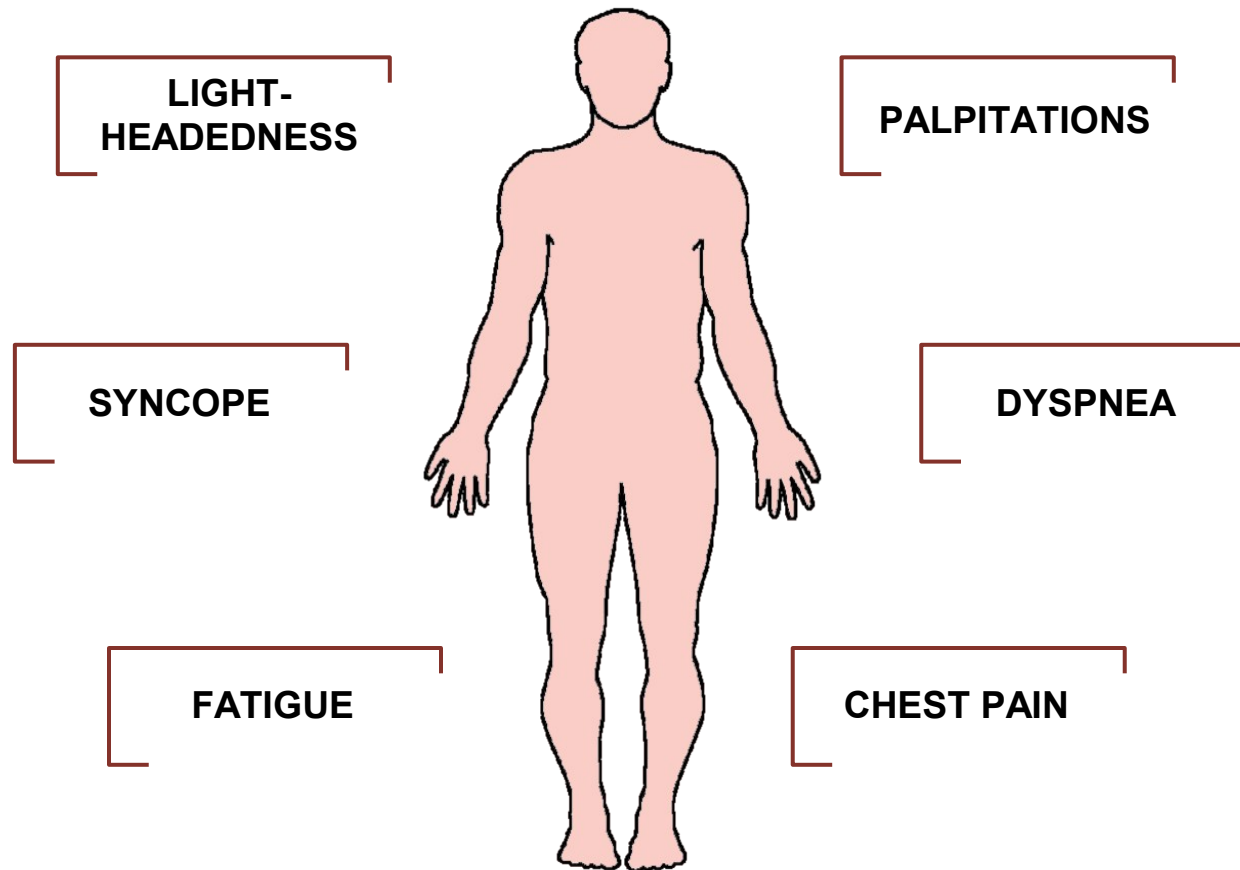


AF May Present with a Wide Range of Symptoms



- AF may also be asymptomatic

Asymptomatic AF is Common

- At least 33% of AF patients could be asymptomatic¹
- Holter and transtelephonic monitoring studies have demonstrated that asymptomatic episodes of paroxysmal AF are 10-12 times more frequent than symptomatic episodes^{2,3}
- AF episodes may go unnoticed if asymptomatic, yet could still have long term deleterious consequences for the patient²

1. Savelieva I, et al. *Pacing Clin Electrophysiol.* 2000;23:145-148

2. Page RL, et al. *Circulation.* 2003;107:1141-1145

3. Defaye P, et al. *Pacing Clin Electrophysiol.* 1998;21:250-255

AF has Serious Consequences

- **Morbidity and Mortality**
 - Near 5-fold increase in risk of stroke¹
 - Stroke associated with AF is typically more severe than ischemic stroke due to other causes²
 - 2-fold increase in risk of mortality³
 - AF promotes heart failure and HF aggravates AF to worsen a patient's overall prognosis⁴
- **Quality of Life**
 - QoL may be considerably impaired due to risk of exacerbation of symptoms⁵

1. Wolf *et al.* *Stroke* 1991;22:983-988
2. Dulli DA *et al.* *Neuroepidemiology*. 2003;22(2):118-23
3. Benjamin EJ *et al.* *Circulation*. 1998;98:946-952
4. Wang TJ *et al.* *Circulation* 2003;107: 2920-2925.
5. Hamer ME *et al.* *Am J Cardiol* 1994;74:826-9.

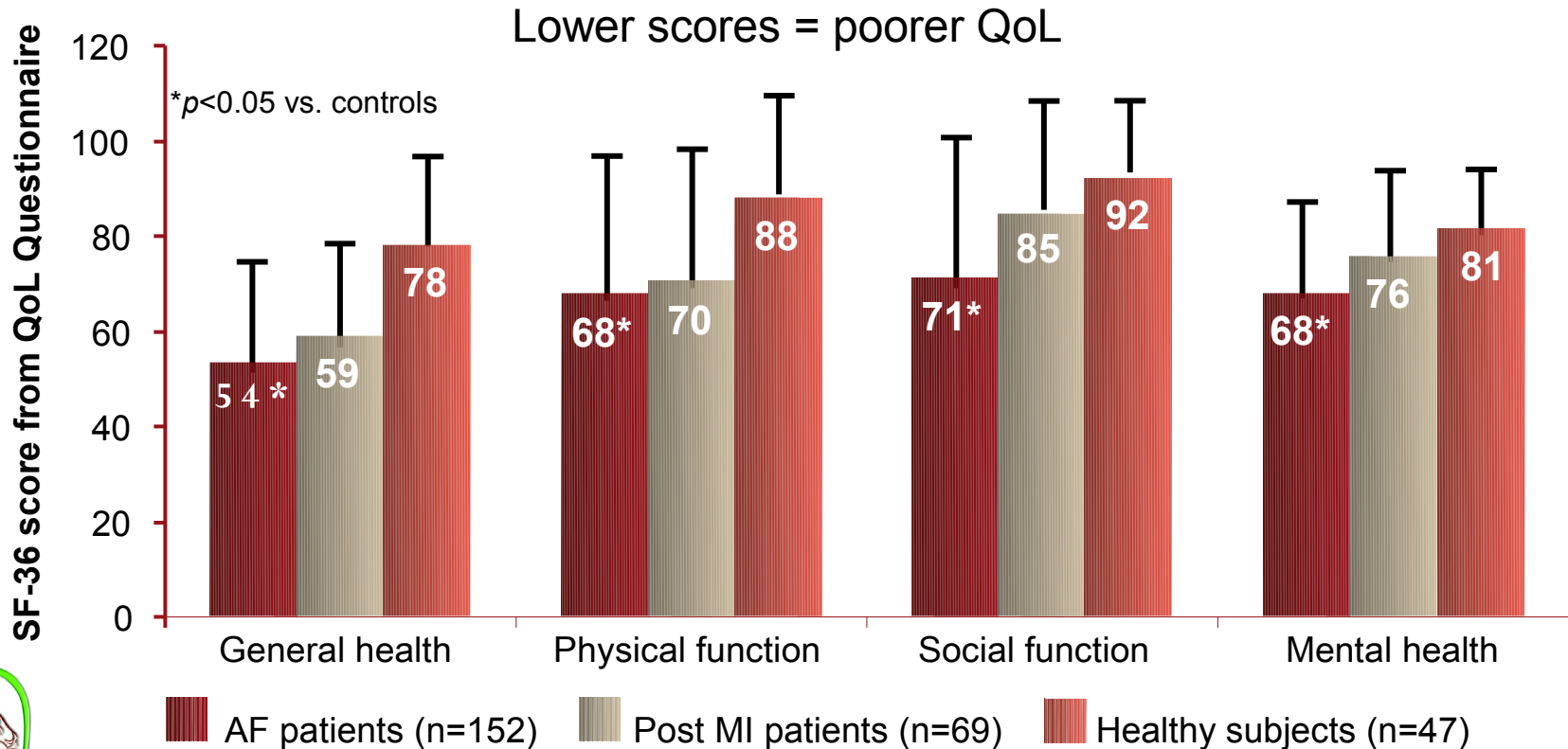
AF May Have a Significant Impact on Quality of Life

- Paroxysmal AF has a significant impact on patient QoL independent of frequency or duration of symptoms^{1,2}
 - Two-thirds of patients reported their symptoms were moderately disruptive to their lives¹
 - These patients could not be distinguished from those that reported no disruption based on the incidence or duration of symptoms¹
- Impairment in QoL seen with AF is similar to that in CHF, MI and angioplasty³
- One-third of AF patients experience anxiety or depression significantly correlated with QoL⁴

1. Van den Burg MP *et al. Neth J Med* 2005;63:170-174.
 2. Hamer ME *et al. Am J Cardiol* 1994;74:826-829.
 3. Dorian P *et al. J Am Coll Cardiol.* 2000;36:1303-1309.
 4. Thrall G *et al. Chest* 2007;132:1259-64.

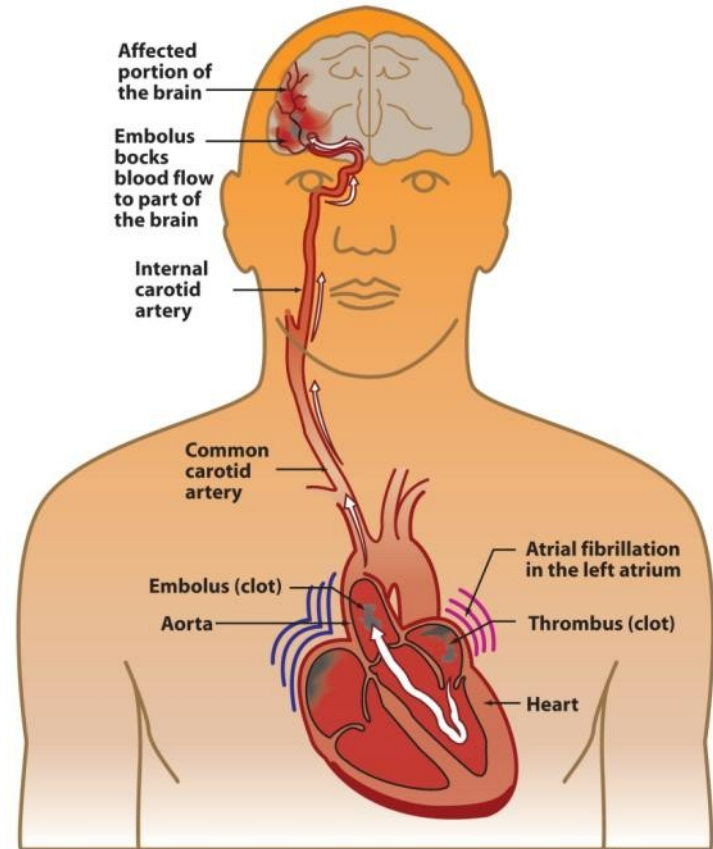
AF May Adversely Affect Quality of Life

- QoL was significantly worse in AF patients than in controls (post MI patients and healthy subjects)



AF is an Independent Risk Factor for Stroke

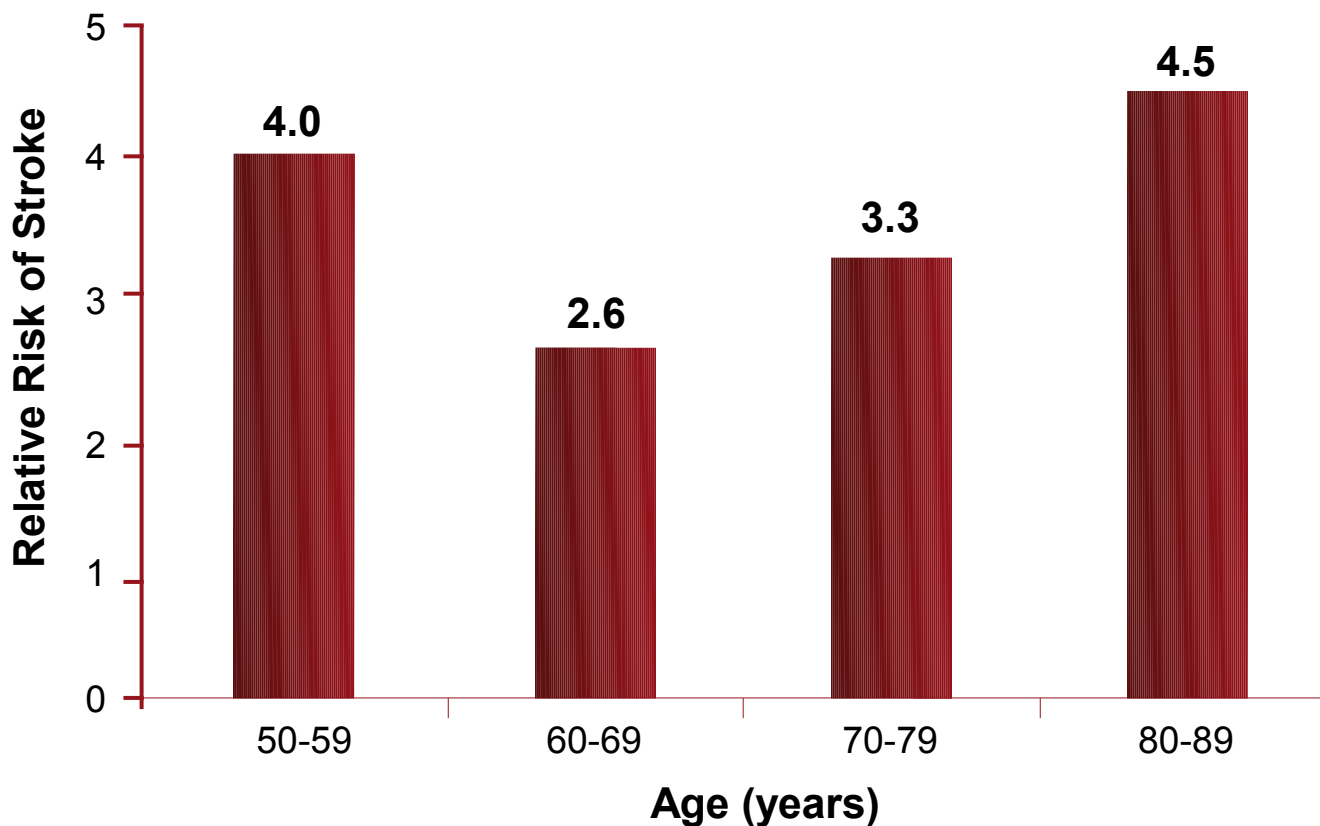
- AF patients have a near 5-fold increased risk of stroke¹
- 1 in every 6 strokes occurs in a patient with AF²
- Ischemic stroke associated with AF is typically more severe than stroke due to other etiologies³
- Stroke risk persists even in asymptomatic AF⁴



1. Wolf *et al.* *Stroke* 1991;22:983-988
 2. Fuster V, *et al.* *Circulation*. 2006;114:e257-e354;
 3. Dulli DA, *et al.* *Neuroepidemiology*. 2003;22:118-123.
 4. Page RL, *et al.* *Circulation*. 2003;107:1141-1145.

AF Increases the Risk of Stroke by Nearly 5-fold

Framingham



$p < 0.001$ vs. Non-AF patients

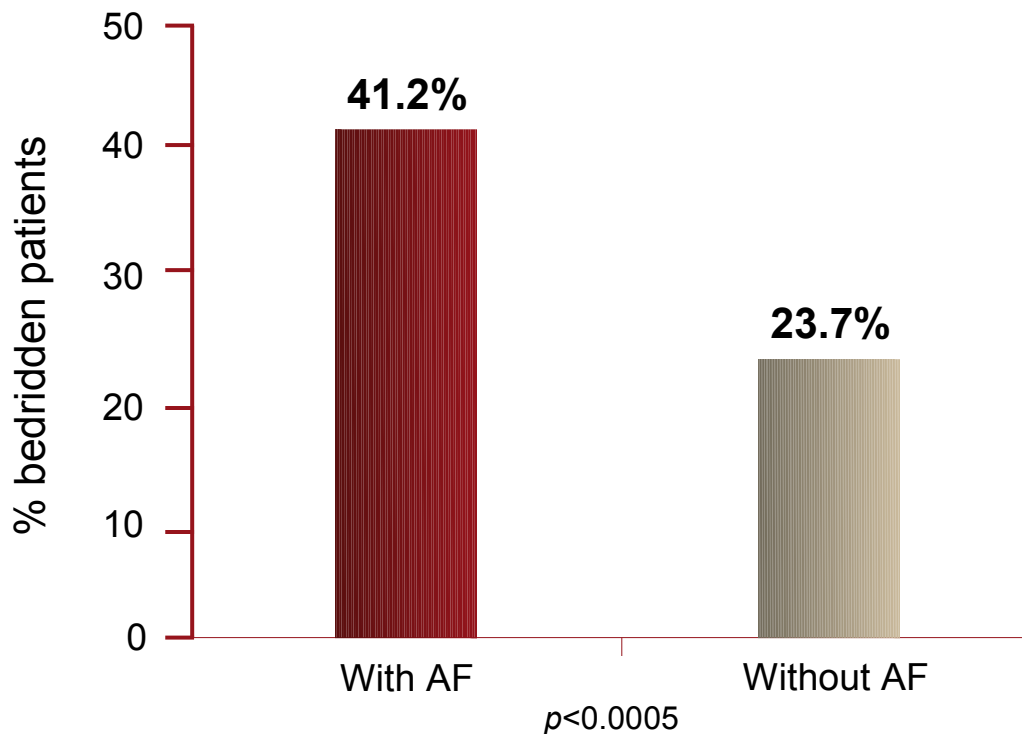
AF Adversely Affects Stroke Outcomes

- AF-associated ischemic stroke is more severe than non-AF stroke¹
- AF increases 30-day stroke-related mortality
 - 25% of patients with AF-related stroke died vs. 14% in non-AF strokes¹
- Ischemic stroke associated with AF is almost twice as likely to be fatal compared with non-AF stroke¹
- Survival is poorer and recurrence higher following AF-related stroke¹
 - By 1 year, 63% AF patients vs. 34% non-AF patients died
 - By 1 year, stroke recurred in 23% AF patients vs. 8% non-AF patients
- Functional outcome is significantly poorer in patients with AF²

1. Lin HJ *et al.* *Stroke* 1996;27:1760-1764

2. Firedman PJ. *Stroke* 1991;2:209-214.

Ischemic Stroke Associated with AF is Typically More Severe than Stroke due to Other Etiologies



- Odds ratio for bedridden state following stroke due to AF was 2.23 (95% CI, 1.87-2.59; $p < 0.0005$)

AF Increases the Risk of Stroke Recurrence and Post-Stroke Mortality

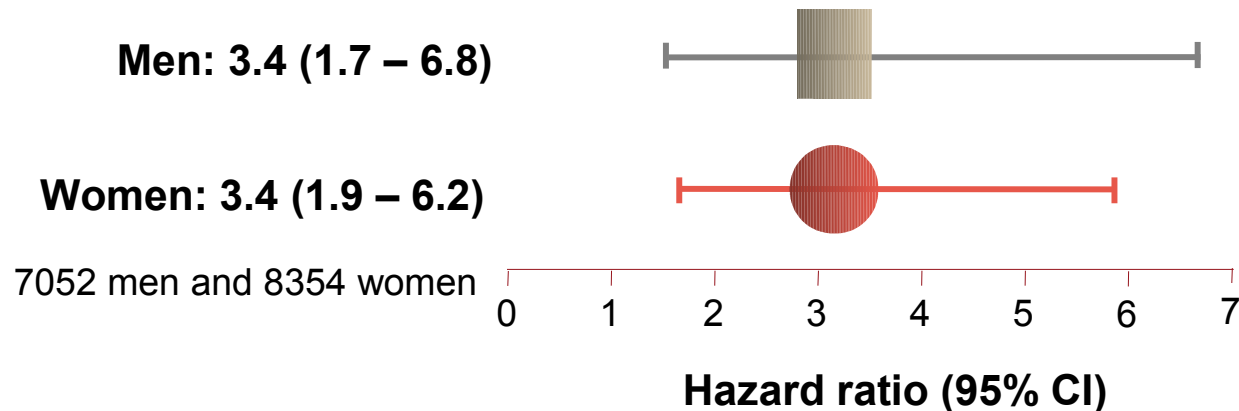
Framingham

	AF patients	Non-AF patients	
1-year stroke recurrence	23%	8%	$p < 0.001$
30-day post stroke mortality	25%	14%	OR 1.84 (95% CI, 1.04 to 3.27)
1-year post stroke mortality	63%	34%	$p < 0.001$

AF Increases the Risk of Heart Failure

Renfrew/Paisley

Risk of heart failure in AF patients compared to non-AF patients



- The Renfrew Paisley study showed that the presence of AF was an independent predictor of heart failure in men and women

AF Worsens the Prognosis of Patients with Comorbidities

Patients with new onset AF	Events	Risk
Hypertension¹ • n=8851 • Follow-up: 4.8 ± 1 years	Cardiovascular events	X 1.88
	Fatal and non-fatal stroke	X 3
	Hospitalisation for heart failure	X 5
CHF² • n=1470 • Follow-up: 5.6 years	Mortality in men	X 1.6
	Mortality in women	X 2.7
MI³ • n= 17944 • Follow-up: 4 years	In-hospital mortality	X 1.98
	Long-term mortality (4 years)	X 1.78

1. Adapted from Wachtell K, *et al. J Am Coll Cardiol.* 2005;45:712-719.

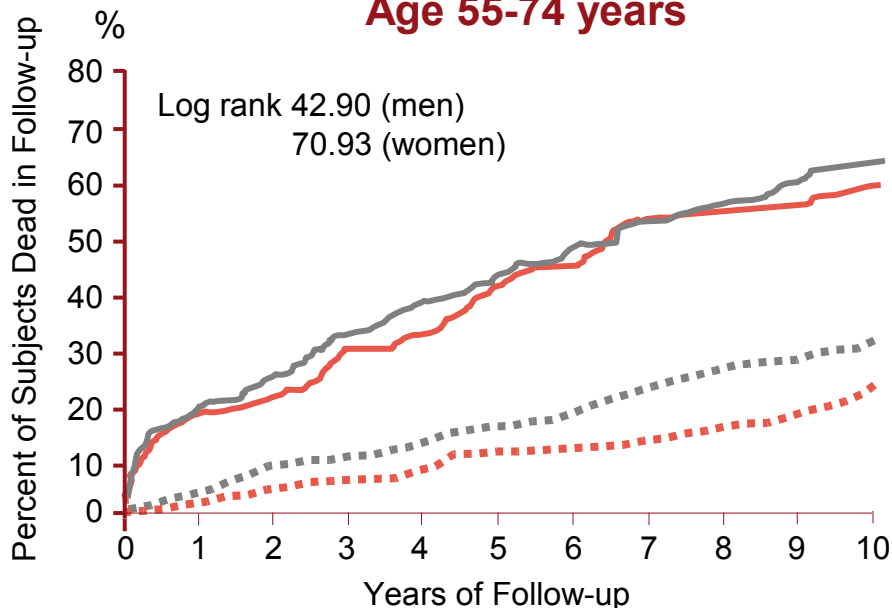
2. Adapted from Wang *et al. Circulation* 2003;107:2920-2925.

3. Adapted from Pizzetti F, *et al. Heart.* 2001;86:527-532.

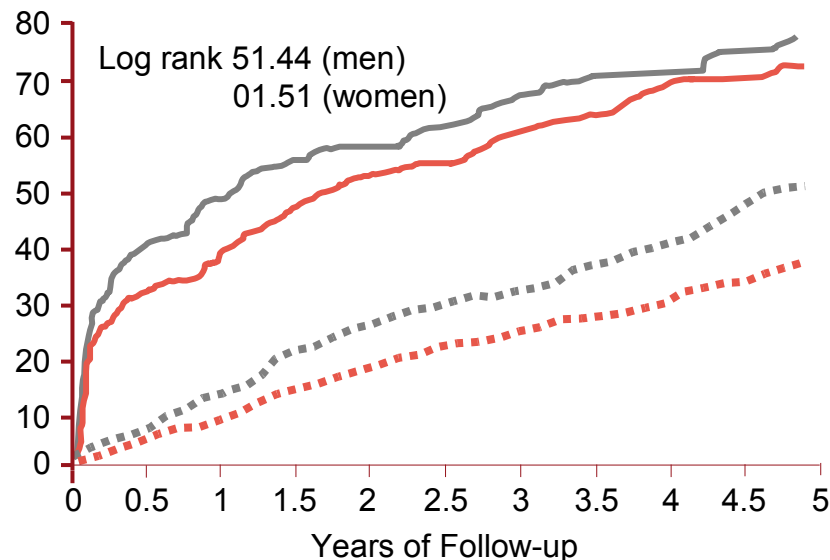
AF Approximately Doubles the Risk of Mortality in Younger and Older Patients

Framingham

Age 55-74 years



Age 75-94 years

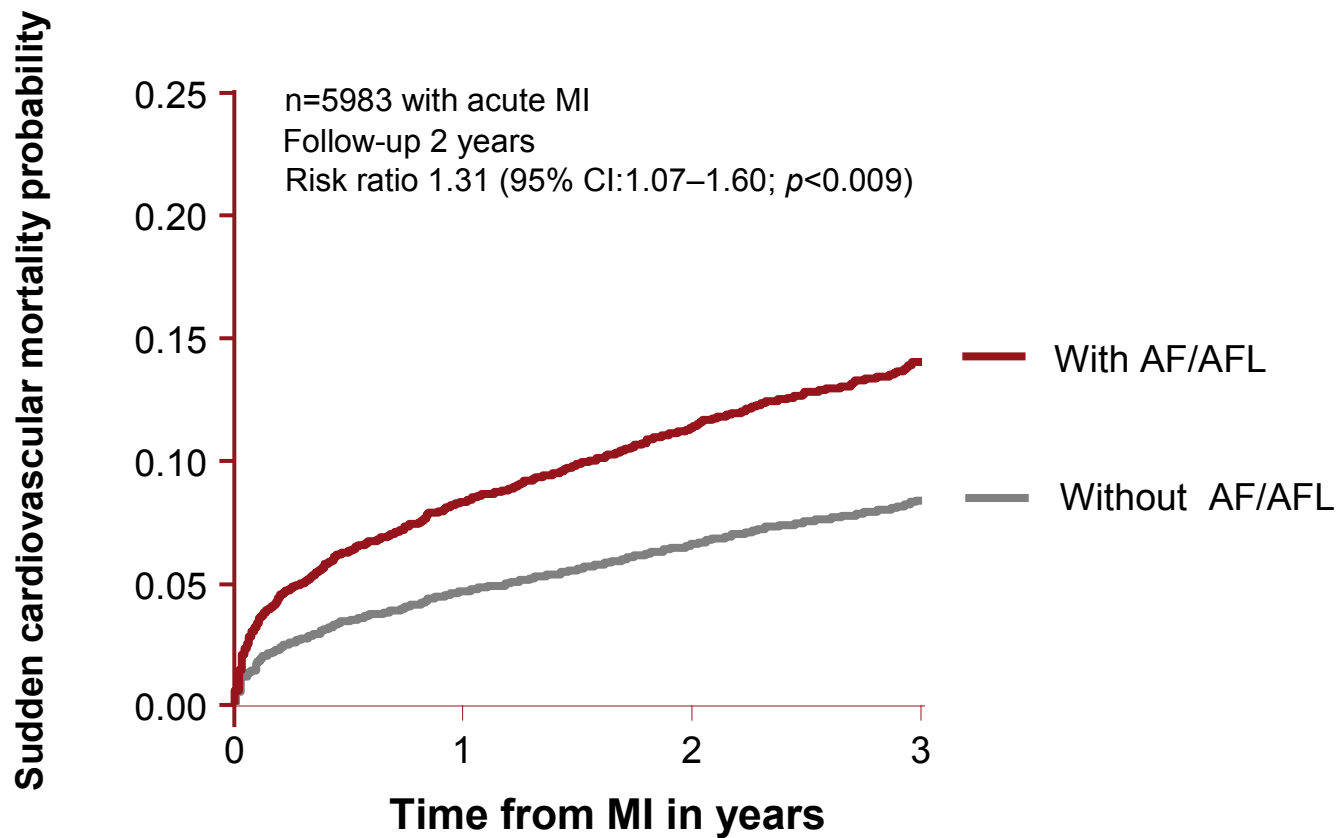


- Men AF (n=159)
- Women AF (n=133)
- - - Men no AF (n=318)
- - - Women no AF (n=266)

- Men AF (n=137)
- Women AF (n=192)
- - - Men no AF (n=274)
- - - Women no AF (n=384)

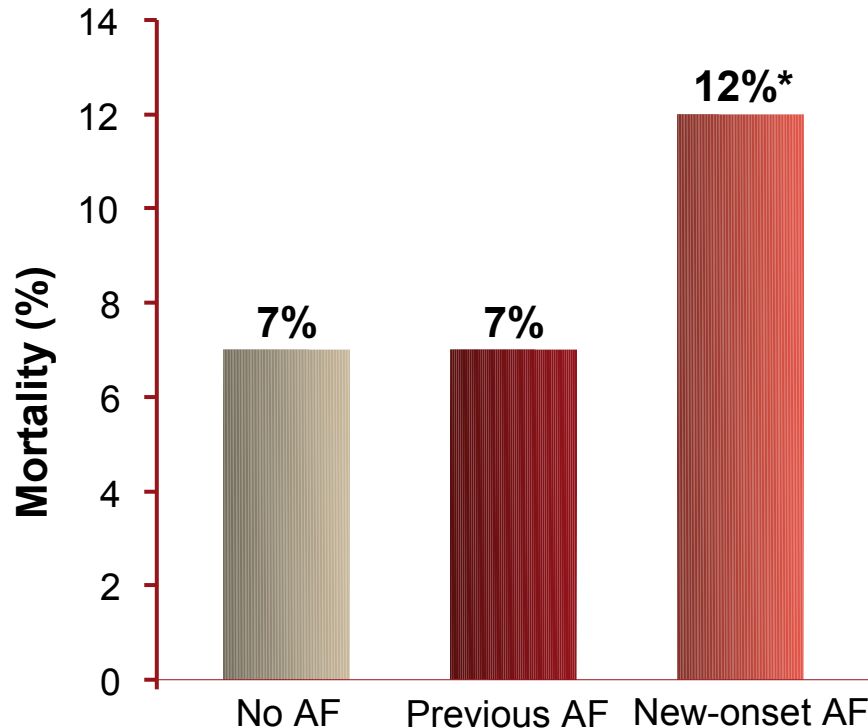
AF Increases the Risk of Sudden Death

TRACE



New-Onset AF increases In-Hospital Mortality and Hospital Stays

EuroHeart Failure Survey



- New-onset AF is an independent predictor of
 - In-hospital mortality
 - Longer ICU stay
 - Longer hospital stay

* $p < 0.001$ vs patients with previous AF and without AF

Rivero-Ayerza et al. *Eur Heart J.* 2008;29:1618-1624.

AF Leads to Hospitalisation

- AF is the leading cause of hospitalisations for arrhythmia
 - AF accounts for approximately one third of hospitalisations for cardiac rhythm disturbances¹
- AF hospitalisations have increased dramatically in recent years

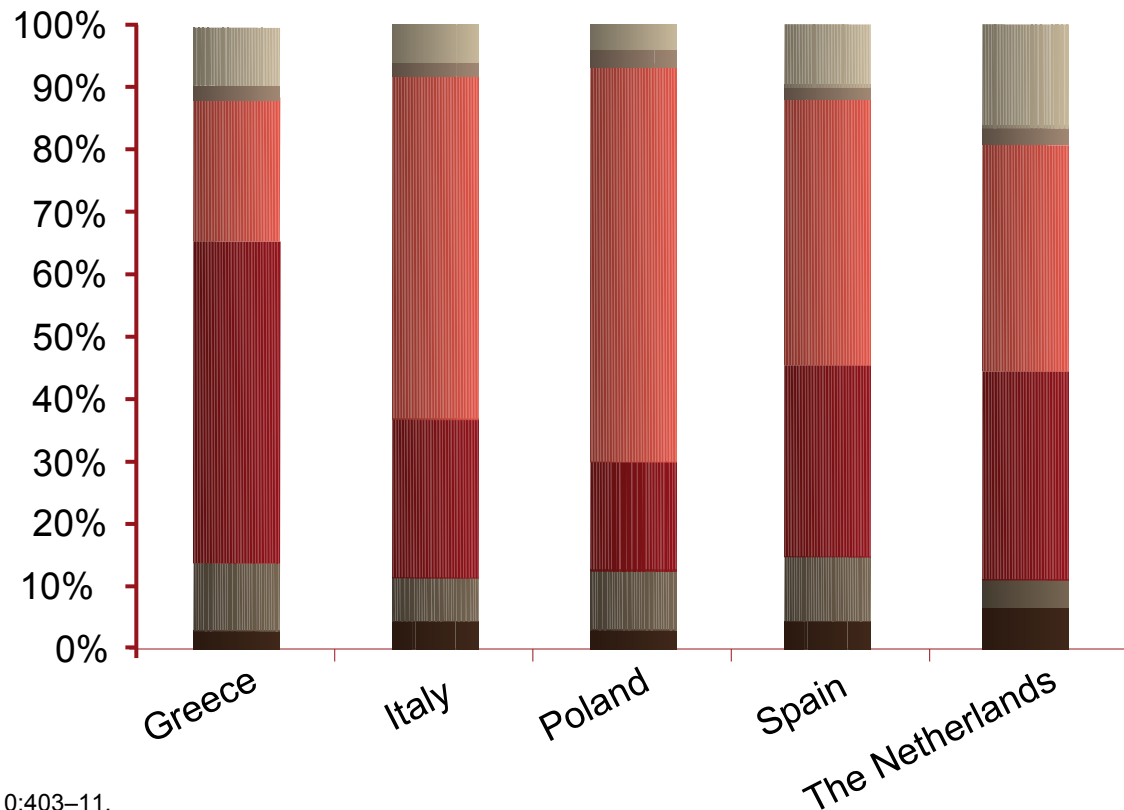
Hospitalisations
X 2 to 3
(US - 1985 to 1999)²

1. Go AS *et al.* *JAMA* 2001;285:2370-5.
2. Wattigney WA, *Circulation*. 2003;108:711-716.

Hospitalisations Represent a Major Driver in Cost of Care of AF Patients (EU)

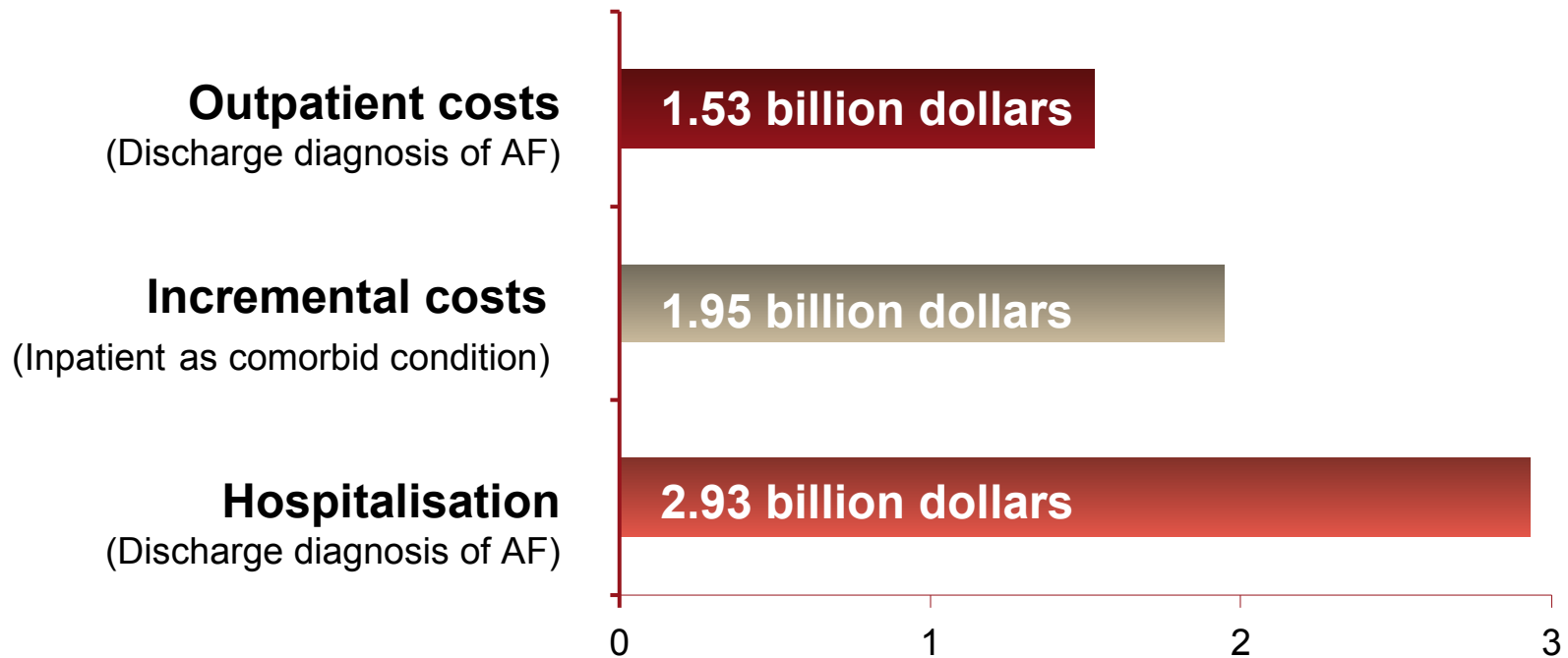
- 70% of the cost of AF management is driven by inpatient care and interventional procedures

EuroHeart Survey (2004-2005)



Hospitalisations Represent a Major Driver in Cost of Care of AF Patients (US)

- In 2001, AF management cost about 6.65 billion Dollars* in the US and was mainly driven by inpatient care



* Does not include prescription costs
 Coyne K et al. *Value Health* 2006;9(5):348-56.

The Consequences of AF – Key Points

- AF may adversely affect Quality of Life
- Beyond stroke, AF increases the risk of CV morbidity and mortality
 - AF increases the risk of stroke and heart failure
 - AF worsens the prognosis of patients with comorbidities
 - AF doubles the risk of mortality
 - AF is an independent risk factor for sudden death
- AF has a significant socio-economic impact
 - AF is the leading cause of hospitalisations for arrhythmia
 - AF hospitalisations have dramatically increased in recent years
 - The high cost of AF management is mainly driven by hospitalisation