

# “Who needs DC Cardioversion?”

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# A rhetorical question?

	<b>Patients (n= )</b>	<b>1° outcome</b>	<b>Comments</b>
<b>PIAF</b>	252	Symptoms	No difference
<b>STAF</b>	200	MACE & stroke	No difference
<b>RACE</b>	522	CV death, admissions, stroke, bleed	No difference
<b>HOT- CAFE</b>	205	Death, stroke, bleed	No difference
<b>AFFIRM</b>	4060	Overall mortality	No difference

## **Influence of the randomized trials, AFFIRM and RACE, on the management of atrial fibrillation in two University Medical Centers.**

Mason PK, Wood MA, Lake D, Dimarco JP.  
*Am J Cardiol.* 2005 May 15;95(10):1248-50.

From January 1998 to March 2002, monthly averages:

- **31 +/- 8** elective cardioversions and
- **6 +/- 3** AV Node ablations performed.

From April 2002 to December 2003, the monthly averages:

- **21 +/- 6** cardioversions ( $p = 0.001$ ) and
- **9 +/- 3** ablations ( $p = 0.001$ ).

# Why is this so surprising?

- AF is associated with an increased mortality
- Thus eliminating AF should improve mortality...

*So why is this not the case?*

# Some questions to think about

- Do anti-arrhythmics increase mortality?
- Is AF mortality related to stroke alone, and hence continuing warfarin is the key?
- Strategy *versus* Reality: does rhythm control = no AF?
- Do beta-blockers & digoxin confer an advantage, especially when concomitant heart disease is present?

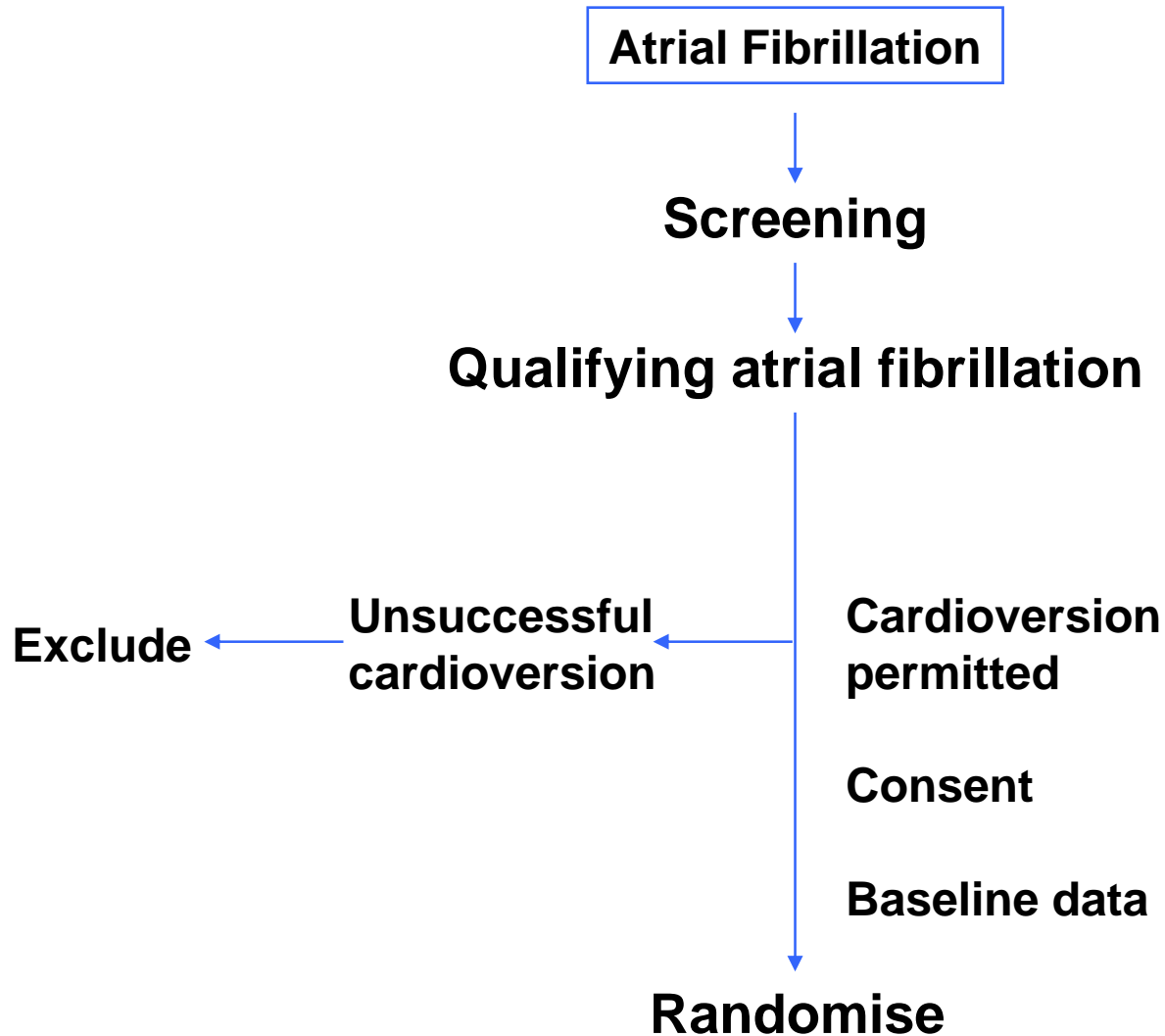
# AFFIRM

- Atrial Fibrillation Follow-up Investigation of Rhythm Management
- Hypothesis: Effect on mortality of antiarrhythmic therapy to maintain sinus rhythm vs. ventricular rate control alone, in the presence of anticoagulation
- Primary endpoint: Total mortality
- Secondary endpoint: Disabling CVA  
Cost of therapy  
Quality of life

# AFFIRM Inclusion Criteria

- Age  $\geq$  65 yrs
- Age  $<$  65 yrs + 1 or more risk factors
- 1 episode of AF, duration  $>$  6 hours, within 6 months

# AFFIRM Study Protocol



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Randomize

**Heart rate control  
anticoagulation**

**STEP I**

**Maintain sinus rhythm  
anticoagulation**

Antithrombotic therapy per guidelines  
Follow-up  
≥ 2 pharmacologic trials

Antithrombotic therapy per guidelines  
Cardioversion prn  
Follow-up  
≥ 2 pharmacologic trials

Protocol-specified innovative  
therapy for heart rate control,  
or continue step I  
pharmacologic trials

**STEP II**

Protocol-specified innovative therapy  
for maintenance of sinus rhythm,  
or continue step I pharmacologic  
trials and prn cardioversion

Antithrombotic therapy per guidelines  
Follow-up

Antithrombotic therapy per guidelines  
Cardioversion prn  
Follow-up

# AFFIRM study

- >65 yrs old
- Randomised to Rhythm control or Rate control
- Rhythm = amiodarone, sotalol, some class Ic drugs + DC cardioversion
- Warfarin stopped at 6-12 weeks post DCC if in SR

# Cause of death in AFFIRM

TABLE 1. Mechanism of Death in the AFFIRM Study

Mode of Death	Rate Control (n=2027), n	Rhythm Control (n=2033), n	P *
Total deaths	310	356	0.07
Cardiac	130	129	0.95
Arrhythmic	79	77	0.88
Nonarrhythmic	43	46	0.75
CHF or shock, with MI	7	7	
CHF or shock, no MI	26	27	
Cardiac surgery/procedure	6	5	
Other/unknown	4	7	
Uncertain	8	6	0.60
Vascular	37	35	0.82
CNS	28	28	>0.99
Ischemic strokes	17	15	
CNS hemorrhage	11	13	
Other	9	7	
Noncardiovascular	113	169	0.0008
Pulmonary	23	39	0.04
Cancer	52	81	0.01
Other/uncertain	38	49	0.24
Unclassifiable	30	23	0.34

MI indicates myocardial infarction.

\*Log rank test, unadjusted for multiple analyses.

- At total of 666 patients died in AFFIRM
- Most differences non-significant (statistically)

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**TABLE 2. Characteristics of Cardiac Deaths in the AFFIRM Study**

Mode of Death	Rate Control (n=2027), n (%)	Rhythm Control (n=2033), n (%)	<i>P</i> *
Total cardiac deaths	130 (100)	129 (100)	...
Death associated with ischemia	23 (18)	18 (14)	0.41
Duration of symptoms <24 hours	18 (38)	23 (43)	0.60
Death witnessed	67 (58)	71 (64)	0.38
Death during sleep	27 (21)	7 (5)	0.007
Onset of terminal event in hospital	35 (27)	42 (33)	0.32
Rhythm associated with terminal event			0.75
Never monitored	62 (48)	65 (51)	
Monitored before and during collapse	20 (16)	22 (17)	
Monitored only after collapse	47 (36)	41 (32)	
Time from onset of collapse to monitoring, min, mean±SD	20±20	18±13	0.59
If monitored, first rhythm			0.61
VF	21 (31)	17 (27)	
VT	3 (4)	6 (10)	
Asystole	21 (31)	22 (35)	
Other	22 (33)	17 (27)	

Percentages reported are proportions.

\**P* value associated with  $\chi^2$  test for homogeneity or *t* test.

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# Conclusion

- No increase in AAD death/cardiac death
- No difference in strokes *including ischaemic and haemorrhagic*
- *Conclude AADs are safe, and no additional benefit with beta-blockers or digoxin?*

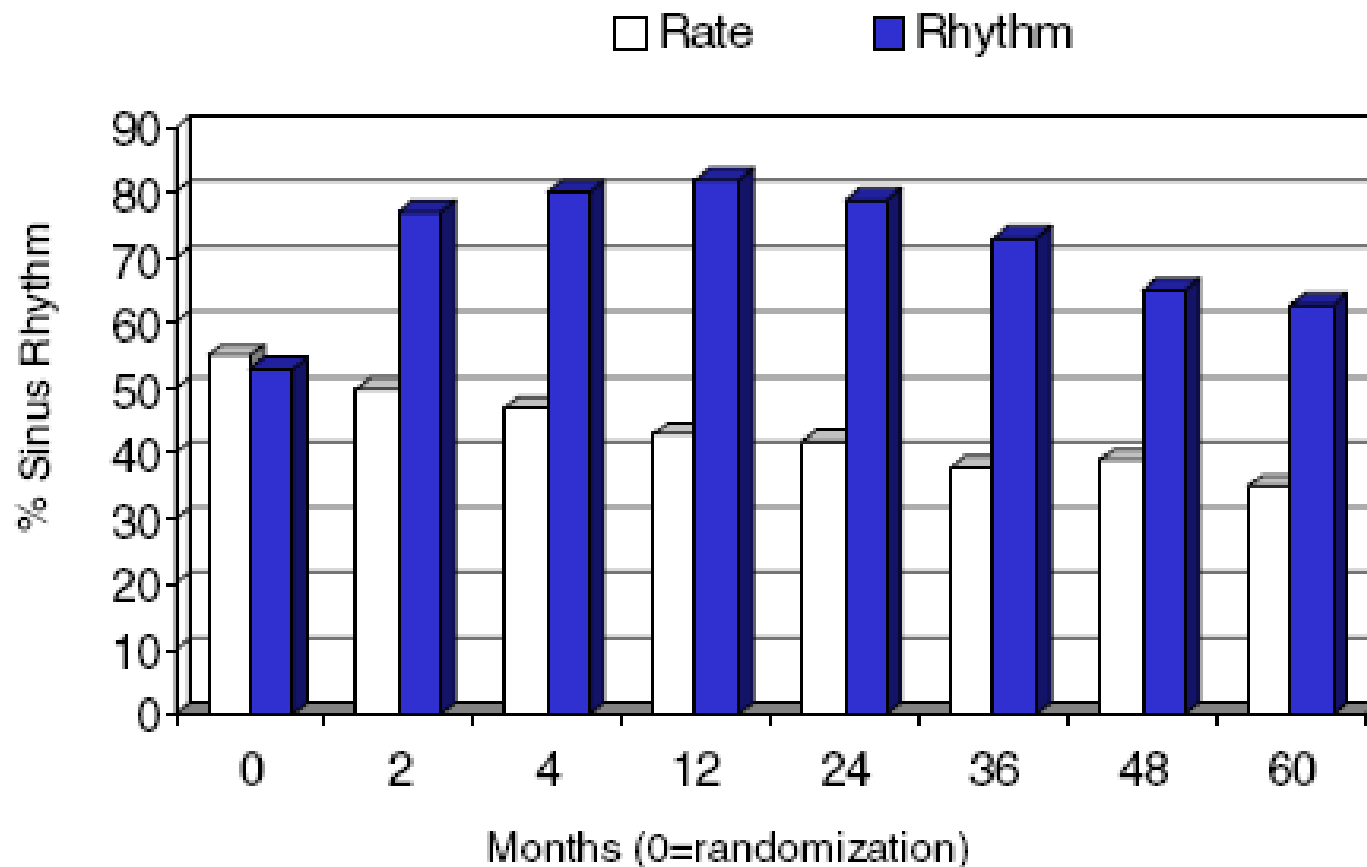
# Conclusion II

- Bizarrely increase risk of cancer (predominantly lung ca.) in rhythm control & increased risk of dying in sleep with rate control

# Strategy v. Reality

- Randomisation occurred in SR for 54% of patients
- At the end of the study 35% of those assigned to rate control remained in SR
- Rhythm control was maintained in 82%, although no monitoring was performed in between visits for ECGs

# Does rhythm control actually mean “staying in SR”?



*Fig. 2. Prevalence of sinus rhythm over the course of 60 months in the AFFIRM trial.*

- Cross-over occurred in 12% of **rate** control patients...
- ...and 29% of rhythm control due to “an inability to maintain SR” and “Drug intolerances”.
- Final analysis was “intention to treat”.

- *Thus in final analysis a difference in rhythm was only present in 30% of the entire study population*

# Additional drug effects?

- Commonest drug used in Rhythm arm was Amiodarone (60%)
- Previous studies have linked amiodarone with increased non-cardiac deaths (e.g. EMIAT and AVID) but other studies have not found this association

# Additional drug effects?

- Is warfarin beneficial in cancer?
  - Some evidence linking it with an anti-neoplastic effect, particularly in context of metastases
  - Also may aid combat the hyper-coagulable state of cancer

# In Summary

- Employing a “Rhythm-control strategy” will not:
  - Improve mortality
  - Decrease stroke
  - Improve symptoms (*when applied regardless of symptoms at baseline!*)
  - Decrease hospitalisations (data not shown)

# In Summary (II)

- Anti-coagulation in AF patients should be based upon risk assessment, such as CHADS2 score *regardless of apparent rhythm at follow up.*

# What we don't know...

- Is which sub-groups (if any) might benefit from DCC and AADs?
- Whether non-pharmacological measures might confer benefits (e.g. Successful catheter ablation)

# To answer the question: *Who needs DCC?*

- Those with secondary AF (post CABG, post pneumonia, etc)
- Those post ablation
- Those who stay in SR without drugs and are willing to stay on warfarin depending on CHADS2 score!

Thank you