HeFSSA Practitioners Program 2013

08:00 – 08:30	Registration
08:30 – 09:15	Clinical Case Presentation 1
09:15 – 10:00	Clinical Case Presentation 2
10:00 – 10:30	Tea Break
10:30 – 11:15	Clinical Case Presentation 3
11:15 – 11:45	ESC Guidelines on Chronic Heart Failure
11:45 – 12:00	Questionnaire
12:00 – 14:00	Lunch

Heart Failure Society of South Africa [HeFSSA]

A case of ischaemic cardiomyopathy

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The story starts with…..
(2010)

- 66 year old man
- Smoker
- Father underwent CABG in his 50's
- Frequent NSAID use for back pain
- Not on any other medication
- Had an anterior STEMI – treated
- Re –admitted 3 months later with recu anterior myocardial infarction - PCI to LAD

Prevention is better than cure!

- Preservation of myocardium in order to prevent ischaemic left ventricular dysfunction is critical in preventing heart failure/death due to ischaemic cardiomyopathy
- Good secondary prevention and lifestyle modification

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Back to our patient

- Discharged on:
- Atenolol 50 mg 2x/day
- Simvastatin 20 mg daily
- Aspirin 150 mg daily
- Clopidogrel 75 mg daily
- Perindopril 4 mg daily

- Did not return for completion of revascularisation.

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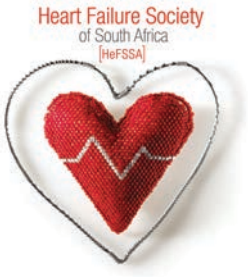
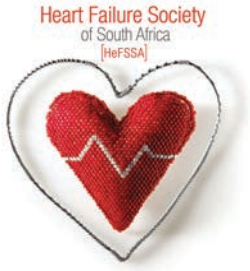
Progress over the next 12 months

- Doing reasonably well
- Very infrequent angina on moderate exertion, readily treated with short-acting nitrates
- Manages to stop smoking
- Develops a cough on the perindopril – therefore this was stopped
- Clopidogrel stopped after 12 months
- Class 1 – 2 NYHA – manages to do be reasonably active



Patient moves from JHB to CT

- Sees his new general practitioner because he finds that over the last 3 months he has become progressively more short of breath – now short of breath on walking even small distances
- He vehemently denies that he has had any chest pain recently
- Current medication:
  - Atenolol 50 mg 2x/day
  - Ecotrin 81 mg daily
  - Simvastatin 10 mg daily



Clinical findings

- All pulses palpable
- Mild pedal oedema
- No pallor
- JVP raised – 8cm above sternomanubrial angle
- Apex beat displaced – dyskinetic
- Soft pansystolic murmur
- S1 and S2 normal, no S3 heard

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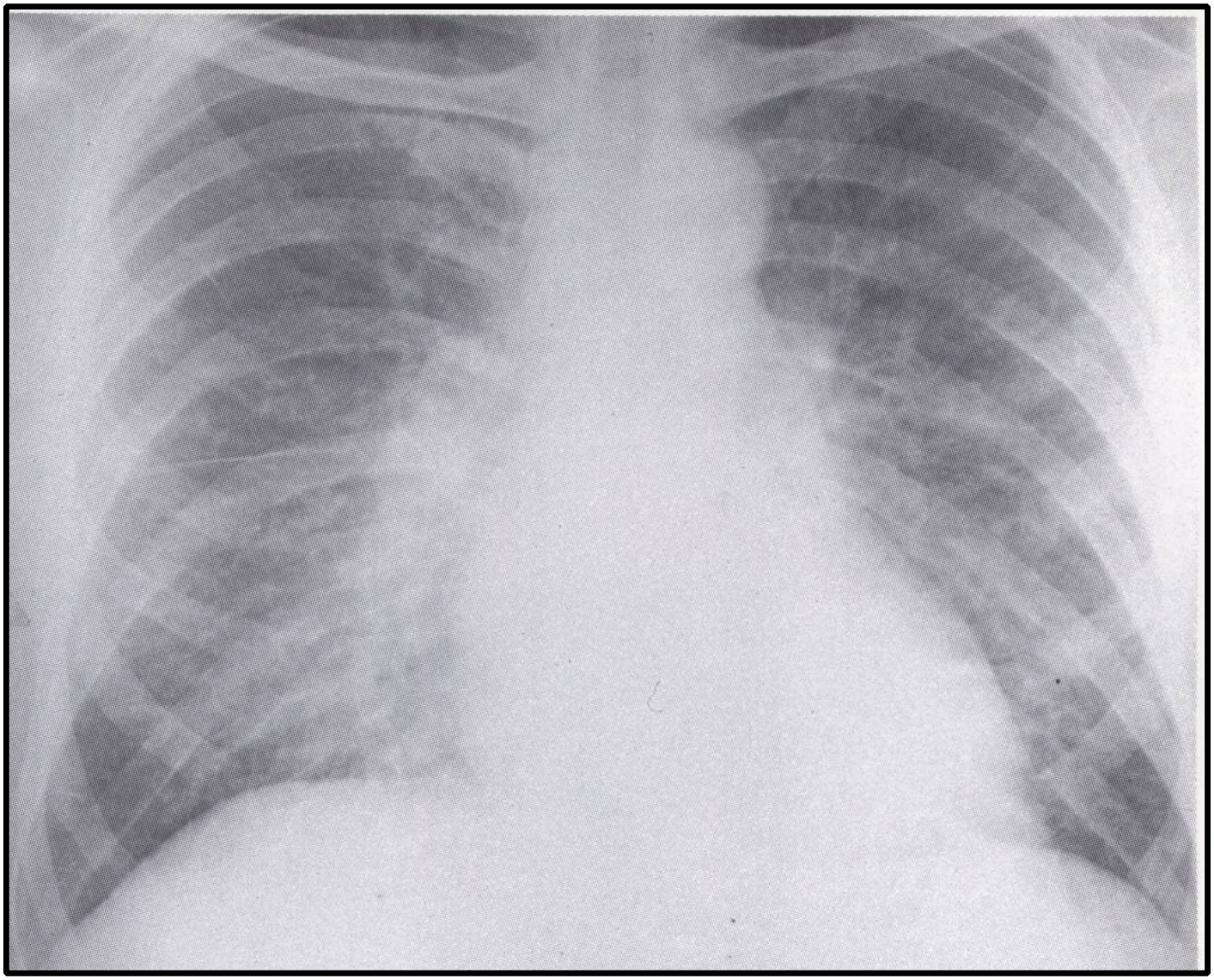
CXR



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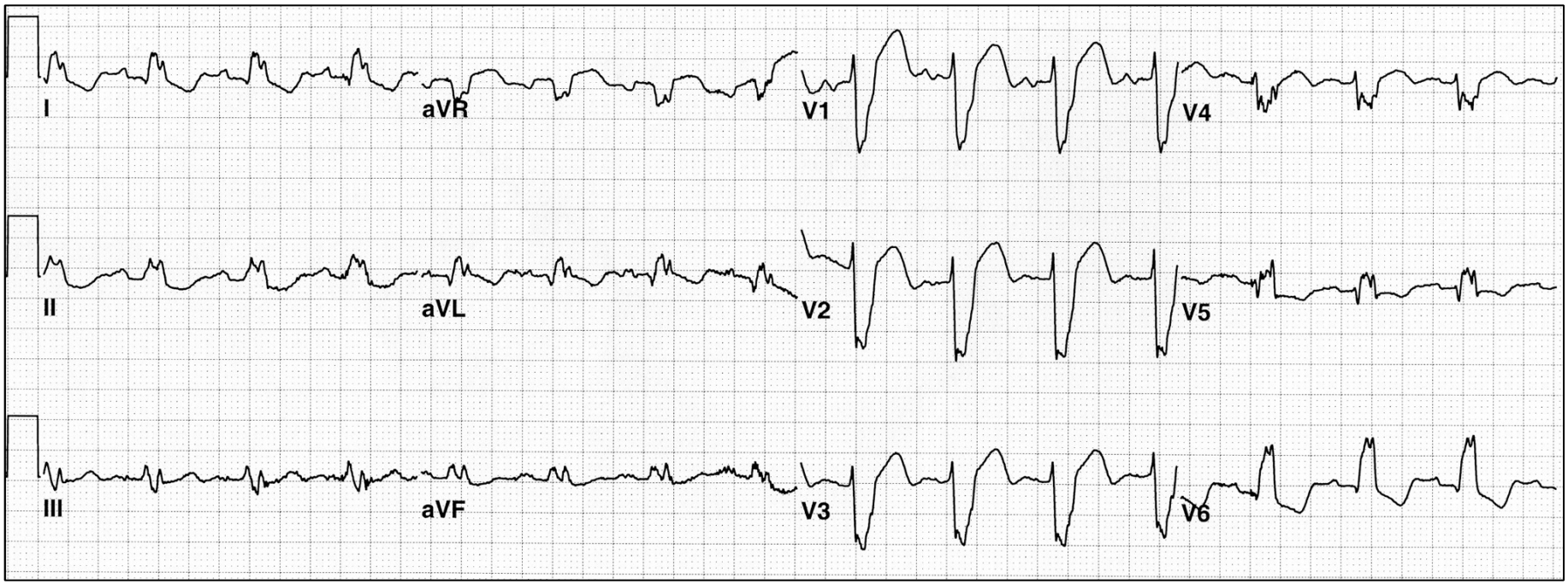
ECG



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Echocardiography

- Quantification of LV function and regional wall motion abnormality (Our patient EF: 25%, global impairment of LV function)
- Rule out significant valvular heart disease which may contribute to the presentation (Our patient: mild mitral regurgitation only)
- Look for other abnormalities: e. g. LV clot (our patient: none)

BLOOD RESULTS

- CEU - Assess renal function and electrolytes as this can affect decisions re. drug therapy and can itself contribute to worsening cardiac failure (our patient: normal)
- FBC - Make sure the patient is not anaemic as this can make CCF symptoms worse (our patient: normal
- TSH - If you do not check it, you cannot diag hypothyroidism (our patient normal)

What medication should this man be on?

First-up the therapy we know saves lives (and reduces heart failure recurrence!)

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Pharmacological therapy

- Beta-blockers
- The only beta-blockers that have been tested in RCT's are: metoprolol, bisoprolol and carvedilol
- These have been titrated to **target dosages NOT target heart rates** in the trials

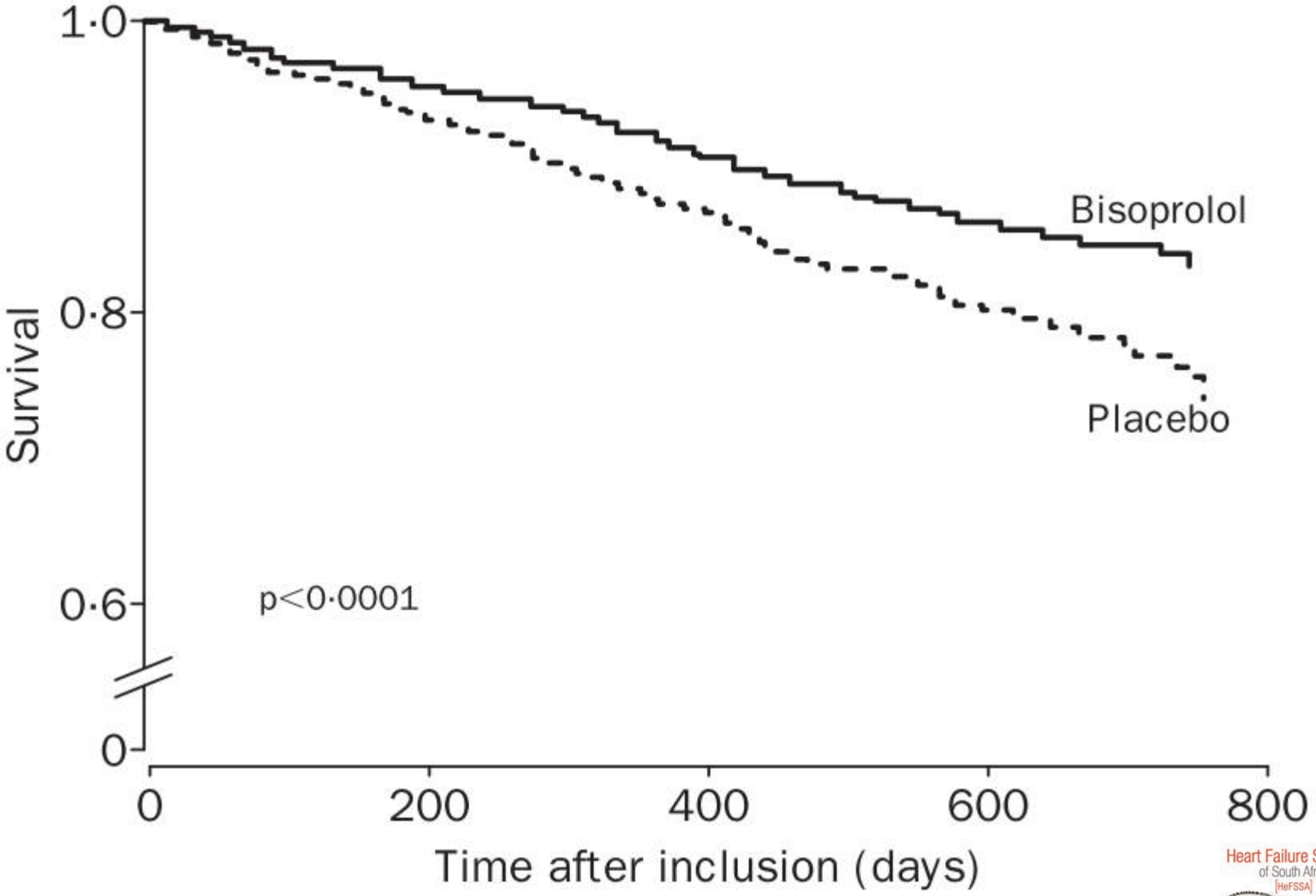

Figure 2: **Survival curves**

Lancet 1999; **353:** 9–13

	Starting dose (mg)	Target dose (mg)
Beta-blocker		
Bisoprolol	1.25 o.d.	10 o.d.
Carvedilol	3.125 b.i.d.	25–50 b.i.d.
Metoprolol succinate (CR/XL)	12.5/25 o.d.	200 o.d.
Nebivolol[c]	1.25 o.d.	10 o.d.
ARB		

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ESC Guideline 2012, pg 21

Pharmacological interventions

- ACE-inhibitors

	Starting dose (mg)	Target dose (mg)
ACE inhibitor		
Captopril[a]	6.25 t.i.d.	50 t.i.d.
Enalapril	2.5 b.i.d.	10–20 b.i.d.
Lisinopril[b]	2.5–5.0 o.d.	20–35 o.d.
Ramipril	2.5 o.d.	5 b.i.d.
Trandolapril[a]	0.5 o.d.	4 o.d.

ESC Guideline 2012, pg 21

	Starting dose (mg)	Target dose (mg)
ARB		
Candesartan	4 or 8 o.d.	32 o.d.
Valsartan	40 b.i.d.	160 b.i.d.
Losartan[b,c]	50 o.d.	150 o.d.

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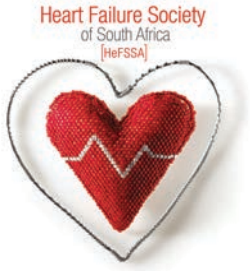
ESC Guideline 2012, pg 21

ACE-inhibitors – special considerations

- Cough is no uncommon (~5%) – often well tolerated with reassurance but may have to switch to ARB
- Angio-oedema – serious complication but rare
- Expect a creatinine rise of up to ~20% - this does not mean one has to stop the drug
- May cause hyperkalaemia
- Postural hypotension a major problem especially with concurrent diuretic use – reduce dosage of diuretic as needed



Pharmacological interventions

- Aldosterone antagonists
- 2 available: spironolactone and eplerenone
- Problems of both: they can cause hyperkalaemia and for this reason are contraindicated in patients with renal failure
- Spironolactone: gynaecomastia

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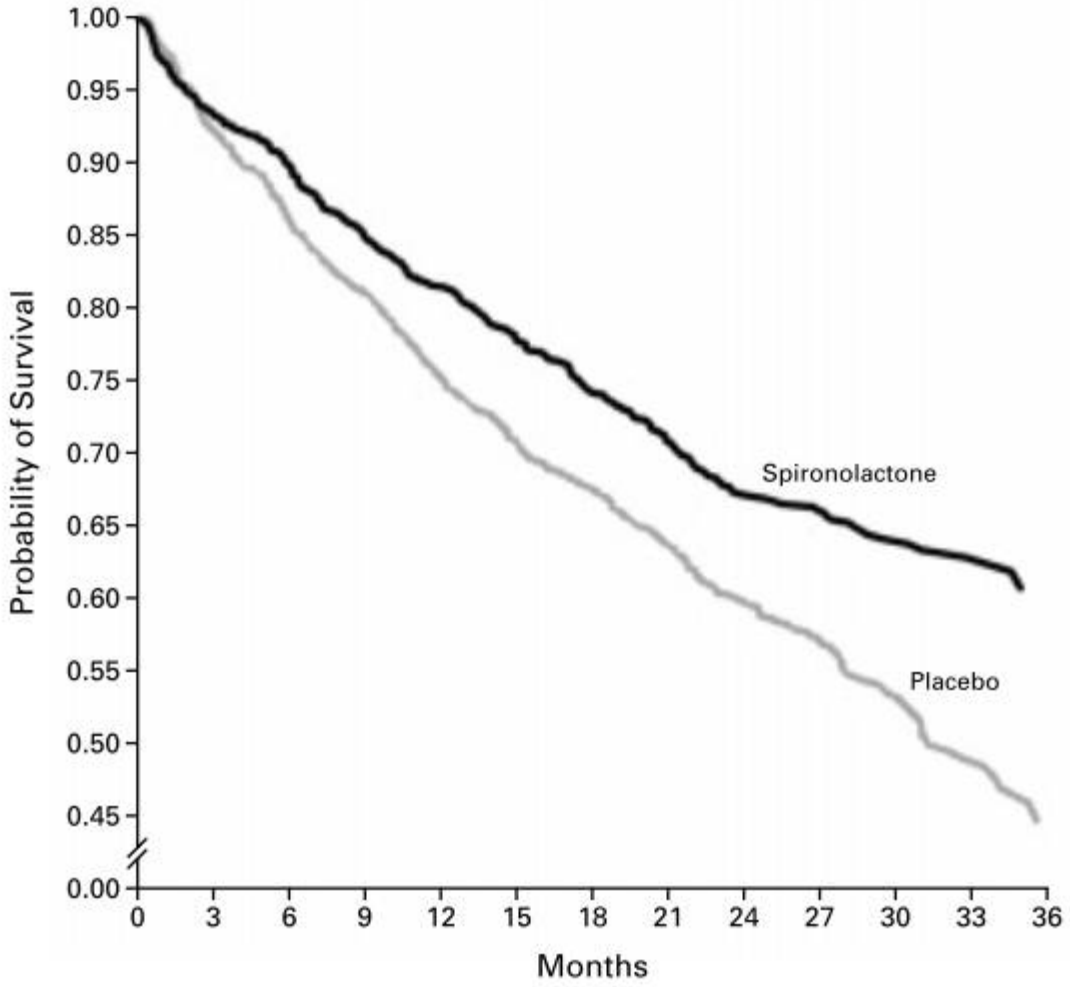

No. at Risk													
Placebo	841	775	723	678	628	592	565	483	379	280	179	92	36
Spironolactone	822	766	739	698	669	639	608	526	419	316	193	122	43

Figure 1. Kaplan–Meier Analysis of the Probability of Survival among Patients in the Placebo Group and Patients in the Spironolactone Group.

The risk of death was 30 percent lower among patients in the spironolactone group than among patients in the placebo group ($P<0.001$).

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N Engl J Med 1999:341:709-17

Aldosterone antagonists are now indicated in class 2 NYHA (not only class 3 NYHA) patients (evidence for class eplerenone)

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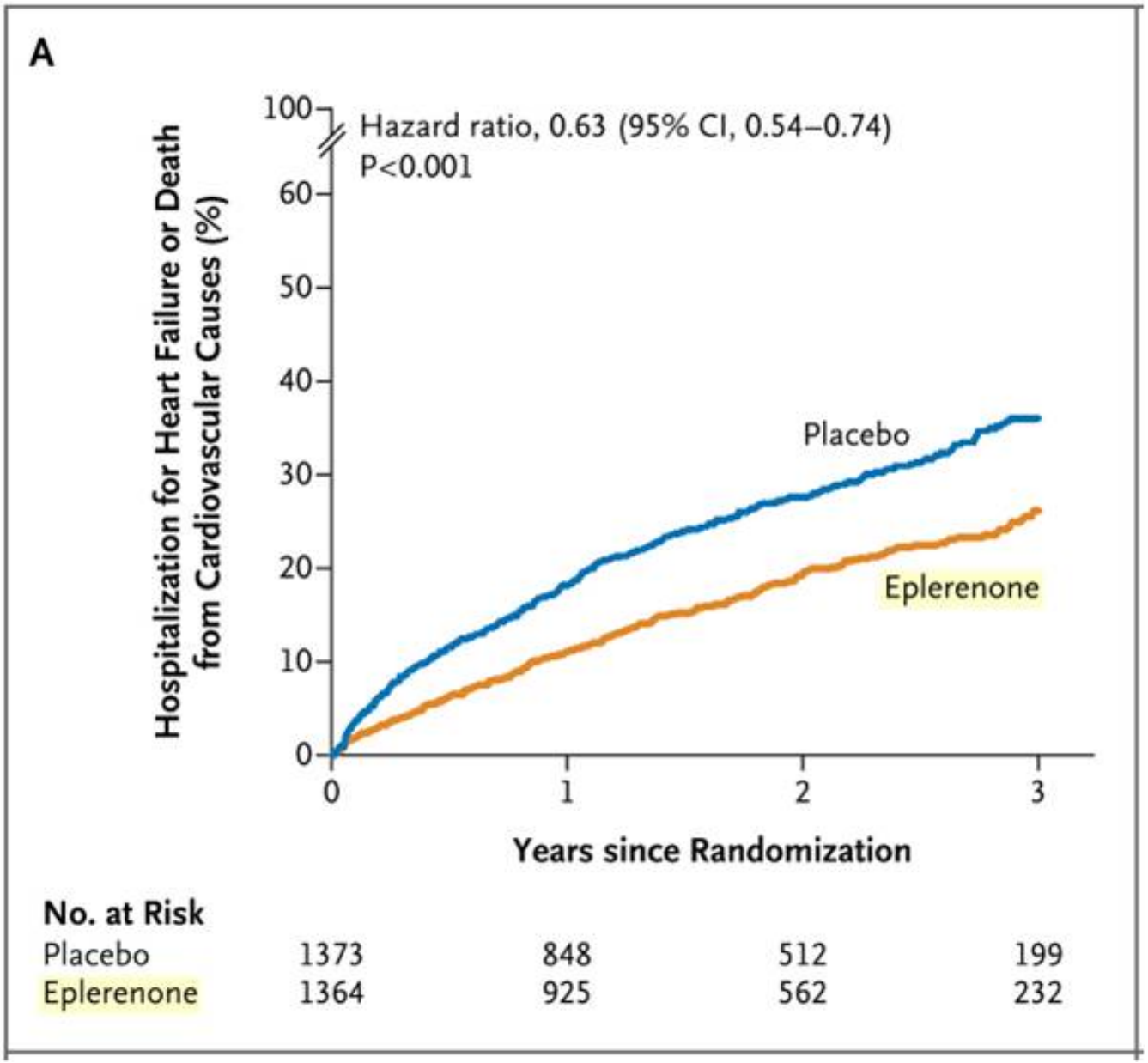

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N Engl J Med 2011;364:11-21.

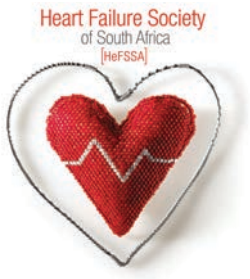
	Starting dose (mg)	Target dose (mg)
MRA		
Eplerenone	25 o.d.	50 o.d.
Spironolactone	25 o.d.	25–50 o.d.

Heart Failure Society of South Africa [HeFSSA]

ESC Guideline 2012, pg 21

Back to our patient….

- Started on:
  - Carvedilol 3.125 mg 2x/day gradually increased to 12.5 mg 2x/day (he did not tolerate a higher dose, felt “ill” on 25 mg 2x/day
  - Valsartan 80 mg 2x/day
  - Furosemide 40 mg 2x/day
  - Continued Aspirin and Simvastatin
- Advised to avoid NSAIDs
- Followed up after 1 month of above therapy



Did not feel better! STILL short of breath on minimal exertion

What next?

- Escalate therapy with one of the following:
  - Add an ARB
  - Ivabradine
  - Digoxin
  - Hydrallazine and long-acting nitrates

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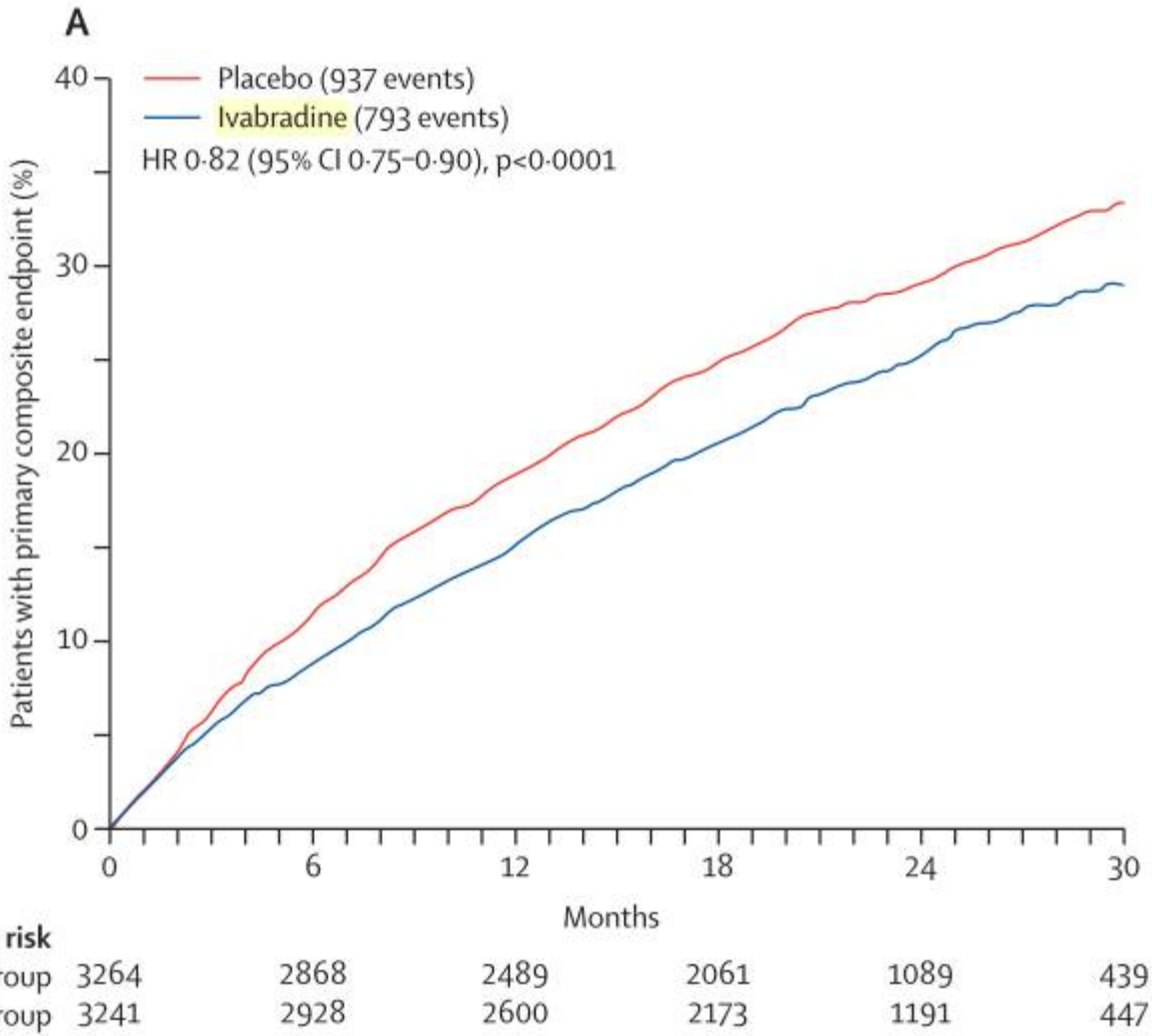
Ivabradine (SHIFT trial)



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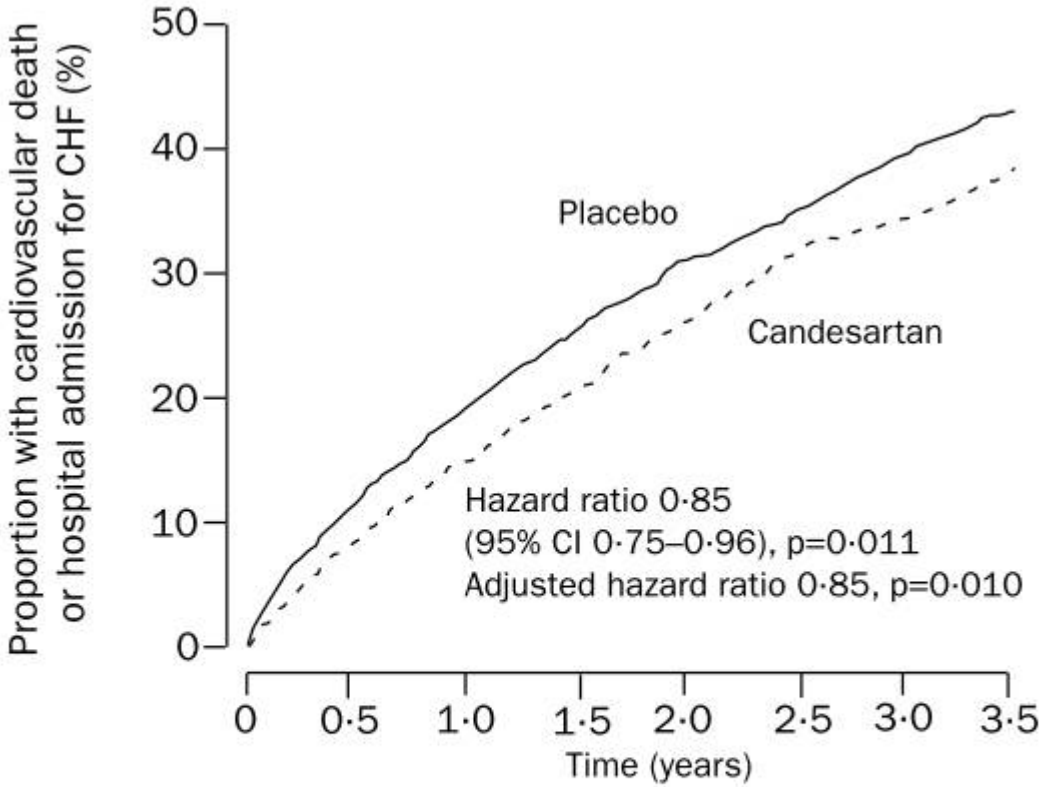
Lancet 2010; 376: 875–85

What is Ivabradine?

- Slow down the discharge rate of the sinus node by inhibiting the If current
- It does NOT work for rate control in AF as it only works on the sinus node
- It is available in South Africa for patients with symptomatic heart failure who have resting heart rates >77 bpm
- Most notable side-effect: phosphenes

ARB



Number at risk

Candesartan	1276	1176	1063	948	457
Placebo	1272	1136	1013	906	422

Figure 2: **Kaplan-Meier cumulative event curves for primary outcome**

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Lancet 2003; **362:** 767–71

	Candesartan (n=1276)	Placebo (n=1272)	p
Cause of discontinuation			
Hypotension	58 (4·5)	40 (3·1)	0·079
Increase in creatinine	100 (7·8)	52 (4·1)	0·0001
Hyperkalaemia	44 (3·4)	9 (0·7)	<0·0001
Any adverse event or laboratory abnormality	309 (24·2)	233 (18·3)	0·0003

Table 4: **Permanent study-drug discontinuation for adverse events**

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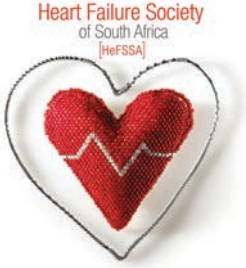


Lancet 2003; **362:** 767–71

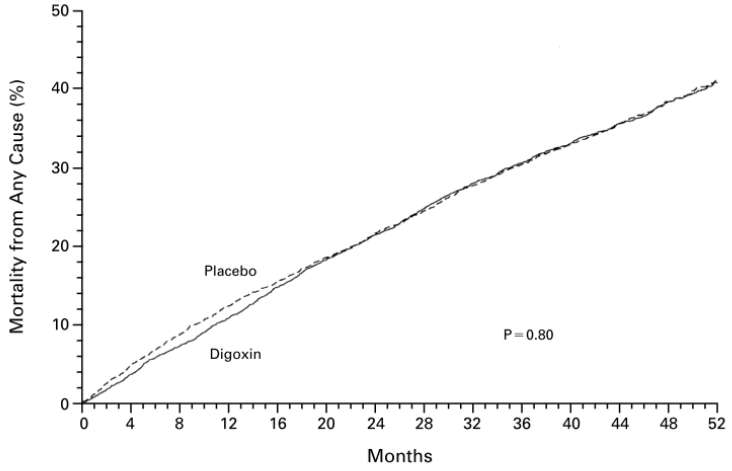
Digoxin

The New England Journal of Medicine

VOLUME 336 FEBRUARY 20, 1997 NUMBER 8

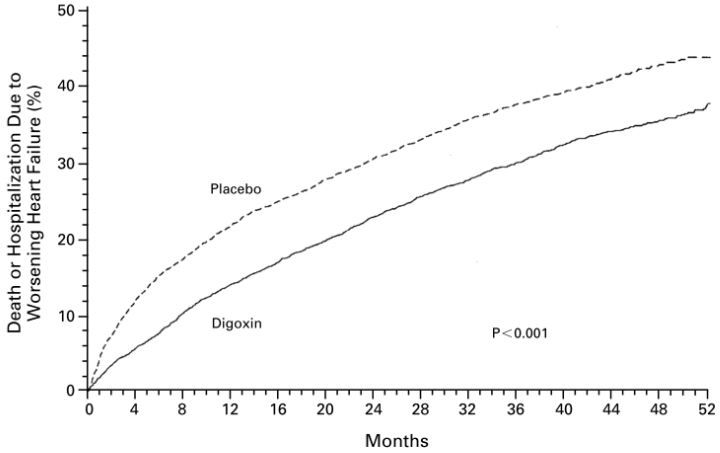
THE EFFECT OF DIGOXIN ON MORTALITY AND MORBIDITY IN PATIENTS WITH HEART FAILURE

THE DIGITALIS INVESTIGATION GROUP*



No. of Patients at Risk														
Placebo	3403	3239	3105	2976	2868	2758	2652	2551	2205	1881	1506	1168	734	339
Digoxin	3397	3269	3144	3019	2882	2759	2644	2531	2184	1840	1475	1156	737	335

Figure 1. Mortality in the Digoxin and Placebo Groups.
The number of patients at risk at each four-month interval is shown below the figure.



No. of Patients at Risk														
Placebo	3403	2915	2674	2473	2328	2197	2071	1954	1659	1397	1111	859	546	250
Digoxin	3397	3120	2888	2696	2544	2392	2241	2115	1825	1521	1188	916	578	255

Figure 3. Incidence of Death or Hospitalization Due to Worsening Heart Failure in the Digoxin and Placebo Groups.
The number of patients at risk at each four-month interval is shown below the figure.

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N Engl J Med 1997; 336: 525

Hydrallazine (225 mg) and long-acting nitrates (60 mg)

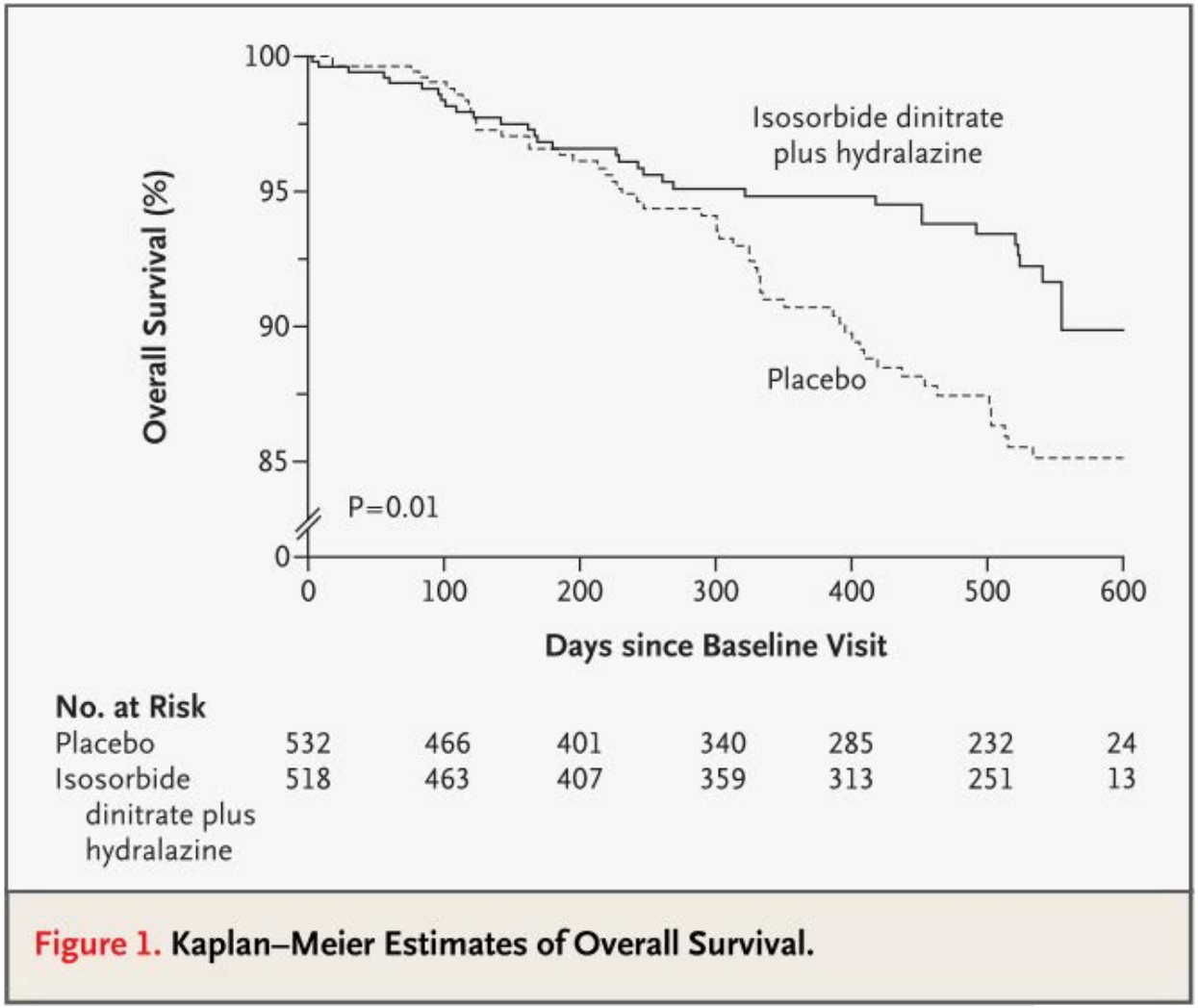

Figure 1. Kaplan–Meier Estimates of Overall Survival.

Heart Failure Society of South Africa [HeFSSA]

N Engl J Med 2004;351:2049-57.

In our patient….

- Ivabradine was not readily accessible
- ARB not added as his potassium on spironolactone and ACE-inhibitor was already 5.2
- Digoxin added

Heart Failure Society of South Africa [HeFSSA]

Should he be on a statin?

Effect of rosuvastatin in patients with chronic heart failure (the GISSI-HF trial): a randomised, double-blind, placebo-controlled trial

*GISSI-HF investigators**

Summary

Background Large observational studies, small prospective studies and post-hoc analyses of randomised clinical trials have suggested that statins could be beneficial in patients with chronic heart failure. However, previous studies have been methodologically weak. We investigated the efficacy and safety of the statin rosuvastatin in patients with heart failure.

Lancet 2008; 372: 1231–39

Published Online
August 31, 2008
DOI:10.1016/S0140-6736(08)61240-4

ORIGINAL ARTICLE

Rosuvastatin in Older Patients with Systolic Heart Failure

John Kjekshus, M.D., Ph.D., Eduard Apetrei, M.D., Ph.D., Vivencio Barrios, M.D., Ph.D., Michael Böhm, M.D., Ph.D., John G.F. Cleland, M.D., Jan H. Cornel, M.D., Ph.D., Peter Dunselman, M.D., Ph.D., Cândida Fonseca, M.D., Assen Goudev, M.D., Ph.D., Peer Grande, M.D., Ph.D., Lars Gullestad, M.D., Ph.D., Åke Hjalmarson, M.D., Ph.D., Jaromir Hradec, M.D., Ph.D., András Jánosi, M.D., D.Sc., Gabriel Kamenský, M.D., Ph.D., Michel Komajda, M.D., Jerzy Korewicki, M.D., Ph.D., Timo Kuusi, M.D., Ph.D., François Mach, M.D., Vyacheslav Mareev, M.D., Ph.D., John J.V. McMurray, M.D., Naresh Ranjith, M.D., Maria Schaufelberger, M.D., Ph.D., Johan Vanhaecke, M.D., Ph.D., Dirk J. van Veldhuisen, M.D., Ph.D., Finn Waagstein, M.D., Ph.D., Hans Wedel, Ph.D., and John Wikstrand, M.D., Ph.D., for the CORONA Group*

N Engl J Med 2007;357:2248-61

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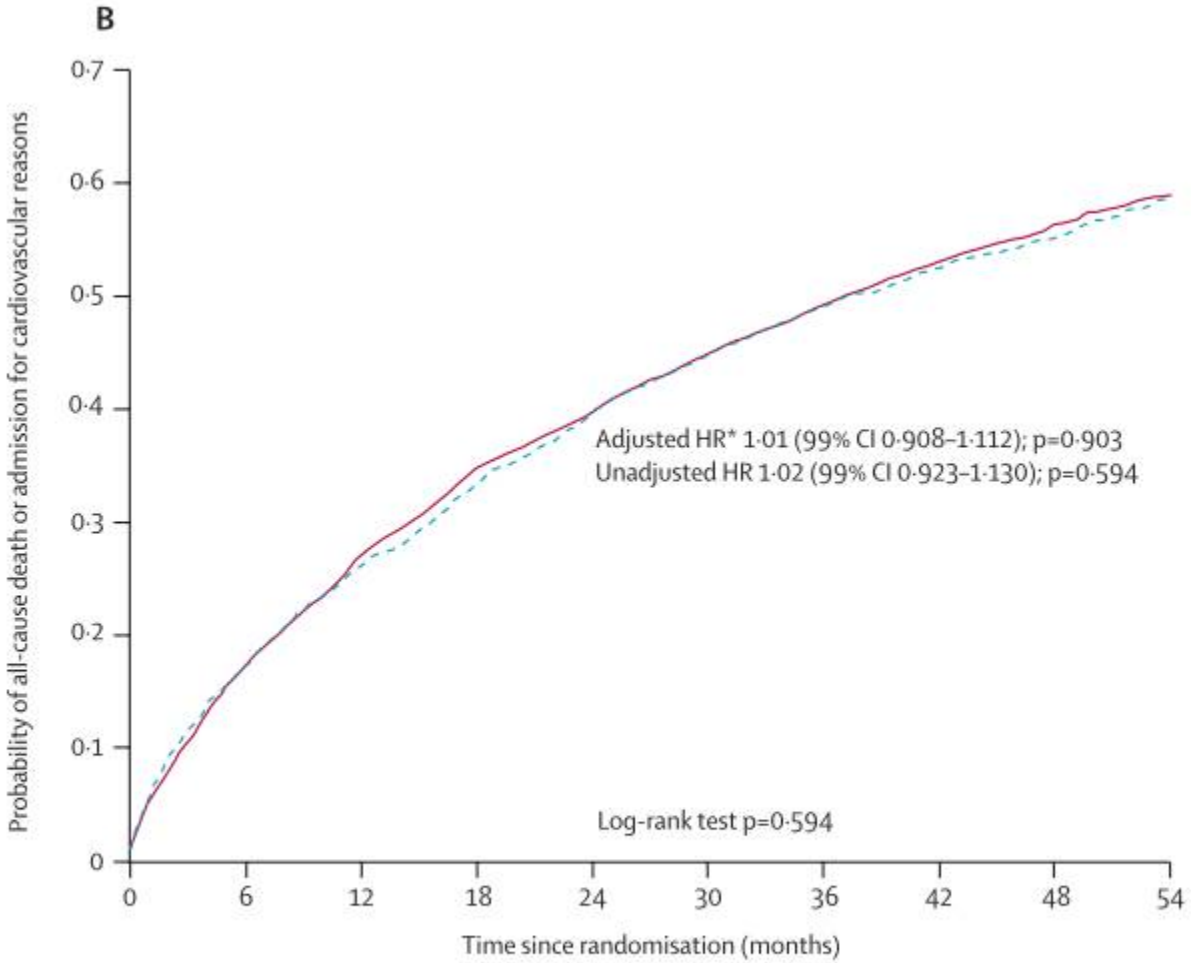

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Lancet 2008; 372: 1231–39

In addition….

- Patients with symptomatic heart failure despite good medical therapy should be considered for cardiac resynchronisation therapy (CRT)
- CRT is achieved by the implantation of a biventricular pacemaker

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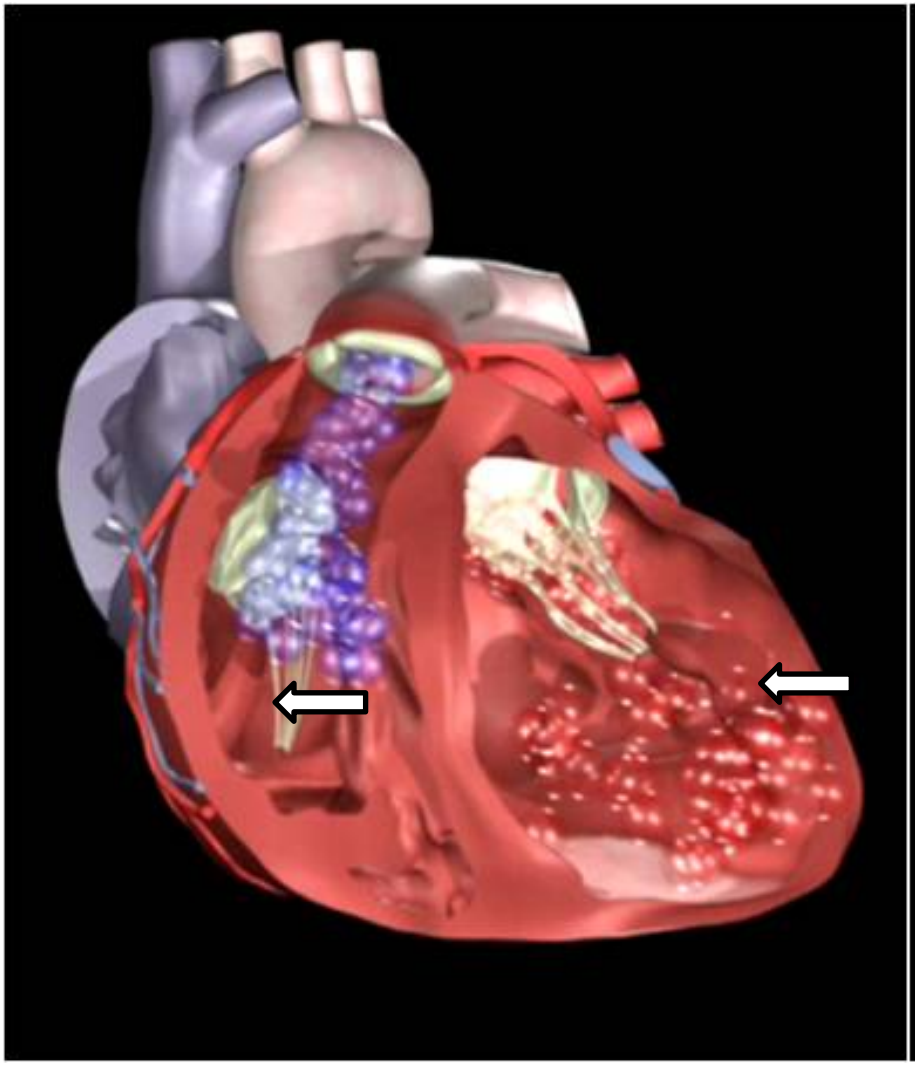
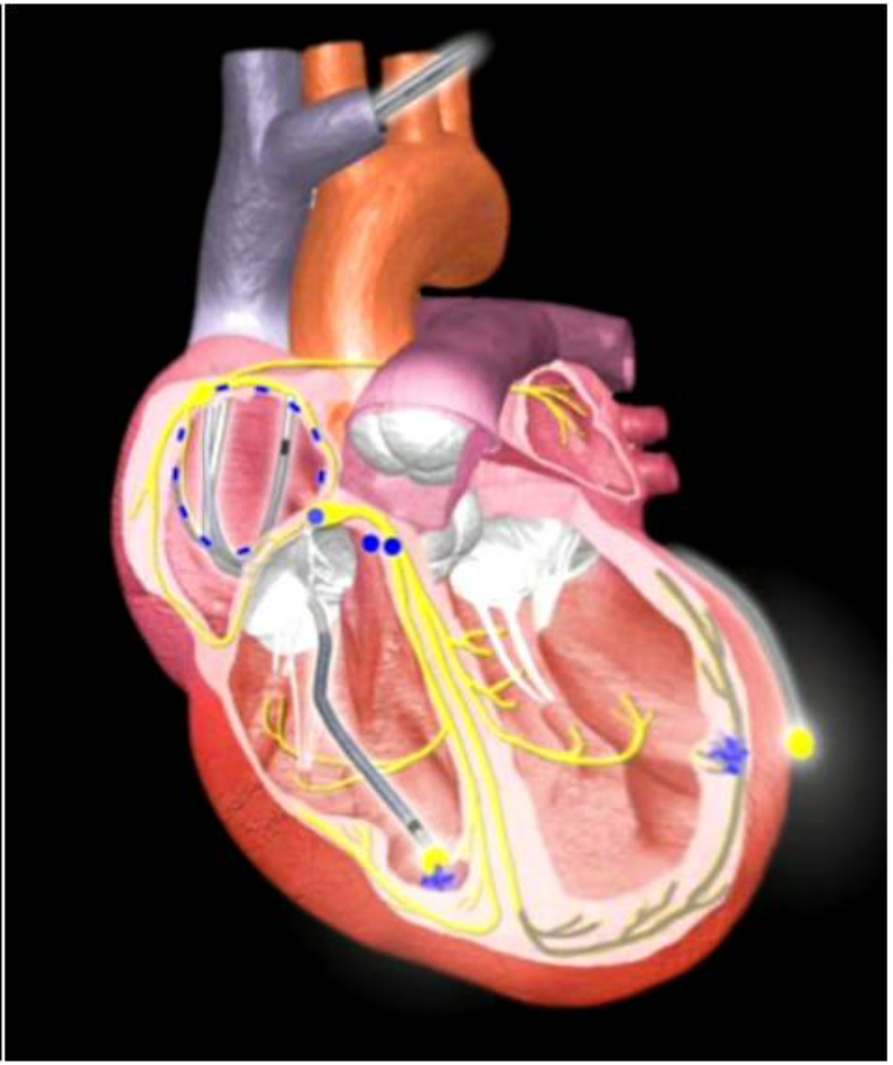
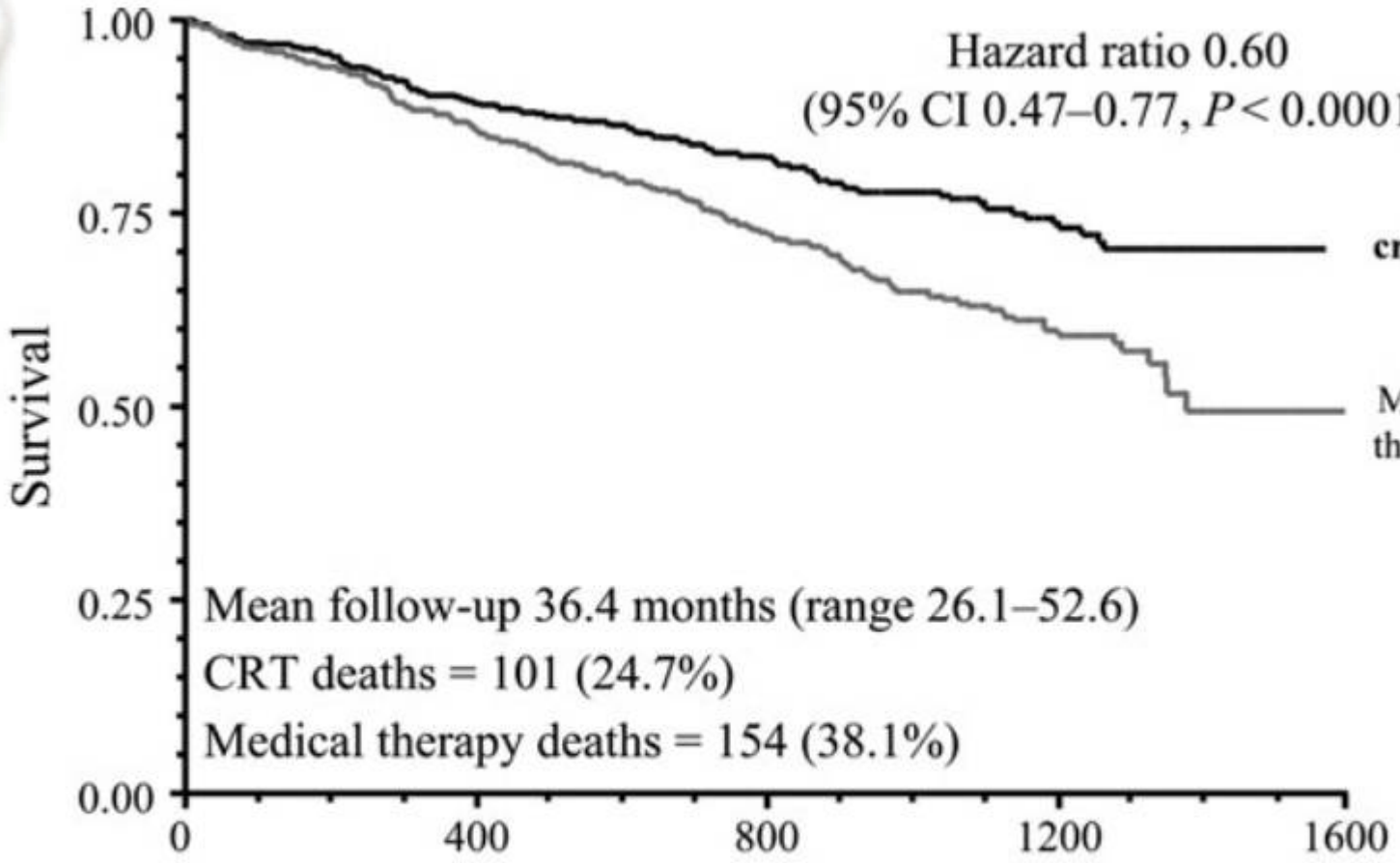
What is “CRT”?







Number at risk

CRT	409	383	358	338	209	85	9
Medical therapy	404	372	331	298	178	63	6

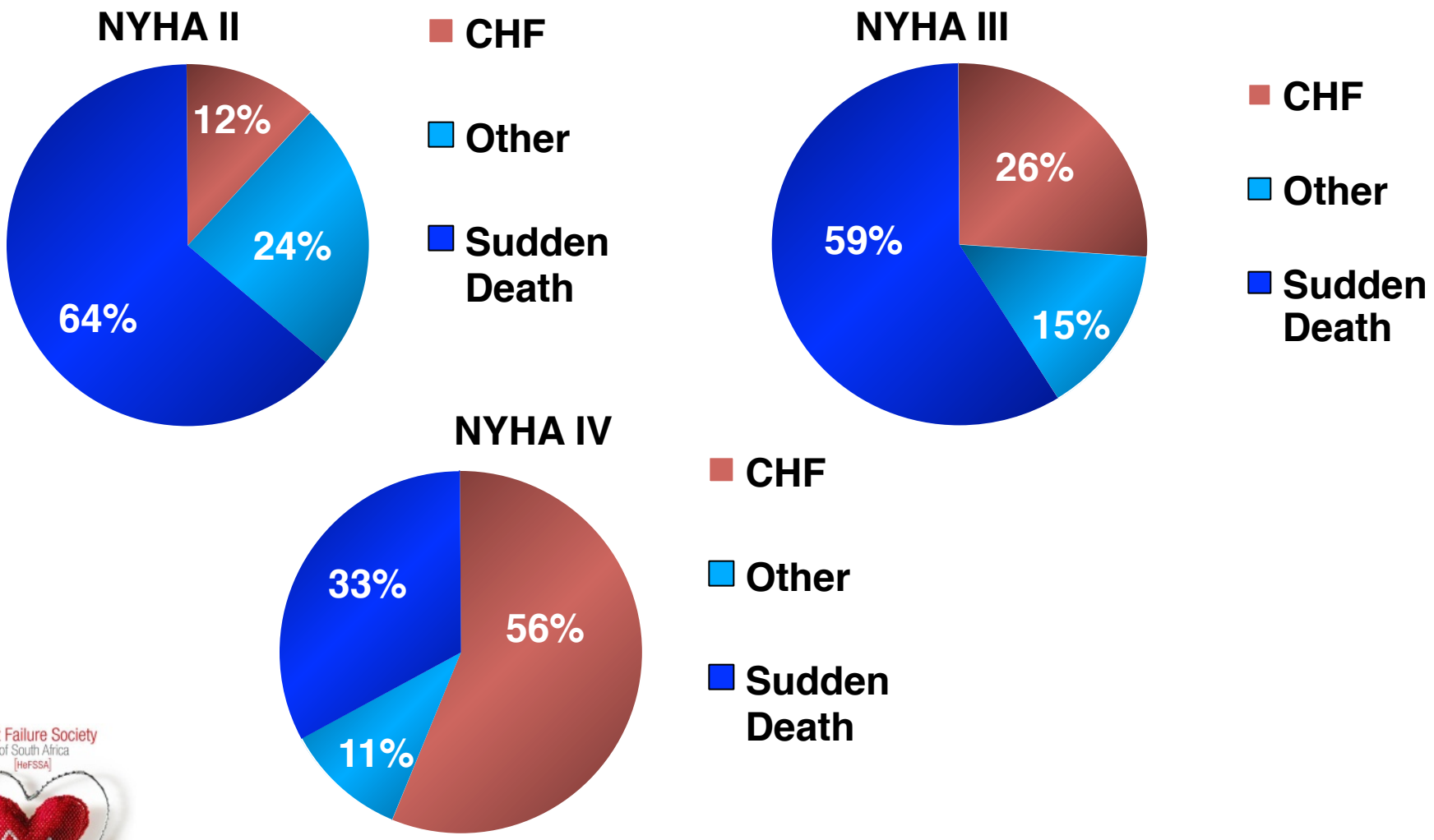
Figure 1 The Kaplan–Meier estimates of the time to all-cause mortality.

European Heart Journal (2006) **27**, 1928–1932

One more thing….

- The cause of death in many patients with cardiomyopathies is sudden cardiac death secondary to malignant ventricular tachyarrhythmias
- Anti-arrhythmics do NOT work to prevent these
- The only therapy available for this is implantation of an internal cardioverter defibrillator (ICD)

Severity of Heart Failure



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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.

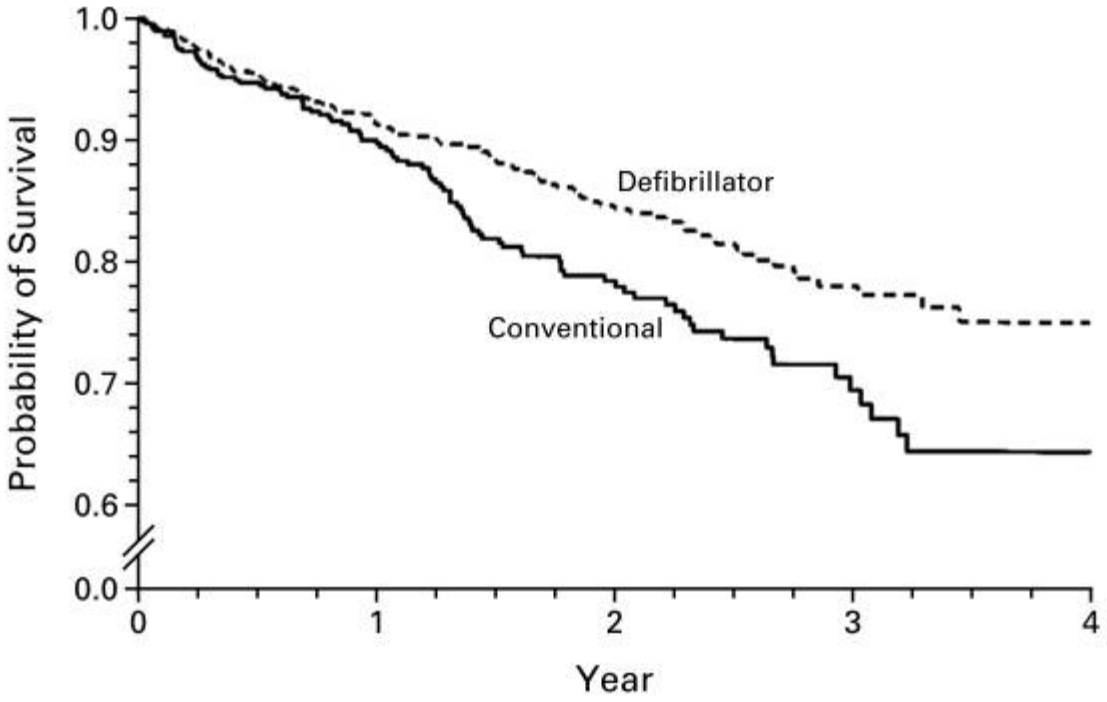
Heart Failure Society of South Africa [HeFSSA]

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

ICD's save lives!



No. at Risk					
Defibrillator	742	503 (0.91)	274 (0.84)	110 (0.78)	9
Conventional	490	329 (0.90)	170 (0.78)	65 (0.69)	3

Figure 2. Kaplan–Meier Estimates of the Probability of Survival in the Group Assigned to Receive an Implantable Defibrillator and the Group Assigned to Receive Conventional Medical Therapy.

The difference in survival between the two groups was significant (nominal P=0.007, by the log-rank test).

Heart Failure Society of South Africa [HeFSSA]

N Engl J Med 2002;346:877-83.

Our patient…..

- Received a combination device: biventricular pacemaker with ICD function
- He improved to the extent that we were able to increase the carvedilol to target dose
- He is now off diuretic completely
- Has had one ICD discharge – inappropriate, he had gone into AF which was then cardioverted by the ICD
- Has been initiated on warfarin for this episode of atrial fibrillation

Do not forget that some patients may qualify for heart transplantation/LV assist devices

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