ESC CONGRESS 2023

Friday, 25 August – Monday, 28 August 2023
Amsterdam, Netherlands

KEY HIGHLIGHTS

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ABSTRACT SUMMARIES

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2023 FOCUSED UPDATE OF THE ESC GUIDELINES FOR CHRONIC HEART FAILURE

PRESENTED BY ROY STUART GARDNER | 26 AUGUST 2023

More than 10 RCTs have been released since the publication of 2021 HF guidelines, necessitating a focused update

CHF

HFmrEF

Recommendation	Class
An SGLT2i (**dapagliflozin or empagliflozin**) is recommended in patients with HFmrEF to reduce the risk of HF hospitalization or CV death	IA

Management of patients with HFmrEF

- Diuretics for fluid retention (Class I)
- Dapagliflozin/ Empagliflozin (Class I)
- ACEI/ARNI/ARB (Class IIb)
- MRA (Class IIb)
- BB (Class IIb)

First available algorithm on HFmrEF management
(based on *EMPEROR-Preserved* and *DELIVER trials*)

HFpEF

Recommendation	Class
An SGLT2i (**dapagliflozin or empagliflozin**) is recommended in patients with HFpEF to reduce the risk of HF hospitalization or CV death	IA

Management of patients with HFpEF

- Diuretics for fluid retention (Class I)
- Dapagliflozin/Empagliflozin (Class I)
- Treatment for etiology, CV and non-CV comorbodities (Class I)

Addition of dapagliflozin/empagliflozin use in the 2021 algorithm
(based on *EMPEROR-Preserved* and *DELIVER trials*)

AHF

Pre-discharge and early post-discharge follow-up

Recommendation	Class
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 an HF hospitalization** is recommended to reduce the risk of HF rehospitalization or death	IB

Based on STRONG-HF trial

Comorbidities

Prevention of HF in patients with T2D and CKD

Recommendation	Class
In patients with T2D and CKD, SGLT2i (**dapagliflozin or empagliflozin**) are recommended to reduce the risk of HF hospitalization or CV death	IA
In patients with T2D and CKD, **finerenone** is recommended to reduce the risk of HF hospitalization	IA

Based on EMPA-KIDNEY, DAPA-CKD, FIDELIO-DKD, FIGARO-DKD and pooled analyses

Class of recommendation 1: Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective. Is recommended or is indicated. Level of evidence A: Data derived from multiple randomized clinical trials or meta-analyses. Level of evidence B: Data derived from a single randomized clinical trial or large non-randomized studies.

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THE GLOBAL BURDEN OF HEART FAILURE: A SYSTEMATIC ANALYSIS FOR THE GLOBAL BURDEN OF DISEASE STUDY 2021

PRESENTED BY NIKKI DECLEENE | 25 AUGUST 2023

Study design

GBD 2021

A comprehensive picture of mortality and disability worldwide

- **10000** collaborators
- Estimates for **1990–2021**
- **204** countries/territories
- **409** diseases
- **88** risk factors

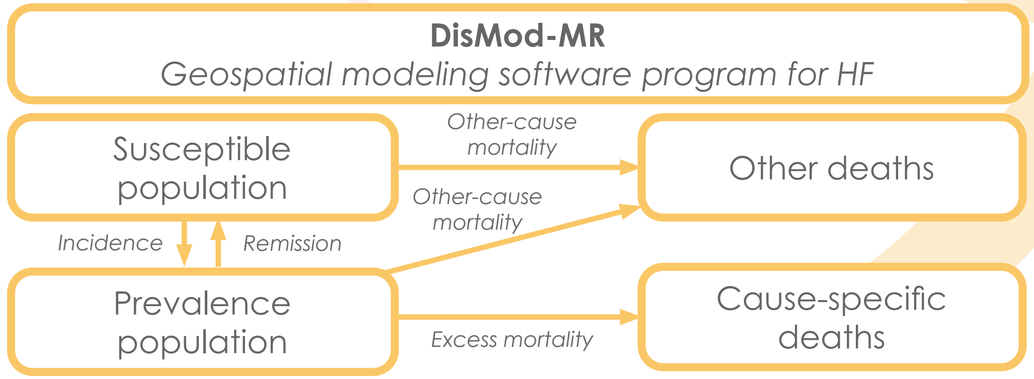
HF data

- **121** published studies from **30** countries
- **Population-representative** data
- ICD-coded records from **29** countries
- Met/could be adjusted to **GBD case definition of HF***

Modeling HF

DisMod-MR

Geospatial modeling software program for HF



*Follows the universal definition of HF in the AHA/ACC definition of a diagnosis based on a structured set of clinical signs and symptoms and includes people with current/previous symptoms of HF.

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THE GLOBAL BURDEN OF HEART FAILURE: A SYSTEMATIC ANALYSIS FOR THE GLOBAL BURDEN OF DISEASE STUDY 2021

PRESENTED BY NIKKI DECLEENE | 25 AUGUST 2023

Key findings

Prevalence of HF

56 million cases worldwide in 2021

Age

↑ With age	High income APAC Central Europe Latin America
↓ With age	Sub-Saharan Africa

Geographical location

↑ North America	888 per 100,000
↓ High income APAC	487 per 100,000

Sex

↑ Males vs Females	402–1350 per 100,000 vs 247–1004 per 100,000

Trends over time

Top 3 regions with largest increase over time	1. South Asia (540–599 per 100,000) 2. Southeast Asia 3. East Asia

Populations-based estimates are essential to guide public health policy and interventions, especially as populations age and risk profiles change

Knowledge of the global epidemiology is key to preventing and treating underlying etiologies, and decreasing the overall burden of HF

DE NOVO HEART FAILURE: WHEN TO START TREATMENT WITH AN ARNI AND SGLT2I

PRESENTED BY JAVED BUTLER | 25 AUGUST 2023

Most HF patients are not on optimal medical therapy

The use of **ARNI** vs **SGLT2i** is often debated, and both therapies remain underutilized. Thus, the rapid initiation of optimal GDMT in HF is recommended.

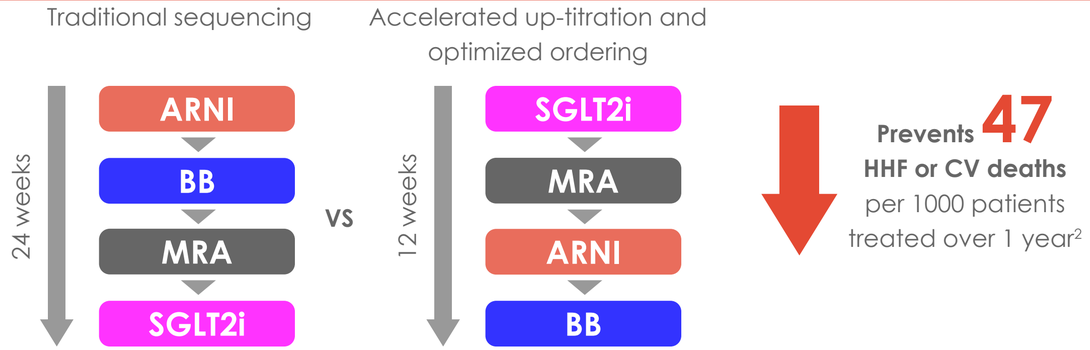
Being comprehensive matters!

Comprehensive therapy (ARNI + BB + MRA + SGLT2i)

Increased mean overall survival by 6.3 years

vs conventional therapy (ACEi/ARB + BB)[1]

Rapid up-titration and optimized ordering



Prevents 47 HHF or CV deaths per 1000 patients treated over 1 year[2]

ARNI vs. SGLT2i

High-level comparison

Properties	ARNI	SGLT2i
Large high caliber RCT data	Yes	Yes
Mortality and morbility benefit	Yes	Yes
Health status benefit	Yes	Yes
Remodeling	Yes - not randomized	Yes - not randomized
SCD benefit	Yes	Likely
Data in HFrEF	Yes	Yes
Data in HHF	Yes	Across EF
HFrEF, HFmrEF	Up to 60%	No
Sex difference?	?	Yes
Glycemic/Metabolic benefit	Possibly	Yes
CKD benefit	Significant	Little
Effect on blood pressuressure	Significant	Little
Diurectic properties	Yes	Yes
Head to head comparisonson	No - no baseline SGLT2i	No - 15-20% baseline ARNI
Dosing	3 steps BID	1 step QD
Cost	Not generic	Not generic

Both ARNI and SGLT2i are beneficial in HF regardless of order of initiation, however:

- ✓ SGLT2i is the only foundational therapy that can be used **without modification in multiple HF phenotypes**
- ✓ SGLT2i are **simple** to use — Single dose — Once daily — No titration
- ✓ SGLT2i may **improve the tolerance** of other HF therapies

1. Vaduganathan M, et al. *Lancet*. 2020;396:121-128.
2. Shen L, et al. *Eur Heart J*. 2022;43:2573-2587.

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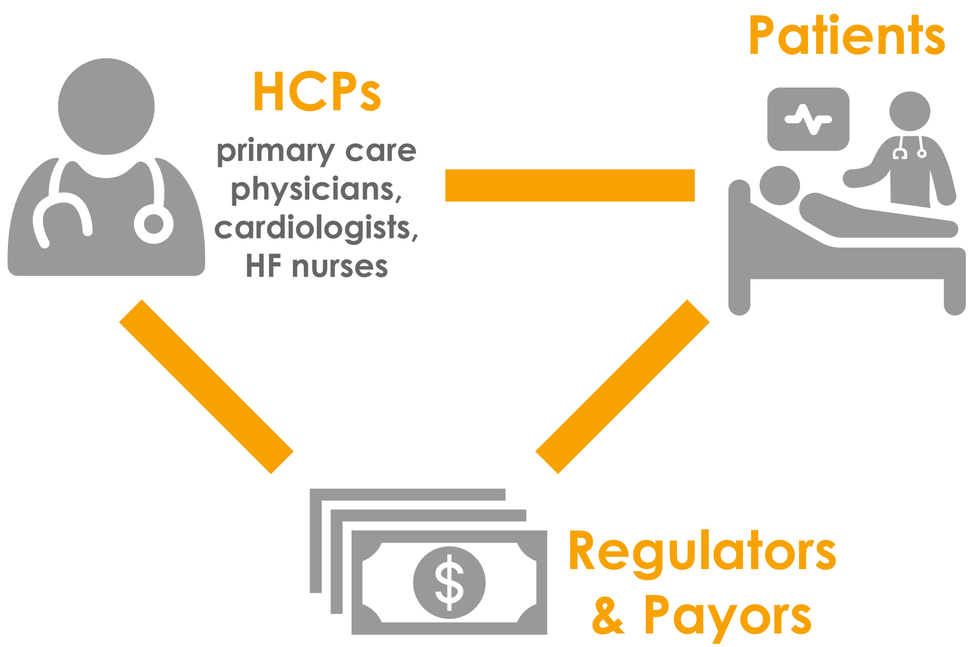
GLOBAL CHALLENGES IN HEART FAILURE: WHAT CAN WE LEARN FROM EACH OTHER?

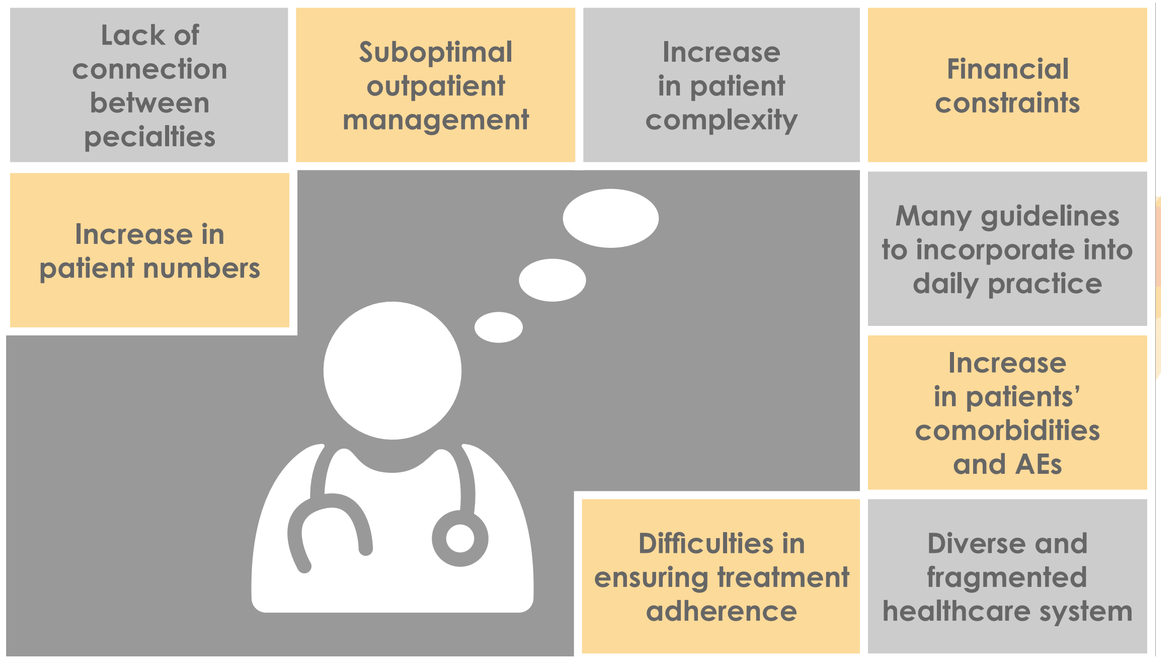
PRESENTED BY ALEJANDRO RECIO MAYORAL | 25 AUGUST 2023

Optimizing the management and treatment of HF is a major public health priority

HF care is complex and involves various stakeholders[1]



Key challenges for HF care team[1]



1. Jankowska EA, et al. *ESC Heart Fail*. 2023;10:2159-2169.

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GLOBAL CHALLENGES IN HEART FAILURE: WHAT CAN WE LEARN FROM EACH OTHER?

PRESENTED BY ALEJANDRO RECIO MAYORAL | 25 AUGUST 2023

All major guidelines strongly support a global HF care that focuses on structured multidisciplinary HF services

Multidisciplinary HF care is associated with improved outcomes:[2-4]

21–26% reduction in ACM

26–47% reduction in HHF

Such structured multidisciplinary HF care aims to:

Deliver **customized holistic care** that responds to changing patient needs and transition across the healthcare settings

- ✓ Accurate diagnosis
- ✓ Implementation of appropriate evidence-based therapy
- ✓ Education for both the patient and their carers

Components of the multidisciplinary HF care programme:[5]

- **Optimized management**
- ✓ Lifestyle choices, pharmacological and devices
- **Patient education**
- **Psychosocial support**
- **Follow-up after discharge**
- ✓ Clinic, home visits, telephone/telemonitoring
- **Access to:**
- ✓ Advanced treatment options
- ✓ Supportive/palliative care

Global heart failure care focuses on structured multidisciplinary HF services to ensure that patients receive the right care from the right person at the right time

2. Takeda A, et al. *Cochrane Database Syst Rev*. 2012 Sep 12;(9):CD002752. 3. Holland R, et al. *Heart*. 2005;91:899-906.
4. McAlister FA, et al. *J Am Coll Cardiol*. 2004;44:810-819. 5. McDonagh TA, et al. *Eur Heart J*. 2021;42:3599-3726.

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PRACTICAL GUIDANCE TO IMPLEMENT HEART FAILURE TREATMENT WITH SGLT2I IN THE HOSPITAL SETTING

PRESENTED BY ILEANA PINA, ANTONIO BAYES GENIS, JOHN R TEERLINK, MIKHAIL KOSIBOROD | 26 AUGUST 2023

Guidelines recommend SGLT2i for patients with HF across the LVEF spectrum, but the implementation of GDMT is suboptimal[1]

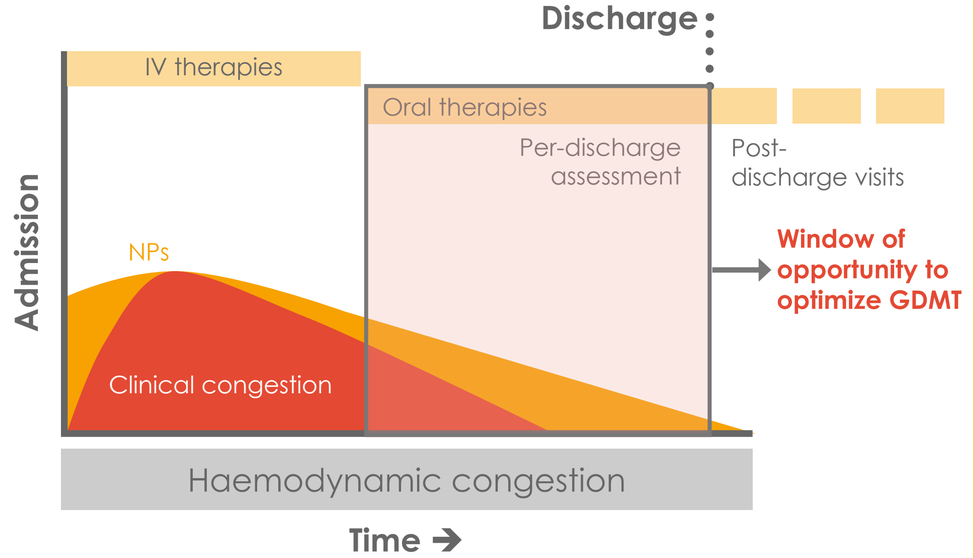
Clinical inertia has a major role in the lack of prescription of GDMT[1–3]

Physicians[2,3]
- Non-prescription of GDMT
- Not reaching target doses
- Risk treatment paradox

Patients[2,3]
- Old age/frailty
- Comorbidities
- Poor adherence
- Lack of awareness

Healthcare systems[2]
- Fragmented, isolated care
- Poor patient follow-up
- Outdated protocols

Hospitalization is a key opportunity to break clinical inertia and improve long-term outcomes for patients with HF[1]



1. Metra M, et al. *Eur J Heart Fail*. 2023;25:1115-1131. 2. Verhestraeten C, et al. *Heart Fail Rev*. 2021;26:1359-1370.
3. Greene SJ, et al. *Eur J Heart Fail.* 2023;23:1343-1345.

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SGLT2i are simple to initiate and associated with early clinical benefit in hospitalized patients who had been stabilized following an acute HF event[4,5]

In the EMPULSE trial, in-hospital initiation of empagliflozin was associated with:

- Significantly reduced risk of death and first HF event vs placebo[6]
- Clinical benefit across age, eGFR or LVEF subgroups[5]
- Early and sustained improvements in symptoms, physical limitations and QoL[7]
- AE rates that are similar to placebo group[5,6]

Considerations for implementation of SGLT2i in the hospital setting

Age
Consistent benefits across age and LVEF subgroups[8,9]

Side effects
AEs such as genital tract infections are often mild, responsive to treatment and do not usually require discontinuation[12–14]

Kidney function
Consistent benefits across the spectrum of kidney function; favorable effects on renal function[8,10]

Other drugs
Increased likelihood of tolerance of other GDMT and reduced need for diuretic dose escalation[12,13]

Blood pressure
Tolerability in patients with low BP[11]

Initiation during hospital stay
1–5 days after hospitalization or at the time of discharge

4. Tromp J, et al. *Eur J Heart Fail*. 2021;23:826-834. 5. Voors AA, et al. *Nat Med*. 2022;28:568-574. 6. Voors AA, et al. Presented at AHA 2021 Scientific Sessions, 13-15 Novmeber 2021. 7. Kosiborod MN, et al. *Circulation*. 2022;146:279-288. 8. Vaduganathan M, et al. *Lancet*. 2022;400:757-767. 9. Filippatos G, et al. *Eur J Heart Fail*. 2022;24:2297-2304. 10. Voors AA, et al. *Eur J Heart Fail*. 2022;24:1844-1852. 11. Böhm M, et al. *J Am Coll Cardiol*. 2021;78:1337-1348. 12. Jardiance® Summary of Product Characteristics. Boehringer Ingelheim International GmbH. 13. Farxiga® Summary of Product Characteristics. AstraZeneca AB. 14. Engelhardt K, et al. *Ann Pharmacother*. 2021;55:543-548.

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PRACTICAL GUIDANCE TO IMPLEMENT HEART FAILURE TREATMENT WITH SGLT2I IN THE OUTPATIENT SETTING

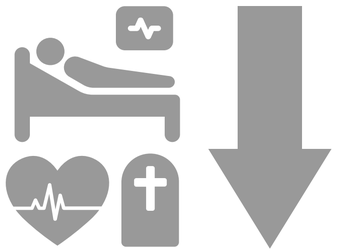
PRESENTED BY STEFAN ANKER, THERESA MCDONAGH, JAVED BUTLER, MARIA ROSA COSTANZO, SHELLEY ZIEROTH | 27 AUGUST 2023

Optimal global implementation of SGLT2i in HF could result in a significant real-world benefit[1]

Global prevalence of HF: **64 million**

Estimated patients with HF eligible for SGLT2i: **50 million**

Optimal implementation of SGLT2i globally



7–8 million
projected reduction in worsening HF events or CV deaths*

*Based on NNT to prevent worsening HF event/CV death[5,6,10–12]

Guidelines recommend early administration of SGLT2i for patients with HF irrespective of LVEF

HFrEF

There are fundamental changes in the approach to HF treatment[2–4]

1. **No fixed order** for sequence of therapies
2. **Prioritize initiation** over up-titration of dose
3. **Speed** of initiating lifesaving therapies **matters**

HFmrEF | HFpEF

Underdiagnosis is a huge problem in HFpEF and is often missed in patients with multiple comorbidities

We can't treat what we can't see

In studies documenting under diagnosis of HF, most patients (76%) with unrecognized HF were found to have HFpEF[5]

HFpEF (76.1%) | **HFrEF (18.5%)** | **Isolated RHF (5.4%)**

Score-based algorithms such as **H_2FPEF score[6]** or **HFA-PEFF algorithm[7]** can help indicate the likelihood of HFpEF

1. Talha KM, et al. *Eur J Heart Fail*. 2023;25:999. 2. Heidenreich, PA et al. *J Am Coll Cardiol*. 2022;79:e263. 3. Metra M et al, *Eur J Heart Fail.* 2023;25:1115. 4. McDonagh T, et al. *Eur Heart J*. 2023;ehad195. 5. van Riet EES, et al. *Eur J Heart Fail*. 2014;16:772. 6. Reddy YNV, et al. Circulation. 2018;138:861. 7. Pleske B, et al. *Eur Heart J*. 2019;40:3297.

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SGLT2i are simple to use

- Single dose[8,9]
- Once daily[8,9]
- No titration[8,9]
- With/without food[8,9]
- Any time of the day, but regularly[8,9]

An echocardiogram may not be required to initiate SGLT2i treatment

SGLT2i may improve tolerance of other HF therapies

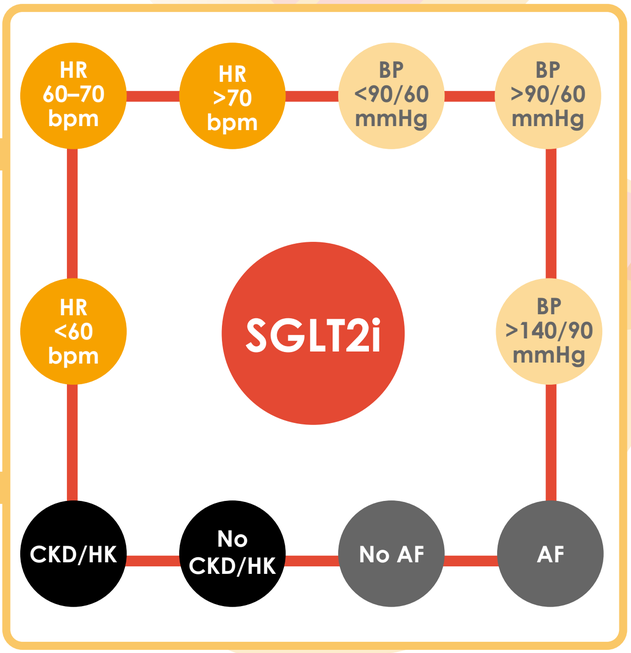
- K^+ Decreased risk of hyperkalemia
- Slow progression of renal dysfunction
- Minimal to no effect on BP

May improve the tolerance of **ARNI, MRA and BB**

SGLT2i are the only foundational therapy that can be used without modification for the multiple patient phenotypes based on

- BP
- Heart rate
- Kidney function
- AF

Education has a key role in empowering and reassuring patients, thus helping to **maximize the benefit** and **minimize the side effects of SGLT2i**



7. Pleske B, et al. *Eur Heart J*. 2019;40:3297. 8. Jardiance® Summary of Product Characteristics, BI international GmbH. 9. Forxiga® Summary of Product Characteristics. AstraZeneca AB. 10. Greene SJ, et al. *Eur J Heart Fail*. 2021;23:1525. 11. Docherly KF, Petrie MC. *Heart*. 2022;108:312.

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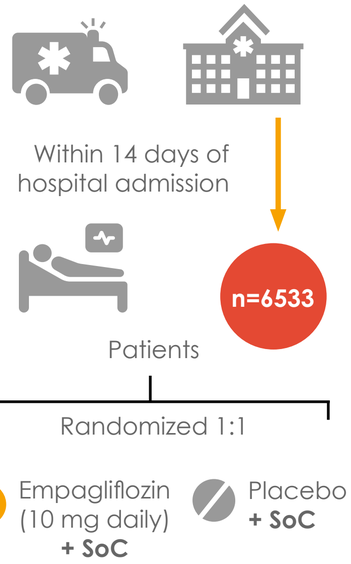
BASELINE CHARACTERISTICS OF PATIENTS ENROLLED IN THE EMPACT-MI TRIAL

PRESENTED BY JAVED BUTLER | 25 AUGUST 2023

Study design

EMPACT

Double-blind, randomized, placebo-controlled, event-driven trial to evaluate the efficacy and safety of **empagliflozin compared with placebo**, in addition to standard of care, in patients with **acute MI and high risk of new-onset HF or mortality**



Key eligibility criteria
- Hospital admission for spontaneous AMI
- Signs and symptoms of congestion requiring treatment or newly developed LVEF <45% AND
- One additional HF risk factor (enrichment criterion)*
- No history of HF

Primary endpoint:
- Composite endpoint of time to first event of HHF or ACM

Secondary endpoints:
Total number of:
- HHF or ACM
- Non-elective CV hospitalizations or ACM
- Non-elective all-cause hospitalizations or ACM
- Hospitalizations for MI or ACM

Patients enrolled in EMPACT-MI

6522 participants randomized 1:1 (empagliflozin 10 mg or placebo once-daily) at 451 sites across 22 countries

Mean age: 64 yrs	**Male: 75%**	**White race: 84%**	**prior AMI: 13%**	**Median time from AMI to randomization: 5 days**
T2D: 32%	**STEMI: 74%**	**PCI: 88.8%**	**CABG: 0.5%**	

57% with acute signs or symptoms of congestion requiring treatment

78% with newly depressed LVEF <45%

36% met both criteria

78% participants had 1–3 enrichment criteria*

Most common enrichment criteria

50% aged ≥65 yrs

32% T2D

31% 3-vessel CAD

EMPACT-MI revealed similar rates of comorbidities, background GDMT, statin and antiplatelet therapy, and revascularization compared to PARADISE-MI

EMPACT-MI includes participants across a spectrum of relevant characteristics, including a wide range of acute signs or symptoms of congestion, the entire spectrum of LVEF, and a range of additional risk factors, which will allow **broad applicability of trial findings to clinical practice**

*Age ≥65 years, LVEF <35%, prior MI, eGFR <60 ml/min/1.73 m², atrial fibrillation, T2D, elevated NT-proBNP/BNP, uric acid, elevated PASP, 3-vessel CAD, PAD.

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RECORD MI: HEART FAILURE COMPLICATING ACUTE MYOCARDIAL INFARCTION

PRESENTED BY JAVED BUTLER | 28 AUGUST 2023

Study design

Retrospective analysis of adults with a discharge diagnosis of MI across 28 hospital EHR in the BSW Health (US) (Jan 2015 to Dec 2021)

6804
eligible patients

Aged ≥18 years
Discharge diagnosis of MI

6556
discharged alive

STEMI (n=1487)
Non-STEMI (n=5609)

5047
no prior history of HF

STEMI (n=1356)
Non-STEMI (n=3691)

1578
developed incident HF

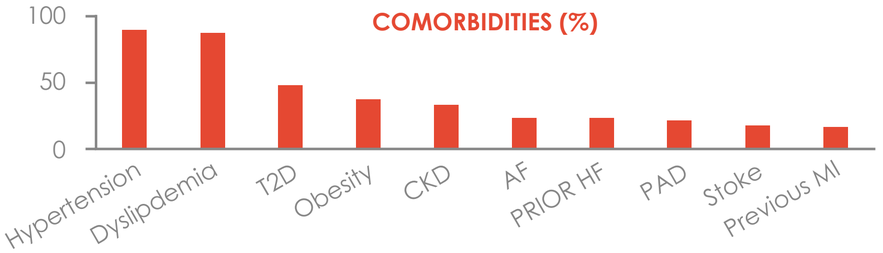
STEMI (n=438)
Non-STEMI (n=1140)

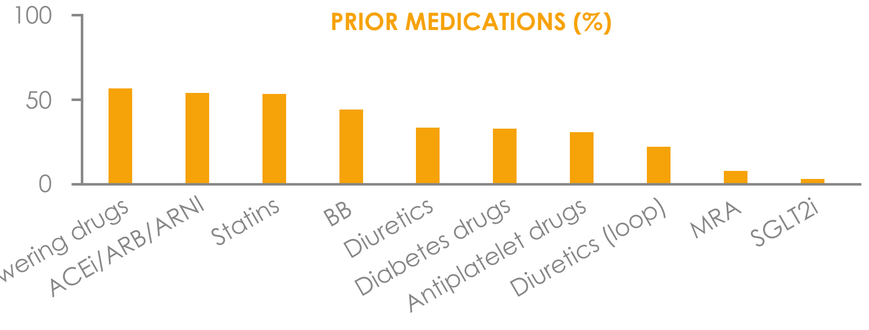
Key demographics and patient characteristics

MEDIAN AGE
68.9 years

FEMALE
40.3%

MEDIAN LVEF
52.5%





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RECORD MI: HEART FAILURE COMPLICATING ACUTE MYOCARDIAL INFARCTION

PRESENTED BY JAVED BUTLER | 28 AUGUST 2023

Outcomes at 1 year

Among patients who were discharged alive, a lower proportion of patients in the **STEMI** vs **non-STEMI group** had:

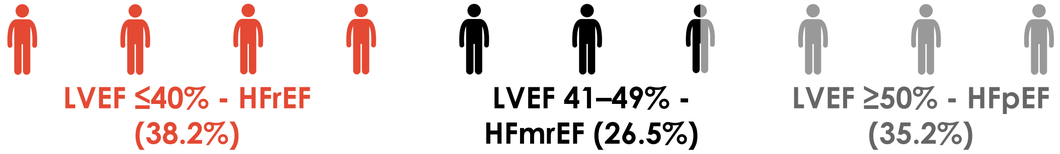
- **Recurrent MI**: 4.0% vs 6.4%
- **All-cause mortality**: 6.1% vs 11.3%
- **All-cause rehospitalization**: 26.8% vs 37.6%
- **CV hospitalization**: 12.0% vs 18.0%

Patients with no prior history of HF (n=5047)

Among patients with no prior history of HF, a higher proportion of patients who developed incident HF vs those who did not develop HF had:

- **Recurrent MI**: 9.2 % vs 2.5%
- **All-cause mortality**: 11.0% vs 5.0%
- **All-cause rehospitalization**: 54.7% vs 17.2%
- **CV hospitalization**: 29.0% vs 5.3%

Distribution of incident HF types



The study findings underscore the importance of developing novel therapeutic strategies to mitigate post-MI HF risk

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ABBREVIATION LIST

ACC, American College of Cardiology

ACEI, angiotensin-converting enzyme inhibitor

ACM, arrhythmogenic cardiomyopathy

AE, adverse event

AF, atrial fibrillation

AHA, American Heart Association

AMI, acute myocardial infarction

APAC, Asia Pacific

ARB, angiotensin receptor blocker

ARNI, angiotensin receptor neprilysin inhibitor

BB, beta-blocker

BID, twice daily

BP, blood pressure

BSW HEALTH, Baylor Scott & White Health

CABG, coronary artery bypass graft

CAD, coronary artery disease

CKD, chronic kidney disease

CV, cardiovascular

EHR, electronic health record

ESC, European Society of Cardiology

DISMOD-MR, Disease Modelling Meta-Regression

EGFR, estimated glomerular filtration rate

GBD, Global Burden of Disease

GDMT, guideline-directed medical therapy

HCP, healthcare professional

HF, heart failure

HFA-PEFF, Heart Failure Association Pre-test assessment, Echocardiographic & natriuretic peptide score

HHF, hypertensive heart failure

HK, hyperkalemia

HR, heart rate

HRmrEF, heart failure with mildly reduced ejection fraction

HfpEF, heart failure with preserved ejection fraction

HFrEF, heart failure with reduced ejection fraction

HR-QOL, heath-related quality of life

ICD, International Classification of Diseases

IV, intravenous

LVEF, left ventricular ejection fraction

MI, myocardial infarction

MRA, magnetic resonance angiography

NT-proBNP, N-terminal prohormone of brain natriuretic peptide

PAD, peripheral arterial disease

PCI, percutaneous coronary intervention

QD, once daily

QOL, quality of life

RCT, randomized controlled trial

RHF, right-sided heart failure

SCD, sudden cardiac death

SGLT2I, sodium sodium-glucose cotransporter-2 inhibitor

SOC, standard of care

STEMI, ST-segment elevation myocardial infarction

SU, sulfonylurea

T1D, Type 1 diabetes

T2D, Type 2 diabetes