

XI Reunión. Estado del Arte en  
**INSUFICIENCIA CARDIACA**

PRÁCTICA CLÍNICA Y MODELOS ORGANIZATIVOS

Sede: Hotel Meliá MaríaPita, A Coruña

**A CORUÑA** 27-28 SEPTIEMBRE 2024



XI Meeting. State of the Art in  
**HEART FAILURE**

CLINICAL PRACTICE AND ORGANIZATIONAL MODELS

Venue: Hotel Meliá MaríaPita, A Coruña

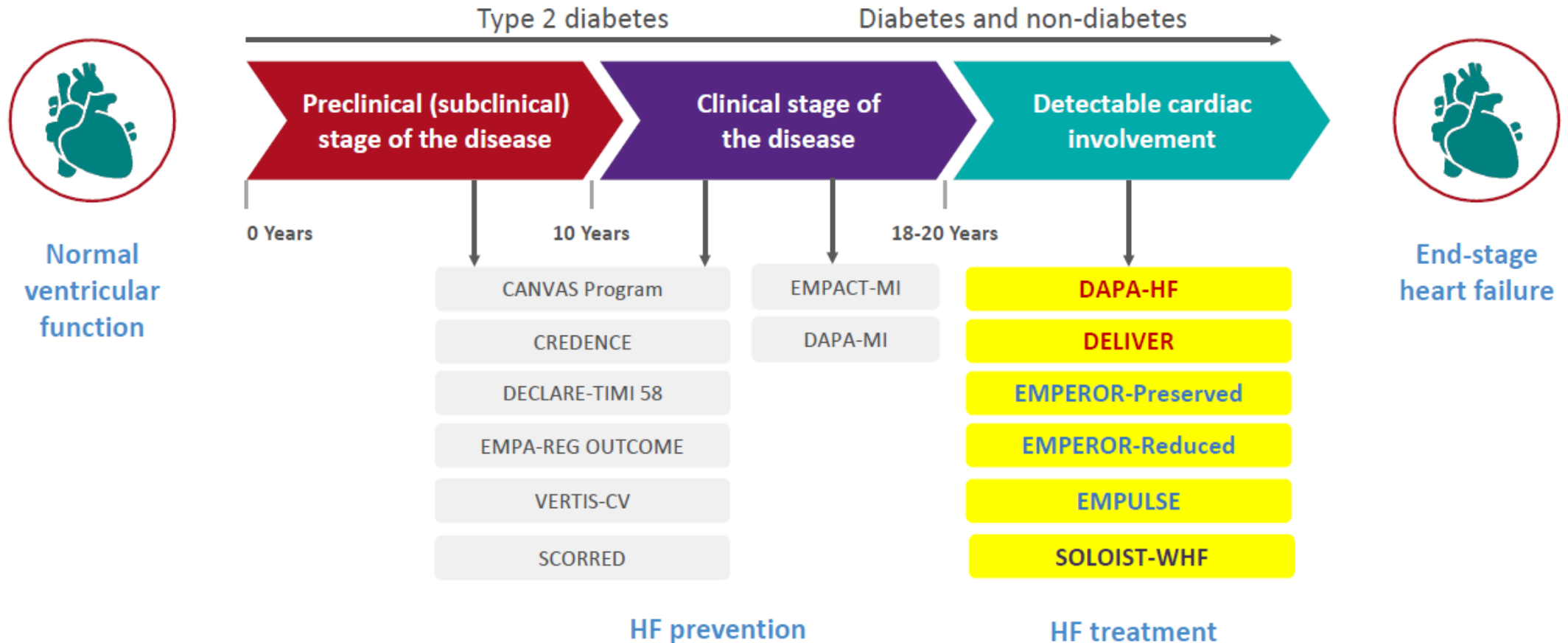
#ACoruñaHF2024

**A CORUÑA** 27-28 SEPTEMBER 2024

# SGLT2i in HF regardless of LVEF. Practical approach.

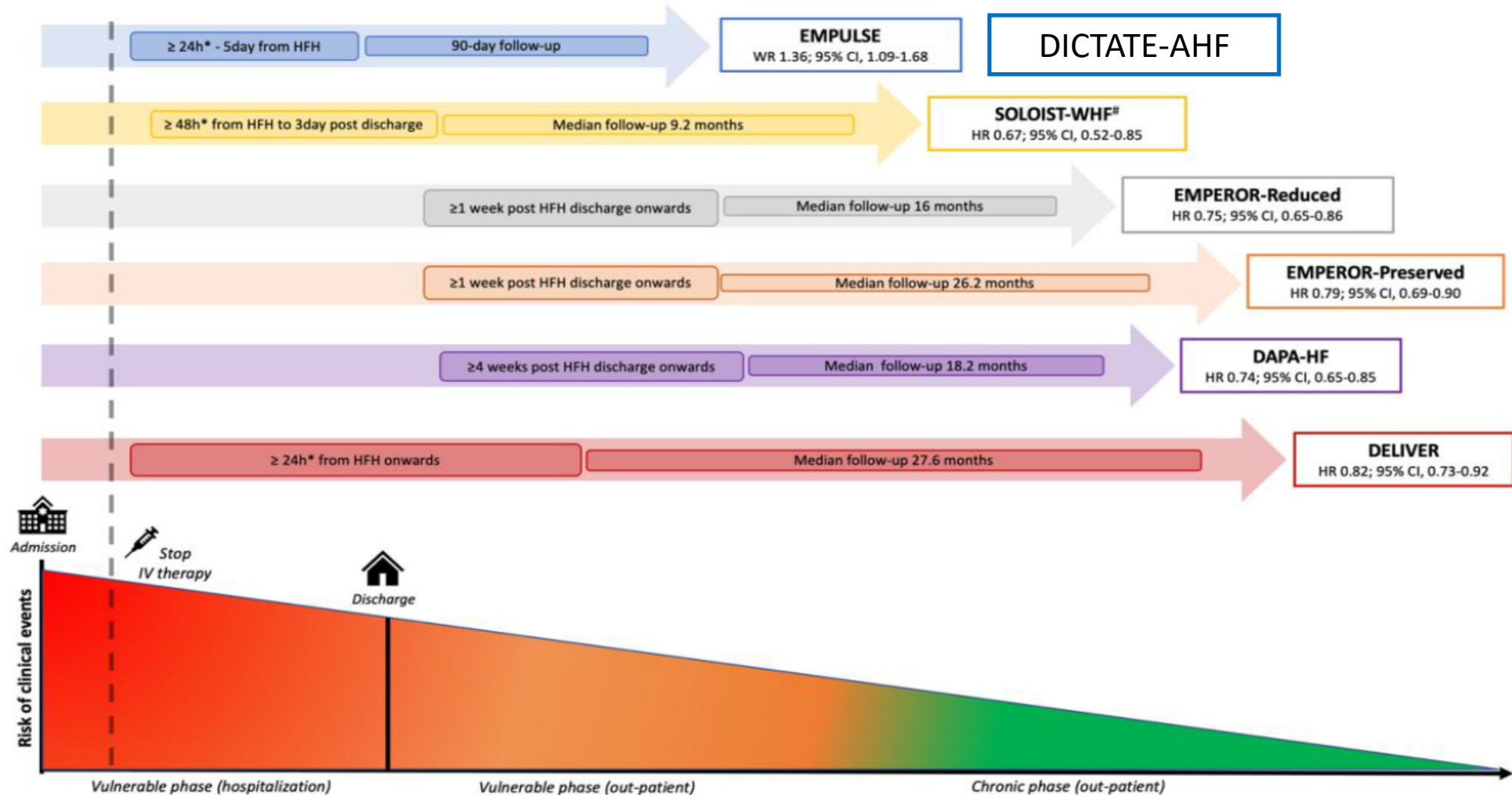
*Carolina Ortiz Cortés  
Cardiology Department  
Alcorcón Foundation Hospital, Madrid, Spain*

# Story of SGLT2i. Across the whole spectrum LVEF



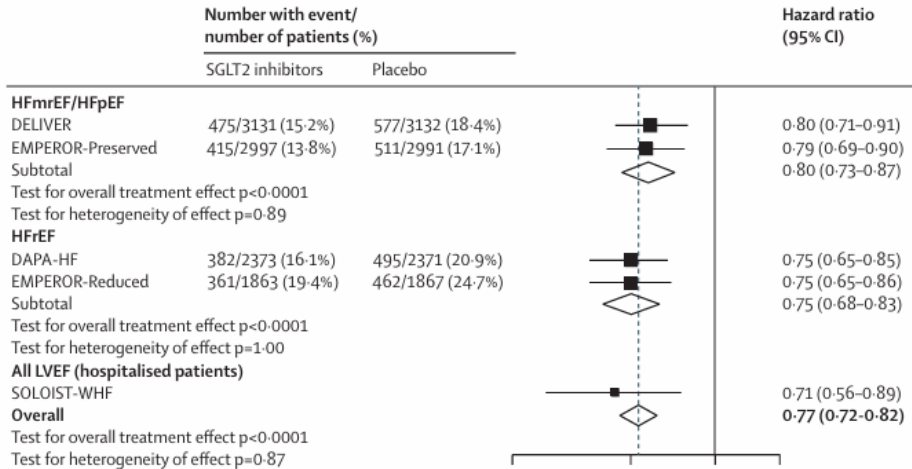
Adapted from Bhatt DL et al. *Cell Metab.* 2019;30:847-9

# SGLT2i in heart failure

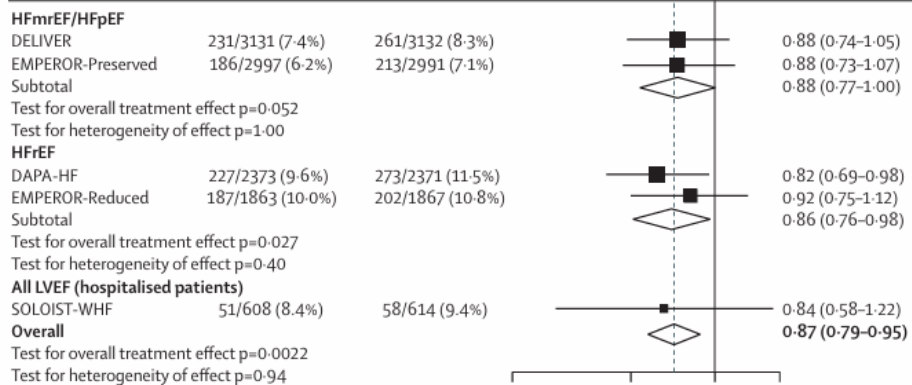


# Meta-Analysis of 5 LCT

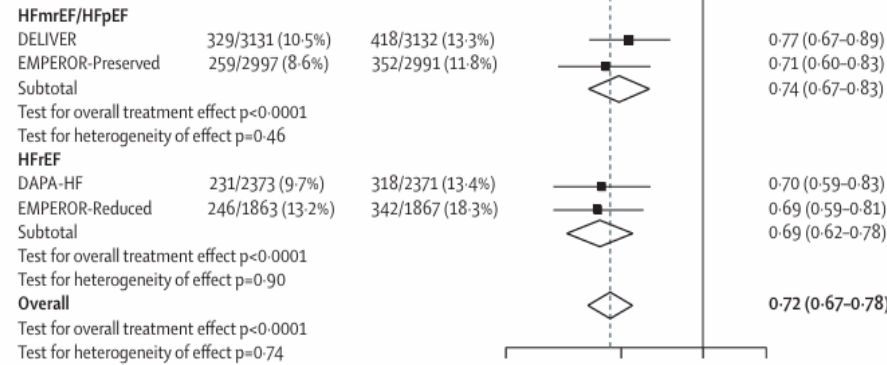
## Cardiovascular death or heart failure hospitalisation



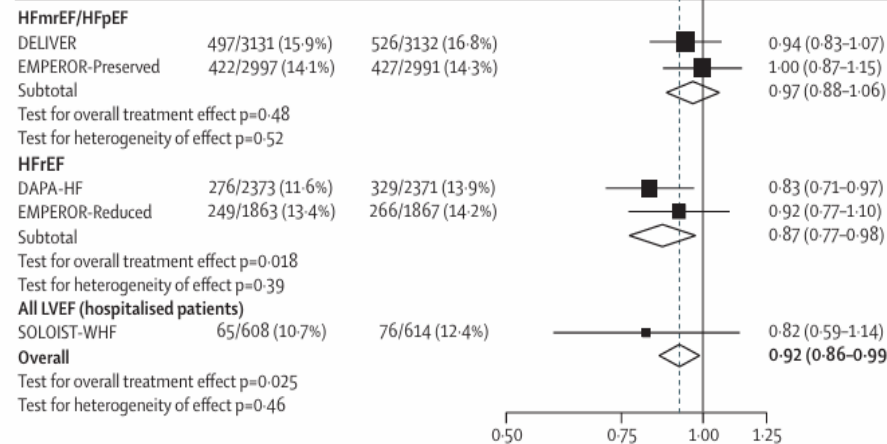
## Cardiovascular death



## Heart failure hospitalisation



## All-cause death



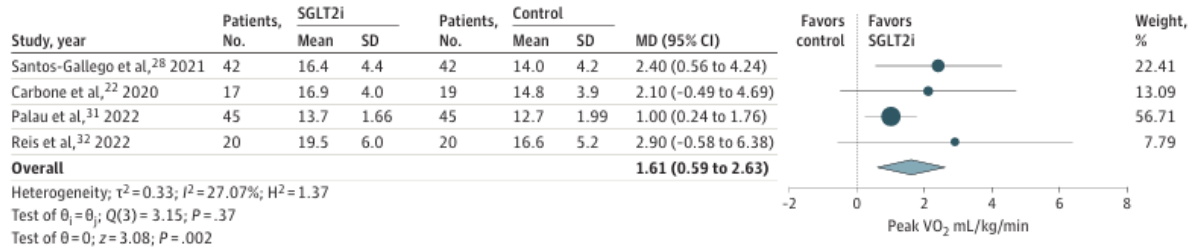
21.947 ptes SGLT2i reduced:

- ✓ 23 % the risk of composite CV death or HF hospitalization
- ✓ 13% of CV death
- ✓ 8% All-cause death
- ✓ 28% HF hospitalization

Lancet. 2022 Sep 3;400(10354):757-767

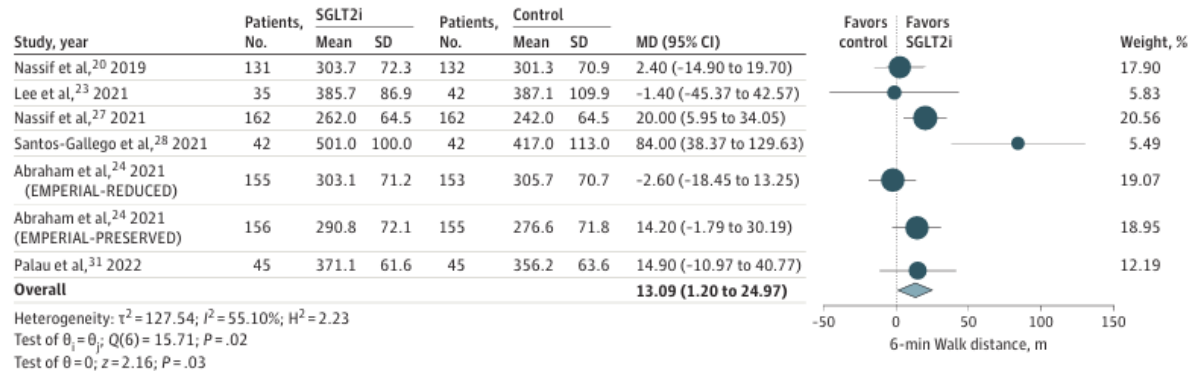
# SGLT2 in Functional Capacity and QoL

Figure 2. Association of SGLT2i Treatment With Peak Oxygen Consumption



Peak oxygen consumption (VO<sub>2</sub>) was measured as milliliters per kilogram per minute. MD indicates mean difference; SGLT2i, sodium glucose cotransporter-2 inhibitor.

Figure 3. Association of SGLT2i Treatment With 6-Minute Walk Distance



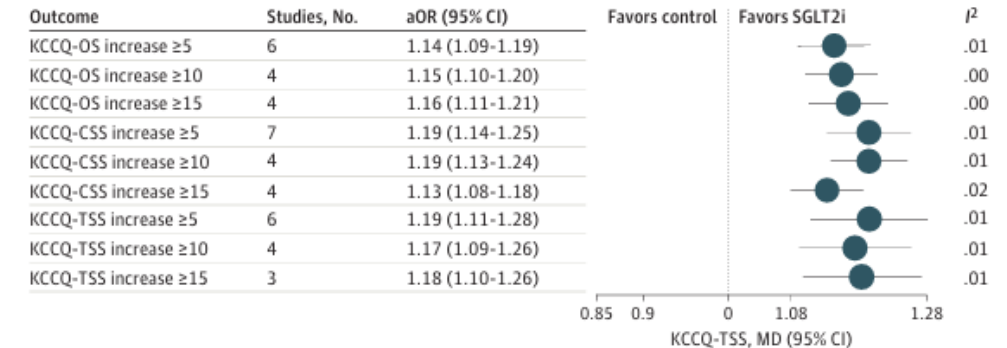
The 6-minute walk distance was measured in meters. MD indicates mean difference; SGLT2i, sodium glucose cotransporter-2 inhibitor.

JAMA Network | **Open**

Original Investigation | Cardiology

## SGLT2 Inhibitors, Functional Capacity, and Quality of Life in Patients With Heart Failure A Systematic Review and Meta-Analysis

Michael Gao, MD; Kirtipal Bhatia, MD; Arjun Kapoor, MD; Juan Badimon, PhD; Sean P. Pinney, MD; Donna M. Mancini, MD; Carlos G. Santos-Gallego, MD; Anuradha Lala, MD



JAMA Netw Open. 2024 Apr 1;7(4):e245135

# Broad population benefit

Secondary analysis of SGLT2 inhibitors trials in HF showed a clinical benefit regardless:

- ✓ age
- ✓ frailty
- ✓ aetiology
- ✓ body mass index(BMI)
- ✓ liver and renal function
- ✓ AF
- ✓ Background therapy
- ✓ severity of HFH

ESC Heart Fail. 2024 May 28.



# SGLT2i in patients with HF and chronic kidney disease

**Table 1** Effect of SGLT2 inhibitors on the change of renal function and kidney outcomes

	Mean baseline eGFR (mL/min/1.73 m <sup>2</sup> )	Mean absolute eGFR dip in the SGLT2 inhibitor group (mL/min/1.73 m <sup>2</sup> )	Mean slope of eGFR change (mL/min/1.73 m <sup>2</sup> per year)	Between-groups difference in eGFR slope (95% CI)	Renal adverse outcomes
DAPA-HF	66	-4.2	Dapagliflozin, -1.09 vs. placebo, -2.85	1.73 (1.10; 2.37) mL/min/1.73 m <sup>2</sup> per year; <i>P</i> < 0.001	HR 0.71 (95% CI, 0.44-1.16) <sup>a</sup>
EMPEROR-Reduced	62	-3.8	Empagliflozin, -0.55 vs. placebo, -2.28	1.73 (1.10; 2.37) mL/min/1.73 m <sup>2</sup> per year; <i>P</i> < 0.001	HR 0.50 (95% CI, 0.32-0.77) <sup>b</sup>
EMPEROR-Preserved	61	–	Empagliflozin, -1.25 vs. placebo, -2.62	1.36 (1.06; 1.66) mL/min/1.73 m <sup>2</sup> per year; <i>P</i> < 0.001	HR 0.95 (95% CI, 0.73-1.24) <sup>b</sup>
DELIVER	61	- 3.7	Dapagliflozin, 1.0 vs. placebo, -1.5	1.4 (1.0; 1.8) mL/min/1.73 m <sup>2</sup> per year; <i>P</i> < 0.001	HR 1.08, (95% CI, 0.79-1.49) <sup>a</sup>
SOLOIST-WHF	50 (median)	–	Sotagliflozin, -0.34 vs. placebo, -0.18	-0.16 (-1.30; 0.98) mL/min/1.73 m <sup>2</sup> per year; <i>P</i> = NS	–
EMPULSE	52 (median)	–	–	–	Not possible to fit a model due to low event rate <sup>c</sup>

The dash stands for not reported or not investigated data.

Abbreviations: CI, confidence interval; eGFR, estimated glomerular filtration rate; NS, non-significant; HR, hazard ratio.

<sup>a</sup>Composite of sustained reduction of ≥50% in the eGFR for ≥28 days or sustained eGFR < 15 mL/min/1.73m<sup>2</sup> for ≥28 days or long-term dialysis treatment or renal transplantation or death from renal causes.

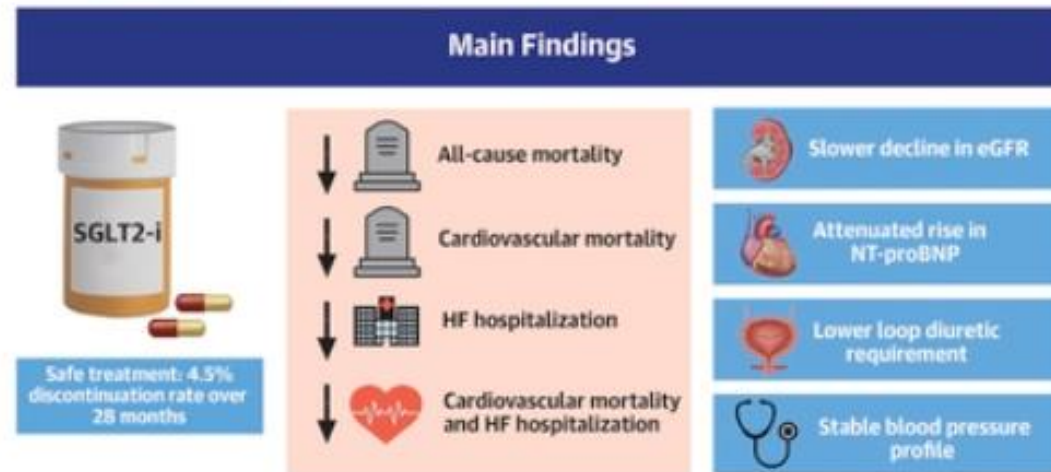
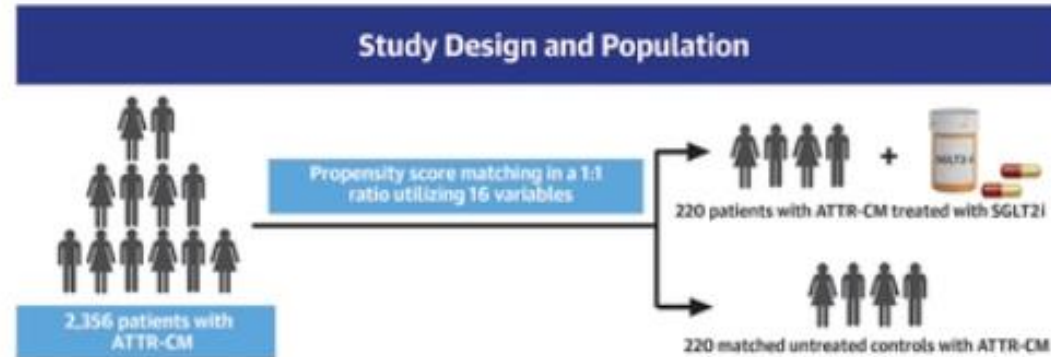
<sup>b</sup>Composite of ≥40% sustained decline eGFR or end-stage renal disease (defined as: 1) chronic dialysis; 2) renal transplantation; or 3) a sustained eGFR <15 mL/min/1.73 m<sup>2</sup> [for patients with baseline eGFR ≥30] or sustained eGFR < 10 mL/min/1.73m<sup>2</sup> [for patients with baseline eGFR <30 mL/min/1.73 m<sup>2</sup>]).

<sup>c</sup>Occurrence of chronic dialysis or renal transplant or sustained reduction of ≥40% eGFR or sustained eGFR <15 mL/min/1.73 m<sup>2</sup> [for patients with baseline eGFR ≥30] or sustained eGFR < 10 mL/min/1.73 m<sup>2</sup> [for patients with baseline eGFR <30 mL/min/1.73 m<sup>2</sup>]).

American Journal of Cardiovascular Drugs (2023) 23:609–621

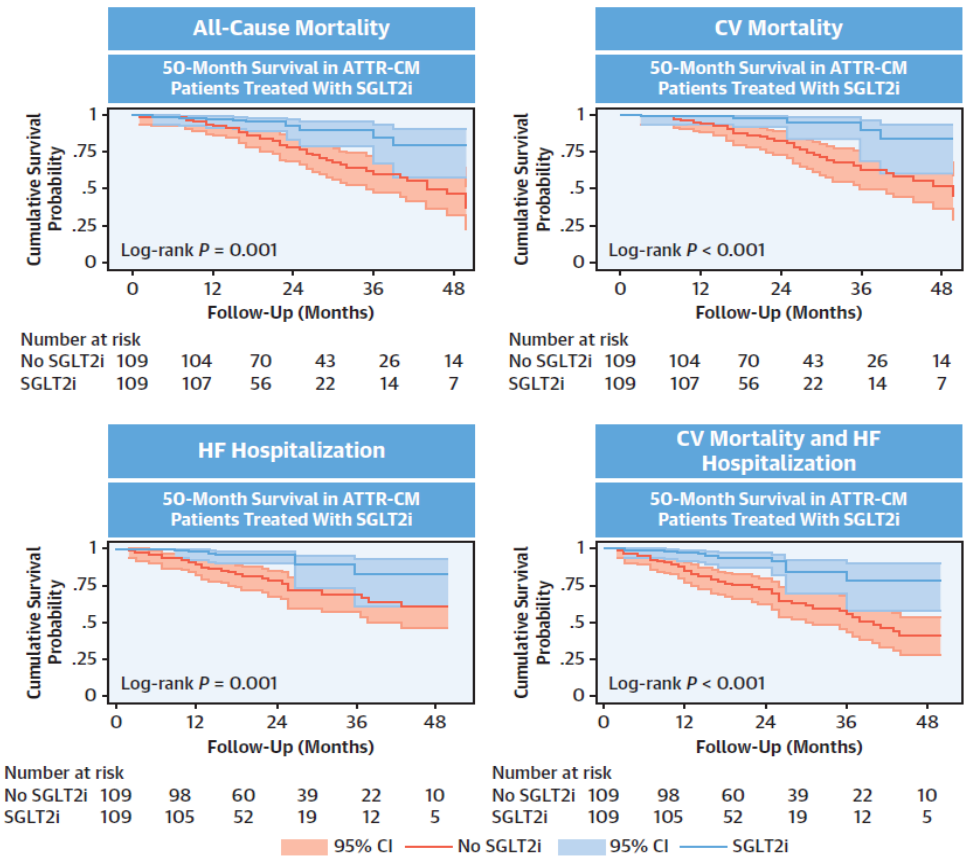
# SGLT2 in TTR amyloid

## CENTRAL ILLUSTRATION: Sodium-Glucose Cotransporter 2 Inhibitors in Transthyretin Amyloid Cardiomyopathy



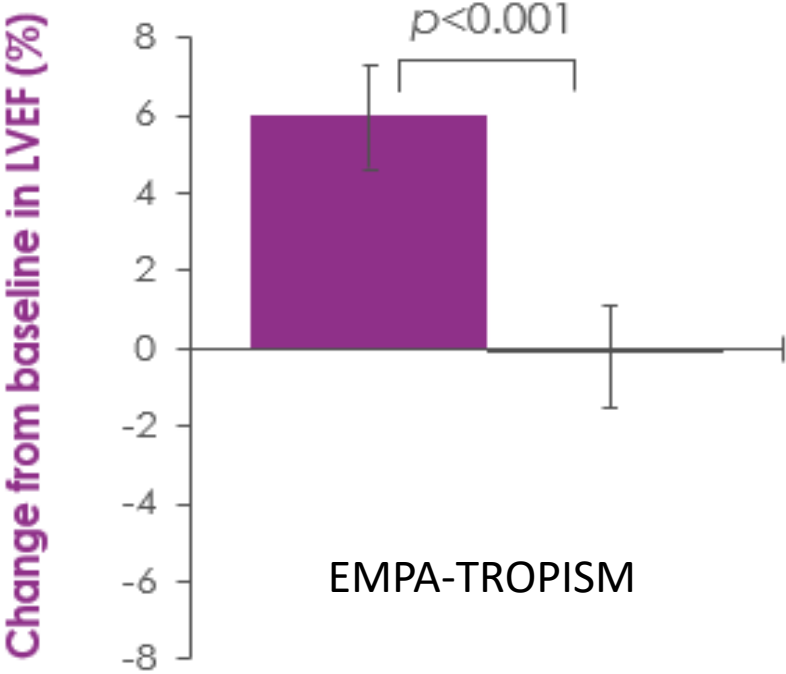
Porcari A, et al. J Am Coll Cardiol. 2024;83(24):2411-2422.

FIGURE 3 Survival and HF Hospitalizations in ATTR-CM According to SGLT2i Treatment



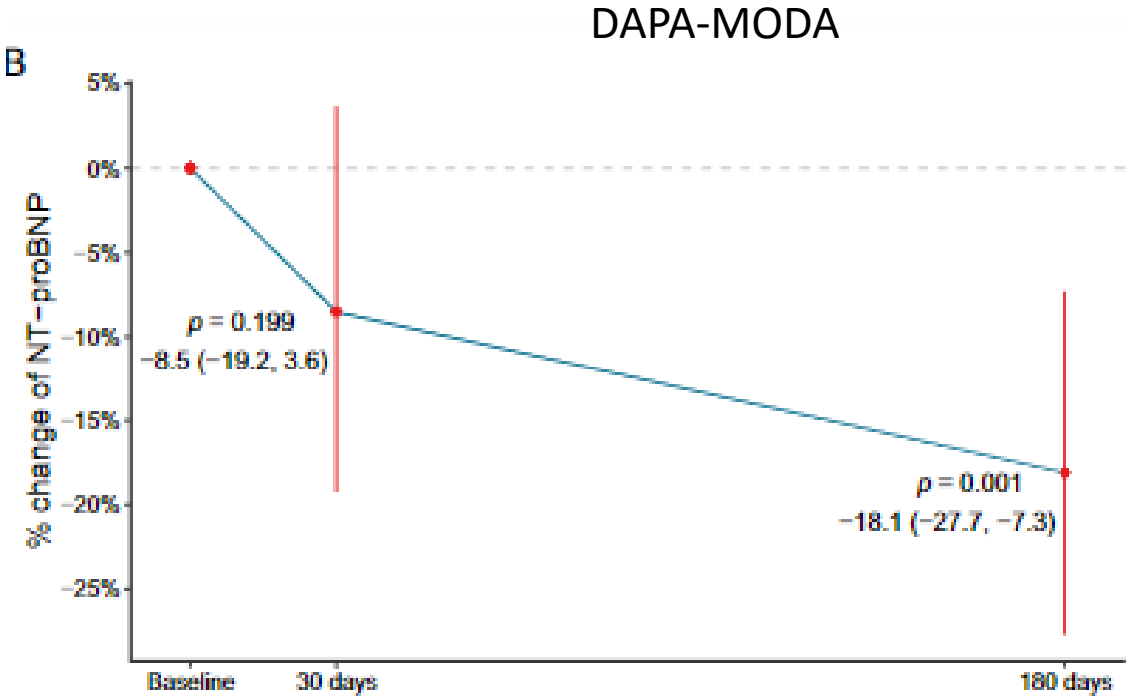


# Remodeling with iSGLT2



Values at:

Baseline	36.2±8.2	36.5±8.0
6 months	42.2±9.2	36.3±8.5



Santos-Gallego CG et al. *J Am Coll Cardiol.* 2021;77:243; Pascual Figal .D *Eur J Heart Fail.* 2023. doi: 10.1002/ejhf.2884.

# SGLTi in first step in all Guidelines

## Management of HFrEF

To reduce mortality - for all patients

ACE-I/ARNI

BB

MRA

SGLT2i

To reduce HF hospitalization/mortality - for selected patients

Volume overload

Diuretics

SR with LBBB  $\geq 150$  ms

CRT-P/D

SR with LBBB 130–149 ms or non LBBB  $\geq 150$  ms

CRT-P/D

Ischaemic aetiology

ICD

Non-ischaemic aetiology

ICD

Atrial fibrillation

Anticoagulation

Atrial fibrillation

Digoxin

PVI

Coronary artery disease

CABG

Iron deficiency

Ferric carboxymaltose

Aortic stenosis

SAVR/TAVI

Mitral regurgitation

TEE MV Repair

Heart rate SR  $>70$  bpm

Ivabradine

Black Race

Hydralazine/ISDN

ACE-I/ARNI intolerance

ARB

For selected advanced HF patients

Heart transplantation

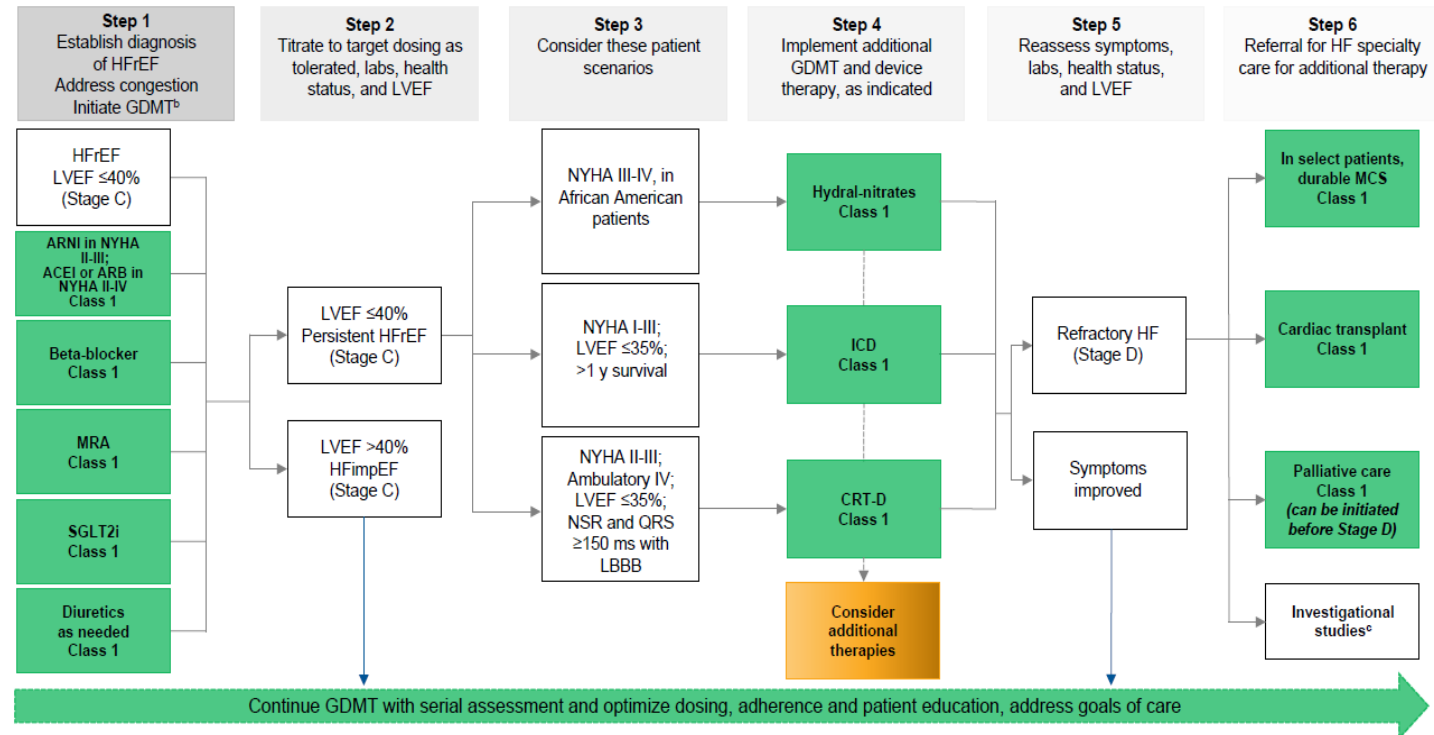
MCS as BTT/BTC

Long-term MCS as DT

To reduce HF hospitalization and improve QOL - for all patients

Exercise rehabilitation

Multi-professional disease management



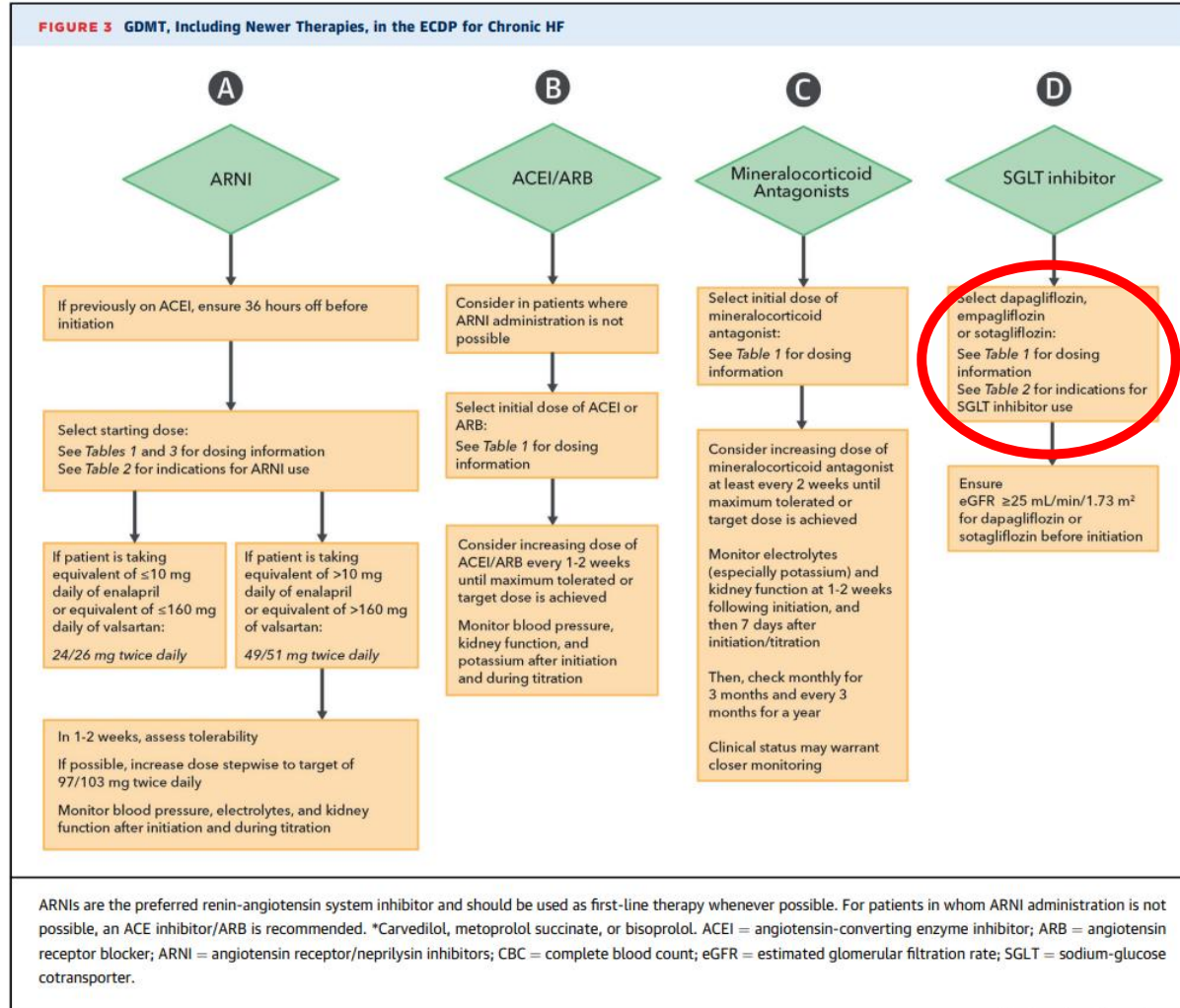
Eur J Heart Fail. 2022 Jan;24(1):4-131

Circulation. 2022 May 3;145(18):e1033.

#ACORUÑAHF2024



# SGLTi first step in all HF patients. Guidelines



Continued on the next page

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PUBLISHED BY ELSEVIER

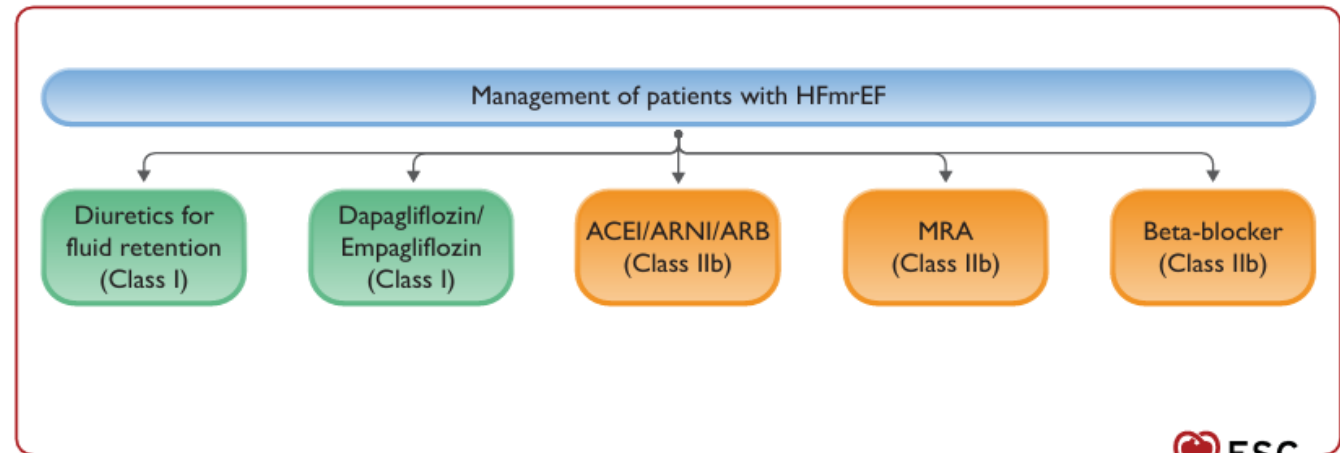
VOL. ■, NO. ■, 2024

EXPERT CONSENSUS DECISION PATHWAY

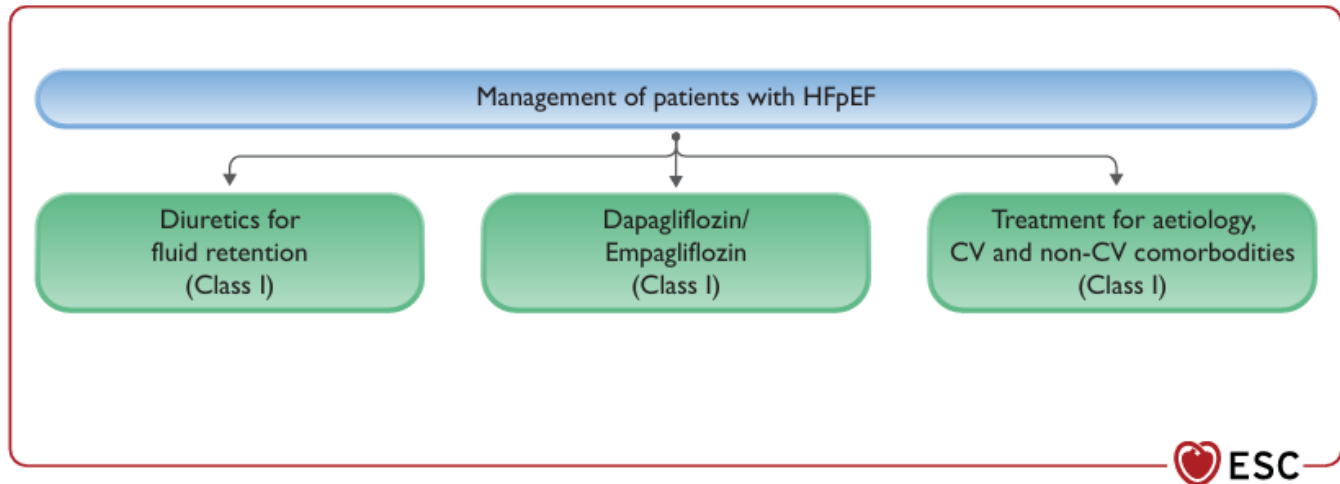
**2024 ACC Expert Consensus Decision Pathway for Treatment of Heart Failure With Reduced Ejection Fraction**

A Report of the American College of Cardiology Solution Set Oversight Committee

# SGLT<sub>i</sub> first step in all HF patients. Guidelines



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



European Heart Journal (2023) 44, 3627–3639

# Timing for initiation of SGLT2 inhibitors. The earlier the better.

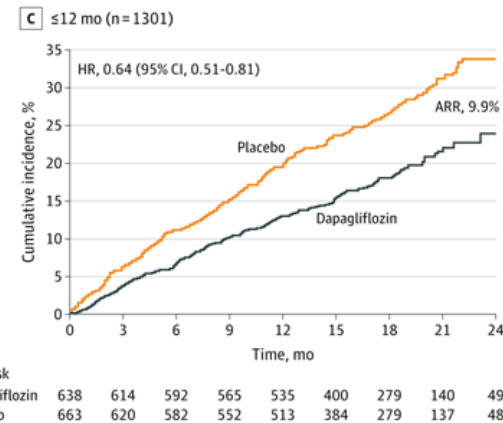
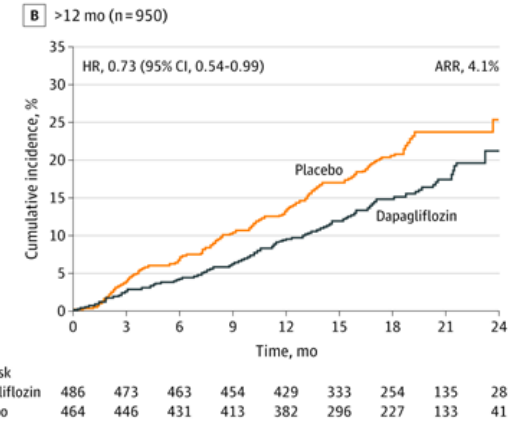
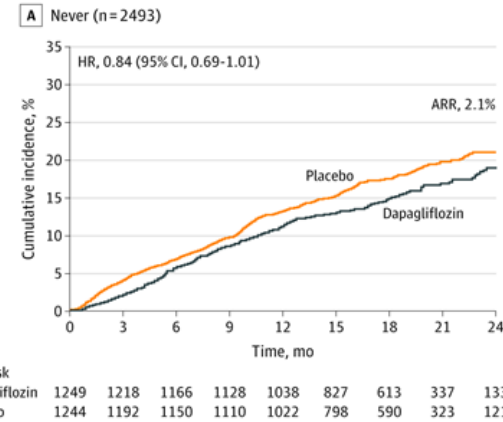
Evidence-based, **the earlier the better. Very early benefit.**

## Reduction in clinical events in patients with HFrEF:

- ✓ Dapagliflozin: **at 28 days** (HR 0.51)
- ✓ Empagliflozin: **at 12 days** (HR 0.76).

## Results in patients with HFmrEF/HFpEF:

- ✓ Dapagliflozin: **at 2 weeks** (HR 0.45).
- ✓ Empagliflozin: **at 18 days** (HR 0.41).



**Even more crucial in patients at higher risk, such as those with a recent episode of AHF!!!**

JAMA Cardiol 2021;6:499-507

Eur J Heart Fail 2022;24:245-248.

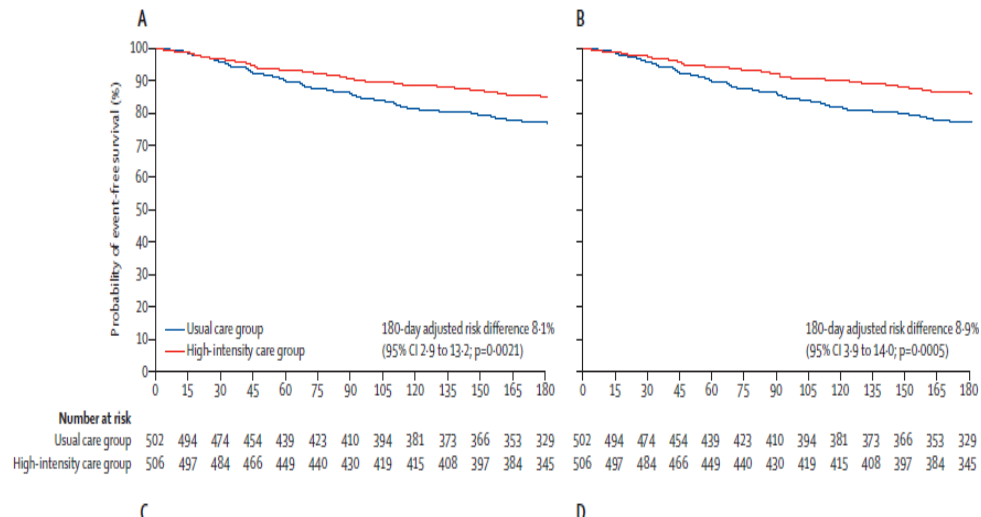
JAMA Cardiol 2022;7:1259-1263

Circulation 2021;143:326-336.

# Timing for initiation of SGLT2 inhibitors. The earlier the better, from the hospital

Safety, tolerability, and efficacy of up-titration of guideline-directed medical therapies for acute heart failure (STRONG-HF): a multinational, open-label, randomised, trial

Alexandre Mebazaa, Beth Davison, Ovidiu Chioncel, Alain Cohen-Solal, Rafael Diaz, Gerasimos Filippatos, Marco Metra, Piotr Ponikowski, Karen Shiwa, Adriaan A Voors, Christopher Edwards, Maria Novosadova, Koji Takagi, Albertino Damasceno, Hadiza Saidu, Etienne Gayat, Peter S Pang, Jelena Celutkiene, Gad Cotter



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

Recommendation	Class <sup>a</sup>	Level <sup>b</sup>
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. <sup>c,d,e 16</sup>	I	B

European Heart Journal (2023) 44, 3627–3639



# when to start iSGLT2???

Very early benefit  
Independent of LVEF  
Good safety profile

Initiation on clinical suspicion of HF while waiting for echocardiography???

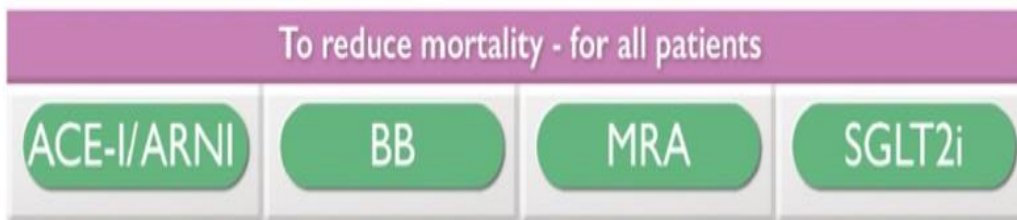
**Unlocking the potential of natriuretic peptide testing in primary care: A roadmap for early heart failure diagnosis**

Antoni Bayes-Genis<sup>1\*</sup> and Giuseppe Rosano<sup>2</sup>

# Quadruple therapy in HFrEF ambulatory patients

## Management of HFrEF

To reduce mortality - for all patients

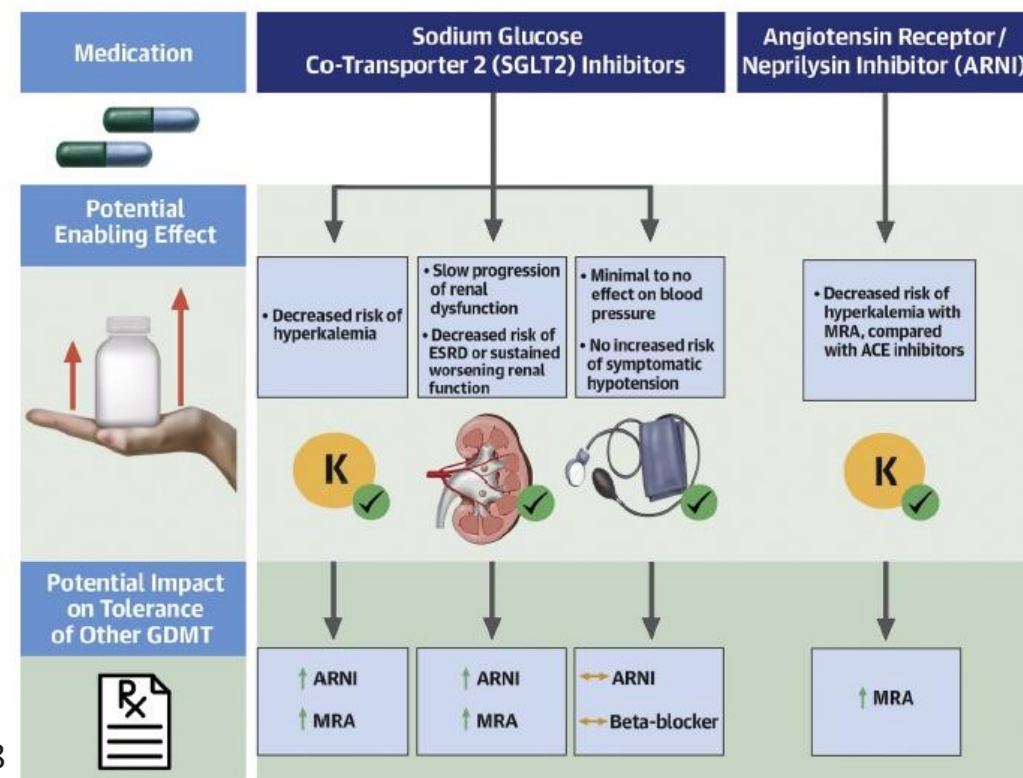


### Initiation and sequencing of treatment:

- ✓ Individualised: according to patient profile and clinical scenario.
- ✓ Based on different clinical variables: BP, HR, renal function and potassium.

Eur J Heart Fail. 2021 Sep;23(9):1525-1528

## SGLT2 inh: tolerance-facilitating drugs for others



# iSGLT2 initiation in acute heart failure

**Table 1** A practical guide to sodium-glucose co-transporter 2 inhibitors utilization in acute heart failure patients

---

## I. Eligibility

AHF patients, irrespective of diabetes status, LVEF, or chronic decompensated vs. de novo AHF

## II. Exclusion

eGFR < 20 mL/min/1.73 m<sup>2</sup>

Symptomatic hypotension (caution in patients with SBP < 100 mmHg)

Use of IV vasodilators, inotropes, or increase in IV loop diuretics within the past 6 h

Type 1 diabetes

History of ketoacidosis

## III. Caution

Hypovolaemic patients

History of severe UTIs or urosepsis

## IV. Monitoring

Blood pressure (at least daily while in-hospital)

Baseline and periodic monitoring of renal function (daily while in-hospital)<sup>a</sup>

Monitor volume status with clinical examination (at least daily while in-hospital)

Acute illness or major surgery<sup>b</sup>

## V. Information for patients

Genital hygiene (daily)

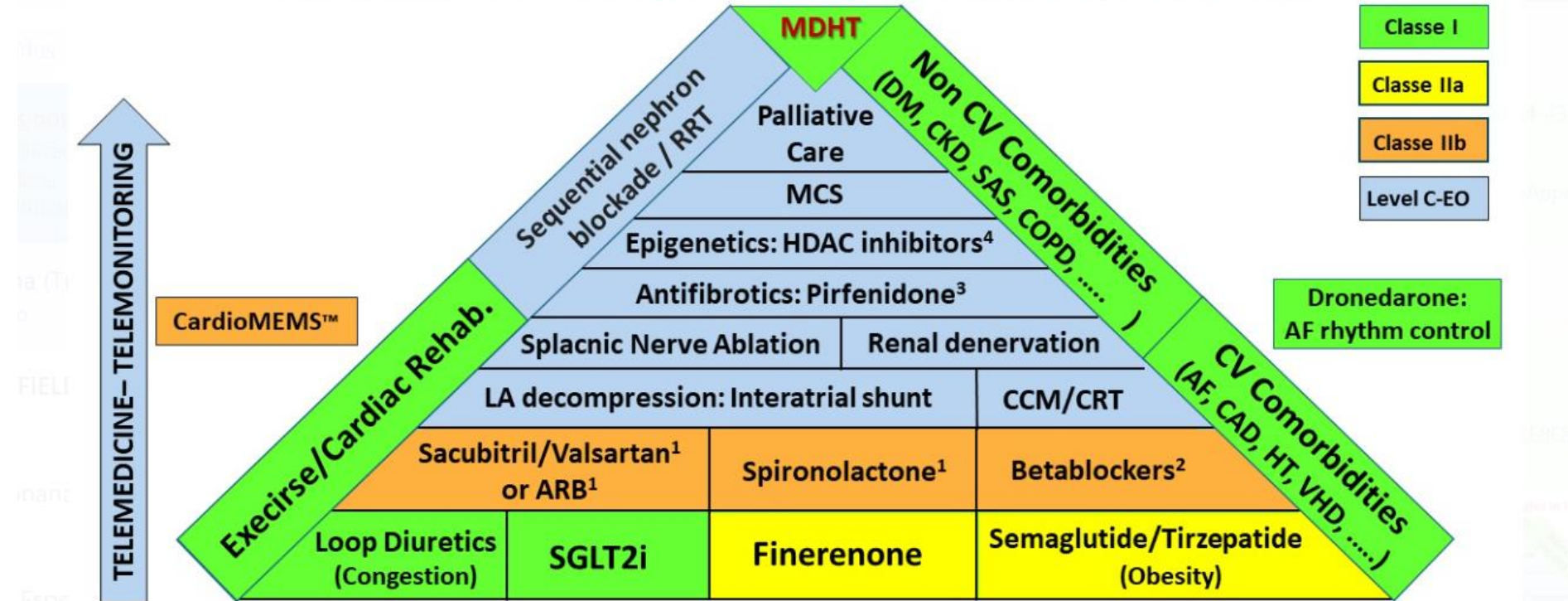
Ensure adequate hydration and balanced diet

---

ESC Heart Fail. 2022 Dec;9(6):4344-4347

# Therapeutic agents for the management of heart failure with mildly reduced and preserved ejection fraction.

## Established and emergent strategies in HFpEF management



1. FDA/AHA recommendation. 2. If CAD and/or AF with high heart rate. In sinus rhythm evaluate chronotropic incompetence. 3. Phase 2 trials. 4. Phase 1 trials

AF: Atrial Fibrillation; ARB: Angiotensin Receptor Blockers; CAD: Coronary Artery Disease; CCM: Cardiac contractility modulation; CKD: Chronic Kidney Disease; COPD: Chronic Obstructive Pulmonary Disease; CRT: Cardiac Resynchronization Therapy; CV: Cardiovascular; DM: Diabetes Mellitus; EO: Expert Opinion; HDAC: Histone Deacetylase; HFpEF: Heart Failure with Preserved Ejection Fraction; HT: Hypertension; LA: Left Atrium; MCS: Mechanical Circulatory Support; MDHT: Multidisciplinary Heart Team; RRT: Renal Replacement Treatment; SAS: Sleep Apnea Syndrome; SGLT2i: Sodium-glucose Cotransporter-2 Inhibitors. VHD:Valvular Heart Disease

© @Dr\_Manito

# Management of Concomitant Medications

## Diuretics:

- ✓ iSGLT2i are well tolerated and effective regardless of diuretic use or dose.
- ✓ The majority of patients did not change their diuretic dose throughout follow-up (almost 75% at 18 months).
- ✓ Consider downtitrating by 50 % in patients without signs of volume overload on >40 mg furosemide, 20 mg torsemide, or 1 mg bumetanide daily.

# Management of Concomitant Medications

## Antihypertensive drugs

- ✓ SGLT2i show a modest effect on BP (−1.32 and 1.06 mmHg in S and D BP, respectively)
- ✓ Even in patients with lower BP below 110 mmHg, they appear to have no change or even increase.
- ✓ Dose reduction of antihypertensives is not generally recommended but may be considered in patients with baseline systolic blood pressure  $\leq$  100 mmHg or those experiencing symptomatic hypotension.

## Hypoglycaemic drugs

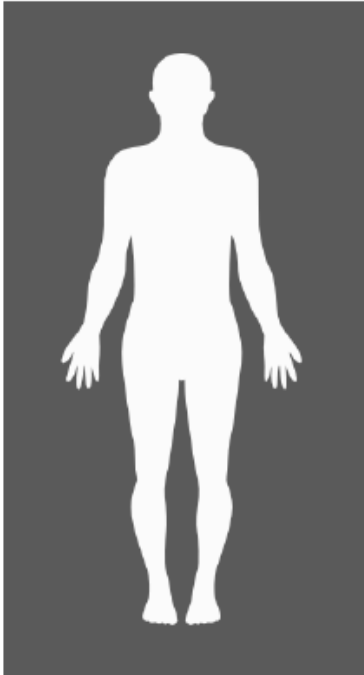



- ✓ Reassess glucose-lowering medications when starting SGLT2 inhibitors in HF patients with T2D, especially for those on insulin or secretagogues if HbA1c  $<$  7.5% or with hypoglycemia history. Generally, no dose adjustment is needed unless high hypoglycemia risk exists.



# Safety and Prevention of Adverse Effects

## Genital infections

### Management and treatment

		<b>Raise awareness</b> at the start of SGLT2 inhibitor treatment to <b>promote early intervention</b>
		<b>Provide practical hygiene advice</b> to patients and their partners to <b>prevent</b> genital infections
		Topical treatments or appropriate oral treatments can be used for <b>mild to moderate infections</b>

Genital infections usually occur early during treatment exposure and are not serious

# Practical guide to initiation of SGLT2i in patients with HF

## Eligible patients

- All symptomatic HF patients, regardless of LVEF, diabetic status and care setting



## Contraindications

- Type 1 diabetes mellitus or history of ketoacidosis
- Hypotension (caution if SBP <100 mmHg)
- Severe CKD (dapagliflozin: eGFR <25 ml/min/1.73m<sup>2</sup>; empagliflozin: eGFR <20 ml/min/1.73m<sup>2</sup>)<sup>a</sup>
- Pregnancy/risk of pregnancy and breastfeeding period
- Caution in patients with history of recurrent genital or urinary tract infections
- In AHF, use of inotropes within the last 24h or use of IV vasodilators or LD escalation within the last 6h



## Dose

- 10 mg once daily for both dapagliflozin and empagliflozin (irrespective of food)



## Monitoring

- Check renal function when starting the therapy and then after 1-2 weeks<sup>a,b</sup>
- Blood glucose (if SGLT2 inhibitors are used in association with anti-diabetic drugs – mainly insulin and insulin secretagogues)
- Acute illness or major surgery<sup>c</sup>



## Patient/caregiver counselling

- Ensure adequate daily genital hygiene
- Watch for symptoms of volume depletion<sup>d</sup>, uro-genital infections<sup>e</sup> and diabetic ketoacidosis<sup>f</sup>
- Avoid dehydration, low carbohydrate (ketogenic) diet and excessive alcohol consumption



THANK YOU