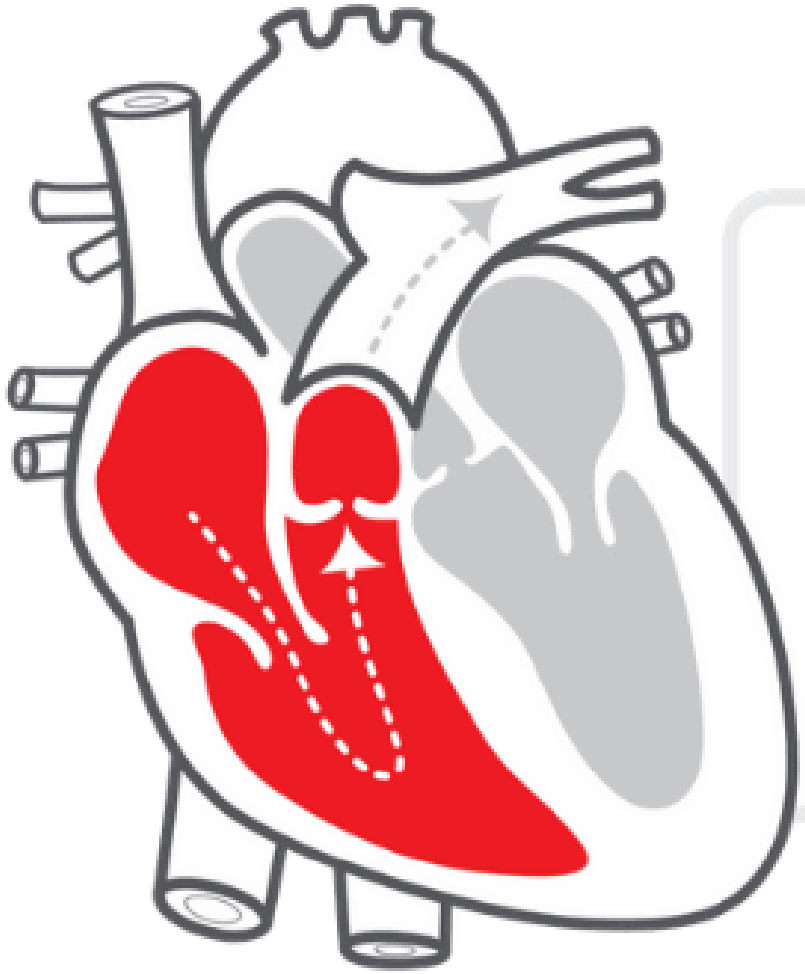
Congestive Heart Failure

Jan 25 2024

Radhika Nandur Bukkapatnam

What is Congestive Heart Failure?



It is a medical condition where the **HEART** cannot pump enough **blood** around the body as well as it should.

Congestive Heart Failure

Classification

Based on the Side of the Heart Affected

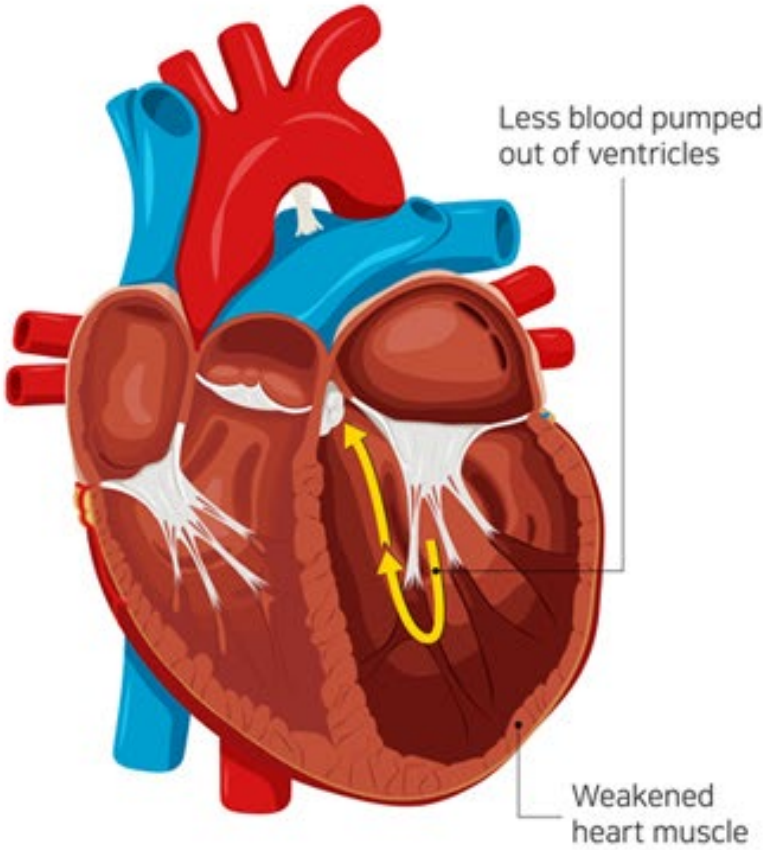
- **Left** Heart Failure
  - MI, Aortic Valve Disease, Mitral Stenosis, etc.
- **Right** Heart Failure
  - Pulmonary Stenosis, PH, PE, Chronic Lung Disease
- **Biventricular** Heart Failure
  - Cardiomyopathies
  - Right failure follows left

Based on Acute or Chronic

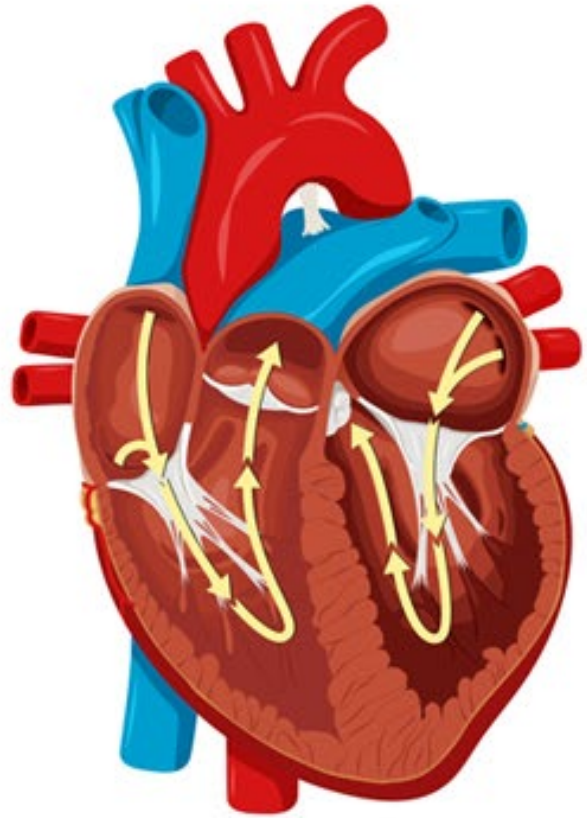
- **Acute** Heart Failure
  - Acute MI, Severe HTN, Acute Myocarditis, PE (Right Heart Failure)
- **Chronic** Heart Failure
  - Can develop in all types of heart failure
  - Recurrent Attacks
  - Persistent Symptoms

Based on Ejection Fraction (EF)

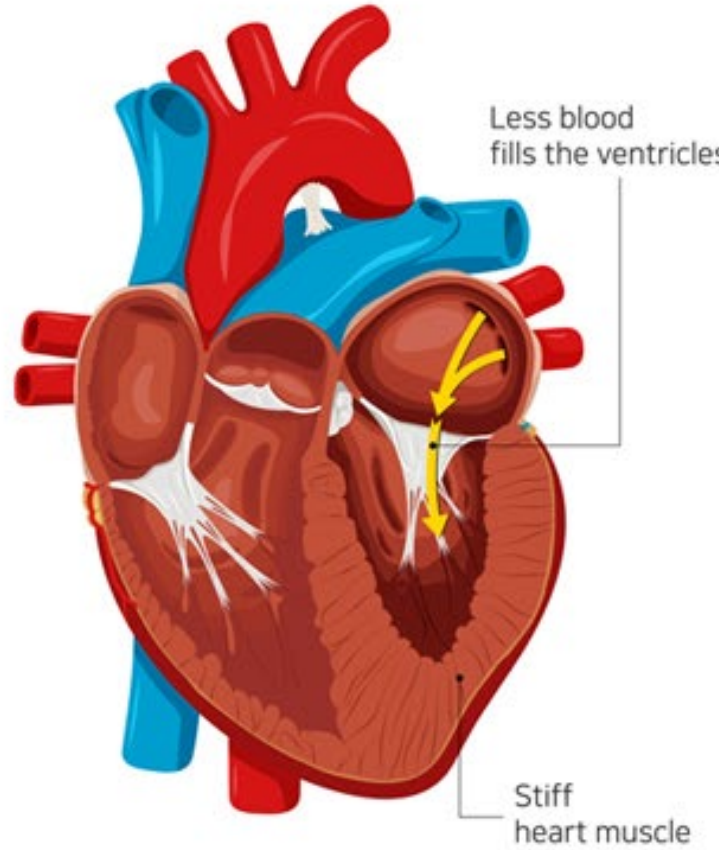
- Heart Failure with Reduced Ejection Fraction (HFrEF)
  - **EF < 40%**
- Heart Failure with Preserved Ejection Fraction (HFpEF)
  - **EF > 50%**
- Heart Failure with Mid-Range Ejection Fraction (HFmrEF)
  - **EF = 40-50%**



Systolic Dysfunction

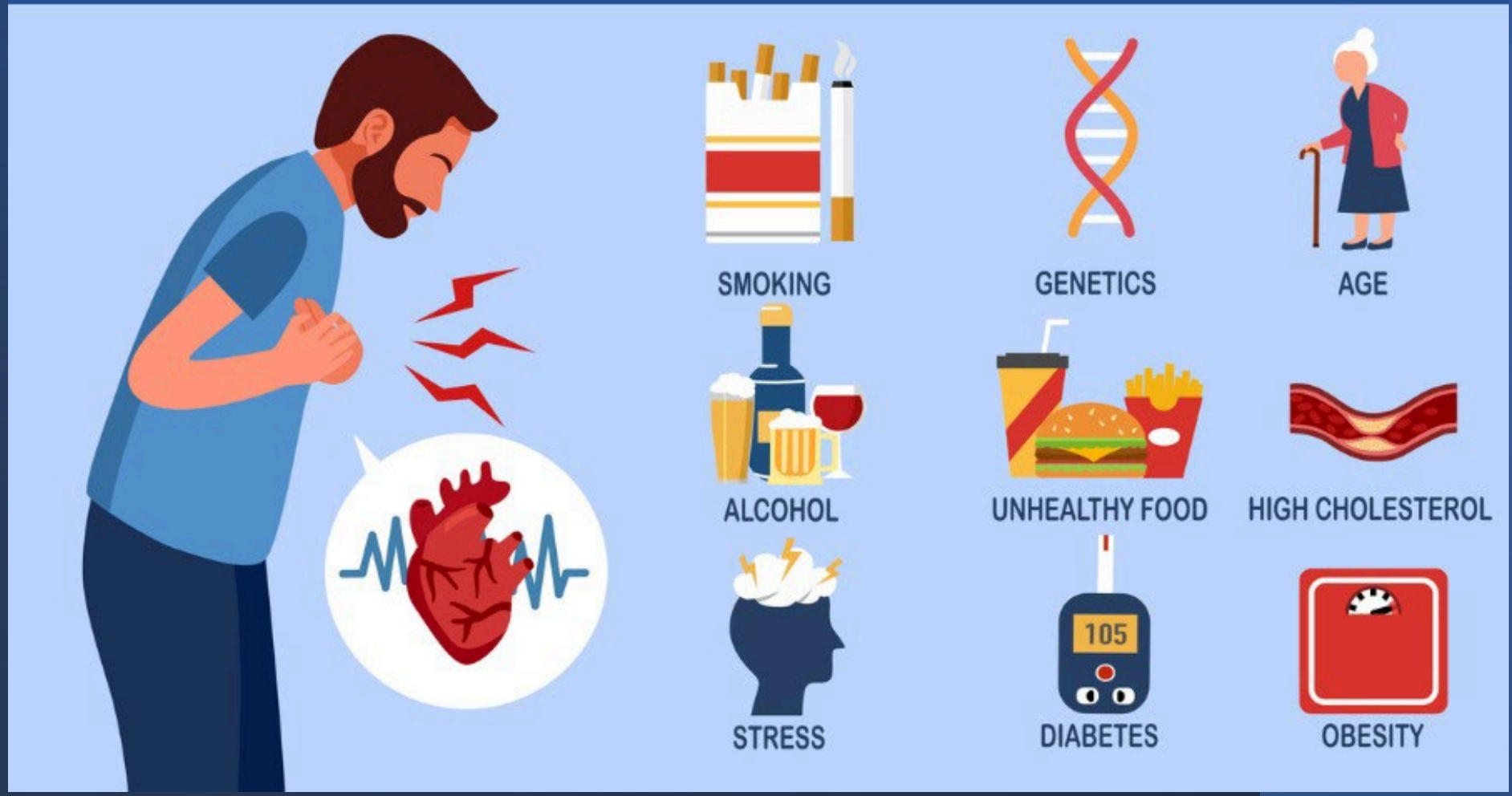


Normal

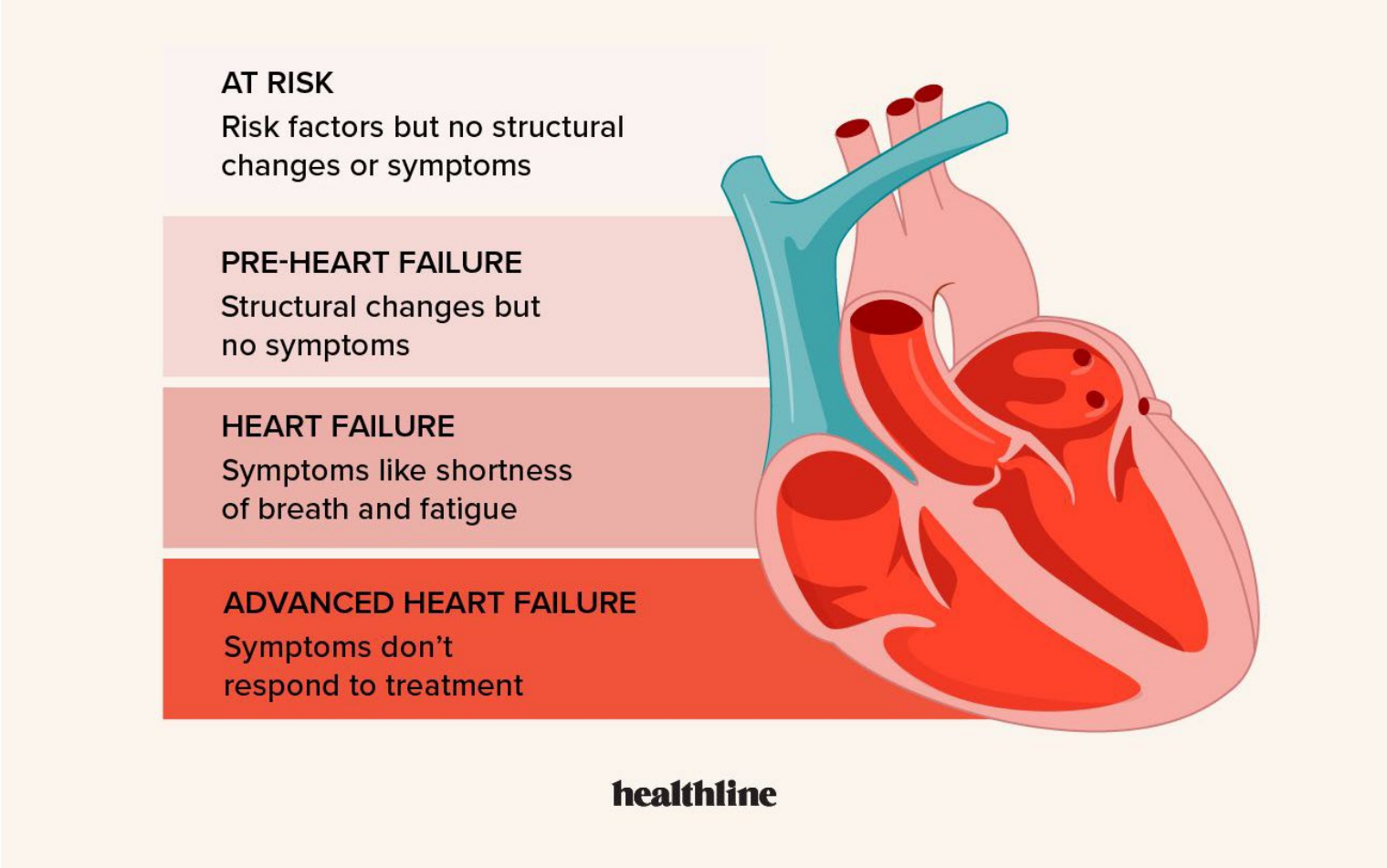


Diastolic Dysfunction

HEART DISEASE RISK FACTORS



STAGES OF HEART FAILURE



NYHA Class	Level of Clinical Impairment
I 	No limitation of physical activity. Ordinary physical activity does not cause undue breathlessness, fatigue, or palpitations.
II 	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in undue breathlessness, fatigue, or palpitations.
III 	Marked limitation of physical activity. Comfortable at rest, but less than ordinary physical activity results in undue breathlessness, fatigue, or palpitations.
IV 	Unable to carry on any physical activity without discomfort. Symptoms at rest can be present. If any physical activity is undertaken, discomfort is increased.

Congestive Heart Failure Symptoms

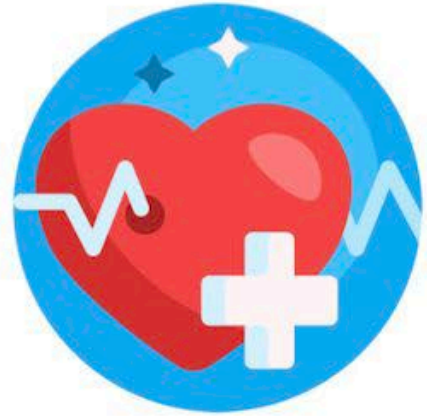
Shortness of breath & cough

Swelling of feet, ankles & legs

Weight gain

Tiredness or fatigue

Congestive Heart Failure



Signs

- Tachycardia
  - Fast heart rate
- Peripheral Cyanosis
  - Bluish discoloration to hands, feet, fingers, etc.
- Cold extremities
- Jugular Venous Distension
  - Swollen jugular vein
- Ascites
  - Fluid buildup in abdomen

- Dependent Pitting Edema
  - Swelling commonly in feet and ankles
- Hepatomegaly/Splenomegaly
  - Enlarged liver/spleen
- Abnormal Heart Sounds
  - Additional heart sounds, murmurs, etc.
- Abnormal Lung Sounds
  - Rhonchi, crackles, etc.

Congestive Heart Failure

Diagnosis

- Chest X-Ray (CXR)
  - Cardiomegaly
  - Pulmonary Edema
  - Pleural Effusion
  - Kerley B Lines
- Electrocardiogram (ECG)
  - Ventricular Hypertrophy
  - Arrhythmias
  - Ischemia
  - Low-voltage QRS

- Echocardiography (ECHO)
  - Ultrasound of the heart
  - Structural/Functional abnormalities of the heart
- Blood Tests
  - CBC, chemistry, glucose, LFTs, BNP, troponin, etc.
- Other Imaging Modalities
  - Cardiac CT/MRI
  - Nuclear Imaging

Congestive Heart Failure

Treatment

General Measures

- Treat underlying cause or precipitating factors
- Diet modifications
  - Sodium restriction
  - Possible fluid restriction
- Adequate rest
- Mild exercise
- Alcohol/Smoking cessation
- Adequate oxygen
- Health maintenance
  - Vaccines, wellness checks

Medications

- Diuretics
- ACE Inhibitors
- Angiotensin Receptor Blockers (ARBs)
- Beta Blockers
- Cardiac Glycosides

Surgical

- Revascularization
  - Angioplasty, CABG
- Valve Repair/Replacement

Device Therapy

- Cardiac Resynchronization (CRT)
  - Biventricular pacing
- Implantable Cardioverter Defibrillator (ICD)
  - To reduce incidence of cardiac death seen
- Ventricular Assisted Devices (VAD)
  - Often used as a bridge while waiting for definitive therapy

Congestive Heart Failure

Treatment - Diuretics

Class	Action	Medications	Oral Dose	Side Effects
Loop Diuretics	Sodium, Potassium & Water Excretion	Furosemide Torsemide Bumetanide	20-40 mg od/bd 10-20 mg od 0.5-1.0 mg od/bd	Hypokalemia, hyponatremia, hypotension, hypomagnesemia, hyperuricemia
Thiazide & Thiazide-like Diuretics	Sodium, Potassium & Water Excretion	Hydrochlorothiazide Chlorthalidone Metolazone	25 mg od/bd 12.5-25 mg od 2.5-5 mg od	Hypokalemia, hyponatremia, hypotension, hypercalcemia, hyperuricemia
Mineralocorticoid Receptor Antagonists	Sodium & Water Excretion Potassium Retention	Spironolactone Eplerenone	25-50 mg od 25 mg od	Hyperkalemia, acute renal dysfunction, gynecomastia (spironolactone)
Potassium Sparing	Sodium & Water Excretion Potassium Retention	Amiloride Triamterene	12.5-25 mg od 50-75 mg bd	Hyperkalemia, aggravate renal dysfunction, GI side effects

Congestive Heart Failure

Treatment - Medications

Class	Action	Medications	Oral Dose	Side Effects
Angiotensin Converting Enzyme Inhibitor (ACEI)	Inhibit conversion of Angiotensin I to Angiotensin II	Captopril Lisinopril Enalapril Ramipril Perindopril	6.25-25 mg TID 2.5-10 mg OD 2.5-10 mg BID 1.25-10 mg OD 4-8 mg OD	Hypotension, cough, aggravation of renal failure, hyperkalemia, angioedema
Angiotensin Receptor Blocker (ARB)	Block action of Angiotensin II on Angiotensin II Receptors	Losartan Valsartan Candesartan	12.5-25 mg BID 40-80 mg BID 4-32 mg OD	Hypotension, angioedema, aggravation of renal failure, hyperkalemia
Beta Blockers (BB)	Block Alpha, Beta-1 & Beta-2 Receptors	Carvedilol Bisoprolol Metoprolol (SR)	3.125-25 mg BID 1.25-25 mg OD 12.5 – 200 mg OD	Bradycardia, heart blocks, fatigue, aggravation of asthma, low BP
Digoxin	Positive inotropic effect. Inhibition of AV node by increased vagal tone	Digoxin	0.125-0.25 mg OD	Cardiac arrhythmias, visual disturbances. GI disturbances
Ivabradine	Selective blockade of pacemaker “funny” current in SA node	Ivabradine	5-7.5 mg BID	Sinus bradycardia, sinus node dysfunction, AV blocks

Congestive Heart Failure

Prognosis

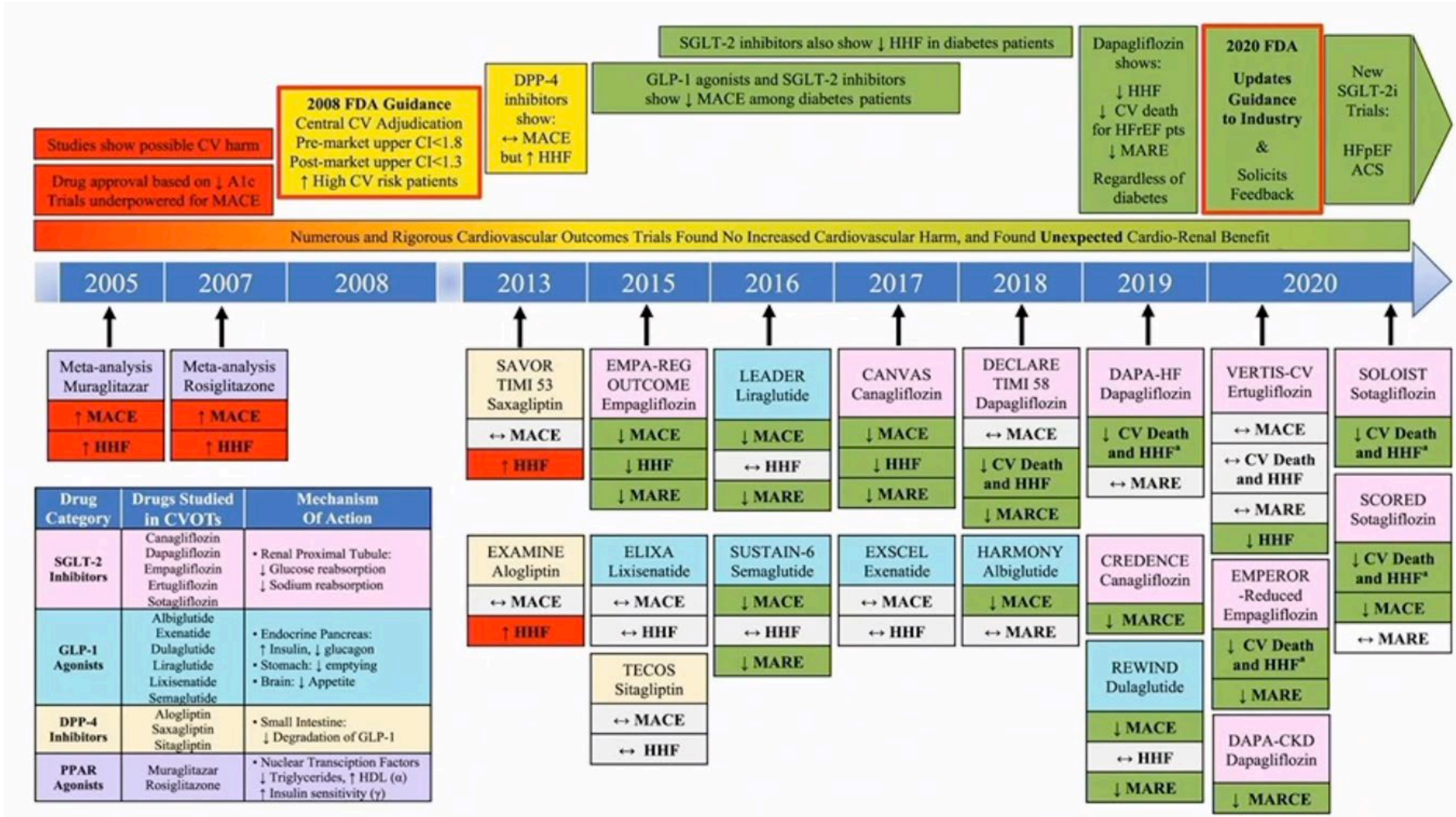
Factors that contribute to a worse prognosis include:

- Persistent Hyponatremia
- Markedly Elevated BNP
- Hypotension
  - Systolic < 120 mmHg
- Presence of 3rd Heart Sound

- Severe/Uncontrolled Diabetes
- Severe Anemia
- Cardiac Cachexia
- Need for Frequent Hospitalizations

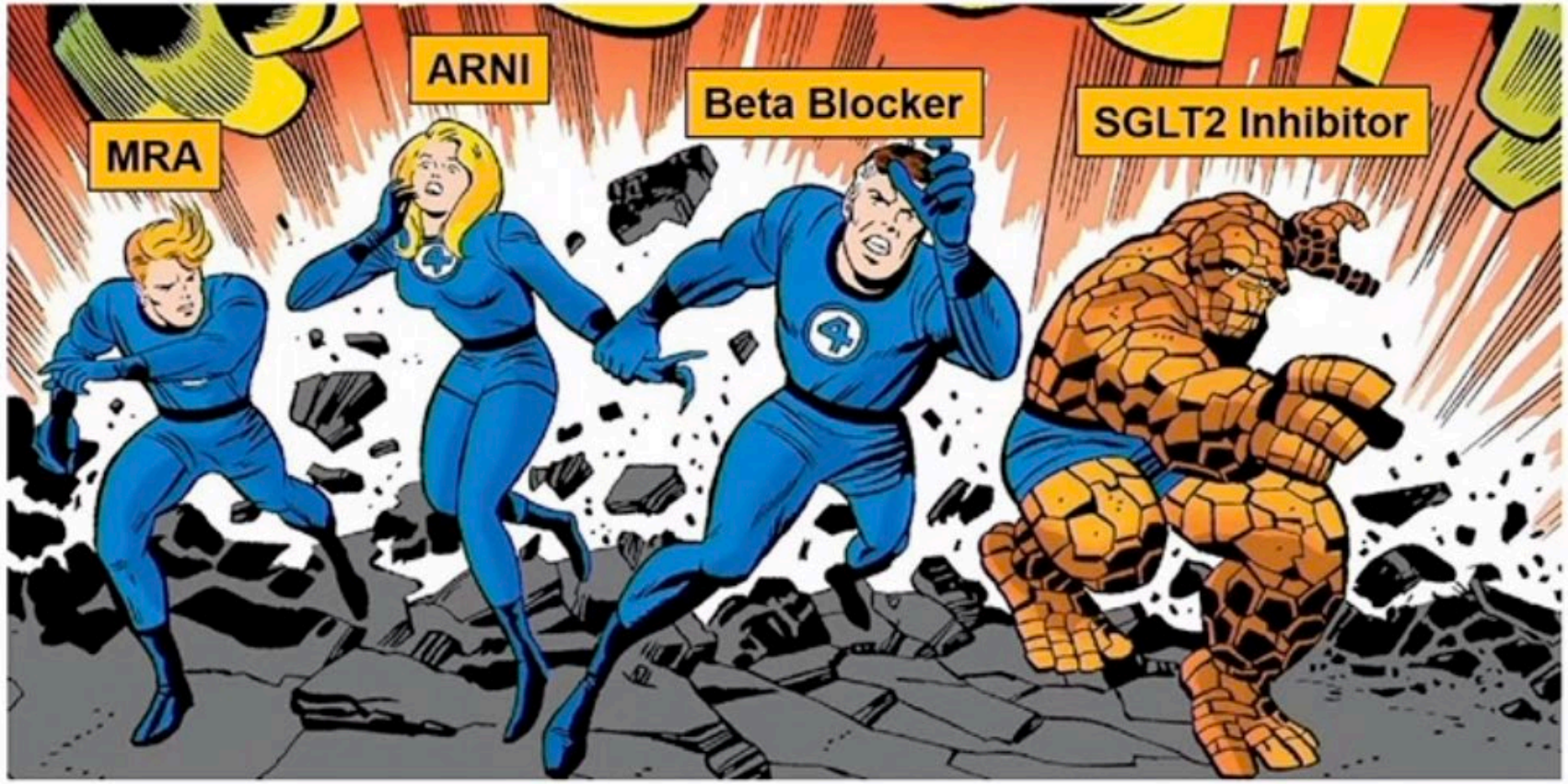
One-year survival in NYHA class II or III heart failure is about 85%

One-year survival in NYHA class IV heart failure is about 35%



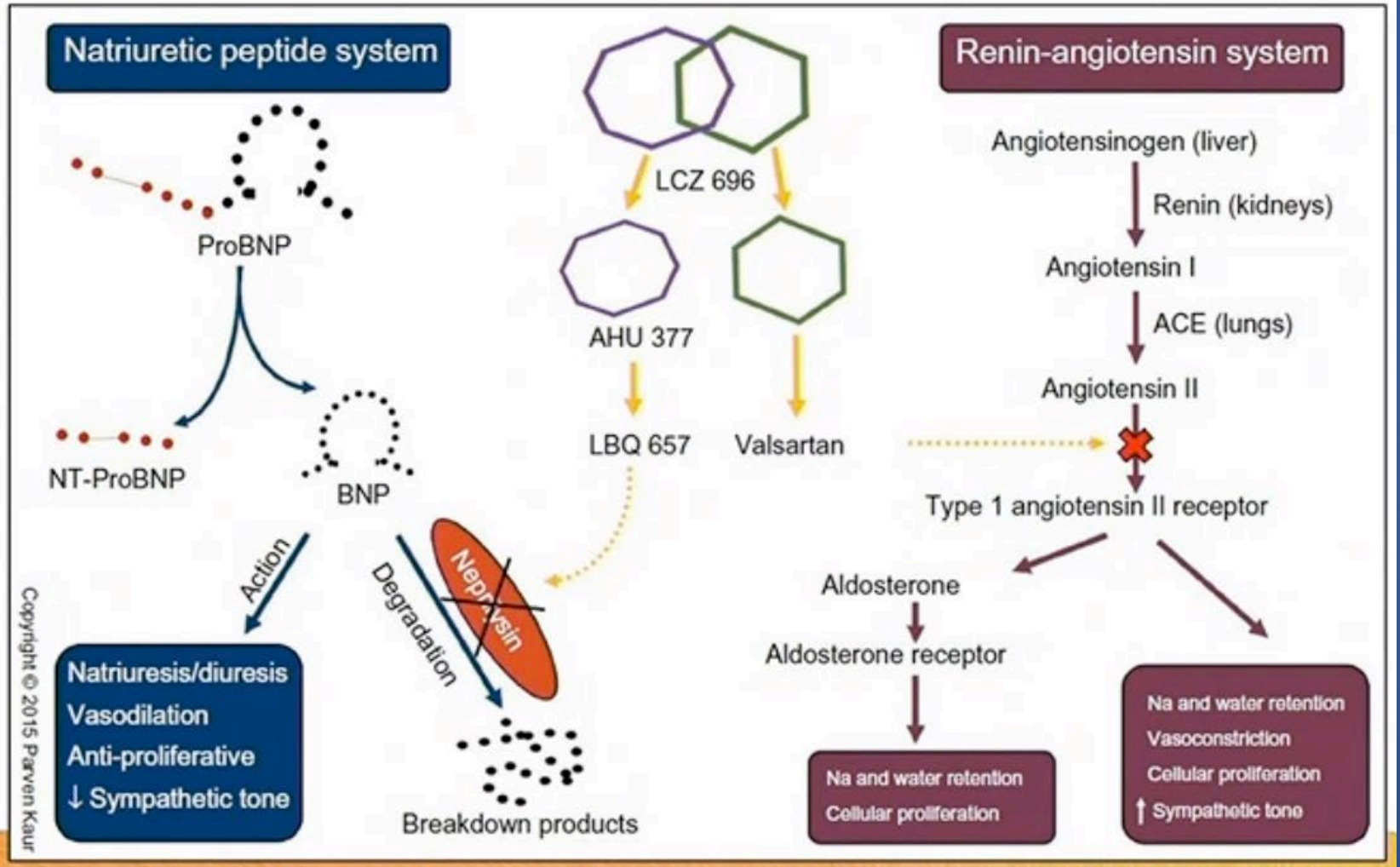
Drug Category	Drugs Studied in CVOTs	Mechanism Of Action
SGLT-2 Inhibitors	Canagliflozin Dapagliflozin Empagliflozin Ertugliflozin Sotagliflozin	• Renal Proximal Tubule: ↓ Glucose reabsorption ↓ Sodium reabsorption
GLP-1 Agonists	Albiglutide Exenatide Dulaglutide Liraglutide Lixisenatide Semaglutide	• Endocrine Pancreas: ↑ Insulin, ↓ glucagon • Stomach: ↓ emptying • Brain: ↓ Appetite
DPP-4 Inhibitors	Alogliptin Saxagliptin Sitagliptin	• Small Intestine: ↓ Degradation of GLP-1
PPAR Agonists	Muraglitazar Rosiglitazone	• Nuclear Transciption Factors ↓ Triglycerides, ↑ HDL (α) ↑ Insulin sensitivity (γ)

The Fantastic Four of HFrEF Management



Angiotensin-Receptor Neprilysin Inhibitor (ARNI) – Sacubitril/Valsartan

- Approved by the FDA July 2015
- First-in-class ARNI



Singh JS, et al. Vascular Health and Risk Management. 2015:11 283–295

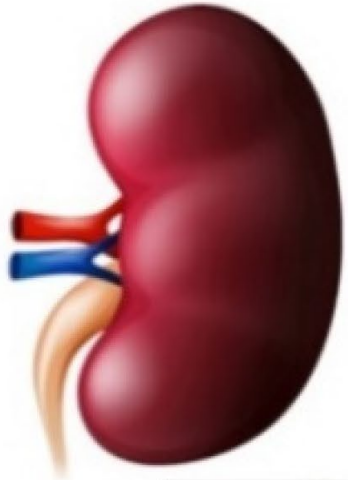

LOW STARTING DOSE
PRESCRIPTION ONLY MEDICINE
KEEP OUT OF REACH OF CHILDREN
Entresto 24/26
24.3 mg sacubitril/25.7 mg valsartan
Oral use
56 film-coated tablets
AUST R 234219
NOVARTIS
one tablet twice daily
24 mg/26 mg
Step up after
2–4 weeks
RECOMMENDED
STARTING DOSE
PRESCRIPTION ONLY MEDICINE
KEEP OUT OF REACH OF CHILDREN
Entresto 49/51
48.6 mg sacubitril/51.4 mg valsartan
Oral use
56 film-coated tablets
AUST R 234222
NOVARTIS
one tablet twice daily
49 mg/51 mg
Step up after
2–4 weeks
TARGET DOSE
PRESCRIPTION ONLY MEDICINE
KEEP OUT OF REACH OF CHILDREN
Entresto 97/103
97.2 mg sacubitril/102.8 mg valsartan
Oral use
56 film-coated tablets
AUST R 234218
NOVARTIS
one tablet twice daily
97 mg/103 mg

Clinical Use of Sacubitril/Valsartan (Entresto®)

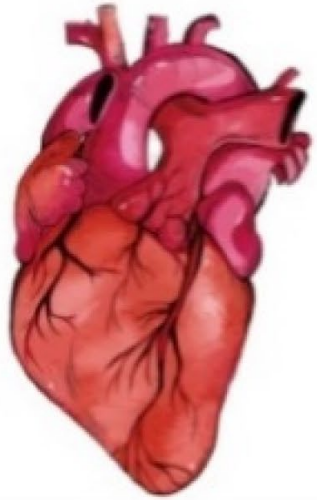
Characteristic	Recommendations
Dosing	Starting dose: 49/51 mg twice daily ➔ Step two: 97/103 mg twice daily Use the lower starting dose of 24/26 mg twice daily in the following situations: • Patients naïve to ACE-I/ARB or on a low dose of these agents • Severe kidney impairment (CrCl <30 mL/min) • Moderate hepatic impairment (Child-Pugh B Classification)
Adverse Effects	ARNI compared to enalapril, respectively (PARADIM-HF) • Symptomatic hypotension (14% vs. 9%) • Elevated SCr ≥2.5 (5% vs 6.5%) • Elevated potassium >5.5 (20% vs 23%) • Cough (11% vs 14%) • Angioedema (0.4% vs. 0.3%)
Contraindications	• Pregnancy • History of angioedema • Concomitant use with ACE-I, ARBs, aliskiren

NOTE:
Sacubitril/Valsartan can be safely initiated during hospitalization for ADHF (PIONEER-HF)

SGLT2 Inhibitors

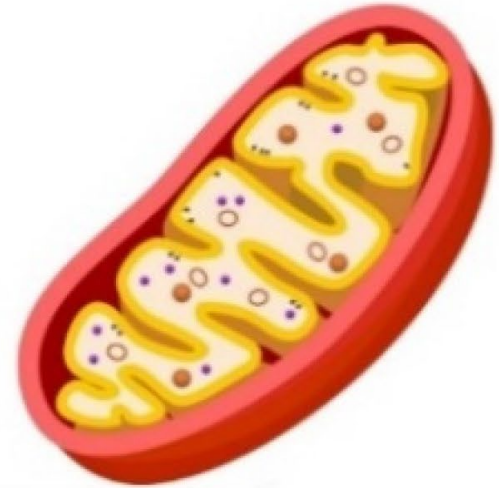


- Diuretic effect
- Glycosuria
- Nephroprotection
- Erythropioetin increase

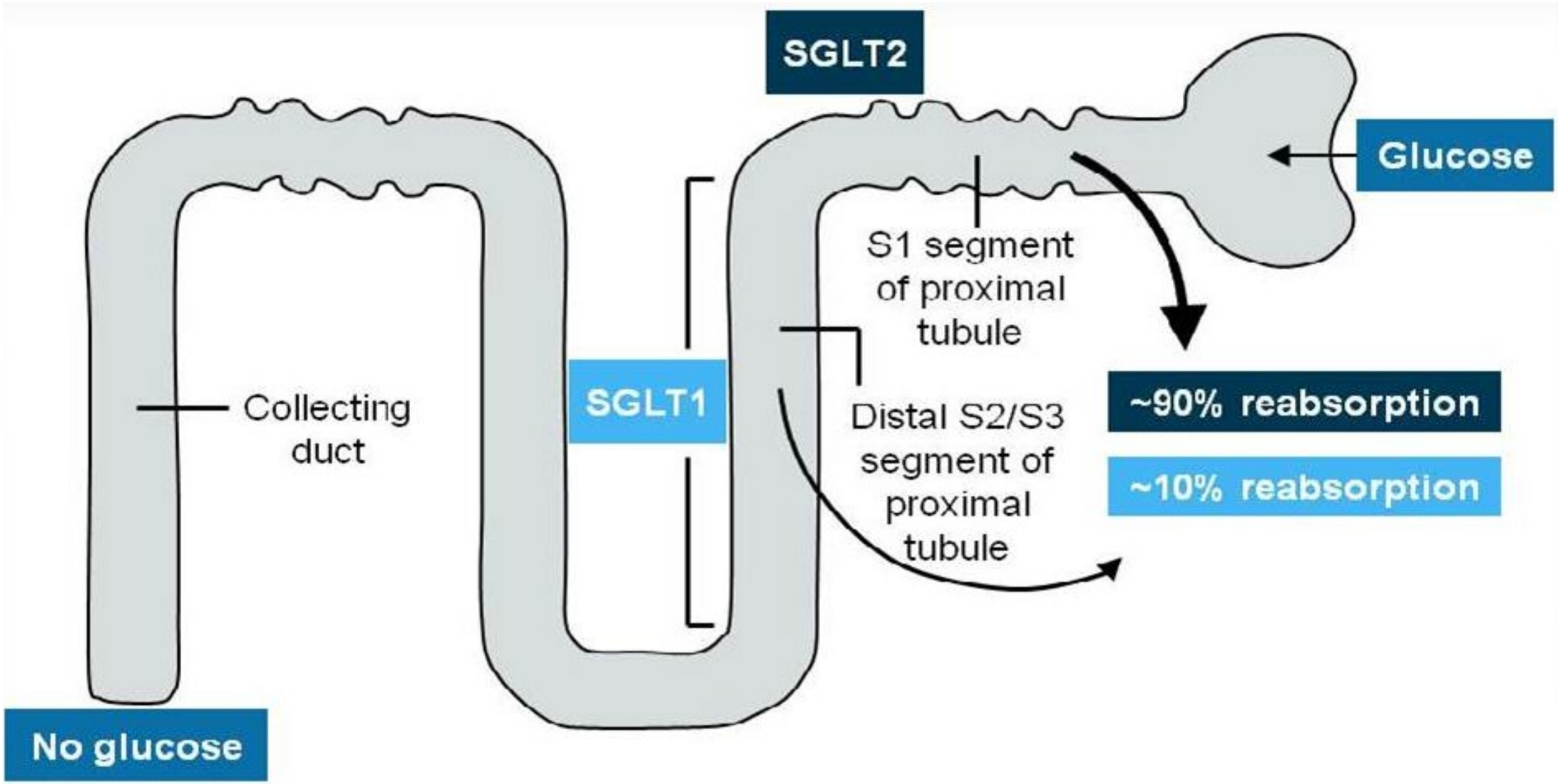


- Decreased left ventricular mass
- Improved diastolic function

- Reduced vascular stiffness
- Improved endothelial function



- Increased utilization of ketone bodies
- Improved energy processes


SGLT2
Glucose
S1 segment of proximal tubule
Collecting duct
SGLT1
Distal S2/S3 segment of proximal tubule
~90% reabsorption
~10% reabsorption
No glucose

Cardiovascular Trials of SGLT 2 Inhibitors

Characteristic	DAPA-HF	EMPEROR-REDUCED
Study Population	N=4744 24% female, 70% white **100% LVEF ≤ 40%** **42% T2DM**	N=3730 24% female, 70% white **100% LVEF ≤ 40%** **50% T2DM**
Intervention	Dapagliflozin 10 mg daily	Empagliflozin 10 mg daily
Primary Outcome (composite)	HHF, urgent visit, or CV death	CV death or HHF
Primary Outcome Results	HR 0.74 (0.65 to 0.85) **NNT = 20**	HR 0.75 (0.65 to 0.86) **NNT= 19**
Secondary Outcome Results	• 25% RRR in CV death/HHF • 17% RRR in death from any cause	• 30% RRR in total HHF • No statistical difference in death from any cause
Other Notes	***Findings were <u>independent</u> of diabetes status***	

N Engl J Med 2019; 381:1995-2008
N Engl J Med 2020; 383:1413-1424
N Engl J Med 2021; 384:117-128


Jardiance®
25 mg
Film-coated tablets
Empagliflozin
Oral use
30 film-coated tablets
Jardiance®
10 mg
Film-coated tablets
Empagliflozin
Oral use
30 film-coated tablets

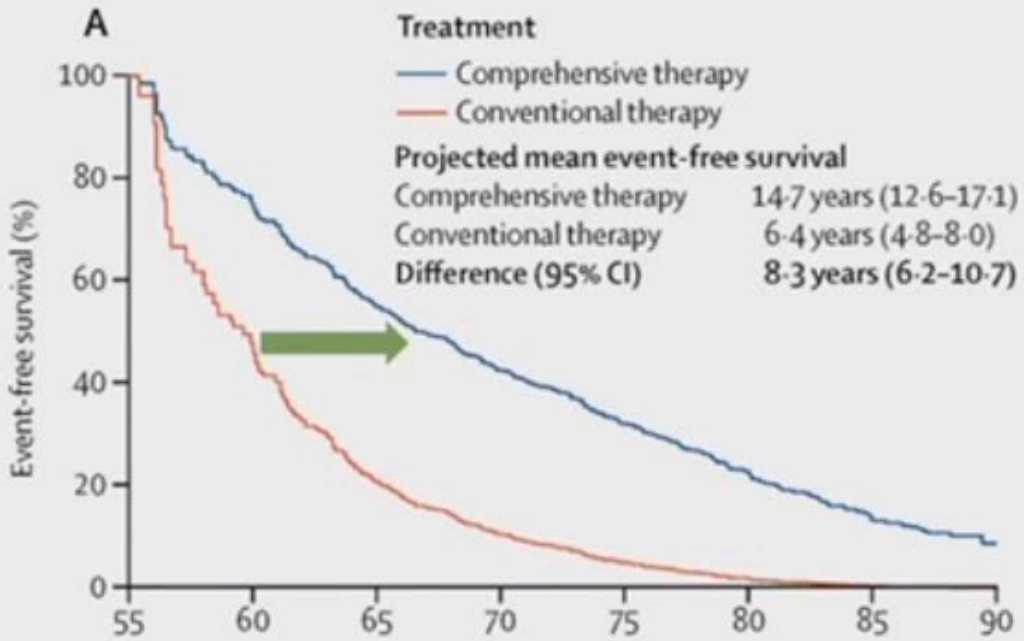

forxiga
dapagliflozin
10mg
28 film-coated tablets

Clinical Use of SGLT2 Inhibitors in HF

Characteristic	Recommendations
Dosing	Dapagliflozin: 10 mg once daily (OK to initiate if eGFR ≥ 25) • To reduce the risk of CV death and HHF in adults with HFrEF Empagliflozin: 10 mg once daily (OK to initiate if eGFR ≥ 20) • To reduce the risk of CV death and HHF in adults with HF
Adverse Effects	Dapagliflozin compared to placebo, respectively, (DAPA-HF) • Hypotension (0.3% vs. 0.5%) • Volume depletion (7.2% vs. 6.5%) • Urinary tract infection (0.5% vs. 0.7%) • Any DKA (3 cases vs. 0 cases) Empagliflozin compared to placebo, respectively (EMPEROR-REDUCED) • Symptomatic hypotension (5.7% vs. 5.5%) • Volume depletion (10.6% vs. 9.9%) • Genital infections (1.7% vs. 0.6%) • No cases of DKA in either group
Contraindications	• On dialysis

Farxiga® Package Insert
Jardiance® Package Insert
N Engl J Med 2019; 381:1995-2008
N Engl J Med 2020; 383:1413-1424

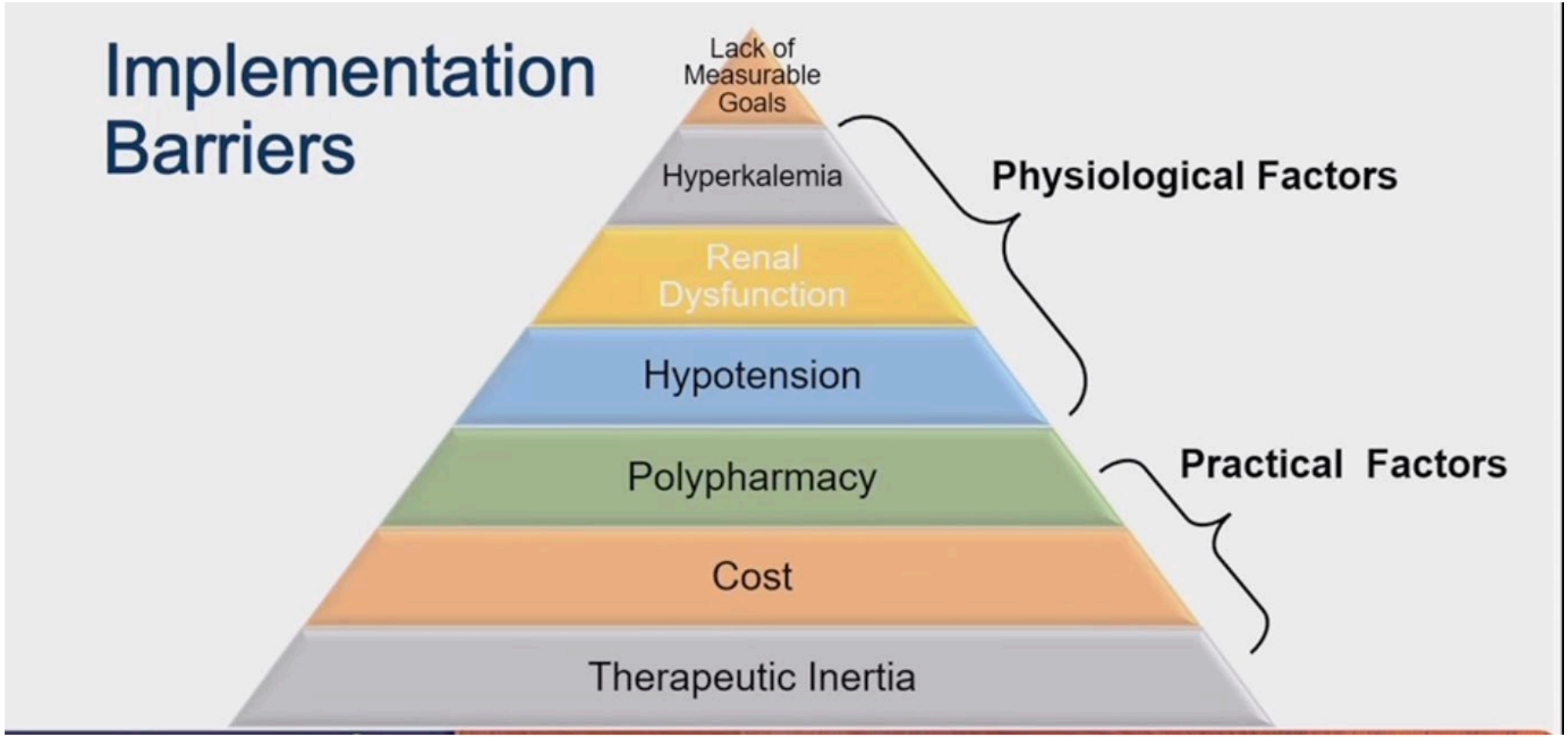
Comprehensive Guideline Directed Medical Therapy (GDMT) Extends Lives and Reduces Hospitalizations



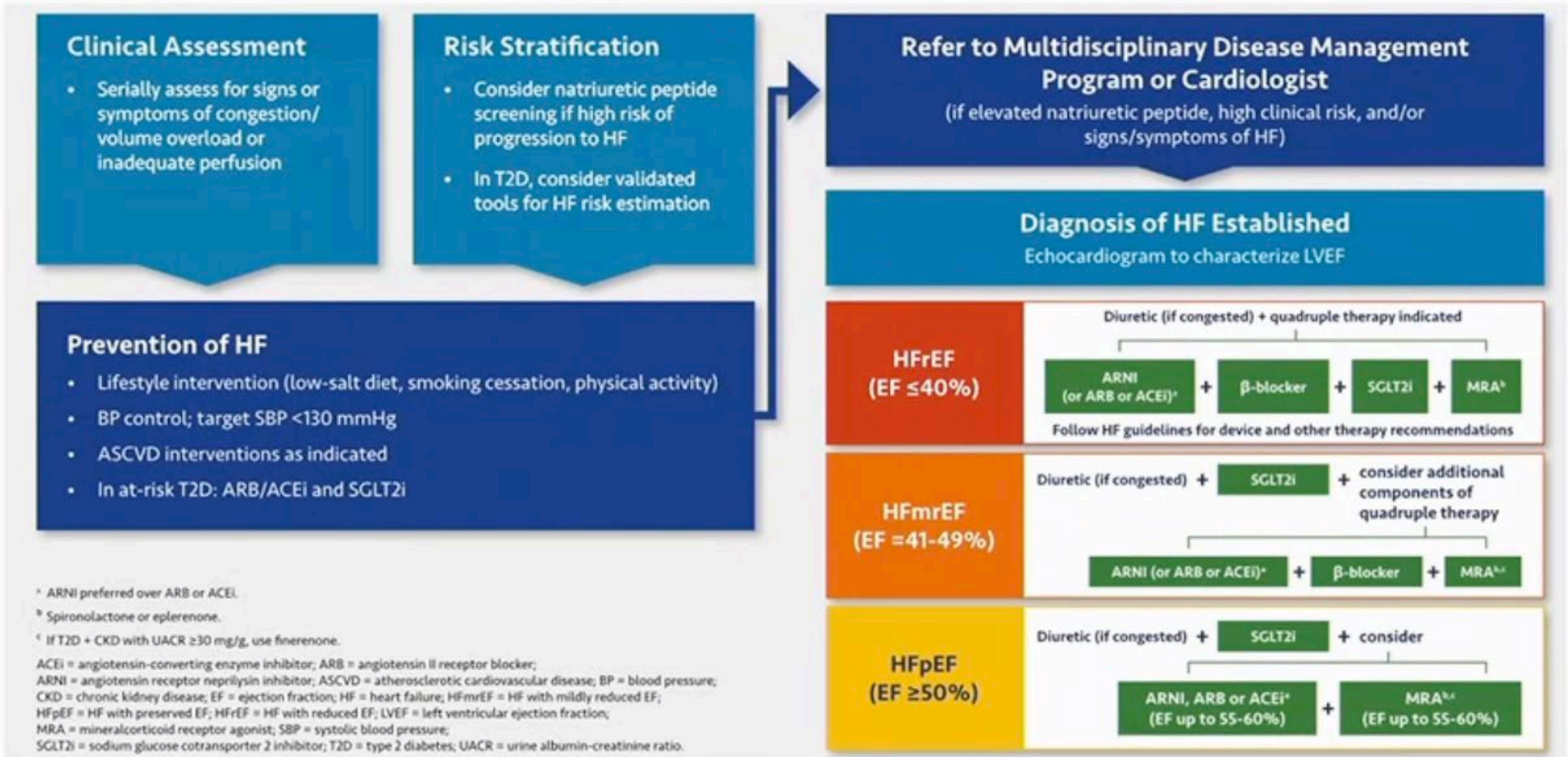
In a 55-year-old HFrEF patient, ARNI + βB + MRA + SGLT2i estimated to extend event-free survival by **8.3 years** vs. ACEI + βB alone

Vaduganathan et al. *Lancet*. 2020.

Barriers to Guideline Directed Medical Therapy



Prevention and Management of Heart Failure



[a] ARNI preferred over ARB or ACEi.

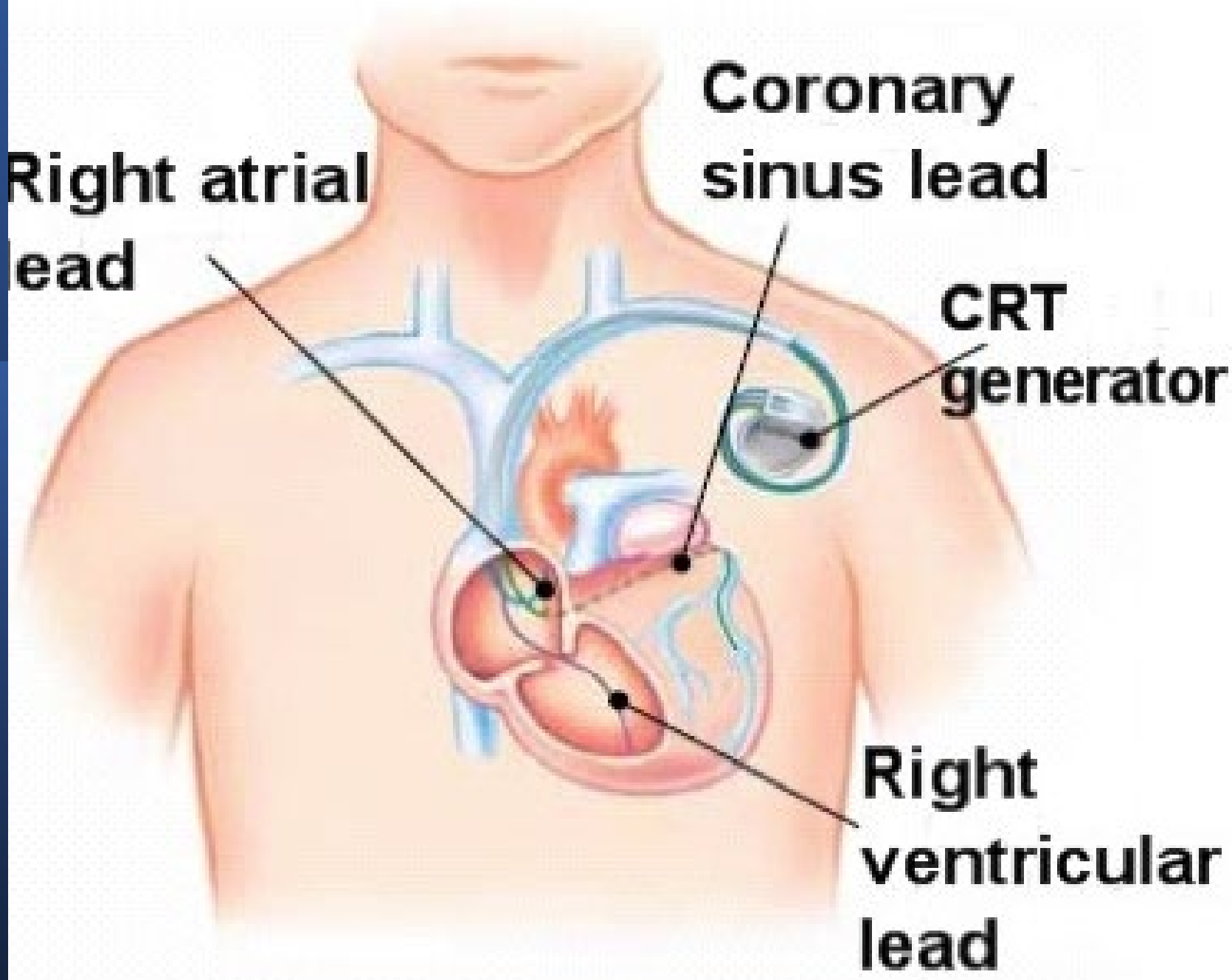
[b] Spironolactone or eplerenone.

[c] If T2D + CKD with UACR ≥30 mg/g, use finerenone.

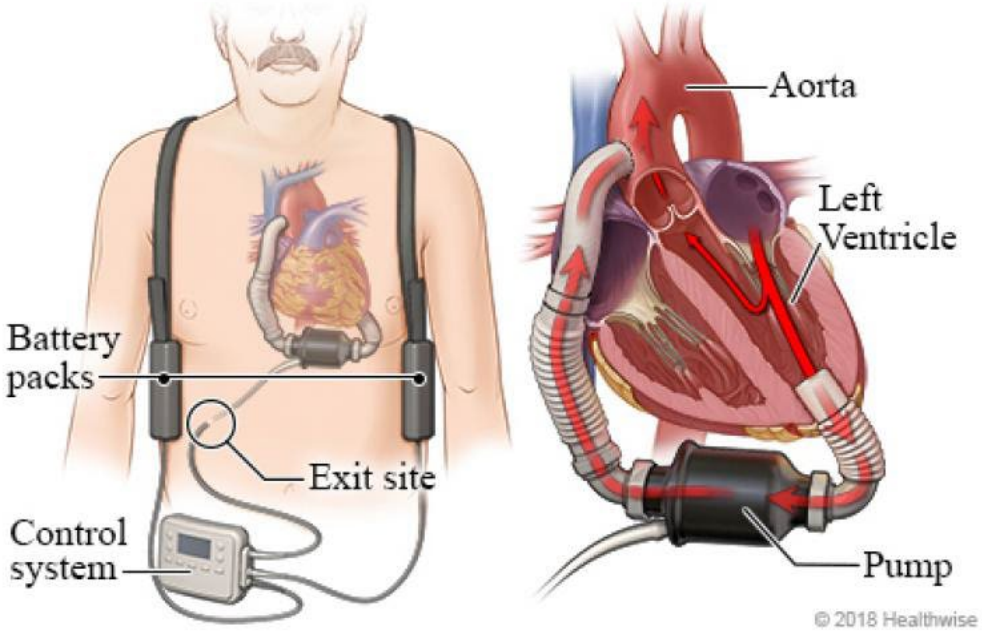
ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor blocker; ARNI = angiotensin receptor neprilysin inhibitor; ASCVD = atherosclerotic cardiovascular disease; BP = blood pressure; CKD = chronic kidney disease; EF = ejection fraction; HF = heart failure; HFmrEF = HF with mildly reduced EF; HFpEF = HF with preserved EF; HFrEF = HF with reduced EF; LVEF = left ventricular ejection fraction; MRA = mineralcorticoid receptor agonist; SBP = systolic blood pressure; SGLT2i = sodium glucose cotransporter 2 inhibitor; T2D = type 2 diabetes; UACR = urine albumin-creatinine ratio.

Handelsman Y et al, Journal of Diabetes and Its Complicitous 36:Feb 2022

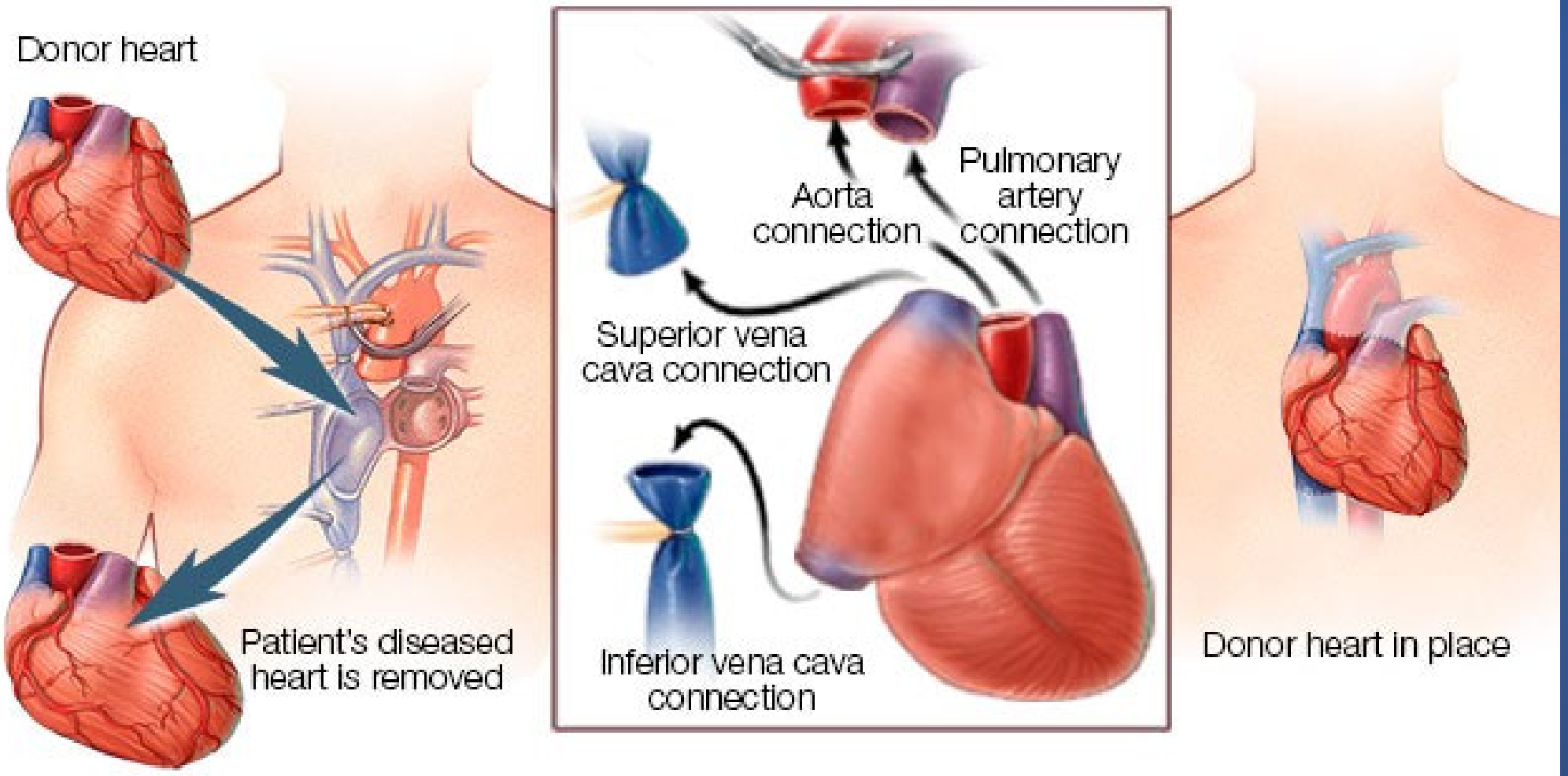
Device Therapy for CHF



Ventricular Assist Devices



Heart transplant procedure



Thank You