KHRS 2023

Toward better risk stratification for stroke prevention in AF : *Beyond the CHA_2DS_2VASc Score*

GREGORY Y H LIP MD FRCP (Lond Edin Glasg) FACC FESC FEHRA

Price-Evans Chair of Cardiovascular Medicine, University of Liverpool, UK
National Institute for Health Research (NIHR) Senior Investigator
Distinguished Professor, Aalborg University, Denmark

Professor of Cardiovascular Medicine, Liverpool John Moores University;
Adjunct Professor, Yonsei University, Seoul; Adjunct Professor, Seoul National University, South Korea

Liverpool Centre for **Cardiovascular Science**

Declaration of Interests

- Guideline membership/reviewing: ESC Guidelines on Atrial Fibrillation 2010 and Focused Update 2012, 2020; ESC Guidelines on Heart Failure, 2012; American College of Chest Physicians Antithrombotic Therapy Guidelines for Atrial Fibrillation, 2012; NICE Guidelines on Atrial Fibrillation, 2006 and 2014; NICE Quality Standards on Atrial Fibrillation 2015; ESC Cardio-oncology Task Force, 2015; ESC Working Group on Thrombosis position documents (2011-). Chairman, Scientific Documents Committee, European Heart Rhythm Association (EHRA). Chairman, 2018 CHEST guidelines from American College of Chest Physicians. Writing Group, 2021 Asia Pacific Heart Rhythm Society Guidelines on Stroke Prevention.

- Steering Committees/trials: Includes steering committees for various Phase II and III studies, Health Economics & Outcomes Research, etc. Investigator in various clinical trials in cardiovascular disease, including those on antithrombotic therapies in atrial fibrillation, acute coronary syndrome, lipids, etc.

- Editorial Roles: Editor-in-Chief (clinical), Thrombosis & Haemostasis; Associate Editor, Europace; Guest Editor, Circulation, American Heart Journal.

- Consultant/Advisor/Speaker:
  - Consultant and Speaker for BMS/Pfizer, Boehringer Ingelheim and Daiichi-Sankyo. No direct personal fees.

Stroke risk factors in patients with Atrial Fibrillation

Hindricks et al Eur Heart J 2020 doi:10.1093/eurheartj/ehaa612

Most commonly studied clinical risk factors (a systematic review)[324]	Positive studies/All studies	Other clinical risk factors[325]	Imaging biomarkers[291,326–328]	Blood/urine biomarkers[329–332]
Stroke/TIA/systemic embolism	15/16	Impaired renal function/ CKD	*Echocardiography*	Cardiac troponin T and I Natriuretic peptides Cystatin C Proteinuria CrCl/eGFR CRP IL-6 GDF-15 von Willebrand factor D-dimer
Hypertension	11/20	OSA	LA dilatation Spontaneous contrast or thrombus in LA Low LAA velocities Complex aortic plaque	
Ageing (per decade)	9/13	HCM		
Structural heart disease	9/13	Amyloidosis in degenerative cerebral and heart diseases		
Diabetes mellitus	9/14	Hyperlipidaemia		
Vascular disease	6/17	Smoking	*Cerebral imaging*	
CHF/LV dysfunction	7/18	Metabolic syndrome[333]	Small-vessel disease	
Sex category (female)	8/22	Malignancy		

CHF = congestive heart failure; CKD = chronic kidney disease; CrCl = creatinine clearance; CRP = C-reactive protein; eGFR = estimated glomerular filtration rate; GDF-15 = growth differentiation factor-15; IL-6 = interleukin 6; LA = left atrium; LAA = left atrial appendage; LV = left ventricular; OSA = obstructive sleep apnoea; TIA = transient ischaemic attack.

The CHA_2DS_2-VASc score

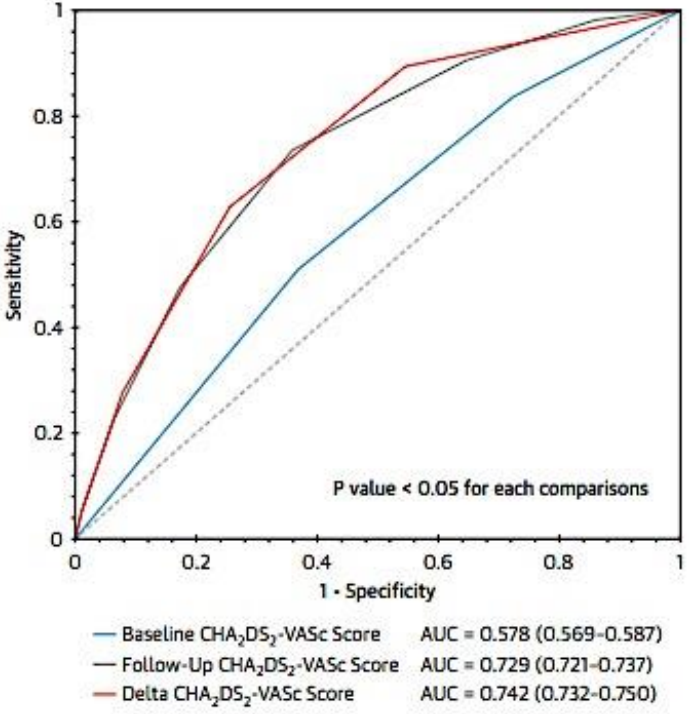
a) Risk factors for stroke and thromboembolism in non-valvular AF	
'Major' risk factors	'Clinically relevant non-major' risk factors
Previous stroke, TIA or systemic embolism Age ≥ 75 years	Heart failure or moderate to severe LV systolic dysfunction [e.g. LV EF ≤ 40%] Hypertension - Diabetes mellitus Female sex - Age 65-74 years Vascular disease*

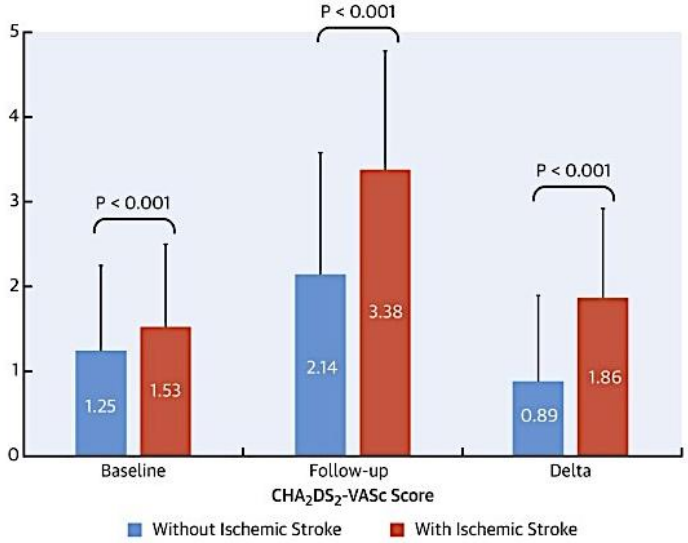
Stroke risk factors	Score
Congestive heart failure/LV dysfunction	1
Hypertension	1
Aged ≥75 years	2
Diabetes mellitus	1
Stroke/TIA/TE	2
Vascular disease [prior MI, PAD, or aortic plaque]	1
Aged 65–74 years	1
Sex category [i.e. female gender]	1

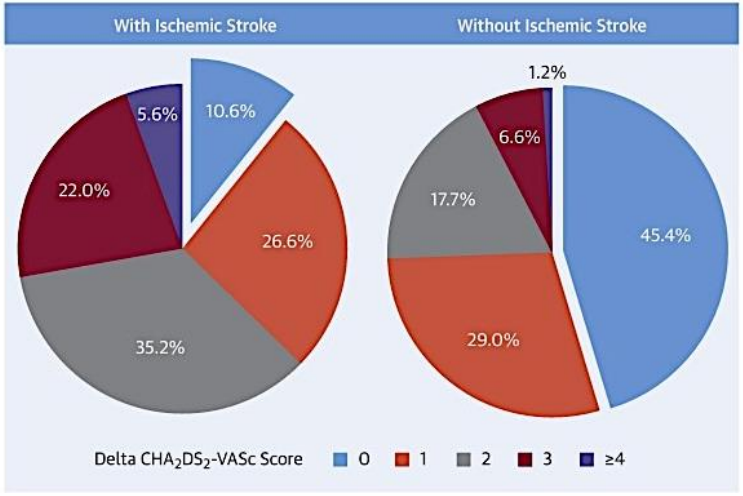
Lip et al. Chest. 2010;137:263-72.

CHA_2DS_2-VASc Scores of Patients With AF ±Ischemic Stroke: Baseline, Follow-Up, Delta

Chao, Lip et al J Am Coll Cardiol. 2018;71(2):122–32.

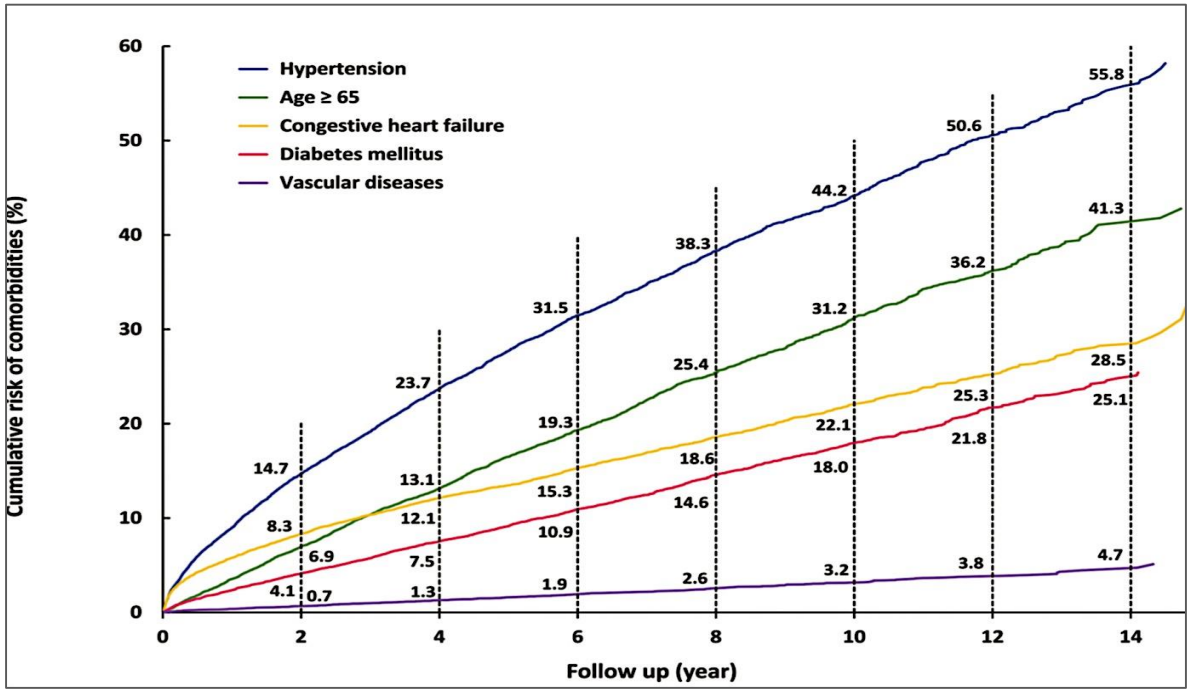






Incident Co-Morbidities in AF Patients Initially with a CHA_2DS_2-VASc Score of 0 (Males) or 1 (Females): Implications for Reassessment of Stroke Risk in Initially 'Low-Risk' Patients

Chao .. Lip et al
Thromb Haemost. 2019 Jul;119(7):1162-1170. .



- In 80% of patients who acquired a comorbidity (HF, hypertension, diabetes or vascular disease), the new condition occurred after 4.2 months of AF diagnosis.
- Time from incident comorbidity to ischaemic stroke was >4.4 months for 90% of patients suffering stroke.

3-4 months may be a reasonable time interval at which stroke risk should be re-assessed, so that OACs could be prescribed timely.

Stroke risk factors in patients with Atrial Fibrillation

Hindricks et al Eur Heart J 2020 doi:10.1093/eurheartj/ehaa612

Most commonly studied clinical risk factors (a systematic review)[324]	Positive studies/All studies	Other clinical risk factors[325]	Imaging biomarkers[291,326–328]	Blood/urine biomarkers[329–332]
Stroke/TIA/systemic embolism	15/16	Impaired renal function/ CKD	*Echocardiography*	Cardiac troponin T and I
Hypertension	11/20	OSA	LA dilatation	Natriuretic peptides
Ageing (per decade)	9/13	HCM	Spontaneous contrast or thrombus in LA	Cystatin C
Structural heart disease	9/13	Amyloidosis in degenerative cerebral and heart diseases	Low LAA velocities	Proteinuria
Diabetes mellitus	9/14	Hyperlipidaemia	Complex aortic plaque	CrCl/eGFR
Vascular disease	6/17	Smoking	*Cerebral imaging*	CRP
CHF/LV dysfunction	7/18	Metabolic syndrome[333]	Small-vessel disease	IL-6
Sex category (female)	8/22	Malignancy		GDF-15
				von Willebrand factor
				D-dimer

CHF = congestive heart failure; CKD = chronic kidney disease; CrCl = creatinine clearance; CRP = C-reactive protein; eGFR = estimated glomerular filtration rate; GDF-15 = growth differentiation factor-15; IL-6 = interleukin 6; LA = left atrium; LAA = left atrial appendage; LV = left ventricular; OSA = obstructive sleep apnoea; TIA = transient ischaemic attack.

Does chronic kidney disease improve predictive value of the $CHADS_2$ and CHA_2DS_2-VASc stroke stratification risk scores for AF?

Roldan … Lip
Thromb Haemostat 2013
May 2;109(5):956-60.

Evaluating renal function in AF patients is important as CKD would confer a poor overall prognosis

Adding CKD to the $CHADS_2$ and CHA_2DS_2-VASc stroke risk scores did not independently add predictive information.

Stroke/systemic embolism	C-statistic (95% CI)	P	Relative IDI	P
$CHADS_2$	0.650 (0.619–0.680)			
$CHADS_2$+CKD	0.636 (0.605–0.666)	0.442	0.7%	0.260
CHA_2DS_2-VASc	0.623 (0.592–0.654)			
CHA_2DS_2-VASc+CKD	0.612 (0.580–0.642)	0.451	0.3%	0.122
Thrombotic events	**C-statistic (95% CI)**	**P**	**Relative IDI**	**P**
$CHADS_2$	0.628 (0.597–0.658)			
$CHADS_2$+CKD	0.629 (0.598–0.660)	0.917	0.3%	0.552
CHA_2DS_2-VASc	0.634 (0.603–0.664)			
CHA_2DS_2-VASc+CKD	0.636 (0.605–0.666)	0.908	0.7%	0.502
All cause death	**C-statistic (95% CI)**	**P**	**Relative IDI**	**P**
$CHADS_2$	0.668 (0.638–0.698)			
$CHADS_2$+CKD	0.685 (0.655–0.714)	0.244	-2.5%	0.236
CHA_2DS_2-VASc	0.657 (0.627–0.687)			
CHA_2DS_2-VASc+CKD	0.672 (0.642–0.702)	0.224	-1.8%	0.290

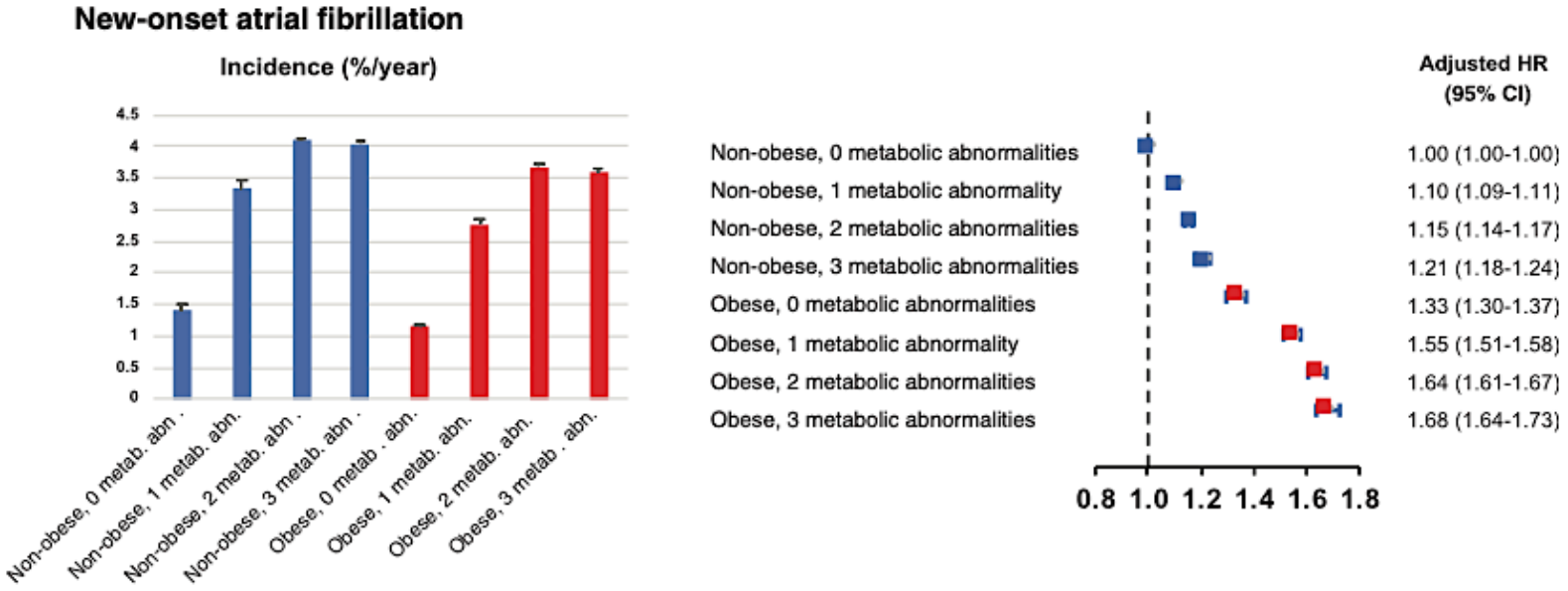
$CHADS_2$: congestive heart failure, hypertension, age ≥75, diabetes mellitus, and prior stroke or transient ischaemic attack; CHA_2DS_2-VASc: congestive heart failure, hypertension, age ≥75, diabetes mellitus, prior stroke or transient ischaemic attack, vascular disease, age 65–74, female; CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate; CKD: we add 1 point for eGRF 30–60 and 2 points for eGFR<30.

Evaluating increased predictive ability of Chronic Kidney Disease (CKD) adding to clinical risk scores ($CHADS_2$ and CHA_2DS_2-VASc) using C-statistics and and IDI indexes.
N=978

Metabolically healthy obesity and cardiovascular events: A nationwide cohort study

Fauchier … Lip, Fauchier. Diabetes Obes Metab. 2021 DOI: 10.1111/dom.14492

Phenotypes defined by obesity and three metabolic abnormalities (diabetes, hypertension and hyperlipidaemia)



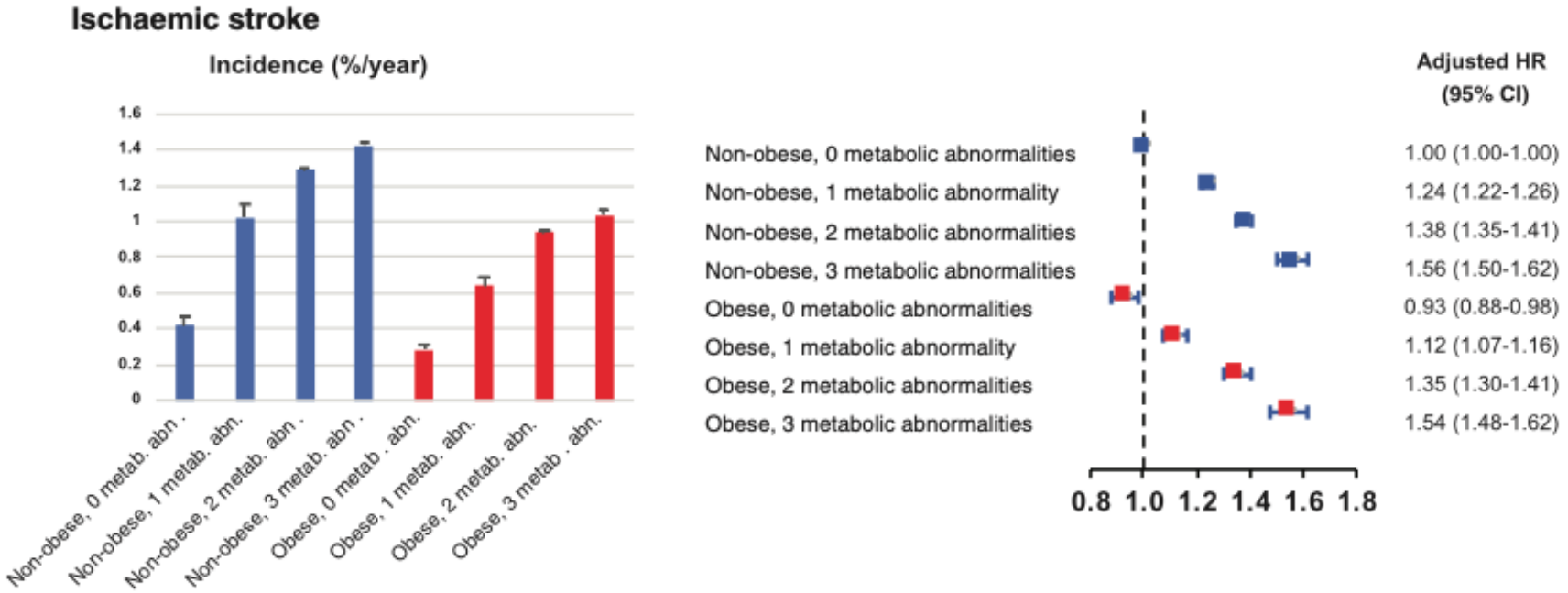
'… individuals with MHO did not have a higher risk of myocardial infarction, ischaemic stroke or cardiovascular death than metabolically healthy individuals with no obesity.

By contrast, they had a higher risk of new-onset HF and new-onset AF.'

Metabolically healthy obesity and cardiovascular events: A nationwide cohort study

Fauchier … Lip, Fauchier. Diabetes Obes Metab. 2021 DOI: 10.1111/dom.14492

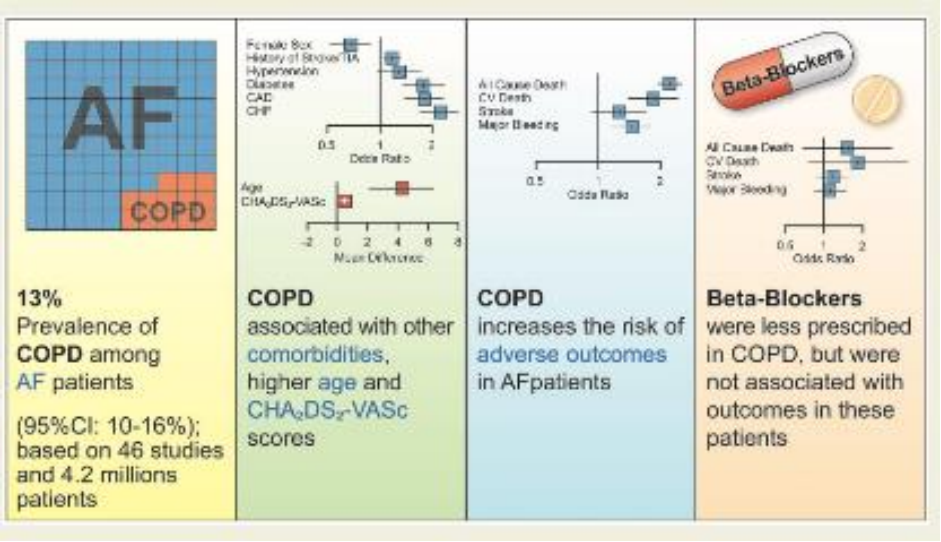
Phenotypes defined by obesity and three metabolic abnormalities (diabetes, hypertension and hyperlipidaemia)

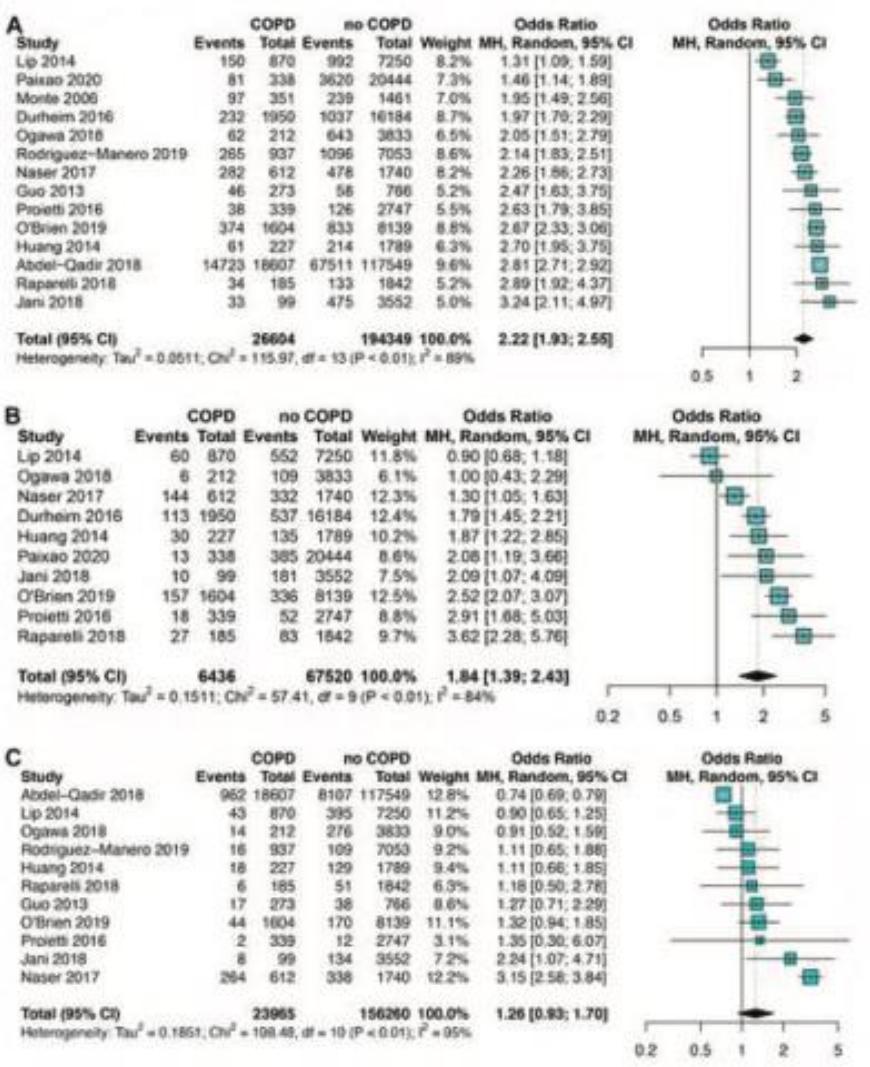


'… individuals with MHO did not have a higher risk of myocardial infarction, ischaemic stroke or cardiovascular death than metabolically healthy individuals with no obesity.
By contrast, they had a higher risk of new-onset HF and new-onset AF.'

Risk of outcomes in AF patients with COPD vs. non-COPD.

Romiti .. Lip, Proietti.
Eur Heart J 2021 doi:10.1093/eurheartj/ehab453





(A) All-cause death; (B) cardiovascular death; (C) ischemic stroke

Stroke risk factors in patients with Atrial Fibrillation

Hindricks et al Eur Heart J 2020 doi:10.1093/eurheartj/ehaa612

Most commonly studied clinical risk factors (a systematic review)[324]	Positive studies/All studies	Other clinical risk factors[325]	Imaging biomarkers[291,326–328]	Blood/urine biomarkers[329–332]
Stroke/TIA/systemic embolism	15/16	Impaired renal function/ CKD	*Echocardiography*	Cardiac troponin T and I
Hypertension	11/20	OSA	LA dilatation	Natriuretic peptides
Ageing (per decade)	9/13	HCM	Spontaneous contrast or thrombus in LA	Cystatin C
Structural heart disease	9/13	Amyloidosis in degenerative cerebral and heart diseases	Low LAA velocities	Proteinuria
Diabetes mellitus	9/14	Hyperlipidaemia	Complex aortic plaque	CrCl/eGFR
Vascular disease	6/17	Smoking	*Cerebral imaging*	CRP
CHF/LV dysfunction	7/18	Metabolic syndrome[333]	Small-vessel disease	IL-6
Sex category (female)	8/22	Malignancy		GDF-15
				von Willebrand factor
				D-dimer

CHF = congestive heart failure; CKD = chronic kidney disease; CrCl = creatinine clearance; CRP = C-reactive protein; eGFR = estimated glomerular filtration rate; GDF-15 = growth differentiation factor-15; IL-6 = interleukin 6; LA = left atrium; LAA = left atrial appendage; LV = left ventricular; OSA = obstructive sleep apnoea; TIA = transient ischaemic attack.

Summary of biomarkers associated with atrial fibrillation and outcome measures.

Tidbury.. Lip.
Expert Review of Precision Medicine and Drug Development 2020
https://doi.org/10.1080/23808993.2020.1804864

Biomarkers	AF incidence	Stroke risk	Bleeding risk	All-cause mortality	Recurrence
NT-proBNP	*	*		*	
Troponins	*	*		*	
CRP	*				*
IL-6		*			
vWF		*			
D-dimer		*			
GDF-15			*	*	
TGF-β1	*				*
Galectin-3	*				*
sST2	*			*	*
LA size and function	*	*			*
LAA morphology		*			
Myocardial fibrosis (MRI-LGE)		*			*
4q25 locus	*	*			

* An association between the biomarker and outcome has been identified i clinical trials. AF, atrial fibrillation; CRP, C-reactive protein;GDF-15, growt differentiation factor-15; IL-6, interleukin-6; LA, left atrium; LAA, left atria appendage; MRI-LGE, magnetic resonance imaging-late enhanced gadolinium NT-proBNP, N-terminal-pro B-type natriuretic peptide; sST2, soluble suppres sion of tumorigenicity 2; TGF-β1, transforming- growth factor-β1; vWF, vo Willebrand factor.

Additive Role of Plasma vWf Levels to Clinical Factors for Risk Stratification in AF

Lip et al Stroke 2006;37:2294-2300

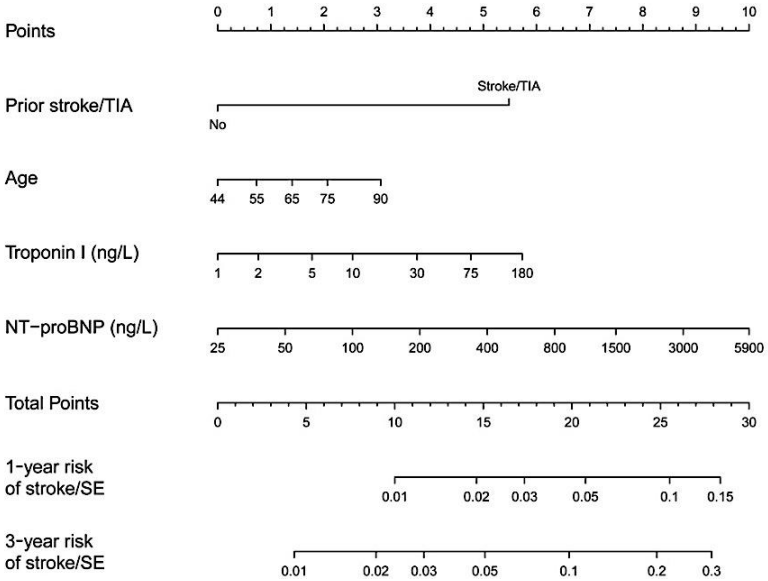
Risk score level	Annualized Rate (95% CI)	vWf Level	Annualized Rate (95% CI)
Ischemic stroke			
Birm, low	0 (0–0)	Low High	0 0
Birm, moderate	1.95 (1.17–2.92)	Low High	1.44 (0.69–2.48) 3.18 (1.44–5.59)
Birm, high	5.75 (3.68–8.28)	Low High	4.88 (2.51–8.04) 6.98 (3.59–11.5)
$CHADS_2$, low	0.65 (0.12–1.60)	Low High	0.54 (0.05–1.56) 1.09 (0.00–4.27)
$CHADS_2$, moderate	2.72 (1.76–3.89)	Low High	2.24 (1.22–3.56) 3.73 (1.85–6.26)
$CHADS_2$, high	7.03 (3.92–11.0)	Low High	5.68 (2.04–11.1) 8.37 (3.79–14.7)

Annualized Stroke Event Rates for Birmingham (Birm) and $CHADS_2$ Risk Scores by vWf level

...

high plasma vWf level was defined as the top tertile (>158 IU/dL) of vWf levels in the study cohort. Low plasma vWf levels were defined as <158 IU/dL

	Full cohort
Derivation cohort	
ABC-stroke (troponin I)	0.68 (0.65, 0.71)
ABC-stroke (troponin T)	0.67 (0.65, 0.70)
CHA_2DS_2-VASc	0.62 (0.60, 0.65)
Validation cohort	
ABC-stroke (troponin T)	0.66 (0.58, 0.74)
CHA_2DS_2-VASc	0.58 (0.49, 0.67)



ABC (age, biomarkers, clinical history) stroke risk score: a biomarker-based risk score for predicting stroke in AF

Hijazi et al Eur Heart J 2016 doi:10.1093/eurheartj/ehw054

- ABC score derived from a cohort on anticoagulant treatment (ARISTOTLE trial) and validated in a mixed population cohort—some treated with anticoagulation and some not (49%).
- Laboratories and commercial assays have variance and differences in reproducibility or lower limits of detection.

Biomarkers (whether blood, urine, or imaging-based) will always improve on risk prediction scores based on clinical factors … *at least statistically* [Note c-indexes all <0.70]

Long-Term Stroke Risk Prediction in Patients with AF: Comparison of ABC-Stroke & CHA_2DS_2-VASc Scores

Rivera-Caravaca .. .. Lip, Marin. J Am Heart Assoc. 2017;6:e006490. DOI: 10.1161/JAHA.117.006490

	C-Index	95% CI	*P* Value	z Statistic*	*P* Value*	IDI	*P* Value	NRI	*P* Value
At 3.5 y									
ABC-stroke score	0.663	0.634 to 0.690	<0.001	1.998	0.046	0.019	0.002	0.002	0.903
CHA_2DS_2-VASc score	0.600	0.567 to 0.625	<0.001						
At 6.5 years									
ABC-stroke score	0.662	0.633 to 0.690	<0.001	1.574	0.116	0.019	0.002	−0.053	<0.001
CHA_2DS_2-VASc score	0.620	0.590 to 0.648	<0.001						

ABC-stroke indicates age, biomarkers (N-terminal fragment B-type natriuretic peptide, high-sensitivity troponin), and clinical history (prior stroke/transient ischemic attack); CHA2DS2-VASc, cardiac failure or dysfunction, hypertension, age ≥75 (doubled), diabetes mellitus, stroke (doubled)—vascular disease, age 65 to 74 years and sex category (female); IDI, integrated discriminatory improvement; NRI, net reclassification index; ROC, receiver operating characteristic.
*For C-index comparison.

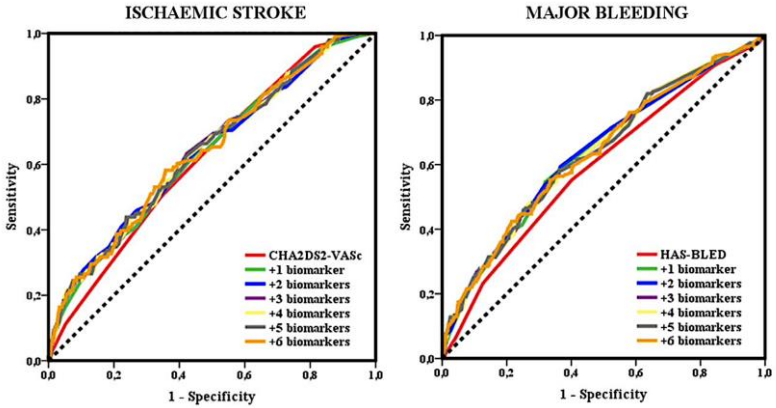
- At 6.5 years, 6.64% patients categorized as low-medium risk with ABC-stroke score experienced an ischemic stroke, vs 1.59% low-medium risk with CHA_2DS_2-VASc score.
- Patients at low-medium risk with ABC-stroke had a median CHA_2DS_2-VASc score of 3 (IQR 2–4) and a high risk of stroke per every CHA_2DS_2-VASc score point (hazard ratio, 1.3; 95% CI, 1.09-1.70, p=0.007)

ABC-stroke score did not provide better long term predictive accuracy for stroke in 'real world' AF patients. CHA_2DS_2-VASc score performed well in identifying patients at "low risk," better than ABC-stroke

Refining Stroke and Bleeding Prediction in Atrial Fibrillation by Adding Consecutive Biomarkers to Clinical Risk Scores

Rivera-Caravaca .. Lip, Roldan. Stroke 2019;50(6):1372-1379.

Adding consecutive biomarkers, the predictive ability of CHA_2DS_2-VASc for ischemic stroke was not increased, whereas the predictive ability of HAS-BLED for major bleeding was only slightly enhanced statistically.



The net benefit and clinical usefulness of the biomarker-based models were marginal in comparison to the original scores based on clinical risk factors.

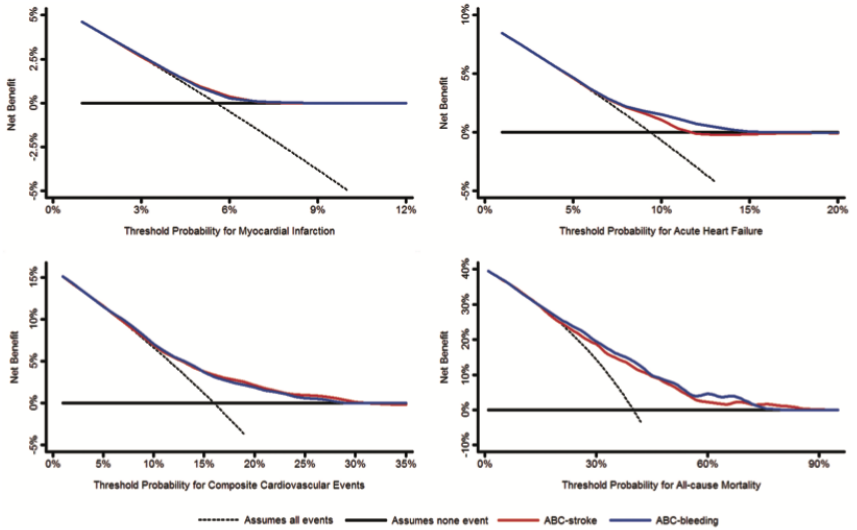
	C Index	95% CI	*Z* Score*	*P* Value*	IDI, %	95% CI	*P* Value	NRI, %	95% CI	*P* Value
Ischemic stroke										
CHA_2DS_2-VASc	0.621	0.589–0.652	…	…	…	…	…	…	…	…
+1 biomarker	0.634	0.602–0.655	0.721	0.471	1.70	0.00/4.40	0.060	−2.80	−13.20/19.00	0.667
+2 biomarkers	0.638	0.606–0.669	0.915	0.360	2.30	0.10/5.30	0.020	−5.60	−16.10/13.70	0.587
+3 biomarkers	0.641	0.610–0.672	1.153	0.249	2.70	0.70/5.30	<0.001	−4.50	−16.60/16.10	0.766
+4 biomarkers	0.639	0.607–0.670	1.024	0.306	2.70	0.60/5.50	0.020	−4.50	−14.10/15.30	0.826
+5 biomarkers	0.639	0.608–0.670	1.012	0.312	2.60	0.01/6.20	0.040	−3.30	−17.40/17.60	0.766
+6 biomarkers	0.639	0.608–0.670	1.022	0.307	2.60	0.30/6.20	0.020	−0.70	−10.90/16.70	0.999
Major bleeding										
HAS-BLED	0.600	0.561–0.625	…	…	…	…	…	…	…	
+1 biomarkers	0.636	0.605–0.667	2.158	0.031	4.00	0.90/7.80	<0.001	22.60	3.80/32.60	<0.001
+2 biomarkers	0.639	0.607–0.669	2.275	0.023	4.90	1.00/8.80	0.030	20.10	0.20/32.90	0.040
+3 biomarkers	0.639	0.607–0.669	2.249	0.025	5.20	1.90/8.90	<0.001	19.20	1.40/32.50	0.020
+4 biomarkers	0.638	0.606–0.669	2.188	0.029	5.00	1.60/8.70	<0.001	19.40	3.00/33.70	0.020
+5 biomarkers	0.635	0.604–0.666	2.003	0.045	5.00	1.90/8.80	<0.001	19.60	4.80/32.70	<0.001
+6 biomarkers	0.635	0.604–0.666	2.023	0.043	5.30	1.90/9.20	0.020	20.30	0.40/34.20	0.020

Predicting Adverse Events beyond Stroke and Bleeding with the ABC-Stroke and ABC-Bleeding Scores in Patients with AF: The Murcia AF Project

Camelo-Castillo .. Lip et al Thromb Haemost 2020;120(8):1200-1207.

	ABC-stroke	ABC-bleeding	*p*-Value[a]
	c-index (95% CI)	c-index (95% CI)	
Myocardial infarction	0.535 (0.504–0.566)	0.542 (0.511–0.572)	0.880
Acute heart failure	0.600 (0.564–0.624)	0.614 (0.584–0.644)	0.504
Composite cardiovascular events	0.644 (0.615–0.674)	0.644 (0.613–0.672)	0.946
All-cause mortality	0.704 (0.676–0.732)	0.726 (0.698–0.753)	0.187

[a]*p*-Value for c-index comparison.



Decision curve analyses for the primary endpoints.

- The ABC-stroke and ABC-bleeding scores demonstrated similar predictive ability for outcomes beyond stroke and bleeding, including MI, acute HF, a composite of cardiovascular events, and all-cause deaths.

Consistent with nonspecificity of biomarkers that predict "sick" patients or poor prognosis overall.

European Heart Journal Advance Access published December 20, 2012

European Heart Journal
doi:10.1093/eurheartj/ehs435

REVIEW

Controversies in cardiovascular medicine

Stroke and bleeding risk assessment in atrial fibrillation: when, how, and why?

Gregory Y.H. Lip*

University of Birmingham Centre for Cardiovascular Sciences, City Hospital, Birmingham B18 7QH, UK

Received 2 October 2012; revised 3 November 2012; accepted 25 November 2012

'….. the value of clinical risk scores would be enhanced by biomarkers that can include blood markers (e.g. vWf), urine (for example, proteinuria, eGFR or creatinine clearance), cardiac imaging (echocardiography, whether transthoracic or transoesophageal) and/or cerebral imaging (e.g. CT or MRI imaging) which can offer incremental predictive value for the identification of 'high risk' subjects.

…… this would be at the cost of reduced simplicity and practicality, limiting its (immediate) 'quick' use in everyday clinical practice'

Beyond CHA_2DS_2VASc ….. there remains a high residual risk

Cause of Death and Predictors of All-Cause Mortality in Anticoagulated Patients With Nonvalvular AF: Data From ROCKET AF

Pokorney et al J Am Heart Assoc. 2016;5: e002197 doi: 10.1161/JAHA.115.002197

	Rivaroxaban (n=582)	Warfarin (n=632)	HR (95% CI)	*P* Value
All-cause mortality	582 (4.5)	632 (4.9)	0.92 (0.82–1.03)	0.15
Vascular death	375 (2.9)	401 (3.1)	0.94 (0.81–1.08)	0.35
Nonvascular death	148 (1.2)	157 (1.2)	0.94 (0.75–1.18)	0.61
Death unknown cause	59 (0.5)	74 (0.6)	0.80 (0.57–1.12)	0.20
Sudden/unwitnessed death	169 (1.3)	174 (1.4)	0.97 (0.79–1.20)	0.79
CHF/shock cause of death	88 (0.7)	69 (0.5)	1.28 (0.93–1.75)	0.13
Malignancy cause of death	63 (0.5)	55 (0.4)	1.14 (0.80–1.64)	0.46
Intracranial hemorrhage death	27 (0.2)	43 (0.3)	0.63 (0.39–1.02)	0.06

Data are summarized as number of events (event rate per 100 patient-years of follow-up), unless otherwise indicated. CHF indicates congestive heart failure; HR, hazard ratio.

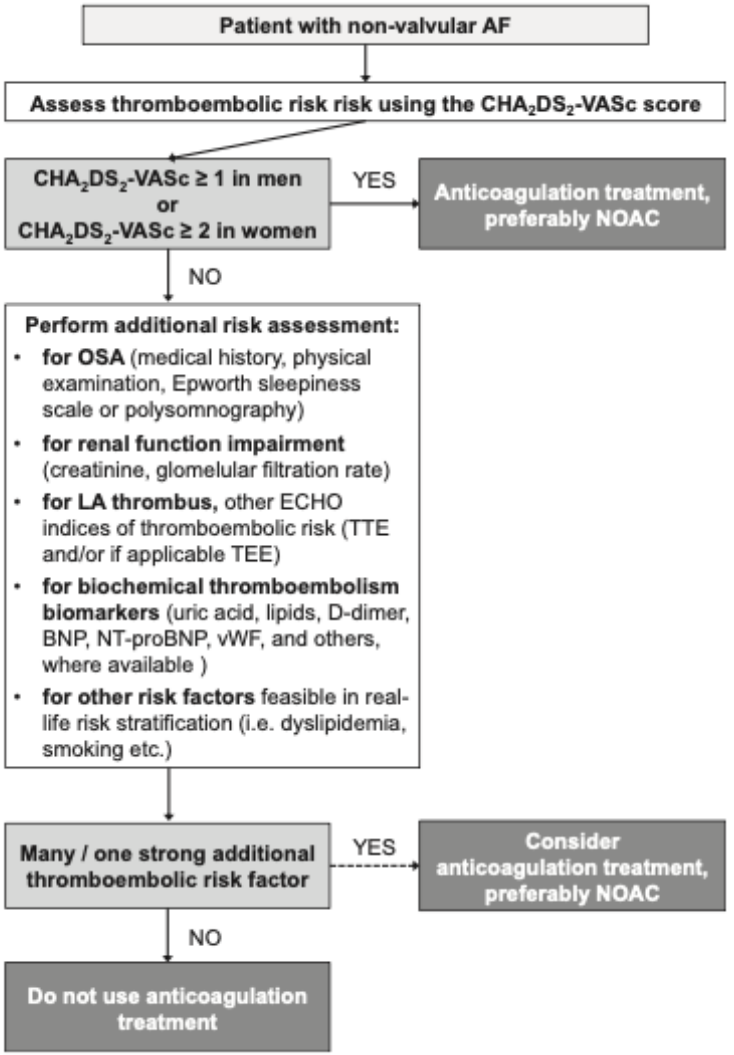
AF patients anticoagulated for nonvalvular atrial fibrillation, ~7 in 10 deaths were cardiovascular, whereas <1 in 10 deaths were caused by nonhemorrhagic stroke or systemic embolism.

Optimal prevention and treatment of heart failure, renal impairment, chronic obstructive pulmonary disease, and diabetes may improve survival.

We make it complicated ……

Stroke Risk Factors Beyond the CHA_2DS_2-VASc Score: Can We Improve Our Identification of "High Stroke Risk" Patients With Atrial Fibrillation?

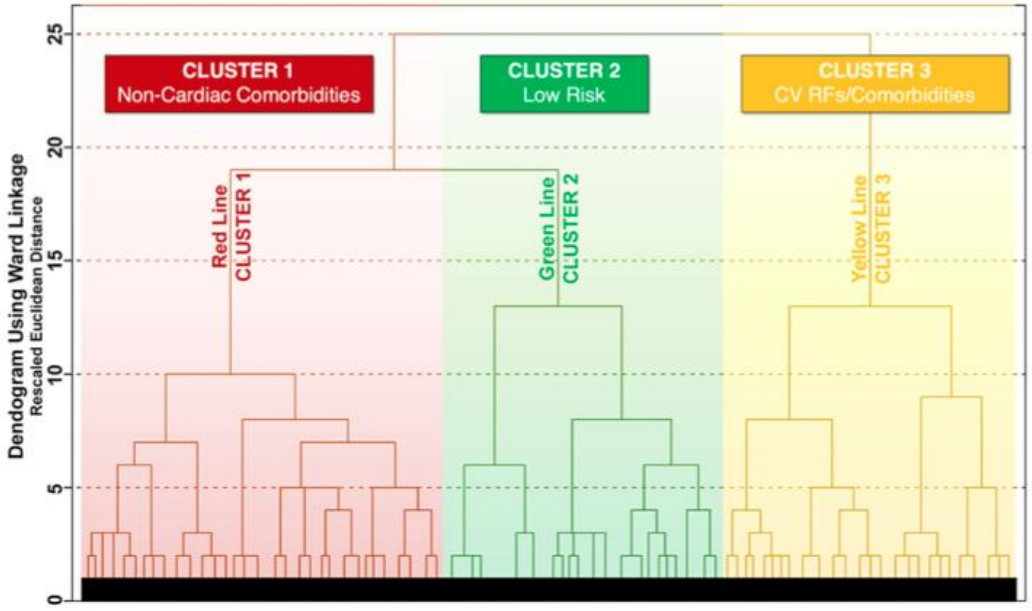
Szymanski .. Lip et al Am J Cardiol 2015
http://dx.doi.org/10.1016/j.amjcard.2015.08.049

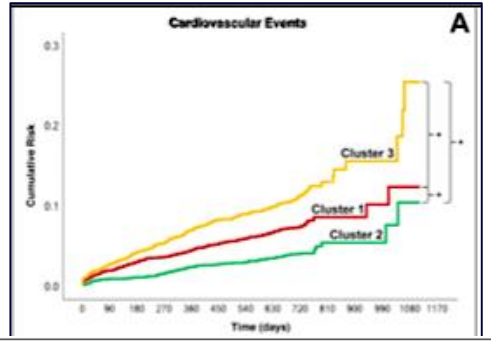


Proposed flow chart for thromboembolic risk assessment in atrial fibrillation patients

Impact of clinical phenotypes on management and outcomes in European AF patients: the ESC-EHRA EORP-AF General Long- Term Registry

Proietti …Lip. BMC Medicine 2021 19:256
https://doi.org/10.1186/s12916-021-02120-3





	Univariate		Multivariable[a]	
	HR (95% CI)	***P***	**HR (95% CI)**	***P***
Cardiovascular Events, *n* (%)				
Cluster 1	1.85 [1.46–2.34]	< .001	1.88 [1.48–2.38]	< .001
Cluster 2 (Ref.)	–	–	–	–
Cluster 3	2.82 [2.24–3.55]	< .001	2.87 [2.27–3.62]	< .001
All-cause death, *n* (%)				
Cluster 1	2.55 [2.03–3.21]	< .001	2.50 [1.98–3.15]	< .001
Cluster 2 (Ref.)	–	–	–	–
Cluster 3	3.55 [2.83–4.46]	< .001	3.42 [2.72–4.31]	< .001
Composite outcome, *n* (%)				
Cluster 1	2.09 [1.74–2.51]	< .001	2.09 [1.74–2.51]	< .001
Cluster 2 (Ref.)	–	–	–	–
Cluster 3	2.81 [2.34–3.37]	< .001	2.79 [2.32–3.35]	< .001

Legend: [a]adjusted for type of AF, EHRA score, use of OAC. *HR* hazard ratio. For other acronyms, please see previous tables' legends

Improving dynamic stroke risk prediction in non-anticoagulated patients with and without AF: comparing common clinical risk scores and ML algorithms

Lip et al EHJ-QCCO 2021: doi:10.1093/ehjqcco/qcab037

The future? Complicated …

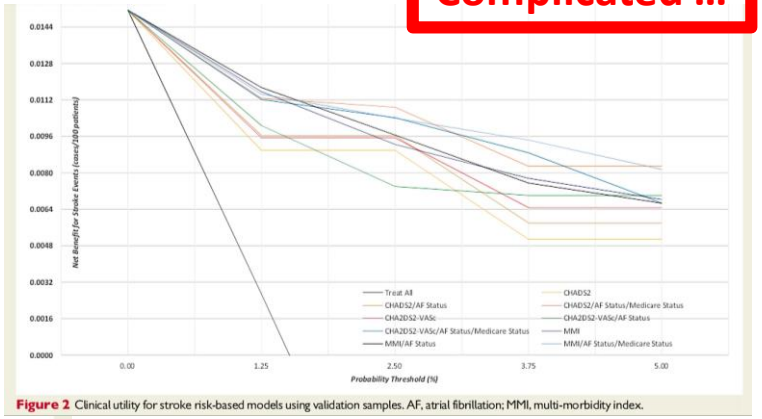


Figure 2 Clinical utility for stroke risk-based models using validation samples. AF, atrial fibrillation; MMI, multi-morbidity index.

The best prediction model was derived on the basis of non-linear formulations using ML criteria, with the highest c-index was obtained for logistic regression [0.892; 95% CI 0.886–0.898] with consistency on external validation (0.891; 95% CI 0.882–0.9).

These were significantly higher than those based on the conventional stroke risk scores ($CHADS_2$: 0.7488, 95% CI 0.746–0.7516; CHA_2DS_2-VASc: 0.7801, 95% CI 0.7772–0.7831) and multi-morbid index (0.8508, 95% CI 0.8483–0.8532).

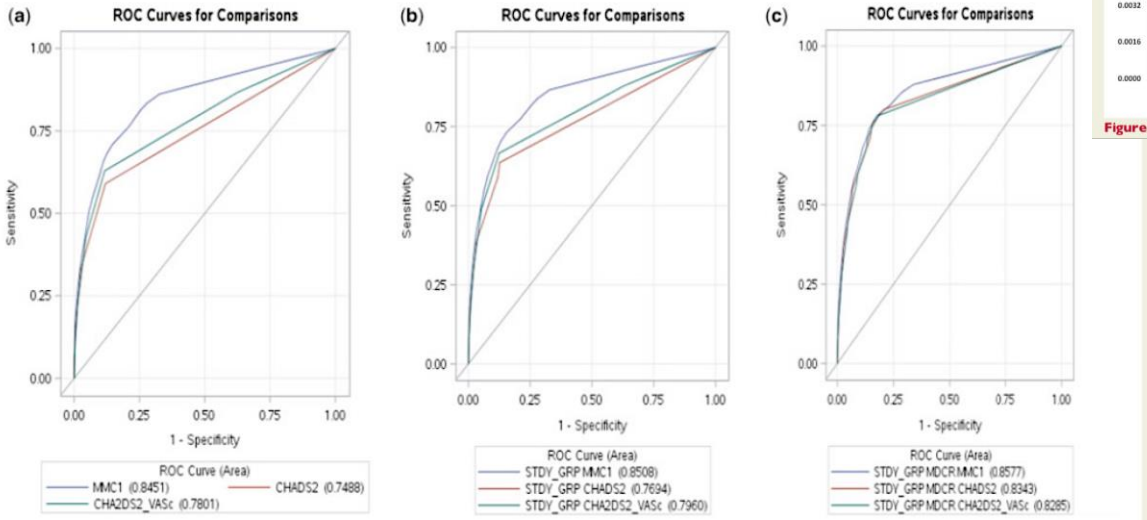


Figure 1 External validation for three sets of three clinical rule-based models: (*A*) Set 1: multi-morbid index 'MMC1' (C index 0.8451, 95% CI 0.8427–0.8476), $CHADS_2$ (C index 0.7488, 95% CI 0.746–0.7516), CHA_2DS_2VASc (C index 0.7801, 95% CI 0.7772–0.7831); (*B*) Set 2: multi-morbid index/AF status (C index 0.8508, 95%CI 0.8483–0.8532), $CHADS_2$/AF status (C index 0.7694, 95% CI 0.7667–0.7722), CHA_2DS_2VASc/AF status (C index 0.796, 95% CI 0.7931–0.7989); (*C*) Set 3: multi-morbid index/AF status/Medicare status (C index 0.8577, 95% CI 0.8553–0.86), $CHADS_2$/AF status/Medicare status (C index 0.8343, 95% CI 0.8319–0.8368), CHA_2DS_2VASc/AF status/Medicare status (C index 0.8285, 95% CI 0.8259–0.8312).

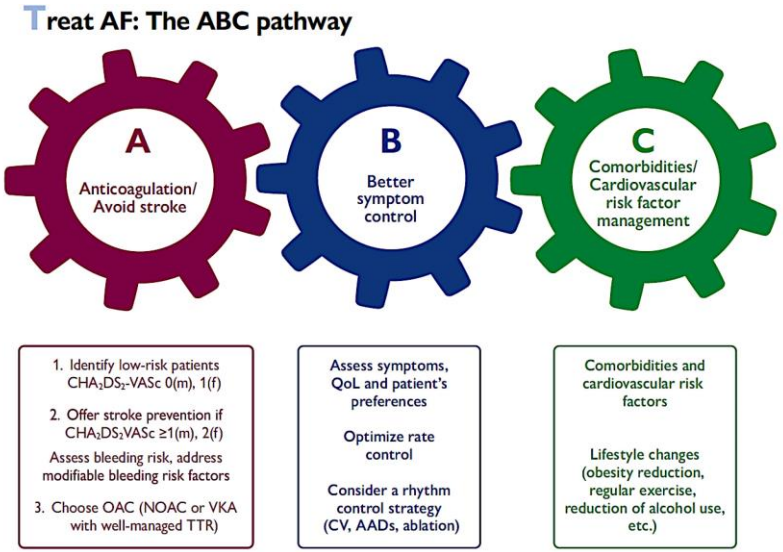
Or we can keep it simple and practical ……

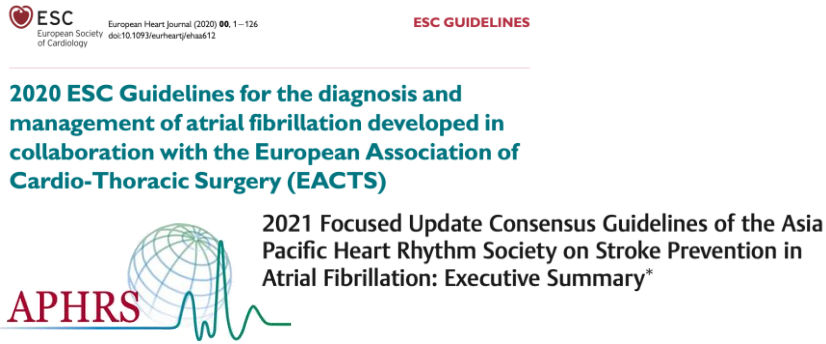
‘A’ Avoid stroke/anticoagulation

The default is stroke prevention* unless ‘low risk’

…given the limitations of (all) risk scores

*Stroke prevention means oral anticoagulation, whether as well managed warfarin with good TTR (>70%) or (ideally) NOAC





Thinking outside the CHA_2DS_2VASc Box ….

Let me conclude with this:

Impact of adherence to the ABC pathway on clinical outcomes in patients with AF

Romiti .. Lip, Proietti. Thromb Haemostat 2022 Mar;122(3):406-414