Sociedad Peruana de Medicina Interna
VI Curso Internacional y XLVI Curso de Terapéutica y Prevención en Medicina

Lima, 22 de marzo de 2025

Titulación en falla cardíaca con fracción de eyección reducida

Armando Lionel Godoy Palomino

Cardiólogo Clínico

Profesor Universidad Nacional Mayor de San Marcos

Instituto Nacional Cardiovascular INCOR

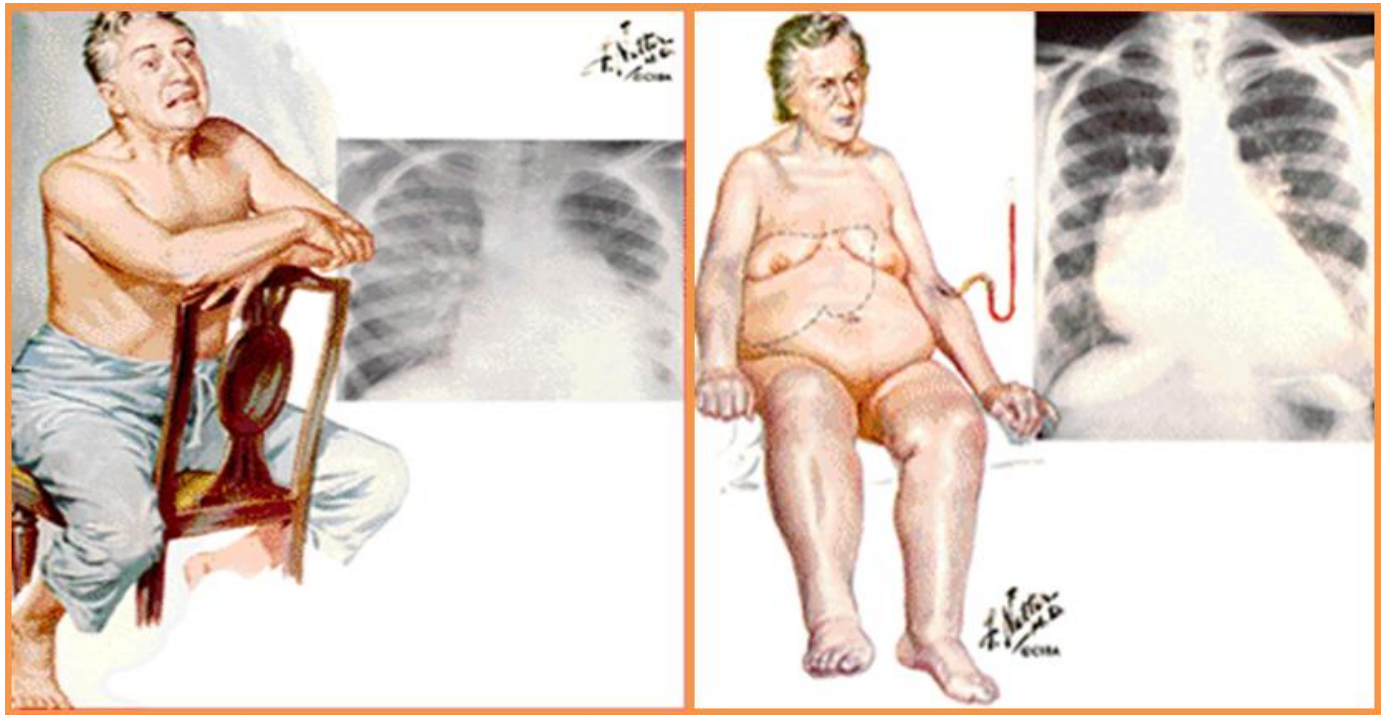
Clínica Delgado AUNA

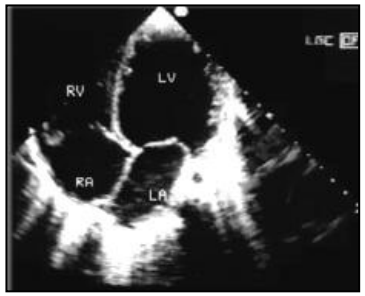
Conflictos de interés:

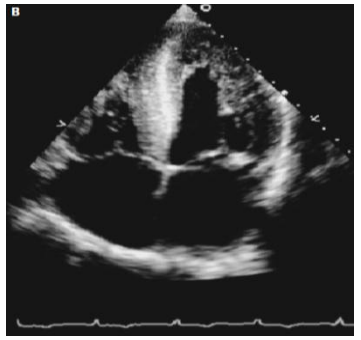
Investigador principal de ensayos de falla cardíaca: PARADIGM-HF, PARAGON-HF, VICTORIA, DELIVER, VICTOR, BALANCED-HF.

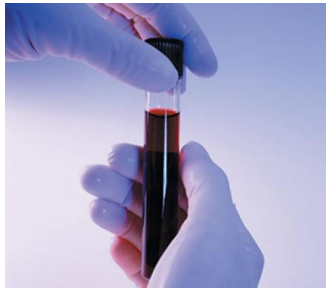
Vocero de AstraZeneca, Farmakonsuma, MSN, Merck Serono, Abbott, MSD, Novartis, Bayer, Tecnofarma, Pfizer, Boehringer Ingelheim, Sanofi Aventis, Ohm.

Introducción





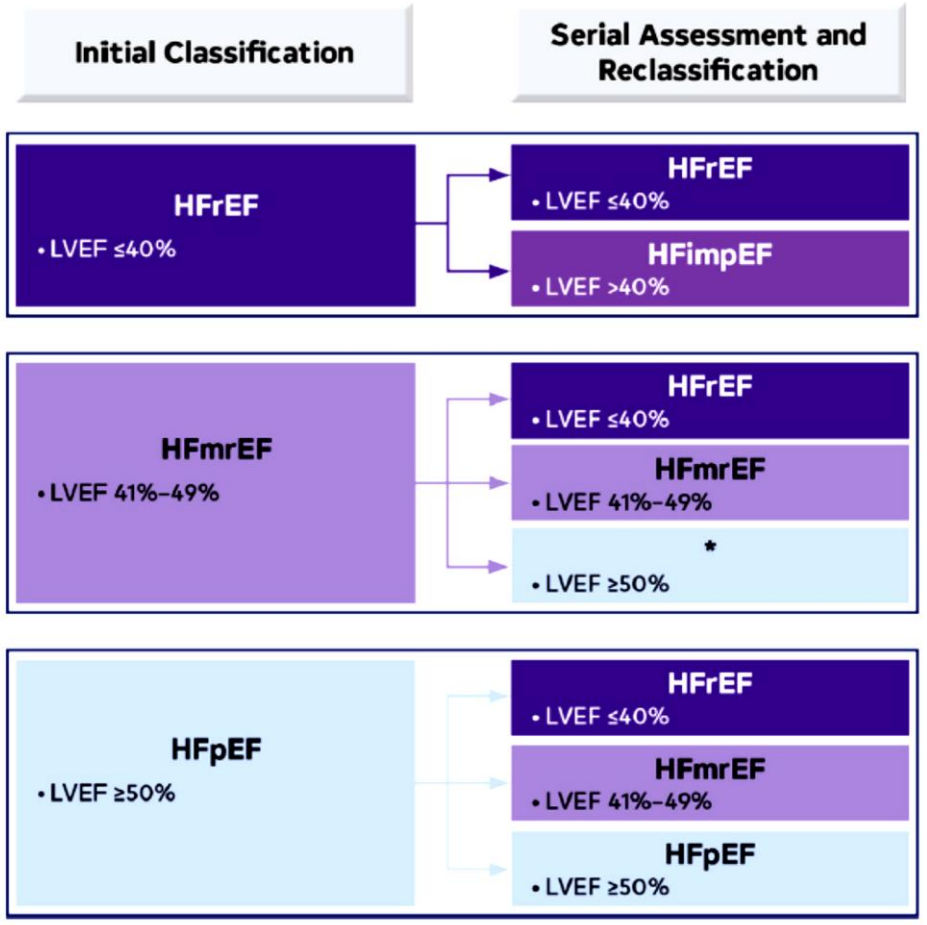




"No he de volver a escribir
como lo hice cuando el
corazón era joven
y sobre mí el firmamento"

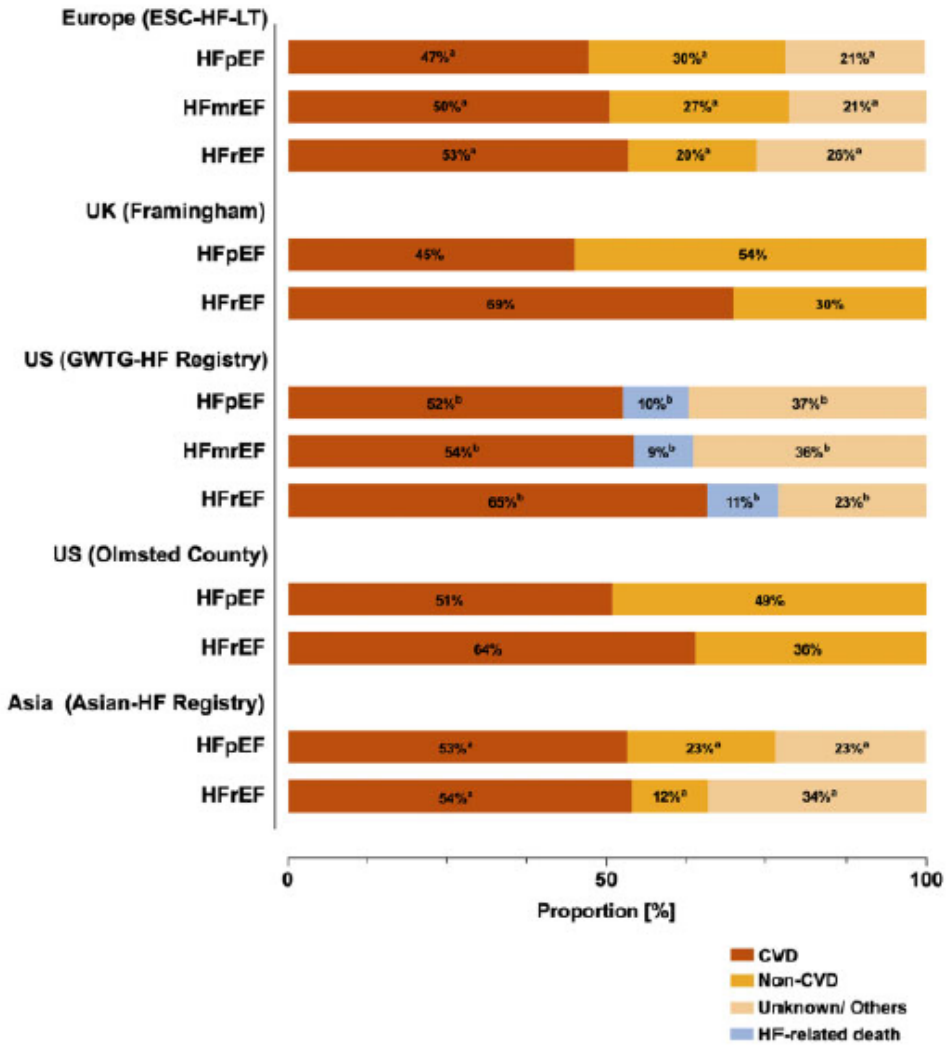
Definiciones y trayectoria de fenotipos de falla cardiaca

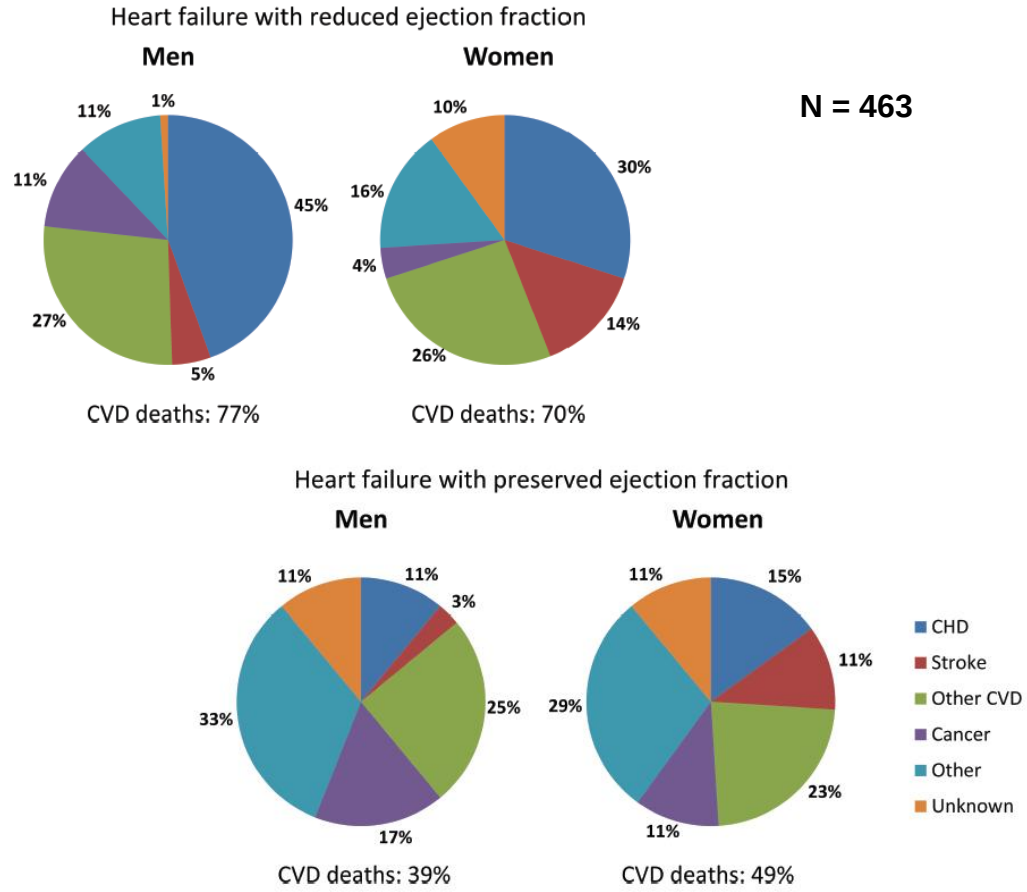
Type of HF According to LVEF	Criteria
HFrEF (HF with reduced EF)	LVEF ≤40%
HFimpEF (HF with improved EF)	Previous LVEF ≤40% and a follow-up measurement of LVEF >40%
HFmrEF (HF with mildly reduced EF)	LVEF 41%–49% Evidence of spontaneous or provokable increased LV filling pressures (eg, elevated natriuretic peptide, noninvasive and invasive hemodynamic measurement)
HFpEF (HF with preserved EF)	LVEF ≥50% Evidence of spontaneous or provokable increased LV filling pressures (eg, elevated natriuretic peptide, noninvasive and invasive hemodynamic measurement)



2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure Treatment. J Am Coll Cardiol 2022

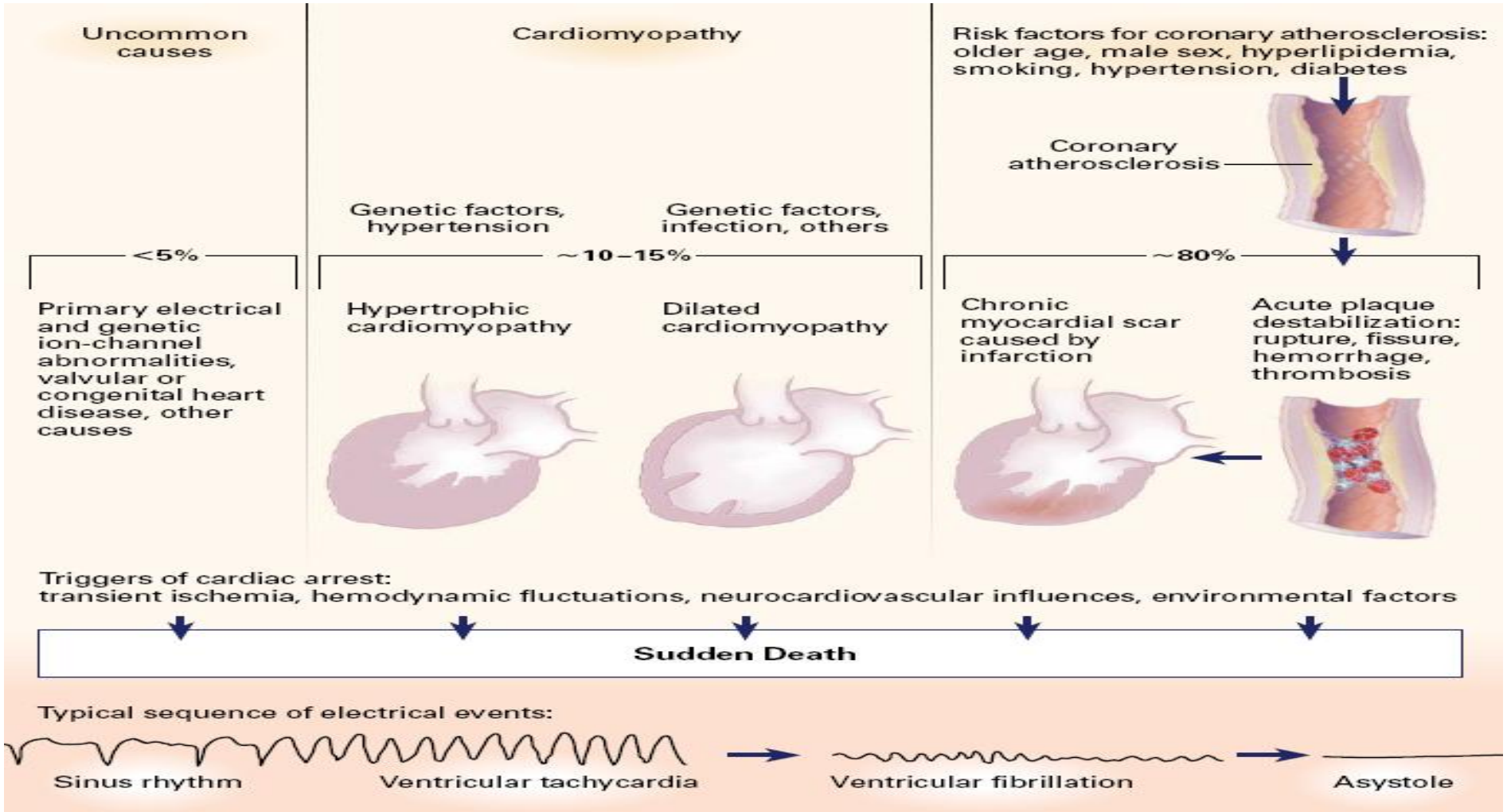
Muerte en los fenotipos de insuficiencia cardíaca





Savarese G, et al. Cardiovasc Res 2022;118:3272-87
Lee DS, et al. Circ Heart Fail 2011;4:36-43

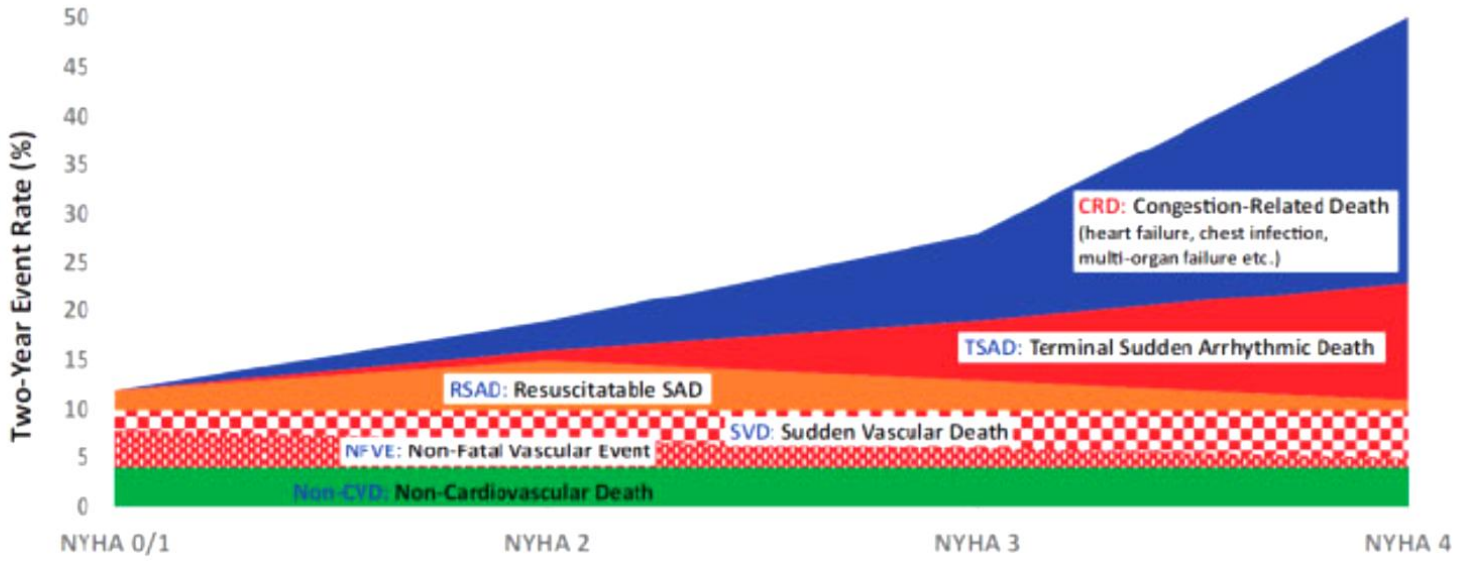
Muerte súbita en la insuficiencia cardíaca



Huikuri HV, Castellanos A, Myergurg R. N Engl J Med 2001;345:1473-83

Clase funcional NYHA y tipo de muerte en falla cardíaca

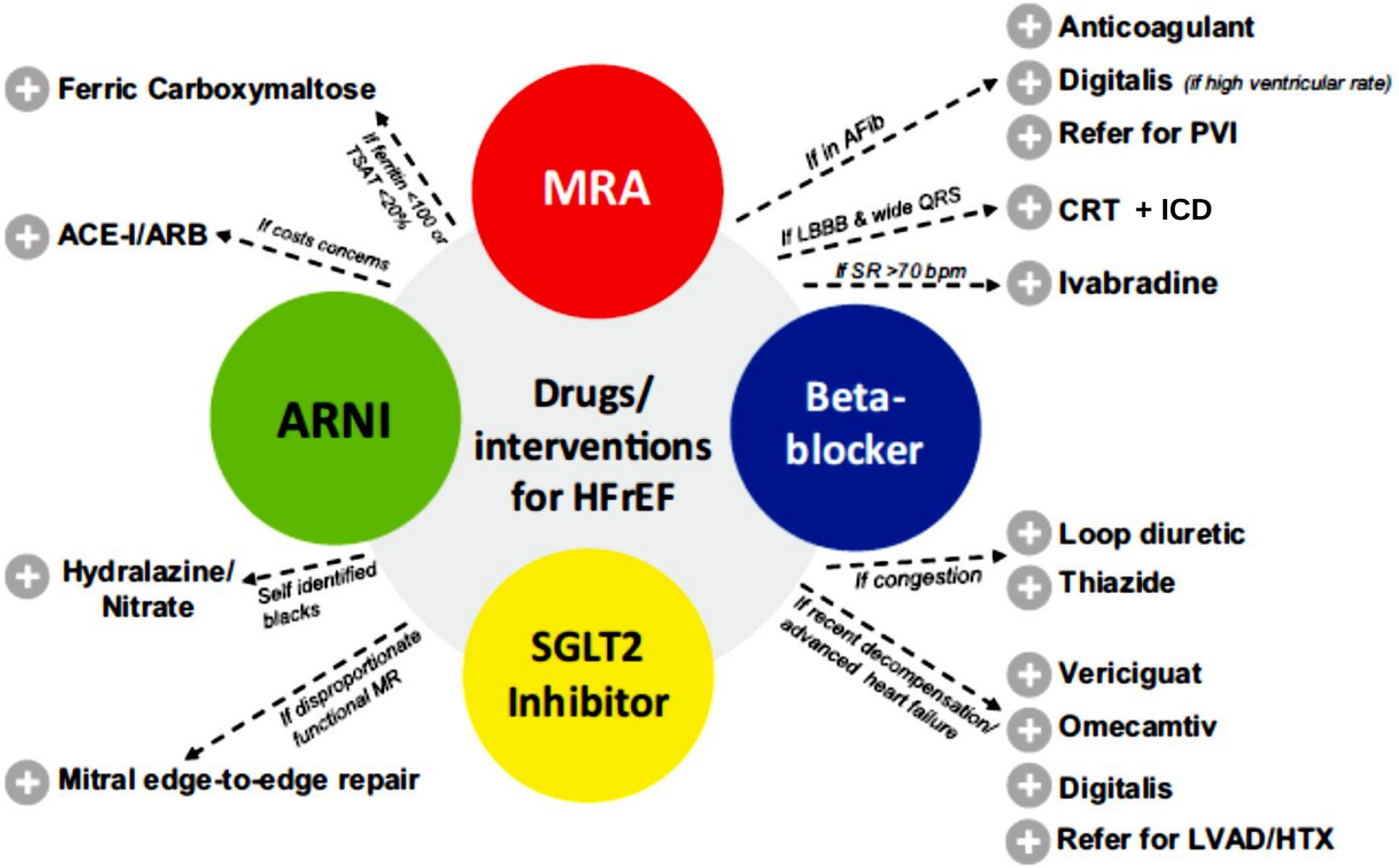
Class I	No limitation of physical activity. Ordinary physical activity does not cause undue breathlessness, fatigue, or palpitations.
Class II	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in undue breathlessness, fatigue, or palpitations.
Class III	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity results undue breathlessness, fatigue, or palpitations.
Class IV	Unable to carry on any physical activity without discomfort. Symptoms at rest can be present. If any physical activity is undertaken, discomfort is increased.



	NYHA 0/1		NYHA 2		NYHA 3		NYHA 4	
	Absolute Rate	% of Events	Absolute Rate	% of Events	Absolute Rate	% of Events	Absolute Rate	% of Events
CRD	0%	0%	3%	16%	9%	32%	27%	54%
TSAD	<1%	<1%	1%	5%	6%	21%	12%	24%
RSAD	2%	17%	5%	26%	3%	11%	1%	2%
SVD	2%	17%	3%	16%	4%	14%	5%	10%
NFVE	4%	33%	3%	16%	2%	7%	1%	2%
Non-CVD	4%	33%	4%	21%	4%	14%	4%	8%

Eur Heart J (2021) 00, 1-128 doi:10.1093/eurheartj/ehab368
Cleland JGF, et al. Eur Heart J 2019;40:2128-30

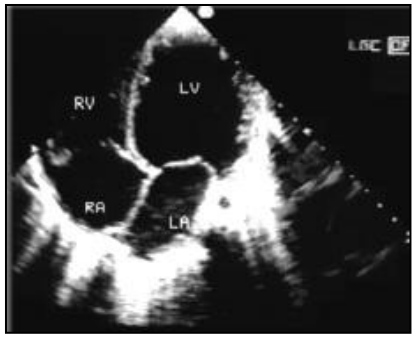
Tratamiento cuádruple de la IC-FE r

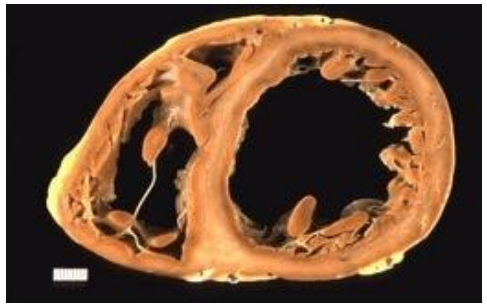


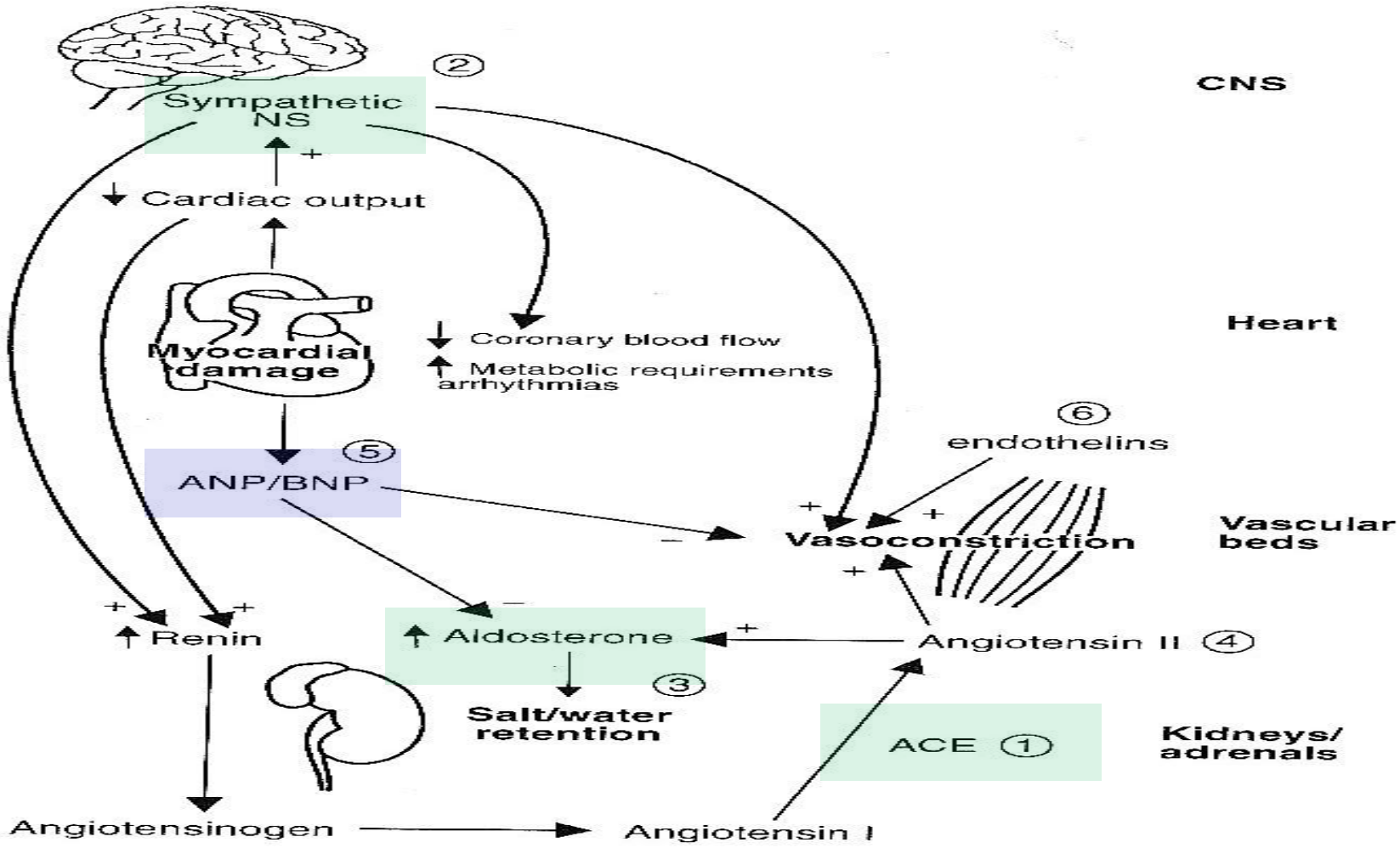
Bauersachs J. Eur Heart J 2021;42:481-3

Las neurohormonas de siempre

Bloqueo/modulación neurohumoral progresivo



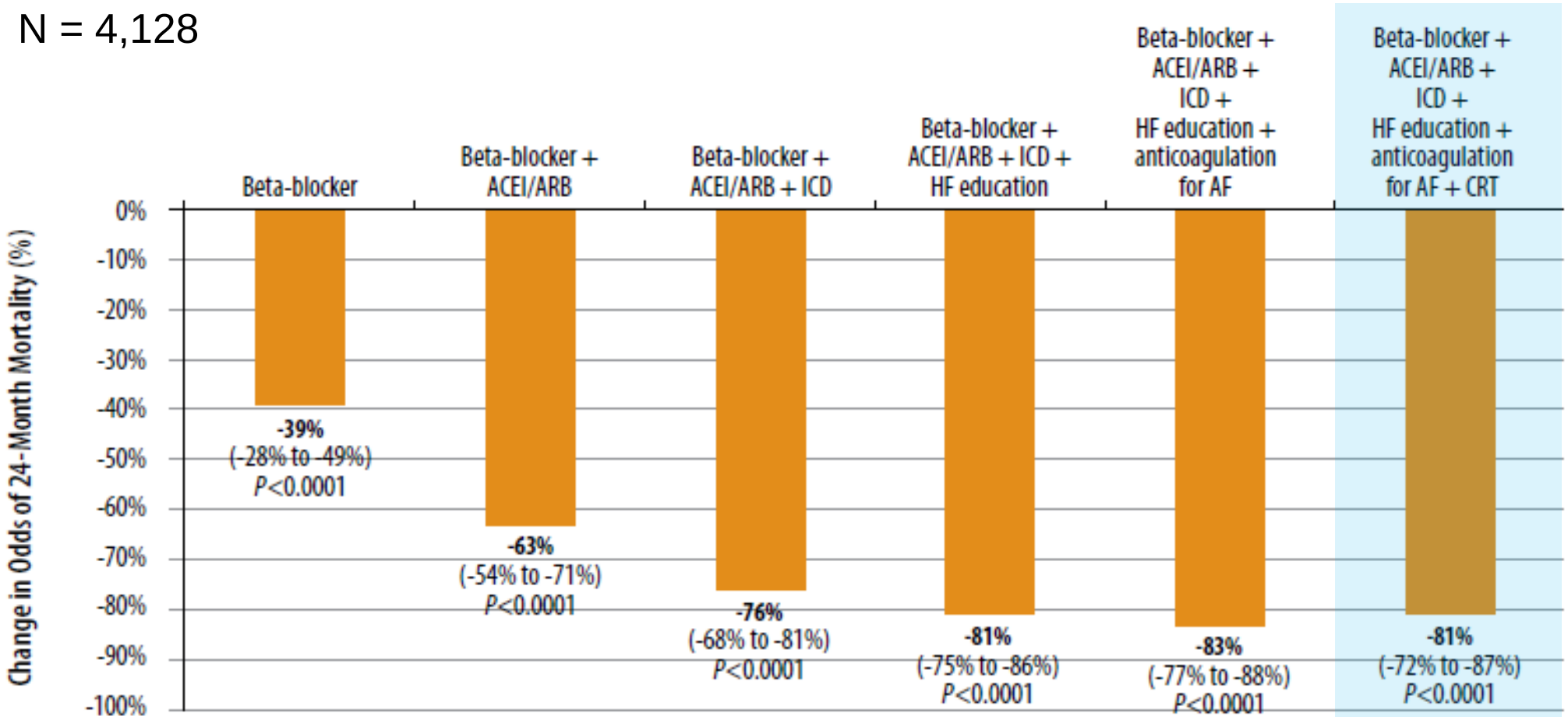




McEwan J. Current Issues in Cardiology. Pp. 142. BMJ 1998

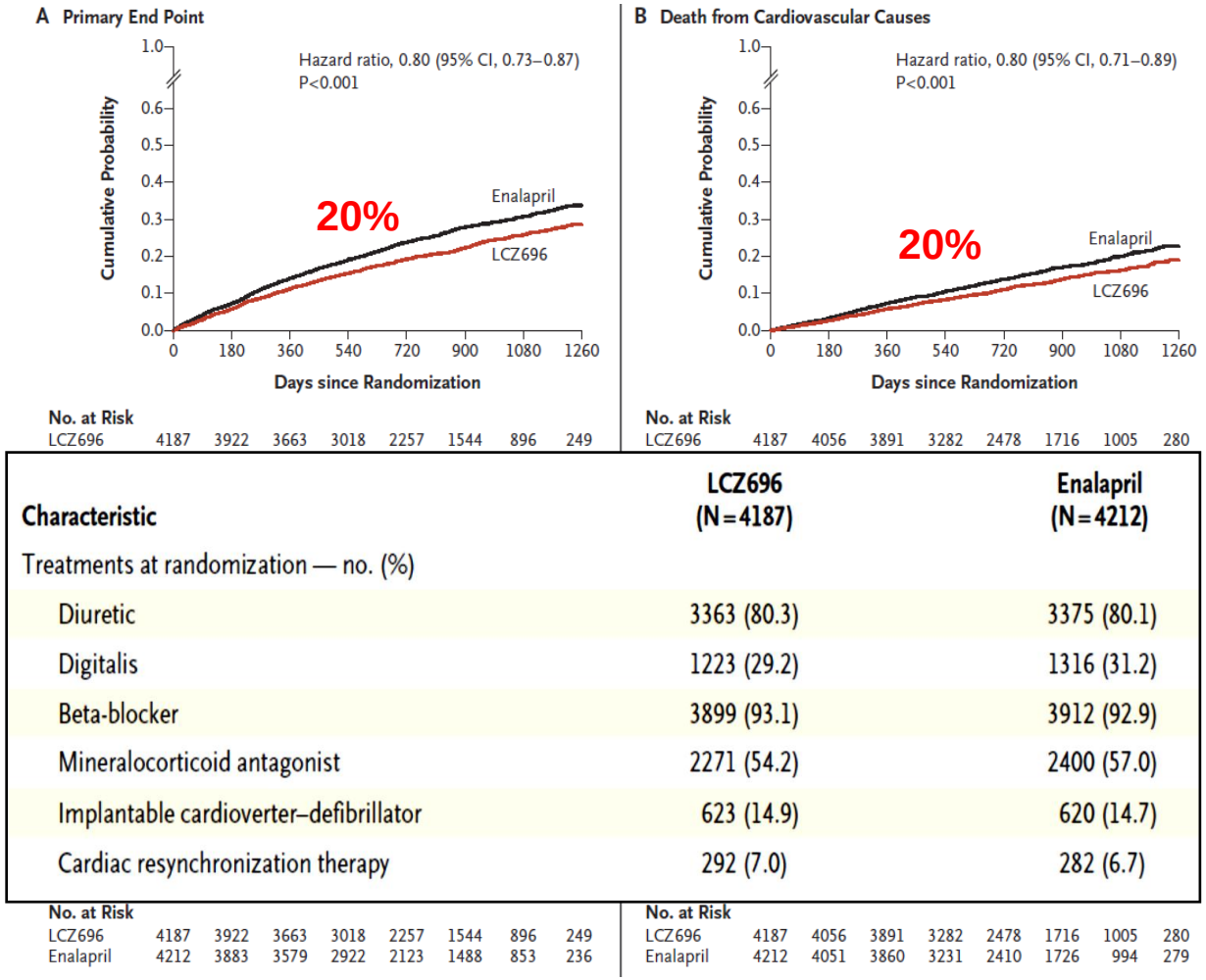
Tratamiento combinado en IC-FE r (IMPROVE-HF)

N = 4,128

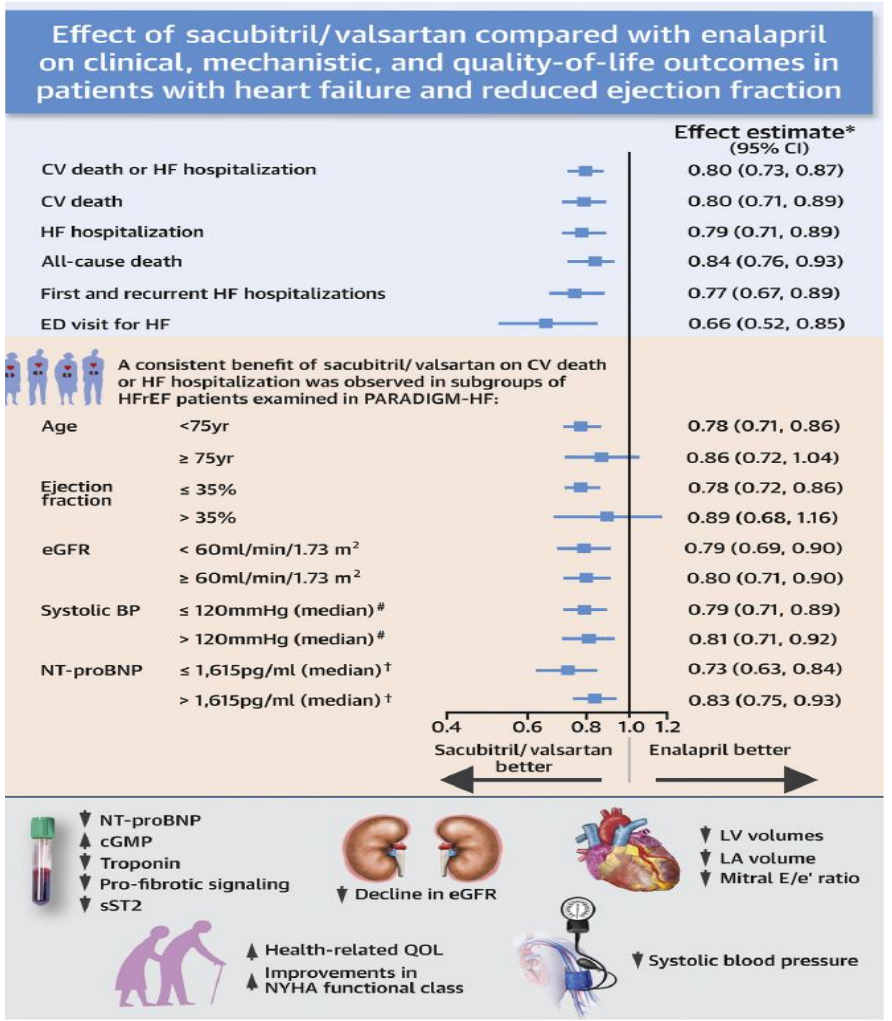


Fonarow GC, Albert NM, Curtis AB et al. J Am Heart 2012;1:16-26

Valsartán/sacubitril (PARADIGM-HF, estadio C)

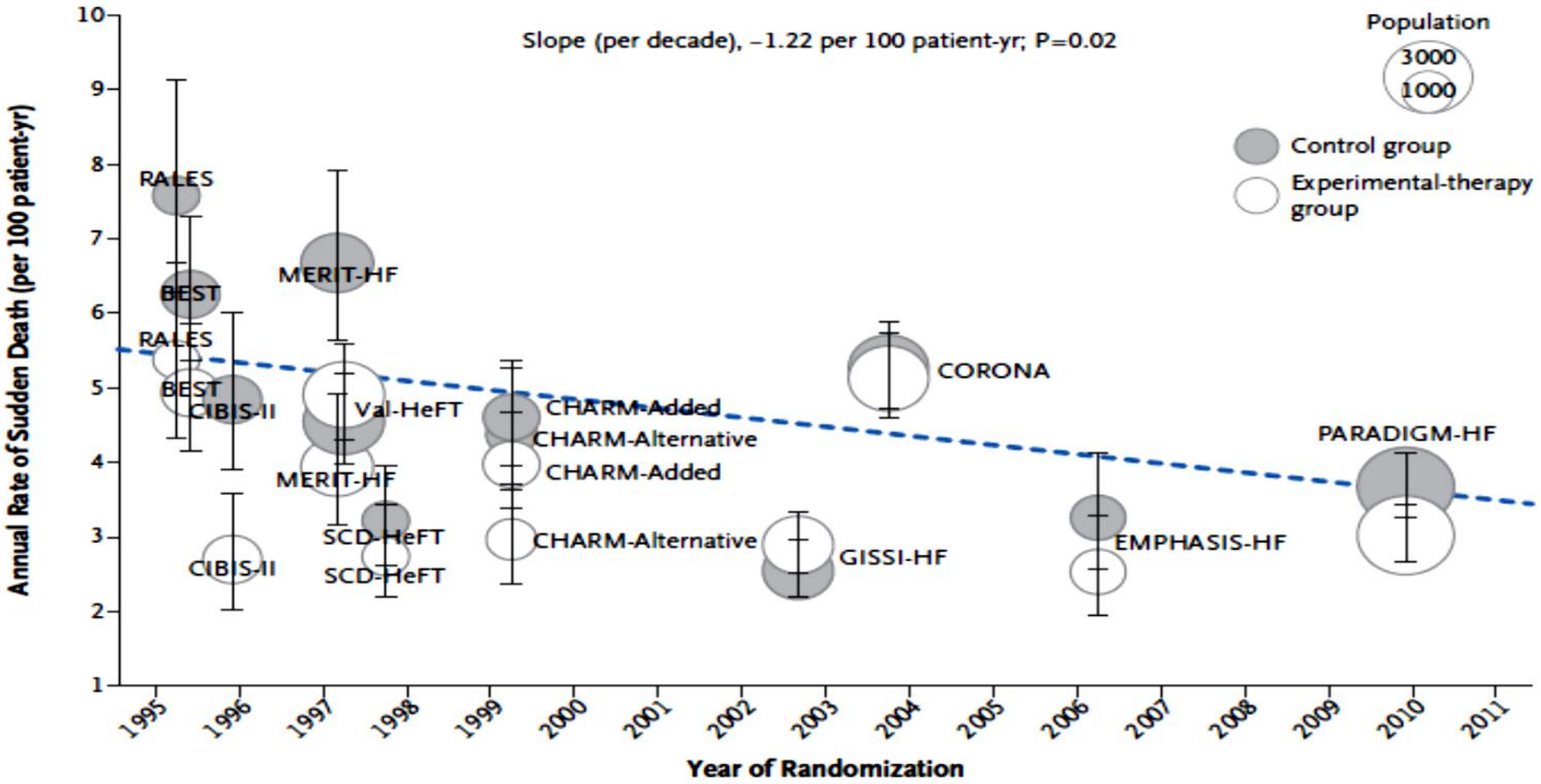


Characteristic	LCZ696 (N=4187)	Enalapril (N=4212)
Treatments at randomization — no. (%)		
Diuretic	3363 (80.3)	3375 (80.1)
Digitalis	1223 (29.2)	1316 (31.2)
Beta-blocker	3899 (93.1)	3912 (92.9)
Mineralocorticoid antagonist	2271 (54.2)	2400 (57.0)
Implantable cardioverter–defibrillator	623 (14.9)	620 (14.7)
Cardiac resynchronization therapy	292 (7.0)	282 (6.7)



McMurray JJV, et al. N Engl J Med 2014;371:993-1004
Docherty KF, et al. J Am Coll Cardiol HF 2020;8:800-10

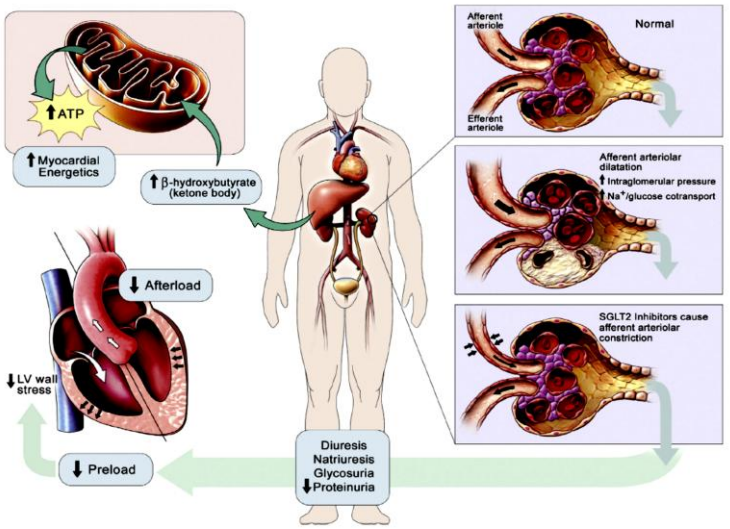
Pronóstico de la muerte súbita



Shen L, et al. N Engl J Med 2017;377:41-5

Terapia cuádruple de nuestros días: más allá de las neurohormonas

iSGLT2 en insuficiencia cardíaca

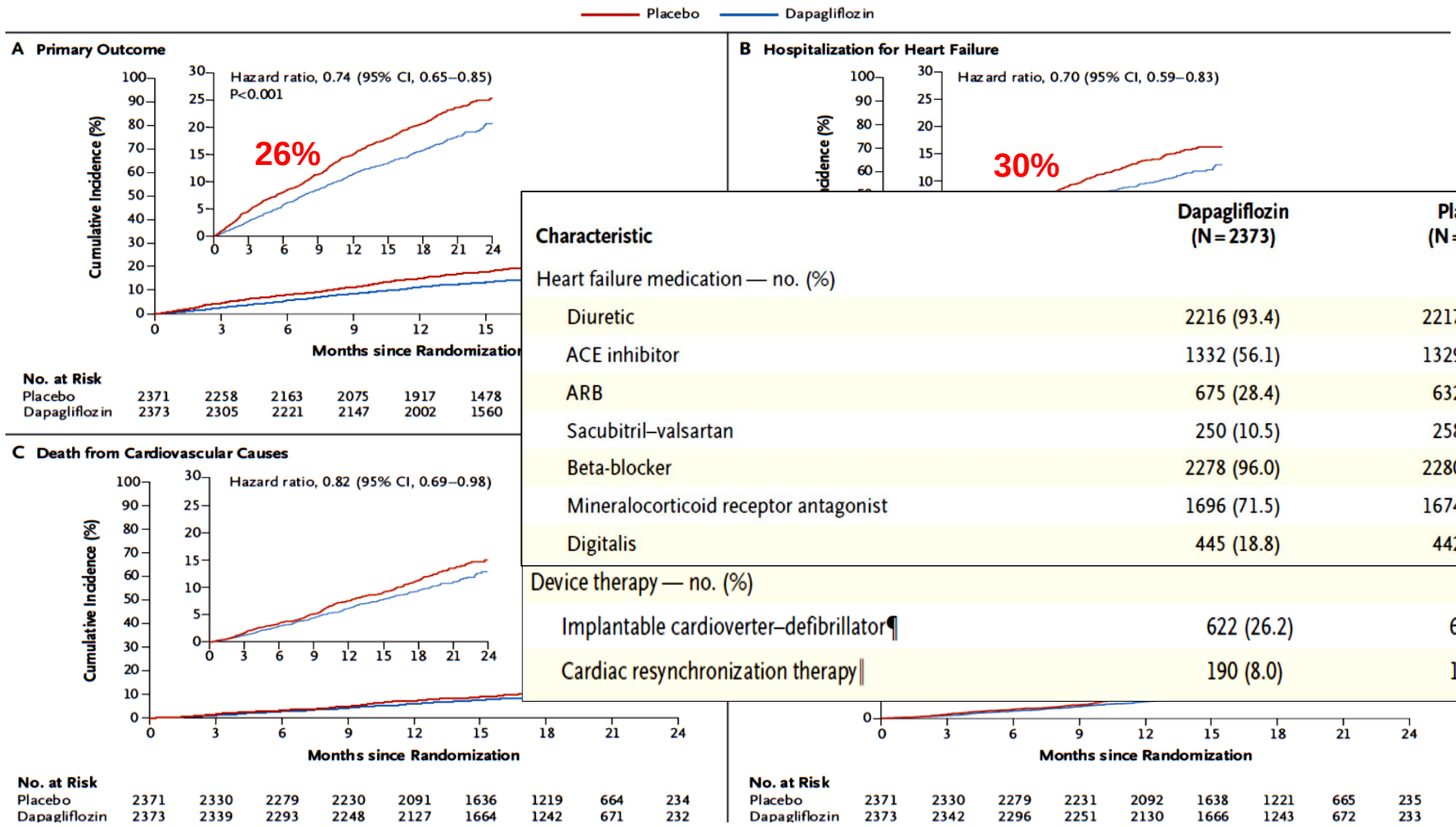


N = 71,553

Trial	Patient Population	Active Treatment Assignment	Effect on Time to First Hospitalization for Heart Failure HR (95% CI)
EMPA-REG OUTCOMES	7,020 patients with type 2 diabetes	Empagliflozin	0.65 (0.50-0.85)
CANVAS	10,142 patients with type 2 diabetes	Canagliflozin	0.67 (0.52-0.87)
DECLARE-TIMI58	17,160 patients with type 2 diabetes	Dapagliflozin	0.73 (0.61-0.88)
VERTIS-CV	8,246 patients with type 2 diabetes	Ertugliflozin	0.70 (0.54-0.90)
CREDENCE	4,401 patients with type 2 diabetes with chronic kidney disease	Canagliflozin	0.61 (0.47-0.80)
DAPA-CKD	4,304 patients with chronic kidney disease, 67% with diabetes	Dapagliflozin	0.51 (0.34-0.76)
SCORED	10,584 patients with type 2 diabetes with chronic kidney disease	Sotagliflozin	0.67 (0.55-0.82)
DAPA-HF	4,744 patients with chronic heart failure and reduced ejection fraction, 42% with diabetes	Dapagliflozin	0.70 (0.59-0.83)
EMPEROR-Reduced	3,730 patients with chronic heart failure with reduced ejection fraction, 50% with diabetes	Empagliflozin	0.69 (0.59-0.81)
SOLOIST	1,222 with type 2 diabetes with worsening heart failure, with reduced and preserved ejection fraction	Sotagliflozin	0.64 (0.49-0.83)

Verma S, et al. JAMA Cardiology 2017;2:939-40
Packer M. JACC Heart Fail 2021;9:535-49

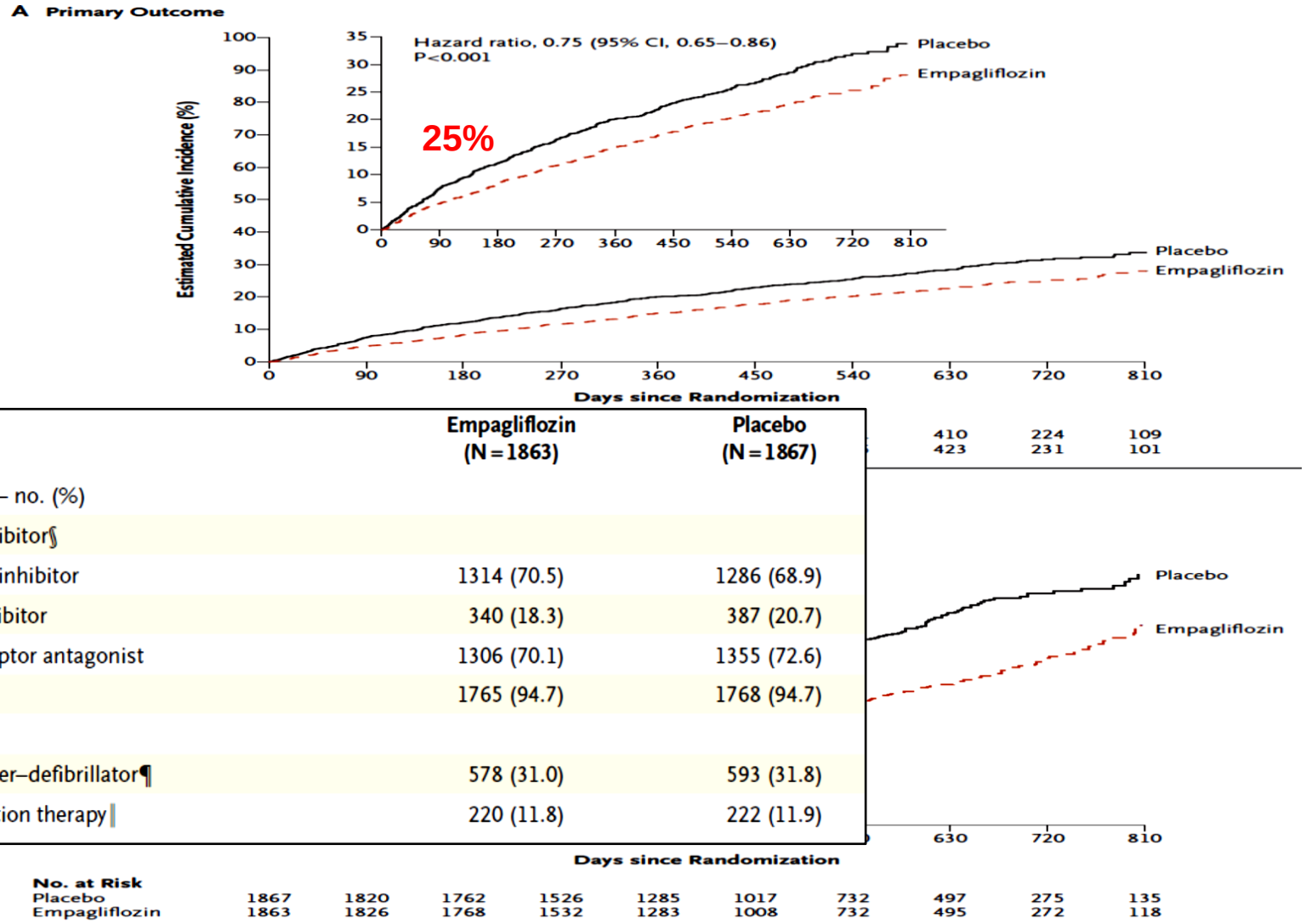
Dapagliflozina (DAPA-HF, estadio C)



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)
Device therapy — no. (%)		
Implantable cardioverter–defibrillator¶	622 (26.2)	620 (26.1)
Cardiac resynchronization therapy‖	190 (8.0)	164 (6.9)

DAPA-HF Investigators. N Engl J Med 2019 doi:10.1056/NEJMoa1911303

Empagliflozina (EMPEROR-Reduced, estadio C)

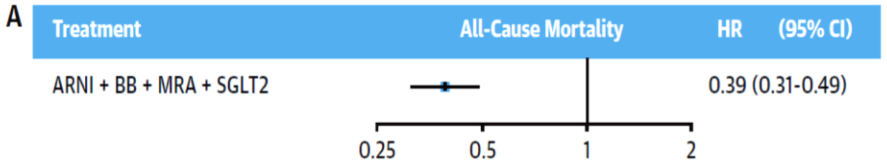


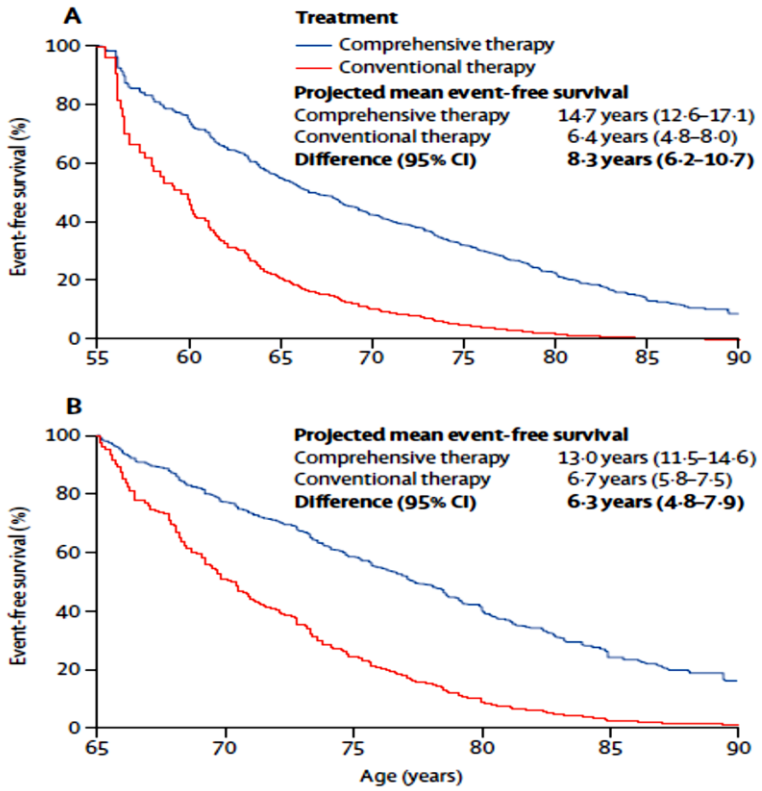
Characteristic	Empagliflozin (N=1863)	Placebo (N=1867)
Heart failure medication — no. (%)		
Renin–angiotensin inhibitor§		
Without neprilysin inhibitor	1314 (70.5)	1286 (68.9)
With neprilysin inhibitor	340 (18.3)	387 (20.7)
Mineralocorticoid receptor antagonist	1306 (70.1)	1355 (72.6)
Beta-blocker	1765 (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)

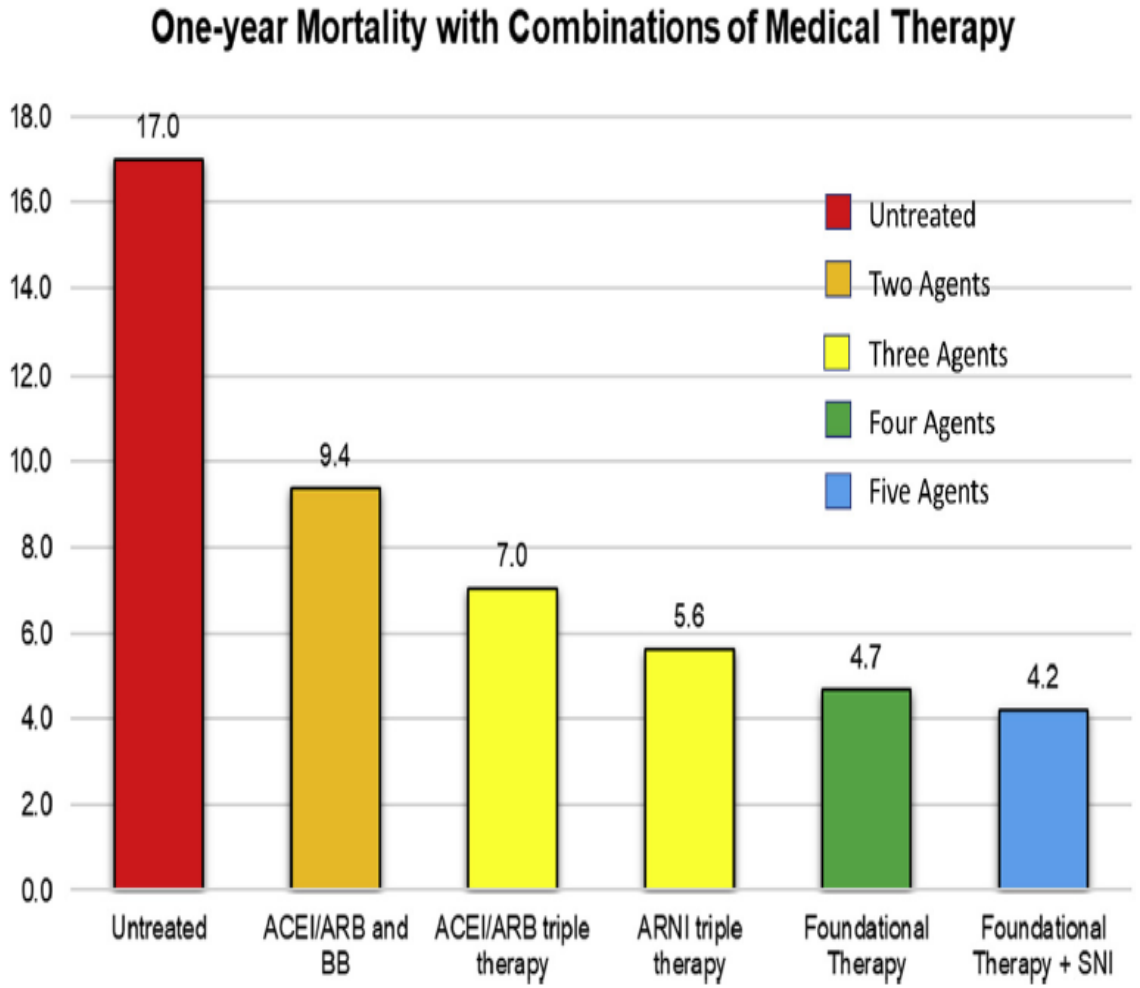
EMPEROR-Reduced Investigators. N Engl J Med 2020 doi:10.1056/NEJMoa2022190

Beneficios de la terapia cuádruple en la IC-FE r

N = 95,444

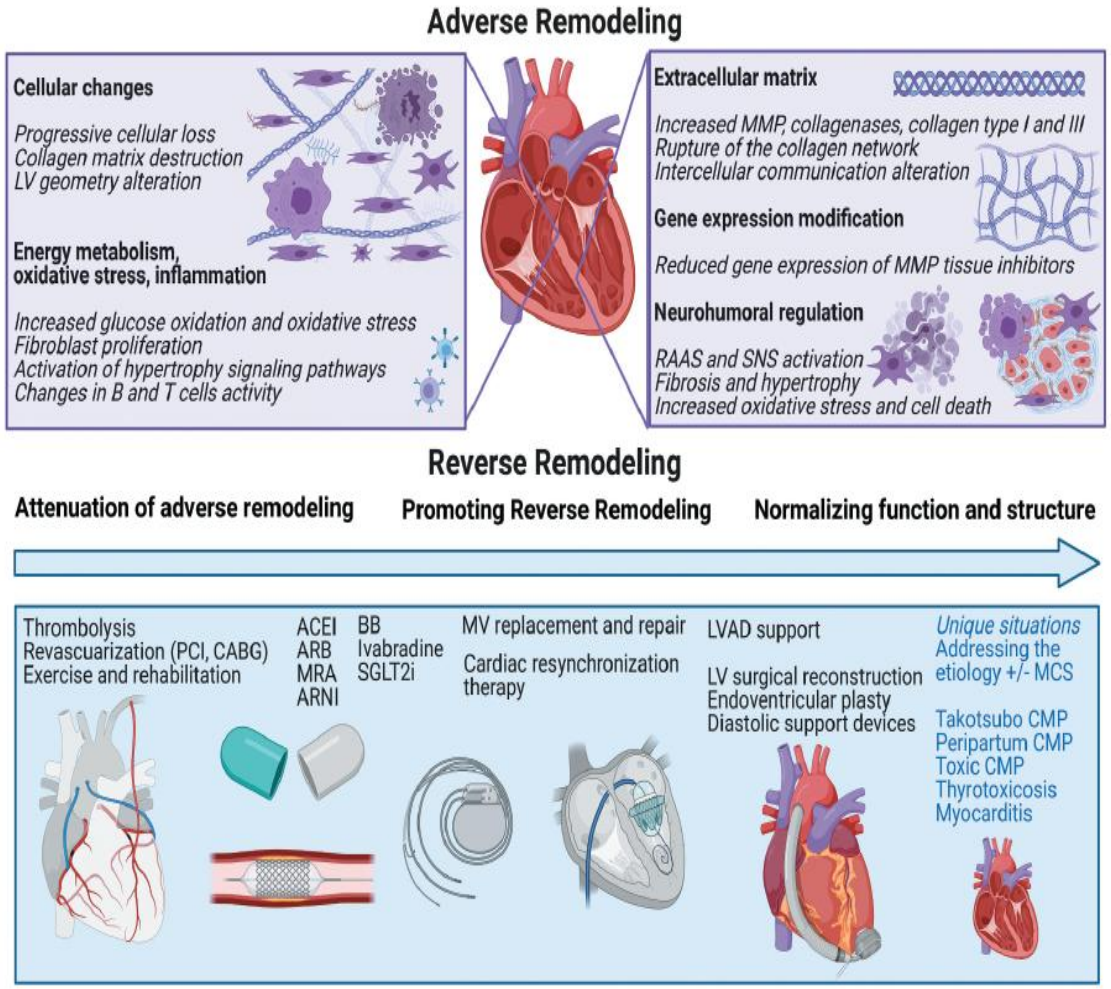


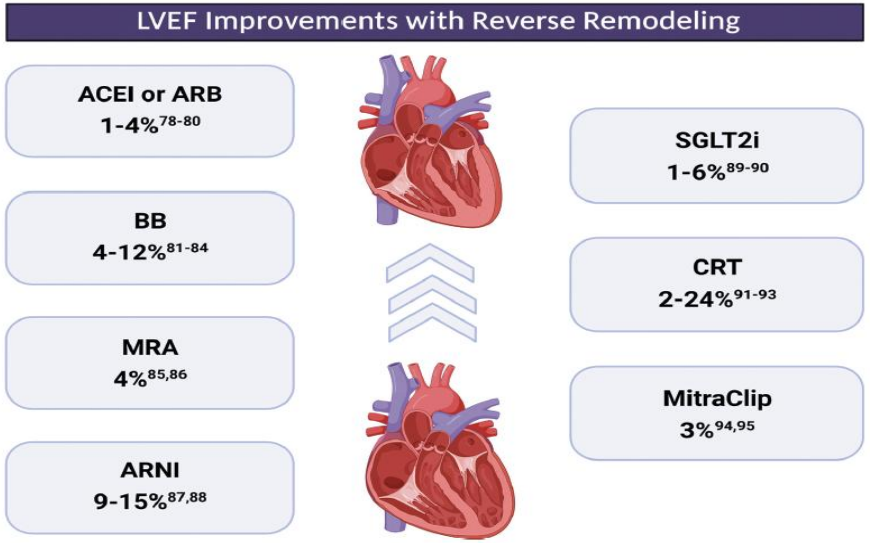




Tromp J, et al. J Am Coll Cardiol HF 2022:10;73-84
Vaduganathan M, et al. Lancet 2020 https://doi.org/10.1016/S0140-6736(20)30748-0
Miller RJH, Howlett JG, Fine NM. Can J Cardiol 2021;37:632-43

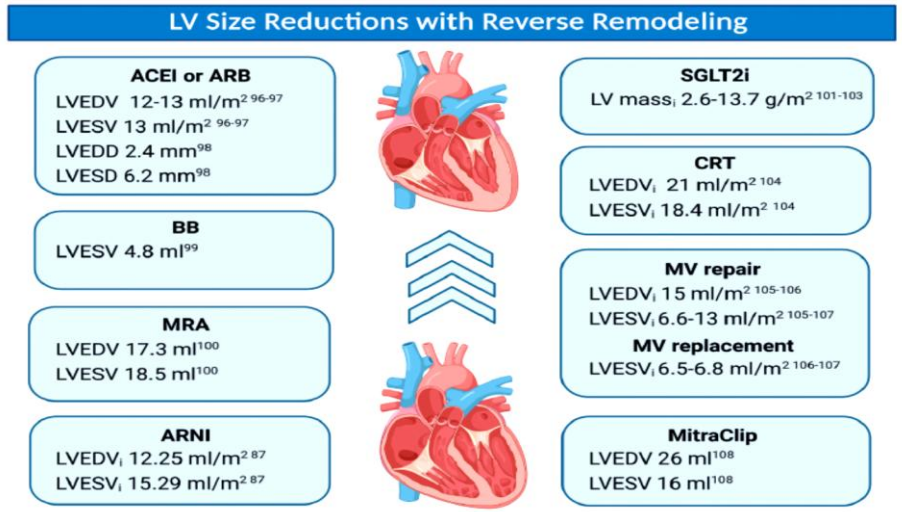
Remodelación reversa y terapias en IC-FE r





FE VI

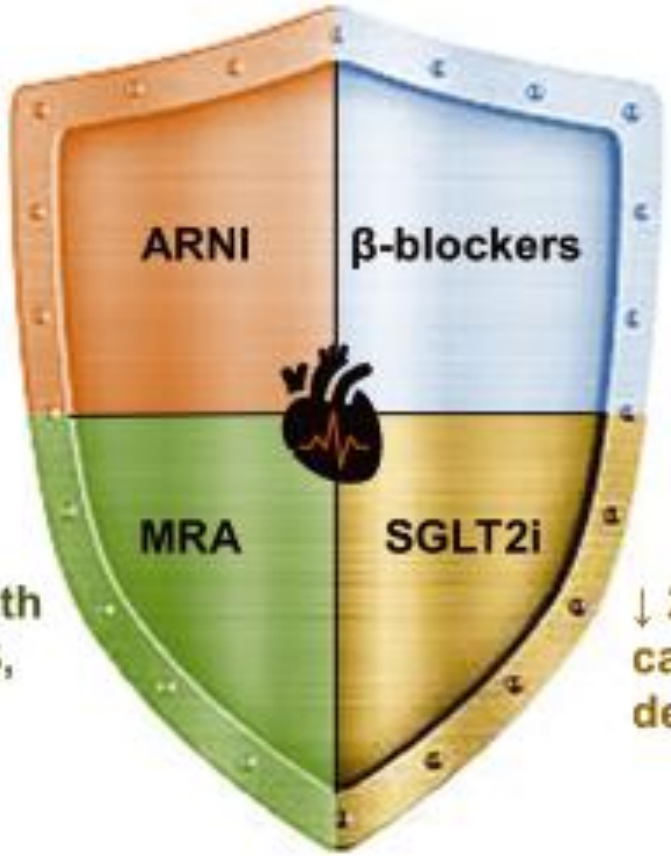
Vol.



Boulet J, Merha M.STRUCTURAL HEART 2021;5:466-81

Disminución del RR de muerte súbita con terapia cuádruple

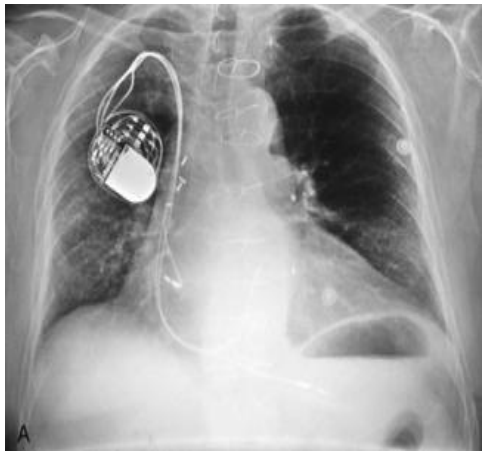
↓ 20% in sudden death &
↓ 21% in VA, ICD shock, or resuscitated cardiac arrest vs. ACEi in PARADIGM-HF



↓ 31% in sudden death based on meta-analysis of trials

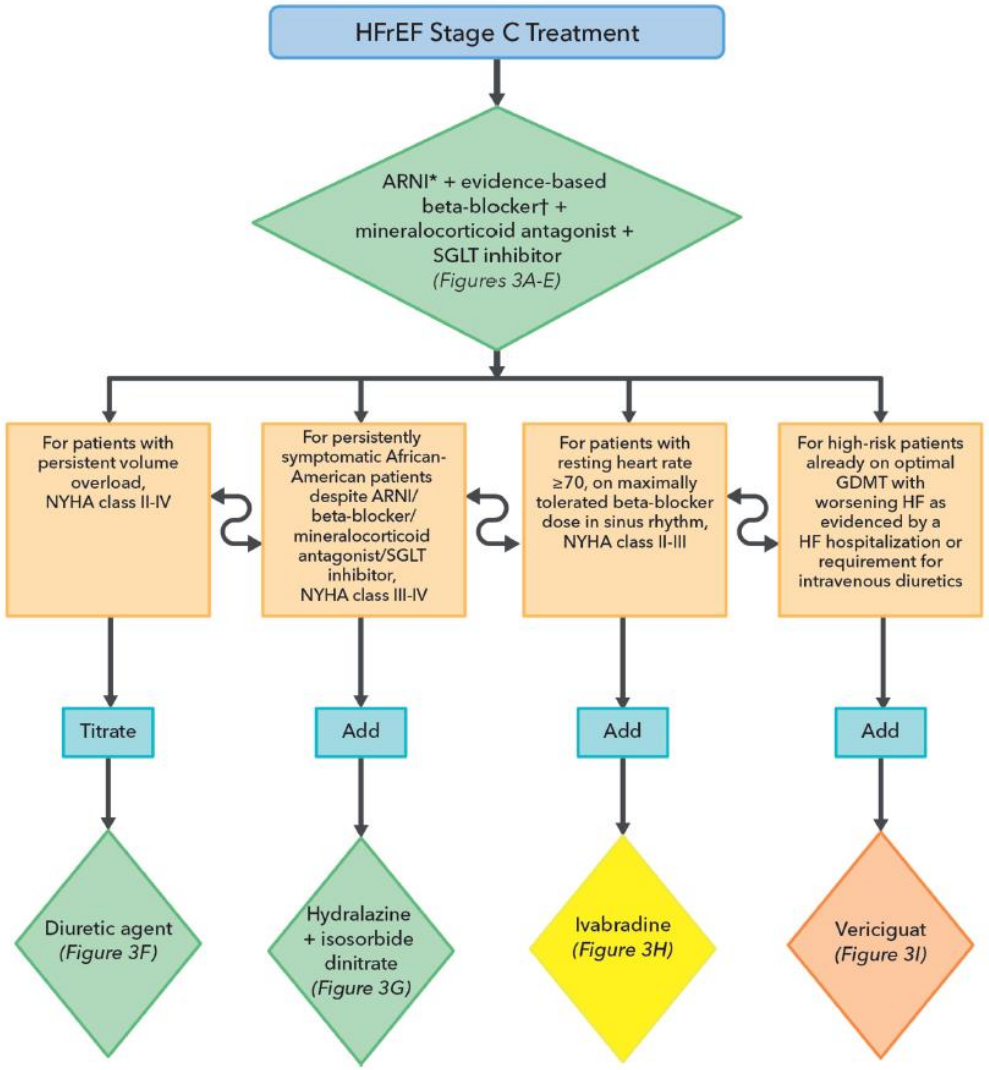
↓ 23% in sudden death in RALES, EPHESUS, and EMPHASIS-HF

↓ 21% in VA, resuscitated cardiac arrest, or sudden death in DAPA-HF



Varshney AS, Singh JP, Vaduganathan M. Eur J Heart Fail 2022;24:562-4

Guía ACC 2024 de IC-FE r (estadio C)



	Starting Dose	Target Dose
Beta-blockers		
Bisoprolol	1.25 mg once daily	10 mg once daily
Carvedilol	3.125 mg twice daily	25 mg twice daily for weight <85 kg and 50 mg twice daily for weight ≥85 kg
Metoprolol succinate	12.5-25 mg daily	200 mg daily
ARNI		
Sacubitril/valsartan	24/26 mg to 49/51 mg twice daily	97/103 mg twice daily
ACE inhibitors		
Captopril	6.25 mg 3× daily	50 mg 3× daily
Enalapril	2.5 mg twice daily	10-20 mg twice daily
Lisinopril	2.5-5 mg daily	20-40 mg daily
Ramipril	1.25 mg daily	10 mg daily
ARBs		
Candesartan	4-8 mg daily	32 mg daily
Losartan	25-50 mg daily	150 mg daily
Valsartan	40 mg twice daily	160 mg twice daily
Mineralocorticoid antagonists		
Eplerenone	25 mg daily	50 mg daily
Spironolactone	12.5-25 mg daily	25-50 mg daily
SGLT inhibitors		
Dapagliflozin	10 mg daily	10 mg daily
Empagliflozin	10 mg daily	10 mg daily
Sotagliflozin	200 mg daily	400 mg daily
Vasodilators		
Hydralazine	25 mg 3× daily	75 mg 3× daily
Isosorbide dinitrate†	20 mg 3× daily	40 mg 3× daily
Fixed-dose combination isosorbide dinitrate/hydralazine‡	20 mg/37.5 mg (one tab) 3× daily	2 tabs 3× daily
Ivabradine		
Ivabradine	2.5-5 mg twice daily	Titrate to heart rate 50-60 beats/min. Maximum dose 7.5 mg twice daily
Oral soluble guanylyl cyclase stimulator		
Vericiguat	2.5 mg daily	10 mg daily

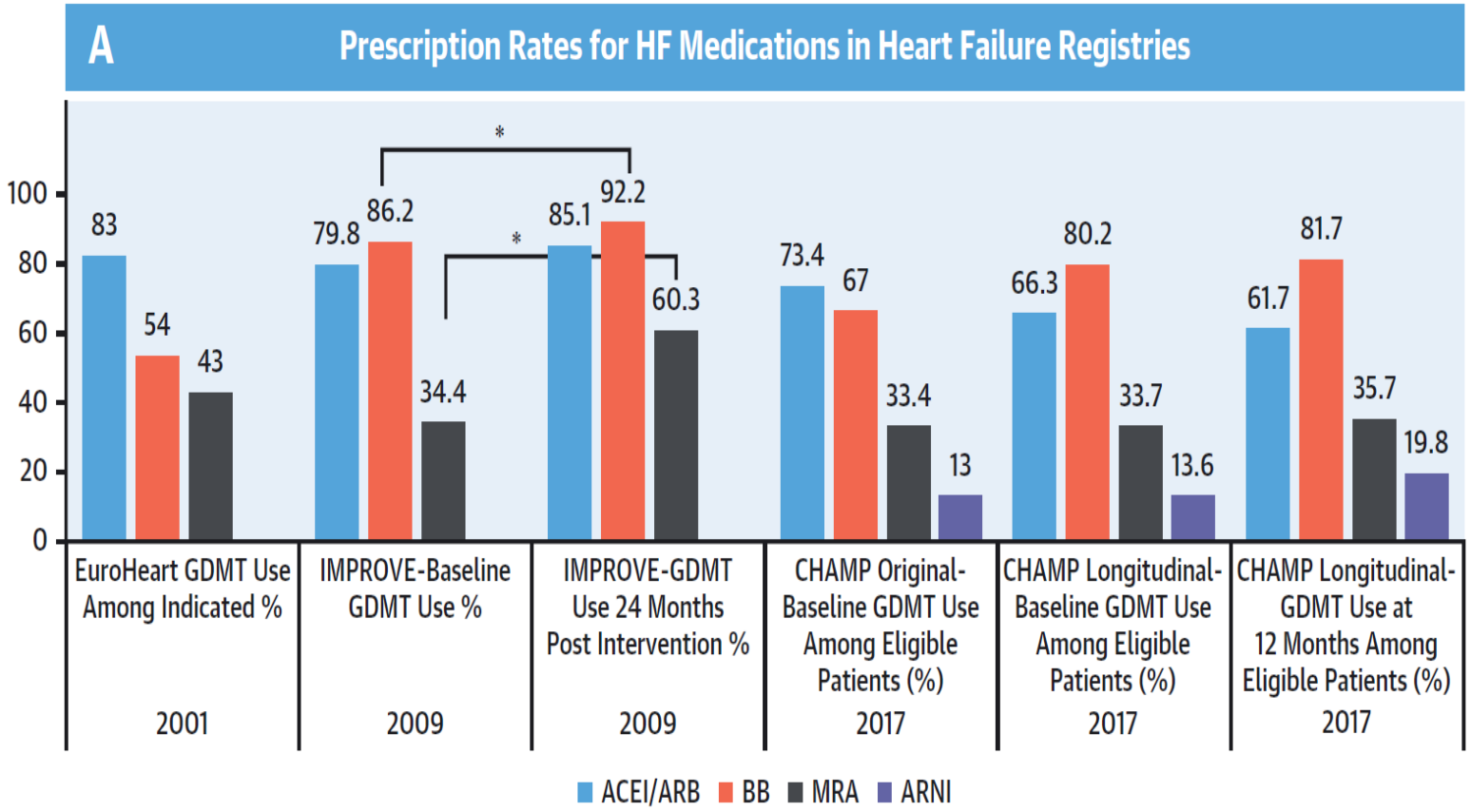
J Am Coll Cardiol 2024:83:1444-88

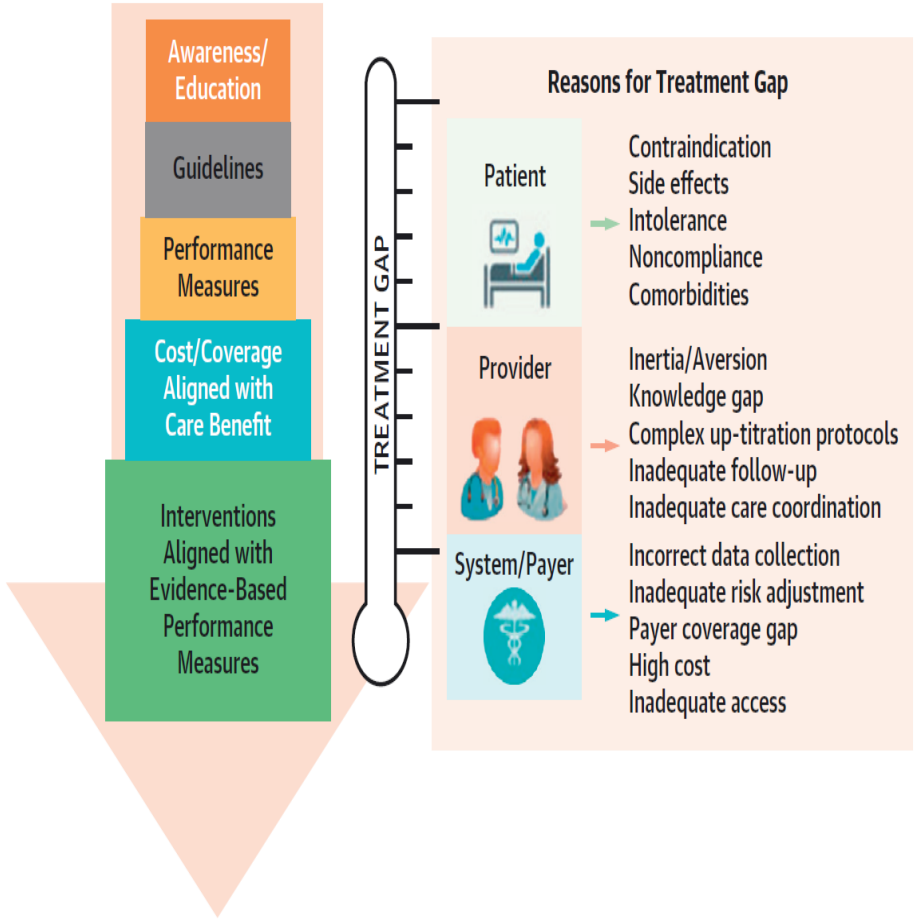
Seguridad de la terapia en IC-FE r

Class	Parameters for assessment	Allowable lab for initiation/titration	Allowable clinical finding	Lab parameter of intolerance
ARNI (first) or ACEI/ARB	Lightheaded, postural symptoms sCr, K+, SBP Both classes	eGFR > 30, K+ < 5.2 Both classes	ARNI, SBP > 100 mm Hg, ACEI/ARB, SBP > 90 mm Hg, no symptomatic hypotension	Creatinine > 30% over baseline, K+ > 5.5 Both classes
BB	Lightheaded, postural symptoms HR	Absence of high-grade AV block or pauses > 3 sec	SBP > 95 mm Hg HR > 60 bpm, No symptomatic hypotension or worsening HF	Heart block
MRA	Lightheaded, postural symptoms sCr, K+, SBP	eGFR > 30, K+ < 5.0	SBP > 80 mm Hg, No symptomatic hypotension	Creatinine > 30% over baseline, K+ > 5.5
SGLT2i	Lightheaded, postural symptoms sCr, SBP	eGFR > 25, stable blood glucose control if diabetes mellitus	SBP > 90 mm Hg, No symptomatic hypotension or volume depletion	Elevated lactate or ketones (if DM), creatinine > 30% from baseline

Miller RJH, Howlett JG, Fine NM. Can J Cardiol 2021;37:632-43

Inercia a pesar de las evidencias de tratamiento





Patolia H, et al. J Am Coll Cardiol 2023;82:529-43

Efectos colaterales, comorbilidades en la terapia de IC-FE r

Drug	Common side effects
Diuretics	Hypotension; hypokalaemia; hypomagnesaemia; hyponatraemia; hyperuricemia; hypovolaemia/dehydration; rise in creatinine, urea
ACEi/ARB	Cough; hypotension; rise in urea, creatinine, potassium
ARNI	Hypotension; rise in creatinine, potassium; angioedema
Beta-blockers	Worsening HF; low heart rate; hypotension
Ivabradine	Low heart rate; visual phenomena
MRA	Rise in creatinine, potassium; breast discomfort or gynaecomastia
SGLT2i	Genital infection (in diabetic patients)

Comorbidity	GDMT	Precaution	Comment
Coronary artery disease and angina	✓		Beta-blockers and ivabradine may help control symptoms
Diabetes	✓		GDMT have shown similar benefits in diabetic patients
Lung disease		Asthma is a relative contraindication to beta-blocker; starting with low doses of cardio-selective beta-blocker may allow its use	Beta-blockers can be given in COPD
Depression	✓		Depression is associated with low adherence to medication
Erectile dysfunction	✓		Thiazides, spironolactone and beta-blockers (nebivolol preferred) may aggravate erectile dysfunction
Iron deficiency/anaemia	✓		
Kidney dysfunction		ACEi, ARB, ARNI, MRA may have some limitations (see text)	Diuretics may need higher doses to be effective
Cachexia		ACEi, ARB, ARNI should be up-titrated carefully because of orthostatic hypotension	

Rossano GMC, et al. Eur J Heart Fail 2021;23:872-81

Terapia de base en los ensayos de IC-FE r

Baseline Therapy in the Various Heart Failure Trials

Therapy	Trial (Year)	ACE Inhibitors/ Angiotensin Receptor Blockers	Beta-Blocker	Mineralocorticoid Receptor Antagonist	Angiotensin Receptor Neprilysin Inhibitor
ACE inhibitors	CONSENSUS (1987)	-	<5%	50%-55%	-
	SOLVD (1991)	-	8%	9%	-
	V-HeFT II (1991)	-	Not reported	Not reported	-
Beta-blockers	USCS (1996)	>95%	-	Not reported	-
	MERIT-HF (1999)	>95%	-	Not reported	-
	CIBIS-II (1999)	>95%	-	Not reported	-
Mineralocorticoid receptor antagonist	RALES (1999)	92%	10%-11%	-	-
	EMPHASIS-HF (2011)	93%-94%	86%-87%	-	-
Combination vasodilator	A-HeFT (2004)	86%-87%	73%-74%	38%-40%	-
I_f channel blocker	SHIFT (2010)	90%	93%	60%	-
Angiotensin receptor neprilysin inhibitor	PARADIGM-HF (2014)	100%	93%	56%	-
Sodium-glucose cotransporter 2 inhibitor	DAPA-HF (2019)	94%	96%	71%	11%
	EMPEROR- Reduced (2020)	70%	95%	71%	20%
Soluble guanylate cyclase stimulator	VICTORIA (2020)	74%	93%	70%	15%

Bhatt AS, et al. J Am Coll Cardiol HF 2021;9:1-12

Dosis medias y descontinuación en los ensayos de IC-FE r

	RASi	BB	MRA	ARNI	ARNI	SGLT2i
Trial	SOLVD-treatment	MERIT-HF	EMPHASIS-HF	PARADIGM-HF	PARADIGM-HF vs. SOLVD-treatment and CHARM-alternative	DAPA-HF
Number of patients	2569	3991	2737	8399	–	4744
study patients	NYHA II–IV, LVEF ≤ 35%	NYHA II–IV, LVEF ≤ 40%	NYHA II, LVEF ≤ 35%	NYHA II–IV, LVEF ≤ 40%	–	NYHA II–IV, LVEF ≤ 40%
Key baseline therapy	BB 8%, potassium sparing diuretic 9%	RASi 96%, MRA 8%	RASi 94%, BB 87%	RASi 100%, BB 93%, MRA 56%	–	RASi 94%, BB 96%, MRA 71%, ARNI 11%
Test treatment	Enalapril	Metoprolol CR/XL	Eplerenone	Sacubitril/valsartan	Sacubitril/valsartan	Dapagliflozin
Control treatment	Placebo	Placebo	Placebo	Enalapril	Putative placebo	Placebo
Discontinuation percentage in the experimental arm	32.5%	13.9%	16.3%	17.8%	–	10.5%
Mean daily dose in those taking the study drug/ target dose	16.6 mg/20 mg	159 mg/ 200 mg	39.1 ± 13.8 mg/50 mg	375 ± 71 mg/ 400 mg	–	98.1% taking the target dose of 10 mg daily

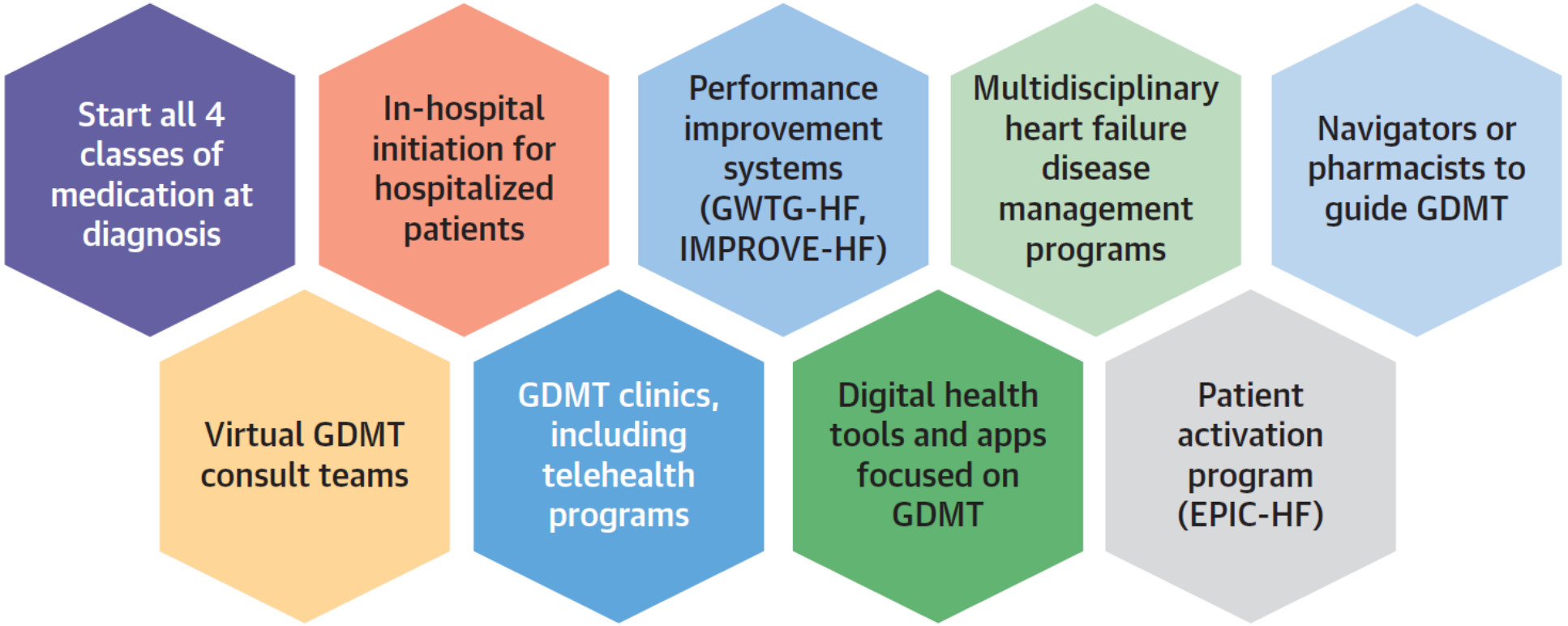
Shen L, et al. Eur Heart J 2022;43:2573-87

Exclusiones renales en los ensayos de IC-FE r

Trial; Author; Year	Pts (*n*)	Design	Main Eligibility Criteria	Primary Outcome	Mean Follow up (years)	Renal Function Exclusion	CKD Groups (eGFR, mL/min/ 1.73 m^2)	Main Findings
CONSENSUS; 1987; The CONSENSUS Trial Study Group	253	Enalapril vs. Pl.	Congested HF, NYHA IV, cardiomegaly on chest X-ray	ACM	0.5	Serum creatinine concentration > 3.4 mg/dL	NA	Enalapril significantly reduced ACM in patients with sCr > 1.39 mg/dL compared to pl. (30% vs. 55%) but did not have a significant effect in those with sCr < 1.39 mg/dL.
RALES; 1999; Kulbertus et al.	1663	Spironolactone vs. Pl.	LVEF < 35%; NYHA III–IV; creatinine ≤ 2.5 mmol/L	ACM	2	creatinine ≥ 2.5 mg/dL	<60 (*n* = 792) 47.62% ≥60 (*n* = 866) 52.07%	Individuals with reduced baseline eGFR exhibited similar relative risk reductions in all-cause death and the combined. Endpoint of death or hospital stayed for HF as those with normal renal function and greater absolute risk reduction compared with those with a higher baseline eGFR.
EMPHASIS-HF, 2001; Zannad et al. [30]	2737	Eplerenone vs. Pl.	LVEF ≤ 35%; NYHA II; eGFR ≥ 30 mL/min/1.73 m	CV death or HFH	1.75	eGFR < 30 mL/min/1.73 m	<60 (*n* = 912) 33.32% ≥60 (*n* = 1821) 66.53%	Eplerenone, as compared with placebo, reduced both the risk of death and the risk of hospitalization in HFrEF patients with CKD.
PARADIGM-HF; 2014; Solomon et al.	8442	Enalapril vs. Sac/Val	LVEF ≤ 40%; NYHA III–V; eGFR ≥ 30 mL/min/ 1.73 m^2	CV death or HFH	2.25	eGFR ≤ 30 mL/min/ 1.73 m^2	<60 (*n* = 3061) 36.2% ≥60 (*n* = 5338) 63.2%	Compared with enalapril, sacubitril and valsartan led to a slower rate of decrease in the eGFR and improved CV outcomes, even in patients with CKD.
DAPA-HF; 2019; Mc Murray et al. [45]	4744	Dapaglifozin vs. Pl.	LVEF ≤ 40%; NYHA III–V; eGFR ≥ 30 mL/min/ 1.73 m^2	WHF or CV death	1.5	eGFR < 30 mL/min/ 1.73 m^2	<60 (*n* = 1926) 41% ≥60 (*n* = 2816) 59, 35%	The effect of dapagliflozin on the primary and secondary outcomes did not differ by eGFR category or examining eGFR as a continuous variable.
EMPEROR reduced; 2020; Packer et al.;	3730	Empaglifozin vs. Pl.	LVEF ≤ 40%; NYHA IIIV; eGFR ≥ 20 mL/min/ 1.73 m^2	WHF or CV death	1.3	eGFR < 20 mL/min/ 1.73 m^2	<60 (*n* = 1978) 53, 2% ≥60 (*n* = 1746) 46.8%	Empagliflozin reduced the primary outcome and total HF hospitalizations in patients with and without CKD.

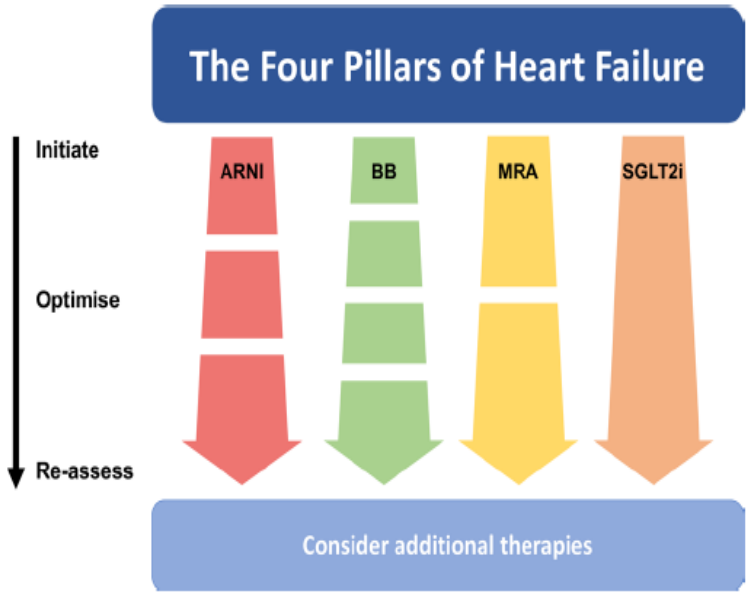
Shen L, et al. Eur Heart J 2022;43:2573-87

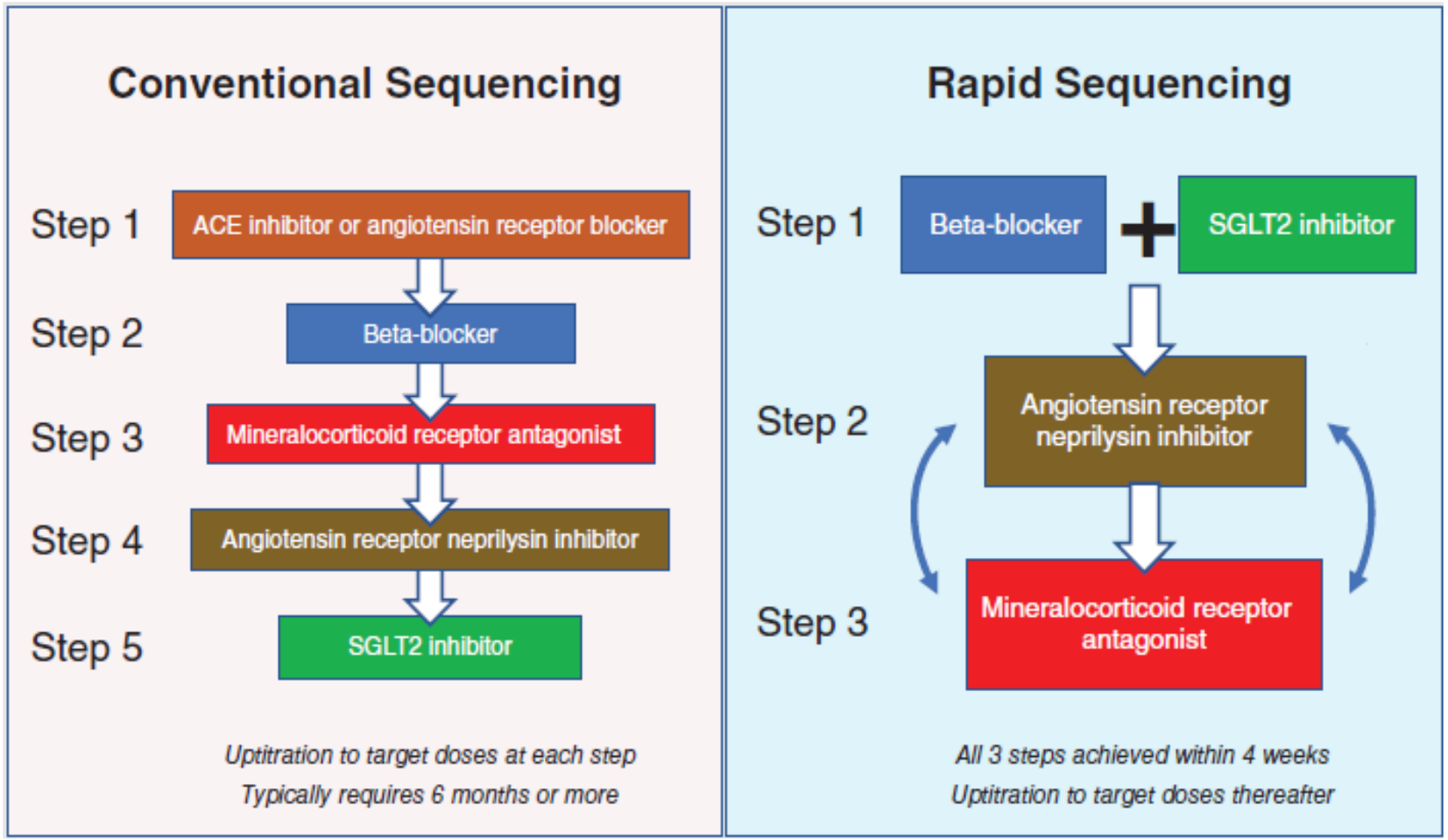
Estrategias para facilitar el inicio de GDMT en IC-FE r



Patolia H, et al. J Am Coll Cardiol 202;82:529-43

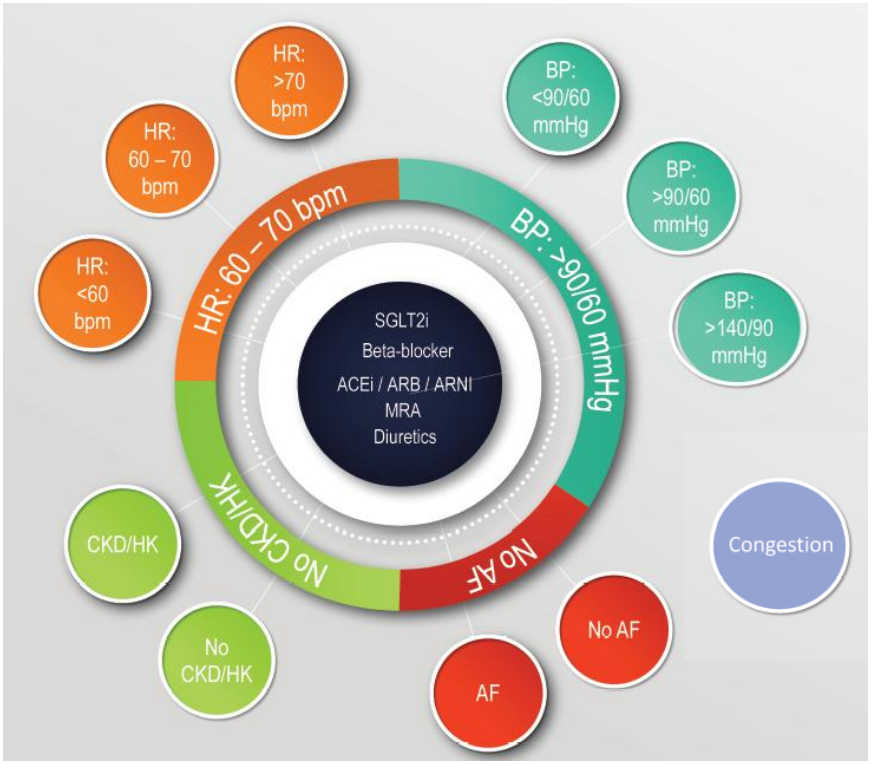
Titulación de la terapia cuádruple en IC-FE r





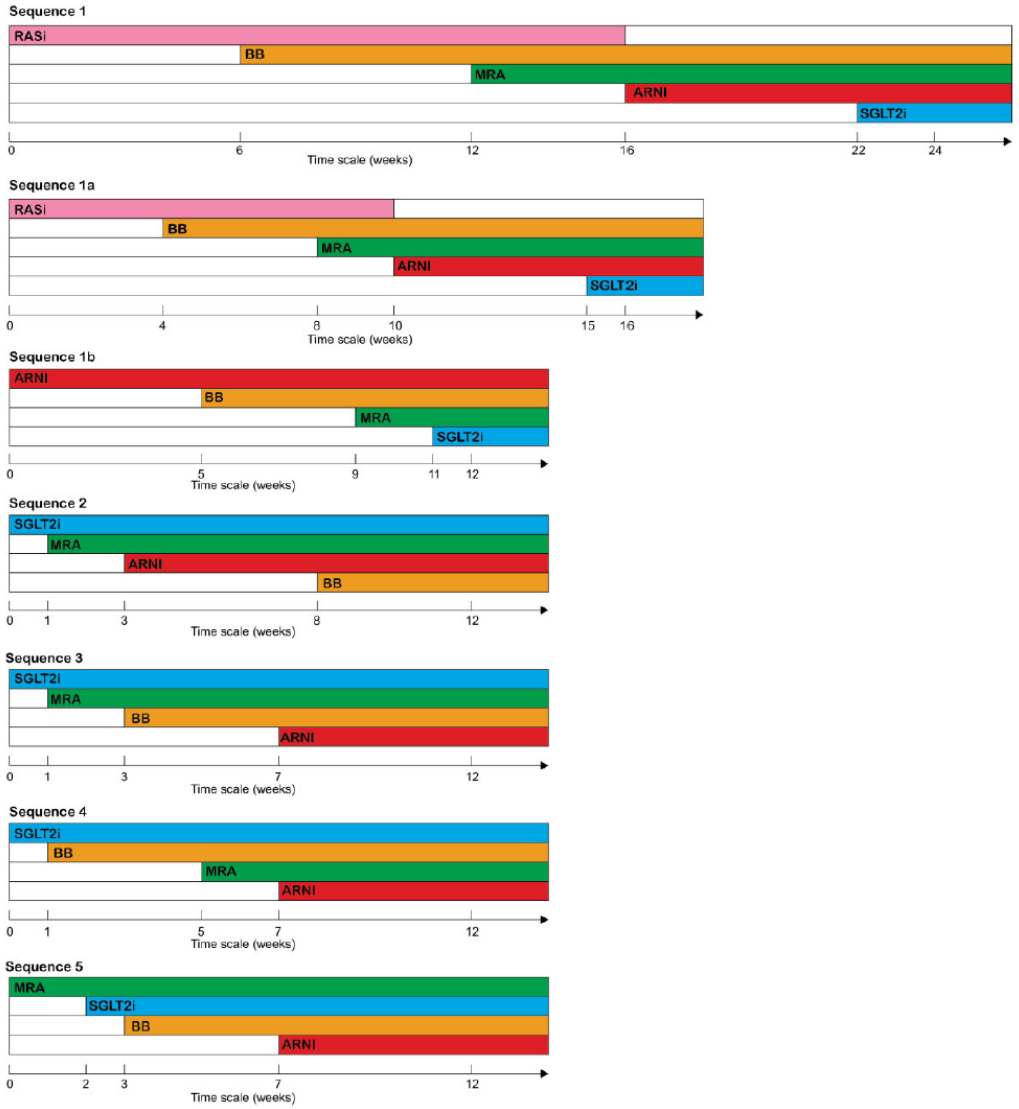
Straw S, McGinlay M, Witte KK. Open Heart 2021;8:e001585
Packer M, McMurray JJV. Eur J Heart Fail 2021 doi:10.1002/ejhf.2149

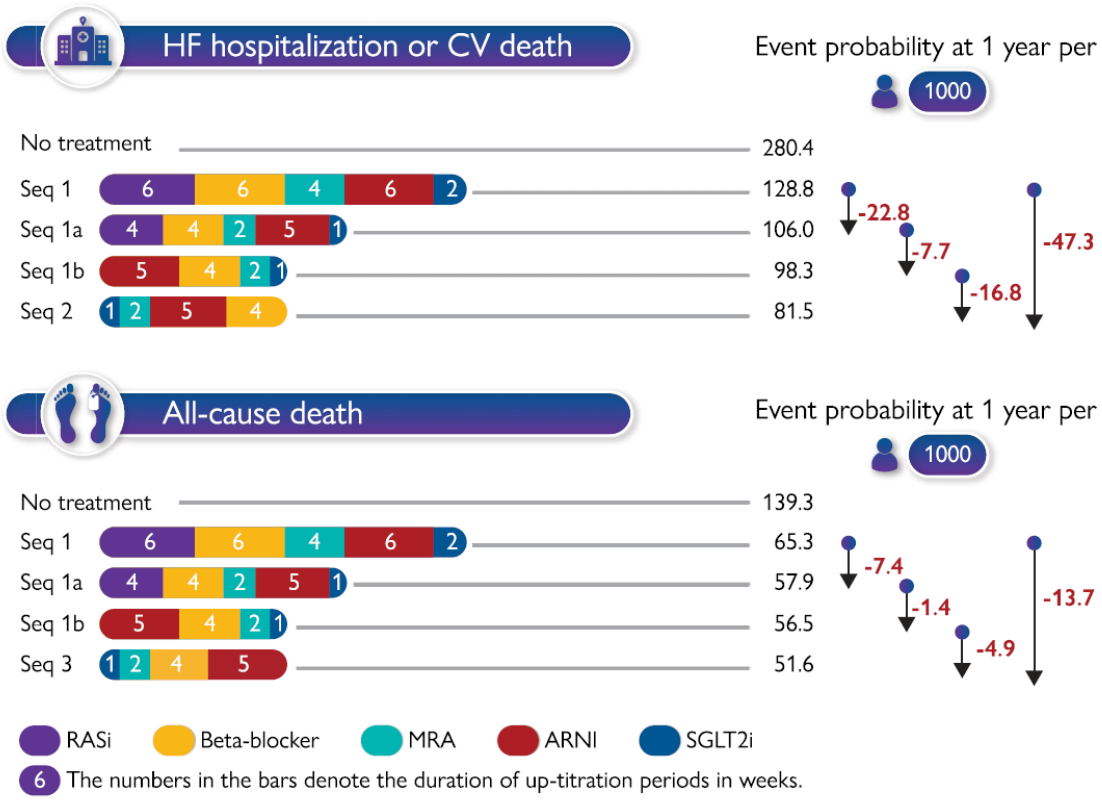
Perfiles de los pacientes con IC-FE r para GDMT



Rosano GMC, et al. Eur J Heart Fail 2021;23:872-81

Titulación acelerada y tratamiento secuencial ordenado optimizado en IC-FE r



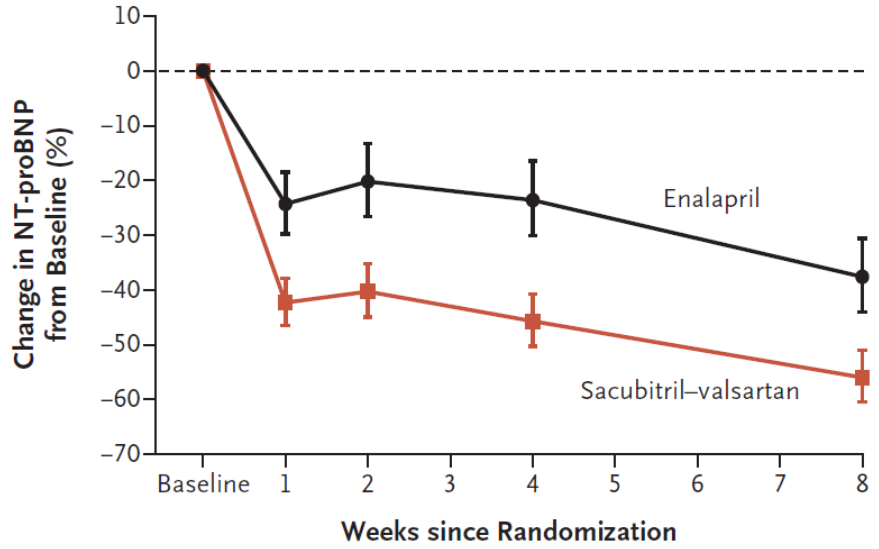


Shen L, et al. Eur Heart J 2022;43:2573-87

Escenarios de titulación: hospitalización, transición

PIONEER-HF (INRA en IC-EF r descompensada)

Outcome	Sacubitril–Valsartan (N = 440)	Enalapril (N = 441)	Sacubitril–Valsartan vs. Enalapril
Key safety outcomes — no. (%)			**Relative risk (95% CI)**
Worsening renal function†	60 (13.6)	65 (14.7)	0.93 (0.67 to 1.28)
Hyperkalemia	51 (11.6)	41 (9.3)	1.25 (0.84 to 1.84)
Symptomatic hypotension	66 (15.0)	56 (12.7)	1.18 (0.85 to 1.64)
Angioedema	1 (0.2)	6 (1.4)	0.17 (0.02 to 1.38)
Secondary biomarker outcomes — % (95% CI)‡			**Ratio of change (95% CI)**
Change in high-sensitivity troponin T concentration	−36.6 (−40.8 to −32.0)	−25.2 (−30.2 to −19.9)	0.85 (0.77 to 0.94)
Change in B-type natriuretic peptide concentration	−28.7 (−35.5 to −21.3)	−33.1 (−39.5 to −25.9)	1.07 (0.92 to 1.23)
Change in ratio of B-type natriuretic peptide to NT-proBNP	35.2 (28.8 to 42.0)	−8.3 (−3.6 to −12.7)	1.48 (1.38 to 1.58)
Exploratory clinical outcomes — no. (%)			**Hazard ratio (95% CI)§**
Composite of clinical events	249 (56.6)	264 (59.9)	0.93 (0.78 to 1.10)
Death	10 (2.3)	15 (3.4)	0.66 (0.30 to 1.48)
Rehospitalization for heart failure	35 (8.0)	61 (13.8)	0.56 (0.37 to 0.84)
Implantation of left ventricular assist device	1 (0.2)	1 (0.2)	0.99 (0.06 to 15.97)
Inclusion on list for heart transplantation	0	0	NA
Unplanned outpatient visit leading to use of intravenous diuretics	2 (0.5)	2 (0.5)	1.00 (0.14 to 7.07)
Use of additional drug for heart failure	78 (17.7)	84 (19.0)	0.92 (0.67 to 1.25)
Increase in dose of diuretics of >50%	218 (49.5)	222 (50.3)	0.98 (0.81 to 1.18)
Composite of serious clinical events¶	41 (9.3)	74 (16.8)	0.54 (0.37 to 0.79)



No. at Risk

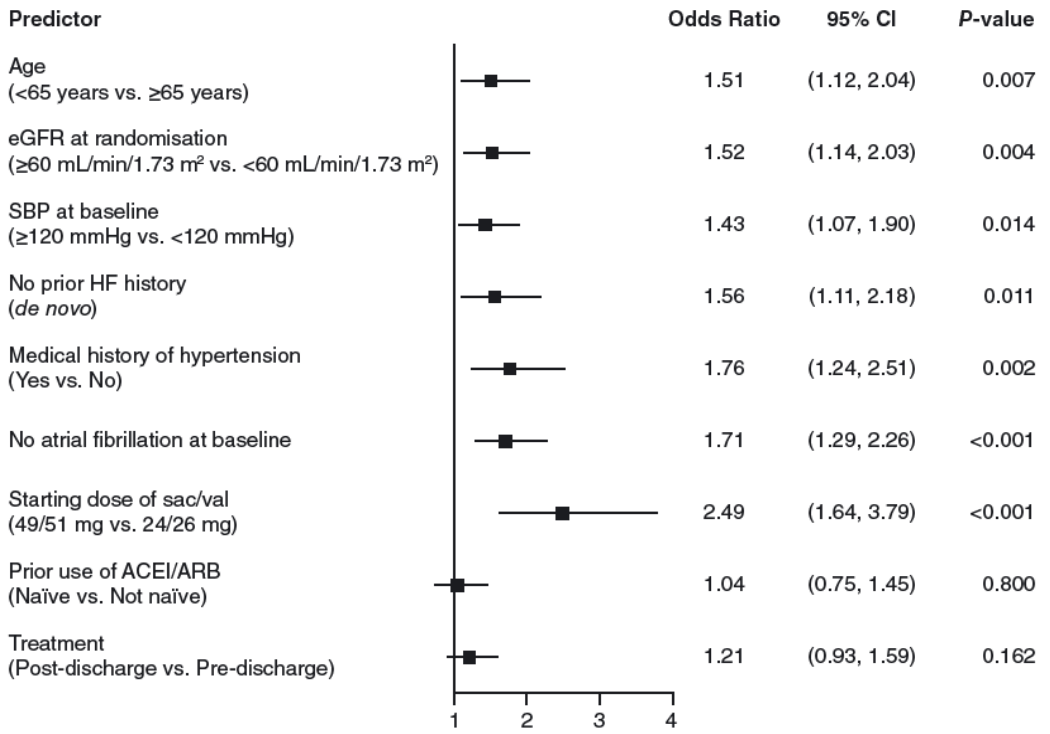
Enalapril	394	359	351	350		348
Sacubitril–valsartan	397	355	363	365		349

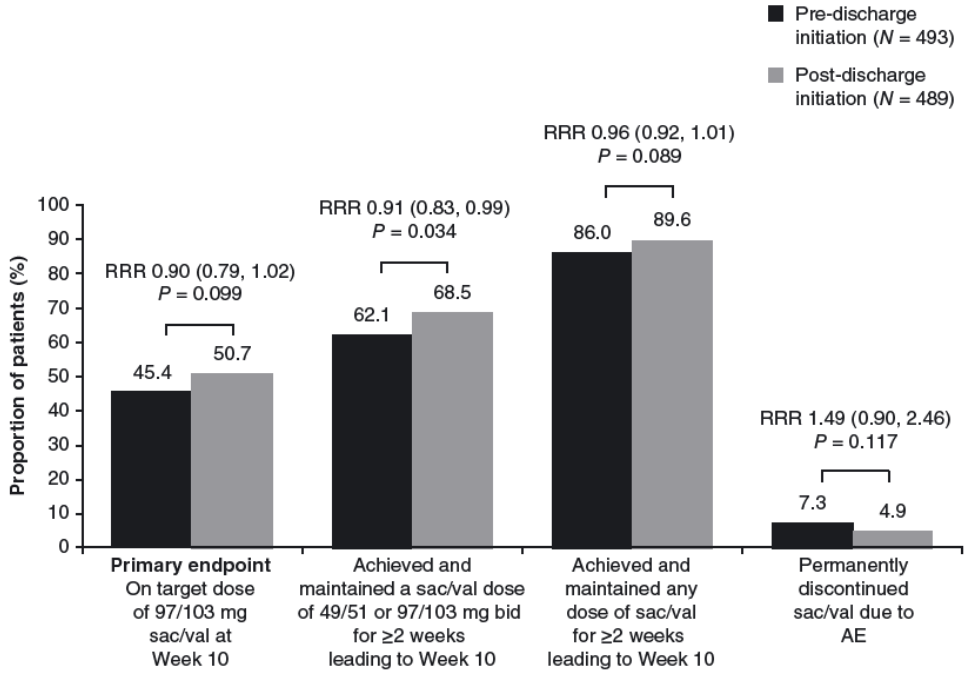
Previous use of medication — no. (%)		
ACE inhibitor or ARB	208 (47.3)	214 (48.5)
Beta-blocker	262 (59.5)	263 (59.6)
MRA	48 (10.9)	40 (9.1)
Loop diuretic	262 (59.5)	240 (54.4)
Hydralazine	30 (6.8)	33 (7.5)
Nitrate	43 (9.8)	40 (9.1)
Digoxin	41 (9.3)	35 (7.9)

PIONEER-HF[58] 2019	ADHF	Patients with primary diagnosis of ADHF LVEF ≤40% NT-proBNP ≥1,600 pg/mL or BNP >400 pg/mL	Sacubitril-valsartan vs enalapril	Significant reduction in NT-proBNP in sacubitril-valsartan group compared with enalapril (46.7% vs -25.3%; ratio of change: 0.71; 95% CI: 0.63-0.81; $P < 0.001$)

PIONEER-HF Investigators. N Eng J Med 2019;380:539-48
Bozkurt B, et al. JACC: BASIC TO TRANSLATIONAL SCIENCE 2023;8:88-105

TRANSITION (INRA en IC-FE r descompensada)



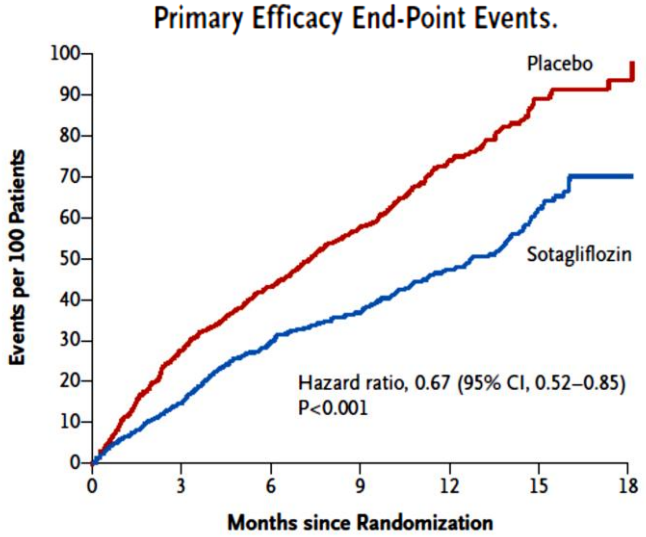


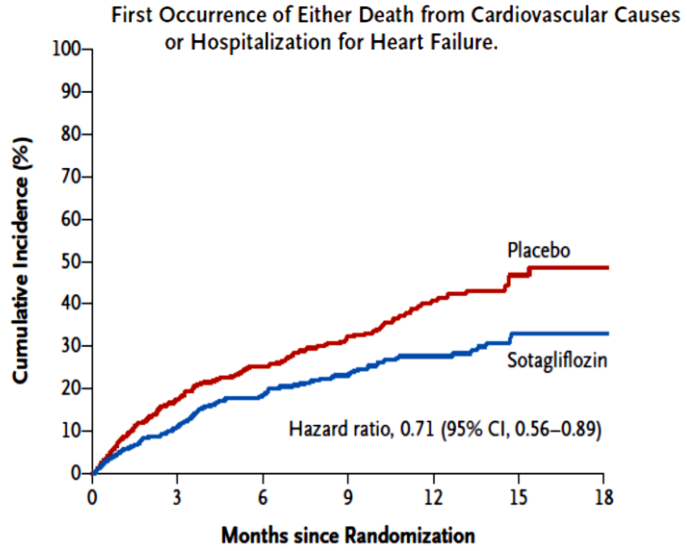
Cardiac resynchronisation therapy	38 (7.7)	50 (10.1)	88 (8.9)
Implantable defibrillator insertion	73 (14.7)	79 (15.9)	152 (15.3)
Medications by randomisation strata, *n* (%)			
ACEI	250 (50.5)	253 (51.0)	503 (50.8)
ARB	123 (24.8)	124 (25.0)	247 (24.9)
ACEI/ARB naïve	122 (24.6)	119 (24.0)	241 (24.3)
Other HF- and CV-related medications prior to admission, *n* (%)			
Beta-blocker	213 (43.0)	233 (47.0)	446 (45.0)
MRA	169 (34.1)	181 (36.5)	350 (35.3)
Diuretic	248 (50.1)	261 (52.6)	509 (51.4)
Loop diuretics	238 (48.1)	245 (49.4)	483 (48.7)
Thiazide diuretics	15 (3.0)	13 (2.6)	28 (2.8)
Cardiac glycosides	63 (12.7)	45 (9.1)	108 (10.9)
Nitrates	31 (6.3)	45 (9.1)	76 (7.7)

TRANSITION[62] 2019	ADHF	Patients hospitalized for ADHF with NYHA functional class II-IV, SBP ≥100 mm Hg, and LVEF ≤40%	Open-label LCZ696 sacubitril-valsartan	Comparable proportions of patients in the pre- and postdischarge initiation groups achieved the target dose of 97/103 mg twice daily at wk 10

TRANSITION Investigators. Eur J Heart Fail 2019;21:998-1007
Bozkurt B, et al. JACC: BASIC TO TRANSLATIONAL SCIENCE 2023;8:88-105

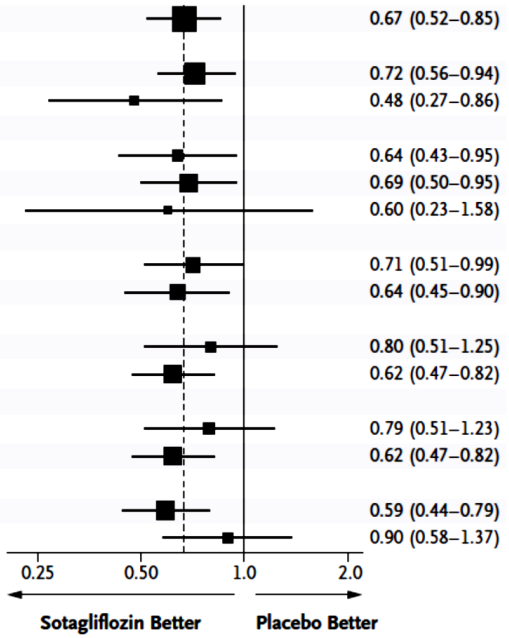
SOLOIST-WHF (sotagliflozina en IC descompensada)





Left ventricular ejection fraction		
Median value (IQR) — %	35 (28–47)	35 (28–45)
<50% — no. (%)¶	481 (79.1)	485 (79.0)

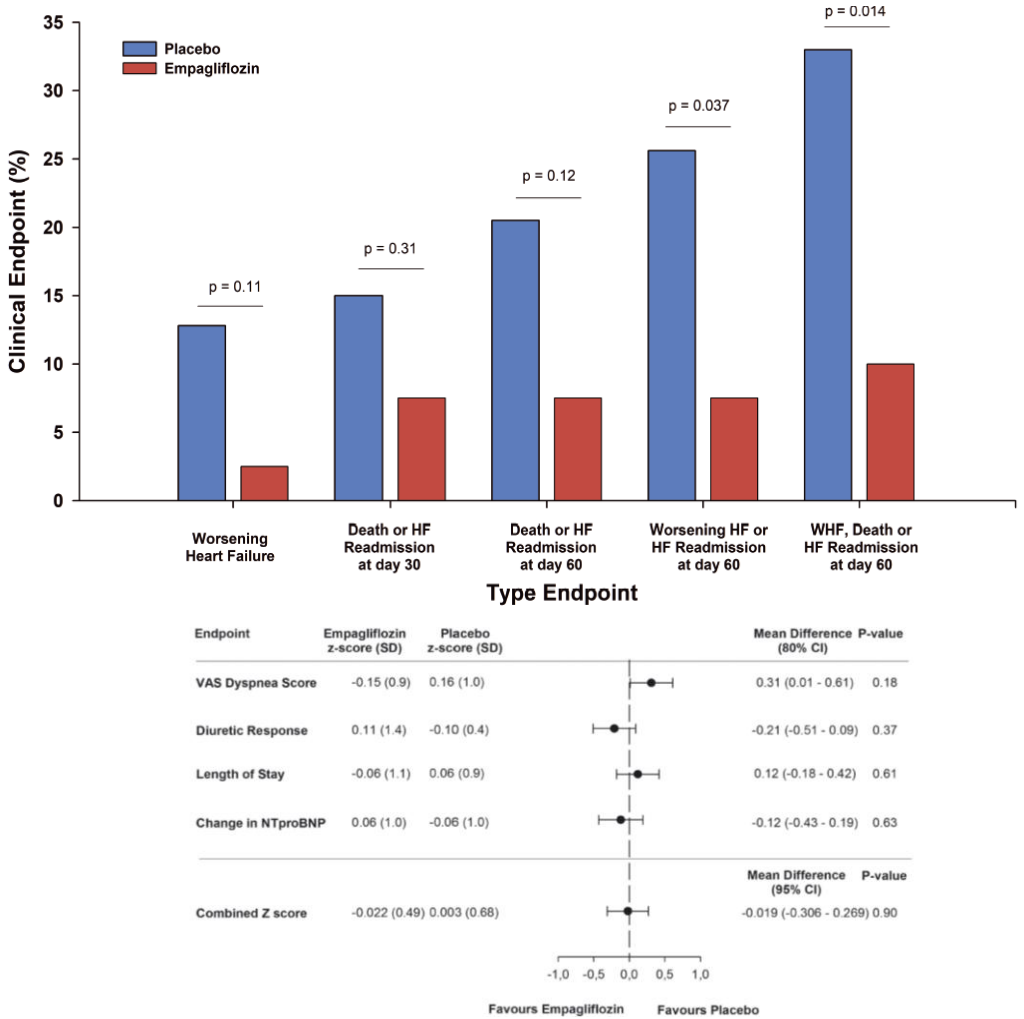
Subgroup	No. of Patients	Sotagliflozin	Placebo
		events per 100 patient-yr	
Overall	1222	51.0	76.3
LVEF			
<50%	966	56.9	79.9
≥50%	256	30.6	64.0
Geographic region			
North America or Latin America	346	68.3	103.0
ırope	800	44.1	64.7
Rest of the world	76	48.4	78.3
Timing of first dose			
Before discharge	596	52.1	76.6
After discharge	626	50.0	76.1
Sex			
Female	412	41.9	52.0
Male	810	55.7	89.3
Age			
<65 yr	364	57.1	71.1
≥65 yr	858	48.0	78.5
Estimated GFR			
<60 ml/min/1.73 m²	854	50.1	85.8
≥60 ml/min/1.73 m²	368	53.1	58.1



SOLOIST trial investigators. N Engl J Med 2020 doi:10.1056/NEJMMoa2030183

EMPA-RESPONSE-AHF (empagliflozina en ICA)

Variable	Randomized treatment		*P*-value
	Empagliflozin	Placebo	
Patients (*n*)	40	39	
Age (years)	79 (73–83)	73 (61–83)	0.14
Female sex, *n* (%)	16 (40)	10 (26)	0.17
Caucasian race (%)	100	95	0.15
Body weight at baseline (kg)	87 ± 23	83 ± 20	0.42
SBP (mmHg)	127 ± 22	121 ± 25	0.25
DBP (mmHg)	76 ± 15	72 ± 15	0.27
HR (bpm)	83 ± 19	80 ± 23	0.50
Respiratory rate (breaths/min)	19 ± 4	20 ± 5	0.60
NYHA class III/IV (%)	92	97	0.57
LVEF if known (%) (*n* = 46)	36 ± 17	37 ± 14	0.87
De novo acute HF (%)	48	46	0.90
Ischaemic aetiology (%)	28	29	0.89
Medical history (%)			
Myocardial infarction	30	38	0.43
Hypertension	68	56	0.31
Atrial fibrillation/flutter	78	64	0.19
Diabetes mellitus type 2	38	28	0.38
Cerebrovascular accident	5	5	0.98
COPD	28	26	0.85
Cancer	38	13	0.012
Medical therapy (%)			
ACEi	40	47	0.51
ARB	5	3	0.45
ARNI	5	3	0.52
Beta-blocker	70	66	0.69
MRA	48	45	0.81
Loop diuretic	100	100	NA
Intravenous vasodilator	10	3	0.36
ICD	8	23	0.054
CRT	15	13	0.78
Laboratory at baseline			
NT-proBNP (pg/mL)	4406 (2873–6979)	6168 (3180–10 489)	0.14
Serum creatinine (μmol/L)	114 ± 34	116 ± 33	0.72
eGFR (mL/min/1.73 m^2)	55 ± 18	55 ± 18	0.97
Sodium (mmol/L)	135 ± 17	135 ± 5	0.99



EMPA-RESPONSE-AHF. Eur J Heart Fail 2020;22:713-22

Titulación intensiva pos ICA (STRONG-HF)

	High-intensity care group (n=542)	Usual care group (n=536)	Adjusted treatment effect (95% CI)	p value
Vital signs				
Systolic blood pressure, mm Hg				
Baseline	123·4 (13·30)	122·2 (12·56)	..	..
Day 90	119·0 (15·93)	123·8 (15·29)	..	..
Adjusted mean change	−3·7 (0·92)	1·6 (0·94)	−5·4 (−7·2 to −3·5)*	<0·0001
Diastolic blood pressure, mm Hg				
Baseline	76·7 (10·22)	75·9 (8·71)	..	..
Day 90	74·0 (10·41)	75·9 (10·14)	..	..
Adjusted mean change	−2·4 (0·59)	−0·07 (0·61)	−2·3 (−3·5 to −1·1)*	0·0001
Heart rate, beats per min				
Baseline	78·5 (11·78)	78·8 (11·82)	..	..
Day 90	71·3 (13·30)	77·3 (12·61)	..	..
Adjusted mean change	−7·8 (0·77)	−2·0 (0·79)	−5·8 (−7·3 to −4·3)*	<0·0001
Potassium, mmol/L				
Baseline	4·27 (0·455)	4·26 (0·442)	..	..
Day 90	4·60 (0·471)	4·45 (0·504)	..	..
Adjusted mean change	0·32 (0·030)	0·17 (0·031)	0·15 (0·09 to 0·21)*	<0·0001
Urea, mmol/L				
Baseline	8·11 (3·59)	7·96 (3·40)	..	..
Day 90	7·84 (3·83)	7·93 (4·01)	..	..
Adjusted mean change	0·10 (0·223)	0·37 (0·229)	−0·27 (−0·71 to 0·18)*	0·24
eGFR, ml/min per 1·73 m²				
Baseline	61·92 (19·92)	62·89 (21·83)	..	..
Day 90	62·13 (21·54)	63·01 (21·71)	..	..
Adjusted mean change	1·50 (0·94)	1·85 (0·97)	−0·35 (−2·22 to 1·52)*	0·71

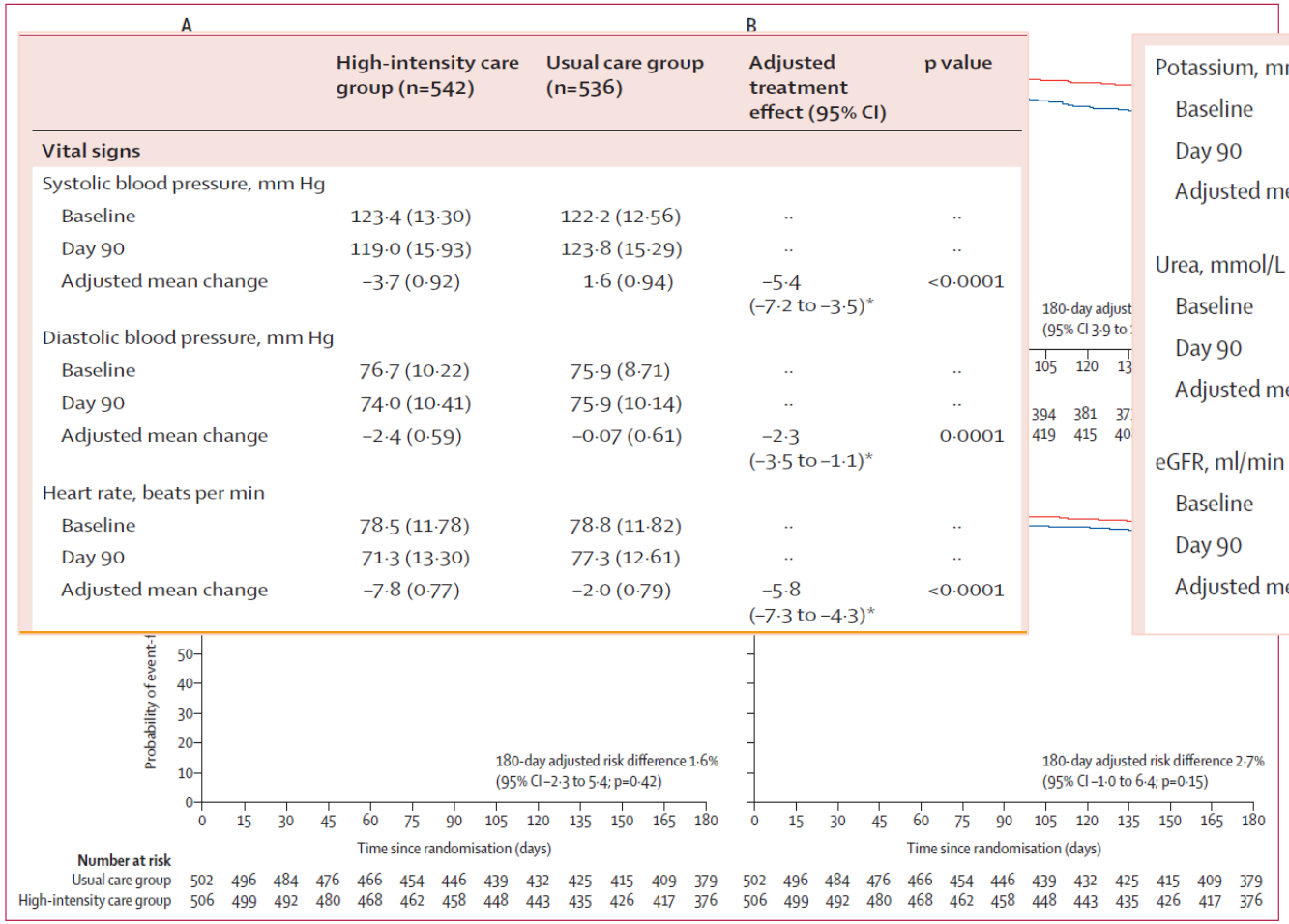


Figure 3: Adjusted Kaplan-Meier estimates of cumulative event-free survival with down-weighting of cohort 1 for all-cause death or heart failure readmission (A), all-cause death or heart failure excluding deaths due to COVID-19 (B), all-cause mortality (C), and all-cause mortality excluding deaths due to COVID-19 (D), from randomisation up to day 180
Adjusted 180-day risk differences are given. Analyses excluding COVID-19-related deaths were prespecified sensitivity analyses.

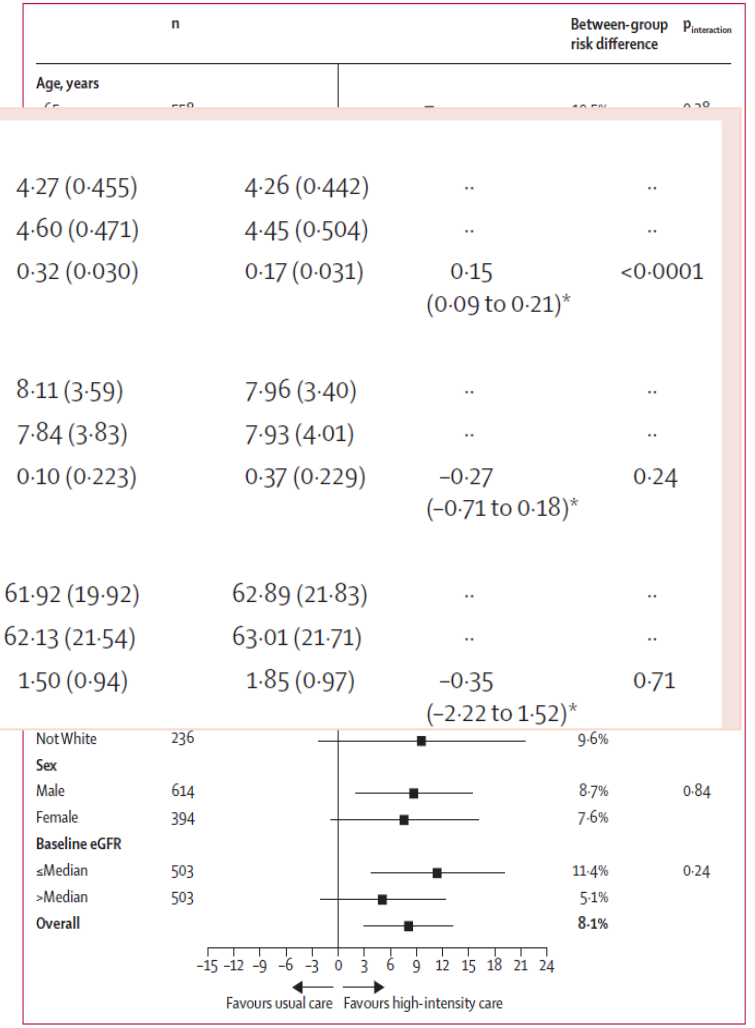
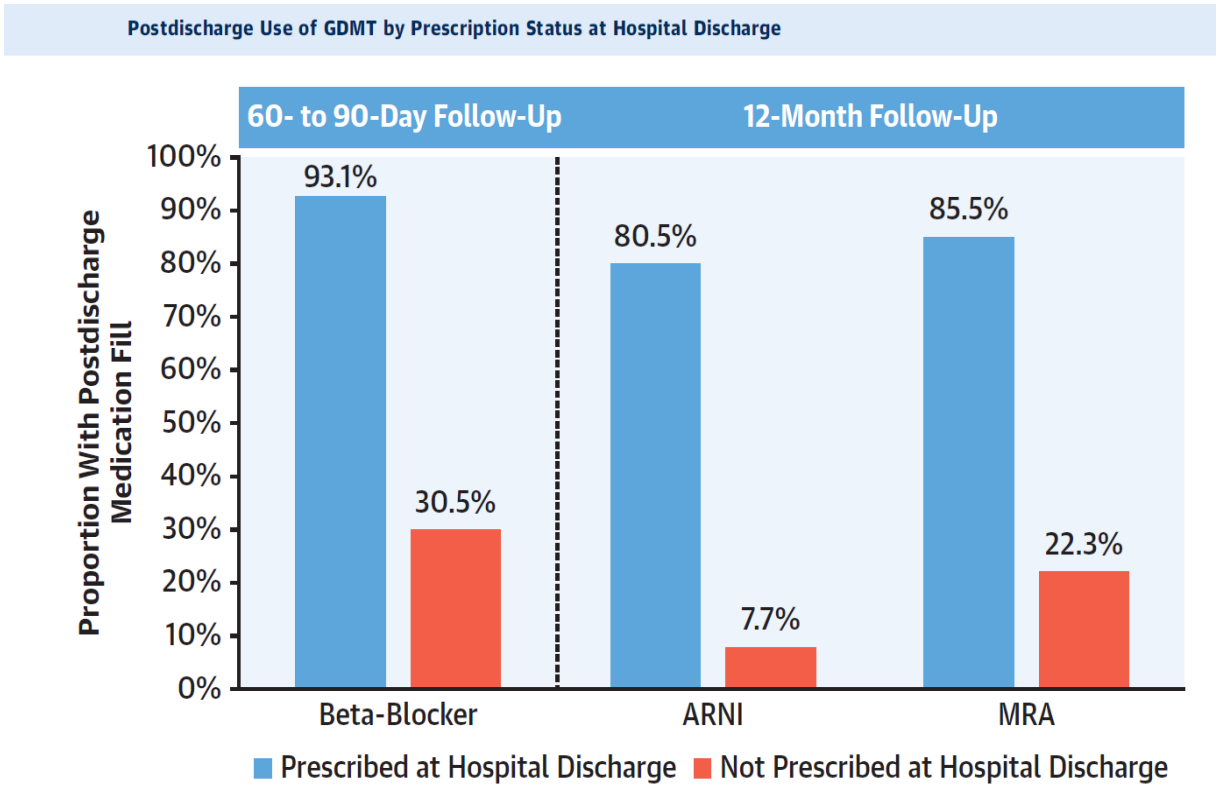
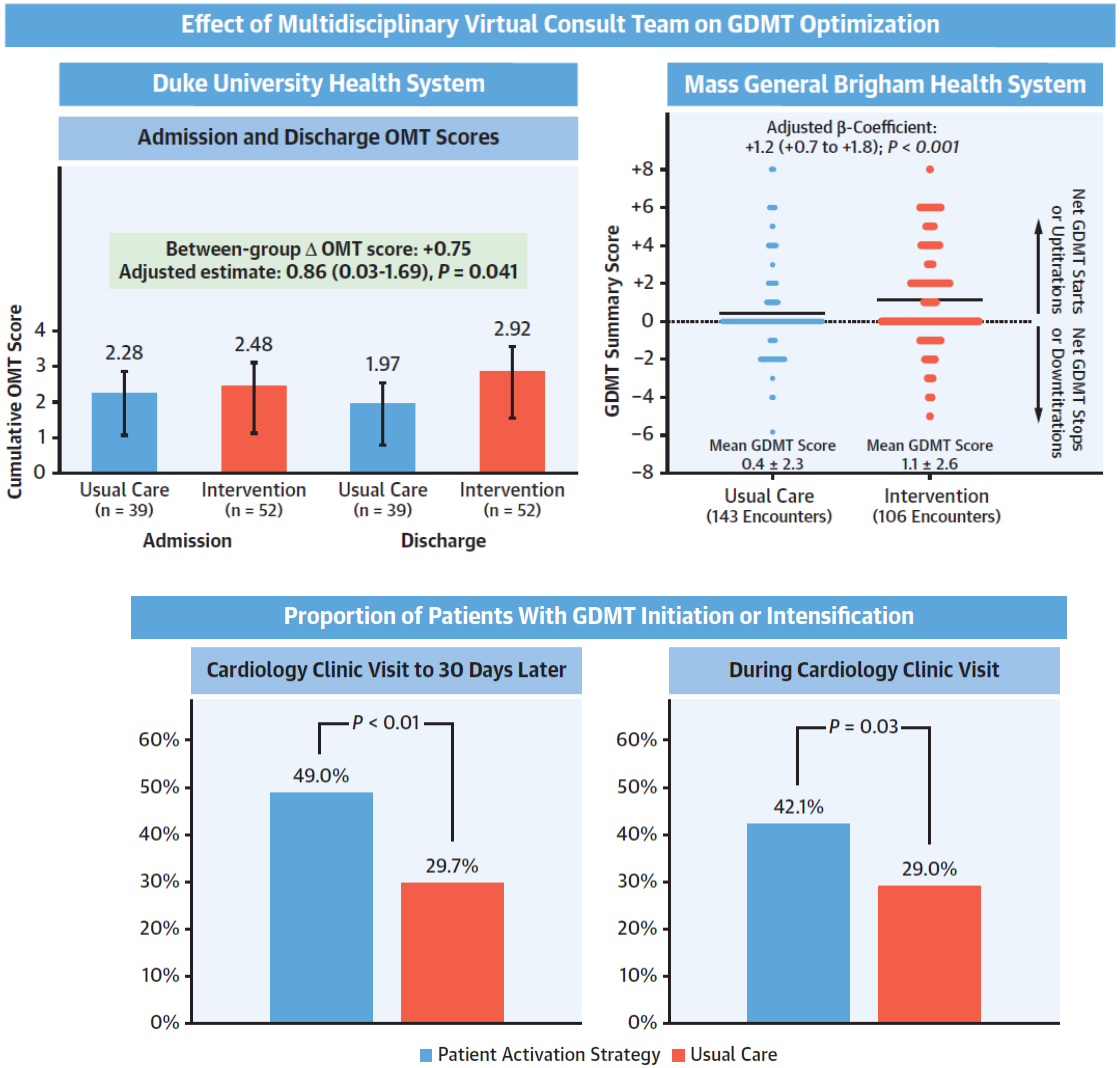


Figure 4: Prespecified and post-hoc subgroup analysis of primary endpoint (difference in 180-day risk of all-cause death or heart failure readmission)

STRONG-HF. Lancet 2020;400:1938-52

Estrategias para facilitar el mantenimiento de GDMT en IC-FE r





Patolia H, et al. J Am Coll Cardiol 202;82:529-43

Hipotensión, disfunción renal

Hipotensión en el tratamiento de la IC-FE r

Hypotension in heart failure is less harmful if associated with high or increasing doses of heart failure medication: Insights from the Swedish Heart Failure Registry

SwedeHF Heart Failure Registry

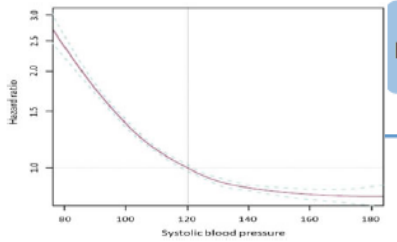
Linked registries

National patient registry

Cause of death registry

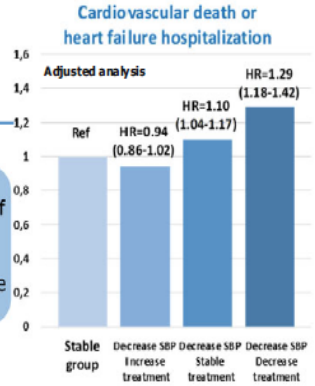
Study population

42,040 patients with **HFrEF**, enrolled between 2000-2018



The risk of CV death/HF hospitalization with lower systolic BP

Decreasing systolic BP was associated with higher risk of CVD/HFH in patients with stable/decreasing HF medication dose, not in those increasing doses



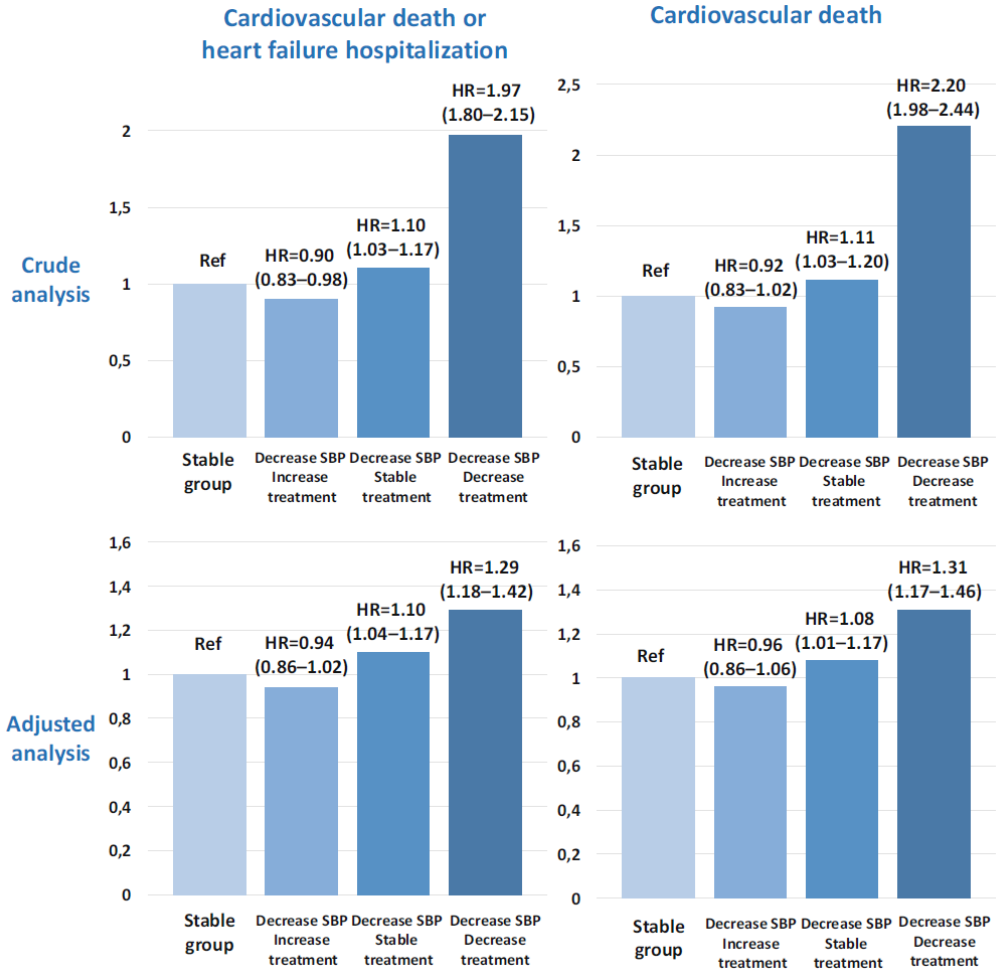
Cardiovascular death or heart failure hospitalization

	Subgroup	Adjusted HR for 1 mmHg increase in SBP (95% CI)	P-value	Interaction P-value
Interaction of SBP with RAS inhibitors dose	No RASI	0.90 (0.89-0.92)	<0.001	0.016
	RASI dose <50%	0.92 (0.91-0.94)	<0.001	
	RASI dose >=50%	0.93 (0.92-0.94)	<0.001	
Interaction of SBP with BB dose	No BB	0.90 (0.88-0.92)	<0.001	0.016
	BB dose <50%	0.92 (0.91-0.94)	<0.001	
	BB dosse >=50%	0.93 (0.92-0.94)	<0.001	
Interaction of SBP with MRA dose	No MRA	0.93 (0.92-0.94)	<0.001	0.010
	MRA	0.91 (0.90-0.92)	<0.001	

Lower baseline systolic BP was associated with higher risk of CV death/HF hospitalization, which was less high risk under optimized drug therapy

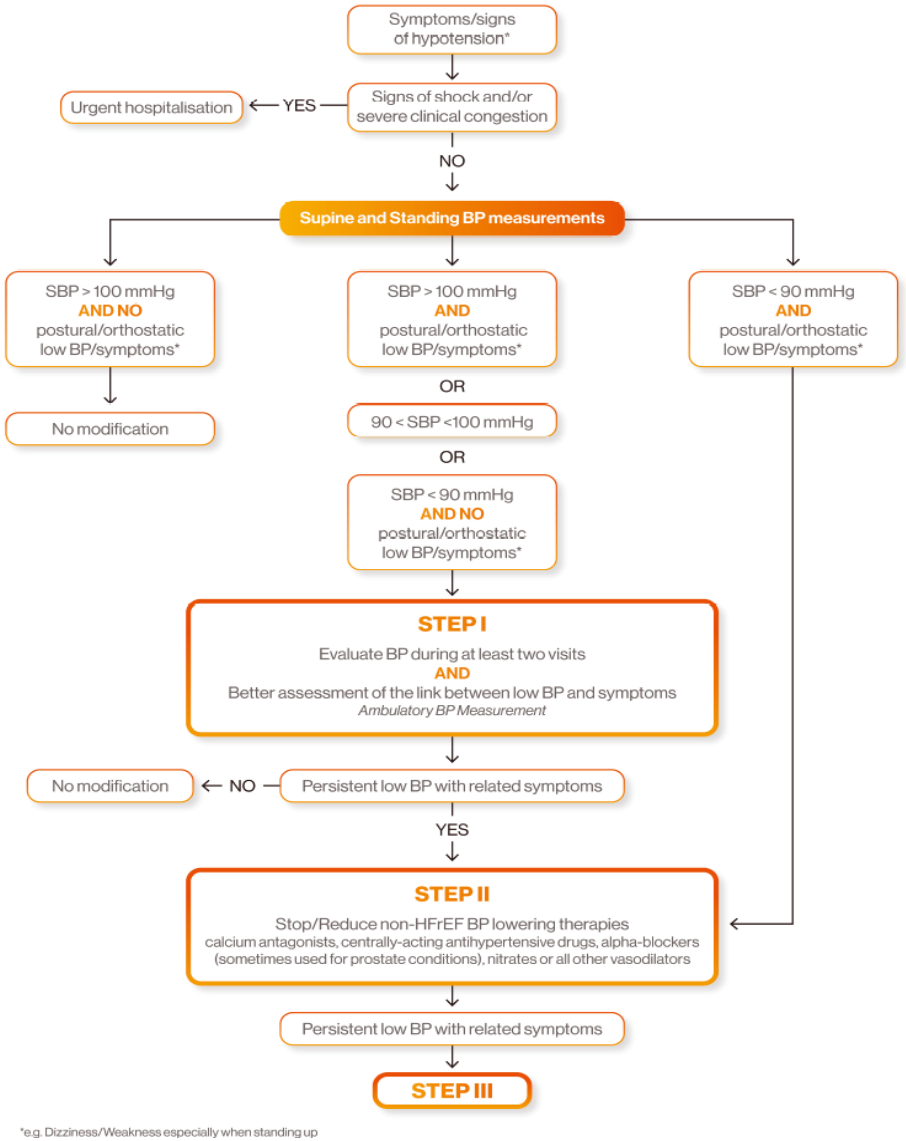
We assessed: i) interaction systolic BP x HF medication with outcomes and ii) prognostic impact of BP decrease (spontaneous or related to HF medications' uptitration)

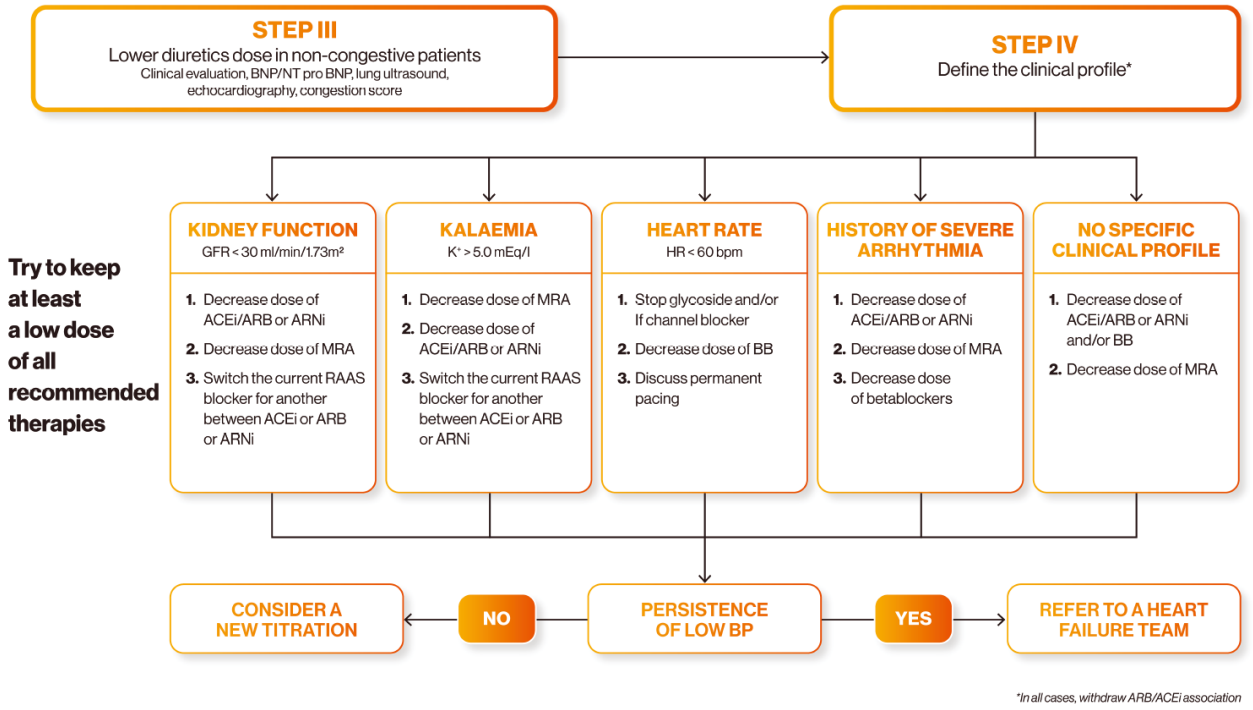
The association of lower systolic BP with higher risk of CVD/HFH is attenuated in patients with optimized HF medication, and it should not limit medication optimization



SwedeHF registry. Eur J Heart Fail 2024;26:359-69

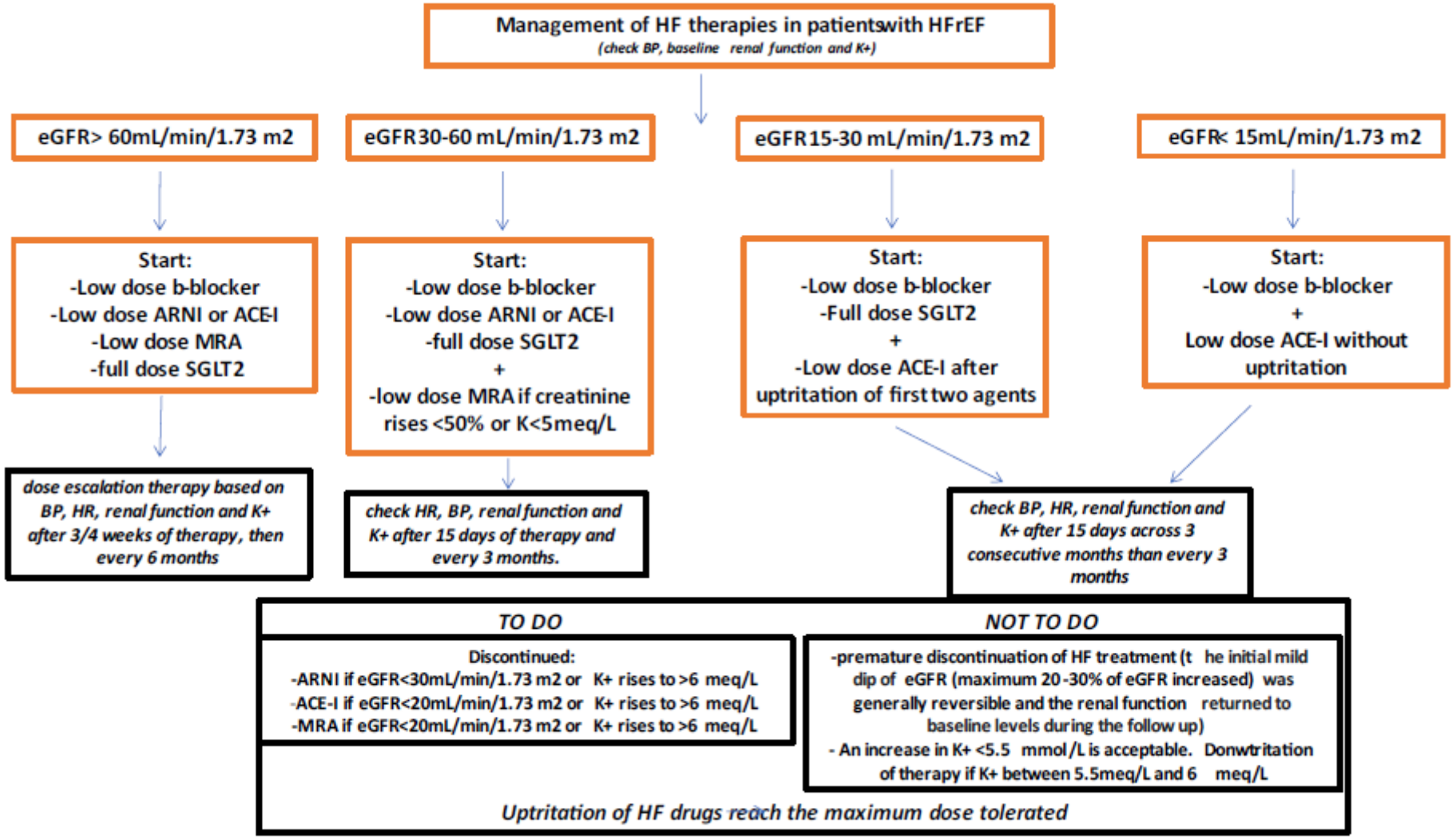
Hipotensión, disfunción renal e hiperkalemia en el tratamiento de la IC-FE r





Cautela J, et al. Eur J Heart Fail 2020;22:1357-65

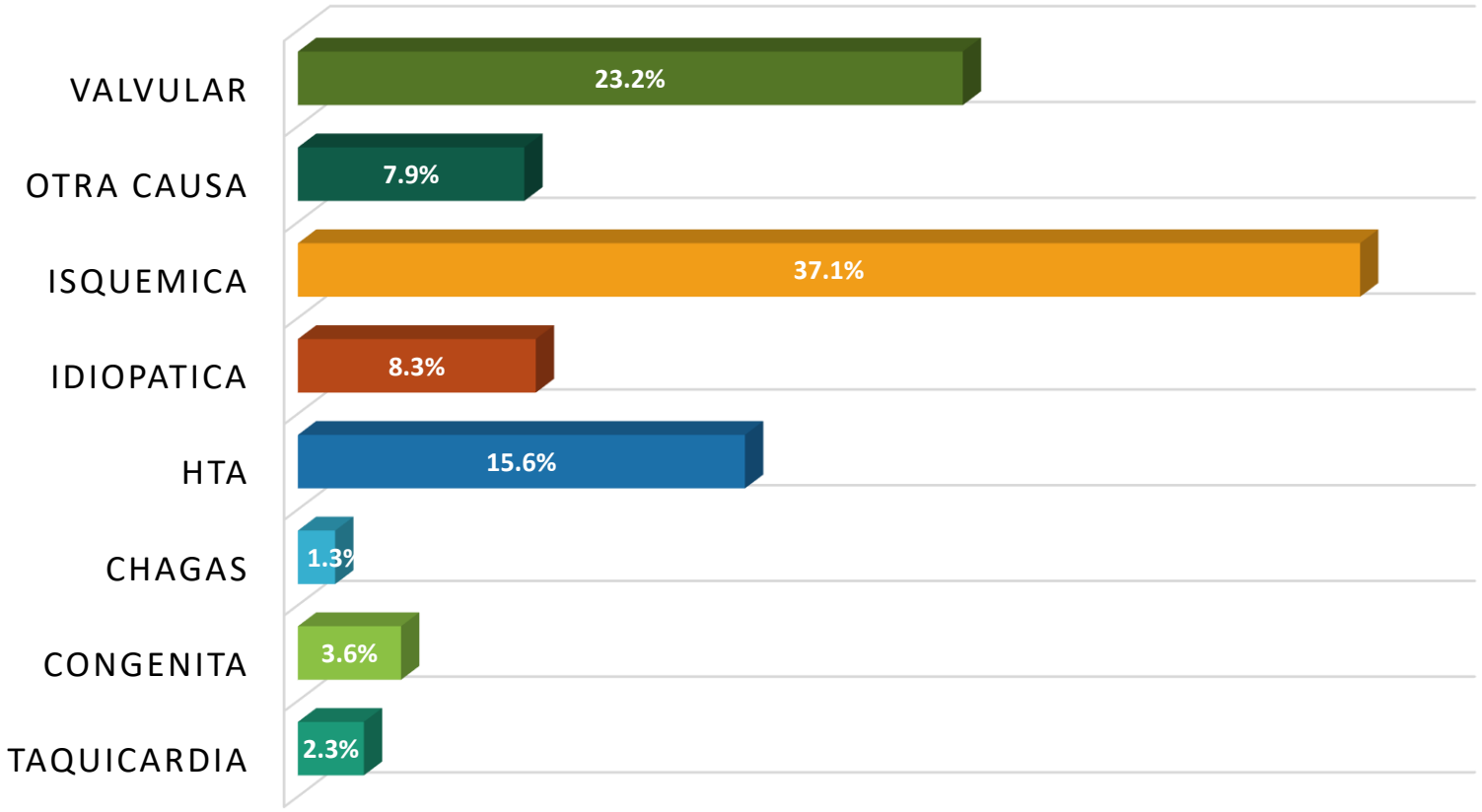
Función renal en el tratamiento de la IC-FE r



Beltrami M, et al. J Clin Med 2022,11,2243

A modo de conclusiones

Etiologías y prevalencias de los fenotipos en Perú



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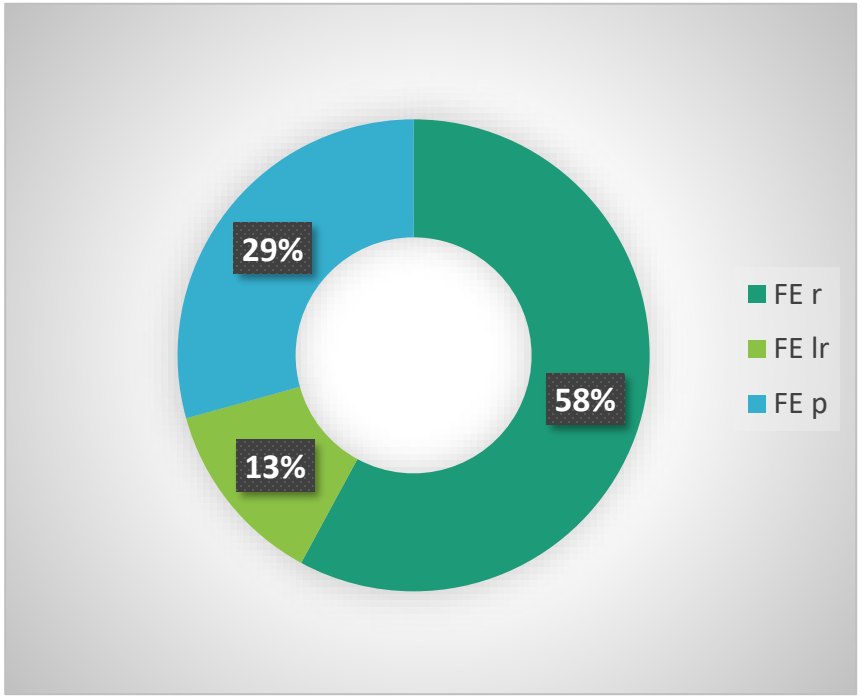

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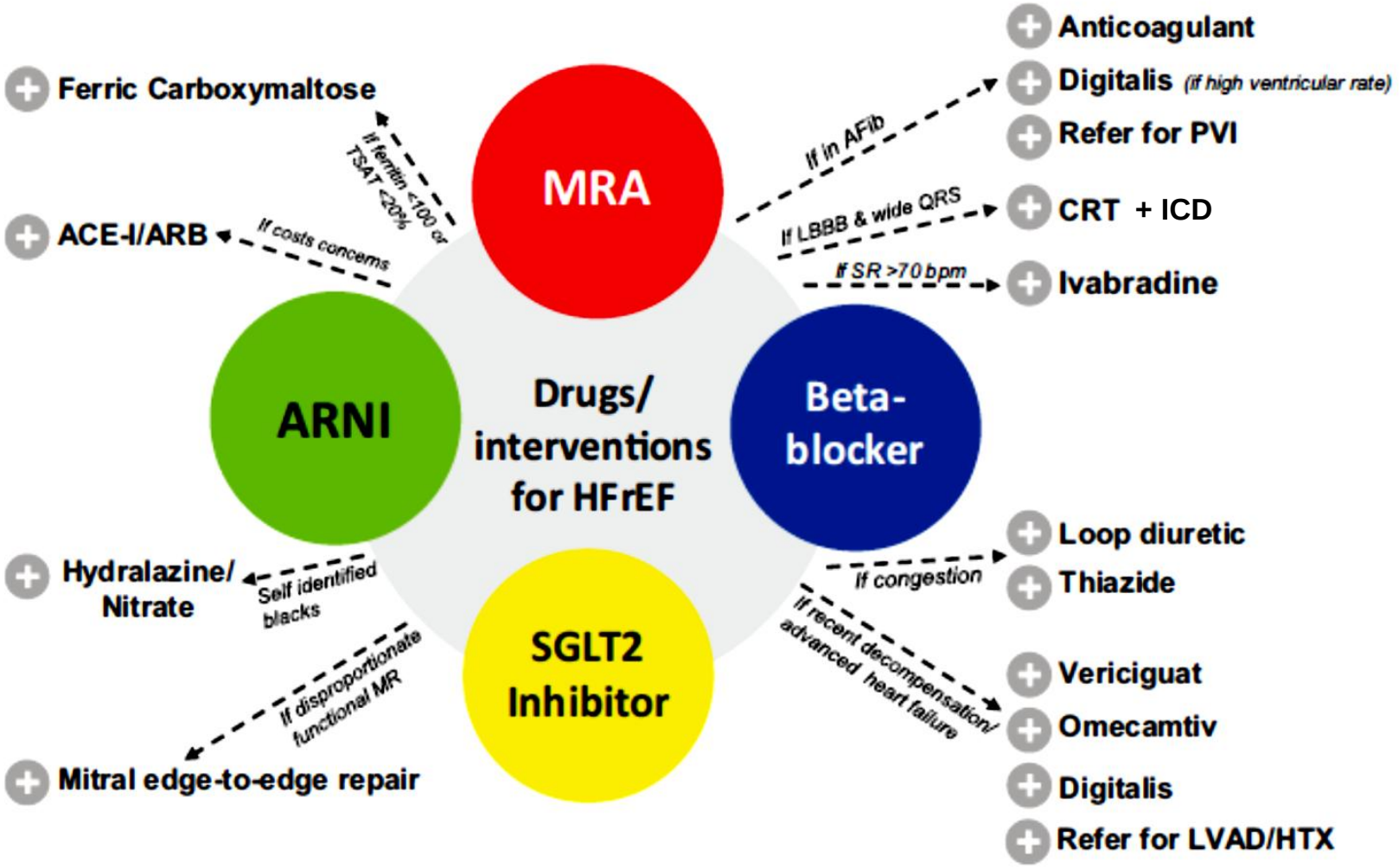
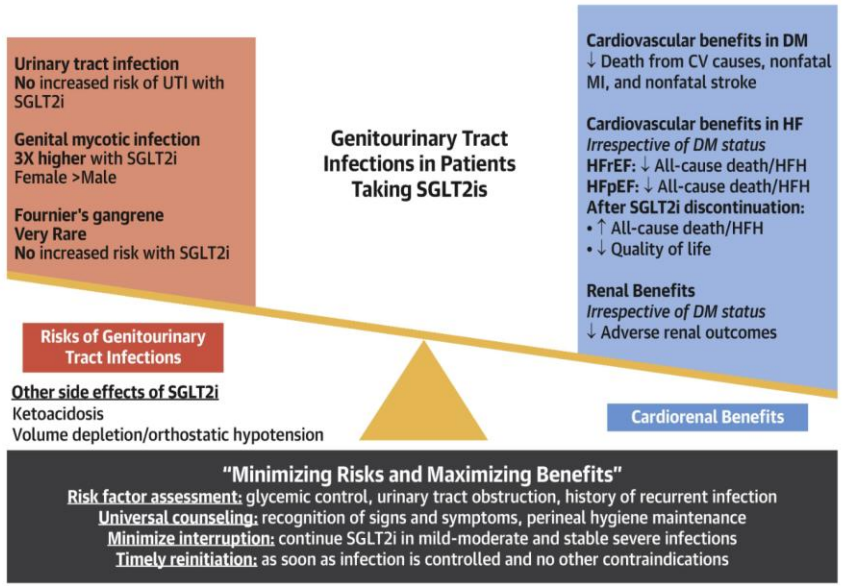
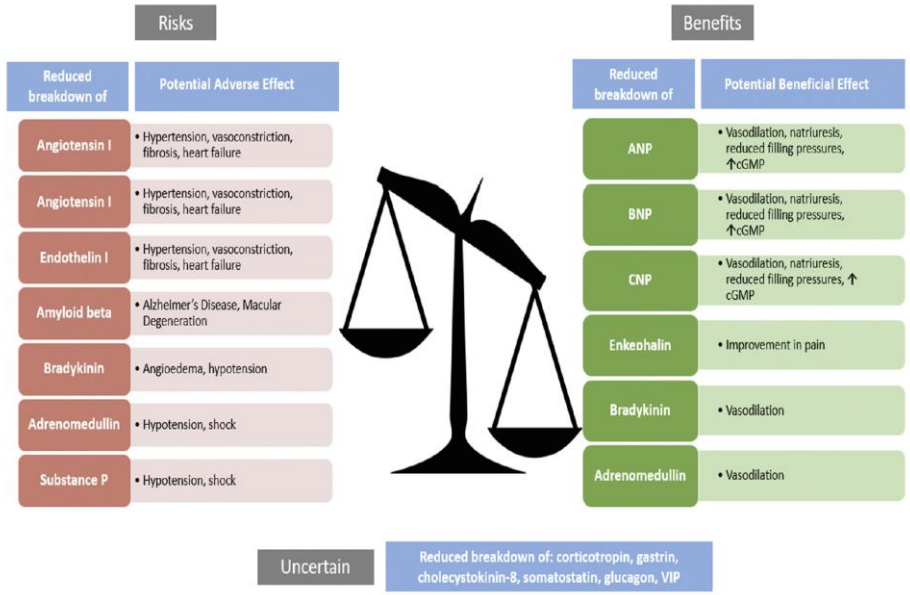
Tratamiento cuádruple actual de la IC-FE r

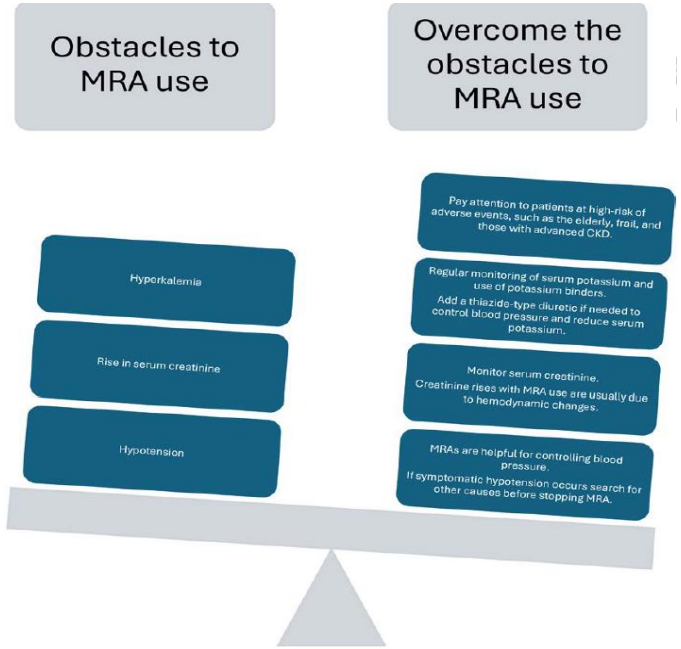


Bauersachs J. Eur Heart J 2021;42:481-3

Obstáculos para el uso de la terapia fundamental

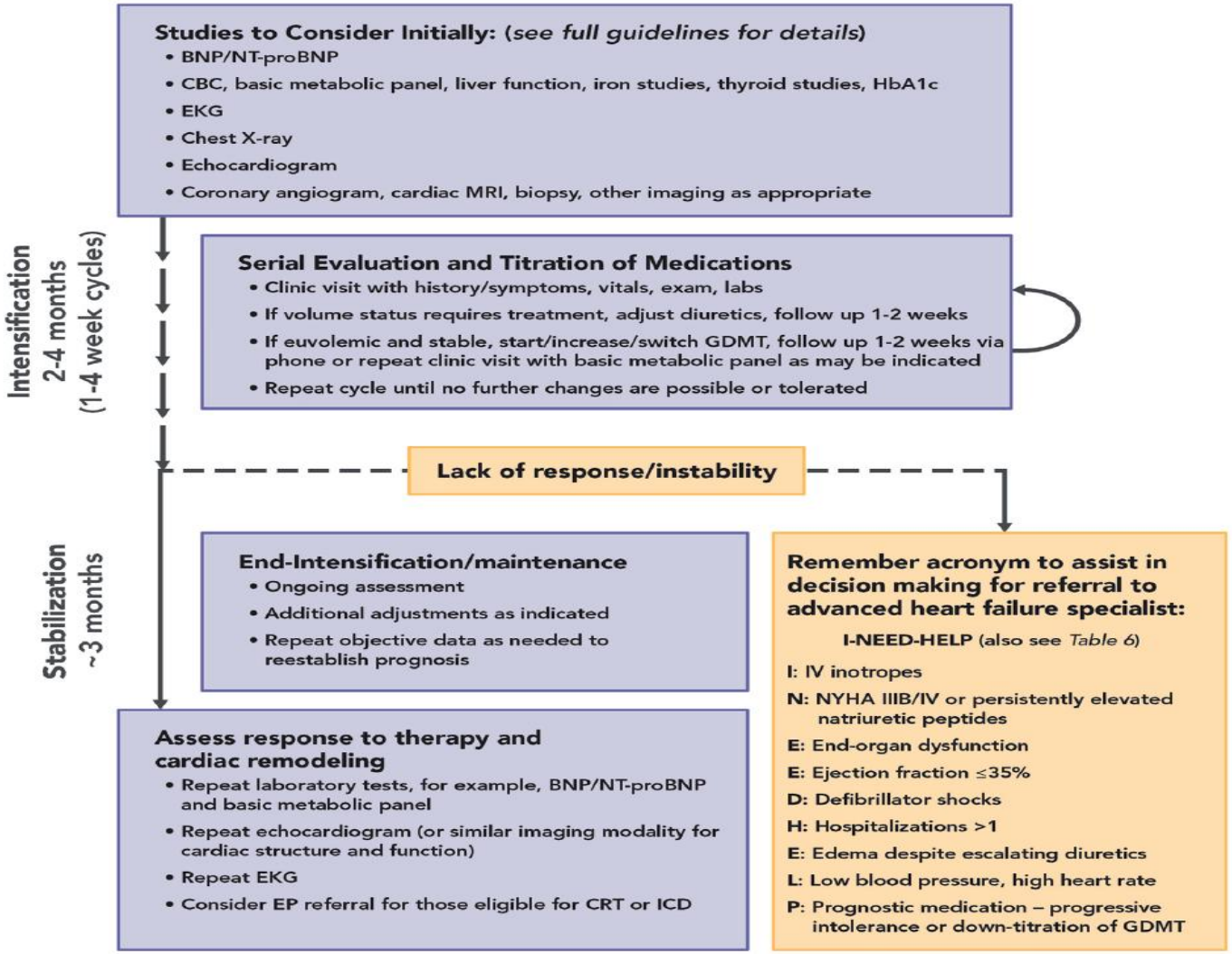






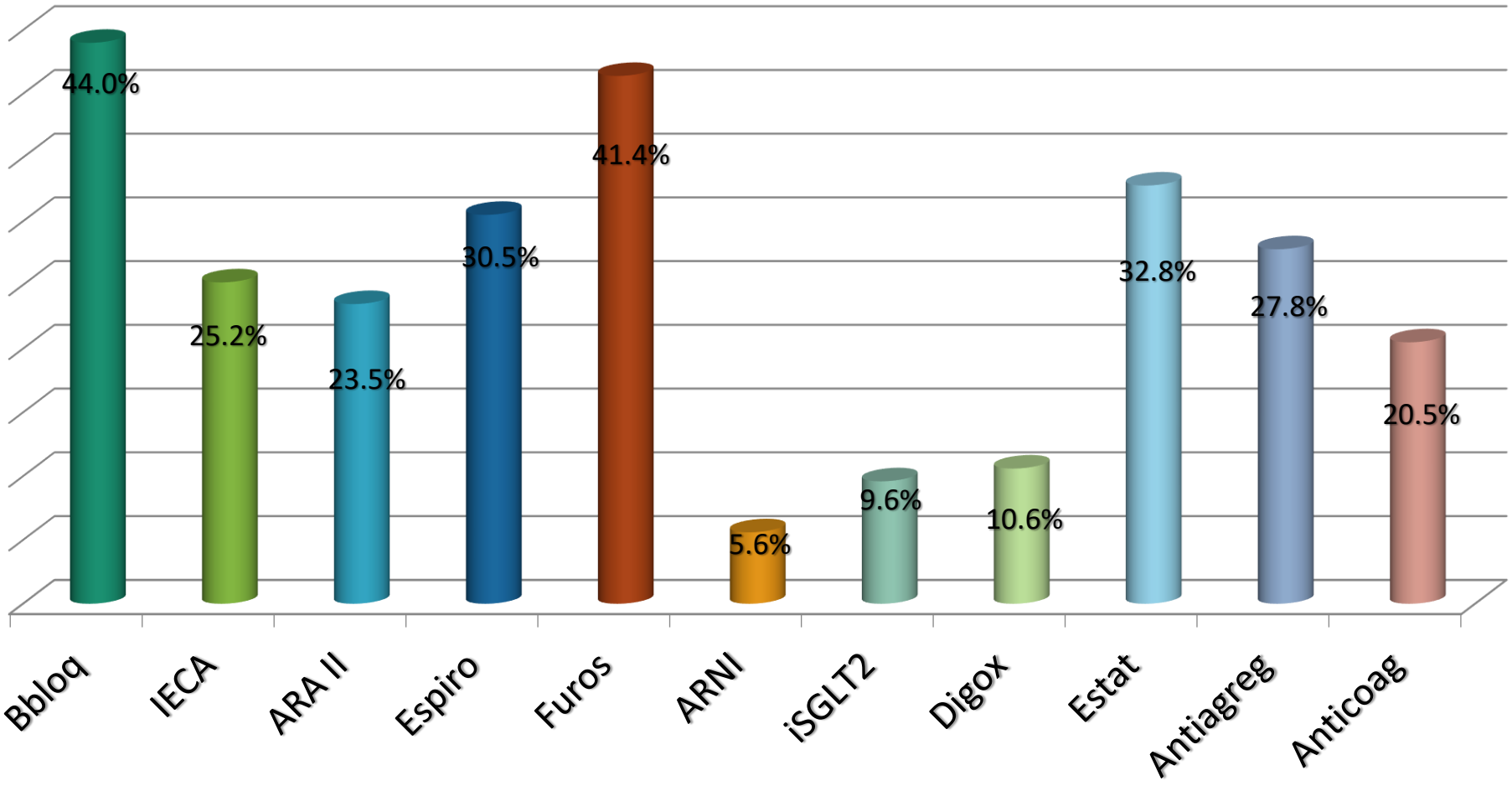
Kittipibul V, et al. J Am Coll Cardiol 2024;83:1568-78
Bozkurt B, et al. JACC: BASIC TO TRANSLATIONAL SCIENCE 2023;8:88-105
Ferreira JP, et al. Circ Heart Fail 2024;17:e011629.Doi:10.1161/CIRCHEARTFAILURE.124.011629

Intensificación, titulación y referencia al especialista



Yancy C, et al. J Am Coll Cardiol 2017. https://doi.org/10.1016/j.jack.2017.11.025

Medicación previa a la hospitalización índice



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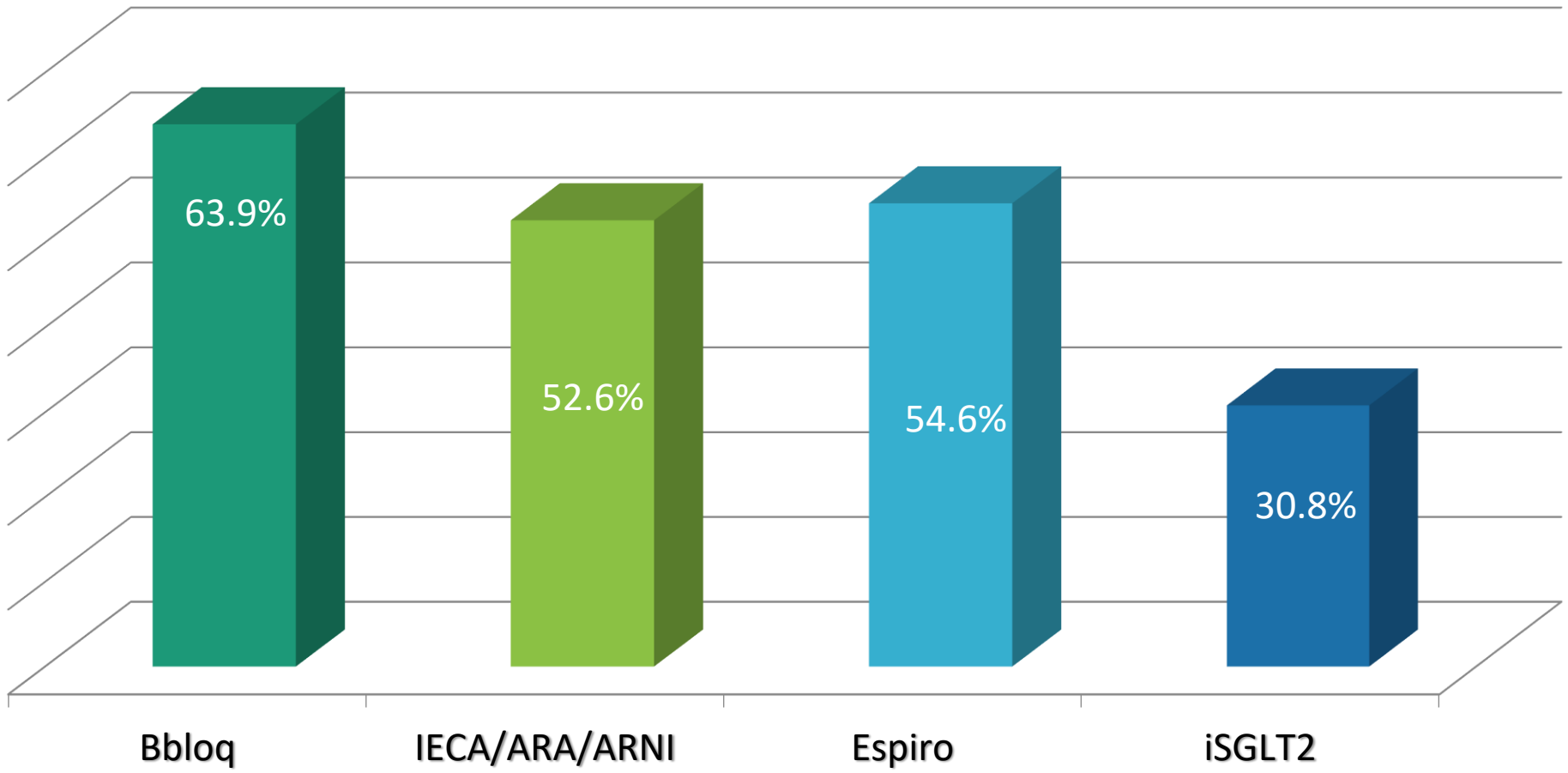
Medicación al alta hospitalaria



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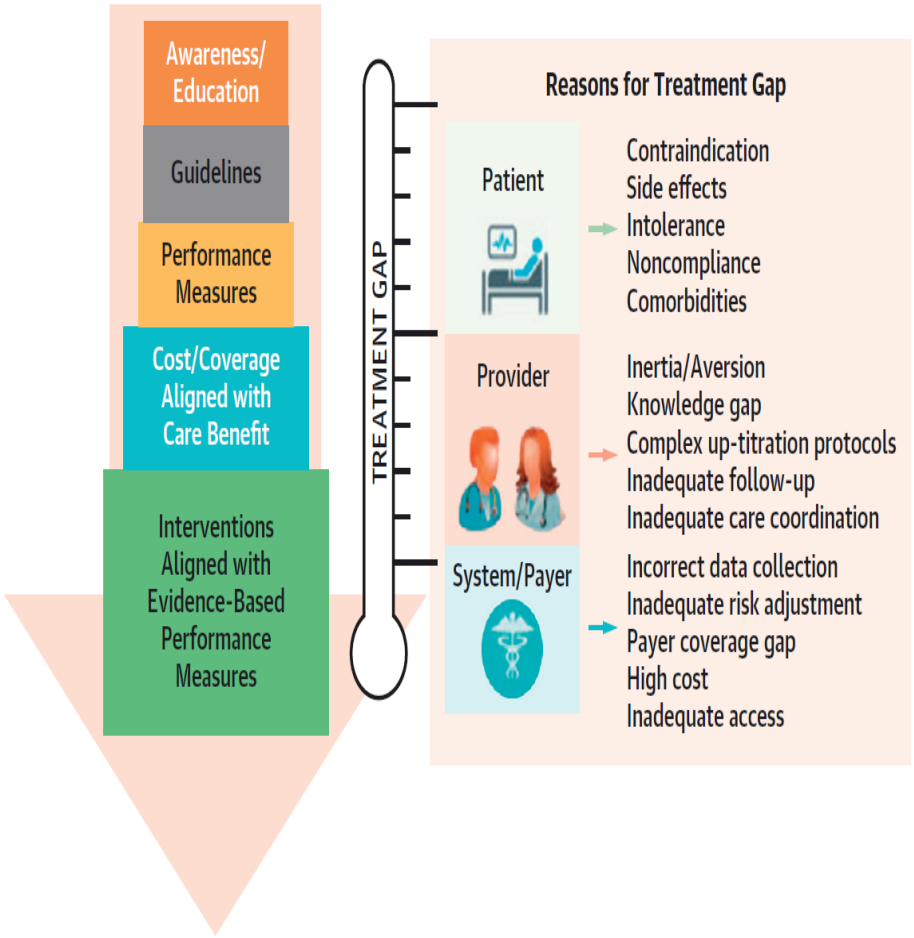
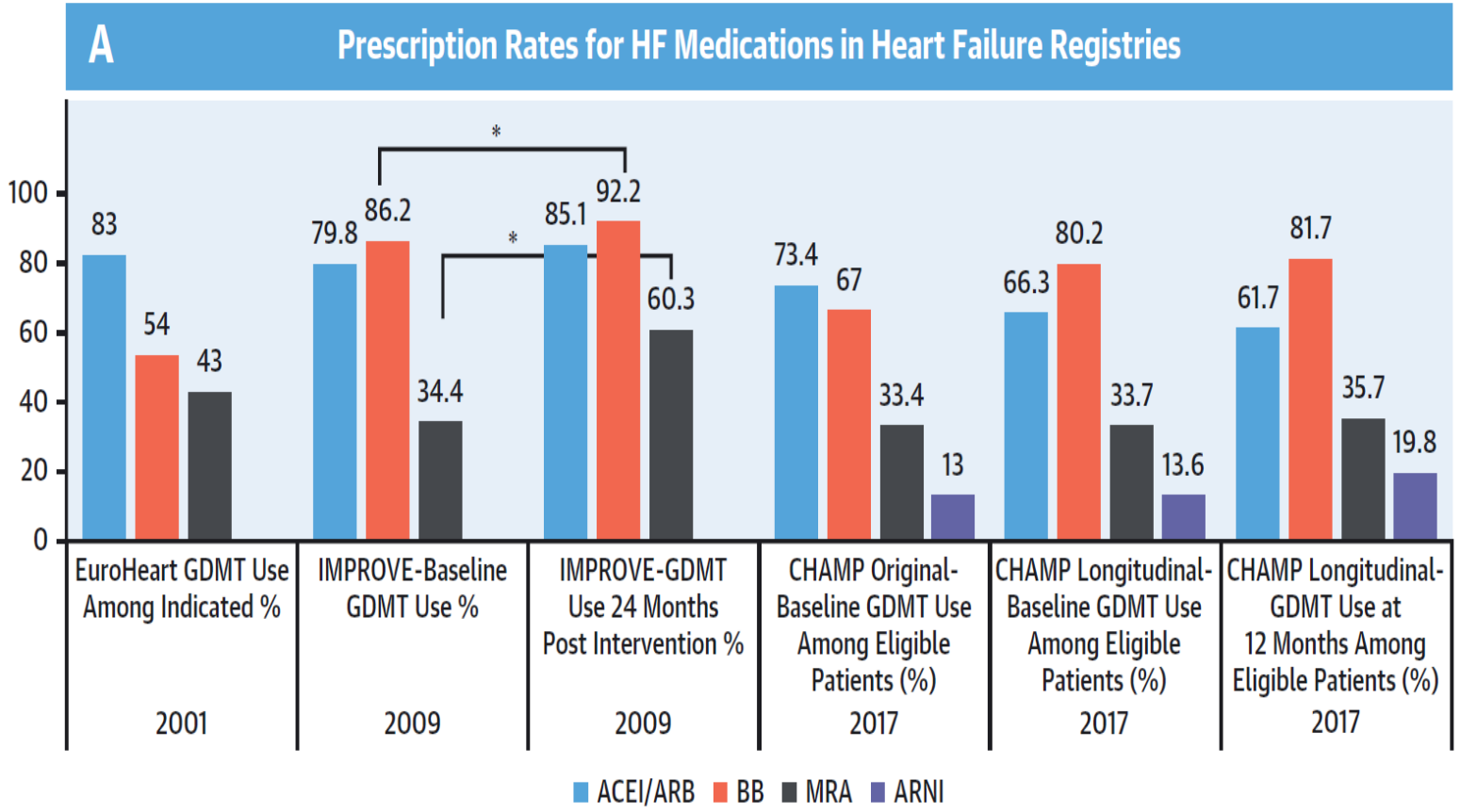
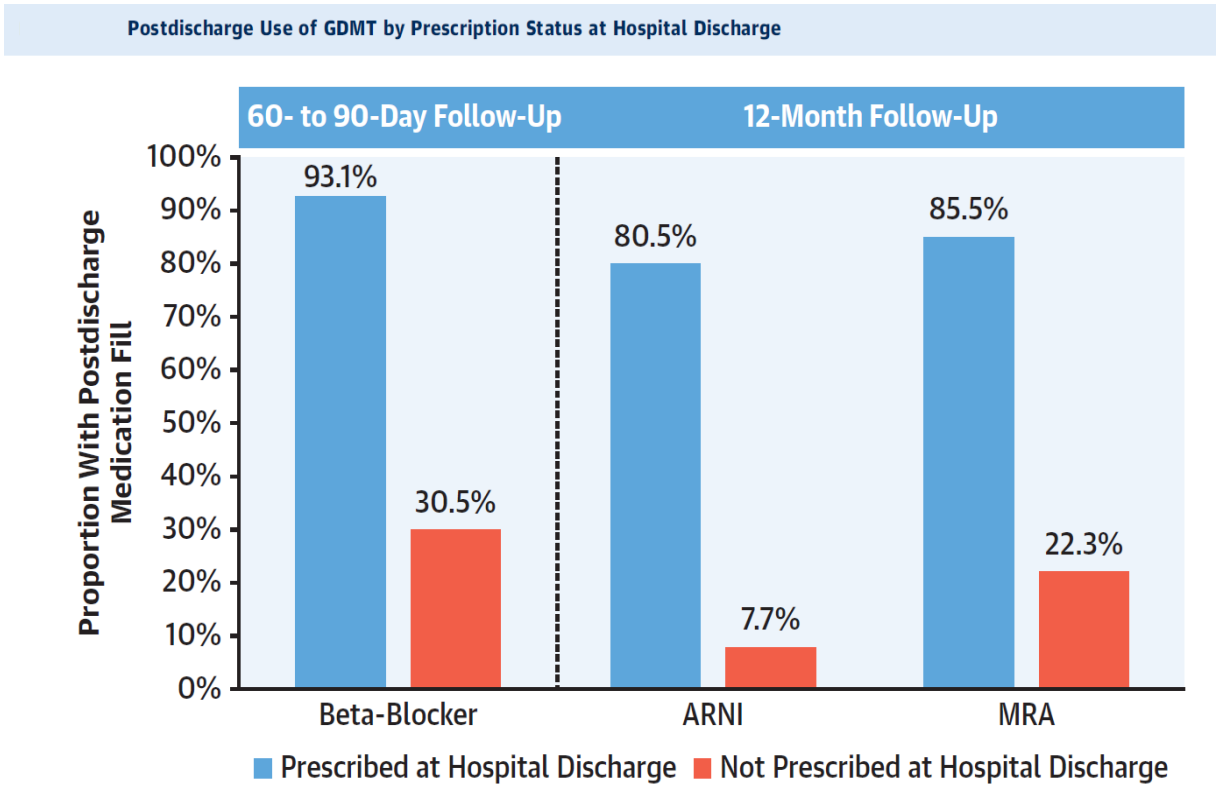
Vacíos a pesar de las evidencias de tratamiento

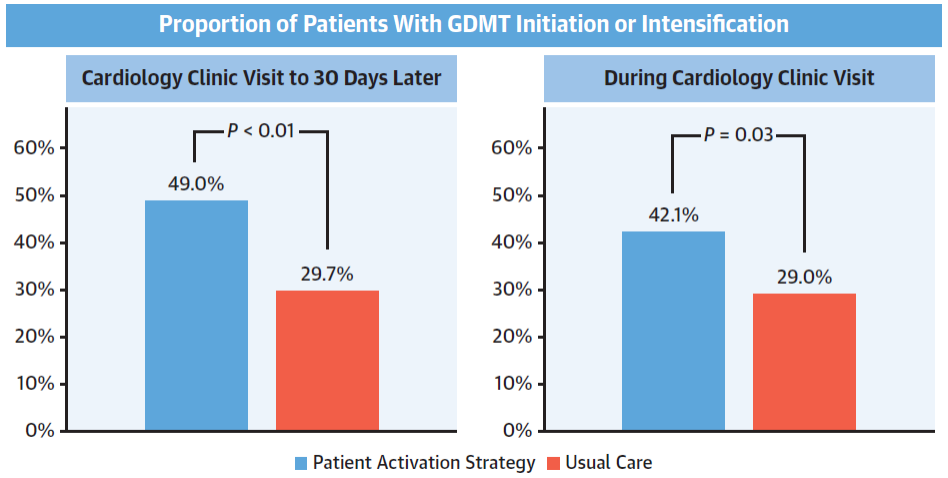


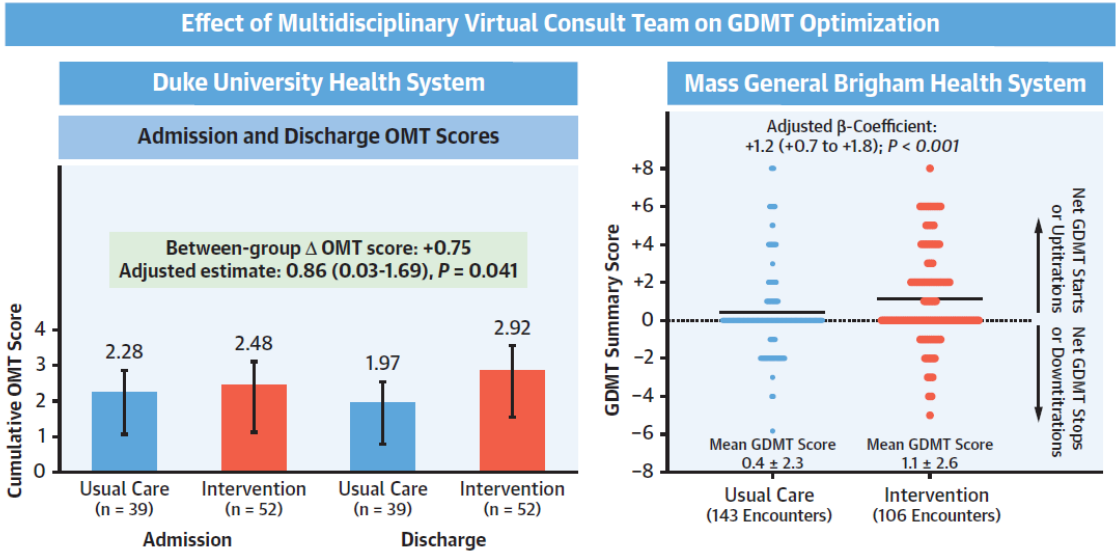


Patolia H, et al. J Am Coll Cardiol 2023;82:529-43

Estrategias para facilitar el inicio/titulación de GDMT en IC-FE r

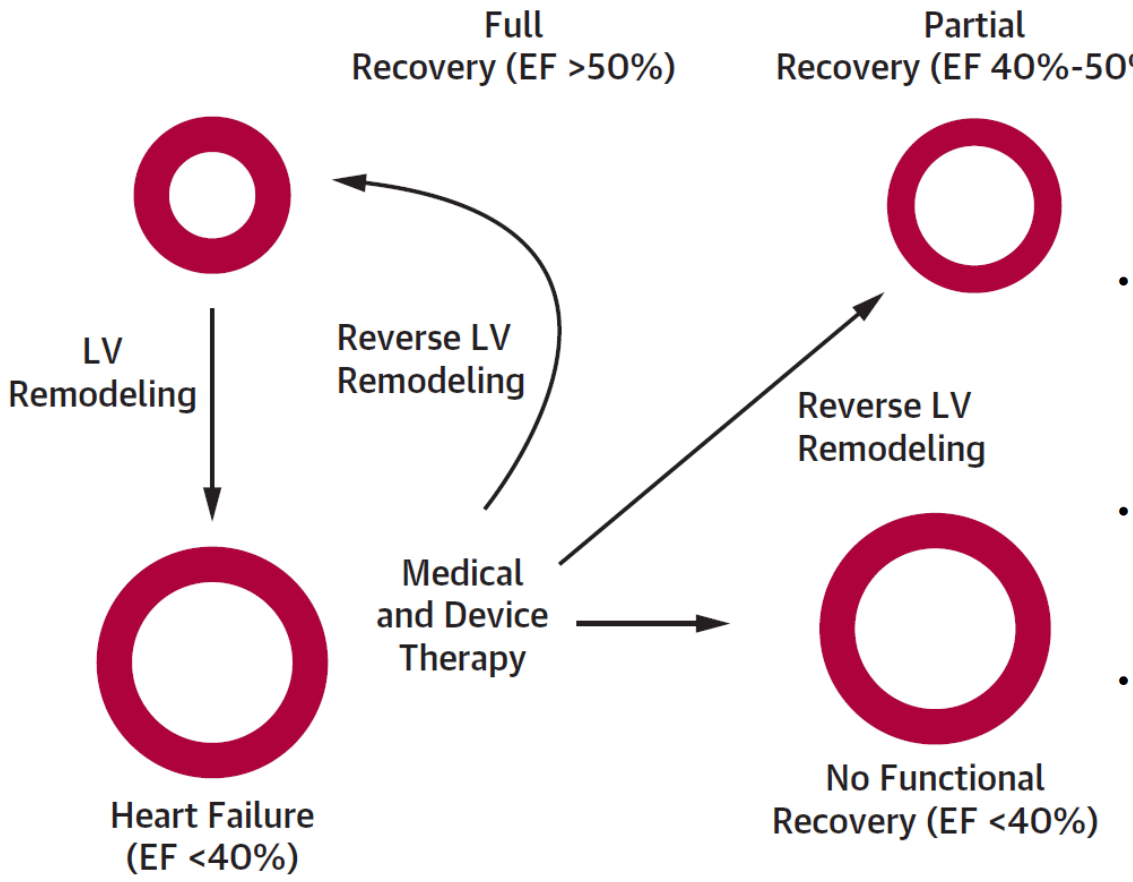




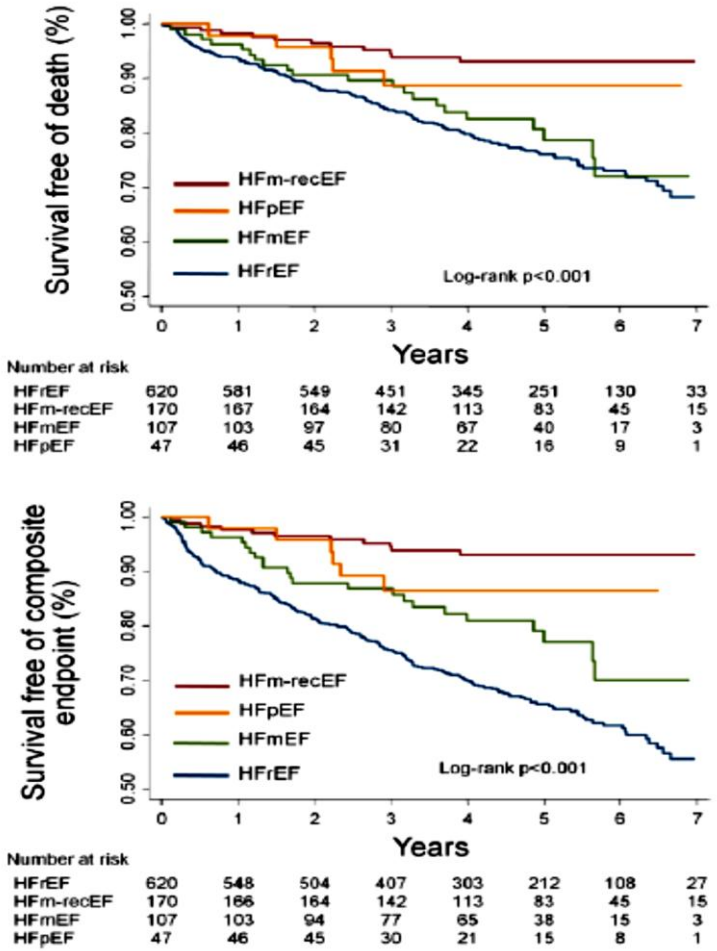


Patolia H, et al. J Am Coll Cardiol 202;82:529-43

Insuficiencia cardiaca con FE VI recuperada (IC-FE rec)



- A working definition of HFrecEF that is consistent with the majority of studies in the literature includes the following: 1) documentation of a decreased LVEF <40% at baseline; 2) ≥10% absolute improvement in LVEF; and 3) a second measurement of LVEF >40%.
- Guideline-directed medical and device therapy for patients with HFrecEF should be continued indefinitely until the biology and clinical epidemiology of HFrecEF is better understood.
- HFrecEF patients should have close clinical follow-up due to the high risk of heart failure relapse.



Wilcox JE, et al. J Am Coll Cardiol 2020;76:719-34
Nadruz W, et al. Circ Heart Fail 2016;9:e002826

Conclusiones

. El tratamiento farmacológico cuádruple en la IC-FE r debe indicarse temprano y debe titularse, salvo contraindicaciones.

. Las dosis óptimas tolerables conllevan a mayores beneficios.

. Lograr las dosis óptimas tolerables en menor tiempo es más beneficioso.

. La presión arterial, frecuencia cardíaca, función renal y kalemia son determinantes de titulación, entre otras.

. Debemos evitar la inercia terapéutica.

. Debemos educar y cambiar el sistema.

. “Mientras nuestro paciente piense y orine” asumo que vamos bien.

Agp/2025