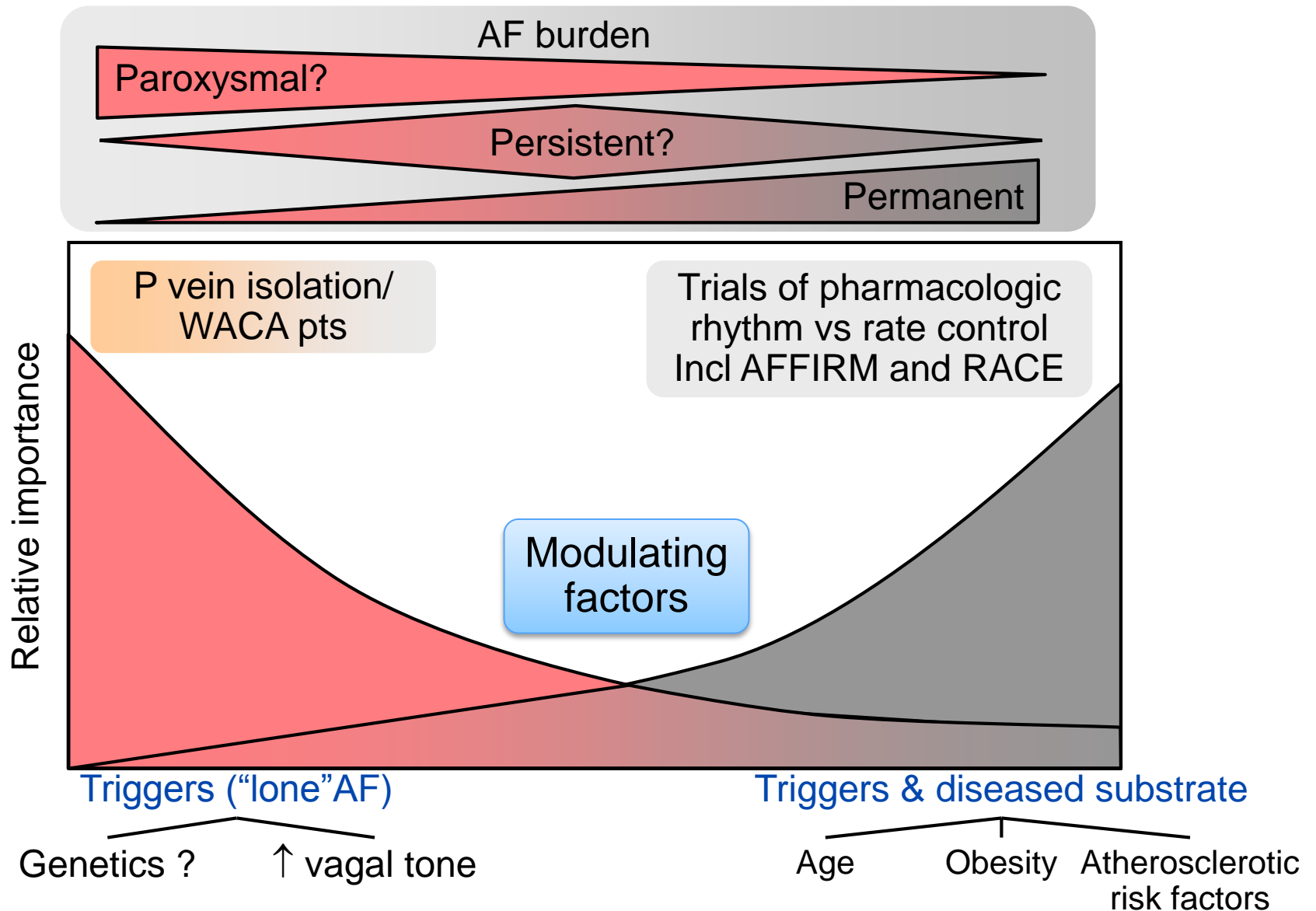


Controversies in Risk Stratification

Things are not as simple as they seem

Banff 2017

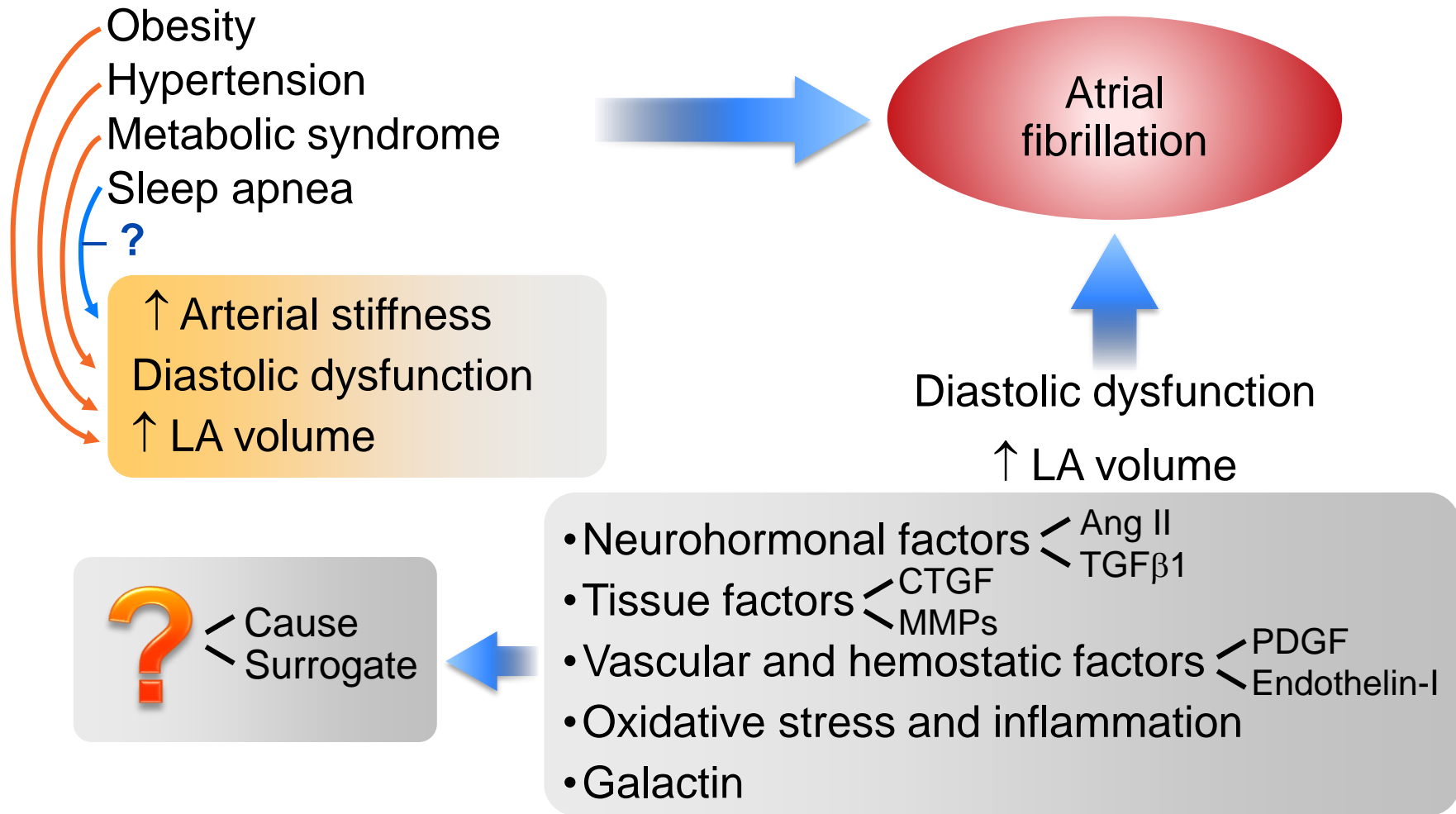
Triggers vs Substrate in Pathophysiology of AF



Wyse & Gersh: Circ, 2004

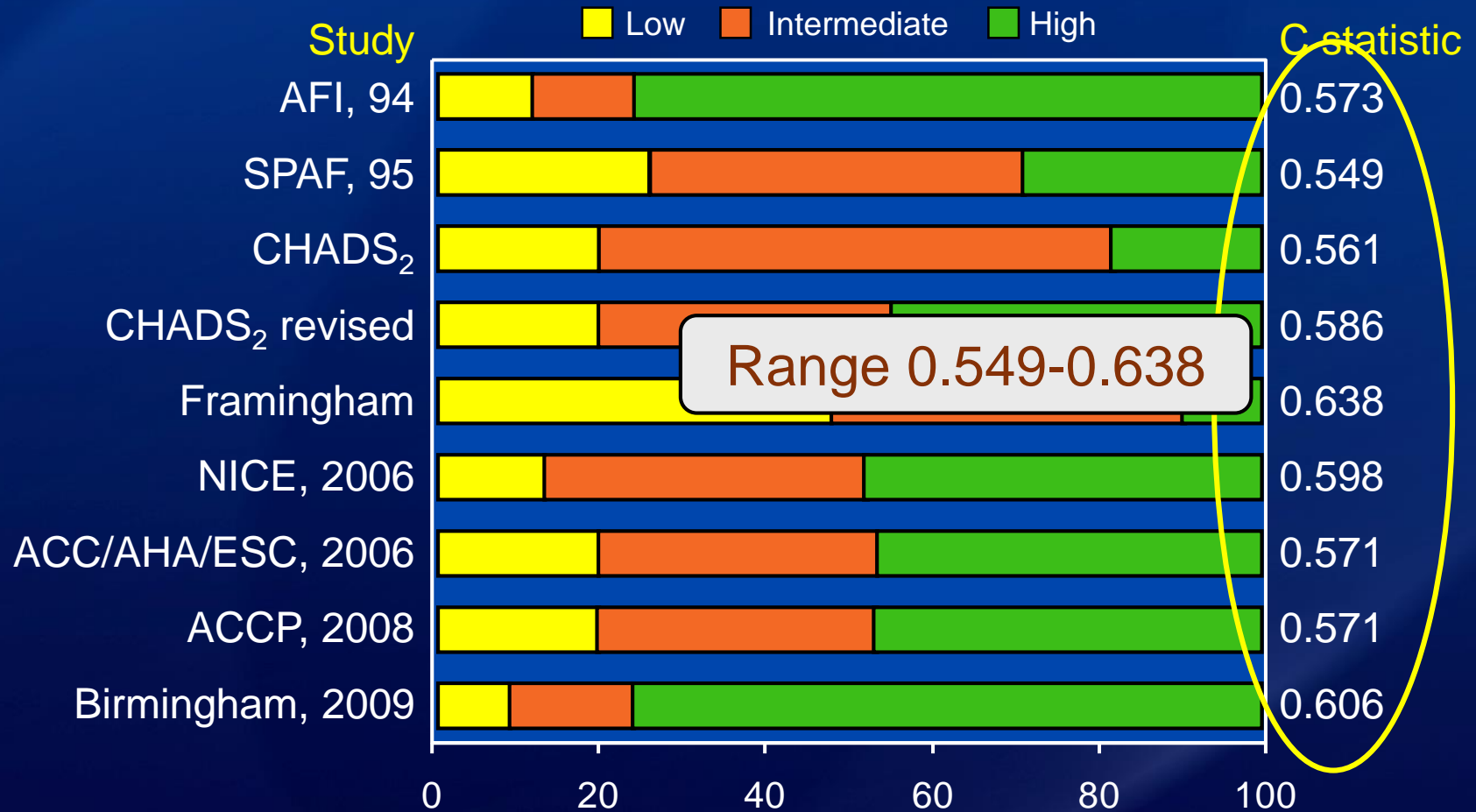
A Fib as a Vascular Disease

Suggestive Evidence



Tsang and Gersh: EHJ 2008; JACC 2008; AJC 2008;
AJC 2006; JACC 2006; JACC 2003; JACC 2002

Performance of Contemporary Risk Stratification Schemes



Lip: Chest, 2010

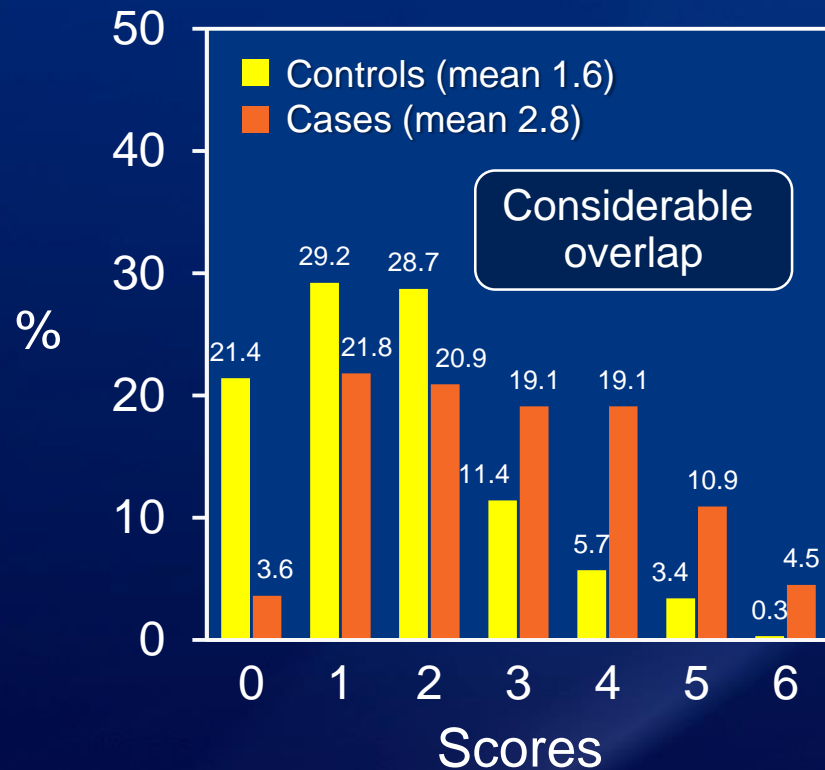
CHADS₂ Score and Left Atrial Thrombi in AF

- Case control study

Cases

- 110 pt
- NVAF
- LAA thrombus
- TEE

Distribution of Scores



Wysosinski: AHJ, 2010

Atrial Fibrillation Guidelines

Risk	Recommended therapy	
	ESC 2016	AHA/ACC/HRS 2014
Risk factors (no.) CHA ₂ DS ₂ -VASc = 0	No antithrombotic therapy (IIIB)	No antithrombotic therapy
CHA ₂ DS ₂ -VASc = 1*	<i>OAC > (Class IIaB) (NOAC > VKA)</i>	None or OAC or ASA
CHA ₂ DS ₂ -VASc ≥ 2	<i>NOAC > VKA (IA)</i>	NOAC or VKA
Mechanical prosthetic valve	VKA: INR 2.0-3.0 (AVR) VKA: INR 2.5-3.5 (MVR)	

*Female ≥2

ESC Guidelines: Eur Heart J, 2012

AHA/ACC/HRS Guidelines Circulation, 2014

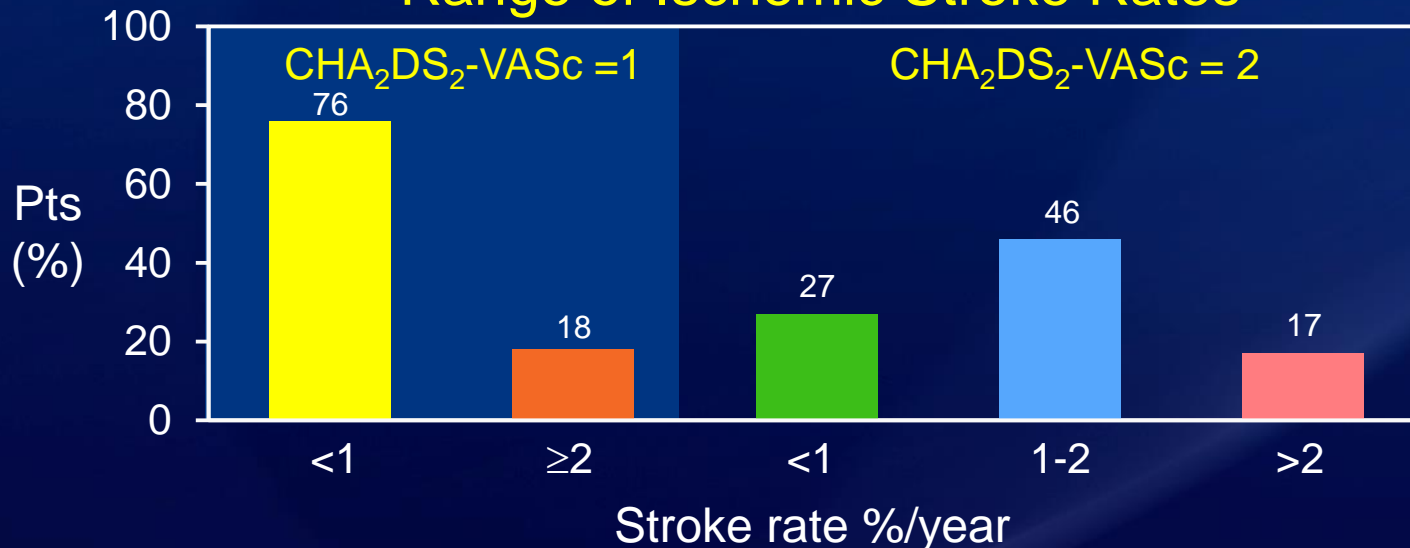
Wide Variation in Reported Rates of Stroke Across Cohorts of Patients with AF

- 34 studies
- Patients with non-valvular AF

Results

- Overall stroke rates ranged 0.45-9.28%/year
- Heterogeneity in stroke rates $P < 0.001$
- Mean North American stroke rate $< 1/3$ of mean European stroke rate

Range of Ischemic Stroke Rates



Benefit of Anticoagulation Unlikely in Patients With Atrial Fibrillation and a CHA₂DS₂-VASc Score of 1



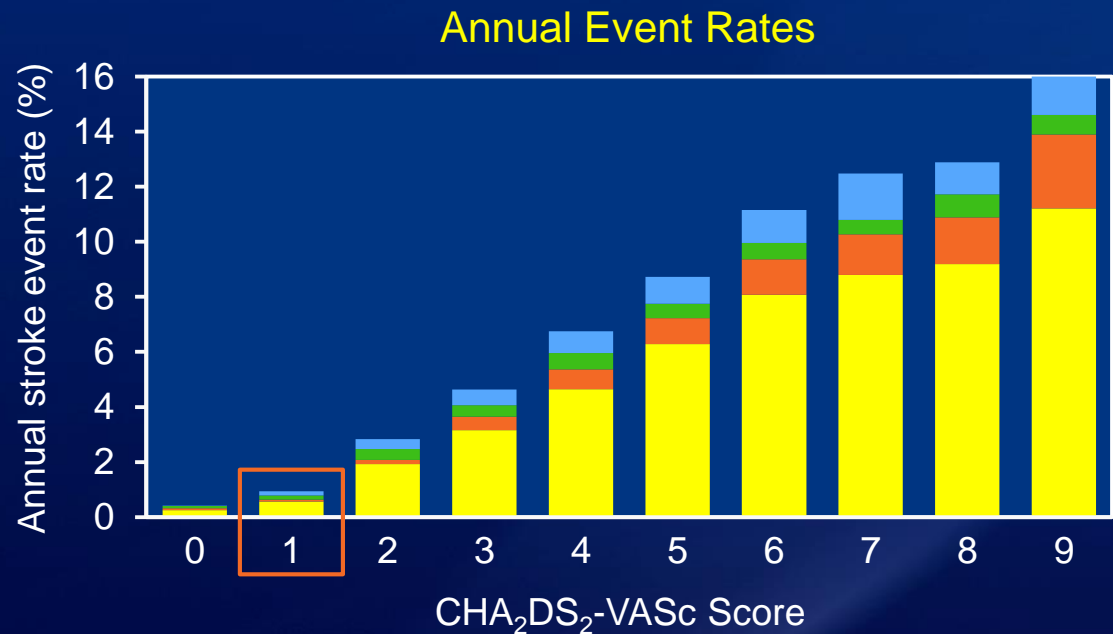
Leif Friberg, MD, PhD,* Mika Skeppholm, MD, PhD,* Andreas Terént, MD, PhD†

JACC, 2015

- 140,420 patients
- Swedish nationwide health registry

Exclusions

- Valvular AF
- Warfarin exposure
- 4 week quarantine period after diagnosis



“Tipping point”
1.7%/yr – Warfarin
0.9%/yr – NOAC

- +TIA
- +Pulmonary Embolism
- +Unspecified Stroke/+Systemic Embolism
- Ischemic stroke only

Adherence to Warfarin and NOAC – Clinical Outcomes

Insurance Administrative Claims Database (USA – 100 Million Enrollees Over 20 Yr Period)

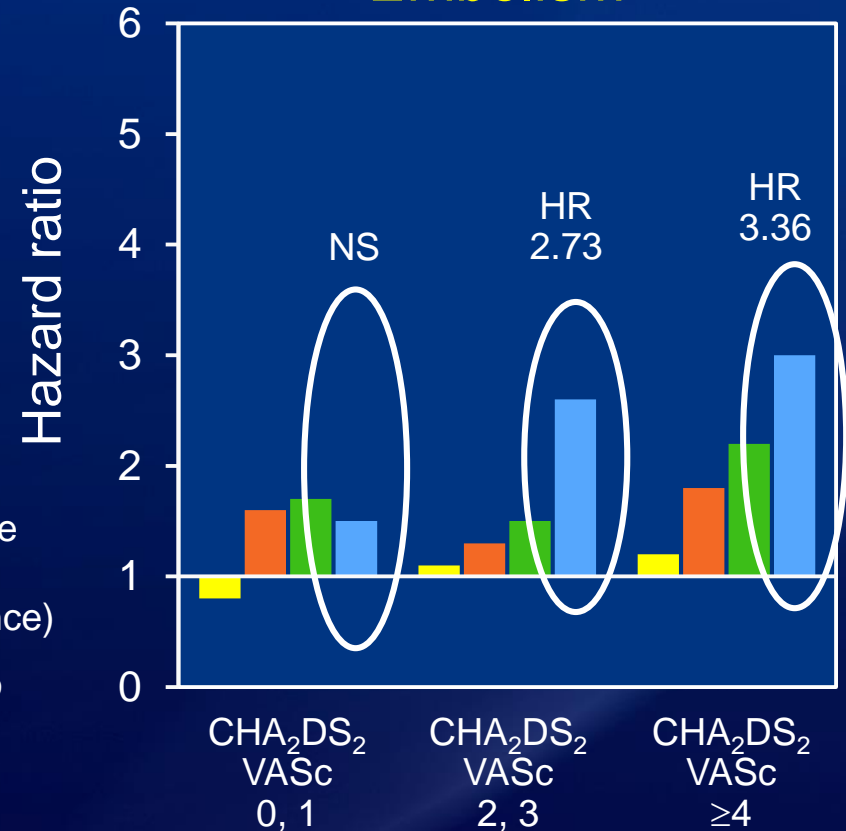
- 64,661 pt
- 2000-2014
- AF (OAC)
 - Warfarin
 - Dabigatran
 - Rivaroxatan
 - Apixiban

Adherence
(≥80 days covered
by OAC)
|
43.2%

Cumulative time
off OACs
(<1 wk as reference)

- 1 wk-1 mo
- 1-3 mo
- 3-6 mo
- ≥6 mo

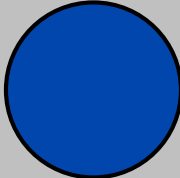









Stroke or Systemic Embolism



Noseworthy P (In Press)

Risk Factors for Thromboembolic Events in Atrial Fibrillation Patients

Are all 1 pointers equal ?

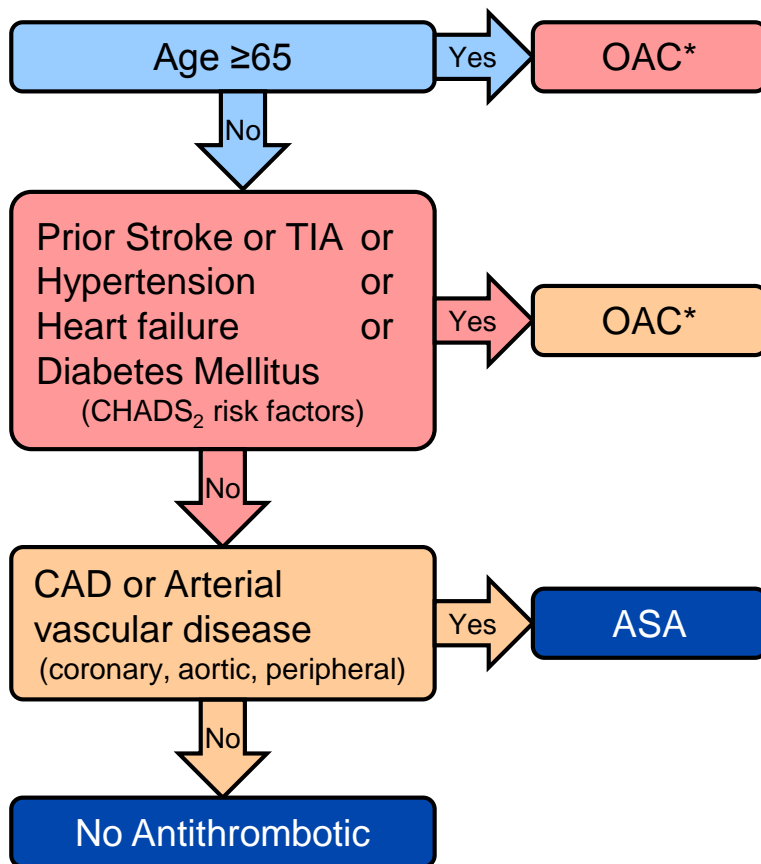
Risk Factor	Hazard ratio estimates	CHA ₂ DS ₂ -VASc Points
Age ≥75 years (reference <65 years)		2
Age 65-74 years (reference <65 years)		1
Previous Ischemic Stroke		2
Female Gender		1
Vascular Disease		1
Hypertension		1
Diabetes Mellitus		1
History of heart failure		1
History of intracranial bleeding		0
Reference		

Argulian: Am J Med, 2015; Camm: EHJ, 2012; Friberg: EHJ, 2012

Society Guidelines

2014 Focused Update of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation

The “CCS Algorithm” for OAC Therapy in AF



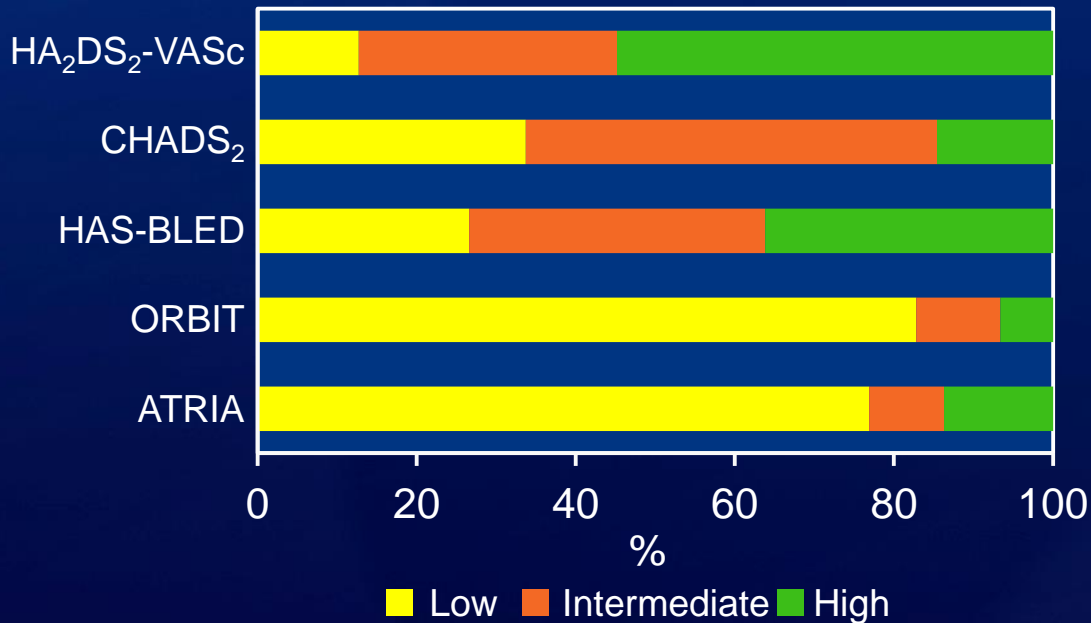
Consider and modify (if possible) all factors influencing risk of bleeding during OAC treatment (hypertension, antiplatelet drugs, NSAIDs, excessive alcohol, labile INRs) and specifically bleeding risks for NOACs (low eGFR, age ≥75, low body weight).

***NOAC preferred**

Comparison of Stroke and Bleeding Scores in Patients on NOACS

- 39,539 patients
- U.S. commercial insurance database

Stratification of Bleeding Risk



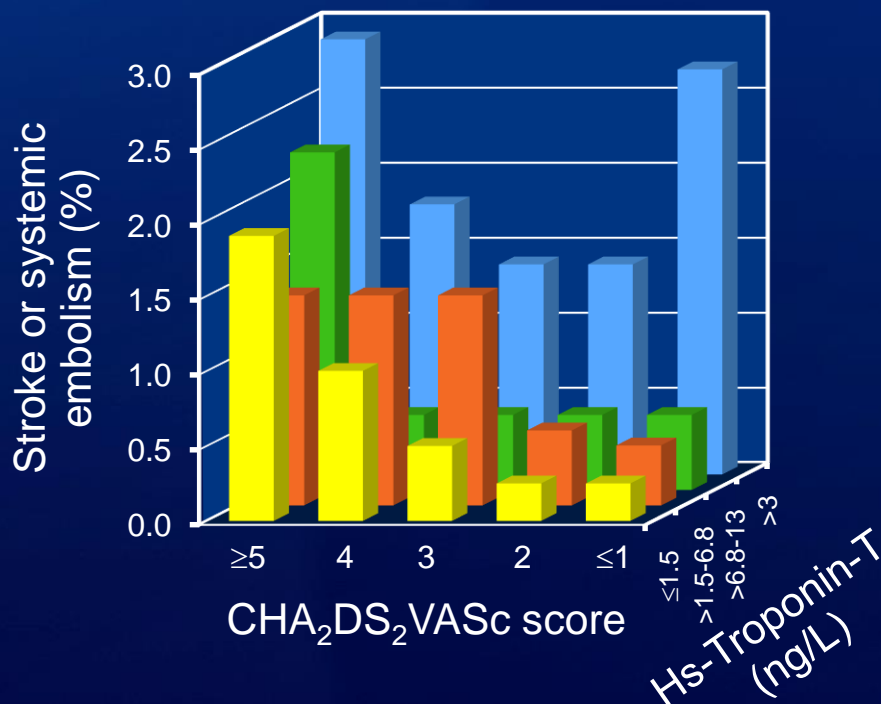
C-statistic	
Major bleeding	Intracranial bleeding
0.65	0.61
0.64	0.66
0.64	0.63
0.60	0.55
0.60	0.55

Yao and Noseworthy in press

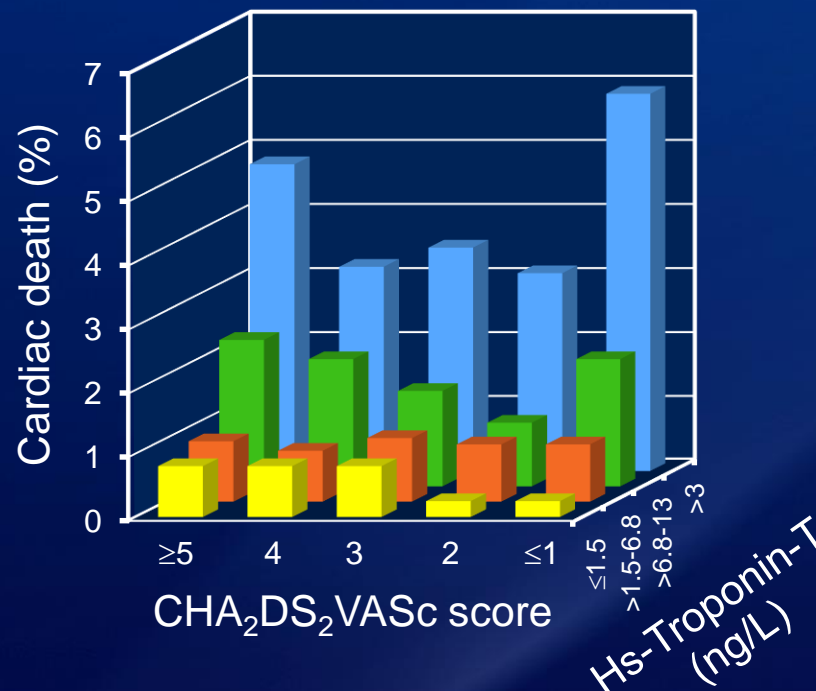
Outcomes in Patients with AF Stratified by CHADS₂ VASc Score and hs-TnT

12,892 Patients ARISTOTLE Trial

Stroke and Systemic Embolism



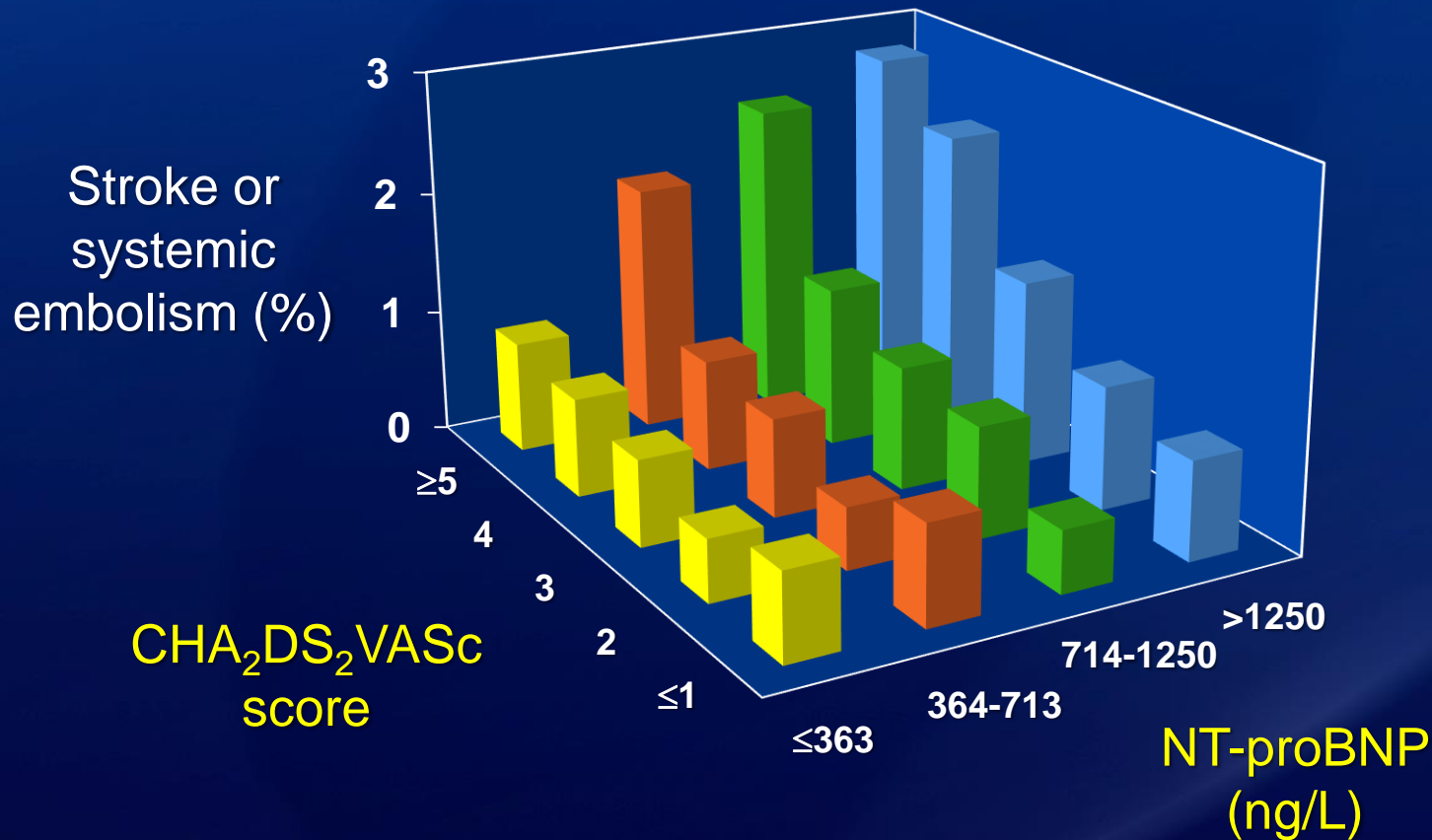
Cardiac Death



Hijazi: JACC, 2014

Stroke and Systemic TE and NT-proBNP in Patients With AFib

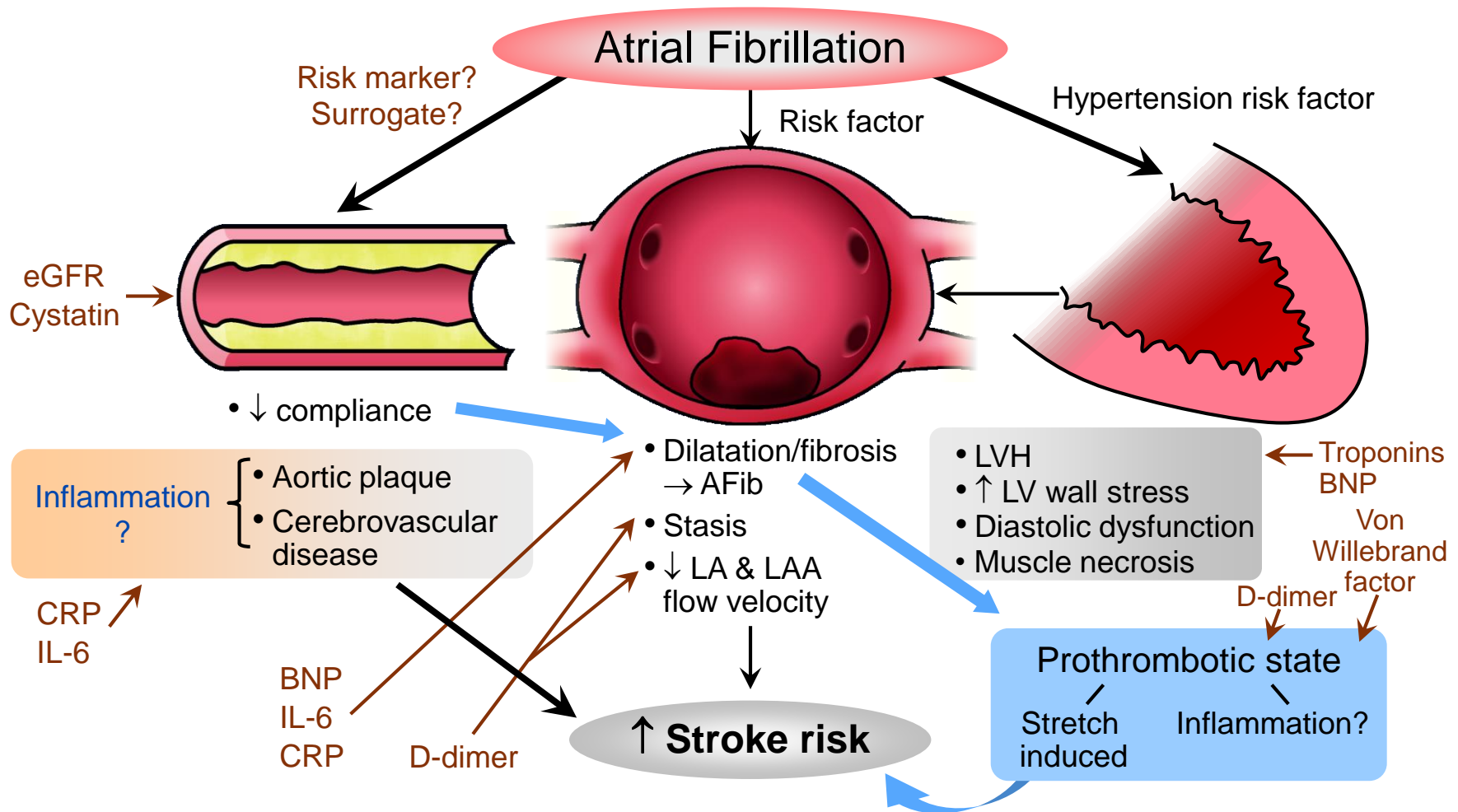
18,201 Patients – ARISTOTLE Trial
Stratified by CHAD₂ VASc Score



Hijazi: JACC, I 2013

Atrial Fibrillation and the Risk of Stroke

Potential Role of Biomarkers



Assessment of Stroke Risk in AF

Risk scores (CHADS2, CHA2DS2,-VASC and ATRIA)

Crucial to basic risk assessment

Modifying factors incl. LAA morphology
Role of comorbidities
Patients represented in clinical trials ?

Impact of other disease states,
eg. HCM, prosthetic valves

Limitations of Risk Stratification Scores for Atrial Fibrillation

The AF population is very heterogeneous regarding stroke risk

- Different classifications in measuring stroke rates lead to overestimates
- Incorporation of other embolic episodes into determinants of stroke risk may be misleading
- Current risk stratification schema are based primarily upon **clinical** risk factors

- Differential weight of **individual** risk factors
- Performance varies according to baseline risk of stroke which is variable among populations



What will be the role of biomarkers and imaging

What gets us into trouble is not
what we don't know

It is what we know for sure that
just ain't so

Mark Twain