Update on Atrial Fibrillation

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Disclosures

- None

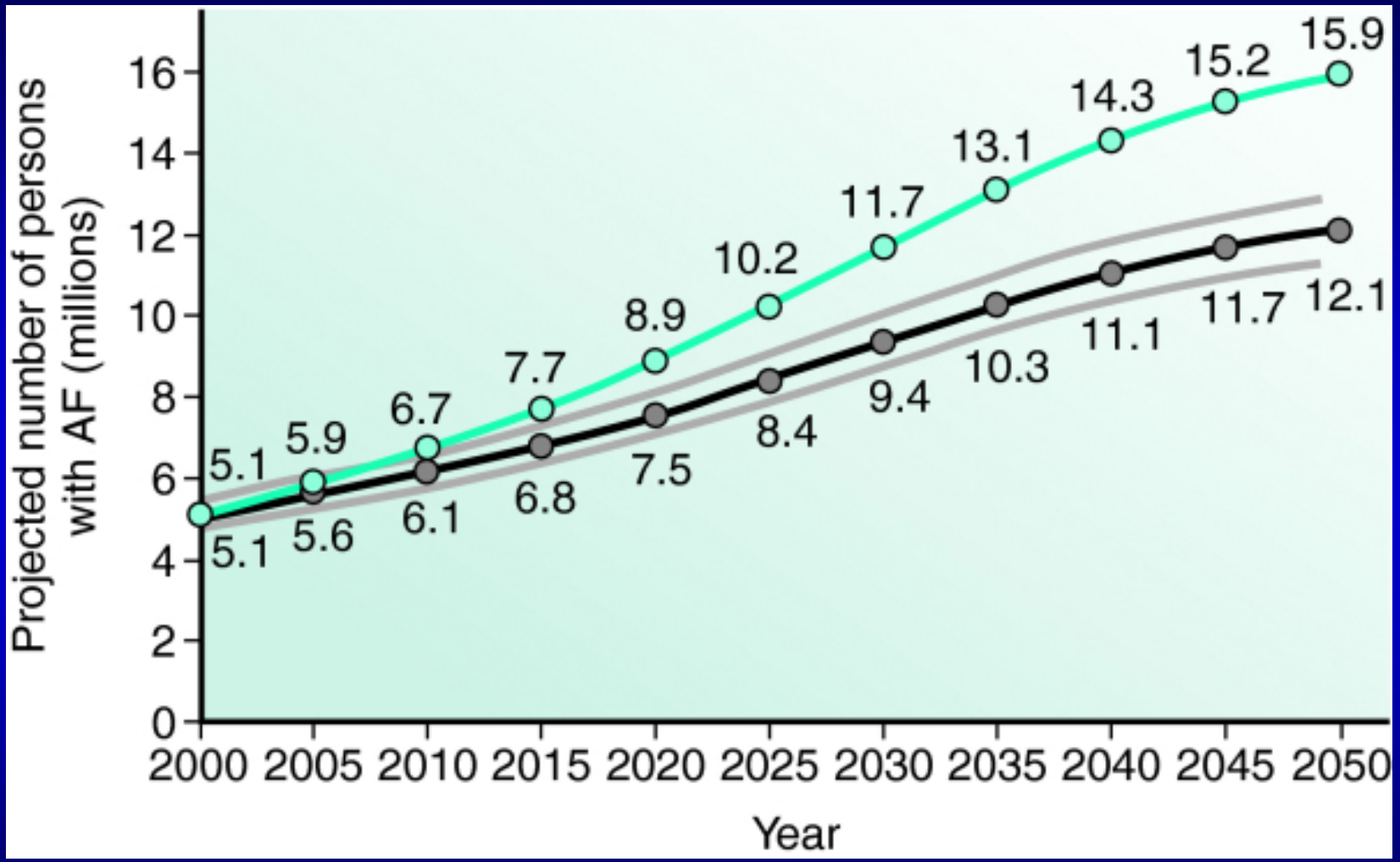
Atrial Fibrillation

- **Objectives**
  - Review epidemiology and morbidity/mortality associated with AF
  - Review landmark drug trials aimed at rhythm control.
  - Review efficacy of AF ablation
  - Discuss novel ablation techniques
  - Review long term outcomes associated with AF ablation

Atrial Fibrillation

- **Most common arrhythmia in clinical practice.**
- Prevalence increases with age.
- Incidence is more prevalent among men
- .1 % per year in patients younger than 40.
- 1.5-2.5% in patients older than 80.
- Estimated at 12 million by 2050.

Atrial Fibrillation

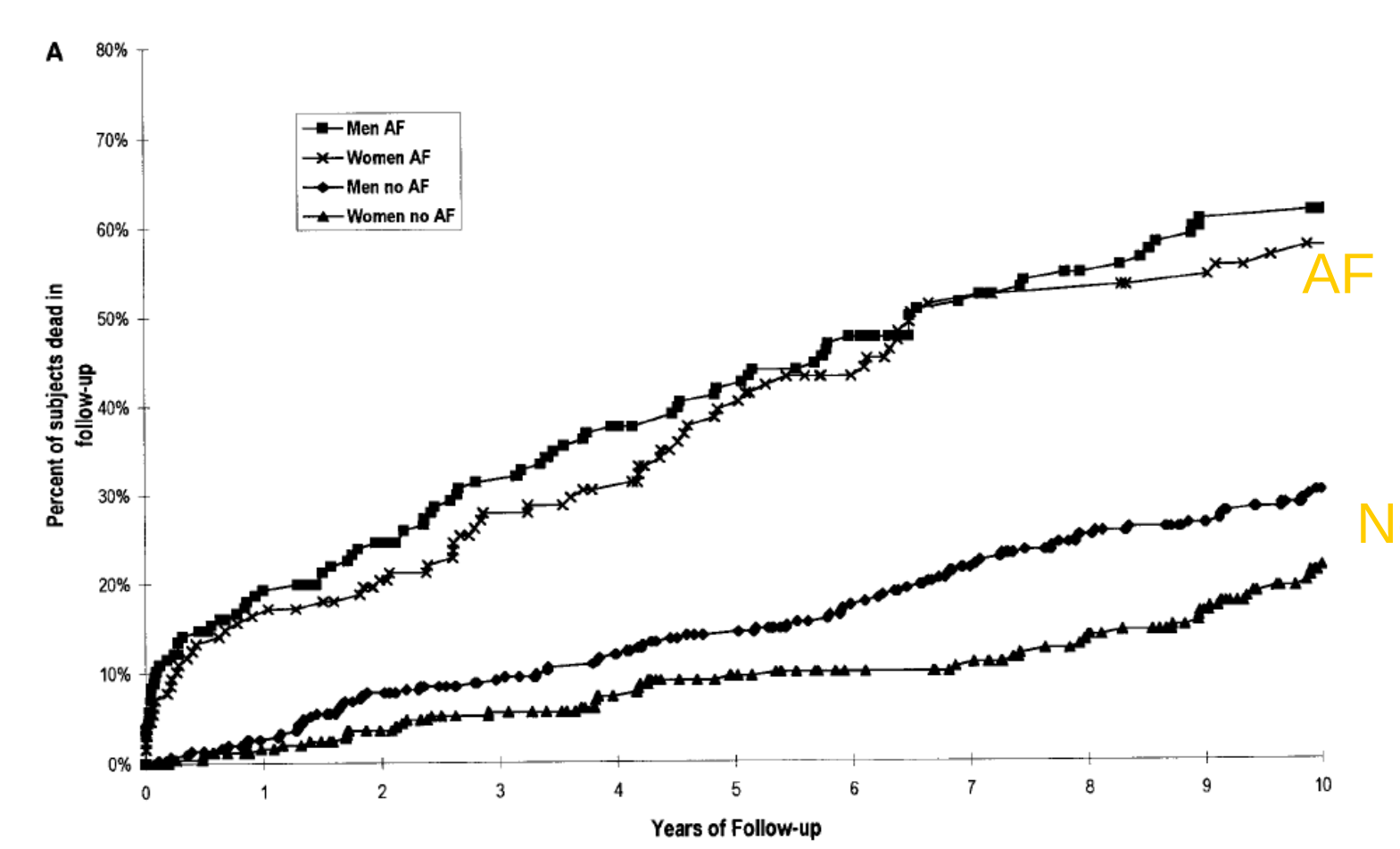


Miayasaka et al. Circulation 2006; 114:119-125

Atrial Fibrillation

- 1/3 of hospitalizations for cardiac rhythm disturbances.
- 2.2 million in the US have paroxysmal or persistent AF.
- Increased mortality, morbidity.
- 5% rate of ischemic stroke in nonvalvular AF:
  - 5-7 times that of people without AF.
  - 1/6 strokes occurs in people with AF.
  - Higher rates in patients with rheumatic heart disease.

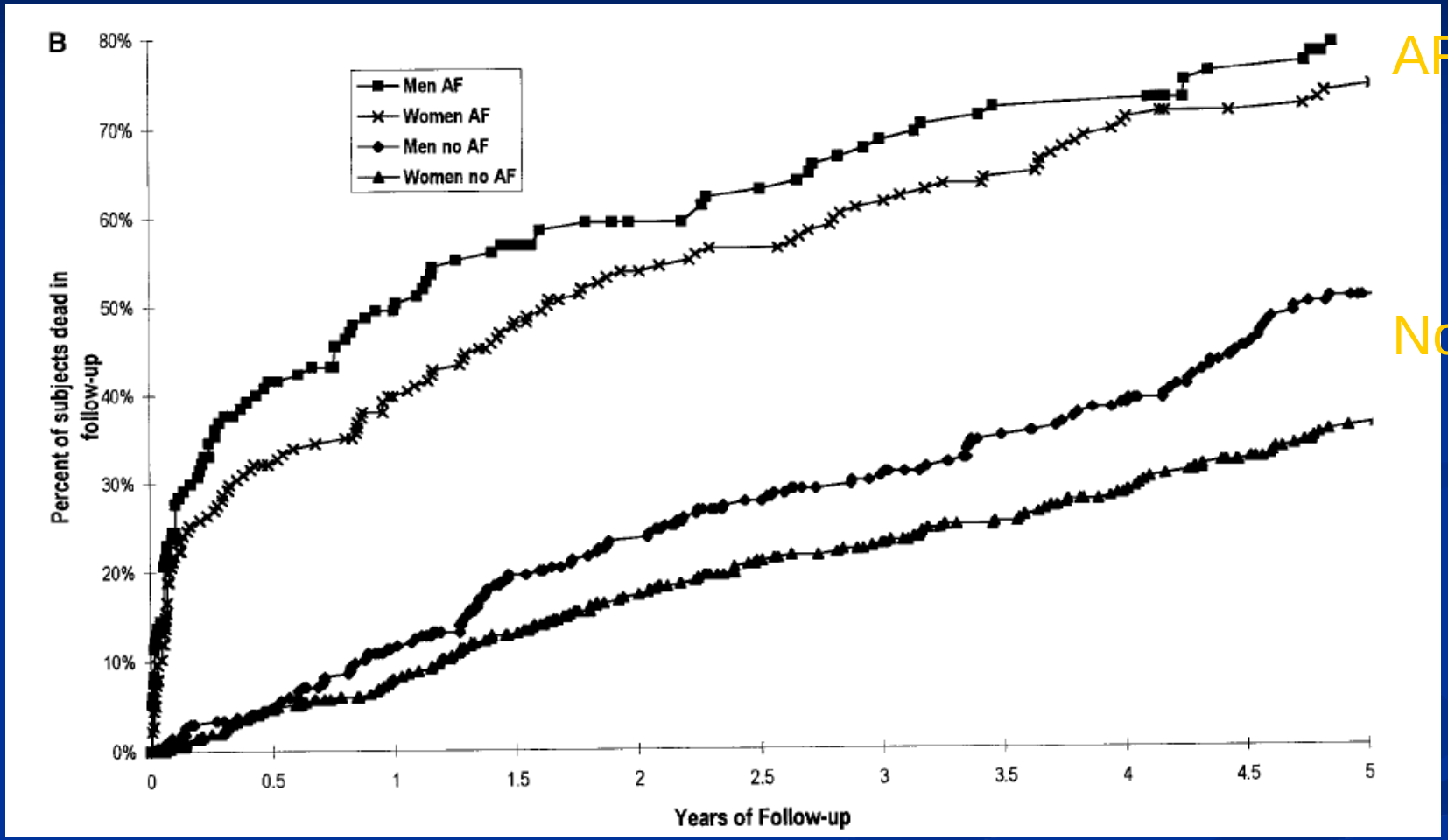
Framingham Mortality



Patient (Ages 55-74) Mortality

Benjamin et al. Circulation 1998

Mortality

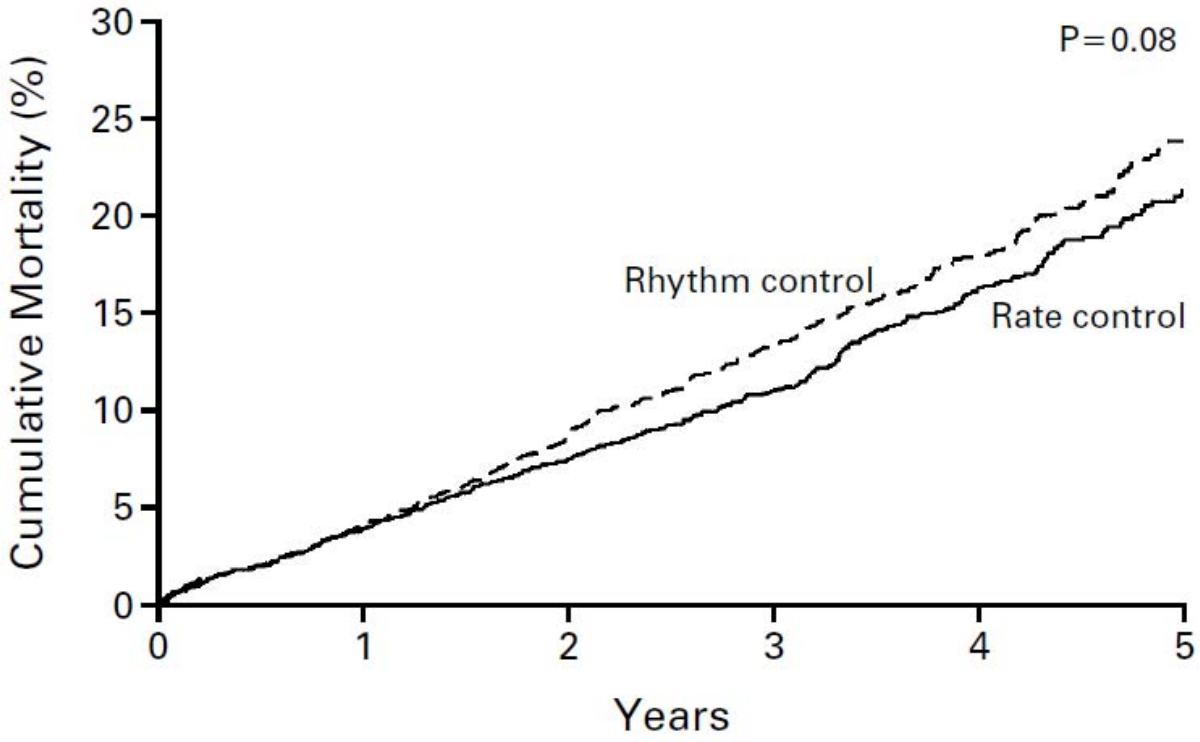


Patient (75-94) Mortality

Rate Control Vs Rhythm Control: Survival

- Hypothesis tested that maintenance of rhythm control would significantly improve mortality associated with AF.

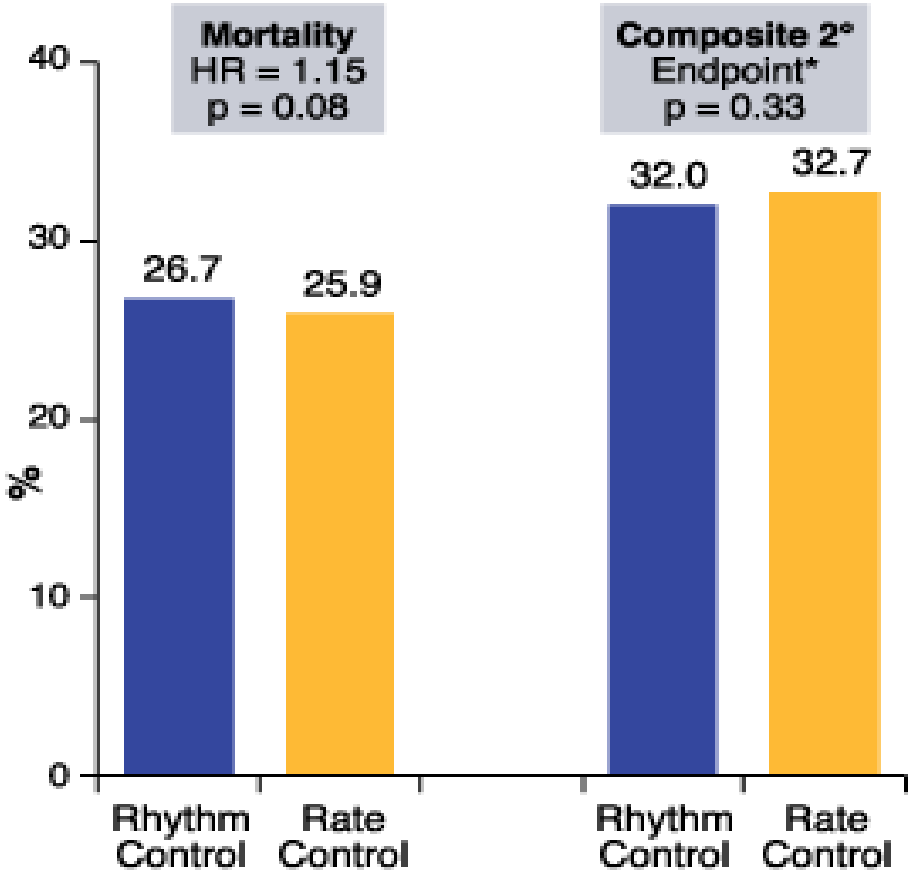
The AFFIRM Trial



No. of Deaths		number (percent)				
Rhythm control	0	80 (4)	175 (9)	257 (13)	314 (18)	352 (24)
Rate control	0	78 (4)	148 (7)	210 (11)	275 (16)	306 (21)

The AFFIRM Trial

Trial Design: AFFIRM was a multi-center randomized trial of rhythm control (n=2,033) vs rate control (n=2,027) in patients with atrial fibrillation and a high risk of stroke or death. Patients were followed for 5 years. The primary endpoint was all-cause mortality.



www.cardiosource.com

Results

- All cause mortality did not differ between the rate and rhythm control arms
- Hospitalization rate was higher in the rhythm control arm (80% vs 73%, $p<0.001$)

Conclusions

- There is no survival benefit to the strategy of rhythm control in elderly patients with atrial fibrillation

Limitations

- Trial enrolled high-risk elderly patients; extrapolation of results to other subgroups may not be appropriate

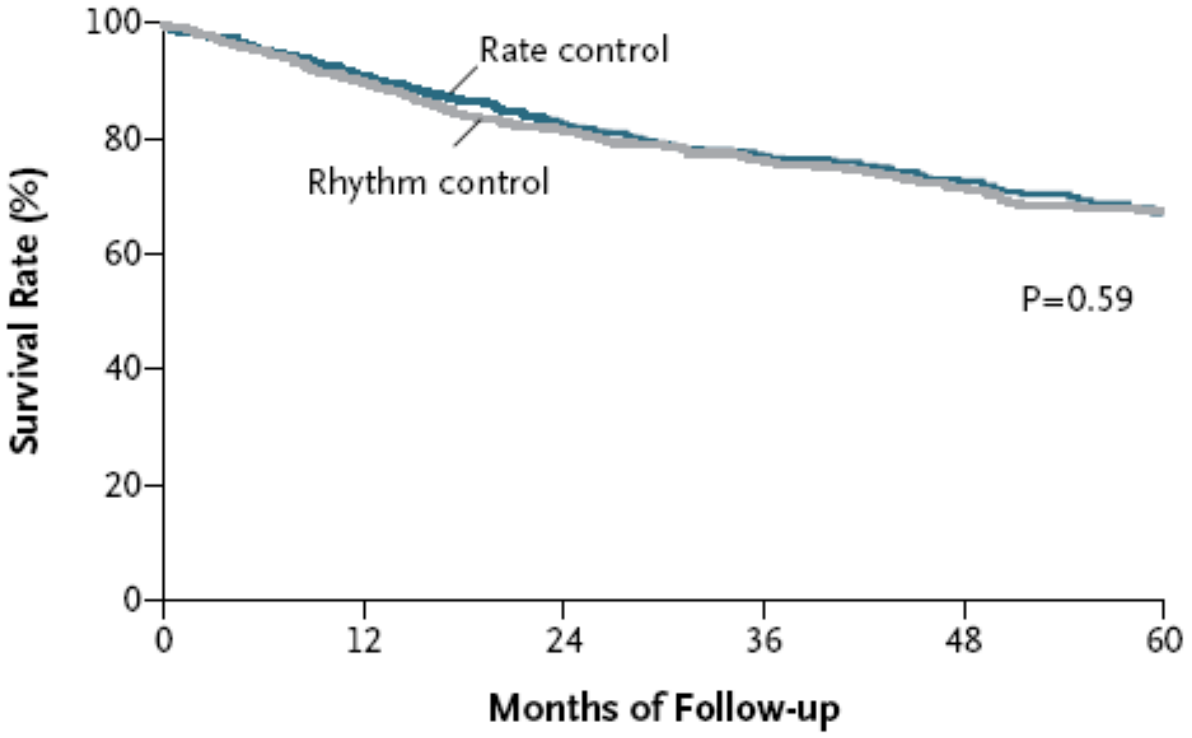
* Composite of death, disabling stroke, disabling anoxic encephalopathy, major bleeding, and cardiac arrest

N Engl J Med 2002; 347:1825-33.

AF-CHF Trial

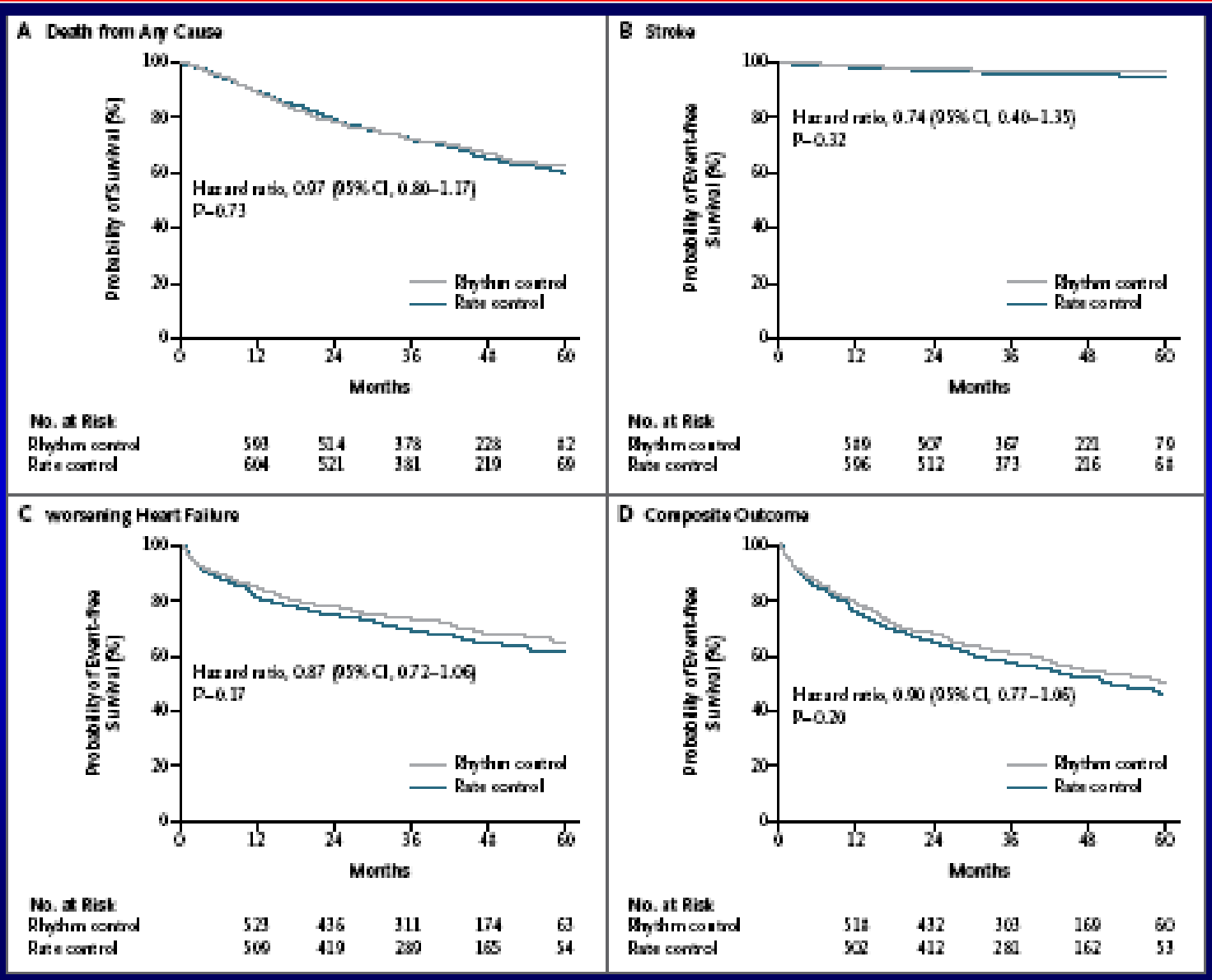
- 1376 patients
  - LVEF <35%, AF, sxs of CHF randomized
    - rate vs rhythm approach
    - Follow-up 37 months.
- Primary outcome
  - time to death from cardiovascular causes.

AF-CHF: Primary Outcome



No. at Risk					
Rhythm control	593	514	378	228	82
Rate control	604	521	381	219	69

AF-CHF Secondary Outcomes



Rate Control Vs Rhythm Control: Survival

- Six randomized trials comparing rate vs rhythm control
  - •No survival advantage with rhythm control.
  - •AFFIRM and RACE studies demonstrated trend toward increase mortality in rhythm arm.

RATE VS RHYTHM
THE BATTLE BEGINS

PRESUMED BENEFIT OF NSR
Fewer sxs/better exercise tolerance
Lower risk of stroke
Long term anticogulation not needed
Better survival

PRESUMPTIONS SHATTERED…

PRESUMED BENEFIT OF NSR	OUTCOME
Fewer sxs/better exercise tolerance	No diff. in functional status
Lower risk of stroke	More strokes in NSR arm
Long term anticogulation not needed	More strokes occurred off coumadin or INR<2.
Better survival	No diff. in survival; trend toward inc late risk

Atrial Fibrillation

So can we conclude that rate control strategy is better than rhythm control?

Performance and Analysis of Clinical Trials

- Trials were performed with ITT.
- Younger patients with stroke risk factors not included
- Symptomatic patients excluded.
  - compromise applicability of study to overall AF population.
- Therapeutic interventions did not investigate outcome of specific drug.
- Anticoagulation discontinued in more patients randomized to rhythm control, thus more thromboembolic complications.

ns

Non ITT Observations

- In AFFIRM substudy with on treatment analysis, SR maintenance was associated with decreased risk of death (HR 0.53), however AADs (mostly amio) were associated with offsetting increased mortality.

- Restoration and maintenance of NSR was correlated with significantly lower risk than placebo for all-cause CHF rehospitalizations.

BOTTOM LINE

- New Therapy needed!!!!!

Atrial Fibrillation

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Circumferential Pulmonary-Vein Ablation for Chronic Atrial Fibrillation

Hakan Oral, M.D., Carlo Pappone, M.D., Aman Chugh, M.D., Eric Good, D.O., Frank Bogun, M.D., Frank Pelosi, Jr., M.D., Eric R. Bates, M.D., Michael H. Lehmann, M.D., Gabriele Vicedomini, M.D., Giuseppe Augello, M.D., Eustachio Agricola, M.D., Simone Sala, M.D., Vincenzo Santinelli, M.D., and Fred Morady, M.D.

2006

Atrial Fibrillation

- 2002-2004 - 146 patients with chronic AF (six mos) randomized to amio (control) or in combo with PVI.
- Exclusion criteria as shown on right

Table 1. Exclusion Criteria.

Age <18 or >70 yr
Left atrial diameter >55 mm
Left ventricular ejection fraction <30 percent
Contraindication to amiodarone therapy or anticoagulation with warfarin
Presence of a mechanical prosthetic valve
History of a cerebrovascular accident
Presence of left atrial thrombus on transesophageal echocardiography
Prior attempt at catheter or surgical ablation for atrial fibrillation

Study Design

- Study design – determine efficacy of PVI in absence of AAD.
- Amiodarone 3 mos following.
- Cardioversion performed if AF developed in first 3 mos.

Table 2. Characteristics of the Patients.*

Characteristic	Control (N = 69)	Circumferential Pulmonary-Vein Ablation (N = 77)
Age (yr)	58±8	55±9†
Sex (no. of patients)		
Male	62	67
Female	7	10
Duration of atrial fibrillation (yr)	4±4	5±4
Left atrial diameter (mm)	45±5	45±6
Left ventricular ejection fraction (%)	56±7	55±7
Structural heart disease (no. of patients)	6	6
Nonischemic cardiomyopathy	1	2
Coronary artery disease	4	3
Valvular heart disease	0	1
Congenital heart disease	1	0
No. of previously ineffective anti-arrhythmic drugs	2.1±1.2	2.0±1.2
No. of prior cardioversions	1.7±1.0	2.2±1.7

Younger patients than AFFIRM

DCCV

18 in PVI group

67 in Control group

Repeat ablation

25 in PVI group

20 for AF

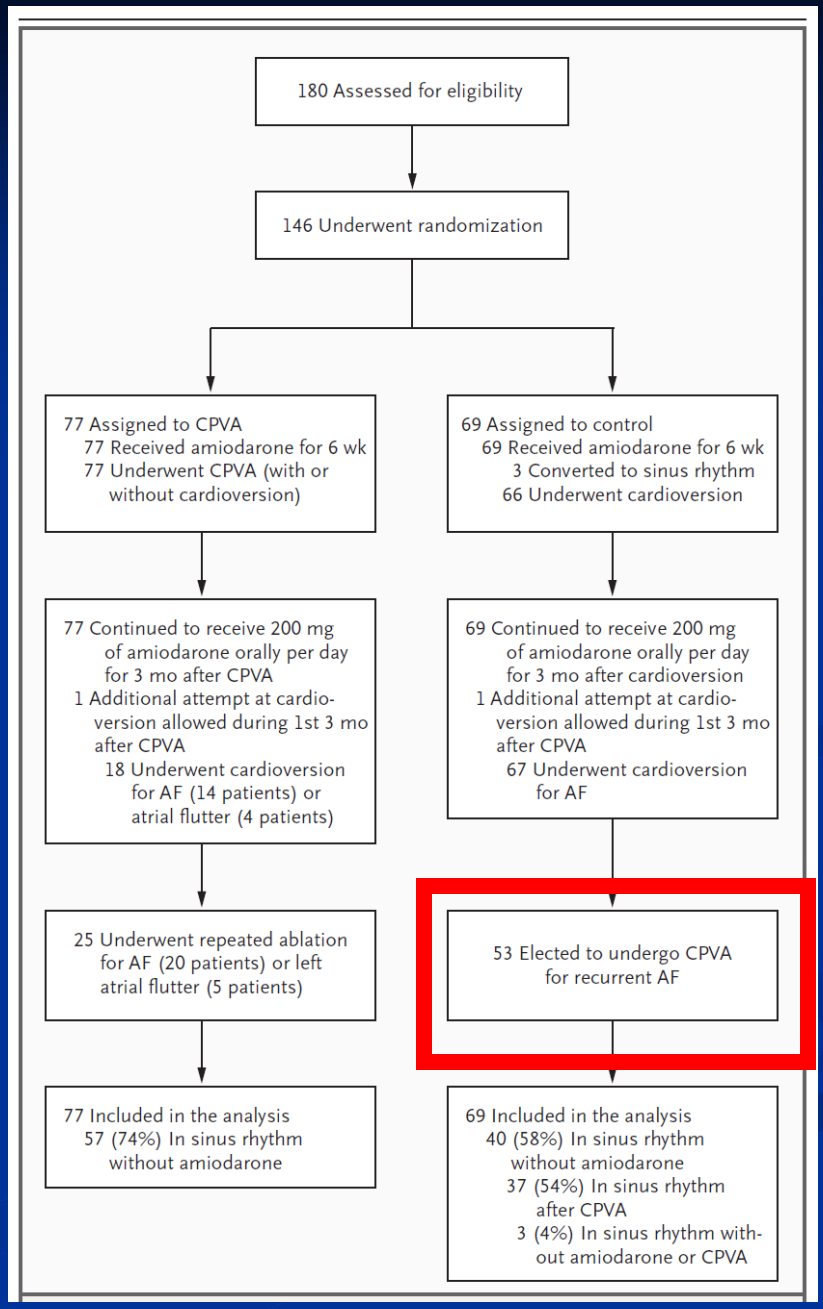
5 for AFL

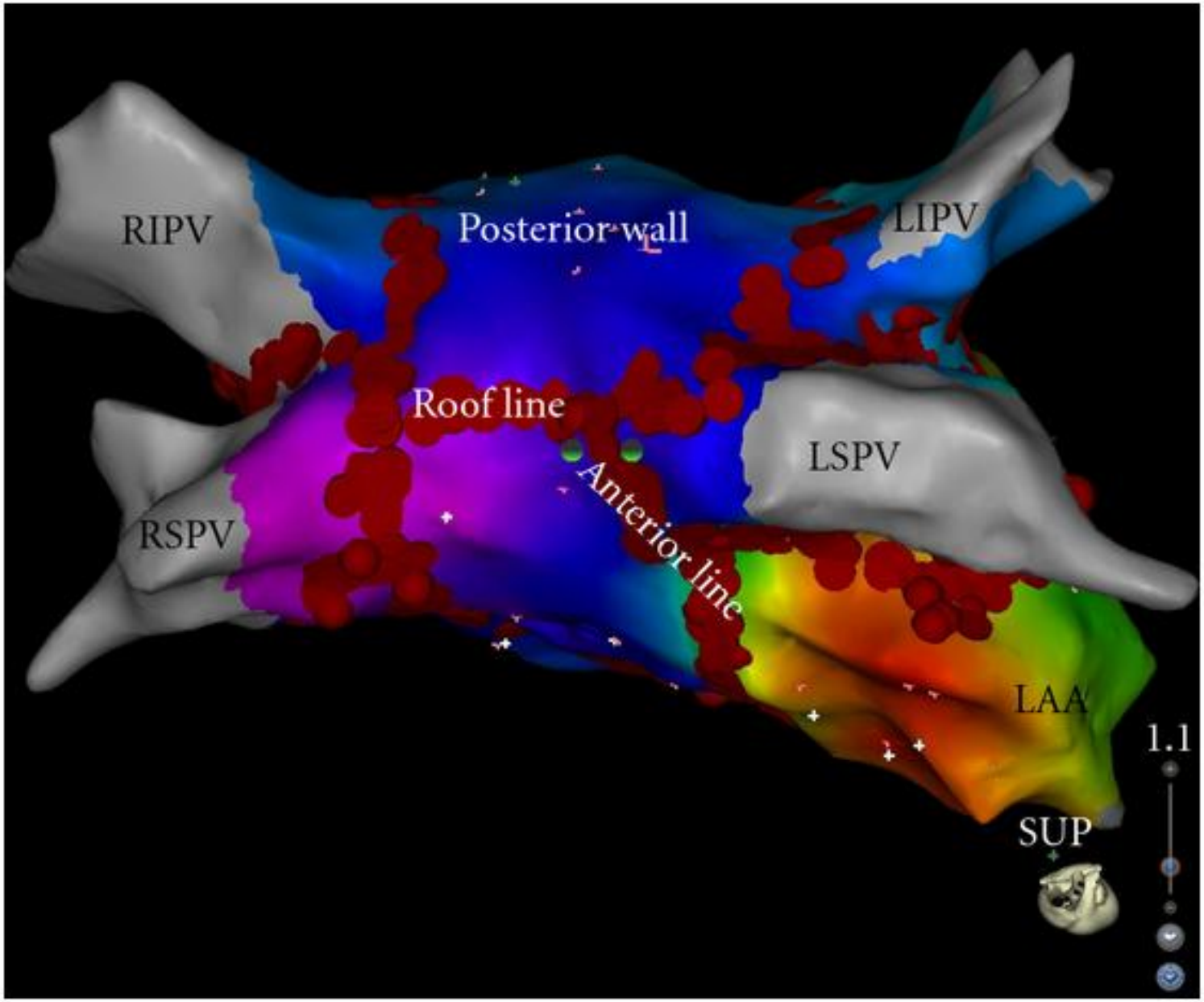
SR –

PVI - 74% in SR without amio

Control- If AF persisted after 3 mos → PVI vs amio

- **only 3 in SR without PVI or amio**




RIPV
Posterior wall
LIPV
Roof line
LSPV
Anterior line
RSPV
LAA
1.1
SUP

Arctic Front Cryocatheter and Ablation Methods

Cryoballoon design

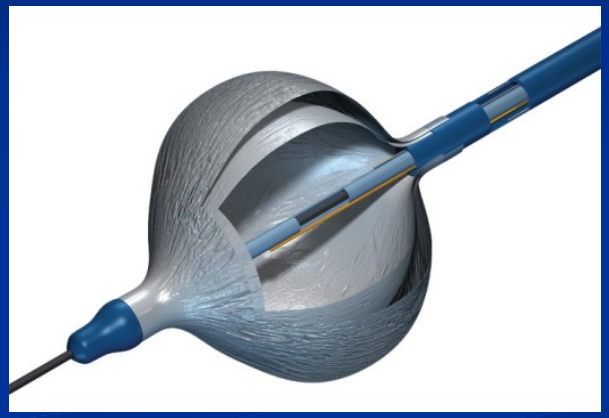
Cryoballoon sizes	23 and 28 mm
Structure	Double balloon
Cooling (in balloon)	Liquid → gas transition

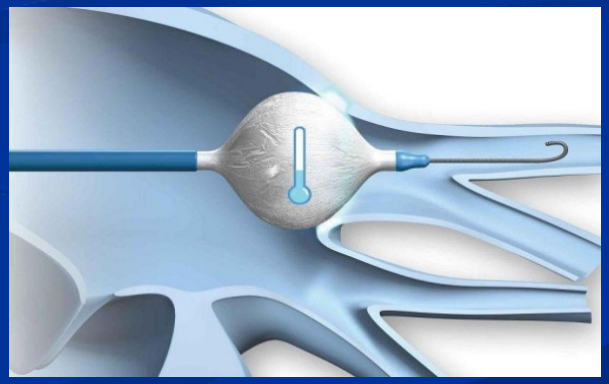
Balloon delivery

Catheter	Steerable
Sheath	14 French deflectable
Ablation	PVI w / no lines

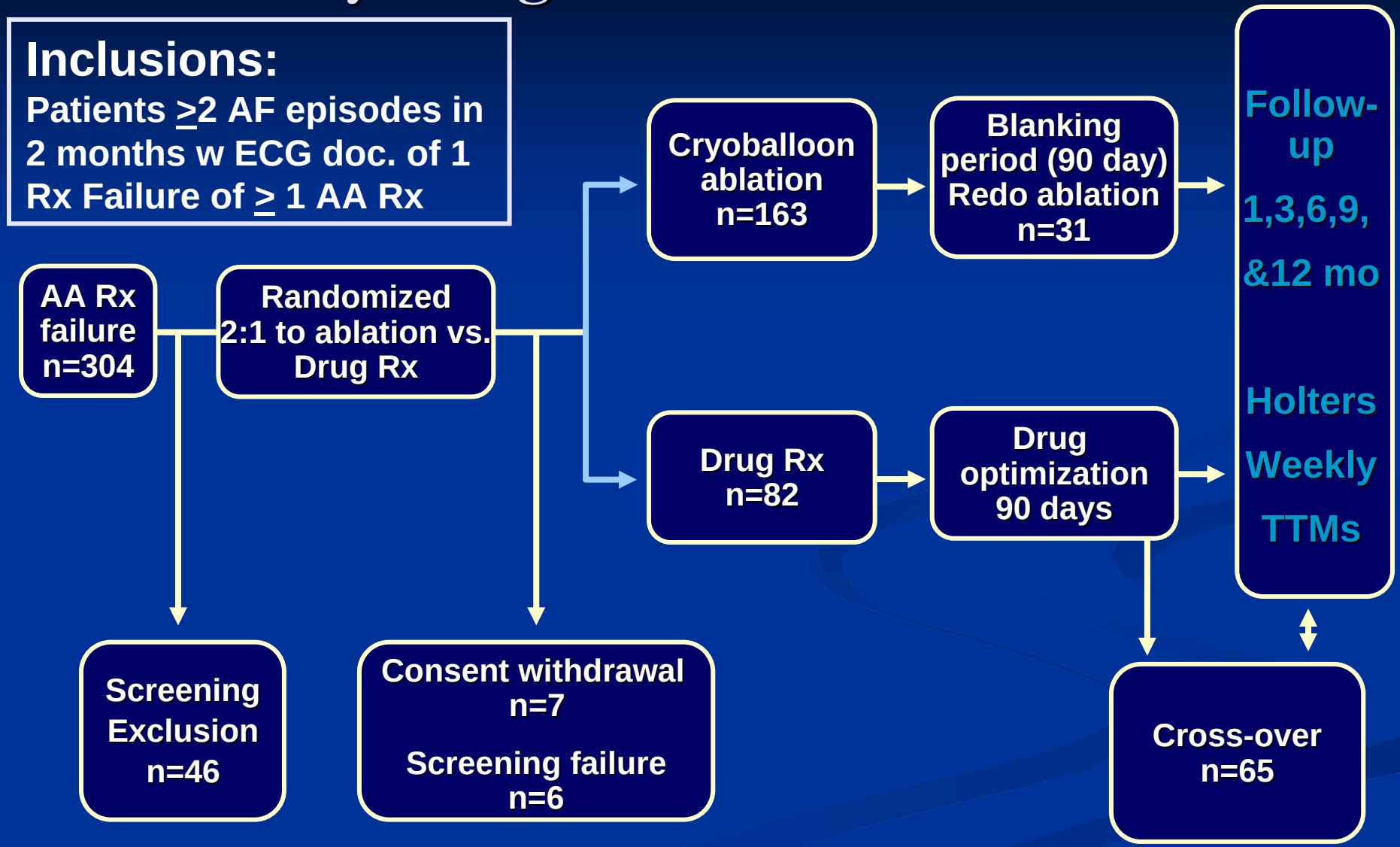
Focal Catheter

9 Fr, 8mm tip

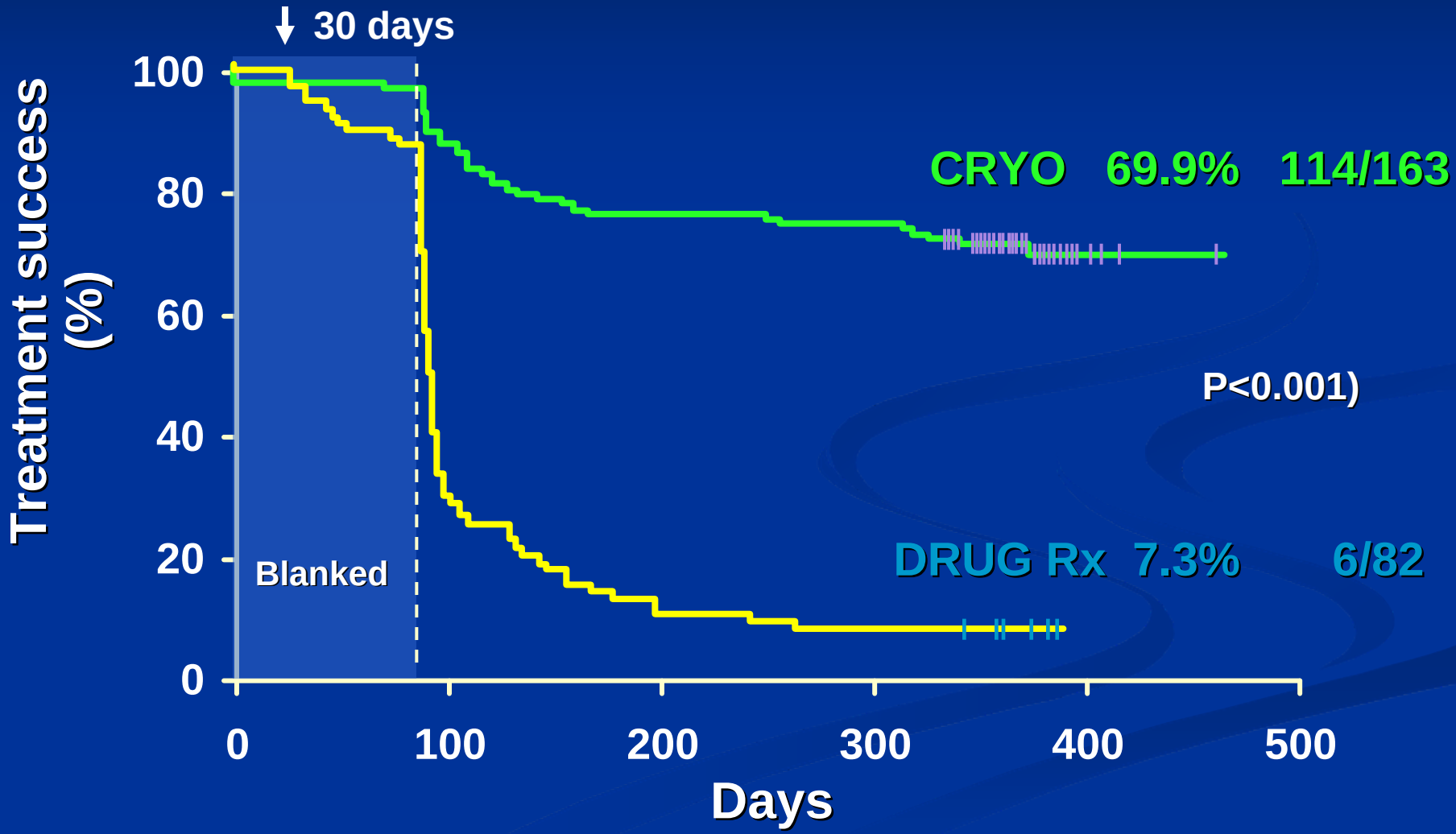




Study Design of the STOP-AF Trial



Primary Effectiveness Analysis
Treatment Success



KM estimate 68.6% (SE 3.9%) vs 7.3% (SE 2.9%)

CLINICAL RESEARCH Clinical Trials

Mortality, Morbidity, and Quality of Life After Circumferential Pulmonary Vein Ablation for Atrial Fibrillation

Outcomes From a Controlled Nonrandomized Long-Term Study

Carlo Pappone, MD, PHD,* Salvatore Rosanio, MD, PHD,* Giuseppe Augello, MD,* Giuseppe Gallus, PHD,† Gabriele Vicedomini, MD,* Patrizio Mazzone, MD,* Simone Gulletta, MD,* Filippo Gugliotta, RT,* Alessia Pappone, MD,* Vincenzo Santinelli, MD,* Valter Tortoriello, MD,* Simone Sala, MD,* Alberto Zangrillo, MD,‡ Giuseppe Crescenzi, MD,‡ Stefano Benussi, MD,§ Ottavio Alfieri, MD§

Milan, Italy

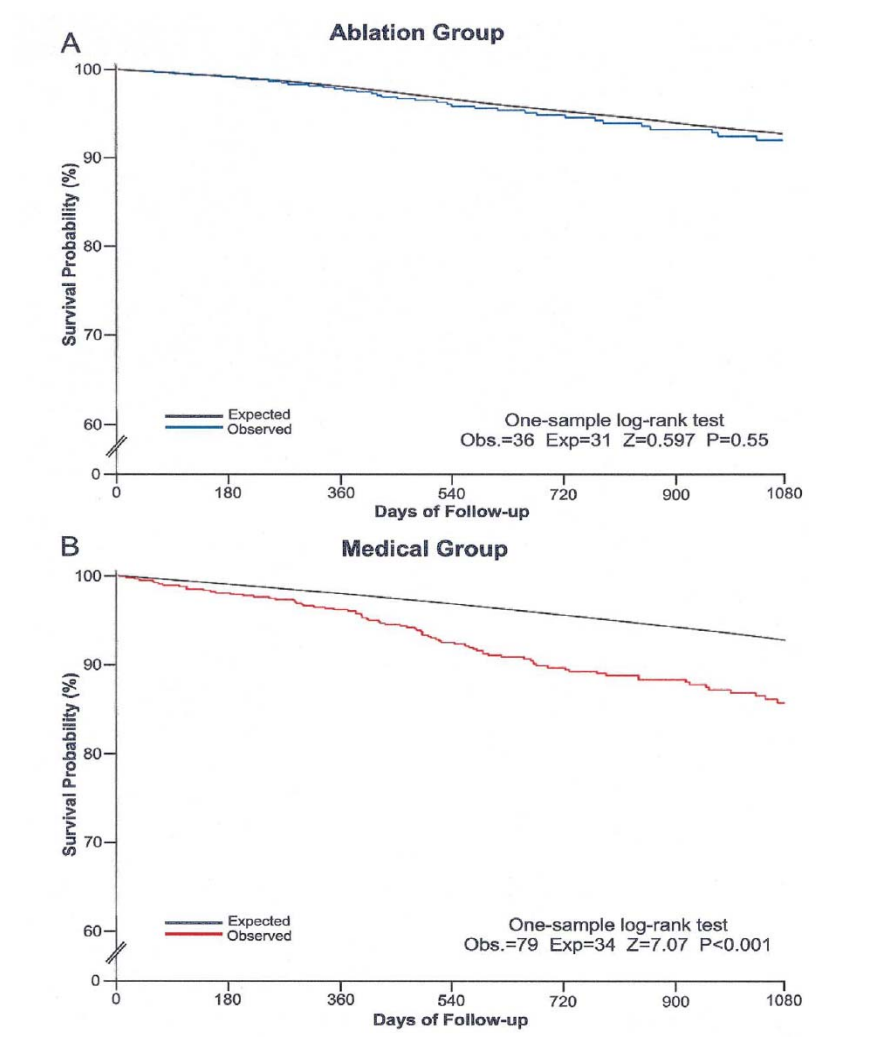
Study population 1998-2000
1,171 consecutive patients from Italy
With symptomatic AF referred to San Raffaele University.

Report on clinical course of those undergoing PVI vs medical RX

Investigate the potential of ablation to maintain SR over time

Hope that mortality/morbidity reduced with qol improvement

Survival



Survival compared to age and gender Matched controls

Patients Treated with Catheter Ablation for Atrial Fibrillation Have Long-Term Rates of Death, Stroke, and Dementia Similar to Patients Without Atrial Fibrillation

T. JARED BUNCH, M.D.,*,† BRIAN G. CRANDALL, M.D.,*,† J. PETER WEISS,*,†
HEIDI T. MAY, PH.D., M.S.P.H.,† TAMI L. BAIR,† JEFFREY S. OSBORN, M.D.,*,†
JEFFREY L. ANDERSON, M.D.,† JOSEPH B. MUHLESTEIN, M.D.,†
BENJAMIN D. HORNE, PH.D., M.P.H.,† DONALD L. LAPPE, M.D.,† and JOHN D. DAY, M.D.*,†

From the *Intermountain Heart Rhythm Specialists, and †Department of Cardiology, Intermountain Medical Center, Murray, Utah, USA

JCE 2011; 22: 839-845

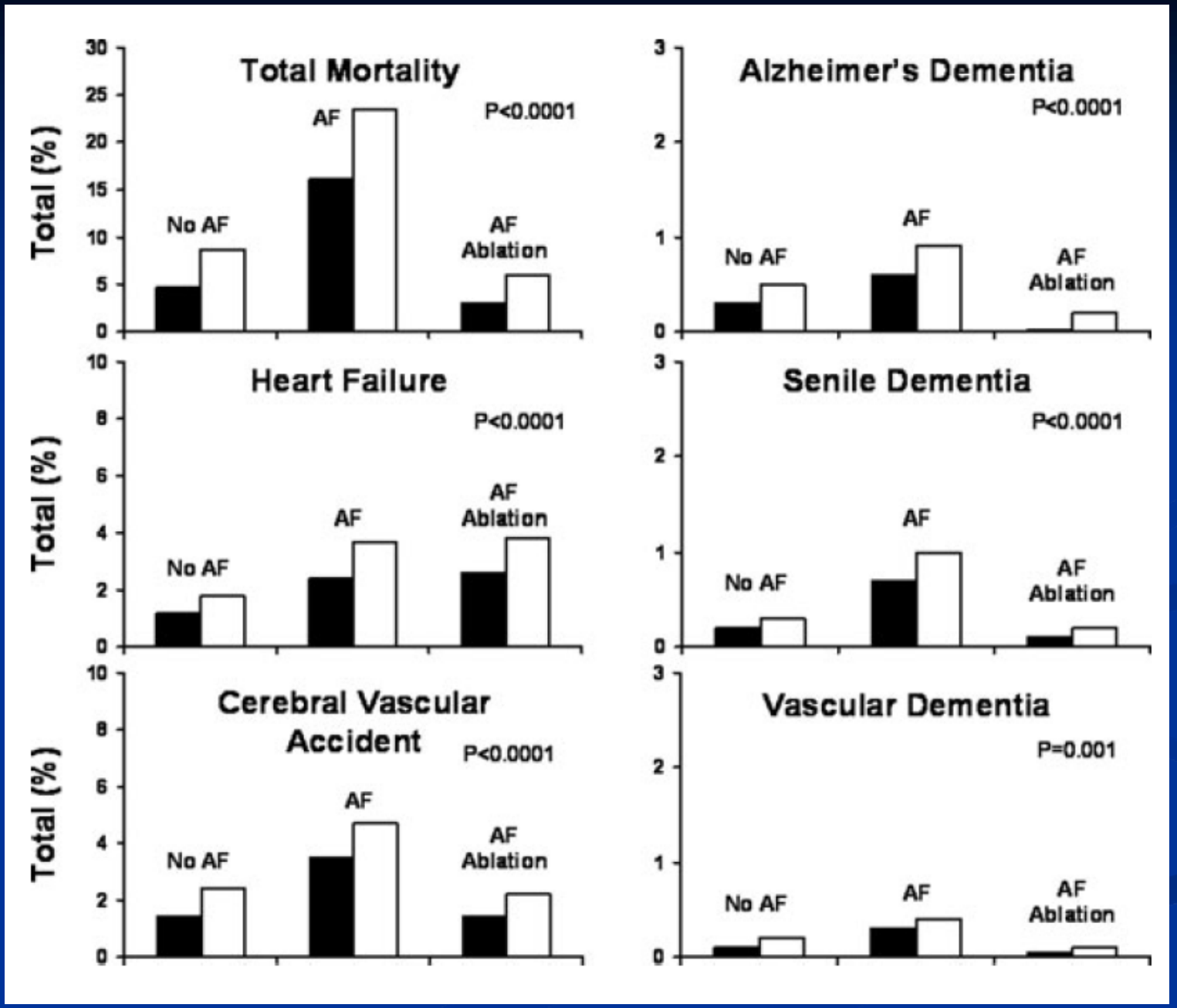
TABLE 1

Baseline Demographics of the AF Patients That Underwent an Ablation, a 4:1 Control Population of Age- and Sex-Matched AF Patients That Did Not Receive an Ablation, and a 4:1 Control Population of Age- and Sex-Matched Patients Without AF

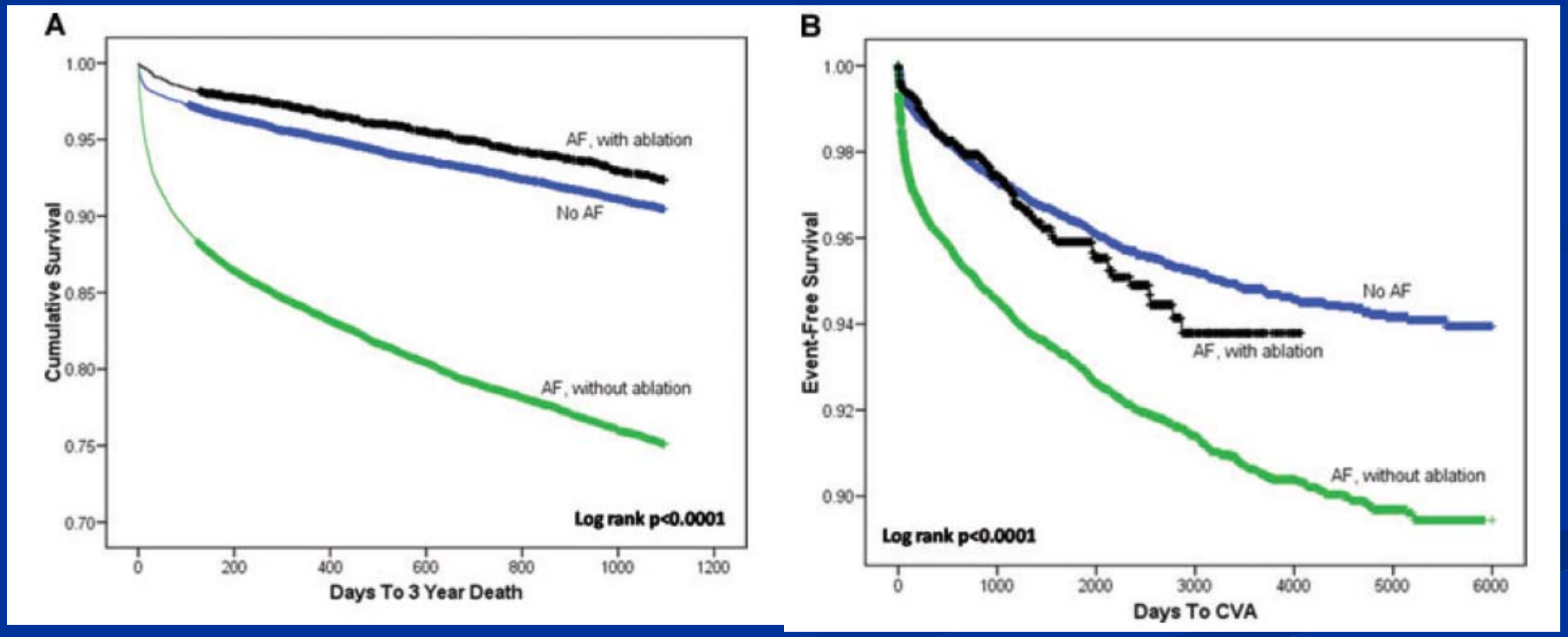
Characteristic	No AF (n = 16,848)	AF, No Ablation (n = 16,848)	AF, Ablation (n = 4,212)	P-Value
Age (years)*,†,†	64.1 ± 13.0	66.0 ± 13.3	64.8 ± 12.7	<0.0001
Sex (male)	60.8%	60.8%	60.8%	1.00
Diabetes*,†,†	19.0%	21.1%	16.3%	<0.0001
Hypertension*,†,†	41.2%	45.3%	47.8%	<0.0001
Hyperlipidemia*,†,†	58.4%	37.3%	44.0%	<0.0001
CHF*,†,†	14.5%	23.6%	29.5%	<0.0001
Renal failure*	5.6%	7.8%	7.5%	<0.0001
TIA history	4.0%	4.2%	4.6%	0.16
CVA history*,†	4.4%	6.3%	4.5%	<0.0001
MI history*,†	10.0%	6.4%	6.4%	<0.0001

*P< 0.05: no AF versus AF, no ablation.
†P< 0.05: AF, no ablation versus AF, ablation.
†P< 0.05: no AF versus AF, ablation.

JCE 2011; 22: 839-845



JCE 2011; 22: 839-845



JCE 2011; 22: 839-845

Catheter Ablation for Atrial Fibrillation

Are Results Maintained at 5 Years of Follow-Up?

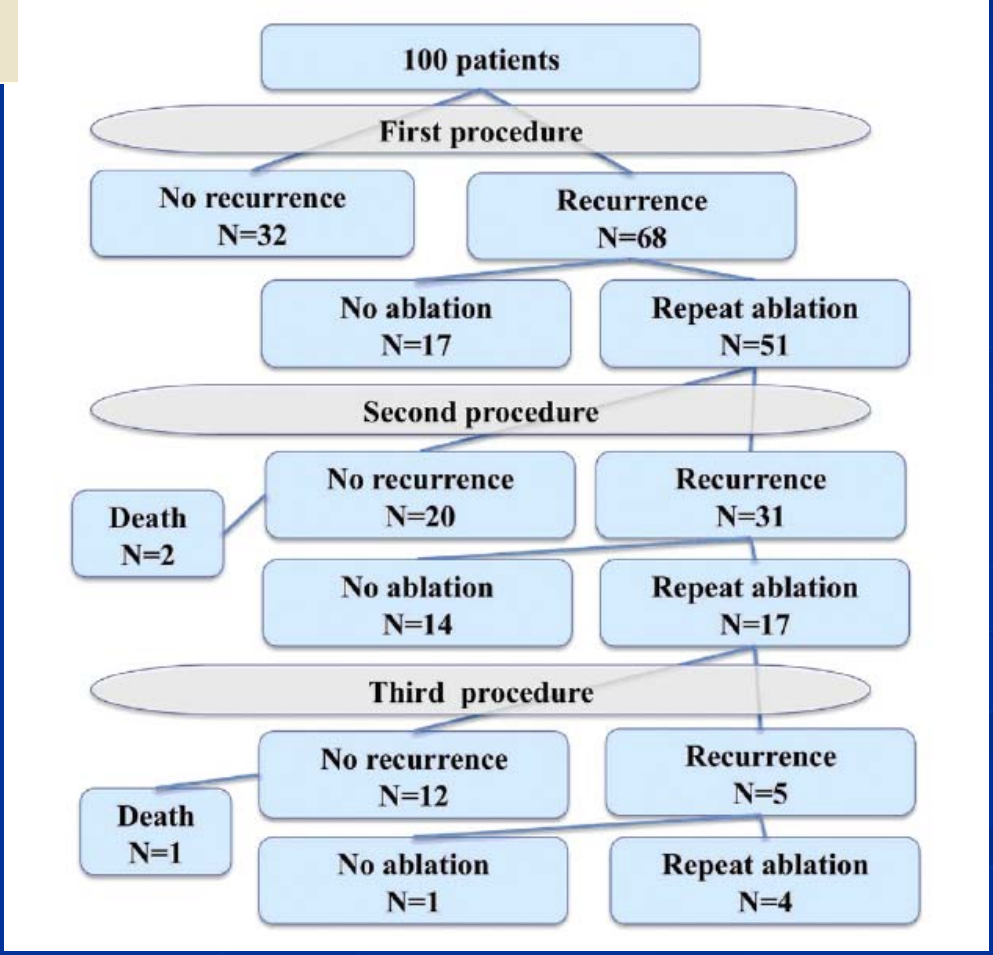
Rukshen Weerasooriya, BMEDSC(HONS), MBBS,*† Paul Khairy, MD, PHD,‡ Jean Litalien, MD,* Laurent Macle, MD,‡ Meleze Hocini, MD,* Frederic Sacher, MD,* Nicolas Lellouche, MD,* Sebastien Knecht, MD,* Matthew Wright, PHD, MD,* Isabelle Nault, MD,* Shinsuke Miyazaki, MD,* Christophe Scavee, MD,* Jacques Clementy, MD,* Michel Haissaguerre, MD,* Pierre Jais, MD*

Bordeaux-Pessac, France; Crawley, Western Australia; and Montreal, Quebec, Canada

JACC 2011

Catheter Ablation for Atrial Fibrillation

Study Flow Chart



Catheter Ablation for Atrial Fibrillation

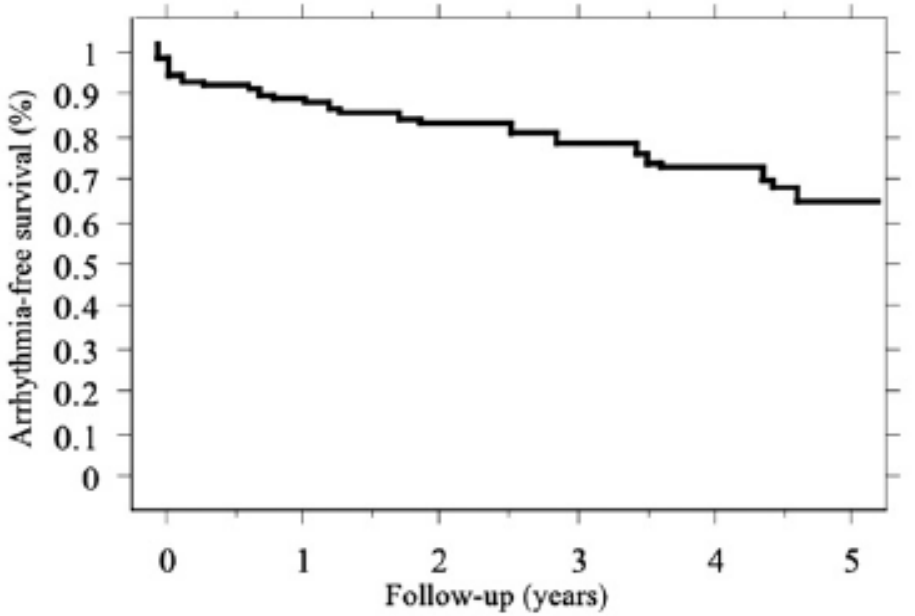
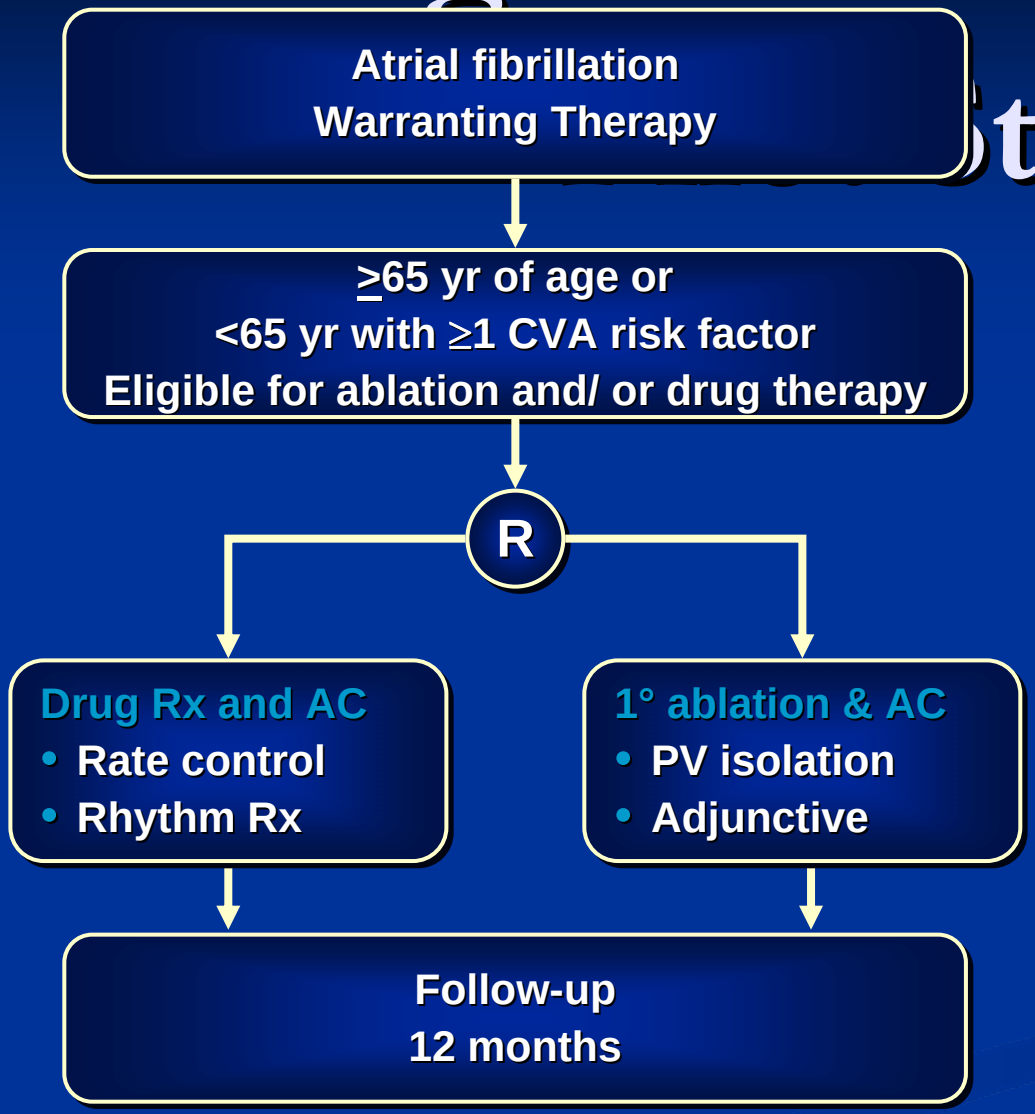


Figure 3 Multiple Procedure Success

Catheter Ablation for Atrial Fibrillation

- **Results**
  - **Multivariate analysis**
    - Valvular heart disease (HR: 6.0, 95% CI: 2.0 to 17.6; p= 0.0012)
    - nonischemic dilated cardiomyopathy (HR: 34.0, 95% CI: 6.3 to 182.1; p= 0.0001)
- **Complications.**
  - No deaths
  - cardiac tamponade (surgical intervention, n =3),
  - pericardial effusion conservative management (n =3)
  - PV stenosis (asymptomatic) (n =1)
  - arteriovenous femoral fistulae (n =1)
  - femoral false aneurysm (n =1)
  - anaphylactic shock from propofol (n =1)
  - VF secondary to cardioversion (n =1).

Design of the CABANA Study



Inclusion Criteria

- ≥2 paroxysmal AF episodes (≥1 hour) over 4 mos or ≥1 persistent AF episode (>1 week)
- ≥65 yr of age, or <65 yr with ≥1 risk factors
  - Hypertension
  - Diabetes
  - Heart failure
  - Prior CVA or TIA
  - LA size >5.0 cm (Vol In ≥40 cc/m^2)
  - EF ≤35 %
- Eligible for ablation and ≥2 rhythm control and/or ≥3 rate control drugs

CABANA Pilot Study; ACC 2010

CABANA Pilot Study
Baseline Characteristics in 60 Patients

Age (yrs)	61±10	
Age <65 yrs old with ≥2 risk factors	25	66%
Gender Male / Female (%)	77%	23%
Hypertension (%)	48	80%
Diabetes (%)	11	18%
CAD (%)	21	35%
Prior MI (%)	6	10%
Prior CABG/PTCA (%)	13	22%
Dilated cardiomyopathy (%)	10	17%
Congestive heart failure	13	22%
Ejection fraction (%)	55 ± 10	
LA size (mm)	4.4±1.0	
Left atrial enlargement		
None (%)	8	16%
Mild–moderate (%)	27	54%
Severe (%)	15	30%
CHADS2 score		
≤1	36	61%
≥2	23	39%

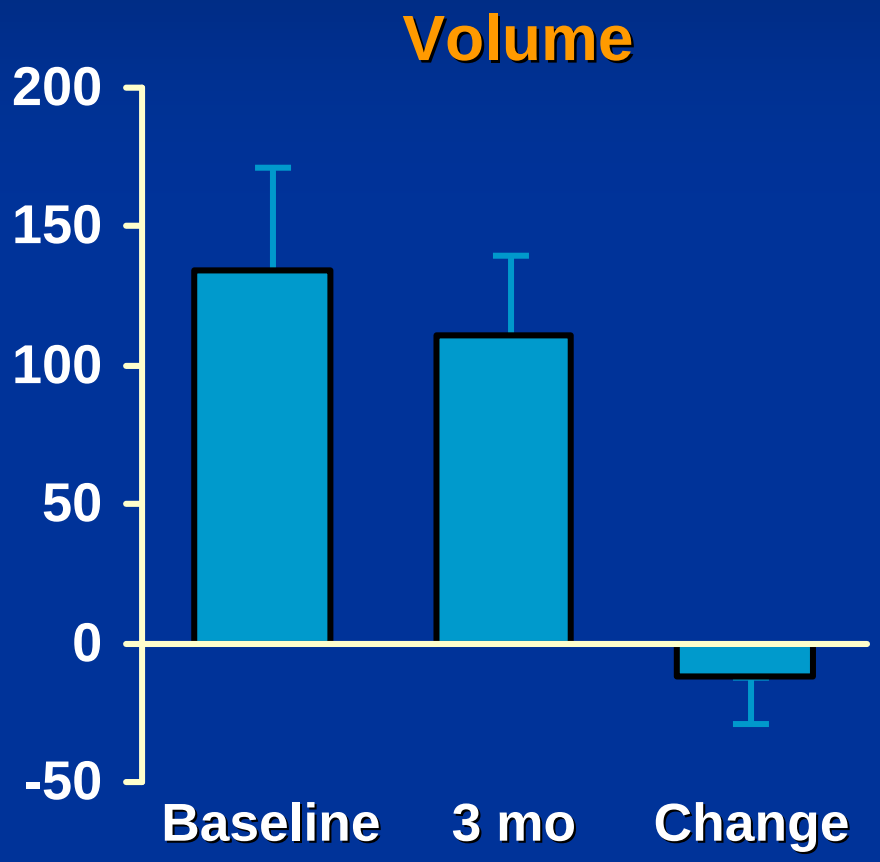
CABANA Pilot Study; ACC 2010

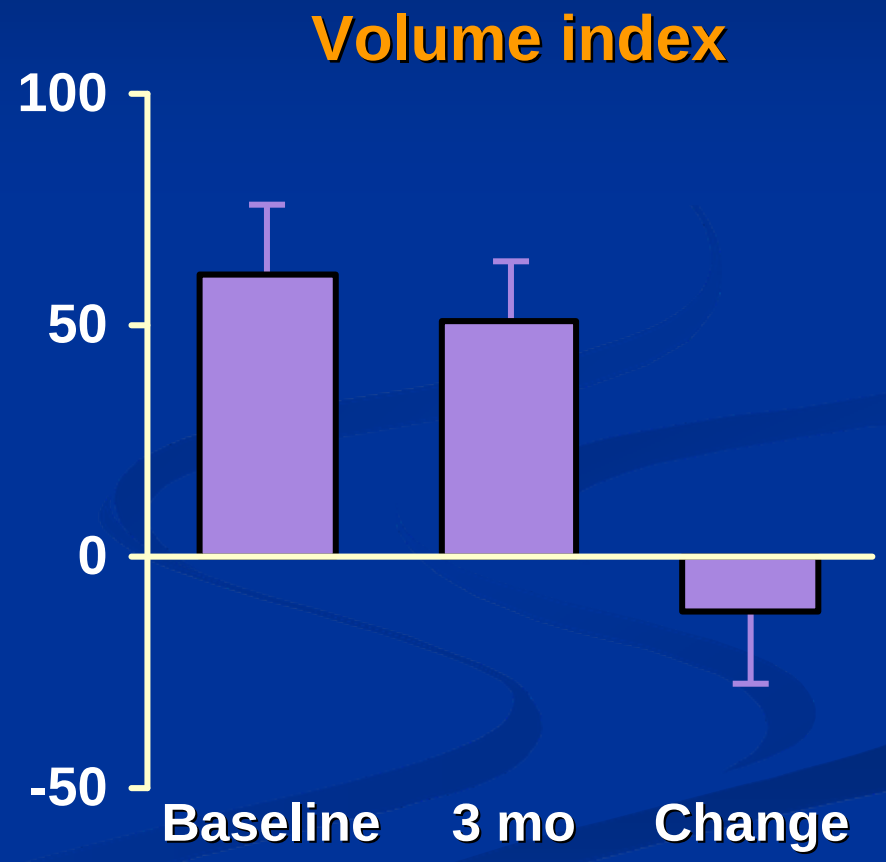
CABANA Pilot Study
Arrhythmia History

Type of AF		
Paroxysmal	**19**	**32%**
Persistent	**22**	**37%**
Long standing persistent	**19**	**32%**
Years since first AF episode (yrs)	**3.3±4.6**	
CCS AF severity		
Class 1-2	**18**	**32%**
Class 3-4	**35**	**61%**
Prior anti-arrhythmic drugs (no.)		
0	**42**	**70%**
1	**15**	**25%**
2	**3**	**5%**
Hospitalized for AF	**28**	**47%**
Direct current cardio-version	**32**	**53%**
History of atrial flutter	**14**	**23%**

CABANA Pilot Study; ACC 2010

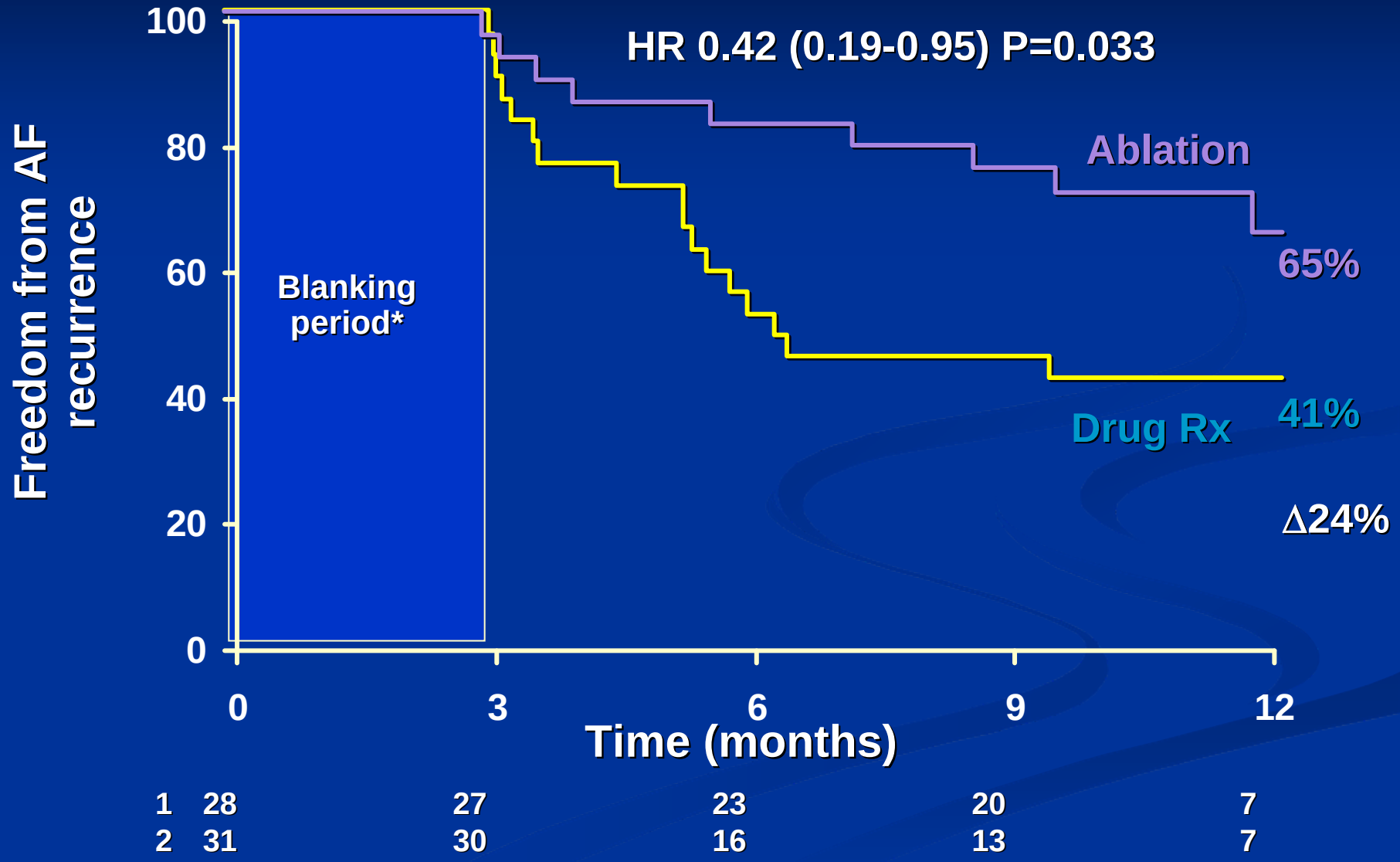
CABANA Pilot Study
Change in LA Size in Ablated Patients





CABANA Pilot Study; ACC 2010

Freedom from Recurrence of *Symptomatic* Atrial Fibrillation Post Blanking Period



Adverse Events in the CABANA Pilot Study

	Ablation n=29	Drug Rx n=31
DVT (%)	1 (3.4)	
AV fistula/pseudo aneurysm (%)	2 (6.8)	
CVA/TIA (%)	1 (3.4)	
PV stenosis		
Moderate (50-75%)	1 (3.4)	
Severe (75-95%)	0 (0)	
Atrial esophageal fistula (%)	0 (0)	
Tamponade (%)	1 (3.4)	
Congestive heart failure (%)	3 (10.2)	1 (3.2)
Volume overload (%)	2 (6.8)	0 (0)
Myocardial infarction (%)	1 (3.4)	0 (0)
Bradycardia (%)	1 (3.4)	0 (0)
Ventricular tachycardia (%)	0 (0)	1 (3.2)
Atrial flutter (%)	0 (0)	1 (3.2)
LFT increase (%)	0 (0)	1 (3.2)
UTI (%)	1 (3.4)	0 (0)
Death, Cardiac Arrest, CVA	0 (0)	0 (0)

CABANA Pilot Study; ACC 2010

Conclusion of the CABANA Pilot Study

- **Ablative intervention was more effective than drug therapy for preventing recurrent *symptomatic* atrial fibrillation**
- **This pilot study establishes the feasibility and importance of conducting a pivotal trial for establishing long-term outcome, mortality, quality of life, and cost of therapy for AF**