Several compensatory mechanisms are activated in response to heart failure

- HF activates compensatory mechanisms, some of which contribute to the symptoms, signs and poor natural history of HF

HF activates compensatory mechanisms, some of which contribute to the symptoms, signs and poor natural history of HF

- Ventricular filling pressure increased (pre-load)
- Cardiac output decreased
- Increased total systemic vascular resistance
- Arterial impedance increased (after-load)

Compensatory responses:
1) Activation of the sympatho-adrenal system
2) Activation of the RAAS
3) Activation of the endothelin system
4) Other renal mechanisms for conservation of sodium and water
   a. proximal tubular sodium reabsorption (mechanism remains unclear)
   b. anti-diuretic hormone

HF = heart failure  RAAS = Renin-Angiotensin Aldosterone system
Kumar, Abbas. Lange 2002.373-387-50
### 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 (HF(r)EF)</td>
<td>≤40%</td>
<td>Also referred to as <strong>systolic HF</strong>. Randomized clinical trials have mainly enrolled patients with HF(r)EF 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 (HF(p)EF)</td>
<td>≥50%</td>
<td>Also referred to as <strong>diastolic HF</strong>. Several different criteria have been used to further define HF(p)EF. The diagnosis of HF(p)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. HF(p)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 patient with HF(p)EF.</td>
</tr>
<tr>
<td>b. HF(p)EF, Improved</td>
<td>&lt;40%</td>
<td>It has been recognized that a subset of patients with HF(p)EF previously had HF(r)EF. 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>
**Guidelines**

**ACEI, ARBs**

Heart failure therapy follows a symptom-based treatment algorithm (NICE)

- **New diagnosis**
  - Start ACEI and titrate upwards
  - Or if ACEI not tolerated (e.g. due to severe cough)
    - Consider ARB

- **Generalist**
  - Add diuretic
    - Diuretic therapy is likely to be required to control congestive symptoms and fluid retention
  - Add digoxin
    - If a patient in sinus rhythm remains symptomatic despite therapy with a diuretic, ACEI (or ARB) and β-blocker or if patient is in atrial fibrillation then use as first-line therapy

- **Specialist input**
  - Add β-blocker and titrate upwards

- **Specialist**
  - Add spironolactone
    - If patient remains moderately to severely symptomatic despite optimal drug therapy listed above
  - Seek specialist advice for further options

National Institute for Clinical Excellence (NICE); Chronic heart failure clinical guideline 5; July 2003.
Diuretics are recommended in patients with HFrEF with fluid retention

ACE Inhibitors
ACE inhibitors are recommended for all patients with HFrEF

ARBs
ARBs are recommended in patients with HFrEF who are ACE inhibitor intolerant
ARBs are reasonable as alternatives to ACE inhibitor as first line therapy in HFrEF
The addition of an ARB may be considered in persistently symptomatic patients with HFrEF on GDMT
Routine combined use of an ACE inhibitor, ARB, and aldosterone antagonist is potentially harmful
Evidences

ACEI

CONSENSUS trial (1987)
Enalapril therapy in patients with severe HF

Primary endpoint:
All-cause mortality at 6 months

Conclusions: enalapril significantly reduced the risk of mortality at 6 months and at 1 year vs placebo in patients with severe HF

*On top of standard therapy for heart failure
CONSENSUS: Cooperative North Scandinavian Enalapril Survival Study; NYHA: New York Heart Association; QD: once daily
**SOLVD treatment trial (1991)**

*Enalapril therapy in patients with HF*

- NYHA I–IV, LVEF ≤35%, standard therapy
- **Enalapril**: 2.5–20 mg QD
  - n=1285
- **Placebo**: n=1284

Primary endpoint: All-cause mortality at follow-up

Conclusions: Enalapril* significantly reduced the risk of mortality versus placebo in patients with HF and reduced ejection fractions.

*On top of standard therapy for HF*


**ATLAS trial (1999)**

*Lisinopril therapy in patients with chronic HF*

- NYHA II–IV, LVEF ≥30%
- **Lisinopril**: 32.5–35 mg QD
  - n=1568
- **Placebo**: n=1596

Primary endpoint: All-cause mortality at follow-up

Conclusions: Patients with HF should not be maintained on low doses of an ACEI except when these are the only doses that can be tolerated.

*On top of standard therapy for HF*

Evidences

**ARBs**

---

**Val-HeFT trial (2001)**

*Valsartan therapy in patients with chronic heart failure*

Conclusions: valsartan significantly reduced the combined endpoint of mortality and morbidity, and improved clinical signs and symptoms in patients with HF vs placebo.

*On top of standard therapy for HF.*
†Defined as the incidence of cardiac arrest with resuscitation, hospitalization for HF, or receipt of intravenous inotropic or vasodilator therapy for ≥4 hours.

Val-HeFT: Valsartan Heart Failure Trial; BID: twice daily; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; QD: once daily

**CHARM-Added trial (2003)**

*Candesartan therapy in patients with chronic heart failure*

Conclusions: Addition of candesartan to ACEI therapy led to significant reductions in CV events in patients with chronic HF and reduced LVEF

On top of therapy with a proven ACE inhibitor regimen

CHARM-Added: Candesartan in Heart failure Assessment of Reduction in Mortality and Morbidity in patients with HFrEF who were on ACE inhibitors; ACEI: angiotensin-converting enzyme inhibitor; CV: cardiovascular; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; QD: once daily


---

**CHARM-Alternative trial (2003)**

*Candesartan therapy in patients with chronic heart failure*

Conclusions: Candesartan significantly reduced CV mortality and morbidity vs placebo in patients with symptomatic chronic HF and intolerance to ACEIs

On top of therapy with a proven ACE inhibitor regimen

CHARM-Alternative: Candesartan in Heart failure Assessment of Reduction in Mortality and Morbidity: CV: cardiovascular; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; QD: once daily


---

*Primary endpoint: composite of CV mortality or hospitalizations for chronic HF*

*Placebo vs. Candesartan: 15% relative risk reduction p=0.011*

*Placebo vs. Candesartan: 30% relative risk reduction p<0.0001*
HEAAL trial (2009)

Losartan therapy in patients with heart failure

**Conclusions:** Losartan 150 mg reduced the risk of mortality or hospitalization versus losartan 50 mg in patients with HF

HEAAL: Heart failure Endpoint evaluation of Angiotensin II Antagonist Losartan; ACEI: angiotensin-converting enzyme inhibitor; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; QD: once daily

Konstam et al. Lancet. 2009;374:1840-1848
Heart failure therapy follows a symptom-based treatment algorithm (NICE)

**New diagnosis**
- Add diuretic
- Diuretic therapy is likely to be required to control congestive symptoms and fluid retention
- Add digoxin
- If a patient in sinus rhythm remains symptomatic despite therapy with a diuretic, ACEI (or ARB) and β-blocker or if patient is in atrial fibrillation then use as first-line therapy

**Seek specialist advice for further options**

**Add a beta-blocker**

**Add ACE inhibitor (or ARB if not tolerated)**
- Still NYHA class II-IV?
  - Yes
    - Add a MR antagonist
    - Still NYHA class II-IV?
  - No
- Add a beta-blocker

**Add spironolactone**
- If patient remains moderately to severely symptomatic despite optimal drug therapy listed above

**European Heart Journal (2012) 33, 1787–1847**
**European Journal of Heart Failure (2012) 14, 803–869**
Pharmacological Therapy for Management of Stage C HF HFrEF (cont.)

<table>
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<tr>
<th>Recommendations</th>
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Evidences

*Beta-blockers*
β-blockers reduce the risk of mortality versus placebo in patients with chronic heart failure

CIBIS II Cardiac Insufficiency Bisoprolol Study II; COPERNICUS = Carvedilol Prospective Randomized Cumulative Survival; MERIT-HF = Metoprolol CR/XL Randomized Intervention Trial in Congestive Heart Failure


Guidelines

Aldosterone Antagonists
Heart failure therapy follows a symptom-based treatment algorithm (NICE)

- **Generalist**
  - Add diuretic
  - Diuretic therapy is likely to be required to control congestive symptoms and fluid retention
  - Add digoxin
  - If a patient in sinus rhythm remains symptomatic despite therapy with a diuretic, ACEI (or ARB) and β-blocker or if patient is in atrial fibrillation then use as first-line therapy

- **New diagnosis**
  - Start ACEI and titrate upwards
  - Or if ACEI not tolerated (e.g. due to severe cough) Consider ARB

- **Specialist**
  - Add β-blocker and titrate upwards
  - Add spironolactone if patient remains moderately to severely symptomatic despite optimal drug therapy listed above
  - Seek specialist advice for further options

- **Specialist input**

- **ACE inhibitor (or ARB if not tolerated)**
  - Add a beta-blocker
  - Still NYHA class II-IV?
    - Yes
      - Add a MR antagonist
    - No
  - Or if ACEI not tolerated (e.g. due to severe cough) Consider ARB
  - Start ACEI and titrate upwards

National Institute for Clinical Excellence (NICE); Chronic heart failure clinical guideline 5; July 2003.
Pharmacological Therapy for Management of Stage C HFrEF (cont.)

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</tr>
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</table>

Evidences

Aldosterone Antagonists
MRAs: trial evidence and subsequent update in the ESC 2012 HF guidelines

- Trials comparing an MRA with placebo (added to an ACEi and a β-blocker) in HF-REF
  - RALES
    - 1,663 NYHA class III/IV patients
    - 95% ACEI/10% β-blocker
    - RRR (95% CI) 30 (18–40)% p<0.001
    - Spironolactone
    - Placebo

  - EMPHASIS-HF
    - 2,737 NYHA class II patients
    - 90% ACE-I or ARB/87% β-blocker
    - RRR (95% CI) 22 (5–36)% p=0.0139
    - Eplerenone
    - Placebo

ESC 2012 HF guidelines:

Guidelines

Ivabradine
Pharmacological therapy – Next step

Still NYHA class II-IV?

Yes \rightarrow \text{No}

LVEF \leq 35%?

Yes \rightarrow \text{No}

Sinus rhythm, HR \geq 70 beats/min?

Yes \rightarrow \text{No}

Add ivabradine

Evidences

Ivabradine
**Ivabradine**: trial evidence for use in patients with systolic HF and subsequent update in the ESC 2012 HF guidelines

- **SHIFT**: Systolic Heart failure treatment with the If inhibitor ivabradine Trial – primary composite endpoint (CV death or hospitalization for worsening HF)

![Cumulative frequency (%)](image)

- Hazard ratio (HR) (95% CI), 0.82 (0.75-0.90)
- p<0.0001

Guidelines

**Digoxin and H-ISDN**

When to consider CRT and ICD

When to consider CRT and ICD

- **Still NYHA class II-IV and LVEF ≤35%?**
  - Yes
    - QRS duration ≥120 ms?
      - Yes
        - Consider CRT-P/CRT-D
      - No
        - Consider ICD
  - No

- **Still NYHA class II-IV?**
  - Yes
    - No further specific treatment
      - Continue in disease management programme
  - No

- **Consider digoxin and/or H-ISDN**
  - If end-stage consider LVAD and/or transplantation

Pharmacological therapy

Other treatments with less certain benefits in systolic HF (2)

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Digoxin</strong></td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>May be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF ≤45% who are unable to tolerate a beta-blocker (l-arginine is an alternative in patients with a heart rate ≥70 b.p.m.). Patients should also receive an ACE inhibitor (or ARB) and an MRA (or ARB).</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>H-ISDN</strong></td>
<td>IIb</td>
<td>P</td>
</tr>
<tr>
<td>May be considered as an alternative to an ACE inhibitor or ARB, if neither is tolerated, to reduce the risk of HF hospitalization and risk of premature death in patients with an EF ≤45% and dilated LV (or EF ≤35%). Patients should also receive a beta-blocker and an MRA.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>May be considered to reduce the risk of HF hospitalization and risk of premature death in patients with an EF ≤45% and dilated LV (or EF ≤35%) and persisting symptoms (NYHA class II–IV) despite treatment with a beta-blocker, ACE inhibitor (or ARB), and an MRA (or ARB).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>An n-3 PUFA preparation may be considered to reduce the risk of death and the risk of cardiovascular hospitalization in patients treated with an ACE inhibitor (or ARB), beta-blocker, and an MRA (or ARB).</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

European Heart Journal (2012) 33, 1787–1847
European Journal of Heart Failure (2012) 14, 803–869
### Pharmacologic Therapy for Management of Stage C HFrEF (cont.)

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Digoxin</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digoxin can be beneficial in patients with HFrEF</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td><strong>Anticoagulation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with chronic HF with permanent/persistent/paroxysmal AF and an additional risk factor for cardioembolic stroke should receive chronic anticoagulant therapy*</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>The selection of an anticoagulant agent should be individualized</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Anticoagulation is reasonable for patients with chronic HF who have permanent/persistent/paroxysmal AF but without an additional risk factor for cardioembolic stroke*</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Anticoagulation is not recommended in patients with chronic HFrEF without AF, prior thromboembolic event, or a cardioembolic source</td>
<td>III: No Benefit</td>
<td>B</td>
</tr>
<tr>
<td><strong>Statins</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Statins are not beneficial as adjunctive therapy when prescribed solely for HF</td>
<td>III: No Benefit</td>
<td>A</td>
</tr>
<tr>
<td><strong>Omega-3 Fatty Acids</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omega-3 PUFA supplementation is reasonable to use as adjunctive therapy in HFrEF or HFrEF patients</td>
<td>IIa</td>
<td>B</td>
</tr>
</tbody>
</table>

### Evidences
- **Digoxin and H-ISDN**
**Digitalis (1997)**

*Digoxin in patients with chronic heart failure*

**Conclusions:** Digoxin* did not reduce all-cause mortality vs placebo, but it reduced the rate of hospitalization overall and for worsening HF

---

**V-HeFT- I (1986)**

*Hydralazine-Isosorbide Dinitrate in patients with chronic heart failure*

**Conclusions:** H-ISDN showed favorable effects on LV function and mortality when added to digoxin and diuretic therapy in patients with chronic HF

---

*On top of diuretics and ACEI*ns

LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; QD: once daily


A-HeFT trial (2004)

**Hydralazine-Isosorbide Dinitrate in black patients with advanced HF**

- **Randomization**: Placebo vs H-ISDN
  - Placebo: n=532
  - H-ISDN: 225/120 mg QD; n=518

**Primary endpoint**: composite of death, first hospitalization for HF, and patient-reported functional status at 6 months

**Conclusions**: H-ISDN plus standard therapy significantly increased survival vs placebo among black patients with advanced HF

- **NYHA III–IV, LVEF ≤35%**
- **Survival (%)**

V-HeFT-II (1991)

**Enalapril therapy vs hydralazine-isosorbide dinitrate in men with HF**

- **Randomization**: Hyd: 300 mg QD; ISDN: 160 mg QD
  - Hyd: n=401
  - ISDN: n=403

**Primary endpoint**: All-cause mortality at 2 years

**Conclusions**: enalapril significantly reduced the risk of mortality vs H-ISDN in symptomatic men with reduced ejection fractions

- **Men, LVEF <45%, symptomatic**
- **Cumulative mortality rate**

---

*On top of standard therapy for HF*

H-ISDN: Hydralazine-Isosorbide Dinitrate; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; QD: once daily.


**Medical Therapy for Stage C HF\(_r\)EF:** 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>

**Guidelines**

*CRT-ICD, Surgical devices*
When to consider CRT and ICD

- Still NYHA class II-IV and LVEF ≤35%?
  - Yes → QRS duration ≥120 ms?
    - Yes → Consider CRT-D
    - No → Consider ICD
  - No → No further specific treatment

- Still NYHA class II-IV?
  - Yes → Continue in disease management programme
  - No → Consider digoxin and/or H-NSIN
  - If end-stage consider LVAD and/or transplantation

An expanded indication for cardiac resynchronization therapy (CRT)

Recommendations for the use CRT where the evidence is strong—patients in sinus rhythm with NYHA functional class II heart failure and a persistently reduced ejection fraction, despite optimal pharmacological therapy.

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>LBBB QRS morphology</td>
<td></td>
<td>A</td>
</tr>
</tbody>
</table>

CRT, preferably CRT-D is recommended in patients in sinus rhythm with a QRS duration of ≥130 ms, LBBB QRS morphology, and an EF ≤30%, who are expected to survive for >1 year with good functional status, to reduce the risk of HF hospitalization and the risk of premature death.

2 trials: MADIT-CRT and RAFT
CRT Indications

**Symptoms**
- NYHA Class I, II, III, IV
- Class IV
- Ambulatory
- Resting

**ECG**
- Rhythm
- Sinus
- AF
- QRS duration
- 120-149 ms
- 150 ms

**QRS pattern**
- LBBB
- Non-LBBB

**Echocardiography**
- LVEF
- 30%
- 35%
- 40%

Evidences

**CRT-ICD, Surgical devices**

Nabil Farag
**Non-surgical devices** and the ESC 2012 HF guideline recommendations

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Trial</th>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRT</td>
<td>MADIT-CRT</td>
<td>CRT in systolic HF and mild symptoms</td>
</tr>
<tr>
<td>CRT</td>
<td>RAFT</td>
<td>CRT in systolic HF and mild symptoms</td>
</tr>
<tr>
<td>Transcatheter aortic valve implantation (TAVI)</td>
<td>PARTNER trials</td>
<td>Role of transcatheter aortic valve implantation</td>
</tr>
</tbody>
</table>

- **CRT in systolic HF with mild symptoms:**
  - Recommendation for the use of CRT where the evidence is strong – patients in sinus rhythm with HF NYHA functional class II and a persistently reduced ejection fraction, despite optimal pharmacological therapy.


**SCD-HeFT (2005)**

Aniodarone or an Implantable Cardioverter-Defibrillator for Congestive Heart Failure

- Symptomatic, LVEF ≤35%
- Primary endpoint: All cause Mortality

**Conclusions:** In patients with NYHA class II or III CHF and LVEF of 35 percent or less, amiodarone has no favorable effect on survival, whereas single-lead, shock-only ICD therapy reduces overall mortality by 23 percent.

*There were no significant differences among the three groups, except in the use of beta blockers at the time of the last follow-up visit (P<0.001). SCD-HeFT: Sudden Cardiac Death in Heart Failure Trial.

COMPANION (2004) Cardiac-Resynchronization Therapy with or without an Implantable Defibrillator in Advanced Chronic Heart Failure

**Conclusions:** In patients with advanced heart failure and a prolonged QRS interval, cardiac-resynchronization therapy decreases the combined risk of death from any cause or first hospitalization and, when combined with an implantable defibrillator, significantly reduces mortality.

*Surgery/surgical devices* and the ESC 2012 HF guideline recommendations

<table>
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<th>Treatment</th>
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<tr>
<td>VAD</td>
<td>Heart Mate II trial</td>
<td>Continuous vs pulsatile flow</td>
</tr>
<tr>
<td>Coronary artery bypass graft (CABG)</td>
<td>STITCH</td>
<td>Role in patients with systolic HF</td>
</tr>
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ESC 2012 HF guidelines recognise the growing use of VADs as a bridge to transplantation and as destination therapy:

- McMurray et al. *Eur Heart J* 2012
Advanced heart failure treated with continuous-flow left ventricular assist device

Conclusions: Treatment with a continuous-flow left ventricular assist device in patients with advanced heart failure significantly improved the probability of survival free from stroke and device failure at 2 years as compared with a pulsatile device. Both devices significantly improved the quality of life and functional capacity.

LVAD = left ventricular assist device.
Heart Failure with Preserved Ejection Fraction (HFpEF)

Guidelines
Treatment for patients with HFpEF and the ESC 2012 HF guideline recommendations

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<td>ARB</td>
<td>FPRESERVE</td>
<td>Efficacy and safety of irbesartan in HF-PEF – neutral results</td>
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- ESC 2012 HF guidelines:
  - No treatment has been shown to reduce mortality and morbidity in HFpEF
  - Diuretics are used to control sodium and water retention and to relieve breathlessness and edema
  - Drugs that should be avoided in HF-REF should also be avoided in HF-PEF, with the exception of calcium channel blockers (CCBs)

McMurray JJ et al., Eur Heart J (2012) 33, 1787–1847
Major trials in HFpEF

Unmet need in chronic heart failure

To date, no therapy has been proven to reduce morbidity and mortality in patients with HFpEF.

- **I-PRESERVE**
  - Primary composite endpoint of death from any cause or hospitalization for a cardiovascular cause (HF, MI, unstable angina, arrhythmia, or stroke) in HF patients with LVEF ≥45%
  - HR=0.95 (95% CI, 0.86 to 1.05); p=0.35

- **CHARM-preserved**
  - Primary composite outcome of cardiovascular death or admission to hospital for chronic HF in HF patients with LVEF >40%
  - HR=0.89 (95% CI, 0.77–1.03); p=0.118

Adjusting for HR=0.86, p=0.051

**TOPCAT (2014)**

**Spironolactone for Heart Failure with Preserved Ejection Fraction**

Conclusions: In patients with heart failure and a preserved ejection fraction, treatment with spironolactone did not significantly reduce the incidence of the primary composite outcome of death from cardiovascular causes, aborted cardiac arrest, or hospitalization for the management of heart failure.

**TOPCAT**: Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist

It takes a Taskforce to develop a Guideline...

But it takes THOUSANDS to reach Evidence...

**Summary**

- ACEIs, ARBs, β-blockers and MRAs are effective in reducing CV morbidity and mortality in patients with chronic HFrEF\(^1^–^6\)
  - Despite the availability of proven treatment options for chronic HFrEF, mortality is high\(^1^–^4\); nearly half of patients die within 5 years of diagnosis\(^5\)
  - Devices therapy (ICD & CRT) and VADs are seen to be life-saving in selected patients

- HFrEF is associated with high levels of morbidity and mortality\(^8\)
  - No proven therapies exist for the treatment of HFpEF

**References**


HFrEF = heart failure with reduced ejection fraction  
HFpEF = heart failure with preserved ejection fraction