# What should I know about the 2022 AHA/ACC/HFSA Heart Failure Management Guidelines?

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# Objectives

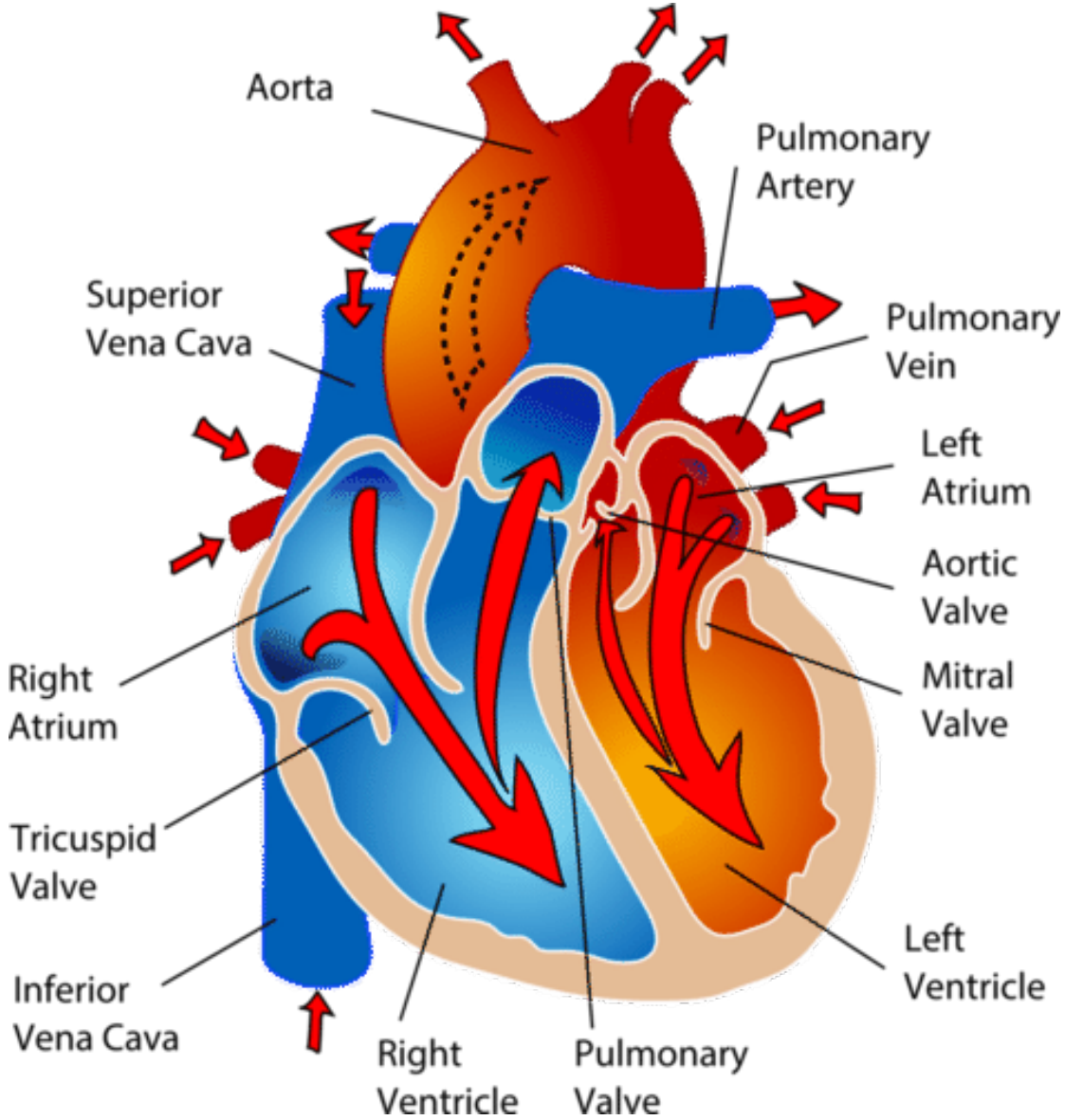
Upon the completion of this conference, the participant will be able to

1. Explain the value of clinical guidelines in pharmacy practice.
2. Discuss current recommendations for heart failure treatment.
3. Explain the importance of using evidence-based guidelines in the management of heart failure.
4. Describe the guideline-directed medical therapy for HF patients.
5. Identify the risks and benefits of the different medications, old and new, to meet heart failure treatment goals.
6. Value the role of the pharmacist.

# Definition

Heart Failure (HF) is a **syndrome** with symptoms and signs that result from any structural or functional impairment of ventricular filling or ejection of blood.

- The heart is unable to provide adequate blood supply to throughout the body.






Heidenreich P, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. J Am Coll Cardiol. 2022 May, 79 (17) e263–e421.https://doi.org/10.1016/j.jacc.2021.12.012

# Epidemiology

1,000,000 new cases diagnosed each year

1ry diagnosis for hospital discharge ~1 million annually.

HF affects nearly 6.5 million Americans. (2019).

HF is an increasingly prevalent disease state and is projected to affect > 8 million people older than age 18 years by 2030.*

The annual expenditures for HF : >$30 billion; ~$70 million by 2030

5-year survival ~ 42%

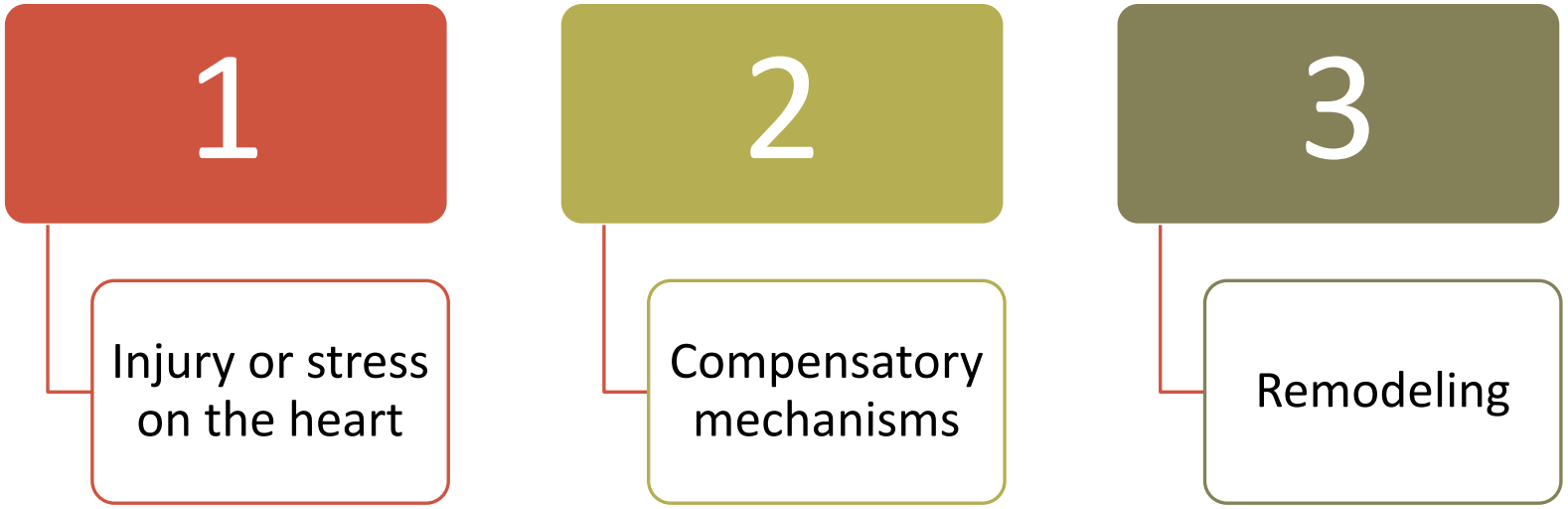
Mortality increases with symptom severity

Total deaths caused by HF have increased from 275,000 in 2009 to 310,000 in 2014**

Sudden death~ 40% of patients

Benjamin EJ, Virani SS, Callaway CW, et al. Heart disease and stroke statistics—2018 Update: A report from the American Heart Association. *Circulation*. 2018;137:e67–e492.
Benjamin EJ, Muntner P, Alonso A, et al. Heart disease and stroke statistics-2019 update: a report from he American Heart Association. Circulation. 2019;139: e56–528.
Heidenreich PA, Albert NM, Allen LA, et al. Forecasting the impact of heart failure in the United States: a policy statement from the American Heart Association. Circ Heart Fail. 2013;6:606–19
Tsao CW, Aday AW, Almarzooq ZI, et al. Heart disease and stroke statistics—2022 update: a report from the American Heart Association. *Circulation*. 2022;145:e153-e639.*3. Cleland JG, Chiswell K, Teerlink JR, et al. Predictors of postdischarge outcomes from information acquire shortly after admission for acute heart failure: a report from the placebo-controlled randomized study of the selective A1 adenosine receptor antagonist rolofylline for patients hospitalized with acute decompensated heart failure and volume overload to assess treatment effect on congestion and renal function (PROTECT) study. Circ Heart Fail. 2014;7:76–87.**

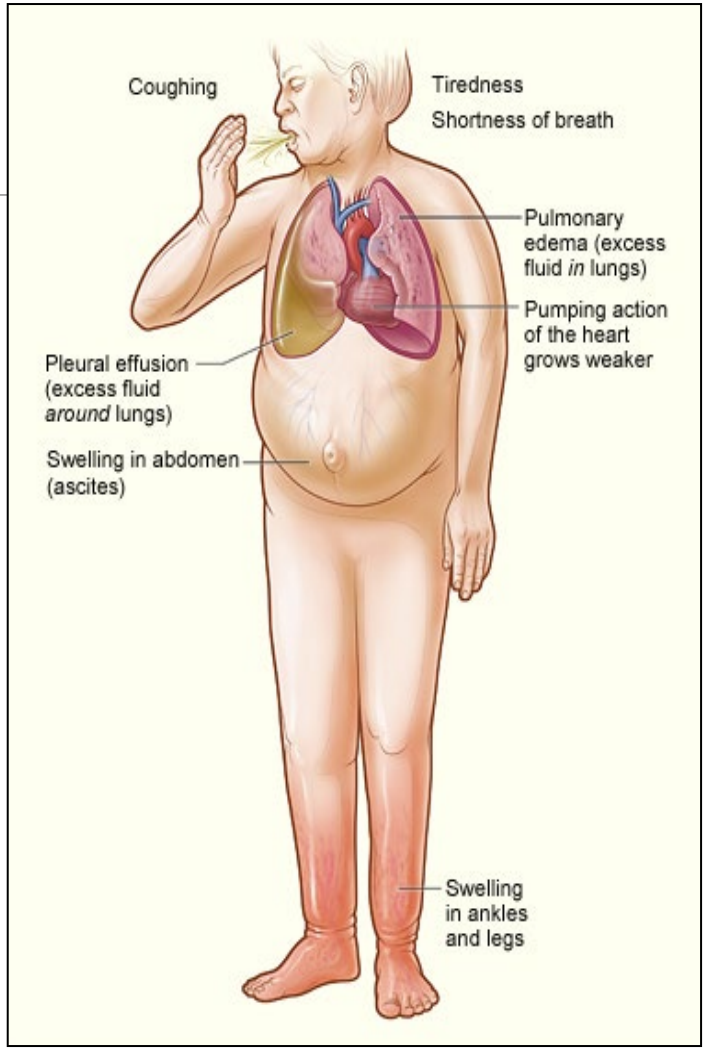
# Pathophysiology



# Which are the Symptoms of Heart Failure?

Think **FACES**…

- **F**atigue
- **A**ctivities limited
- **C**hest congestion or Cough
- **E**dema or ankle swelling
- **S**hortness of breath




http://www.nhlbi.nih.gov/health/dci/Diseases/Hf/HF_SignsAndSymptoms.html

# Classification of Heart Failure based on Left Ventricular Ejection Fraction

| | |
|---|---|
| HF with reduced EF (HFrEF) | HF with LVEF ≤ 40% (0.4) |
| HF with mildly reduced EF (HFmrEF) * | HF with LVEF 41%-49% (0.41-0.49) |
| HF with preserved EF (HFpEF) | HF with LVEF ≥ 50% (0.5) |
| HF with improved EF (HFimpEF) | HF with baseline LVEF ≤ 40% (0.4), a ≥ 10-point increase from baseline LVEF, and a second measurement of LVEF > 40% (0.4) |

HF, heart failure; LVEF, left ventricular ejection fraction.
*also known as mid range

All patients with current or prior HF symptoms, irrespective of EF, should be considered for:

GUIDELINE-DIRECTED MEDICAL THERAPY (GDMT).

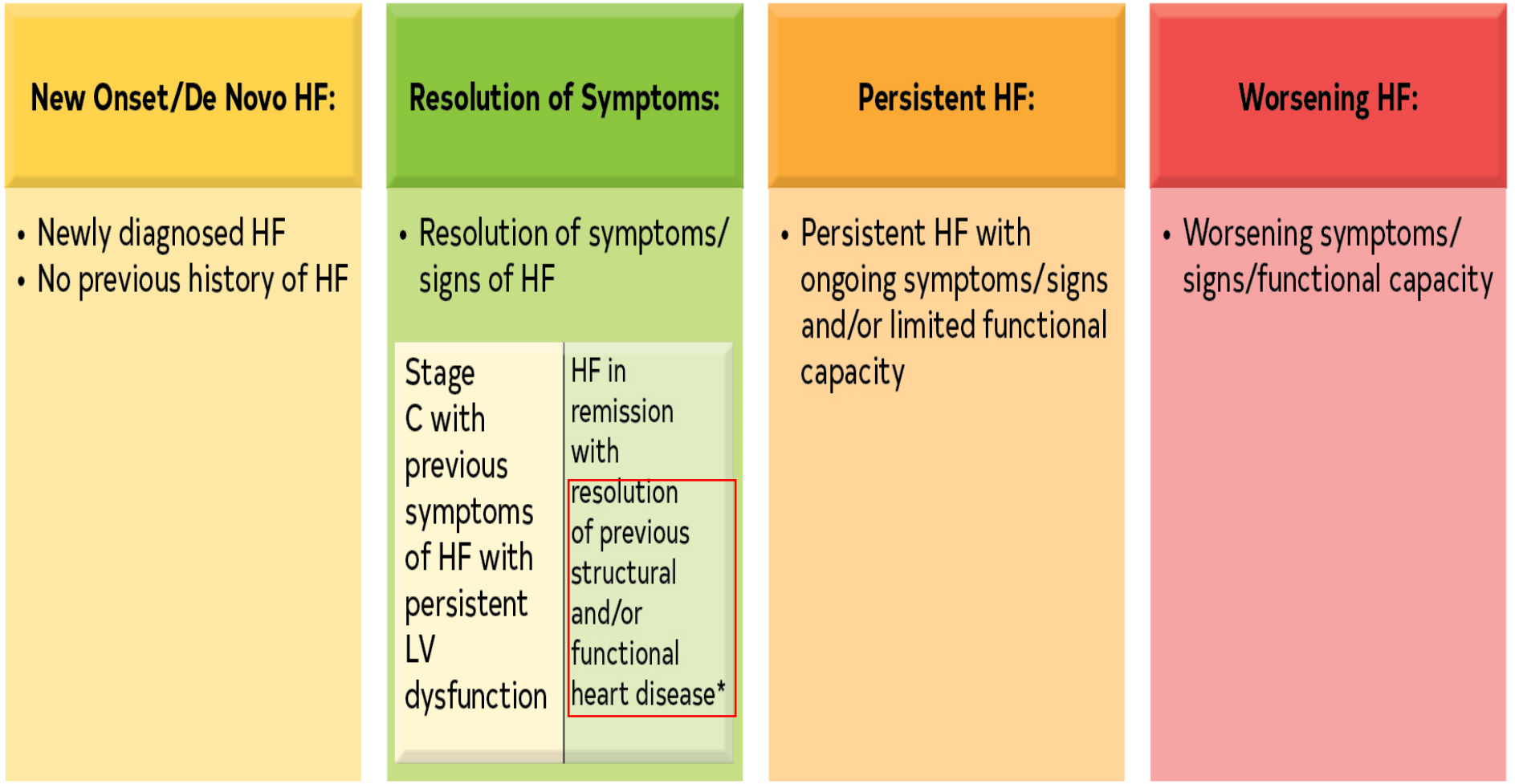
Heidenreich P, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. *J Am Coll Cardiol.* 2022 May, 79 (17) e263–e421.https://doi.org/10.1016/j.jacc.2021.12.012

Parker R.B., & Rodgers J (2021). Chronic heart failure. DiPiro J.T., & Yee G.C., & Michael Posey L.L., & Haines S.T., & Nolin T.D., & Ellingrod V.L.(Eds.), *DiPiro: Pharmacotherapy A Pathophysiologic Approach, 12e*. McGraw Hill. https://accesspharmacy.mhmedical.com/content.aspx?bookid=3097&sectionid=267924089

| STAGES* | DEFINITION | Class | NEW YORK HEART ASSOCIATION FUNCTIONAL CLASSIFICATION |
|---|---|---|---|
| Stage A<br>At-risk for heart failure | Patients at risk for HF but without current or prior symptoms or signs of HF and without structural, biomarker, or genetic markers of heart disease.<br>• Patients with HTN, CVD, DM, obesity, known exposure to cardiotoxins, family history of cardiomyopathy | | |
| Stage B<br>Pre-heart failure | Patients without current or prior symptoms or signs of HF but evidence of one of the following:<br>• Structural heart disease: e.g., LVH, chamber enlargement, wall motion abnormality, myocardial tissue abnormality, valvular heart disease<br>• Abnormal cardiac function: e.g., reduced LV or RV systolic function, evidence of increased filling pressures or abnormal diastolic dysfunction<br>• Elevated natriuretic peptide levels or elevated cardiac troponin levels in the setting of exposure to cardiotoxins | I | No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF. |
| Stage C<br>Heart failure | Patients with current or prior symptoms and/or signs of HF caused by structural and/or cardiac abnormality.<br>• HF in remission or persistent HF | I | No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF. |
| | | II | Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in symptoms of HF |
| | | III | Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes symptoms of HF |
| | | IV | Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest. |
| Stage D<br>Advanced heart failure | Severe symptoms and/or signs of HF at rest, recurrent hospitalizations despite GDMT, refractory or intolerant to GDMT.<br>• Requiring advanced therapies such as consideration for transplant, mechanical circulatory support, or palliative care | IV | Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest. |

*Adapted from: Bozkurt B, Coats AJ, Tsutsui H, et al. Universal Definition and Classification of Heart Failure: A Report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure. *J Card Fail*. 2021 CVD, cardiovascular disease; DM, diabetes; GDMT, guideline-directed medical therapy; HF, heart failure; HTN, hypertension; LV, left ventricle; LVH, left ventricular hypertrophy; RV, right ventricle.

# Figure 2. Trajectory of Class C HF



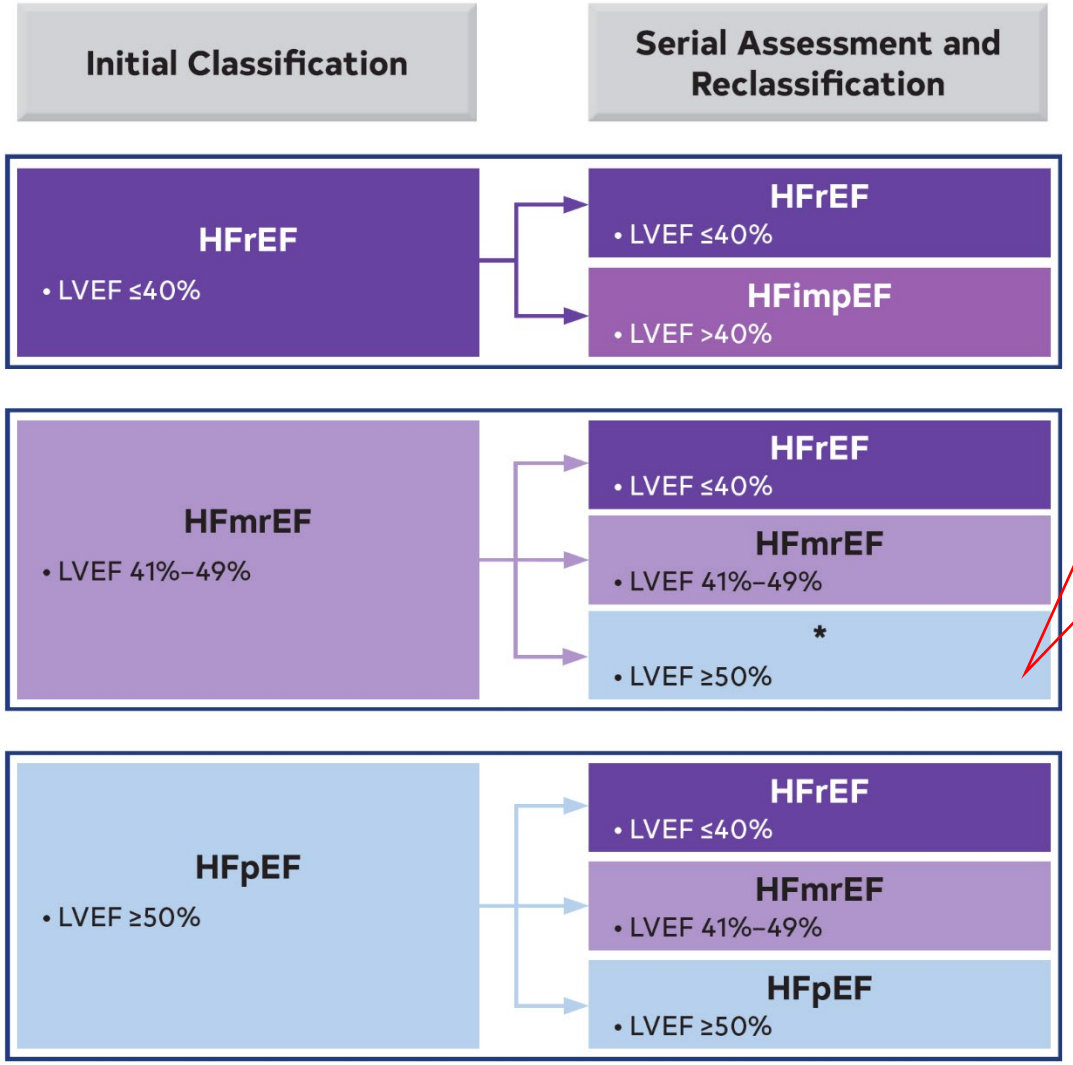

**The trajectory of stage C HF is displayed. Patients whose symptoms and signs of HF are resolved are still stage C and should be treated accordingly. If all HF symptoms, signs, and structural abnormalities resolve, the patient is considered to have HF in remission.**

***Full resolution of structural and functional cardiac abnormalities is uncommon.**

**HF indicates heart failure; and LV, left ventricular.**

2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Published online ahead of print April 1, 2022, available at: Circulation. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001063 And Journal of the American College of Cardiology published online ahead of print April 1, 2022. J Am Coll Cardiol. https://www.jacc.org/doi/10.1016/j.jacc.2021.12.012

# Figure 3. Classification and Trajectories of HF Based on LVEF




**Limited evidence** re: how to treat patients who improve their **LVEF from mildly reduced (41%-49%) to ≥50%.**

**(HFmrEF or HFpEF ?)**

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# Table 2. Applying American College of Cardiology/American Heart Association Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care (Updated May 2019)*

| CLASS (STRENGTH) OF RECOMMENDATION | |
|---|---|
| **CLASS 1 (STRONG)** | **Benefit >>> Risk** |
| **Suggested phrases for writing recommendations:**<br>• Is recommended<br>• Is indicated/useful/effective/beneficial<br>• Should be performed/administered/other<br>• Comparative-Effectiveness Phrases†:<br>– Treatment/strategy A is recommended/indicated in preference to treatment B<br>– Treatment A should be chosen over treatment B | |
| **CLASS 2a (MODERATE)** | **Benefit >> Risk** |
| **Suggested phrases for writing recommendations:**<br>• Is reasonable<br>• Can be useful/effective/beneficial<br>• Comparative-Effectiveness Phrases†:<br>– Treatment/strategy A is probably recommended/indicated in preference to treatment B<br>– It is reasonable to choose treatment A over treatment B | |
| **CLASS 2b (WEAK)** | **Benefit ≥ Risk** |
| **Suggested phrases for writing recommendations:**<br>• May/might be reasonable<br>• May/might be considered<br>• Usefulness/effectiveness is unknown/unclear/uncertain or not well-established | |
| **CLASS 3: No Benefit (MODERATE)**<br>**(Generally, LOE A or B use only)** | **Benefit = Risk** |
| **Suggested phrases for writing recommendations:**<br>• Is not recommended<br>• Is not indicated/useful/effective/beneficial<br>• Should not be performed/administered/other | |
| **Class 3: Harm (STRONG)** | **Risk > Benefit** |
| **Suggested phrases for writing recommendations:**<br>• Potentially harmful<br>• Causes harm<br>• Associated with excess morbidity/mortality<br>• Should not be performed/administered/other | |

| LEVEL (QUALITY) OF EVIDENCE‡ | |
|---|---|
| **LEVEL A** | |
| • High-quality evidence‡ from more than 1 RCT<br>• Meta-analyses of high-quality RCTs<br>• One or more RCTs corroborated by high-quality registry studies | |
| **LEVEL B-R** | **(Randomized)** |
| • Moderate-quality evidence‡ from 1 or more RCTs<br>• Meta-analyses of moderate-quality RCTs | |
| **LEVEL B-NR** | **(Nonrandomized)** |
| • Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies<br>• Meta-analyses of such studies | |
| **LEVEL C-LD** | **(Limited Data)** |
| • Randomized or nonrandomized observational or registry studies with limitations of design or execution<br>• Meta-analyses of such studies<br>• Physiological or mechanistic studies in human subjects | |
| **LEVEL C-EO** | **(Expert Opinion)** |
| • Consensus of expert opinion based on clinical experience | |

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR 1 and 2a; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely-used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

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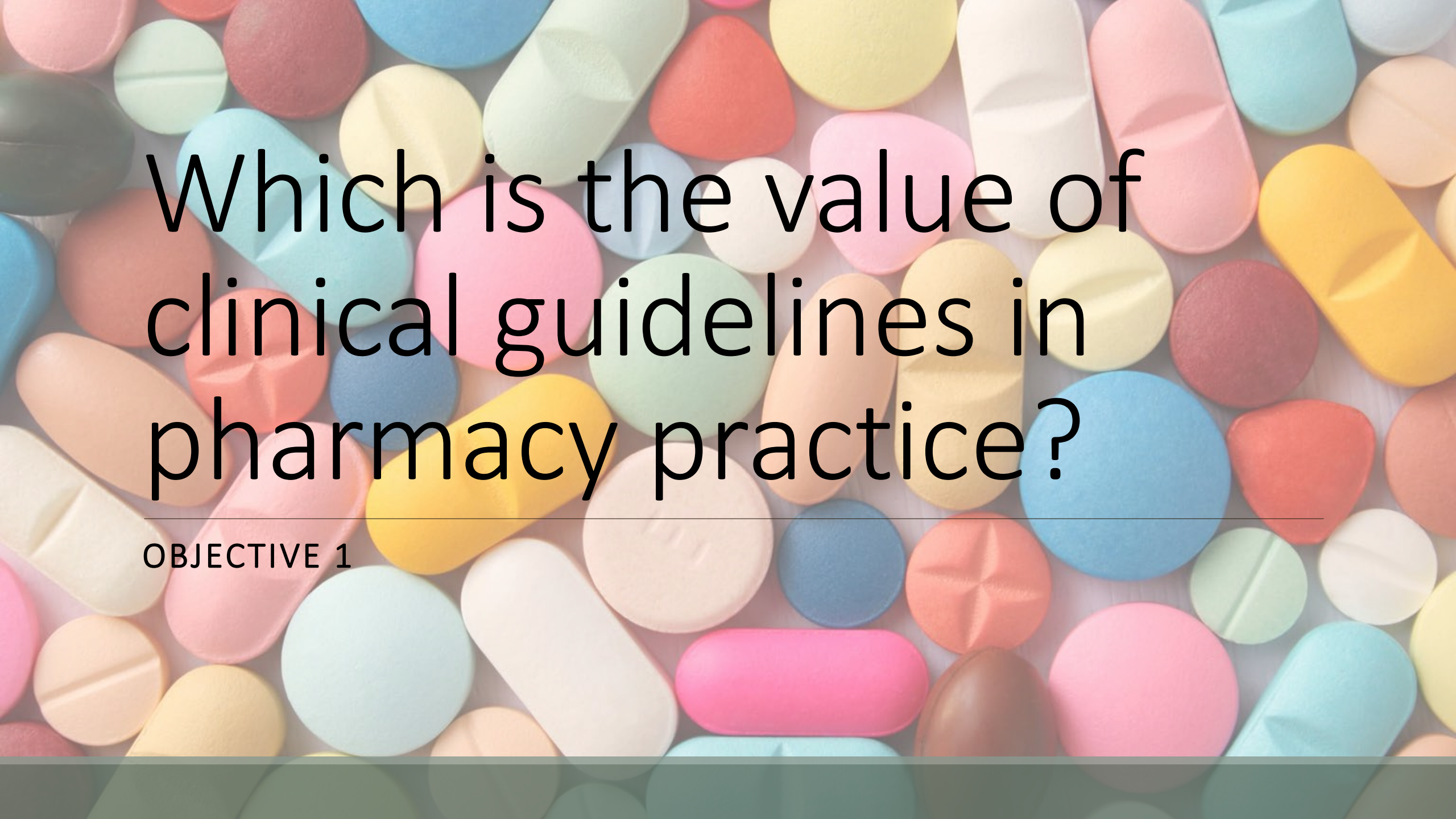

# Which is the value of clinical guidelines in pharmacy practice?

OBJECTIVE 1

# 2022 guideline is intended to provide:

These are **patient-centric** recommendations for clinicians to prevent, diagnose, and manage patients with heart failure.

It is the **most up-to-date evidence** to direct the clinician in patient decision-making.

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# HF Treatment Goals

| | |
|---|---|
| Prolong | Survival |
| Improve | Quality of life |
| Decrease | Hospitalizations |
| Slow | Disease progression |

# Question 1

The purpose of publishing clinical guidelines is to…

a. Make sure the recommendations are always applied
b. Provide a body of reference for best decisions based on clinical experience
c. Offer recommendations to help practitioners and patients make decisions about appropriate health care for specific conditions
d. All answers are correct

# Current recommendations for heart failure treatment

OBJECTIVE 2

# 2022 AHA/ACC/HFSA Heart Failure Guideline: Key Points - **New terminology**

| Stage | Primary Prevention Recommendations |
|---|---|
| A<br>At-risk for HF | Management of risk factors<br>Screening<br><br>Lifestyle modification |
| B<br>Pre-HF | |

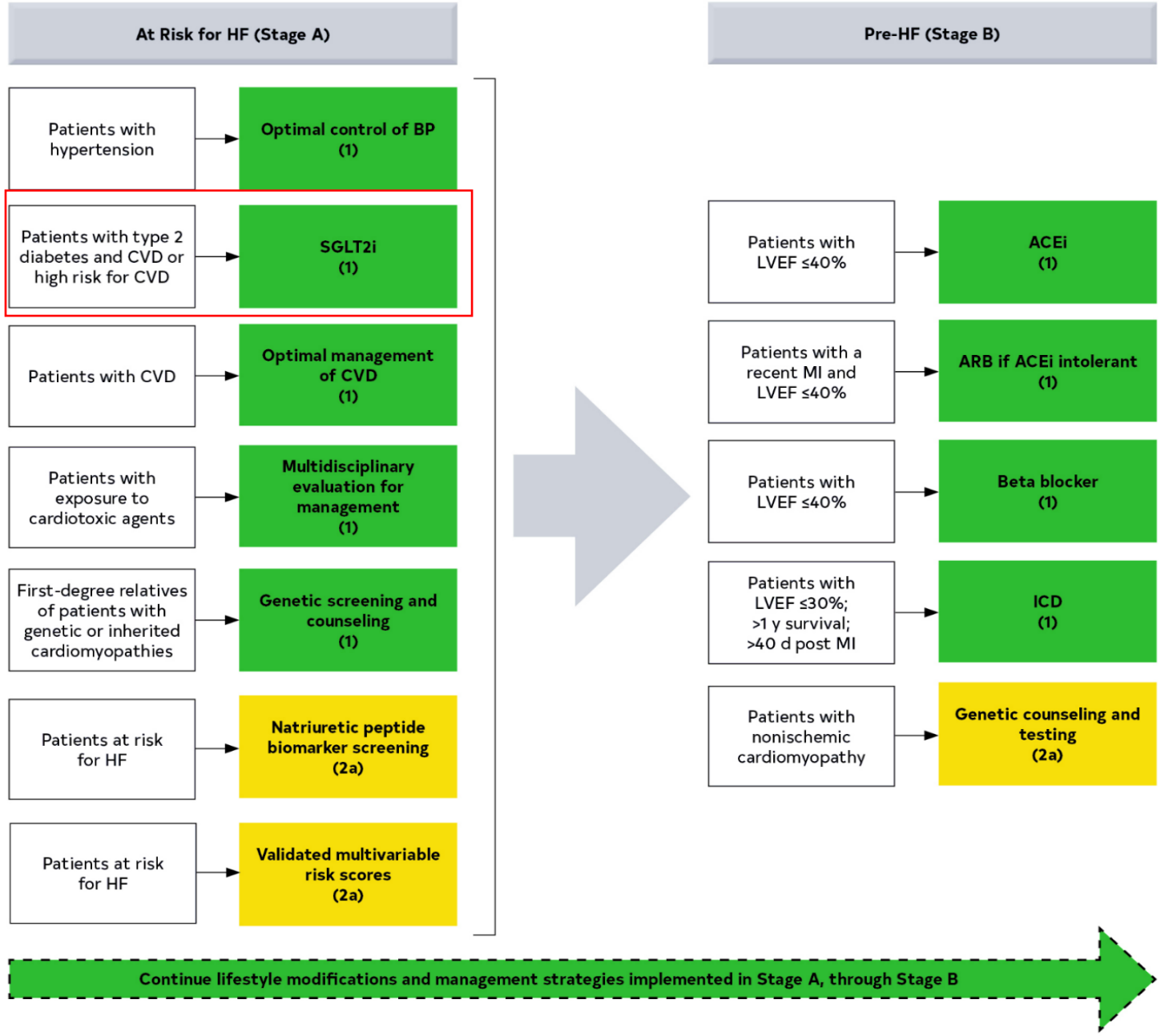
Adapted from: Heidenreich P, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. *J Am Coll Cardiol.* 2022 May, 79 (17) e263 e421.**https://doi.org/10.1016/j.jacc.2021.12.012**

# 2022 AHA/ACC/HFSA Heart Failure Guideline
# Recommendations for Patients at Risk for HF (Stage A: Primary Prevention)

| **Recommendations for Patients at Risk for HF (Stage A: Primary Prevention)**<br>**Referenced studies that support the recommendations are summarized in the Online Data Supplements.** | | |
|---|---|---|
| **COR** | **LOE** | **Recommendations** |
| **I** | **A** | 1. In patients with **hypertension**, blood pressure should be controlled in accordance with GDMT for hypertension to **prevent symptomatic** HF.1–9 |
| **I** | **A** | 2. In patients with **type 2 diabetes** and either established **CVD or at high cardiovascular risk**, **SGLT2i** should be used to **prevent hospitalizations** for HF.10–12 |
| **I** | **B-NR** | 3. In the general population, **healthy lifestyle habits** such as regular physical activity, maintaining normal weight, healthy dietary patterns, and avoiding smoking are helpful to reduce future risk of HF.13–21 |
| **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.22,23 |
| **2a** | **B-NR** | 5. In the general population, validated **multivariable risk scores** can be useful to estimate subsequent risk of incident HF.24–26 |

Adapted from: 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Published online ahead of print April 1, 2022, available at: Circulation. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001063 And Journal of the American College of Cardiology published online ahead of print April 1, 2022. J Am Coll Cardiol. https://www.jacc.org/doi/10.1016/j.jacc.2021.12.012

# Figure 5. Recommendations (Class 1 and 2a) for Patients at Risk of HF (Stage A) and Those With Pre-HF (Stage B)




**Colors correspond to COR in Table 2.**

**Class 1 and Class 2a recommendations** for patients at risk for HF (stage A) and those with pre-HF (stage B) are shown. Management strategies implemented in patients at risk for HF (stage A) should be continued though stage B.

ACEi indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BP, blood pressure; CVD, cardiovascular disease; HF, heart failure; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; MI, myocardial infarction; and SGLT2i, **sodium glucose cotransporter 2 inhibitor.**

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# SGLT2 inhibitors

Prevent the reabsorption of glucose filtered through the kidneys, facilitating glucose excretion in the urine.

First-line agents with COR I for **stage C or D HFrEF** in patients WITHOUT diabetes who were treated according to previous guidelines.

# SGLT2 inhibitors

PROVEN cardioprotective effects in HF patients **regardless of the presence of diabetes**

- Decrease blood pressure
- Natriuresis
- Diuresis
- Improve cardiac energy metabolism
- Prevent of inflammation
- Improve glucose control
- Weight loss

Lopaschuk GD, Verma S. Mechanisms of cardiovascular benefits of sodium glucose co-transporter 2 (SGLT2) inhibitors: a state-of-the-art review. JACC Basic Transl Sci. 2020;5(6):632-644.

# SGLT2 inhibitors

| SGLT2 inhibitor | FDA approval | Indications | Dose |
|---|---|---|---|
| Invokana (canagliflozin) | 2013 | Type 2 diabetes | 100 – 300 mg daily |
| Dapagliflozin | 2014 | Type 2 diabetes<br><br>Heart failure | Type 2 diabetes:<br>5 – 10 mg daily<br><br>Heart failure:<br>10 mg daily |
| Empagliflozin | 2014 | Type 2 diabetes<br><br>Heart failure– to reduce the risk of CV death plus hospitalization | Type 2 diabetes:<br>10 – 25 mg daily<br><br>Heart failure:<br>10 mg daily |
| Steglatro (ertugliflozin) | 2017 | Type 2 diabetes | 5 – 15 mg daily |

Adapted from: **What Are SGLT2 Inhibitors and How Do They Work?**
Available at: https://www.healthline.com/health/type-2-diabetes/sglt2-inhibitors#benefits

# Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction (DAPA-HF) 2019 - **milder HF**

PRIMARY ENDPOINT: reduces the risk of CV DEATH and worsening HF event (hospitalization, urgent HF visit requiring IV therapy) – 26% decrease composite

Mortality – 17% reduction

Kansas City Cardiomyopathy Questionnaire (KCCQ) – 17% improvement (significant)

Reduces the risk of further worsening of kidney disease and slow the progression toward end-stage. No differences regarding renal decline, dialysis and transplant

NNT to prevent 1 event was 21

Packer M, Anker SD, Butler J, et al. Cardiovascular and renal outcomes with empagliflozin in heart failure. N Engl J Med. 2020;383:1413-1424.
McMurray JJV, Solomon SD, Inzucchi SE, et al. Dapagliflozin in patients with heart failure and reduced ejection fraction. N Engl J Med. 2019;381:1995-2008. Packer M, Anker SD, Butler J, et al. Cardiovascular and renal outcomes with empagliflozin in heart failure. N Engl J Med. 2020;383:1413-1424.
McMurray JJV, Solomon SD, Inzucchi SE, et al. Dapagliflozin in patients with heart failure and reduced ejection fraction. N Engl J Med. 2019;381:1995-2008.

# SGLT2 Inhibitor - dapagliflozin

| Indication | Dose | Pharmacologic Effects |
| --- | --- | --- |
| • DMT2<br>• Improves the glycemic control in adults<br>• Decreases glucose, A1c, blood pressure and weight<br>• HFrEF<br>  • (EF ≤40%) with or without diabetes<br>  • NYHA class II–IV HF*<br>  • Administered in conjunction with a background of GDMT for HF | • 10mg QD<br>• 5mg if hypovolemia, hypotension or renal dysfunction | • Osmotic diuresis/natriuresis<br>• Reduces preload and afterload<br>• Reverse remodeling ?<br>• Reduces CV death 18% and HF hospitalization in patients w or w/o DM 30% (class effect) |

*Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction. N Engl J Med 2019;381:1995-2008.

Maddox et al. 2021 Update to 2017 ECDP for Optimization of Heart Failure Treatment J A C C V O L . 7 7 , NO . 6 , F E B R U A R Y 1 6 , 2 0 2 1 : 7 7 2 – 8 1 0

# SGLT2 Inhibitor - dapagliflozin

| Side effects | Interactions | Contraindications |
| --- | --- | --- |
| • Genitourinary infections 6%<br>• Genitourinary fungal infections 3-8%<br>• Nasopharyngitis 7%<br>• Hypovolemia<br>• Hypoglycemia<br>• Hyperkalemia<br>• Ketoacidosis | • Antidiabetic agents<br>• Quinolones<br>• SSRI<br>• Salicylates<br>• Androgens<br>• Alpha lipoic acid<br>• Thiazide and thiazide like diuretics<br>• Diuretics<br>• Others | • History of serious hypersensitivity to dapagliflozin or any component of the formulation<br>• Severe renal impairment (eGFR <30 mL/minute/1.73 $m^2$)<br>• End -stage renal disease (ESRD)<br>• Dialysis |

*Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction. N Engl J Med 2019;381:1995-2008.

Maddox et al. 2021 Update to 2017 ECDP for Optimization of Heart Failure Treatment J A C C V O L . 7 7 , NO . 6 , F E B R U A R Y 1 6 , 2 0 2 1 : 7 7 2 – 8 1 0

# SGLT2 inhibitors - empagliflozin

| | EMPEROR-Reduced |
|---|---|
| P | symptomatic stable HFrEF (EF ≤40%) on excellent baseline GDMT |
| I | 10mg |
| C | Placebo |
| O | Reduced CV death or hospitalization 19.4% vs 24.7% |

EMPagliflozin outcomE tRial in Patients With chrOnic heaRt Failure With Reduced Ejection Fraction (EMPEROR-Reduced)
**Empagliflozin** Outcome Trial in Patients with Chronic Heart Failure with Preserved Ejection Fraction

# EMPagliflozin outcomE tRial in Patients With chrOnic heaRt Failure With Reduced Ejection Fraction (EMPEROR-Reduced) 2020 – **Severe HF**

| | |
|---|---|
| CV death or hospitalization | Patients with DM RRR 28% |
| | Patients without DM RRR 22% |
| Hospitalization for HF | 30% reduction |
| Renal death, dialysis or profound GFR reduction | 50% reduction |

Packer M, Anker SD, Butler J, et al. Cardiovascular and renal outcomes with empagliflozin in heart failure. N Engl J Med. 2020;383:1413-1424.
McMurray JJV, Solomon SD, Inzucchi SE, et al. Dapagliflozin in patients with heart failure and reduced ejection fraction. N Engl J Med. 2019;381:1995-2008
Packer M, Anker SD, Butler J, et al. Cardiovascular and renal outcomes with empagliflozin in heart failure. N Engl J Med. 2020;383:1413-1424.
McMurray JJV, Solomon SD, Inzucchi SE, et al. Dapagliflozin in patients with heart failure and reduced ejection fraction. N Engl J Med. 2019;381:1995-2008..

# Table 12. Commonly Used Oral Diuretics in Treatment of Congestion for Chronic HF

| Drug | Initial Daily Dose | Maximum Total Daily Dose | Duration of Action |
|---|---|---|---|
| **Loop diuretics** | | | |
| Bumetanide | 0.5–1.0 mg once or twice | 10 mg | 4–6 h |
| **Furosemide** | 20–40 mg once or twice | 600 mg | 6–8 h |
| Torsemide | 10–20 mg once | 200 mg | 12–16 h |

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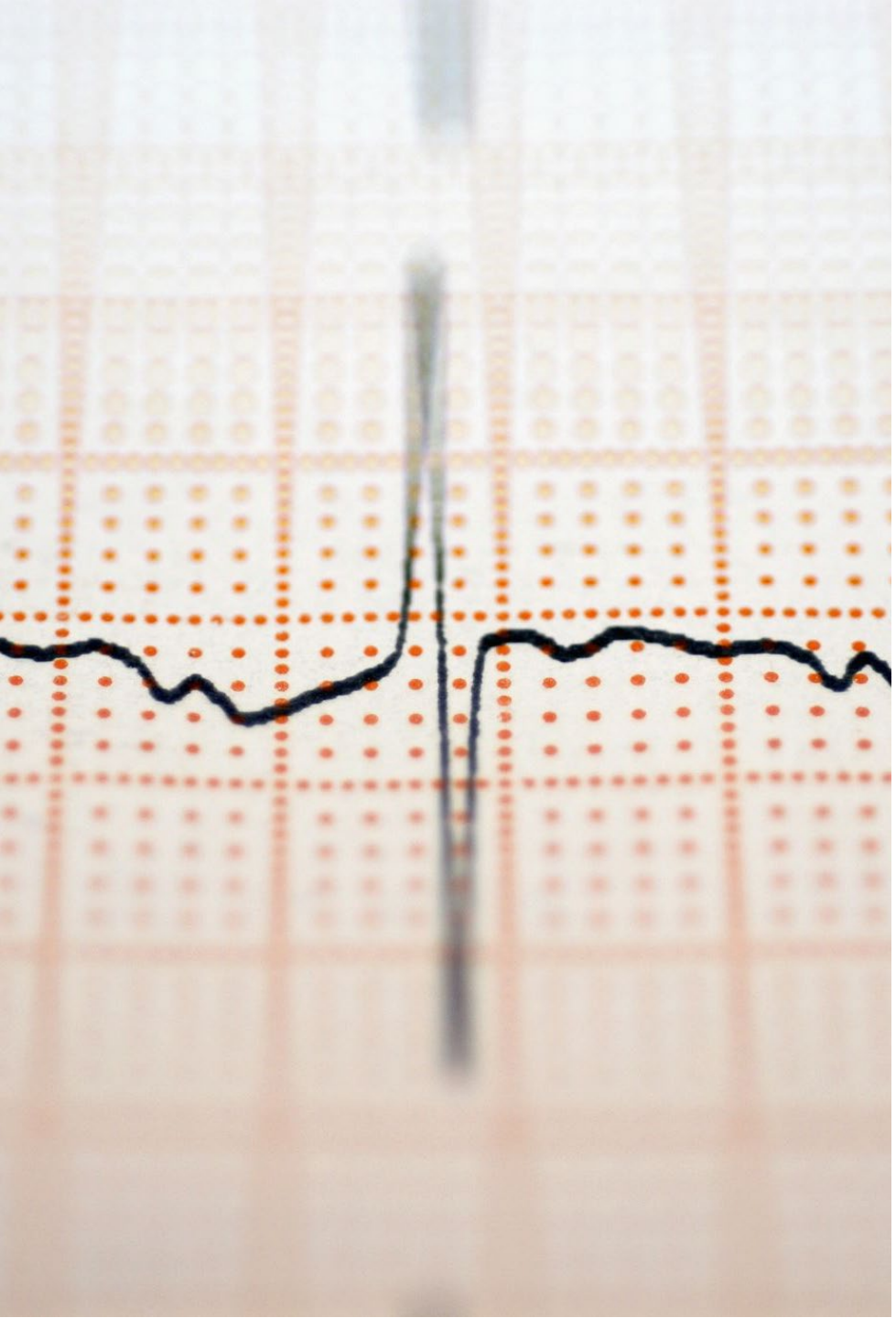
# 2022 AHA/ACC/HFSA Heart Failure Guideline STAGE C HF

## Nonpharmacological Interventions

Because of the complexity of HF management and coordination of other health and social services required, HF care is ideally provided by multidisciplinary teams27–30 that include cardiologists, nurses, and **pharmacists who specialize in HF** as well as dieticians, mental health clinicians, social workers, primary care clinicians, and additional specialists.31–33

| 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.1–6 |

| Recommendations for Management of Stage C HF: Activity, Exercise Prescription, and Cardiac Rehabilitation<br>Referenced studies that support the recommendations are summa- rized in the Online Data Supplements. | | |
|---|---|---|
| **COR** | **LOE** | **Recommendations** |
| **I** | **A** | 1. For patients with HF **who are able to participate**, **exercise training** (or regular physical activity) is recommended to improve functional status, exercise performance, and QOL.1–9 |
| **2a** | **B-NR** | 2. In patients with HF, a **cardiac rehabilitation program** can be useful to improve functional capacity, exercise tolerance, and health-related QOL.1,2,5,6,8 |



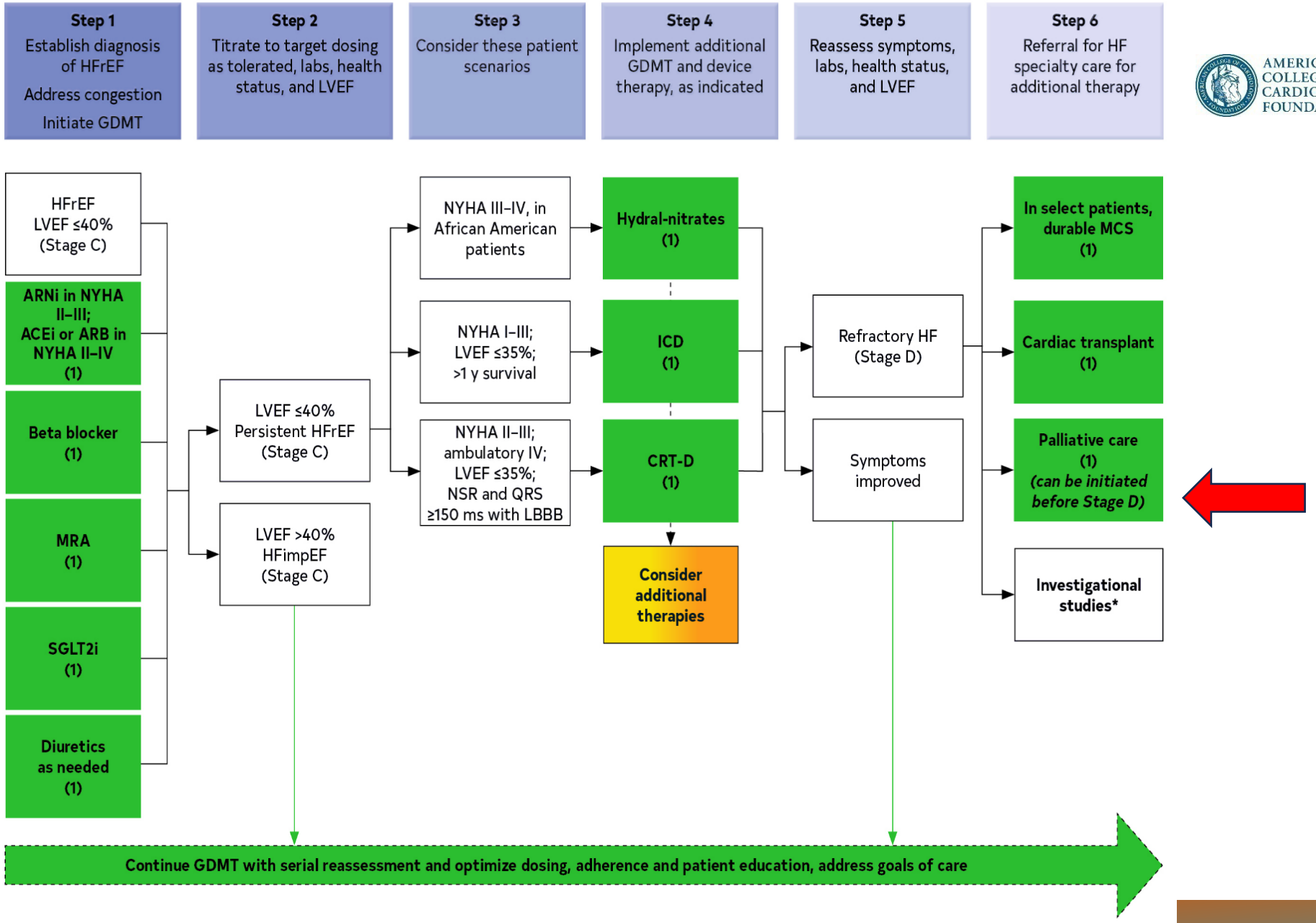
# 2022 Heart Failure Guideline Six-Step Algorithm of HFrEF – Stages C and D

HEIDENREICH PA, BOZKURT B, AGUILAR D, ET AL. 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. CIRCULATION. 2022;145(18):E895-E1032.

# Figure 6. Treatment of HFrEF Stages C and D

**Colors correspond to COR in Table 2.**

Treatment recommendations for patients with HFrEF are displayed. 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.




Adapted from: 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Published online ahead of print April 1, 2022, available at: Circulation. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001063 And Journal of the American College of Cardiology published online ahead of print April 1, 2022. J Am Coll Cardiol. https://www.jacc.org/doi/10.1016/j.jacc.2021.12.012

# 2022 AHA/ACC/HFSA Heart Failure Guideline

| **Recommendations for Diuretics and Decongestion Strategies in Patients With HF Referenced studies that support the recommendations are summarized in the Online Data Supplements.** | | |
|---|---|---|
| **COR** | **LOE** | **Recommendations** |
| **I** | **B-NR** | 1. In patients with HF who have **fluid retention**, **diuretics** are recommended to relieve congestion, improve symptoms, and prevent worsening HF.1–5 |
| **I** | **B-NR** | 2. For patients with HF and congestive symptoms, **addition of a thiazide** (e.g., metolazone) to treatment with a loop diuretic should be **reserved for patients who do not respond to moderate- or high-dose loop diuretics** to minimize electrolyte abnormalities.6 |

Adapted from: 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Published online ahead of print April 1, 2022, available at: Circulation. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001063 And Journal of the American College of Cardiology published online ahead of print April 1, 2022. J Am Coll Cardiol. https://www.jacc.org/doi/10.1016/j.jacc.2021.12.012

# Table 12. Commonly Used Oral Diuretics in Treatment of Congestion for Chronic HF (con't.)

| Drug | Initial Daily Dose | Maximum Total Daily Dose | Duration of Action |
|---|---|---|---|
| **Thiazide diuretics** | | | |
| **Chlorothiazide** | 250–500 mg once or twice | 1000 mg | 6–12 h |
| Chlorthalidone | 12.5–25 mg once | 100 mg | 24–72 h |
| Hydrochloro-thiazide | 25 mg once or twice | 200 mg | 6–12 h |
| Indapamide | 2.5 mg once | 5 mg | 36 h |
| **Metolazone** | 2.5 mg once | 20 mg | 12–24 h |

**HF indicates heart failure.**

Adapted from: 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Published online ahead of print April 1, 2022, available at: Circulation. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001063 And Journal of the American College of Cardiology published online ahead of print April 1, 2022. J Am Coll Cardiol. https://www.jacc.org/doi/10.1016/j.jacc.2021.12.012

# Question 2

According to current heart failure treatment guidelines, the following is recommended **as needed** for most patients with heart failure with reduced ejection fraction (**HFrEF**) Stage C

a. Empagliflozin
b. Spironolactone
c. Metoprolol succinate
d. Furosemide
e. Sacubitril/Valsartan

# 2022 AHA/ACC/HFS A Heart Failure Guideline

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

| Recommendations for Renin-Angiotensin System Inhibition With ACEi or ARB or ARNi<br>Referenced studies that support the recommendations are summarized in the Online Data Supplements. | | |
|---|---|---|
| **COR** | **LOE** | **Recommendations** |
| **I** | **A** | 1. In patients with HFrEF and NYHA class II to III symptoms, the use of **ARNi** is recommended to reduce morbidity and mortality.1–5 |
| **I** | **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.6–13 |
| **I** | **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.14–18 |
| **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**.19–25 |
| **I** | **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**.1–5 |
| **Value Statement: High Value (A)** | | 6. In patients with chronic symptomatic HFrEF, treatment with an **ARNi instead of an ACEi provides high economic value**.26–29 |
| **3: Harm** | **B-R** | 7. ARNi should not be administered concomitantly with ACEi or within 36 hours of the last dose of an ACEi.30,31 |
| **3: Harm** | **C-LD** | 8. ARNi should not be administered to patients with any history of angioedema.32–35 |
| **3: Harm** | **C-LD** | 9. ACEi should not be administered to patients with any history of angioedema.36–39 |

Adapted from: 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Published online ahead of print April 1, 2022, available at: Circulation. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001063 And Journal of the American College of Cardiology published online ahead of print April 1, 2022. J Am Coll Cardiol. https://www.jacc.org/doi/10.1016/j.jacc.2021.12.012

# Table 14. Drugs Commonly Used for HFrEF (Stage C HF)

| Drug | Initial Daily Dose(s) | Target Doses(s) | Mean Doses Achieved in Clinical Trials | References |
|---|---|---|---|---|
| **ACEi** | | | | |
| Captopril | 6.25 mg 3 times daily | 50 mg 3 times daily | 122.7 mg total daily | (19) |
| Enalapril | 2.5 mg twice daily | 10–20 mg twice daily | 16.6 mg total daily | (3) |
| Fosinopril | 5–10 mg once daily | 40 mg once daily | NA | … |
| Lisinopril | 2.5–5 mg once daily | 20–40 mg once daily | 32.5–35.0 mg total daily | (17) |
| Perindopril | 2 mg once daily | 8–16 mg once daily | NA | … |
| Quinapril | 5 mg twice daily | 20 mg twice daily | NA | … |
| Ramipril | 1.25–2.5 mg once daily | 10 mg once daily | NA | … |
| Trandolapril | 1 mg once daily | 4 mg once daily | NA | … |

Adapted from: 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Published online ahead of print April 1, 2022, available at: Circulation. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001063 And Journal of the American College of Cardiology published online ahead of print April 1, 2022. J Am Coll Cardiol. https://www.jacc.org/doi/10.1016/j.jacc.2021.12.012

# Table 14. Drugs Commonly Used for HFrEF (Stage C HF) (con't.)

| Drug | Initial Daily Dose(s) | Target Doses(s) | Mean Doses Achieved in Clinical Trials | References |
|---|---|---|---|---|
| **ARB** | | | | |
| Candesartan | 4–8 mg once daily | 32 mg once daily | 24 mg total daily | (20) |
| Losartan | 25–50 mg once daily | 50–150 mg once daily | 129 mg total daily | (18) |
| Valsartan | 20–40 mg once daily | 160 mg twice daily | 254 mg total daily | (21) |
| **ARNi** | | | | |
| Sacubitril-valsartan | 49 mg sacubitril and 51 mg valsartan twice daily (therapy may be initiated at 24 mg sacubitril and 26 mg valsartan twice daily) | 97 mg sacubitril and 103 mg valsartan twice daily | 182 mg sacubitril and 193 mg valsartan total daily | (22) |

Adapted from: 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Published online ahead of print April 1, 2022, available at: Circulation. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001063 And Journal of the American College of Cardiology published online ahead of print April 1, 2022. J Am Coll Cardiol. https://www.jacc.org/doi/10.1016/j.jacc.2021.12.012

# Angiotensin II Receptor Blocker/Neprilysin Inhibitor (ARNi):

# sacubitril/valsartan

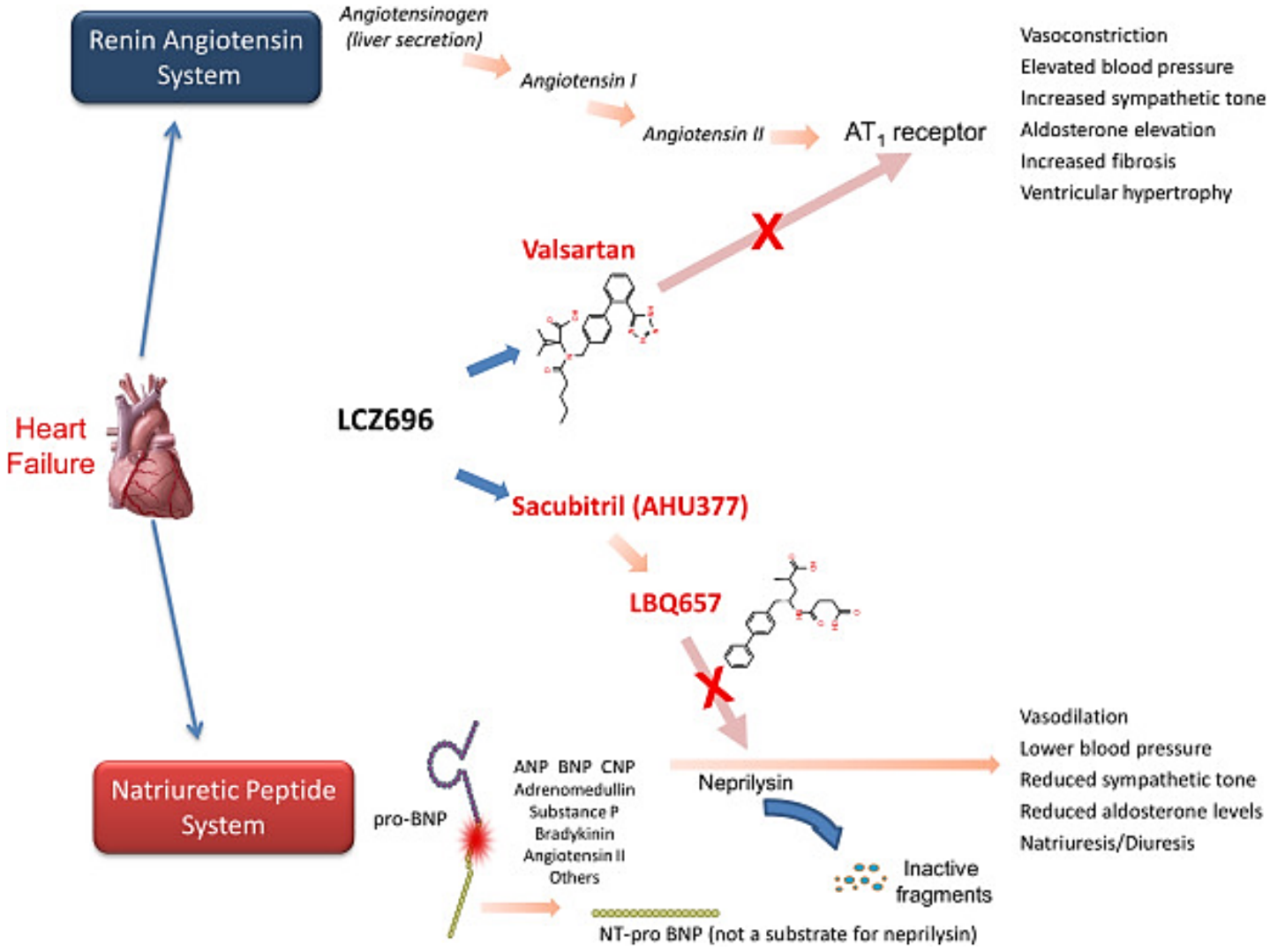



Image: Vardeny O, Miller R, Solomon SD. Combined neprilysin and renin-angiotensin system inhibition for the treatment of heart failure. *JACC Heart Fail.* 2014;2:663–670.

# ARNi: sacubitril/valsartan

| Combination | MOA | MORE effective vs. ACEI alone |
| --- | --- | --- |
| Valsartan + Sacubitril (first "angiotensin receptor/neprilysin inhibitor" = ARNI) | • Sacubitril works by inhibiting the enzyme neprilysin, to increase the concentration of bradykinin, **natriuretic peptides** and adrenomedullin.<br>Increases sodium loss and vasodilation | • ACEI vs ARNI - LVEF increased from 28.2% to 37.8%<br>• Naïve to ACEI LVEF increased 12%<br>• Reverse remodeling **<br>• Prevents 1:21 CV death or heart failure hospitalization (treated over 2 years) vs enalapril 10 mg BID*<br>• Absolute 4.7% reduction in the primary outcome of CV death or HF hospitalization<br>• 20% reduction in SCD |

*McMurray JJ, Packer M, Desai AS, et al. Angiotensin-neprilysin inhibition versus enalapril in heart failure. N Engl J Med. 2014;371:993–1004. (**PARADIGM-HF**)
** Desai AS, Solomon SD, Shah AM, et al. Effect of sacubitril-valsartan vs enalapril on aortic stiffness in patients with heart failure and reduced ejection fraction a randomized clinical trial. JAMA. 2019;322:1–10. (**EVALUATE-HF**)

# ARNi: sacubitril/valsartan

| Place in therapy | Caution | Dosing |
|---|---|---|
| **2021:**<br>**De novo patients, Stage C- preferred agent***<br><br>**2017:**<br>**Stage C - Consider a switch from the ACEI or ARB to ARNI** in patients taking **target doses** of a std. regimen (ACEI or ARB, BB, and an aldosterone antagonist), **especially after a recent HF hospitalization**. | • **De novo patients- caution hypotension and advanced HF**<br><br>• **Make sure systolic BP is >100mmHg**<br><br>• **Wait at least 36 hours** after ACEI is stopped before starting ARNI | • 24/26 mg BID naïve patients or severe renal disease.<br>F/U: 2-4 weeks.<br><br>• 49/51 mg tabs BID for most patients. To switch from low dose enalapril or valsartan (or equivalent dose).<br>F/U: 2-4 weeks.<br><br>• Titration: every 2 to 4 wks. based on BP, aiming for a dose of 97/103 mg BID |

*Maddox et al. 2021 Update to 2017 ECDP for Optimizatin of Heart Failure Treatment J A C C V O L . 7 7 , NO . 6 , F E B R U A R Y 1 6 , 2 0 2 1 : 7 7 2 – 8 1 0

McMurray JJ, Packer M, Desai AS, et al. Angiotensin-neprilysin inhibition versus enalapril in heart failure. N Engl J Med. 2014;371:993–1004. (**PARADIGM-HF**)

# ARNi: sacubitril/valsartan

## Cost

~ $ 400.00- 600.00 /month*

## Hypotension

Don't suggest lowering the beta-blocker dose

Instead, the diuretic dose reduction, lower ARNi dose or stop *Entresto* and restart an ACEI or ARB.

## Angioedema

Avoid ARNi in patients with previous angioedema.

Blacks are at higher risk for angioedema.

Smokers

A Multicenter, Randomized, Double-blind, Active-controlled Study to Evaluate the Effects of LCZ696 Compared to Valsartan on Cognitive Function in Patients With Chronic Heart Failure and Preserved Ejection Fraction

* Good Rx – Entresto Available at: https://www.goodrx.com/entresto?dosage=97mg-103mg&form=tablet&label_override=Entresto&quantity=60&sort_type=popularity

# 2022 AHA/ACC/HFSA Heart Failure Guideline

| **Recommendation for Beta Blockers**<br>**Referenced studies that support the recommendation are summarized in the Online Data Supplements.** | | |
|---|---|---|
| **COR** | **LOE** | **Recommendation** |
| I | A | 1. In patients with HFrEF, with current or previous symptoms, use of 1 of the 3 beta blockers proven to reduce mortality (eg, bisoprolol, carvedilol, sustained-release metoprolol succinate) is recommended to reduce mortality and hospitalizations.1–3 |
| **Value Statement: High Value (A)** | | 2. In patients with HFrEF, with current or previous symptoms, **beta-blocker therapy provides high economic value**.4–8 |

Adapted from: 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Published online ahead of print April 1, 2022, available at: Circulation. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001063 And Journal of the American College of Cardiology published online ahead of print April 1, 2022. J Am Coll Cardiol. https://www.jacc.org/doi/10.1016/j.jacc.2021.12.012

# Table 14. Drugs Commonly Used for HFrEF (Stage C HF) (con't.)

| Drug | Initial Daily Dose(s) | Target Doses(s) | Mean Doses Achieved in Clinical Trials | References |
|---|---|---|---|---|
| **Beta blockers** | | | | |
| Bisoprolol | 1.25 mg once daily | 10 mg once daily | 8.6 mg total daily | (1) |
| Carvedilol | 3.125 mg twice daily | 25–50 mg twice daily | 37 mg total daily | (23) |
| Carvedilol CR | 10 mg once daily | 80 mg once daily | NA | … |
| Metoprolol succinate extended release (metoprolol CR/XL) | 12.5–25 mg once daily | 200 mg once daily | 159 mg total daily | (11) |
| **Mineralocorticoid receptor antagonists** | | | | |
| Spironolactone | 12.5–25 mg once daily | 25–50 mg once daily | 26 mg total daily | (6) |
| Eplerenone | 25 mg once daily | 50 mg once daily | 42.6 mg total daily | (13) |

Adapted from: 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Published online ahead of print April 1, 2022, available at: Circulation. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001063 And Journal of the American College of Cardiology published online ahead of print April 1, 2022. J Am Coll Cardiol. https://www.jacc.org/doi/10.1016/j.jacc.2021.12.012

# 2022 AHA/ACC/HFSA Heart Failure Guideline

| Recommendations for Mineralocorticoid Receptor Antagonists (MRAs) Referenced studies that support the recommendations are summarized in the Online Data Supplements. | | |
|---|---|---|
| **COR** | **LOE** | **Recommendations** |
| **I** | **A** | 1. In patients with **HFrEF and NYHA class II to IV symptoms**, an MRA (spironolactone or eplerenone) is recommended to reduce morbidity and mortality, if eGFR is >30 mL/min/1.73 m2 and serum potassium is <5.0 mEq/L. Careful monitoring of potassium, renal function, and diuretic dosing should be performed at initiation and closely monitored thereafter to minimize risk of hyperkalemia and renal insufficiency.1–3 |
| **Value Statement: High Value (A)** | | 2. In patients with HFrEF and NYHA class II to IV symptoms, **MRA therapy provides high economic value**.4–7 |
| **3: Harm** | **B-NR** | 3. In patients taking MRA whose serum potassium cannot be maintained at <5.5 mEq/L, MRA should be discontinued to avoid life- threatening hyperkalemia.8,9 |

Adapted from: 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Published online ahead of print April 1, 2022, available at: Circulation. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001063 And Journal of the American College of Cardiology published online ahead of print April 1, 2022. J Am Coll Cardiol. https://www.jacc.org/doi/10.1016/j.jacc.2021.12.012

# Strategies to Minimize the Risk of Hyperkalemia in Patients Treated with Aldosterone Antagonists

| | |
|---|---|
| Caution | • Avoid higher doses of ACE inhibitors: captopril ≥75 mg/d; enalapril or lisinopril ≥10 mg/d<br>• Discontinued or reduced potassium supplements<br>• Avoid foods high in potassium and NSAIDs |
| Check potassium levels and renal function | • At 3d and 1wk after initiating therapy and at least once a mo. for the first 3 mo. and every 3 mo. thereafter.<br>• When adding or increasing the dose of ACEI or ARBs<br>• Avoid triple combination of ACEI, ARB, and aldosterone receptor antagonist<br>• Discontinue or reduce if potassium levels >5.5 mEq/L unless other causes are identified |
| Impaired renal function is a risk factor for hyperkalemia if: | • Increased risk if serum creatinine is >1.6 mg/dL.*<br>• A CrCl >30 mL/min/1.73 $m^2$ is recommended in elderly patients or with low muscle mass<br>• Do not initiate if baseline serum $K^+$ >5.0 mEq/L. |
| Patient education | • Instruct to stop the aldosterone receptor antagonist in case of diarrhea, dehydration or interrupted loop diuretic therapy |

*Although the entry criteria for the trials of aldosterone antagonists included creatinine <2.5 mg/dL, the majority of patients had much lower creatinine; in 1 trial (425), 95% of patients had creatinine ≤1.7mg/dL. ACE indicates angiotensin-converting enzyme.

Adapted from: Yancy, CW et al. JACC Vol. 62(16).e147-239 2013 ACCF/AHA Heart Failure Guideline

# Table 14. Drugs Commonly Used for HFrEF (Stage C HF) (con't.)

| Drug | Initial Daily Dose(s) | Target Doses(s) | Mean Doses Achieved in Clinical Trials | References |
|---|---|---|---|---|
| **SGLT2i** | | | | |
| Dapagliflozin | 10 mg once daily | 10 mg once daily | 9.8 mg total daily | (8) |
| Empagliflozin | 10 mg once daily | 10 mg once daily | NR | (9) |
| **Isosorbide dinitrate and Hydralazine** | | | | |
| Fixed dose combination | 20 mg isosorbide dinitrate and 37.5 mg hydralazine 3 times daily | 40 mg isosorbide dinitrate and 75 mg hydralazine 3 times daily | 90 mg isosorbide dinitrate and ~175 mg hydralazine total daily | (10) |
| Isosorbide dinitrate and hydralazine | 20–30 mg isosorbide dinitrate and 25–50 mg hydralazine 3–4 times daily | 120 mg isosorbide dinitrate total daily in divided doses and 300 mg hydralazine total daily in divided doses | NA | (24) |

Adapted from: 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Published online ahead of print April 1, 2022, available at: Circulation. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001063 And Journal of the American College of Cardiology published online ahead of print April 1, 2022. J Am Coll Cardiol. https://www.jacc.org/doi/10.1016/j.jacc.2021.12.012

# 2022 AHA/ACC/HFSA Heart Failure Guideline

| **Recommendation for SGLT2i**<br>**Referenced studies that support the recommendation are summarized in the Online Data Supplements.** | | |
|---|---|---|
| **COR** | **LOE** | **Recommendation** |
| **I** | **A** | 1. In patients with symptomatic chronic HFrEF, SGLT2i are recommended to **reduce hospitalization for HF and cardiovascular mortality, irrespective of the presence of type 2 diabetes**.1,2 |
| **Value Statement: Intermediate Value (A)** | | 2. In patients with symptomatic chronic HFrEF, **SGLT2i** therapy provides **intermediate economic value**.3,4 |

Adapted from: 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Published online ahead of print April 1, 2022, available at: Circulation. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001063 And Journal of the American College of Cardiology published online ahead of print April 1, 2022. J Am Coll Cardiol. https://www.jacc.org/doi/10.1016/j.jacc.2021.12.012

# Table 14. Drugs Commonly Used for HFrEF (Stage C HF) (con't.)

| Drug | Initial Daily Dose(s) | Target Doses(s) | Mean Doses Achieved in Clinical Trials | References |
|---|---|---|---|---|
| **$I_f$ Channel inhibitor** | | | | |
| Ivabradine | 5 mg twice daily | 7.5 mg twice daily | 12.8 total daily | (25-27) |
| **Soluble guanylate cyclase stimulator** | | | | |
| Vericiguat | 2.5 mg once daily | 10 mg once daily | 9.2 mg total daily | (28) |
| Digoxin | 0.125–0.25 mg daily (modified according to monogram) | Individualized variable dose to achieve serum digoxin concentration 0.5–<0.9 ng/mL | NA | (29, 30) |

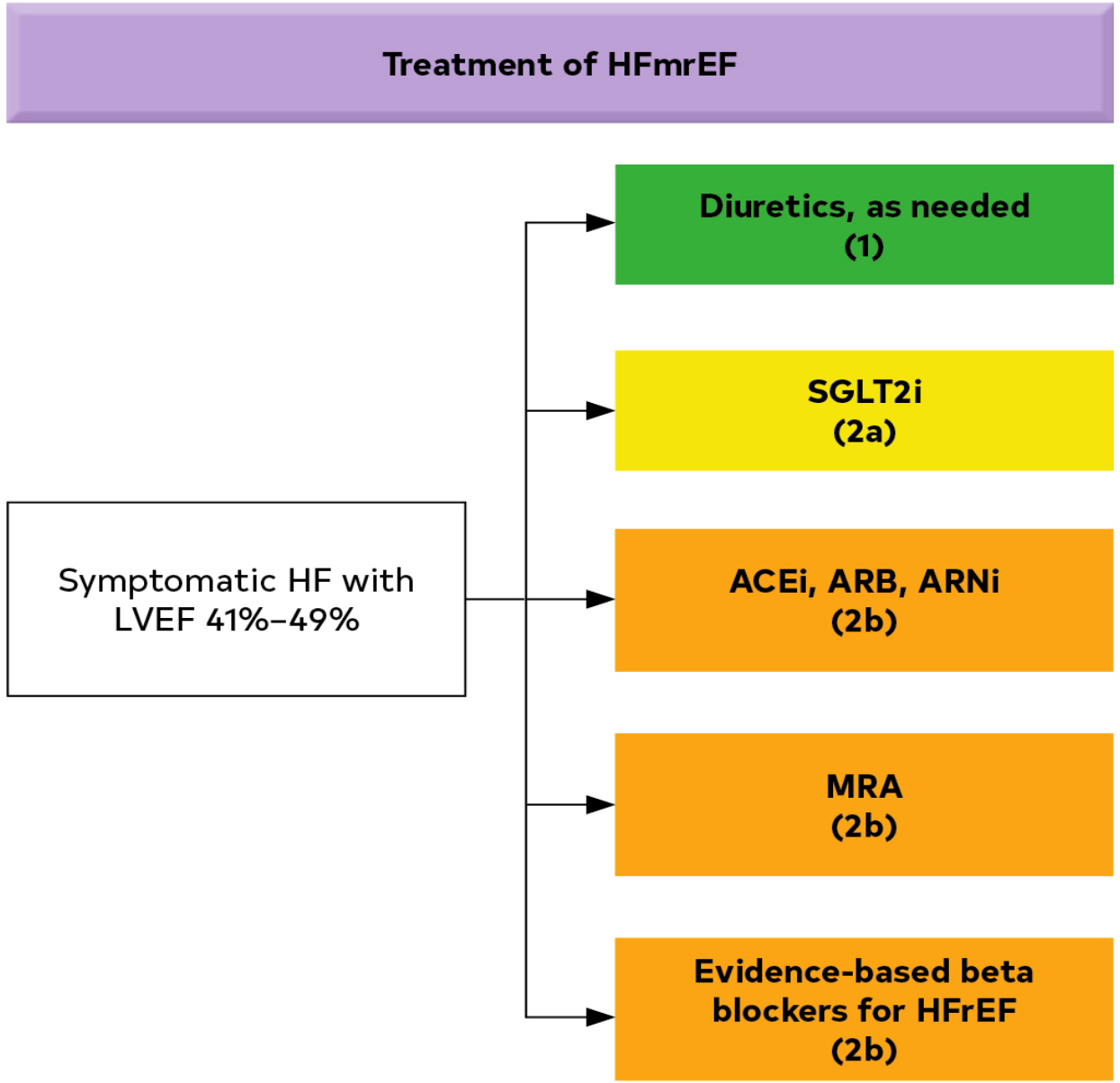
**ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CR, controlled release; CR/XL, controlled release/extended release; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; NA, not applicable; NR, not reported; and SGLT2i, sodium glucose cotransporter 2 inhibitor.**

Adapted from: 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Published online ahead of print April 1, 2022, available at: Circulation. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001063 And Journal of the American College of Cardiology published online ahead of print April 1, 2022. J Am Coll Cardiol. https://www.jacc.org/doi/10.1016/j.jacc.2021.12.012

# 2022 AHA/ACC/HFSA Heart Failure Guideline

| **Recommendation for Pharmacological Treatment for Stage C HFrEF:**<br>**Soluble Guanylyl Cyclase Stimulators**<br>**REFERENCED studies that support the recommendation are summarized in the Online Data Supplements.** | | |
|---|---|---|
| **COR** | **LOE** | **Recommendation** |
| **2b** | **B-R** | 1. In selected high-risk patients with HFrEF and **recent worsening of HF already** on GDMT, an oral soluble guanylate cyclase stimulator (**vericiguat**) may be considered to reduce HF hospitalization and cardiovascular death.1 |

# Figure 11. Recommendations for Patients With Mildly Reduced LVEF (41%–49%)




**Colors correspond to COR in Table 2.**

Medication recommendations for HFmrEF are displayed.

ACEi indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNi, angiotensin receptor- neprilysin inhibitor; HRmrEF, heart failure with mildly reduced ejection fraction; HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; and SGLT2i, sodium- glucose cotransporter 2 inhibitor.

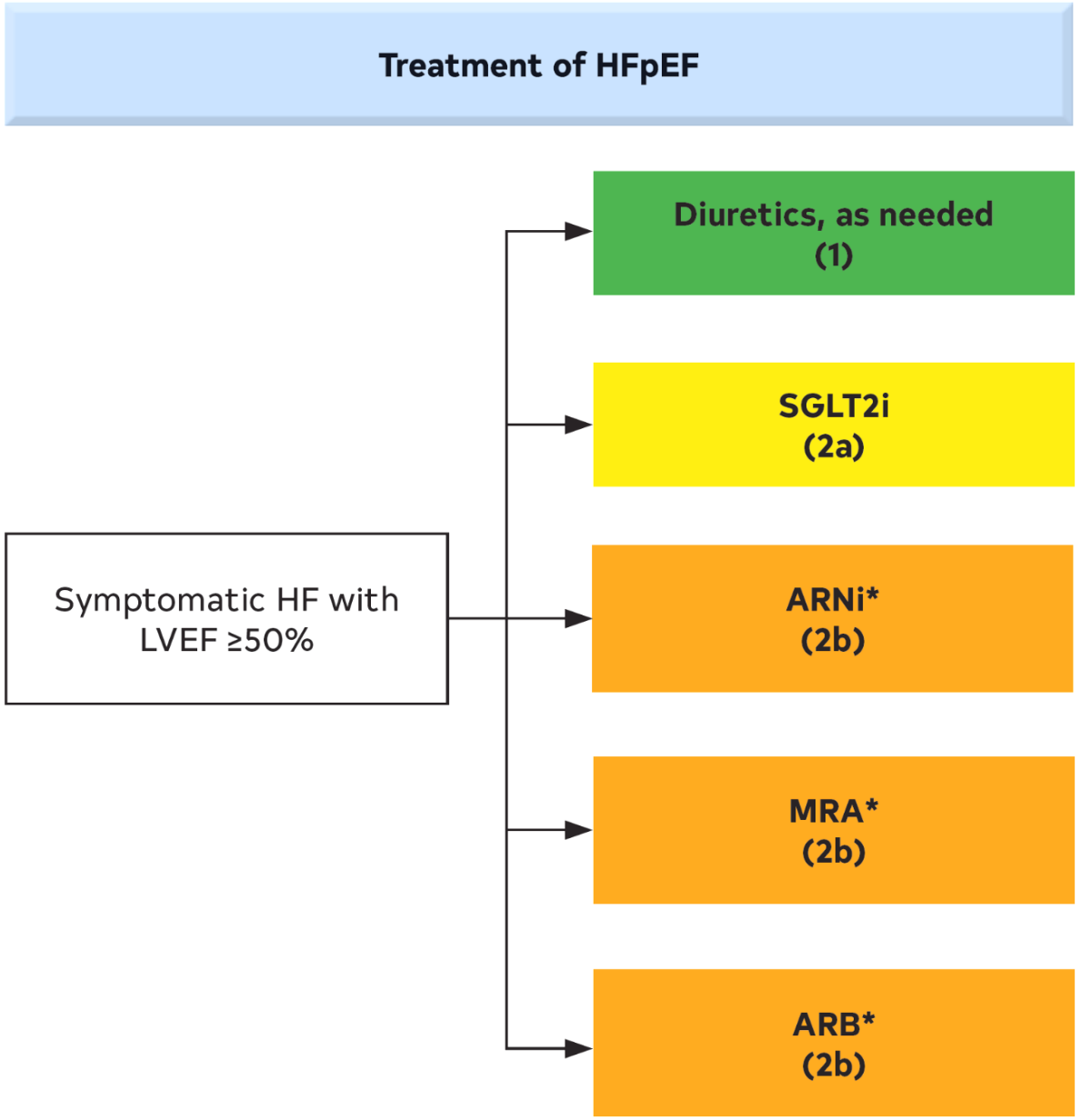
Adapted from: 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Published online ahead of print April 1, 2022, available at: Circulation. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001063 And Journal of the American College of Cardiology published online ahead of print April 1, 2022. J Am Coll Cardiol. https://www.jacc.org/doi/10.1016/j.jacc.2021.12.012

# 2022 AHA/ACC/HFSA Heart Failure Guideline: **HFmrEF**

| **Recommendations for HF With Mildly Reduced Ejection Fraction Referenced studies that support the recommendations are summarized in the Online Data Supplements.** | | |
|---|---|---|
| **COR** | **LOE** | **Recommendations** |
| **2a** | **B-R** | 1. In patients with HFmrEF, **SGLT2i** can be beneficial in decreasing HF hospitalizations and cardiovascular mortality.1 |
| **2b** | **B-NR** | 2. Among patients with current or previous symptomatic HFmrEF (LVEF, 41%–49%), use of evidence-based beta blockers for HFrEF, ARNi, ACEi, or ARB, and MRAs may be considered to reduce the risk of HF hospitalization and cardiovascular mortality, particularly among patients with LVEF on the lower end of this spectrum.2–9 |

Adapted from: 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Published online ahead of print April 1, 2022, available at: Circulation. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001063 And Journal of the American College of Cardiology published online ahead of print April 1, 2022. J Am Coll Cardiol. https://www.jacc.org/doi/10.1016/j.jacc.2021.12.012

# Figure 12. Recommendations for Patients With Preserved LVEF (≥50%)




**Colors correspond to COR in Table 2.**

Medication recommendations for HFpEF are displayed.

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

ARB indicates angiotensin receptor blocker; ARNi, angiotensin receptor-neprilysin inhibitor; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; and SGLT2i, sodium-glucose cotransporter 2 inhibitor.

Adapted from: 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Published online ahead of print April 1, 2022, available at: Circulation. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001063 And Journal of the American College of Cardiology published online ahead of print April 1, 2022. J Am Coll Cardiol. https://www.jacc.org/doi/10.1016/j.jacc.2021.12.012

# SGLT2 inhibitors - empagliflozin

| EMPEROR-Preserved | |
|---|---|
| P | symptomatic HFpEF (EF >40%) NYHA class II to IV; DM (49%); a HF hospitalization within the past year |
| I | 10mg |
| C | Placebo |
| O | Reduced the combined risk of CV death or hospitalization for HF (13.8% vs. 17.1%)<br>Slowed decline in renal function |

EMPagliflozin outcomE tRial in Patients With chrOnic heaRt Failure With Reduced Ejection Fraction (EMPEROR-Reduced)
**Empagliflozin** Outcome Trial in Patients with Chronic Heart Failure with Preserved Ejection Fraction

# SGLT-2 inhibitors and HFpEF: meta-analysis - five trials
## (DELIVER; EMPEROR-Preserved; DAPA-HF; EMPEROR-Reduced; SOLOIST-WHF)

| Majority of patients… | Results from EMPEROR-Preserved and DELIVER | Overall |
|---|---|---|
| • **NYHA class II** symptoms<br>• Baseline median **N-terminal (NT)-pro hormone BNP** that ranged from 974 pg/mL to 1910 pg/mL<br>• **Minimum eGFR** ranged from 20 - 30 mL/min/1.73m2 | • Reduction in both:<br>• Time to cardiovascular death (HR 0.88; 95% CI 0.77-1.00)<br>• Time to first hospitalization for HF (HR 0.74; 95% CI 0.67-0.83)<br>• **Extend to patients with an LVEF >60%** | • RRR 28%: NTT 28 patients to prevent one CV death or hospitalization for HF event |

Vaduganathan M, Docherty KF, Claggett BL, et al. SGLT-2 inhibitors in patients with heart failure: a comprehensive meta-analysis of five randomised controlled trials. Lancet. 2022;400:757-767.

# SGLT-2 inhibitors and HFpEF

**Table 1** Key Trials Examining SGLT2i in HFpEF

| Trial | Trial Population | Primary Findings | Adverse Events |
|---|---|---|---|
| EMPEROR-Preserved (n = 5988) | All patients LVEF >40%<br>66% with LVEF ≥50%<br>49% with diabetes<br>Mean age 71 years<br>Mean eGFR 60 mL/min/1.73 $m^2$ | Empagliflozin 10 mg reduced the risk of cardiovascular death or HF hospitalizations, mainly driven by a 29% reduction in hospitalizations | *Most common ADEs:*<br>Hypotension<br>Acute kidney injury<br>Uncomplicated genital and urinary tract infections |
| PRESERVED-HF (n = 324) | HFpEF, LVEF ≥45% (mean EF = 60%), elevated natriuretic peptides (NTproBNP or BNP)<br>55% with diabetes<br>Median age 70 years<br>Baseline eGFR = 55 mL/min/1.73 $m^2$ | Dapagliflozin 10 mg improved symptoms and physical limitations in HF in 12 weeks as measured by KCCQ-CS | *Most common ADEs:*<br>Volume depletion<br>Acute kidney injury<br><br>No DKA, severe hypoglycemia, or amputations |
| CHIEF-HF (n = 448) | 59.6% with HFpEF (EF ≥50%)<br>27.9% with diabetes<br>>50% of patients aged ≥65 years | Canagliflozin 100 mg resulted rapid improvement of HF symptoms as evaluated using the KCCQ | 9.9% of all participants had serious ADEs (hospitalization or ED visit) |
| DELIVER (n = 6263) | LVEF >40%<br>Patients aged ≥40 years<br>NYHA class II to IV symptoms<br>45% had diabetes | Dapagliflozin 10 mg reduced composite endpoint of HF hospitalizations and cardiovascular death by 18%. | *Serious ADEs (including death):*<br>43.5% of dapagliflozin patients and 45.5% of placebo patients |

*ADEs: adverse events; BNP: brain natriuretic peptide; DKA: diabetic ketoacidosis; ED: emergency department; EF: ejection fraction; eGFR: estimated glomerular ejection fraction; HF: heart failure; HFpEF: HF with preserved EF; KCCQ-CS: Kansas City Cardiomyopathy Questionnaire–clinical summary; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; NTproBNP: N-terminal pro hormone BNP; SGLT2i: sodium glucose cotransporter 2 inhibitors. Source: References 7-12.*

Investigating SGLT2 Inhibitors in Heart Failure. *US Pharm*. 2023;48(3):45-48.
Kansas City Cardiomyopathy Questionnaire Clinical Summary (KCCQ-CS)

# 2022 AHA/ACC/HFSA Heart Failure Guideline:

# Key Points - HFimpEF

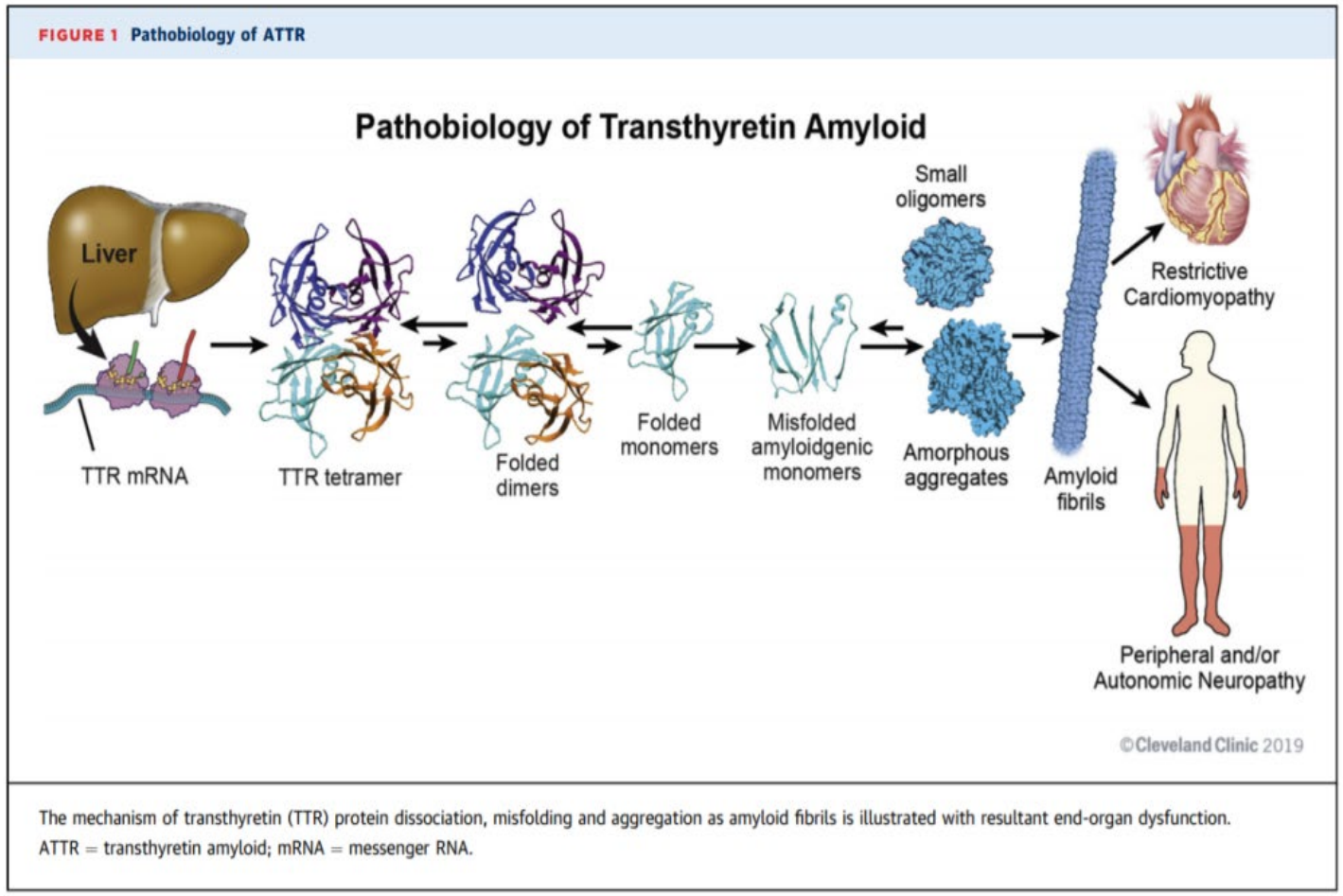
There is little data to guide management of patients with **HFimpEF**, a small, randomized trial (TRED-HF, 2019) demonstrated a high rate of relapse of dilated cardiomyopathy (44%) within 6 mo. of discontinuation of GDMT.

Therefore, it is recommended that GDMT be continued in patients with **HFimpEF**, including those who are asymptomatic, to prevent relapse of HF and LV dysfunction.

Heidenreich P, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. *J Am Coll Cardiol.* 2022 May, 79 (17) e263–e421.**https://doi.org/10.1016/j.jacc.2021.12.012**

# Transthyretin Amyloid Cardiomyopathy

Amyloid cardiomyopathy [AL-CM]) or transthyretin amyloidosis (ATTR-CM)



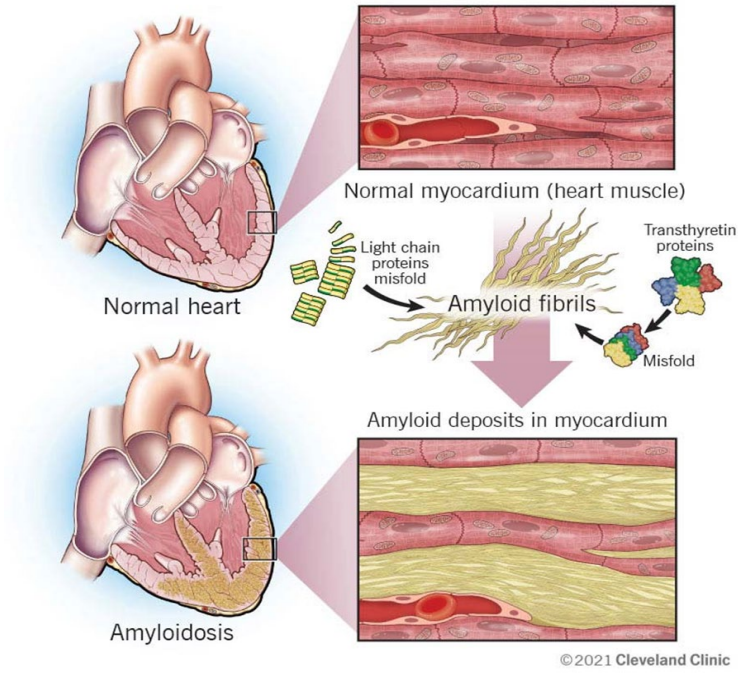
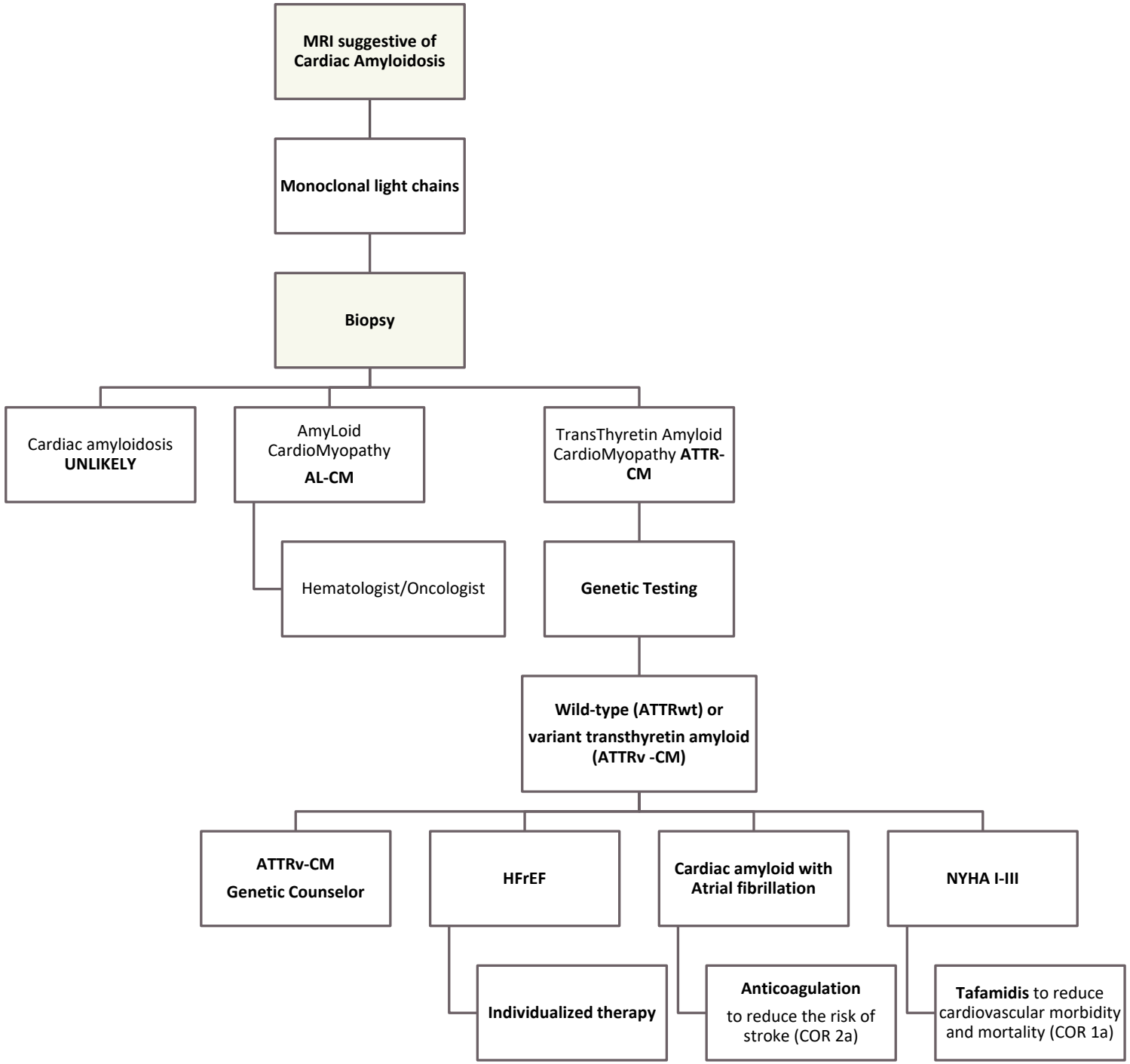




Image available at: https://my.clevelandclinic.org/health/diseases/22598-cardiac-amyloidosis Retrieved 07 24 2023.
Image available at: https://phoenixcardiology.wordpress.com/tag/transthyretin-amyloid-cardiomyopathy/ Retrieved 07 24 2023.

# 2022 AHA/ACC/HFSA Heart Failure Guideline:

# Key Points – Cardiac Amyloidosis

TransThyretin Amyloid CardioMyopathy




**Adapted from**: Heidenreich P, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. *J Am Coll Cardiol.* 2022 May, 79 (17) e263–e421.**https://doi.org/10.1016/j.jacc.2021.12.012**

# 2022 AHA/ACC/HFSA Heart Failure Guideline: HFpEF

Cardiac Amyloidosis

QALY = Quality Adjusted Life Year

| Recommendations for Treatment of Cardiac Amyloidosis Referenced studies that support the recommendations are summarized in the Online Data Supplements. | | |
|---|---|---|
| **COR** | **LOE** | **Recommendations** |
| **I** | **B-R** | 1. In select patients with wild-type or variant transthyretin cardiac amyloidosis and NYHA class I to III HF symptoms, **transthyretin tetramer stabilizer therapy ( )** is indicated to reduce cardiovascular morbidity and mortality.1 |
| **Value Statement: Low Value (B-NR)** | | 2. At 2020 list prices, tafamidis provides **low economic value (>$180000 per QALY gained)** in patients with HF with wild-type or variant transthyretin cardiac amyloidosis.2 |
| **2a** | **C-LD** | 3. In patients with cardiac **amyloidosis and AF, anticoagulation** is reasonable to reduce the risk of stroke **regardless of the CHA2DS2-VASc** (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, stroke or transient ischemic attack [TIA], vascular disease, age 65 to 74 years, sex category) score.3,4 |

Adapted from: 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Published online ahead of print April 1, 2022, available at: Circulation. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001063 And Journal of the American College of Cardiology published online ahead of print April 1, 2022. J Am Coll Cardiol. https://www.jacc.org/doi/10.1016/j.jacc.2021.12.012

# Tafamidis

## Approved in the US in 2019

## Indication

- confirmation of the presence of **amyloid deposits -** biopsy from the heart or other tissues (e.g., fat aspirate, gastrointestinal mucosa sites, salivary glands, or bone marrow)

## Dose

- 61 mg single capsule
- 20 mg four capsules (80 mg)

## MOA

- **stabilizes** the transthyretin (TTR) **tetramer** by binding to the thyroxine-binding sites
- **slows** its disassociation into **monomers**
- **halts** the amyloid **deposition process**

Kittleson MM, Maurer MS, Ambardekar AV, et al. Cardiac Amyloidosis: Evolving Diagnosis and Management: A Scientific Statement From the American Heart Association. Circulation 2020;Jun 1:[Epub ahead of print].

Mauer MS, et al. Tafamidis treatment for patients with transthyretin amyloid cardiomyopathy. New England Journal of Medicine. 2018;379:1007.

# Tafamidis

**The Transthyretin Amyloidosis Cardiomyopathy Clinical Trial (ATTR-ACT) – 2018**

- **Reduced all-cause mortality vs. placebo** (29.5% vs 42.9%; HR 0.70 [95% CI 0.51-0.96])
- **Reduced the rate of hospitalizations** due to cardiovascular complications (RRR 0.68 vs. 0.70 per year [95%CI 0.56-0.81])
- Lower rate of decline in distance for the 6-minute walk test (P<0.001)
- Lower rate of decline in KCCQ-OS score (P<0.001).
- The incidence and types of adverse events were similar in the two groups.
- **No difference in the primary outcome between hereditary and wild type ATTR patients was observed**

Kittleson MM, Maurer MS, Ambardekar AV, et al. Cardiac Amyloidosis: Evolving Diagnosis and Management: A Scientific Statement From the American Heart Association. Circulation 2020;Jun 1:[Epub ahead of print].
Mauer MS, et al. Tafamidis treatment for patients with transthyretin amyloid cardiomyopathy. New England Journal of Medicine. 2018;379:1007

*Kansas City Cardiomyopathy Questionnaire Overall Summary Score = KCCQ-OS score*

# Question 3

For patients with heart failure with reduced ejection fraction (**HFrEF**) the use of the following medications is considered as **high value** therapies, **except**:

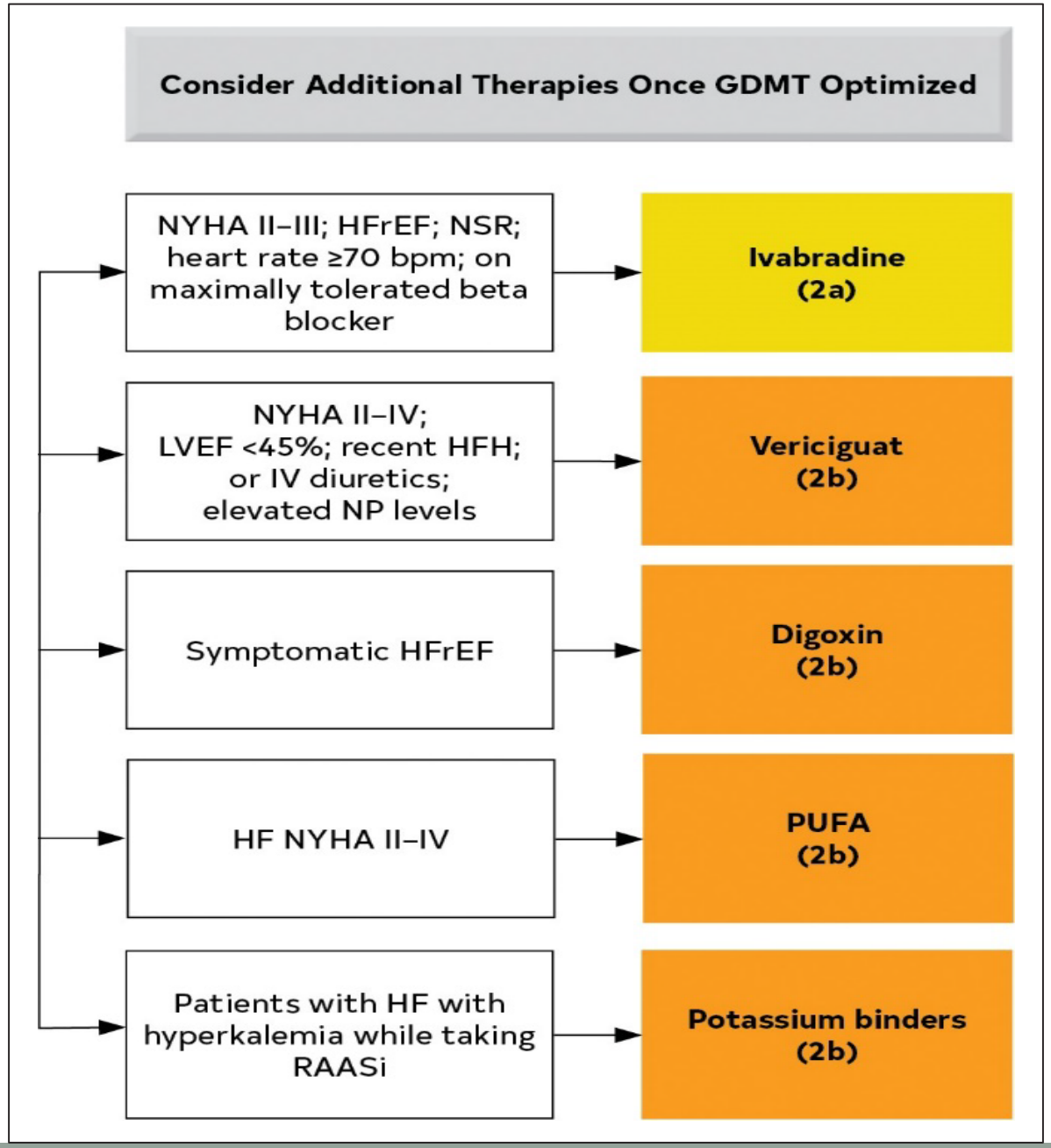
a. Lisinopril

b. Spironolactone

c. Metoprolol succinate

d. Isosorbide dinitrate/hydralazine

e. Tafadamis




# 2022 AHA/ACC/HFSA Heart Failure Guideline

**Figure 7. Additional Medical Therapies for Patients With HFrEF.** Colors correspond to COR in Table 2. Recommendations for additional medical therapies that may be considered for patients with HF are shown. GDMT indicates guideline-directed medical therapy; HF, heart failure; HFH, heart failure hospitalization; HFrEF, heart failure with reduced ejection fraction; IV, intravenous; LVEF, left ventricular ejection fraction; LVESD, left ventricular end systolic dimension; MV, mitral valve; MR, mitral regurgitation; NP, natriuretic peptide; NSR, normal sinus rhythm; NYHA, New York Heart Association; and RAASi, renin-angiotensin-aldosterone system inhibitors.

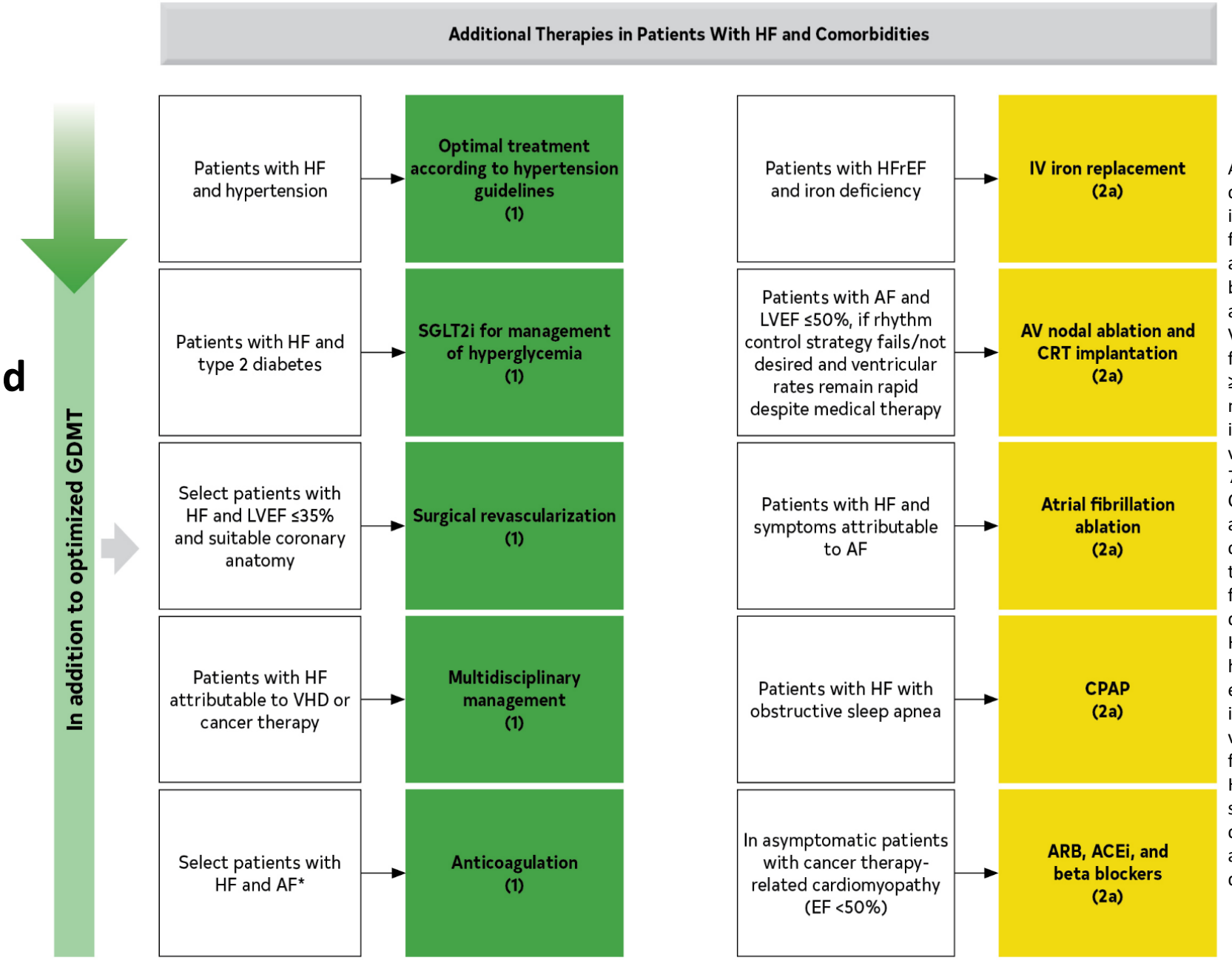
n-3 polyunsaturated fatty acids (PUFAs)

Adapted from: 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Published online ahead of print April 1, 2022, available at: Circulation. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001063 And Journal of the American College of Cardiology published online ahead of print April 1, 2022. J Am Coll Cardiol. https://www.jacc.org/doi/10.1016/j.jacc.2021.12.012

# Figure 14. Recommendations for Treatment of Patients With HF and Selected Comorbidities

**Colors correspond to COR in Table 2.**

Recommendations for treatment of patients with HF and select comorbidities are displayed.
*Patients with chronic HF with permanent-persistent-paroxysmal AF and a CHA2DS2-VASc score of ≥2 (for men) and ≥3 (for women).




ACEi indicates angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin receptor blocker; AV, atrioventricular; CHA2DS2-VASc, congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, stroke or transient ischemic attack [TIA], vascular disease, age 65 to 74 years, sex category; CPAP, continuous positive airway pressure; CRT, cardiac resynchronization therapy; EF, ejection fraction; GDMT, guideline-directed medical therapy; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; IV, intravenous; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; SGLT2i, sodium-glucose cotransporter 2 inhibitor; and VHD, valvular heart disease.

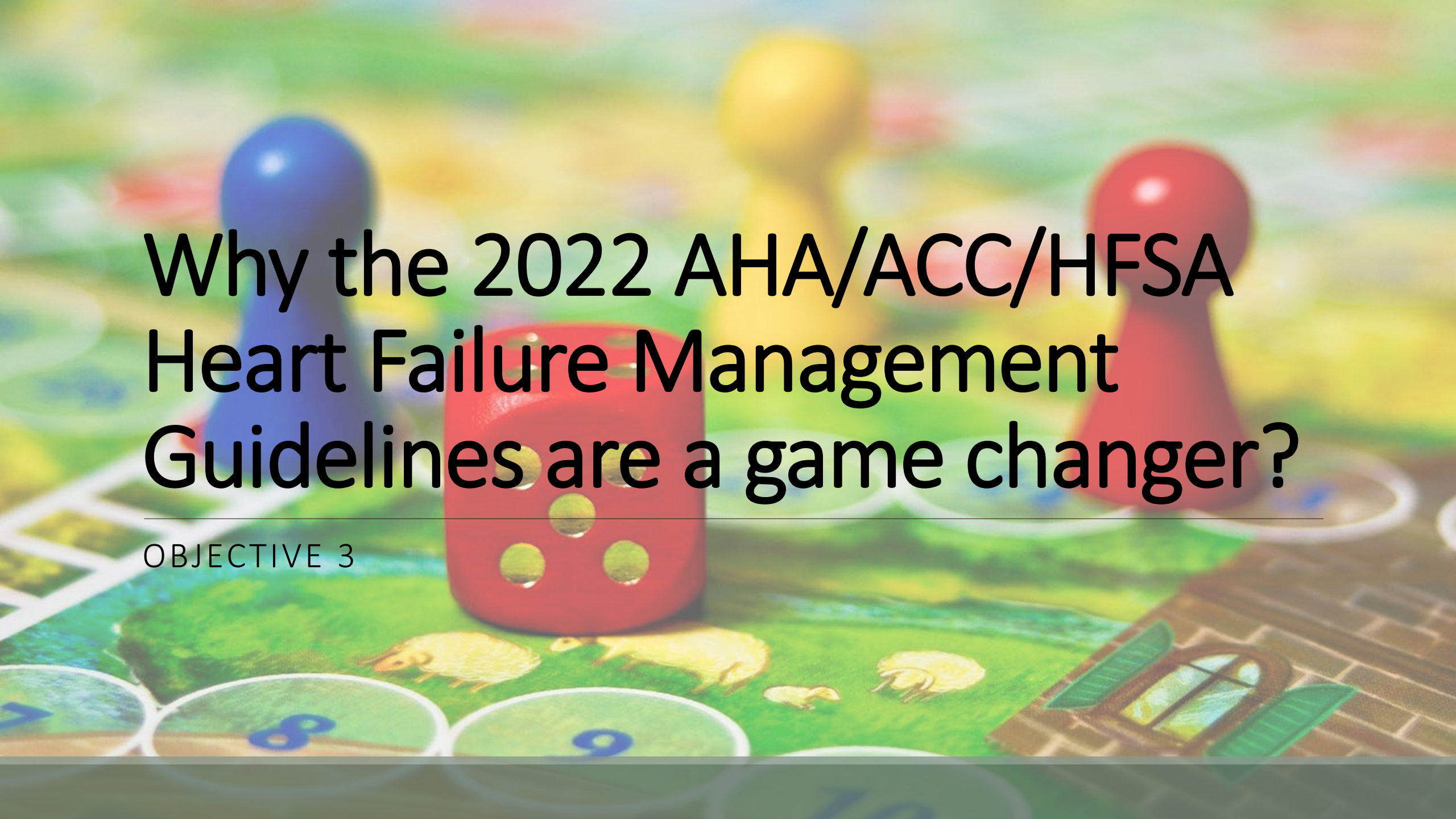


Adapted from: 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Published online ahead of print April 1, 2022, available at: Circulation. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001063 And Journal of the American College of Cardiology published online ahead of print April 1, 2022. J Am Coll Cardiol. https://www.jacc.org/doi/10.1016/j.jacc.2021.12.012

# Question 4

Current heart failure treatment **Class 1 recommendations** for patients with preserved ejection fraction (HFpEF) includes the use of **SGLT2i** medications.

a. True
b. False



# Why the 2022 AHA/ACC/HFSA Heart Failure Management Guidelines are a game changer?

OBJECTIVE 3

# 2022 AHA/ACC/HFSA Heart Failure Guideline: **Key Points**

GDMT has expanded to include four classes

1. Sodium-glucose cotransporter-2 inhibitors (SGLT2i)
2. Renin-angiotensin system inhibition (RASi) with angiotensin receptor- neprilysin inhibitors (ARNi), angiotensin-converting enzyme inhibitors (ACEi), or angiotensin-II receptor blockers (ARBs) alone
3. Beta blockers (BBs)
4. Mineralocorticoid receptor antagonists (MRAs)

Heidenreich P, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. *J Am Coll Cardiol.* 2022 May, 79 (17) e263–e421.**https://doi.org/10.1016/j.jacc.2021.12.012**

# 2022 AHA/ACC/HFSA Heart Failure Guideline: Key Points

New recommendations were made for the use of **SGLT2i** in HF

1. Chronic HFrEF with symptomatic - to reduce hospitalization and cardiovascular mortality, regardless of the presence of type 2 diabetes (COR 1a).

2. HFmrEF and HFpEF - can be beneficial (COR 2a).

Heidenreich P, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. *J Am Coll Cardiol.* 2022 May, 79 (17) e263–e421.**https://doi.org/10.1016/j.jacc.2021.12.012**

# 2022 AHA/ACC/HFSA Heart Failure Guideline: **Key Points**

**ARNi is now recommended as first-line** RASi to reduce morbidity and mortality in HFrEF (COR 1a).

ACEi is recommended when ARNi is not feasible, and ARB in those who are ACEi intolerant and when ARNi is not feasible.

In symptomatic patients with HFrEF who tolerate ACEi or ARB, replacement with ARNi is recommended for further reduction in morbidity and mortality.

Heidenreich P, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. *J Am Coll Cardiol.* 2022 May, 79 (17) e263–e421.**https://doi.org/10.1016/j.jacc.2021.12.012**


# Guideline-Directed Medical Therapy (GDMT) for HF Patients

Image: attribution unknown

# Why to use the GDMT and reach Target Doses?

- In patients with HF and asymptomatic recovered dilated cardiomyopathy whose LVEF improved from <40% to ≥50%, 44% relapsed upon withdrawal of their cardiac medications*

Change the Management of Patients With Heart Failure (CHAMP-HF) target doses at baseline**

- MRAs - 25.4%
- BBs - 20.3%
- ACEi/ARBs - 11.1%
- ARNi - 1.7%

*Halliday BP, Wassall R, Lota AS, 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;393(10166):61-73.

**Greene SJ, Fonarow GC, DeVore AD, et al. Titration of medical therapy for heart failure with reduced ejection fraction. *J Am Coll Cardiol*. 2019;73(19):2365-2383.

# Risks and benefits of new and old medications to meet heart failure treatment goals

OBJECTIVE 5

# 2022 AHA/ACC/HFSA Heart Failure Guideline: **Key Points**

**High value therapies** (<$60,000/quality-adjusted life year gained) include **ARNi, ACEi, ARB, beta blocker, MRA, hydralazine and isosorbide dinitrate in African Americans**, implantable cardioverter-defibrillator (**ICD**), and cardiac resynchronization therapy (**CRT**)

**SGLT2i** and cardiac transplantation are of **intermediate value**

**Tafamidis** for amyloid was identified as **low value** (>$180,000/quality-adjusted life year gained)

Mechanical circulatory support and pulmonary pressure monitoring are of **uncertain value**

Heidenreich P, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. *J Am Coll Cardiol.* 2022 May, 79 (17) e263–e421.**https://doi.org/10.1016/j.jacc.2021.12.012**

# **Referral** to an advanced HF: *I NEED HELP*

| | |
|---|---|
| I | Intravenous inotropes |
| | |
| N | New York Heart Association (NYHA) class IIIB to IV or persistently elevated natriuretic peptides |
| E | End-organ dysfunction |
| E | EF <35% |
| D | Defibrillator shocks |
| | |
| H | Hospitalizations >1 |
| E | Edema despite escalating diuretics |
| L | Low systolic BP <90, high heart rate |
| P | Prognostic medication; progressive intolerance or down-titration of GDMT |

Baumwol J. "I Need Help"-A mnemonic to aid timely referral in advanced heart failure. J Heart Lung Transplant. 2017 May;36(5):593-594. doi: 10.1016/j.healun.2017.02.010. Epub 2017 Feb 10. PMID: 28258792.

# 2022 AHA/ACC/HFSA Heart Failure Guideline: Key Points

Timely **referral** for HF specialty care to

- Review HF management
- Assess suitability for advanced HF therapies

Management of **comorbid conditions** in patients with HF may be beneficial.

The new guideline provides recommendations for **select patients:**

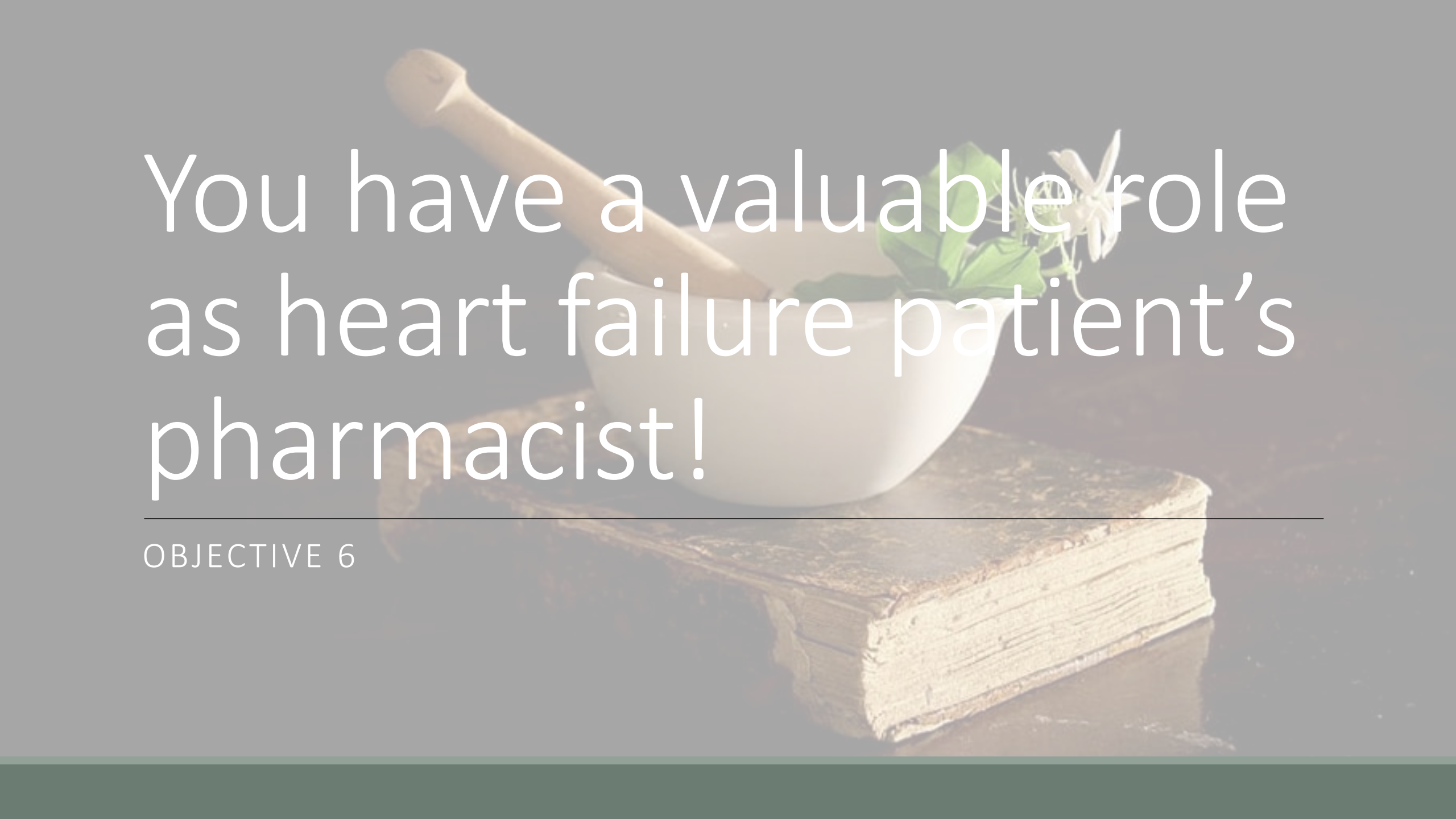
- Anemia
- Iron deficiency
- Hypertension
- Sleep disorders
- Type 2 diabetes
- Atrial fibrillation
- Coronary artery disease
- Malignancy

Heidenreich P, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. *J Am Coll Cardiol.* 2022 May, 79 (17) e263–e421.**https://doi.org/10.1016/j.jacc.2021.12.012**

# Question 5

Clinical guidelines offer evidence-based information for the management of patients with heart failure **comorbid conditions** such as:

a. Anemia and Iron deficiency
b. Hypertension, coronary artery disease and atrial fibrillation
c. Sleep disorders and type 2 diabetes
d. Malignancy
e. All answers are correct



# You have a valuable role as heart failure patient's pharmacist!

OBJECTIVE 6


# Pharmacist's role: Patient education

In-home medication reconciliation

Prevention of medication-related problems such as adverse drug events, medication errors, and drug-drug interactions

Increases in knowledge, health literacy

Improvements in medication adherence

Improvements in self management, self-maintenance, and self-confidence among HF patients


# Pharmacist's role: Patient education

| | | |
|---|---|---|
| Optimization of medication regimens | Up - titration every two weeks (symptoms, labs and vital signs) | |
| | HFrEF - CV death and hospitalization risk reduction | 62% vs conventional treatment* |

*Tsao CW, Aday AW, Almarzooq ZI, et al. Heart disease and stroke statistics—2022 update: a report from the American Heart Association. Circulation. 2022;145(8):e153-e639.

Milfred-Laforest SK, Chow SL, Didomenico RJ, et al. **Clinical pharmacy services** in heart failure: an opinion paper from the Heart Failure Society of America and American College of Clinical Pharmacy Cardiology Practice and Research Network. J Card Fail. 2013;19(5):354-369.



# Pharmacist's role: Impact on HF patients

- Reductions in all-cause mortality
- Decreases in HF and/or all-cause readmission
- Decreases in HF hospitalizations
- Increases in prescribing of GDMT to goal
- Symptom control
- Quality of life
- Reductions in time to follow-up in bridge patients
- Improvements in clinical outcomes

Lisi Donna M. Medication-Focused Overview of the 2022 AHA/ACC/HFSA Heart Failure Management Guideline. February 1, 2023. Acceded May 1, 2023.

# Pharmacist's Role

| Stage A |
| --- |
| • Educate about modifiable risk factors<br>• Help avoid and monitor cardiotoxic agents<br>• Recommend the use of SGLT2i for DMT2 patients with high risk for CVD (COR 1, LOE A)<br>• Participate of the team-based approach to assess natriuretic peptides and provide GDMT<br>• Use multivariable scores to determine further risks<br>  • Framingham Heart Failure Risk Score<br>  • Health Aging, and Body Composition (ABC) Heart Failure Score<br>  • Atherosclerosis Risk in Communities (ARIC) Risk Score |

| Stage B |
| --- |
| • Emphasize on risks prevention and treatment of structural disease<br>  • ACEi/ARB > BB<br>• Avoid the use of DHP, Glitazones<br>• Refer for *Implantable Cardioverter Defibrillator* (ICD) - selected patients<br>• Pooled Cohort Equations to Prevent HF |

# Pharmacist's Role

| Stage C |
| --- |
| • Vaccinate against respiratory infections<br>• Screen/refer for depression, social isolation, fragility, health literacy<br>• Educate regarding sodium restriction, exercise and cardiac rehabilitation |

| Stage D |
| --- |
| • Educate about fluid restriction<br>  • Fluid restriction and diuretics use<br>  • Nitroglycerin/Nitroprusside IV<br>  • IV inotropes<br>  • Bridge therapy to MCS/transplant<br>  • Palliative therapy |

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