INNOVATION IN HEART FAILURE: IMAGINING THE NEXT DECADE OF CARE

March 20th, 2026

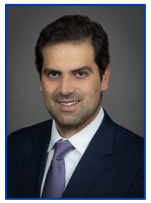
Deane Smith, MD and Snehal R Patel, MD
Co-Directors of the Center for Heart Failure, Transplant and Mechanical Circulatory Support

Sandra Atlas Bass Heart Hospital
Northwell Health®

No Disclosures

CENTER FOR HEART FAILURE, TRANSPLANT, AND MCS

Metro/Mid-Hudson Region



Miguel Alvarez-Villela, MD
Interventional Heart Failure Physician

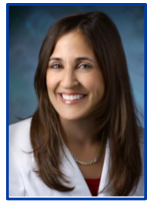
Email: malvarezvill@northwell.edu

Ravi Shah, MD
Associate Director, CCU at LHH
Heart Failure Physician

Email: rshah49@northwell.edu

Kenneth Dulnuan, MD
Director, Heart Failure at SIUH

Email: kdulnuan@northwell.edu



Gerin Stevens, MD, PhD
Heart Failure Physician

Email: gstevens1@northwell.edu

Spencer D. Liu, MD
Interventional Heart Failure Physician

Email: sliu19@northwell.edu

Sirish Vullaganti, MD, MSc
Director, Heart Failure at LHH

Email: svullaganti@northwell.edu

Sabarivinoth Rangasamy, MD
Director, Heart Failure at NWH

Email: srangasamy@northwell.edu

Jasjit Bhinder, MD
Heart Failure Physician

Email:
Jasjit.Bhinder@nuvancehealth.org

James Lyons, MD
Heart Failure System Medical Director at Nuvance Health

Email:
James.Lyons@NuvanceHealth.org

Central Region

Maria Avila, MD
Director, Heart Transplant

Email: mavila4@northwell.edu

David Mintz, MD
Heart Failure Physician

Email: dmintz@northwell.edu

Lauren Cooper, MD, MHS
Director, Heart Failure at NSUH

Email: lcooper6@northwell.edu

Snehal Patel, MD
System Director, Heart Failure

Email: spatel28@northwell.edu

Sandeep Jauhar, MD, PhD
Heart Failure Physician

Email: sjauhar@northwell.edu

Dipan Uppal, MD
Heart Failure Physician

Email: duppal@northwell.edu

Simon Maybaum, MD
Heart Failure Physician

Email: smaybaum@northwell.edu

Deane Smith, MD
Surgical Director, Heart Transplant

Email: dsmith86@northwell.edu

Aaron Weiss, MD, PhD
Cardiac Surgeon

Email: aweiss12@northwell.edu

Eastern Region

Kristin Stawiarski, MD
Heart Failure Physician

Email: kstawiarski@northwell.edu

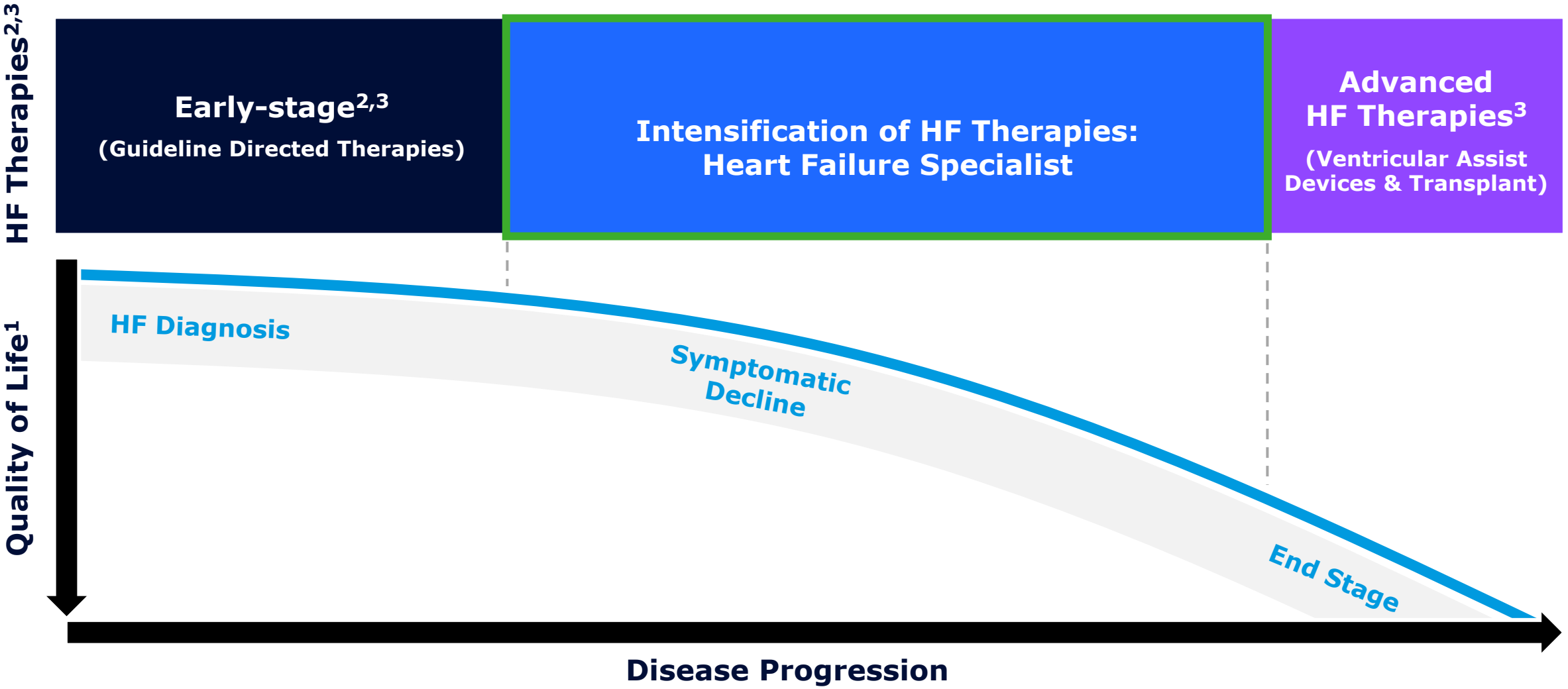
Sarumathi Thangavel, MD
Heart Failure Physician

Email: sthangavel@northwell.edu

Edlira Tam, DO
Heart Failure Physician

Email:

CLINICAL COURSE OF HEART FAILURE – ROLE OF THE HF TEAM AT NORTHWELL



1. Adapted from Greenhalgh T, et al. BMC Cardiovasc Disord. 2017;17:156; 2. Adapted from Estep JD, et al. J Card Fail. 2024;30:1472-1488; 3. Heidenreich PA, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Circulation. 2022;145:e895-e1032.

AGENDA

1. Scale of improvement in clinical outcomes for HFrEF with GDMT.
2. Defining residual risk in HFrEF despite 4 pillar GDMT.
3. Role of the HF specialist (at Northwell) addressing this residual risk moving forward.

1985: WHAT IS THE 1-YEAR MORTALITY OF HFREF?

65-YEAR-OLD | EF 25% | NYHA III

A. 10%

B. 25%

C. 50%

D. 75%

1985: WHAT IS THE 1-YEAR MORTALITY OF HFREF?

65-YEAR-OLD | EF 25% | NYHA III

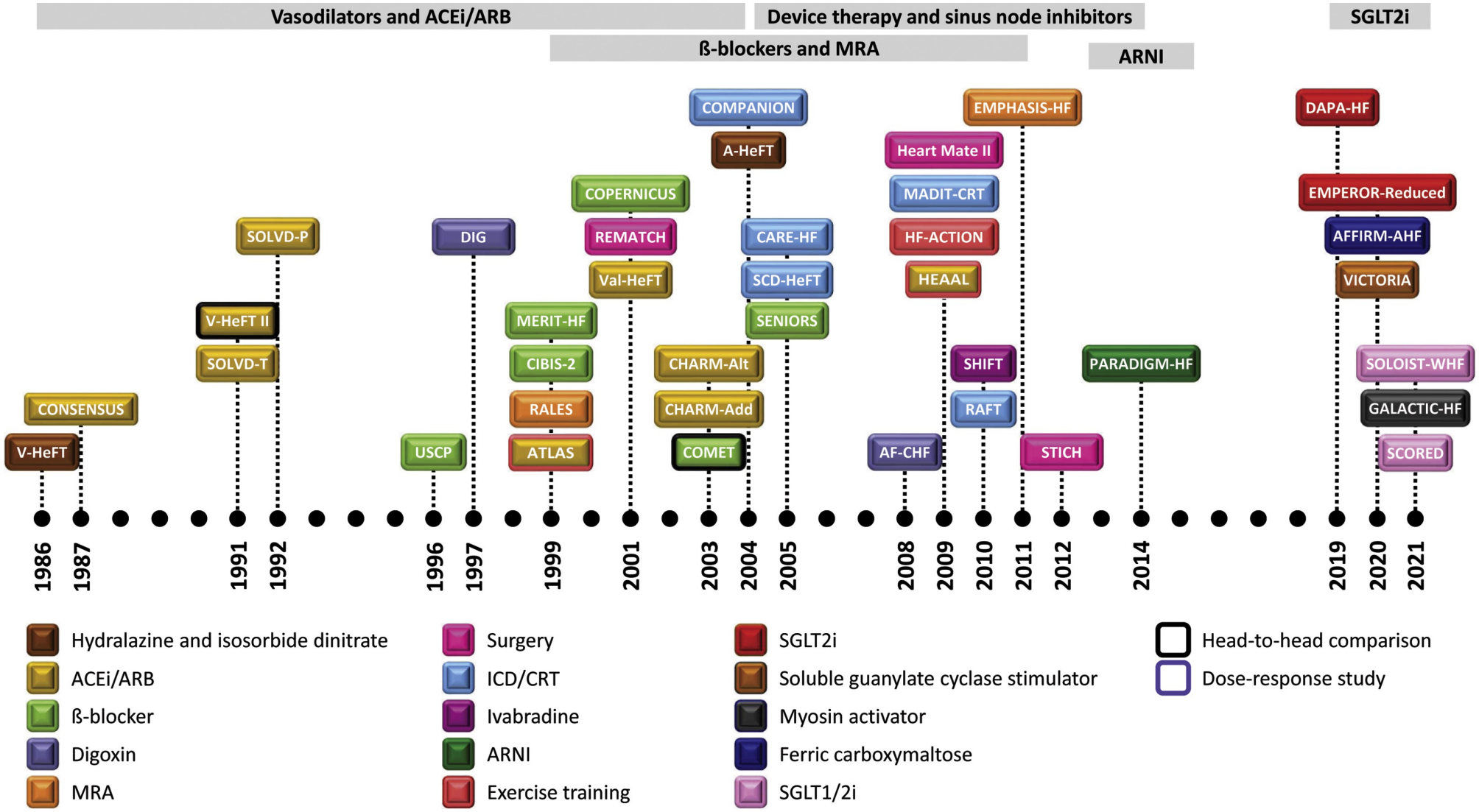
A. 10%

B. 25% (V-HeFT I placebo arm 1986)

C. 50%

D. 75%

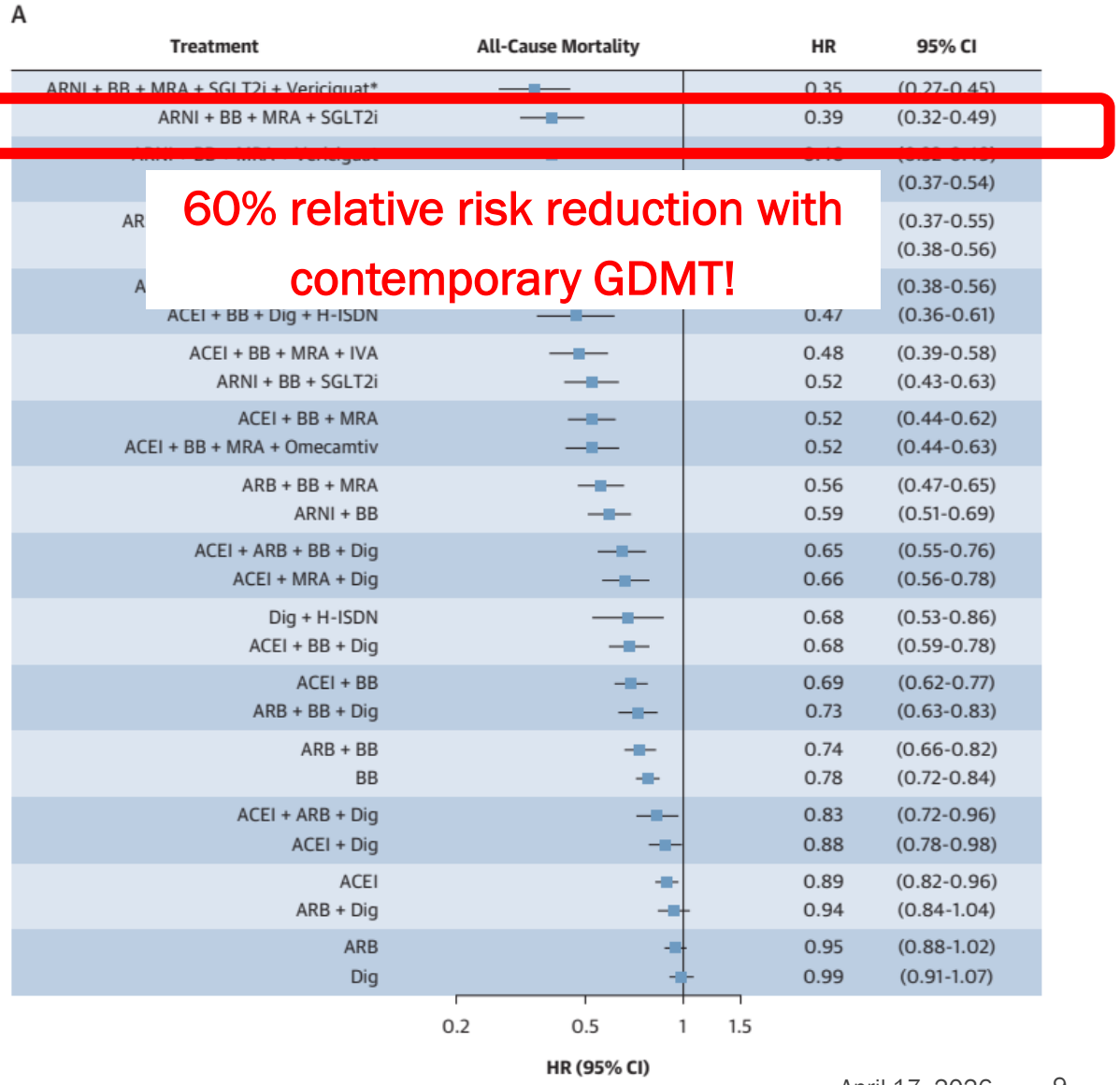
SINCE THEN, ADVANCES IN THERAPIES FOR HFREF HAVE IMPROVED OVERALL OUTCOMES



Sharma A, Verma S, Bhatt D, et al. Optimizing Foundational Therapies in Patients With HFrEF. JACC: BTS. 2022

MAGNITUDE OF MORTALITY RISK REDUCTION WITH GDMT

Therapy Class	Approximate Relative Risk Reduction
Beta Blockers	~35%
MRA	~30%
ACEi/ARB	~15-20%
ARNI	~15-20%
SGLT2 inhibitors	~15-20%



60% relative risk reduction with contemporary GDMT!

1. ACC/AHA HF Guidelines 2022
2. Van Essen, et al. JACC 2025.

2025: WHAT IS THE 1-YEAR MORTALITY OF HFREF ON CONTEMPORARY THERAPY?

65-YEAR-OLD | EF 25% | NYHA III

A. 5%

B. 10%

C. 15%

D. 25%

2025: WHAT IS THE 1-YEAR MORTALITY OF HFREF ON CONTEMPORARY THERAPY?

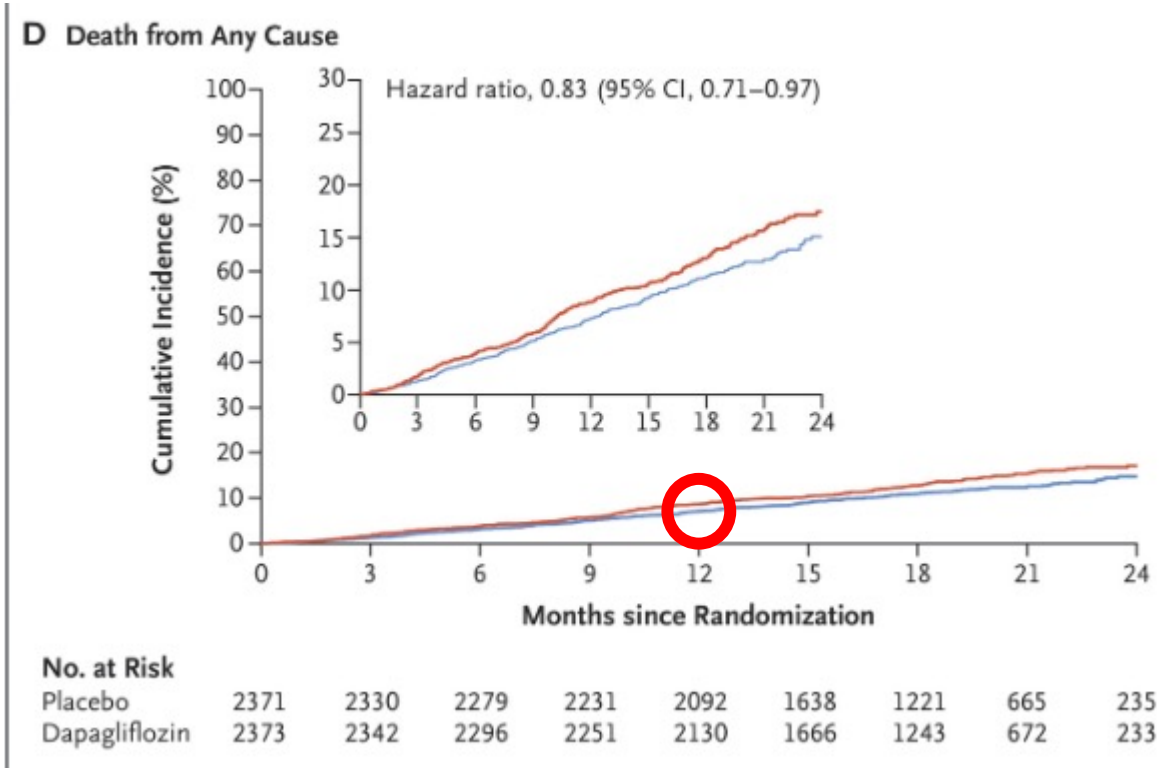
65-YEAR-OLD | EF 25% | NYHA III

A. 5%

B. 10% (DAPA HF, 2019. Treatment arm)

C. 15%

D. 25%



MODERN HFREF THERAPY HAS IMPROVED SURVIVAL — BUT NOT ENOUGH

Vericiguat in patients with chronic heart failure and reduced ejecti

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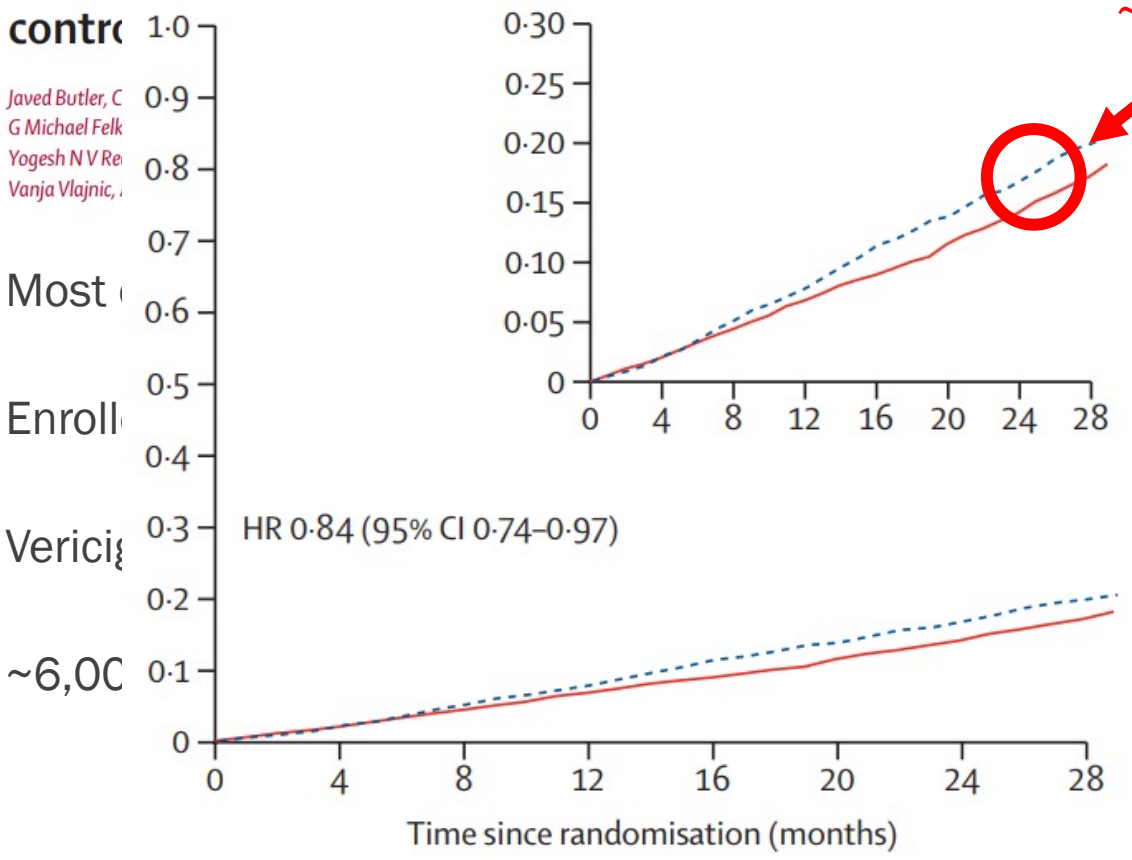
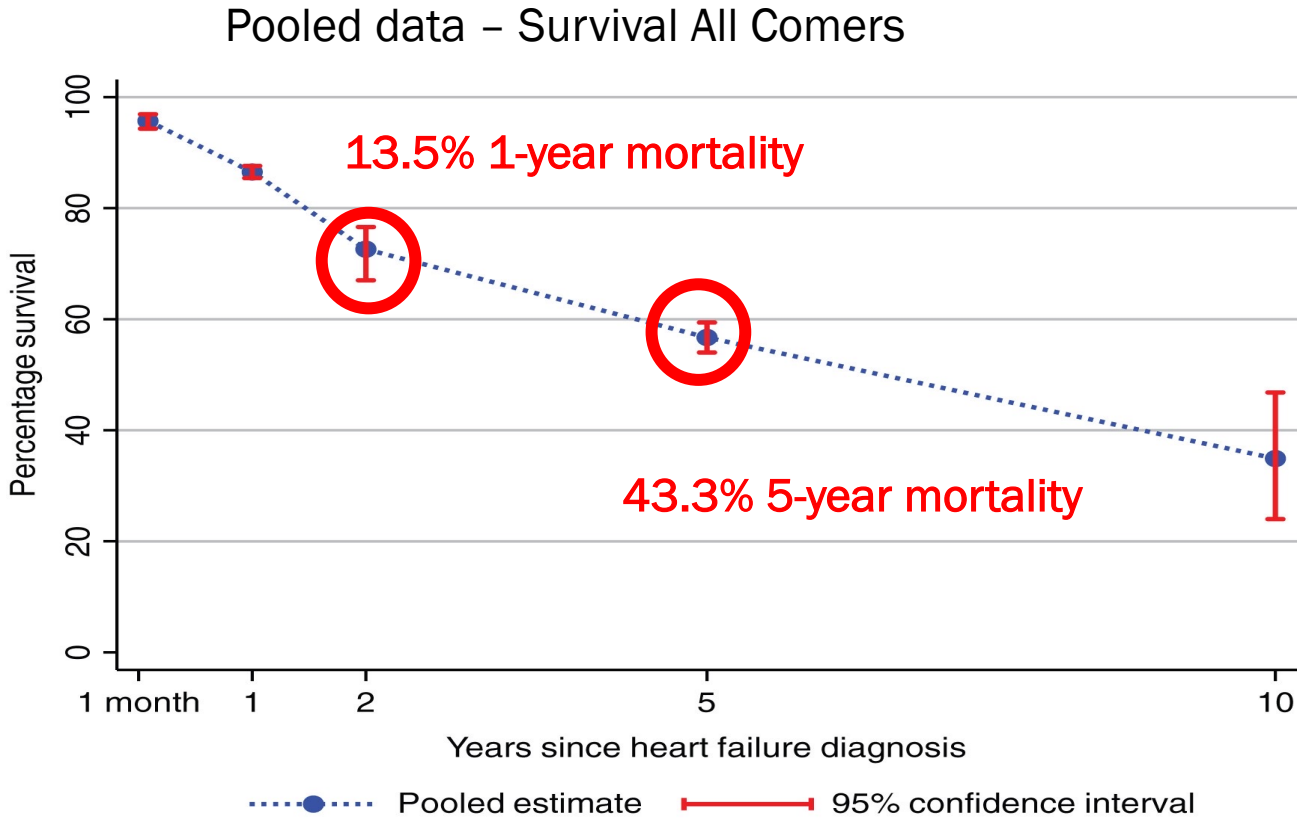
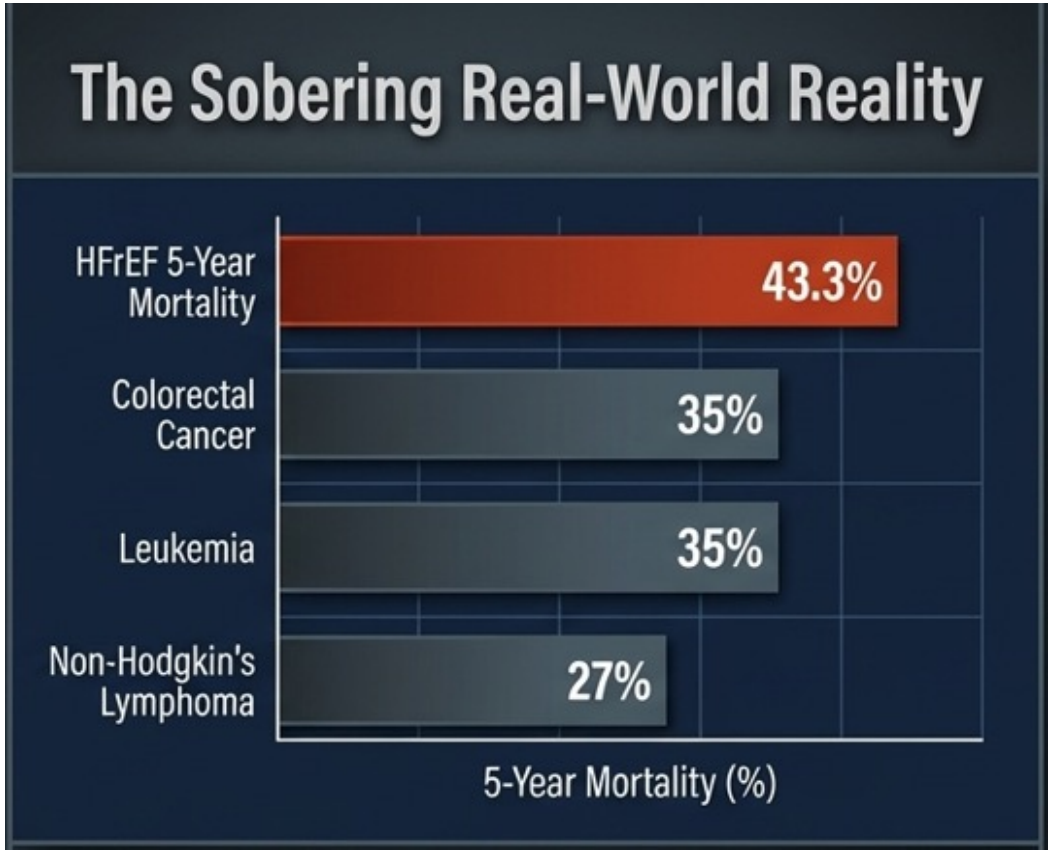


~16% 2 year mortality

	Vericiguat group (n=3053)	Placebo group (n=3052)
(Continued from previous column)		
ass		
	2411 (79·0%)	2411 (79·0%)
III	635 (20·8%)	633 (20·7%)
IV	7 (0·2%)	8 (0·3%)
LVEF, %	30·5% (7·0)	30·4% (7·0)
eGFR, mL/min per 1·73 m²	70·9 (23·8)	70·8 (24·3)
<15	3 (0·1%)	4 (0·1%)
≥15 to <30	118 (3·9%)	125 (4·1%)
≥30 to <60	921 (30·2%)	940 (30·8%)
≥60	1954 (64·0%)	1921 (62·9%)
Missing	57 (1·9%)	62 (2·0%)
Medical therapy		
Loop diuretics	2131 (69·8%)	2129 (69·8%)
β blockers	2886 (94·5%)	2880 (94·4%)
Angiotensin-converting enzyme inhibitor or angiotensin receptor blocker	1150 (37·7%)	1188 (38·9%)
Angiotensin receptor–neprilysin inhibitor	1734 (56·8%)	1682 (55·1%)
Mineralocorticoid receptor antagonist	2358 (77·2%)	2390 (78·3%)
SGLT2 inhibitor	1812 (59·4%)	1798 (58·9%)
Implantable cardioverter defibrillator	993 (32·5%)	1016 (33·3%)
Cardiac resynchronisation therapy	464 (15·2%)	440 (14·4%)

REAL WORLD DATA IS EVEN MORE SOBERING THAN CLINICAL TRIAL DATA WITH OUTCOMES WORSE THAN COMMON CANCERS

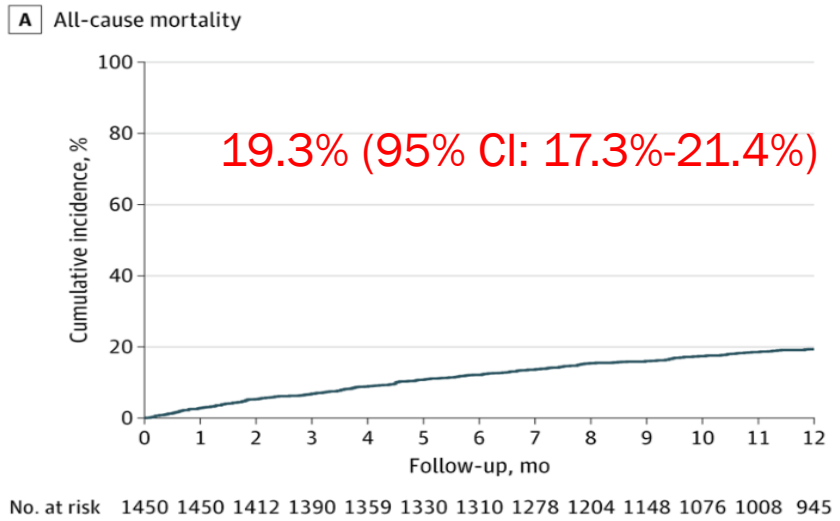


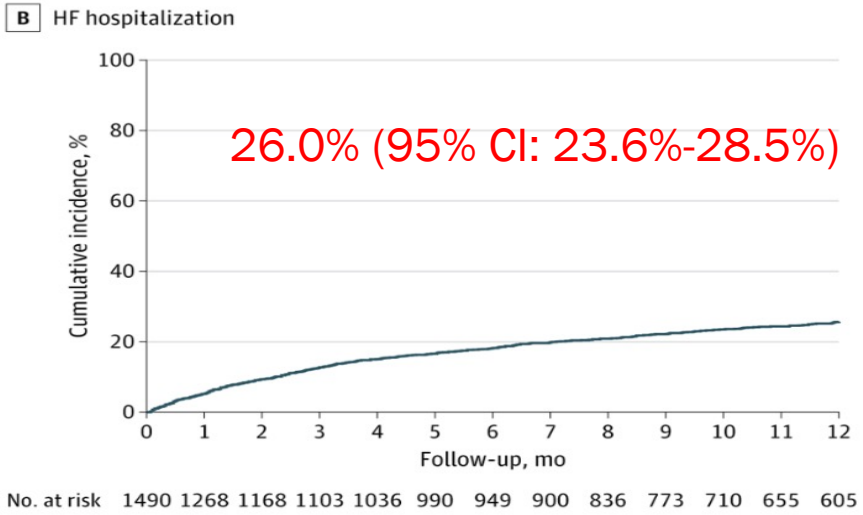


Eur J Heart Fail, Volume 21, Issue 11, November 2019, Pages 1306–1325.

WORSENING HEART FAILURE MARKS A SHARP INFLECTION IN RISK

- GWTG registry:
- 20,000 pts post hospital discharge b/w 2021-2023
- Focus on 1490 (7.2%) patients discharged on quad therapy.
- At 1 year:
  - 1 in 5 dead
  - 1 in 4 re-hospitalized





Greene et al. JAMA Cardiol. 2026.

ROLE OF THE HEART FAILURE PROGRAM

Guideline Directed Medical Therapy

Implementation Clinic

Remote Hemodynamic Monitoring

CardioMEMS

Cordella

Intermediate Device Therapies

Barostim

CCM

Investigational Therapies

Corcinch

Omecamtiv Mecarbil

Other Additional Agents/Therapies

Access to Advanced Therapies

Left Ventricular Assist Device (LVAD)

Transplant

THE IMPLEMENTATION GAP IN GDMT

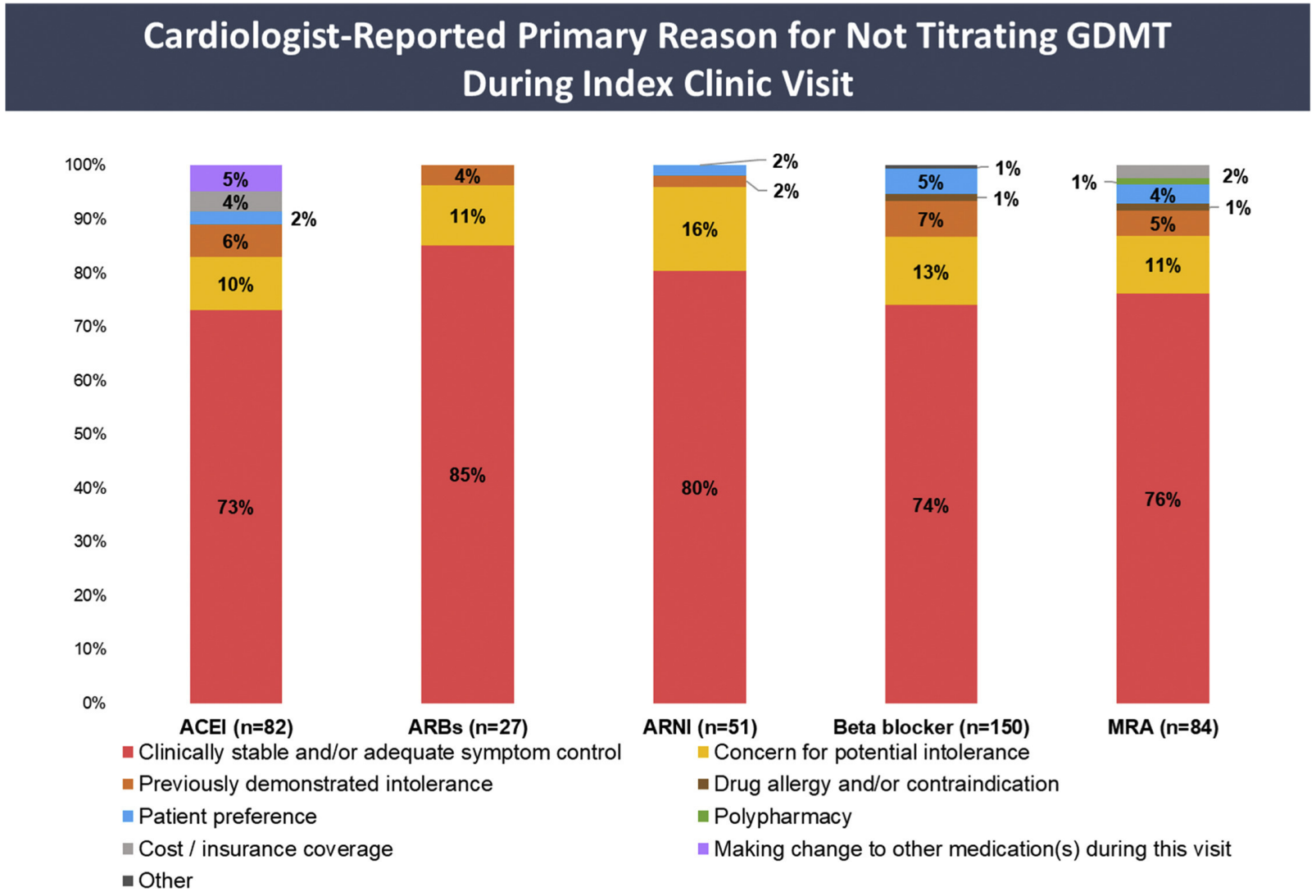
1. <u>CHAMP–HF REGISTRY:</u> 150 sites contributing data on outpatient HF mgmnt and outcomes
2. Analysis of 3,500 [illegible] age of 66±12 and LVEF 29%±8%
3. Only 22% were prescribed all three therapies.
   - 26% not on ACE/ARB/ARNI
   - 33% not on beta blocker
   - 66% not on MRA

Addressing the implementation gap will have a larger effect than any other one strategy

	ACEI/ARB	ARNI	ACEI/ARB/ ARNI	Beta-Blocker	MRA
Without Contraindication and Not Treated	1374	3029	920	1159	2317
Treated	2107	452	2536	2351	1163
With Contraindication	37	37	62	8	38

Greene et al. JACC. 2024.

WHY DOES THIS GAP EXISTS? SURVEY OF CARDIOLOGISTS



Greene, S. et al. JCF. 2025

Clinical and Systemic Barriers to Target Titration

Implementing GDMT is really hard!

Hemodynamic & Physiologic Constraints

- Symptomatic hypotension and borderline

Polypharmacy Burden

- Patient reluctance to manage multiple

ules

The Northwell HF clinics are structured to handle these issues and provide persistence in implementing GDMT.

Socioeconomic & Access Factors

- Restrictive insurance coverage and prior authorizations
- Prohibitive out-of-pocket costs for novel agents

Monitoring Fatigue

- The logistical burden of frequent vital monitoring
- Patient fatigue with continuous laboratory checks for renal function and electrolytes

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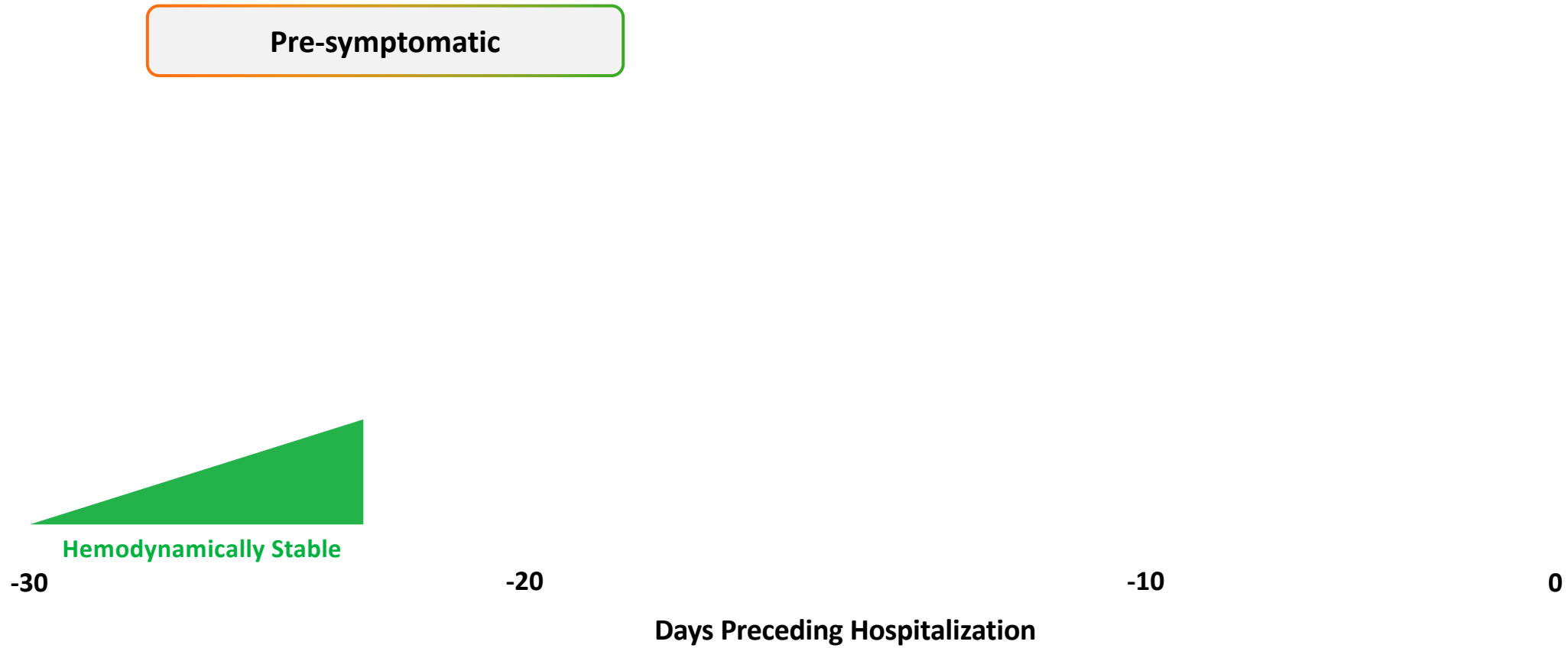
INTRA-CARDIAC AND PULMONARY ARTERY PRESSURES BEGAN TO RISE ABOUT 30 DAYS PRIOR TO HF SYMPTOMS



Adamson PB. Pathophysiology of the transition from chronic compensated and acute decompensated heart failure: new insights from continuous monitoring devices. *Current Heart Failure Reports.* 2009;6(4):287-292. doi:10.1007/s11897-009-0039-z

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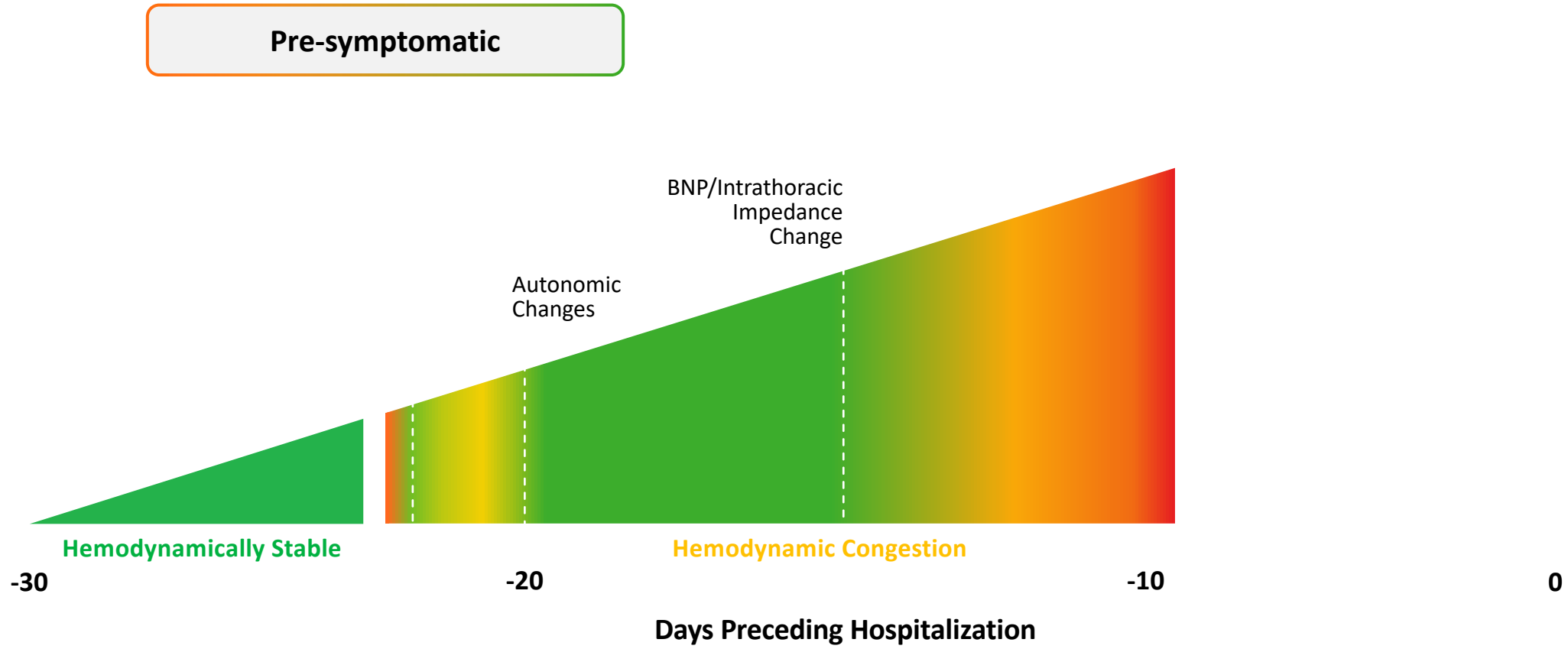

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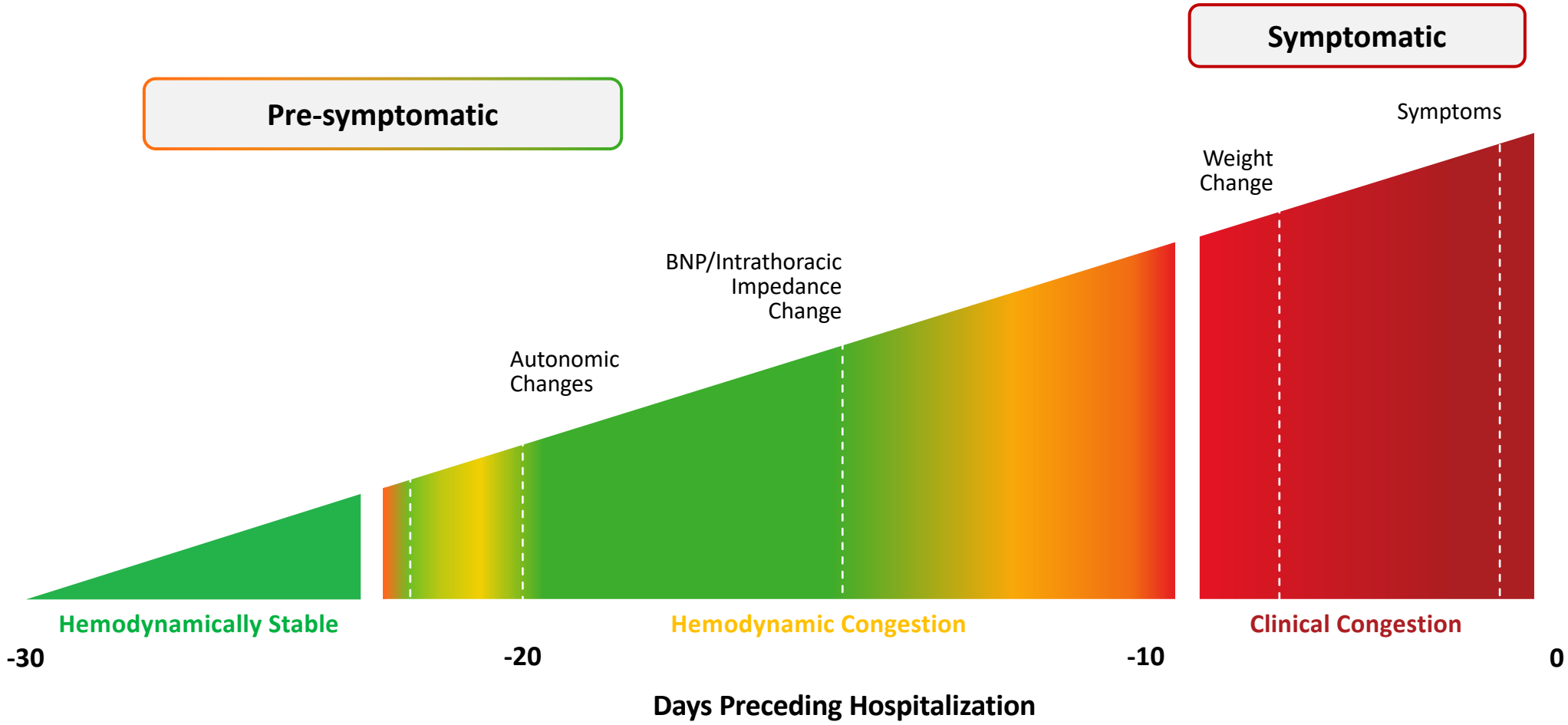

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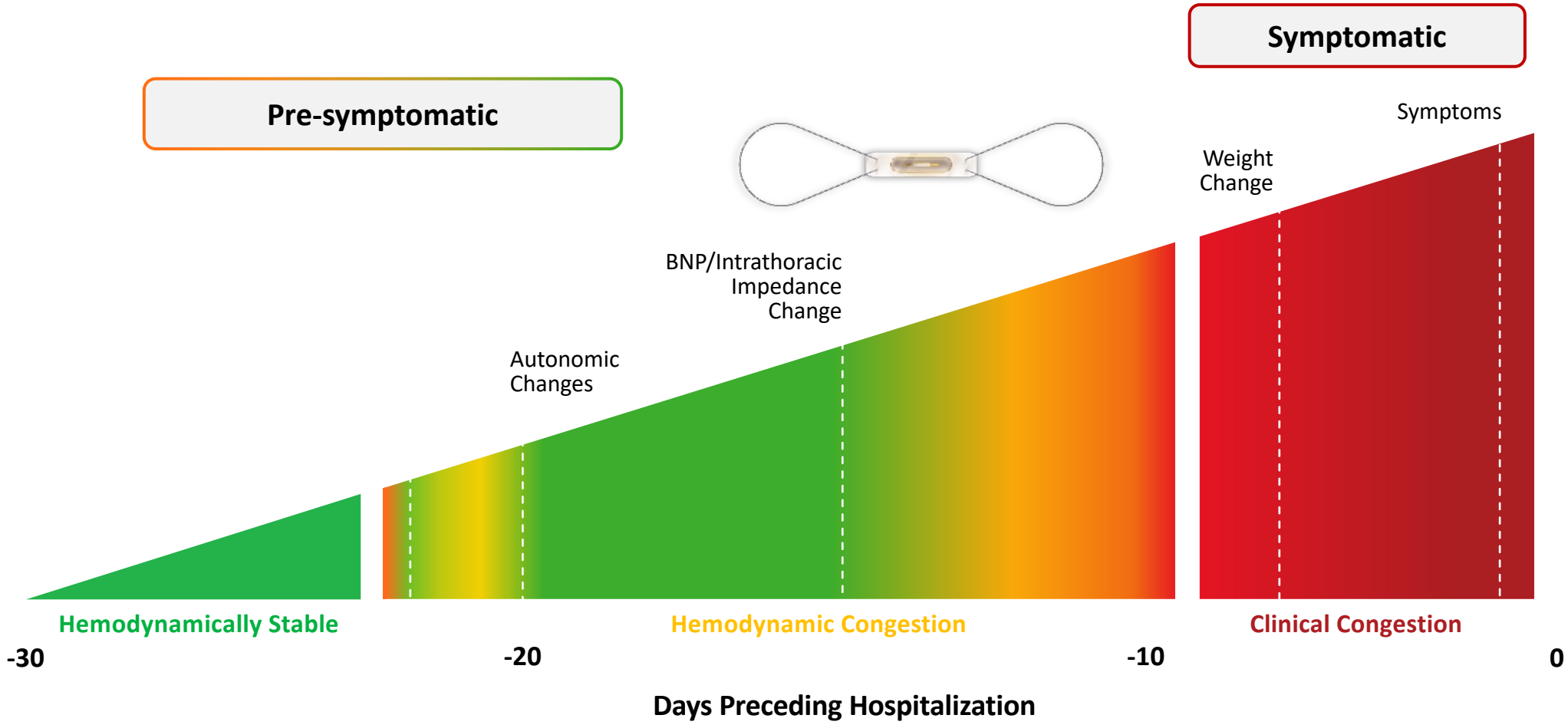

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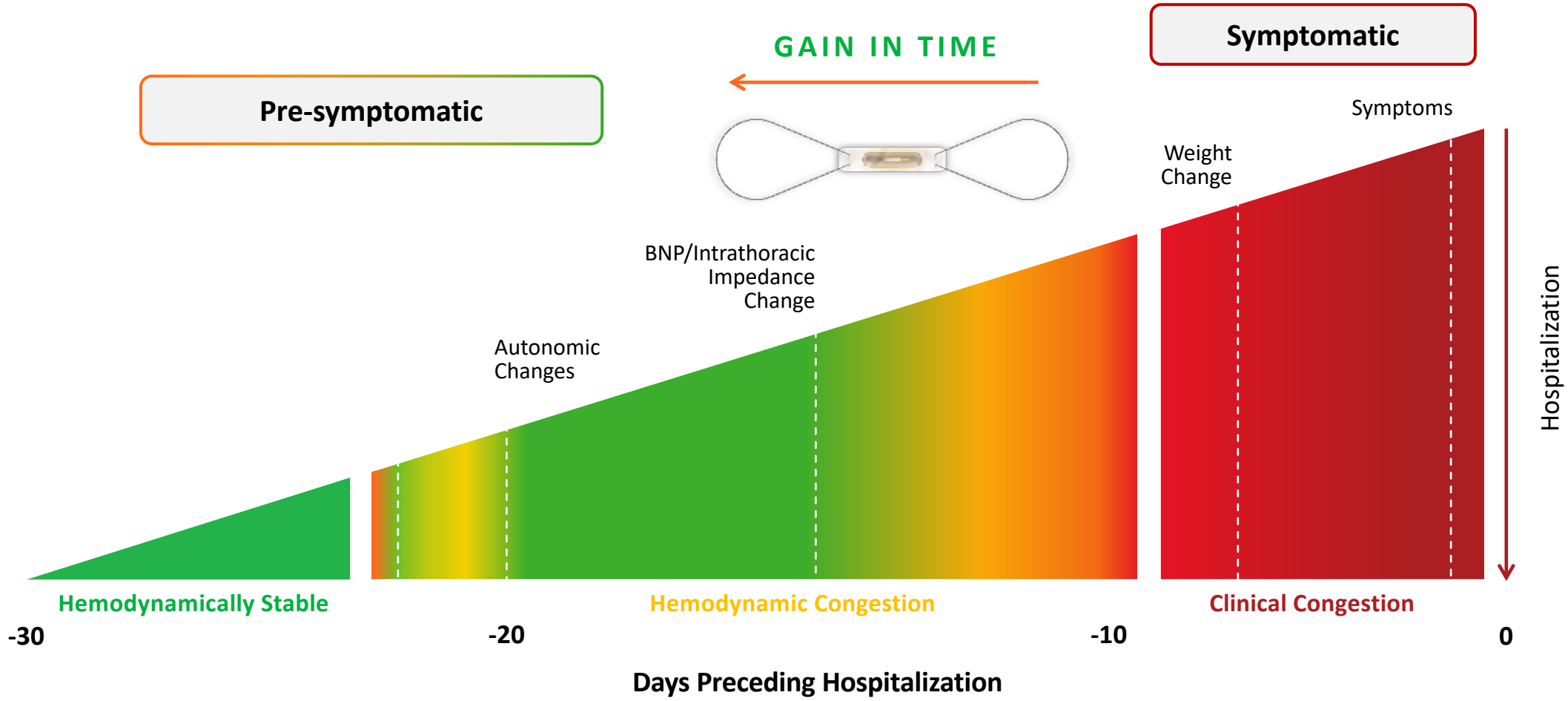

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THE CHAMPION STUDY

Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomised controlled trial

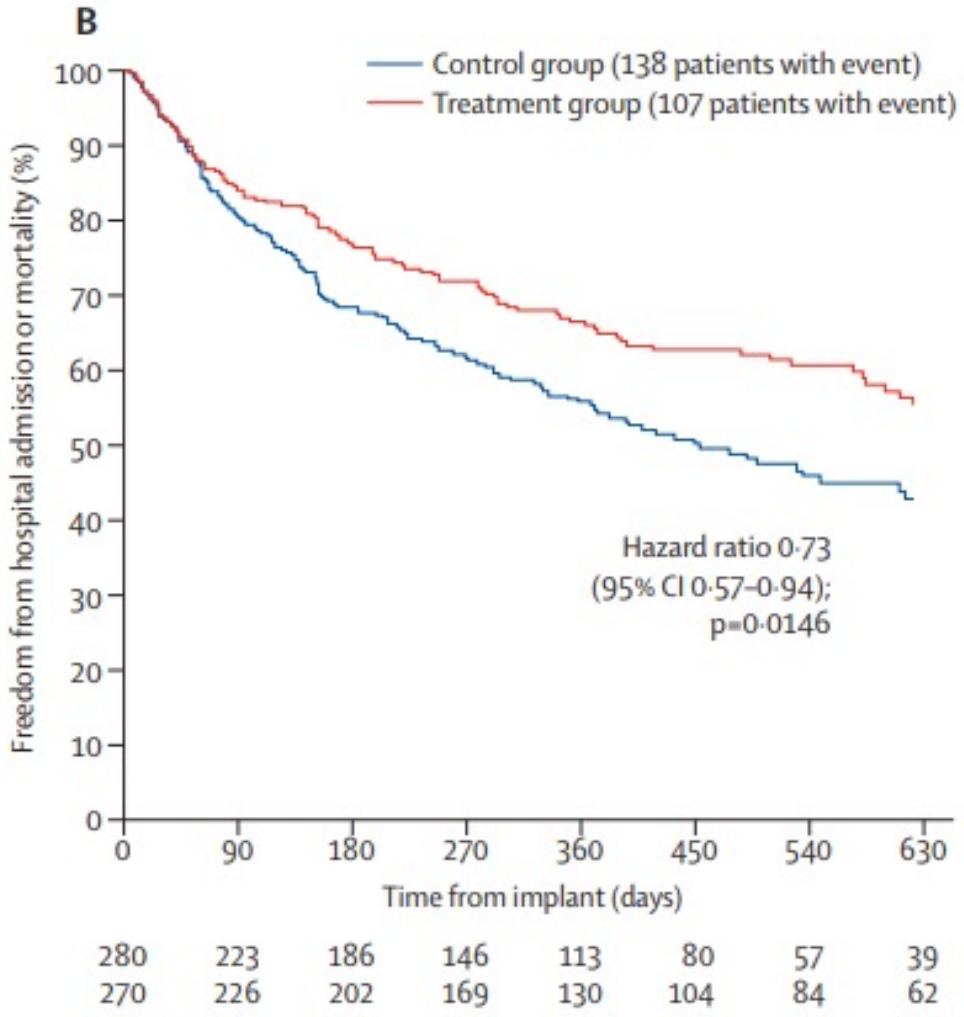
*William T Abraham, Philip B Adamson, Robert C Bourge, Mark F Aaron, Maria Rosa Costanzo, Lynne W Stevenson, Warren Strickland, Suresh Neelagaru, Nirav Raval, Steven Krueger, Stanislav Weiner, David Shavelle, Bradley Jeffries, Jay S Yadav, for the CHAMPION Trial Study Group**

550 pts with NYHA III HF and admission within prior year.

After CardioMEMS implant randomized to active monitoring vs control.

At 6 mos f/u the treatment group had:

- A greater reduction in mPAP
- Fewer hospitalizations for HF
- More days alive outside hospital
- Better quality of life

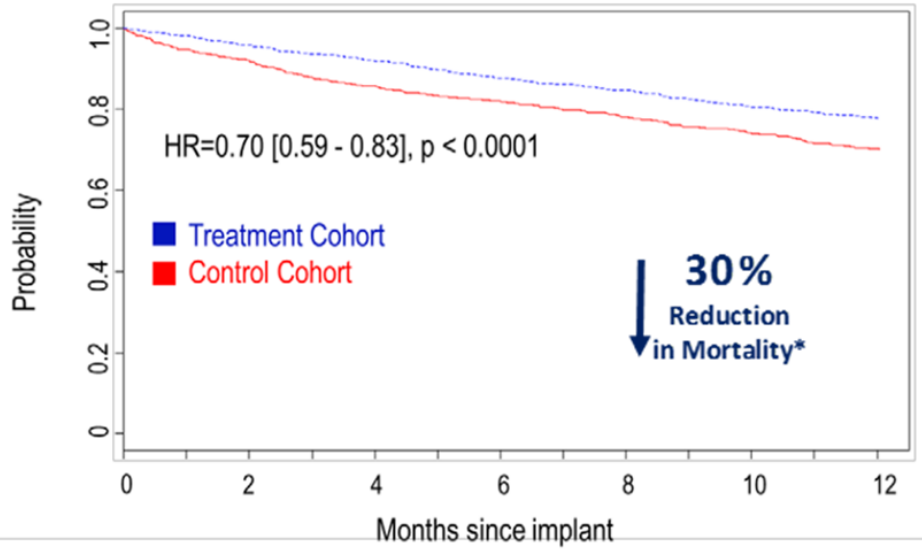


Abraham et al. Lancet. 2011.

CARDIOMEMS HF SYSTEM AND MORTALITY

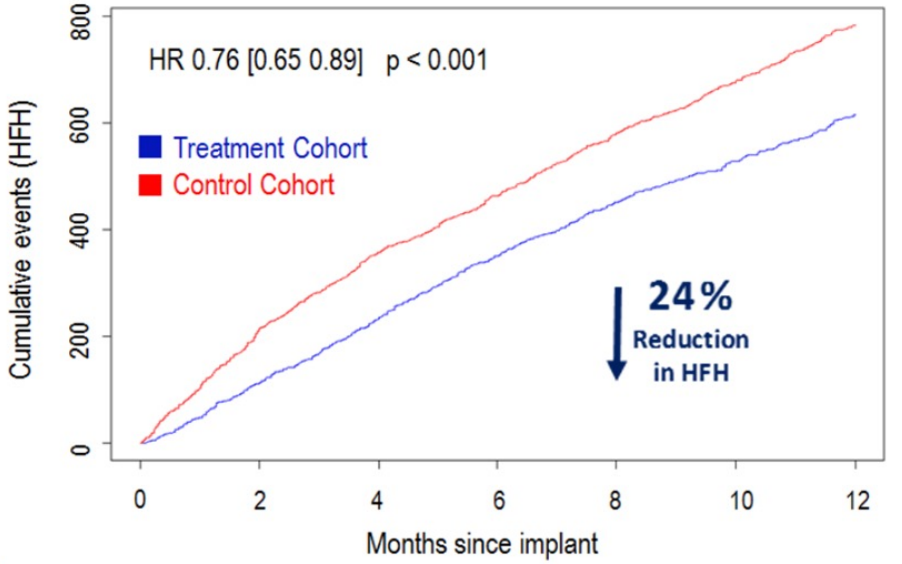
30% REDUCTION IN MORTALITY AT ONE YEAR

Kaplan-Meier Survival after implant or index date



Number at risk							
Treatment cohort	1087	1037	991	944	908	862	830
Control cohort	1087	1000	931	891	850	805	764

Cumulative HFH events after implant or index date



Number at risk							
Treatment cohort	1087	1037	991	944	908	862	830
Control cohort	1087	1000	931	891	850	805	764

SINCE CHAMPION, THERE HAVE BEEN CONSISTENT OUTCOMES SUPPORTED BY MULTIPLE STUDY DESIGNS

RANDOMIZED CONTROLLED

- **CHAMPION** (N = 550)
- **GUIDE-HF RANDOMIZED ARM** (N = 1,000)
- **MONITOR-HF (EUROPEAN)** (N = 348)

SINGLE-ARM

- **U.S. POST-APPROVAL** (N = 1,200)
- **MEMS-HF (EUROPEAN)** (N = 234)
- **COAST-HF (TOTAL COHORT)** (N = 321)
- **GUIDE-HF SINGLE ARM** (N = 1,001)

PROPENSITY-MATCHED

- **ABRAHAM MEDICARE** (N = 2,174)
- **KRIMM 5-YR OUTCOMES** (N = 7,128)

SUMMARY OF KEY CLINICAL OUTCOMES SHOWN IN THESE ANALYSIS

REDUCTION IN PA PRESSURES[23-31]

REDUCTION IN HEART FAILURE HOSPITALIZATIONS[23-31,33,34]

IMPROVED SURVIVAL[23,36-37]

OPTIMIZED MEDICAL MANAGEMENT[23-24,26-27,36-37]

HFpEF AND HFrEF PATIENTS[23-24,26-30,32]

IMPROVED QOL[23,26,29]

NORTHWELL CARDIOMEMS PROGRAM – TRANSITION TO CENTRALIZED REMOTE MONITORING

- **Problem:**

  CardioMEMS requires significant personnel time to follow and respond to transmissions.

  Expanding access to technology and adherence to transmission are an opportunity for improvement.

- **Proposal:**

  Centralized management with communication to local sites.

  2 RNs, 1 biller, 1 secretary

  Codified treatment algorithm

  Financial analysis project this to be net neutral. Quality of care potential remains high.

  Go Live July 2027

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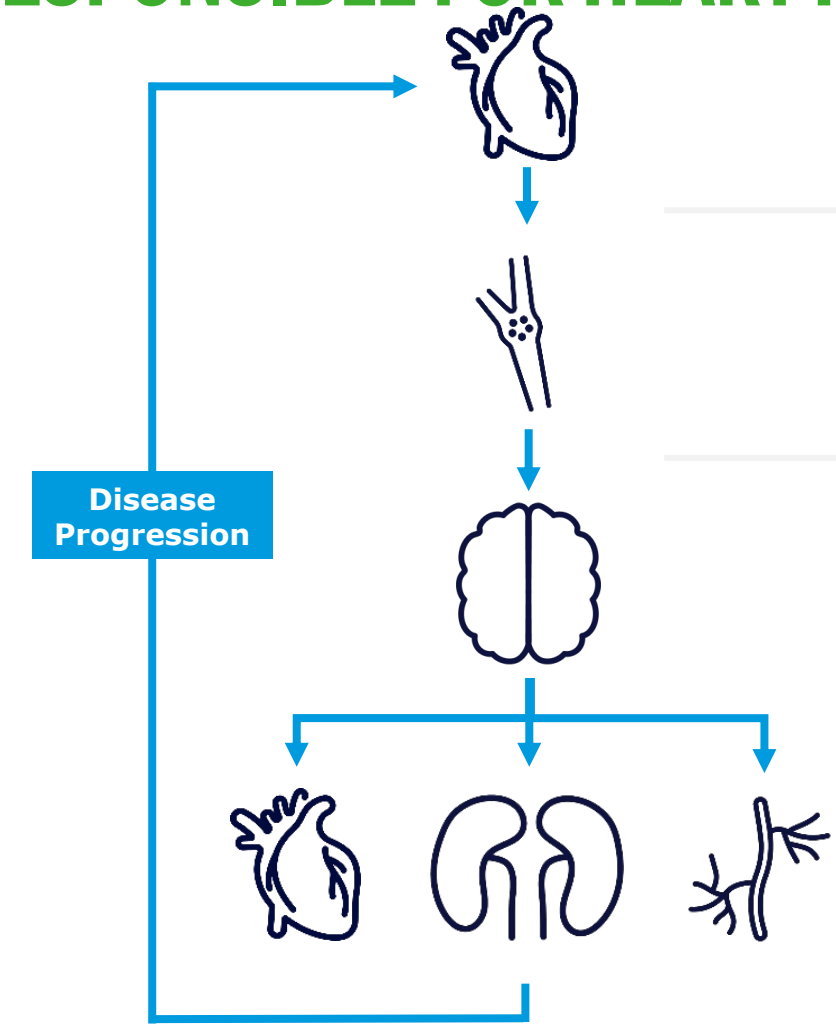
BAROSTIM TARGETS THE NEUROHORMONAL PATHWAYS RESPONSIBLE FOR HEART FAILURE PROGRESSION

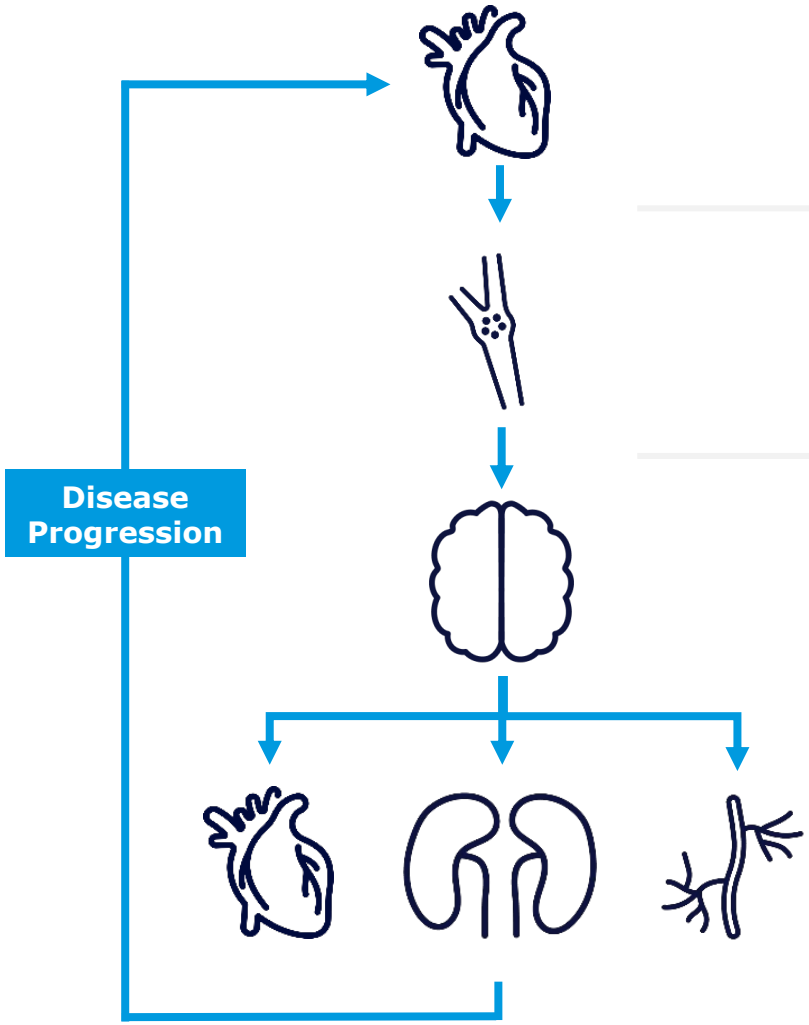


1. Weakened heart & heart failure symptoms
   - ↓ **Contractility**
2. **Reduced stretch sensed by baroreceptors**
   - ↓ **Baroreceptor Signaling**
3. Brain interprets as acute hemorrhage or dehydration and activates neurohormonal systems
   - ↑ **Sympathetic Activity**
   - ↑ **RAAS Activation**
   - ↓ **Parasympathetic Activity**
4. Chronic excess neurohormones* produce adverse hemodynamic effects & organ toxicity
   - ↓ **Cardiovascular Function**
   - ↑ **Heart Failure Symptoms**

* Norepinephrine, Angiotensin II, Aldosterone, etc.

Adapted from Packer M. J Am Coll Cardiol. 1992;20:248-54; Hartupee J and Mann DL. Nat Rev Cardiol. 2017;14:30-38; Mann DL and Felker GM. Circ Res. 2021;128:1435-1450.

DRUG THERAPIES WORK BY BLOCKING SPECIFIC EXCESS NEUROHORMONES



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Neurohormonal blockade is the basis of drug therapy

4. Chronic excess neurohormones* produce adverse hemodynamic effects & organ toxicity
   - ↓ **Cardiovascular Function**
   - ↑ **Heart Failure Symptoms**

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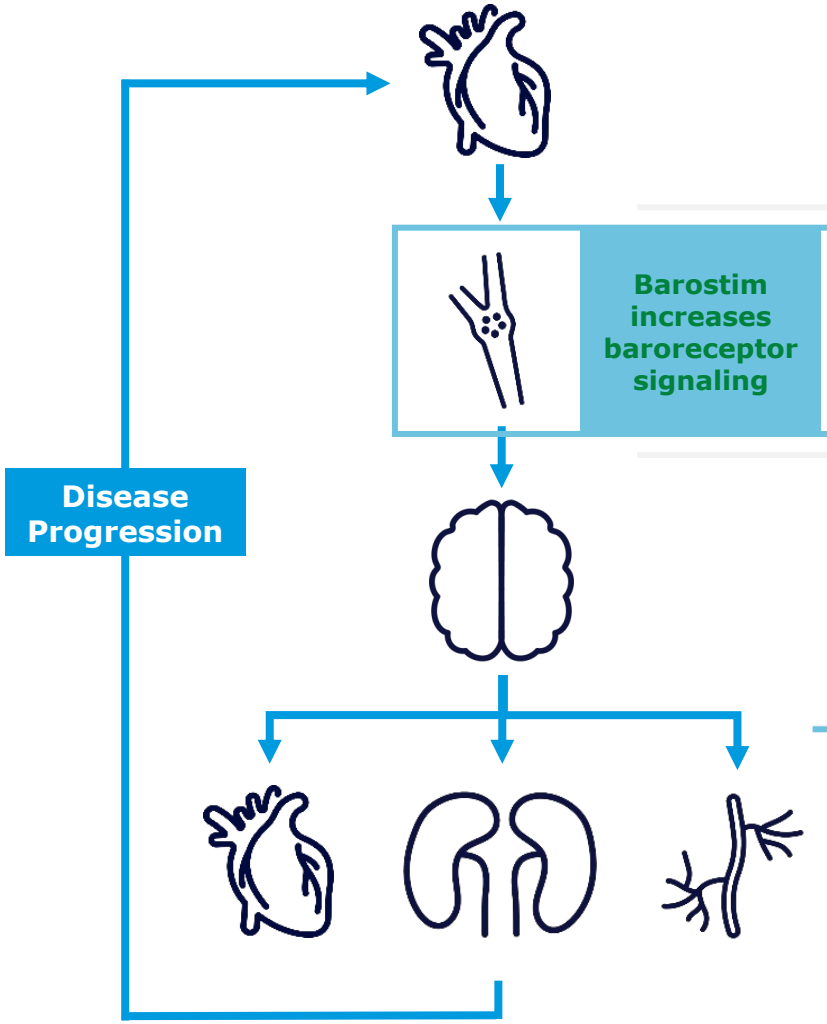
BAROSTIM COMPLEMENTS DRUG THERAPY BY ACTING UPSTREAM TO RESTORE BARORECEPTOR SIGNALING



1. Weakened heart & heart failure symptoms → ↓ Contractility

Barostim increases baroreceptor signaling

2. Reduced stretch sensed by baroreceptors → ↓ Baroreceptor Signaling

3. Brain interprets as acute hemorrhage or dehydration and activates neurohormonal systems → ↑ Sympathetic Activity; ↑ RAAS Activation; ↓ Parasympathetic Activity

Neurohormonal blockade is the basis of drug therapy

4. Chronic excess neurohormones* produce adverse hemodynamic effects & organ toxicity → ↓ Cardiovascular Function; ↑ Heart Failure Symptoms

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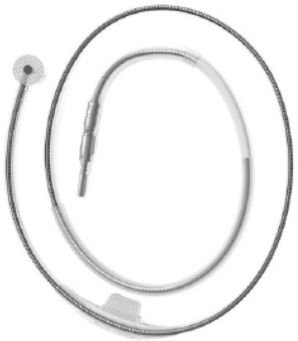
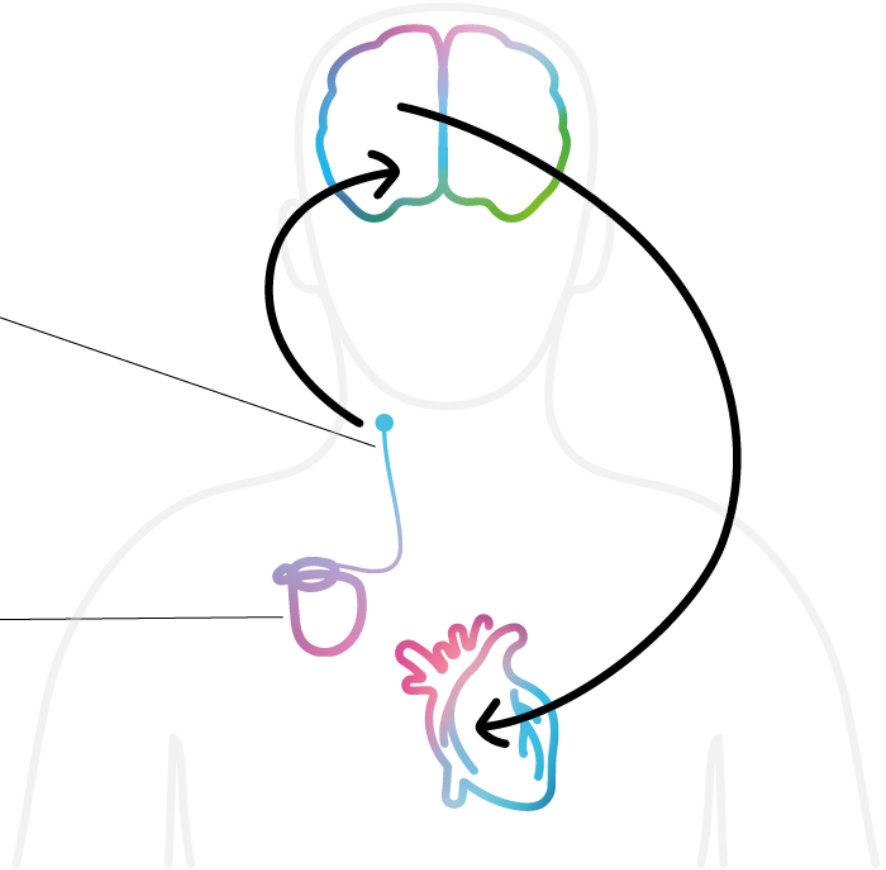
BAROSTIM DEVICE



Small wire, called a lead, is implanted on the carotid artery

Pulse generator, similar to a pacemaker, is implanted under the skin



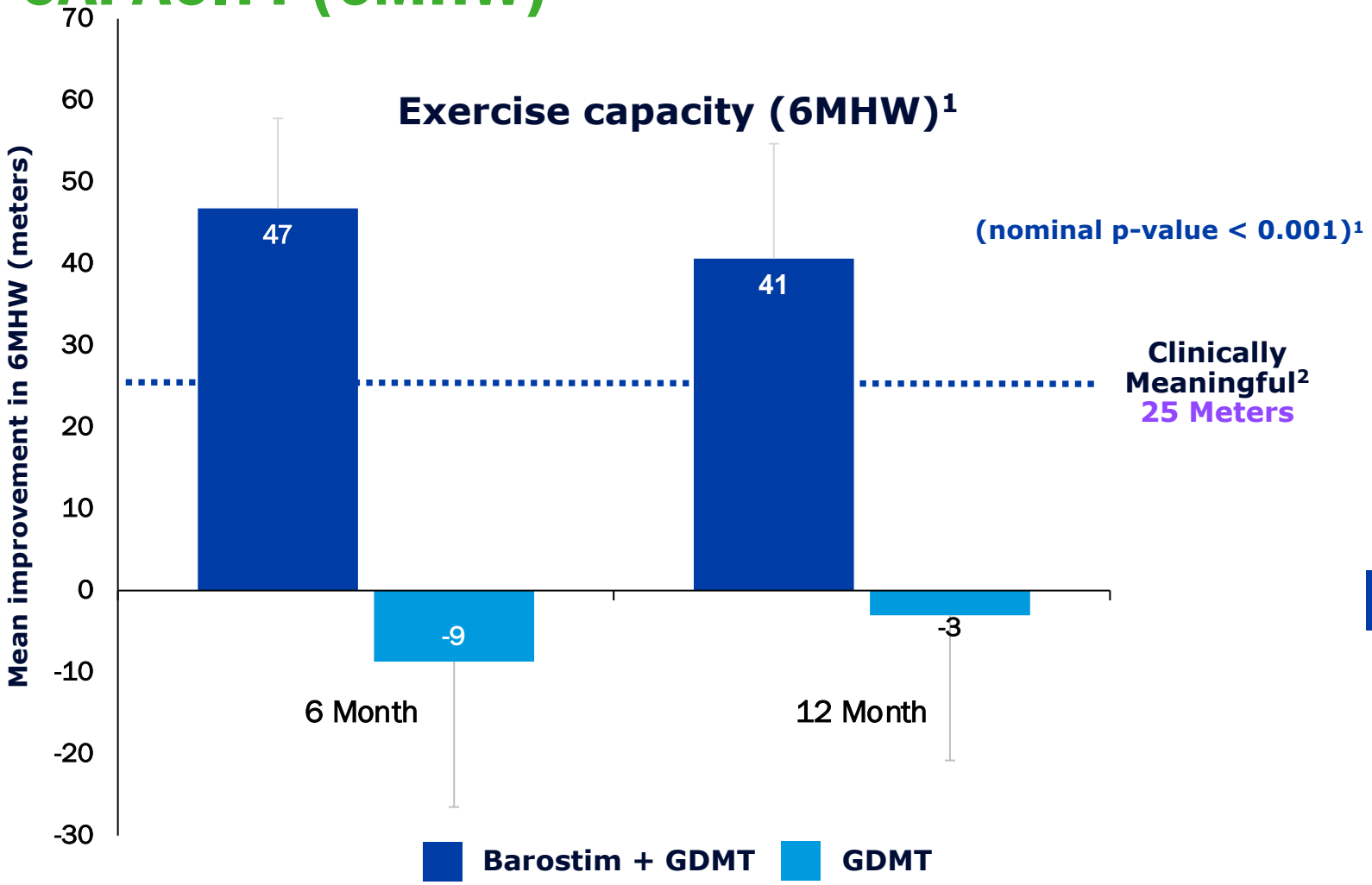
THE BEAT-HF TRIAL: BASELINE DEMOGRAPHICS

	Barostim (n=163)	Control (n=160)
Demographics		
Age at Screening (years)	63 ± 11	63 ± 10
Gender (Female)	28 (17.2%)	35 (21.9%)
Race (Caucasian)	120 (73.6%)	116 (72.5%)
Heart failure and physical status		
SBP (mmHg)	120 ± 16	121 ± 16
DBP (mmHg)	74 ± 10	73 ± 10
HR (bpm)	75 ± 10	75 ± 11
BMI (kg/m2)	31 ± 5	31 ± 5
eGFR	62.5 ± 16.3	61.1 ± 18.9
NYHA: Class III	155 (95.1%)	151 (94.4%)
LVEF (%)	27 ± 6	28 ± 6
6 Minute Walk (m)	314 ± 66	300 ± 71
QOL	53 ± 24	51 ± 24
NT-proBNP (pg/mL)	736 (474, 1057)	704 (442, 1044)
LBBB	4 (2.5%)	2 (1.3%)
>=1 HF Hospitalization	66 (40.5%)	79 (49.4%)
Number of HF Hospitalizations	0.6 ± 0.9	0.7 ± 0.8

	Barostim (n=163)	Control (n=160)
Co-Morbidities		
Coronary Artery Disease	104 (63.8%)	107 (66.9%)
Atrial Fibrillation	53 (32.5%)	66 (41.3%)
Stroke or TIA	29 (17.8%)	37 (23.1%)
Chronic Kidney Disease	45 (27.6%)	43 (26.9%)
Type II Diabetes	74 (45.4%)	80 (50.0%)
Heart failure treatment		
Number of Meds	4.0 ± 1.3	4.1 ± 1.5
ACE-I / ARB / ARNI	143 (88%)	129 (81%)
ARNI	57 (35%)	43 (27%)
Beta-Blocker	152 (93%)	147 (92%)
MRA	74 (45%)	64 (40%)
Diuretic	138 (85%)	139 (87%)
Ivabradine	4 (2.5%)	9 (5.6%)
ICD	125 (77%)	127 (79%)

Zile MR, et al. Eur J Heart Fail. 2024;26:1051-1061.

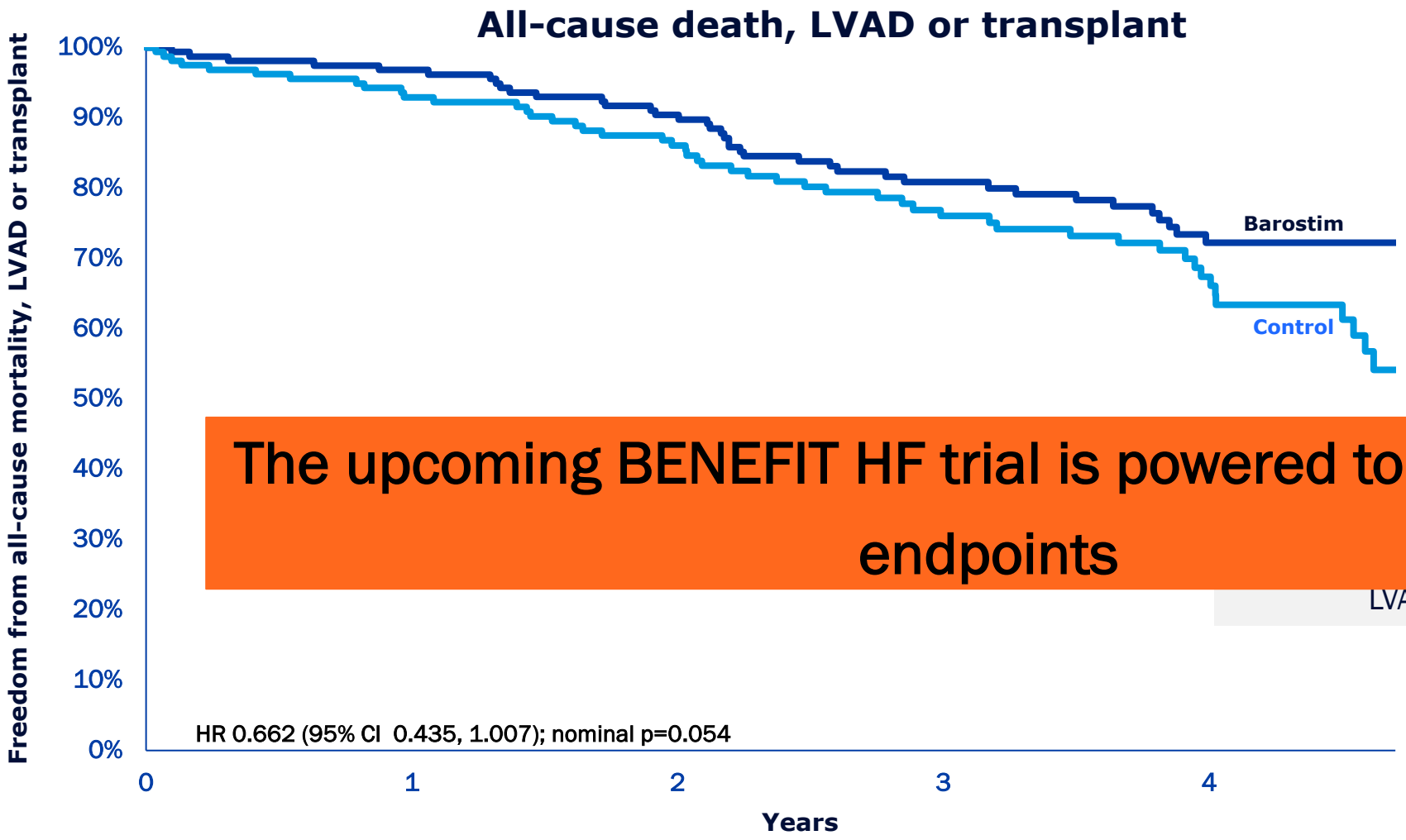
BAROSTIM PROVIDED SIGNIFICANT IMPROVEMENT IN EXERCISE CAPACITY (6MHW)



CRT trial results at 6 months*		
CONTAK CD[3]	NYHA III or IV LVEF ≤ 35% QRS > 120ms	39m
MIRACLE[4]	NYHA III or IV LVEF ≤ 35% QRS > 130ms	29m

Zile MR, et al. Eur J Heart Fail. 2024;26:1051-1061; 2. Gremeaux V, et al. Arch Phys Med Rehabil. 2011;92:611-619; 3. Higgins SL, et al. J Am Coll Cardiol. 2003;42:1454-1459; 4. Abraham WT, et al. N Engl J Med. 2002;346:1845-1853.

REDUCTION IN ALL-CAUSE DEATH, LVAD OR TRANSPLANT



The upcoming BENEFIT HF trial is powered to explore hard endpoints

% of
LVAD or heart transplant

Zile MR, et al. Eur J Heart Fail. 2024;26:1051-1061.

ROLE OF THE HEART FAILURE PROGRAM

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Barostim

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Corcinch

Omecamtiv Mecarbil

Other Additional Agents/Therapies

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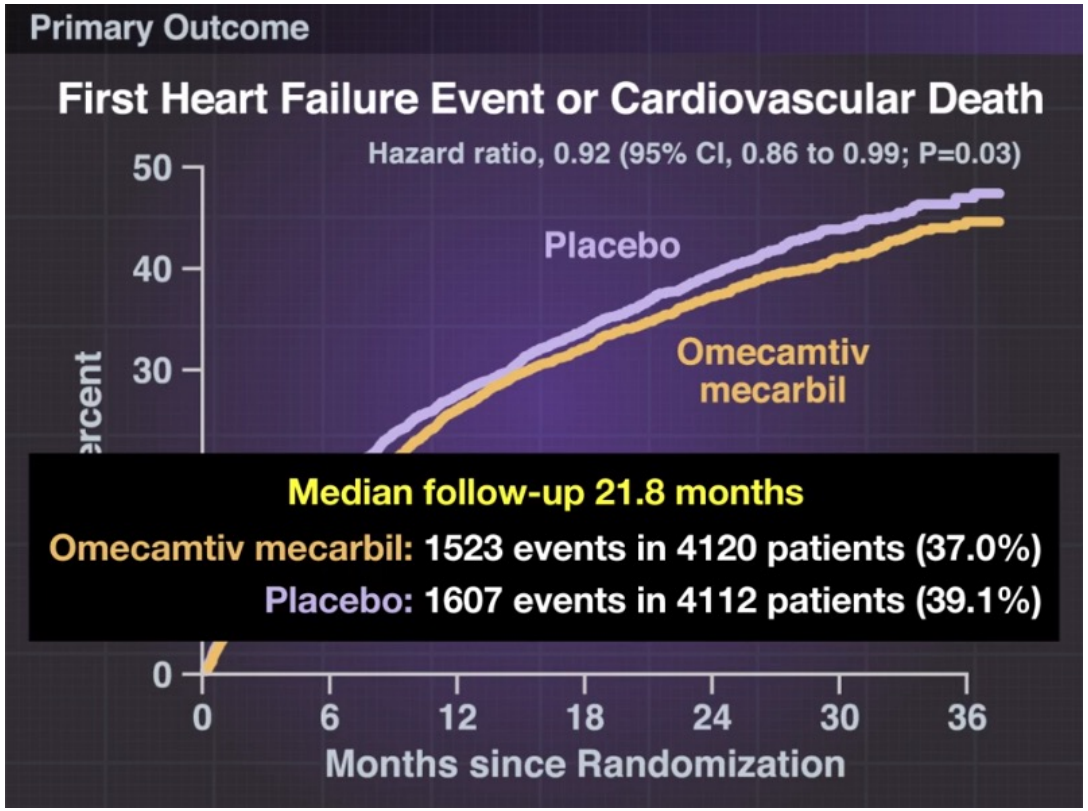
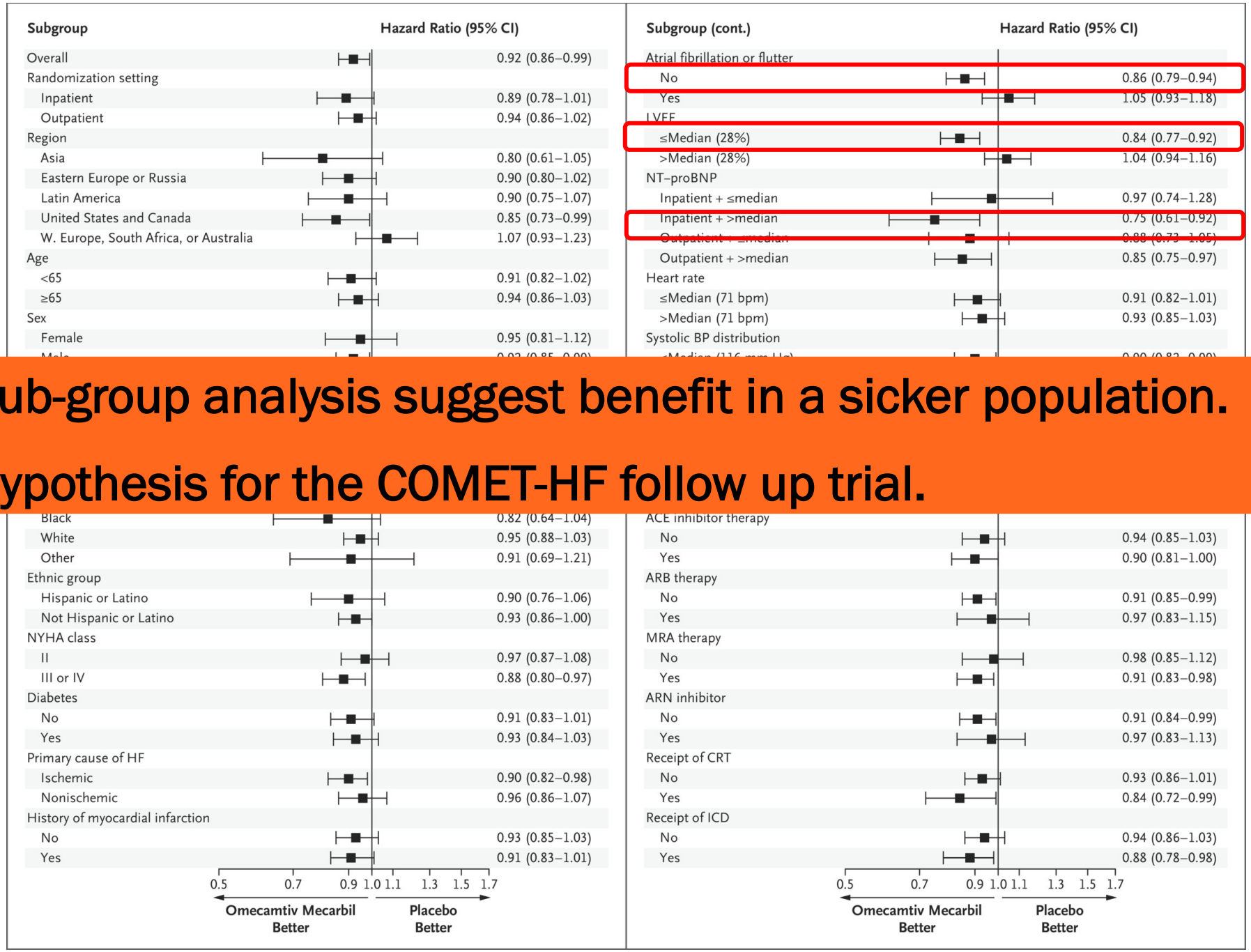
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 14, 2021 VOL. 384 NO. 2

Cardiac Myosin Activation with Omecamtiv Mecarbil in Systolic Heart Failure

- Omercamtiv Mecarbil a novel agent – cardiac myosin activator that improves cardiac function without increasing myocardial oxygen demand.
- Symptomatic chronic heart failure study.
- Primary endpoint was neutral.





Sub-group analysis suggest benefit in a sicker population.

Hypothesis for the COMET-HF follow up trial.

COMET HF Study

A Multi-Center, Double-Blind, Randomized, Placebo-Controlled Trial to Assess Efficacy and Safety of Omecamtiv Mecarbil in Patients with Symptomatic Heart Failure with Severely Reduced Ejection Fraction

PI:
Dr. Dipan Uppal
Sub-Is
Dr. Snehal Patel
Dr. Simon Maybaum

Coordinators:
Dhruti Patel

Inclusion Criteria

- Age: 18-85 years
- Have a history of chronic HFrEF, requiring Rx for a minimum of 3 months prior to screening
- Are receiving oral loop diuretics on a regular schedule
- Patient w/out AFF on screening EKG: LVEF <30% within 6 months of screening, proBNP ≥1000 pg/ml
- Patients w/AFF: LVEF <25% within 6 months of screening, proBNP ≥3000 pg/ml, not currently taking digoxin
- HFH criteria - are currently hospitalized with primary reason of HF or had HF event within 12 months prior to screening or (i) at leadt 50% or 1.5 fold increase in daily loop diuretic-equivalent dose (ii) addition of a new diuretic class to loop diuretic
- Are established on regional SOC HF therapies for at least 30 days prior to screening.
- SBP ≤140 mmHg

Overall sample size: 2050 patients
Randomized Arm: 1800 patients

Objectives

The overall objectives of COMET-HF trial are:

1) To evaluate the efficacy of omecamtiv mecarbil compared with placebo on the risk of HF outcomes in patients with symptomatic HFrEF and severely reduced ejection fraction in the setting of guideline-directed medical therapy per local standard of care

2) To evaluate the effect of omecamtiv mecarbil compared with placebo on risk of CV death and HF event, irreversible morbidity/mortality related to HFrEF, on risk of all-cause mortality

Endpoints

Primary Endpoint- Time to the first event of the following components: • CV death • HF event • LVAD implantation or cardiac transplantation • Stroke

Secondary Endpoint- Time to the first event of the following components: • CV death • HF event • Time to the first HF hospitalization

ACTIVELY ENROLLING at NSUH

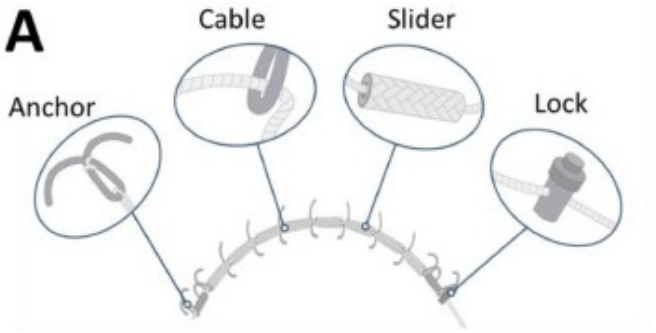
Please reach out to Dr. Uppal
duppal@northwell.edu

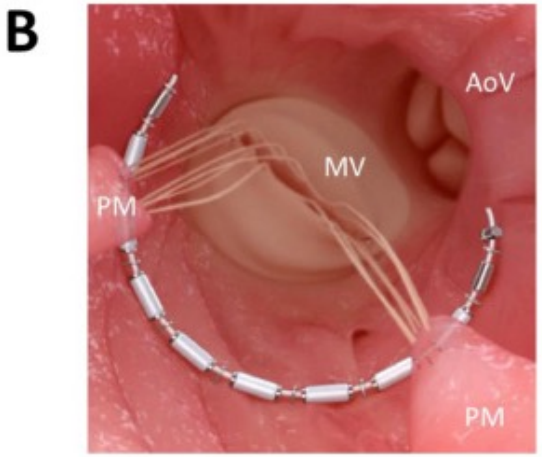
Exclusi

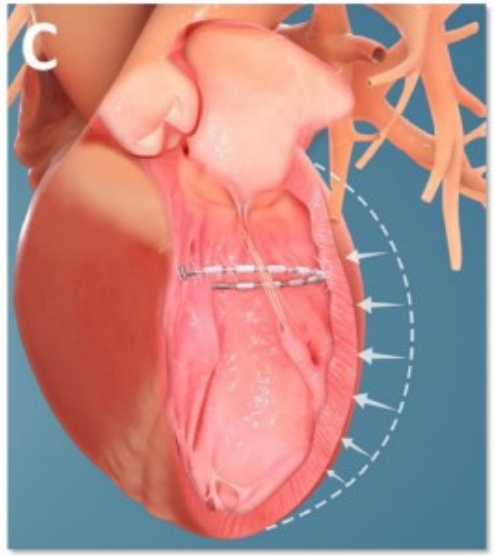
- Have AFF on the screening I… digoxin
- Have had acute coronary sy… surgery, any coronary revas… resynchronization therapy within 3 months of screening
- Are receiving iv inotropes or vasopressors ≤ 3 days, mechanical hemodynamic support or mechanical ventilation ≤ 7 days prior to screening
- Are receiving iv diuretics, iv vasodilators, or supplemental oxygen therapy ≤ 12 hours prior to screening (exception – nocturnal supplement O2 for sleep apnea)
- History of any solid organ transplant
- Have an estimated glomerular filtration rate (eGFR) < 20 mL/min/1.73m2 or receiving dialysis at screening
- Are receiving treatment in another investigational device or drug study or are within 30 days of ending such investigational treatment at screening.
- Have previously received omecamtiv mecarbil
- Primary infiltrative cardiomyopathy (eg: cardiac amyloidosis) or severe stenotic valvular disease.

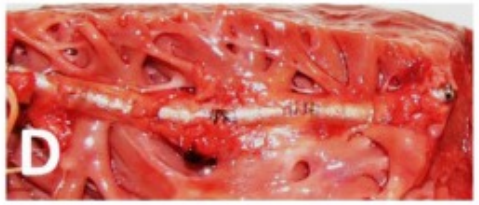
TRANSCATHETER LEFT VENTRICULAR RESTORATION – ACCUCINCH

LV REMODELING CONTINUES BEYOND IMMEDIATE PROCEDURE









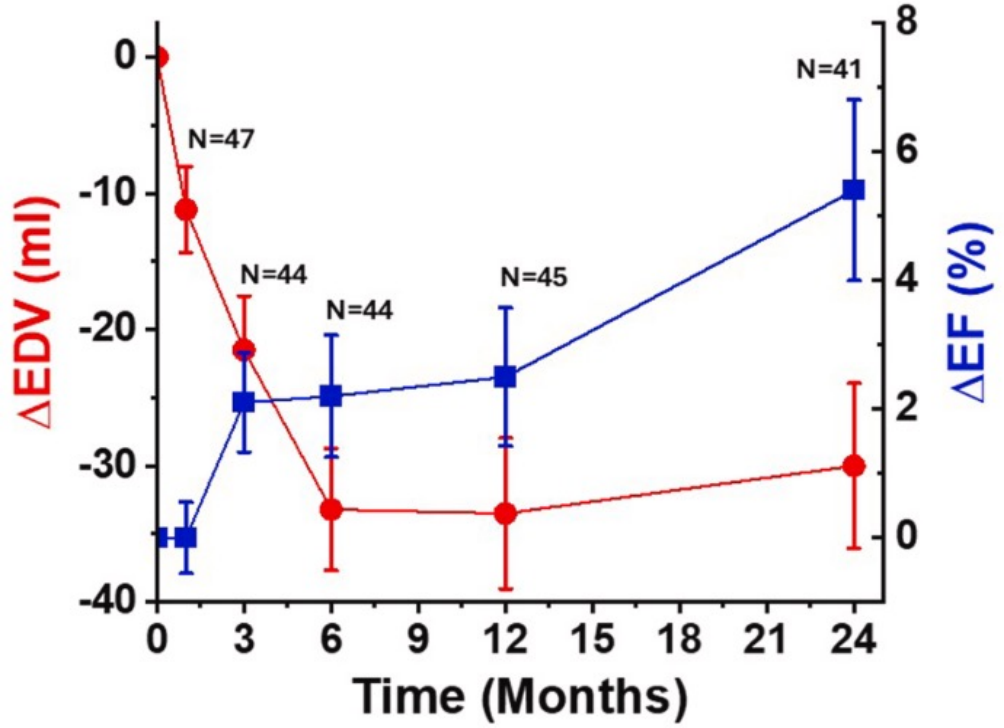


FIGURE 1

Kurlianskaya, A et al. Struct Heart. 2025

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TAKE HOME POINTS/CONCLUSIONS

1. Contemporary therapy for HFrEF has reduced mortality by 60% over the past 40 years.

2. Despite these improvements, residual risk of poor outcomes remains high, emphasized by a 5-year mortality over 40% in all comers (worse than common cancers).

3. The role of the HF specialist (at Northwell) is to address this residual risk.
   - Implementation of GDMT.
   - Remote monitoring of intracardiac pressures.
   - Barostim and other devices specifically targeting novel pathways
   - Access to investigational therapies.

REFERRAL PATHWAYS

Phone Number: (844) HEART-93

Heart Failure Email: heartfailure@northwell.edu

Allscripts/Epic: Advanced Heart Failure Referral Order

All referral pathways are handled by our centralized team that can direct patients to the nearest heart failure location.