

# Review of the 2022 Heart Failure Guidelines

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**Chair, ACC Council for Heart Failure and Transplantation**

**Director, Heart Failure Program,**

**Indiana University, Indianapolis, USA**

## AHA/ACC/HFSA CLINICAL PRACTICE GUIDELINE

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# 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

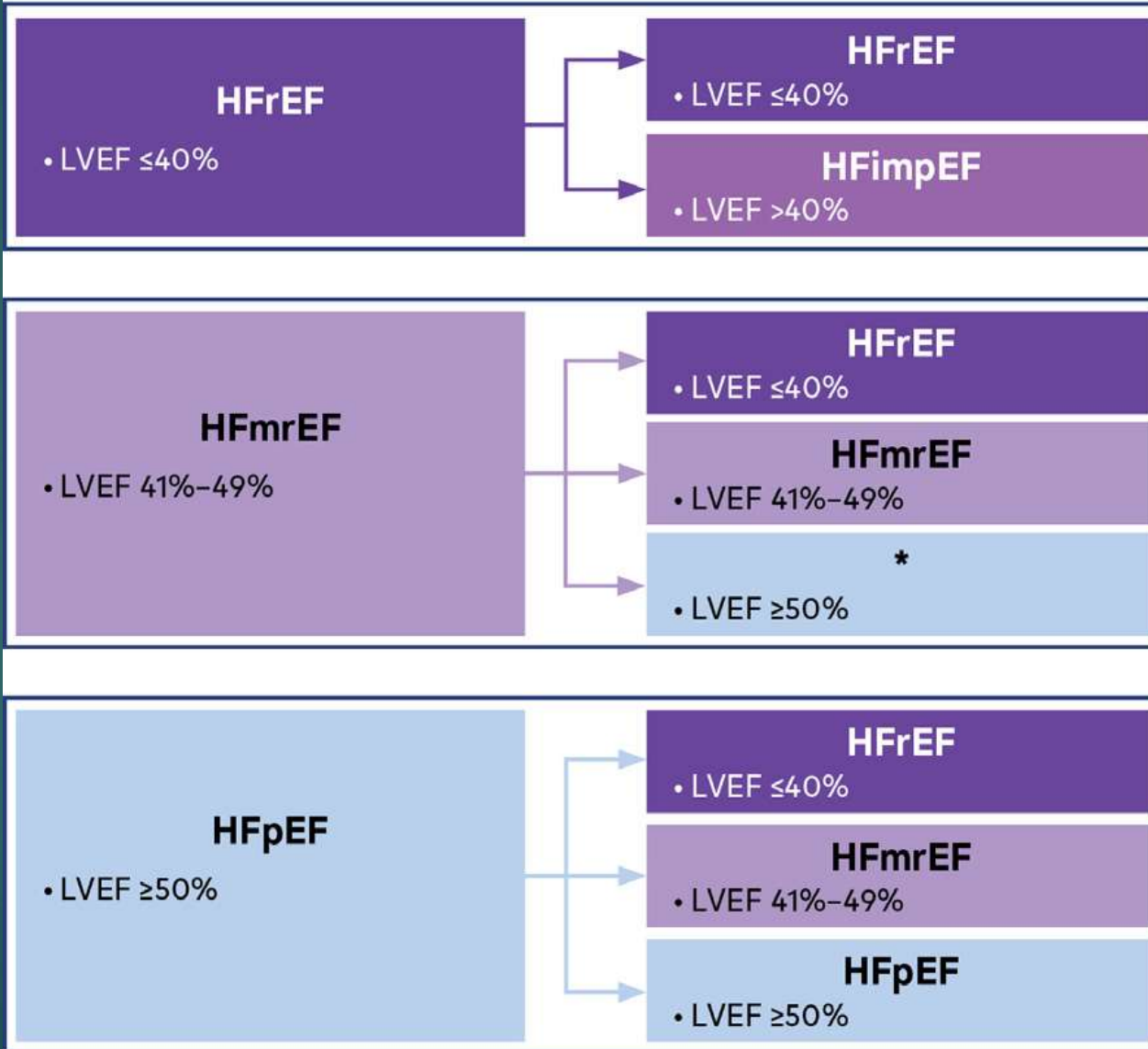
### Writing Committee Members\*

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## Initial Classification

## Serial Assessment and Reclassification

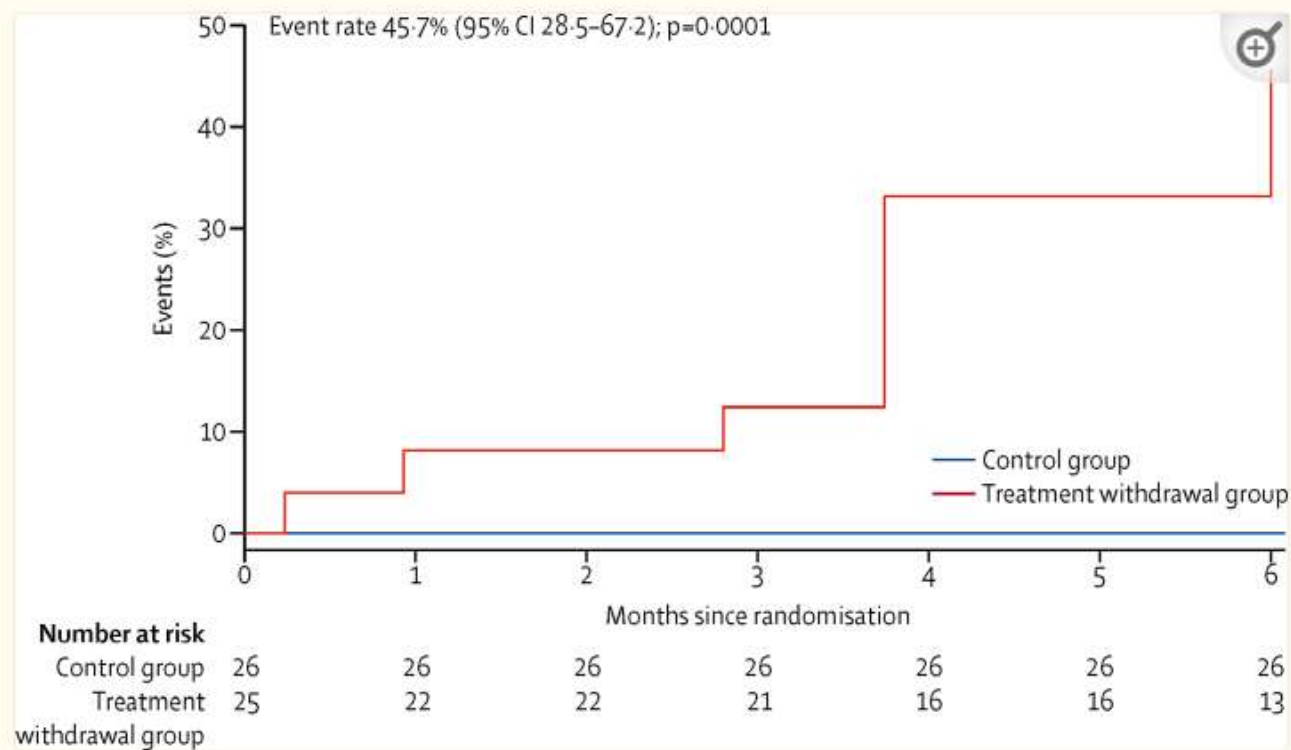


COR	LOE	Recommendation
1	B-R	In patients with HFimpEF after treatment, GDMT should be continued to prevent relapse of HF and left ventricular dysfunction, even in patients who may become asymptomatic. <sup>36</sup>

# Non-ischemic cardiomyopathy with recovered EF

Previous dilated CMP  
EF<40%  
Recovered to >50%  
Normal LV size  
Normal BNP

Primary end point: relapse  
EF decrease by 10% to <50%  
LVEDV increase by >10%  
2x NT-proBNP to >400  
HF



**Figure 3**

Kaplan-Meier curve of time to primary endpoint in randomised phase, according to treatment group

One patient dropped out at 7 days.

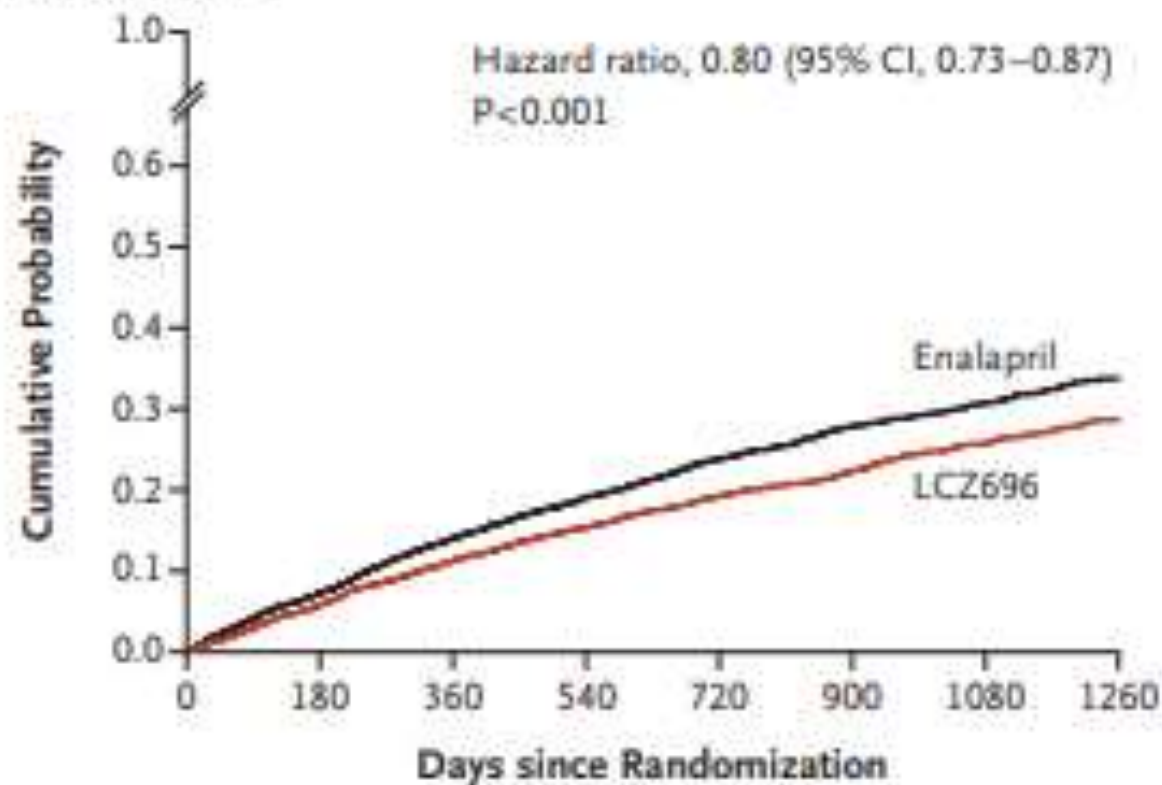


## Recommendations for Renin-Angiotensin System Inhibition With ACEi or ARB or ARNi

Referenced studies that support the recommendations are

COR	LOE	Recommendations
1	A	1. In patients with HFrEF and NYHA class II to III symptoms, the use of ARNi is recommended to reduce morbidity and mortality. <sup>1-5</sup>
1	A	2. In patients with previous or current symptoms of chronic HFrEF, the use of ACEi is beneficial to reduce morbidity and mortality when the use of ARNi is not feasible. <sup>6-13</sup>
1	A	3. In patients with previous or current symptoms of chronic HFrEF who are intolerant to ACEi because of cough or angioedema and when the use of ARNi is not feasible, the use of ARB is recommended to reduce morbidity and mortality. <sup>14-18</sup>
Value Statement: High Value (A)		4. In patients with previous or current symptoms of chronic HFrEF, in whom ARNi is not feasible, treatment with an ACEi or ARB provides high economic value. <sup>19-25</sup>
1	B-R	5. In patients with chronic symptomatic HFrEF NYHA class II or III who tolerate an ACEi or ARB, replacement by an ARNi is recommended to further reduce morbidity and mortality. <sup>1-5</sup>
Value Statement: High Value (A)		6. In patients with chronic symptomatic HFrEF, treatment with an ARNi instead of an ACEi provides high economic value. <sup>26-28</sup>
3: Harm	B-R	7. ARNi should not be administered concomitantly with ACEi or within 36 hours of the last dose of an ACEi. <sup>30,31</sup>
3: Harm	C-LD	8. ARNi should not be administered to patients with any history of angioedema. <sup>32-35</sup>
3: Harm	C-LD	9. ACEi should not be administered to patients with any history of angioedema. <sup>36-39</sup>

# A Primary End Point



## No. at Risk

LCZ696	4187	3922	3663	3018	2257	1544	896	249
Enalapril	4212	3883	3579	2922	2123	1488	853	236

EF  $\leq$  40%  
NYHA II-IV (>99% NYHA II-III)

Randomized

LCZ696 200 mg twice daily  
or enalapril 10 mg twice daily

The primary outcome: a composite of death from CV causes or hospitalization for HF

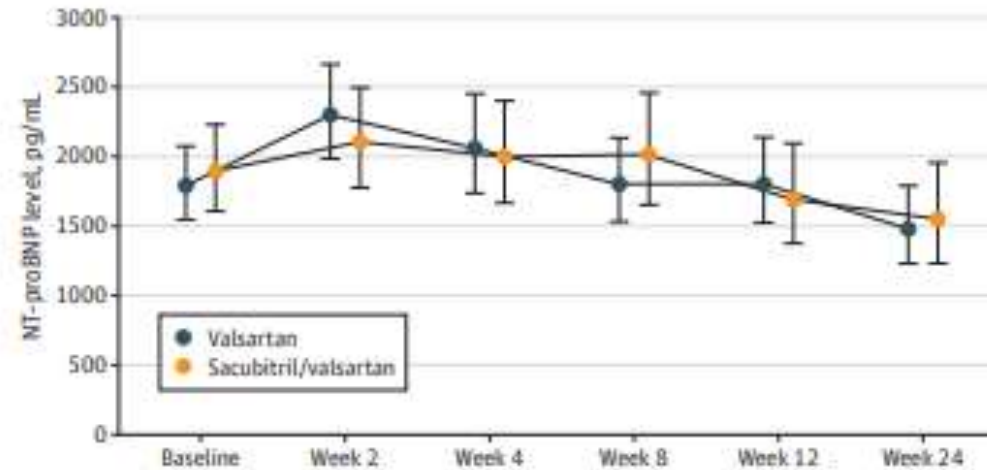
**Paradigm-HF**

McMurrey N Engl J Med . 2014 Sep 11;371(11):993-1004.

- ▶ EF  $\leq$  35%
- ▶ NYHA IV
- ▶ sacubitril/valsartan (target dose, 200 mg twice daily)  
or valsartan (target dose, 160 mg twice daily)

Figure 2. Change in N-Terminal Pro-Brain Natriuretic Peptide (NT-proBNP) Levels

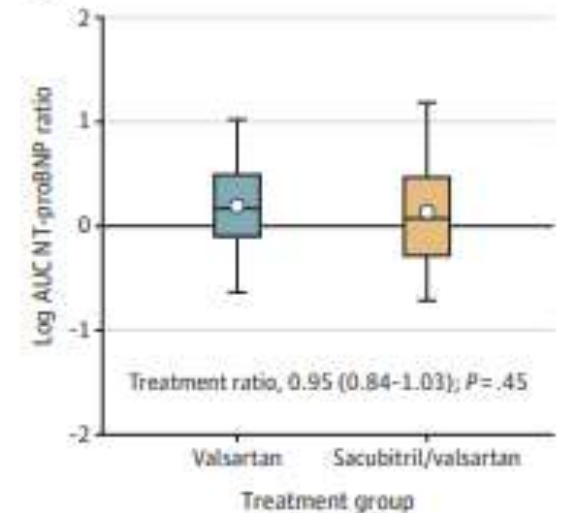
**A** Geometric mean NT-proBNP level



No. with data

Valsartan	162	155	154	144	145	124
Sacubitril/valsartan	161	156	153	143	140	118

**B** Log AUC NT-proBNP



Primary endpoint: change in NTproBNP after 24 weeks of therapy

The Life trial      Mann JAMA Cardiol . 2022 Jan 1;7(1):17-25.



**TABLE 1** Reasons for Discontinuation of Sacubitril/Valsartan During Run-In<sup>a</sup>

Reason	Number
Systolic arterial blood pressure <90 mm Hg with symptoms of hypotension	23
Systolic arterial blood pressure <90 mm Hg without symptoms of hypotension	20
Symptoms of hypotension/dizziness with systolic arterial blood pressure >90 mm Hg	14
Renal dysfunction (creatinine >2 mg/dL)	9
Hyperkalemia	2
Possible allergic reaction or rash	5
Other	7

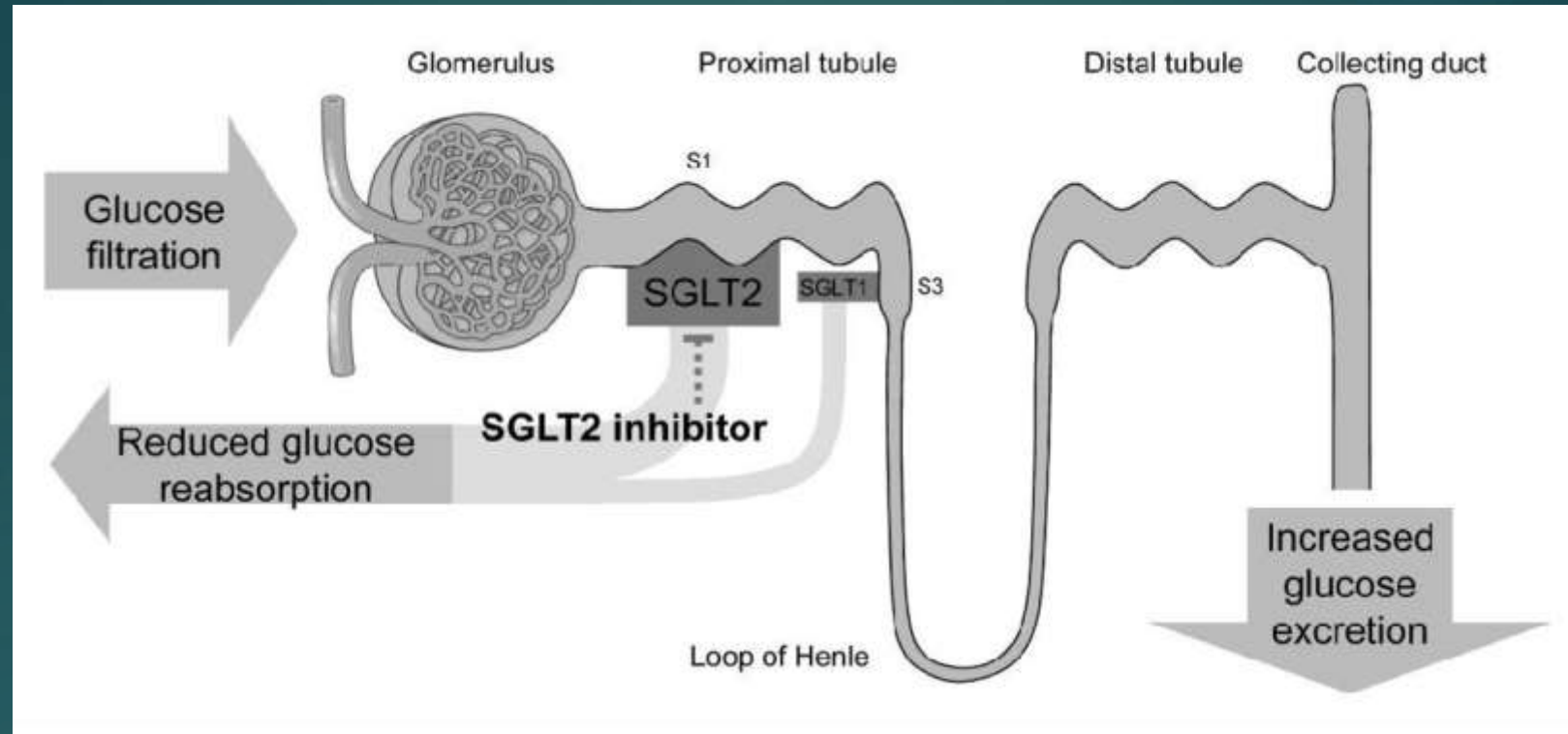
<sup>a</sup>Multiple reasons may be selected for one subject discontinuation.

18% were intolerant  
of  
sacubitril/valsartan

# SGLT2i

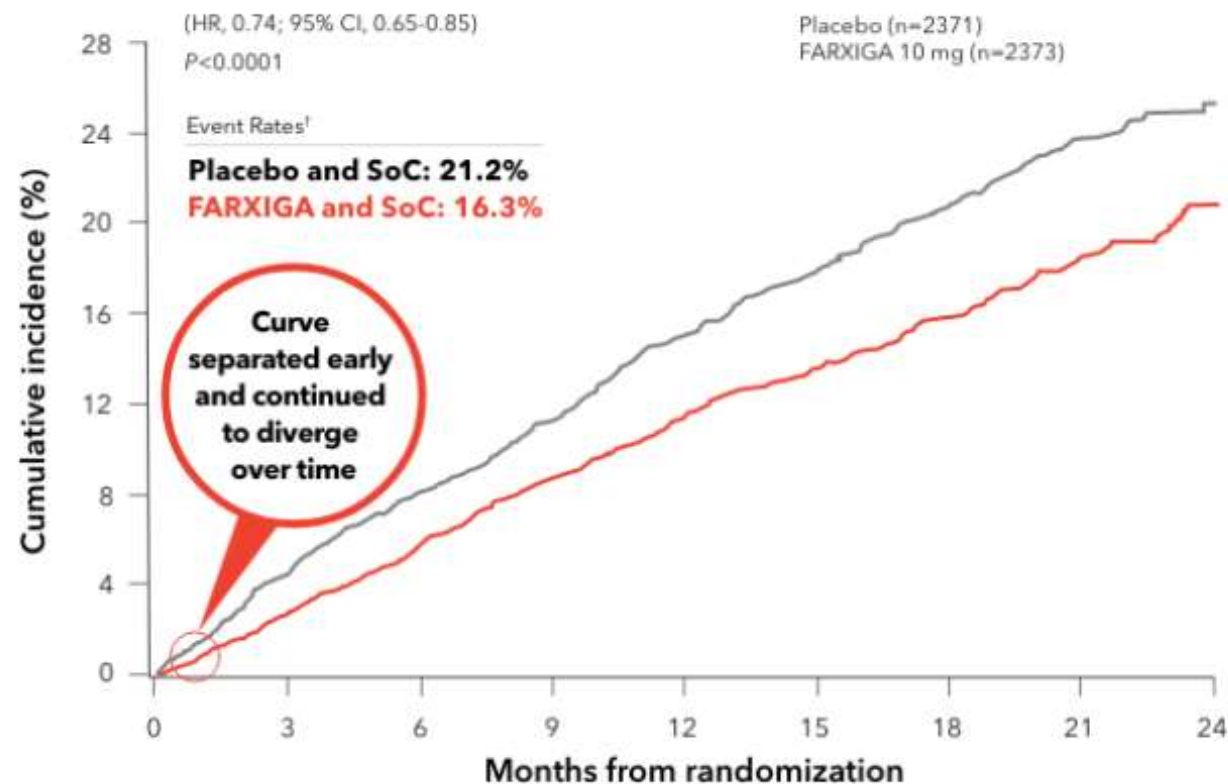
Guideline-directed medical therapy for HF with reduced EF now includes 4 medication classes, including sodium-glucose cotransporter-2 inhibitors (SGLT2i).

COR	LOE	Recommendation
1	A	In patients with symptomatic chronic HFrEF, an SGLT2i is recommended to reduce hospitalization for HF and cardiovascular mortality, irrespective of the presence of type 2 diabetes. <sup>31,32</sup>



SGLT2 inhibitors-  
Inhibit 30-50% of  
Renal Glucose  
Absorption

## Primary end point: Composite of CV death or hospitalization for heart failure<sup>1,2,\*</sup>



↓ **26%** RRR

**4.9%** ARR

👤 **NNT=21**

## DAPA-HF

NYHA class II,III,IV

EF <40%

With or without Diabetes

CV death

↓ **18%** RRR

$P=0.0294$   
(HR, 0.82; 95% CI, 0.69-0.98)

**1.9%** ARR<sup>†</sup>

Hospitalization for heart failure

↓ **30%** RRR

$P < 0.0001$   
(HR, 0.70; 95% CI, 0.59-0.83)

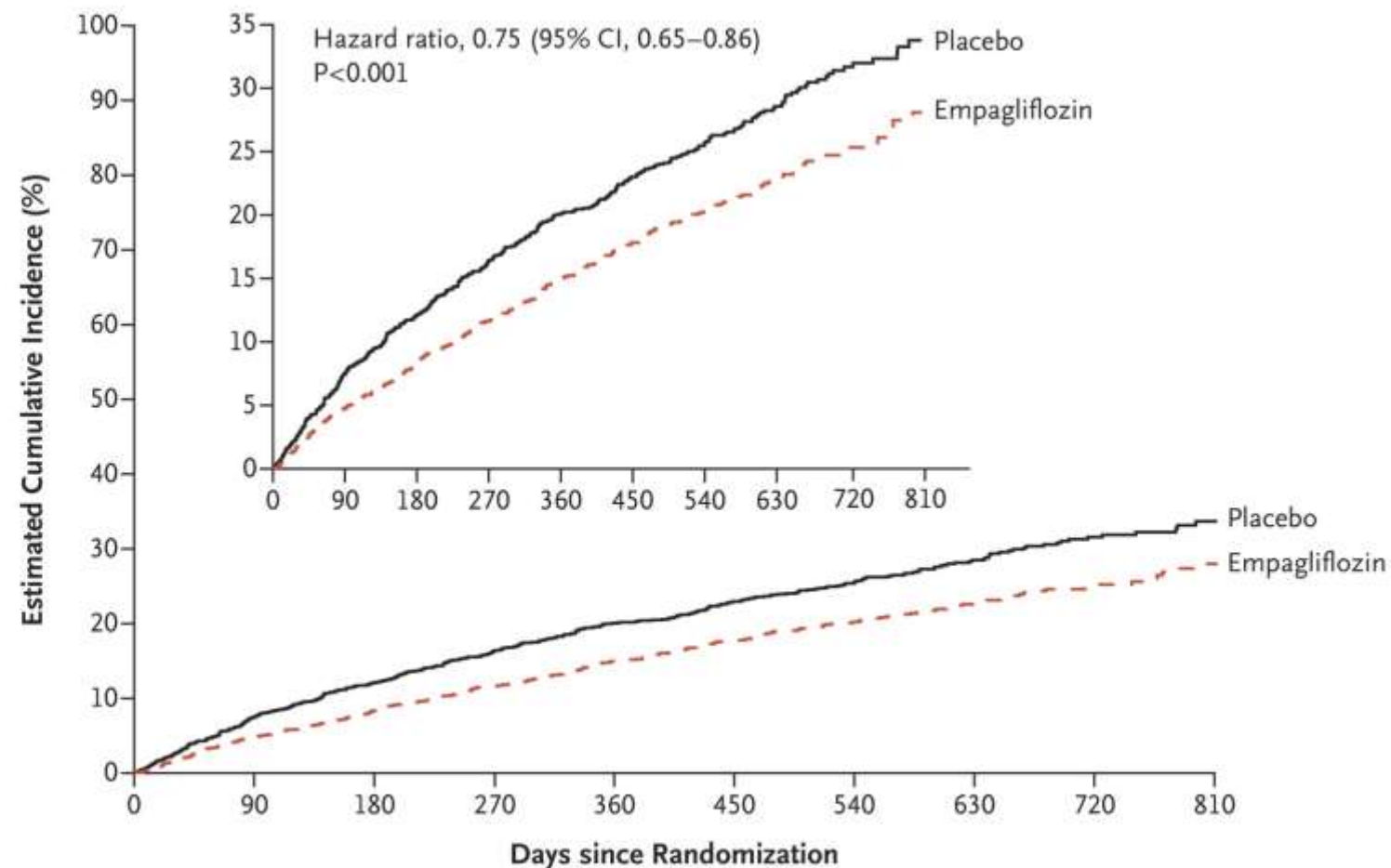
**3.7%** ARR<sup>†</sup>

# EMPEROR Reduced

Empagliflozin

3700 patients  
NYHA II,III,IV  
EF <40%

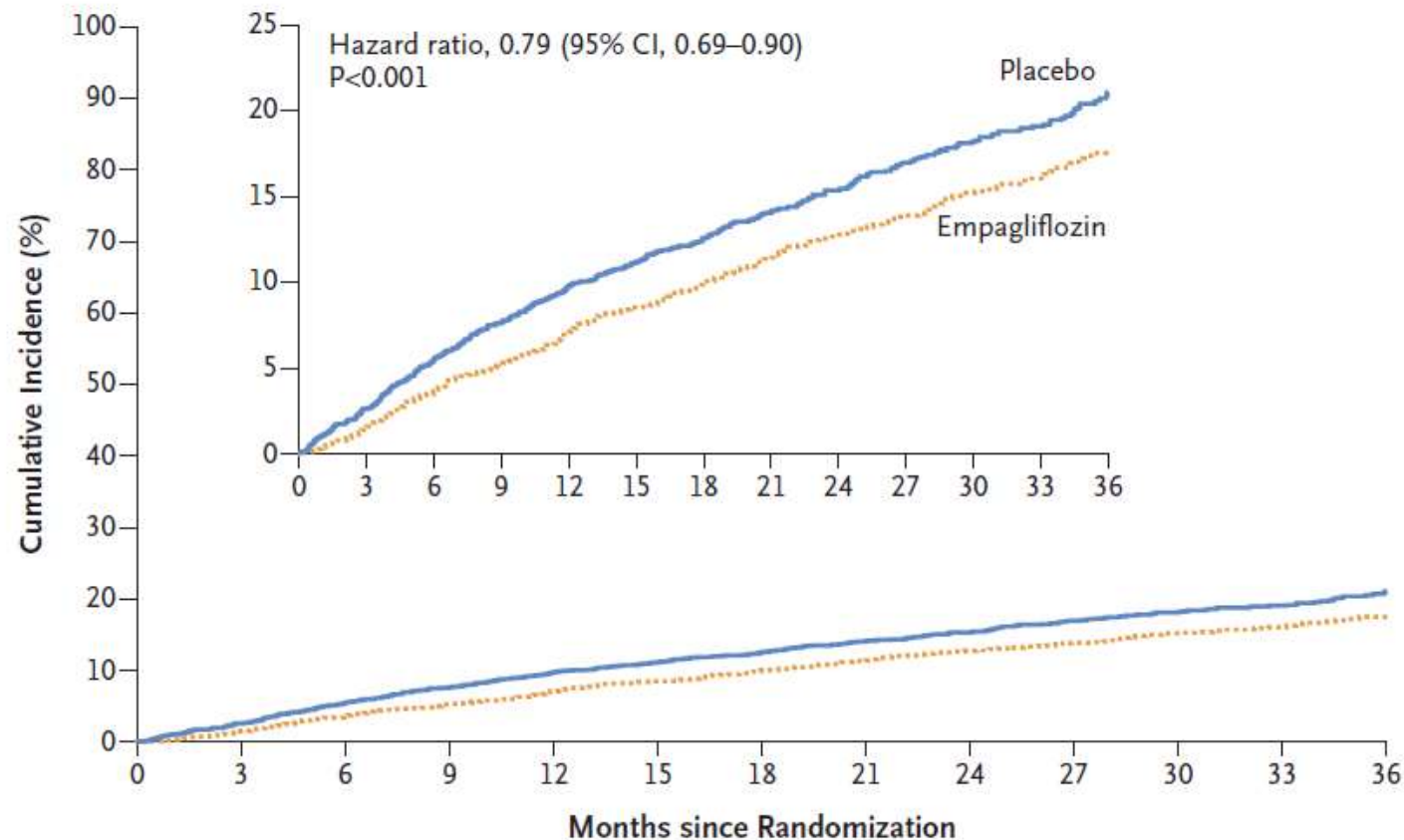
A Primary Outcome



No. at Risk

Placebo	1867	1715	1612	1345	1108	854	611	410	224	109
Empagliflozin	1863	1763	1677	1424	1172	909	645	423	231	101





**No. 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

**Figure 1. Primary Outcome, a Composite of Cardiovascular Death or Hospitalization for Heart Failure.**

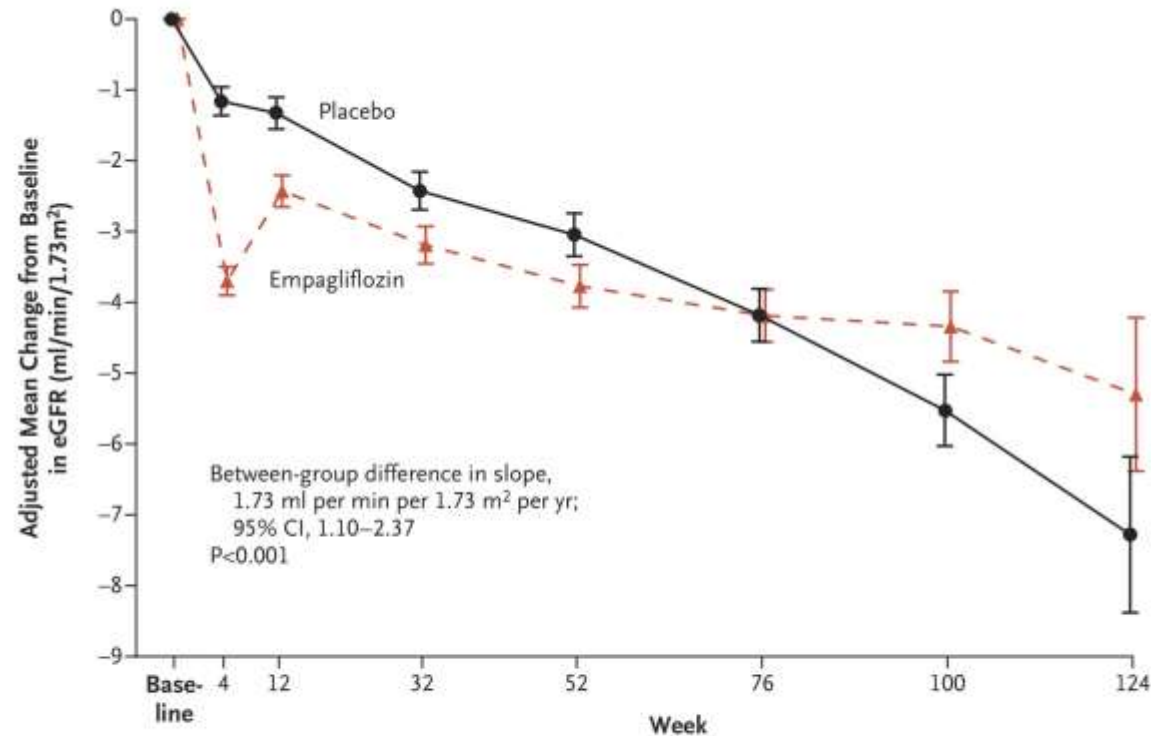
The estimated cumulative incidence of the primary outcome in the two groups is shown. The inset shows the data on an expanded y axis.

Anker et al EMPEROR-preserved

EF >40%  
NYHA class II,III,IV  
LAE or LVH  
BMI <45  
Stable diuretic dose

# EMPEROR- Reduced- Renal benefits

## Slower decline in GFR in SGLT 2 inhibitor group



No. at Risk  
Placebo  
Empagliflozin

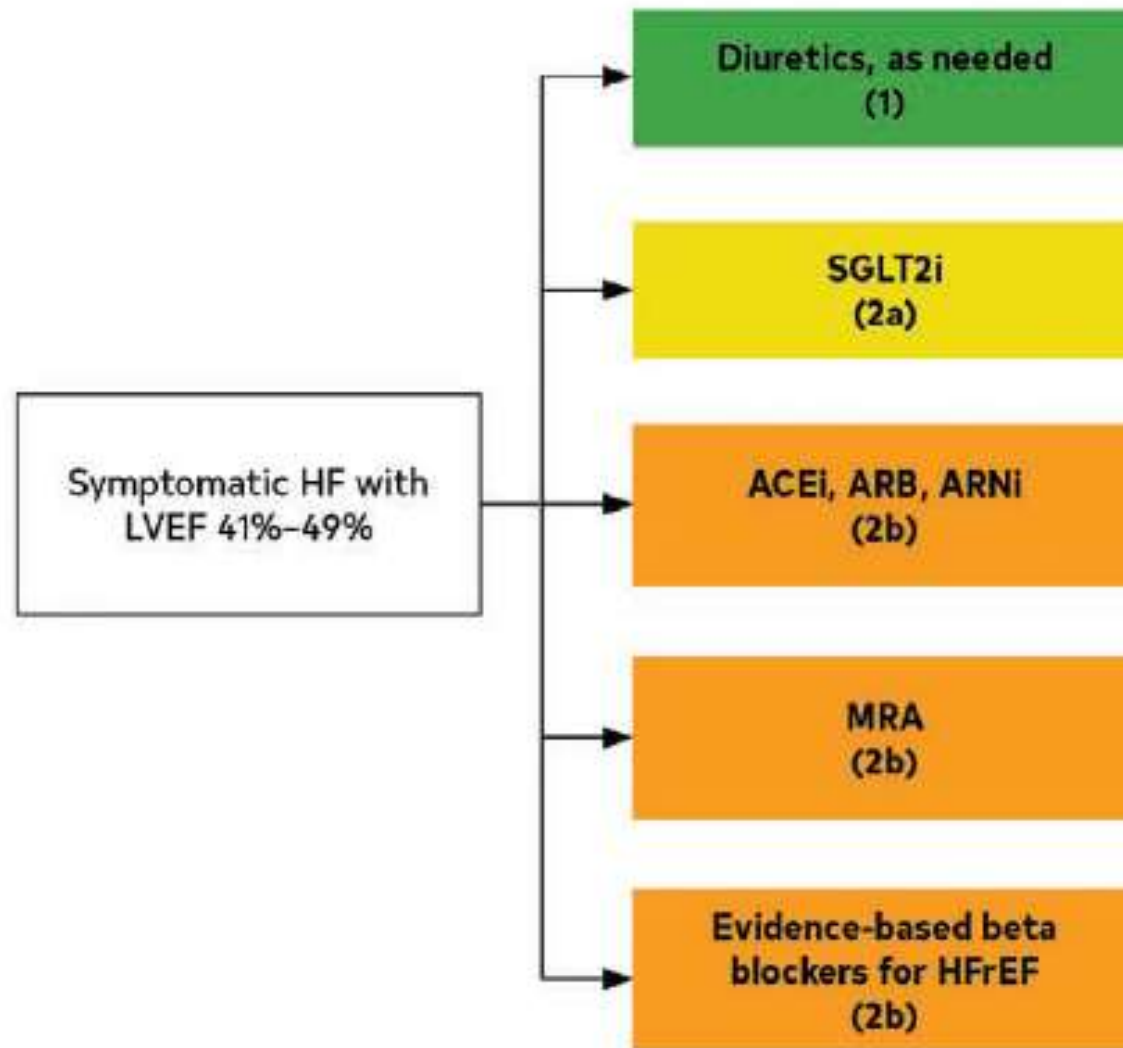
1792	1765	1683	1500	1146	745	343	76
1799	1782	1720	1554	1166	753	356	80

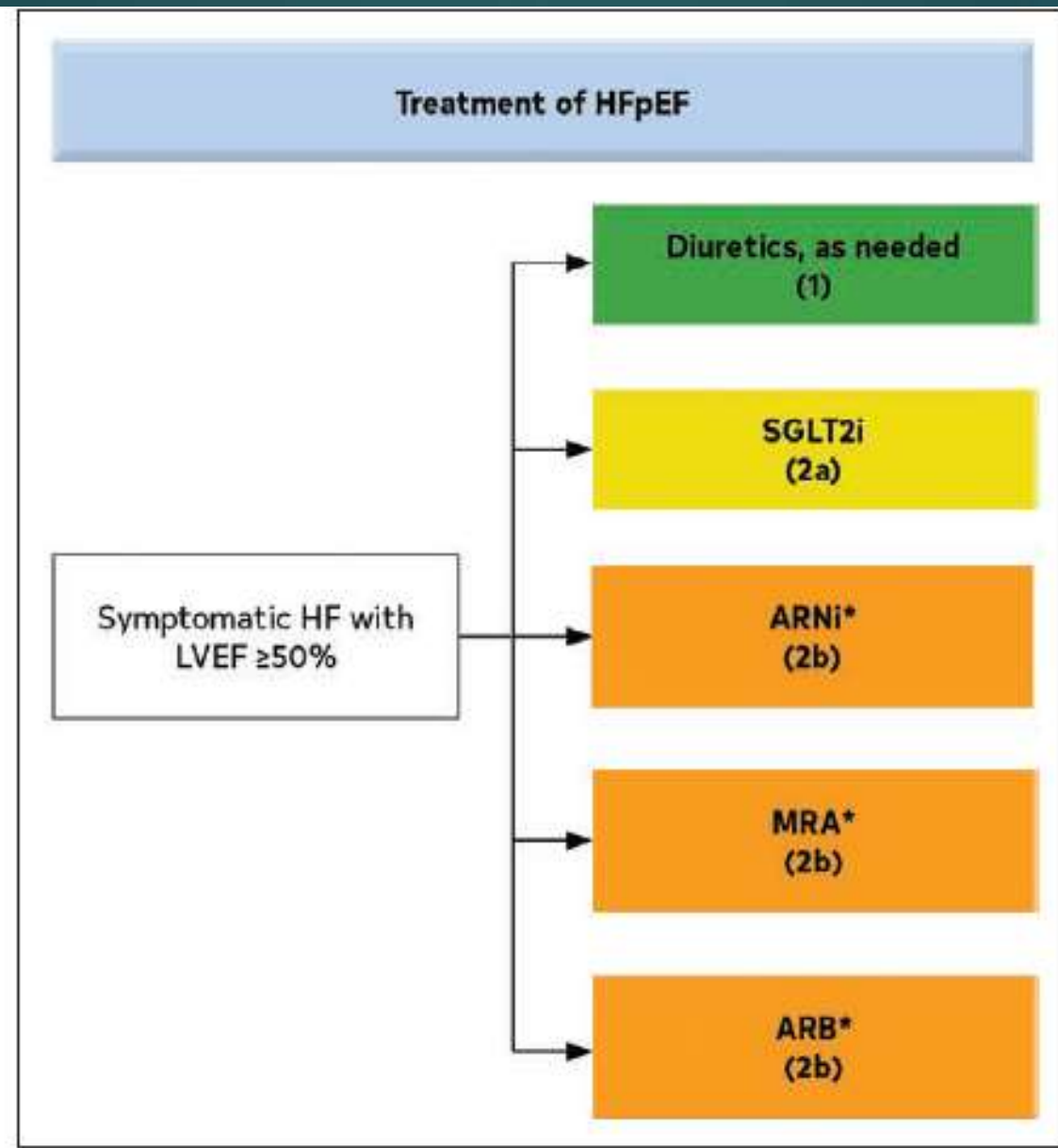
Secondary outcome

Decline in GFR -0.55 vs-  
2.28ml/1.73 body surface  
area/year

**50% Decrease in Renal Events**  
**p<0.001**

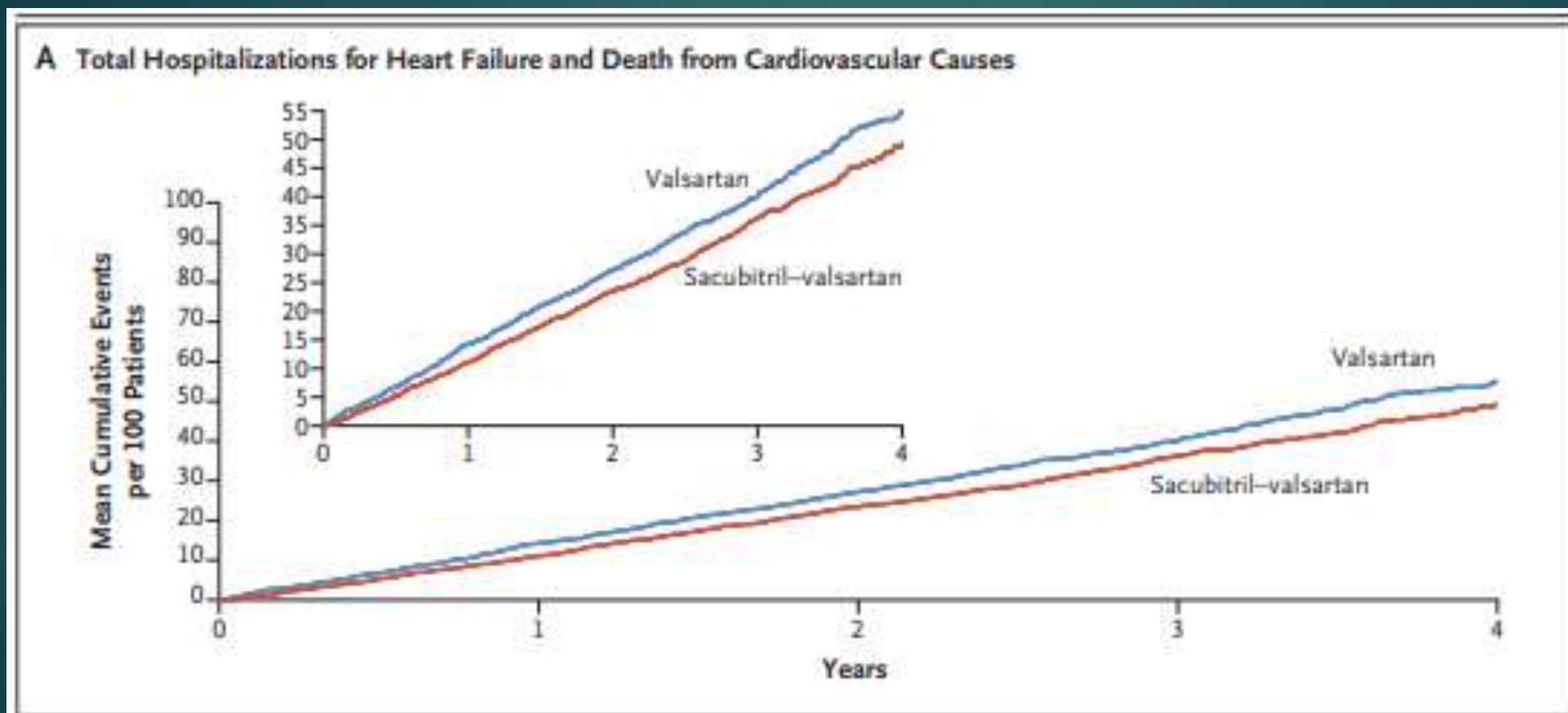
## Treatment of HFmrEF





**Figure 12.** Recommendations for Patients With Preserved LVEF ( $\geq 50\%$ ).

# PARAGON HF, $p=0.06$



NYHA) class II to IV  
EF 45% or higher,  
elevated level of  
natriuretic peptides,  
and structural heart  
disease

Sacubitril-valsartan  
(target dose, 97 mg  
of sacubitril with 103  
mg of valsartan twice  
daily) or valsartan  
(target dose, 160 mg  
twice daily

Solomon SD, McMurray JJV, Anand IS, et al. N Engl J Med.  
2019;381:1609–1620



## CHAMP-HF Registry Data

- ▶ Only 1% of eligible patients were simultaneously treated with target ACEI/ARB/ARNI, beta-blocker, and MRA therapy
- ▶ <25% patients simultaneously received any dose of all 3 medications



**Gregg Fonarow MD**

@gcfmd

Efficacy of ARNI+MRA+SGLT2i by EF

Outcome: CV💀 / HF🏠

EF 0-40%: ⬇️ 62% (CI 53-70)

EF 45-54%: ⬇️ 51% (CI 26-68)

EF 55-64%: ⬇️ 46% (CI 20-63)

EF  $\geq 65\%$ : ⬆️ 17% (CI -35-+210)

Delta in response to GDMT as function of EF categorization

Vaduganathan  
Circulation.  
2022 May  
23. doi:  
10.1161/CIRCULATION  
HA.121.0589  
29.

A Cluster Randomized **PR**agmatic  
Trial Aimed At Impr**O**ving Use Of  
Guideline Directed **M**edical Therapy  
In Out**P**atient**T**s With **H**ear**t F**ailure:  
**PROMPT-HF**

### Adherence to Evidence Based Therapies in HFrEF

Your patient meets the criteria for having Heart Failure with reduced Ejection Fraction. Relevant values are listed below:

LVEF	30%	4/7/2021
BP	140/90	8/16/2019
Potassium	6.0	8/21/2019
Heart Rate	55	8/16/2019
eGFR	55	4/9/2021

#### Current Heart Failure Therapies:

**Beta Blocker: None**

Note: Patient excluded from Beta Blocker therapy due to last heart rate being <60

Last Heart Rate: 55

#### Current ACE/ARB/ARNI Therapy

Angiotensin II Receptor Blocker-Nephrilysin Inhibitor Comb. (ARNI)

 sacubitril-valsartan (ENTRESTO) 24-26 mg tablet 1 tablet

**MRA: None**

Note: Patient excluded from MRA therapy due to one of following:

- most recent serum potassium >5 mmol/L
- Patient's last eGFR <30 mL/min/1.73m<sup>2</sup>
- Patient currently receiving potassium sparing diuretic

**SGLT2i: None**

In order to improve the care of patients with HFrEF, we have included the evidence based medical therapy order set for each of the recommended medications.

*This patient is part of a randomized clinical trial. The guideline-recommended treatment for heart failure in the alert IS NOT a substitute for clinical judgment and individual-patient-centered decision making. Evidenced-based therapies include those that may not be listed here due to patient allergy or contraindication. Please consult with the attending provider before making any clinical decisions. There are clinical reasons why these recommendations may not apply to your patient. For full treatment guidelines, click [here](#)*

Open Order Set

Do Not Open

Y HP - PROMPT HF IP - MMT MEDS [Preview](#)


### Acknowledge Reason

I will adjust medications

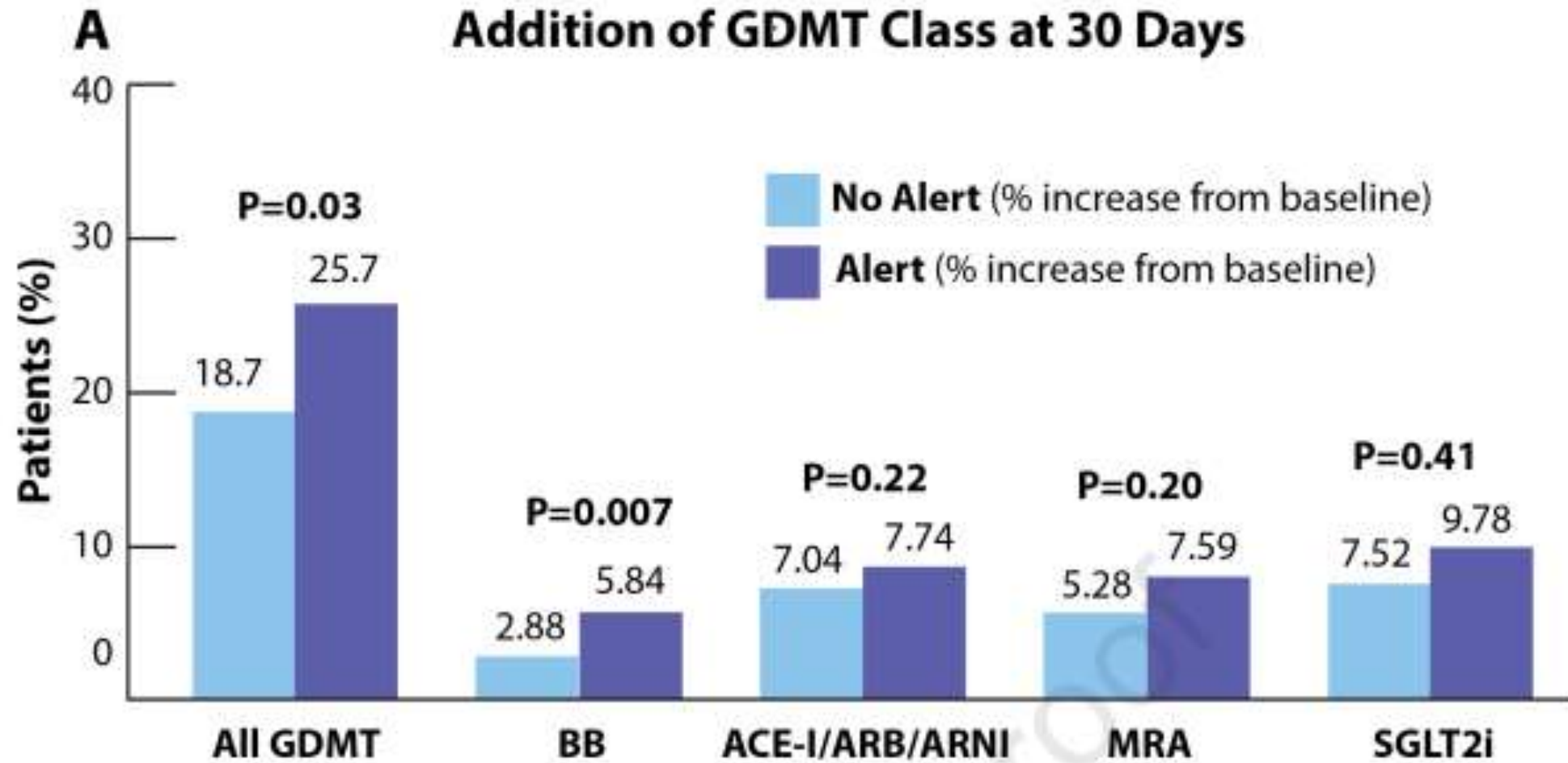
Med changes not clinically indicated

Remind me in 2 days

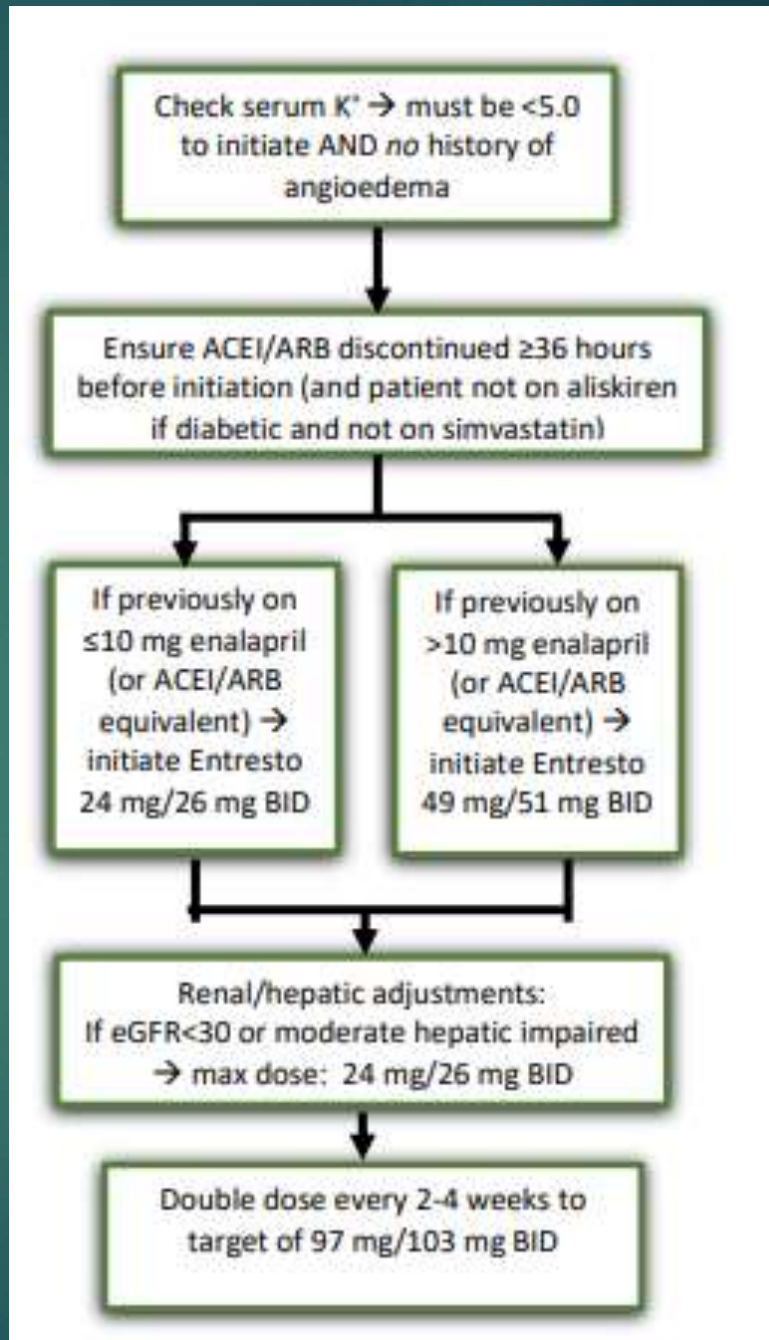
 Accept

- 
- ▶ 100 providers randomized to either an alert or usual care.
  - ▶ The primary outcome: an increase in the number of GDMT classes prescribed at 30 days post-randomization.
  - ▶ 25% implemented the recommendations,
  - ▶ 14% reported that patients weren't suitable candidates
  - ▶ 49% postponed changes
  - ▶ 12% ignored the alert





# Sacubitril/Valsartan





# 2013

## Class IIa

1. Sodium restriction is reasonable for patients with symptomatic HF to reduce congestive symptoms. (*Level of Evidence: C*)



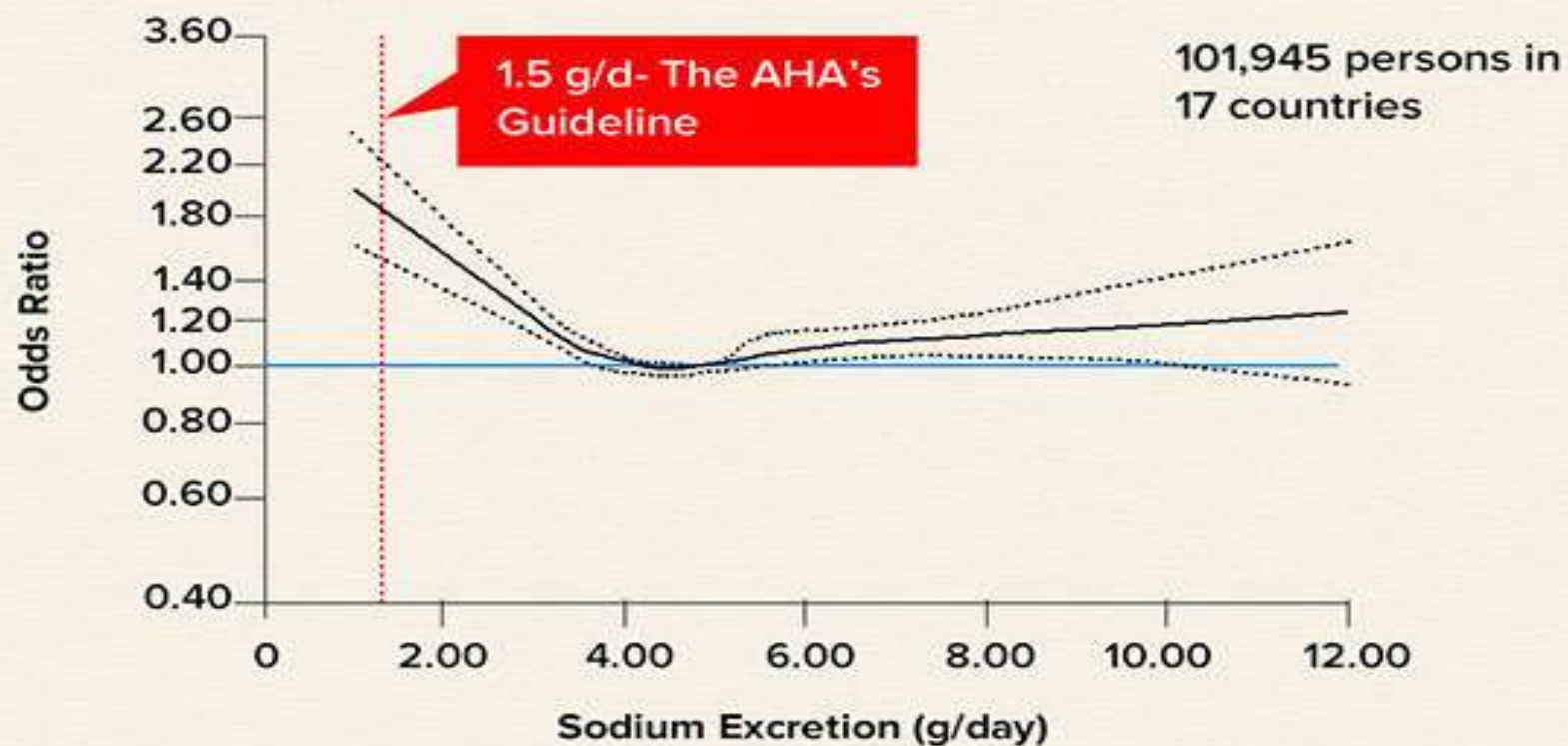
# 2022

## 7.1.2. Dietary Sodium Restriction

Recommendation for Dietary Sodium Restriction		
COR	LOE	Recommendation
2a	C-LD	1. For patients with stage C HF, avoiding excessive sodium intake is reasonable to reduce congestive symptoms. <sup>1-6</sup>



## Estimated Sodium Excretion and Risk of Death or Cardiovascular Events



No. of Events	101	1,023	1,437	597	126	25
No. at Risk	1817	30,124	46,663	18,395	3885	756





Canadian **VIGOUR** Centre  
Bridging Hearts and Minds


# Study of Dietary Intervention Under 100 MMOL in Heart Failure

## SODIUM-HF

Justin A. Ezekowitz, MBBCh MSc, on behalf of the SODIUM-HF  
investigators

Professor, University of Alberta  
Co-Director, Canadian VIGOUR Centre  
Cardiologist, Mazankowski Alberta Heart Institute  
ACC 2022



 @sodiumhf

# SODIUM-HF: Intervention

Patients randomized to one of two study arms:

## 1. Low-sodium containing diet

- <1500 mg daily (<65 mmol/daily)

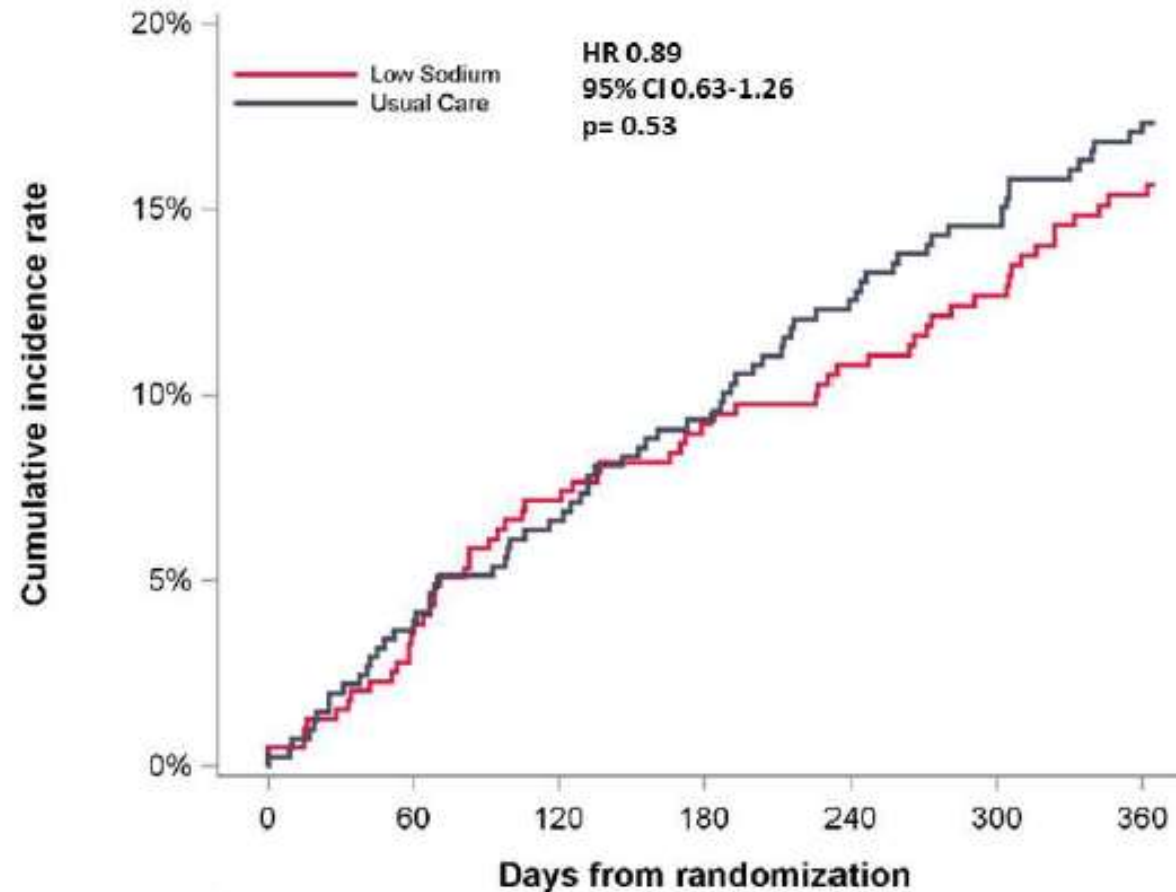
## 2. Usual care

- general advice to limit dietary sodium as provided in routine clinical practice

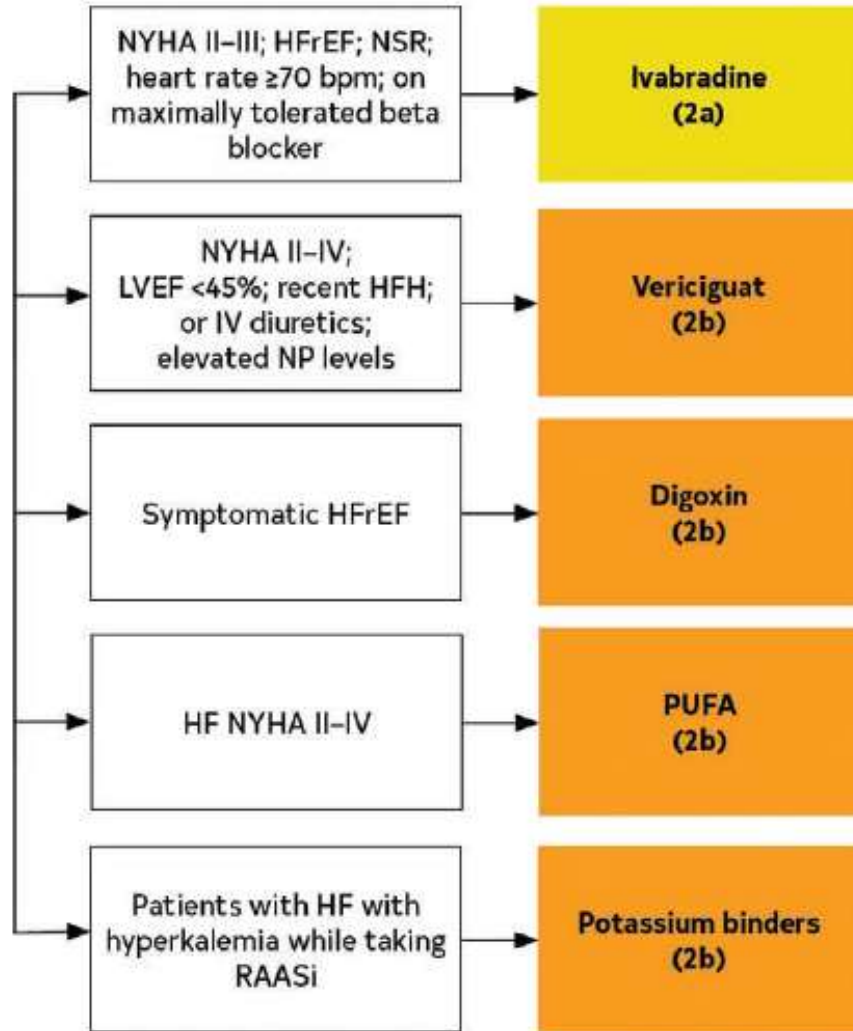


# Primary Outcome

CV related hospitalization/ED visit or all-cause mortality



**Consider Additional Therapies Once GDMT Optimized**



2b	B-R	1. In patients with HF class II to IV symptoms, omega-3 polyunsaturated fatty acid (PUFA) supplementation may be reasonable to use as adjunctive therapy to reduce mortality and cardiovascular hospitalizations. <sup>1-4</sup>
2b	B-R	2. In patients with HF who experience hyperkalemia (serum potassium level $\geq 5.5$ mEq/L) while taking a renin-angiotensin-aldosterone system inhibitor (RAASi), the effectiveness of potassium binders (patiromer, sodium zirconium cyclosilicate) to improve outcomes by facilitating continuation of RAASi therapy is uncertain. <sup>5,6</sup>



## 10.2. Management of AF in HF

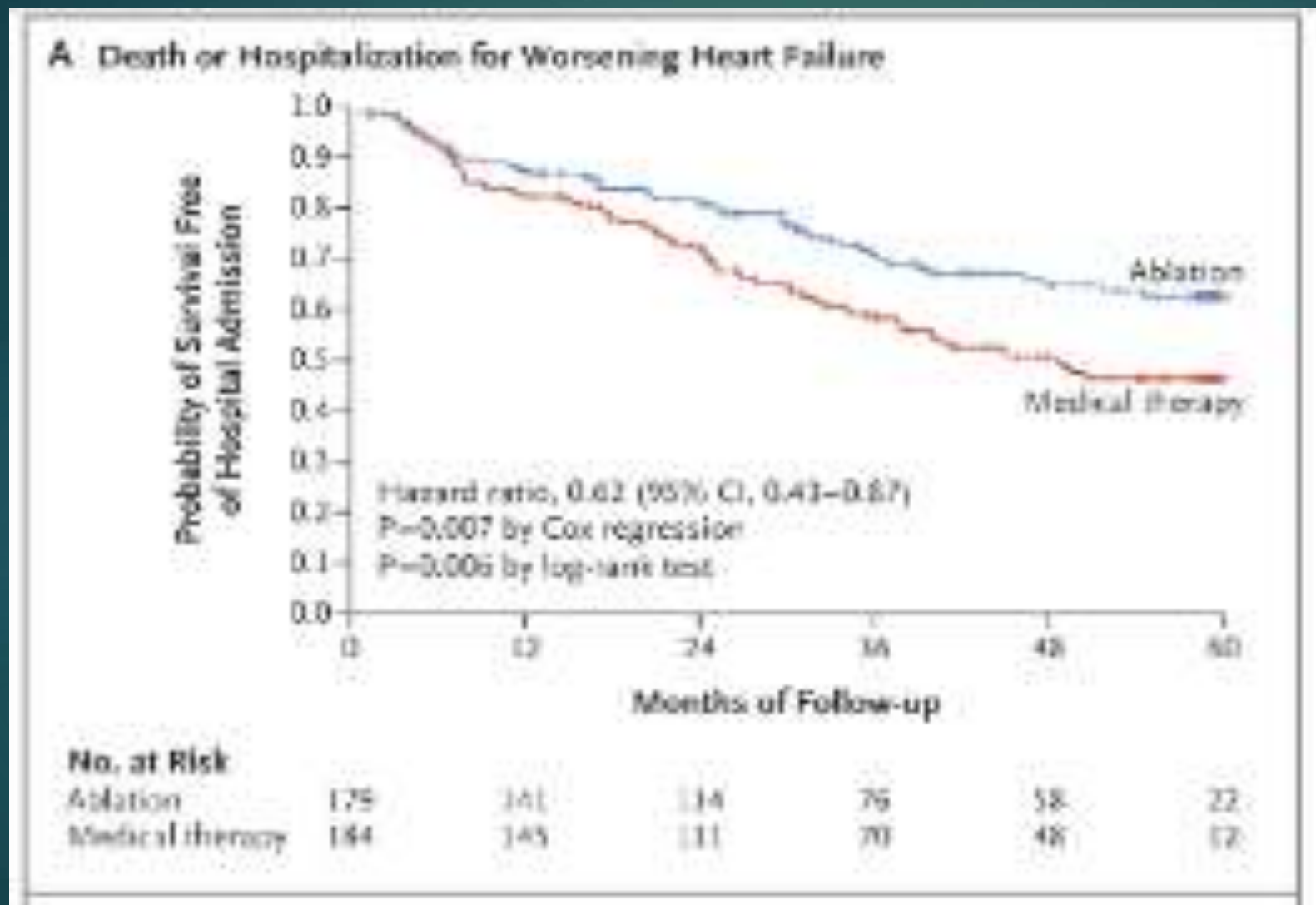
### Recommendations for Management of AF in HF

Referenced studies that support the recommendations are summarized in the [Online Data Supplements](#).

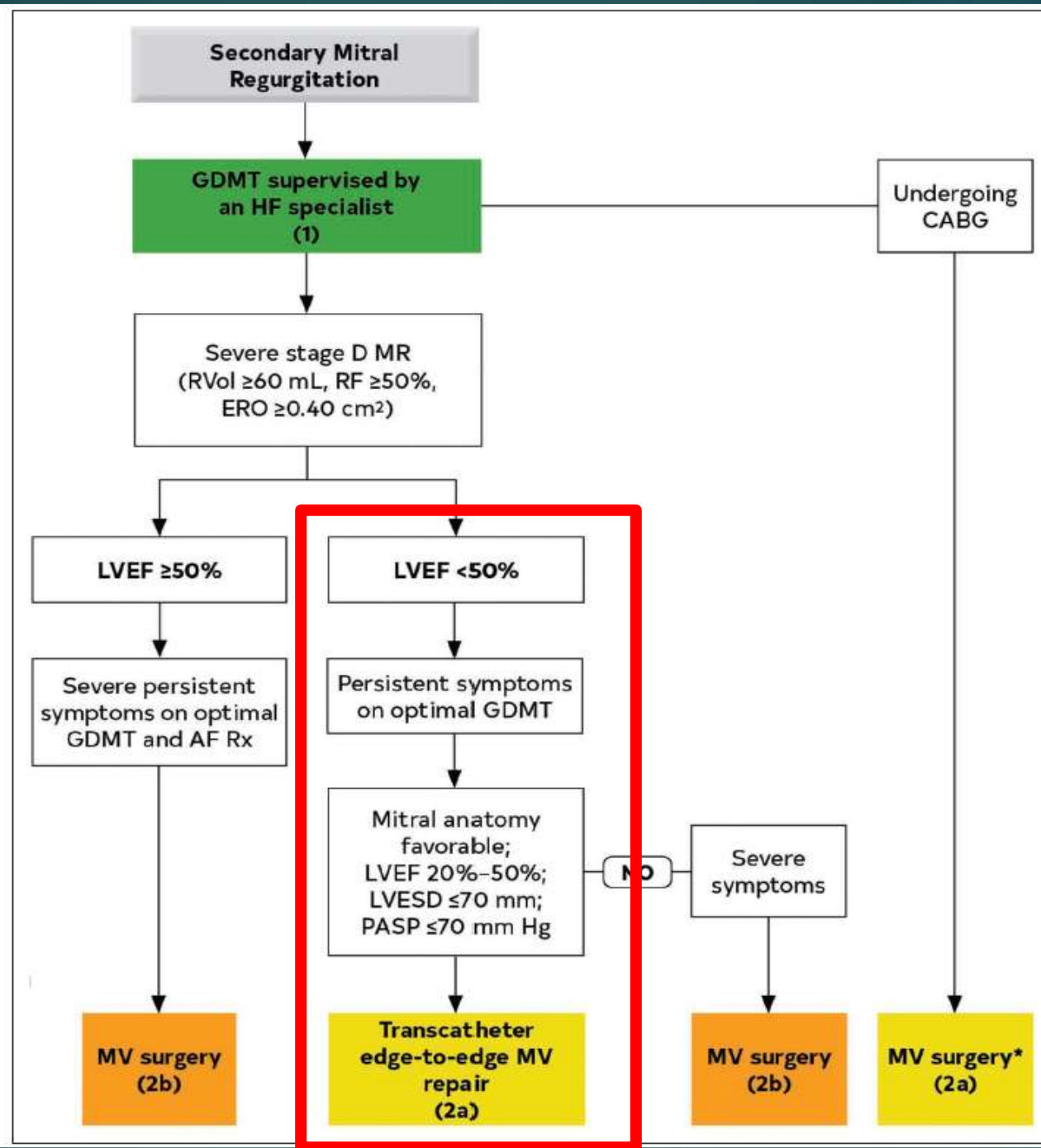
COR	LOE	Recommendations
1	A	1. Patients with chronic HF with permanent-persistent-paroxysmal AF and a CHA <sub>2</sub> DS <sub>2</sub> -VASc score of $\geq 2$ (for men) and $\geq 3$ (for women) should receive chronic anticoagulant therapy. <sup>1-5</sup>
1	A	2. For patients with chronic HF with permanent-persistent-paroxysmal AF, DOAC is recommended over warfarin. <sup>6-10</sup>
2a	B-R	3. For patients with HF and symptoms caused by AF, AF ablation is reasonable to improve symptoms and QOL. <sup>11-14</sup>
2a	B-R	4. For patients with AF and LVEF $\leq 50\%$ , if a rhythm control strategy fails or is not desired, and ventricular rates remain rapid despite medical therapy, atrioventricular nodal ablation with implantation of a CRT device is reasonable. <sup>15-22</sup>
2a	B-NR	5. For patients with chronic HF and permanent-persistent-paroxysmal AF, chronic anticoagulant therapy is reasonable for men and women without additional risk factors. <sup>23-28</sup>



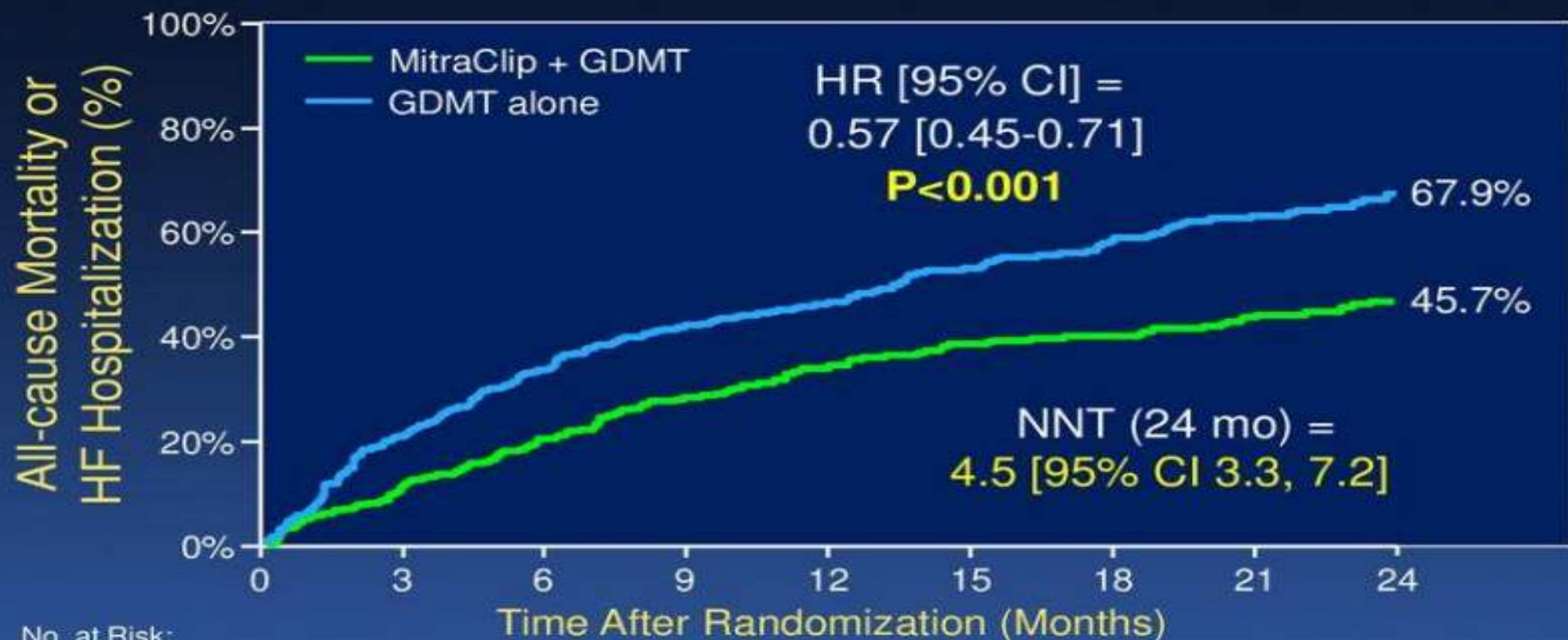
# CASTLE



Marrouche NEJM 2028



# Death or HF Hospitalization



No. at Risk:

MitraClip + GDMT	302	264	238	215	194	154	145	126	97
GDMT alone	312	244	205	174	153	117	90	75	55

**Adult Echo**

TIS0.7

MI 0.3

**X7-2t**

17Hz

13cm

**2D**

67%

C 50

P Off

Gen

**CF**

48%

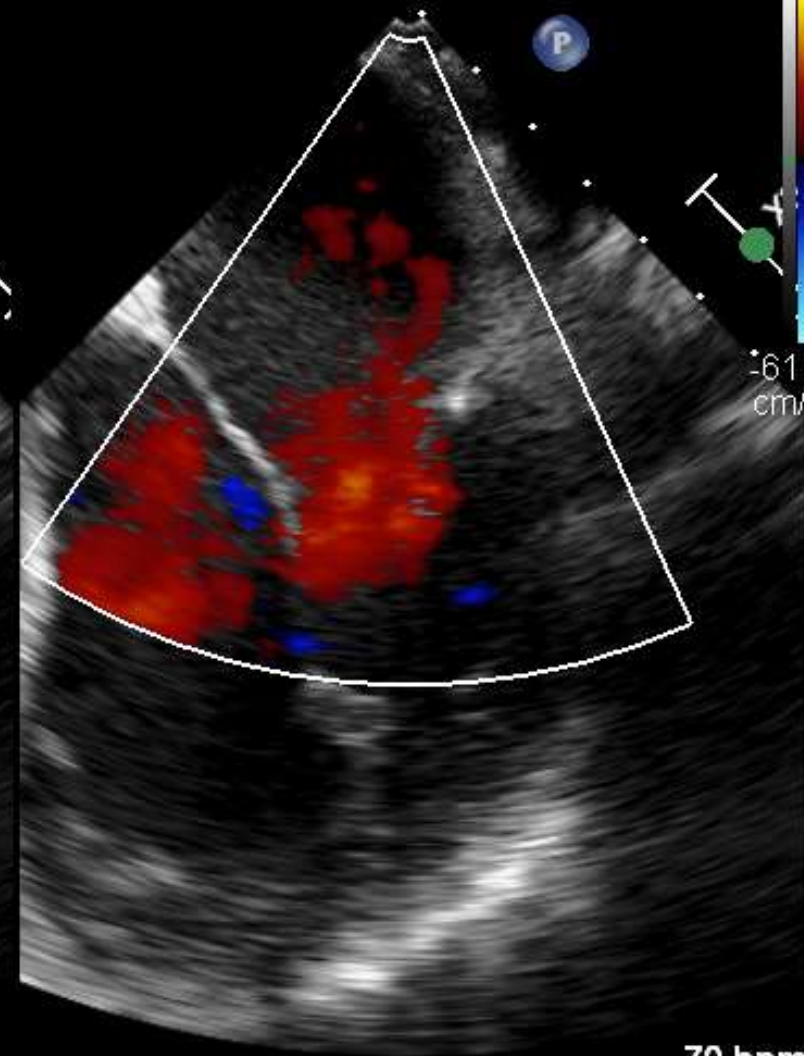
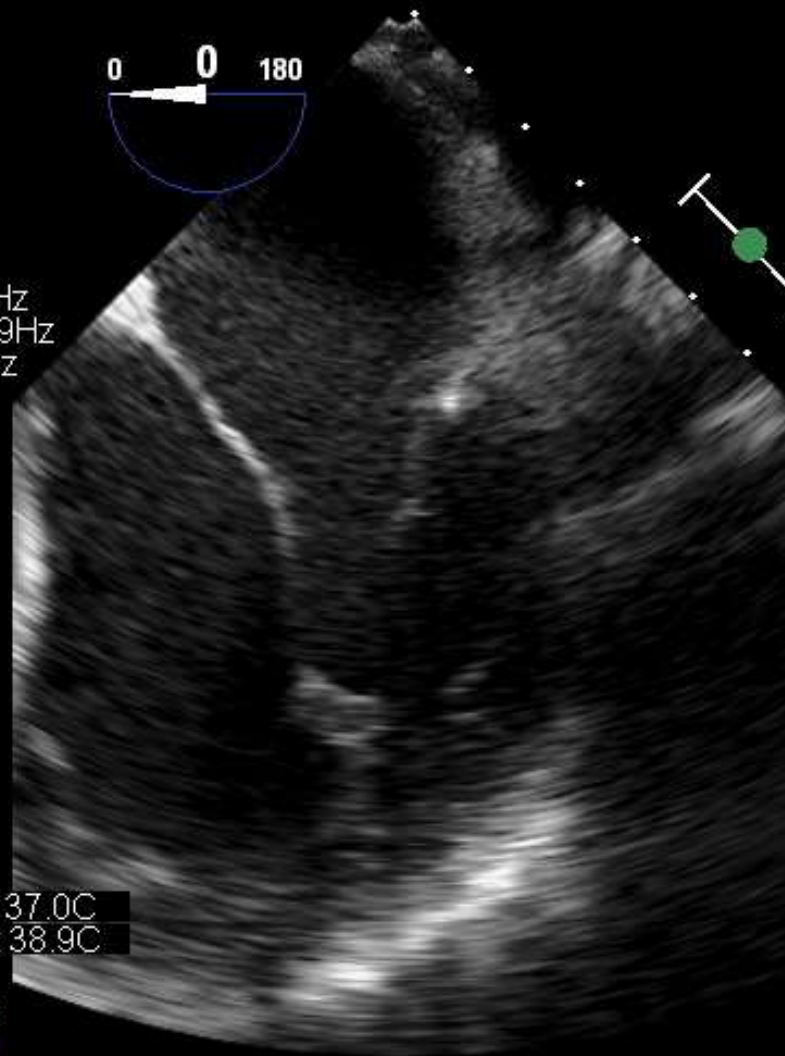
7104Hz

WF 639Hz

4.4MHz



PAT T: 37.0C  
TEE T: 38.9C



M4  
+61.6

-61.6  
cm/s

70 bpm



IRAVANI, MOUSTAFA 76679628

IU Methodist

EPIQ 7C

06/10/2021

04:12:29PM

Adult Echo

TIS0.7

MI 0.3

X7-2t

17Hz

13cm

2D

59%

C 50

P Off

Gen

CF

48%

7104Hz

VWF 639Hz

4.4MHz

0 135 180

PAT T: 37.0C

TEE T: 39.6C

M4

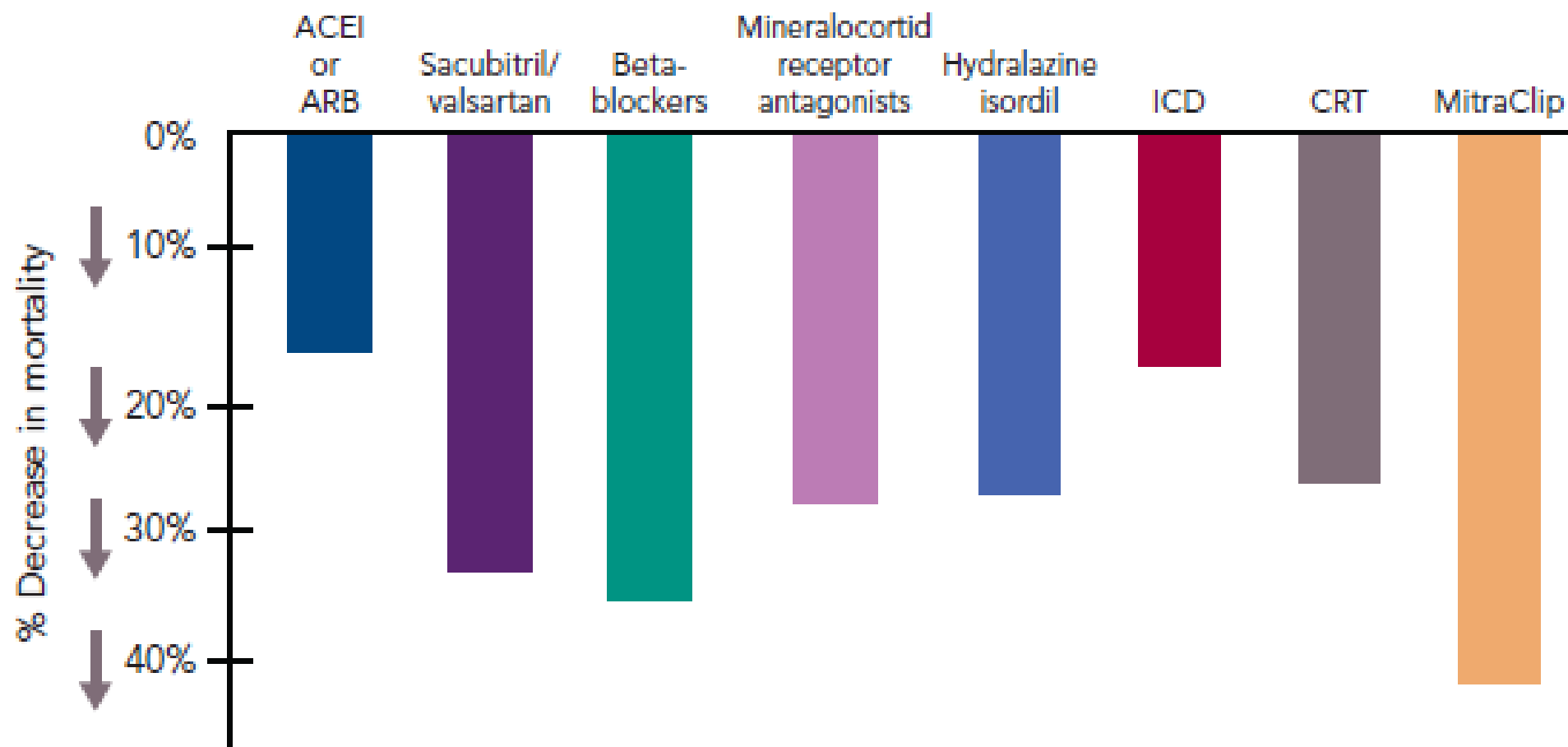
+61.6

-61.6  
cm/s

77 bpm



# Mortality reduction in Heart Failure

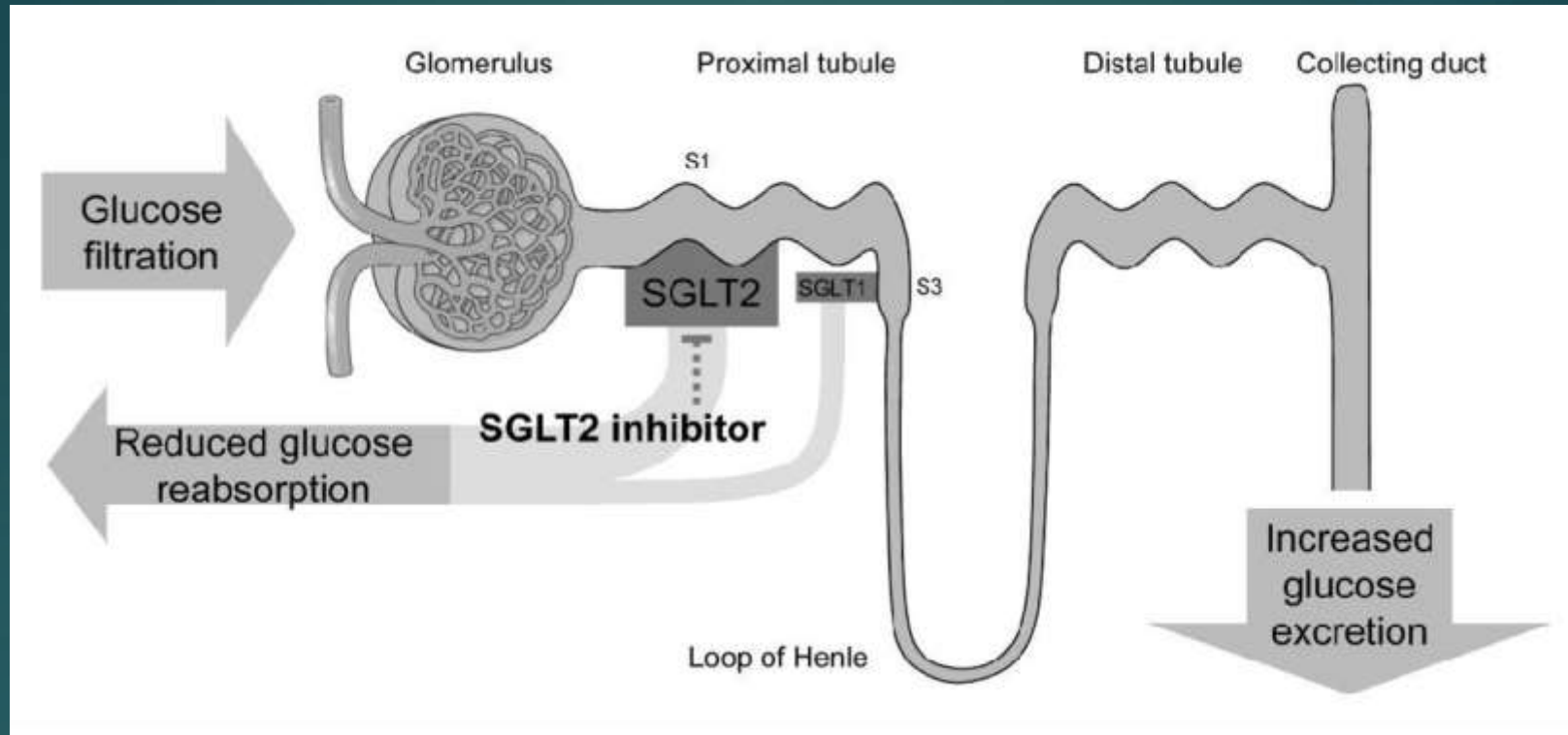


# Conclusions

- ▶ Recovered LVEF: continue GDMT
- ▶ ARNI→ACE→ARBs
- ▶ SGLT2 inhibitors – any LVEF
- ▶ Afib: rhythm control
- ▶ Severe MR: consider mitralclip



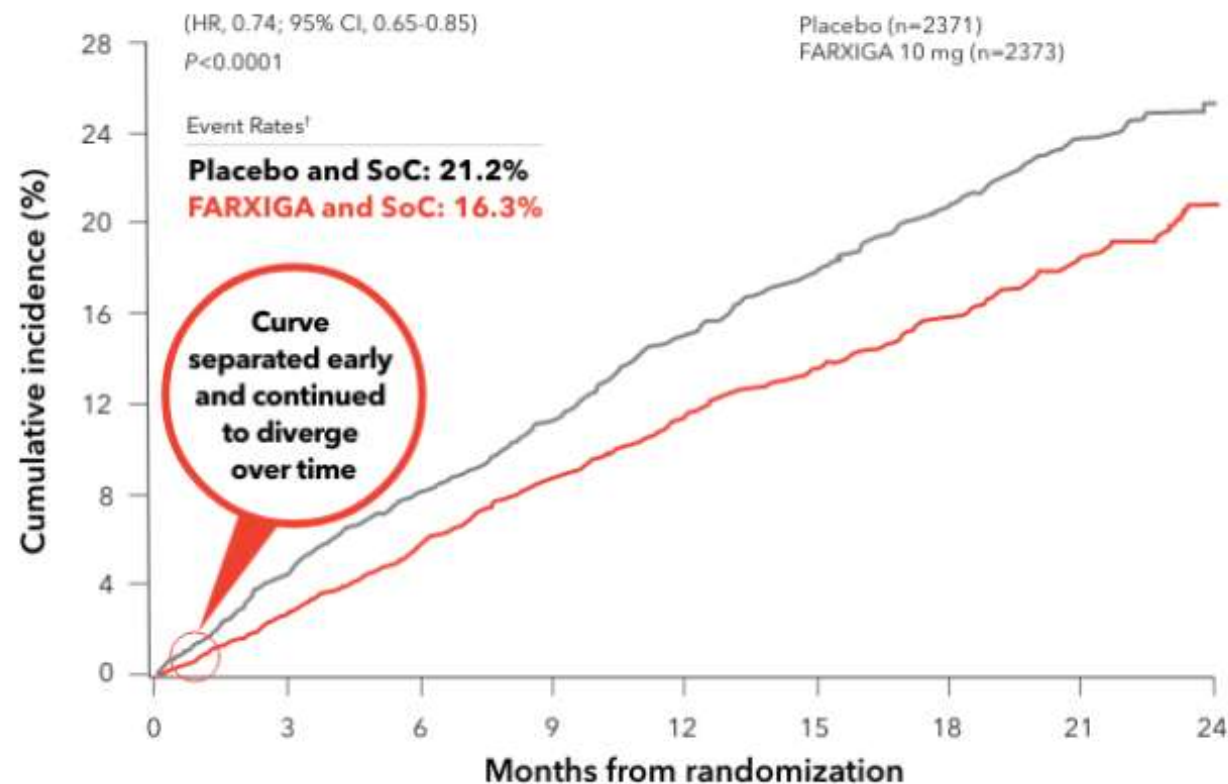
T



SGLT2 inhibitors-  
Inhibit 30-50% of  
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Absorption



## Primary end point: Composite of CV death or hospitalization for heart failure<sup>1,2,\*</sup>



↓ **26%** RRR

**4.9%** ARR

👤 **NNT=21**

## DAPA-HF

NYHA class II,III,IV

EF <40%

With or without Diabetes

CV death

↓ **18%** RRR

$P=0.0294$   
(HR, 0.82; 95% CI, 0.69-0.98)

**1.9%** ARR<sup>†</sup>

Hospitalization for heart failure

↓ **30%** RRR

$P < 0.0001$   
(HR, 0.70; 95% CI, 0.59-0.83)

**3.7%** ARR<sup>†</sup>

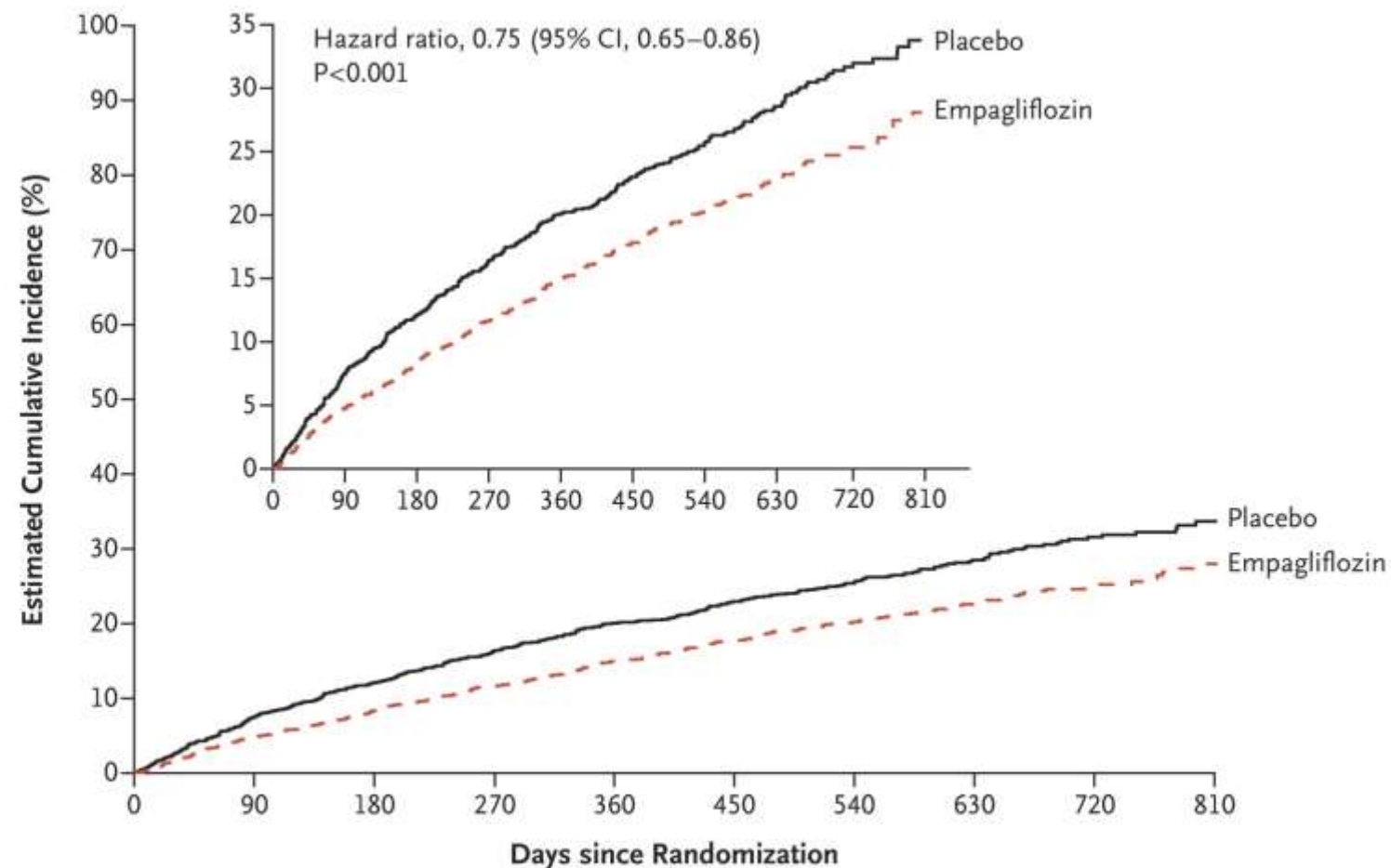


# EMPEROR Reduced

Empagliflozin

3700 patients  
NYHA II,III,IV  
EF <40%

A Primary Outcome

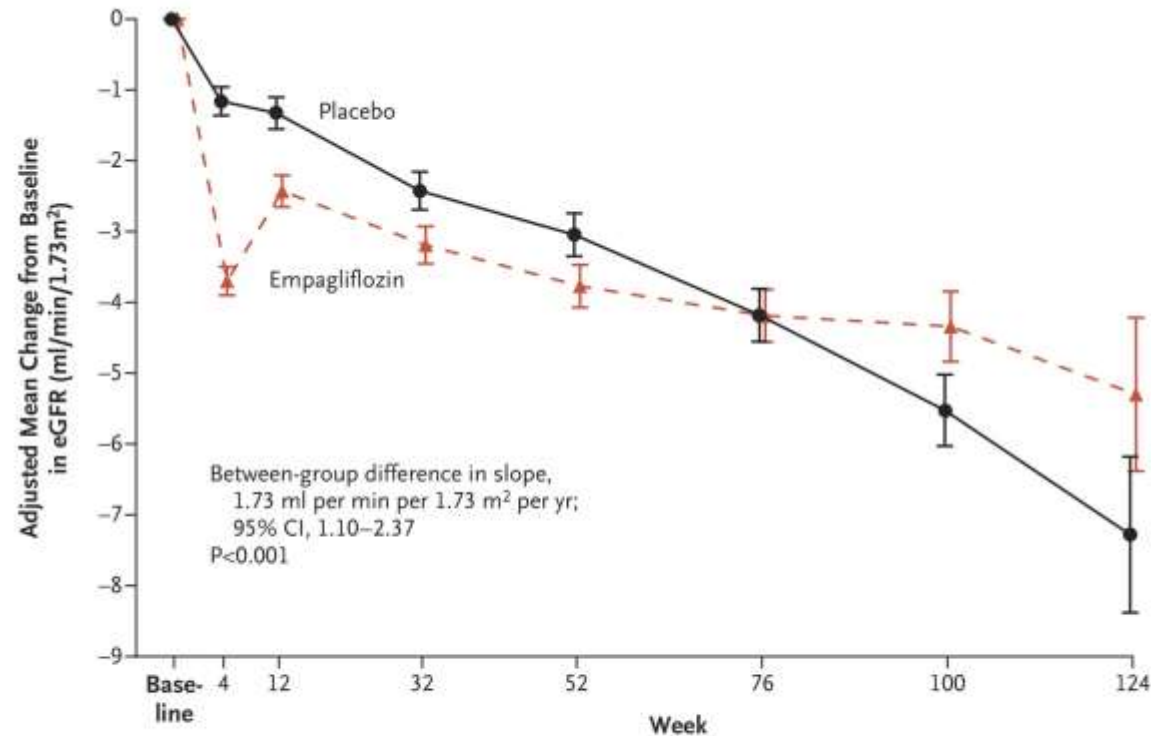


No. at Risk

Placebo	1867	1715	1612	1345	1108	854	611	410	224	109
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# EMPEROR- Reduced- Renal benefits

## Slower decline in GFR in SGLT 2 inhibitor group



No. at Risk  
Placebo  
Empagliflozin

1792	1765	1683	1500	1146	745	343	76
1799	1782	1720	1554	1166	753	356	80

Secondary outcome

Decline in GFR -0.55 vs-  
2.28ml/1.73 body surface  
area/year

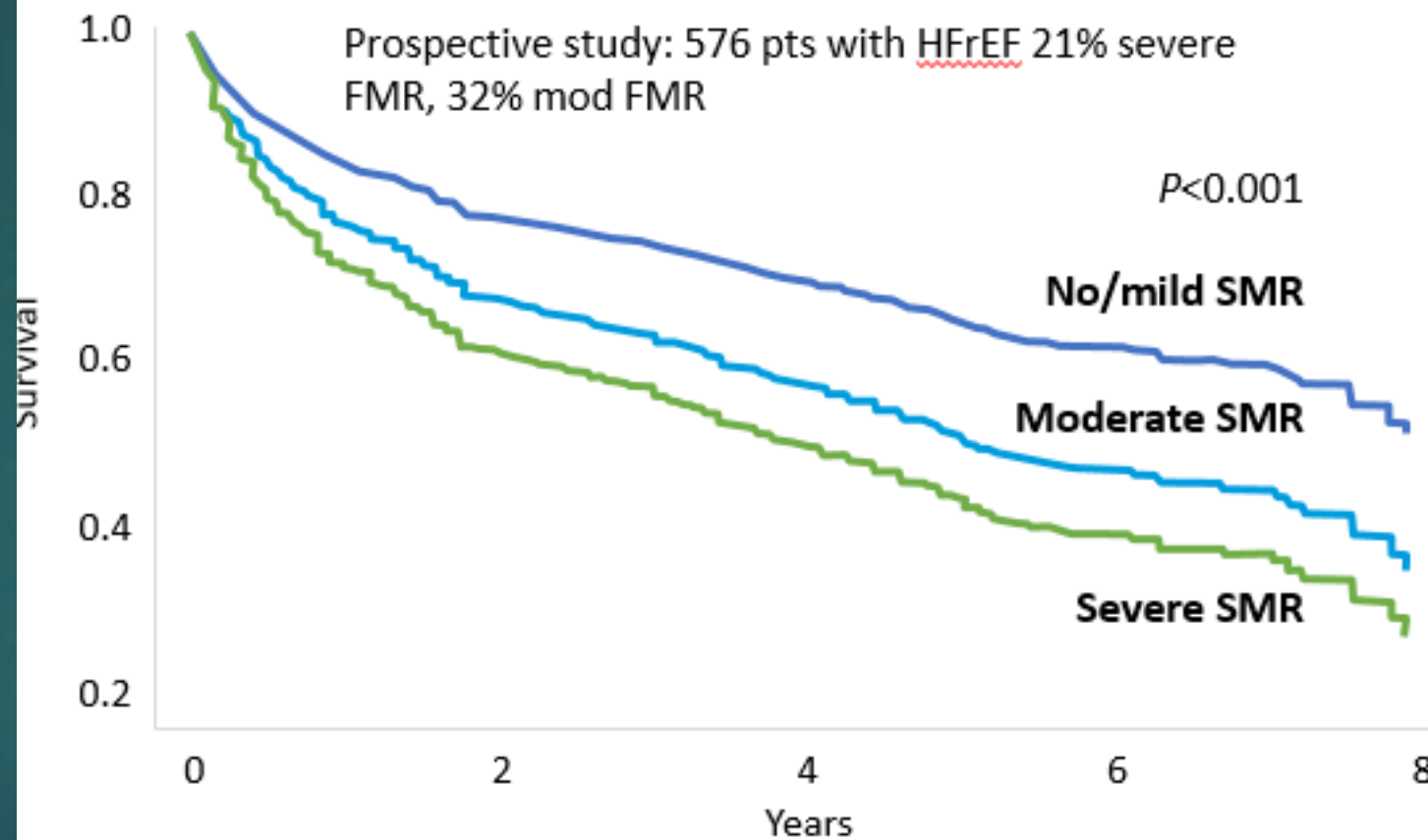
**50% Decrease in Renal Events**  
**p<0.001**

# Diastolic Heart Failure and SGLT2 inhibitors

▶ **EMPEROR –Preserved**

▶ **Deliver**

## SEVERE SECONDARY MR IS AN INDEPENDENT PREDICTOR OF MORTALITY<sup>6</sup>



Jung B, et al. *Eur Heart J*. 2003;24:1231-1243.

# Diastolic Heart Failure and SGLT2 inhibitors

▶ **EMPEROR –Preserved**

▶ **Deliver**



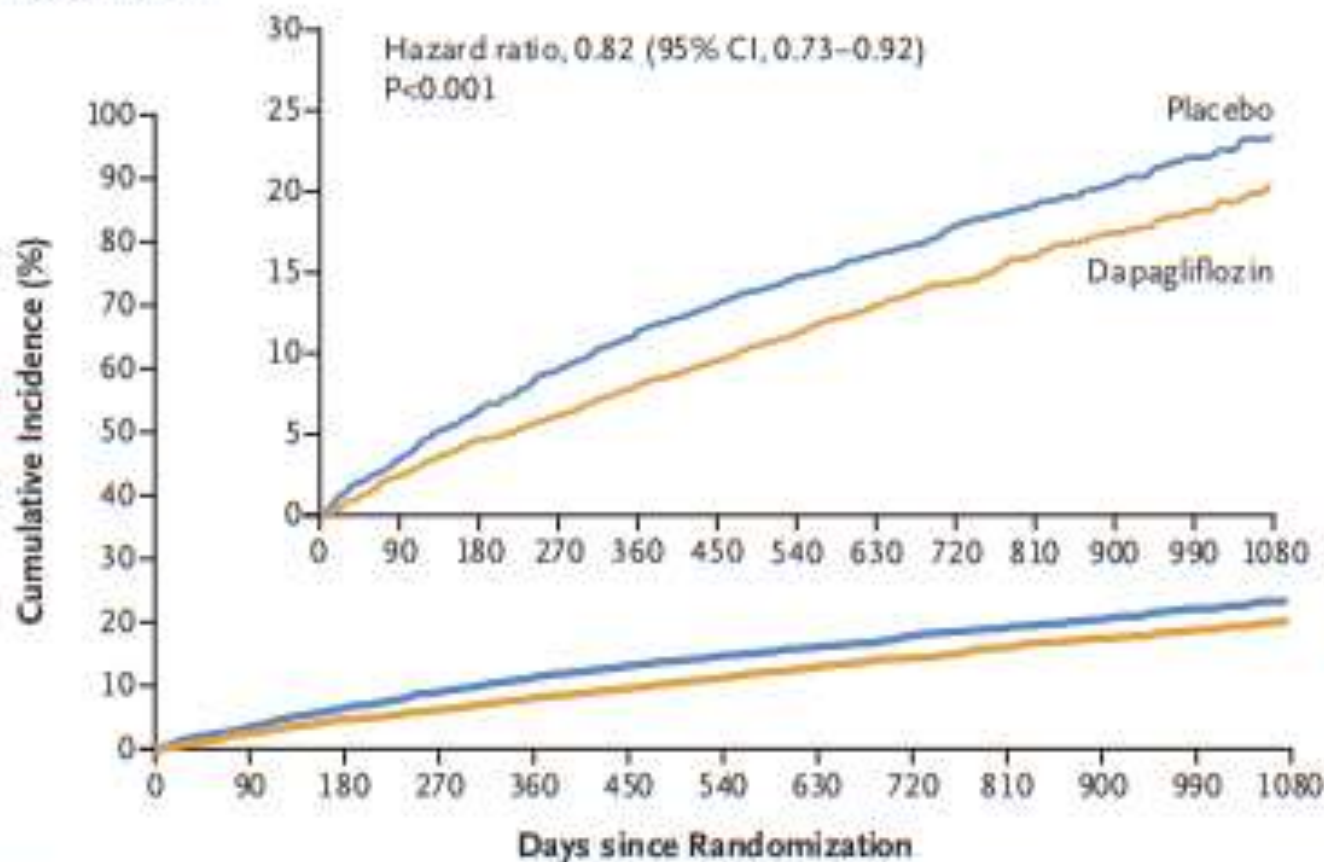
**FIGURE 5** The MitraClip Device



Close-up views of the MitraClip device's fabric-covered clip (**left**) and guiding catheter with clip delivery system (**right**). Images courtesy of Abbott Vascular, Menlo Park, California.

# DELIVER: Dapagliflozin

A Primary Outcome



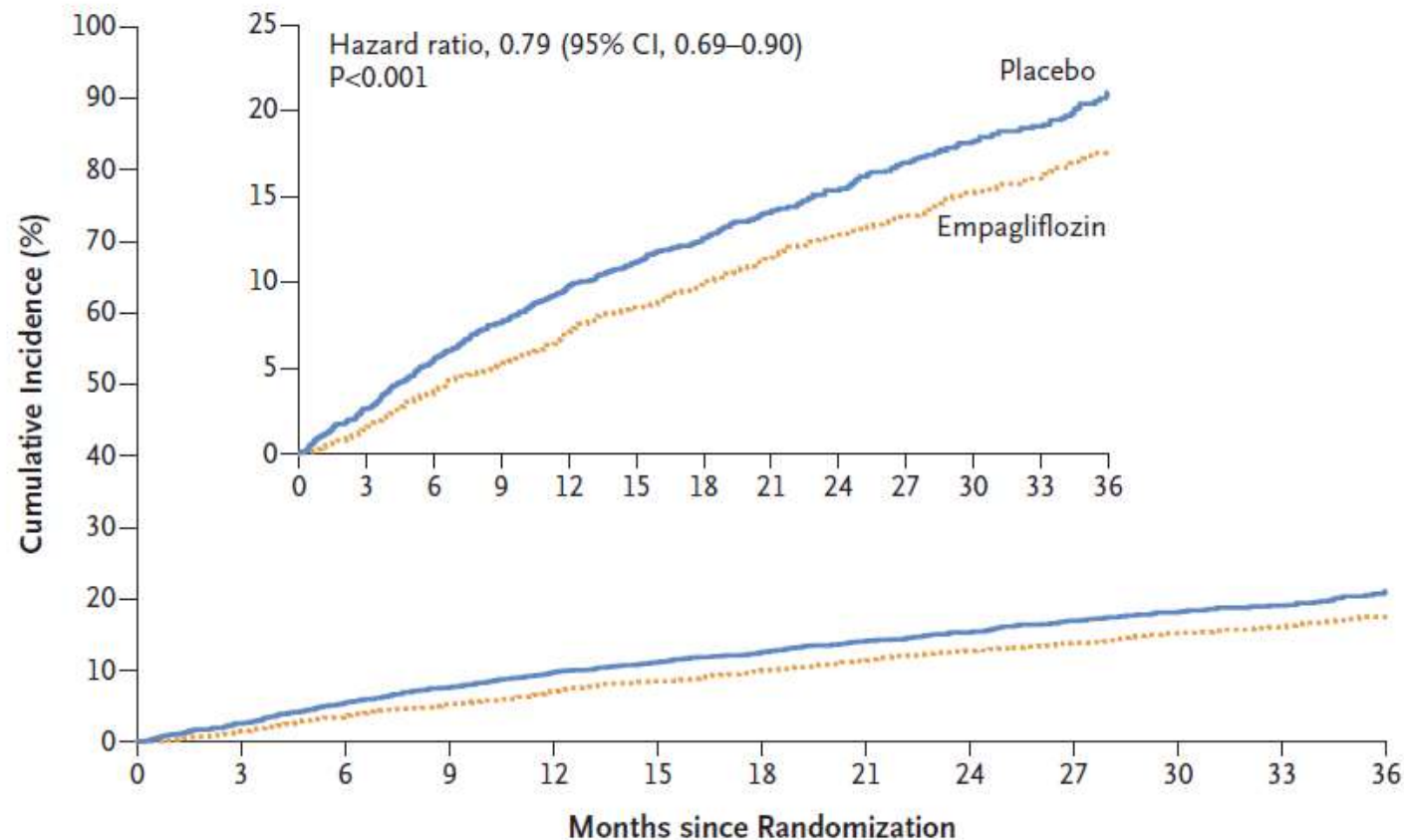
No. at Risk

Placebo	3132	3007	2896	2799	2710	2608	2318	2080	1923	1554	1140	772	383
Dapagliflozin	3131	3040	2949	2885	2807	2716	2401	2147	1982	1603	1181	801	389

EF>40%  
had evidence of  
structural heart disease;  
and had an elevated  
natriuretic peptide level

Worsening HF or CV  
death

Solomon NEJM 2022



#### No. 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

**Figure 1. Primary Outcome, a Composite of Cardiovascular Death or Hospitalization for Heart Failure.**

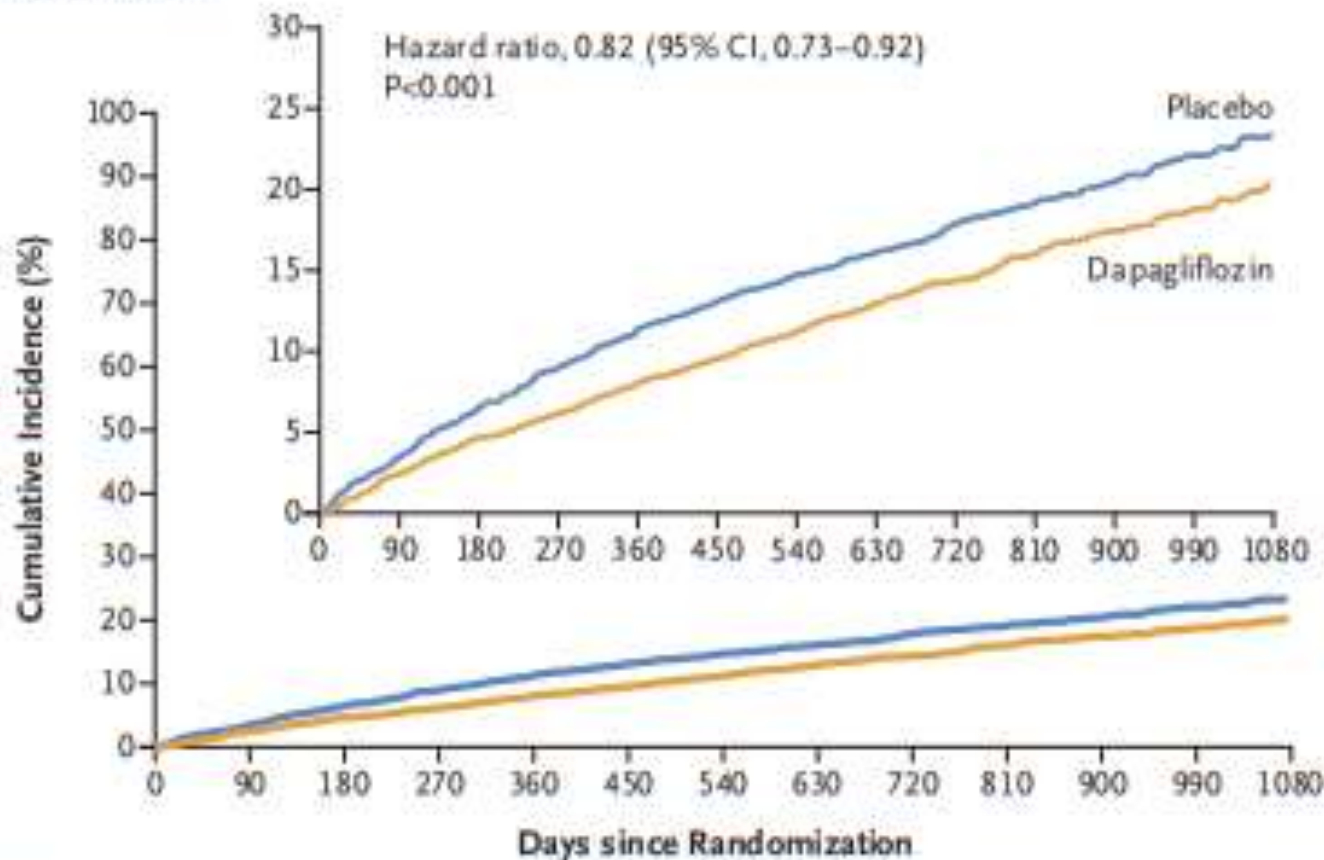
The estimated cumulative incidence of the primary outcome in the two groups is shown. The inset shows the data on an expanded y axis.

Anker et al EMPEROR-preserved

EF >40%  
NYHA class II,III,IV  
LAE or LVH  
BMI <45  
Stable diuretic dose

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## A Primary Outcome



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# 63 year old male

- ▶ Presented with severe chest pain
- ▶ Anterior MI
- ▶ 100% LAD occlusion, moderate RCA disease and severe Cx disease
- ▶ Referred for CABG, declined, multiple stents
- ▶ LVEF 20%, moderate MR
- ▶ VT storm, ablation, ICD implanted





# The COAPT Trial

Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation

A parallel-controlled, open-label, multicenter trial in ~610 patients with heart failure and moderate-to-severe (3+) or severe (4+) secondary MR who remained symptomatic despite maximally-tolerated GDMT



\*Stratified by cardiomyopathy etiology (ischemic vs. non-ischemic) and site

# Multiple admissions for syncope/falls/shortness of breath



**1**

**B-R**

4. For patients who have LVEF  $\leq 35\%$ , sinus rhythm, left bundle branch block (LBBB) with a QRS duration  $\geq 150$  ms, and NYHA class II, III, or ambulatory IV symptoms on GDMT, CRT is indicated to reduce total mortality, reduce hospitalizations, and improve symptoms and QOL.<sup>18-21</sup>





IRAVANI, MOUSTAFA 76679628

IU Methodist

EPIQ 7C

06/10/2021 03:04:10PM

Adult Echo

TIS0.1

MI 0.3

X7-2t

3D Beats 1

10Hz

7.8cm

3D Zoom

2D / 3D

% 61 / 17

C 50 / 30

Gen



M4

PAT T: 37.0C  
TEE T: 40.2C

IRAVANI, MOUSTAFA 76679628

IU Methodist

EPIQ 7C

06/10/2021 04:01:56PM

Adult Echo

TIS0.1

MI 0.3

X7-2t

3D Beats 1

10Hz

8.0cm

3D Zoom

2D / 3D

% 54 / 9

C 50 / 30

Gen



M4

PAT T: 37.0C  
TEE T: 39.8C

76 bpm