Guideline Directed Management of Heart Failure

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Disclosures

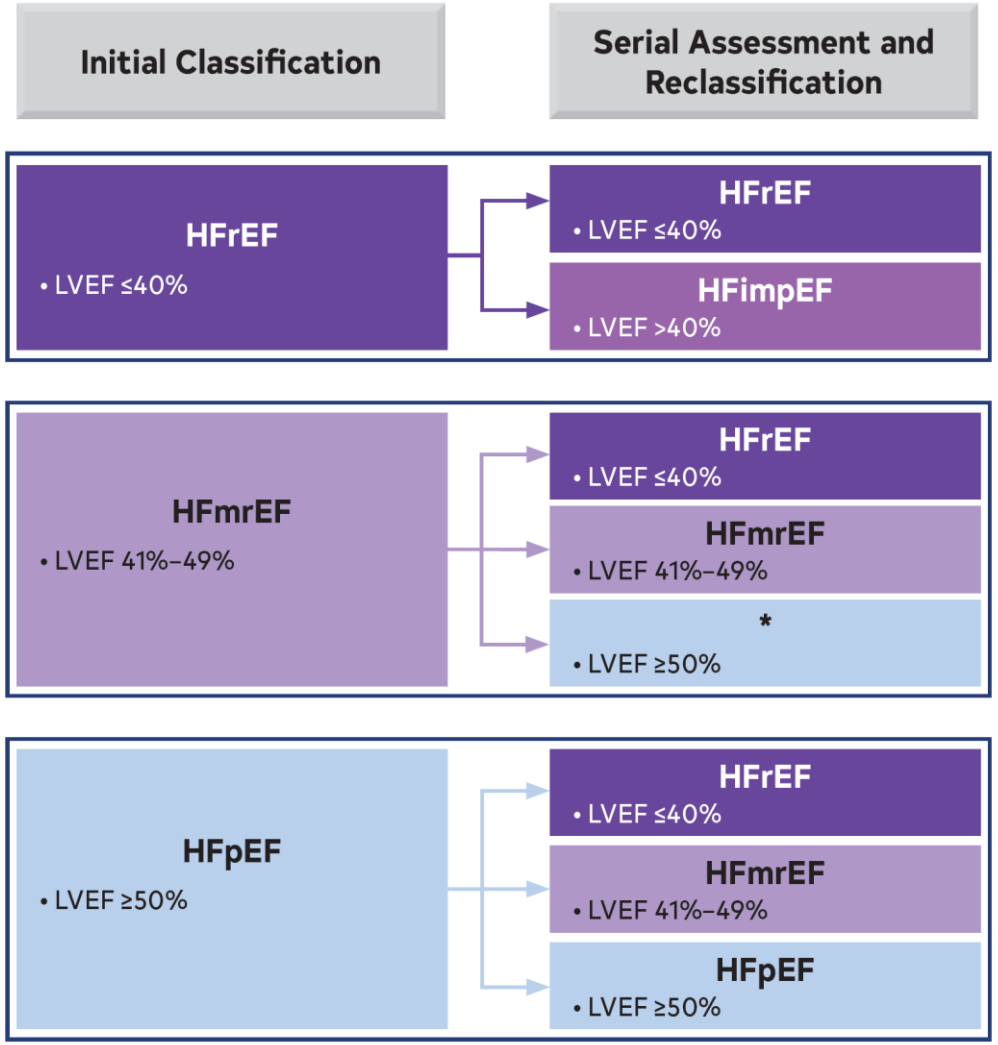
- **Clinical Event Committee**: Abbott, GUIDE HF Trial
- **Consultation:** Astra Zeneca, Amgen, Bristol Myers Squibb, scPharmaceuticals, Baxter, Sanofi-Aventis, Relypsa, Vifor, Boehringer Ingelheim
- **DSMC:** Anthem Trial, Liva Nova

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

Endorsed by the Heart Failure Society of America

Heidenreich P, Bozkurt B et al. 2022 AHA/ACC/HFSA Guideline
https://doi.org/10.1016/j.jacc.2021.12.012, https://www.ahajournals.org/doi/10.1161/CIR.0000000000001063

Classification and Trajectories of HF Based on LVEF



Heidenreich P, Bozkurt B et al. 2022 AHA/ACC/HFSA Guideline, https://doi.org/10.1016/j.jacc.2021.12.012, https://www.ahajournals.org/doi/10.1161/CIR.0000000000001063

2022 ACC/AHA/HFSA Guidelines
Diagnostic Criteria Based on LVEF

TABLE 4 Classification of HF by LVEF

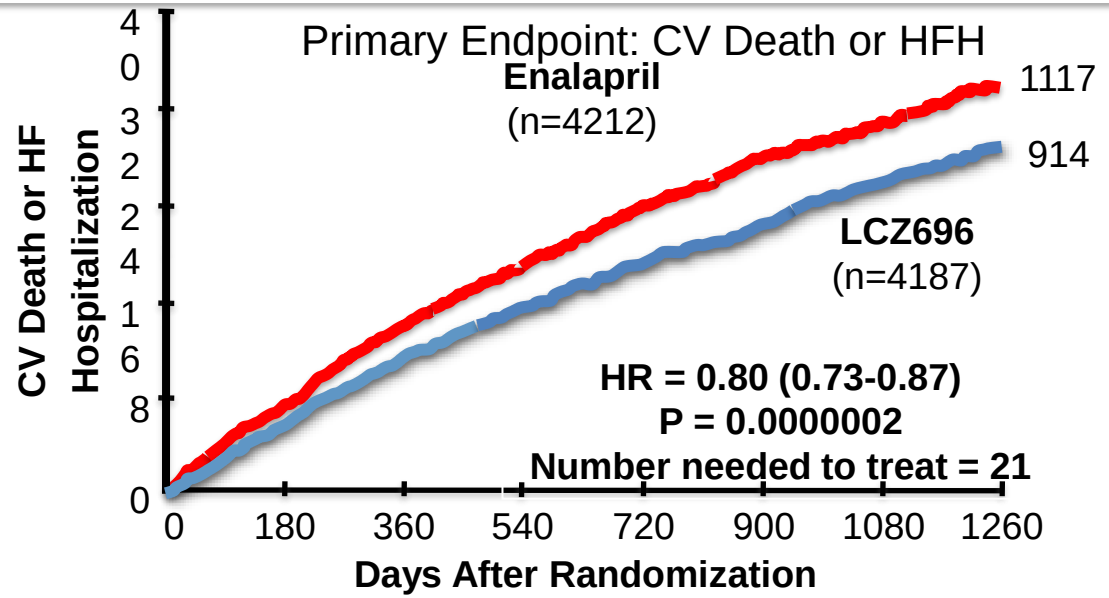
Type of HF According to LVEF	Criteria
HFrEF (HF with reduced EF)	■ LVEF ≤40%
HFimpEF (HF with improved EF)	■ Previous LVEF ≤40% and a follow-up measurement of LVEF >40%
HFmrEF (HF with mildly reduced EF)	■ LVEF 41%–49% ■ Evidence of spontaneous or provokable increased LV filling pressures (e.g., elevated natriuretic peptide, noninvasive and invasive hemodynamic measurement)
HFpEF (HF with preserved EF)	■ LVEF ≥50% ■ Evidence of spontaneous or provokable increased LV filling pressures (e.g., elevated natriuretic peptide, noninvasive and invasive hemodynamic measurement)

Heidenreich P, Bozkurt B et al. 2022 AHA/ACC/HFSA Guideline, https://doi.org/10.1016/j.jacc.2021.12.012, https://www.ahajournals.org/doi/10.1161/CIR.0000000000001063

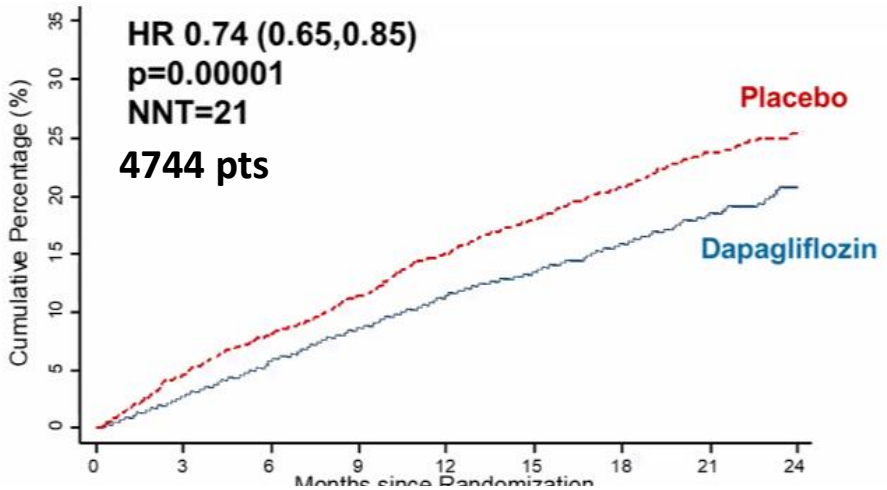
Current Evidence in Treatment of HFrEF

ARNi & SGLT2i in HFrEF

PARADIGM



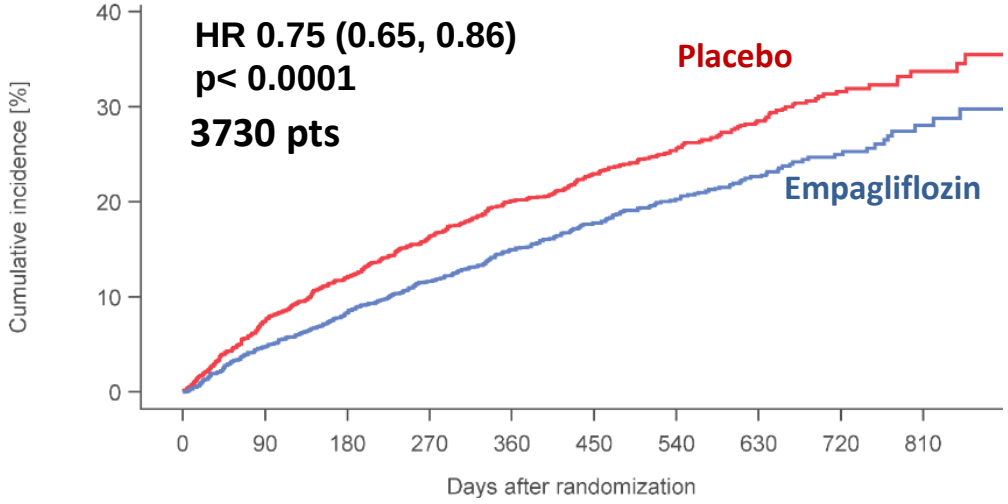
DAPA-HF



55% was without DM, 41 % had CKD

N Engl J Med 2019;381:1995-2008

EMPEROR-Reduced



50% was without DM, 48 % had CKD

Packer M et al. NEJM, August 29

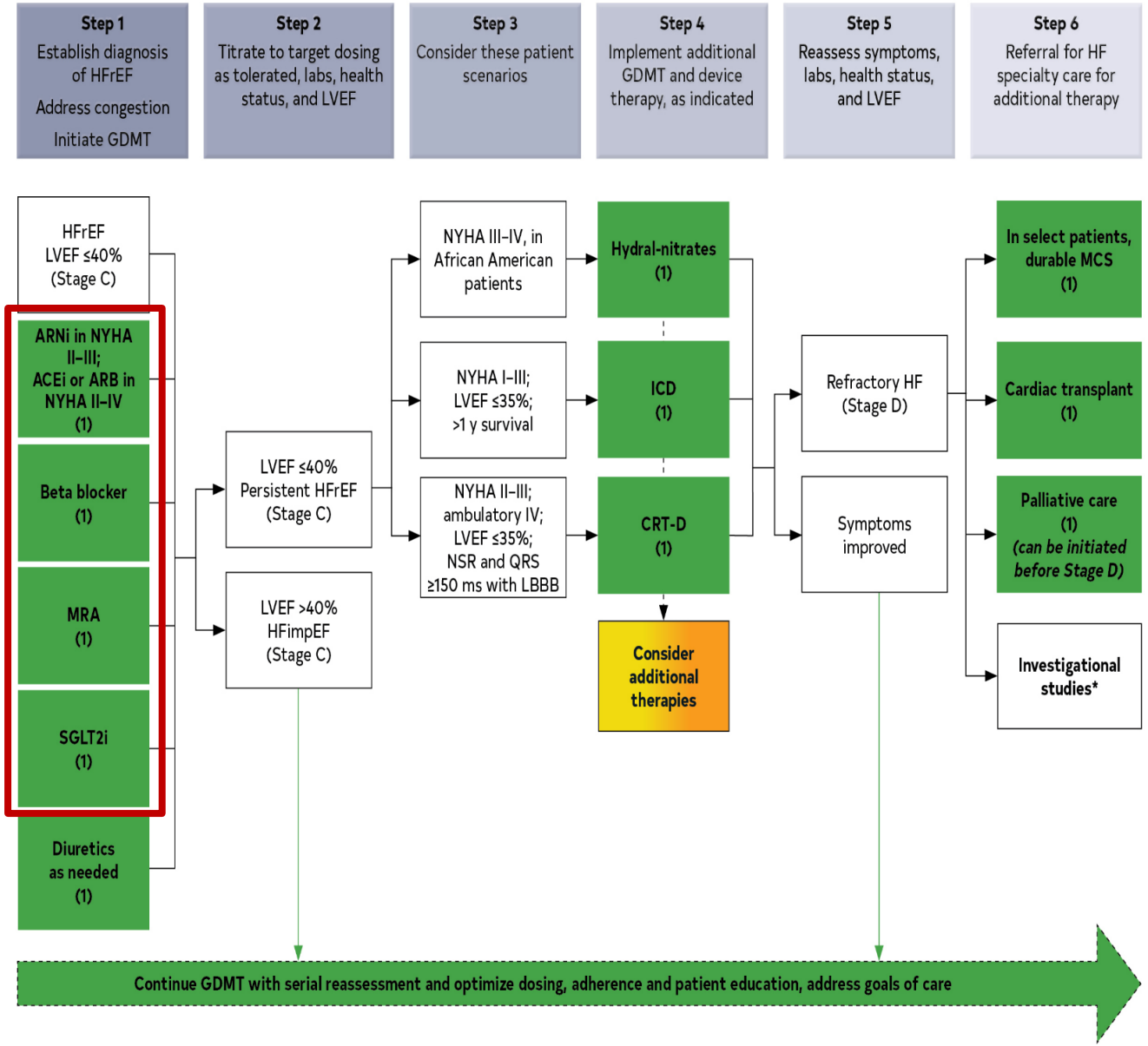
STEP 1

Treatment of HFrEF Stages C and D

Step 1 medications may be started simultaneously at initial (low) doses recommended for HFrEF.

Alternatively, these medications may be started sequentially, with sequence guided by clinical or other factors, without need to achieve target dosing before initiating next medication.

Medication doses should be increased to target as tolerated.



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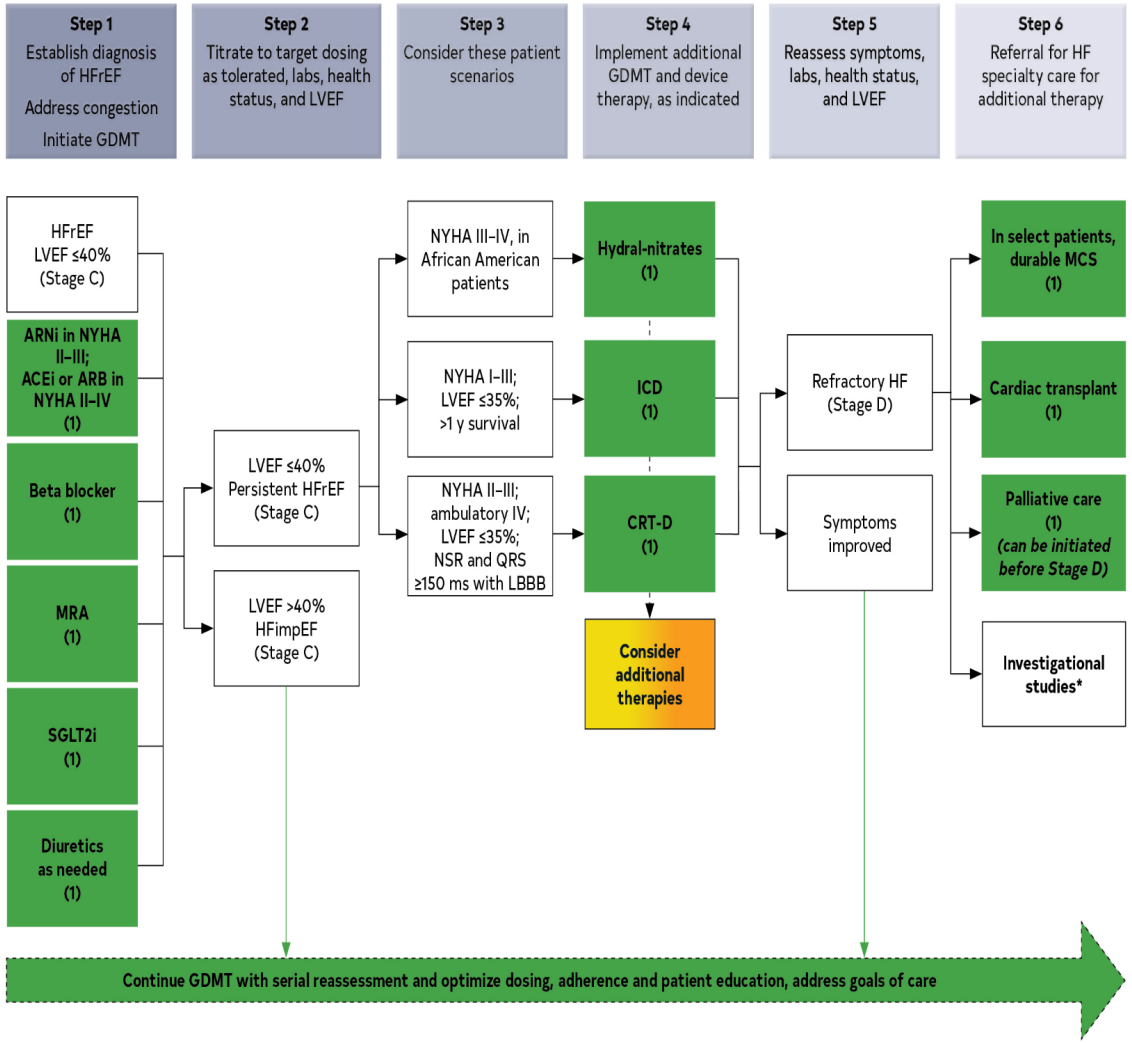

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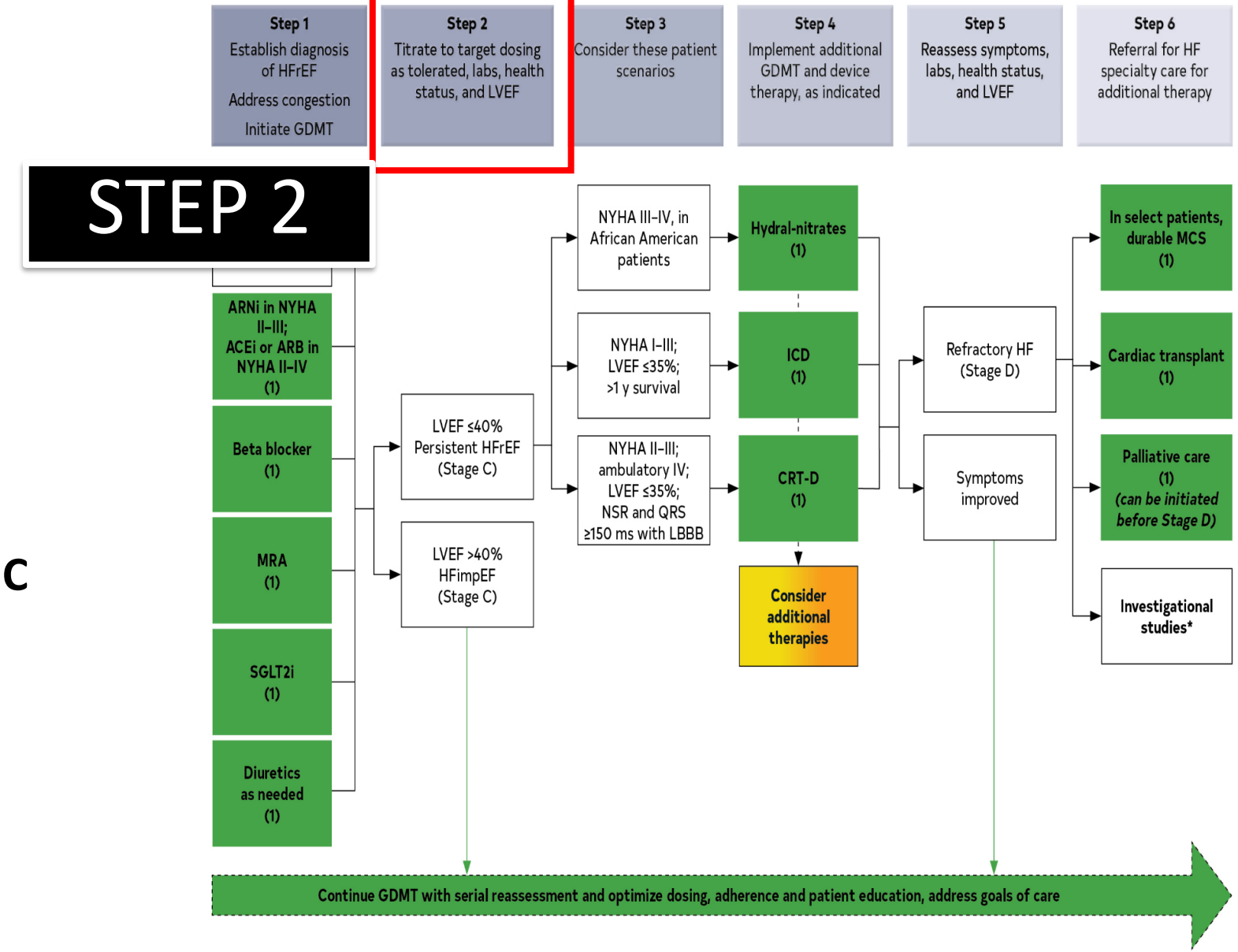
STEP 2



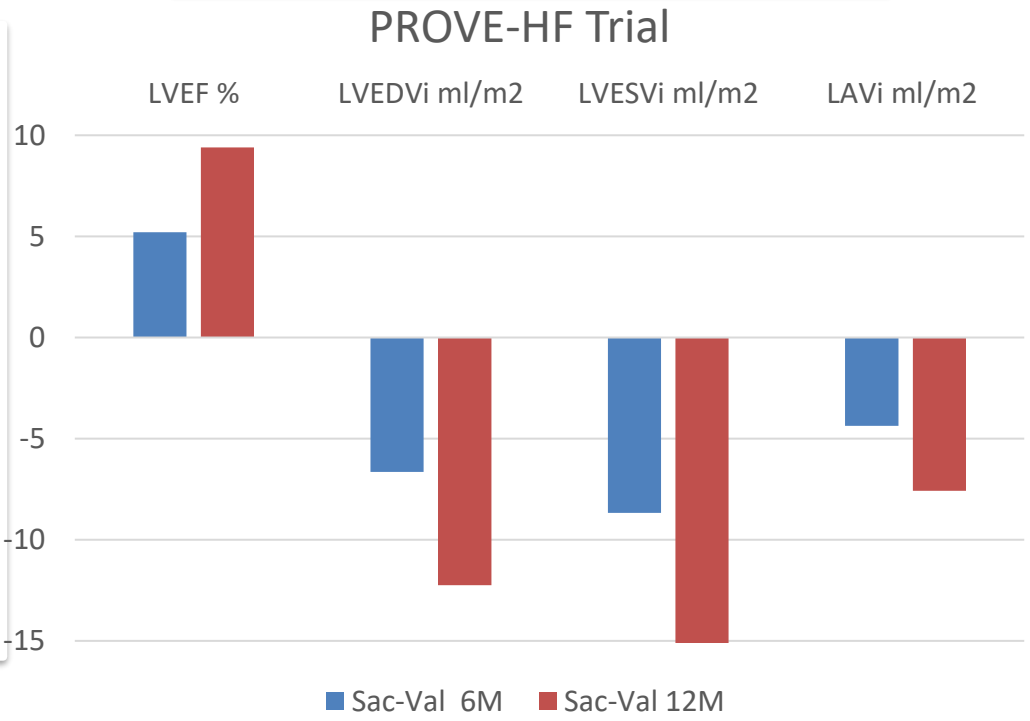
Treatment of HFrEF Stages C and D

Heidenreich P, Bozkurt B et al. 2022 AHA/ACC/HFSA Guideline, https://doi.org/10.1016/j.jacc.2021.12.012, https://www.ahajournals.org/doi/10.1161/CIR.0000000000001063

Reversal of Remodeling with GDMT

ARNi

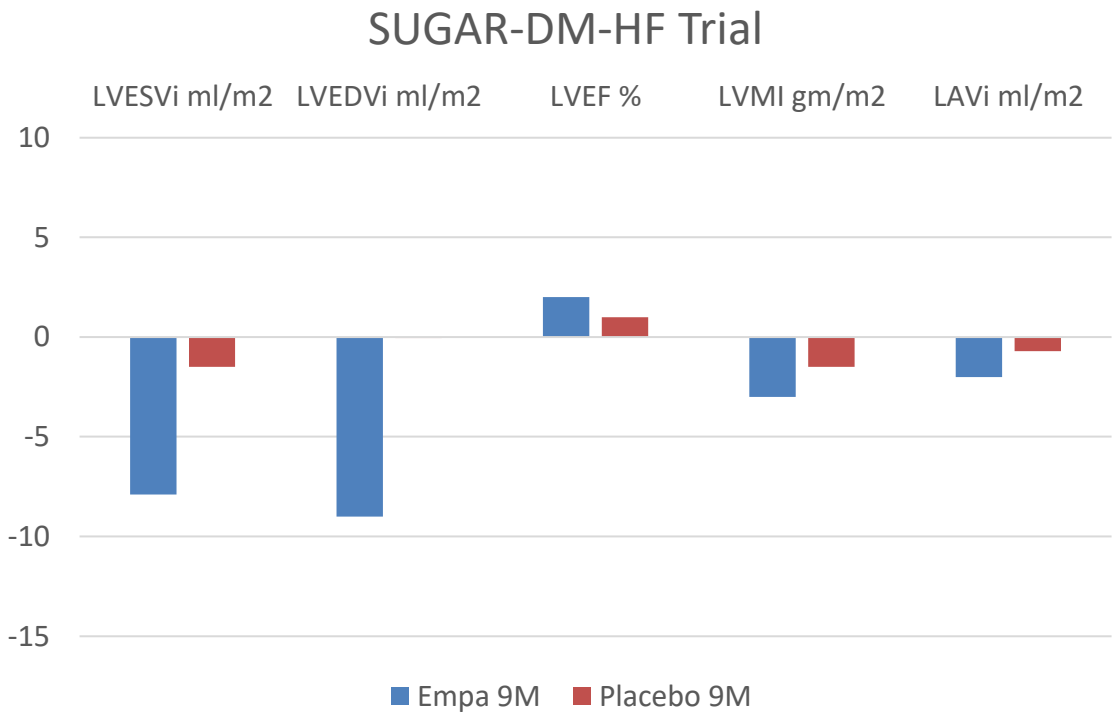
12 months in PROVE HF



JAMA. 2019;322(11):1085-1095.

SGLT2i

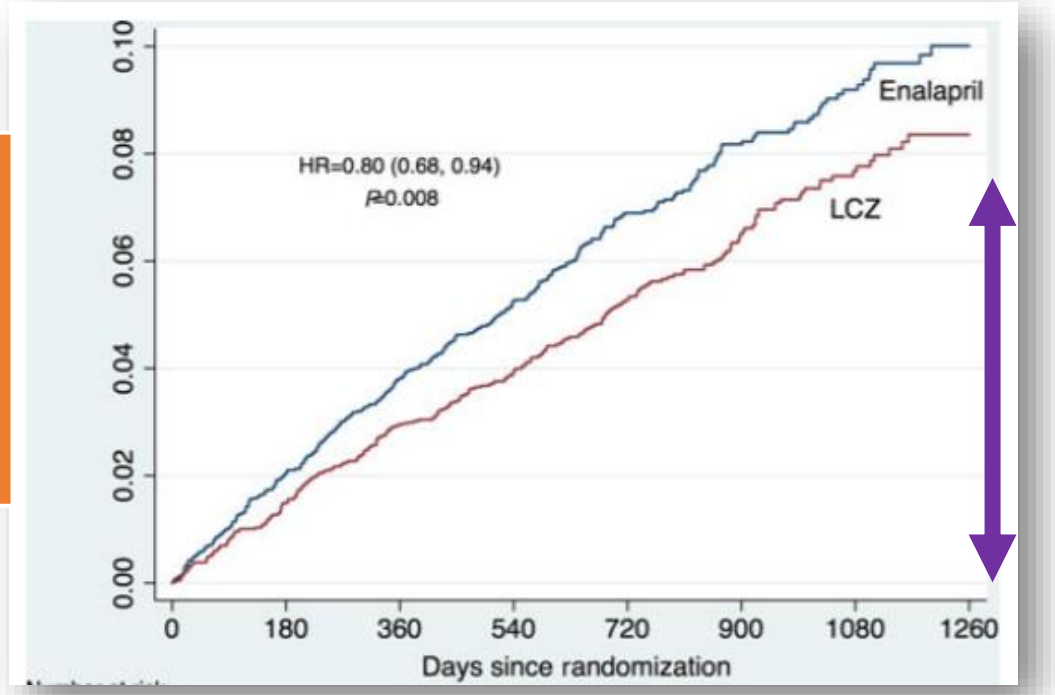
9 months in SUGAR DM



Lee M. Et al. Circulation. 2021;143:516–525.

Reduced SCD with GDMT

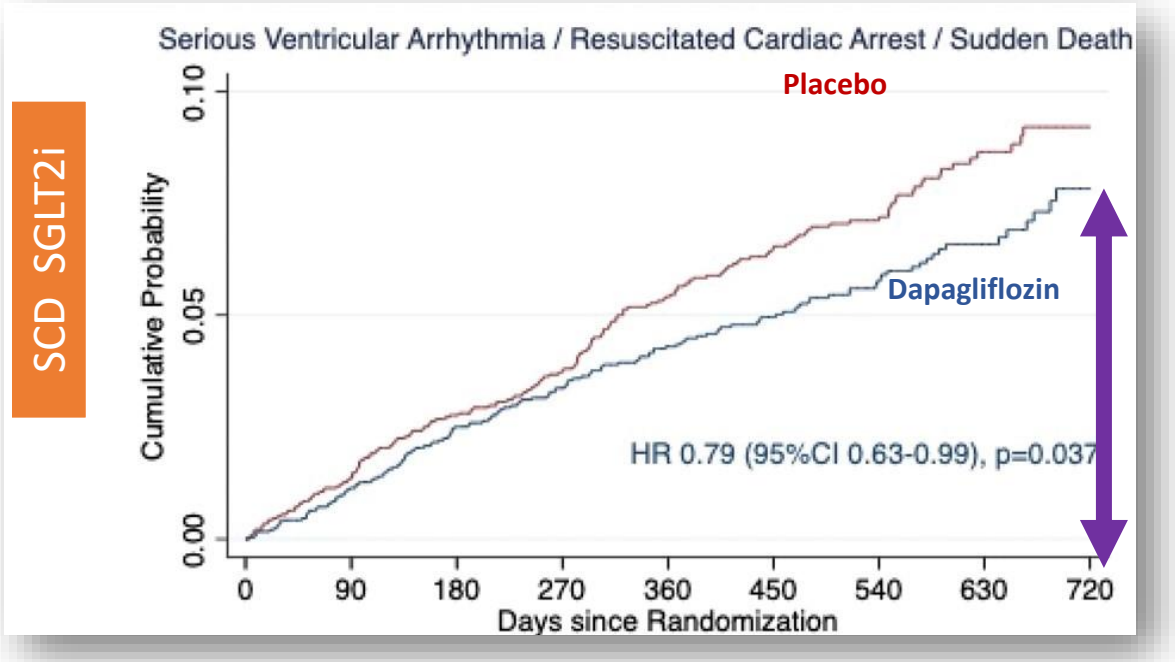
SCD ARNi



Desai AS. Et al Eur Heart J. 2015 Aug 7;36(30):1990-7. PMID: 26022006

SCD Placebo 3.3/1000 pt-yr, Dapagliflozin 2.7/1000 pt-yr, HR: 0.81 (0.62-1.07)

SCD SGLT2i



Curtain J. et al. DAPA-HF Eur Heart J . 2021 Sep 21;42(36):3727-3738.

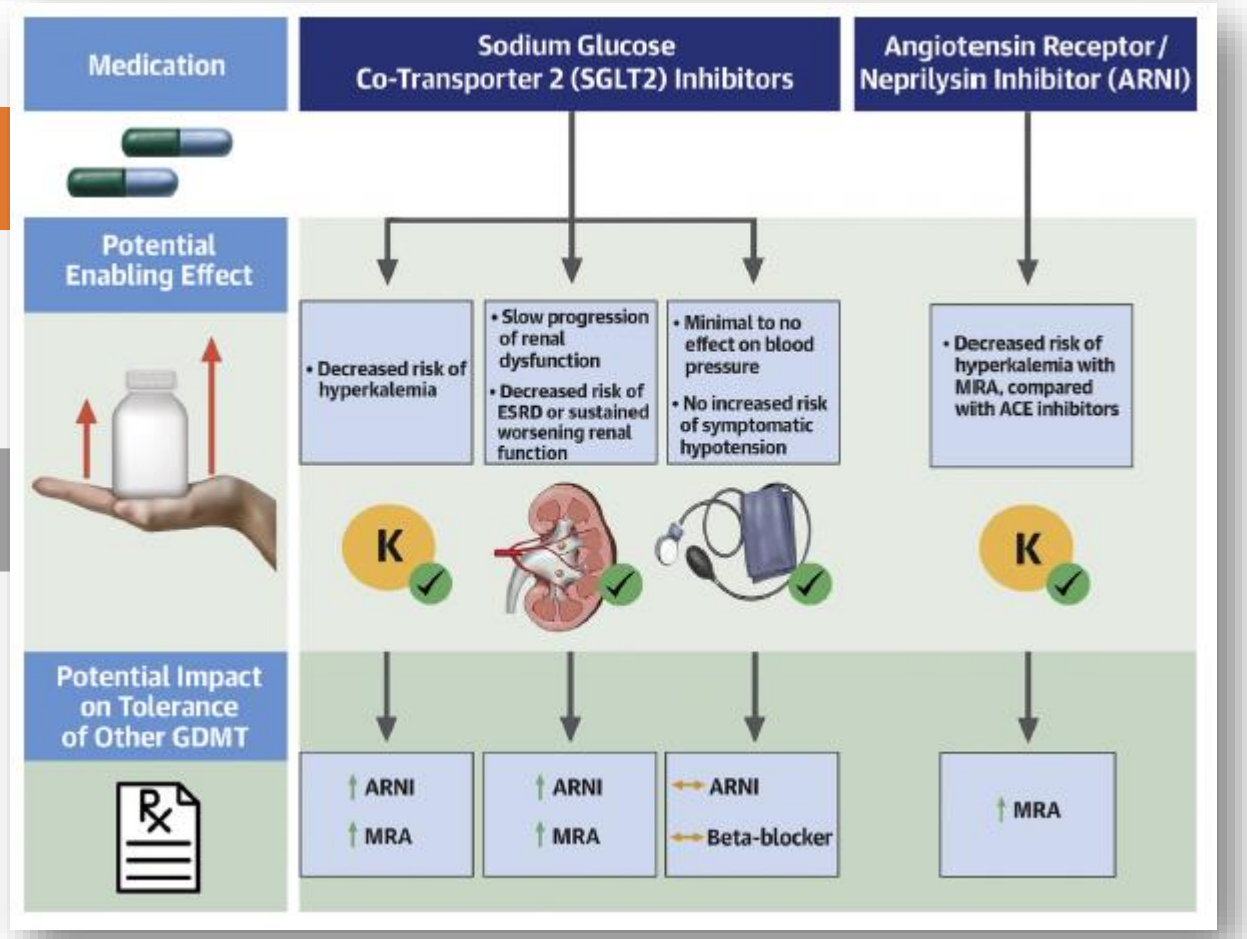
New Agents Enable Initiation of Other GDMT

SGLT2i

- Reduction in decline in eGFR
- No increase in hyperkalemia
- Less MRA discontinuation

ARNi

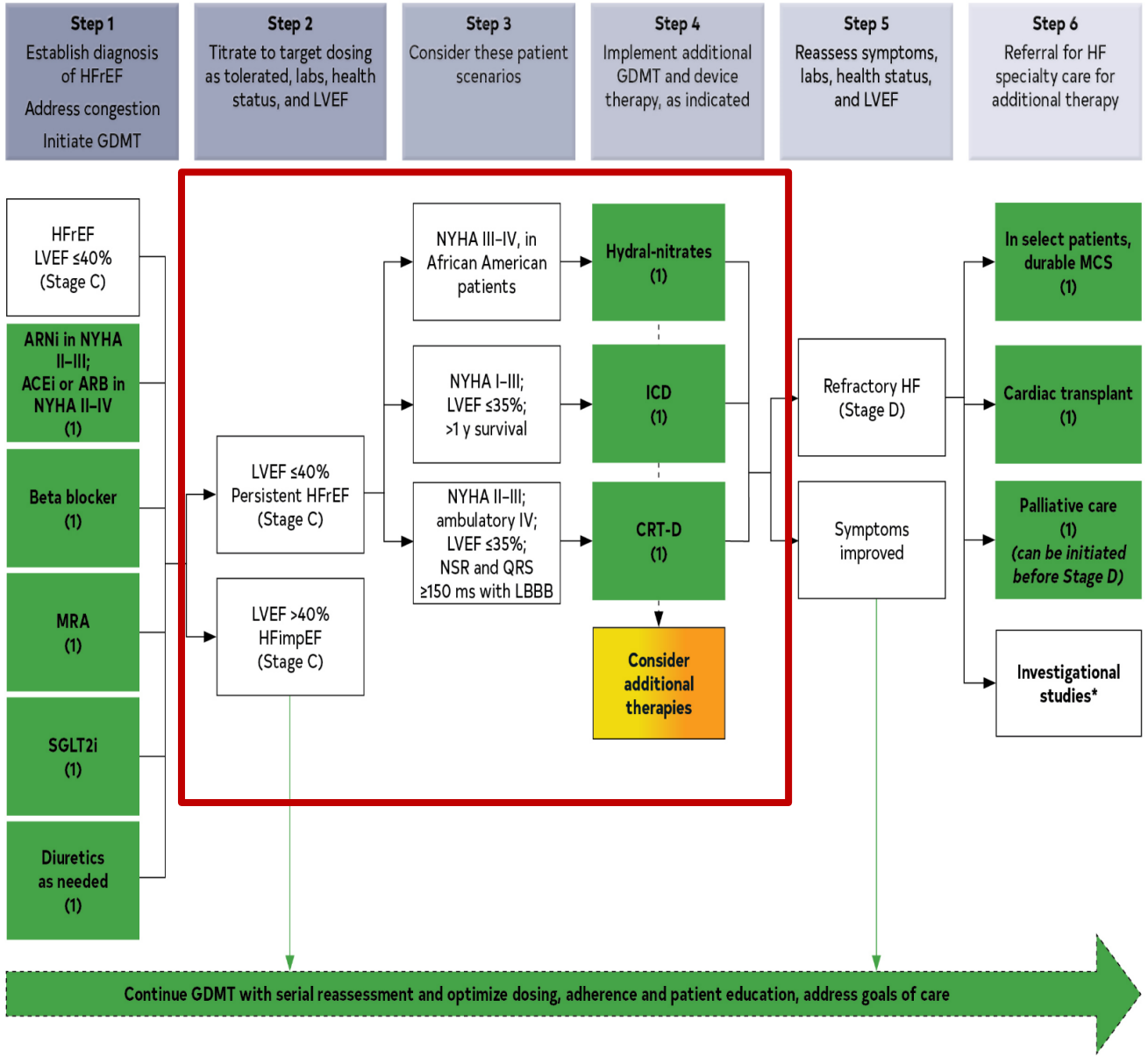
- Lower K levels or hyperkalemia
- Reduction in decline in eGFR



Desai A JAMA Cardiology 2016, Ferreira et al. JACC 77:11, 23 March 2021, 1397-1407, Greene JACC 77 2021

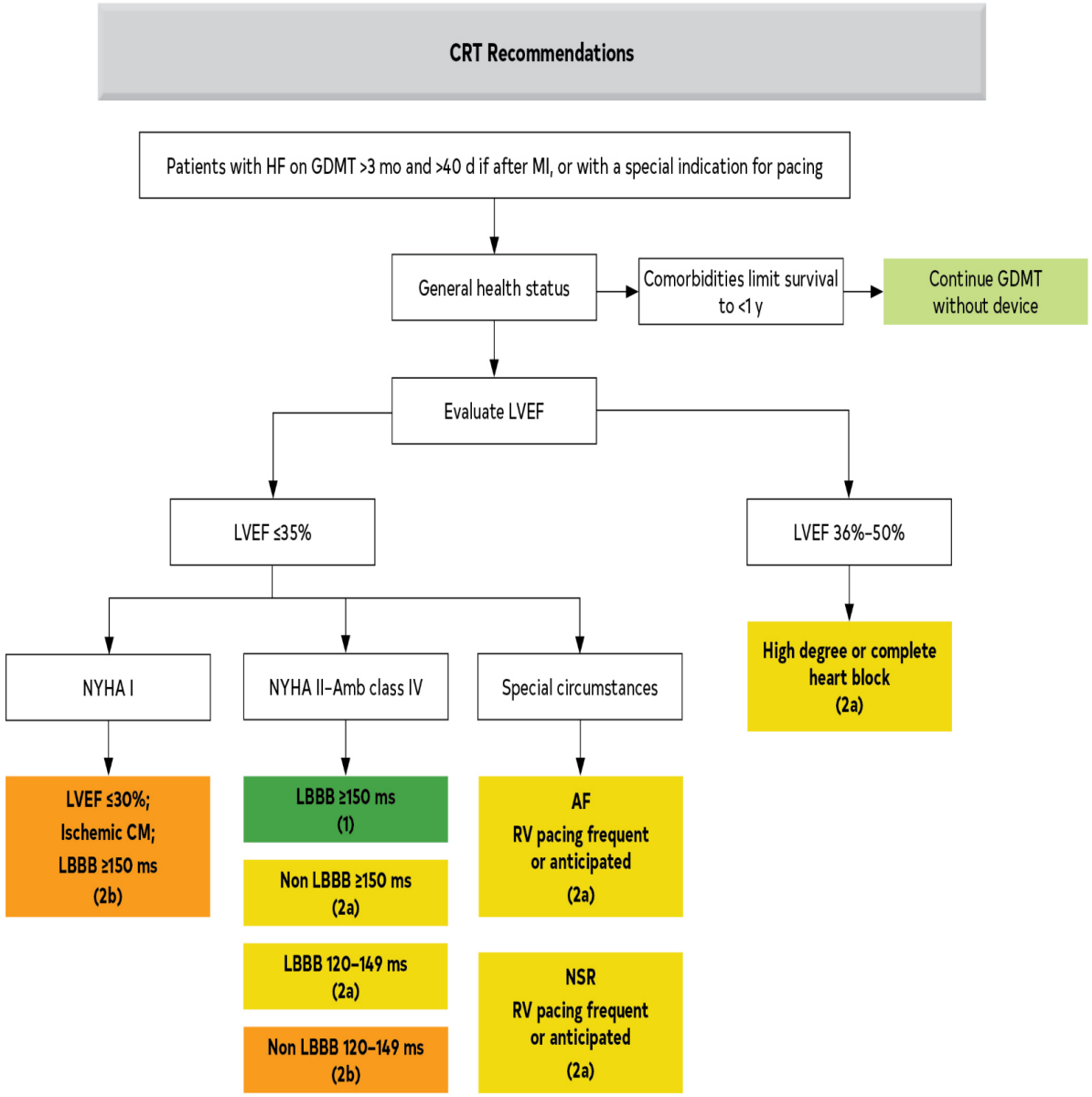
Treatment of HFrEF Stages C and D

STEPS 3&4



Heidenreich P, Bozkurt B et al. 2022 AHA/ACC/HFSA Guideline, https://doi.org/10.1016/j.jacc.2021.12.012, https://www.ahajournals.org/doi/10.1161/CIR.0000000000001063

Algorithm for CRT Indications in Patients With Cardiomyopathy or HFrEF

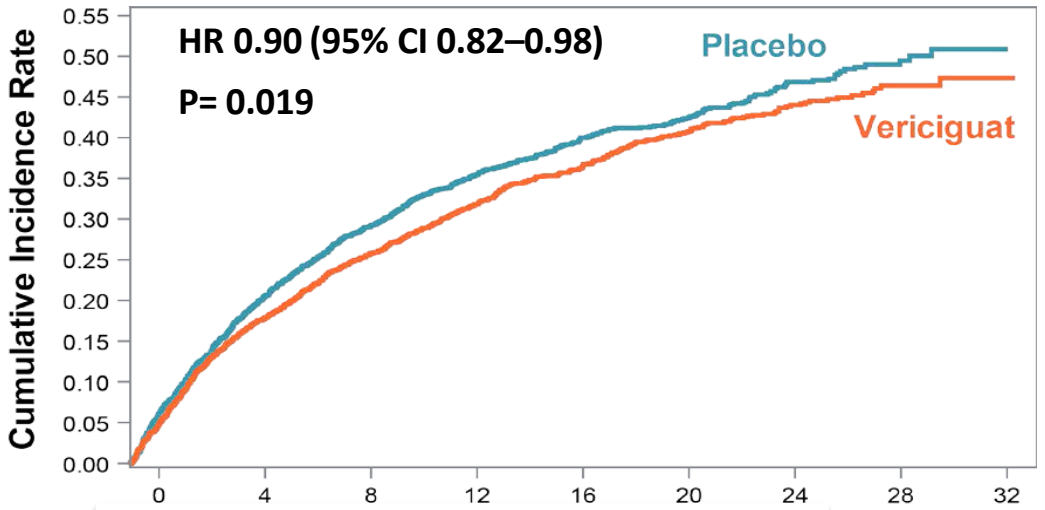


Additional Therapies in HFrEF

Vericiguat and Omecamtiv (not FDA approved)

Primary Endpoint: CV Death or HFH

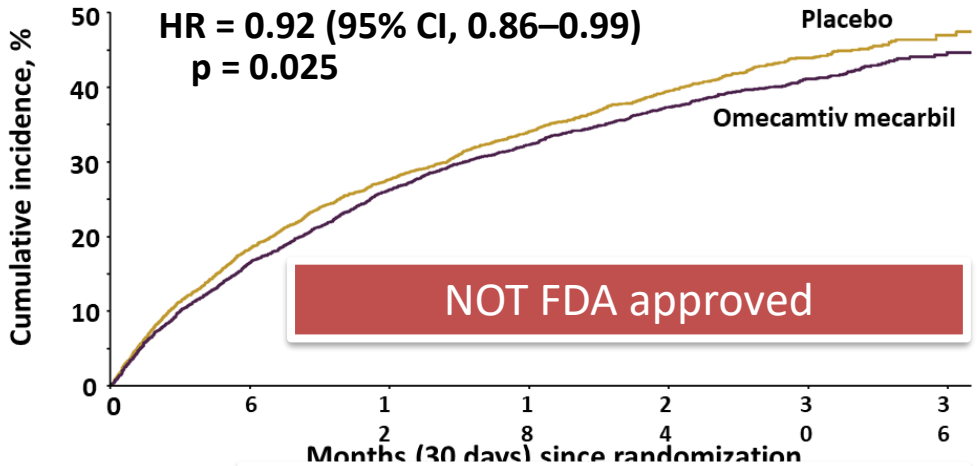
VICTORIA



Inclusion:
- NYHA class II-IV, recent HFH/IV Diur
- LVEF < 45%
- NT-proBNP ≥1000 pg/ml*

Exclusion:
- eGFR <15 ml/min/1.73 m²
- SBP <100mmHg

GALACTIC-HF



Inclusion:
- NYHA class II-IV, current HF Hosp or HF Hosp/UC within 1 yr
- LVEF ≤ 35%
- NT-proBNP ≥400 pg/ml*

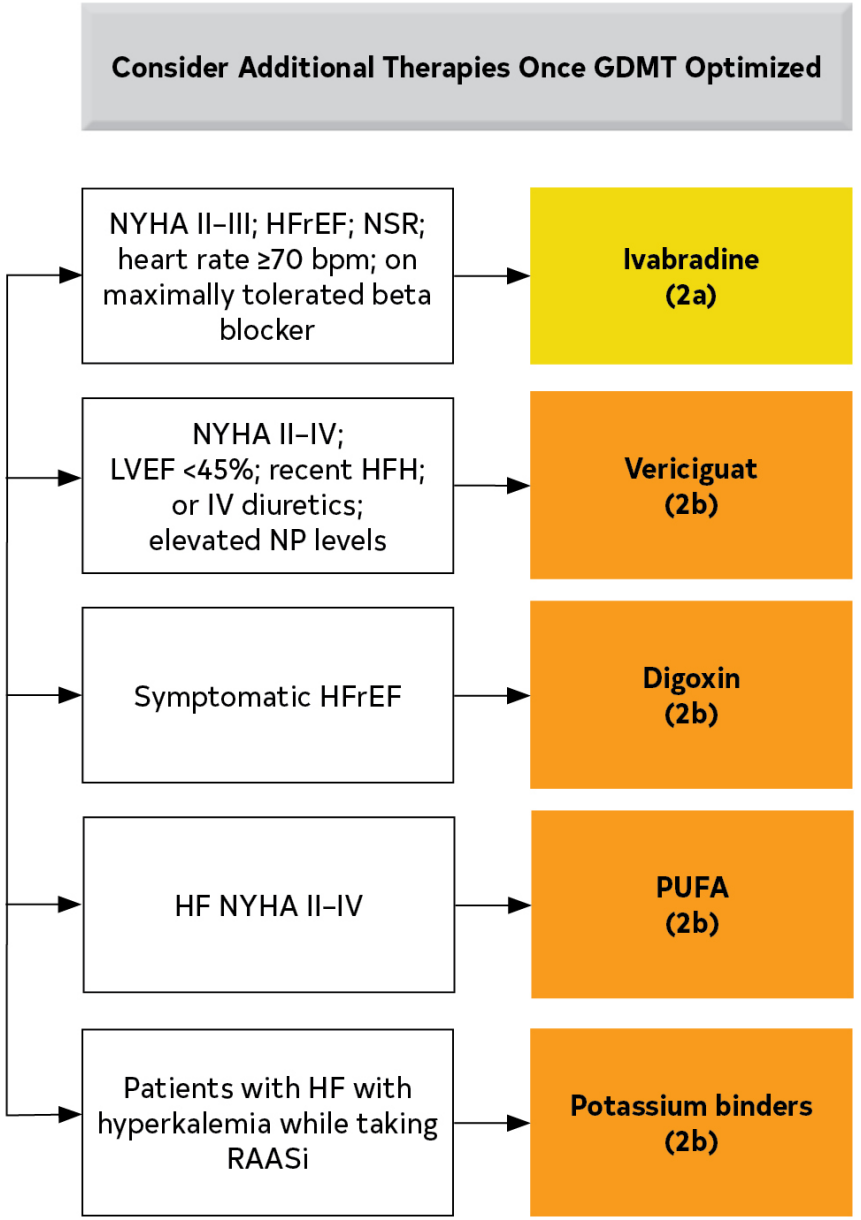
Exclusion:
- eGFR <20 ml/min/1.73 m²
- SBP <85 mmHg

No reduction in CV Death

Armstrong P et al. N Engl J Med 2020;382:1883-93.

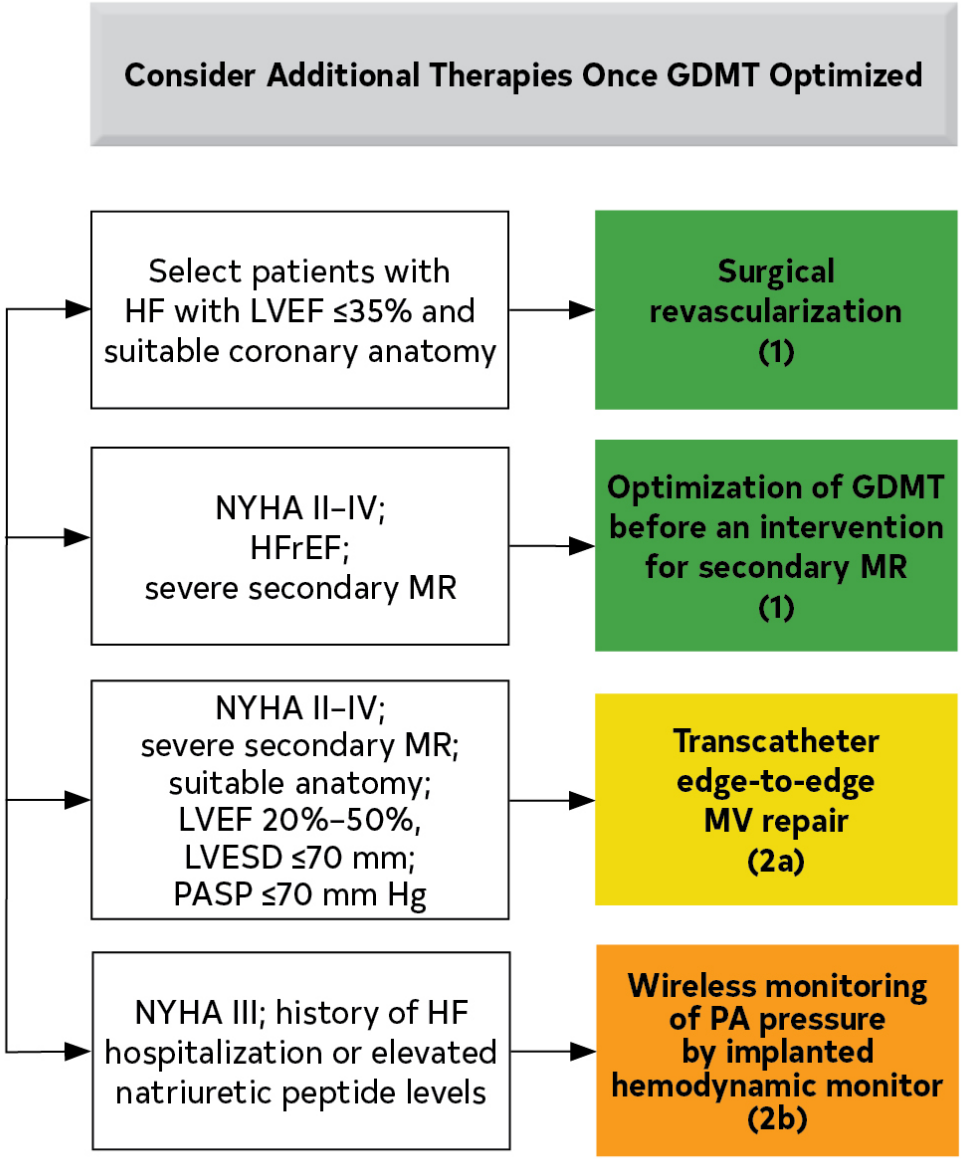
Teerlink J et al. N Engl J Med 2020; 11/13/2020, *AHA LBCT*

Additional Medical Therapies for Patients With HFrEF



Heidenreich P, Bozkurt B et al. 2022 AHA/ACC/HFSA Guideline

Additional Device Therapies

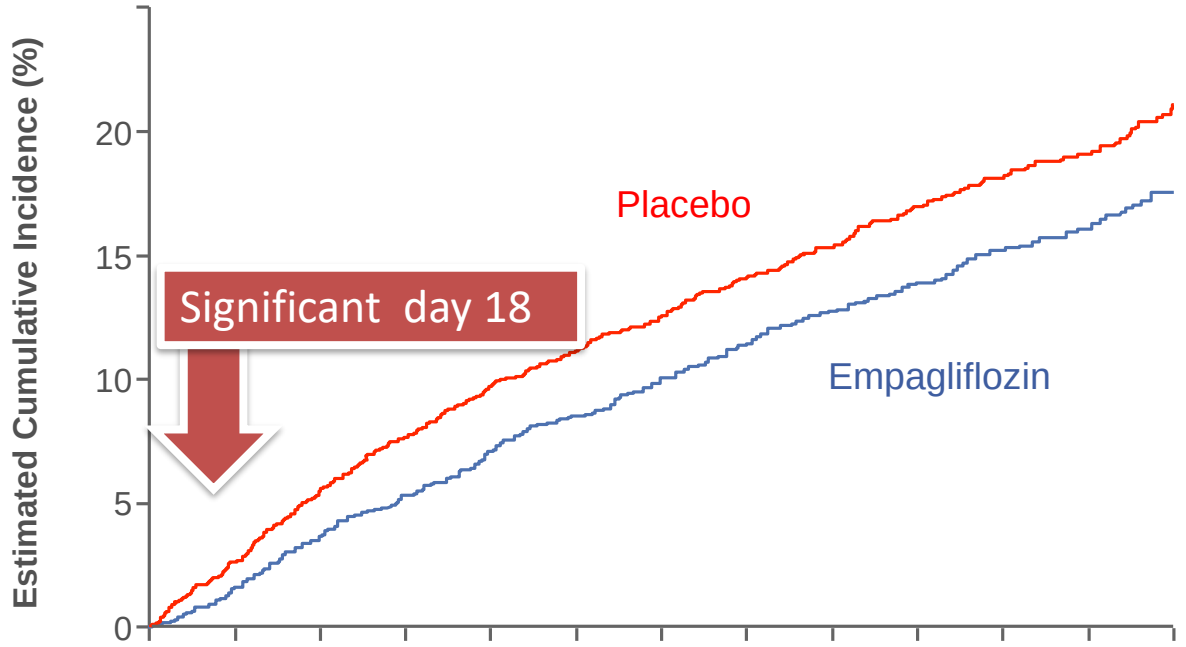


Heidenreich P, Bozkurt B et al. 2022 AHA/ACC/HFSA Guideline

HFmrEF, HFpEF

HFpEF: EMPEROR-Preserved Trial

~3000 pts NYHA Class II-IV HF, LVEF > 40 % elevated BNP
ARNi (sacubitril valsartan) vs valsartan



HR 0.79
(95% CI 0.69, 0.90)
P = 0.0003

Placebo:
511 patients with event
Rate: 8.7 per 100 patient-years

Empagliflozin:
415 patients with event
Rate: 6.9 per 100 patient-years

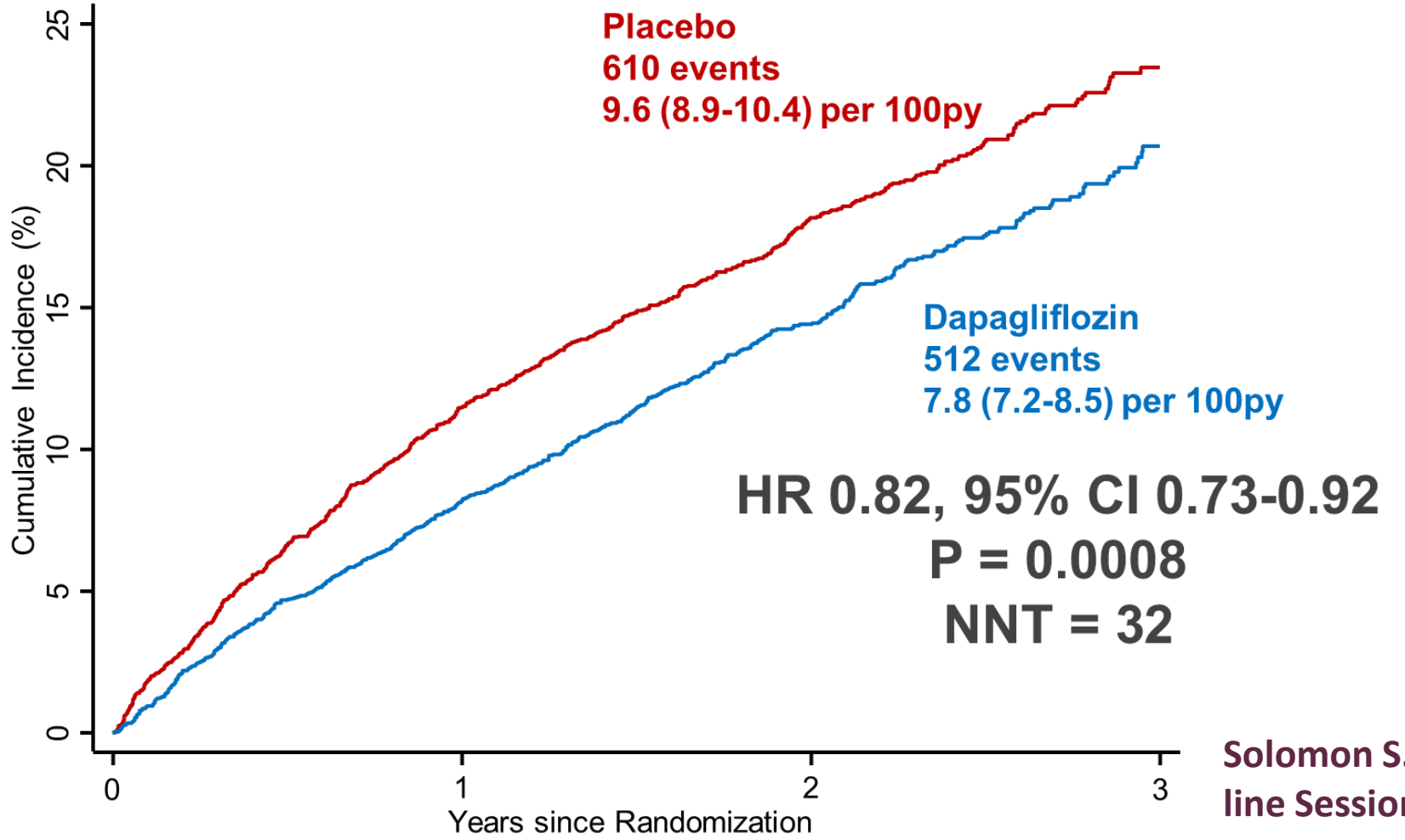
RRR 21%

NNT=31

During a median trial period of 26 months.

Anker et al NEJM 2021 DOI: 10.1056/NEJMoa2107038

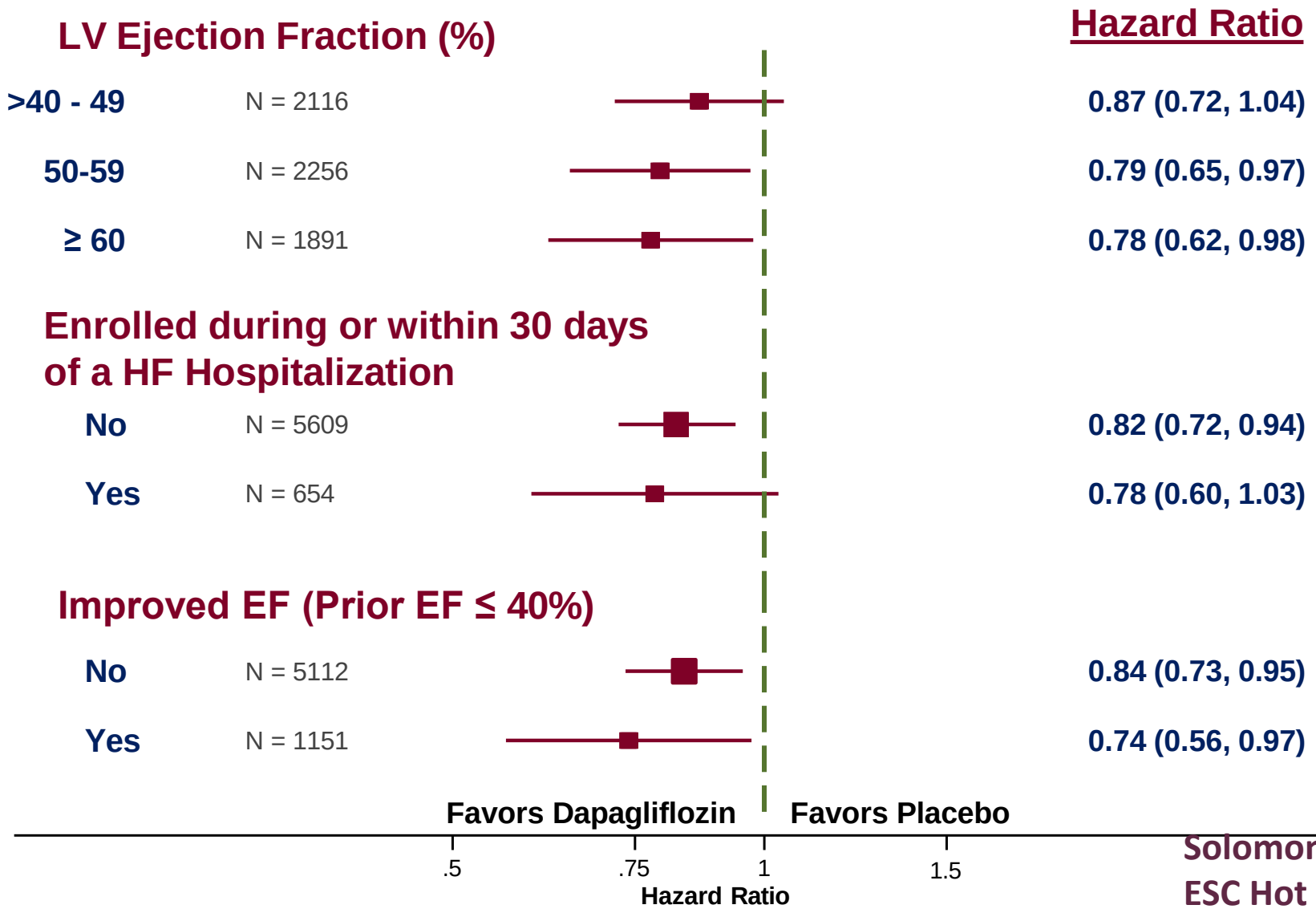
Primary Endpoint: CV Death or Worsening HF



Solomon S. DELIVER ESC Hot line Sessions August 2022

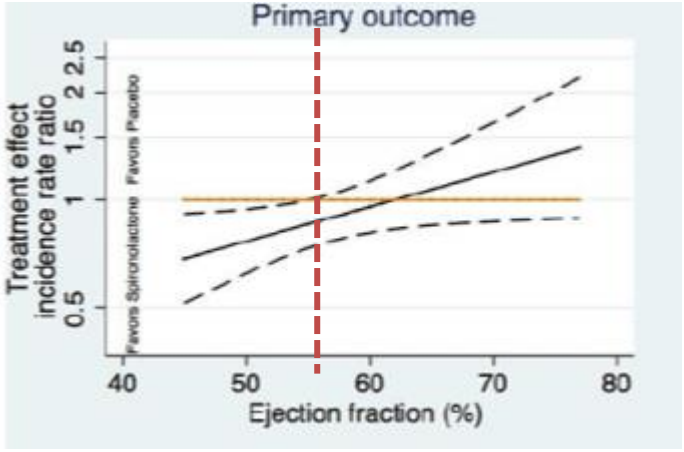
- Largest RCT of **well-treated** patients with **HFmrEF and HFpEF**
- broader population including **HFimpEF (18%), HFmrEF (34%), LVEF 50-59% (36%), LVEF>60% (30%)** and recently hospitalized patients (16% within 3 mo)
- Compared with other recent trials, higher risk: comorbidities, lower LVEF, and higher NT-proBNP levels.

Primary Endpoint in Prespecified Subgroups

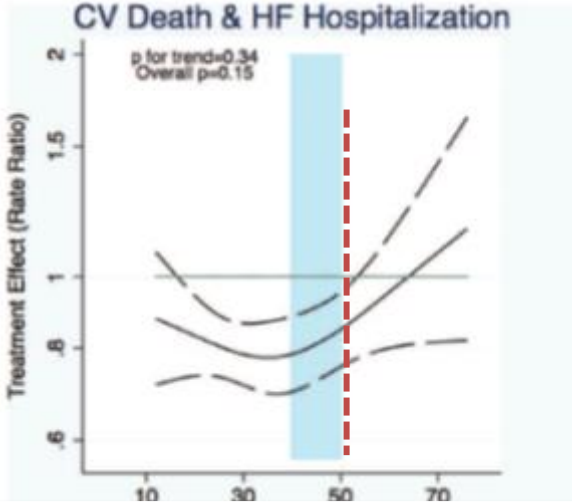


Benefit with ARB, MRA, ARNi, SGLT2i in HFmrEF

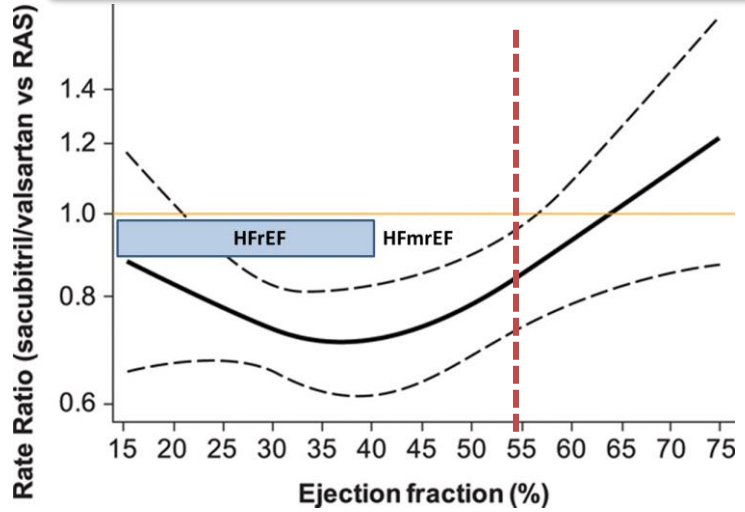
Spironolactone: TOPCAT
Solomon et al, 2016



EHJ ARB: CHARM-PRESERVED
Lund L et al, EJHF, 2018

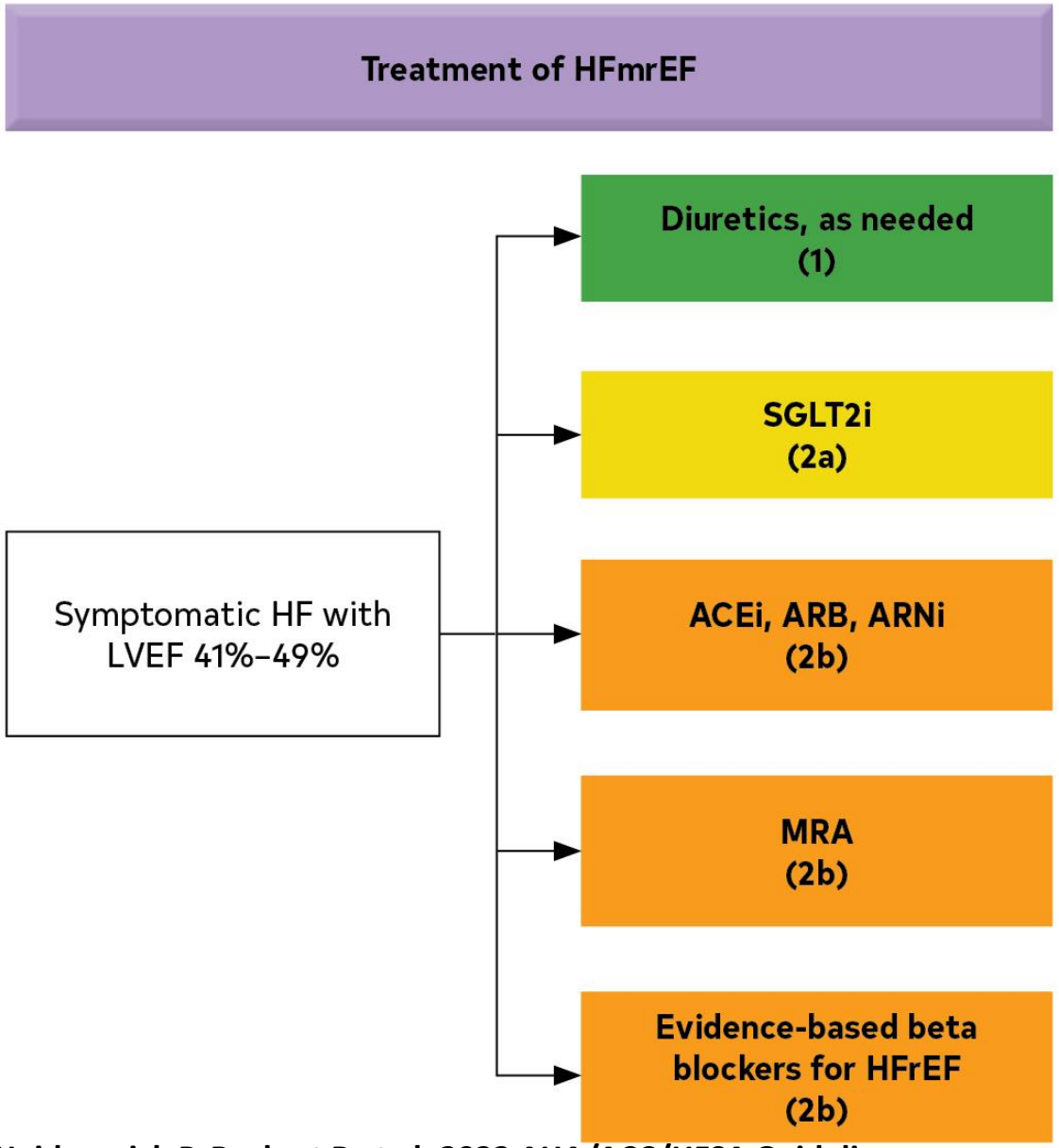


ARNI: PARAGON-HF.
Solomon et al, Circulation, 2020



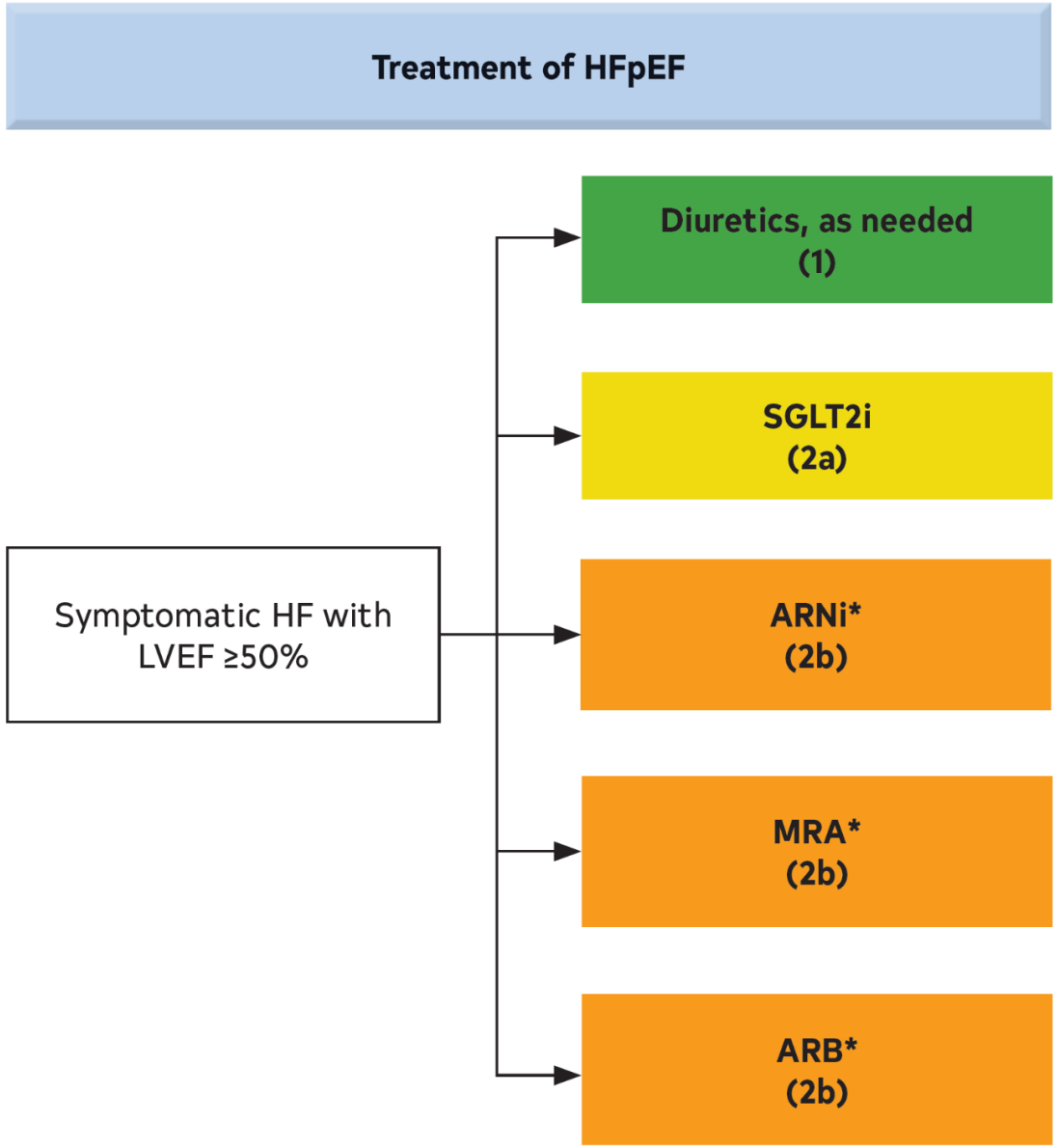
EMPEROR PRESERVED and PARAGON
Packer Circulation. 2021;143:337–349

Recommendations for Patients With Mildly Reduced LVEF (41%–49%)



Heidenreich P, Bozkurt B et al. 2022 AHA/ACC/HFSA Guideline

Recommendations for Patients With Preserved LVEF (≥50%)



Medication recommendations for HFpEF are displayed.

*Greater benefit in patients with LVEF closer to 50%.

Heidenreich P, Bozkurt B et al. 2022 AHA/ACC/HFSA Guideline

HFimpEF

TRED-HF Trial Conclusions

- Withdrawal of pharmacological HF therapy from patients deemed to have recovered DCM resulted in relapse in ~40% of cases

- Improvement in function represents *remission* rather than *permanent recovery* for many patients

Halliday BP, et al. Withdrawal of pharmacological treatment for heart failure in patients with recovered dilated cardiomyopathy (TRED-HF): an open-label, pilot, randomised trial. Lancet. 2019 Jan 5;393(10166):61-73.

HF With improved Ejection Fraction

Recommendation for HF With Improved Ejection Fraction		
Referenced studies that support the recommendation are summarized in the Online Data Supplements.		
COR	**LOE**	**Recommendation**
1	**B-R**	**1. In HFimpEF after treatment, GDMT should be continued to prevent relapse of HF and LV dysfunction, even in patients who may become asymptomatic.**

Heidenreich P, Bozkurt B et al. 2022 AHA/ACC/HFSA Guideline, https://doi.org/10.1016/j.jacc.2021.12.012, https://www.ahajournals.org/doi/10.1161/CIR.0000000000001063

Hospitalized HF Patients

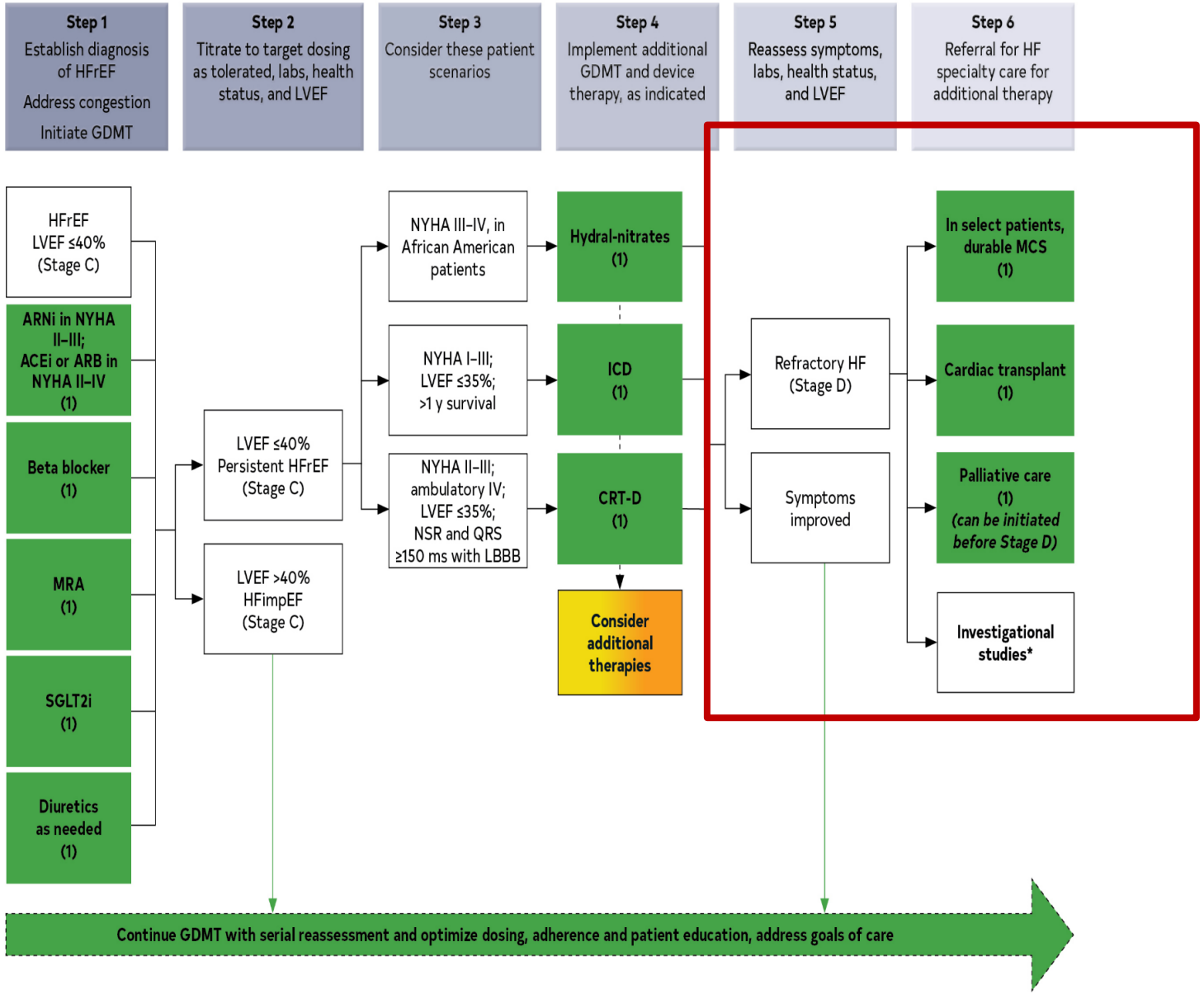
Maintenance or Optimization of GDMT During Hospitalization

Recommendations for Maintenance or Optimization of GDMT During Hospitalization Referenced studies that support the recommendations are summarized in the Online Data Supplements.		
COR	**LOE**	**Recommendations**
1	**B-NR**	**1. In patients with HFrEF requiring hospitalization, preexisting GDMT should be continued and optimized to improve outcomes, unless contraindicated.**
1	**B-NR**	**2. In patients experiencing mild decrease of renal function or asymptomatic reduction of blood pressure during HF hospitalization, diuresis and other GDMT should not routinely be discontinued.**
1	**B-NR**	**3. In patients with HFrEF, GDMT should be initiated during hospitalization after clinical stability is achieved.**
1	**B-NR**	**4. In patients with HFrEF, if discontinuation of GDMT is necessary during hospitalization, it should be reinitiated and further optimized as soon as possible.**

Heidenreich P, Bozkurt B et al. 2022 AHA/ACC/HFSA Guideline

Advanced HF Patients

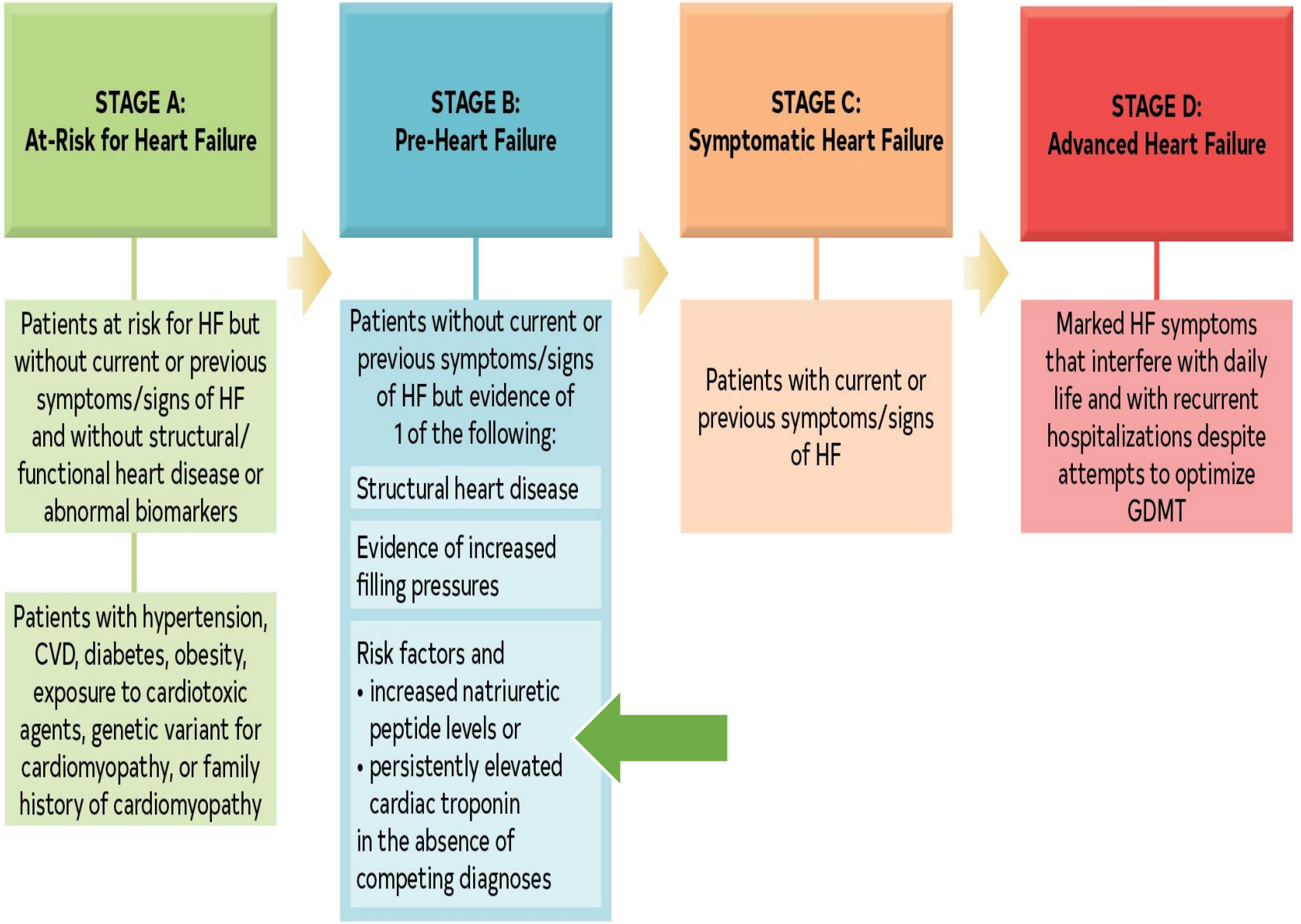
Treatment of HFrEF Stage D



Heidenreich P, Bozkurt B et al. 2022 AHA/ACC/HFSA Guideline, https://doi.org/10.1016/j.jacc.2021.12.012, https://www.ahajournals.org/doi/10.1161/CIR.0000000000001063

At-Risk for HF (Stage A)
Pre-HF (Stage B)

ACC/AHA Stages of HF



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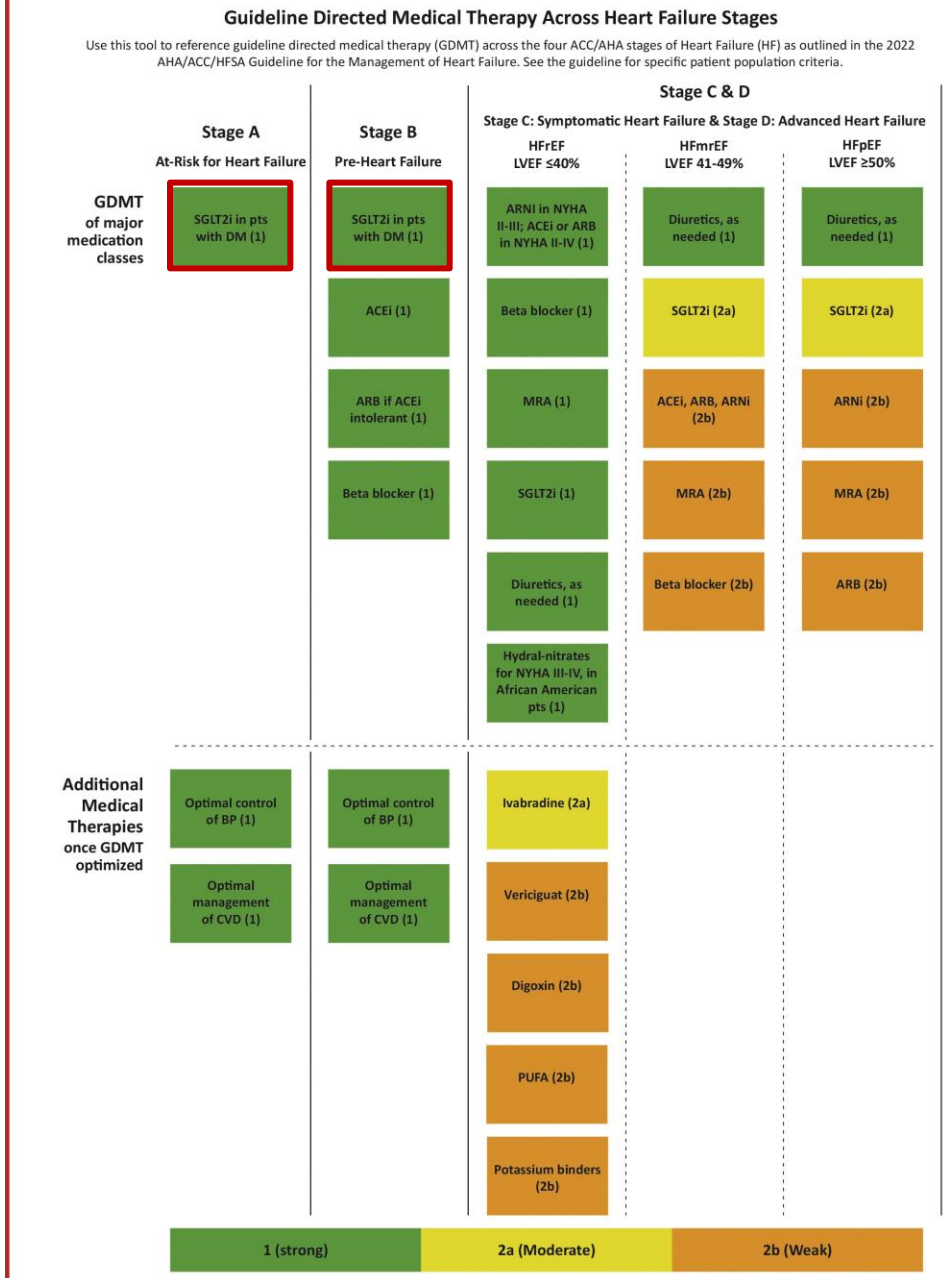
CENTRAL ILLUSTRATION: 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure



Heidenreich PA, et al. J Am Coll Cardiol. 10.1016/j.jacc.2021.12.012

STOP- HF Trial RCT (n=1374)

BNP testing baseline & annually

STOP HF

INTERVENTION (KNOW BNP)

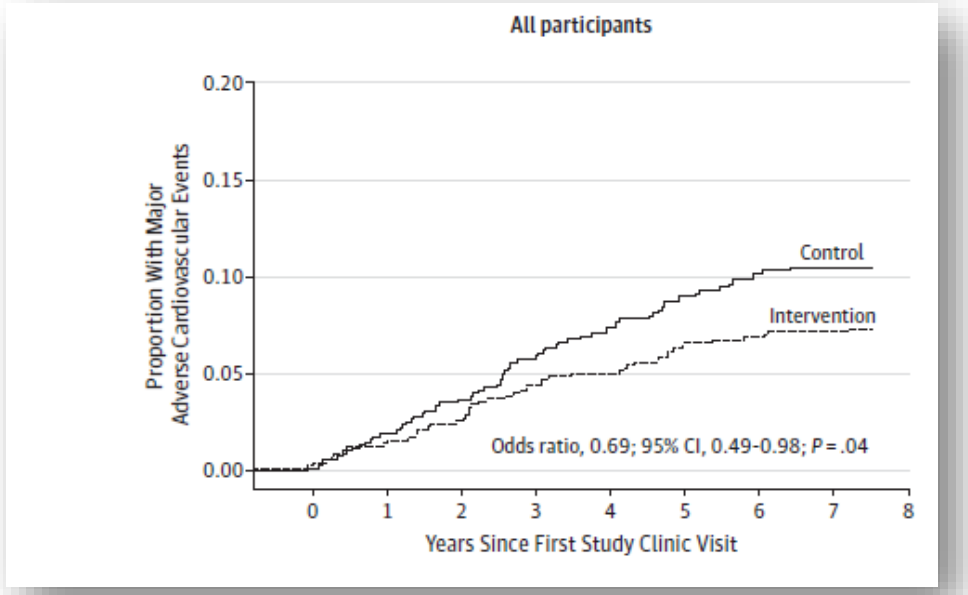
CONTROL (NO KNOWLEDGE OF BNP)

BNP ≥ 50 ng/L

- CV referral, cardiologist led W/U & team management
- Doppler Echocardiography
- Risk factor management, coaching by specialist nurse on adherence, LSM
- Collaborative care, annual specialized CV review
- Repeat echocardiography, BNP, other

BNP < 50 ng/L

- Same as control



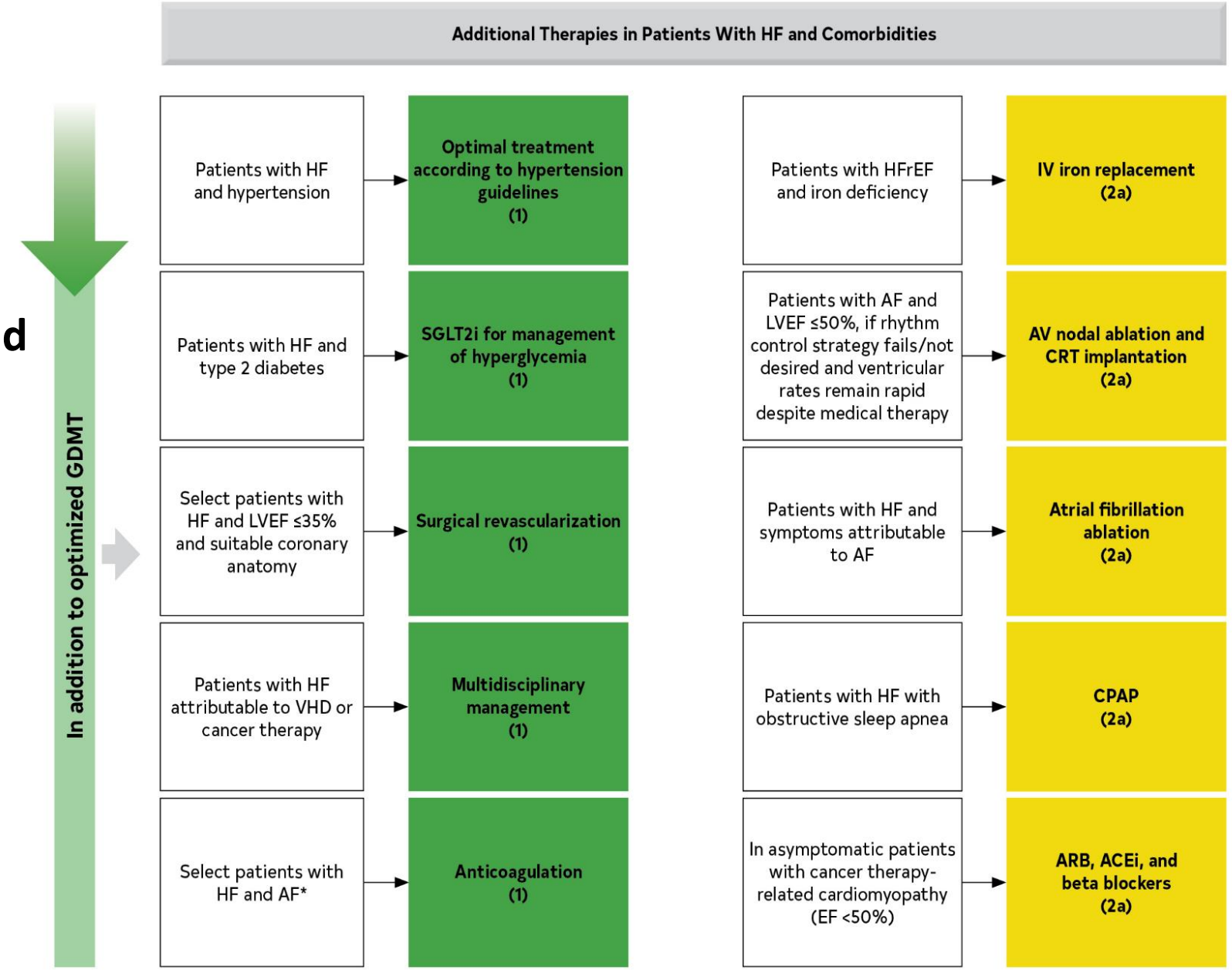
Ledwidge et al.JAMA. 2013 Jul 3;310(1):66-74.

Patients at Risk for HF (Stage A: Primary Prevention) (con't.)

2a	B-R	4. For patients at risk of developing HF, natriuretic peptide biomarker–based screening followed by team-based care, including a cardiovascular specialist optimizing GDMT, can be useful to prevent the development of LV dysfunction (systolic or diastolic) or new-onset HF.

Treatment of Comorbidities in HF

Recommendations for Treatment of Patients With HF and Selected Comorbidities



Summary: 2022 HF Guidelines

HFrEF

COR	LOE	
1	A	In patients with HFrEF, ARNi or ACEi/ARB, SGLT2i, BB, MRA are recommended to reduce morbidity and CV mortality

HFmrEF

2a	B-R	In patients with HFmrEF, SGLT2i can be beneficial in decreasing HFH and cardiovascular mortality
2b	B-NR	Among patients with symptomatic HFmrEF, use of BB, ARNi, ACEi or ARB, and MRAs may be considered to reduce the risk of HFH and CV mortality, particularly among patients with LVEF on the lower end of this spectrum.

HFpEF

2a	B-R	In patients with HFpEF, SGLT2i can be beneficial in decreasing HFH and cardiovascular mortality
2b	B-NR	In selected patients with HFpEF, MRA, ARB, or ARNi may be considered to decrease hospitalizations particularly among patients with LVEF on the lower end of this spectrum.

HFimpEF

1	B-R	In HFimpEF after treatment, GDMT should be continued to prevent relapse of HF and LV dysfunction, even in patients who may become asymptomatic.

Summary: Treatment Across Stages of HF: At risk, Pre-HF, HF to Advanced HF