

**Westcliffe Medical Practice**  
ShIPLEY

Westcliffe Cardiology Service

# Under 60 With Atrial Fibrillation: Options and Access

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GPwSI Cardiology

# Conflicts of interest

## Speaker fees, Honorarium and grants

Boehringer Ingelheim

Sanofi Aventis

Bayer

Pfizer

Spacelabs

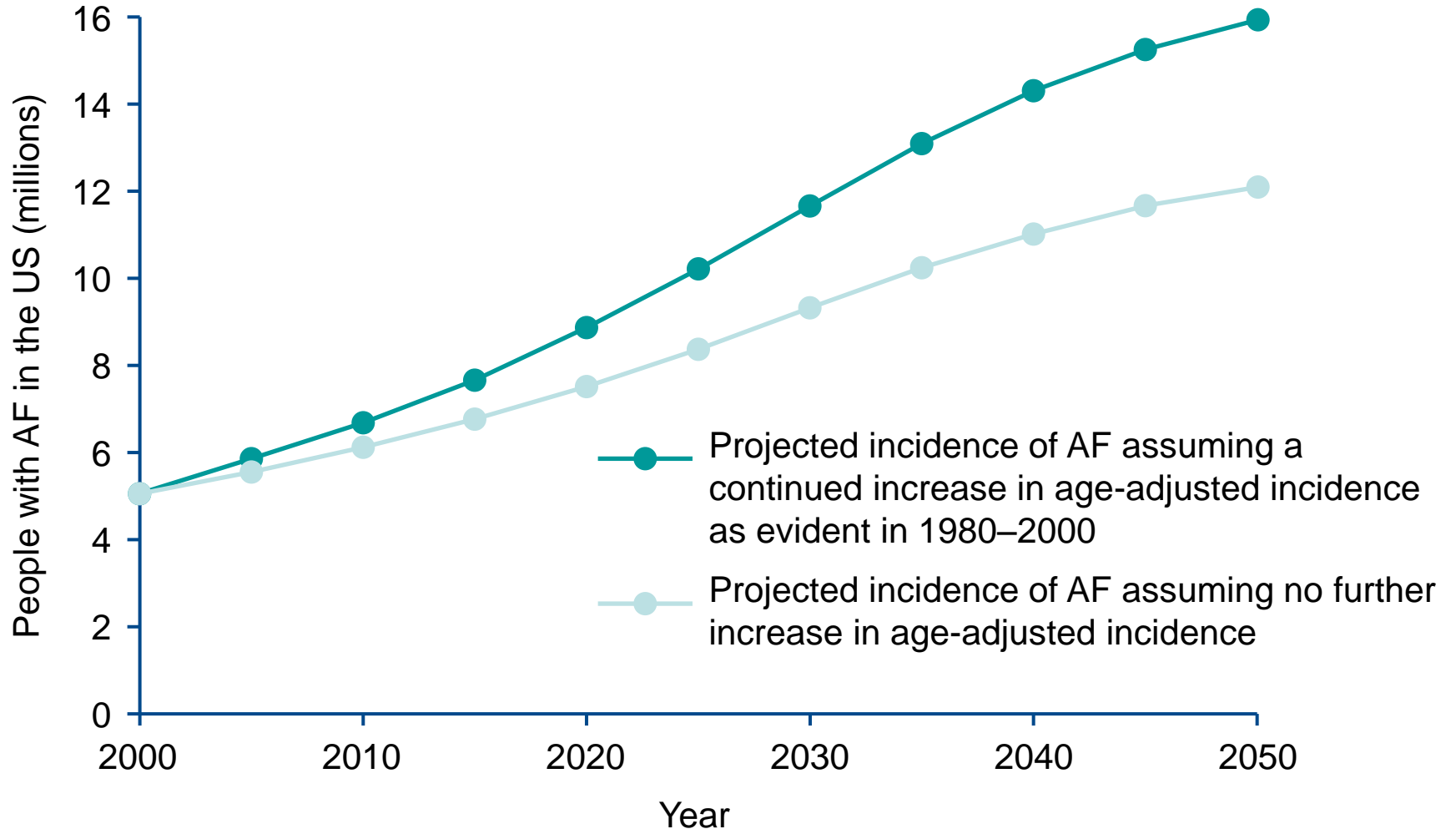
# Atrial Fibrillation

- First described by Sir William Harvey in 17th century:
  - observed chaotic motion of atria in open chest animal
- ECG findings described in 1909 by Sir Thomas Lewis:
  - “irregular or fibrillatory waves and irregular ventricular response” or “absent atrial activity with grossly irregular ventricular response”

# AF is a common disorder

- AF is the most common heart arrhythmia, with a prevalence of approximately 1.2% in primary care in the UK<sup>1</sup>
- Estimated numbers affected by AF:
  - England: 600,000<sup>1</sup>
  - Europe: 4.5 million<sup>2</sup>
  - USA: 5.1 million<sup>3</sup>
- Nearly one in four people at age 55 years will go on to develop AF (24% of men and 22% of women)<sup>4</sup>

## Prevalence of AF predicted to more than double by 2050



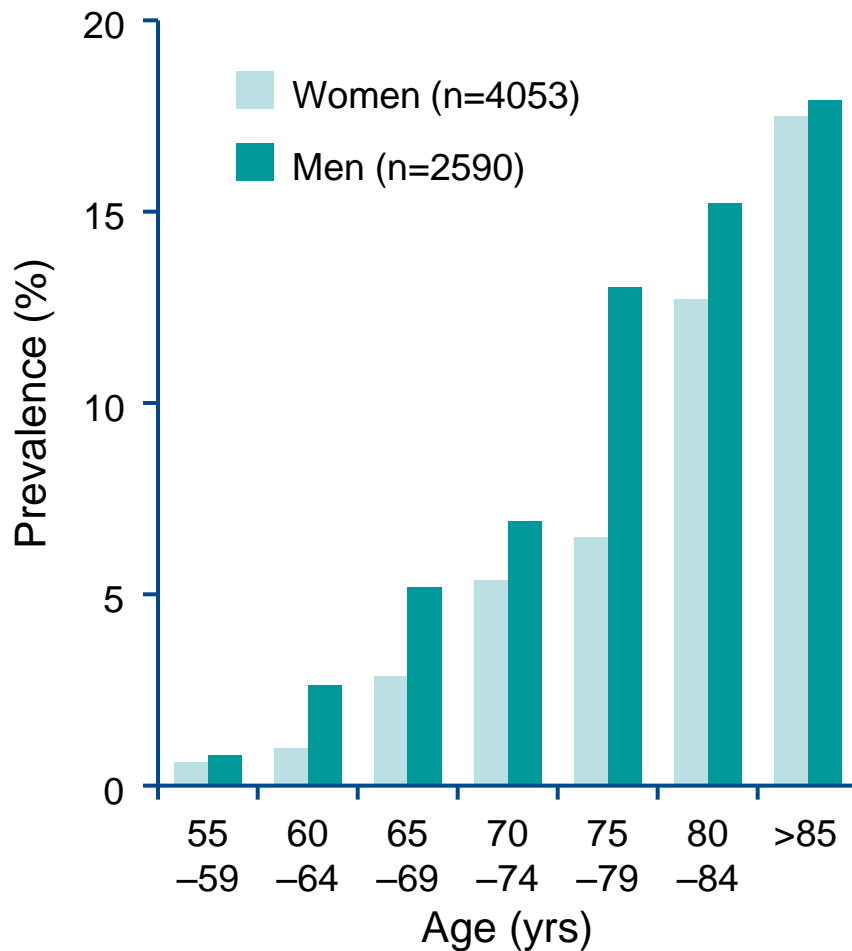
# Incidence and Prevalence of Atrial Fibrillation

Age (Yrs)	Manitoba F/U Study		Framingham	
	Prevalence	Incidence	Prevalence	Incidence
20	0	0	-	-
30	0	0	-	-
40	1.1	0.3	0.4	0
50	5.1	0.7	0.8	0.4
60	18.0	3.5	1.9	0.9
70	54.4	8.6	9.1	4.5
80	92.7	16.3	21.9	12.5
90	105	-	-	-

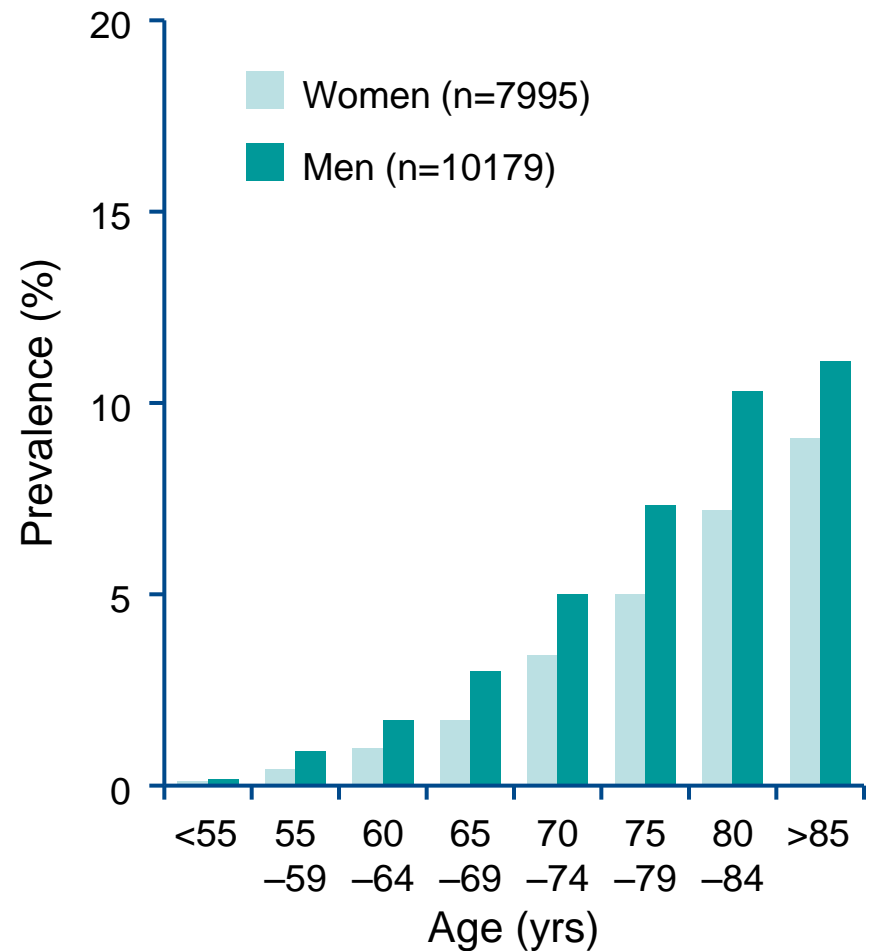
Incidence per 100,000 patient years. Prevalence per 1000,000 patients

## Prevalence of AF increases with age

**European age-related prevalence<sup>1</sup>**



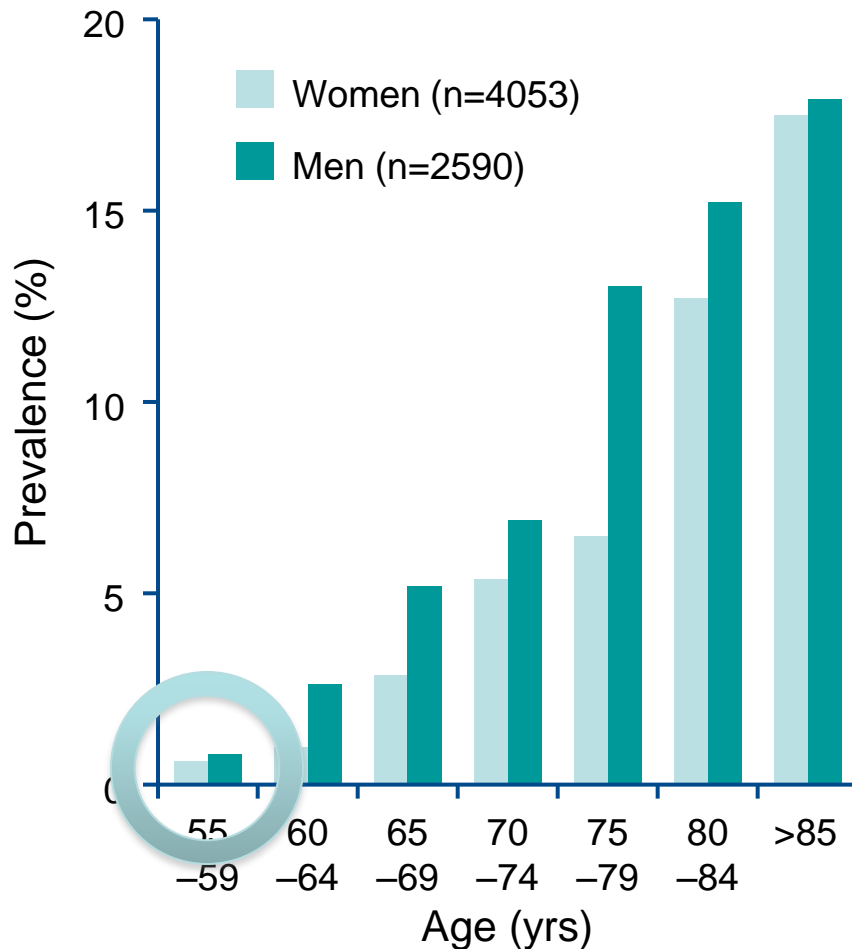
**US age-related prevalence<sup>2</sup>**



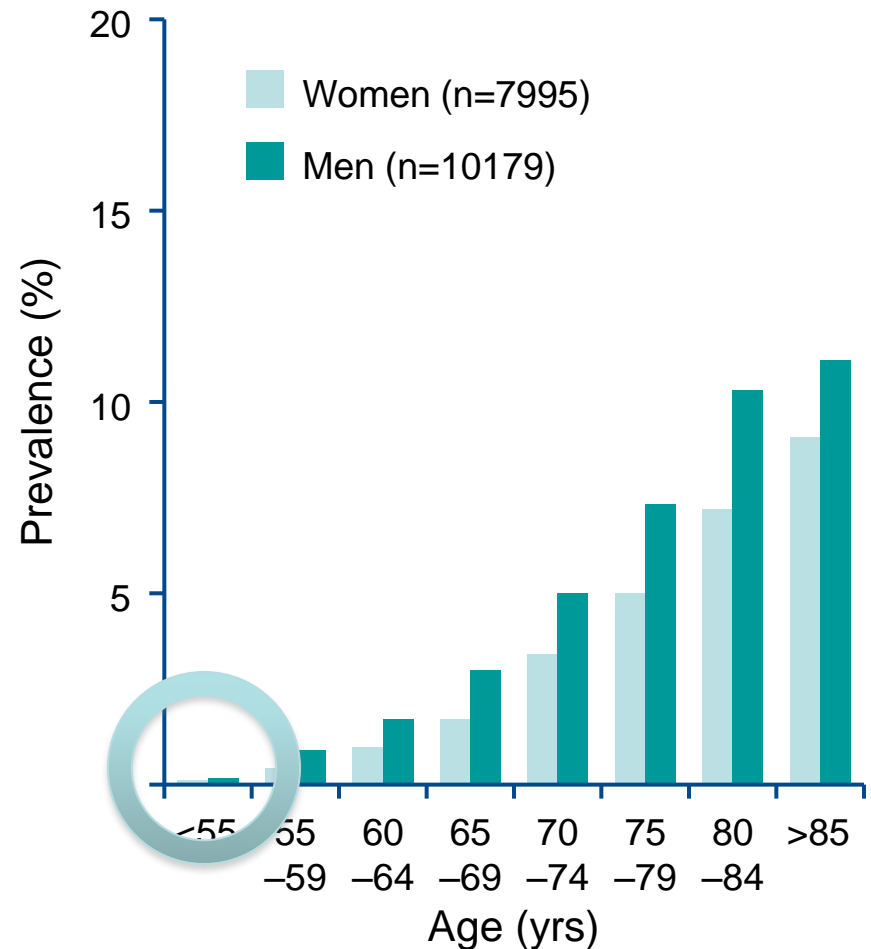
1. Heeringa J et al. Eur Heart J 2006;27:949-53; 2. Go AS et al. JAMA 2001;285:2370-5

## Prevalence of AF increases with age

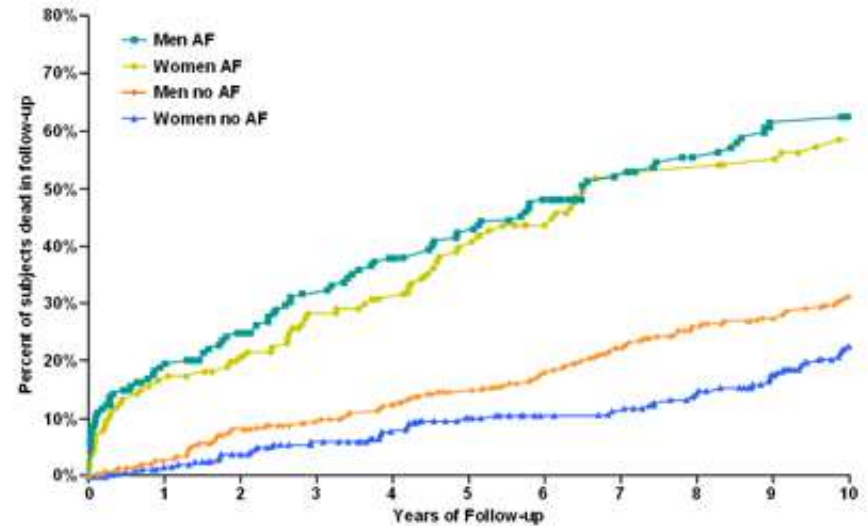
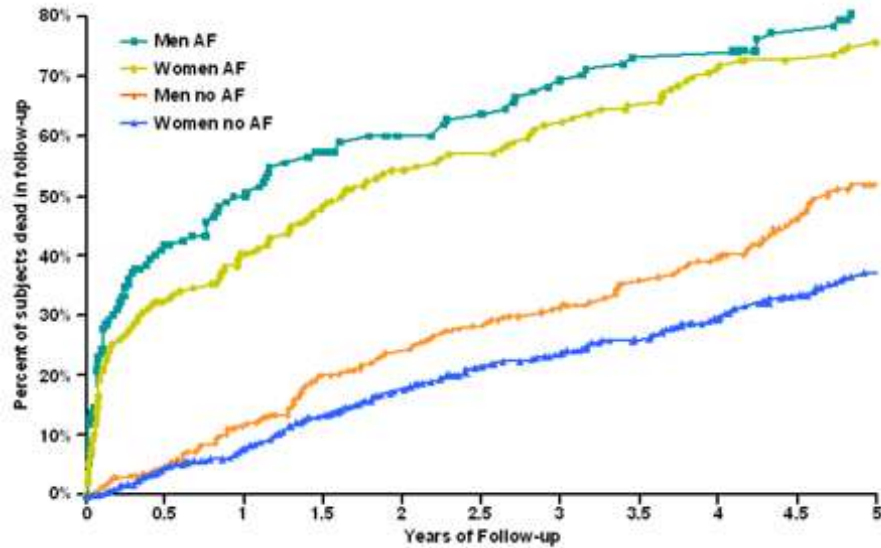
European age-related prevalence<sup>1</sup>



US age-related prevalence<sup>2</sup>



## AF Affects Life Expectancy



## Rate or rhythm

....do we really need to restore and maintain sinus rhythm, or can we simply maintain heart rate control?

## Rate vs Rhythm Control

### Favours rate control

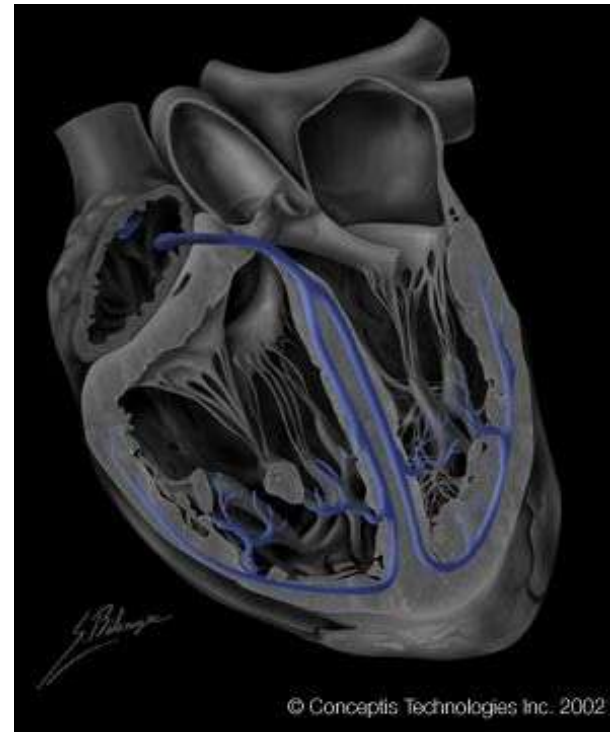
- Persistent Afib
- Recurrent Afib
- Less symptomatic
- $\geq 65$  years of age
- Male Hypertension
- No History of CHF
- Previous rhythm Rx failure
- Patient preference

### Favours rhythm control

- Paroxysmal Afib
- First episode Afib
- More Symptomatic
- $< 65$  years of age
- Female
- No hypertension
- History of CHF
- No previous rhythm Rx
- Patient preference

# AFFIRM

**A**trial  
**F**ibrillation  
**F**ollow-up  
**I**nvestigation of  
**R**hythm  
**M**anagement



# Inclusion criteria

Wanted to focus on the elderly

- >65 years of age
- Patients where the atrial fibrillation itself was a risk for morbidity or mortality
- Able to tolerate at least 2 drug regimens in both treatment arms

# AFFIRM Trial

- 4060 patients with atrial fibrillation of less than 6 months duration
- Rate control with digoxin, beta blocker or calcium channel blocker and anticoagulation with warfarin or
- Rhythm control with the most effective anti-arrhythmic drug and anticoagulation with warfarin
- Amiodarone 39% (60% at 3 years), sotalol 33%, other treatments 1-10%
- Follow-up 3.5 years

# AFFIRM Trial

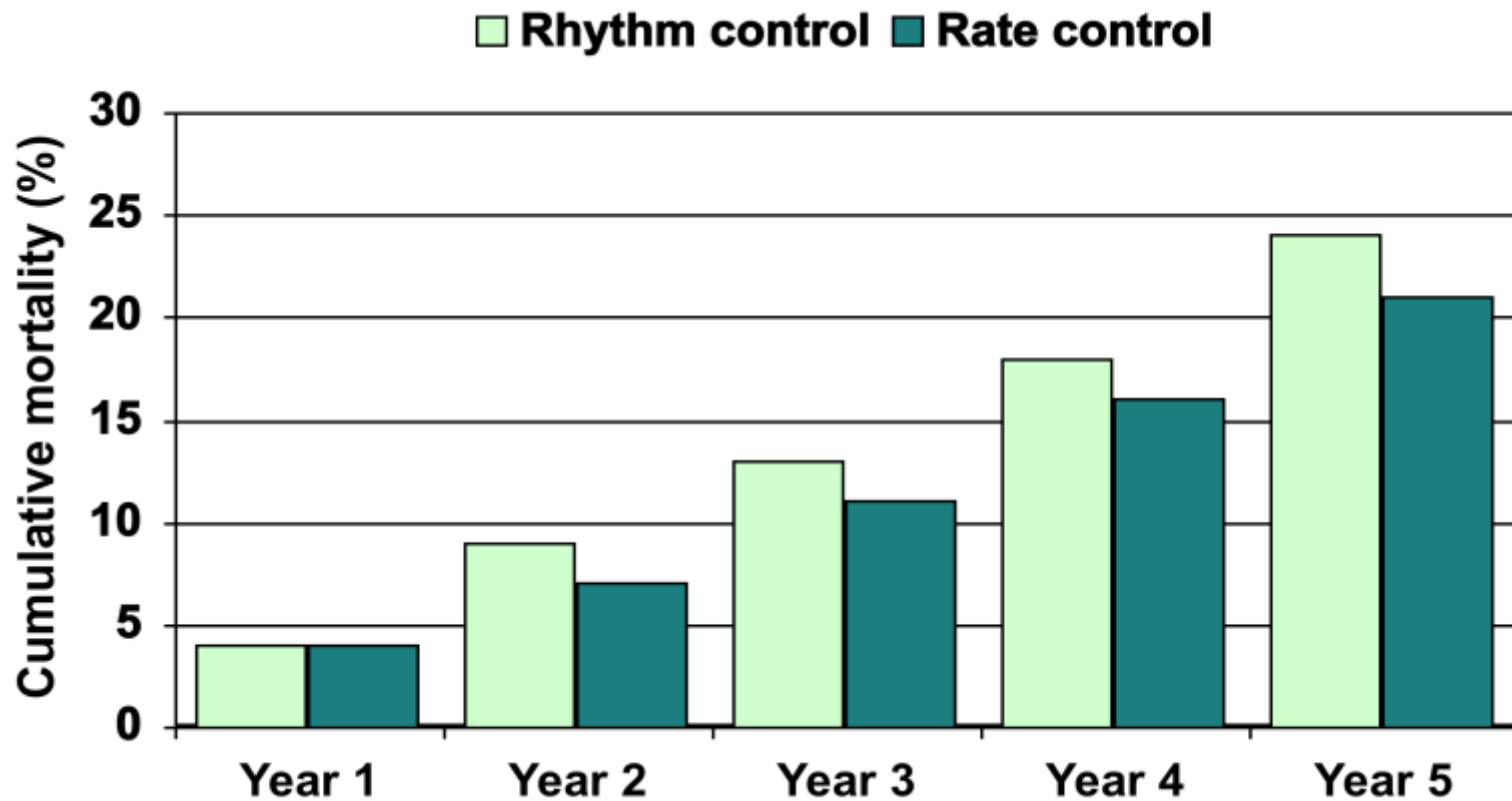
Patients were randomized to a strategy, not a specific drug regimen

- Pharmacological therapies: allowed any drug approved by North American regulatory authorities. Drugs could be added if they were approved during the trial
- Nonpharmacological therapies: allowed designated therapies once a patient failed 2 drug therapies

# AFFIRM Trial

- Results:
  - No difference in all cause mortality (1° endpoint)
  - Trend towards better survival with rate control
  - No difference in death, ischaemic stroke, anoxic encephalopathy, major bleeding or cardiac arrest (2° endpoints)
  - No difference in quality of life or functional status including cardiovascular death, CHF, thromboembolism severe bleeding, pacemaker implantation or side effects of anti-arrhythmic therapy between the two strategies:

# Mortality results



# Prevalence of warfarin

Greater prevalence of warfarin use in rate-control arm

- Rate-control arm: >85% throughout the trial
- Rhythm-control arm: >70% throughout the trial

# CAN SINUS RHYTHM IMPROVE SURVIVAL?

## Predictors of Mortality in AFFIRM

TABLE 2. Covariates Significantly Associated With Survival Results With Echocardiographic Data Included

Covariate	P	HR	HR: 99% Confidence Limits	
			Lower	Upper
Age at enrollment*	<0.0001	1.06	1.05	1.08
Coronary artery disease	<0.0001	1.56	1.20	2.04
Congestive heart failure	<0.0001	1.57	1.18	2.09
Diabetes	<0.0001	1.56	1.17	2.07
Stroke or transient ischemic attack	<0.0001	1.70	1.24	2.33
Smoking	<0.0001	1.78	1.25	2.53
Left ventricular dysfunction	0.0065	1.36	1.02	1.81
Mitral regurgitation	0.0043	1.36	1.03	1.80
Sinus rhythm	<0.0001	0.53	0.39	0.72
Warfarin use	<0.0001	0.50	0.37	0.69
Digoxin use	0.0007	1.42	1.09	1.86
Rhythm-control drug use	0.0005	1.49	1.11	2.01

\*Per year of age.

# Predictors of Atrial Fibrillation Recurrence

- Age > 70
- Afib duration > 3 months
- Hypertension
- Heart Failure
- LA enlargement
- Rheumatic heart disease

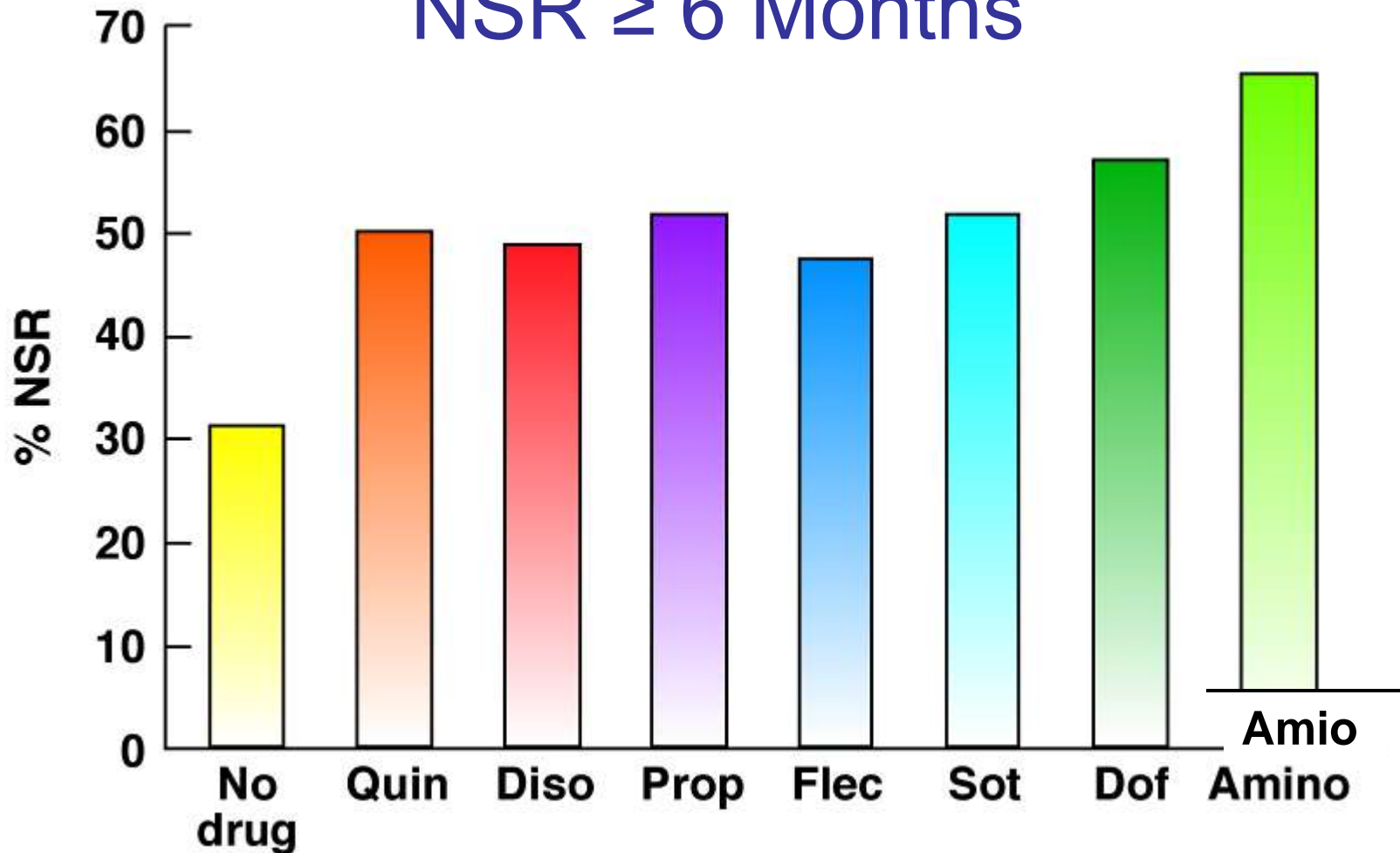
# Maintenance of NSR

- One year recurrence rate 75% in absence of anti-arrhythmic drug
- Higher risk of pro-arrhythmia with underlying structural heart disease
- Amiodarone more efficacious but significant side effects
- Other agents have potential for pro-arrhythmia in patients with underlying heart disease

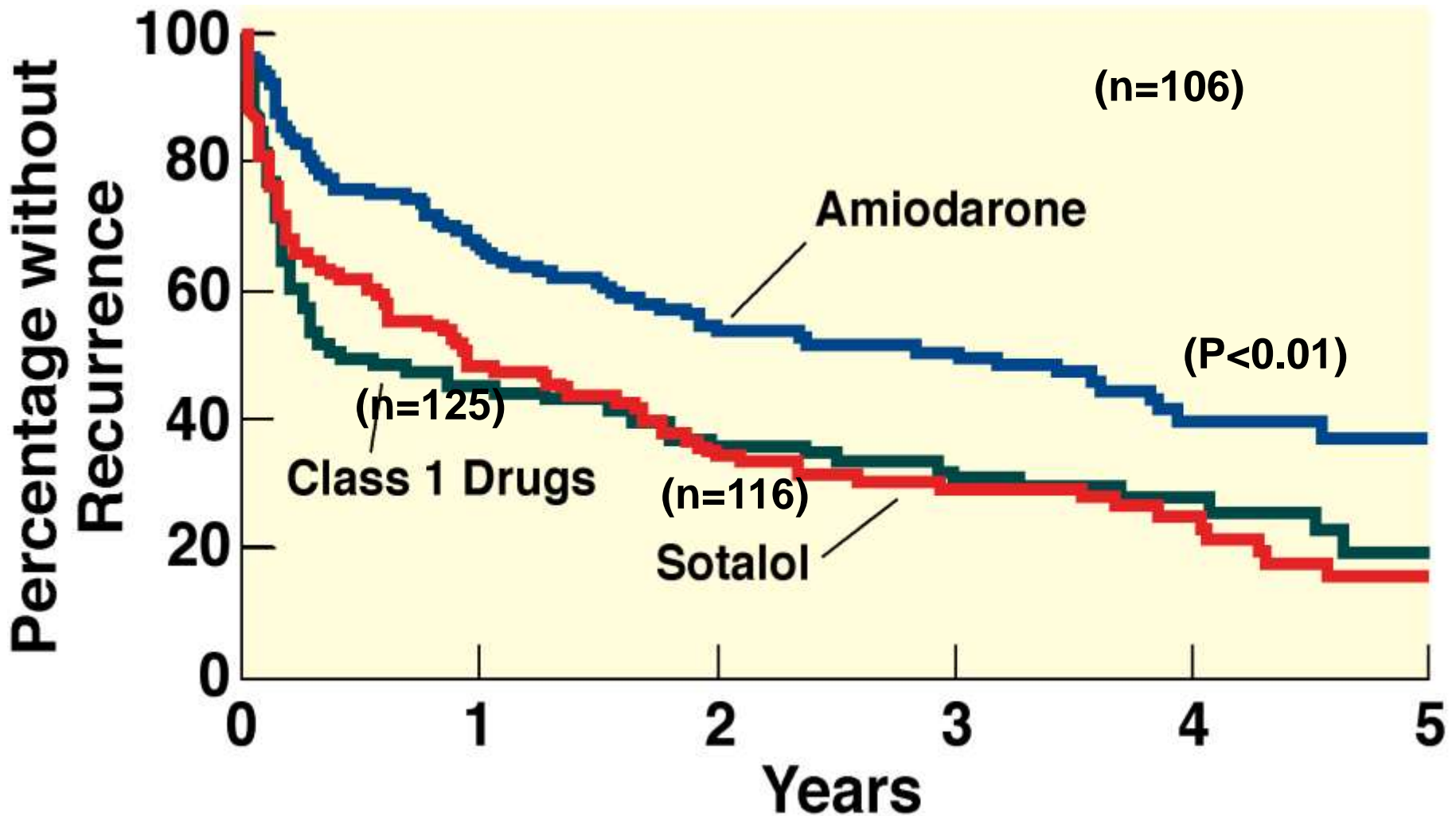
# Maintenance of NSR in Patients with Structurally Normal Hearts

- **Propafenone**
- **Flecainide**
- **Sotalol**
- **Amiodarone**
- **Disopyramide**
- **Dronedarone**

# Antiarrhythmic Drugs: Efficacy Maintaining NSR $\geq$ 6 Months



# AFFIRM: Antiarrhythmic drug Substudy



# Adverse Effects of Amiodarone

- Excess bradycardia/heart block
- Corneal microdeposits
- Phtosensitivity/ skin pigmentation
- Hyper/hypothroidism
- Pulmonary fibrosis/interstitial pneumonitis
- Hepatotoxicity
- Peripheral neuropathy

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# Catheter Ablation Therapy for Atrial Fibrillation

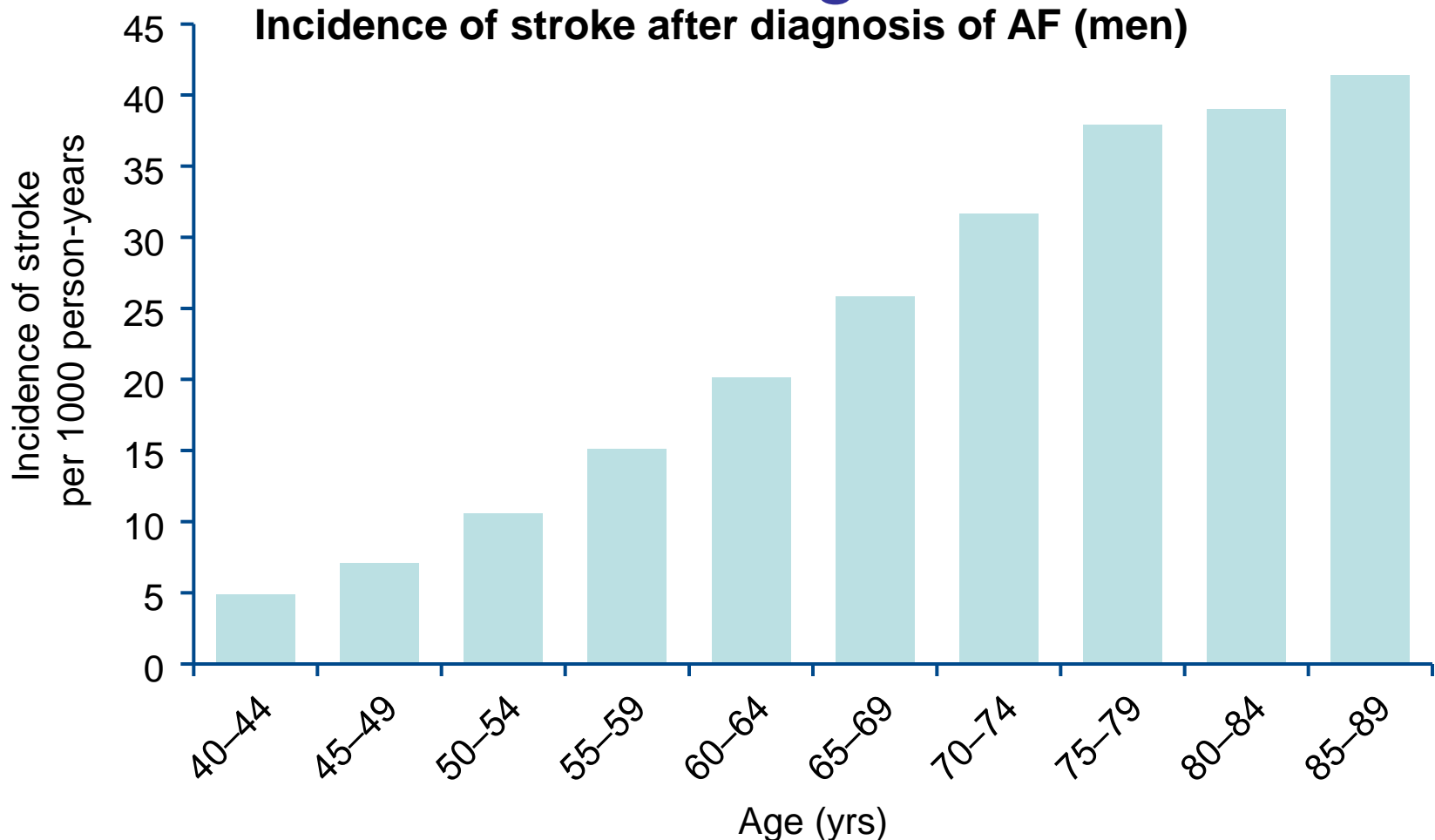
## Stroke is a frequent complication of AF

- 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>

# 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>

# Incidence of stroke in AF patients increases with age



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

Frost L et al. Neuroepidemiology 2007;28:109-15

# Risk Stratification for Patients with AF

	Annual Stroke Rate %	
AGE Years	No other Risk Factors	One or More Additional Risk Factors
< 65	1.0	4.9
65-75	4.3	5.7
> 75	3.5	8.1

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Don't forget the person!



**August 2009**



**Mid December 2009**



**Christmas Eve 2009**



**Mid January 2010**



**Early February 2010**

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**Shipley**

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# My Friend Jon

## Summary

- The evidence in the younger person is not as substantial as the older
- As non-pharmacological rhythm strategies develop this should be seen as an option
- The stroke risk in the younger normal heart is so low that no intervention may be required
- Never forget how people can feel about developing atrial fibrillation at a young age

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Thank you for your attention

**Question**

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