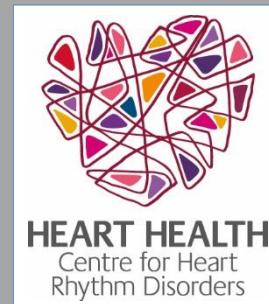


Obesity and Arrhythmia

Rajeev K. Pathak MBBS, PhD

Department of Cardiac Electrophysiology
Hospital of University of Pennsylvania

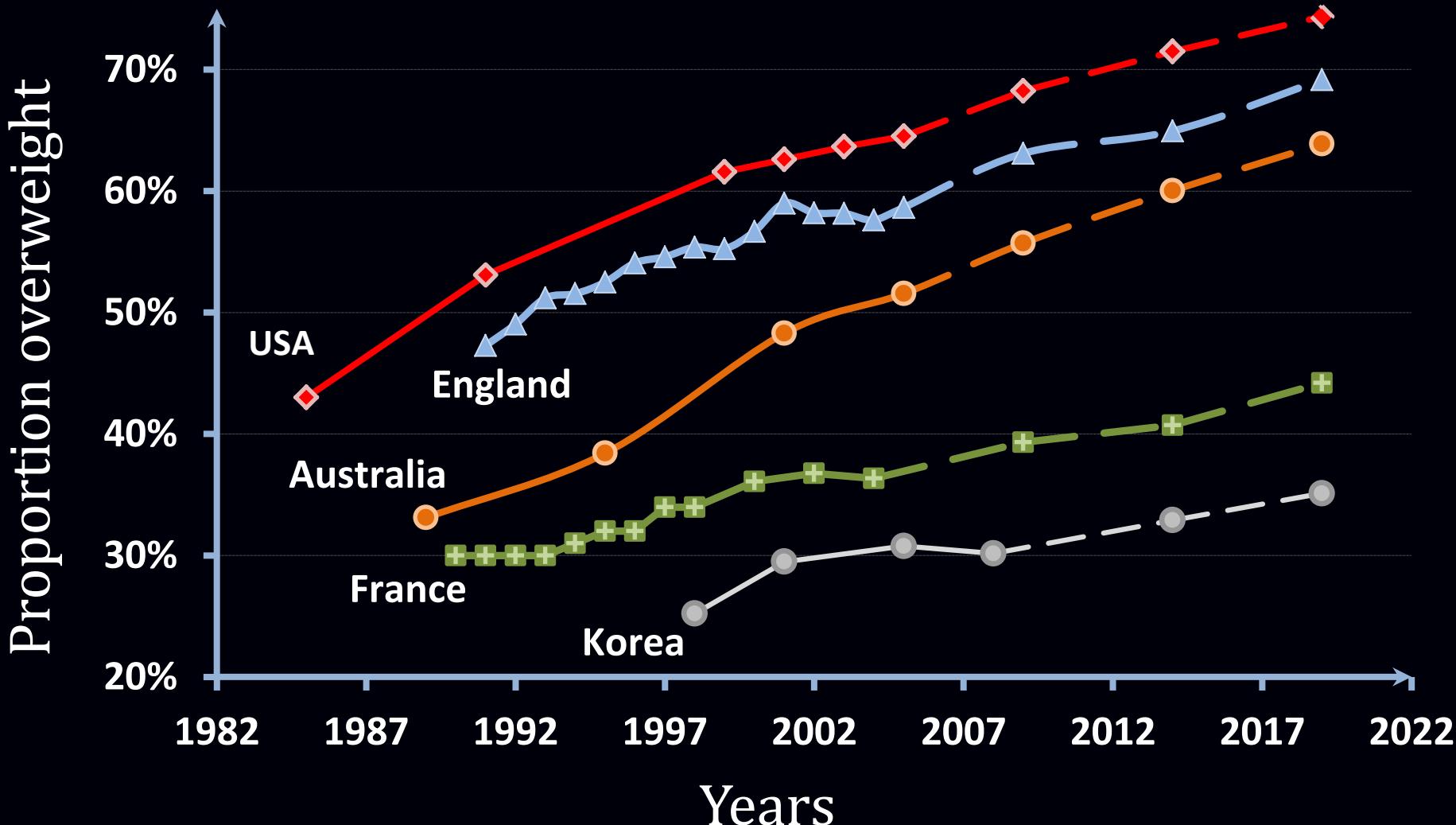


THE UNIVERSITY
*of*ADELAIDE

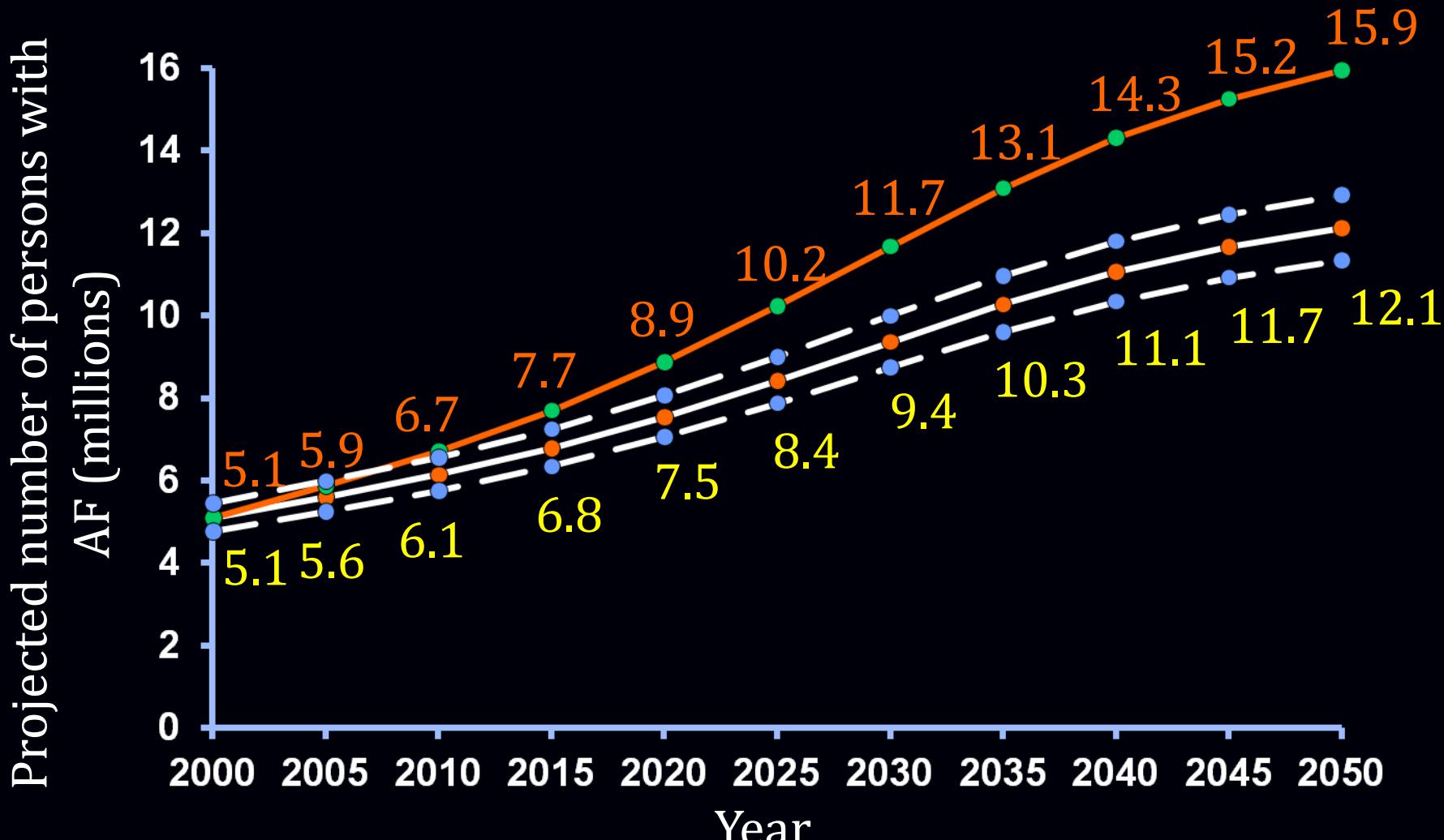
Disclosure

Nil Applicable

Obesity: Past and Projected rate

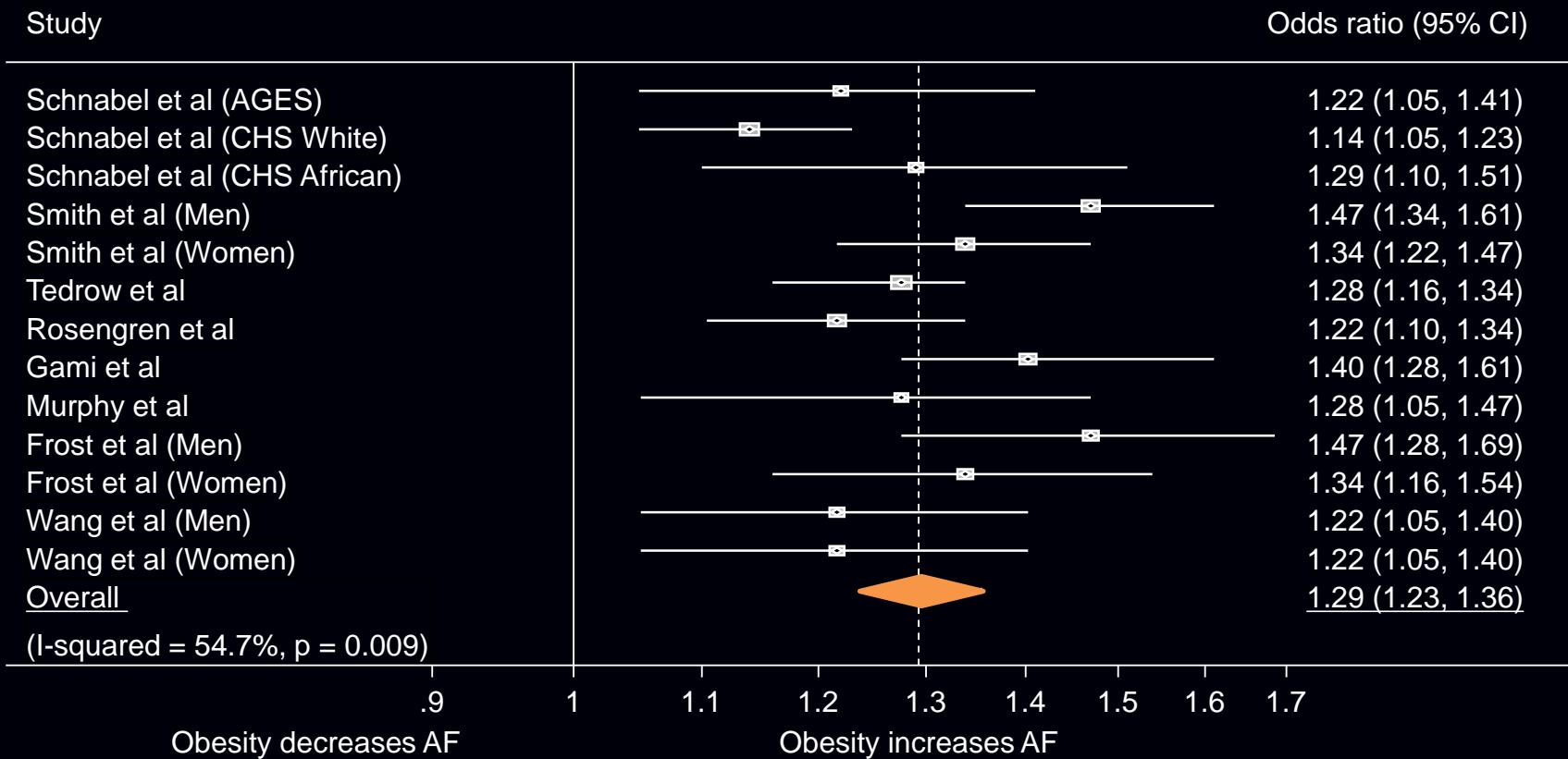


Projected Prevalence of AF

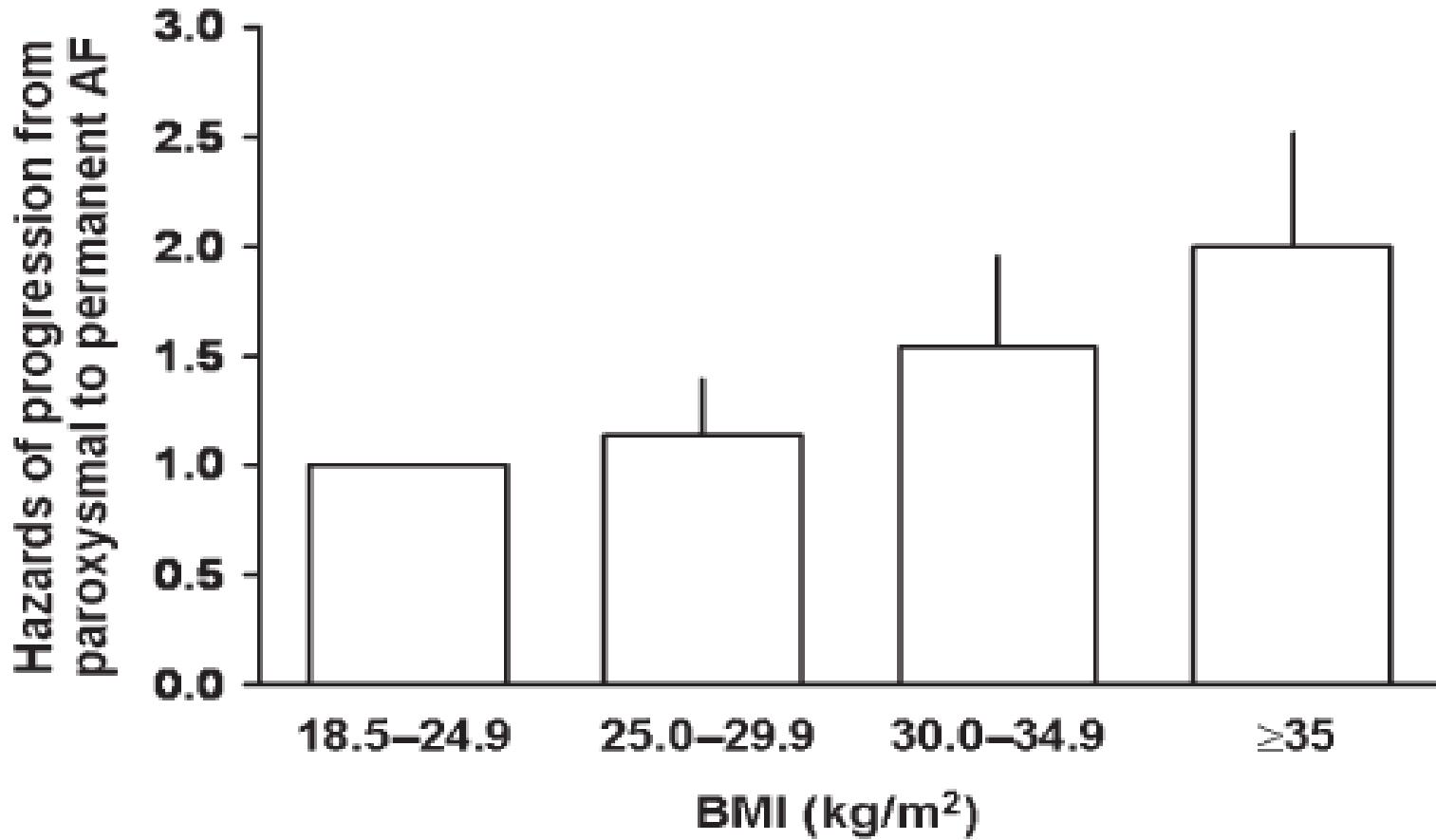


Obesity and incident AF: meta-analysis of 51 studies including 626,603 individuals

29% greater AF risk for every 5 BMI units

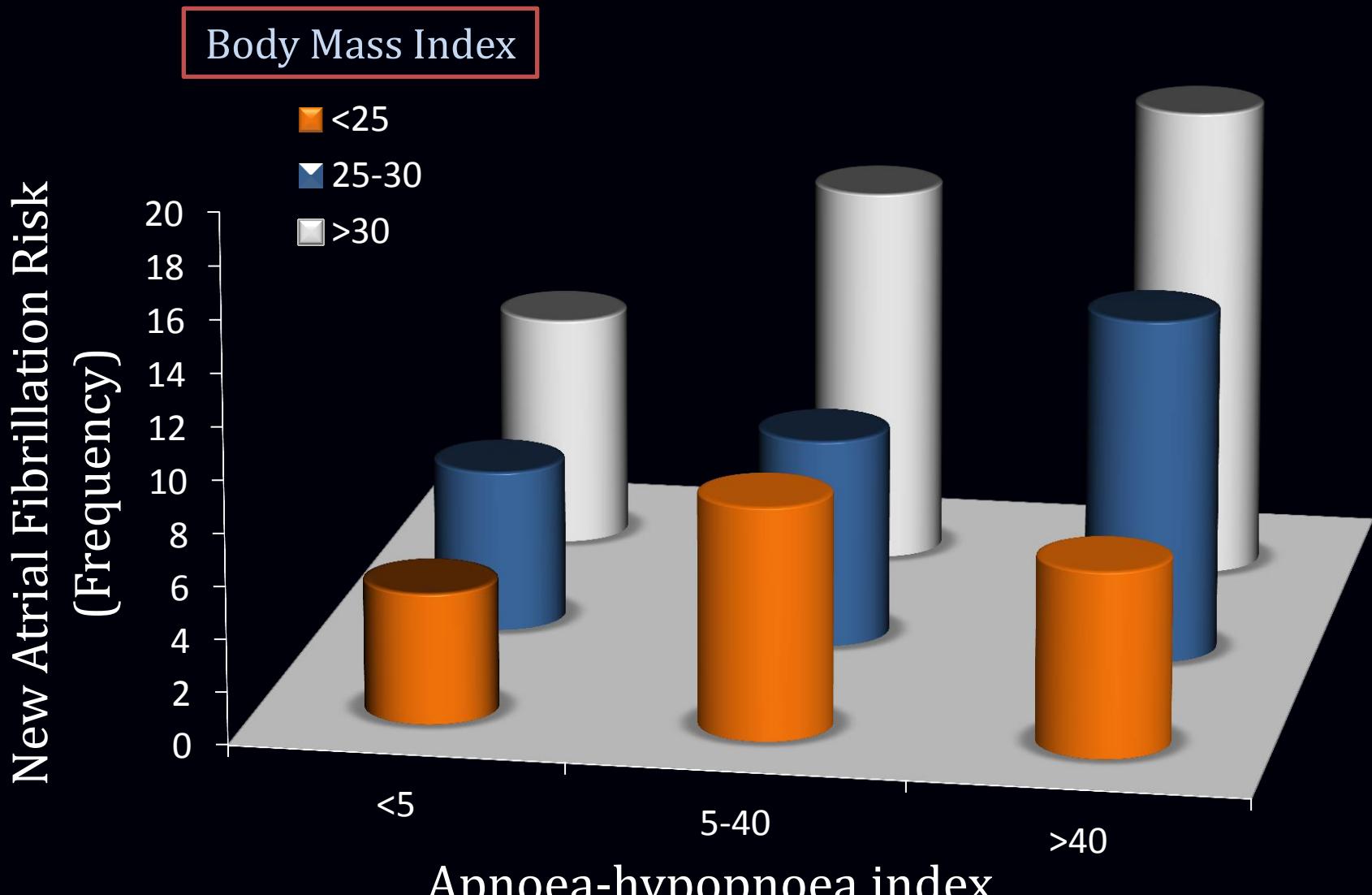


Dose-response of obesity & progression of AF

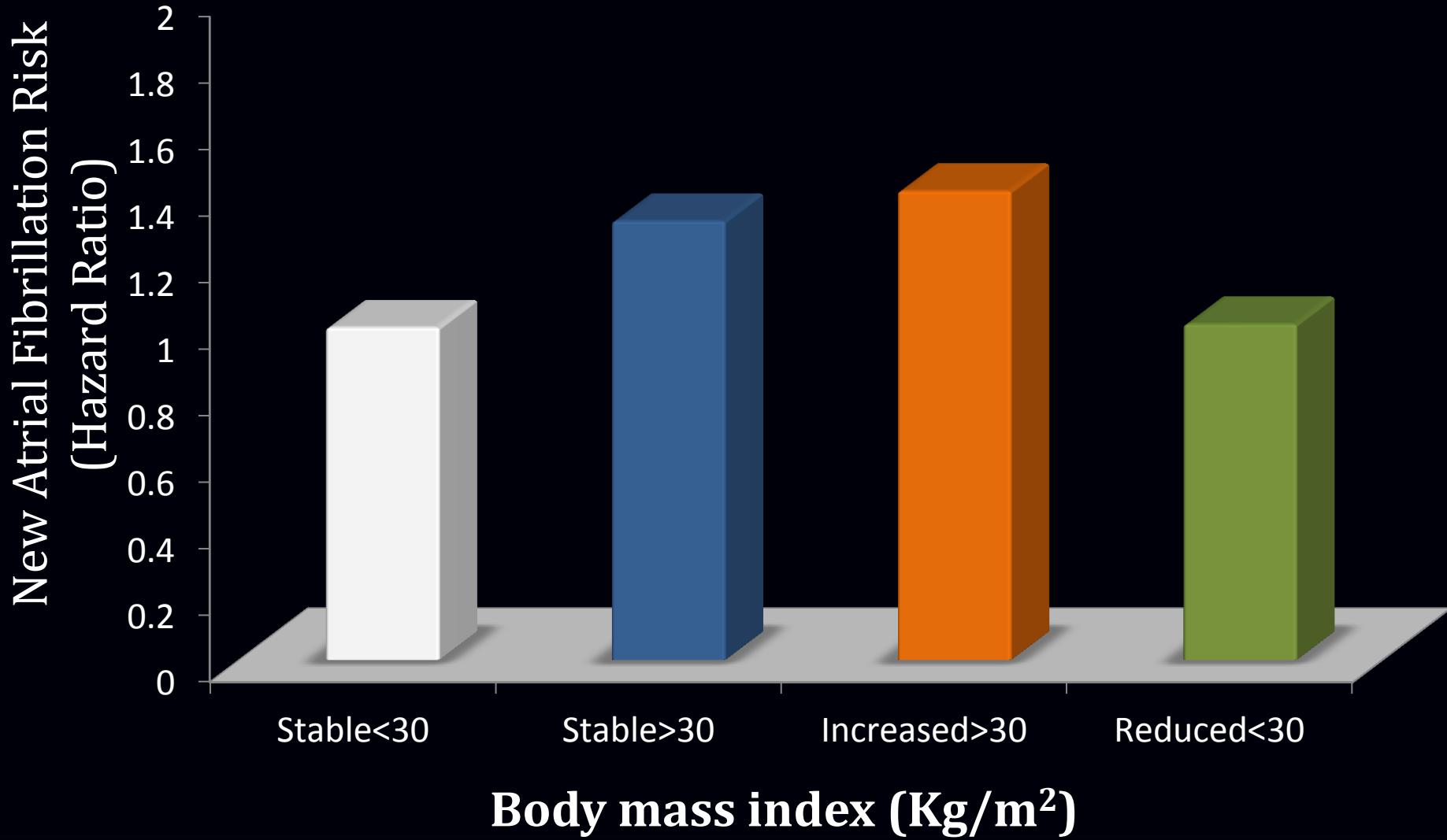


Tsang et al. EHJ, 2008

Obesity, Sleep Apnea and AF



Weight Change and AF Risk





JACC
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

Long-Term Effect of Goal-Directed Weight Management in an Atrial Fibrillation Cohort

A Long-Term Follow-Up Study (LEGACY)



Rajeev K. Pathak, MBBS,* Melissa E. Middeldorp,* Megan Meredith,* Abhinav B. Mehta, MACTSt,†
Rajiv Mahajan, MD, PhD,* Christopher X. Wong, MBBS, PhD,*‡ Darragh Twomey, MBBS,* Adrian D. Elliott, PhD,*§
Jonathan M. Kalman, MBBS, PhD,¶ Walter P. Abhayaratna, MBBS, PhD,# Dennis H. Lau, MBBS, PhD,*
Prashanthan Sanders, MBBS, PhD*

VOL. 65, NO. 20, 2015

<http://dx.doi.org/10.1016/j.jacc.2015.03.002>

Assessed for Eligibility
N=1415



Patients with BMI ≥ 27
N=825



Weight Management



Final Cohort
N=355



**<3%WL or
WG
N=117**



**3-9%WL
N=103**



**$\geq 10\%$ WL
N=135**

Met Exclusion Criteria (N=293)

Terminal Cancer (N=10)
Inflammatory Dx (N=20)
Permanent AF (N=84)
AV Node ablation (N=12)
AF ablation (N=90)
Severe Medical Illness (N=77)

**Patients from other States
(N=177)**

Impact on Risk Factors

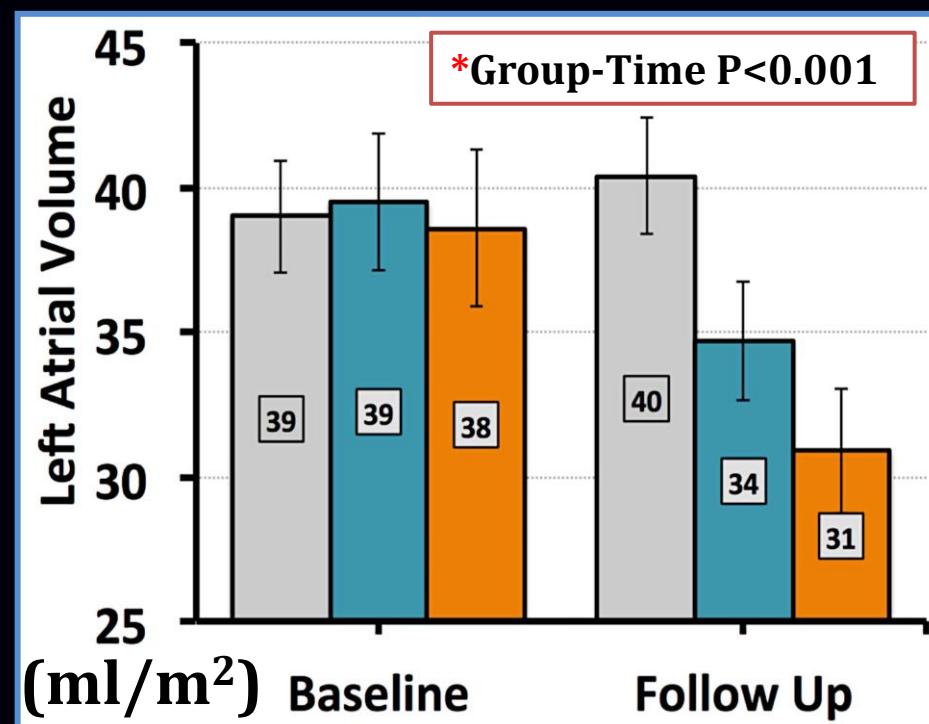
	<3% Wt Loss N= 117		3-9% Wt Loss N = 103		≥10% Wt Loss N = 135		P Value
	Baseline	Follow Up	Baseline	Follow Up	Baseline	Follow Up	
SBP (mmHg)	146±17	139±15	144±17	134±14	147±17	129±12	<0.001
Anti-HTN, n	0.8±1.0	1.0±0.7	0.7±0.8	0.7±0.6	1.0±0.9	0.5±0.6	<0.001
DM with HbA1c≥7, n (%)	34 (29)	23 (20)	28 (27)	15 (15)	40 (30)	5 (4)	<0.001
Fasting Insulin (mU/L)	14.5±6.9	17.3±9.6	16.9±6.1	14.8±9.4	18.3±7.1	8.4±3.9	<0.001
LDL Level (mg/dL)	104±35	108±31	116±35	93±23	116±37	89±31	<0.001
TG Level (mg/dL)	141±62	159±62	141±53	115±53	141±62	97±35	<0.001
Lipid Rx n (%)	56 (48)	54 (46)	45 (44)	38 (37)	66 (49)	37 (27)	<0.001

Structural Remodeling

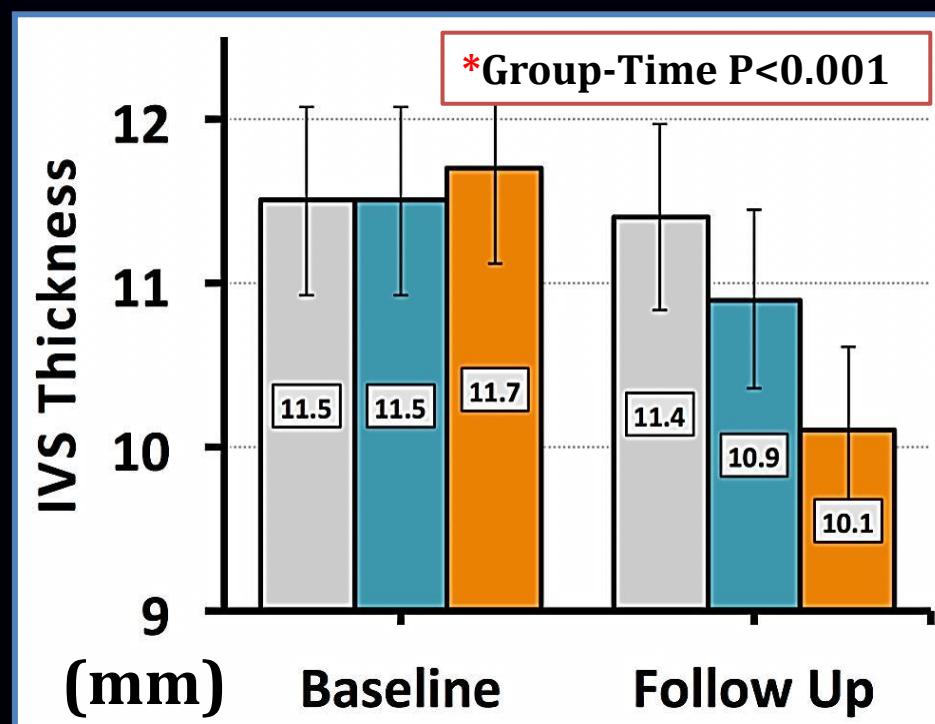
Legend:

- <3% WL
- 3-9% WL
- ≥10% WL

LA Volume (Indexed)



Septal Dimension

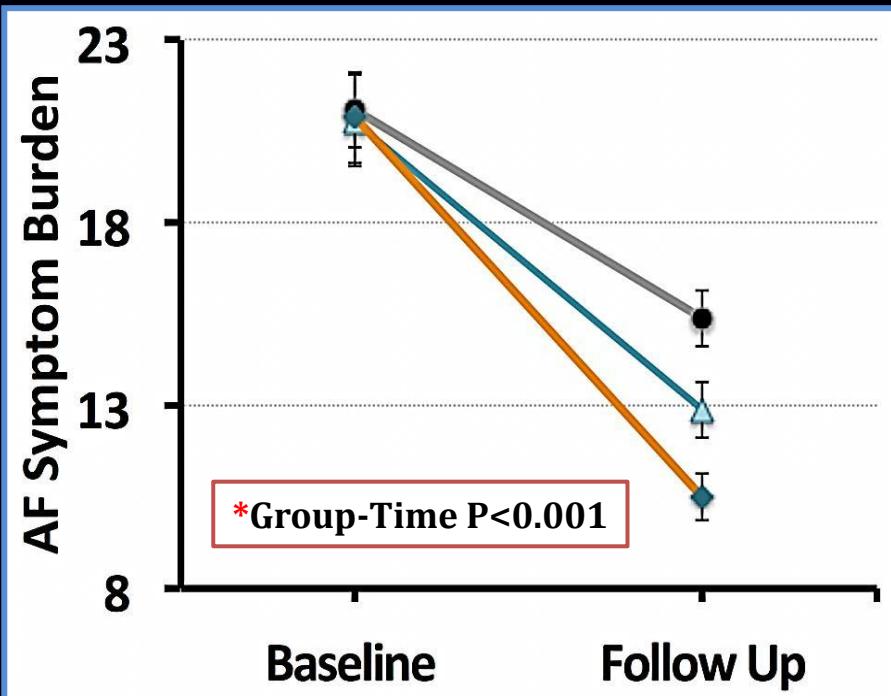


Impact on AF Symptoms

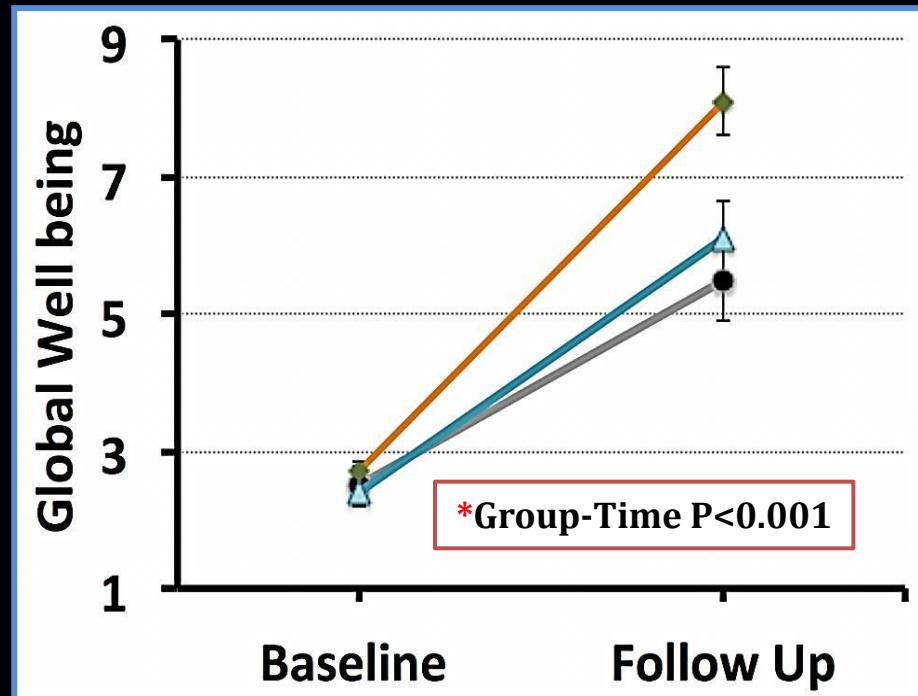
Legend:

- <3% WL
- 3-9% WL
- ≥10% WL

AF Symptom Burden



Global Well Being Score

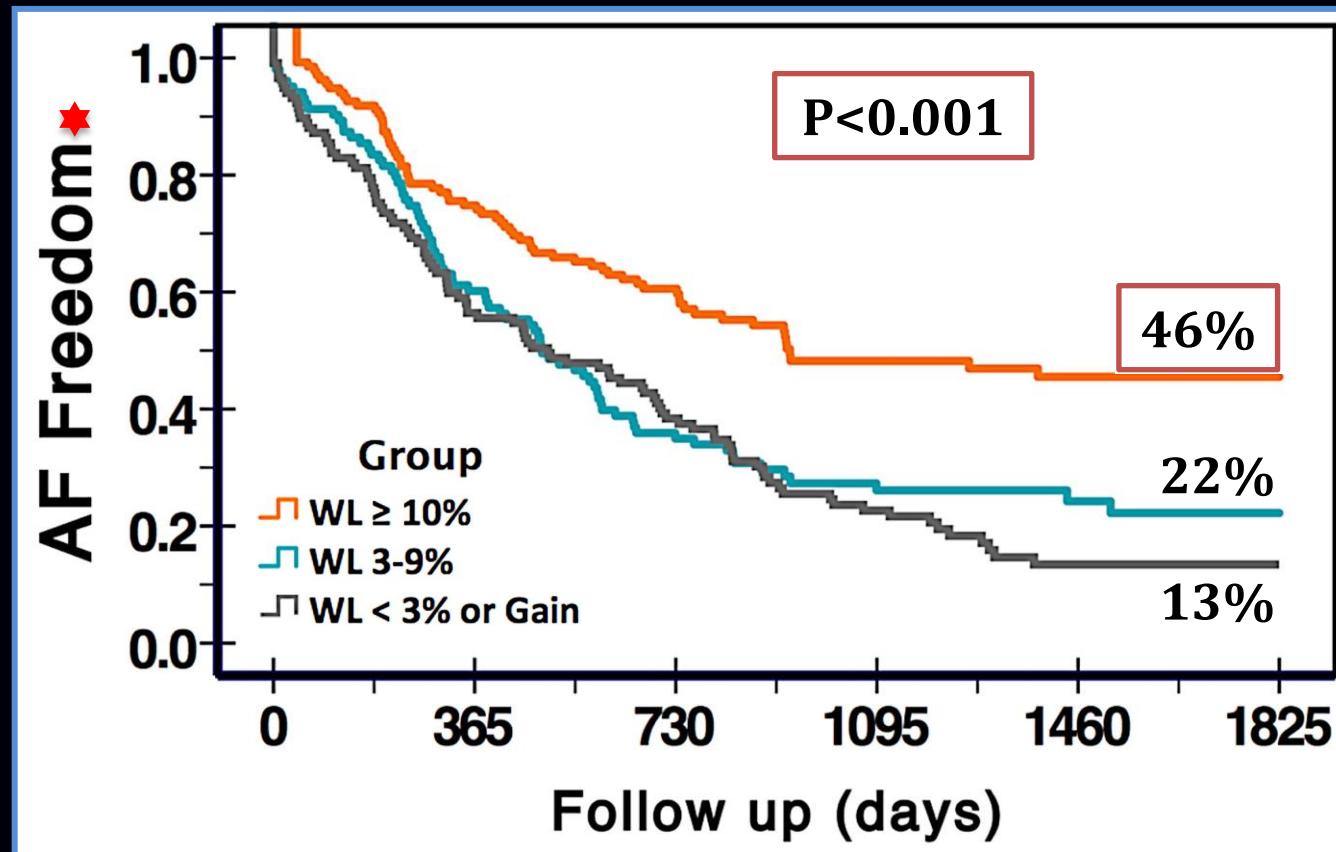


*Group-Time P<0.001

*Group-Time P<0.001

AF Freedom: Drug & Ablation-Free

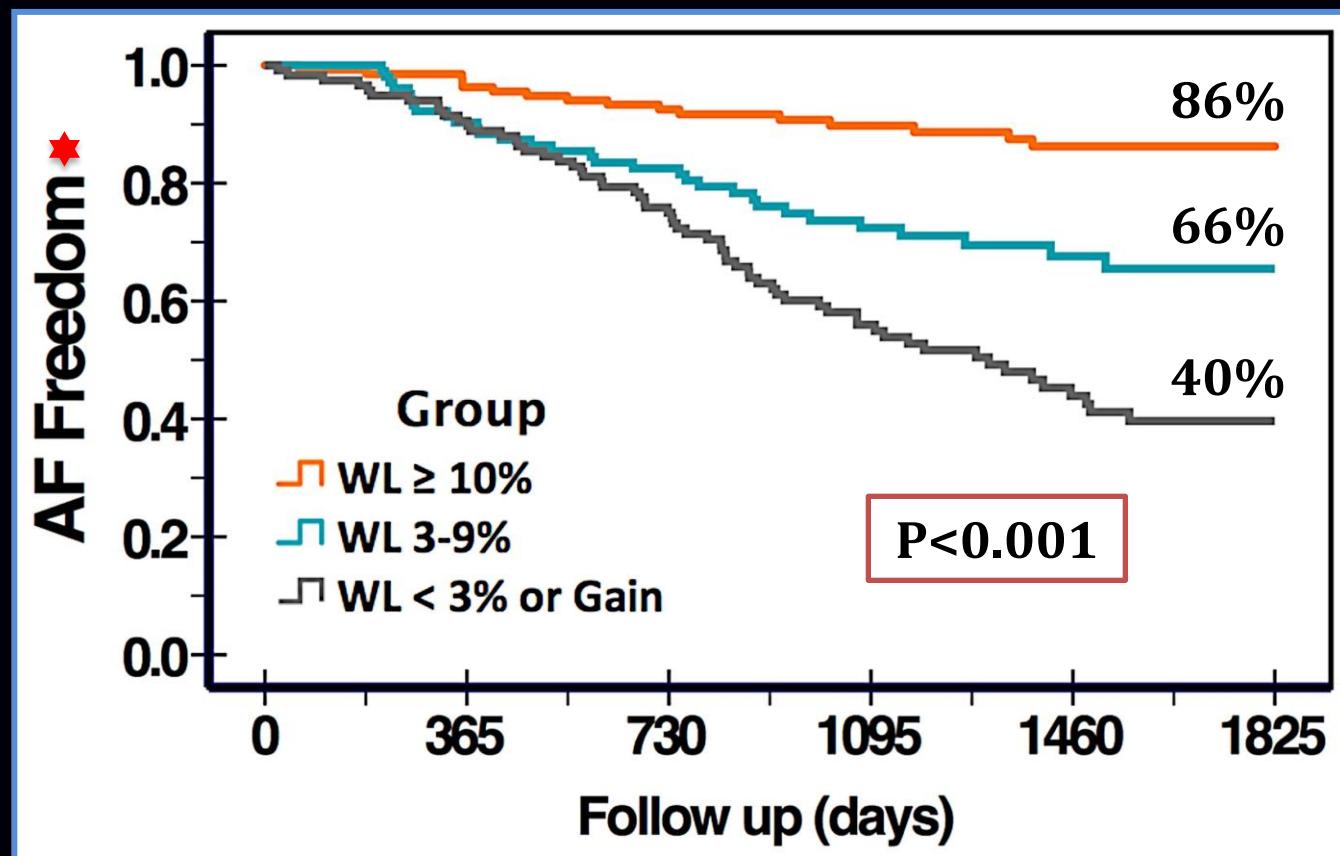
★ Without
AAD or
ablation



Days	0	365	730	1095	1460	1825
≥10%WL	135	101	72	42	31	18
3-9% WL	103	62	36	22	13	7
<3% WL	117	66	44	22	11	9

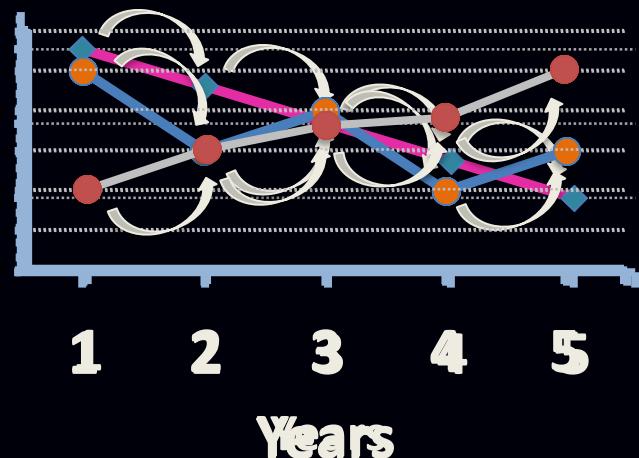
Total Arrhythmia-Free Survival

★ With
AAD +/-
ablation



Days	0	365	730	1095	1460	1825
≥10%WL	135	130	114	86	67	36
3-9% WL	103	93	83	57	35	22
<3% WL	117	105	85	53	32	22

Effect of Weight Loss Trend



Yearly Weight Trend (N=344)

Linear Weight Loss
N=141 (41%)

Weight Fluctuation
N=179 (52%)

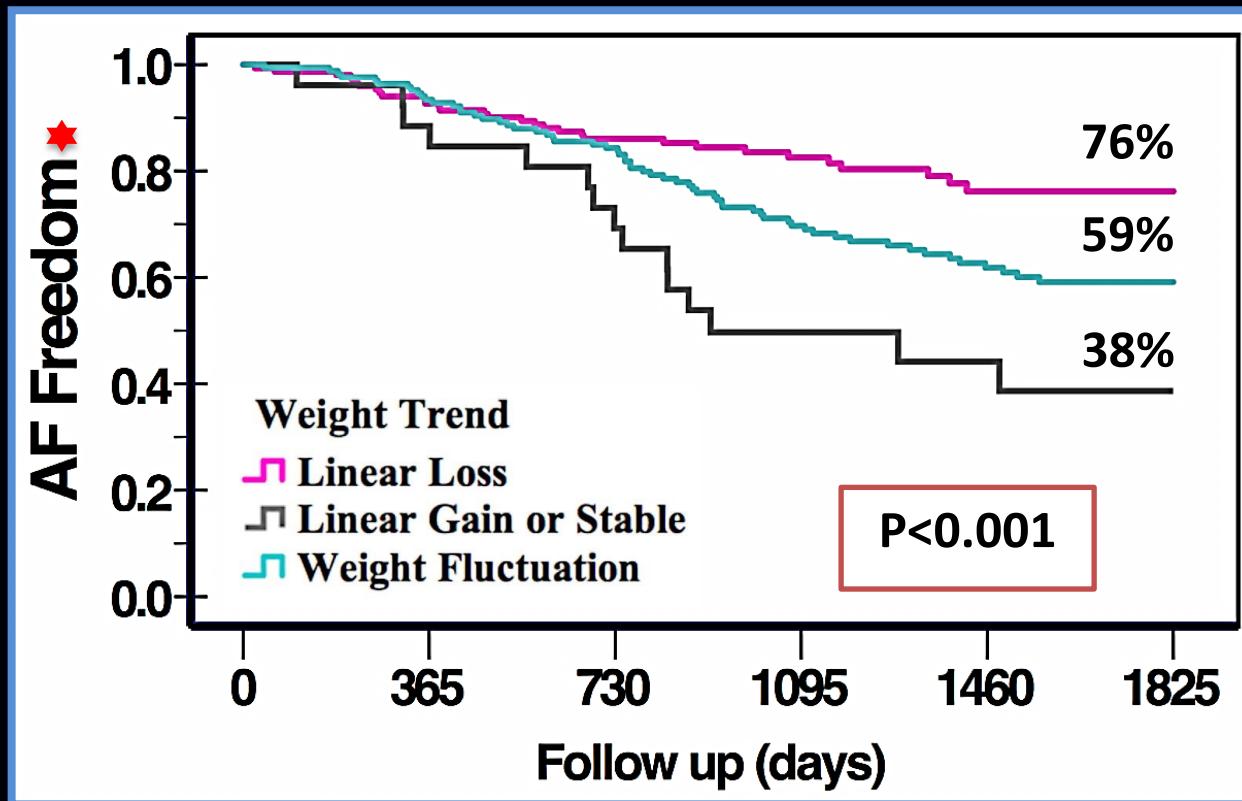
Linear Gain
N=24 (7%)

<2%WF
N=54

2-5%WF
N=68

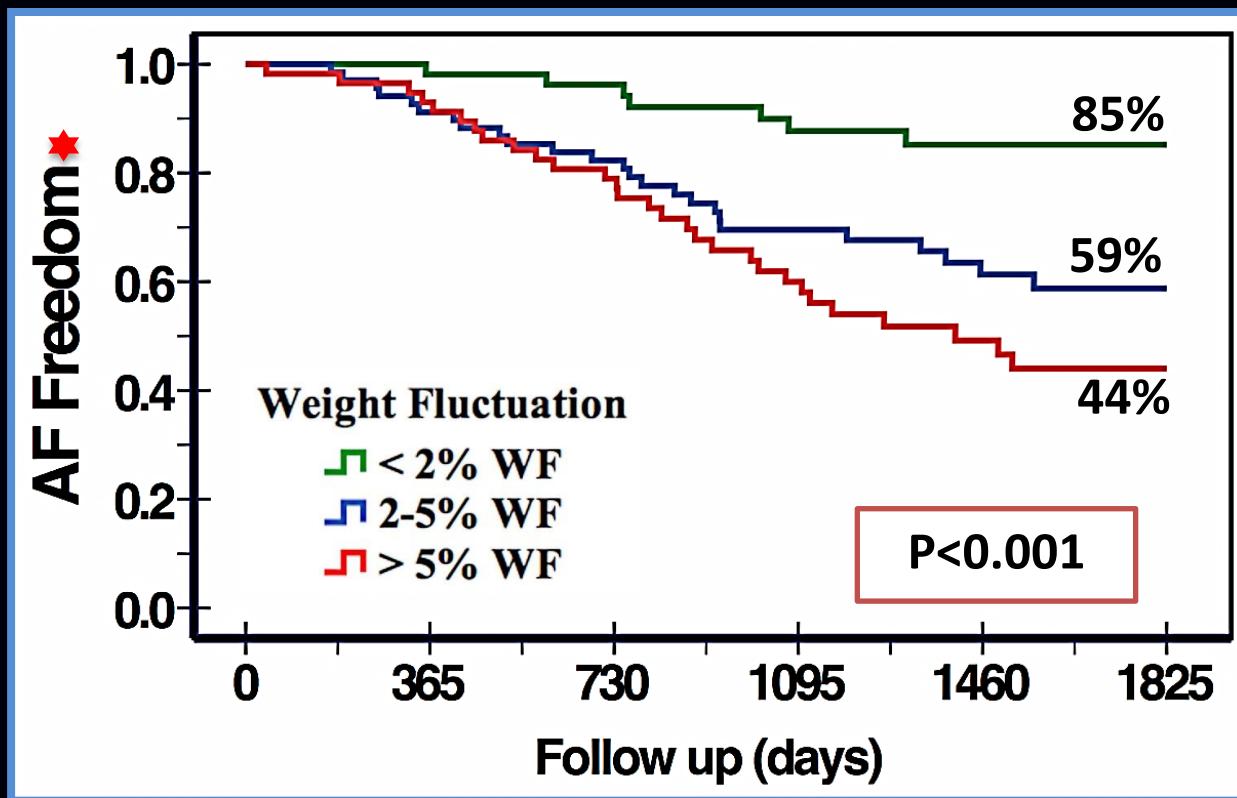
>5%WF
N=57

Weight Loss Trend



Days	0	365	730	1095	1460	1825
Linear Loss	141	130	122	80	52	29
Wt. Fluctuation	179	165	140	99	71	44
Linear Gain	24	20	18	12	8	5

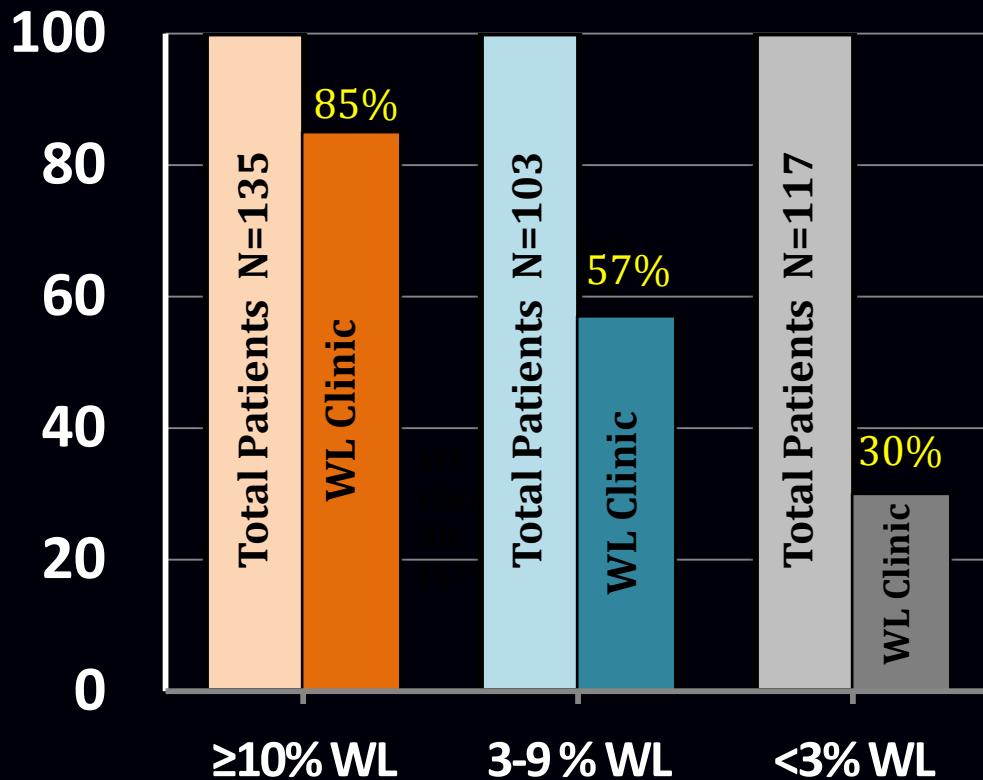
Effect of Weight Fluctuation



Days	0	365	730	1095	1460	1825
<2% WF	54	52	49	39	33	19
2-5% WF	68	62	54	39	27	15
>5% WF	57	53	45	31	19	14

Implications of Dedicated Weight Loss Clinic

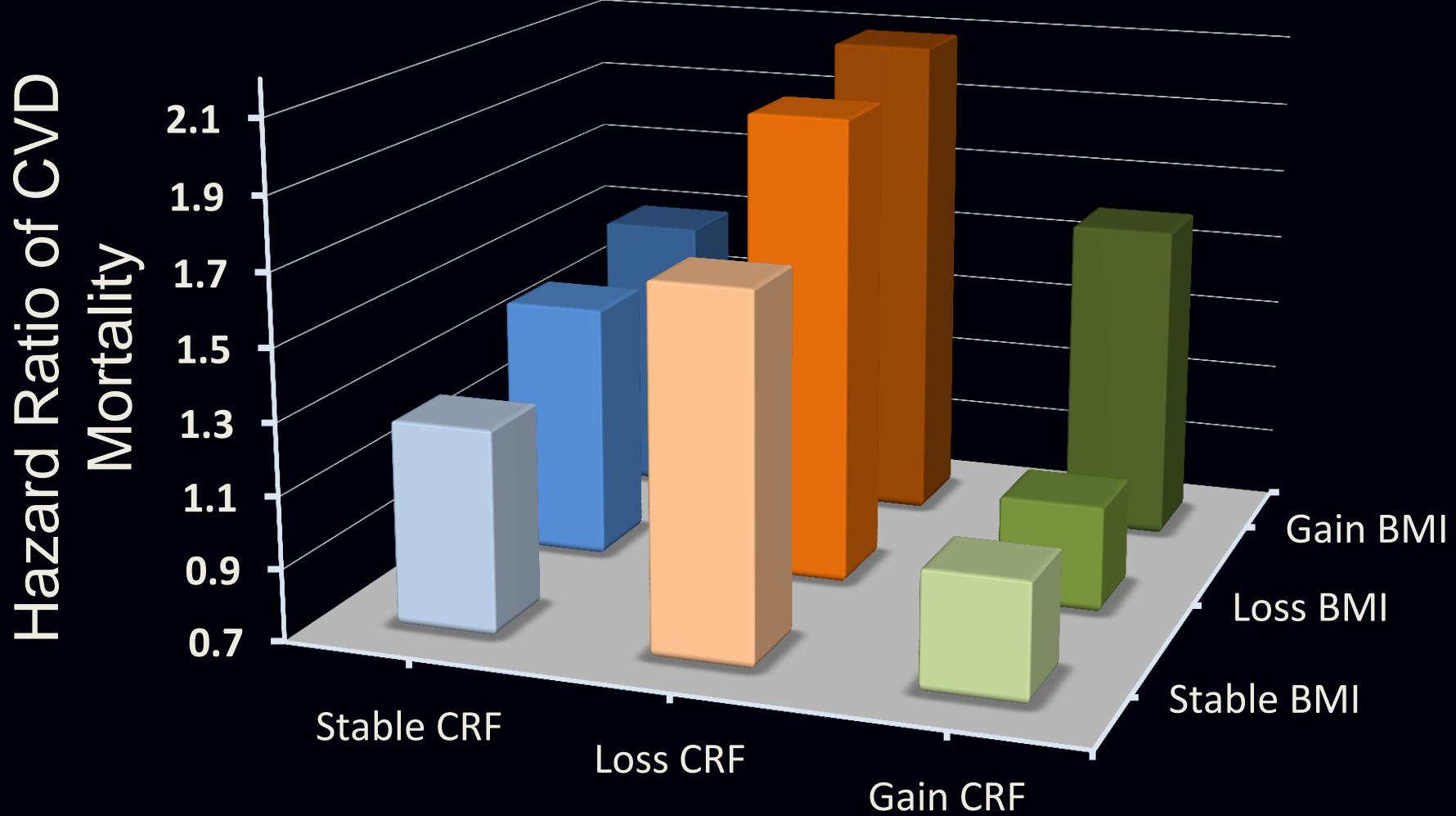
Successful Weight Loss



Weight Maintenance

- 52 patients lost $>10\%$ weight in first year
- 34/52 (66%) maintained WL
- 30/34 (85%) attended WL clinic
- 18 regained weight, only 2 (11%) attended clinic

BMI and Cardio Respiratory Fitness





JACC

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

Impact of CARDIORespiratory FITness on Arrhythmia Recurrence in Obese Individuals With Atrial Fibrillation

The CARDIO-FIT Study

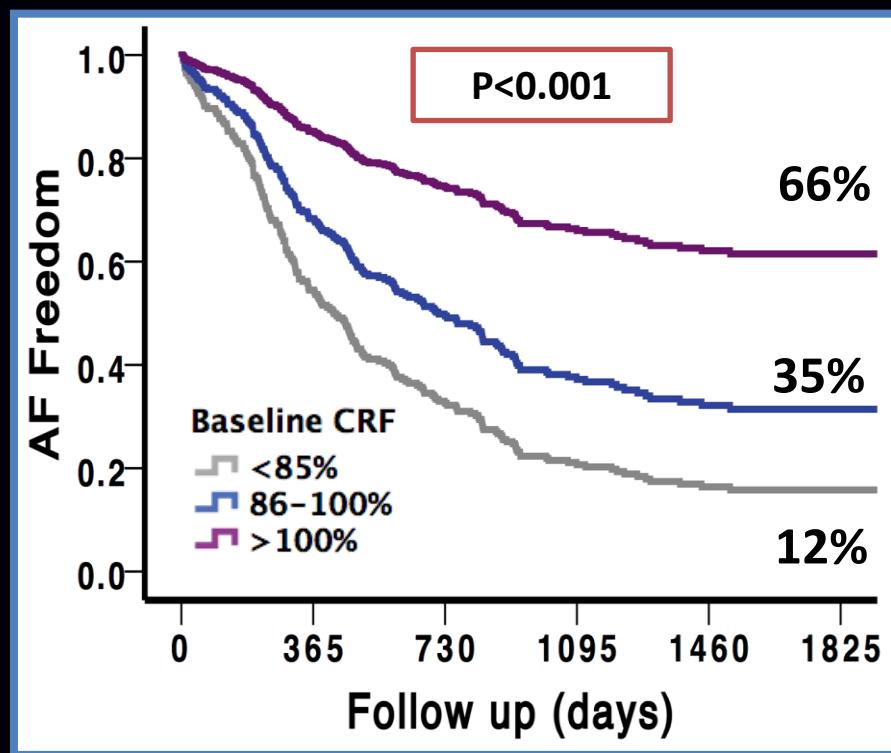
Rajeev K. Pathak, MBBS,* Adrian Elliott, PhD,* Melissa E. Middeldorp,* Megan Meredith,*
Abhinav B. Mehta, M Act St,† Rajiv Mahajan, MD, PhD,* Jeroen M.L. Hendriks, PhD,* Darragh Twomey, MBBS,*
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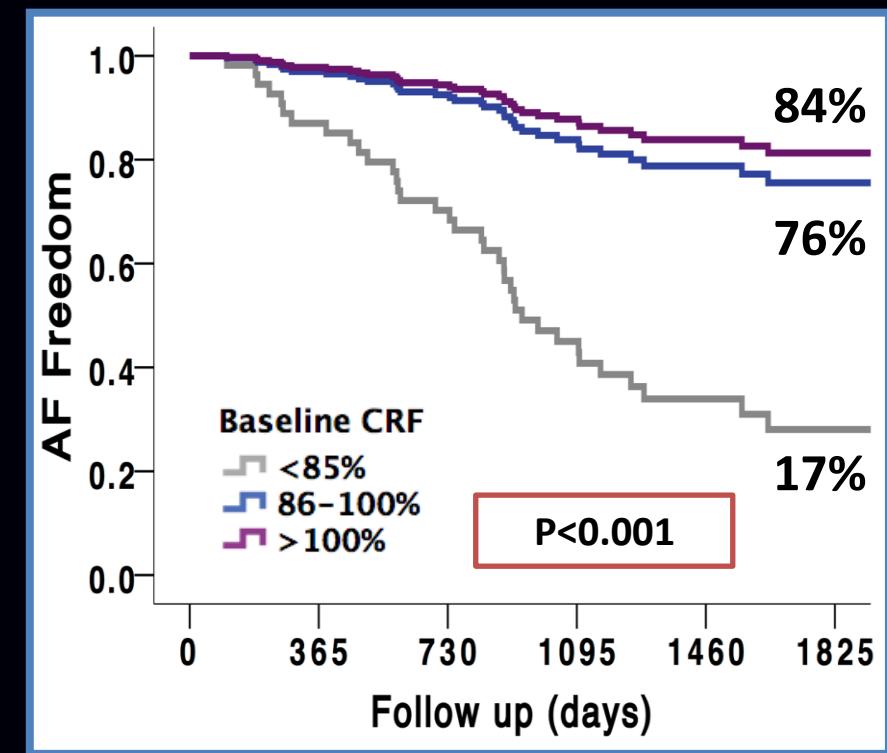
VOL. 66, NO. 9, 2015
<http://dx.doi.org/10.1016/j.jacc.2015.06.488>

Fitness and Obesity

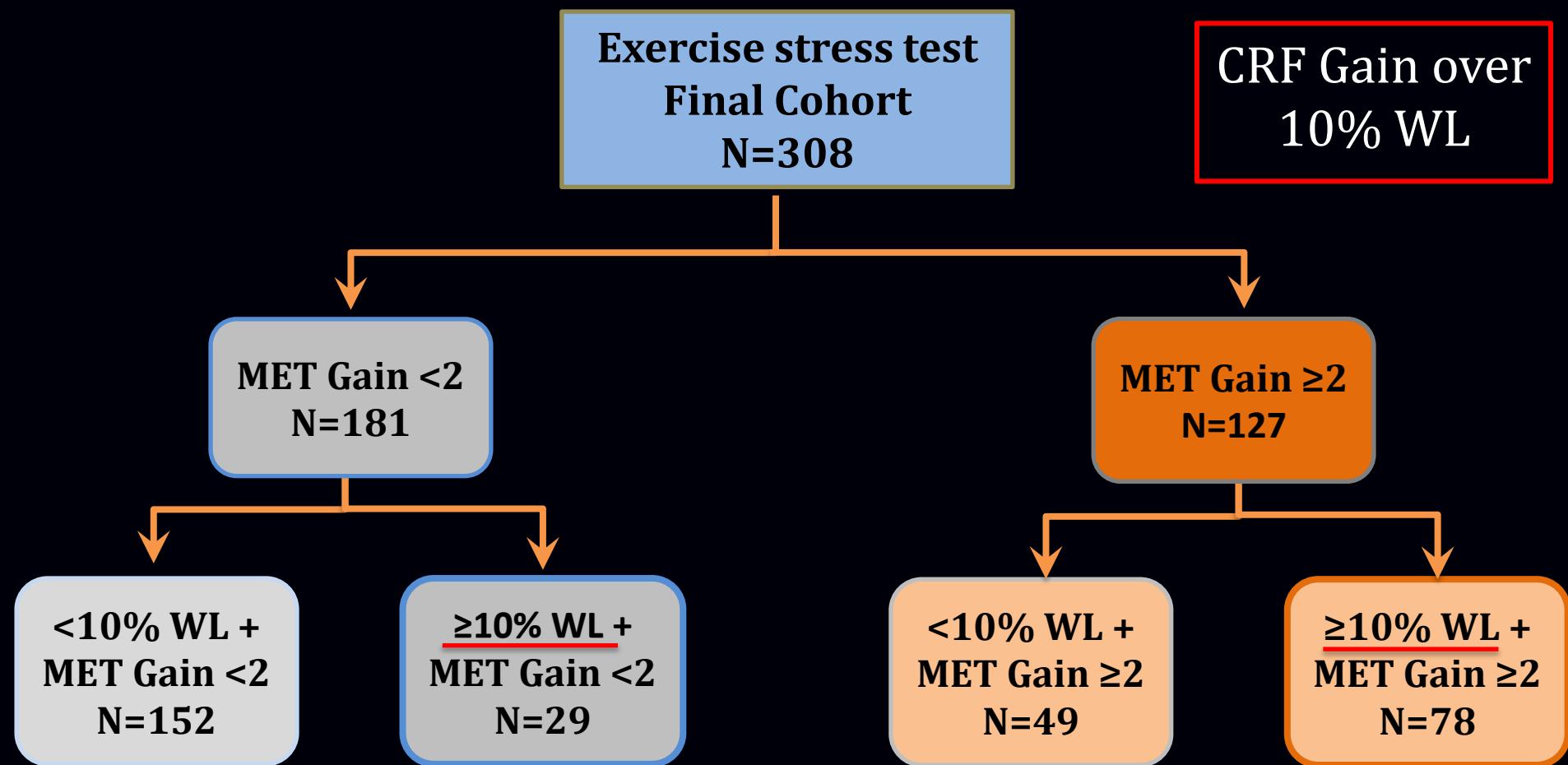
Without rhythm control strategies



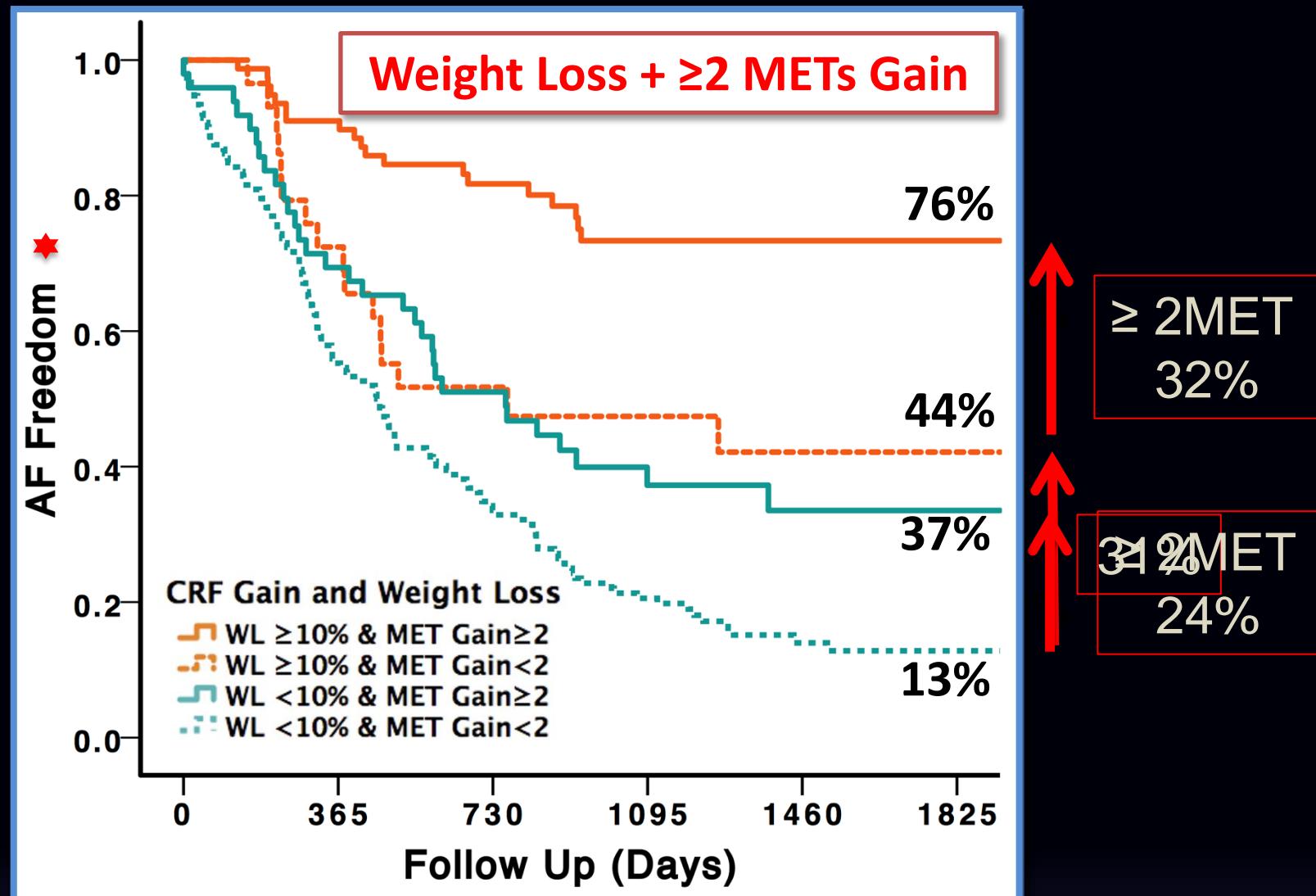
With rhythm control strategies



Weight Loss and CRF

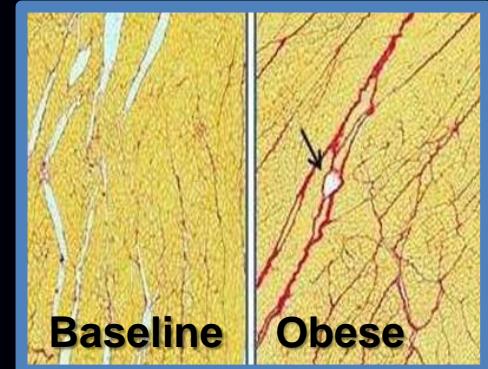
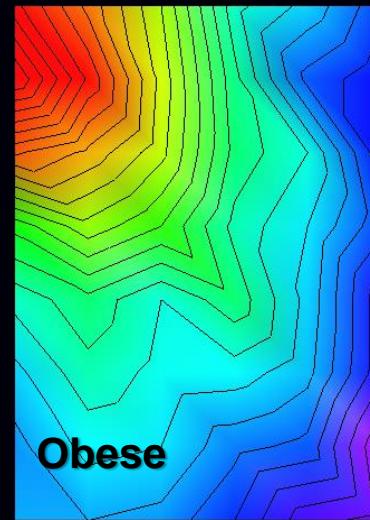
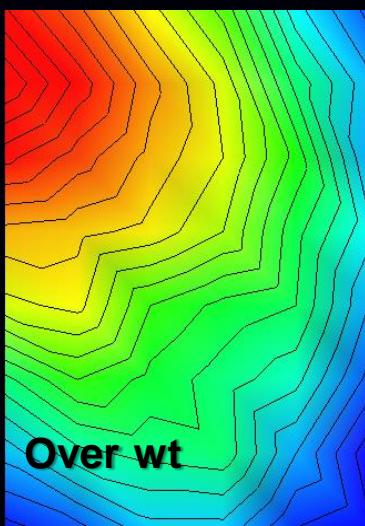
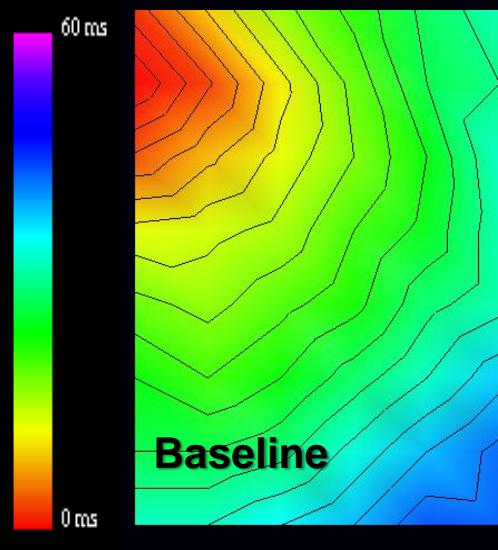


Weight Loss and CRF Drug & Ablation-Free AF freedom

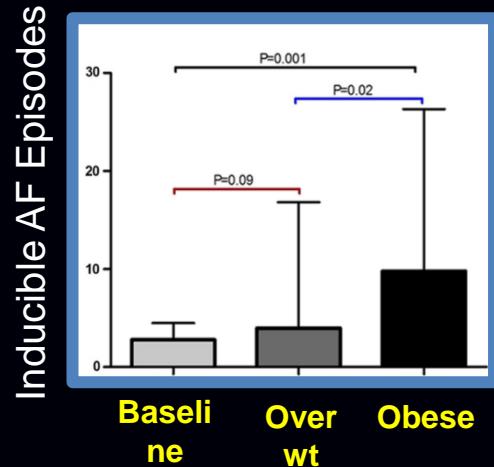


Atrial substrate due to progressive weight gain & obesity

Atrial Fibrosis

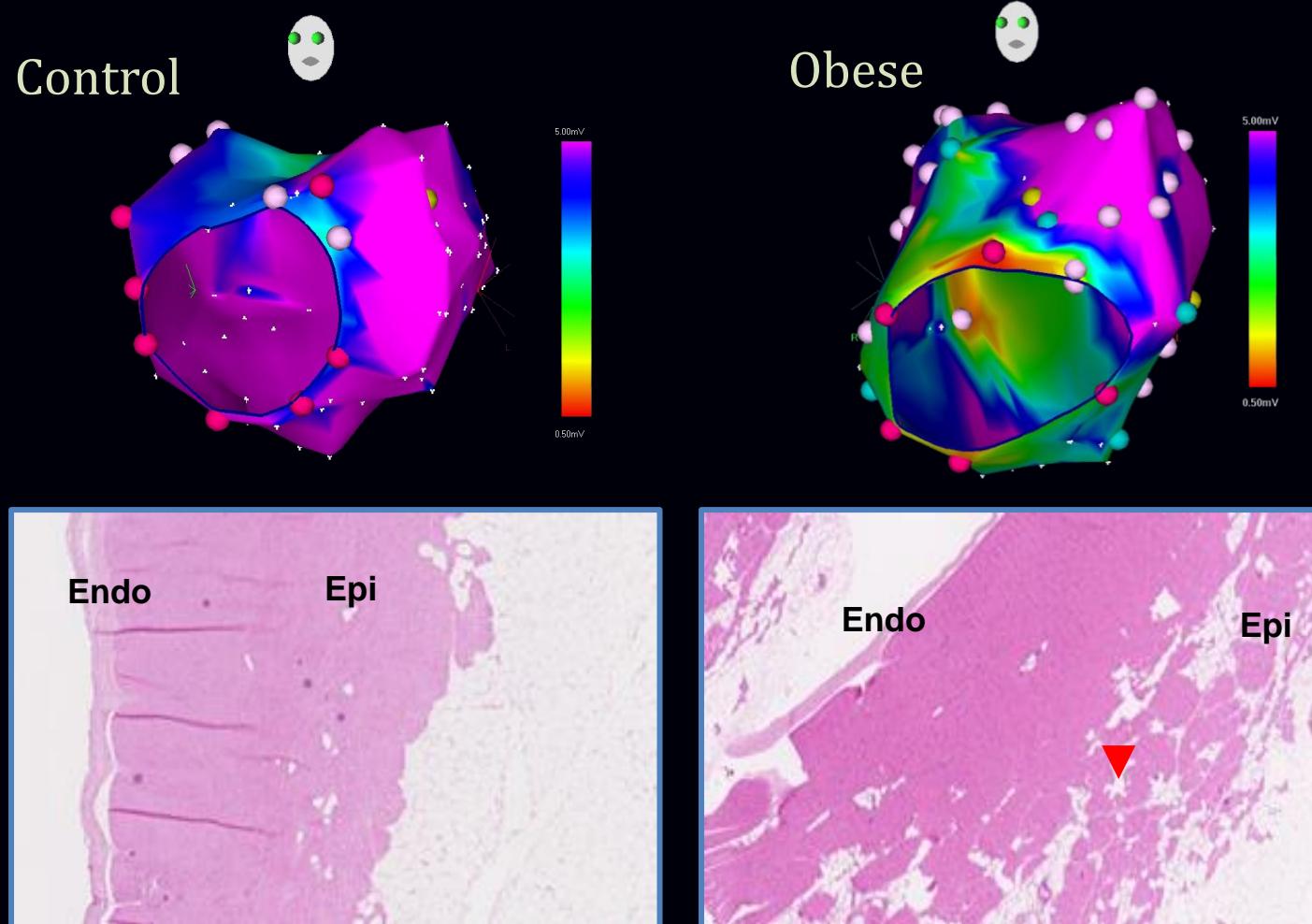


AF Inducibility



Abed H et al, Heart Rhythm 2013

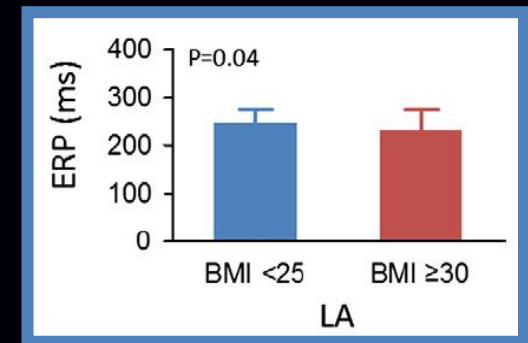
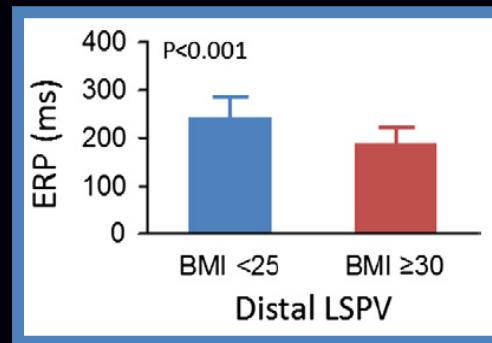
Fatty infiltration: a new substrate for AF



Mahajan R et al, JACC 2015

Electrical and hemodynamic changes associated with obesity

- ↓ERP
- ↑LA pressure
- ↑LA volume
- ↓LA strain



Characteristic	BMI <25 kg/m ² (n = 19)	BMI ≥30 kg/m ² (n = 44)	Total (N = 63)	p Value
LVEDV index, ml/m ²	42.5 (36.6, 47.5)	42.1 (36.8, 50.0)	42.2 (36.8, 48.5)	0.94*
LVESV index, ml/m ²	15.0 (12.5, 7.5)	15.9 (12.8, 20.5)	15.3 (12.8, 20.4)	0.59*
LVEF, %	64.7 (62.1, 66.7)	62.5 (56.3, 68.3)	64.0 (57.7, 67.5)	0.67*
LAVI end-diastole, ml/m ²	10.3 (6.8, 18.0)	20.3 (14.5, 29.5)	17.9 (11.1, 24.3)	0.002*
LAVI pre-A, ml/m ²	16.8 (11.6, 27.7)	24.4 (19.3, 38.7)	24.1 (16.0, 31.4)	0.006*
LAEF, %	33.7 ± 12.3	22.2 ± 11.6	25.7 ± 12.9	0.001
E flow velocity, m/s	76.8 ± 21.8	76.7 ± 16.6	76.7 ± 18.1	0.99
A flow velocity, m/s	48.6 ± 18.2	44.3 ± 16.2	45.6 ± 16.8	0.37
E/A ratio	1.6 (1.3, 1.8)	1.6 (1.3, 2.4)	1.6 (1.3, 2.2)	0.40*
Deceleration time, ms	191.3 ± 40.0	200.6 ± 40.1	197.9 ± 40.0	0.41
LA septal E velocity, m/s	9.1 ± 4.1	8.5 ± 2.7	8.7 ± 3.2	0.51
E/E' ratio	8.2 (6.3, 11.8)	8.7 (6.6, 12.3)	8.7 (6.6, 12.3)	0.69*
LA strain pre-A, %	8.8 ± 2.8	5.5 ± 3.1	6.5 ± 3.4	<0.001

Munger TM et al, JACC 2012

Aggressive Risk factor REduction STudy: implications for the substrate for Atrial Fibrillation (ARREST-AF: Substrate Study)

Pathak et al, AHA YIA 2015/CSANZ YIA 2015

Hypothesis

Aggressive risk factor management, results
in reversal of the substrate for AF

**Consecutive Patients
Symptomatic AF
N=112**

**Patients with $BMI \geq 27 + \geq 1$ risk factors (HTN, DM, OSA, Lipids)
N=67**

Exclusion Criteria

Previous AF ablation or Permanent AF
Amiodarone <6 months
H/O Recent MI or cardiac surgery <12M
Active malignancy
Autoimmune diseases
Severe renal or hepatic failure

Randomisation to Aggressive Risk Factor Management
ANZCTR : ACTRN12613000444785

**Control Group
N=34**

**RFM Group
N=33**

Follow Up 3 monthly

**≥ 6 months of Standard care
N=26**

**$>10\% WL + \geq 6$ months of RFM
N=24**

Moved Interstate, N= 7 (4CTL, 3 RFM)
Refused further participation, N=10

Baseline Investigations

EP study
Cardiac MRI + Bloods

Mean Follow up : 12.3 ± 1.1 Months

Follow Up Investigations
EP study
Cardiac MRI + Bloods

Risk factor management

Weight Management and Exercise

Structured Program
Dedicated Clinic
Meal Plan
Initial Target:
 $>10\%$ WL
Final Target:
 $BMI < 27 \text{ kg/m}^2$
Lifestyle journal
30 minutes 3-4 times weekly to 200 Min

Hyperlipidemia

Lifestyle measures
At 3 months LDL $> 2.6 \text{ mmol/L}$ - start statin
Add Fibrate if TG $> 2.6 \text{ mmol/L}$
Start Fibrate if TG $> 5.6 \text{ mmol/L}$

Glucose Tolerance

Glucose tolerance test
Lifestyle measures
 $HbA1c > 6.5$ at 3 months – start Metformin
Diabetes clinic

Hypertension

Measure BP 2-3 times daily, No added salt diet
Aim of :
 $< 130/80 \text{ mmHg}$ at rest
 $< 200/100$ at peak exercise

Sleep Apnea

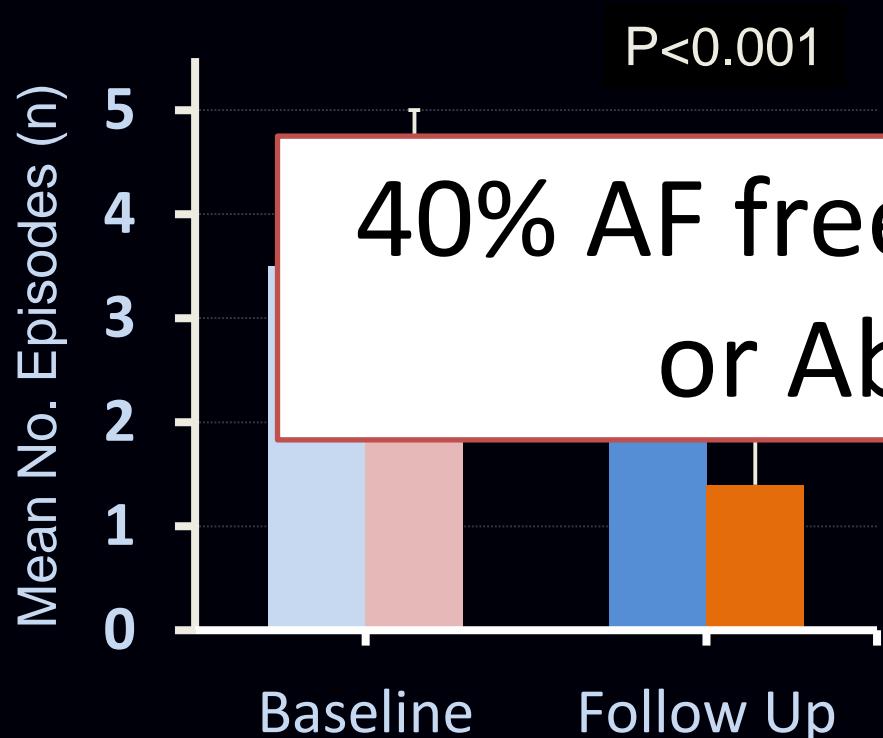
Formal overnight sleep study
 $AHI \geq 30/\text{hour}$: CPAP
Use Log in diary

Tobacco and alcohol use

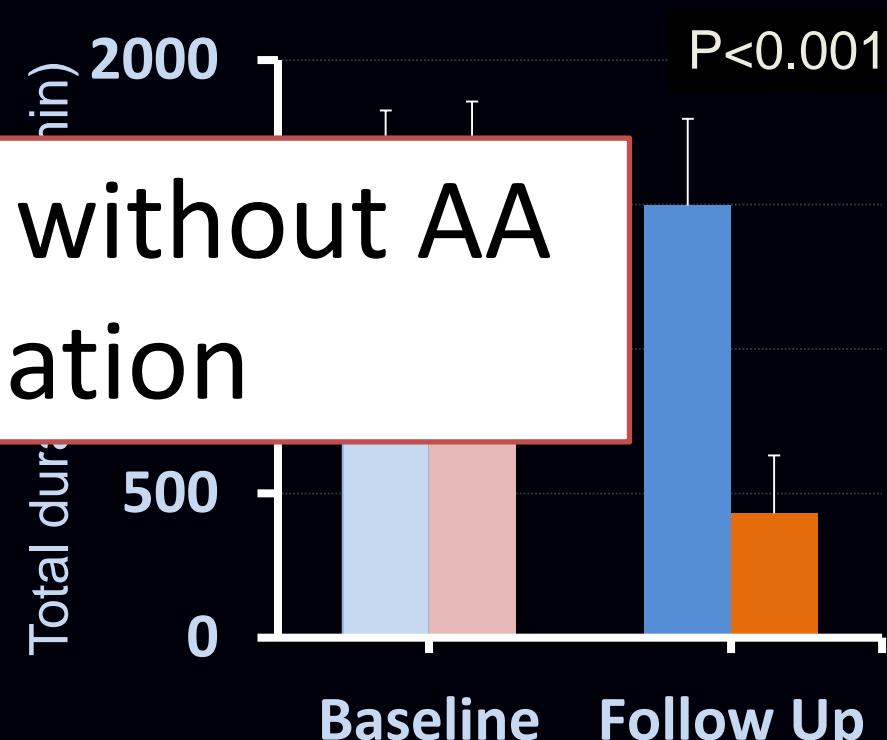
- Smoking cessation
- Alcohol reduction to $\leq 30 \text{ g/week}$

Atrial Fibrillation detected by 7days Holter

Mean Number of AF
Episodes



Total Duration of AF



Δ Mean no. AA : Control : 0.4 ± 0.2 ; RFM Group: - 0.7 ± 0.1

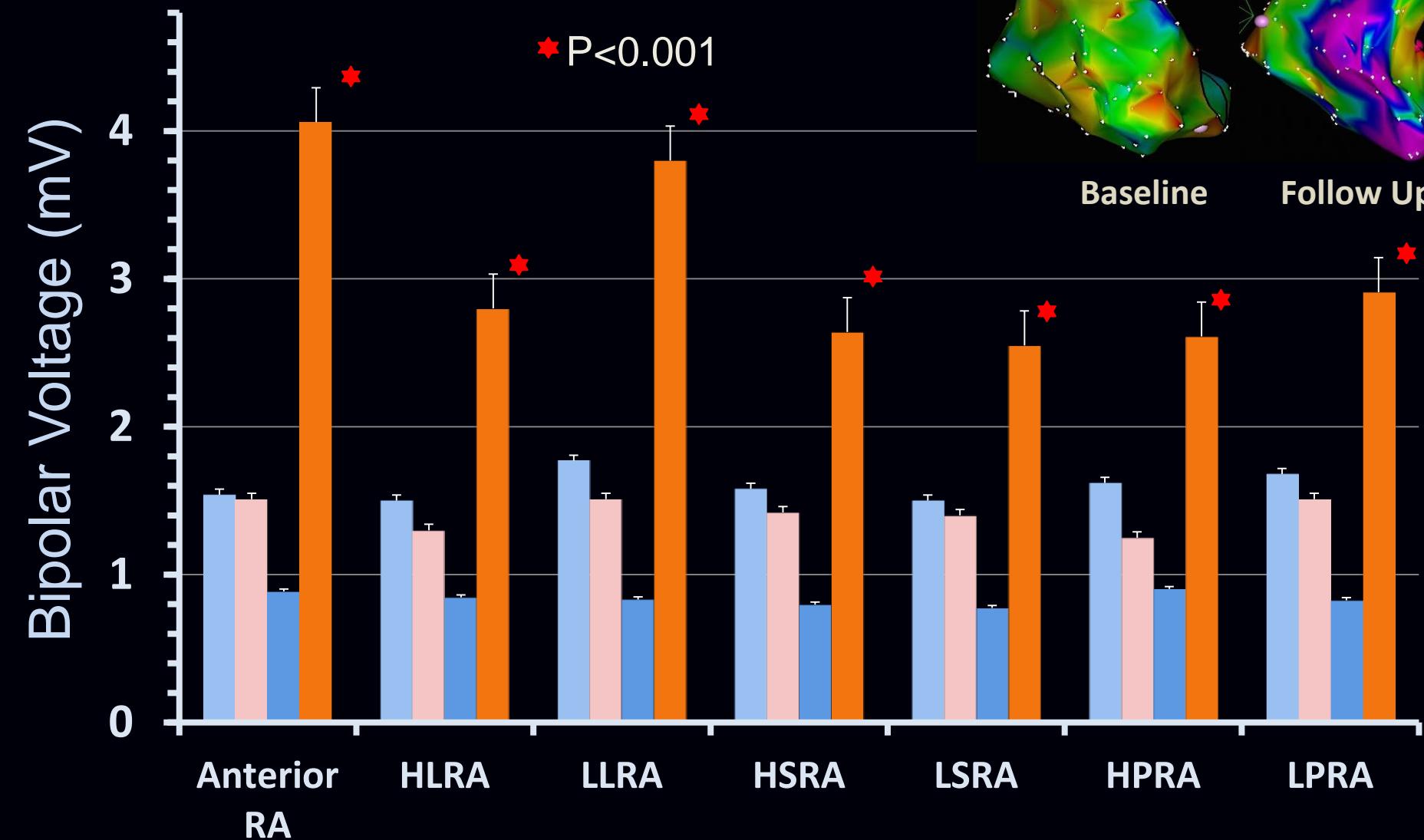
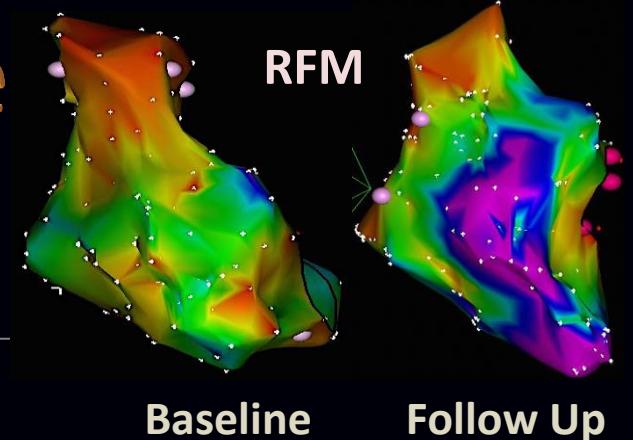
■ CTL_Baseline

■ RFM_Baseline

■ CTL_Follow Up

■ RFM_Follow Up

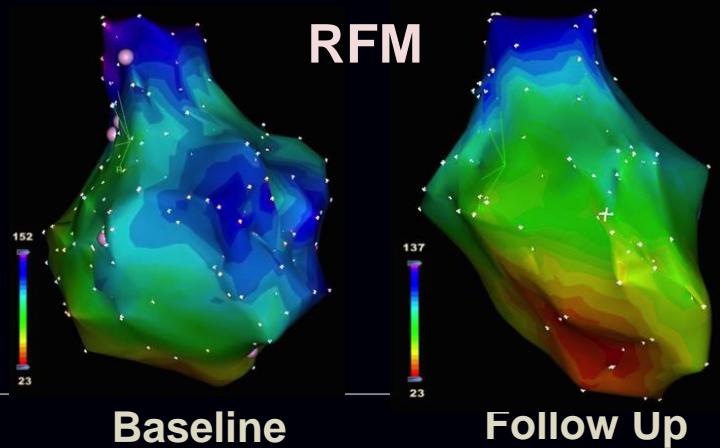
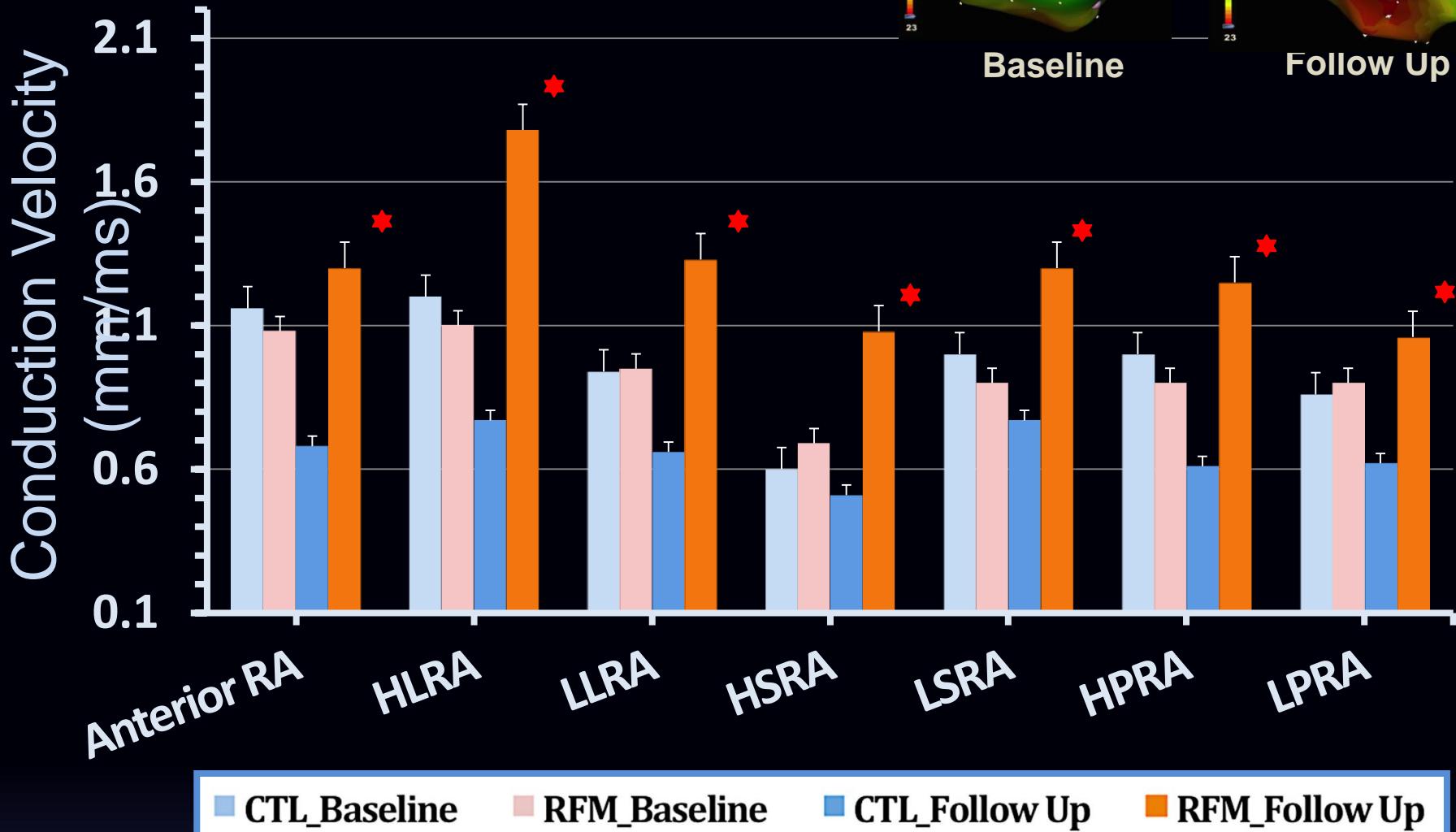
Regional Bipolar Voltage



■ CTL_Baseline ■ CTL_Follow up ■ RFM_Baseline ■ RFM_Follow up

Regional Conduction Velocity

* P<0.02



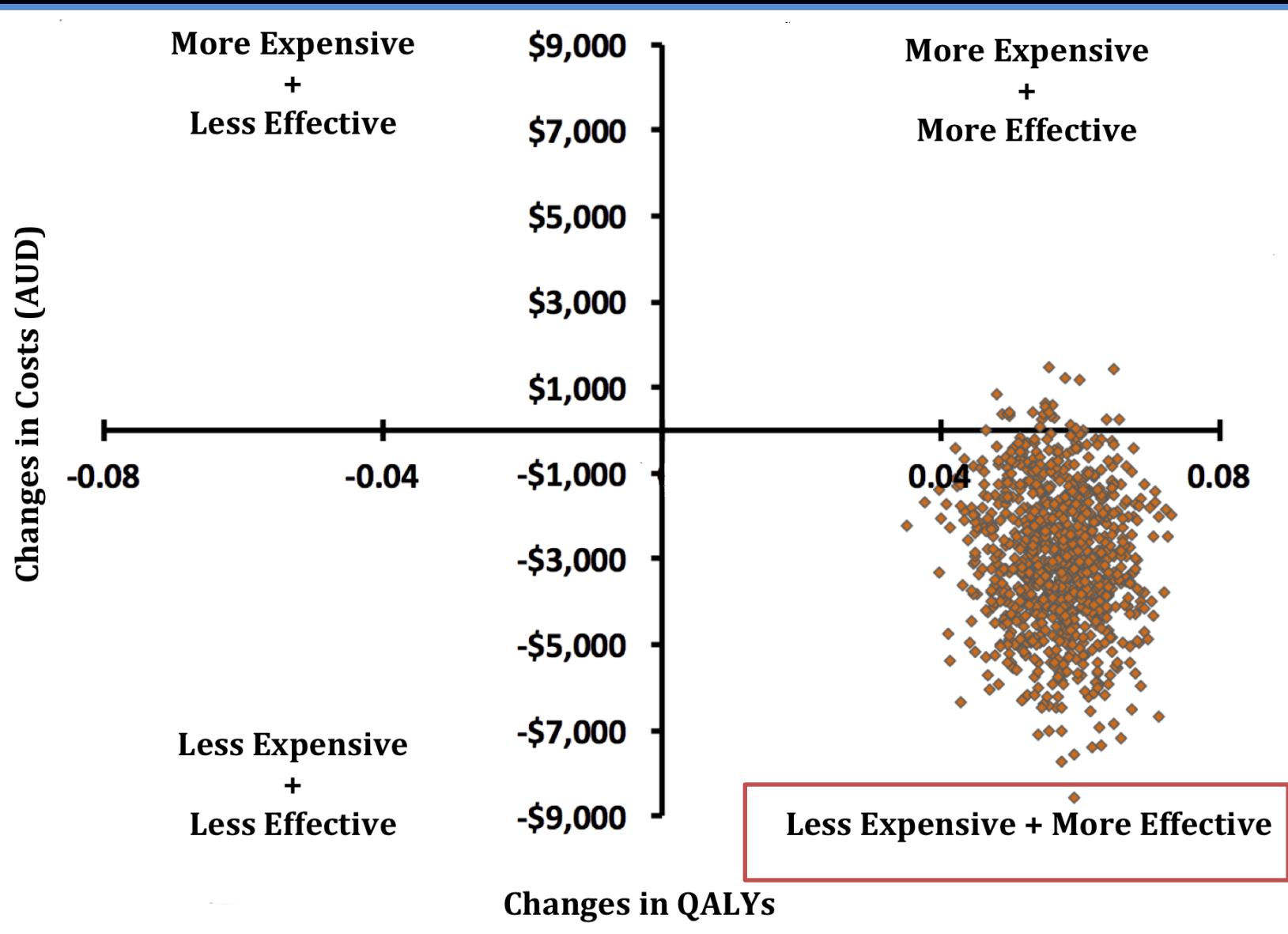
Conclusions

- Obesity is associated with electrical and structural remodeling, increased risk of AF
- Sustained weight loss is associated with dose dependent reduction in AF burden
- Cardiorespiratory fitness gain provides incremental gain over weight loss in long-term freedom from AF
- Weight loss leads to marked improvement in structural and electrical properties of heart
- A dedicated clinic improves patient engagement, promoting treatment adherence, preventing weight regain and fluctuation

Health Care Utilisation

	Control Group (N=147)	RFM Group (N=208)	P Value
Medication Use			
Anti-arrhythmic use	0.91 ±0.6	0.26±0.5	0.003
Anti-Hypertensive medication	0.78±0.6	0.53±0.7	0.043
Lipid Therapy	81 (64)	73 (40)	0.032
CPAP Use	62 (43)	70 (34)	0.098
Interventional Procedure			
Cardioversion	1.51±2.3	0.89±1.5	0.002
Single AF Ablation	43 (29)	86 (41)	0.009
2nd Procedure	24 (16%)	15 (7)	
3rd Procedure	5 (3)	3 (1)	
In Patient Visits			
ED presentation	0.76±1.2	0.18±0.5	< 0.001
Hospitalization for AF	1.15±1.6	0.74±1.3	0.034
Out Patient Visits			
Specialist - Planned	14±3	10±2	0.01
Specialist Visit - Unplanned	1.94±2.0	0.19±0.4	<0.001

Incremental Cost Effectiveness Plane



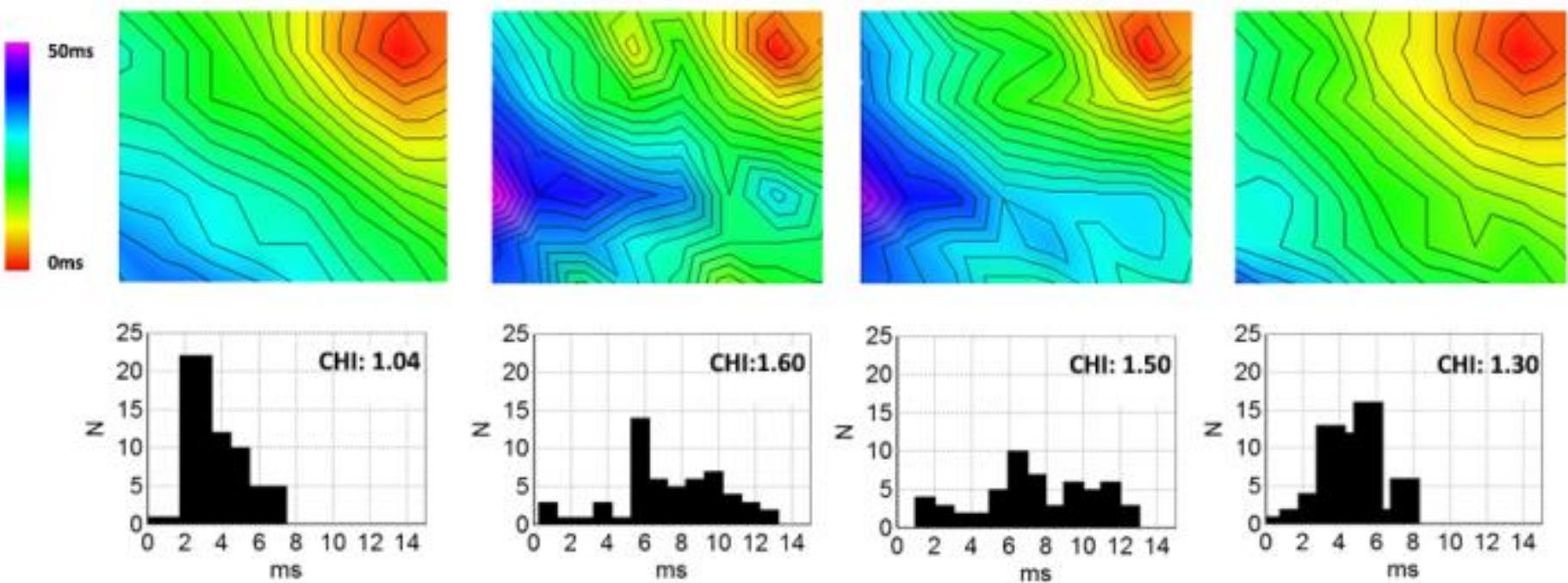
Reversal of AF substrate with Weight reduction

Lean Control

Obese

15% Wt Loss

30% Wt Loss



Reversal of Atrial Fibrosis with Weight Reduction

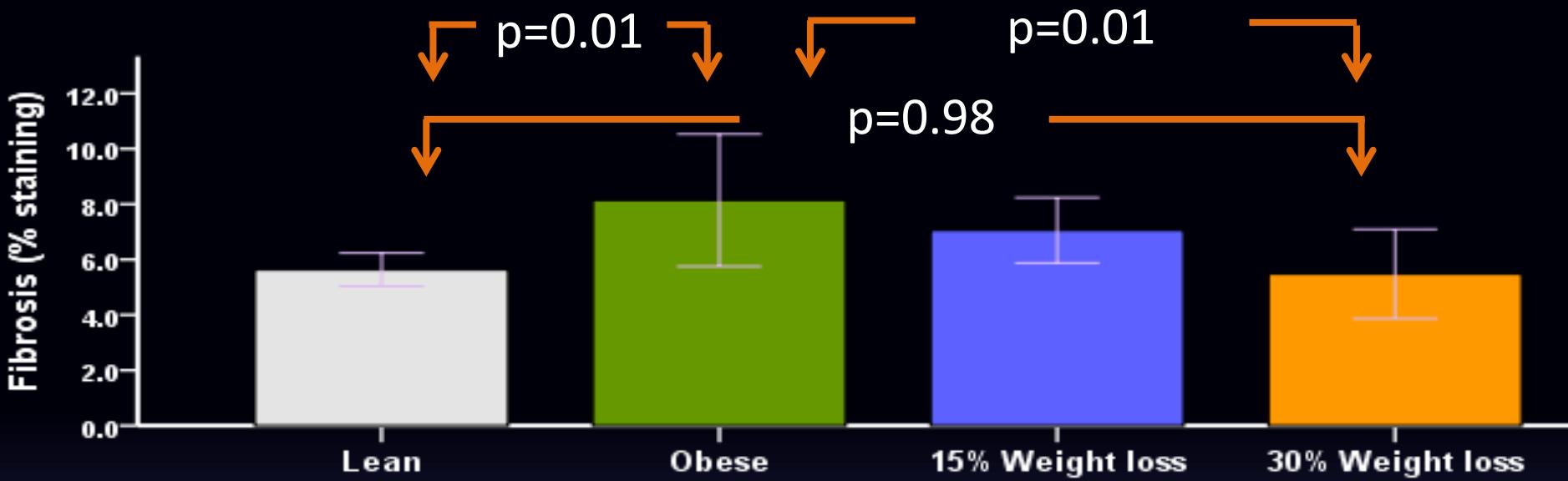
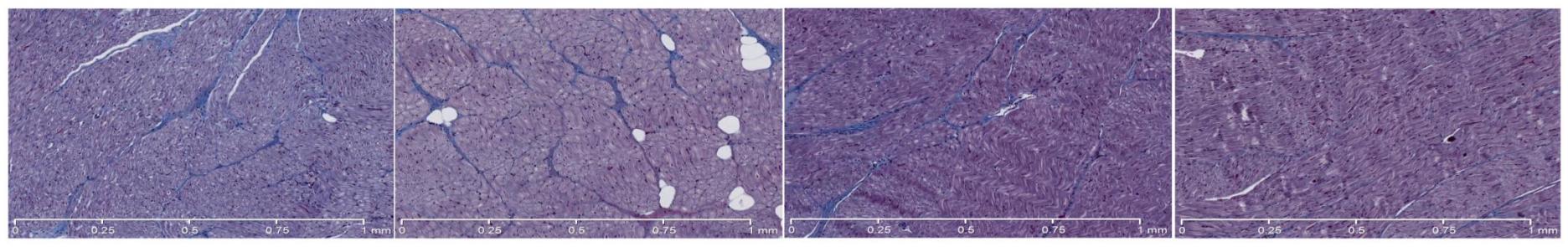
Masson's Trichrome

Lean Control

Obese

15% Wt Loss

30% Wt Loss



Improvement in Atrial Inflammation with weight loss

Lean Control

Obese

15% Wt Loss

30% Wt Loss

