11th ANNUAL HEART FAILURE UPDATE 2024

Friday May 24 - Saturday May 25

Marriott Chateau Champlain, Montreal, Quebec

CHFS SCIC Canadian Heart Failure Society / Société canadienne d'insuffisance cardiaque

𝕏 @CanHFSociety #HFupdate

Trainee Competition Awards

Dr. Aws Almufleh

Heart Failure Update 2024
Trainee Research Competition

Winner
Kevin Ma
University of Alberta
Guideline Directed Medical Therapy in Heart Failure Patients with Advanced Chronic Kidney Disease: A Prospective Study from the Heart Function Clinic Registry

Runner-up
Mohammed Adam Benharrats
Université de Sherbrooke
Acute Myocarditis and Pericarditis in PASC (Post-Acute Sequelae of COVID-19): Initial Insights From the IMPACT-COVID-19 Study

Heart Failure Update 2024
Trainee Research Competition

Finalist
Florence Bernier
Université de Montréal
Patient selection for advanced therapies in heart failure, can we agree to disagree?

Finalist
Amir Razaghizad
McGill University
Cardiovascular Phenotypes in Type 2 Diabetes: Latent Profile Analysis of the CANVAS program and CREDENCE trial

Plenary 2: Clinical Pearls and Conundrums in HF Clinical Care

Plenary Opening Remarks

Stephanie Poon
MD, MSc, FRCPC

Faculty

Co-chairs:

- Stephanie Poon, MD, MSc, FRCPC
- Biykem Bozkurt, MD, PhD, FACC, FHFSA, FACP

Presenters:

- Abhinav Sharma, MD , PhD
- Scott Solomon, MD
- Anique Ducharme, MD, MSc, FRCPC, FACC, FCCS, FHSA(h)
- Justin Ezekowitz, MB, BCH, MSc, FRCPC, FACC, FAHA, FESC
- Jillianne Code, PhD

Disclosures

	Dr. Poon	Dr. Bozkurt
Any direct financial payments including receipt of honoraria	No disclosures	Abbott, Abiomed, American Regent, Amgen, Astra Zeneca, Bayer, Boehringer Ingelheim, Merck, Respicardia/Zoll, Roche, Sanofi-Aventis, Vifor.
Membership on advisory boards or speakers' bureaus	Servier, Bayer, Boehringer Ingelheim	No disclosures
Funded grants or clinical trials	Boehringer Ingelheim	No disclosures
All other investments or relationships that could be seen by a reasonable, well-informed participant as having the potential to influence the content of the educational activity	No disclosures	No disclosures

Plenary Agenda

TIME	TOPIC
3:00 p.m. – 3:05 p.m.	**Plenary Opening Remarks & Trainee Competition Awards** Dr. Stephanie Poon and Dr. Aws Almufleh
3:05 p.m. – 3:20 p.m.	**JACC HF: Great Papers of the Past Year** Dr. Biykem Bozkurt
3:20 p.m. – 3:35 p.m.	**ABC's of De-congesting "Congestive" Heart Failure** Dr. Abhinav Sharma
3:35 p.m. – 3:50 p.m.	**A Treasure Chest of Late Breaking Clinical Trials: A Clinical Trialist's Perspective** Dr. Scott Solomon
3:50 p.m. – 4:05 p.m.	**DEBATE: Is Canada ready for Implantable Hemodynamic Monitoring?** Dr. Anique Ducharme & Dr. Justin Ezekowitz
4:05 p.m. – 4:10 p.m.	**Lived Experience Commentary** Dr. Jillianne Code
4:10 p.m. – 4:30 p.m.	**Plenary Q&A** All panelists

Housekeeping

- To collect your MOC Section 1 credits, please remember to complete both the session evaluation and the congress evaluation
- The evaluation QR code can be found on your tables and will be displayed on the screen after the presentation

Great HF Papers of the Past Year

Biykem Bozkurt, MD PhD, FACC, FAHA, FHFSA,
The Mary and Gordon Cain Chair & Professor of Medicine
Senior Dean of Faculty at Baylor College of Medicine
W.A. “Tex” and Deborah Moncrief, Jr., Chair
Director, Winters Center for HF Research
Baylor College of Medicine, Houston, TX
Editor-in-Chief, JACC: Heart Failure

Disclosures

- Consultation: Amgen, Baxter , Bayer , Daiichi Sankyo, Johnson & Johnson, Merck, Sanofi-Aventis, Abiomed, Regeneron, Roche, Cytokinetics, AstraZeneca, Boehringer Ingelheim, Novo Nordisk, Vifor, Respicardia/Zoll
- Data Safety Monitoring Committee: LivaNova, Cardurion, Renovacor
- Clinical Endpoints Committee: Abbott, NIH

Learning Objectives

1. Highlight some of the most provocative and impactful research in heart failure and cardiomyopathies over the past year
2. Discuss how the results of these trials could change the way that we currently manage patients with heart failure and/or cardiomyopathies

Major Progress

Update in Management of HFpEF, HFrEF

Management of Comorbidities Obesity, Afib, CKD, Prevention of HF

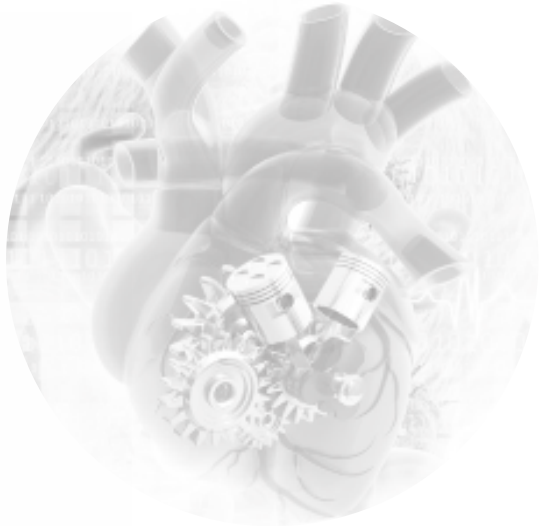
Devices, Technology, Wearables, Shock, VAD/Tx

Genetic, Cardiomyopathies Myocarditis, Pregnancy

Major Progress

Update in Management of HFpEF, HFrEF

Management of Comorbidities Obesity, Afib, CKD, Prevention of HF



Devices, Technology, Wearables, Shock, VAD/Tx

Genetic, Cardiomyopathies Myocarditis, Pregnancy

SGLT2i now First Line in Treatment of HFpEF

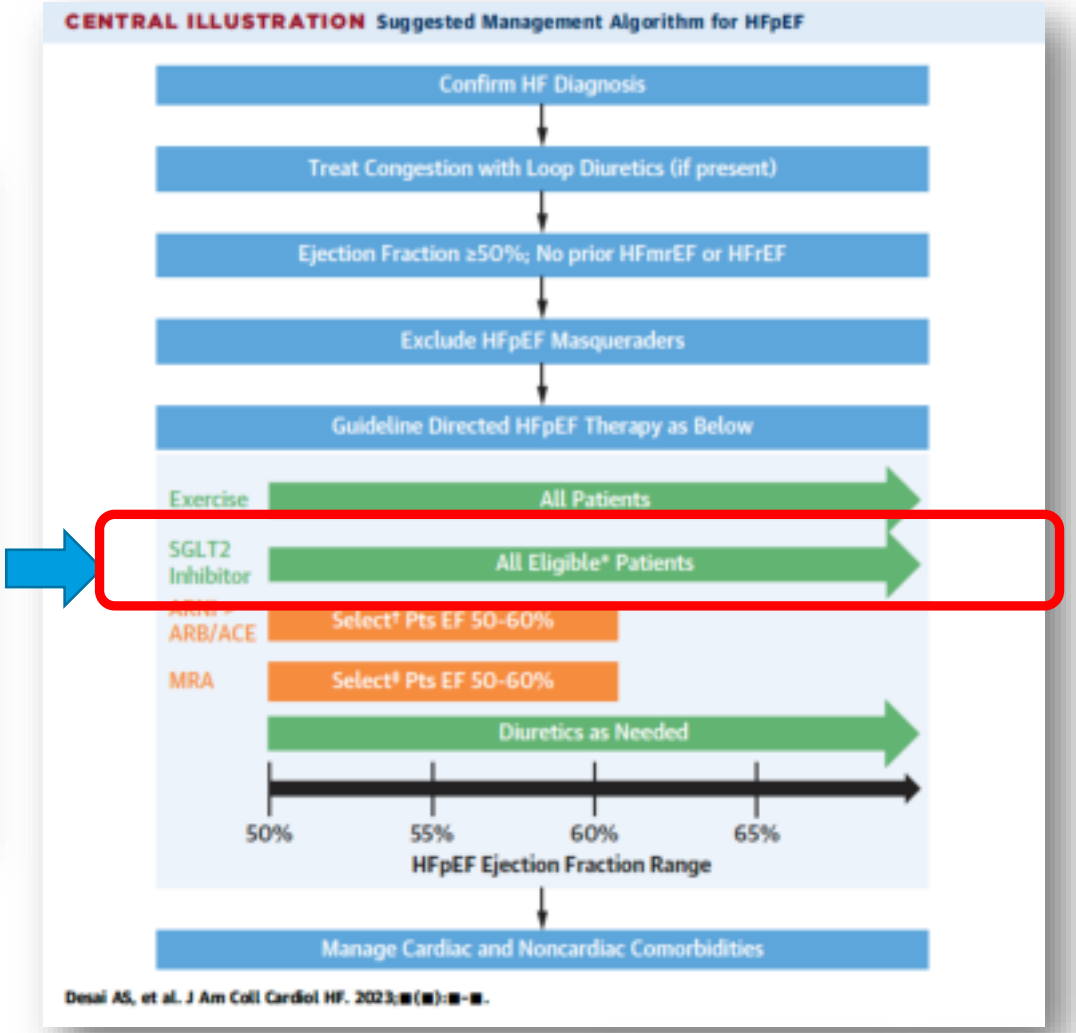
How to Manage Heart Failure With Preserved Ejection Fraction

Practical Guidance for Clinicians

Akshay S. Desai, MD, MPH,[a] Carolyn S.P. Lam, MBBS, PhD,[b,c] John J.V. McMurray, MD,[d] Margaret M. Redfield, MD[e]

HIGHLIGHTS

- Effective pharmacologic therapy is now available to modify disease progression in HFpEF.
- After confirming the diagnosis and excluding alternatives, clinicians should aggressively manage congestion, address comorbidities, and initiate evidence-based medical treatment.
- SGLT2 inhibitors are appropriate for most patients with HFpEF, and addition of an ARNI and/or MRA may be appropriate for many.
- Exercise and lifestyle modification to facilitate weight reduction are appropriate for all patients.

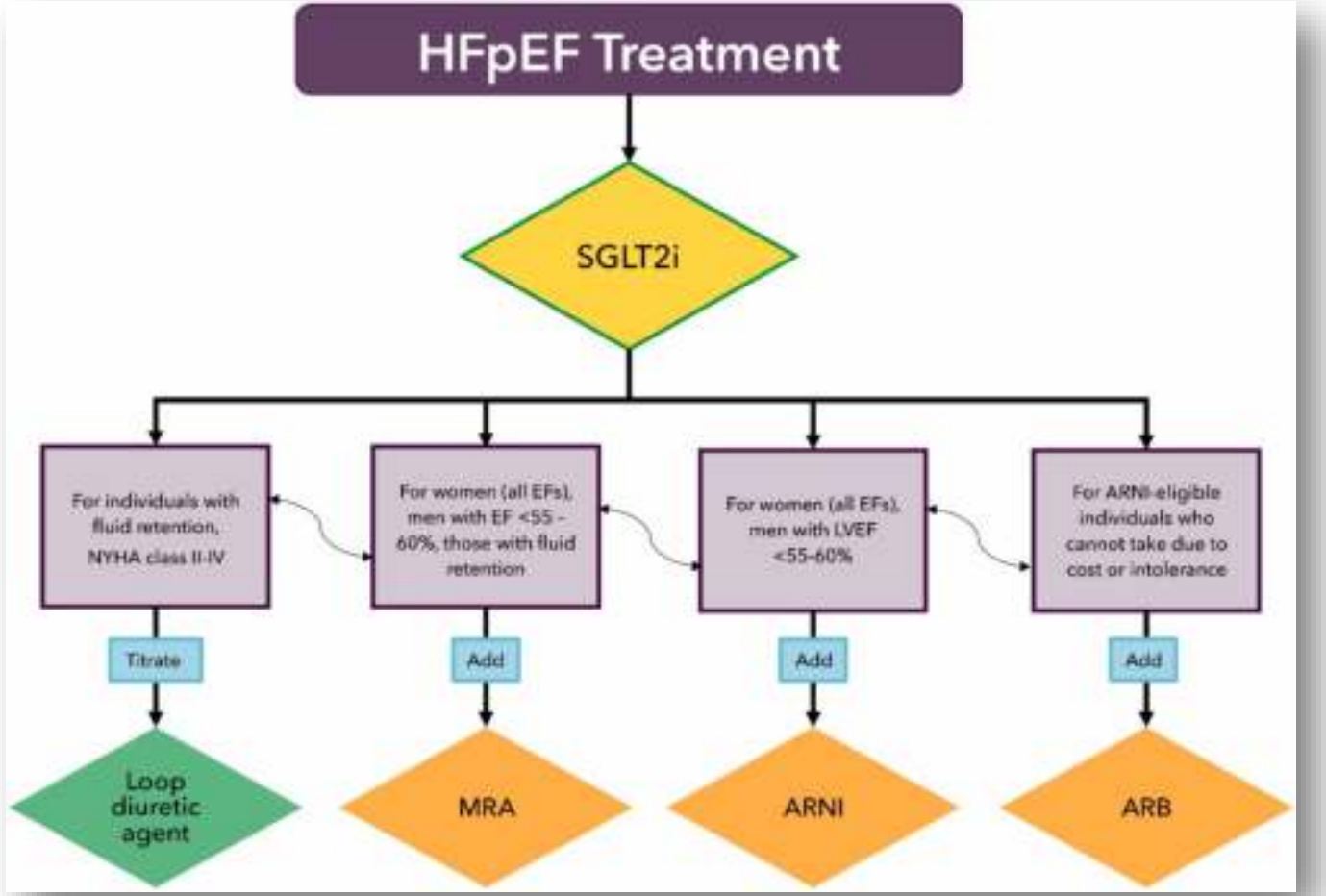


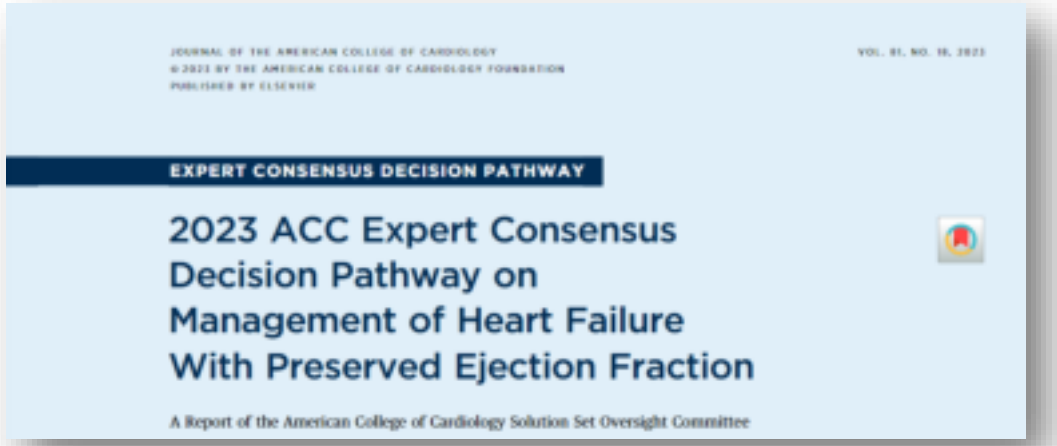
JACC MOST TALKED ABOUT ARTICLES

JACC MOST READ ARTICLES

Desai, A, Lam, C, McMurray, J. et al. How to Manage Heart Failure With Preserved Ejection Fraction: Practical Guidance for Clinicians. J Am Coll Cardiol HF. 2023 Jun, 11 (6) 619–636.

SGLT2i now First Line in Treatment of HFpEF





JACC MOST READ ARTICLES

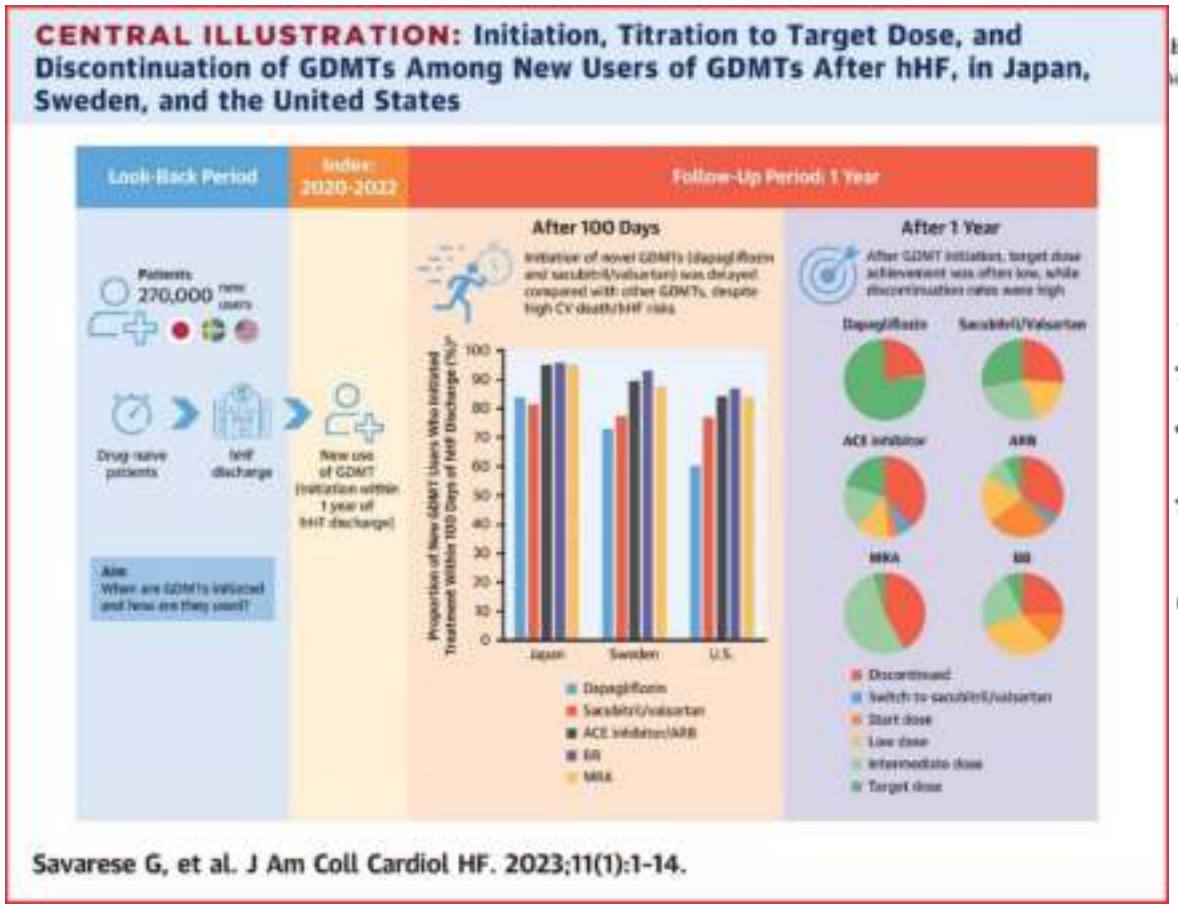
Kittleson, M, et al. 2023 ACC Expert Consensus Decision Pathway on Management of HFpEF. J Am Coll Cardiol. 2023 May, 81 (18) 1835–1878.

RWE: HF Drug Treatment Inertia, Discontinuation after Hospitalization

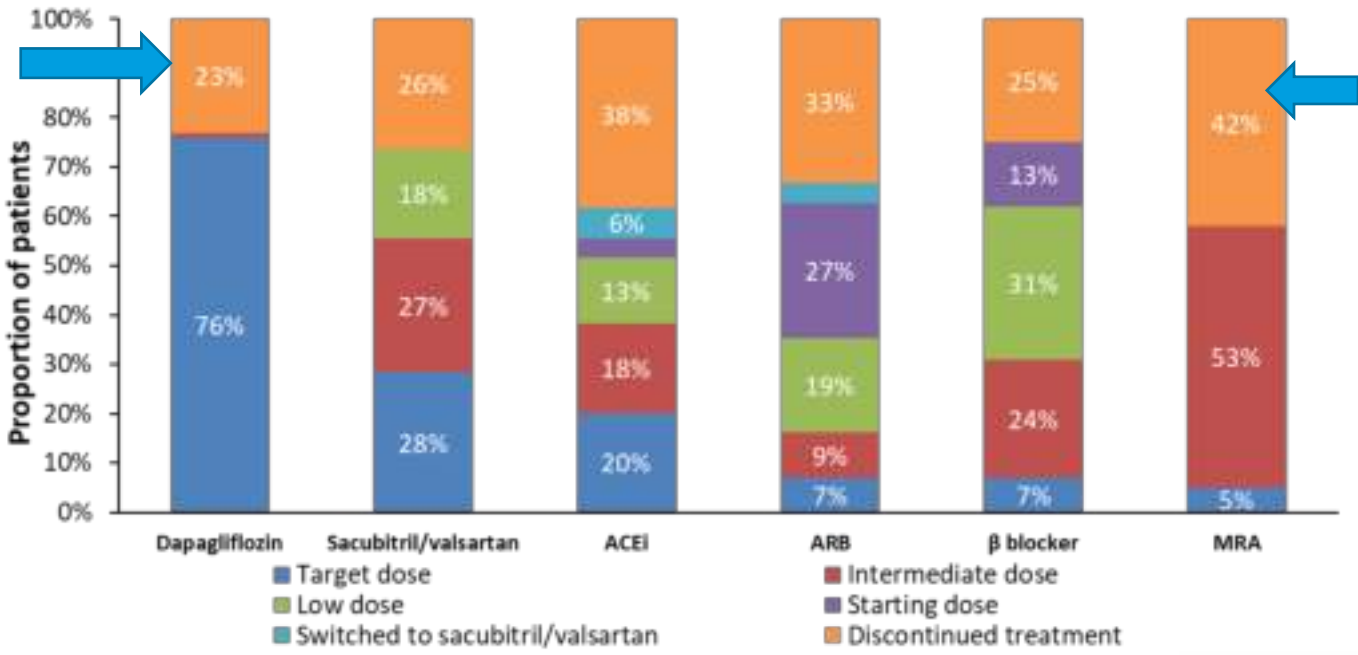
Heart Failure Drug Treatment—Inertia, Titration, and Discontinuation

A Multinational Observational Study (EVOLUTION HF)

266,589 patients in US, Japan, Sweden
12 mo after hHF



Savarese G, et al. J Am Coll Cardiol HF. 2023;11(1):1-14.



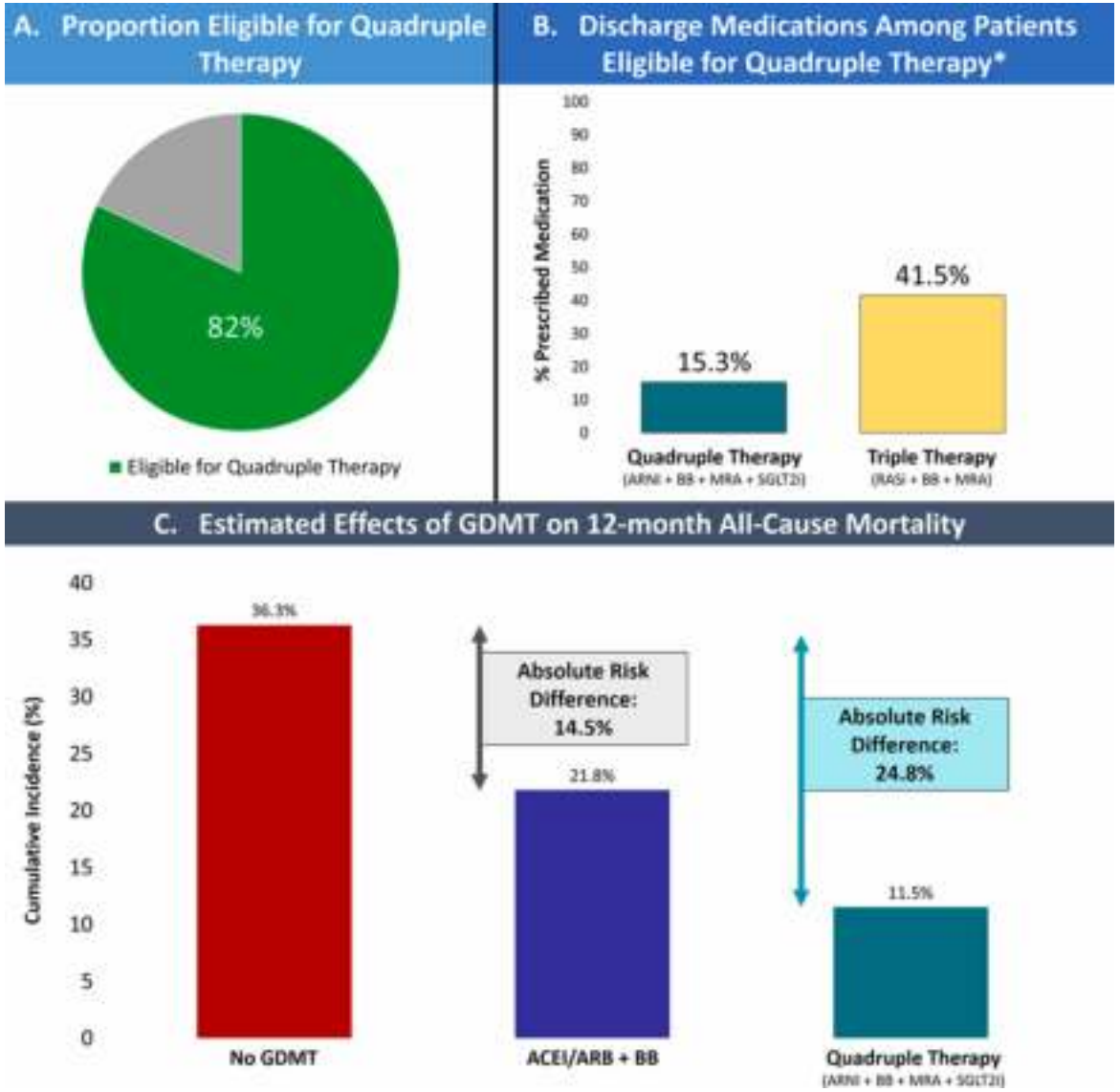
Novel HFrEF GDMTs are initiated later than other GDMTs following hHF

JACC MOST READ ARTICLES

Savarese G, Kishi T, Vardeny O, Adamsson Eryd S, Bodegård J, Lund LH, Thuresson M, Bozkurt B. Heart Failure Drug Treatment-Inertia, Titration, and Discontinuation: A Multinational Observational Study (EVOLUTION HF). JACC Heart Fail. 2023 Jan;11(1):1-14. PMID: 36202739.

ACC.24
Simultaneous pub.

RWE: Lag in Initiation of in-Hospital Quadruple Therapy



- Among hospitalized pts for newly diagnosed HFrEF in the GWTG-HF registry (2016-2023), 88% were eligible, but 15 % were prescribed quadruple therapy
- Despite a projected aRR of 25% of 12-month all-cause mortality

Greene, S, et al. Eligibility and Projected Benefits of Rapid Initiation of Quadruple Medical Therapy for Newly Diagnosed HF. *J Am Coll Cardiol HF*. .https://doi.org/10.1016/j.jchf.2024.03.001

Comparison of US and European HF Guidelines

	ACC/AHA/HFSA		ESC
HFrEF	• ARNi preferred over ACEi • ↑ COR for H+ISDN in self-identified Black patients • Adjunctive PUFA & K⁺ binders • ↓ QRSd threshold for CRT	• Similar diagnostic tools • ARNi/ACEi/ARB + BB + MRA + SGLT2i • Rapid GDMT initiation and optimization • ICD in iCM if LVEF ≤35%	• ACEi or ARNi preferred • ↑ COR for intravenous iron supplementation • ↓ threshold for MV TEER • ↓ COR for ICD in niCM
HFmrEF & HFimpEF	• HFimpEF explicitly included as HF subtype	• ARNi/ACEi/ARB + BB + MRA + SGLT2i • GDMT should be continued in HFimpEF	• HFimpEF implicitly included as HF subtype
HFpEF	• ARNi/ARB and MRA selectively recommended in addition to SGLT2i	• Simplified diagnostic approaches • SGLT2i as foundational therapy • Focus on comorbidity management	• No other pharmacotherapies recommended
Key Strengths	• Formal cost/value statements • Emphasis on HF trajectory • Explicit attention to equity & healthcare disparities • Pledge for continuous & dynamic guideline updates	• Patient-centered recommendations • Multistakeholder representation • Simplified treatment algorithms • Focus on special populations and HF prevention	• Patient-centered deliverables • High-yield practical guidance for GDMT use • Focus on CKD as risk factor • Explicit guidance to facilitate patients' self-care goals

Table: Comparison of American and European Medical Therapy Recommendations for the Management of HF

Condition	Recommendation	ACC/AHA/HFSA		ESC	
HFrEF	Diuretics to alleviate signs/symptoms of congestion	1	B-NR	1	C
	ACEi if ARNi not feasible	1	A	-	-
	ACEi to reduce morbidity and mortality	-	-	1	A
	ARNi to reduce morbidity and mortality	1	A	-	-
	ARNi as a replacement for ACEi	1	B-R	1	B
	ARB if intolerant of ACEi and ARNi not feasible	1	A	1	B
	BB to reduce mortality and hospitalizations	1	A	1	A
	MRA to reduce morbidity and mortality	1	A	1	A
	SGLT2i to reduce HF hospitalization and CV death	1	A	1	A
	H+ISDN to reduce morbidity and mortality in self-identified Black patients	1	A	2a	B
	H+ISDN if unable to tolerate or contraindicated for first-line agents	2b	C-LD	2b	B
	Digoxin if symptomatic despite GDMT (or intolerant to GDMT)	2b	B-R	-	-
	Digoxin if symptomatic in SR despite ACEi (or ARNi) + BB + MRA	-	-	2b	B
	Ivabradine if symptomatic with LVEF ≤35% on GDMT (including maximally tolerated BB), in SR with rate ≥70 beats per minute	2a	B-R	2a	B
	Potassium binders in patients with hyperkalemia on GDMT	2b	B-R	-	-
	PUFA if NYHA II-IV	2b	B-R	-	-
	Vericiguat if NYHA II-IV with worsening HF despite GDMT	2b	B-R	2b	B
HFmrEF	Diuretics to alleviate signs/symptoms of congestion	-	-	1	C
	SGLT2i to reduce HF hospitalizations or CV death	2a	B-R	1	A
	ACEi/ARB/ARNi, BB, and MRA to reduce morbidity and mortality	2b	B-NR	2b	C
HFpEF	Diuretics to alleviate signs/symptoms of congestion	1	C-LD	1	C
	SGLT2i to decrease HF hospitalizations or CV death	2a	B-R	1	A
	ARB, ARNi, MRA to decrease hospitalizations	2b	B-R	-	-
HFimpEF	Continue GDMT even if asymptomatic to prevent HF relapse	1	B-R	-	-

Ostrominski, J, et al. Contemporary American and European Guidelines for the Management of Heart Failure: JACC: Heart Failure Guideline Comparison.
J Am Coll Cardiol HF.https://doi.org/10.1016/j.jchf.2024.02.020

Combination Therapy in HFmrEF and HFpEF: Network Meta-Analysis

Recent pub.

CENTRAL ILLUSTRATION: Combination Treatment Effects

A Complex Intervention	Primary Outcome	HR	[95% CI]	z	P Value
ARNI + BB + MRA + SGLT2i		0.47	[0.31–0.70]	−3.70	<0.01
RASi + BB + MRA + SGLT2i		0.51	[0.34–0.74]	−3.46	<0.01
ARNI + MRA + SGLT2i		0.56	[0.43–0.71]	−4.61	<0.01
ARNI + BB + SGLT2i		0.57	[0.40–0.82]	−3.04	<0.01
ARNI + BB + MRA		0.58	[0.39–0.86]	−2.70	<0.01
RASi + BB + SGLT2i		0.62	[0.44–0.87]	−2.76	<0.01
RASi + BB + MRA		0.63	[0.43–0.92]	−2.41	0.02
MRA + SGLT2i		0.66	[0.54–0.80]	−4.18	<0.01
ARNI + SGLT2i		0.68	[0.57–0.81]	−4.29	<0.01
ARNI + MRA		0.69	[0.55–0.88]	−3.08	<0.01
ARNI + BB		0.71	[0.50–1.01]	−1.91	0.06
RASi + BB		0.77	[0.55–1.07]	−1.56	0.12
RASi + Dig		0.81	[0.63–1.04]	−1.69	0.09
BB		0.84	[0.61–1.15]	−1.08	0.28
RASi		0.92	[0.83–1.01]	−1.75	0.08

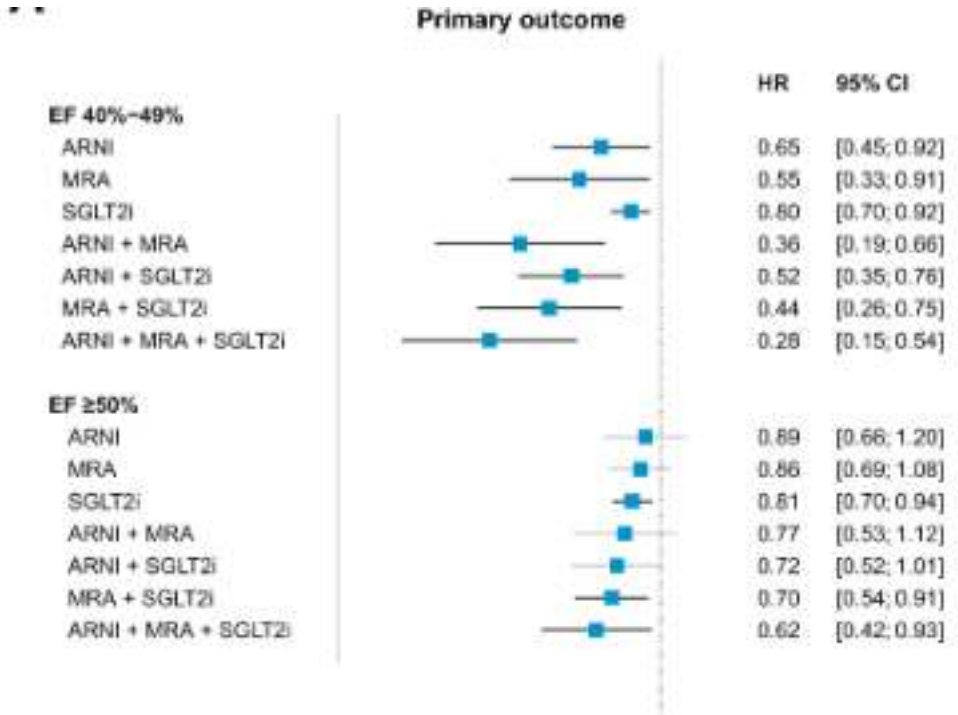
0.5 1 2

B Complex Intervention	Cardiovascular Death	HR	[95% CI]	z	P Value
ARNI + BB + MRA + SGLT2i		0.55	[0.32–0.95]	−2.16	0.03
RASi + BB + MRA + SGLT2i		0.58	[0.35–0.96]	−2.14	0.03
ARNI + BB + MRA		0.62	[0.37–1.04]	−1.82	0.07
ARNI + MRA + SGLT2i		0.63	[0.43–0.91]	−2.43	0.01
RASi + BB + MRA		0.64	[0.40–1.05]	−1.78	0.07
MRA + SGLT2i		0.67	[0.50–0.89]	−2.71	<0.01
ARNI + MRA		0.70	[0.49–0.99]	−2.00	0.05
ARNI + BB + SGLT2i		0.75	[0.47–1.19]	−1.22	0.22
RASi + BB + SGLT2i		0.78	[0.51–1.20]	−1.13	0.26
ARNI + BB		0.83	[0.53–1.30]	−0.80	0.42
ARNI + SGLT2i		0.85	[0.65–1.10]	−1.21	0.23
RASi + BB		0.87	[0.58–1.30]	−0.67	0.50
BB		0.88	[0.60–1.29]	−0.65	0.52
RASi		0.99	[0.87–1.12]	−0.18	0.85
RASi + Dig		0.99	[0.71–1.38]	−0.07	0.95

0.5 1 2

Zafeiropoulos S, et al. J Am Coll Cardiol HF. 2024;12(4):616–627.

- In patients with HF and LVEF>40%, quadruple ARNI, BB, MRA, SGLT2i ➔largest reduction in the risk of CV death and HHF
- The benefit more pronounced in HFmrEF patients.

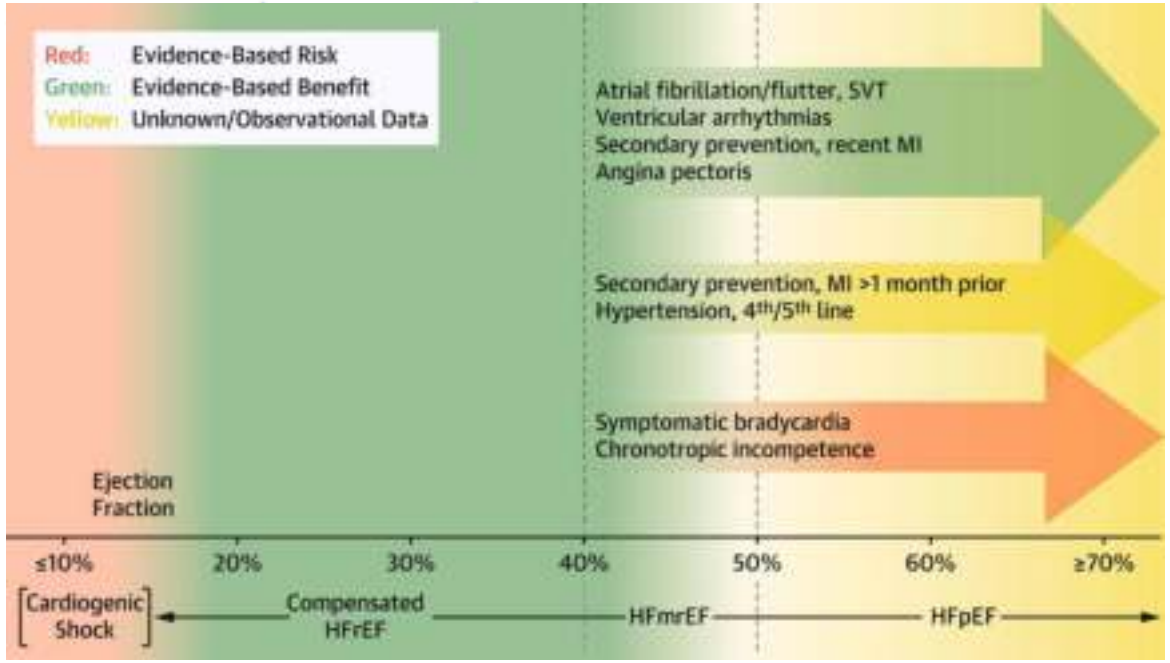


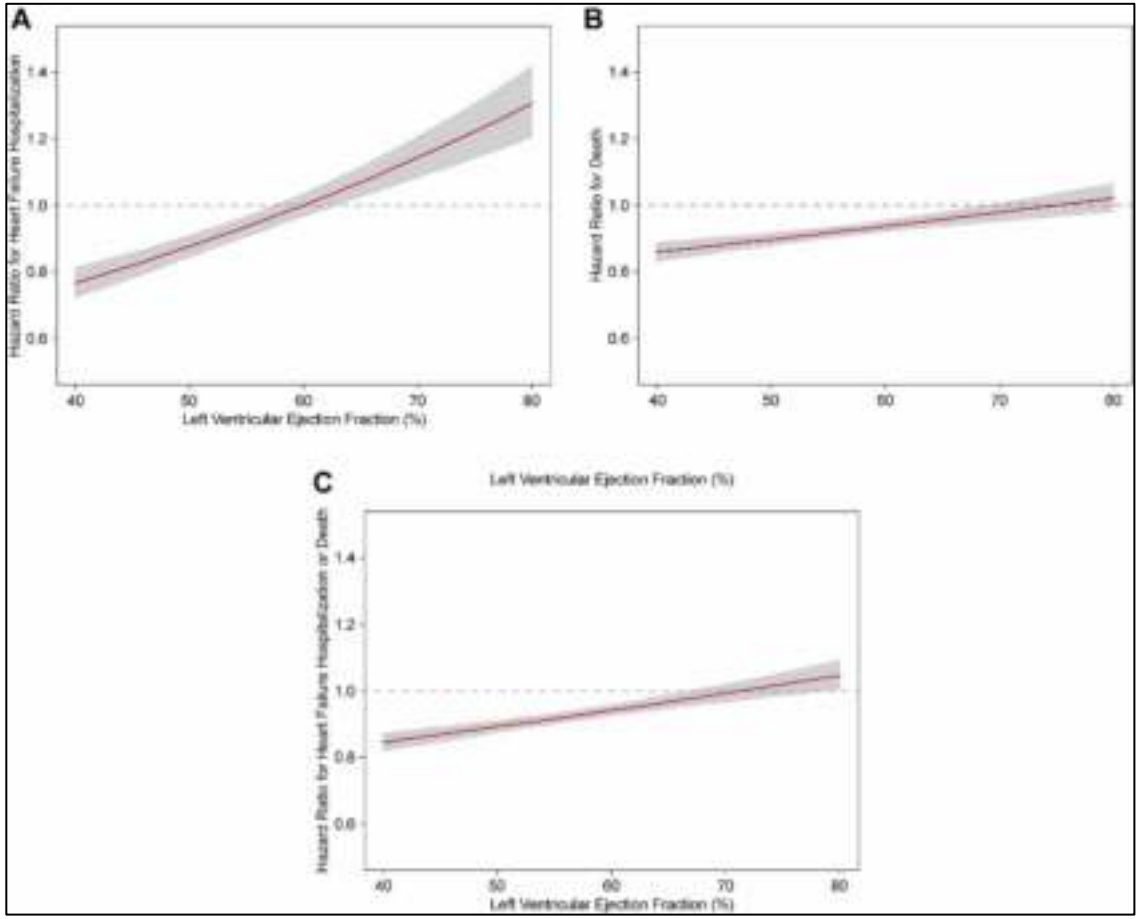
Zafeiropoulos, S, Farmakis, I, Milioglou, I. et al. Pharmacological Treatments in Heart Failure With Mildly Reduced and Preserved Ejection Fraction: Systematic Review and Network Meta-Analysis. J Am Coll Cardiol HF. 2024 Apr, 12 (4) 616–627.

Lack-of RWE of Benefit with β-Blockers in HFpEF

Beta-Blocker Use and Heart Failure Outcomes in Mildly Reduced and Preserved Ejection Fraction

Suzanne V. Arnold, MD, MHA,[a] Daniel N. Silverman, MD,[b,c] Kensey Gosch, MS,[a] Michael E. Nassif, MD, MS,[a]





Among 435,897 real-world patients with HF EF ≥40% , BB use associated with a ↑ risk of HFH as EF ↑, with potential benefit in patients with HFmrEF and potential risk in patients with higher EF (>60%)

JACC MOST READ ARTICLES

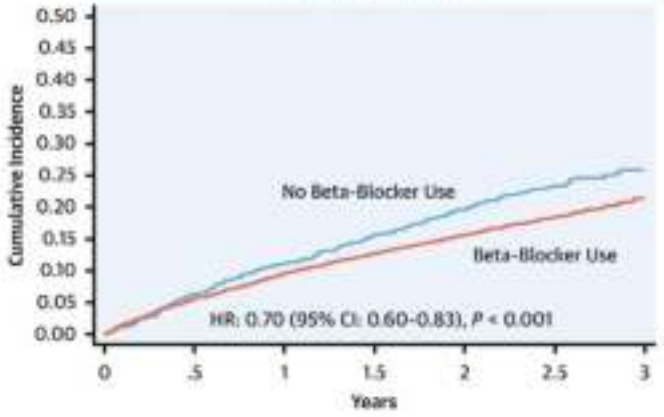
Arnold SV, et al. Beta-Blocker Use and Heart Failure Outcomes in Mildly Reduced and Preserved Ejection Fraction. JACC Heart Fail. 2023 Aug;11(8 Pt 1):893-900. PMID: 37140513.

Recent pub.

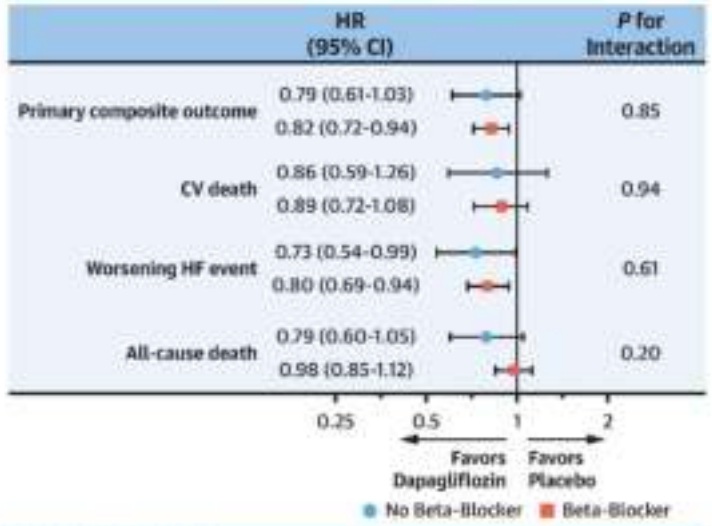
β-Blocker Use Not Associated with Increased Risk in Patients with HFmrEF or HFpEF: The DELIVER Trial

CENTRAL ILLUSTRATION: Beta-Blocker Use, Clinical Outcomes, and Treatment Response to Dapagliflozin

Beta-Blocker Use Not Associated With Higher Risk of CV Death or Worsening HF



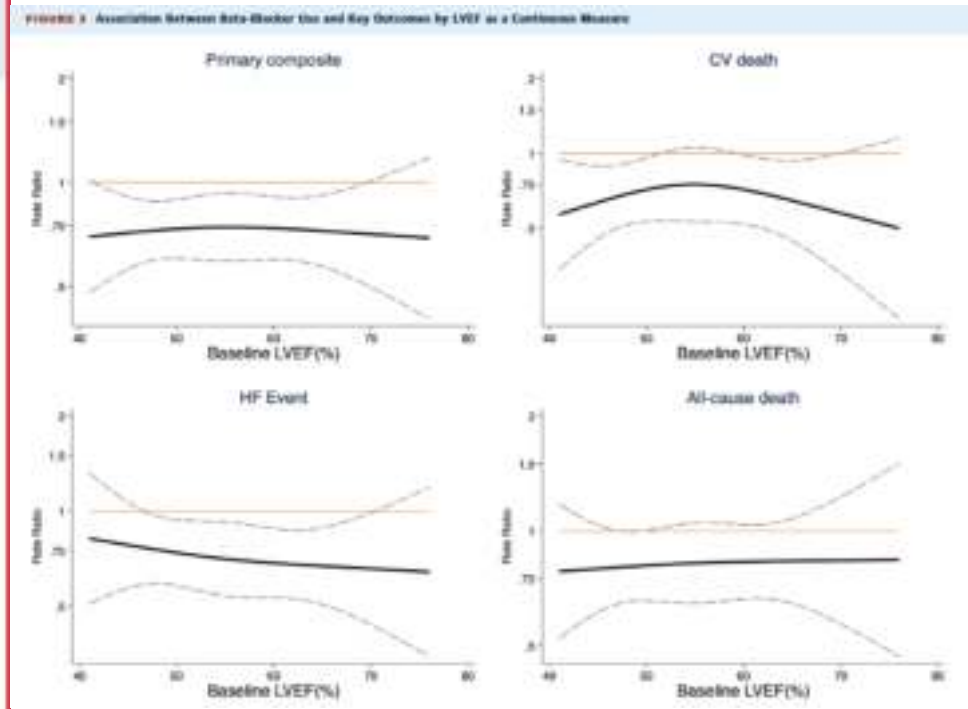
Consistent Benefits With Dapagliflozin Irrespective of Beta-Blocker Use



In the DELIVER trial of 6,263 participants with HF with LVEF >40%:

- 83% were treated with beta-blockers, with the vast majority having 1 or more potential indications such as hypertension, atrial fibrillation/flutter, previous LVEF ≤40%, and CAD.
- Beta-blocker use was not associated with adverse HF outcomes and mortality.
- Dapagliflozin consistently reduced CV death or worsening HF events, regardless of baseline beta-blocker use.

Peikert A, et al. J Am Coll Cardiol HF. 2024;12(4):631-644.



The associations between b-blocker use and clinical outcomes were not modified by LVEF categorical or continuous (ns)

PARAGLIDE: ARNi stabilized post WHF in HF EF>40%

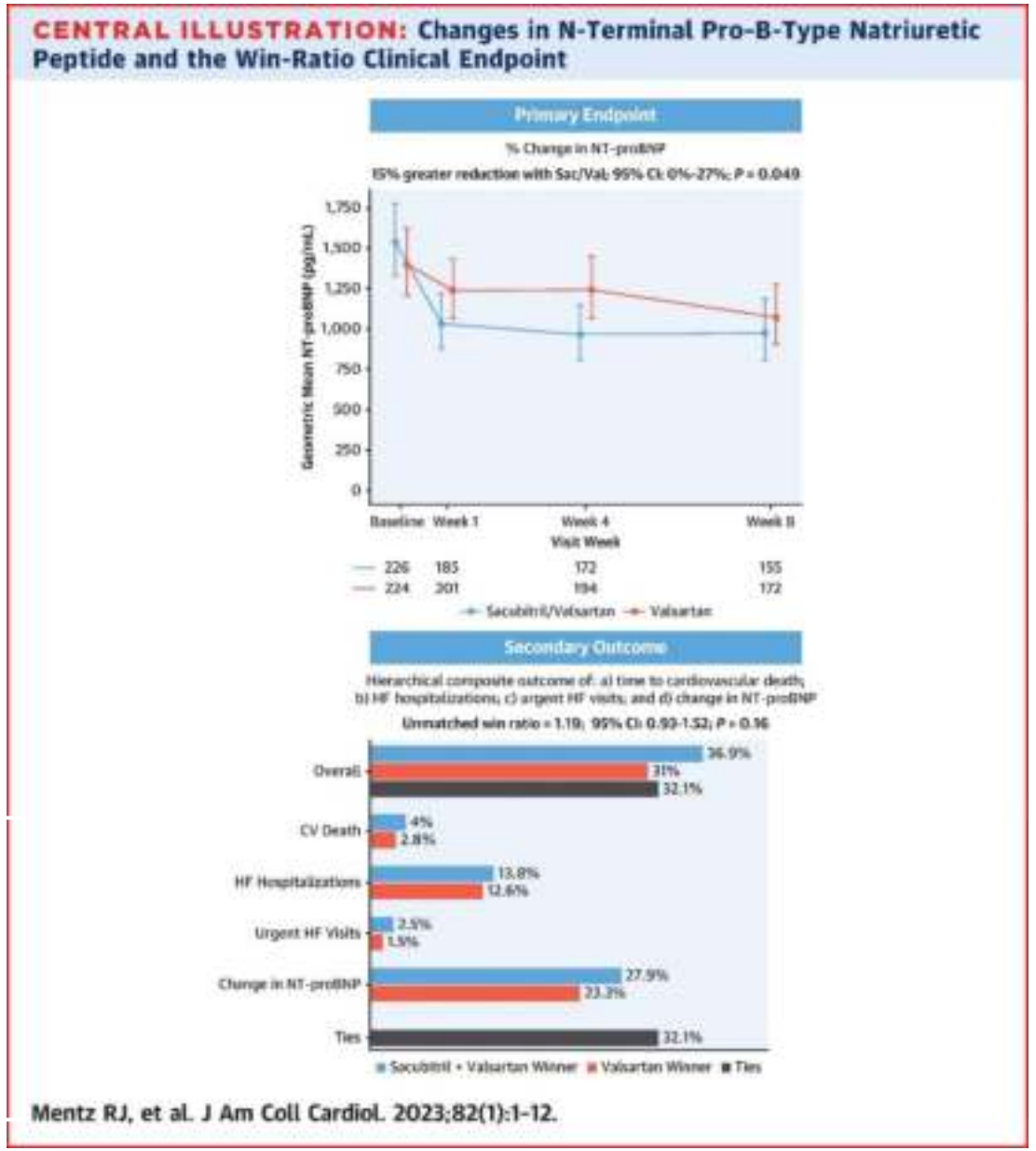
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 82, NO. 1, 2023

ORIGINAL INVESTIGATIONS

Angiotensin-Neprilysin Inhibition in Patients With Mildly Reduced or Preserved Ejection Fraction and Worsening Heart Failure

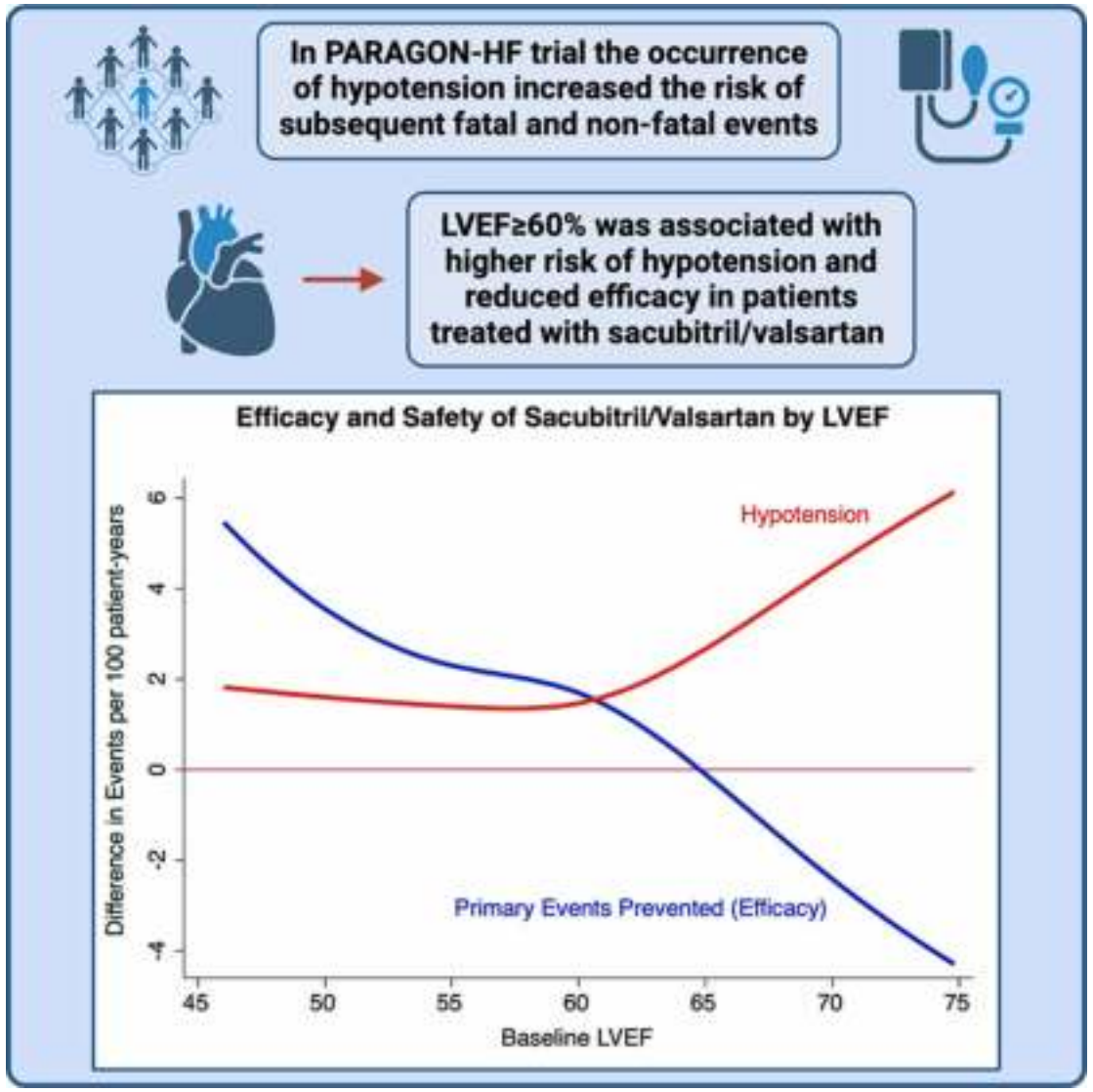
Robert J. Mentz, MD,[a] Jonathan H. Ward, PharmD,[b] Adrian F. Hernandez, MD, MHS,[a] Serge Lepage, MD,[c] David A. Morrow, MD, MPH,[d] Samiha Sarwat, PhD,[b] Kavita Sharma, MD,[e] Randall C. Starling, MD, MPH,[f] Eric J. Velazquez, MD,[g] Kristin M. Williamson, PharmD,[b] Akshay S. Desai, MD, MPH,[d] Shelley Zieroth, MD,[h] Scott D. Solomon, MD,[d] Eugene Braunwald, MD,[d] on behalf of the PARAGLIDE-HF Investigators

- 466 pts EF>40% within 30 days of WHF
- Greater NT-proBNP with ARNi
- Hierarchical outcome ns
- Larger treatment effect EF≤60



Recent pub.

Heterogeneity: LVEF>60% Associated with Higher Risk of Hypotension & Reduced Efficacy with ARNi in PARAGON Trial

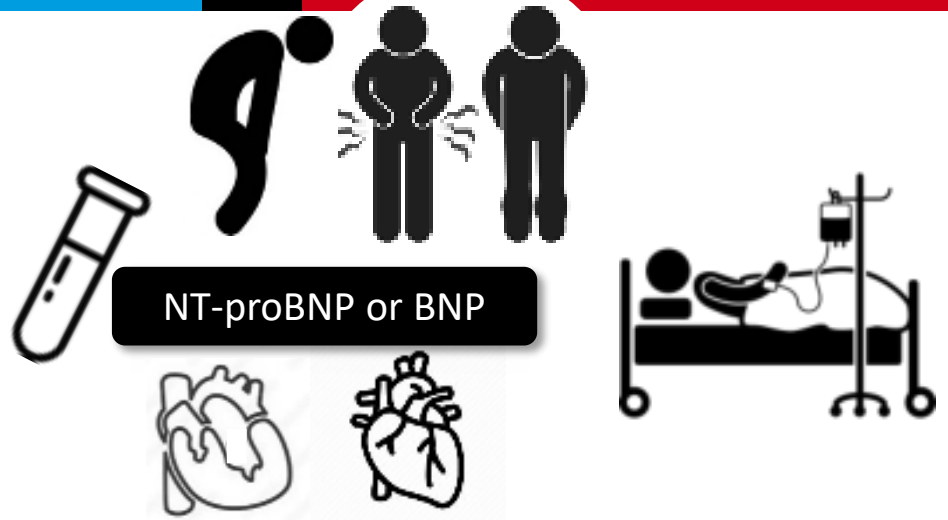


- 13% experienced hypotension, more frequently in the sacubitril/valsartan arm ($p<0.001$).
- Patients with hypotension had higher risk of CVD and total HFH (RR 1.63; CI 1.27-2.09; $p<0.001$) and all-cause death (HR 1.62; CI 1.28-2.05; $p<0.001$).
- LVEF≥60% experienced substantially higher treatment-related risks of hypotension.

Foà, A, et al. Sacubitril/Valsartan-Related Hypotension in Patients with Heart Failure and Preserved or Mildly Reduced Ejection Fraction. J Am Coll Cardiol. null2024, 0 (0) .https://doi.org/10.1016/j.jacc.2024.02.035

Response to Treatment

Treatment



Assess Response to Therapy

- Symptoms, Signs, Functional Capacity, NYHA Class, QoL
- Natriuretic Peptides and Other Laboratory Markers
- Cardiac Function and Reversal of Remodeling
- Re-hospitalizations, Days Alive and Outside Hospital

First Line Quadruple Therapy *(Induction Therapy)*

SGLT2i | ARNi/ACEi | BB | MRA

In any order, initiate in 4-6 weeks

Optimize doses of quadruple therapy

Add-on Therapies *(Consolidation Therapy)*

Hydralazine -Nitrates* | ICD | CRT-D

Treatment of specific etiologies

Ivabradine | Digoxin | Vericiguat

Decongestion, Life Style Modification

Treatment of Comorbidities

SGLT2i in DM | Hypertension | Valvular

IV Iron in Iron Deficiency | Sleep Apnea | Atrial Fibrillation

Other comorbidities

Responsive to Therapy

- Improving HF → Optimize GDMT
- HF in Remission → Continue GDMT

Nonresponsive to Therapy

- Persistent HF
- Worsening HF

→ Escalate GDMT; Close Follow-Up; HF Specialists; Additional & Advanced Therapies

Improvement expected within 3-6 months

HF Diagnosis, GDMT Initiation and Optimization

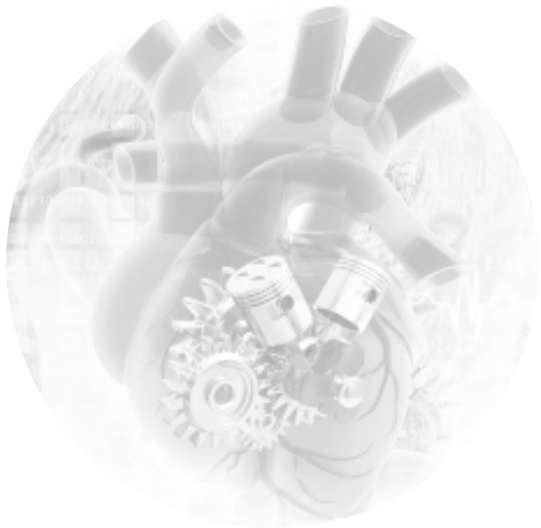
Assess Response to Therapy

Bozkurt B. JACC Heart Fail . 2023 Jun;11(6):729-732.

Major Progress

Update in Management of HFpEF, HFrEF

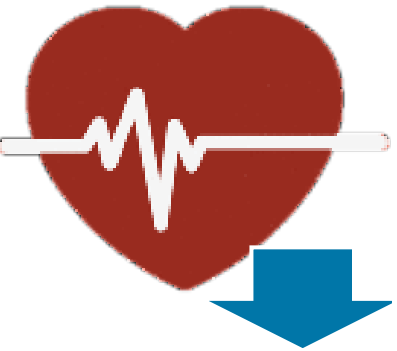
Management of Comorbidities Obesity, Afib, CKD, Prevention of HF



Devices, Technology, Wearables, Shock, VAD/Tx

Genetic, Cardiomyopathies Myocarditis, Pregnancy

SELECT Trial: Effect of s.c. Semaglutide in CVOT in Obesity and CVD

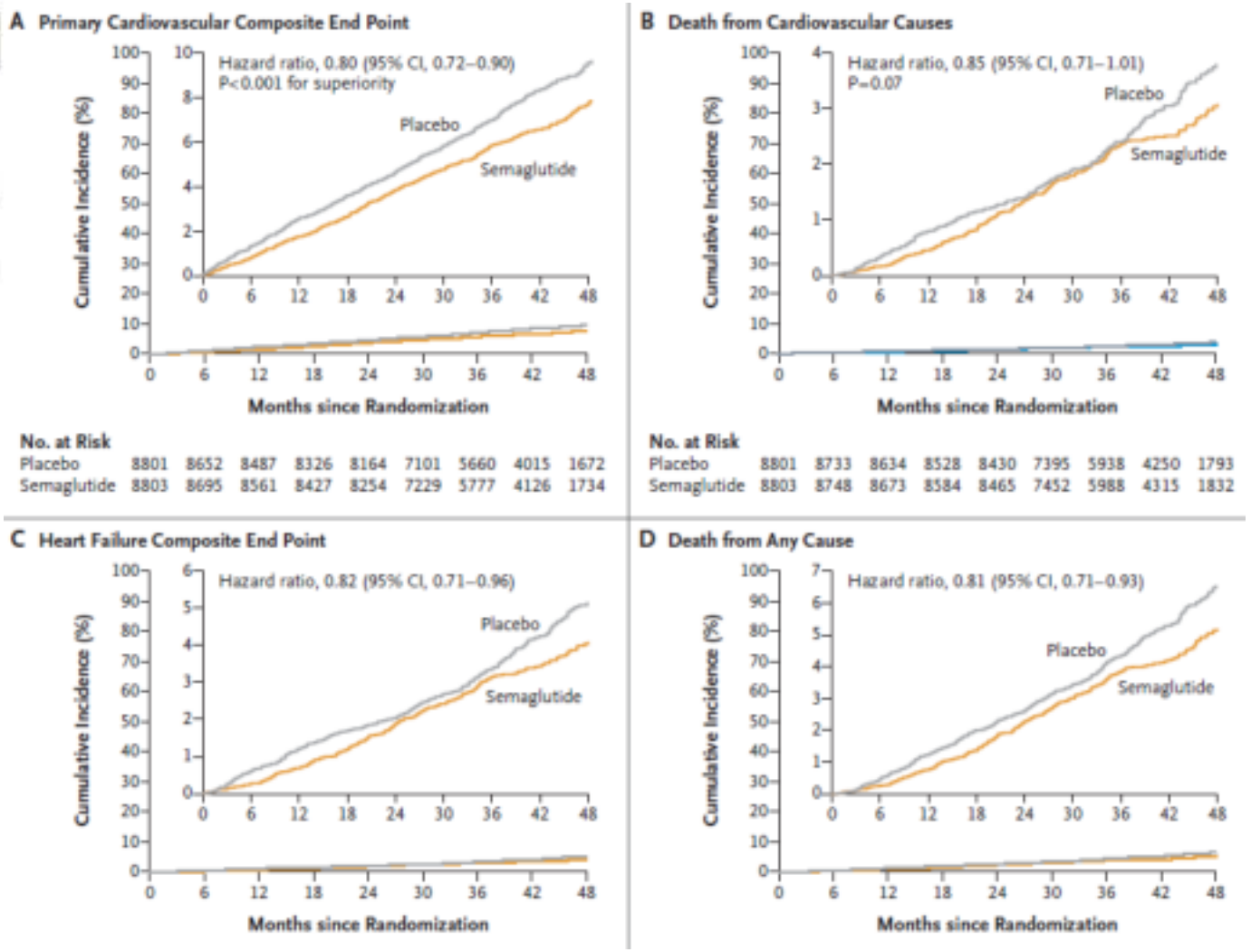


ORIGINAL ARTICLE

Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes

A. Michael Lincoff, M.D., Kirstine Brown-Frandsen, M.D., Helen M. Colhoun, M.D., John Deanfield, M.D., Scott S. Emerson, M.D., Ph.D., Sille Esbjerg, M.Sc., Søren Hardt-Lindberg, M.D., Ph.D., G. Kees Hovingh, M.D., Ph.D., Steven E. Kahn, M.B., Ch.B., Robert F. Kushner, M.D., Ildiko Lingvay, M.D., M.P.H., Tugce K. Oral, M.D., Marie M. Michelsen, M.D., Ph.D., Jorge Plutzky, M.D., Christoffer W. Tornøe, Ph.D., and Donna H. Ryan, M.D., for the SELECT Trial Investigators*

- Semaglutide 2.4 mg reduced composite CV death, non-fatal MI or nonfatal stroke) by 20% over five years in adults with overweight or obesity
- 17,604 adults aged ≥ 45 years with overweight or obesity and established CVD with no prior history of diabetes.
- All three components of the primary endpoint contributed to the superior MACE reduction



Obese

- Lifestyle Modification
- GLP1RA
- GLP1RA+ GIP
- GLP1RA + Lifestyle modification
- Other drugs or bariatric surgery ?

Obese-Pre-HF

- In DM: SGLT2i
- GLP1RA?
- GLP1RA + SGLT2i?
- Other, bariatric sx?

Obese-HFpEF

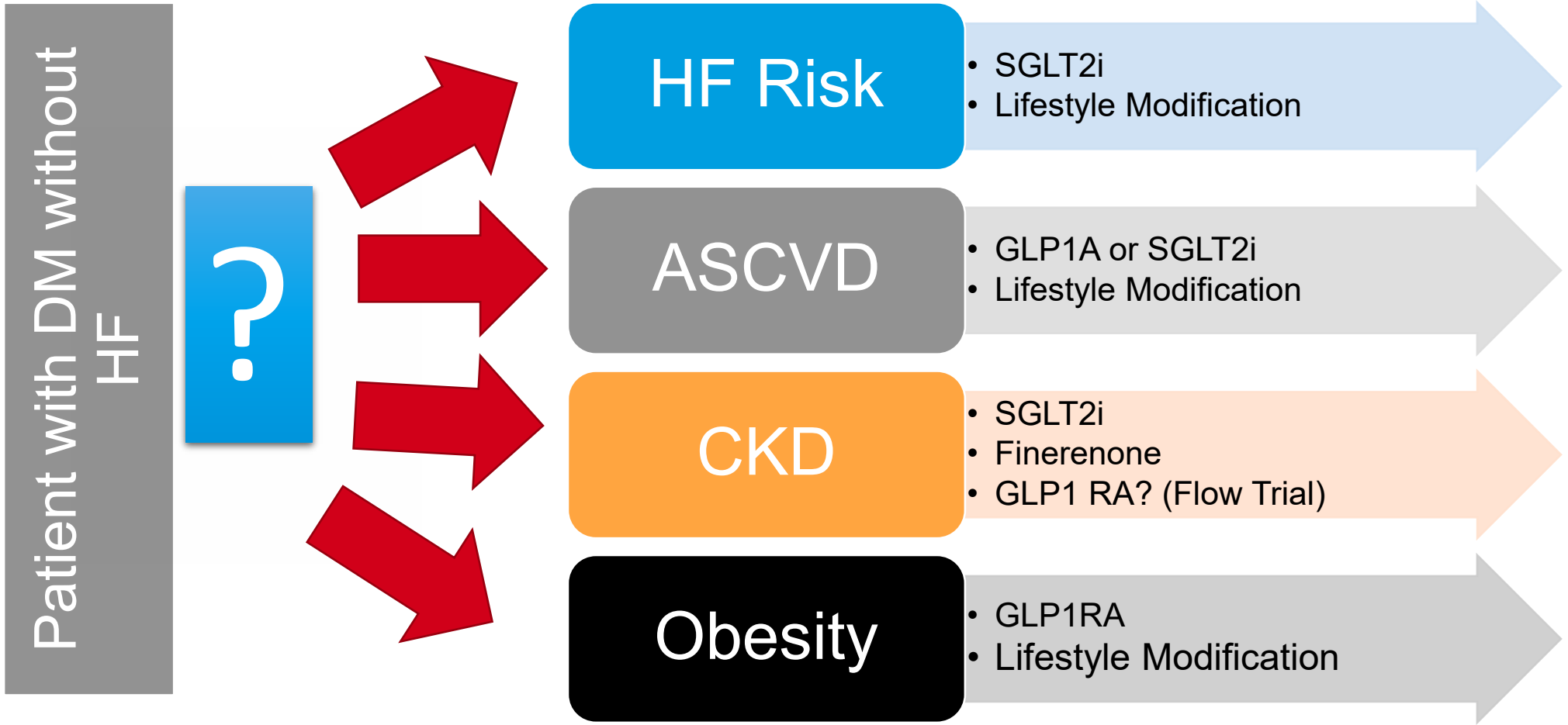
- GLP1RA
- GLP1RA+ SGLT2i?

Obese-HFrEF

- SGLT2i
- SGLT2i + GLP1RA? (safety & efficacy)

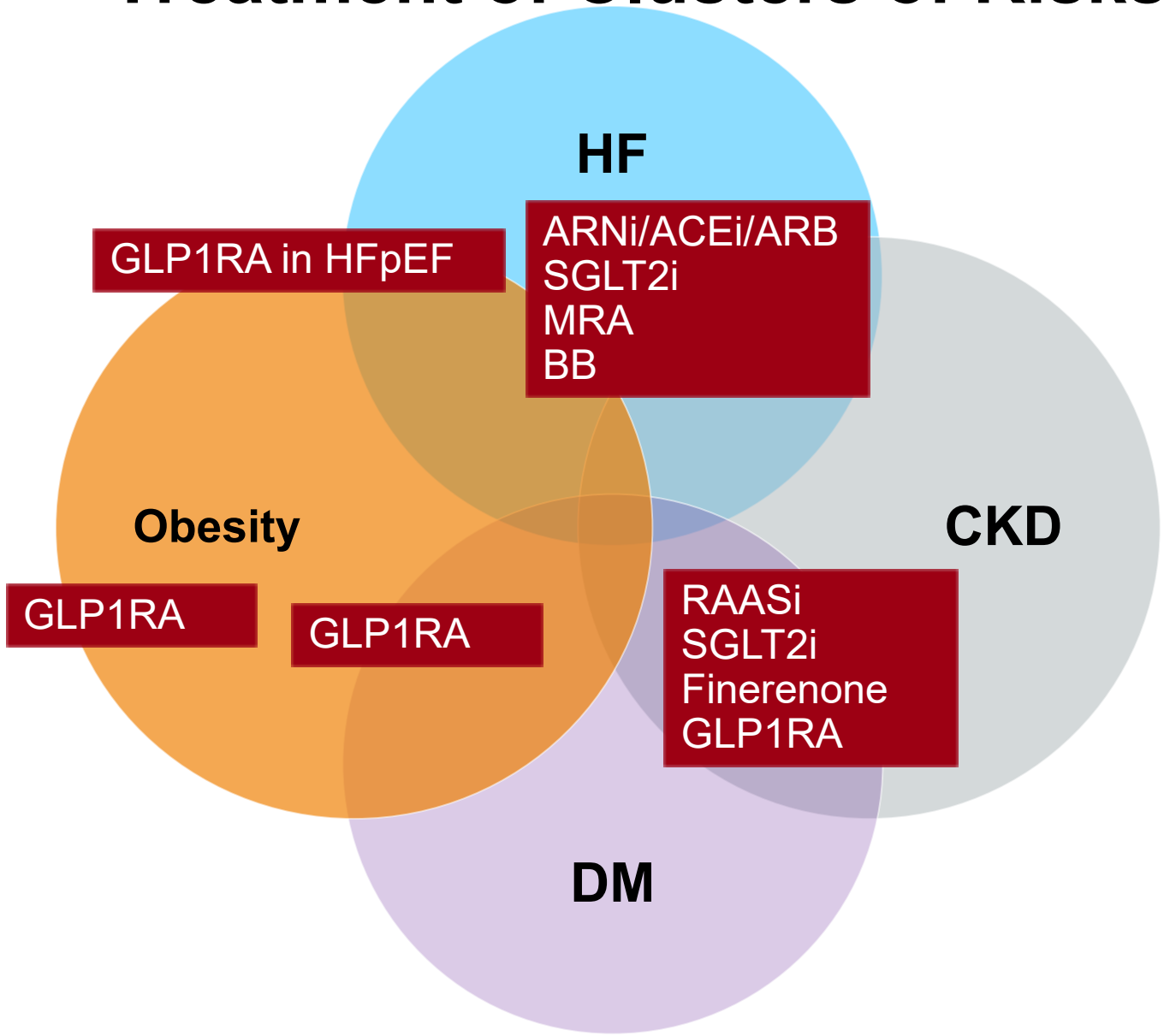
Combination Therapies?

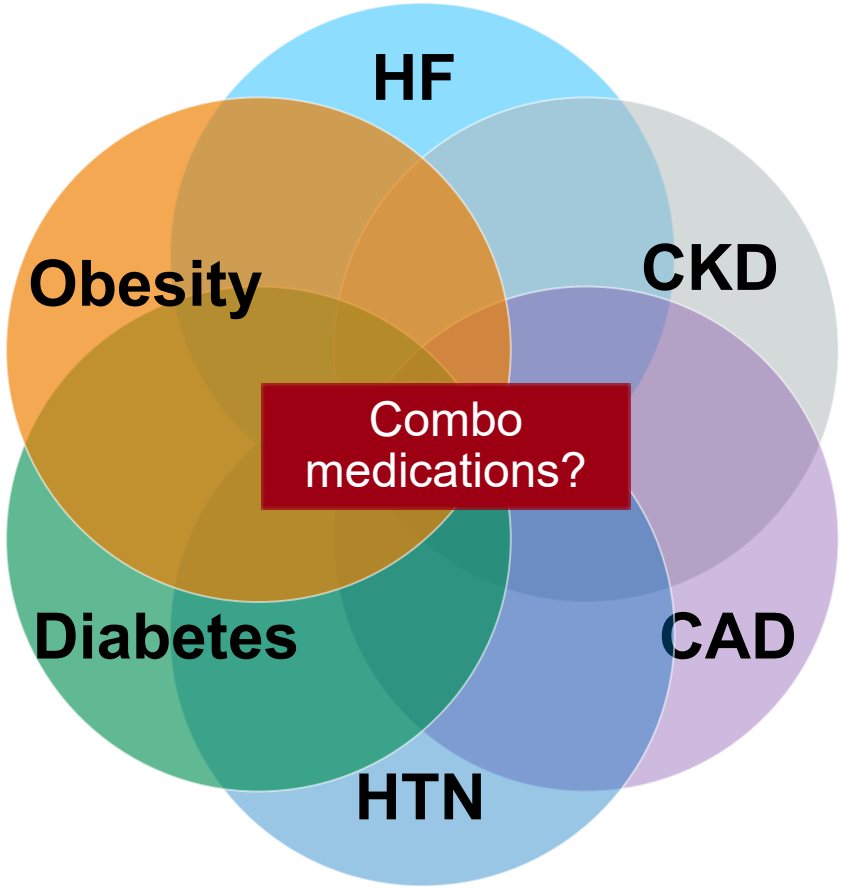
Prevention or Treatment of Pre-HF
Treatment of According to Additional Risk in DM



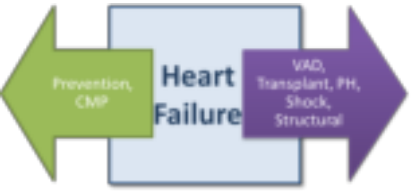
Role of Biomarkers & Clusters of Risk

Treatment of Clusters of Risks to Prevent Heart Failure





Bozkurt B. JACC Heart Fail . 2024 Feb;12(2):417-420. doi:10.1016/j.jchf.2023.12.008.

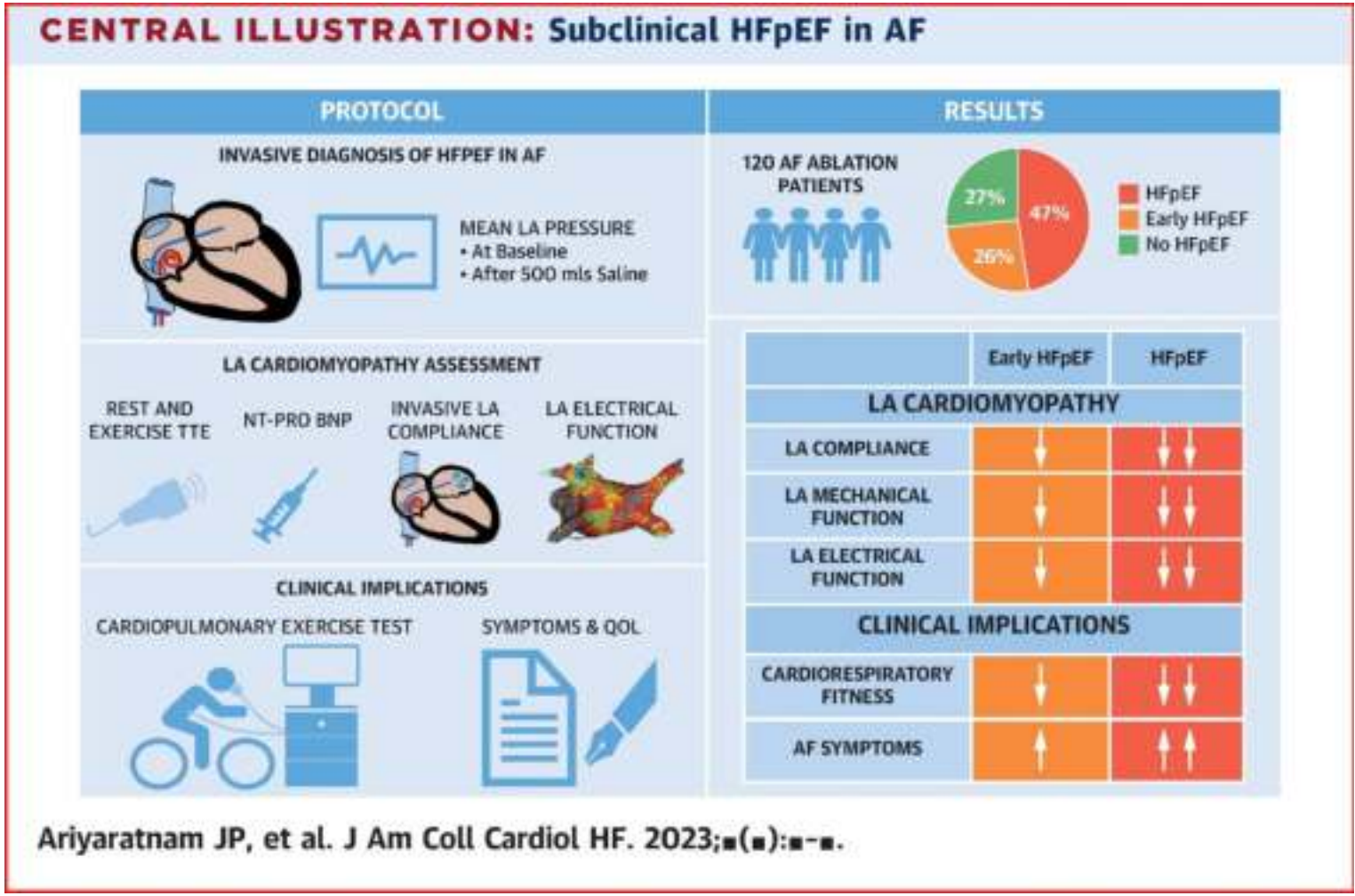


Subclinical HFpEF in Patients Referred for AF Ablation

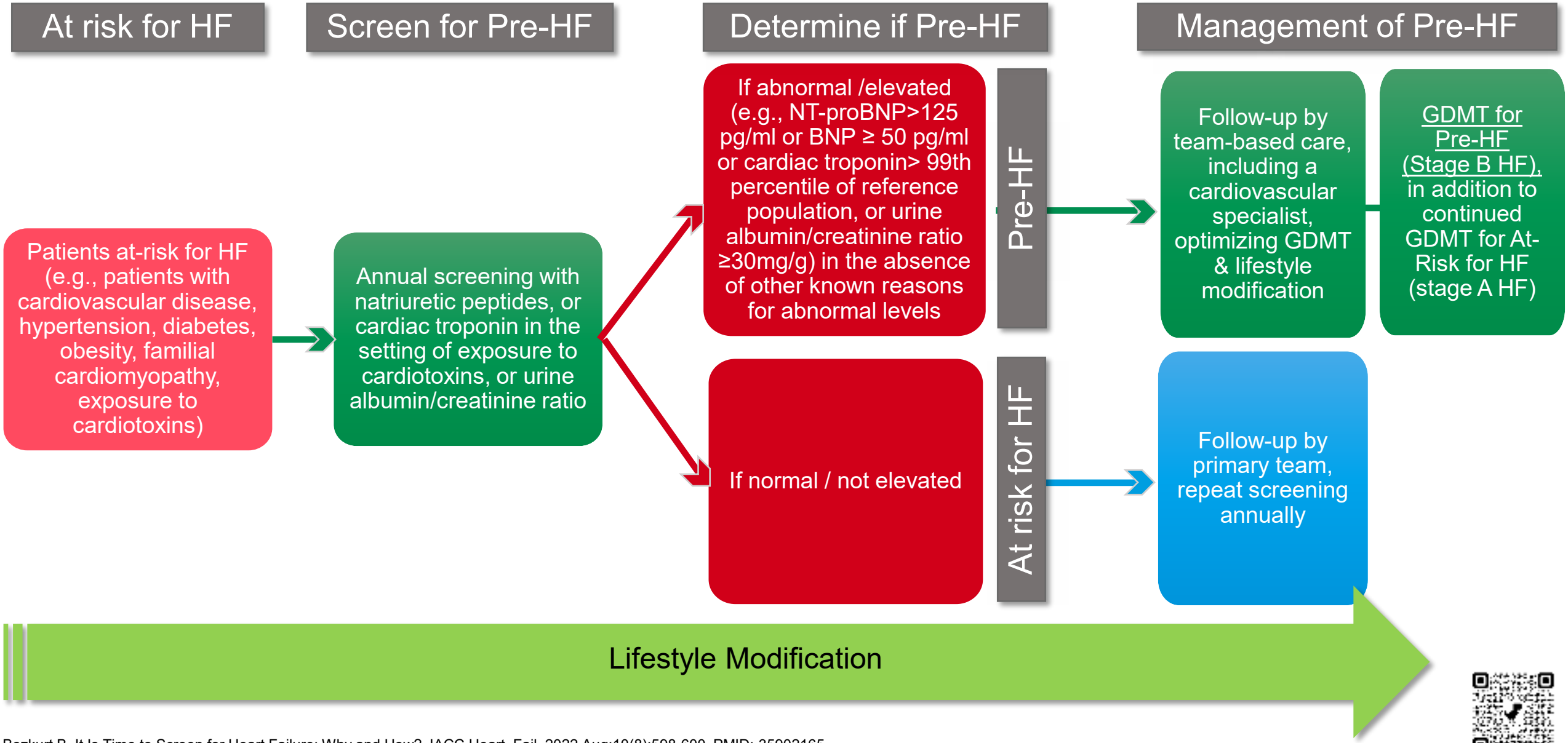
Identification of Subclinical Heart Failure With Preserved Ejection Fraction in Patients With Symptomatic Atrial Fibrillation

Jonathan P. Ariyaratnam, MB, BCom,[a] Adrian D. Elliott, PhD,[a,c] Ricardo S. Mishima, MD, PhD,[a] Kadhim Kadhim, MBCoB, PhD,[a] Olivia McNamee, RN,[a] Pawel Kuklik, PhD,[b] Mehrdad Emami, MD,[a] Varun Malik, MBBS, PhD,[a] John L. Fitzgerald, MBBS,[a] Celine Gallagher, PhD,[a] Dennis H. Lau, MBBS, PhD,[a] Prashanthan Sanders, MBBS, PhD[a,c]

- Lower LA compliance
- Decreased LA emptying fraction
- Decreased LA voltage
- Decreased VO2peak
- Increased AF symptom burden



Evolving Concepts in Screening for HF



Bozkurt B. It Is Time to Screen for Heart Failure: Why and How? JACC Heart Fail. 2022 Aug;10(8):598-600. PMID: 35902165.

Major Progress

Update in Management of HFpEF, HFrEF

Management of Comorbidities Obesity, Afib, CKD, Prevention of HF

Devices, Technology, Wearables, Shock, VAD/Tx

Genetic, Cardiomyopathies Myocarditis, Pregnancy

Evolving Device Interventions in HF

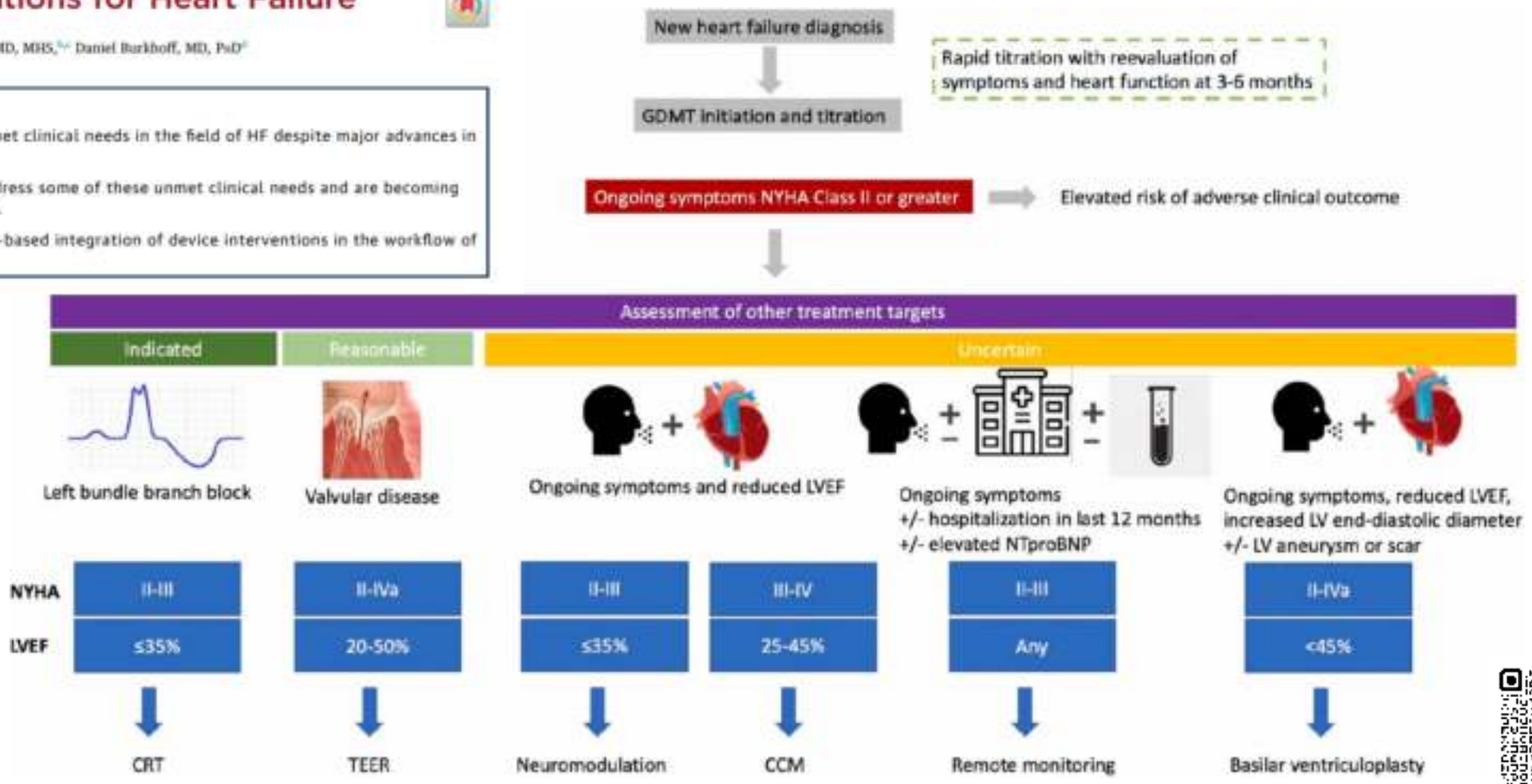
STATE-OF-THE-ART REVIEW

Device Interventions for Heart Failure

Husam M. Salah, MD,[a] Marat Fudim, MD, MHS,[b,c] Daniel Burkhoff, MD, PhD[d]

HIGHLIGHTS

- There remain significant unmet clinical needs in the field of HF despite major advances in drug therapy.
- Device interventions can address some of these unmet clinical needs and are becoming integral for HF management.
- There is a need for evidence-based integration of device interventions in the workflow of HF management.

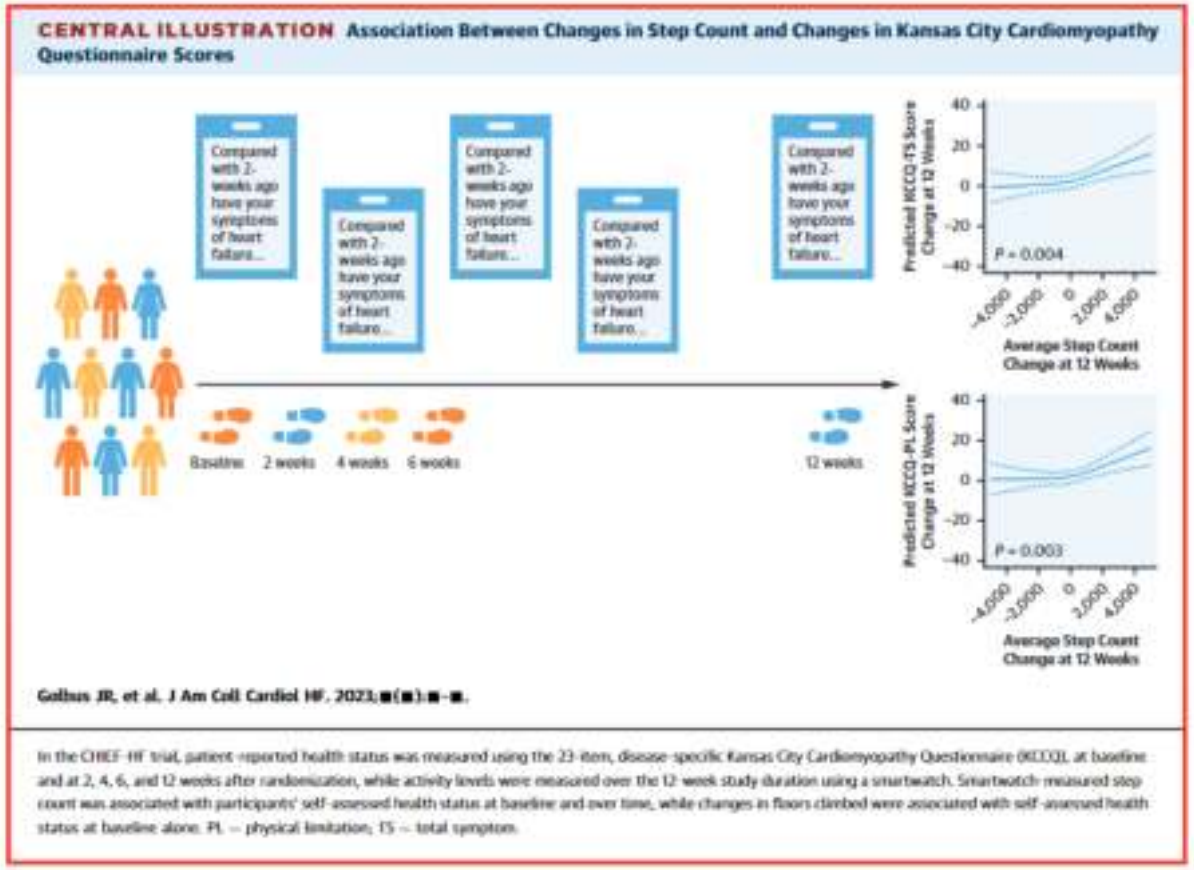


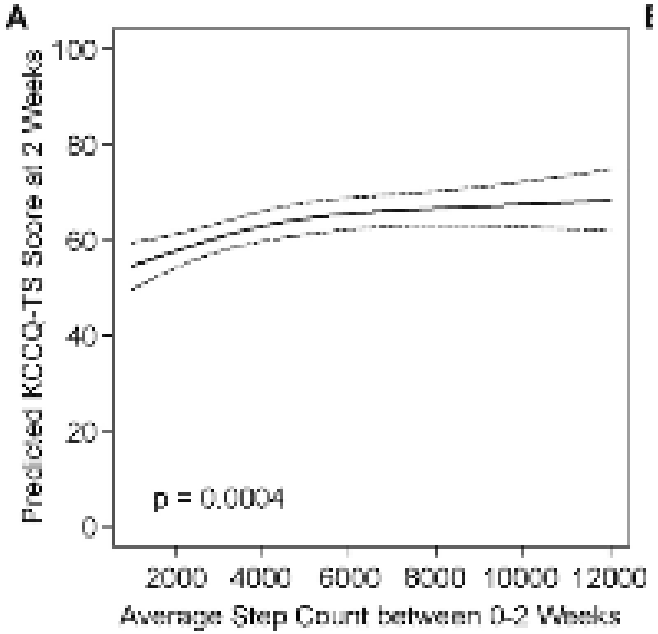
Salah HM, Fudim M, Burkhoff D. Device Interventions for Heart Failure. JACC Heart Fail. 2023 Aug;11(8 Pt 2):1039-1054. PMID: 37611987.

Wearable Devices: Step Count Associated with PROs

Association Between Wearable Device Measured Activity and Patient-Reported Outcomes for Heart Failure

Jessica R. Golbus, MD, MS,[a,b] Kensey Gosch, MS,[c] Mary C. Birmingham, PharmD,[d] Javed Butler, MD, MPH, MBA,[e] Ildiko Lingvay, MD, MPH, MSCS,[f] David E. Lanfear, MD, MS,[g] Antonio Abbate, MD,[h] Mikhail L. Kosiborod, MD, MS,[c] C.V. Damaraju, PhD,[d] James L. Januzzi, MD,[i] John Spertus, MD, MPH,[c,*] Brahmajee K. Nallamothu, MD, MPH[a,b,j,*]





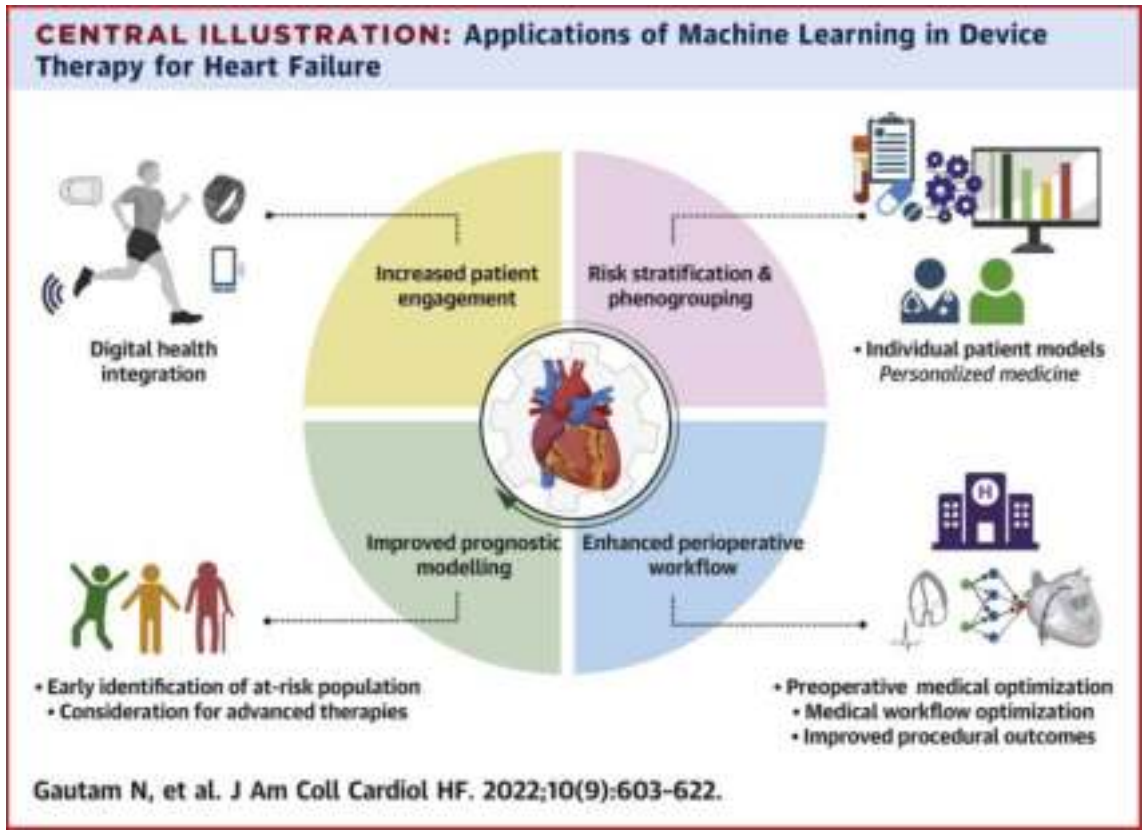
Machine Learning: From Voice Recognition, Risk Prediction to Patient Education

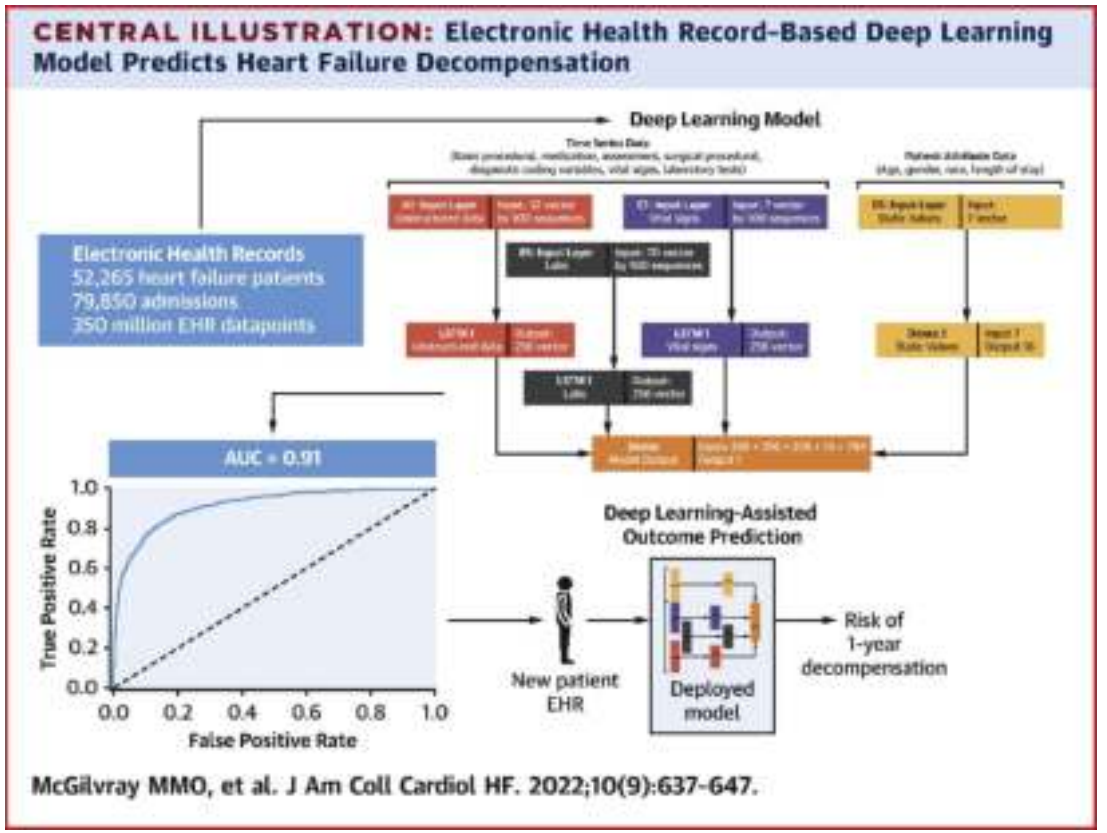
Contemporary Applications of Machine Learning for Device Therapy in HF

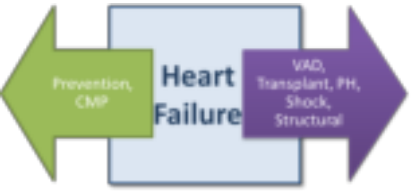
Nitesh Gautam, Sai Nikhila Ghanta Alex Clausen, Prachi Saluja, Kalai Sivakumar, Gaurav Dhar, Qi Chang, Deeptankar DeMazumder, Mark G Rabbat, Stephen J Greene, Marat Fudim, Subhi J Al'Aref

Electronic Health Record-Based Deep Learning Prediction of Death or Severe Decompensation in HF Patients

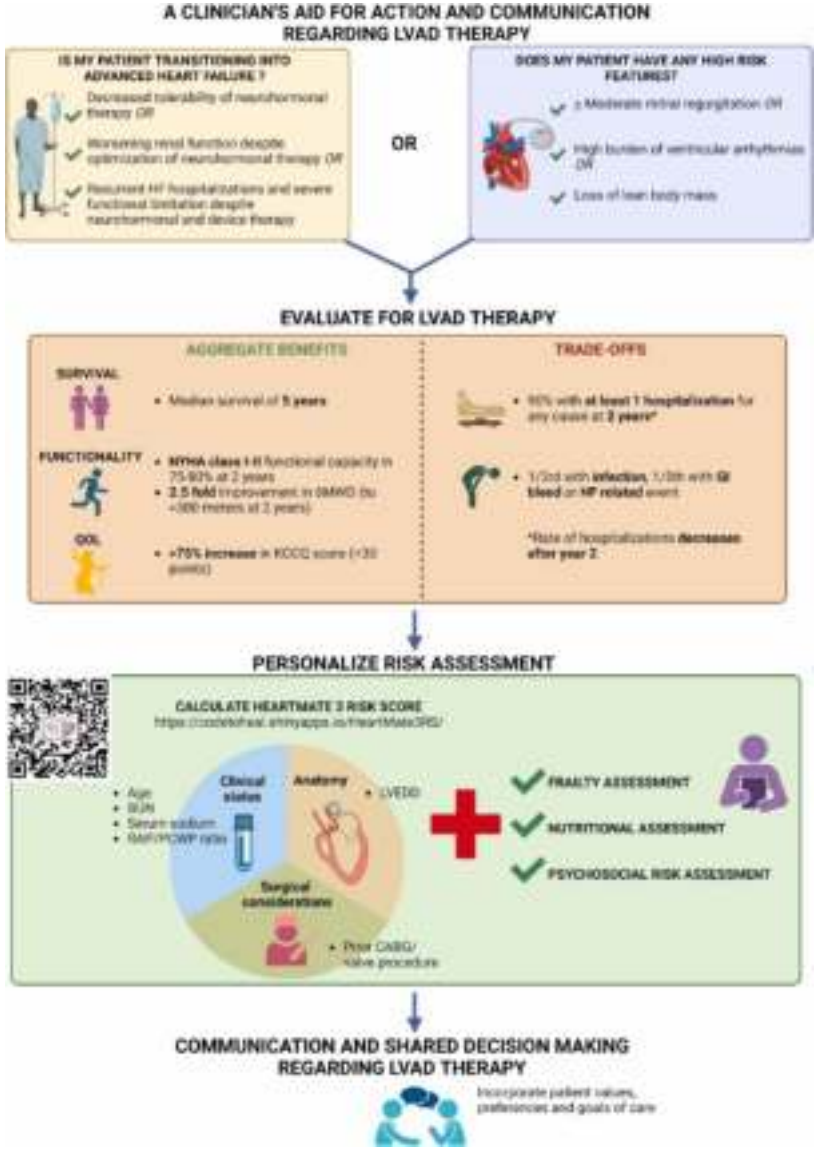
Martha M.O. McGilvray MSt, MD a, Jeffrey Heaton PhD b, Aixia Guo PhD, M. Faraz Masood MD, Brian P. Cupps PhD, Marci Damiano RN, MSN, Michael K. Pasque MD, Randi Foraker PhD







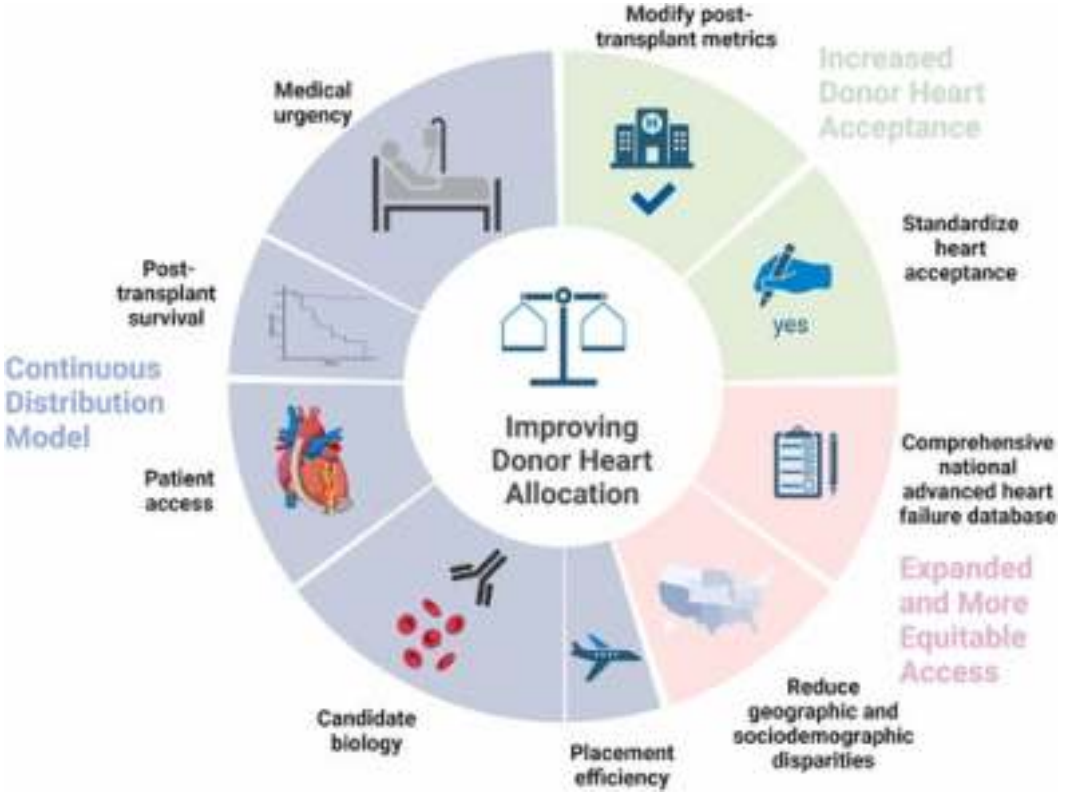
Life-Prolonging Benefits of LVAD Therapy in Advanced HF



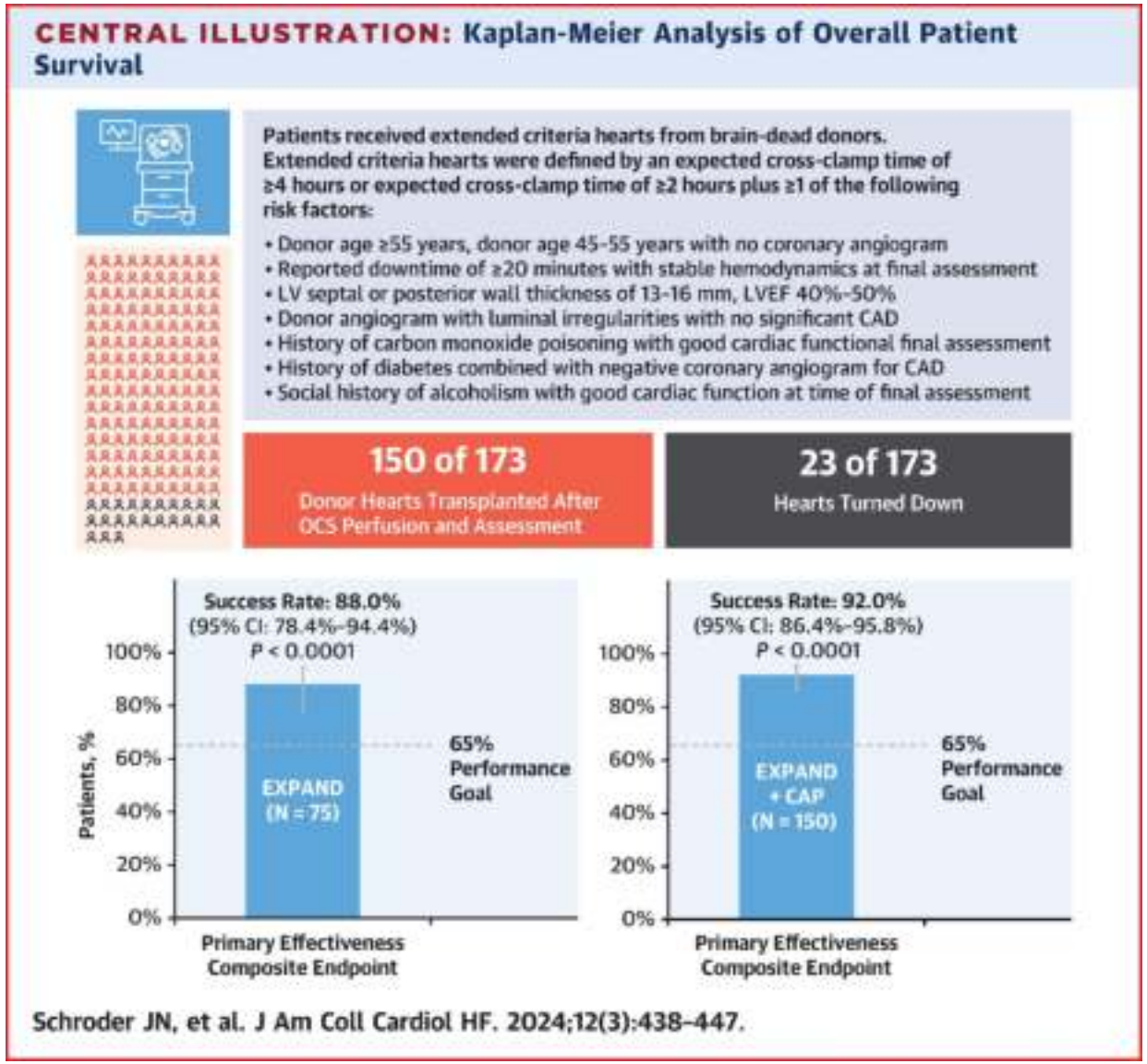
Mehra MR, Nayak A, Desai AS. Life-Prolonging Benefits of LVAD Therapy in Advanced Heart Failure: A Clinician's Action and Communication Aid. JACC Heart Fail. 2023 Aug;11(8 Pt 1):1011-1017 PMID: 37226447.

Ongoing Discussion - Heart Transplant Allocation

- Impact of the 2018 UNOS Heart Transplant Policy Changes on Patient Outcomes (SoA)
  Neil S. Maitra, Samuel J. Dugger, Isabel C. Balachandran, Andrew B. Civitello, Prateeti Khazanie, and Joseph G. Rogers
- The Accuracy of Initial U.S. Heart Transplant Candidate Rankings
  Kenley M. Pelzer, Kevin C. Zhang, Kevin A. Lazenby, Nikhil Narang, Matthew M. Churpek, Allen S. Anderson, and William F. Parker
- The Future of Heart Allocation Policy: Patient-Specific Variables Over Treatment Strategy
  Maryjane Farr and Nicholas S. Hendren
- Developing a System for Best Performance for Cardiac Transplantation
  Jesse D. Schold, Jordan Hoffman, and Joseph Cleveland
- How to Make the Transplantation Allocation System Better
  Kiran K. Khush, Alexander T. Sandhu, and William F. Parker



Organ Preservation Techniques: Increasing Utilization of Extended Criteria Donor Hearts for Transplantation: The Organ Case System (OCS) Heart EXPAND Trial



- >50% of hearts enrolled had multiple risk factors that resulted in them being declined for transplantation on UNOS match run on average 51 times before being accepted.
- Organ Case System Heart perfusion resulted in 87% successful utilization of these donor hearts for transplantation with excellent patient survival to 2 years post-transplant and low rates of severe primary graft dysfunction.

Evolving Concepts in Noninvasive Heart Transplant Rejection Surveillance

The End of Endomyocardial Biopsy?

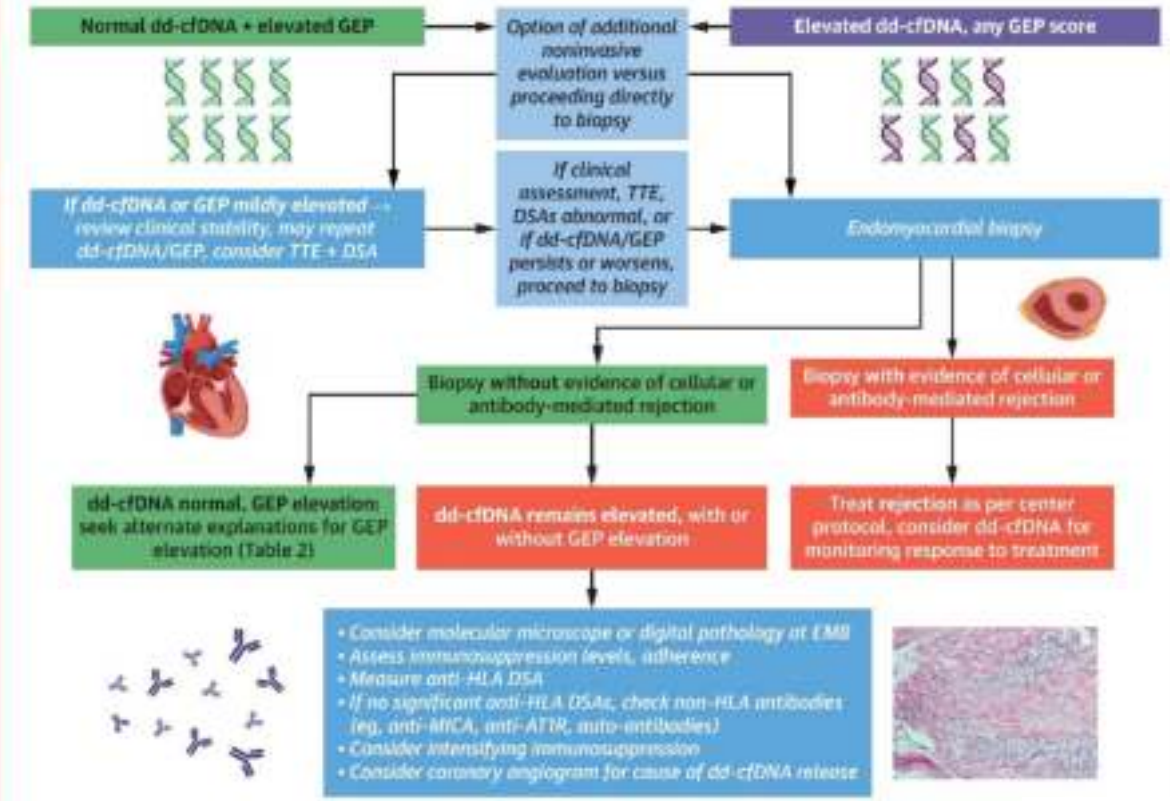
A Practical Guide for Noninvasive Heart Transplant Rejection Surveillance

Luise Holzhauser, MD,[a] Ersilia M. DeFilippis, MD,[b] Andriana Nikolova, MD, PhD,[c] Mirnela Byku, MD, PhD,[d] Johanna P. Contreras, MD,[e] Teresa De Marco, MD,[f] Shelley Hall, MD,[g] Kiran K. Khush, MD, MAS,[h] Amanda R. Vest, MBBS, MPH[i]

HIGHLIGHTS

- Rejection surveillance using gene expression profiling and donor-derived cell-free DNA (dd-cfDNA) is noninferior to endomyocardial biopsy.
- Transitioning away from traditional biopsy surveillance raises many practical questions.
- In this paper, we provide guidance for the transition and early implementation process.
- The clinical value of dd-cfDNA may offer benefits beyond current surveillance strategies, pending future prospective studies.

CENTRAL ILLUSTRATION: Flowchart Proposing Interpretation of Noninvasive Surveillance With a Combination of Gene Expression Profiling and dd-cfDNA

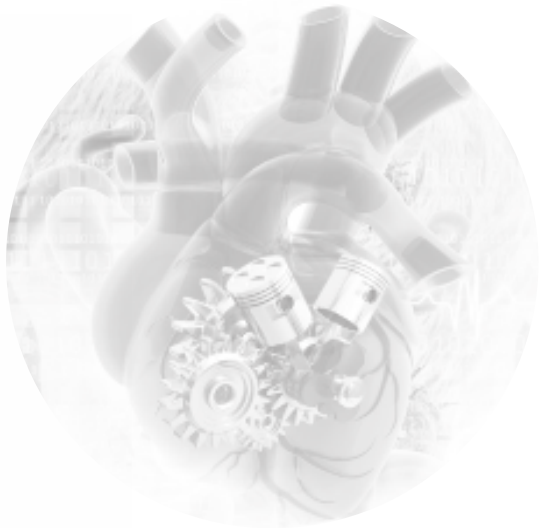


Holzhauser L, et al. J Am Coll Cardiol HF. 2023;11(3):263-276.

Major Progress

Update in Management of HFpEF, HFrEF

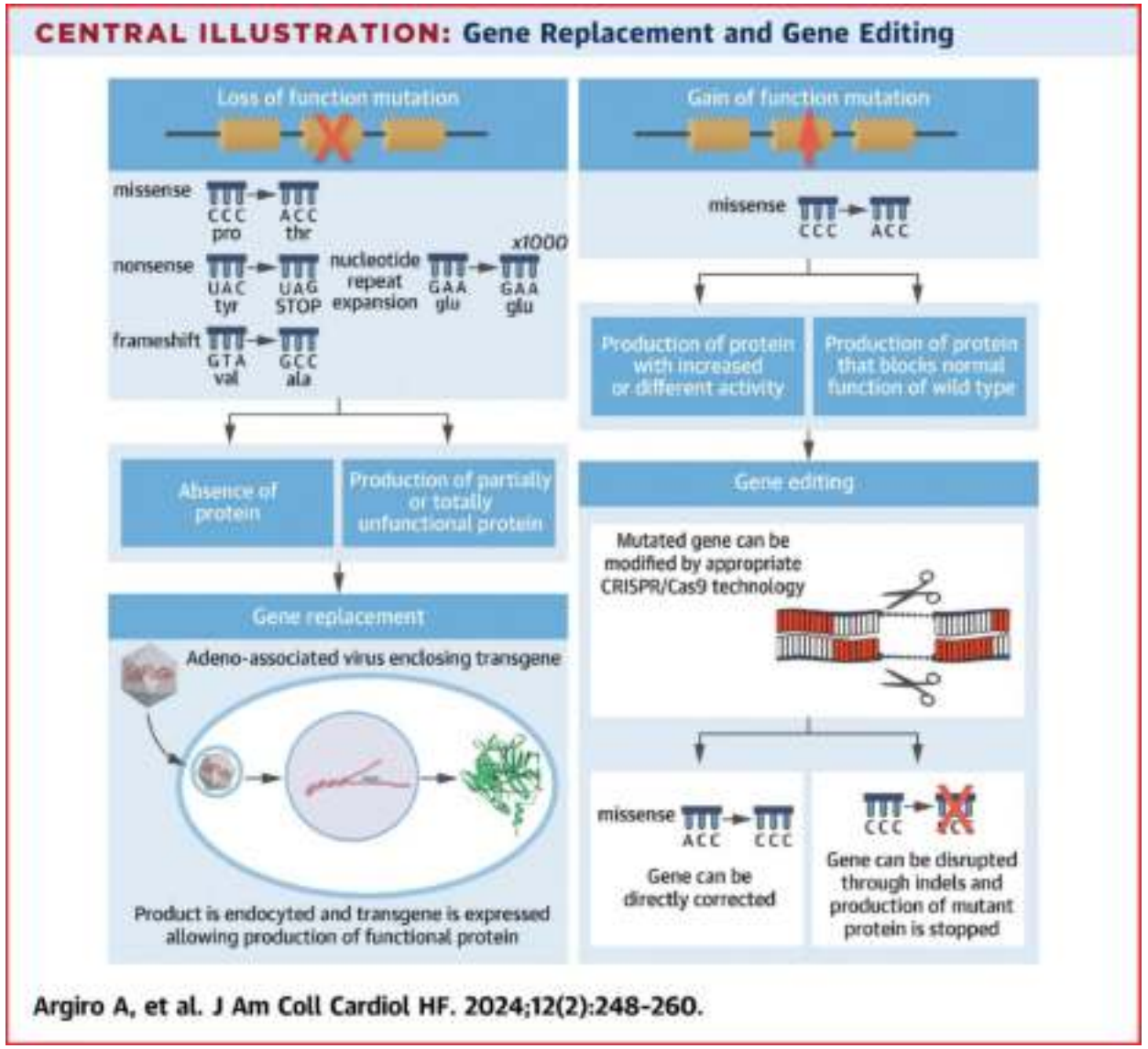
Management of Comorbidities Obesity, Afib, CKD, Prevention of HF



Devices, Technology, Wearables, Shock, VAD/Tx

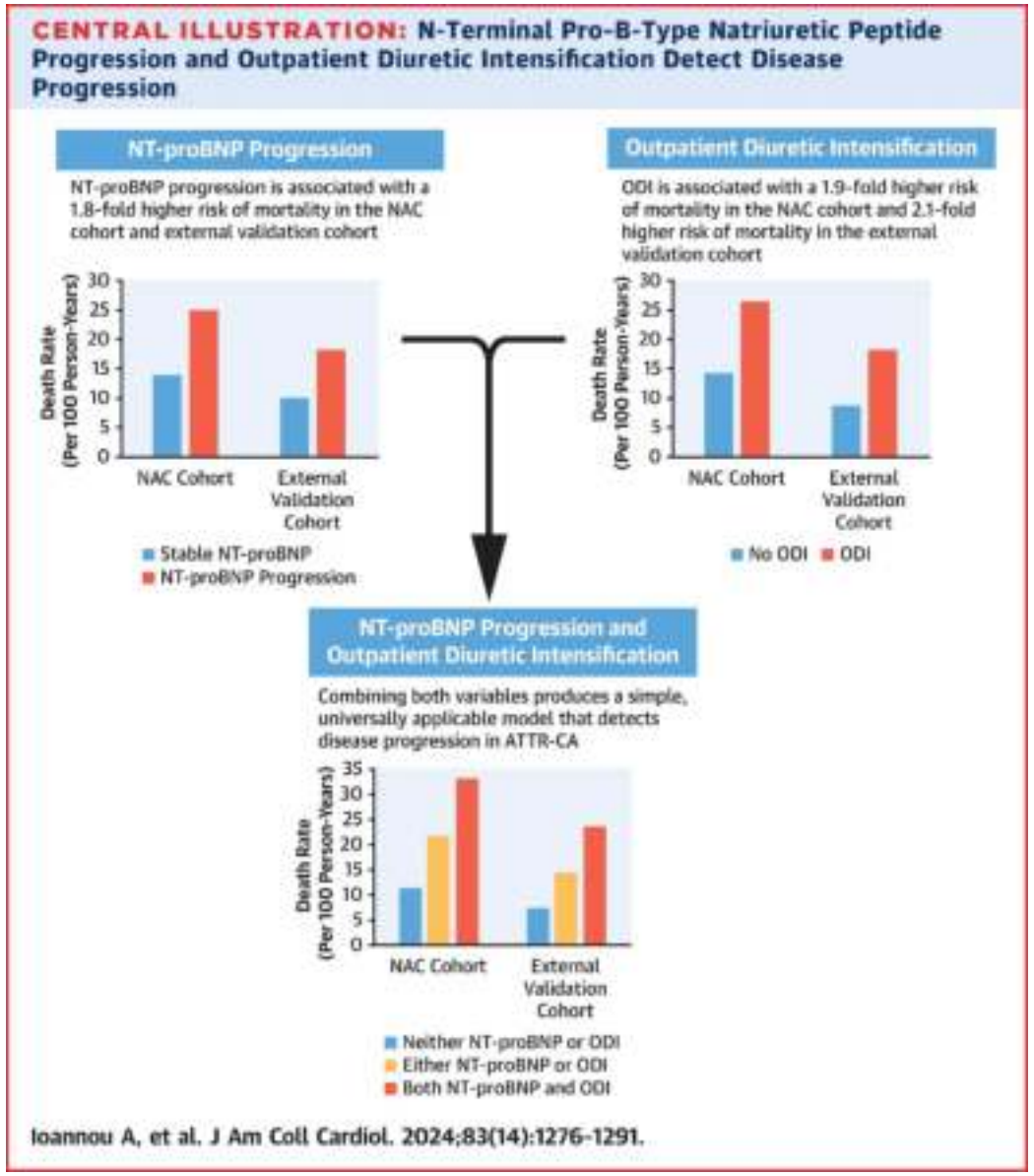
Genetic, Cardiomyopathies Myocarditis, Pregnancy

Gene Therapy in Cardiomyopathies



- Gene therapy for Duchenne muscular dystrophy approved
- Pivotal clinical trials are testing gene therapy approaches in Danon disease and Fabry disease.
- Promising results shown in animal models of gene therapy in HCM and arrhythmogenic cardiomyopathy

NP and Diuretic Need as Markers of Disease Progression in Cardiac ATTR Amyloidosis



JACC: HEART FAILURE
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VOL. 11, NO. 9, 2023

STATE-OF-THE-ART REVIEW

Heart Failure in Pregnancy

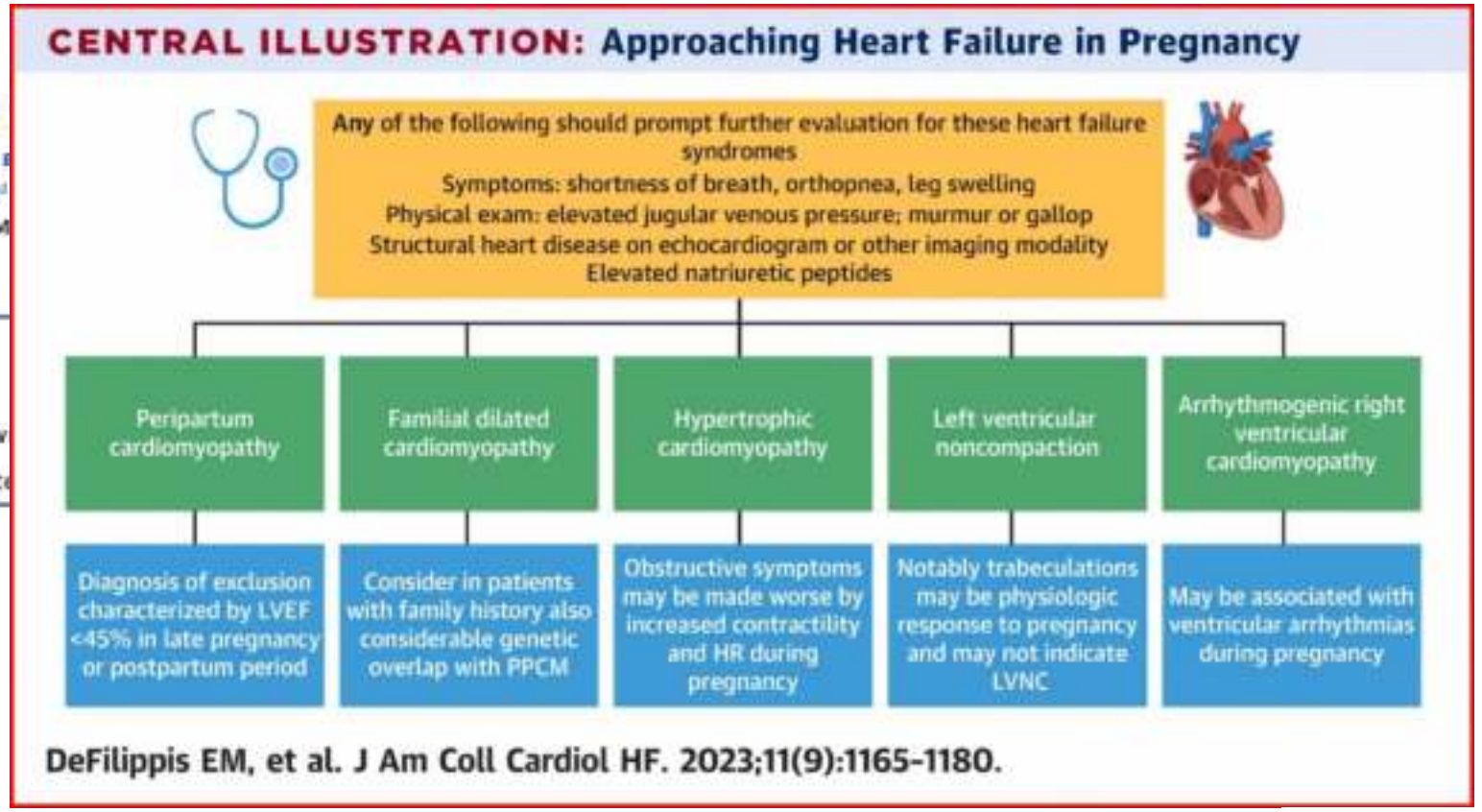
Cardio-Obstetrics and Heart Failure

JACC: Heart Failure State-of-the-Art Review

Ersilia M. DeFilippis, MD,[a] Catriona Bhagra, MD,[b] Jillian Casale, PharmD,[c] Patricia Ging, MSc,[d] Francesca Macera, MD,[e,f] Lynn Punnoose, MD,[g] Kismet Rasmusson, DNP,[h] Garima Sharma, M[i] Sara Thorne, MD,[j] Mary Norine Walsh, MD,[k] Michelle M. Kittleson, MD, PhD[m]

HIGHLIGHTS

- Maternal mortality continues to rise in the United States.
- A comprehensive preconception risk assessment is necessary for women w
- Multidisciplinary cardio-obstetric teams are necessary for improving mat



DeFilippis, E, Bhagra, C, Casale, J. et al. Cardio-Obstetrics and Heart Failure: *JACC: Heart Failure* State-of-the-Art Review. *J Am Coll Cardiol HF.* 2023 Sep, 11 (9) 1165–1180.

Reproductive Factors Associated with Risk of HF

Female Reproductive Factors and Risk of New-Onset Heart Failure

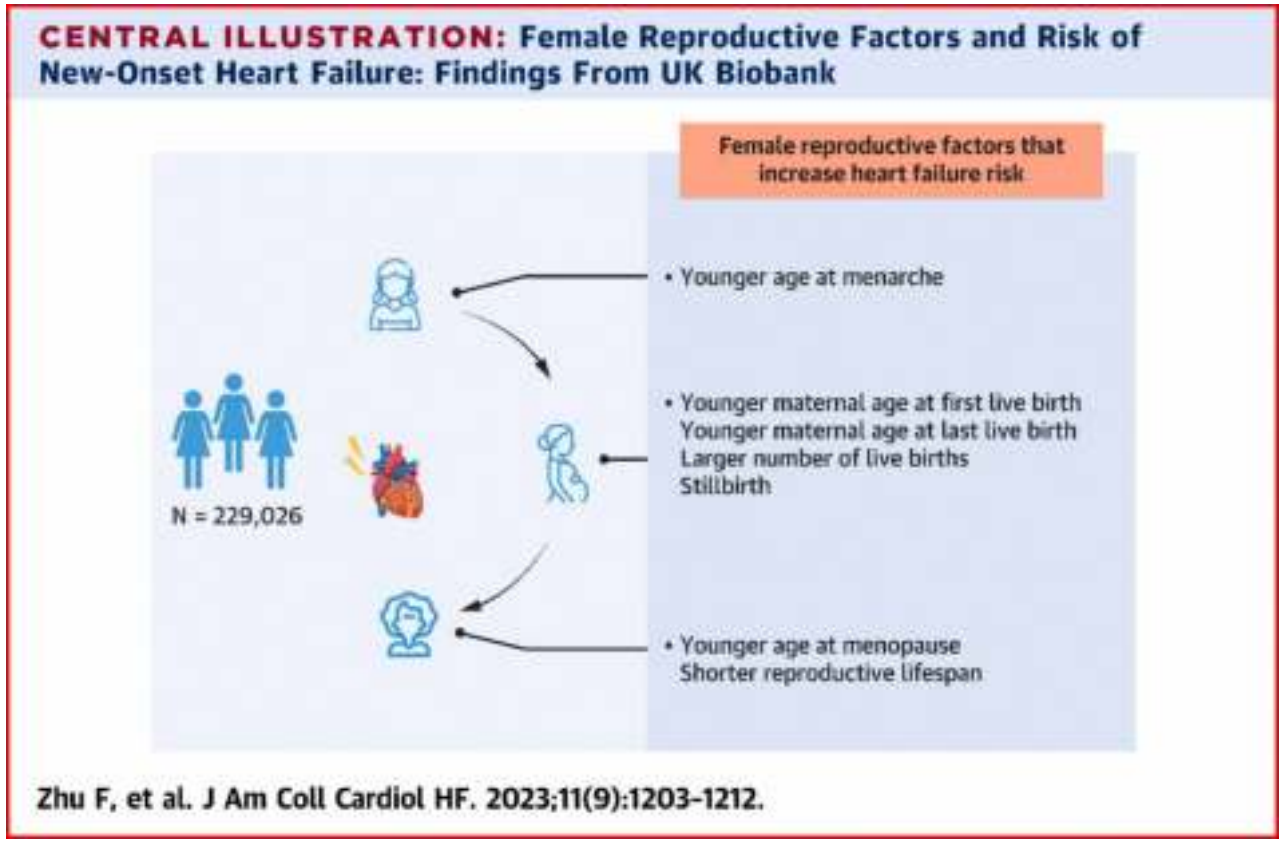
Findings From UK Biobank

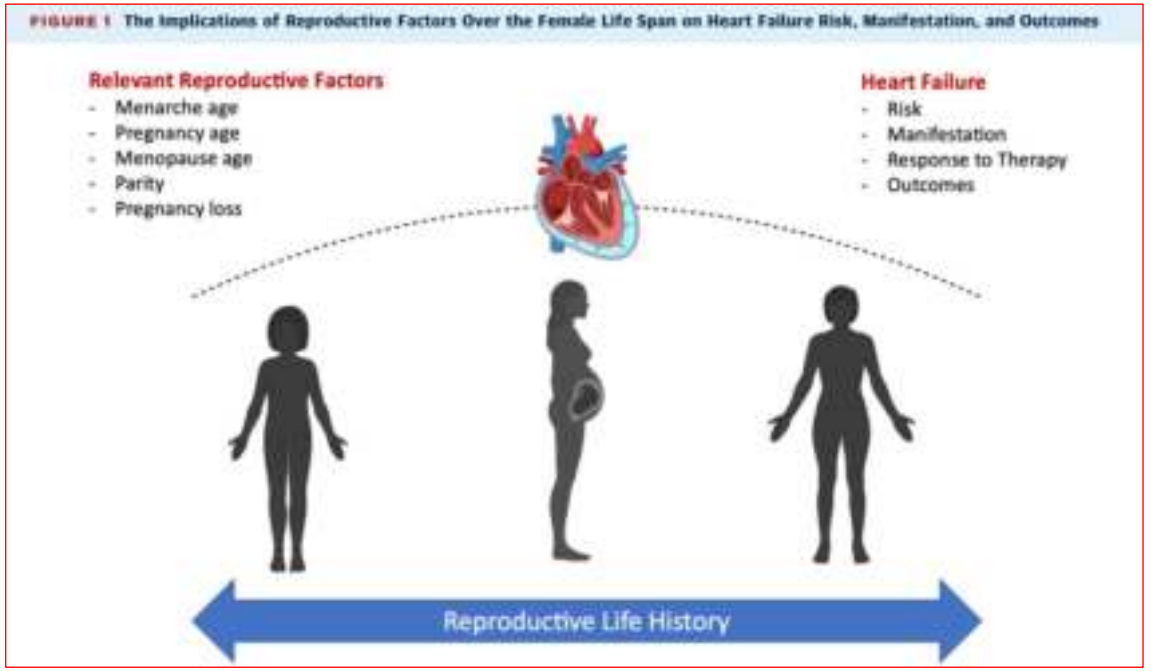
Fang Zhu, MSc, MPH,[a,*] Hongchao Qi, MD, MSc,[a,b,*] Maxime Bos, PhD,[a] Eric Boersma, MSc, PhD,[c] Maryam Kavousi, MD, PhD[a]

Reproductive History Assessments in Cardiovascular Care

We Need to Start by Asking*

Paz (Upasana) Tayal, PhD,[a] Anuradha Lala, MD[b]





Global Variations According to Sex in Patients Hospitalized for HF

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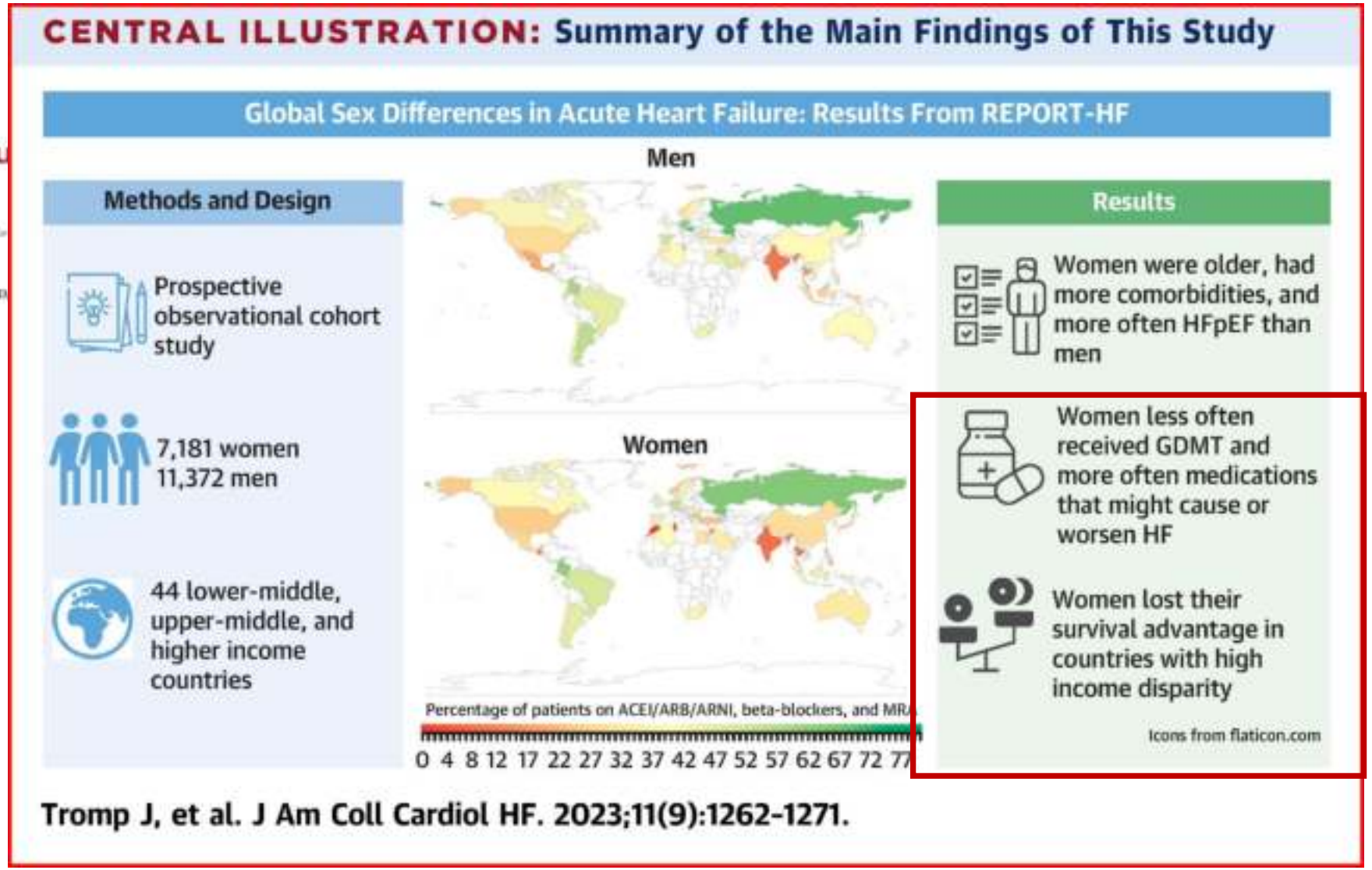
Global Variations According to Sex in Patients Hospitalized for Heart Failu in the REPORT-HF Registry

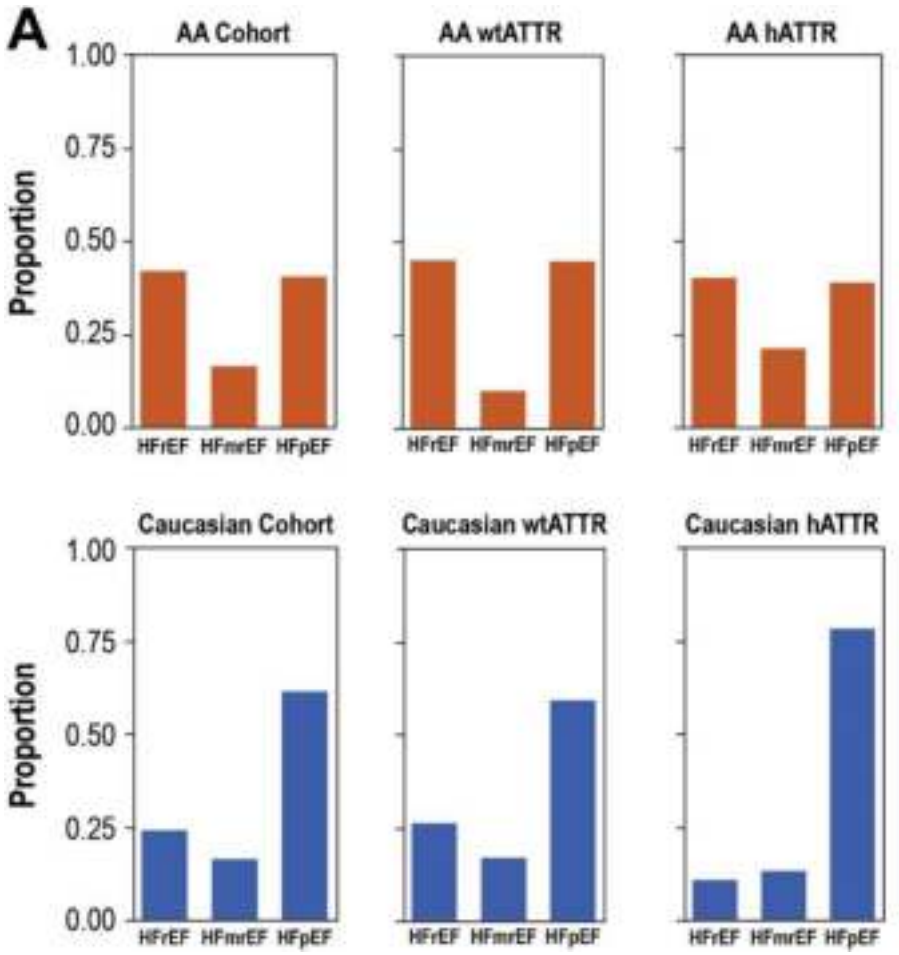
Jasper Tromp, MD, PhD, MPH,[a,b] Justin A. Ezekowitz, MBBCh, MSc,[c] Wouter Ouwerkerk, PhD,[d,e] Chanchal Chandramouli, PhD,[e,f] Kai Hang Yiu, MBBS, PhD,[f,g] Christiane E. Angermann, MD,[h] Ulf Dahlström, MD, PhD,[i] Georg Ertl, MD,[h] Mahmoud Hassanein, MD,[j] Sergio V. Perrone, MD,[k] Mathieu Ghadanfar, MD,[l] Anja Schweizer, PhD,[m] Achim Obergfell, MD,[m] Kenneth Dickstein, MD, Sean P. Collins, MD, MSc,[n] Gerasimos Filippatos, MD,[o,p] John G.F. Cleland, MD, PhD,[q,r] Carolyn S.P. Lam, MBBS, PhD[b,s]

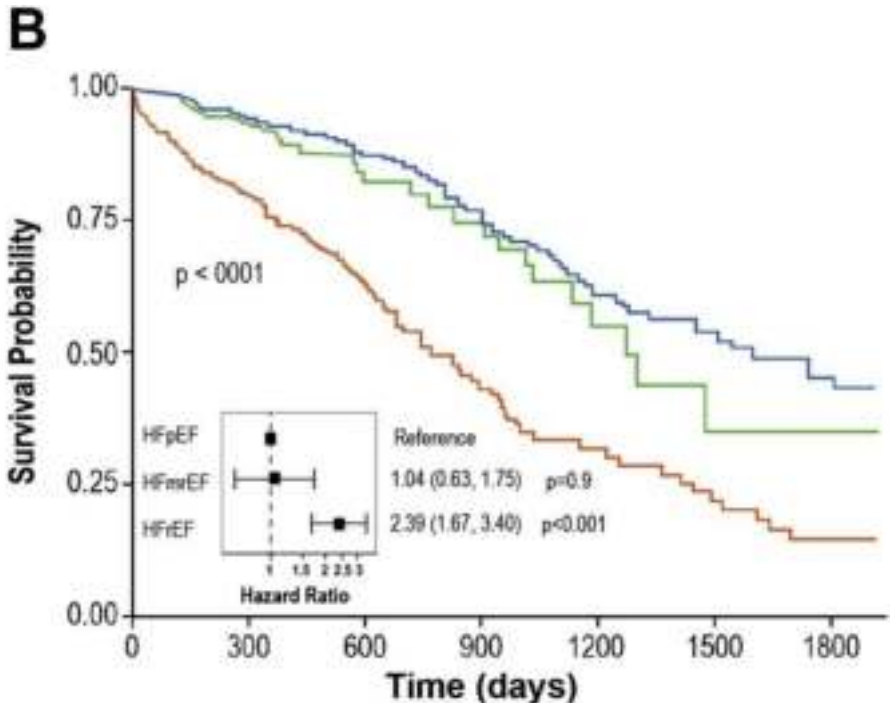


Tromp J, et al. J Am Coll Cardiol HF. 2023;11(9):1262-1271.

Racial and Genetic Differences in Presentation of Transthyretin Amyloid Cardiomyopathy With Impaired Left Ventricular Function

Trejeeve Martyn MD, Joshua Saef MD, Anusha Ray Dey BS, Rola Khedraki MD, Vardhmaan Jain MD, Patrick Collier MD, PhD, Wael A. Jaber MD, Jerry D. Estep MD, Mazen Hanna MD, W.H. Wilson Tang MD





Black patients with ATTR-CM were more likely to present with HFrEF compared with Caucasian patients

JACC Heart Fail . 2022 Sep;10(9):689-691

Bereavement, Social Isolation in HF

Bereavement and Prognosis in Heart Failure

A Swedish Cohort Study

Hua Chen, MSc,[a] Dang Wei, MD, MSc,[a] Imre Janszky, MD, PhD,[a,b] Ulf Dahlström, MD, PhD,[c] Mikael Rostila, PhD,[d,e] Krisztina D. László, PhD[a]

- Swedish Heart Failure Registry 2000-2018
- Death of a family member associated with 29% increase in mortality, regardless of cause

Enhancing patient spirituality (finding meaning and purpose) through palliative care may help to improve quality of life and outcomes in HF

STATE-OF-THE-ART REVIEW

Spirituality in Patients With Heart Failure

Rachel S. Tobin, MD,[a] Michael F. Cosiano, MD,[a] Christopher M. O'Connor, MD,[b] Mona Fiuzat, PharmD,[a] Bradi B. Granger, PhD,[c] Joseph G. Rogers, MD,[a,d] James A. Tulsky, MD,[e] Karen E. Steinhauser, PhD,[a,f] Robert J. Mentz[a,g]

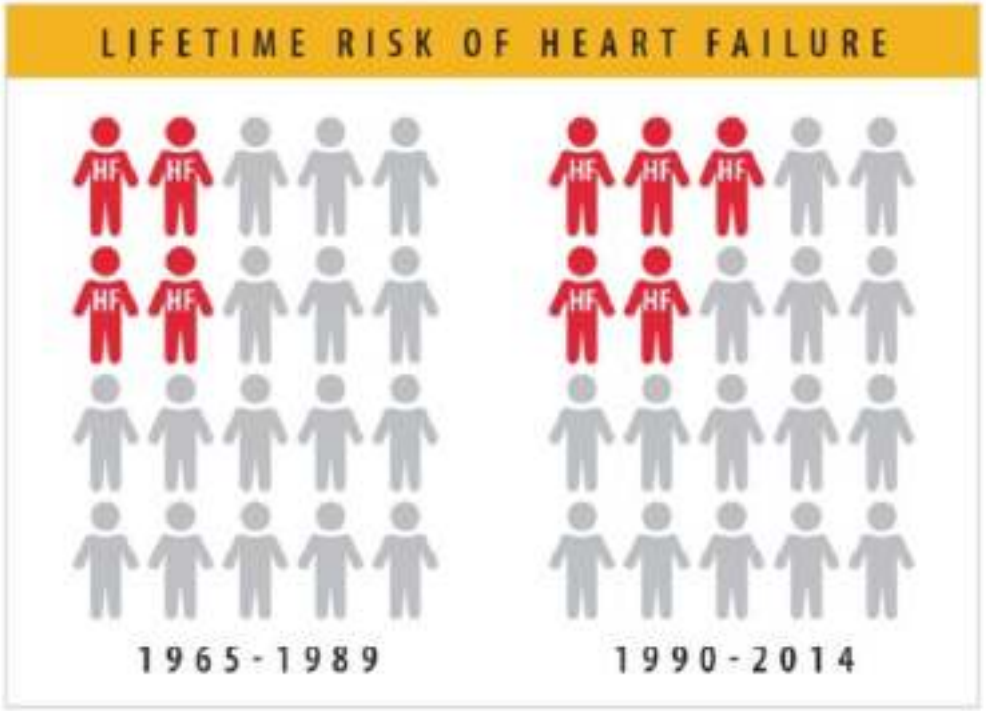
Association of Social Isolation and Loneliness With Incident Heart Failure in a Population-Based Cohort Study

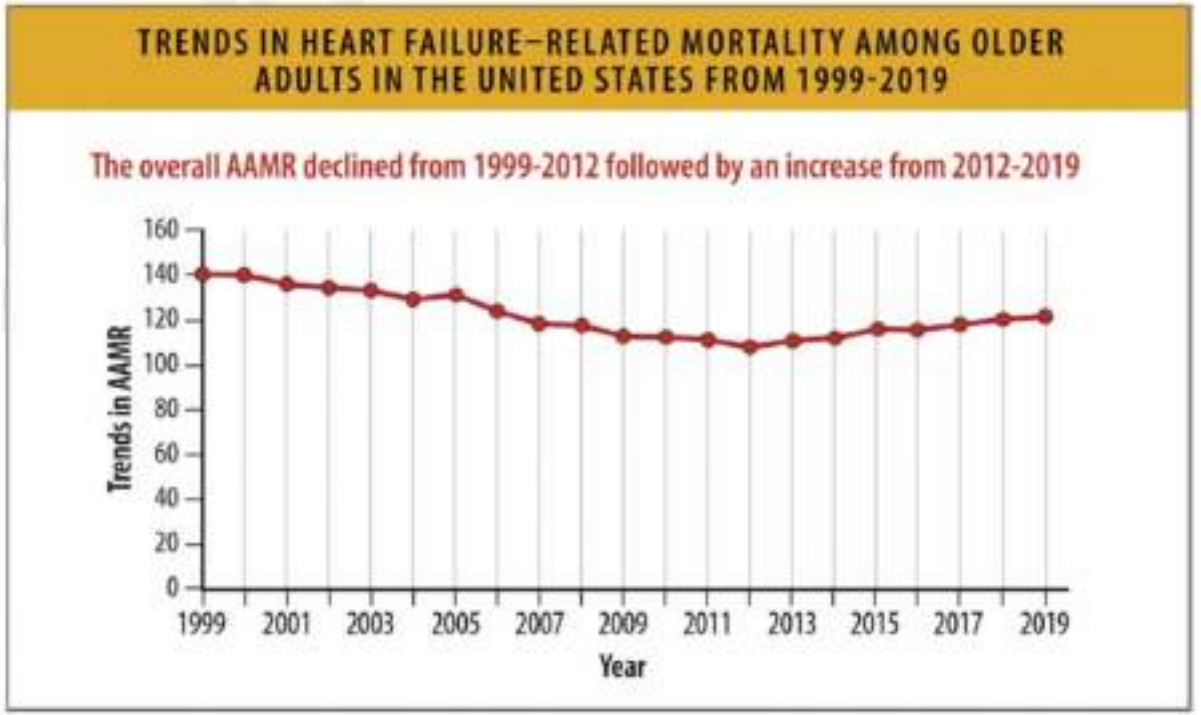
Yannis Yan Liang, MD, PhD,[a,b,c,*] Yilin Chen, MD,[a,d,e] Hongliang Feng, MD, PhD,[a,e] Xiangxin Liu, MD, PhD,[a,f] Qi-Yong H. Ai, MD, PhD,[g] Huachen Xue, MSc,[h] Xinyue Shu,[i] Foqian Weng,[i] Zhixuan He,[i] Jiacheng Ma, BS,[h] Huan Ma, MD, PhD,[a,b] Sizhi Ai, MD, PhD,[i] Qingshan Geng, MD, PhD,[a,b] Jihui Zhang, MD, PhD[b,j]

UK Biobank: Social Isolation and Loneliness associated with heightened risk for incident HF

HFSTATS
EPIDEMIOLOGY AND OUTCOMES
Heart Failure Epidemiology and Outcomes Statistics:
A Report of the Heart Failure Society of America

Lifetime Risk of HF and HF Mortality Rates are Increasing

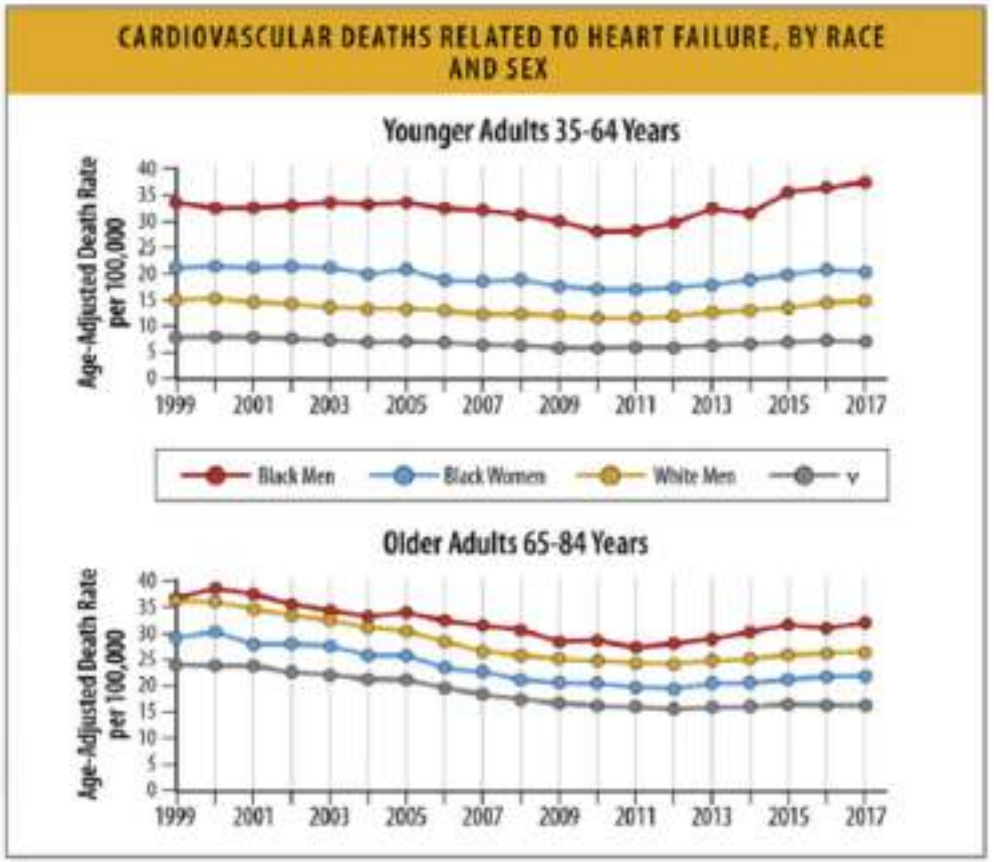


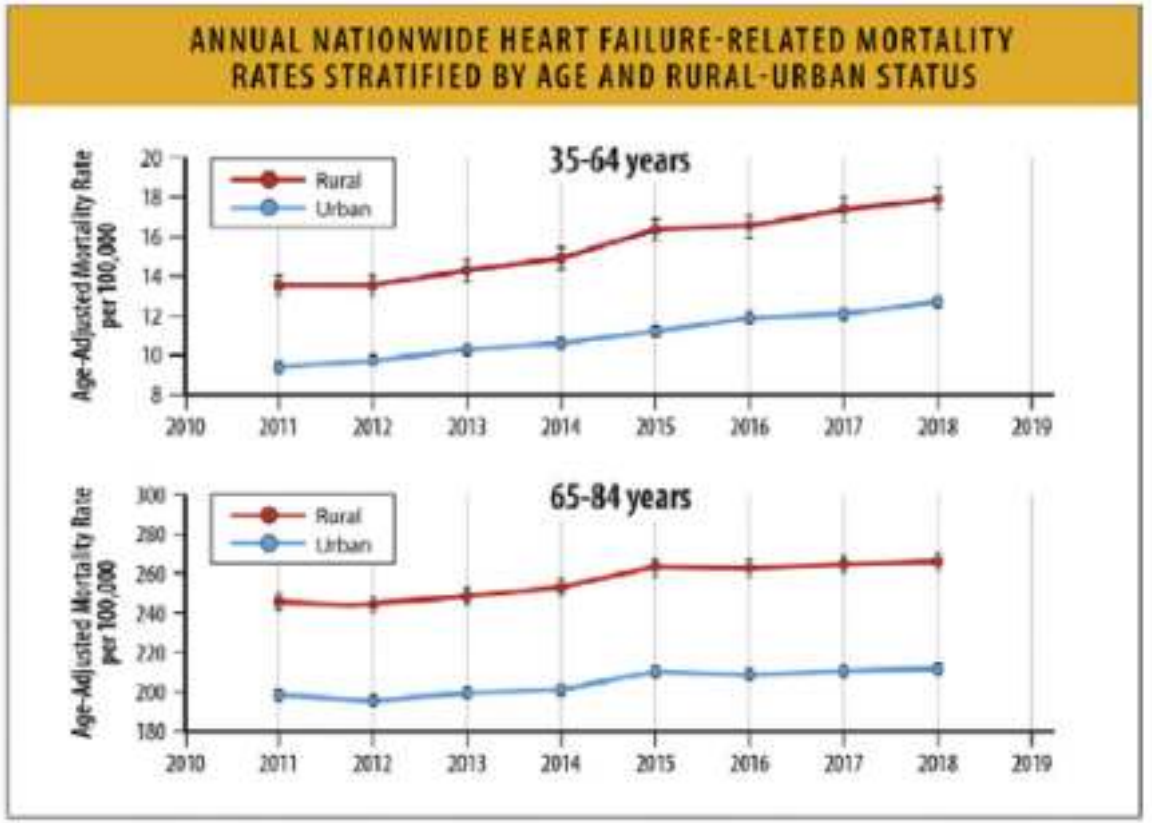


HF Stats. Bozkurt B et al. J Card Fail. 2023 Oct;29(10):1412-1451.

HFSTATS
EPIDEMIOLOGY AND OUTCOMES
Heart Failure Epidemiology and Outcomes Statistics:
A Report of the Heart Failure Society of America

Higher HF Mortality Rates

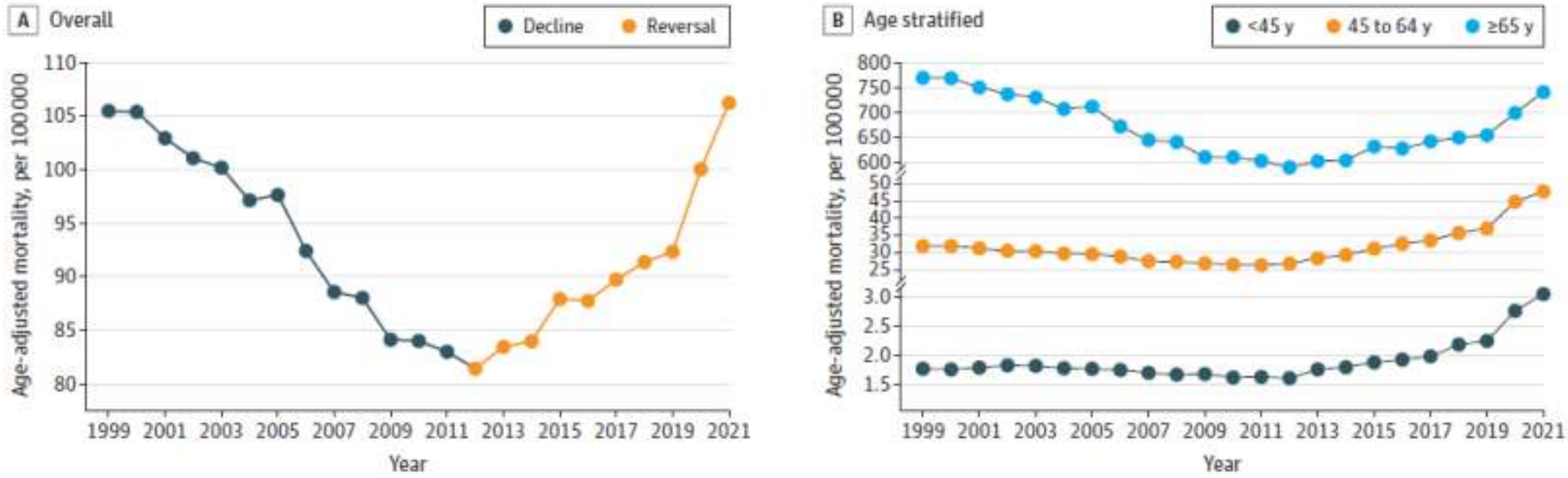




HF Stats. Bozkurt B et al. J Card Fail. 2023 Oct;29(10):1412-1451.

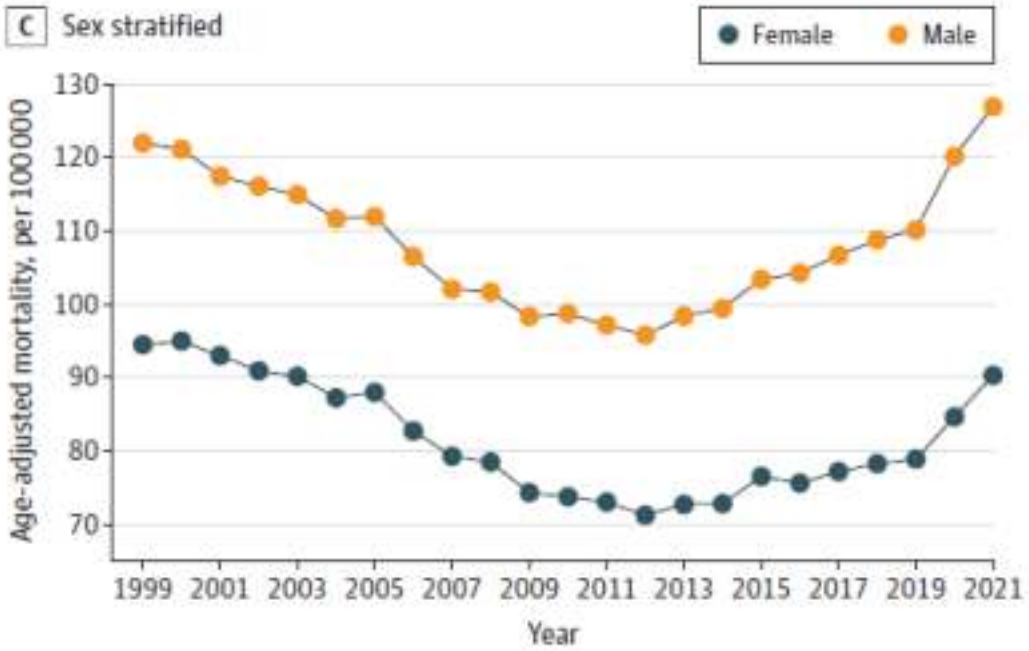
Recent Trends

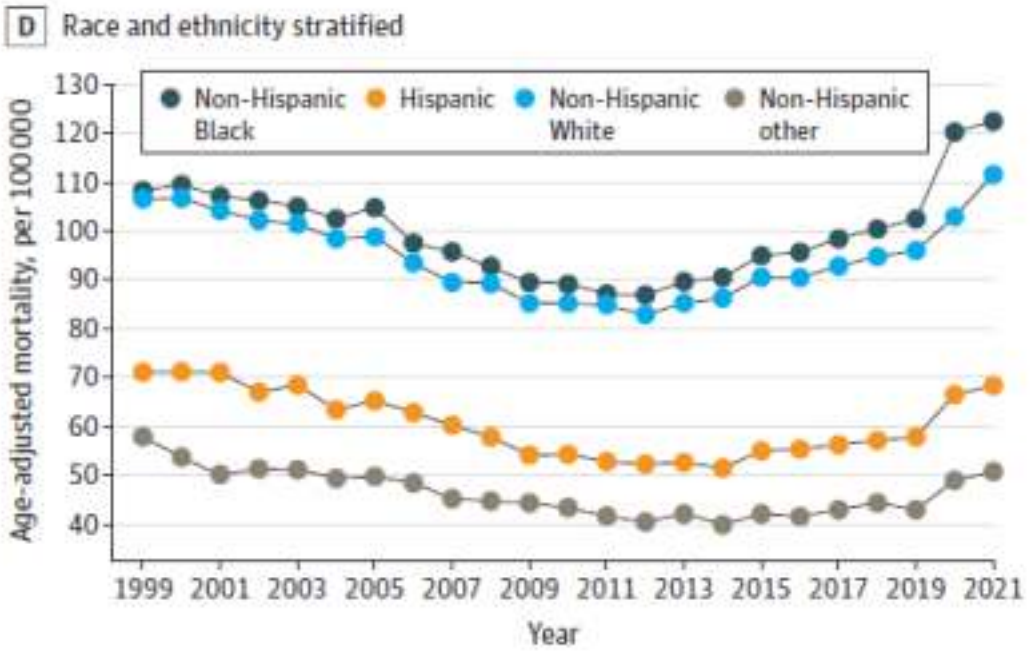
Figure. Temporal Trends in Heart Failure-Related Mortality in the US, 1999 to 2021



Sayed A. et al. Reversals in the Decline of Heart Failure Mortality in the US, 1999 to 2021 JAMA Cardiology Published online April 24, 2024

Recent Trends





Sayed A. et al. Reversals in the Decline of Heart Failure Mortality in the US, 1999 to 2021 JAMA Cardiology Published online April 24, 2024

ABC's of De-congesting "Congestive" Heart Failure

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Disclosures

	Dr. Abhinav Sharma
Any direct financial payments including receipt of honoraria	Boehringer Ingelheim, Novartis, Novo Nordisk, CHFS, HF Update, CCS
Membership on advisory boards or speakers' bureaus	AstraZeneca, Boehringer Ingelheim, Eli-Lilly, Servier, Novo Nordisk, Abbott
Funded grants or clinical trials	AstraZeneca, Boehringer-Ingelheim, Medtronic, Merck, Novartis, Novo Nordisk, Takeda Development Center Americas, Inc., Roche Diagnostics, Janssen
All other investments or relationships that could be seen by a reasonable, well-informed participant as having the potential to influence the content of the educational activity	Boehringer-Ingelheim, Boston Scientific Corporation, Janssen

Learning Objectives

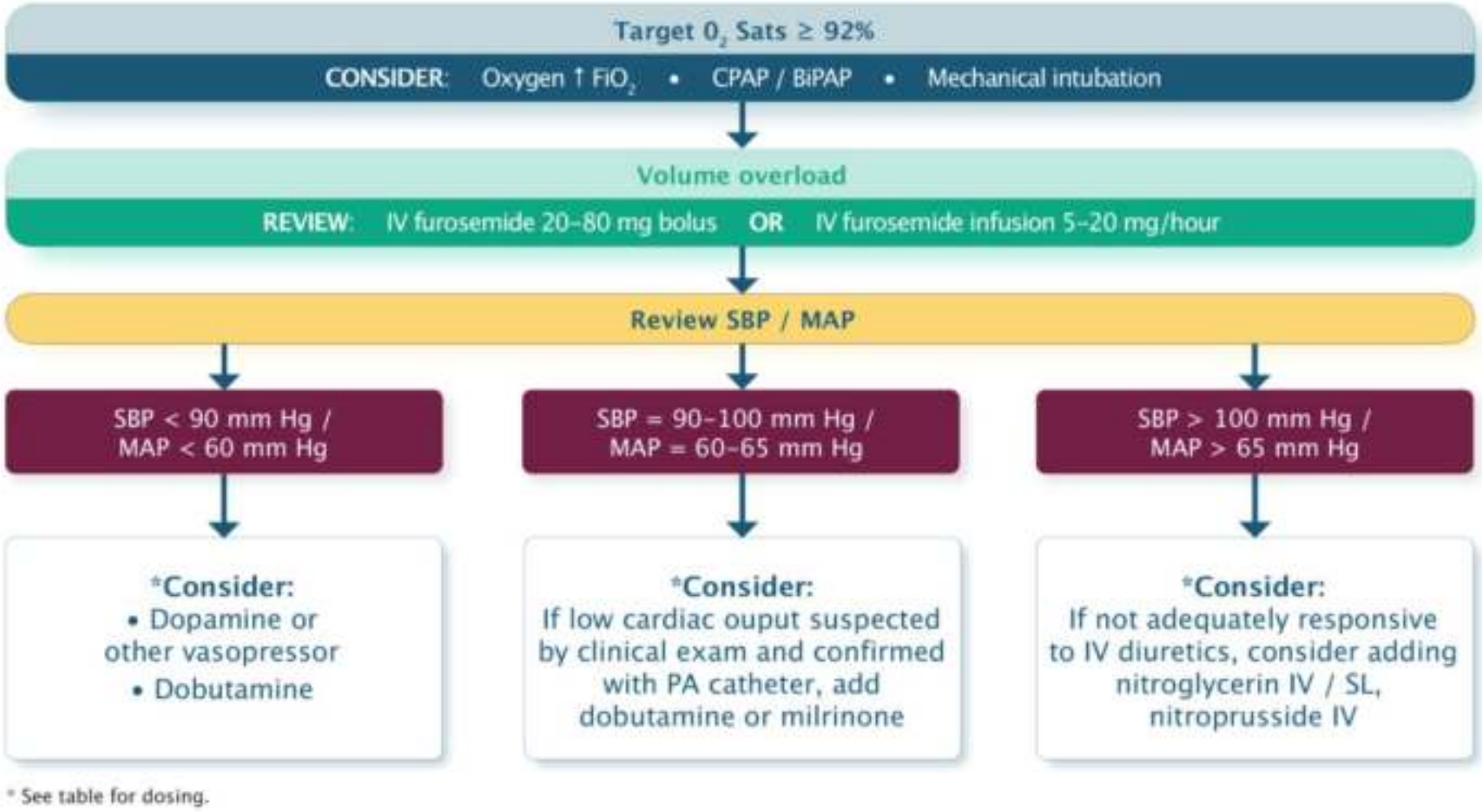
1. Provide an overview of medical therapies that can be used to decongest patients with acute heart failure
2. Define diuretic resistance
3. Describe strategies that can be used to decongest patients who have diuretic resistance

CASE

- 69-year-old female
- Prior history of acute MI, T2DM
- Presenting with two weeks history of shortness of breath and leg swelling

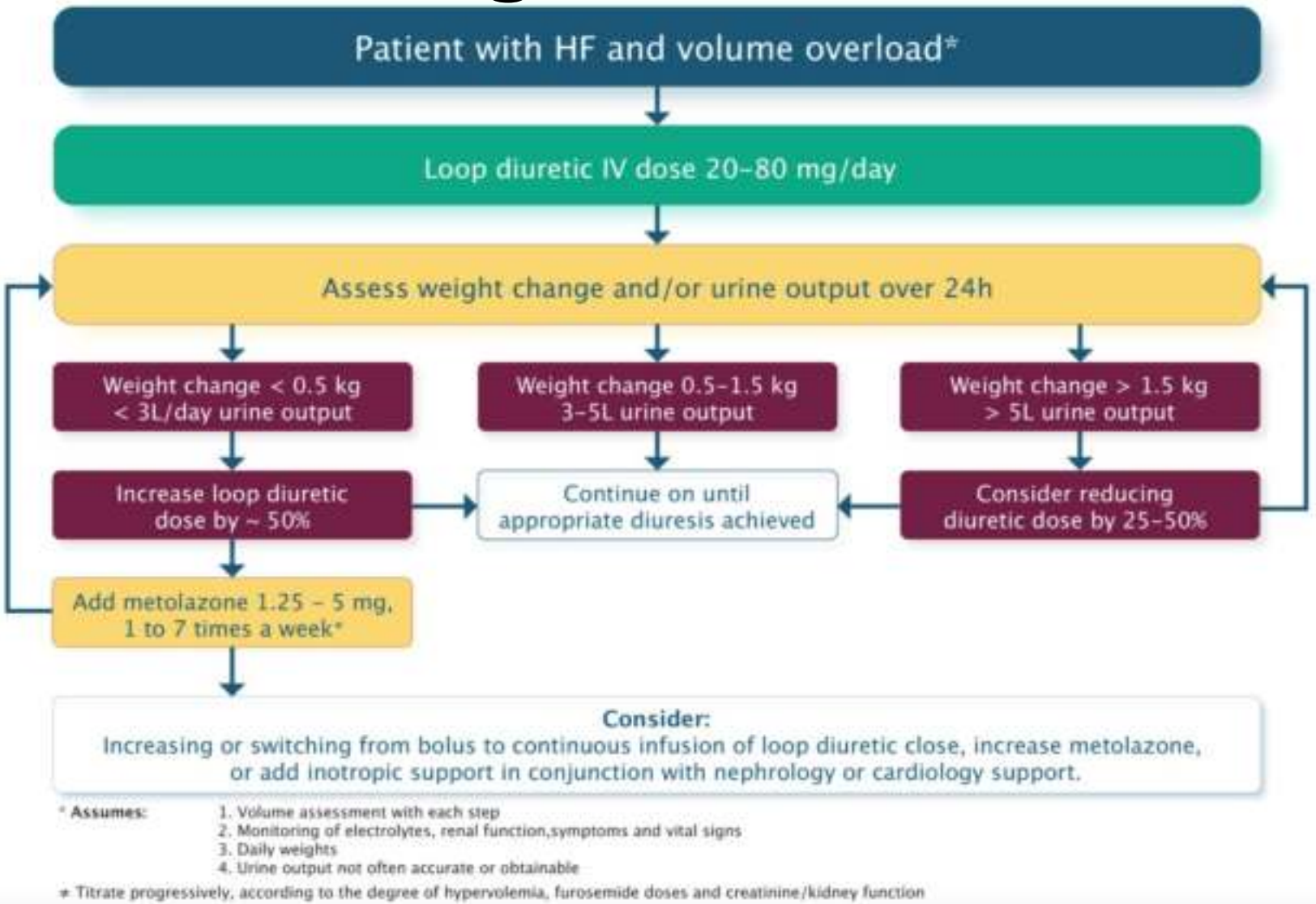
  - BP 100/70, HR 80, 95% RA
  - JVP elevated, bilateral edema and crackles
  - Current creatinine 210 µmol/L (BL 150)

Initial Treatments



* See table for dosing.

Treatment Targets



Response

- The patient does not make much urine and has minimal improvements in symptoms
- Creatinine also goes up slightly to 240 µmol/L
- Is there anything else we can do?

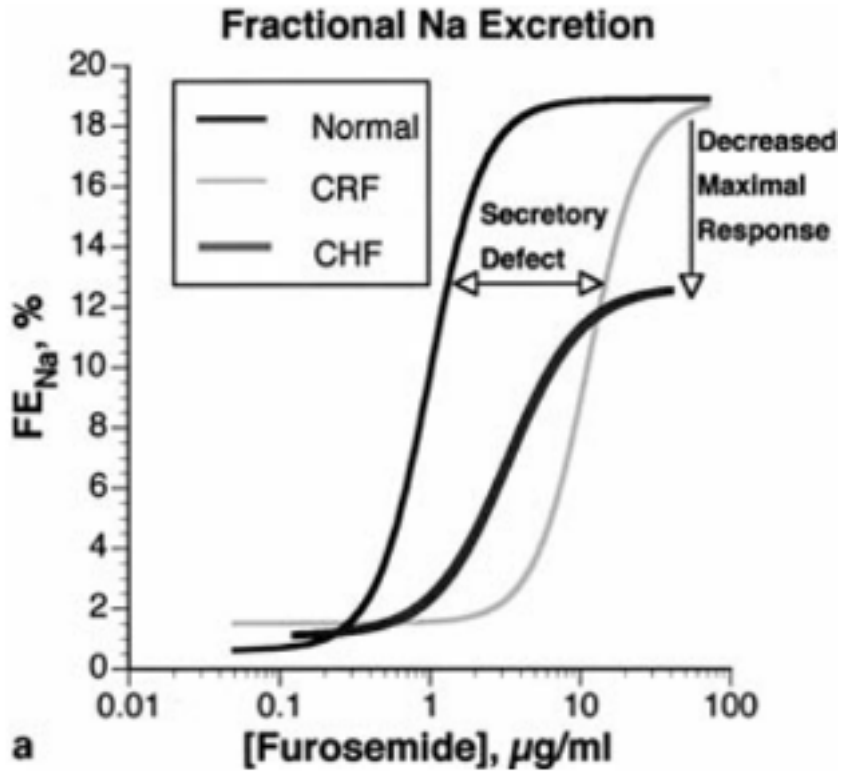
What is Diuretic Resistance

CARDIOLOGY

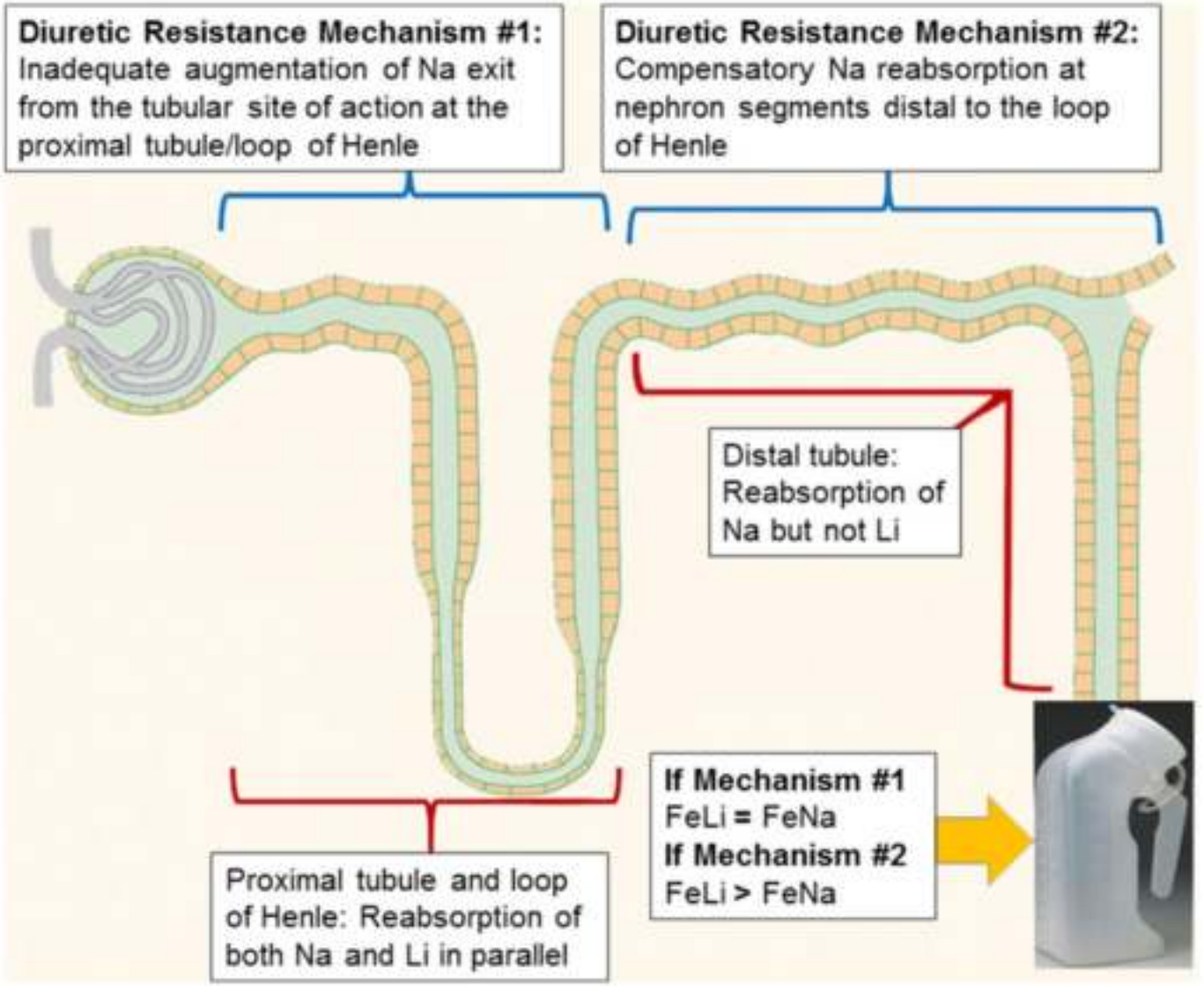
Cardiology 2001;96:132–143

Diuretic Therapy and Resistance in Congestive Heart Failure

An edematous patient may be deemed resistant to diuretic drugs when moderate doses of a loop diuretic do not achieve the desired ECF volume reduction.



Mechanisms of Diuretic Resistance



Diuretic Resistance and Outcomes

Author (year)	Metric	Findings in patients with low diuretic efficacy
Testani et al. (2014)[11]	Net fluid loss	Higher all-cause mortality after 5 years (Penn Cohort)/180 days (Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness Cohort)
Valente et al. (2014)[5]	Weight loss	Higher heart failure readmissions after 60 daysHigher death, heart failure or renal-related readmissions after 60 daysHigher all-cause mortality after 180 days
Voors et al. (2014)[22]	Weight loss	Higher death, heart failure or renal-related readmissions after 60 daysNeutral effect on all-cause mortality after 180 days
Singh et al. (2014)[12]	Urinary sodiumFurosemide concentration	Higher death, transplantation or heart failure readmission after 5 months
ter Maaten et al. (2015)[18]	Weight lossUrine output	Higher death or heart failure readmission after 30 days
Verbrugge et al. (2015)[10]	Natriuresis	Higher death or heart failure readmission after 188 days
Kumar et al. (2015)[19]	Fractional sodium excretion	Higher all-cause mortality after 30 days
Ter Maaten et al. (2016)[20]	Chloride levels	Higher mortality through 180 days
Aronson et al. (2016)[56]	Net fluid lossUrine output	Higher all-cause mortality after 6 months

Adapted from Verbrugge FH, Mullens W & Tang WH (2016).[13]

The Furosemide Stress Test: 1.0-1.5 mg/kg IV

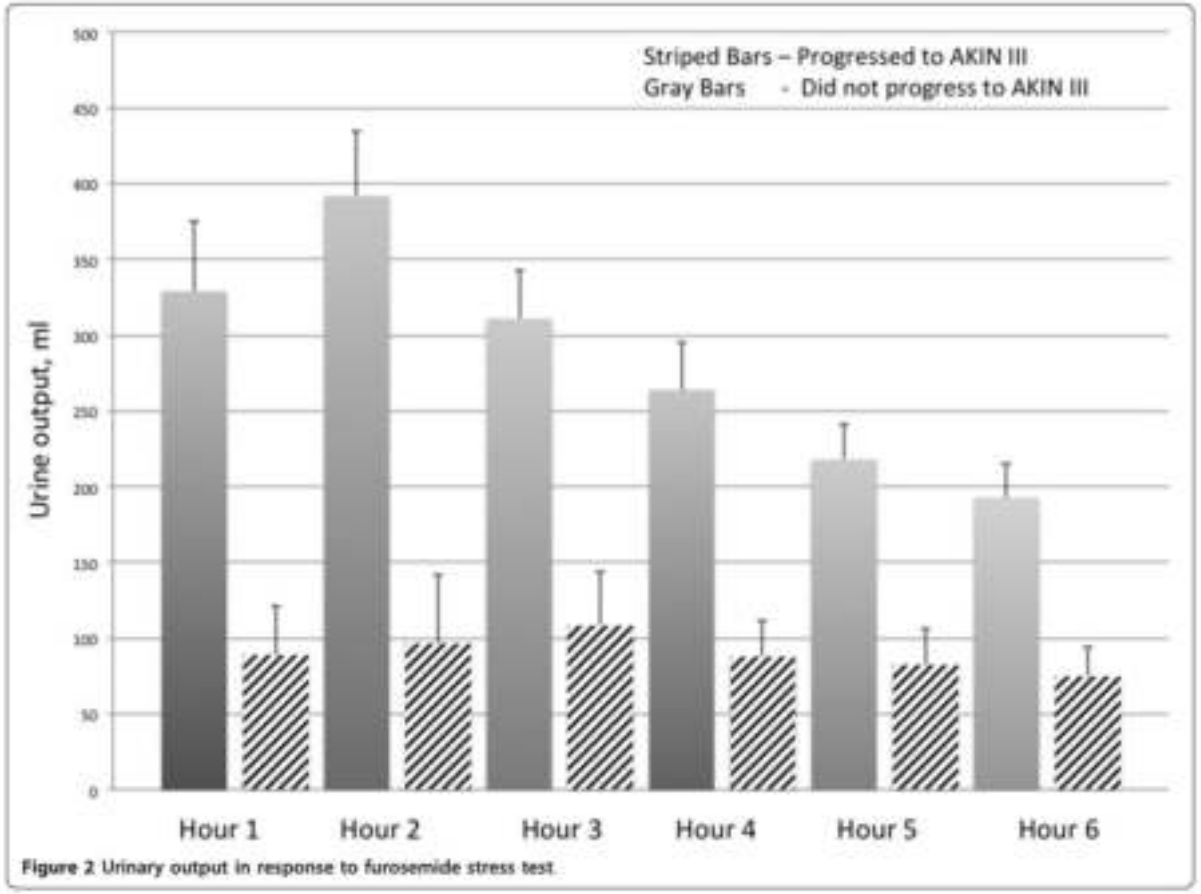


Figure 2 Urinary output in response to furosemide stress test.

- Intravenous dose of 1.5 mg/kg of furosemide
- Urine output < 200 ml (100 ml/h) in the first two hours after furosemide administration

Table 4 Sensitivity and specificity of two hour urine thresholds for progression to AKIN stage III

A

	Combined cohort	
Total urine output over 2 hours	Sensitivity	Specificity
≤100 ml	90.2%	60.0%
<200 ml	87.1%	84.1%
<300 ml	85.3%	88.0%
<400 ml	66.7%	88.0%
<500 ml	50.5%	88.0%

B Sensitivity and specificity of two hour urine thresholds for progression to AKIN III or death

	Combined cohort	
Total urine output over two hours	Sensitivity	Specificity
<100 ml	93.3%	53.2%
<200 ml	90%	74.2%
<300 ml	87.8%	77.4%
<400 ml	66.7%	77.4%
<500 ml	53.3%	77.4%

JASN 2015; 26: 2023; Critical Care 2013; 17: R207

Proximal or Distal Sequential Blockade?

- Currently the mainstay to augment diuretic response is thiazide (metolazone)

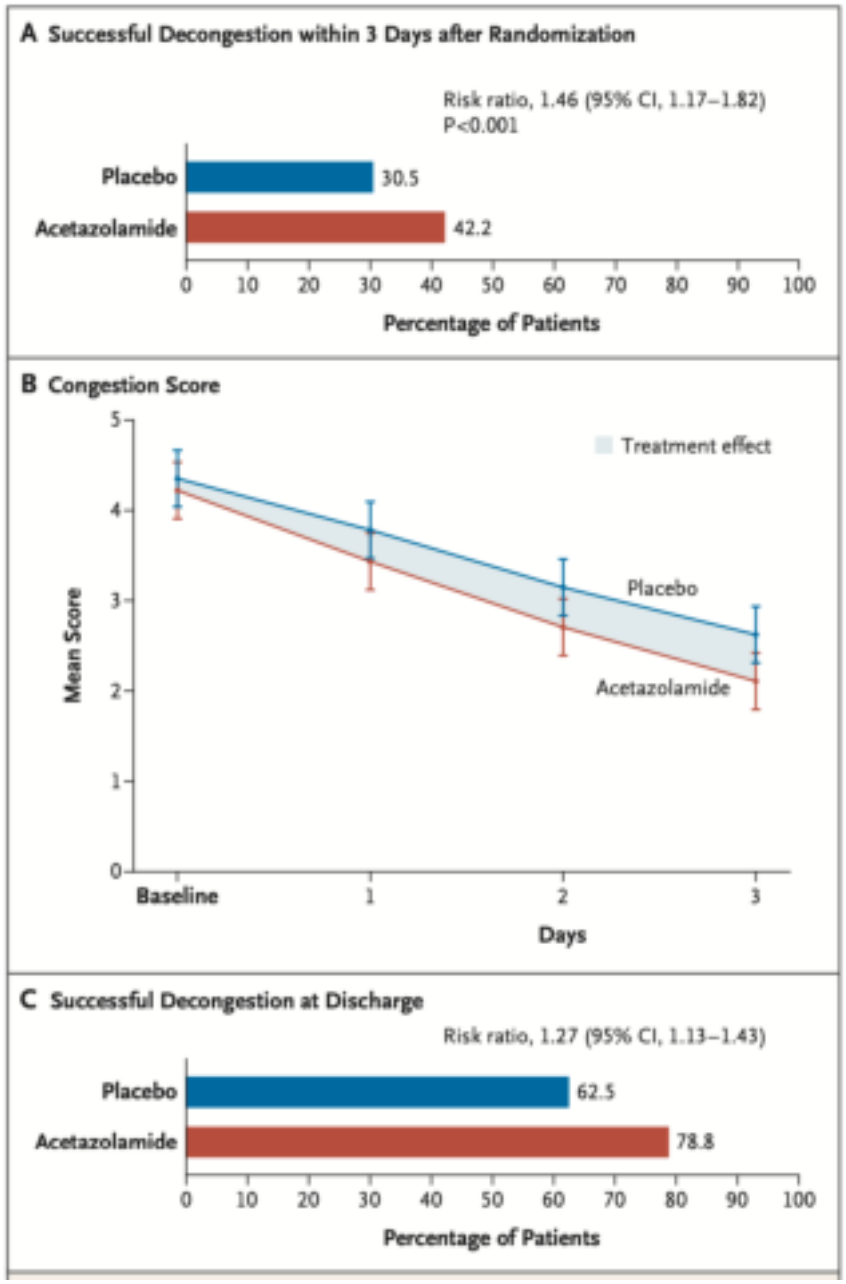
- What are the other options:
  - Acetazolamide?
  - SGLT-2 inhibitors?

Acetazolamide in Acute Decompensated Heart Failure with Volume Overload

Authors: Wilfried Mullens, M.D., Ph.D., Jeroen Dauw, M.D., Pieter Martens, M.D., Ph.D., Frederik H. Verbrugge, M.D., Ph.D., Petra Nijst, M.D., Ph.D., Evelyne Meekers, M.D., Katrien Tartaglia, M.Sc., +16, for the ADVOR Study Group* Author Info & Affiliations

Published August 26, 2022 | N Engl J Med 2022;387:1185-1195 | DOI: 10.1056/NEJMoa2203094

VOL. 387 NO. 13



- Death or hospitalization for AHF: 29% vs. 28%
- Length of stay: 8.8 vs. 9.9 days
- Safety endpoint (creat. x 2 or ΔGFR -50% or dialysis during hospitalization): 0.8 % vs. 2.7 % (p = 0.10)

Subgroup	Placebo	Acetazolamide	Risk Ratio (95% CI)
	no. of patients/total no.		
Overall	79/259	108/256	1.46 (1.17–1.82)
Age			
≤79 yr	43/130	59/132	1.36 (1.02–1.82)
>79 yr	36/129	49/124	1.56 (1.11–2.21)
Left ventricular ejection fraction			
≤40%	36/111	43/111	1.24 (0.88–1.75)
>40%	43/148	65/145	1.63 (1.22–2.19)
NT-proBNP			
≤6173 pg/ml	51/122	68/132	1.35 (1.06–1.74)
>6173 pg/ml	27/135	38/120	1.61 (1.06–2.44)
Sex			
Female	37/104	36/88	1.21 (0.86–1.71)
Male	42/155	72/168	1.67 (1.24–2.25)
Estimated GFR			
<39 ml/min/1.73 m^2	33/135	53/125	1.77 (1.25–2.50)
≥39 ml/min/1.73 m^2	46/124	55/131	1.23 (0.92–1.65)
Cause of heart failure			
Ischemic	37/113	48/118	1.35 (0.97–1.87)
Nonischemic	42/146	60/138	1.57 (1.16–2.12)
Home maintenance loop diuretic dose			
≤60 mg furosemide equivalent	42/136	67/127	1.78 (1.33–2.36)
>60 mg furosemide equivalent	37/123	41/129	1.08 (0.76–1.55)
Baseline congestion score			
≤4	60/145	82/155	1.38 (1.10–1.74)
>4	19/114	26/101	1.62 (0.96–2.73)
Atrial fibrillation			
No	20/71	31/71	1.76 (1.14–2.72)
Yes	59/188	77/185	1.35 (1.04–1.75)

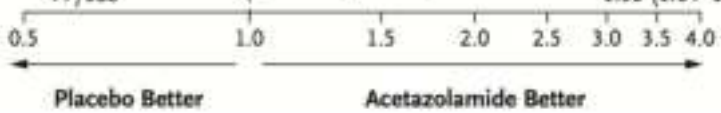
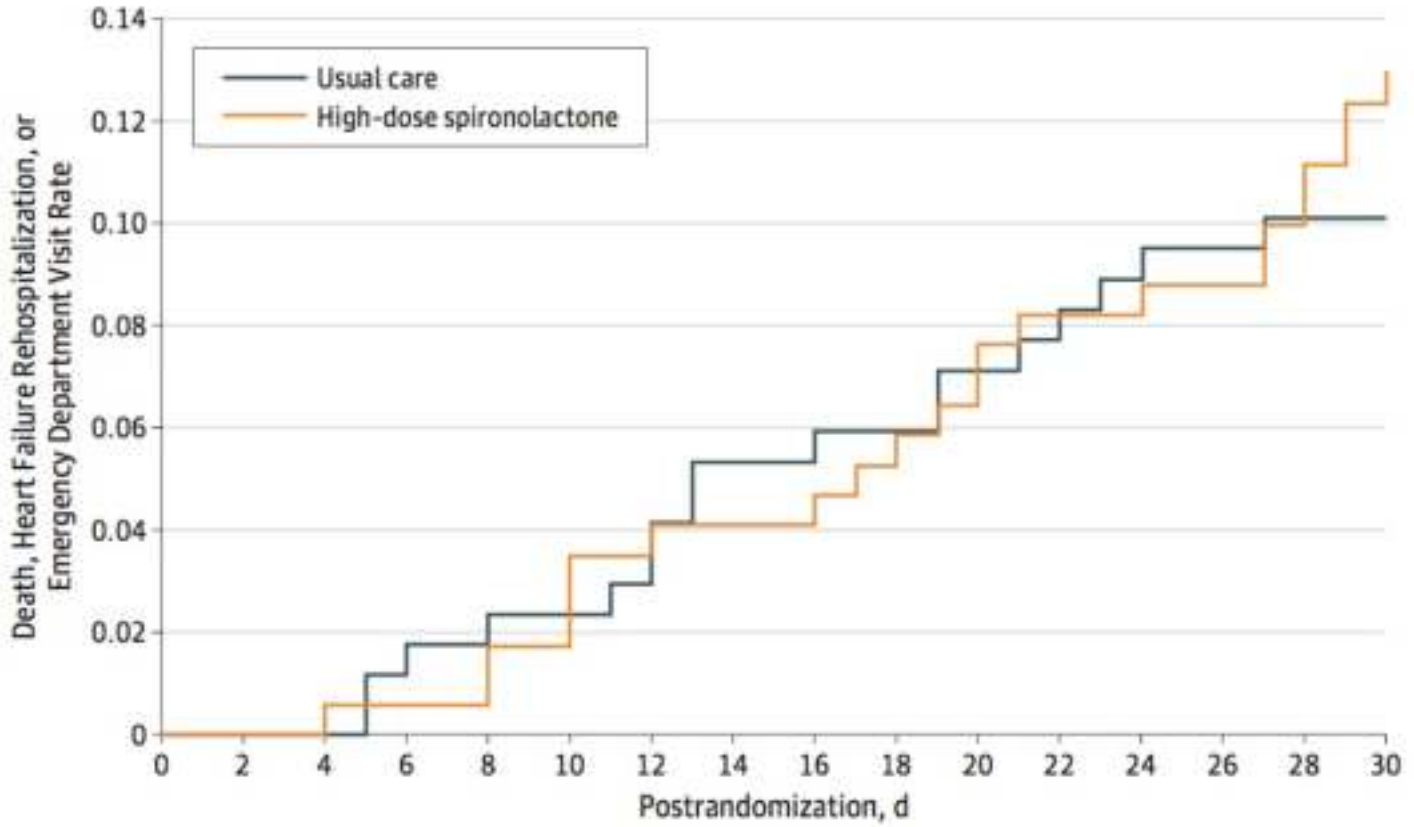


Figure 2. Subgroup Analysis.

Subgroups that were defined according to age, the N-terminal pro–B-type natriuretic peptide (NT-proBNP) level, the estimated glomerular filtration rate (GFR), the home maintenance dose of loop diuretic, and the baseline congestion score were based on observed median values at randomization.

MRAs in Acute HF (ATHENA-HF)

Figure 2. Time to First Heart Failure Rehospitalization, Emergency Department Visit, or Death



No. at risk

Usual care	178	176	171	166	165	164	163	159	159	158	156	155	153	152	147	137
High-dose spironolactone	182	175	173	171	171	167	164	163	163	161	159	156	156	155	153	141

JAMA Cardiol. 2017; 2(9): 950-958

CLOROTIC Trial

Key Question

Does the addition of hydrochlorothiazide to standard intravenous loop-diuretic therapy improve the diuretic response in patients with acute heart failure (AHF)?

Key Finding

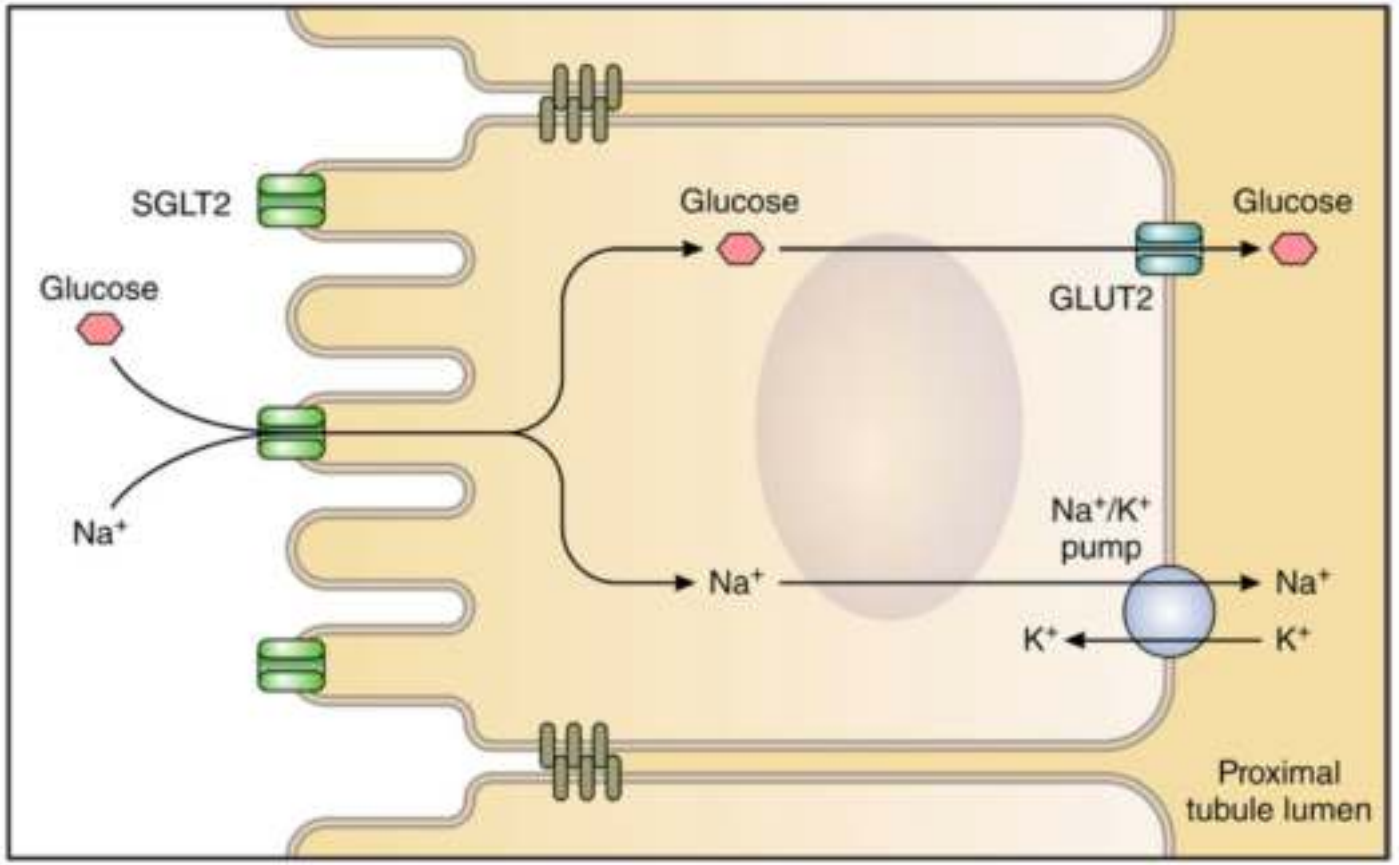
In patients with AHF, the combination of oral hydrochlorothiazide with intravenous loop diuretics improved the diuretic response but was associated with worsening renal function.

Take Home Message

The addition of hydrochlorothiazide to intravenous loop diuretics improves the diuretic response in patients with decompensated heart failure at the cost of worsening renal function.

Mechanism of Action in the Proximal Tubule

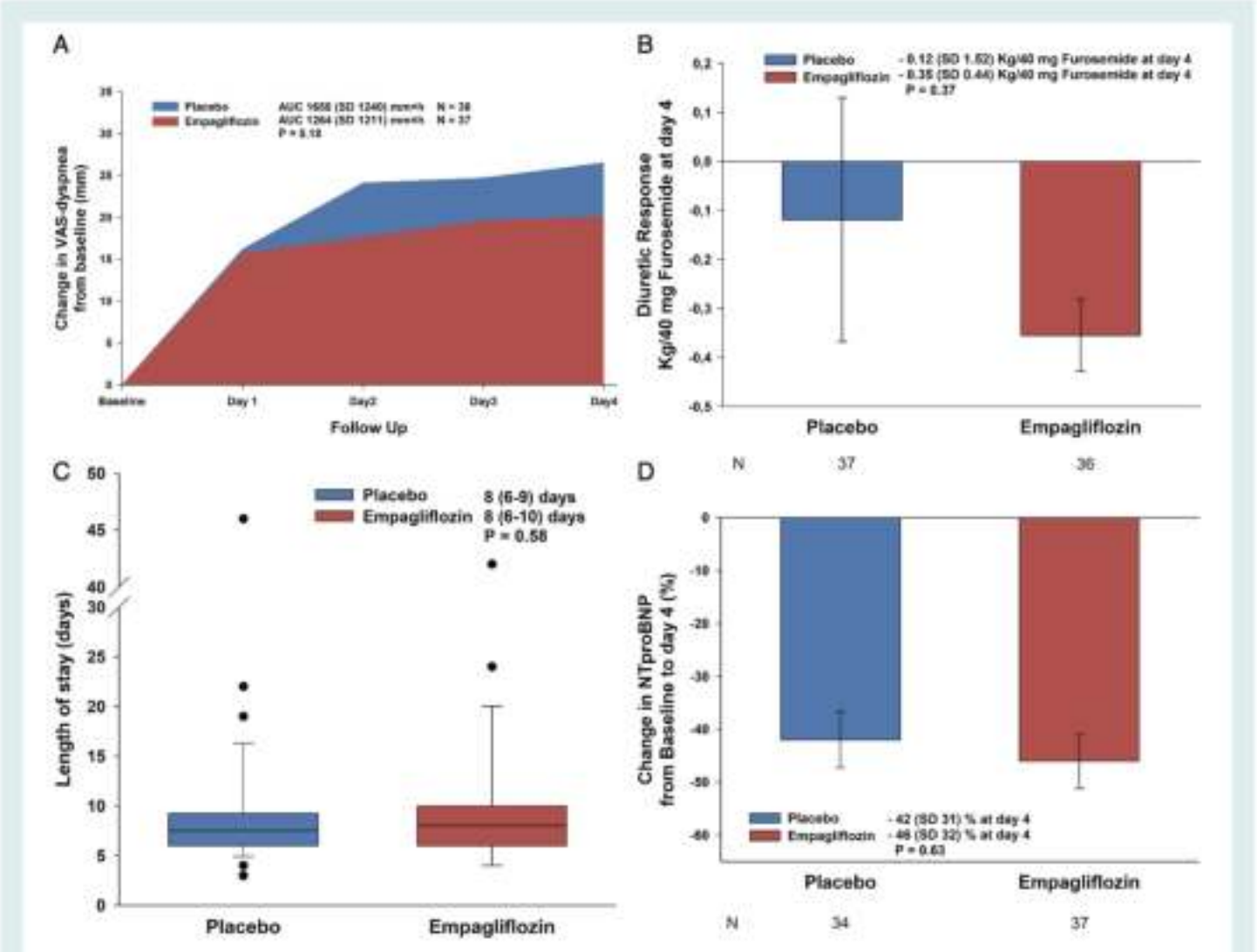
- SGLT-2 inhibitors block sodium and glucose reabsorption at the proximal tubular level



Circulation 2016; 134: 752

SGLT-2s in Acute Heart Failure

- EMPA-RESPONSE-AHF
- Acutely decompensated heart failure (N=80). Randomized to receive 10 mg of empagliflozin vs. placebo



European Journal of Heart Failure (2020) 22, 713–722

SGLT-2s in Acute Heart Failure

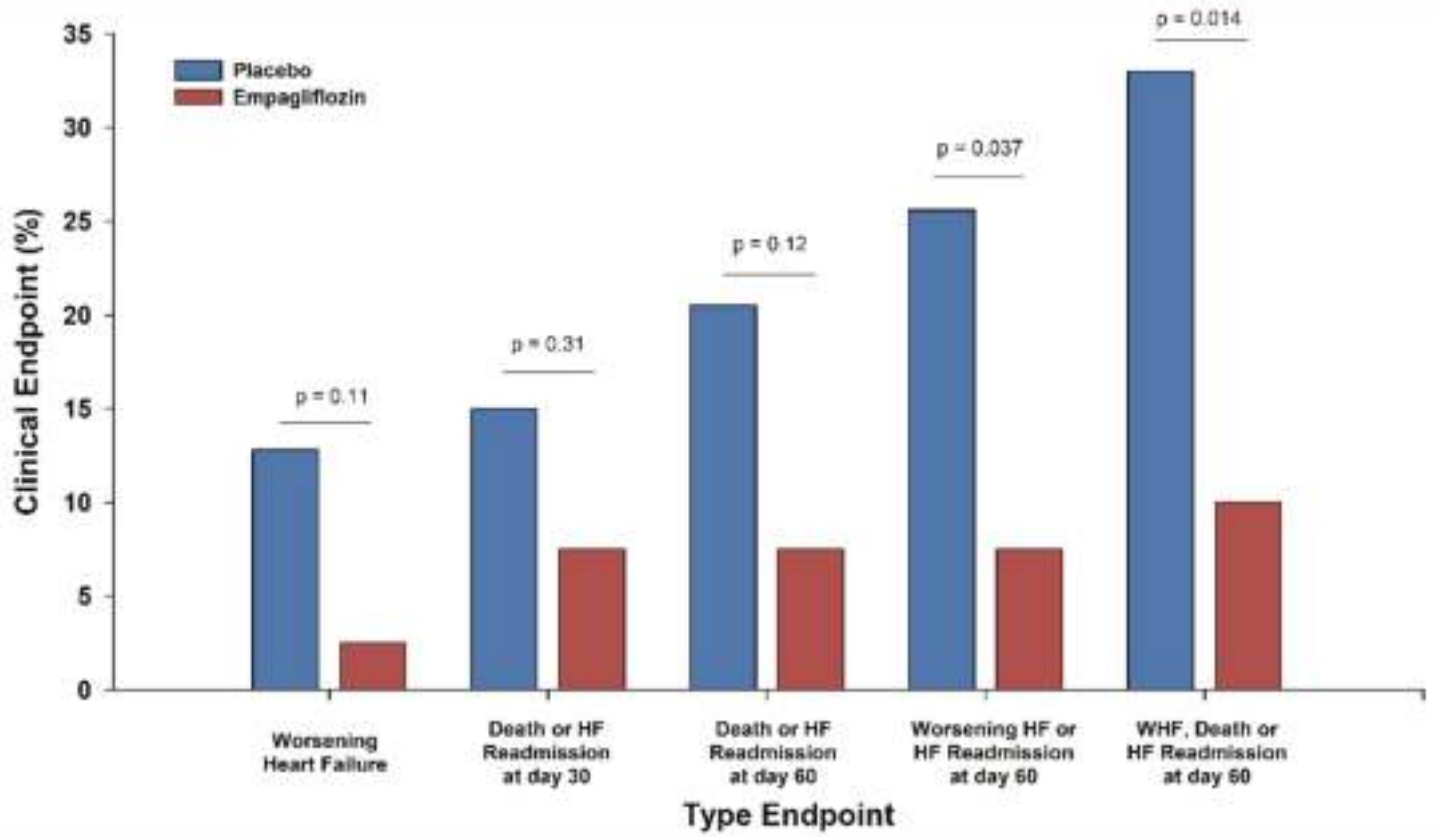


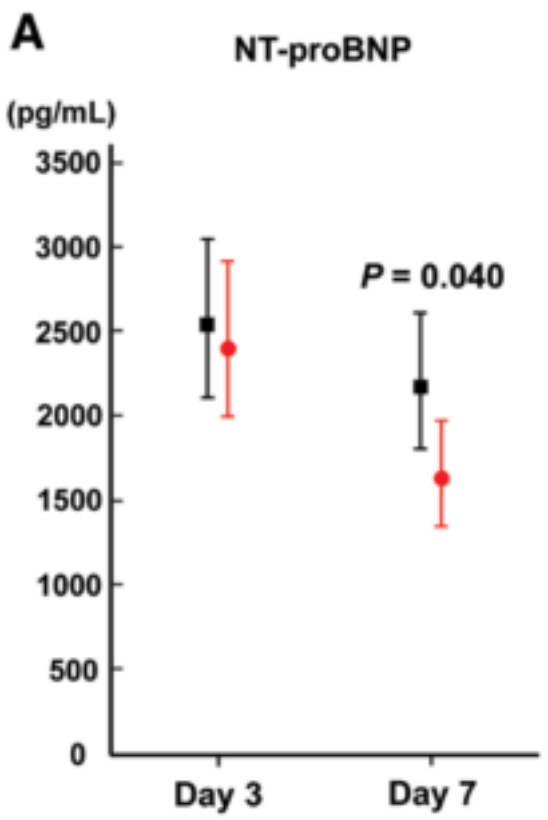
Figure 4 Clinical events. HF, heart failure; WHF, worsening heart failure.

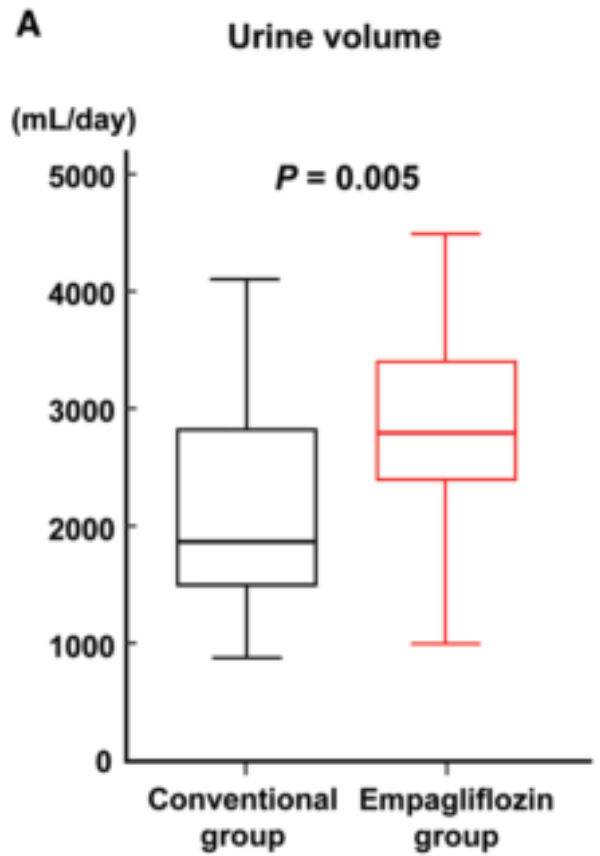
Effect of Empagliflozin on Decongestion RCT

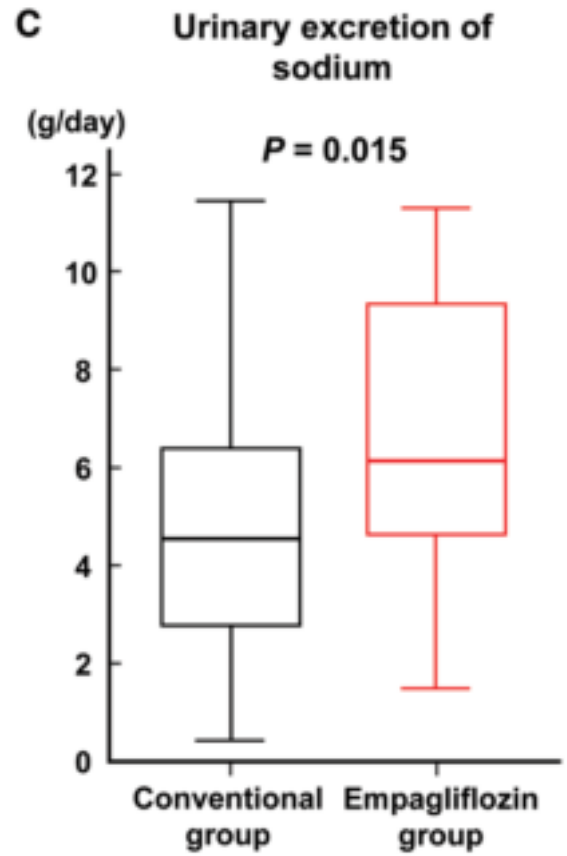
- P: Patients with type 2 DM, acutely decompensated heart failure, and eGFR > 15
- I/C: empagliflozin 10 mg or conventional glucose-lowering therapy (N=59)
- Outcomes: BNP levels on day 7; urine output during the first 24 hours

Circ Heart Fail 2021;14(3):e007048.

Effect of Empagliflozin on Decongestion

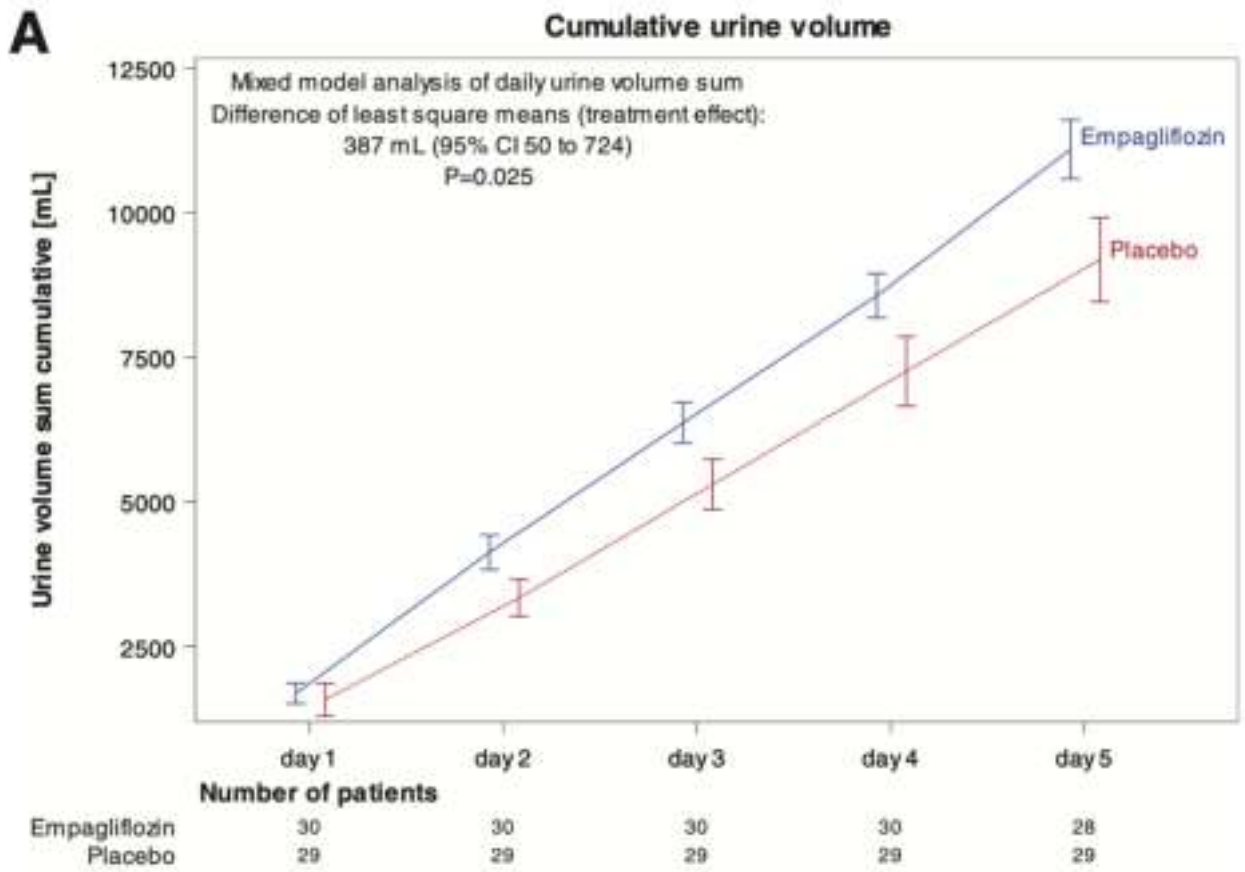






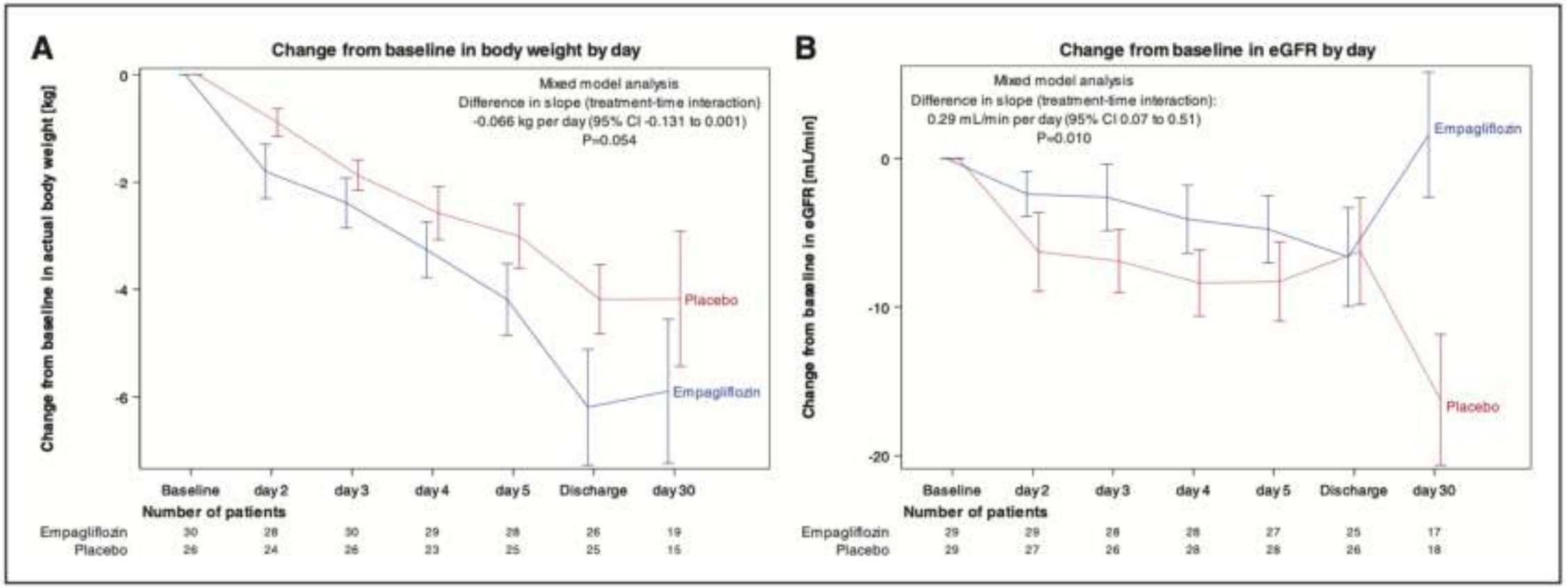
EMPAG-HF

- P: Patients with acutely decompensated heart failure and eGFR≥30; excluded if acute cardiorenal syndrome
- I/C: empagliflozin 25 mg or placebo (N=60)
- Outcome: urine output over 5 days



Circulation 2022; 146: 289–98

EMPAG-HF



Circulation 2022; 146: 289–98

Ultrafiltration or Diuretics

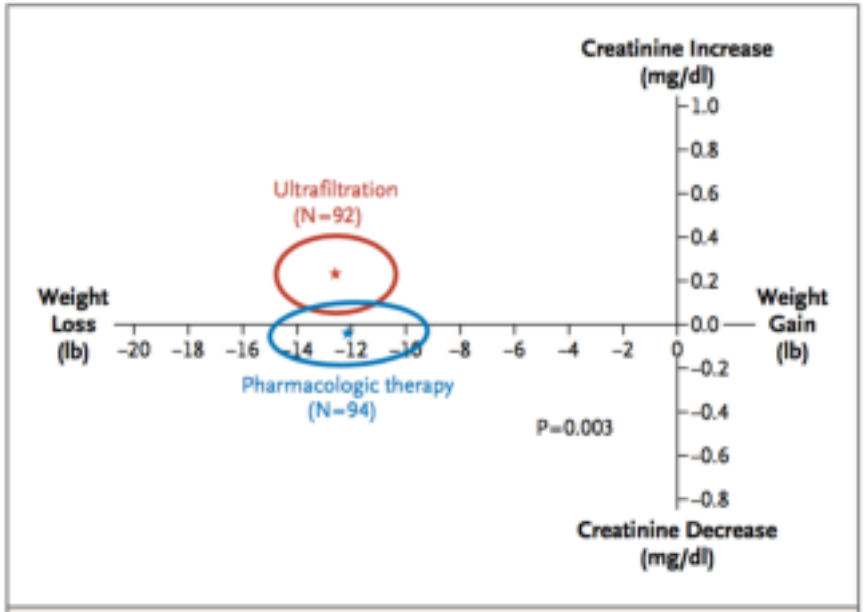


Figure 1. Changes in Serum Creatinine and Weight at 96 Hours (Bivariate Response).

The ellipses represent the 95% confidence regions and the stars the exact values for the mean changes in the serum creatinine level and weight at 96 hours in the ultrafiltration group and the pharmacologic-therapy group. Data from two patients who had been randomly assigned to the ultrafiltration group were excluded from the analysis: baseline creatinine measurements were missing for one patient, and all post-baseline creatinine measurements were missing for the other patient. To convert the values for creatinine to micromoles per liter, multiply by 88.4. To convert the values for weight to kilograms, multiply by 0.45.

AT RANDOMIZATION – STEPPED PHARMACOLOGIC CARE ARM

UO > 5 L/day → Reduce current diuretic regimen *if desired*
UO 3-5 L/day → Continue current diuretic regimen
UO < 3 L/day → See table

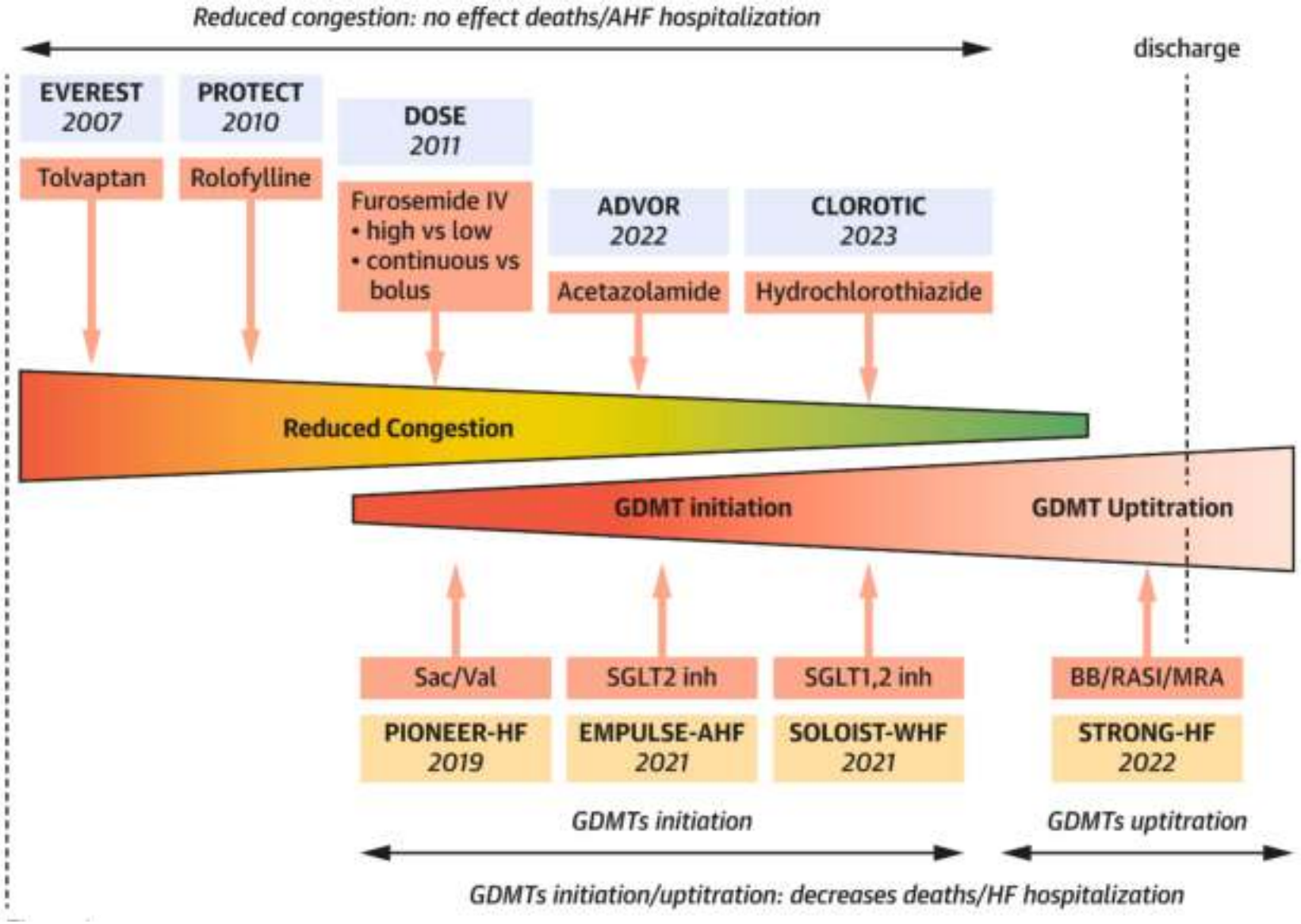
	Current Dose		Suggested Dose	
	loop (/day)	thiazide	loop (/day)	thiazide
A	≤ 80	+ or -	40 mg iv bolus+ 5 mg/hr	0
B	81-160	+ or -	80 mg iv bolus+ 10 mg/hr	5 mg metazolone QD
C	161-240	+ or -	80 mg iv bolus+ 20 mg/hr	5 mg metazolone BID
D	> 240	+ or -	80 mg iv bolus+ 30 mg/hr	5 mg metazolone BID

NEJM 2012; 367: 2296-304

Conclusion

- Decongestion through intravenous furosemide remains a cornerstone of management of patients with acute worsening of heart failure
- Diuretic resistance is associated with worse outcomes, yet diagnosis can be challenging
- Multiple options are now present to augment diuresis: acetazolamide, thiazide, and SGLT2i

Conclusion


Reduced congestion: no effect deaths/AHF hospitalization
discharge
EVEREST 2007
PROTECT 2010
DOSE 2011
Tolvaptan
Rolofylline
Furosemide IV
• high vs low
• continuous vs bolus
ADVOR 2022
CLOROTIC 2023
Acetazolamide
Hydrochlorothiazide
Reduced Congestion
GDMT initiation
GDMT Uptitration
Sac/Val
SGLT2 inh
SGLT1,2 inh
BB/RASI/MRA
PIONEER-HF 2019
EMPULSE-AHF 2021
SOLOIST-WHF 2021
STRONG-HF 2022
GDMTs initiation
GDMTs uptitration
GDMTs initiation/uptitration: decreases deaths/HF hospitalization

A Treasure Chest of Late Breaking Clinical Trials: A Clinical Trialist's Perspective

Scott D. Solomon, MD
The Edward D. Frohlich Distinguished Chair
Professor of Medicine, Harvard Medical School
Brigham and Women's Hospital
Editor, Braunwald's Heart Disease

Disclosures

	Dr. Scott Solomon
Any direct financial payments including receipt of honoraria	Abbott, Action, Akros, Alexion, Alnylam, Amgen, Arena, AstraZeneca, Bayer, BMS, Cardior, Cardurion, Corvia, Cytokinetics, GSK, Lilly, Novartis, Roche, Theracos, Quantum Genomics, Tenaya, Sanofi-Pasteur, Dinaqor, Tremeau, CellProThera, Moderna, American Regent, Sarepta, Lexicon, Anacardio, Akros, Valo
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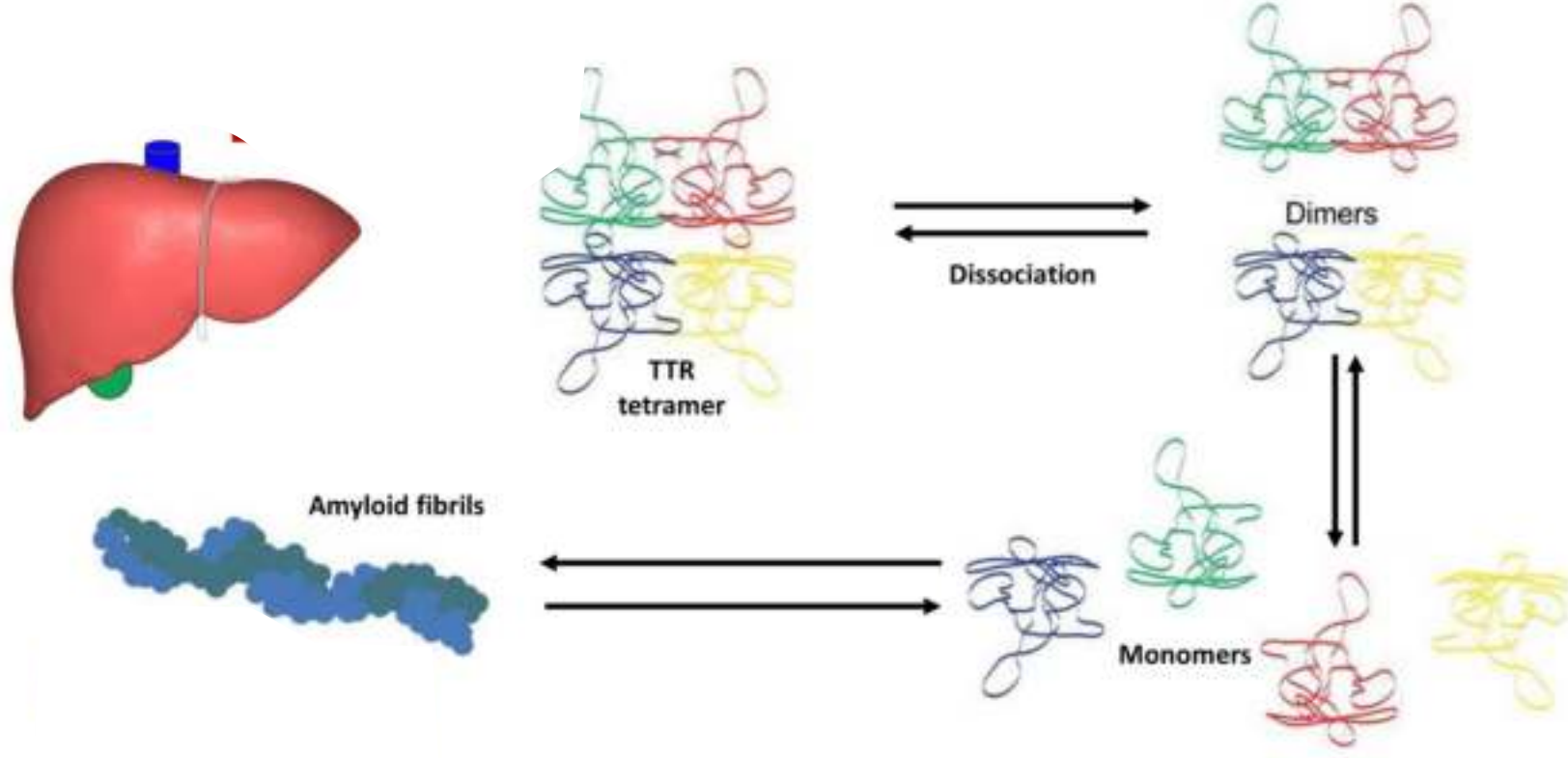
Funded grants or clinical trials	Alexion, Alnylam, Applied Therapeutics, AstraZeneca, Bellerophon, Bayer, BMS, Boston Scientific, Cytokinetics, Edgewise, Eidos/BridgeBio, Gossamer, GSK, Ionis, Lilly,NIH/NHLBI, Novartis, NovoNordisk, Respicardia, Sanofi, Pasteur, Tenaya, Theracos, US2.AI
All other investments or relationships that could be seen by a reasonable, well-informed participant as having the potential to influence the content of the educational activity	No disclosures

Learning Objectives

1. Provide an update on HF clinical trials supporting new therapies and new indications for known therapies
2. Discuss HF clinical trial endpoints and their impact on clinical care decisions

Amyloid Heart Disease

Current and Future Specific Therapy for ATTR



Yadav JD et al. Ann Pharmotherapy 2021

TTR = transthyretin

Efficacy and Safety of Acoramidis in Transthyretin Amyloid Cardiomyopathy

Results of the ATTRibute-CM Trial

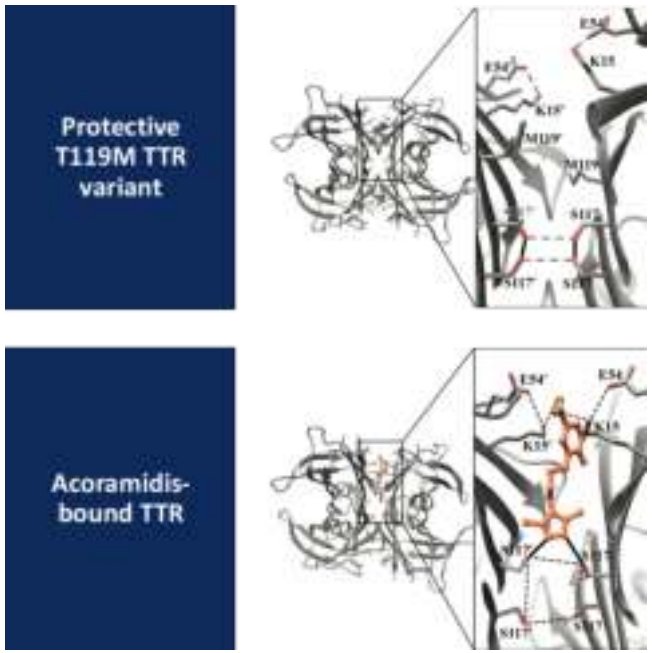
Julian D. Gillmore,[1] Daniel P. Judge,[2] Francesco Cappelli,[3] Marianna Fontana,[1] Pablo Garcia-Pavia,[4,5,6] Simon Gibbs,[7] Martha Grogan,[8] Mazen Hanna,[9] James Hoffman,[10] Ahmad Masri,[11] Mathew S. Maurer,[12] Jose Nativi-Nicolau,[13] Laura Obici,[14] Frank Rockhold,[15, 16] Keyur B. Shah,[17] Prem Soman,[18] Jyotsna Garg,[15] Karen Chiswell,[15] Haolin Xu,[15] Xiaofan Cao,[19] Ted Lystig,[19] Uma Sinha,[19] and Jonathan C. Fox[19]

[1]National Amyloidosis Centre, Division of Medicine, University College London, Royal Free Hospital, London, UK; [2] The Medical University of South Carolina, Charleston, SC, USA, [3]Tuscan Regional Amyloidosis Centre, Careggi University Hospital, Florence, Italy;[4]Heart Failure and Inherited Cardiac Diseases Unit, Department of Cardiology, Hospital Universitario Puerta der Hierro Majadahonda, CIBERCV, Manuel de Falla 2, 28222 Madrid, Spain; [5]Universidad Francisco de Vitoria (UFV), Pozuelo de Alarcon, Spain; [6]European Reference Network for Rare, Low Prevalence and Complex Diseases of the Heart-ERN GUARD-Heart; [7]The Victorian and Tasmanian Amyloidosis Service, Department of Haematology, Monash University Eastern health Clinical School, Box Hill, Victoria, Australia; [8]Department of Cardiovascular Diseases, Mayo Clinic, Rochester, MN, USA; [9] Department of Cardiovascular Medicine, Cleveland Clinic, Cleveland, OH, USA; [10] Sylvester Comprehensive Cancer Center, University of Miami, Miami, FL, USA; [11]Cardiac Amyloidosis Program, Knight Cardiovascular Institute, Oregon Health and Science University, Portland, OR, USA; [12]Cardiac Amyloidosis Program, Division of Cardiology, Columbia College of Physicians and Surgeons, New York NY, USA; [13] Amyloidosis Program, Department of Transplant,, Mayo Clinic, Jacksonville, FL, USA; [14]Amyloidosis Research and Treatment Center, IRCCS Fondazione Policlinico San Matteo, Pavia, Italy; [15]Duke Clinical Research Institute, Durham, NC, USA; [16]Duke University Medical Center, Durham, NC, USA; [17]The Pauley Heart Center, Virginia Commonwealth University, Richmond, VA, USA; [18]Divison of Cardiology, University of Pittsburgh Medical Center, Pittsburgh, PA, USA; [19]BridgeBio Pharma, San Francisco, CA, USA

27 Aug 2023

Acoramidis binding uniquely mimics structure of protective TTR mutation T119M

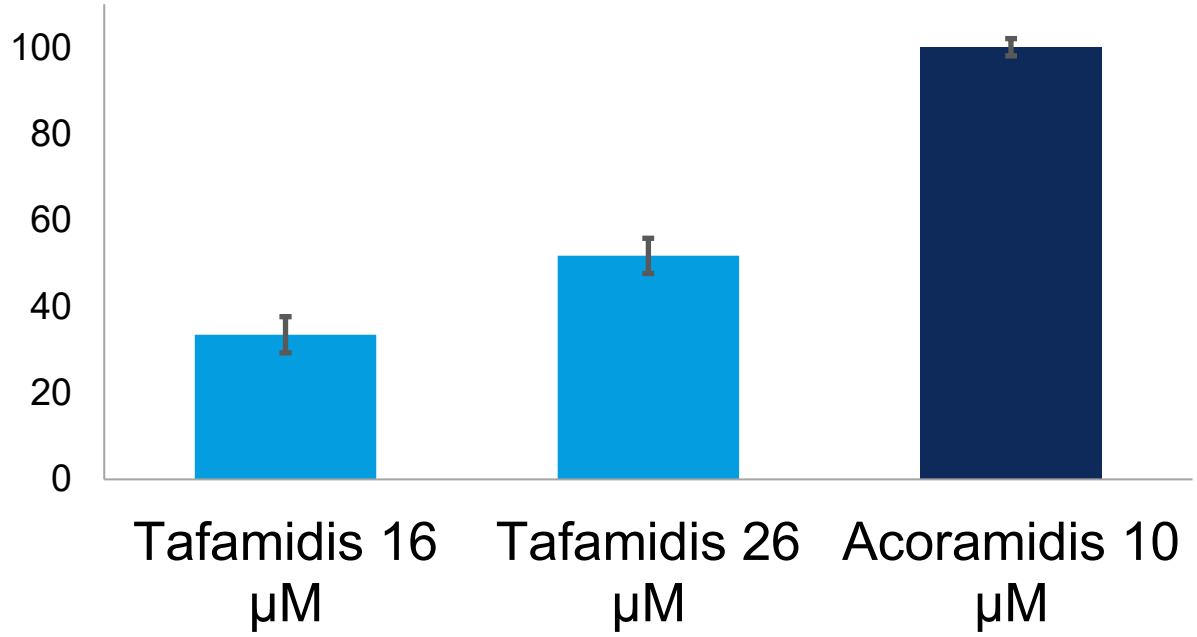
Mimics a naturally-occurring variant of the TTR gene (T119M) that is considered a “rescue mutation”



- Mimics a naturally-occurring variant of the TTR gene (T199M) that is considered a “rescue mutation” found in some healthy family members who also have deleterious ATTR mutations –thought to be “super-stabilizing”
- Induces H-bonds , shown to near-completely stabilize TTR in vitro

TTR target site occupancy by FPE assay[1]

%, mean +/- SD



Acoramidis demonstrated near-complete TTR stabilization in vitro at clinical concentrations

ATTRibute-CM: Study Design

30-month primary endpoint:
Hierarchical analysis consisting of all-cause mortality, cumulative frequency of CVH, change from baseline in NT-proBNP, and change from baseline in 6MWD

Key eligibility criteria

- Subjects with diagnosed ATTR-CM (WT or variant)
- NYHA Class I-III
- ATTR-positive biopsy or 99mTc scan
- Light chain amyloidosis excluded if diagnosis by 99mTc

Screening and randomization

800 mg acoramidis HCl twice daily
N = 421

placebo twice daily
N = 211

Efficacy assessment included 611 participants in the pre-specified mITT population (eGFR ≥30 mL/min/1.73 m^2)

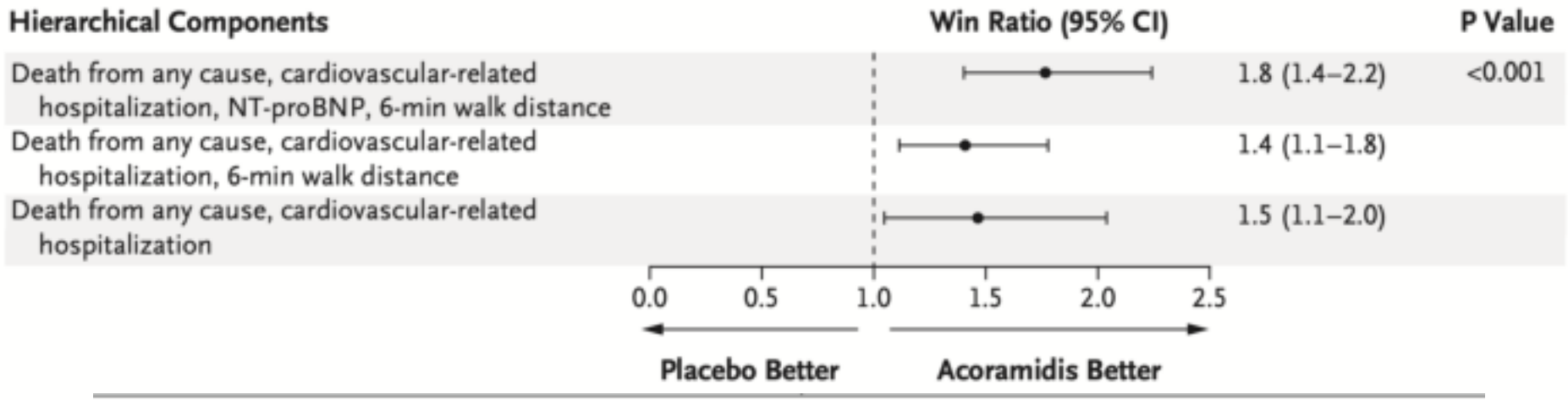
Tafamidis usage allowed after Month 12

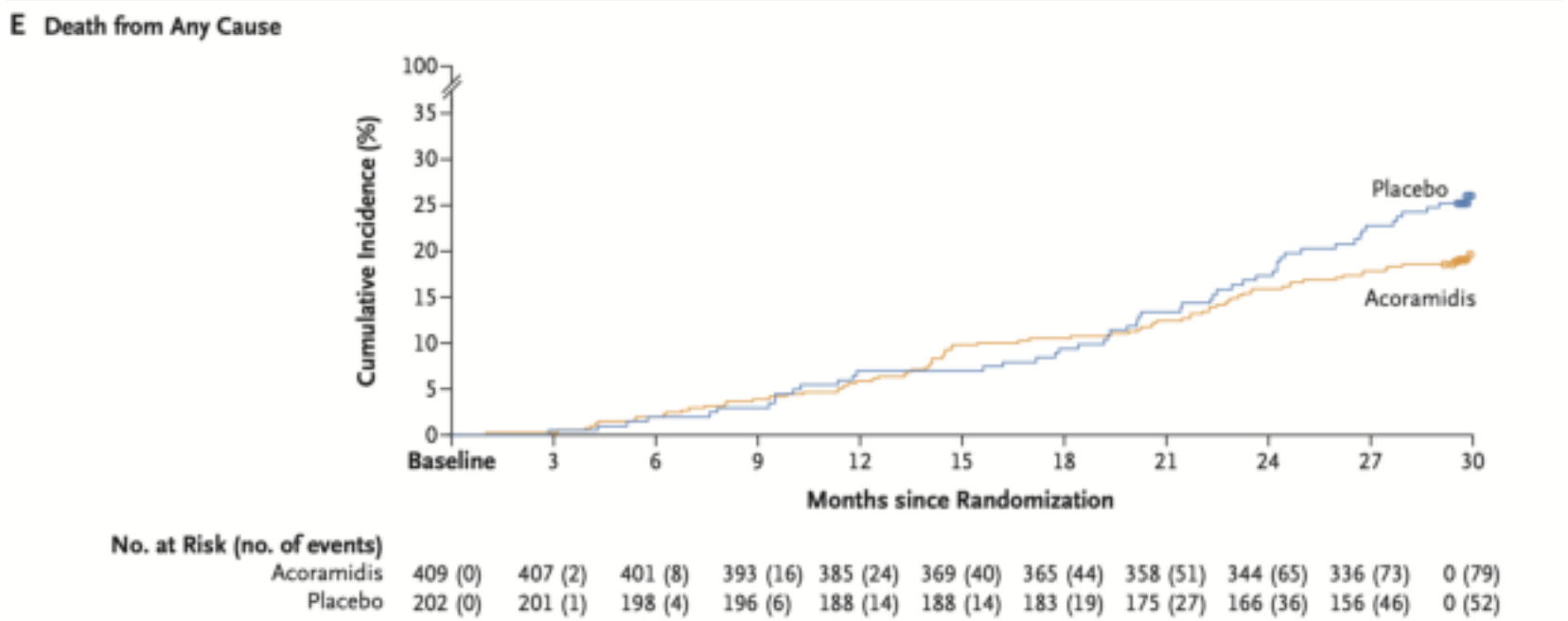
800 mg acoramidis HCl twice daily

Open-label extension

6MWD = Six-minute walk distance; NYHA = New York heart association; 99mTc = Technetium labeled pyrophosphate (PYP) or bisphosphonate (e.g., DPD); mITT = Modified intent-to-treat.
eGFR = Estimated glomerular filtration rate. ClinicalTrials.gov identifier: NCT03860935.

Acoramidis in ATTR-CM





CRISPR-Cas9 Gene Editing for TTR Knockdown (NTLA-2001)

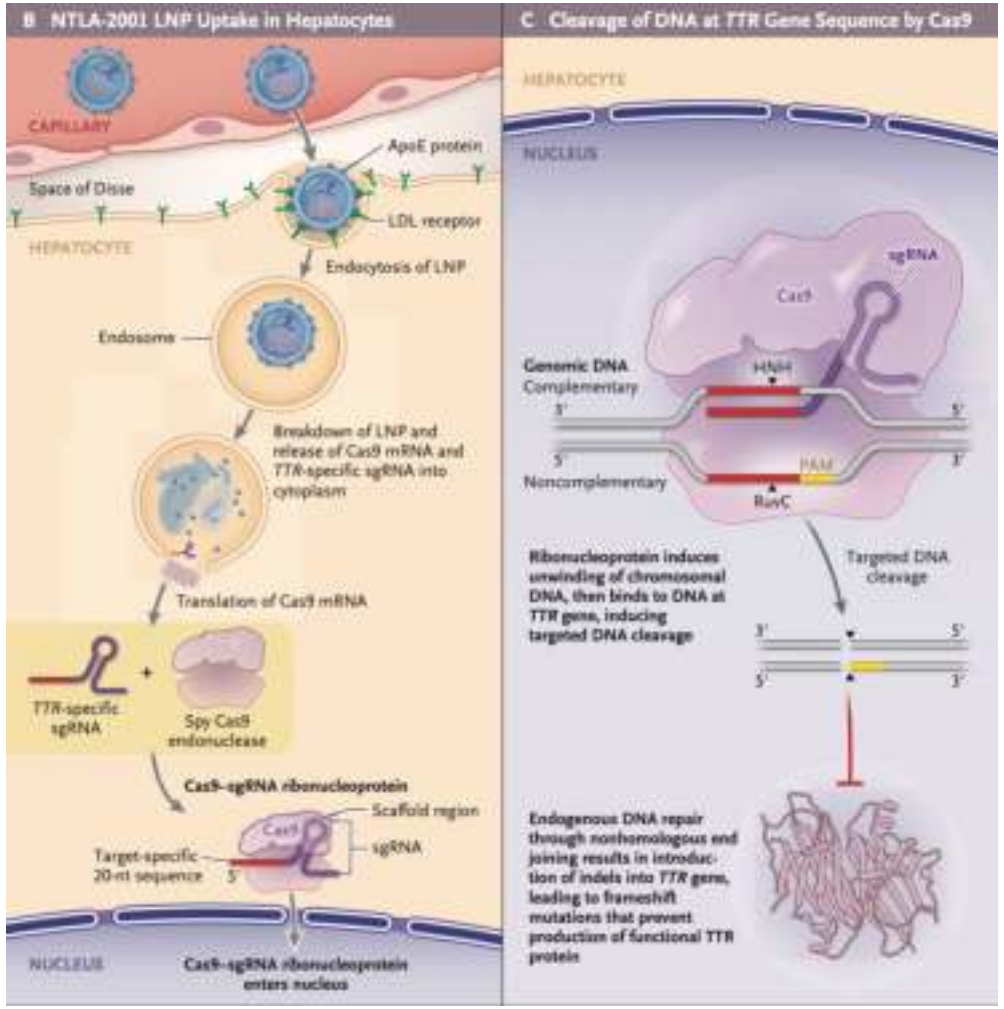
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 5, 2021 VOL. 385 NO. 6

CRISPR-Cas9 In Vivo Gene Editing for Transthyretin Amyloidosis

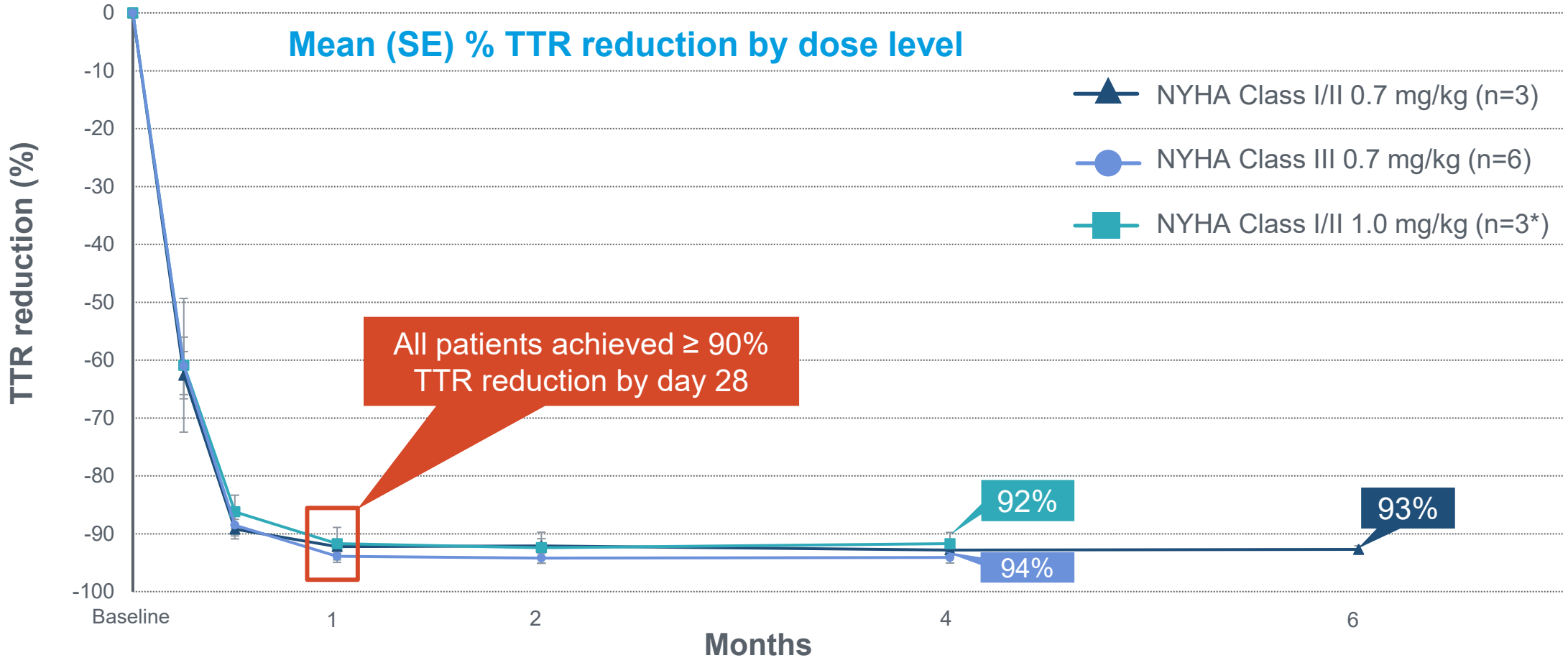
Julian D. Gillmore, M.D., Ph.D., Ed Gane, M.B., Ch.B., Jorg Taubel, M.D., Justin Kao, M.B., Ch.B., Marianna Fontana, M.D., Ph.D., Michael L. Maitland, M.D., Ph.D., Jessica Seitzer, B.S., Daniel O'Connell, Ph.D., Kathryn R. Walsh, Ph.D., Kristy Wood, Ph.D., Jonathan Phillips, Ph.D., Yuanxin Xu, M.D., Ph.D., Adam Amaral, B.A., Adam P. Boyd, Ph.D., Jeffrey E. Cehelsky, M.B.A., Mark D. McKee, M.D., Andrew Schiermeier, Ph.D., Olivier Harari, M.B., B.Chir., Ph.D., Andrew Murphy, Ph.D., Christos A. Kyratsous, Ph.D., Brian Zambrowicz, Ph.D., Randy Soltys, Ph.D., David E. Gutstein, M.D., John Leonard, M.D., Laura Sepp-Lorenzino, Ph.D., and David Lebwohl, M.D.

- NTLA-2001 is a CAS9 mRNA and a single guide RNA specific to the human TTR gene encapsulated in a lipid nanoparticle.
- Precisely targeted DNA cleavages result in initiation of Endogenous DNA-repair mechanisms which then introduce insertions or deletions of bases
- Results in a “knockout” mutation with reduction of functional target gene mRNA levels leading to reduced levels of target protein



NTLA-2001 Resulted in Rapid and Deep Serum TTR Reduction Sustained Through 4-6 Months Across All Patients

?potential for greater knockdown than other strategies



Data Cut Off: August 25, 2022
SE, standard error; **TTR**, transthyretin
*n=2 at Month 2 (missed patient visit)

Gillmore J et al. AHA 2022

Perspective: ATTR-CM

- Multiple therapies being tested in ATTR-CM – but declining event rates in earlier diagnosed patients makes trials challenging
- What's coming in ATTR-CM:
  - HELIOS-B – siRNA – to be presented later this year
  - CardioTTRansform – oligo silencer – likely 2025
  - MAGNITUDE-CM -gene therapy knockdown - recruiting
  - DepleTTR-CM - antibody depleter therapy - recruiting

Hypertrophic Cardiomyopathy

Am. J. Hum. Genet. 47:389–394, 1990

A Locus for Familial Hypertrophic Cardiomyopathy Is Closely Linked to the Cardiac Myosin Heavy Chain Genes, CRI-L436, and CRI-L329 on Chromosome 14 at q11-q12

Scott D. Solomon,* Anja A. T. Geisterfer-Lowrance,* Hans-Peter Vosberg,§ Gudrun Hiller,§ John A. Jarcho,* Cynthia C. Morton,† Wesley O. McBride,‖ Anna L. Mitchell,‖ Allen E. Bale,‖ William J. McKenna,# J. G. Seidman,‡ and Christine E. Seidman*

Mavacamten for treatment of symptomatic obstructive hypertrophic cardiomyopathy (EXPLORER-HCM): a randomised, double-blind, placebo-controlled, phase 3 trial

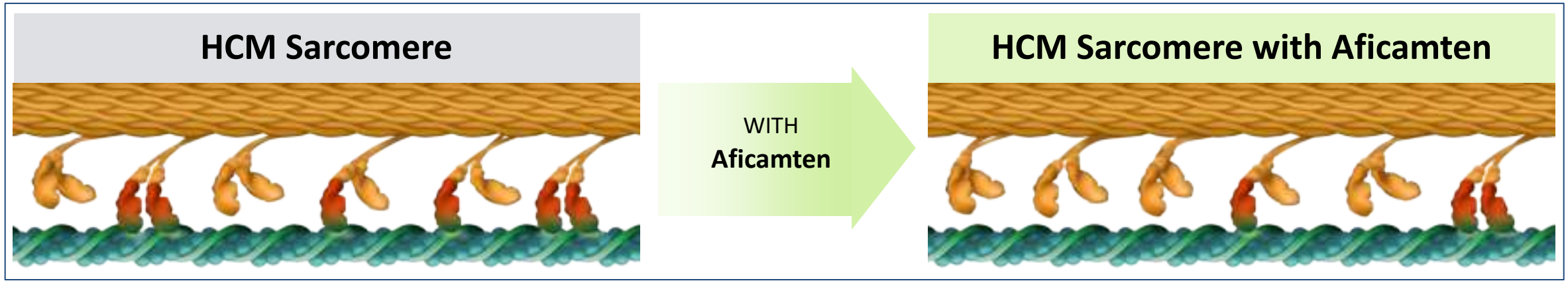
*Iacopo Olivotto, Artur Oreziak, Roberto Barriales-Villa, Theodore P Abraham, Ahmad Masri, Pablo Garcia-Pavia, Sara Saberi, Neal K Lakdawala, Matthew T Wheeler, Anjali Owens, Milos Kubanek, Wojciech Wojakowski, Morten K Jensen, Juan Gimeno-Blanes, Kia Afshar, Jonathan Myers, Sheila M Hegde, Scott D Solomon, Amy J Sehnert, David Zhang, Wanying Li, Mondira Bhattacharya, Jay M Edelberg, Cynthia Burstein Waldman, Steven J Lester, Andrew Wang, Carolyn Y Ho, Daniel Jacoby, on behalf of EXPLORER-HCM study investigators**

Aficamten for the Treatment of Symptomatic Obstructive Hypertrophic Cardiomyopathy

SEQUOIA-HCM, an international multicenter Phase 3 trial

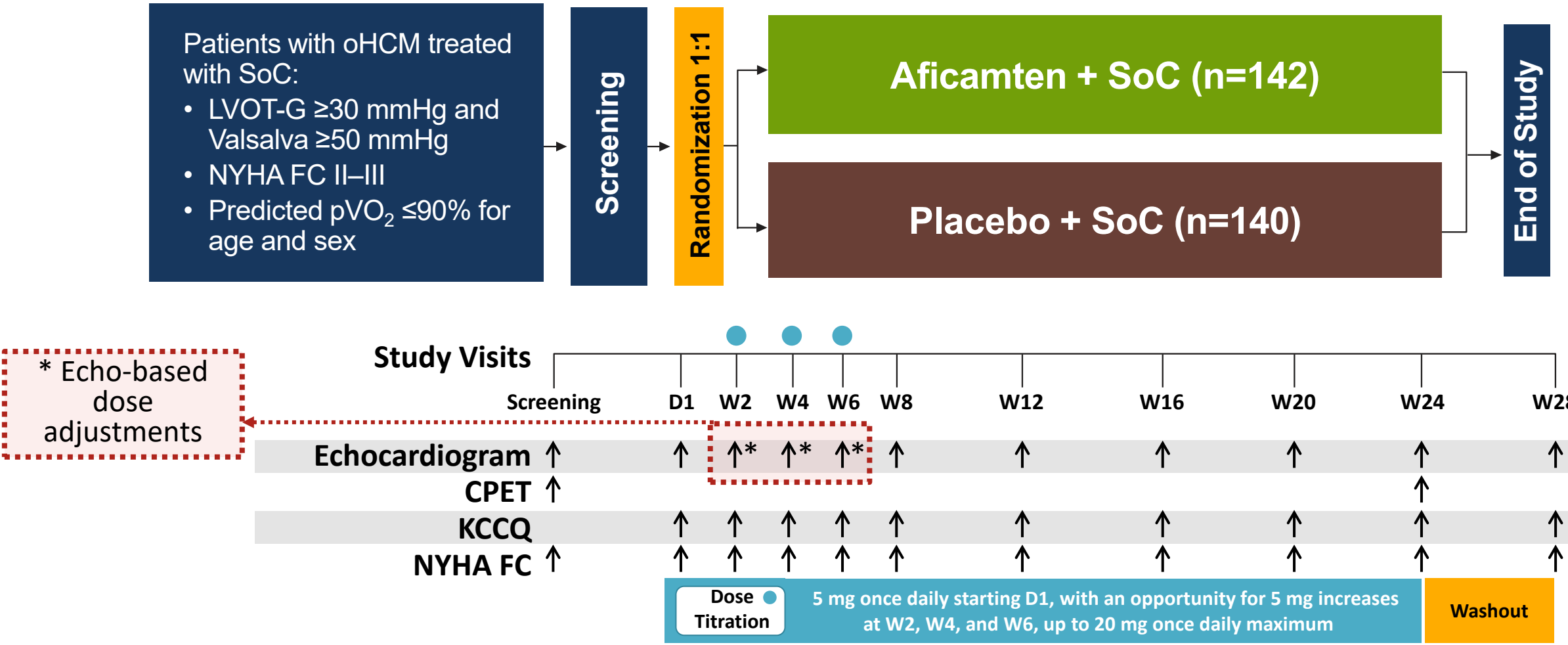
May 13, 2024

Aficamten – Mechanism and Key Pharmacologic Features



- **Once daily dosing with half-life → 3.4 days**
  - Steady state achieved by 2 weeks, allowing rapid dose adjustments
  - Rapid reversibility
- **Shallow dose–response relationship (wide therapeutic window)**
  - Small changes in LVEF as aficamten dose is increased
  - No need for serum plasma drug concentration monitoring
- **Minimal drug-drug interactions** → No clinically significant CYP inhibition or induction

SEQUOIA-HCM – Study Design

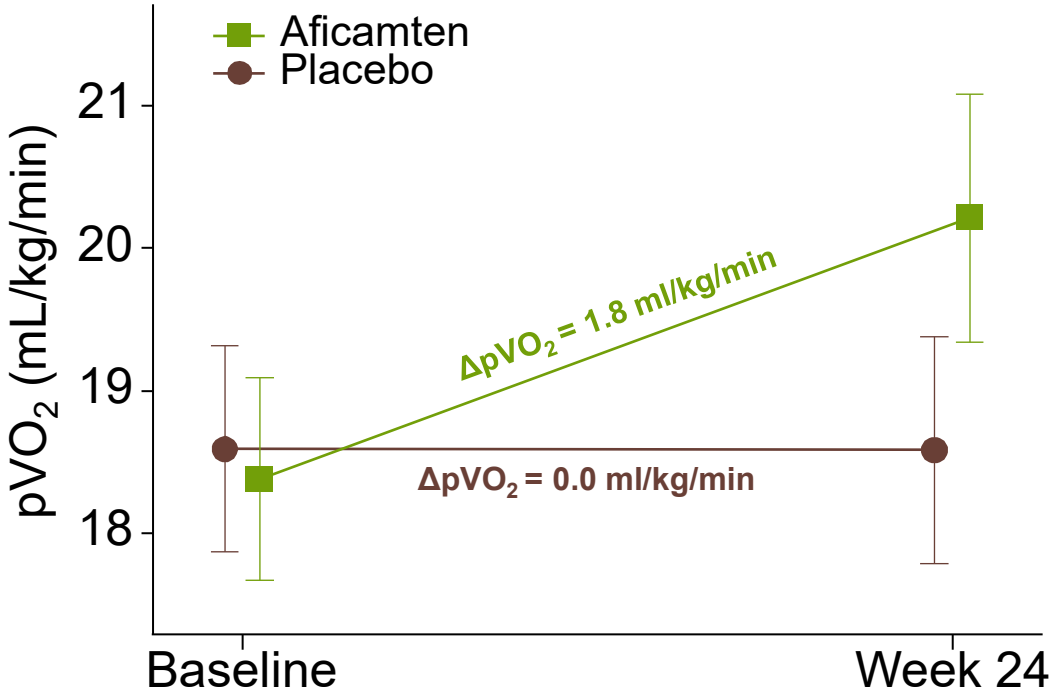


CPET, cardiopulmonary exercise testing; D, day; IP, investigational product; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVOT-G, left ventricular outflow tract obstruction gradient; NYHA FC, New York Heart Association functional class; SoC, standard of care; W, week.

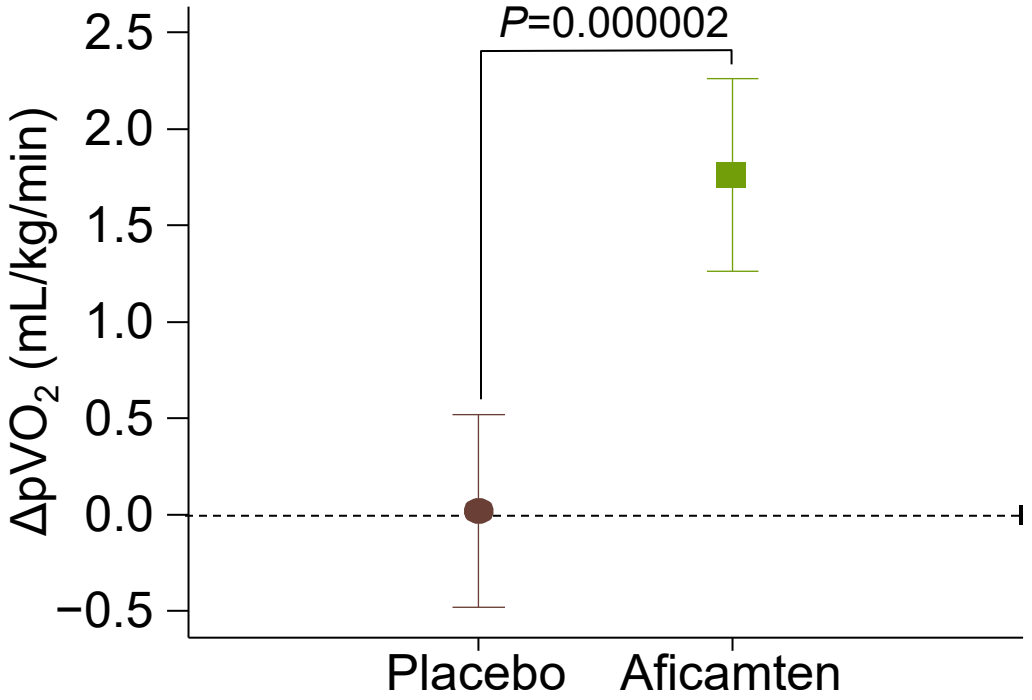
Coats CJ, et al. *J Am Coll Cardiol HF* 2024;12:199–215.

Subgroup Analyses – Change in pVO_2

Absolute Change from Baseline to Week 24



LS mean Change from Baseline to Week 24



Data are mean and 95% CI

LS mean difference (SE) vs placebo

1.74 mL/kg/min (0.36)

Subgroup Analyses – Change in pVO_2

	n (Afi/Plb)	Aficamten LS mean	Placebo LS mean	Mean difference (95% CI)
Age				
<65 y	85/84	2.4	0.4	2.0 (1.1, 2.8)
≥65 y	57/56	0.9	−0.5	1.4 (0.3, 2.5)
Sex				
Male	86/81	2.5	0.7	1.8 (0.9, 2.7)
Female	56/59	0.6	−0.8	1.4 (0.4, 2.5)
Baseline BMI				
<30 kg/m^2	97/94	1.9	0.1	1.8 (1.0, 2.7)
≥30 kg/m^2	45/46	1.4	−0.2	1.6 (0.3, 2.8)
Baseline Median LVEF				
≤75.6%	73/68	1.9	0.0	1.8 (0.8, 2.8)
>75.6%	69/72	1.7	0.0	1.6 (0.6, 2.6)
Baseline NYHA FC				
Class II	108/106	2.0	0.3	1.7 (0.9, 2.5)
Class III /IV	34/34	1.0	−0.9	1.9 (0.5, 3.3)
Baseline Median KCCQ-CSS				
≤78.1	67/75	1.7	−0.1	1.8 (0.8, 2.8)
>78.1	75/65	1.8	0.1	1.7 (0.7, 2.6)
Baseline Median NT-proBNP				
≤ 788 pg/mL	66/73	2.2	0.6	1.7 (0.7, 2.7)
> 788 pg/mL	73/65	1.4	−0.6	2.0 (1.0, 2.9)
CPET Modality				
Treadmill	78/77	2.5	0.2	2.3 (1.4, 3.2)
Bicycle	64/63	0.9	−0.1	1.0 (−0.0, 2.1)
Baseline Median pVO_2				
≤18.4 mL/kg/min	74/67	1.5	−0.1	1.6 (0.6, 2.5)
>18.4 mL/kg/min	68/73	2.0	0.1	1.9 (1.0, 2.9)
Baseline Beta-Blocker Use				
Yes	86/87	1.4	−0.2	1.6 (0.7, 2.5)
No	56/53	2.2	0.2	1.9 (0.8, 3.1)
Baseline Median Resting LVOT				
≤51.1 mmHg	72/69	1.8	0.5	1.3 (0.3, 2.3)
>51.1 mmHg	70/71	1.7	−0.4	2.1 (1.2, 3.1)
Genotype				
Positive	20/22	1.6	−1.0	2.6 (0.9, 4.2)
Negative	71/70	1.4	−0.1	1.4 (0.5, 2.3)

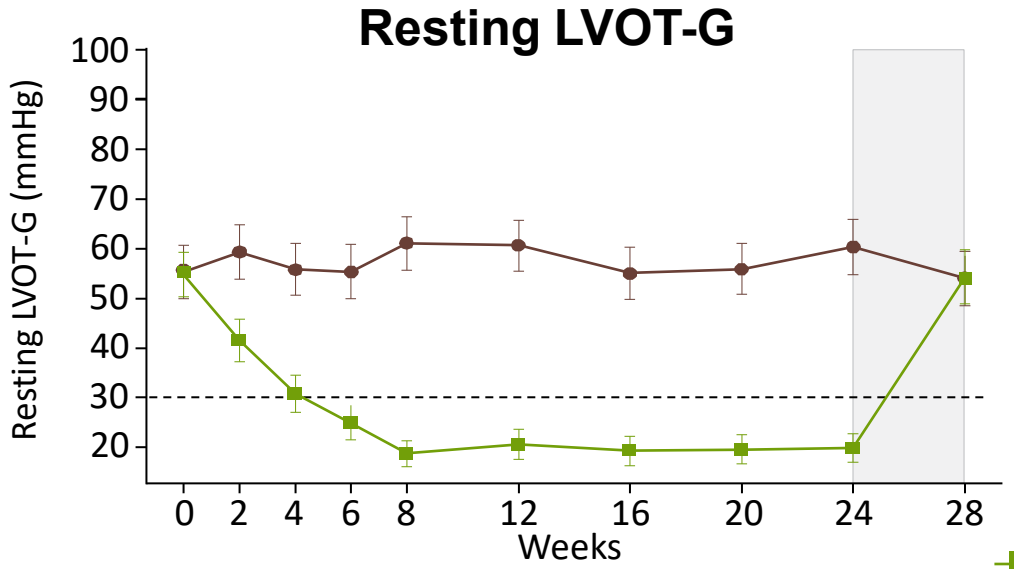
Interaction *P* values were >0.05 for all prespecified subgroups

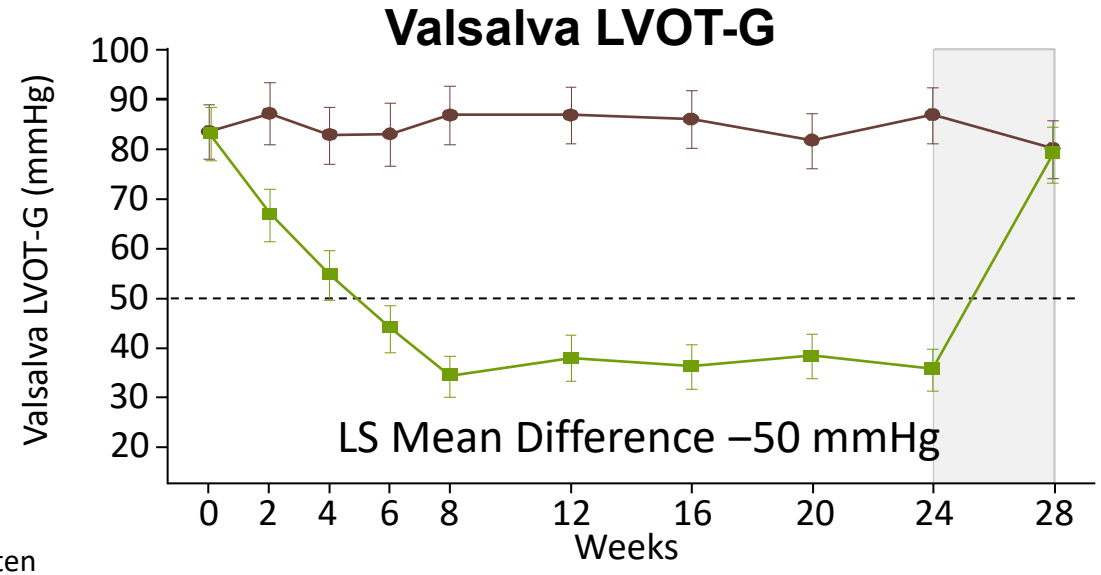
BMI, body mass index; CPET, cardiopulmonary exercise test; KCCQ-CCS, Kansas City Cardiomyopathy Questionnaire-Clinical Summary Score; LVEF, left ventricular ejection fraction; LS, least squares; LVOT, left ventricular outflow tract; NT-proBNP, N-terminal pro–B-type natriuretic peptide; NYHA FC, New York Heart Association functional class; pVO_2, peak oxygen uptake.

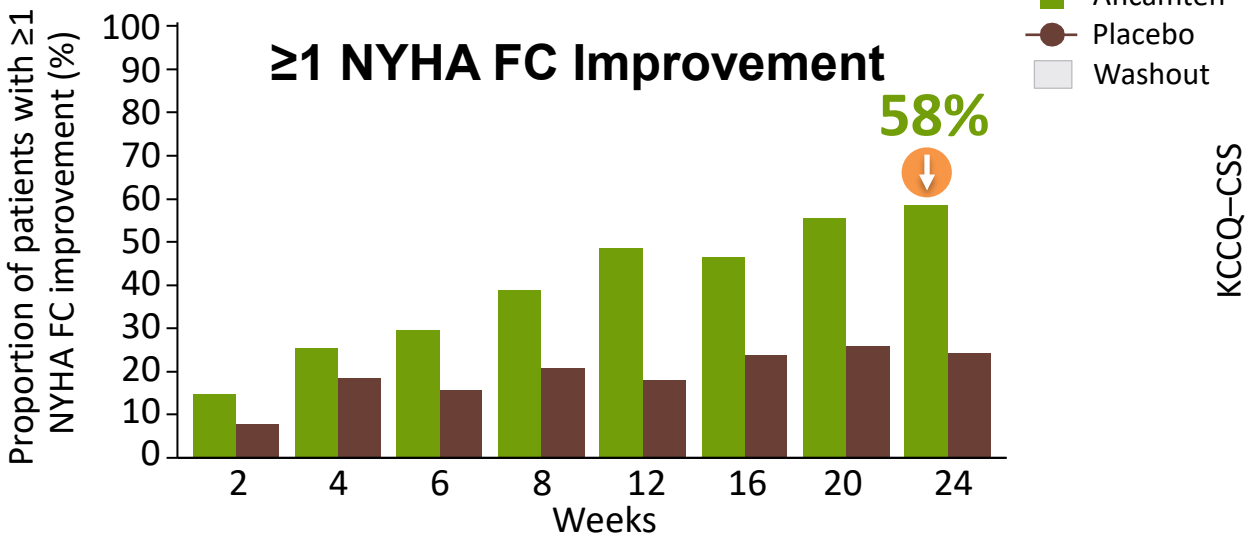
Overview of All Prespecified Endpoints

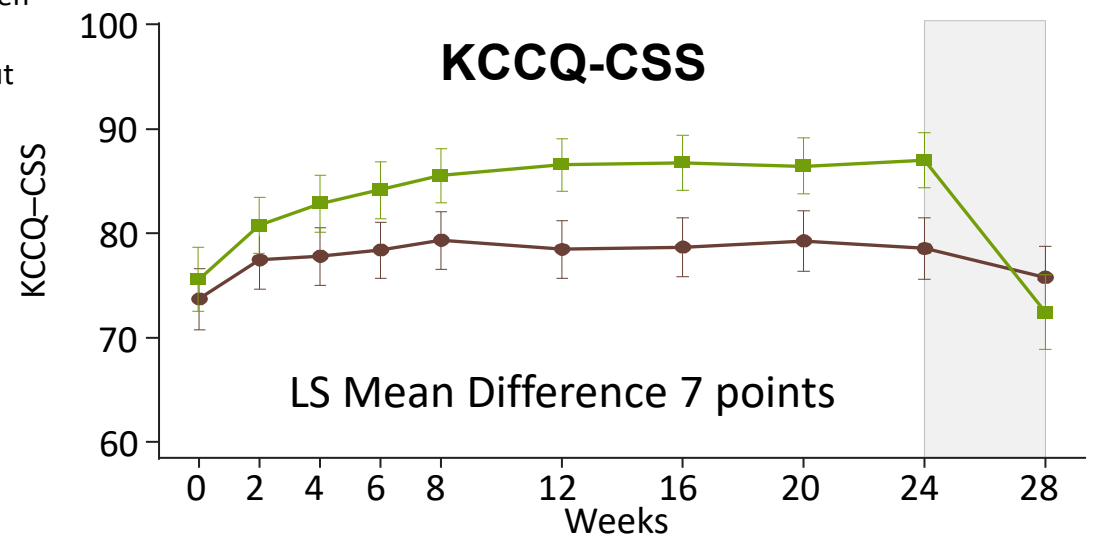
Endpoints	*P* value
Primary Endpoint	
pVO_2 change from baseline to Week 24	**<0.0001**
Secondary Endpoints	
1. KCCQ-CSS change from baseline to Week 24	**<0.0001**
2. % NYHA class improvement by at least 1 class at Week 24	**<0.0001**
3. Valsalva LVOT-G change from baseline to Week 24	**<0.0001**
4. % Valsalva LVOT-G <30 mmHg at Week 24	**<0.0001**
5. Duration of SRT-eligible during 24 weeks of treatment	**<0.0001**
6. KCCQ-CSS change from baseline to Week 12	**<0.0001**
7. % NYHA class improvement by at least 1 class at Week 12	**<0.0001**
8. Valsalva LVOT-G change from baseline to Week 12	**<0.0001**
9. % Valsalva LVOT-G <30 mmHg at Week 12	**<0.0001**
10. Total workload change from baseline to Week 24	**<0.0001**

Secondary and Exploratory Endpoints





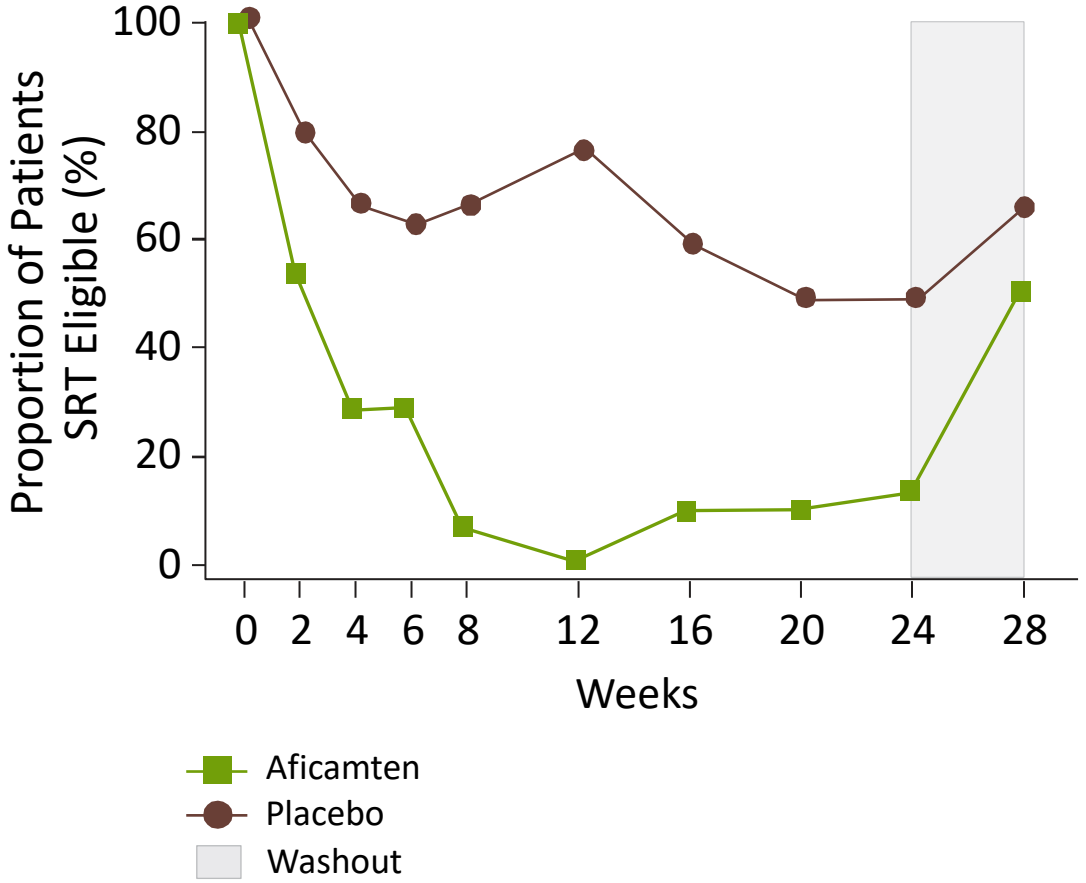




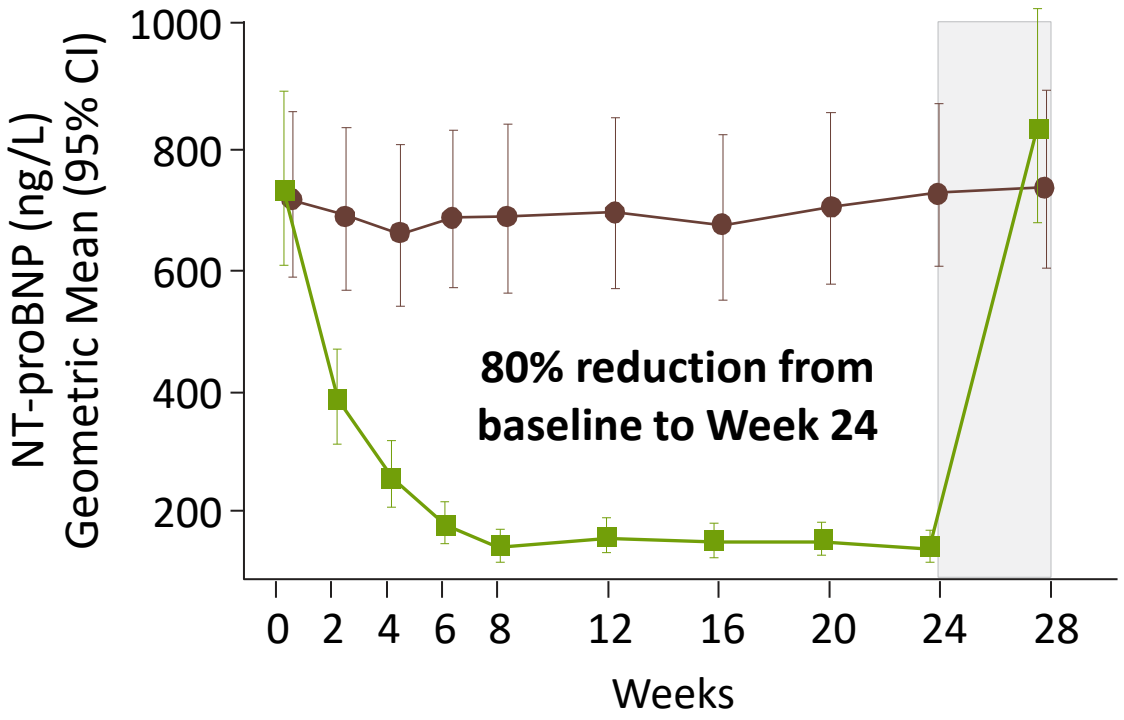
Error bars are 95% CI

Secondary and Exploratory Endpoints

Guideline Eligibility for SRT



NT-proBNP



Number of patients

Aficamten	139	141	141	139	139	139	137	139	136	135
Placebo	138	138	139	136	137	135	135	137	134	135

Safety Outcomes

AEs with ≥5% incidence

Event, n (%)	Placebo (n=140)	Aficamten (n=142)
Overall AEs	99 (70.7)	105 (73.9)
Headache	10 (7.1)	11 (7.7)
Hypertension	3 (2.1)	11 (7.7)
Palpitations	4 (2.9)	10 (7.0)
Upper respiratory infection	12 (8.6)	9 (6.3)
COVID-19	9 (6.4)	8 (5.6)
Dyspnea	8 (5.7)	8 (5.6)
SAEs	13 (9.3)	8 (5.6)
Cardiac AEs	21 (15.0)	24 (16.9)
Discontinuations	4 (2.9)	5 (3.5)
New-onset AF	1 (0.7)	1 (0.7)
Appropriate ICD shock	1 (0.7)	0
LVEF <50% by core laboratory[a]	1 (0.7)	5 (3.5)
Dose reduction based on site-read LVEF <50%	1 (0.7)	7 (4.9)

[a] 1 placebo- and 1 aficamten-treated patient overlap with dose reduction based on site-read LVEF <50%.

There were no serious adverse cardiovascular events associated with aficamten treatment in SEQUOIA-HCM

AE, adverse event; SAE, serious adverse event.

Perspective: Aficamten in HCM

- In patients with symptomatic oHCM, aficamten resulted in clinically meaningful improvements in exercise capacity, decreased burden of limiting symptoms, and dramatically reduced gradients.
- Adds to rich data with mavacamten regarding myosin inhibition in HCM
- Somewhat improved pharmacokinetics of aficamten may translate to better safety

SGLT-2 Inhibitors Post-MI

SGLT-2 inhibitors in patients with heart failure: a comprehensive meta-analysis of five randomised controlled trials

Muthiah Vaduganathan, Kieran F Docherty*, Brian L Claggett, Pardeep S Jhund, Rudolf A de Boer, Adrian F Hernandez, Silvio E Inzucchi, Mikhail N Kosiborod, Carolyn S P Lam, Felipe Martinez, Sanjiv J Shah, Akshay S Desai, John J V McMurray†, Scott D Solomon†*

Vaduganathan et al. ESC-Hotline; Lancet 2022

TRIAL DESIGN

Main Inclusion Criteria

- MI (NSTEMI or STEMI) < 10 days
- Impaired LV systolic function or Q-wave MI
- Hemodynamically stable

Main Exclusion Criteria

- Type 1 or type 2 diabetes
- Chronic symptomatic HF with a prior HHF within the last year and known reduced EF (LVEF ≤ 40 %)
- eGFR <20 mL/min/1.73 m²

Key assumptions

- 4000 patients
- Minimum follow up 3 months
- Assumed true win ratio 1.2
- Total trial duration 2.5 years
- Power 80%, *P*<0.05

MI: myocardial infarction, NSTEMI: non-ST-elevation MI, STEMI: ST-elevation MI, HF: heart failure, HHF: hospitalization for heart failure, EF: ejection fraction
eGFR: estimated glomerular filtration rate

ENDPOINTS

The composite of CV death and hospitalization for heart failure was initially chosen as the primary outcome.
During the trial, it became evident that the number primary composite outcomes was substantially lower than anticipated.
Thus, in Feb 2023, the trial was modified to a hierarchical composite outcome approach with cardiometabolic outcomes.[1]

Primary

The hierarchical (win ratio) composite outcomes:

- Death (first cardiovascular death, followed by non-cardiovascular death)
- Hospitalization due to heart failure (first adjudicated, followed by investigator reported)
- Non-fatal myocardial infarction
- Atrial fibrillation/flutter event
- New diagnosis of type 2 diabetes
- NYHA functional class at last visit
- Body weight decrease at least 5% at last visit

Key secondary

- Primary outcome excluding body weight component

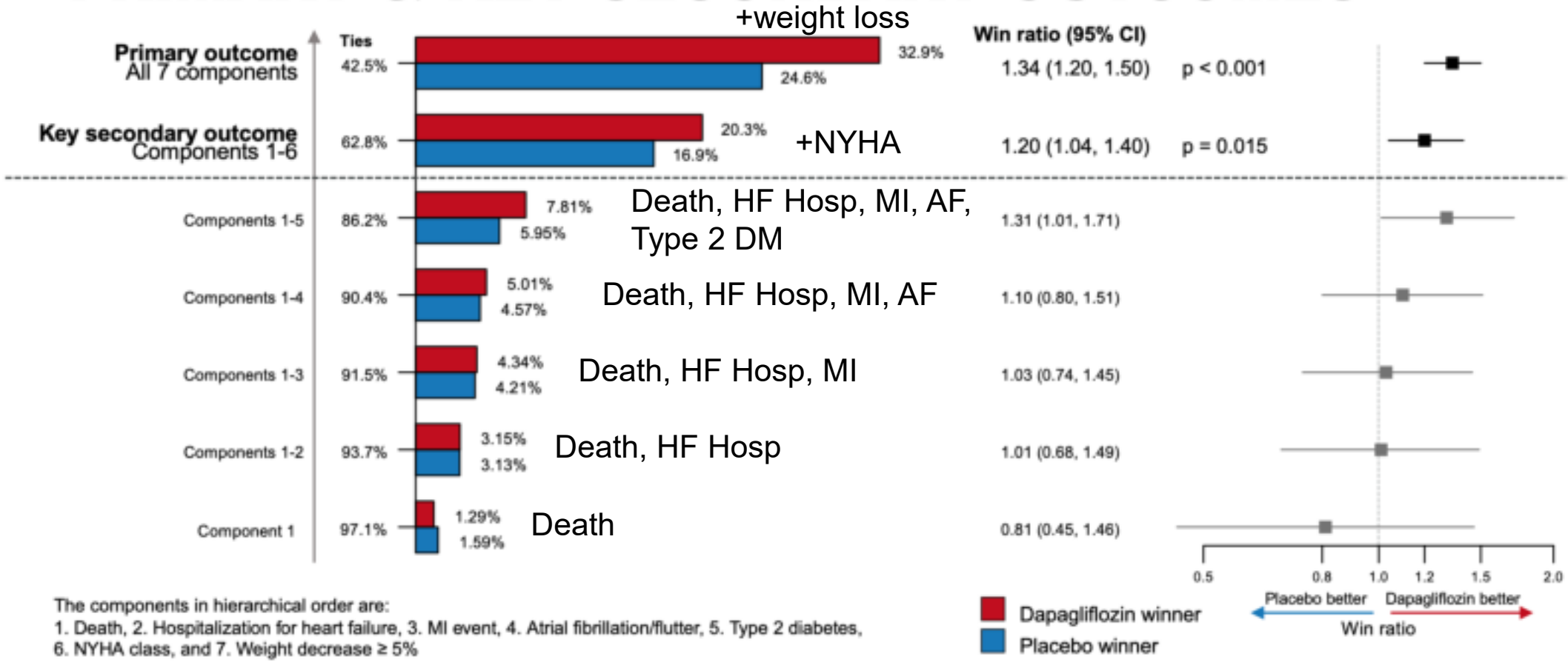
Other secondary

- Time to the first occurrence of any of the components of the composite:
  - Hospitalization for heart failure
  - Cardiovascular death

1. James S et al. *Am Heart J* 2023. doi: 10.1016/j.ahj.2023.08.008.

NYHA, New York Heart Association

PRIMARY & KEY SECONDARY OUTCOMES



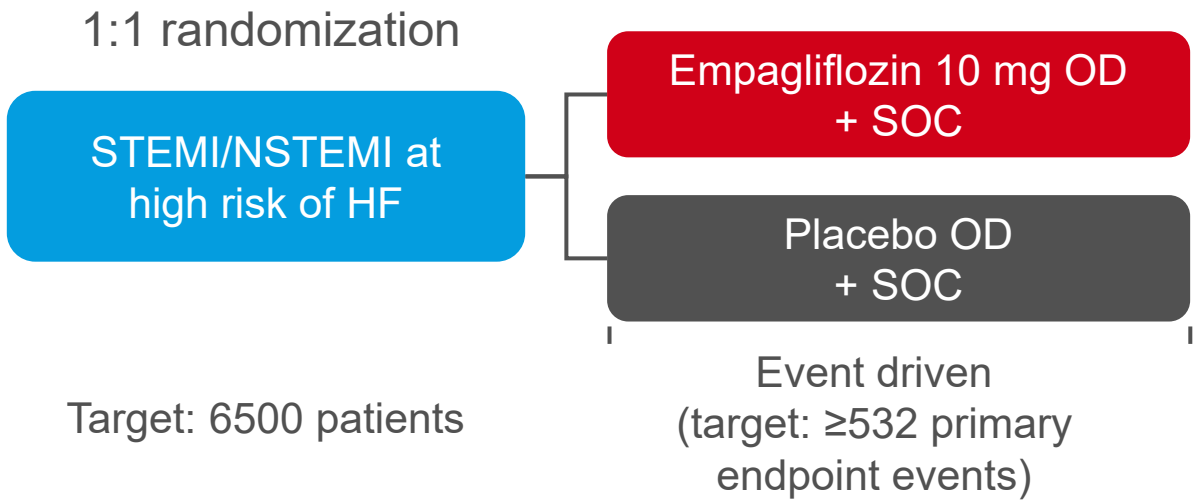
The components in hierarchical order are:
1. Death, 2. Hospitalization for heart failure, 3. MI event, 4. Atrial fibrillation/flutter, 5. Type 2 diabetes, 6. NYHA class, and 7. Weight decrease ≥ 5%

EMPACT-MI was Conducted to Evaluate Efficacy and Safety of Empagliflozin in Patients After Acute MI

EMPACT-MI

Streamlined, multicentre, randomized, double-blind, phase III, placebo-controlled superiority trial

Primary endpoint: time to first heart failure hospitalization or all-cause mortality



EMPACT-MI was a streamlined trial:

- Use of inclusion/exclusion criteria readily available in routine care
- Mainly remote follow-up visits
- Streamlined data collection incl. focused collection of safety information
- Blinded investigator review instead of central adjudication, additionally supported by structured data collection

NSTEMI, non-ST-segment elevation myocardial infarction; OD, once daily; SOC, standard of care; STEMI, ST-segment elevation myocardial infarction.

Key Eligibility Criteria

EMPACT-MI

INCLUSION

Diagnosis of spontaneous acute MI
- **STEMI or NSTEMI**
- Randomization **≤14 days** after hospital admission

High risk of HF, defined as either:
- Signs or symptoms of **congestion** requiring treatment during index hospitalization **OR**
- Newly developed **LVEF <45%**

At least one HF risk factor : Age ≥65 years; LVEF <35%; prior MI; eGFR <60 mL/min/1.73 m^2;* atrial fibrillation;† type 2 diabetes; elevated NT-proBNP/BNP;‡ elevated uric acid;§ PASP (RVSP) ≥40 mmHg;¶ no revascularization for the index MI; 3-vessel coronary artery disease; peripheral artery disease

EXCLUSION

Diagnosis of chronic HF prior to index MI

SBP ≤90 mmHg at randomization

Cardiogenic shock or use of IV inotropes in last 24 hours before randomization

Current or planned treatment with an SGLT2 inhibitor

Any current severe (stenotic or regurgitant) valvular heart disease

eGFR <20 mL/min/1.73 m^2

Type 1 diabetes mellitus

*Using CKD-EPI formula based on creatinine from local lab at any time during index hospitalization. †Persistent or permanent, if paroxysmal, only valid if associated with index MI; ‡NT-proBNP ≥1400 pg/mL for patients in sinus rhythm, ≥2800 pg/mL if atrial fibrillation; BNP ≥350 pg/mL for patients in sinus rhythm, ≥700 pg/mL if atrial fibrillation, measured at any time during hospitalization. §Uric acid ≥7.5 mg/dL (≥446 µmol/L), measured at any time during hospitalization. ¶Pulmonary Artery Systolic Pressure [or right ventricular systolic pressure]. eGFR, estimated glomerular filtration rate; IV, intravenous; (NT-pro)BNP, (N-terminal prohormone of) brain natriuretic peptide; SBP, systolic blood pressure.

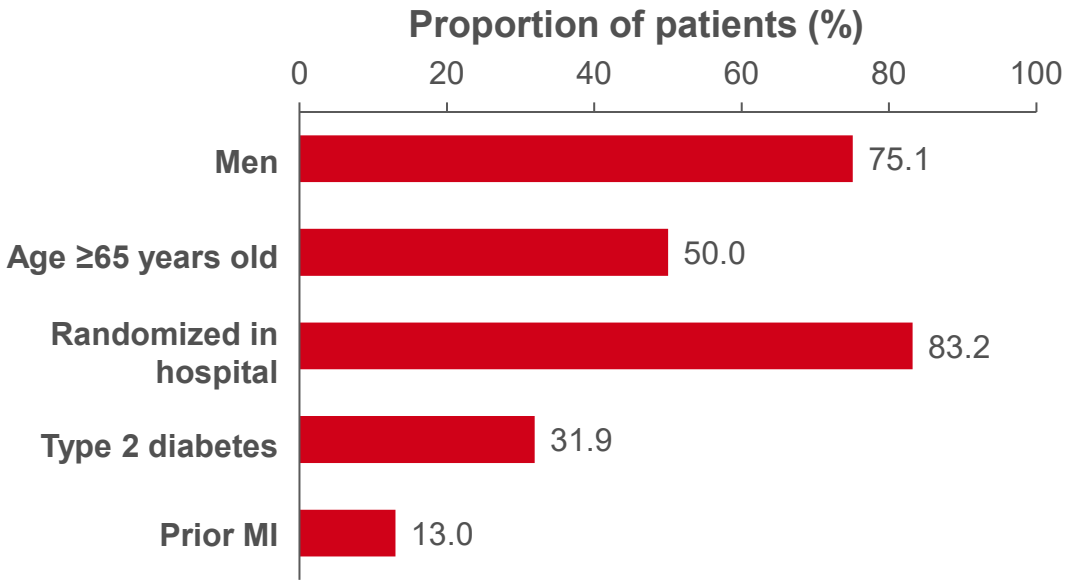
EMPACT-MI: Patient Population

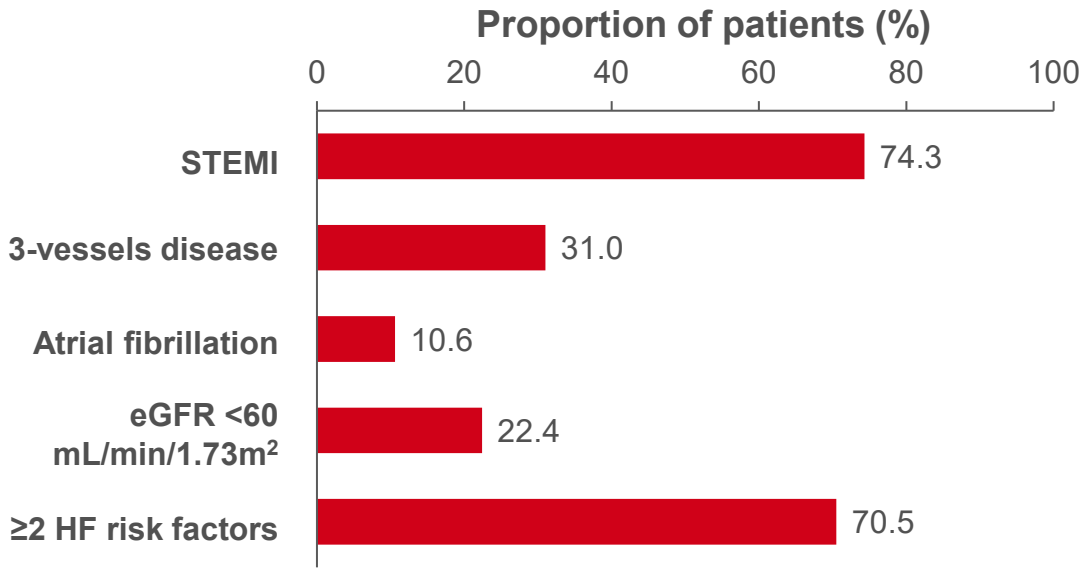
EMPACT-MI

Patients with signs and symptoms of congestion requiring treatment: n=3715 (57.0%)

Patients with both: n=2323 (35.6%)

Patients with LVEF <45%;* n=5112 (78.4%)

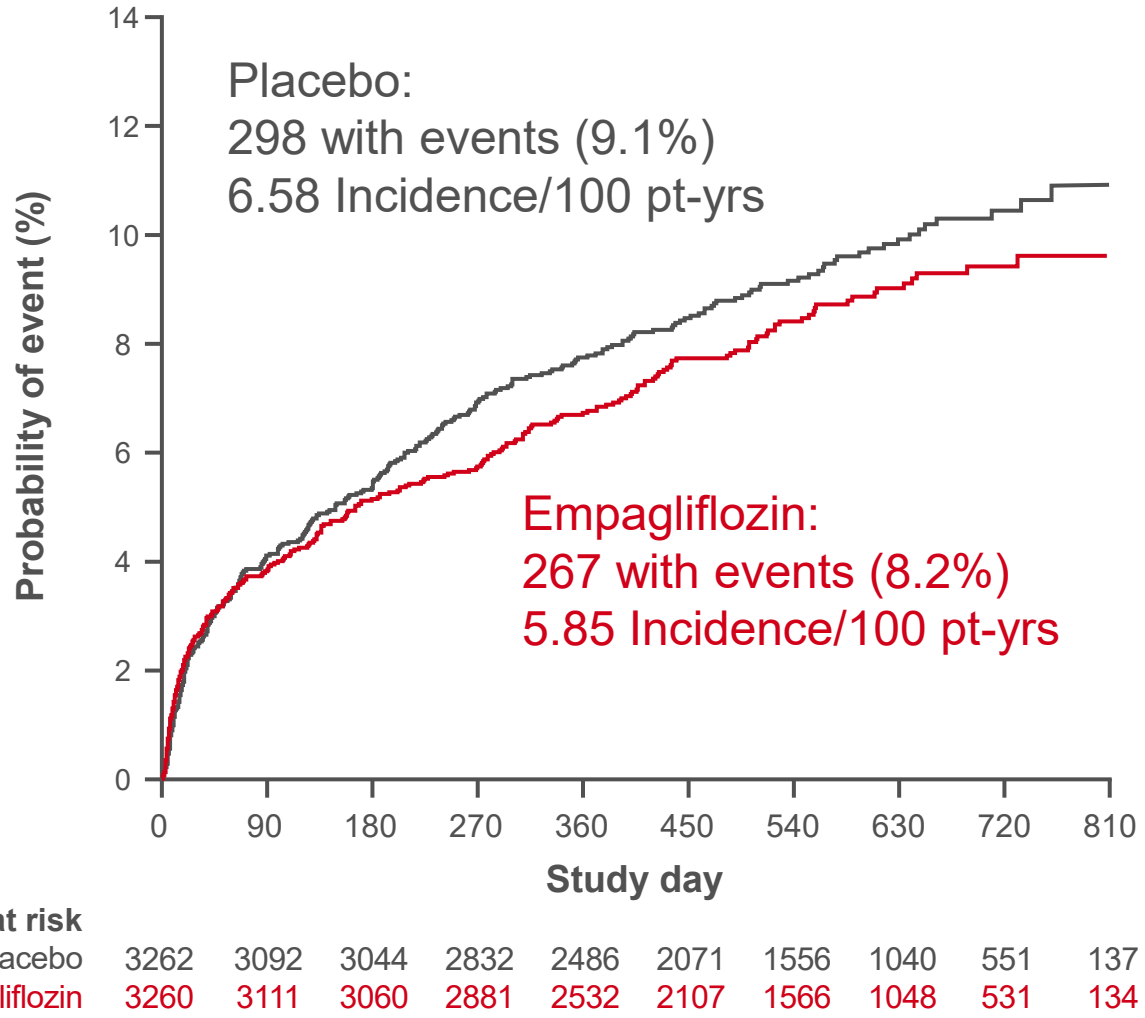




*52 patients had missing LVEF.
≥2 enrichment criteria: Except for eGFR, laboratory values and pulmonary artery pressure have been optional to be reported beyond meeting the inclusion criterion of providing at least 1 enrichment criterion.

Primary Endpoint

EMPACT-MI



HR 0.90 (95% CI: 0.76, 1.06)
p=0.21

565 primary endpoint events

- 271 (48%) first events: HHF
- 294 (52%) first events: death

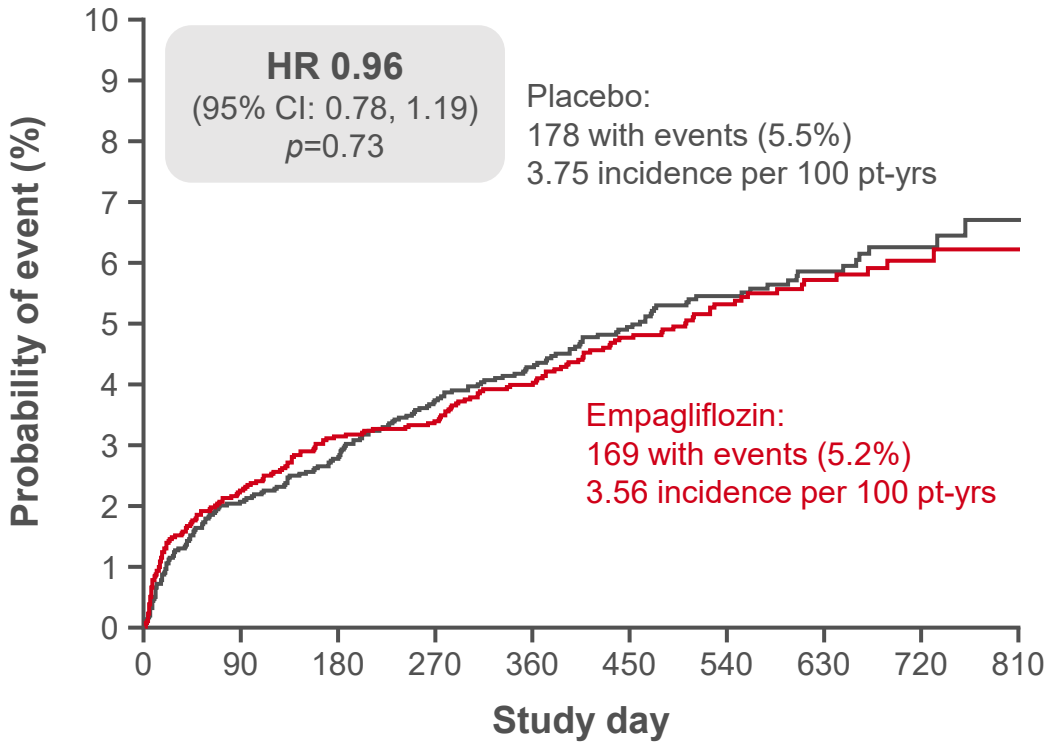
CI, confidence interval; HHF, hospitalization for heart failure; HR, hazard ratio; pt-yrs, patient-years.

Components of Primary Endpoint

EMPACT-MI

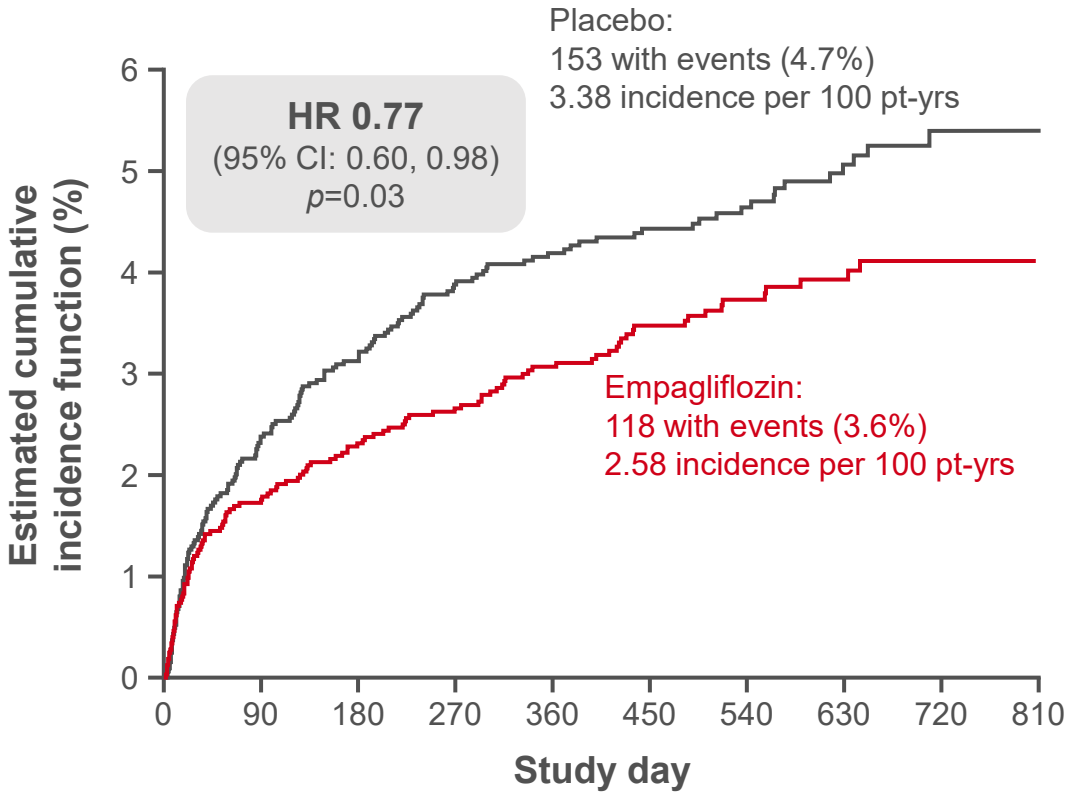
Time to all-cause mortality

347 deaths: 263 (76%) CV death; 84 (24%) non-CV death



No. at risk										
Placebo	3262	3186	3159	2975	2632	2207	1660	1111	593	148
Empagliflozin	3260	3177	3148	2995	2639	2218	1658	1119	572	153

Time to first HHF



	3262	3092	3044	2832	2486	2071	1556	1040	551	137
	3260	3111	3060	2881	2532	2107	1566	1048	531	134

Perspective: SGLT-2 Inhibitors Post-MI

- You can't make "better" better…… the majority of well treated, well re-perfused patients enrolled in post-MI trials are not at risk for heart failure and won't benefit from SGLT2 inhibitors
- However, SGLT2 inhibitors are SAFE post-MI, and anyone with another indication "discovered" at time of MI (i.e., DM or CKD) should be treated with SGLT2 inhibitors, as should patients who develop HF symptoms in follow-up


3.37
THANK YOU

DEBATE: Is Canada ready for Implantable Hemodynamic Monitoring?

Anique Ducharme
MD, MSc, FRCPC, FACC, FCCS, FHSA(h)

Justin Ezekowitz
MB, BCH, MSc, FRCPC, FACC, FAHA, FESC

Disclosures

	Dr. Anique Ducharme	Dr. Justin Ezekowitz
Any direct financial payments including receipt of honoraria	CCS (not-for-profit)	AstraZeneca, Bayer, Boehringer Ingelheim, Novartis, Novo Nordisk, Otsuka; serves as an advisor to US2.ai.
Membership on advisory boards or speakers' bureaus	Abbott, AstraZeneca, Bayer, Boehringer-Ingelheim, GlaxoSmithKline, Novartis, Novo Nordisk	No disclosures
Funded grants or clinical trials	Abbott, Astra-Zeneca, Bayer, BioBridge, Merck, Novartis, Novo Nordisk, Pfizer	American Regent, Applied Therapeutics, AstraZeneca, Bayer, Cytokinetics, Merck & Co, Novo Nordisk, Otsuka; CIHR, Heart and Stroke Foundation, NIH, PCORI;
All other investments or relationships that could be seen by a reasonable, well-informed participant as having the potential to influence the content of the educational activity	No disclosures	CCS, CHFS, AHA, ESC, ACC, HFSA, AHS, UofA, CVC

Learning Objectives

1. Provide an overview of trials that focus on the use of implantable hemodynamic monitoring in patients with heart failure
2. Highlight benefits of using implantable hemodynamic monitoring in patients with heart failure
3. Identify potential barriers to widespread utilization of implantable hemodynamic monitoring in patients with heart failure

Is Canada ready for Implantable Hemodynamic Monitoring?

<No / Non>

Justin A. Ezekowitz, MBBCh MSc
Professor and Director, Cardiovascular Research University of Alberta
Co-Director, Canadian VIGOUR Centre, University of Alberta
Cardiologist, Mazankowski Alberta Heart Institute
President, Canadian Heart Failure Society
AHS Chair in Cardiac Sciences
May 2024

Disclosures / COI / RWI / RWA

- Available: thecvc.ca

Cardiovascular Research Institute

Top 10 reasons IHM is a ‘non’

1. Invasive
2. Complications of device
3. Data alarms – the false and misinterpreted alarms
4. Privacy / data breaches
5. Cost / cost utility borderline
6. The people cost (specialized training)
7. Longevity of device
8. Patient compliance
9. RCTs do not suggest major benefit for QOL or mortality
10. Anique Ducharme is an author

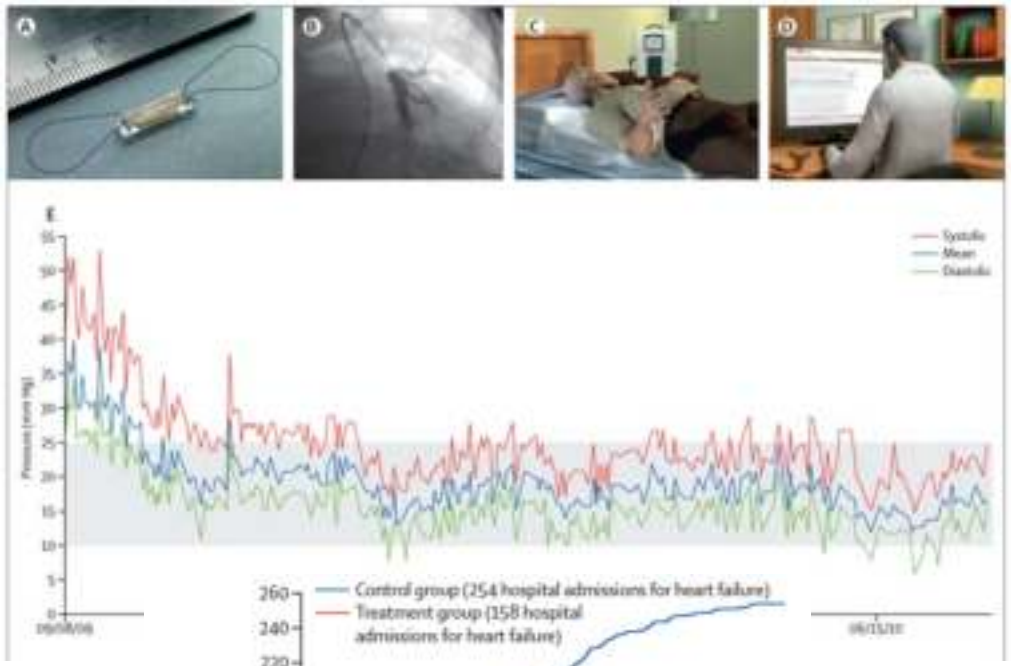
Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomised controlled trial

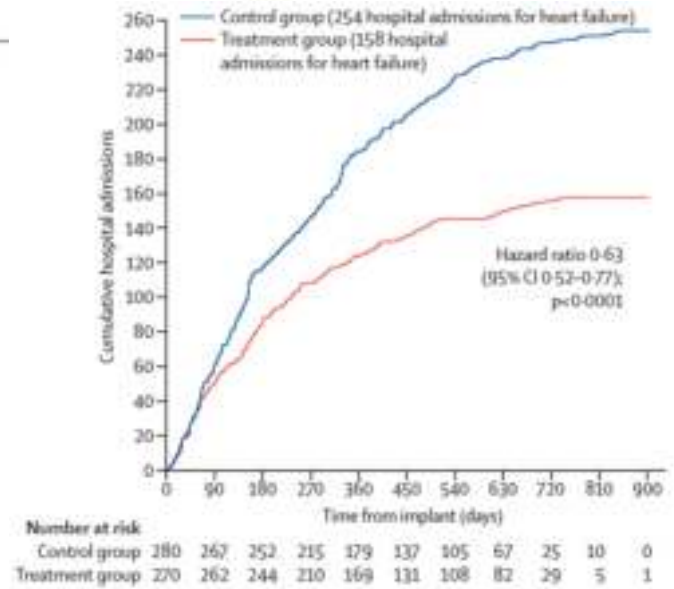
William T Abraham, Philip B Adamson, Robert C Bourge, Mark F Aaron, Maria Rosa Costanzo, Lynne W Stevenson, Warren Strickland, Suresh Neelagaru, Mona Raval, Steven Krueger, Stanislav Weiner, David Shilowitz, Bradley Jeffries, Jay S Yadav, for the CHAMPION Trial Study Group*

Lancet 2011; 377: 658–66

Summary

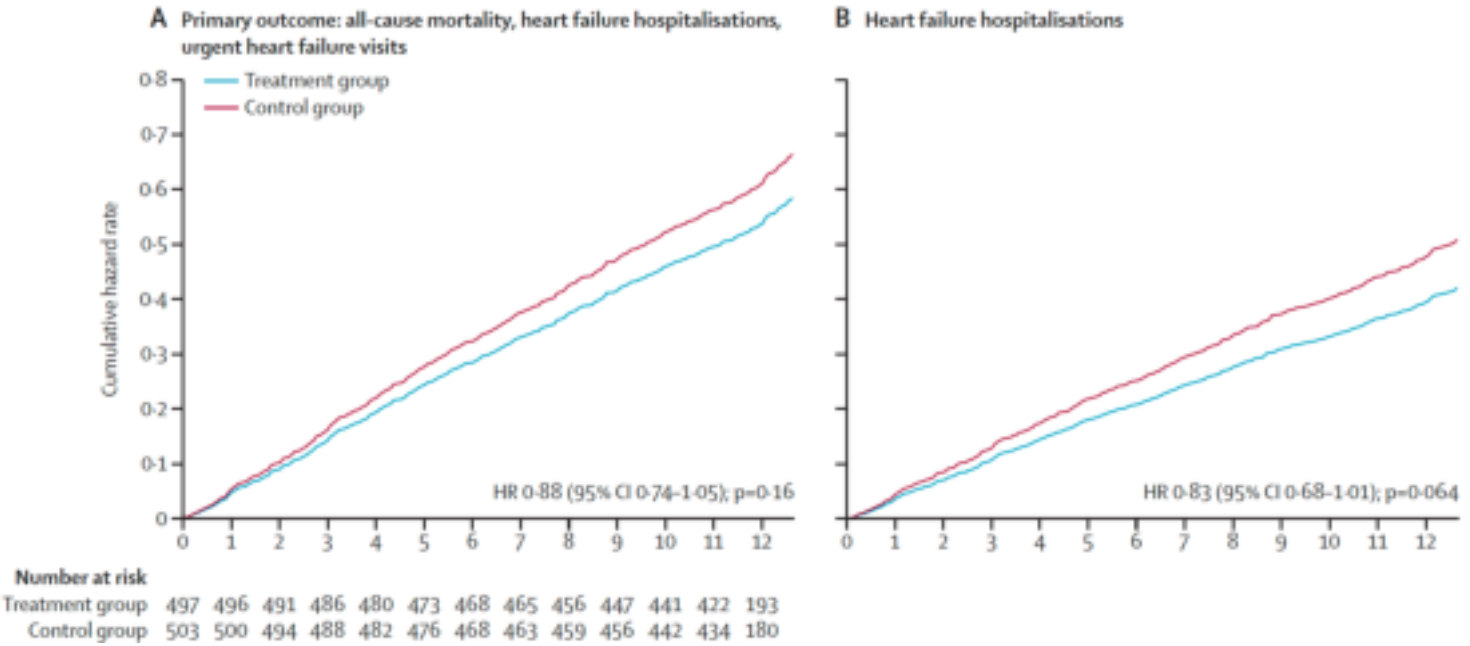
Background Results of previous studies support the hypothesis that implantable haemodynamic monitoring

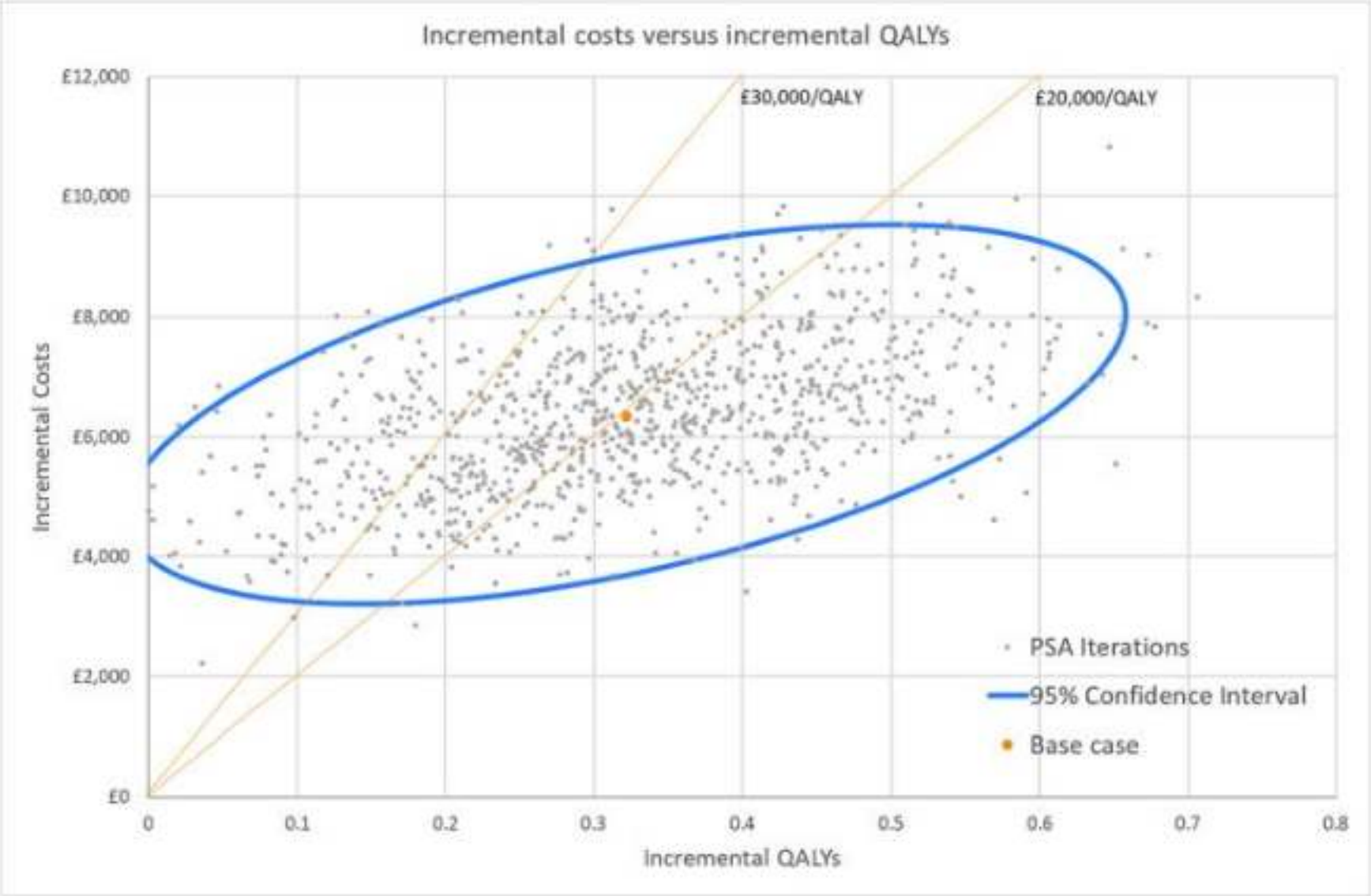




Haemodynamic-guided management of heart failure (GUIDE-HF): a randomised controlled trial

JoAnn Lindenfeld, Michael R Zile, Akshay S Desai, Kunjan Bhatt, Anique Ducharme, Douglas Horstmanshof, Selim R Krim, Alan Maisel, Mandeep R Mehra, Sara Paul, Samuel F Sears, Andrew J Sauer, Frank Smart, Marcel Zughaib, Paige Castaneda, Jean Kelly, Nessa Johnson, Poornima Sood, Greg Ginn, John Henderson, Philip B Adamson, Maria Rosa Costanzo





"Our model suggests that CardioMEMS is likely to be cost-effective in the United Kingdom, at the currently considered thresholds of **£20 000–30 000/QALY.**"

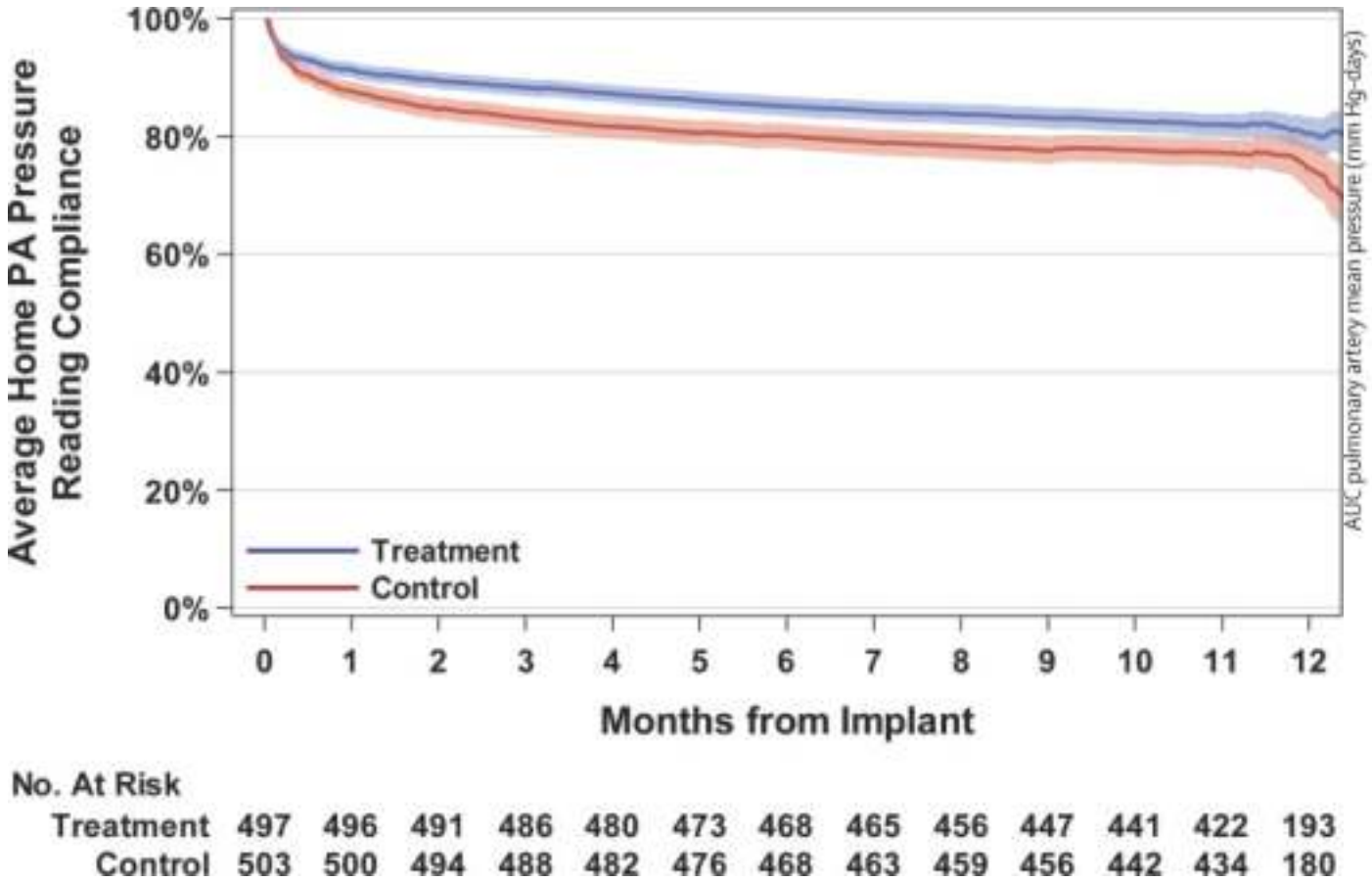
Cowie, ESC Heart Fail. 2023 Oct; 10(5): 3046–3054

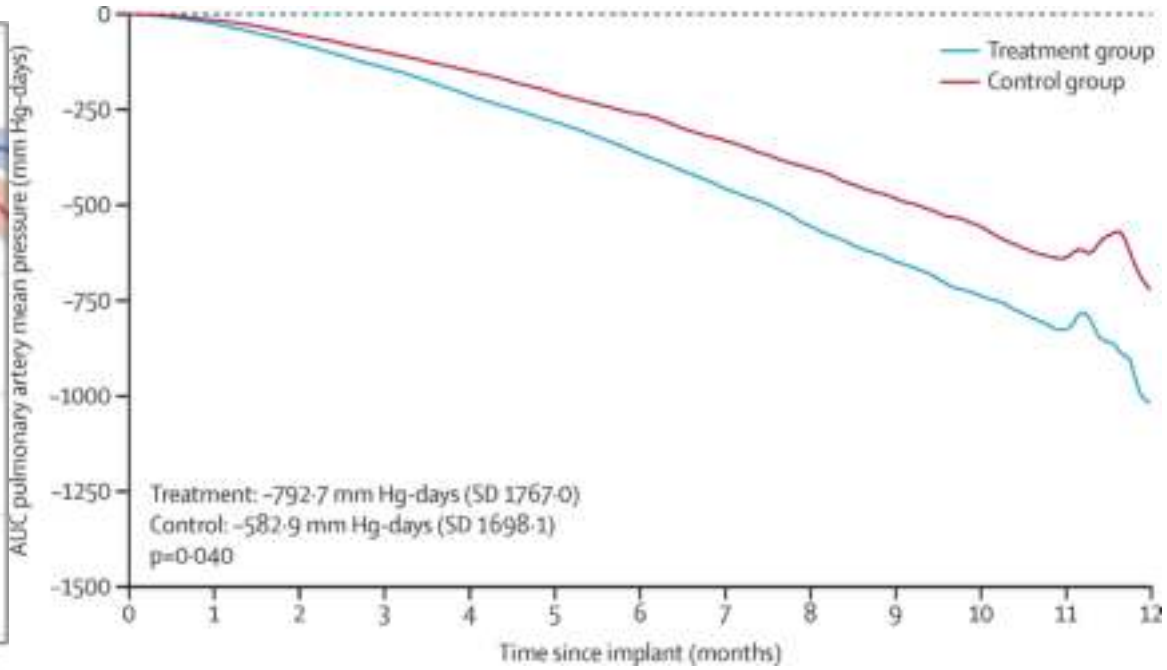
Meanwhile in Canada:

- ….and a device cost of $17,500, the **additional** cost of using CardioMEMS in one NYHA class III patient would be $14,734.

https://muhc.ca/sites/default/files/micro/m-TAU/TAU_CardioMEMS_report_final_2022.pdf

Patient ‘Compliance’ still matters





During the 12 months of follow-up, mean pulmonary artery pressure averaged around ~ 2 mm Hg lower compared with baseline with monitoring

Lindenfeld, *Lancet* 2021; Zile et al EHJ 2022 doi: 10.1093/eurheartj/ehac114; Cleland, *Lancet* 2021

Expensive diuretic titration machine?

- Most common ways it c/should work: medication changes to prevent HFH
- Medication Changes / month
  - IHM = 0.835 vs Control = 0.475 ($p<0.001$; pre-covid)
  - IHM = 0.675 vs Control = 0.425 (p=ns; post-covid)

- Of the 3237 medication changes in 775 patients, 2364 changes (73%) were diuretics

- ? What about GDMT = no change reported to date

Zile et al EHJ 2022 doi: 10.1093/eurheartj/ehac114

QOL / mortality no different

- KCCQ, EQ-5-D, 6 minute walk test = **No** difference
- Mortality = **No** difference
  - CV = 30/497 (6%) for cardioMems, vs 24/503 (5%) control

- COVID-19 analysis was the same:
  - The treatment effect change was not due to COVID-19-related events.
  - Patient management sustained but not intensified during COVID-19
  - Patient status improved during COVID-19 and pulmonary artery pressure reduced in <u>both</u> groups.

Lindenfeld, *Lancet* 2021; Zile et al *EHJ* 2022 doi: 10.1093/eurheartj/ehac114


Heart Failure
& World Congress on Acute Heart Failure
2022

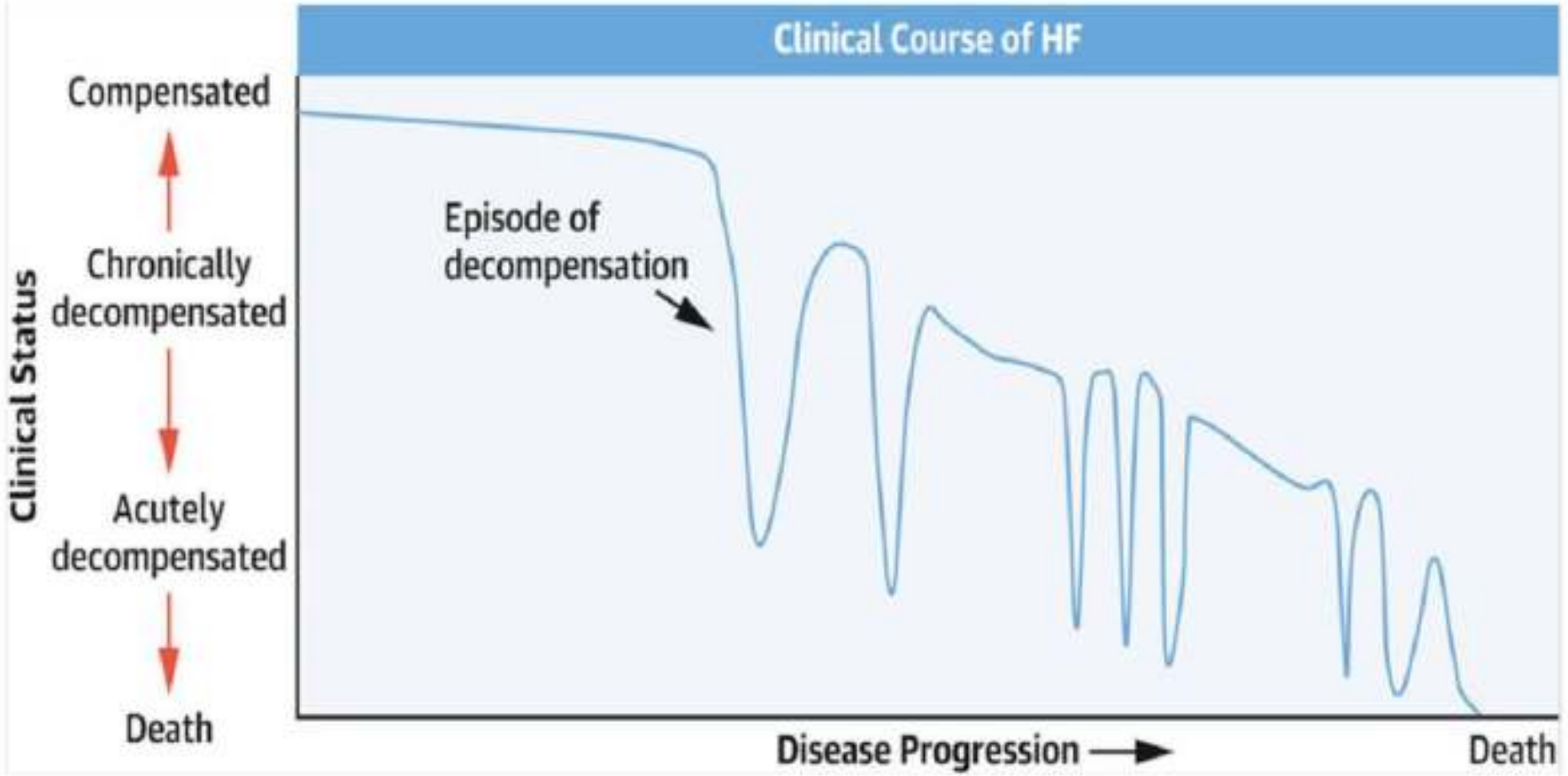
PLENARY Session 2

Clinical Pearls and Conundrums in HF Clinical Care
DEBATE: Is Canada ready for Implantable Hemodynamic Monitoring?

Anique Ducharme MD, MSc, FRCPC, FCCS, FHFSA(h)
Canadian Heart Failure Society – Immediate Past President
Director, Heart Failure clinic, Montreal Heart Institute,
Professor of medicine, University of Montreal, Montréal (Canada)
Chair holder, University of Montreal Fondation Marcelle et Jean Coutu, Cal et Janine Moisan for better practices in advanced heart failure

Friday, May 24th, 2024; TIME: 3:00–4:30 p.m
co-present a 15-minute debate
(Followed by a 25-min panel discussion and Q&A at the end of the plenary session);

Heart Failure Management 1.0

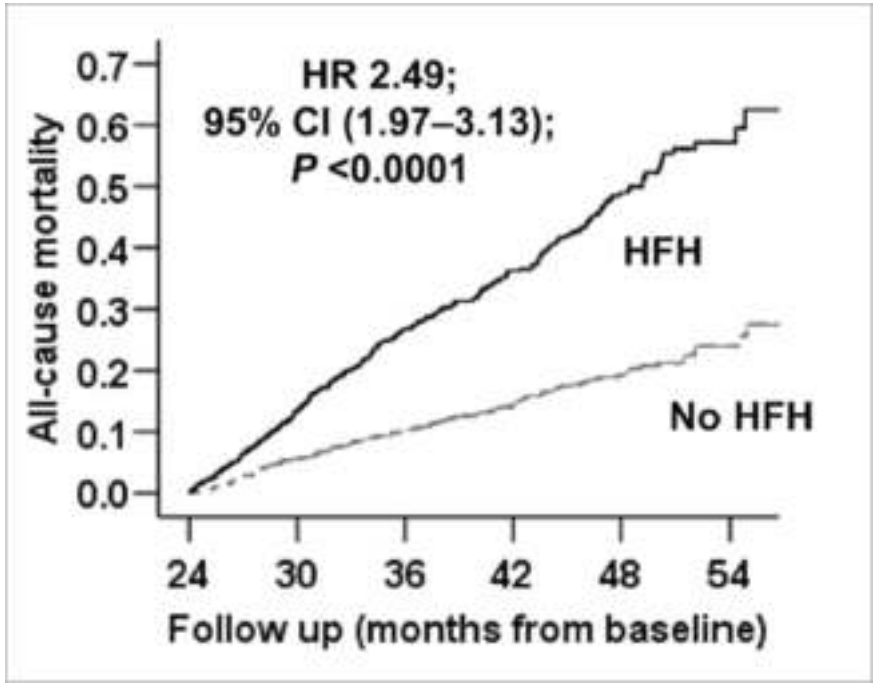


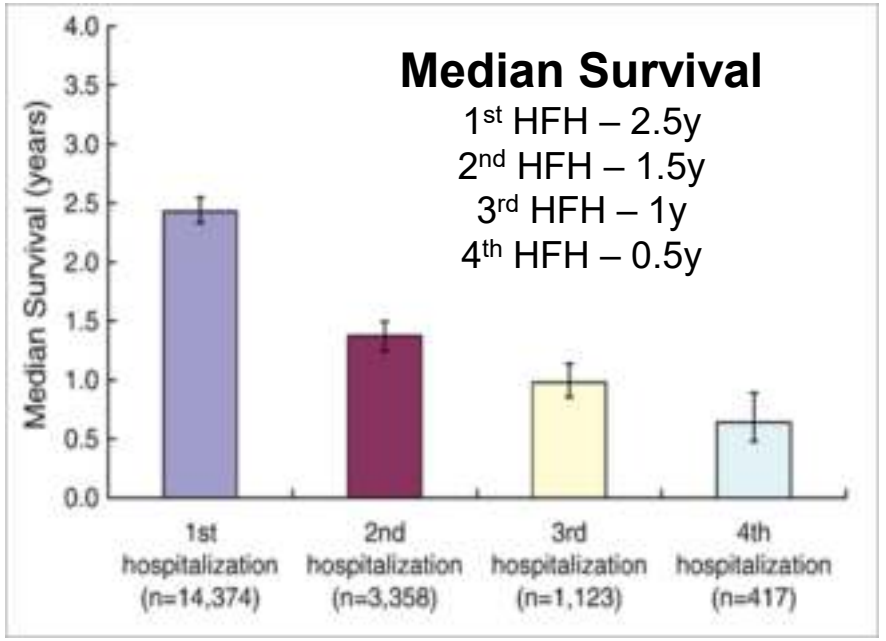
Januzzi, JL and Butler, J. J Am Coll Cardiol 2022 Jul, 80 (2) 123-125

Justin’s View of the Present…

https://petedeutschman.com/2018/04/20/what-is-the-purpose-of-a-rear-view-mirror/

Heart Failure Hospitalizations is a Sentinel Event

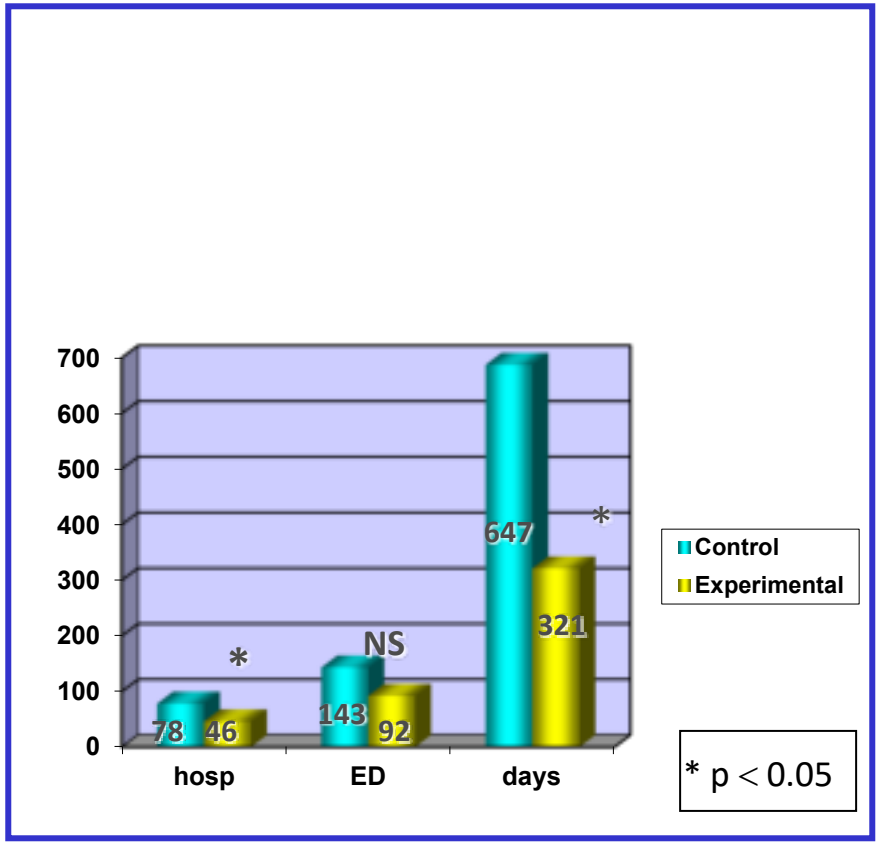


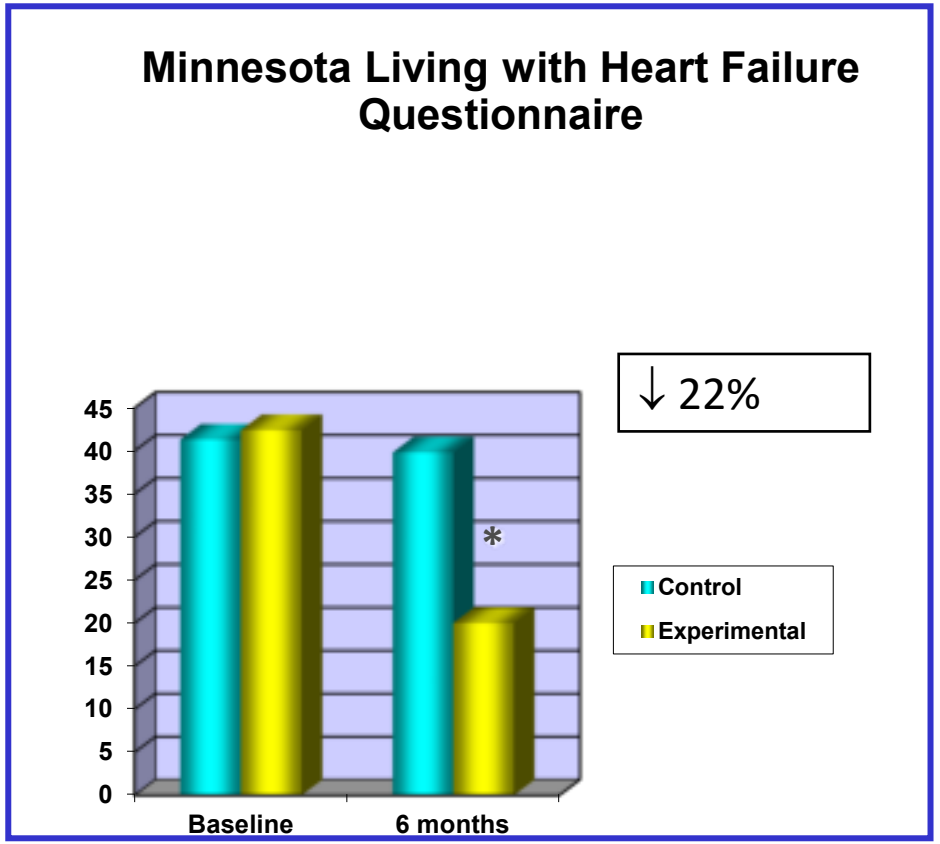


Medicare beneficiaries **risk adjusted 1-year mortality** after HFH **29.6%**

Ahmed, et al, J Card Fail 2008;14:221.
Setoguchi et, Stevenson, Schneeweiss. Am H J. 2007;154:260-6.
Chen et al JAMA 2011;306(15):1669-1678.

Disease Management Programs for HF
Results after 6 Months of Follow-up

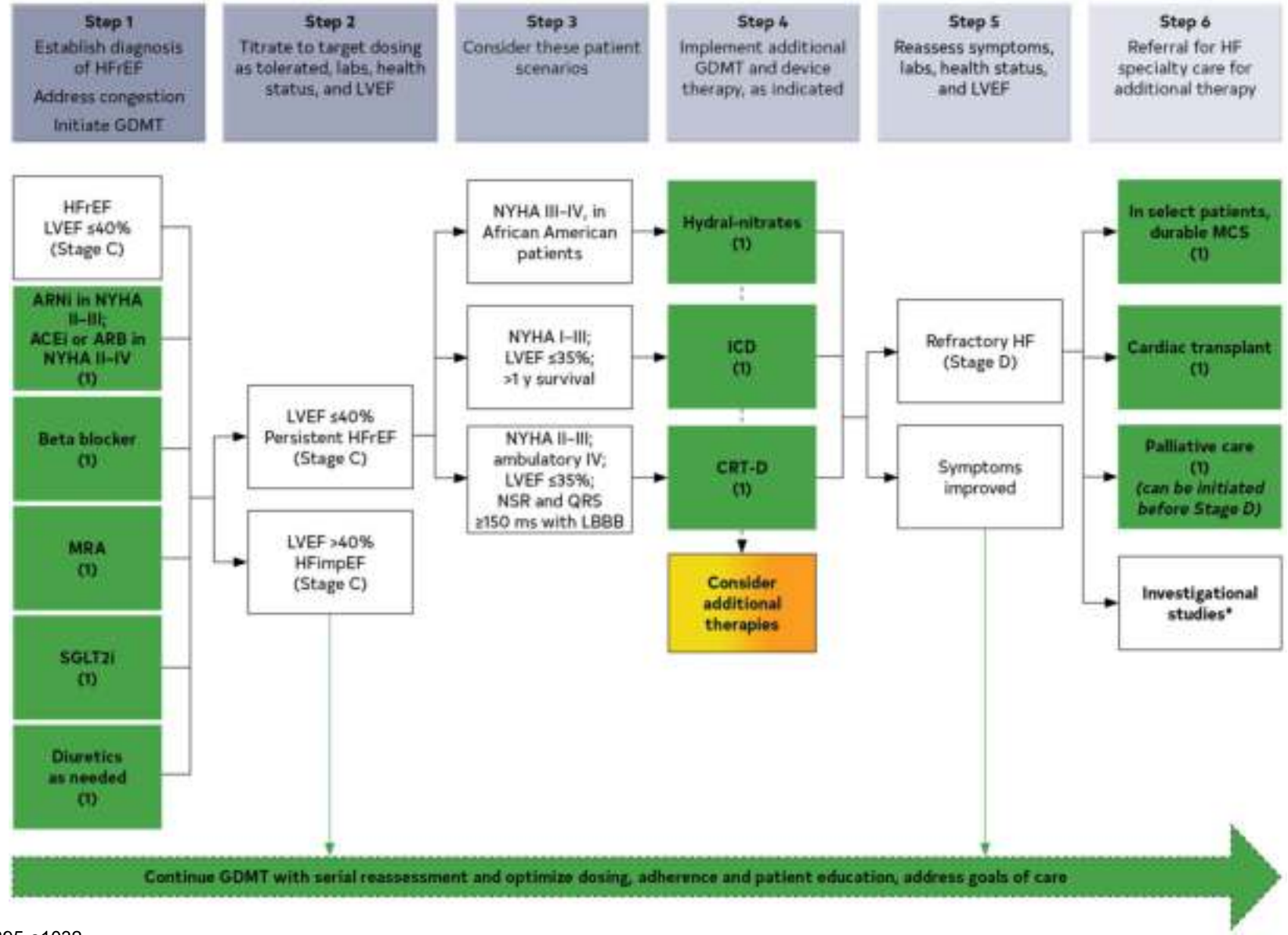




DELTA (%)	**41**	**35**	**53**

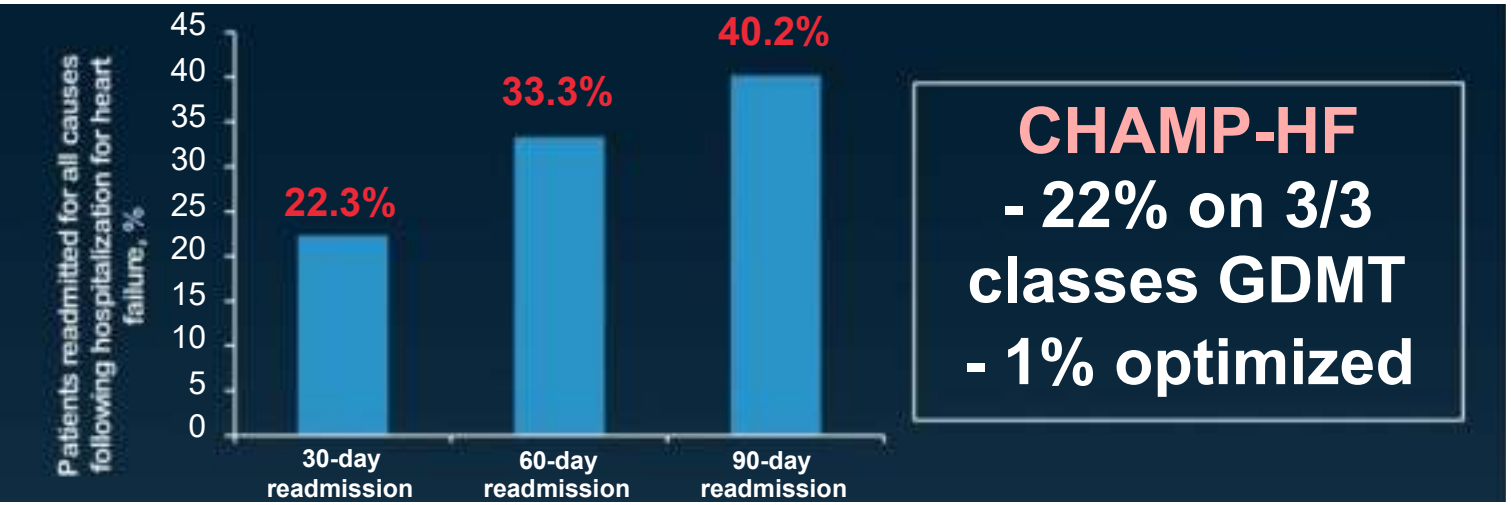
Ducharme *et al*, CMAJ 2005; 173:40-45

Heart Failure Management 2.0



Heidenrich et al. Circulation. 2022;145:e895-e1032

Why Remote Patients Monitoring in HF? Mismatch outcomes vs resources



- High readmission/mortality rates[1]
- Low rates GDMT utilization[2] with poor GDMT titration[3]
- clinical inertia -> 48.6% visits without any GDMT changes despite not at target dose

1 Solomon SD Circ 2017;10:63-70 2. Greene S JACC 2018 Jul, 72 (4) 351-366; ; 3. Swat S JACC: HF Vol 11 (11), No 2023, 1592-944.
4. AAMC 2022 Physician Specialty Data report 5. Kaiser Family Foundation Data; 5. Kaiser Family Foundation Data

Management Based on Signs and Symptoms or Non-hemodynamic Parameters Does Not Work

	TRIAL	n	PARAMETER MONITORED	IMPACT ON PREVENTION	JOURNAL
Clinical Congestion (Symptoms)	**Tele-HF**[28]	1,653	Signs/symptoms, daily weights	**None**	*The New England Journal of Medicine*, 2010
	TIM-HF[29]	710	Signs/symptoms, daily weights	**None**	*Circulation*, 2011
	TEN-HMS[30]	426	Signs/symptoms, daily weights, BP, nurse telephone support	**None**	*The New England Journal of Medicine*, 2005
	BeAT-HF[31]	1,437	Signs/symptoms, daily weights, nurse communications	**None**	*JAMA Internal Medicine*, 2016
	EMPOWER[32]	552	Daily weights, electronic pill dispenser	**None**	*JAMA Internal Medicine,* 2022
Non-hemodynamic markers	**DOT-HF**[33]	335	Intrathoracic impedance with patient alert	**Increased**	*Circulation*, 2011
	OptiLink[34]	1,002	Intrathoracic impedance	**None**	*European Heart Journal*, 2016
	REM-HF[35]	1,650	Remote monitoring via ICD, CRT-D or CRT-P	**None**	*European Heart Journal*, 2017
	MORE- CARE[36]	865	Remote monitoring of advanced diagnostics via CRT-D	**None**	*Journal of Medical Internet Research*, 2013
	Total	**8,630**	**Multiple trials showing no benefit with traditional management**	**Total**	

Heart Failure Management 2.0

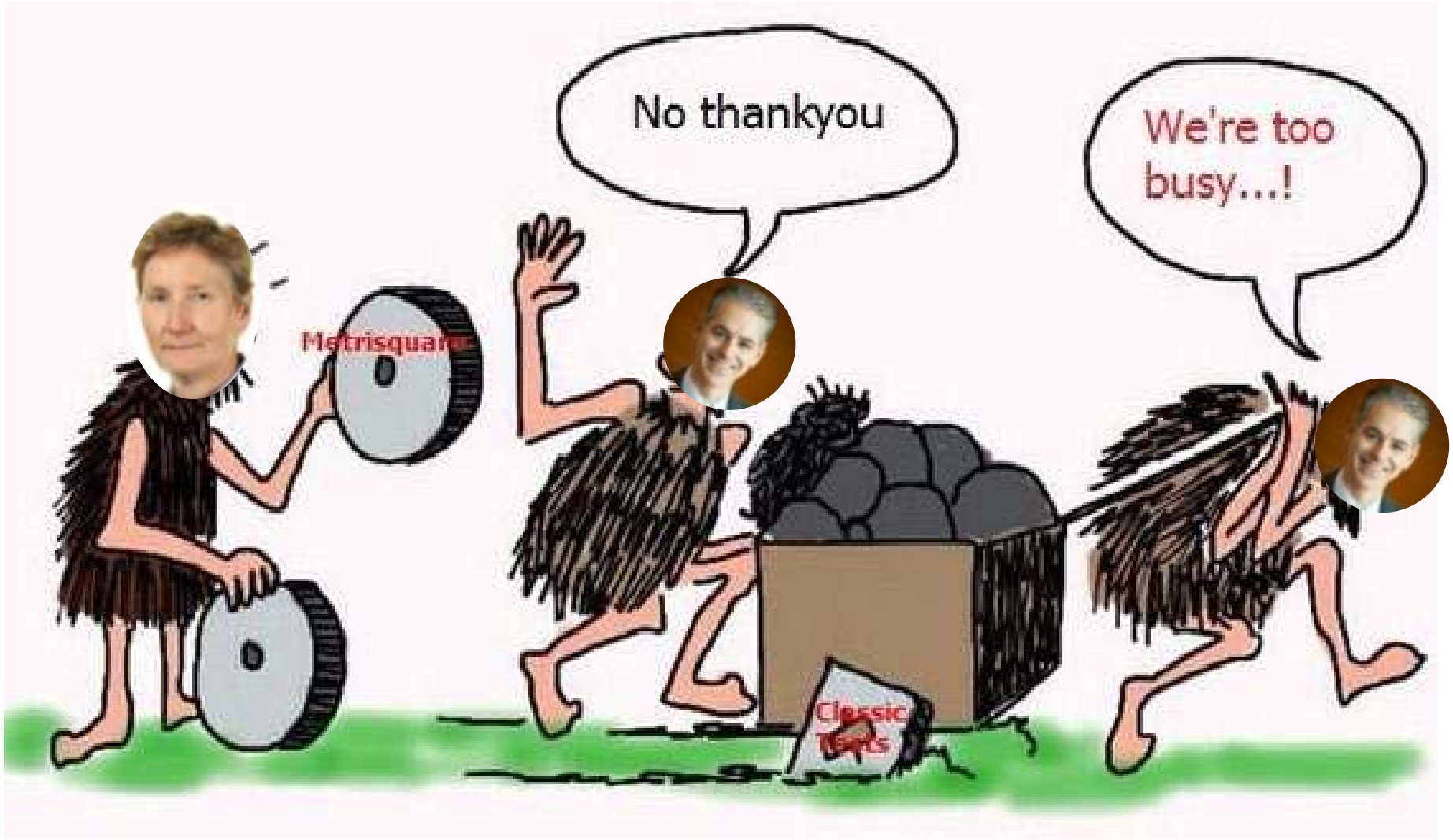
Reactive

Generic

Dogmatic

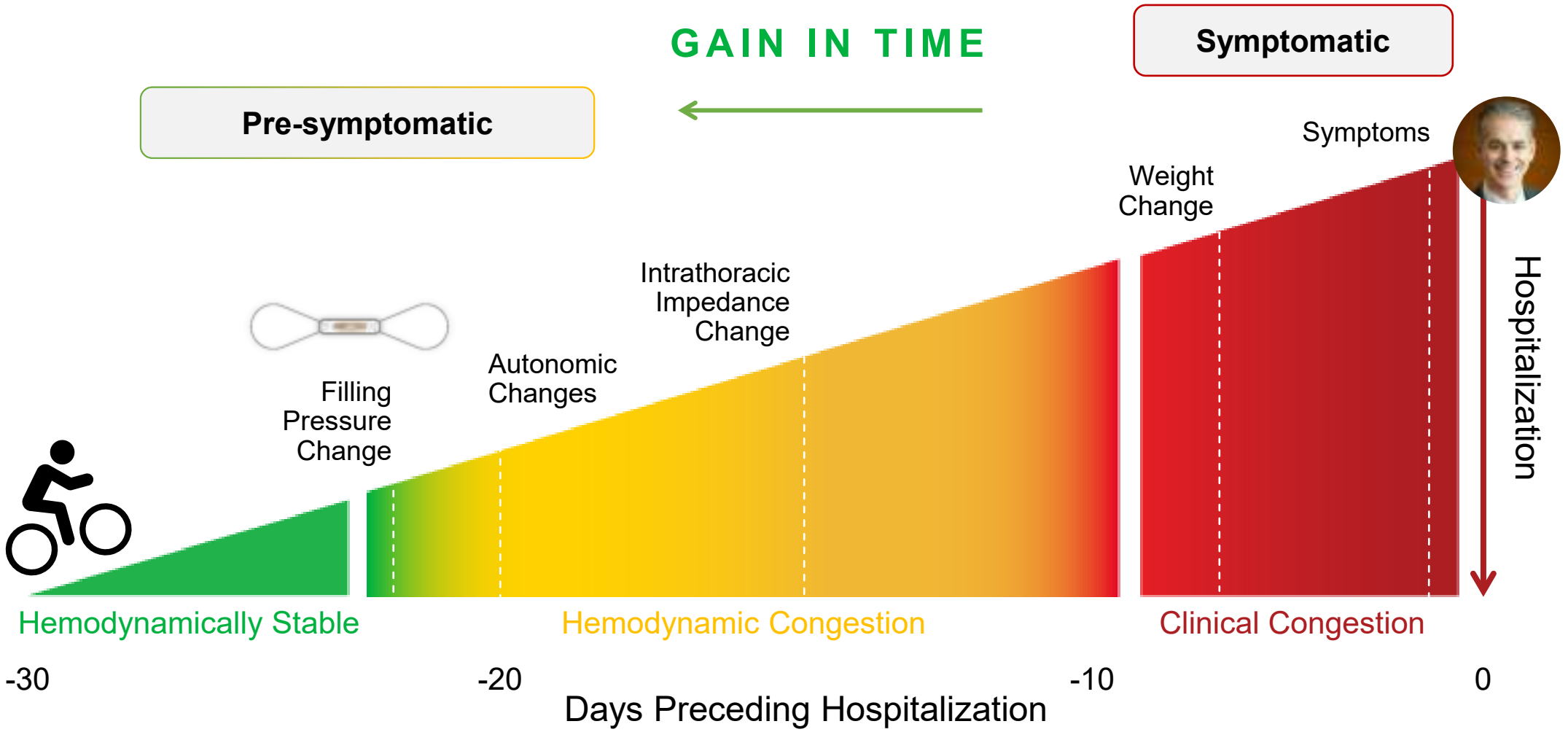
Modified from: P Mc Cann, THT 2024

We Must To Do Things Differently…



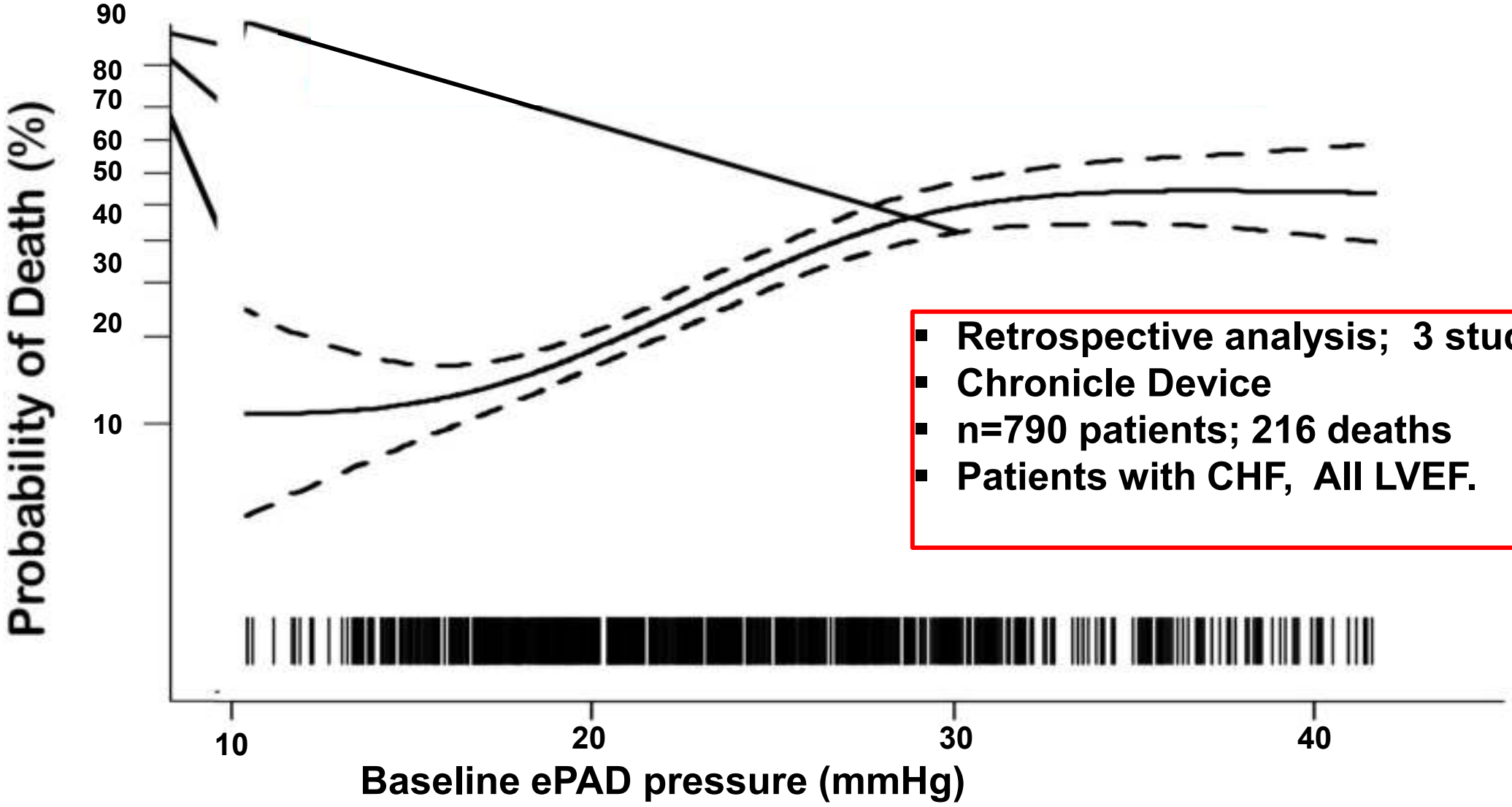
https://s-media-cache-ak0.pinimg.com

Heart Failure Progression is Like a Hill Ride



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;6:287-292.

Baseline Filling Pressure Predicts Mortality In CHF Patients

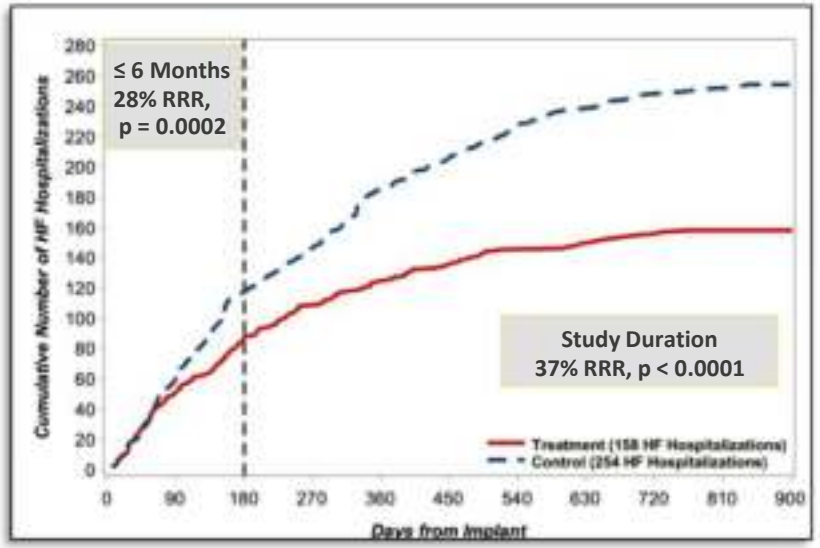


- Retrospective analysis; 3 studies
- Chronicle Device
- n=790 patients; 216 deaths
- Patients with CHF, All LVEF.

Zile et al, Circ-HF. 2017.

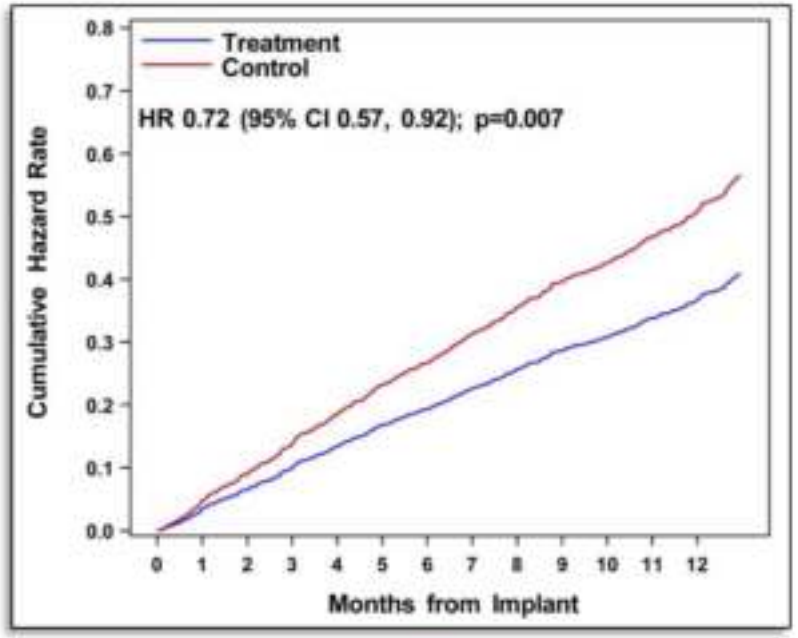
Robust Evidence of Reduction in HF Hospitalizations with Ambulatory Hemodynamic Management

CHAMPION (N=550)



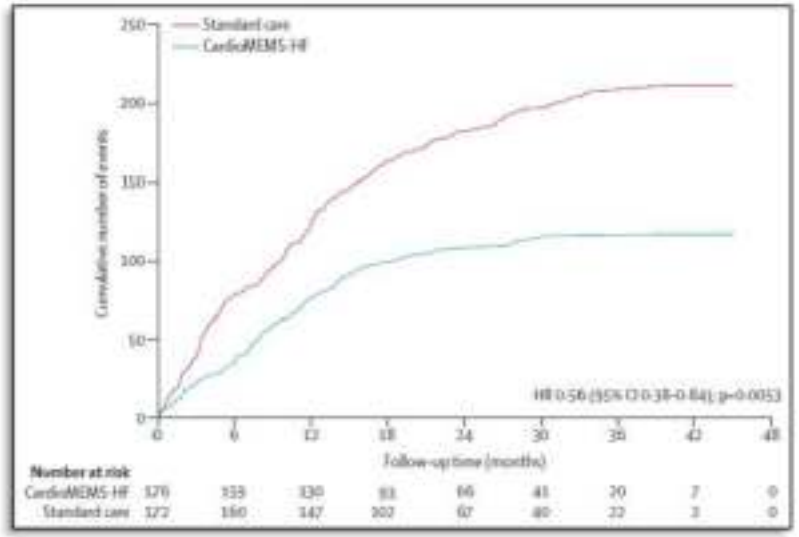
28%

GUIDE-HF (N=1000)



28%

MONITOR-HF (N=348)



44%

Consistent effects regardless of EF and in those without prior HFH

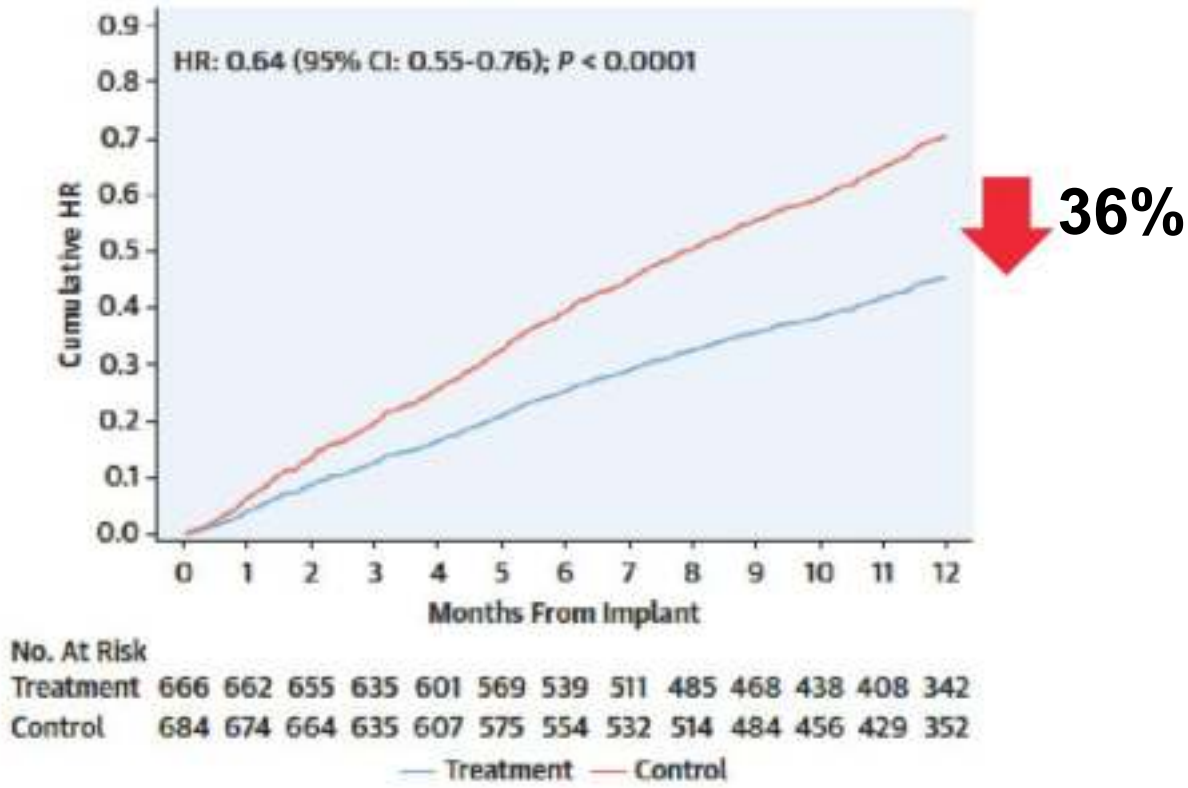
Modified from: AS Desai. THT 2024

Brugts JJ Lancet 2023; Lindenfield J Lancet, 2021; Abraham WT Lancet 2011

Lower Rates of HFH and Mortality with Hemodynamic Management in HFrEF

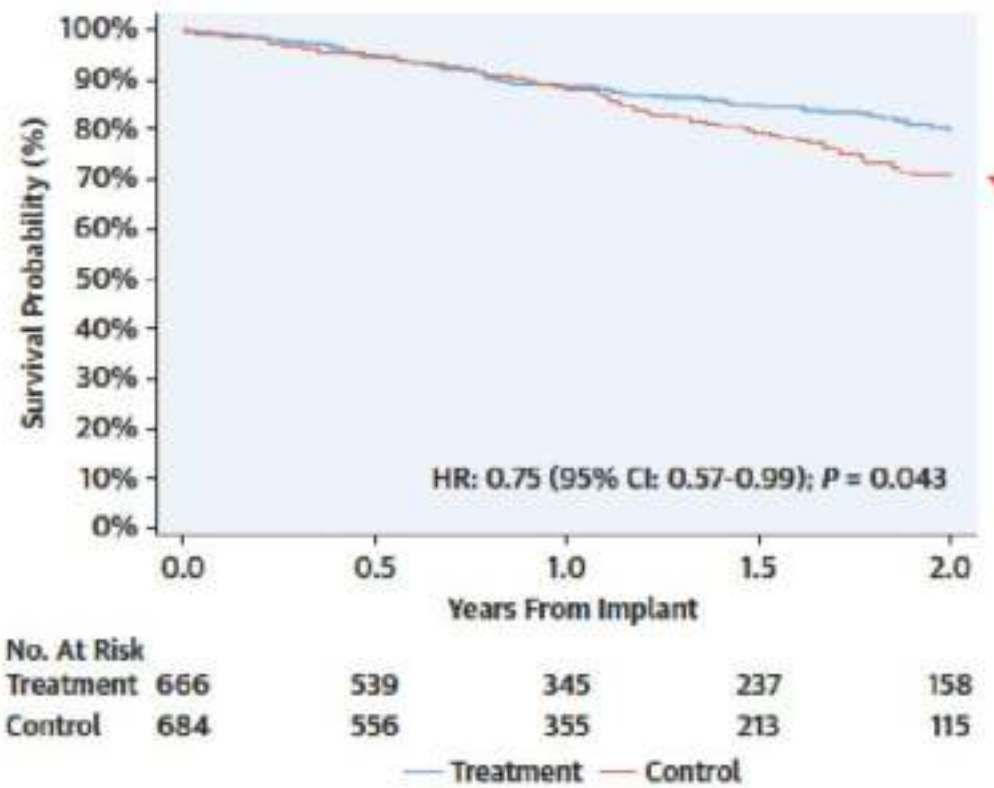
Pooled CHAMPION, GUIDE-HF, LAPTOP-HF

HF HOSPITALIZATIONS



36%

MORTALITY



25%

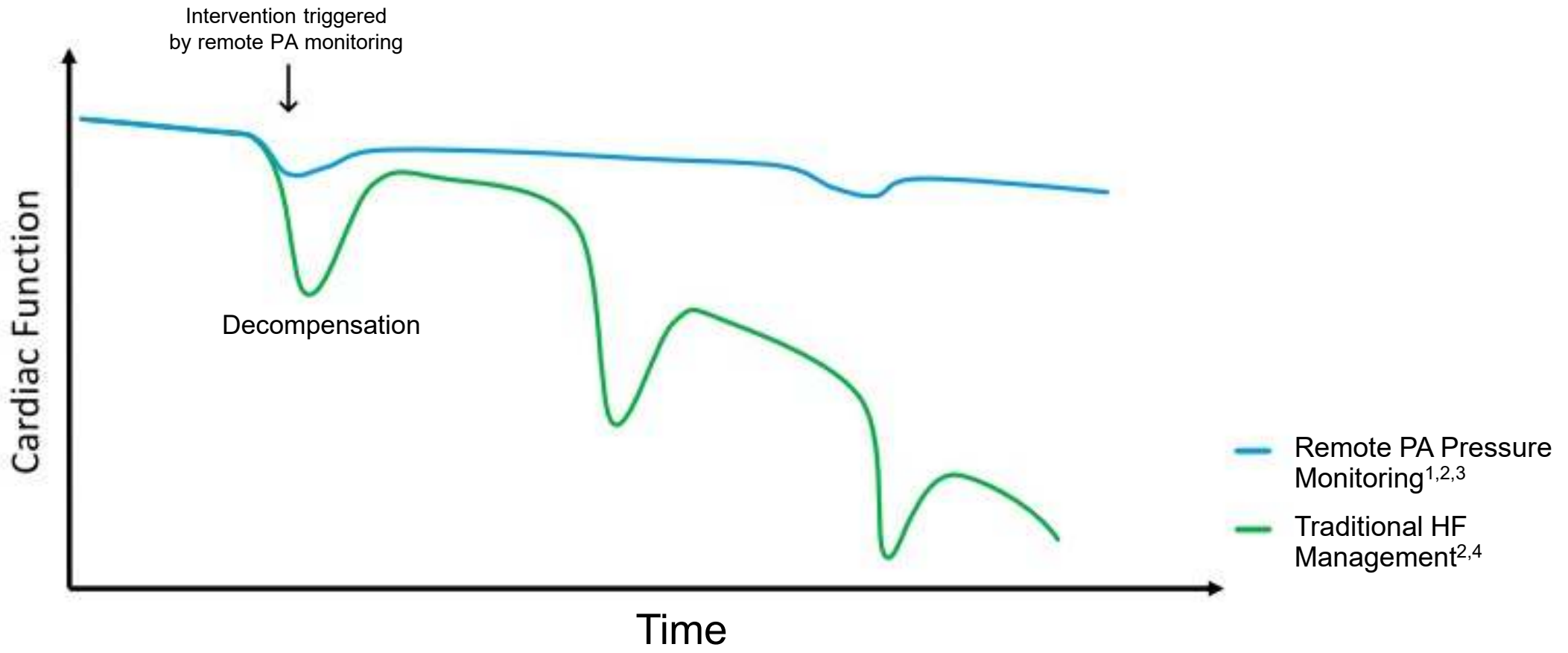
Trials of novel PAP sensors, LAP and IVC pressure sensors ongoing

Lindenfeld J, et al. J Am Coll Cardiol 2024

Modified from: AS Desai. THT 2024

Slow the Progression of Heart Failure

REMOTE PA PRESSURE MANAGEMENT PROVIDES EARLY DETECTION OF ELEVATED PAP



1. Cowie MR, et al. *ESC Heart Fail.* 2021. **2.** Angermann C, et al. *Eur J Heart Fail.* 2020.
2. **3.** Lindenfeld J, et al. *The Lancet.* 2021. **4.** Gheorghiade MD, et al. *Am J. Cardiol,* 2005.

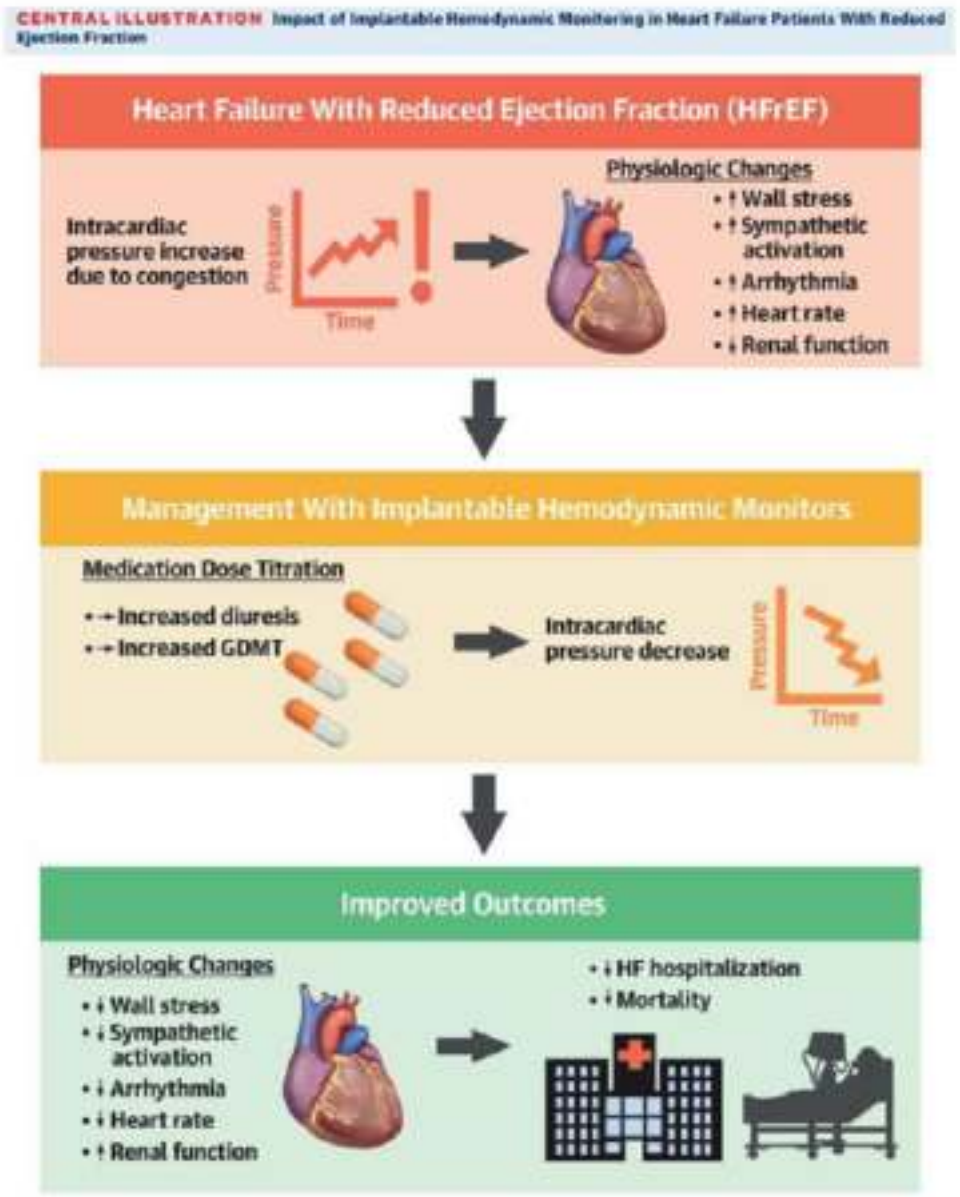
HF Management 3.0

PROACTIVE

TAILORI

EVIDENCE BASED

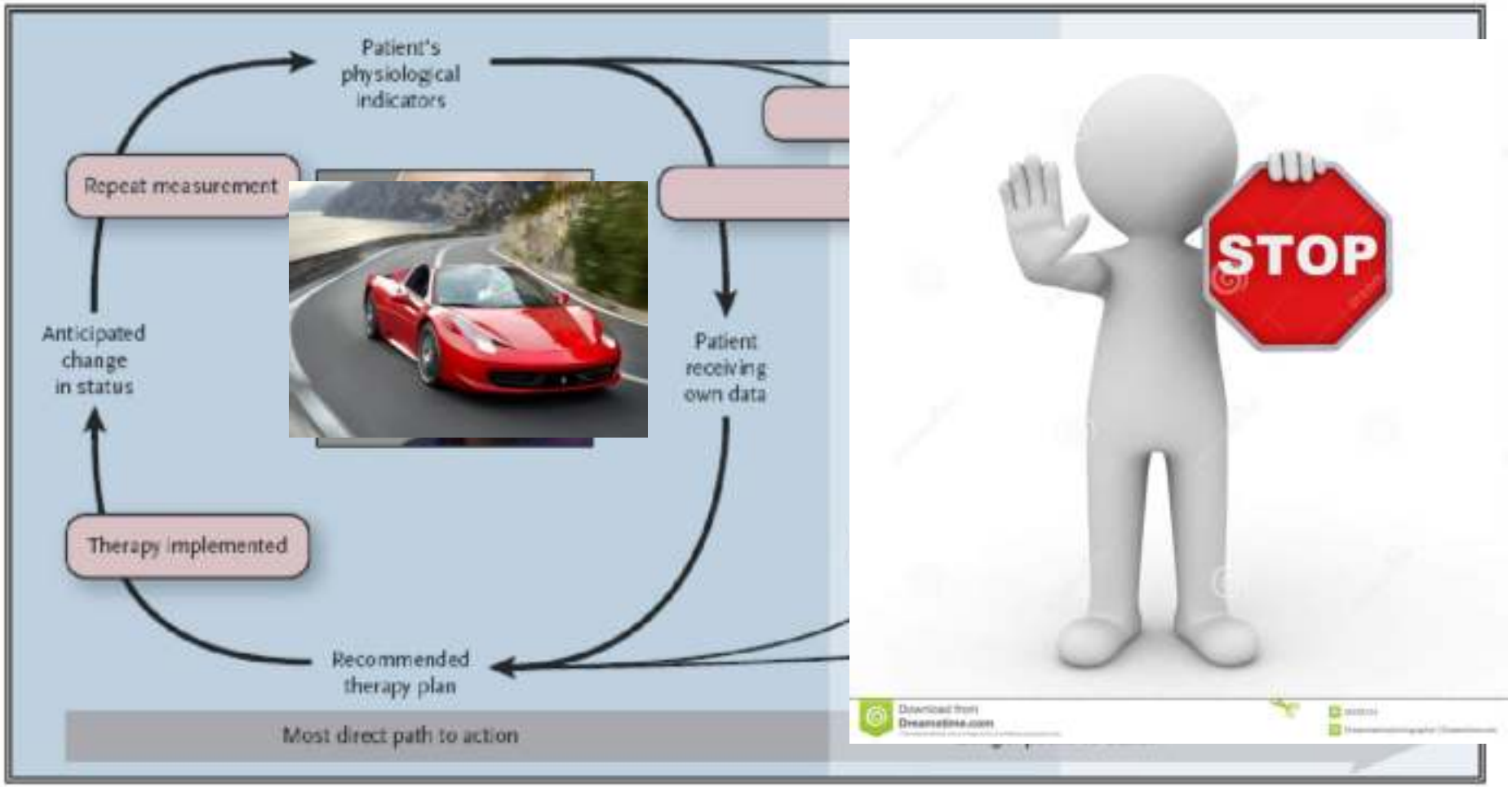
INFORMATION BASED



Lindenfeld et al JACC VOL.83, NO.6 2024 FEBRUARY 13, 2024:682 - 694

Modified from: P Mc Cann, THT 2024

The Patient at the Centre: Empowerment



Desai AS and Warner-Stevenson L. Editorial. NEJM Nov 2010

Is Canada Ready for Implantable Hemodynamic Monitoring?

- The indirect measures of congestion available for monitoring HF remotely are not good
  - Weight, Blood Pressure, Symptoms, Impedance
- Managing Heart Failure by **Managing Pressures**
  - ↓↓↓ HFH, regardless of LVEF (since 2011)
  - Improve survival (HFrEF)
- The real question: What does **Justin** want?

Lived Experience Commentary

Jillianne Code
PhD

Disclosures

No disclosures

Q&A Period

All panelists

THANK YOU!

Please remember to complete the session evaluation

Next Up! ***Day 1 Highlights from the Co-Chairs*** **and** ***Welcome Reception & Networking Event in the Exhibit Hall (Samuel ABC)***

Co-Chair Highlights
Plenary 1:
Healing Hearts

Closing the Gaps: A Call to Action

Implement Evidence-Based Strategies

Adopt and scale up interventions proven to increase GDMT use such as CDST, transitional care programs, and prescription coverage. Leverage multi-disciplinary teams and enhanced interdisciplinary collaboration.

Ensure Equitable Access

Prioritize underserved populations and address socioeconomic determinants to guarantee all Canadians receive high-quality, guideline-concordant heart failure care regardless of background or circumstances.

Tailor Solutions for Local Contexts

Recognize diverse barriers across health systems, clinics, providers, and patients. Adapt evidence-based strategies to local settings through stakeholder engagement and pragmatic trials evaluating implementation outcomes.

Engaging Patients as Partners

Develop and implement culturally appropriate education, self-management support tools in collaboration with patients to improve adherence & address barriers. Focus on PREMS and PROMS that are meaningful to patients/families.

Coordinate System-Wide Approach

Engage policymakers, health authorities, clinicians, researchers, industry, and patient advocates in a coordinated, multi-level effort to develop, fund, and operationalize implementation solutions.

Integrated Model to HF Care for JHB HF Patients

Co-developed model over last year – and continue to refine as we move ahead

In-person clinics (across 5 JHB communities)

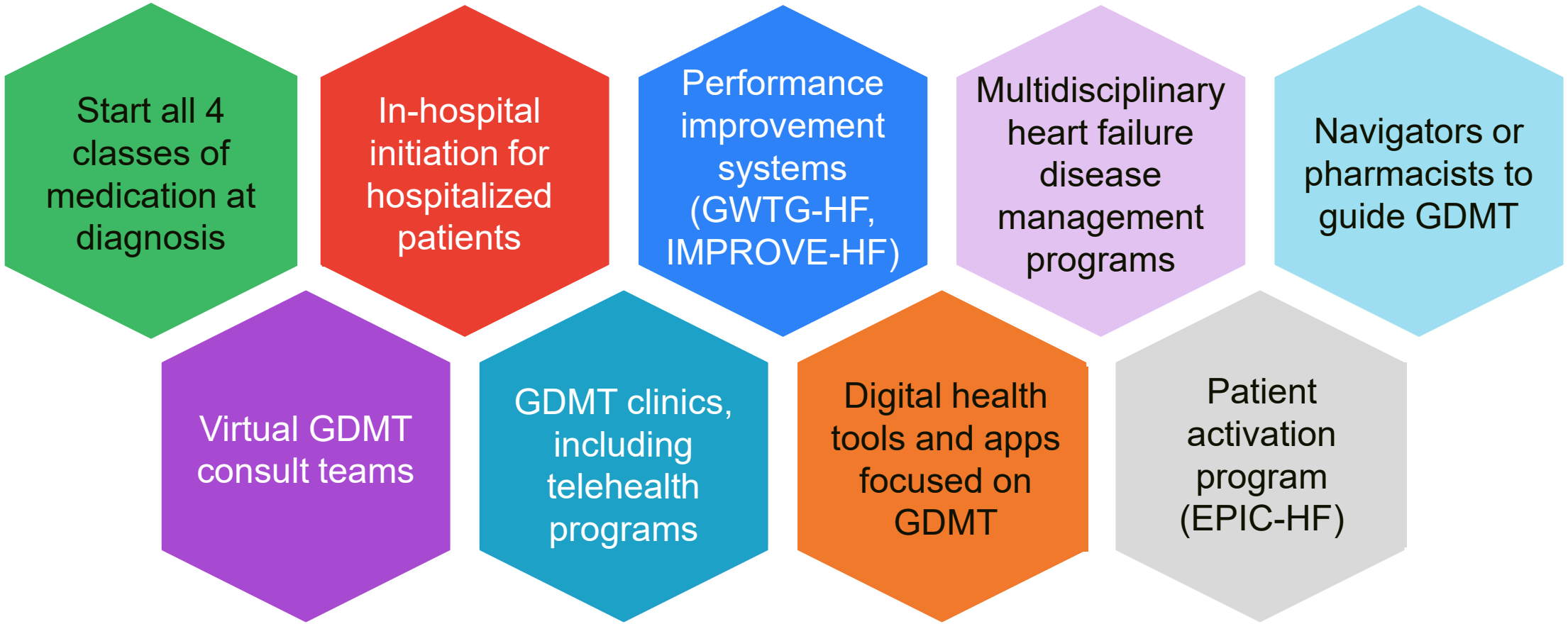
+

Support through virtual clinics

+

Working closely with WAHA based Clinical Coordinator

Strategies to Help Facilitate GDMT Initiation



Patolia H…Greene SJ. *JACC* 2023

Conclusions

Use	Use positive and understandable language to communicate and engage with patients and care partners
Acknowledge	Acknowledge the longitudinal journey and transitions when caring for HF patients
Apply	Apply methods to improve resiliency in patients and in health care practitioners

Co-Chair Highlights
Plenary 2:
Clinical Pearls and Conundrums

JACC HF: Great Papers in Past Year Dr. Bozkurt

Major Progress

Update in Management of HFpEF, HFrEF

Management of Comorbidities Obesity, Afib, CKD, Prevention of HF

Devices, Technology, Wearables, Shock, VAD/Tx

Genetic, Cardiomyopathies Myocarditis, Pregnancy

Combination Therapy in HFmrEF and HFpEF: Network Meta-Analysis

Recent pub.

CENTRAL ILLUSTRATION: Combination Treatment Effects

A Complex Intervention	Primary Outcome	HR	[95% CI]	z	P Value
ARNI + BB + MRA + SGLT2i		0.47	[0.31–0.70]	−3.70	<0.01
RASi + BB + MRA + SGLT2i		0.51	[0.34–0.74]	−3.46	<0.01
ARNI + MRA + SGLT2i		0.56	[0.43–0.71]	−4.61	<0.01
ARNI + BB + SGLT2i		0.57	[0.40–0.82]	−3.04	<0.01
ARNI + BB + MRA		0.58	[0.39–0.86]	−2.70	<0.01
RASi + BB + SGLT2i		0.62	[0.44–0.87]	−2.76	<0.01
RASi + BB + MRA		0.63	[0.43–0.92]	−2.41	0.02
MRA + SGLT2i		0.66	[0.54–0.80]	−4.18	<0.01
ARNI + SGLT2i		0.68	[0.57–0.81]	−4.29	<0.01
ARNI + MRA		0.69	[0.55–0.88]	−3.08	<0.01
ARNI + BB		0.71	[0.50–1.01]	−1.91	0.06
RASi + BB		0.77	[0.55–1.07]	−1.56	0.12
RASi + Dig		0.81	[0.63–1.04]	−1.69	0.09
BB		0.84	[0.61–1.15]	−1.08	0.28
RASi		0.92	[0.83–1.01]	−1.75	0.08

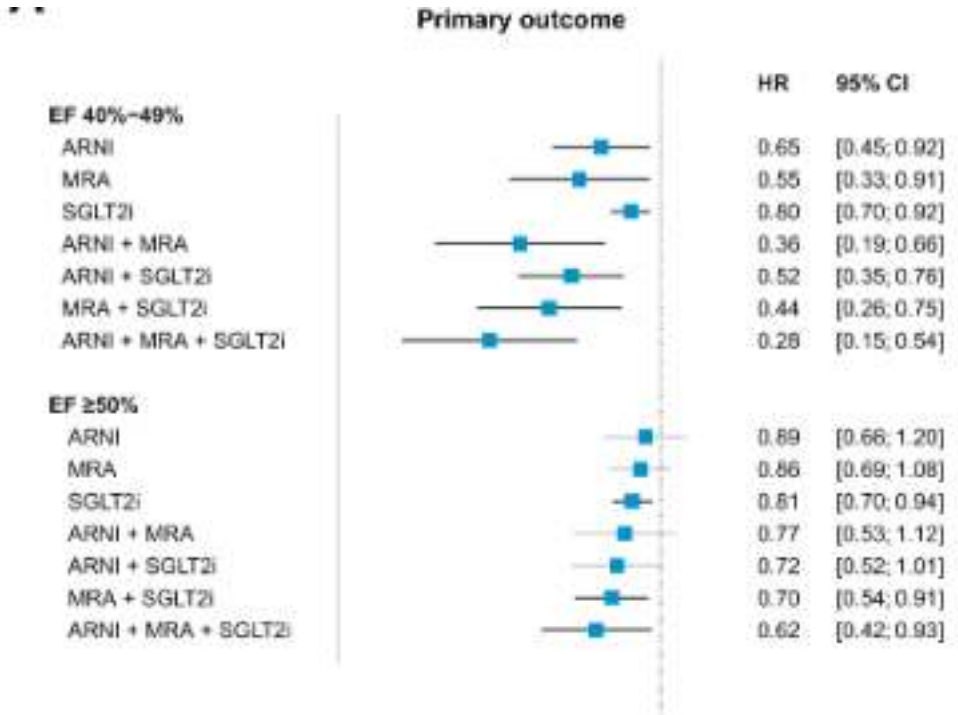
0.5 1 2

B Complex Intervention	Cardiovascular Death	HR	[95% CI]	z	P Value
ARNI + BB + MRA + SGLT2i		0.55	[0.32–0.95]	−2.16	0.03
RASi + BB + MRA + SGLT2i		0.58	[0.35–0.96]	−2.14	0.03
ARNI + BB + MRA		0.62	[0.37–1.04]	−1.82	0.07
ARNI + MRA + SGLT2i		0.63	[0.43–0.91]	−2.43	0.01
RASi + BB + MRA		0.64	[0.40–1.05]	−1.78	0.07
MRA + SGLT2i		0.67	[0.50–0.89]	−2.71	<0.01
ARNI + MRA		0.70	[0.49–0.99]	−2.00	0.05
ARNI + BB + SGLT2i		0.75	[0.47–1.19]	−1.22	0.22
RASi + BB + SGLT2i		0.78	[0.51–1.20]	−1.13	0.26
ARNI + BB		0.83	[0.53–1.30]	−0.80	0.42
ARNI + SGLT2i		0.85	[0.65–1.10]	−1.21	0.23
RASi + BB		0.87	[0.58–1.30]	−0.67	0.50
BB		0.88	[0.60–1.29]	−0.65	0.52
RASi		0.99	[0.87–1.12]	−0.18	0.85
RASi + Dig		0.99	[0.71–1.38]	−0.07	0.95

0.5 1 2

Zafeiropoulos S, et al. J Am Coll Cardiol HF. 2024;12(4):616–627.

- In patients with HF and LVEF>40%, quadruple ARNI, BB, MRA, SGLT2i ➔largest reduction in the risk of CV death and HHF
- The benefit more pronounced in HFmrEF patients.



Zafeiropoulos, S, Farmakis, I, Milioglou, I. et al. Pharmacological Treatments in Heart Failure With Mildly Reduced and Preserved Ejection Fraction: Systematic Review and Network Meta-Analysis. J Am Coll Cardiol HF. 2024 Apr, 12 (4) 616–627.

PARAGLIDE: ARNi stabilized post WHF in HF EF>40%

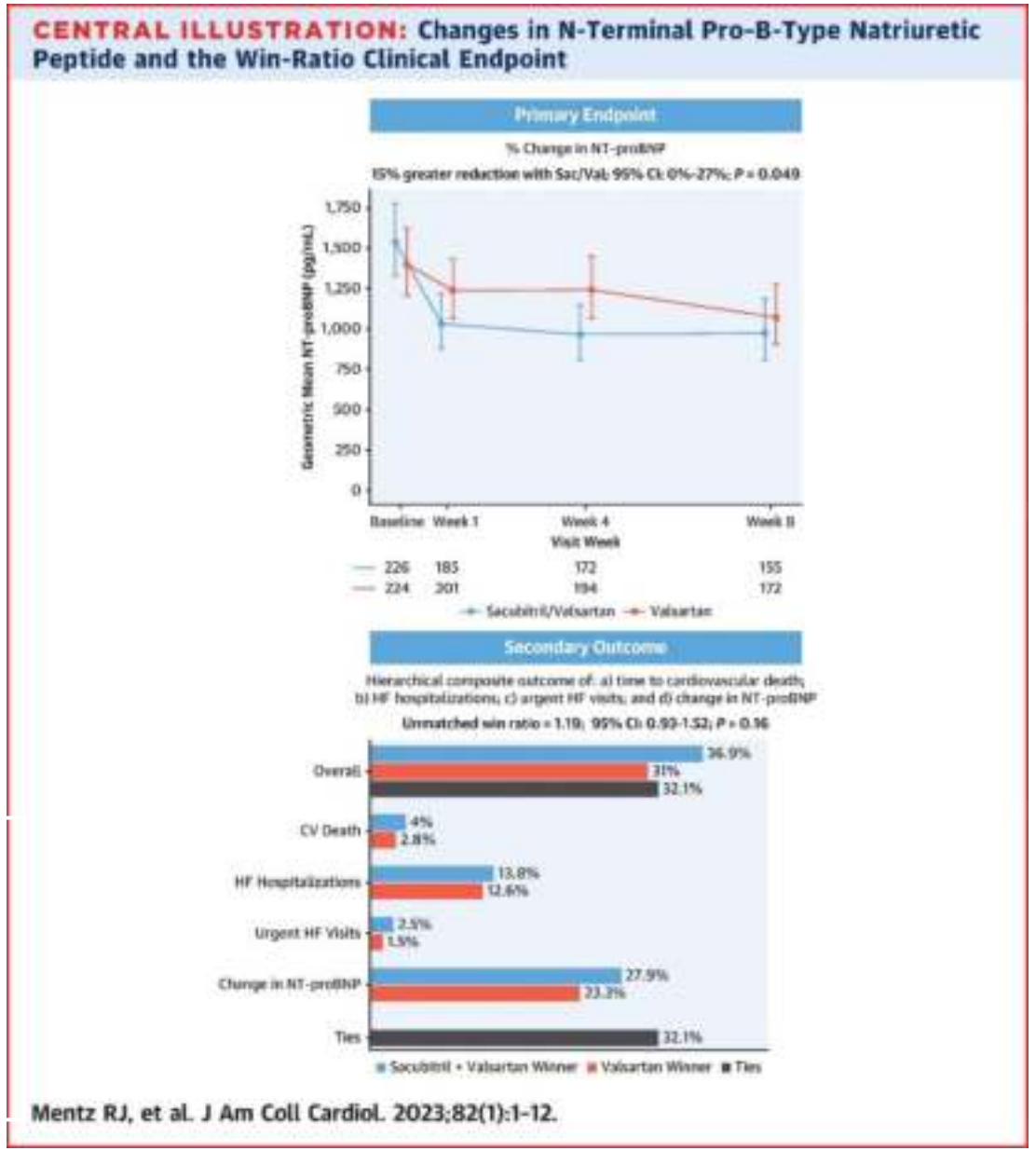
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 82, NO. 1, 2023

ORIGINAL INVESTIGATIONS

Angiotensin-Neprilysin Inhibition in Patients With Mildly Reduced or Preserved Ejection Fraction and Worsening Heart Failure

Robert J. Mentz, MD,[a] Jonathan H. Ward, PharmD,[b] Adrian F. Hernandez, MD, MHS,[a] Serge Lepage, MD,[c] David A. Morrow, MD, MPH,[d] Samiha Sarwat, PhD,[b] Kavita Sharma, MD,[e] Randall C. Starling, MD, MPH,[f] Eric J. Velazquez, MD,[g] Kristin M. Williamson, PharmD,[b] Akshay S. Desai, MD, MPH,[d] Shelley Zieroth, MD,[h] Scott D. Solomon, MD,[d] Eugene Braunwald, MD,[d] on behalf of the PARAGLIDE-HF Investigators

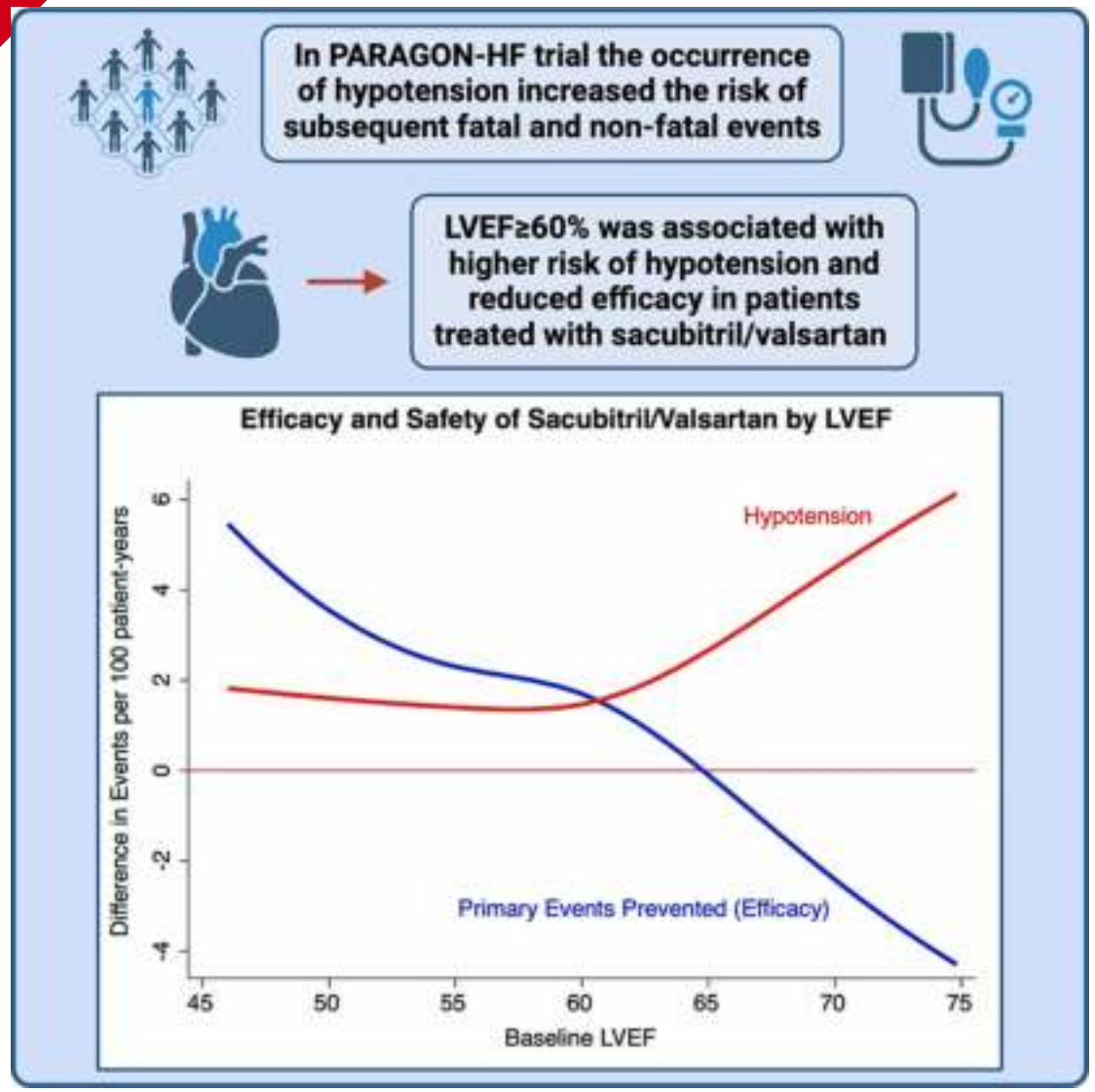
- 466 pts EF>40% within 30 days of WHF
- Greater NT-proBNP with ARNi
- Hierarchical outcome ns
- Larger treatment effect EF≤60



Mentz RJ, et al. J Am Coll Cardiol. 2023;82(1):1-12.

Recent pub.

Heterogeneity: LVEF>60% Associated with Higher Risk of Hypotension & Reduced Efficacy with ARNi in PARAGON Trial



- 13% experienced hypotension, more frequently in the sacubitril/valsartan arm ($p<0.001$).
- Patients with hypotension had higher risk of CVD and total HFH (RR 1.63; CI 1.27-2.09; $p<0.001$) and all-cause death (HR 1.62; CI 1.28-2.05; $p<0.001$).
- LVEF≥60% experienced substantially higher treatment-related risks of hypotension.

Foà, A, et al. Sacubitril/Valsartan-Related Hypotension in Patients with Heart Failure and Preserved or Mildly Reduced Ejection Fraction. J Am Coll Cardiol. null2024, 0 (0) .https://doi.org/10.1016/j.jacc.2024.02.035

Comparison of US and European HF Guidelines

	ACC/AHA/HFSA		ESC
HFrEF	• ARNi preferred over ACEi • ↑ COR for H+ISDN in self-identified Black patients • Adjunctive PUFA & K⁺ binders • ↓ QRSd threshold for CRT	• Similar diagnostic tools • ARNi/ACEi/ARB + BB + MRA + SGLT2i • Rapid GDMT initiation and optimization • ICD in iCM if LVEF ≤35%	• ACEi or ARNi preferred • ↑ COR for intravenous iron supplementation • ↓ threshold for MV TEER • ↓ COR for ICD in niCM
HFmrEF & HFimpEF	• HFimpEF explicitly included as HF subtype	• ARNi/ACEi/ARB + BB + MRA + SGLT2i • GDMT should be continued in HFimpEF	• HFimpEF implicitly included as HF subtype
HFpEF	• ARNi/ARB and MRA selectively recommended in addition to SGLT2i	• Simplified diagnostic approaches • SGLT2i as foundational therapy • Focus on comorbidity management	• No other pharmacotherapies recommended
Key Strengths	• Formal cost/value statements • Emphasis on HF trajectory • Explicit attention to equity & healthcare disparities • Pledge for continuous & dynamic guideline updates	• Patient-centered recommendations • Multistakeholder representation • Simplified treatment algorithms • Focus on special populations and HF prevention	• Patient-centered deliverables • High-yield practical guidance for GDMT use • Focus on CKD as risk factor • Explicit guidance to facilitate patients' self-care goals

Table: Comparison of American and European Medical Therapy Recommendations for the Management of HF

Condition	Recommendation	ACC/AHA/HFSA		ESC	
HFrEF	Diuretics to alleviate signs/symptoms of congestion	1	B-NR	1	C
	ACEi if ARNi not feasible	1	A	-	-
	ACEi to reduce morbidity and mortality	-	-	1	A
	ARNi to reduce morbidity and mortality	1	A	-	-
	ARNi as a replacement for ACEi	1	B-R	1	B
	ARB if intolerant of ACEi and ARNi not feasible	1	A	1	B
	BB to reduce mortality and hospitalizations	1	A	1	A
	MRA to reduce morbidity and mortality	1	A	1	A
	SGLT2i to reduce HF hospitalization and CV death	1	A	1	A
	H+ISDN to reduce morbidity and mortality in self-identified Black patients	1	A	2a	B
	H+ISDN if unable to tolerate or contraindicated for first-line agents	2b	C-LD	2b	B
	Digoxin if symptomatic despite GDMT (or intolerant to GDMT)	2b	B-R	-	-
	Digoxin if symptomatic in SR despite ACEi (or ARNi) + BB + MRA	-	-	2b	B
	Ivabradine if symptomatic with LVEF ≤35% on GDMT (including maximally tolerated BB), in SR with rate ≥70 beats per minute	2a	B-R	2a	B
	Potassium binders in patients with hyperkalemia on GDMT	2b	B-R	-	-
	PUFA if NYHA II-IV	2b	B-R	-	-
	Vericiguat if NYHA II-IV with worsening HF despite GDMT	2b	B-R	2b	B
HFmrEF	Diuretics to alleviate signs/symptoms of congestion	-	-	1	C
	SGLT2i to reduce HF hospitalizations or CV death	2a	B-R	1	A
	ACEi/ARB/ARNi, BB, and MRA to reduce morbidity and mortality	2b	B-NR	2b	C
HFpEF	Diuretics to alleviate signs/symptoms of congestion	1	C-LD	1	C
	SGLT2i to decrease HF hospitalizations or CV death	2a	B-R	1	A
	ARB, ARNi, MRA to decrease hospitalizations	2b	B-R	-	-
HFimpEF	Continue GDMT even if asymptomatic to prevent HF relapse	1	B-R	-	-

Ostrominski, J, et al. Contemporary American and European Guidelines for the Management of Heart Failure: JACC: Heart Failure Guideline Comparison. J Am Coll Cardiol HF.https://doi.org/10.1016/j.jchf.2024.02.020

Global Variations According to Sex in Patients Hospitalized for HF

JACC: HEART FAILURE
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Global Variations According to Sex in Patients Hospitalized for Heart Failu in the REPORT-HF Registry

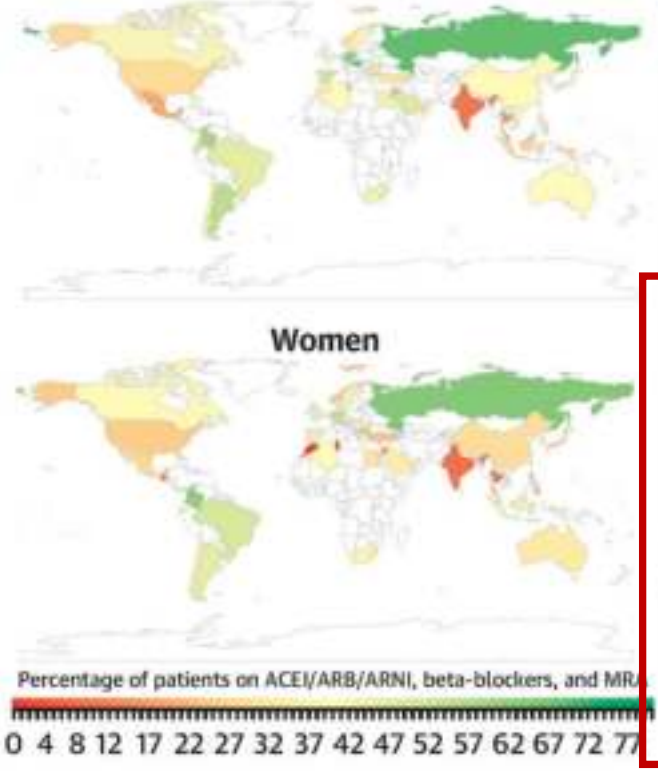
Jasper Tromp, MD, PhD, MPH,[a,b] Justin A. Ezekowitz, MBBCh, MSc,[c] Wouter Ouwerkerk, PhD,[d,e] Chanchal Chandramouli, PhD,[b,f] Kai Hang Yiu, MBBS, PhD,[f,g] Christiane E. Angermann, MD,[h] Ulf Dahlström, MD, PhD,[i] Georg Ertl, MD,[h] Mahmoud Hassanein, MD,[j] Sergio V. Perrone, MD,[k] Mathieu Ghadanfar, MD,[l] Anja Schweizer, PhD,[m] Achim Obergfell, MD,[m] Kenneth Dickstein, MD, Sean P. Collins, MD, MSc,[n] Gerasimos Filippatos, MD,[o,p] John G.F. Cleland, MD, PhD,[q,r] Carolyn S.P. Lam, MBBS, PhD[b,s,t]

CENTRAL ILLUSTRATION: Summary of the Main Findings of This Study

Global Sex Differences in Acute Heart Failure: Results From REPORT-HF

Methods and Design

- Prospective observational cohort study
- 7,181 women 11,372 men
- 44 lower-middle, upper-middle, and higher income countries



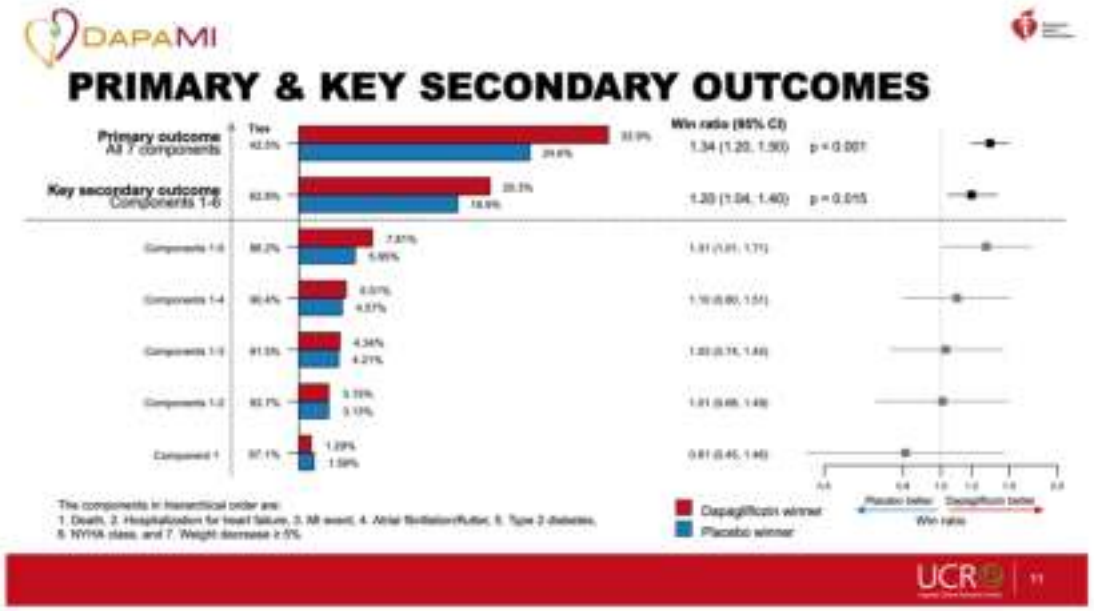
Results

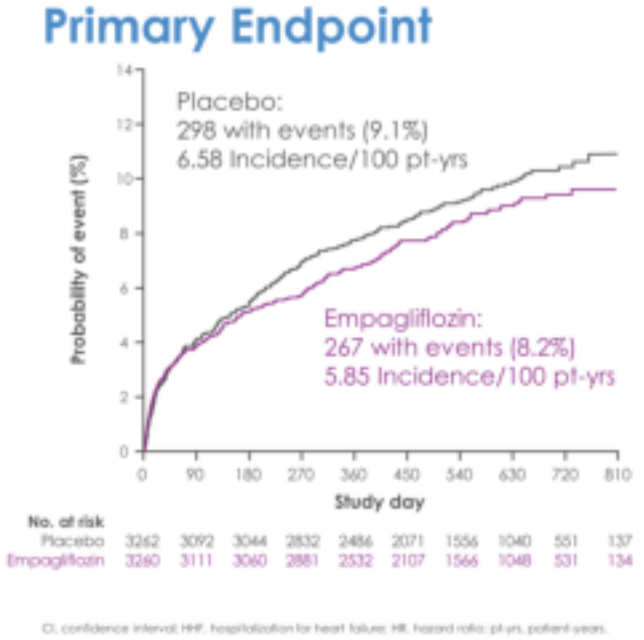
- Women were older, had more comorbidities, and more often HFpEF than men
- Women less often received GDMT and more often medications that might cause or worsen HF
- Women lost their survival advantage in countries with high income disparity

Icons from flaticon.com

Tromp J, et al. J Am Coll Cardiol HF. 2023;11(9):1262-1271.

Late-Breaking Clinical Trials: Dr. Solomon





HR 0.90 (95% CI: 0.76, 1.06)
p=0.21

565 primary endpoint events
- **271 (48%) first events: HHF**
- **294 (52%) first events: death**

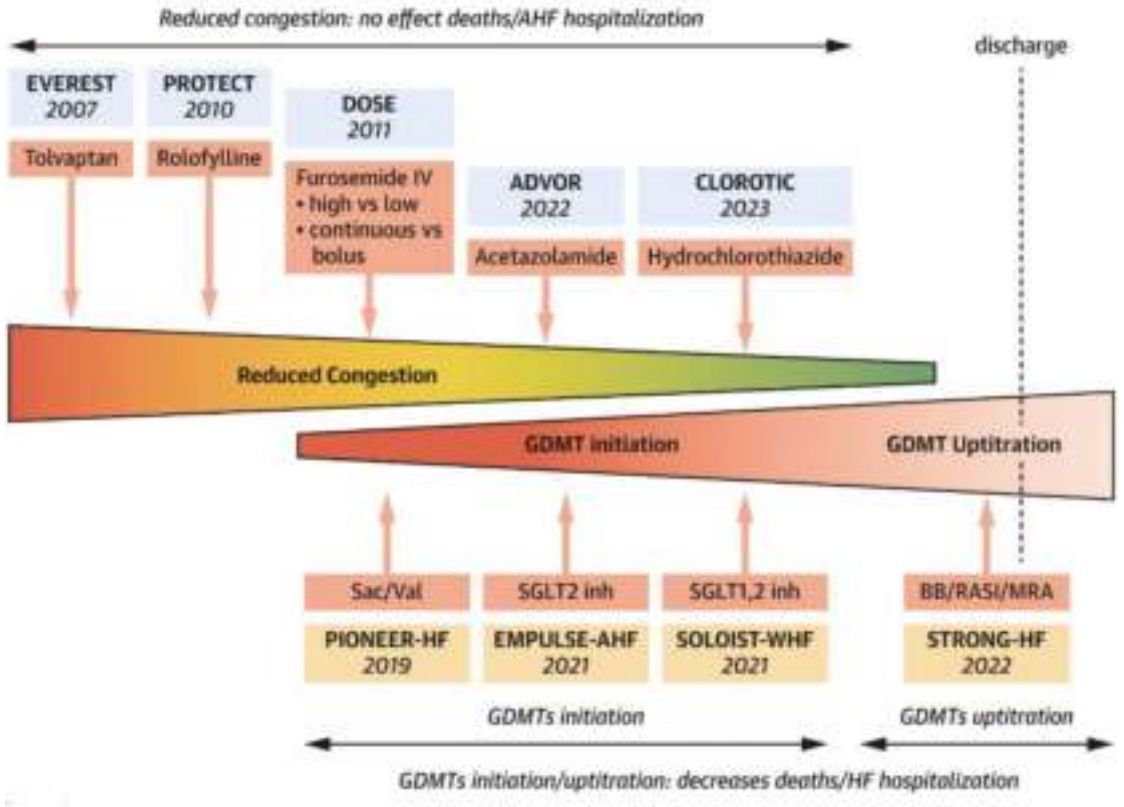
EMPACT-MI

Perspective: SGLT-2 Inhibitors Post-MI

- You can't make "better" better…… the majority of well treated, well re-perfused patients enrolled in post-MI trials are not at risk for heart failure and won't benefit from SGLT2 inhibitors
- However, SGLT2 inhibitors are SAFE post-MI, and anyone with another indication "discovered" at time of MI (i.e., DM or CKD) should be treated with SGLT2 inhibitors, as should patients who develop HF symptoms in follow-up

ABC's of De-congesting "Congestive" Heart Failure: Dr. Sharma

- Decongestion through intravenous furosemide remains a cornerstone of management of patients with acute worsening of heart failure
- Diuretic resistance is associated with worse outcomes, yet diagnosis can be challenging
- Multiple options are now present to augment diuresis: acetazolamide, thiazide, and SGLT2i



Cotter JACC 2024