HFA Heart Failure Association
European Society of Cardiology
САНУ СРПСКА АКАДЕМИЈА НАУКА И УМЕТНОСТИ
УНИВЕРЗИТЕТ У БЕОГРАДУ МЕДИЦИНСКИ ФАКУЛТЕТ
KLINIČKI CENTAR SRBIJE
Heart failure Society of Serbia

Prof. dr Petar M. Seferovic, MD, PhD, FESC, FACC

Chair, ESC Task force on Eastern Countries

Co-Editor for Eastern Europe, European Heart Journal

Vice-president, European Society of Cardiology (2020-2022)

SGLT2 inhibitors from HFrEF to HFmrEF and HFpEF

Academician, Serbian Academy of Sciences and Arts

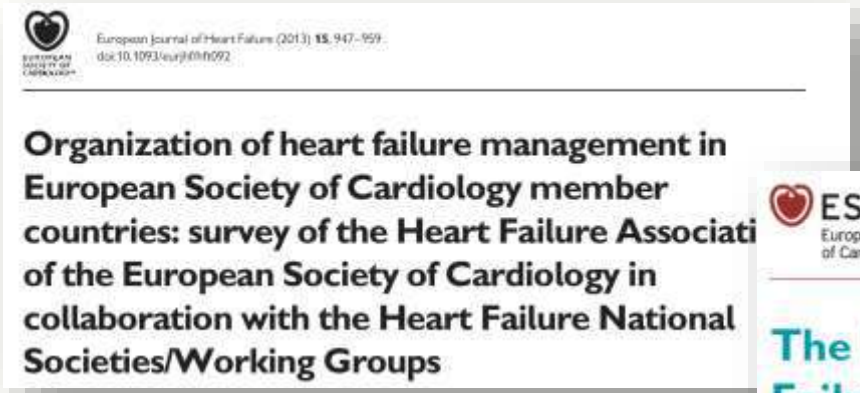
Professor of Cardiology, Belgrade University School of Medicine

President, Heart failure Society of Serbia

ESC/HFA long-term mission:

Surveillance of HF epidemiology and management capacities in ESC member countries

2013 Survey


European Journal of Heart Failure (2013) 15, 947–959
doi:10.1093/eurjhf/hft092

Organization of heart failure management in European Society of Cardiology member countries: survey of the Heart Failure Associati of the European Society of Cardiology in collaboration with the Heart Failure National Societies/Working Groups

2019 HFA Atlas


ESC European Society of Cardiology

European Journal of Heart Failure (2021)
doi:10.1002/ejhf.2143

RESEARCH ARTICLE

The Heart Failure Association Atlas: Heart Failure Epidemiology and Management Statistics 2019

2025 European HF Survey

Heart Failure & World Congress on Acute Heart Failure 2025

2019 HFA Atlas vs 2025 European HF Survey

Heart failure incidence

Median incidence 2019:

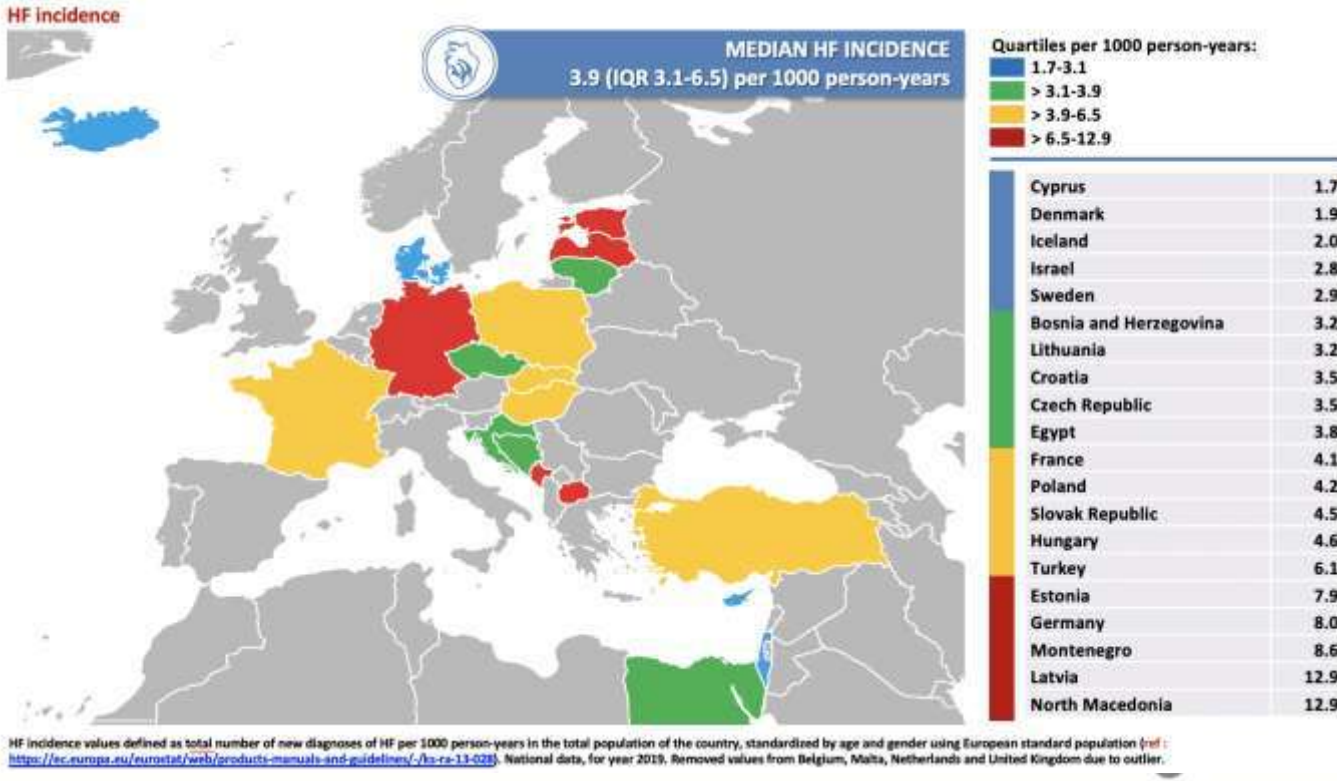
3.2 new cases per 1000 PY

Incidence: number of new cases of heart failure per 1000 person-years. **Data in blue letters derived from**: national statistics, governmental and/or ministry of health documents and prospective national registries/surveys; **Data in orange letters derived from**: publications based on defined populations (e.g. regional registries/surveys).

Acute Heart Failure 2025

Median incidence 2025:

3.9 new cases per 1000 PY



HF incidence values defined as total number of new diagnoses of HF per 1000 person-years in the total population of the country, standardized by age and gender using European standard population (ref : https://ec.europa.eu/eurostat/web/products-manuals-and-guidelines/-/ks-ra-13-028). National data, for year 2019. Removed values from Belgium, Malta, Netherlands and United Kingdom due to outlier.

Seferović P, Polovina M, Savarese G, et al. Eur J Heart Fail. 2025 Accepted

2019 HFA Atlas vs 2025 European HF Survey

Heart failure prevalence

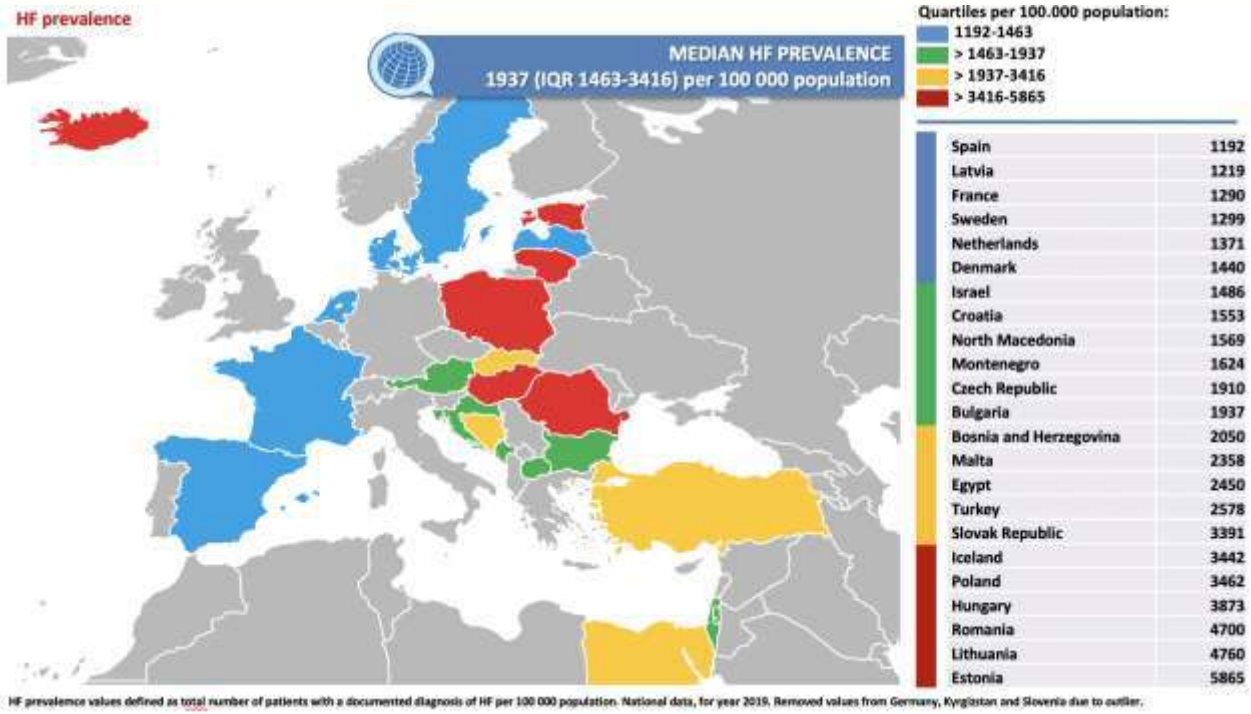
Median prevalence 2019:

1.7% total population

Seferović P et al. Eur J Heart Fail.2021 Jun;23(6):906-914

Median prevalence 2025:

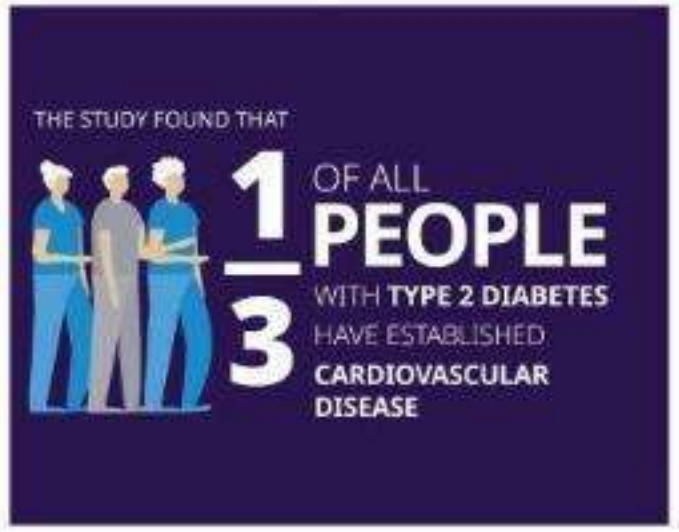
1.9% total population

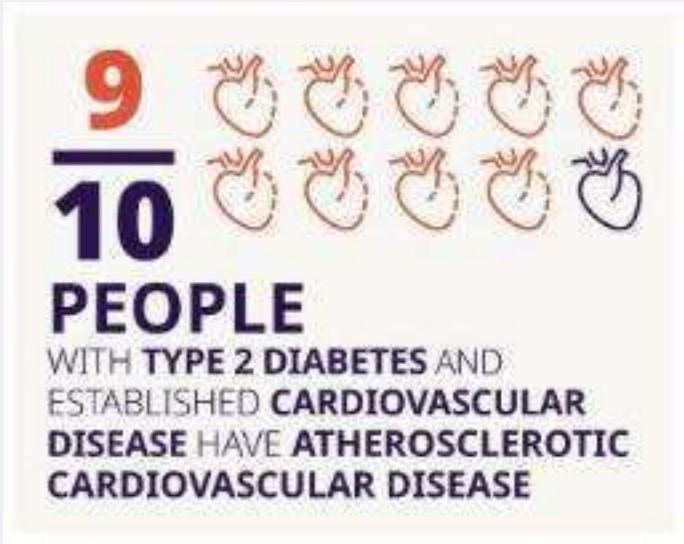


Seferović P, Polovina M, Savarese G, et al. Eur J Heart Fail. 2025 Accepted

CAPTURE: a cross-sectional study of the contemporary (2019) prevalence of cardiovascular disease in adults with type 2 diabetes across 13 countries

Cardiovascular disease must be prioritised as a key factor in the management of type 2 diabetes



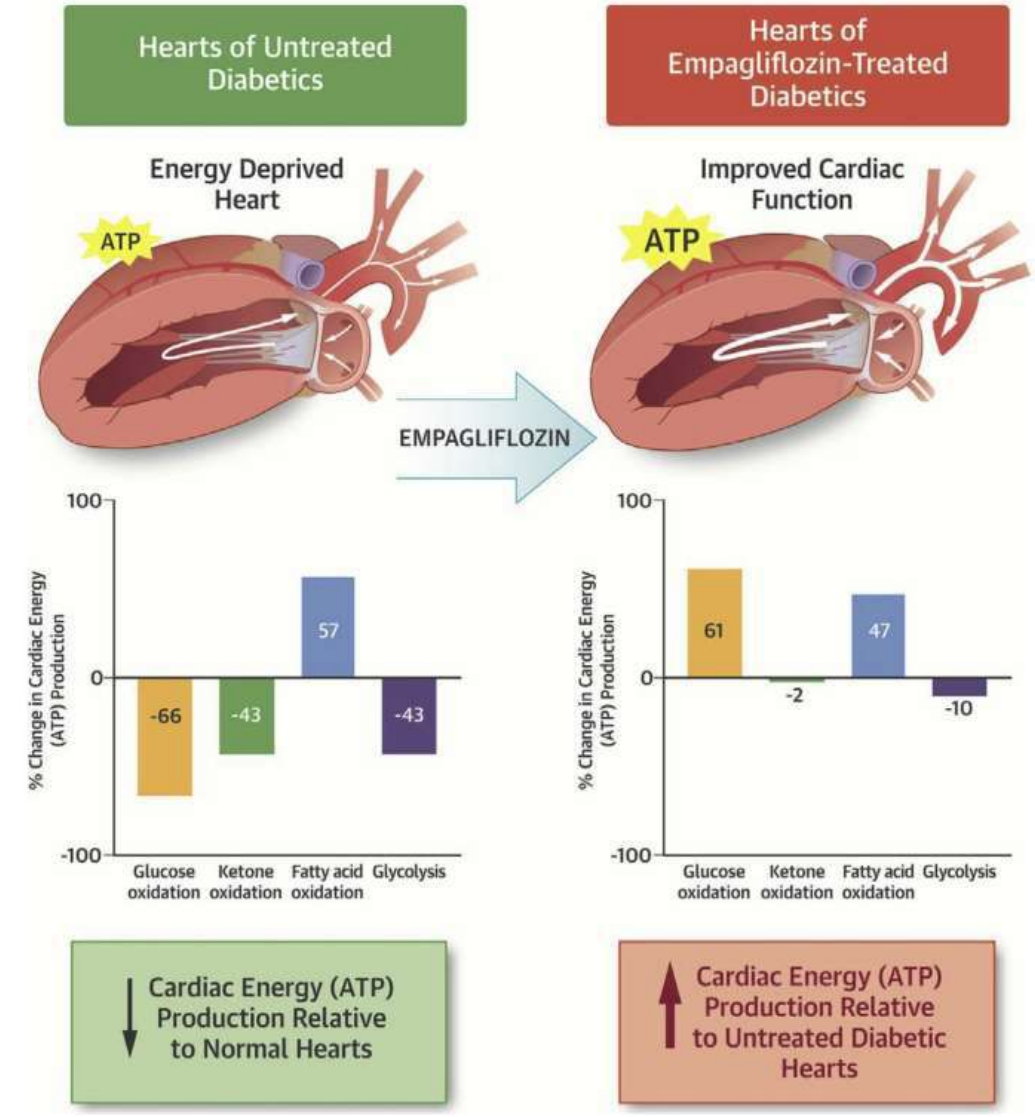


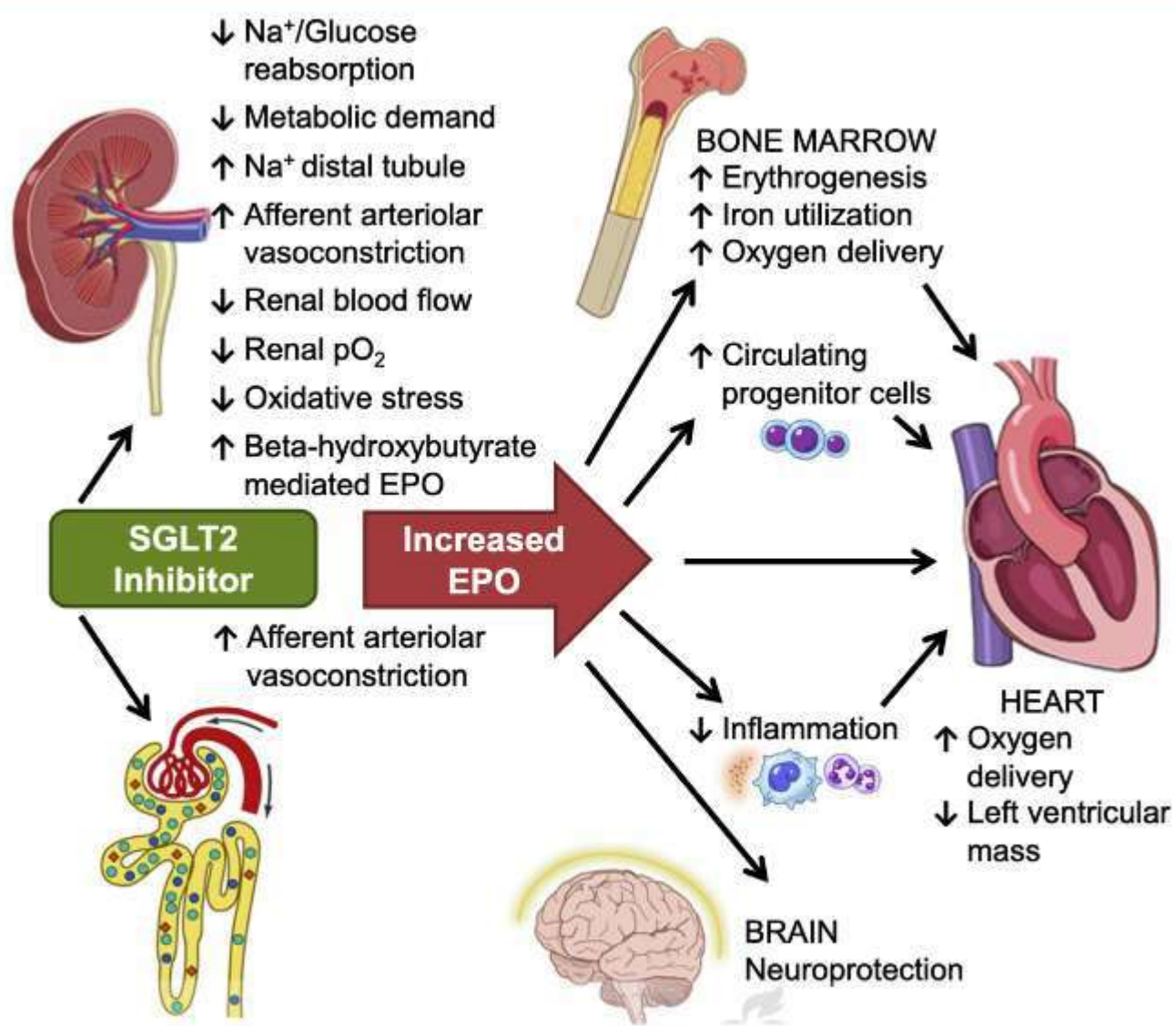
ASCVD prevalence within the T2D population is **high** but the **vast majority** are **not being managed** with **treatments that are proven to reduce the risk** of life-altering cardiovascular events.

Cardiovascular risk active screen should be prioritised.

Mosenzon O, Alguwaihes A, Arenas Leon J.L., et al. CAPTURE: a cross-sectional study of the contemporary (2019) prevalence of cardiovascular disease in adults with type 2 diabetes across 13 countries. Abstract 158. Presented at the 56th Annual Meeting of the European Association of the Study of Diabetes, Macrovascular complications and beyond, 10:15 CEST on 24 September 2020.

SGLT2 inhibition
Mechanisms of the cardio-/nephroprotective effects





Lopaschuk, G.D. et al. J Am Coll Cardiol Basic Trans Science. 2020;5(6):632–44

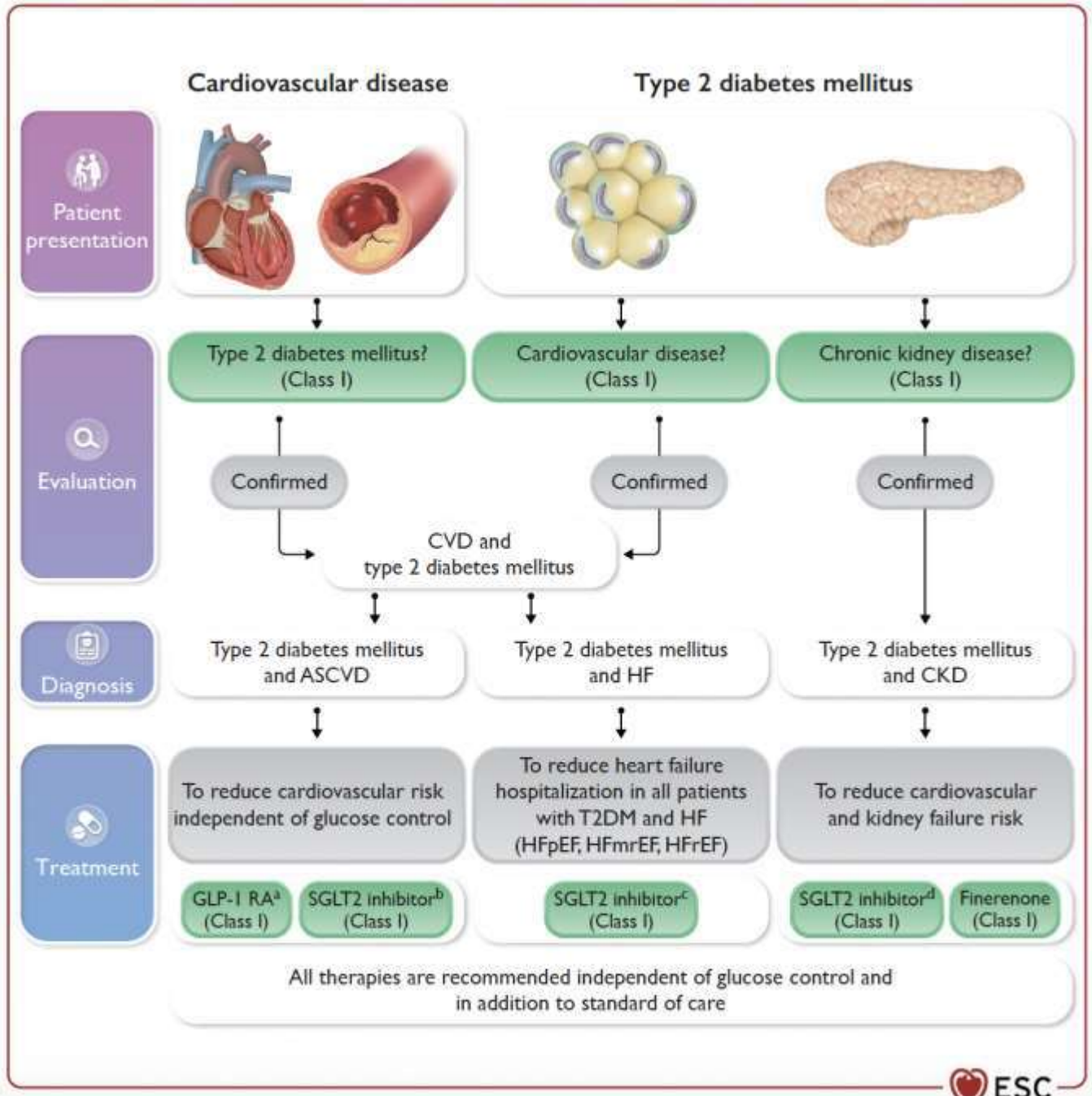
SGLT2 inhibitors have multiple CV benefits in patients with T2DM

	EMPA-REG OUTCOME[1] (empagliflozin)	CANVAS Program[2] (canagliflozin)	DECLARE-TIMI 58[3] (dapagliflozin)
 HHF	**HR 0.65** (95% CI 0.50, 0.85) *p*=0.002*	**HR 0.67** (95% CI 0.52, 0.87)†	**HR 0.73** (95% CI 0.61, 0.88)†
 CV death	**HR 0.62** (95% CI 0.49, 0.77) *p*<0.001*	**HR 0.87** (95% CI 0.72, 1.06)†	**HR 0.98** (95% CI 0.82, 1.17)†
 3P-MACE	**HR 0.86** (95% CI 0.74, 0.99) *p*=0.04	**HR 0.86** (95% CI 0.75, 0.97) *p*=0.02‡	**HR 0.93** (95% CI 0.84, 1.03) *p*=0.17

Comparison of studies should be interpreted with caution due to differences in study design, populations and methodology
p-values are for superiority
*Nominal *p*-value; †Exploratory outcome, no *p*-value is reported – only nominal effect estimate is given; ‡Testing for superiority for 3P-MACE was part of the statistical analysis plan but was not part of the hierarchical testing strategy
HHF, hospitalisation for heart failure
1. Zinman B *et al. N Engl J Med* 2015;373:2117; 2. Neal B *et al. N Engl J Med* 2017;377:644; 3. Wiviott S *et al. N Engl J Med* 2019;380:347

2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes

Management of cardiovascular disease in patients with T2DM: clinical approach and key recommendations



Marx N et al. European Heart Journal (2023) 00, 1–98

2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes

Special considerations for the glucose-lowering medication in patients with T2DM, with and without CV disease

Special considerations for glucose-lowering medications in patients with T2DM with and without HF		
It is recommended to switch glucose-lowering treatment from agents without proven CV benefit or proven safety to agents with proven CV benefit.	I	C

Marx N et al. European Heart Journal (2023) 00, 1–98

Trilateral Cooperation Project

Starting date: Munich, March 22 nd, 2019

Petar M. Seferovic
President of HFA

HFA
Heart Failure
Association
European Society of Cardiology

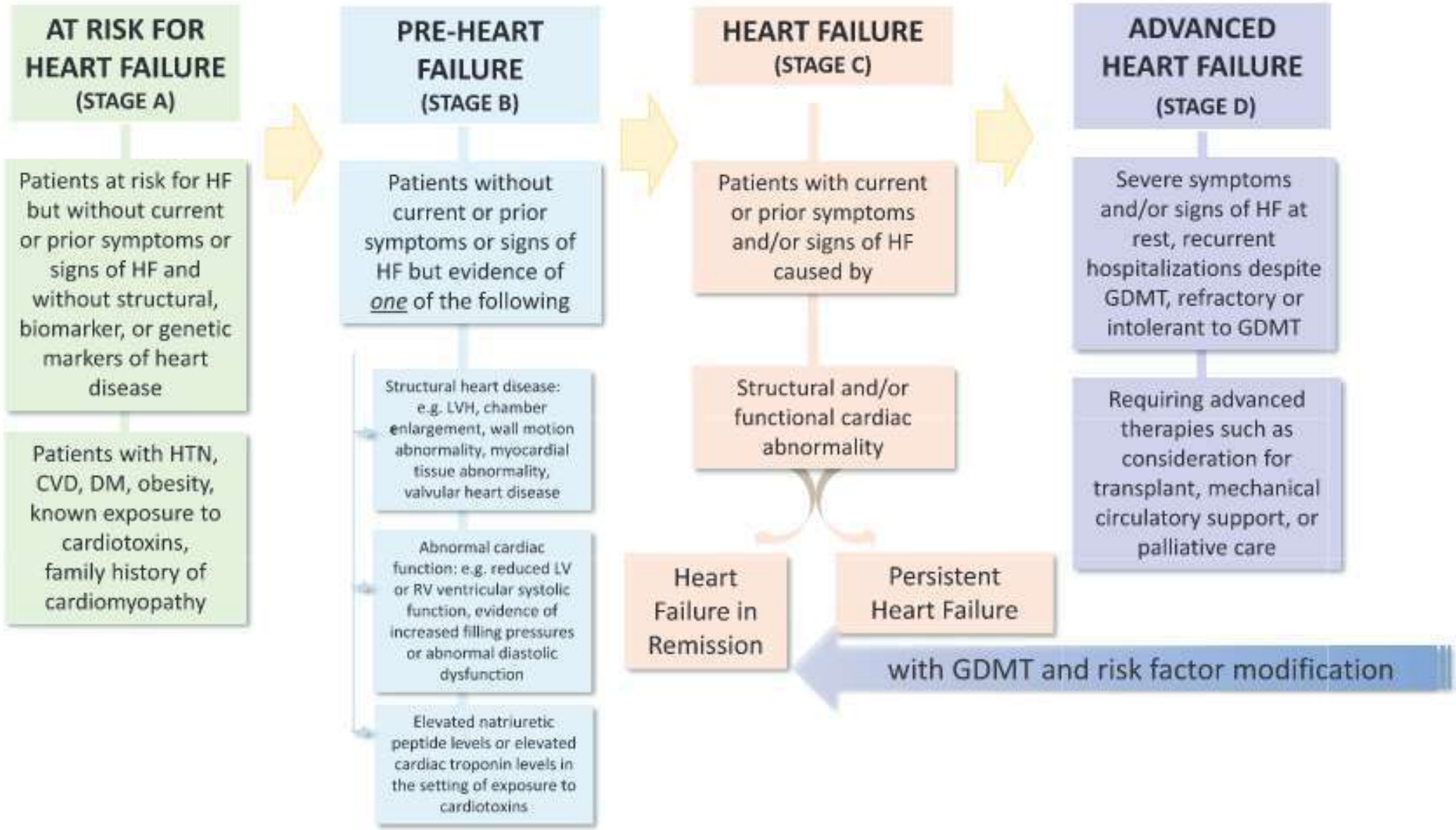
Randall Starling
President of HFSA

HFSA
HEART FAILURE SOCIETY OF AMERICA

Hiroyuki Tsutsui
President of JHFS

The Japanese
Heart Failure Society

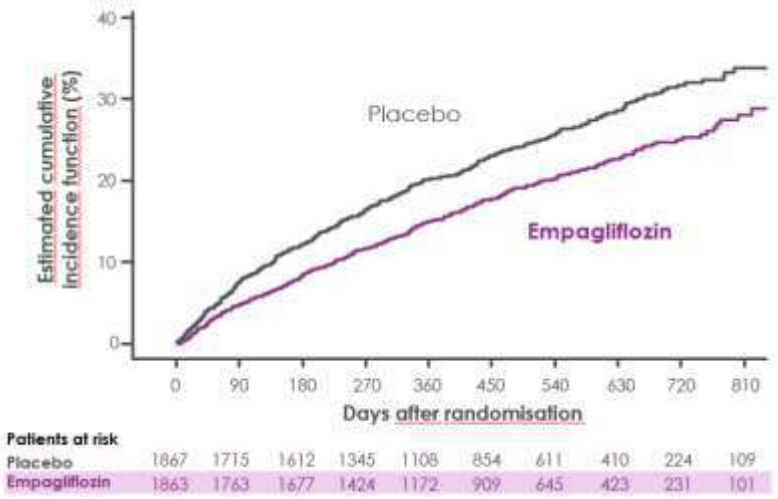
Stages in the development and progression of heart failure



European Journal of Heart Failure (2021)23, 352–380; Journal of Cardiac Failure (2021)27(4) 387-413

EMPEROR Reduced

Primary endpoint: First adjudicated CV death or HF hospitalisation



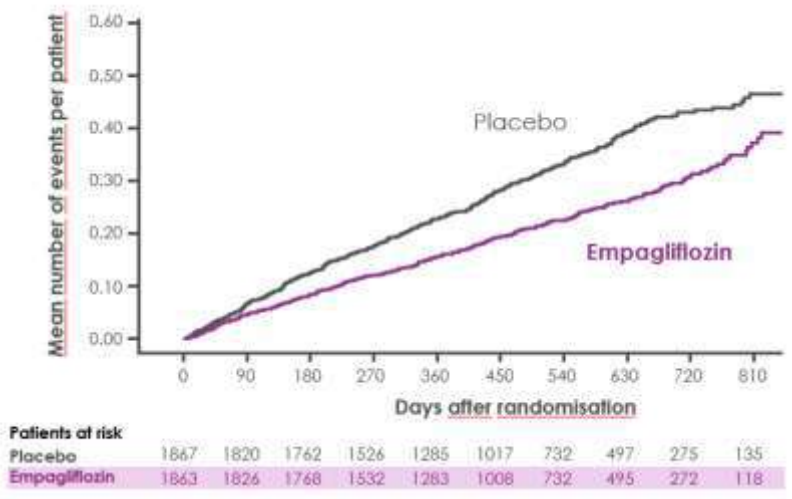
RRR 25%

ARR 5.2%

NNT = 19

HR 0.75
(95% CI 0.65, 0.86)
p<0.001

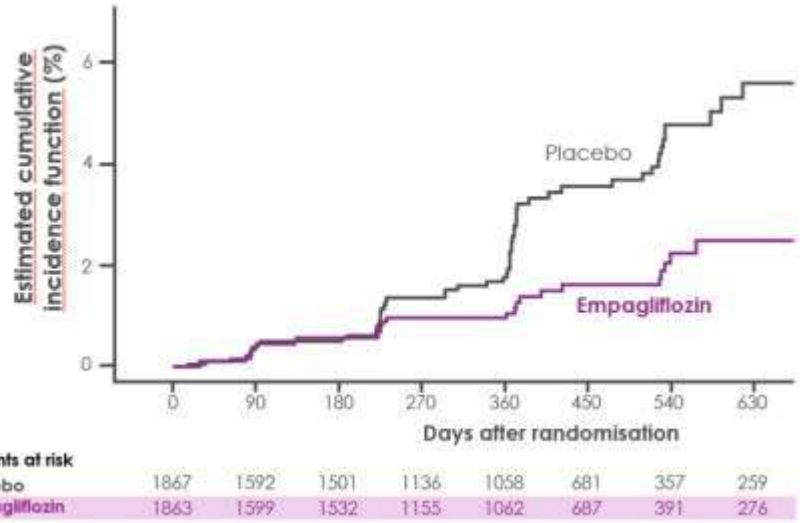
Key secondary: Adjudicated total HF hospitalisations (first and recurrent)



RRR 30%

HR 0.70
(95% CI 0.58, 0.85)
p<0.001

Composite renal endpoint (ESKD or sustained profound decrease in eGFR)



RRR 50%

ARR 1.5%

HR 0.50
(95% CI 0.32, 0.77)

N Engl J Med 2020; 383:1413-1424

Dapagliflozin: The first and only SGLT2 inhibitor to significantly reduce CV mortality in HFrEF patients, with and without T2D[1,2]

DAPA-HF[1]

N=4744

- LVEF ≤40%
- Elevated NT-proBNP
- eGFR ≥30 mL/min/1.73 m^2

1:1 randomization

DAPA 10 mg | **Placebo**

Median follow-up: 18.2 months

Primary endpoint[1]

Composite of CV death or worsening HF (hHF or an urgent HF visit)

Secondary endpoints[1]

- CV death or hHF
- Total number of hHF (first and recurrent) and CV death
- Change in KCCQ-TSS from baseline to 8 months
- ≥50% sustained decline in eGFR, ESKD or renal death
- All-cause mortality

Baseline characteristics[3]

1437 pg/mL
Median NT-proBNP

31%
Average LVEF

55%
Without T2D

41%
With an eGFR <60 mL/min/1.73 m^2

1. McMurray JJV et al. *N Engl J Med.* 2019;381(21):1995-2008; 2. Packer M et al. *N Engl J Med.* 2020;383(15):1413-1423; 3. McMurray JJV et al. *Eur J Heart Fail.* 2019;21:1402-1411.

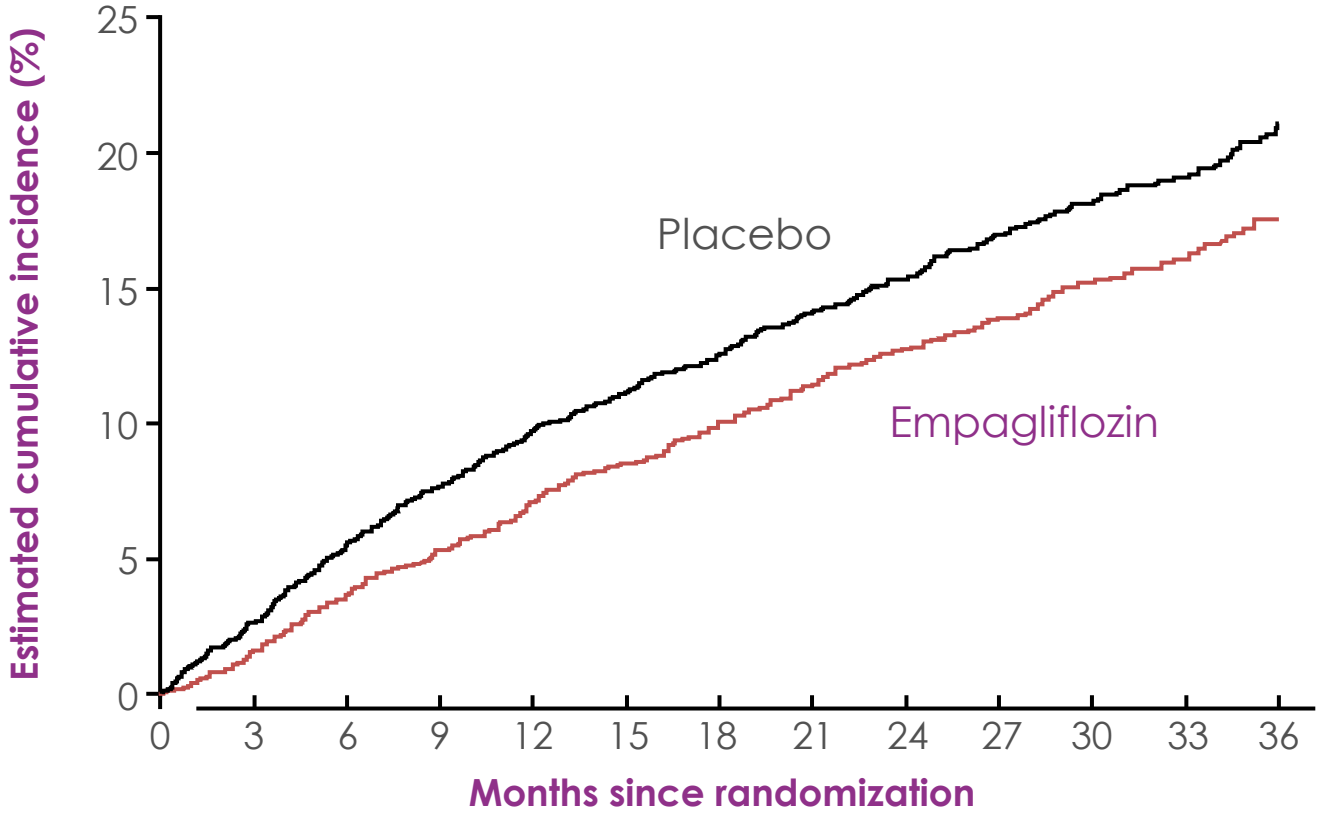
Pharmacological treatments indicated in patients with (NYHA class II-IV) heart failure with reduced ejection fraction (LVEF ≤40%)

Recommendations	Class	Level
An ACE-I is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.	I	A
A beta-blocker is recommended for patients with stable HFrEF to reduce the risk of HF hospitalization and death.	I	A
An MRA is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.	I	A
Dapagliflozin or empagliflozin are recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.	I	A
Sacubitril/valsartan is recommended as a replacement for an ACE-I in patients with HFrEF to reduce the risk of HF hospitalization and death.	I	B

ACE-I = angiotensin-converting enzyme inhibitor; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; LVEF = left ventricular ejection fraction; MRA = mineralocorticoid receptor antagonist; NYHA= New York Heart Association.

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure
(European Heart Journal 2021 – doi:10.1093/eurheartj/ehab368)

EMPEROR-preserved: Reduction of composite primary endpoint of CV death/HHF



Patients at risk

Placebo	2991	2888	2786	2706	2627	2424	2066	1821	1534	1278	961	681	400
Empagliflozin	2997	2928	2843	2780	2708	2491	2134	1858	1578	1332	1005	709	402

RRR 21%

ARR 3.3%

NNT*=31

HR: 0.79
(95% CI: 0.69, 0.90)
p<0.001

Empagliflozin:
415 (13.8%) patients with event
Rate: 6.9/100 patient-years
Placebo:
511 (17.1%) patients with event
Rate: 8.7/100 patient-years

*During a median trial period of 26 months. ARR, absolute risk reduction; CI, confidence interval; CV, cardiovascular; HHF, hospitalization for heart failure; HR, hazard ratio; NNT, number needed to treat; RRR, relative risk reduction. Anker S *et al. N Engl J Med*. 2021 Aug 27. doi: 10.1056/NEJMoa2107038.

DELIVER

Largest and Broadest Trial to Date in Patients with Heart Failure and Mildly Reduced or Preserved Ejection Fraction

International | Multicenter | Parallel-group | Event-driven | Randomized | Double-blind

Inclusion Criteria

353 Sites

20 Countries

6263 Patients

- Age ≥40 with/without T2D
- Symptomatic HF
- LVEF >40%[a]
- Ambulatory or hospitalized
- Elevated NT-proBNP levels
- eGFR ≥25 mL/min/1.73 m^2

Randomized 1:1[b]

Stop when ~1117 primary events are reached

Dapagliflozin 10 mg vs **Placebo**

Baseline Characteristics

Older, Symptomatic Cohort

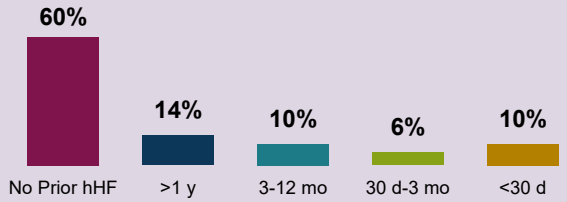
72 years Mean Age
44% Women
75% NYHA Class II
25% NYHA Class III
Moderate Symptomatic Impairment[c]

High Rate of Comorbidities

45% T2D
45% BMI ≥30 kg/m^2
89% Hypertension
57% History of AF/AFL
51% Coronary artery disease
61 mL/min/1.73 m^2 Mean eGFR

Elevated Risk

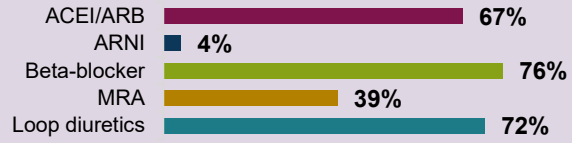
- Median NT-proBNP: **1011 pg/mL**
- **16%** enrolled during or <90 days of hospitalization
- History of hospitalization for HF:



Well-represented LVEF Groups

- Mean LVEF: **54%**
- Patients with prior LVEF ≤40%[3]: **~18%**

High Use of HF Medical Therapies



[a]Patients with prior LVEF ≤40% were also included; [b]Stratified by T2D status (established diagnosis/HbA1c ≥6.5% at enrollment); [c]Mean baseline KCCQ -CSS, -OSS, and -TSS were 68, 67, and 70, respectively.

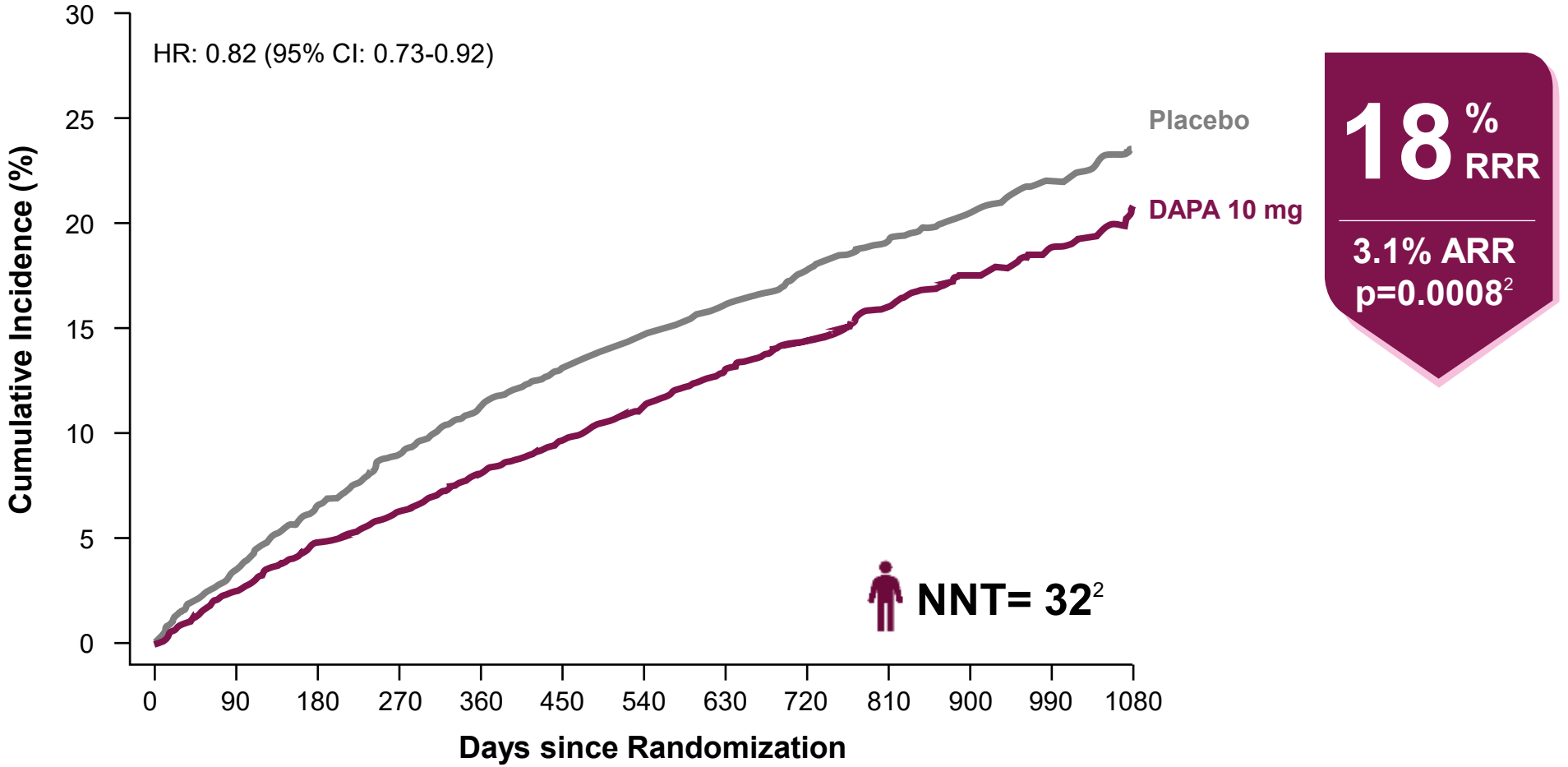
Solomon SD et al. Dapagliflozin in Heart Failure with Mildly Reduced or Preserved Ejection Fraction. N Engl J Med. 2022 Aug 27.

Dapagliflozin significantly reduced the risk of CV death or worsening HF[a] in patients with LVEF >40%[1]

DELIVER

Primary Endpoint

Composite of CV Death or Worsening HF[a]



[a]hHF or an urgent HF visit.

Solomon SD et al. Dapagliflozin in Heart Failure with Mildly Reduced or Preserved Ejection Fraction. N Engl J Med. 2022 Aug 27.

How does SGLT2i reduce cardiovascular mortality?

Mediation analysis of the EMPA-REG OUTCOME trial

Favourable haemodinamic effects:

decongestion?

Changes of plasma volume

(**increasing haematocrit and haemoglobin**) mediated **~50%** of risk reduction in CV death with empagliflozin versus placebo.

Table 2—Univariable mediation analysis of risk of CV death with empagliflozin versus placebo: time-dependent covariate analysis adjusting for the change from baseline in each variable

	HR for CV death with empagliflozin vs. placebo (95% CI)	Percentage mediation
Unadjusted	0.615 (0.491, 0.770)	
Adjusted for		
HbA_{1c}	0.624 (0.496, 0.785)	3.0
FPG	0.665 (0.529, 0.837)	16.1
SBP	0.593 (0.473, 0.743)	−7.5
DBP	0.614 (0.490, 0.769)	−0.3
Heart rate	0.621 (0.495, 0.780)	2.0
LDL-C	0.596 (0.475, 0.748)	−6.5
HDL-C	0.636 (0.506, 0.799)	6.9
logTG	0.604 (0.482, 0.758)	−3.7
FFAs	0.586 (0.463, 0.741)	−9.9
logUACR	0.649 (0.518, 0.815)	11.1
eGFR (MDRD)	0.631 (0.504, 0.790)	5.3
eGFR (CKD-EPI)	0.632 (0.505, 0.791)	5.6
Weight	0.579 (0.461, 0.727)	−12.4
BMI	0.578 (0.460, 0.726)	−12.8
WC	0.598 (0.477, 0.750)	−5.8
Hematocrit	0.791 (0.626, 1.000)	51.8
Hemoglobin	0.780 (0.619, 0.983)	48.9
Albumin	0.696 (0.555, 0.873)	25.5
Uric acid	0.693 (0.553, 0.869)	24.6

Cox proportional hazards regression analysis in patients treated with one or more doses of study drug. FFA, free fatty acid; HDL-C, HDL cholesterol; LDL-C, LDL cholesterol; TG, triglyceride; WC, waist circumference.

Inzucchi SE et al. Diabetes Care 2018;41:356–363

The prevention of HF hospitalisation

The integrity of clinical decision making

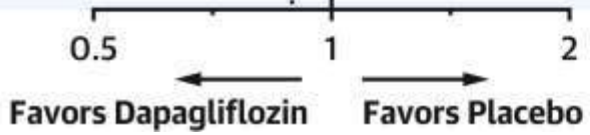
- Primary prevention
- In type 2 diabetes, with or without atherosclerotic CV disease (EMPA-REG OUTCOME, CANVAS, VERITIS-CV)
- In chronic kidney disease, with or
- without diabetes (CREDENCE,
- DAPA-CKD, SCORED)
- Secundary prevention
- HFrEF (EMPEROR-reduced, DAPA-HF)
- HFpEF (EMPEROR-preserved)

Dapagliflozin reduces the risk of all hospitalisations: DELIVER

Patients with HFpEF are older, multimorbid and at risk of non-CV hospitalisation

- **Treatment with dapagliflozin vs. placebo was associated with a 11% lower risk of all hospitalisations, with a number needed to prevent one HF hospitalisation of 26 patients.**

	Total # of Events					
	Dapagliflozin	Placebo	Rate Ratio (95% CI)	Rate Ratio	(95% CI)	*P* Value
All-Cause Hospitalization	2,226	2,484		0.89	(0.82-0.98)	0.015
Top Causes of Hospitalization						
Cardiac	906	1,080		0.84	(0.73-0.95)	0.008
Noncardiac	1,320	1,404		0.94	(0.85-1.04)	0.22
Infectious	524	535		0.98	(0.85-1.13)	0.76
Nervous System	176	162		1.08	(0.86-1.36)	0.49
Gastrointestinal	94	162		0.58	(0.43-0.74)	<0.001
Renal/Urinary	107	131		0.82	(0.60-1.11)	0.20
Respiratory/Thoracic	109	115		0.95	(0.68-1.31)	0.74
Injury, Poisoning, or Procedural	96	110		0.87	(0.64-1.18)	0.38
Vascular	100	82		1.22	(0.88-1.69)	0.24
Cancer	90	89		1.01	(0.74-1.38)	0.95
Metabolism/Nutrition	78	85		0.92	(0.64-1.32)	0.64



Vaduganathan M et al. JACC. 2023 Mar, 81 (10) 1004–1006

Why do SGLT2 inhibitors reduce heart failure hospitalization?

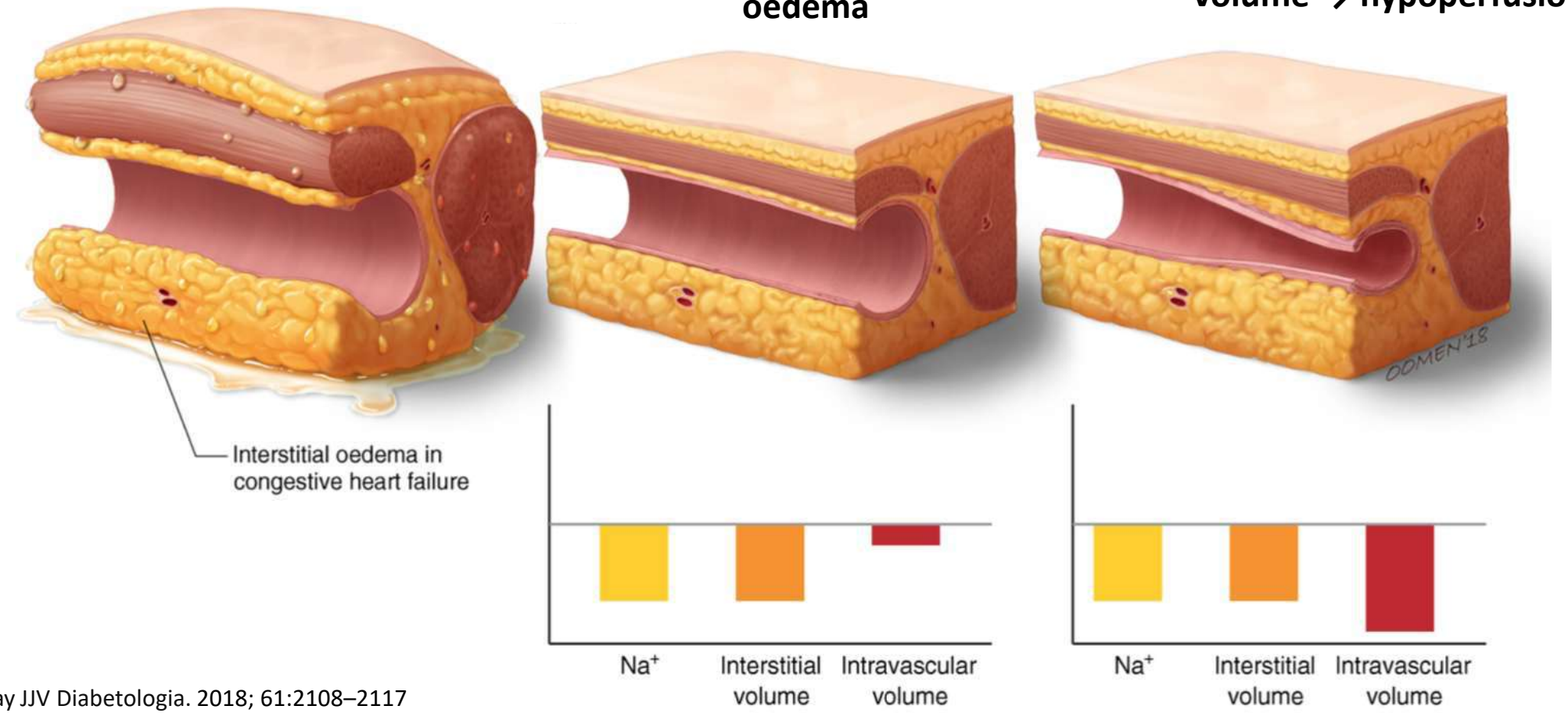
A differential volume regulation hypothesis

based on a mathematical model

Interstitial oedema in heart failure

SGLT2 inhibitors may selectively reduce interstitial oedema

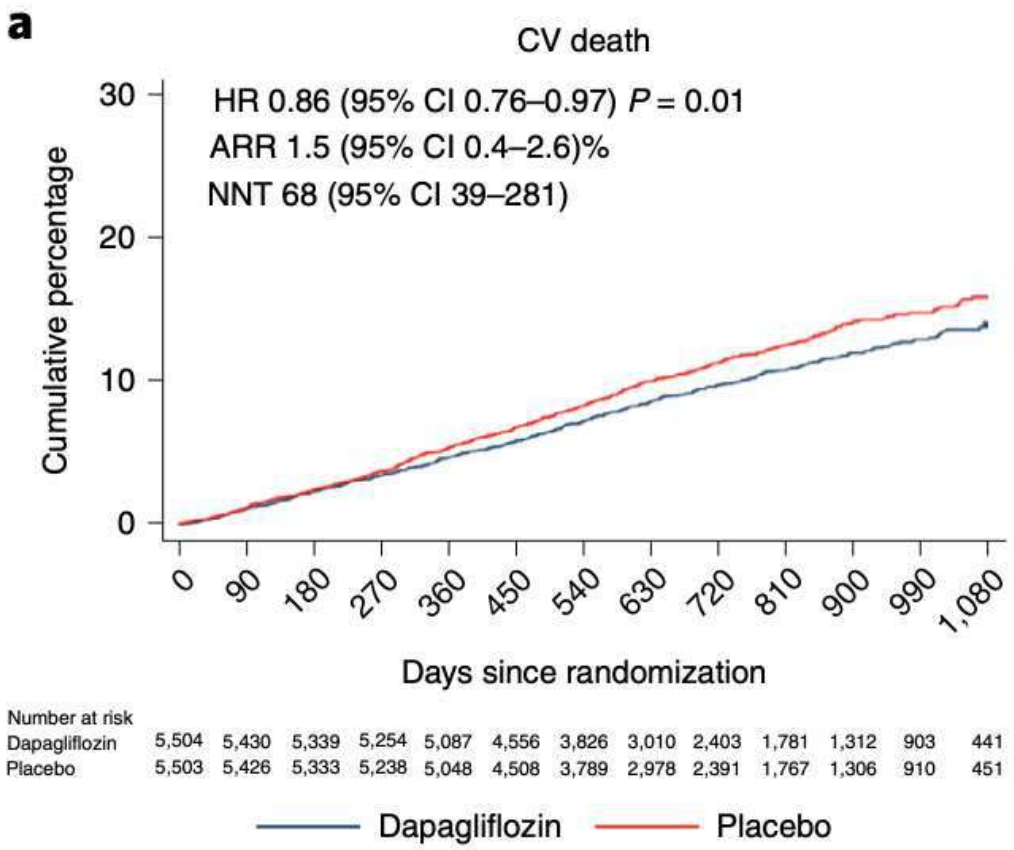
Traditional diuretics may reduce both interstitial oedema and IV volume → hypoperfusion

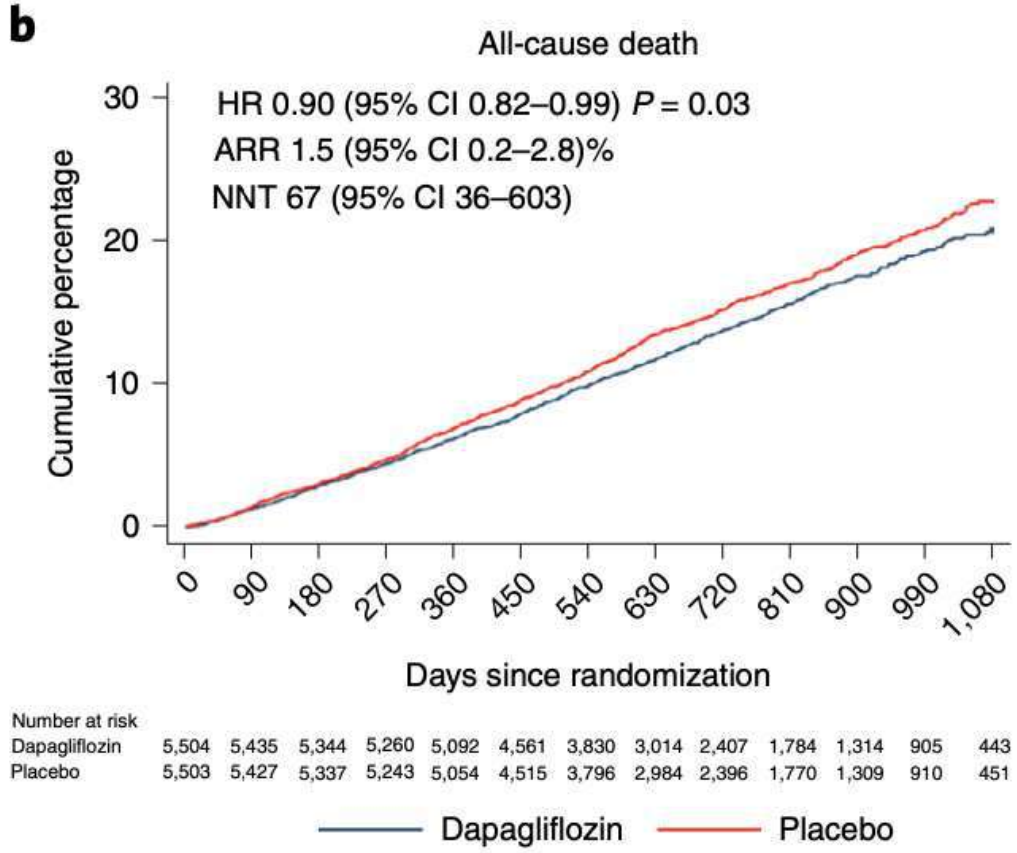


Verma S McMurray JJV Diabetologia. 2018; 61:2108–2117

Dapagliflozin across the range of ejection fraction in patients with heart failure: a patient-level, pooled meta-analysis of DAPA-HF and DELIVER

Across the range of LVEF dapagliflozin reduced the risk of all-cause and CV death: pooled analysis DAPA-HF and DELIVER



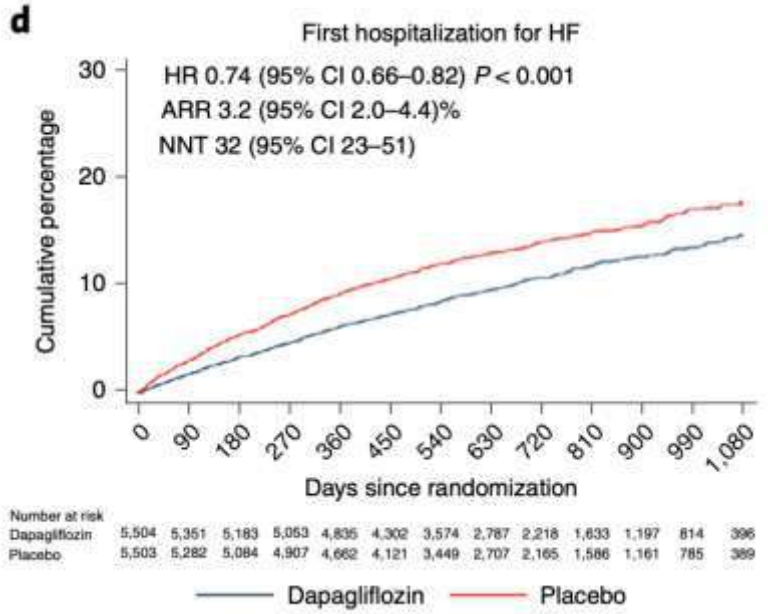


Jhund P et al. NATuRE MEDICINE | VOL 28 | 2022 | 1956–1964

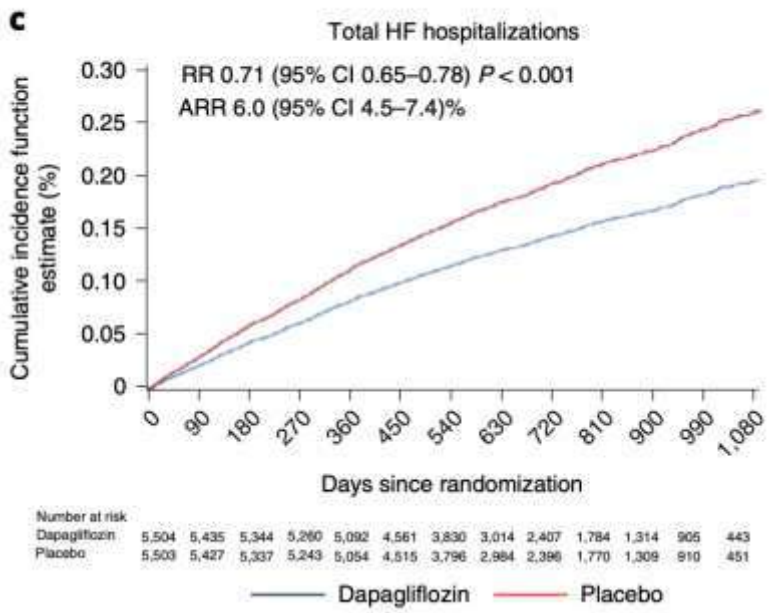
Dapagliflozin across the range of ejection fraction in patients with heart failure: a patient-level, pooled meta-analysis of DAPA-HF and DELIVER

Across the range of LVEF dapagliflozin reduced the risk of major CV complications: pooled analysis DAPA-HF and DELIVER

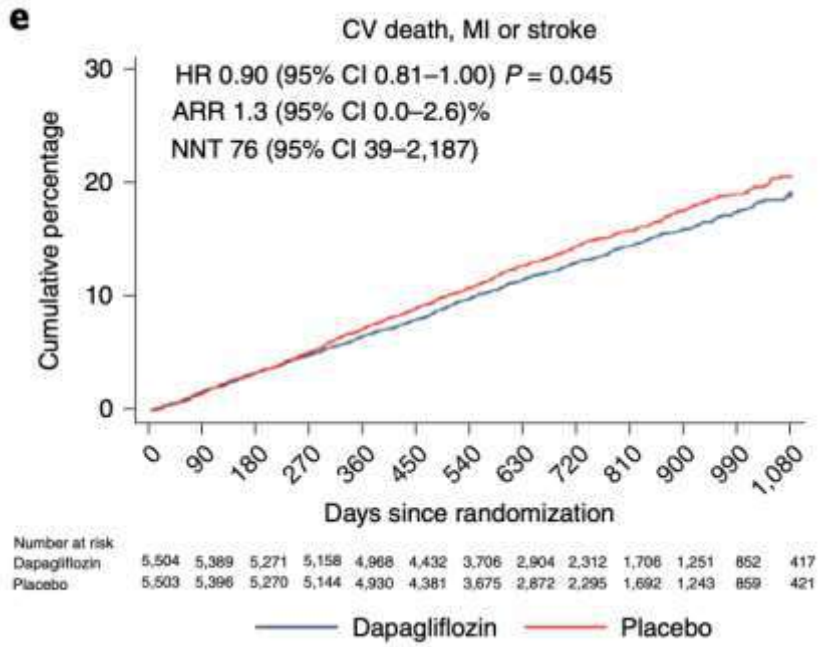
First HF hospitalisation



Total HF hospitalisation



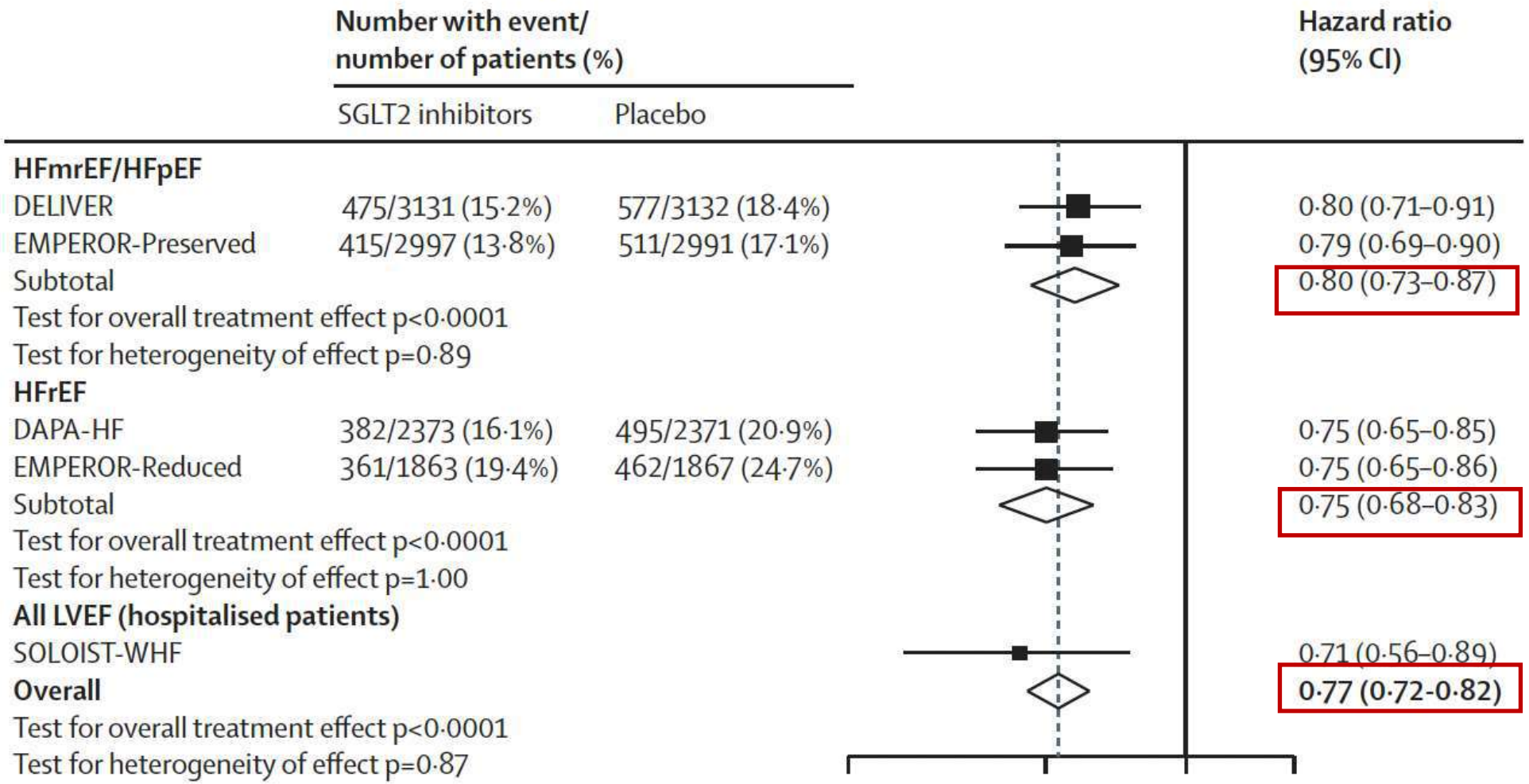
MACE



Jhund P et al. NATuRE MEDICINE | VOL 28 | 2022 | 1956–1964

SGLT-2 inhibitors in patients with heart failure: a comprehensive meta-analysis of five randomised controlled trials

Across all LVEF, 23% risk reduction in CV death/HF hospitalisation



Vaduganathan M et al. Lancet. 2022 Sep 3;400(10354):757-767

HEART FAILURE AND CARDIOMYOPATHIES

EDITOR'S CHOICE

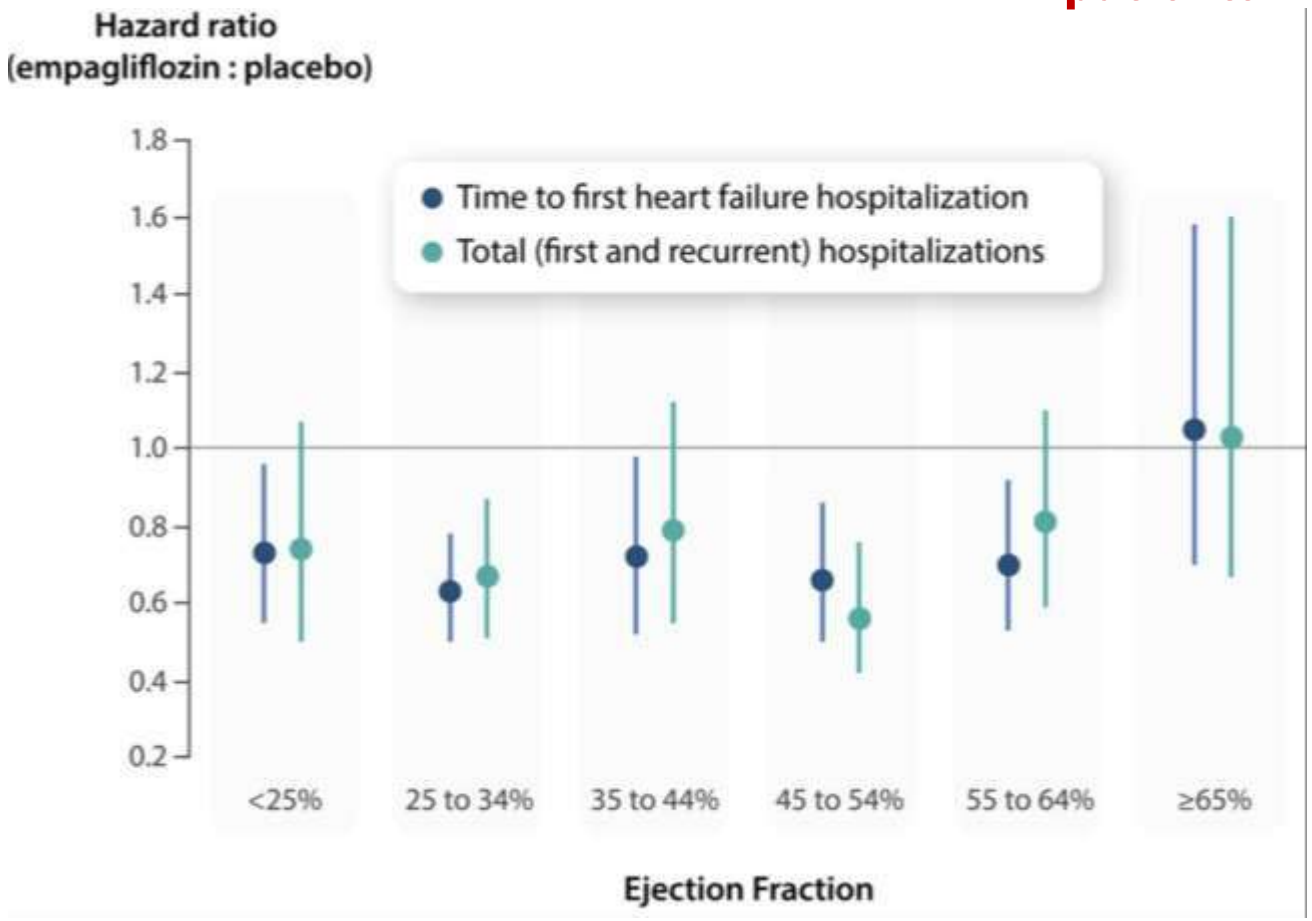
Effect of empagliflozin in patients with heart failure across the spectrum of left ventricular ejection fraction

Javed Butler and others

European Heart Journal, Volume 43, Issue 5, 1 February 2022, Pages 416–424,

Article highlight:

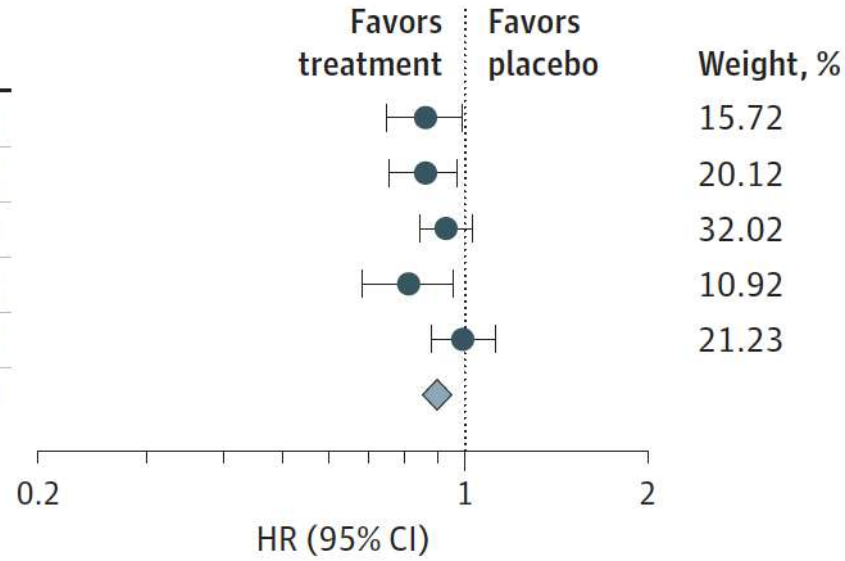
EMPEROR-pooled analysis: the magnitude of the effect of empagliflozin on HF outcomes and health status was similar across LVEF <25% to <65%, but it was attenuated in patients with LVEF ≥65%.



SGLT2 inhibitors: impact on major cardiovascular outcomes in type 2 diabetes

Meta-analysis, 4 different SGLT2 inhibitors (empagliflozin, canagliflozin, dapagliflozin, ertugliflozin), n=46,969 pts with T2DM (66% with CVD)

	Treatment		Placebo		
	No./total No.	Rate/1000 patient-years	No./total No.	Rate/1000 patient-years	Hazard ratio (95% CI)
EMPA-REG OUTCOME	490/4687	37.4	282/2333	43.9	0.86 (0.74-0.99)
CANVAS program	NA/5795	26.9	NA/4347	31.5	0.86 (0.75-0.97)
DECLARE-TIMI 58	756/8582	22.6	803/8578	24.2	0.93 (0.84-1.03)
CREDENCE	217/2202	38.7	269/2199	48.7	0.80 (0.67-0.95)
VERTIS CV	735/5499	40.0	368/2747	40.3	0.99 (0.88-1.12)
Fixed-effects model (Q = 5.22; *df* = 4; *P* = .27; I^2 = 23.4%)					0.90 (0.85-0.95)



Reduction in the risk of MACE without evidence of a considerable heterogeneity between the trials

McGuire DK, Shih WJ, Cosentino F et al. JAMA Cardiol. 2021;6(2):148-158.

SGLT-2 inhibitors in patients with heart failure: a comprehensive meta-analysis of five randomised controlled trials

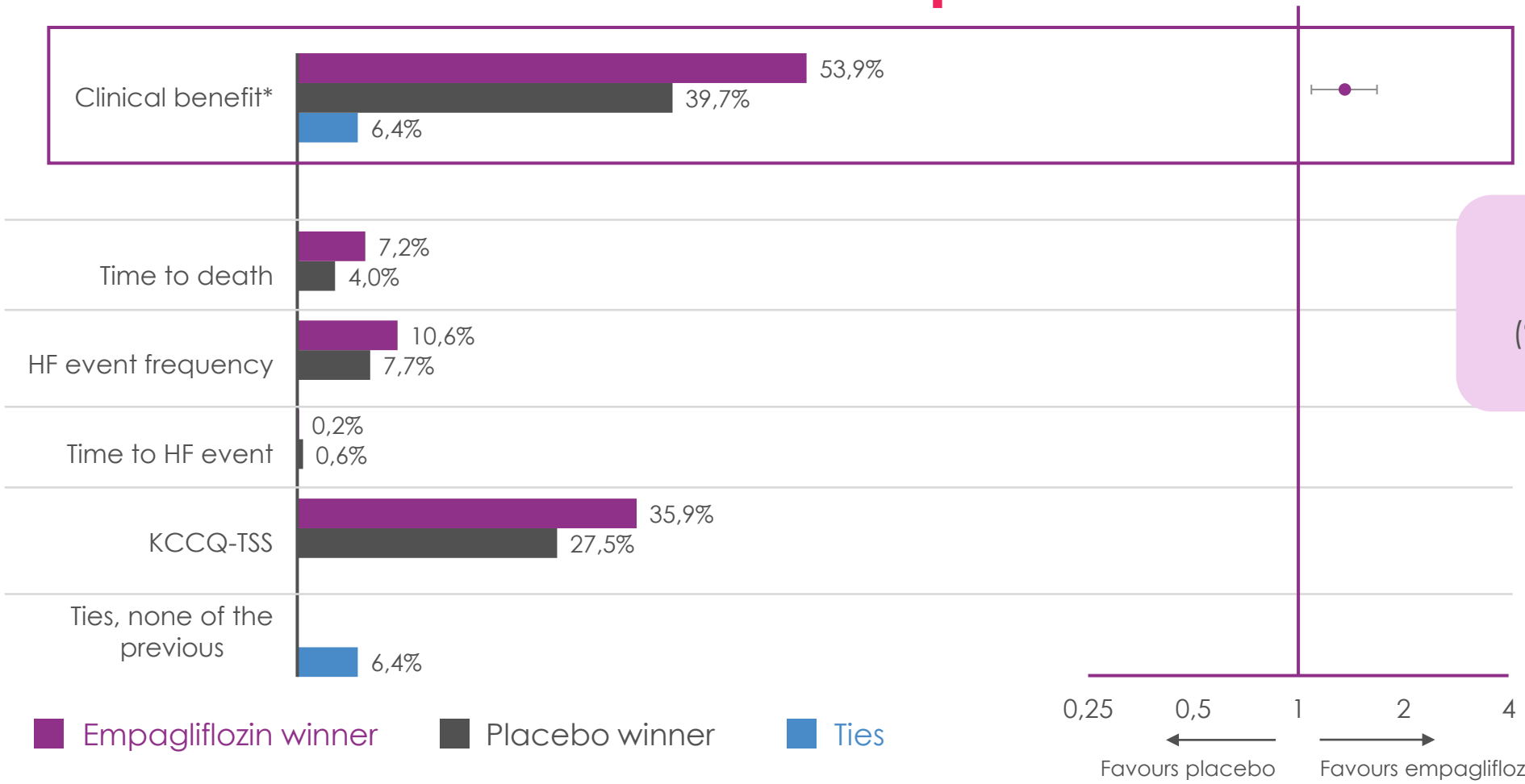
Favourable safety profile

	DELIVER		EMPEROR-Preserved	
	Dapagliflozin (n=3126)	Placebo (n=3127)	Empagliflozin (n=2996)	Placebo (n=2989)
Any serious adverse event	1361 (43·5%)	1423 (45·5%)	1436 (47·9%)	1543 (51·6%)
Amputation	19 (0·6%)	25 (0·8 %)	16 (0·5%)	23 (0·8%)
Diabetic ketoacidosis	2 (0·1%)	0 (0·0 %)	4 (0·1%)	5 (0·2%)
Hypoglycaemia	6 (0·2 %)	7 (0·2 %)	73 (2·4%)	78 (2·6%)
Renal	73 (2·3 %)	79 (2·5 %)	363 (12·1%)	384 (12·8%)

Vaduganathan M et al. Lancet. 2022 Sep 3;400(10354):757-767

EMPULSE

Empagliflozin is likely to produce a 36% more clinical benefit vs placebo



Stratified win ratio: 1.36
(95% CI: 1.09, 1.68)
p=0.0054

Death:
Empagliflozin: 4.2%
Placebo: 8.3%

HF event:
Empagliflozin: 10.6%
Placebo: 14.7%

Numbers reflect percentage of comparisons. For the components of the win ratio these numbers do not reflect randomized comparisons. *Composite of death, number of HFEs (including HHFs, urgent HF visits and unplanned outpatient visits), time to first HFE and ≥5 point difference in the KCCQ-TSS change from baseline after 90 days of treatment. CI, confidence interval; HF, heart failure; HFE, heart failure event; HHF, hospitalization for heart failure; KCCQ-TSS, Kansas City Cardiomyopathy Questionnaire Total Symptom Score. Voors AA *et al. Nat Med.* 2022;doi:10.1038/s41591-021-01659-1.

FAST TRACK CLINICAL RESEARCH

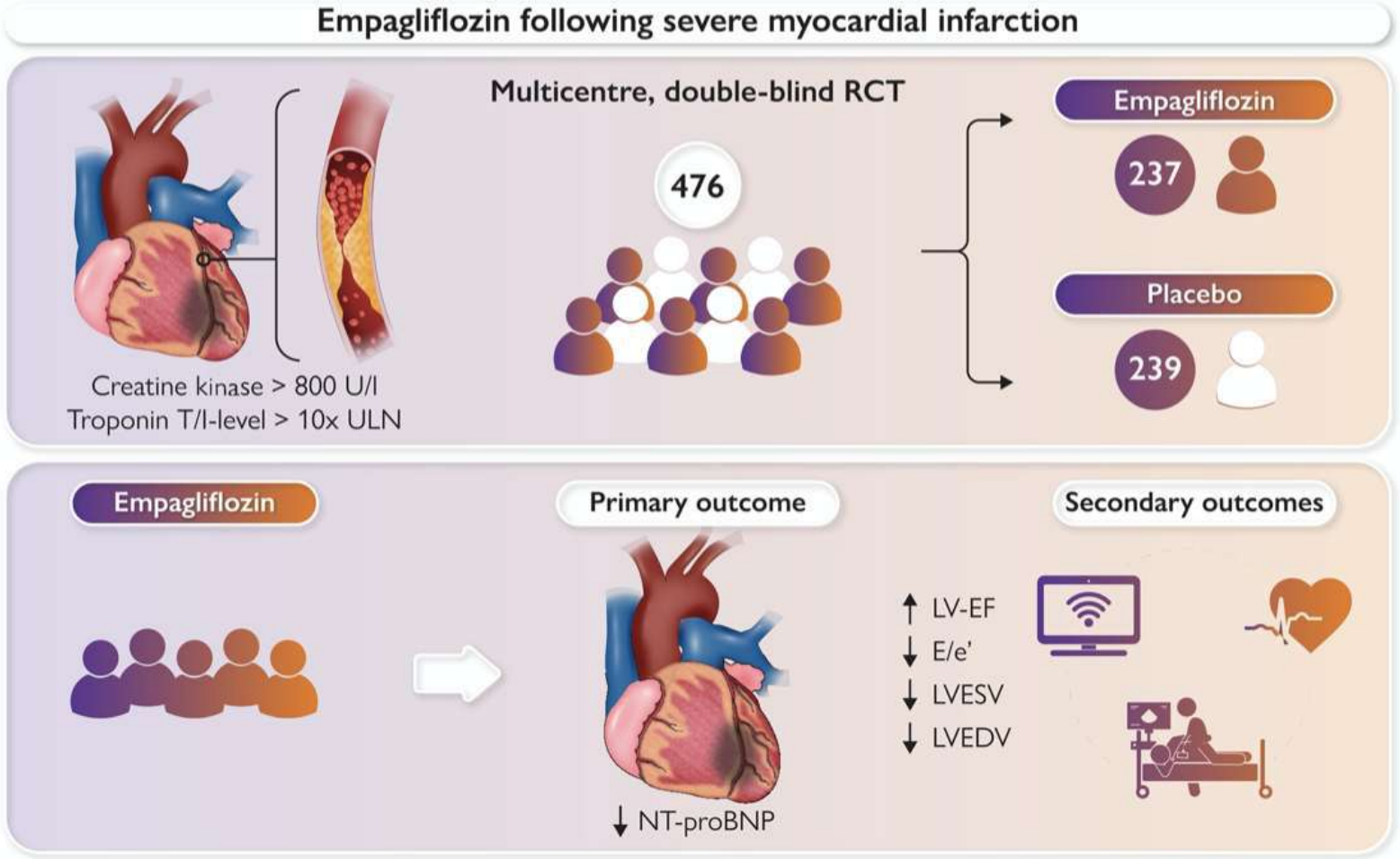
Empagliflozin in acute myocardial infarction: the EMMY trial

Dirk von Lewinski and others

European Heart Journal, Volume 43, Issue 41, 1 November 2022, Pages 4421–4432,

Article highlight:

Us of empagliflozin after AMI provides a significantly greater NT-proBNP reduction and an improvement in echocardiographic parameters.

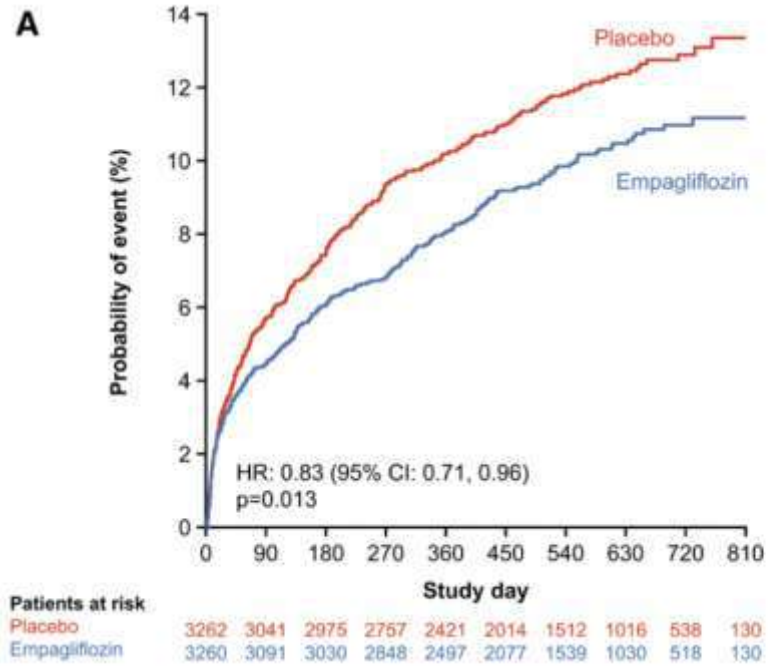


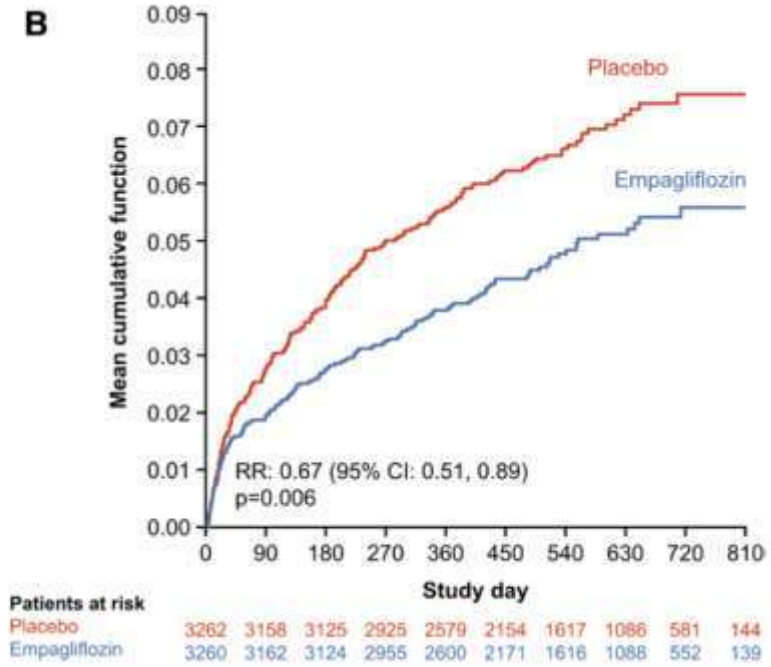
Empagliflozin and risk of HF hospitalisation after AMI

EMPACT-MI

- Empagliflozin vs. placebo
- 1 – 14 days after AMI, FUP 17.2 m
- Inclusion criteria:
  - AMI
  - LVEF ≤ 45% and/or
  - Signs/symptoms of congestion
  - + one or more risk augmenting factors.
- Primary endpoint first HF hospitalisation HF or all-cause death: HR, 0.90; 95% CI, 0.76–1.06; P=0.21

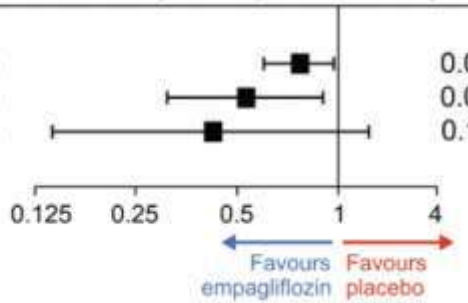
Lower risk of first and total HF hospitalisations





Lower risk of repeat HF hospitalisations

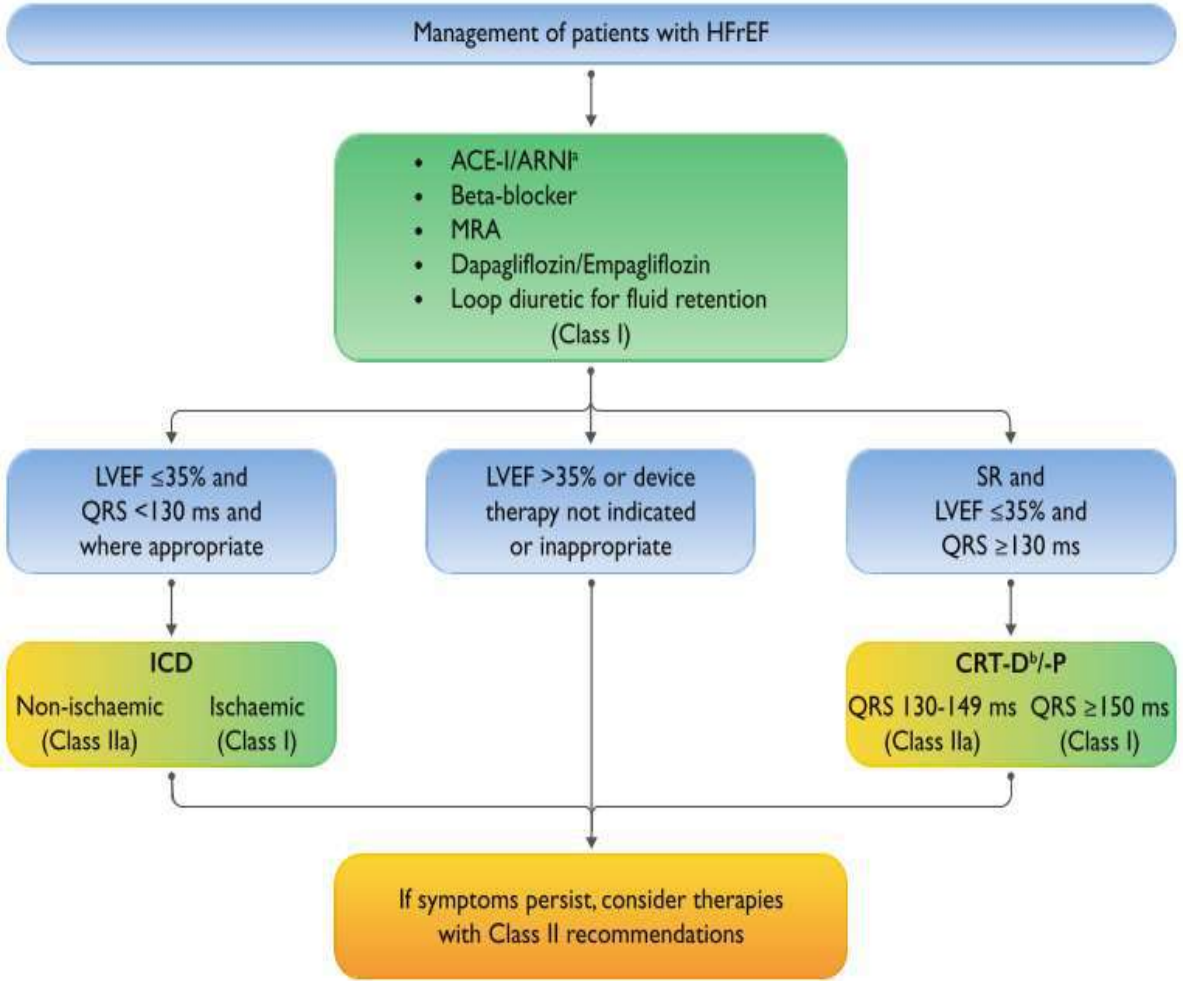
Variable	Number of patients (%) Empagliflozin (n=3260)	Placebo (n=3262)	Hazard ratio (95% CI)	p-value
Time to HHF by number of events (Wei-Lin-Weisfeld model)				
≥1 event	98 (3.0)	114 (3.5)	0.77 (0.60, 0.98)	0.032
≥2 events	15 (0.5)	27 (0.8)	0.53 (0.31, 0.91)	0.021
≥3 events	1 (<0.1)	9 (0.3)	0.42 (0.14, 1.24)	0.117
Test for consistency, *p*=0.290				



Hernandez A et al. Circulation. 2024;149:1627–1638

ESC
European Society of Cardiology

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



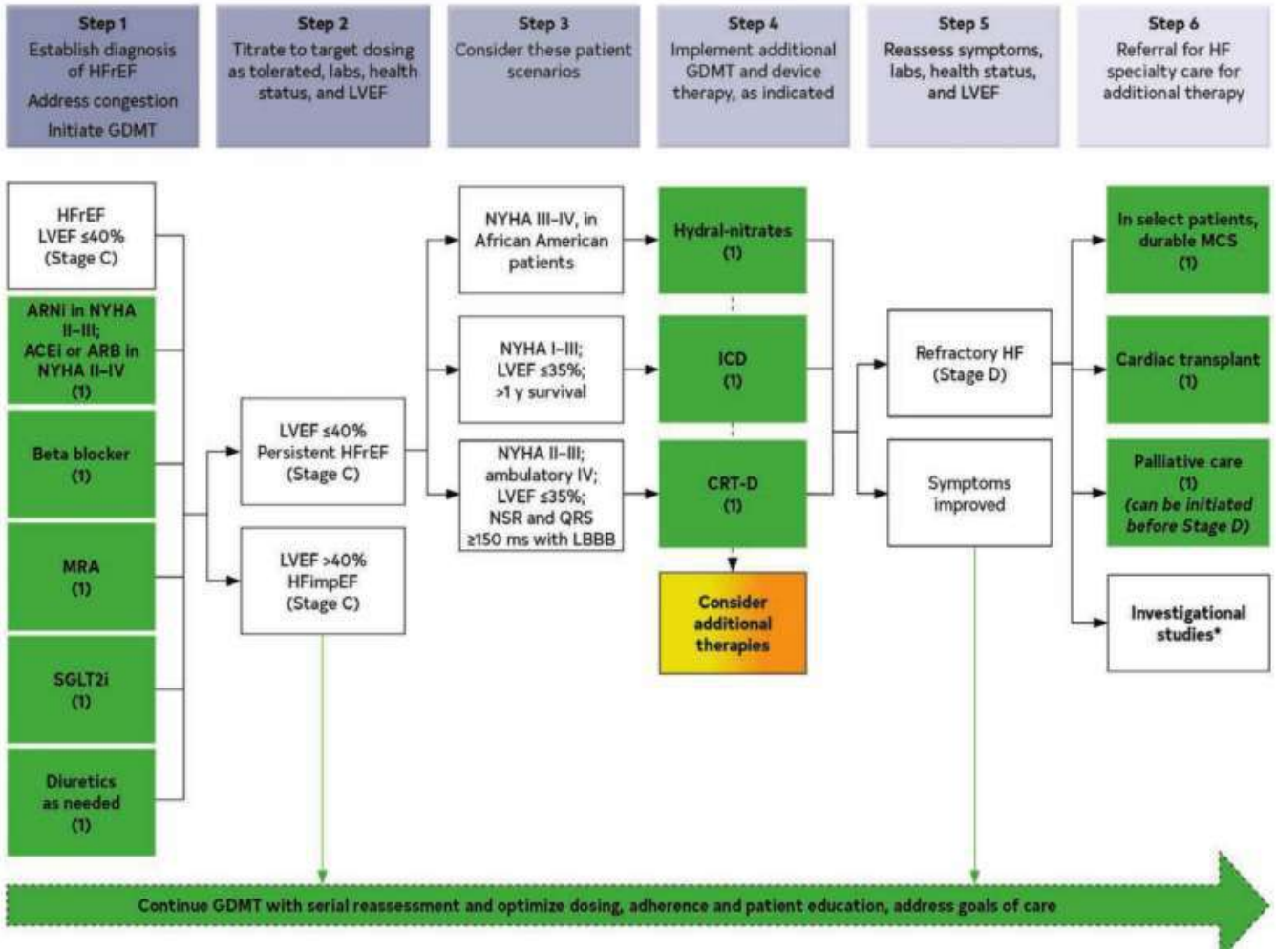
American Heart Association.

AMERICAN COLLEGE of CARDIOLOGY

HFSA
HEART FAILURE SOCIETY OF AMERICA

CLINICAL PRACTICE GUIDELINE: FULL TEXT

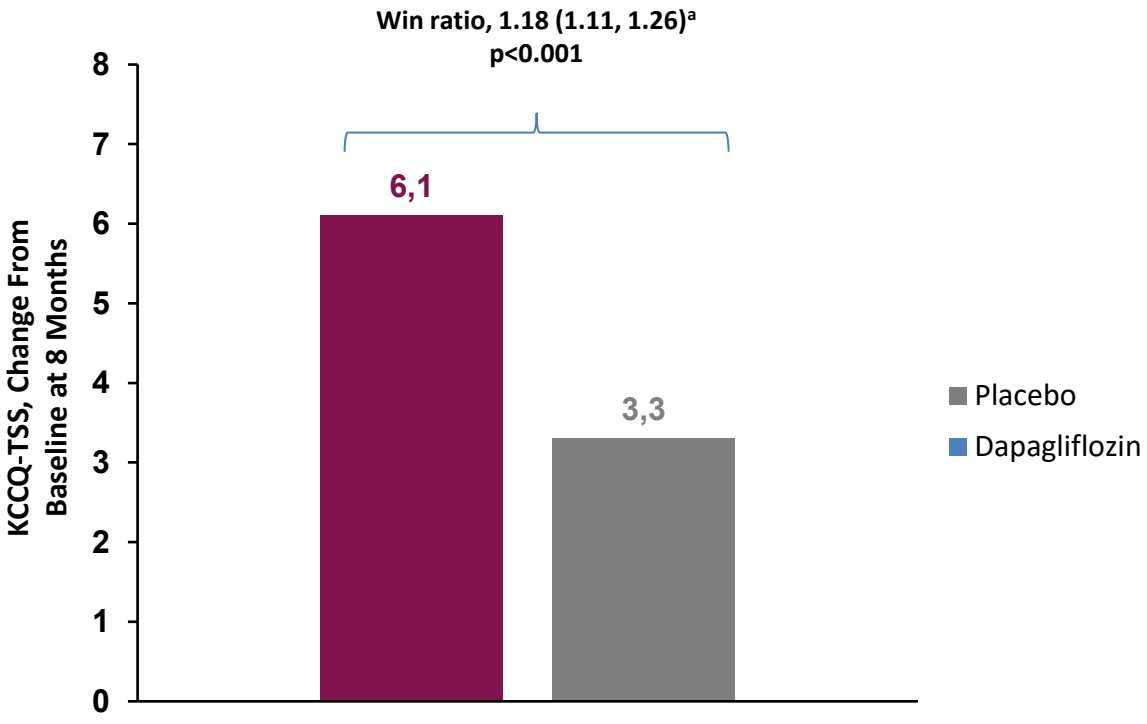
2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure



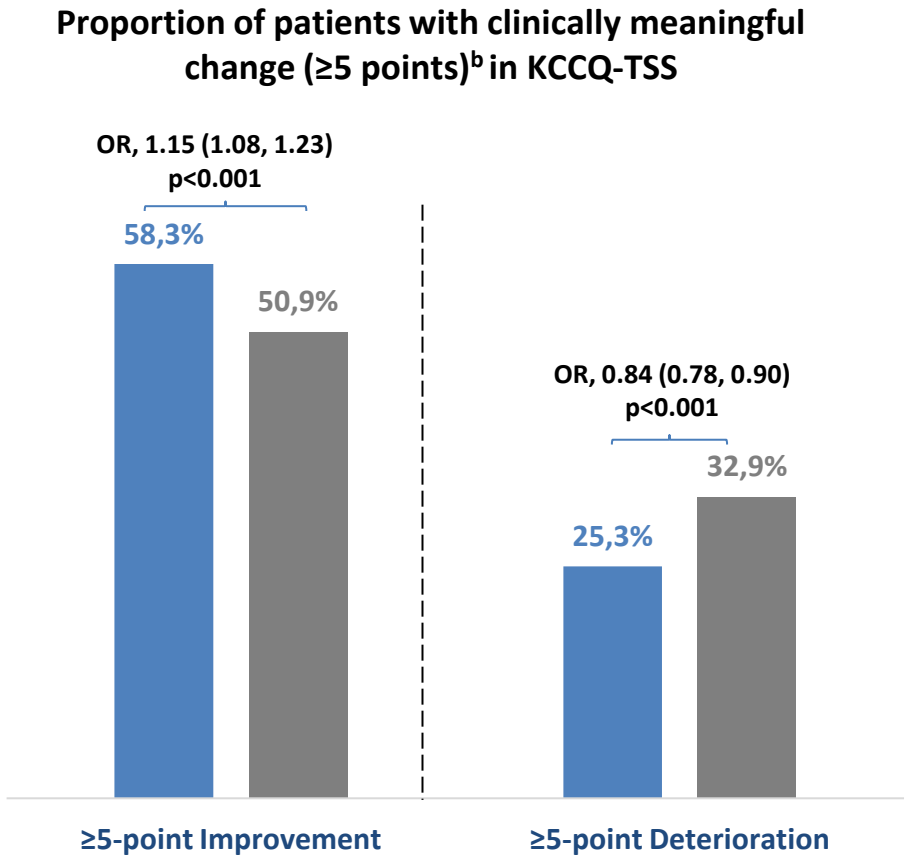
EHJ 2021;00:1-128; Circulation. 2022;145:00–00

Secondary Endpoint: Health Status Assessed By Change from Baseline in KCCQ-TSS at 8 Months

Patients on dapagliflozin were 18% more likely to have symptom benefit (improvement in KCCQ-TSS) compared to placebo



Symptom improvement was more common and deterioration was less common with dapagliflozin



[a]Win ratio >1 indicates superiority of dapagliflozin over placebo; [b]Taking account of death.
KCCQ-TSS = Kansas City Cardiomyopathy Questionnaire Total Symptom Score; OR = odds ratio.
McMurray JJV et al. *N Engl J Med*. 2019;381:1995-2008.

CLINICAL RESEARCH

EDITOR'S CHOICE

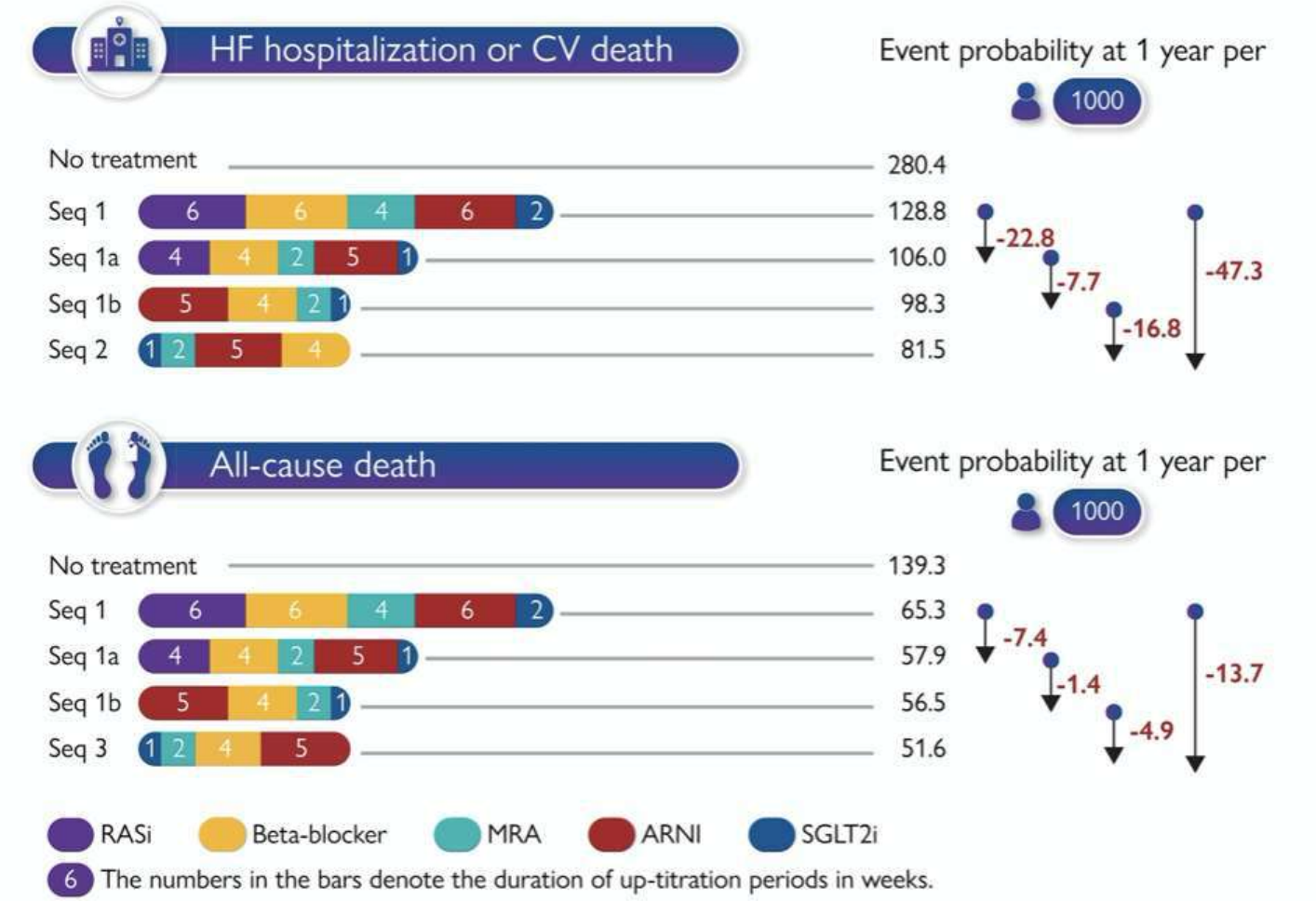
Accelerated and personalized therapy for heart failure with reduced ejection fraction

Li Shen and others

European Heart Journal, Volume 43, Issue 27, 14 July 2022, Pages 2573–2587,

Article highlight:

Accelerated up-titration and optimized ordering can prevent at least 14 deaths and 47 HF hospitalisations/CV deaths per 1000 treated HFrEF patients over the first 12 months.



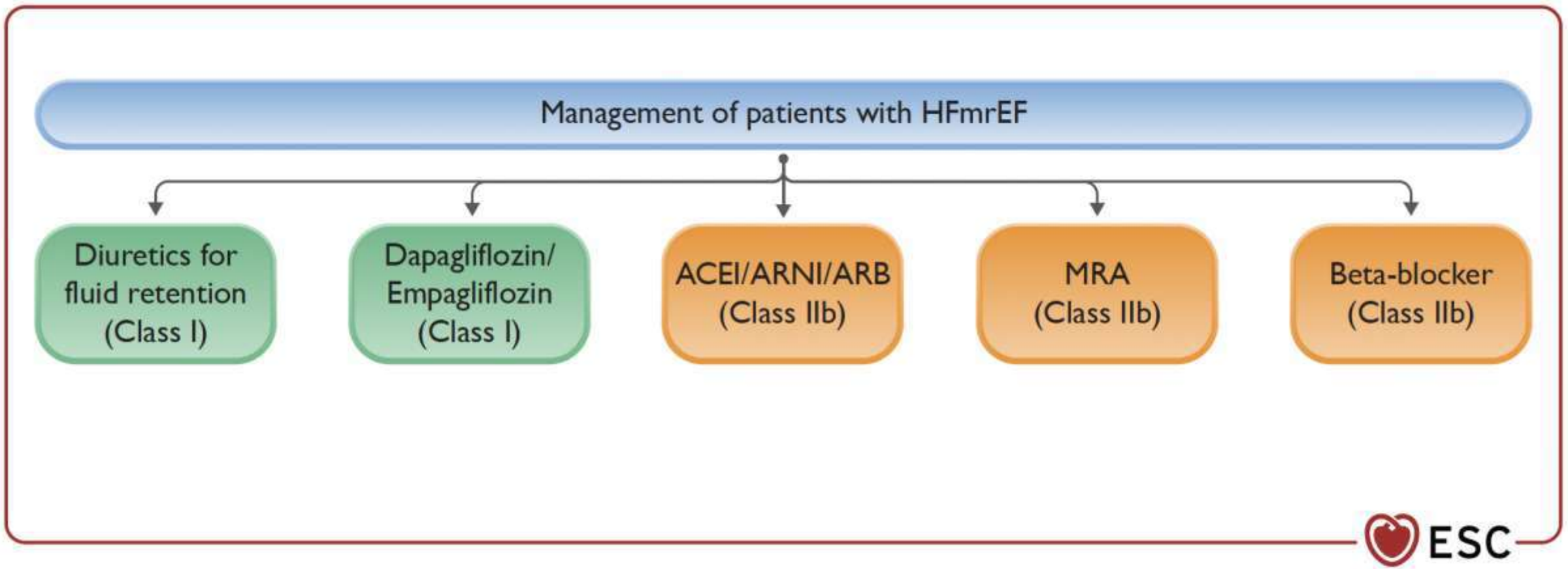
2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Recommendation for the treatment of patients with symptomatic HFmrEF

Recommendation	Class[a]	Level[b]
An SGLT2 inhibitor (dapagliflozin or empagliflozin) is recommended in patients with HFmrEF to reduce the risk of HF hospitalization or CV death.[c] [6,8]	I	A

Mc Donagh T et al. European Heart Journal (2023) 00, 1–13

2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure



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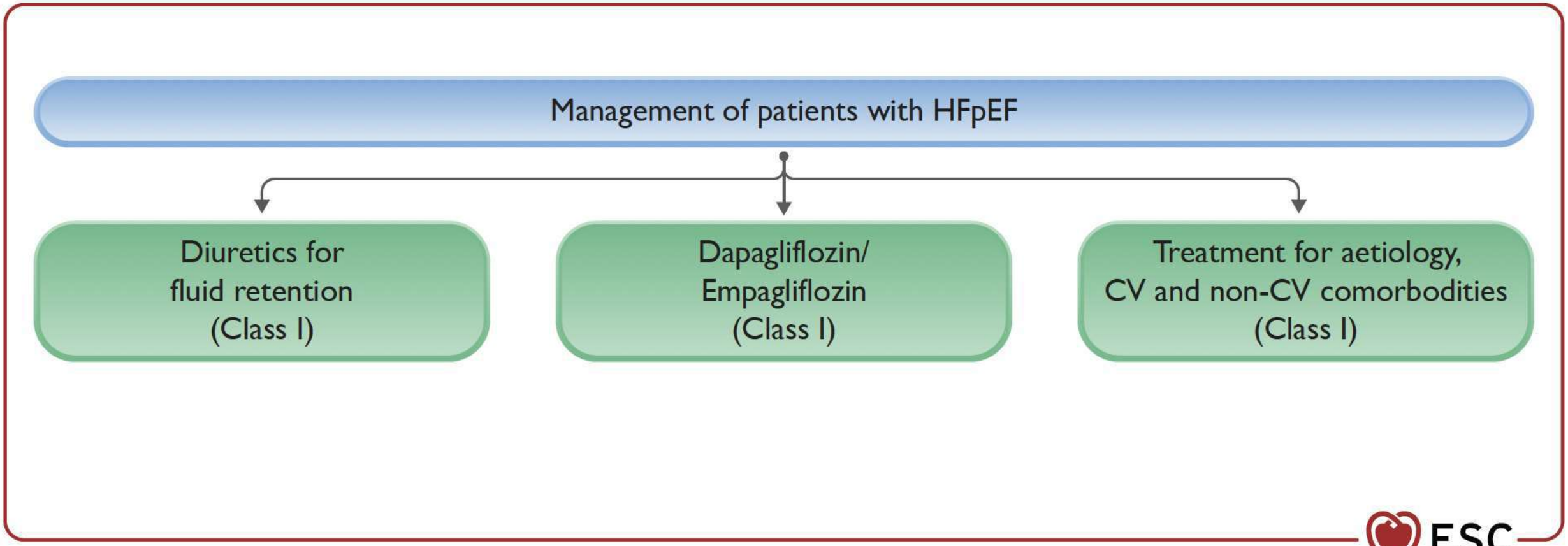


Mc Donagh T et al. European Heart Journal (2023) 00, 1–13

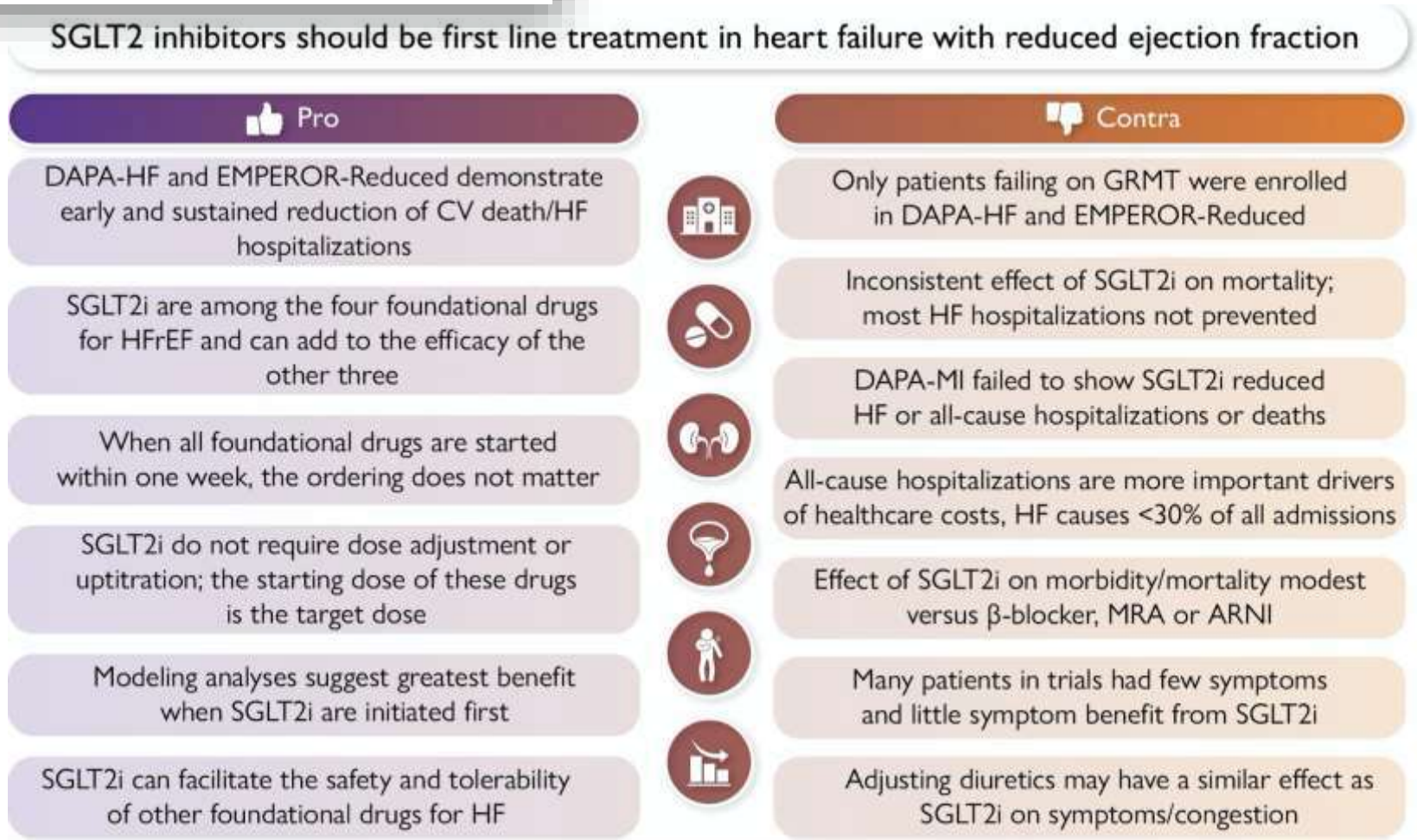
JOURNAL ARTICLE EDITOR'S CHOICE

Great Debate: SGLT2 inhibitors should be first-line treatment in heart failure with reduced ejection fraction FREE

Milton Packer, John G F Cleland, Johann Bauersachs ✉ Author Notes

EHJ
Great debate

- **With an introduction by J Bauersachs, M. Packer and J. Cleland discuss scientific evidence for the use of SGLT2 inhibitors as first-line HFrEF treatment.**

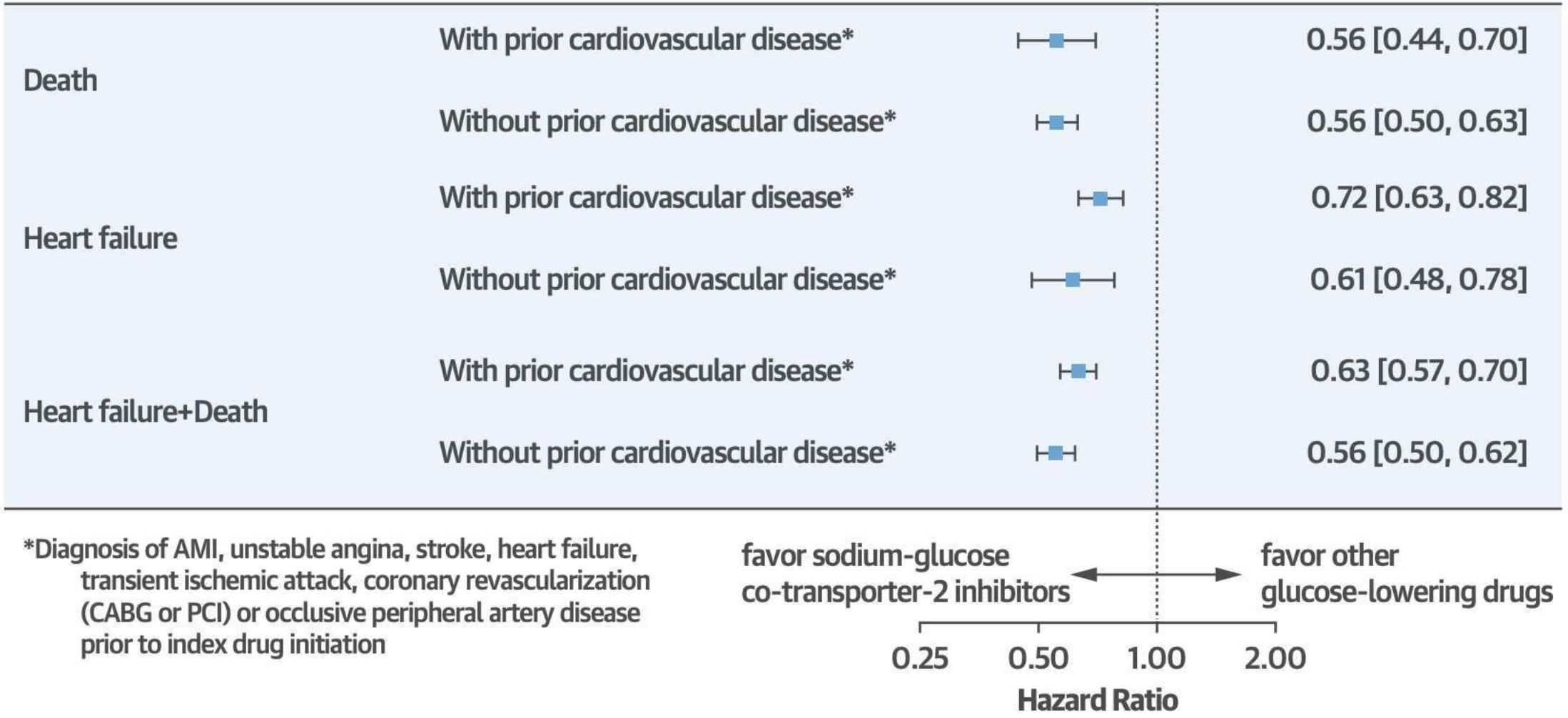


European Heart Journal, Volume 45, Issue 25, 1 July 2024, Pages 2186–2196

SGLT-2 Inhibitors and Cardiovascular Risk

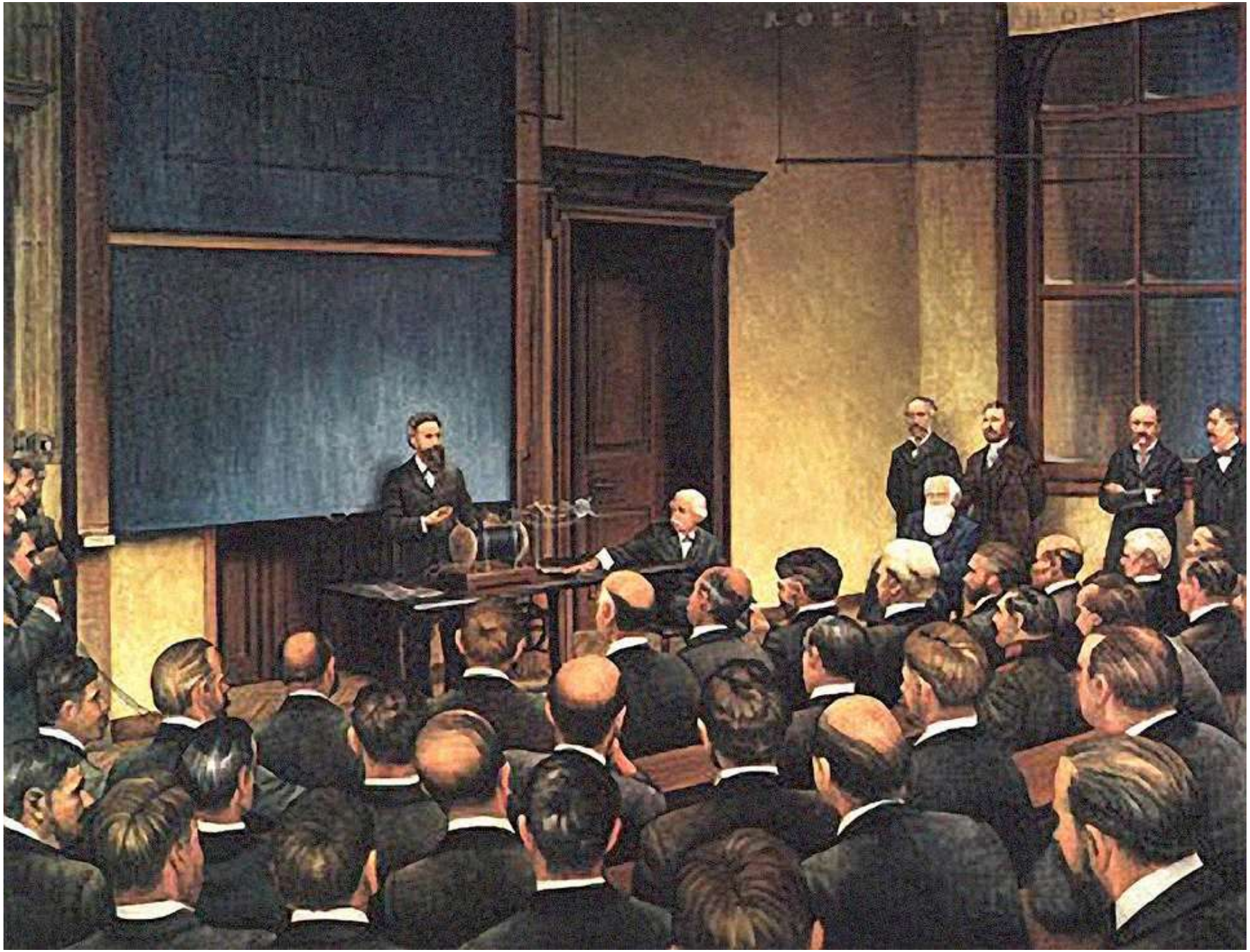
An Analysis of CVD-REAL

SGLT2I (empagliflozin) are effective even in patients without known VCD.



*Diagnosis of AMI, unstable angina, stroke, heart failure, transient ischemic attack, coronary revascularization (CABG or PCI) or occlusive peripheral artery disease prior to index drug initiation

Cavender, M.A. et al. J Am Coll Cardiol. 2018;71(22):2497-506.



- On the evening of January 23, 1896, Wilhelm Conrad Röentgen (University of Würzburg, Germany) ,
- demonstrated for the first time the use of x-ray photograph

- The news traveled fast, and within a year, x-ray equipment was being employed world-wide.

- Later research revealed many diagnostic and therapeutic applications of x-rays.

ESC Textbook of heart failure