

When the drugs don't work

When to refer in AF

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Clinical Lead NHS-Improvement

Food for thought...

- 150,000 strokes per year in the UK¹
- 410 per day
- 17 per hour
- Within the next four hours, 10 patients with AF will have suffered a stroke
- 8 would have been known to be high risk of stroke
- 6 should have been on warfarin
- 3 will go home
- 5 will end up in residential care
- 2 will die....

www.stroke.org.uk

THINK WHY?

Think about the cause

- Ischaemic heart disease
 - Can be the presenting feature of AMI
- Hypertension
- Valvular Heart Disease
- Thyrotoxicosis
- Cardiomyopathy
- Infection
- Alcohol
- Idiopathic

Think about the investigations

- 12 Lead ECG
- Full Blood Count
- Electrolytes
- Liver Function including the Gamma GT
- Thyroid Function

THINK CAN I LOOK AFTER THEM?

Are they one of the below?

- Where an other cause is identified
 - Thyrotoxicosis
 - Cardiomyopathy
- Recent onset where cardioversion is appropriate
- Unresponsive to normal medication
- Associated with syncope
- Associated with valvular disease
- If diagnosis is in doubt

REFER THEM TO A SPECIALIST

THINK RATE?

How Are They?

- Acutely Unwell
- Breathless
- Suffering Palpitations
- Asymptomatic
- Tachycardic

If the Heart Rate is Fast

Slow it down

- Beta-blockers
- Rate Limiting Calcium Channel Blockers
- Digoxin
- New medications on the way

Refer them to a cardiologist

- If the Heart Rate is Slow

Speed it up

- Stop rate limiting drugs
- Ask about symptoms
 - No symptoms-Monitor them
- Otherwise

Refer them to a cardiologist

THINK RHYTHM?

How Are They?

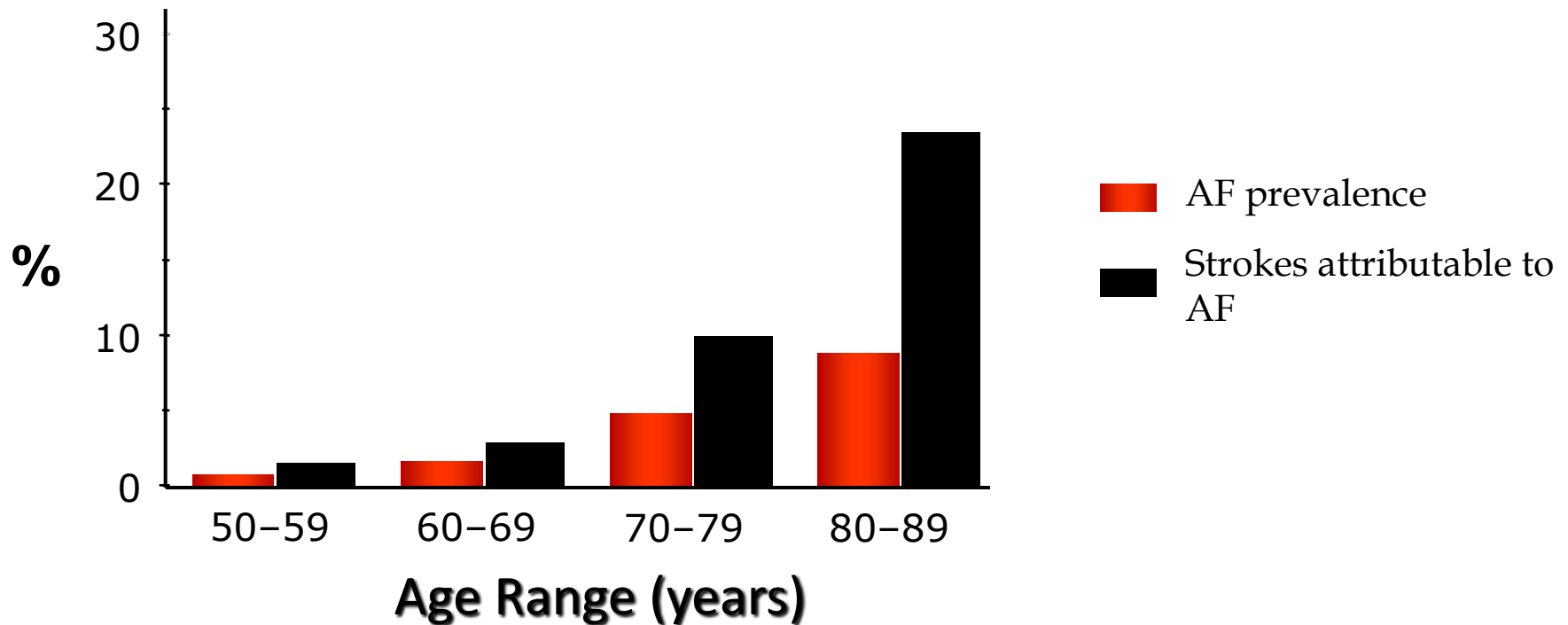
- Controlled heart rate-Yes
- But
 - Breathless
 - Suffering Palpitations
 - Tired

Refer them to a cardiologist

What About the Stroke Risk

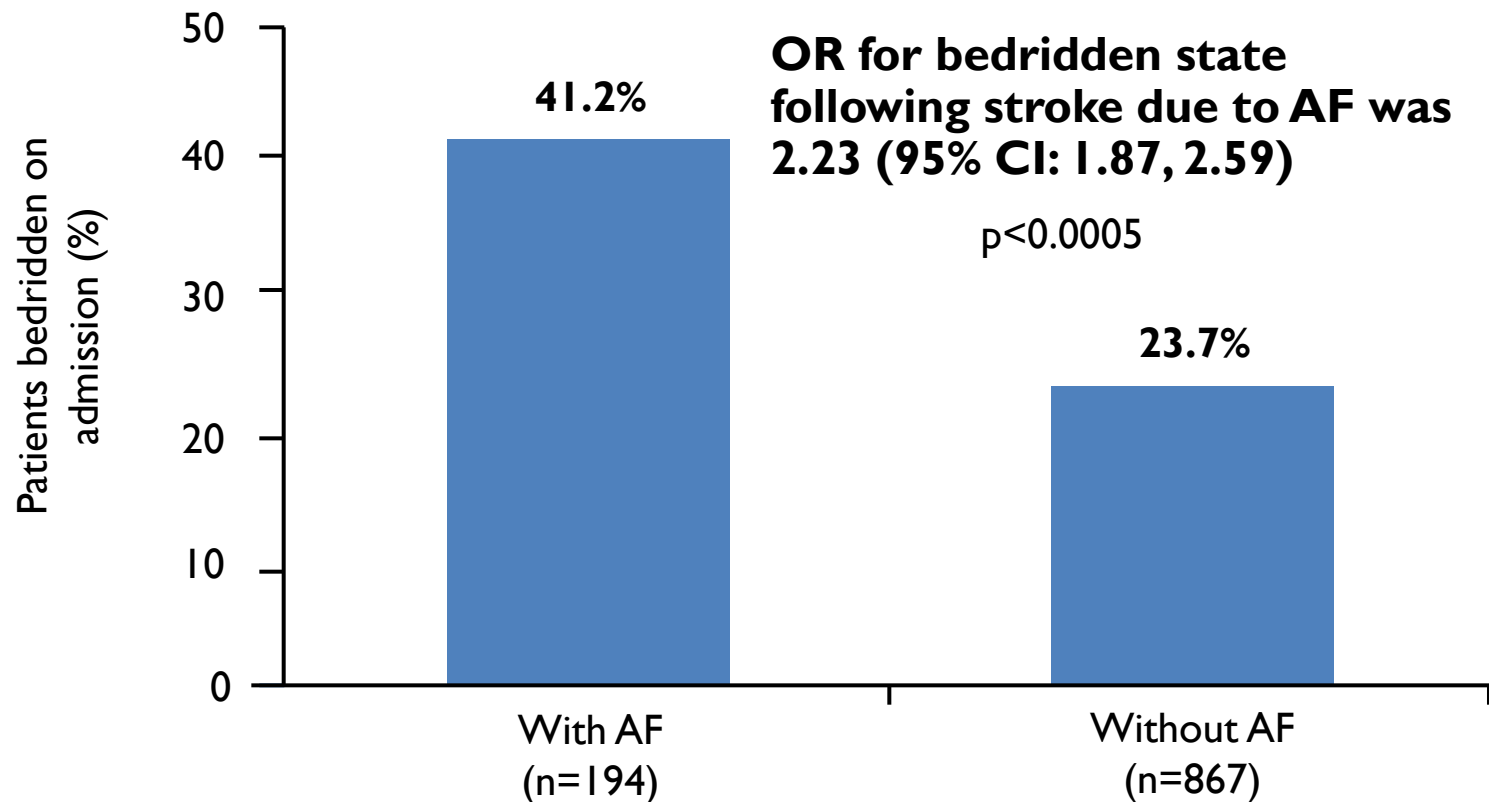
One sixth of all strokes are attributable to AF

Framingham Study



The Impact of AF on Stroke Outcomes

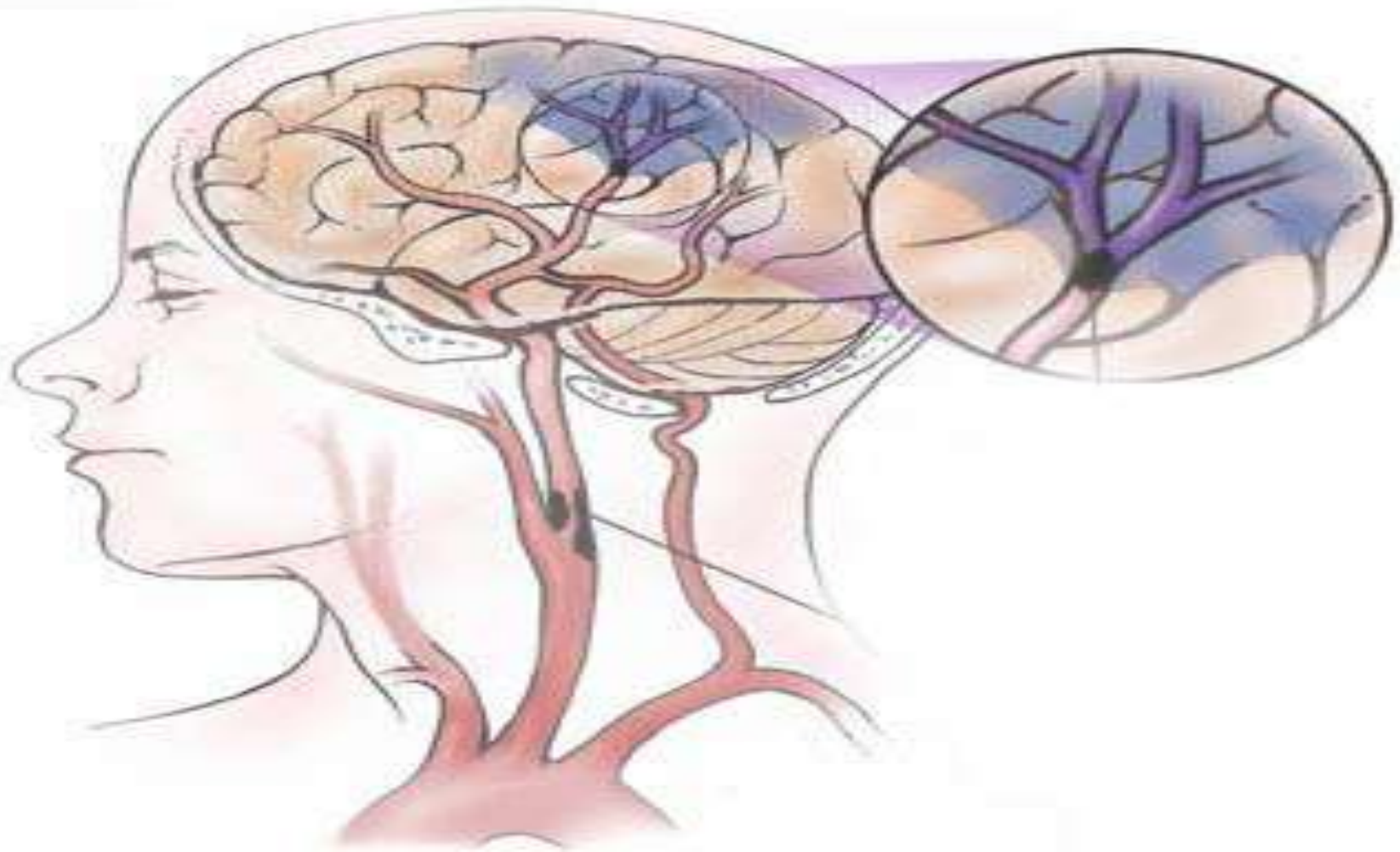
- Functional outcomes of stroke are significantly worse in patients with AF, and more patients remain bedridden



StrokeImprovement

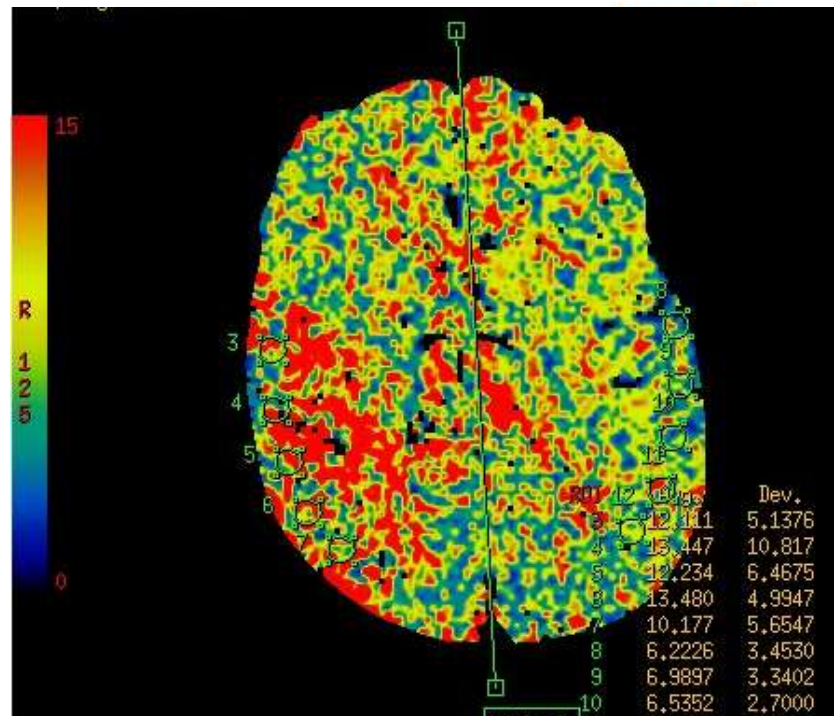
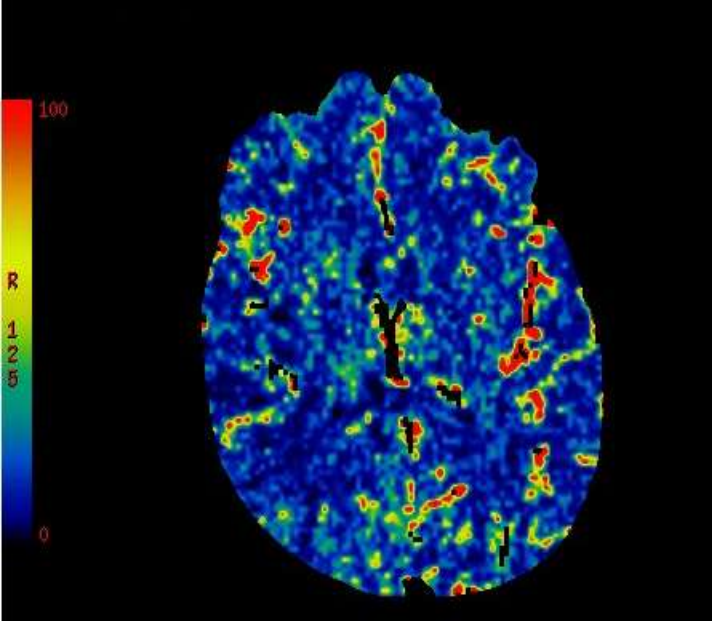
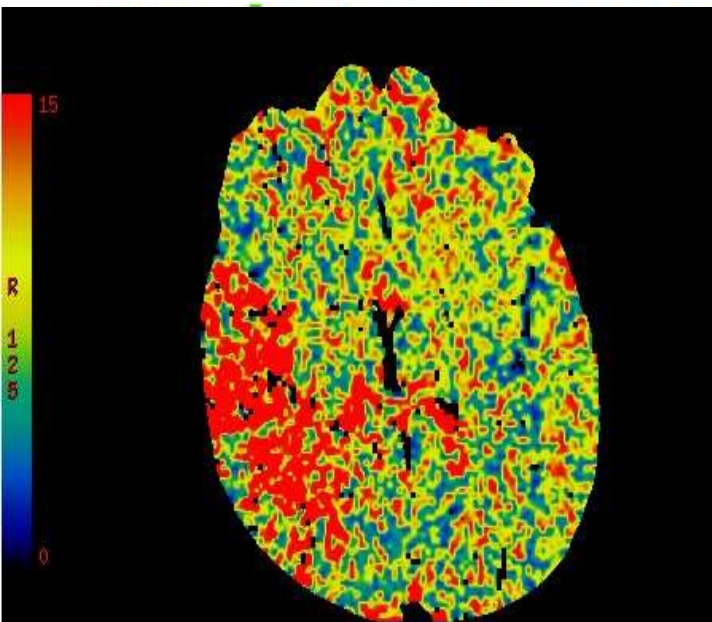
NHS Improvement 

Large artery stroke; cardioembolic or atherothrombotic

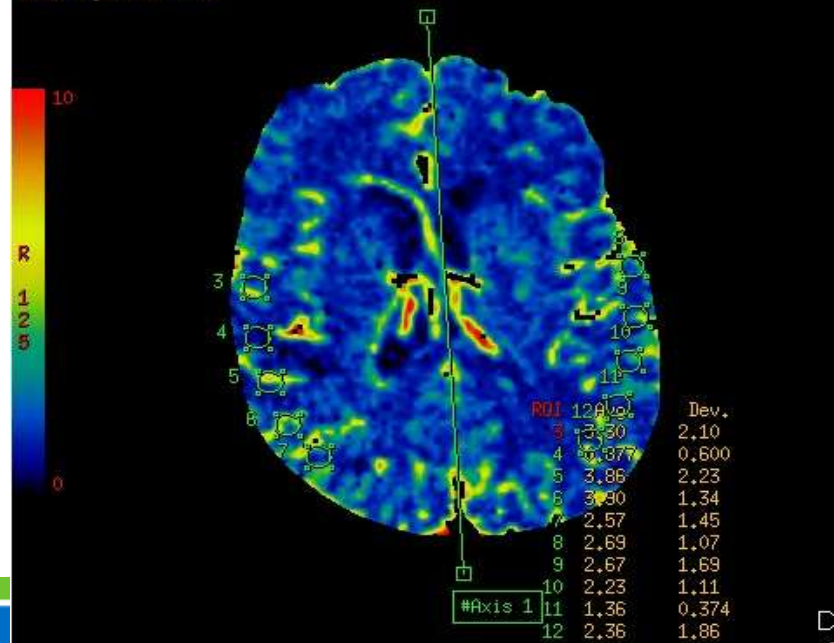


nt

MTT



DOB: AUGUST 29 1973



#Axis 1



What is PAF?

What is PAF?

- European Society of Cardiology **Clinical Practice Guidelines**
- **Atrial Fibrillation (Management of)**
- **Published 2010**

- “Paroxysmal AF is self-terminating, usually within 48 h. Although AF paroxysms may continue for up to 7 days, the 48 h time point is clinically important—after this the likelihood of spontaneous conversion is low and anticoagulation must be considered”
- “An irregular pulse should always raise the suspicion of AF, but an ECG recording is necessary to diagnose AF. Any arrhythmia that has the ECG characteristics of AF and lasts sufficiently long for a 12-lead ECG to be recorded, or at least 30 s on a rhythm strip, should be considered as AF”
- “PAF vs salvo of atrial ectopy”

- <http://www.escardio.org/guidelines-surveys/esc-guidelines/pages/atrial-fibrillation.aspx>
- Kirchhof P, et al. Outcome parameters for trials in atrial fibrillation: executive summary. Recommendations from a consensus conference organized by the German Atrial Fibrillation Competence NETwork (AFNET) and the European Heart Rhythm Association (EHRA). Eur Heart J 2007;28:2803–2817.

- Paroxysmal AF is also associated with the same risk of stroke as persistent AF (12% per year) hence its detection and treatment becomes necessary as secondary prevention for cerebrovascular disease.

Stroke 1982;13:382-837

- Patients with paroxysmal AF should be regarded as having a stroke risk similar to those with persistent or permanent AF, in the presence of risk factors.
- The risk of stroke linked to atrial flutter has been studied retrospectively in a large number of older patients, and was similar to that seen in AF. Thus, thromboprophylaxis in patients with atrial flutter should follow the same guidelines as in AF patients.

ESC Guidelines 2010

BUT...

- ESC 3.3 'Natural' time course
- AF progresses from short, rare episodes, to longer and more frequent attacks. Over time (years), many patients will develop sustained forms of AF.
- In patients with AIS, ≥ 70 atrial premature beats/24 hours are a marker for individuals who are at greater risk to develop or have PAF(1).

What if large artery stroke and Intracranial/extracranial vessels normal?

- Just anticoagulate?
- Anticoagulate if >70 APB/24hrs on monitor
- Anticoagulate if <30 sec AF run on monitor?
- Anticoagulate if >30 sec AF run on monitor?
- Other? (TOE?)

(1) Wallmann et al. Frequent Atrial premature beats predict PAF in stroke patients
Stroke 2007;38:2292-2294

Who to anticoagulate?

OBJECTIVES IN MANAGEMENT OF AF

- (1) Prevention of thrombo-embolism.
- (2) Symptom relief.
- (3) Optimal management of concomitant cardiovascular disease.
- (4) Rate control.
- (5) Correction of rhythm disturbance.

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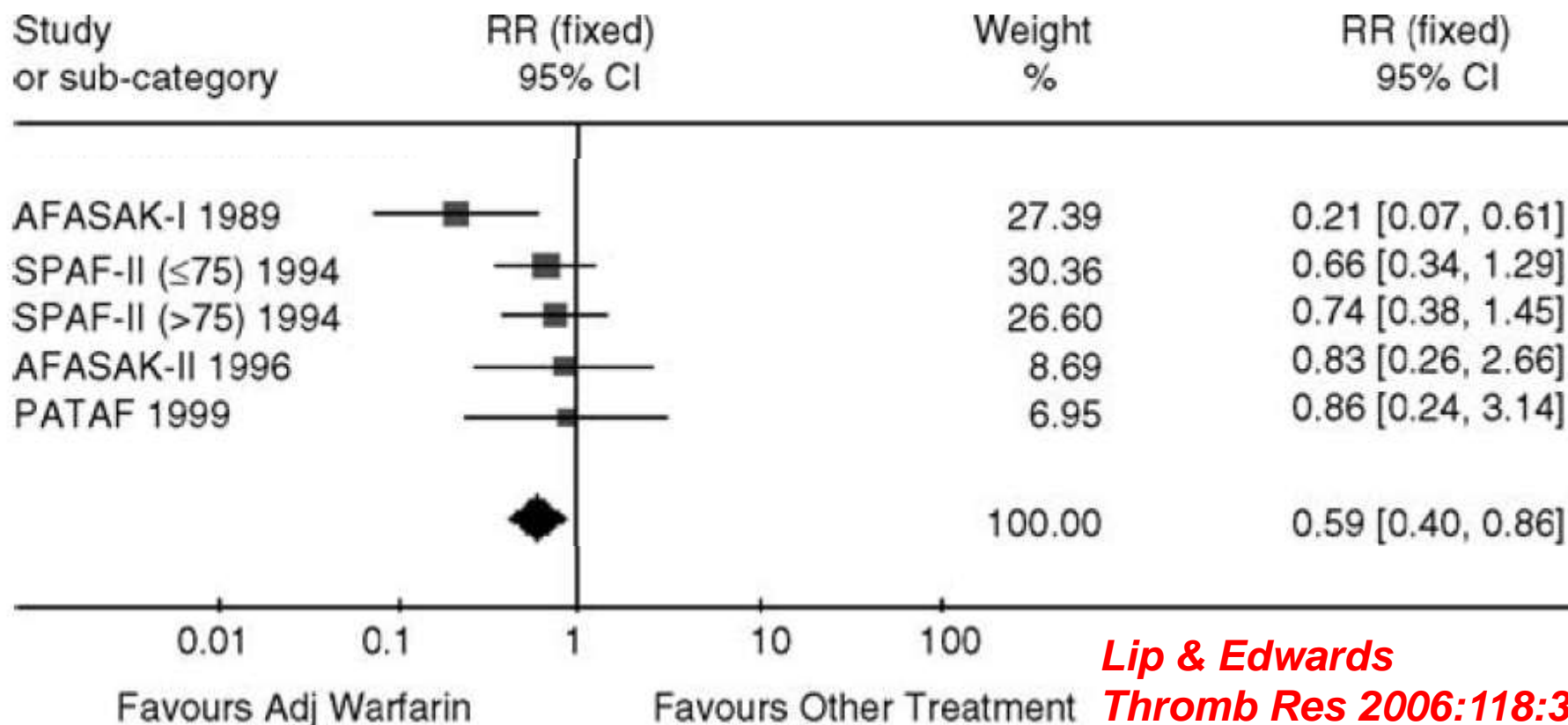
THROMBOPROPHYLAXIS IN AF

- WARFARIN
- ASPIRIN
- ASPIRIN + CLOPIDOGREL
- DIRECT THROMBIN INHIBITORS
- FACTOR X_a ANTAGONISTS

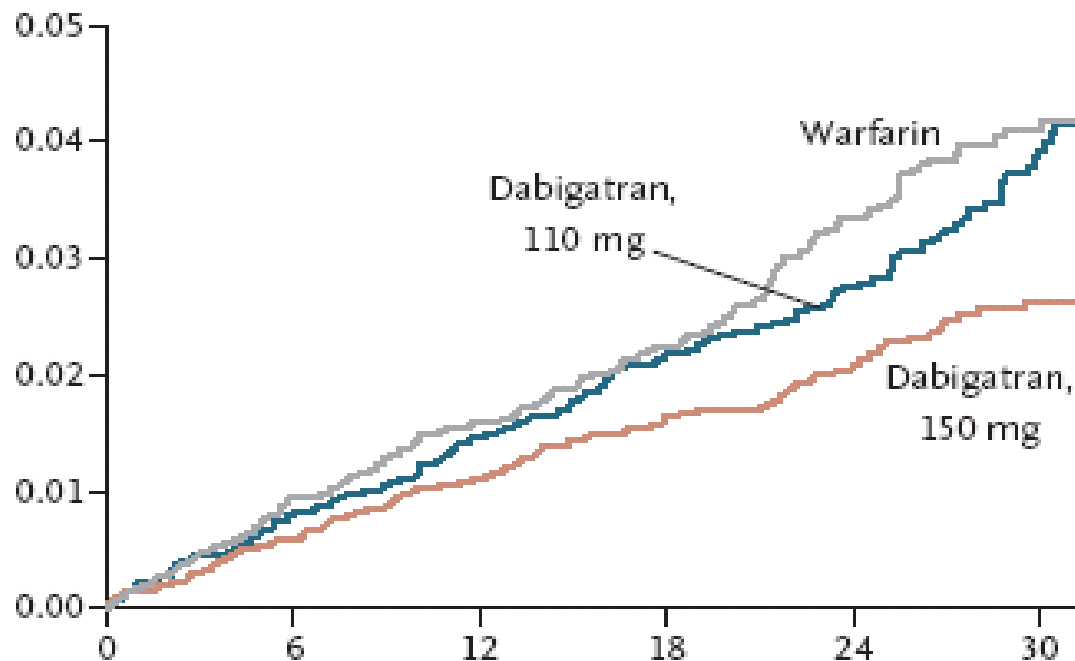
META-ANALYSIS OF ADJUSTED DOSE

WARFARIN vs ASPIRIN

ISCHAEMIC STROKE/SYSTEMIC EMBOLISM

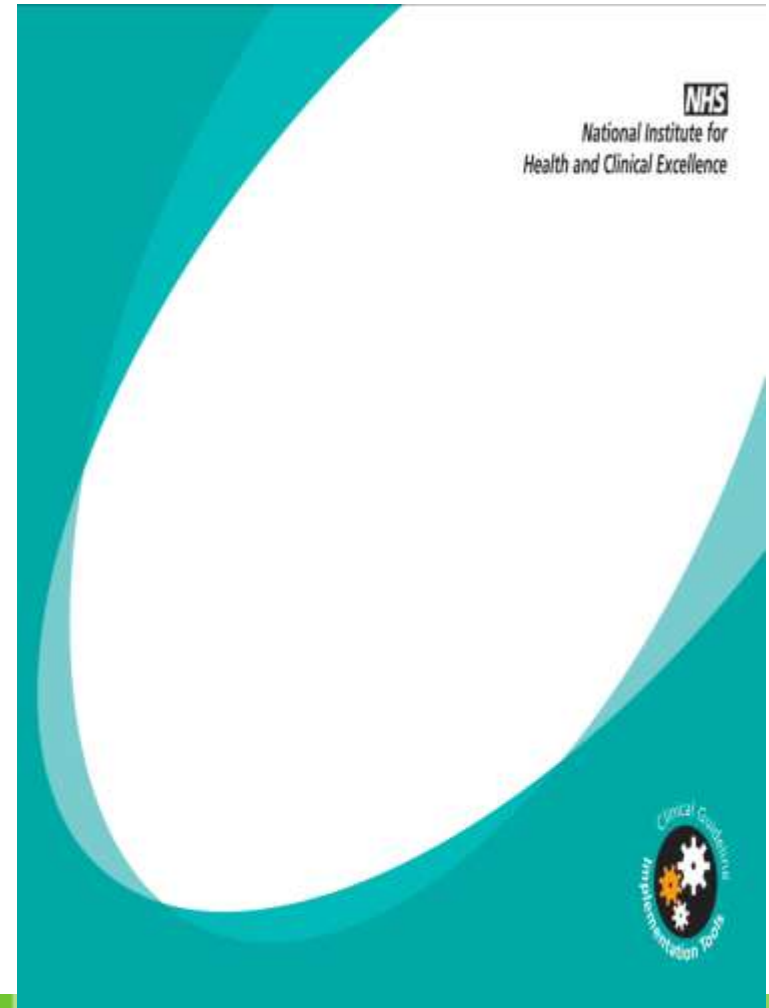
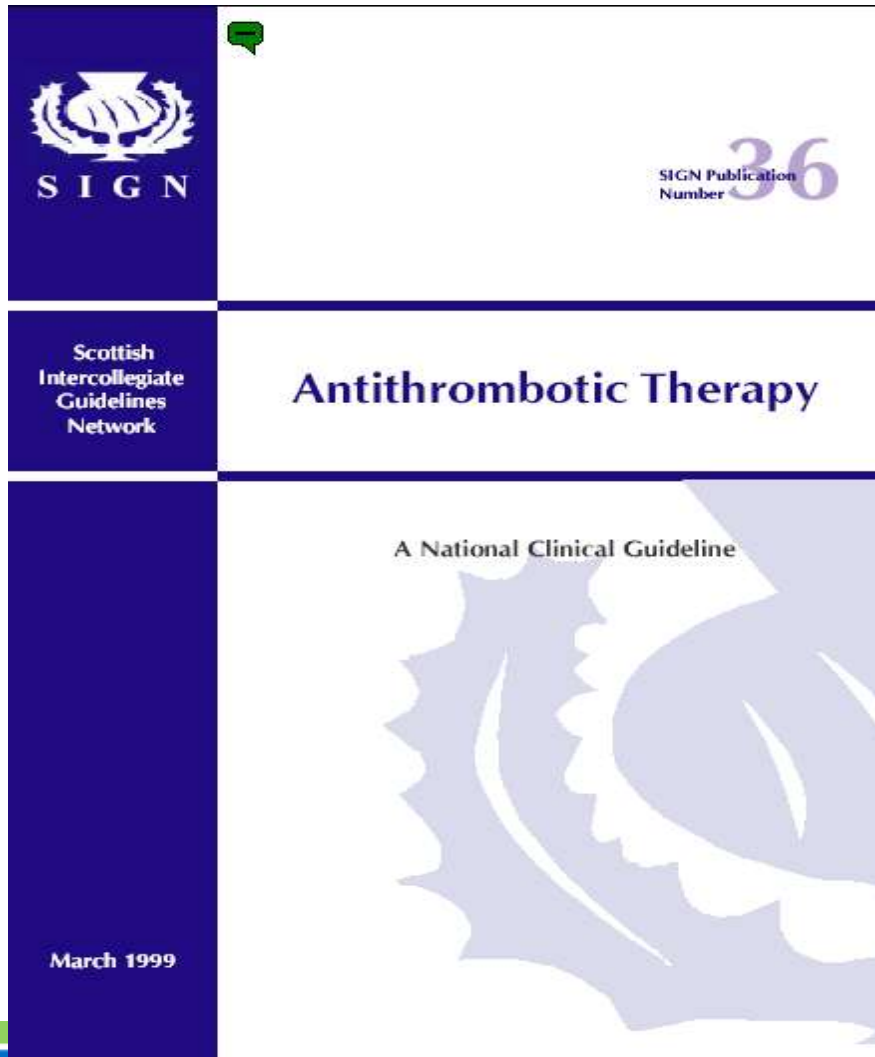


RE-LY Study Stroke or Systemic embolism



NEJM, Sept 2009

PREVENTION OF STROKE/THROMBOEMBOLISM



PREDICTOR OF THROMBOEMBOLIC RISK IN AF - CHADS₂

- Congestive heart failure

- History of hypertension

- Age > 75 years

- Diabetes

- Prior stroke or TIA (X2)

SCORE ANNUAL RISK

0 – 1 1.9% - 2.8%

2 – 4 4.0% - 5.9%

5 – 6 12.5% - 18.2%

AF Investigators Arch Intern Med 2001;154:1449

ESC 2010

- De-emphasize the use of the 'low', 'moderate', and 'high' risk categorizations
- Recognize that risk is a continuum.
- Recommend a more detailed stroke risk assessment

- Large proportion of subjects into the 'moderate risk' category
- Current treatment guidelines recommend the use of either warfarin or aspirin in such patients, causing confusion over which therapy should really be prescribed
- Alternatively, classification as 'moderate risk' is often used as an excuse not to give anticoagulation, since the guidelines 'allow' aspirin.

CHA2DS2-VASc 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

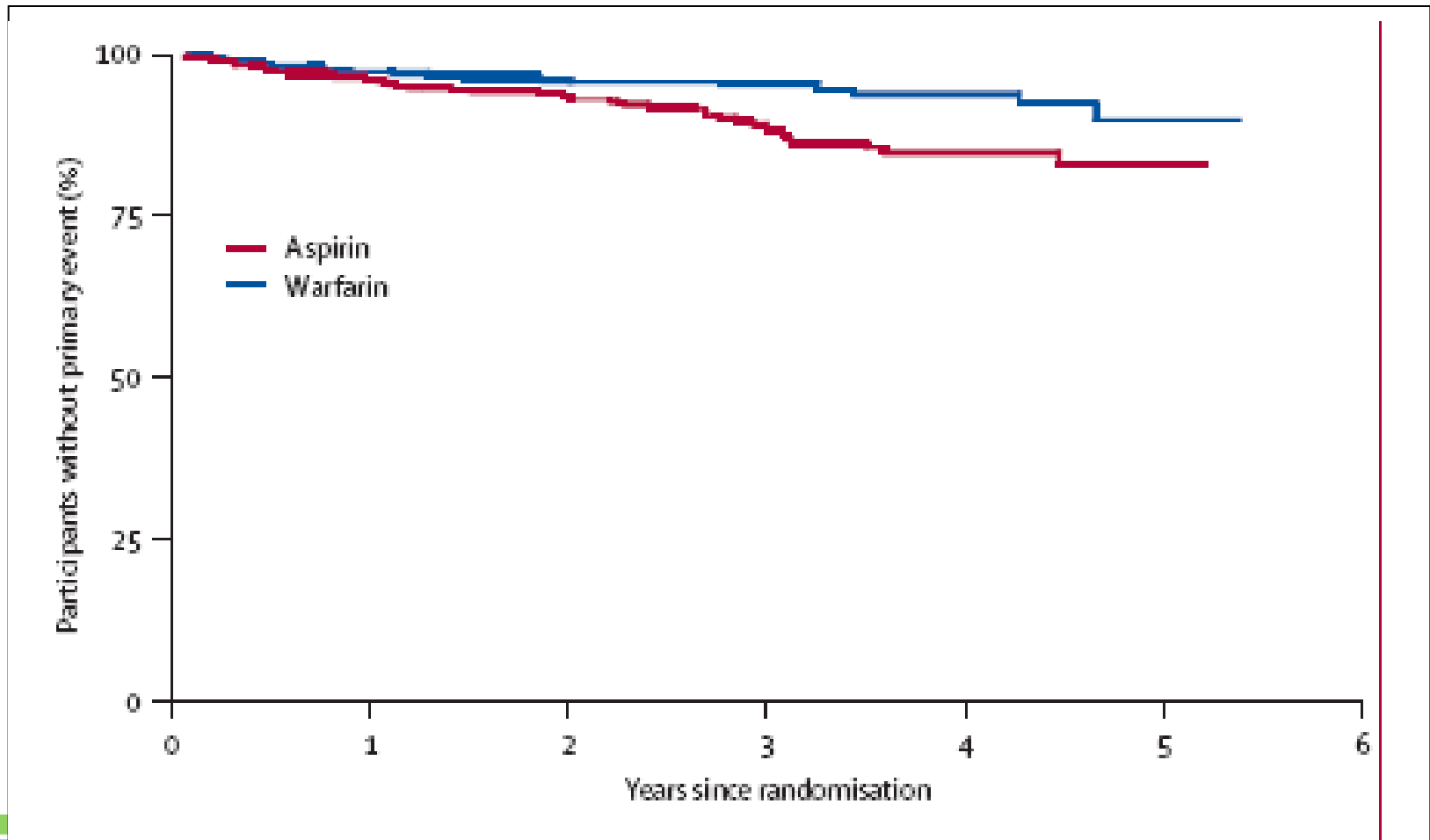
Maximum score 10

- Those patients with one major risk factor or ≥ 2 'clinically relevant non-major' stroke risk factors (essentially CHA2D2-VASc score of ≥ 2) should be treated with [oral anticoagulation](#).
- Those with one 'clinically relevant non-major' stroke (ie. [CHA2D2-VASc score of 1](#)) can be treated with oral anticoagulation or aspirin, although [oral anticoagulation is suggested rather than aspirin](#), given recent data in such patients
- Low risk patients (CHA2D2-VASc score=0) are those with no risk factors, and given that such patients are 'truly low risk' treatment with aspirin or (preferably) no antithrombotic therapy is appropriate.

WARFARIN vs ASPIRIN IN THE OVER

75s: BAFTA TRIAL

Mant Lancet 2007;370:493

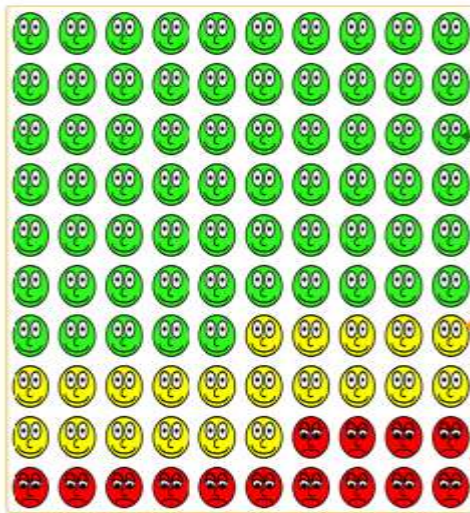


Risk of stroke p.a.

Risk group	Untreated	Aspirin	Warfarin	NNT*
Very high Previous ischaemic stroke or TIA	12%	10%	5%	13
High Age over 65 and one other risk factor: – hypertension – diabetes mellitus – heart failure – LV dysfunction	5-8%	4-6%	2-3%	22-47
Moderate – Age over 65, no other risk factors – Age under 65, other risk factors	3-5%	2-4%	1-2%	47-83
Low Age under 65, no other risk factors	1.2%	1%	c. 0.5%	200

Risk of Major Haemorrhage with Age p.a.

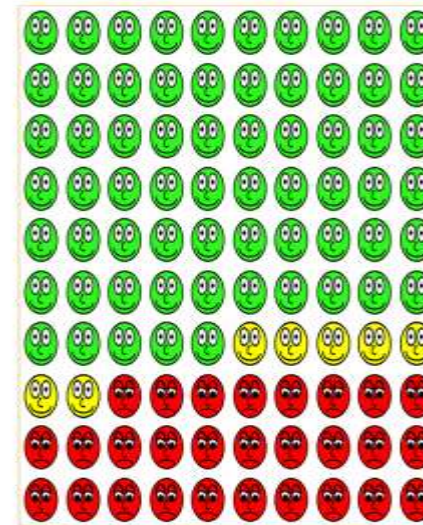
Age Range	Warfarin	Aspirin	Relative Risk
75-79	1.1%	0.8%	1.44
80-84	2.3%	2.4%	0.96
85+	2.9%	3.7%	0.77



These 65 people will not have a stroke whether or not they take warfarin

These 21 people will be saved from having a stroke by taking warfarin

These 14 people will have a stroke, even though they take warfarin



These 65 people will not have a stroke whether or not they take aspirin

These 7 people will be saved from having a stroke by taking aspirin

These 28 people will have a stroke, even though they take aspirin

StrokeImprovement AFFIRM TRIAL

Wyse NEJM 2002;347:1825

- At 5 years, SR present in 35% of rate control group vs 63% of rhythm control
- >90% of rate control group remained on warfarin vs 70% in rhythm control group
- Majority of strokes occurred in patients not taking warfarin or with INR<2.0
- QoL substudy showed no difference between rate vs rhythm control groups

Opportunities to prevent stroke in patients with AF...

- Detection and anticoagulation
 - of those known to have AF
 - of those not known to have AF
- Detection after TIA/CVA
- Improving quality of anticoagulation

Incidence of new diagnoses of AF and PAF in TIA population

- Patients with AF are often asymptomatic or have only minimal symptoms or vague, non-specific symptoms, hence any asymptomatic paroxysmal episodes of AF become difficult to monitor. (1)
- In about one-third of patients, the patient is not aware of so-called 'asymptomatic AF'.
- Shorter and asymptomatic episodes of AF may be biomarkers of more prolonged or clinically significant episodes of AF hence the importance of its detection.

(1) *Asymptomatic arrhythmias in patients with symptomatic paroxysmal atrial fibrillation and paroxysmal supraventricular tachycardia. Wilkinson WE, Clair WK, McCarthy EA, Pritchett ELC Circulation 1994; 89: 224-227*

- Various techniques are used to detect episodes of AF post-stroke; these can be non-invasive or invasive. Duration of monitoring can also vary from a few hours to a few days.
- Available non-continuous ECG methods include scheduled or symptom-activated standard ECGs, Holter (24 h to 7 days) monitoring and transtelephonic recordings, patient- and automatically activated devices, and external loop recorders.
- A systematic review of 5 cohort studies evaluated 24 hour Holter monitoring:
 - New AF diagnosis made in 3.8%-6.1% (average 4.6%)
 - Compared with 5.7%-7.2% using Event loop recorders ⁽³⁾

(3) Non Invasive cardiac monitoring for detecting PAF/Flutter after ischaemic stroke; systems review Stroke 2007;38:2935-40

- Comparative study between holter, memory loop recorders and auto-triggered memory loop recorder picked up new AF at a rate of 6.7%, 17% and 36% respectively. (4)
- Continuous long term ECG recorder (40-100 hours duration) in those with negative 24 hour monitoring showed PAF in 31% of study group. (5)
- Despite these studies, there remains little guidance on the optimal strategy for detecting AF or PAF post stroke or TIA.

(4) Comp of autotriggered MLR versus MLR vs 24 hour holter;DMJ Cardiology 2005:1:95 (9)

(5) Automatc long term recording in patients withnegative 24 hour tape;Pacing clin Ep 2002:25

ESC Guidance 2010 - Tools for non-continuous ECG monitoring

- In paroxysmal AF, prolonged noncontinuous recording will facilitate AF detection. It has been estimated that 7 day Holter ECG recording or daily and symptom-activated event recordings may document the arrhythmia in around 70% of AF patients, and that their negative predictive value for the absence of AF is between 30 and 50%.
- In stroke survivors, a step-wise addition of five daily short-term ECGs, one 24 h Holter ECG, and another 7 day Holter ECG will each increase the detection rate of AF by a similar extent.

- We aimed to evaluate the incidence the new diagnoses of AF and PAF in our TIA population using a combination of standard 12 lead ECG, inpatient and outpatient cardiac monitoring.
- 1st January 2008 to 1st July 2008
- All patients presenting with a TIA underwent evaluation of underlying cardiac rhythm.
- We instituted the following pathway for identification of AF and PAF:

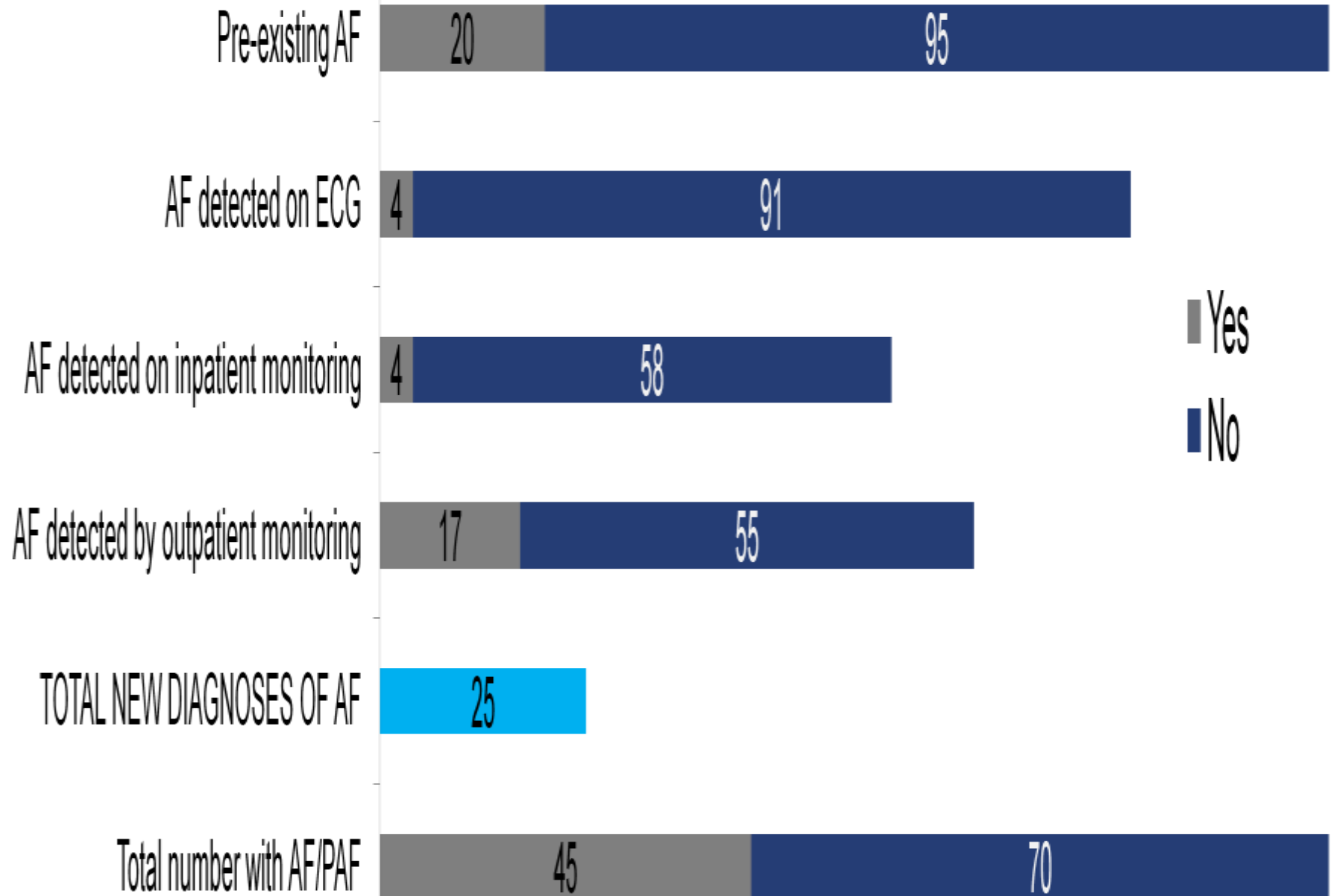
- The primary endpoint was detection of AF or PAF.
- The secondary endpoint was anticoagulation treatment with warfarin.

Results

- There were 115 patients with TIAs in the study period.
- The mean age was 77.2 years old (range 45-93).
- 95 were in sinus rhythm and had no prior history of PAF.
- 62 underwent inpatient monitoring.
- 72 underwent outpatient 3 day monitoring.

StrokeImprovement

NHS Improvement 



Warfarin Treatment for AF and PAF	
Previous diagnosis of AF/PAF – On warfarin	4/20
Previous diagnosis of AF / PAF – Not on warfarin	16/20
New treatment with warfarin for old AF/PAF	10/16 (total 14/20)
New diagnosis of AF/PAF with ECG or monitoring	25
Warfarin started for new diagnoses of AF/PAF	25 / 25 (100%)
Total number of patients on warfarin for AF/PAF	39 / 45 (86.7%)

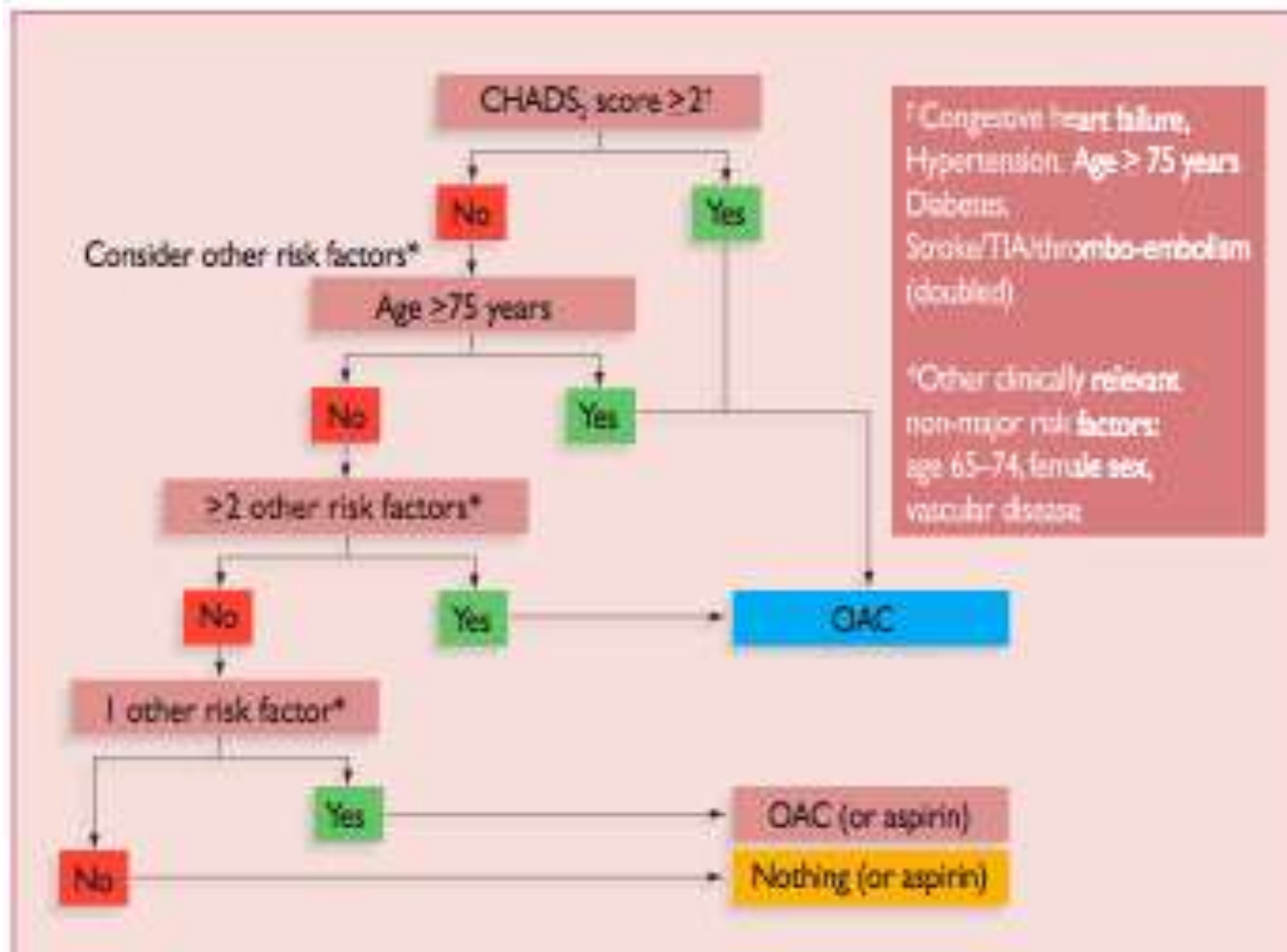
Discussion

- This intensive cardiac rhythm monitoring strategy after TIA identifies a significant proportion of patients with previously unknown AF or PAF in our population ($25/95 = 26.3\%$).
- This high level of AF and PAF detection may be a reflection of our relatively elderly population.
- Outpatient 72 hour tape found a large burden of undiagnosed AF or PAF ($17/72 = 23.6\%$)
- The identification of AF and PAF led to high rates of anticoagulation prescribing.

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

Summary

Who to refer:

- People with complex causes
- People with complex hearts
- People who are going too slow
- People going too fast despite medication
- People with symptoms despite good rate management
- People who are contra-indicated to warfarin
- People who are very high bleeding risk and stroke risk

Thank you for your attention

Question

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The PCCS

The Big Quiz!

The London Room

15:45