Disclosures

None

Objectives

1. Understand the prevalence and significant of heart failure
2. Recognize the pharmacological therapies used in heart failure
3. Evaluate the role of emerging device therapies

Heart Failure is a Public Health Crisis

- Approximately 6.7 million people in the US have CHF
- By 2050, >11 million people in the US

- HF mortality and hospitalization rates have been increasing since 2012
  - Significant acceleration 2020-2021

- HF accounted for 45% of cardiovascular deaths in the US in 2021

Lifetime risk of developing heart failure is now 1 in 4

1 million new HF cases are diagnosed each year

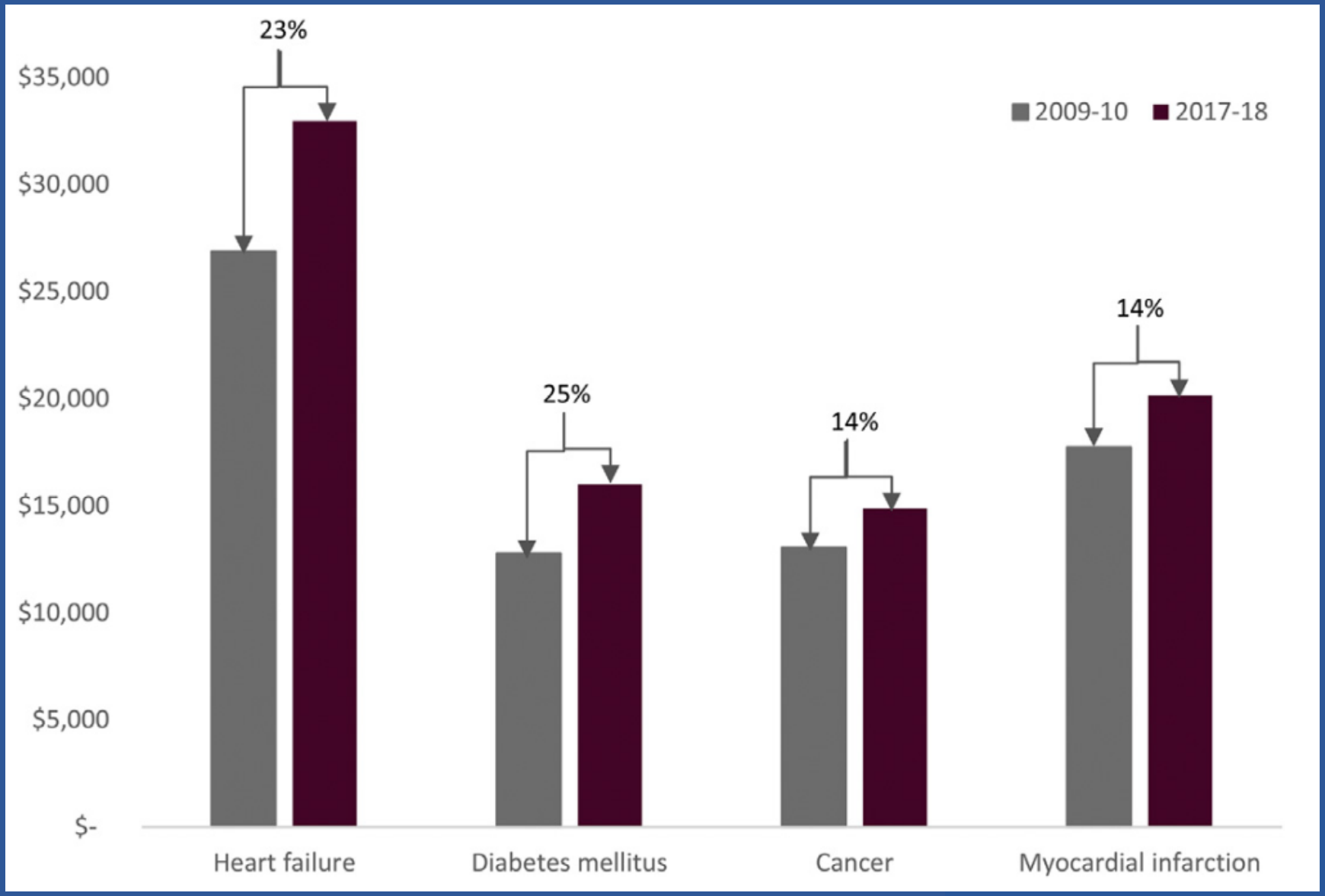
The proportion of younger patients with HF is increasing compared to older patients

Heart Failure is Costly and Expensive

In the US, total cost for heart failure care in 2020 was $43.6 billion

By 2030, an expected increase to $70 billion – 127% increase!

Cook C, Cole G, Asaria P, Jamil R, Francis DP. "The annual global economic burden of heart failure." *Circulation: Heart Failure*. 2014



Bhatnager et al. *J Am Coll Cardiol HF.* 2022 Aug, 10 (8) 571–580.

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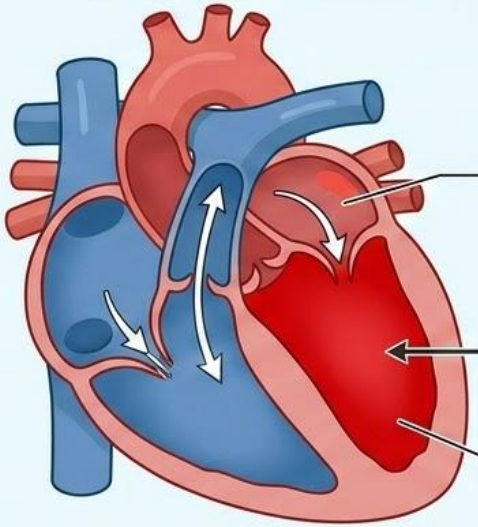
What is heart failure?

According to the American Heart Association and American College of Cardiology,

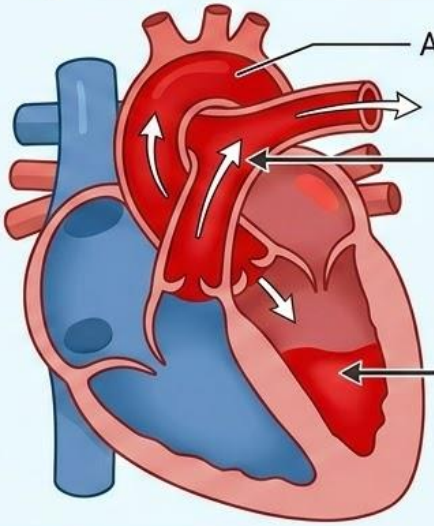
> ***"A complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill or eject blood"***

EJECTION FRACTION (EF)

1. DIASTOLE (RELAXED & FULL)



2. SYSTOLE (CONTRACTED & PUMPING)



EJECTION FRACTION (EF) CALCULATION

$$EF\ (\%) = \left(\frac{\text{Stroke Volume}}{\text{End-Diastolic Volume}}\right) \times 100$$

$$EF\ (\%) = \left(\frac{80\ \text{mL}}{120\ \text{mL}}\right) \times 100 = 66\%$$

RESULT: EF = 66% (Normal Range)

Normal Range: 50% - 70%

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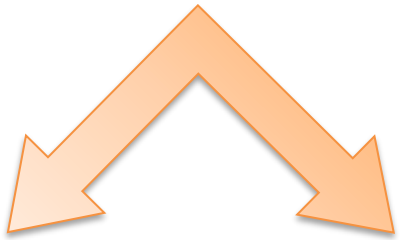
Types of Heart Failure



Heart Failure with Preserved Ejection Fraction

=

Diastolic Heart Failure

Heart Failure with Reduced Ejection Fraction

=

Systolic Heart Failure

SYMPTOMS

Rapid changes in weight

Extreme tiredness or weakness

Feeling light-headed

Swelling in the ankles, feet, legs or tummy

Rapid or irregular heartbeat

Shortness of breath

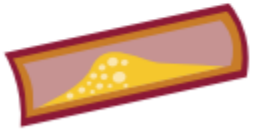
Trouble breathing when lying down

Over 6 million Americans have heart failure

It is the **leading cause of hospitalization** for people 65+

COMMON CAUSES

Coronary artery disease



Heart attack

Diabetes

High blood pressure

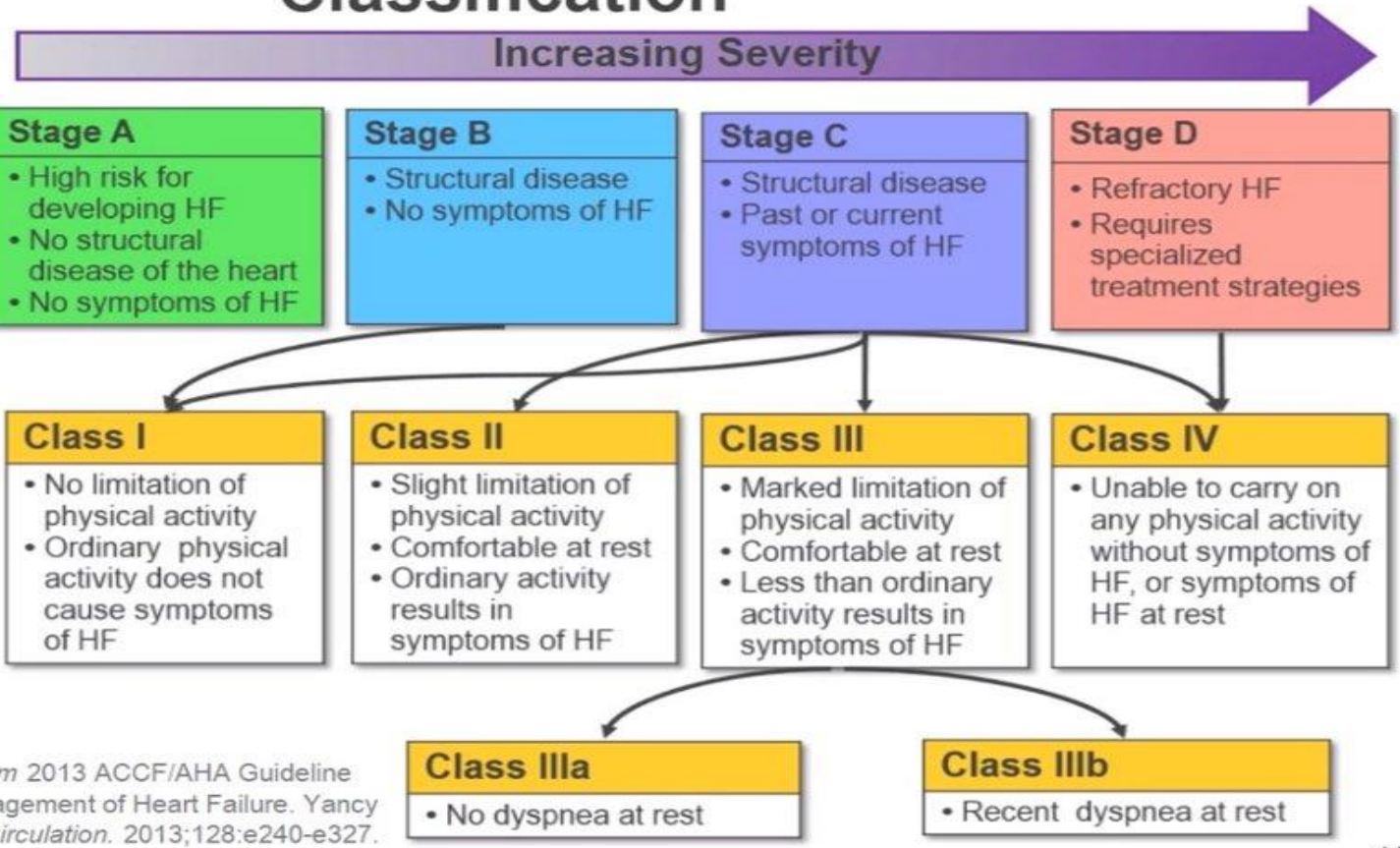
Heart rhythm disorders

- Heart inflammation
- Valve problems
- Congenital heart problems
- Obesity
- Some cancer treatments

For more information, visit *CardioSmart.org/HeartFailure*

@ACCinTouch #CardioSmart

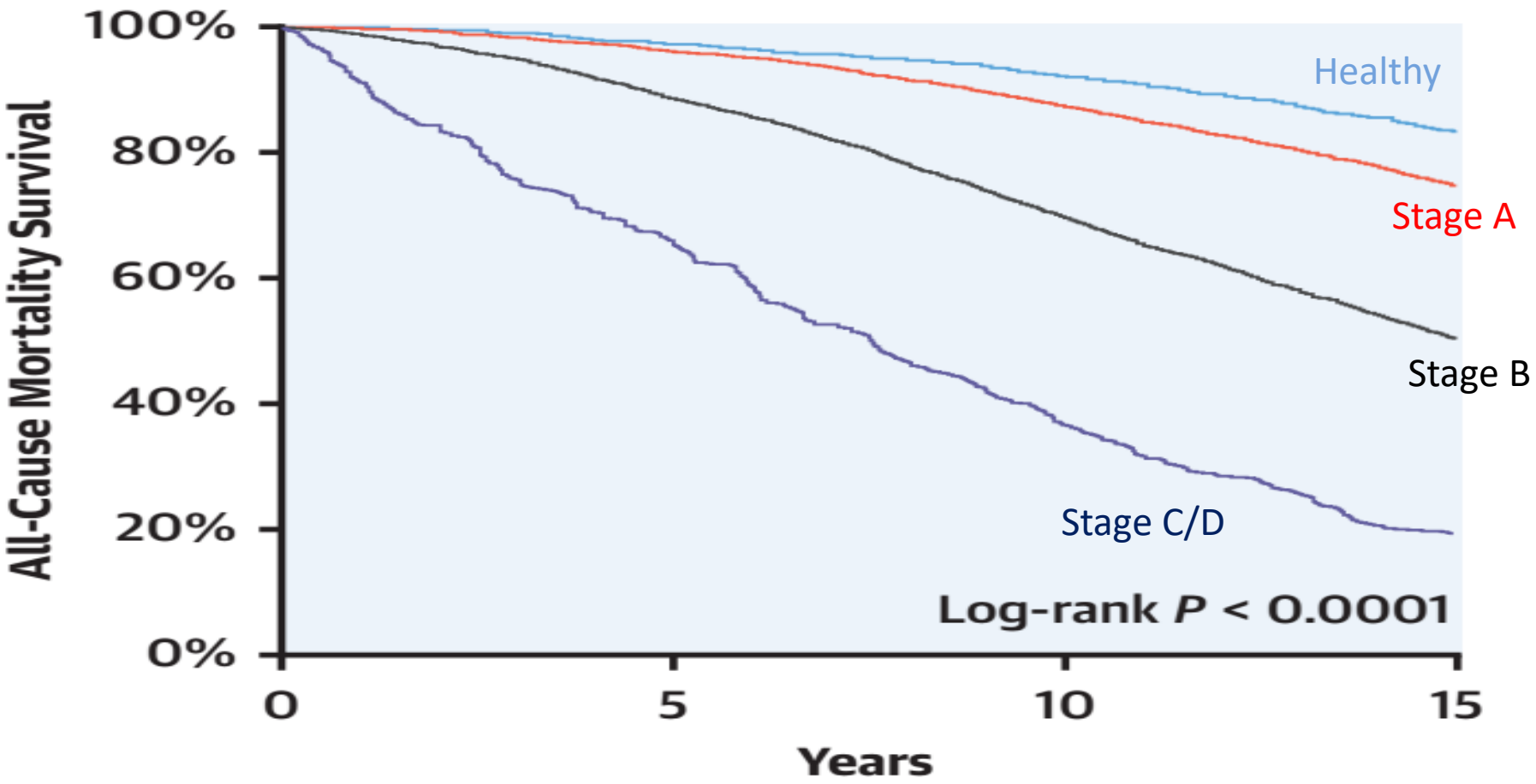
HF Severity: ACC/AHA Stages and NYHA Functional Classification



Modified from 2013 ACCF/AHA Guideline for the Management of Heart Failure. Yancy CW, et al. *Circulation.* 2013;128:e240-e327.

SPOTLIGHT SERIES

Survival in Heart Failure



Pandey A, et al. *JACC Heart Fail*. 2023;11(7):814–825

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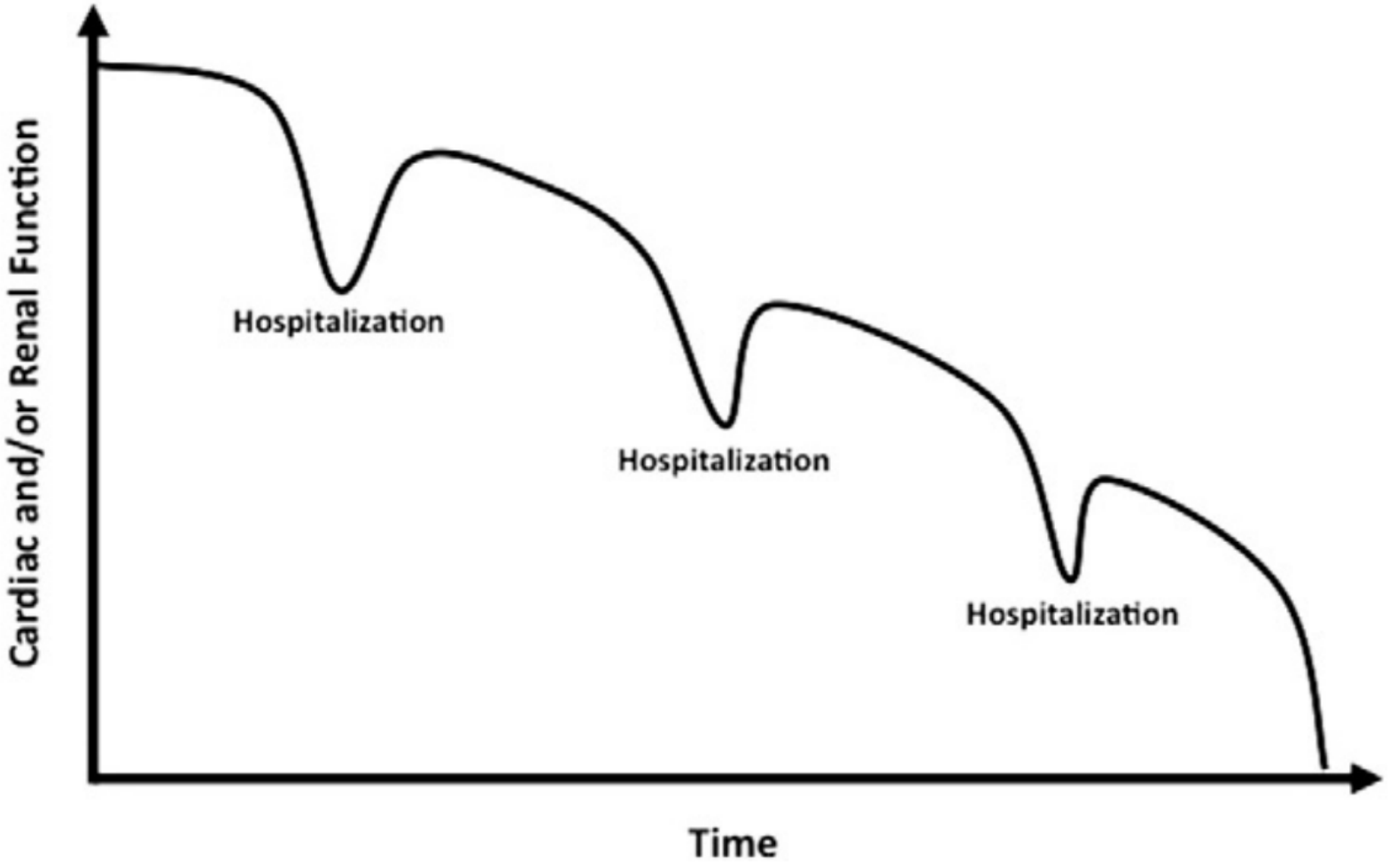
Heart Failure is a Progressive Disease



Hsiao R. Contemporary Treatment of Acute Heart Failure. Prog Cardiovasc Dis. 2016 Jan-Feb;58(4):367-78.

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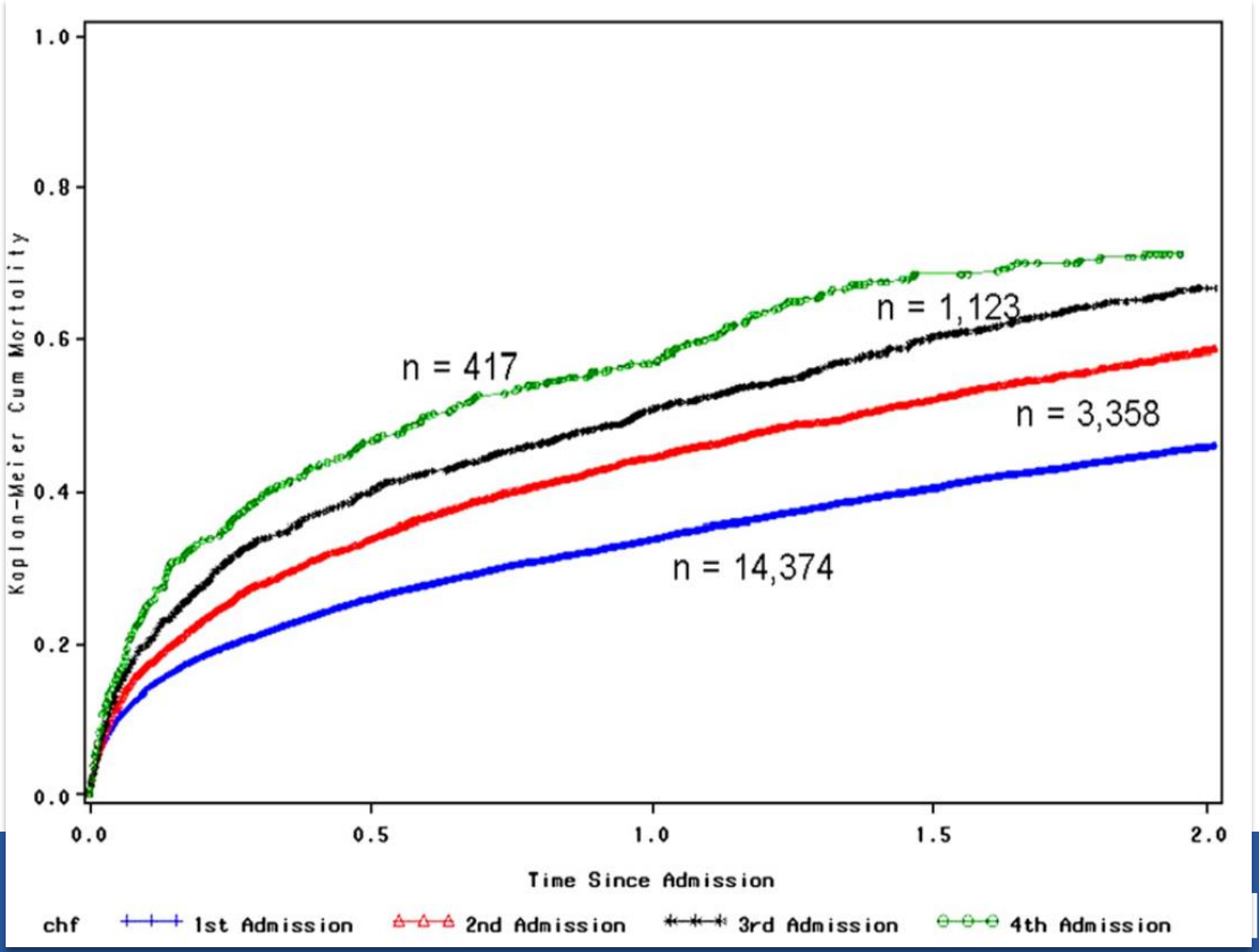
Repeat Hospitalizations Predict Mortality



Setoguchi S et al. *Am Heart J*. 2007;154(2):260–266.

Heart failure with reduced ejection fraction (HFrEF)

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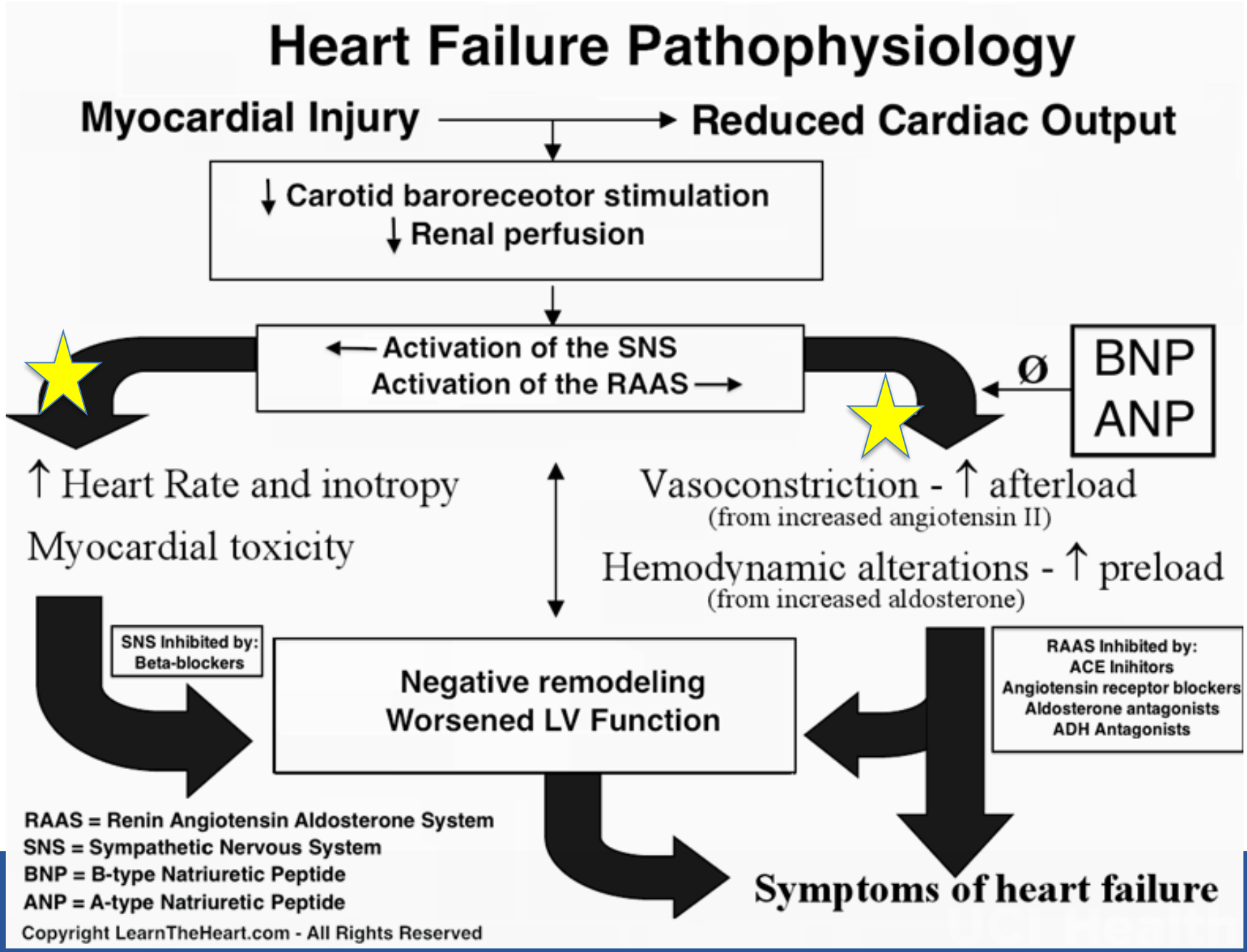
Heart Failure Pathophysiology
Myocardial Injury
Reduced Cardiac Output
↓ Carotid baroreceotor stimulation
↓ Renal perfusion
← Activation of the SNS
Activation of the RAAS →
ø
BNP
ANP
↑ Heart Rate and inotropy
Myocardial toxicity
Vasoconstriction - ↑ afterload
(from increased angiotensin II)
Hemodynamic alterations - ↑ preload
(from increased aldosterone)
SNS Inhibited by:
Beta-blockers
Negative remodeling
Worsened LV Function
RAAS Inhibited by:
ACE Inihitors
Angiotensin receptor blockers
Aldosterone antagonists
ADH Antagonists
RAAS = Renin Angiotensin Aldosterone System
SNS = Sympathetic Nervous System
BNP = B-type Natriuretic Peptide
ANP = A-type Natriuretic Peptide
Symptoms of heart failure
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Four Pillars of HF Therapy

- RAAS Inhibitors
- Beta Blockers
- Mineralocorticoid Receptor Antagonists
- SGLT2 inhibitors

Four Pillars of HF Therapy Reduce Mortality and Morbidity

The Pillar	Common Names	The "Job Description"	The Big Benefit
1. The Stress Relievers	Entresto (ARNI)	Widens blood vessels to lower "push-back" on the heart.	Lowers blood pressure and prevents heart stretching.
2. The Heart Protectors	Carvedilol, Metoprolol	Keeps the heart from beating too fast or working too hard.	Allows the heart to rest and refill properly.
3. The Fluid Balancers	Spironolactone	Blocks "scarring" hormones and prevents salt buildup.	Protects the heart's shape and reduces swelling.
4. The Engine Tuners	Jardiance, Farxiga	Helps the heart use energy better and clears excess sugar/salt.	Dramatically reduces hospital stays and protects kidneys.

Heart failure with preserved ejection fraction (HFpEF)

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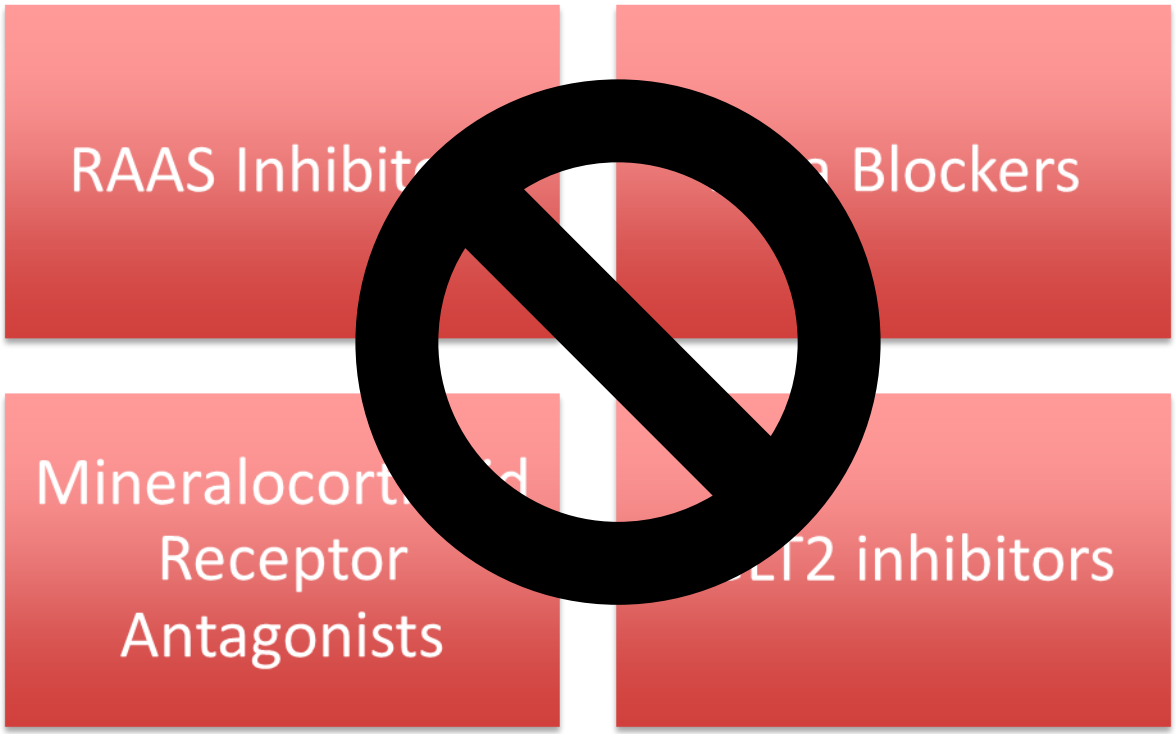
Pathophysiology is driven by systemic inflammation resulting from comorbidities such as obesity, diabetes, and chronic kidney disease

Inflammation causing microvascular dysfunction and fibrosis of the heart

Traditional HFrEF Pillars of Therapy ≠ HFpEF Therapy

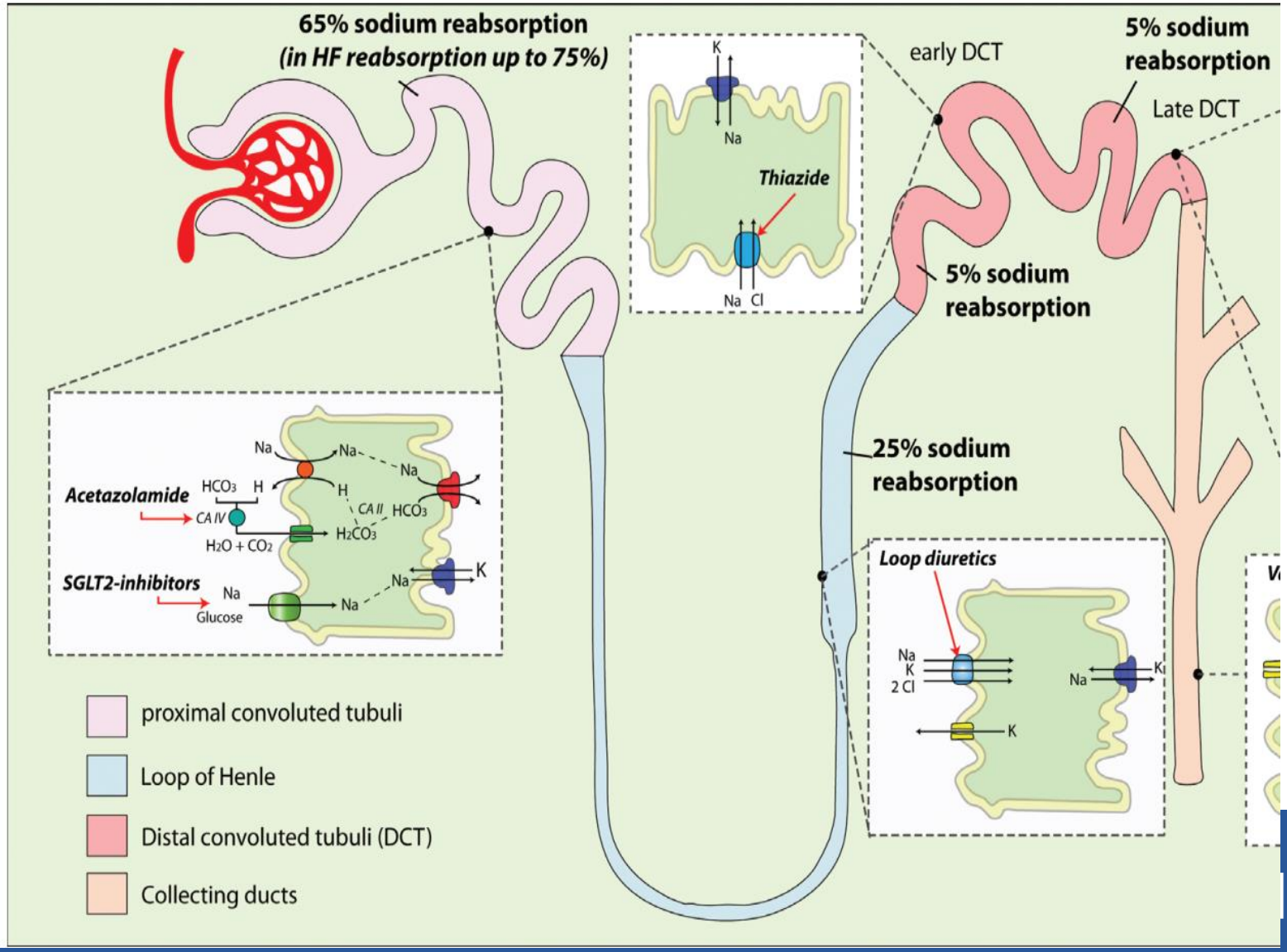


Promising New Medications for HFpEF

1. SGLT2 inhibitors
2. Nonsteroidal mineralocorticoid receptor antagonist
3. GLP-1 receptor agonists

4. Angiotensin receptor neprilysin inhibitors

SGLT2 inhibitors



Nonsteroidal Mineralocorticoid Receptor Antagonists (Finerenone)

First approved MRA to improve outcomes in EF ≥ 40%

Finerenone reduced the risk of cardiovascular death and total HF events by 16%

Steroidal MRAs (spironolactone or eplerenone) have not been shown to reduce CV death

- Benefit was seen in CHF hospitalizations

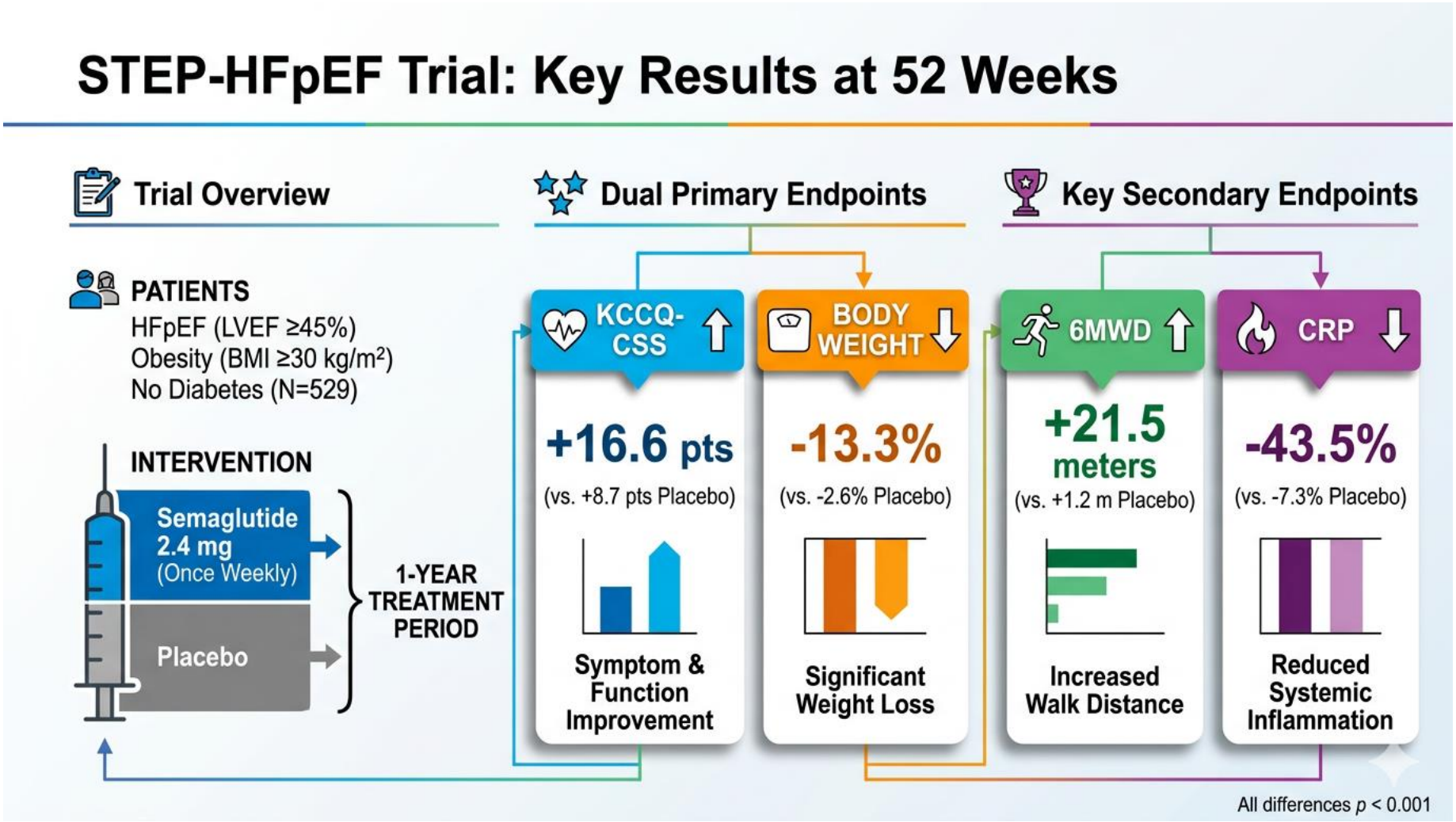
GLP-1 Receptor Agonists

Mimic the natural incretin hormone GLP-1

- Enhances insulin secretion
- Reduces glucagon
- Slows gastric emptying to promote satiety

Promote significant weight loss and glycemic control

STEP-HFpEF Trial: Key Results at 52 Weeks



STEP-HFpEF Trial. N Engl J Med. 2023 Sep 21;389(12):1069-1084.

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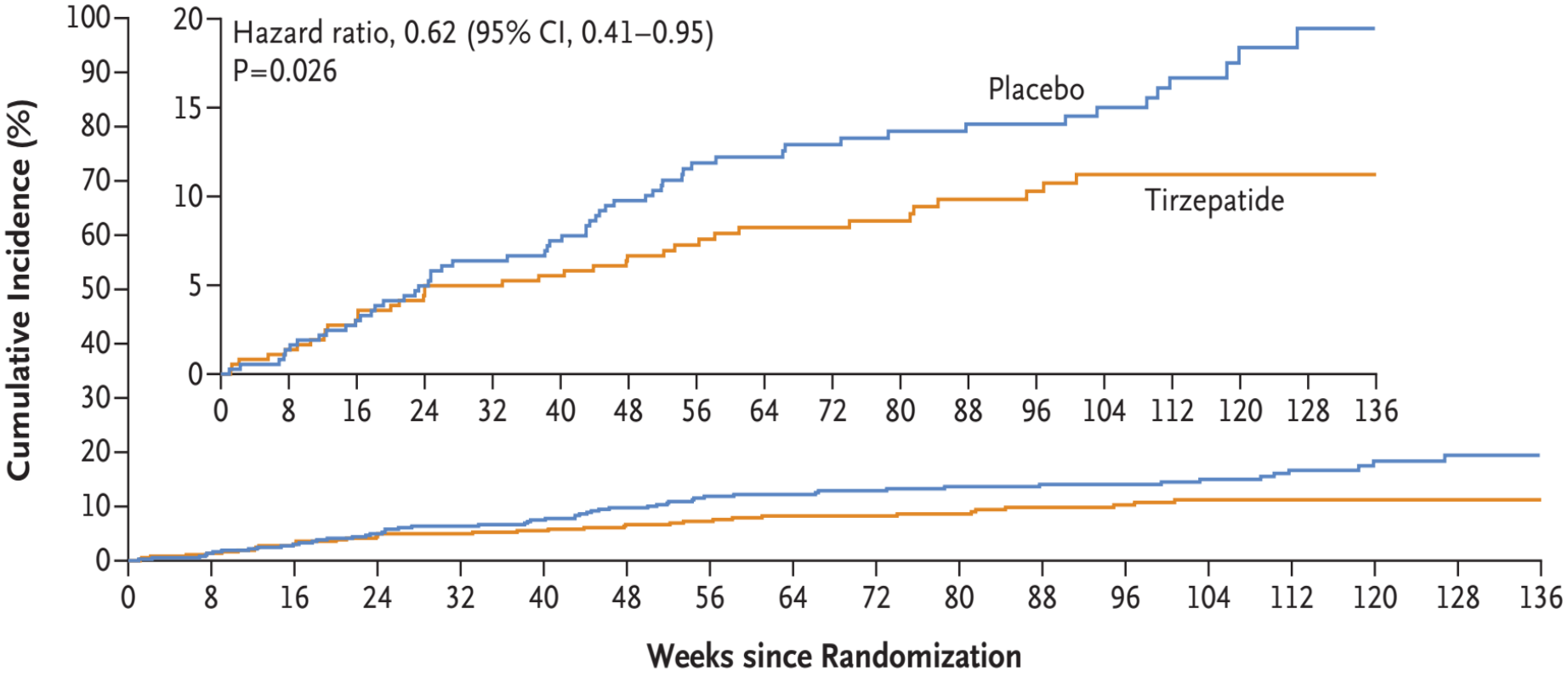
GLP-1 Improves Cardiovascular Events in HFpEF



Packer M; SUMMIT Trial Study Group. Tirzepatide for Heart Failure with Preserved Ejection Fraction and Obesity. N Engl J Med. 2025 Jan 30;392(5):427-437.

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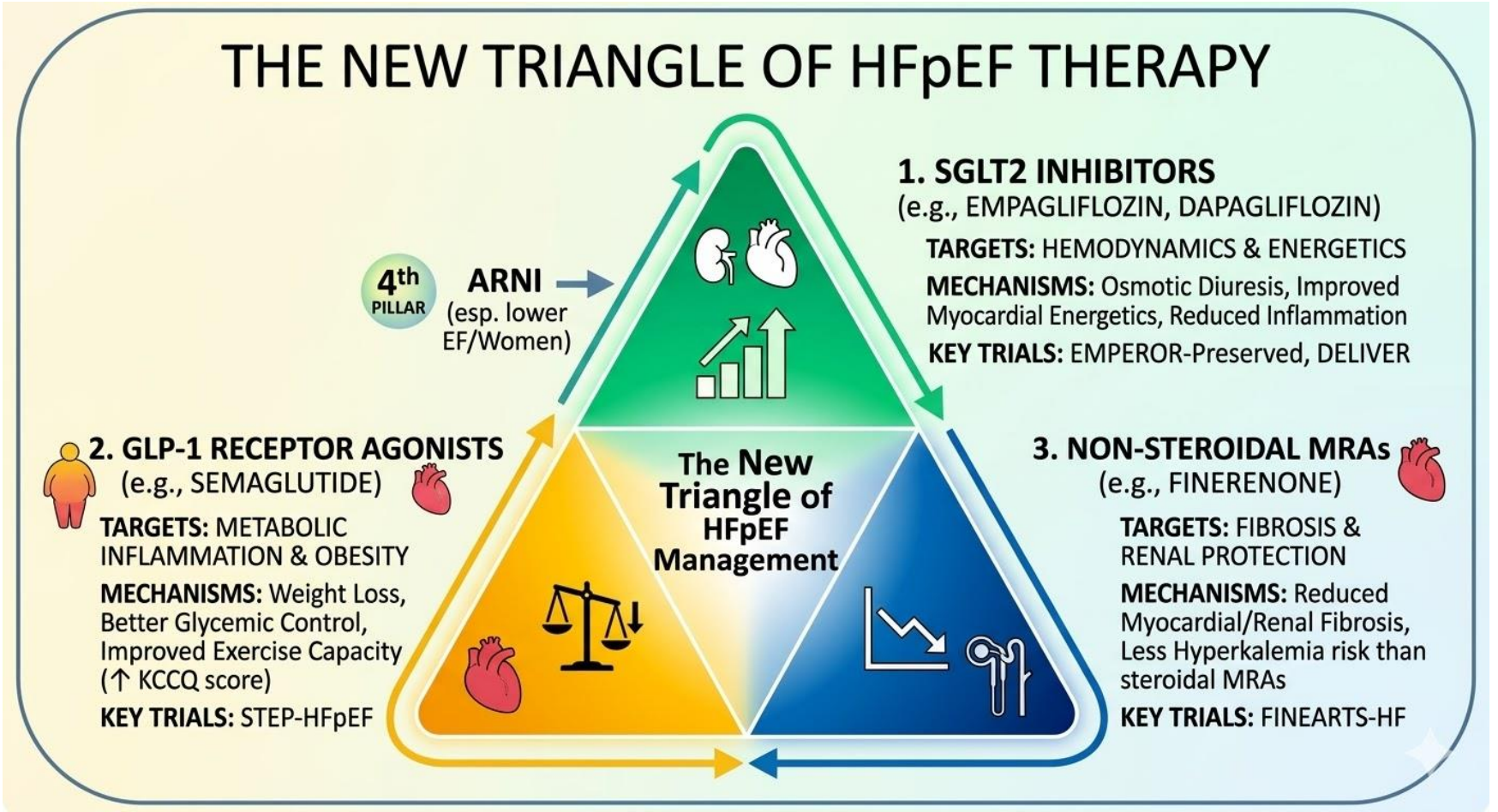
Frontiers of HFpEF Therapy



Additional Therapies in HF

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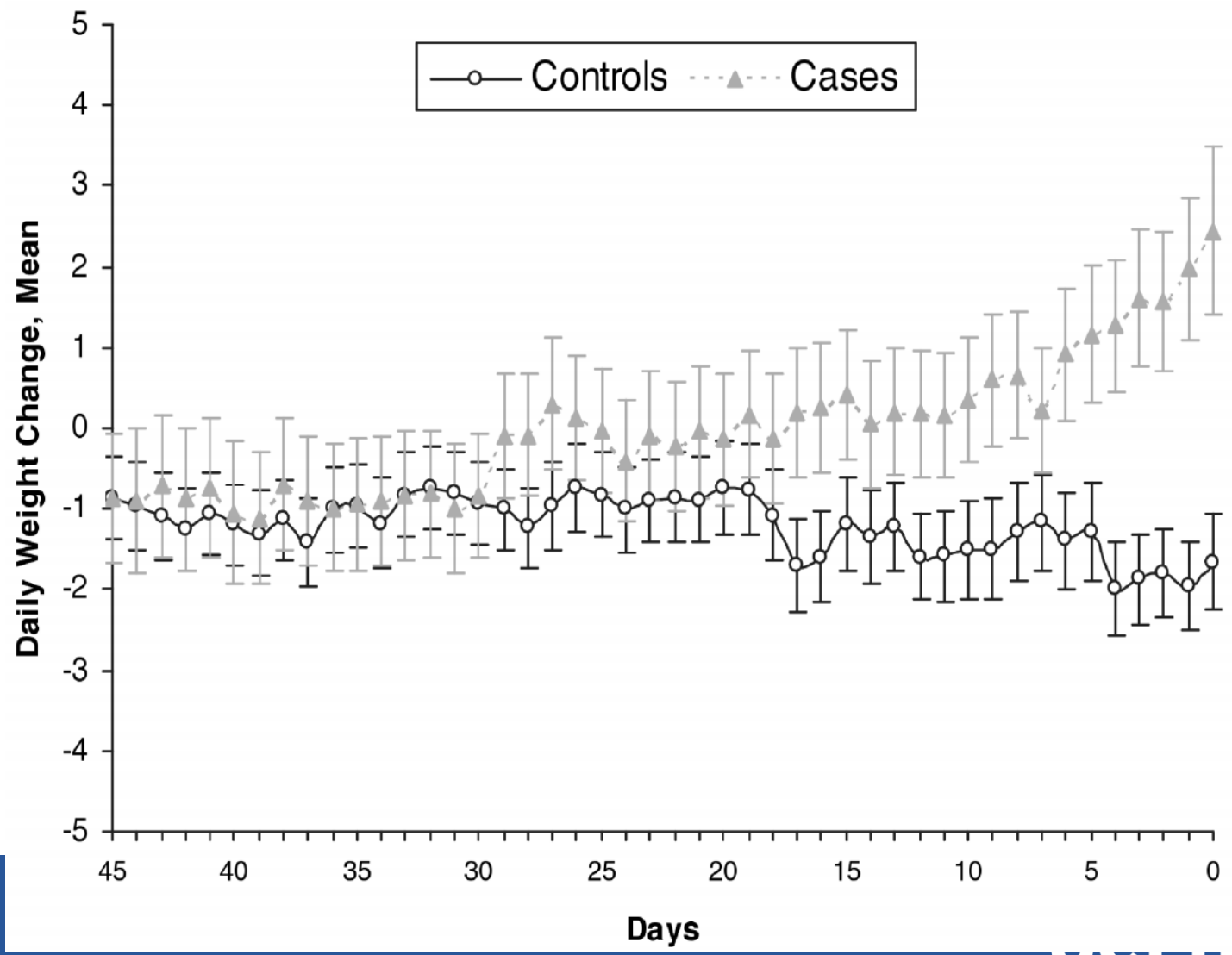
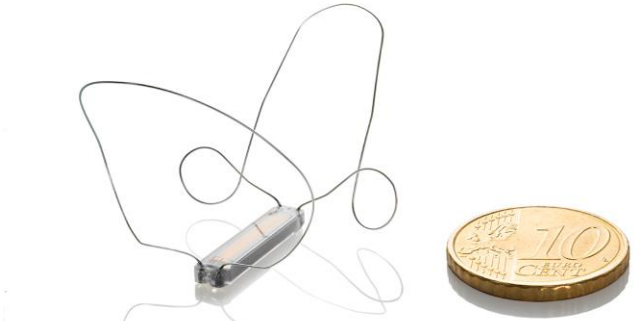


Chaudhry S. Patterns of weight change preceding hospitalization for heart failure. *Circulation*. 2007 Oct 2;116(14):1549-54

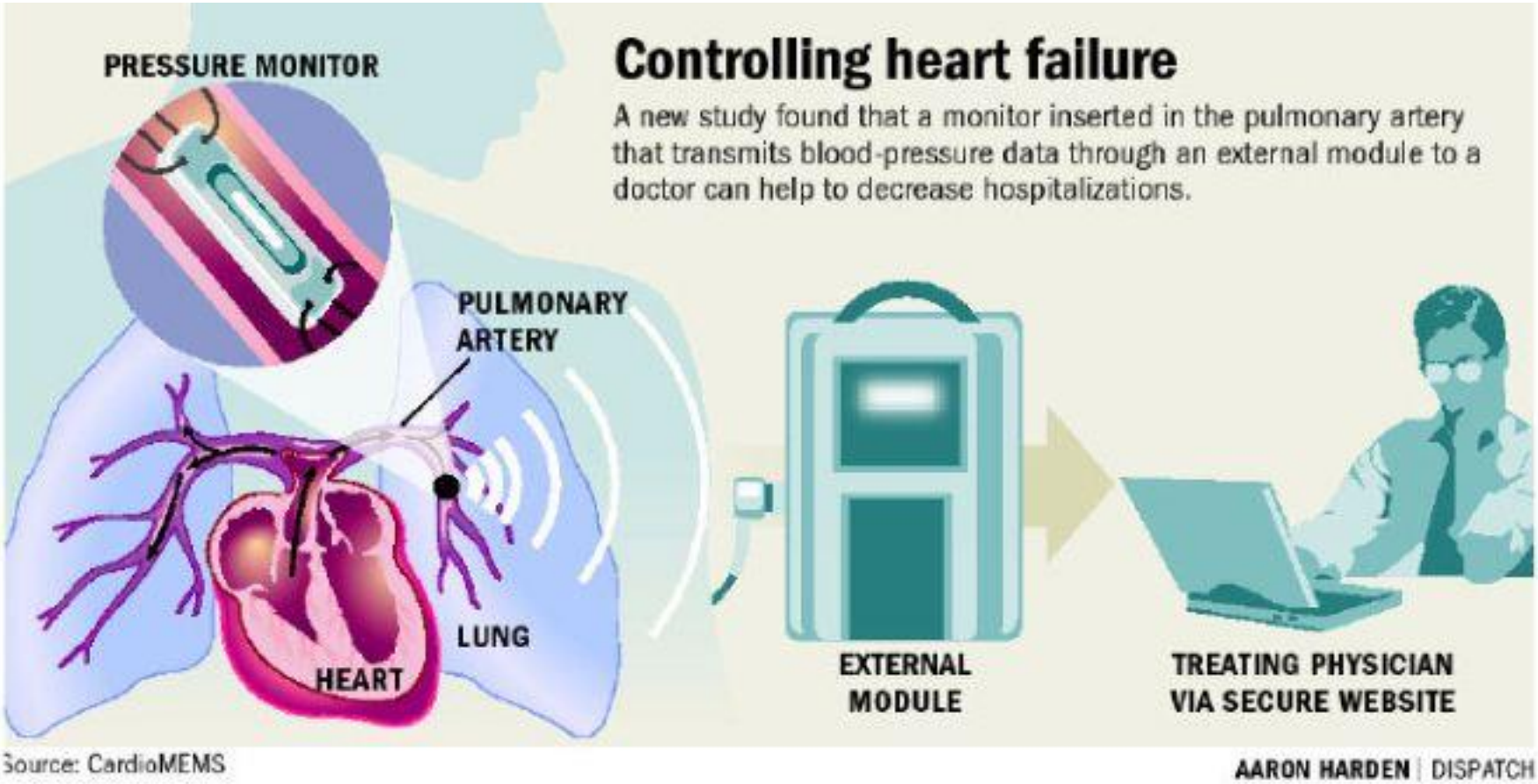
Remote Patient Monitoring Systems

1. CardioMEMS

2. Cordella PA Sensor

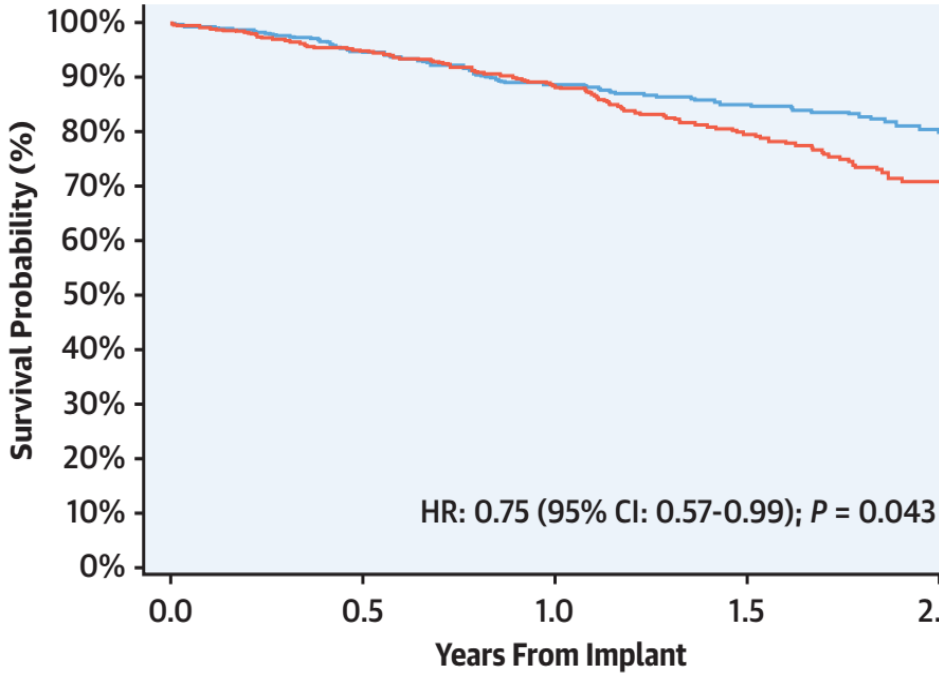


CardioMEMS

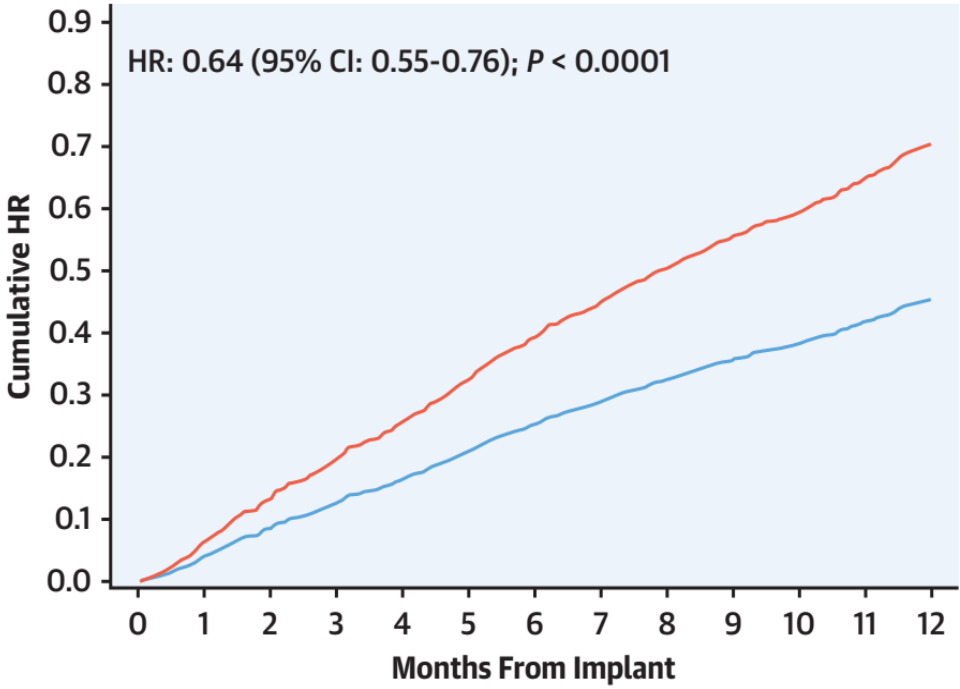

PRESSURE MONITOR
Controlling heart failure
A new study found that a monitor inserted in the pulmonary artery that transmits blood-pressure data through an external module to a doctor can help to decrease hospitalizations.
PULMONARY ARTERY
LUNG
HEART
EXTERNAL MODULE
TREATING PHYSICIAN VIA SECURE WEBSITE
Source: CardioMEMS
AARON HARDEN | DISPATCH

Cardiomems Reduces Hospitalizations and Mortality

Mortality



Hospitalizations



Lindenfeld, J, Costanzo, M, Zile, M. et al. *JACC.* 2024 Feb, 83 (6) 682–694.

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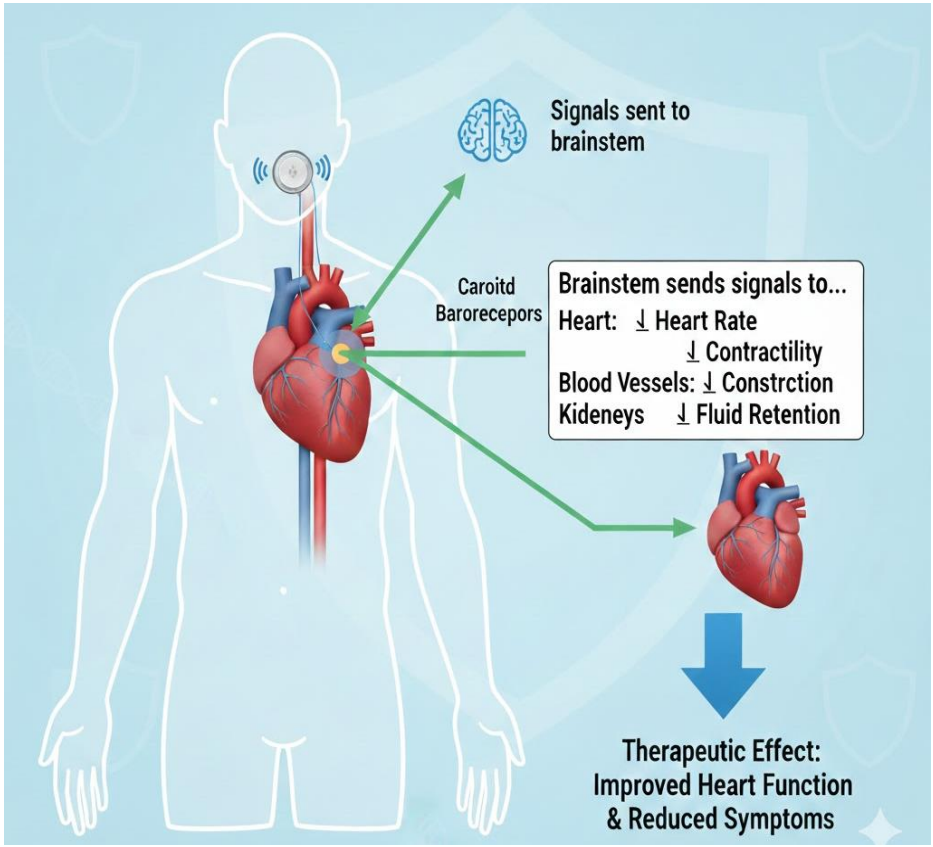
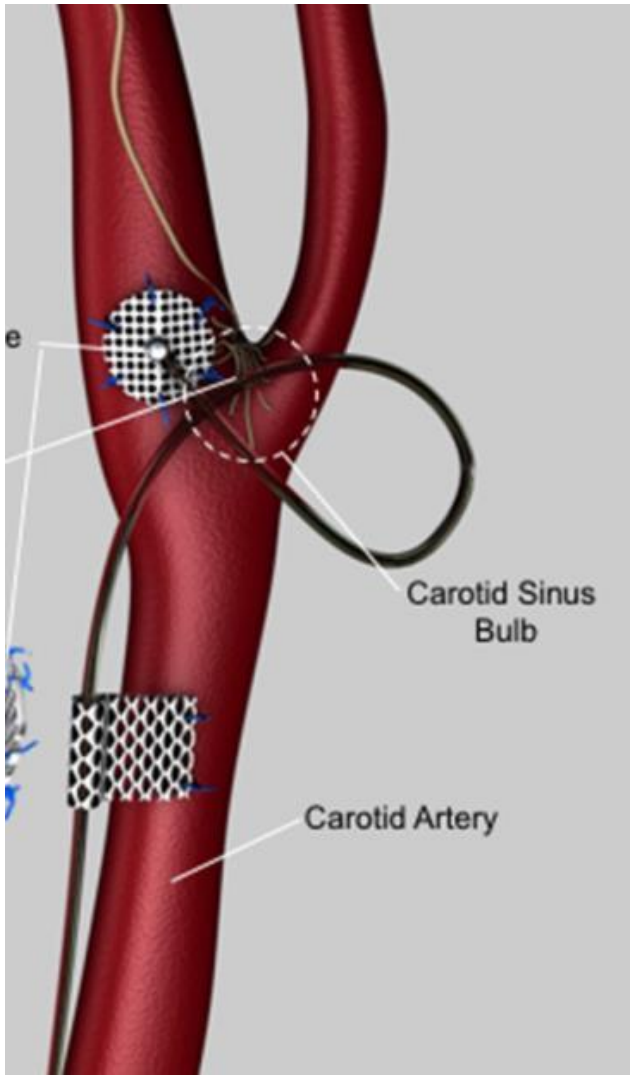
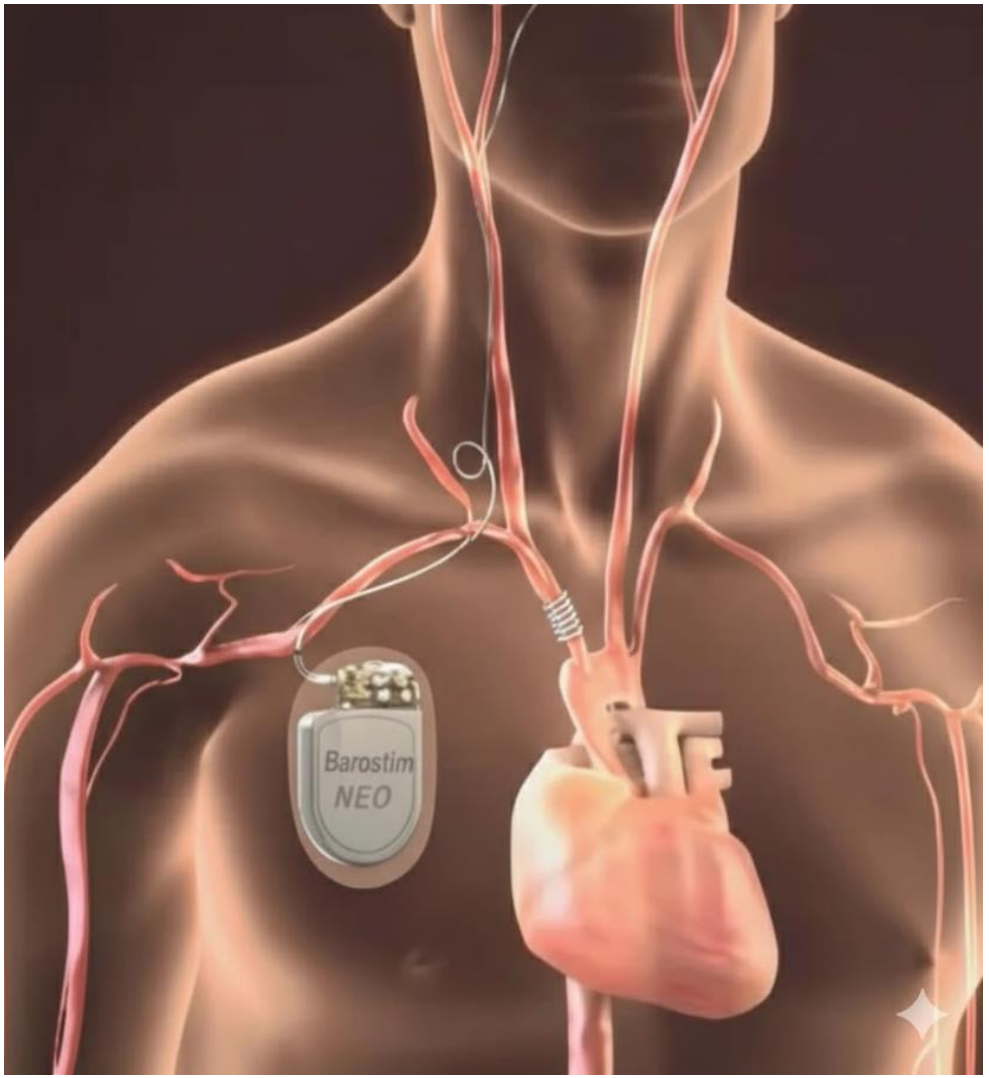
Barostim Device

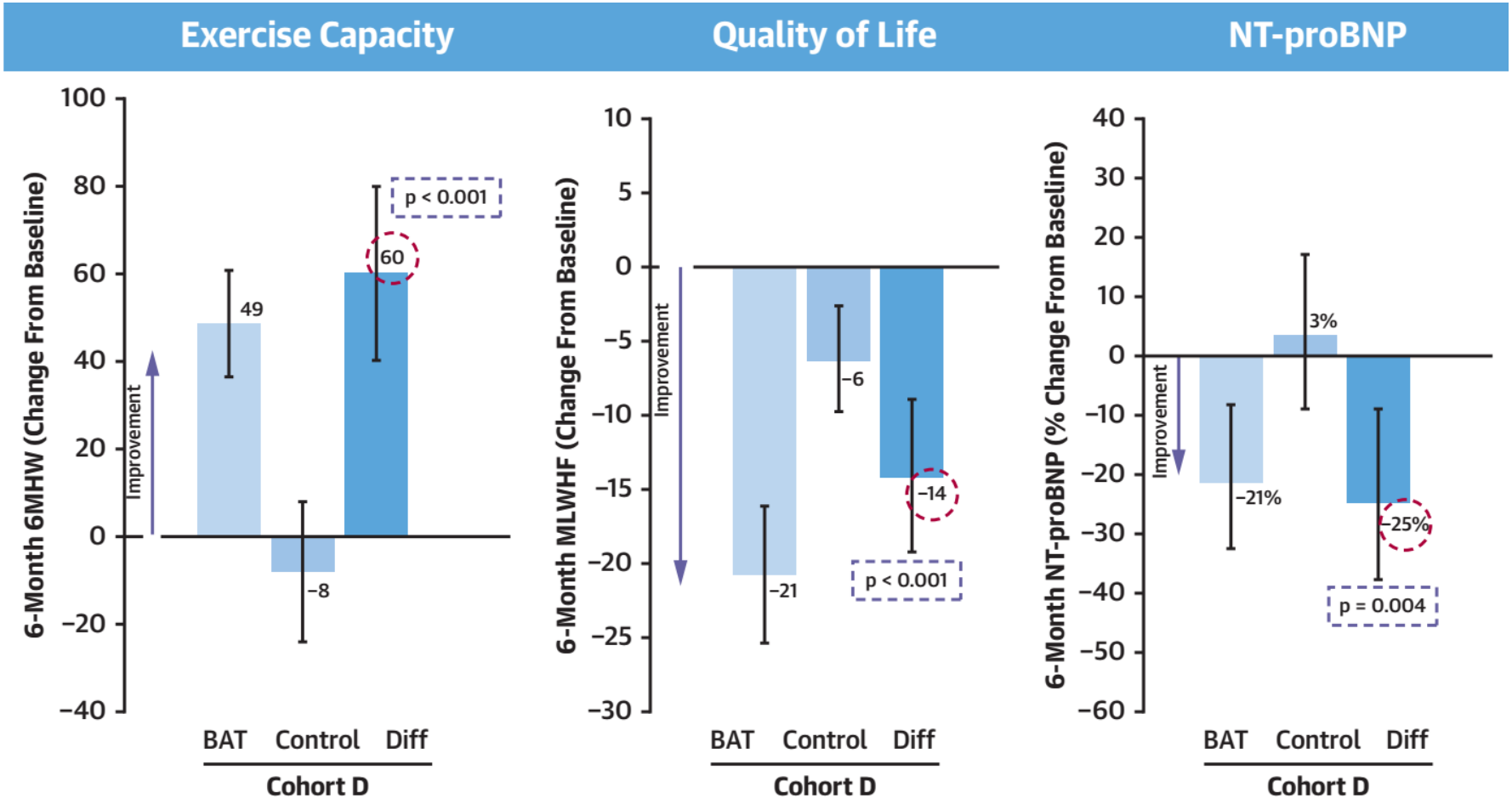
Baroreflex activation therapy

Afferent signaling to the brain from the carotid sinus nerve to reduce sympathetic activity and increase parasympathetic signaling to the heart




Carotid Sinus
Bulb
Carotid Artery


Barostim
NEO



Zile, M.R. et al. J Am Coll Cardiol. 2020;76(1):1-13.

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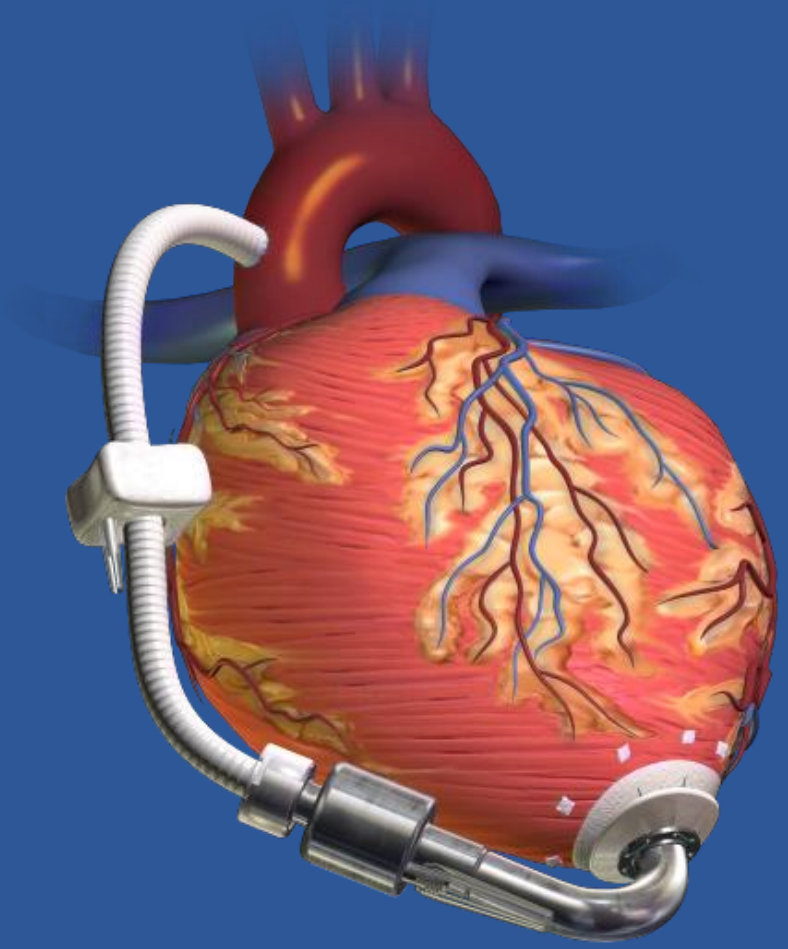

Durable left ventricular assist device

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Transplants are considered the ‘gold standard’ in stage D… but the supply of donor hearts is limited

“Proposing heart transplantation to cure heart failure is analogous to proposing the lottery to cure poverty.”

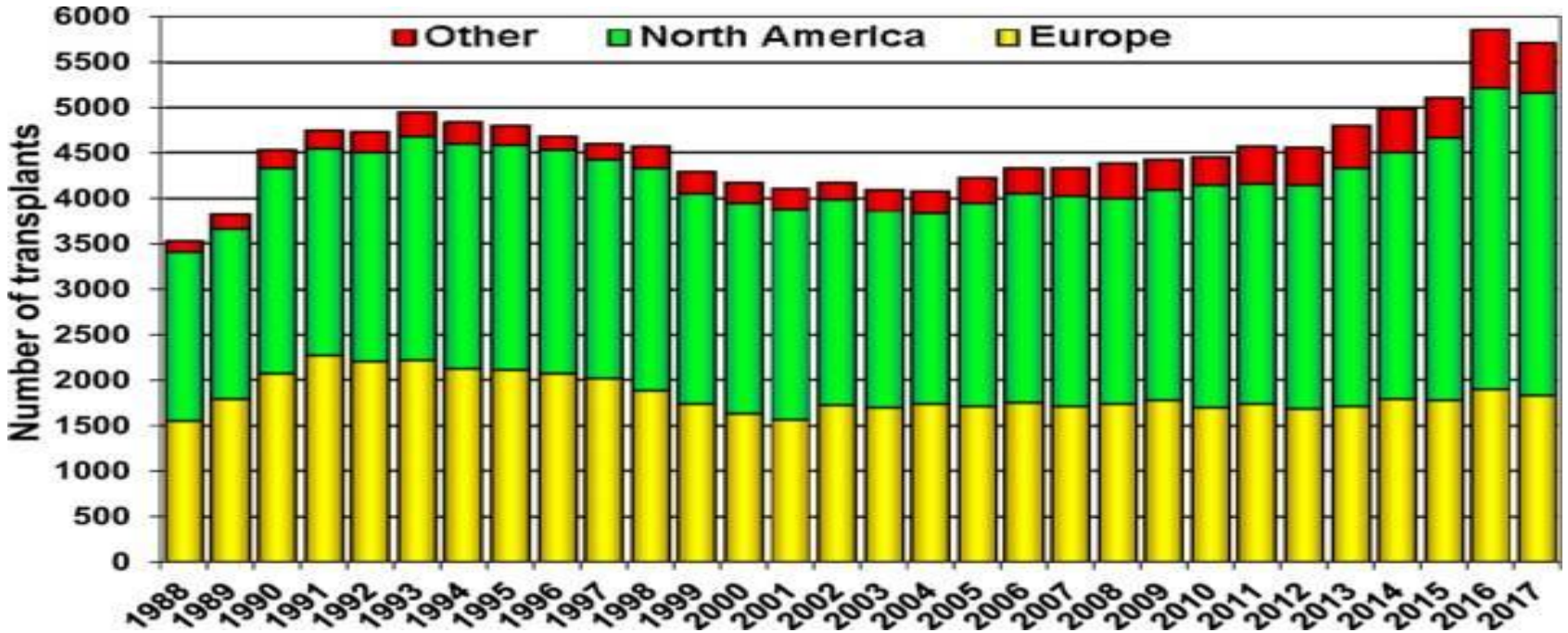
– LW Stevenson[3]

670,000 new cases of heart failure each year[1]

25,000 appropriate candidates for advanced therapies[1]

2,500 hearts available for transplant annually[2]

<10% patients benefit from transplant[1]



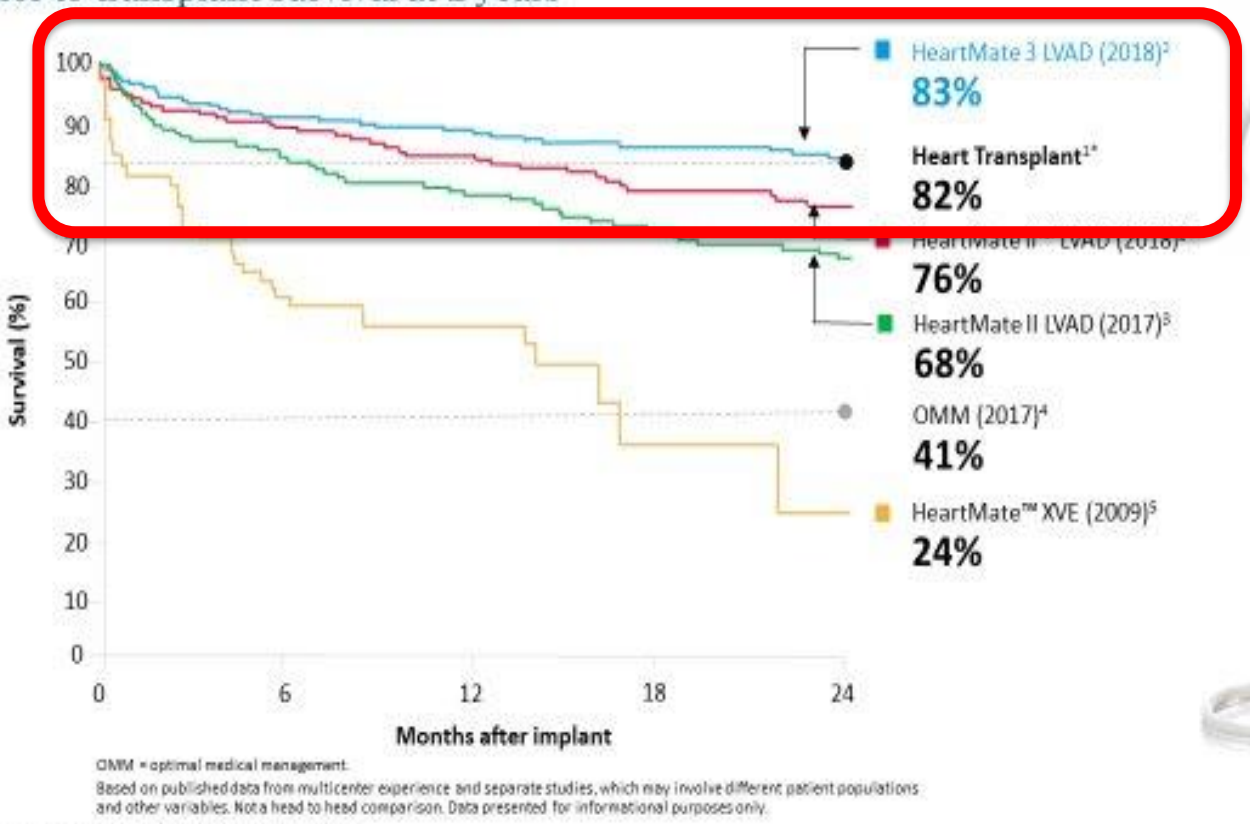
Left ventricular assist device (LVAD)

- A mechanical pump designed to increase the blood flow for patients who have heart failure.

- Functions to take blood from the left ventricle and pumps it out of the aorta to the rest of the body

A new standard in survival has been set with HeartMate 3™ LVAD

Now comparable to transplant survival at 2 years[1*]

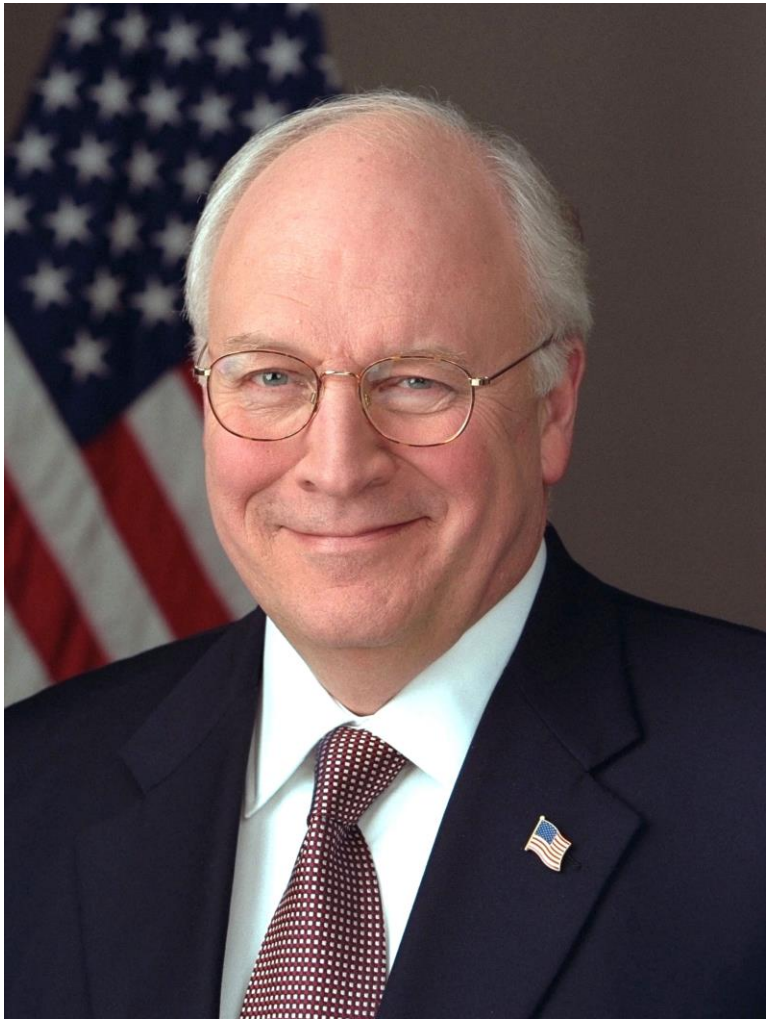


OMM = optimal medical management.

Based on published data from multicenter experience and separate studies, which may involve different patient populations and other variables. Not a head to head comparison. Data presented for informational purposes only.

*82% 2-year survival for heart transplant patients between 2009 and 2015.[1]

References: 1. Lund LF, Khush KK, Cherikh WS, et al. The Registry of the International Society for Heart and Lung Transplantation: Thirty-fourth Adult Heart Transplantation Report—2017; Focus theme: allograft ischemic time. *J Heart Lung Transplant.* 2017;36:1037-1046. 2. Mehra MR, Goldstein DJ, Uriel N, et al. Two-Year Outcomes with a Magnetically Levitated Cardiac Pump in Heart Failure. *N Engl J Med.* 2018;378(15):1386-1395. 3. Rogers JG, Pagani FD, Tatooles AJ, et al. Intrapericardial Left Ventricular Assist Device for Advanced Heart Failure. *N Engl J Med.* 2017;376:451-60. 4. Starling RC, Estep JD, Horstmanshof DA, et al. Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management in Ambulatory Heart Failure Patients: The ROADMAP Study 2-Year Results. *J Am Coll Cardiol HF.* 2017;5:518-527. 5. Slaughter MS, Rogers JG, Milano CA, et al. Advanced heart failure treated with continuous-flow left ventricular assist device. *N Engl J Med.* 2009;361:2241-2251.



Future Directions: Clinical Trials and Beyond

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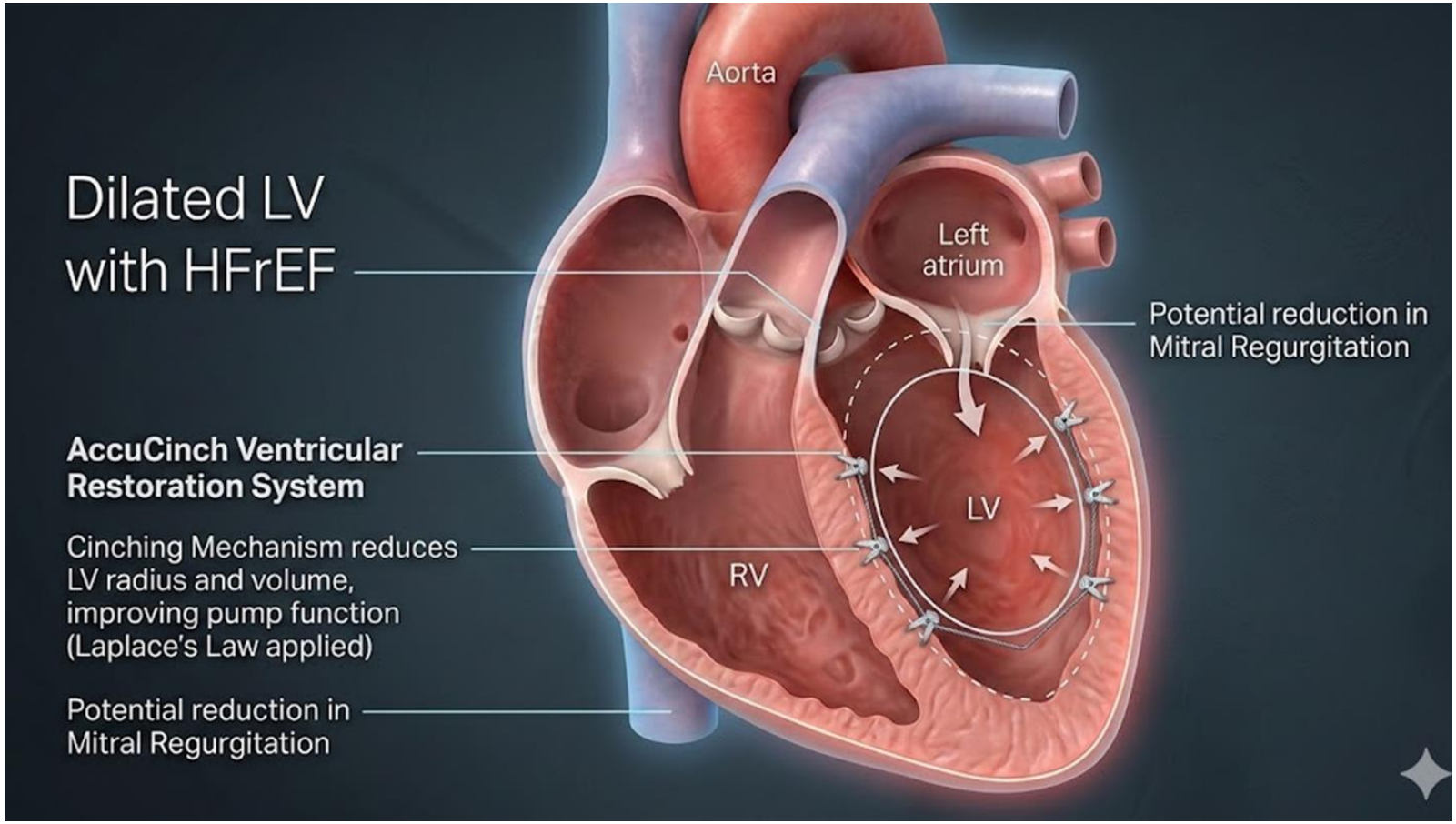
CCR

Trial Name	Mechanism / Intervention	Target Population	Status
HERMES	Anti-inflammatory (IL-6 inhibitor)	HF with high CRP (Inflammation)	Enrolling
Maridebart	GLP-1/GIP (Weight & CV management)	HFpEF / HFmrEF + Obesity	Enrolling
ALT-FLOW II	Interatrial Shunt (Device)	HFpEF / HFmrEF	Enrolling
CORCINCH-HF	Ventricular Restoration (Device)	Symptomatic HFrEF	Enrolling
FASTR-II	Reprieve System (Fluid Mgmt)	Acute Decompensated HF	Enrolling
RENEU-HF	JK07 (Regenerative/Biologic)	HFrEF and HFpEF	Limited

AccuCinch Ventricular Restoration System



https://youtu.be/MGD9_xt_llQ?t=30

Take Home Points

- Heart failure is a prevalent, costly disease with significant morbidity and mortality
- The “Four Pillars” are first-line and the gold standard in pharmacological treatments for HFrEF
- HFpEF is no longer untreatable
- Innovative and new technologies include remote monitoring and devices that are under investigation

Thank You!

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