# How to control atrial fibrillation in 2013

## The ideal patient for a rate control strategy

L. Pison, MD

Advances in Cardiac Arrhythmias and Great Innovations in Cardiology - Torino, September 28th 2013

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# Disclosures

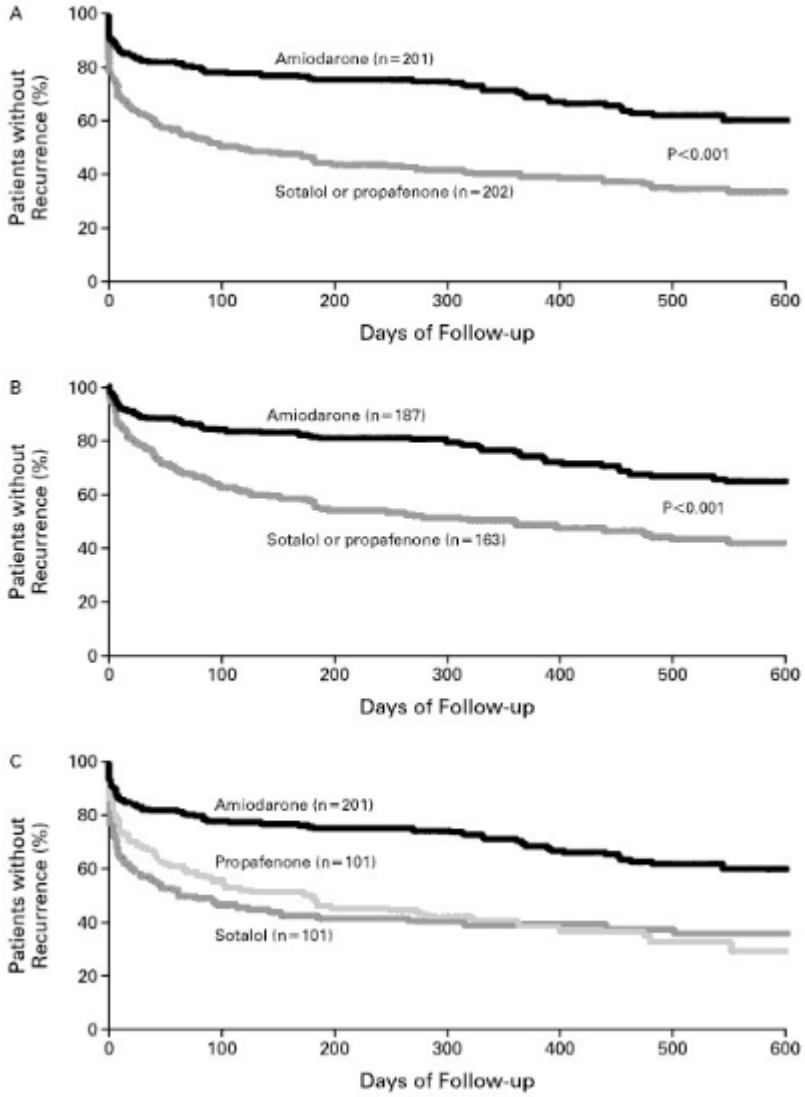
- Consultant to Atricure

# Setting the stage

- US > 3 million people, EU > 4.5 million people
- AF =
  - 5-fold increased risk of stroke
  - 3-fold increased risk of heart failure
  - diminished quality of live
  - increased health care costs

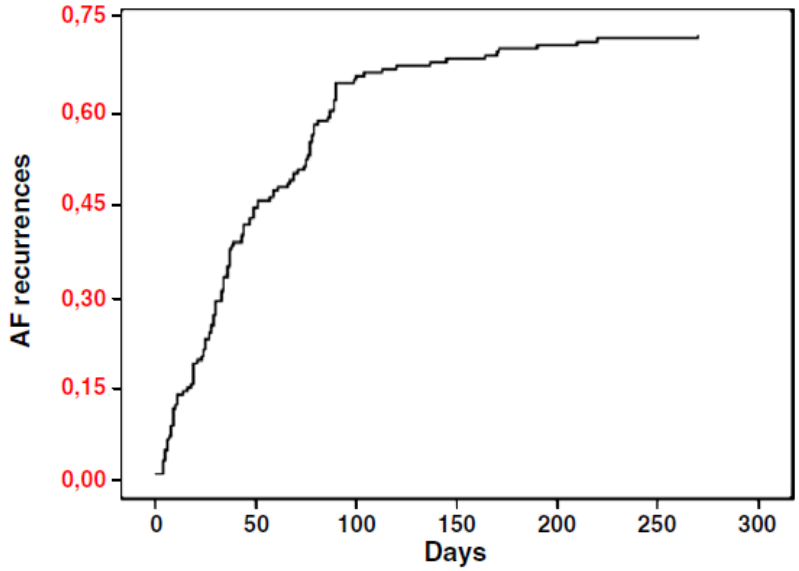
Fuster et al, JACC 2011 Go et al, JAMA 2001 Stewart et al, Heart 2004 Wolf et al, Stroke 1991
Krahn et al, Am J Med 1995 Dorian et al, Am Heart J 2002 Woodchis et al, Value Health 2012 Wolowacz et al, Europace 2011

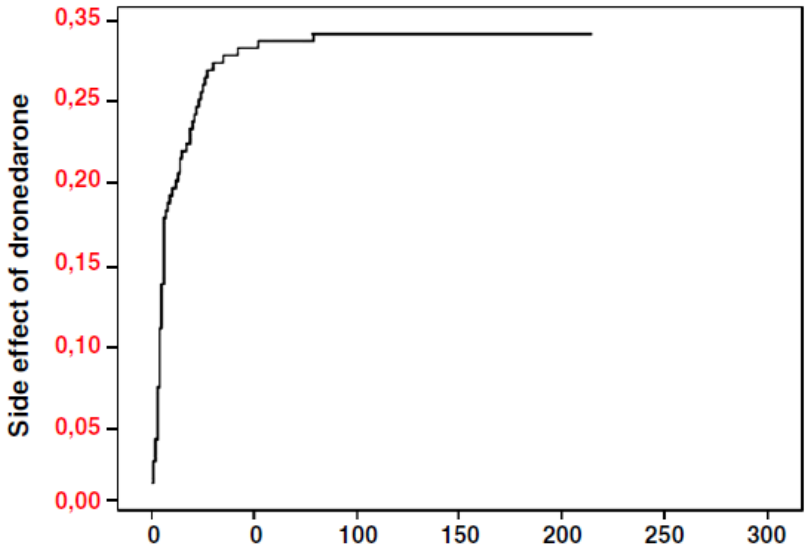
- **Rate controle**: a traditional front-line and well-tolerated therapeutic option
- **Rhythm controle**:
  - seemingly preferable?
    - improved cardiac function
    - avoidance of electrical and mechanical remodelling
  - important limitations!
    - limited efficacy of currently available AAD
    - catheter ablation: recurrence rate and lack of very-long term data



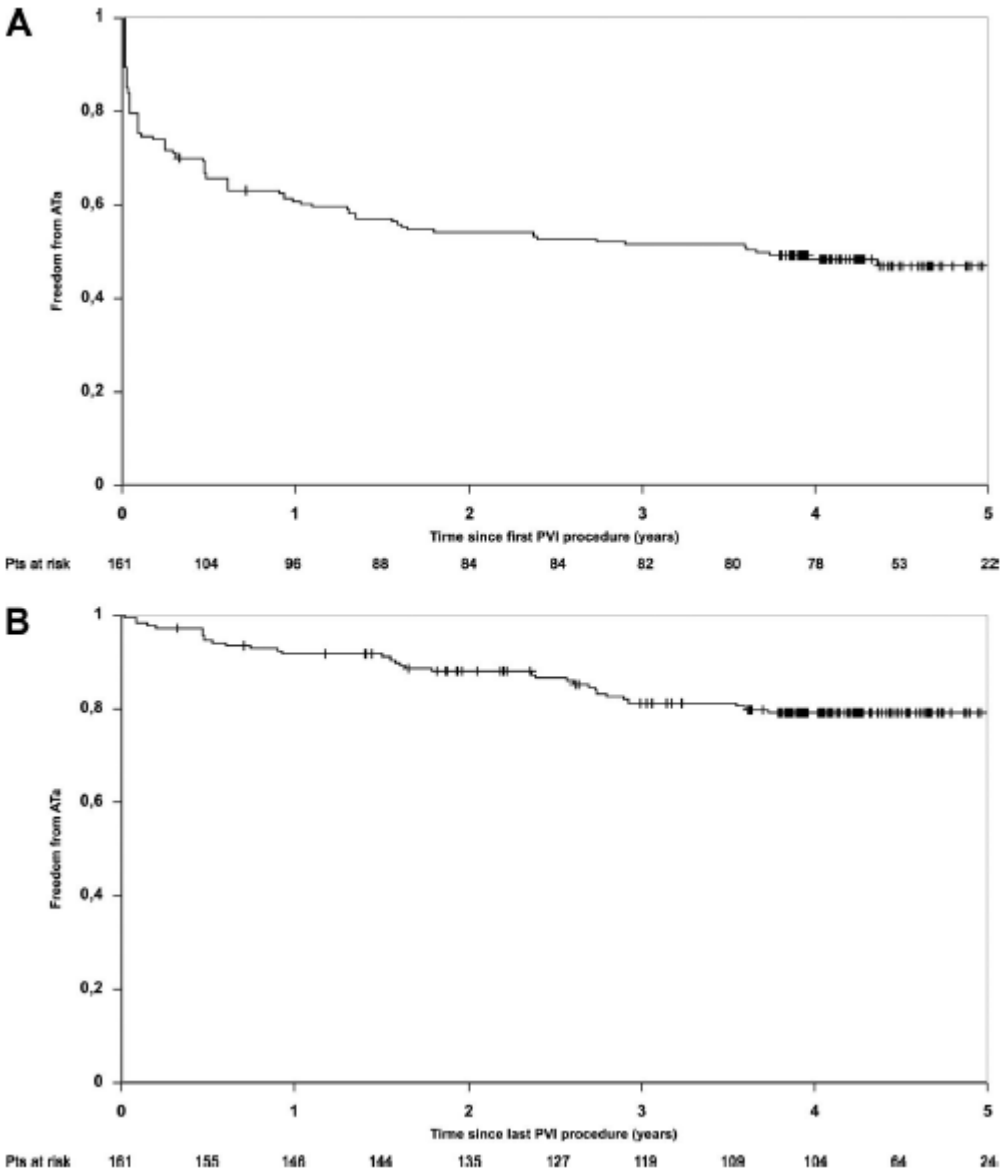

Roy et al, NEJM 2000

# Magdeburg Dronedarone Registry (MADRE study)




Said et al, International Journal of Cardiology 2013




Ouyang et al, Circulation 2010

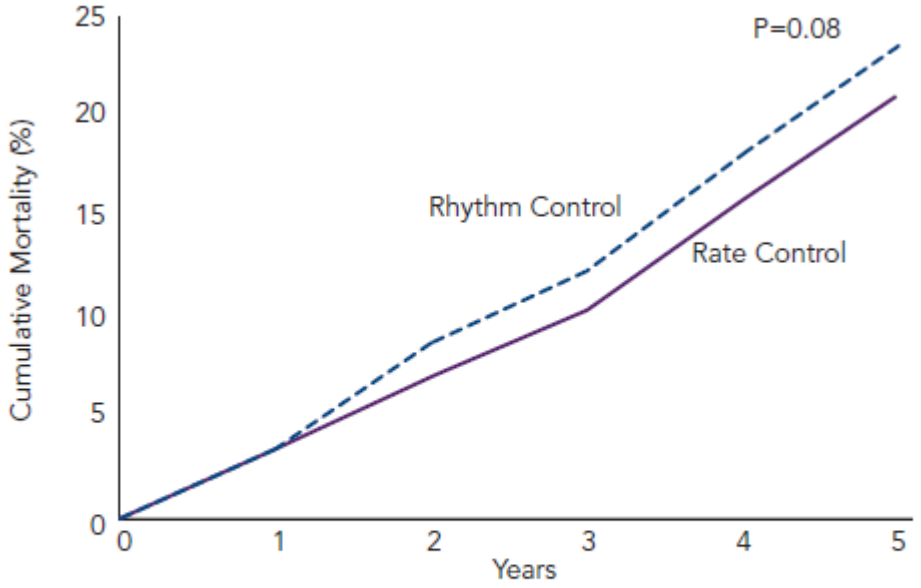
The New England
Journal of Medicine



VOLUME 347 DECEMBER 5, 2002 NUMBER 23

# A COMPARISON OF RATE CONTROL AND RHYTHM CONTROL IN PATIENTS WITH ATRIAL FIBRILLATION

THE ATRIAL FIBRILLATION FOLLOW-UP INVESTIGATION OF RHYTHM MANAGEMENT (AFFIRM) INVESTIGATORS*

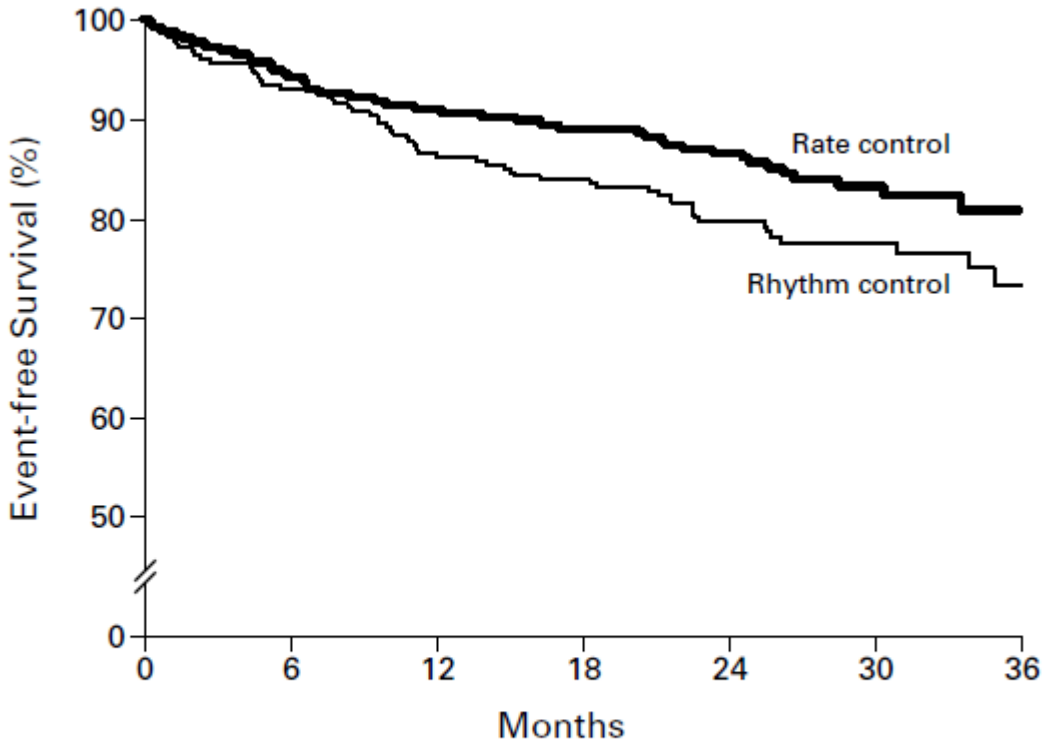



| No. of deaths | | Number (%) | | | | |
|---|---|---|---|---|---|---|
| Rhythm control | 0 | 80(4) | 175(9) | 257(13) | 314(18) | 352(24) |
| Rate comntrol | 0 | 78(4) | 148(7) | 210(11) | 275(16) | 306(21) |

The New England Journal of Medicine

# A COMPARISON OF RATE CONTROL AND RHYTHM CONTROL IN PATIENTS WITH RECURRENT PERSISTENT ATRIAL FIBRILLATION

Isabelle C. Van Gelder, M.D., Vincent E. Hagens, M.D., Hans A. Bosker, M.D., J. Herre Kingma, M.D., Otto Kamp, M.D., Tsjerk Kingma, M.Sc., Salah A. Said, M.D., Julius I. Darmanata, M.D., Alphons J.M. Timmermans, M.D., Jan G.P. Tijssen, Ph.D., and Harry J.G.M. Crijns, M.D., for the Rate Control versus Electrical Cardioversion for Persistent Atrial Fibrillation Study Group*




| No. at Risk | | | | | | | |
|---|---|---|---|---|---|---|---|
| Rate control | 256 | 239 | 232 | 222 | 212 | 99 | 25 |
| Rhythm control | 266 | 243 | 224 | 218 | 207 | 85 | 24 |

The New England Journal of Medicine

# A COMPARISON OF RATE CONTROL AND RHYTHM CONTROL IN PATIENTS WITH RECURRENT PERSISTENT ATRIAL FIBRILLATION

ISABELLE C. VAN GELDER, M.D., VINCENT E. HAGENS, M.D., HANS A. BOSKER, M.D., J. HERRE KINGMA, M.D., OTTO KAMP, M.D., TSJERK KINGMA, M.SC., SALAH A. SAID, M.D., JULIUS I. DARMANATA, M.D., ALPHONS J.M. TIMMERMANS, M.D., JAN G.P. TIJSSEN, PH.D., AND HARRY J.G.M. CRIJNS, M.D., FOR THE RATE CONTROL VERSUS ELECTRICAL CARDIOVERSION FOR PERSISTENT ATRIAL FIBRILLATION STUDY GROUP*

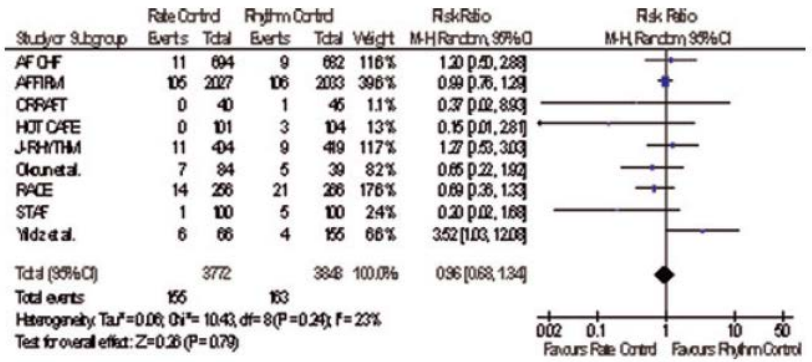
- Rate controle:
  - As effective as rhythm controle in managment of AF
  - Potential advantages:
    - Lower risk of adverse drug effects
    - Higher cost-effectiveness
    - Decreased incidence of hospitalisations

- Various meta-analyses have shown that a rate control strategy is at least as effective as rhythm control in patients with AF when comparing endpoints such as cardiovascular and all-cause mortality

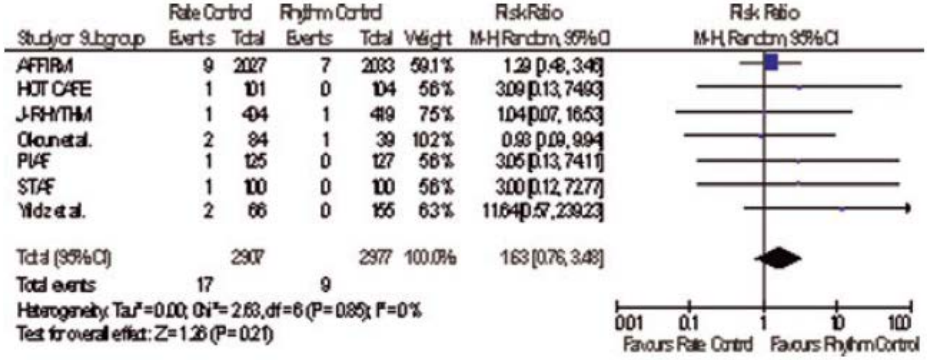
→ majority of patients in these trials were elderly patients without highly symptomatic AF

Kumana et al, Br J Clin Pharmacol 2005
Caldiera et al, Eur J Intern Med 2011

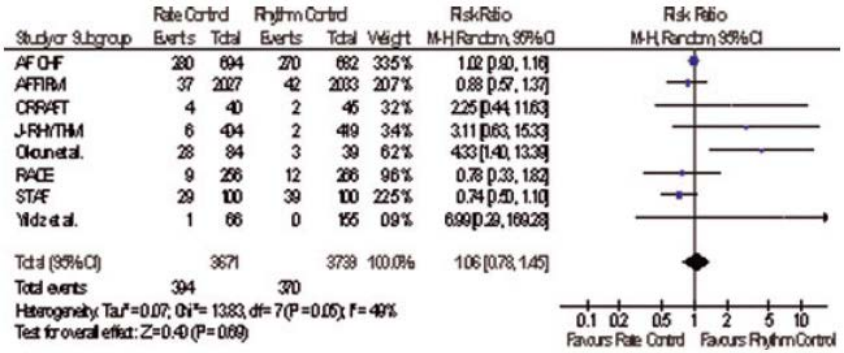
de Denus et al, Arch Intern Med 2005
Caldeira et al, Arch Cardiovasc Dis 2012



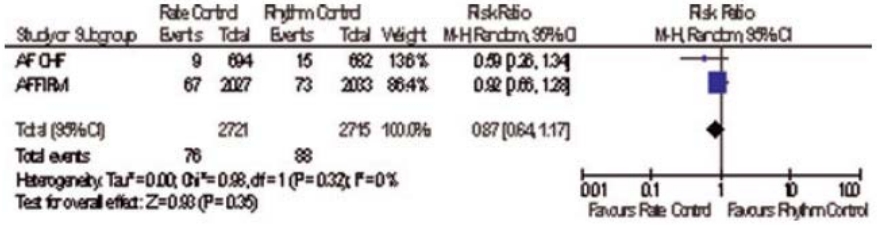

= Stroke




= Systemic embolism

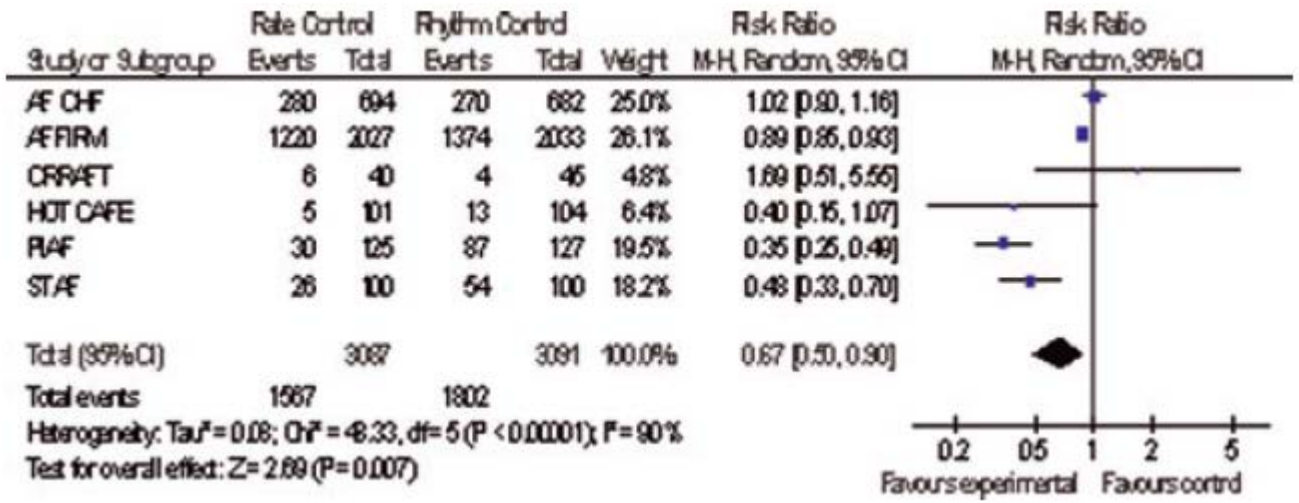



= Heart failure




= Myocardial infarction

Chatterjee et al, Pacing Clin Electrophysiol 2013

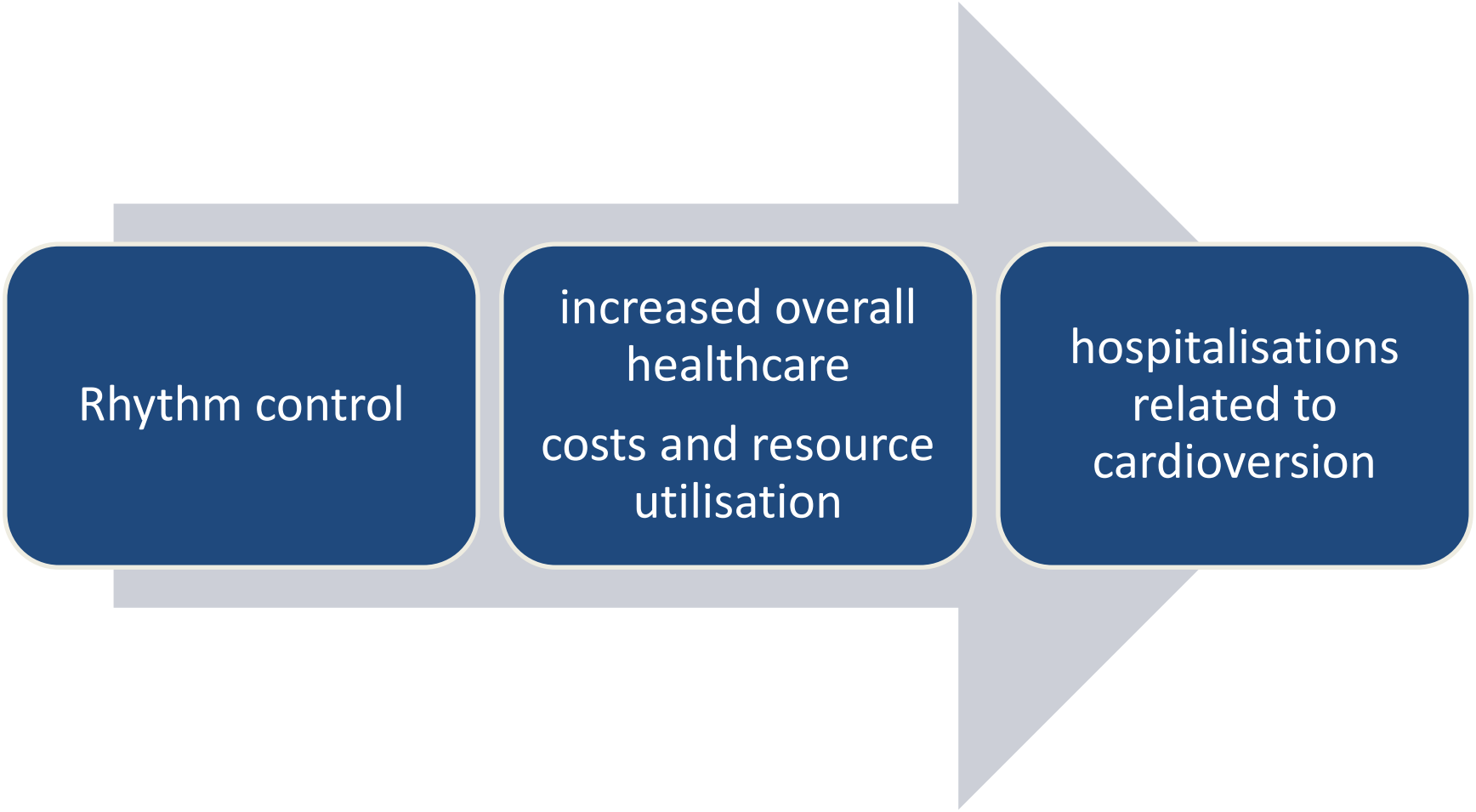



Rhythm controle: higher incidence of hospitalisations

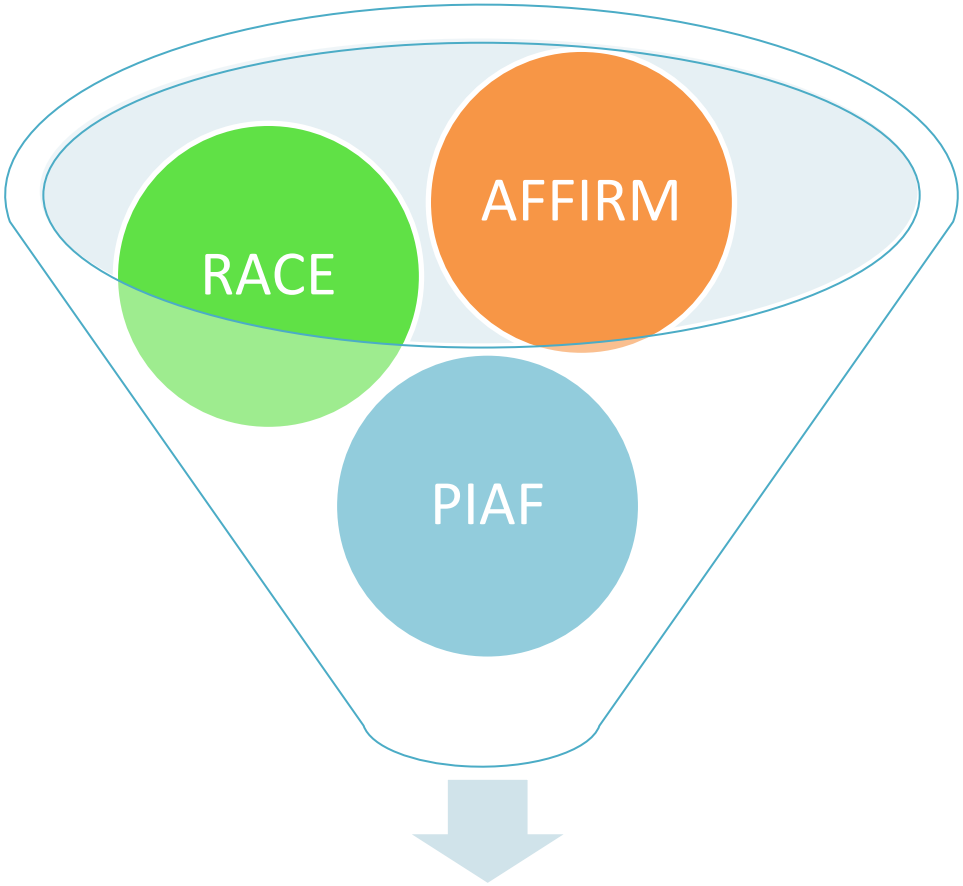
- rhythm control by cardioversion in a monitored setting
- adverse effects and arrhythmias secondary to the use of AAD

Chatterjee et al, Pacing Clin Electrophysiol 2013

# HOT CAFE trial

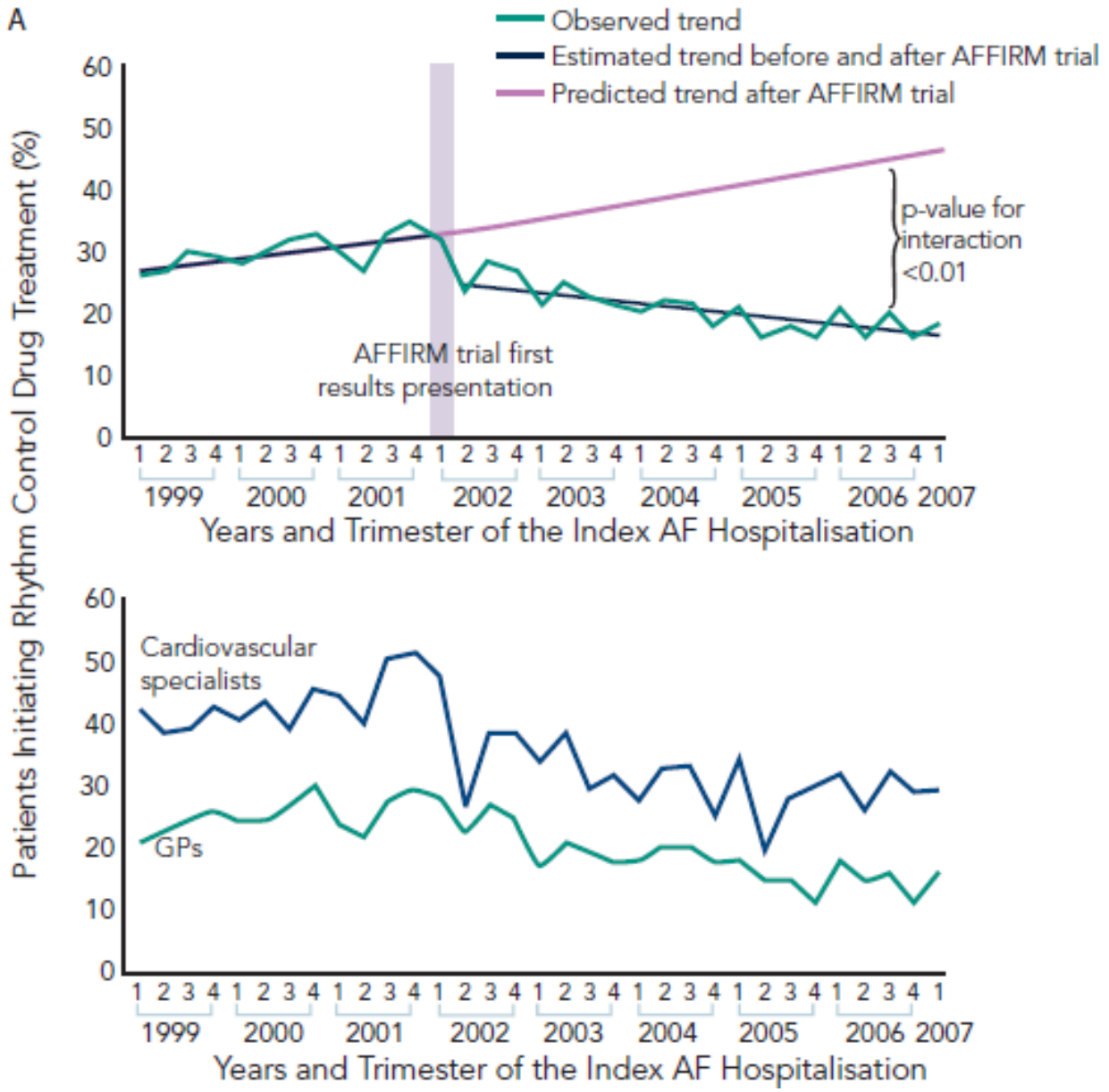



Opolski et al, Chest 2004




More hospitalisations with rhythm control strategy

Wyse et al, NEJM 2002 Van Gelder et al, NEJM 2002 Hohnloser et al, Lancet 2000




Pilote et al, Can J Cardiol 2013 Andrade et al, Heart Rhythm 2010

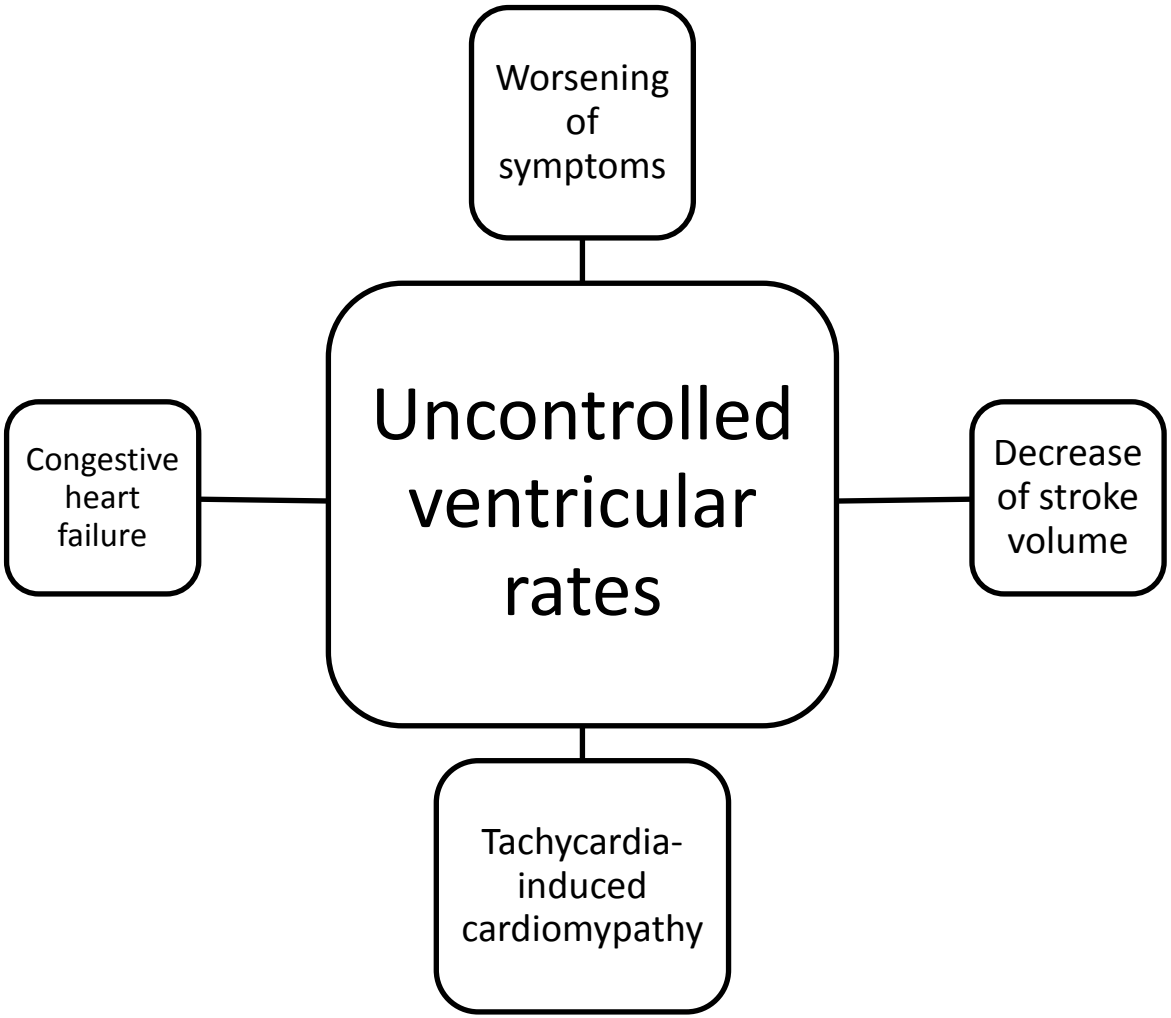
Martin-Doyle et al, J Cardiovasc Electrophysiol 2011 Ionscu-Ittu et al, Arch Intern Med 2012

# Aims of Rate Control

- **Decrease AF Symptoms**
- **Reduce risk of Cardiomyopathy**



Camm AJ, et al. Eur Heart J 2010


Worsening of symptoms
Uncontrolled ventricular rates
Congestive heart failure
Decrease of stroke volume
Tachycardia-induced cardiomypathy

# Adequate rate control?

- AFFIRM: average heart rate ≤80 bpm at rest and a maximum heart rate ≤110 bpm during either a six-minute walk or moderate exercise
- RACE: resting heart rate <100 bpm

- Subgroup analyses AFFIRM and RACE: patients with resting heart rates > 100 bpm had worse outcome
  - impact of better rate control?
  - co-morbidities resulting in both higher heart rates and worse outcomes?

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# Lenient versus Strict Rate Control in Patients with Atrial Fibrillation

Isabelle C. Van Gelder, M.D., Hessel F. Groenveld, M.D.,
Harry J.G.M. Crijns, M.D., Ype S. Tuininga, M.D., Jan G.P. Tijssen, Ph.D.,
A. Marco Alings, M.D., Hans L. Hillege, M.D., Johanna A. Bergsma-Kadijk, M.Sc.,
Jan H. Cornel, M.D., Otto Kamp, M.D., Raymond Tukkie, M.D.,
Hans A. Bosker, M.D., Dirk J. Van Veldhuisen, M.D.,
and Maarten P. Van den Berg, M.D., for the RACE II Investigators*

Van Gelder IC, et al. NEJM 2010

# Permanent AF > 80 bpm

## lenient

HR < 110 bpm
(12 lead ECG)

## strict

HR < 80 bpm (12 lead ECG)

and

HR < 110 bpm (at 25% of maximal exercise)

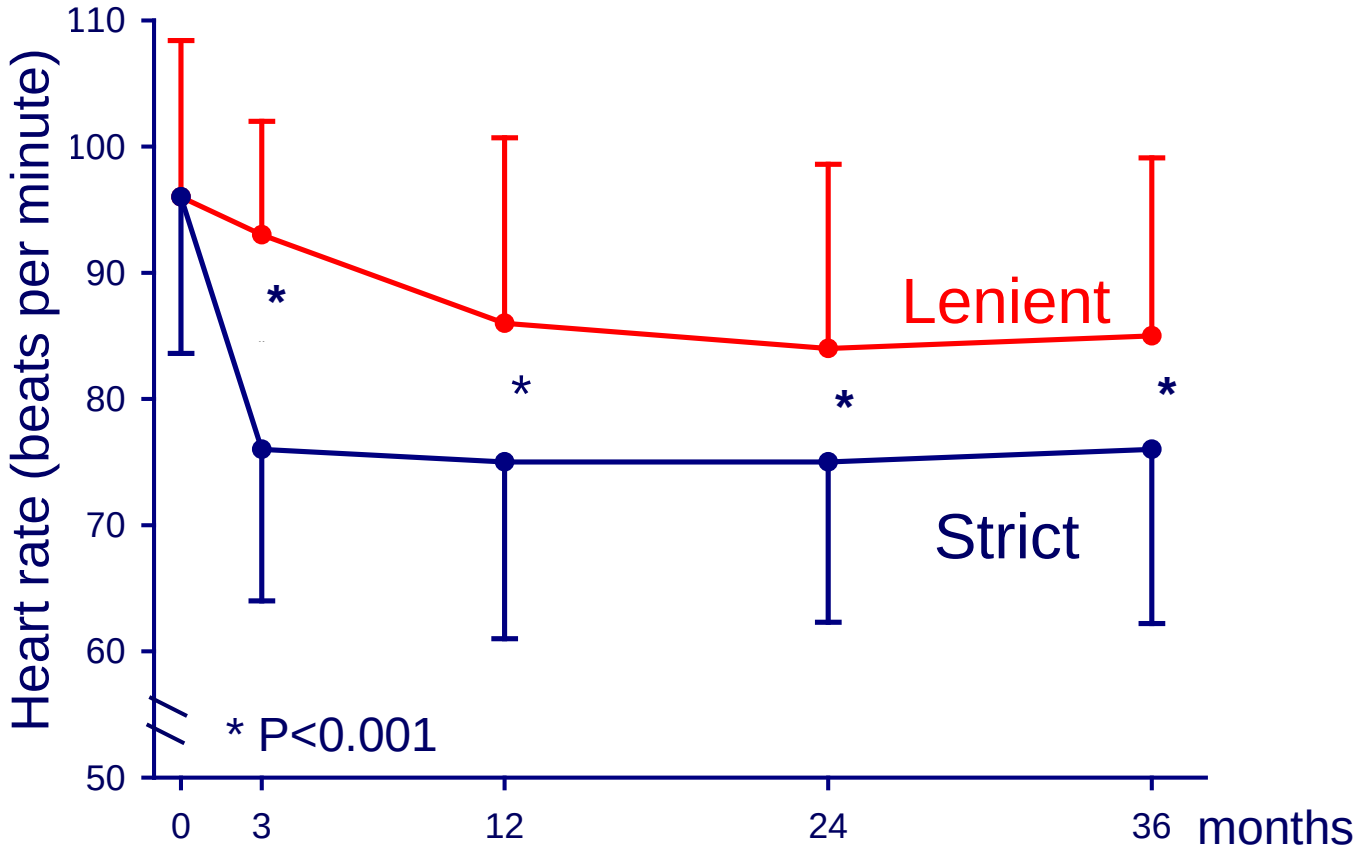
After achieving rate control target:

Holter for safety

funded by the Netherlands Heart Foundation

Van Gelder IC, et al. NEJM 2010

# Heart rate during study

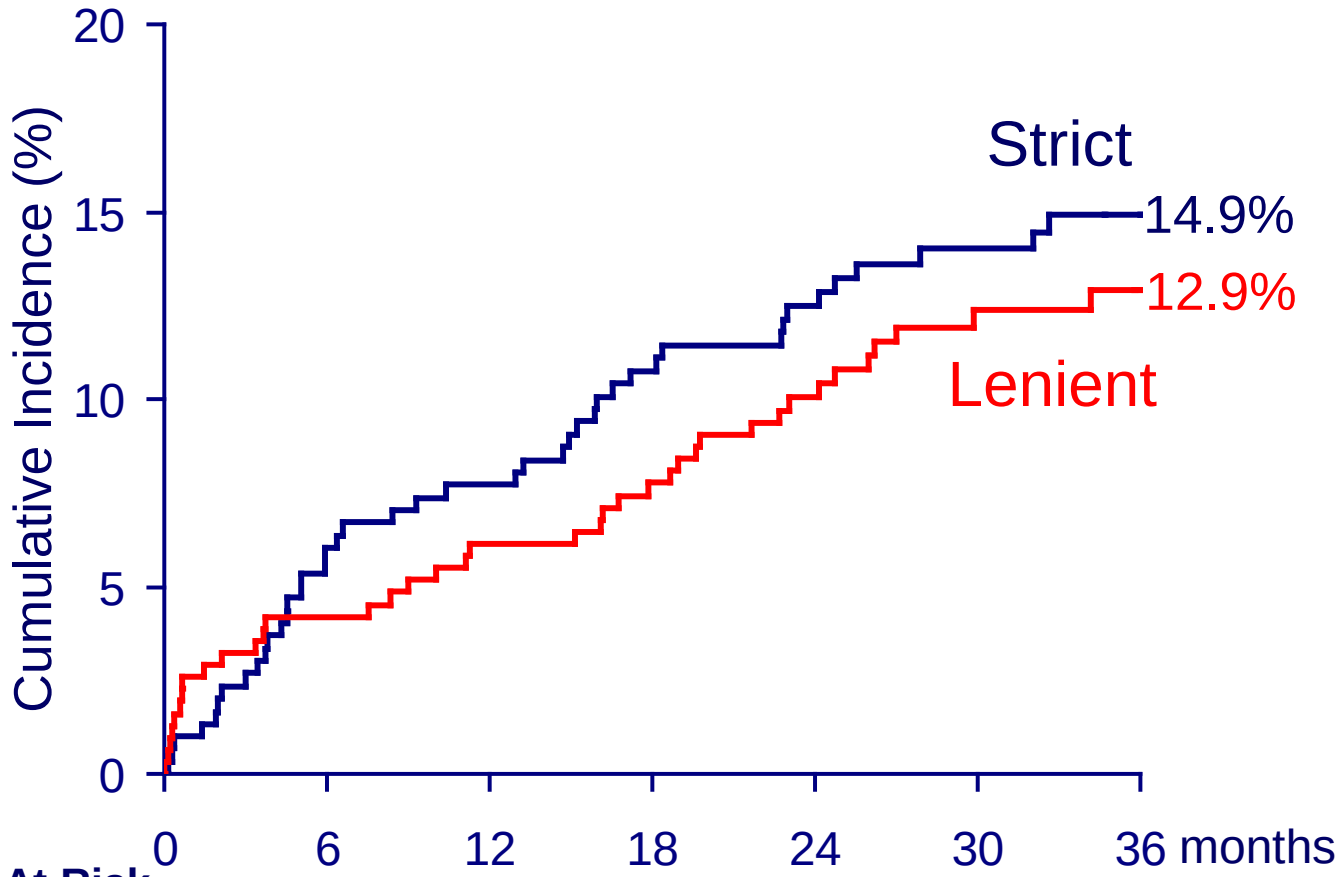



| No. At Risk | | | | | |
|---|---|---|---|---|---|
| **Lenient** | 311 | 311 | 302 | 291 | 237 |
| **Strict** | 303 | 303 | 284 | 277 | 240 |

Van Gelder IC, New Engl J Med 2010

funded by the Netherlands Heart Foundation

# Cumulative incidence primary outcome

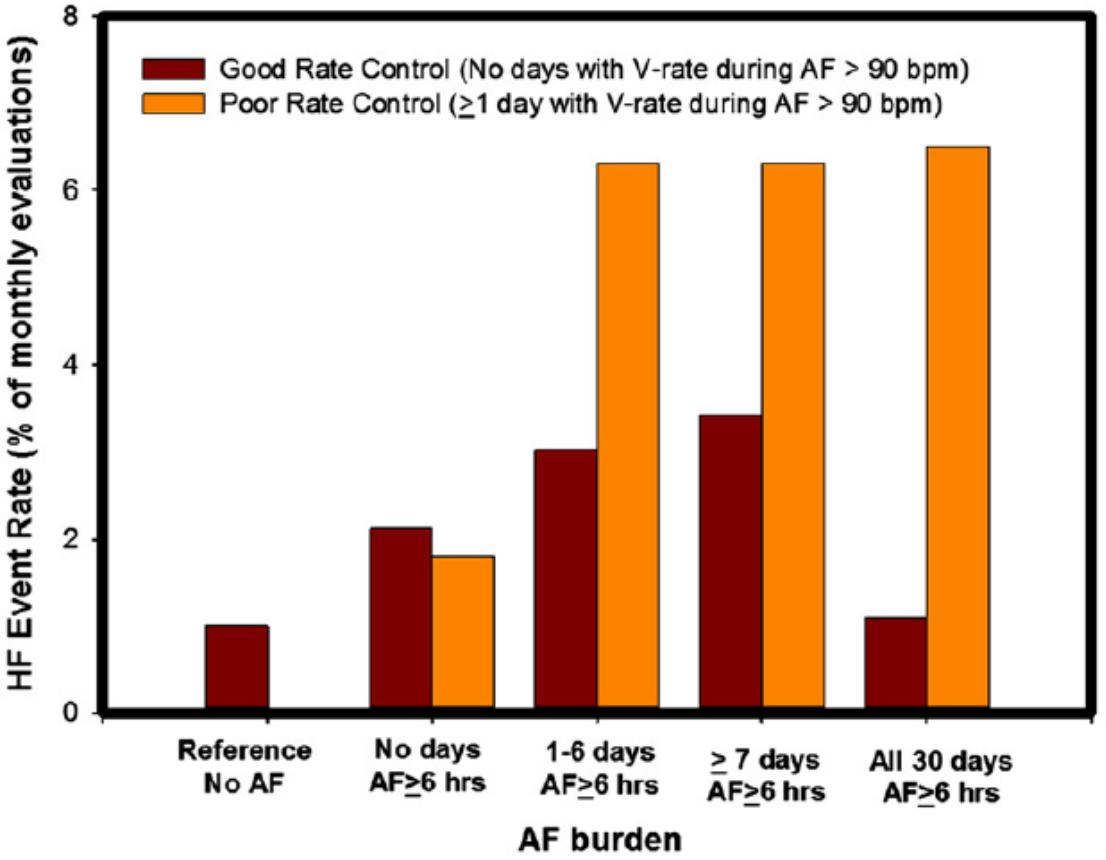



| No. At Risk | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Strict** | 303 | 282 | 273 | 262 | 246 | 212 | 131 |
| **Lenient** | 311 | 298 | 290 | 285 | 255 | 218 | 138 |

Van Gelder IC, et al. NEJM 2010

funded by the Netherlands Heart Foundation

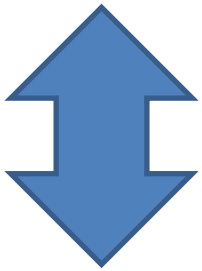
# However…




| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Adjusted Hazard Ratio | Reference | **2.1*** | **2.0** | **2.8#** | **5.3*** | **3.9*** | **5.8*** | **1.2** | **6.7*** | *$P < .001$; #$P = .006$ |
| Evaluations | 10,375 | 3283 | 333 | 300 | 126 | 354 | 96 | 611 | 93 | |
| Patients | 1042 | 419 | 138 | 135 | 90 | 116 | 60 | 118 | 31 | |

# Methods of Achieving Rate Control in Patients with Atrial Fibrillation

- AFFIRM:
  - β-blockers ± digoxin: 70% succes
  - calcium channel antagonists ± digoxin: 54% succes



- RATAF (Ulimoen et al, Am J Cardiol 2013)
  - diltiazem 360 mg/d superior to verapamil 240 mg/d, metoprolol 100 mg/d and carvedilol 25 mg/d

# Recommendations for acute rate control

| Recommendations | Class[a] | Level[b] | Ref.[c] |
|---|---|---|---|
| In the acute setting in the absence of pre-excitation, i.v. administration of β-blockers or non-dihydropyridine calcium channel antagonists is recommended to slow the ventricular response to AF, exercising caution in patients with hypotension or heart failure. | I | A | 100 |



100. Segal JB, et al., J Fam Pract 2000

- Digoxin as single agent:
  - Not as effective as β-blockers or calcium blockers
  - Efficacy further reduced in states of high sympathetic tone
- IV amiodarone:
  - May be particularly effective in critically ill patients who develop uncontrolled and haemodynamically compromising high ventricular rates during AF
  - Controlling effects attributed to its calcium channel blocking as well to its antiadrenergic properties

# Recommendations for acute rate control

| Recommendations | Class[a] | Level[b] | Ref.[c] |
|---|---|---|---|
| In the acute setting, i.v. administration of digitalis or amiodarone is recommended to control the heart rate in patients with AF and concomitant heart failure, or in the setting of hypotension. | I | B | 101 |



101. Hou ZY, et al., Eur Heart J 1995

# AV node ablation and permanent pacemaker implantation

- AF with difficult to control rapid ventricular rates
- Two randomised clinical studies:
  - Severely symptomatic paroxysmal AF (Brignole et al, Circulation 1997)
  - Chronic AF and heart failure (Brignole et al, Circulation 1998)
- Highly effective in controlling AF symptoms, improving quality of life and general wellbeing (Rodriguez et al, Am J Cardiol 1993 – Lee et al, JACC 1998 – Kay et al, JICE 1998 – Fitzpatrick et al, Am Heart J 1996)
- Decrease in healthcare costs:
  - ↓ hospitalisations,
  - ↓ outpatient visits and
  - ↓ AAD use

# AV node ablation and permanent pacemaker implantation

- Caution:
  - Avoid single chamber system in paroxysmal AF (Schuchert et al, Cardiology 1997 – Marshall et al, Heart 1998)
  - Biventricular pacemaker should be preferred in patients with impaired left ventricular function (not tachycardia induced) (Wilkoff et al, JAMA 2002 – Doshi et al, JCE 2005)
  - Thromboembolic risk remains

# Conclusions

- Rate control: therapeutically convenient option in patients who are older, minimally symptomatic and those who might not tolerate the adverse effects of currently available AADs
- Currently available data supports the use of lenient rate control as a front-line strategy over strict rate control for most patients treated with rate control, although heart failure patients may benefit from more aggressive rate control targets

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