"Who Are HBR Patients?“

Identification of HBR Patients in Clinical Practice

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Presenter Disclosure Information

Name: Dominick J Angiolillo

Within the past 12 months, the presenter or their spouse/partner have had a financial interest/arrangement or affiliation with the organization listed below.

Received payment as an individual for:
a) Consulting fee or honorarium from Amgen, Bayer, Chiesi, Sanofi, Eli Lilly, Daiichi-Sankyo, The Medicines Company, AstraZeneca, Merck, Abbott Vascular, Pfizer, and PLx Pharma;
b) Honorarium for participation in review activities (DSMB member) from CeloNova, Johnson & Johnson, St. Jude, and Sunovion.
c) Honorarium from the American Board of Internal Medicine (Interventional Cardiology Subspecialty Exam Writing Committee Member)

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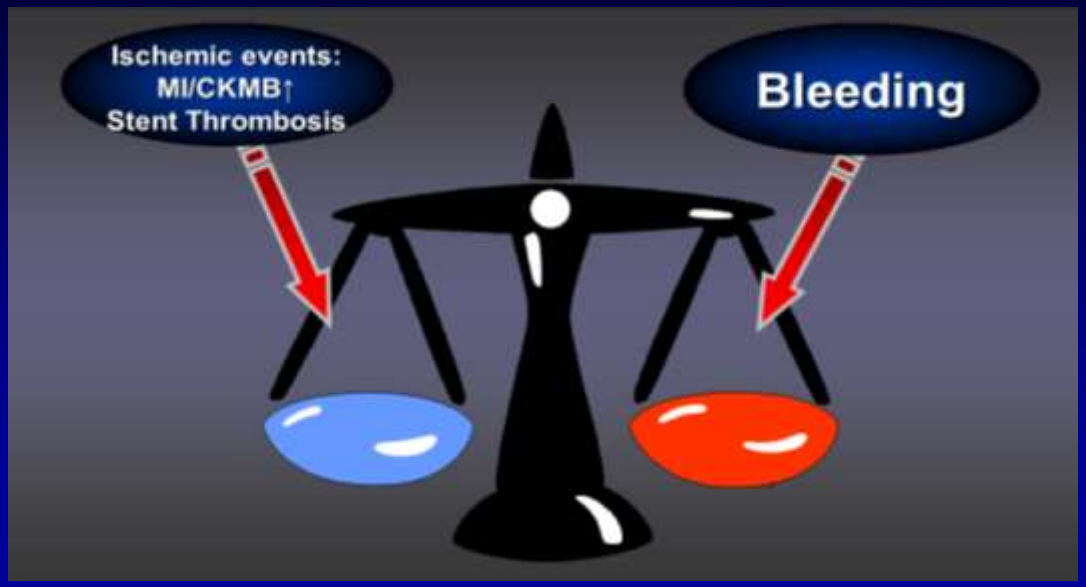
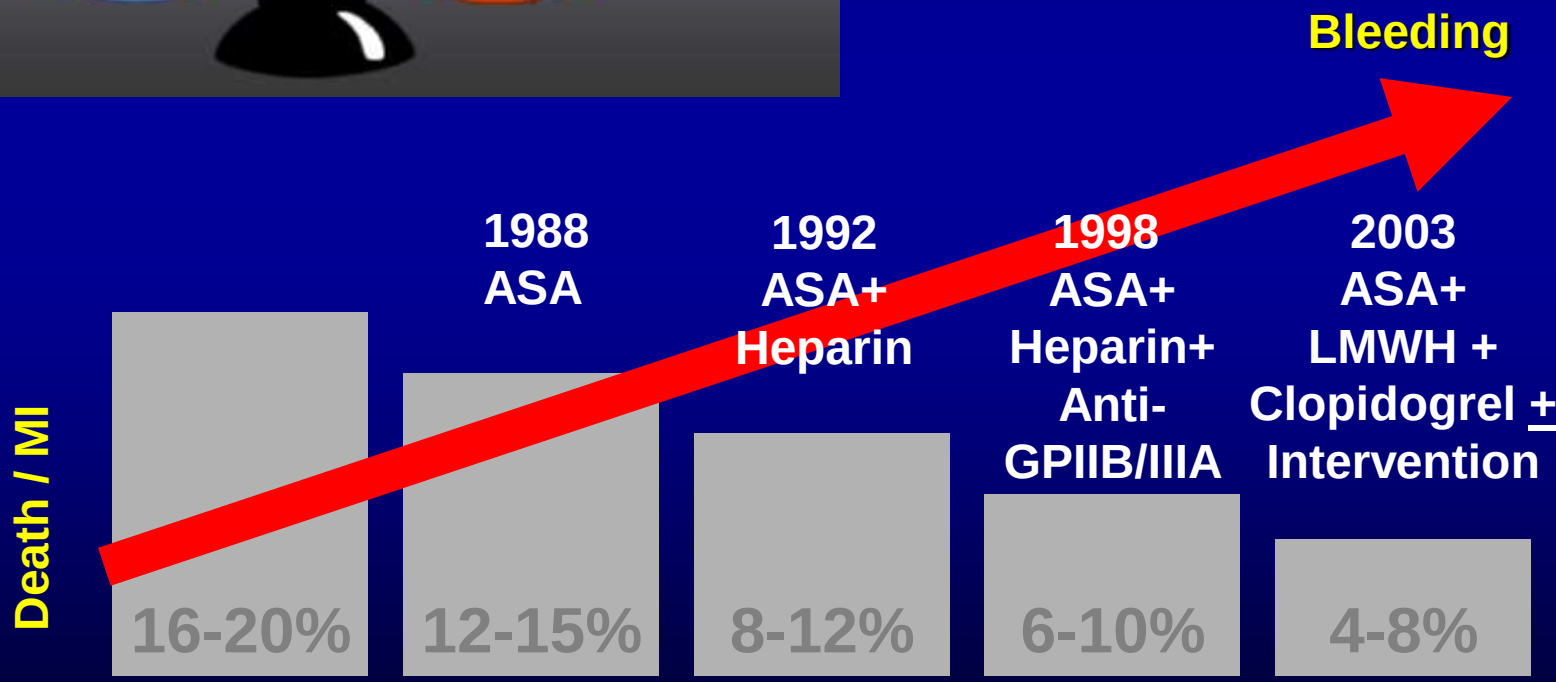
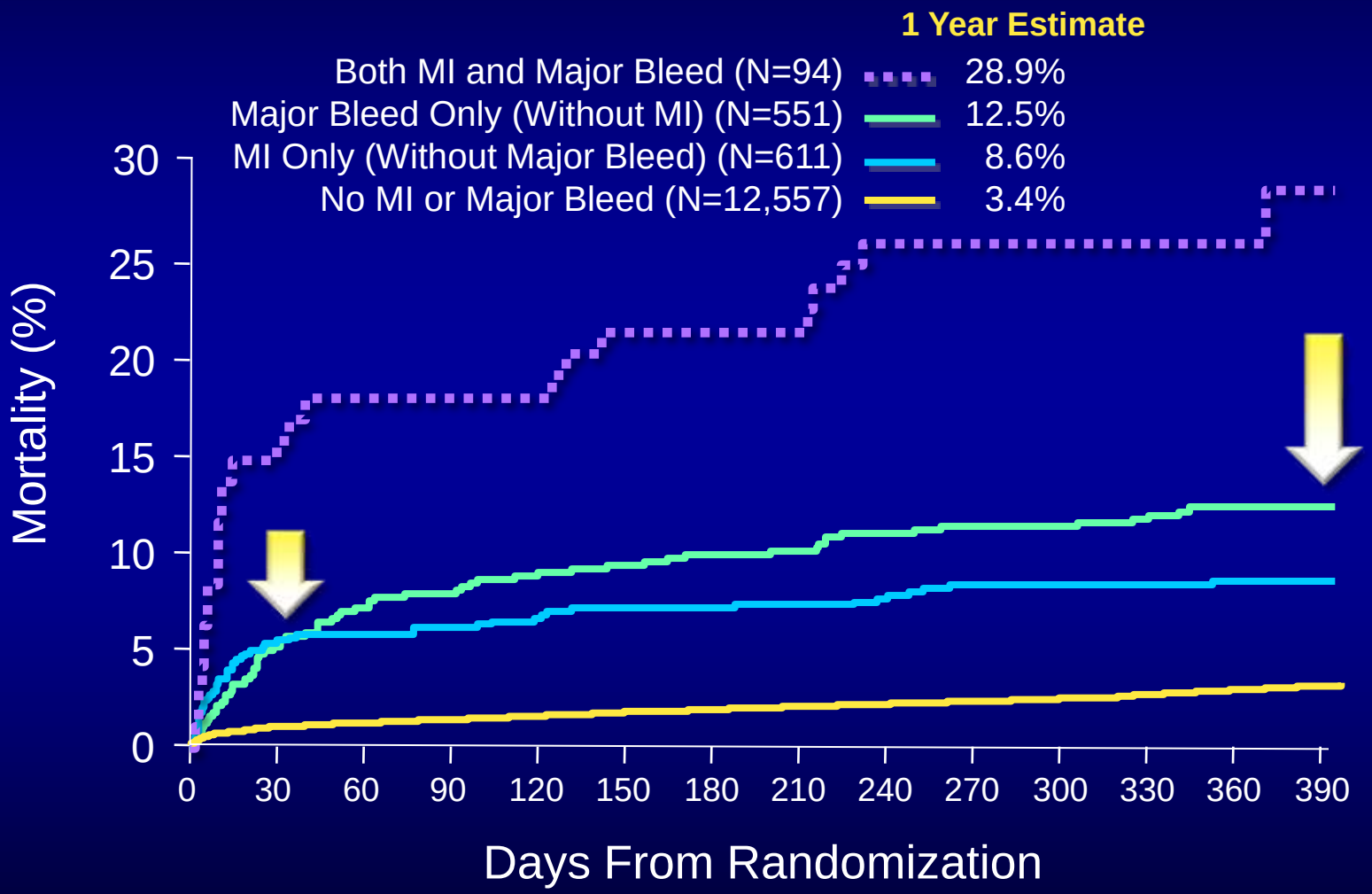
c) Federal agency: NIH

Increased Efficacy at the Price of Increased Bleeding





Impact of MI and Major Bleeding (Non-CABG) in the First 30 Days on Risk of Death Over 1 Year



CABG=coronary artery bypass graft; MI=myocardial infarction.

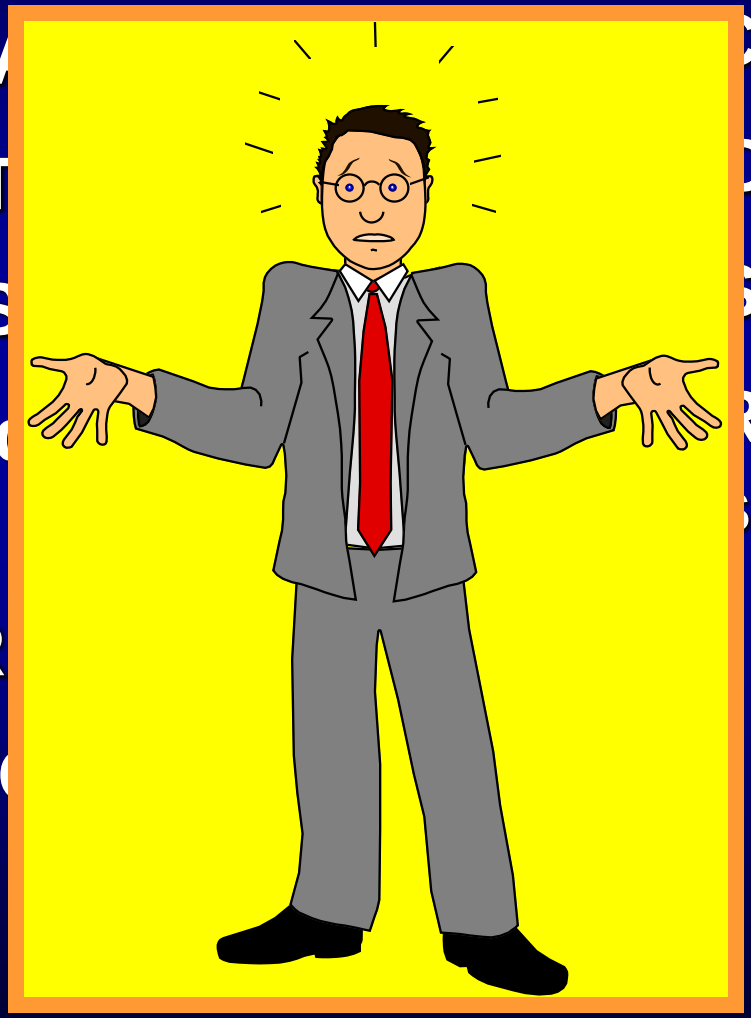
Mehran R, et al. *Eur Heart J.* 2009;30(12):1457-1466.

How do we identify High Bleeding Risk (HBR) patients?

Risk Scores for Bleeding

Models to predict bleeding in ACS/PCI

- REPLA
- ACUIT
- OASIS
- Poole
  Trials
- CHAR
- GUST



CH Registry

CE

SADE

R CathPCI
stry

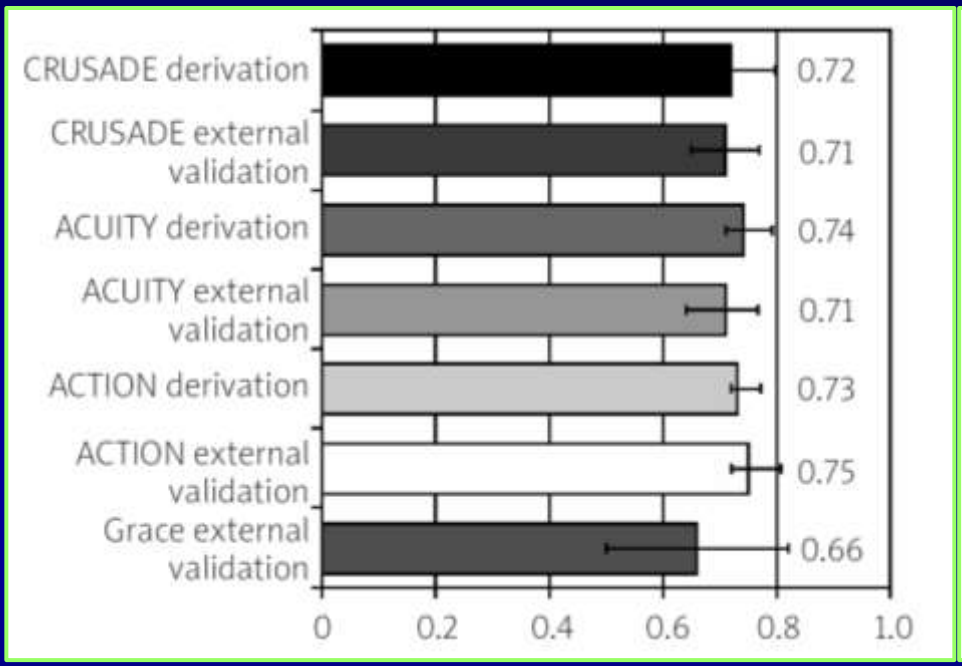
Models to predict bleeding in ACS/PCI
Variables for risk scores

Variable	CRUSADE	ACUITY	ACTION	GRACE
Blood pressure	x		x	x
Heart rate	x		x	x
Diabetes mellitus	x		x	
Prior vascular disease	x			
Heart failure at presentation	x			
Gender	x	x	x	
Creatinine or clearance	x	x	x	xx
Baseline hematocrit/anemia	x	x	x	
Age		x	x	x
White blood cell count		x		
Killip class				x

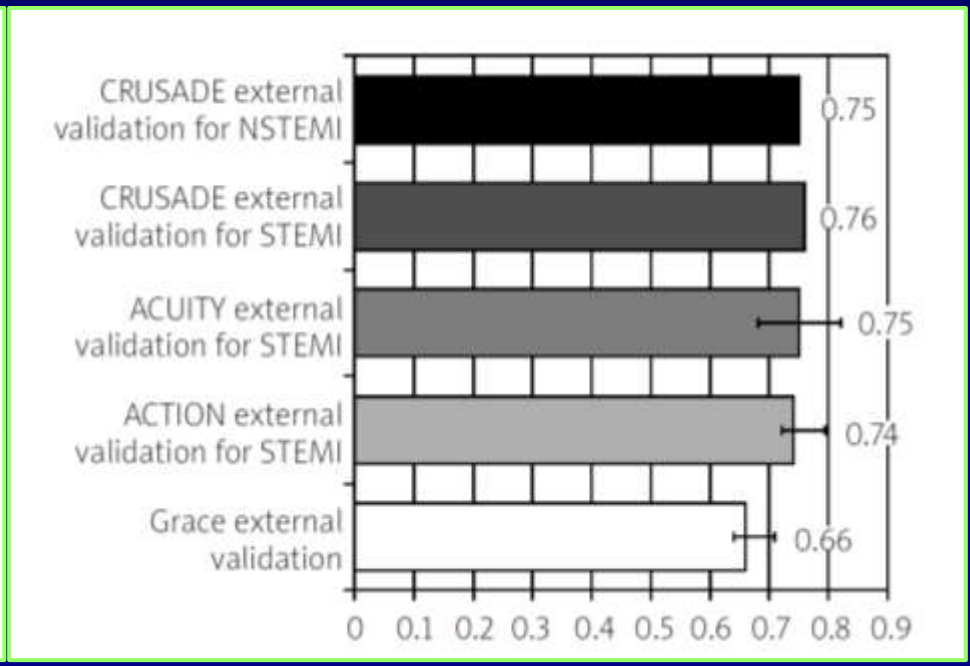
Overall, variables not consistently predictive across scoring systems
(e.g., <50% of variables present in most or all scores)

Taha S et al. Postepy Kardiol Interwencyjnej. 2015;11:182-90

Accuracy of scores across patient subsets



Accuracy of different scores (derivation and validation) for all ACS patients



Accuracy of different scores (external validation) for STEMI and NSTEMI

Overall, within NCDR CathPCI Registry, consistent accuracy according to clinical presentation (STEMI), gender (females), age (>70y), risk factors (DM), management (non-CABG) with a c-index ~0.70 range

(*Rao SV et al. JACC Cardiovasc Interv 2013;6:897-904*)

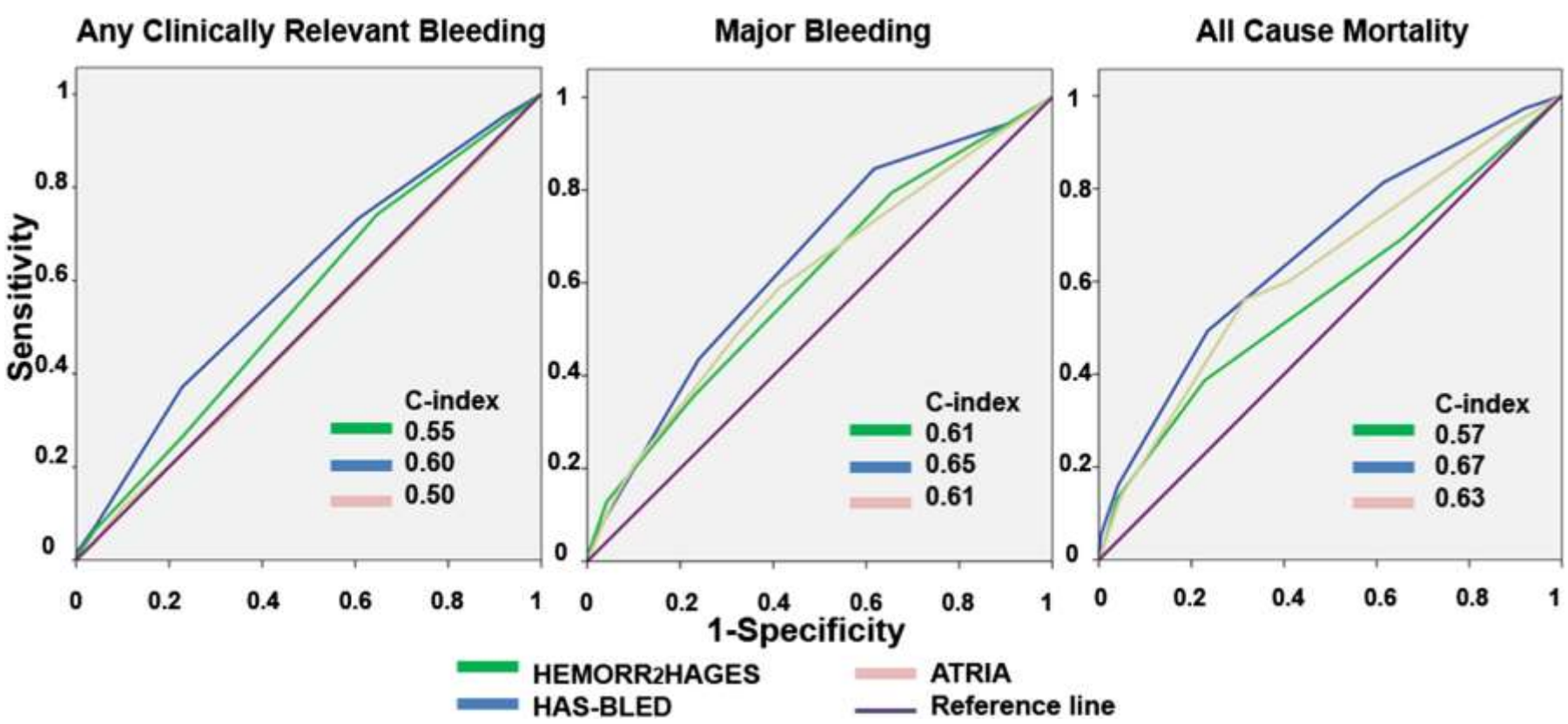
Taha S et al. Postepy Kardiol Interwencyjnej. 2015;11:182-90

Scoring systems cannot always be universally applied

There are different HBR species: AF vs non-AF

HAS-BLED, the best score for bleeding?

2293 anticoagulated patients wth AF from the AMADEUS trial



Apostolakis S, et al. J Am Coll Cardiol. 2012;60:861-7

HAS-BLED is as good as a flip of a coin

ESC Guidelines for Atrial Fibrillation

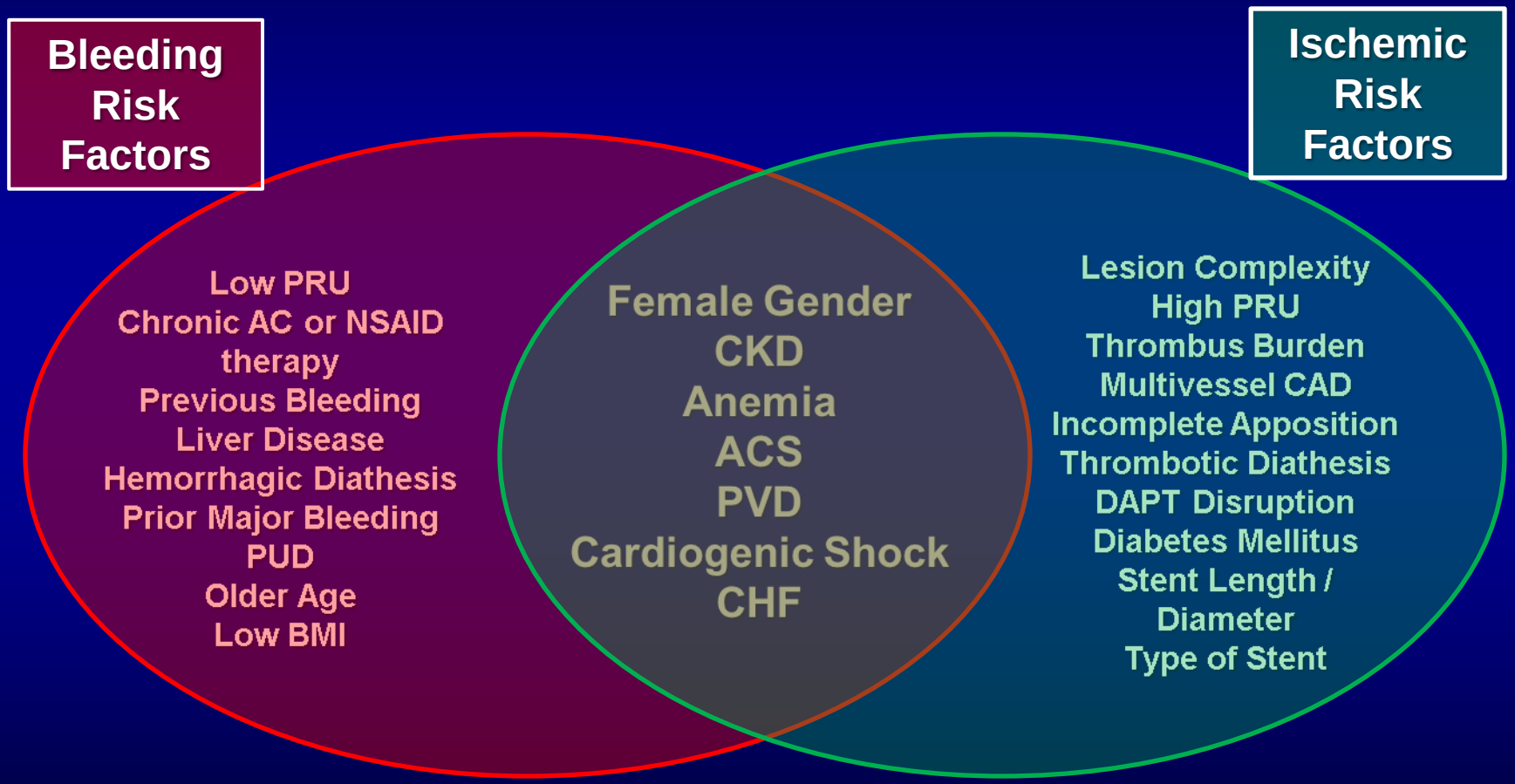
Recommendations for Prediction of Stroke and Bleeding Risk

Bleeding risk scores should be considered in AF patients on oral anticoagulation to identify modifiable risk factors for major bleeding.	IIa	B

A high bleeding risk score should generally not result in withholding OAC.

Kirchhof P et al. Eur Heart J. 2016 [ePub Ahead of print]

Overlap Between Bleeding and Ischemic Risk Clinical Factors



Bleeding Versus Ischemic Events

Which is Worse?

Bleeding Versus Ischemic Events Which is Worse?

Major bleeds and MI have similar overall strength of association with mortality in the first year after ACS. MI is correlated with an increase in short-term risk, whereas major bleeding correlates with a more prolonged mortality risk.

MI defined as a troponin leak ≠ Intracranial hemorrhage

Dropping dead ≠ Bleeding requiring transfusion

Debilitating stroke ≠ >5 cm hematoma

The Devil is in the Details

<u>Take home message</u>:

- **Know the source of your scores (if you use them)**
- **Know the definition of the endpoints (ischemic and bleeding)**
- **Know patient preference (you might be surprised)**

Scores to define optimal DAPT duration

General Concepts and Challenges

- **Ideally, it would be desirable to personalize DAPT duration based on a prediction rule that easily identifies patients at high bleeding risk and separates those who benefit from shortening (*e.g., high bleeding risk & low risk of ischemia*) vs prolonging (*e.g., non-high bleeding risk & high risk of ischemia*) DAPT.**
- **However, because risk factors for ischemia and bleeding largely overlap, modelling of such an algorithm is challenging.**
- **Ideally, a scoring system that concomitantly takes into account both bleeding and ischemic risk would be practical.**
- **Need for large derivation data set which require external validation (ideally in different patient cohorts).**

Capodanno D, Angiolillo DJ. Lancet 2017; 389:987-989.

Scores to define optimal DAPT duration

Key Criteria of an Ideal Scoring System

- Ease of use
- Precise
- Accurate

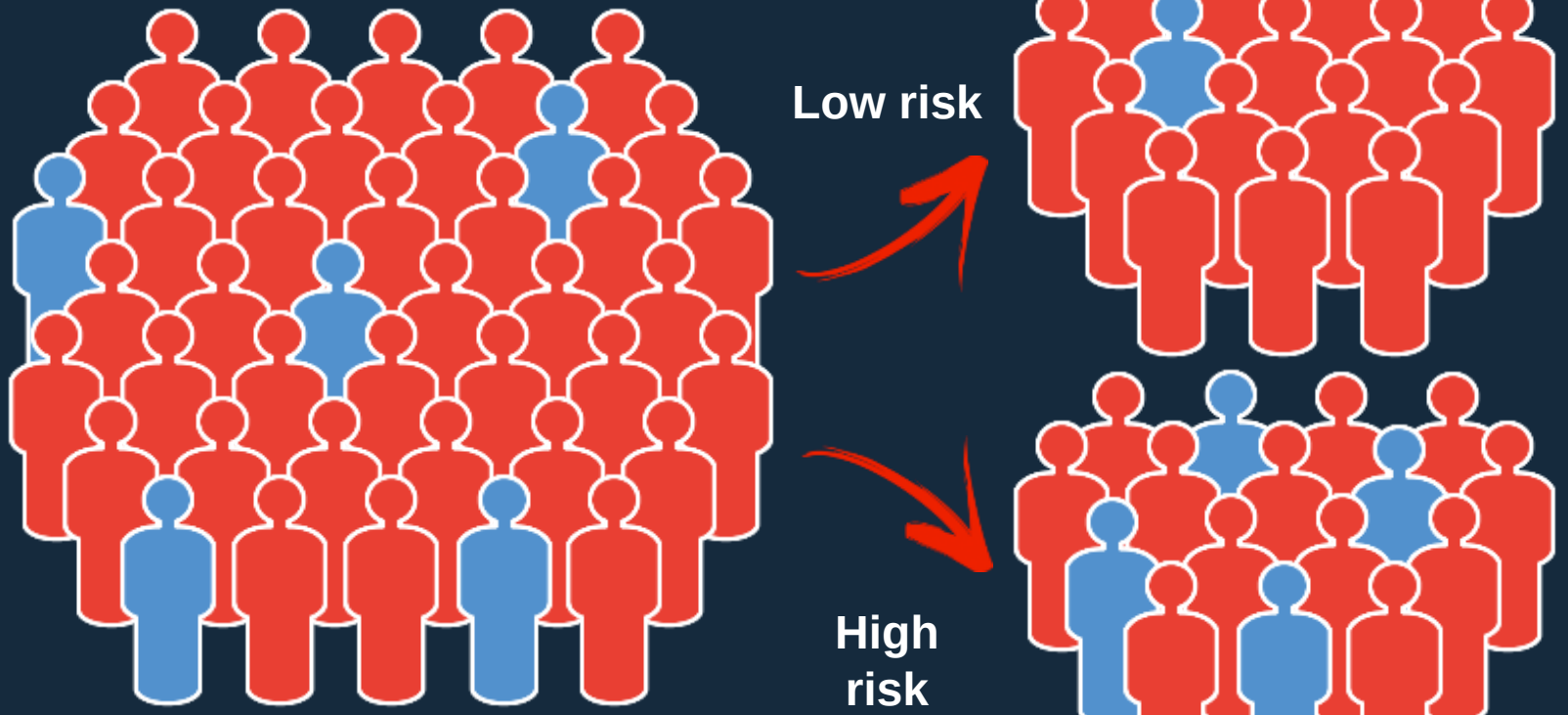
Capodanno D, Angiolillo DJ. Lancet 2017; 389:987-989.

Risk Scores for DAPT Duration

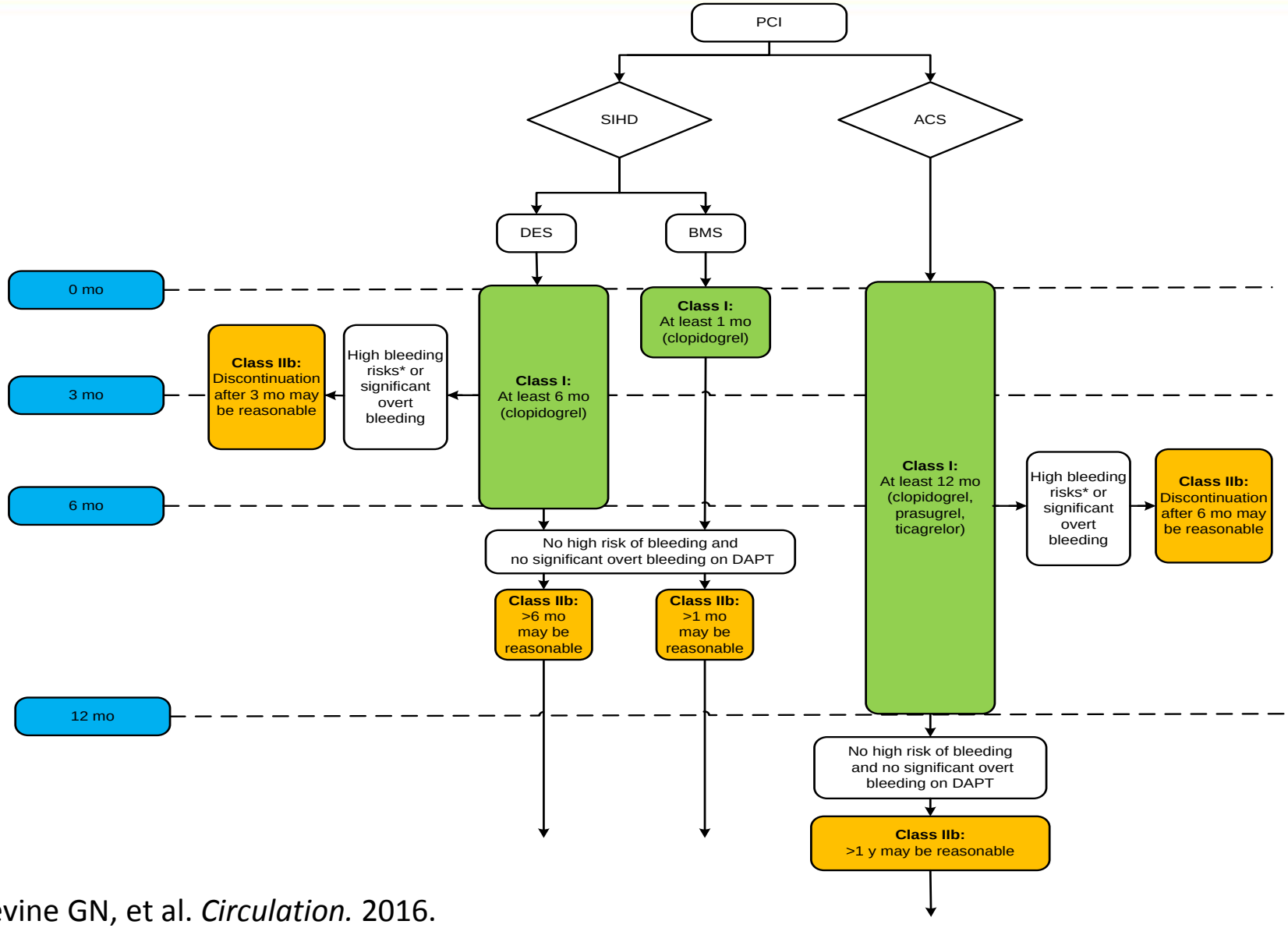
Score	Number of variables	Development cohort (patients, design)	Setting	Predicted outcome(s)	Validation cohort(s) (patients, c-index)
DAPT	5 clinical, 3 procedural	N=11,648, multicentre randomized clinical trial	PCI patients on DAPT who were event-free for 12 months	Ischemia and bleeding between 12 and 30 months after PCI	N=8,136, 0.64 for both ischemia and bleeding
PARIS	Coronary thrombosis risk score: 6 clinical Major bleeding risk score: 6 clinical	N=4,190 patients, multicentre registry	PCI patients on DAPT	Ischemia and bleeding at 24 months after PCI	N=8,665, 0.65 for ischemia and 0.64 for bleeding
PRECISE-DAPT	5 clinical	N=14,963, pooled analysis of randomized clinical trials	PCI patients on DAPT	Bleeding at 12 months after PCI	N=8,595, 0.70 N=6,172, 0.66

Capodanno D, Angiolillo DJ. Lancet 2017; 389:987-989.

Categorization is Useful, But Sometimes Simplistic



Treatment Algorithm for Duration of $P2Y_{12}$ Inhibitor Therapy in Patients Treated With PCI



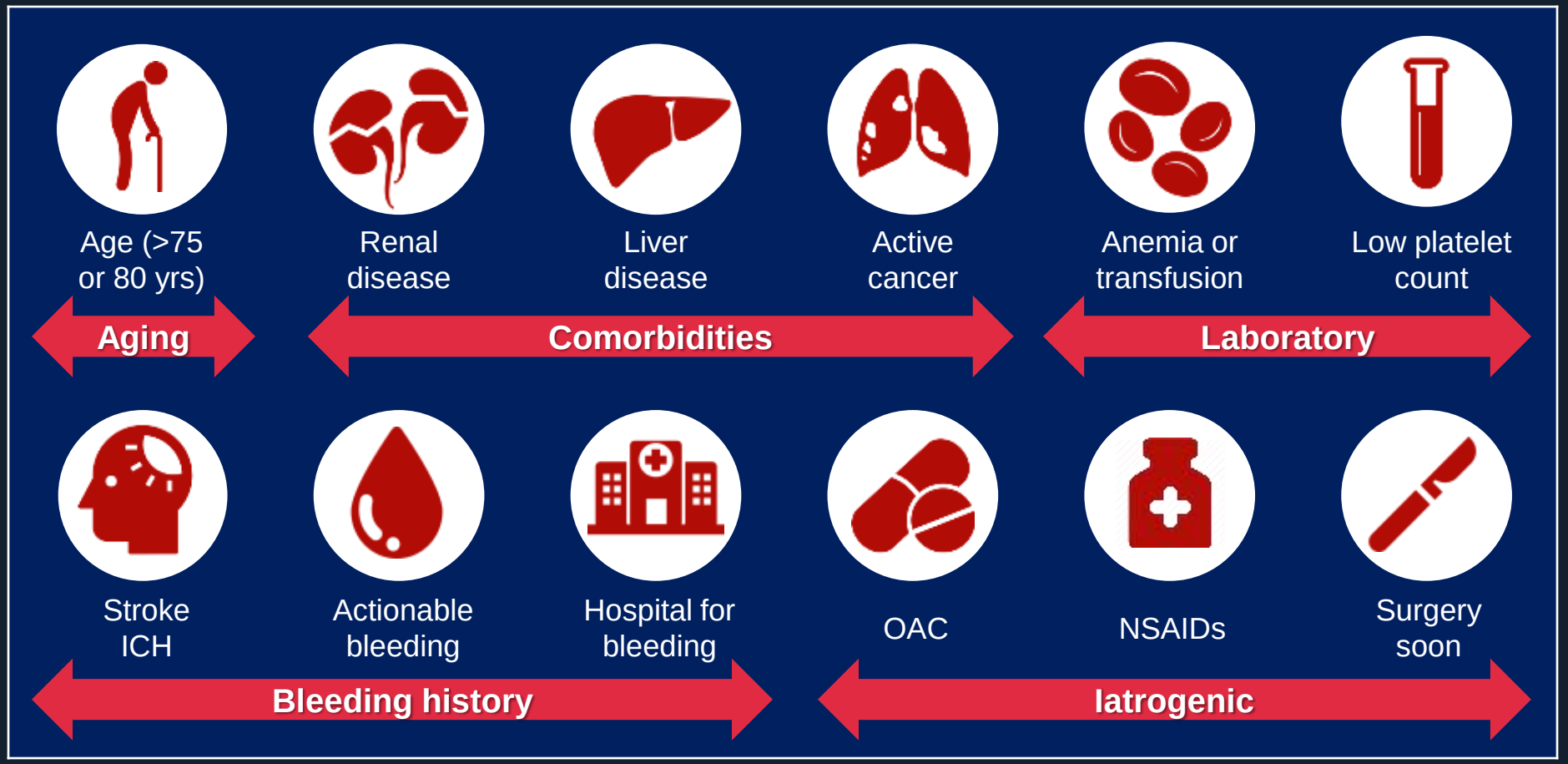
Levine GN, et al. *Circulation.* 2016.

Clinical and Procedural Factors Associated with Increased Ischemic Risk or Increased Bleeding Risk

Increased Ischemic Risk/ Risk of Stent Thrombosis (May favor longer duration DAPT)	Increased Bleeding Risk (May favor shorter duration DAPT)
Increased Ischemic Risk • Advanced age • ACS presentation • Multiple prior MI • Extensive CAD • Diabetes mellitus • CKD **Increased Risk of Stent Thrombosis** • ACS presentation • Diabetes mellitus • Left ventricular ejection fraction <40% • First generation drug-eluting stent • Stent under-sizing or under-deployment • Small stent diameter or greater stent length • Bifurcation stents • In-stent restenosis	• History of prior bleeding • Oral anticoagulant therapy • Female sex • Advanced age • Low body weight • CKD • Diabetes mellitus • Anemia • Chronic steroid or NSAID therapy

Levine GN, et al. *Circulation.* 2016.

Reasons of High Bleeding Risk After PCI with DAPT (LEADERS FREE Like Criteria)



Conclusions

- Identification of HBR patients is critical for optimizing antithrombotic therapies (i.e., reduce bleeding risk and enhance efficacy).
- The main challenge is represented by the overlap in risk factors for bleeding and ischemic/thrombotic risk.
- Risk scores are currently available and easy to use.
- Risk scores (when applied in the correct context) are overall precise, but with a degree of accuracy which is overall modest/good – underscores the need to further refine tools to identify HBR patients.
- Critical clinical judgment is paramount in defining antithrombotic treatment regimens (drug type, dose, duration, etc).
- Prospective studies to validate tailored approaches (whether device or drug based) selectively conducted in HBR patients (specifically defined) are warranted.