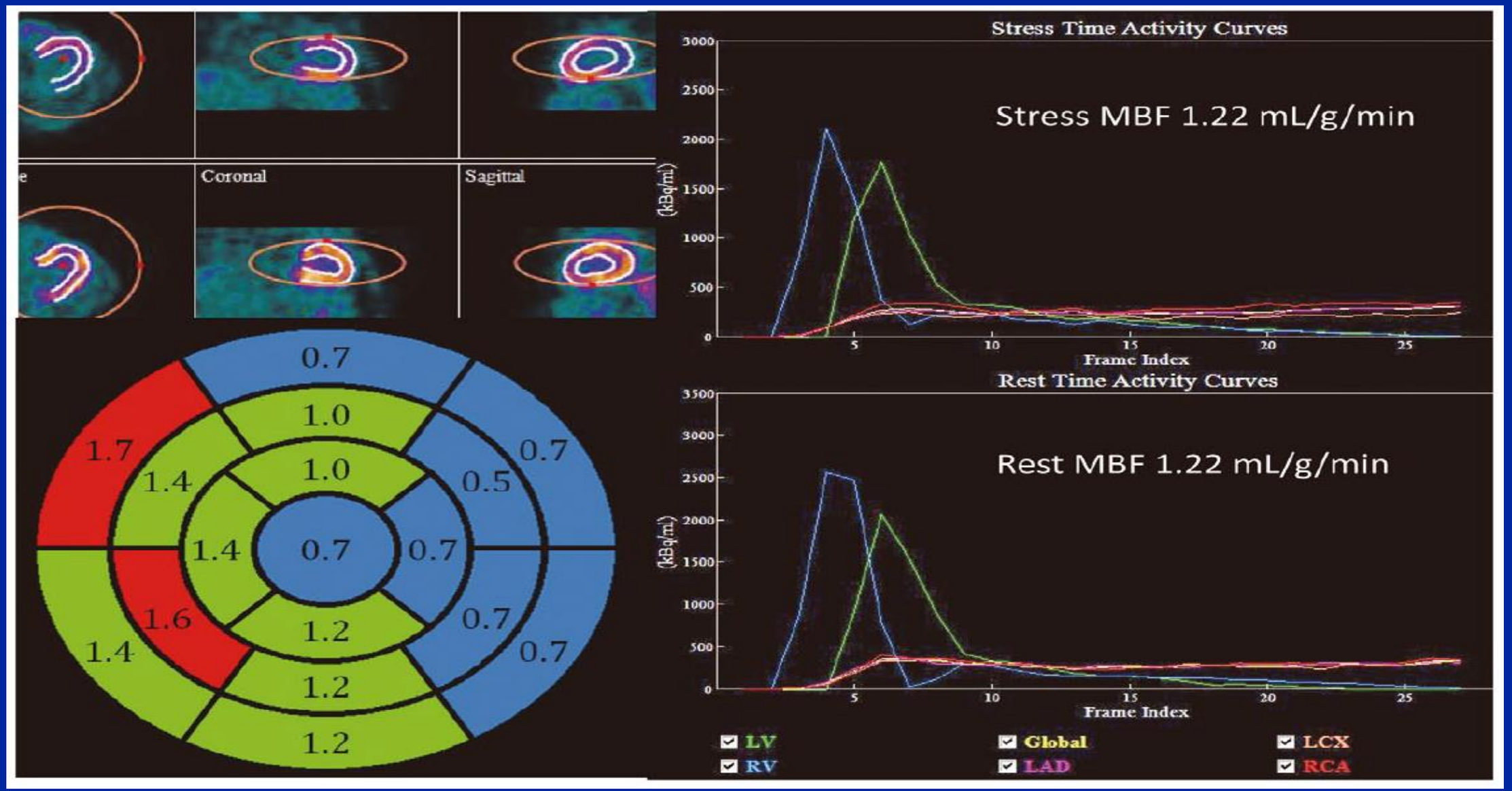
➔ **Measures *integrated* hemodynamic effects of epicardial CAD, diffuse atherosclerosis, vessel remodeling and microvascular dysfunction on myocardial tissue perfusion**



$$CFR = \frac{MBF_{\text{peak hyperemia}}}{MBF_{\text{rest}}}$$

VR Taqueti and MF Di Carli 2014

Time-activity Curves And A Polar Map Of 17-segment Coronary Flow Reserve



B Tu et. al. Ann Intern Med. 2014;161:724

Coronary Calcification on the Diagnostic Performance of CT Angiography Derived FFR

Coronary calcification was assessed by using the Agatston score (AS) in 214 patients suspected of having CAD who underwent coronary CTA, FFR_{CT}, and FFR. The diagnostic performance of FFR_{CT} (≤0.80) in identifying vessel-specific ischemia (FFR ≤0.80) was investigated across AS quartiles. FFR_{CT} provided high and superior diagnostic performance compared with coronary CTA interpretation alone in patients and vessels with a high AS.

***NXT Trial** (BL Nørgaard et al.), J Am Coll Cardiol Img **2015;** 8:1045*

CFR and the Microcirculation

Cardiac Imaging

Multiparametric Cardiovascular Magnetic Resonance Assessment of Cardiac Allograft Vasculopathy

Christopher A. Miller, BSc, MBChB,*†‡ Jaydeep Sarma, MA, MB BChir, PhD,*‡
Josephine H. Naish, PhD,† Nizar Yonan, MD,*‡ Simon G. Williams, MD,*‡ Steven M. Shaw, PhD,*‡
David Clark, BSc,§ Keith Pearce, BSc,* Martin Stout, PhD,* Rahul Potluri, MBChB,*†
Alex Borg, MD,* Glyn Coutts, PhD,‖ Saqib Chowdhary, PhD,*‡ Gerry P. McCann, MD,¶
Geoffrey J. M. Parker, PhD,† Simon G. Ray, MD,*‡ Matthias Schmitt, MD, PhD*‡

Manchester and Leicester, United Kingdom

JACC: CARDIOVASCULAR IMAGING
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VOL. 7, NO. 11, 2014
ISSN 1936-878X/$36.00
http://dx.doi.org/10.1016/j.jcmg.2014.07.011

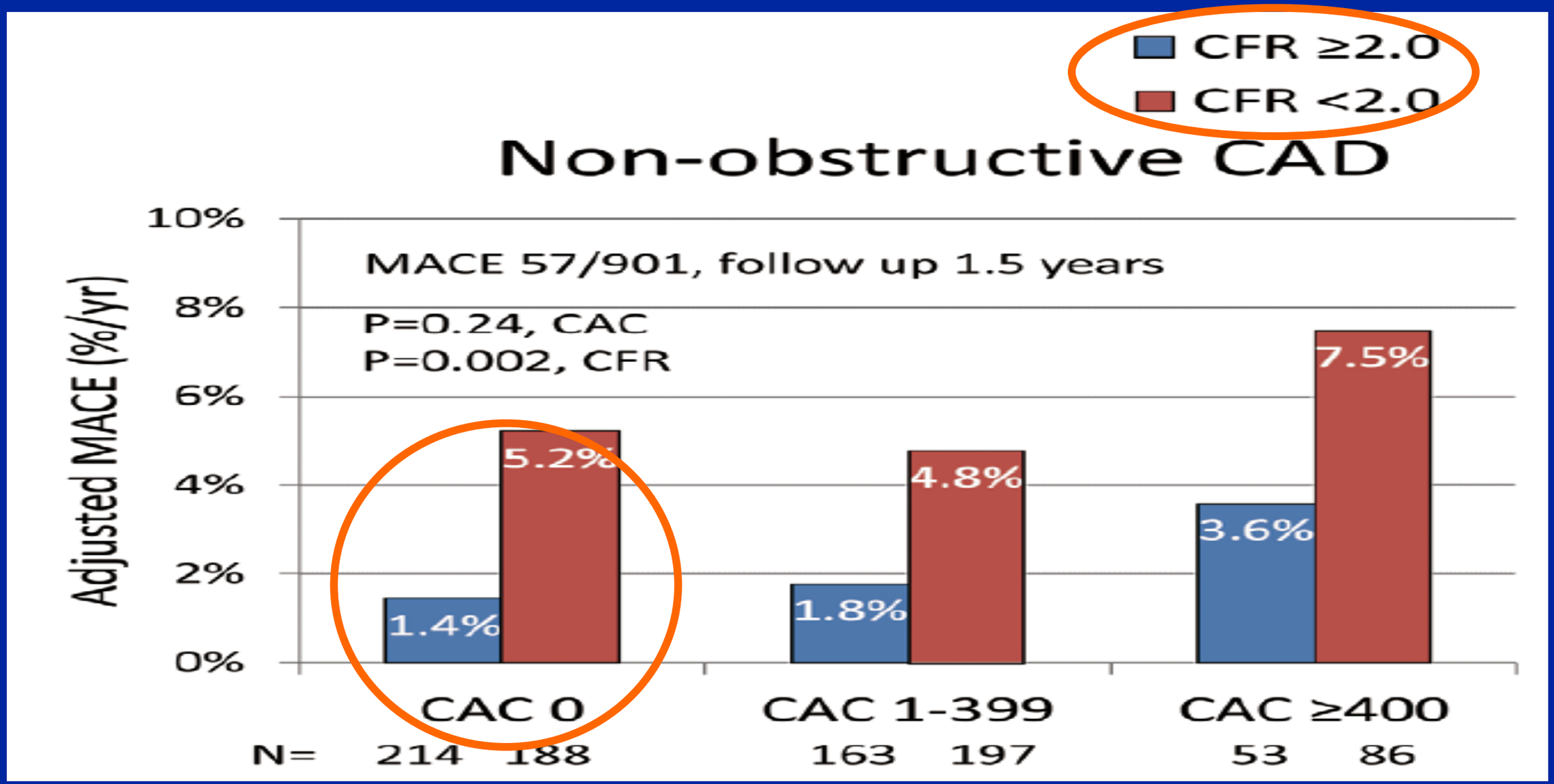
Diagnostic Accuracy of Myocardial Magnetic Resonance Perfusion to Diagnose Ischemic Stenosis With Fractional Flow Reserve as Reference

Systematic Review and Meta-Analysis

Min Li, MD, Tao Zhou, MD, Lin-feng Yang, MD, Zhao-hui Peng, MD, Juan Ding, MD, Gang Sun, MD, PhD

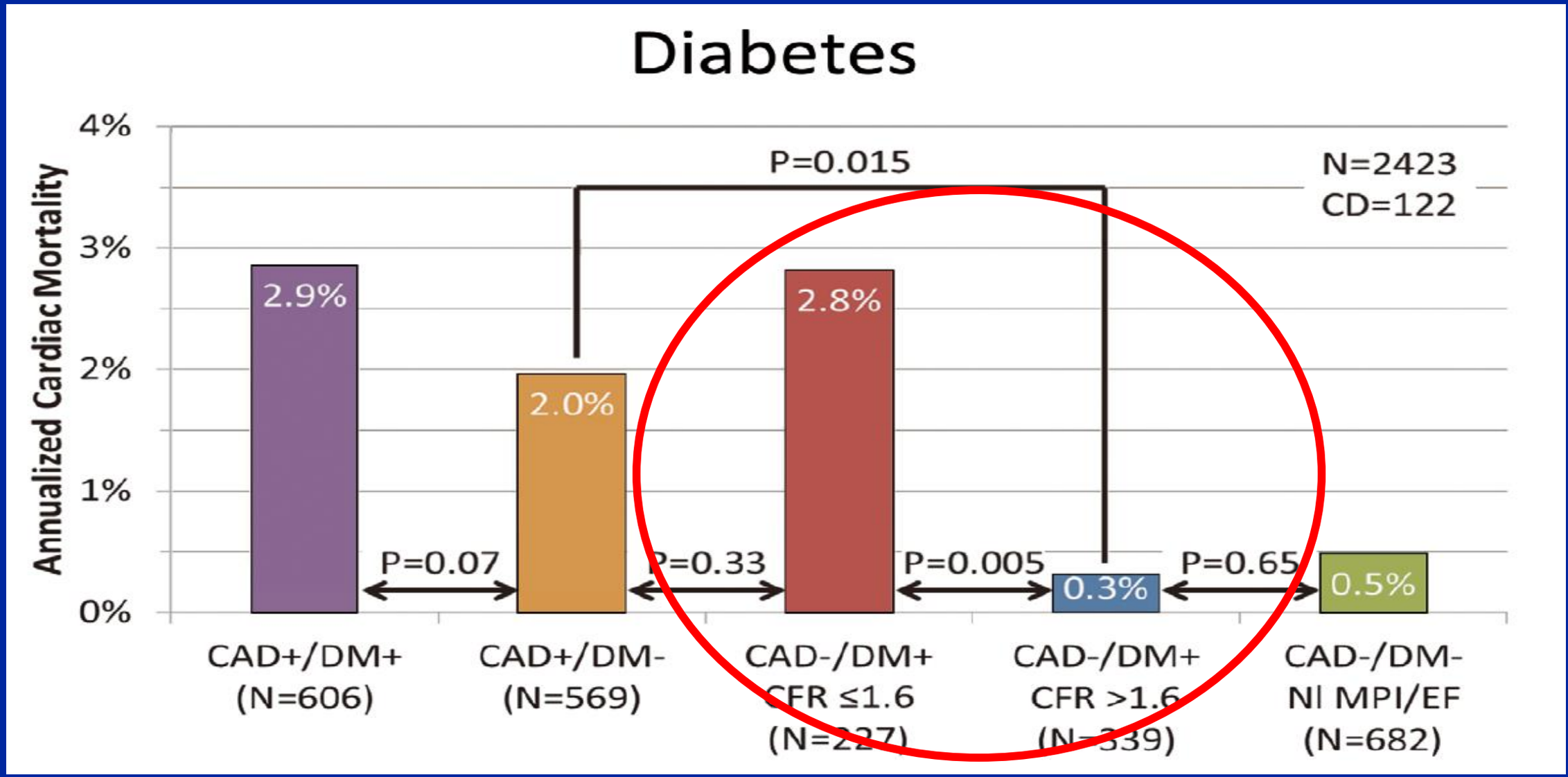
JACC 2014;63:799 - JACC Imag. 2014;7: 1936

1a. Impaired CFR & Zero CAC - MACE



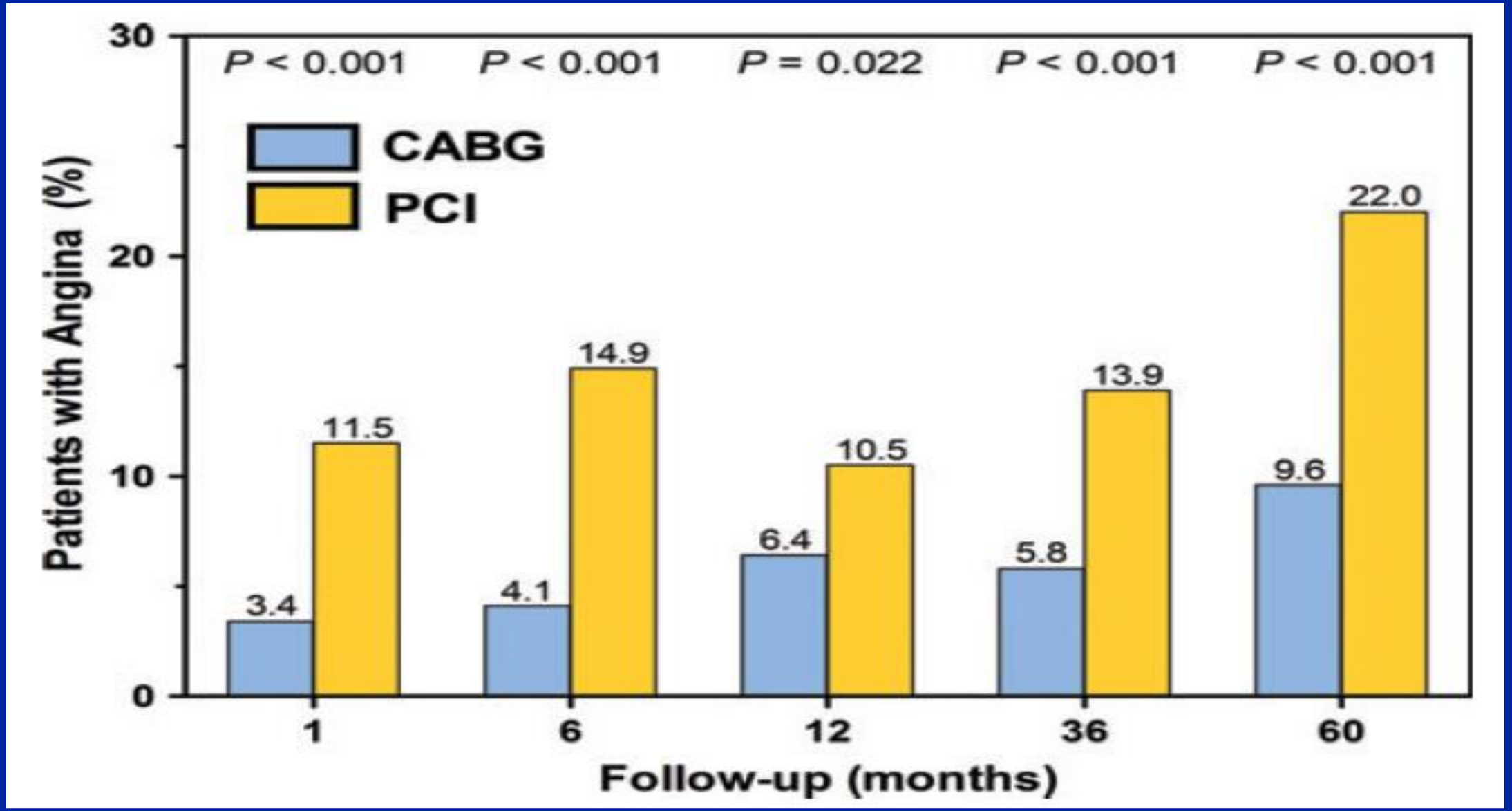
M Naya et. al. JACC 2013;61:2098 - M Naya et. al. Circ J 2015; 79: 15

1b. Diabetes - CFR w/wo Epicardial CAD, Relation To Cardiac Death



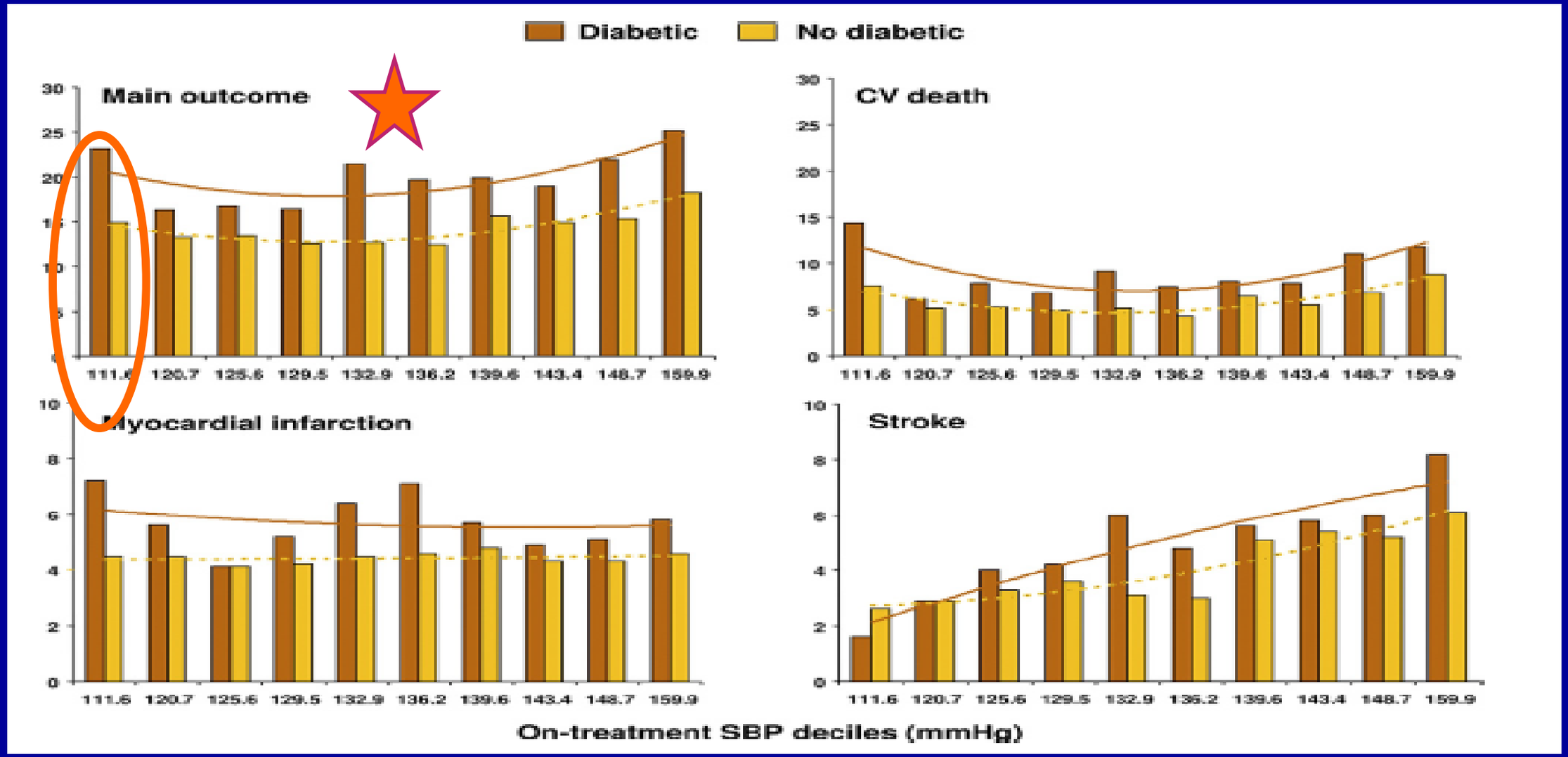
VL Murthy et. al. Circulation 2012;126:1858 - M Naya et. al. Circ J 2015; 79: 15

1c. Angina During Follow-up



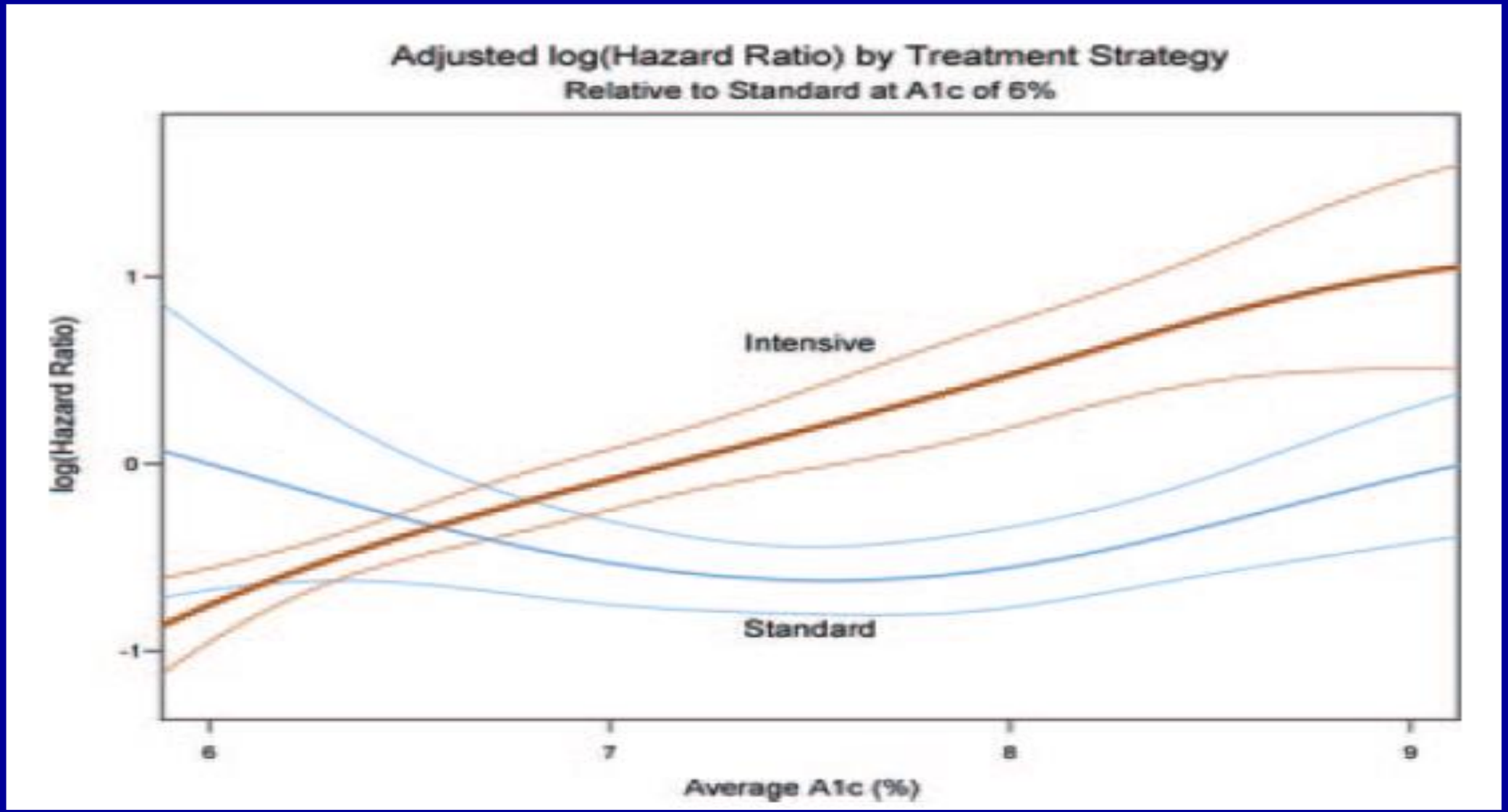
SJ Head et. al. EHJ. 2014;35:2821 – No Stad. Signif in FREEEDOM

1d. Proportion of Outcome Events by Achieved SBP - ONTARGET Trial



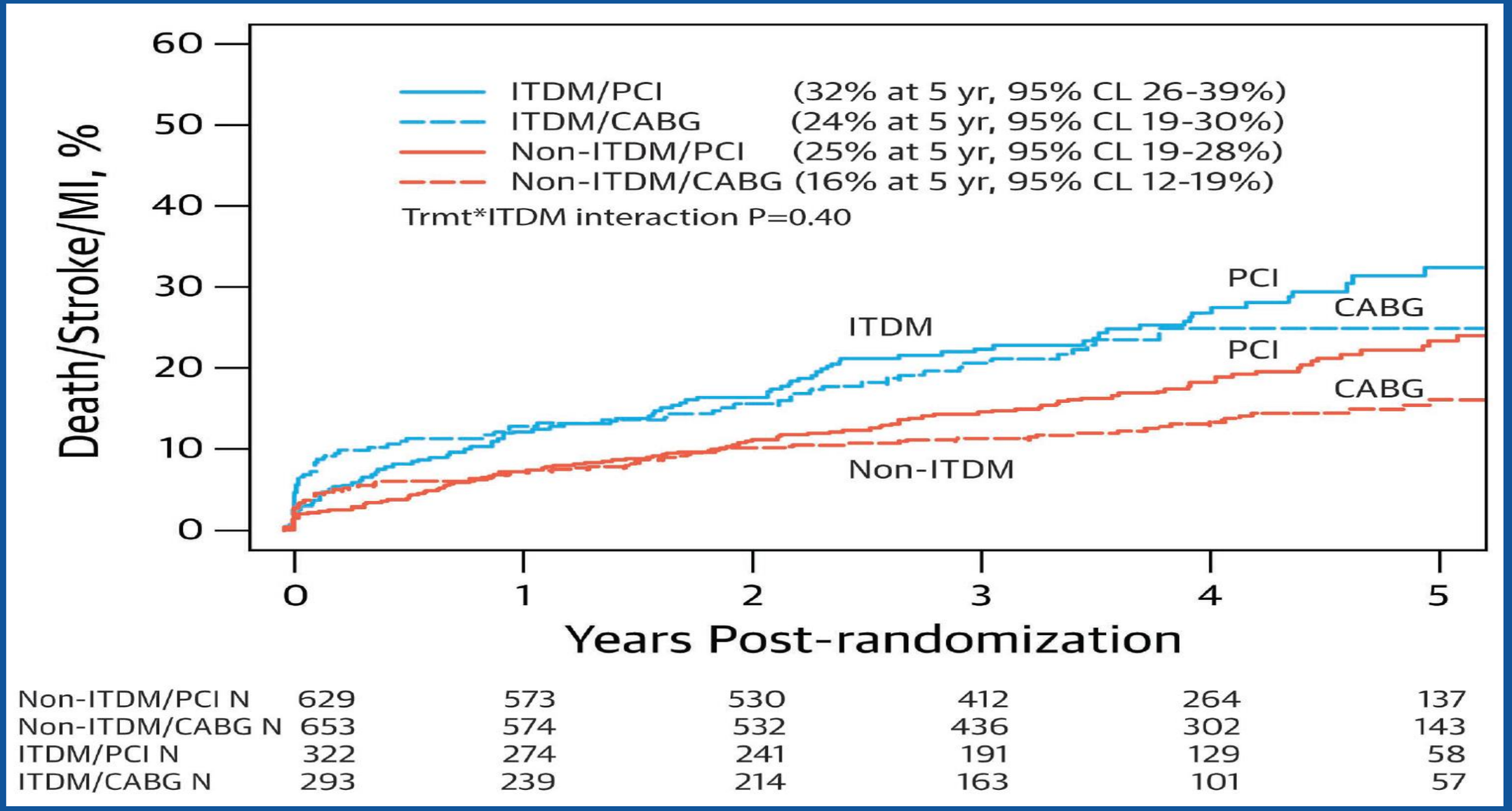
ONTARGET (J Redon et. al.)J ACC2012;59:74 – Microvasculature, Underperfusion ?
FREEDOM (M Farkoug, V Fuster) 2015 (In Press)

1e. Mortality in the ACCORD Population Over a Range of On-treatment HbA1c Values



ACCORD (MC Riddle et al) Circ 2010;122:844 - *Microvascular / Catecholamines ?*

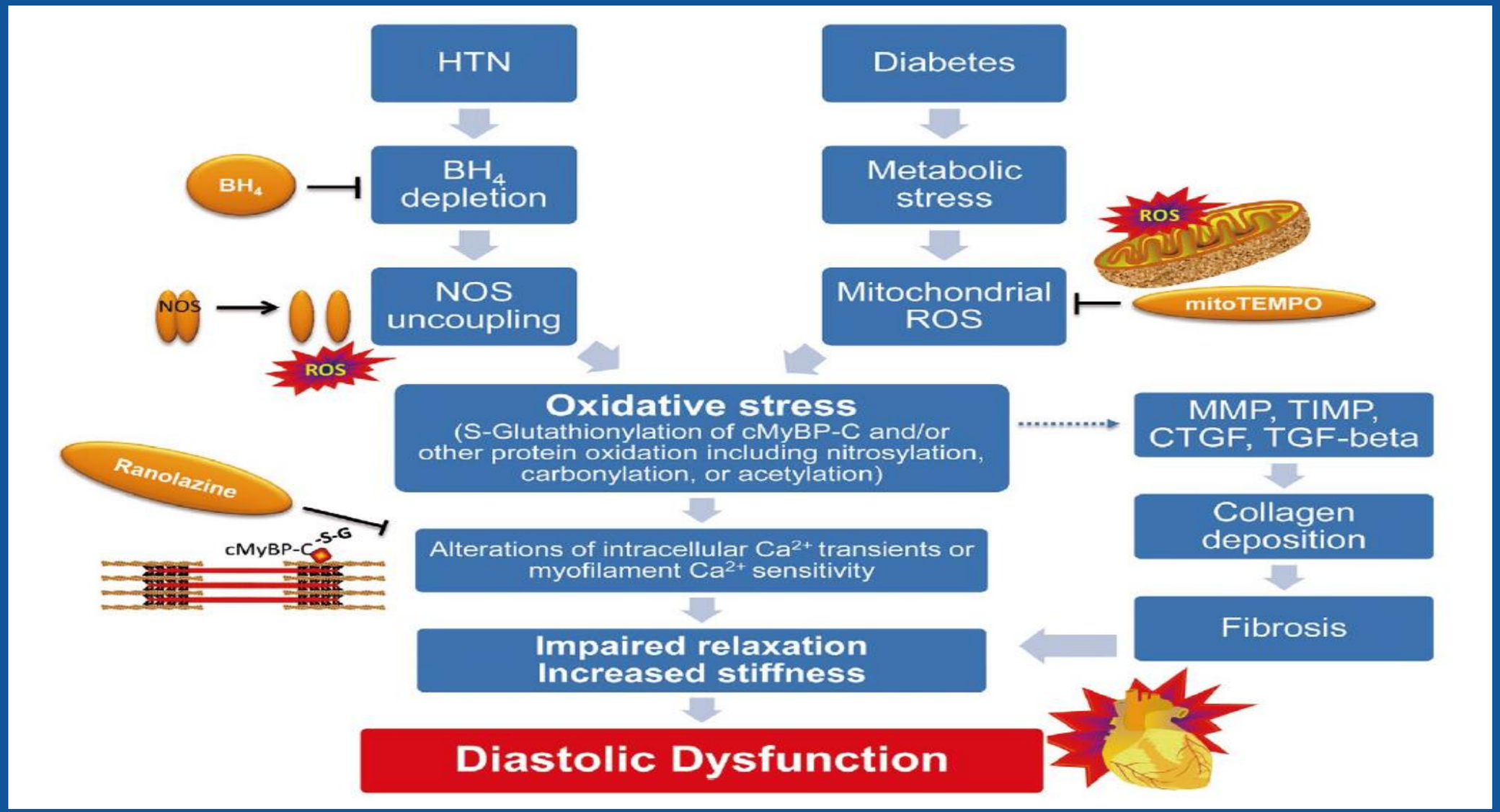
1f. PCI versus CABG in Insulin and Non-Insulin Treated Diabetic Patients: Results from the FREEDOM Trial



Non-ITDM/PCI N	629	573	530	412	264	137
Non-ITDM/CABG N	653	574	532	436	302	143
ITDM/PCI N	322	274	241	191	129	58
ITDM/CABG N	293	239	214	163	101	57

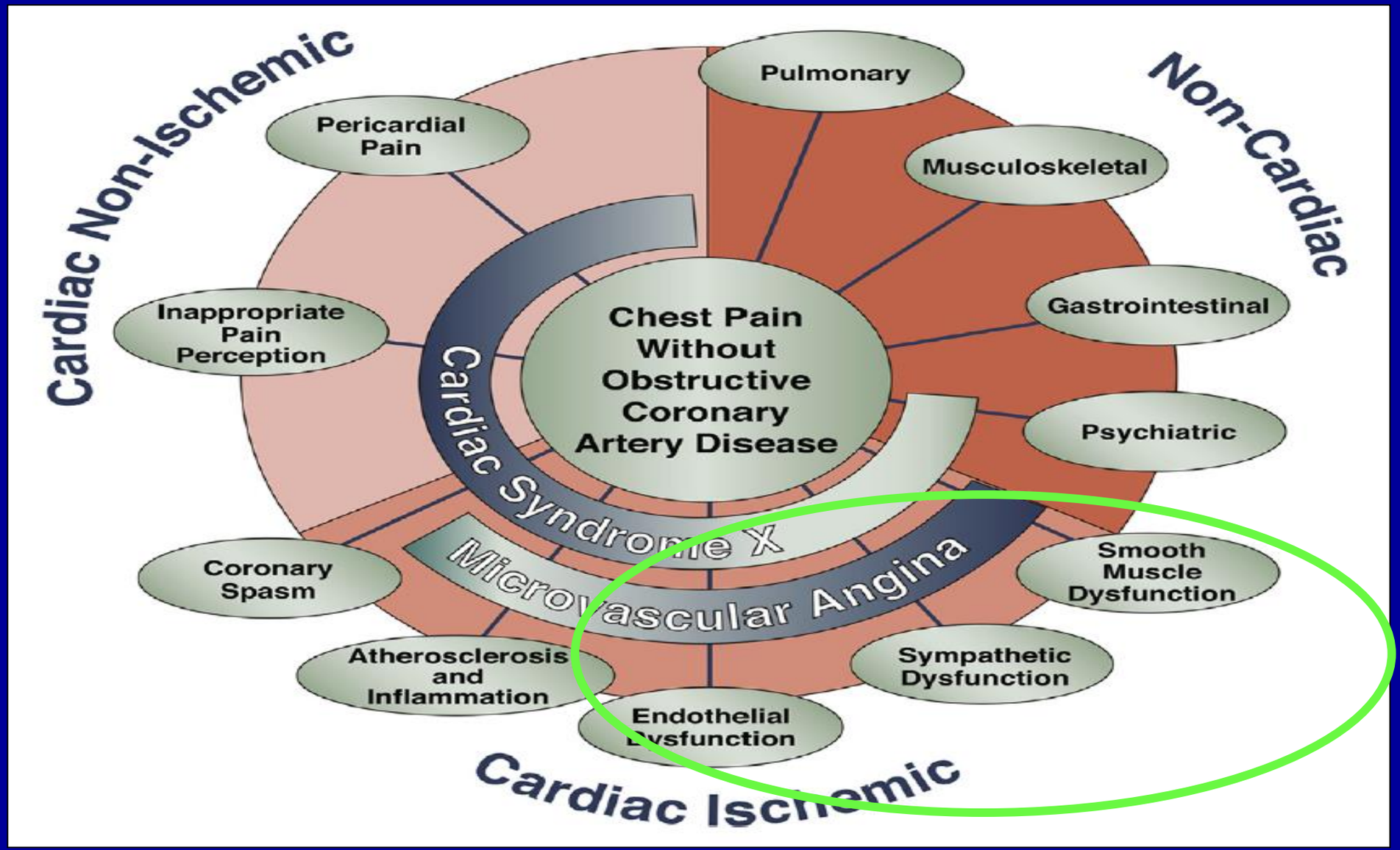
FREEDOM (GD Dangas, V Fuster et. al.) JACC 2014; 64: 1189

1g. Diastolic Dysfunction & Microcirculation



EM Jeong et. al. Circ J 2015; 79: 470

Etiologies of Chest Pain Without Obstructive CAD



MA Marinescu et. al. J Am Coll Cardiol Img 2015;8:210

COMPLEX, STABLE CORONARY DISEASE

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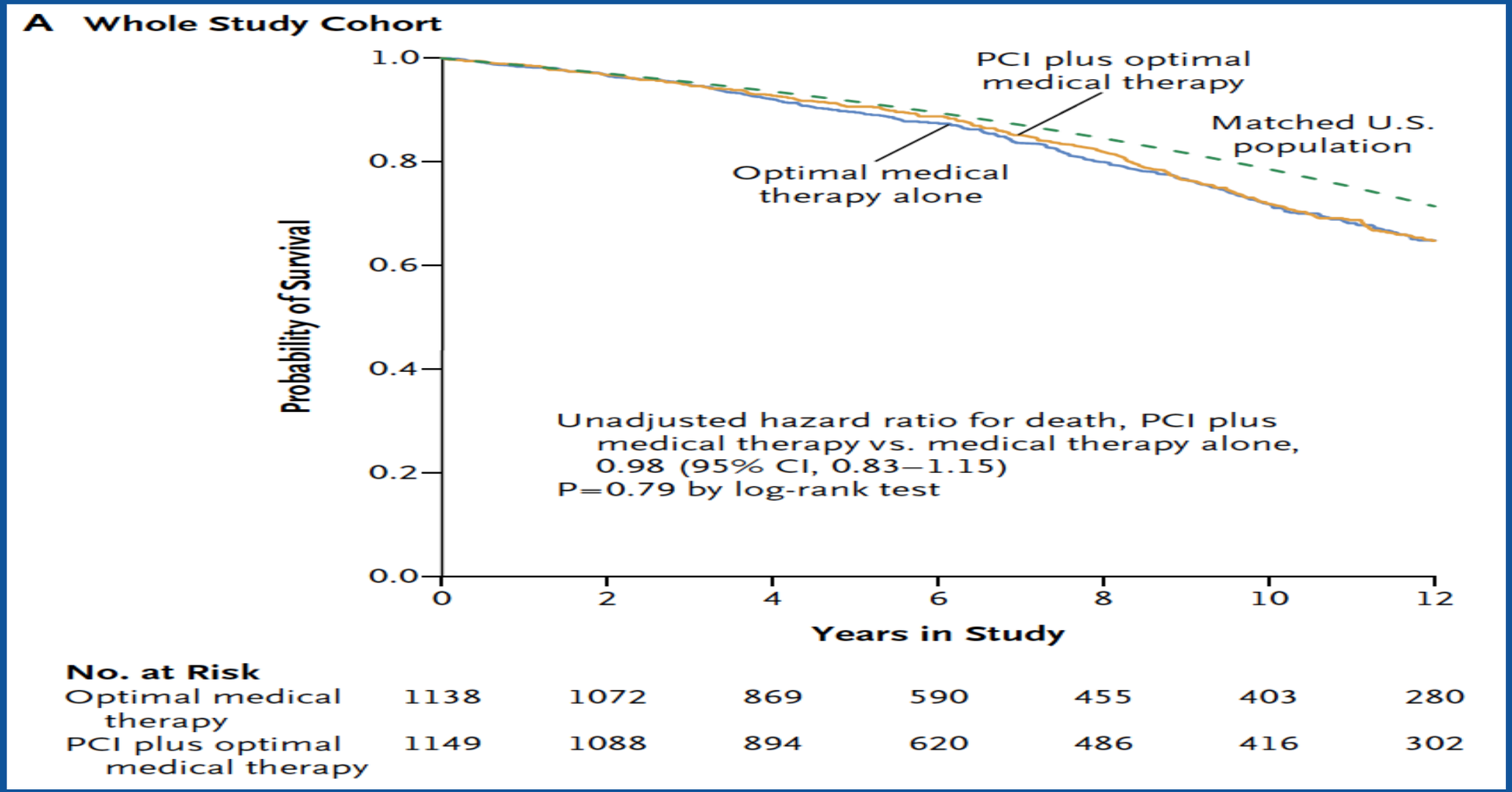
SYNTAX	+	-	++	-	++	CABG > PCI SYNTAX Score
						PCI "ISCHEMIA" Score
FAME	-	+	+	+	+	CABG / PCI = MT X.OV.ER 42%
COURAGE	-	-	+	+	+	PCI = MT "ISCHEMIA">10%-Events
FREEDOM	+	+	++	(+)	+	CABG > PCI No Freedom of Choice?

Conditions Methods-Interests Conclusions

PCI and Long-Term Survival in Patients with Stable Ischemic Heart Disease



No. at Risk							
Optimal medical therapy	1138	1072	869	590	455	403	280
PCI plus optimal medical therapy	1149	1088	894	620	486	416	302

COURAGE (SP Sedlis et. al.) NEJM 2015;373:1937

Effect of PCI on Long-Term Survival in Patients with Stable Ischemic Heart Disease

Extended survival information was available for 1211 patients -53% of the original population-. During an extended-follow-up of up to 15 years, we did not find a difference in survival between and initial strategy of PCI plus medical therapy and medical therapy alone in patients with stable ischemic heart disease.

COURAGE (SP Sedlis et al.) N Engl J Med 2015; 373:1937

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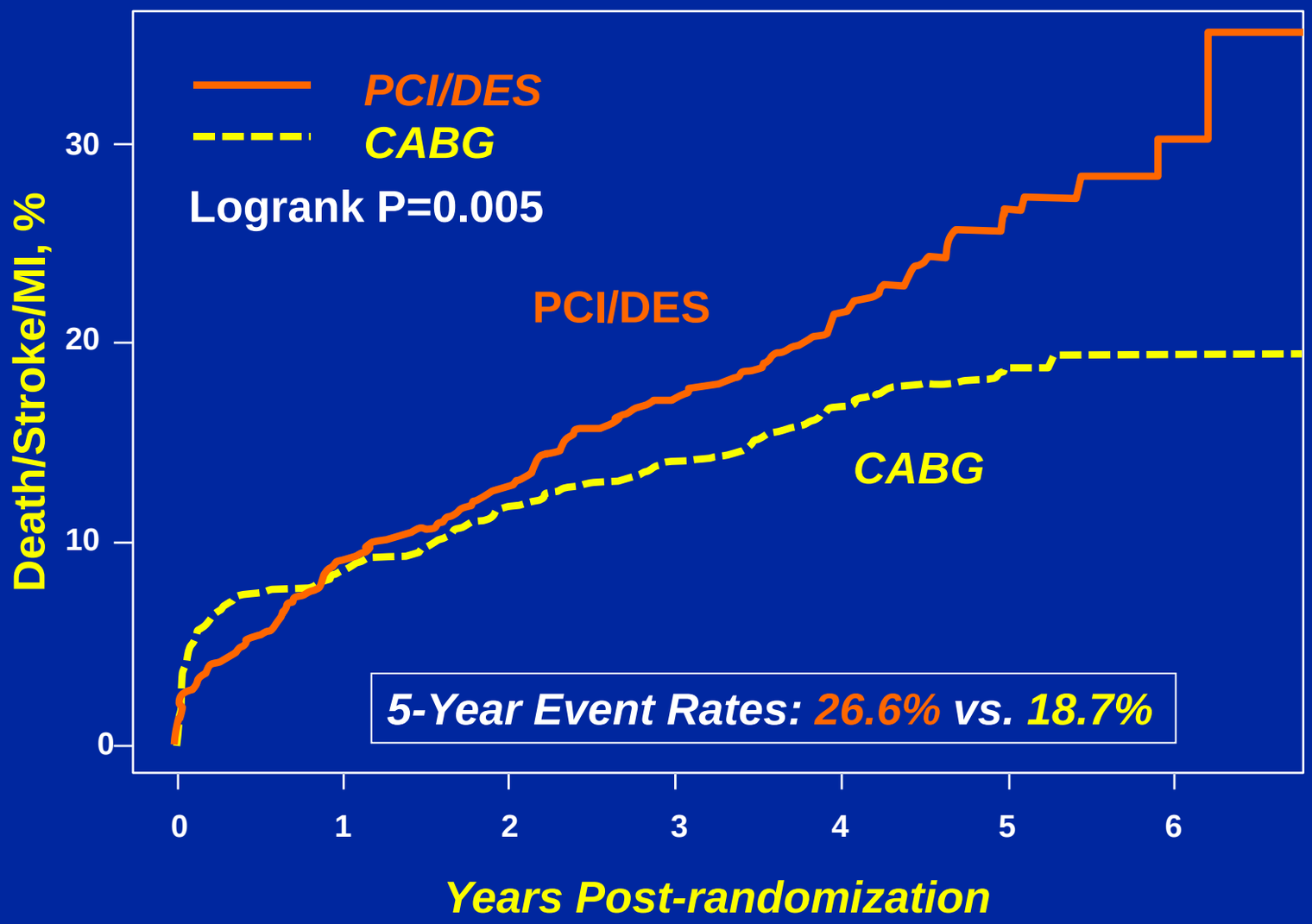
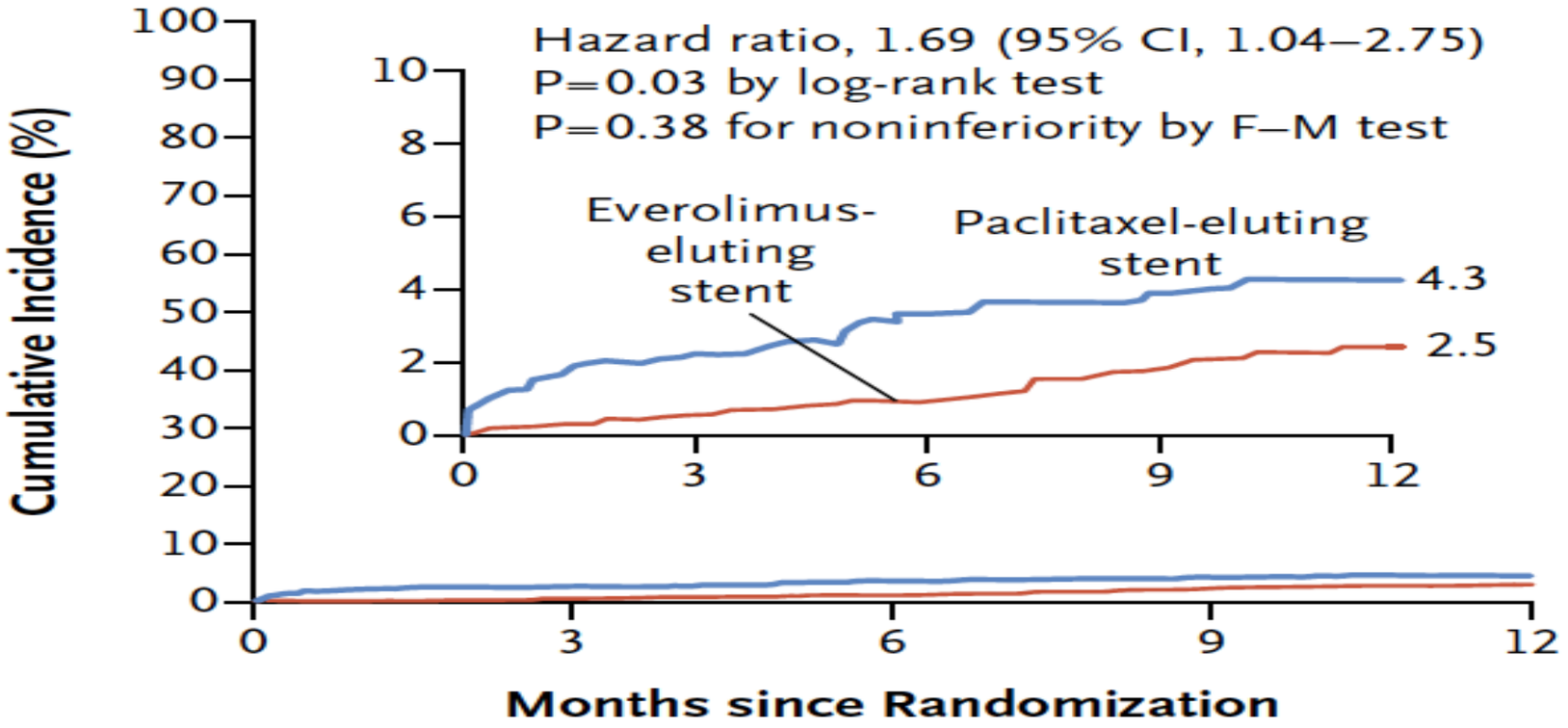
FREEDOM TRIAL – MI / DEATH / STROKE



New Engl. J. Med . 2012; 367: 2375 – All Subgroups (Syntax etc)
(Circ Cardiovasc Interv. 2014;7:518 – Newer Generation DES, Still Gap)

Paclitaxel-Eluting vs Everolimus-Eluting Coronary Stents in Diabetes

C Cardiac Death or Target-Vessel Myocardial Infarction



No. at Risk

Paclitaxel-eluting stent	914	843	824	798	723
Everolimus-eluting stent	916	857	849	825	739

TUXEDO-India (U Kaul et. al.) NEJM 2015;373:1709

ACC/AHA - Recommendations for CAD Revascularization In Patients with Diabetes

2012 Recommendation	2014 Focused Update Recommendations	Comments
Class IIa	Class I	
1. CABG is probably recommended in preference to PCI to improve survival in patients with multivessel CAD and diabetes mellitus, particularly if a LIMA graft can be anastomosed to the LAD artery.[58–65] *(Level of Evidence: B)*	1. A Heart Team approach to revascularization is recommended in patients with diabetes mellitus and complex multivessel CAD.[66] *(Level of Evidence: C)*	New recommendation
	2. CABG is generally recommended in preference to PCI to improve survival in patients with diabetes mellitus and multivessel CAD for which revascularization is likely to improve survival (3-vessel CAD or complex 2-vessel CAD involving the proximal LAD), particularly if a LIMA graft can be anastomosed to the LAD artery, provided the patient is a good candidate for surgery.[58–69] *(Level of Evidence: B)*	Modified recommendation (Class of Recommendation changed from IIa to I, wording modified, additional RCT added).

Circulation. 2014;130:1749

Recommendations	Class[a]	Level[b]	Ref[c]
In patients presenting with STEMI, primary PCI is recommended over fibrinolysis if it can be performed within recommended time limits.	I	A	363
In patients with NSTE-ACS, an early invasive strategy is recommended over non-invasive management.	I	A	180,338, 364–366
In stable patients with multivessel CAD and/or evidence of ischaemia, revascularization is indicated in order to reduce cardiac adverse events.	I	B	93,367
In patients with stable multivessel CAD and an acceptable surgical risk, CABG is recommended over PCI.	I	A	106,175,349
In patients with stable multivessel CAD and SYNTAX score ≤22, PCI should be considered as alternative to CABG.	IIa	B	346,350
New-generation DES are recommended over BMS.	I	A	351,352
Bilateral mammary artery grafting should be considered.	IIa	B	368
In patients on metformin, renal function should be carefully monitored for 2 to 3 days after coronary angiography/PCI.	I	C	

Specific Recommendations For Revascularization In Patients With Diabetes

*The Task Force on Myocardial Revascularization of the **ESC and the EACTS***
(S Windecker et. al.) Eur Heart J. 2014;35:2541

Patient-level Pooled-Analysis of the BARI 2D, COURAGE and FREEDOM Trials

Comparative Assessment of Medical Therapy, PCI, or CABG on Clinical Outcomes in Diabetic Patients with Stable CAD According Angiography and LV Function

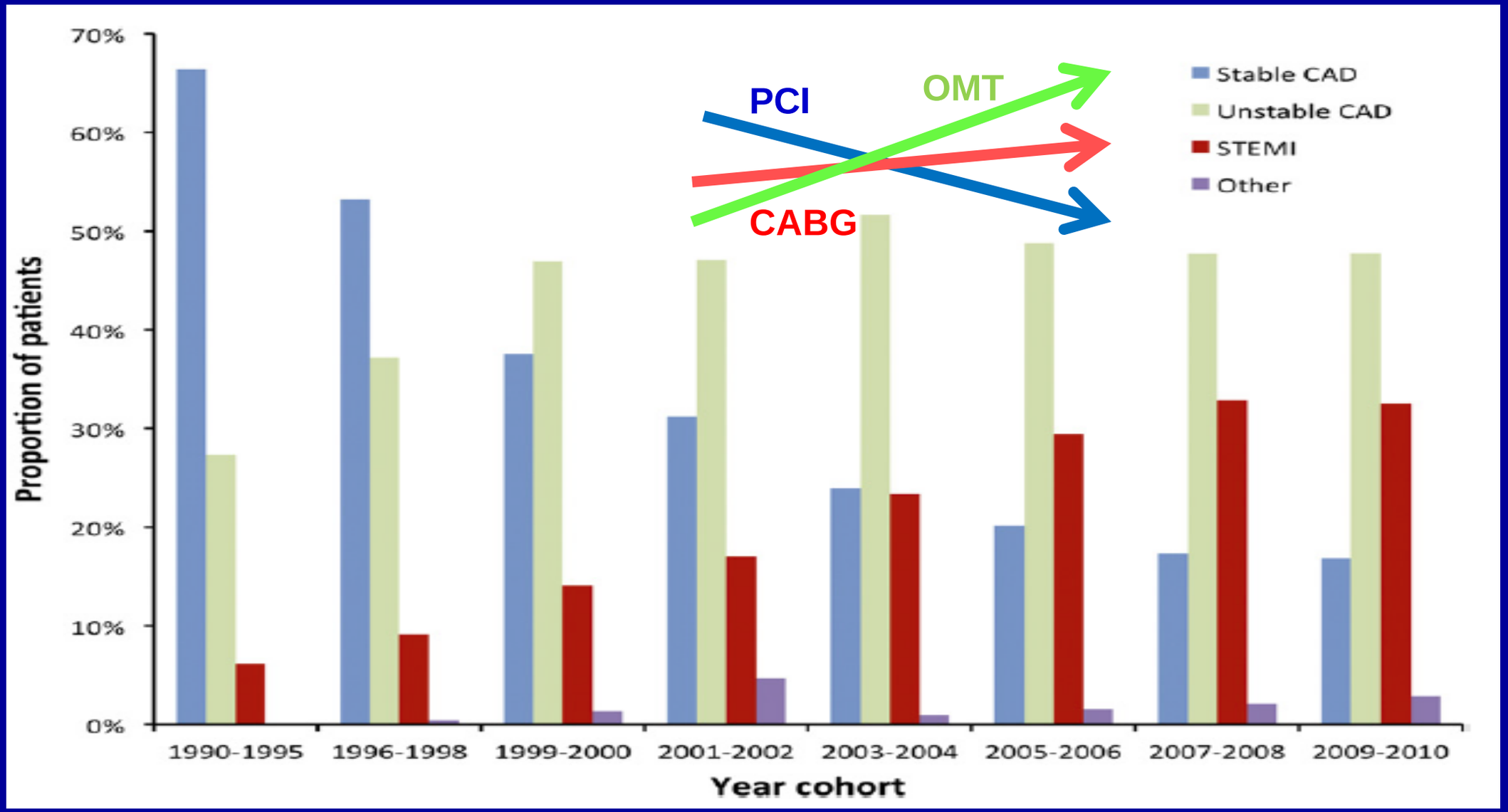
GBJ Mancini, ME Farkouh, BR Chaitman,
WE Boden, RL Frye, PM Hartigan, H Vlachos,
FS Siami, MS Sidhu, VA Bittner, V Fuster, MM Brooks

AHA Annual Scientific Sessions, Orlando 2015

Patients with T2DM and SIHD:

- ***All comparisons between OMT and PCI + OMT were neutral***
- ***CABG + OMT compared with PCI + OMT reduced the risk of the primary composite of death, MI or stroke by 35%***
- ***These results were noted especially in patients with 2- and 3-vessel disease, whether the pLAD was involved or not and with preserved EF***
- ***There was a strong indication of similar benefit with 1-vessel/LAD disease or with EF < 50%***

Future For PCI / CABG – OMT ADHERENCE



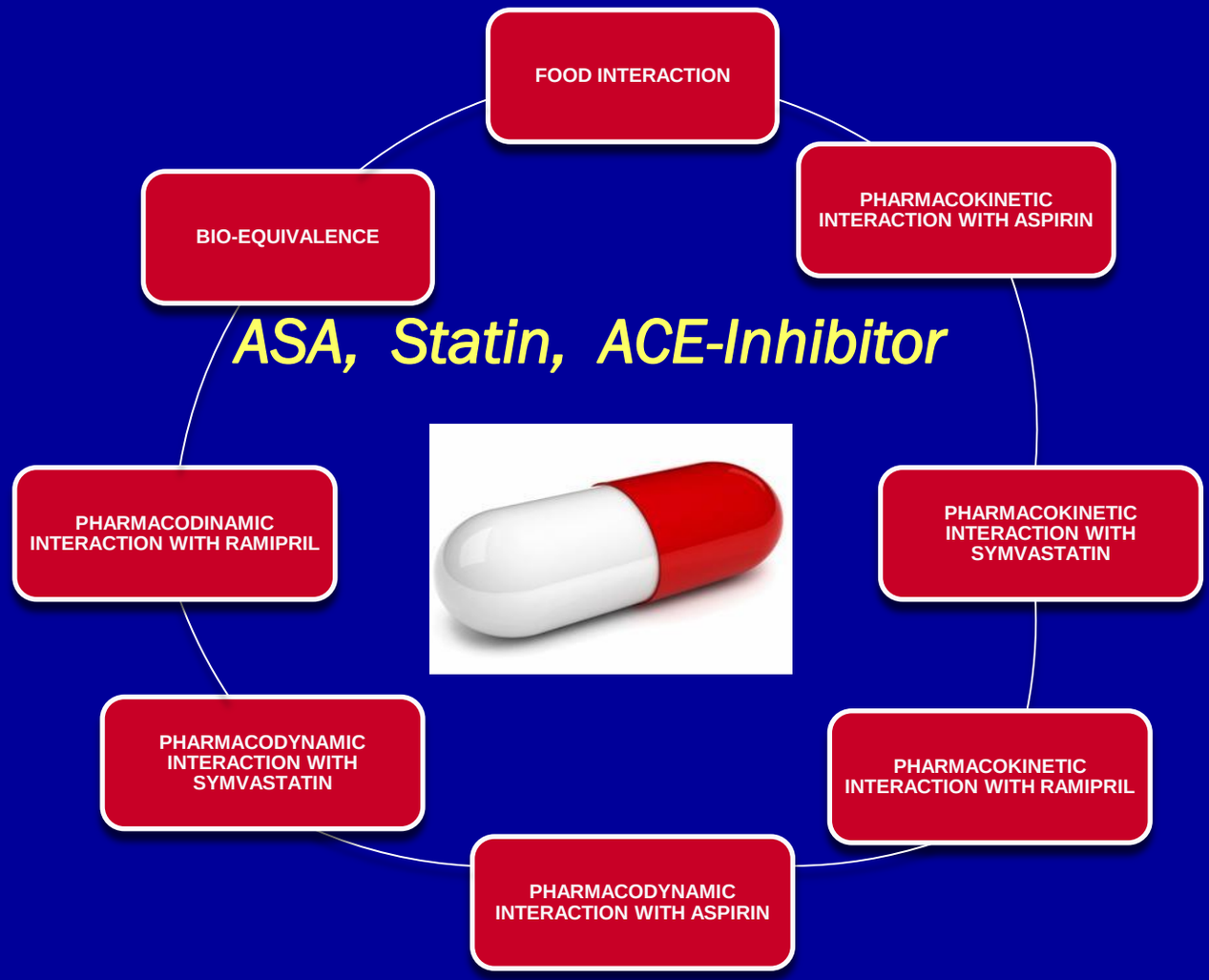
SCAAR (ML Fokkema et.al.) JACC 2013;61:1222 - Swedish Registry (VF.Modified)
Diabetes Trialists' Collaboration – 2015 (In Press)- FREEDOM, BARI 2D, COURAGE

2. CV Drugs Underuse - Polypill, 2ary Prevention.

FOCUS 1 & 2

- Argentina
- Brazil
- Paraguay
- Italy
- Spain

FREEDOM
AETNA-DIABETES
SECURE-EC 2015



Am. H J 2011;162:811

Semin.Thor.Cardiov.Surg 2011;23:24

JACC, 2014; 64:2071

Approved in 22 Countries

*** Valentín Fuster (inventor)**

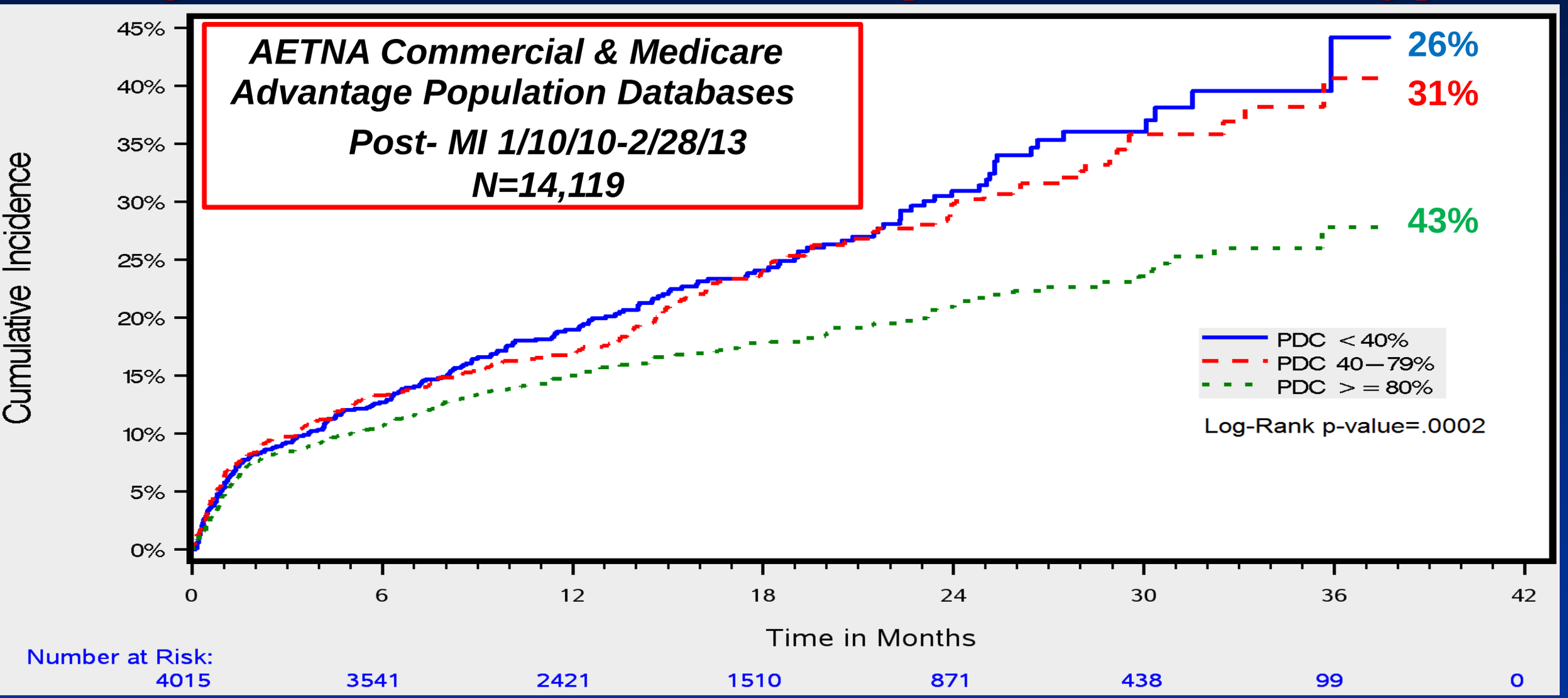
2a. ADHERENCE FOR RISK FACTOR CONTROL?

Risk Factors - Proportion of Participants at Goal % – 1 year

Trials	LDL	SBP	DBP	Hb A1C	Meet Goals Base	Meet Goals FU
BARI-2D	75	56	70	52	14	20
COURAGE	51	55	55	59	12	19
FREEDOM	55	63	53	55	12	20

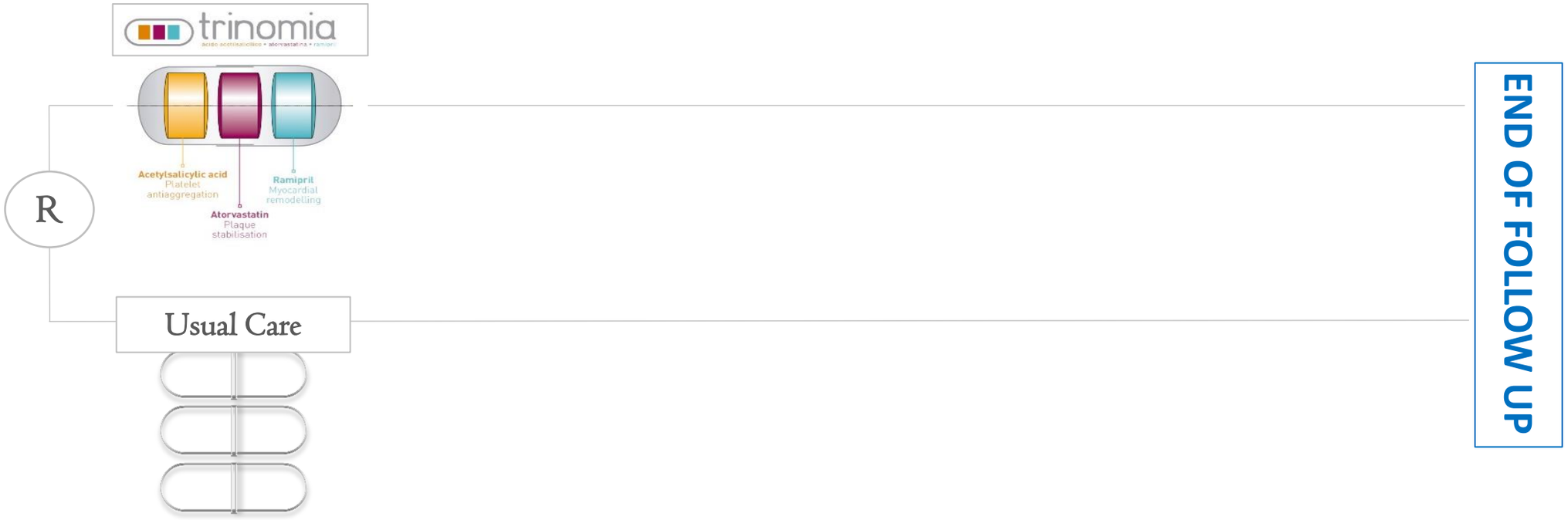
Freedom, Bari-2D, Courage Investigators, JACC 2013;61:1607
PURE (S Yusuf et al.) Lancet 2011; Aug 28 - Poor Countries,7% !!!
NHANES, AHA, NHLBI-JNC-7, NHLBI-NCEP – Significant < Adherence
P Muntner, V Fuster et al., AHJ 2011; 161: 719 – 49 seconds !!!!

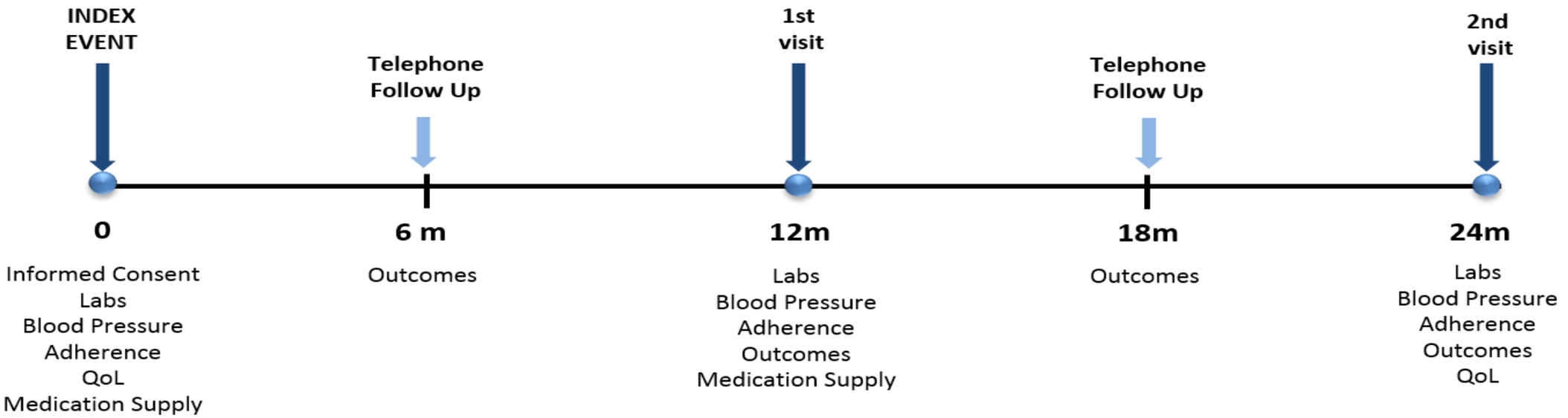
2b. Time to Major CV Event by Adherence Levels (Post-MI Study)



Sameer Bansilal et al.: ESC 2014 Registry Hotline Aug 31, 2014

2c. SECURE | Visiting Schema





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2010's[1]. PCI <, CABG > (DM), Microc., OMT

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ACC - New York, Dec. 11, 2015

No Disclosures

CABG Versus PCI

Greater Benefit in Long-Term Outcomes With Multiple Arterial Bypass Grafting

Robert H. Habib, PhD,*†‡ Kamellia R. Dimitrova, MD,§ Sanaa A. Badour, MD,† Maroun B. Yammine, MD,† Abdul-Karim M. El-Hage-Sleiman, MD,† Darryl M. Hoffman, MD,§ Charles M. Geller, MD,§ Thomas A. Schwann, MD,‖ Robert F. Tranbaugh, MD§

The Choice of Conduits in Coronary Artery Bypass Surgery

Mario Gaudino, MD,*† David Taggart, PhD,‡ Hisayoshi Suma, MD,§ John D. Puskas, MD,‖ Filippo Crea, MD,† Massimo Massetti, MD†

J Am Coll Cardiol 2015;66:1417 - J Am Coll Cardiol 2015;66:1729

FFR vs Angiography for Guidance of PCI in Multivessel CAD, 5-Year Follow-up

In the FAME study, FFR-guided PCI improved outcome compared with angiography-guided PCI for up to 2 years of follow-up. The aim in this study was to investigate whether the favourable clinical outcome with the FFR-guided PCI in the FAME study persisted over a 5-year follow-up. The results confirm the long-term safety of FFR-guided PCI in patients with multivessel disease. A strategy of FFR-guided PCI resulted in a significant decrease of major adverse cardiac events for up to 2 years after the index procedure. From 2 years to 5 years, the risks for both groups developed similarly. This clinical outcome in the FFR-guided group was achieved with a lower number of stented arteries and less resource use. These results indicate that FFR guidance of multivessel PCI should be the standard of care in most patients.

FAME (LX van Nunen et al.), The Lancet 2015; 386:1853

FRACTIONAL FLOW RESERVE - STATEMENTS

1. **Blood flow across a coronary stenosis during maximum vasodilation, divided by expected blood flow in its absence.**
2. **Measured with pressure sensors as the ratio of distal coronary to aortic pressure during maximum vasodilation, and expressed as %.**
3. **FFR of less than 75% is highly correlated with ischaemia.**
4. **FFR of 75-80% is the grey zone and might be associated with ischaemia and predictive of need for revascularization.**
5. **FFR of less than 80% was regarded as significant in FAME and treated with coronary stenting.**

FAME (LX van Nunen et al., The Lancet 2015; 386:1853