

CHA₂DS₂-VASc 1: to anticoagulate or not?

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

The CHA₂DS₂-VASc score

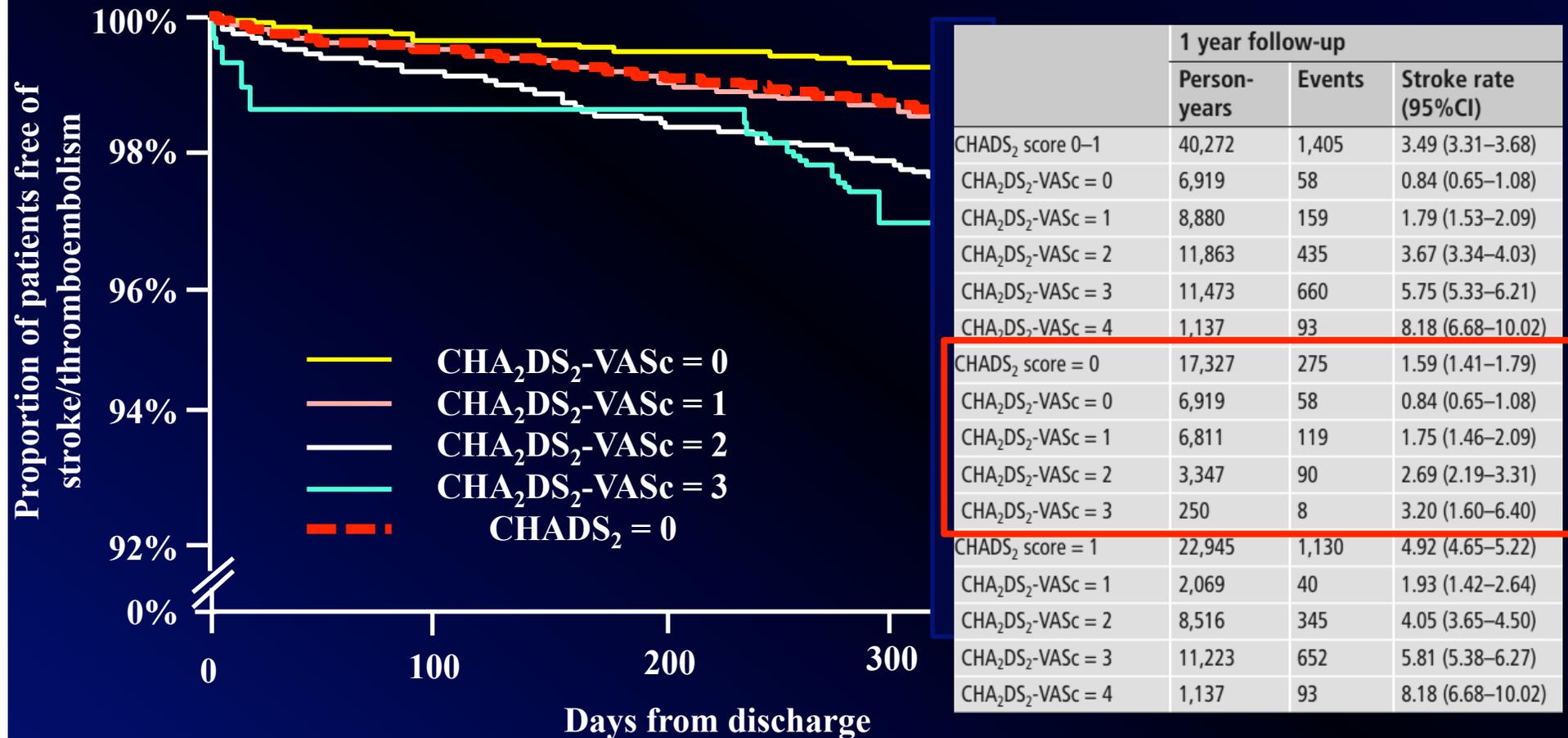
*Camm, Kirchhof, Lip et al
Eur Heart J 2010; 31, 2369–2429*

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 \geq 75 years	Heart failure or moderate to severe LV systolic dysfunction [e.g. LV EF \leq 40%] Hypertension - Diabetes mellitus Female sex - Age 65-74 years Vascular disease*

Stroke risk factors	Score
<u>C</u> ongestive heart failure/LV dysfunction	1
<u>H</u> ypertension	1
<u>A</u> ged \geq 75 years	2
<u>D</u> iabetes mellitus	1
<u>S</u> troke/TIA/TE	2
<u>V</u> ascular disease [prior MI, PAD, or aortic plaque]	1
<u>A</u> ged 65–74 years	1
<u>S</u> ex category [i.e. female gender]	1

The value of the CHA₂DS₂-VASc score for refining stroke risk stratification in patients with a CHADS₂ score 0-1

Olesen et al *Thromb Haemost.* 2012 Jun;107(6):1172-9



In patients with a CHADS₂=0, c-statistic was 0.573 (0.539-0.608) and increased to 0.641 (0.610-0.671) when CHA₂DS₂-VASc was included.

Reliable identification of 'truly low' thromboembolic risk in patients initially diagnosed with 'lone' AF:

Belgrade AF Study

Potpara ... Lip. Circ Arrhythmia Electrophysiol 2012;5(2):319-26

Predictive ability and Multivariable Relationships of CHADS₂, CHA₂DS₂-VASc, and van Walraven Scores of 0 With the Absence of Ischemic Strokes During Follow-Up

		Predictive ability of score=0			Multivariable analysis		
<i>Risk score of 0</i>	<i>C-statistic</i>	<i>95%CI</i>	<i>p</i>	<i>OR</i>	<i>95%CI</i>	<i>p</i>	
CHADS₂	0.58	0.38-0.79	0.426	0.359	
CHA₂DS₂-VASc	0.72	0.61-0.84	0.031	5.1	1.5-16.8	0.008	
Van Walraven	0.65	0.46-0.85	0.133	0.100	

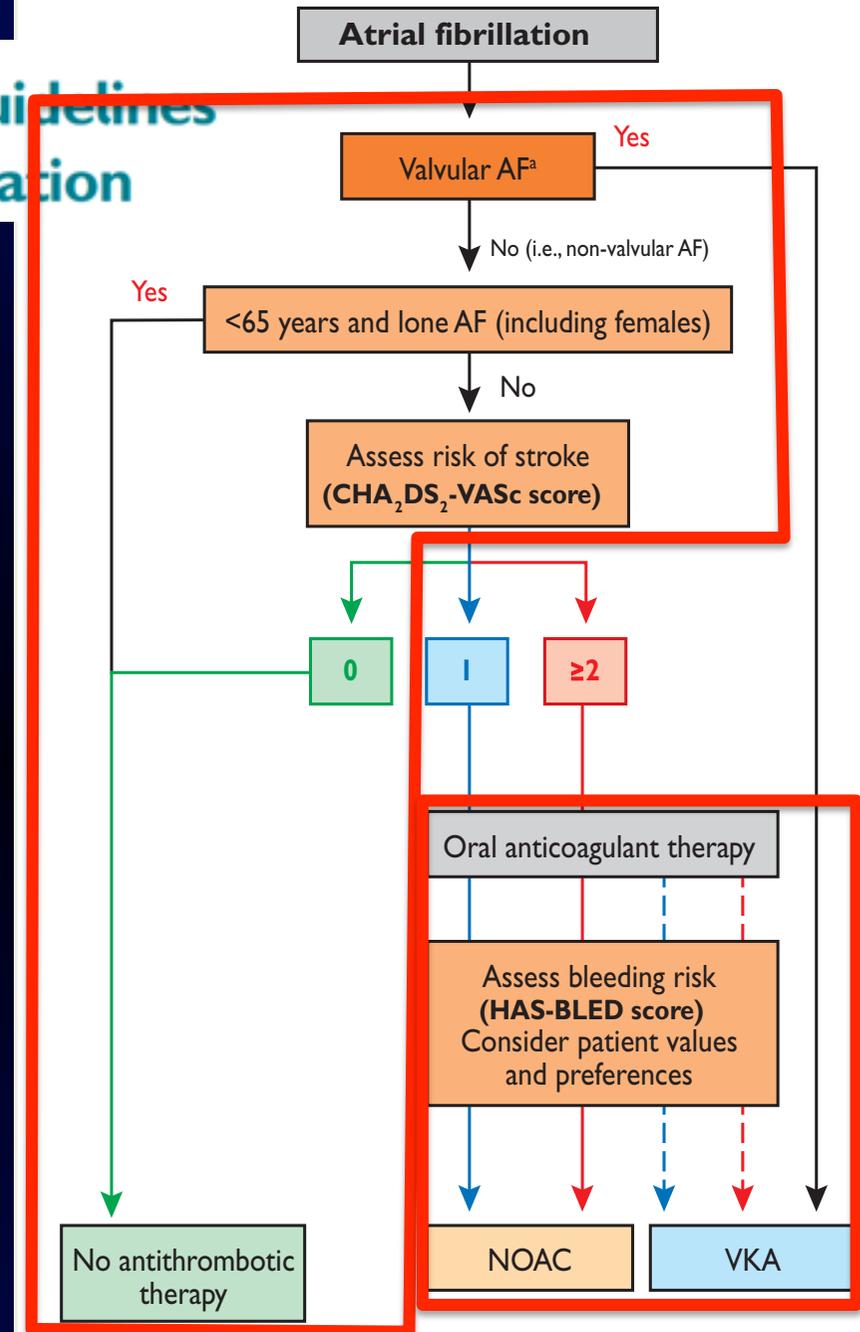
The CHA₂DS₂-VASc score reliably identified the 'lone' AF patients who were at 'truly low risk' for thromboembolism, and was the only tested risk stratification scheme with a significant predictive ability for thromboembolism amongst lone AF patients.

2012 focused update of the ESC Guidelines for the management of atrial fibrillation

‘This guideline strongly recommends a practice shift towards greater focus on identification of ‘truly low risk’ patients with AF (who do not need any antithrombotic therapy), instead of trying to focus on identifying ‘high risk patients’”

SIMPLICITY IS BEST

*European Heart Journal 2012
doi:10.1093/eurheartj/ehs253*



2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation

January C et al Circulation 2014 DOI: 10.1161/CIR.0000000000000041

Antithrombotic therapy based on shared decision-making, discussion of risks of stroke and bleeding, and patient's preferences

CHA₂DS₂-VASc score recommended to assess stroke risk

Warfarin recommended with mechanical heart valves.
Target INR intensity should be based on the type and location of prosthesis

If end-stage CKD (CrCl <15 mL/min) or on hemodialysis, it is reasonable to prescribe warfarin for OAC [NOACs not recommended]

Prior stroke, TIA, or CHA₂DS₂-VASc ≥2

OAC, either VKA or NOAC (dabigatran, rivaroxaban or apixaban) (Class I)

CHA₂DS₂-VASc=1

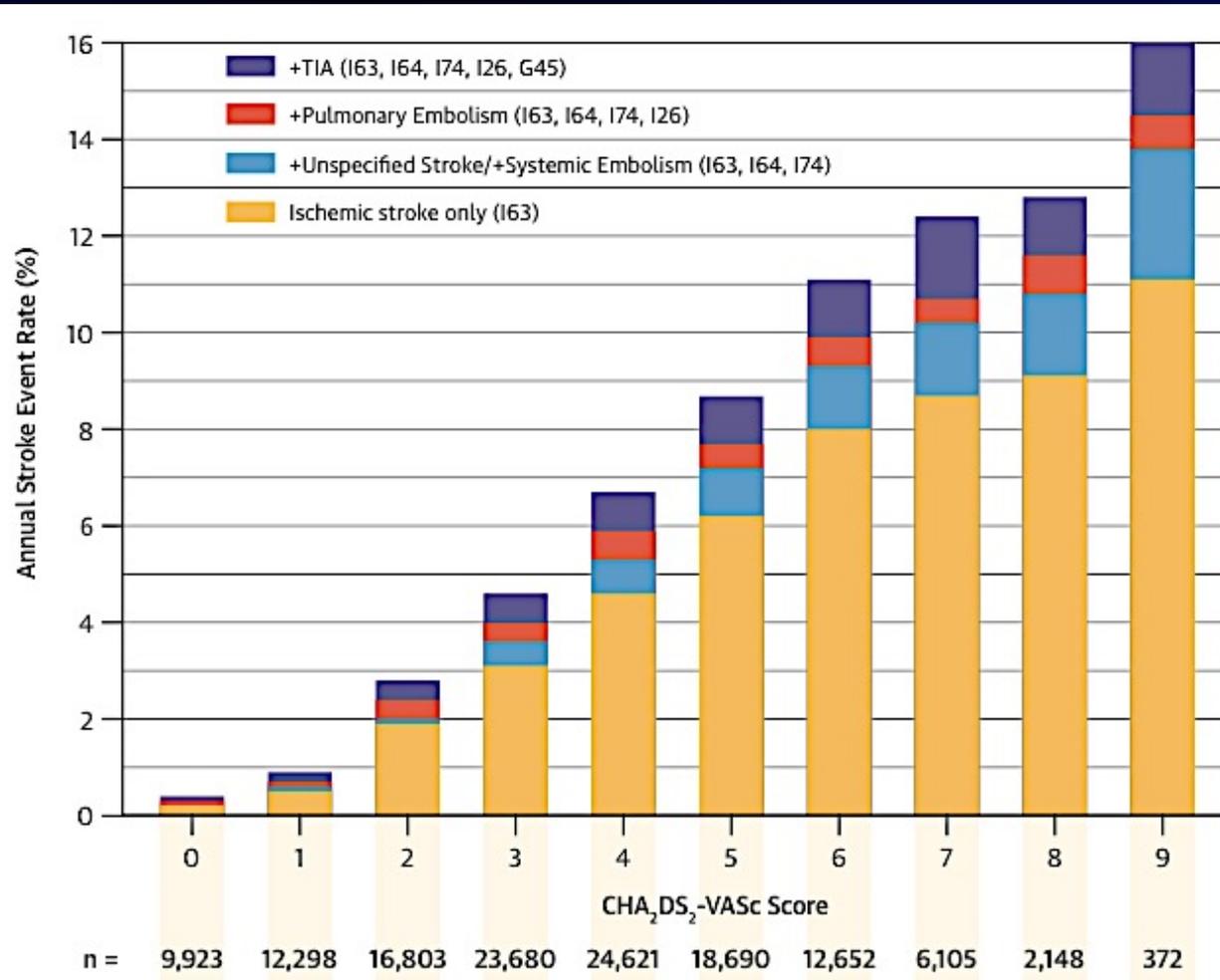
No antithrombotic therapy or treatment with OAC or aspirin (Class IIb)

CHA₂DS₂-VASc score of 0

No antithrombotic Rx (Class IIa)

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

Friberg et al J Am Coll Cardiol 2015;65:225–32



140,420 patients with a diagnosis of nonvalvular AF in the Swedish National Patient Register between July 1, 2005, and June 31, 2010, who had not been exposed to warfarin at any time during follow-up.

At a CHA₂D₂-VASc score of 1, the annual event rates varied between 0.5% and 0.9%, depending on whether only ischemic strokes were counted or a more inclusive endpoint was used

‘The risk of ischemic stroke in patients with AF and a CHA₂D₂-VASc score of 1 seems to be lower than previously reported’

CHA₂DS₂-VASc=1: Is it worth taking the risk?

Commentary on Friberg et al

<http://www.practiceupdate.com/content/benefit-of-anticoagulation-unlikely-in-atrial-fibrillation-and-a-cha2ds2-vasc-score-of-1/21229/7/2/1>

- Focus on headline “ischemic stroke” rates clearly results in absolute rates lower than the more traditional “all stroke and systemic embolism” endpoints in randomized clinical trials of stroke prevention.
 - OAC reduces the risk for ALL stroke/systemic embolism by 64% and all-cause mortality by 26% compared with placebo/control.
- Exclusion of patients who were treated with warfarin 6 months prior to baseline, but also patients who received warfarin treatment during follow-up.
 - The latter approach can introduce a bias away from the null hypothesis (that patients with a CHA₂DS₂-VASc score of 1 for males and 2 for females will benefit from OAC treatment).
 - All events studied for the excluded patients are omitted by this “conditioning on the future” approach.

Stroke risk in atrial fibrillation: Do we anticoagulate CHADS₂ or CHA₂DS₂-VASc ≥ 1 , or higher?

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Thromb Haemost. DOI: <http://dx.doi.org/10.1160/TH15-02-0154>.

The risks of risk scores for stroke risk assessment in atrial fibrillation

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Thromb Haemost. DOI: <http://dx.doi.org/10.1160/TH15-03-0210>.

Event rates from various studies investigating AF patients off oral anticoagulant treatment and stratified according to ESC/NICE guidelines recommendations

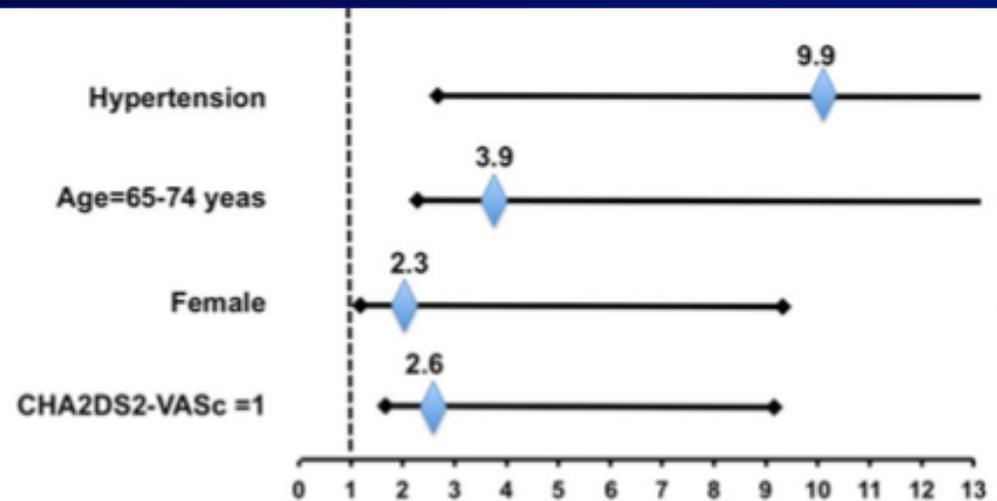
Nielsen and Chao. *Thromb Haemostat* 2015 DOI: <http://dx.doi.org/10.1160/TH15-03-0210>.

Authors	Year of publication	Study period	Data source	Number of patients	Outcome of interest	Event rate in CHA ₂ DS ₂ -VASc score of 0	Event rate in CHA ₂ DS ₂ -VASc score 1
Friberg et al. (22)	2012	2005 to 2008	Nationwide cohort	90,706	Ischaemic stroke	0.2 %/year (n=15)	0.6 %/year (n=63)
Olesen et al. (25)	2012	1997–2006	Nationwide cohort	73,538	Ischaemic stroke/SE/PE	0.78 %/year	2.01 %/year
Singer et al. (26)	2013	1996 to 1997	Ambulatory based cohort	10,927	Ischaemic stroke/ thromboembolic events	0.04 %/year	0.55 %/year
Taillandier et al. (27)	2013	2000 to 2010	Community based cohort	8,962	Ischaemic stroke/ thromboembolism	0.69 %/year	NR
Lip et al. (8)	2014	1999–2012	Nationwide cohort	47,090	Ischaemic stroke/SE/TIA	1.13 %/year	2.94 %/year
Huang et al. (28)	2014	1997 to 2011	Hospital based cohort	548	Ischaemic stroke	2.4 %/year	6.6 %/year
Chao et al. (29)	2014	1996–2011	National Health Insurance Research Database	9,416	Ischaemic stroke	1.15 %/year	NR
Chao et al. (30)	2015	1996 to 2011	National Health Insurance Research Database	12,935	Ischaemic stroke	NR	2.75 %/year
Lip et al. (9)	2015	1998–2012	Nationwide cohort	39,400	Ischaemic stroke	0.49 %/year	1.50 %/year
Lip et al. (4)	2015	1999–2012	Nationwide cohort	22,582	Ischaemic stroke/SE/TIA	1.13 %/year	4.32 %/year

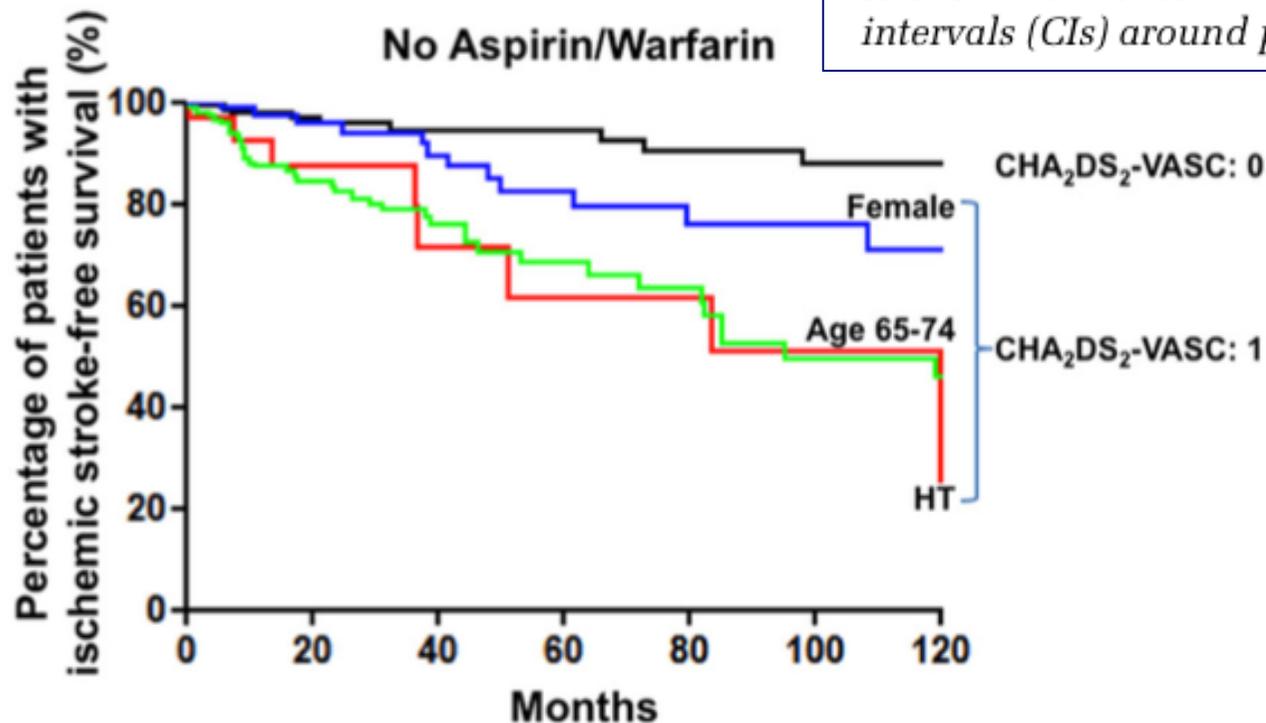
ESC: European Society of Cardiology. NICE: National Institute of Clinical Excellence. OAC: Oral anticoagulant. SE: Systemic embolism. PE: Pulmonary embolism. TIA: Transient ischaemic attack. Yr: Year. NR: Not reported.

Refinement of Ischemic Stroke Risk in Patients with AF & CHA₂DS₂-VASc 1

Huang et al
 PACE 2014 doi: 10.1111/pace.12445



Relative effects of individual components constituting CHA₂DS₂-VASc score of 1 on ischemic stroke. Horizontal lines represent 95% confident intervals (CIs) around point estimates.

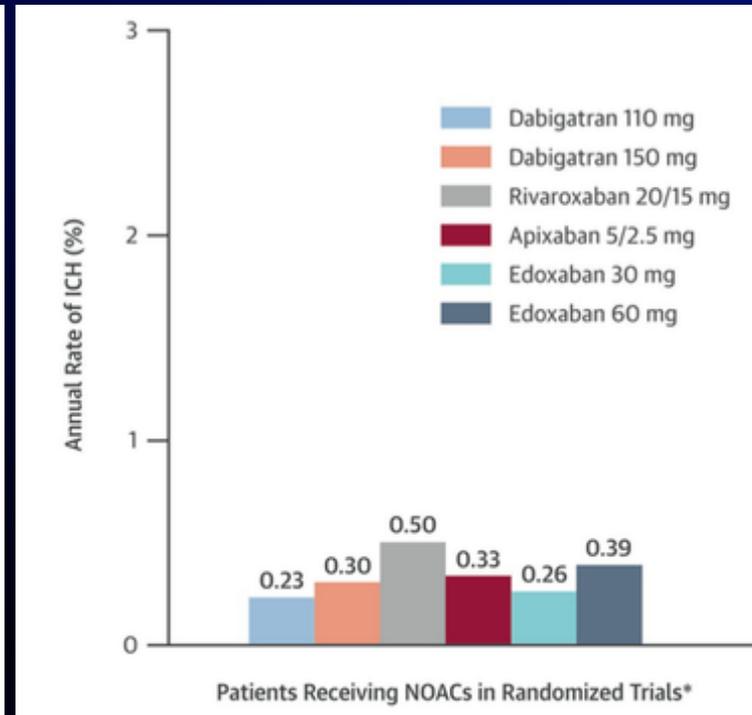
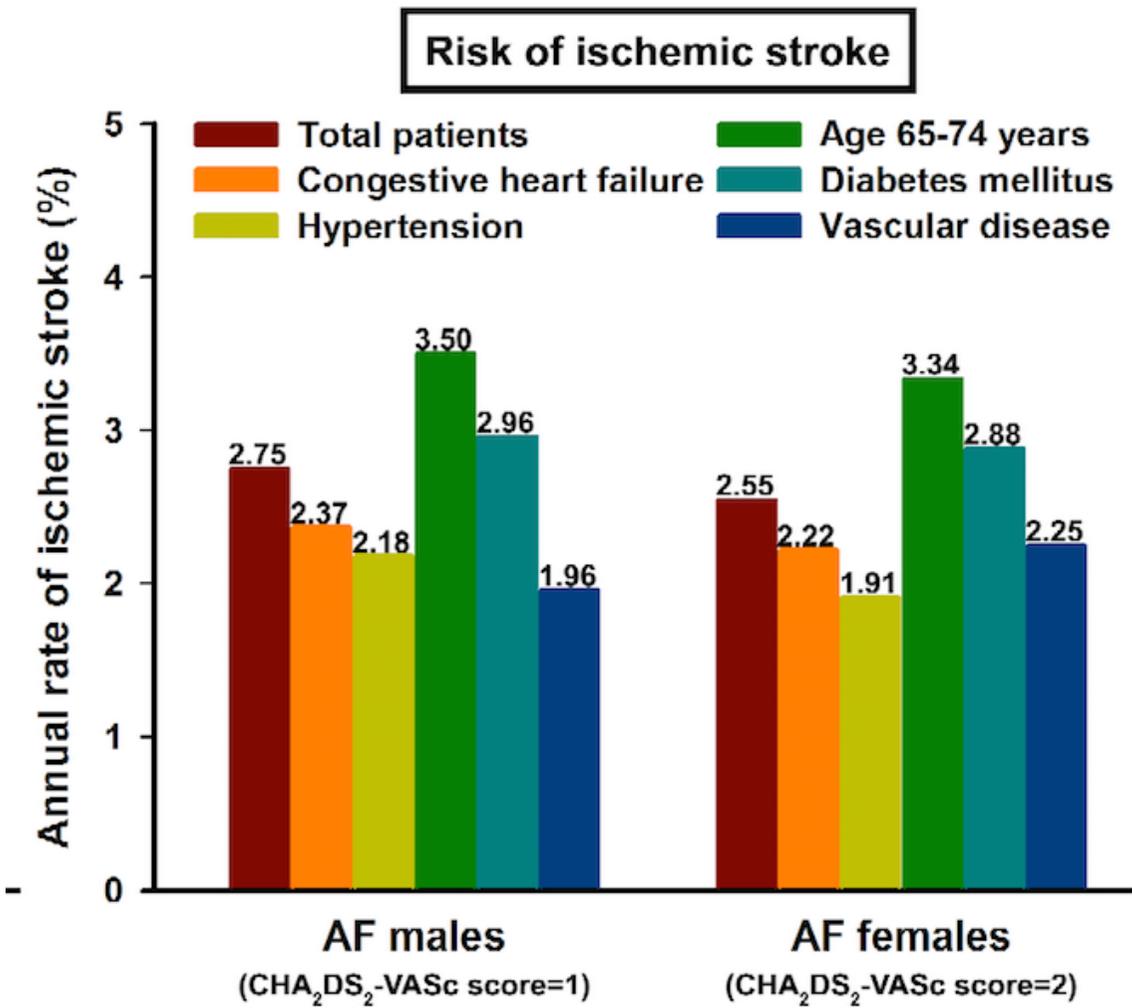


Mean follow-up of 38.5 ± 51.0 months (1,758 patient-years),

- 17 strokes occurred in patients with CHA₂DS₂-VASc 0 (annual ischemic stroke risk: 2.4% per year);
- 70 strokes in patients with CHA₂DS₂-VASc 1 (annual ischemic stroke risk: 6.6% per year, HR: 2.58, 95% CI: 1.67-3.97, P = 0.0002).

Is OAC Necessary in AF Patients with a CHA₂DS₂-VASc Score=1 (males) or 2 (females)? A nationwide cohort study

Chao, Liu ... Lip, Chen. JACC 2014. Presented at ESC 2014

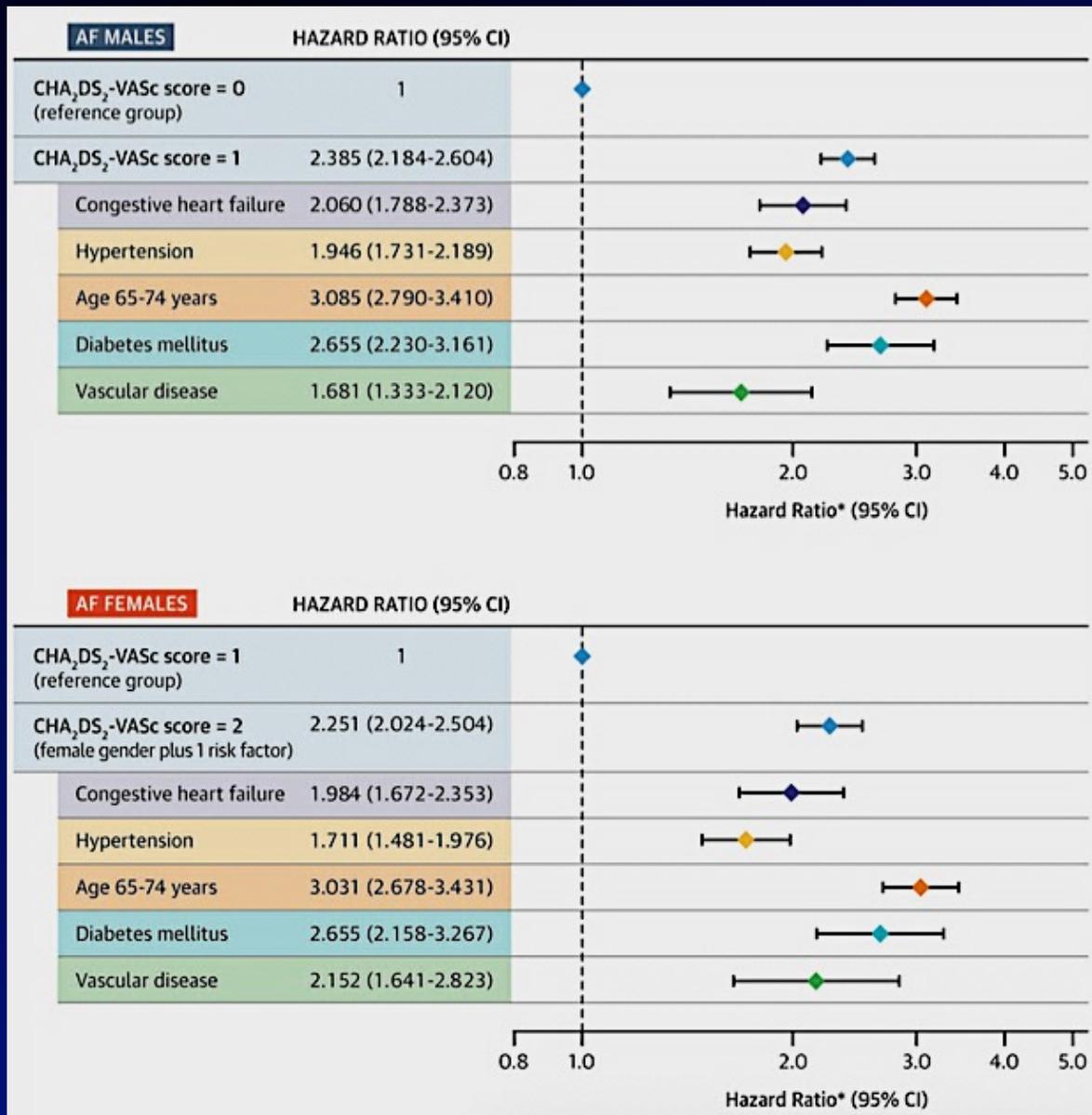


Ischaemic stroke rates in non-anticoagulated male and female patients with 1 additional stroke risk factor

OAC should be considered for AF patients with 1 additional stroke risk factors (ie. CHA₂DS₂-VASc score of 1 (males) or 2 (females))

Is OAC Necessary in AF Patients with a CHA₂DS₂-VASc Score=1 (males) or 2 (females)? A nationwide cohort study

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Ischaemic stroke rates in non-anticoagulated male and female patients with 1 additional stroke risk factor

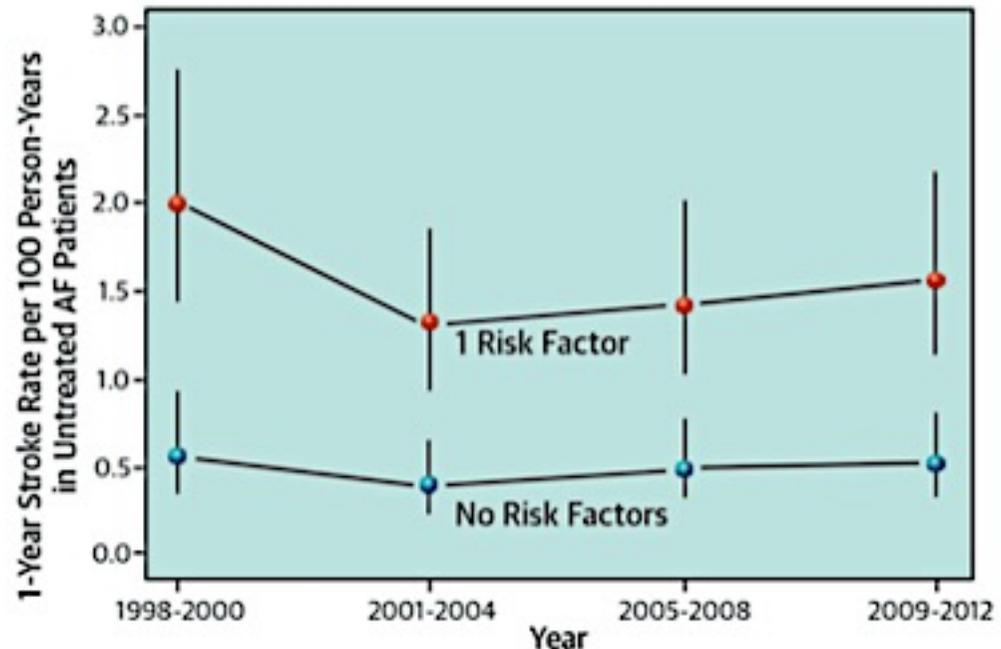
Oral anticoagulants should be considered for AF patients with 1 additional stroke risk factors (ie. CHA₂DS₂-VASc score of 1 (males) or 2 (females))

OAC, Aspirin, or No Therapy in Patients With Nonvalvular AF With 0 or 1 Stroke Risk Factor Based on CHA₂DS₂-VASc

Lip et al JACC 2015
<http://dx.doi.org/10.1016/j.jacc.2015.01.044>

Stroke event rates for untreated low-risk patients (CHA₂DS₂-VASc 1/4 0 [male], 1 [female]) were 0.49 per 100 person-years at 1 year and 0.47 per 100 person-years at full FU.

The presence of 1 additional stroke risk factor (CHA₂DS₂-VASc= 1 [male], = 2 [female]) among untreated patients increased the stroke rate at 1 year to 1.55 per 100 person-years, representing a significant 3.01-fold increase.



OAC, Aspirin, or No Therapy in Patients With Nonvalvular AF With 0 or 1 Stroke Risk Factor Based on CHA₂DS₂-VASc score

Lip et al JACC 2015 <http://dx.doi.org/10.1016/j.jacc.2015.01.044>

Event Rates Per 100 PYs at 1 Year FU
According to Treatment Strategy Initiated at
Day 14 After Discharge With Incident AF

	No Rx	Aspirin	Warfarin
No risk factors			
Ischaemic stroke	0.49	0.78	0.88
Death	3.87	3.12	2.20
ICH	0.15	0.10	0.16
1 risk factor			
Ischaemic stroke	1.50	1.45	1.02
Death	11.3	5.66	4.00
ICH	0.36	0.20	0.44

Low-risk patients) have a truly low risk for stroke and bleeding.

With 1 additional stroke risk factor, there was a significant increase in event rates (particularly mortality) if non-anticoagulated.

CHA₂DS₂-VASc 1: to anticoagulate or not?

- Risk scores are designed to be reductionist and simple to facilitate their practical and broad use in various (and busy) clinical settings.
 - This is not indicative of a failure of CHA₂DS₂-VASc as a stroke risk score, as it is not necessary for risk scores to identify exact risk but to provide useful thresholds at which important dichotomous clinical decisions are made; for example, use of anticoagulation vs no anticoagulation.

Although the actual stroke risk may vary with respect to any given score in an individual patient, we should be less obsessed with identifying the “exact” stroke risk, which is not possible given the basic fact that a patient’s clinical status does not remain static, and in most patients with at least one risk factor for stroke, we should be considering OAC as they are at an elevated risk.

The ESC and NICE guidelines recommend a two-step approach.

- Step 1: Initially identify the low-risk patients; then
- Step 2: Offer OAC to those with one or more stroke risk factors. As the decision is made for OAC, step 2 is irrespective of whether we are dealing with a CHA₂DS₂-VASc score 2, 3, 4 or more!