American Heart Association

Get With The Guidelines HF®
A review- 2017 Focused Update of the ACC/AHA/HFSA Heart Failure Guidelines

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Professor, Medical Social Science
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No relevant disclosures
Our Presenter

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• Editor duties: JAMA Cardiology, Deputy Editor; Journal of the American College of Cardiology- senior associate editor (HF); American Journal of Cardiology, American Heart Journal, Circulation; Circulation-Heart Failure- editorial boards

• Guideline writing committees: Chair, ACC/AHA, chronic HF; member, atrial fibrillation; hypertrophic cardiomyopathy; syncope guideline committees. Chair, Performance Measures, Sudden Cardiac Death; Chair, ACC HF Consensus Pathways

• Federal appointments: FDA: Immediate Past Chair, Cardiovascular Device Panel; ad hoc consultant; NIH – Scientific Management and Review Board; AHRQ- adhoc consultant; NHLBI- consultant; PCORI- former methodology committee member; IOM- writing group member

• Volunteer Appointments: American Heart Association- President, American Heart Association, 2009-2010; American College of Cardiology, Founder- CREDO
A review - 2017 Focused Update of the ACC/AHA/HFSA Heart Failure Guidelines

• Incorporating new clinical practice guidelines
  – What’s new?
  – How will practice be changed?
• PREVENTION; a new reality in heart failure
• Identifying a new phenotype- heart failure with improved ejection fraction
  – What is this?
  – What’s the natural history?
  – Can it be manipulated?
• Heart Failure with preserved Ejection Fraction
• Important Co-Morbidities in Heart Failure
Comparison of short-term vs lifetime cumulative risks of CHF for men and women at selected index ages

ONE IN FIVE INDIVIDUALS WILL DEVELOP HF

NHANES indicates National Health and Nutrition Examination Survey.
Source: National Center for Health Statistics and National Heart, Lung, and Blood Institute.
• HF prevalence: 5.7 million (2009 to 2012) to 6.5 million (2011 to 2014)
• Five-year survival of HF s/p MI:
  – improved in 2001 to 2010 versus 1990 to 2000, from 54% to 61%.
• Greater adherence to the AHA’s Life Simple 7 guidelines associated with a lower lifetime risk of HF
• Of incident hospitalized HF events, 53% had HFrEF; 47% had HFpEF
• Black males had the highest proportion of hospitalized HFrEF fraction (70%)
• white females had the highest proportion of hospitalized HFpEF (59%)
**Stages, Phenotypes and Treatment of HF**

**At Risk for Heart Failure**

- **STAGE A**
  - At high risk for HF but without structural heart disease or symptoms of HF
  - e.g., Patients with:
    - HTN
    - Atherosclerotic disease
    - DM
    - Obesity
    - Metabolic syndrome or Patients
    - Using cardiotoxins
    - With family history of cardiomyopathy

  **THERAPY**
  - Goals
    - Heart healthy lifestyle
    - Prevent vascular, coronary disease
    - Prevent LV structural abnormalities
  - Drugs
    - ACEI or ARB in appropriate patients for vascular disease or DM
    - Statins as appropriate

- **STAGE B**
  - Structural heart disease but without signs or symptoms of HF
  - e.g., Patients with:
    - Previous MI
    - LV remodeling including LVH and low EF
    - Asymptomatic valvular disease

  **THERAPY**
  - Goals
    - Prevent HF symptoms
    - Prevent further cardiac remodeling
  - Drugs
    - ACEI or ARB as appropriate
    - Beta blockers as appropriate
  - In selected patients
    - ICD
    - Revascularization or valvular surgery as appropriate

  **THERAPY**
  - Development of symptoms of HF
  - e.g., Patients with:
    - Structural heart disease and
    - HF signs and symptoms

- **STAGE C**
  - Structural heart disease with prior or current symptoms of HF
  - e.g., Patients with:
    - Known structural heart disease and
    - HF signs and symptoms

  **THERAPY**
  - Goals
    - Control symptoms
    - Patient education
    - Prevent hospitalization
    - Prevent mortality
  - Drugs for routine use
    - Diuretics for fluid retention
    - ACEI or ARB
    - Beta blockers
    - Aldosterone antagonists
  - Drugs for use in selected patients
    - Hydralazine/isosorbide dinitrate
    - ACEI and ARB
    - Digoxin
  - In selected patients
    - CRT
    - ICD
    - Revascularization or valvular surgery as appropriate

- **STAGE D**
  - Refractory HF
  - Refractory symptoms of HF at rest, despite GDMT
  - e.g., Patients with:
    - Marked HF symptoms at rest
    - Recurrent hospitalizations despite GDMT

  **THERAPY**
  - Goals
    - Control symptoms
    - Improve HRQOL
    - Reduce hospital readmissions
    - Establish patient’s end-of-life goals
  - Options
    - Advanced care measures
    - Heart transplant
    - Chronic inotropes
    - Temporary or permanent MCS
    - Experimental surgery or drugs
    - Palliative care and hospice
    - ICD deactivation

**Heart Failure**

- **HFpEF**
- **HFrEF**

**HELPING CARDIOVASCULAR PROFESSIONALS**


Yancy C, et al. JACC, 2013
HFrEF Stage C
NYHA Class I – IV
Treatment:

Class I, LOE A
ACEI or ARB AND Beta Blocker

For all volume overload, NYHA class II-IV patients
Add
Class I, LOE C
Loop Diuretics

For persistently symptomatic African Americans, NYHA class III-IV
Add
Class I, LOE A
Hydral-Nitrates

For NYHA class II-IV patients. Provided estimated creatinine >30 mL/min and K+ <5.0 mEq/dL
Add
Class I, LOE A
Aldosterone Antagonist

Medical Therapy for Stage C HFrEF: Magnitude of Benefit Demonstrated in RCTs

<table>
<thead>
<tr>
<th>GDMT</th>
<th>RR Reduction in Mortality</th>
<th>NNT for Mortality Reduction (Standardized to 36 mo)</th>
<th>RR Reduction in HF Hospitalizations</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitor or ARB</td>
<td>17%</td>
<td>26</td>
<td>31%</td>
</tr>
<tr>
<td>Beta blocker</td>
<td>34%</td>
<td>9</td>
<td>41%</td>
</tr>
<tr>
<td>Aldosterone antagonist</td>
<td>30%</td>
<td>6</td>
<td>35%</td>
</tr>
<tr>
<td>Hydralazine/nitrate</td>
<td>43%</td>
<td>7</td>
<td>33%</td>
</tr>
</tbody>
</table>

A review- 2017 Focused Update of the ACC/AHA/HFSA Heart Failure Guidelines

• Incorporating new clinical practice guidelines
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• Heart Failure with preserved Ejection Fraction
• Important Co-Morbidities in Heart Failure
New ACC/AHA/HFSA Guidelines

2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America

Developed in Collaboration With the American Academy of Family Physicians, American College of Chest Physicians, and International Society for Heart and Lung Transplantation

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Citation

This slide set was adapted from the 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure (Journal of the American College of Cardiology). Published on April 28, 2017, available at: Yancy, et. al. ACC/AHA/HFSA 2017 Heart Failure Focused Update

The full-text guidelines are also available on the following Web sites:
• American College of Cardiology (www.acc.org)
• American Heart Association (professional.heart.org)
• Heart Failure Society of America (www.hfsa.org)
Special Thanks To

The Heart Failure Focused Update
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PARADIGM-HF: Cardiovascular Death or Heart Failure Hospitalization (Primary Endpoint)

Kaplan-Meier Estimate of Cumulative Rates (%)

**Enalapril (n=4212)**

**LCZ696 (n=4187)**

HR = 0.80 (0.73-0.87)

P = 0.0000004

Number needed to treat = 21

Patients at Risk

<table>
<thead>
<tr>
<th></th>
<th>LCZ696</th>
<th>Enalapril</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>3922</td>
<td>3883</td>
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<td></td>
<td>3663</td>
<td>3579</td>
</tr>
<tr>
<td></td>
<td>3018</td>
<td>2922</td>
</tr>
<tr>
<td></td>
<td>2257</td>
<td>2123</td>
</tr>
<tr>
<td></td>
<td>1544</td>
<td>1488</td>
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<tr>
<td></td>
<td>896</td>
<td>853</td>
</tr>
<tr>
<td></td>
<td>249</td>
<td>236</td>
</tr>
</tbody>
</table>
Simplified Schematic of the Renin–Angiotensin–Aldosterone System

Angiotensinoogen → Renin → Ang-I → ACE2 → Ang-(1-9) → NEP → Ang-(1-7) → ANG II → AR-1

Heart: Pathological hypertrophy, fibrosis
Vasculature: Vasoconstriction, Oxidative stress remodelling
Kidneys: Aldosterone release, Na reabsorption
CNS: Norepinephrine release

Biological Actions

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Simplified Schematic of the Natriuretic Peptide System (NPS)
Ivabradine Inhibition of hyperpolarization-activated cyclic nucleotide–gated (HCN) channels.

Mitchell A. Psotka, and John R. Teerlink Circulation. 2016;133:2066-2075
Primary composite endpoint
(CV death or hospital admission for worsening HF)

Hospitalization for HF

Cumulative frequency (%)

HR = 0.74 (0.66–0.83)

Placebo

Ivabradine

26%

<table>
<thead>
<tr>
<th>Patient population</th>
<th>Treatment</th>
<th>Recommendation and LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2013 ACC/AHA guidelines</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>For all patients with HFrEF with volume overload, NYHA class II–IV</td>
<td>• Loop diuretics</td>
<td>Class I, LOE C</td>
</tr>
<tr>
<td></td>
<td>• In addition to ACE inhibitor or ARB and β-blocker</td>
<td></td>
</tr>
<tr>
<td>For persistently symptomatic African American patients, NYHA class III–IV, to reduce morbidity and mortality</td>
<td>• Hydral-nitrates</td>
<td>Class I, LOE A</td>
</tr>
<tr>
<td></td>
<td>• In addition to ACE inhibitor, or ARB and β-blocker</td>
<td></td>
</tr>
<tr>
<td>For patients with NYHA class II–IV with eGFR &gt;30 ml/min/1.73m² and K⁺ &lt;5.0 mEq/l, to reduce morbidity and mortality</td>
<td>• Mineralocorticoid-receptor antagonists</td>
<td>Class I, LOE A</td>
</tr>
<tr>
<td></td>
<td>• In addition to ACE inhibitor or ARB in conjunction with β-blocker</td>
<td></td>
</tr>
<tr>
<td><strong>2016 ACC/AHA/HFSA guideline update</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>For patients with chronic HFrEF, to reduce morbidity and mortality</td>
<td>• ARNI in conjunction with β-blocker</td>
<td>Class I, LOE B–R</td>
</tr>
<tr>
<td>For patients with chronic symptomatic HFrEF, NYHA class II–III, who tolerate an ACE inhibitor or ARB</td>
<td>• ARNI to replace an ACE inhibitor or ARB</td>
<td>Class I, LOE B–R</td>
</tr>
<tr>
<td>For patients with stable chronic HFrEF (LVEF ≤35%), NYHA class II–III, who are in sinus rhythm with a heart rate ≥70 bpm at rest, to reduce heart failure hospitalization</td>
<td>• Ivabradine in addition to ACE inhibitor or ARB and β-blocker</td>
<td>Class IIa, LOE B–R</td>
</tr>
</tbody>
</table>
Stage C
# Pharmacological Treatment for Stage C HF With Reduced EF

## Renin-Angiotensin System Inhibition With ACE-Inhibitor or ARB or ARNI

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
<th>Comment/Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>ACE-I: A</td>
<td>The clinical strategy of inhibition of the renin-angiotensin system with ACE inhibitors (Level of Evidence: A), OR ARBs (Level of Evidence: A), OR ARNI (Level of Evidence: B-R) in conjunction with evidence-based beta blockers, and aldosterone antagonists in selected patients, is recommended for patients with chronic HFrEF to reduce morbidity and mortality.</td>
<td>NEW: New clinical trial data prompted clarification and important updates.</td>
</tr>
</tbody>
</table>
## Pharmacological Treatment for Stage C HF With Reduced EF

### Renin-Angiotensin System Inhibition With ACE-Inhibitor or ARB or ARNI

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
<th>Comment/ Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>ACE-I:A</td>
<td>The use of ACE inhibitors is beneficial for patients with prior or current symptoms of chronic HFrEF to reduce morbidity and mortality.</td>
<td>2013 recommendation repeated for clarity in this section.</td>
</tr>
<tr>
<td>I</td>
<td>ARB:A</td>
<td>The use of ARBs to reduce morbidity and mortality is recommended in patients with prior or current symptoms of chronic HFrEF who are intolerant to ACE inhibitors because of cough or angioedema.</td>
<td>2013 recommendation repeated for clarity in this section.</td>
</tr>
</tbody>
</table>
### Renin-Angiotensin System Inhibition With ACE-Inhibitor or ARB or ARNI

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
<th>Comment/Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>ARNI</td>
<td>In patients with chronic symptomatic HFrEF NYHA class II or III who tolerate an ACE inhibitor or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality.</td>
<td>NEW: New clinical trial data necessitated this recommendation.</td>
</tr>
</tbody>
</table>
### Renin-Angiotensin System Inhibition With ACE-Inhibitor or ARB or ARNI

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
<th>Comment/Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>III: Harm</td>
<td>B-R</td>
<td>ARNI should not be administered concomitantly with ACE inhibitors or within 36 hours of the last dose of an ACE inhibitor.</td>
<td><strong>NEW</strong>: Available evidence demonstrates a potential signal of harm for a concomitant use of ACE inhibitors and ARNI.</td>
</tr>
<tr>
<td>III: Harm</td>
<td>C-EO</td>
<td>ARNI should not be administered to patients with a history of angioedema.</td>
<td><strong>NEW</strong>: New clinical trial data.</td>
</tr>
</tbody>
</table>
### Ivabradine

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
<th>Comment/Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIa</td>
<td>B-R</td>
<td>Ivabradine can be beneficial to reduce HF hospitalization for patients with symptomatic (NYHA class II-III) stable chronic HFrEF (LVEF ≤35%) who are receiving GDEM*, including a beta blocker at maximum tolerated dose, and who are in sinus rhythm with a heart rate of 70 bpm or greater at rest.</td>
<td>NEW: New clinical trial data.</td>
</tr>
</tbody>
</table>

*In other parts of the document, the term “GDMT” has been used to denote guideline-directed management and therapy. In this recommendation, however, the term “GDEM” has been used to denote this same concept in order to reflect the original wording of the recommendation that initially appeared in the “2016 ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure”.

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**Pharmacological Treatment for Stage C HF With Reduced EF**
Treatment of HFrEF Stage C and D

Step 1
Establish Dx of HFrEF; assess volume; initiate GDMT

Step 2
Consider the following patient scenarios

Step 3
Implement indicated GDMT. Choices are not mutually exclusive, and no order is inferred

Step 4
Reassess symptoms

Step 5
Consider additional therapy

ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor-blocker; ARNI, angiotensin receptor-neprilysin inhibitor; BP, blood pressure; bpm, beats per minute; C/I, contraindication; COR, Class of Recommendation; CrCl, creatinine clearance; CRT-D, cardiac resynchronization therapy–device; Dx, diagnosis; GDMT, guideline-directed management and therapy; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; ICD, implantable cardioverter-defibrillator; ISDN/HYD, isosorbide dinitrate hydral-nitrates; K+, potassium; LBBB, left bundle-branch block; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NSR, normal sinus rhythm; and NYHA, New York Heart Association.

†Hydral-Nitrates green box: The combination of ISDN/HYD with ARNI has not been robustly tested. BP response should be carefully monitored.
‡See 2013 HF guideline.
§Participation in investigational studies is also appropriate for stage C, NYHA class II and III HF.

Helping Cardiovascular Professionals
ESC HFrEF Treatment Algorithm

Patient with symptomatic HFrEF

Therapy with ACE-I and beta-blocker (Up-titrare to maximum tolerated evidence-based doses)

Still symptomatic and LVEF ≤35%

No

Add MR antagonist (up-titrare to maximum tolerated evidence-based dose)

Still symptomatic and LVEF ≤35%

No

Yes

Able to tolerate ACEI (or ARB)

Sinus rhythm, QRS duration ≥130 msec

Sinus rhythm, HR ≥70 bpm

ARNI to replace ACE-I

Evaluate need for CRT

Ivabradine

These above treatments may be combined if indicated

Resistant symptoms

Yes

Consider digoxin or H-ISDN or LVAD, or heart transplantation

No further action required

Consider reducing diuretic dose

No
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Stages, Phenotypes and Treatment of HF

**STAGE A**
At high risk for HF but without structural heart disease or symptoms of HF

**STAGE B**
Structural heart disease but without signs or symptoms of HF

**STAGE C**
Structural heart disease with prior or current symptoms of HF

**STAGE D**
Refractory HF

---

**THERAPY**

**Goals**
- Prevent HF symptoms
- Prevent further cardiac remodeling

**Drugs**
- ACEI or ARB as appropriate
- Beta blockers as appropriate

**In selected patients**
- ICD
- Revascularization or valvular surgery as appropriate

---

**THERAPY**

**Goals**
- Control symptoms
- Improve HRQOL
- Prevent hospitalization
- Prevent mortality

**Drugs for routine use**
- Diuretics for fluid retention
- ACEI or ARB
- Beta blockers
- Aldosterone antagonists

**Drugs for use in selected patients**
- Hydralazine/isosorbide dinitrate
- ACEI and ARB
- Digoxin

**In selected patients**
- CRT
- ICD
- Revascularization or valvular surgery as appropriate

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**THERAPY**

**Goals**
- Patient education
- Prevent hospitalization
- Prevent mortality

**Drugs for routine use**
- ACEI or ARB

**Options**
- Advanced care measures
- Heart transplant
- Chronic inotropes
- Temporary or permanent MCS
- Experimental surgery or drugs
- Palliative care and hospice
- ICD deactivation

---

**At Risk for Heart Failure**

- E.g., Patients with:
  - HTN
  - Atherosclerotic disease
  - DM
  - Obesity
  - Metabolic syndrome
  - Using cardiotoxins
  - With family history of cardiomyopathy

**Heart Failure**

- E.g., Patients with:
  - Marked HF symptoms at rest
  - Recurrent hospitalizations despite GDMT

---

Helping Cardiovascular Professionals

Yancy C, et al. JACC, 2013
Prevalence and prognostic significance of HF Stages

Survival (years)

Ammar et al. *Circulation* 2007; 115:1563
Lifetime risk for HF; indexed to blood pressure & sex

- Men:
  - BP <140/<90: 15.6%
  - BP 140-159/90-99: 23.2%
  - BP ≥160/≥100: 27.4%

- Women:
  - BP <140/<90: 12%
  - BP 140-159/90-99: 20.4%
  - BP ≥160/≥100: 29.5%
Primary and Secondary Outcomes and Renal Outcomes.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intensive Treatment</th>
<th>Standard Treatment</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of patients (%)</td>
<td>% per year</td>
<td>no. of patients (%)</td>
<td>% per year</td>
</tr>
<tr>
<td>All participants (N = 4678)</td>
<td>243 (5.2)</td>
<td>1.65</td>
<td>319 (6.8)</td>
<td>2.19</td>
</tr>
<tr>
<td>Primary outcome</td>
<td>97 (2.1)</td>
<td>0.65</td>
<td>116 (2.5)</td>
<td>0.78</td>
</tr>
<tr>
<td>Secondary outcomes</td>
<td>40 (0.9)</td>
<td>0.27</td>
<td>40 (0.9)</td>
<td>0.27</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>62 (1.3)</td>
<td>0.41</td>
<td>70 (1.5)</td>
<td>0.47</td>
</tr>
<tr>
<td>Stroke</td>
<td>62 (1.3)</td>
<td>0.41</td>
<td>100 (2.1)</td>
<td>0.67</td>
</tr>
<tr>
<td>Heart failure</td>
<td>37 (0.8)</td>
<td>0.25</td>
<td>65 (1.4)</td>
<td>0.43</td>
</tr>
<tr>
<td>Death from cardiovascular causes</td>
<td>155 (3.3)</td>
<td>1.03</td>
<td>210 (4.5)</td>
<td>1.40</td>
</tr>
<tr>
<td>Death from any cause</td>
<td>332 (7.1)</td>
<td>2.25</td>
<td>423 (9.0)</td>
<td>2.90</td>
</tr>
<tr>
<td>Participants with CKD at baseline (N = 1330)</td>
<td>14 (1.1)</td>
<td>0.33</td>
<td>15 (1.1)</td>
<td>0.36</td>
</tr>
<tr>
<td>Composite renal outcome</td>
<td>10 (0.8)</td>
<td>0.23</td>
<td>11 (0.8)</td>
<td>0.26</td>
</tr>
<tr>
<td>≥50% reduction in estimated GFR</td>
<td>6 (0.5)</td>
<td>0.14</td>
<td>10 (0.8)</td>
<td>0.24</td>
</tr>
<tr>
<td>Long-term dialysis</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Kidney transplantation</td>
<td>49/526 (9.3)</td>
<td>3.02</td>
<td>59/500 (11.8)</td>
<td>3.90</td>
</tr>
<tr>
<td>Incident albuminuria</td>
<td>127 (3.8)</td>
<td>1.21</td>
<td>37 (1.1)</td>
<td>0.35</td>
</tr>
<tr>
<td>Participants without CKD at baseline (N = 3332)</td>
<td>110/1769 (6.2)</td>
<td>2.00</td>
<td>135/1831 (7.4)</td>
<td>2.41</td>
</tr>
</tbody>
</table>

* CI denotes confidence interval, and CKD chronic kidney disease.
† The primary outcome was the first occurrence of myocardial infarction, acute coronary syndrome, stroke, heart failure, or death from cardiovascular causes.
‡ The composite renal outcome for participants with CKD at baseline was the first occurrence of a reduction in the estimated GFR of 50% or more, long-term dialysis, or kidney transplantation.
§ Incident albuminuria was defined by a doubling of the ratio of urinary albumin (in milligrams) to creatinine (in grams) from less than 10 at baseline to greater than 10 during follow-up. The denominators for number of patients represent those without albuminuria at baseline.
¶ No long-term dialysis or kidney transplantation was reported among participants without CKD at baseline.
**Treatment of Hypertension to Prevent HF:**

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of participants</th>
<th>Inclusion criteria</th>
<th>Intervention</th>
<th>Duration (yr)</th>
<th>Mean BP difference between groups (mmHg)</th>
<th>Absolute rates of heart failure</th>
<th>Relative reduction of heart failure (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SHEP 1997</td>
<td>4,736</td>
<td>≥ 60 yrs; SBP ≥ 160 mmHg</td>
<td>Chlorthalidone ± atenolol</td>
<td>4.5</td>
<td>-26.0 / -8.9</td>
<td>2.3% vs. 4.4%</td>
<td>RR 0.51 (0.37-0.71)</td>
</tr>
<tr>
<td>HYVET 2008</td>
<td>3,845</td>
<td>≥ 80 yrs; SBP ≥ 160 mmHg</td>
<td>Indapamide ± perindopril</td>
<td>2.1</td>
<td>-15.0 / -6.1</td>
<td>5.3% vs. 14.8%</td>
<td>RR 0.36 (0.22-0.58)</td>
</tr>
<tr>
<td>ALLHAT 2002</td>
<td>33,357</td>
<td>≥ 55 years; HTN + 1 CV risk factor</td>
<td>Chlorthalidone vs. Amlodipine; Chlorthalidone vs. Lisinopril</td>
<td>4.9</td>
<td>-0.8 / +0.8; -2.0 / 0</td>
<td>7.7% vs. 10.2%; 7.7% vs. 8.7%</td>
<td>RR 0.62 (0.48-0.75); RR 0.81 (0.69-0.93)</td>
</tr>
<tr>
<td>HOPE 2000</td>
<td>9,297</td>
<td>≥ 55 years; vascular disease or DM + 1 CV risk factor</td>
<td>Ramipril</td>
<td>4.5</td>
<td>-3 / -2</td>
<td>9.0% vs. 11.5%</td>
<td>RR 0.77 (0.67-0.87)</td>
</tr>
<tr>
<td>SPRINT 2015</td>
<td>9,361</td>
<td>SBP ≥ 130 mmHg; increased CVD risk without DM</td>
<td>SBP target &lt;120 mmHg vs. SBP target &lt;140 mmHg</td>
<td>3.3</td>
<td>-18.2 / -9.4</td>
<td>1.3%/yr vs. 2.1%/yr</td>
<td>HR 0.62 (0.45-0.84)</td>
</tr>
</tbody>
</table>

For ALLHAT, mean blood pressure differences. Data for the chlorthalidone vs. doxazosin comparison is not presented since this arm was terminated early due to harm from doxazosin.

*Helping Cardiovascular Professionals Learn. Advance. Heal.*
### Treating Hypertension to Reduce the Incidence of HF

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<td>I</td>
<td>B-R</td>
<td>In patients at increased risk, stage A HF, the optimal blood pressure in those with hypertension should be less than 130/80 mm Hg.</td>
<td>NEW: Recommendation reflects new RCT data.</td>
</tr>
</tbody>
</table>
New Guideline Takeaway messages:  

Part I

• New effective medical therapies have now been fully incorporated in evidence based guideline directed treatment algorithms
• There is an increasing complexity in the treatment of HFrEF; this will require careful assessment of the clinical context/scenario
• Powerful new data should drive the PREVENTION of heart failure
• Avoiding entry into the “HF Club” is the best therapeutic approach
A review- 2017 Focused Update of the ACC/AHA/HFSA Heart Failure Guidelines

• Incorporating new clinical practice guidelines
  – What’s new?
  – How will practice be changed?
• PREVENTION; a new reality in heart failure
• Identifying a new phenotype- heart failure with improved ejection fraction
  – What is this?
  – What’s the natural history?
  – Can it be manipulated?
• Heart Failure with preserved Ejection Fraction
• Important Co-Morbidities in Heart Failure
A new classification?

ESC HF GUIDELINES 2016

Table 3.1
Definition of heart failure with preserved (HFpEF), mid-range (HFmrEF) and reduced ejection fraction (HFrEF)

<table>
<thead>
<tr>
<th>Type of HF</th>
<th>HFrEF</th>
<th>HFmrEF</th>
<th>HFpEF</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Symptoms ± Signs(^a)</td>
<td>Symptoms ± Signs(^a)</td>
<td>Symptoms ± Signs(^a)</td>
</tr>
<tr>
<td>2</td>
<td>LVEF &lt;40%</td>
<td>LVEF 40–49%</td>
<td>LVEF ≥50%</td>
</tr>
<tr>
<td>3</td>
<td>–</td>
<td>Elevated levels of natriuretic peptides(^b); At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).</td>
<td>Elevated levels of natriuretic peptides(^b); At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).</td>
</tr>
</tbody>
</table>
# Definition of Heart Failure

<table>
<thead>
<tr>
<th>Classification</th>
<th>Ejection Fraction</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Heart Failure with Reduced Ejection Fraction (HFrEF)</td>
<td>≤40%</td>
<td>Also referred to as systolic HF. Randomized clinical trials have mainly enrolled patients with HFrEF and it is only in these patients that efficacious therapies have been demonstrated to date.</td>
</tr>
<tr>
<td>II. Heart Failure with Preserved Ejection Fraction (HFpEF)</td>
<td>≥50%</td>
<td>Also referred to as diastolic HF. Several different criteria have been used to further define HFpEF. The diagnosis of HFpEF is challenging because it is largely one of excluding other potential noncardiac causes of symptoms suggestive of HF. To date, efficacious therapies have not been identified.</td>
</tr>
<tr>
<td>a. HFpEF, Borderline</td>
<td>41% to 49%</td>
<td>These patients fall into a borderline or intermediate group. Their characteristics, treatment patterns, and outcomes appear similar to those of patient with HFpEF.</td>
</tr>
<tr>
<td>b. HFpEF, Improved</td>
<td>&gt;40%</td>
<td>It has been recognized that a subset of patients with HFpEF previously had HFrEF. These patients with improvement or recovery in EF may be clinically distinct from those with persistently preserved or reduced EF. Further research is needed to better characterize these patients.</td>
</tr>
</tbody>
</table>
Characteristics and Outcomes of Adult Outpatients With Heart Failure and Improved or Recovered Ejection Fraction

Andreas P. Kalogeropoulos, MD, MPH, PhD; Gregg C. Fonarow, MD; Vasiliki Georgiopoulou, MD, MPH, PhD; Gregory Burkman, MD; Sarawut Siwamogsatham, MD; Akash Patel, MD; Song Li, MD; Lampros Papadimitriou, MD, PhD; Javed Butler, MD, MPH, MBA
Heart Failure with Improved EF?

Kalogeropoulos, A. et al. JAMA Cardiology 2016

- 2166 patients followed over 3 years
- 62% HFrEF
- 38% HFpEF
- 16.2% had HFpEF with previous evidence of LVEF < 0.40
- Mortality at 3 years: 16.3%; 13.2%; 4.8%
Kaplan-Meier Curves, Adjusted for Age and Sex, Across the 3 Heart Failure Groups
The stratified log-rank $\chi^2$ was 15.0 (P < .001) for difference in mortality between groups. HfPEF indicates heart failure with preserved ejection fraction; HFrecEF, heart failure with recovered ejection fraction; and HFrEF, heart failure with reduced ejection fraction.
A  Death

Cumulative Mortality, %

Time, mo

HFrEF
HFpEF
HFrecEF

0 0 5 10 15 20
0 6 12 18 24 30 36

16.3%
13.2%
4.8%
D  Death or heart failure hospitalization

![Graph showing cumulative event rate percentage over time.](chart)

- Time, mo
- Cumulative Event Rate, %
- 40.1%
- 28.9%
- 11.8%
Figure 1. The MCS investigational setting is a unique transformative “research vehicle” that could help advance the science of cardiac recovery, HF reversal and MCS innovation. AVR: Aortic valve replacement/repair, CRT: Cardiac resynchronization, HF: Heart fai...
A new HF phenotype 2016

Editorial  |  July 06, 2016

Heart Failure—A New Phenotype Emerges

Jane E. Wilcox, MD, MSc1; Clyde W. Yancy, MD, MSc1,2

[+] Author Affiliations

*JAMA Cardiol.* Published online July 06, 2016. doi:10.1001/jamacardio.2016.1356
HF improvedEF? - (Takeaways, Part II)

Wilcox J, Yancy CW. JAMA Cardiology 2016

• Spontaneous Myocardial Recovery/Repair
  – Ischemia/revascularization
  – Arrhythmia management; AF/VT ablation
  – Neuregulin pathways
• Reverse Remodeling – super-responders
  – Restoration of beta receptor density
  – Active collagen turnover
  – Pharmacogenomics
• Reversible illnesses; e.g., myocarditis, metabolic cardiomyopathies, peripartum cardiomyopathy
• Myocardial Recovery LVAD supported
  – Restoration of calcium handling; restored mitochondrial function

• TREATMENT?
  – Similar to HFrEF or HFpEF or both?
A review- 2017 Focused Update of the ACC/AHA/HFSA Heart Failure Guidelines

• Incorporating new clinical practice guidelines
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• Heart Failure with preserved Ejection Fraction
• Important Co-Morbidities in Heart Failure
Treatment of HFpEF & the important co-morbidities
Longitudinal plots of blood pressure, potassium, and creatinine over the first 12 months of follow-up by treatment and region.

Pfeffer M A et al. Circulation. 2015;131:34-42
Kaplan-Meier plots of primary outcome and 2 major components.

Pfeffer M A et al. Circulation. 2015;131:34-42
Spironolactone among Repository Participants in the TOPCAT Trial.

A Participants Who Reported Taking Assigned Spironolactone or Placebo

- Placebo: 82/90 in Russia (N=160) and 91/105 in the United States and Canada (N=206)
- Spironolactone: 66/70 in Russia and 76/101 in the United States and Canada

B Participants Who Reported Taking Spironolactone but Had No Detectable Canrenone Concentration

- Russia (N=66): 30 with detectable canrenone
- United States and Canada (N=76): 3 with detectable canrenone

C Median Canrenone Concentration among Participants Who Reported Taking Spironolactone

- Russia
  - Spearman correlation: 0.09 (P=0.47)
- United States and Canada
  - Spearman correlation: 0.43 (P<0.001)

D Median Canrenone Concentration among Participants Who Reported Taking Spironolactone and Had Detectable Canrenone Concentration

E Mean Change in Serum Potassium Level from Baseline to 12 mo

- 0.34 (95% CI, 0.24 to 0.43) P=0.001 vs. baseline

F Mean Change in Aldosterone Level from Baseline to 12 mo

- 66 (95% CI, 48 to 84) P<0.001 vs. baseline
- 49 (95% CI, 89 to 9) P=0.02 vs. baseline
# Pharmacological Treatment for Stage C HF With Preserved EF

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
<th>Comment/Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>B</td>
<td>Systolic and diastolic blood pressure should be controlled in patients with HFpEF in accordance with published clinical practice guidelines to prevent morbidity</td>
<td>2013 recommendation remains current.</td>
</tr>
<tr>
<td>I</td>
<td>C</td>
<td>Diuretics should be used for relief of symptoms due to volume overload in patients with HFpEF.</td>
<td>2013 recommendation remains current.</td>
</tr>
</tbody>
</table>
## Pharmacological Treatment for Stage C HF With Preserved EF

<table>
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<tr>
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<th>Recommendations</th>
<th>Comment/Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ila</td>
<td>C</td>
<td>Coronary revascularization is reasonable in patients with CAD in whom symptoms (angina) or demonstrable myocardial ischemia is judged to be having an adverse effect on symptomatic HFpEF despite GDMT.</td>
<td>2013 recommendation remains current.</td>
</tr>
<tr>
<td>Ila</td>
<td>C</td>
<td>Management of AF according to published clinical practice guidelines in patients with HFpEF is reasonable to improve symptomatic HF.</td>
<td>2013 recommendation remains current.</td>
</tr>
<tr>
<td>Ila</td>
<td>C</td>
<td>The use of beta-blocking agents, ACE inhibitors, and ARBs in patients with hypertension is reasonable to control blood pressure in patients with HFpEF.</td>
<td>2013 recommendation remains current.</td>
</tr>
</tbody>
</table>
## Pharmacological Treatment for Stage C HF With Preserved EF

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<tr>
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</thead>
<tbody>
<tr>
<td>IIb</td>
<td>B-R</td>
<td>In appropriately selected patients with HFpEF (with EF ≥45%, elevated BNP levels or HF admission within 1 year, estimated glomerular filtration rate &gt;30 mL/min, creatinine &lt;2.5 mg/dL, potassium &lt;5.0 mEq/L), aldosterone receptor antagonists might be considered to decrease hospitalizations.</td>
<td>NEW: Current recommendation reflects new RCT data.</td>
</tr>
<tr>
<td>IIb</td>
<td>B</td>
<td>The use of ARBs might be considered to decrease hospitalizations for patients with HFpEF.</td>
<td>2013 recommendation remains current.</td>
</tr>
</tbody>
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## Pharmacological Treatment for Stage C HF With Preserved EF

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</tr>
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<tbody>
<tr>
<td>III: No Benefit</td>
<td>B-R</td>
<td>Routine use of nitrates or phosphodiesterase-5 inhibitors to increase activity or QoL in patients with HFpEF is ineffective.</td>
<td>NEW: Current recommendation reflects new data from RCTs.</td>
</tr>
<tr>
<td>III: No Benefit</td>
<td>C</td>
<td>Routine use of nutritional supplements is not recommended for patients with HFpEF.</td>
<td>2013 recommendation remains current.</td>
</tr>
</tbody>
</table>
Important Comorbidities in HF
Anemia
<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
<th>Comment/Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIb</td>
<td>B-R</td>
<td>In patients with NYHA class II and III HF and iron deficiency (ferritin &lt;100 ng/mL or 100 to 300 ng/mL if transferrin saturation is &lt;20%), intravenous iron replacement might be reasonable to improve functional status and QoL.</td>
<td>NEW: New evidence consistent with therapeutic benefit.</td>
</tr>
<tr>
<td>III: No Benefit</td>
<td>B-R</td>
<td>In patients with HF and anemia, erythropoietin-stimulating agents should not be used to improve morbidity and mortality.</td>
<td>NEW: Current recommendation reflects new evidence demonstrating absence of therapeutic benefit.</td>
</tr>
</tbody>
</table>
Hypertension
(New Section)
Treating Hypertension to Reduce the Incidence of HF

<table>
<thead>
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<tr>
<td>I</td>
<td>B-R</td>
<td>In patients at increased risk, stage A HF, the optimal blood pressure in those with hypertension should be less than 130/80 mm Hg.</td>
<td>NEW: Recommendation reflects new RCT data.</td>
</tr>
</tbody>
</table>
## Treating Hypertension in Stage C HF\(r\)EF

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</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>C-EO</td>
<td>Patients with HF(r)EF and hypertension should be prescribed GDMT titrated to attain systolic blood pressure less than 130 mm Hg.</td>
<td>NEW: Recommendation has been adapted from recent clinical trial data but not specifically tested per se in a randomized trial of patients with HF.</td>
</tr>
</tbody>
</table>
# Treating Hypertension in Stage C HFpEF

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<tr>
<td>I</td>
<td>C-LD</td>
<td>Patients with HFpEF and persistent hypertension after management of volume overload should be prescribed GDMT titrated to attain systolic blood pressure less than 130 mm Hg.</td>
<td>NEW: New target goal blood pressure based on updated interpretation of recent clinical trial data.</td>
</tr>
</tbody>
</table>
"A mediocre physician treats advanced disease... A good physician treats disease... A great physician prevents disease" – Chinese proverb

We should all aim to be great physicians
Sleep Disorders
(Moved from Section 7.3.1.4, Treatment of Sleep Disorders in the 2013 HF guideline)
## Sleep Disorders

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<tbody>
<tr>
<td>IIa</td>
<td>C-LD</td>
<td>In patients with NYHA class II–IV HF and suspicion of sleep disordered breathing or excessive daytime sleepiness, a formal sleep assessment is reasonable.</td>
<td>NEW: Recommendation reflects clinical necessity to distinguish obstructive versus central sleep apnea.</td>
</tr>
<tr>
<td>IIb</td>
<td>B-R</td>
<td>In patients with cardiovascular disease and obstructive sleep apnea, CPAP may be reasonable to improve sleep quality and daytime sleepiness.</td>
<td>NEW: New data demonstrate the limited scope of benefit expected from CPAP for obstructive sleep apnea.</td>
</tr>
<tr>
<td>III: Harm</td>
<td>B-R</td>
<td>In patients with NYHA class II–IV HFrEF and central sleep apnea, adaptive servo-ventilation causes harm.</td>
<td>NEW: New data demonstrate a signal of harm when adaptive servo-ventilation is used for central sleep apnea.</td>
</tr>
</tbody>
</table>
Fig. 1. Associations between heart failure with preserved ejection fraction (HFpEF) and heart failure with reduced ejection fraction (HFrEF), with comorbidities. Pathways linking several common comorbidities to disease progression in both HFpEF and HFrEF are...

**Targeting Comorbidities in Elderly Patients With Heart Failure: The OPTIMIZE-HFPEF Trial**

Journal of Cardiac Failure, Volume 22, Issue 7, 2016, 545–547  
Robert J. Mentz, Thomas M. Maddox

http://dx.doi.org/10.1016/j.cardfail.2016.03.002
New Guideline Takeaways- HFpEF & the Important Co-Morbidities; *Part III*

THE FIRST EVIDENCE BASED GUIDELINE DIRECTED THERAPY FOR HFpEF HAS BEEN ENDORSED (MODESTLY); MORE RESEARCH IS NEEDED

- **Anemia**
  - Fe deficiency; intravenous iron preferable to oral iron

- **Sleep Apnea**
  - Do NOT use servo control support for central sleep apnea
  - CPAP only for OSA
  - Sleep studies are indicated
  - No impact on HF outcomes but sleep quality is improved

- **Hypertension**
  - New target: < 130/80 mmHg in HF with HTN

- **Bidirectional effect**
  - Co0morbidities exaggerate adverse clinical outcomes and symptoms

- **Causative inferences**
  - especially with HFpEF
Final Takeaways

• The treatment of heart failure continues to evolve with new therapies and emerging new devices
• New treatment algorithms address the increasing complexity of HF therapy
• A specific intervention is now indicated for HFpEF
• Co-Morbidities matter; overzealous treatment may lead to harm
• PREVENTION is a new reality
“A mediocre physician treats advanced disease… A good physician treats disease … A great physician prevents disease” – Chinese proverb

We should all aim to be great physicians
Questions?
Thank you!
More Questions about Get With The Guidelines?

Visit heart.org/quality to find your local Get With The Guidelines representative.

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