

Foundations of Cardiometabolic Health Certification Course

Certified Cardiometabolic Health Professional (CCHP)



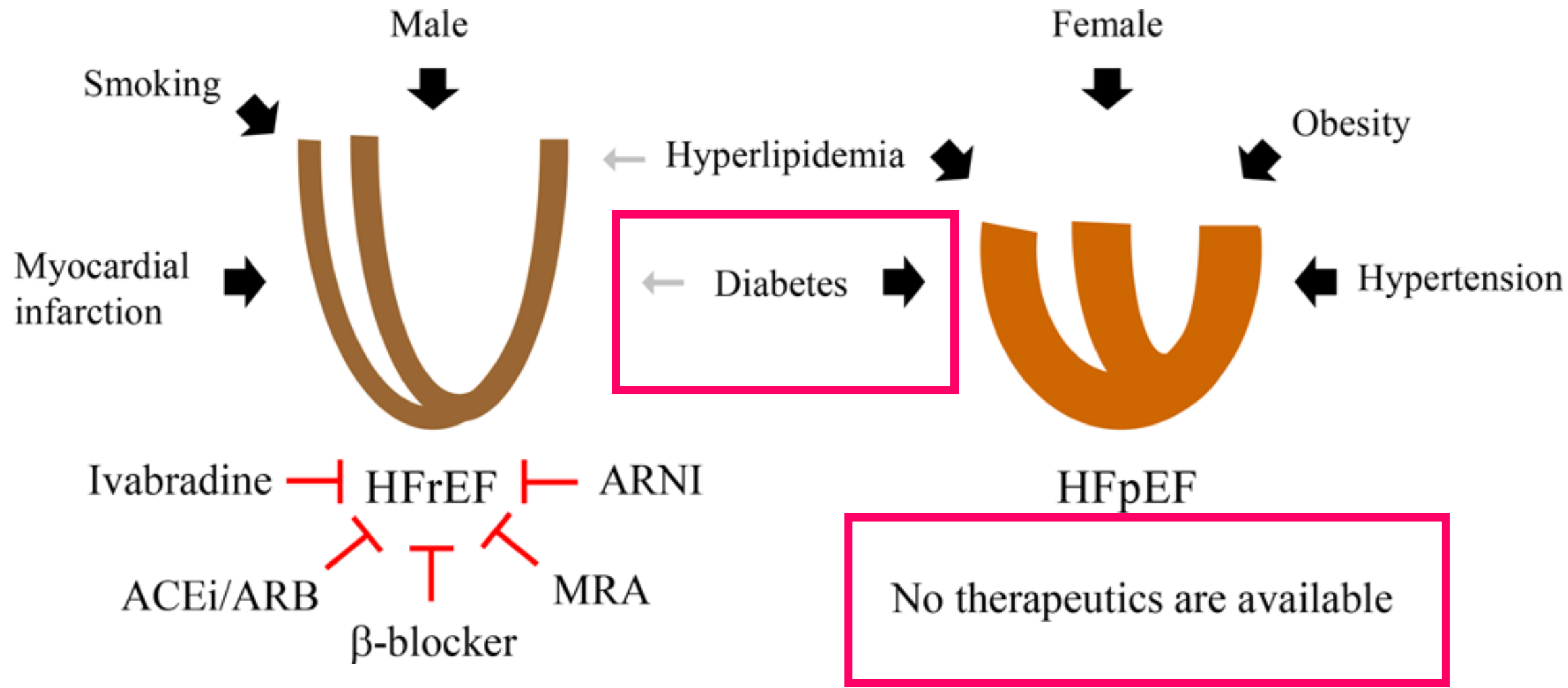
Heart Failure and Sudden Death

Keith C. Ferdinand, MD, FACC, FAHA, FASPC, FNLA
Gerald S. Berenson Endowed Chair in Preventative Cardiology
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Tulane University School of Medicine
New Orleans, LA

Goals

- Update diagnostic criteria for the effective management of patients with heart failure (HF)
- Integrate current guideline-directed medical therapy (GDMT) and newer outcome studies.
- Develop new approaches to HF management in patients with/without diabetes with SGLT2 inhibitors.
- Review best practices to achieve successful HF care

Comorbidity Associated With Each Type of HF: Present and Future Directions



Ejection Fraction Defined

HF with reduced EF (HFrEF):

- HF with LVEF $\leq 40\%$

HF with mildly reduced EF (HFmrEF):

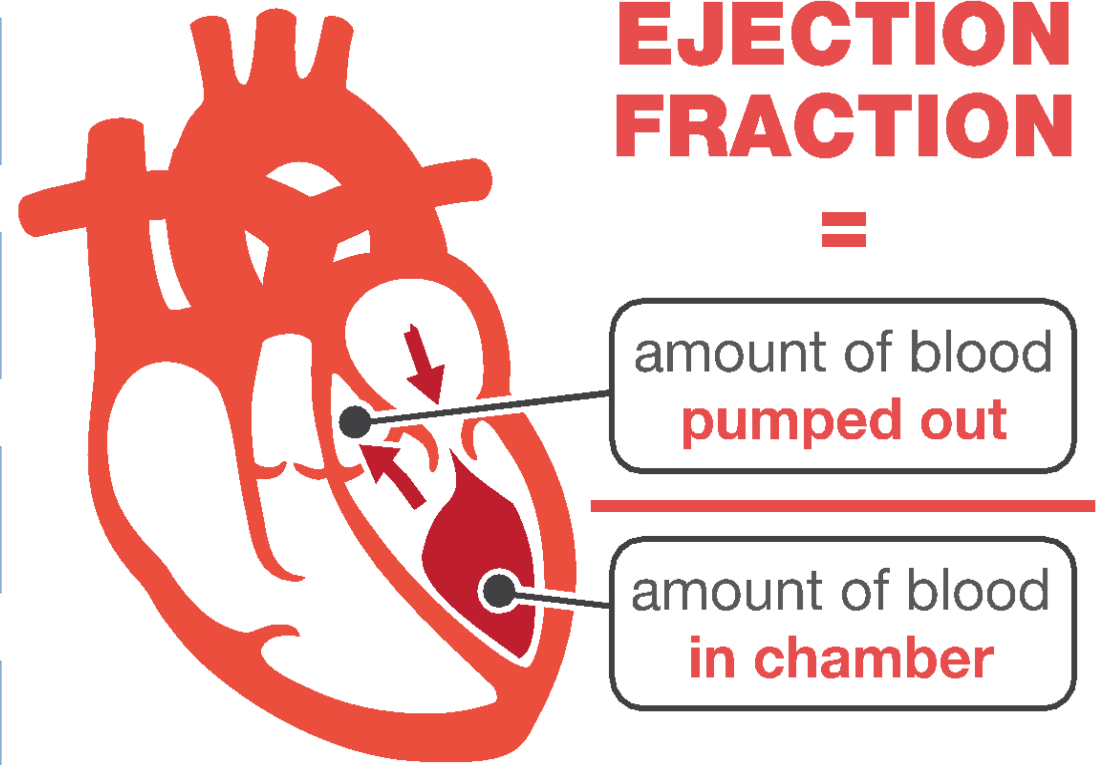
- HF with LVEF 41–49%

HF with preserved EF (HFpEF):

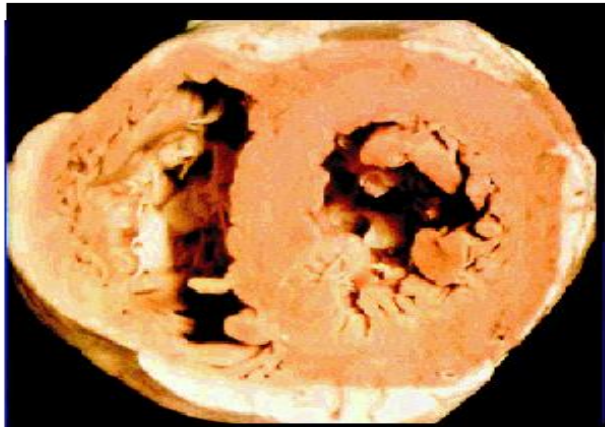
- HF with LVEF $\geq 50\%$

HF with improved EF (HFimpEF):

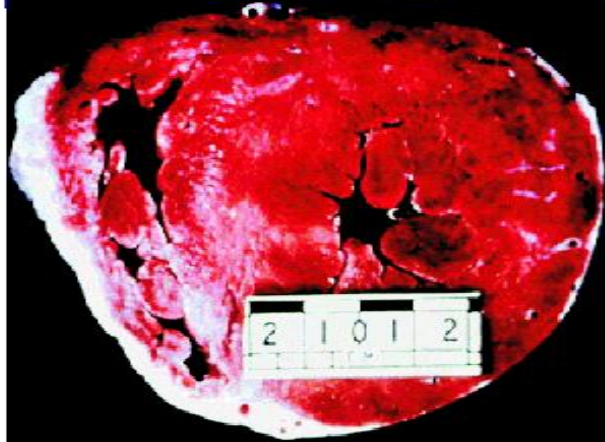
- HF with a baseline LVEF $\leq 40\%$, a ≥ 10 point increase from baseline LVEF, and a second measurement of LVEF $> 40\%$



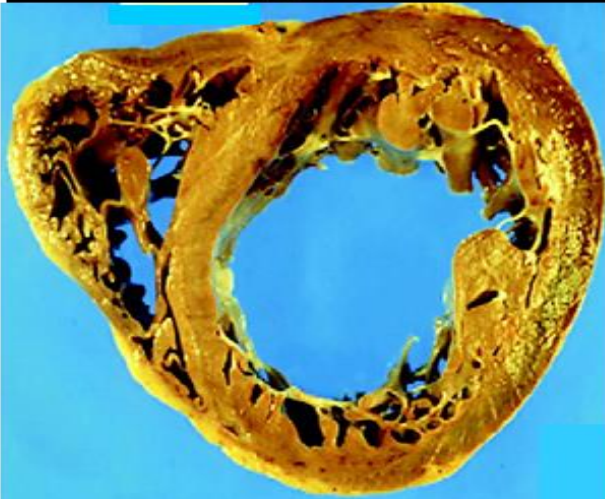
1. Normal Heart →



2. HF with Preserved Ejection Fraction (HFpEF) →



3. HF with Reduced Ejection Fraction (HFrEF) →



**HF pathology:
heart size,
wall thickness**

Classification of HF according to LVEF

Type of HF According to LVEF	Criteria
HFrEF (HF with reduced EF)	LVEF \leq 40%
HFimpEF (HF with improved EF)	Previous LVEF \leq 40% and a follow-up measurement of LVEF $>$ 40%
HFmrEF (HF with mildly reduced EF)	LVEF 41% - 49%. Evidence of spontaneous or provokable increased LV filling pressures (e.g. elevated natriuretic peptide, noninvasive and invasive hemodynamic measurement)
HFpEF (HF with preserved EF)	LVEF \geq 50%. Evidence of spontaneous or provokable increased LV filling pressures (e.g., elevated natriuretic peptide, noninvasive and invasive hemodynamic measurement)

LVEF: left ventricular ejection fraction

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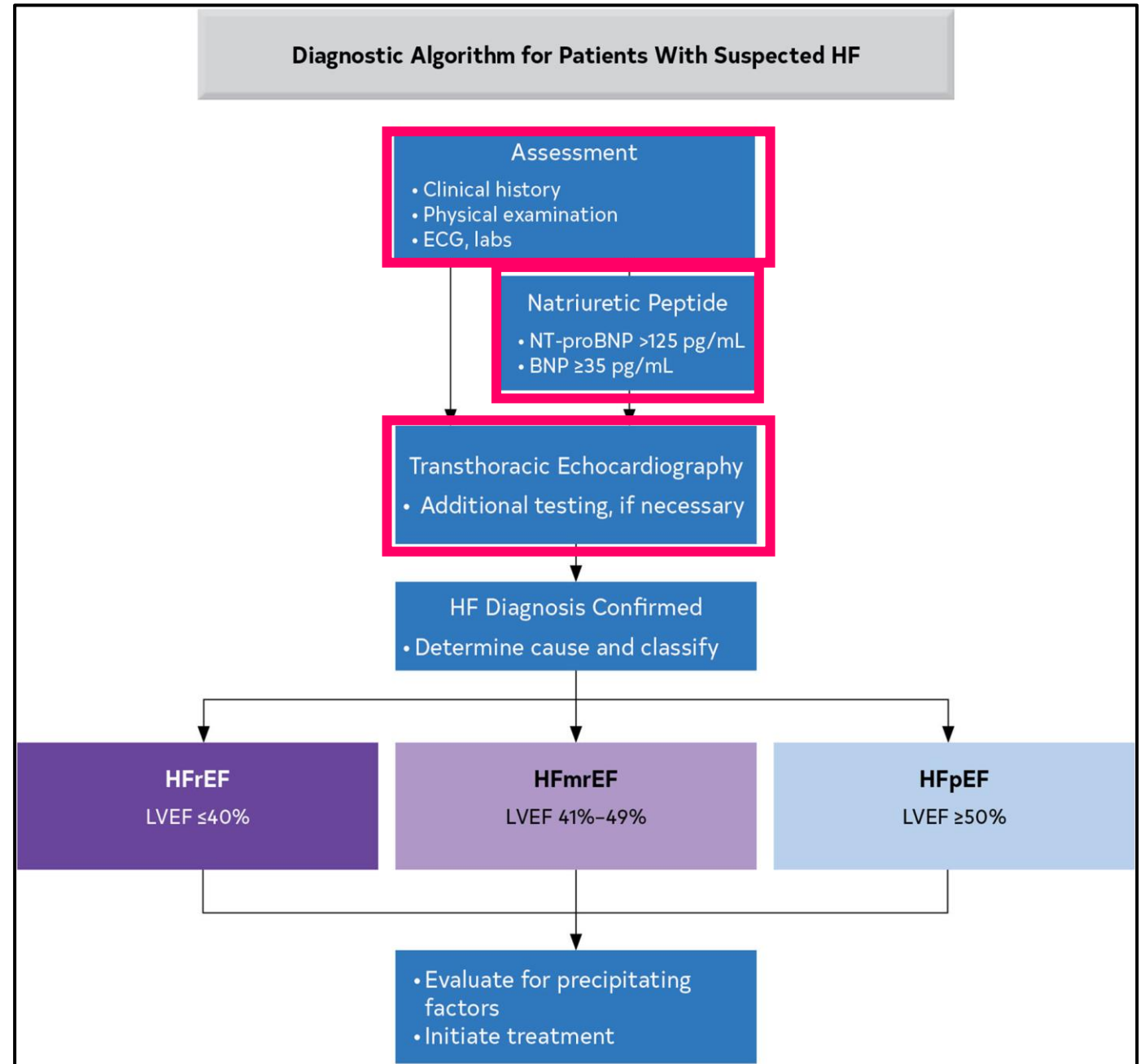
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Diagnosis of Heart Failure

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Diagnosis of HF



Symptoms and/or signs
of HF caused by a
structural and/or
functional cardiac
abnormality

corroborated by *at least one* of the following

Elevated natriuretic
peptide levels

or

Objective evidence of
cardiogenic pulmonary or
systemic congestion

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Epidemiology, Disparities, and Treatment of Heart Failure

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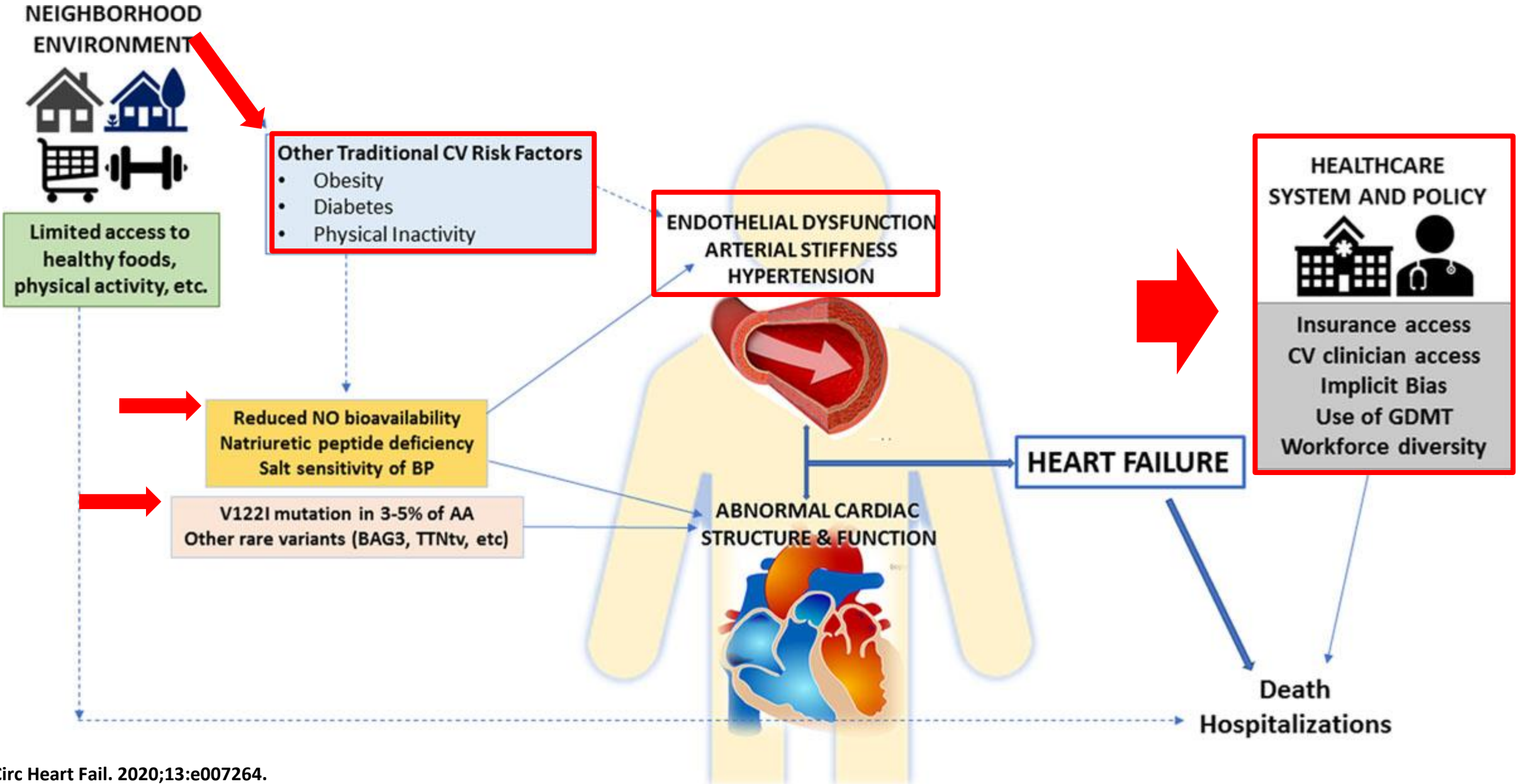
Circulation: Heart Failure

ADVANCES IN HEART FAILURE

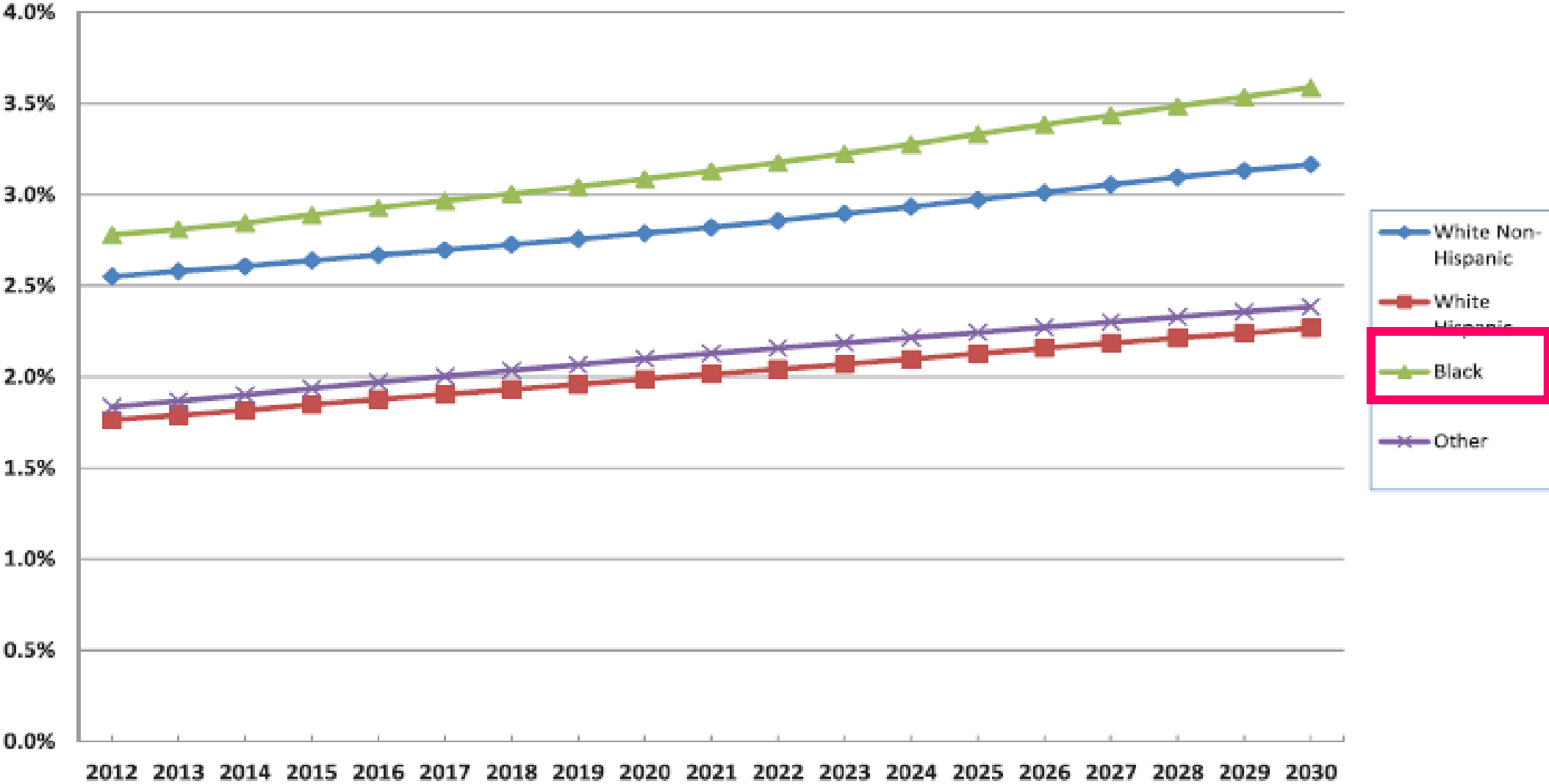
Understanding the Complexity of Heart Failure Risk and Treatment in Black Patients

Aditi Nayak, MD; Albert J. Hicks, MD, MPH; Alanna A. Morris , MD, MSc

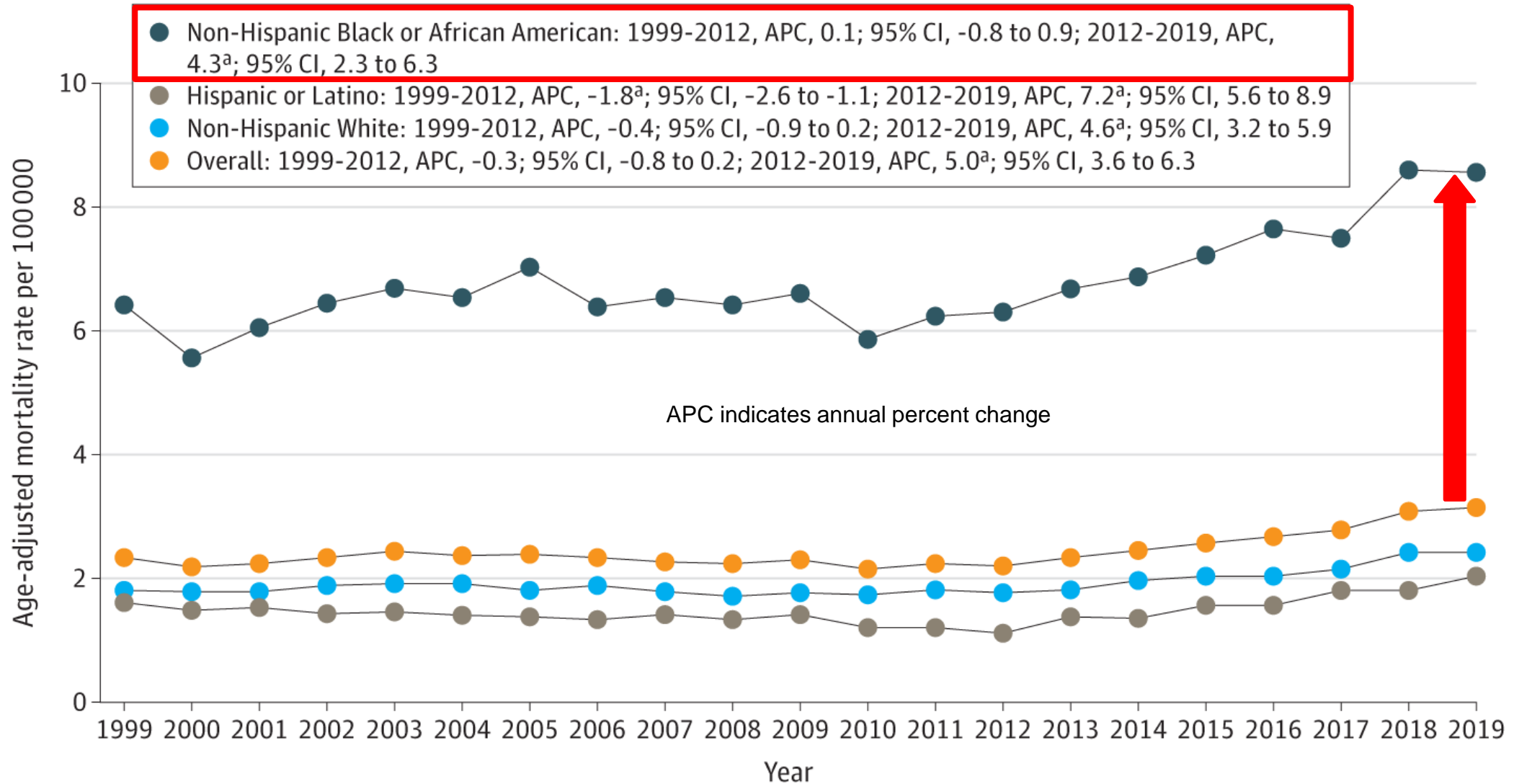
Multiple Levels of Influence on Racial Disparities in HF Incidence and Clinical Outcomes Once Clinical Disease has Manifested



Projected HF: Race/ethnicity 2012-2030



Trends HF-Related Age-Adjusted Mortality Rates, Race/Ethnicity US Young Adults , 1999-2019, ^aP < .05.



● Non-Hispanic Black or African American: 1999-2012, APC, 0.1; 95% CI, -0.8 to 0.9; 2012-2019, APC, 4.3^a; 95% CI, 2.3 to 6.3
● Hispanic or Latino: 1999-2012, APC, -1.8^a; 95% CI, -2.6 to -1.1; 2012-2019, APC, 7.2^a; 95% CI, 5.6 to 8.9
● Non-Hispanic White: 1999-2012, APC, -0.4; 95% CI, -0.9 to 0.2; 2012-2019, APC, 4.6^a; 95% CI, 3.2 to 5.9
● Overall: 1999-2012, APC, -0.3; 95% CI, -0.8 to 0.2; 2012-2019, APC, 5.0^a; 95% CI, 3.6 to 6.3

Why Are AAs More at Risk for HF?

Modifiable RFs

- Hypertension, DM, obesity, LVH, smoking, and CKD are more common in AAs

Neurohormonal imbalances and endothelial dysfunction

- Derangements in the RAS and adrenergic axes as well as impaired endothelial function are more common in AAs

Genetic polymorphisms – Least Common Cause

- Several polymorphisms associated with HF (beta 1 adrenergic receptor, alpha 2c receptor, aldosterone synthase, G protein, transforming growth factor beta, NO synthase, and transthyretin)

Socioeconomic factors and quality of care

- Low SES and discrimination from health care providers serve as barriers to attaining treatment goals in AAs

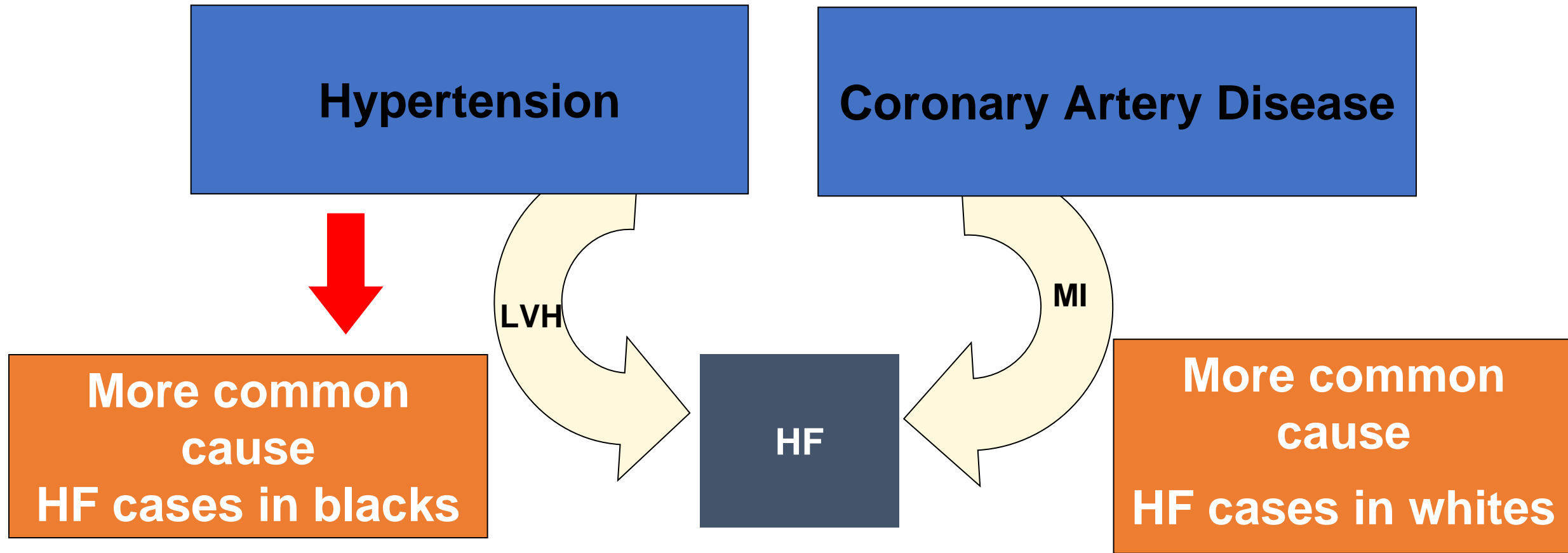
Which is the least convincing cause of most cases of heart failure in African American individuals?

- A. Modifiable risk factor
- B. Neuronal or hormonal imbalances
- C. Genetic polymorphism
- D. Social economic factors and quality of care

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Etiology of Heart Failure in African American Individuals



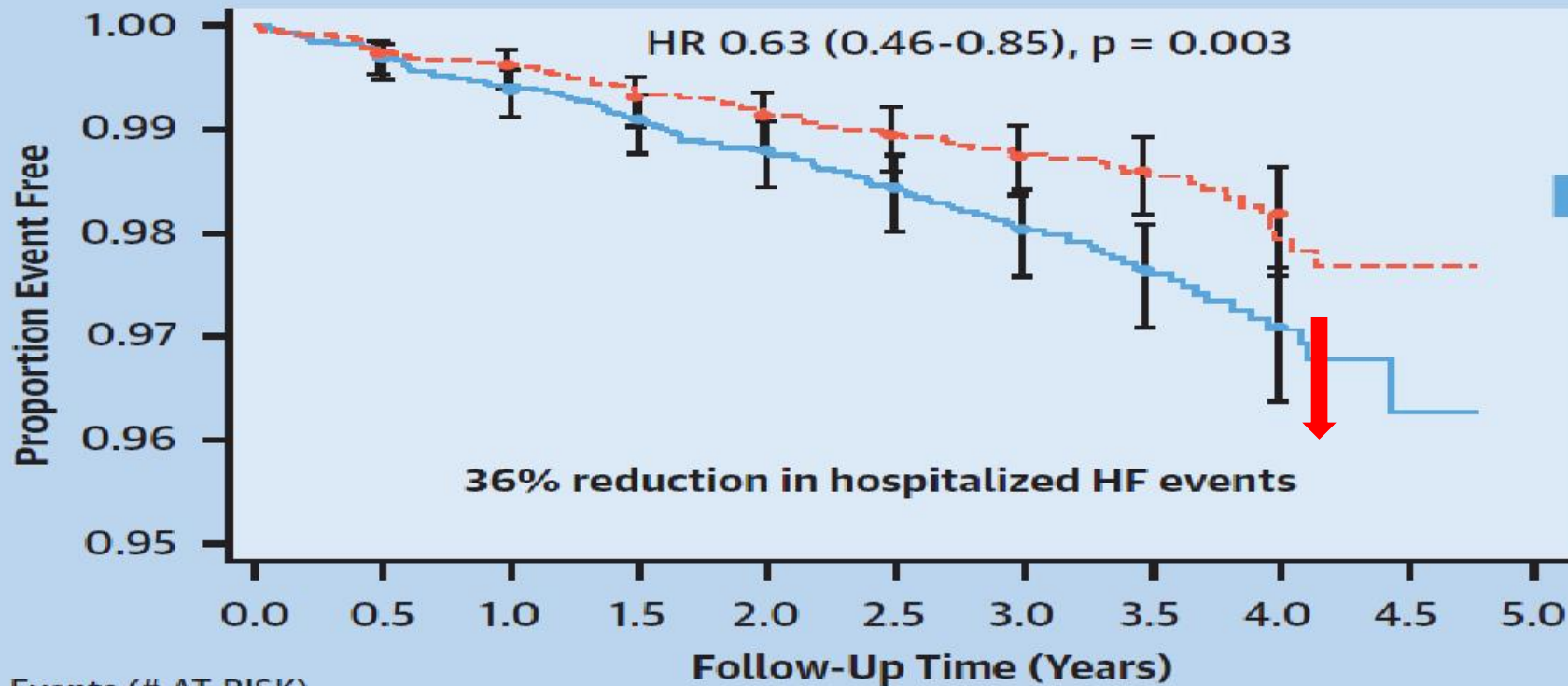
LVH=left ventricular hypertrophy.

HF=heart failure. MI=myocardial infarction

Systolic BP Intervention Trial (SPRINT) (n = 9,361)
(mean age 68 years; 28% ≥ age 75)

Intensive arm
(SBP <120 mm of Hg)
(n = 4,678)

Standard arm
(SBP <140 mm of Hg)
(n = 4,683)



Events (# AT RISK)

Intensive 0 (4678) 11 (4563) 16 (4491) 30 (4421) 39 (4371) 47 (4148) 54 (3120) 59 (1878) 66 (883) 68 (126)

Standard 0 (4683) 12 (4559) 26 (4493) 41 (4423) 55 (4346) 70 (4127) 85 (3070) 94 (1833) 102 (848) 105 (130)

Standard Intensive

HF
Prevention
in Older
Patients
Using
Intensive
BP
Reduction

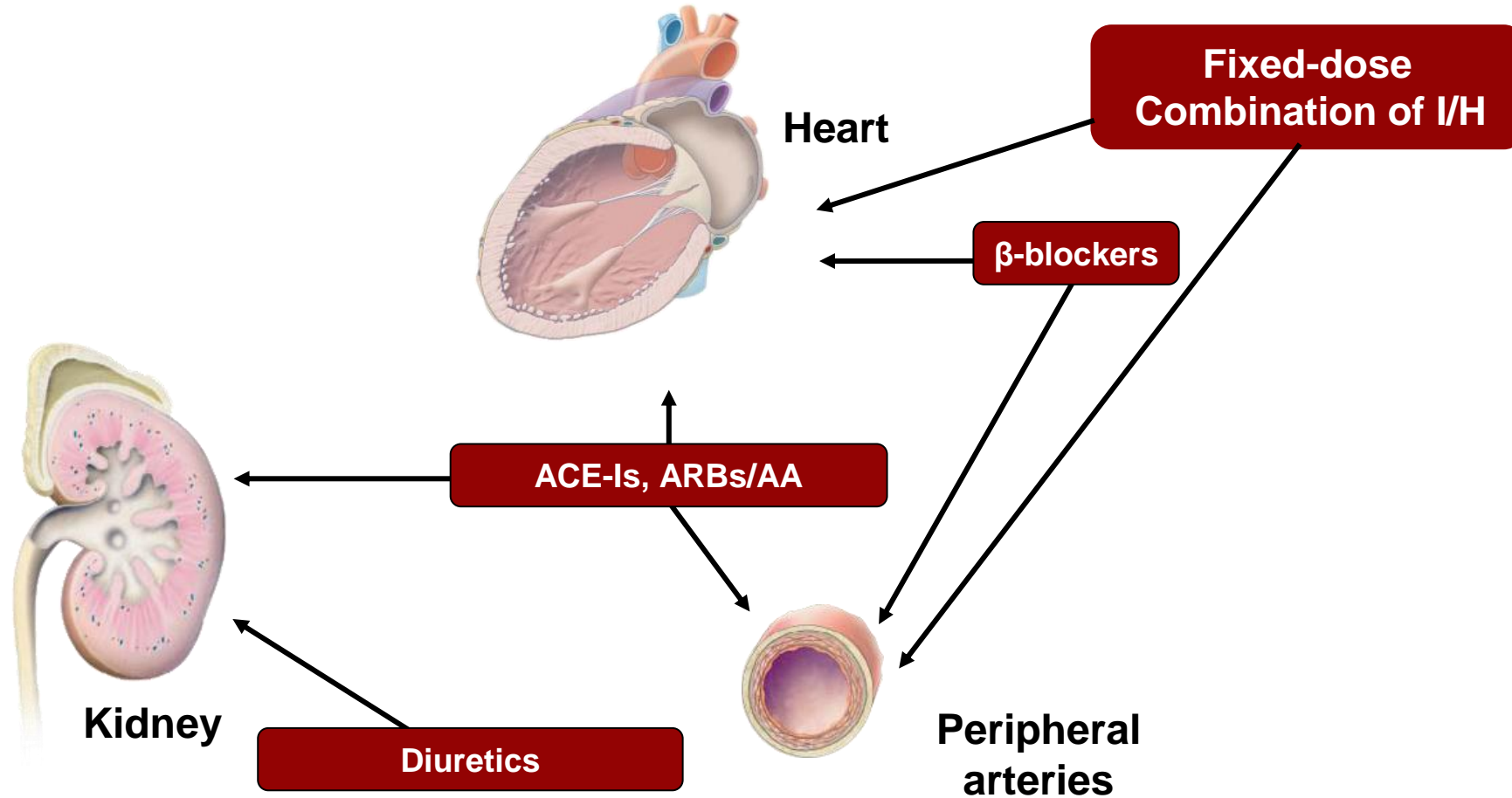
Guideline Directed Medical Therapy Stage C HFrEF: RTCs Magnitude of Benefits

GDMT	RR Reduction in Mortality	NNT Mortality Reduction (Standardized to 36 mo)	RR Reduction in HF Hospitalizations
ACE inhibitor or ARB	17%	26	31%
Beta blocker	34%	9	41%
Aldosterone antagonist	30%	6	35%
Hydralazine/nitrate	43%	7	33%
SGLT-2 Inhibitors	17%	22	31%

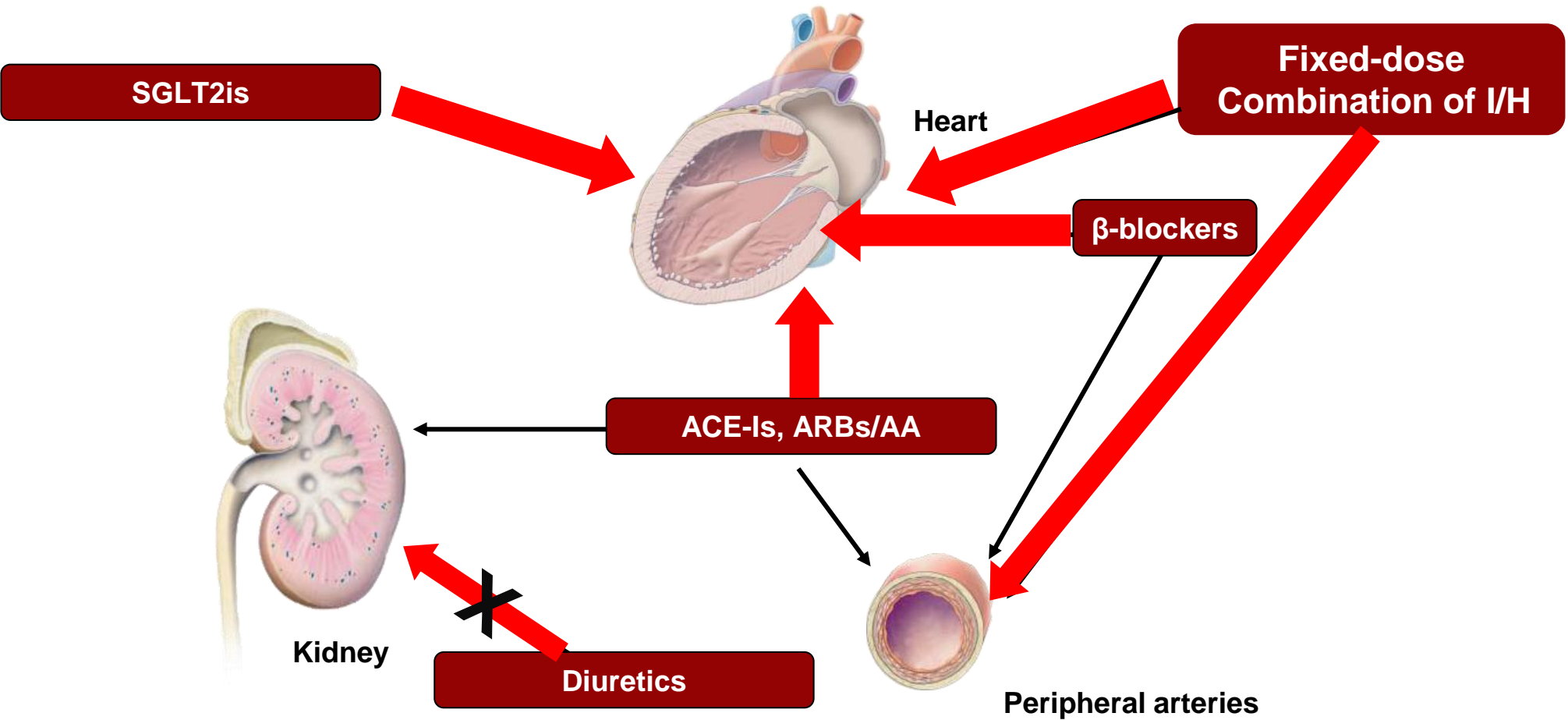
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Standard Care Treatment with HFrEF

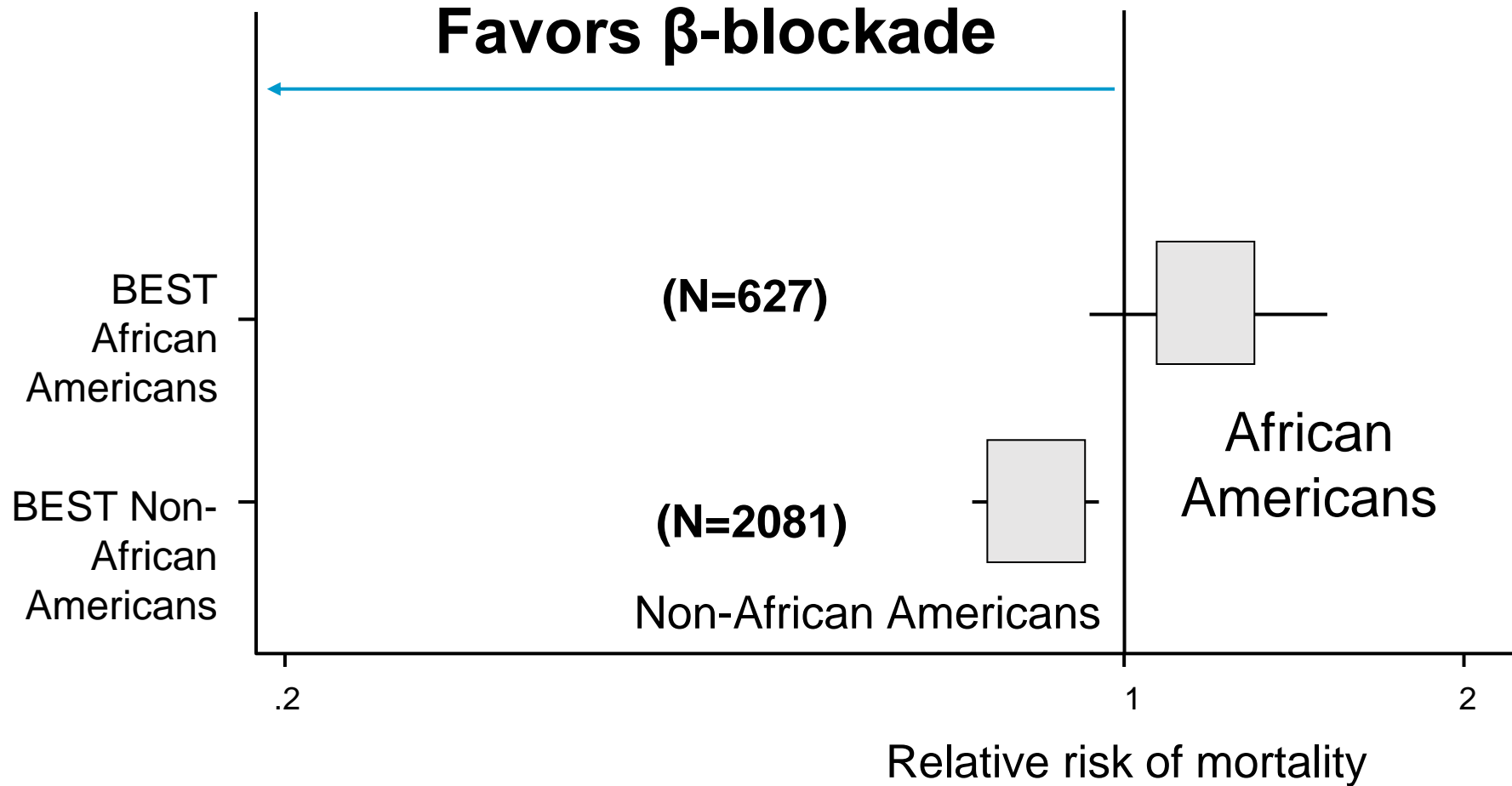


Standard Care Treatment with HFrEF

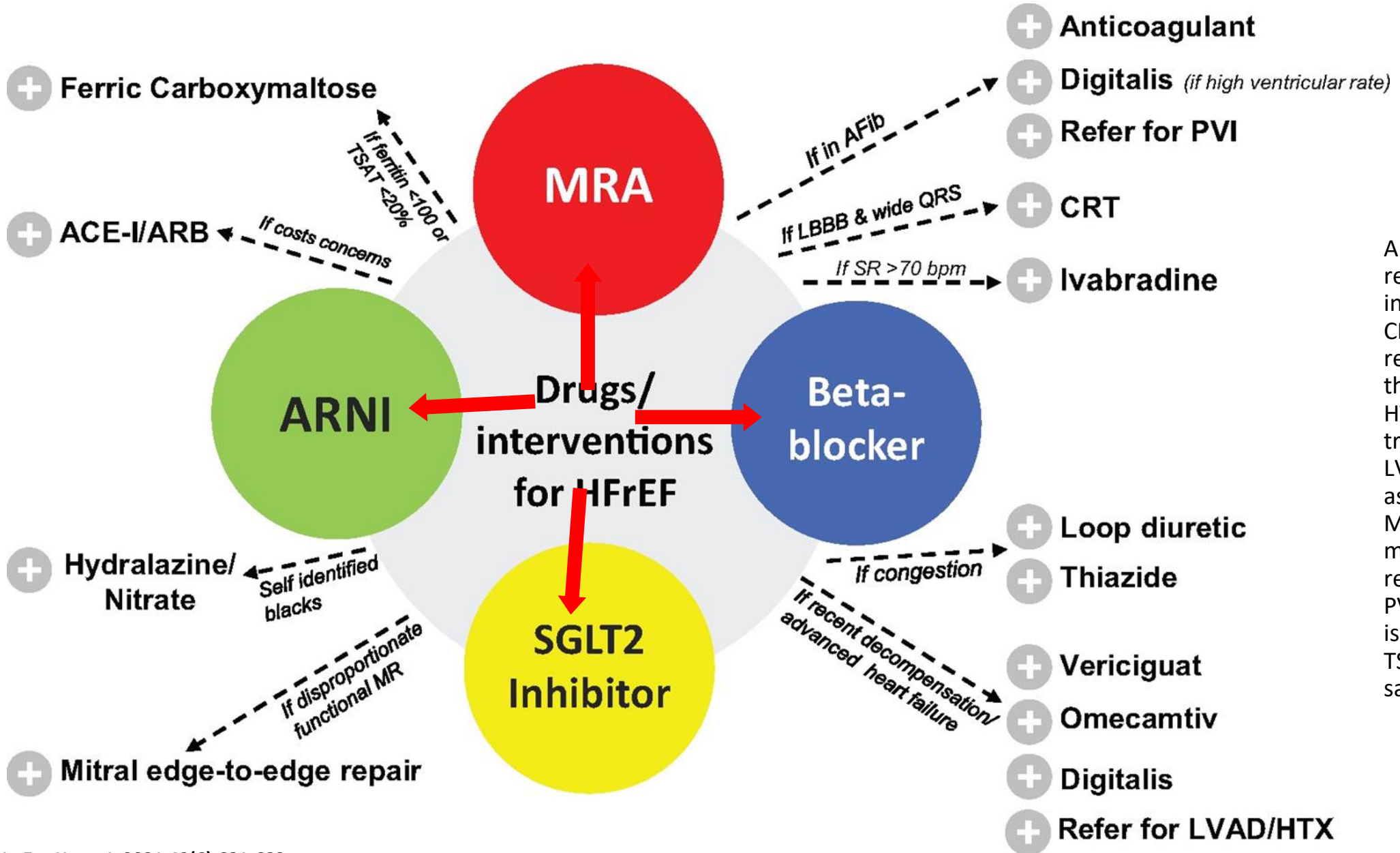


Modified from Jessup M, Brozena S. N Engl J Med. 2003;348:2007-2018.
Heidenreich PA et al. JACC. 2022; 79.17: e263-e421

BEST : No Survival Advantage with β -blocker Bucindolol in African Americans with HF



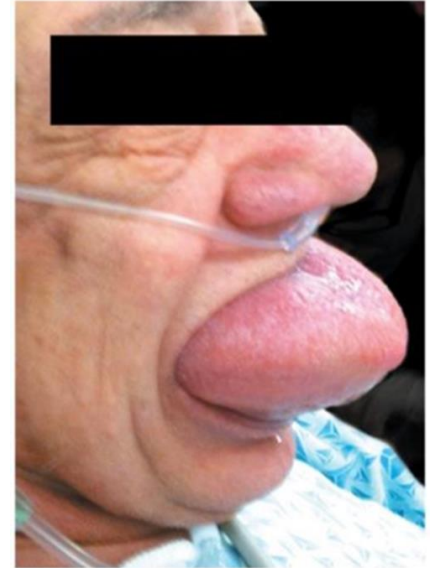
Heart Failure Drug Treatment: the HFrEF Fantastic Four



ARNI, angiotensin receptor/neprilysin inhibitor;
 CRT, cardiac resynchronization therapy;
 HTX, heart transplantation;
 LVAD, left ventricular assist device;
 MRA, mineralocorticoid receptor antagonist;
 PVI, pulmonary vein isolation;
 TSAT, transferrin saturation.

Angioedema

- Inhibition of ACE may prompt ↓ angiotensin II production and ↑ bradykinin level
- Resulting in regional vasodilatation and ↑vascular permeability that are characteristic of angioedema.
- Angioedema onset can occur even after long-term use of ACEIs



Drugs Commonly Used for HFrEF (Stage C HF)

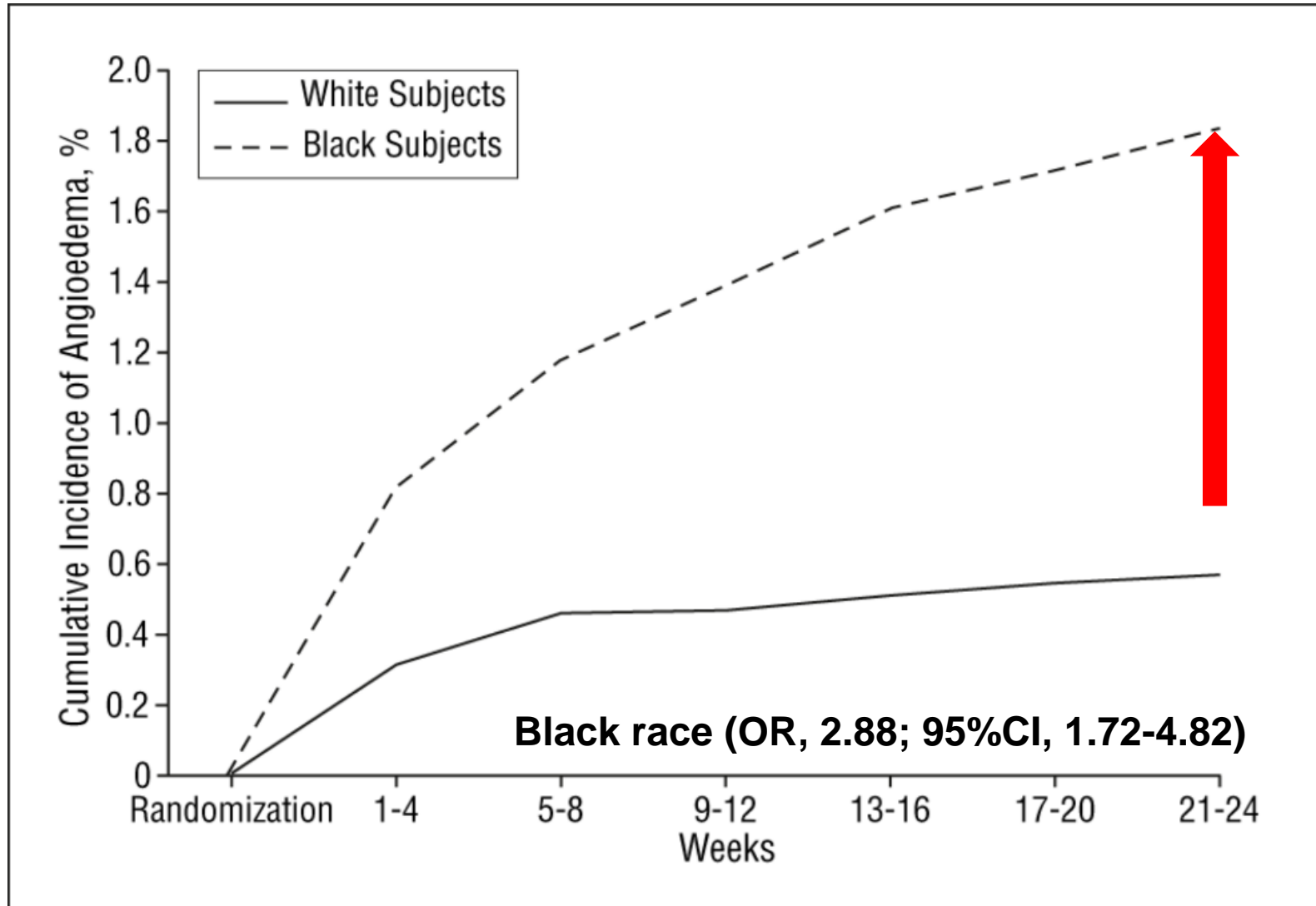
Drug	Initial Daily Dose(s)	Max. Doses(s)	Mean Doses Achieved in RTCs
<i>Beta Blockers</i>			
Bisoprolol	1.25 mg once daily	10 mg once daily	8.6 mg/d
Carvedilol	3.125 mg twice daily	50 mg twice daily	37 mg/d
Metoprolol succinate ER (metoprolol CR/XL)	12.5 to 25 mg once daily	200 mg once daily	15 mg/d

Angioedema

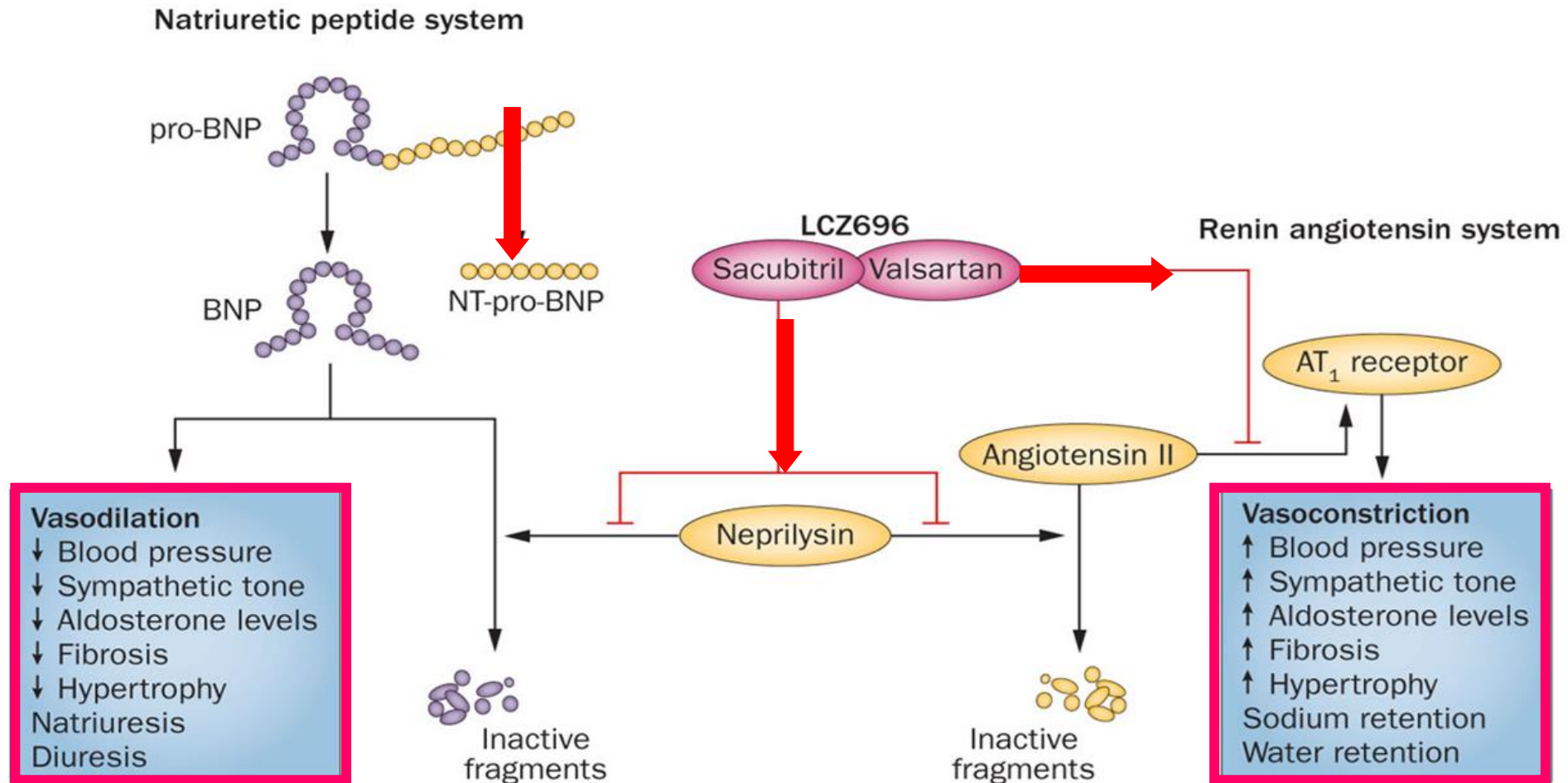
	Total	Blacks	Non-blacks
Chlorthalidone	8 / 15,255 0.1%	2 / 5,369 <0.1%	6 / 9,886 0.1%
Lisinopril	41 / 9,054 0.5%	23 / 3,210 0.7%	18 / 5,844 0.3%
	p<.001	p<.001	p=.002

There were 3 cases (<0.1%) of angioedema in the amlodipine group (comparison to chlorthalidone not significant).

Incidence and Characteristics of Angioedema Associated With Enalapril



N=12,557
Hypertension treated with
Enalapril



Sacubitril/Valsartan

- FDA approved to reduce risk of CV death and hospitalization in patients with chronic HF (NYHA Class II-IV) and reduced EF
 - ACC/AHA/HFSA Guidelines:
 - Recommend sacubitril/valsartan with:
 - NYHA class II or III HF and reduced EF
 - Who tolerate an ACEi or ARB
- Replacement of ACEI/ARB with angiotensin receptor neprilysin inhibitor (ARNI)
 - Recommended to further reduce morbidity/mortality
 - Close surveillance of serum potassium and creatinine (LOE I-BR)

The NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

NOVEMBER 11, 2004

VOL. 351 NO. 20

Combination of Isosorbide Dinitrate and Hydralazine in Blacks with Heart Failure

Anne L. Taylor, M.D., Susan Ziesche, R.N., Clyde Yancy, M.D., Peter Carson, M.D., Ralph D'Agostino, Jr., Ph.D., Keith Ferdinand, M.D., Malcolm Taylor, M.D., Kirkwood Adams, M.D., Michael Sabolinski, M.D., Manuel Worcel, M.D., and Jay N. Cohn, M.D., for the African-American Heart Failure Trial Investigators*

ABSTRACT

BACKGROUND

We examined whether a fixed dose of both isosorbide dinitrate and hydralazine provides additional benefit in blacks with advanced heart failure, a subgroup previously noted to have a favorable response to this therapy.

METHODS

A total of 1050 black patients who had New York Heart Association class III or IV heart failure with dilated ventricles were randomly assigned to receive a fixed dose of isosorbide dinitrate plus hydralazine or placebo in addition to standard therapy for heart failure. The primary end point was a composite score made up of weighted values for death from any cause, a first hospitalization for heart failure, and change in the quality of life.

From the University of Minnesota (A.L.T., J.N.C.) and Minneapolis Veterans Affairs Hospital (S.Z.) — both in Minneapolis; University of Texas Southwestern Medical Center, Dallas (C.Y.); Veterans Affairs Medical Center, Washington, D.C. (P.C.); Wake Forest University, School of Medicine, Winston-Salem, N.C. (R.D.); Heartbeats Life Center and Xavier University, New Orleans (K.F.); Jackson Cardiology Associates, Jackson, Miss. (M.T.); Association of Black Cardiologists, Atlanta (M.T.); University of North Carolina, Chapel Hill (K.A.); and NitroMed, Lexington, Mass. (M.S., M.W.)

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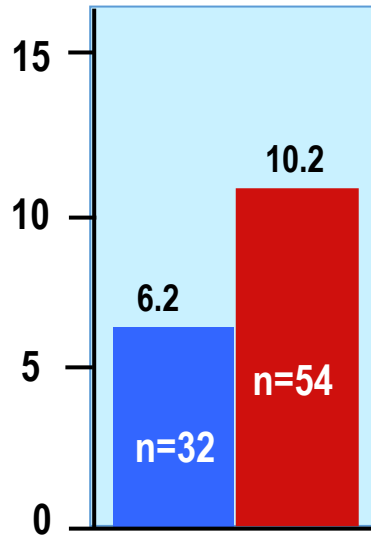
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CONCLUSIONS

The addition of a fixed dose of isosorbide dinitrate plus hydralazine to standard therapy for heart failure including neurohormonal blockers is efficacious and increases survival among black patients with advanced heart failure.

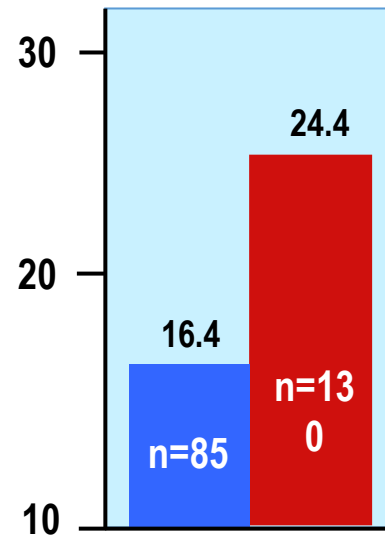
A-HeFT Trial Summary

All-Cause Mortality (%)



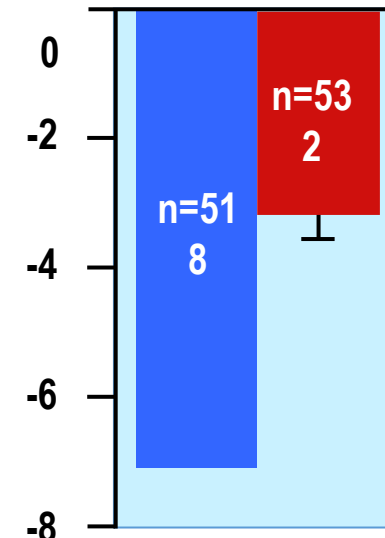
P=0.012

First HF Hospitalization (%)



P<0.001

Patient Reported Functional Status



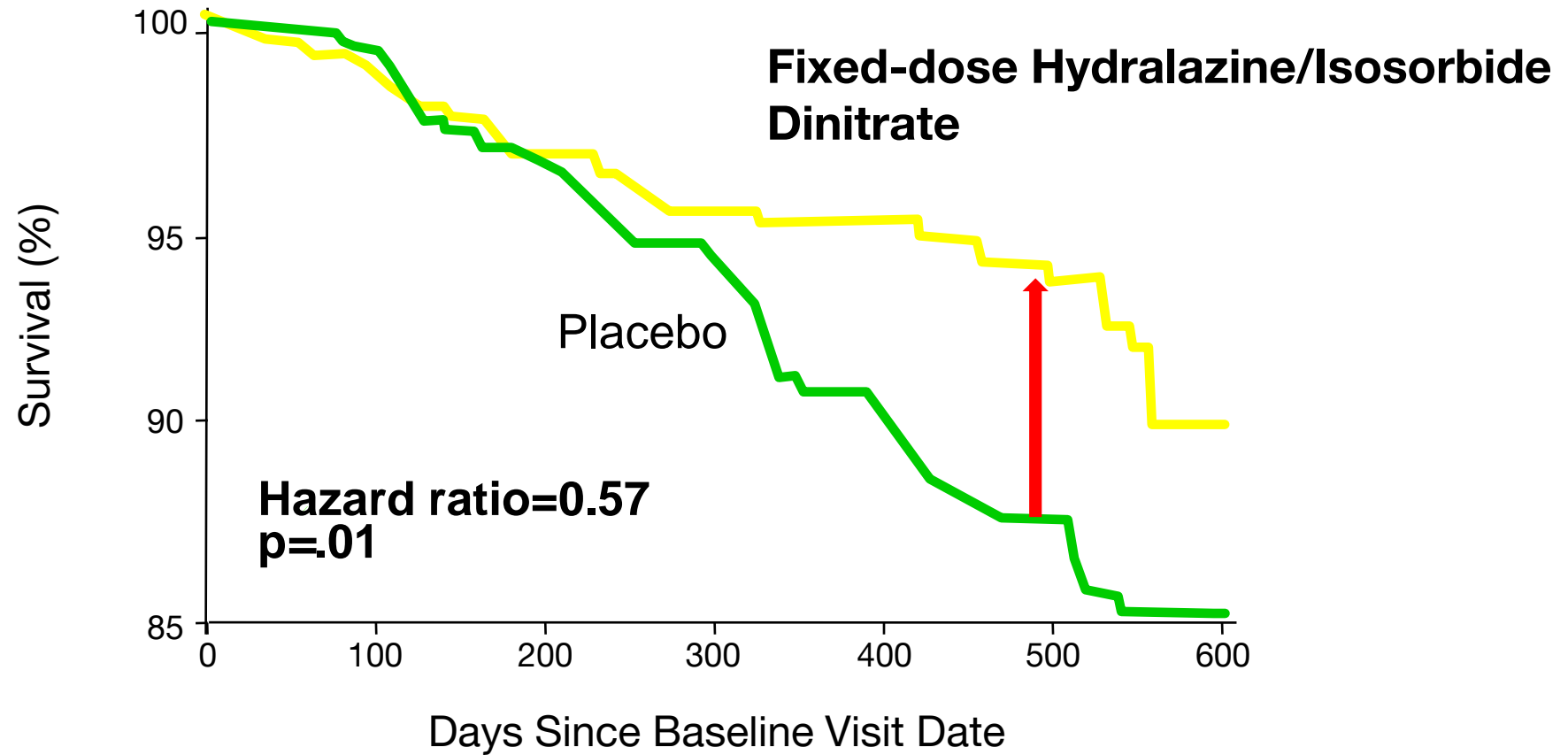
P<0.01

 FDC I/H + Standard Therapies

 Placebo + Standard Therapies

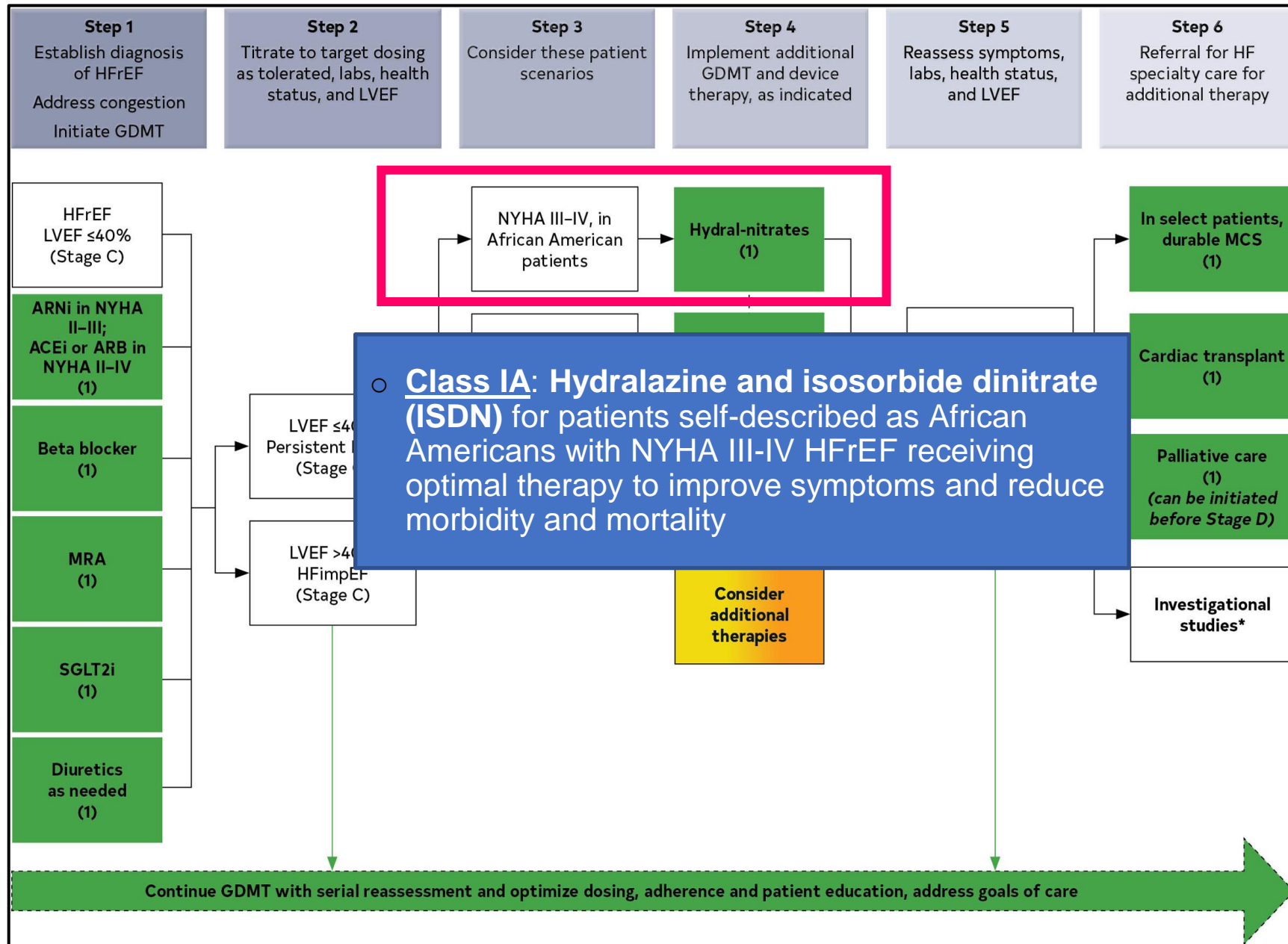
N=1050

A-HeFT: All-Cause Mortality

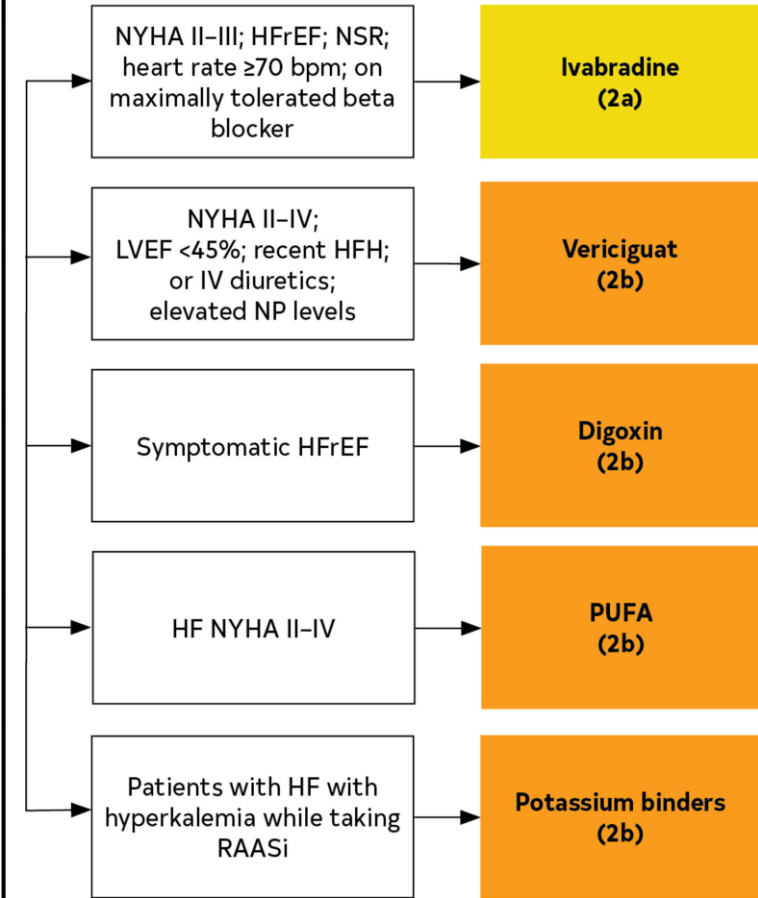


Fixed-dose I/H	518	463	407	359	313	251	13
Placebo	532	466	401	340	285	232	24

Heart Failure: HFrEF Treatment



Consider Additional Therapies Once GDMT Optimized



Heart Failure Readmission- Risk Factors

- **Clinical Factors**

- Advanced age
- Renal disease
- **Prior HF admission**
- **Black race**

- **Behavioral Factors**

- **Non-adherence**
- Dementia
- Depression

Patient Centric Factors

Distressing symptoms

Unavoidable progression of illness

Influence of psychosocial factors

Good but imperfect self-care adherence

Health system failures

On Admission to Hospital - Identify Barriers to Implementation of Treatment Plans

- Cognitive difficulties
- **Impaired learning capabilities**
- Poor communication skills
- Depression/Anxiety
- Adverse Coping Skills
- **Lack of caregiver/family support**

- Comorbidity burden
- **Language barriers**
- **Financial constraints**
- Transportation limitations

Cardiac Rehabilitation in HF

- Specific exercise prescription (intensity, frequency, duration, and progression of training)
- Together with behavioral and lifestyle risk reduction,
- Health education, and
- Personal counseling

Cardiac Rehabilitation

Cardiac Rehab Participation Rates by Race (601,000 Medicare Patients)



Cardiac Rehabilitation



**Only 10% of eligible patients
with heart failure are referred**



**Less than 3% of eligible patients
with heart failure attend
at least 1 session**

Referral

Many People Who Can Benefit Are Not Being Referred



Minority status predicts lower referral and participation rates.

Women, minorities, older people, and those with other medical conditions are under-referred to cardiac rehab.



One of the best predictors of cardiac rehab referral is whether the eligible person speaks English.

Asian Americans are 18 times more likely to speak limited English, compared to white people.



Black women are 60% less likely to be referred and enroll in cardiac rehab programs, compared to white women.

We Know What Works to Improve Referral Rates



Automatic, systematic referral to cardiac rehab at discharge can help connect eligible people with these programs.



Strong coordination among inpatient, home health, and outpatient cardiac rehab programs boosts referral rates as well as participation rates and outcomes.



Patients' medical teams and families can support and encourage participation in cardiac rehab programs.

Awareness campaigns should be aimed at people and caregivers.

Which is true regarding referral for cardiac rehab?

- a) Younger people are referred more often than older people
- b) Women are referred more often than men
- c) One of the best predictors of cardiac rehab is English speaking
- d) Minority individuals are more often referred to cardiac rehab

Which is true regarding referral for cardiac rehab?

- a) Younger people are referred more often than older people
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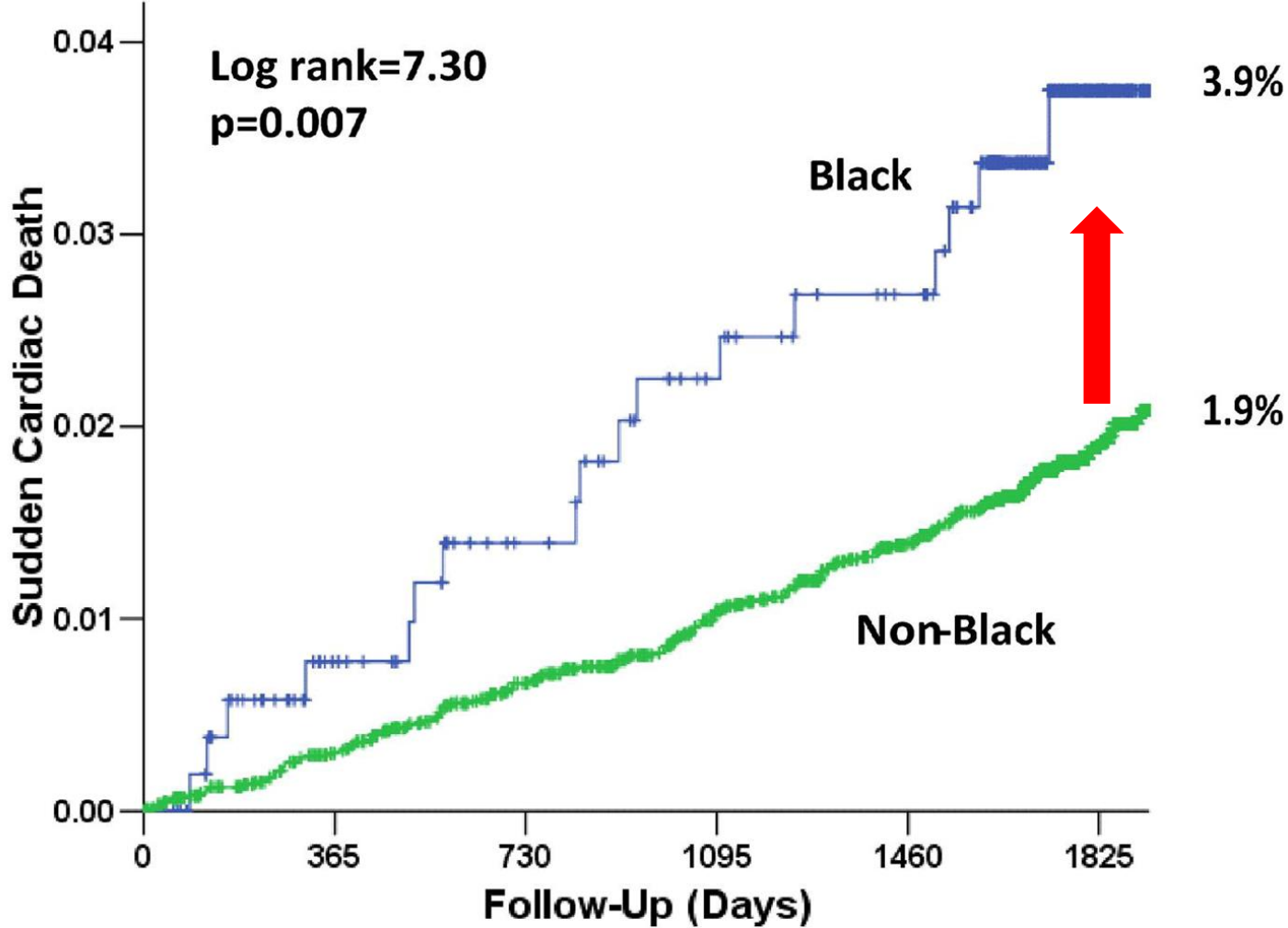


Sudden Cardiac Death

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Racial Differences SCD Hypertensive Patients: LIFE Losartan Study

5-Year SCD
Incidence



Number at Risk

Black	533	495	475	459	446	154
Non-Black	8660	8548	8413	8242	8075	3476

Sudden Cardiac Arrest (SCA) and Sudden Cardiac Death (SCD) higher in AAs vs. Whites

- Primarily higher burden of traditional and nontraditional (eg, sickle cell trait) CVD risk factors
- SCN5A-1103Y -common missense variant, of African ancestry, cardiac sodium channel gene.
- SCN5A-1103Y interacts with QT-prolonging to promote ventricular arrhythmias at high risk for SC
- Gene-environment interaction: SCN5A-1103Y (JHS-15.4%) and hypokalemia influences QT interval prolongation in AAs
- Out-of-hospital SCA: AAs 2X as likely to experience SCD
- AAs SCA on average >6 years younger than whites.

Age-specific Incidence of Sudden Cardiac Arrest in Oregon Sudden Unexpected Death Study (Oregon SUDS), 2002 to 2005

