The 4th Indonesian Symposium on Heart Failure and Cardiometabolic Disease

Choosing The Right Path for CV Mortality Reduction in Heart Failure

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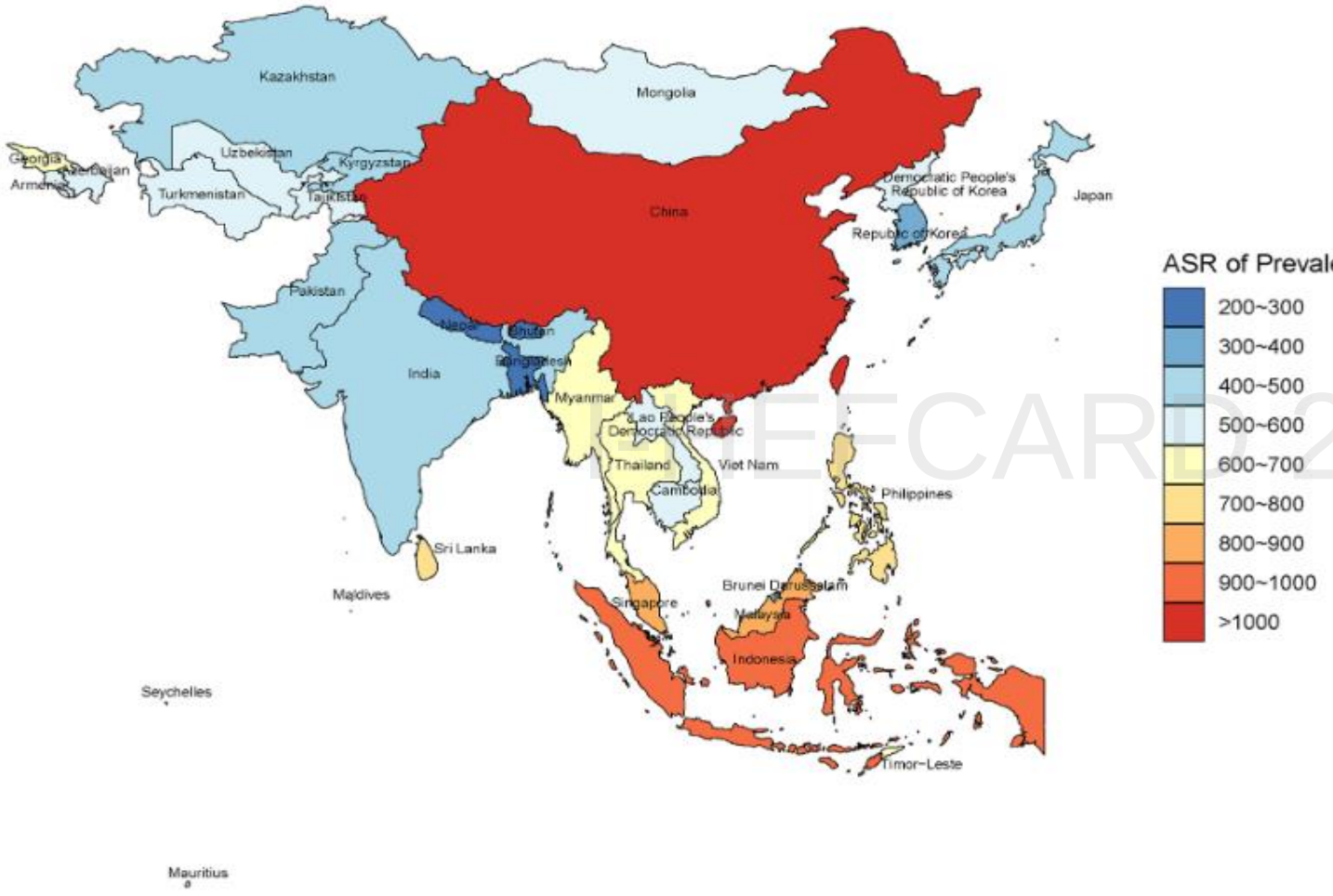
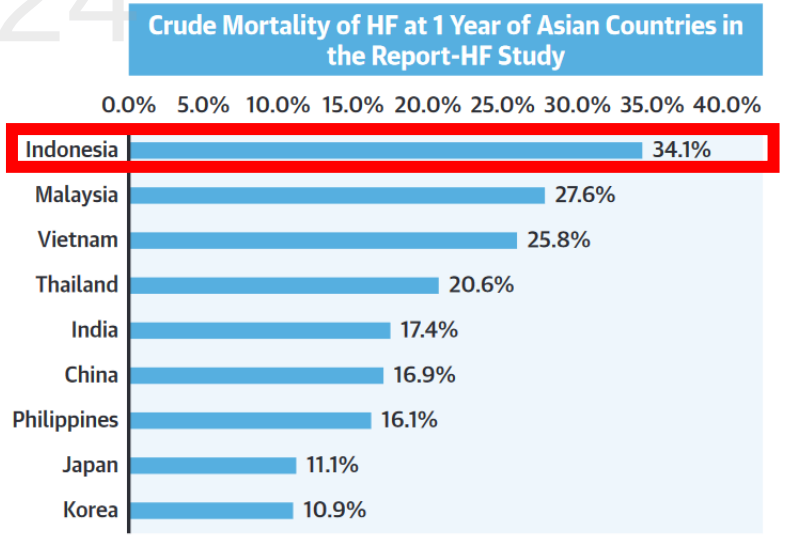
How Big is HF in Indonesia?

FIGURE 1 **Age-Standardized Prevalence Rate of Heart Failure in Asia From GBD 2019**



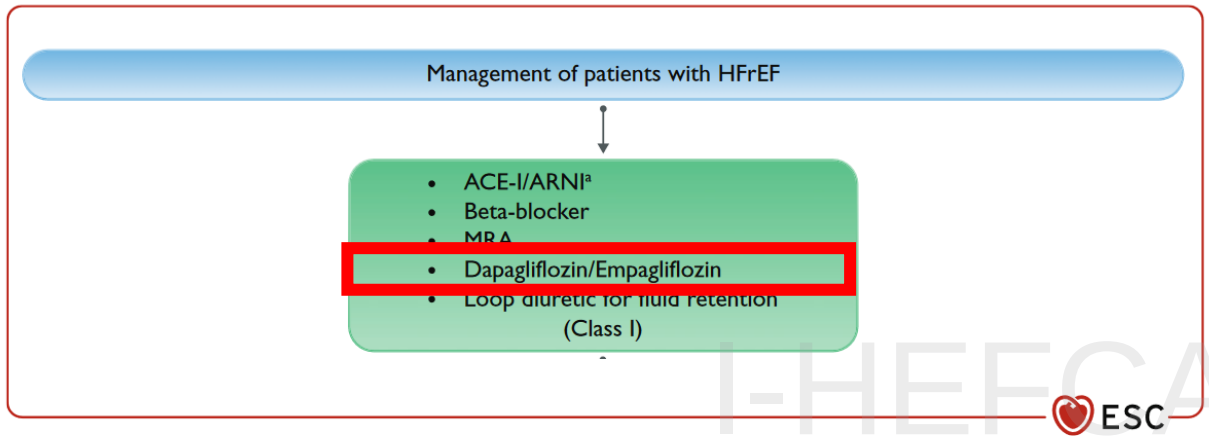
From the GBD (Global Burden of Disease) data, the national and territorial age-standardized rate (ASR) of heart failure prevalence ranged from 211.86 to 1,032.84 cases per 100,000 population in Asia. China (1,032.84), Indonesia (900.90), and Malaysia (809.47) are the 3 highest nations in terms of ASR for prevalence of HF in 2019. Conversely, Nepal (211.86), Bhutan (255.54), and Bangladesh (275.00) reported the lowest rates.

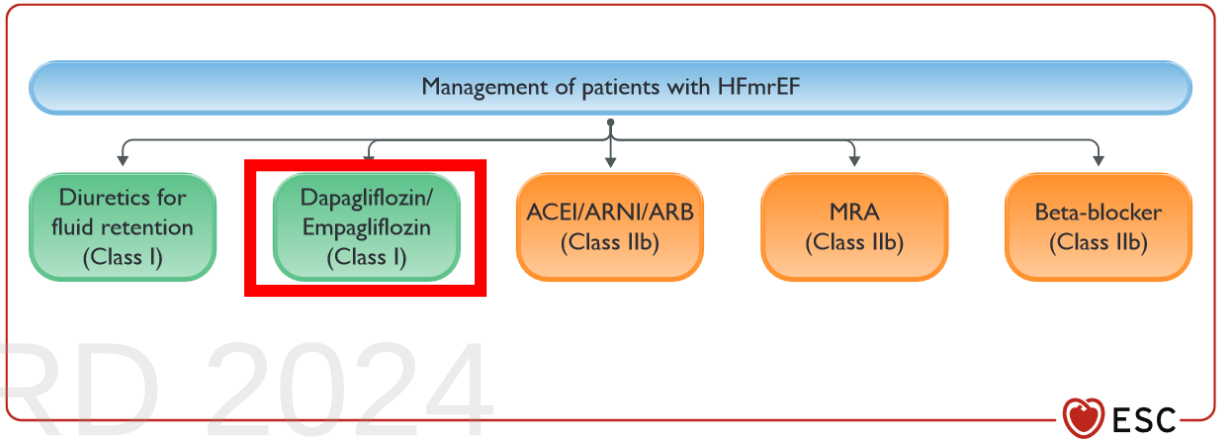
The 1-Year Mortality of Asian HF Patients Is Still High, Especially in Southeast and South Asia: CV Death is the Primary Cause of Death for HF

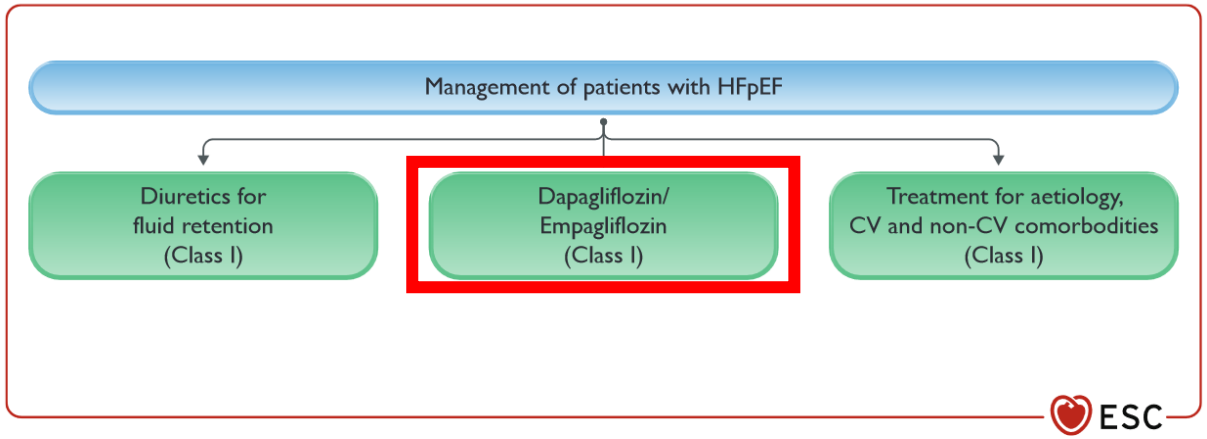


Feng J, et al. JACC: Asia. 2024;4(4):249–264.

Which Drug Reduced Death on HF Across LVEF?

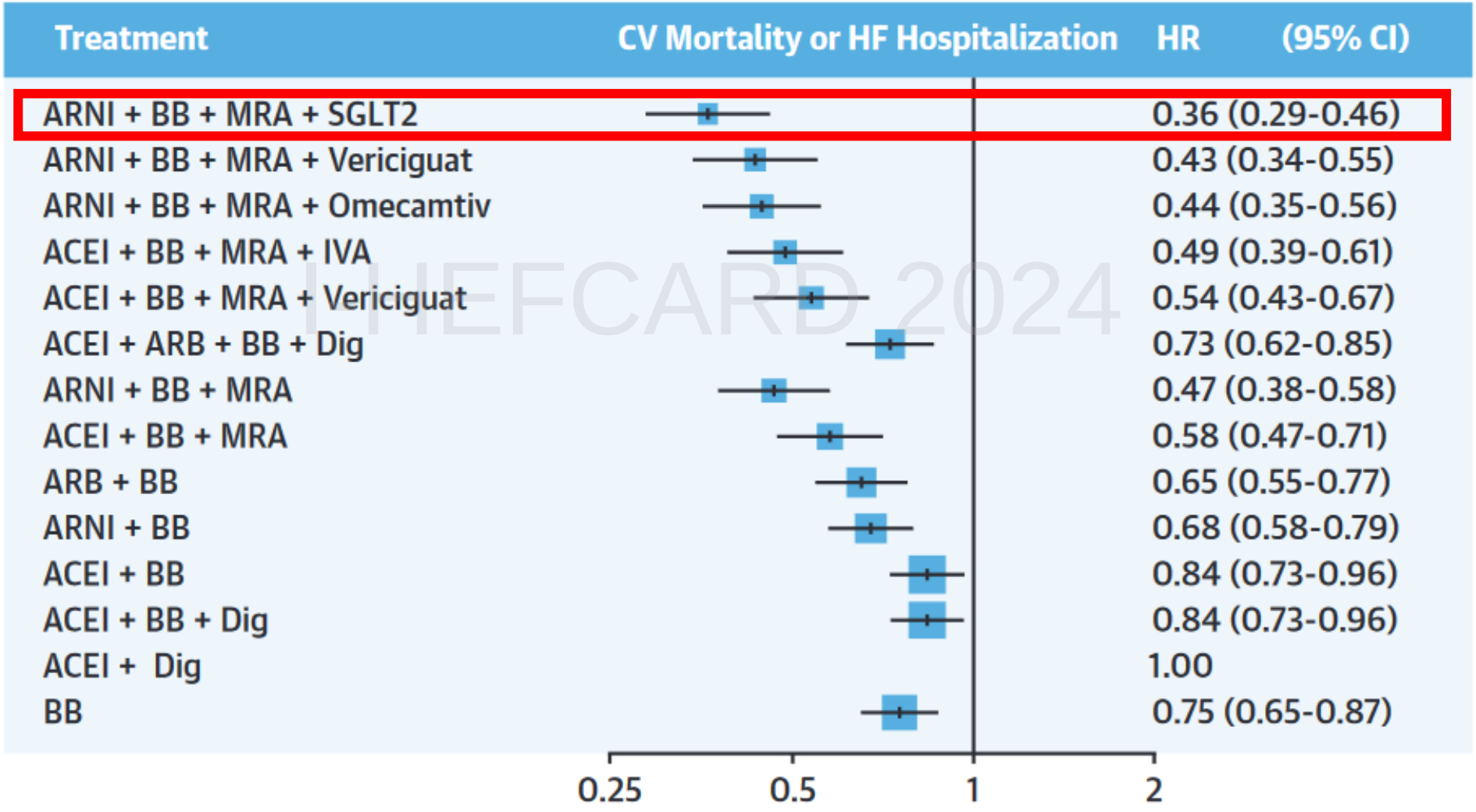






European Heart Journal, 2023, https://doi.org/10.1093/eurheartj/ehad195

Relative Risk Reduction of Different Pharmacological Treatment Combinations for Heart Failure



Tromp J. et al .J Am Coll Cardiol HF 2022;10:73–84

Heart Failure in Numbers

	Total (N=18 102)	Central and South America (n=2525)	Eastern Europe (n=2761)	Eastern Mediterranean region and Africa (n=2172)	North America (n=1565)	Southeast Asia (n=2292)	Western Europe (n=3489)	Western Pacific (n=3298)	p value*
(Continued from previous page)									
Medication at 6-month follow-up									
ACEi or ARB†	9189 (59%)	1272 (61%)	1704 (69%)	1140 (63%)	712 (53%)	876 (44%)	1923 (64%)	1562 (55%)	<0·0001
β blocker†	10 437 (67%)	1400 (67%)	1883 (76%)	1222 (68%)	1057 (78%)	925 (47%)	2330 (78%)	1620 (57%)	<0·0001
Diuretics†	11 176 (67%)	1345 (65%)	1923 (78%)	1376 (63%)	1078 (80%)	1326 (67%)	2516 (84%)	1614 (57%)	<0·0001
MRA†	6608 (43%)	9539 (45%)	1289 (52%)	573 (32%)	469 (35%)	528 (27%)	1411 (47%)	1399 (50%)	<0·0001
Length of stay, days†	8 (5–12)	8 (5–14)	9 (6–13)	6 (4–10)	6 (4–10)	6 (4–8)	9 (6–13)	9 (7–14)	<0·0001
1-year mortality	3461 (20%)	547 (23%)	439 (16%)	472 (22%)	324 (21%)	470 (21%)	668 (20%)	541 (17%)	<0·0001
Hospitalisation									
Hospitalised for any cause	6674 (38%)	799 (33%)	1062 (39%)	773 (36%)	955 (62%)	428 (19%)	1583 (47%)	1074 (34%)	<0·0001
Hospitalised for heart failure	3940 (22%)	482 (20%)	654 (24%)	478 (23%)	626 (41%)	240 (11%)	826 (24%)	634 (20%)	<0·0001
Death or heart failure hospitalisation	6928 (39%)	972 (40%)	1038 (38%)	913 (43%)	830 (54%)	673 (30%)	1395 (41%)	1107 (35%)	<0·0001

Data are n (%), unless otherwise stated. BMI=body-mass index. DCHF=decompensated chronic heart failure. NYHA=New York Heart Association. LVEF=left ventricular ejection fraction. JVP=jugular venous pressure. ACEi=angiotensin-converting enzyme inhibitor. ARB=angiotensin receptor blocker. MRA=mineralocorticoid receptor antagonist. *All comparisons p<0·001. †No data missing.

Table 1: **Differences between patients according to region**

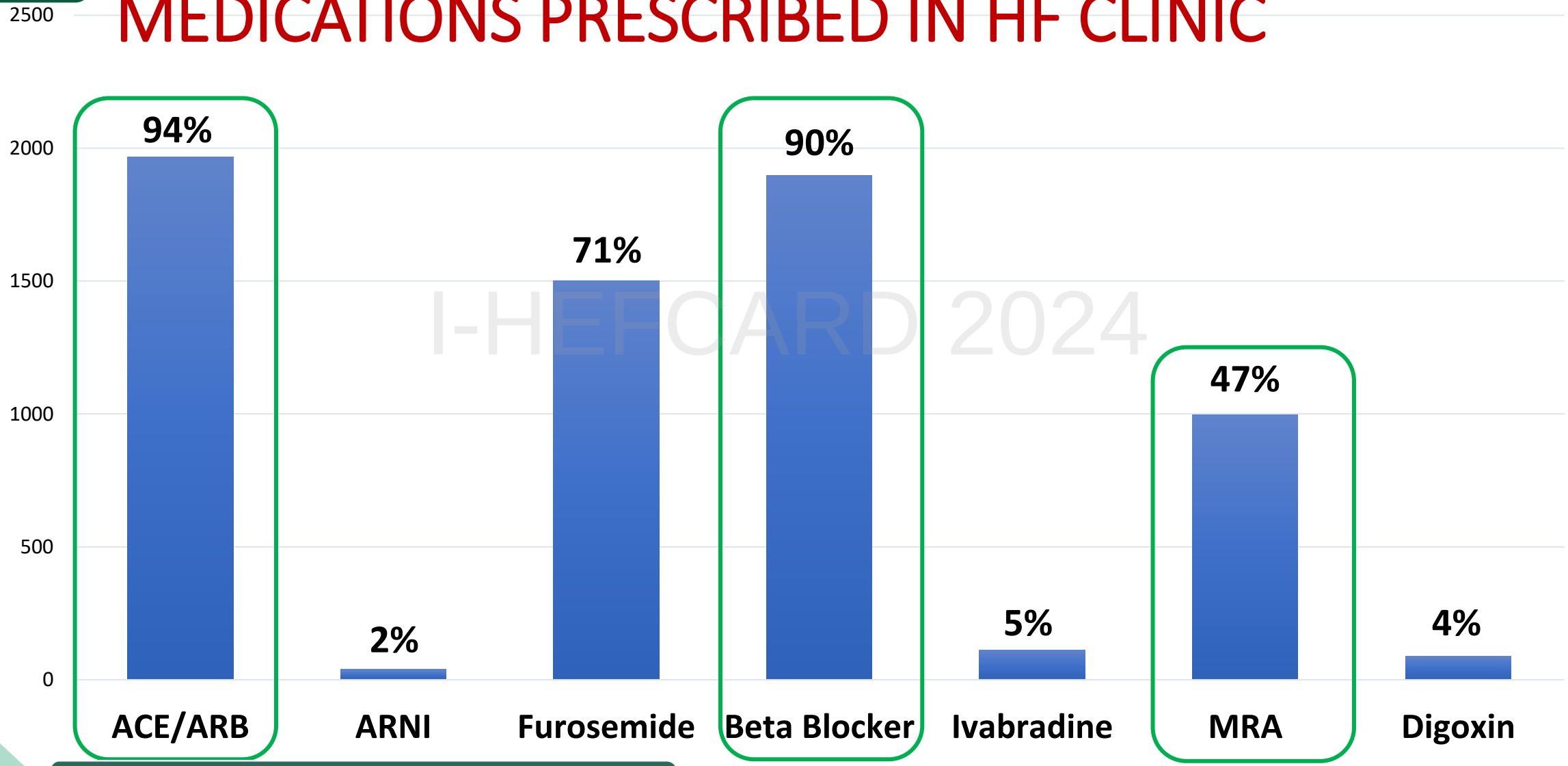
Tromp J, et al. Lancet Glob Health 2020; 8: e411–22

InaHF Registry – Data from 2018-2021

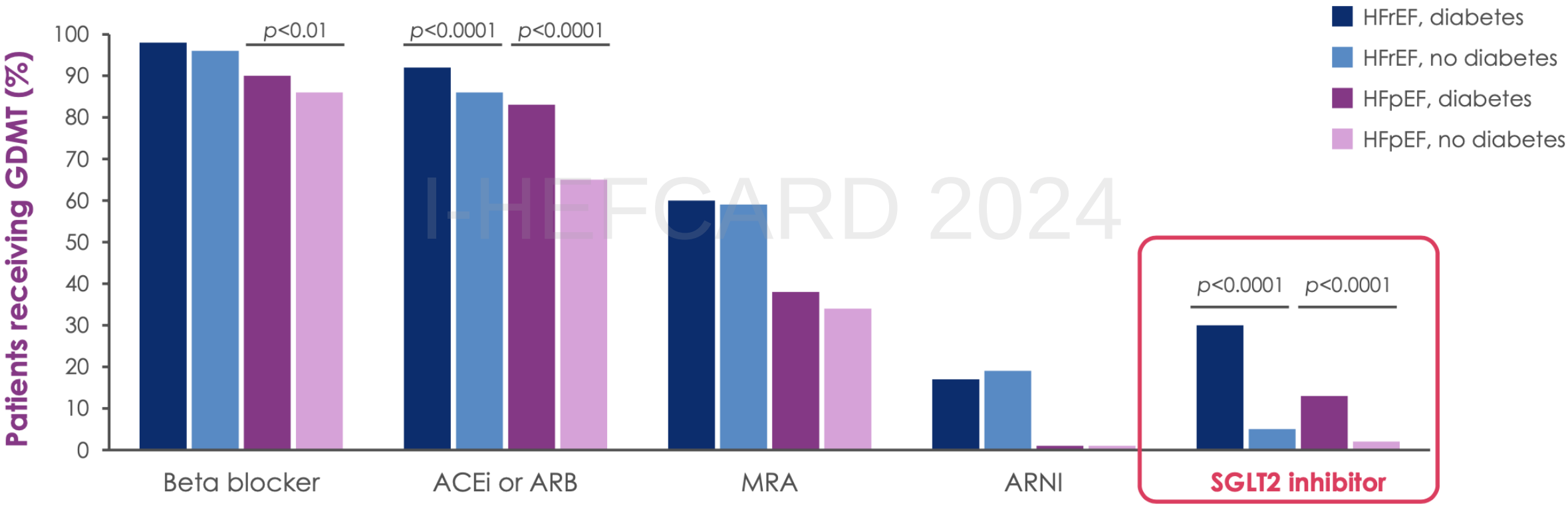
- **2103 heart failure patients** from **10 healthcare facilities in** Indonesia.

	No. of patients	Percentage (%)
RSUD Tangerang, Banten	522	24.8
RS Universitas Sebelas Maret, Solo	482	22.9
RS dr Sardjito, Yogyakarta	403	19.2
RS Harapan Kita, Jakarta	223	10.6
RS Awal Bros, Pekanbaru	132	6.3
RSUD Cibinong, Jawa Barat	93	4.4
RS Hasan Sadikin, Bandung	72	3.4
RSUD Arifin Achmad, Pekanbaru	65	3.1
RSPAD Gatot Subroto, Jakarta	60	2.9
RSUP Adam Malik, Medan	51	2.4
Total	2103	100

MEDICATIONS PRESCRIBED IN HF CLINIC



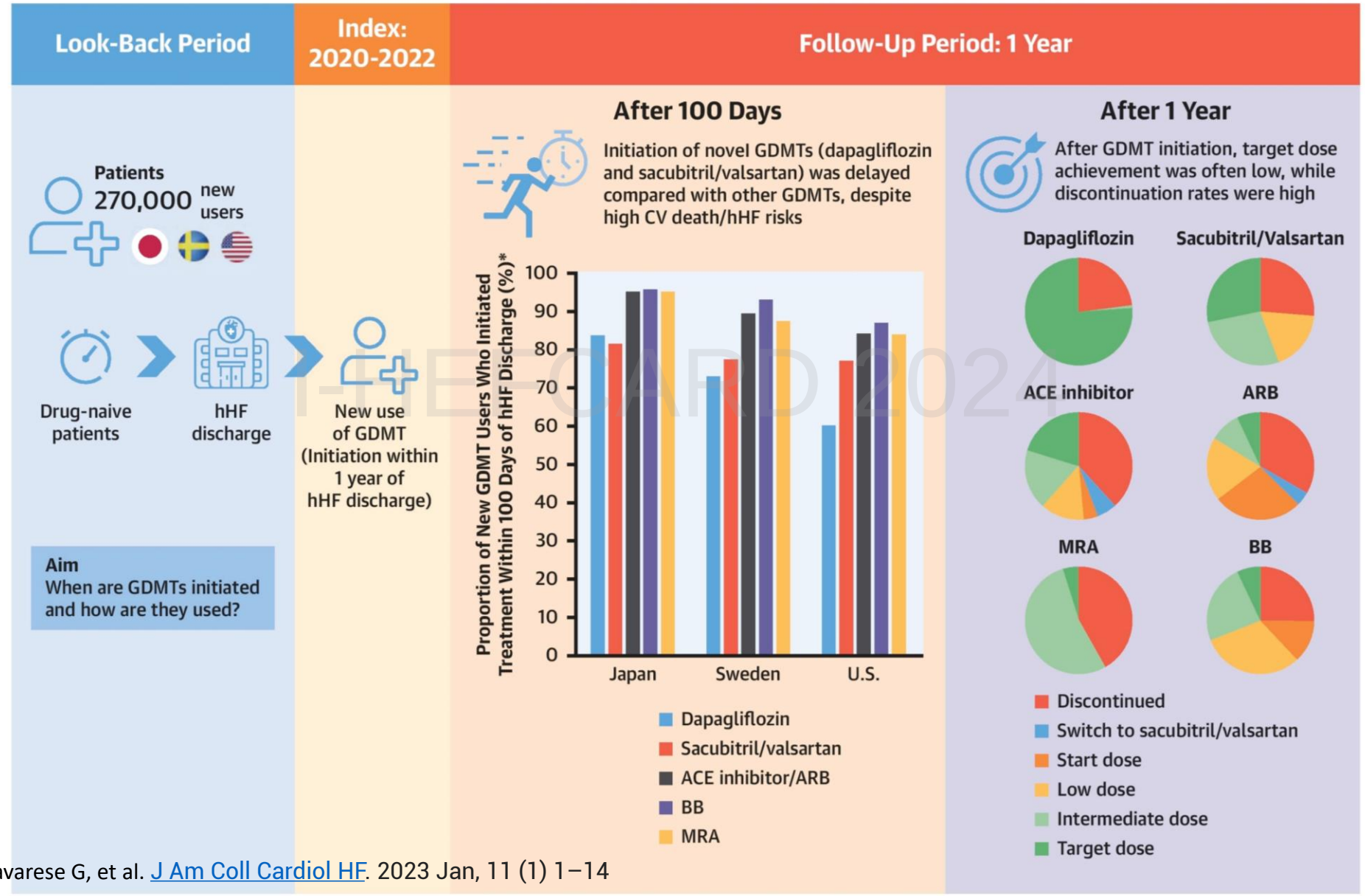
Newer GDMTs are Underutilized in HF Patients



ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor–neprilysin inhibitor; GDMT, guideline-directed medical therapy; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; MRA, mineralocorticoid receptor antagonist; SGLT2, sodium-glucose co-transporter-2. Figure redrawn from data in Table 1 of Canonico ME *et al. JACC Heart Fail.* 2022;10:989.

https://doi.org/10.1016/j.jchf.2022.09.013

Initiation, Titration to Target Dose, and Discontinuation of GDMT Among New User after hHF



Savarese G, et al. J Am Coll Cardiol HF. 2023 Jan, 11 (1) 1–14

Treatment Patterns, Outcomes, and Persistence to Newly Started HF Medications in Patients with Worsening HF: A Cohort Study from US and Germany

Retrospective cohort study of patients with prevalent HF and a HFH from 2016-19

1 year persistence (no treatment gap of > 2 months) to HF medications among new users

Medication	Germany			USA		
	New users *N*	Persistence (%)	Mean time to discontinuation, days (SD)	New users *N*	Persistence (%)	Mean time to discontinuation, days (SD)
Beta-blocker	2530	63.4	161.3 (85.7)	3009	50.1	132.1 (100.1)
ACE inhibitor	2263	48.3	151.1 (82.3)	3001	33.5	119.7 (96.4)
ARB	1742	61.0	149.6 (87.5)	2834	38.2	123.8 (97.3)
MRA	4277	28.1	147.4 (86.0)	5526	39.9	126.7 (97.6)
Digoxin/digitoxin	1048	51.5	158.7 (87.0)	1896	43.7	123.4 (95.8)
Ivabradine	164	67.1	158.8 (95.2)	95	44.2	123.5 (94.4)
ARNI	851	76.3	142.6 (102.4)	2142	47.2	133.6 (101.5)
SGLT2i	271	60.1	153.3 (105.7)	239	41.4	133.1 (98.3)
Loop diuretics	4637	54.1	155.1 (90.3)	5016	41.8	128.2 (99.20)

~ 5 months

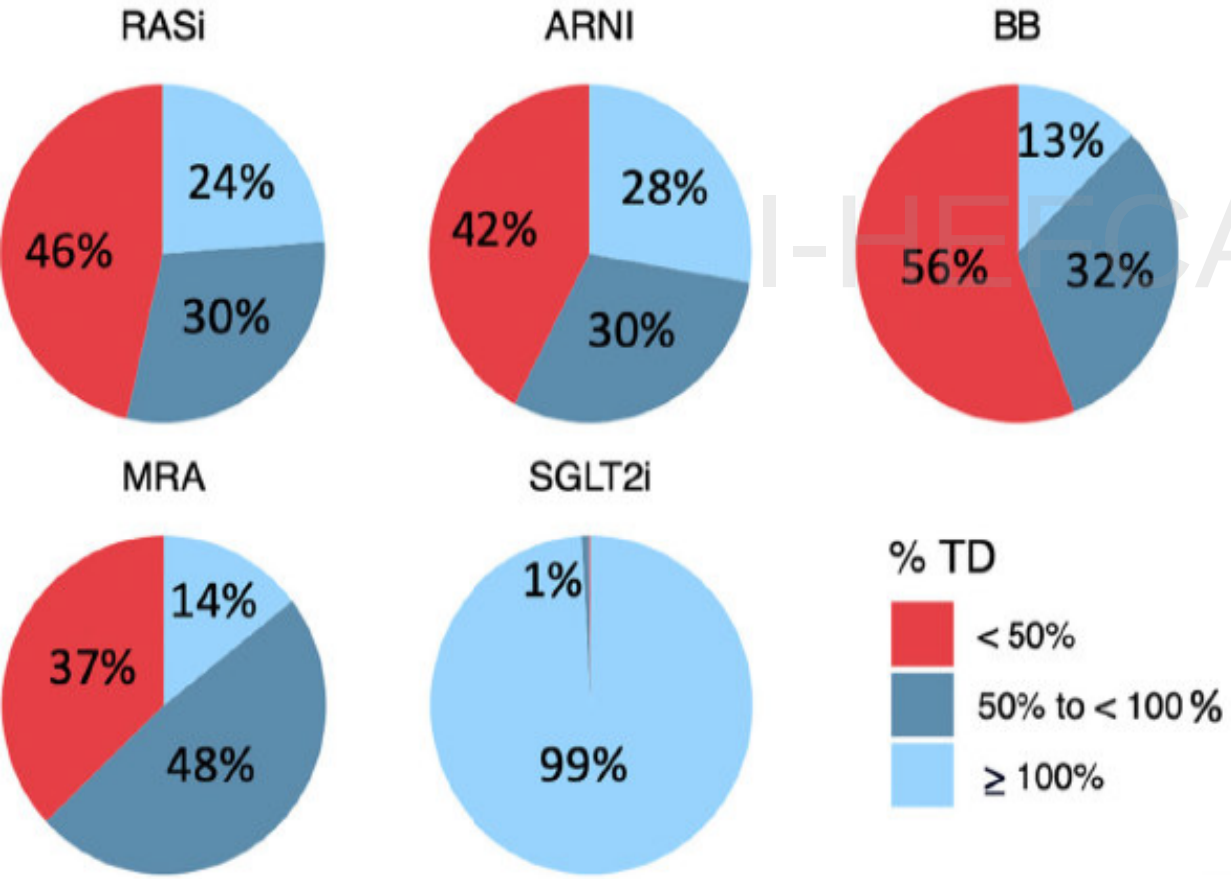
~ 4 months

Michel A et al. American Journal of Cardiovascular Drugs 2024; https://doi.org/10.1007/s40256-024-00643-7.

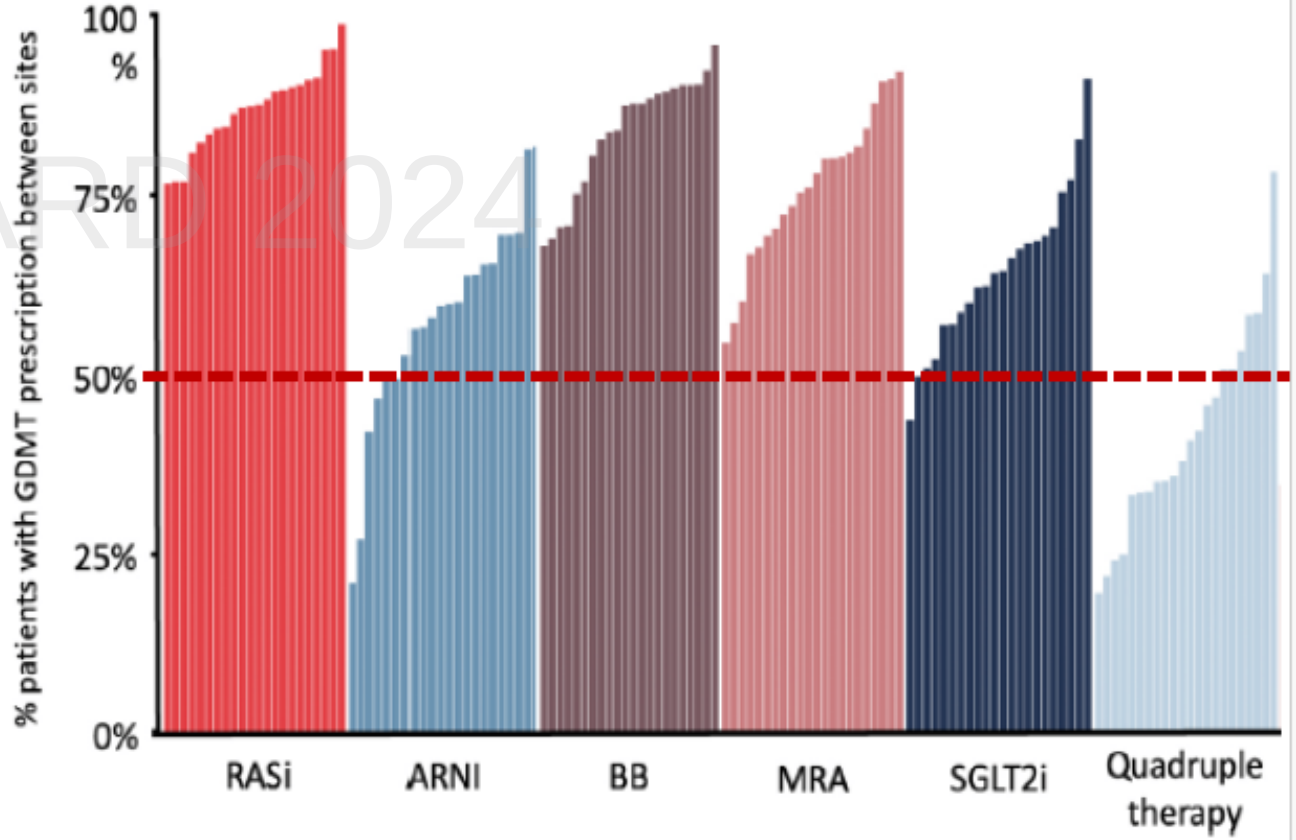
Contemporary guideline-directed medical therapy in de novo, chronic, and worsening HF patients: First data from the TITRATE-HF study

TITRATE-HF: ongoing long-term HF registry conducted in the Netherlands. Overall, 4288 patients from 48 hospitals were included; 1732 presented de novo, 2240 chronic, and 316 with worsening HF.

Percentage of target dose for each drug class, stratified by <50% vs 50%-100% vs ≥100% of target dose

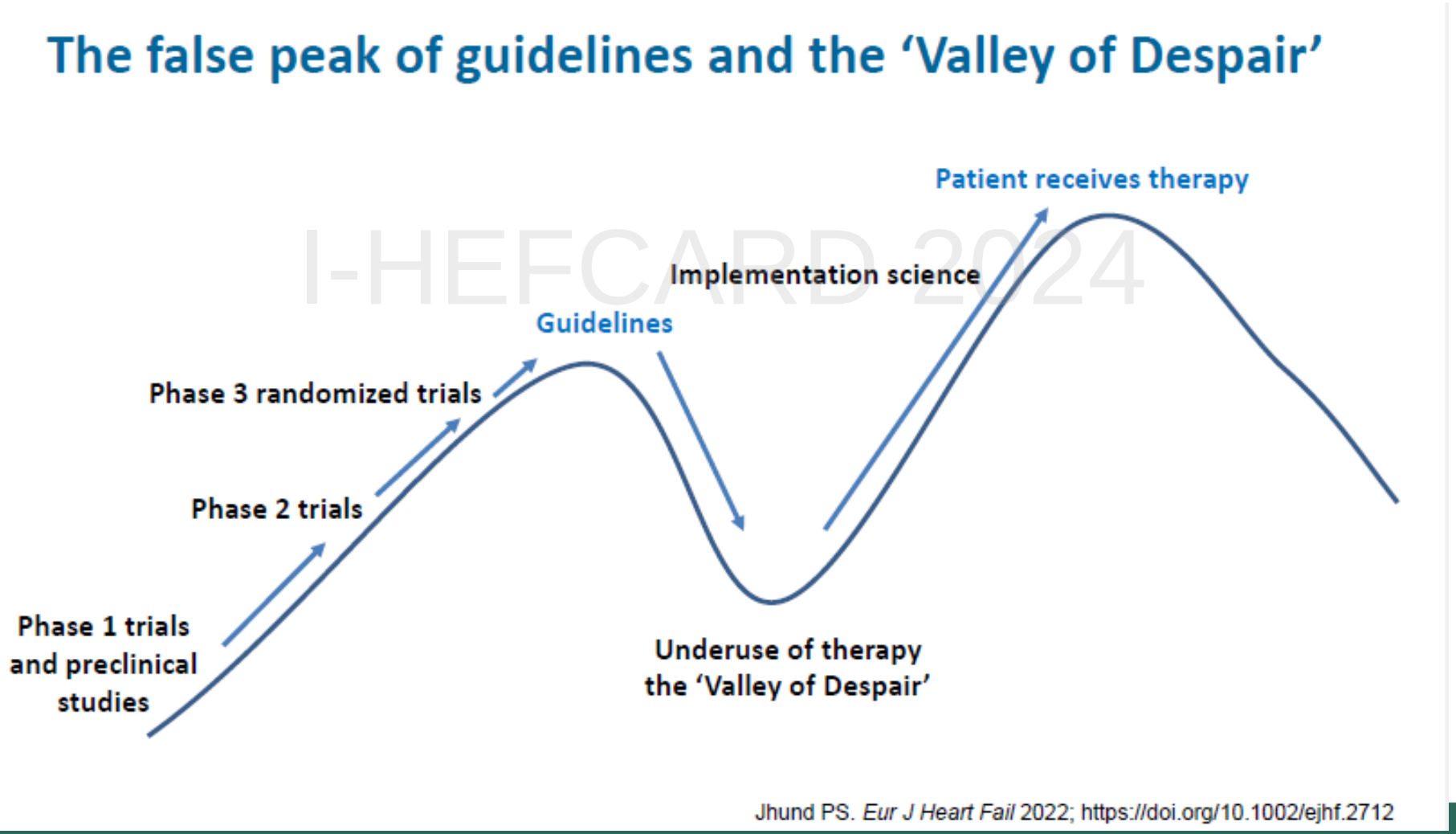


Differences in GDMT use in HFrEF patients between participating sites with ≥50 enrolled patients



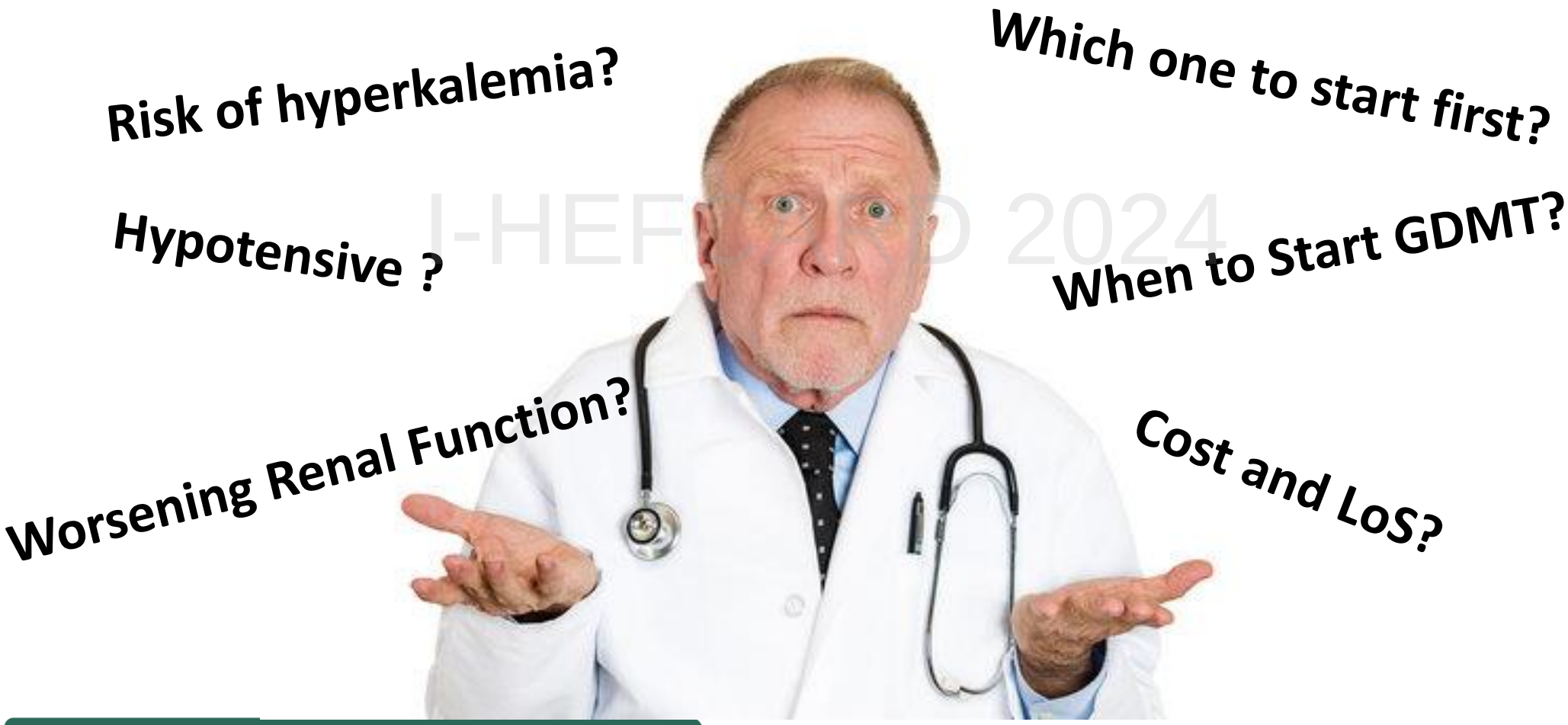
Malgie J et al. European Journal of Heart Failure (2024) doi:10.1002/ejhf.3267

Why There's Unmeet Point between Guidelines and Real World Data?



Jhund PS. *Eur J Heart Fail* 2022; https://doi.org/10.1002/ejhf.2712

Which path do I choose to reduce mortality in my HF patient?



Clinical Inertia

"the lack of treatment intensification in a patient not at evidence based goals for care…"

Principal factors : System-related (20%), **patient-related (30%), physician-related (50%)**

The main causes for non-prescription of GDMT in HF:

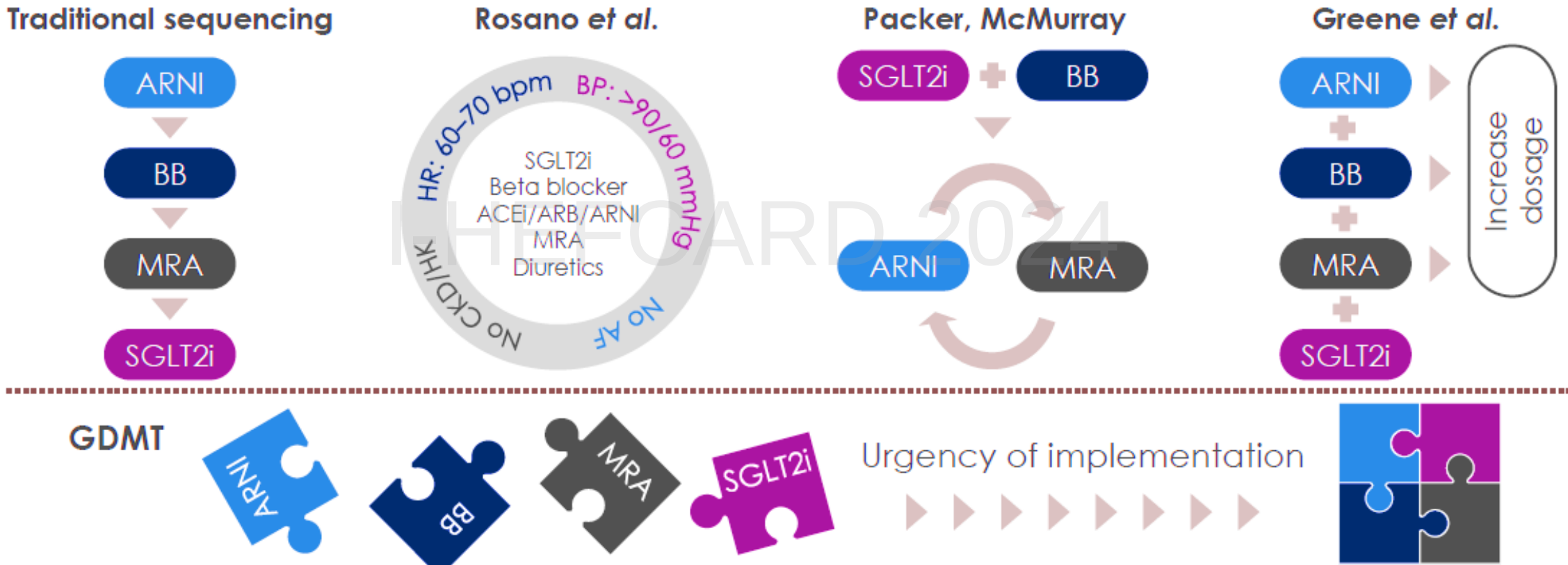
	QUALIFY *(Komajda M, et al, 2016)*	ESC HF Long-Term Registry *(Crespo-Leiro MG, et al. 2015)*	TSOC-HFrEF *(Chang HY, et al. 2017)*
ACEi/ARB	Worsening renal function, hypotension, cough	Worsening renal function, hypotension	Worsening renal function
BB	Worsening of asthma & COPD, Hypotension, bradycardia, fatigue	Hypotension, bronchospasm	Worsening of asthma & COPD, older age
MRA	Hyperkalemia, renal dysfuction	Hyperkalemia, renal dysfuction	Renal dysfuction, older age

Physician Related Factor :

- **Physician lack of awareness of the importance of reaching target dose**
- **Physician forgot to increase dose**
- **Physician do not see an indication**
- **Physician forget to prescribe**
- **Physician concerns about AE**

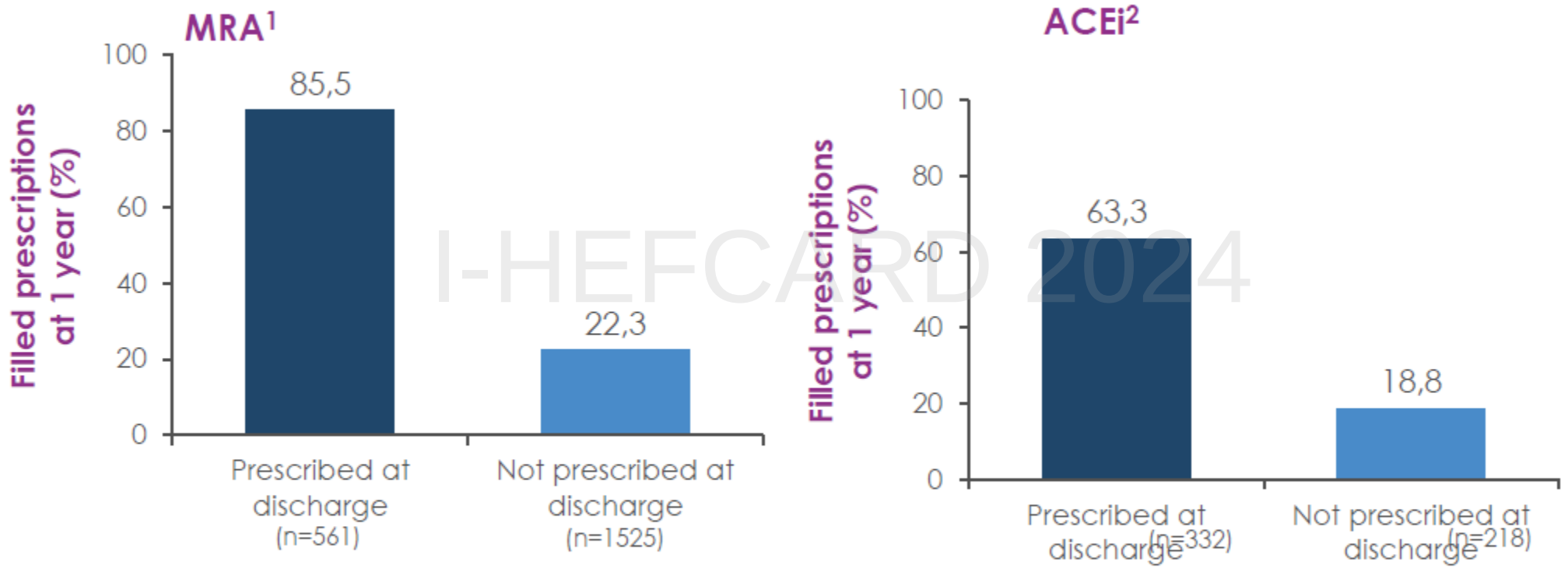
Greene SJ, et al. Heart Fail Rev 2021

Sequencing in HFrEF: Guidelines tell us *what* to do, but not *how* to do it!



ACEi, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor–neprilysin inhibitor; BB, beta blocker; BP, blood pressure; bpm, beats per minute; CKD, chronic kidney disease; GDMT, guideline-directed medical therapy; HFrEF, heart failure with reduced ejection fraction; HK, hyperkalaemia; HR, heart rate; MRA, mineralocorticoid receptor antagonist; SGLT2i, sodium-glucose co-transporter-2 inhibitor. Adapted from Malgie J *et al. Heart Fail Rev.* 2023;28:1221. References cited: Rosano GMC *et al. Eur J Heart Fail.* 2021;23:872; Packer M, McMurray JJV. *Eur J Heart Fail.* 2021;23:882; Greene SJ *et al. JAMA Cardiol.* 2021;6:743.

Increase adherence to heart failure guidelines by initiating treatment in hospital



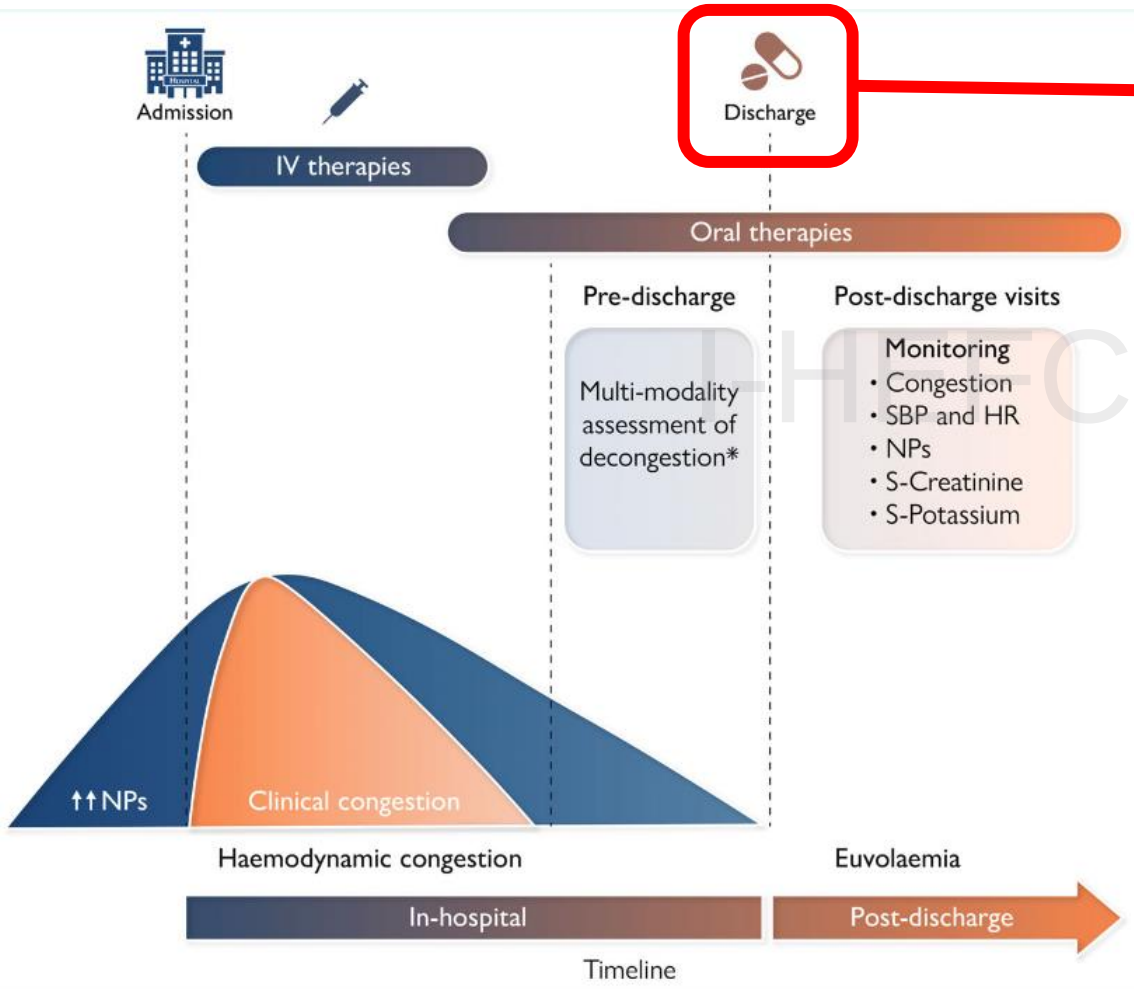
Early treatment initiation of GDMT in the hospital is associated with improved adherence

ACEi, angiotensin-converting enzyme inhibitor; GDMT, guideline-directed medical therapy; MRA, mineralocorticoid receptor antagonist.

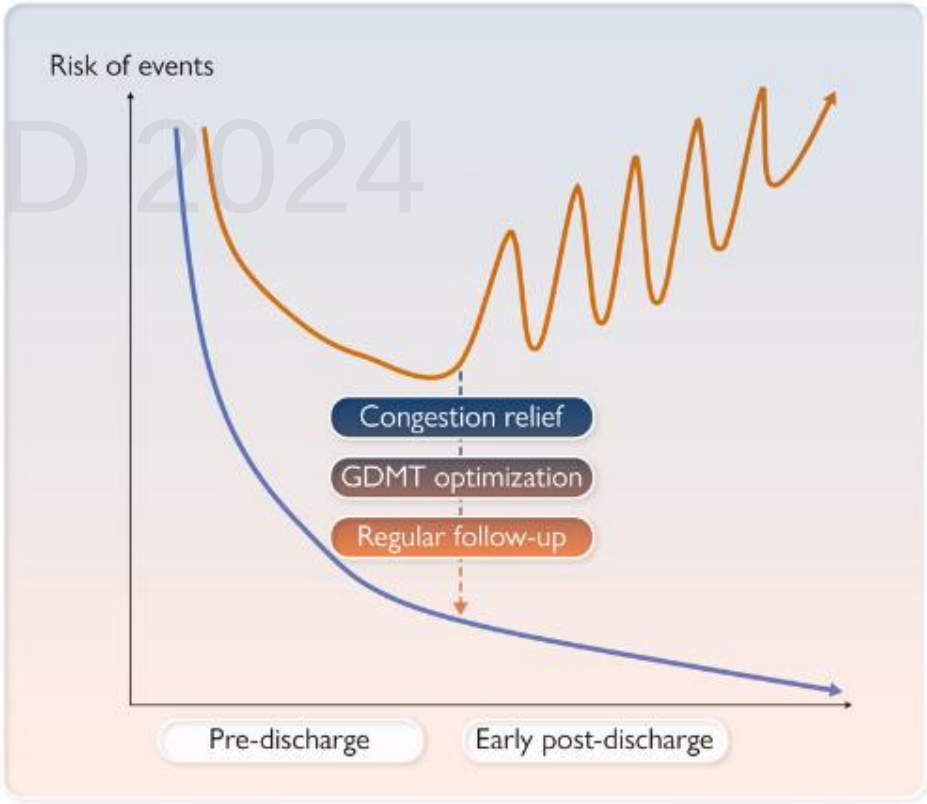
1. Curtis LH *et al. Am Heart J.* 2013;165:979; 2. Butler J *et al. J Am Coll Cardiol.* 2004;43:2036.

Hospitalization is a key opportunity to optimize GDMT

Management of patients with HF according to hospitalization phase

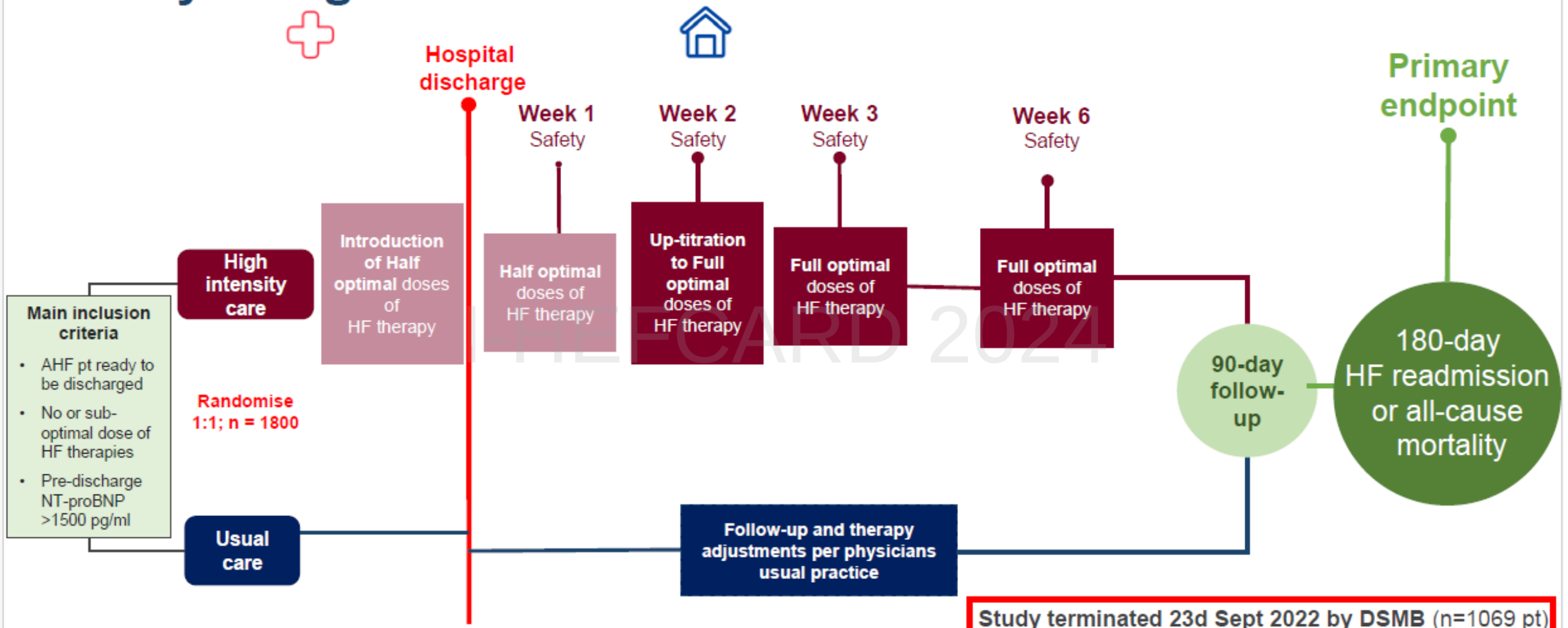


Before discharge from hospital, **oral therapies should be optimized** in patients with heart failure



Study design

STRONG-HF
CONTEMPORARY POST-DISCHARGE MANAGEMENT IN HEART-FAILURE



HF therapy: combining ACEi/ARB/ARNi & BB & MRA
Safety = clinical exam & biology (NT-proBNP, K, Creat, hemoglobin)

Study terminated 23d Sept 2022 by DSMB (n=1069 pt)

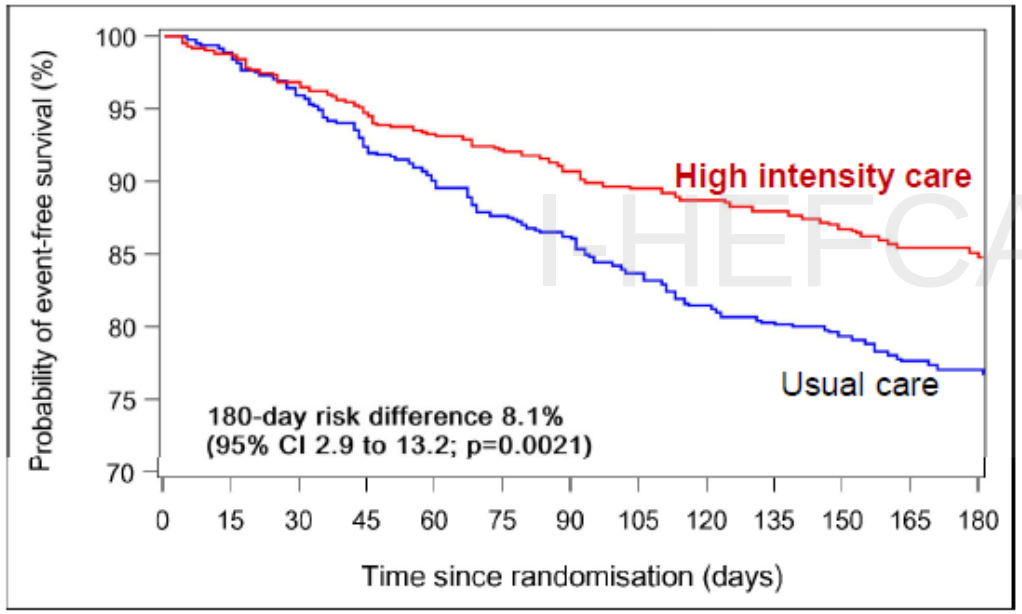
- larger than expected difference in primary endpoint
- unethical to keep patients in usual care

ACEi, angiotensin converting enzyme inhibitors; AHF, acute heart failure; ARB, angiotensin receptor blockers; BB, beta blockers; HF, heart failure; MRA, mineralcorticoid receptor antagonists; NT-proBNP, N-terminal pro B-type natriuretic peptide

Mebazaa A, LBCT presentation at the AHA 2022

STRONG-HF
CONTEMPORARY POST-DISCHARGE MANAGEMENT IN HEART-FAILURE

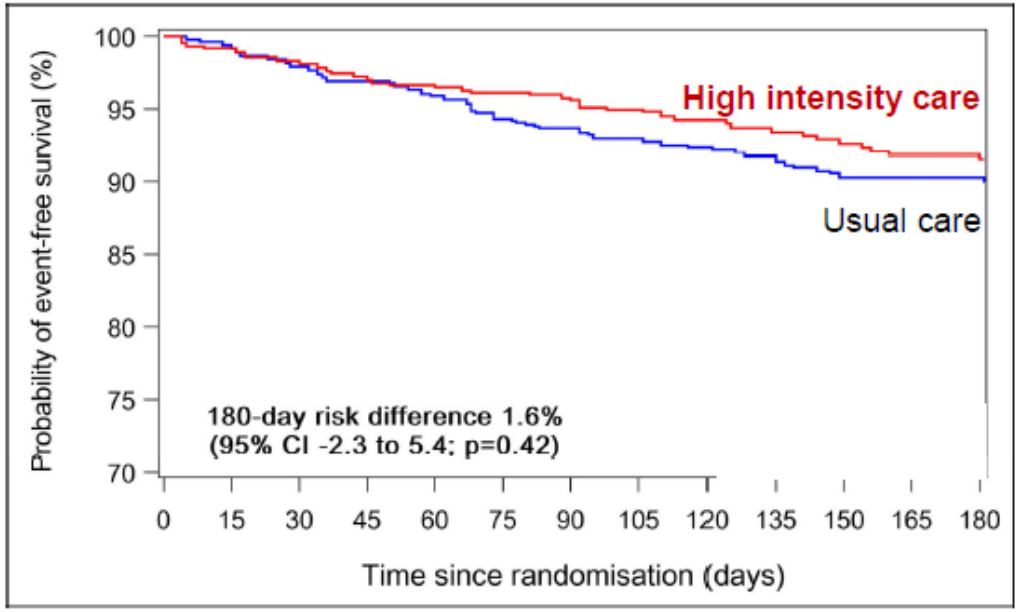
Primary endpoint:
180-Day Readmission for HF or All-Cause Death



Secondary endpoints:
Change from Baseline to Day 90 in EQ-5D VAS

High Intensity	Usual Care	Treatment effect	P value
10.7 (0.9)	7.2 (0.9)	3.5 (1.7 to 5.2)	< 0.0001

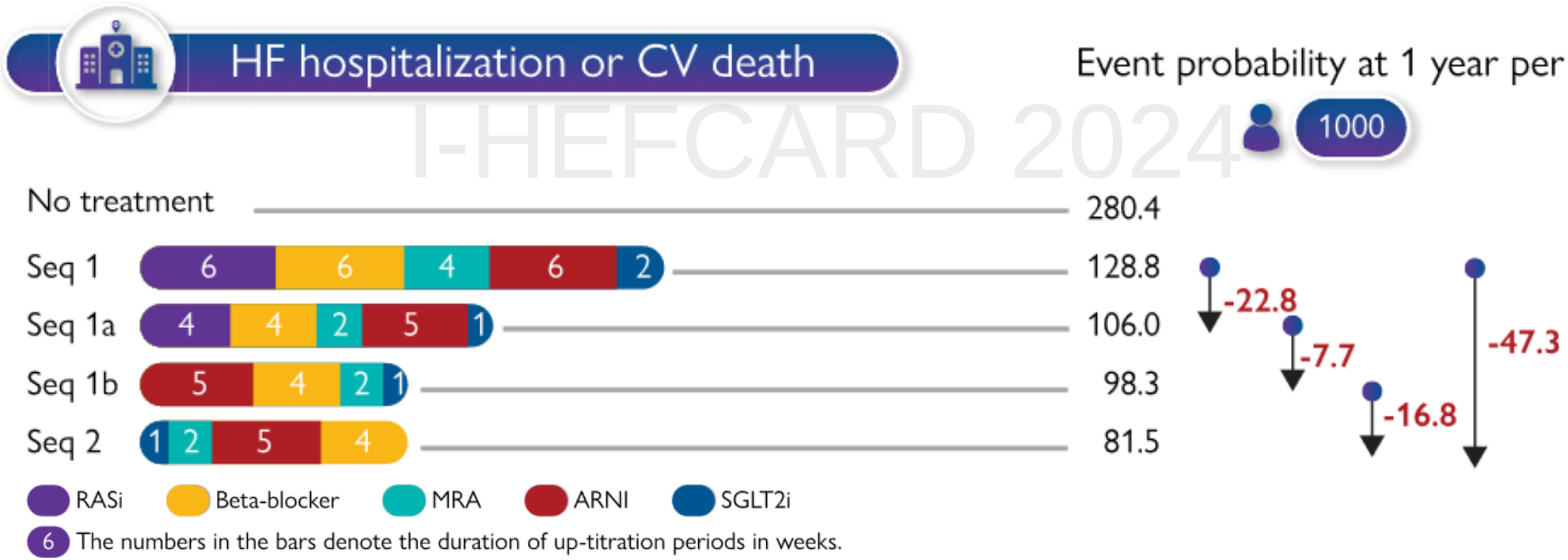
180-Day All-Cause Death



Mebazaa A, LBCT presentation at the AHA 2022

Speed matters: Models of optimized treatment sequencing in HFrEF

- Initiating an SGLT2 inhibitor and an MRA first in the treatment sequence vs conventional sequence → achieves quadruple therapy faster and may prevent more deaths and hospital admissions



Shen L, et al. 2022 Jul 14;43(27):2573-2587. doi: 10.1093/eurheartj/ehac210

Time is Prognosis!

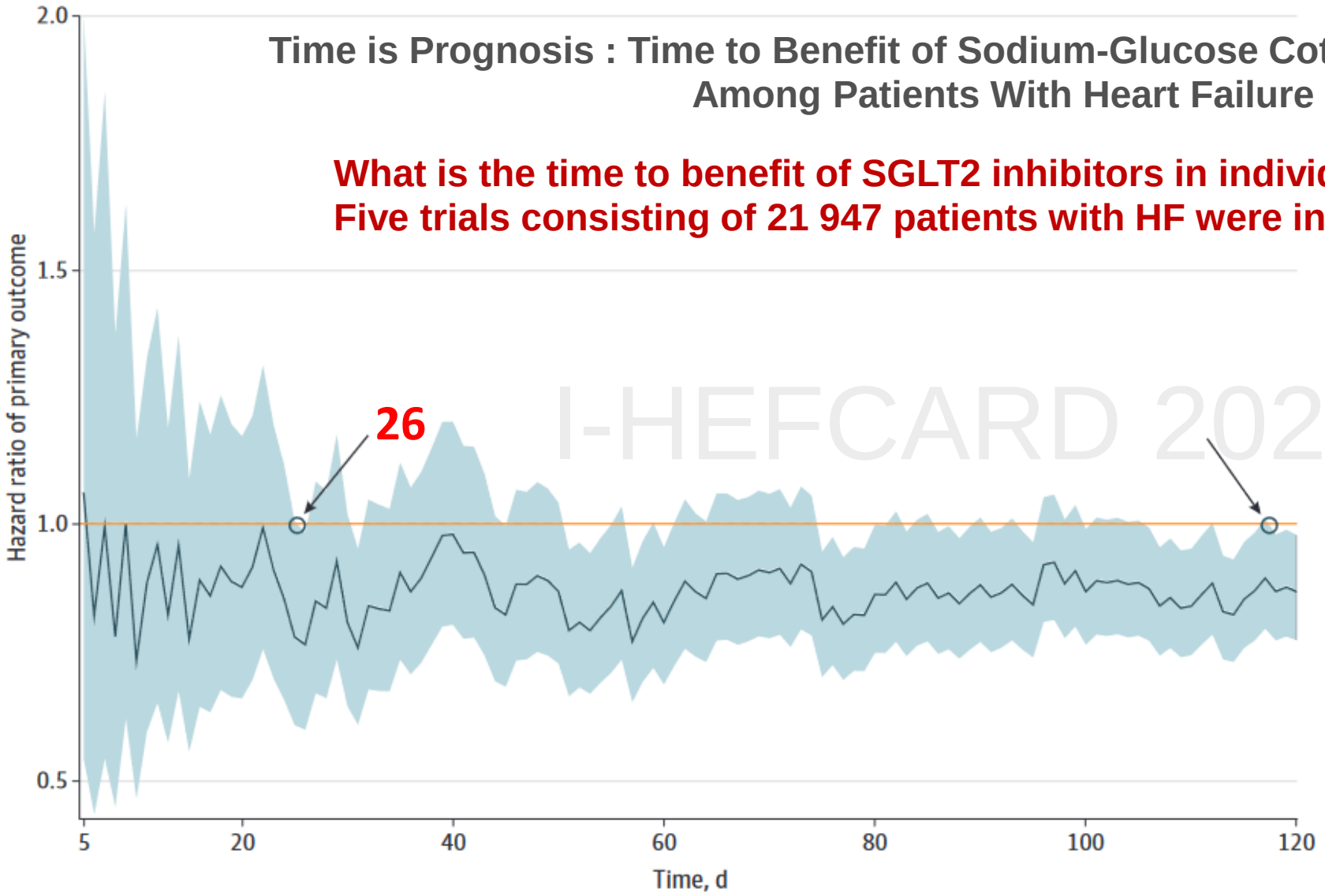
Recommendation Table 3 — Recommendation for pre-discharge and early post-discharge follow-up of patients hospitalized for acute heart failure

Recommendation	Class[a]	Level[b]
An intensive strategy of initiation and rapid up-titration of evidence-based treatment before discharge and during frequent and careful follow-up visits in the first 6 weeks following a HF hospitalization is recommended to reduce the risk of HF rehospitalization or death.[c,d,e] [16]	I	B

European Heart Journal, 2023, https://doi.org/10.1093/eurheartj/ehad195

Time is Prognosis : Time to Benefit of Sodium-Glucose Cotransporter-2 Inhibitors Among Patients With Heart Failure

What is the time to benefit of SGLT2 inhibitors in individuals with HF ?
Five trials consisting of 21 947 patients with HF were included

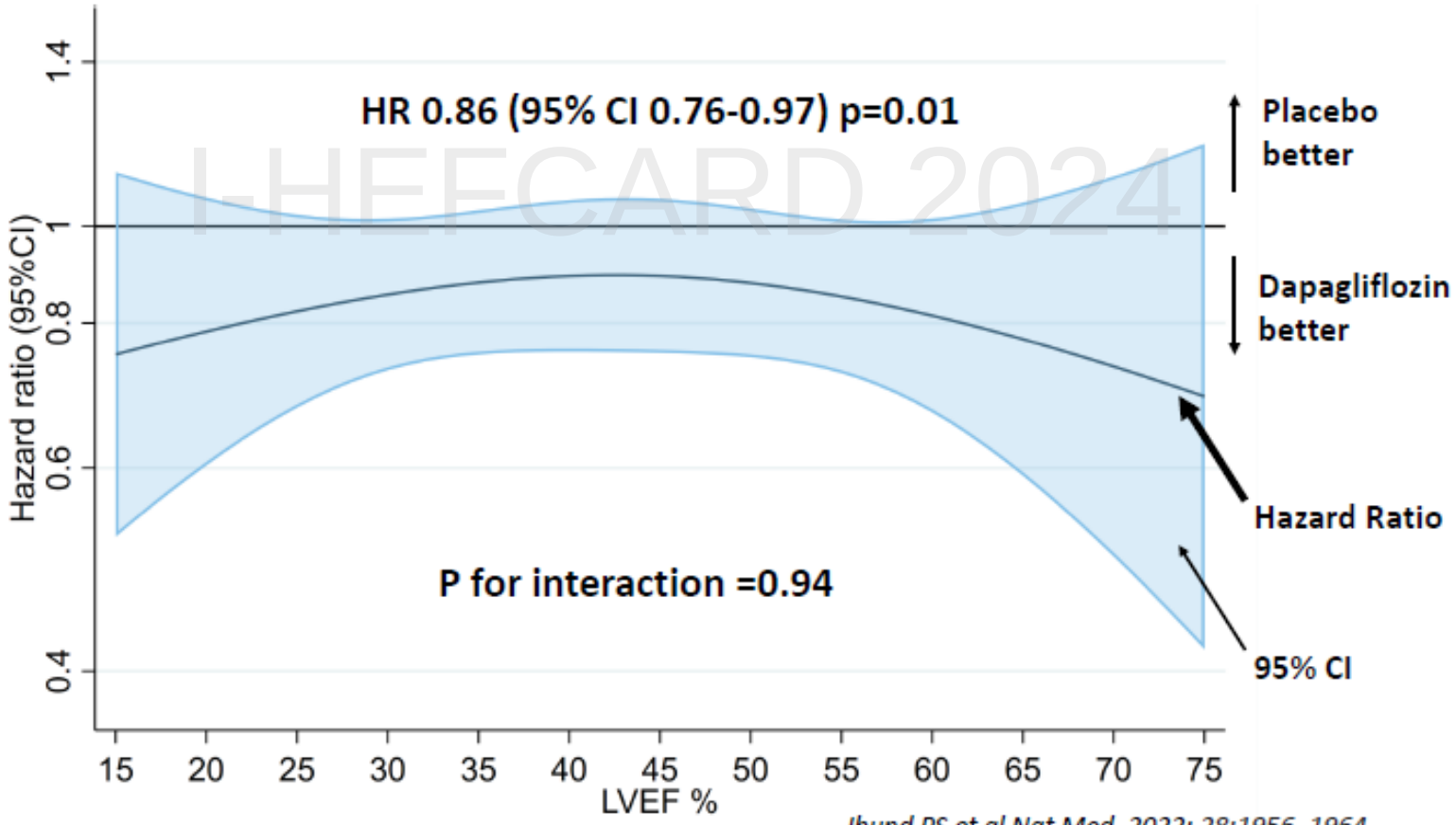


Shaded regions indicate 95% CIs. In panel B, left arrow indicates the time to first nominal statistically significant clinical benefit (26 days [0.86 months]); right arrow, time to consistently reach statistically significant clinical benefit and sustain it thereafter (118 days [3.93 months]). SGLT2 indicates sodium-glucose cotransporter 2.

Chen KY, et al. JAMA Network Open. 2023;6(8):e2330754. doi:10.1001/jamanetworkopen.2023.30754

SGLT2i Reduced CV Mortality Across EF

DAPA-HF & DELIVER pooled: Cardiovascular death

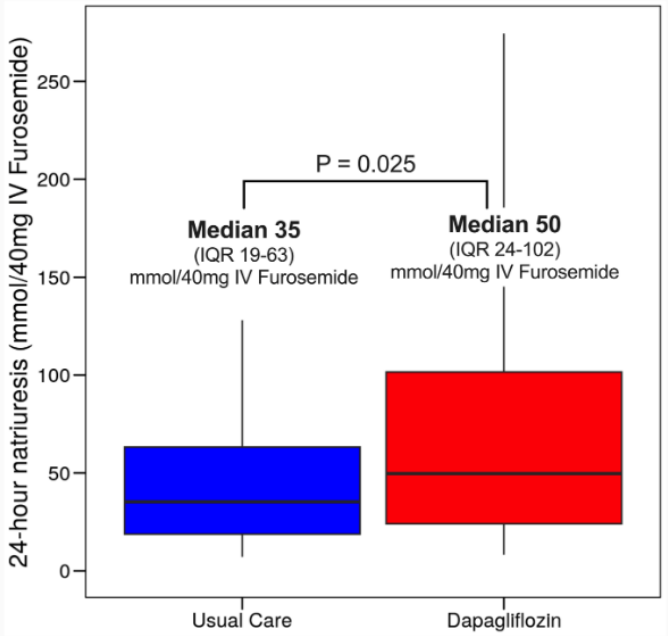


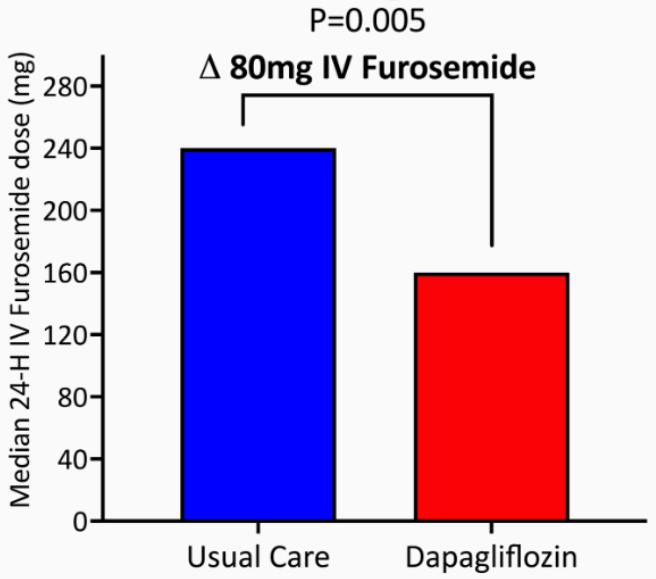
Jhund PS et al Nat Med. 2022; 28:1956–1964

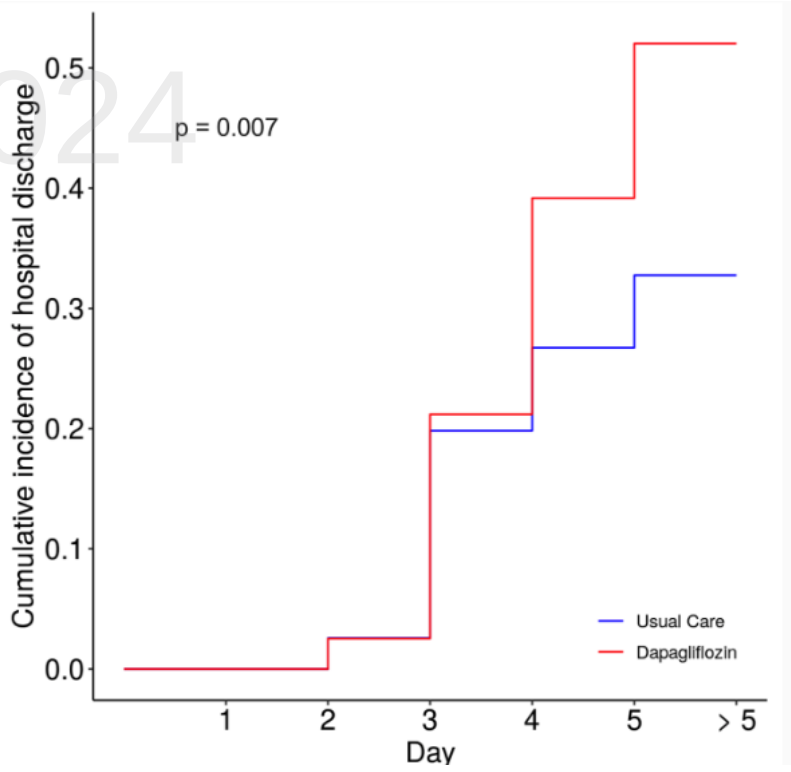
Acute HF→ early initiation of dapagliflozin in AHF to safely facilitate decongestion and GDMT optimization

- Dapagliflozin improve diuretic efficiency by:
  - **Increased natriuresis and diuresis per 40mg of IV furosemide**
  - **Decreased total dose and duration of loop diuretics required**
  - **Decreased time to hospital discharge**

Improved 24-Hour Natriuresis with Dapagliflozin





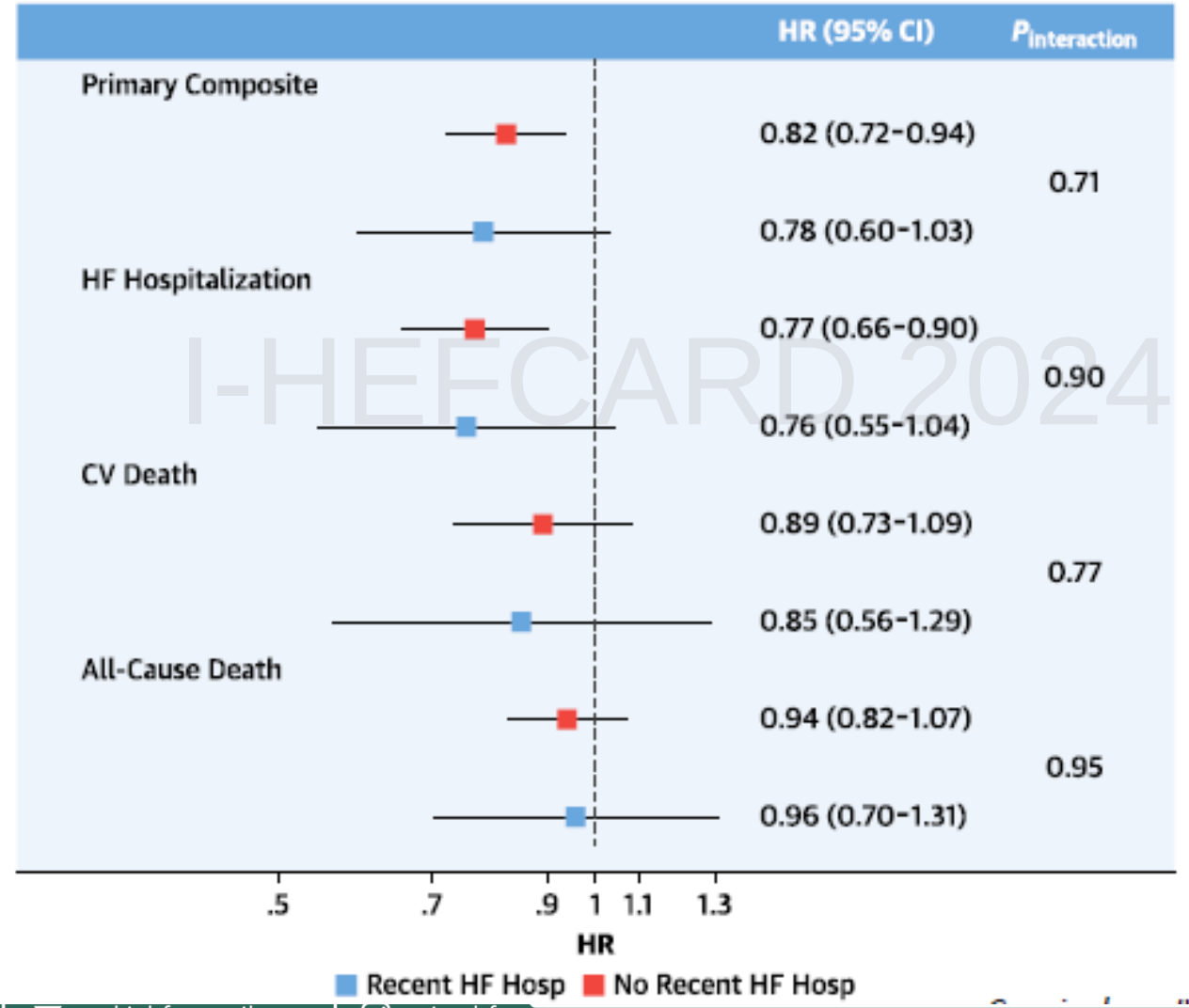


ESC Congress 2023
Amsterdam & Online

In Indonesia, Dapagliflozin is indicated for the treatment of symptomatic chronic heart failure.

J Am Col Cardiol. 2024 Apr 9;83(14):1295-1306. doi: 10.1016/j.jacc.2024.02.009.

Using dapagliflozin in recently hospitalised patients: DELIVER



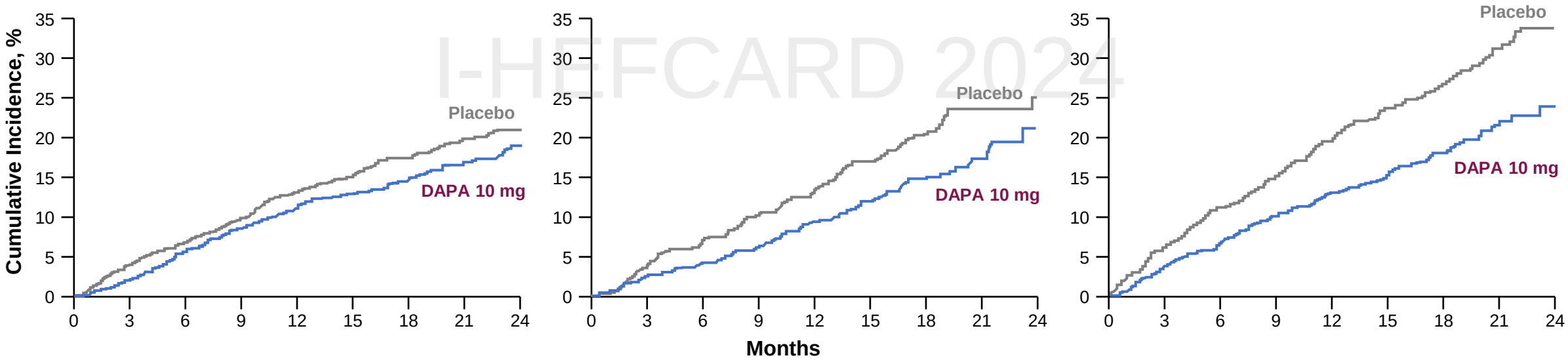
Cunningham JW et al JACC.2022; 80:1302–10

CV Death or Worsening HF[a] by Timing of Most Recent hHF[b]

None (n=2493)	
RRR	16%
ARR	2.1%
HR (95% CI)	0.84 (0.69-1.01)

>12 months (n=950)	
RRR	27%
ARR	4.1%
HR (95% CI)	0.73 (0.54-0.99)

≤12 months (n=1301)	
RRR	36%
ARR	9.9%
HR (95% CI)	0.64 (0.51-0.81)



RRR p-trend=0.07 | **ARR p-trend=0.05**

[a]Worsening HF includes hHF or urgent HF visit; [b]Timing of hHF relative to trial enrollment.

ARR = absolute risk reduction; CV = cardiovascular; DAPA = dapagliflozin; HF = heart failure; hHF = hospitalization for heart failure; HR = hazard ratio; RRR = relative risk reduction.

Berg DD et al. *JAMA Cardiol*. 2021;6:499-507.

Hyperkalemia Events in the DAPA-HF Trial

Dapagliflozin may attenuate the risk of moderate/severe hyperkalemia in patients treated with an MRA at baseline

Endpoint	Dapagliflozin 10 mg		Placebo		HR (95% CI)	p-value	Interaction p-value[a]
	n/N (%)	Rate per 100 pt-yrs	n/N (%)	Rate per 100 pt-yrs			
Mild Hyperkalemia (>5.5 mmol/L)							
No MRA at baseline	63/660 (9.6)	7.2	57/682 (8.4)	6.4	1.20 (0.84-1.72)	0.316	0.13
MRA at baseline	180/1632 (11.0)	8.7	204/1625 (12.6)	10.0	0.86 (0.70-1.05)	0.144	
Moderate/Severe Hyperkalemia (>6.0 mmol/L)							
No MRA at baseline	13/675 (1.9)	1.4	11/695 (1.6)	1.2	1.17 (0.52-2.62)	0.707	0.08
MRA at baseline	21/1683(1.3)	0.9	40/1666(2.4)	1.8	0.50 (0.29-0.85)	0.01	

[a]A non-significant result for an interaction test can be interpreted as consistency of effect across the subgroup.[2]

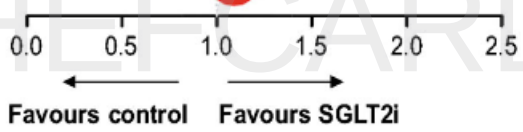
HR = hazard ratio; MRA = mineralocorticoid-receptor antagonist; pt-yrs = patient-years.

1. Shen L et al. *JACC Heart Fail.* 2021;9:254-264; 2. Alosh M et al. *J Biopharm Stat*. 2015;25:1161-1178.

Side effects and initiation barriers for SGLT2 inhibitors
A systematic review and meta-analysis

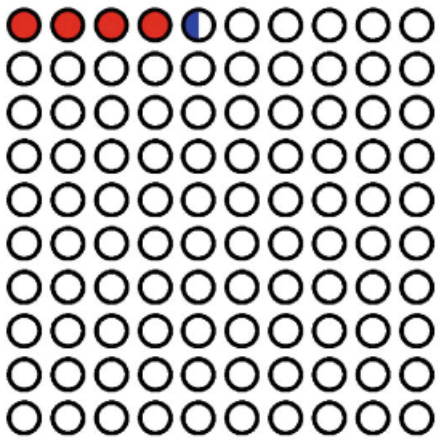
A Hypotension

Study	SGLT2i Events	SGLT2i Total events	SGLT2i Event rate	Control Events	Control Total events	Control Event rate	Risk ratio (95%CI)	
DAPA HF	7	2,368	0.30%	11	2,368	0.46%	0.64	(0.25–1.64)
EMPEROR-Reduced	176	1,863	9.45%	163	1,867	8.73%	1.08	(0.88–1.33)
SOLOIST-WHF	36	605	5.95%	28	611	4.58%	1.30	(0.80–2.10)
TOTAL	219	4,836	4.53%	202	4,846	4.17%	1.09	(0.91–1.31)



p=0.36

B Rate of hypotension



Total 100%

Placebo

Excess on SGLT2-i

No hypotension

4.5% SGLT2-i

4.1% Placebo

Excess of hypotension on SGLT2-i is 0.4% ➡ hypotension truly-related to SGLT2-i could be expected in 1 from 250 patients treated with SGLT2-i

- reported in **4.5% on SGLT2 inhibitors vs. 4.1% of patients on placebo** (RR 1.09, 95% CI 0.91–1.31, p = 0.36)
- The excess of **hypotension on SGLT2i was 0.4% over placebo → 1/250 patient on treatment with SGLT2 inhibitors develop symptomatic hypotension** as a consequence of SGLT2i therapy

Vukadinovic D, et al. Eur J of Heart Fail (2022) 24, 1625–1632. doi:10.1002/ejhf.2584

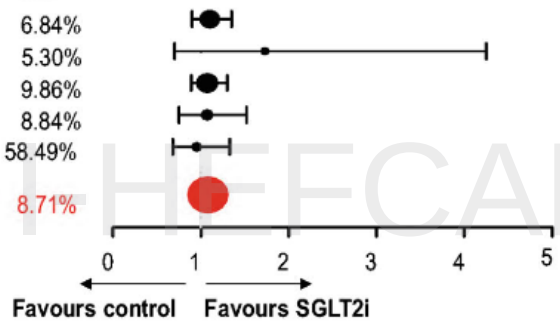
Side effects and initiation barriers for SGLT2 inhibitors

A systematic review and meta-analysis

A Volume depletion

Study	SGLT2i Events	SGLT2i Total events	SGLT2i Event rate	Control Events	Control Total events	Control Event rate	Risk ratio (95%CI)	
DAPA-HF	178	2,368	7.52%	162	2,368	6.84%	1.10	(0.90–1.35)
DEFINE-HF	12	131	9.16%	7	132	5.30%	1.73	(0.70–4.25)
EMPEROR-Reduced	197	1,863	10.57%	184	1,867	9.86%	1.07	(0.89–1.30)
SOLOIST-WHF	57	605	9.42%	54	611	8.84%	1.07	(0.75–1.52)
SUGAR-DM-HF	29	52	55.77%	31	53	58.49%	0.95	(0.68–1.33)
TOTAL	473	5,019	9.42%	438	5,031	8.71%	1.07	(0.95–1.21)

p=0.25



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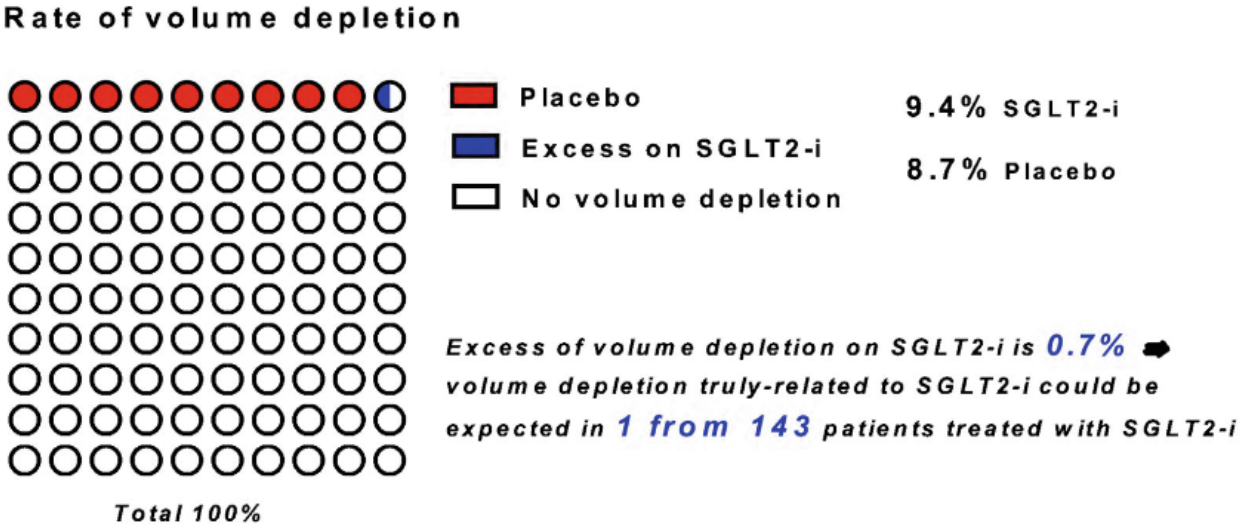


- Volume depletion was defined: **dehydration, hypovolaemia or hypotension**.
- Volume depletion → **9.4% on SGLT2i and in 8.7% on placebo** (RR 1.07, 95% CI 0.95–1.21, p = 0.25) (Figure 2A) (p for heterogeneity = 0.80, I2 = 0%)
- The **excess of volume depletion on SGLT2i was 0.7% over placebo, indicating that approximately 1/143 patients** on treatment with SGLT2i would develop signs of volume depletion as a consequence of SGLT2 inhibitor therapy

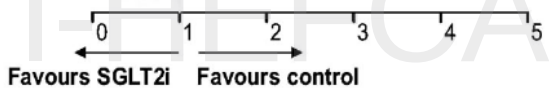
Vukadinovic D, et al. Eur J of Heart Fail (2022) 24, 1625–1632. doi:10.1002/ejhf.2584

Side effects and initiation barriers for SGLT2 inhibitors

A systematic review and meta-analysis

A Acute Kidney Injury

Study	SGLT2i Events	SGLT2i Total events	SGLT2i Event rate	Control Events	Control Total events	Control Event rate	Risk ratio (95%CI)
DAPA HF	23	2,368	0.97%	46	2,368	1.94%	0.50 (0.30– 0.82)
EMPEROR-Reduced	46	1,863	2.47%	67	1,867	3.59%	0.69 (0.48– 1.00)
SOLOIST-WHF	25	605	4.13%	27	611	4.42%	0.94 (0.55– 1.59)
SUGAR-DM-HF	1	52	1.92%	0	53	0.00%	3.06 (0.13–73.36)
TOTAL	95	4,888	1.94%	140	4,899	2.86%	0.69 (0.51– 0.93) p=0.02



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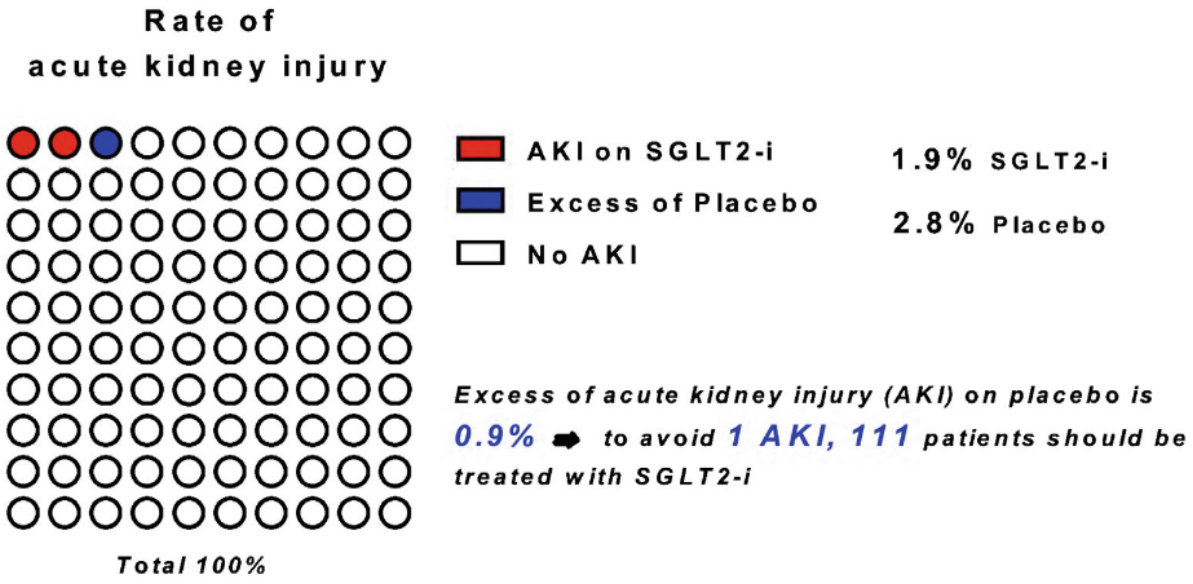

- Acute kidney injury was defined as doubling of baseline serum creatinine values.
- **1.9% on SGLT2i and in 2.8% on placebo** (RR 0.69, 95% CI 0.51–0.93, p = 0.02)
- **The excess of AKI on placebo over SGLT2i was 0.9%** and the corresponding NNH was 111 → **111 patients should be treated with SGLT2 inhibitors to avoid one AKI event**

Vukainovic D, et al. Eur J of Heart Fail (2022) 24, 1625–1632. doi:10.1002/ejhf.2584

Impact of diabetes on the effects of sodium glucose co-transporter-2 inhibitors on kidney outcomes: collaborative meta-analysis of large placebo-controlled trials

The Nuffield Department of Population Health Renal Studies Group and the SGLT2 inhibitor Meta-Analysis Cardio-Renal Trialists' Consortium**

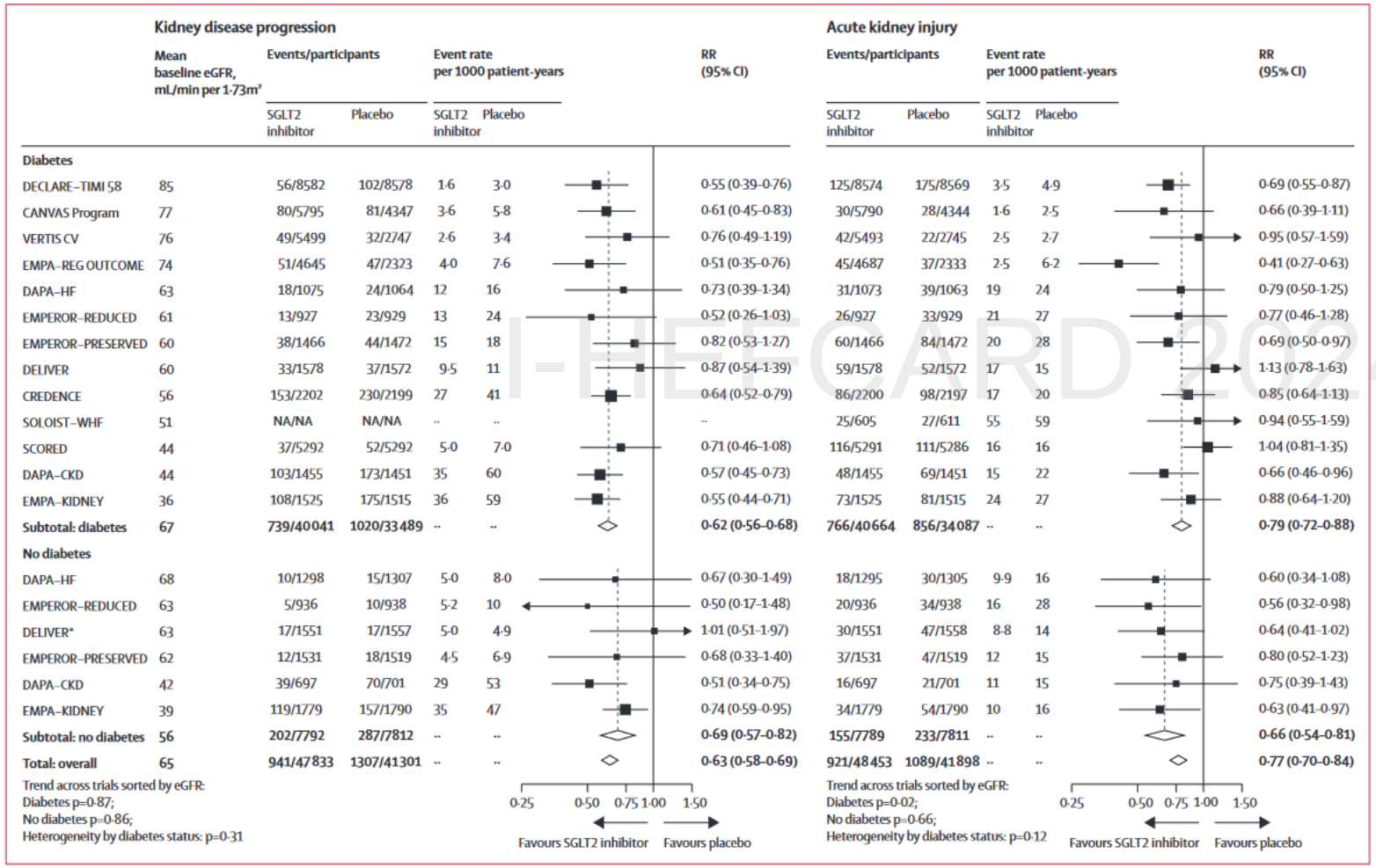

Figure 1: **Effect of sodium glucose co-transporter-2 inhibition on kidney disease outcomes by diabetes status**
Kidney disease progression was defined as a sustained decrease in eGFR (≥50%) from randomisation, a sustained low eGFR, end-stage kidney disease, or death from kidney failure in all presented trials. Outcome definition details for each trial are provided in the appendix (pp 9–11). Rate values are not presented for the combined subtotal and total populations due to the heterogeneity in rates across the individual trials. eGFR=estimated glomerular filtration rate. RR=relative risk. SGLT2=sodium glucose co-transporter-2. NA=not available. *One participant without diabetes in DELIVER was missing a baseline creatinine measurement and was excluded.

- 13 trials; 90,409 pts.
- **37% RRR kidney disease progression**
- **23% RRR AKI**
- Similar benefit with and without diabetes.
- Similar benefit regardless of cause of CKD.

Risk Benefit Ratio on SGLT2i in HF

	Endpoint	SGLT2-I	Control group	RR (95 CI)	ARD %	NNT-B or NNT-H	NNT-H/ NNT-B
Benefit	Acute kidney injury	1.9%	2.8%	0.68 (0.53 – 0.88)	0.9	111 (NNT-B)	/
Risk	Hypotension	4.5%	4.1%	1.09 (0.91-1.31)	0.4	250 (NNT-H)	2.25
	Volume depletion	9.4%	8.7%	1.08 (0.96 – 1.22)	0.7	143 (NNT-H)	1.28

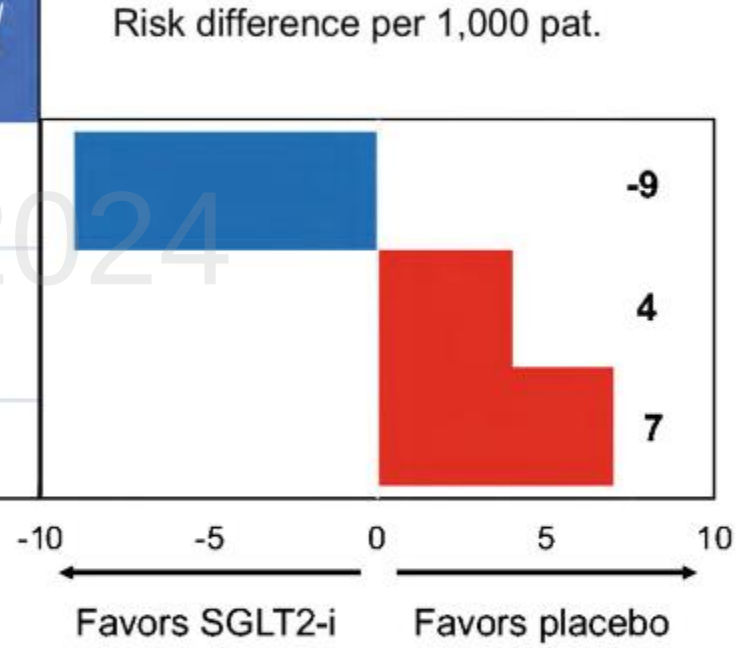

Figure 4 Key benefit–risk summary table with embedded risk difference forest plot per 1000 patients. ARD, absolute risk difference; CI, confidence interval; NNT-B, number needed to treat for benefit; NNT-H, number needed to treat for harm; RR, risk ratio; SGLT2-i, sodium–glucose cotransporter 2 inhibitor.

Vukainovic D, et al. Eur J of Heart Fail (2022) 24, 1625–1632. doi:10.1002/ejhf.2584

Take Home Points

- Mortality in HF patients is stil skyrocketing in Indonesia → most of them because of inertia
- 50% inertia → health care providers (lack of awareness of importance of GDMT, forget to increase the dose, afraid of AEs)
- Growing evidence supporting early initiation of GDMT (including SGLT2i) in the hospital setting (as soon as clinical stability is achieved), with a well-planned transtition to chronic care
- Hospitalization for HF favors clinicians with ideal window to initiate and adjust the GDMT (with rapid concurrent administration)
- Once the diagnosis of HF is made a SGLT2 inhibitor should be started, so it can improves morbidity and mortality in patients with heart failure irrespective of ejection fraction, once daily, no need uptitration
- The drug will only work if you prescribe it!

4th I-HEF CARD

The 4th Indonesian Symposium on Heart Failure and Cardiometabolic Disease

The 4th Indonesia Symposium on Heart Failure and Cardiometabo

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Ir. Budi Gunadi Sadikin, CHFC., CLU | dr. Radityo Prakoso, SpJP(K), FIHA, FAPSIC, FAsCC, FESC, FACC, FSCAI

dr. Hawani Sasmaya, Sp.JP (K), FIHA, FHFA | Dr. dr. Sally Aman Nasution, Sp.PD-KKV, FINASIM, FACP

dr. Siti Elkana Nauli, Sp.JP(K), FIHA, FAsCC, FHFA | dr. Rarsari Soerarso, Sp.JP(K), MARS, FIHA, FHFA

dr. Irnizarifka, Sp.JP (K), FIHA, FAPSC, FAsCC, FHFA | Prof. Dr. dr. Trisulo Wasyanto, Sp.JP(K), FIHA, FAPSC, FAsCC

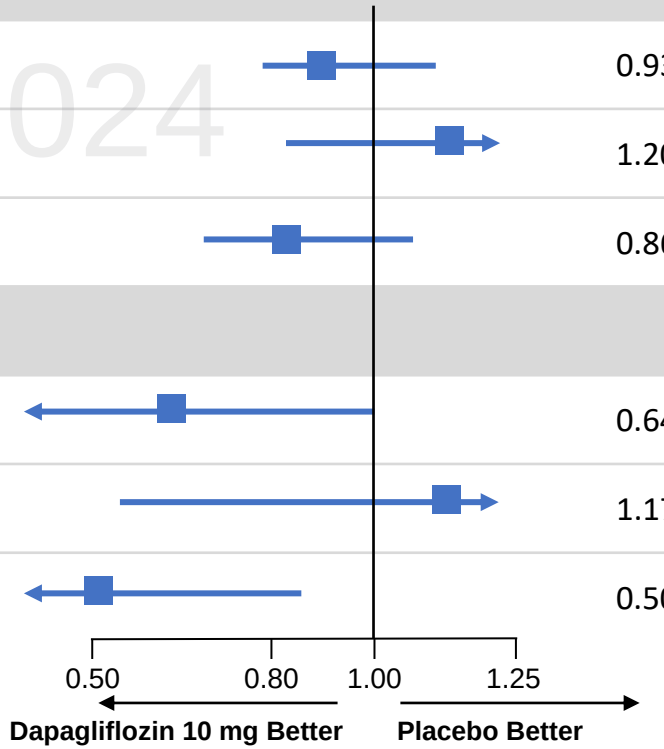
and many more

Back-up/additional slides

Hyperkalemia Events in the DAPA-HF Trial

Dapagliflozin may attenuate the risk of moderate/severe hyperkalemia in patients treated with an MRA at baseline

Endpoint	Dapagliflozin 10 mg n/N	Dapagliflozin 10 mg Rate per 100 pt-yrs	Placebo n/N	Placebo Rate per 100 pt-yrs	HR (95% CI)
Mild Hyperkalemia (>5.5 mmol/L)					
All patients	245/2298	8.2	262/2310	8.8	0.93 (0.78, 1.11)
No MRA at baseline	63/661	7.1	58/684	6.5	1.20 (0.84, 1.72)
MRA at baseline	182/1637	8.6	204/1626	9.8	0.86 (0.70, 1.05)
Moderate/Severe Hyperkalemia (>6.0 mmol/L)					
All patients	36/2364	1.1	51/2364	1.6	0.64 (0.42, 0.99)
No MRA at baseline	13/676	1.4	11/697	1.1	1.17 (0.52, 2.62)
MRA at baseline	23/1688	1.0	40/1667	1.7	0.50 (0.29, 0.85)



HFrEF = heart failure with reduced ejection fraction; HR = hazard ratio; MRA = mineralocorticoid-receptor antagonist; n = number of events; pt-yrs = patient-years.
Kristensen SL. Presented at: ESC Congress - The Digital Experience; August 29-September 1, 2020.

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Hyperkalemia Events in the DAPA-HF Trial

Dapagliflozin may attenuate the risk of moderate/severe hyperkalemia in patients treated with an MRA at baseline

Endpoint	Dapagliflozin 10 mg		Placebo		HR (95% CI)	p-value	Interaction p-value[a]
	n/N (%)	Rate per 100 pt-yrs	n/N (%)	Rate per 100 pt-yrs			
Mild Hyperkalemia (>5.5 mmol/L)							
No MRA at baseline	63/660 (9.6)	7.2	57/682 (8.4)	6.4	1.20 (0.84-1.72)	0.316	0.13
MRA at baseline	180/1632 (11.0)	8.7	204/1625 (12.6)	10.0	0.86 (0.70-1.05)	0.144	
Moderate/Severe Hyperkalemia (>6.0 mmol/L)							
No MRA at baseline	13/675 (1.9)	1.4	11/695 (1.6)	1.2	1.17 (0.52-2.62)	0.707	0.08
MRA at baseline	21/1683(1.3)	0.9	40/1666(2.4)	1.8	0.50 (0.29-0.85)	0.01	

[a] A non-significant result for an interaction test can be interpreted as consistency of effect across the subgroup.[2]

HR = hazard ratio; MRA = mineralocorticoid-receptor antagonist; pt-yrs = patient-years.

1. Shen L et al. *JACC Heart Fail.* 2021;9:254-264; 2. Alosh M et al. *J Biopharm Stat*. 2015;25:1161-1178.

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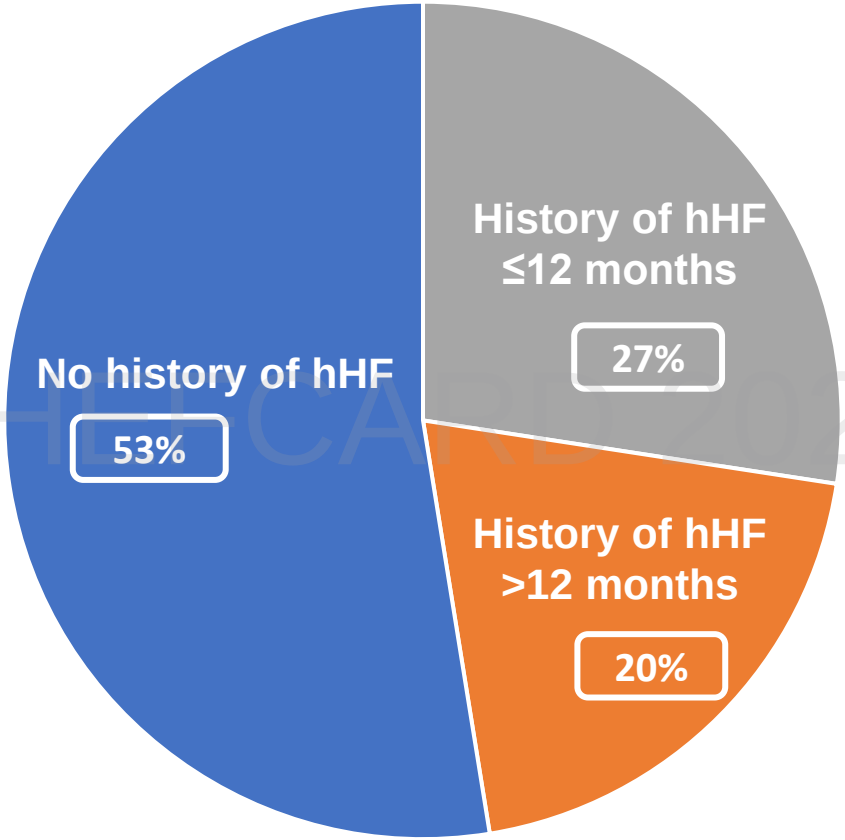
DAPA-HF
Clinical Benefit Analysis: Onset and Timing From Prior hHF

hHF = hospitalization for heart failure.

Distribution of Patients by History of hHF



N=4744

hHF = hospitalization for heart failure.

Berg DD et al. *JAMA Cardiol*. 2021;6:499-507.

Baseline Characteristics by Timing of Most Recent hHF[1,a]

Characteristic	No history (n=2493)	>12 months (n=950)	≤12 months (n=1301)	p-value
Mean age, year	66.7	66.9	65.2	<0.001
Female, %	23.7	22.6	23.3	0.80
eGFR[2], mL/min/1.73m^2	66	64	66	0.002
NT-proBNP, pg/mL	1400	1526	1486	0.09
LVEF, %	31.3	30.6	30.9	0.009
NYHA Class, %				
II	67.9	74.5	61.6	<0.001
III	31.6	24.8	36.4	
IV	0.5	0.6	1.9	
Ischemic etiology, %	57.8	55.7	54.0	0.03

[a]Timing of hHF relative to trial enrollment.

eGFR = estimated glomerular filtration rate; hHF = hospitalization for heart failure; LVEF = left ventricular ejection fraction; NT-proBNP = N-terminal pro-B-type natriuretic peptide; NYHA = New York Heart Association.

1. Berg DD et al. *JAMA Cardiol*. 2021;6:499-507; 2. Sabatine MS et al. Presented at: AHA Scientific Sessions; November 16-18, 2019; Philadelphia, PA.

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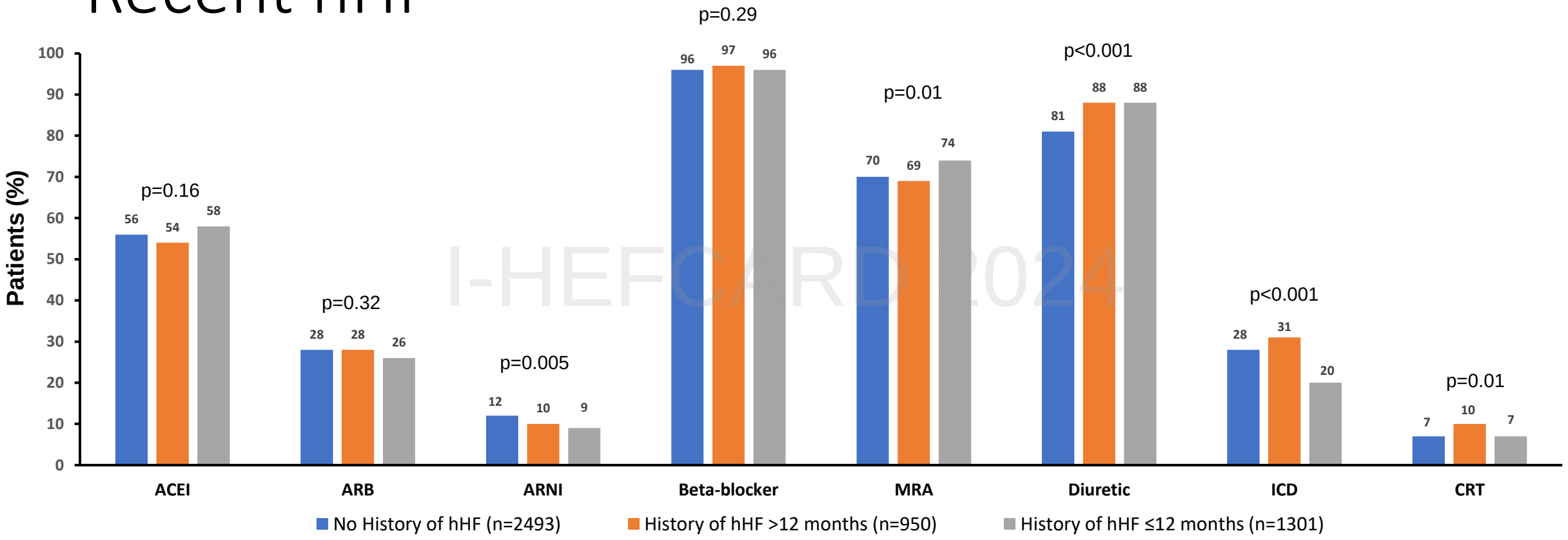
Baseline HF Treatments by Timing of Most Recent hHF[a]

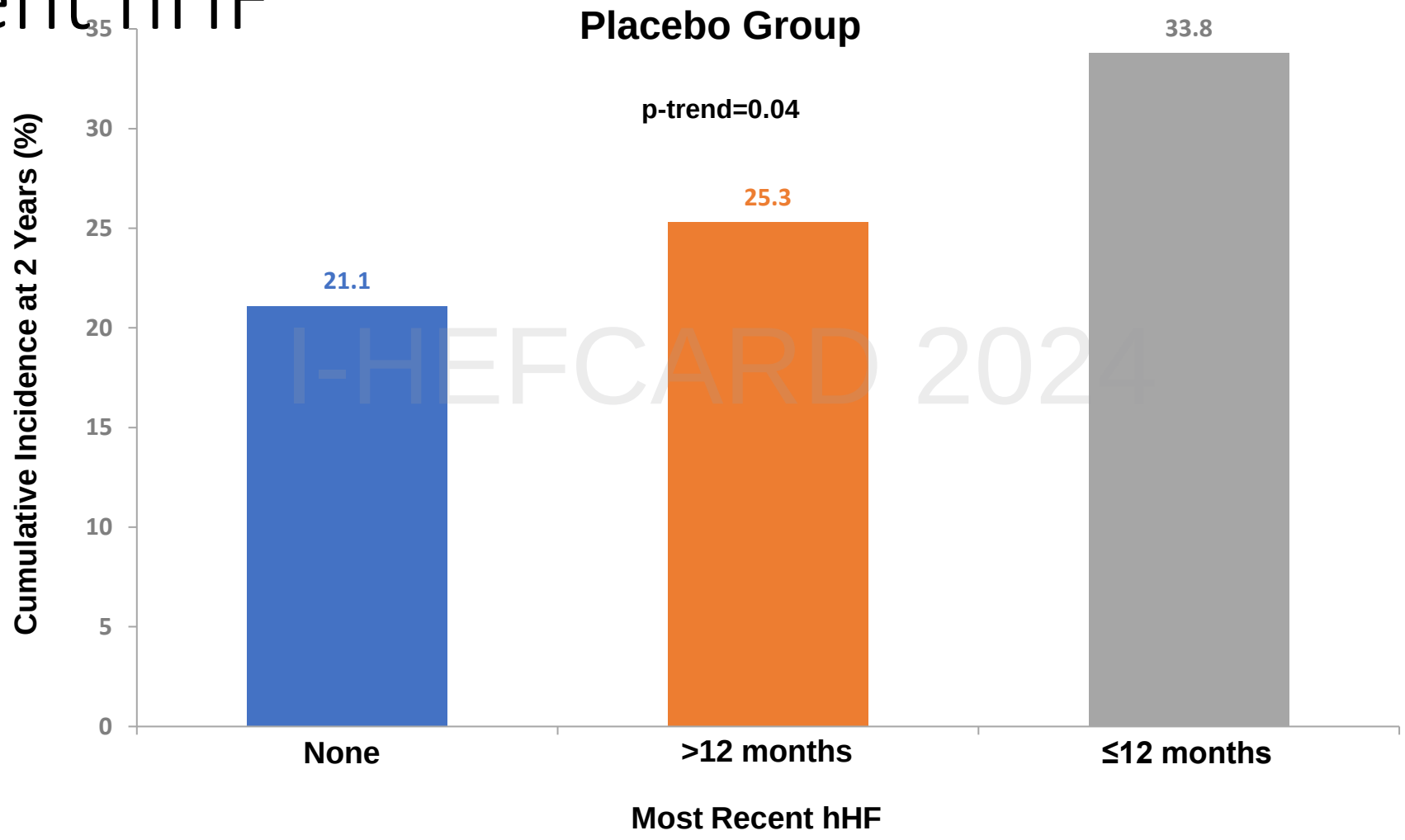


[a]Timing of hHF relative to trial enrollment.

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin-receptor blocker; ARNI = angiotensin-receptor neprilysin inhibitor; CRT = cardiac resynchronization therapy; HF = heart failure; hHF = hospitalization for heart failure; ICD = implantable cardioverter-defibrillator; MRA = mineralocorticoid receptor antagonist.

Berg DD et al. *JAMA Cardiol*. 2021;6:499-507.

CV Death or Worsening HF[a] by Timing of Most Recent hHF[b]



[a]Worsening HF includes hHF or urgent HF visit [b]Timing of hHF relative to trial enrollment.

CV = cardiovascular; HF = heart failure; hHF = hospitalization for heart failure.

Berg DD et al. *JAMA Cardiol*. 2021;6:499-507.

Summary: DAPA-HF Clinical Benefit Analysis: Onset and Timing From Most Recent hHF

- This assessment from the DAPA-HF trial was a *post hoc* analysis.
- The reduction in the primary endpoint of CV death and worsening HF events[a] occurred as early as 28 days.
- The risk of CV death and worsening HF events[a] was lower with dapagliflozin versus placebo in patients with HFrEF regardless of timing of most recent hHF.
- Patients with a more recent HF hospitalization tended to experience greater relative risk reductions and correspondingly greater absolute risk reductions in the primary outcome at 2 years with dapagliflozin.

[a]Worsening HF includes hHF or urgent HF visit.

CV = cardiovascular; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; hHF = hospitalization for heart failure.

Berg DD et al. *JAMA Cardiol*. 2021;6:499-507.