

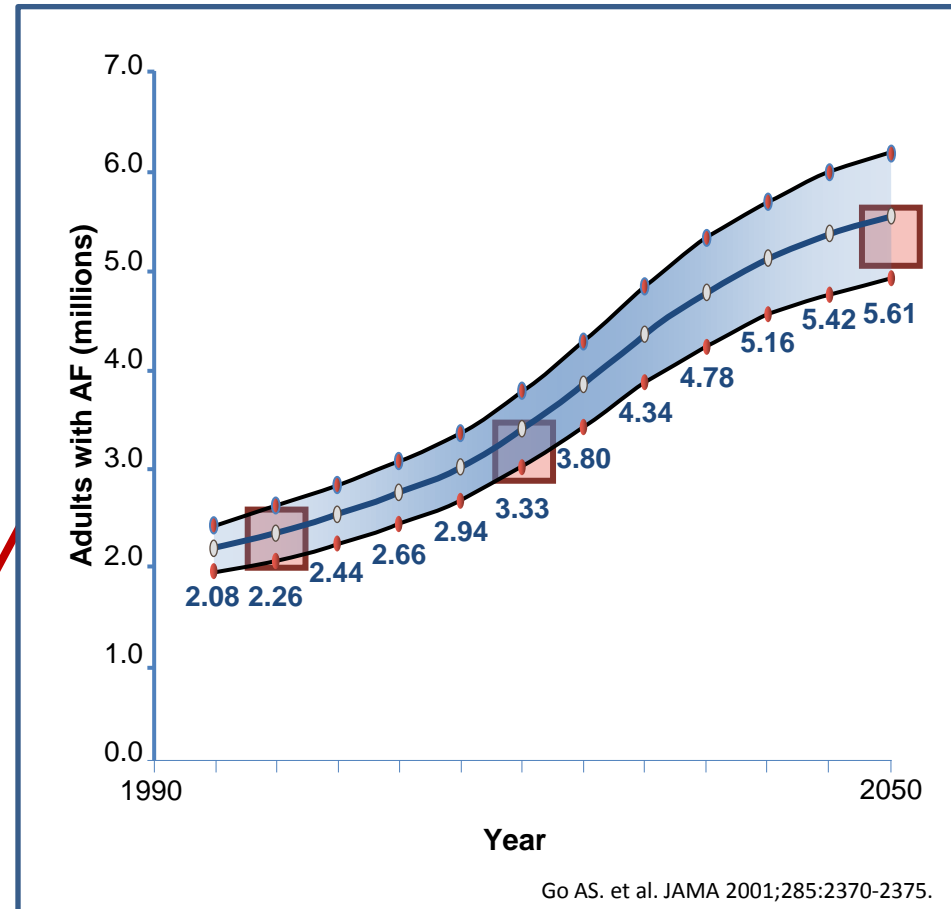
# New therapeutic options in atrial fibrillation

Hielko Miljoen  
UZA Edegem, BE

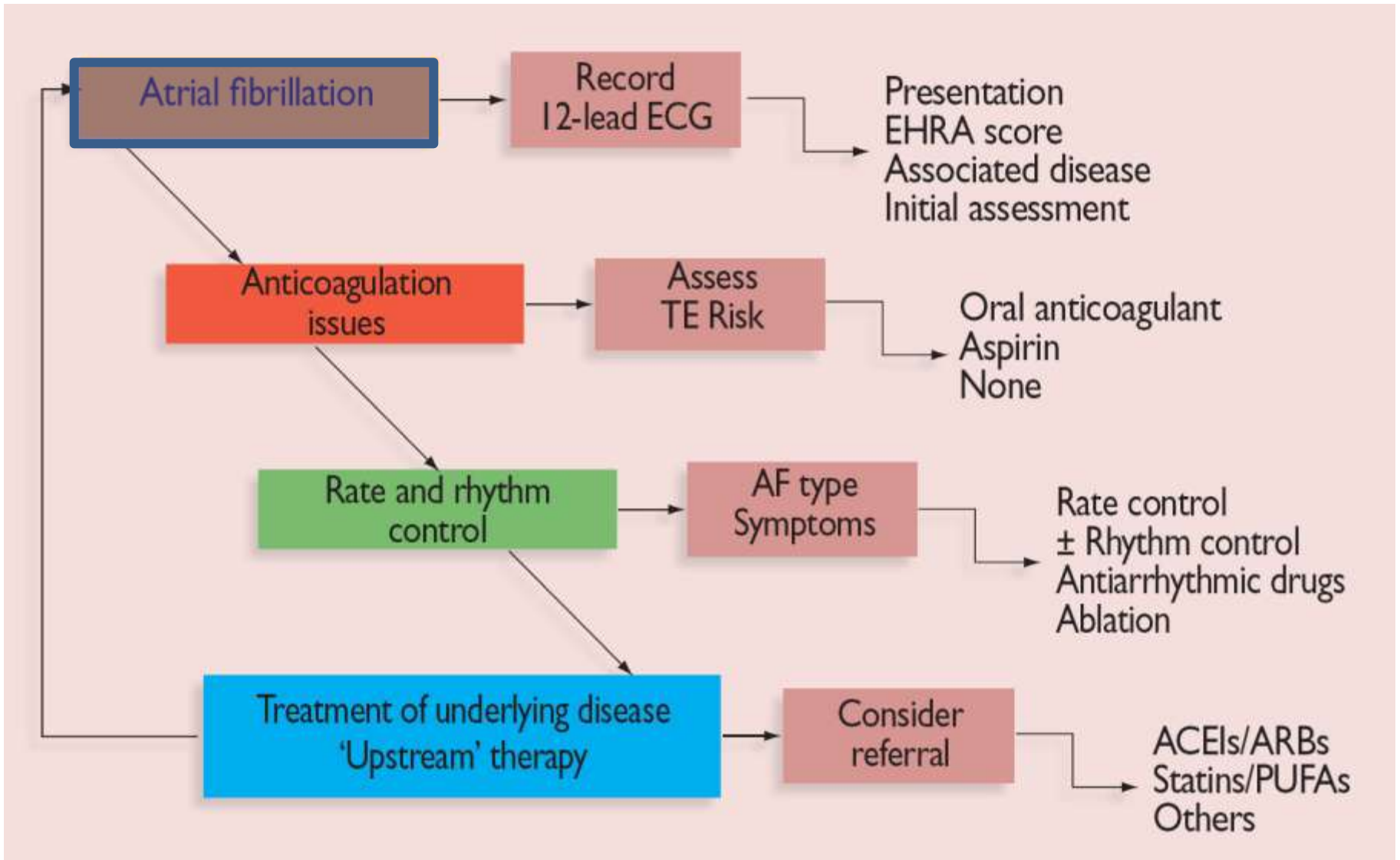
**NO DISCLOSURES**

# Natural History of Atrial Fibrillation

Outcome parameter	Relative change in AF patients
1. Death	Death rate doubled.
2. Stroke (includes haemorrhagic stroke and cerebral bleeds)	Stroke risk increased; AF is associated with more severe stroke.
3. Hospitalizations	Hospitalizations are frequent in AF patients and may contribute to reduced quality of life.
4. Quality of life and exercise capacity	Wide variation, from no effect to major reduction. AF can cause marked distress through palpitations and other AF-related symptoms.
5. Left ventricular function	Wide variation, from no change to tachycardiomyopathy with acute heart failure.



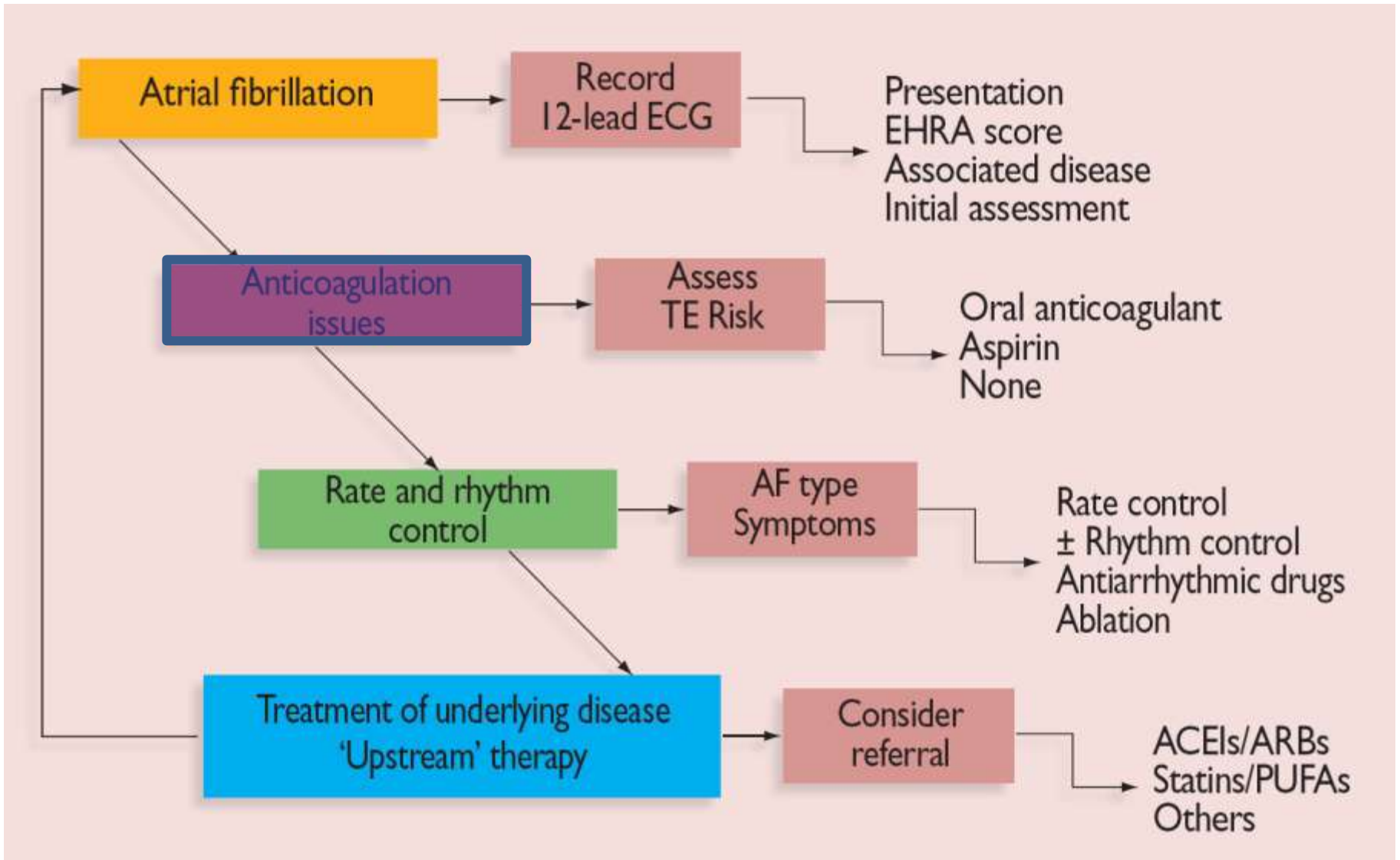
Time





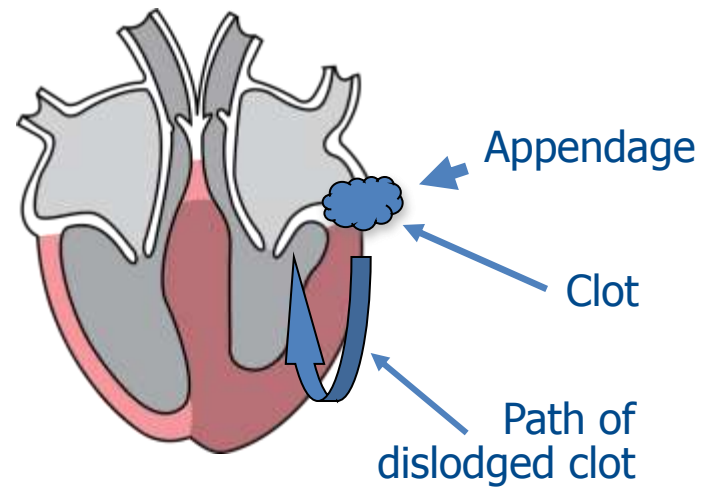
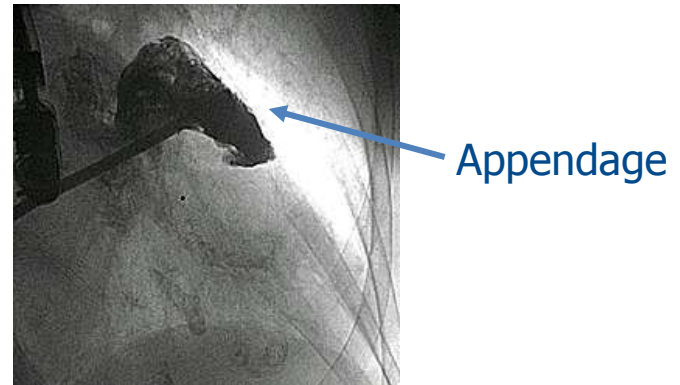
## Classification of AF-related symptoms (EHRA score)

<b>EHRA class</b>	<b>Explanation</b>
<b>EHRA I</b>	‘No symptoms’
<b>EHRA II</b>	‘Mild symptoms’; normal daily activity not affected
<b>EHRA III</b>	‘Severe symptoms’; normal daily activity affected
<b>EHRA IV</b>	‘Disabling symptoms’; normal daily activity discontinued



# Risk of Thrombus in AF

- Atria do not contract properly leading to stasis in the left atrium and appendage (LAA)
- LAA is a small muscular pouch attached to the main atrial chamber
- In non-valvular AF, ~90% of atrial thrombi occur in the LAA



**Sintrom 4 mg**

Acenocumarol

comprimidos

Via oral



**Marcoumar<sup>®</sup>**

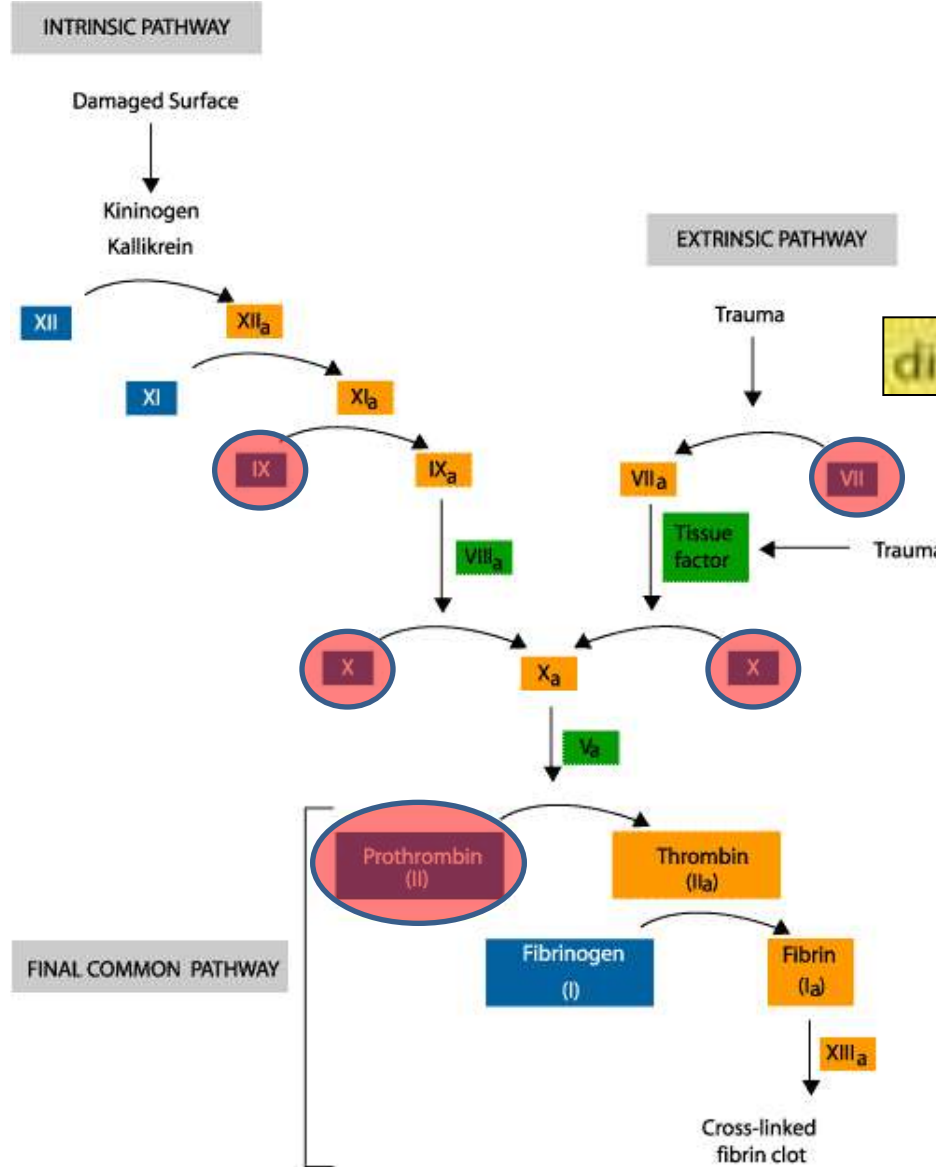
fenprocoumon

**3 mg**

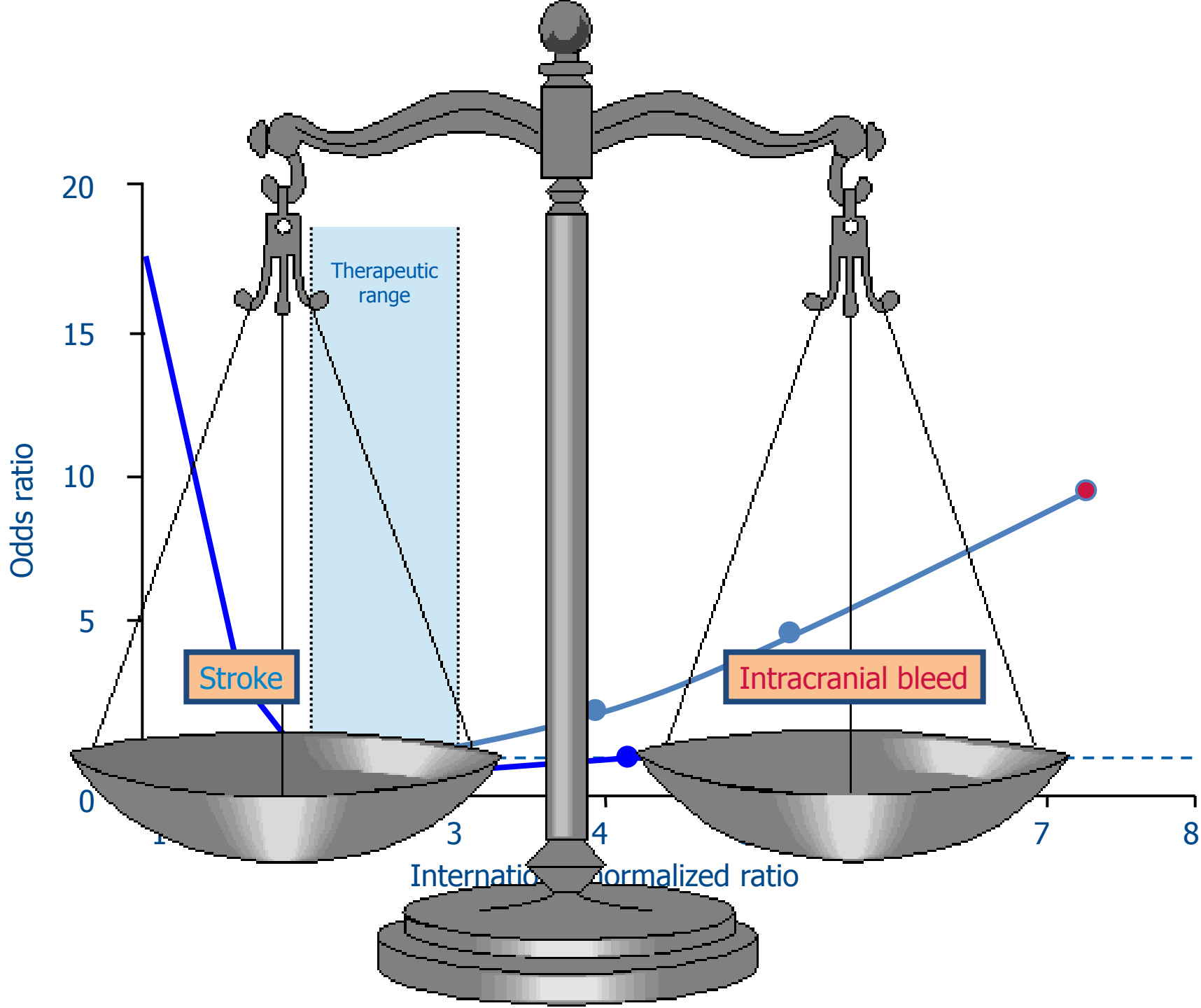
250 tabletten



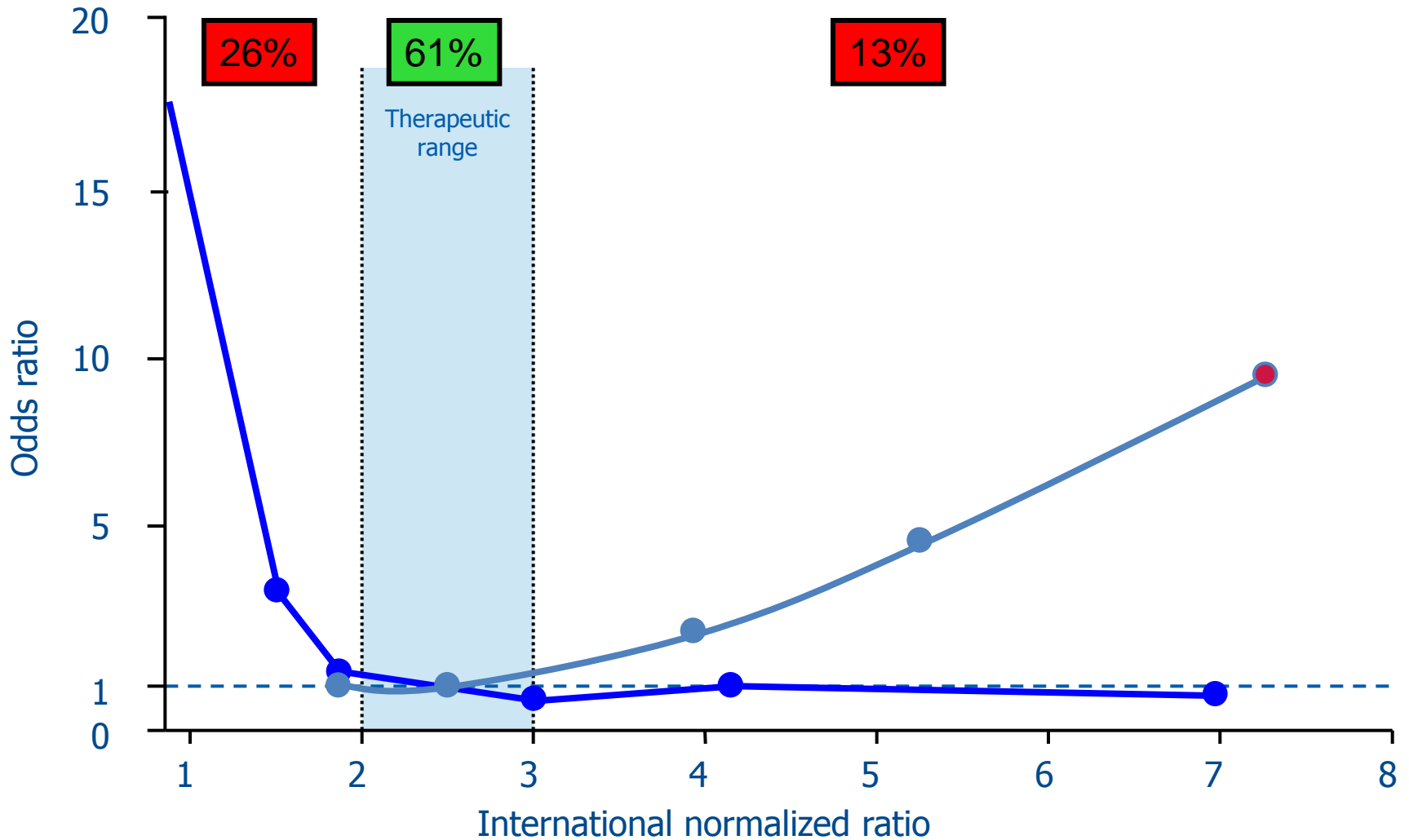
# R/ Warfarin



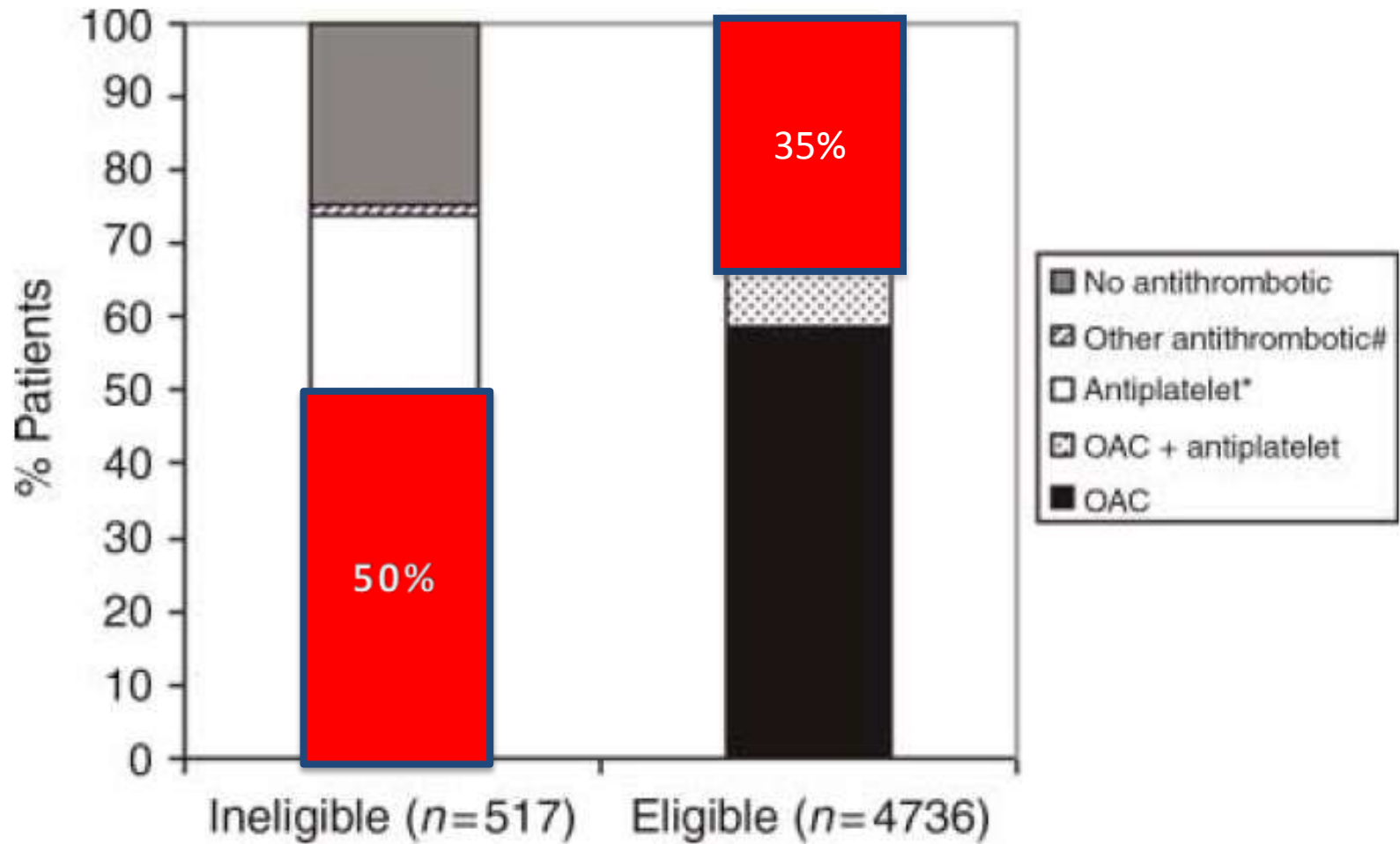




# Time in Target Range INR



# Real Life OAC Prescription





# Requirements of new antithrombotic agents

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At least as effective as warfarin

Predictable response

Wide therapeutic window

Low incidence and severity of adverse effects

Oral fixed dose

No need for routine anticoagulation monitoring

Low potential for food or drug interactions

Fast onset and offset of action

Cost-effective

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# Novel Antithrombotic Therapies

Tissue factor/VIIa

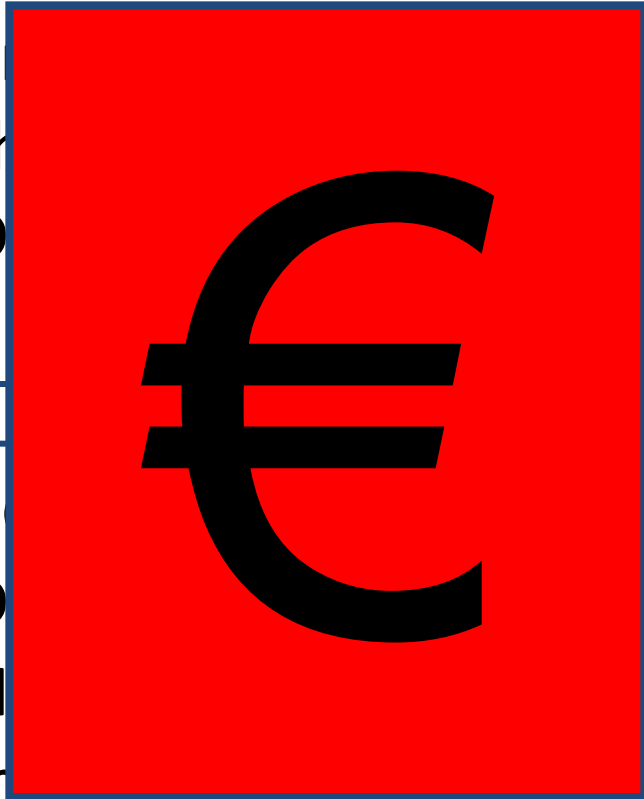


# Direct Thrombin Inhibitor(s)

stroke or systemic

## Conclusions Re-Ly:

- Dabi 110 bid as effective
- Dabi 150 bid as effective



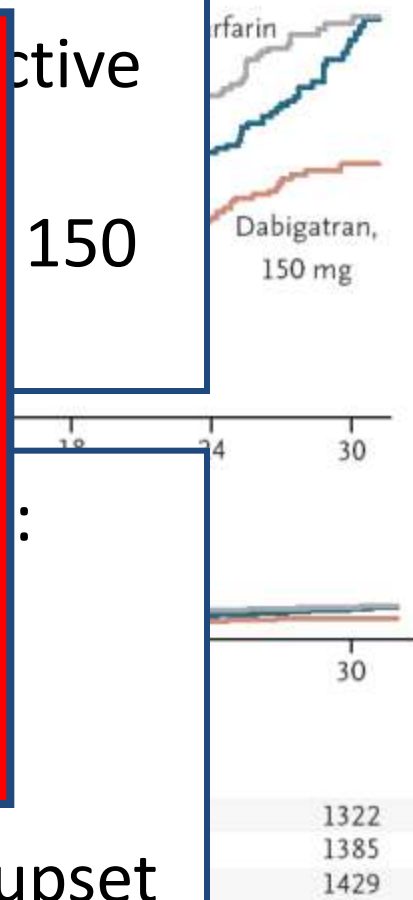
## Side Effects:

- Dizziness
- Headache
- Indigestion
- Mild stomach pain or upset
- Nausea

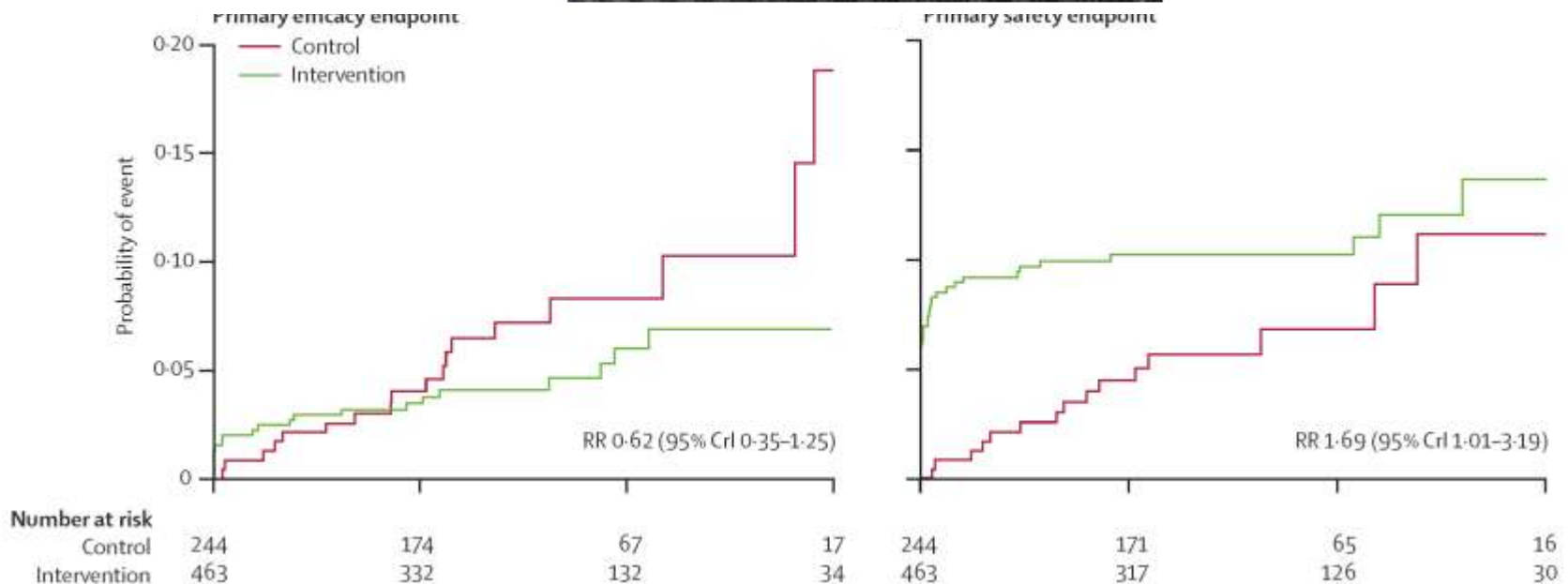
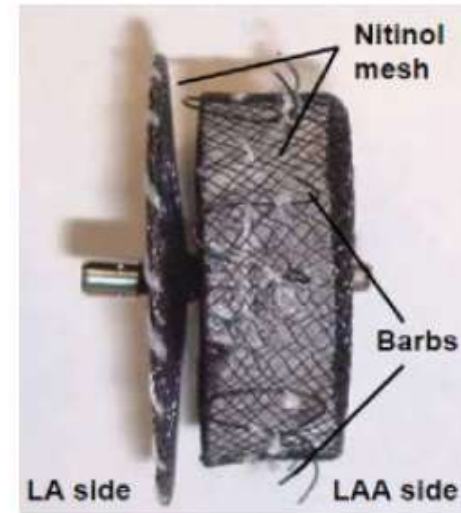
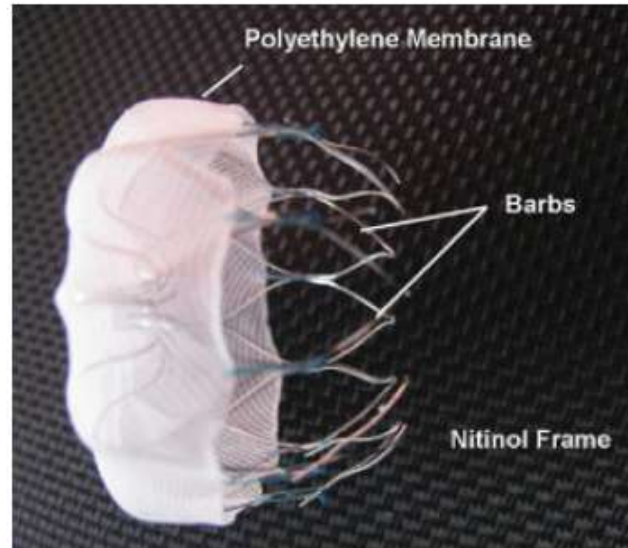
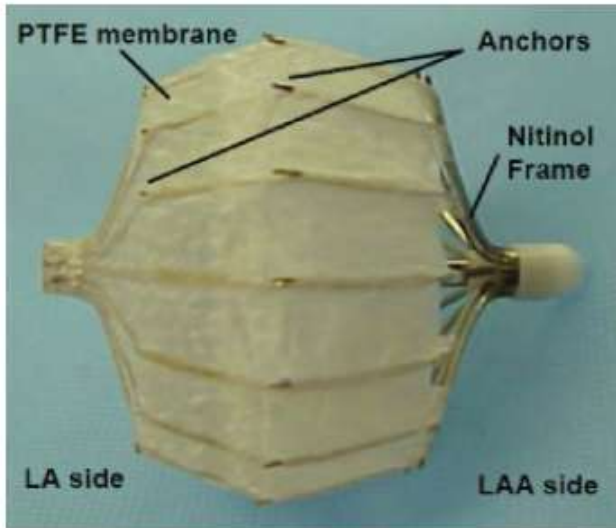
Cumulative Hazard Rate

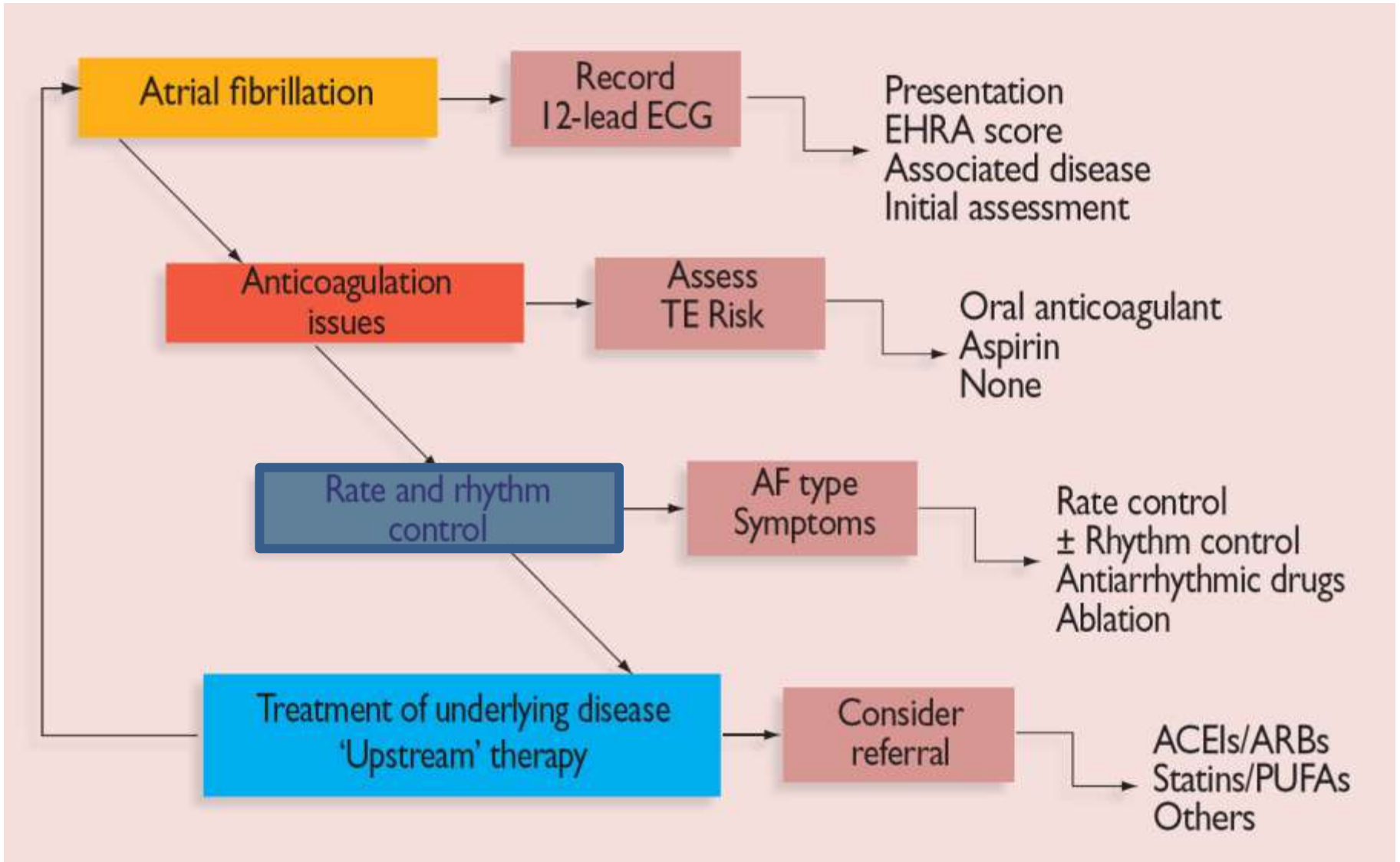
No. at Risk

Warfarin  
Dabigatran, 110 mg  
Dabigatran, 150 mg



# LAA Occlusion





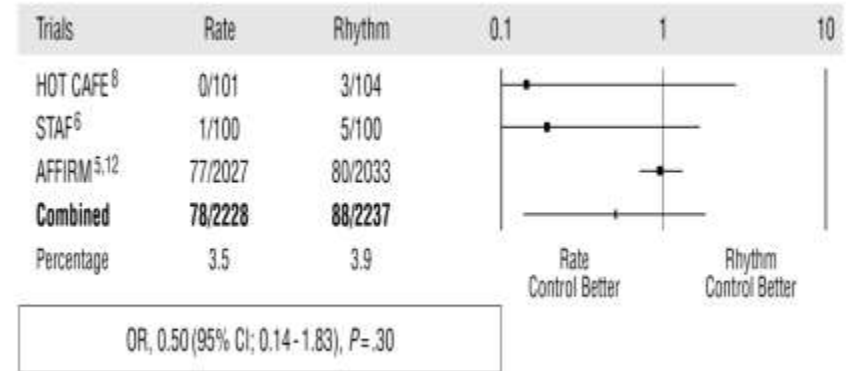
# Rate or Rhythm

## QOL



Jenkins et al. Am Heart J 2005;149:112-20

## CVA



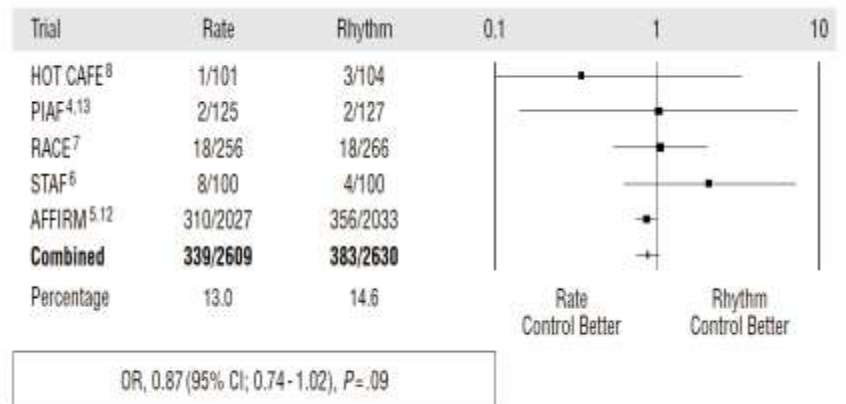
De Denus et al. Arch Intern Med. 2005;165:258-262

## Heart Failure

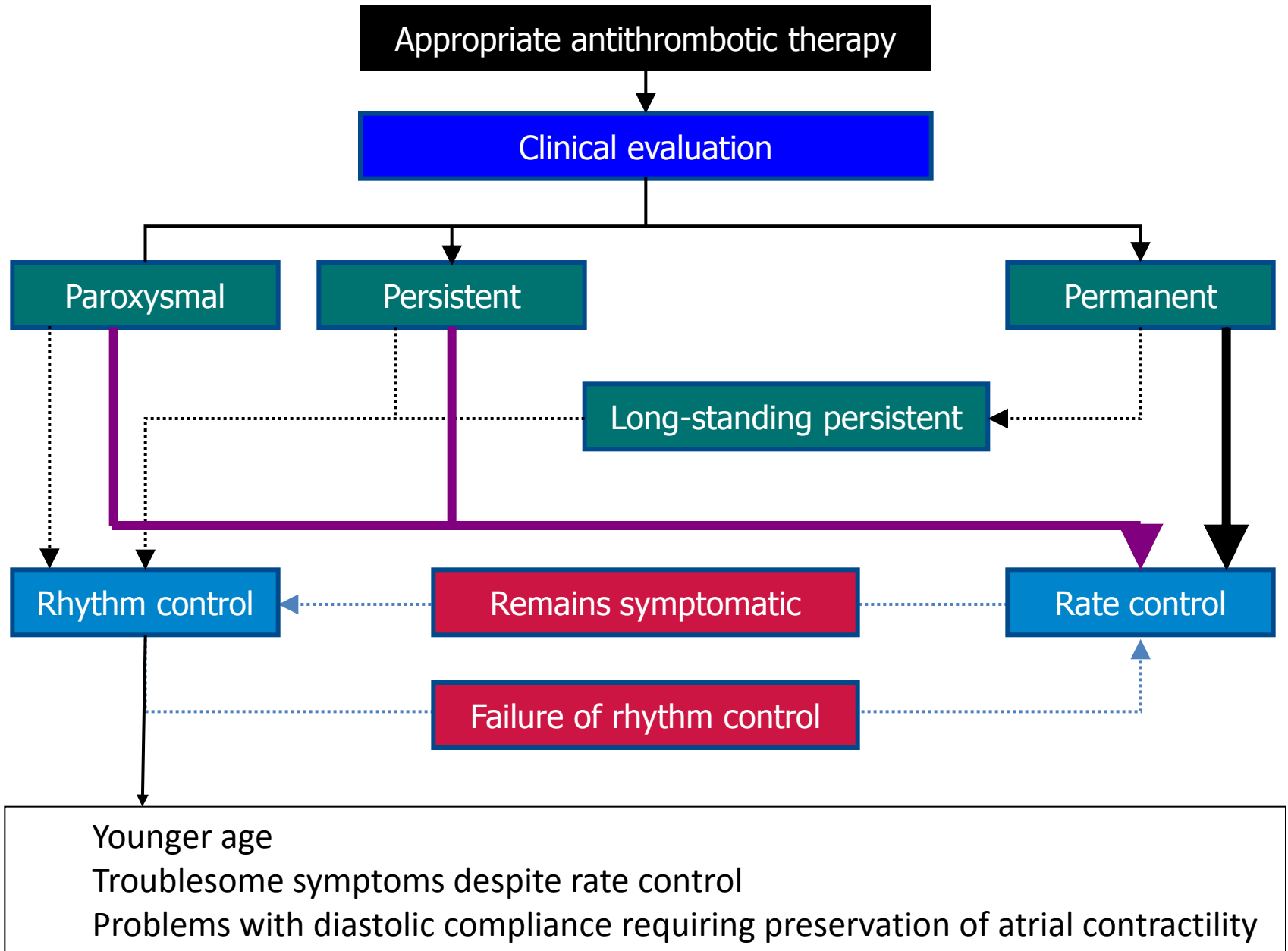
EVENT	OVERALL (N=4060)	RATE- CONTROL GROUP	RHYTHM- CONTROL GROUP	P VALUE†
		(N=2027)	(N=2033)	
	no. of patients (%)			
Congestive heart failure	79 (2.4)	37 (2.1)	42 (2.7)	0.58
Pulmonary event	132 (4.6)	24 (1.7)	108 (7.3)	<0.001
Gastrointestinal event	162 (5.0)	35 (2.1)	127 (8.0)	<0.001
Bradycardia	169 (5.1)	64 (4.2)	105 (6.0)	0.001
Prolongation of the corrected QT interval (>520 msec)	35 (1.1)	4 (0.3)	31 (1.9)	<0.001
Other	590 (19.8)	176 (14.0)	414 (25.4)	<0.001

N Engl J Med 2002;347:1825

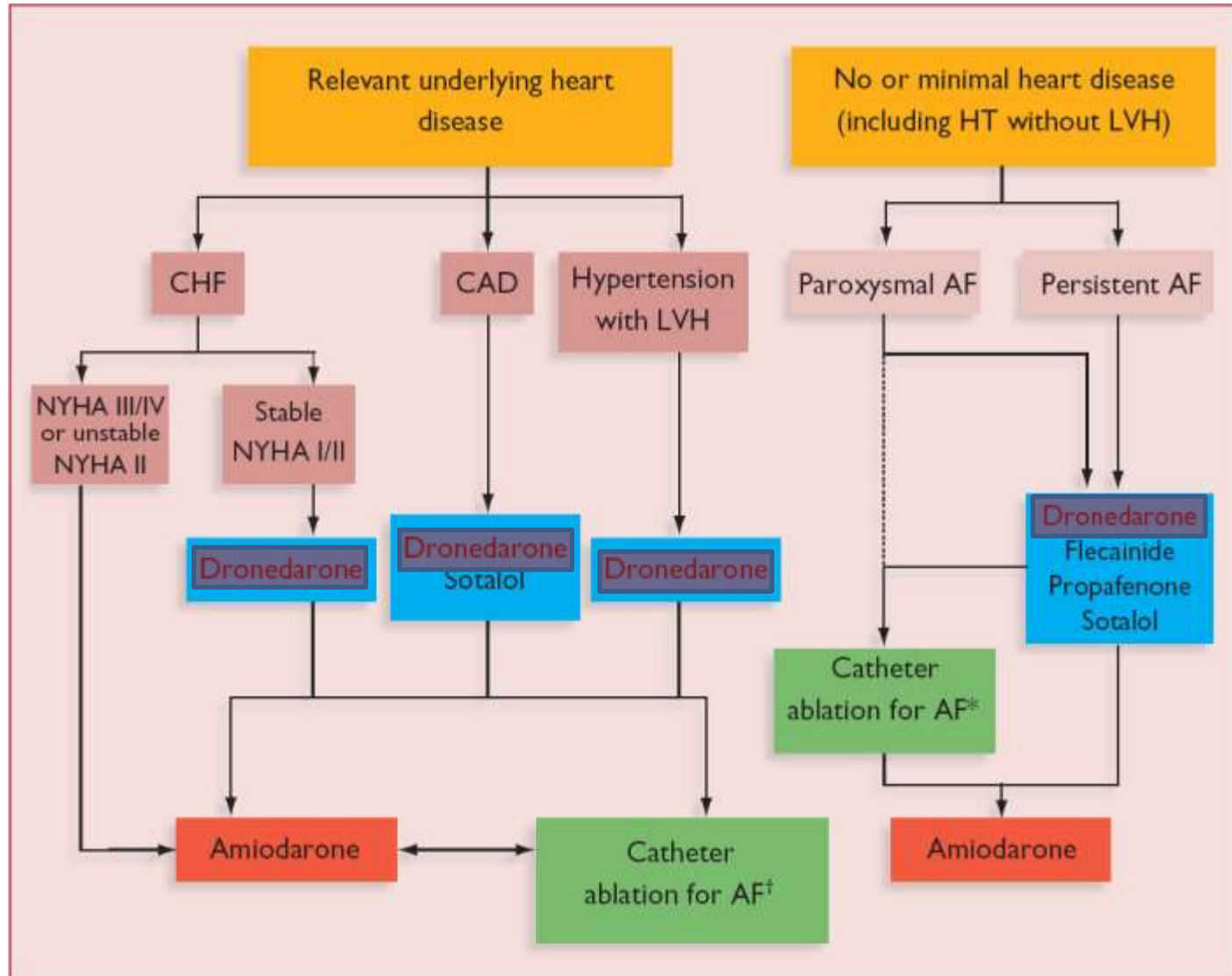
## Mortality



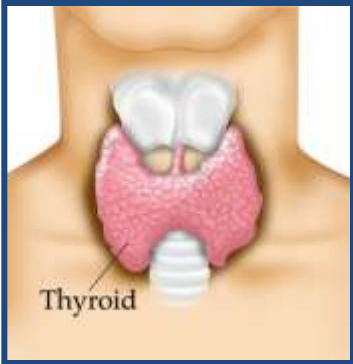
De Denus et al. Arch Intern Med. 2005;165:258-262



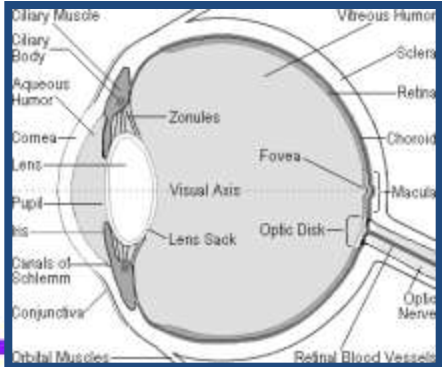
# Long-Term Rhythm Control



# Efficacy AAD



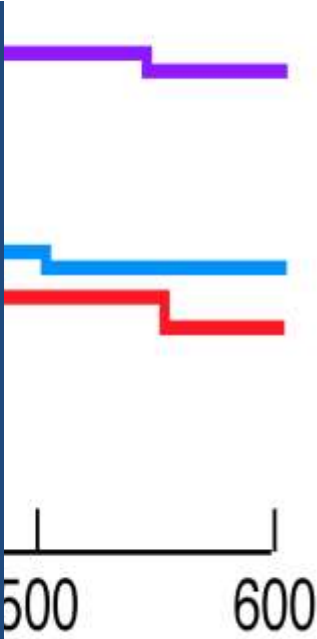
Amiodarone (n=201)



Patients with



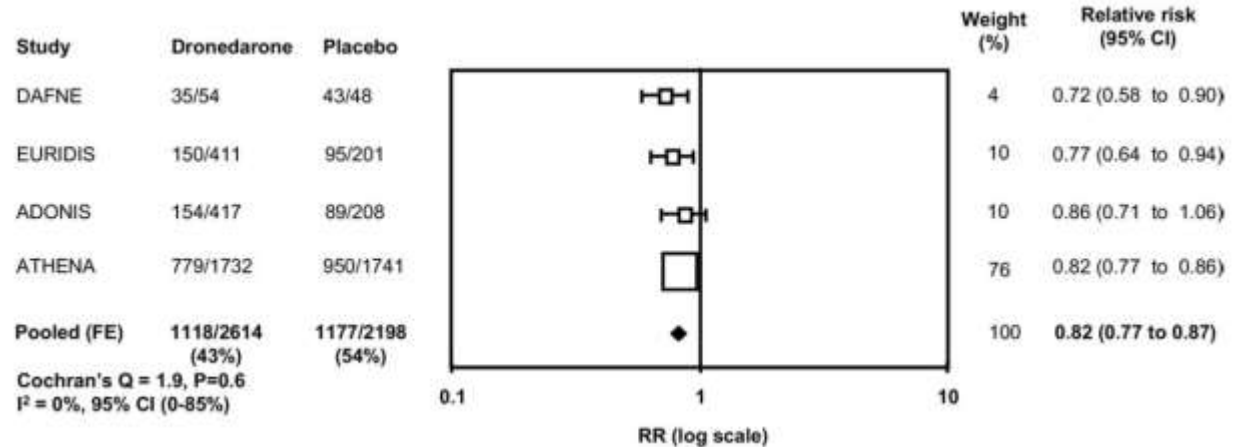
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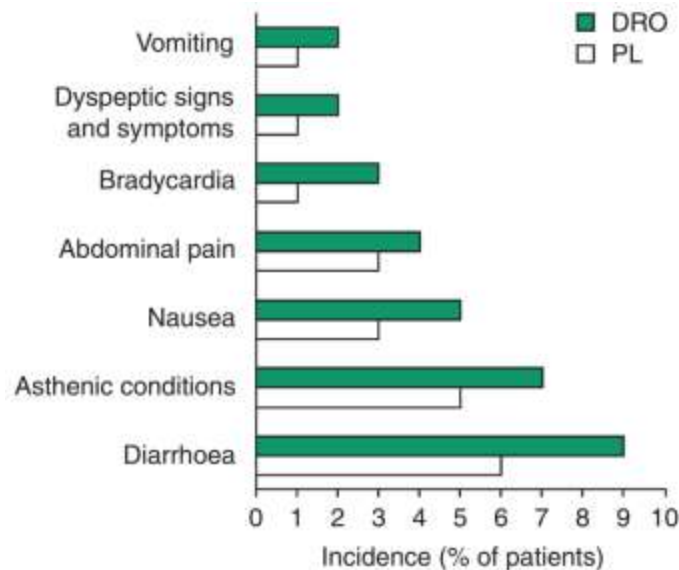
Days of Follow up

# Dronedarone

## Maintenance of Sinus Rhythm vs. Placebo



## Side Effects

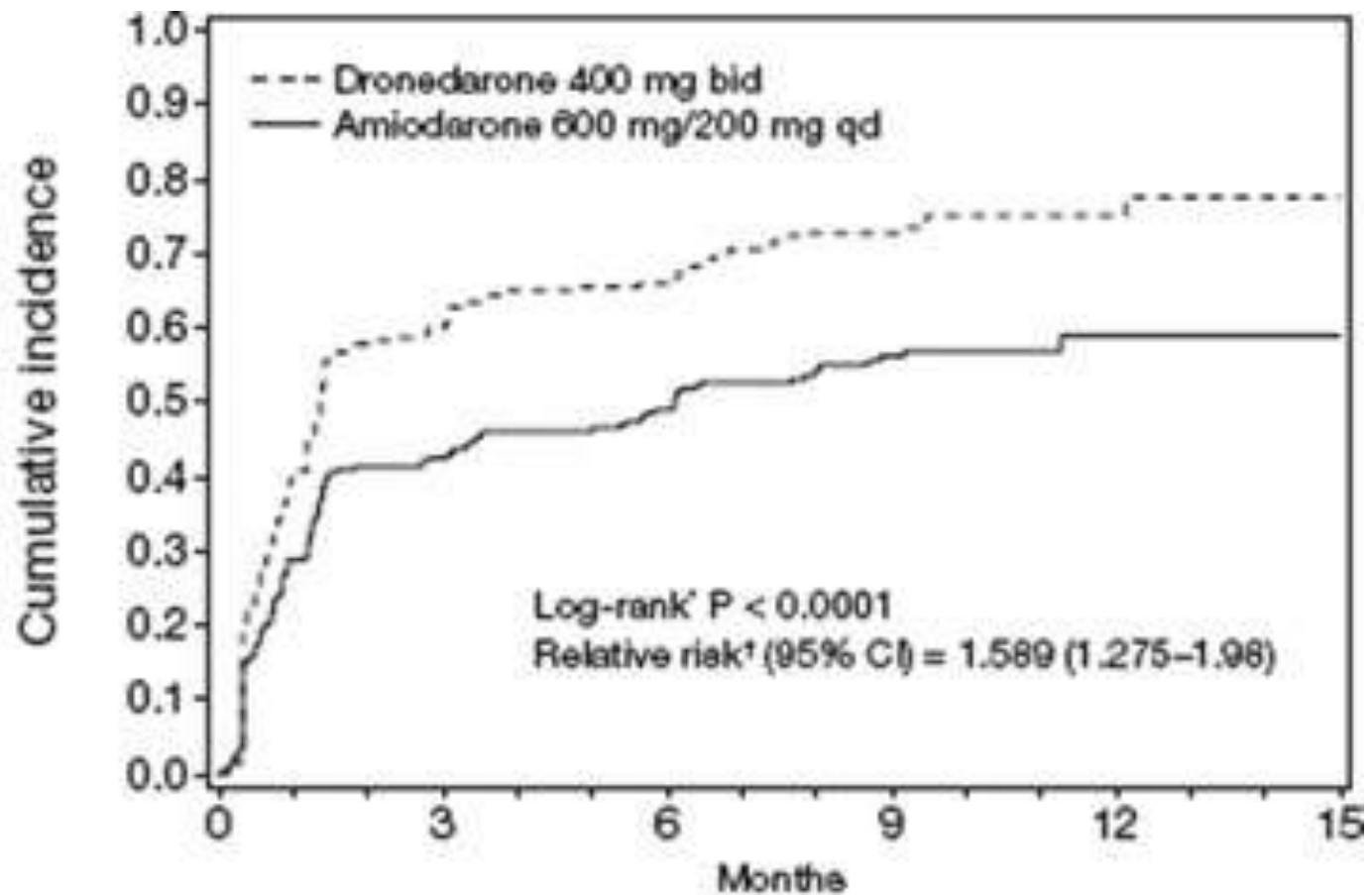


Liver enzymes (?)

Contra-indicated in NYHA III-IV

Decrease in incidence of CVA

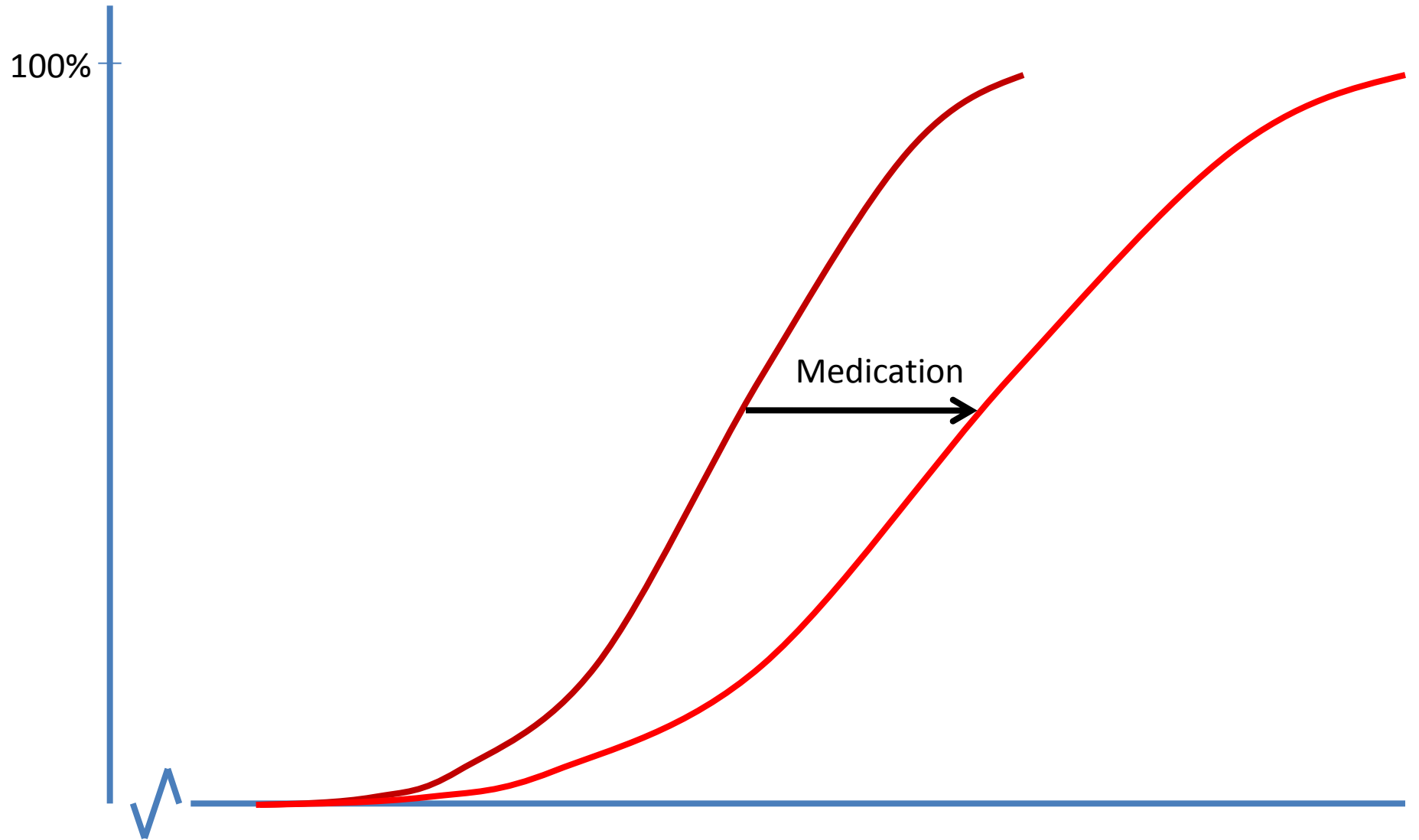
Reduces cardiovascular mortality but not overall mortality



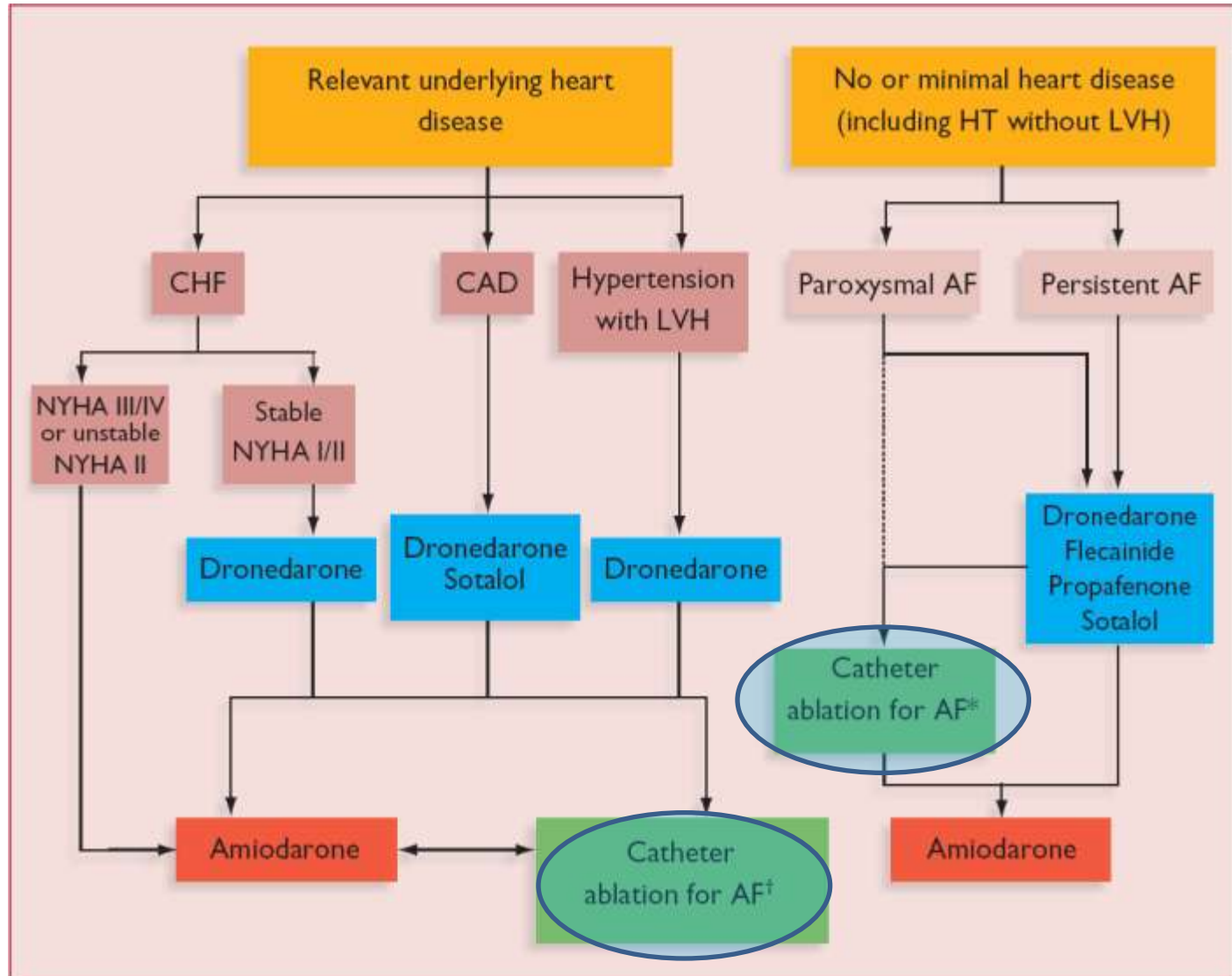
Patients at risk:

Dronedarone	249	99	84	40	12	0
Amiodarone	255	146	126	61	13	0

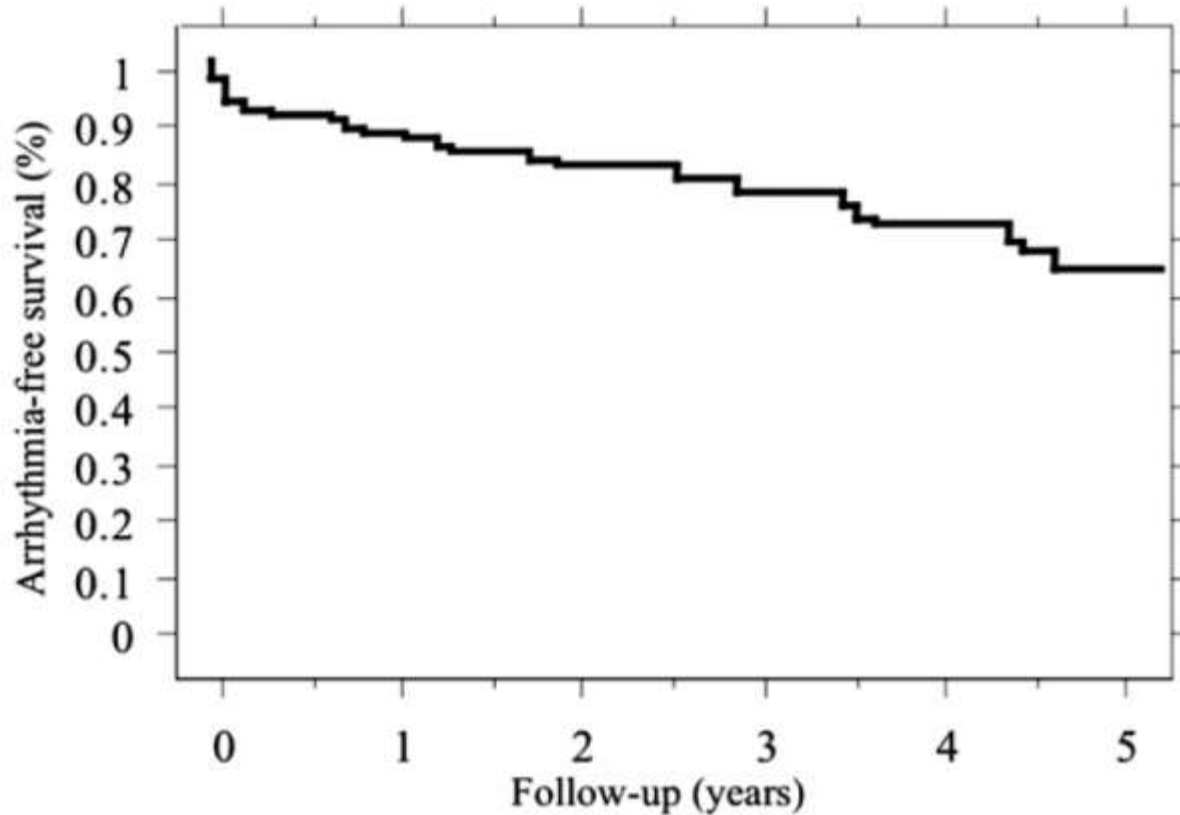
# Rhythm Control



# Long-Term Rhythm Control

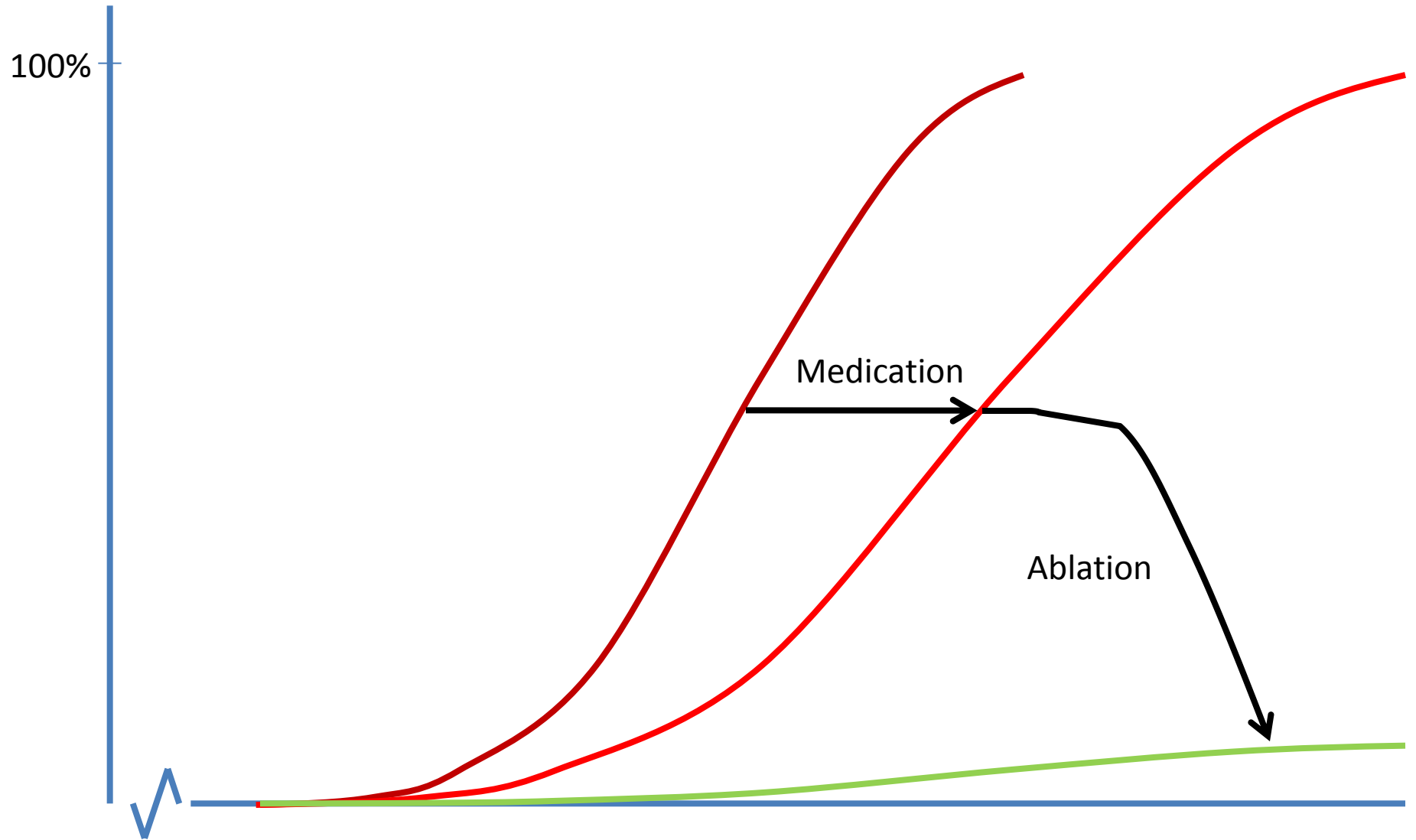


# Ablation – Longer-Term Results



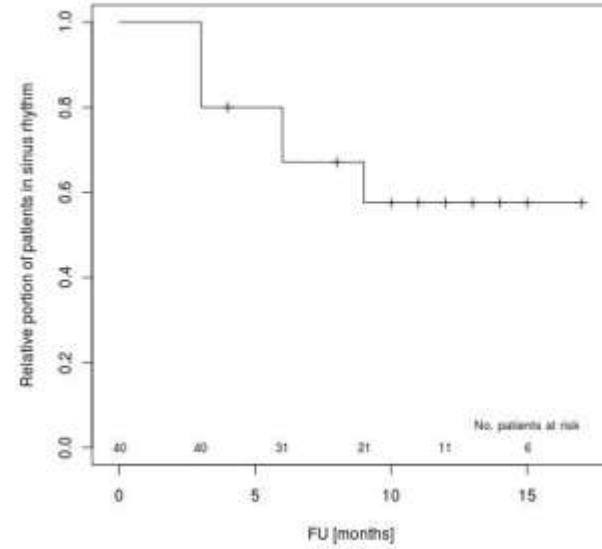
<b>Number at risk</b>	<b>100</b>	<b>78</b>	<b>71</b>	<b>67</b>	<b>54</b>	<b>18</b>
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# Rhythm Control

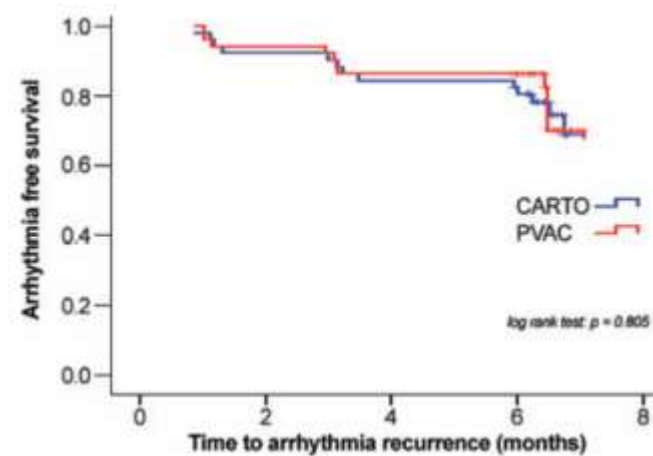


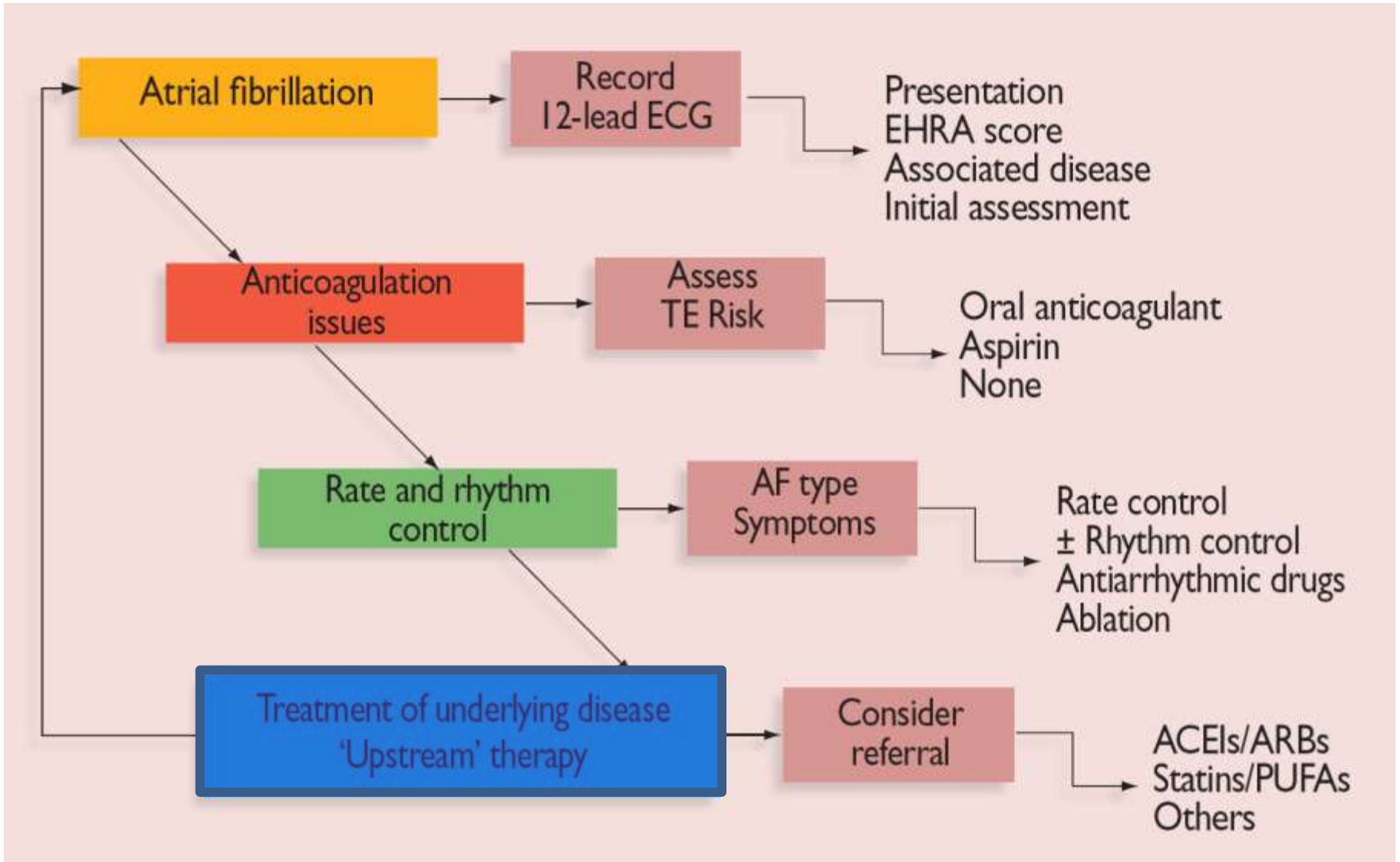
# Novelties in Ablation

## Balloons

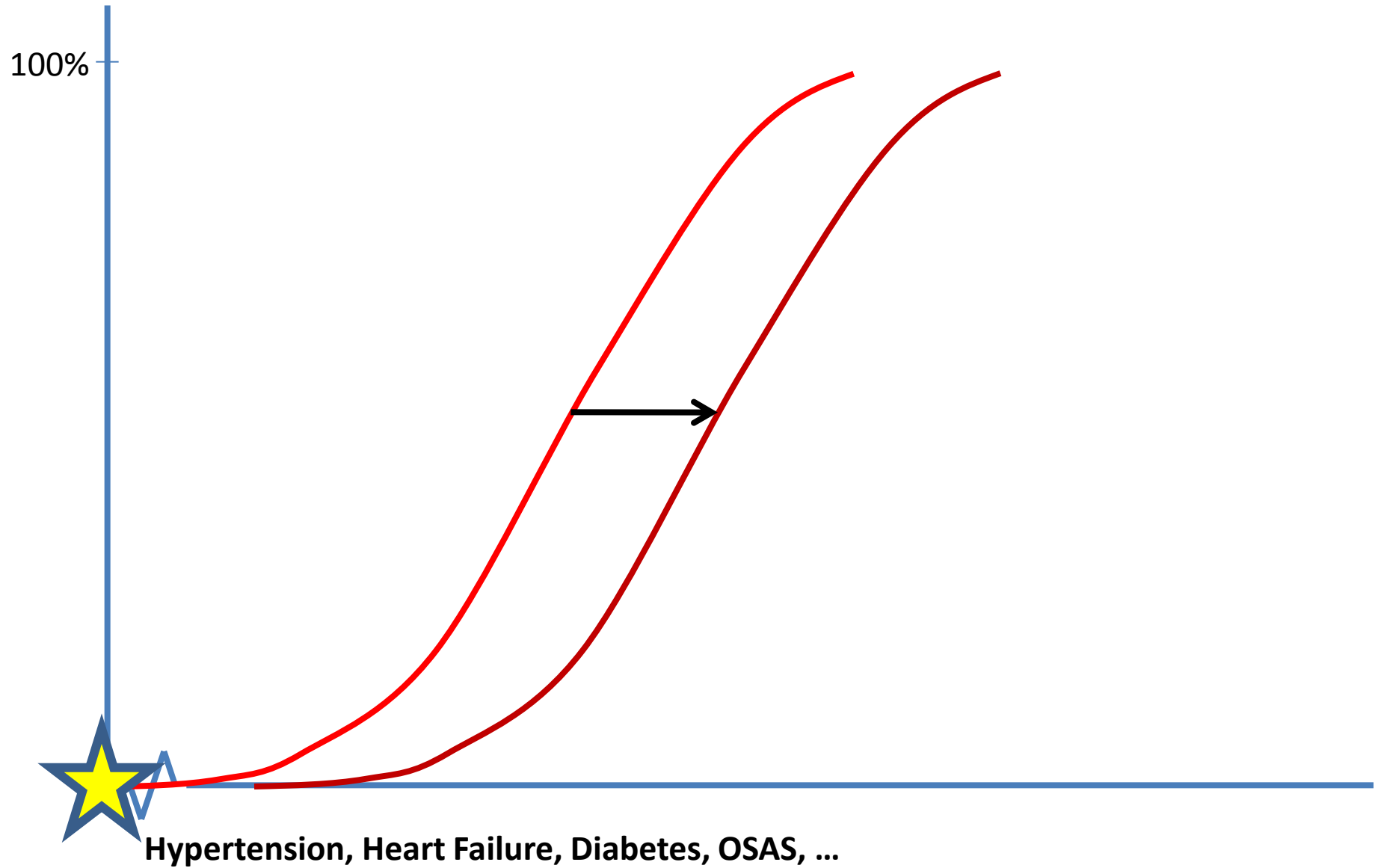


## Multielectrode catheters



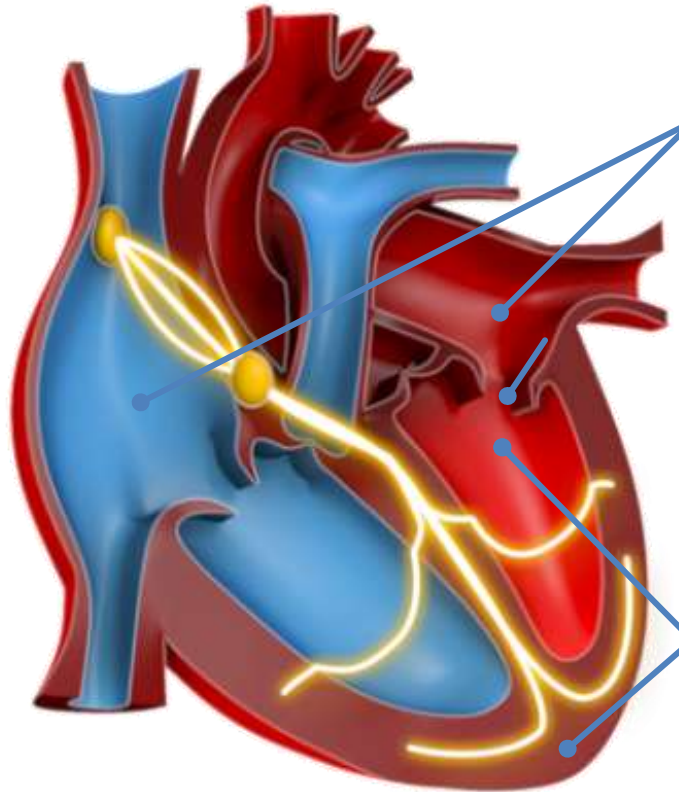
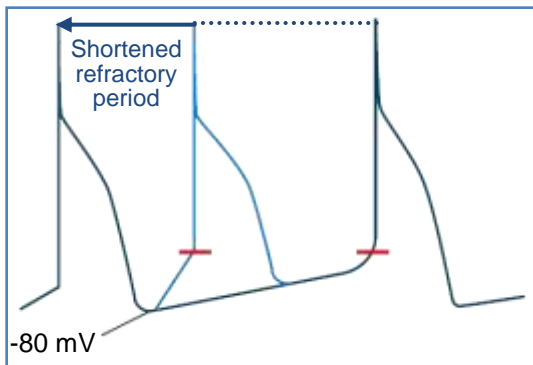


# Atrial Remodelling



- **Electrical remodelling**

- Shortening of atrial refractory periods
- Occurs rapidly (within several days) and contributes to the increased stability of AF



- **Contractile remodelling**

- Reduced atrial contractility
- Sets the stage for thrombus formation
- May lead to atrial dilation further altering electrophysiologic properties
- Occurs rapidly

- **Structural remodelling**

- Histologic changes
- Left atrium and left atrial appendage enlargement
- Decrease in cardiac output
- Occurs after a period of weeks to months

# Upstream Therapies

- RAAS Inhibition:
  - Heart Failure: Yes
  - Hypertension: Probably
  - Secondary prevention: ?
- Statins:
  - Post operative: Yes
  - Other: ?
- PUFA
  - ?

# Future Challenges

