

Assessing other risks and symptoms

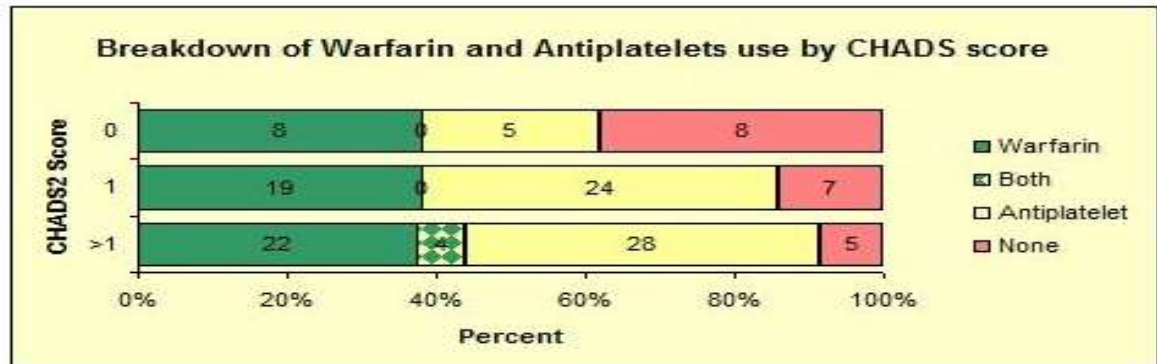
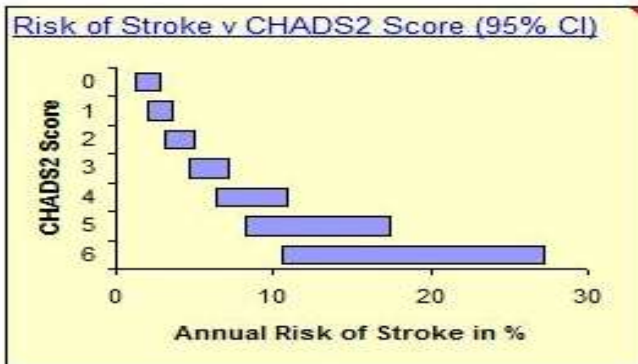
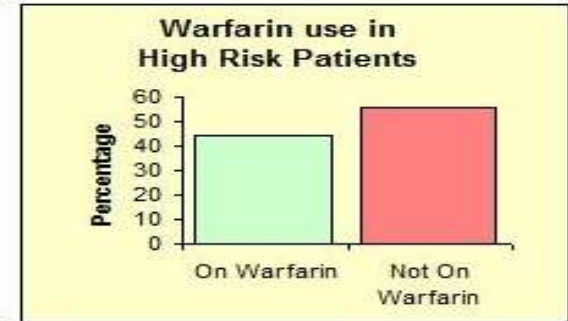
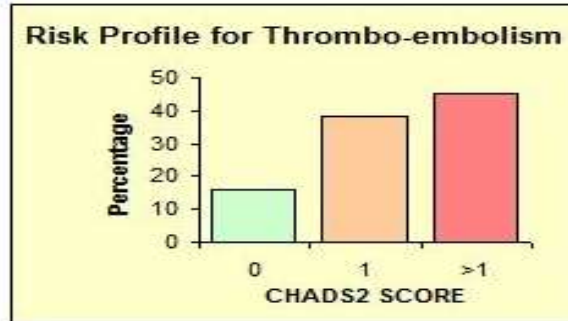
Anti arrhythmic drugs in the  
treatment pathway

AFA October 2011

# The scale of the problem of atrial fibrillation

# GRASP - AF tool

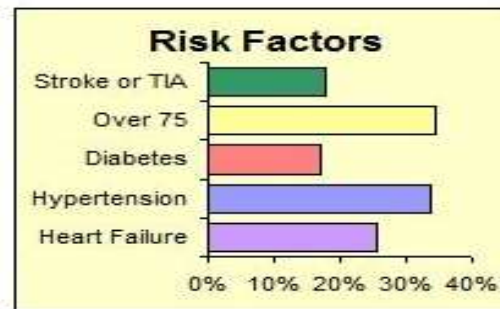
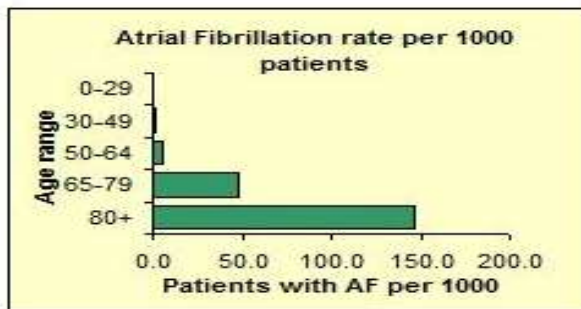
Practice Name	Any Practice	
Date of Audit	7th July 2008	
Total Practice Population	9824	
No. with Atrial Fibrillation	130	0.32%
No. over 65 with AF		0.85%



Strokes Expected Annually in untreated group of 33

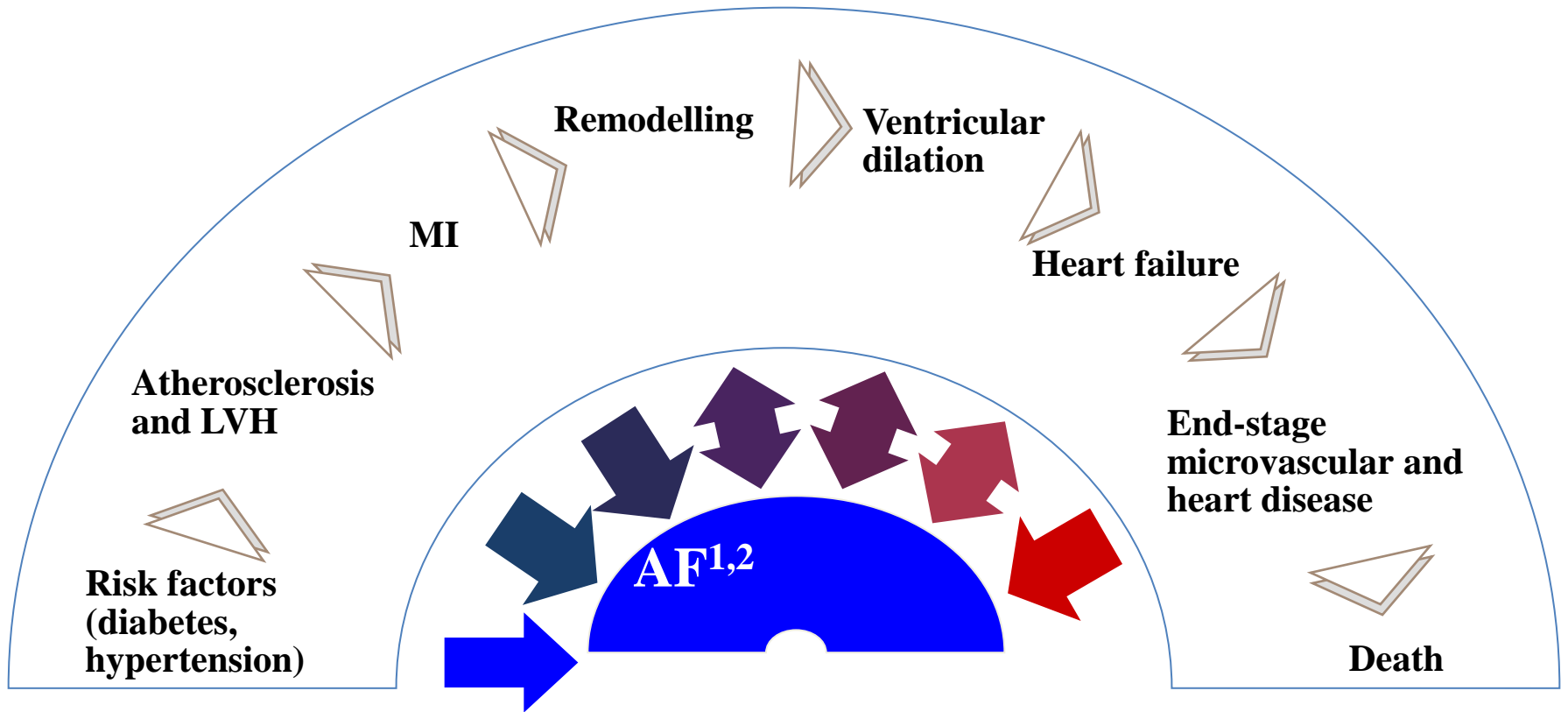
# 2.0

(95% CI 1.4 to 2.6)



[ADVICE](#)  
[REFERENCES](#)  
[PODCAST](#)

# AF is a final common pathway



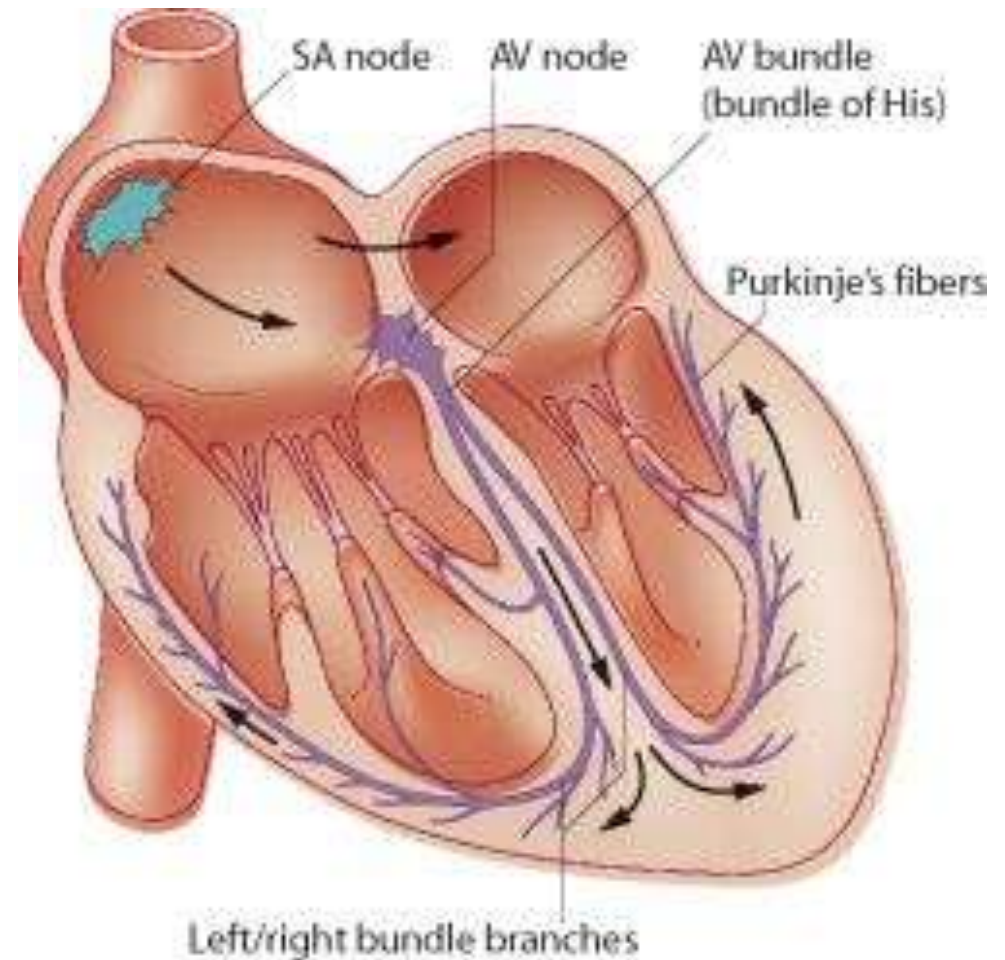
# Other diseases impacting on AF

- Hypertension
- Coronary heart disease
- Heart muscle disease

Focus today on  
Anti-arrhythmic drugs

# Strategies for rhythm management

- Rhythm control
- Rate control



# Strategies for rhythm management

- Rhythm control
  - Cardioversion
  - Anti-arrhythmic drug therapy
  - Ablation

# Strategies for rhythm management

## – Rhythm control

- Cardioversion
- Anti-arrhythmic drug therapy
- Ablation

## – Rate control

- Anti-arrhythmic drug therapy
- Pacing + A-V node ablation

# Strategies for rhythm management

## – Rhythm control

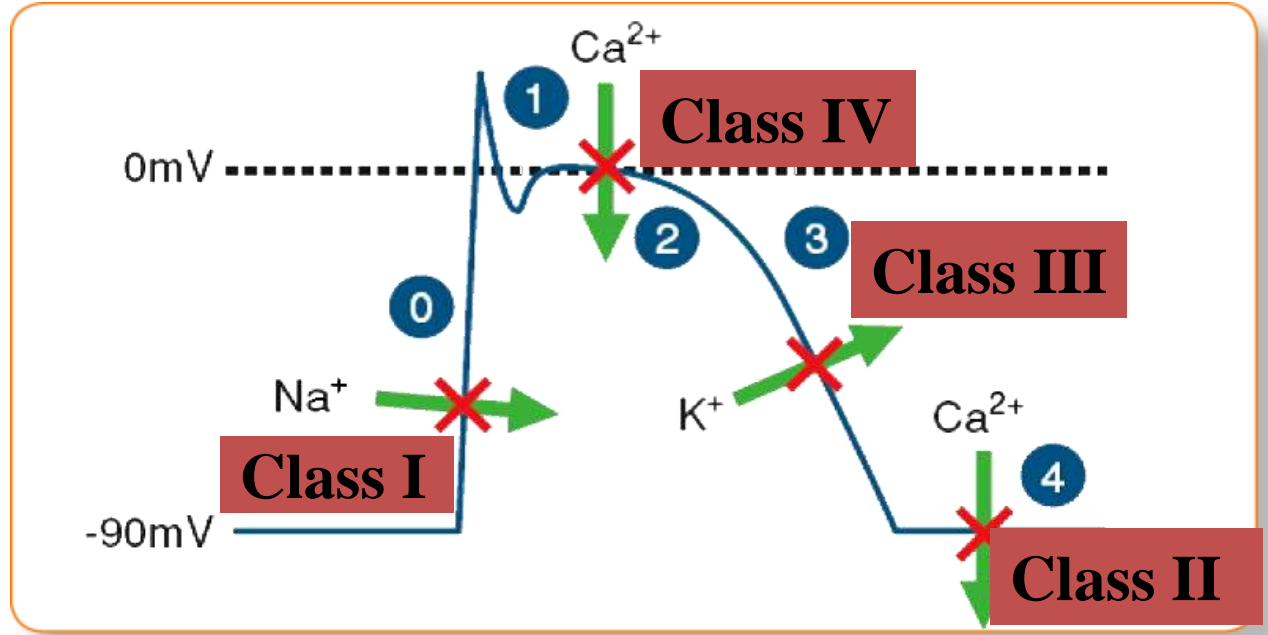
- Cardioversion
- Anti-arrhythmic drug therapy
- Ablation

## – Rate control

- Anti-arrhythmic drug therapy
- Pacing + A-V node ablation

# Classification of anti-arrhythmic drugs

- AADs have distinct characteristics depending on which ion channels they block

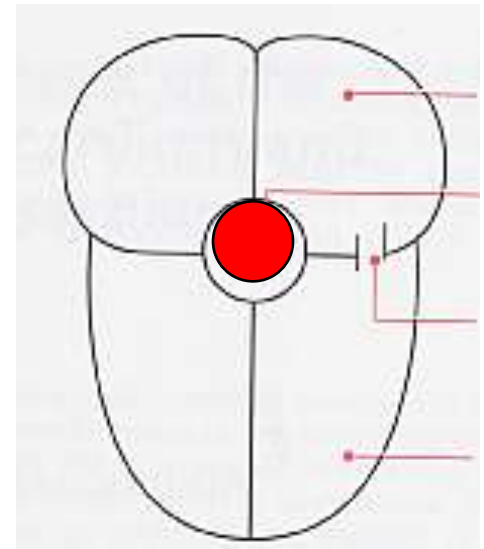


	Vaughan-Williams class			
	I (incl. IA, IB, IC)	II	III	IV
Channels blocked	Na <sup>+</sup>	β-receptors	K <sup>+</sup>	Ca <sup>2+</sup>
Action potential phase	0	4	3	2
Main uses in AF	Rhythm control	Rate control	Rhythm control	Rate control

# Classes of anti-arrhythmic drug

- **Class I - Sodium channel blockers**
  - Slow conduction of cardiac impulse
- **Class II - Beta blockers**
  - Oppose the effects of adrenaline on the heart
- **Class III - Drugs like amiodarone**
  - Prolong duration of the heart's electrical activity
- **Class IV - Calcium blockers**
  - Slow conduction from atrium to ventricle

# Drugs for rate control



## Class II

- Beta-blockers (e.g. propranolol)

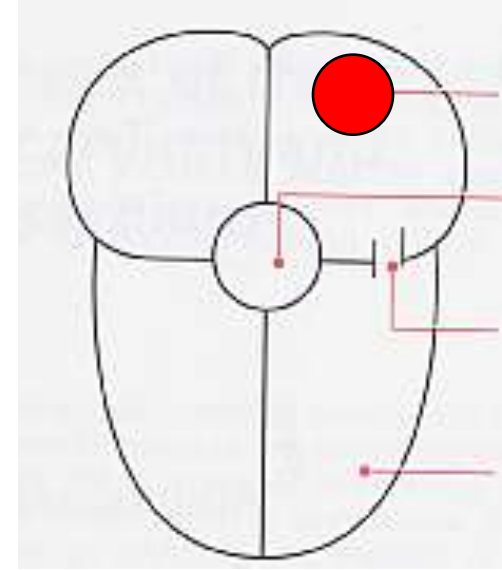
## Class IV

- Non-dihydropyridine calcium channel antagonists (verapamil and diltiazem)

## Cardiac glycoside

- Digoxin

# Drugs for rhythm control



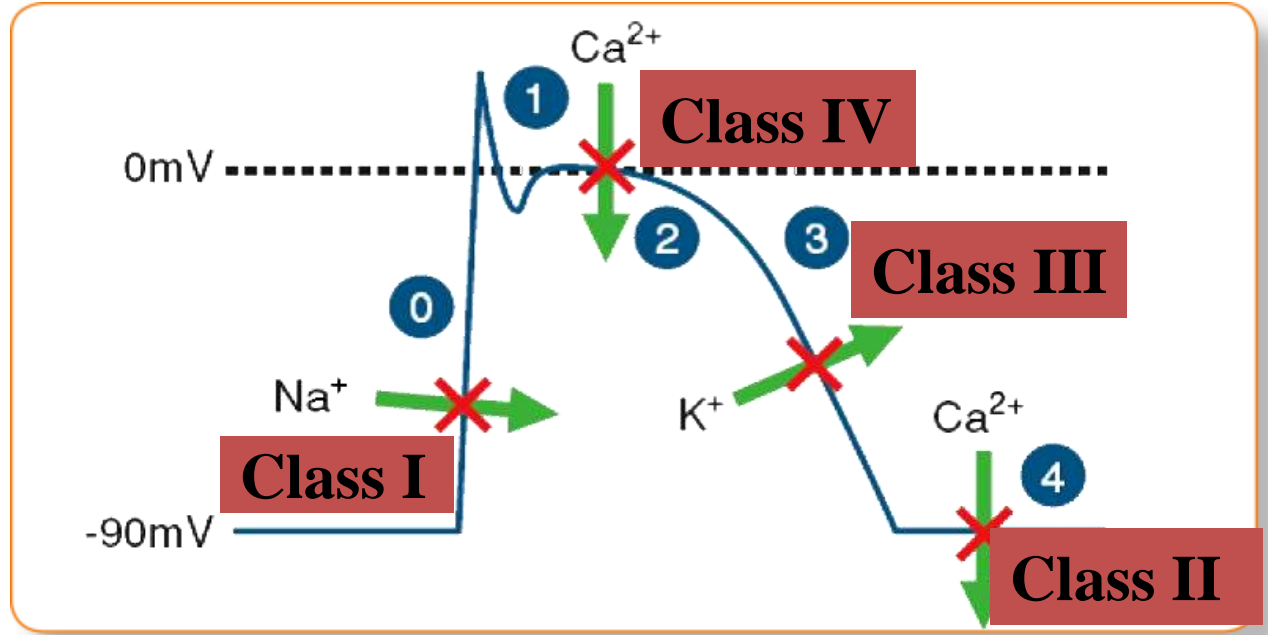
<b>Class IA</b>	<ul style="list-style-type: none"><li>• Disopyramide</li><li>• Procainamide</li></ul>
<b>Class IB</b>	<ul style="list-style-type: none"><li>• (none)</li></ul>
<b>Class IC</b>	<ul style="list-style-type: none"><li>• Flecainide</li><li>• Propafenone</li></ul>
<b>Class II</b>	<ul style="list-style-type: none"><li>• Beta-blockers</li></ul>
<b>Class III</b>	<ul style="list-style-type: none"><li>• Amiodarone</li><li>• Sotalol</li></ul>

AF=atrial fibrillation

NICE Clinical Guideline 36. Available at: [www.nice.org.uk/CG036](http://www.nice.org.uk/CG036)

# Classification of anti-arrhythmic drugs

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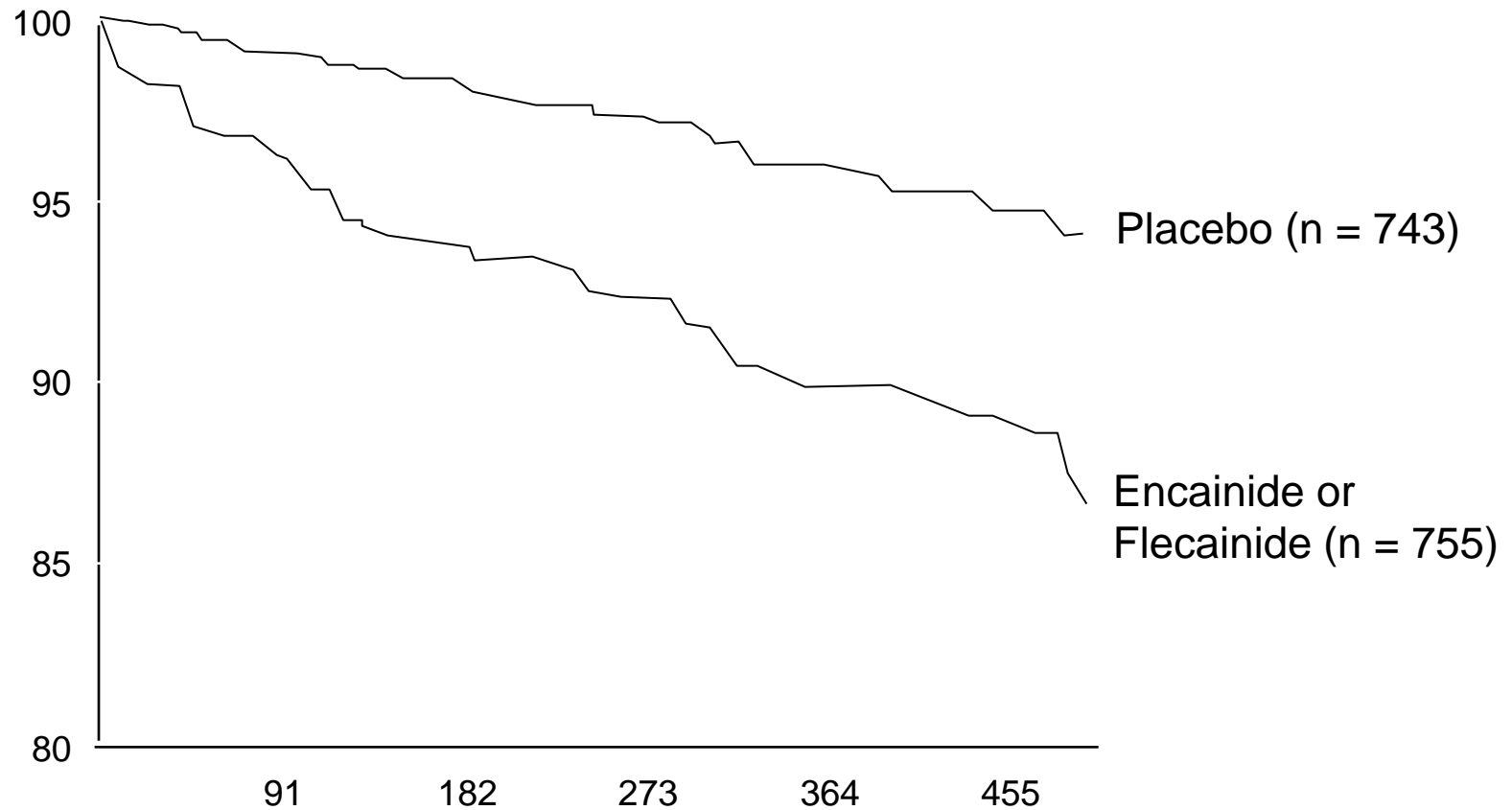


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# **Characterization of a new oral antiarrhythmic drug, flecainide (R818)**

- **J. Campbell Cowan, E. Miles Vaughan Williams**
- The Department of Pharmacology, South Parks Road, Oxford University, Oxford, OX1 3QT, U.K.
- Received 6 January 1981; revised 24 March 1981; Accepted 19 May 1981. Available online 20 November 2002.

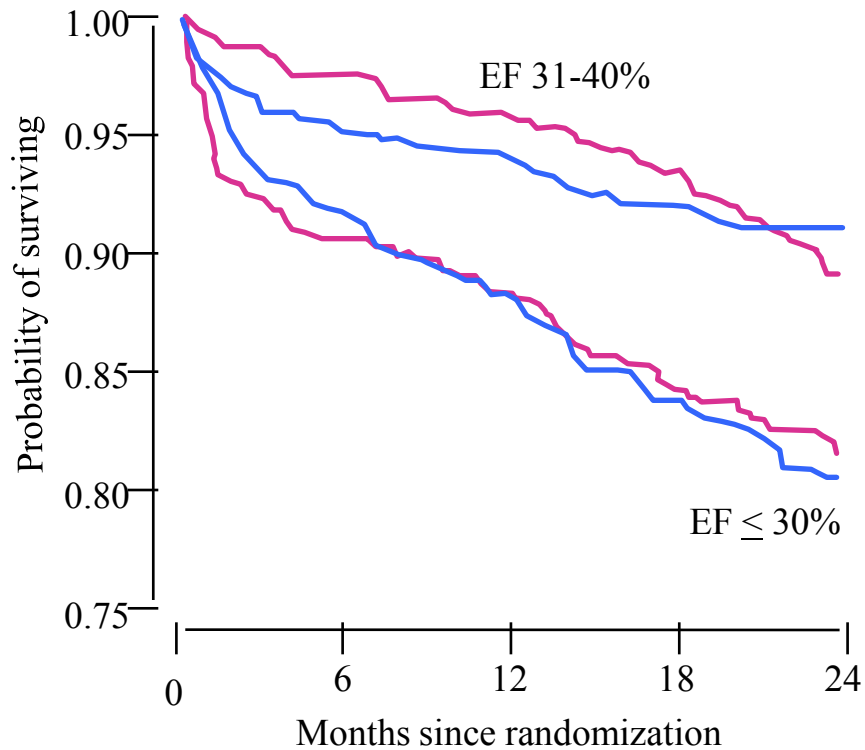
# Flecainide - CAST study 1991



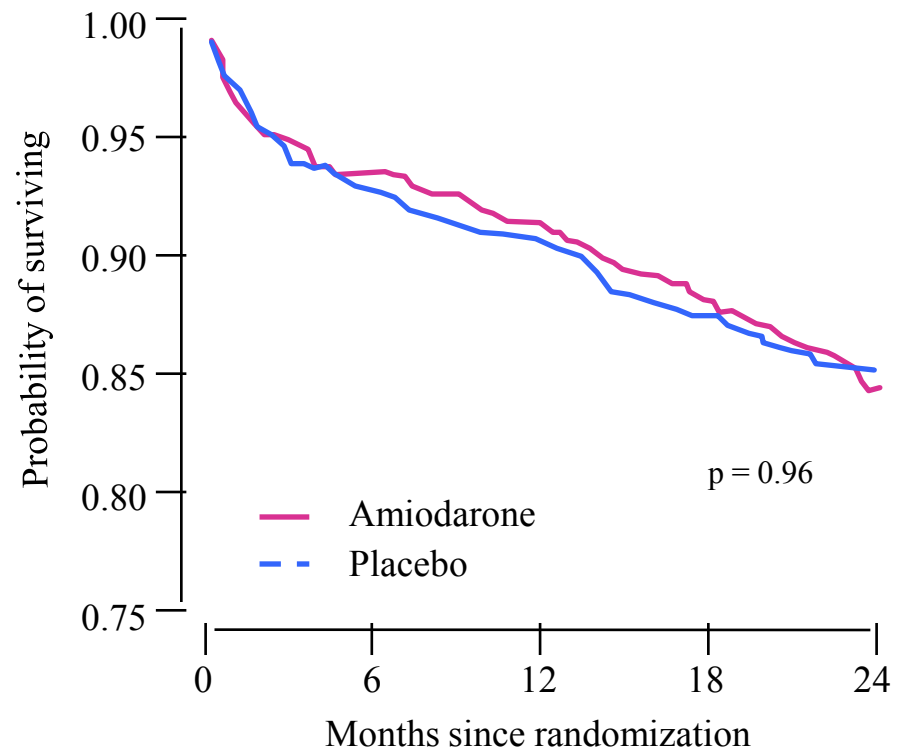
# EMIAT Results

## All-Cause Mortality

By group and ejection fraction



By group



# Amiodarone toxicity / side effects

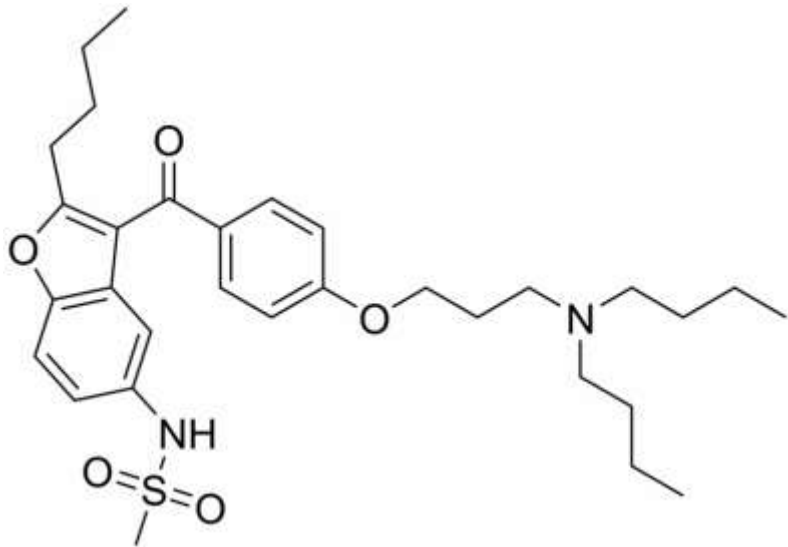
## Toxicity

- Pulmonary fibrosis
- Hypo- or hyper-thyroidism
- Liver failure
- Bone marrow suppression
- Renal failure
- Photosensitivity
- Corneal deposits

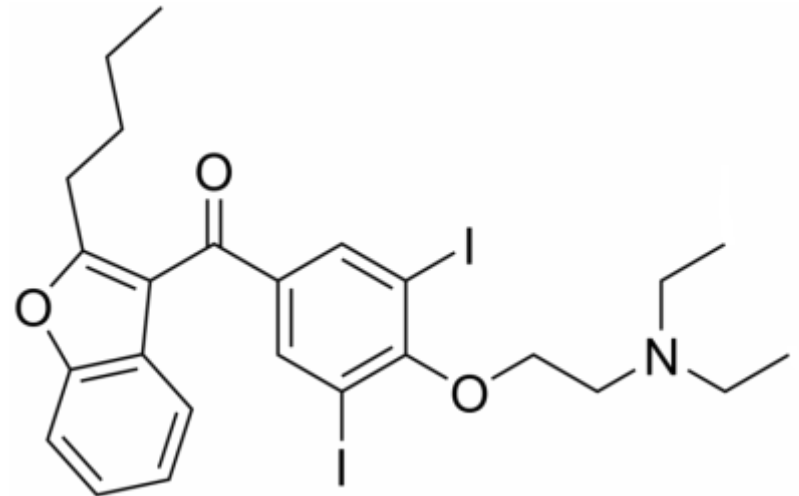
## Side effects

- Myalgias
- Gait disturbance
- Insomnia
- Prolongation of coagulation time (PT)  
(need to reduce coumadin dosage)
- Digoxin toxicity (need to reduce digoxin dosage)

# Dronedarone structure



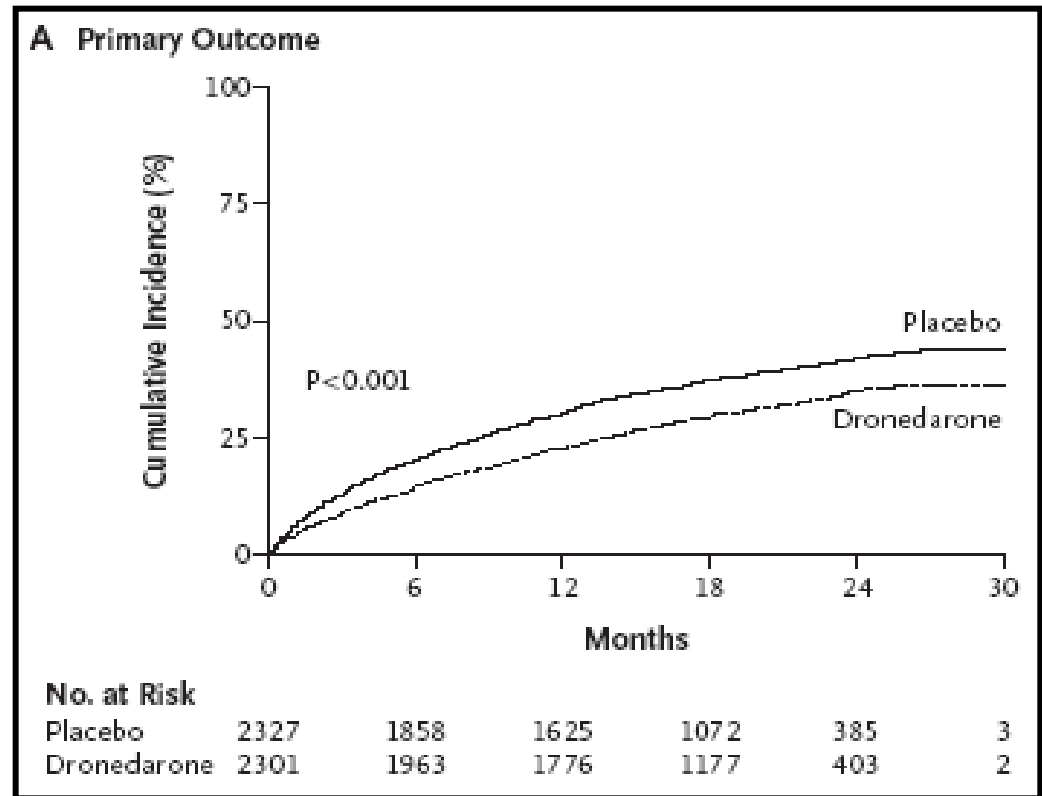
Dronedarone



Amiodarone

# Dronedarone: ATHENA

- 4628 pts randomised to Dronedarone or Placebo
- Paroxysmal or recently Persistent AF or Flutter
- $\geq 70/75$  yrs old, and at least 1 risk factor
- Primary outcome: Time to 1<sup>st</sup> hospitalisation or death



# Dronedarone - problems

- Patients with heart failure – ANDROMEDA study

# Dronedarone - problems

- Patients with heart failure – ANDROMEDA study
- Concern over potential hepatotoxicity

# **Dronedarone advisory - 19 January 2011**

## **Information on severe liver injury associated with the use of Multaq (dronedarone).**

### **Dear Healthcare Professional**

#### **Summary**

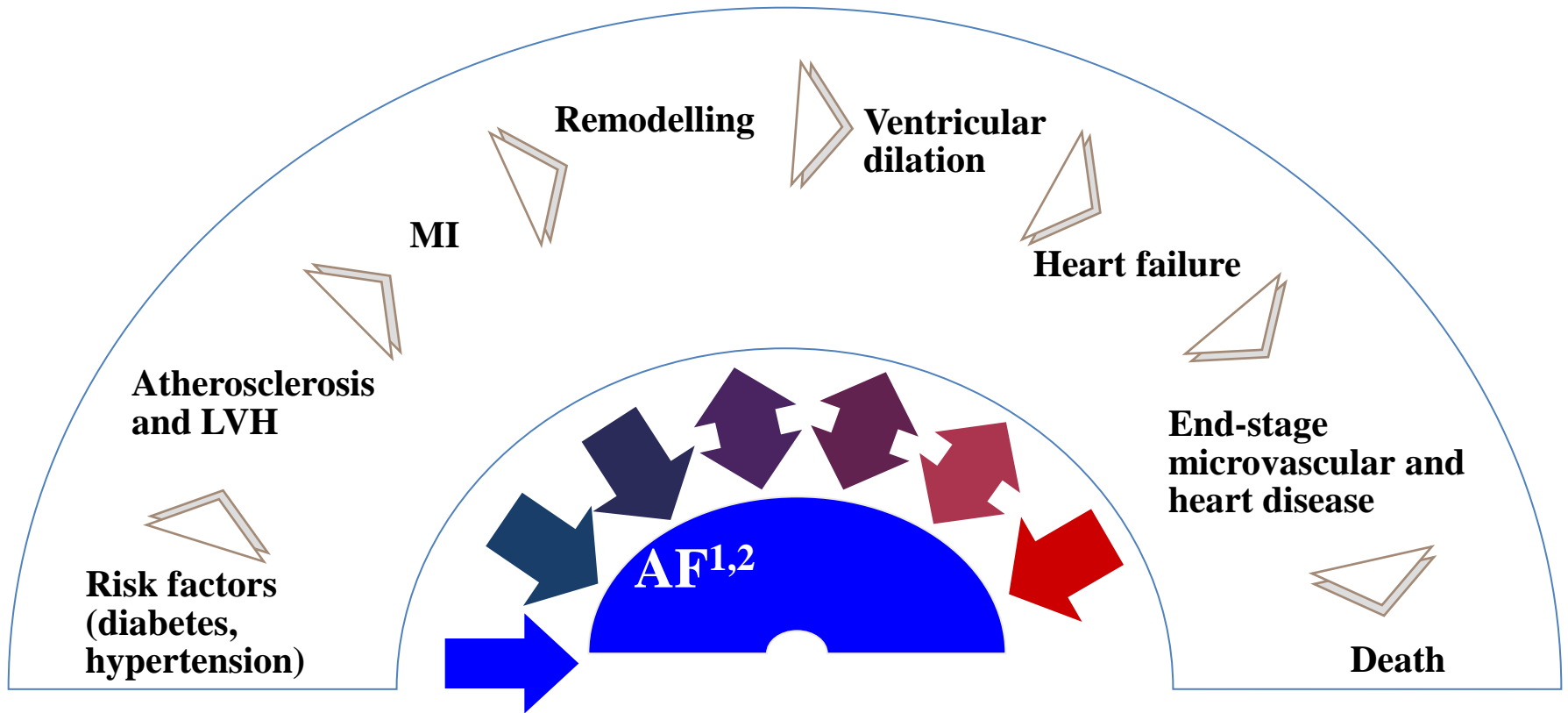
- Cases of liver injury, including two cases of liver failure requiring transplantation have been reported in patients receiving dronedarone. Some of these cases have occurred early after start of treatment.

○Liver function tests should be performed prior to initiation of treatment with dronedarone and then repeated monthly for six months, at months 9 and 12, and periodically thereafter.

# Dronedarone - problems

- Patients with heart failure – ANDROMEDA study
- Concern over potential hepatotoxicity
- Concern over adverse effects in patients with permanent AF – PALLAS study

# The spectrum of AF



# Anti-arrhythmic drugs

- No problems with rate control strategy
- But issues with drugs for rhythm control
  - Side effects
  - Potential for serious adverse reactions
  - Risks increase with extent of heart disease
- In considering drugs for rhythm control, need to give very serious consideration to alternative strategies
  - Rate control
  - Ablation