Reflections on the Ideal Stratification Tool: Beyond the SYNTAX score

Corrado Tamburino, MD, PhD

Full Professor of Cardiology, Director of Postgraduate School of Cardiology
Chief Cardiovascular Department, Director Cardiology Division, Interventional Cardiology and Heart Failure Unit, University of Catania, Ferrarotto Hospital, Catania, Italy

Disclosure statement of financial interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below

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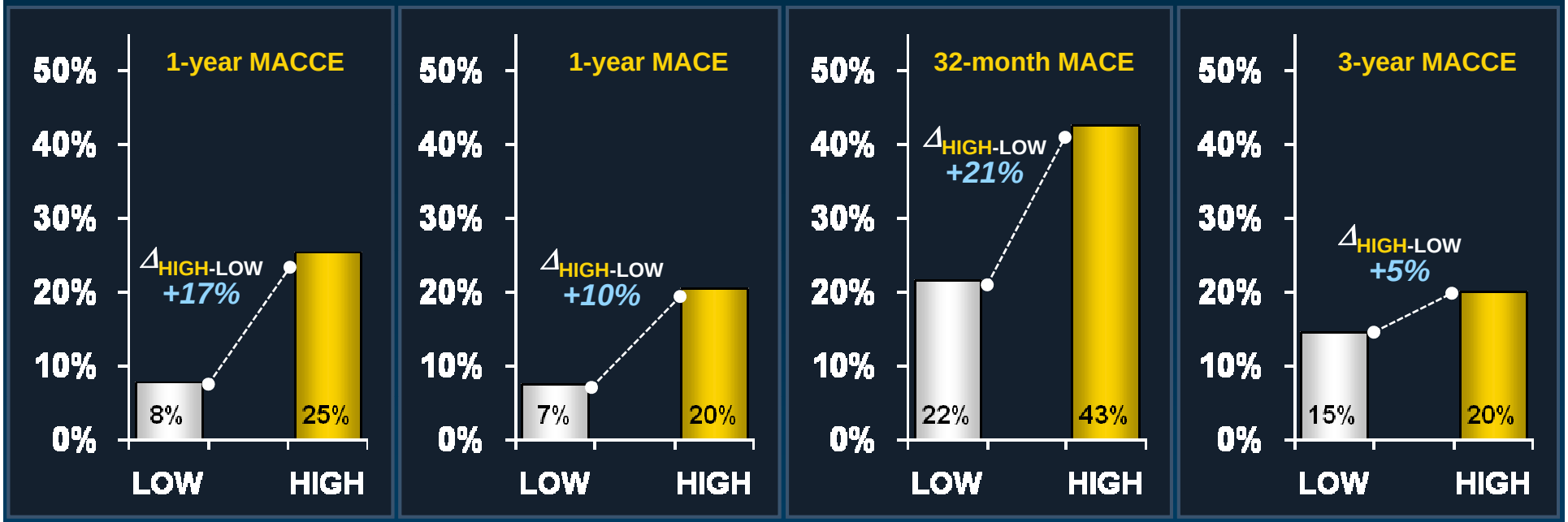
Integrating the Synergy between percutaneous coronary intervention with Taxus and Cardiac Surgery (SYNTAX) score into practice: Use, pitfalls, and new directions

Davide Capodanno, MD,[a,b] and Corrado Tamburino, MD, PhD[a,b] *Catania, Italy*

Risk stratification is key in optimizing care of patients undergoing percutaneous coronary intervention (PCI). Score algorithms, in particular, are useful prognostic tools to select the most appropriate strategy of treatment and help patients and their families to get a better understanding of issues relevant to treatment strategies and subsequent risks. Most scores tested in the setting of PCI focus on clinical variables. The SYNTAX score is a semiquantitative angiographic score developed to prospectively characterize the disease complexity of the coronary vasculature. This scoring system has recently been assessed in numerous cohorts of patients undergoing coronary revascularization by PCI or bypass surgery. When using the SYNTAX score, however, physicians are still challenged with a labor-intensive calculation and conflicting results from validation studies. Understanding how the SYNTAX score works, for which patients it works best, and whether it predicts accurately enough for its purpose is of paramount importance to get the maximum benefit from its application. The present article provides an overview of the background and the currently available evidences on the use of the SYNTAX score in patients undergoing coronary revascularization along with its limitations. (Am Heart J 2011;161:462-70.)

Fact #1 –The SYNTAX score usefully discriminates MACE and MACCE between patients at low risk and those at high risk in patients undergoing left main PCI



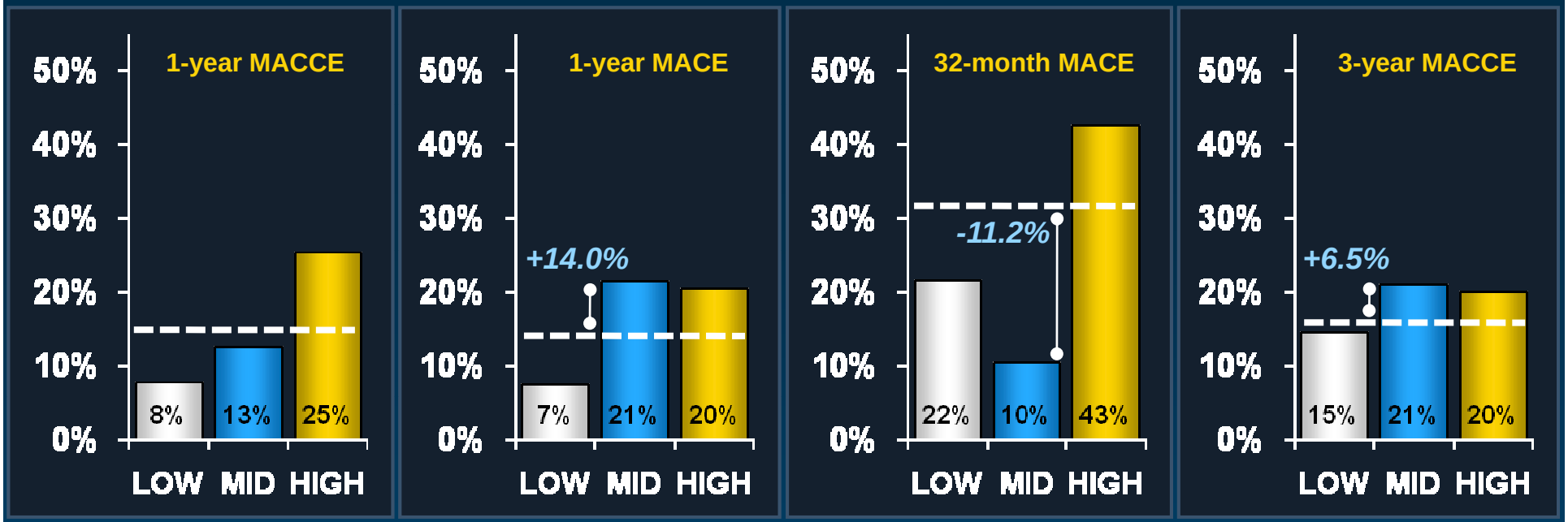
SYNTAX
Circulation 2010

Capodanno et al.
Circ Card Interv 2009

Brito et al.
EuroPCR 2010

MAIN COMPARE
JACC Interv 2010

Fact #2 – In observational registries, the intermediate tertile is frequently poorly calibrated with respect to the outcomes of the high and low tertiles



SYNTAX
Circulation 2010

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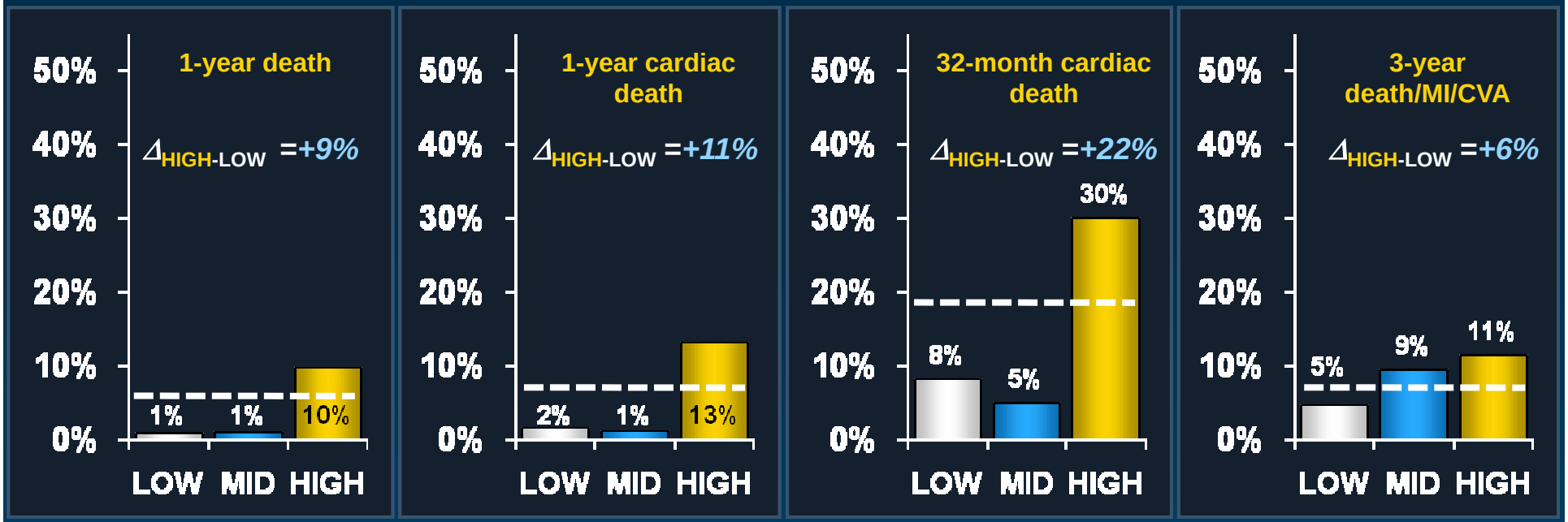
EuroPCR 2010

MAIN COMPARE
JACC Interv 2010

Expected risk for the intermediate stratum

Fact #3 – The SYNTAX score is also a good predictor of hard events but, once again, the intermediate stratum is frequently not well calibrated



SYNTAX
Circulation 2010

Capodanno et al.
Circ Card Interv 2009

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MAIN COMPARE
JACC Interv 2010

– – – – – Expected risk for the intermediate stratum

Indications for CABG vs PCI in stable patients with lesions suitable for both procedures and low predicted surgical mortality

Subset of CAD by anatomy	Favours CABG	Favours PCI
1VD or 2VD – non proximal LAD	IIb C	I C
1VD or 2VD – proximal LAD	I A	IIa B
3VD simple lesions, full functional revascularization achievable with PCI, SYNTAX score ≤ 22	I A	IIa B
3VD complex lesions, incomplete revascularization 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, bifurcation)	I A	IIb B
Left main + 2VD or 3VD, SYNTAX score ≤ 32	I A	IIb B
Left main + 2VD or 3VD, SYNTAX score ≥ 33	I A	III B

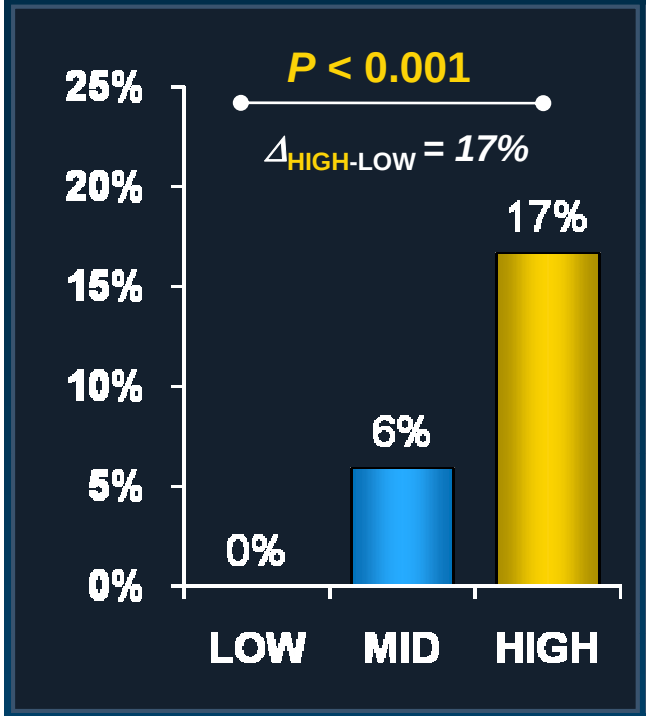
Prognostic models cannot be fully appreciated without the use of Discrimination and Calibration

- **Discrimination** is the probability that the test will assign higher values of risk to patients who will go on to have events compared with those who will not. It is measured with the c-statistic, which ranges from 0.50 (no discrimination) to 1.0 (perfect discrimination).
- **Calibration** is the ratio of predicted risk to observed risk. It is measured with the Hosmer Lemeshow test (the lower, the better).

Cardiac death to 24 months by EuroSCORE, ACEF and SYNTAX score strata

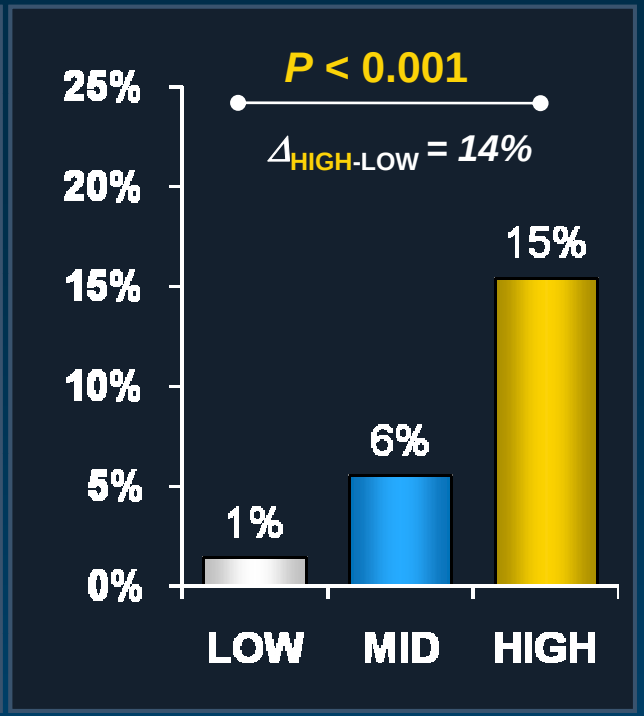
PCI cohort (n = 400)

EuroSCORE



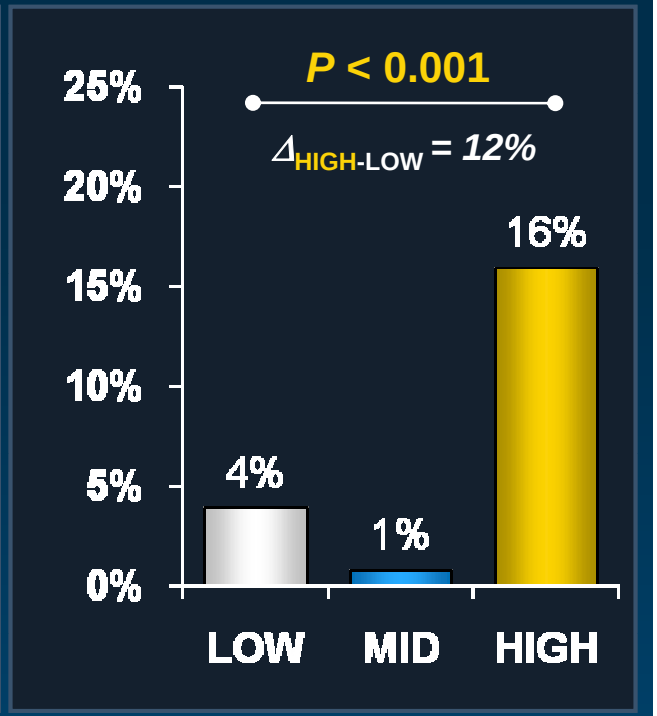
Hosmer-Lemeshow: 1.607 ☹
c-statistic: 0.69 😐

ACEF score



Hosmer-Lemeshow: 0.216 ☺
c-statistic : 0.69 😐

SYNTAX score

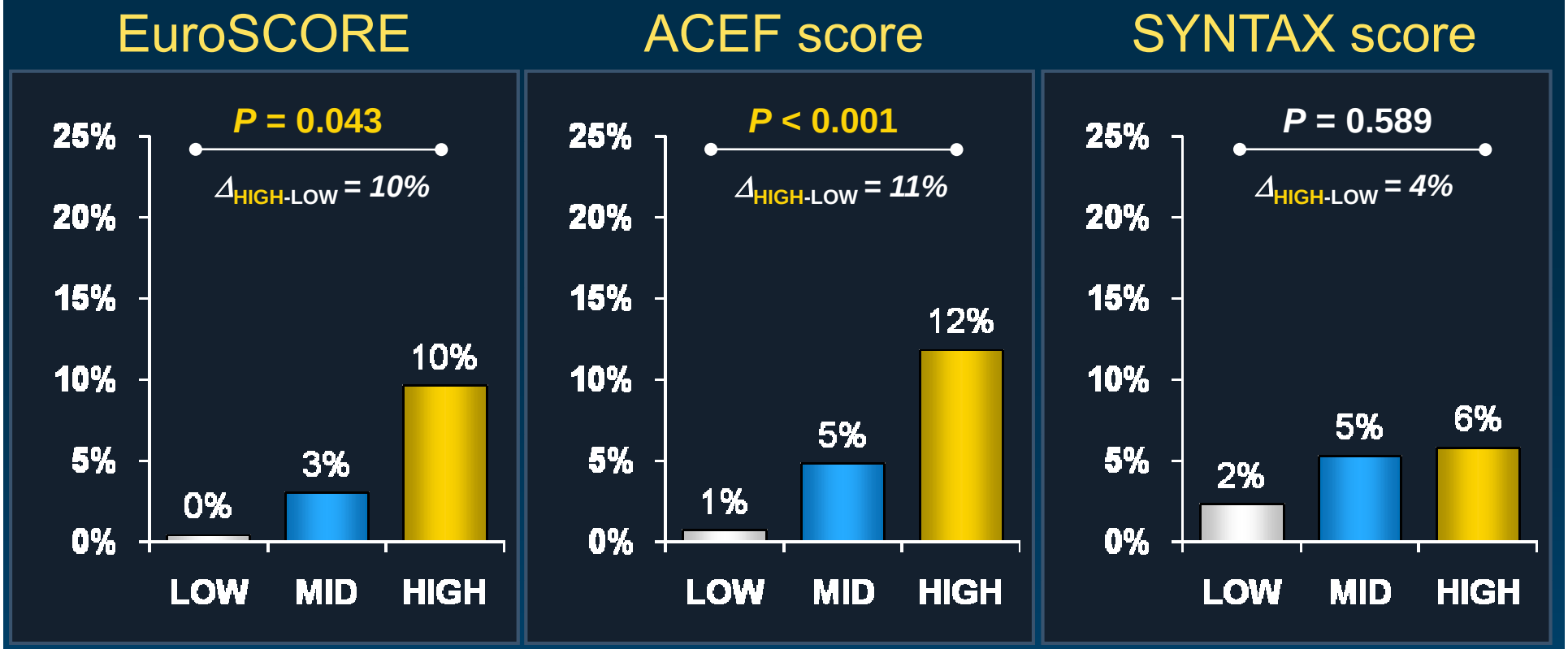


Hosmer-Lemeshow: 2.448 ☹
c-statistic : 0.73 ☺

Capodanno, et al. *JACC Interv* 2011;4:287-97

Cardiac death to 24 months by EuroSCORE, ACEF and SYNTAX score strata

CABG cohort (n = 549)



Hosmer-Lemeshow: 0.321 ☺
c-statistic: 0.62 ☹

Hosmer-Lemeshow: 0.426 ☺
c-statistic: 0.74 ☺

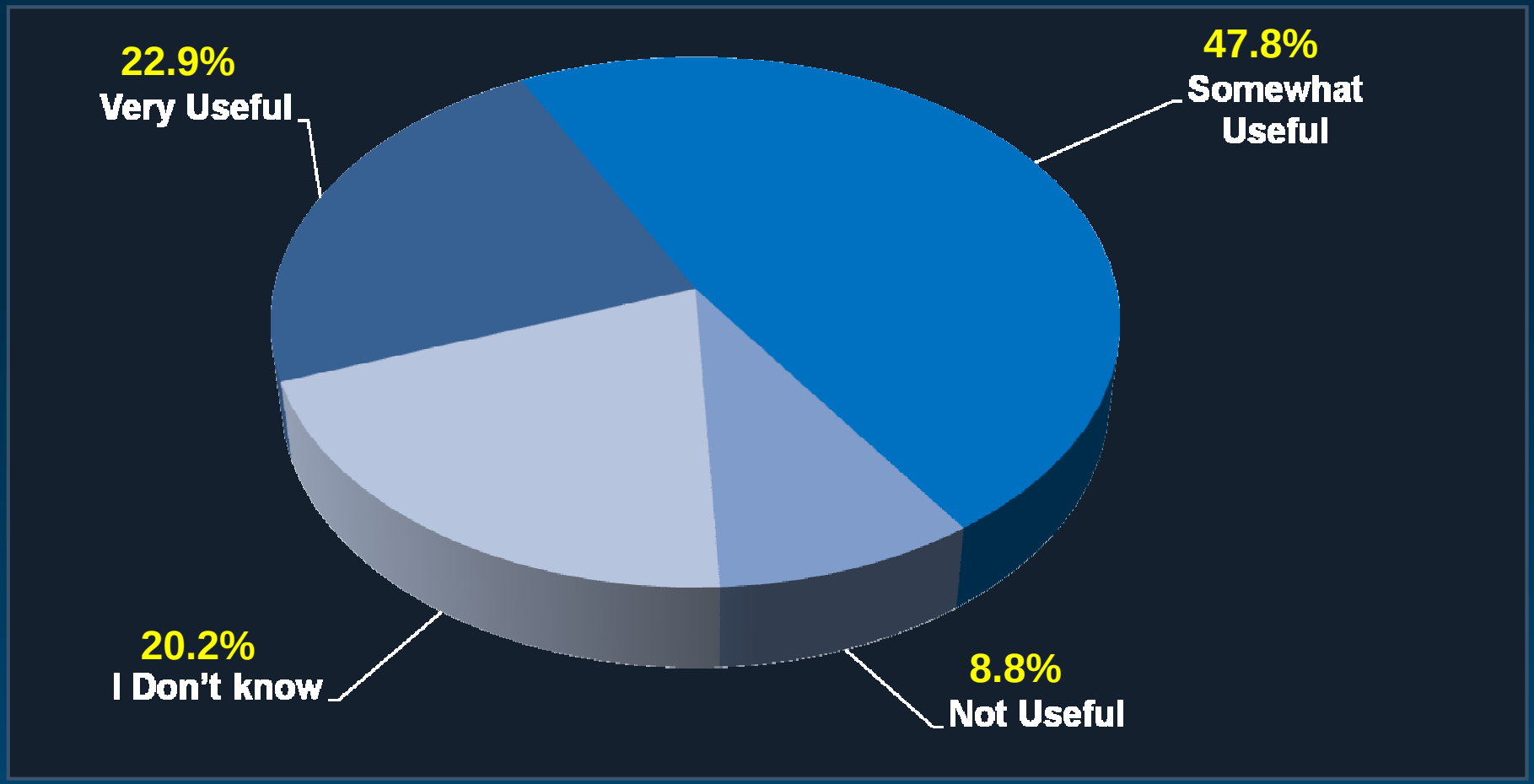
Hosmer-Lemeshow: 0.098 ☺
c-statistic: 0.56 ☹

Capodanno, et al. *JACC Interv* 2011;4:287-97

Pitfalls and issues relevant to SYNTAX score application in clinical practice

- **Does not include any subset of lesions** (i.e. in-stent restenosis, stenotic bypass grafts, coronary anomalies, muscular bridges, aneurysms)
- **Time-consuming**
- Interobserver and intraobserver **variability**
- **Does not account for clinical or procedural variables** that are known for impacting the outcomes during and after PCI

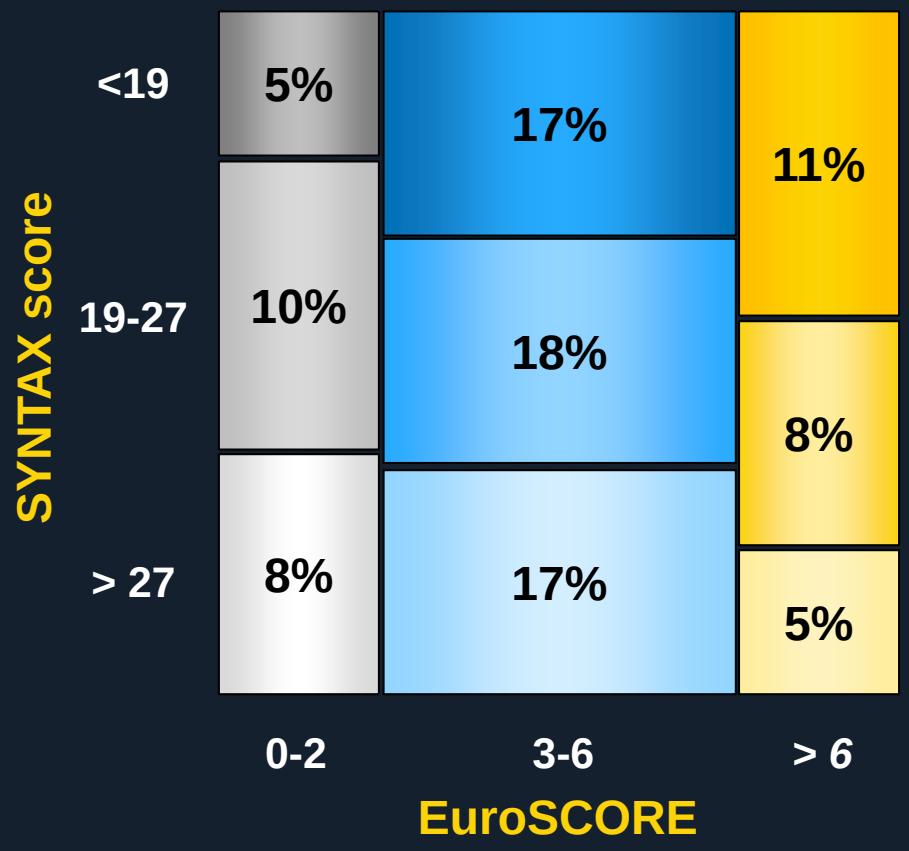
If you have used the SYNTAX score, how would you rate its worth as a clinical tool?



A sample of comments from TCTmd.com readers who took the survey

- "It gives us information we already know"
- "The concept is more practical than the score"
- "An app would be helpful so computer use in the cath lab isn't necessary"
- "It is a useful but incomplete tool"
- "A clinical Syntax score is needed"

Why do we need both clinical and angiographic variables?



Clinical and angiographic scores summarize very different information in 255 patients with unprotected LM

Low Spearman rank correlation coefficient between SYNTAX score and EuroSCORE (R_S=0.204, p = 0.001)

The frequency of patients for each cross-tabulation cell is shown within a rectangle that is proportional in size to the frequency

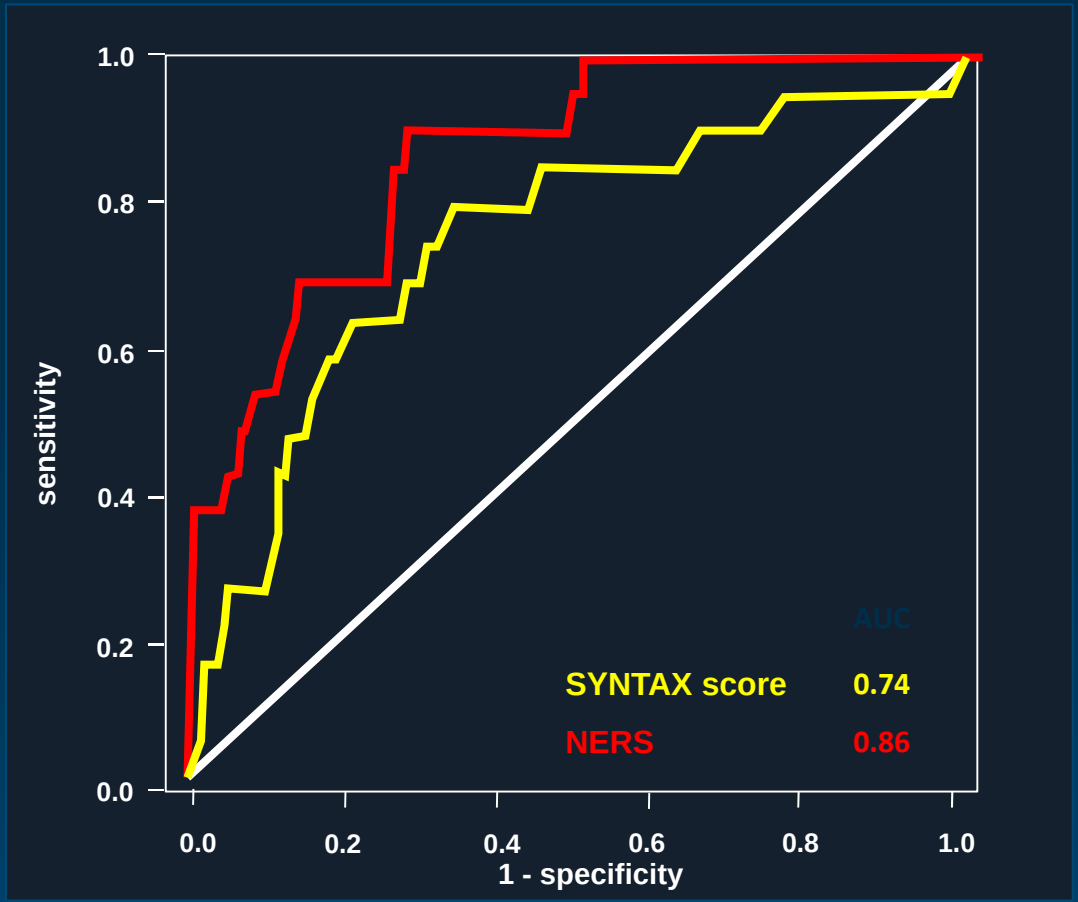
The New Risk Stratification (NERS)

NERS = 17 clinical, 4 procedural, and 33 angiographic variables = 54

ROC curve for cardiac mortality of 337 LM patients

Significant differences in AUC versus SYNTAX score for cardiogenic death, MI, TVR, ST and MACE

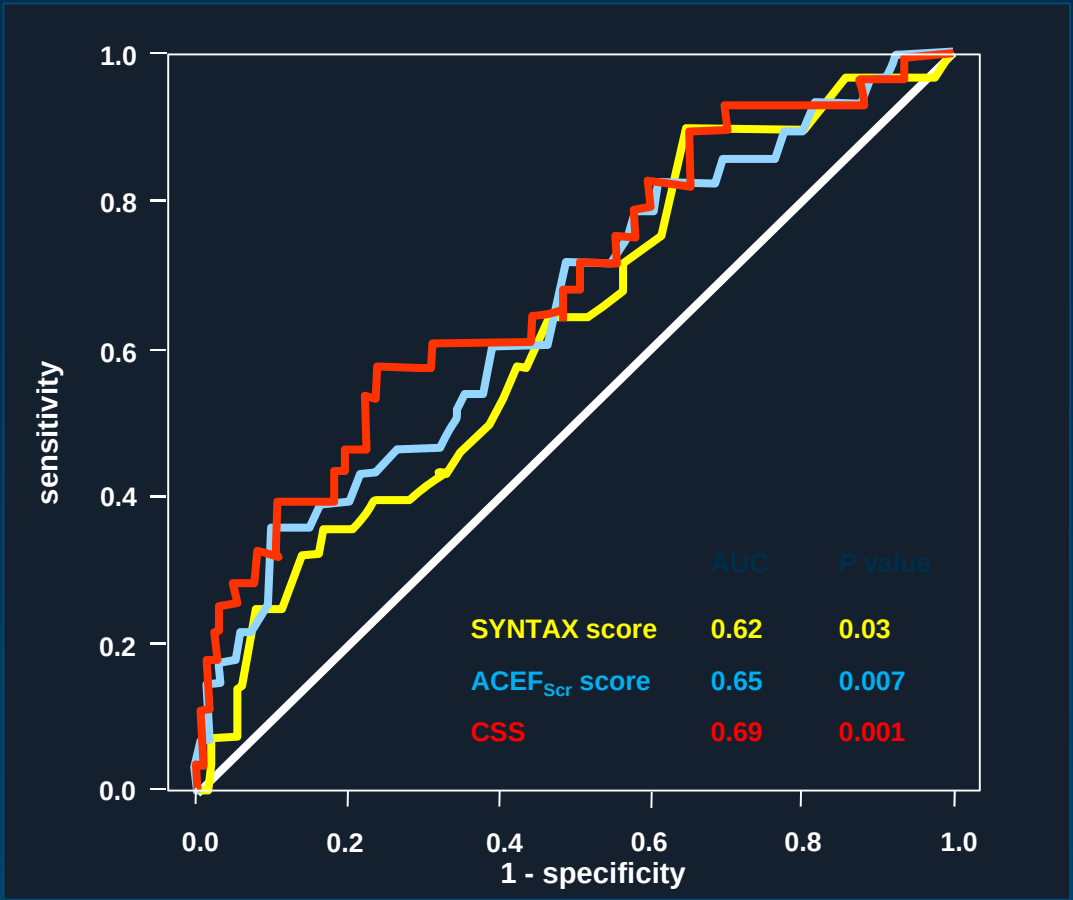
Comprehensive but labor intensive, needs 4 procedural variables. Utility in decision making needs to be further elucidated



Chen et al, *JACC Cardiovasc Interv* 2010;3:632-41

The Clinical SYNTAX score (CSS)

Clinical SYNTAX score = **SYNTAX score** * **$ACEF_{Scr}$**



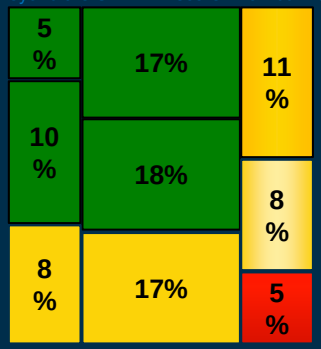
ROC curve for 5-year mortality of 512 MVD patients enrolled in the ARTS II study

High potential for improving risk prediction in LM

No external validation yet to support this hypothesis

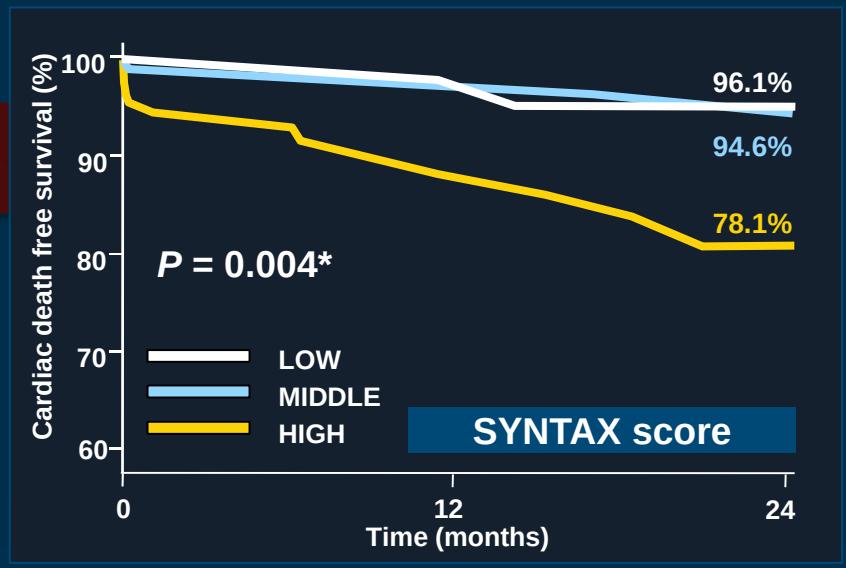
Garg et al, *Circ Cardiovasc Interv* 2010;159:103-9

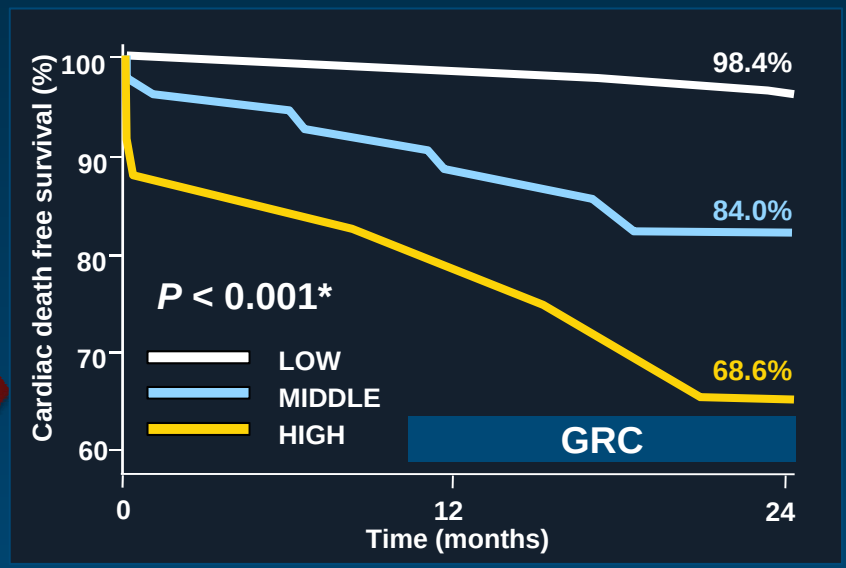
The Global Risk Classification (GRC)



EuroSCORE	SYNTAX score < 19	SYNTAX score 19-27	SYNTAX score > 27
0-2	L	L	I
3-6	L	L	I
> 6	I	I	H

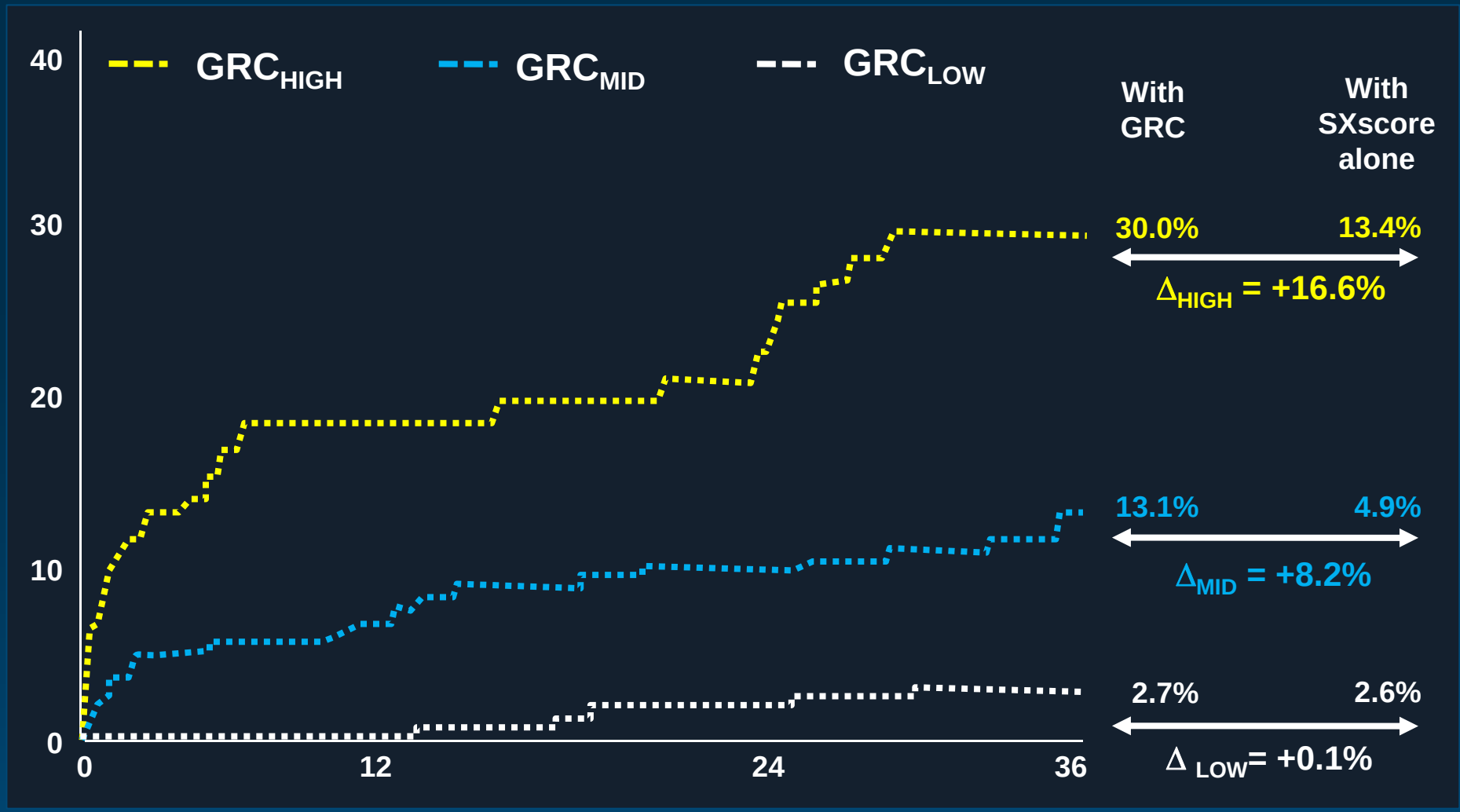
Improved calibration





* log rank test; n = 255 LM patients undergoing PCI

3-year Death Stratified by SXscore and GRC in the SYNTAX LM Cohort



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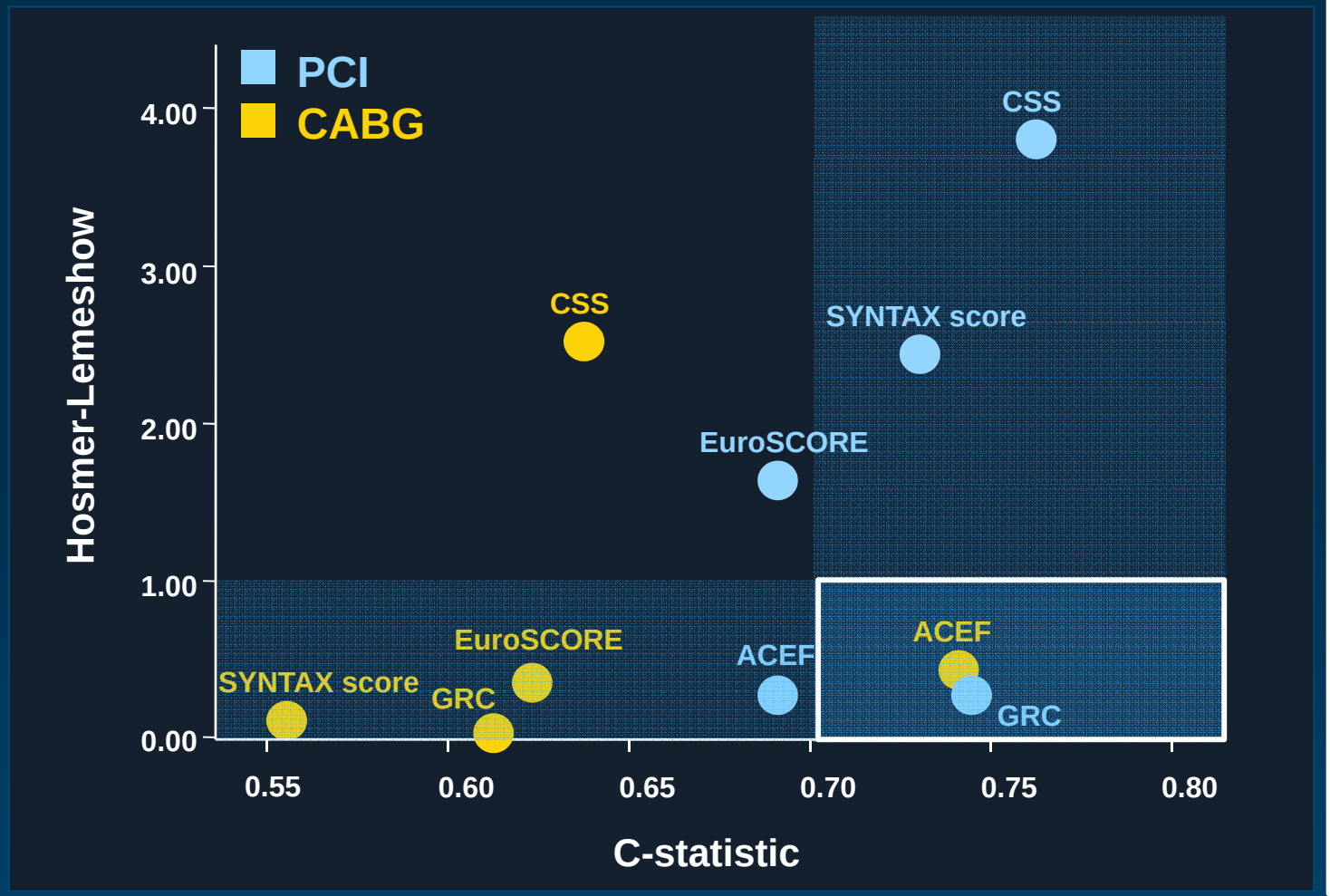
Prediction accuracy of different risk models



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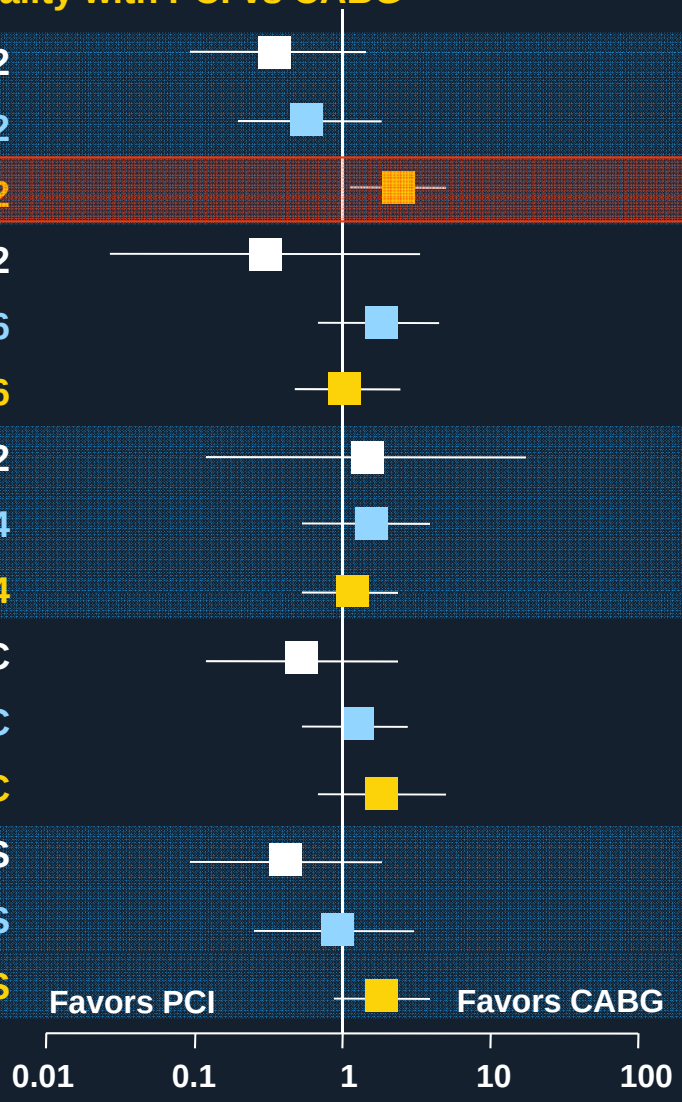
24-month cardiac mortality with PCI vs CABG*



	HR	LCL	UCL	p
SYNTAX score 0-22	0.348	0.084	1.445	0.146
SYNTAX score 23-32	0.582	0.177	1.910	0.372
SYNTAX score > 32	2.323	1.091	4.945	0.029
EuroSCORE 0-2	0.293	0.025	3.482	0.331
EuroSCORE 3-6	1.753	0.709	4.339	0.224
EuroSCORE > 6	1.091	0.452	2.638	0.846
ACEF 0-1.2	1.431	0.115	17.804	0.781
ACEF 1.2-1.4	1.511	0.552	4.134	0.421
ACEF > 1.4	1.107	0.521	2.352	0.793
LOW GRC	0.557	0.129	2.407	0.434
MID GRC	1.174	0.475	2.904	0.728
HIGH GRC	1.760	0.648	4.779	0.267
LOW CSS	0.467	0.103	2.122	0.324
MID CSS	0.929	0.268	3.218	0.908
HIGH CSS	1.711	0.810	3.615	0.159

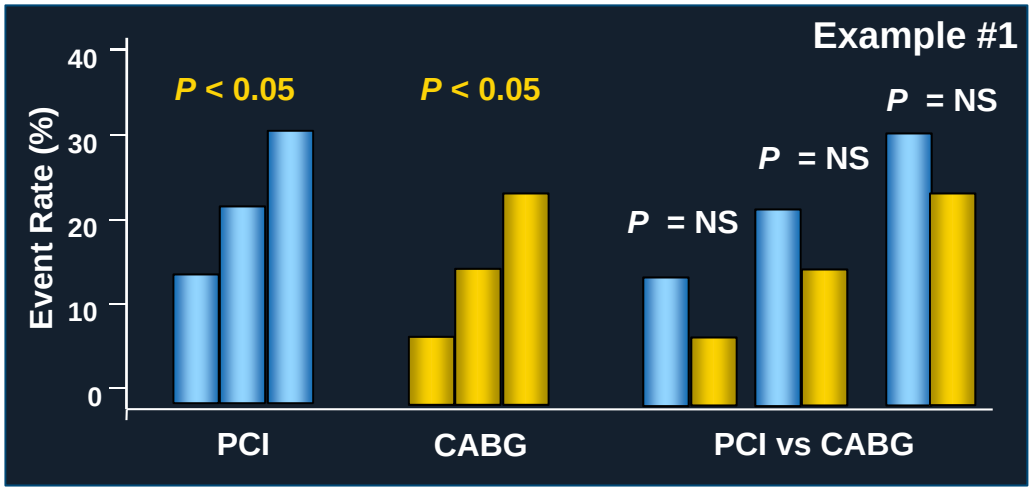
* adjusted by propensity score; HR indicates hazard ratio; LCL indicates lower confidence limit; UCL indicates upper confidence limit

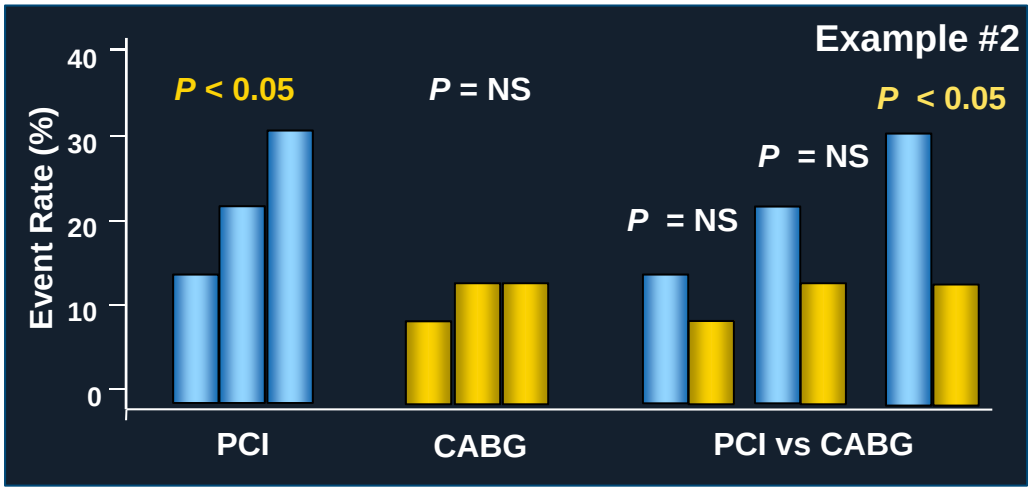
Capodanno, et al. *JACC Interv* 2011;4:287-97

Why does it happen? An egg of Columbus

Good risk stratification both in PCI and CABG

Good risk stratification in PCI and BAD risk stratification in CABG





Closing remarks

- The ideal stratification tool should be both discriminative and calibrated
- Adding clinical variables requires more time, but improves the discrimination and calibration ability of the SYNTAX score alone for **prognostic purposes**.
- On the other side, the **good predictive ability in the PCI scenario along with the poor predictive ability in the CABG scenario** make the SYNTAX score the preferable tool to guide **decision-making** in LM CAD