Program:

Module 1:

- Definition and Classification
- Epidemiology of Heart Failure
- Pathophysiology of Heart Failure
- Specific Diseases causing Heart Failure and practical case studies

Module 2:

- Diagnosis and Investigation of HF and Practical Case Studies
- Treatment of Heart Failure and Practical Case Studies

Treatment Approach for the Patient with Heart Failure

Stage A

At high risk, no structural disease

Therapy

- Treat Hypertension
- Treat lipid disorders
- Encourage regular exercise
- Discourage alcohol intake
- ACE inhibition

Stage B

Structural heart disease, asymptomatic

Therapy

- All measures under stage A
- ACE inhibitors in appropriate patients
- Beta-blockers in appropriate patients

Stage C

Structural heart disease with prior/ current symptoms of HF

Therapy

- All measures under stage A

Drugs:

- Diuretics
- ACE inhibitors
- Beta-blockers
- Digitalis
- Dietary salt restriction

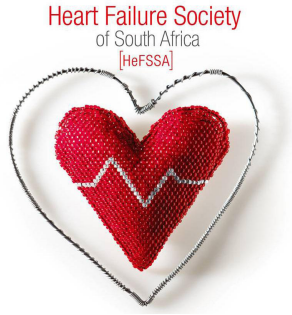
Stage D

Refractory HF requiring specialized interventions

Therapy

- All measures under stages A,B, and C
- Mechanical assist devices
- Heart transplantation
- Continuous (not intermittent) IV inotropic infusions for palliation
- Hospice care

Hunt, SA, et al ACC/AHA Guidelines for the Evaluation and Management of Chronic Heart Failure in the Adult, 2001



Treatment of Heart Failure

Two distinct settings:

Treatment of Acute Decompensated Heart Failure

Goal:

Stabilise the patient, return the filling pressures to as close as possible to normal and restore organ perfusion.

Chronic Stable Heart Failure

Goal:

Enhance survival and minimise symptoms.

At All Times Treat Important

Precipitating Factors

Change a compensated condition to frank heart failure. (Can occur in up to 93% of patients)

Ghali et al. Arch Int Med 1986

- Inappropriate reduction in therapy
- Arrhythmias (including abnormal intra-ventricular conduction)
- Myocardial infarction/ischaemia
- Systemic infection
- Pulmonary embolism
- Drugs causing myocardial depression

-Oestrogens, corticosteroids, NSAIDS.
- Development of another form of heart disease

Pharmacologic Management

ACE Inhibitors

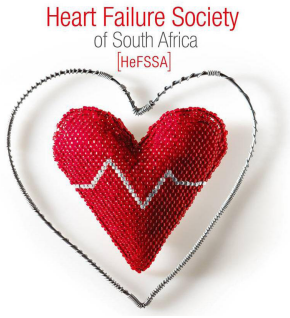
- Blocks the conversion of angiotensin I to angiotensin II; prevents functional deterioration.
- Recommended for all heart failure patients.
- Relieves symptoms and improves exercise tolerance.
- Reduces risk of death and decreases disease progression.
- Benefits may not be apparent for 1-2 months after initiation.

Heart Failure Society of South Africa [HeFSSA]

Pharmacologic Management

Angiotensin Receptor Blockers (ARBs)

- Block AT_1 receptors, which bind circulating angiotensin II.
- Examples: valsartan, candesartan, losartan.
- Should not be considered equivalent or superior to ACE inhibitors.
- In clinical practice, ARBs should be used to treat patients who are ACE intolerant due to intractable cough or who develop angioedema.



Pharmacologic Management

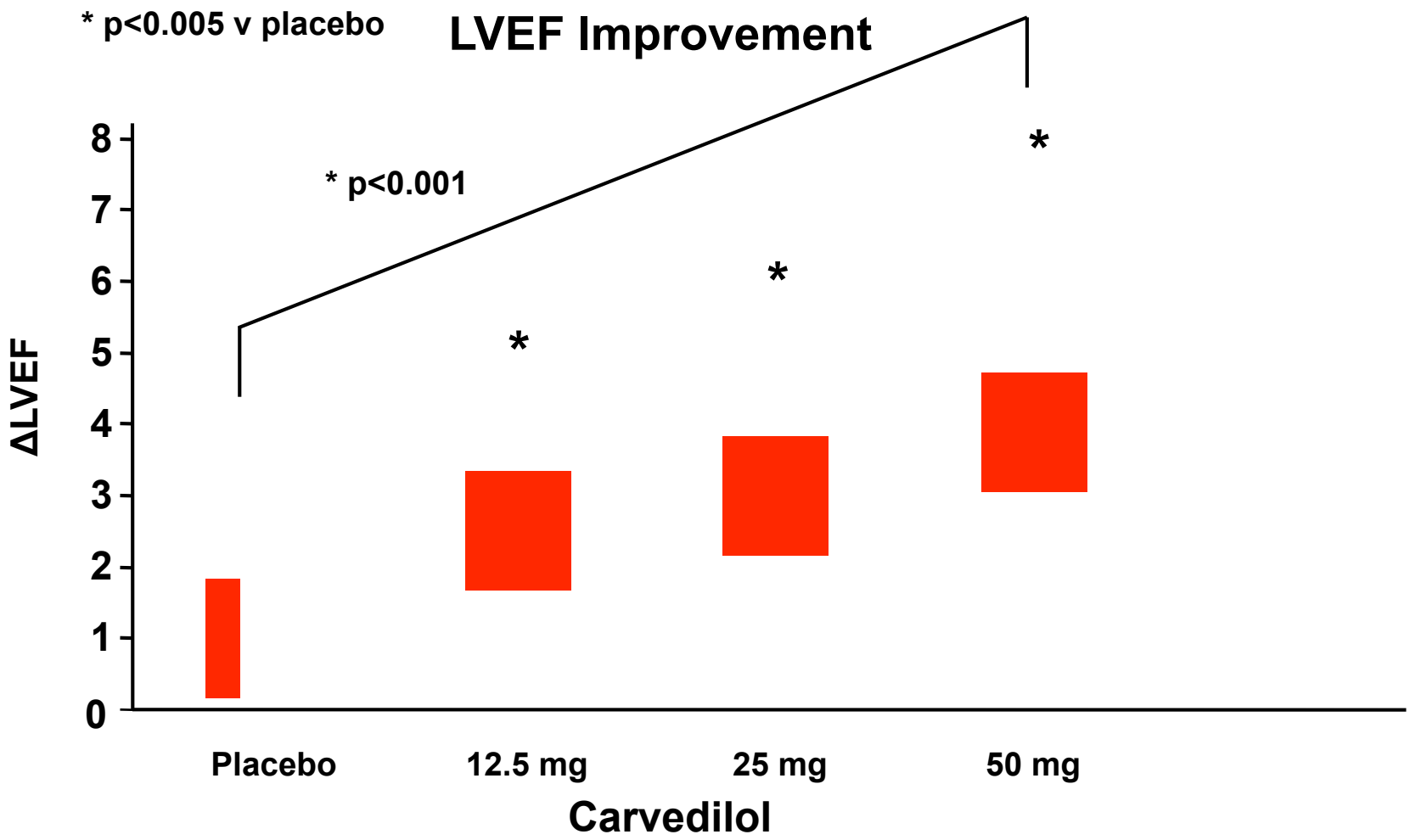
Beta-Blockers

- Cardioprotective effects due to blockade of excessive SNS stimulation.
- In the short-term, beta blocker decreases myocardial contractility; increase in EF after 1-3 months of use.
- Long-term, placebo-controlled trials have shown symptomatic improvement in patients treated with certain beta-blockers.[1]
- When combined with conventional HF therapy, beta-blockers reduce the combined risk of morbidity and mortality, or disease progression.[1]

1 *Hunt, SA, et al ACC/AHA Guidelines for the Evaluation and Management of Chronic Heart Failure in the Adult, 2001 p. 20.*

Heart Failure Society of South Africa [HFSSA]

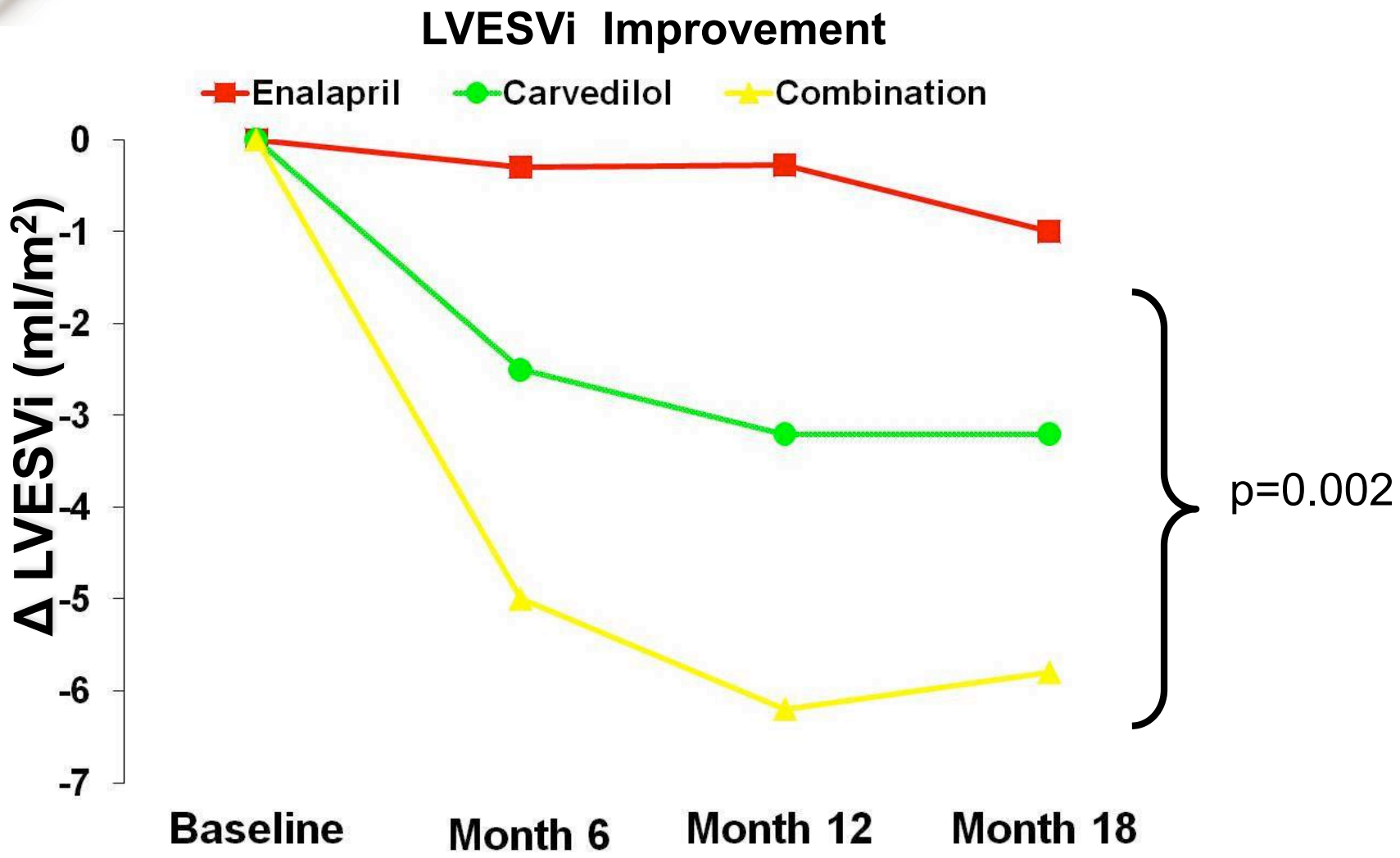
MOCHA: β blocker therapy reverses remodelling over 6 months



Bristow, M. R. et al. Circulation 1996;94:2807-2816

Heart Failure Society of South Africa [HeFSSA]

CARMEN: β blocker + ACE inhibitor therapy reverses remodelling over 18 months



Remme et al Cardiovasc Drugs and Therapy 2004;18;57-66

Pharmacologic Management

Aldosterone Antagonists

- Generally well-tolerated.
- Shown to reduce heart failure-related morbidity and mortality.
- Generally reserved for patients with NYHA Class III-IV HF.
- Side effects include hyperkalemia and gynecomastia. Potassium and creatinine levels should be closely monitored.

Diuretics

Fluid retention may increase cardiac output by a Frank-Starling mechanism.

Other consequences of fluid retention include:

Increase diastolic pressure

thus

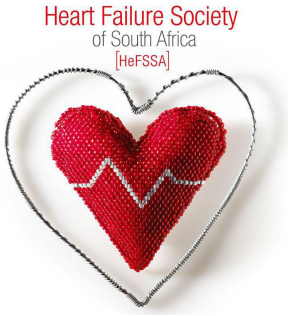
Increase in wall stress

thus

Hypertrophy and remodelling

There may be oedema, dyspnoea and pulmonary oedema.

Hence the use of diuretics



Classes of Diuretics

Loop Diuretics

Furosemide, turasemide, bumetamide

Thiazide and Thiazide-like

Potassium Sparing Diuretics

Amiloride, triamterine

Mineralo Corticoid Inhibitory

Spironolactone

Carbonic Anhydrase Inhibitors

Acetezolamide (diamox)

Diuretics

With the exception of spironolactone (an aldosterone antagonist) diuretics do not influence the natural history of chronic heart failure.

Bristow MR et al. Heart Disease. P562. Ed Braunwald, Zipes, Lippy, WB Saunders 2001

However….

Diuretics potentially improve congestive symptoms and may slow down ventricular remodelling.

Problems Encountered With Diuretics

1. Metabolic Side Effects

   Hyperglycaemia, hyperuricaemia

2. Electrolyte Imbalance

3. Volume Depletion

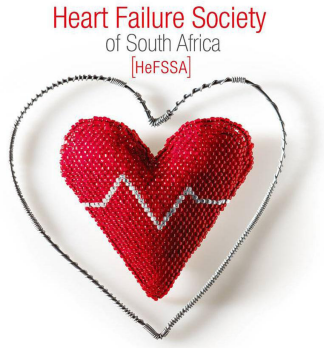
   Hypertension, interference with other medications (Ace I, ARB, beta blockade)

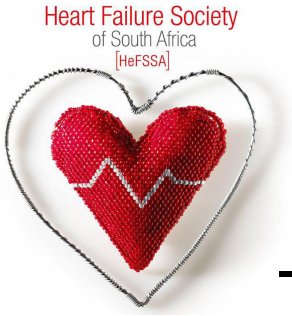
4. Diuretic Resistance (Na=sodium)

   - Net gain of Na with a high Na diet
   - Compensatory hypertrophy of tubular epithelial cells distal to their site of action
   - Other drugs NSAIDS
   - ↓ Renal perfusion

Cardiac Glycosides

- Have a definite inotropic effect (more Starling curve -calcium mediated).
- Does not decrease mortality.
- Beneficial effects in mild to moderate failure in sinus rhythm.
- Requires vigilance regarding toxic accumulation (NB: GFR, body mass).
- Measurement of serum levels advisable.
- Contra-indicated in predominantly diastolic dysfunction.





Medications Which Increase Serum Digoxin Levels Mainly By ↓ Renal Clearance

Amiodarone
Verapamil
Nifedipine
Diltiazem
Quinidine
Propafenone
Captopril
Carvedilol
Saint John's wort

Amiloride
Triamterene
Macrolide Antibiotics
Tetracycline
Indomethacin
Alprazolam
Itraconazole
Cyclosporine Spironolactone

Vasodilators

Decrease arteriolar tone ↑ CO

Decrease venous preload ↓ congestion

Acute Phase

Sodium nitroprusside

Nitrates initially may also have a beneficial primary coronary effect, secondary ↑CO.

Chronic Stable Phase

Oral Nitrates – Note: Avoid nitrate resistance by having a drug free time.

Hydrallazine – Need for 3-4 times daily dose. (major increase in systemic and pulmonary afterload).

Anticoagulants

The presence of heart failure markedly lowers the threshold for instituting anticoagulant therapy e.g. atrial fibrillation, bed rest.

Timing is Everything

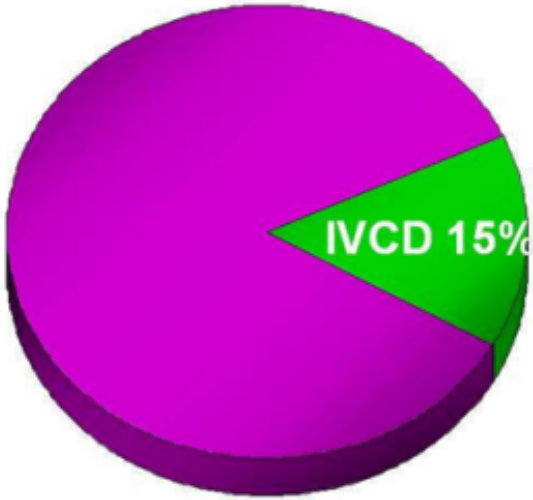
"Either my watch has stopped or this guy is dead."

Groucho Marx: A day at the races.

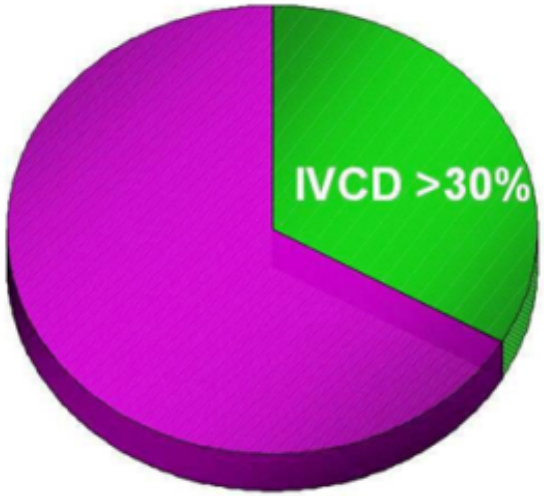
Heart Failure Society of South Africa [HeFSSA]

Prevalence of Inter- or Intraventricular Conduction Delay

General HF Population[1,2]



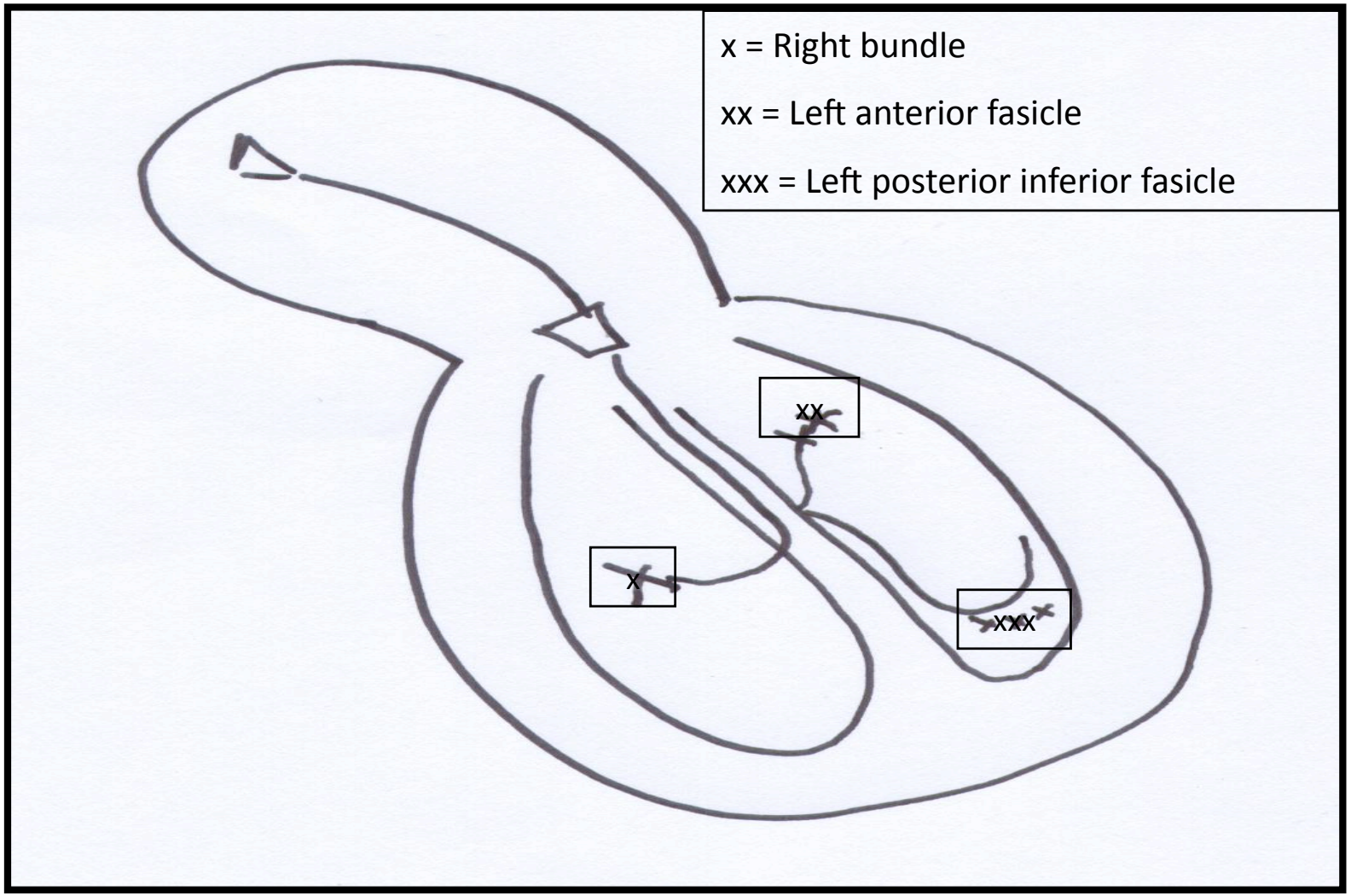
Moderate to Severe HF Population[3,4,5]



[1] Havranek E, Masoudi F, Westfall K, et al. *Am Heart J* 2002;143:412-417
[2] Shenkman H, McKinnon J, Khandelwal A, et al. *Circulation* 2000;102(18 Suppl II): abstract 2293
[3] Schoeller R, Andersen D, Buttner P, et al. *Am J Cardiol.* 1993;71:720-726
[4] Aaronson K, Schwartz J, Chen T, et al. *Circulation* 1997;95:2660-2667
[5] Farwell D, Patel N, Hall A, et al. *Eur Heart J* 2000;21:1246-1250

Determinants of Cardiac Synchrony
Interventricular Synchrony

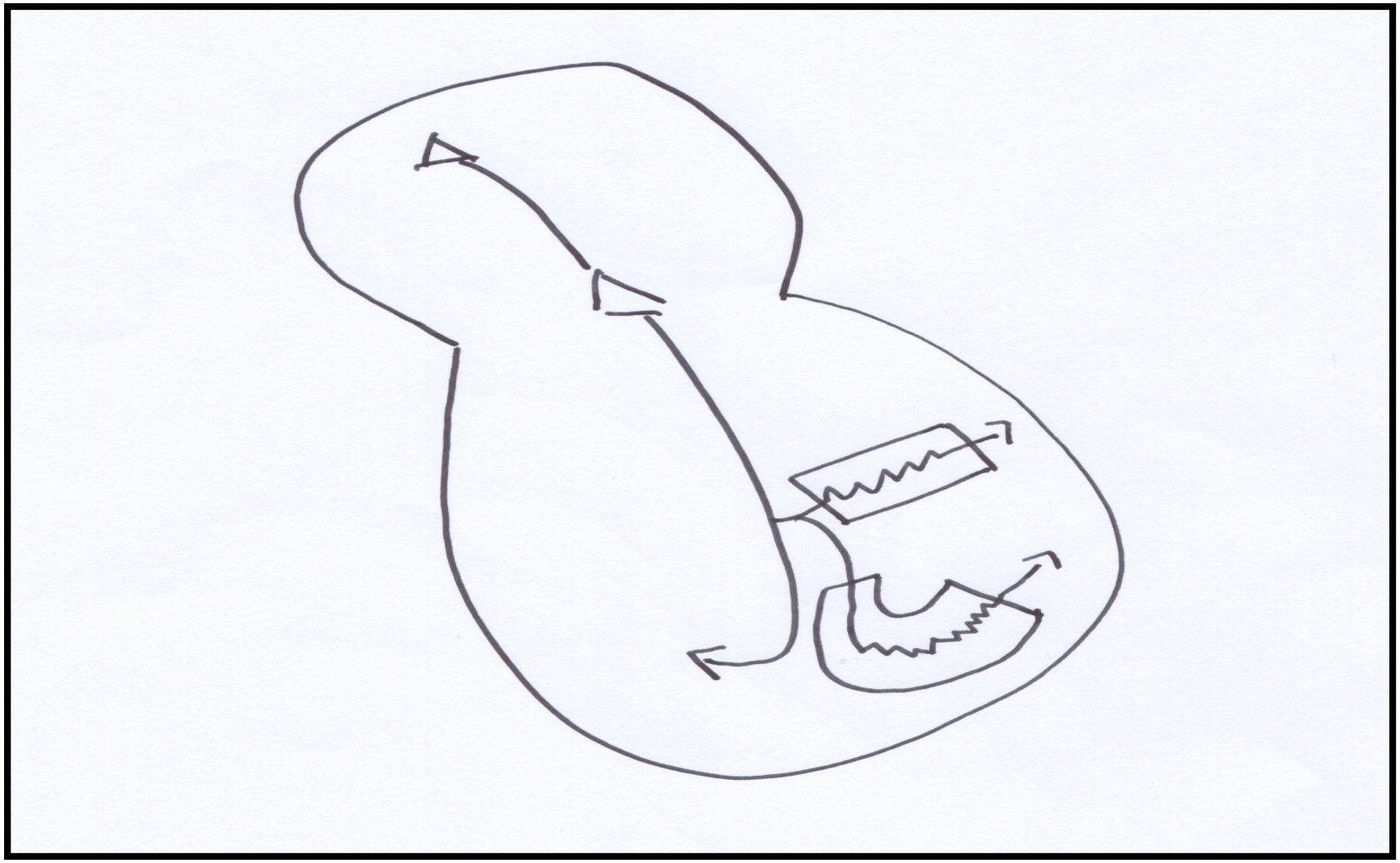
Determinants: Bundle branches



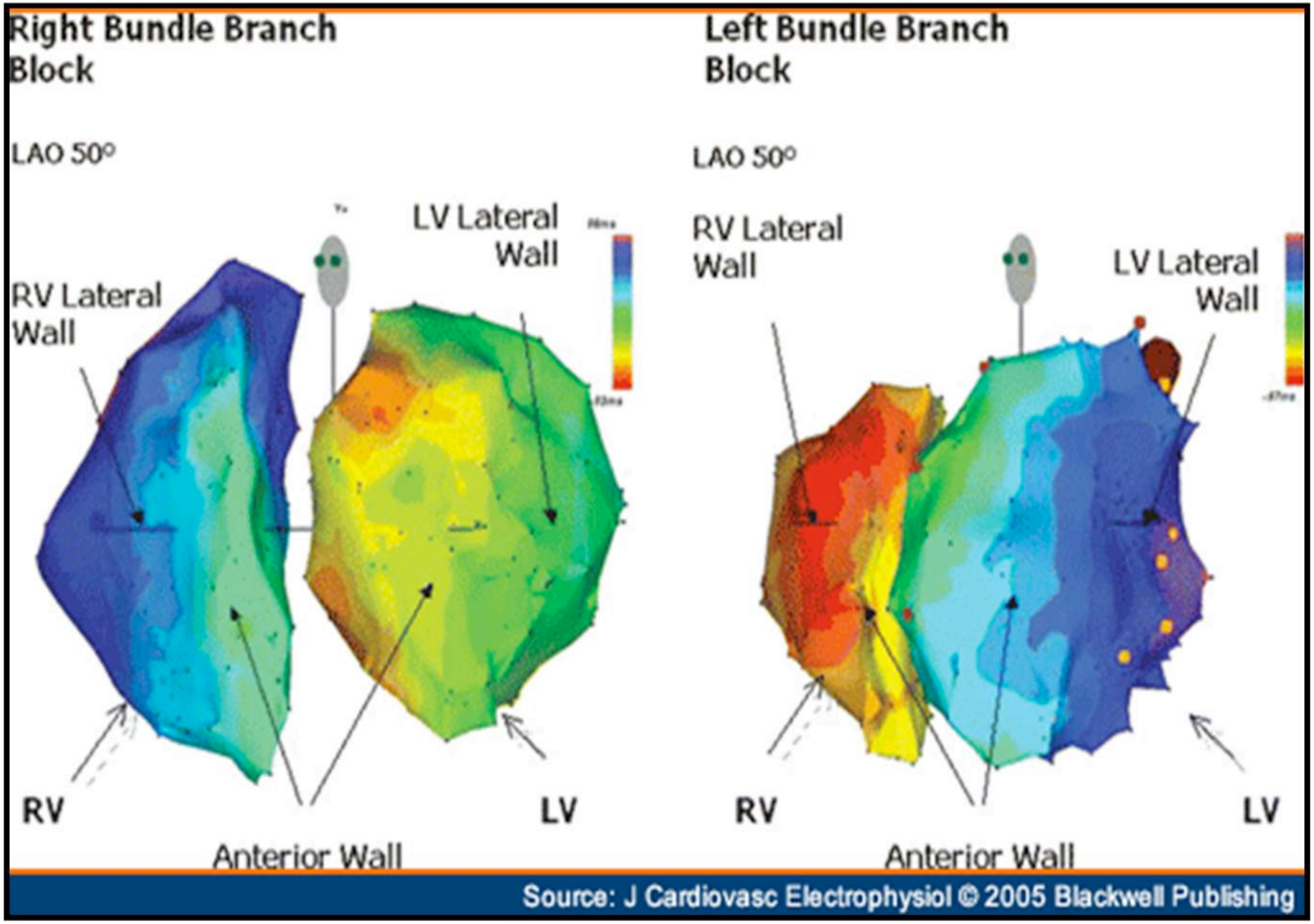
Determinants of Cardiac Synchrony

Intraventricular Synchrony

Mainly affects LV (scar etc)



Bundle Branch Patterns of Activation

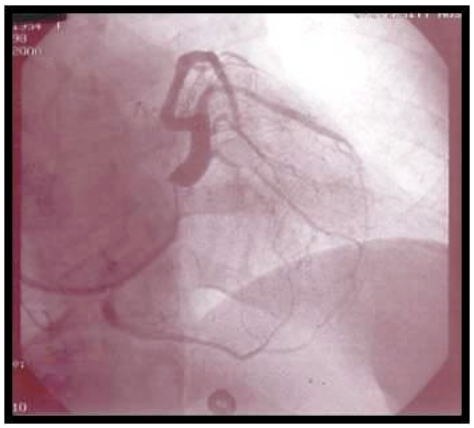


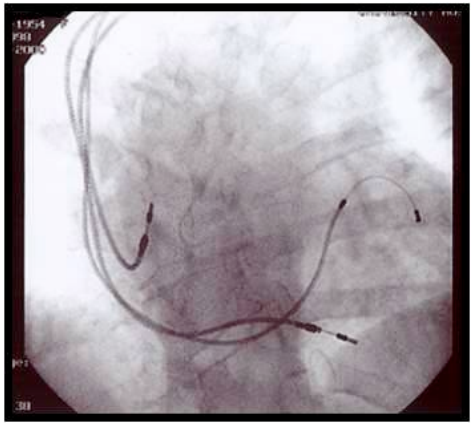
Achieving Cardiac Resynchronization

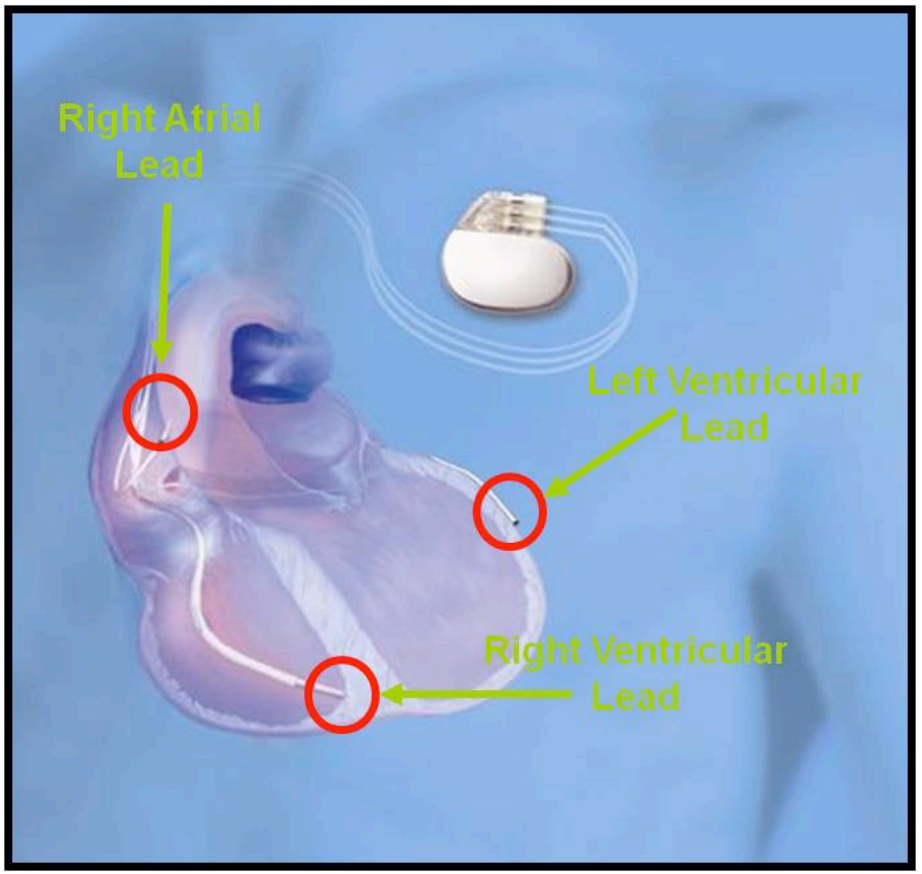
Goal: Atrial synchronous biventricular pacing

Transvenous approach for left ventricular lead via coronary sinus

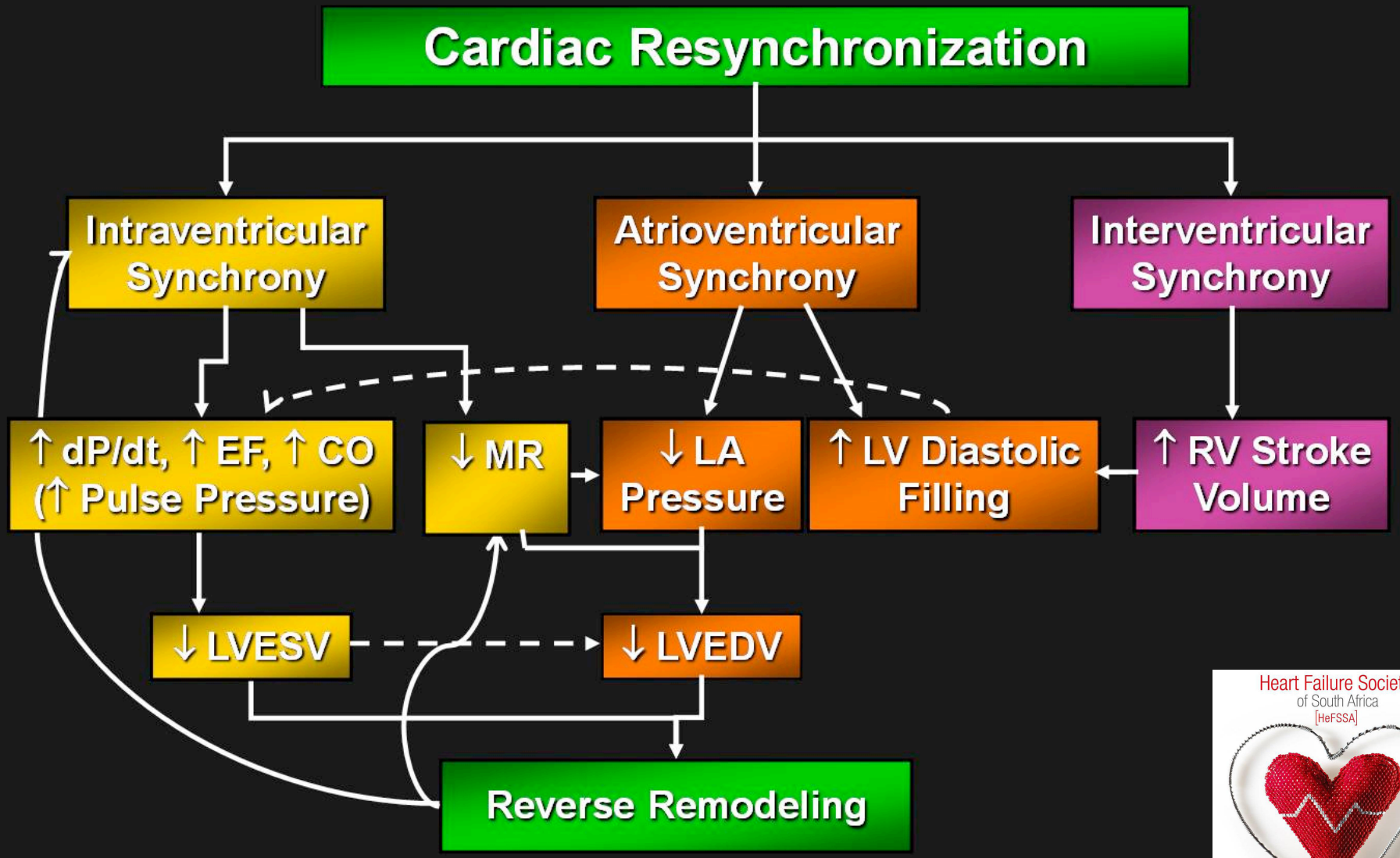
Back-up epicardial approach







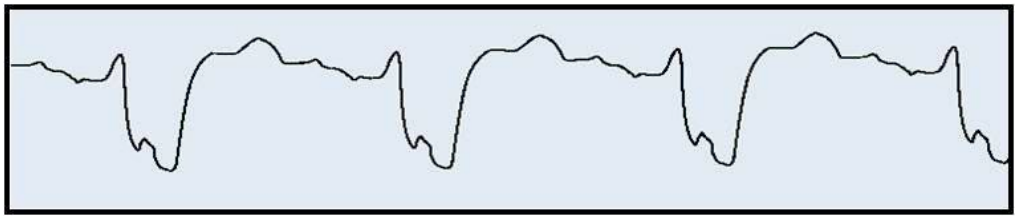
Summary of Proposed Mechanisms Therapy



Yu C-M, Chau E, Sanderson J, et al. *Circulation* 2002;105:438-445

Ventricular Dysynchrony and Cardiac Resynchronization

Ventricular Dysynchrony[1]

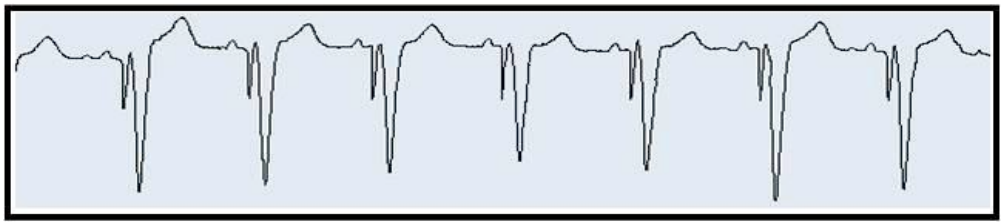


Electrical: Inter- or Intraventricular conduction delays typically manifested as left bundle branch block

Structural: disruption of myocardial collagen matrix impairing electrical conduction and mechanical efficiency

Mechanical: Regional wall motion abnormalities with increased workload and stress—compromising ventricular mechanics

Cardiac Resynchronization



Therapeutic intent of atrial synchronized biventricular pacing

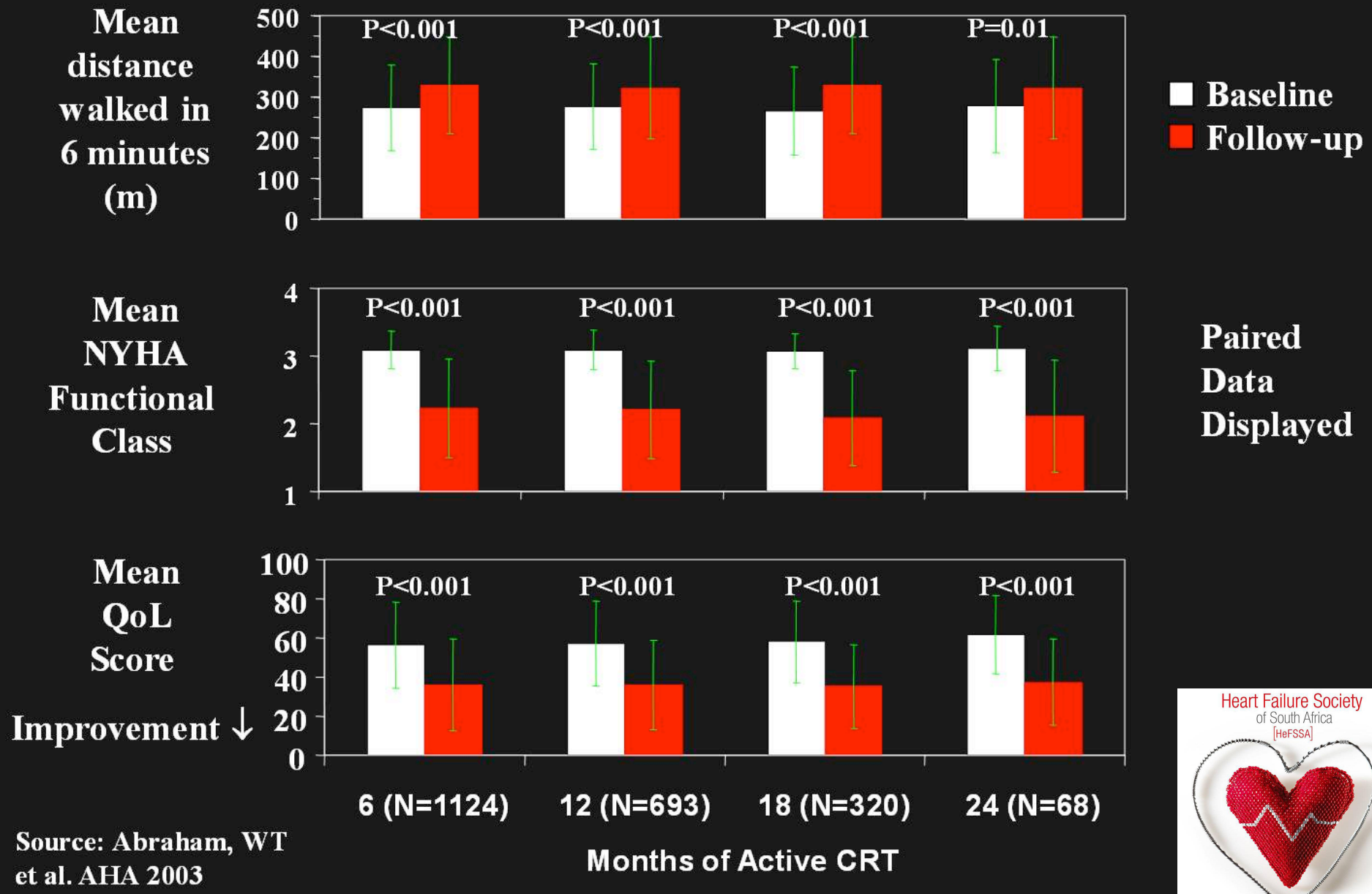
- Modification of interventricular, intraventricular, and atrial-ventricular activation sequences in patients with ventricular dysynchrony
- Complement to optimal medical therapy

Heart Failure Society of South Africa [HeFSSA]

[1] *Tavazzi L. Eur Heart J 2000;21:1211-1214*

Benefits Sustained Through 2 Years

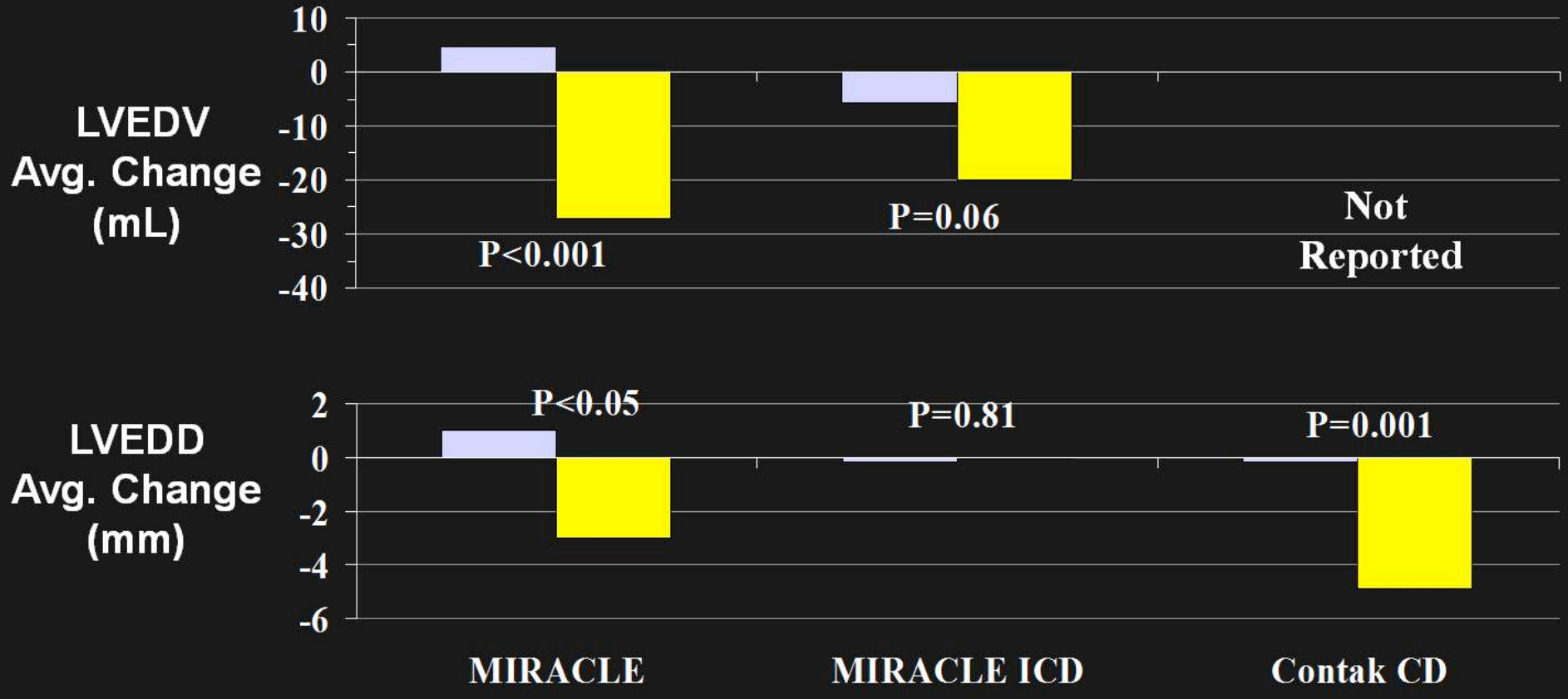
MIRACLE Study Program



Source: Abraham, WT et al. AHA 2003

Heart Failure Society of South Africa [HeFSSA]

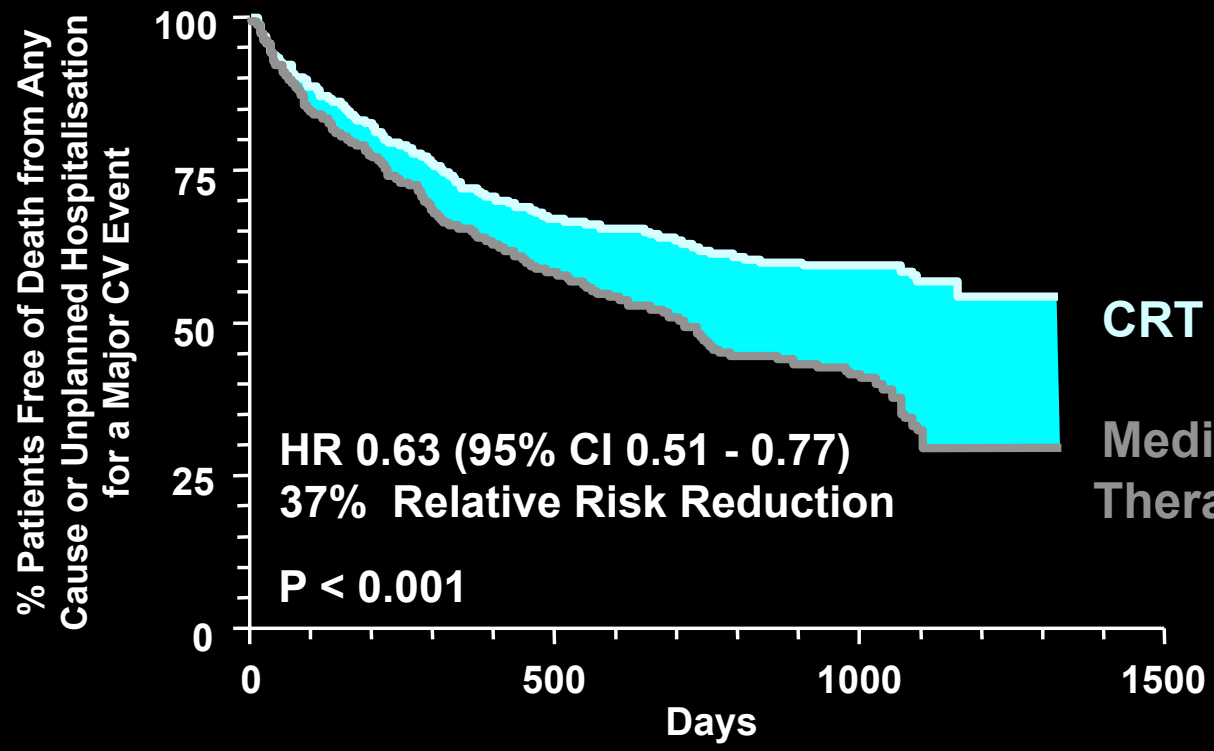
CRT Effect on LV Structure at 6 Months in Moderate to Severe Heart Failure



Data sources: MIRACLE: *Circulation* 2003;107:1985-1990
MIRACLE ICD:*JAMA* 2003;289:2685-2694
Contak CD: *J Am Coll Cardiol* 2003;2003;42:1454-1459

Heart Failure Society of South Africa [HeFSSA]

CARE-HF: CRT reduces death or unplanned hospitalisation for CV events in NYHA III/IV



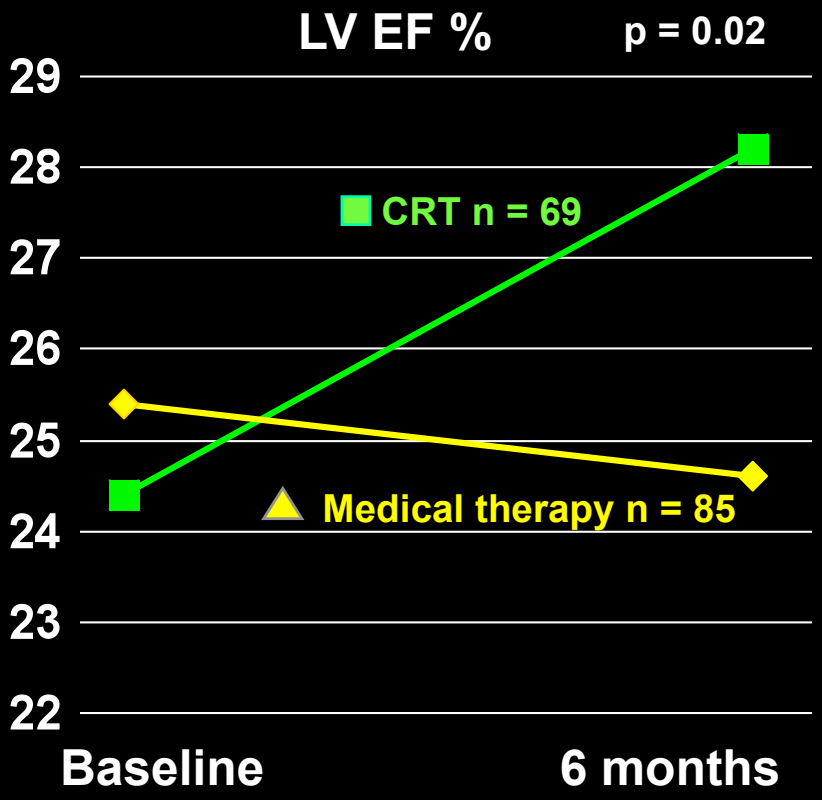
37% risk reduction with CRT

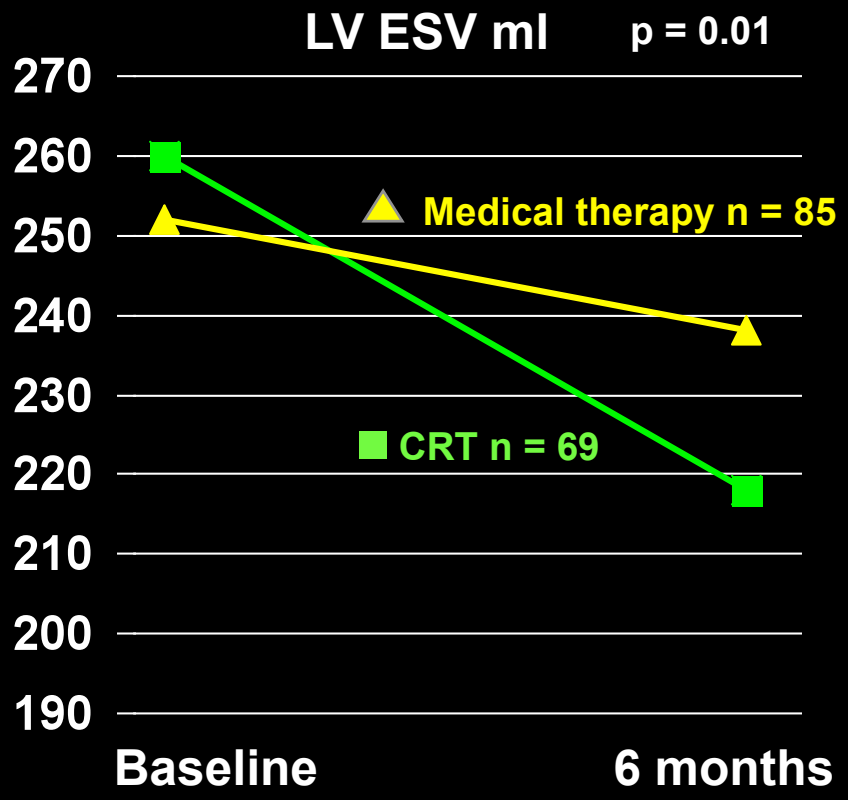
No. at Risk						
CRT	409	323	273	166	68	7
Medical Therapy	404	292	232	118	48	3

Cleland JGF. N Engl J Med. 2005;352:1539-1549.

Heart Failure Society of South Africa [HeFSSA]

MICD II: CRT therapy may reverse remodelling over 6 months in mild HF

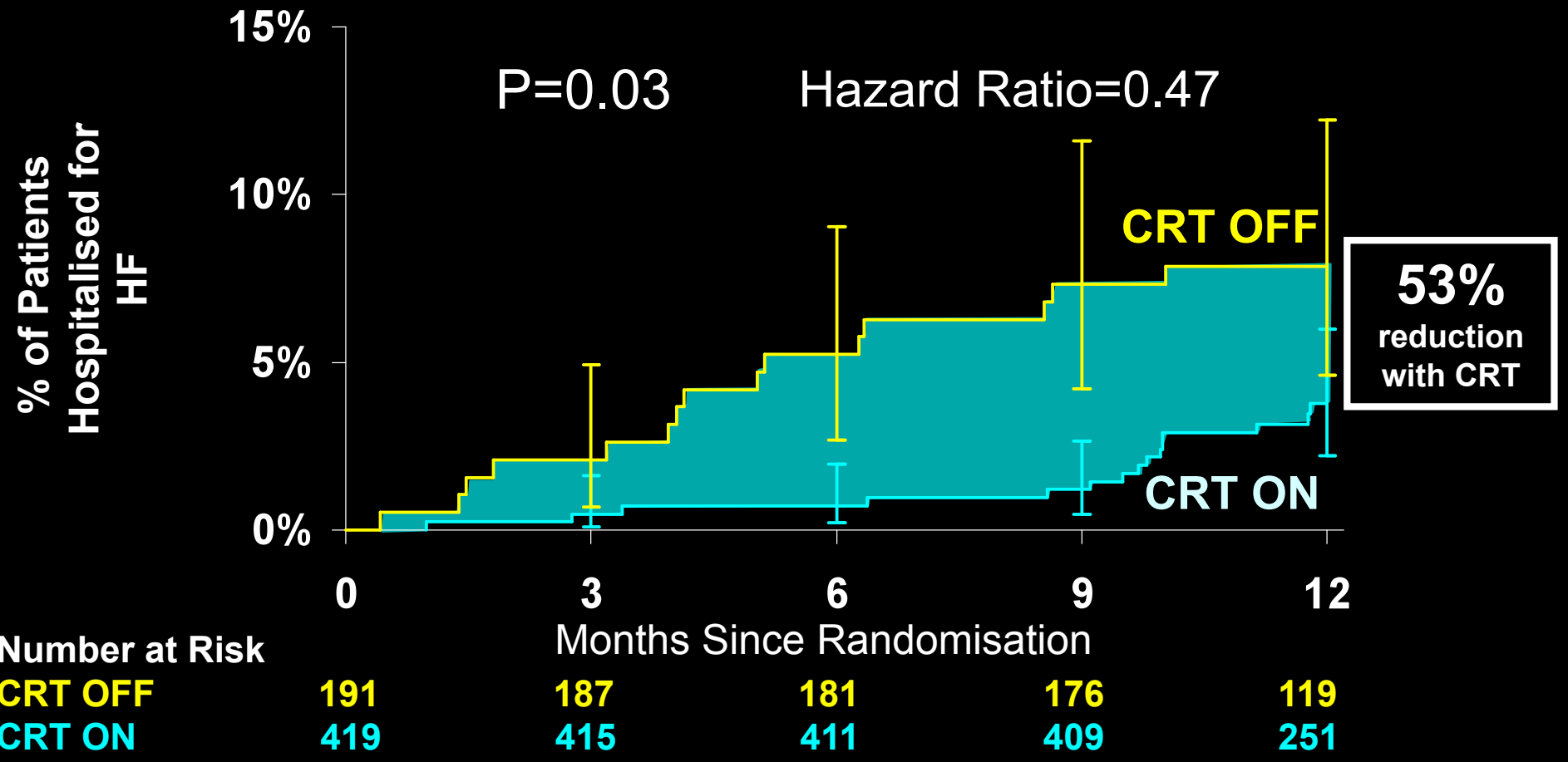




Abraham et al Circulation 2004;110:2864-68

Heart Failure Society of South Africa [HeFSSA]

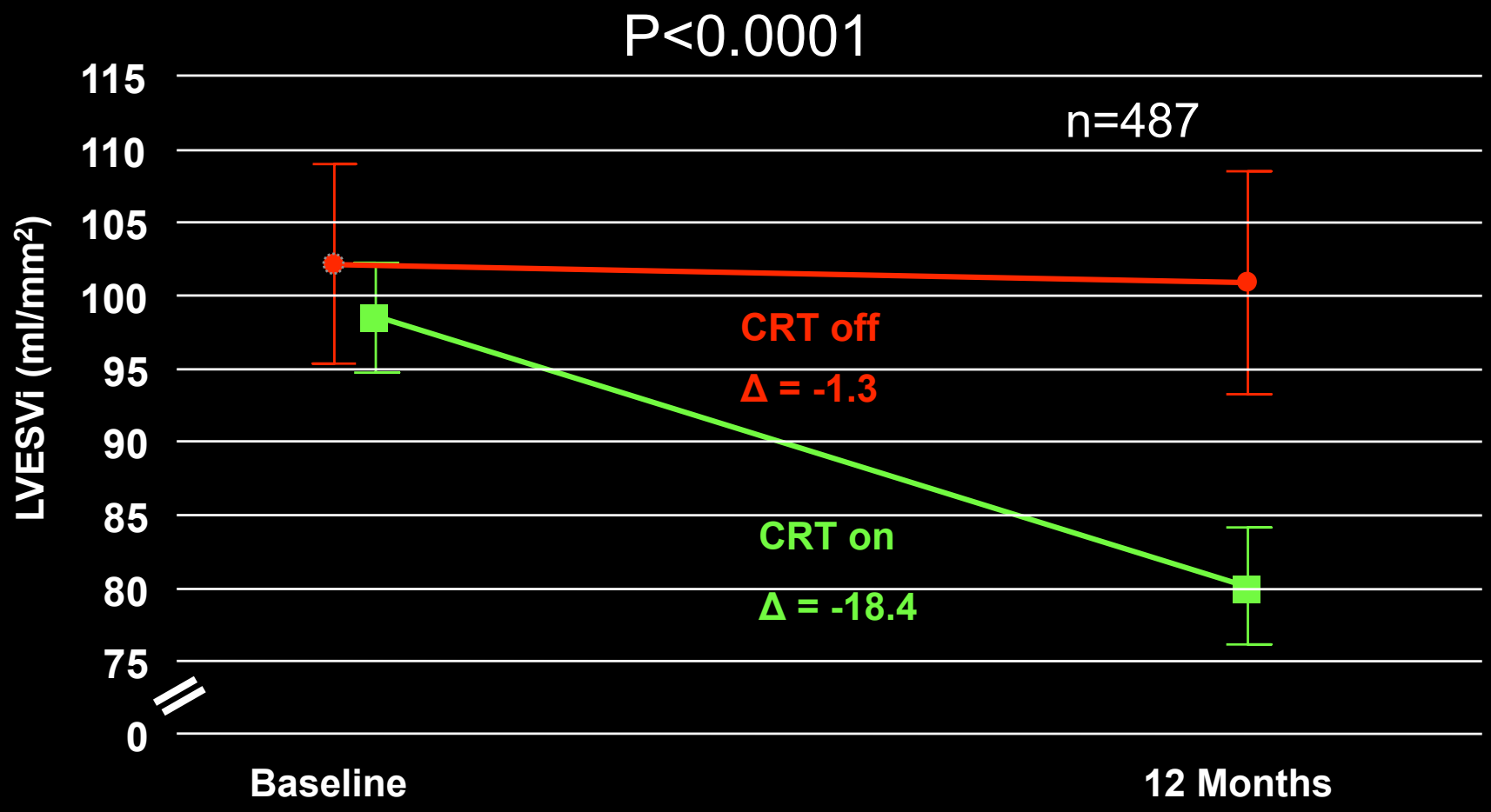
Grade II NYHA



Number at Risk					
CRT OFF	191	187	181	176	119
CRT ON	419	415	411	409	251

Linde C, Abraham WT, Gold WR et al for REVERSE Study Group. J Am Coll Cardiol 2008 Dec 2;52(23):1834-43.

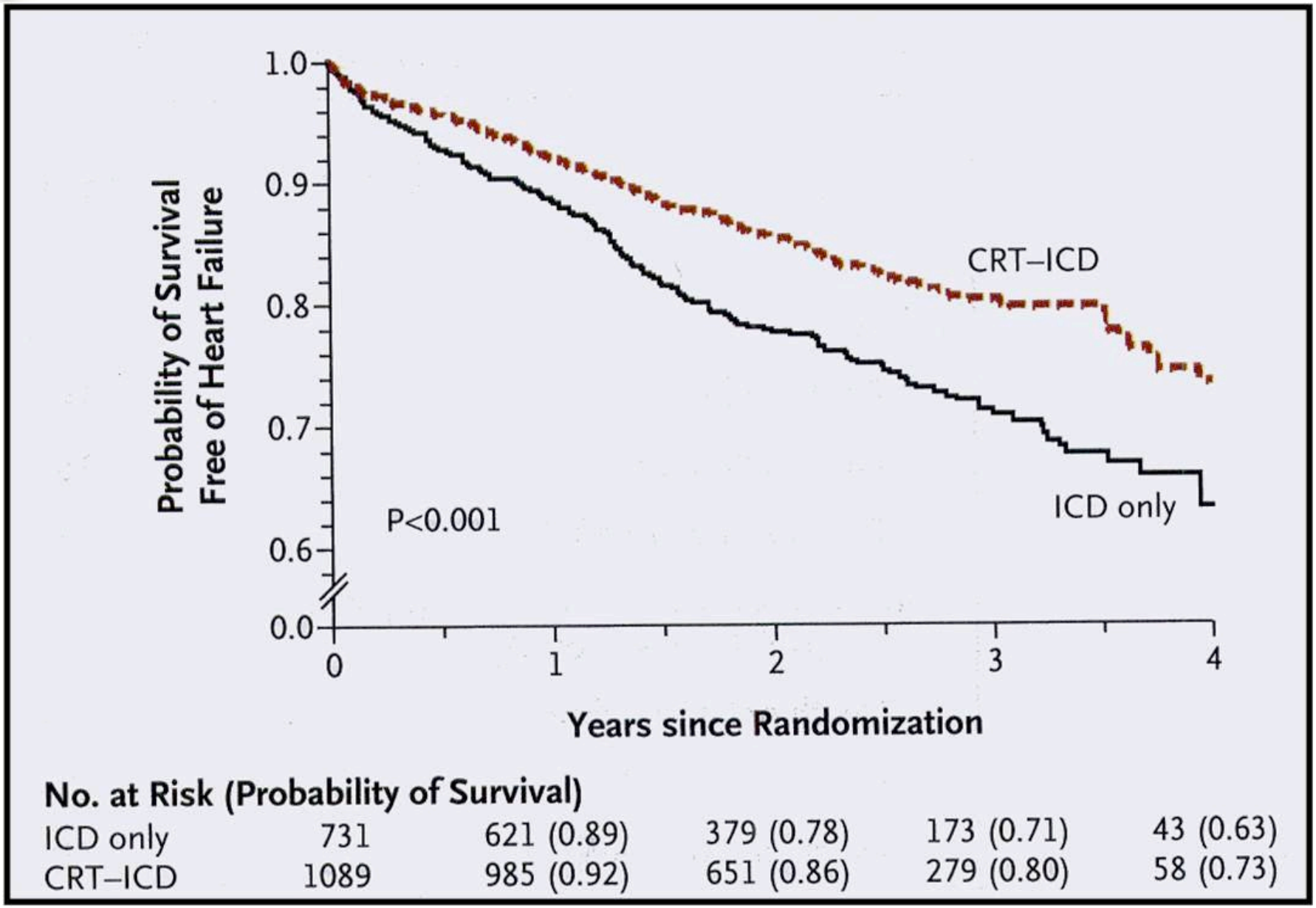
Grade II NYHA



Linde C, Abraham WT, Gold WR et al for REVERSE Study Group. J Am Coll Cardiol 2008 Dec 2;52(23):1834-43.

Heart Failure Society of South Africa [HeFSSA]

Madit CRT



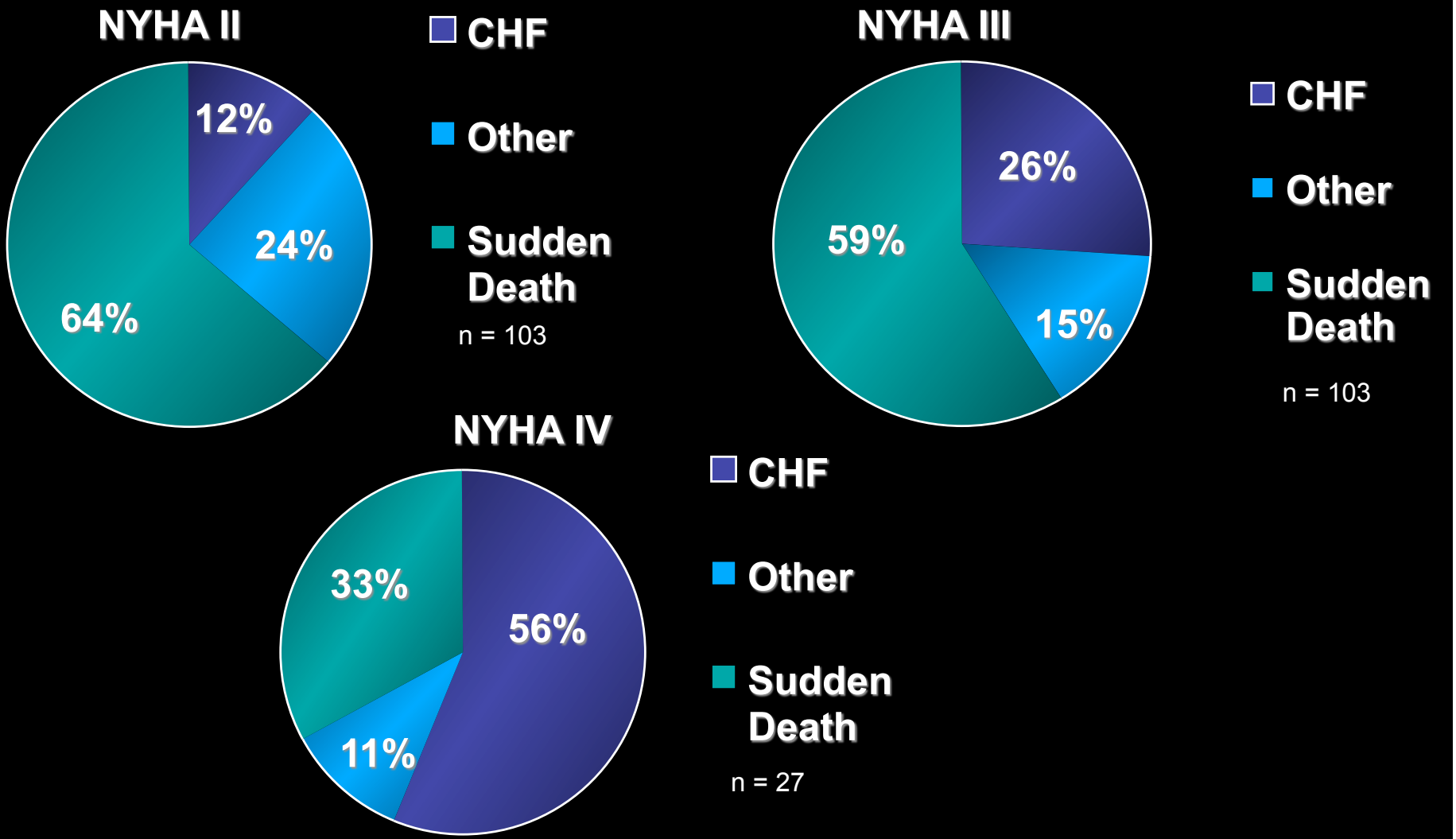
No. at Risk (Probability of Survival)

ICD only	731	621 (0.89)	379 (0.78)	173 (0.71)	43 (0.63)
CRT–ICD	1089	985 (0.92)	651 (0.86)	279 (0.80)	58 (0.73)

NEJM. Oct 2009

Severity of Heart Failure

Modes of Death



MERIT-HF Study Group. Effect of Metoprolol CR/XL in chronic heart failure: Metoprolol CR/XL randomized intervention trial in congestive heart failure (MERIT-HF). LANCET. 1999;353:2001-07.

Prediction of Sudden Death from History – Paris Study

Factors associated with sudden death during follow up (23 years):

- Resting heart rate.
- Systolic and diastolic blood pressure.
- Tobacco consumption.
- Body mass index.
- Diabetes.
- Serum cholesterol.
- Parental history of sudden death.

Most Cardiac Arrests (70%-80%) Occur At Home

Cummins RO et al. *Circulation,* 1991: 83:832-847

Litwin PE et al. *Emerg Med,* 1987: 16:787-791

Summary : Treatment

1. Acute Phase

fluid overload (oedema, pulmonary oedema).
Remove/treat precipitating cause (ischaemia, infection, arrhythmia, thyrotoxicosis)

2. Chronic Phase

Stop the vicious cycle

a. ACE inhibitors, ARB
b. Beta blockers
c. Spironolactone
d. Digoxin (?)
e. Arrhythmias
f. Incoordinate contractions

REST
REVERSE
REPAIR