



Risk Stratification in Atrial Fibrillation

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Stroke is a frequent complication of AF

- Stroke is the leading complication of AF
- Patients with AF have a five-fold higher stroke risk than those without AF¹
- AF doubles the risk of stroke when adjusted for other risk factors²
- Without preventive treatment, each year approximately 1 in 20 patients (5%) with AF will have a stroke³
 - When transient ischaemic attacks and clinically 'silent' strokes are considered, the rate of brain ischaemia associated with non-valvular AF exceeds 7% per year⁴
- It is estimated that 15% of all strokes are caused by AF⁵ and that 12,500 strokes per year in England are directly attributable to AF⁶

Stroke is a serious complication of AF

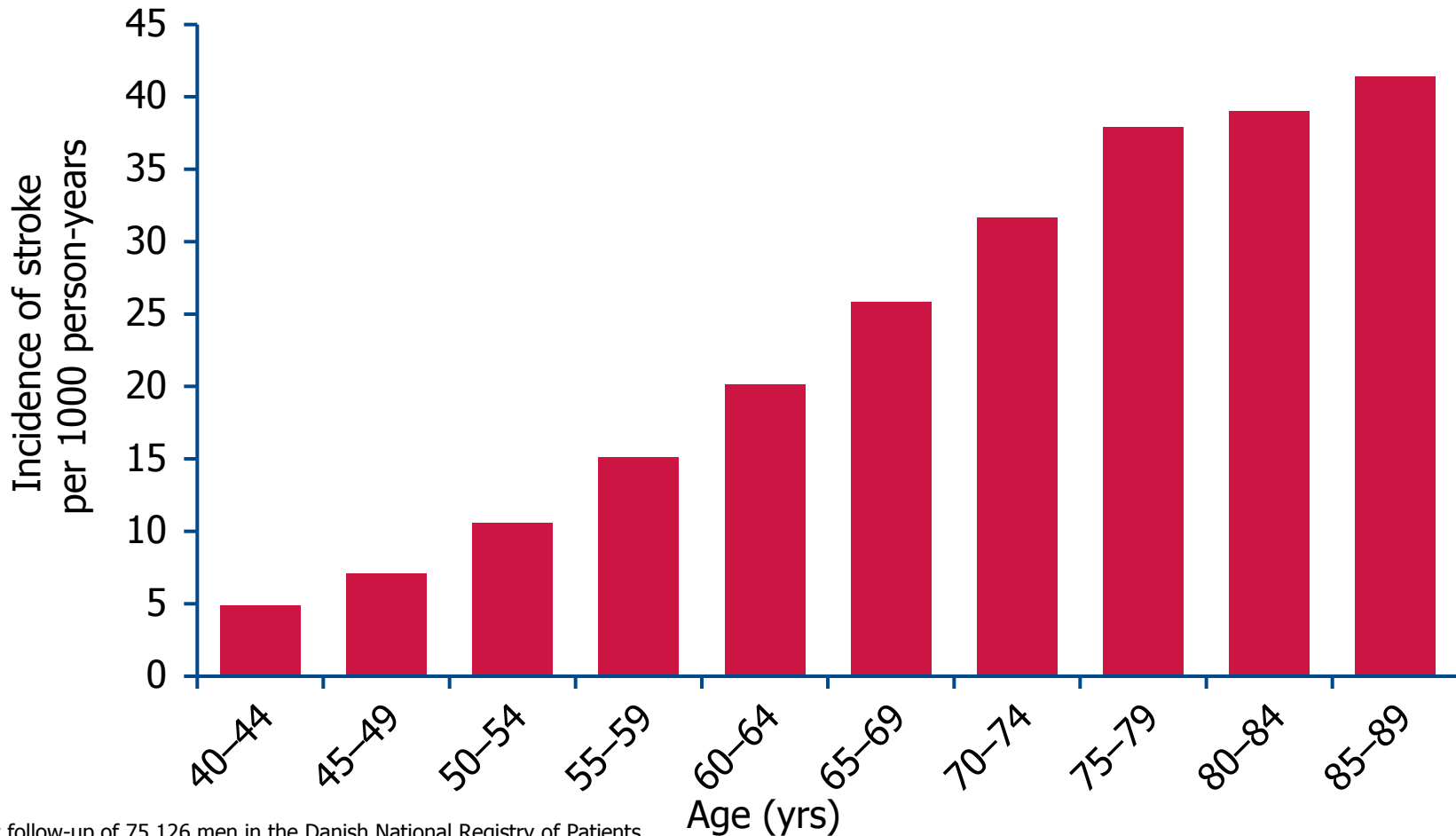
- Stroke in AF is associated with a heavy burden of morbidity and mortality
- AF stroke is usually more severe than stroke due to other causes¹
- Compared with other stroke patients, those with AF are more likely to:
 - Have cortical deficit (e.g. aphasia), severe limb weakness and diminished alertness, and be bedridden on admission²
 - Have longer in-hospital stay with a lower rate of discharge to their own home³
- The mortality rate for patients with AF is double that in people with normal heart rhythm⁴

1. Savelieva I et al. *Ann Med* 2007;39:371–91; 2. Dulli DA et al. *Neuroepidemiology* 2003;22:118–23; 3. NICE clinical guideline 36 June 2006. Available at <http://www.nice.org.uk/guidance/CG36/?c=91497>; accessed April 2010;

4. Benjamin EJ et al. *Circulation* 1998;98:946–52

Incidence of stroke in AF patients increases with age

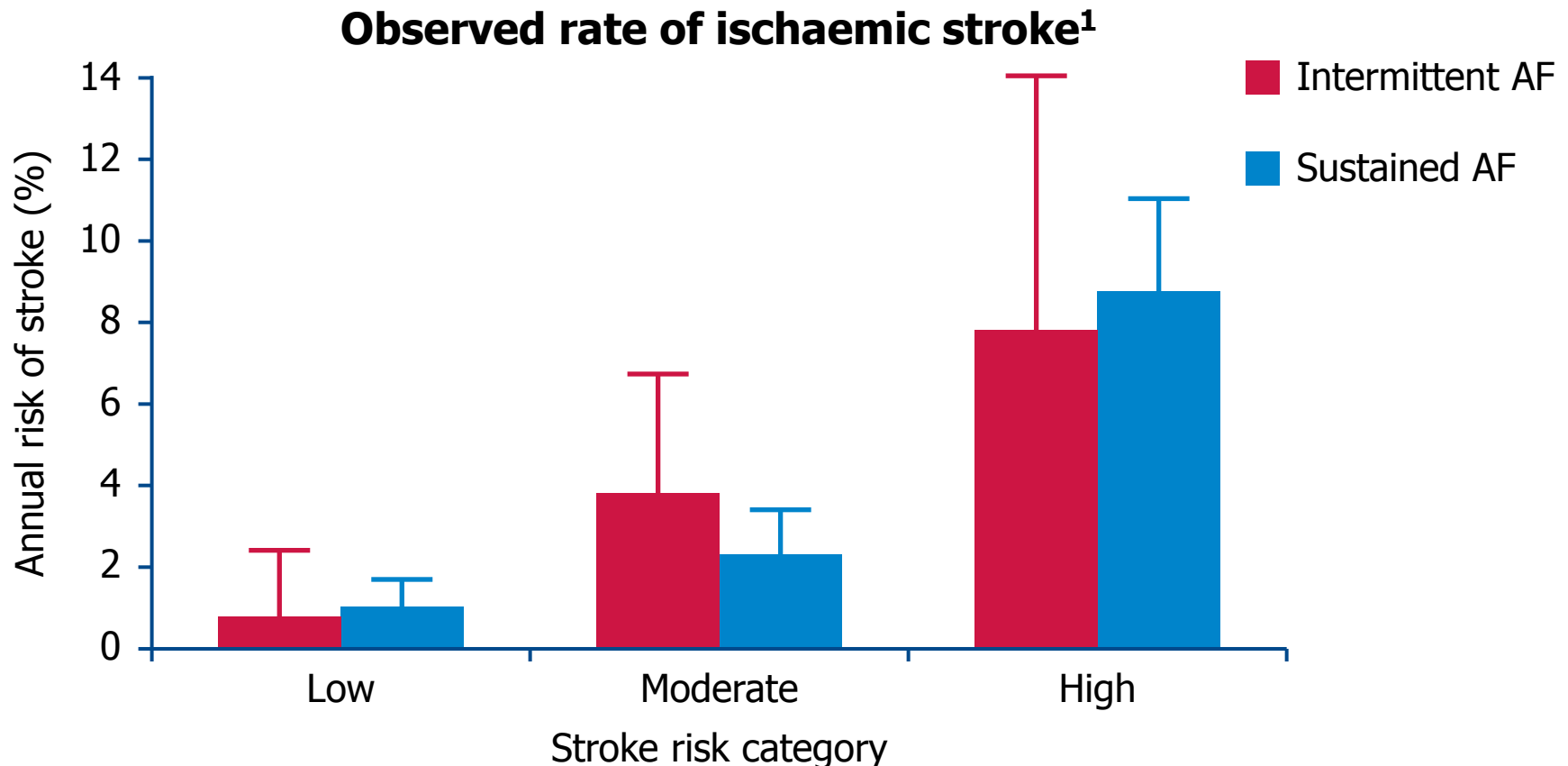
Incidence of stroke after diagnosis of AF (men)



22-year follow-up of 75 126 men in the Danish National Registry of Patients

Stroke risk persists even in asymptomatic/paroxysmal AF

- The risk of stroke with asymptomatic or paroxysmal AF is comparable to that with permanent AF^{1,2}



Risk factors for stroke in patients with AF

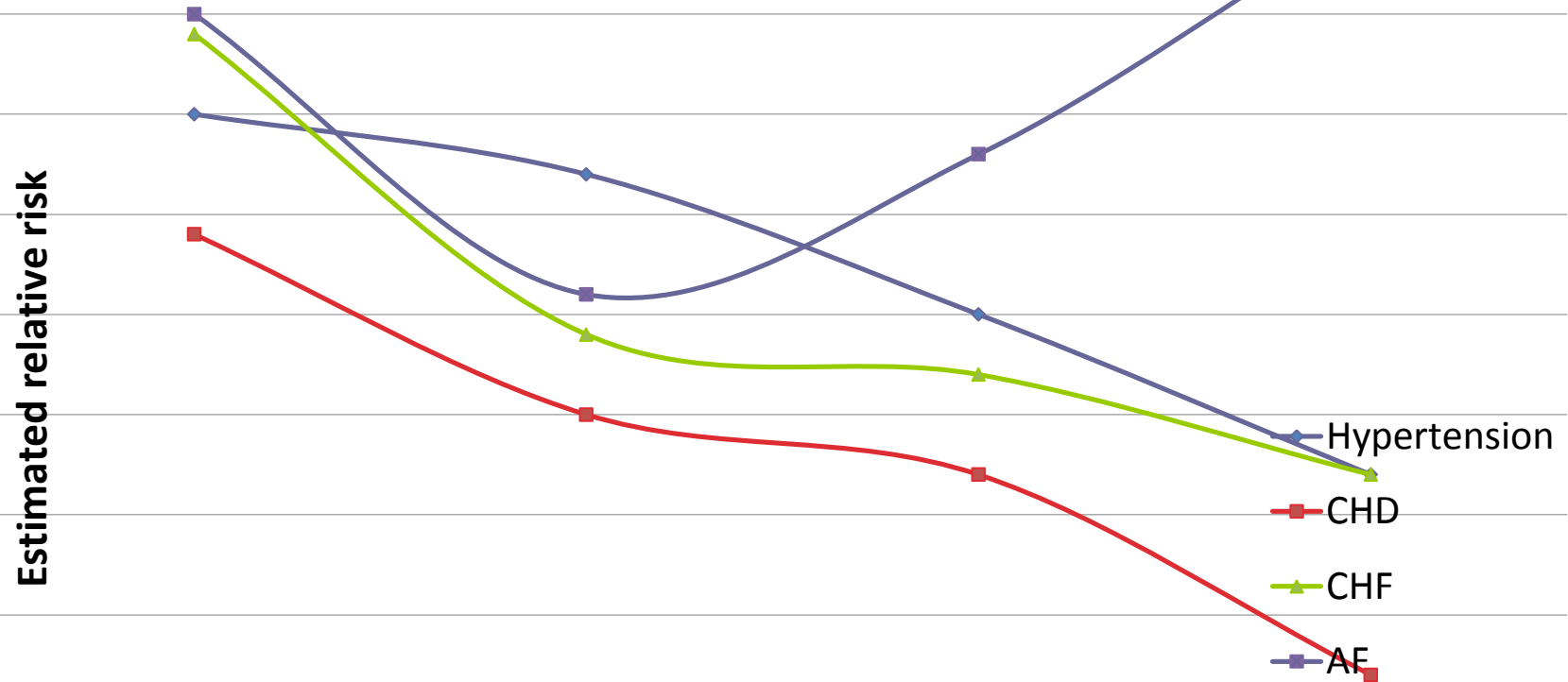
Estimation of stroke risk in AF: CHADS₂

- Most widely used to guide the choice of antithrombotic therapy

CHADS₂ risk criteria	Score
C ardiac failure	1
H ypertension	1
A ge >75 yrs	1
D iabetes mellitus	1
S troke or TIA (previous history)	2

TIA = transient ischaemic attack

Estimated Relative Risk of Stroke for Persons With Given Cardiovascular Condition Compared to Those Without Condition by Age



Risk scheme	Ref	Low risk	Intermediate risk	High risk
AFI Investigators (1994)	23	Age <65y and no risk factors	Age >65y and no other risk factors	Prior stroke/TIA, hypertension, diabetes
Stroke Prevention in AF (SPAF) Investigators	24	No risk factors	Hypertension, Diabetes	Prior stroke/TIA, women >75y, men >75y with hypertension
CHADS ₂ (2001) - classical	25	Score 0	Score 1-2	Score 3-6
CHADS ₂ - revised	...	Score 0	Score 1	Score 2-6
Framingham (2003)	24	Score 0-7	Score 8-15	Score 16-31
NICE guidelines (2006)	12	Age <65y with no moderate/high risk factors	Age ≥65y with no high risk factors Age <75y with hypertension, diabetes or vascular disease*	Previous stroke/TIA or thromboembolic event Age ≥75y with hypertension, diabetes or vascular disease Clinical evidence of valve disease or heart failure, or impaired left ventricular function
ACC/AHA/ESC guidelines (2006)	11	No risk factors	Age ≥75y, or hypertension, or heart failure, or LVEF ≤35%, or diabetes	Previous stroke, TIA or embolism, or ≥2 moderate risk factors of (age ≥75y, hypertension, heart failure, LVEF ≤35%, diabetes)
8 th ACCP guidelines (2008)	10	No risk factors	Age >75y, or hypertension, or moderately or severely impaired LVEF and/or heart failure, or diabetes	Previous stroke, TIA or embolism, or ≥2 moderate risk factors of (age ≥75y, hypertension, moderately or severely impaired LVEF and/or heart failure, diabetes)

Stroke risk assessment

- **Absolute risk (AR) of stroke increases with age and co-morbid conditions**

C	C ongestive heart failure	1
H	H istory of hypertension	1
A	A ge >75 years	1
D	D iabetes	1
S2	P rior stroke	2

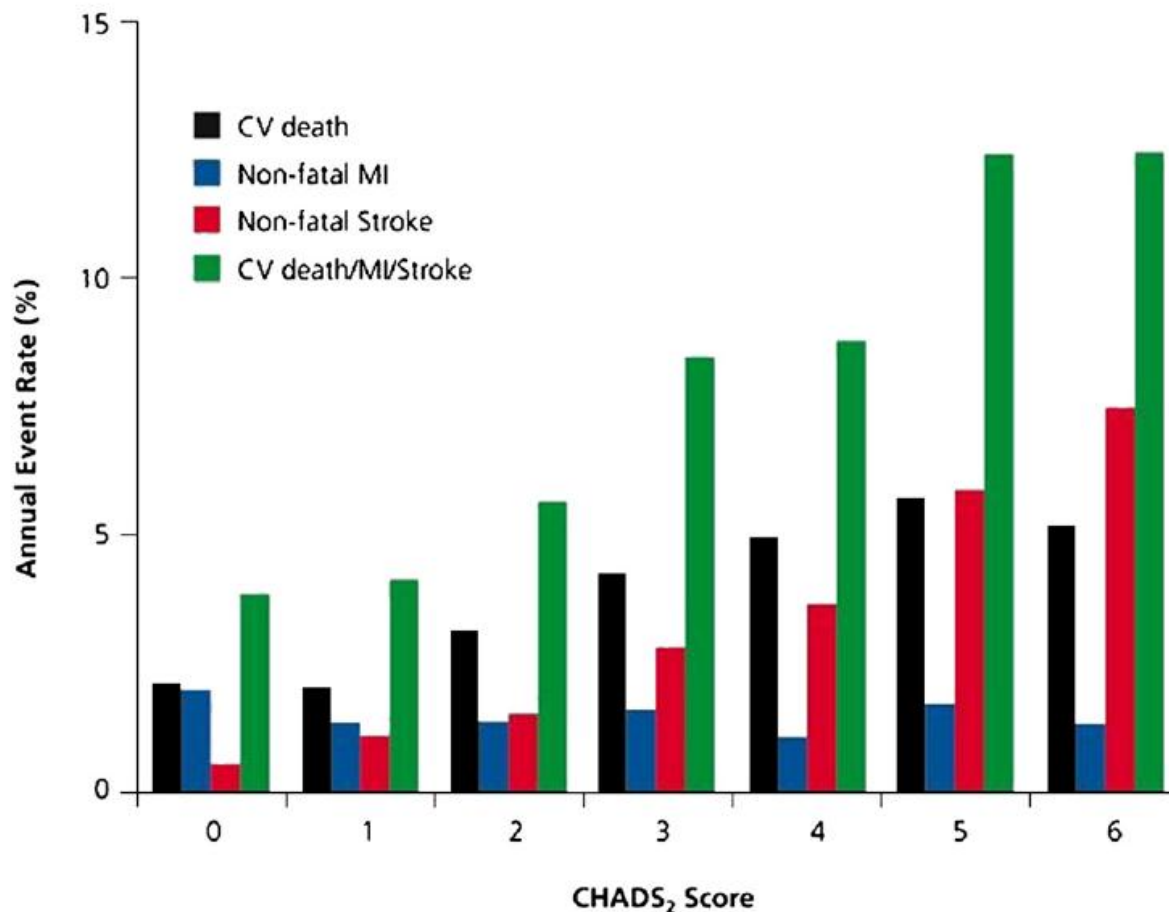
Table 2. Risk of Stroke in National Registry of Atrial Fibrillation (NRAF) Participants, Stratified by CHADS₂ Score*

CHADS ₂ Score	No. of Patients (n = 1733)	No. of Strokes (n = 94)	NRAF Crude Stroke Rate per 100 Patient-Years	NRAF Adjusted Stroke Rate, (95% CI)†
0	120	2	1.2	1.9 (1.2-3.0)
1	463	17	2.8	2.8 (2.0-3.8)
2	523	23	3.6	4.0 (3.1-5.1)
3	337	25	6.4	5.9 (4.6-7.3)
4	220	19	8.0	8.5 (6.3-11.1)
5	65	6	7.7	12.5 (8.2-17.5)
6	5	2	44.0	18.2 (10.5-27.4)

*CHADS₂ score is calculated by adding 1 point for each of the following conditions: recent congestive heart failure, hypertension, age at least 75 years, or diabetes mellitus and adding 2 points for having had a prior stroke or transient ischemic attack. CI indicates confidence interval.

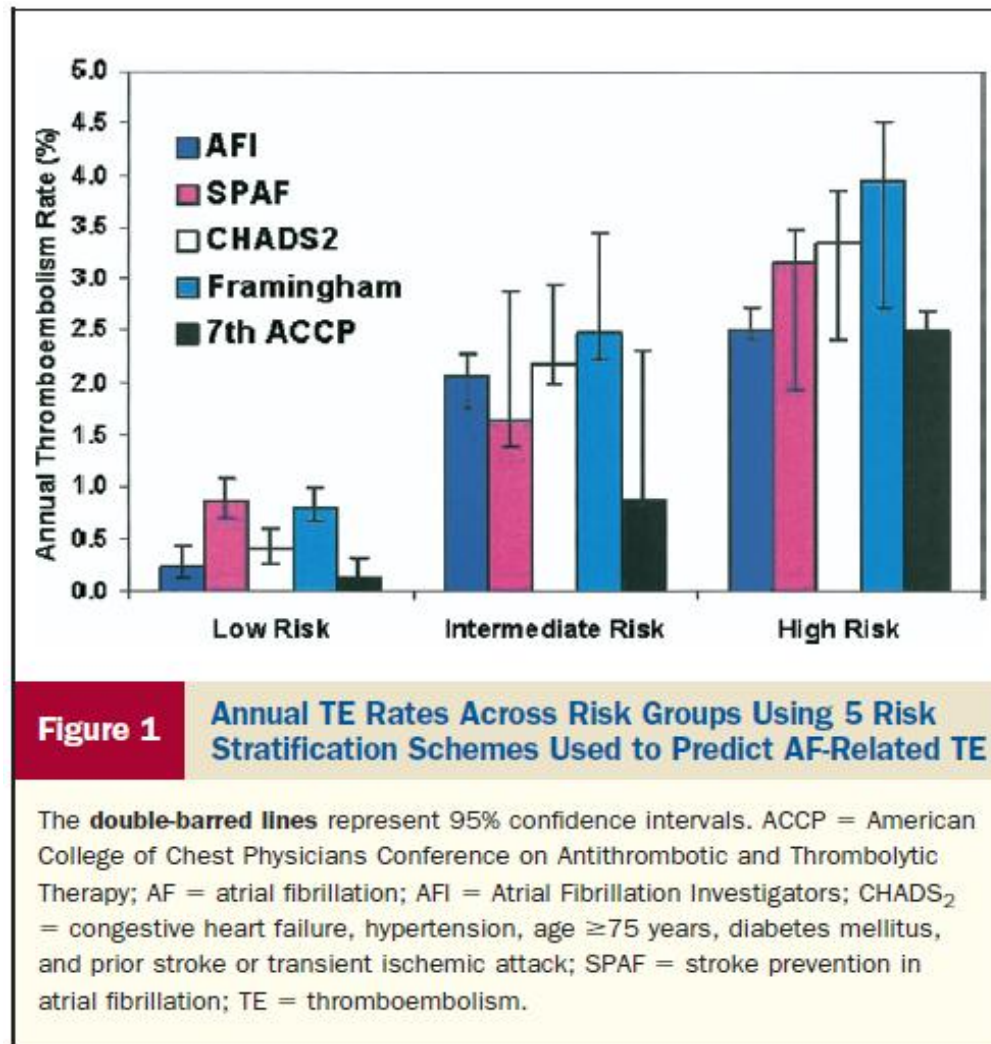
†The adjusted stroke rate is the expected stroke rate per 100 patient-years from the exponential survival model, assuming that aspirin was not taken.

Figure 2



Annual CV event risk in AF patients with various CHADS₂ (congestive heart failure [C], history of hypertension [H], age >75 years [A], DM [D], or history of stroke or TIA [S]) scoring (adjusted for age, sex, smoking, diabetes, hypertension, hypercholesterolemia). Annual event rate of CV death, nonfatal stroke, and combined end point of CV death/nonfatal MI/nonfatal stroke are for patients with higher CHADS₂ scoring, whereas the rate of nonfatal MI was not influenced by CHADS₂ scoring.

Comparison of Risk Stratification Schemes to Predict Thromboembolism in People With Nonvalvular Atrial Fibrillation



Stroke Improvement

Comparison of Risk Stratification Schemes to Predict Thromboembolism in People With Nonvalvular Atrial Fibrillation

Table 3

Proportion of ATRIA Cohort Categorized by 5 Risk Stratification Schemes Used to Predict Atrial Fibrillation-Related Thromboembolism and Discriminatory Ability of Risk Schemes (c-Statistics)

	Risk for Thromboembolism (%)			c-Statistic	
	Low	Intermediate	High	All Patients	Subgroup*
AFI	13.1	24.7	62.3	0.56	0.61
SPAF	27.7	28.5	43.8	0.60	0.65
CHADS ₂	18.8	61.2	20.1	0.58	0.67
Framingham	37.1	46.6	16.4	0.62	0.69
7th ACCP	11.7	7.9	80.4	0.56	0.60

*Subgroup of 5,588 patients not on warfarin at baseline and with continuous follow-up off of warfarin for at least 12 months.

Abbreviations as in Table 1.

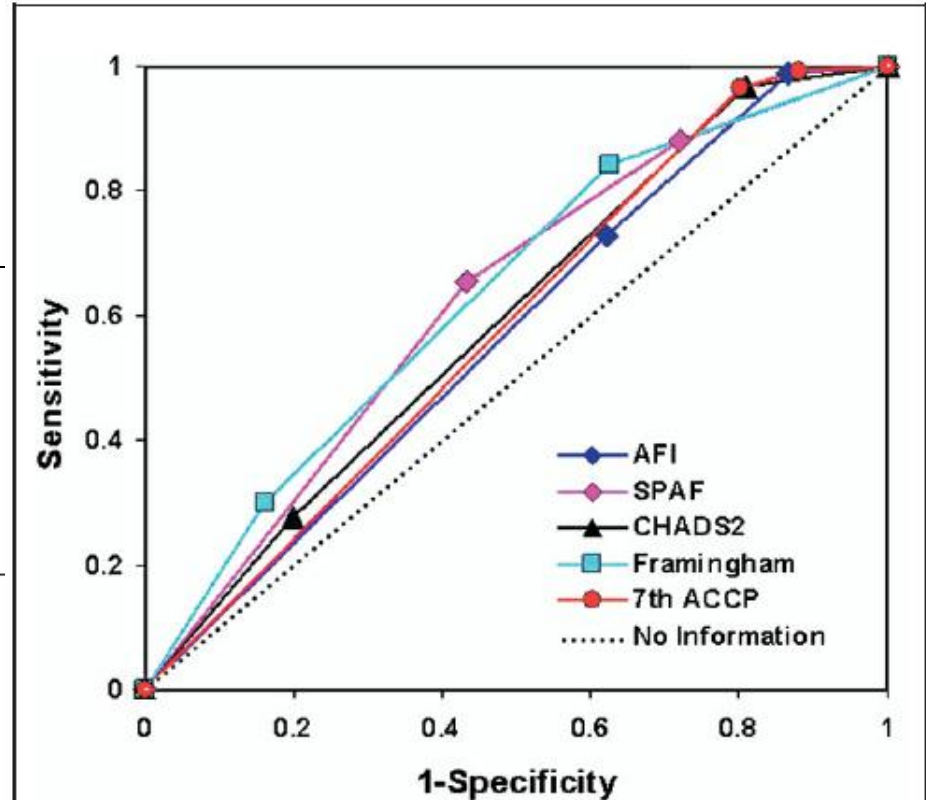


Figure 3

ROC Curves for 5 Risk Stratification Schemes Used to Predict AF-Related Thromboembolism

The 45° dotted line represents the line of no information. ROC = receiver-operating characteristic; other abbreviations as in Figure 1.

Framingham risk prediction schema

Figure 1. Predicted 5-Year Risk of Stroke

Step 1		Step 4		Predicted 5-year Risk of Stroke	
Age, y	Points	Diabetes	Points	Total Points	5- Year Risk, %
55-59	0	No	0	0-1	5
60-62	1	Yes	5	2-3	6
63-66	2			4	7
67-71	3			5	8
72-74	4			6-7	9
75-77	5			8	11
78-81	6			9	12
82-85	7			10	13
86-90	8			11	14
91-93	9			12	16
>93	10			13	18
				14	19
				15	21
				16	24
				17	26
				18	28
				19	31
				20	34
				21	37
				22	41
				23	44
				24	48
				25	51
				26	55
				27	59
				28	63
				29	67
				30	71
				31	75

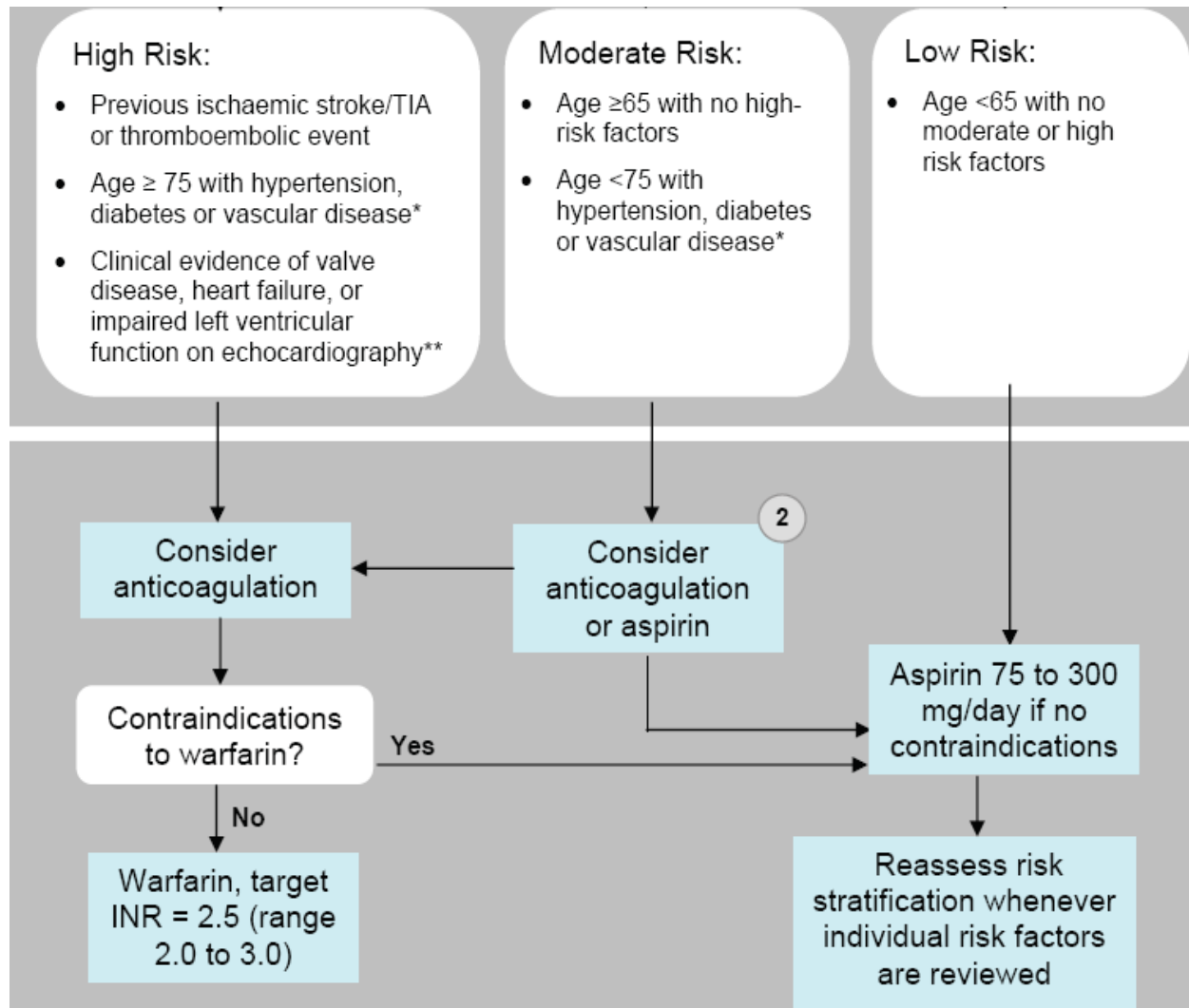
Step 2	
Sex	Points
Men	0
Women	6

Step 3	
Systolic Blood Pressure, mm Hg	Points
<120	0
120-139	1
140-159	2
160-179	3
>179	4

Step 5	
Prior Stroke or TIA	Points
No	0
Yes	6

Step 6	
Add Up Points From Steps 1 Through 5	
Look Up Predicted 5-Year Risk of Stroke in Table	

The point-based risk estimate approximates the more precise equation-based risk function provided as an Excel spreadsheet available at <http://www.nhlbi.nih.gov/about/framingham/stroke.htm>. The point-based risk estimate may differ from the equation-based one, particularly for patients with uncommon combinations of characteristics. TIA indicates transient ischemic attack.

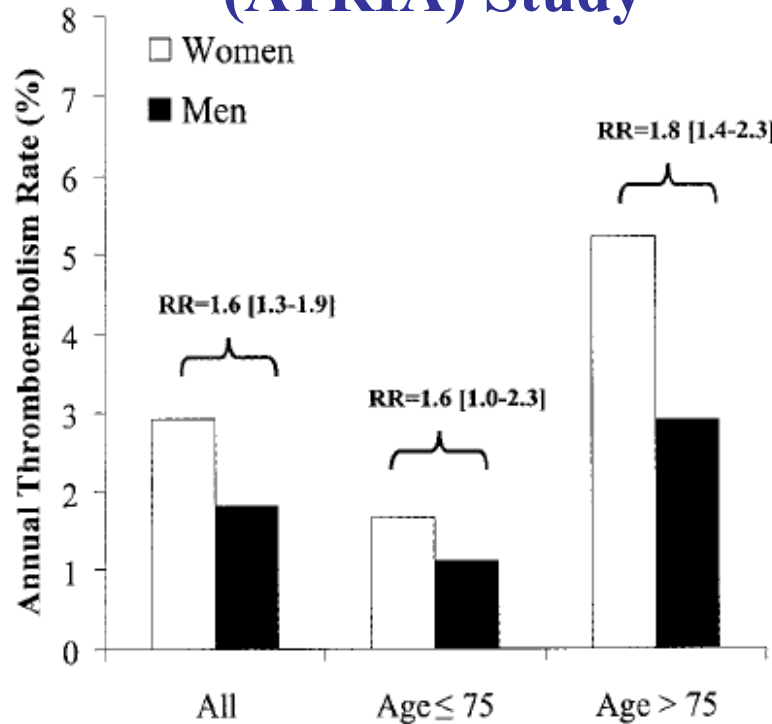


Chronic atrial fibrillation: Incidence, prevalence, and prediction of stroke using the Congestive heart failure, Hypertension, Age >75, Diabetes mellitus, and prior Stroke or transient ischemic attack (CHADS2) risk stratification scheme

Stephan Rietbrock, MD,^a Emma Heeley, PhD,^a Jonathan Plumb, MSc,^b and Tjeerd van Staa, PhD, MD^{a,c} *London, United Kingdom; Ingelheim am Rhein, Germany; and Utrecht, The Netherlands*

Adding sex, the extension of age categories and reweighing of established risk factors improved CHADS2 accuracy (C-statistic 0.68-0.72). Applying the reclassification resulted in a substantial number of patients changing stroke risk category.

Gender Differences in the Risk of Ischemic Stroke and Peripheral Embolism in Atrial Fibrillation (ATRIA) Study



Annualized adjusted rate of thromboembolism (ischemic stroke and peripheral embolism) during off-warfarin periods among women and men with atrial fibrillation with age, prior stroke, hypertension, congestive heart failure, coronary artery disease, diabetes mellitus, and estrogen use controlled for. Age cutoffs of ≤ 75 and > 75 years used as in the SPAF analysis.³ RR indicates adjusted RR and 95% CI.

Prognostic risk of atrial fibrillation in acute myocardial infarction complicated by left ventricular dysfunction: the OPTIMAAL experience

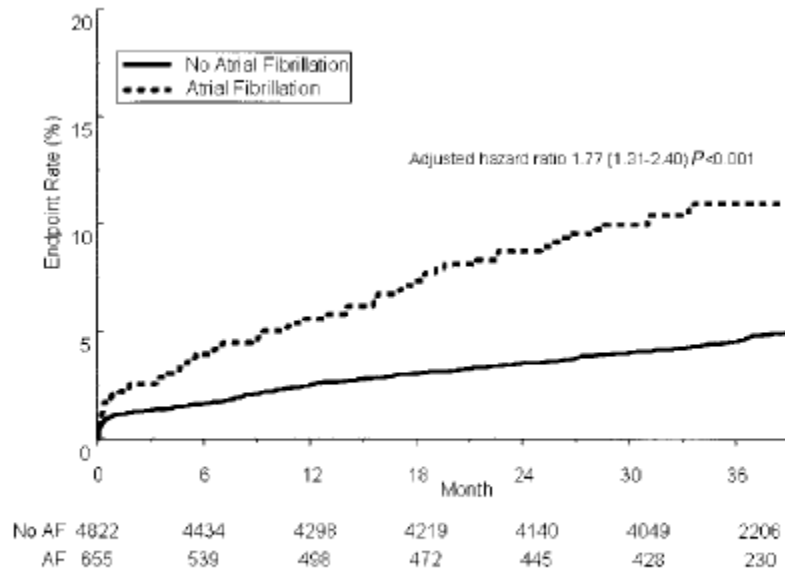


Figure 2 Kaplan-Meier curves for stroke stratified by the presence of AF at baseline.

Transient Atrial Fibrillation Complicating Acute Inferior Myocardial Infarction: Implications for Future Risk of Ischemic Stroke

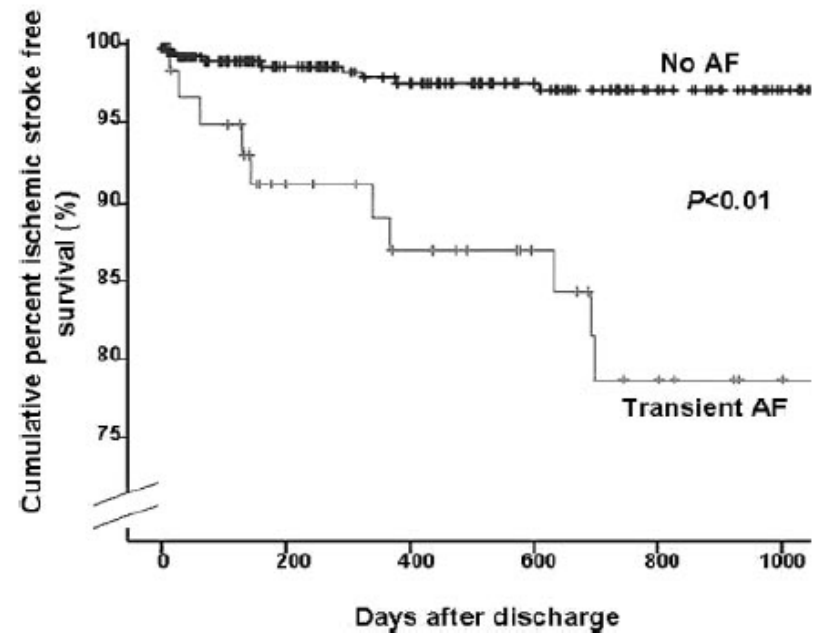


FIGURE 3. Kaplan-Meier curves for the unadjusted rate of occurrence of ischemic stroke in patients with or without transient AF complicating acute ST-segment-elevation MI.

CHA₂DS₂VASc

	Score
Congestive heart failure/left ventricular systolic dysfunction	1
Hypertension	1
Age ≥75	2
Diabetes	1
Stroke / TIA	2
Vascular disease	1
Age 65–74	1
Sex (female)	1

CHA₂DS₂VASc

Validated: The Euro Heart Survey on Atrial Fibrillation

Score	Percent AF population	Adjusted TE rate
0	9.2	0%
1	15.1	0.7%
2	17	1.9%
3	18.7	4.7%
4	19.2	1.9%
5	8.7	3.2%
6	5.3	3.6%
7	2.3	10.1%
8	0.8	14.2%
9	0.01	100%

CHA₂DS₂VASc

- Slightly better c-statistic than CHADS2
- Low risk is virtually no risk
- Score ≥ 2 is suggested to be high risk
- 1.9% annual stroke risk considered high
- 75% of AF population classed at high risk

Considerations on implementation

- Is a traditional three tier system of low – moderate – high risk helpful?
- How big is the moderate risk category?
- How do we balance benefit against risk?
- Where to set the cut offs?
- Does cost come into it?
- How will new oral anticoagulants affect the equation?

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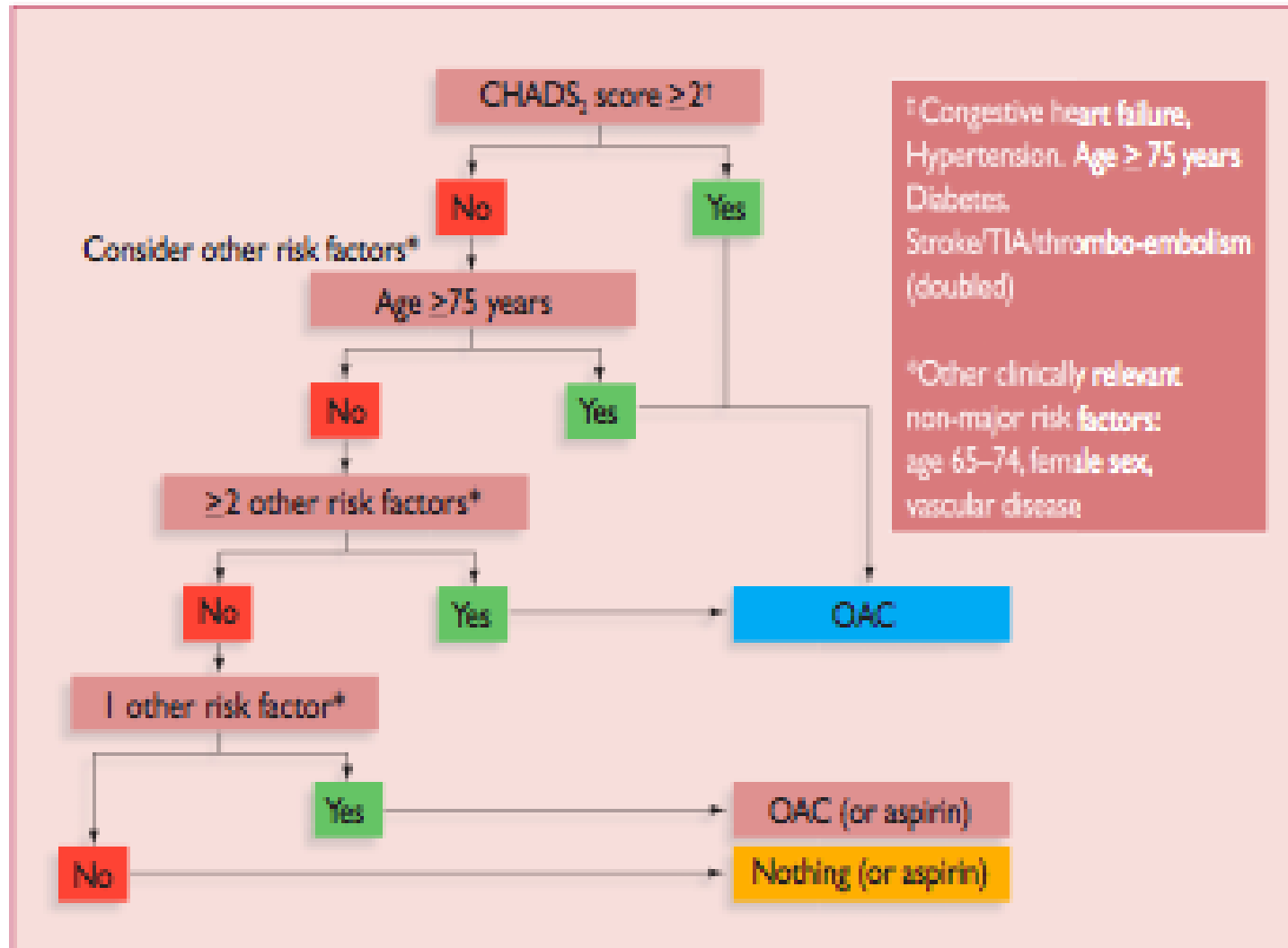
Choice of intervention

CHADS 2 score	Adjusted annual stroke rate (%)	Number needed to treat (NNT)	
0	1.9	53	
1	2.8	36	
2	4.0	25	
3	5.9	17	
4	8.5	12	
5	12.5	8	
6	18.2	5	
BENEFITS OF WARFARIN OUTWEIGH RISKS WHEN CHADS2 ≥2			

An Approach to Risk Assessment

Risk Category	CHA ₂ DS ₂ -VASc Score	Recommended Therapy
One 'major' risk factor or ≥ 2 clinically relevant non-major risk factors	≥ 2	OAC
One clinically relevant non-major risk factor	1	Either OAC or Aspirin but preferably OAC
No risk factors	0	Either aspirin or no therapy

An Approach to Risk Assessment



Balancing risk vs harm

- What's the risk?
 - 1.9% major haemorrhage risk with warfarin in BAFTA¹
 - Haemorrhage risk increases with age (2.9% > 85)
 - 25% of major haemorrhage are due to intracranial haemorrhage
 - 15% mortality of major bleed (Walraven et al²)
- What's the benefit of anticoagulation?
 - 60-70% relative risk reduction of ischaemic stroke³
= NNT of 25 at CHADS2 score of 2 (36 at 1)
- Where's the balance? NNT 25 vs NNH 53
- Is NNT vs NNH too simplistic? NNH of death or lasting disability >200

¹ Mant J et al. Lancet 2007; 370

² Walraven C et al. JAMA 2002; 288

³ Hart RG et al. Ann Intern Med 1999; 131

An Approach to Risk Assessment

HAS-BLED

Letter	Clinical Characteristic	Points Awarded
H	Hypertension	1
A	Abnormal renal and or liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INR	1
E	Elderly (age >65)	1
D	Drugs and or alcohol (1 point each)	1 or 2
		Maximum 9 points

Guidance on Risk Assessment and Stroke Prevention for Atrial Fibrillation: GRASP-AF

Tools to support data collection and
analysis for GRASP AF

Acknowledgement:

- Keith Tyndall, Leeds AF clinic
- James Barrett, Primis+
- West-Yorkshire Cardiovascular Network

The CHART GRASP-AF tool

- CHART is an Excel program (97-2003, 2007)
- The CHART GRASP-AF library is available from NHS Improvement:
<http://www.improvement.nhs.uk/graspaf/>
- Run locally within the practice
- Queries written for the MIQUEST interpreter
- Versions available for all the main GP systems
- Queries can be identifiable or pseudonymised
- Queries extract a set of information about patients with atrial fibrillation

CHART GRASP-AF Tool

- Identifies patients with atrial fibrillation
- Looks for co-morbidities and works out **CHADS2 score** for all
- Determines whether patients are currently on warfarin or aspirin (or both)
- Looks out for recorded reasons for NOT treating with warfarin
- Has a comprehensive 'Advice sheet'

Suite of Tools

- CHART
 - to generate queries
 - for local analysis
- CHART Online
 - for comparative analysis

CHART GRASP AF: Datasheet

MIQUEST response file AFREPA CSV was created on 21/05/09 using Refdate 21/05/09

AF_CHADS_SCORE AFREPA: Report on patients with AF (Pseudonymised)

Reference	Age	Sex	Earliest AF code	Earliest AF date	CHADS2 score	% Annual risk of stroke	Earliest heart failure code	Earliest heart failure date	Earliest hypert code	Earliest hypert date	Age > 75	Earliest DM code	Earliest DM date	Earliest stroke code	Earliest stroke date	Latest warfarin code in L6M	Latest warfarin date in L6M
02QC	89	F	G573.	04/04/92	3	5.90	G580.	09/05/93			89	C1001	13/10/97				
00Df	73	F	G5730	28/11/02	3	5.90			G2...	23/10/04				G65..	11/05/03		
00QS	85	M	G573.	22/02/99	4	8.50	G581.	27/01/03			85			G65..	17/07/93	bs19.	20/01/0
00u9	62	M	G5730	31/03/03	1	2.80			G2...	07/08/97							
01HV	85	F	G573z	02/12/99	2	4.00			G2...	26/01/05	85					bs18.	13/01/0
01Lq	88	F	G5730	03/05/04	4	8.50			G2...	18/11/05	88			G64..	02/06/05		
02DA	71	F	G573.	10/03/03	2	4.00			G2...	11/01/05							

CHART GRASP-AF: Dashboard

Audit of Atrial Fibrillation and CHADS2 Scores

[Classic View](#)

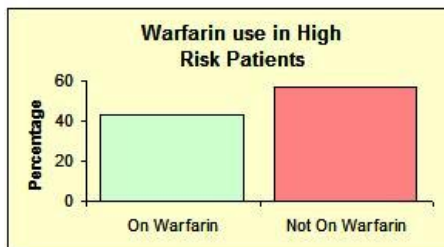
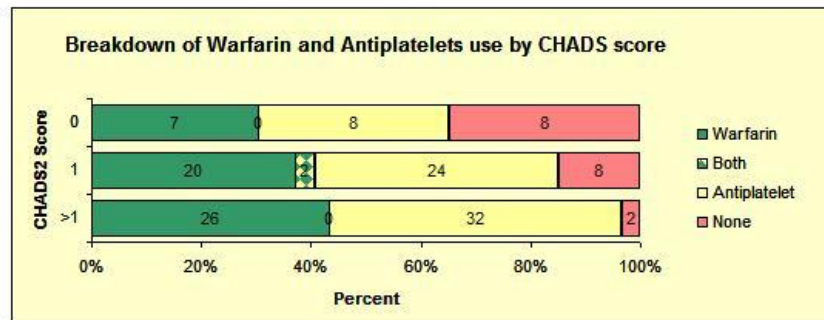
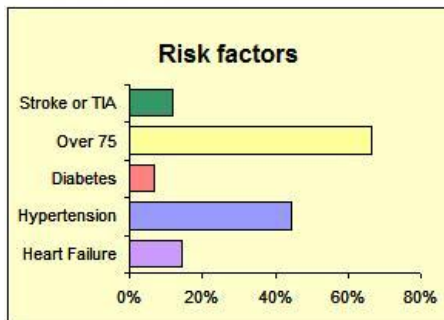
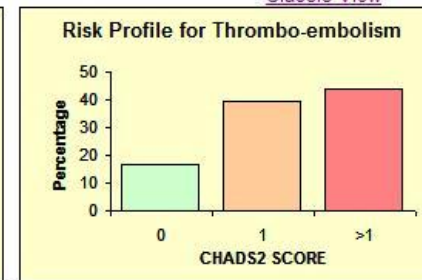
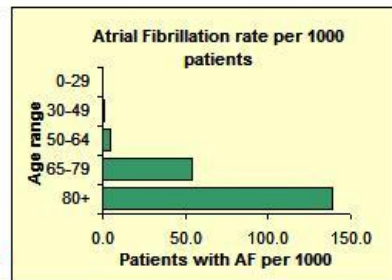
Practice:

Reference Date for Audit 27/03/2009

Total Practice Population 10118

	Total	Percent
No. with Atrial Fibrillation	137	1.35
Percent of over 65s with AF		8.24

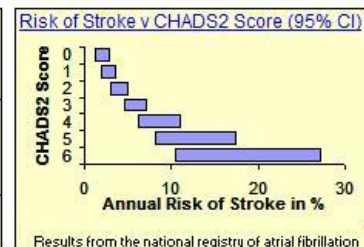
NB: Handling of Warfarin Exclusions



Strokes Expected Annually in the 34 high risk untreated

1.9

(95% CI 1.4 to 2.5)



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Summary

- Big variation in stroke risk amongst AF patients -> importance of risk assessment
- Lots of risk assessment tools – none is perfect
- Ongoing development to improve predictive value, ie CHA₂DS₂VASc
- Majority of AF patients can be classified easily as high or low risk
- Small intermediate risk group requires careful weighing up of risks vs benefits of SPAF
- The cut offs are being re-evaluated
- GRASP-AF makes life easy for the GP.

Thank you for your attention

Question

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