



BAFTA: RCT of warfarin vs aspirin for stroke prevention in atrial fibrillation in a primary care population aged over 75

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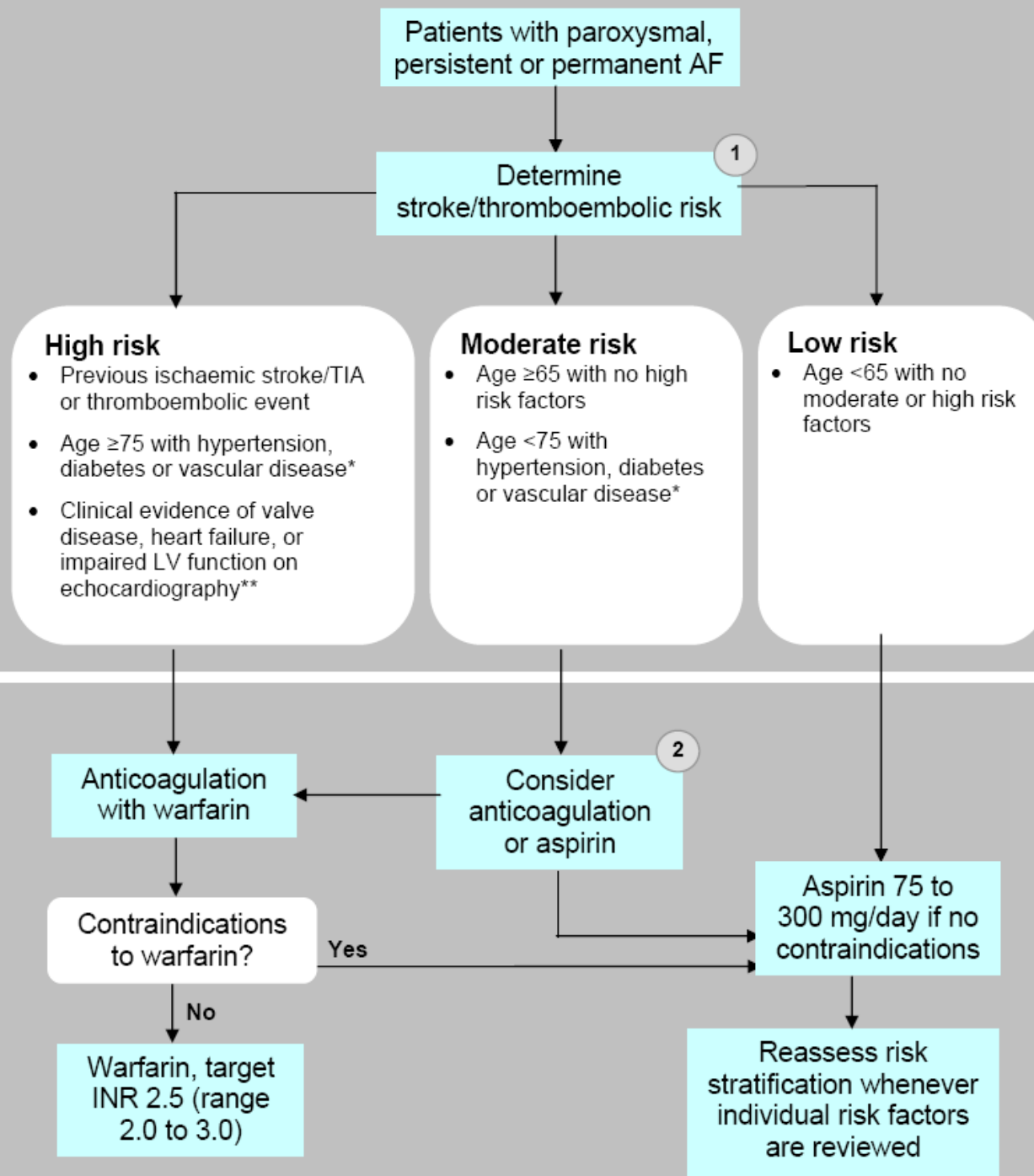
Background

- Importance of atrial fibrillation as a risk factor for stroke in older people
- Strong evidence for effectiveness of warfarin at reducing this risk.....
- But concerns about applicability of this evidence
 - in the elderly
 - In primary care settings
- Uncertainty reflected in current guidelines

Warfarin versus aspirin: in age ≥ 75 (Walraven et al)

Outcome	On aspirin	On warfarin	Rel Risk Reduction/increase	NNT/H pa
Ischaemic stroke	5.9%	3.7%	47%	46
Major bleed	1.5%	3.2%	213%	59

NICE Guideline



NICE guidelines: caution with warfarin

- **Aged over 75**
- On anti-platelet drugs
- Polypharmacy
- Uncontrolled hypertension
- History of bleeding (eg peptic ulcer; cerebral haemorrhage)
- History of poor anticoagulation control

Aim of BAFTA

- To compare the incidence of fatal and non-fatal disabling stroke (ischaemic and haemorrhagic), intra-cranial haemorrhage and other significant arterial embolism in patients randomised to warfarin or aspirin

Methods: participants

- Recruited 2001-2004 from 260 practices
- Age ≥ 75
- ECG confirmed AF
- Exclusions:
 - Rheumatic heart disease
 - History of major haemorrhage
 - Active peptic ulcer disease
 - Allergic hypersensitivity to study medications
 - Terminal illness
 - BP $\geq 180/110$
 - GP not in equipoise

Methods: Interventions

- Aspirin 75mg daily
- Warfarin: target INR 2.5, range 2-3
 - Frequency and method of INR testing at discretion of GP

Methods: Outcome measures

– Primary

- All adjudicated by independent committee blinded to treatment allocation

– Secondary

- Major extra-cranial haemorrhage
- Non-stroke vascular events
- All cause mortality
- Adjudicated by independent clinician blinded to treatment allocation

4,639 cases AF identified by ECG

2,877 excluded

1,762 attended randomisation clinic

789 excluded

485 aspirin

488 warfarin

4 lost to follow up:
3 withdrew consent
1 emigrated

Mean follow up
2.7 years

4 lost to follow up:
3 withdrew consent
1 emigrated

485 analysed

488 analysed

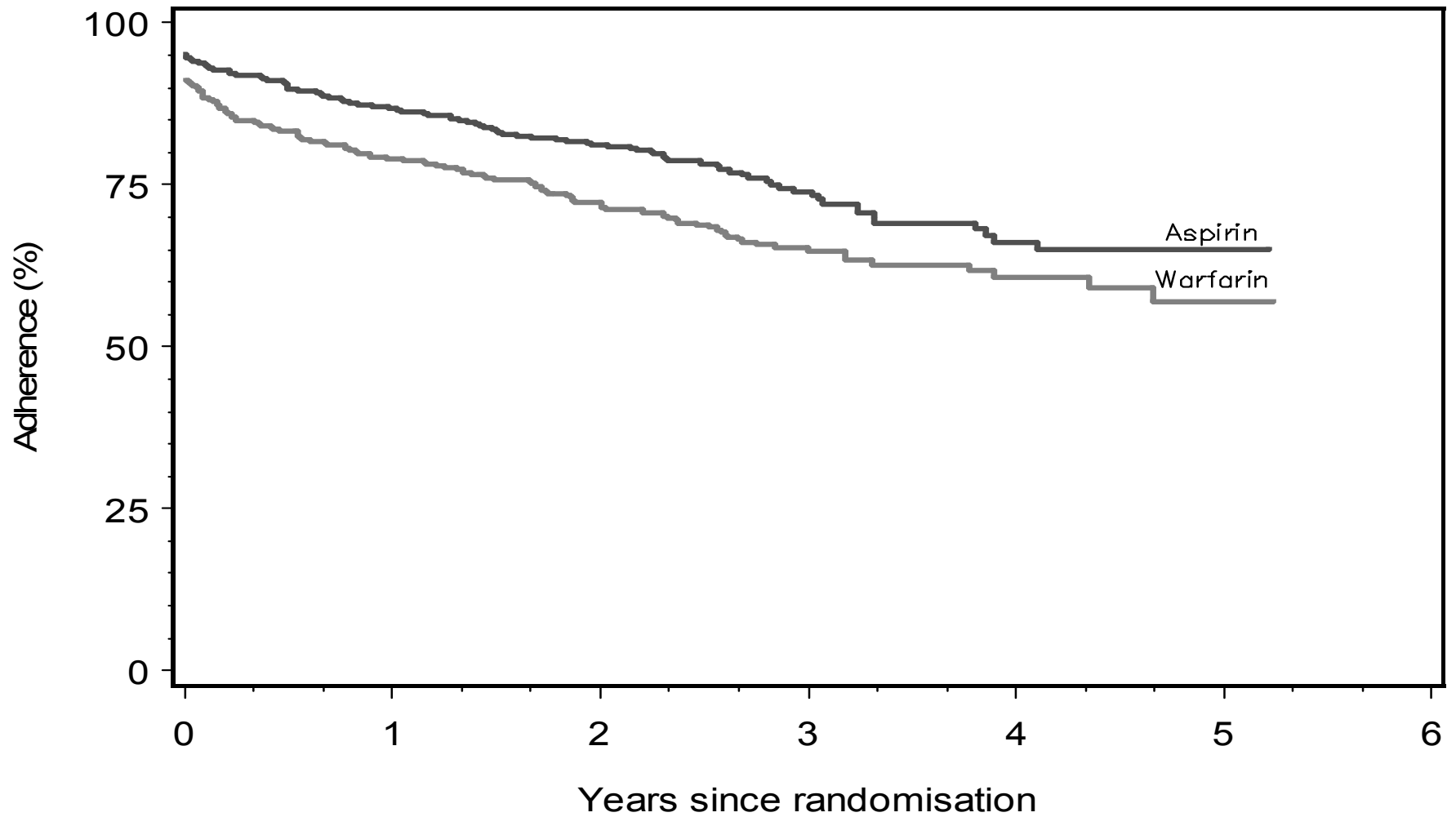
Reasons for non-participation

Not meeting inclusion criteria	224	6.1%
Lack of clinical equipoise	1995	54.4%
Patient decision	905	24.7%
Died/moved away	110	3.0%
No reason given	432	11.8%

Baseline characteristics

	Warfarin	Aspirin
Age (mean)	81.5	81.5
Male	55%	54%
Identified through screening	30%	30%
CHADS 2 score 3-6	28%	28%
On warfarin	40%	39%
History of stroke/ TIA	13%	12%
Hypertension	53%	55%
Blood pressure (mean)	140/78	141/79
Diabetes	14%	13%
Heart failure	20%	19%

Adherence to allocated therapy



INR control in BAFTA

- 67% time in range (2-3)
- 19% below target; 14% above target
- Models of INR control in practices:
 - 22% all done by hospital
 - 30% INR dosing & analysis done by hospital
 - 19% INR analysis alone done by hospital
 - 25% all done by practice
 - (4%?)

Results: primary end point

- Risk of primary end point:
- Warfarin v aspirin
- 1.8% v 3.8%
- RR 0.48 (0.28-0.80)
- $p = 0.0027$

Nature of Primary end points

	warfarin	aspirin
Stroke	21	44
<i>-ischaemic</i>	10	32
<i>-haem</i>	6	5
Subdural	2	1
Embolism	1	3
Total	24	48

Risk of primary event by age (% p.a)

	Warfarin	Aspirin	RRR	P value (interaction)
75-79	2.0	2.8	29%	0.57
80-84	1.1	3.8	70%	0.45
85+	2.8	5.6	50%	

Secondary outcomes: haemorrhage – risk per annum

	warfarin	aspirin	RR (95% CI)
Major extra-cranial	1.4%	1.6%	0.87 (0.43-1.73)
Other hospital admission	1.8%	1.5%	1.22 (0.64-2.36)
All major (including stroke and sub-dural)	1.9%	2.0%	0.96 (0.53-1.75)

Risk of major haemorrhage by age (% p.a)

	Warfarin	Aspirin	RR	P value (interaction)
75-79	1.1	0.8	1.44	0.53
80-84	2.3	2.4	0.96	0.80
85+	2.9	3.7	0.77	

Secondary outcomes: deaths – risk per annum

	Warfarin	Aspirin	RR (95% CI)
All cause	8.0%	8.4%	0.95 (0.72-1.26)
Stroke	1.0%	1.6%	0.59 (0.27-1.24)
Other vascular	3.1%	2.7%	1.16 (0.72-1.88)
Non-vascular	3.8%	4.0%	0.96 (0.64-1.45)

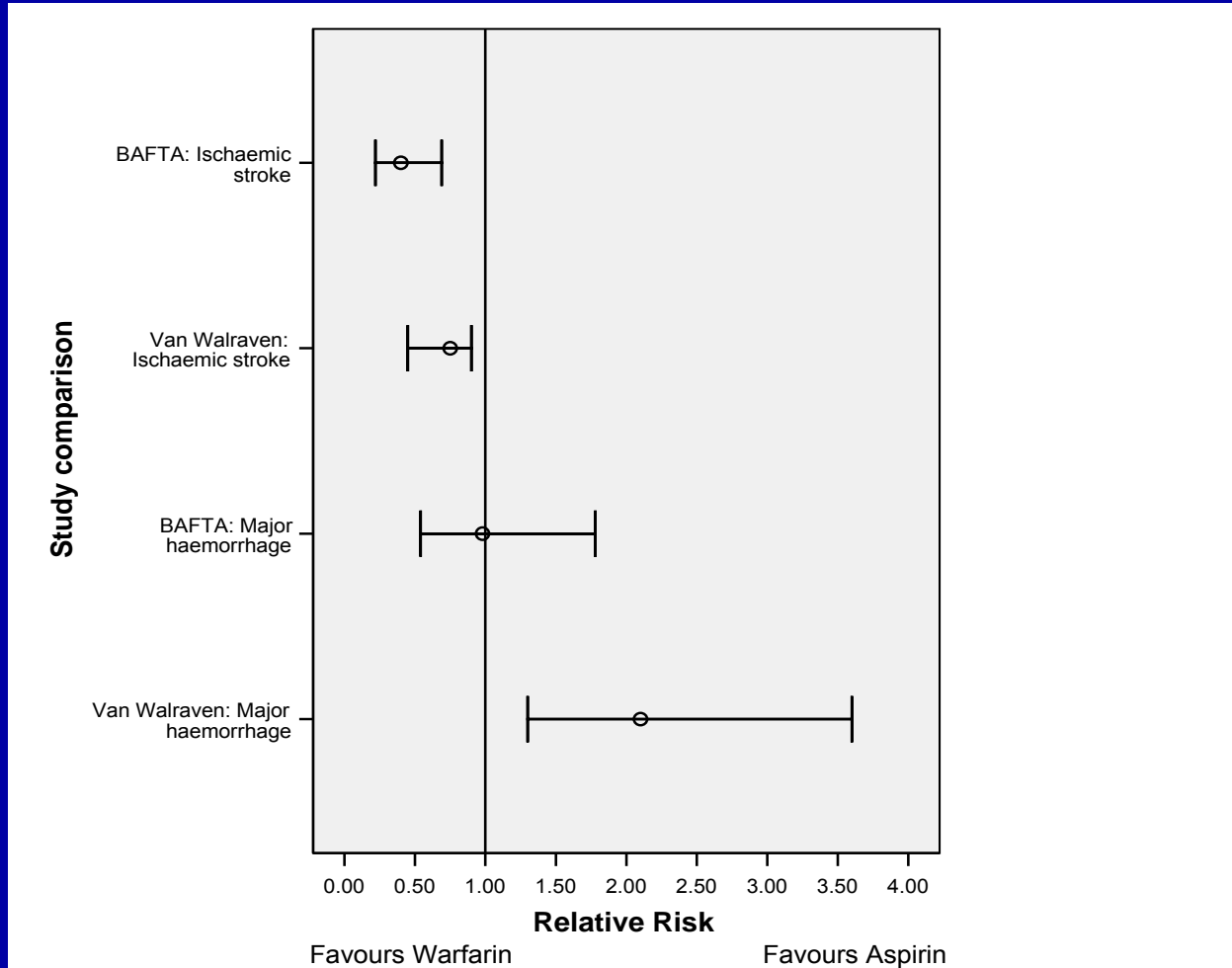
Secondary outcomes: vascular events – risk per annum

	warfarin	aspirin	RR (95% CI)
Myocardial infarction	1.1%	1.2%	0.96 (0.44,2.11)
All non stroke vascular	6.1%	6.3%	0.97 (0.70,1.35)
Major vascular events (stroke, MI, PE, vasc death)	5.9%	8.1%	0.73 (0.53,0.99)

Summary

- Anticoagulation significantly more effective than aspirin in preventing stroke
- No difference in prevention of other vascular events
- No difference in risk of major haemorrhage

Comparison of BAFTA results with previous trial data from age ≥ 75



Discussion

- 21% of people identified to be in atrial fibrillation took part in study
- Cross overs with regard to therapy
 - Both these factors likely to lead to underestimate of potential benefit of warfarin

Conclusion

- Use of anticoagulation rather than aspirin will prevent one primary event for every 53 patients treated per year
- Warfarin could safely be used more widely in the elderly
- Age of itself should not be regarded as a contra-indication to therapy



Acknowledgements



- Writing Committee: J Mant, F Hobbs, K Fletcher, A Roalfe, G Lip, D Fitzmaurice, E Murray
- Additional Trial Management Group Members: R Salter; J Raftery; S Bryan; M Davies
- Trial Steering Committee: S Cobbe, C Baigent, G Fowler, T Meade, M Sudlow, B Clark, K Wheatley
- Data Monitoring & Ethics Committee: P Sandercock; T Peters; R Hart
- Events Adjudication: P Rothwell; A Williams; P Mayer
- Funding: Medical Research Council
- Supported by: Midlands Research Consortium, Other Primary Care Research Networks & Stroke Research Network



Leading science for better health

- Mant J, Hobbs FDR, Fletcher K et al. Warfarin versus aspirin for stroke prevention in an elderly community population with atrial fibrillation (the Birmingham Atrial Fibrillation Treatment of the Aged Study, BAFTA): a randomised controlled trial. *Lancet* 2007; 370: 493–503
- Mant JWF, Richards SH, Hobbs R, et al. Protocol for Birmingham Atrial Fibrillation Treatment of the Aged study (BAFTA): a randomised controlled trial of warfarin versus aspirin for stroke prevention in the management of atrial fibrillation in an elderly primary care population. *BMC Cardiovasc Disord* 2003; 3: 9.