The Fantastic Four of Heart Failure Therapy: A tailored approach

Jens Hitzeroth

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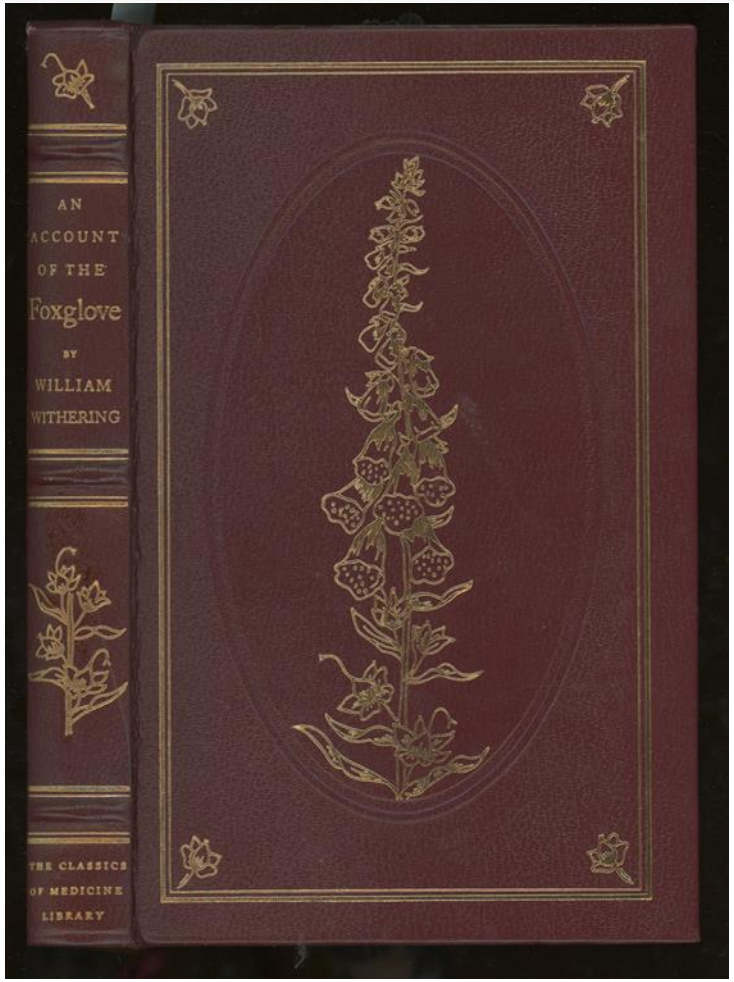

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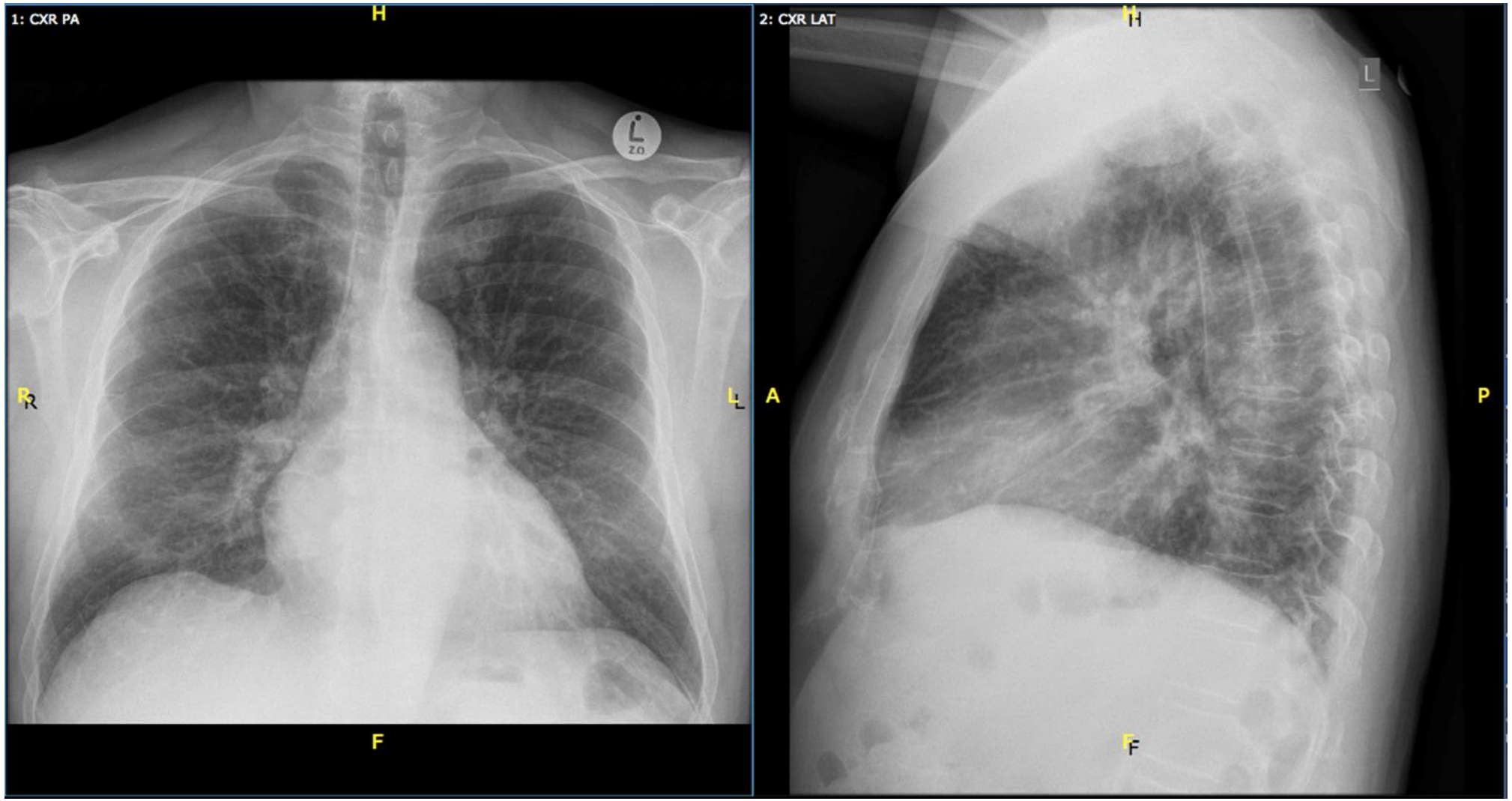
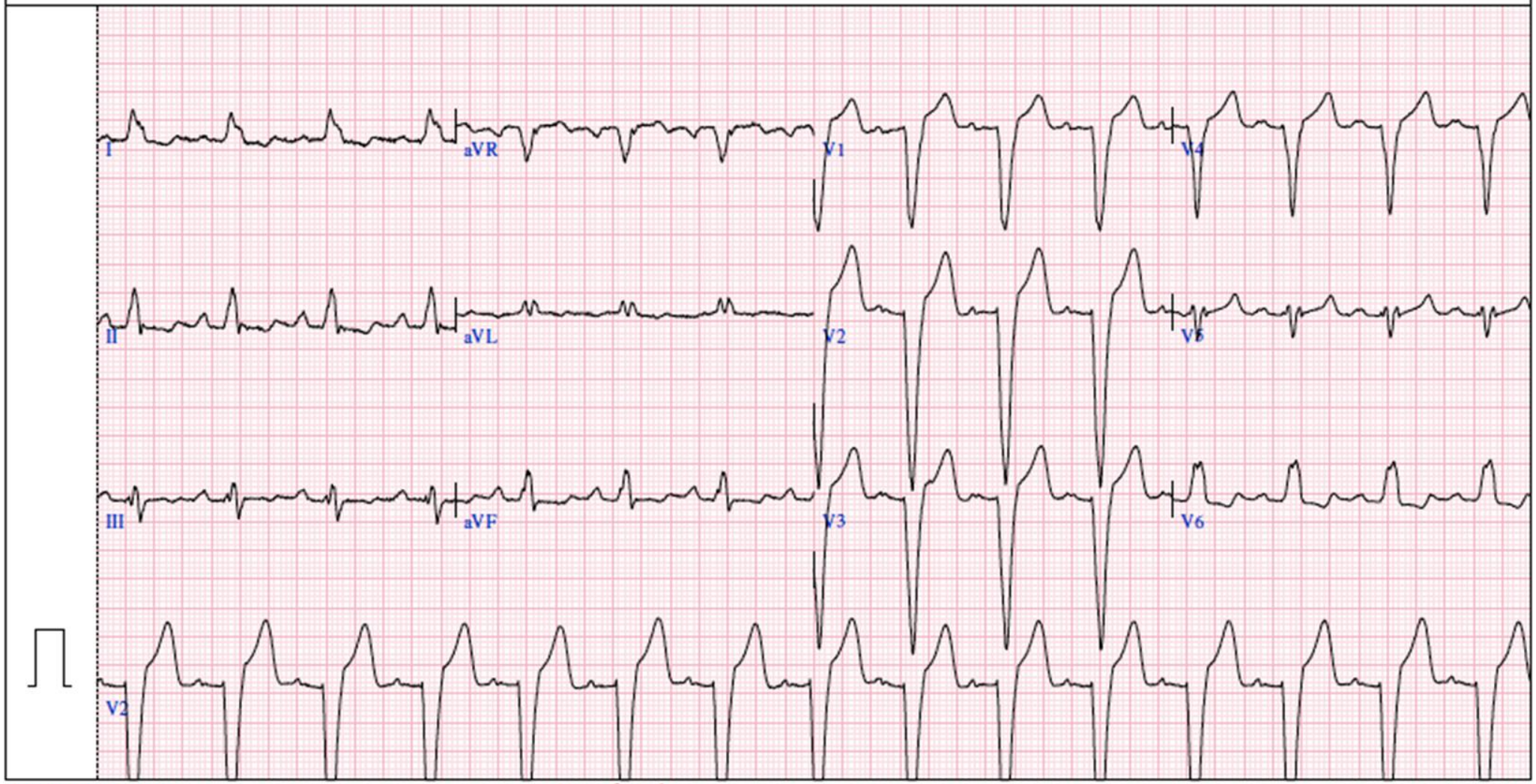
Case - HFrEF

- 45 year old male
- 6/12 history of fatigue
- 2/12 worsening dyspnoea culminating in admission to Milnerton MedicClinic with heart failure
- No chest pain
- No syncope or palpitations
- No other systemic complaints
- Father died of some form of heart disease at a fairly young age
- No recent viral illness
- Non-smoker, occasional alcohol use only
- No history of HPT or DM


1: CXR PA
H
R
L
F
2: CXR LAT
H
L
A
P
F

Vent. Rate	89 bpm	**Technician:**	L Papenfus
PR interval	192 ms	**Interpretation:**	
QRS duration	158 ms	Normal sinus rhythm	
QT/QTC	422/513 ms	Left bundle branch block	
P-R-T axes	73/31/125 °	Abnormal ECG	
P duration	112 ms		
RR/PP interval	672/670 ms		

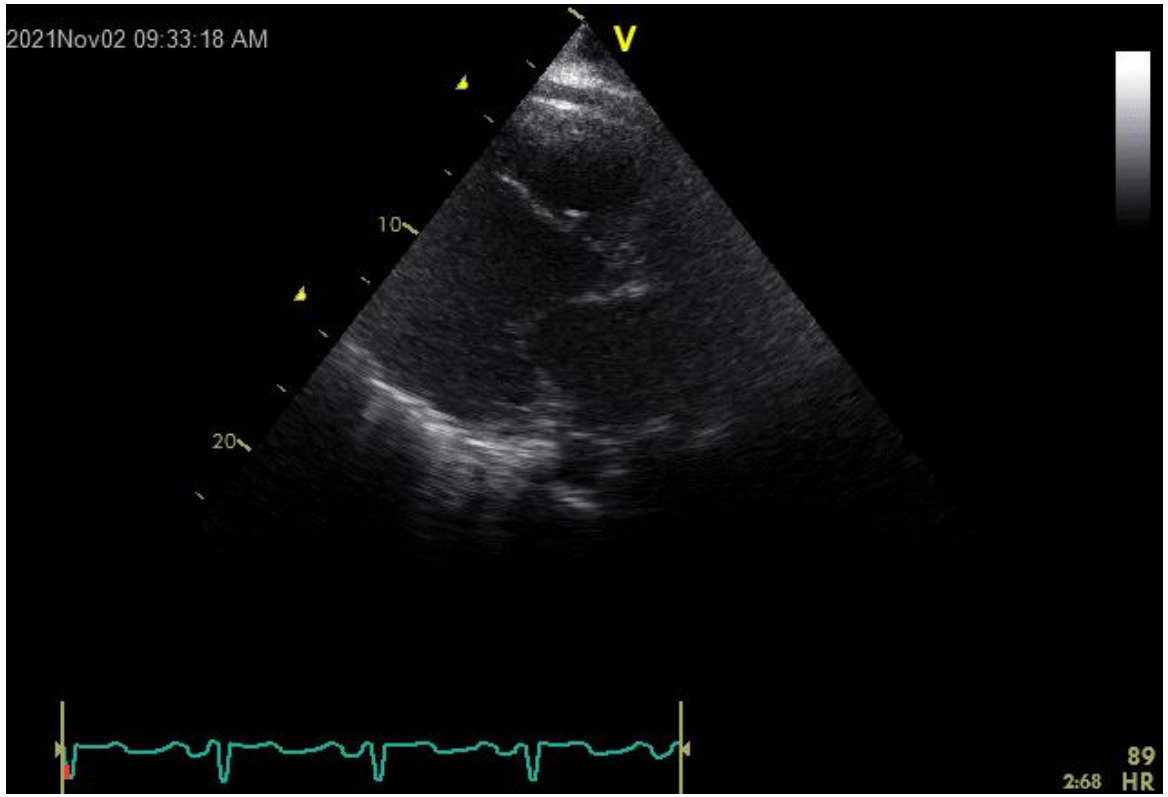


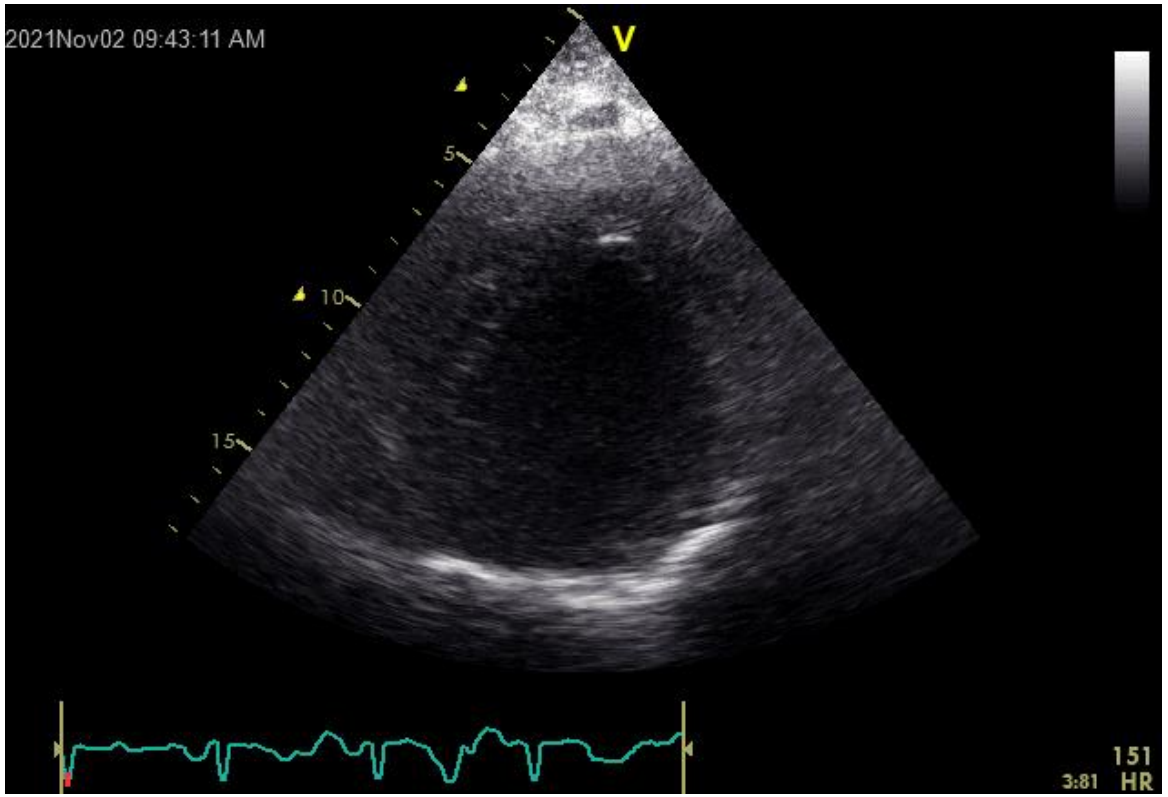
GE CASE V6.72(0)

Unconfirmed

25mm/s 10mm/mV 0.01-150Hz 50Hz Spline 12SL V21

Attending MD: Dr Jens Hitzeroth





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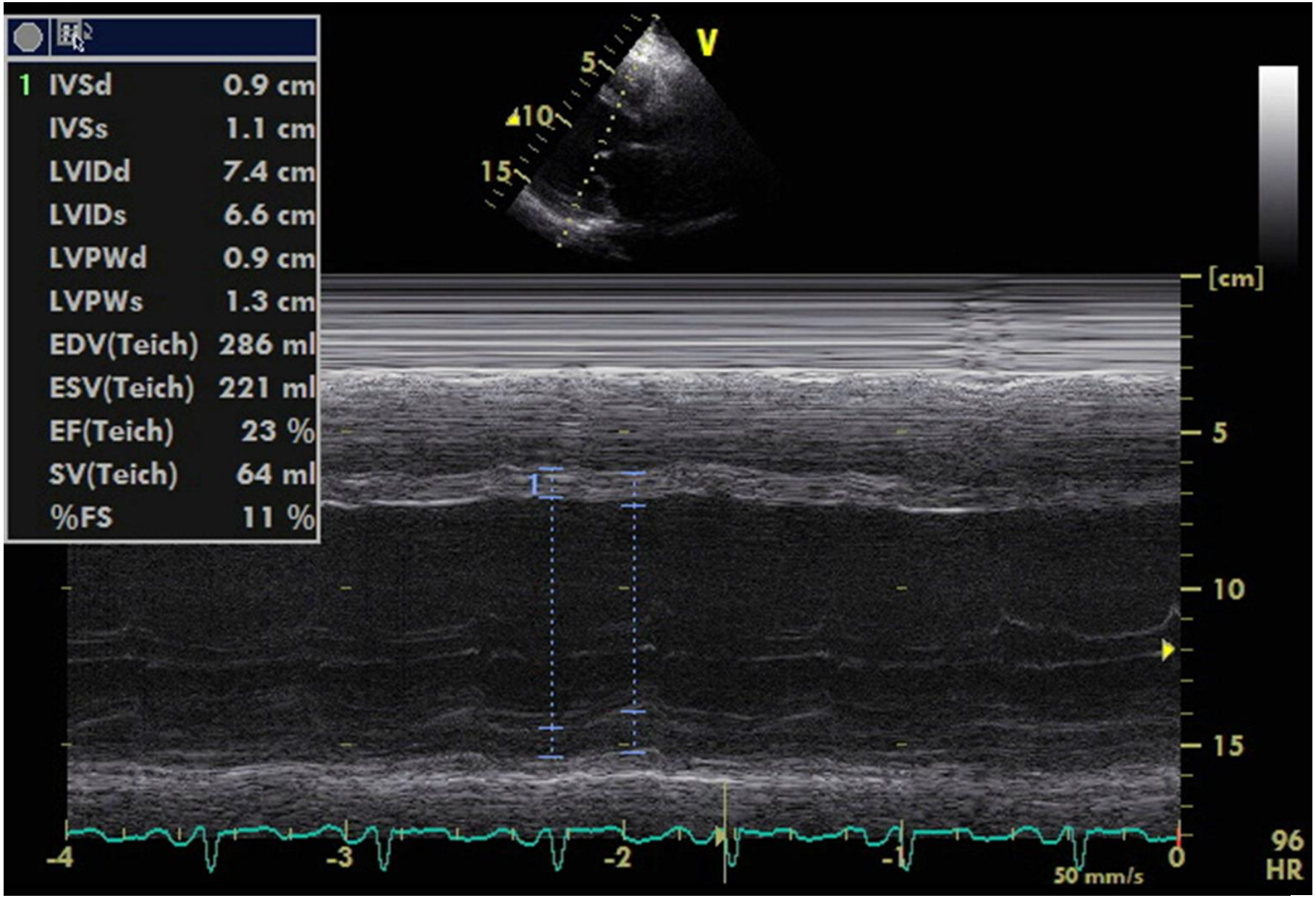

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Test	ABN	Result	Reference	Units
FULL BLOOD COUNT AND ESR				
Haemoglobin		14.8	13.0-17.0	g/dl
Red Cell Count		4.71	4.50-5.50	10 12/l
Haematocrit		42.1	40.0-50.0	%
MCV		89.4	79.1-98.9	fl
MCH		31.4	27.0-32.0	pg
MCHC		35.2	31.0-37.0	g/dl
RDW		11.9	10.0-16.3	%
White Cell Count		5.12	3.92-9.88	10 9/l
Neutrophils		55.7		%
Neutrophils Abs		2.86	2.00-7.50	10 9/l
Lymphocytes		31.3		%
Lymphocytes Abs		1.60	1.00-4.00	10 9/l
Monocytes		10.4		%
Monocytes Abs		0.53	0.18-1.00	10 9/l
Eosinophils		2.0		%
Eosinophils Abs		0.10	0.00-0.45	10 9/l
Basophils		0.6		%
Basophils Abs		0.03	0.00-0.20	10 9/l
Platelet Count		210	150-450	10 9/l
ESR		4	0-15	mm/hr

-------- ENDOCRINOLOGY --------				
Tests	**Result**	**Flag**	**Range**	**Unit**
FREE T4	10.7		7.2 - 16.4	pmol/L
S-TSH	2.13		0.38 - 5.33	mIU/L
THYROID COMMENT	.			

The thyroid results suggest EUTHYROIDISM.
Patients on thyroid replacement therapy:
- the dose is probably adequate.

NT-proBNP	1133		< 125	pg/mL

INTERPRETATION

< 125pg/ml : Congestive Cardiac Failure excluded.
Acute presentations:
< 300pg/ml : Acute CCF unlikely.
> 1800 pg/ml: Acute CCF likely.
300 - 1800 pg/ml: Age related cut-off values required:

Patient age	NT-proBNP values:	
<50 yrs	300 - 450	>450
50 - 75 yrs	300 - 900	>900
>75 yrs	300 - 1800	>1800
Interpretation	Acute CCF less likely. Consider alternative causes.	Acute CCF likely.

Other causes for elevated levels: Acute Coronary Syndrome, pulmonary embolism, shock, atrial arrhythmias, severe pneumonia, renal insufficiency, prior CCF.

BIOCHEMISTRY

Test	Result			Reference		
UE CREATININE(UREA+ELECT+CREAT						
S-SODIUM	135	mmol/L	L	136	-	145
S-POTASSIUM	4.6	mmol/L		3.5	-	5.1
S-CHLORIDE	98	mmol/L		98	-	107
S-TOT. CO2 (bicarbonate)	28	mmol/L		21	-	29
S-UREA	5.8	mmol/L		2.1	-	7.1
S-CREATININE	83	umol/L		80	-	115
eGFR (CKD-EPI-mL/min/1.73m2)	> 89					

COMMENT:
Normal eGFR.

For consultation by referring doctors only, please call:

Dr Willie Hoffman (021) 551 6372
Dr Peter P Tsaagane (011) 710 8050
Dr Fierdoz Omar (021)
Dr Manuel v Deventer (011) 242-7303

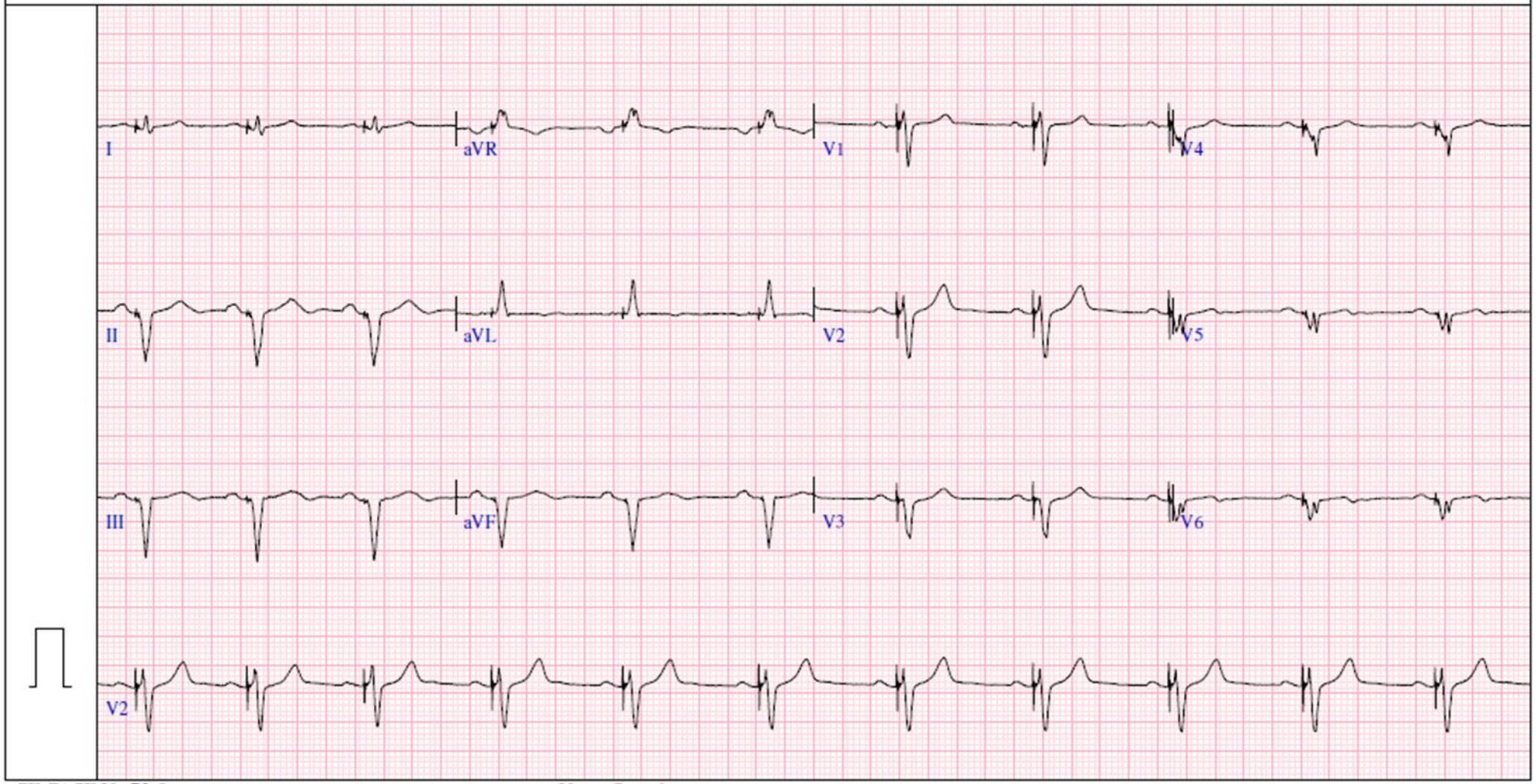
Management

- Does he need additional investigations?
- What therapy is required?
- Would he be a candidate for some form of device?
- What is his prognosis?

12.11.2018 Male
16:05:01 48yrs

Vent. Rate	66 bpm
PR interval	148 ms
QRS duration	130 ms
QT/QTC	438/459 ms
P-R-T axes	67/-81/57 °
P duration	126 ms
RR/PP interval	906/905 ms

Technician: L Papenfus
Interpretation:
Electronic ventricular pacemaker



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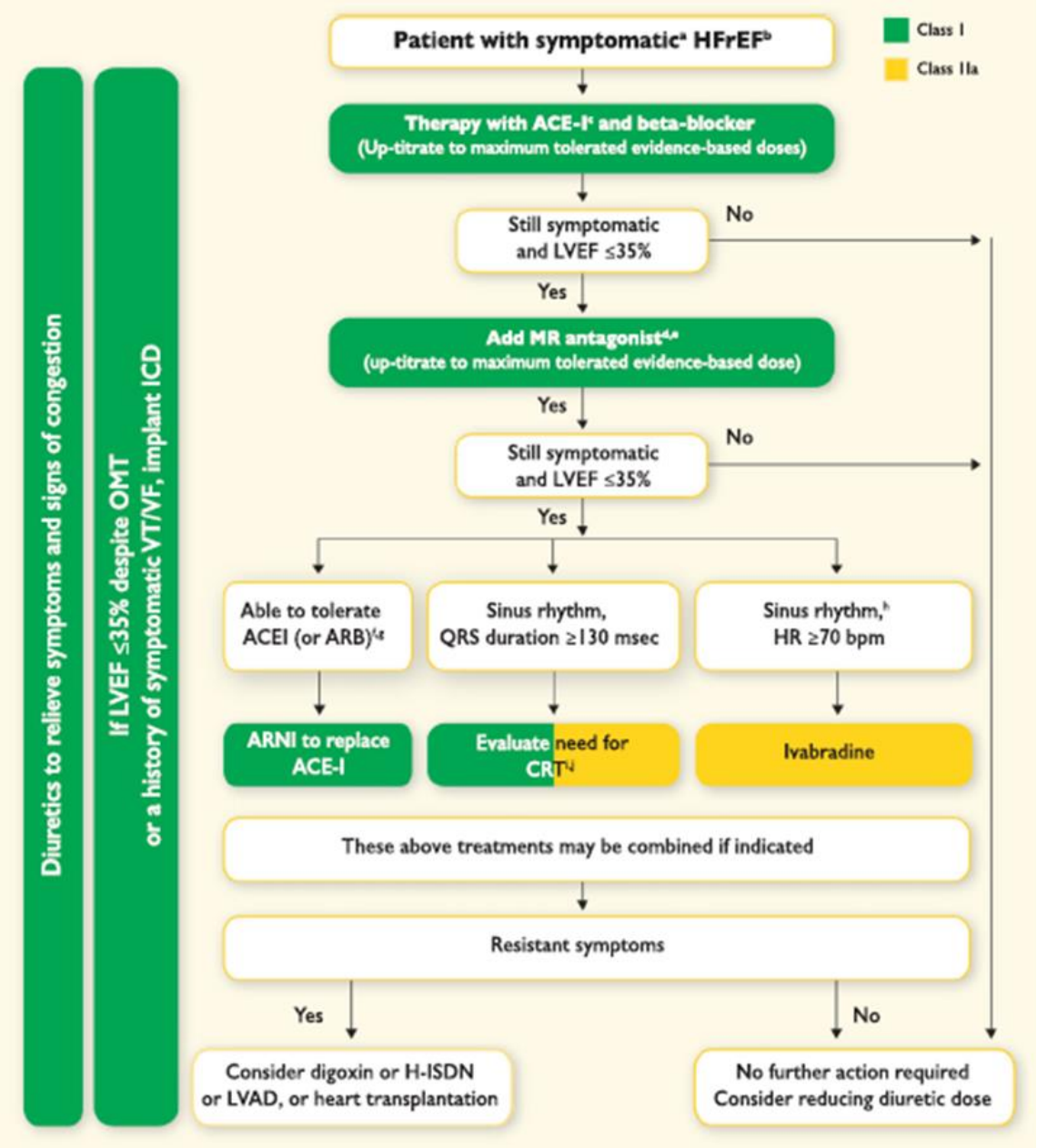

European Heart Journal 2016; 37: 2129–2200

	Starting dose	Target dose
ACE-I		
Captopril[a]	6.25 mg *t.i.d.*	50 mg *t.i.d.*
Enalapril	2.5 mg *b.i.d.*	10–20 mg *b.i.d.*
Lisinopril[b]	2.5–5 mg *o.d.*	20–35 mg *o.d.*
Ramipril	2.5 mg *b.i.d.*	5 mg *b.i.d.*
Trandolapril[a]	0.5 mg *o.d.*	4 mg *o.d.*
ARNI		
Sacubitril/valsartan	49/51 mg *b.i.d.*[c]	97/103 mg *b.i.d.*
Beta-blockers		
Bisoprolol	1.25 mg *o.d.*	10 mg *o.d.*
Carvedilol	3.125 mg *b.i.d.*	25 mg *b.i.d.*[e]
Metoprolol succinate (CR/XL)	12.5–25 mg *o.d.*	200 mg *o.d.*
Nebivolol[d]	1.25 mg *o.d.*	10 mg *o.d.*
MRA		
Eplerenone	25 mg *o.d.*	50 mg *o.d.*
Spironolactone	25 mg *o.d.*[f]	50 mg *o.d.*
SGLT2 inhibitor		
Dapagliflozin	10 mg *o.d.*	10 mg *o.d.*
Empagliflozin	10 mg *o.d.*	10 mg *o.d.*
Other agents		
Candesartan	4 mg *o.d.*	32 mg *o.d.*
Losartan	50 mg *o.d.*	150 mg *o.d.*
Valsartan	40 mg *b.i.d.*	160 mg *b.i.d.*
Ivabradine	5 mg *b.i.d.*	7.5 mg *b.i.d.*
Vericiguat	2.5 mg *o.d.*	10 mg *o.d.*
Digoxin	62.5 µg *o.d.*	250 µg *o.d.*
Hydralazine/ Isosorbide dinitrate	37.5 mg *t.i.d.*/20 mg *t.i.d.*	75 mg *t.i.d.*/40 mg *t.i.d.*

Chronic Heart Failure: Diagnosis and Treatment Algorithm 2020

adapted from ESC HF guideline 2016[1]

Algorithm for the diagnosis of Heart Failure with Reduced Ejection Fraction (HF-REF) or LVEF<40%*

General Assessment

- Risk factor profile (hypertension etc.)
- Family History
- Recent pregnancy < 1 year
- Previous chemotherapy

Symptoms

- Shortness of breath - on effort
  - lying flat
  - during the night
- New cough
- Ankle swelling
- Irregular or fast palpitation
- Effort fatigue
- More frequent nocturia

Signs

Signs of congestion:
- raised JVP
- (tender) hepatomegaly
- peripheral oedema
- ascites

Chest signs:
- inspiratory crackles
- pleural effusion

Signs of heart disease:
- tachycardia
- displaced apex beat
- presence of cardiac murmur
- presence of S3
- cool peripheries

Suspected **Heart Failure / LV Dysfunction** because of signs and symptoms

↓

Assess presence of cardiac disease by ECG, CXR and/or NTproBNP / BNP

→ Normal → HF-REF unlikely

↓ Any abnormalities

Imaging by Echocardiography

→ Normal → HF-REF excluded

↓ LVEF<40%

Assess aetiology, precipitating factor/s and NYHA functional class

→ Additional diagnostic tests in selected cases → Referral to specialist for e.g. CT Coronary Angiogram, cardiac catheterisation, MRI, endomyocardial biopsy

↓ *Choose* ***THERAPY***

Holistic Care

- Fluid restriction ≤ 1.5L
- Salt restriction (in hypertensives only)
- Exercise (once stabilised)
- Heart failure management programme
- Avoid : NSAID, glitazones, CCB (except amlodipine, felodipine)
- Palliative care

Management of HF-REF

Therapy that reduces:

Mortality

ARNI
ACE-I / ARB
B Blocker
Aldosterone Antagonist (MRA)
Hydralazine + Nitrate
SGLT2 Inhibitor
Cardiac resynchronisation therapy (CRT-P/D)
ICD

Hospitalisation

Ivabradine
Digoxin

Symptoms

Diuretic
I.V. Iron

AF Management

Cardioversion
AFlutter RF ablation
Pulmonary vein isolation

Surgical

CABG
Valvular intervention
LV assist device
Heart transplant

Precipitating Factors

Mandatory: U & E and creatinine, Glucose, TSH, FBC
Possible: LFT, Iron study, Calcium, hsTroponin T, Trop I

Special consideration

Digoxin (AF, resistant symptomatic heart failure)
Warfarin (AF, LV clot)
NOAC (Non-valvular AF)
Amiodarone (sustain sinus rhythm and reduce VT in ICD patients)
Aldosterone antagonist (Early post-MI heart failure)
ACE-I + ARB if Aldosterone antagonist (MRA) cannot be used

* Patient with HFmrEF (EF 40-49%) can be treated similarly

Heart Failure Society of South Africa (HEFSSA)

www.hefssa.org

SA Heart

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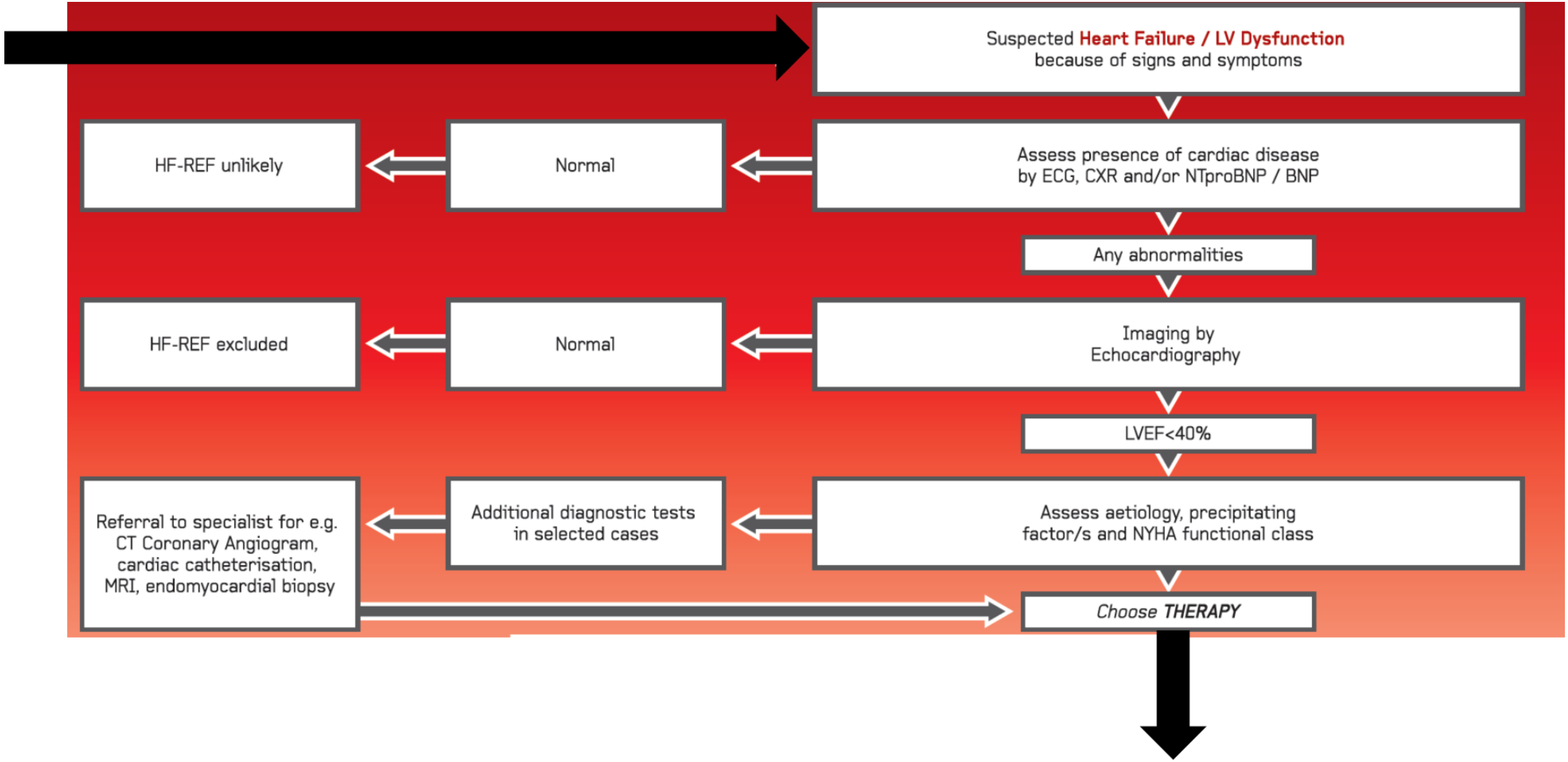
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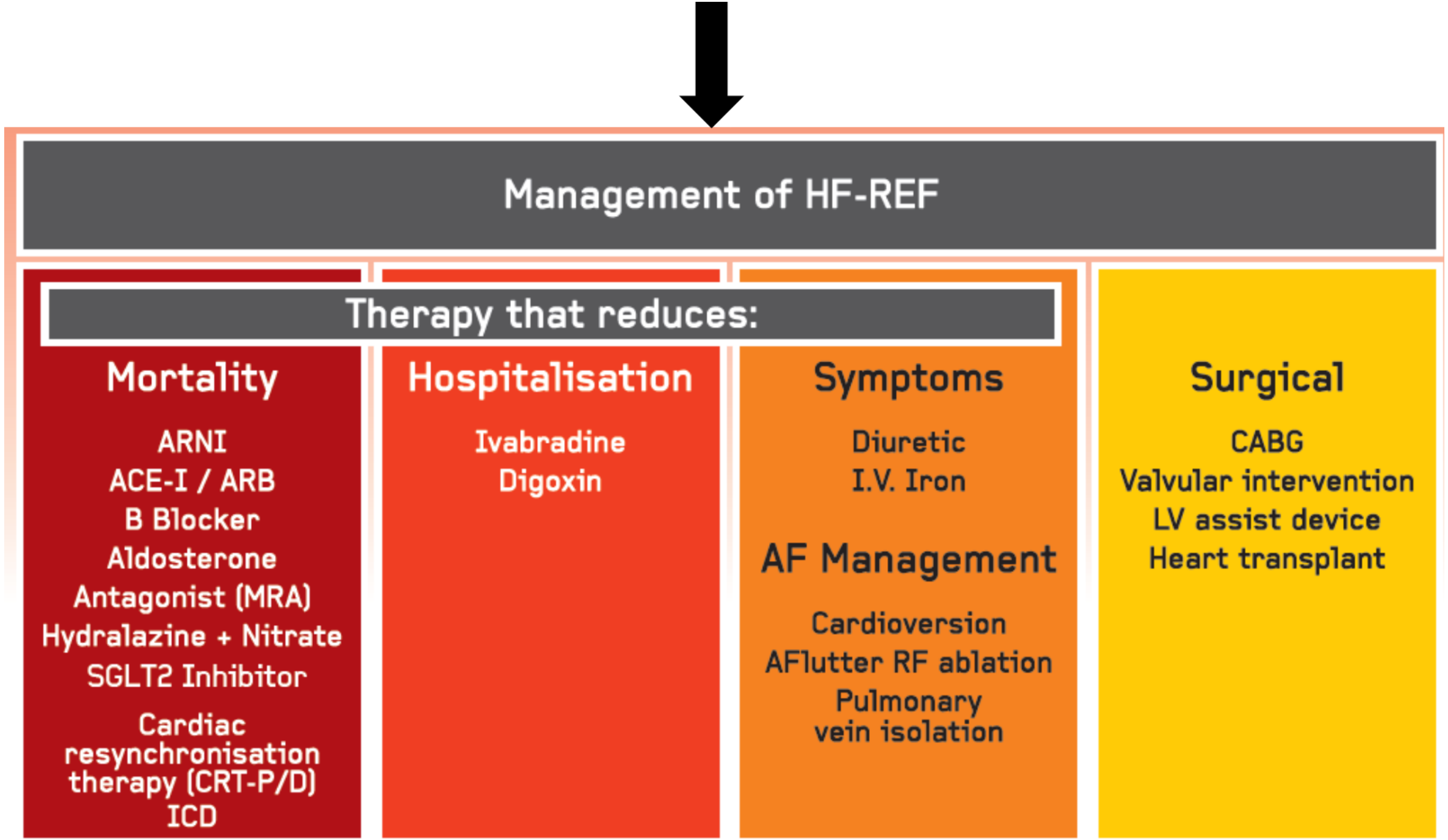
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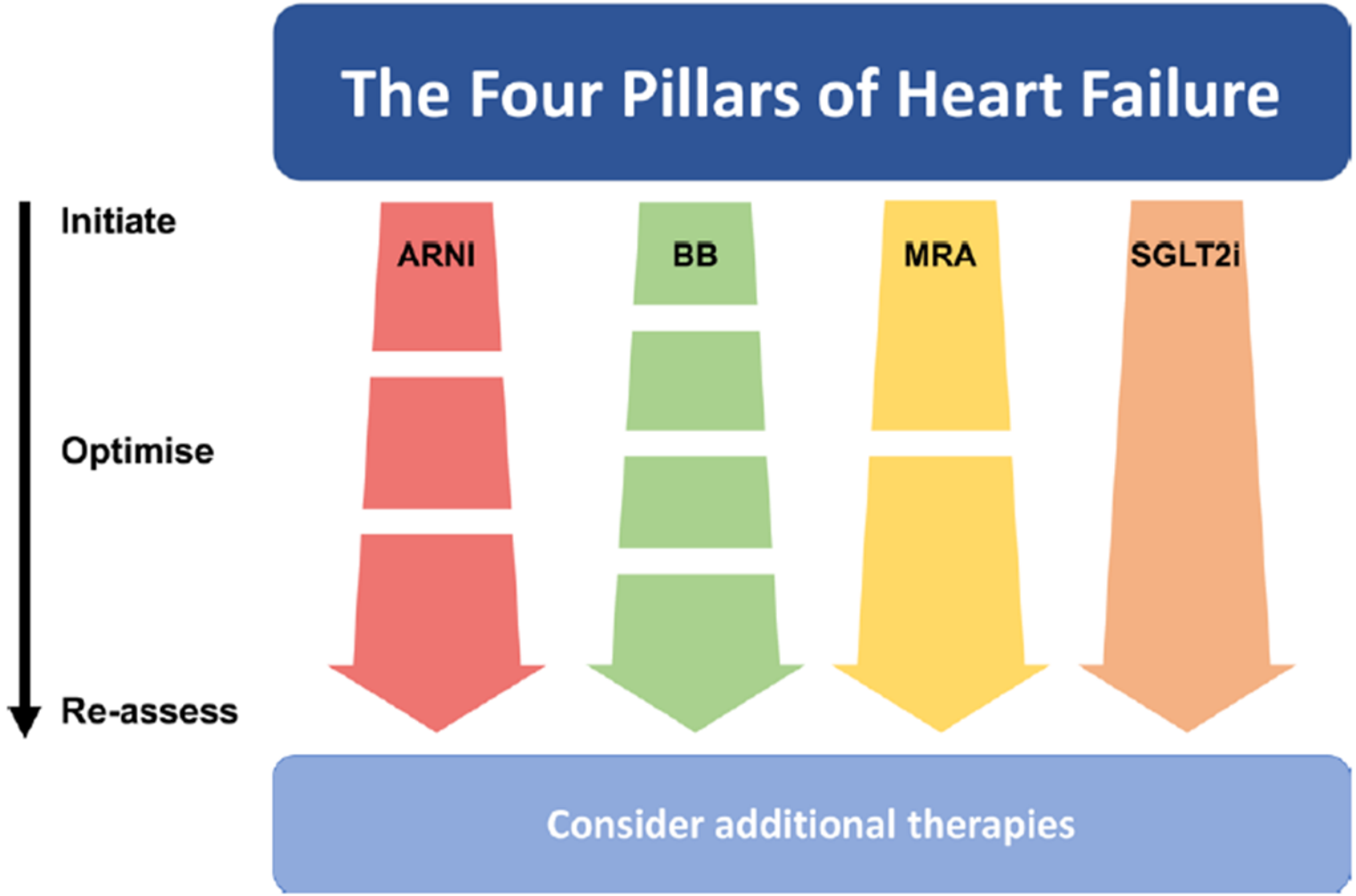

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Open Heart 2021; 8: e001585

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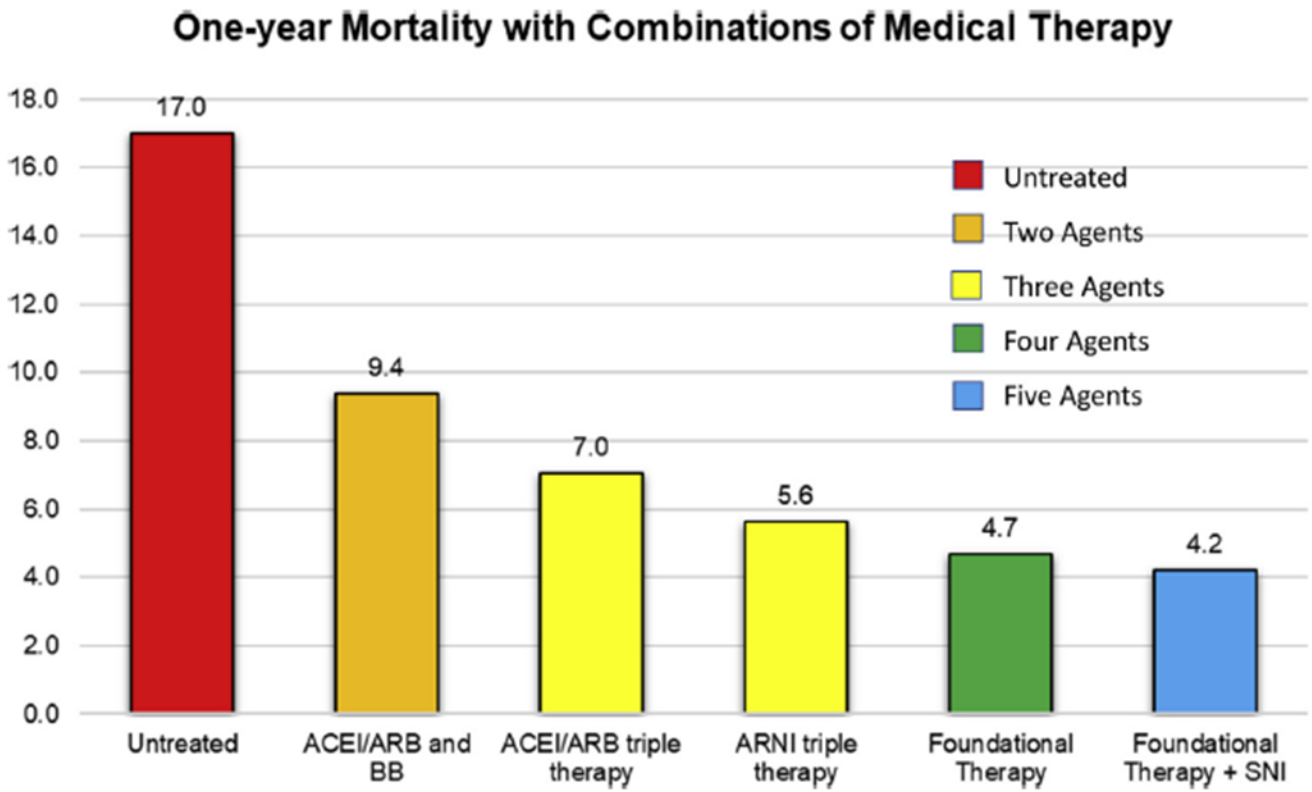

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Canadian Journal of Cardiology 2021; 37: 632 - 643

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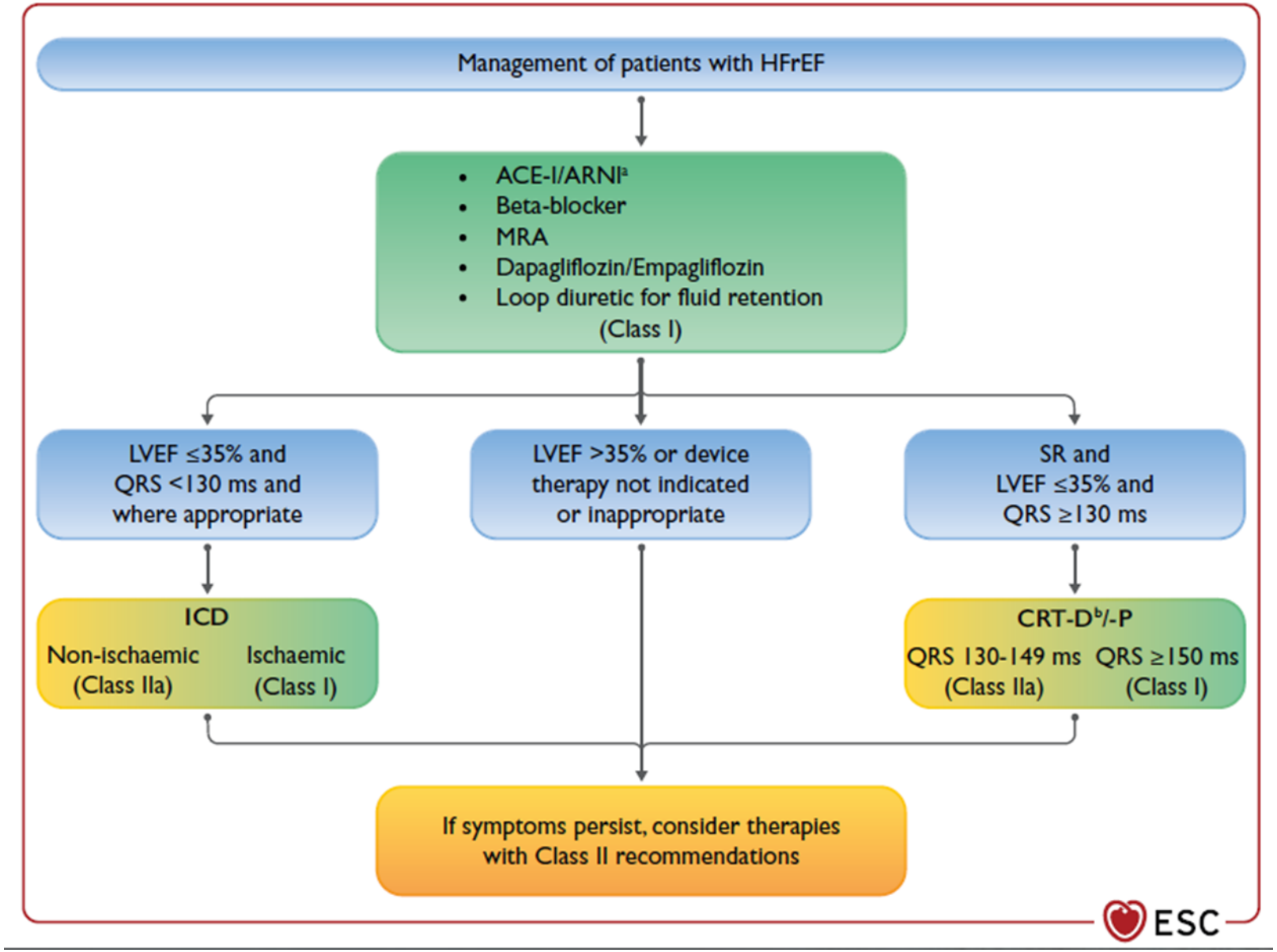

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European Heart Journal 2021; 42: 3599 - 3726

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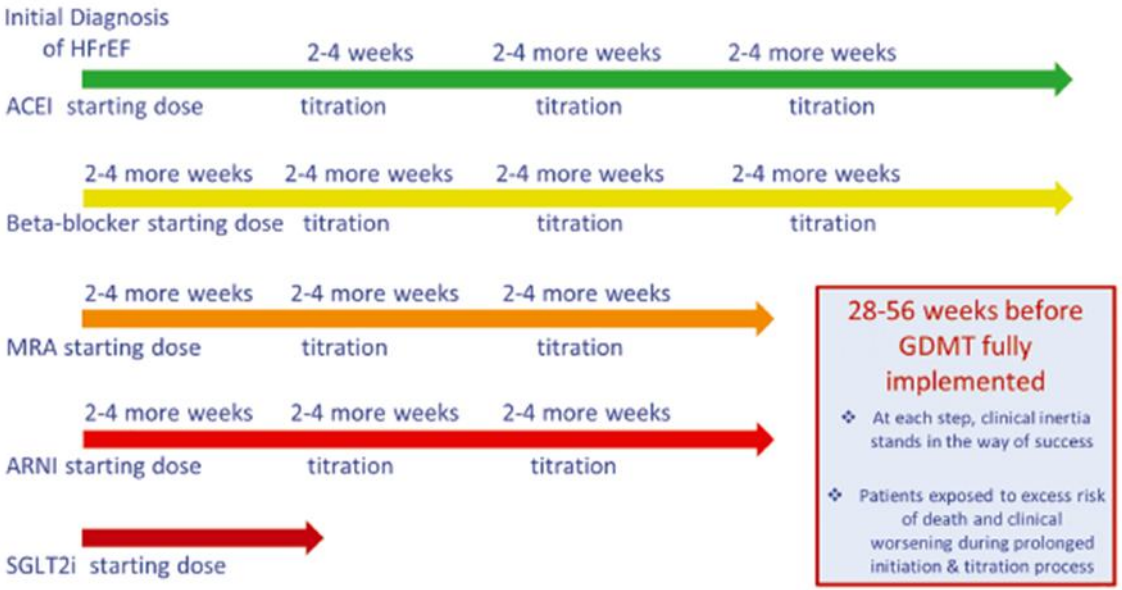
Traditional Serial Strategy



Simultaneous or Rapid Sequence Strategy

GDMT	*Day 1*	Days 7-14	Days 14-28	Days 21-42
ARNI	Initiate, low dose	Continue	Titrate, as tolerated	Titrate, as tolerated
Beta-blocker	Initiate, low dose	Titrate, as tolerated	Titrate, as tolerated	Titrate, as tolerated
MRA	Initiate, low dose	Continue	Titrate, as tolerated	Continue
SGLT2i	Initiate	Continue	Continue	Continue

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Eur H J 2021; 23: 1514–1517

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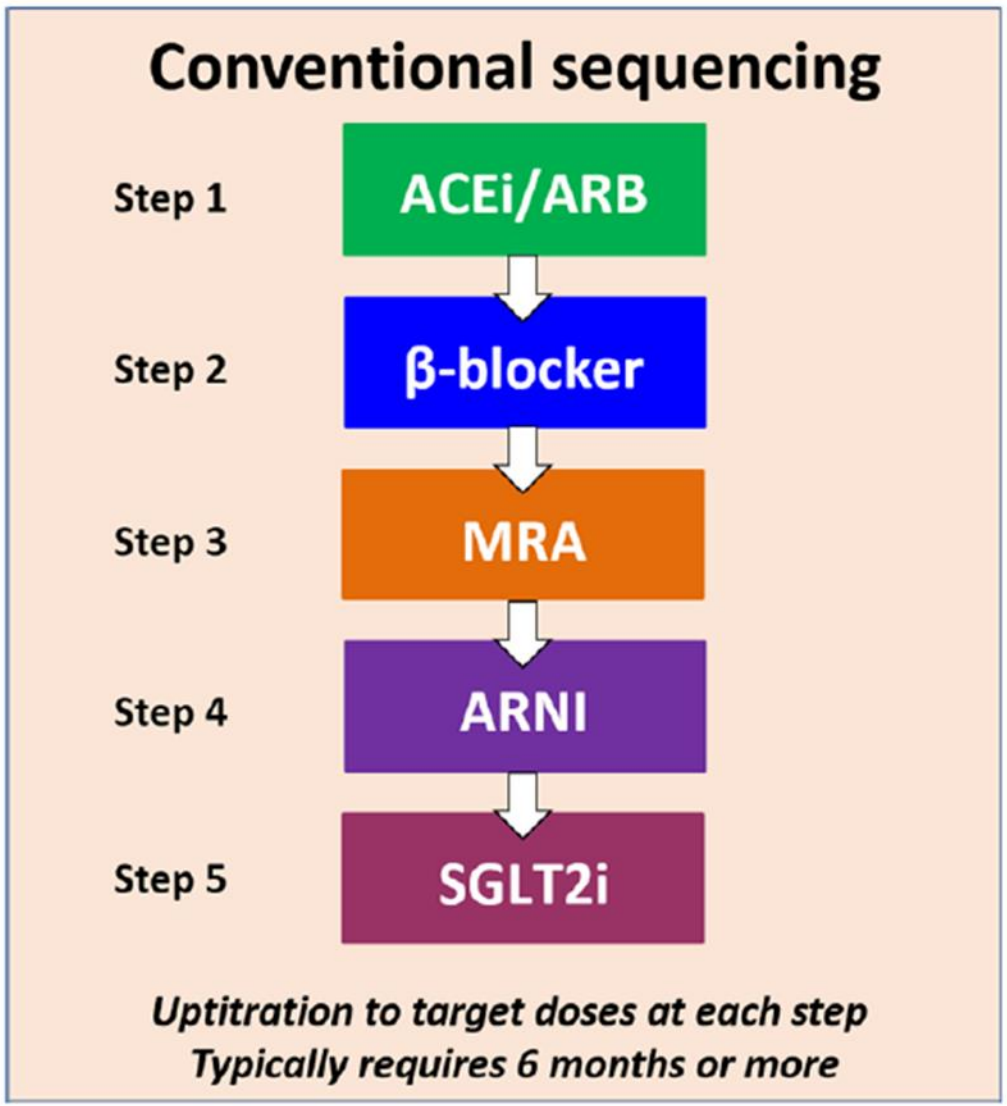

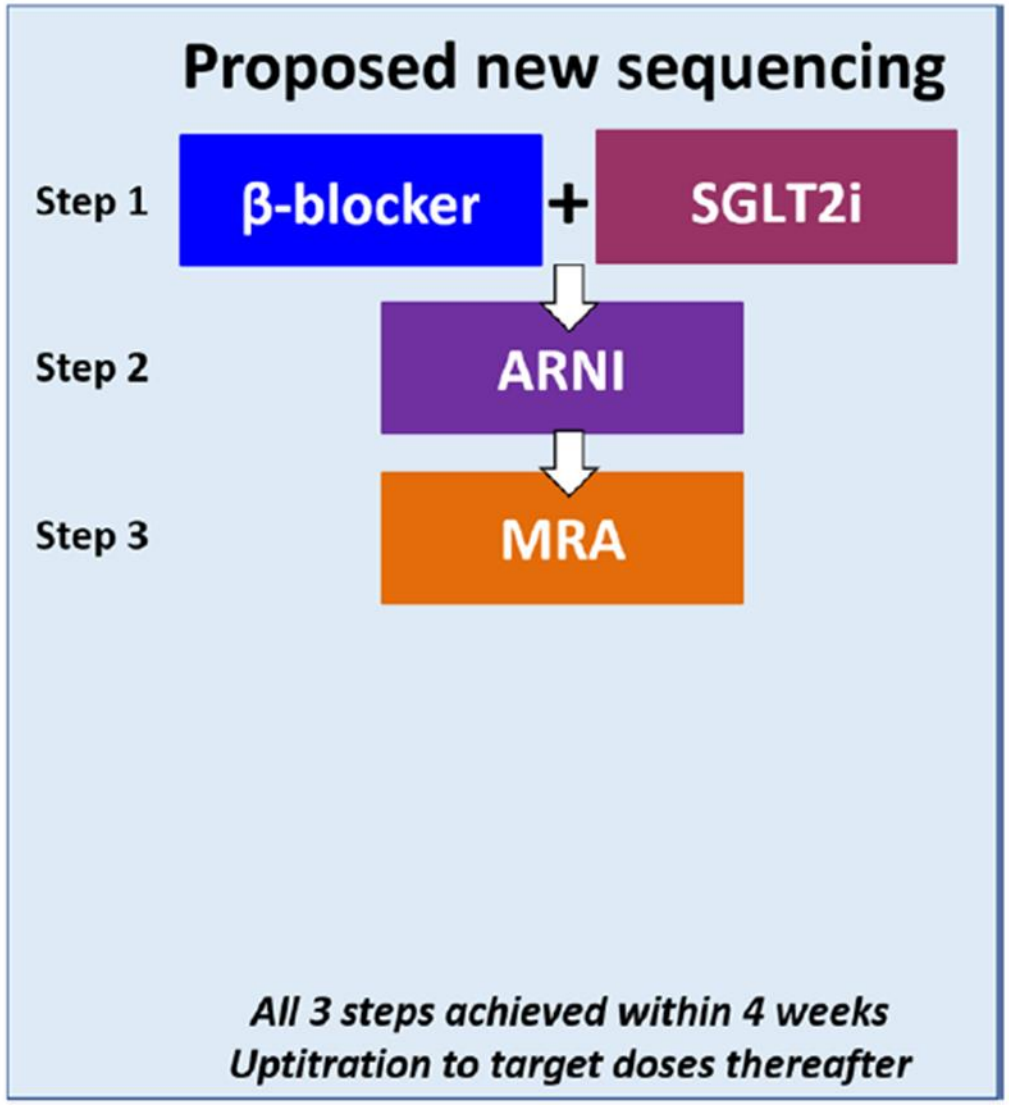

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Circulation 2021;143:875–877

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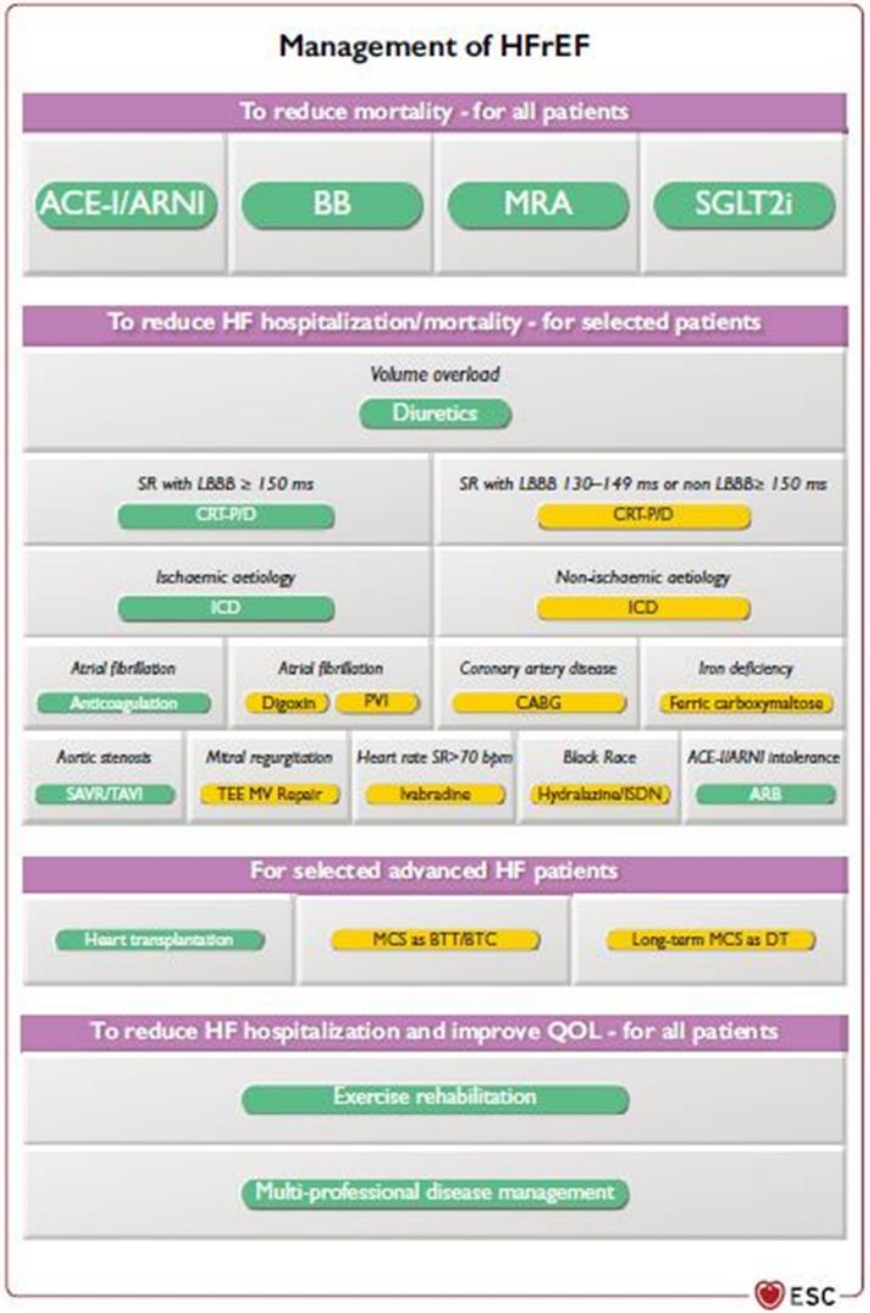
ESC
European Society of Cardiology
European Heart Journal (2021) **00**, 1–128
doi:10.1093/eurheartj/ehab368

ESC GUIDELINES

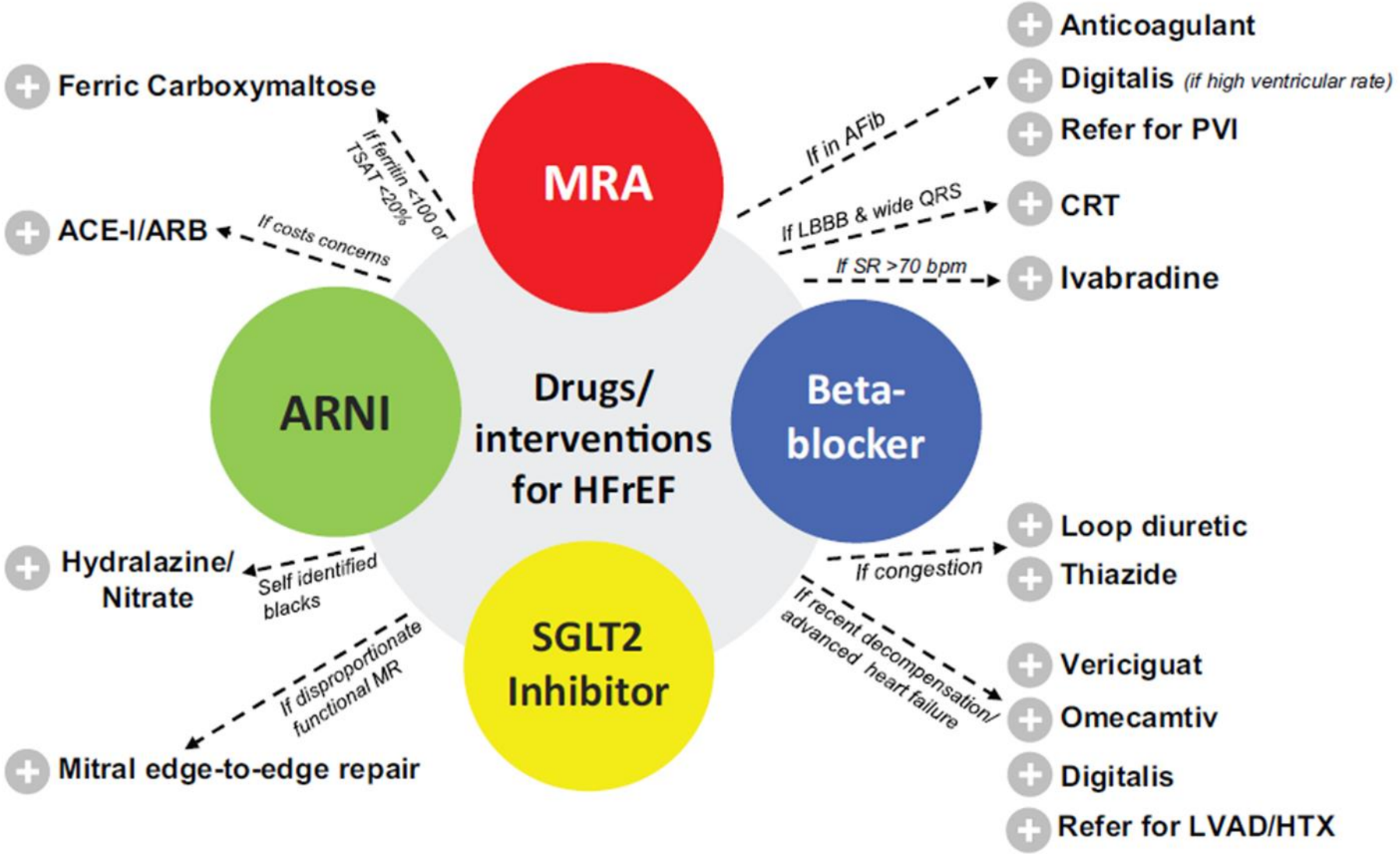
2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

With the special contribution of the Heart Failure Association (HFA) of the ESC



European Heart Journal 2021; 42: 3599 - 3726



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European Heart Journal 2021; 42: 681–683

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[1]ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2016: European Heart Journal (2016) 37, 2129–2200

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Choose THERAPY

Holistic Care

- Fluid restriction ≤ 1.5L
- Salt restriction (in hypertensives only)
- Exercise (once stabilised)
- Heart failure management programme
- Avoid : NSAID, glitazones, CCB (except amlodipine, felodipine)
- Palliative care

Management of HF-REF

Therapy that reduces:

Mortality	Hospitalisation	Symptoms	Surgical
ARNI ACE-I / ARB B Blocker Aldosterone Antagonist (MRA) Hydralazine + Nitrate SGLT2 Inhibitor Cardiac resynchronisation therapy (CRT-P/D) ICD	Ivabradine Digoxin	Diuretic I.V. Iron **AF Management** Cardioversion AFlutter RF ablation Pulmonary vein isolation	CABG Valvular intervention LV assist device Heart transplant

Precipitating Factors

Mandatory: U & E and creatinine, Glucose, TSH, FBC
Possible: LFT, Iron study, Calcium, hsTroponin T, Trop I

Special consideration

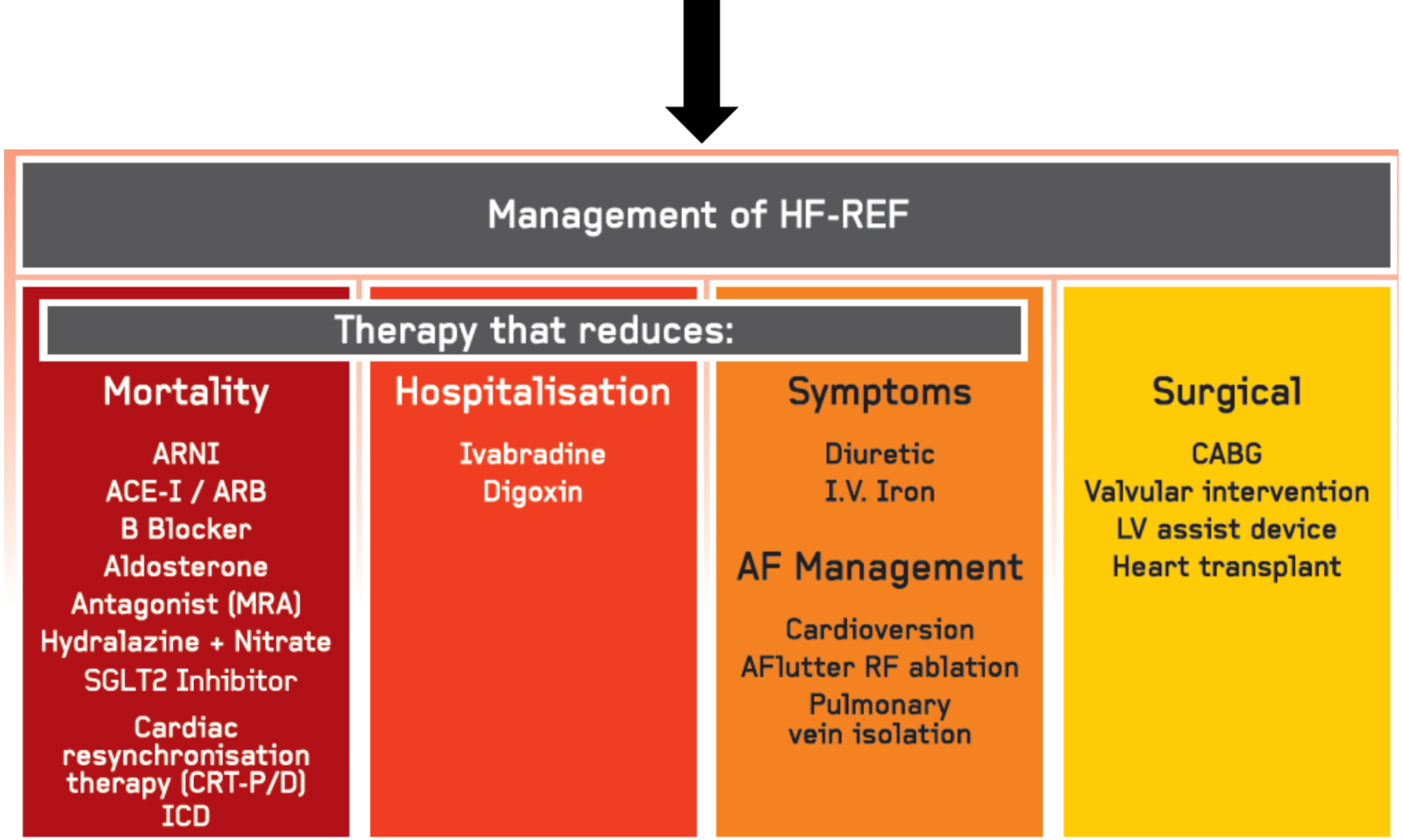
Digoxin (AF, resistant symptomatic heart failure)
Warfarin (AF, LV clot)
NOAC (Non-valvular AF)
Amiodarone (sustain sinus rhythm and reduce VT in ICD patients)
Aldosterone antagonist (Early post-MI heart failure)
ACE-I + ARB if Aldosterone antagonist (MRA) cannot be used

Heart Failure Society of South Africa (HFSSA)

www.hefssa.org

* Patient with HFmrEF (EF 40-49%) can be treated similarly

[1]ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2016: European Heart Journal (2016) 37, 2129–2200



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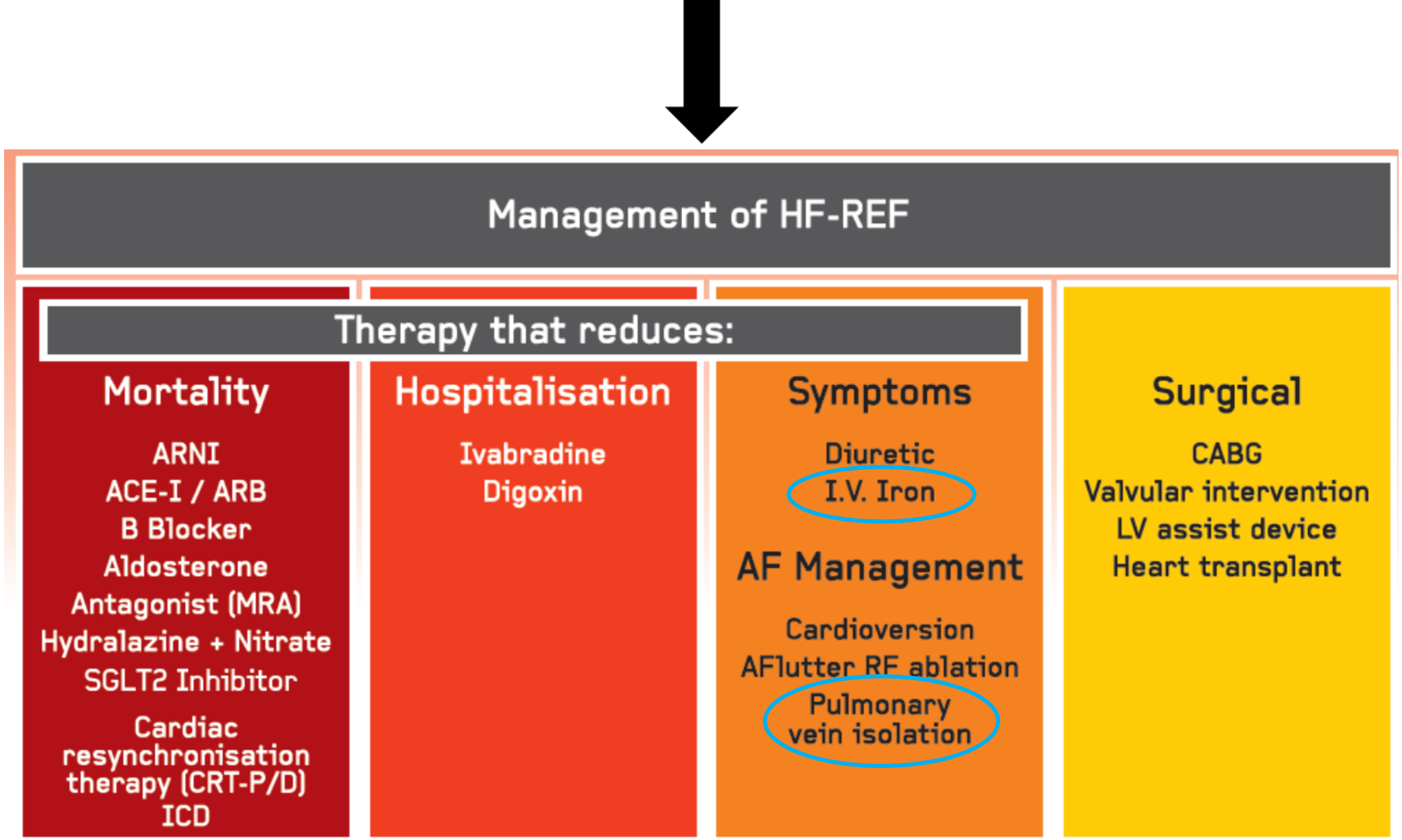
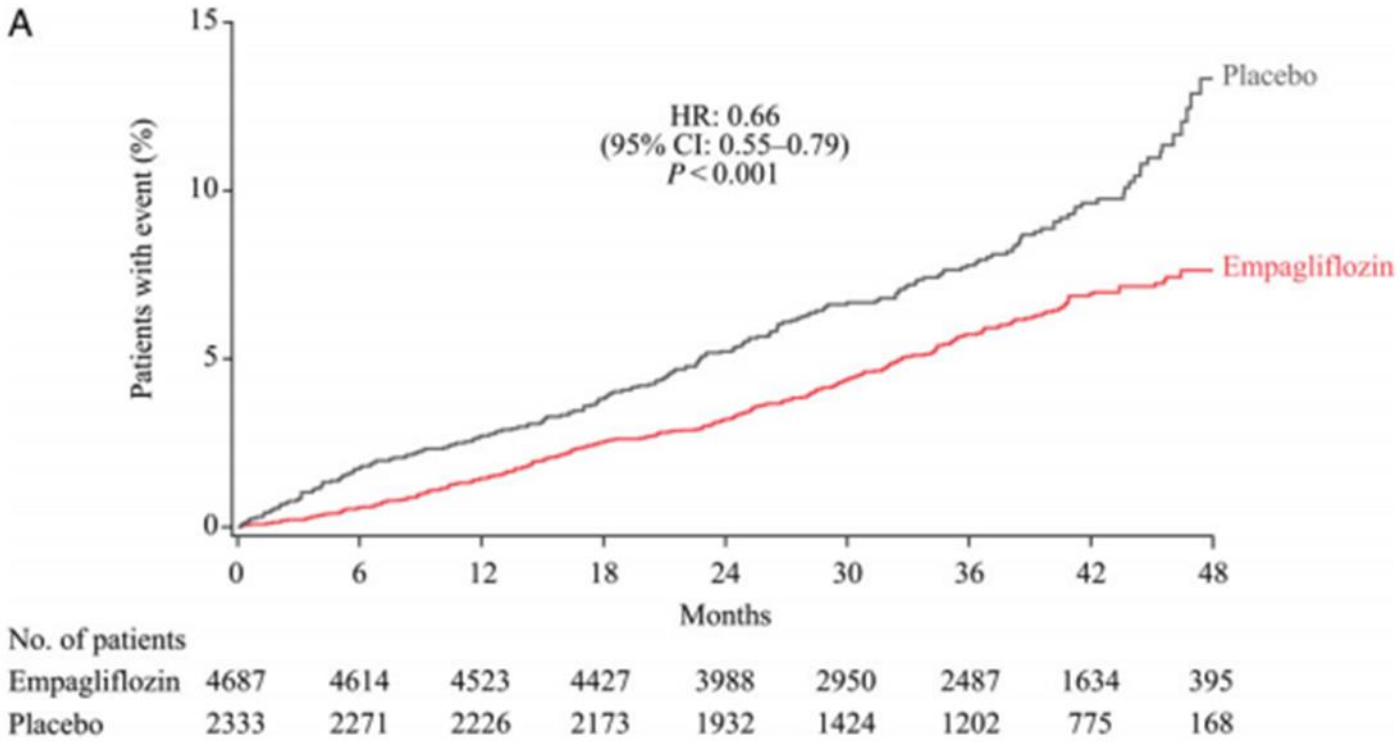

Management of HF-REF
Therapy that reduces:
Mortality
ARNI
ACE-I / ARB
B Blocker
Aldosterone
Antagonist (MRA)
Hydralazine + Nitrate
SGLT2 Inhibitor
Cardiac resynchronisation therapy (CRT-P/D)
ICD
Hospitalisation
Ivabradine
Digoxin
Symptoms
Diuretic
I.V. Iron
AF Management
Cardioversion
AFlutter RF ablation
Pulmonary vein isolation
Surgical
CABG
Valvular intervention
LV assist device
Heart transplant

SGLT2 inhibitors

Heart failure outcomes with empagliflozin in patients with type 2 diabetes at high cardiovascular risk: results of the EMPA-REG OUTCOME® trial

David Fitchett[1*], Bernard Zinman[2,3], Christoph Wanner[4], John M. Lachin[5], Stefan Hantel[6], Afshin Salsali[7], Odd Erik Johansen[8], Hans J. Woerle[9], Uli C. Broedl[9], and Silvio E. Inzucchi[10], on behalf of the EMPA-REG OUTCOME® trial investigators

Time to first hospitalisation for heart failure of CV death



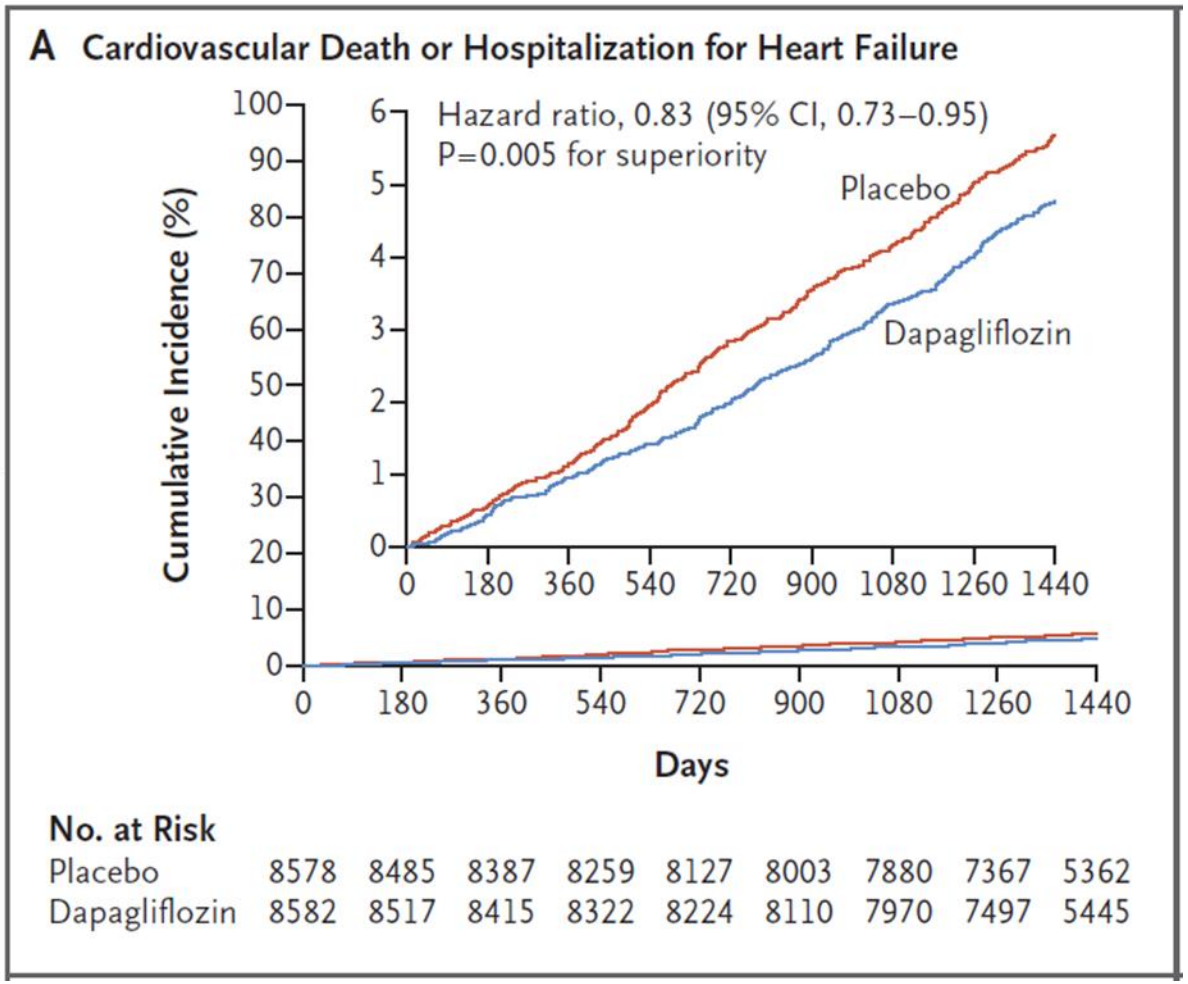
No. of patients									
Empagliflozin	4687	4614	4523	4427	3988	2950	2487	1634	395
Placebo	2333	2271	2226	2173	1932	1424	1202	775	168

Eur Heart J 2016; 37: 1526 - 34

ORIGINAL ARTICLE

Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes

S.D. Wiviott, I. Raz, M.P. Bonaca, O. Mosenzon, E.T. Kato, A. Cahn, M.G. Silverman, T.A. Zelniker, J.F. Kuder, S.A. Murphy, D.L. Bhatt, L.A. Leiter, D.K. McGuire, J.P.H. Wilding, C.T. Ruff, I.A.M. Gause-Nilsson, M. Fredriksson, P.A. Johansson, A.-M. Langkilde, and M.S. Sabatine, for the DECLARE–TIMI 58 Investigators*



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N Engl J Med 2019; 380: 347 - 57

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Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction

J.J.V. McMurray, S.D. Solomon, S.E. Inzucchi, L. Køber, M.N. Kosiborod, F.A. Martinez, P. Ponikowski, M.S. Sabatine, I.S. Anand, J. Bělohlávek, M. Böhm, C.-E. Chiang, V.K. Chopra, R.A. de Boer, A.S. Desai, M. Diez, J. Drozdz, A. Dukát, J. Ge, J.G. Howlett, T. Katova, M. Kitakaze, C.E.A. Ljungman, B. Merkely, J.C. Nicolau, E. O'Meara, M.C. Petrie, P.N. Vinh, M. Schou, S. Tereshchenko, S. Verma, C. Held, D.L. DeMets, K.F. Docherty, P.S. Jhund, O. Bengtsson, M. Sjöstrand, and A.-M. Langkilde, for the DAPA-HF Trial Committees and Investigators*

Characteristics of the Patients at Baseline

Age 66 yrs
Female 23%
NYHA II/III
Ischaemic aetiology ~55%
ICD 25%
CRT 6 – 8%

Characteristic	Dapagliflozin (N=2373)	Placebo (N=2371)
Heart failure medication — no. (%)		
Diuretic	2216 (93.4)	2217 (93.5)
ACE inhibitor	1332 (56.1)	1329 (56.1)
ARB	675 (28.4)	632 (26.7)
Sacubitril–valsartan	250 (10.5)	258 (10.9)
Beta-blocker	2278 (96.0)	2280 (96.2)
Mineralocorticoid receptor antagonist	1696 (71.5)	1674 (70.6)
Digitalis	445 (18.8)	442 (18.6)
Glucose-lowering medication — no./total no. (%)**		
Biguanide	504/993 (50.8)	512/990 (51.7)
Sulfonylurea	228/993 (23.0)	210/990 (21.2)
DPP-4 inhibitor	161/993 (16.2)	149/990 (15.1)
GLP-1 receptor agonist	11/993 (1.1)	10/990 (1.0)
Insulin	274/993 (27.6)	266/990 (26.9)

N Engl J Med 2019; 381: 1995 - 2008

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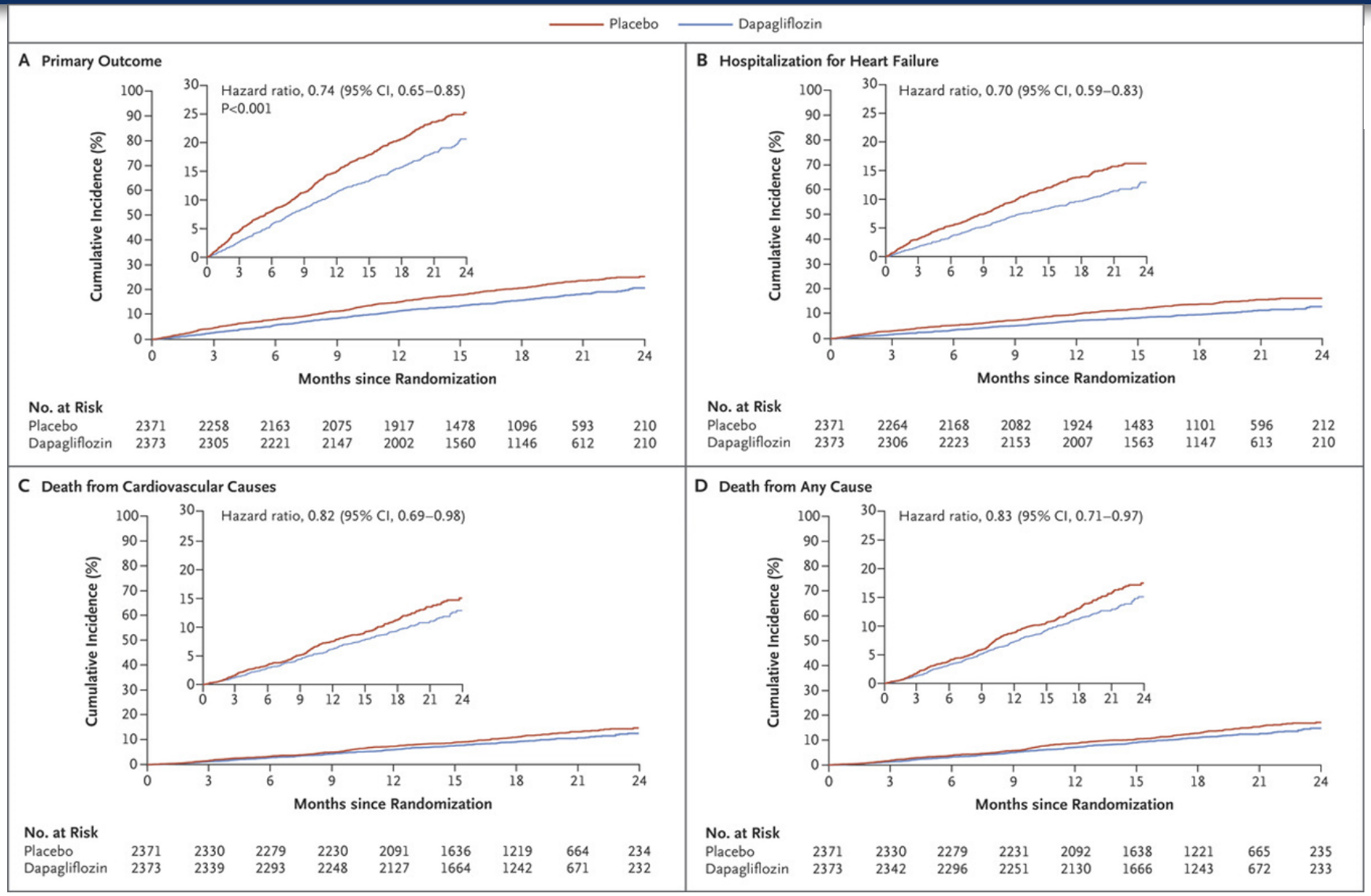
DAPA-HF Trial Cardiovascular Outcomes



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University of Cape Town • iYunivesithi yaseKapa • Universiteit van Kaapstad

N Engl J Med 2019; 381: 1995 - 2008

ORIGINAL ARTICLE

Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure

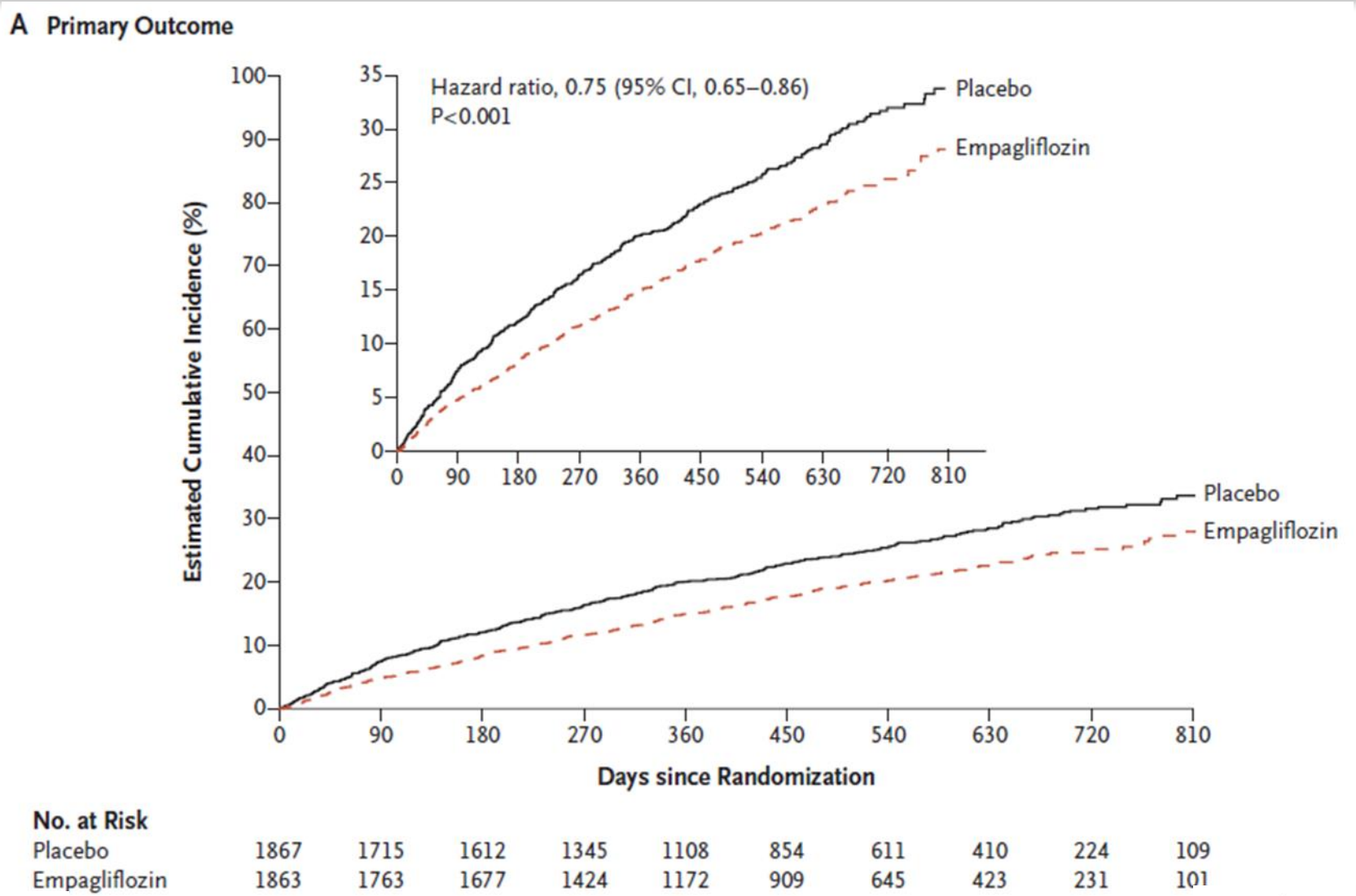
M. Packer, S.D. Anker, J. Butler, G. Filippatos, S.J. Pocock, P. Carson, J. Januzzi, S. Verma, H. Tsutsui, M. Brueckmann, W. Jamal, K. Kimura, J. Schnee, C. Zeller, D. Cotton, E. Bocchi, M. Böhm, D.-J. Choi, V. Chopra, E. Chuquiure, N. Giannetti, S. Janssens, J. Zhang, J.R. Gonzalez Juanatey, S. Kaul, H.-P. Brunner-La Rocca, B. Merkely, S.J. Nicholls, S. Perrone, I. Pina, P. Ponikowski, N. Sattar, M. Senni, M.-F. Seronde, J. Spinar, I. Squire, S. Taddei, C. Wanner, and F. Zannad, for the EMPEROR-Reduced Trial Investigators*

Table 1. (Continued)

Characteristic	Empagliflozin (N=1863)	Placebo (N=1867)
Heart failure medication — no. (%)		
Renin–angiotensin inhibitor§		
Without neprilysin inhibitor	1314 (70.5)	1286 (68.9)
With neprilysin inhibitor	340 (18.3)	387 (20.7)
Mineralocorticoid receptor antagonist	1306 (70.1)	1355 (72.6)
Beta-blocker	1765 (94.7)	1768 (94.7)
Device therapy — no. (%)		
Implantable cardioverter–defibrillator¶	578 (31.0)	593 (31.8)
Cardiac resynchronization therapy‖	220 (11.8)	222 (11.9)

N Engl J Med 2020; 383:1413-1424

Cardiovascular Death or HF Hospitalisation



N Engl J Med 2020; 383:1413-1424

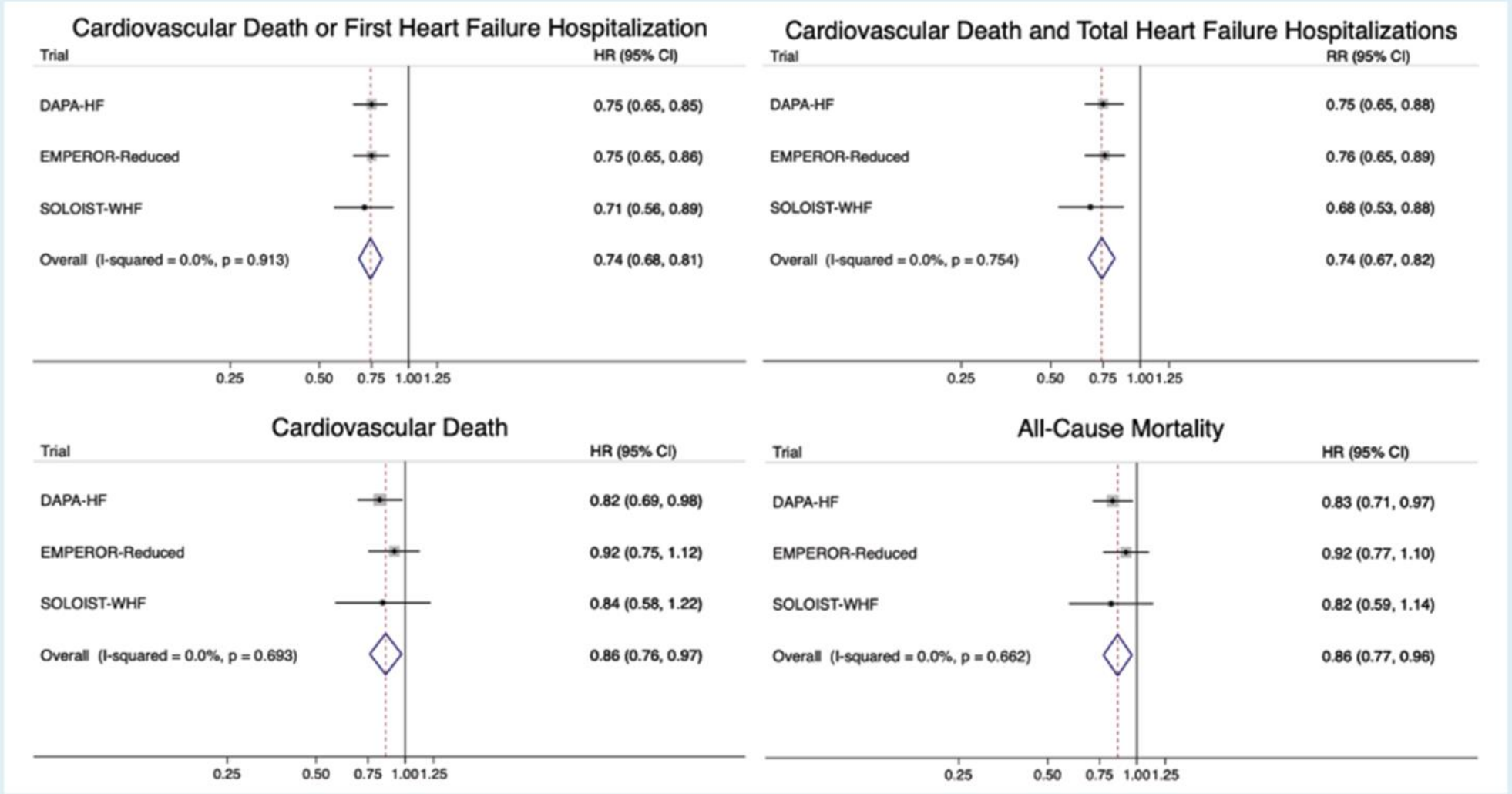
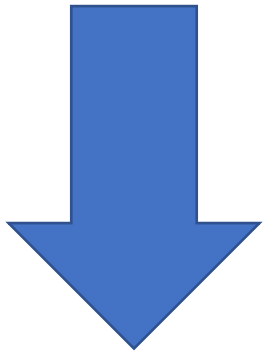


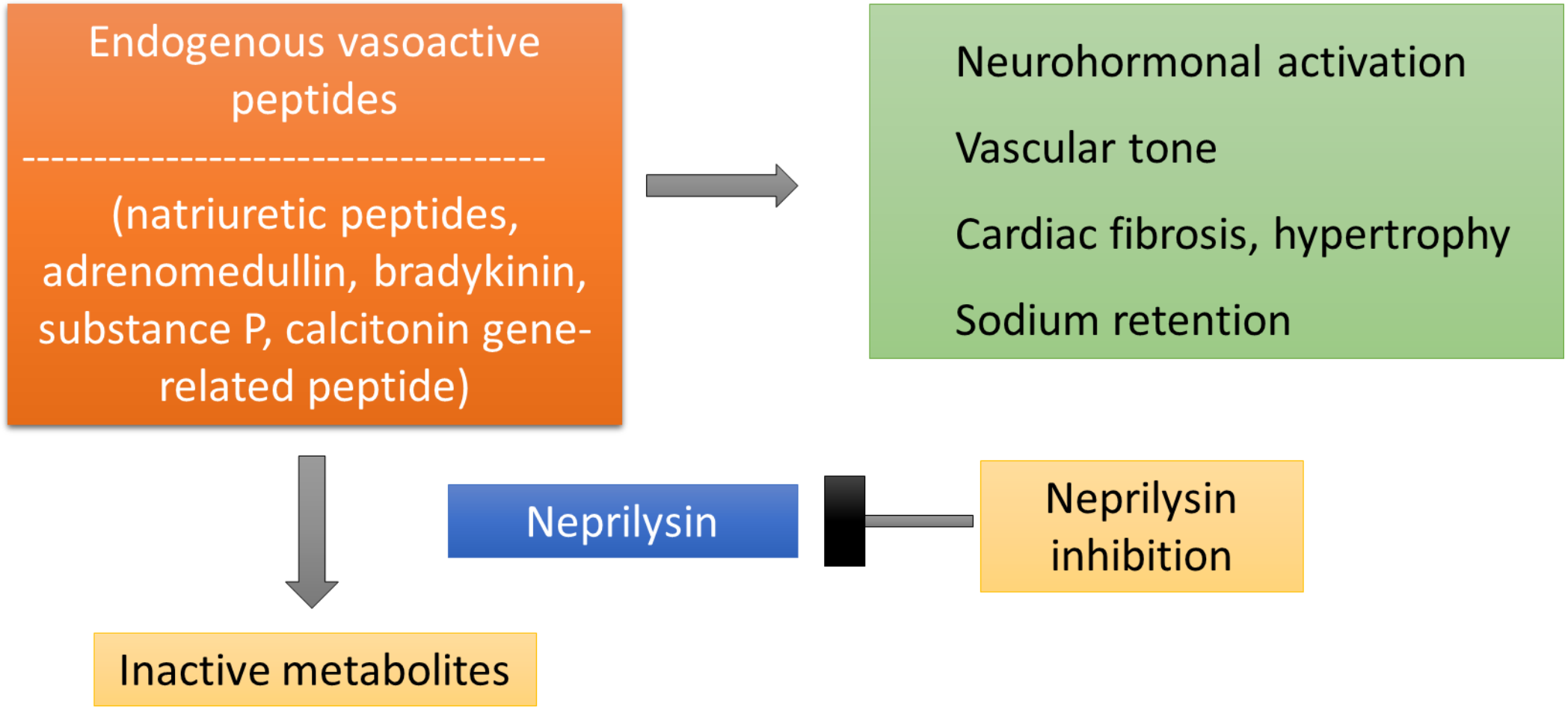
Figure 1 Meta-analysis of DAPA-HF, EMPEROR-Reduced and SOLOIST-WHF. The figure shows pooled treatment effect estimates calculated from the reported individual trial-level estimates using a fixed-effect meta-analysis model. CI, confidence interval; HR, hazard ratio; RR, rate ratio.

ARNI

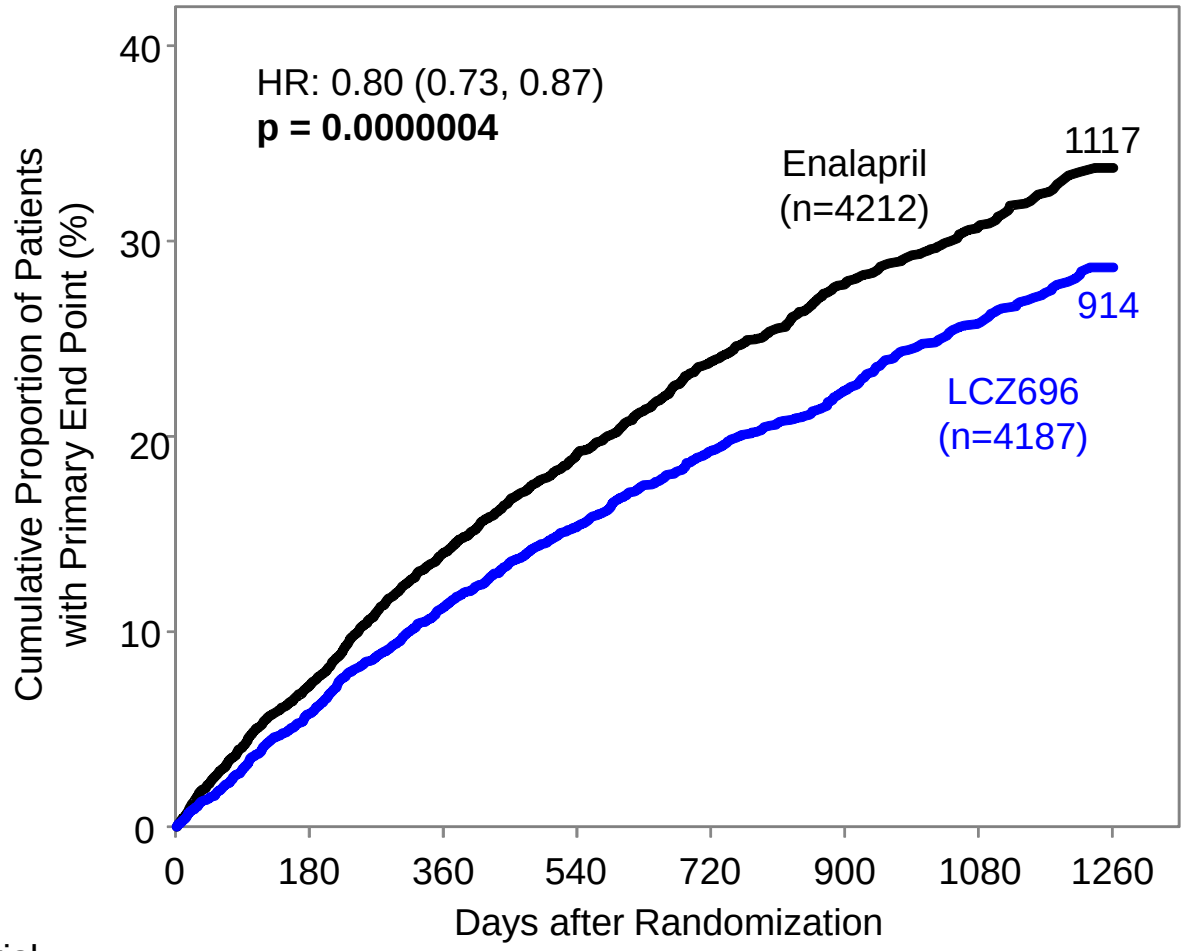


- **Angiotensin Receptor – Neprilysin Inhibitor**

Neprilysin Inhibition potentiates Actions of Vasoactive Peptides beneficial in Heart Failure



Cardiovascular death or heart failure hospitalization



At risk								
Enalapril:	4212	3883	3579	2922	2123	1488	853	236
LCZ696:	4187	3922	3663	3018	2257	1544	896	249

20% RRR in co-primary endpoint with LCZ696+
(ARR = 4.7%)
NNT = 1/ARR x 100 = 21

N Engl J Med 2014; 371:993 - 1004

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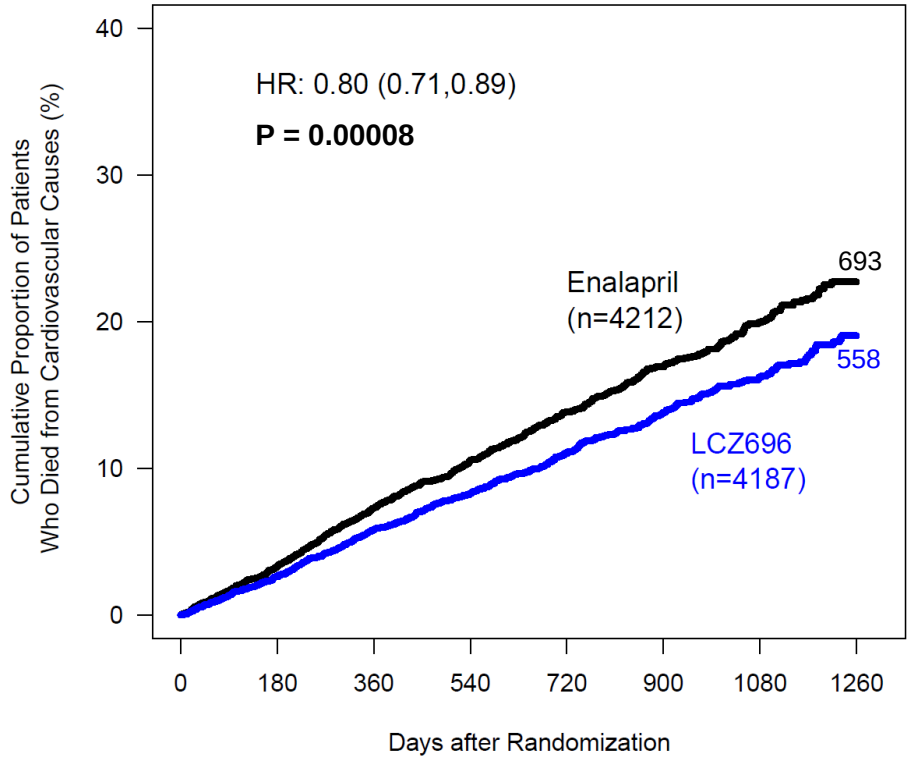
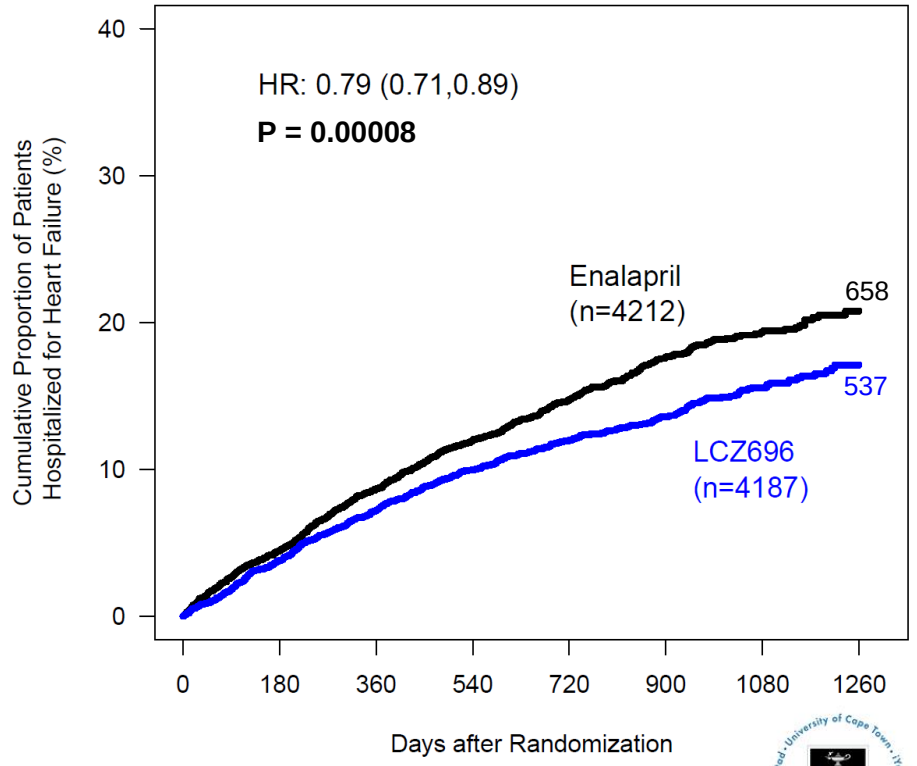
PARADIGM-HF: Components of primary endpoint

Death from CV causes
20% risk reduction
(ARR = 3.2%)
NNT = 1/ARR x 100 = 31



HF hospitalization
21% risk reduction
(ARR = 2.8%)
NNT = 1/ARR x 100 = 36



N Engl J Med 2014; 371:993 - 1004

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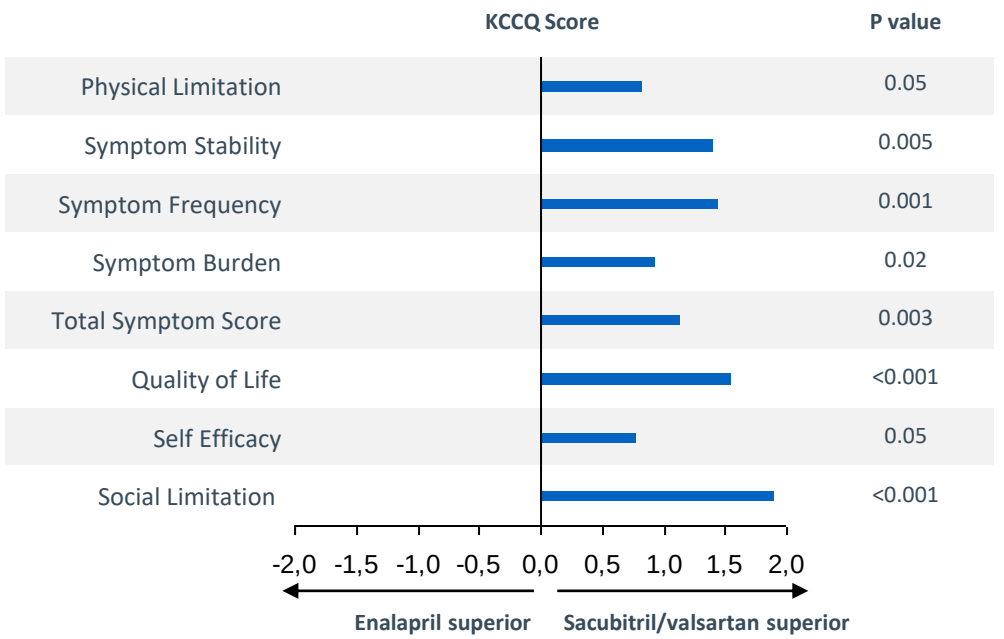
The benefit of Sac/Val is significantly superior vs. enalapril on Quality of Life, in all KCCQ domains*

Entresto® quality of life improvement vs. enalapril

Change vs. baseline for each KCCQ domain at 8 months



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*In surviving patients

KCCQ=Kansas City Cardiomyopathy Questionnaire

Lewis et al. Circ Heart Fail 2017;10:e003430

University of Cape Town · Kaapstad · Yunivesithi yaseKapa · Universiteit van

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Switching 1000 patients from ACE-I/ARB to sacubtril/valsartan avoided:

47 primary endpoints

31 CV deaths

28 patients hospitalised for HF

37 patients hospitalised for any reason

111 admissions for any reason

over a treatment period of 27 months.

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Prospectively defined safety events during

Event, n (%)	LCZ696 (n=4,187)	Enalapril (n=4,212)	p-value
Hypotension			
Symptomatic	588 (14.0)	388 (9.2)	<0.001
Symptomatic with SBP <90 mmHg	112 (2.7)	59 (1.4)	<0.001
Elevated serum creatinine			
≥221 umol/L	139 (3.3)	188 (4.5)	0.007
≥265 umol/L	63 (1.5)	83 (2.0)	0.10
Elevated serum potassium			
>5.5 mmol/L	674 (16.1)	727 (17.3)	0.15
>6.0 mmol/L	181 (4.3)	236 (5.6)	0.007
Cough	474 (11.3)	601 (14.3)	<0.001
Angioedema (adjudicated by a blinded expert committee)			
No treatment or use of antihistamines only	10 (0.2)	5 (0.1)	0.19
Catecholamines or glucocorticoids without hospitalization	6 (0.1)	4 (0.1)	0.52
Hospitalized without airway compromise	3 (0.1)	1 (<0.1)	0.31
Airway compromise	0	0	---

AE: adverse events; SBP: systolic blood pressure

Angioedema:
0,45% Vs. 0,24%

N Engl J Med 2014; 371:993 - 1004

Some practical issues….

- The drug should be titrated upwards carefully as performed in the trial
- The drug was only evaluated in patients who had stable CCF (chronic)
- The drug was only evaluated in patients who did tolerate enalapril 10 mg 2x/day (in the run-in period) – Is it safe in other scenarios?
- ARNI - depending on lab assay may possibly result in elevated BNP measurements at follow-up due as they prevent the breakdown of BNP
- Watch out for hypotension
- Due to the risk of angioedema with neprilysin inhibition allow for a 48 hour period between patients stopping ACE-I and starting ARNI

Iron

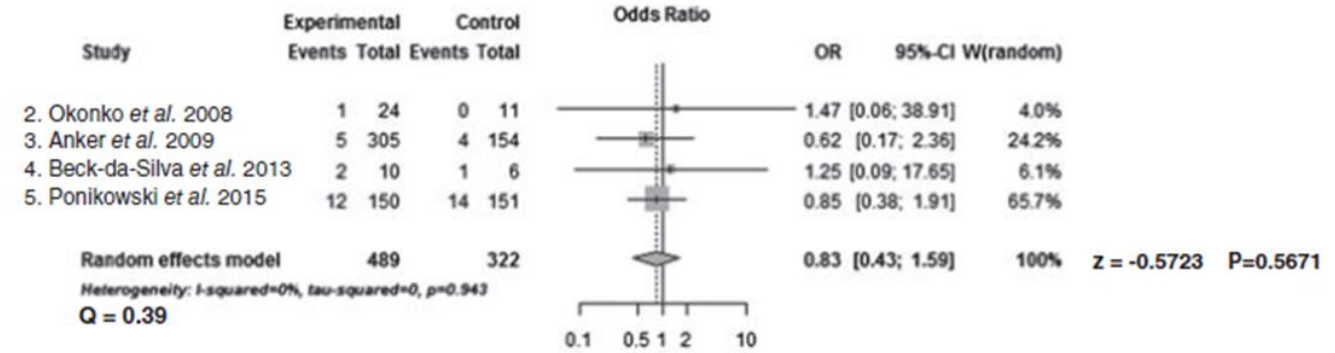
European Journal of Heart Failure (2016) 18, 786–795
doi:10.1002/ejhf.473

REVIEW

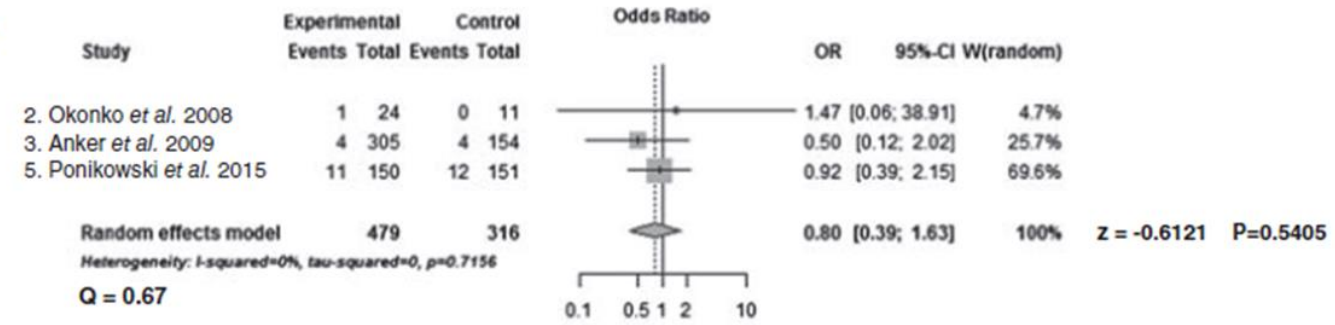
Effects of intravenous iron therapy in iron-deficient patients with systolic heart failure: a meta-analysis of randomized controlled trials

Ewa A. Jankowska[1,2]*, Michał Tkaczyszyn[1,2], Tomasz Suchocki[3], Marcin Drozd[1,2], Stephan von Haehling[4], Wolfram Doehner[5,6], Waldemar Banasiak[2], Gerasimos Filippatos[7], Stefan D. Anker[4], and Piotr Ponikowski[2,8]

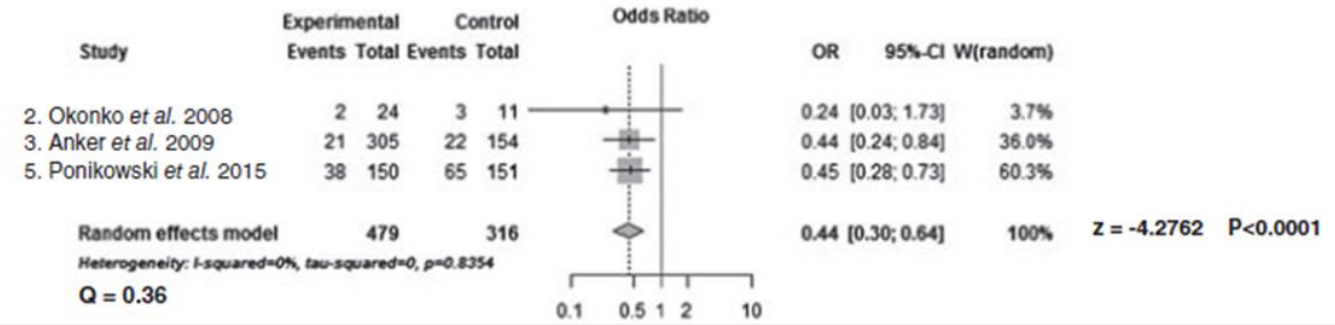
All-cause death



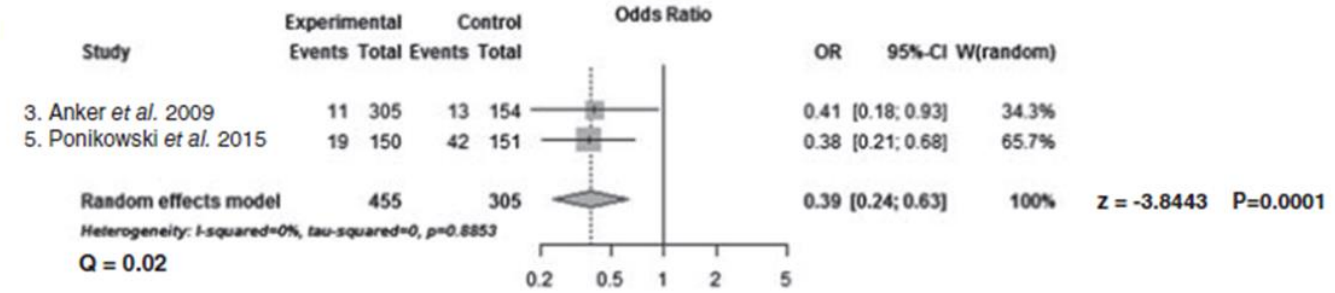
Cardiovascular death



All-cause death or cardiovascular hospitalization



Cardiovascular death or hospitalization for worsening HF



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Eur J of Hear Failure, 2016; 18: 786 - 95

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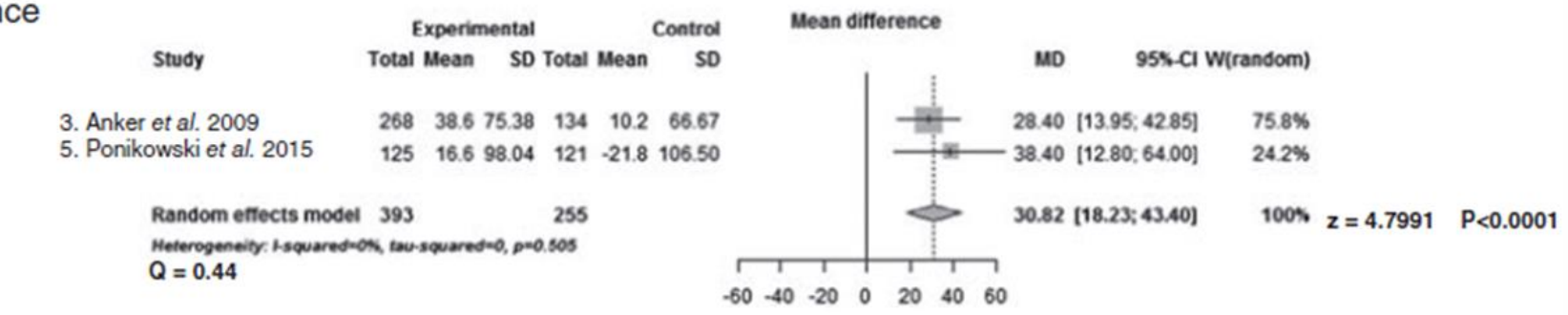
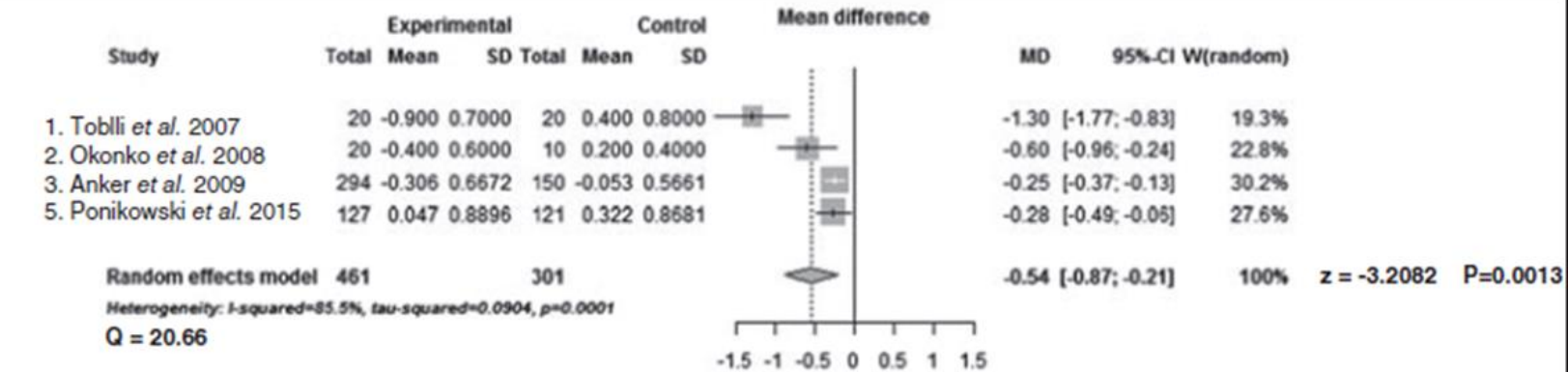
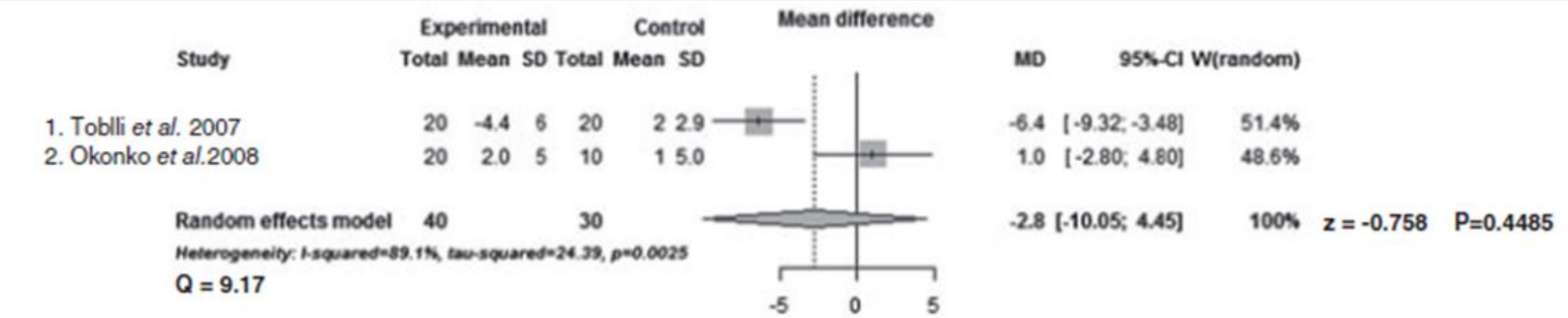
6MWT distance



NYHA class



LVEF



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Eur J of Hear Failure, 2016; 18: 786 - 95

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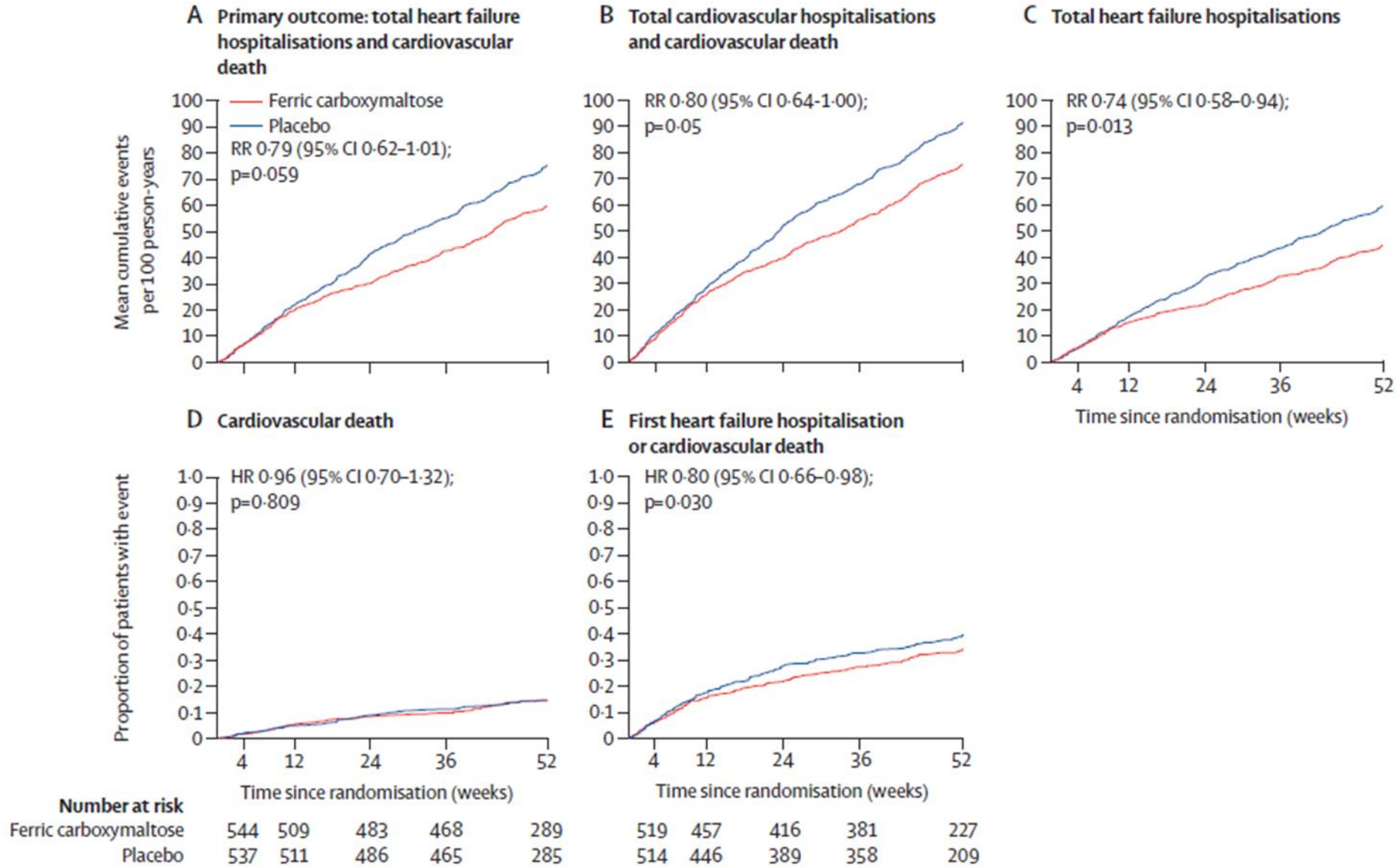
Ferric carboxymaltose for iron deficiency at discharge after acute heart failure: a multicentre, double-blind, randomised, controlled trial

*Piotr Ponikowski, Bridget-Anne Kirwan, Stefan D Anker, Theresa McDonagh, Maria Dorobantu, Jarosław Drozdz, Vincent Fabien, Gerasimos Filippatos, Udo Michael Göhring, Andre Keren, Irakli Khintibidze, Hans Kragten, Felipe A Martinez, Marco Metra, Davor Milicic, José C Nicolau, Marcus Ohlsson, Alexander Parkhomenko, Domingo A Pascual-Figal, Frank Ruschitzka, David Sim, Hadi Skouri, Peter van der Meer, Basil S Lewis, Josep Comin-Colet, Stephan von Haehling, Alain Cohen-Solal, Nicolas Danchin, Wolfram Doehner, Henry J Dargie, Michael Motro, Javed Butler, Tim Friede, Klaus H Jensen, Stuart Pocock, Ewa A Jankowska, on behalf of the AFFIRM-AHF investigators**

Lancet 2020; 396: 1895–904



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Lancet 2020; 396: 1895–904

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Iron deficiency = Ferritin <100 ug/L

or

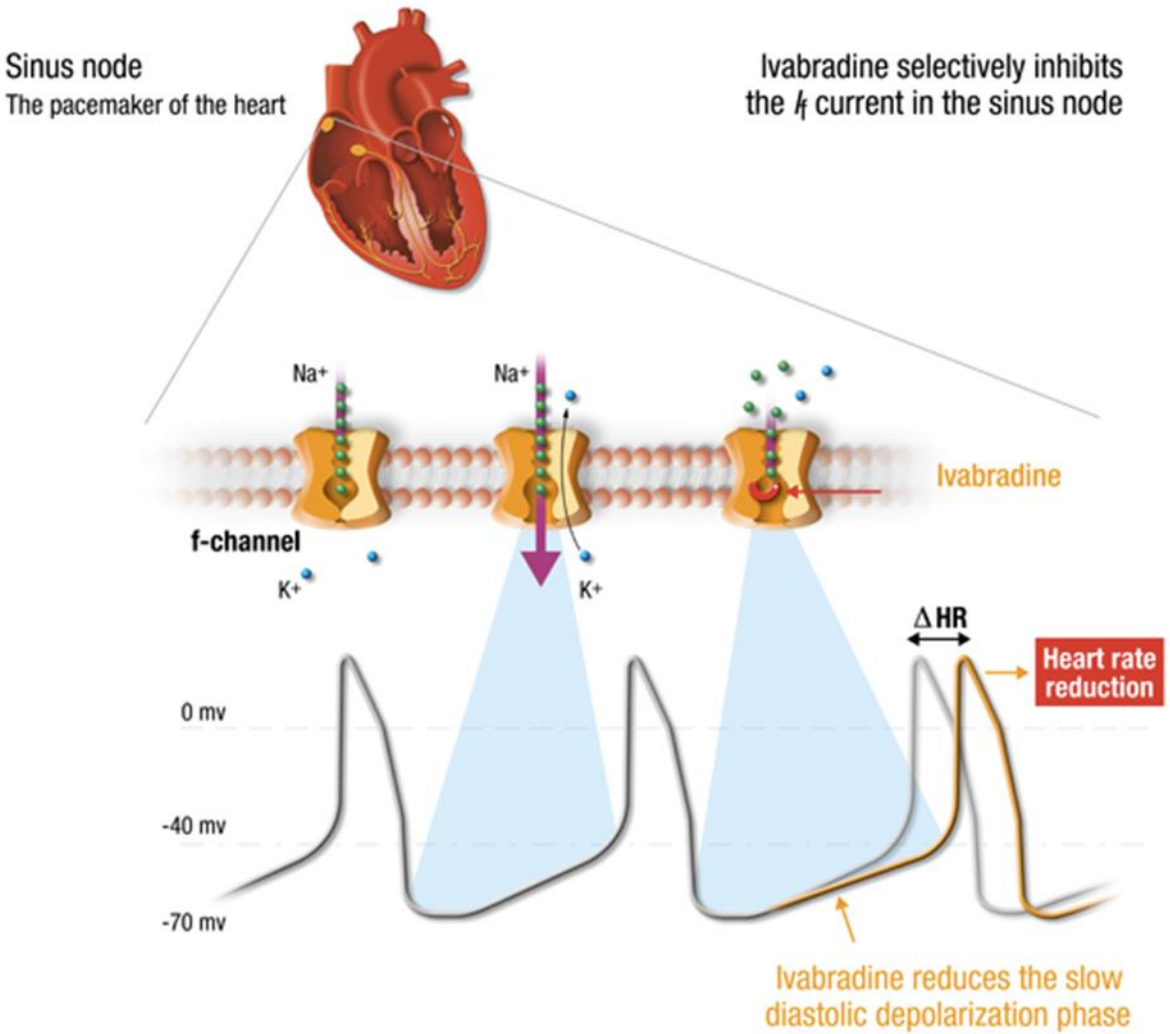
Ferritin 100-299 ug/L & TSAT <20%

Iron dosing

Ferric carboxymaltose – FCM (Ferinject): 500–1000mg single dose, followed by a ferritin/TSAT at 1–3 months, then FCM 500mg to maintain ferritin/TSAT on target. Check haemoglobin/iron studies 1–2 times per year. FCM can be administered over 15 minutes, with minimal risk of adverse effects
Ferric hydroxide surface – FHS (Venofer): 200mg weekly until repletion
Ferric gluconate (Ferrlecit):125–250 mg per IV dose
Ferric hydroxide dextran (Cosmofer): 20 mg/kg over 4-6 hours (maximum daily dose 1000 mg)

Lancet 2020; 396: 1895–904

Ivabradine



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Ivabradine and outcomes in chronic heart failure (SHIFT): a randomised placebo-controlled study

*Karl Swedberg, Michel Komajda, Michael Böhm, Jeffrey S Borer, Ian Ford, Ariane Dubost-Brama, Guy Lerebours, Luigi Tavazzi, on behalf of the SHIFT Investigators**

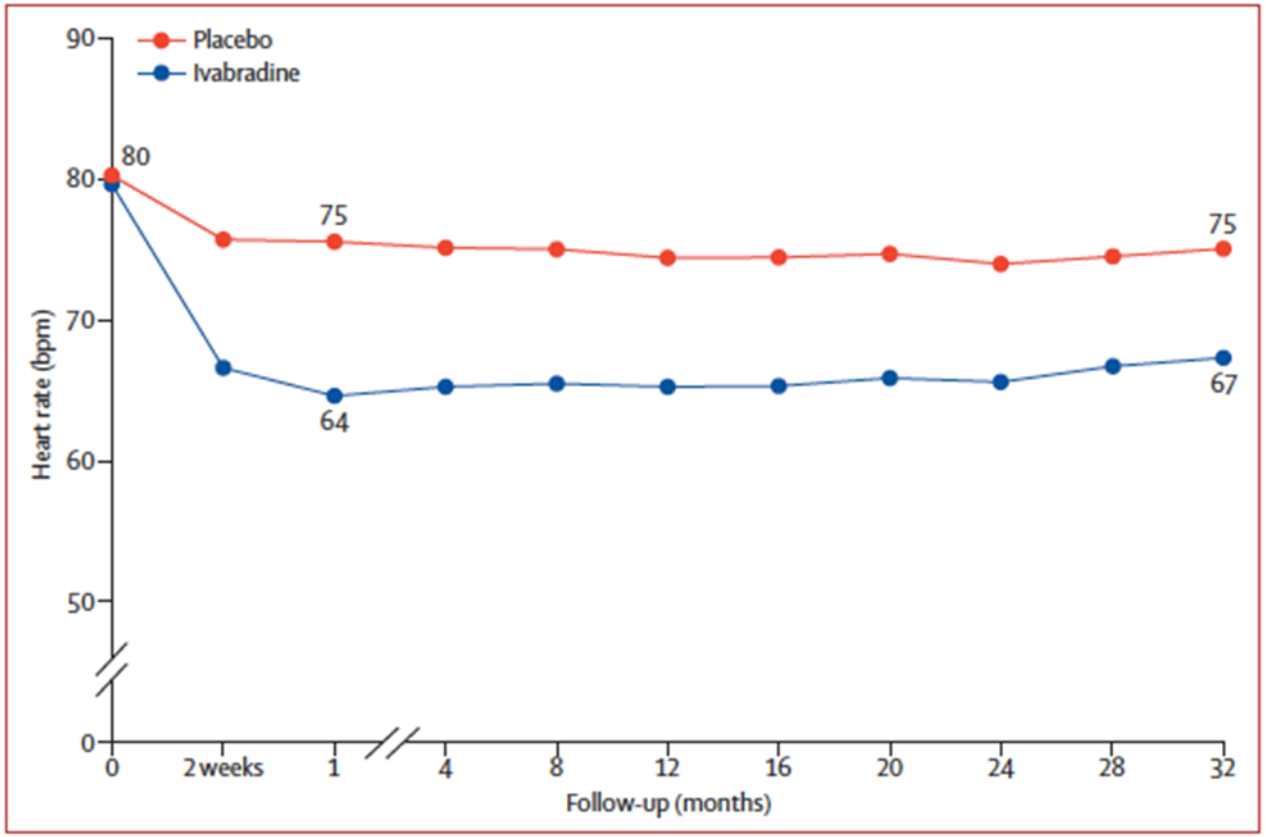

Figure 2: **Mean heart rate during the study in the total study population, by allocation groups**

Lancet 2010; 376: 875–85

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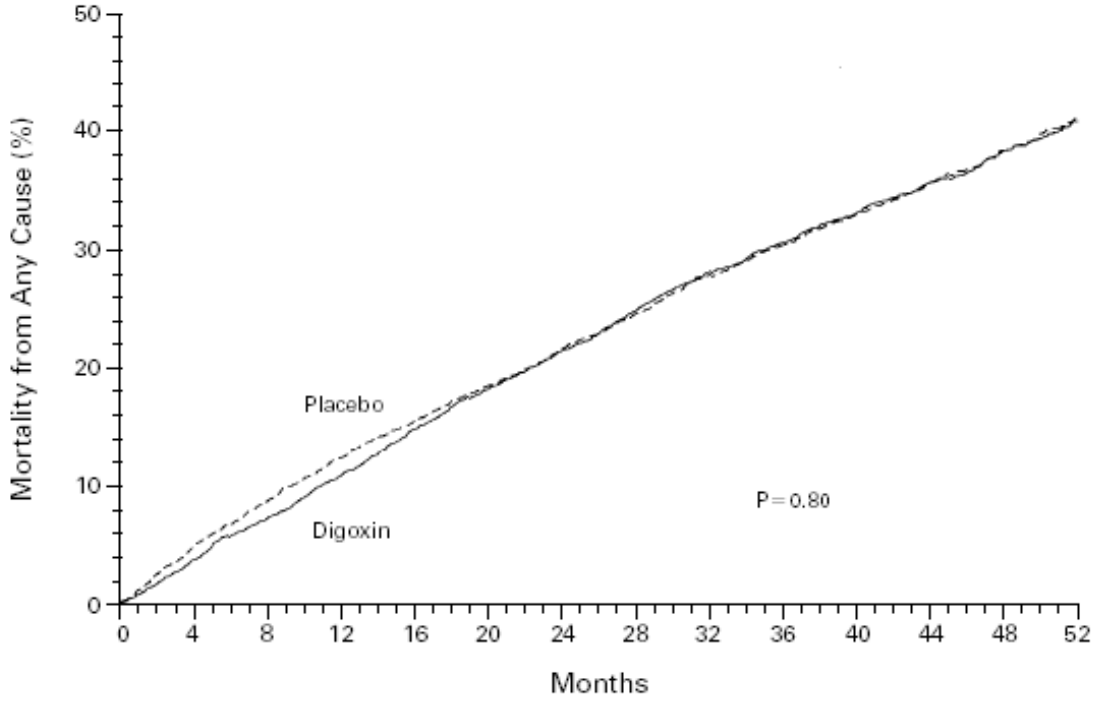
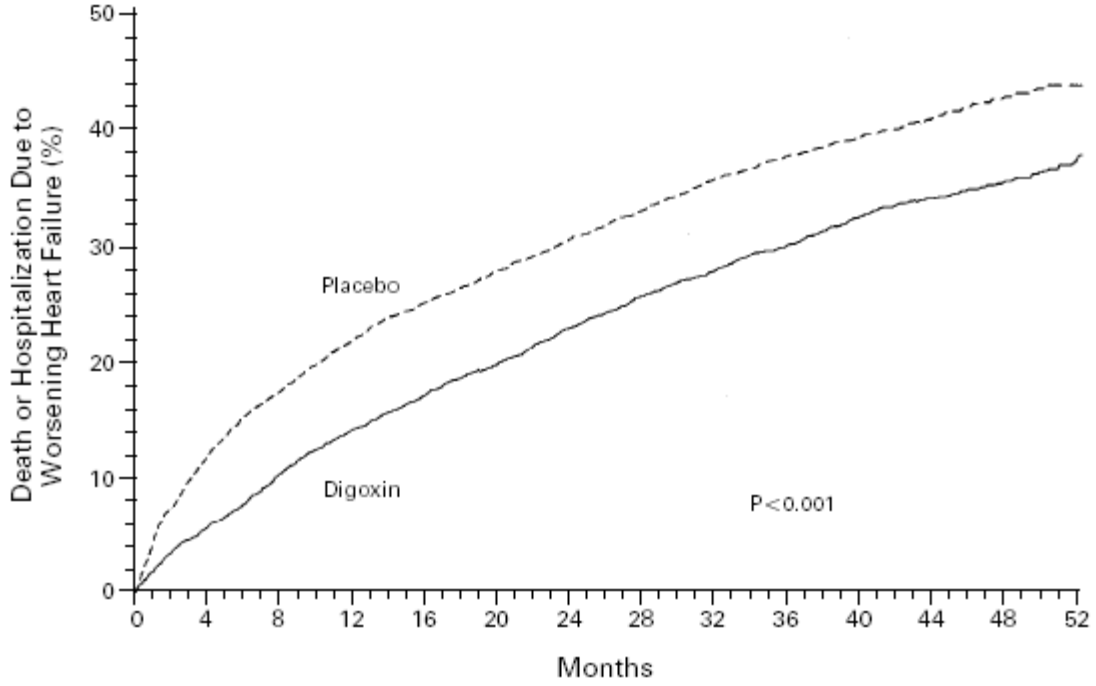
	Ivabradine group (n=3241)	Placebo group (n=3264)	HR (95% CI)	p value
Primary endpoint				
Cardiovascular death or hospital admission for worsening heart failure	793 (24%)	937 (29%)	0·82 (0·75–0·90)	<0·0001
Mortality endpoints				
All-cause mortality	503 (16%)	552 (17%)	0·90 (0·80–1·02)	0·092
Cardiovascular mortality	449 (14%)	491 (15%)	0·91 (0·80–1·03)	0·128
Death from heart failure	113 (3%)	151 (5%)	0·74 (0·58–0·94)	0·014
Other endpoints				
All-cause hospital admission	1231 (38%)	1356 (42%)	0·89 (0·82–0·96)	0·003
Hospital admission for worsening heart failure	514 (16%)	672 (21%)	0·74 (0·66–0·83)	<0·0001
Any cardiovascular hospital admission	977 (30%)	1122 (34%)	0·85 (0·78–0·92)	0·0002
Cardiovascular death, or hospital admission for worsening heart failure, or hospital admission for non-fatal myocardial infarction	825 (25%)	979 (30%)	0·82 (0·74–0·89)	<0·0001

Data are number of first events (%), hazard ratio (HR; 95% CI), and p values.

***Table 3*: Effects on primary and major secondary endpoints**

Digoxin





- **6,800 PATIENTS, MEAN AGE 63 YRS**
- **MOST ON DIURETICS ACE-I**
- **MAJORITY NYHA CLASS II, III**
- **ISCHAEMIA PRIMARY CAUSE IN 70%**
- **LOW DOSE / MONITOR LEVELS**

(N ENGL J MED 1997; 336: 525-33)

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Hydralazine/Nitrates

Hydralazine and nitrates alone or combined for the management of chronic heart failure: A systematic review

Mohamed Farag [a,*], Thato Mabote [a], Ahmad Shoaib [a], Jufen Zhang [a], Ashraf F. Nabhan [c], Andrew L. Clark [a], John G. Cleland [b]

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[b] National Heart & Lung Institute, Imperial College, London, UK
[c] Postgraduate Medical School, Ain Shams University, Cairo, Egypt

Int J Cardiol 2015; 196: 61 - 69

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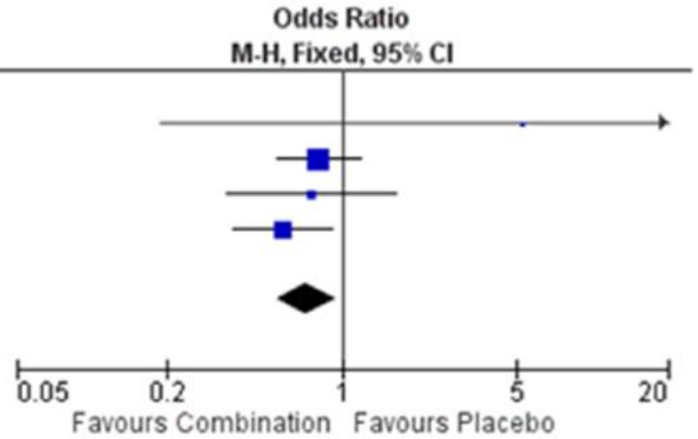
(A)

Study or Subgroup	Combination Events	Total	Placebo Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Franciosa et al	0	11	0	11		Not estimable	1979
Unverferth et al	1	7	0	11	0.3%	5.31 [0.19, 150.08]	1983
V-HeFT I	72	186	120	273	48.0%	0.81 [0.55, 1.18]	1986
Ghose et al	21	50	25	51	11.6%	0.75 [0.34, 1.65]	1992
A-HeFT	32	518	54	532	40.2%	0.58 [0.37, 0.92]	2004
Total (95% CI)		**772**		**878**	**100.0%**	**0.72 [0.55, 0.95]**	
Total events	126		199				

Heterogeneity: $Chi^2 = 2.55$, $df = 3$ ($P = 0.47$); $I^2 = 0\%$
Test for overall effect: $Z = 2.36$ ($P = 0.02$)



(B)

Study or Subgroup	Combination Events	Total	Placebo Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Franciosa et al	0	11	0	11		Not estimable	1979
Unverferth et al	1	7	0	11	0.3%	5.31 [0.19, 150.08]	1983
V-HeFT I	70	186	113	273	50.3%	0.85 [0.58, 1.25]	1986
Ghose et al	18	50	22	51	12.3%	0.74 [0.33, 1.65]	1992
A-HeFT	26	518	45	532	37.1%	0.57 [0.35, 0.94]	2004
Total (95% CI)		**772**		**878**	**100.0%**	**0.75 [0.57, 0.99]**	
Total events	115		180				

Heterogeneity: $Chi^2 = 2.90$, $df = 3$ ($P = 0.41$); $I^2 = 0\%$
Test for overall effect: $Z = 2.02$ ($P = 0.04$)

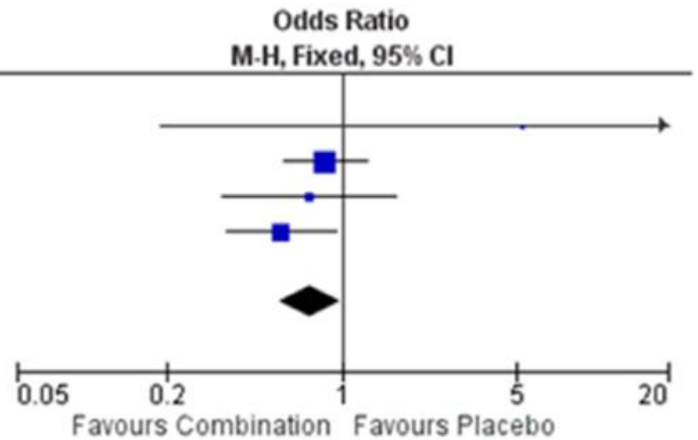


Fig. 1. Mortality with nitrates and hydralazine combination vs. placebo. (A) All-cause mortality, and (B) cardiovascular mortality.

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Int J Cardiol 2015; 196: 61 - 69

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Influenza Vaccination

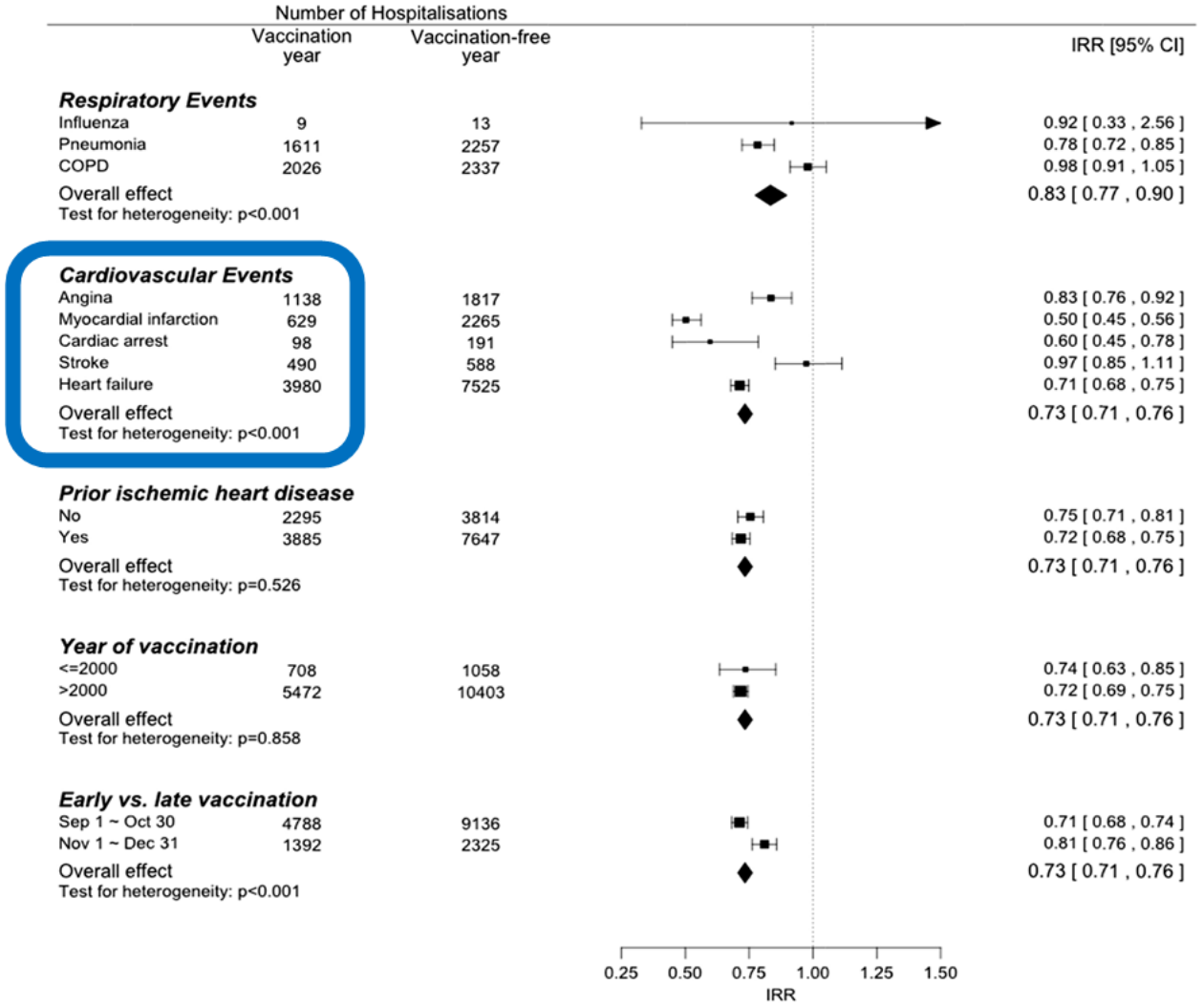

Figure 4 Effect of influenza vaccination on the risk of hospitalizations due to cardiovascular disease, by type of ...

New Therapies

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 14, 2021 VOL. 384 NO. 2

Cardiac Myosin Activation with Omecamtiv Mecarbil in Systolic Heart Failure

N Engl J Med 2021; 384: 105-16

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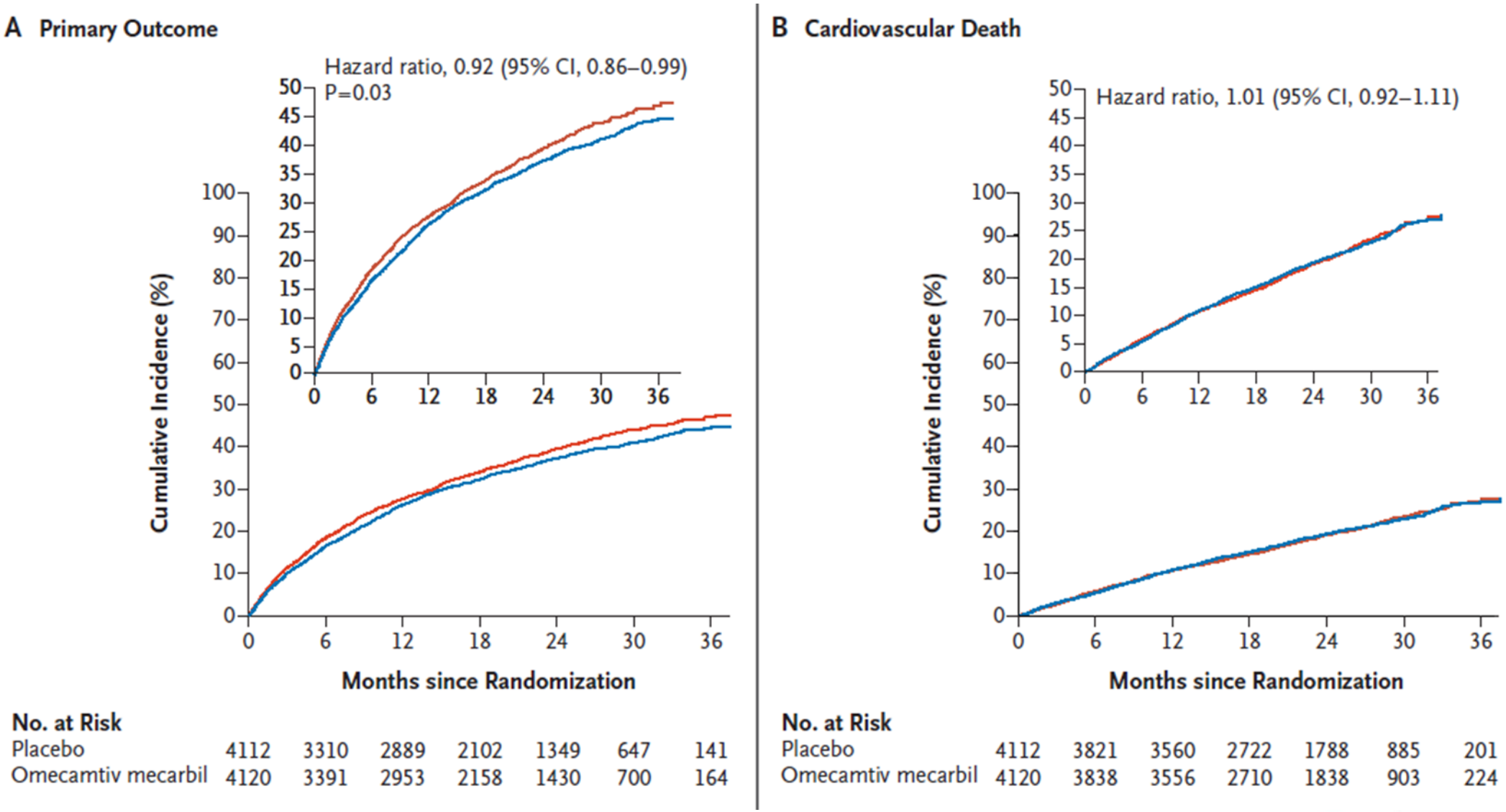

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N Engl J Med 2021; 384: 105-16

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The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 14, 2020 VOL. 382 NO. 20

Vericiguat in Patients with Heart Failure and Reduced Ejection Fraction

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N Engl J Med 2020; 382: 1883-93

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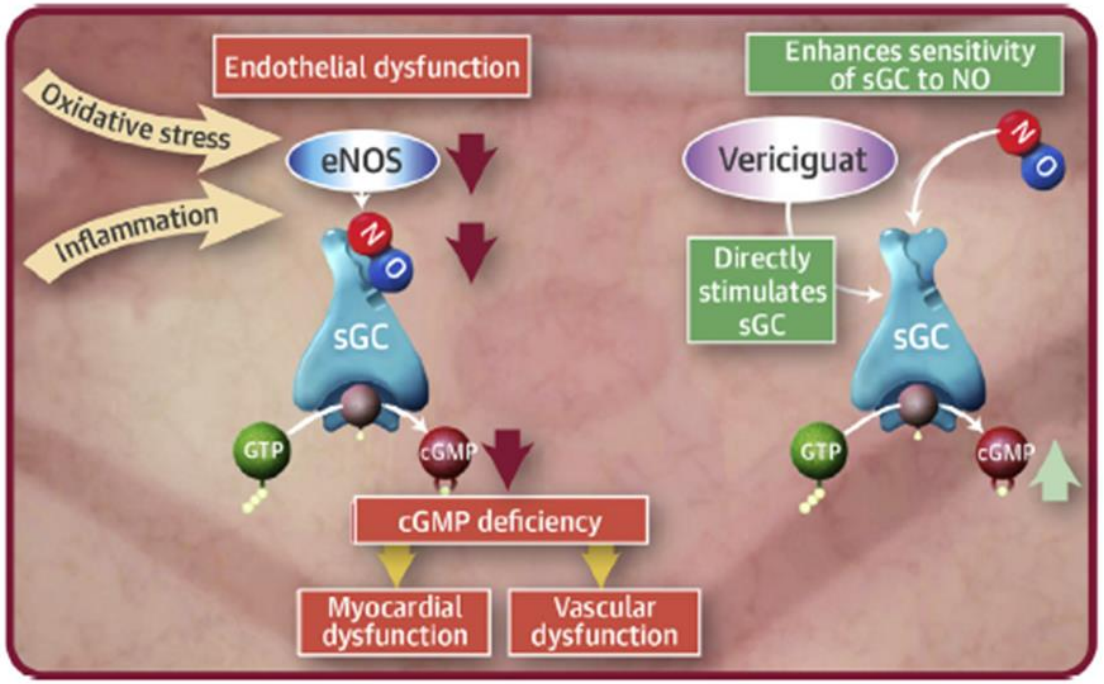
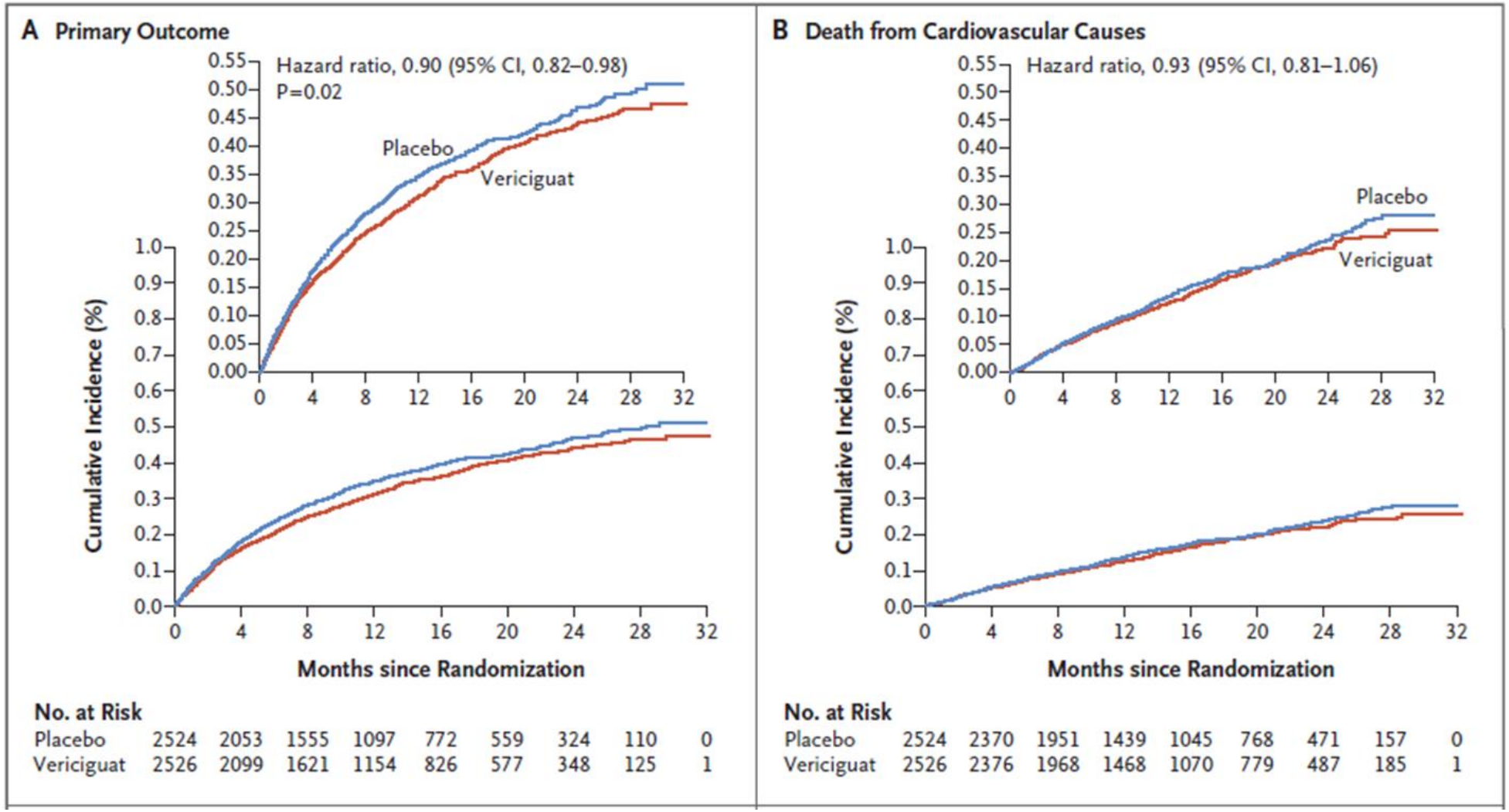
CENTRAL ILLUSTRATION Restoration of Sufficient sGC-cGMP Signaling as Novel Target in HF



Armstrong, P.W. et al. J Am Coll Cardiol HF. 2018;6(2):96-104.

Endothelial dysfunction due to oxidative stress and inflammation reduces nitric oxide bioavailability leading to insufficient activation of sGC. The resulting cGMP deficiency is associated with myocardial dysfunction and impaired endothelium-dependent vasomotor regulation **(orange)**. Vericiguat directly stimulates sGC in a NO-independent manner and by sensitizing the enzyme to endogenous NO **(green)**. cGMP = cyclic guanosine monophosphate; HF = heart failure; NO = nitric oxide; sGC = soluble guanylate cyclase.

N Engl J Med 2020; 382: 1883-93



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N Engl J Med 2020; 382: 1883-93

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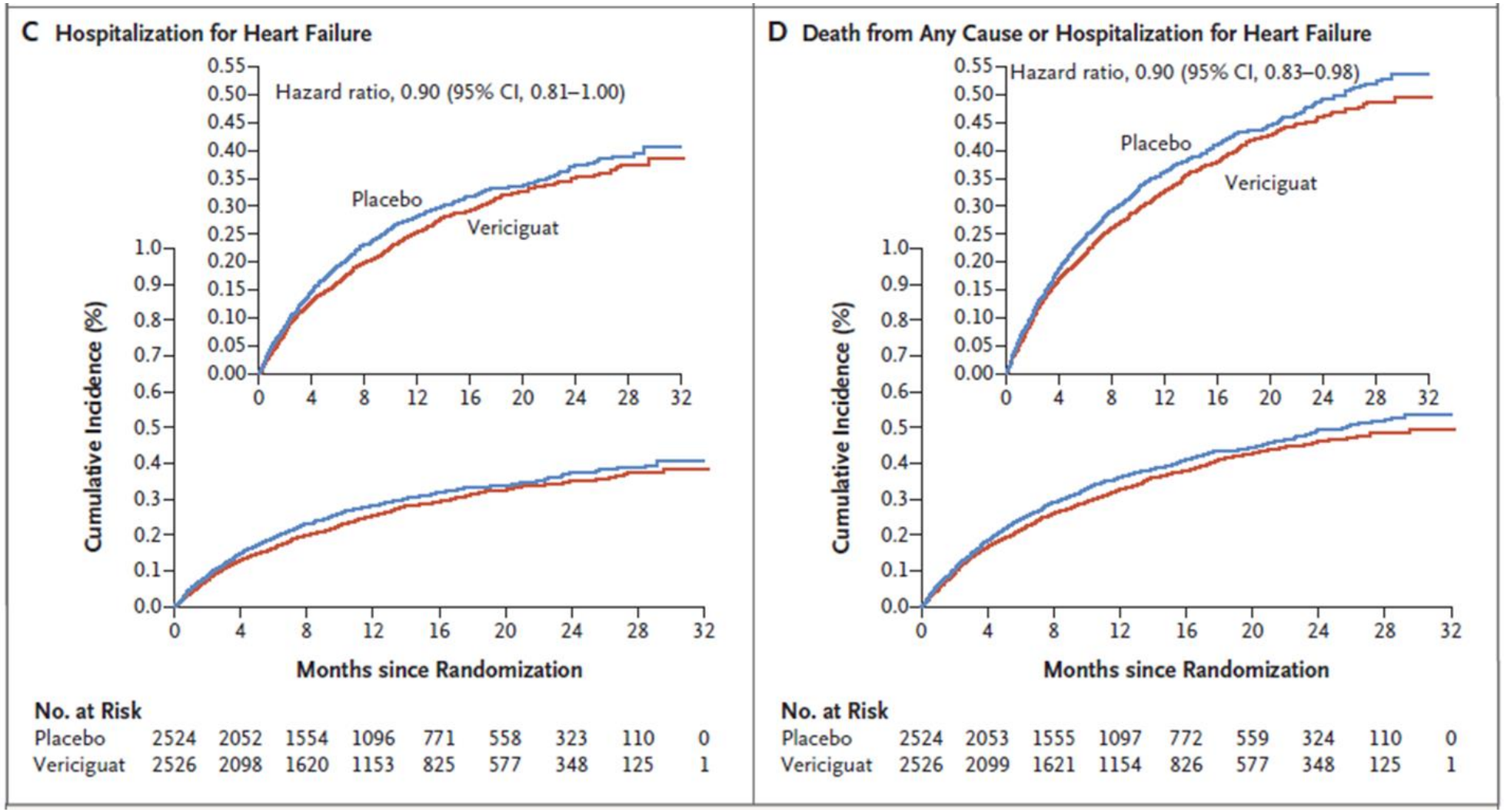

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Thank you for attending!

Please complete the online confirmation of attendance emailed to you post meeting to receive a CPD certificate.

HF ACADEMY COURSE OVERVIEW

This **free CPD accredited educational program** was developed by cardiologists who are members of the Heart Failure Society of South Africa and is aimed at those who are interested in improving services for people with heart failure, including **not only doctors, but also nurses and pharmacists**. The course comprises 5 modules that provide a basic review of heart failure care and each module is individually **CPD accredited for 5 CPD points** with the HPCSA. Following the completion of all 5 modules, a **Certificate of Competency** in basic heart failure management will be awarded by HeFSSA.

COURSE LEARNING OBJECTIVES

- ✓ Raise the awareness of heart failure among health care professionals
- ✓ Improve the prevention, diagnosis, treatment and long – term management of heart failure
- ✓ Ensure equity of care for all patients with heart failure
- ✓ Support and empower patients with heart failure and their families or other caregivers to engage proactively in long – term care

COURSE DIRECTORS

Prof Nash Ranjith
City Hospital
University of KwaZulu Natal

Dr Martin Mpe
Mediclinic Heart Hospital

Prof Nqoba Tsabedze
University of the Witwatersrand

Dr Tony Lachman
Victoria Hospital

Prof Mpiko Ntsekhe
University of Cape Town

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