1. GDMT for HFrEF includes 4 medication classes that include SGLT2i
2. SGLT2i have a 2a recommendation in HFmrEF
3. New recommendations for HFpEF for SGLT2i (2a), MRAs (2b) & ARNi (2b)
4. Improved LVEF refers to HFrEF where LVEF is now >40%; these patients should continue HFrEF treatment
5. Value statements for recommendations where high-quality, cost-effectiveness studies have been published
6. Amyloid heart disease has new recommendations for screening, testing and treatment
7. Evidence supporting increased filling pressures is important for HF diagnosis if LVEF >40%
8. Patients with advanced HF who wish to prolong survival should be referred to a team specializing in HF including palliative care consistent with the patient’s goals of care.

9. Stages of HF were revised to emphasize new terminologies including those “at risk” for HF (stage A) or “pre-HF” (stage B) where primary prevention is important.

10. Recommendations are provided for patients with HF and iron deficiency, anemia, hypertension, sleep disorders, type 2 diabetes, atrial fibrillation, coronary artery disease, and malignancy.
### 1) GDMT for HFrEF includes 4 medication classes

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A</td>
<td>In patients with HFrEF and NYHA class II to III symptoms, the use of ARNi is recommended to reduce morbidity and mortality</td>
</tr>
<tr>
<td>1</td>
<td>A</td>
<td>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</td>
</tr>
<tr>
<td>1</td>
<td>B - R</td>
<td>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</td>
</tr>
<tr>
<td>1</td>
<td>A</td>
<td>In patients with HFrEF, with current or previous symptoms, use of 1 of the 3 beta blockers proven to reduce mortality is recommended to reduce mortality and hospitalizations</td>
</tr>
<tr>
<td>1</td>
<td>A</td>
<td>In patients with HFrEF and NYHA class II to IV symptoms, an MRA is recommended to reduce morbidity and mortality, if eGFR &gt;30 mL/min/1.73 m² and serum potassium is &lt;5.0 mEq/L</td>
</tr>
<tr>
<td>1</td>
<td>A</td>
<td>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</td>
</tr>
</tbody>
</table>

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GDMT for HFrEF

Step 1
Establish diagnosis of HFrEF
Address congestion
Initiate GDMT

Step 2
Titrate to target dosing as tolerated, labs, health status, and LVEF

Step 3
Consider these patient scenarios

Step 4
Implement additional GDMT and device therapy, as indicated

Step 5
Reassess symptoms, labs, health status, and LVEF

Step 6
Referral for HF specialty care for additional therapy

HFrEF
LVEF ≤40%
(Stage C)

ARNI in NYHA II–III
ACEi or ARB in NYHA II–IV
(1)

Beta blocker
(1)

MRA
(1)

SGLT2i
(1)

Diuretics
as needed
(1)

NYHA III–IV, in African American patients

NYHA I–III; LVEF <55%; >1y survival

NYHA II–III; ambulatory IV; LVEF <55%; NSR and QRS ±150 ms with LBBB

LVEF ≥40%
Persistent HFrEF
(Stage C)

Hydral-nitrates
(1)

ICD
(1)

CRT-D
(1)

Symptoms improved

Consider additional therapies

Refractory HF
(Stage D)

In select patients, durable MCS
(1)

Cardiac transplant
(1)

Palliative care
(1)
(can be initiated before Stage D)

Investigational studies*

Continue GDMT with serial reassessment and optimize dosing, adherence and patient education, address goals of care

2022 ACC/AHA/HFSA Guideline for the Management of Heart Failure - DOI: 10.1016/j.cardfail.2022.02.010
2) New recommendations in HFmrEF (LVEF 41-49%)

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>2a</td>
<td>B - R</td>
<td>In patients with HFmrEF, SGLT2i can be beneficial in decreasing HF hospitalizations and cardiovascular mortality</td>
</tr>
<tr>
<td>2b</td>
<td>B - NR</td>
<td>Among patients with current or previous symptomatic HFmrEF, 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</td>
</tr>
</tbody>
</table>

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Recommendations for HFmrEF

Symptomatic HF with LVEF 41%-49%
- Diuretics, as needed (1)
- SGLT2i (2a)
- ACEi, ARB, ARNi (2b)
- MRA (2b)
- Evidence-based beta blockers for HFrEF (2b)

2022 ACC/AHA/HFSA Guideline for the Management of Heart Failure - DOI: 10.1016/j.cardfail.2022.02.010
### 3) New recommendations in HFpEF

<table>
<thead>
<tr>
<th>COR</th>
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<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>2a</td>
<td>B - R</td>
<td>In patients with HFpEF, <strong>SGLT2i</strong> can be beneficial in decreasing HF hospitalizations and cardiovascular mortality</td>
</tr>
<tr>
<td>2b</td>
<td>B - R</td>
<td>In selected patients with HFpEF, <strong>MRAs</strong> may be considered to decrease hospitalizations, particularly among patients with LVEF on the lower end of this spectrum</td>
</tr>
<tr>
<td>2b</td>
<td>B - R</td>
<td>In selected patients with HFpEF, <strong>ARNi</strong> may be considered to decrease hospitalizations, particularly among patients with LVEF on the lower end of this spectrum</td>
</tr>
</tbody>
</table>

Heidenreich PA, *et al.* *J Card Fail* 2022

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Recommendations for HFpEF

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4) Recommendations for HFimpEF

Improved LVEF is used to refer to those with previous HFrEF who now have an LVEF >40%

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>B - R</td>
<td>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</td>
</tr>
</tbody>
</table>
Classification & Trajectories of HF Based on LVEF

Initial Classification

- **HFrEF**
  - LVEF ≤40%

- **HFmrEF**
  - LVEF 41%–49%

- **HFrEF**
  - LVEF ≤40%

  - **HFimpEF**
    - LVEF >40%

  - **HFmrEF**
    - LVEF 41%–49%

    - LVEF ≥50%

Serial Assessment and Reclassification

- **HFrEF**
  - LVEF ≤40%

- **HFmrEF**
  - LVEF 41%–49%

  - LVEF ≥50%

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## 5) Value Statements for Recommendations (1/2)

<table>
<thead>
<tr>
<th>Level</th>
<th>Statements</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>In patients with previous or current symptoms of chronic HFrEF, in whom ARNi is not feasible, treatment with an <strong>ACEi or ARB</strong> provides high economic value</td>
</tr>
<tr>
<td>High</td>
<td>In patients with chronic symptomatic HFrEF, treatment with an <strong>ARNi</strong> instead of an ACEi provides high economic value</td>
</tr>
<tr>
<td>High</td>
<td>In patients with HFrEF, with current or previous symptoms, <strong>beta-blocker</strong> therapy provides high economic value</td>
</tr>
<tr>
<td>High</td>
<td>In patients with HFrEF and NYHA class II to IV symptoms, <strong>MRA</strong> therapy provides high economic value</td>
</tr>
<tr>
<td>High</td>
<td>For patients self-identified as African American with NYHA class III to IV HFrEF who are receiving optimal medical therapy with ACEi or ARB, beta blockers, and MRA, the combination of <strong>hydralazine and isosorbide dinitrate</strong> provides high economic value</td>
</tr>
<tr>
<td>High</td>
<td><strong>A transvenous ICD</strong> provides high economic value in the primary prevention of sudden cardiac death particularly when the patient’s risk of death caused by ventricular arrhythmia is deemed high and the risk of nonarrhythmic death is deemed low based on the patient’s burden of comorbidities and functional status</td>
</tr>
<tr>
<td>High</td>
<td>For patients who have LVEF ≤35%, sinus rhythm, LBBB with a QRS duration of ≥150 ms, and NYHA class II, III, or ambulatory IV symptoms on GDMT, <strong>CRT implantation</strong> provides high economic value</td>
</tr>
</tbody>
</table>

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### Value Statements for Recommendations (2/2)

<table>
<thead>
<tr>
<th>Level</th>
<th>Statements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intermediate</td>
<td>In patients with symptomatic chronic HFrEF, <strong>SGLT2i</strong> therapy provides intermediate economic value</td>
</tr>
<tr>
<td>Intermediate</td>
<td>In patients with stage D (advanced) HF despite GDMT, <strong>cardiac transplantation</strong> provides intermediate economic value</td>
</tr>
<tr>
<td>Low</td>
<td>At 2020 list prices, <strong>tafamidis</strong> provides low economic value (&gt;$180,000 per QALY gained) in patients with HF with wild-type or variant transthyretin cardiac amyloidosis</td>
</tr>
<tr>
<td>Uncertain</td>
<td>In patients with advanced HFrEF who have NYHA class IV symptoms despite GDMT, <strong>durable mechanical circulatory support devices</strong> provide low to intermediate economic value based on current costs and outcomes</td>
</tr>
<tr>
<td>Uncertain</td>
<td>In patients with NYHA class III HF with a HF hospitalization within the previous year, wireless monitoring of the pulmonary artery pressure by an <strong>implanted hemodynamic monitor</strong> provides uncertain value</td>
</tr>
</tbody>
</table>
### 6) New Recommendations for Amyloid Heart Disease

#### Diagnosis of Cardiac Amyloidosis

<table>
<thead>
<tr>
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<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>B - NR</td>
<td>Patients for whom there is a clinical suspicion for cardiac amyloidosis should have screening for serum and urine monoclonal light chains with <strong>serum and urine immunofixation electrophoresis</strong> and <strong>serum free light chains</strong></td>
</tr>
<tr>
<td>1</td>
<td>B - NR</td>
<td>In patients with high clinical suspicion for cardiac amyloidosis, without evidence of serum or urine monoclonal light chains, <strong>bone scintigraphy</strong> should be performed to confirm the presence of transthyretin cardiac amyloidosis</td>
</tr>
<tr>
<td>1</td>
<td>B - NR</td>
<td>In patients for whom a diagnosis of transthyretin cardiac amyloidosis is made, <strong>genetic testing with TTR gene sequencing</strong> is recommended to differentiate hereditary variant from wild-type transthyretin cardiac amyloidosis</td>
</tr>
</tbody>
</table>

Heidenreich PA, et al. J Card Fail 2022
Diagnostic and Treatment of Transthyretin Cardiac Amyloidosis Algorithm

Heidenreich PA, et al. J Card Fail 2022

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JCF Journal of Cardiac Failure
## New Recommendations for Amyloid Heart Disease

### Treatment of Cardiac Amyloidosis

<table>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>B - R</td>
<td>In select patients with wild-type or variant transthyretin cardiac amyloidosis and NYHA class I to III HF symptoms, <strong>transthyretin tetramer stabilizer therapy (tafamidis)</strong> is indicated to reduce cardiovascular morbidity and mortality</td>
</tr>
<tr>
<td>2a</td>
<td>C - LD</td>
<td>In patients with cardiac amyloidosis and AF, <strong>anticoagulation</strong> is reasonable to reduce the risk of stroke regardless of the CHA²DS²-VASc (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, stroke or TIA, vascular disease, age 65 to 74 years, sex category) score</td>
</tr>
</tbody>
</table>

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### Classification of HF by LVEF

<table>
<thead>
<tr>
<th>Type of HF According to LVEF</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HFrEF</strong></td>
<td>LVEF ≤40%</td>
</tr>
<tr>
<td><strong>HFimpEF</strong></td>
<td>Previous LVEF ≤40% and a follow-up measurement of LVEF &gt;40%</td>
</tr>
</tbody>
</table>
| **HFmrEF** | • LVEF 41%–49%  
• Evidence of spontaneous or provokable increased LV filling pressures (e.g., elevated natriuretic peptide, noninvasive and invasive hemodynamic measurement) |
| **HFpEF** | • LVEF ≥50%  
• Evidence of spontaneous or provokable increased LV filling pressures |
8) Patients with advanced HF who wish to prolong survival should be referred to a team specializing in HF

<table>
<thead>
<tr>
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<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>C – LD</td>
<td>In patients with advanced HF, when consistent with the patient’s goals of care, timely <strong>referral for HF specialty</strong> care is recommended to review HF management and assess suitability for advanced HF therapies (e.g., left ventricular assist devices, cardiac transplantation, palliative care, and palliative inotropes)</td>
</tr>
</tbody>
</table>

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9) Revised HF Stages and Primary Prevention

**STAGE A: At-Risk for Heart Failure**
- Patients at risk for HF but without current or previous symptoms/signs of HF and without structural/functional heart disease or abnormal biomarkers
- Patients with hypertension, CVD, diabetes, obesity, exposure to cardiotoxic agents, genetic variant for cardiomyopathy, or family history of cardiomyopathy

**STAGE B: Pre-Heart Failure**
- Patients without current or previous symptoms/signs of HF but evidence of 1 of the following:
  - Structural heart disease
  - Evidence of increased filling pressures
  - Risk factors and:
    - increased natriuretic peptide levels or
    - persistently elevated cardiac troponin in the absence of competing diagnoses

**STAGE C: Symptomatic Heart Failure**
- Patients with current or previous symptoms/signs of HF

**STAGE D: Advanced Heart Failure**
- Marked HF symptoms that interfere with daily life and with recurrent hospitalizations despite attempts to optimize GDMT

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Recommendations for Patients at Risk for HF (Stage A: Primary Prevention)

<table>
<thead>
<tr>
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<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A</td>
<td>In patients with hypertension, <strong>blood pressure</strong> should be controlled in accordance with GDMT for hypertension to prevent symptomatic HF</td>
</tr>
<tr>
<td>1</td>
<td>A</td>
<td>In patients with type 2 diabetes and either established cardiovascular disease or at high cardiovascular risk, <strong>SGLT2i</strong> should be used to prevent hospitalizations for HF</td>
</tr>
<tr>
<td>1</td>
<td>B - NR</td>
<td>In the general population, <strong>healthy lifestyle habits</strong> such as regular physical activity, maintaining normal weight, healthy dietary patterns, and avoiding smoking are helpful to reduce future risk of HF</td>
</tr>
<tr>
<td>2a</td>
<td>B - R</td>
<td>For patients at risk of developing HF, <strong>natriuretic peptide</strong> biomarker–based screening followed by <strong>team-based care</strong>, including a cardiovascular specialist optimizing GDMT, can be useful to prevent the development of LV dysfunction (systolic or diastolic) or new-onset HF</td>
</tr>
<tr>
<td>2a</td>
<td>B - NR</td>
<td>In the general population, <strong>validated multivariable risk scores</strong> can be useful to estimate subsequent risk of incident HF</td>
</tr>
</tbody>
</table>
### Recommendations for Management of Stage B

<table>
<thead>
<tr>
<th>COR</th>
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<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A</td>
<td>In patients with LVEF ≤40%, <strong>ACEi</strong> should be used to prevent symptomatic HF and reduce mortality</td>
</tr>
<tr>
<td>1</td>
<td>A</td>
<td>In patients with a recent or remote history of myocardial infarction or acute coronary syndrome, <strong>statins</strong> should be used to prevent symptomatic HF and adverse cardiovascular events</td>
</tr>
<tr>
<td>1</td>
<td>B - R</td>
<td>In patients with a recent myocardial infarction and LVEF ≤40% who are intolerant to ACEi, <strong>ARB</strong> should be used to prevent symptomatic HF and reduce mortality</td>
</tr>
<tr>
<td>1</td>
<td>B - R</td>
<td>In patients with a recent or remote history of myocardial infarction or acute coronary syndrome and LVEF ≤40%, <strong>evidence-based beta blockers</strong> should be used to reduce mortality</td>
</tr>
<tr>
<td>1</td>
<td>B - R</td>
<td>In patients who are at least 40 days post–myocardial infarction with LVEF ≤30% and NYHA class I symptoms while receiving GDMT and have reasonable expectation of meaningful survival for &gt;1 year, an <strong>ICD</strong> is recommended for primary prevention of sudden cardiac death to reduce total mortality</td>
</tr>
<tr>
<td>1</td>
<td>C - LD</td>
<td>In patients with LVEF ≤40%, <strong>beta blockers</strong> should be used to prevent symptomatic HF</td>
</tr>
</tbody>
</table>

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10) Recommendations for Treatment of Patients With Selected HF and Comorbidities

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Additional Therapies in Patients With HF and Comorbidities

- Patients with HF and hypertension
- Patients with HF and type 2 diabetes
- Select patients with HF and LVEF ≤55% and suitable coronary anatomy
- Patients with HF attributable to VHD or cancer therapy
- Select patients with HF and AF

Optimal treatment according to hypertension guidelines

SGLT2i for management of hyperglycemia

Surgical revascularization

Multidisciplinary management

Anticoagulation

Patients with HF and iron deficiency

Patients with AF and LVEF ≤50%, if rhythm control strategy fails/not desired and ventricular rates remain rapid despite medical therapy

Patients with HF and symptoms attributable to AF

Patients with HF with obstructive sleep apnea

In asymptomatic patients with cancer therapy-related cardiomyopathy (EF <50%)

IV iron replacement

AV nodal ablation and CRT implantation

Atrial fibrillation ablation

CRAP

ARB, ACEi, and beta blockers

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