



# Atrial Fibrillation

News and Views

Hamid Ikram

# Why is AF important?

## 1 of 3 modern CVS Epidemics

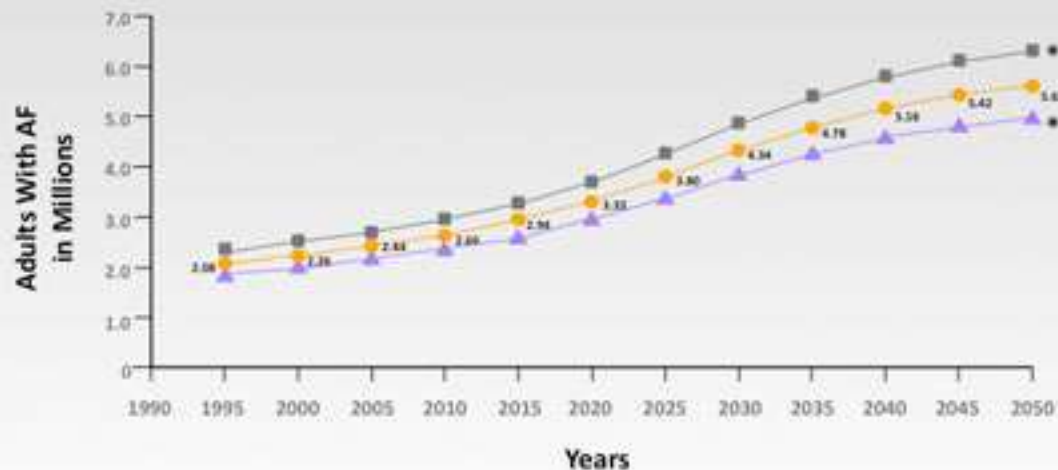
◆ HYPERTENSION

◆ HEART FAILURE

◆ ATRIAL FIBRILLATION

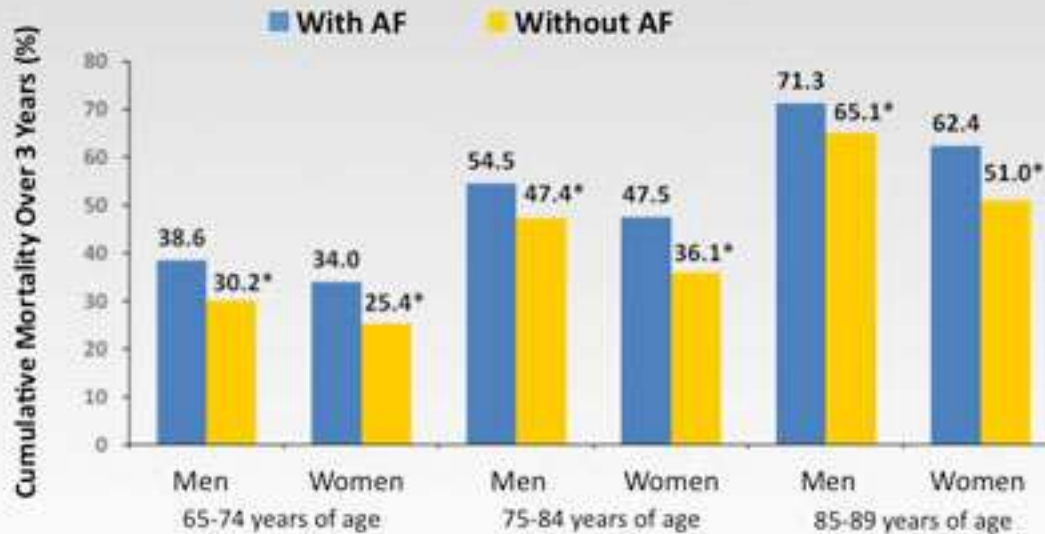
# AF Epidemic: 5.6 Million With AF by 2050

Projected Number of Adults With AF  
in the United States 1995-2050



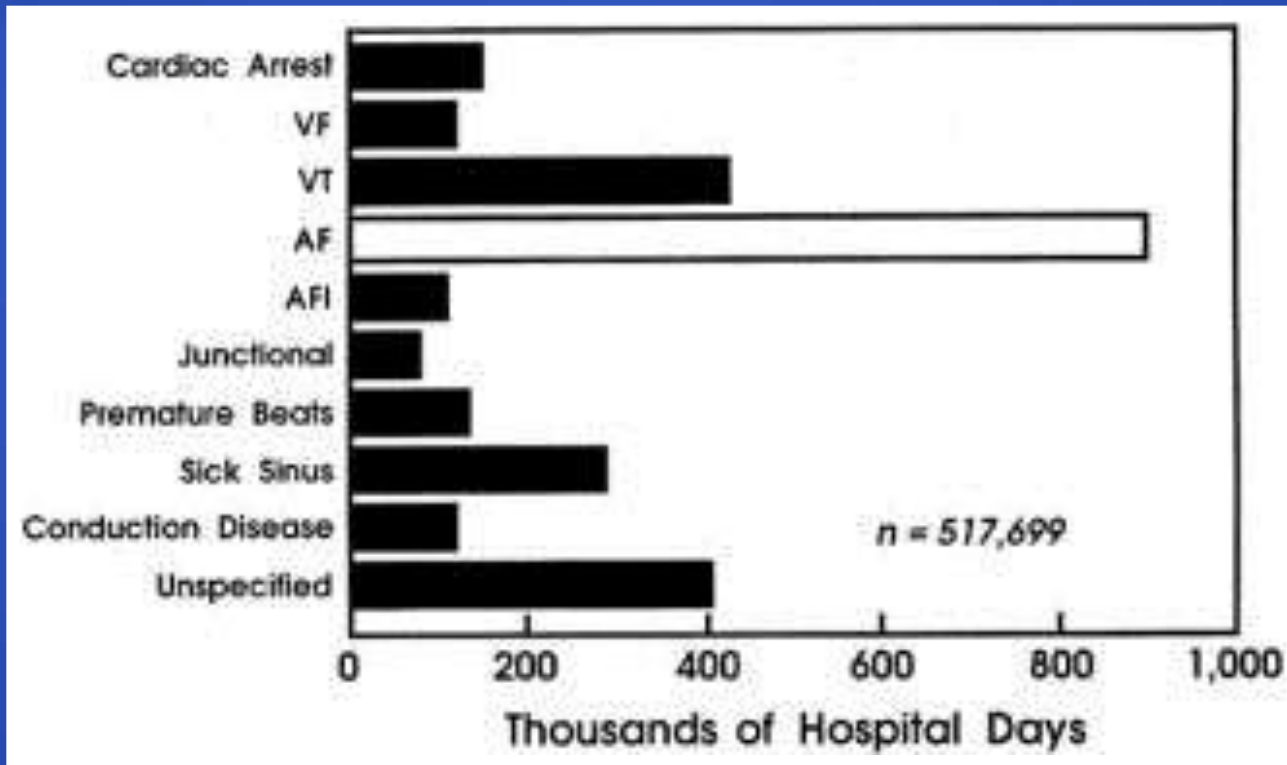
\*Upper and lower curves represent the upper and lower scenarios based on sensitivity analyses.

## AF Is Associated With Increased Mortality



\*Significantly different from patients with AF ( $P < .05$ ).

# Many Hospital Days = \$\$\$\$\$\$.



# # 1 of Obama Administration's Goals in Comparative Effectiveness Research

ENLARGE

THUMBNAILS

## 100 Initial Priority Topics for Comparative Effectiveness Research

**#1 - Compare the effectiveness of treatment strategies for AF including surgery, catheter ablation, and pharmacologic treatment.**



# Causes, Consequences and Natural History

**Table 1.2 Common cardiac and non-cardiac causes of AF**

**Cardiac causes of AF**

*Common cardiac causes:*

ischaemic heart disease  
rheumatic heart disease  
hypertension  
sick sinus syndrome  
pre-excitation syndromes  
(eg Wolff–Parkinson–White).

*Less common cardiac causes:*

cardiomyopathy or heart muscle disease  
pericardial disease (including effusion and  
constrictive pericarditis)  
atrial septal defect  
atrial myxoma.

**Non-cardiac causes of AF**

Acute infections, especially pneumonia

Electrolyte depletion

Lung carcinoma

Other intrathoracic pathology (eg pleural effusion)

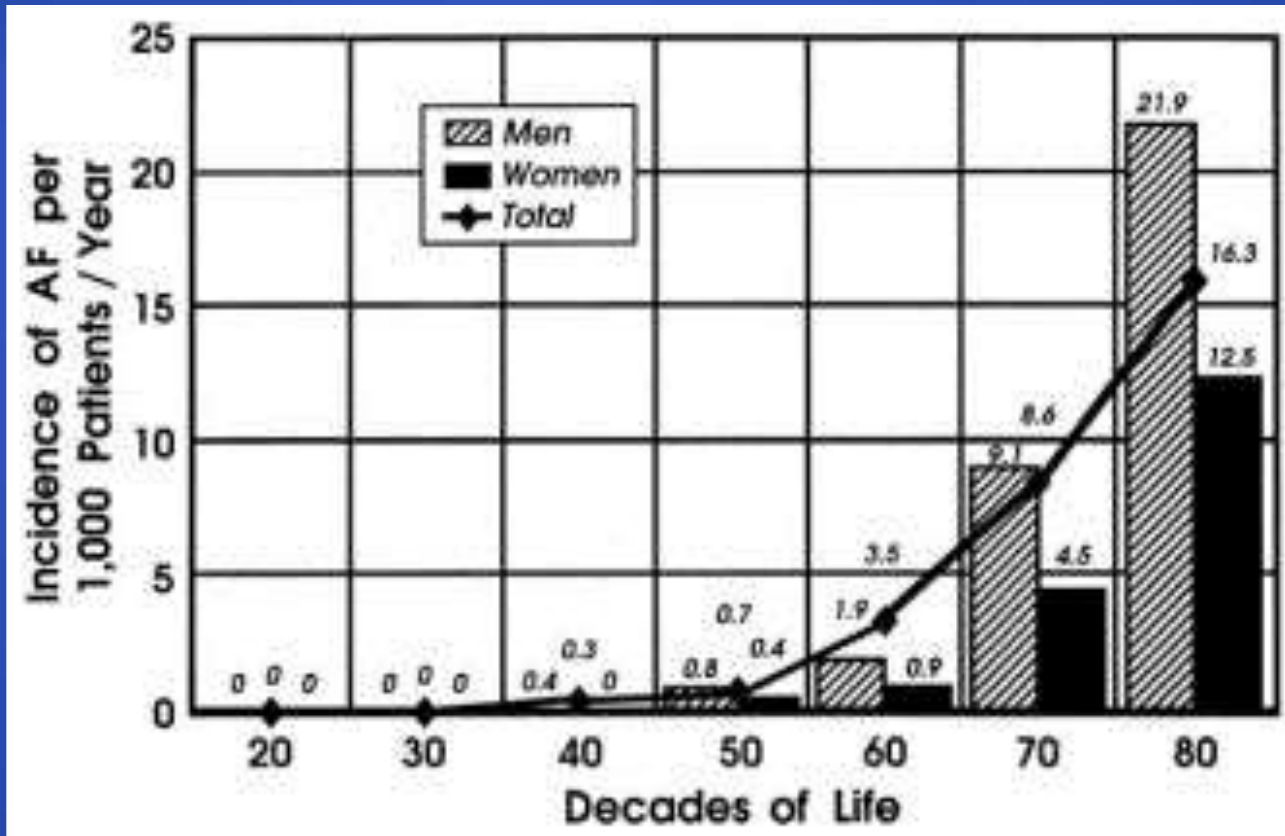
Pulmonary embolism

Thyrotoxicosis

- SSS ie Ageing
- Obesity
- Alcohol and Drugs- therapeutic esp AAD and of course the others



## Incidence increases with age



# The Problems of AF

## Consequences of AF

### Hospitalizations:

- Most common arrhythmia requiring hospitalization
- 2-3x ↑ risk for hospitalization

### Thromboembolism:

- Stroke: 4.5x ↑ risk
- Microemboli: reduced cognitive function
- Prothrombotic state

### Reduced QoL:

- Palpitations, dyspnea, fatigue, ↓ exercise tolerance

### Mortality:

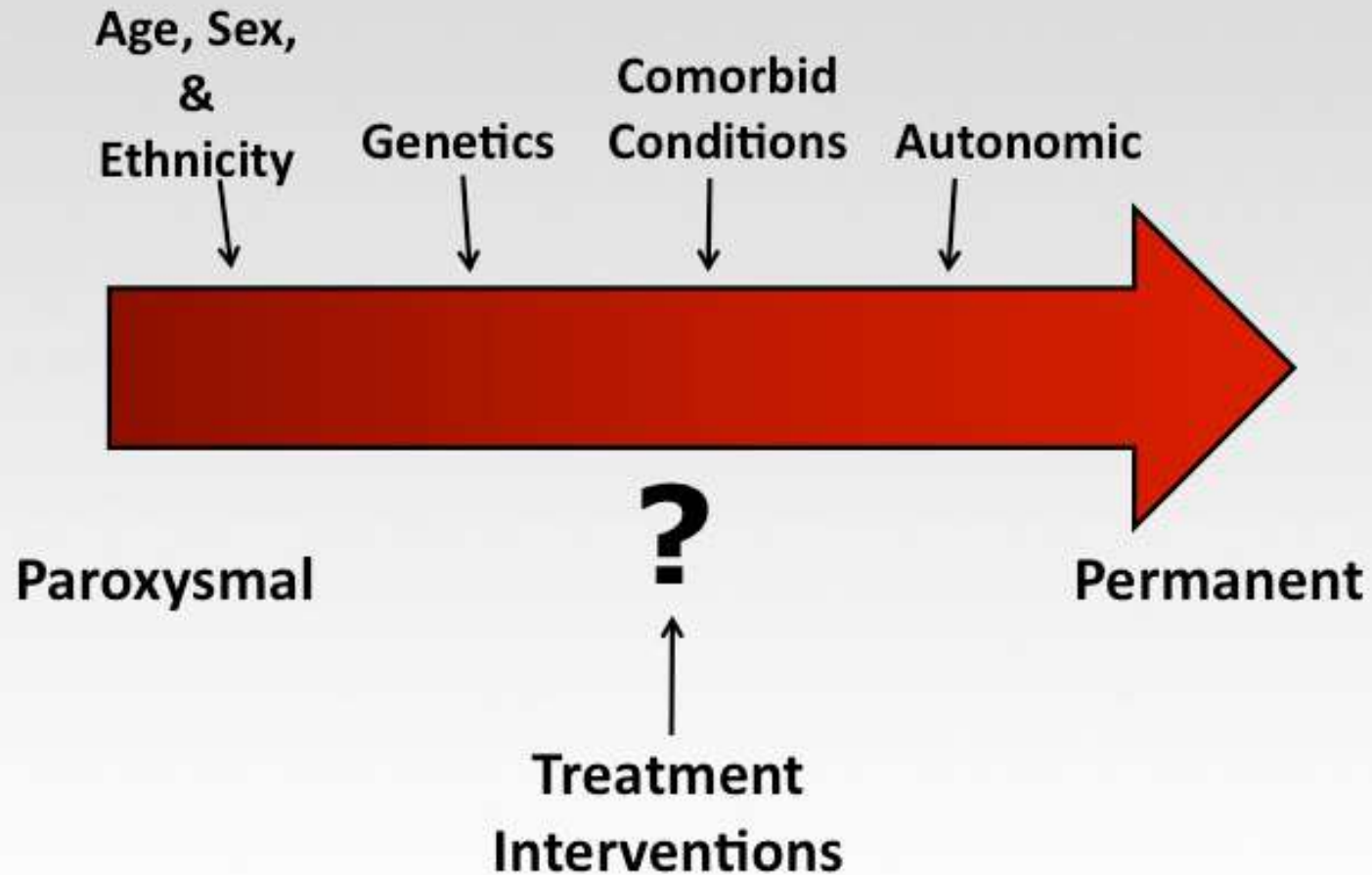
- 2x risk independent of comorbid CV disease
- Sudden death in heart failure and HCM

### Impaired Hemodynamics:

- Loss of atrial kick
- Irregular ventricular contractions
- Heart failure
- Tachycardia-induced cardiomyopathy

# Natural History of AF

## Progression of AF



It is a progressive disorder

# Management Strategies

Rate or Rhythm ?

# Rate vs Rhythm Control

## Sinus Rhythm Strategy:

### Who Are Appropriate Candidates?

- Highly symptomatic with AF
- First episode
- Reversible cause
- Young age
- Symptomatic despite rate control
- Rate-related cardiomyopathy
- LV dysfunction/CHF
- Diastolic dysfunction with symptoms
- HCM or aortic stenosis
- Prior embolic stroke or TIA

# Rate vs Rhythm Control

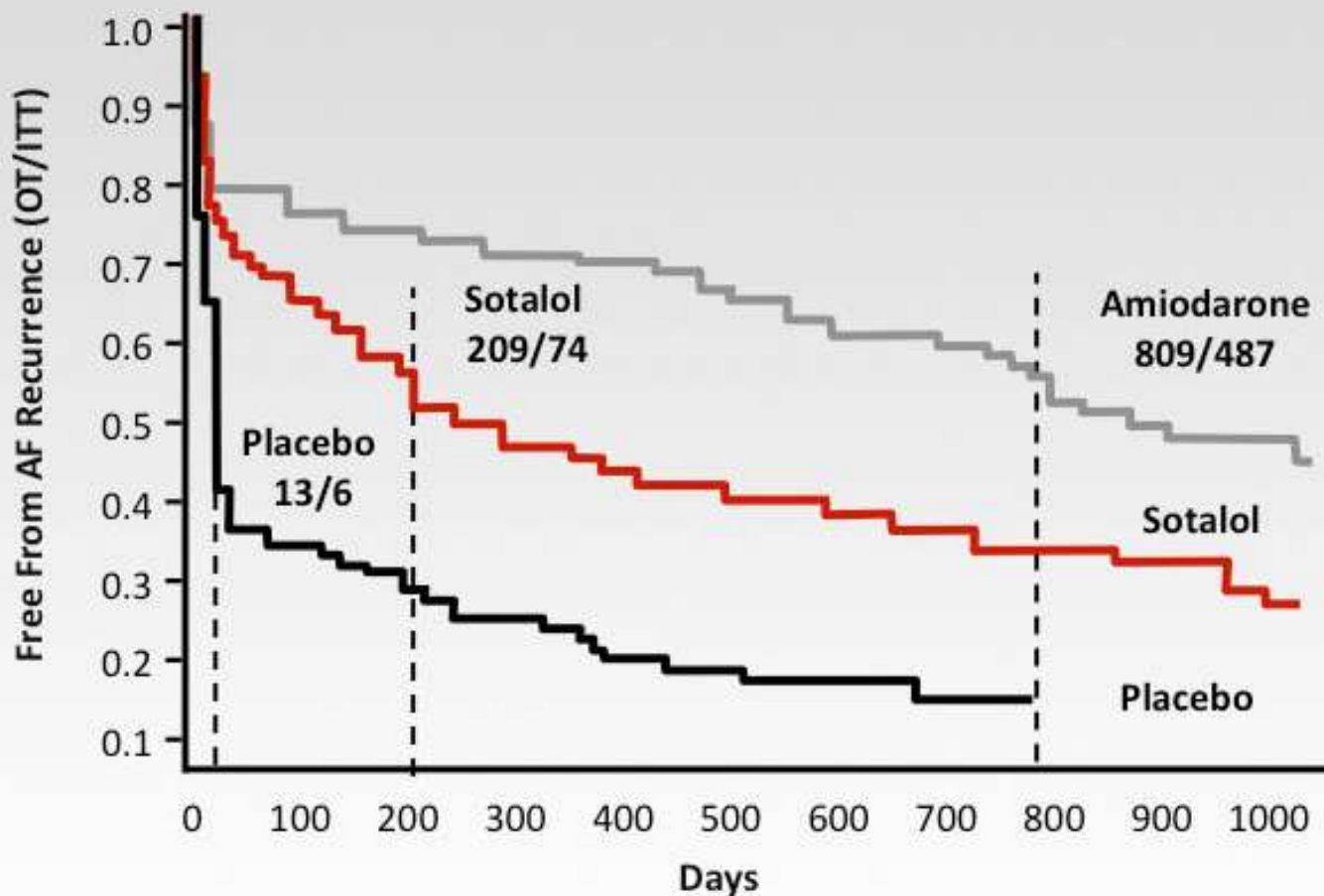
## Strategies for Restoring and Maintaining Normal Sinus Rhythm

- Electrical or pharmacologic cardioversion
- Treatment of reversible causes
- AAD therapy: *Beware of 'Proarrhythmia'*
  - Intermittent
  - Continuous "Pill in Pocket"
- Catheter ablation:
  - PVI (paroxysmal)
  - PVI + substrate modification (persistent)
- Surgical ablation

Pros and Cons of each

# AAD for SR Maintenance

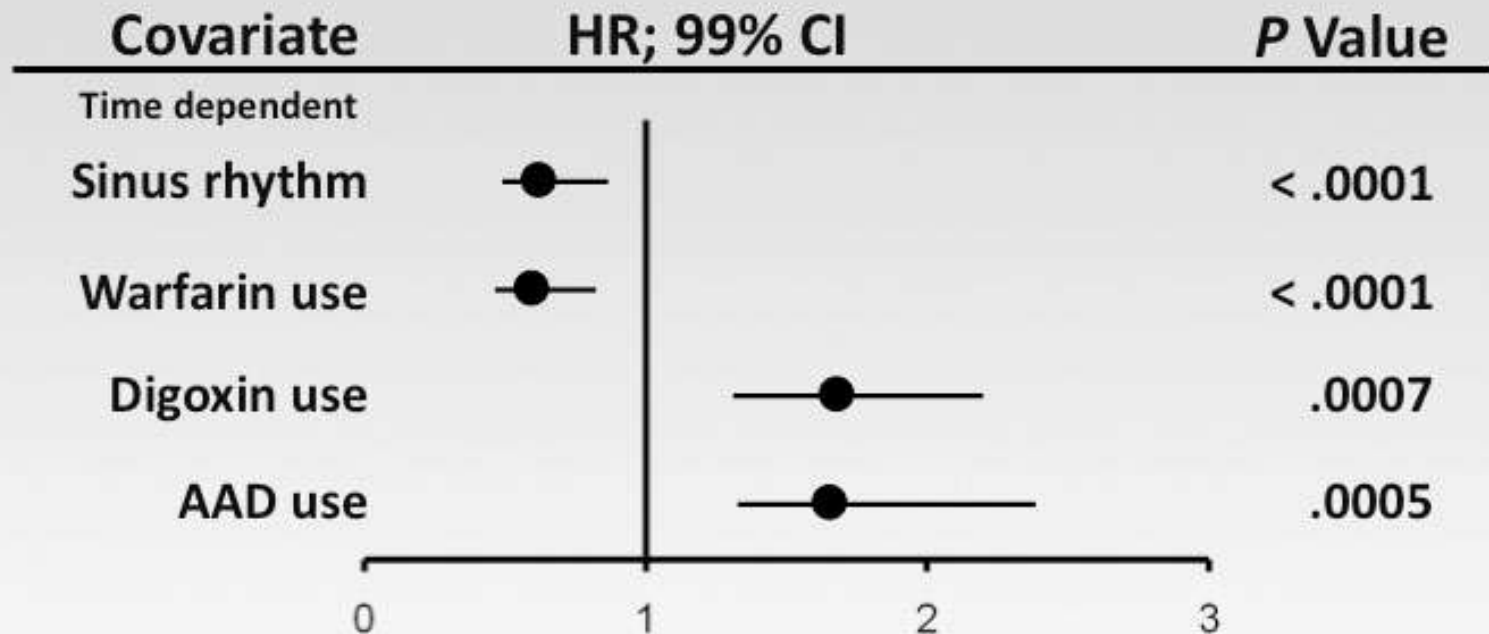
## SAFE-T: Sotalol vs Amiodarone





# Drugs are Dangerous

## AFFIRM: Independent Predictors of Survival



The risks of AADs counterbalance the benefits of sinus rhythm.



# Rate vs Rhythm Control

*Conclusions* Rate control is not inferior to rhythm control for the prevention of death and morbidity from cardiovascular causes and may be appropriate therapy in patients with a recurrence of persistent atrial fibrillation after electrical cardioversion. (N Engl J Med 2002;347:1834-40.)

## The RACE Trial

**DREAM ON!**

## New Pharmacologic Agents for AF

- Multi-ion channel blockers:
  - Dronedarone
  - Budiodarone
- Atrial-selective AADs:
  - $I_{Kur}^-$ ,  $I_{to}$  and  $I_{KACh}^-$  blocker
  - Atrial-selective Na channel blocker
  - Histamine (5-HT<sub>4</sub>) receptor antagonist
- Other ion channel blockers
- Other mechanisms
- Upstream therapies:
  - Statins
  - ACEI/ARB
  - Omega-3 fatty acids
  - Anti-inflammatory drugs

# Intermittent AF

## What Is the Measure of Successful Treatment of AF?

- As with heart failure or angina, success in managing AF is defined as a decrease in:

Frequency  
of  
episodes

Duration  
of  
episodes

Symptoms  
during  
episodes

- Recurrence of AF is not ipso facto drug failure
- AAD efficacy should not be measured simply by time to first recurrence of AF
- Occasional recurrence of AF may be acceptable

# The big issue-AF and Stroke

- ❑ Patients with sustained non-rheumatic AF have 5-7 times the risk of stroke than the GP
- ❑ The risk of stroke and non- CNS embolism are similar in sustained and intermittent AF

# Stroke Risk in Intermittent AF

## CONCLUSIONS

In this large cohort of AF patients given aspirin, those with intermittent AF had stroke rates similar to patients with sustained AF and similar stroke risk factors. Many elderly patients with recurrent intermittent AF have substantial rates of stroke and likely benefit from anticoagulation. High-risk patients with intermittent AF can be identified using the same clinical criteria that apply to patients with sustained AF.

# CHADS<sub>2</sub> Score and Stroke

Annual Stroke Risk

CHADS <sub>2</sub> Score	Stroke Risk %	95% CI
0	1.9	1.2–3.0
1	2.8	2.0–3.8
2	4.0	3.1–5.1
3	5.9	4.6–7.3
4	8.5	6.3–11.1
5	12.5	8.2–17.5
6	18.2	10.5–27.4

*C= CHF*

*H= Hypertension*

*A= Age > 75*

*D= Diabetes*

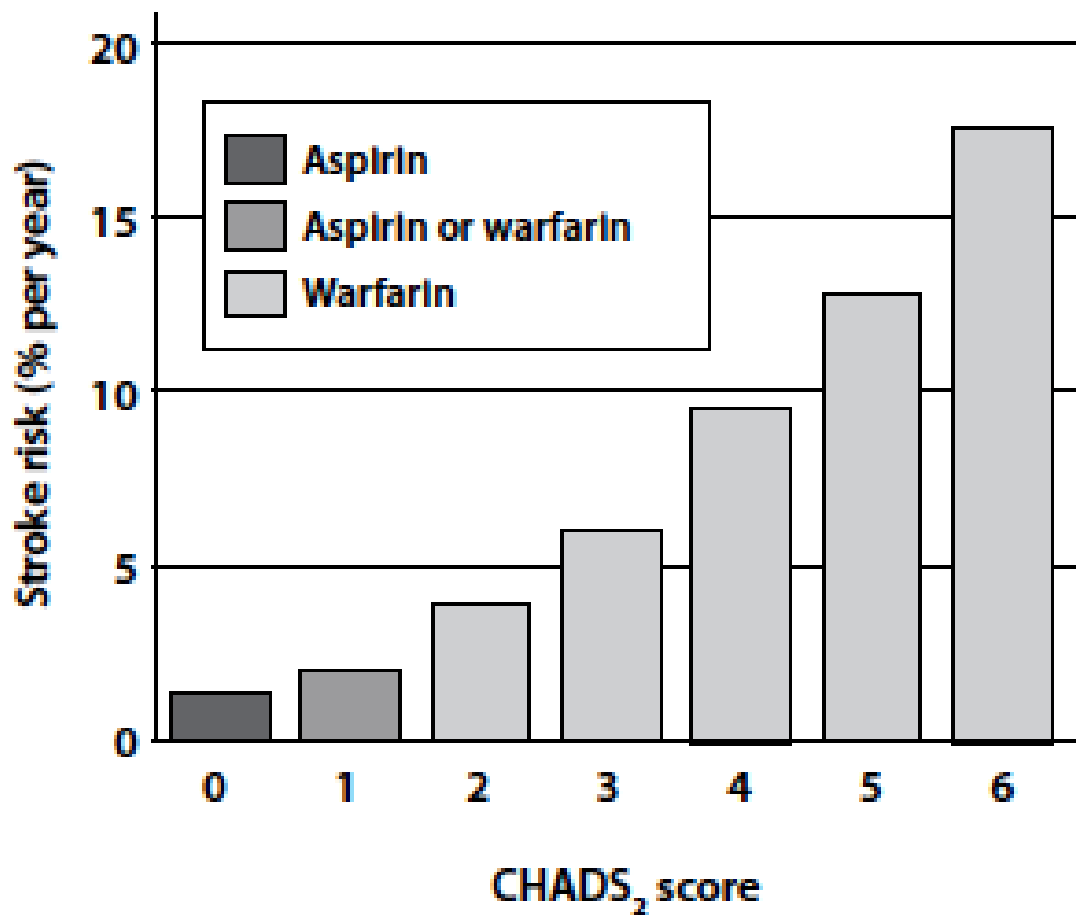
*S= Prior Stroke- 2 points*

## Stroke risk in patients with nonvalvular AF not treated with anticoagulation according to the CHADS<sub>2</sub> index

- CHADS<sub>2</sub> risk criteria and scoring
  - Prior stroke or TIA 2 points
  - Age > 75 years 1 point
  - Hypertension 1 point
  - Diabetes mellitus 1 point
  - Heart failure 1 point

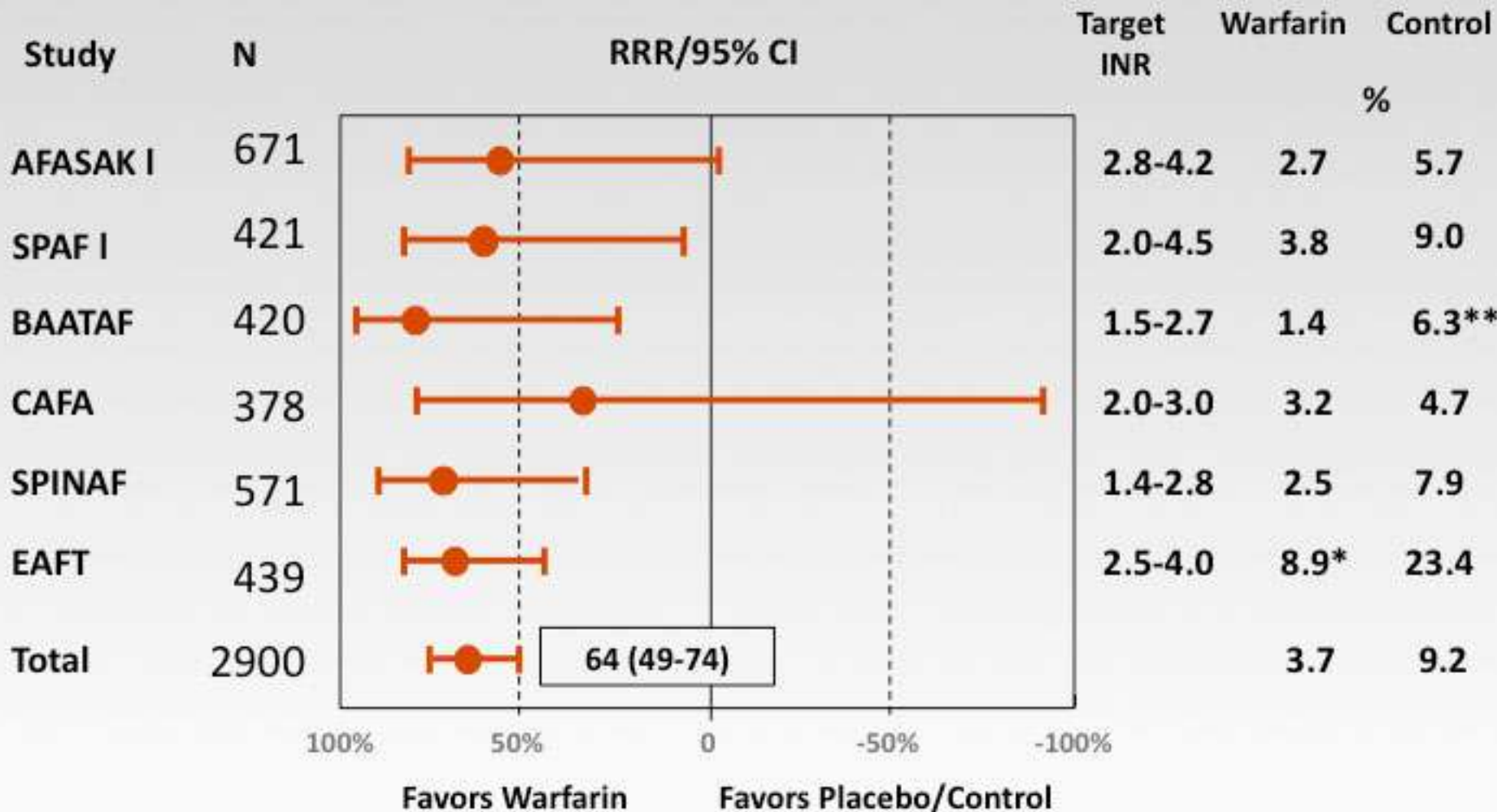
Patients (n = 1733)	Adjusted stroke rate (%/year)* (95% CI)	CHADS <sub>2</sub> score
120	1.9 (1.2–3.0)	0
463	2.8 (2.0–3.8)	1
523	4.0 (3.1–5.1)	2
337	5.9 (4.6–7.3)	3
220	8.5 (6.3–11.1)	4
65	12.5 (8.2–17.5)	5
5	18.2 (10.5–27.4)	6

# ASA OR WARFARIN





# Stroke: Adjusted-Dose Warfarin vs Placebo/Control



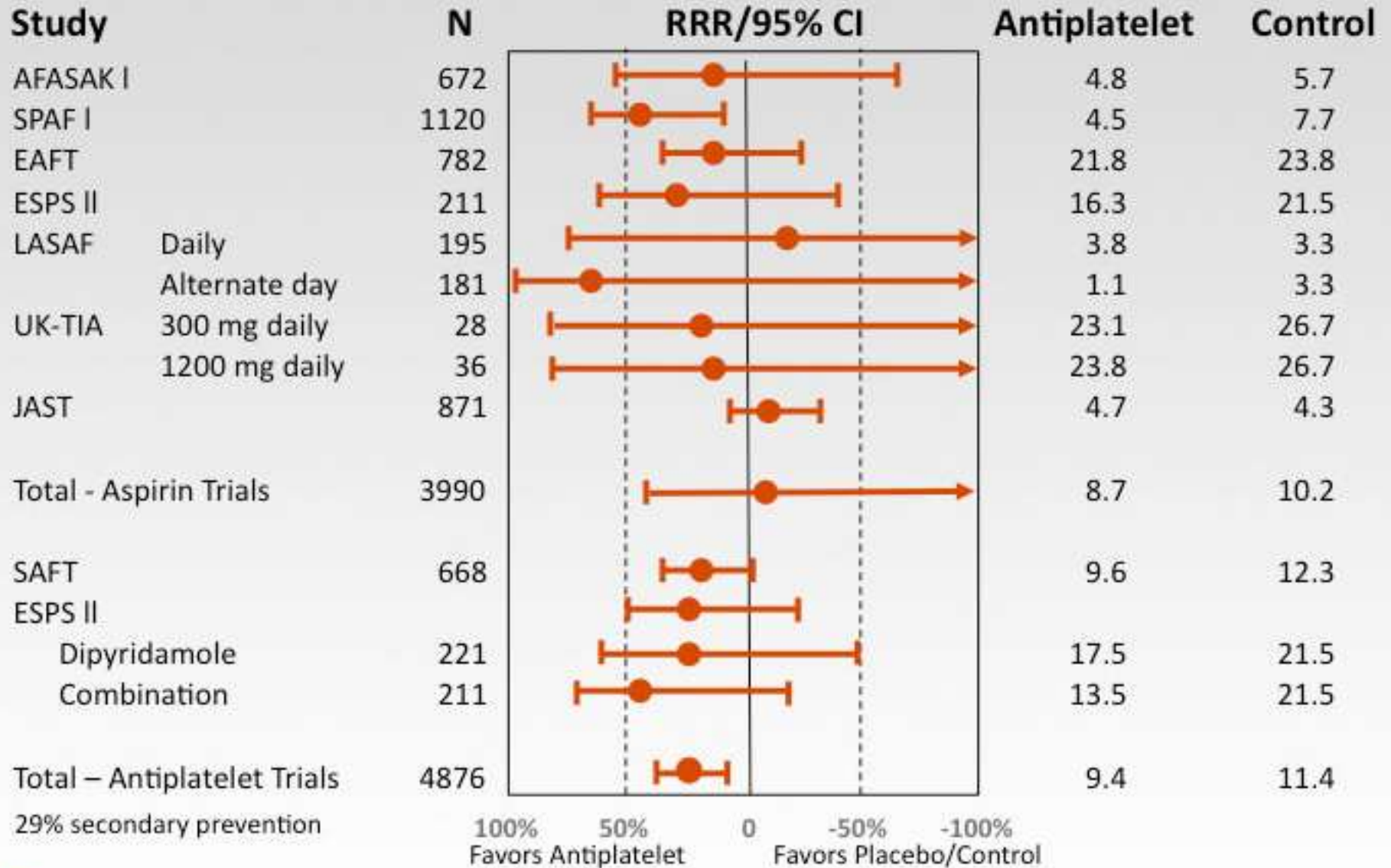
\*Several oral vitamin K antagonists used

\*\*46% of exposure ASA in control group

Reproduced with permission from:

Hart RG, et al. *Ann Intern Med.* 2007;146:857-867.

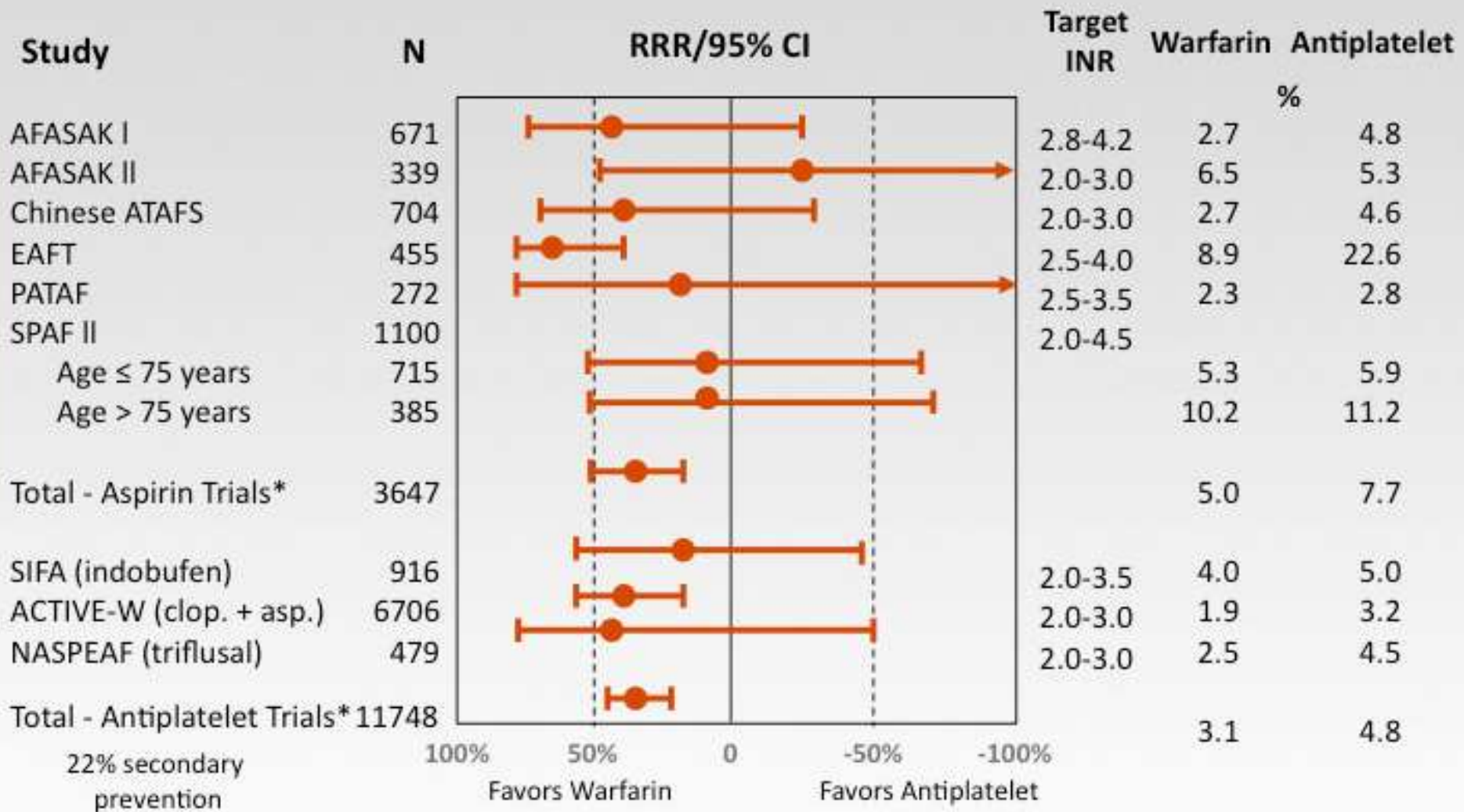
# Stroke: Antiplatelet Agents vs Placebo/Control



Reproduced with permission from:

Hart RG, et al. *Ann Intern Med.* 2007;146:857-867.

# Stroke: Adjusted-Dose Warfarin vs Antiplatelet Rx



\*Includes 2 small trials (n = 106) with only 2 strokes; does not include SPAF III (n = 1044) and part of AFASAK II (n = 341) where antiplatelet groups also received warfarin



**POISON NOT TO BE TAKEN**

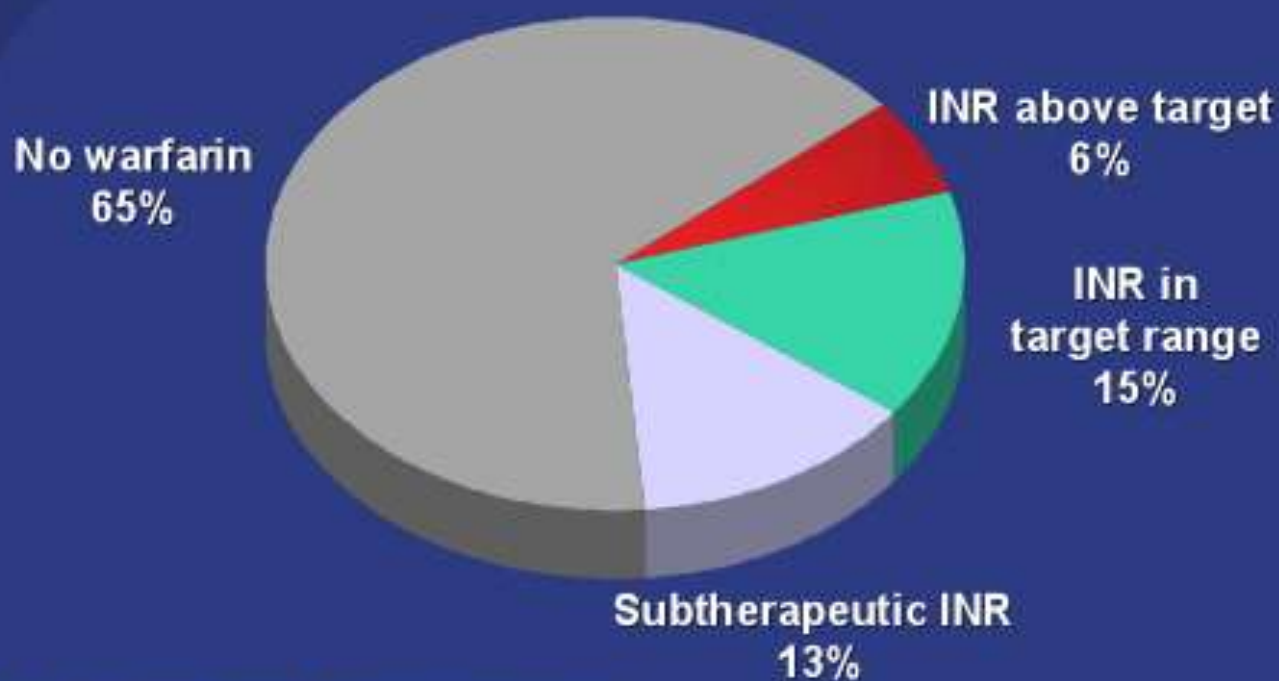


**Who is afraid of big bad Warfarin ?**

# Warfarin for Atrial Fibrillation

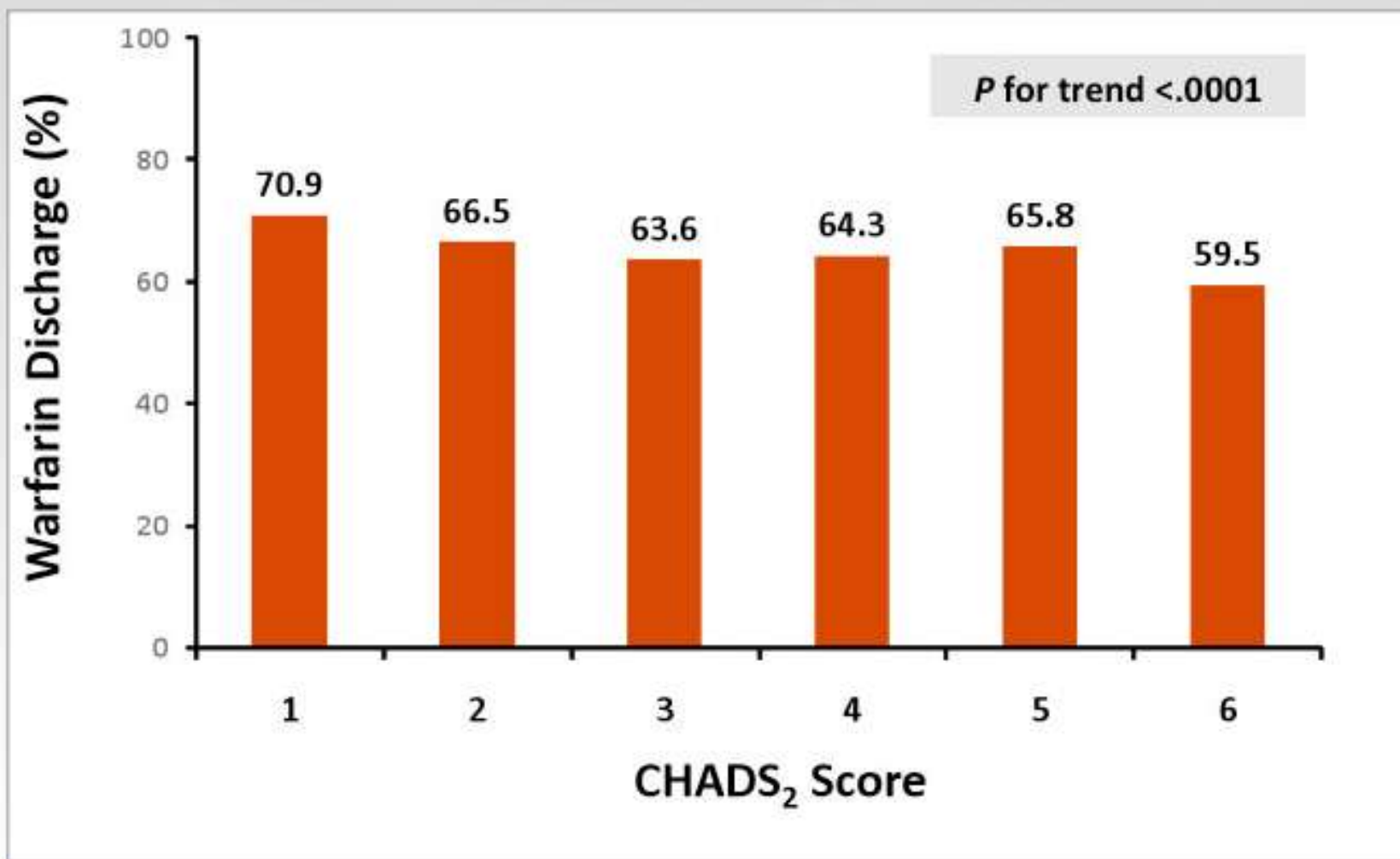
## Limitations Lead to Inadequate Treatment

*Adequacy of Anticoagulation in  
Patients with AF in Primary Care Practice*

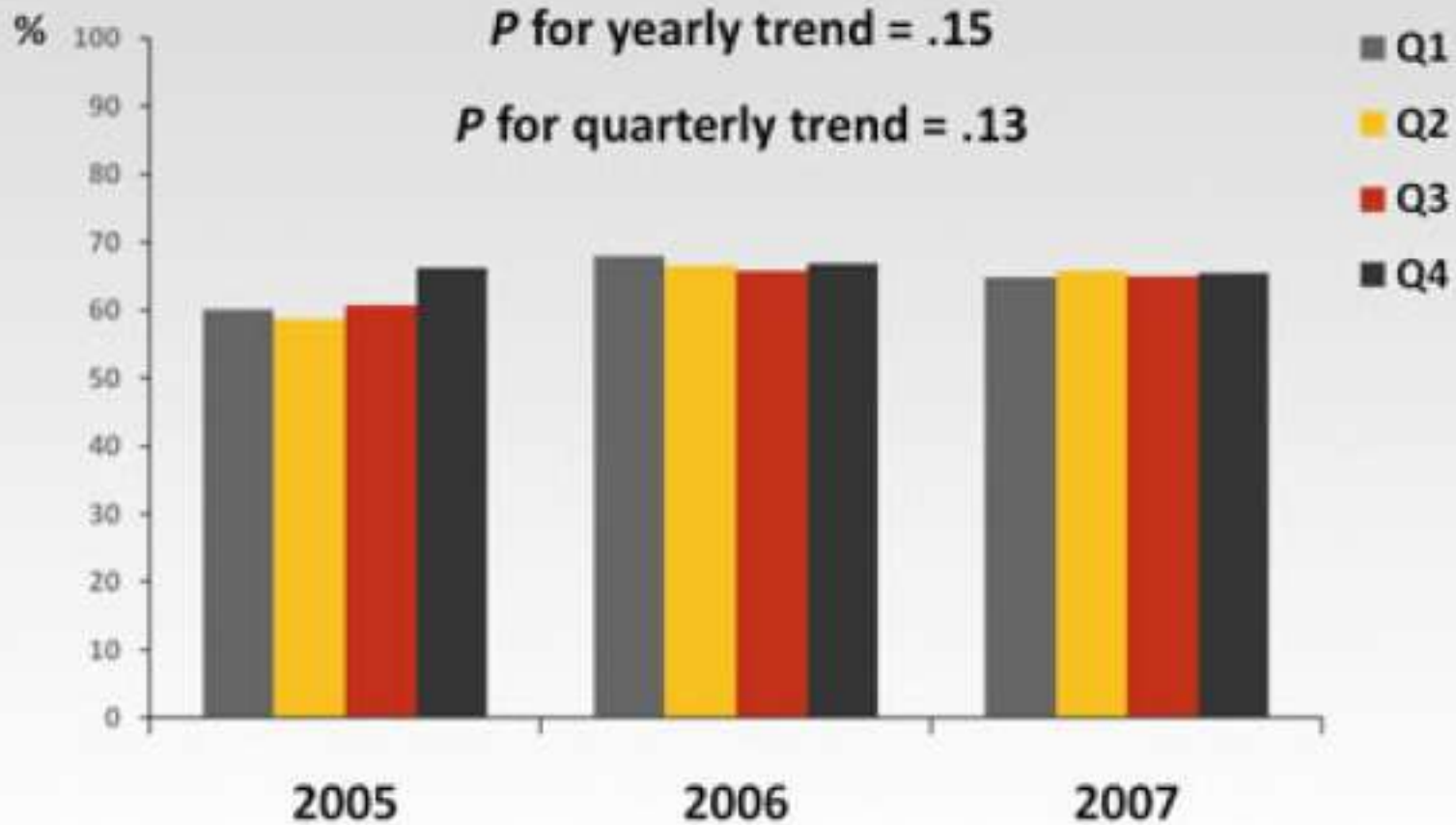


Samsa GP, et al. *Arch Intern Med* 2000;160:967.

# Warfarin Use According to CHADS<sub>2</sub> Scores

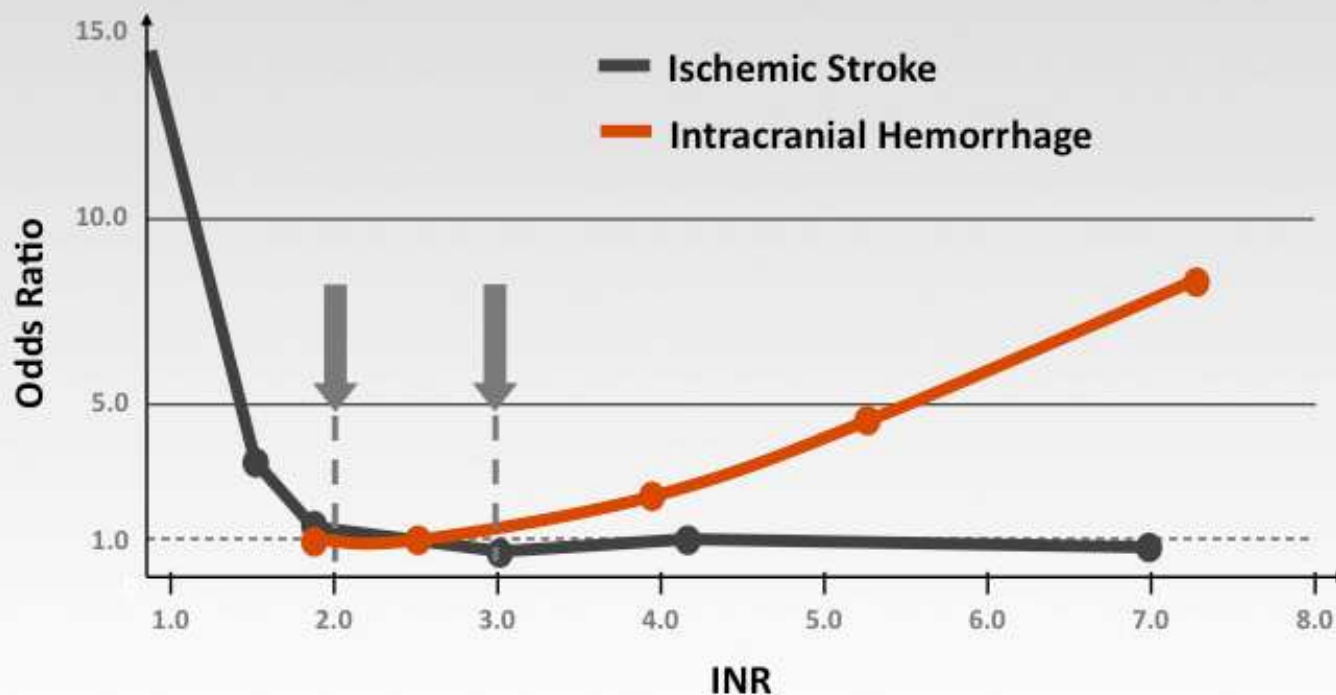


# Warfarin Use Over Time



# The 'J-curve' of Warfarin Therapy

## Optimal INR for Prevention of Stroke and ICH in Relation to Anticoagulation Intensity



Fuster V, et al. *Circulation*. 2006;114:e257-e354.

Adapted from Hylek EM. *Arch Intern Med*. 1994;120:897-902.

Odén A, et al. *Thromb Res*. 2006;117:493-499.



### **Contraindications to warfarin use include:**

- Haemorrhagic tendencies and blood dyscrasias
- Past history of intracranial haemorrhage
- Recent history of GI or GU bleeding (previous six months)
- Uncontrolled hypertension
- Severe liver disease
- Alcoholism
- Recurrent unexplained syncope
- Planned surgery
- Pregnancy

## AHA Performance Measure AF:

- Assessment of thrombotic risk
- Chronic anticoagulation
- Monthly INR measurements

## Other aspects to consider when prescribing warfarin include:

- Comorbidities
- Concomitant use of medications
- Poor compliance with medication and monitoring (e.g. cognitive impairment, confusion, mental illness, inability to access services)
- Activities that increase the risk of trauma
- Increased risk of bleeding in elderly people
- Potential for falls
- Changes in diet, supplement use and general wellbeing (e.g. new illness)

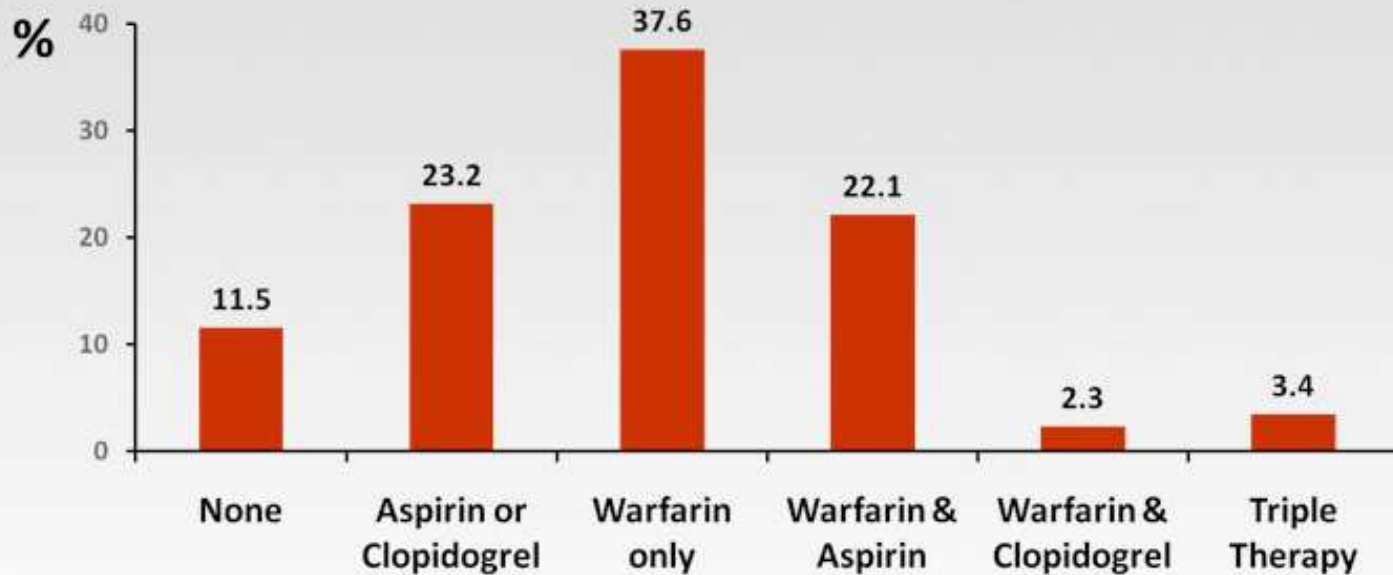
# Important Messages

Warfarin Reduces Risk of Stroke by 68%

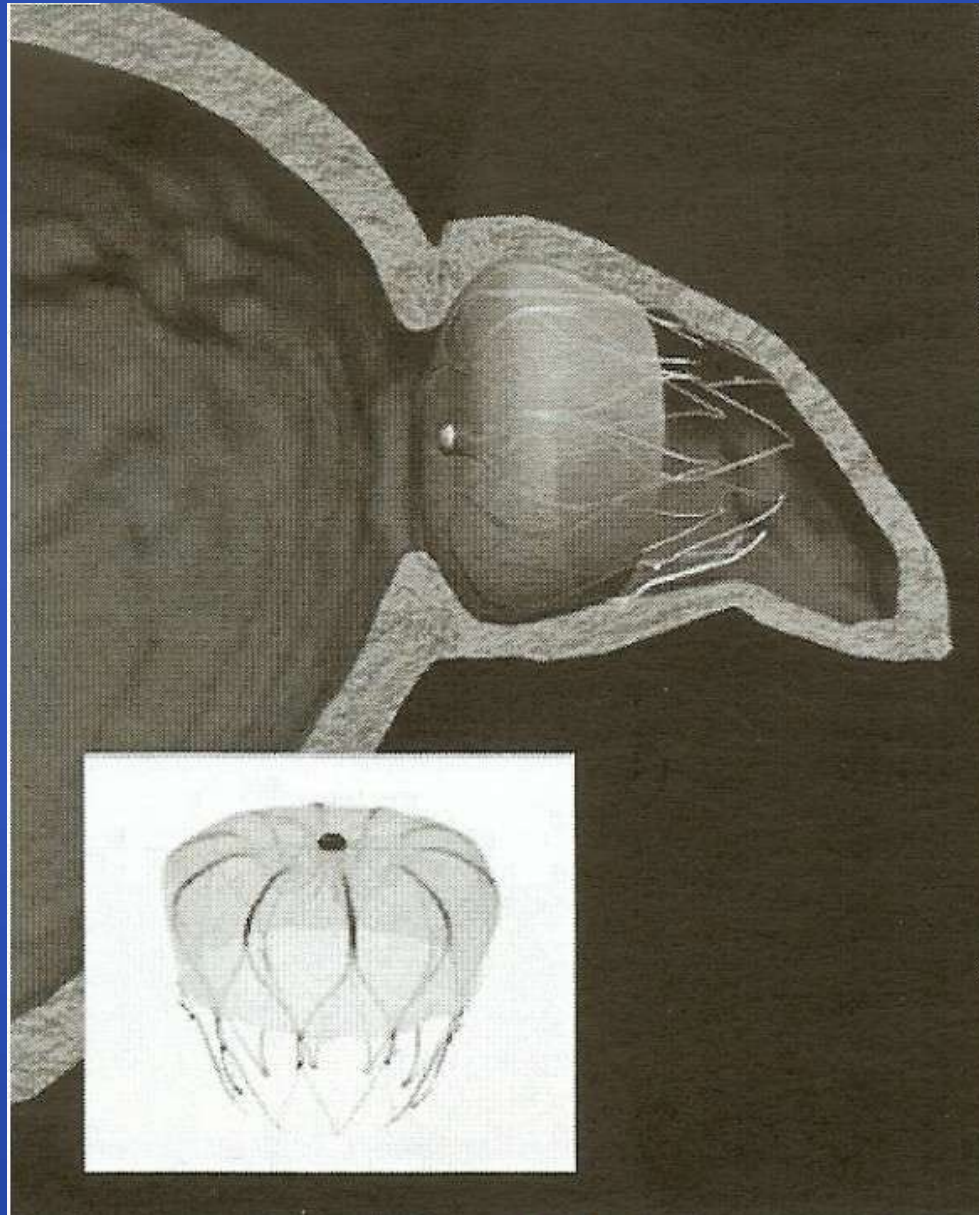
Asprin Reduces Risk of Stroke by 44% (325 mg/ daily)

# Combined ASA/Warfarin Saga

## Discharge Antithrombotic Therapy



# "Watchman"



# Your Take Home Message

- One of the 'Big 3 CVS Epidemics'
- Main causes today are CAD, Hypertension, Ageing [SN Disease], Obesity
- Independent cause of increased mortality
- High morbidity
- Rate control as good as rhythm control for QoL and Survival
- Adequate anticoagulation remains a challenge-CHADS score
- Dangers of Warfarin overstated
- New Therapies on the way- BUT long journey to NZ

# Results

	AF on admission (n = 14,901)	History of AF only (n = 9918)	No AF (n = 47,715)
Age, median	79	79	72
Women	49	49	50
White	82	81	64
LVEF < 40%	40	42	48
Stroke or TIA	16	16	12
Renal insufficiency	18	21	19
ICD	11	11	9
BNP, median	755	760	928



# CHADS score and AC

## Recommendations for anticoagulation

The following treatment strategies were recommended:<sup>[1][2]</sup>

Score	Risk	Anticoagulation Therapy	Considerations
0	Low	Aspirin	Aspirin daily
1	Moderate	Aspirin or Warfarin	Aspirin daily or raise INR to 2.0-3.0, depending on factors such as patient preference
2 or greater	Moderate or High	Warfarin	Raise INR to 2.0-3.0, unless contraindicated (e.g. clinically significant GI bleeding, inability to obtain regular INR screening)