CRT in Atrial Fibrillation Patients: What Evidence Exists?

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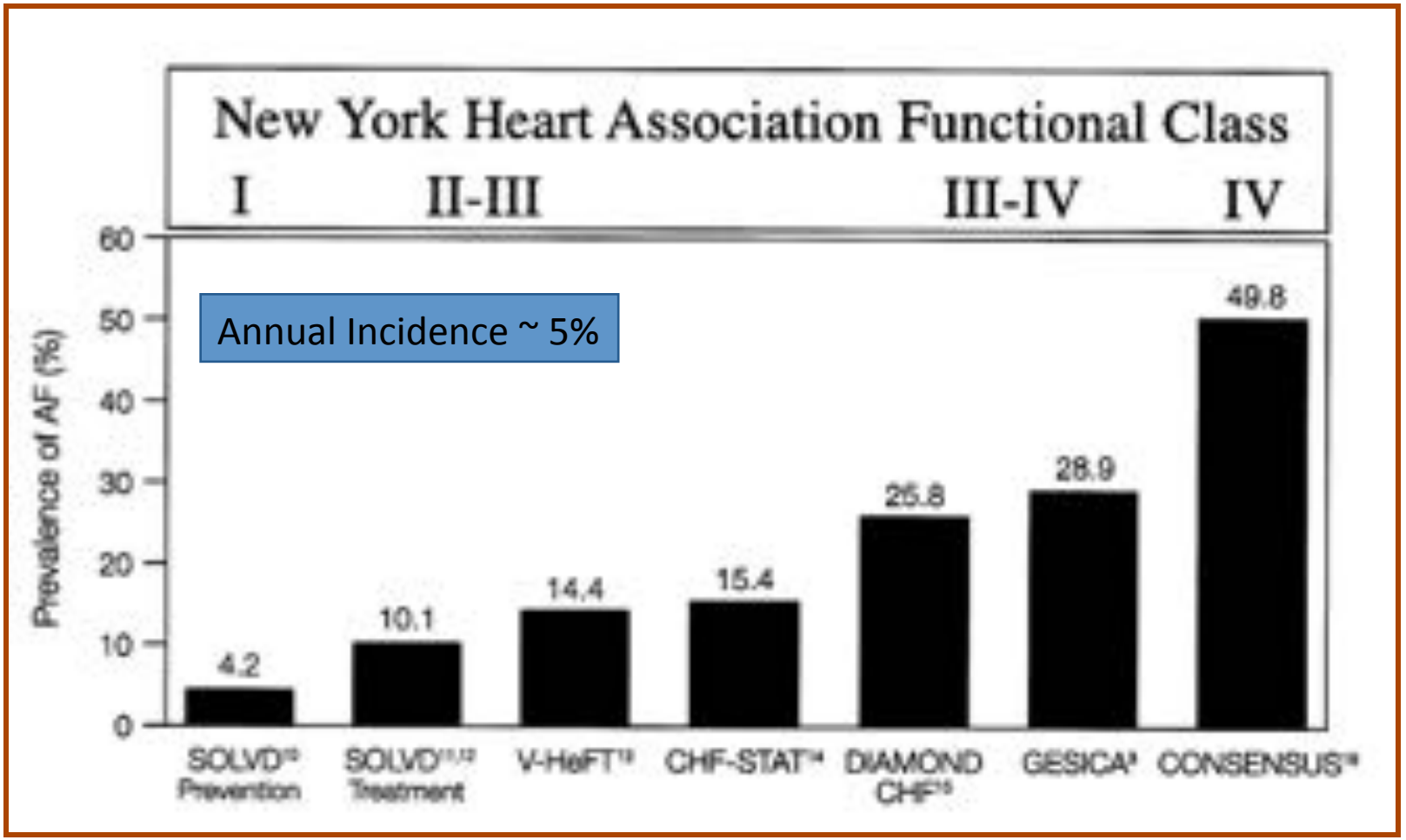
MY CONFLICTS OF INTEREST ARE:

Biosense Webster, Medtronic, Boston Scientific (consultant); Biosense Webster, Medtronic (research support)

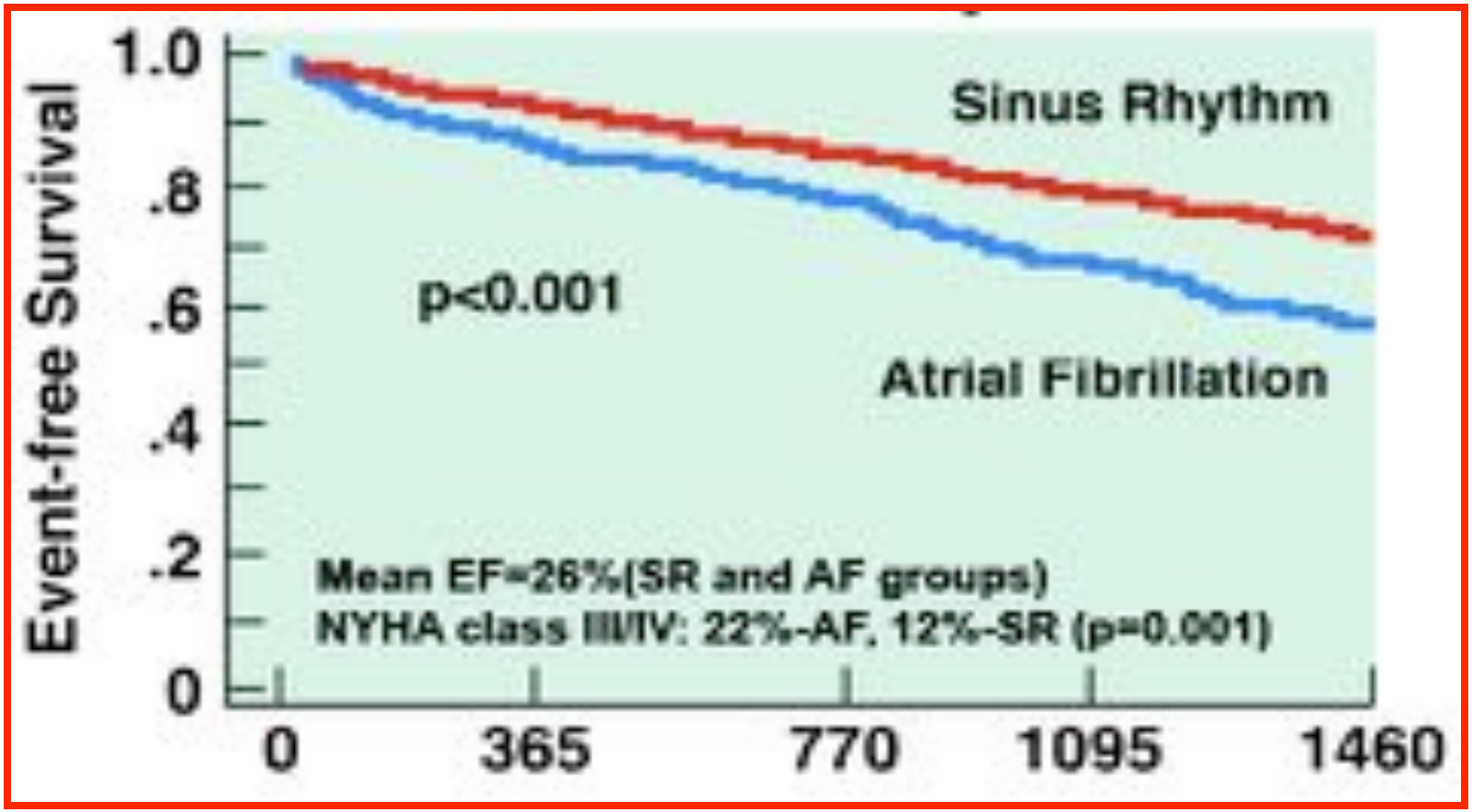
"Since auricular fibrillation so often complicates very serious heart disease, its occurrence may precipitate heart failure or even death, unless successful therapy is quickly instituted."

Paul Dudley White, 1937

Prevalence of AF in Heart Failure



Prognosis is Negatively Influenced by Presence of AF



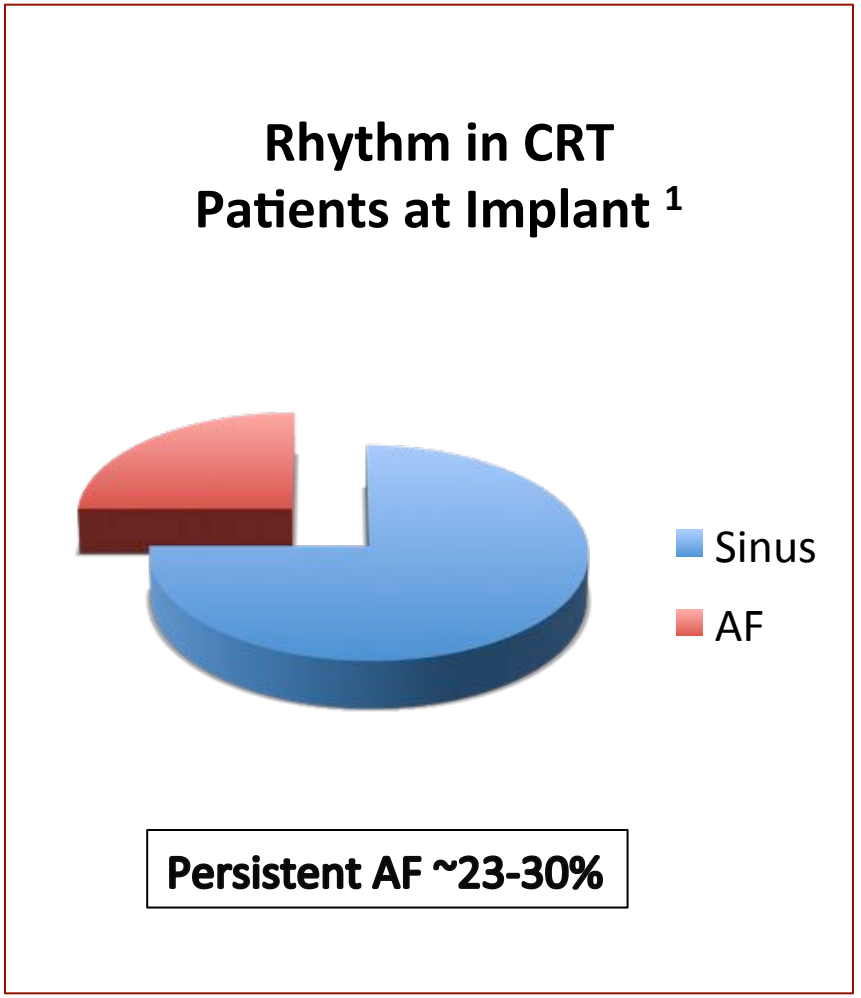
Dries et al/SOLVD; JACC 1998

The Challenge of AF in the CRT Patient With Heart Failure

- CRT depends upon synchronizing ventricular activation via biventricular pacing with atrial activity (ie AV synchrony)
- In the absence of organized atrial activity (eg AF), there can be no coordinated AV synchrony and conducted atrial impulses inevitably compete with pacing impulses to capture the ventricles. To overcome this, one must:
  - Restore sinus rhythm, or
  - Sufficiently control conducted ventricular rate

Atrial Fibrillation in CRT-D Recipients

- New CRT device volume in US approximated 100,000 in 2011
- Annual costs of $1.8 billion
- 2012 NCDR ICD US Registry data: 31% of 326,000 patients had AF[2]
- 2011 NCDR ICD US Registry data: 36% of 87,692 CRT-D patients had AF[2]



[1]Auricchio et al, AJC 2007; Dickstein et al, Eur Heart J 2009; Medtronic, Inc. (internal data)
[2]NCDR ICD Registry 2011-2 Data

Official Guideline Recommendations

Recommendations **ESC 2012**	Class[a]	Level[b]	Ref[c]
Patients in permanent AF			
CRT-P/CRT-D may be considered in patients in NYHA functional class III or ambulatory class IV with a QRS duration ≥120 ms and an EF ≤35%, who are expected to survive with good functional status for >1 year, to reduce the risk of HF worsening if:			
• The patient requires pacing because of an intrinsically slow ventricular rate	IIb	C	–
• The patient is pacemaker dependent as a result of AV nodal ablation	IIa	B	163a
• The patient's ventricular rate is ≤60 b.p.m. at rest and ≤90 b.p.m. on exercise.	IIb	C	–

IIA Recommendation - AHA/ACC/HRS Updated 2012

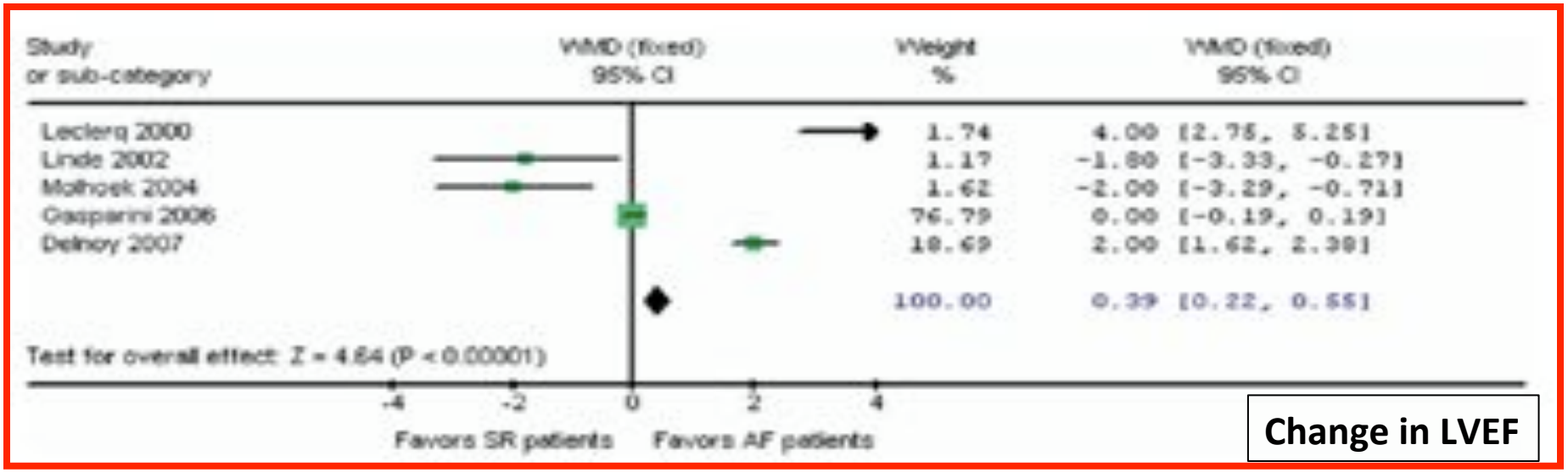
3. CRT can be useful in patients with atrial fibrillation and LVEF less than or equal to 35% on GDMT if a) the patient requires ventricular pacing or otherwise meets CRT criteria and b) AV nodal ablation or pharmacologic rate control will allow near 100% ventricular pacing with CRT.[23–26,26a,48] *(Level of Evidence: B)*

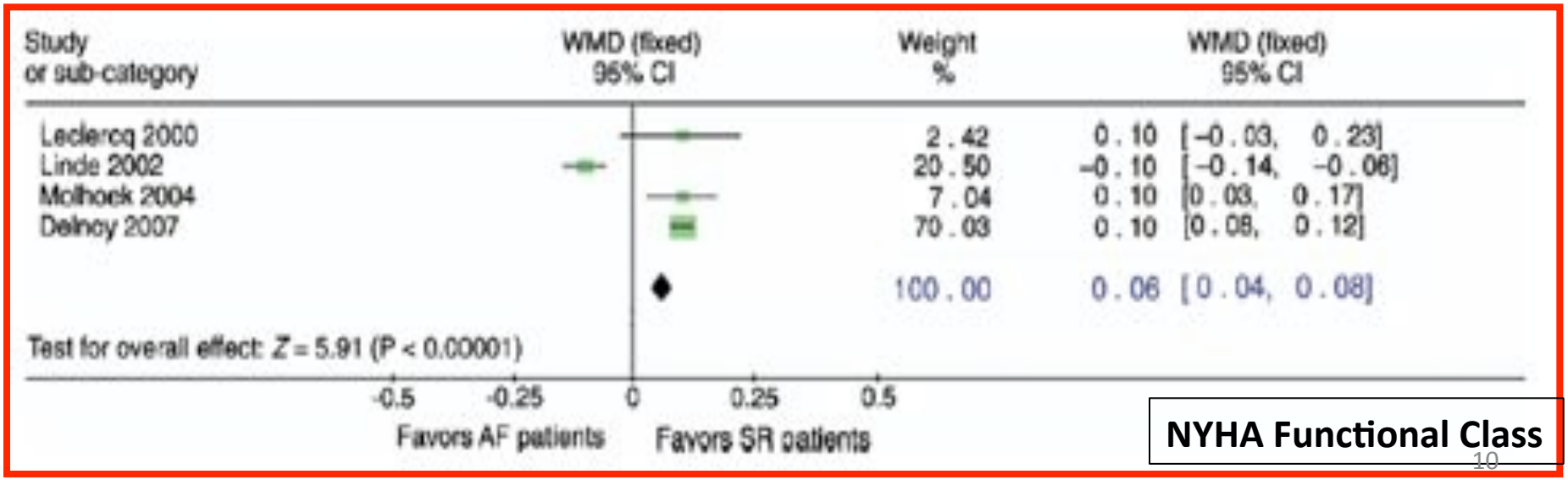
McMurray et al, Eur Heart J 2012; Tracey et al, Circulation 2012

Chronic Absence of RCT Data Limits Formal Recommendations and Clinical Practice

- All seminal RCTs of CRT excluded patients with AF (except very small nonsignificant MUSTIC-AF substudy)
- Published data largely limited to observational studies
- Recent subset of RAFT study in less advanced HF allowed inclusion of “permanent AF” patients

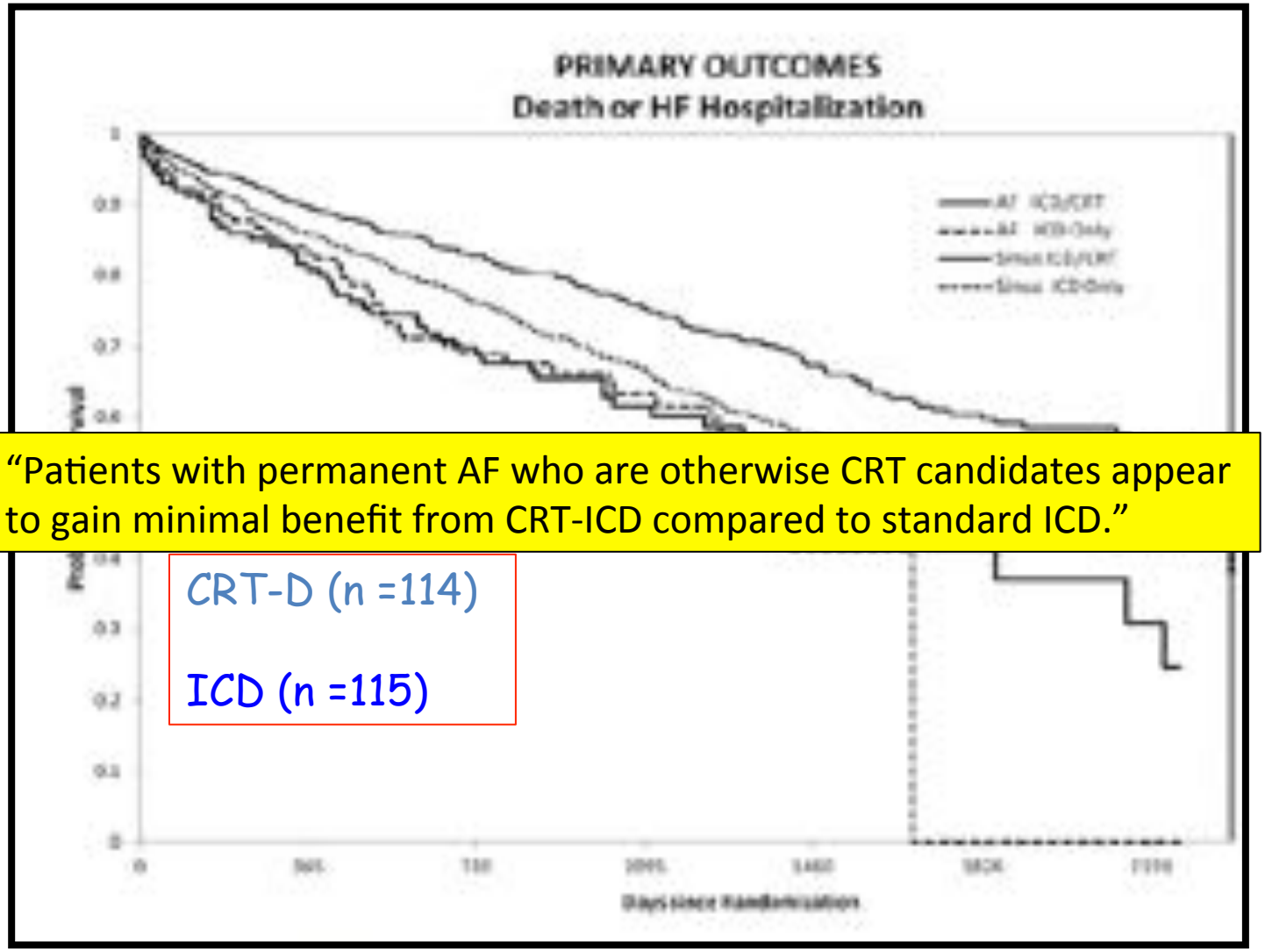
Meta-Analysis of Nonrandomized Cohorts: CRT in AF vs. SR





Upadhyay et al, JACC 2008

RAFT Findings in AF Substudy
(≤60 bpm at rest, ≤90 bpm during 6MHW test)



"Patients with permanent AF who are otherwise CRT candidates appear to gain minimal benefit from CRT-ICD compared to standard ICD."

Healey et al, Circulation HF 2012

RAFT Findings in AF Substudy
(≤60 bpm at rest, ≤90 bpm during 6MHW test)

Table 2. Clinical Outcomes (With HR and 95% CI for CRT-ICD Versus ICD)

	ICD, %	CRT-ICD, %		
Only 1 patient had an AV junc-				
De tion ablation before or within 6 months after randomization.				
Hospitalization				
Death	30.4	36.8	1.04 (0.66–1.62)	0.88
Heart failure	27.8	19.3	0.58 (0.38–1.01)	0.052

During the first 6 months after randomization, there were 34.3% of CRT-treated patients with ≥95% biventricular pacing and 47.1% with biventricular pacing ≥90% of the time.

hospitalization

HR indicates hazard ratio; CRT, cardiac resynchronization; ICD, implantable cardioverter defibrillator.

Healey et al, Circulation HF 2012

The Challenge of AF in the CRT Patient With Heart Failure

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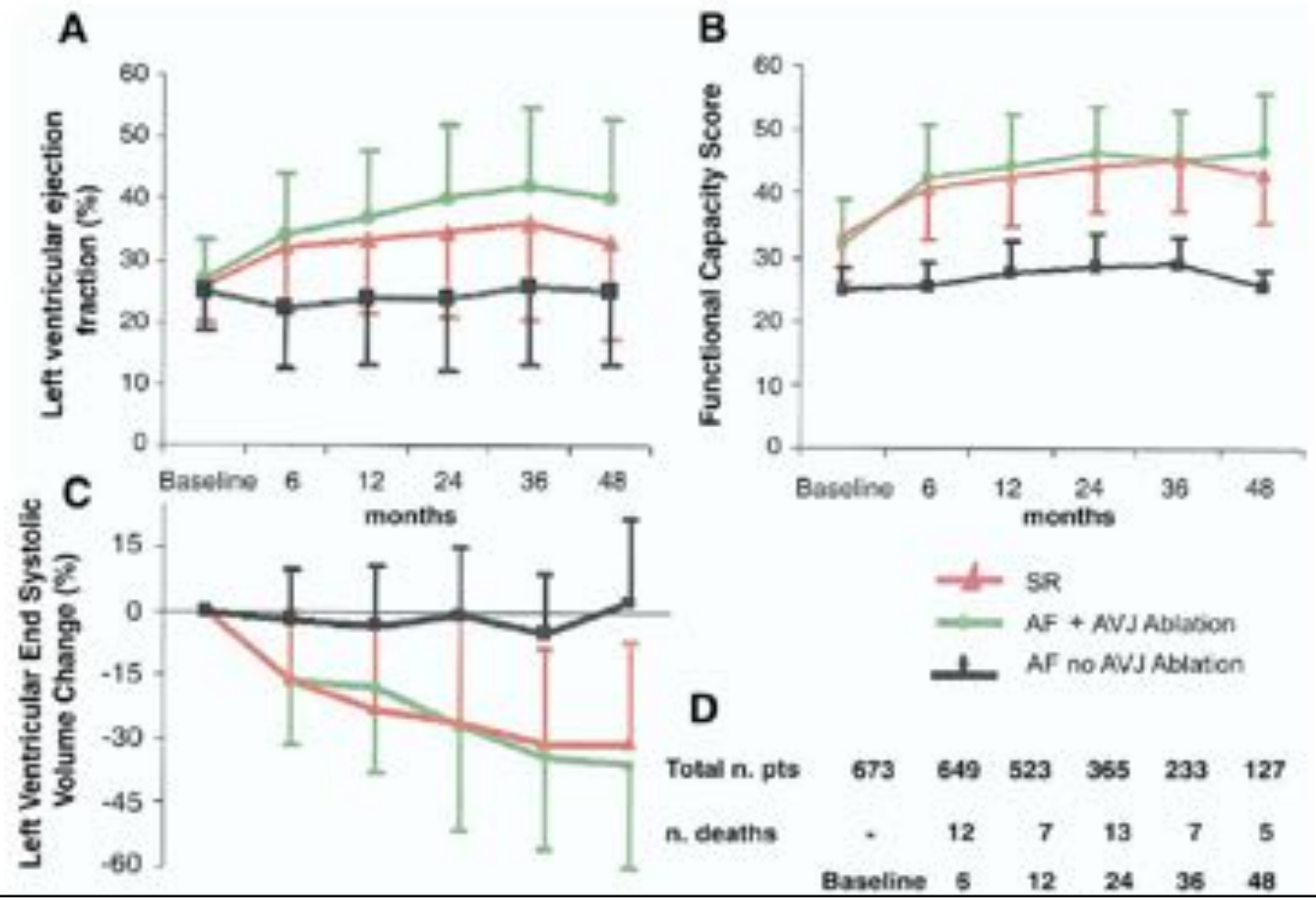
Suggestion That AVJ Ablation Is the Critical Ingredient

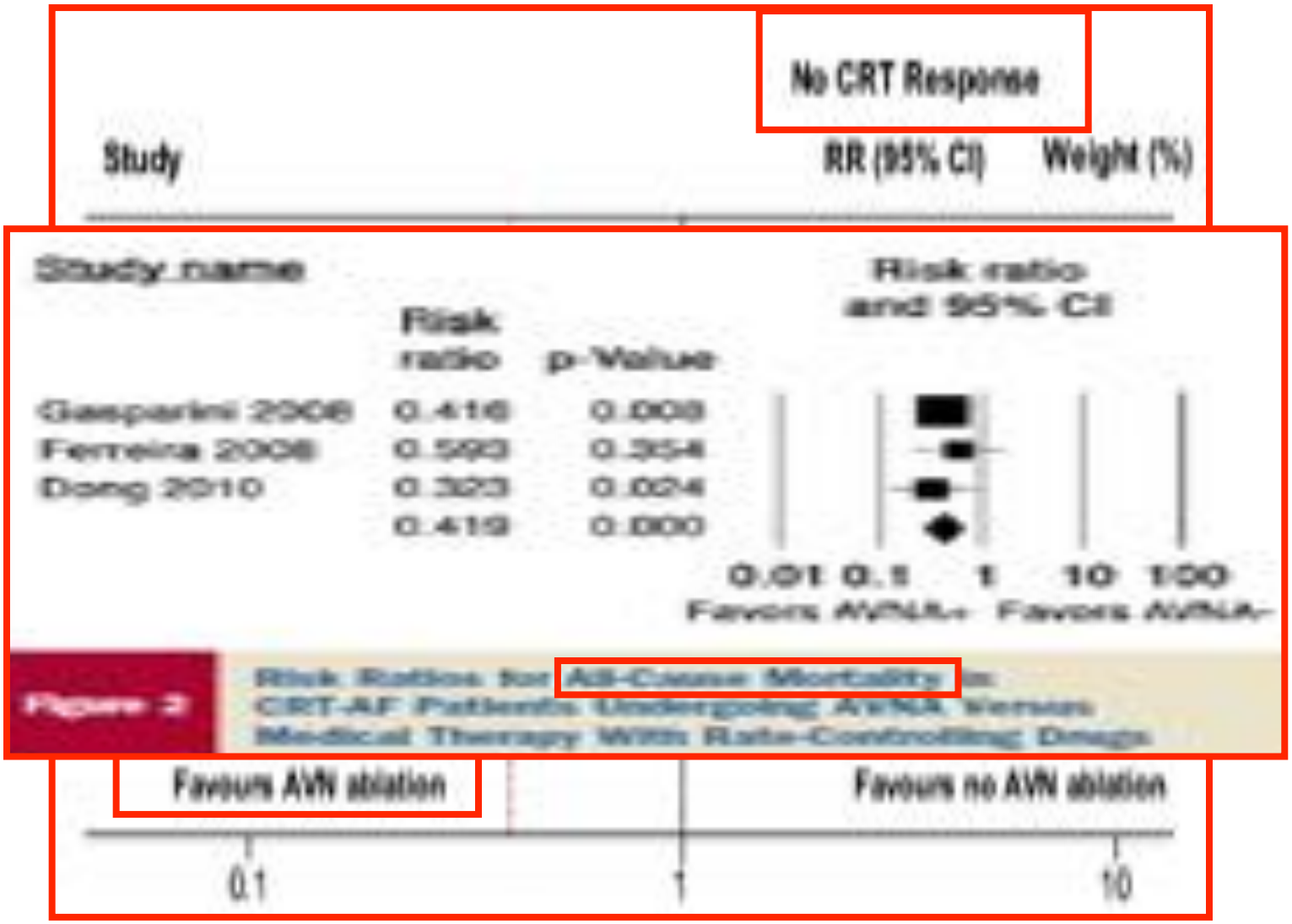
JACC Vol. 48, No. 4, 2006
August 15, 2006:734–43



Current Published Studies of AVJ or No AVJ in AF Patients for CRT

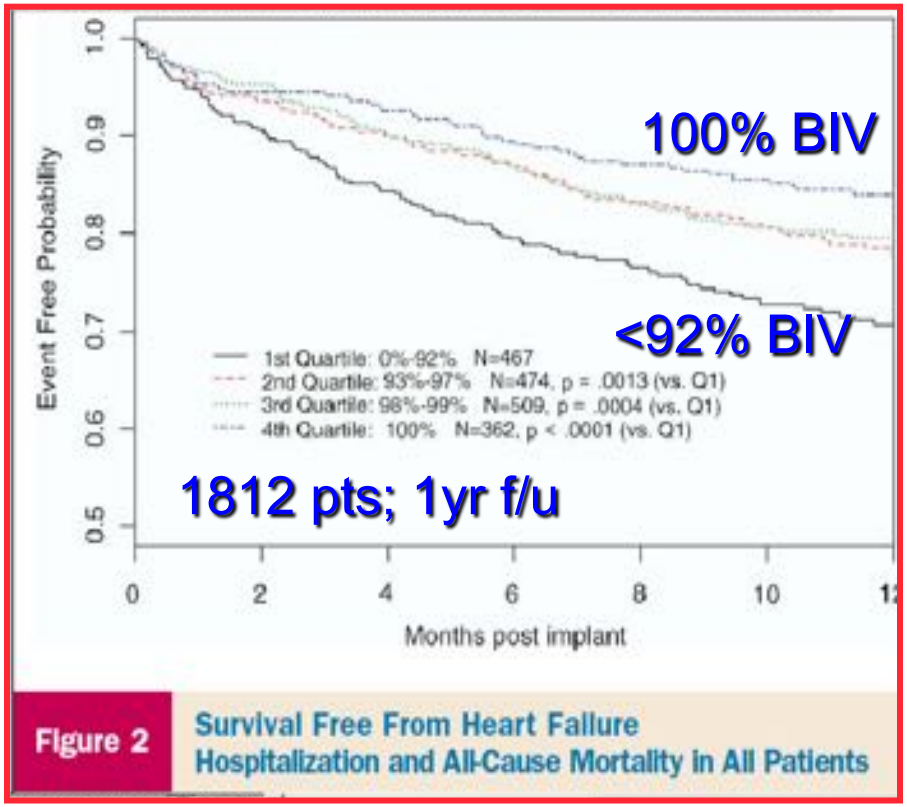
Author	AF+AVJ vs AF-AVJ				
	Sample Size	*HFH*	*2 y Survival*	*CRT response*	*Comments*
Gasparini (JACC 2006)	114/48	--	--	79%/30%	
Gasparini (Eur Heart 2007)	118/125	--	96%/65%	--	
Dong (Heart Rhythm 2010)	45/109	16%/20%	96%/75%	--	AVJ independently predicted survival
Ferreira (Europace 2008)	26/27	15%/41%	95%/62%	85%/52%	AVJ independently predicted response
Molhoek (AJC 2004)	17/13	--	--	71%/54%	AVJ associated with better EF, 6MHW

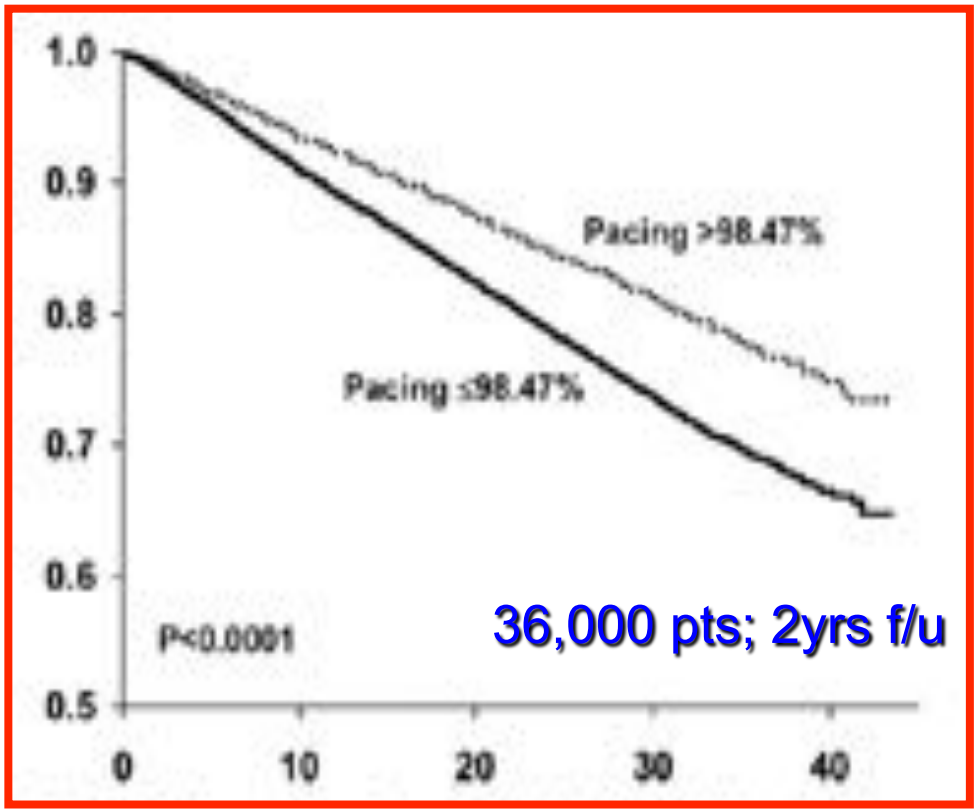
Meta-Analyses of AVJ Ablation in AF Patients for CRT



Wilton et al, Heart Rhythm 2011; Ganesan et al; JACC 2012

The Need for Prevalent Pacing

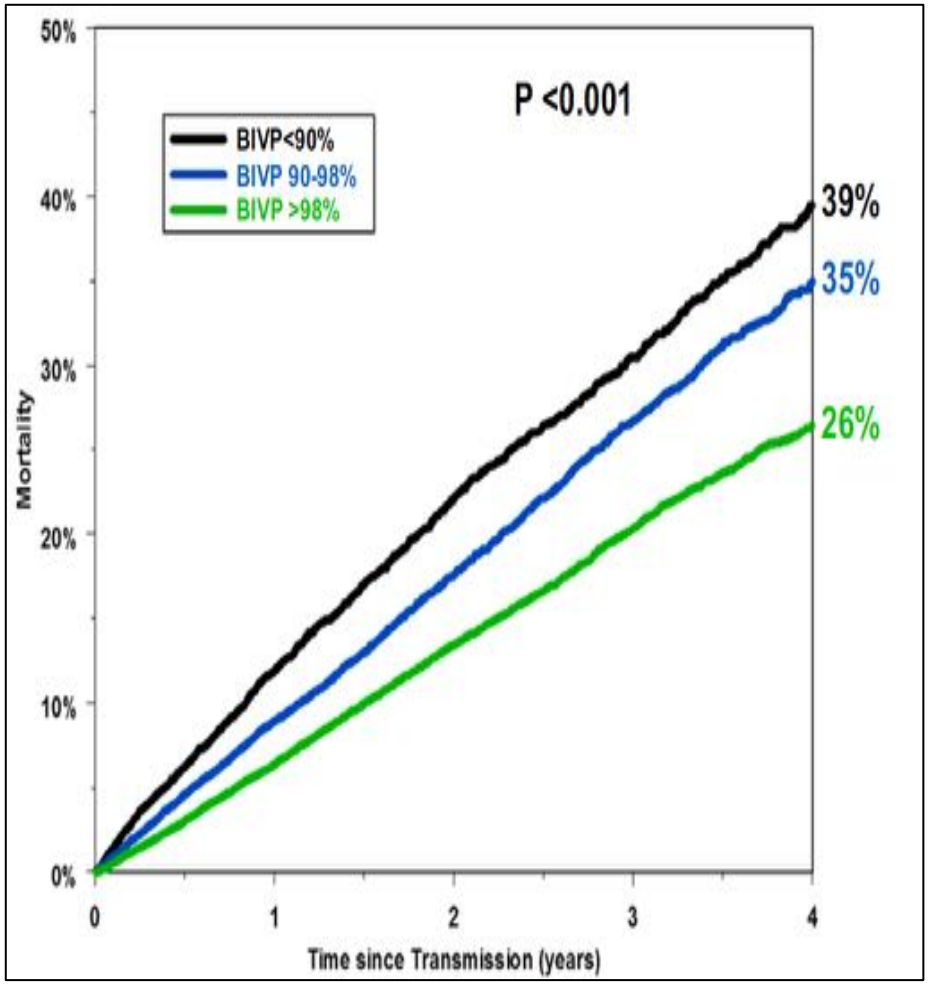


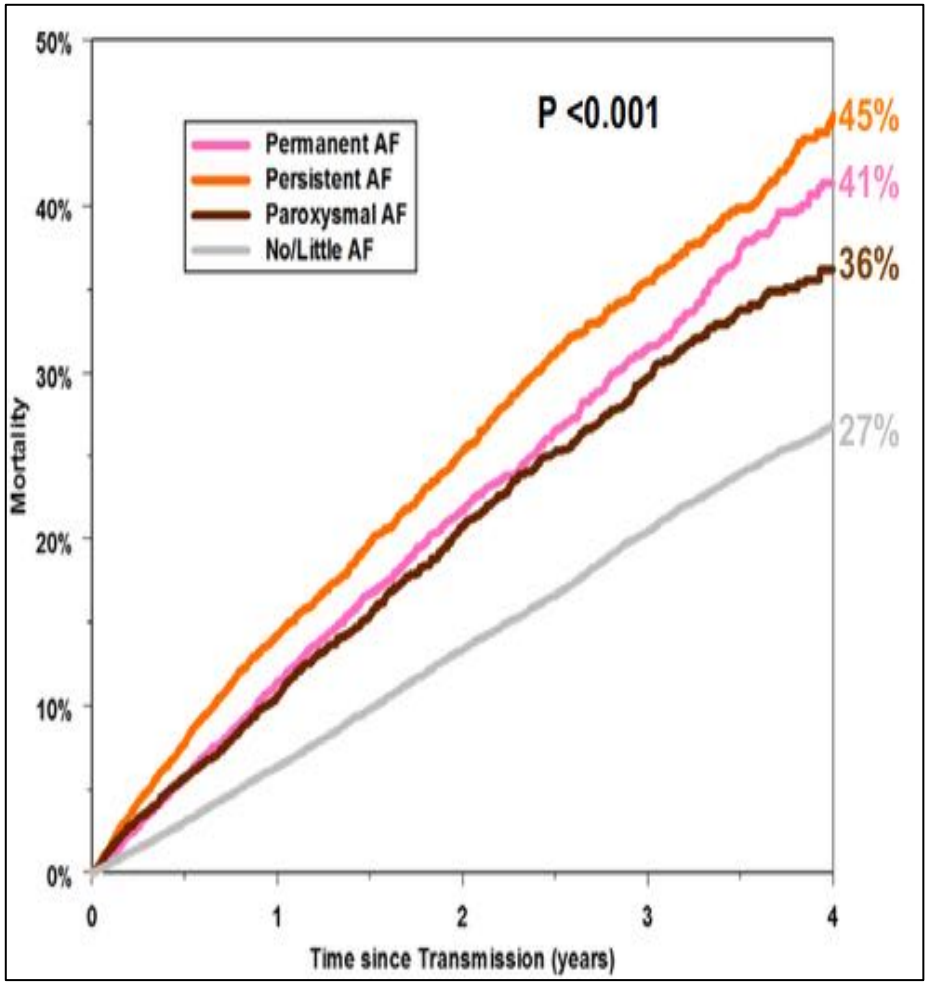


- **Patients with a history of atrial arrhythmia were more likely to be paced < 92% (p < 0.001).**

Kaplan et al, JACC 2009; Hayes et al, Heart Rhythm 2011

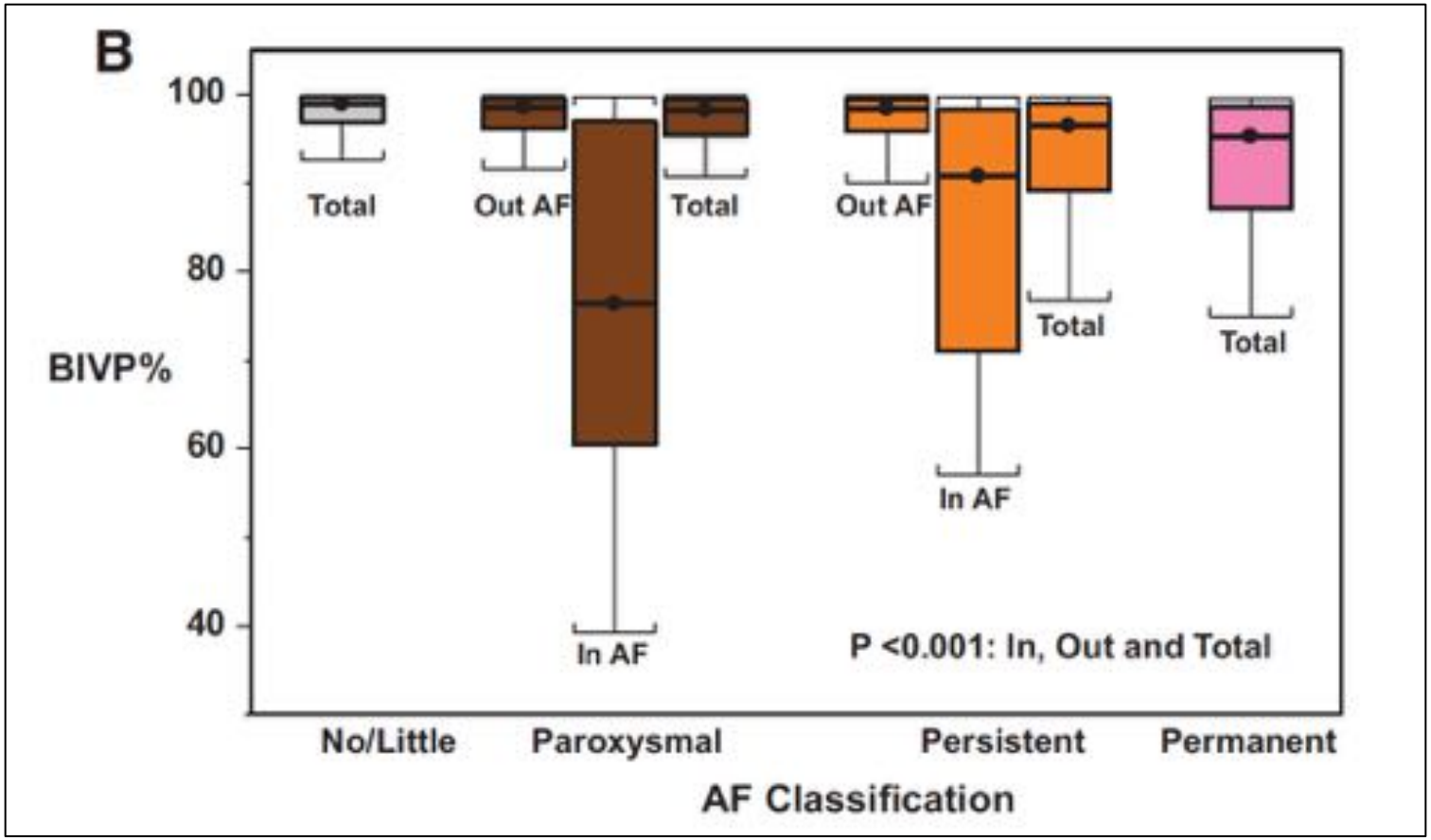
The Benefits of Prevalent Pacing in AF





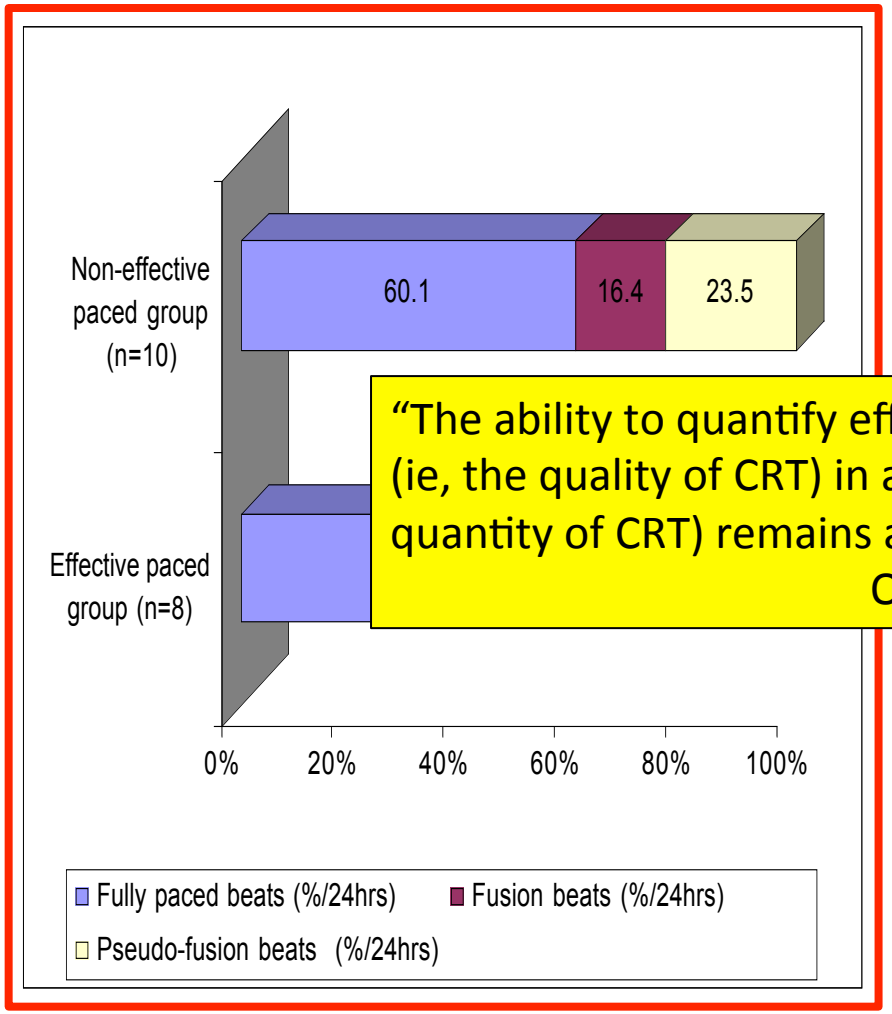
Ousdigian et al, Circ AE 2014

Large Percentage of Real World Patients With AF Who Receive CRT Have Poor Rate Control



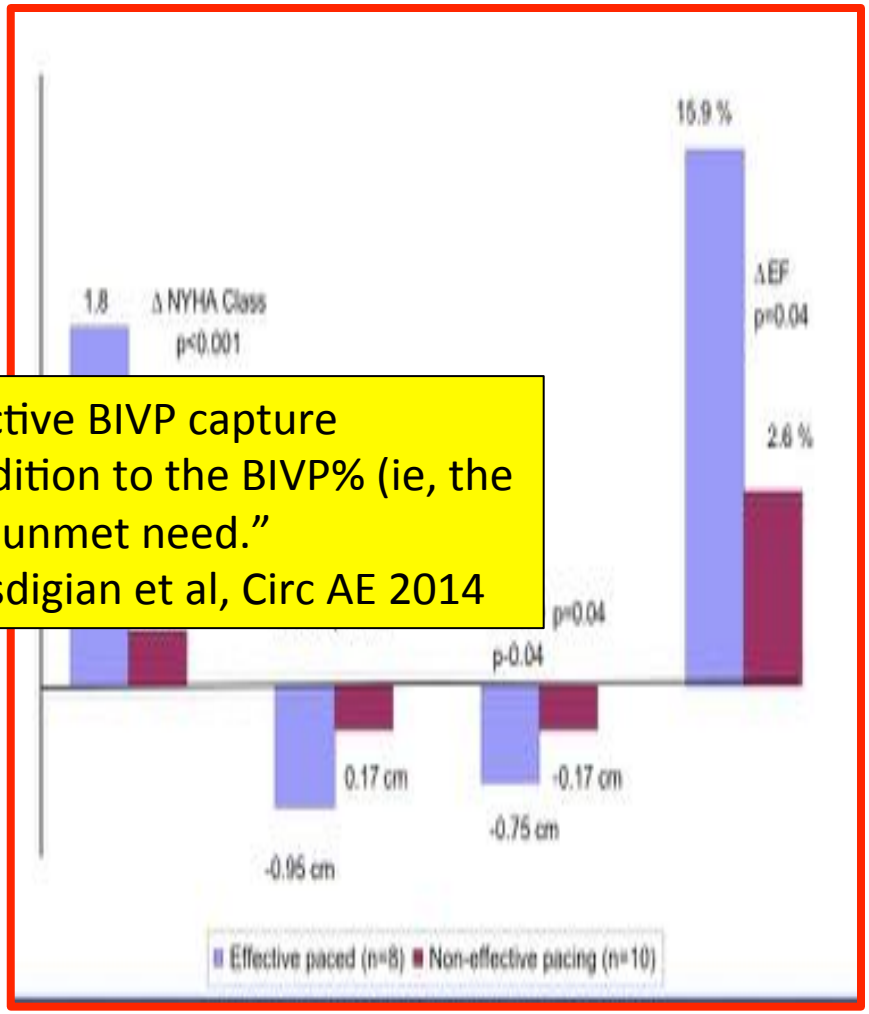
Ousdigian et al, Circ AE 2014

Prevalent Pacing Helps But Is It Enough in Setting of AF and CRT?



"The ability to quantify effective BIVP capture (ie, the quality of CRT) in addition to the BIVP% (ie, the quantity of CRT) remains an unmet need."

Ousdigian et al, Circ AE 2014



Kamath, Steinberg, et al; JACC 2008

Is AF Indication Threatened?
Is Data Excessively Ambiguous?

EDITORIAL COMMENT

Desperately Seeking a Randomized Clinical Trial of Resynchronization Therapy for Patients With Heart Failure and Atrial Fibrillation*

Jonathan S. Steinberg, MD, FACC

New York, New York

JACC 2006

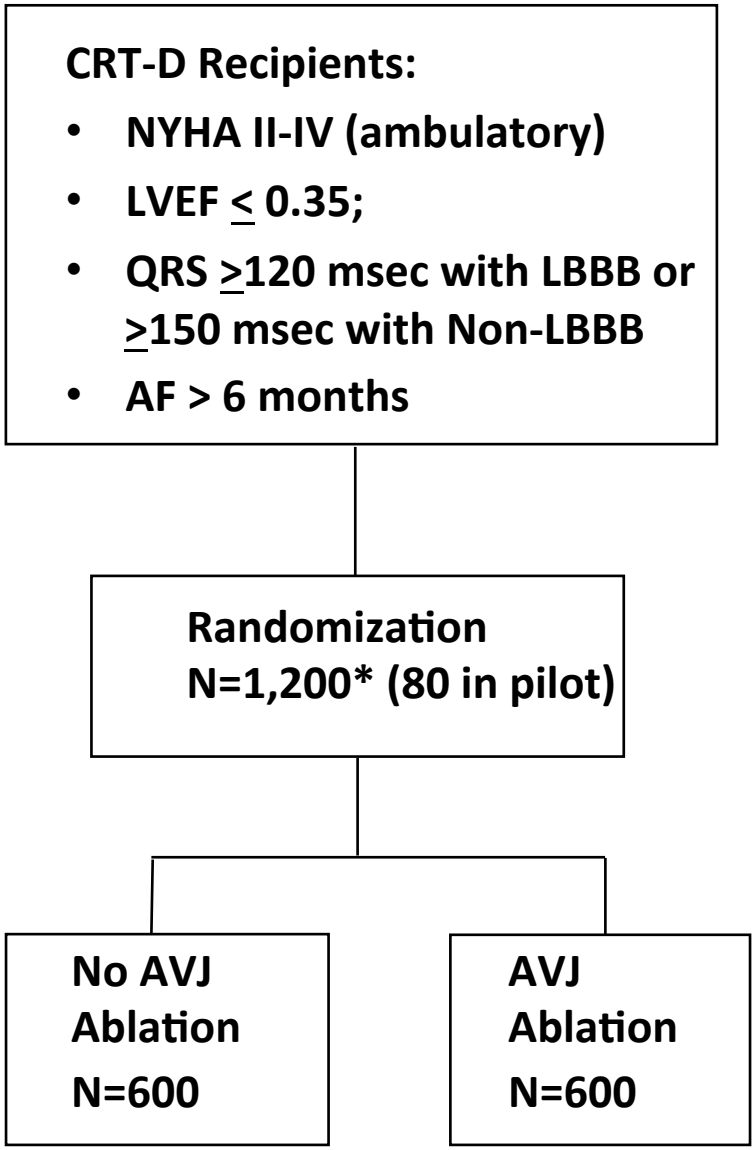
Rationale:

- The absence of strong data and/or RCT is not the same as a negative trial.
- The RAFT study was not designed for AF patients.
- There has been a consistent lack of opportunity to conduct the proper trial.

Randomized Clinical Trial of Junctional AV Ablation for Permanent Atrial Fibrillation in Patients Undergoing Cardiac Resynchronization Therapy (JAVA-CRT): Study Hypothesis

- AVJ ablation in patients with permanent AF who undergo CRT results in improved outcome
  - Greater reduction in LVESV over time (pilot phase)
  - Reduced risk of heart failure event or death

Study Design

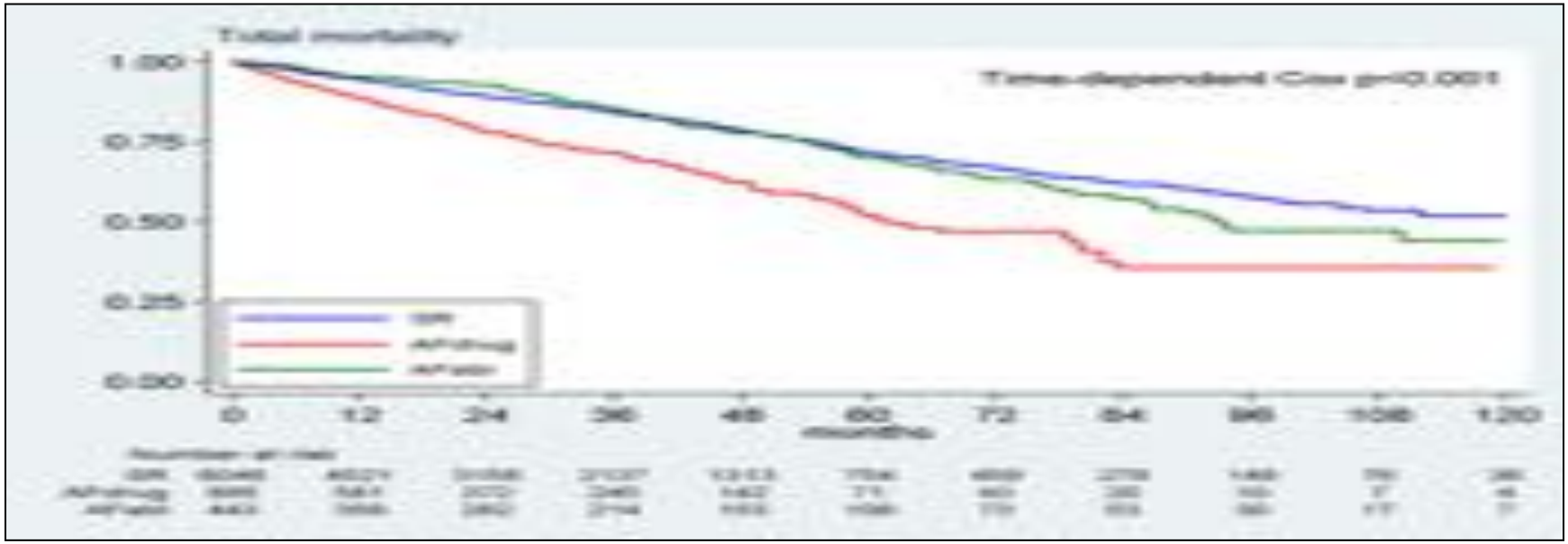


International Trials

- CAAN-AF (Australia)
- APAF-CRT (Italy)

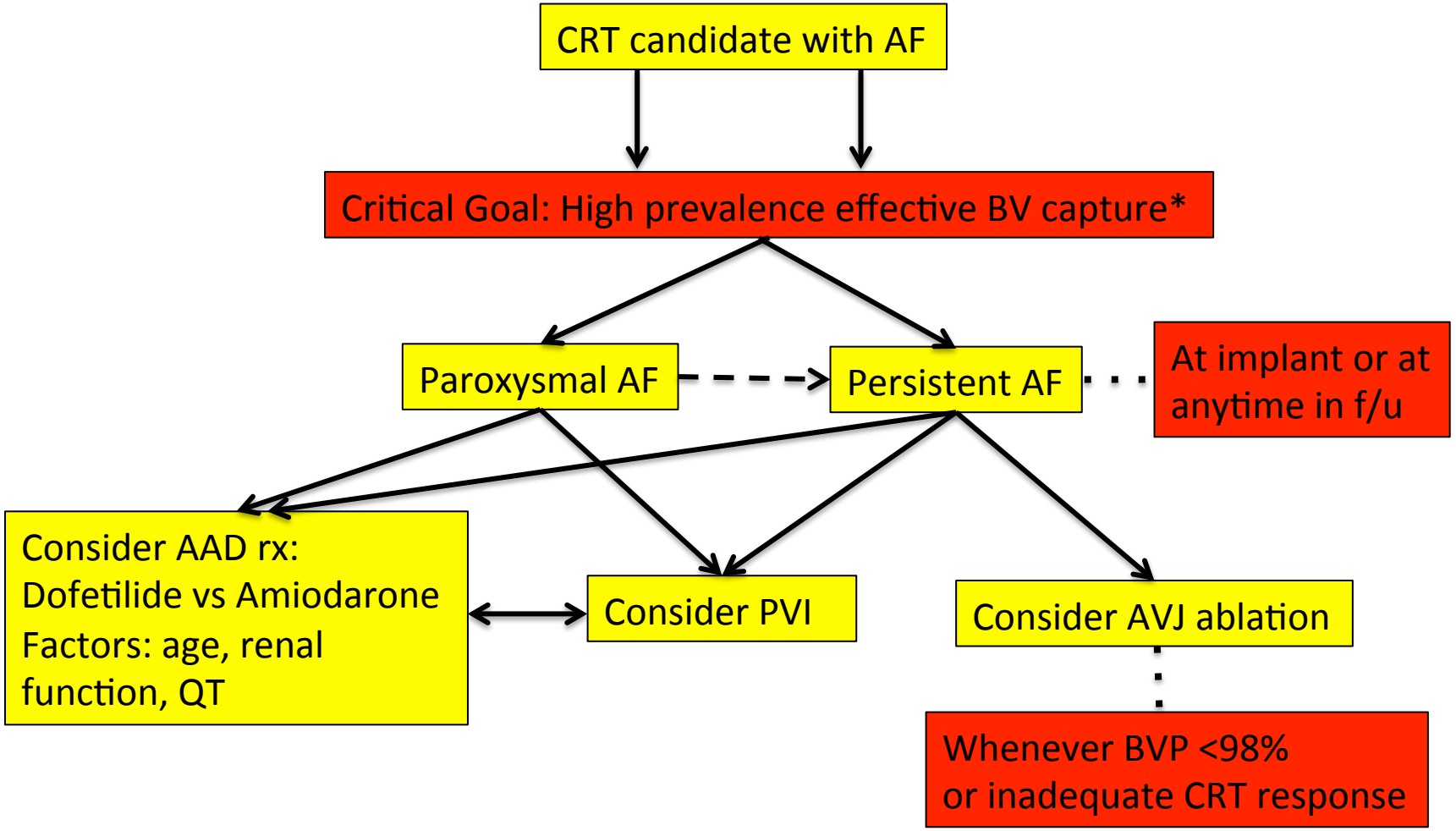
What is Threshold for AVJ Ablation?

- Is fear of PM dependency unfounded?
  - Redundancy of pacing leads (RV and LV)
  - Bipolar or quadripolar leads
  - Intense remote surveillance now routine



CERTIFY Study; JACC HF 2013

Suggested AF Management in Patients With AF, Heart Failure and CRT



* 100% BVP; optimize BB, digoxin

Thank you!