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AMERICAN COLLEGE of CARDIOLOGY

Cardiovascular Symposium India

"Session 5: **Heart Failure; 4 pillars of GDMT for HFrEF"**

Clyde W. Yancy, MD, MSc
Professor of Medicine,
Professor, Medical Social Science
Chief, Cardiology
Associate Director, Bluhm CV Institute
&
Vice-Dean, Diversity & Inclusion
Northwestern University, FSM
&
Deputy Editor, JAMA Cardiology
Twitter: @NMHheartdoc

No relevant disclosures


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Let’s start with
HF in India?

ORIGINAL ARTICLE

Year : 2016 | Volume : 2 | Issue :

Heart failure in India: T

Vivek Chat

Puneet Mis

[1] Departmer

[2] Departmer

[3] Centre for

[4] Departmer

Date of We

Table

Parameter
Age (years)
Male:female ratio
Duration of symptoms (years)
Systolic blood pressure (mmHg)
Diastolic blood pressure (mmHg)
Ejection fraction (%
Peak flow rate
Cause of HF (*n*)

COPD: Chronic ob

Table 4: Key facts regarding heart failure in India

From this study
Prevalence of HF: 1.2/1000 rural population with 2/3 diastolic dysfunction and 1/3 systolic dysfunction
Hospital data: 20% patients came with HF - Causes RHD (52%) >IHD (17%)
Projections
India
16% of the world population
25% of the world CAD
120 million hypertensives
HF outcomes
Admitted patients are very sick
1/3 die during the admission if discharged 1/4 more die in the next 3 months
Causes
The most common causes are RHD and CAD
RHD
Burden 0.25-0.3 million
20% get HF with a 3% annual mortality
CAD
Burden 29.8 million
30 day HF rate of 5%
Hypertension
25-40 in urban, 10-15% in rural with total of 118.2 million
5-10% get HF

RHD: Rheumatic heart disease, CAD: Coronary artery disease, IHD: Ischemic heart disease, HF: Heart failure

ospital

ases (%)
.96)
.67)
80)
80)
8)
8)
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A new definition
of heart failure?

Definition and Universal Classification

Universal Definition and Classification of Heart Failure

A Report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure Consensus Conference

Bozkurt B, Coats A, Tsutsui H. Universal Definition and Classification of Heart Failure. J Card Fail. 2021 Feb 7:S1071-9164(21)00050-6. doi: 10.1016/j.cardfail.2021.01.022. Epub ahead of print. PMID: 33662581.

Definition and Universal Classification

HF with reduced EF (HFrEF):

- HF with LVEF ≤ 40%

HF with mid-range EF (HFmrEF):

- HF with LVEF 41-49%

HF with preserved EF (HFpEF):

- HF with LVEF ≥ 50%

HF with improved EF (HFimpEF):

- HF with a baseline LVEF ≤ 40%, a ≥ 10 point increase from baseline LVEF, and a second measurement of LVEF > 40%

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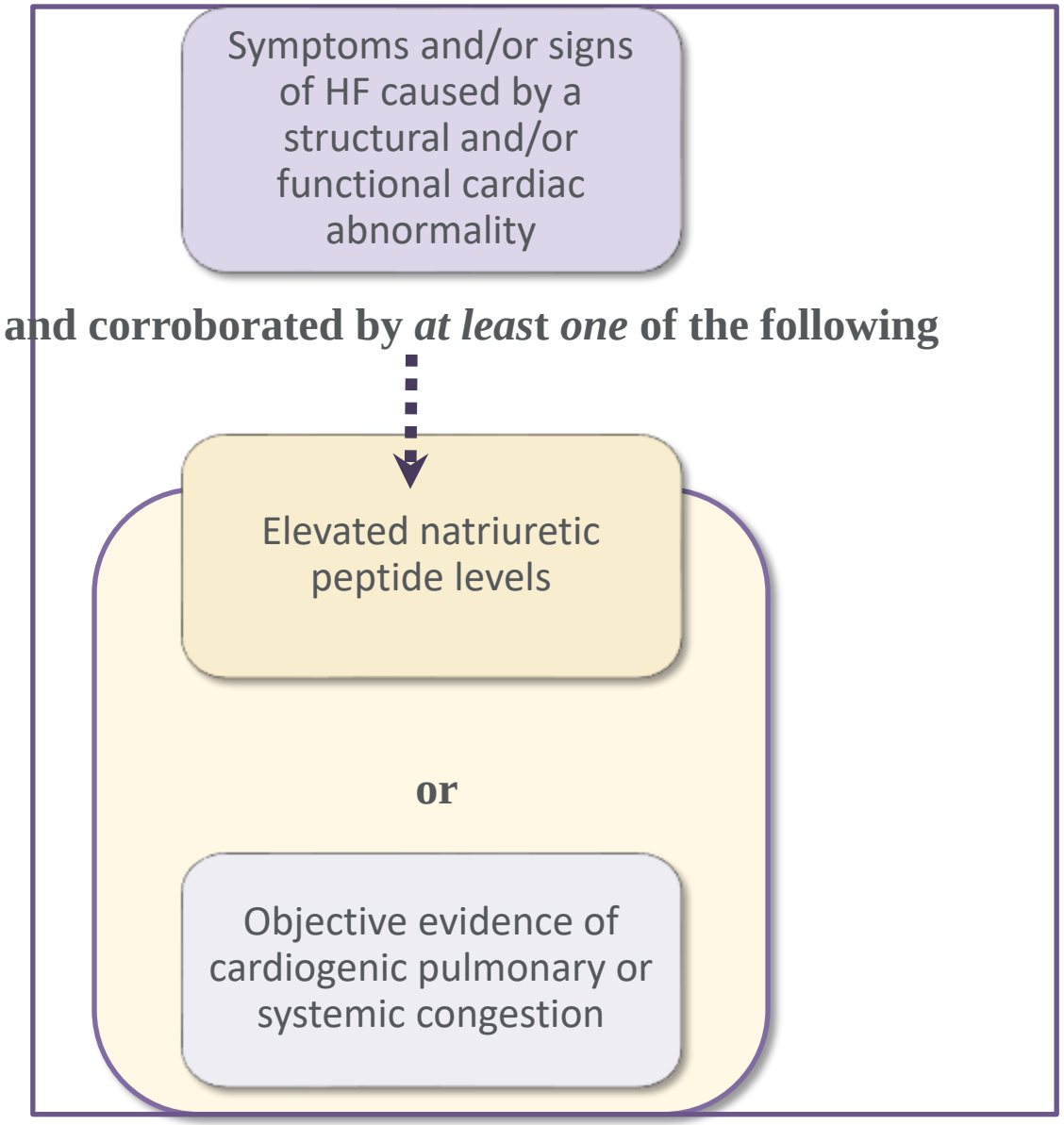
Bozkurt B, Coats A, Tsutsui H. Universal Definition and Classification of Heart Failure. J Card Fail. 2021 Feb 7:S1071-9164(21)00050-6. doi: 10.1016/j.cardfail.2021.01.022. Epub ahead of print. PMID: 33662581.



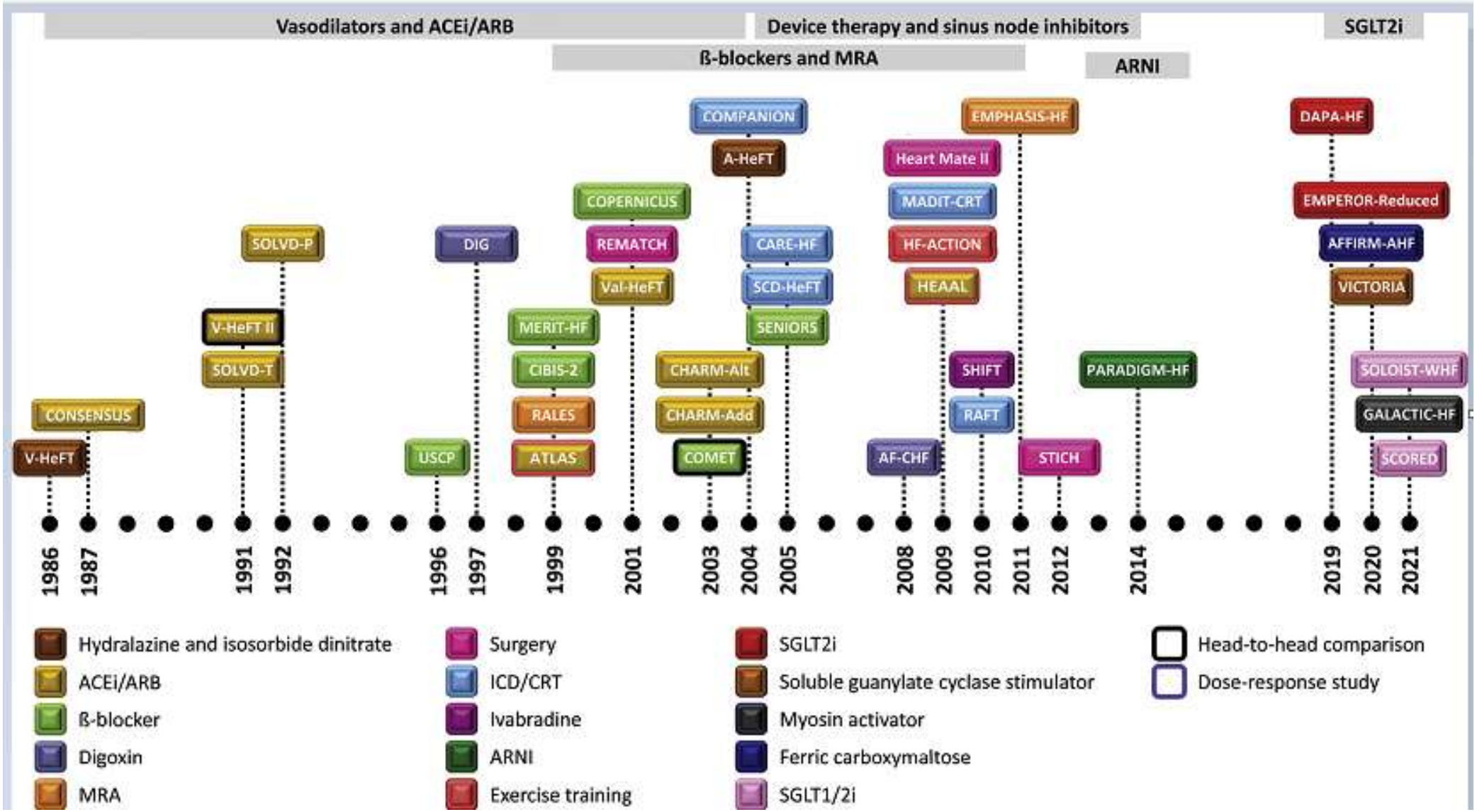
TAKEAWAY?

The new definition?

-symptoms/signs
-objective evidence of heart disease
&
- objective evidence of congestion

Bozkurt B, Coats A, Tsutsui H. Universal Definition and Classification of Heart Failure. J Card Fail. 2021 Feb 7:S1071-9164(21)00050-6. doi: 10.1016/j.cardfail.2021.01.022. Epub ahead of print. PMID: 33662581.

The history of clinical trials informing treatment of HFrEF; *a progression of clinical science*



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Sharma A, et al. J Am Coll Cardiol Basic Trans Science. 2022;7(5):504-517.


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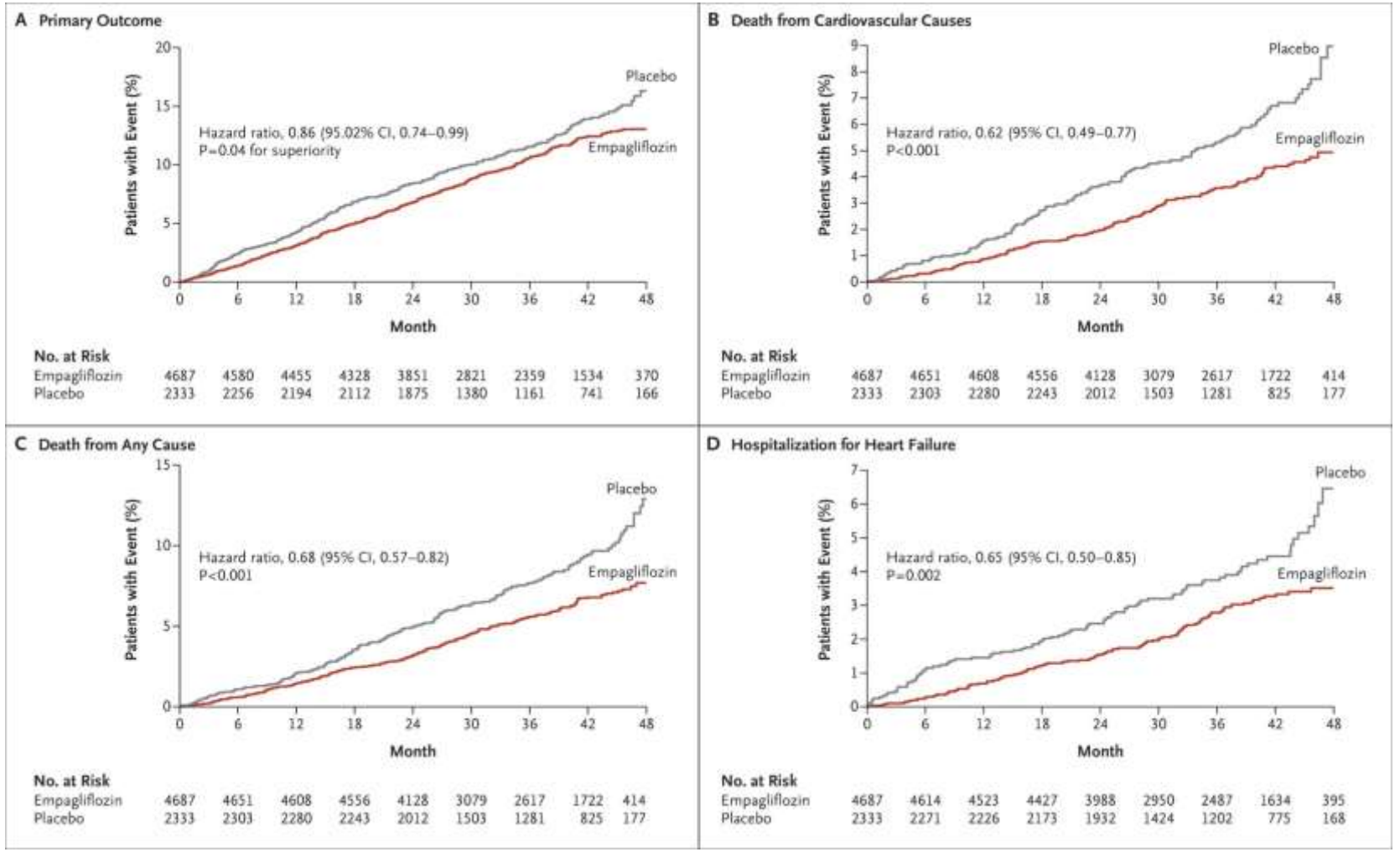
Heart Failure:
A new
generational
paradigm
The SGLT-2 inhibitors; from
prevention to treatment

Cardiovascular Outcomes and Death from Any Cause.



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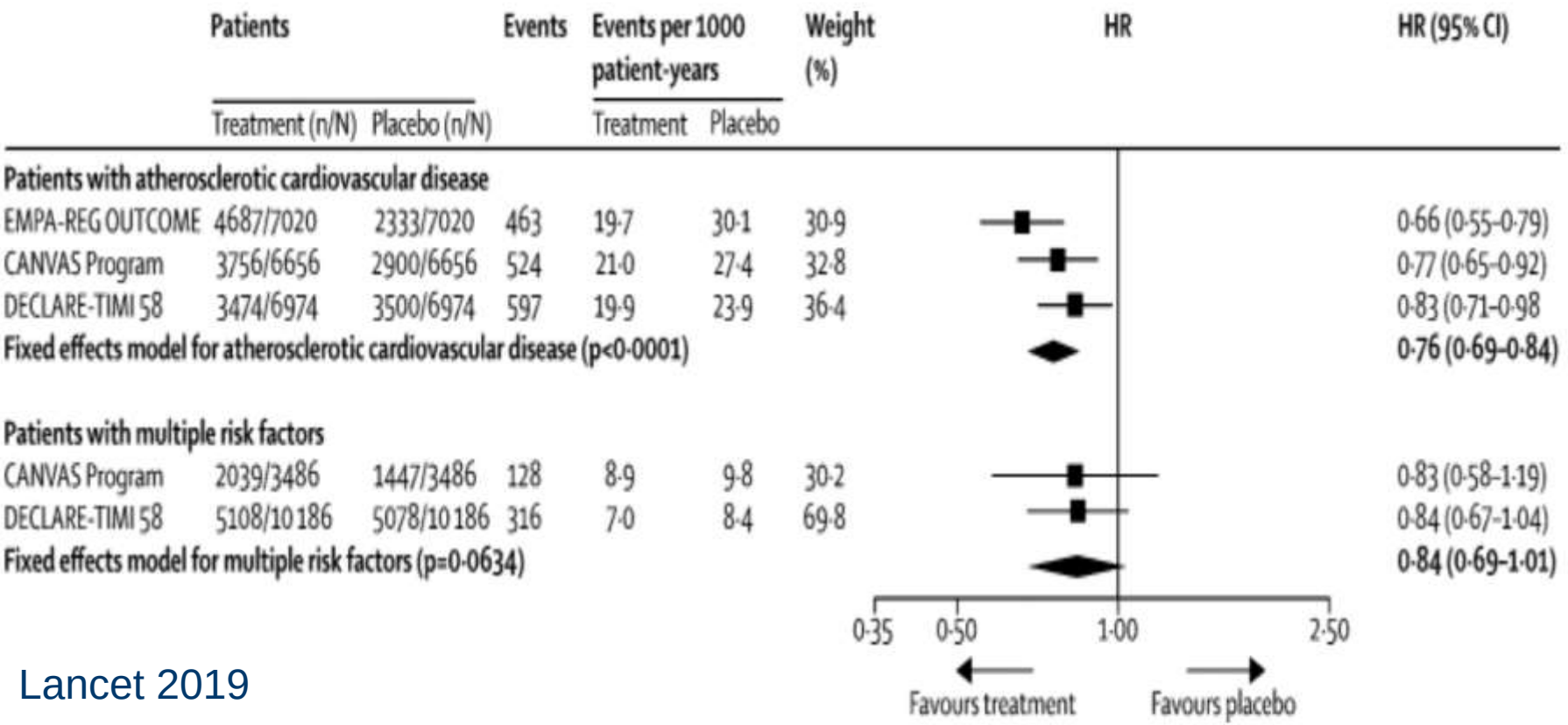
The NEW ENGLAND JOURNAL of MEDICINE

SGLT2 Inhibitors Reduce the Risk of Heart Failure Events in Type 2 Diabetes



Lancet 2019

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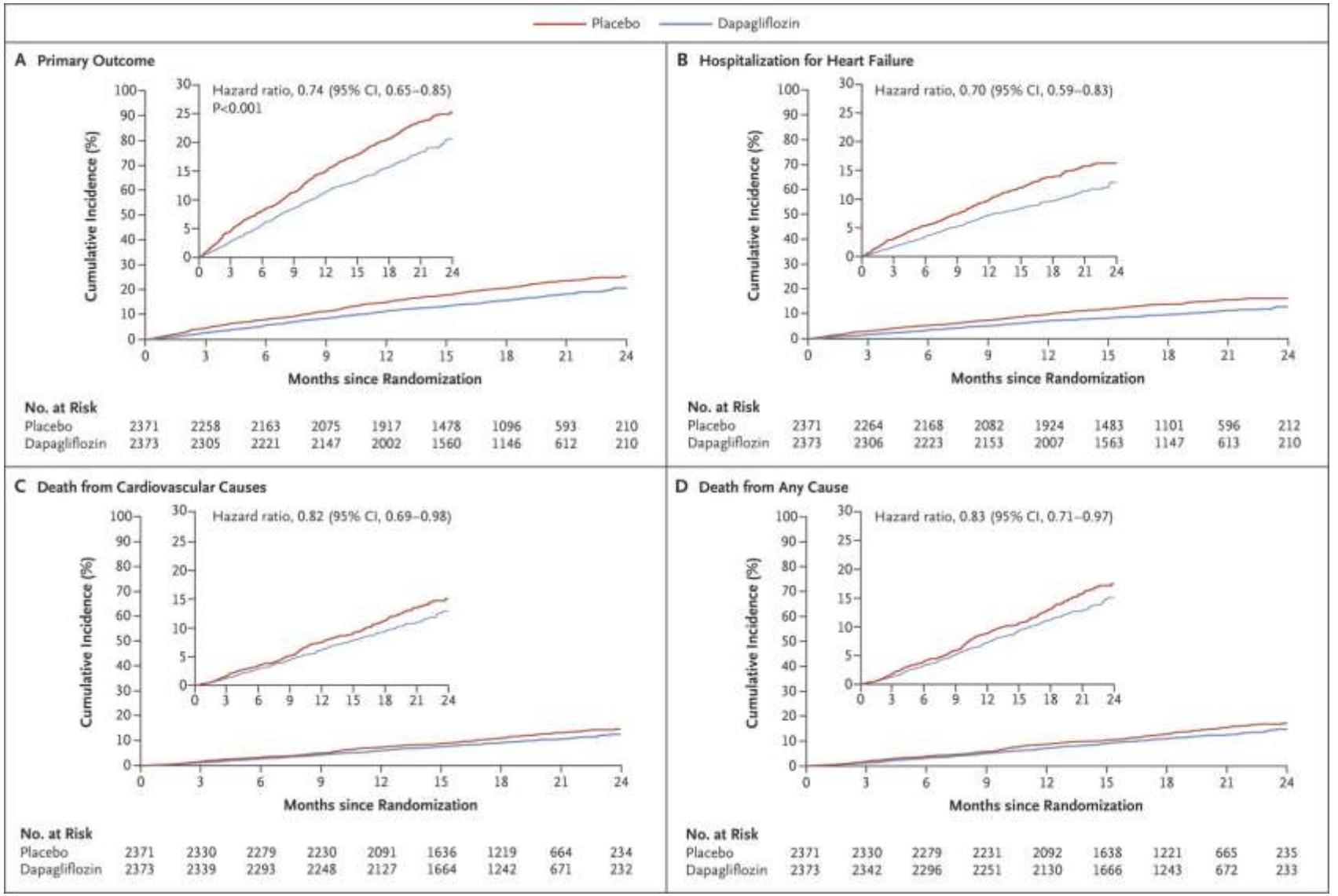
Cardiovascular Outcomes.



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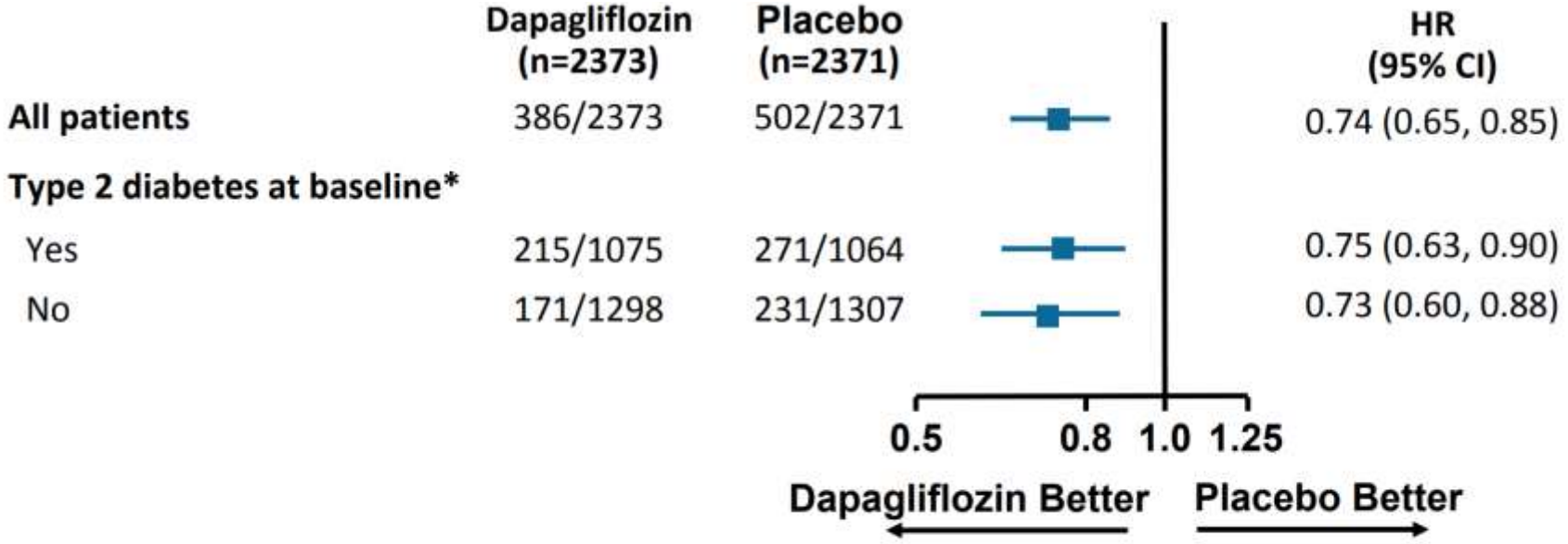
JJ McMurray et al. N Engl J Med 2019. DOI: 10.1056/NEJMoa1911303

DAPA-HF: Effect of Dapagliflozin in Heart Failure, With or Without Diabetes

No diabetes/diabetes subgroup: Primary endpoint

Effect on Primary Endpoint of Cardiovascular Death and Serious Heart Failure Events



*Defined as history of type 2 diabetes or HbA1c ≥6.5% at both enrollment and randomization visits.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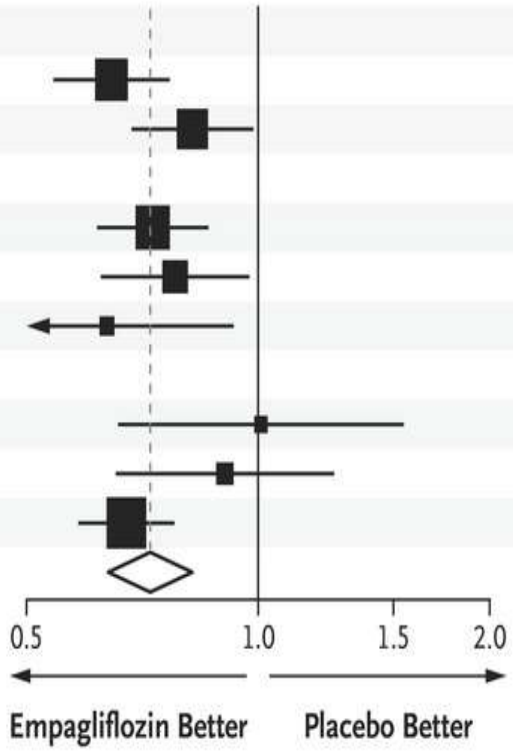
Heart Failure:
A new generational paradigm
The SGLT-2 inhibitors & Renal Function

Primary Outcome in Key Prespecified Subgroups.

Subgroup	Empagliflozin (no. of patients with event/total no.)	Placebo (no. of patients with event/total no.)	Hazard Ratio for Progression of Kidney Disease or Death from Cardiovascular Causes (95% CI)
Diabetes mellitus			
Present	218/1525	306/1515	0.64 (0.54–0.77)
Absent	214/1779	252/1790	0.82 (0.68–0.99)
Estimated GFR			
<30 ml/min/1.73 m^2	247/1131	317/1151	0.73 (0.62–0.86)
≥30 to <45 ml/min/1.73 m^2	140/1467	175/1461	0.78 (0.62–0.97)
≥45 ml/min/1.73 m^2	45/706	66/693	0.64 (0.44–0.93)
Urinary albumin-to-creatinine ratio			
<30	42/665	42/663	1.01 (0.66–1.55)
≥30 to ≤300	67/927	78/937	0.91 (0.65–1.26)
>300	323/1712	438/1705	0.67 (0.58–0.78)
All patients	432/3304	558/3305	0.72 (0.64–0.82)



The EMPA-KIDNEY Collaborative Group. N Engl J Med 2023;388:117-127.

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Heart Failure: A new generational paradigm
The SGLT-2 inhibitors & Time to Benefit

JAMA Cardiol. 2021 May 1;6(5):499-507. doi: 10.1001/jamacardio.2020.7585.

Time to Clinical Benefit of Dapagliflozin and Significance of Prior Heart Failure Hospitalization in Patients With Heart Failure With Reduced Ejection Fraction

David D Berg [1], Pard
Silvio E Inzucchi [4], La
Felipe A Martinez [8], C
John J V McMurray [2]

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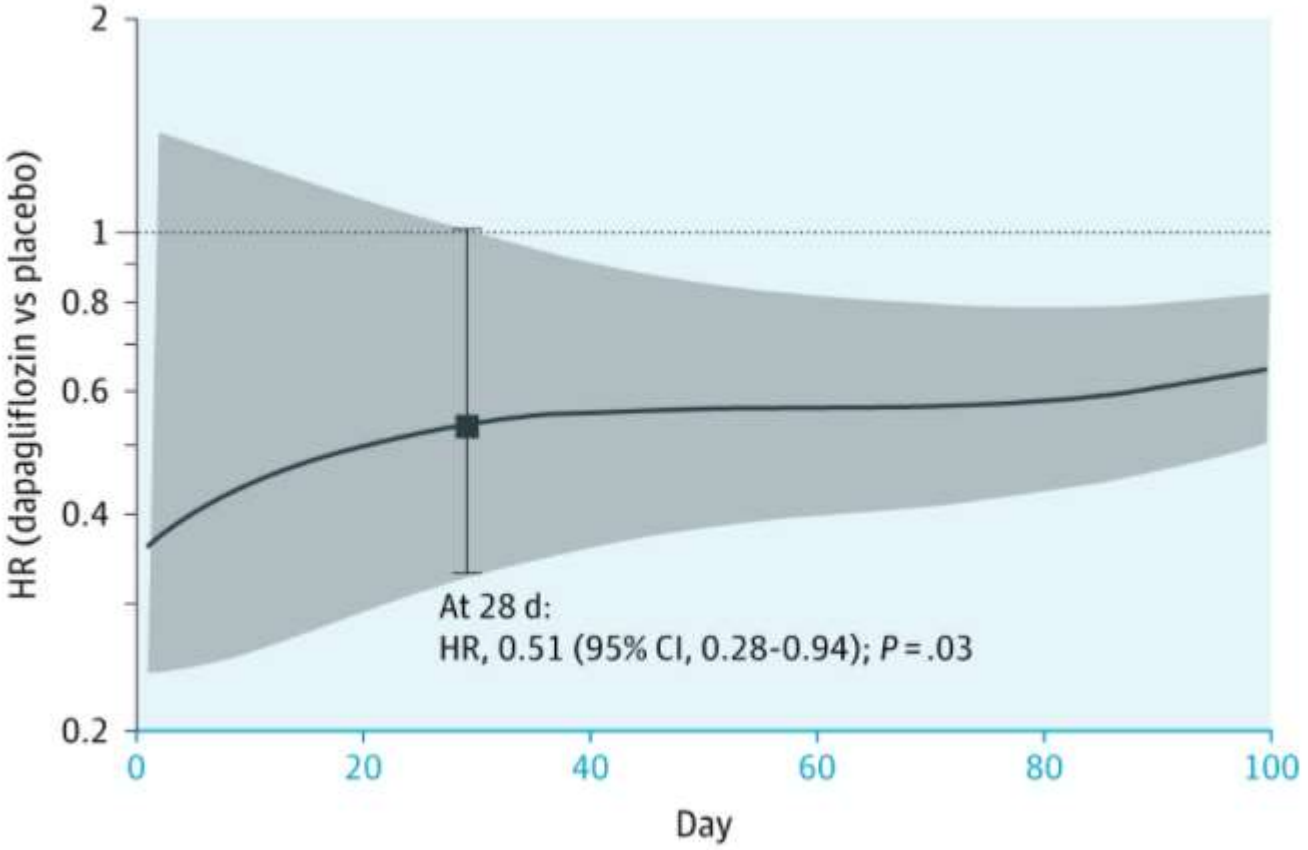
B Worsening heart failure or cardiovascular death, first 100 d



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The Full Portfolio of treatment Choices –SGLT2 I in heart failure

Heart Failure Phenotype	SGLT2i
HFrEF	Guideline indicated therapy; COR I, LOE A: DAPA HF: HR 0.74; CI 0.65 – 0.85; NNT 21 EMPEROR REDUCED; HR 0.75; CI 0. 65 – 0.86; NNT 19
HFpEF	**EMPEROR PRESERVED**; HR 0.79; 0.69 – 0.90; p < 0.001; **DELIVER (2022)**
Hospitalized HF	SOLOIST – WHF: HR 0.67; CI 0.52 -0.85; NNT 54
HF and CKD	DAPA CKD; HR 0.61; CI 0.51 – 0.72; NNT 19 SCORED; (with or without albuminuria)HR 0.74; CI 0.63 – 0.88. EMPA-KIDNEY, 2022

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Treatment of
HFrEF
The Four Pillars

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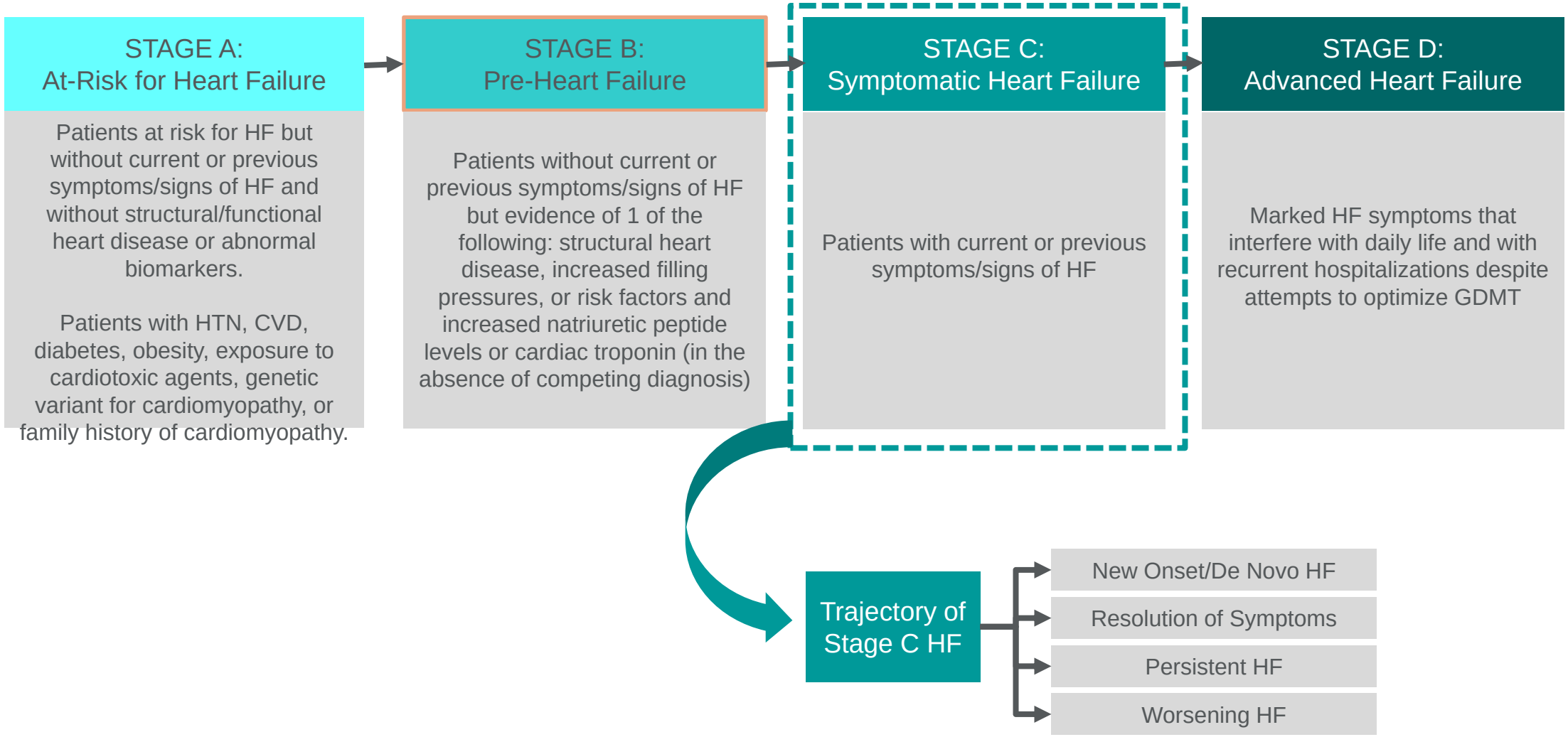
Source Documentation:

New Heart Failure Guidelines AHA/ACC/HFSA, 2022

2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

Clinical Practice Guideline: J Am Coll Cardiol. Apr 01, 2022. Epublished DOI: 10.1016/j.jacc.2021.12.012

Stages of Heart Failure



Abbreviations: CVD indicates cardiovascular disease; GDMT, guideline-directed medical therapy; HF, heart failure; HTN, hypertension; and NYHA, New York Heart Association.

American Heart Association.

Heidenreich, P. A. et al. (2022). 2022 AHA/ACC/HFSA Guideline for Heart Failure. *Circulation*.

Recommendations for Patients at Risk of HF & Pre-HF

At Risk for HF (Stage A)

Primary Prevention

Patients with hypertension	Optimal control of BP (1)
Patients with Type 2 diabetes and CVD or high risk for CVD	SGLT2i (1)
Patients with CVD	Optimal management of CVD (1)
Patients with exposure to cardiotoxic agents	Multidisciplinary evaluation and management (1)
First-degree relatives of patients with genetic or inherited cardiomyopathies	Genetic screening and counselling (1)
Patients at risk for HF	Natriuretic peptide screening (2a)
Patients at risk for HF	Validated multivariable risk score (2a)

Pre-HF (Stage B)

Preventing the Syndrome

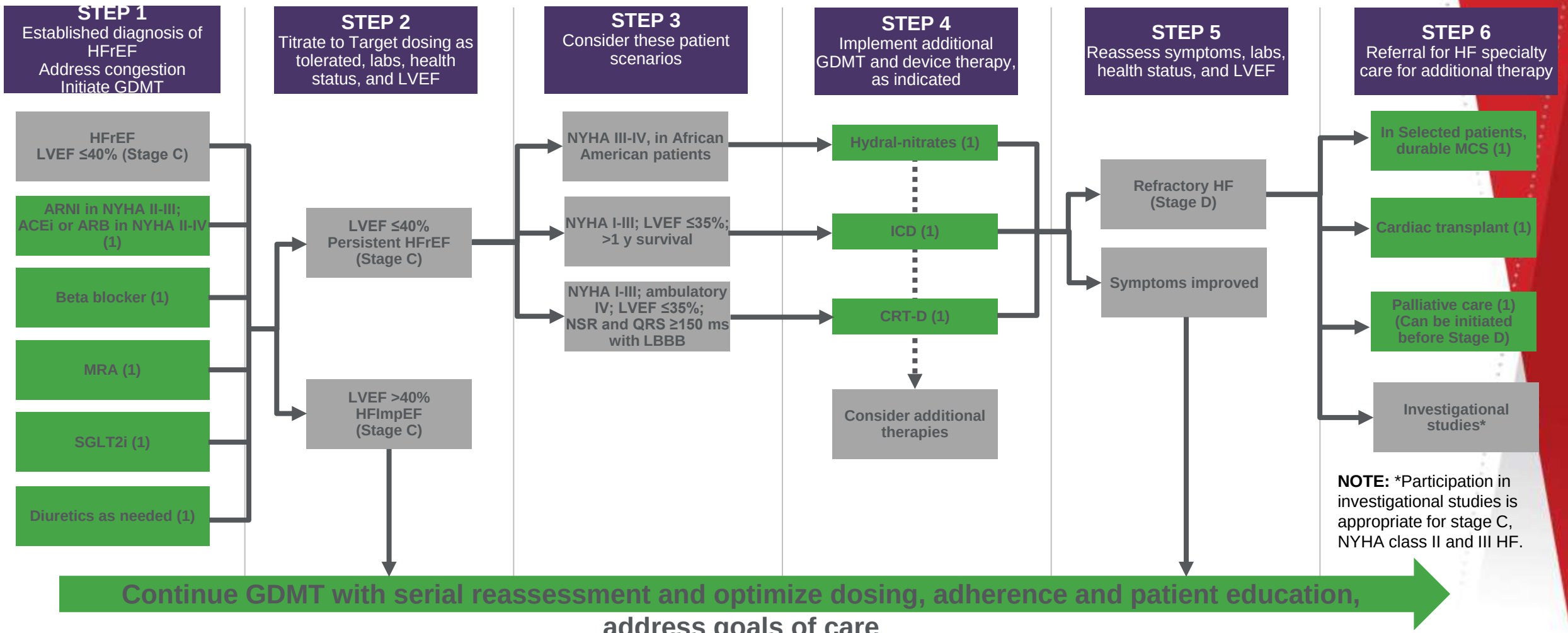
Patients with LVEF ≤ 40%	ACEi (1)
Patient with recent MI and LVEF ≤ 40 %	ARB if ACEi intolerant (1)
Patients with LVEF ≤ 40%	Beta blocker (1)
Patient with LVEF ≤ 30 %; >1 y survival; >40 d post MI	ICD (1)
Patients with nonischemic cardiomyopathy	Genetic counselling and testing (2a)

Continue Lifestyle modification and management strategies implemented in Stage A, through Stage B

Abbreviations: ACEi indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BP, blood pressure; CVD, cardiovascular disease; HF, heart failure; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; MI, myocardial infarction; and SGLT2i, sodium glucose cotransporter 2 inhibitor.

Heidenreich, P. A. et al. (2022). 2022 AHA/ACC/HFSA Guideline for Heart Failure. *Circulation*.

Treatment of HFrEF Stages C and D



Abbreviations: ACEi indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNi, angiotensin receptor-neprilysin inhibitor; CRT, cardiac resynchronization therapy; GDMT, guideline-directed medical therapy; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; hydral-nitrates, hydralazine and isosorbide dinitrate; ICD, implantable cardioverter-defibrillator; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; MCS, mechanical circulatory support; MRA, mineralocorticoid receptor antagonist; NSR, normal sinus rhythm; NYHA, New York Heart Association; SCD, sudden cardiac death; and SGLT2i, sodium-glucose cotransporter 2 inhibitor.

Heidenreich, P. A. et al. (2022). 2022 AHA/ACC/HFSA Guideline for Heart Failure. *Circulation*.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Treatment of HFrEF
The Four Pillars; how best to implement quadruple therapy?
Do we know?

March 31, 2021

Simultaneous or Rapid Sequence Initiation of Quadruple Medical Therapy for Heart Failure—Optimizing Therapy With the Need for Speed

Stephen J. Greene, MD[1,2]; Javed Butler, MD, MPH, MBA[3]; Gregg C. Fonarow, MD[4,5]

» Author Affiliations | Article Information

JAMA Cardiol. 2021;6(7):743-744. doi:10.1001/jamacardio.2021.0496

Early relative risk reduction			Initiation and optimization of medication dosing				
Outcomes	**Change, %**	**CDMMT**	**Day 1**	**Days 7-14**	**Days 14-28**	**Days 21-42**	**After day 42**
CV death or HF hospitalization	-42	ARNI	Initiate at low dose	Continue	Titrate, as tolerated	Titrate, as tolerated	Maintenance or additional titration of the 4 foundational therapies
Death	-25	β-Blocker	Initiate at low dose	Titrate, as tolerated	Titrate, as tolerated	Titrate, as tolerated	Consideration of EP device therapies or transcatheter mitral valve repair
CV death or HF hospitalization	-37	MRA	Initiate at low dose	Continue	Titrate, as tolerated	Continue	Consideration of add-on medications or advanced therapies, if refractory
Death, HF hospitalization,or emergency/ urgent visit for worsening HF	-58	SGLT2i	Initiate	Continue	Continue	Continue	Manage comorbidities

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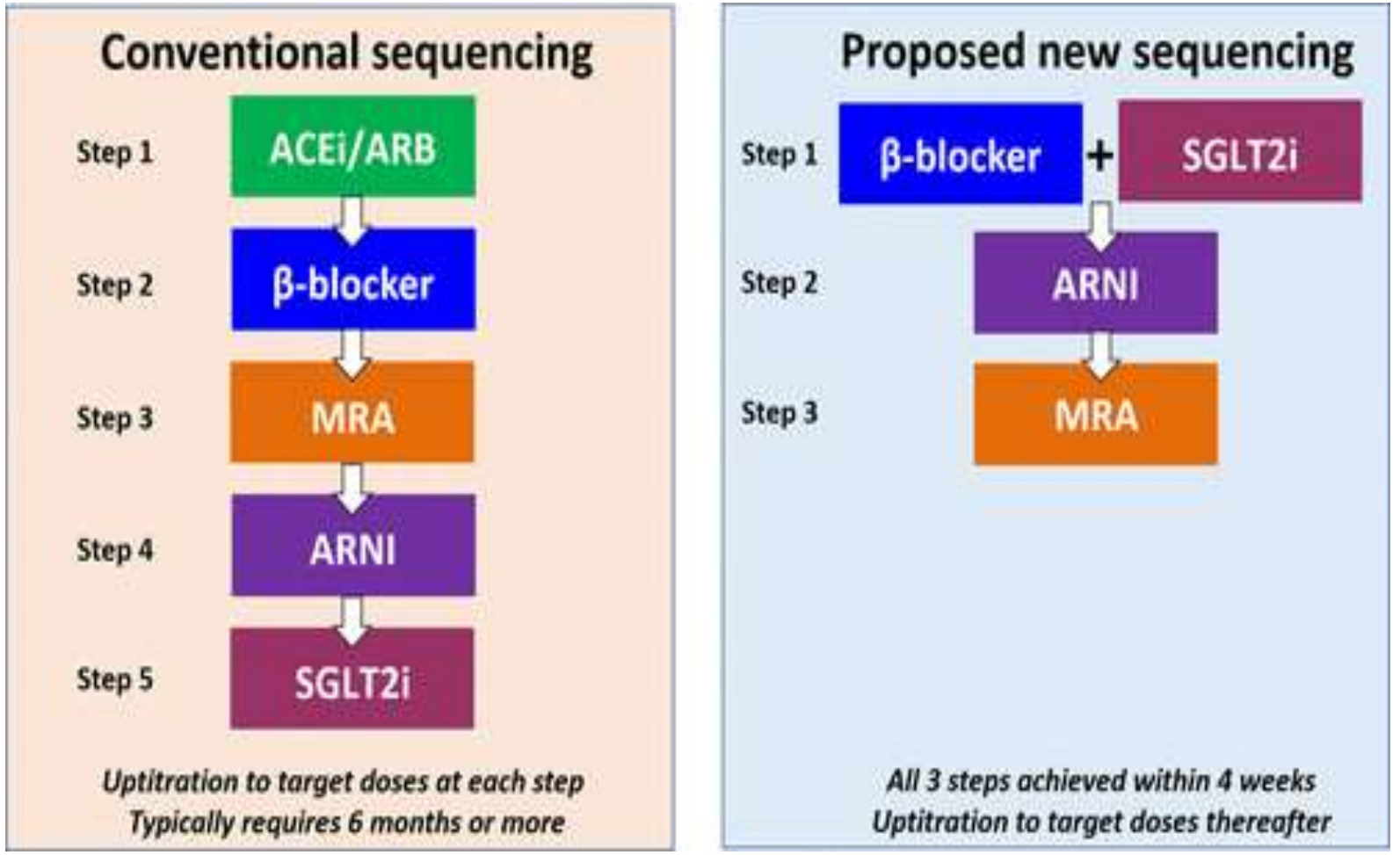
A sequencing approach



John J.V. McMurray. Circulation. How Should We Sequence the Treatments for Heart Failure and a Reduced Ejection Fraction?, Volume: 143, Issue: 9, Pages: 875-877, DOI: (10.1161/CIRCULATIONAHA.120.052926)

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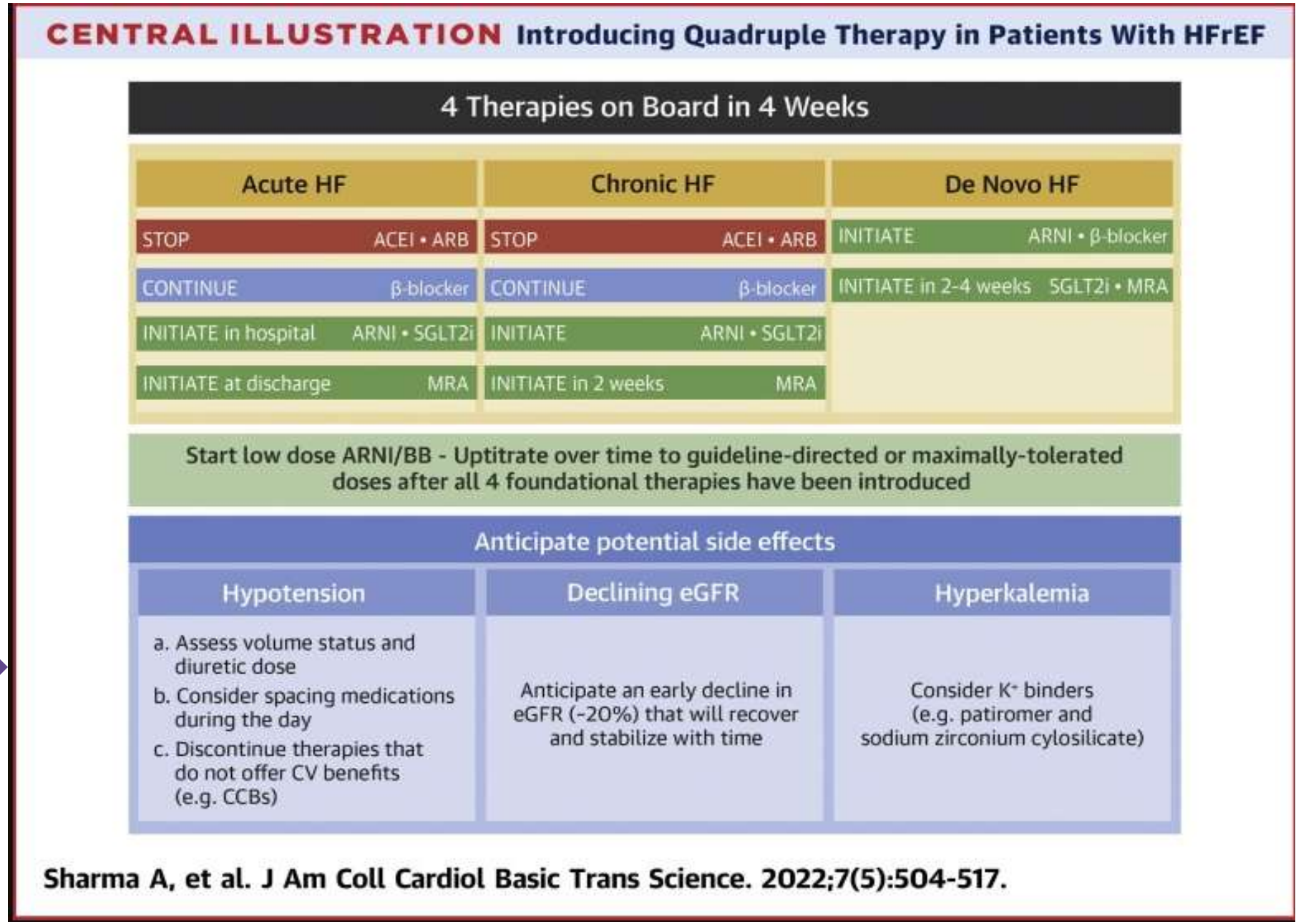

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A different idea…

Viewpoint

November 19, 2020

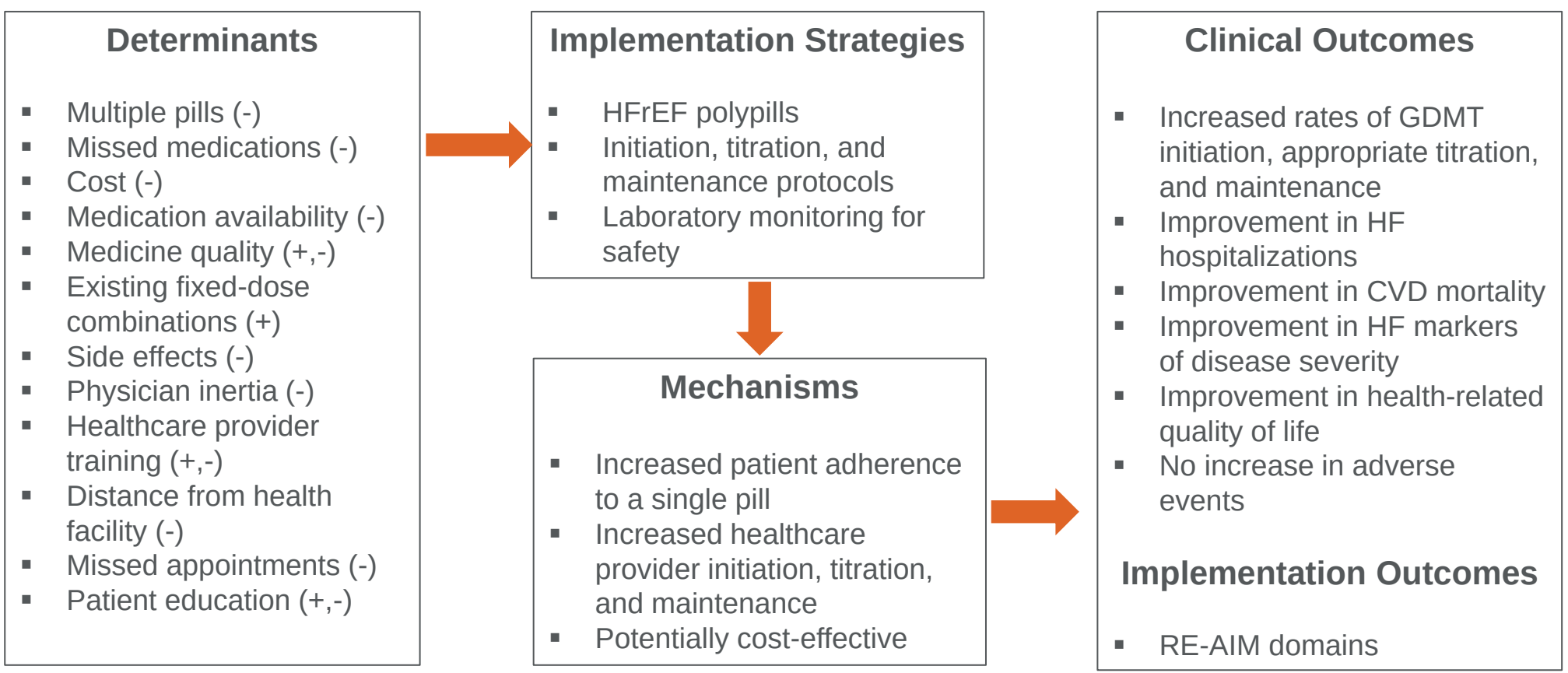
Improving Care for Heart Failure With Reduced Ejection Fraction—A Potential Polypill-Based Strategy

Anubha Agarwal, MD, MSc[1]; Clyde W. Yancy, MD, MSc[1]; Mark D. Huffman, MD, MPH[2,3]

» Author Affiliations | Article Information

JAMA. 2020;324(22):2259-2260. doi:10.1001/jama.2020.21395

HFrEF polypill implementation research logic model



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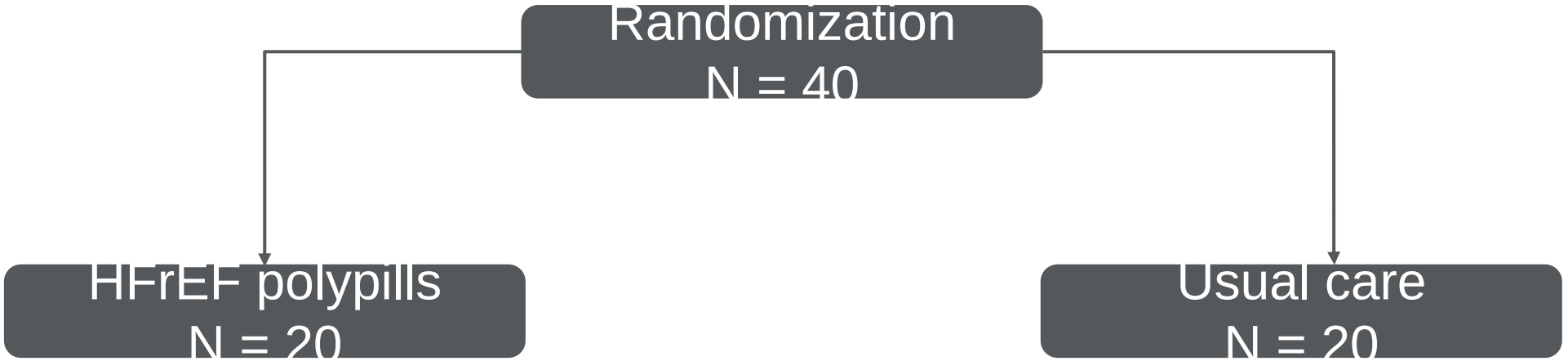
Agarwal A, et al. Unpublished data.

HFrEF Polypill Implementation Strategy in India: A Pilot Randomized Trial



Step 1 (half-dose):	carvedilol CR 5 mg + candesartan 4 mg + eplerenone 12.5 mg
Step 2 (full-dose):	carvedilol CR 10 mg + candesartan 8 mg + eplerenone 25 mg
Step 3 (double-dose):	carvedilol CR 20 mg + candesartan 16 mg + eplerenone 50 mg

Example HFrEF polypill combination, initiation, and titration schedule. Future second-generation HFrEF polypills may include ARNi and/or SGLT2i which are not included in this example due to cost barriers in India.

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PI: A. Agarwal; funded by Northwestern University Institute of Global Health


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Treatment of
HFrEF
The Four Pillars;
what's the potential
benefit?

Cumulative Impact of Evidence-Based Heart Failure with Reduced EF Medical Therapies

	Relative-risk	2 yr Mortality
None	- -	35%
ACEI or ARB	↓ 23%	27%
Beta Blocker	↓ 35%	18%
Aldosterone Ant	↓ 30%	13%
ARNI (replacing ACEI/ARB)	↓ 16%	10.9%
SGLT2 inhibitor	↓ 17%	9.1%

Cumulative risk reduction if all evidence-based medical therapies are used:
Relative risk reduction 74.0%, Absolute risk reduction: 25.9%, NNT = 3.9

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Updated from Fonarow GC, et al. Am Heart 2011;161:1024-1030 and Lancet 2008;372:1195-1196.

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Takeaways:

1. A new generational paradigm now guides best care for HFrEF

2. SGLT2 inhibtors represent breakthrough therapy

3. Ideal care warrants “quadruple therapy”

4. Both implementation and cost remain challenges

Thank you!

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