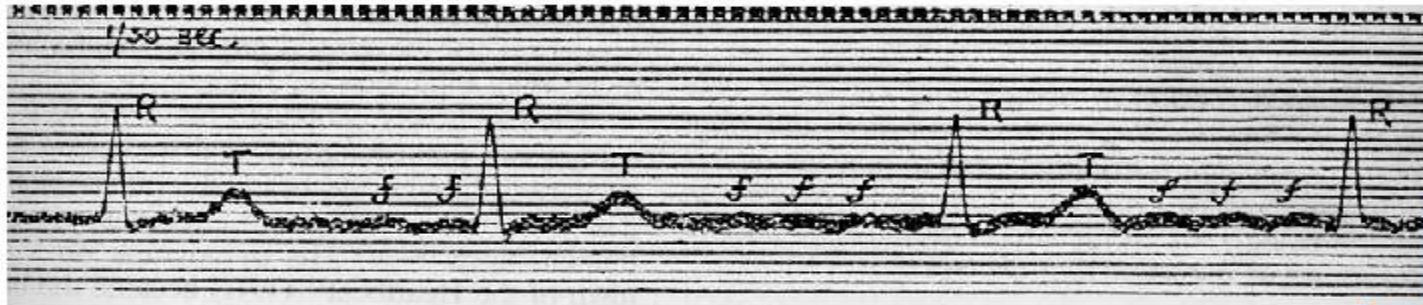


Samer Nasr, M.D.
Mount Lebanon Hospital.

Réduction de la Fibrillation Auriculaire en Pratique de Ville

.....
.....
.....
.....

Treatment of AF. Approaches, results and new technologies...



Recorded and described by Lewis in 1909

Classification

■ Lone atrial fibrillation:

- Younger than 60 years old.
- No clinical or echo evidence of cardiopulmonary disease.
- Favorable prognosis.
- Thromboembolism usually not an issue.

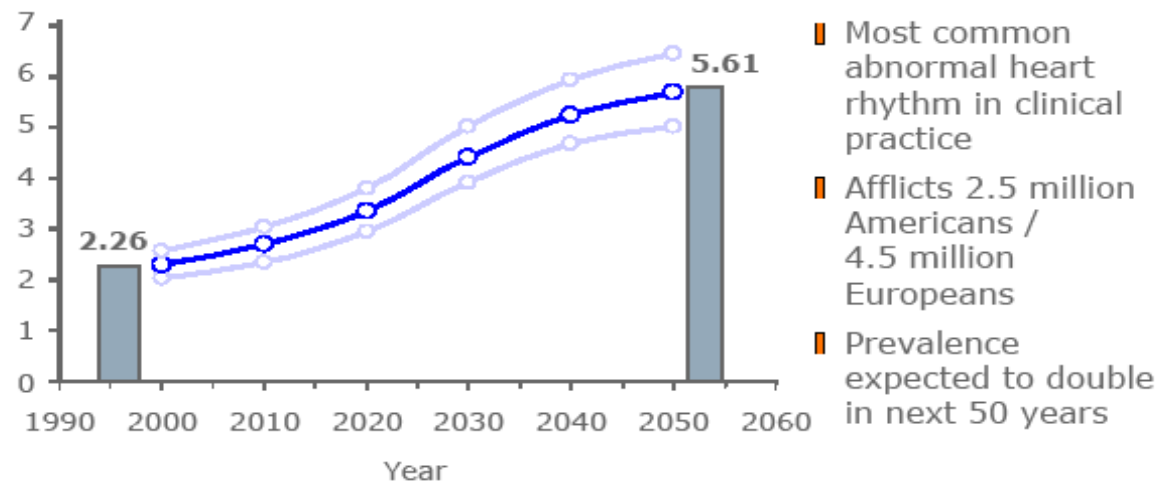
■ Substrate related atrial fibrillation.

- | | | |
|----------------|---------------------|----------------|
| • ETOH | Hyperthyroidism | HTN |
| • Surgery | Metabolic disorders | Cardiomyopathy |
| • MI | Obesity | Sleep apnea |
| • Pericarditis | Valvular disease | |
| • Myocarditis | Heart failure | |
| • PE | CAD | |

Substrate Related Atrial Fibrillation.

Prevalence of Atrial Fibrillation

Patients with Atrial Fibrillation
in millions

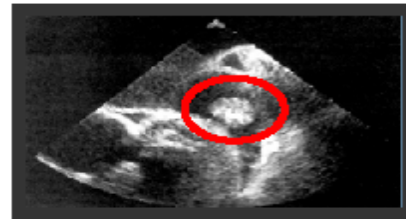


Substrate Related Atrial Fibrillation.

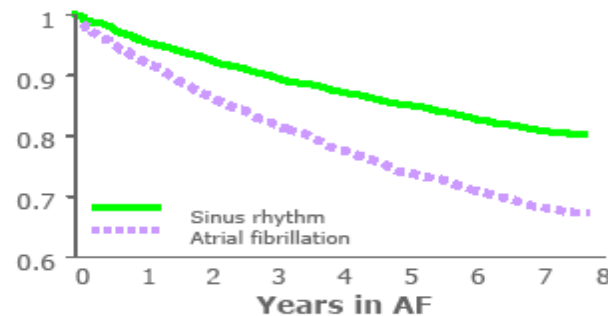
Clinical Consequences of AF (1/2)

- ~1/3 of patients with AF will have a stroke during their life-time
- AF causes 15 - 20% of ischaemic strokes
- Yearly incidence of CVA in patients with AF 4.5% compared to <1% in age-matched controls
- PREVENTABLE**

LAA - Echo



Proportion stroke free



MRI scan



Substrate Related Atrial Fibrillation.

Clinical Consequences of AF (2/2)

Sinus Rhythm



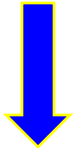
Atrial Fibrillation



- Tachycardia-induced cardiomyopathy
 - Usually with rate persistently > 120 bpm
 - ? time to occur unknown
- **PREVENTABLE & REVERSIBLE**
 - Resolves after rate or rhythm control is achieved

AF: Treatment Options

Rate
normalization



- AV node blockers
 - BB -
 - DIG
 - CA -
 - ...
- AV node ablation

Rhythm
normalization



- AA drugs
 - Ia
 - Ic
 - III
 - New AAd
- Cardioversion
- Non AA drugs
- AF Ablation

Stroke
prevention



Anti –
coagulation

INR: 2-3

Lone Atrial Fibrillation: Outpatient Conversion to NSR.

Lone Atrial Fibrillation

- Rate of progression to permanent atrial fibrillation.
- Prognosis

First Episode



Paroxysmal
(recurrent)



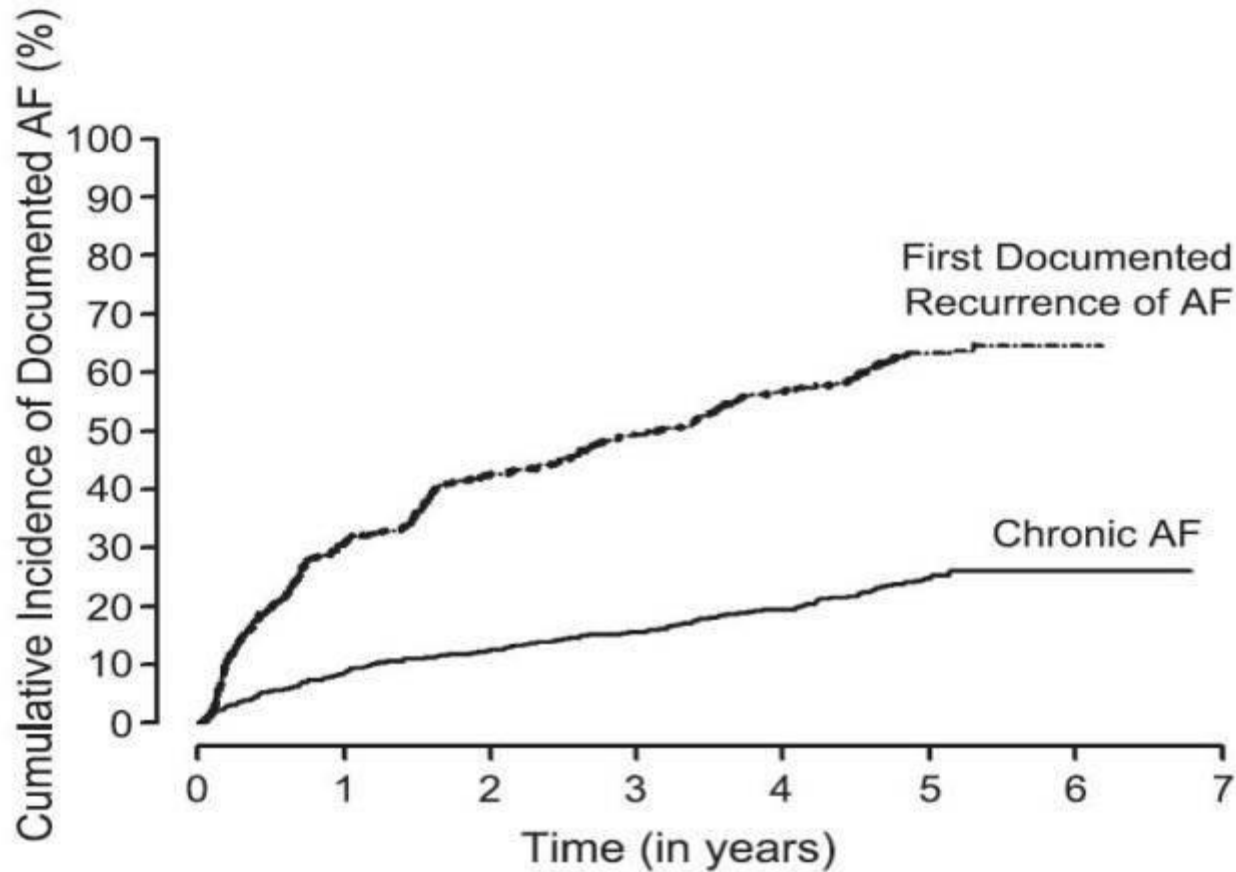
Permanent



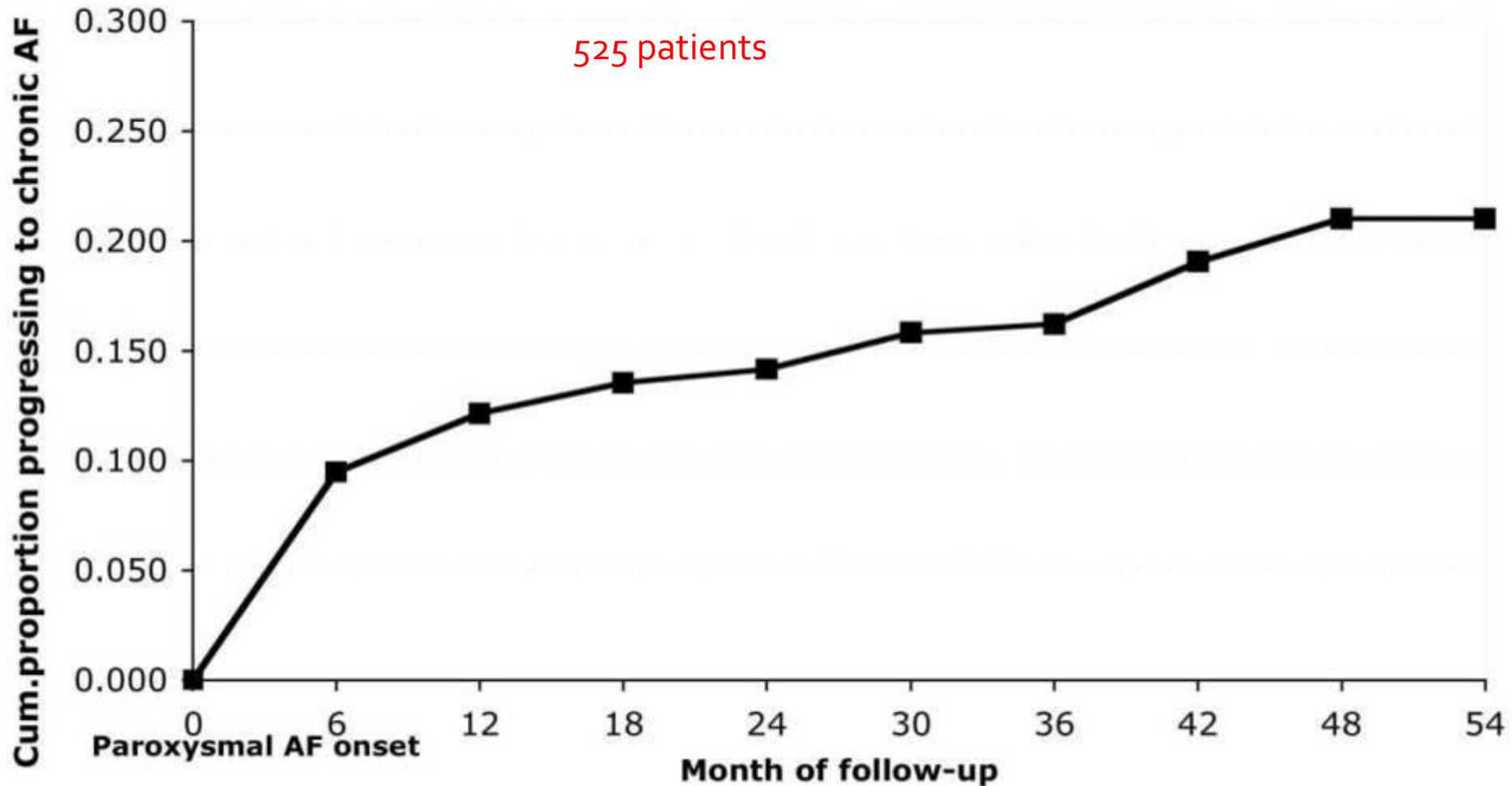
No recurrence

Probability of AF recurrence after the first episode

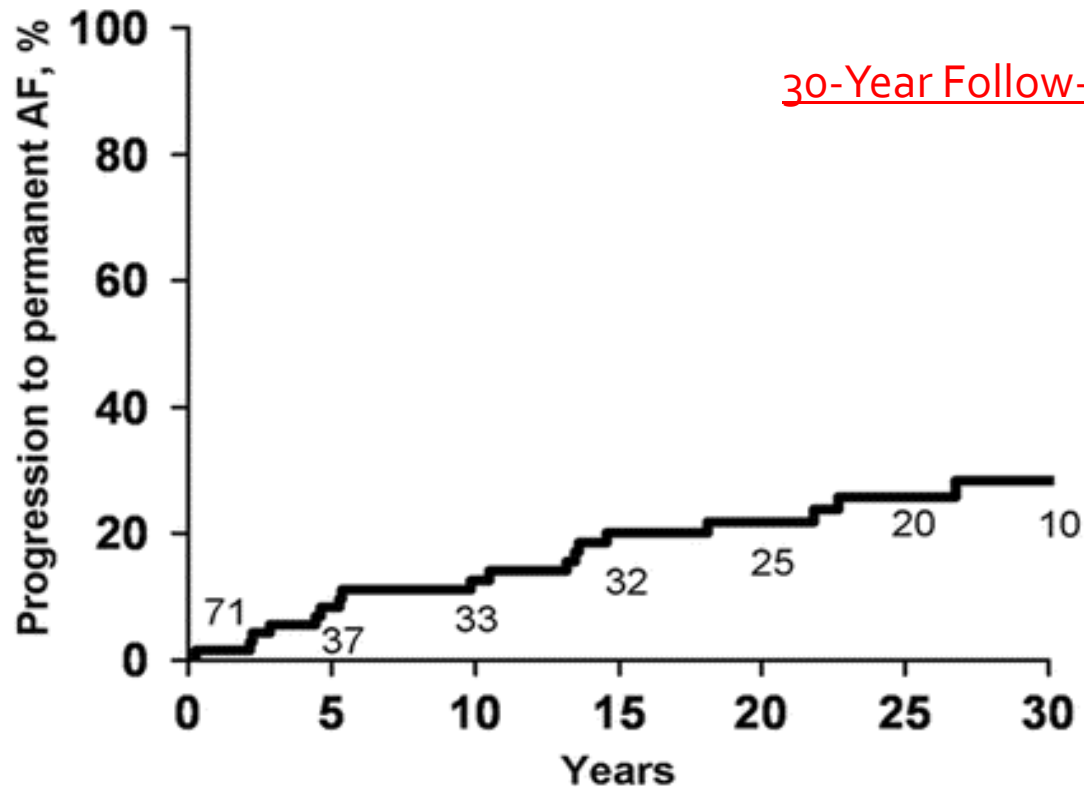
757 patients



Progressing to chronic AF after the first episode







Long-term progression of paroxysmal or persistent lone AF to permanent AF



=> Up to 30% of patients will not recur their AF after the first episode

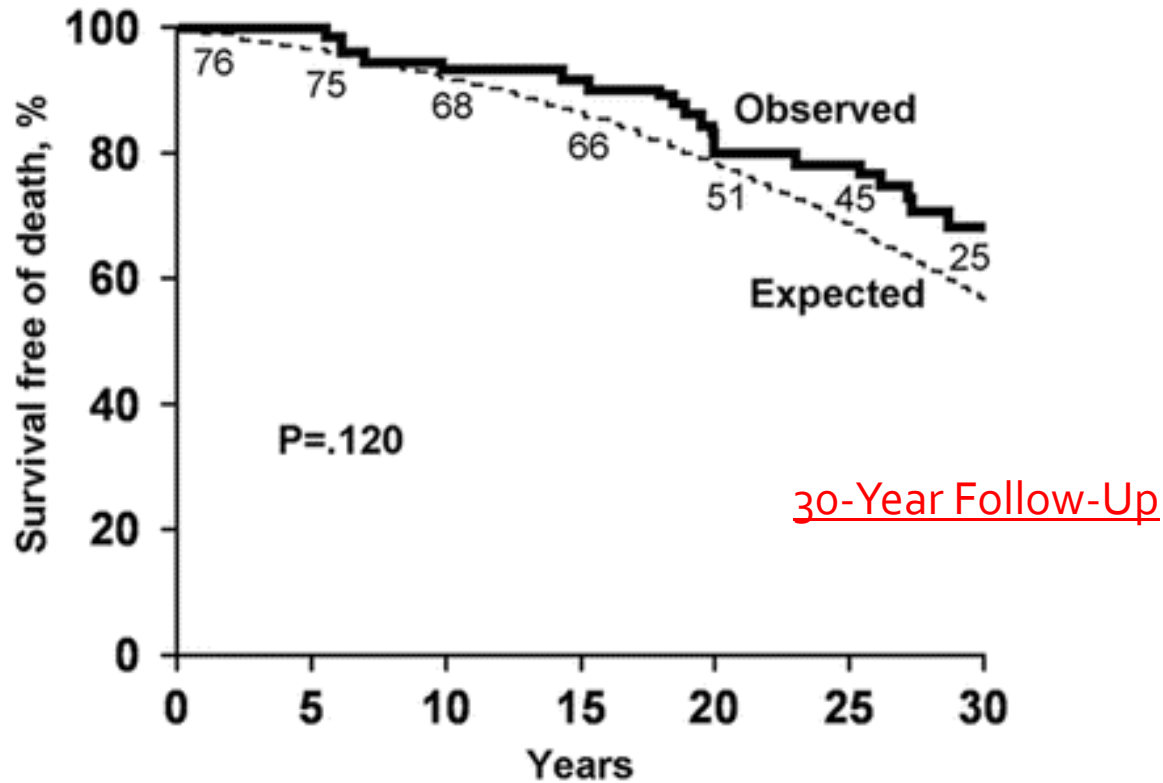
=> the risk of progression to permanent atrial fibrillation is around 20% in young patients

Mortality rate in paroxysmal atrial fibrillation

525 patients 5 y F-U	Age and sex matched Cohort free of AF n = 5000	Paroxysmal AF cohort n = 525
Person-years	14298	1606
Deaths	483	67
Mortality rate/100 person-years (95% CI)	3.38 (3.09–3.69)	4.17 (3.30–5.26)
Relative risk (95% CI)	1 	 1.2 (1.0–1.6)
Adjusted relative risk*(95% CI)	1 	 1.0 (0.75–1.3)

* Relative risk estimated by Cox regression model, including age, sex, smoking, heart failure, ischaemic heart disease, hypertension, cerebrovascular disease and diabetes.

Long-term observed survival in lone AF



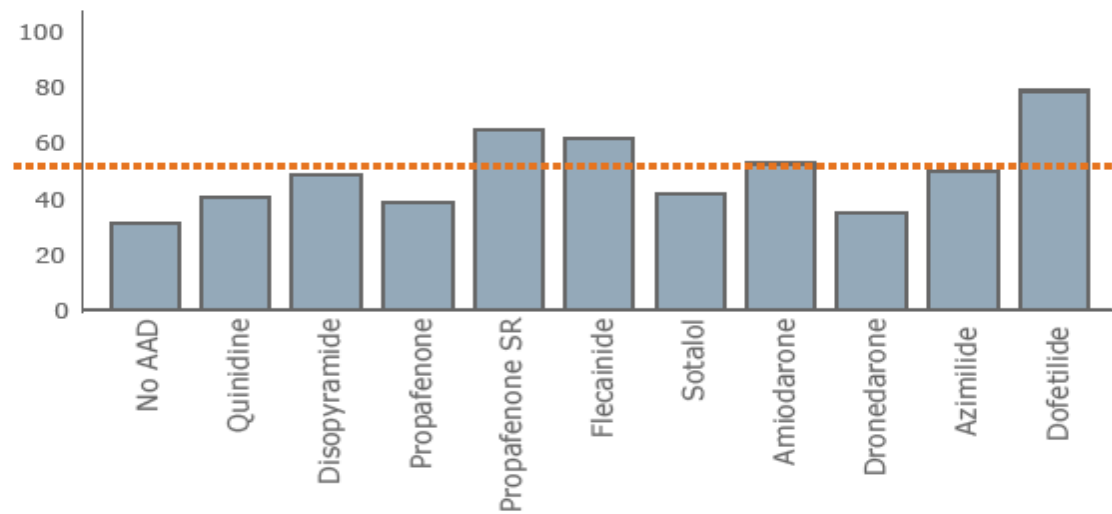
=> Patients with lone atrial fibrillation have a normal life expectancy.

=> Comorbidities significantly modulate AF prognosis and complications: hypertension, diabetes, heart failure, and advancing age ...

Long term efficacy of Anti-arrhythmic drugs

Poor long-term success

Antiarrhythmic drug



CTAF Study: % of Patients Remaining Free of Recurrence of AF

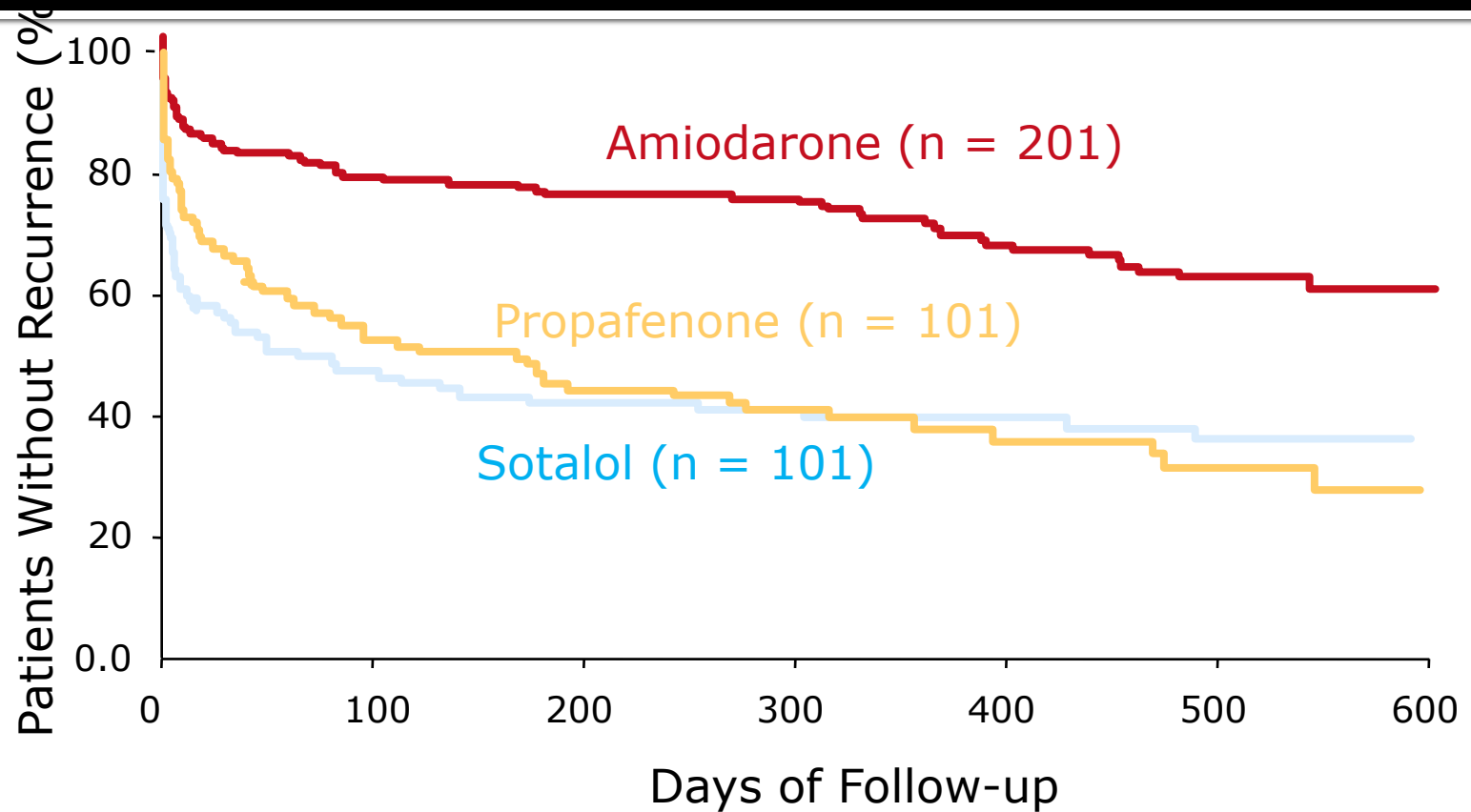


Table 1. Adverse Effects of Oral Amiodarone.

Adverse Effect	Incidence	Recommended Monitoring	Special Considerations
Cardiac		Baseline electrocardiogram at least once during loading period, especially if conduction disease is present; yearly thereafter	Consider reduction of loading dose in elderly patients and those with underlying sinoatrial or atrioventricular conduction disease; reduce dose or discontinue if QT interval exceeds 550 msec
Bradycardia	5%		
Prolonged QT interval	In most patients		
Torsades de pointes	<1%		
Hepatic	15%	Aspartate and alanine aminotransferase measurements at baseline and every 6 months thereafter	Avoid in patients with severe liver disease
Thyroid		Thyroid-function tests at baseline and two or three times a year thereafter	Avoid in presence of preexisting, non-functioning thyroid nodule; higher incidence of thyroid effects in patients with autoimmune thyroid disease
Hyperthyroidism	3%		
Hypothyroidism	20%		
Pulmonary	<3%	Pulmonary-function tests at baseline and if symptoms develop; chest radiograph at baseline and yearly thereafter	Discontinue amiodarone immediately if pulmonary effects suspected
Dermatologic	25–75%	Routine	Recommend use of sunscreen with a high sun protection factor
Neurologic	3–30%	Routine	Consider dose reduction
Ophthalmologic		Examination at baseline if there is underlying abnormality; examinations as needed thereafter	Avoid in presence of preexisting optic neuritis
Corneal deposits	100%		
Optic neuritis	<1%		



Treatment of Paroxysmal Atrial Fibrillation in Outpatient Setting.

- Out patient management of PAF can be performed using:
 - Pill-in- the-pocket.
 - Amiodarone.
 - Dronaderone.

Pill-in-the-pocket

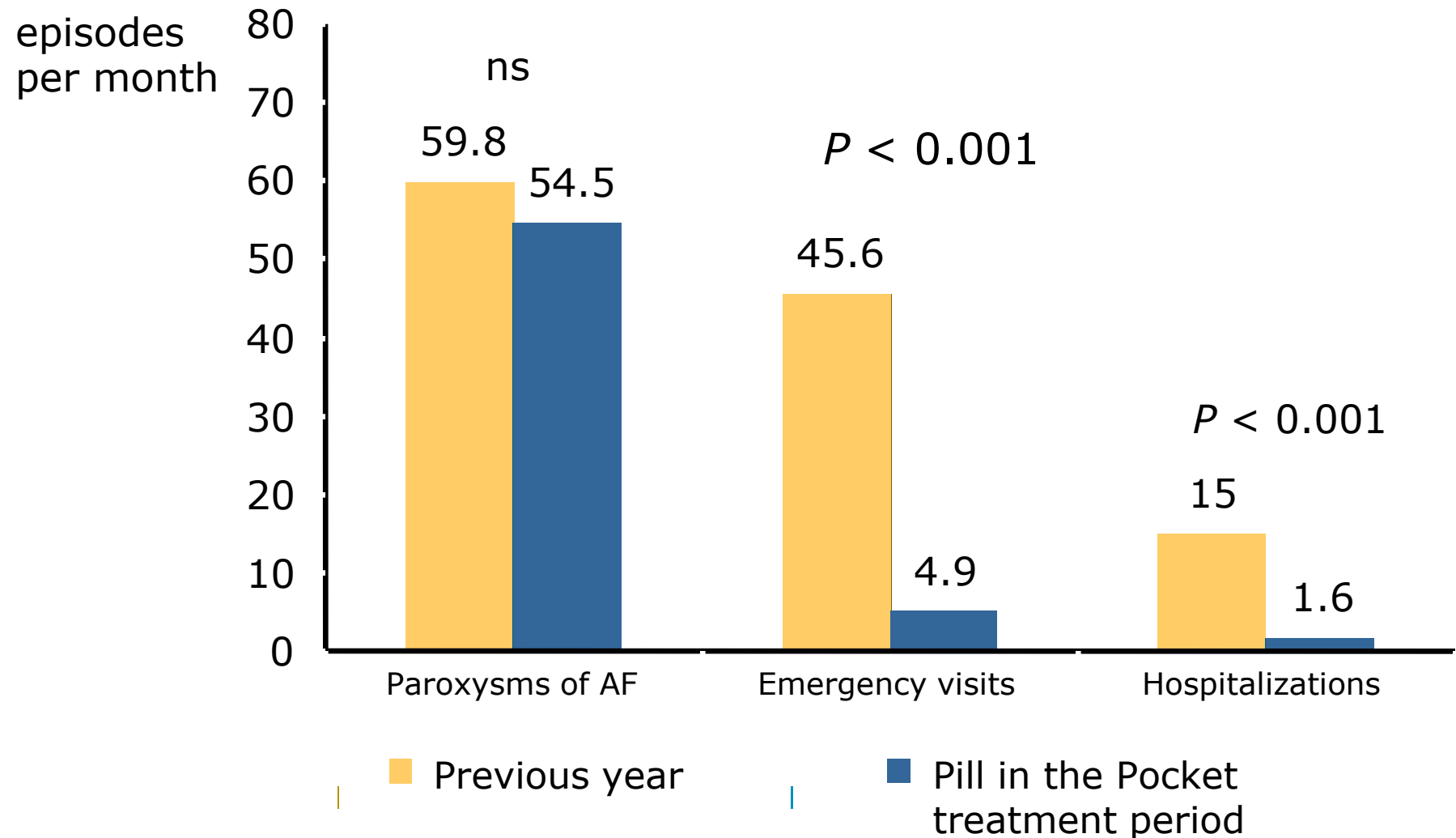
1. A beta-blocker or NDHP Ca-blocker.
 2. Half an hour later ; if symptoms persist:
 - Propafenone:
 - 600 mg if > 70kg
 - 450mg if <70 KG
 - Flecainide:
 - 300 mg if >70 kg.
 - 200 mg if < 70 kg.
- **Only once in 24 hour period.**

Pill-in-the-Pocket

- 268 patients presenting to ER with AF. given Flecanide or Propafenone.
 - 58 had treatment failure or side effects; excluded
 - Out-of-Hospital self administration of Flecanide or Propafenone studied in remaining 210.
 - 79 percent had episodes of arrhythmias
 - 92 % treated 36 ± 93 minutes after sx onset
 - Treatment succesful in 94% of episodes.

• Alboni P, et al. NEJM, 2004;351:23.

“Pill in the Pocket” Technique



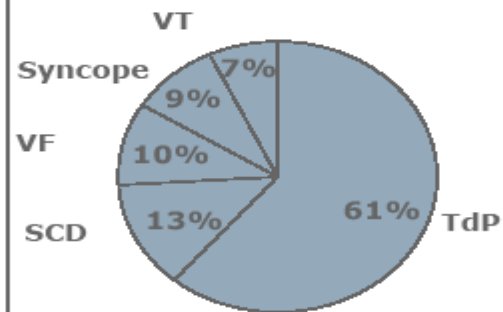
Proarrhythmia in AF patients

Atrial flutter with 1:1 AV conduction

Propafenone, Flecainide	3.7%
Quinidine	2.6%
Procainamide, Disopyramide	~ 1%

Torsade de pointes

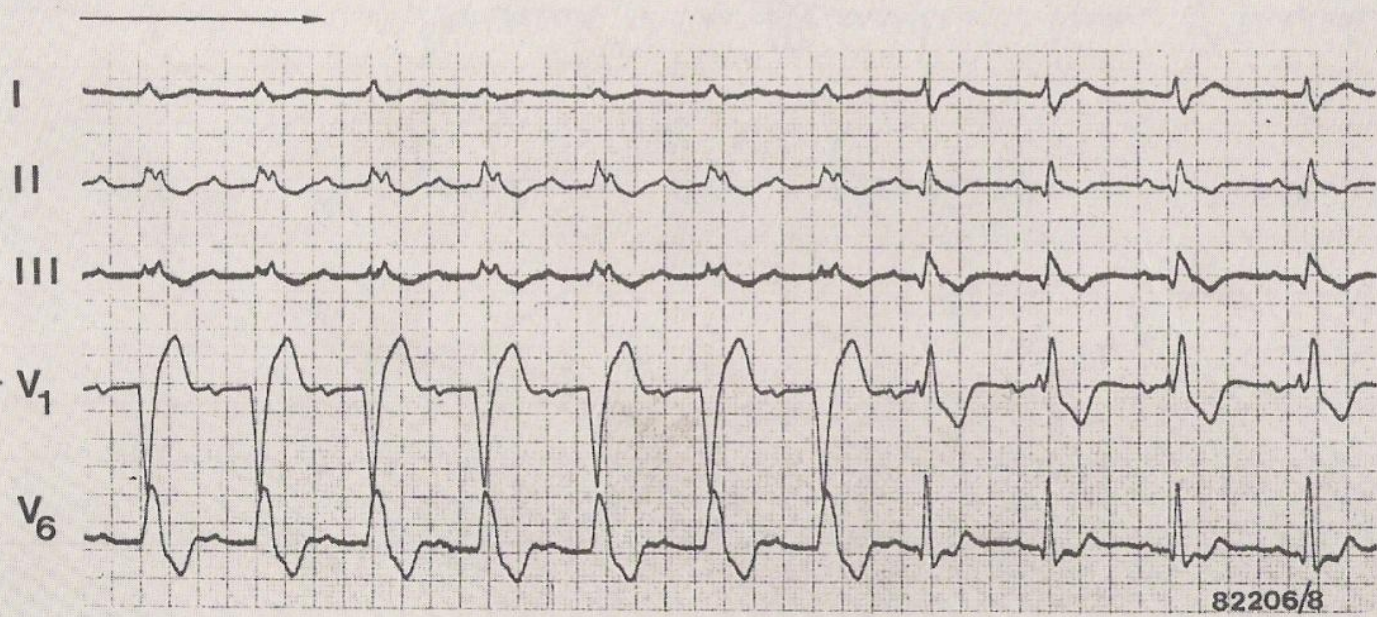
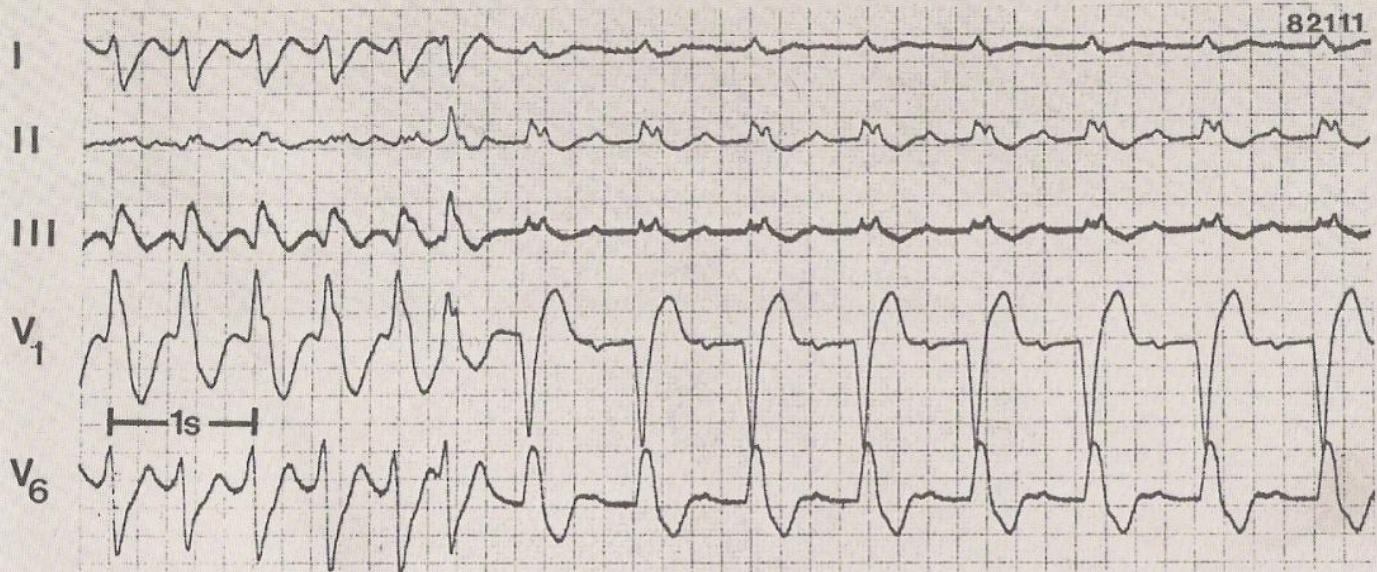
Quinidine	2%
Procainamide	~1 - 2%
Sotalol	1 - 3%
Ibutilide	0.7 - 2.7% sustained, 1.3 - 3.9% non-sustained
Amiodarone	<1%
Dofetilide	0.6%
Azimilide	0.3 - 0.9%



Source: Prystowsky EN. Am J Cardiol 1996;78:35-41; Kowey PR, et al., Am J Cardiol 1996;78:46-52; Friedman PL, et al., Am J Cardiol 1998;82:50N-58N

... For additional safety

- Treat the first episode inpatient with IC antiarrhythmics.
 - Make sure QT interval stays unchanged with therapy.
- Perform exercise stress test on therapy and document QRS interval stability prior to initiating pill-in-the-pocket technique.

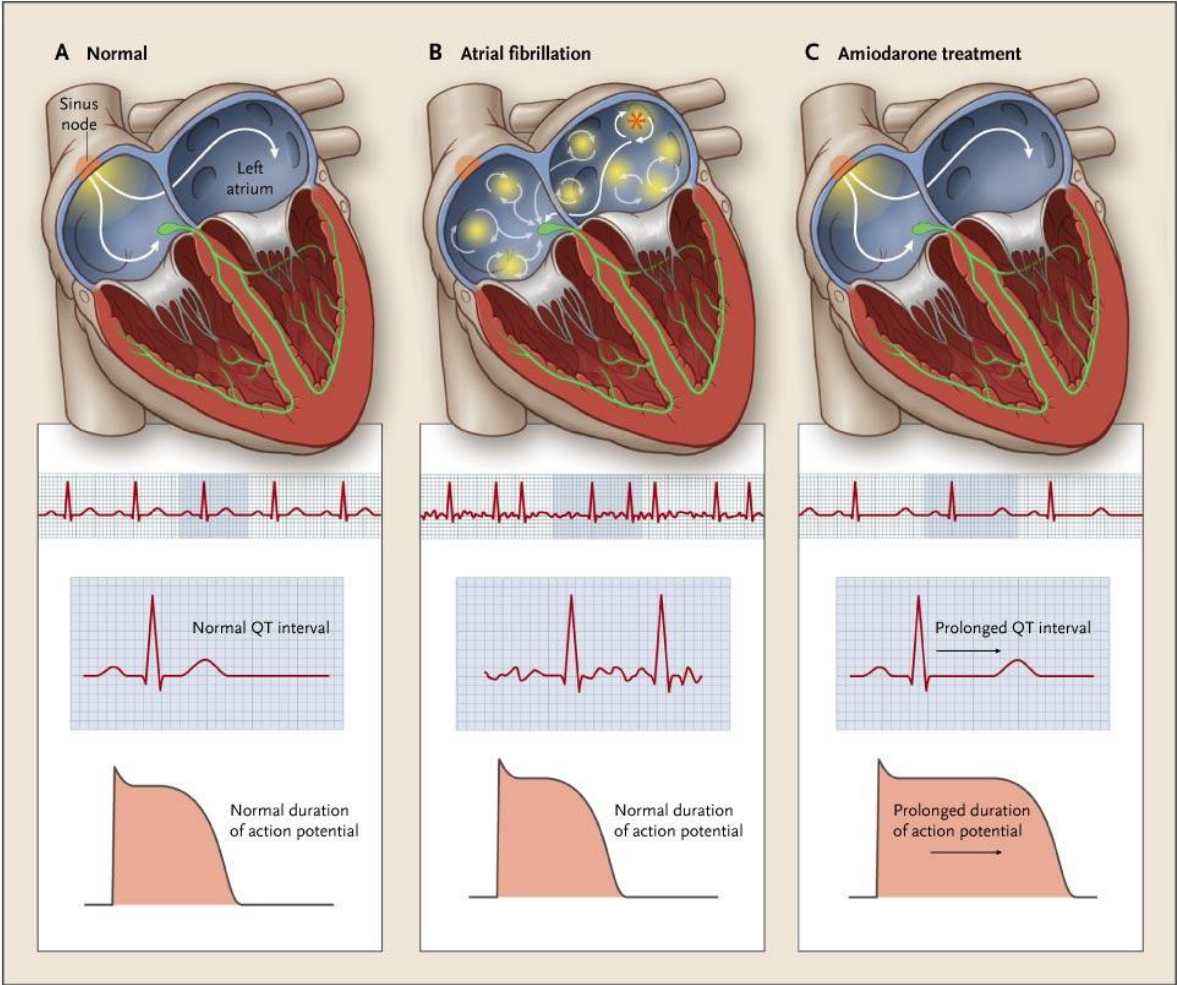


Lone Atrial Fibrillation

- Outpatient therapy of Lone AF can be performed safely and effectively if thorough patient selection with appropriate work up is performed.
- QOL is The main goal of outpatient therapy.

Amiodarone in Outpatient Setting

Dosages and precautions



Recommendations

- Baseline screening studies should include tests of liver, thyroid, and pulmonary function as well as chest radiography.
- It is reasonable to initiate amiodarone therapy in the outpatient setting.



Recommendations

- A slightly reduced loading dose (e.g., 600 mg per day in one dose or divided doses for 3 to 4 weeks) is reasonable.
- The patient should undergo electrocardiography weekly or should be discharged with a loop recorder to monitor heart rhythm, heart rate, and duration of the QT interval.
- If conversion has not occurred by the end of the loading period, electrical cardioversion should be performed, followed by a reduction in the dose of amiodarone to 200 mg daily.



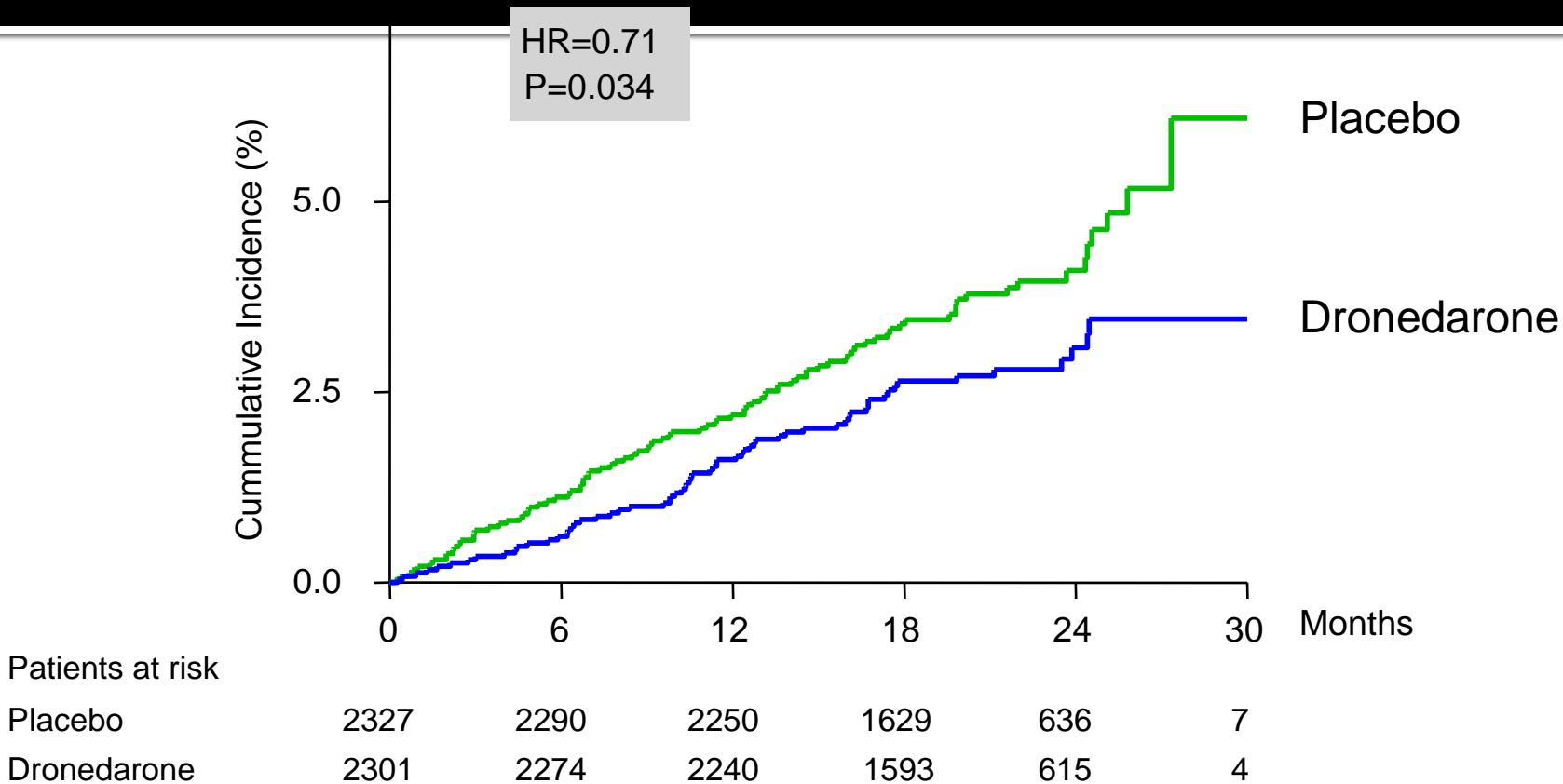
The ATHENA Trial

A placebo-controlled, double-blind, parallel arm Trial to assess the efficacy of **dronedarone** 400 mg bid for the prevention of cardiovascular Hospitalization or death from any cause in pati**EN**ts with **A**trial fibrillation / atrial flutter

ATHENA study

Hohnloser. N Engl J Med 2009;360:668-78.

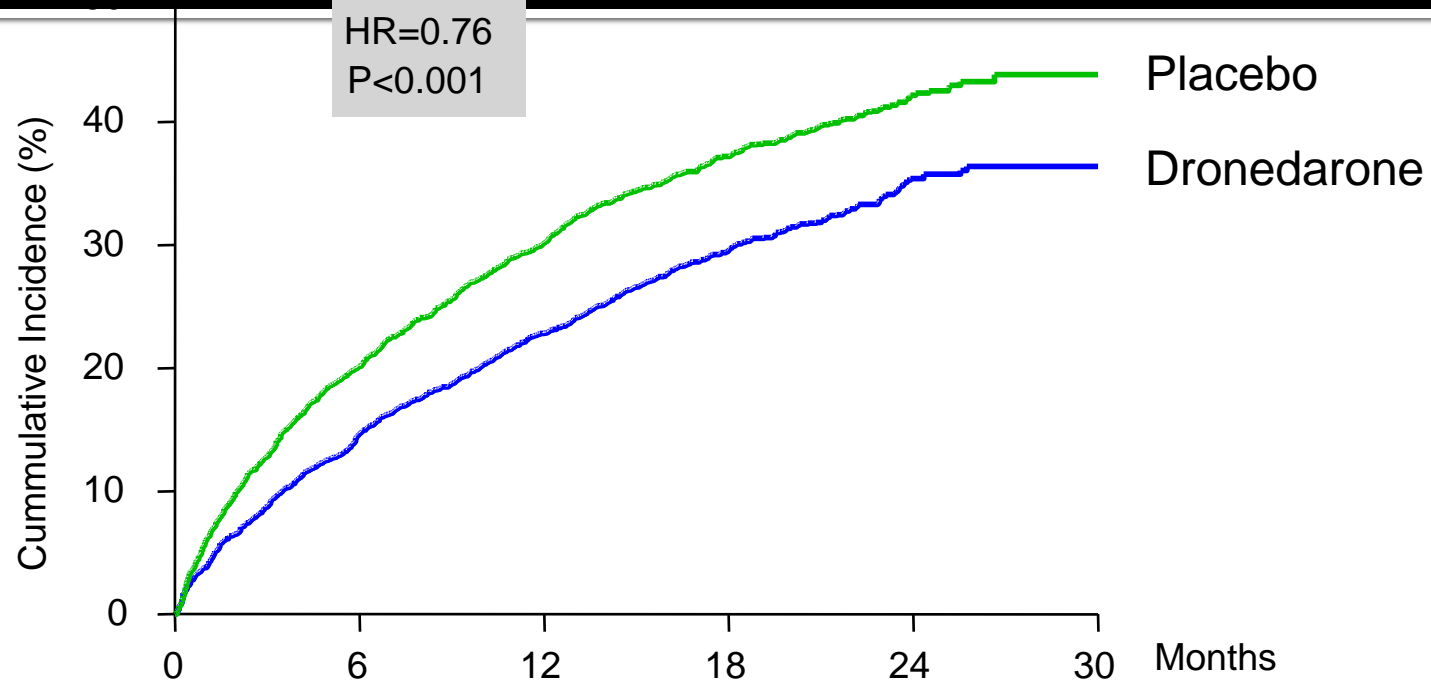
Dronedarone reduces Cardiovascular Death



ATHENA study

Hohnloser. N Engl J Med 2009;360:668-78.

Dronedarone reduces the incidence of cardiovascular hospitalization or death



Patients at risk

Placebo	2327	1858	1625	1072	385	3
Dronedarone	2301	1963	1776	1177	403	2

ATHENA study

Hohnloser. N Engl J Med 2009;360:668-78.

Dronaderone vs Amiodarone

- Meta-analysis on Dronaderone vs Amiodarone: From ANDROMEDA to DIONYSOS.
- Dronaderone less effective than amiodarone for atrial fibrillation with an odds ratio of 0.5 .
 - Less Side Effects.
 - Less efficacy.
- Dronaderone trades efficacy for safety.
 - Piccini et al, J. Am Coll Cardiol. 2009: 54:1089-1095

Conclusion:

- ❖ Lone atrial fibrillation: a benign disease.
- ❖ Strict rules should apply to outpatient therapy.
 - ❖ Careful initial screening for underlying heart disease is imperative.
- ❖ Frequent reevaluation of the substrate is a must to ensure that organic heart disease has not occurred with time.