Heart Failure
**Definition of heart failure**

HF is a clinical syndrome in which patients have the following features:

- **Symptoms typical of HF**
  - (breathlessness at rest or on exercise, fatigue, tiredness, ankle swelling)

- **Signs typical of HF**
  - (tachycardia, tachypnoea, pulmonary rales, pleural effusion, raised jugular venous pressure, peripheral oedema, hepatomegaly)

- **Objective evidence of a structural or functional abnormality of the heart at rest**
  - (cardiomegaly, third heart sound, cardiac murmurs, abnormality on the echocardiogram, raised natriuretic peptide concentration)
Diagnosis

- According to the Working Group in Heart Failure, CHF is a syndrome where the diagnosis has the following essential components:

  - A combination of:
    - Symptoms, typically breathlessness or fatigue
    - Cardiac dysfunction documented at rest

  - The diagnosis is supported by:
    - Response to treatment directed towards heart failure
Incidence

♥ 4.8 million in the United States

♥ 400,000 new cases/year

♥ 20 million patients with asymptomatic LV dysfunction
Incidence continued

❤ 6-10% of patients over 65 y.o.

❤ #1 cause of hospital admission in patients over 65 y.o.

❤ Annual expenditure 20-40 billion/year
Mortality

- 250,000 patients die as a direct result of CHF per year
- 1-year mortality rate = 10%
- 5-year mortality = 50%
Contributors to Increased Incidence

♥ Improvements in:
  ♥ Survival post-MI
  ♥ Technologies (i.e., PCI, stents etc.)
  ♥ Medical Treatments for ischemic heart disease (statin, ACE-I, ASA)
  ♥ Overall survival
Etiology of Chronic Heart Failure

- Coronary artery disease accounts for about 65%
- Non-ischemic Cardiomyopathy:
  - Idiopathic
  - Hypertension
  - Valvular Heart Disease
  - Thyroid
  - Toxic or drug-induced
Etiology of Acute Heart Failure

- Myocardial ischemia-infarction
- Ventricular systolic or diastolic dysfunction
- Mitral valve regurgitation
- Ventricular rupture
- Myocarditis
- Uncontrolled HTN
- Other PE, arrhythmia's, pulmonary HTN
Chronic Heart Failure

Systolic Failure

Diastolic Failure
Diastolic Heart Failure - Definition

- Signs and/or symptoms of CHF

- Normal or mildly reduced left ventricular systolic function (EF > 45%)

- Evidence of abnormal left ventricular relaxation, filling, diastolic distensibility and diastolic stiffness (age adjusted E/A ratio, DT, IVRT, pv-S/D, pvA)
How Do You Find Patients With Diastolic Heart Failure?

- **Patients with hypertension** (25%) and especially if there is sign of left ventricular hypertrophy (90%)

- **Patients with diabetes** and especially in those with complications (neuropathy, nephropathy)

- **Patients with ischaemic heart disease** and angina and no previous myocardial infarction
Epidemiological Aspects of Diastolic Heart Failure

- Symptoms of heart failure with normal left ventricular function is synonymous with diastolic heart failure

- Based on different community studies the prevalence of heart failure with normal systolic function varies between 30-50%

Strong Heart Study (Arizona) et al. Am J Cardiol 2000
Framingham Offspring Study et al. JACC 1999
Hillingdon Study (UK) et al. Eur Heart J 1999
Olmsted County (Minnesota) et al. Circulation 1998
Pathophysiology of Heart Failure: Left Ventricular Remodeling

Left-ventricular (LV) remodeling is defined as a change in LV geometry, mass and volume that occurs over a period of time.
Common Symptoms of Heart Failure

- Dyspnea on exertion
- Paroxysmal nocturnal dyspnea
- Orthopnea
- Fatigue
- Lower extremity edema
- Cough, usually worse at night
- Nausea, vomiting, anorexia, ascites
- Nocturia
- Sleep disorders
Common Physical Findings of Heart Failure

- Elevated jugular venous pressure
- Hepatojugular reflux
- Displaced apical impulse
- S3 gallop
- Pulmonary rales
- Hepatomegaly
- Peripheral edema
- Ascites
- Signs of cardiac cachexia
<table>
<thead>
<tr>
<th>Key features of the clinical examination in patients with heart failure</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Appearance</strong></td>
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<tr>
<td><strong>Pulse</strong></td>
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<tr>
<td><strong>Blood pressure</strong></td>
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<tr>
<td><strong>Fluid overload</strong></td>
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<td></td>
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<td><strong>Lungs</strong></td>
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<td></td>
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<tr>
<td><strong>Heart</strong></td>
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ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure
Flow-chart for the diagnosis of HF in untreated patients with symptoms suggestive of HF using natriuretic peptides

Clinical examination, ECG, Chest X-ray

Natriuretic peptides

- BNP < 100 pg/ml
  - NT-proBNP < 400 pg/ml
  - Chronic HF unlikely

- BNP 100-400 pg/ml
  - NT-proBNP 400-2000 pg/ml
  - Uncertain diagnosis

- BNP > 400 pg/ml
  - NT-proBNP > 2000 pg/ml
  - Chronic HF likely
Tests for diagnosis of heart failure

- ECG
- **Echocardiography**
- Chest X-ray
- Blood count
- Blood chemistry
- Exercise test
- **Natriuretic peptides (BNP)**
- Cardiac cath.
# New York Heart Association Functional Classification

<table>
<thead>
<tr>
<th>I</th>
<th>No limitation of physical activity, no symptoms with ordinary activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>II</td>
<td>Slight limitation, symptoms with ordinary activities</td>
</tr>
<tr>
<td>III</td>
<td>Marked limitation, symptoms with less than ordinary activities</td>
</tr>
<tr>
<td>IV</td>
<td>Severe limitation, symptoms of heart failure at rest</td>
</tr>
</tbody>
</table>
Killip classification

Designed to provide a clinical estimate of the severity of circulatory derangement in the treatment of acute myocardial infarction.

Stage I  No heart failure.
         No clinical signs of cardiac decompensation

Stage II Heart failure.
         Diagnostic criteria include rales, S3 gallop, and pulmonary venous hypertension.
         Pulmonary congestion with wet rales in the lower half of the lung fields.

Stage III Severe heart failure.
         Frank pulmonary oedema with rales throughout the lung fields

Stage IV Cardiogenic shock.
         Signs include hypotension (SBP <90 mmHg), and evidence of peripheral vasoconstriction such as oliguria, cyanosis and sweating.
<table>
<thead>
<tr>
<th>ACC/AHA Stages of HF</th>
<th>NYHA Functional Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage A</strong></td>
<td><strong>Class I</strong></td>
</tr>
<tr>
<td>At high risk for developing HF. No identified structural or functional abnormality; no signs or symptoms.</td>
<td>No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, or dyspnoea.</td>
</tr>
<tr>
<td><strong>Stage B</strong></td>
<td><strong>Class II</strong></td>
</tr>
<tr>
<td>Developed structural heart disease that is strongly associated with the development of HF, but without signs or symptoms.</td>
<td>Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in fatigue, palpitation, or dyspnoea.</td>
</tr>
<tr>
<td><strong>Stage C</strong></td>
<td><strong>Class III</strong></td>
</tr>
<tr>
<td>Symptomatic HF associated with underlying structural heart disease.</td>
<td>Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity results in fatigue, palpitation, or dyspnoea.</td>
</tr>
<tr>
<td><strong>Stage D</strong></td>
<td><strong>Class IV</strong></td>
</tr>
<tr>
<td>Advanced structural heart disease and marked symptoms of HF at rest despite maximal medical therapy.</td>
<td>Unable to carry on any physical activity without discomfort. Symptoms at rest. If any physical activity is undertaken, discomfort is increased.</td>
</tr>
</tbody>
</table>

ACC = American College of Cardiology; AHA, American Heart Association.  
ACC / AHA Guidelines

Stage A
High risk for CHF
No structural heart disease
or CHF symptoms

Stage B
Structural heart disease
No CHF symptoms

Stage C
Structural heart disease
Prior or current CHF symptoms

Stage D
Refractory CHF requiring special interventions
**Stage A**

High risk for CHF
No structural heart disease or CHF symptoms

eg, Patients with:
hypertension, coronary artery disease, diabetes mellitus, or patients using cardiotoxins or with CM

**Therapy:**
treat hypertension, encourage smoking cessation, treat lipid disorders, encourage regular exercise, discourage alcohol intake and illicit drug use, ACE inhibition in appropriate patients
Stage B

Structural heart disease
No CHF symptoms

eg, Patients with:
- previous MI
- LV systolic dysfunction
- asymptomatic valvular disease

Therapy:
All measures under Stage A,
ACE inhibitors in appropriate patients, b blockers in appropriate patients
Stage C

Structural heart disease
Prior or current
CHF symptoms

eg, Patients with:
known structural
heart disease,
shortness of breath
and fatigue
reduced exercise tolerance

Therapy:
All measure under stage A,
drugs for routine use
(diuretics, ACE inhibitors,
b blockers, digitalis),
dietary salt restriction
Stage D

Refractory CHF requiring special interventions

eg, Patients who have marked symptoms at rest despite maximal medical therapy (eg, those who are recurrently hospitalised or cannot be safely discharged from the hospital without specialised interventions)

Therapy:
All measures under Stages A, B and C, mechanical assist devices, heart transplantation, continuous iv inotropic infusions for palliation, hospice care
## Conditions associated with a poor prognosis in HF

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Clinical</th>
<th>Electrophysiological</th>
<th>Functional/Exertional</th>
<th>Laboratory</th>
<th>Imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advanced age*</td>
<td>Hypotension*</td>
<td>Tachycardia</td>
<td>Reduced work, Low peak VO2*</td>
<td>Marked elevation of BNP/NT pro-BNP*</td>
<td>Low LVEF*</td>
</tr>
<tr>
<td>Ischaemic aetiology*</td>
<td>NYHA</td>
<td>Wide QRS*</td>
<td></td>
<td>Hyponatraemia*</td>
<td></td>
</tr>
<tr>
<td>Resuscitated sudden death*</td>
<td>Functional Class III-IV*</td>
<td>LV hypertrophy</td>
<td></td>
<td>Elevated troponin*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Recent HF hospitalization*</td>
<td>Complex ventricular arrhythmias*</td>
<td></td>
<td>Elevated biomarkers, neurohumoral activation*</td>
<td></td>
</tr>
<tr>
<td>Poor compliance</td>
<td>Tachycardia</td>
<td>Low heart rate variability</td>
<td>Poor 6 min walk distance</td>
<td>Elevated creatinine/BUN</td>
<td>Increased LV volumes</td>
</tr>
<tr>
<td>Renal dysfunction</td>
<td>Pulmonary rales</td>
<td>T-wave alternans</td>
<td>High VE/VCO2 slope</td>
<td>Elevated bilirubin</td>
<td>Low cardiac index</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Aortic stenosis</td>
<td>Atrial fibrillation</td>
<td>Periodic breathing</td>
<td>Anaemia</td>
<td>High left ventricular filling pressure</td>
</tr>
<tr>
<td>Anaemia</td>
<td>Low body mass index</td>
<td></td>
<td></td>
<td>Elevated uric acid</td>
<td>Pulmonary hypertension</td>
</tr>
<tr>
<td>COPD</td>
<td>Sleep related breathing disorders</td>
<td></td>
<td></td>
<td></td>
<td>Impaired right ventricular function</td>
</tr>
<tr>
<td>Depression</td>
<td></td>
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</table>
ACE inhibitors

- An ACE inhibitor is recommended in all patients with symptomatic HF and an EF ≤40%

- Treatment with an ACE inhibitor improves LV function, patient well-being, reduces hospital admission for worsening HF and increases survival

Class of recommendation I, level of evidence A

- In hospitalised patients, treatment should be initiated before discharge
ACE Inhibitors: ESC Guidelines

- ACE inhibitors are recommended as first-line therapy in patients with a reduced LV systolic function (LVEF < 40-45%)
- In the absence of fluid retention ACE inhibitors should be given first, in the presence of fluid retention together with diuretics
- ACE inhibitors should be uptitrated to the dosages shown to be effective in large trials
- They should not be titrated based on symptomatic improvement
Management: Angiotensin-Converting Enzyme Inhibitors

ACE inhibitors suppress conversion of angiotensin I to angiotensin II

Benefits of ACE inhibitors

- Reduce cardiac hypertrophy
- Attenuate ventricular remodeling post MI
- Cause peripheral vasodilation
- Decrease sympathetic tone
- Enhance activity of kinin
Clinical Use Of ACE Inhibitors

♥ Recommended for all patients with CHF and systolic dysfunction

♥ Recommended for patients with systolic dysfunction and no symptoms of CHF

♥ Prevents CHF in patients with preserved LV (EF > 40%) and CAD or risk factors (HOPE Trial)
Initiation of ACE inhibitor - Therapy should be initiated with low doses to avoid excessive hypotension.

Target doses - Doses should be slowly titrated to achieve targeted dose used in major clinical trials.
ACE Inhibitors: Adverse Effects

 ♥ Severe hypotension, syncope, renal insufficiency, hyperkalemia and angioedema

 ♥ Some adverse effects can be avoided by initiating and titrating by low doses. Need to monitor BP, lytes and renal function

 ♥ Most frequent side effect is cough (5-15%) - cross sensitivity likely
ACE Inhibitors Cont . . .

♥ Contraindications
  ♥ Allergic reaction
  ♥ Pregnancy
  ♥ Very low BP (<80mmHg)
  ♥ Creatinine > 3
  ♥ Bilateral renal artery stenosis
  ♥ Potassium > 5.5
Angiotensin receptor blockers (ARBs)

- An ARB is recommended in all pts. with HF and an EF $\leq 40\%$ who:
  - remain symptomatic despite optimal Rx with an ACE inhibitor and $\beta$-blocker
  - as an alternative in pts. intolerant of an ACE inhibitor

- Unless pts. are treated with an aldosterone antagonist

- Treatment with an ARB improves LV function, patient well-being and reduces hospital admission for worsening HF

*Class of recommendation I, level of evidence A*

- Treatment reduces the risk of CV death

*Class of recommendation IIa, level of evidence B*

- In hospitalised pts., treatment with an ARB should be initiated before discharge
Angiotensin Receptor Blockers (ARBs)

- ARBs could be considered in patients who do not tolerate ACE inhibitors.
- It has been proven that they are as effective as ACE inhibitors in morbidity reduction.
- In addition to ACE inhibition ARBs improve symptoms and reduce hospitalisations for CHF.
- The addition of ARBs to ACE inhibition and β blockade can be recommended at present.
β-blockade

- A β-blocker should be used in all patients with symptomatic HF and an EF ≤40%.

- β-Blockade improves ventricular function and patient well-being, reduces hospital admission for worsening HF and increases survival.

Class of recommendation I, level of evidence A

- In hospitalised patients, treatment with a β-blocker should be initiated cautiously before discharge.
β Blockade in CHF - ESC Guidelines

- β blocking agents are recommended for the treatment of all patients with stable mild, moderate and severe CHF from ischaemic and non-ischaemic origin... on standard treatment including ACE inhibition and diuretics

- β blocking agents are recommended in patients with LV dysfunction with/without CHF post-MI for survival benefit
ACC / AHA Practice Guidelines: β blockers

• β adrenergic blockade in all stable CHF patients, unless contraindicated

• Patients should have no or minimal evidence of fluid retention and should not have required treatment recently with an intravenous positive inotropic agent
Benefit Of Beta Blockers

♥ Improve symptoms and clinical status
♥ Increase LV ejection fraction
♥ Little effect on exercise tolerance
♥ Reduce frequency of hospitalizations for heart failure
♥ Decrease mortality
Clinical Use Of Beta Blockers

❤️ Recommended for patients with NYHA class II-IV

❤️ General contraindications:
❤️ Decompensated heart failure
❤️ Severe claudication
❤️ Bronchospasm
❤️ Advanced heart block
❤️ Use with caution if patient requires inotropes for support of circulatory function
Clinical Use Cont . . .

♥ Start at very low dose with gradual increments (doubling every 2-4 weeks)
♥ Abrupt withdrawal can lead to dramatic deterioration

♥ Patient education paramount
Beta-Blockers: Adverse Effects

♥ Hypotension
♥ Bradycardia
♥ Worsening heart failure
Aldosterone antagonists

• The addition of an aldosterone antagonist is recommended in all patients with an EF ≤35%, severe symptomatic HF without hyperkalaemia or significant renal dysfunction

• Aldosterone antagonists reduce hospital admission for worsening HF and increase survival when added to existing therapy, including an ACE inhibitor

*Class of recommendation I, level of evidence B*

• In such hospitalised patients, treatment with an aldosterone antagonist should be initiated before discharge

ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure
Aldosterone antagonism is recommended in advanced CHF (NYHA III and IV) in addition to ACE inhibition to improve survival and morbidity.
Aldosterone Antagonists

♥ Angiotensin II causes aldosterone production in the adrenal cortex
♥ Acts on the cortical collecting tubules to conserve sodium

♥ Originally thought to be blocked by ACE inhibitors. Now known that ACE I does not suppress production
Angiotensin I

→

Angiotensin II

→

Hypertrophy

Apoptosis

Aldosterone

→

Spironolactone

→
Aldosterone Antagonists

♥ Potassium-sparing diuretics
♥ Compete with aldosterone for receptor sites in the distal renal tubules
♥ Increase sodium and water excretion while conserving potassium and hydrogen ions
♥ Spironolakton and elprenenon
Aldosterone Antagonist

♥ Consensus Guidelines:
♥ Use in Class III and IV heart failure
♥ Should be given low dose
(12.5mg - 25mg daily)
Aldosterone Antagonists: Averse Effects

♥ Arrhythmia, nervousness, dizziness, fatigue, rash, headache, breast tenderness, enlargement of breast in males, sexual dysfunction, increased hair growth in females

♥ May decrease effects of anticoagulants

♥ Use with caution in renal insufficiency
Digitalis Glycosides

- Cardiac glycosides are recommended in atrial fibrillation and symptomatic CHF in order to improve cardiac function and symptoms.

- A combination of digitalis and beta blockade appears superior to either agent alone.

- In sinus rhythm digoxin may improve the clinical status in persisting CHF symptoms due to LV systolic dysfunction.
Management: Digitalis

❤️ Digitalis glycosides inhibit sodium-potassium adenosine triphosphatase. Inhibition of this enzyme in cardiac cells results in an increase in the contractile state of the heart

❤️ Benefits of digitalis may be related to enzyme inhibition in noncardiac tissue
Clinical Use: Digitalis

♥ Therapy is initiated at dose of .25mg daily. Lower doses such as .125mg daily or every other day, particularly if the patient is elderly or has impaired renal function

♥ Use with caution in patients with significant sinus or atrioventricular block

♥ Not indicated for stabilization of acute decompensated heart failure
Digitalis: Adverse Effects

♥ Cardiac arrhythmia
♥ Gastrointestinal symptoms
♥ Neurologic complaints

♥ Side effects are usually associated with levels >2ng/ml
Management

Treatment: General Measures

Fluid Status

- Compensated
- Non-Compensated
Diuretics

- Diuretics are recommended in patients with clinical signs or symptoms of congestion
- Diuretics provide relief from the symptoms and signs of pulmonary and systemic venous congestion
- Diuretics cause activation of the renin-angiotensin-aldosterone system and should be used in combination with an ACE inhibitor/ARB

Class of recommendation I, level of evidence B

ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure
Adverse Effects: Loop Diuretics

♥ Electrolyte imbalance
♥ Higher incidence of mortality
♥ Hyperuricemia
♥ Ototoxicity
♥ Glucose intolerance
Lifestyle Measures

♥ Sodium restriction (2G/day)
♥ No salt substitutes
♥ Daily weight
♥ Fluid restriction
Lifestyle Measures Cont . . .

♥ Exercise
♥ Avoid heavy lifting
♥ Avoid temperature extremes
Class I recommendations for drugs in patients with symptomatic systolic dysfunction

<table>
<thead>
<tr>
<th>Drug Type</th>
<th>Indication</th>
<th>Class Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitor</td>
<td>All patients*</td>
<td>Class I Level A</td>
</tr>
<tr>
<td>ARB</td>
<td>ACE intolerant/persisting signs or symptoms on ACEI/B-blockade*</td>
<td>Class I Level A</td>
</tr>
<tr>
<td>B-Blocker</td>
<td>All patients*</td>
<td>Class I Level A</td>
</tr>
<tr>
<td>Aldosterone antagonist</td>
<td>Severe symptoms on ACEI*</td>
<td>Class I Level A</td>
</tr>
<tr>
<td>Diuretic</td>
<td>All patients with signs or symptoms of congestion</td>
<td>Class I Level B</td>
</tr>
</tbody>
</table>

*unless contraindications or not tolerated
Management: Devices

- ICD implantable cardioverter-defibrillator
- Cardiac resynchronisation therapy
### Class I recommendations for devices in patients with LV systolic dysfunction

<table>
<thead>
<tr>
<th>ICD</th>
<th></th>
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<tbody>
<tr>
<td>Prior resuscitated cardiac arrest</td>
<td>Class I Level A</td>
<td></td>
</tr>
<tr>
<td>Ischaemic aetiology and &gt;40 days of MI</td>
<td>Class I Level A</td>
<td></td>
</tr>
<tr>
<td>Non-ischaemic aetiology</td>
<td>Class I Level B</td>
<td></td>
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<tr>
<th>CRT</th>
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</thead>
<tbody>
<tr>
<td>NYHA Class III/IV and QRS &gt;120 ms</td>
<td>Class I Level A</td>
<td></td>
</tr>
<tr>
<td>To improve symptoms/reduce hospitalization</td>
<td>Class I Level A</td>
<td></td>
</tr>
<tr>
<td>To reduce mortality</td>
<td>Class I Level A</td>
<td></td>
</tr>
</tbody>
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ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure
Resynchronization Therapy for Heart Failure

Methods:

- **Epicardial Approach**
  - Requires thoracotomy
  - Associated morbidity

- **Transvenous Approach**
  - As practical established
  - Requires access to the coronary sinus
  - Requires leads developed for LV application

Goal: Pace Right and Left Ventricles
Venogram Image of Cardiac Venous System
Lead V3

QRS=160 ms

---Therapy OFF---

---Therapy ON---

QRS=120 ms
Conclusions

- CHF is a very serious condition with a bad prognosis
- Diagnosis of CHF is based on objective evidence of cardiac dysfunction
- Symptoms as well as prognosis can be improved by appropriate therapy
- ACE inhibitors and β-blockers are very well documented and should be considered in all patients to improve survival, hospitalisation rates and QOL
- Dose levels should be titrated as in clinical trials to achieve maximum benefits
- Devices!