MANAGING THE DIFFICULT COMORBIDITY OF ATRIAL FIBRILLATION AND HEART FAILURE

Hong Kong College of Cardiologist ASM 2019

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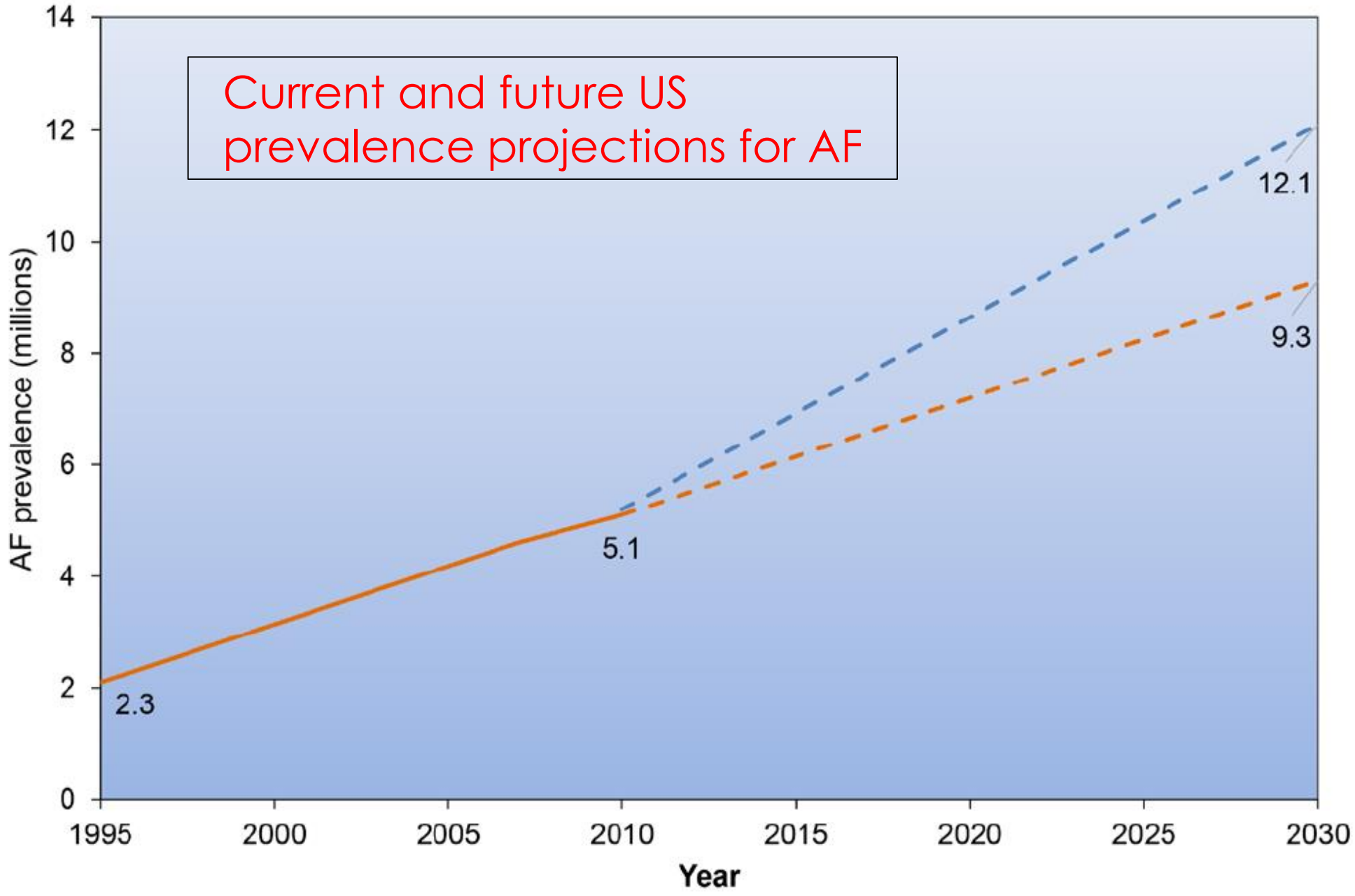
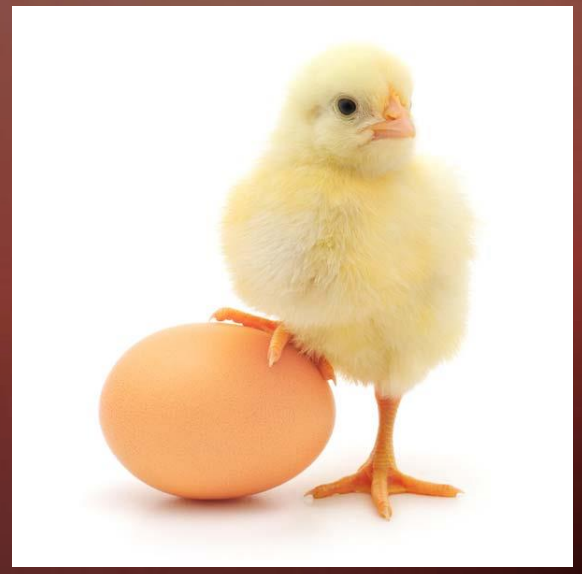
Current and future US prevalence projections for AF

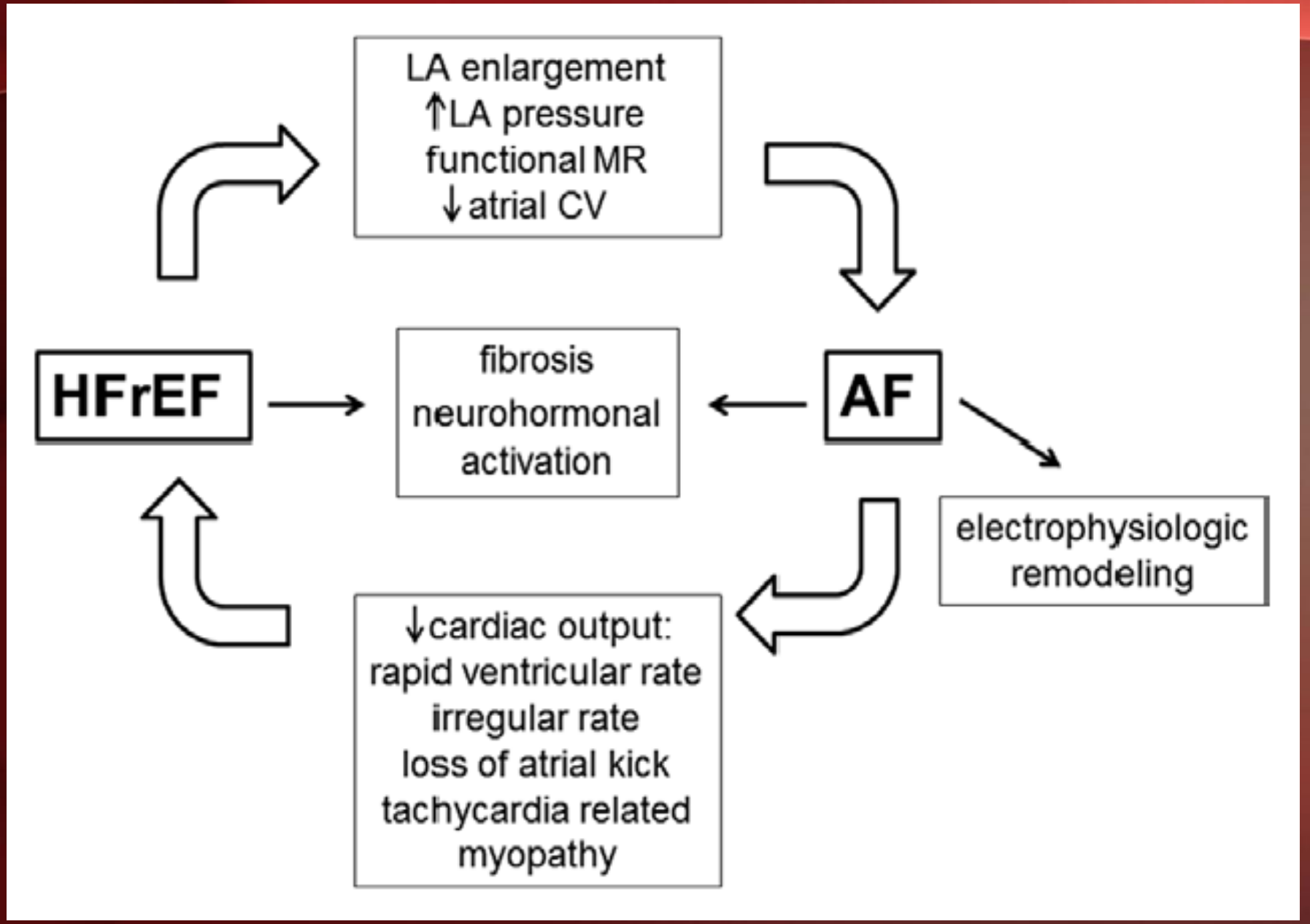


Heart Disease and Stroke Statistics-2019 Update

ATRIAL FIBRILLATION AND HEART FAILURE CHICKEN & EGG

- AF and HF share many fundamental predisposing risk factors
- Aging, Hypertension, Diabetes mellitus, Obesity, Coronary artery disease, Thyrotoxicosis
- Structural heart disease, Chronic lung disease
- Obstructive sleep apnea,
- Alcohol/Stimulant use

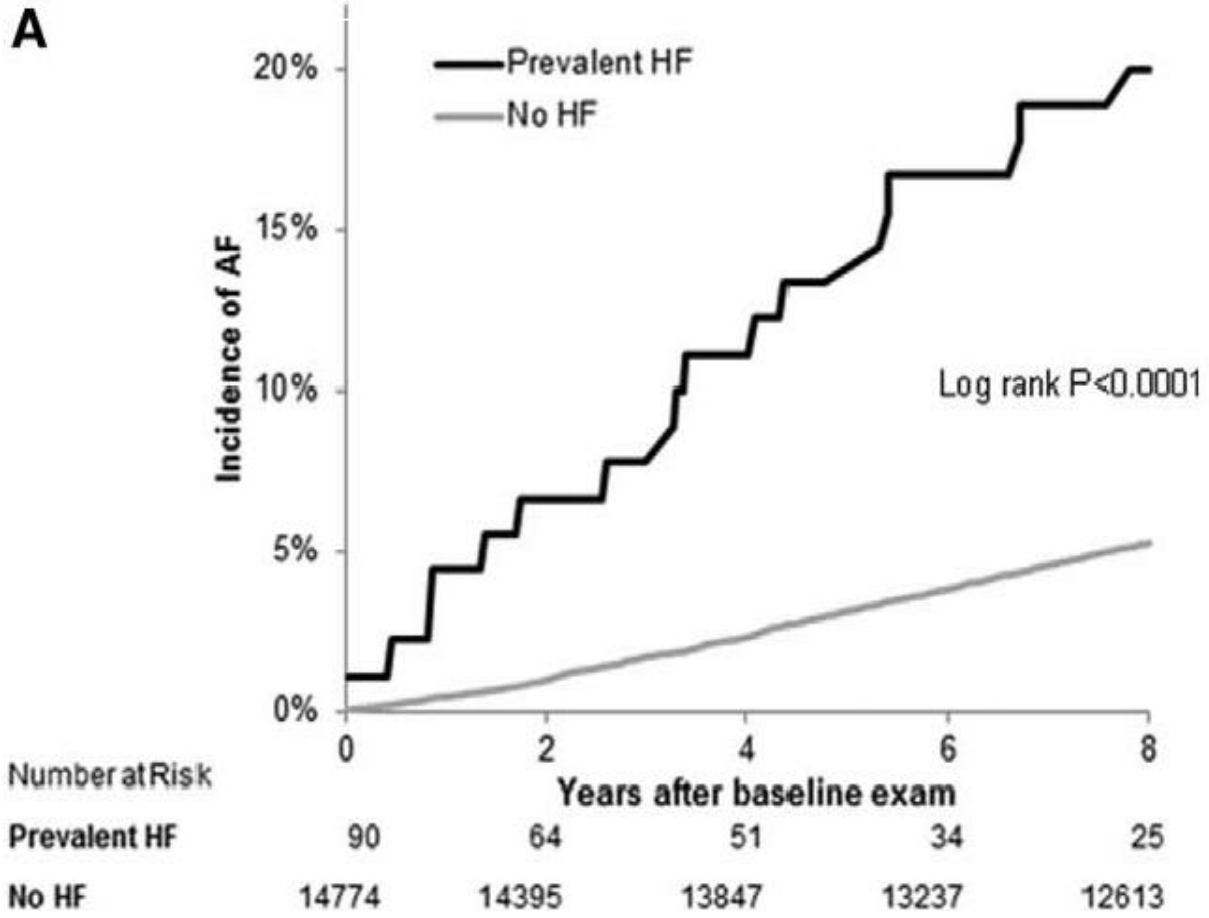




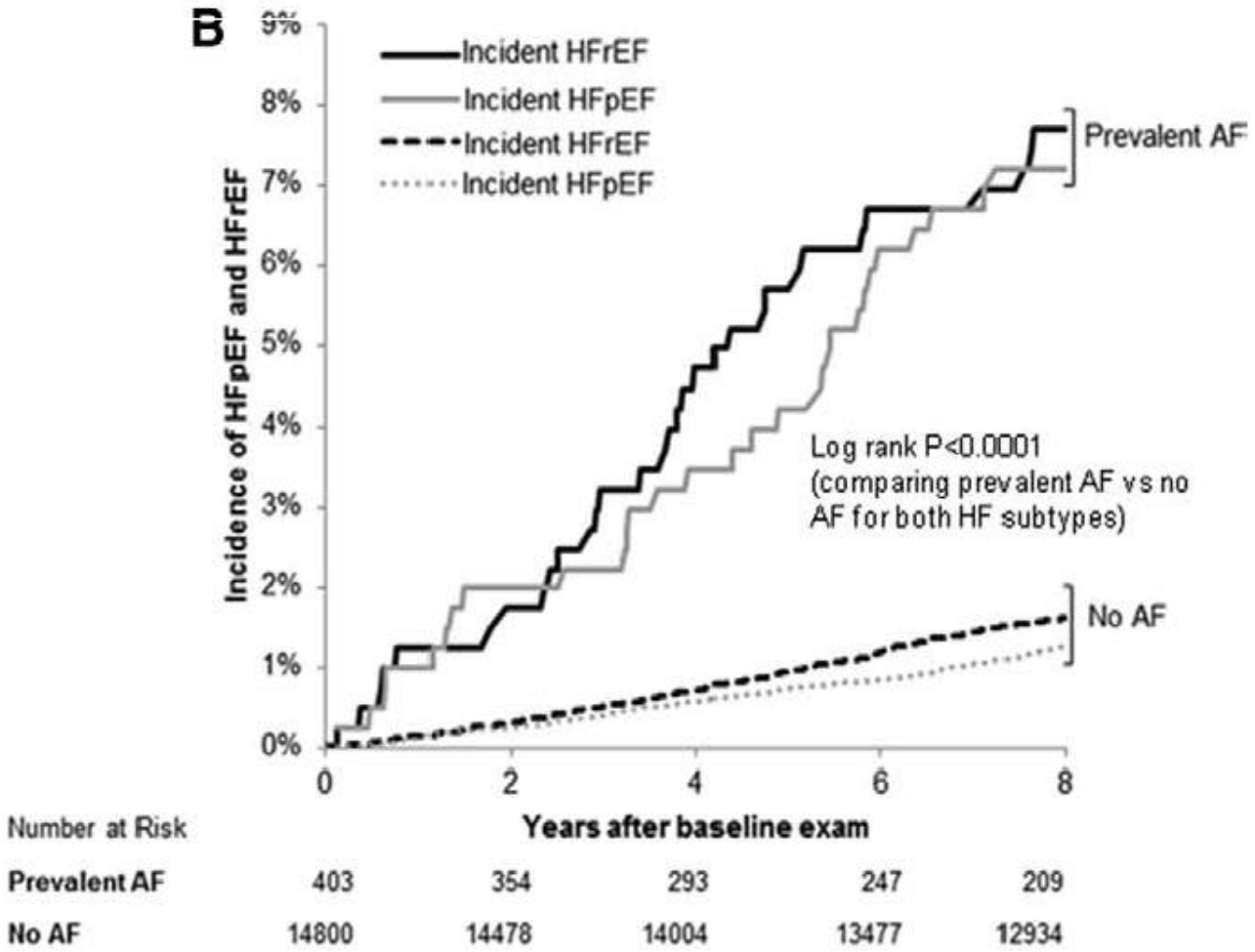
Verma et al Circulation 2017;135:1547-1563

AF BEGETS HEART FAILURE AND VICE VERSA

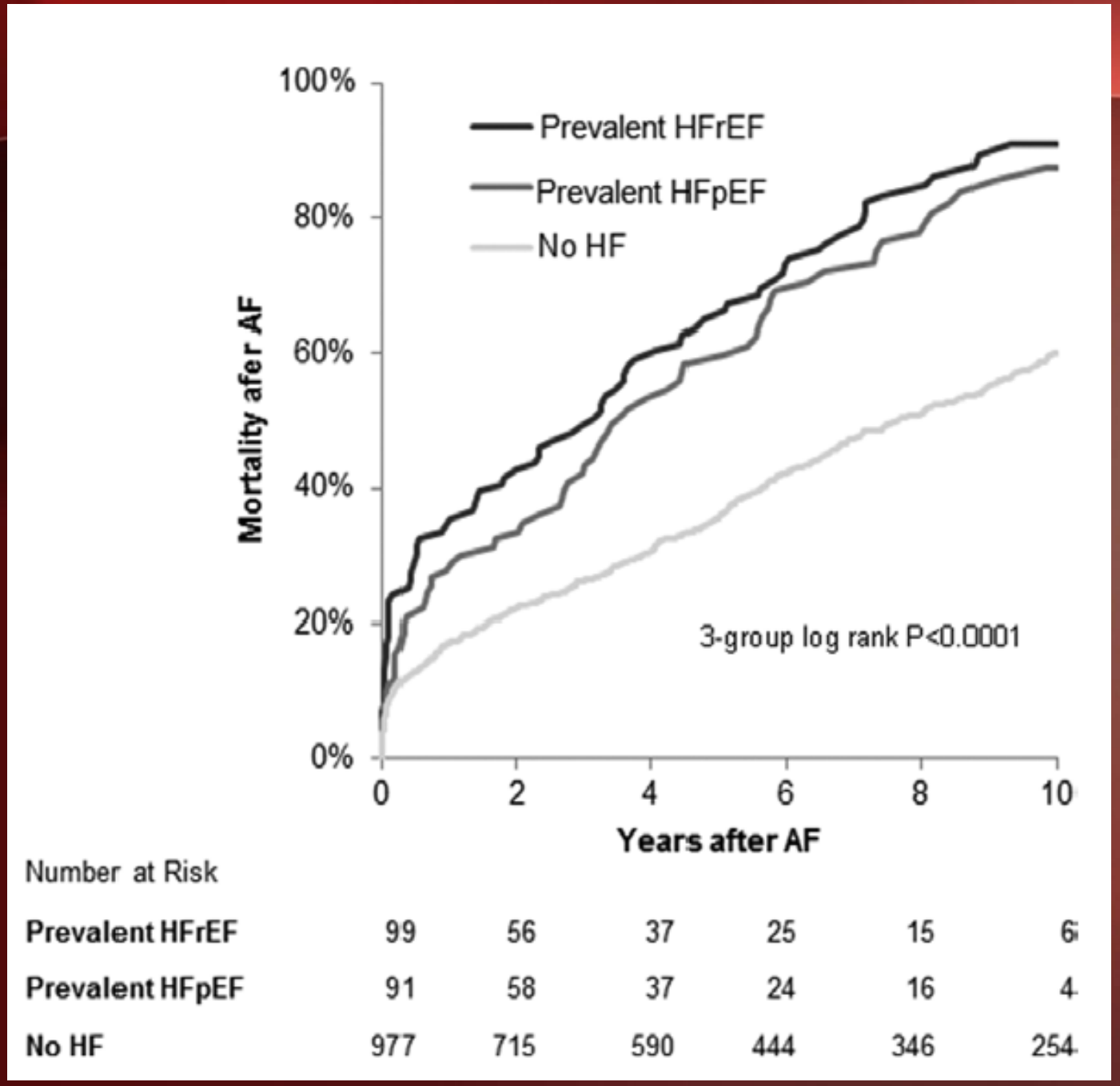
Cumulative incidence of AF



Cumulative incidence of HF



Santhanakrishnan R et al. Circulation 2016;133:484-492



Number at Risk

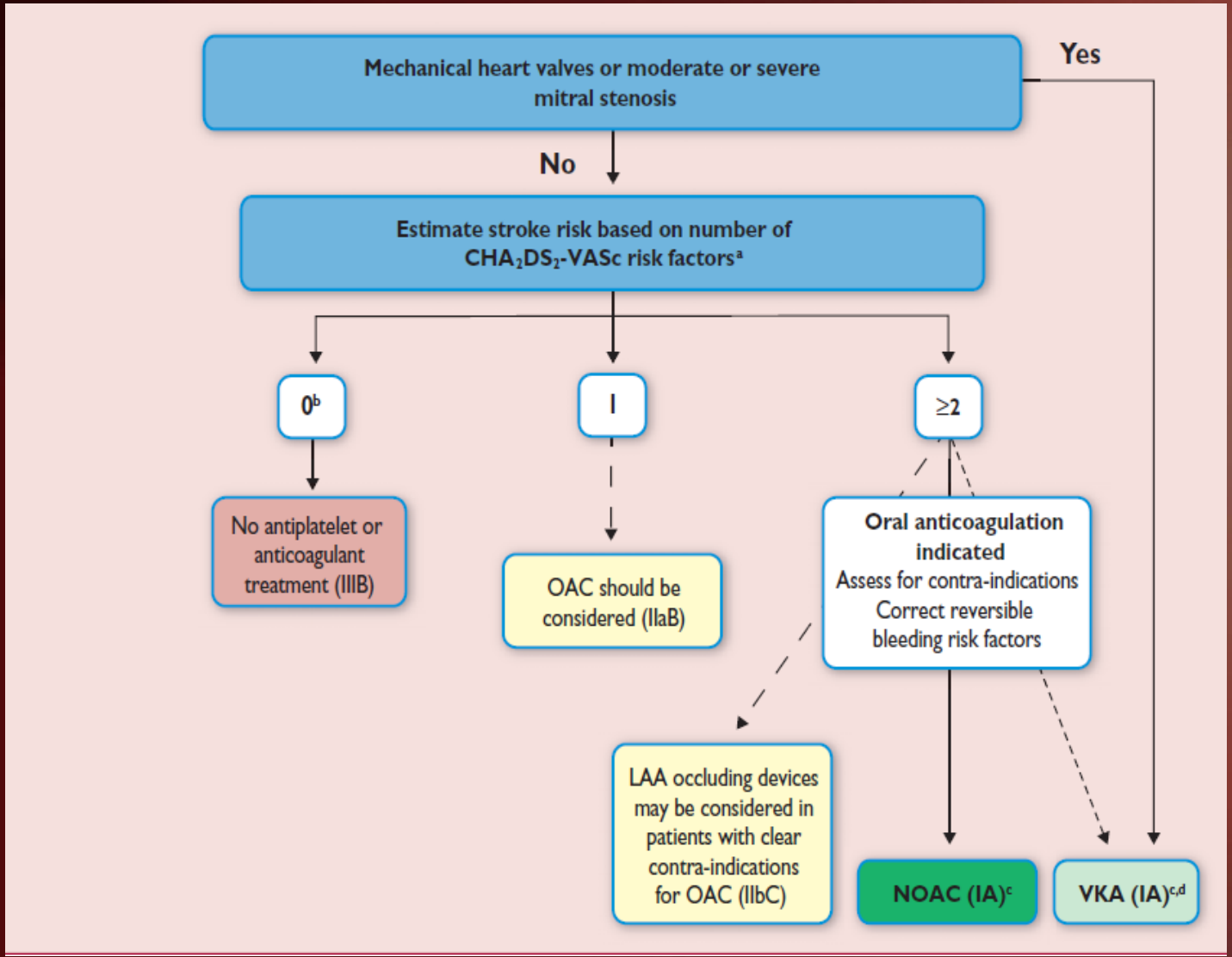
Prevalent HFrEF	99	56	37	25	15	6
Prevalent HFpEF	91	58	37	24	16	4
No HF	977	715	590	444	346	254

Santhanakrishnan R et al. Circulation 2016;133:484-492

MANAGEMENT

- Stroke prevention
- Anti-heart failure Therapy
- Rate control
- Catheter Ablation

2016 ESC GUIDELINES FOR MANAGEMENT OF AF

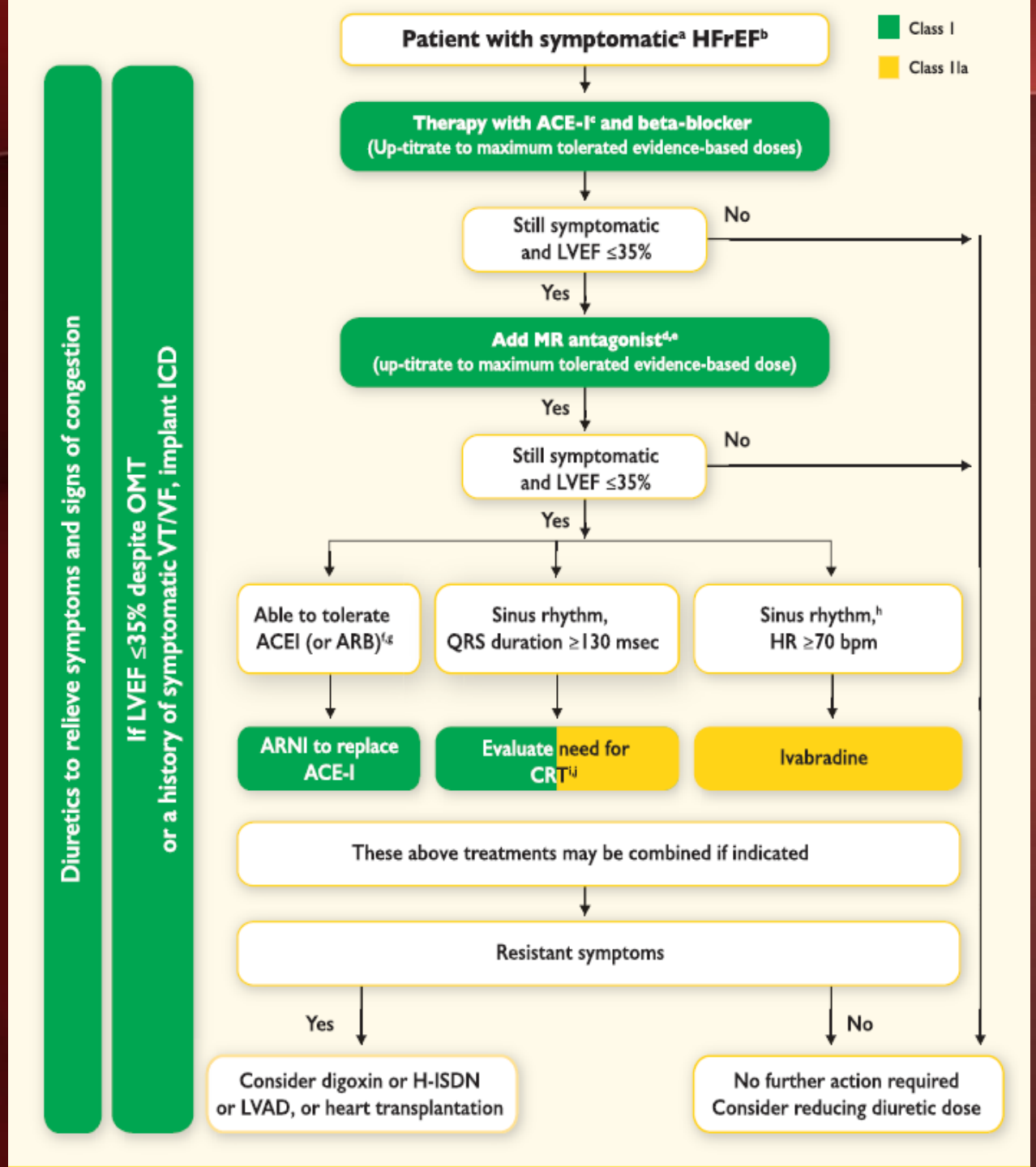


Kirchhof et al. Eur Heart J 2016;37:2893-2962

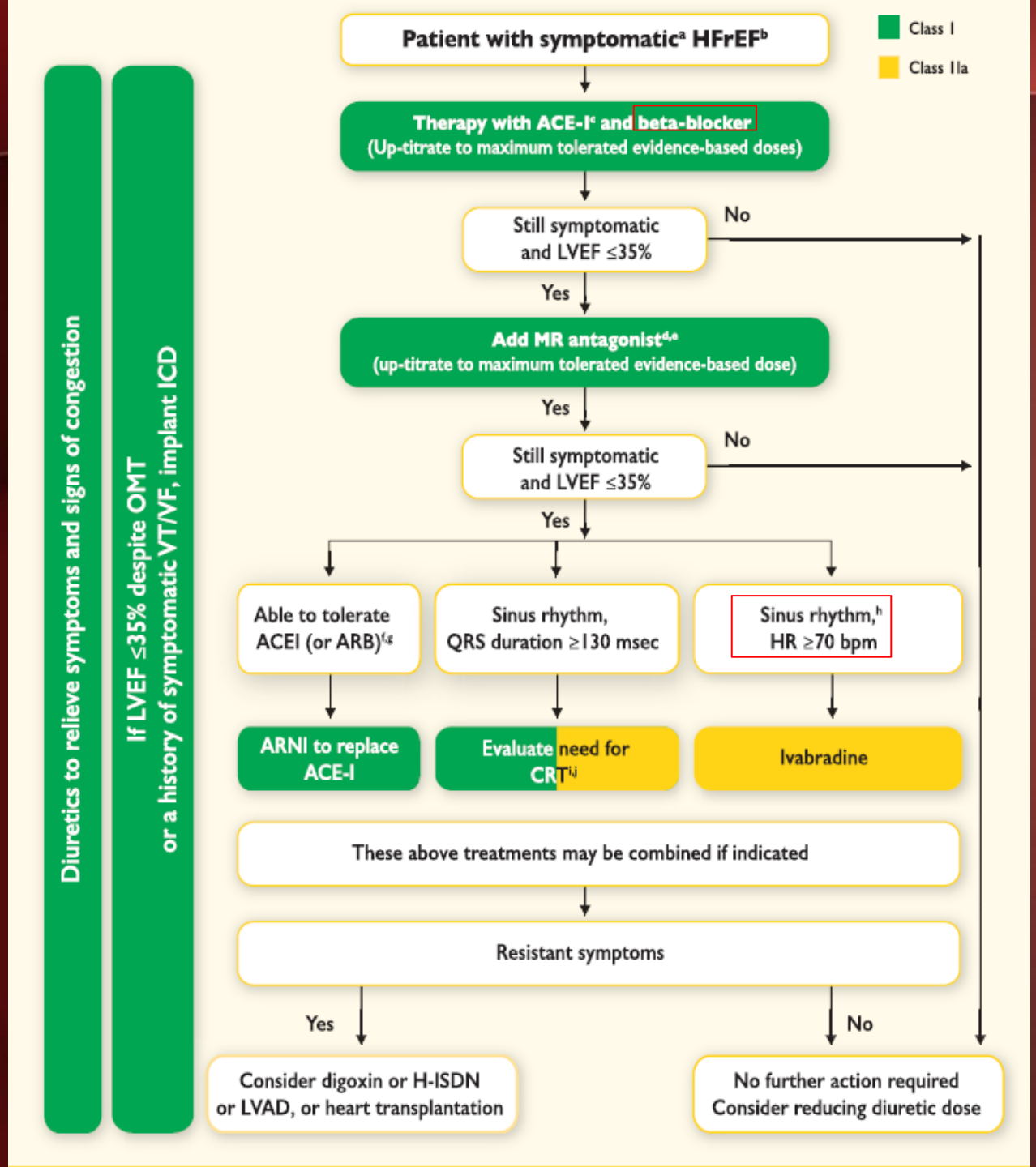
Hazard Ratio of Stroke, TIA, or systemic embolism according to Left ventricular function and Heart Failure Severity (From ACTIVE Study)

Composite Stroke/TIA/ Systemic Embolism, per Year	Risk, N (% per 100 Person Years)			Permanent AF vs Nonpermanent AF		
	Overall (n=3484)	Nonpermanent AF (n=862)	Permanent AF (n=2622)	HR (95% CI)	*P* Value	*P* Value for Interaction
Overall	385 (4.5)	85 (3.8)	300 (4.7)	1.22 (0.96–1.56)	0.10	
HF-PEF	110 (4.3)	27 (3.0)	83 (5.0)	1.61 (1.04–2.49)	0.03	0.047
HF-REF	115 (4.4)	31 (4.8)	84 (4.2)	0.88 (0.58–1.33)	0.54	
LV dysfunction						
None	82 (4.2)	21 (3.0)	61 (4.9)	1.64 (1.00–2.70)	0.05	
Mild	58 (4.2)	14 (3.9)	44 (4.4)	1.13 (0.62–2.06)	0.70	0.13
Moderate	57 (4.6)	13 (4.0)	44 (4.8)	1.19 (0.64–2.21)	0.58	
Severe	27(4.4)	9 (7.0)	18 (3.7)	0.52 (0.23–1.16)	0.11	
NYHA Class						
I	84 (4.8)	23 (3.9)	62 (5.3)	1.33 (0.83–2.16)	0.24	
II	235 (4.5)	51 (3.8)	184 (4.7)	1.24 (0.91–1.69)	0.18	0.91
III or IV	66 (4.0)	11 (3.6)	55 (4.1)	1.14 (0.60–2.17)	0.70	

Sandhu RK et al Stroke 2015;46:667-672

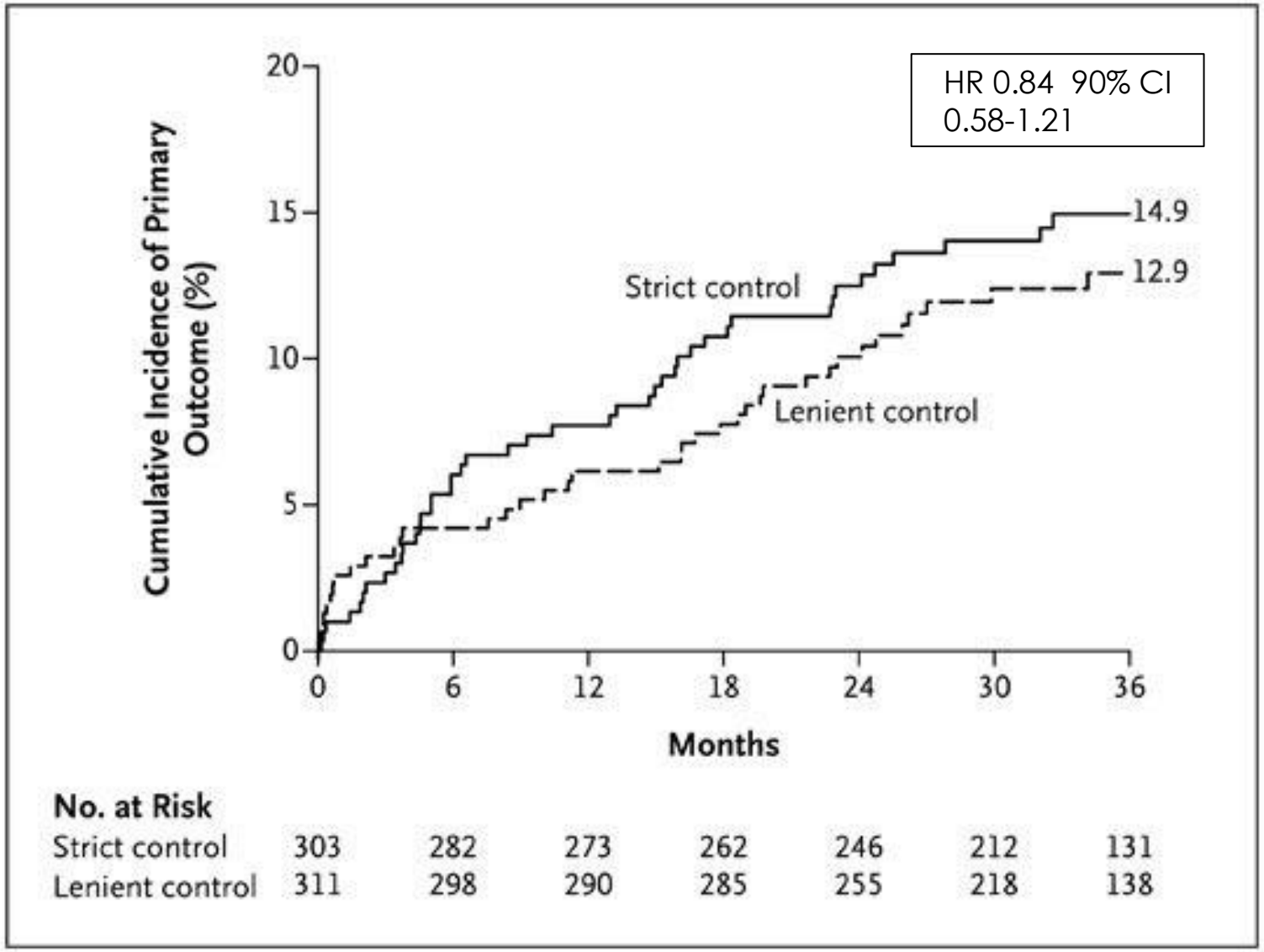


Ponikowski P et al Eur J Heart Fail 2016



Ponikowski P et al Eur J Heart Fail 2016

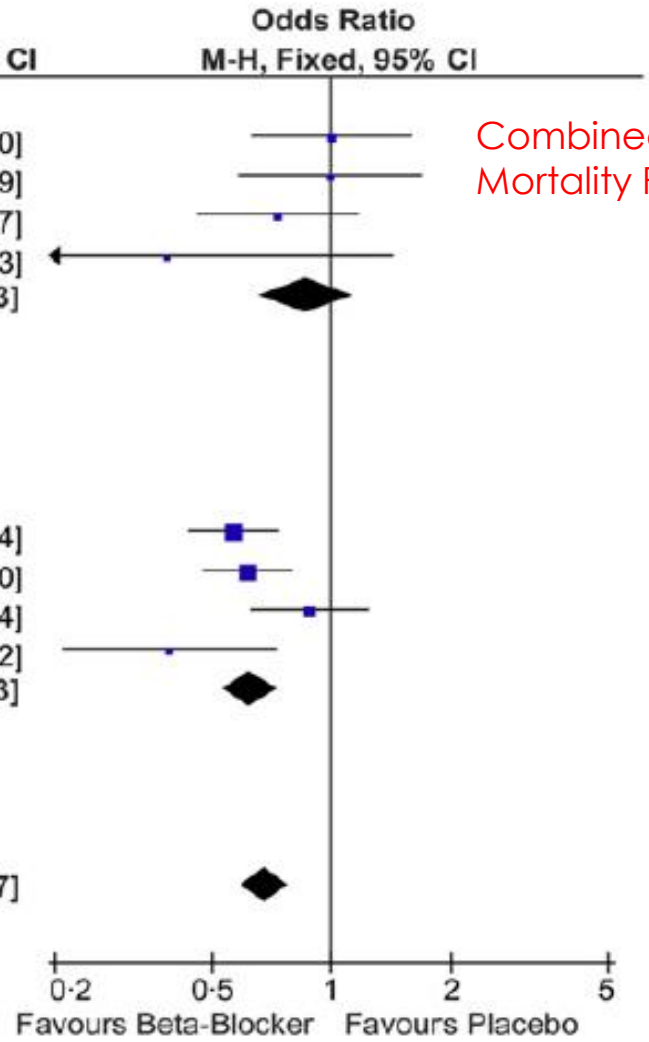
RACE II STUDY



Van Gelder IC et al. N Engl J Med 2010;362:1363-1373

META ANALYSIS: EFFECT OF BETA-BLOCKER IN PATIENTS IN SR VS AF

Study or Subgroup	Beta-Blocker Events	Total	Placebo Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
AF						
CIBIS-II	42	257	43	264	6·9%	1·00 [0·63, 1·60]
MERIT-HF	30	274	31	282	5·3%	1·00 [0·58, 1·69]
SENIORS	38	227	51	237	8·1%	0·73 [0·46, 1·17]
US-Carvedilol	4	84	6	52	1·4%	0·38 [0·10, 1·43]
Subtotal (95% CI)		**842**		**835**	**21·6%**	**0·86 [0·66, 1·13]**
Total events	114		131			
Heterogeneity: Chi² = 2·61, df = 3 (P = 0·46); I² = 0%						
Test for overall effect: Z = 1·07 (P = 0·28)						
SR						
CIBIS-II	105	1014	170	1004	29·7%	0·57 [0·44, 0·74]
MERIT-HF	102	1563	160	1569	29·0%	0·61 [0·47, 0·80]
SENIORS	77	451	84	444	13·6%	0·88 [0·63, 1·24]
US-Carvedilol	18	612	25	346	6·0%	0·39 [0·21, 0·72]
Subtotal (95% CI)		**3640**		**3363**	**78·4%**	**0·63 [0·54, 0·73]**
Total events	302		439			
Heterogeneity: Chi² = 6·71, df = 3 (P = 0·08); I² = 55%						
Test for overall effect: Z = 5·88 (P < 0·00001)						
Total (95% CI)		**4482**		**4198**	**100·0%**	**0·68 [0·59, 0·77]**
Total events	416		570			
Heterogeneity: Chi² = 13·30, df = 7 (P = 0·07); I² = 47%						
Test for overall effect: Z = 5·66 (P < 0·00001)						
Test for subgroup differences: Chi² = 3·97, df = 1 (P = 0·046), I² = 74·8%						

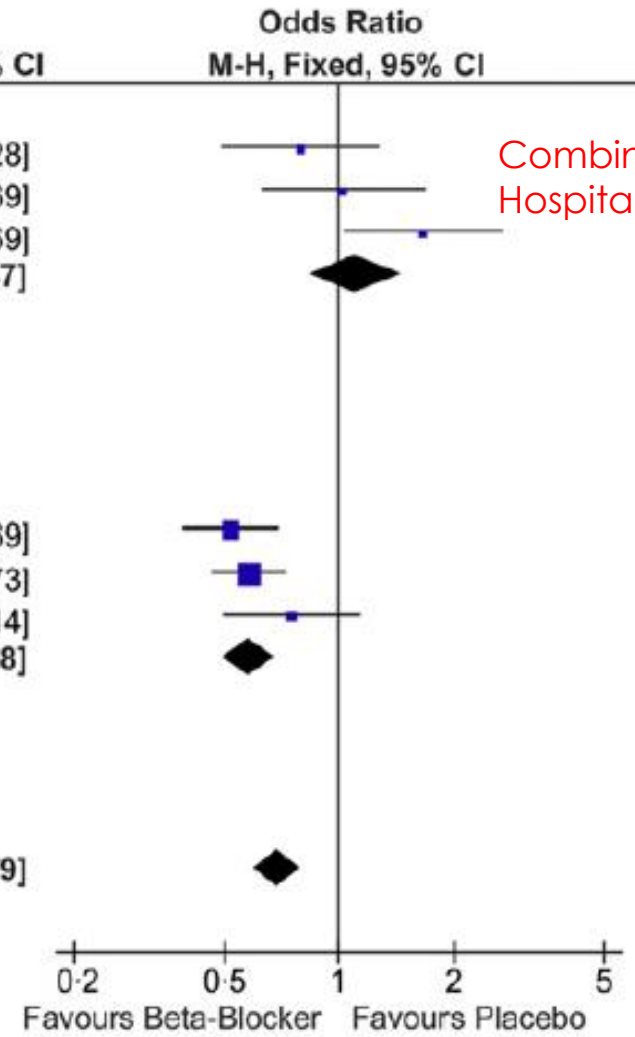


Combined All Cause Mortality Risk

Rienstra M et al J Am Coll Cardiol HF 2013;1:21-8

META ANALYSIS: EFFECT OF BETA-BLOCKER IN PATIENTS IN SR VS AF

Study or Subgroup	Beta-Blocker Events	Total	Placebo Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
AF						
CIBIS-II	36	257	45	264	7·9%	0·79 [0·49, 1·28]
MERIT-HF	37	282	35	274	6·4%	1·03 [0·63, 1·69]
SENIORS	51	227	35	237	5·5%	1·67 [1·04, 2·69]
Subtotal (95% CI)		**766**		**775**	**19·7%**	**1·11 [0·85, 1·47]**
Total events	124		115			
Heterogeneity: Chi² = 4·86, df = 2 (P = 0·09); I² = 59%						
Test for overall effect: Z = 0·77 (P = 0·44)						
SR						
CIBIS-II	81	1014	144	1004	27·5%	0·52 [0·39, 0·69]
MERIT-HF	138	1569	223	1563	42·1%	0·58 [0·46, 0·73]
SENIORS	45	451	57	444	10·7%	0·75 [0·50, 1·14]
Subtotal (95% CI)		**3034**		**3011**	**80·3%**	**0·58 [0·49, 0·68]**
Total events	264		424			
Heterogeneity: Chi² = 2·10, df = 2 (P = 0·35); I² = 5%						
Test for overall effect: Z = 6·53 (P < 0·00001)						
Total (95% CI)		**3800**		**3786**	**100·0%**	**0·69 [0·60, 0·79]**
Total events	388		539			
Heterogeneity: Chi² = 22·45, df = 5 (P = 0·0004); I² = 78%						
Test for overall effect: Z = 5·29 (P < 0·00001)						
Test for subgroup differences: Chi² = 15·81, df = 1 (P < 0·0001), I² = 93·7%						



Combined HF Hospitalization Risk

Rienstra M et al J Am Coll Cardiol HF 2013;1:21-8

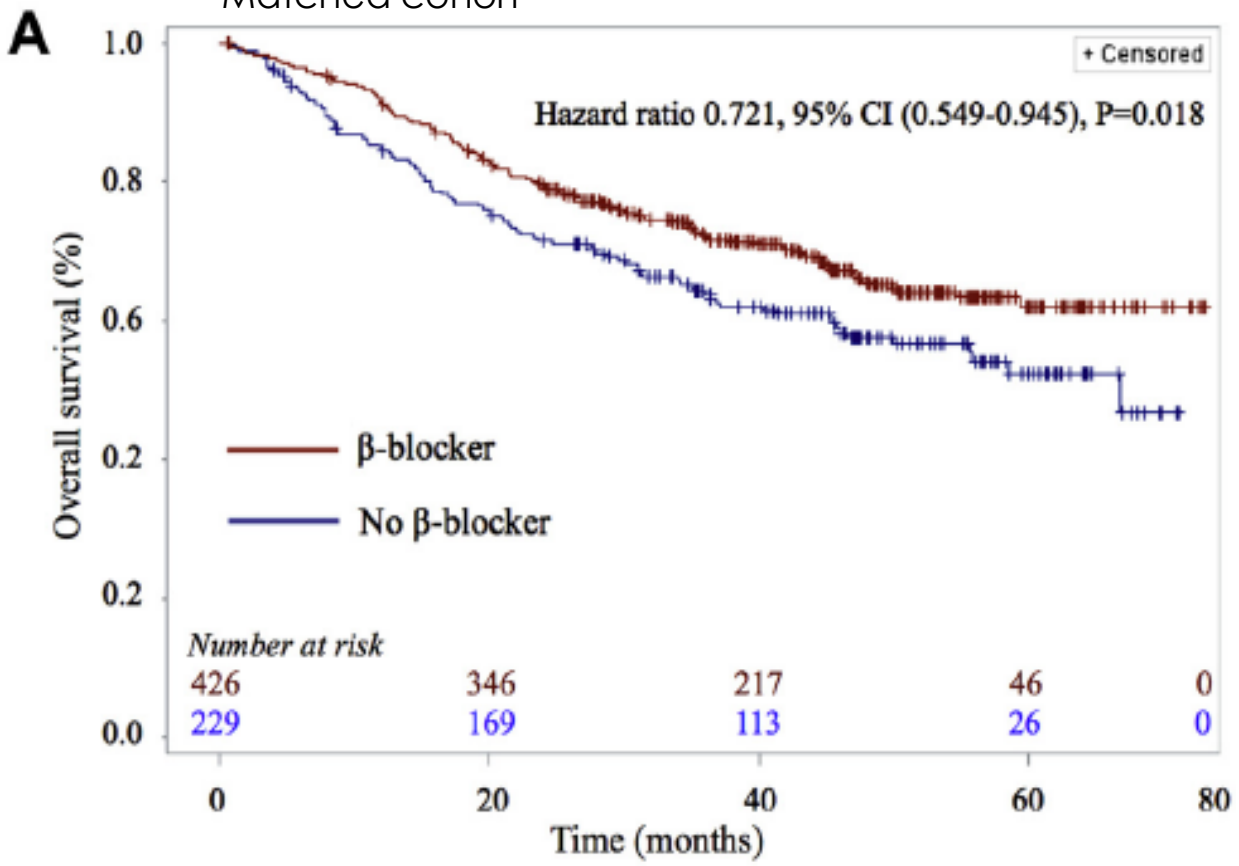
SWEDISH HEART FAILURE REGISTRY

	No. of Deaths/Patients (% Per Person-Year)	Univariable Hazard Ratio (95% CI)	*P* Value	Multivariable Hazard Ratio (95% CI)	*P* Value
β-Blocker use in sinus rhythm				All cause mortality	
HR strata, beats per min			<0.001		<0.001
≤60	670/2565 (7.7%)	Reference	—	Reference	—
61–70	1022/3063 (10.9%)	1.41 (1.27–1.55)	<0.001	1.29 (1.17–1.42)	<0.001
71–80	861/2507 (11.5%)	1.48 (1.34–1.64)	<0.001	1.40 (1·26-1·56)	<0.001
81–90	464/1274 (12.7%)	1.63 (1.45–1.84)	<0.001	1.50 (1.33–1.70)	<0.001
91–100	203/594 (12.4%)	1.58 (1.35–1.85)	<0.001	1.79 (1.52–2.11)	<0.001
>100	127/288 (18.1%)	2.30 (1.90–2.78)	<0.001	2.60 (2.14–3.17)	<0.001
β-Blocker use in atrial fibrillation					
HR strata, beats per min			>0.05		<0.05
≤60	358/792 (15.7%)	Reference		Reference	—
61–70	595/1348 (16.2%)	1.03 (0.90–1.17)	0.697	1.03 (0.90–1.18)	0.700
71–80	753/1787 (15.6%)	0.99 (0.87–1.12)	0.871	1.11 (0.97–1.27)	0.119
81–90	536/1329 (15.5%)	0.98 (0.86–1.12)	0.761	1.10 (0.96–1.27)	0.162
91–100	325/824 (15.1%)	0.96 (0.82–1.11)	0.547	1.09 (0.94–1.28)	0.260
>100	268/659 (15.8%)	1.00 (0.90–1.11)	0.995	1.29 (1.09–1.53)	0.003

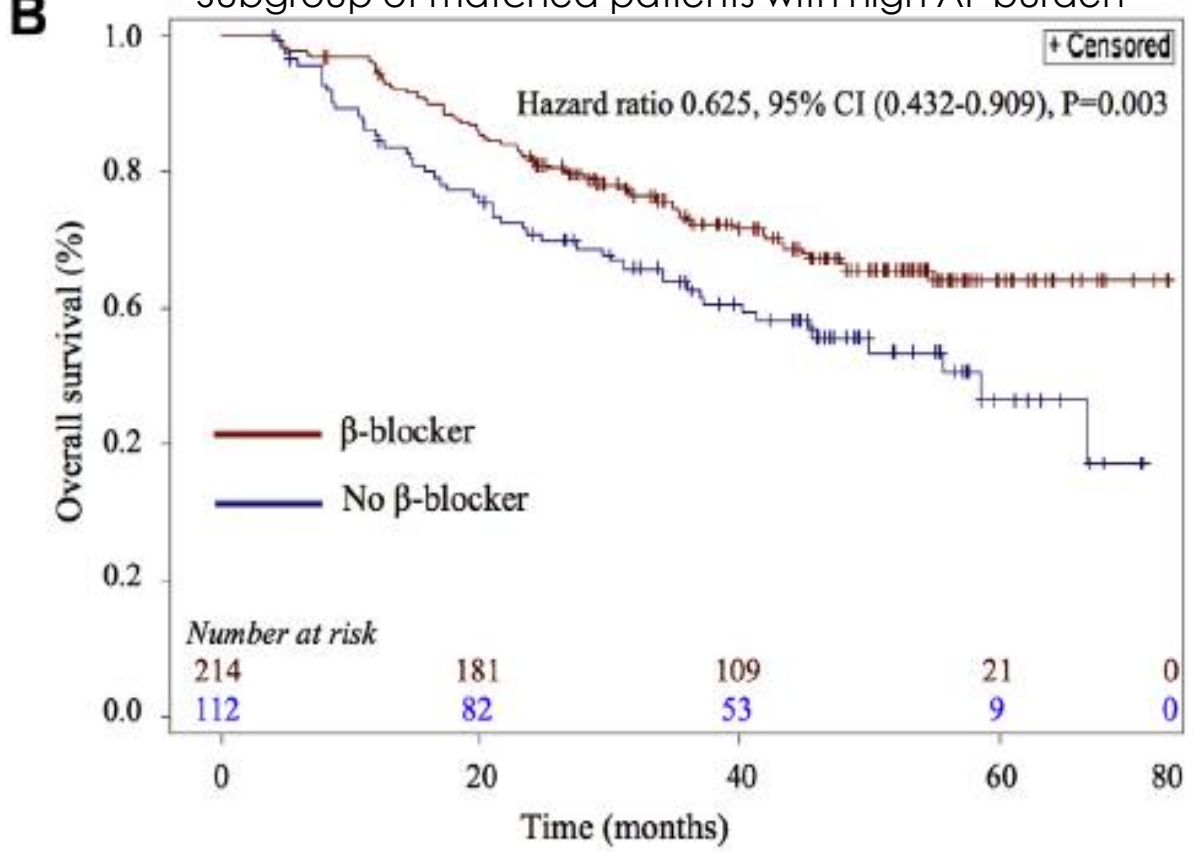
Li SJ et al. Circ Heart Fail. 2015;8:871-879

AF-CHF Sub-study
All Cause Mortality in Patients with and Without Betablocker

Matched cohort

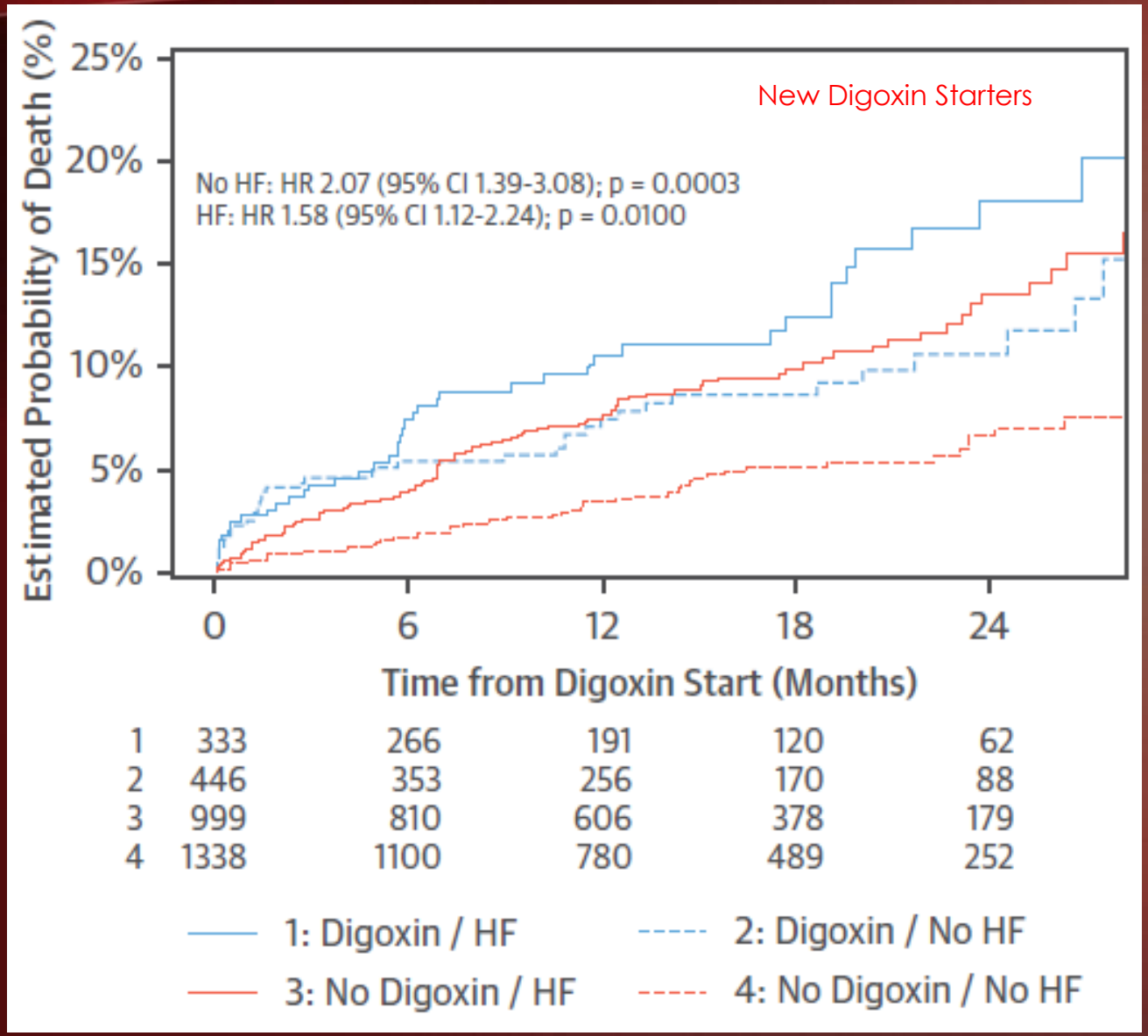


Subgroup of matched patients with high AF burden



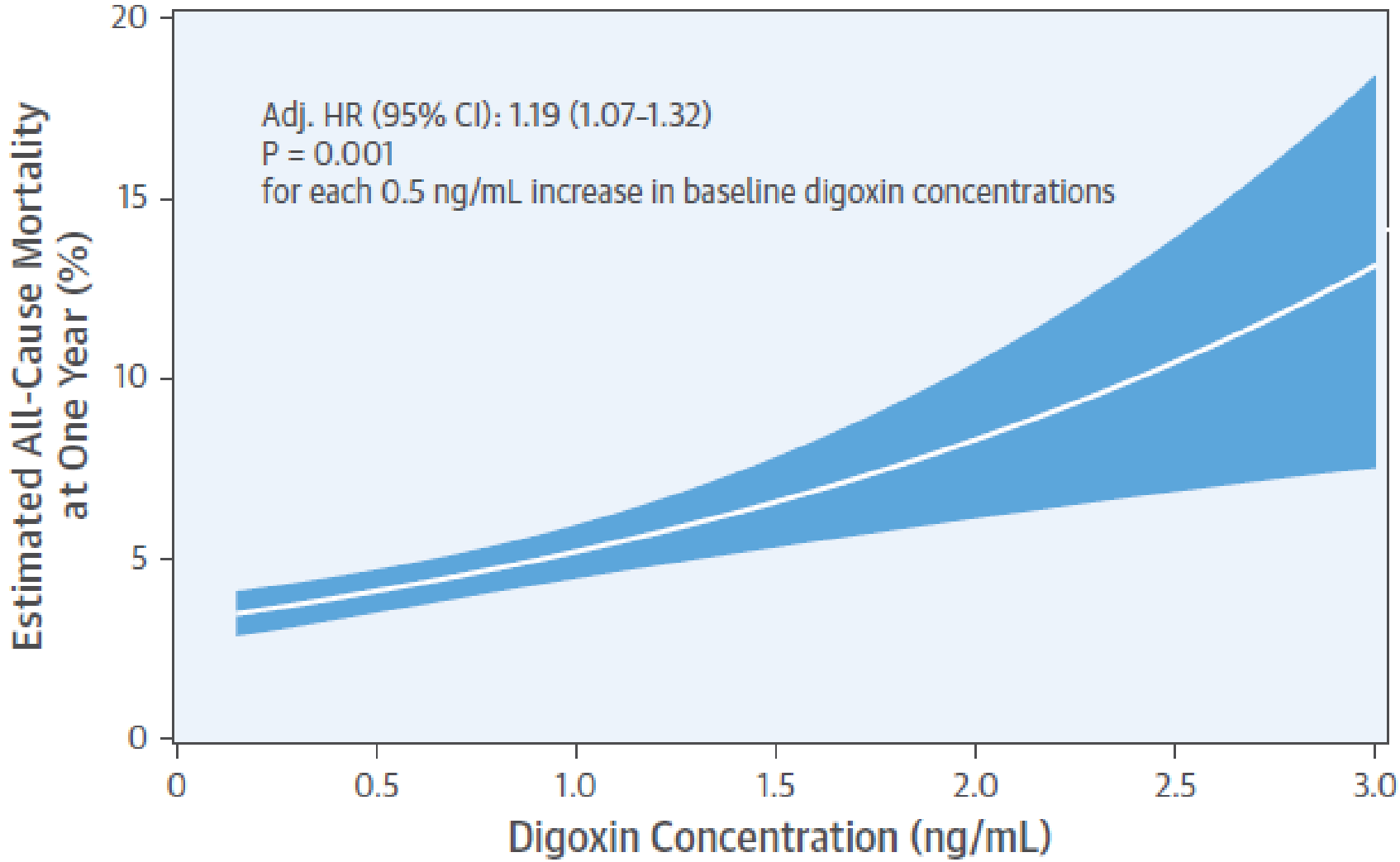
Cadrin-Tourigny J et al. J Am Coll Cardiol HF 2016

DIGOXIN AND MORTALITY IN PATIENTS WITH AF



Lopes RS et al. J Am Coll Cardiol 2018;71:1063-74

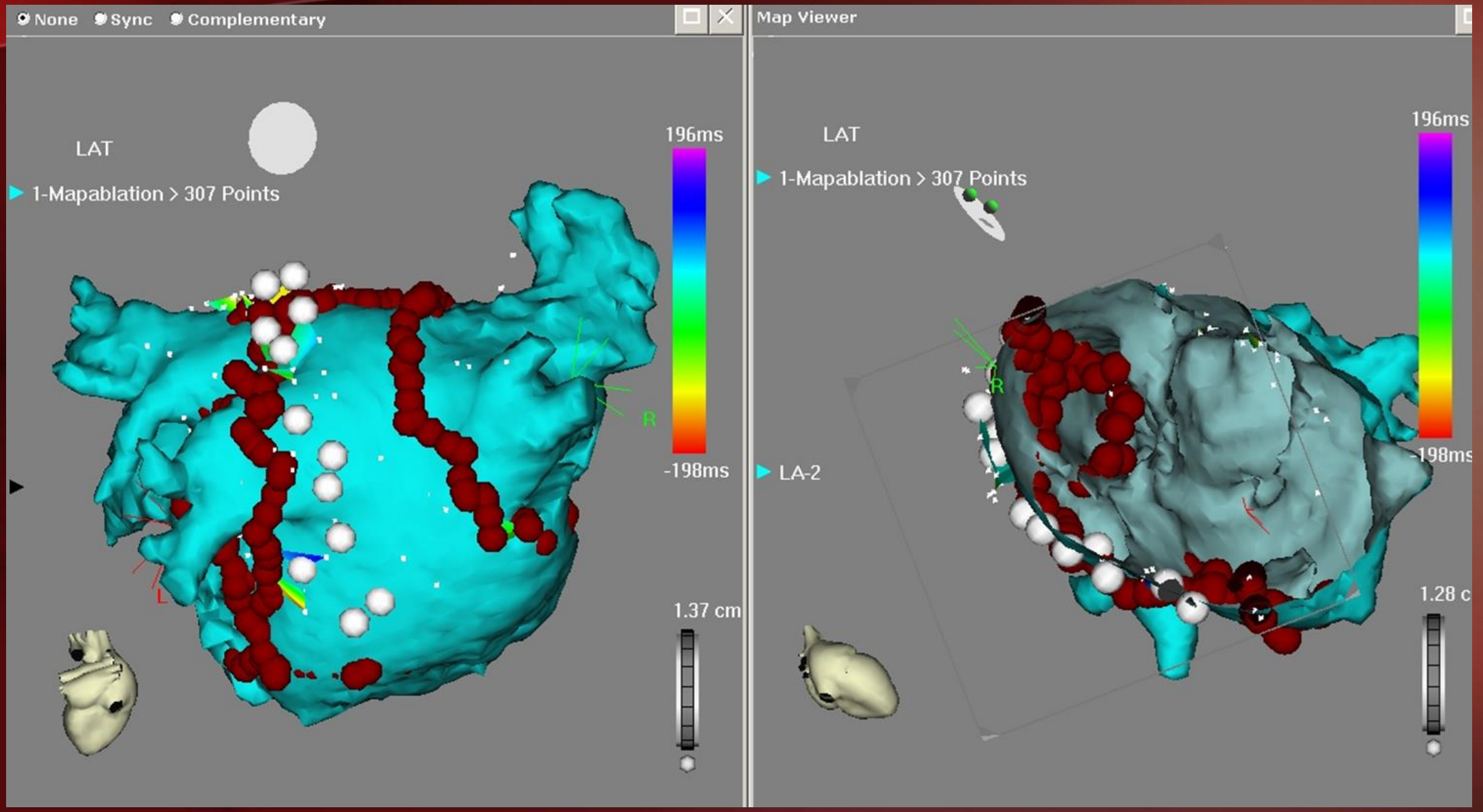
ALL-CAUSE DEATH BY DIGOXIN CONCENTRATION



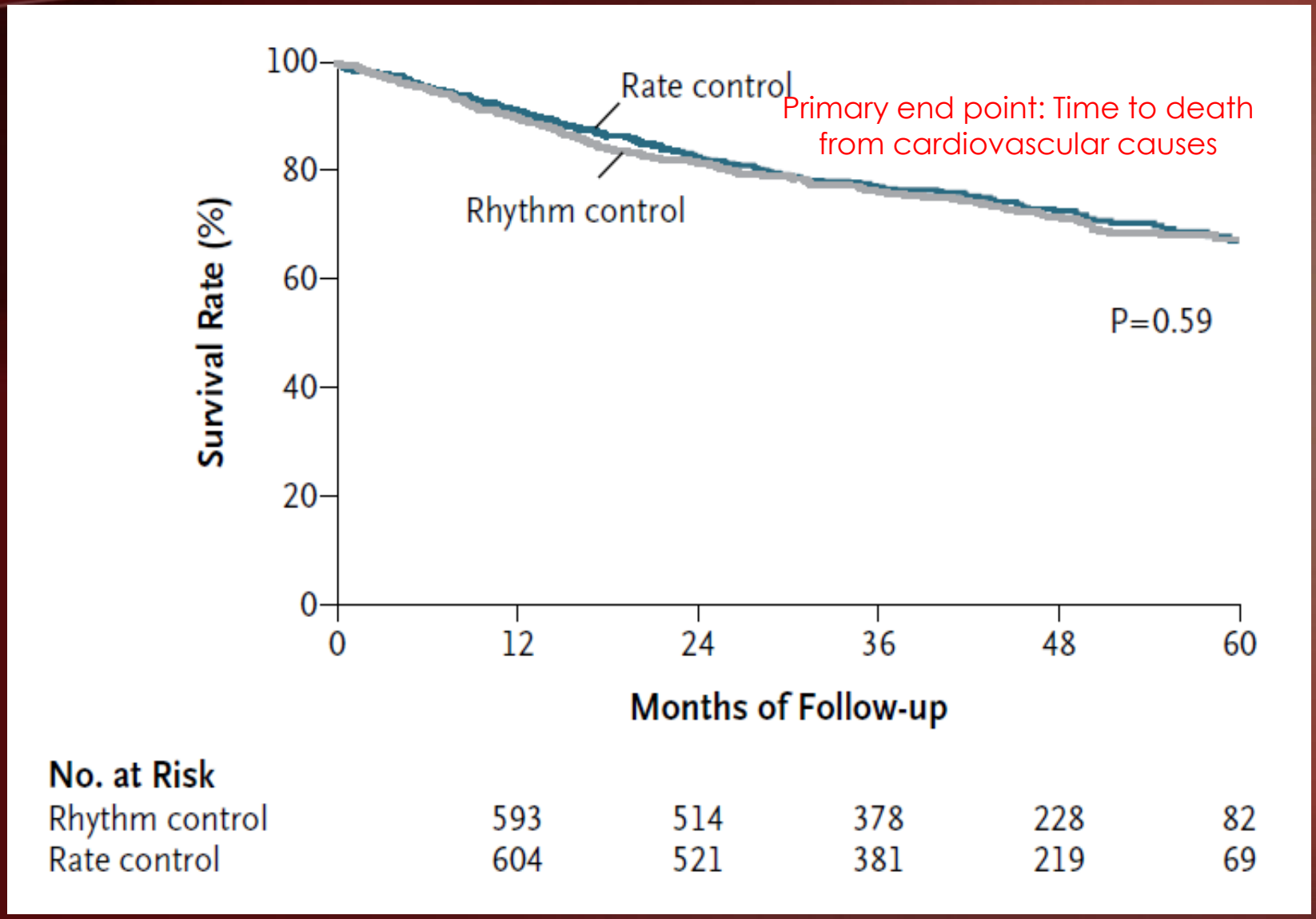
Digoxin level	Adjusted HR	95% CI	P Value
<0.9ng/ml	1.00	0.85 - 1.16	0.96
0.9-12.5ng/ml	1.16	0.87-1.55	0.32
>1.2ng/ml	1.56	1.20-2.04	0.0011

Lopes RS et al. J Am Coll Cardiol 2018;71:1063-74

CATHETER ABLATION

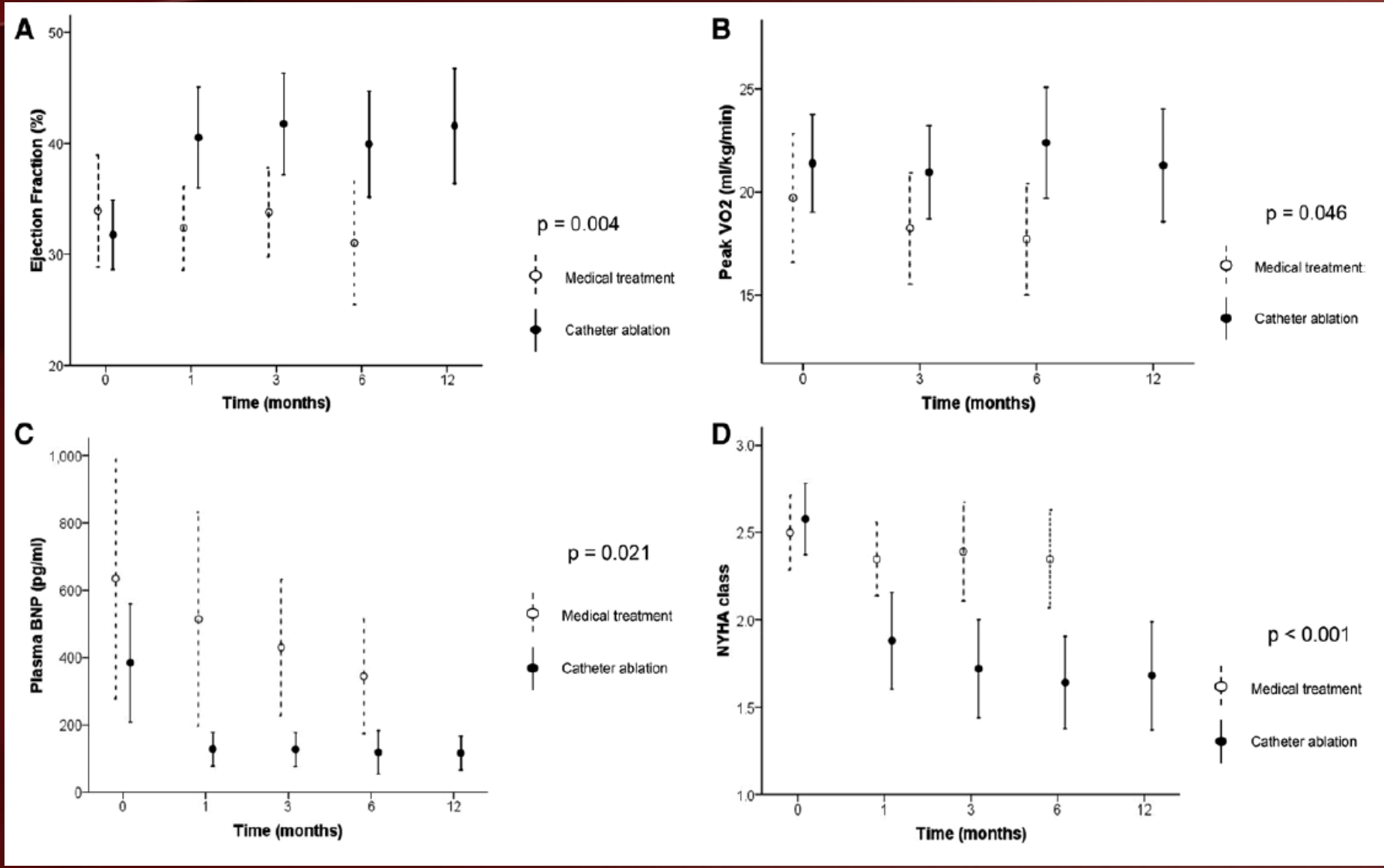


AF-CHF STUDY



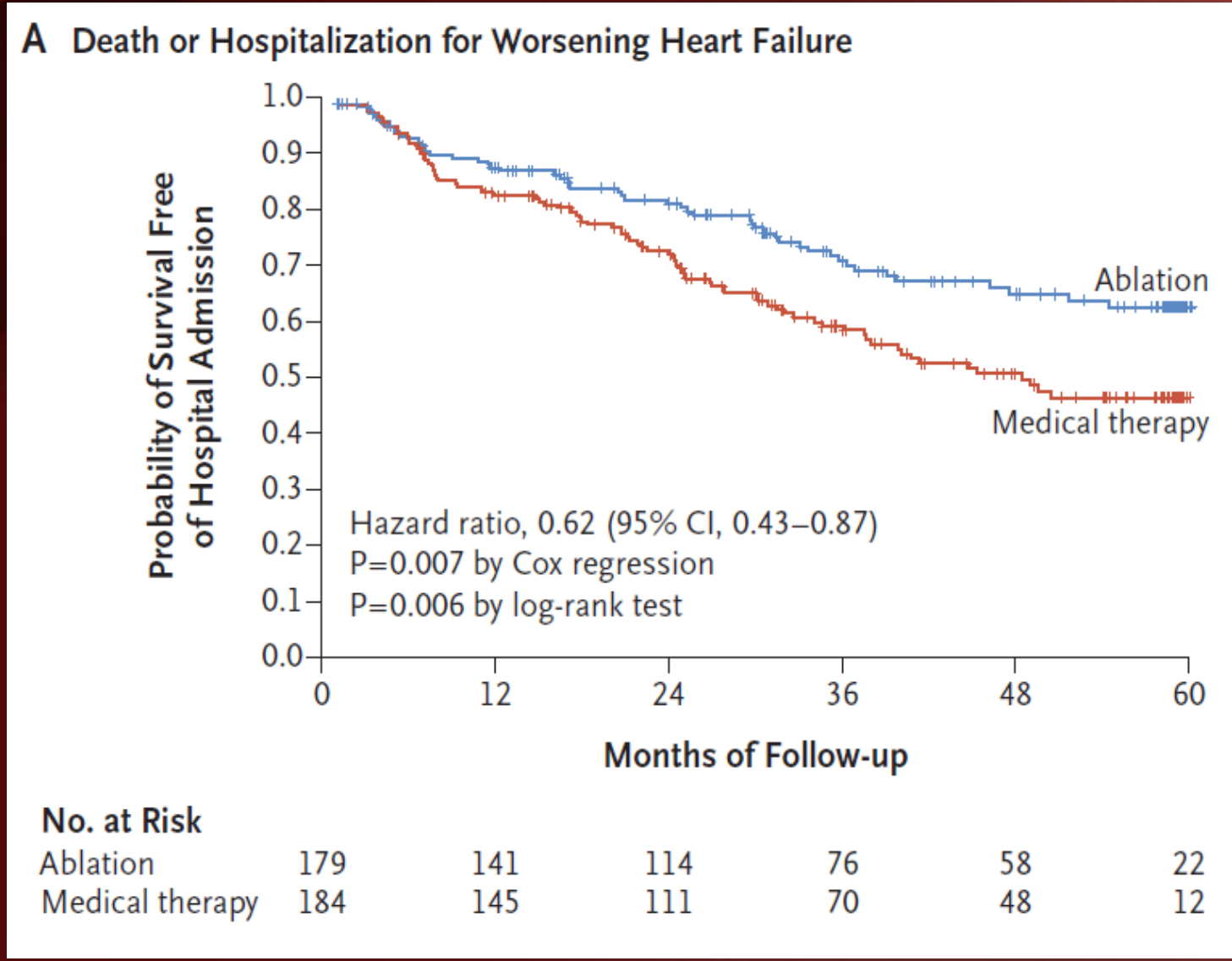
Roy D, et al. N Engl J Med 2008;358:2667-2677

CAMTAF TRIAL



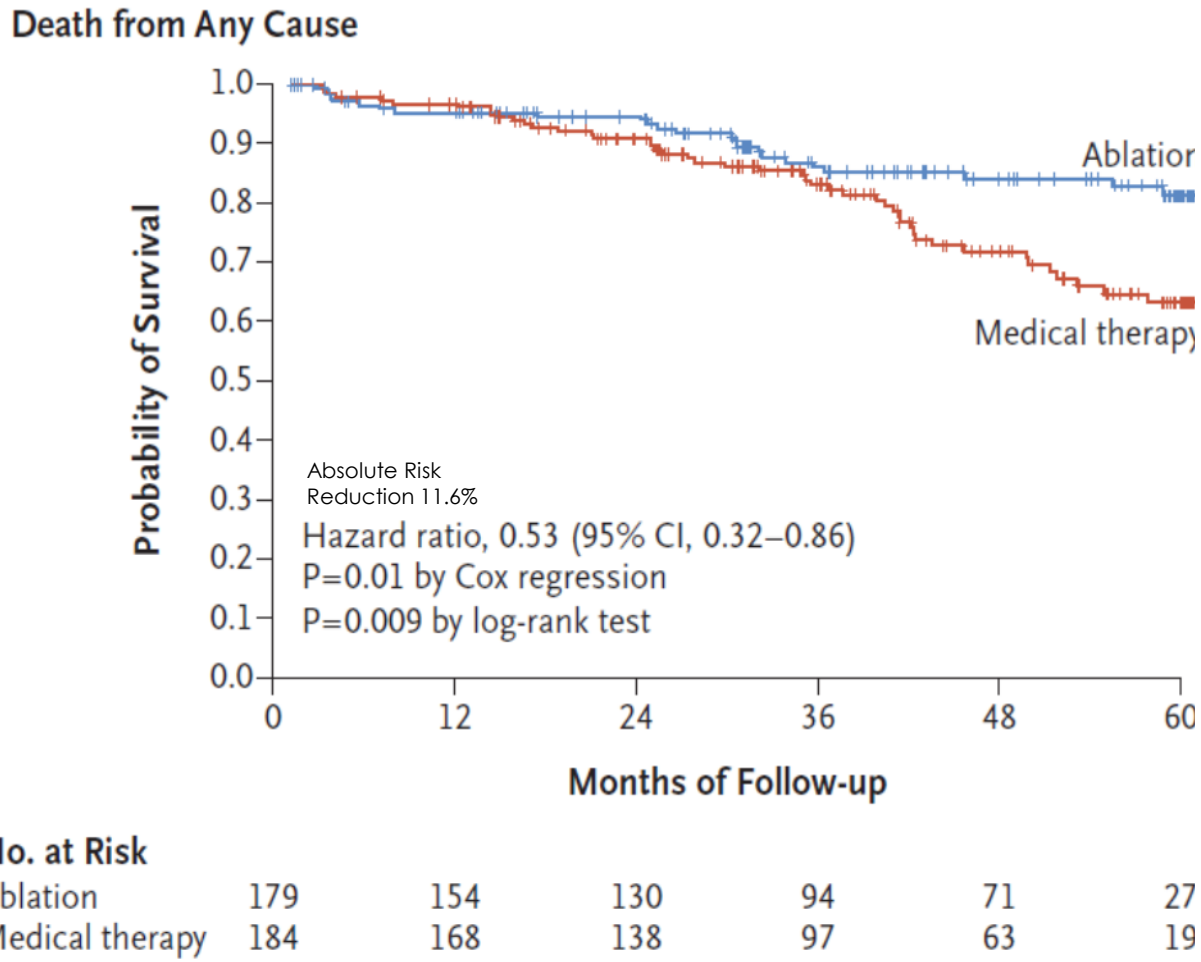
Hunter RJ et al. Cir Arrhythm Electrophysiol 2014;7:31-38

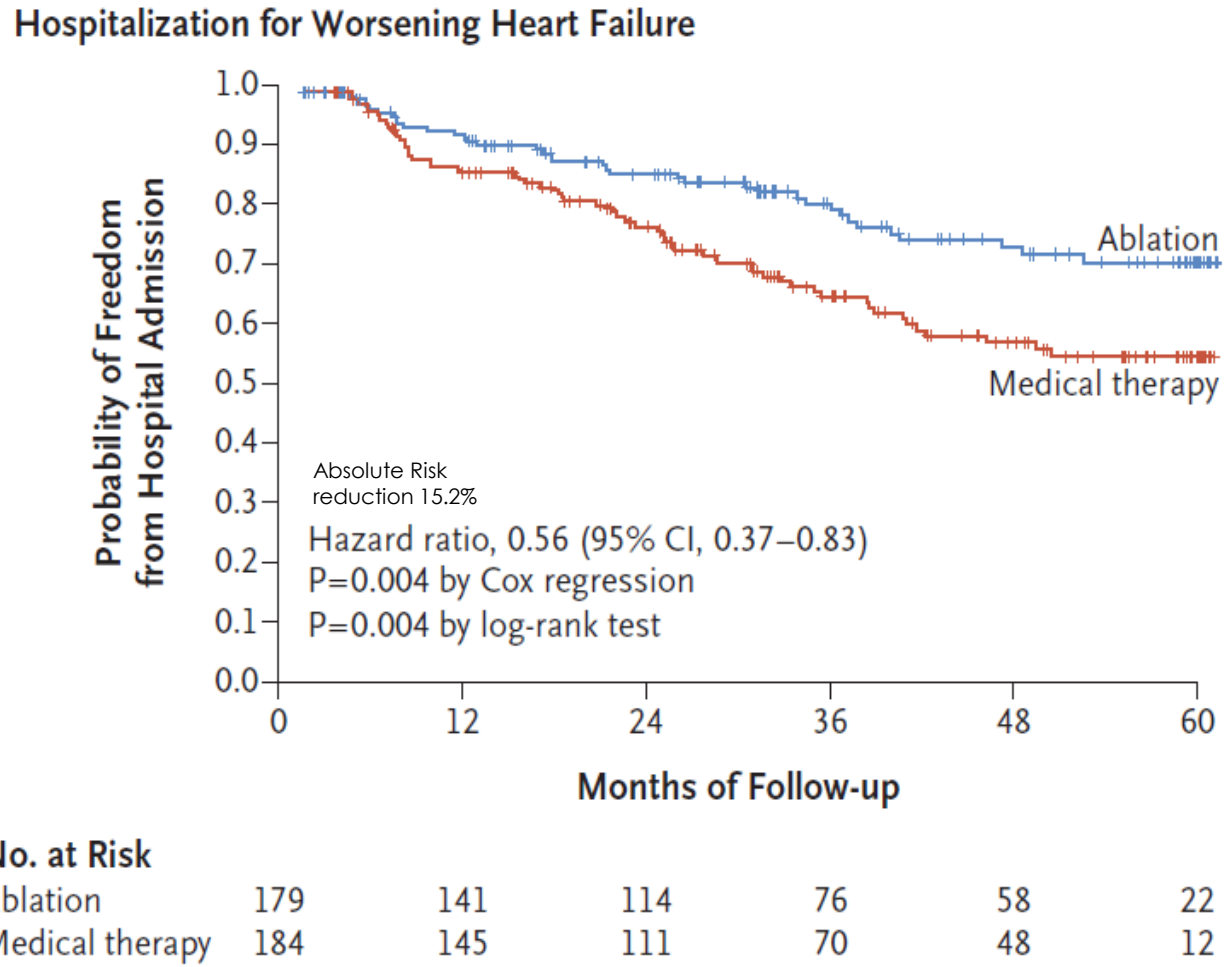
CASTLE-AF STUDY



Marrouche NF et al. N Engl J Med 2018;378:417-427

CASTLE-AF STUDY





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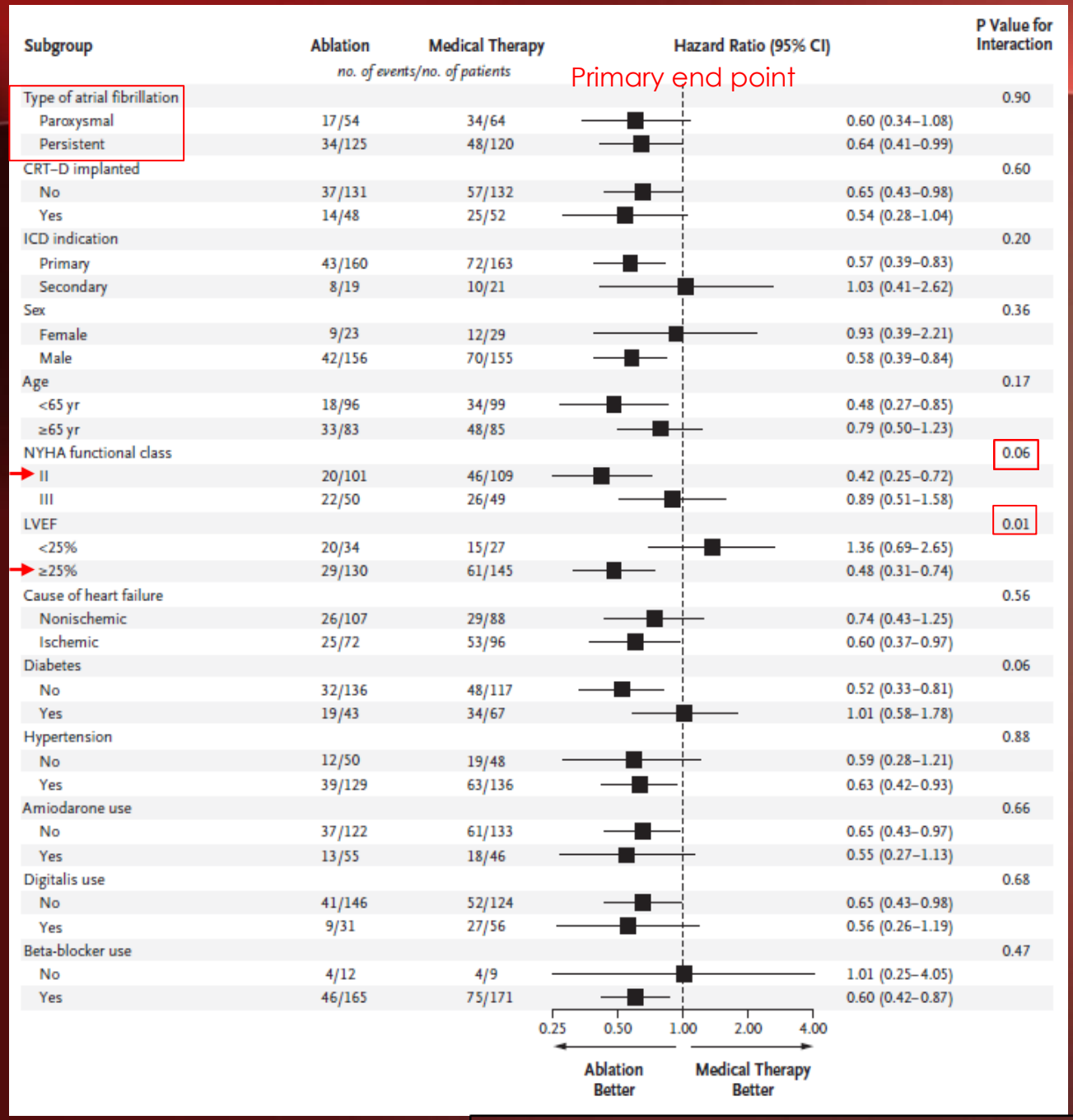
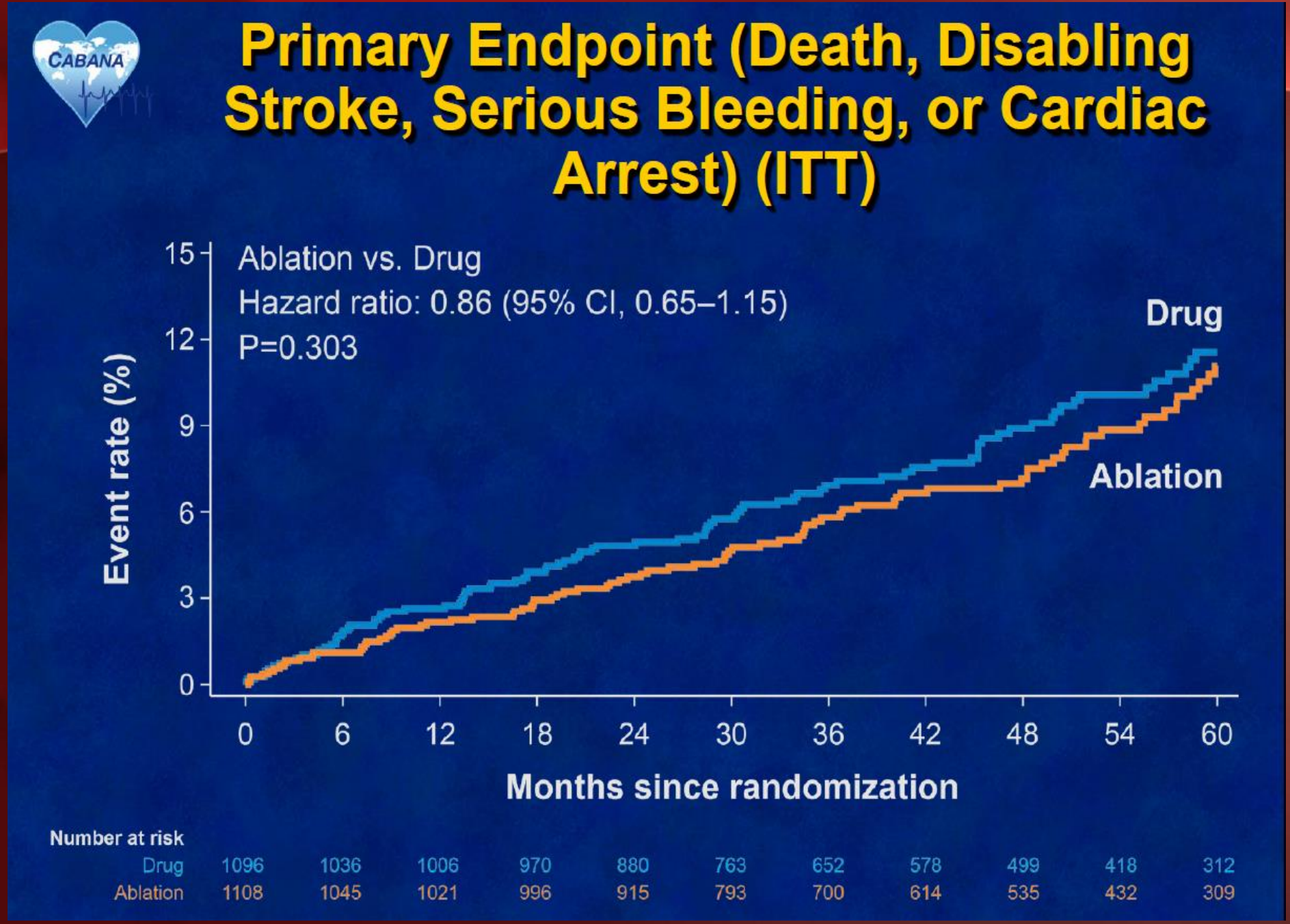


Marrouche NF et al. N Engl J Med 2018;378:417-427

Primary Endpoint (Death, Disabling Stroke, Serious Bleeding, or Cardiac Arrest) (ITT)



Packer DL et al.

Primary Endpoint Sub-group Analysis

All-Cause Mortality, Disabling Stroke, Serious Bleeding, Cardiac Arrest (ITT)

Group	Interaction P-Value	N	Hazard Ratio	95% CI
All Subjects		2204	0.86	0.65, 1.15
Age	0.074			
< 65 years old		766	0.52	0.27, 1.00
≥ 65 and < 75 years old		1130	0.84	0.57, 1.23
≥ 75 years old		308	1.46	0.80, 2.67
Sex	0.161			
Male		1385	0.74	0.52, 1.06
Female		819	1.14	0.70, 1.86
Minority status	0.065			
White		1979	0.96	0.71, 1.31
Minority*		225	0.43	0.20, 0.95
AF type	0.925			
Paroxysmal		946	0.82	0.51, 1.31
Persistent		1042	0.87	0.59, 1.28
Long-standing persistent		215	1.01	0.39, 2.61
Years since onset of AF	0.718			
≤ 1 year		1063	0.83	0.57, 1.21
> 1 year		1122	0.92	0.59, 1.42
Hypertension	0.734			
Absent		427	0.97	0.47, 2.01
Present		1776	0.85	0.62, 1.15
Hypertension with LVH	0.843			
Absent		1176	0.89	0.61, 1.31
Present		587	0.83	0.47, 1.46
Sleep apnea	0.339			
Absent		1695	0.94	0.67, 1.32
Present		508	0.69	0.41, 1.17
BMI	0.378			
< 30		1064	0.74	0.49, 1.11
≥ 30		1106	0.96	0.64, 1.44
CHADS-VASc score	0.716			
≤ 2		959	0.93	0.54, 1.58
> 2		1245	0.83	0.59, 1.16
History of congestive heart failure	0.196			
No		1865	0.95	0.68, 1.32
Yes		337	0.61	0.35, 1.08
Baseline NYHA class	0.147			
No heart failure or Class I		1408	1.04	0.71, 1.52
≥ Class II		778	0.68	0.44, 1.05

* Minority=Hispanic or Latino or non-white race

Packer DL et al.

CONCLUSION

- Atrial fibrillation and Heart Failure share common predisposing risk factors.
- AF begets HF and HF begets AF
- All Heart Failure patients should consider use of oral anti-coagulant for stroke prevention
- Controversy role of Beta-block in heart failure patients with atrial fibrillation
- Digoxin should be avoided in heart failure patients with atrial fibrillation

CONCLUSION

- Target heart rate control in heart failure are different for patients with or without AF
- Evidences suggest catheter ablation can improve left ventricular function, functional state, and mortality in selected AF patient with heart failure