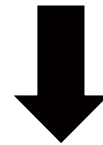


# Stroke prevention in AF

Detection of  
AF



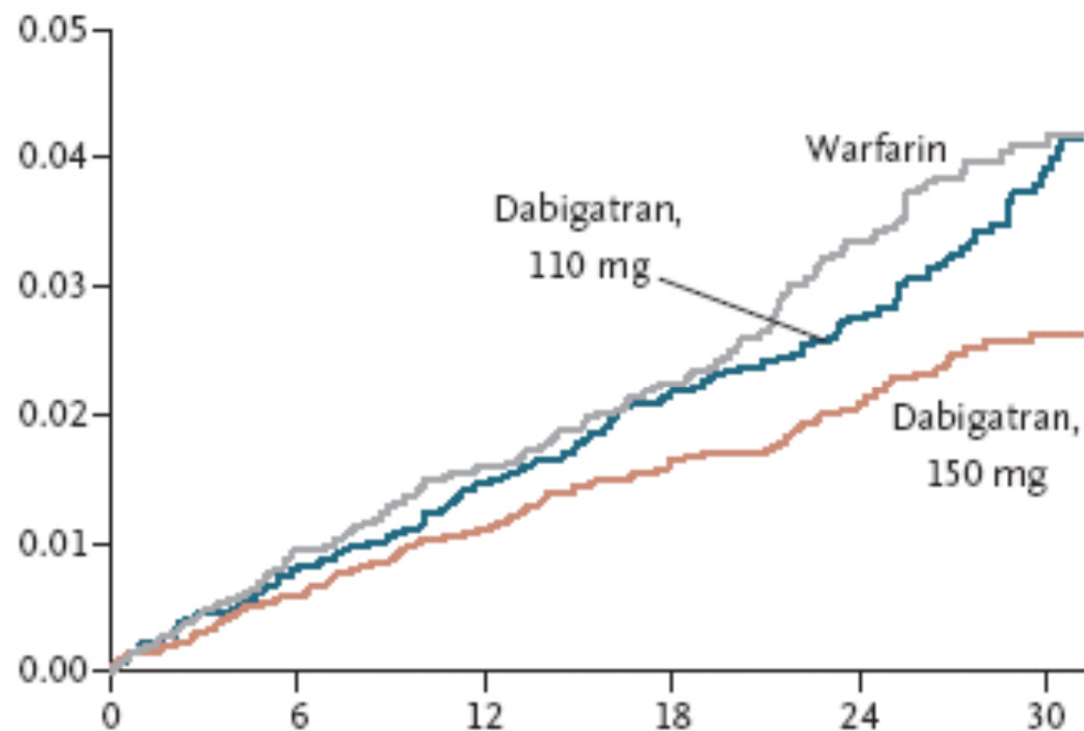
Decision to anti-  
coagulate



Quality of anti-  
coagulation



## RE-LY Study Stroke or Systemic embolism



NEJM, Sept 2009

## RE-LY

Time in therapeutic range

64 %

How does this compare with routine anti -  
coagulant practice?



# Influence of Time in therapeutic range

- What would an improvement of 5 % achieve
- An approximate improvement in odds ratio of 0.23
- Equivalent to NNT of 434
- 189000 patients nationally
- Would prevent 435 strokes
- “Free”



# Potential for stroke prevention

**Detection of AF**

Flu clinic model 361

**Decision to  
anti-coagulate**

GRASP 10%uptake 450

**Quality of  
anti-coagulation**

5% increase in TTR 435



# 1000 High risk AF patients

500 not on warfarin

Strokes

20

500 on warfarin

– 300 therapeutic INR

– 200 sub-therapeutic INR

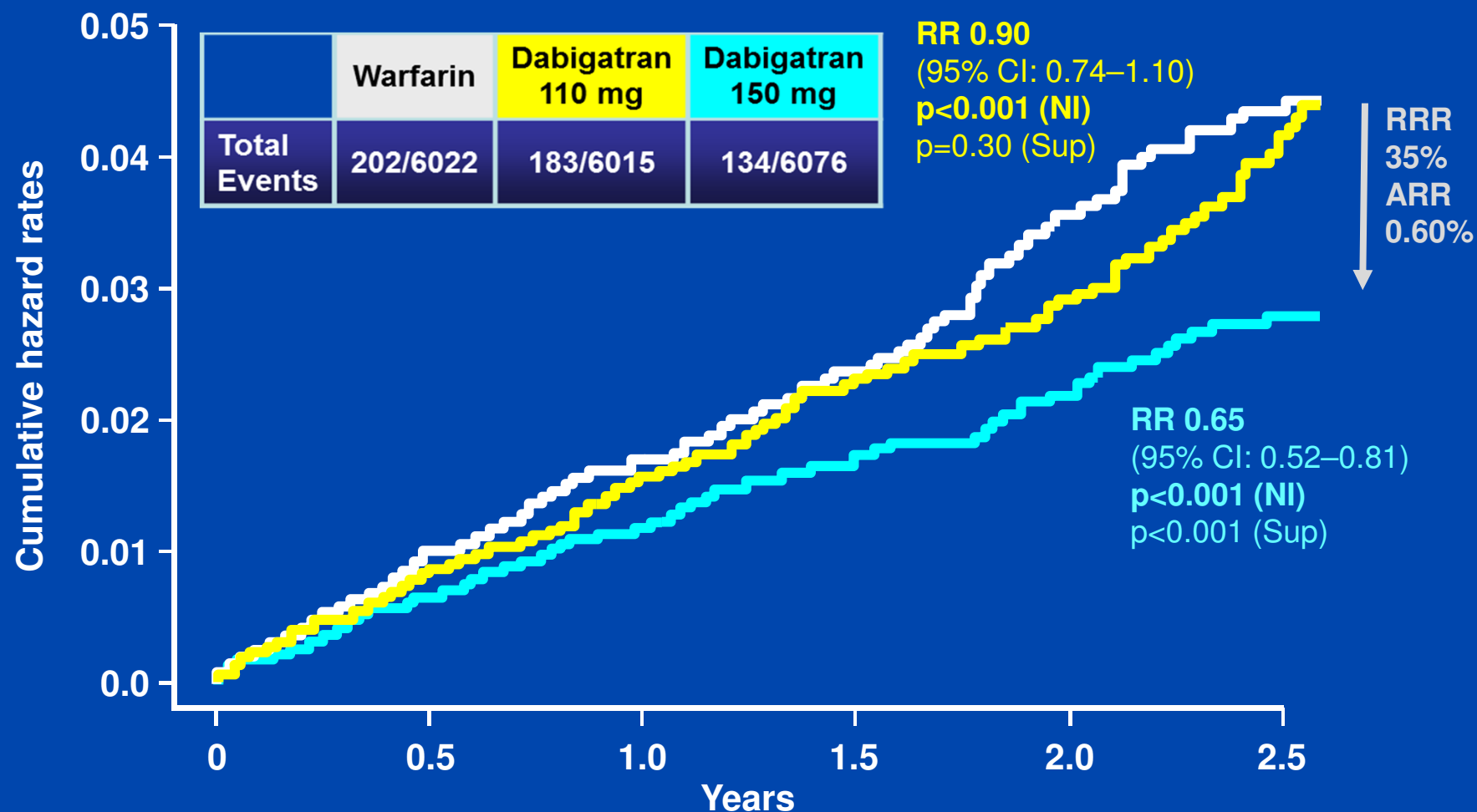
5

8



# How does Pradaxa® compare to warfarin?

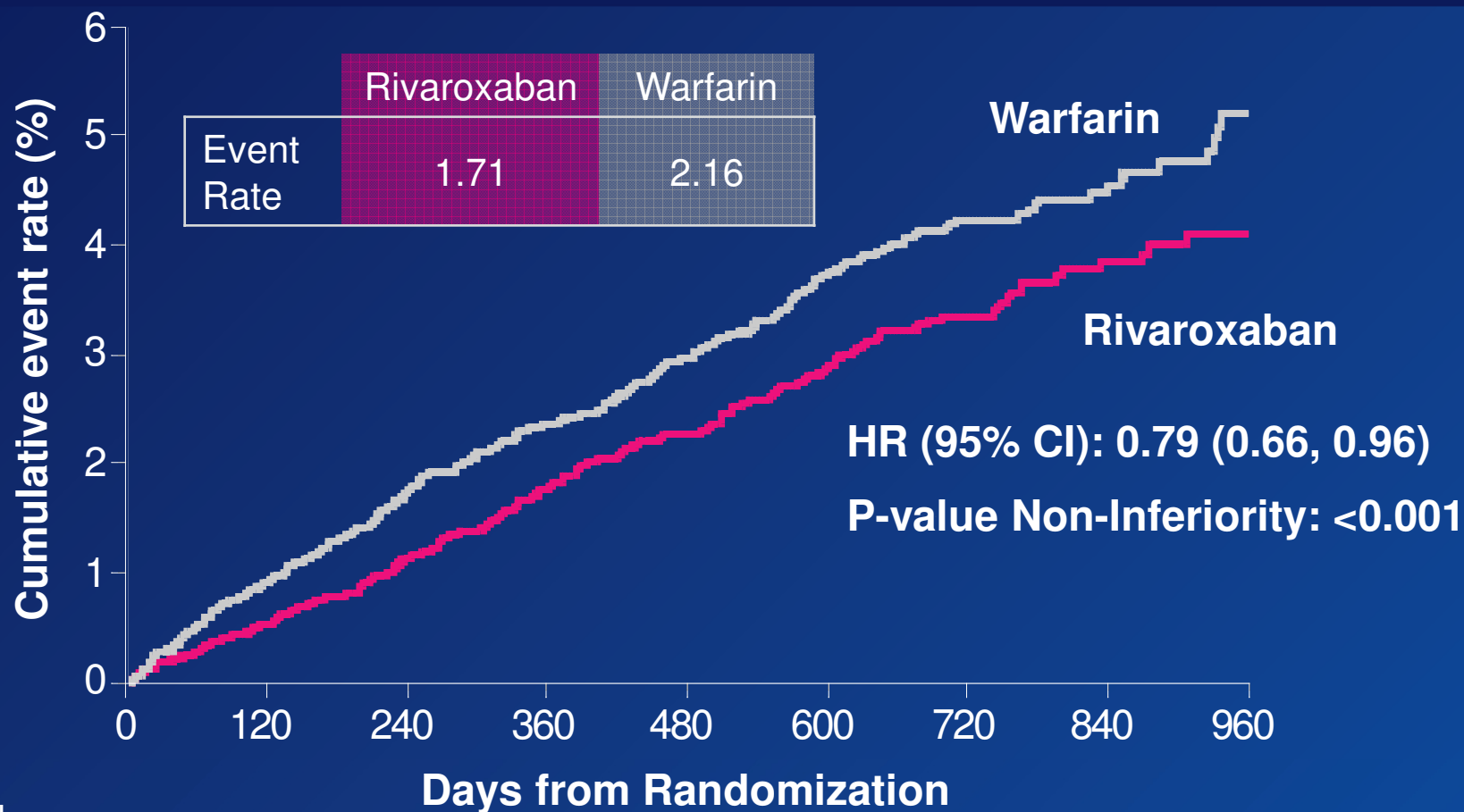
## Time to first stroke / SSE



ARR, absolute risk reduction; RR, relative risk; CI, confidence interval; NI, non-inferior; Sup, superior

# Primary Efficacy Outcome

## Stroke and non-CNS Embolism



No. at risk:

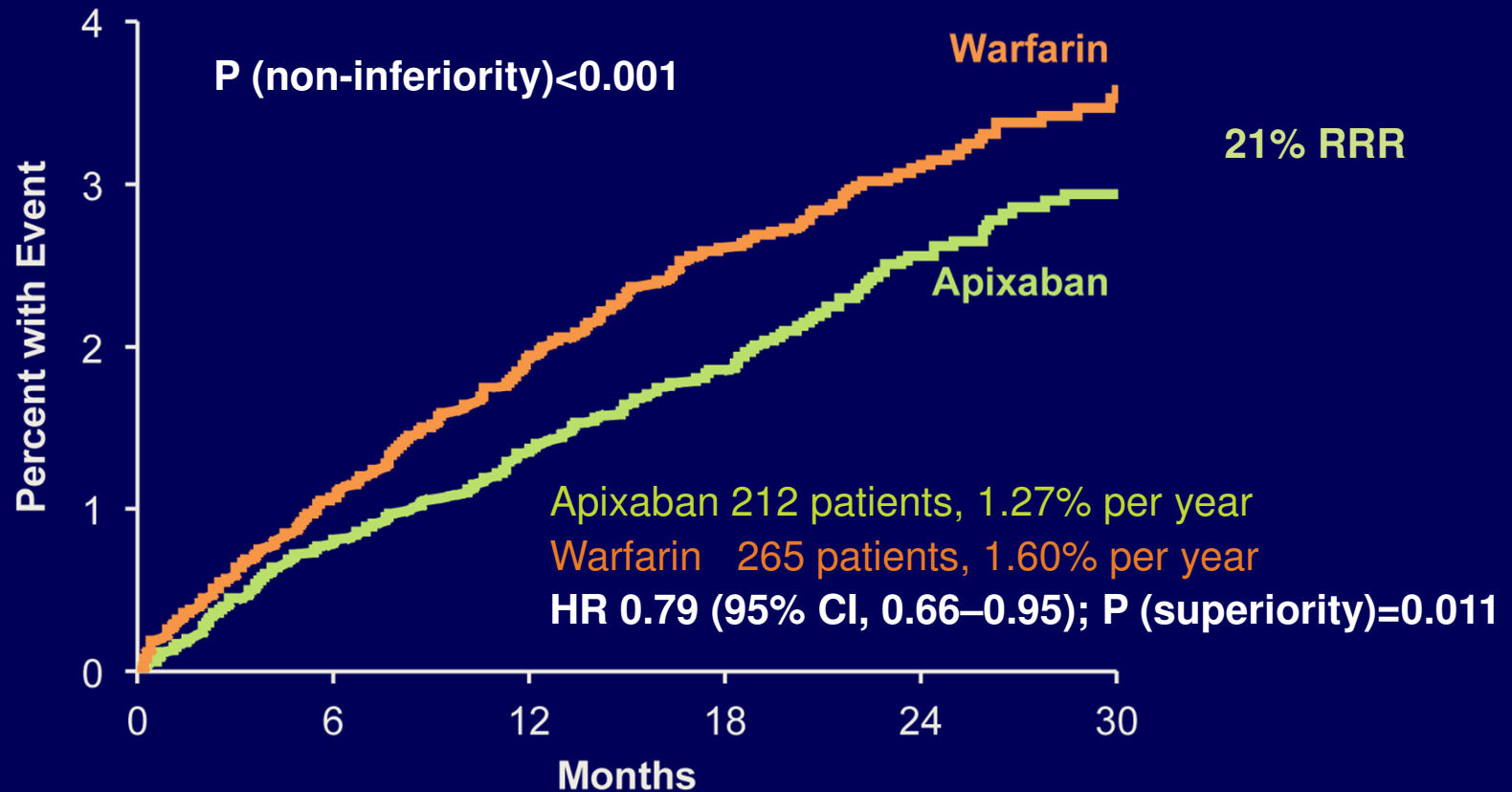
Rivaroxaban	6958	6211	5786	5468	4406	3407	2472	1496	634
Warfarin	7004	6327	5911	5542	4461	3478	2539	1538	655

Event Rates are per 100 patient-years  
Based on Protocol Compliant on Treatment Population



# Primary Outcome

Stroke (ischemic or hemorrhagic) or systemic embolism

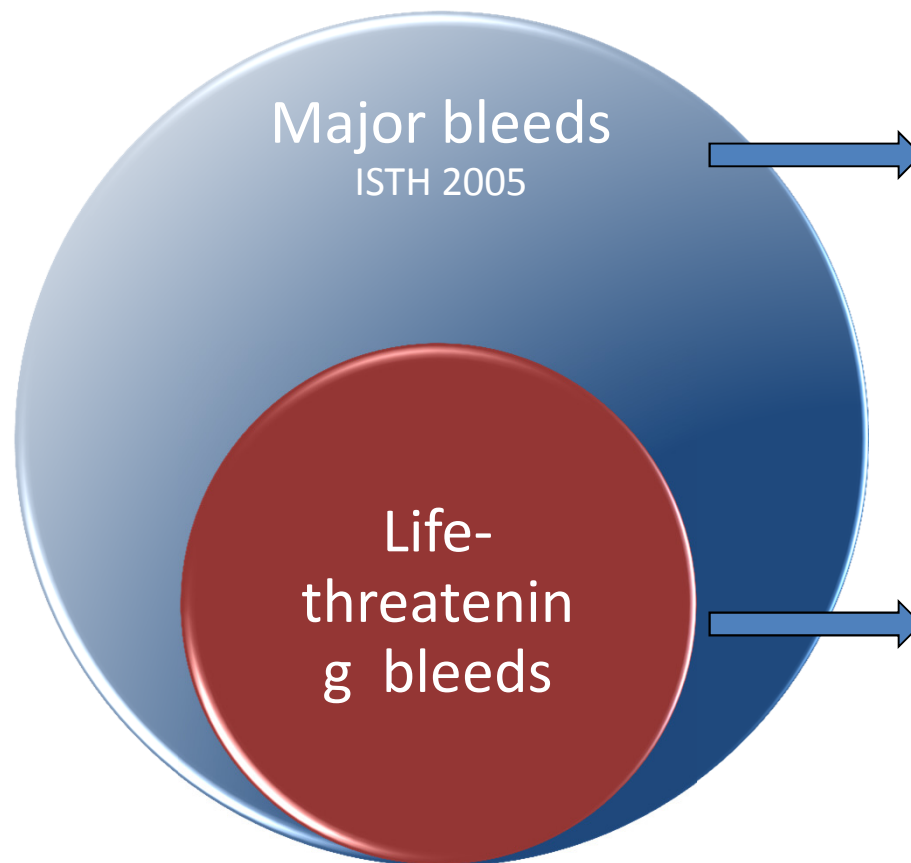


No. at Risk

Apixaban	9120	8726	8440	6051	3464	1754
Warfarin	9081	8620	8301	5972	3405	1768

## Balancing risk vs. Harm

### Do all major haemorrhages matter?



- Major haemorrhage
- Hb drop of  $\geq 2\text{g/dl}$
- Transfusion of  $\geq 2\text{ U}$
- Symptomatic bleeding in critical organ

- Fatal haemorrhage
- Intracranial haemorrhage
- Hb drop of  $\geq 5\text{g/dl}$
- Transfusion of  $\geq 4\text{ U}$
- Inotropic agent support
- Surgery

# An Approach to Risk Assessment

## HAS-BLED

Letter	Clinical Characteristic	Points awarded
H	Hypertension	1
A	Abnormal Renal and Liver Function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Liable INR	1
E	Elderly (age over 65 yrs)	1
D	Drugs and/or Alcohol (1 point each)	1 or 2
		Maximum 9



# An Approach to Risk Assessment

## Atria Risk Score

Clinical Characteristic		Points awarded
Anaemia		3
Severe Renal Failure		3
Age over 75 yrs		2
Prior Bleeding		1
Hypertension		1

## Stroke Prevention and Atrial Fibrillation

Atrial fibrillation (AF) is associated with a five-fold increase in stroke risk and a one in three life time risk of stroke. The cardio-embolic strokes caused by AF are associated with more fatalities than other ischaemic strokes, and are generally more disabling at presentation leading to increased hospital stay, poorer ongoing quality of life and increased discharge to long term care.

Oral anticoagulation is known to be the only effective intervention to reduce the risk of AF related stroke and has also been shown to reduce the damage caused if a stroke occurs. The only role for anti-platelet medication is in those at low risk.

In patients at higher risk of stroke in AF, aspirin is not effective in stroke prevention but carries the same risks as oral anticoagulants.

### Stroke Risk Stratification with an improved CHADS<sub>2</sub>

The CHADSVASc schema is the approved risk schema from the European Society of Cardiology. It is excellent at showing people at low risk (score of zero indicates an annual adjusted risk of 0%), however is harder to remember and has a mild anomaly around its point score for gender. We present another way to see the score.

**C<sub>1</sub> or 2** -Cardiac Disease (1 point LVSD and/or 1 point Vascular disease (IHD and/or PVD))  
**H** -Hypertension  
**A<sub>1</sub> or 2** -Age (1 point 65 to 74; 2 points if 75 or over)  
**D** -Diabetes  
**S<sub>2</sub>** -Stroke or TIA (2 points)

*In a women over the age of 65yrs an additional 1 point should be scored to reflect their increased risk*

### Interpretation

Score of 0, nothing or aspirin  
 Score of 1, aspirin or Oral Anticoagulant  
 Score of 2 or more, oral anticoagulant

### Bleeding Risk Stratification with the ATRIA Bleeding Risk Score

Clearly oral anticoagulants are not without risk as they slow blood clotting. In general it is thought that clinicians tend to over estimate the risks associated with anti-coagulation. Population study data from Finland has shown a decrease in intracerebral haemorrhage (ICH) in the population although there has been a doubling of the level of anticoagulation. This has been further developed to show that warfarin increased the absolute risk rate of ICH by 0.19% giving a numbers needed to harm (NNH) of 526.

A simple validated scoring system for bleeding is the ATRIA schema.

Anaemia 3 points (hemoglobin <13 g/dl in men and <12 g/dl in women)  
 Severe Renal Failure 3 points (eGFR <30 ml/min or dialysis-dependent)  
 Over 75 Years 2 points  
 Previous bleeding 1 point (Any previous significant bleeding)  
 Known Hypertension 1 point (Previously established hypertension, a persistent point)

### Balancing Risk and Benefit

Bleed risk score	Annualised haemorrhage rate	CHA <sub>2</sub> DS <sub>2</sub> VASc	Annual Stroke Risk
Low (0-3)	0.76%	0	0%
		1	1.3%
Intermediate (4)	2.62%	2	2.2%
		3	3.2%
		4	4.0%
High (5-10)	5.76%	5 to 9	6.7-15.2%

**We do not see the strokes and suffering we prevent only the inconvenience of treatment we prescribe**

Dr Duncan Petty-Prescribing Support Services  
 Dr Matthew Fay-GP Westcliffe Medical Centre  
 Mr Greg Fell-Public Health Consultant

# Risk and Benefit

Bleeding Risk Score-ATRIA	Annualised Haemorrhage Risk	CHADSVASc	Annualised Stroke Risk
Low Risk (0-3)	0.76%	0	0%
		1	1.3%
Intermediate Risk (4)	2.62%	2	2.2%
		3	3.2%
		4	4%
High Risk (5-10)	5.76%	5 to 9	6.7-15.2%

## 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 AF<sup>1</sup>
- AF doubles the risk of stroke when adjusted for other risk factors<sup>2</sup>
- Without preventive treatment, each year approximately 1 in 20 patients (5%) with AF will have a stroke<sup>3</sup>
  - When transient ischaemic attacks and clinically 'silent' strokes are considered, the rate of brain ischaemia associated with non-valvular AF exceeds 7% per year<sup>4</sup>
- It is estimated that 15% of all strokes are caused by AF<sup>5</sup> and that 12,500 strokes per year in England are directly attributable to AF<sup>6</sup>

1. NICE clinical guideline 36. June 2006. Available at <http://www.nice.org.uk/guidance/CG36/?c=91497>; accessed April 2010; 2. ACC/AHA/ESC guidelines: Fuster V et al. Circulation 2006;114:e257–354 & Eur Heart J 2006;27:1979–2030; 3. Atrial Fibrillation Investigators. Arch Intern Med 1994;154:1449–57; 4. Carlson M. Medscape Cardiology. 2004;8; available at <http://cme.medscape.com>; accessed Feb 2010; 5. Lip GYH, Lim HS. Lancet Neurol 2007;6:981–93; 6. NHS Improvement. June 2009. Available at [http://www.improvement.nhs.uk/heart/Portals/0/documents2009/AF\\_Combining\\_Guide\\_v2.pdf](http://www.improvement.nhs.uk/heart/Portals/0/documents2009/AF_Combining_Guide_v2.pdf); accessed April 2010

## 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 causes<sup>1</sup>
- 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 admission<sup>2</sup>
  - Have longer in-hospital stay with a lower rate of discharge to their own home<sup>3</sup>
- The mortality rate for patients with AF is double that in people with normal heart rhythm<sup>4</sup>

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



# AF and associated stroke incur substantial healthcare costs<sup>1</sup>

- AF accounts for more than 1% of healthcare expenditure in the UK
- Total costs for treating the 12,500 strokes in England that are attributable to AF is £148 million in the first year
- The cost per stroke due to AF is estimated to be £11,900 in the first year after a stroke occurs

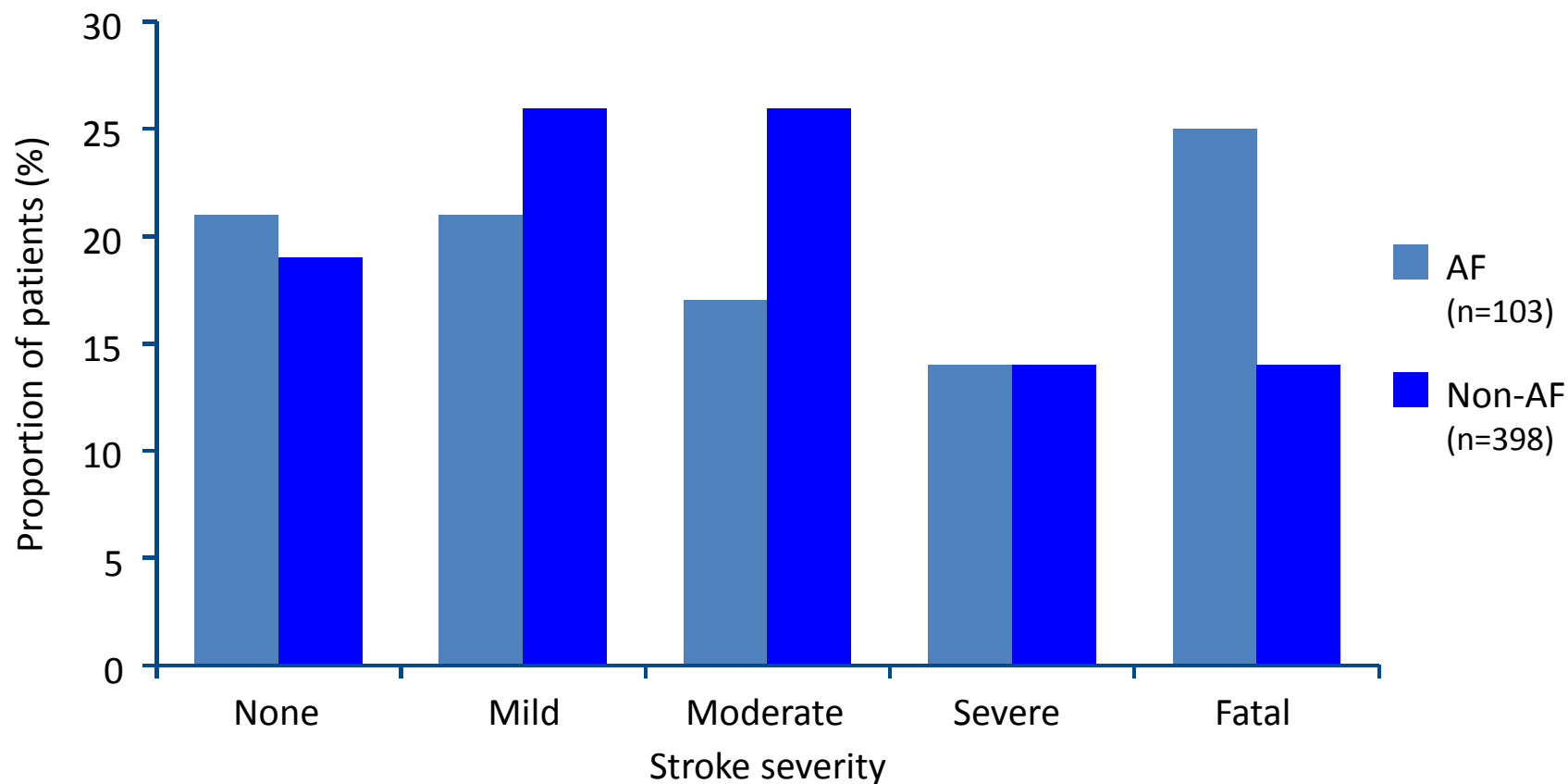
1. NHS Improvement. Commissioning for Stroke Prevention in Primary Care: The Role of Atrial Fibrillation. June 2009.

Available at [http://www.improvement.nhs.uk/heart/Portals/0/documents2009/AF\\_Commissioning\\_Guide\\_v2.pdf](http://www.improvement.nhs.uk/heart/Portals/0/documents2009/AF_Commissioning_Guide_v2.pdf)

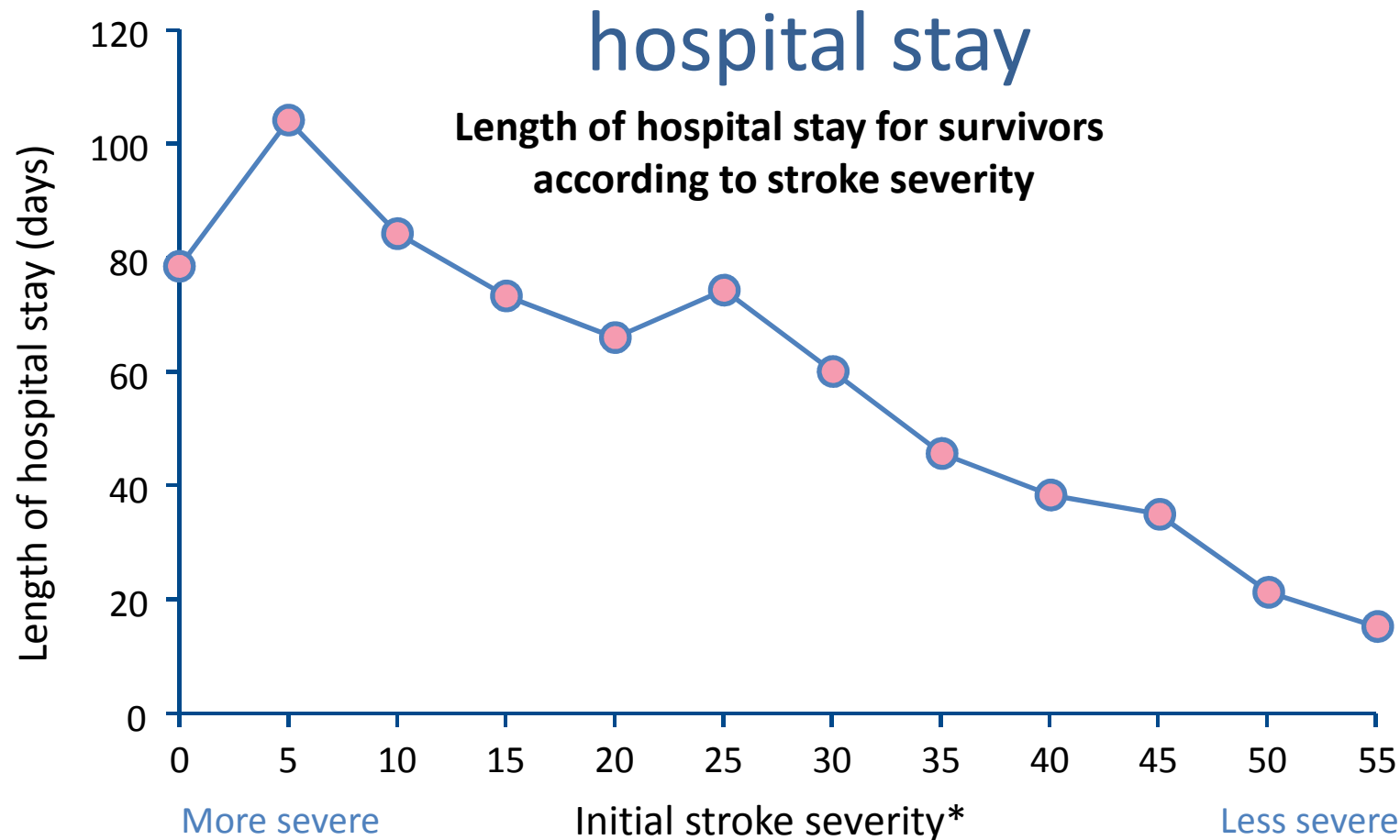
accessed April 2010

# Stroke is more likely to be fatal in patients with AF

P=0.048

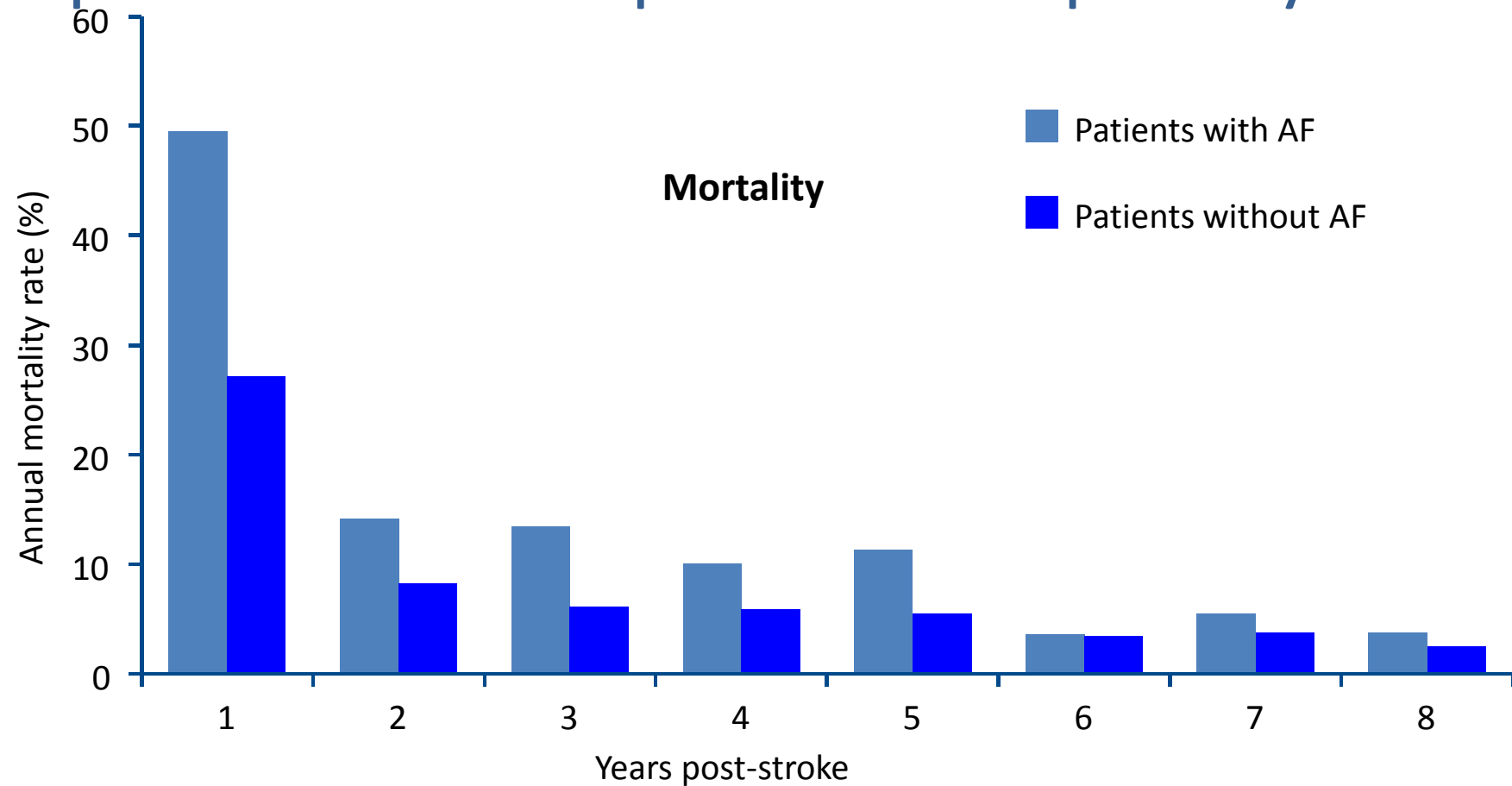


# Stroke severity increases the length of hospital stay



1197 acute stroke patients participating in the Copenhagen Stroke Study; \*Scandinavian Neurological Stroke Score on admission

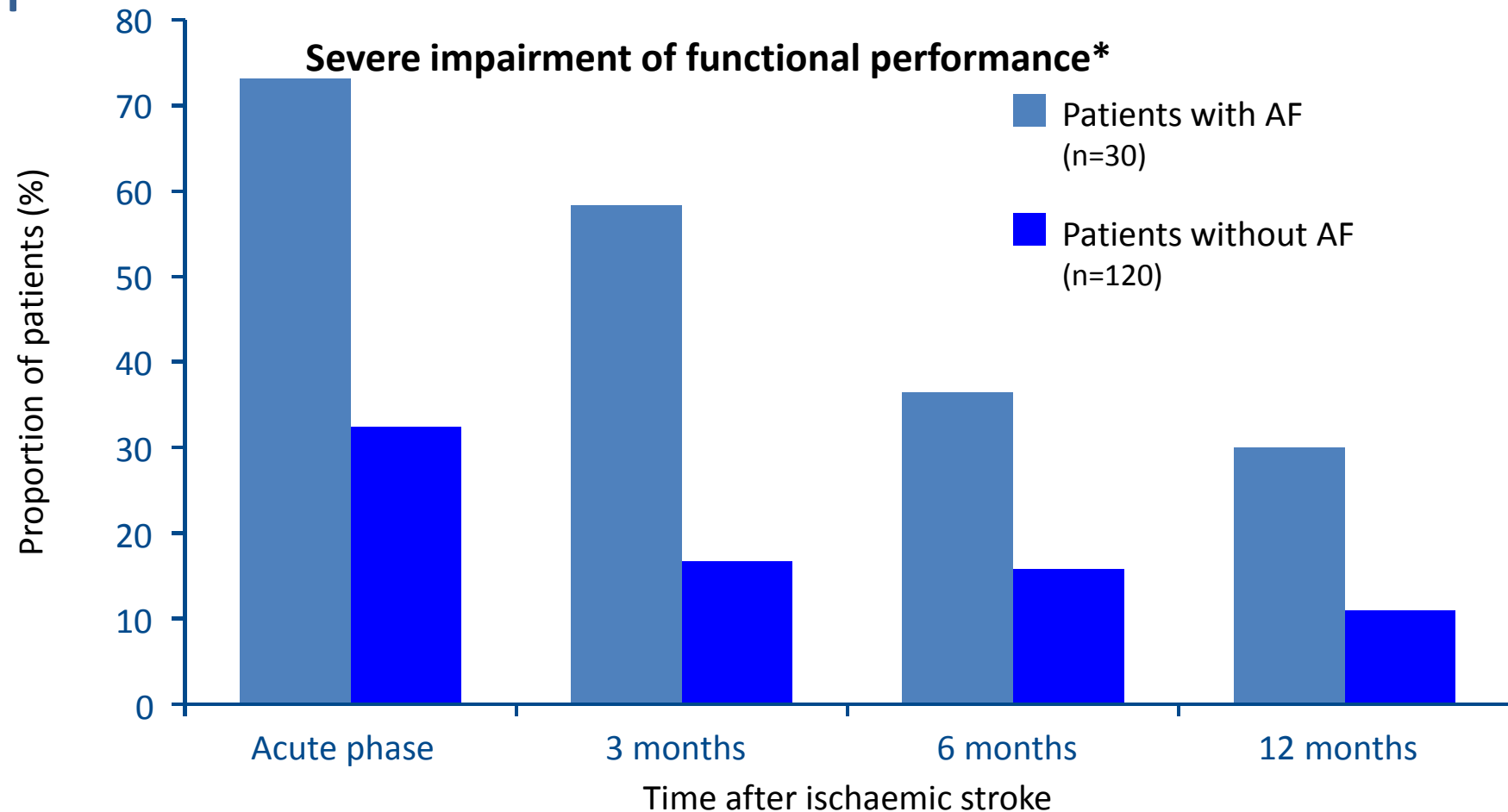
# Increased risk of death after stroke in patients with AF persists for up to 8 years



Population-based study of 3530 patients with ischaemic stroke

Marini C et al. Stroke 2005;36:1115-9

# AF is associated with poorer functional performance in survivors of ischaemic stroke

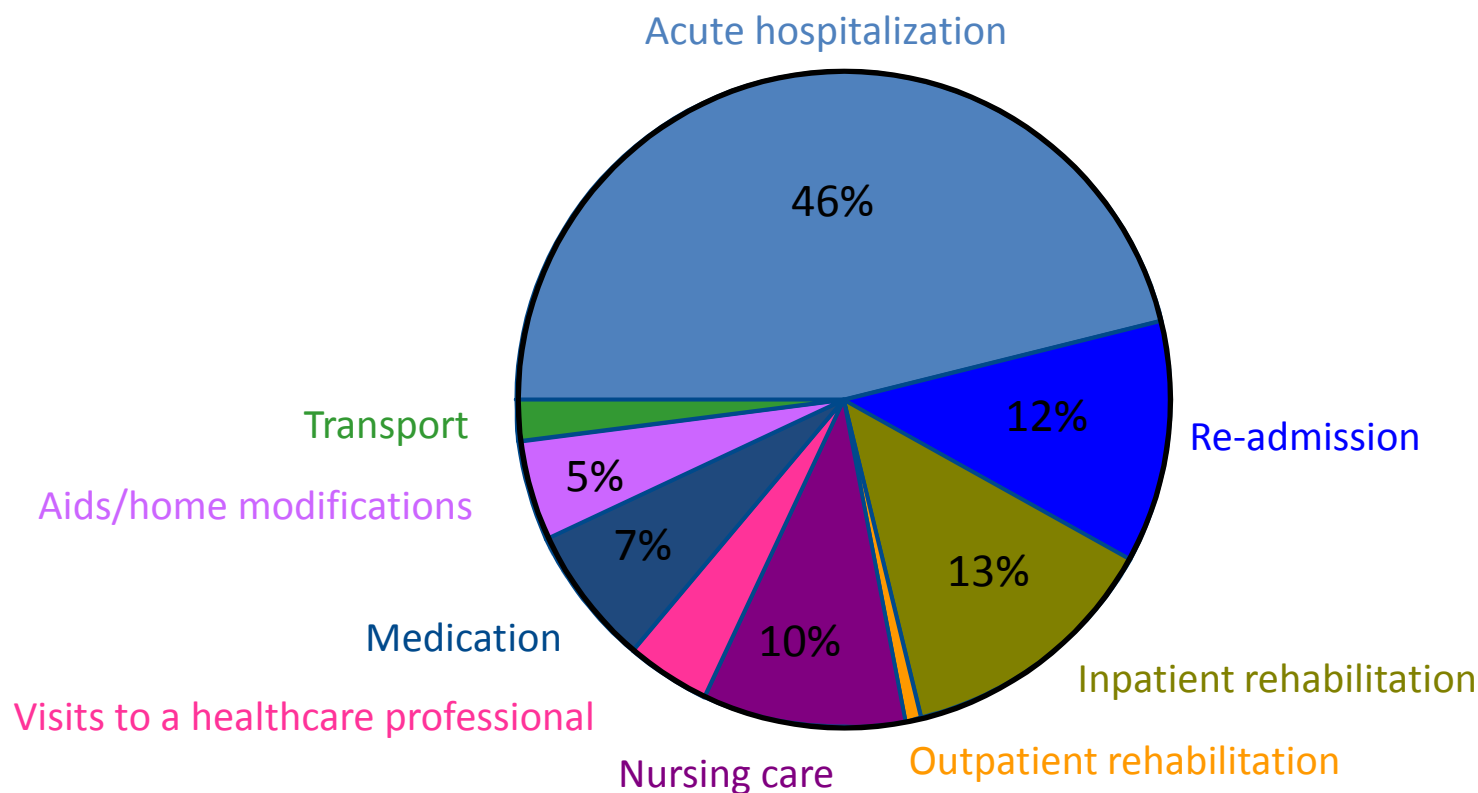


>40-year follow-up of 5070 participants in the Framingham study; \*Barthel Index

Lin HJ et al. Stroke 1996;27:1760-4

# Acute hospitalization accounts for the bulk of AF stroke-related costs

Direct cost components up to 1-year post stroke (% of total direct costs)\*



\*Data analysed as part of the Berlin Acute Stroke Study

Bruggenjurgen B et al. Value Health 2007;10:137-43