The State of Heart Failure: A look at current issues and the future of care
• I will **not** discuss off label use or investigational use in my presentation.

• I **have** financial relationships to disclose:
  – Employee of: **University of Colorado**
  – Consultant for: **Novartis, J&J / Janssen**
  – Stockholder in: None
  – Research support from: **NIH / NHLBI, PCORI**
  – Honoraria from: None
Outline

1. Epidemiology
2. Diagnosis
3. Current treatments
4. Major research
• 5.7 million Americans ≥20 years of age have HF (NHANES 2010-2012)

• Lifetime risk of HF is 20% (for 40 and 80 year olds)

• 75% of HF cases have antecedent hypertension.

• Hospitalization is common
  – 50% of patient readmitted in 6 months
  – 50% of patients dead in <5 years
## AHA Policy Statement

### Forecasting the Impact of Heart Failure in the United States

A Policy Statement From the American Heart Association

Paul A. Heidenreich, MD, MS, FAHA, Chair; Nancy M. Albert, PhD, RN, FAHA;

<table>
<thead>
<tr>
<th>Year</th>
<th>All</th>
<th>18–44 y</th>
<th>45–64 y</th>
<th>65–79 y</th>
<th>≥80 y</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>5813262</td>
<td>396578</td>
<td>1907141</td>
<td>2192233</td>
<td>1317310</td>
</tr>
<tr>
<td>2015</td>
<td>6190606</td>
<td>402926</td>
<td>1949669</td>
<td>2483853</td>
<td>1354158</td>
</tr>
<tr>
<td>2020</td>
<td>6859623</td>
<td>417600</td>
<td>1974585</td>
<td>3004002</td>
<td>1463436</td>
</tr>
<tr>
<td>2025</td>
<td>7644674</td>
<td>434635</td>
<td>1969852</td>
<td>3526347</td>
<td>1713840</td>
</tr>
<tr>
<td>2030</td>
<td>8489428</td>
<td>450275</td>
<td>2000896</td>
<td>3857729</td>
<td>2180528</td>
</tr>
</tbody>
</table>
Incidence down? Prevalence up!
HF is Largely a Disease of the Aged

Median age HF = 76 years
Death and Disease in Life is High
50% older Americans have multimorbidity

3 or more
Managing Multiple Health Problems in Older Adults
#3orMore
Patterns of Comorbidity in Older Adults with Heart Failure: The Cardiovascular Research Network PRESERVE Study

Jane S. Saczynski, PhD, Alan S. Go, MD, David J. Magid, MD, David H. Smith, PhD, David D. McManus, MD, Larry Allen, MD, Jessica Ogarek, MS, Robert J. Goldberg, PhD, and Jerry H. Gurwitz, MD

- 23,435 individuals identified with HF

- Multimorbidity common – addition to HF:
  - 2%: no comorbidity
  - 76%: 3+ co-occurring conditions
  - 52%: 5+ co-occurring conditions

- HFpEF compared to HFrEF:
  - 53% v. 47%
  - mean 4.5 vs 4.4 comorbidities
<table>
<thead>
<tr>
<th>Comorbidity*</th>
<th>All Beneficiaries</th>
<th>HF Definition #1</th>
<th>HF Definition #2</th>
<th>HF Definition #3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specified Heart Arrhythmias</td>
<td>13%</td>
<td>41%</td>
<td>54%</td>
<td>59%</td>
</tr>
<tr>
<td>Diabetes, any manifestation</td>
<td>21%</td>
<td>38%</td>
<td>47%</td>
<td>46%</td>
</tr>
<tr>
<td>COPD</td>
<td>13%</td>
<td>34%</td>
<td>43%</td>
<td>46%</td>
</tr>
<tr>
<td>Vascular Disease</td>
<td>14%</td>
<td>33%</td>
<td>37%</td>
<td>40%</td>
</tr>
<tr>
<td>Cardio-Respiratory Failure/Shock</td>
<td>4%</td>
<td>18%</td>
<td>24%</td>
<td>35%</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>5%</td>
<td>17%</td>
<td>25%</td>
<td>32%</td>
</tr>
<tr>
<td>Angina Pectoris/Old MI</td>
<td>4%</td>
<td>10%</td>
<td>12%</td>
<td>11%</td>
</tr>
<tr>
<td>Ischemic or Unspecified Stroke</td>
<td>4%</td>
<td>11%</td>
<td>12%</td>
<td>12%</td>
</tr>
<tr>
<td>Unstable Angina/Other Acute Ischemic</td>
<td>3%</td>
<td>9%</td>
<td>12%</td>
<td>15%</td>
</tr>
</tbody>
</table>

*Comorbidities were calculated using CMS HCC Risk Adjustment Model

Source: Analysis of 2005 5% sample standard analytic files

COPD: Chronic Obstructive Pulmonary Disease, MI: Myocardial Infarction
Away from HF-Centric Thinking
Psychosocial Considerations

Poverty

World

Income

Absolute

Extremes

Drug

Abuse

Definitions

Education

Drugs

Substance

Alcohol

Psychological

Medical

Health
Definition

• “Heart failure is the inability of the heart to pump blood forward at a sufficient rate to meet the metabolic demands of the body, or the ability to do so only if the cardiac filling pressures are abnormally high.”
STROKE VOLUME PRESERVED BY INCREASED END-DIASTOLIC FILLING / PRESSURE
Ventricular remodeling in diastolic and systolic heart failure

- Normal heart
- Hypertrophied heart (diastolic heart failure)
- Dilated heart (systolic heart failure)

HF is not exactly 2 diseases

De Keulenaer GW, Brutsaert DL. Circ 2009;119:3044
HFrEF, HFP EF, and in between

<table>
<thead>
<tr>
<th>Classification</th>
<th>EF (%)</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 controlled 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 (HFP EF)</td>
<td>≥50</td>
<td>Also referred to as diastolic HF. Several different criteria have been used to further define HFP EF. The diagnosis of HFP EF 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. HFP EF, 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 patients with HFP EF.</td>
</tr>
<tr>
<td>b. HFP EF, improved</td>
<td>&gt;40</td>
<td>It has been recognized that a subset of patients with HFP EF 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>
Summary Goals of E&M

1. Identify underlying **etiology**(ies) of HF
   - Correction not possible for most etiologies

2. Elimination of **exacerbating factors**
   - Adherence, diet, HTN, DM, anemia, ...

3. Reduction of **congestion**

4. Improve **blood flow**
   - Modulate neurohormal activation, synchrony, etc

5. Estimate trajectory and **prognosis**
   - Risk models and milestones; *uncertainty* inherent
   - Advanced therapies? (MCS/Txplt, hospice)
Rx on HF
1) acuity
2) type
3) severity

HFrEF
(LVEF < 40%)

HFpEF
(LVEF > 50%)

RV Failure

Chronic
(Stable)

Volume Control

Acute
(Unstable)
Diuretics: Treatment of Volume Overload

Diuretics

Salt (+Water) Excretion

Intravascular Fluid Volume

Venous Congestion

Dyspnea

Edema
Table 2. Pharmacokinetics of the Loop Diuretics\textsuperscript{12-18}

<table>
<thead>
<tr>
<th>Property</th>
<th>Furosemide</th>
<th>Bumetanide</th>
<th>Torsemide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bioavailability (%)</td>
<td>10–100 (average = 50)</td>
<td>80–100</td>
<td>80–100</td>
</tr>
<tr>
<td>Affected by food</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>Metabolism</td>
<td>50% renal conjugation</td>
<td>50% hepatic</td>
<td>80% hepatic</td>
</tr>
<tr>
<td>Half-life (h)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>normal</td>
<td>1.5–2</td>
<td>1</td>
<td>3–4</td>
</tr>
<tr>
<td>renal dysfunction</td>
<td>2.8</td>
<td>1.6</td>
<td>4–5</td>
</tr>
<tr>
<td>hepatic dysfunction</td>
<td>2.5</td>
<td>2.3</td>
<td>8</td>
</tr>
<tr>
<td>heart failure</td>
<td>2.7</td>
<td>1.3</td>
<td>6</td>
</tr>
<tr>
<td>Onset (min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>oral</td>
<td>30–60</td>
<td>30–60</td>
<td>30–60</td>
</tr>
<tr>
<td>intravenous</td>
<td>5</td>
<td>2–3</td>
<td>unavailable</td>
</tr>
</tbody>
</table>

Potency

Usual 24hr dosing

Cost

\textsuperscript{12-18} Ann Pharmacother 2009;43:1836-47.
Diuretic Dosing

USE ONLY WHAT YOU NEED.

DENVER WATER
denverwater.org
Chronic (Stable)

Acute (Unstable)

HFrEF (LVEF < 40%)

GDMT

HFpEF (LVEF > 50%)

RV Failure
<table>
<thead>
<tr>
<th>Chronic (Stable)</th>
<th>HFpEF (LVEF &gt; 50%)</th>
<th>RV Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute (Unstable)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HFrEF (LVEF &lt; 40%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• BB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• ACEI/ARB (ARNi)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Aldo antagonist</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Hydral / ISDN</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• +/- Digoxin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• ICD/CRT</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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

GDHT
Reverse remodeling Rx for HFrEF: Indicated for nearly all Stage C

- ACEi
- ßB
- NYHA I
- NYHA II
- NYHA III
- NYHA IV
- ?
- ?
- CRT
- AA
Short v. Long Term View

You're going down.
SLOW
PROCEED WITH CAUTION
Predischarge Initiation of Carvedilol in Patients Hospitalized for Decompensated Heart Failure

Results of the Initiation Management Predischarge: Process for Assessment of Carvedilol Therapy in Heart Failure (IMPACT-HF) Trial

Wendy A. Gattis, PharmD,* Christopher M. O’Connor, MD, FACC,* Dianne S. Gallup, MS,* At 60 days 165 patients (91.2%) randomized to predischarge carvedilol initiation were treated with a beta-blocker, compared with 130 patients (73.4%) randomized to initiation postdischarge (p < 0.0001). Predischarge initiation was not associated with an increased risk of serious adverse events. The median length of stay was five days in both groups.

Table 2 Absolute and exposure rates to β-blocker intensification for case and control 30-day time periods, with adjusted odds ratios for exposure

<table>
<thead>
<tr>
<th>Proportion with β-blocker intensification in preceding 30-day window</th>
<th>Adjusted OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CASE (n = 1674)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>2.33% (n = 39)</td>
<td>1.61% (n = 27)</td>
</tr>
<tr>
<td>LVSD</td>
<td>2.44% (n = 14)</td>
<td>2.26% (n = 13)</td>
</tr>
</tbody>
</table>
Hazard ratio = 0.90 (95% CI 0.82–0.99); p = 0.027

Lancet 2009; 374: 1840–48
Real-world HFREF Rx: We CAN improve!

Fonarow GC et al. IMPROVE-HF. Circ 2010;122:585.
Rx on HF 1) acuity 2) type 3) severity

- **Chronic (Stable)**
  - HFrEF (LVEF < 40%)
  - HFpEF (LVEF > 50%)
  - RV Failure

- **Acute (Unstable)**
Table 21. Recommendations for Treatment of HFpEF

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic and diastolic blood pressure should be controlled according to published clinical practice guidelines</td>
<td>I</td>
<td>B²⁷,⁵¹</td>
</tr>
<tr>
<td>Diuretics should be used for relief of symptoms due to volume overload.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Coronary revascularization for patients with CAD in whom angina or demonstrable myocardial ischemia is present despite GDMT</td>
<td>Ila</td>
<td>C</td>
</tr>
<tr>
<td>Management of AF according to published clinical practice guidelines for HFpEF to improve symptomatic HF</td>
<td>Ila</td>
<td>C</td>
</tr>
<tr>
<td>Use of beta-blocking agents, ACE inhibitors, and ARBs for hypertension in HFpEF</td>
<td>Ila</td>
<td>C</td>
</tr>
<tr>
<td>ARBs might be considered to decrease hospitalizations in HFpEF</td>
<td>I</td>
<td>B⁵⁰⁵⁰</td>
</tr>
<tr>
<td>Nutritional supplementation is not recommended in HFpEF</td>
<td>III: No Benefit</td>
<td>C</td>
</tr>
</tbody>
</table>
ARB: HFrEF v. HFpEF

CHARM Alternative

- **HFrEF**
  - Proportion with cardiovascular death or hospital admission for CHF (%)
  - Number at risk:
    - Placebo: 1013, 929, 831, 434, 122
    - Candesartan: 1015, 887, 708, 427, 126

- **HFpEF**
  - Hazard ratio 0.77 (95% CI 0.67–0.89), p=0.0004
  - Adjusted hazard ratio 0.70, p=0.0001

CHARM Preserved

- **I-PRESERVE**
  - Hazard ratio 0.89 (95% CI 0.77–1.03), p=0.118
  - Adjusted hazard ratio 0.86, p=0.051

Number at risk:
- Placebo: 1509, 1458, 1377, 824, 195
- Candesartan: 1514, 1458, 1377, 833, 182
Aldo-DHF

![Graph showing Peak VO2 changes over time with statistical significance values]
### Clinical Outcomes in the TOPCAT Trial, Mean 3.3-Year Follow-up

<table>
<thead>
<tr>
<th>End points</th>
<th>Spironolactone (%) n=1722</th>
<th>Placebo (%) n=1723</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary*</td>
<td>18.6</td>
<td>20.4</td>
<td>0.89 (0.77–1.04)</td>
<td>0.138</td>
</tr>
</tbody>
</table>
### Rx on HF

1) **Acuity**
2) **Type**
3) **Severity**

<table>
<thead>
<tr>
<th>Chronic (Stable)</th>
<th>HFpEF (LVEF &gt; 50%)</th>
<th>RV Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>HFrEF (LVEF &lt; 40%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **HFrEF**: LVEF < 40%
- **HFpEF**: LVEF > 50%
- **RV Failure**
Assess and Adjust Hemodynamics

Congestion at rest?
(e.g. orthopnea, elevated jugular venous pressure, pulmonary rales, S3 gallop, edema)

Congestion at rest?
(No) 
(Warm and Dry) 
(Warm and Wet) 
(Cold and Wet)

Low perfusion at rest?
(e.g. narrow pulse pressure, cool extremities, hypotension)

(A) No
(B) Yes

(A) No
(C) Cold and Dry

(B) Yes
(D) Warm and Wet

Happiness

Dry out (diuretic) +/- vasodilate

IVF challenge
Inotrope?
LVAD, Transplant??
Hospice

Warm up (inotrope), then dry out
Advanced HF Care

- **Transplantation**: Limited resource, $$$
- **Mechanical Assist Devices**: Highly morbid, $$$
- **Inotrope infusion**: Often hastens death
- **Hospice**: Paradigm shift to potentially shorter life for improved quality

Assumption of significant risk (and cost)
Markers of Advanced HF (High Risk)

1. Repeated (≥2) **hospitalizations** or ED visits for HF in the past year
2. Progressive deterioration in **renal** function (end-organ dysfunction)
3. Symptomatic **hypotension**
4. Dose reductions / intolerance of **ACEi** or **BB**
5. Weight loss without other cause (e.g. cardiac **cachexia**)
6. Persistent **dyspnea with simple ADLs**, inability to walk 1 block
7. Repeated **ICD shocks, VT**
8. Daily furosemide equivalent >160 mg/d and/or supplemental metolazone
9. Progressive decline in **serum sodium**, <133 mEq/L
10. High **BNP** (>5x ULN), does not go down 50% with Rx optimization
11. **NO EASILY REVERSIBLE CAUSES OR PRECIPITANTS**
Hospital Care Measures

• 30-day readmissions and mortality rates (outcome measures)

• HF Core Measures going away (process measures)
  – Need for hospitals to use GWTG (different than Core Measures
  – Aligned with 2011 ACC/AHA/PCPI measures and 2013 HF CPG’s)

“In God we trust. All others must bring data”.

W. Edwards Deming
Systems of care critical
Leverage EMR (Epic)
Patient Identification

• Identification algorithm:
  1. Heart failure ICD-9 codes from problem list, OR
  2. BNP >150 pg/ml, OR
  3. IV loop diuretic during current encounter

• Performance: at admission for discharge Dx
  – 97% sensitivity: for final PRIMARY discharge dx HF
  – 75% specificity for patient with HF

• A BPA appears to the admitting or discharging provider and suggests use of the heart failure specific order set
### Please use the Heart Failure Admission Order Set in patients with suspected/actual heart failure. (BPA# 922)

<table>
<thead>
<tr>
<th>Acknowledge reason:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doesn't have HF - don't use HF order set</td>
</tr>
<tr>
<td>Defer decision re: HF admit order set</td>
</tr>
</tbody>
</table>

- **Open Order Set:** UCH Congestive Heart Failure Admission [preview](#)

---

### Please use the Heart Failure Discharge Order Set in patients with suspected/actual heart failure. (BPA# 927)

<table>
<thead>
<tr>
<th>Acknowledge reason:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doesn't have HF - don't use HF order set</td>
</tr>
<tr>
<td>Defer decision re: HF discharge order set</td>
</tr>
<tr>
<td>I will place orderset</td>
</tr>
<tr>
<td>Already ordered</td>
</tr>
</tbody>
</table>

- **Open Order Set:** UCH Congestive Heart Failure Discharge [preview](#)

**The following actions were applied automatically:**
- **Message sent:** This advisory has been sent via In Basket
ACEI/ARB Core Measure — Required

These are required data elements for Core Measure reporting. If LVEF less than 40%, an ACEI OR ARB prescription at discharge is indicated, UNLESS a valid contraindication is provided.

- ACEI/ARB not specifically indicated for heart failure; LVEF greater than or equal to 40%
- ACEI/ARB contraindicated at discharge
- ACEI prescribed
- ARB prescribed

Follow-Up

It is recommended that patients admitted with a heart failure exacerbation should be seen by a provider within **SEVEN DAYS** of discharge.

- Follow-Up has been scheduled.

**Routine, Clinic Performed**, It is very important for you to make and keep the follow-up appointment listed. It is generally recommended that you follow up with a health care provider (e.g. your doctor) within 7 days of hospital discharge following a heart failure exacerbation. We have made an appointment for you:

Name: *****, Date: *****, Time: *****, Location: *****, Phone #: *****
Welcome To The Future
Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomised controlled trial

William T Abraham, Philip B Adamson, Robert C Bourge, Mark F Aaron, Maria Rosa Costanzo, Lynne W Stevenson, Warren Strickland, Suresh Neelagaru, Nirav Raval, Steven Krueger, Stanislav Weiner, David Shavelle, Bradley Jeffries, Jay S Yadav, for the CHAMPION Trial Study Group*
Control group (253 hospital admissions for heart failure)

Treatment group (153 hospital admissions for heart failure)

Hazard ratio 0.64
(95% CI 0.55–0.75);
\( p<0.0001 \)

<table>
<thead>
<tr>
<th>Number at risk</th>
<th>Time from implant (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>280 267 252 215 179 138 105 67</td>
</tr>
<tr>
<td>Treatment group</td>
<td>270 262 244 210 169 131 108 82</td>
</tr>
</tbody>
</table>
Table 1. Inclusion Criteria

Written informed consent and authorization to use and disclose health information.
18 years of age or older.
Diagnosis of HF for $\geq 3$ months, with preserved or reduced LVEF.
Diagnosis of NYHA functional class III HF at screening visit.
If subject has a reduced LVEF, they must be receiving a beta-blocker for 3 months and an ACE-I or ARB for 1 month unless, in the investigator’s opinion, the subject is intolerant to beta-blockers, ACE-I, or ARB. Beta-blocker and ACE-I (or ARB) doses should be stable for 1 month before study entry.
At least 1 HF-related hospitalization within 12 months of screening visit.
BMI $\leq 35$ kg/m². Subjects with BMI $> 35$ kg/m² require additional screening. If the BMI is $> 35$ kg/m² and the chest circumference is $> 52$ in and $< 65$ in, the distance from the skin on the subject’s back to the pulmonary artery must be $< 10$ cm and confirmed by angiogram of the lateral view during the catheterization before placement of the pressure sensor. If the distance is $> 10$ cm, the subject will not receive a sensor and will not be eligible for the study.
Pulmonary artery branch diameter between 7 and 15 mm.
Female subjects of childbearing age with a negative urine or serum pregnancy test at the screening visit and agreeing to use a reliable mechanical or hormonal form of contraception during the study.
Table 2. Exclusion Criteria

- Active infection.
- History of recurrent (>1) pulmonary embolism or deep vein thrombosis.
- Unable to tolerate an RHC, in the investigator’s opinion.
- Implantation of CRT <3 months before enrollment.
- Experienced a major cardiac event (eg, myocardial infarction, stroke) within 2 months of screening visit.
- GFR <25 mL/min or chronic renal dialysis.
- Likely to undergo heart transplantation within 6 months of screening visit.
- Congenital heart disease or mechanical right heart valve(s).
- Diagnosed coagulation disorders.
- Hypersensitivity or allergy to aspirin and/or clopidogrel.
- Enrolled in concurrent studies that may confound the results of this study.
- Clinical condition that would not allow them to complete the study, in the investigator’s opinion.
Practical concerns

• Technical
  – 12-French access

• Work flow
  – Who is responsible?
  – Who needs to be trained?
  – What is being given up to do this?

• Insurance coverage
WARNING
USING WHILE STUPID CAN CAUSE SERIOUS INJURY
Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure

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- LCZ696 200 bid (valsartan + socubutril) v. enalapril 10 bid
- 8441 pts: NYHA II-VI, LVEF <=40%
- Stopped early at 27 months
<table>
<thead>
<tr>
<th>Outcome</th>
<th>LCZ696 (N=4187)</th>
<th>Enalapril (N=4212)</th>
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</thead>
<tbody>
<tr>
<td>Primary composite outcome — no. (%)</td>
<td></td>
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<tr>
<td>Death from cardiovascular causes or first hospitalization for worsening heart failure</td>
<td>914 (21.8)</td>
<td>1117 (26.5)</td>
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<tr>
<td>Death from cardiovascular causes</td>
<td>558 (13.3)</td>
<td>693 (16.5)</td>
</tr>
<tr>
<td>First hospitalization for worsening heart failure</td>
<td>537 (12.8)</td>
<td>658 (15.6)</td>
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<tr>
<td>Secondary outcomes — no. (%)</td>
<td></td>
<td></td>
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<tr>
<td>Death from any cause</td>
<td>711 (17.0)</td>
<td>835 (19.8)</td>
</tr>
<tr>
<td>Change in KCCQ clinical summary score at 8 mo†</td>
<td>−2.99±0.36</td>
<td>−4.63±0.36</td>
</tr>
<tr>
<td>New-onset atrial fibrillation‡</td>
<td>84 (3.1)</td>
<td>83 (3.1)</td>
</tr>
<tr>
<td>Decline in renal function§</td>
<td>94 (2.2)</td>
<td>108 (2.6)</td>
</tr>
</tbody>
</table>
A Primary End Point

Hazard ratio, 0.80 (95% CI, 0.73–0.87)
P<0.001

Cumulative Probability

Days since Randomization

No. at Risk
LCZ696  4187  3922  3663  3018  2257  1544  896  249
Enalapril  4212  3883  3579  2922  2123  1488  853  236
D  Death from Any Cause

Hazard ratio, 0.84 (95% CI, 0.76–0.93)  
P<0.001

Cumulative Probability

No. at Risk
LCZ696  4187  4056  3891  3282  2478  1716  1005  280
Enalapril  4212  4051  3860  3231  2410  1726  994  279
ARB+NEPi (ARNI)

Von Leuder CircHF 2013;594
Other . . .

- Ivrabridine (FDA to review late spring?)
- Subcutaneous ICD (no CRT)
- Vagal / Autonomic stimulation
- Improved mechanical circulatory support
- Ongoing payment reform
- . . .
Some “light” reading

http://circ.ahajournals.org/content/128/16/e240.full.pdf+html

ACCF/AHA Practice Guideline

2013 ACCF/AHA Guideline for the Management of Heart Failure
A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines

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

Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation

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