Guidelines for Prevention and Management of Heart Failure

Anita Deswal, MD, MPH, FAHA, FACC, FHFSA
Ting Tsung and Wei Fong Chao Distinguished Chair
Professor of Medicine
Chair, Department of Cardiology
UT MD Anderson Cancer Center

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Disclosures

- No Financial Disclosures
- American Heart Association Heart Failure Workgroup

Objectives

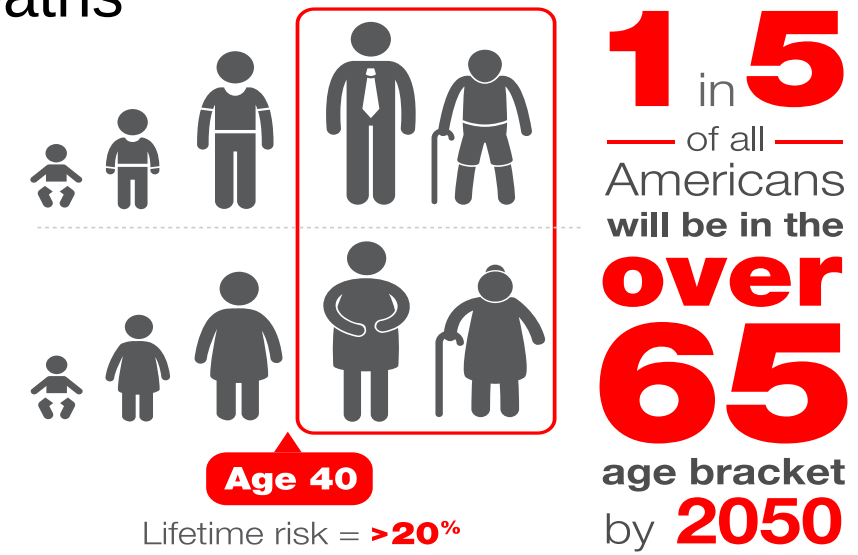
- Articulate the key elements for early detection of heart failure (Stage A) and recommended treatments

- Classify heart failure patients into stages and apply treatments, interventions and processes from the 2013 AHA/ACC/HFSA Heart Failure Guidelines / 2017 focused Update

- List the key pharmacological treatments for HFrEF for heart failure
- List Guideline recommendations for HFpEF

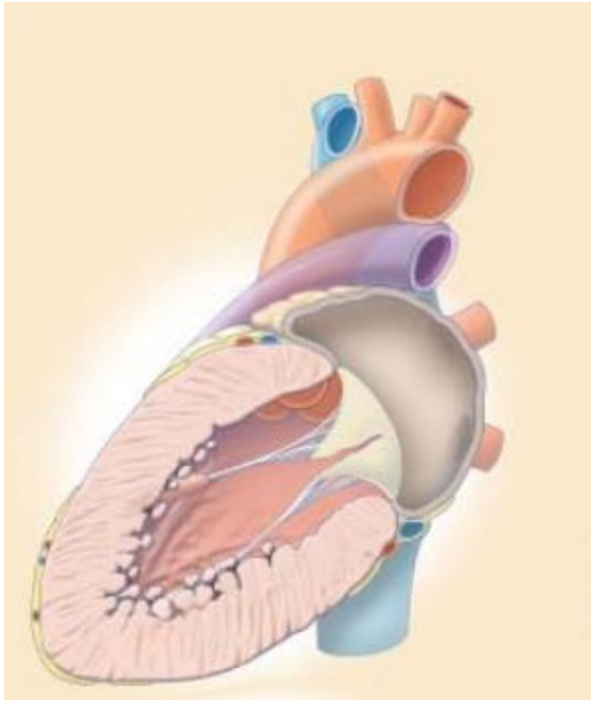
Burden of Heart Failure

- Lifetime risk > 20% for Americans >40 years of age
- 870,000 new cases diagnosed annually
- Prevalence in US: ~ 6.5 million
- 2014: Primary: ≈1.1 million ER visits, 1 million hospitalizations, and 80,000 deaths
- Annual cost of HF care in US ~ 30.7 billion in 2012

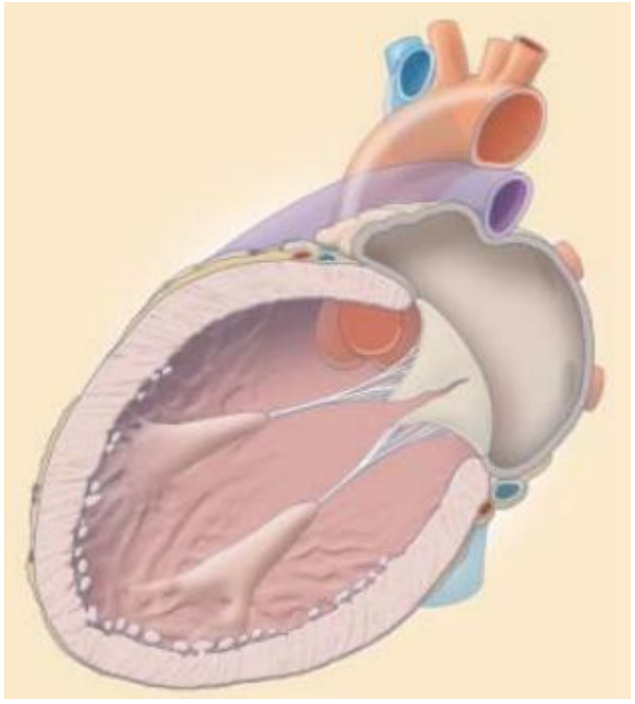


Definition of Heart Failure

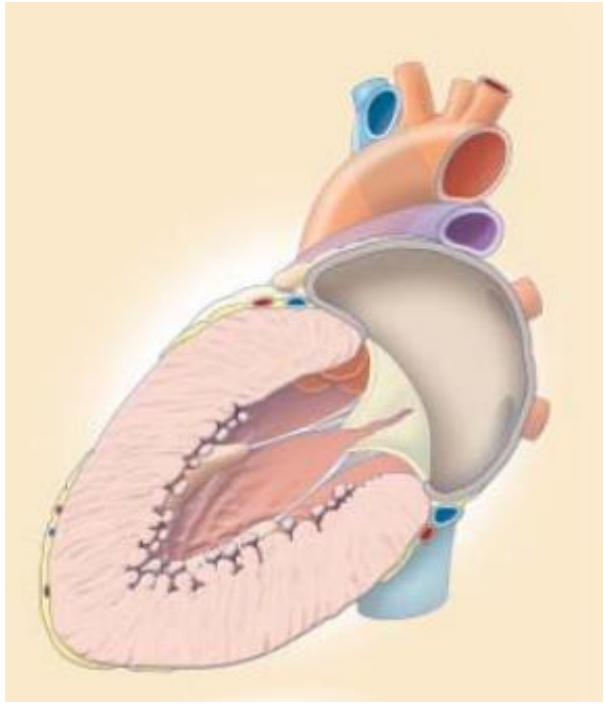
A clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood



Normal Heart



HF with Reduced Ejection Fraction (HF*r*EF)



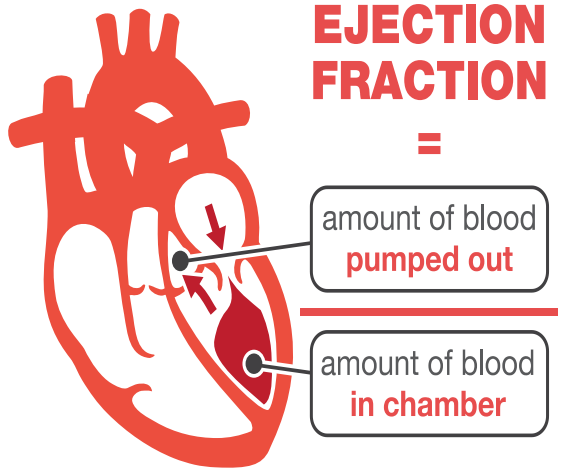
HF with Preserved Ejection Fraction (HF*p*EF)

Jessup M, Brozena SA. *New Engl J Med.* 2003; 348:2007-2018

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

Classification of Heart Failure

Classification	EF (%)	Description
HF*r*EF (HF with reduced EF)	**≤40**	Same as **systolic HF**. RCTs have mainly enrolled patients with HF*r*EF
HF*p*EF (HF with preservedEF)	**≥50**	Same as **diastolic HF**. Diagnosis of HF*p*EF is challenging because it largely involves excluding other potential noncardiac causes of symptoms suggestive of HF.
HF*p*EF, borderline (or HF*m*EF)	**41 – 49**	These patients fall into a borderline or intermediate group.
HF*p*EF improved	**>40**	A subset of patients with HF*p*EF who previously had HF*r*EF. Patients with improvement or recovery in EF may be clinically distinct from those with persistently preserved or reduced EF.

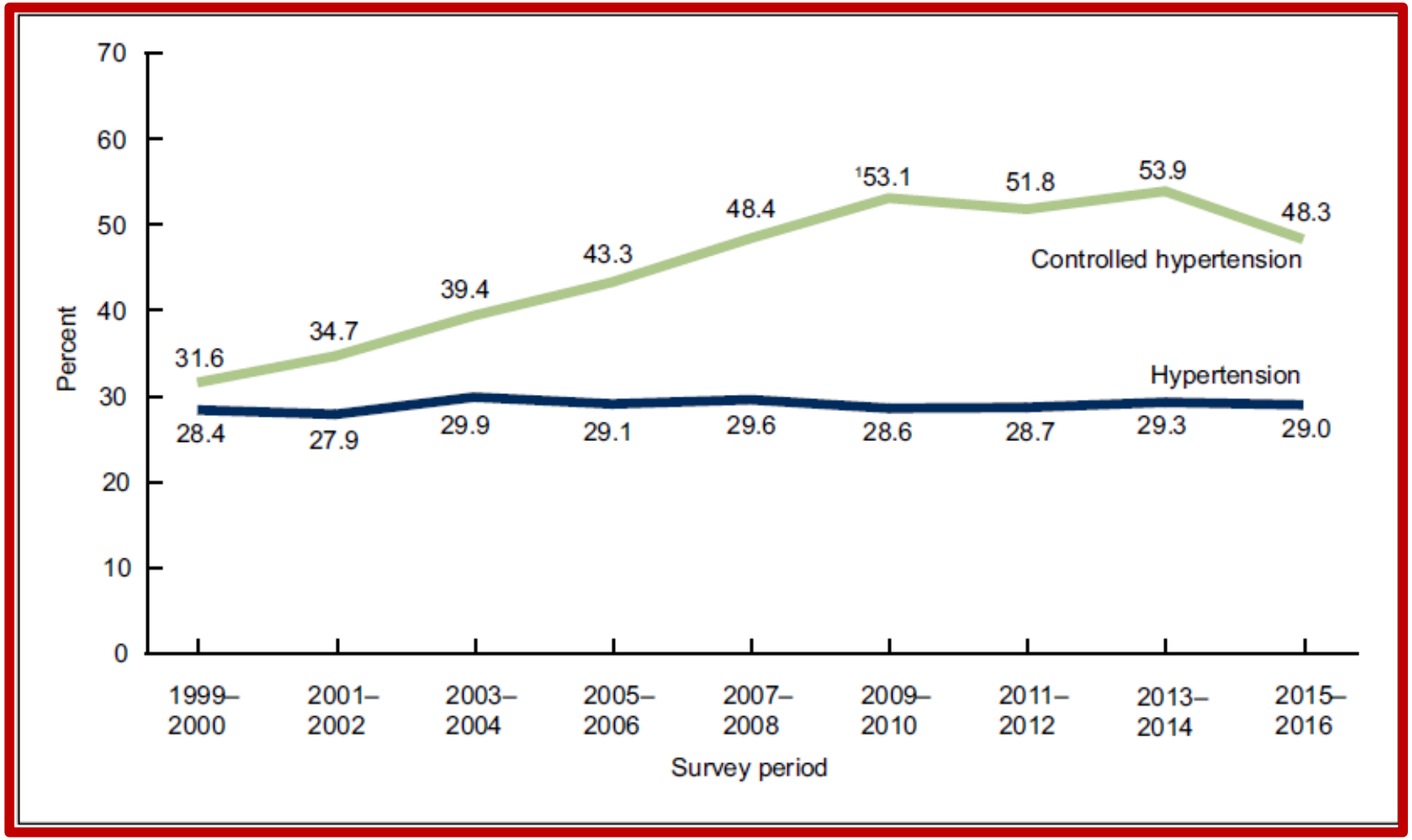


Prevalence of Common Risk Factors for HF/CVD

Behavior/Risk Factor	Prevalence
Smoking, Adults	15.5%
Obesity, Adults	39.6%
Obesity, Youth	18.5%
Low-Density Lipoprotein Cholesterol ≥130 mg/dl, Adults	28.5%
Hypertension, Adults*	45.6%
Diabetes Mellitus, Diagnosed	9.8%
Diabetes Mellitus, Undiagnosed	3.7%
Chronic Kidney Disease	14.8%
Recommended Exercise (2008 guidelines)	22.5%
*Hypertension defined by definition in 2017 ACC/AHA guidelines for hypertension	

Olmstead County: Coronary heart disease, hypertension, diabetes, obesity, and smoking are responsible for 52% of incident HF cases

Age- adjusted trends in Hypertension and controlled hypertension in adults ≥ 18 years in the US



% of individuals with HTN increases with age:

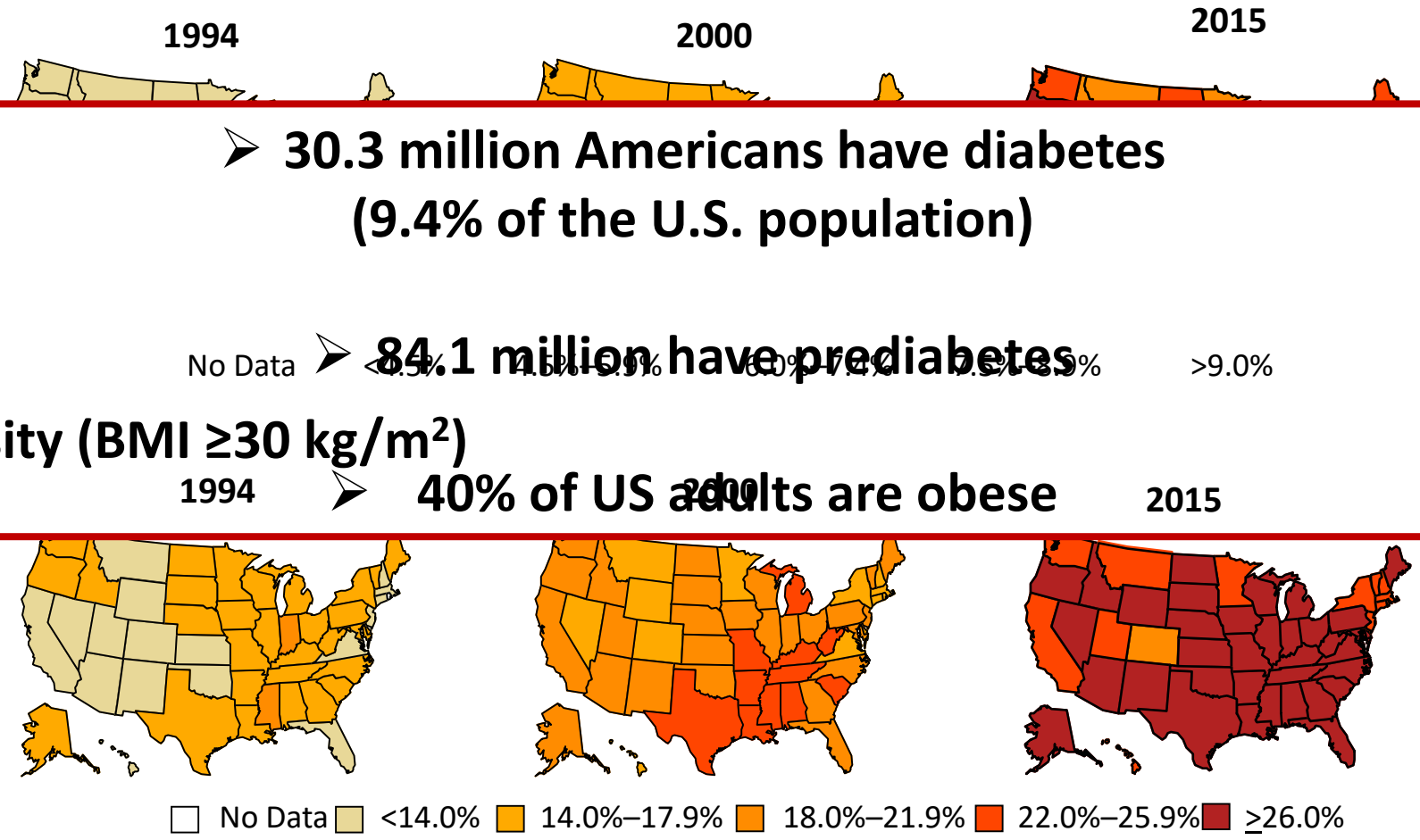
33% among those aged 40–59 and 63% among those aged 60 and over

https://www.cdc.gov/nchs/data/databriefsdb289.pdf

Prevalence of Diabetes and Obesity in the US

Diabetes

Age-adjusted Prevalence

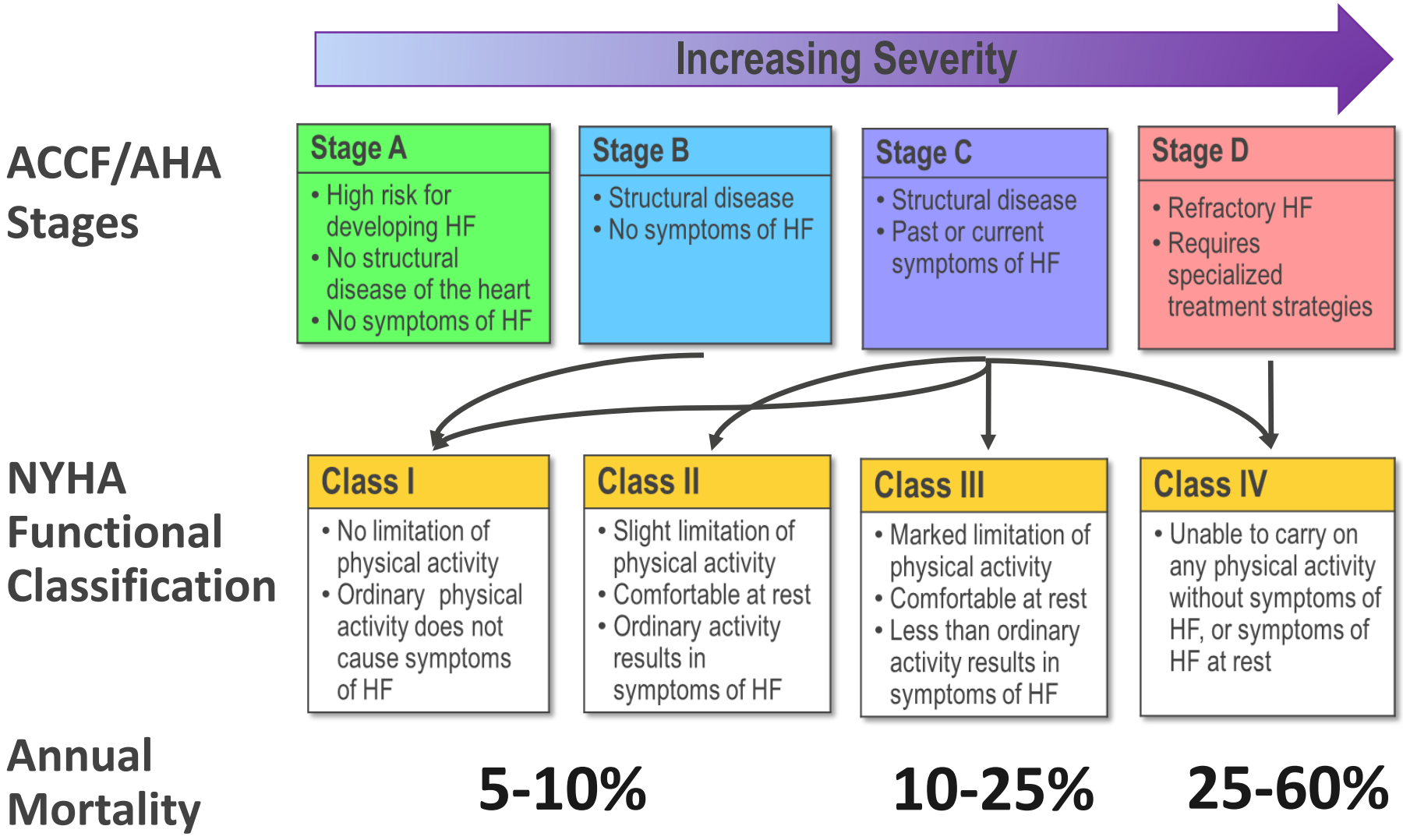


- **30.3 million Americans have diabetes (9.4% of the U.S. population)**
- **84.1 million have prediabetes**

Obesity (BMI ≥30 kg/m²)

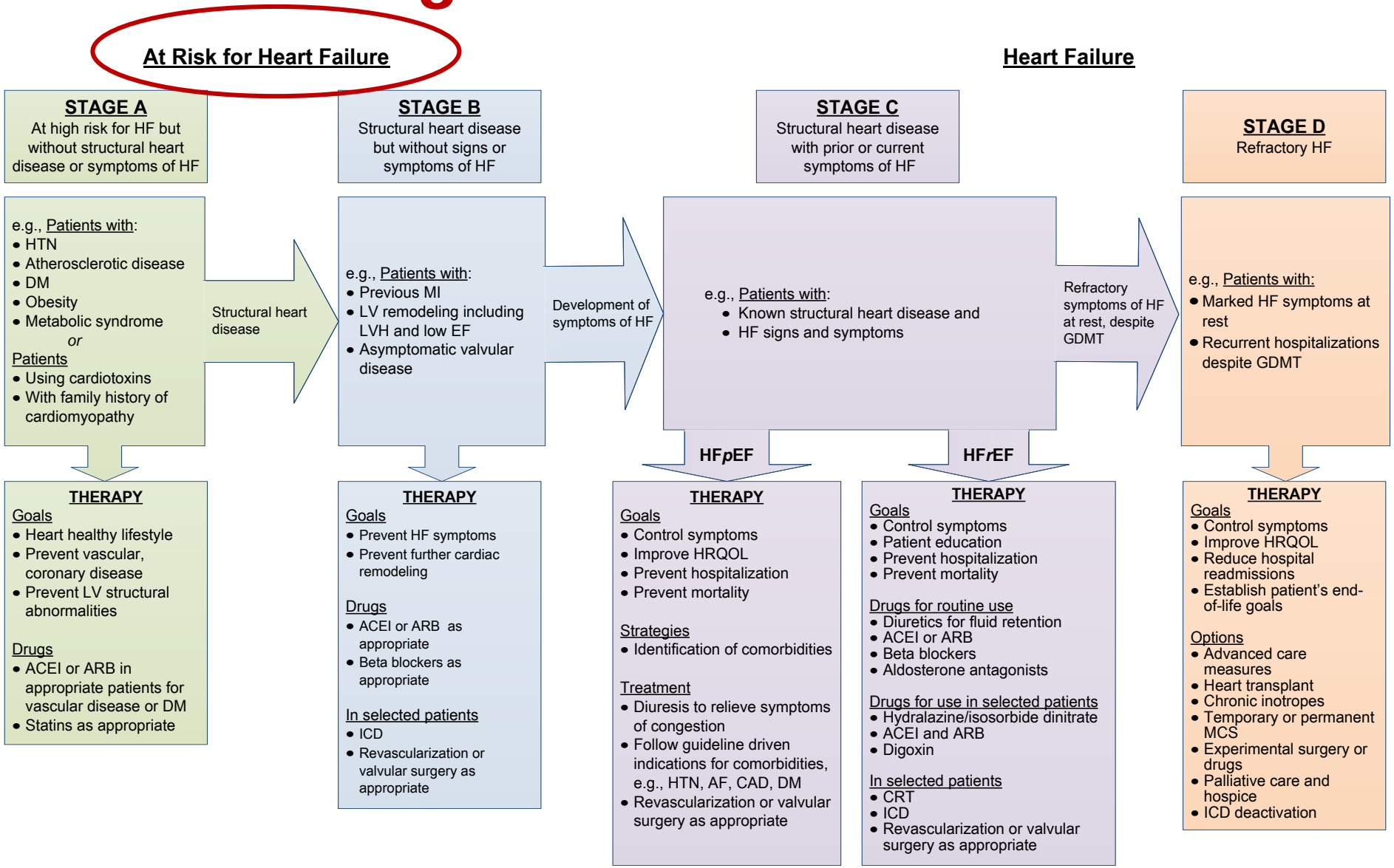
- **40% of US adults are obese**

HF Severity: ACC/AHA Stages and NYHA Functional Classification



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

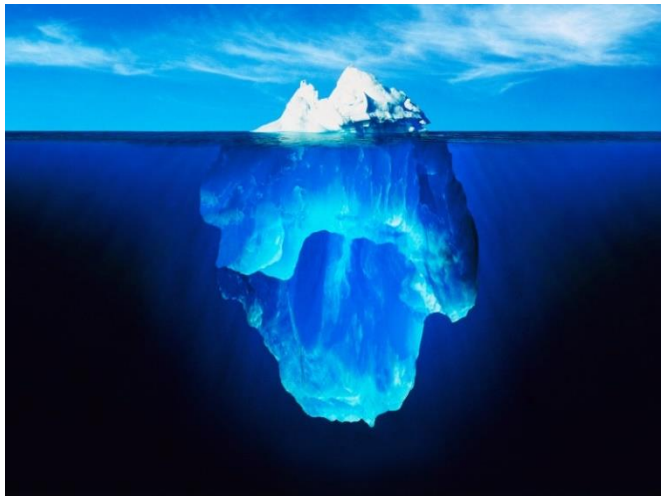
Stages of Heart Failure



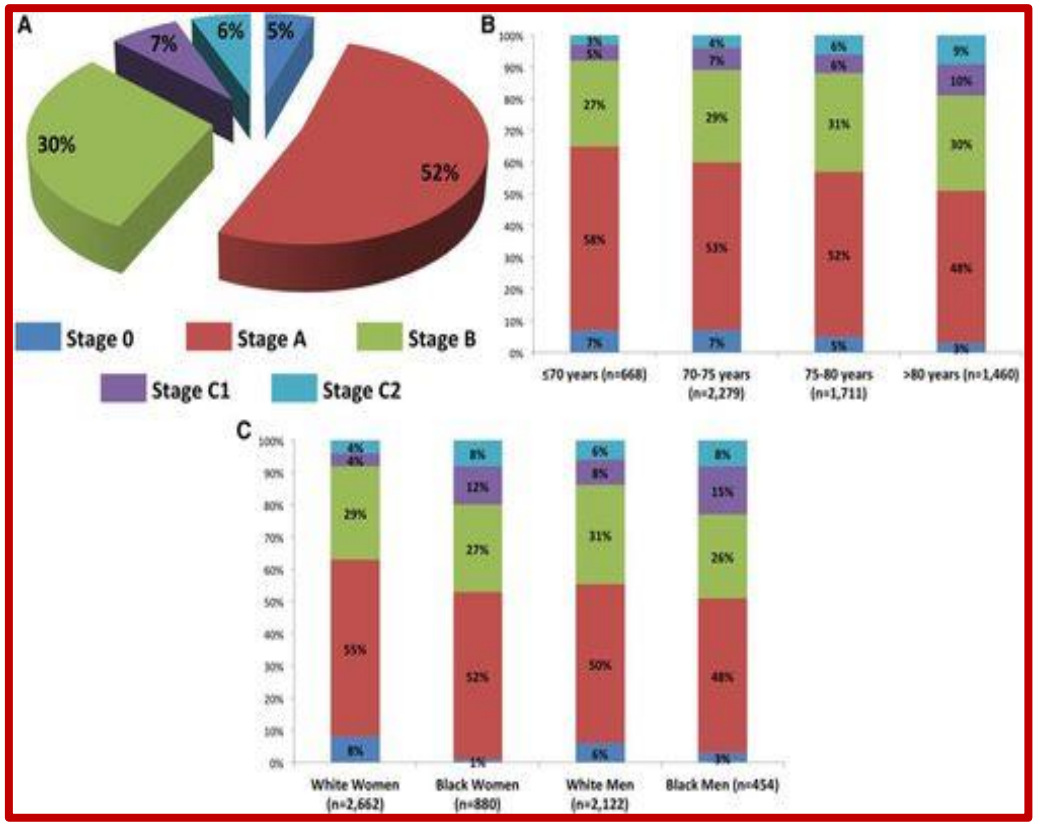
2013 ACCF/AHA Guideline for the Management of Heart Failure. Yancy CW, et al. *Circulation.* 2013;128:e240 e327

Majority of the population is in Stage A/B

Individuals aged >45 yrs:
56% in Stage A/B



Older individuals (67-91 yrs: ARIC)
82% with Stage A/B



Ammar et al Circulation 2007;115:1563 70, Shah AM et al. Circulation 2017;135:224 240

AHA's My Life Check- Life's Simple 7 to stay Heart Healthy

Stage A: 2013

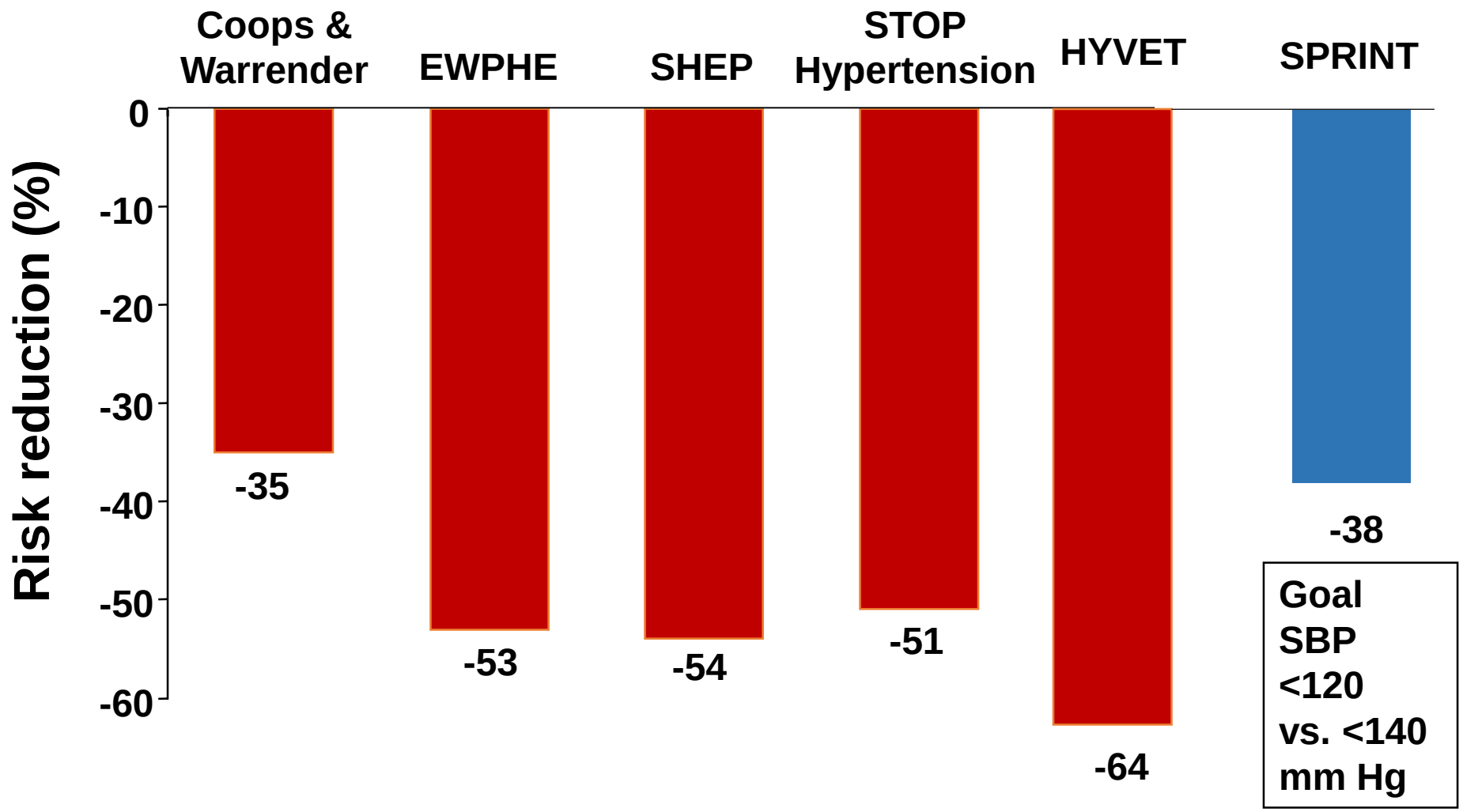
Hypertension and lipid disorders should be controlled in accordance with contemporary guidelines to lower the risk of HF.

Other conditions that may lead to or contribute to HF, such as obesity, diabetes mellitus, tobacco use, and known cardiotoxic agents, should be controlled or avoided.

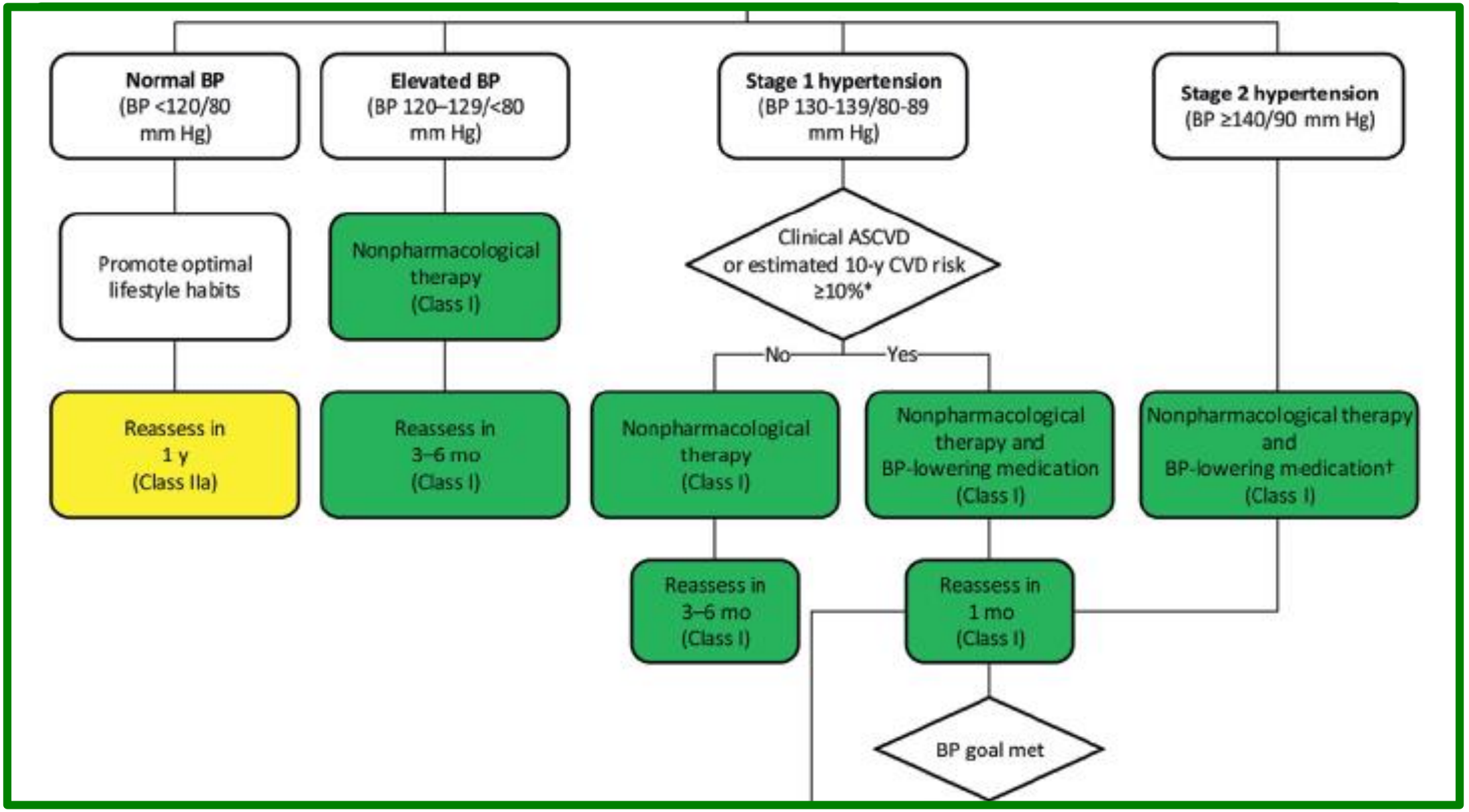
+ 2017

COR	LOE	Recommendations
		In patients at increased risk, stage A HF, the optimal blood pressure in those with hypertension should be less than 130/80 mm Hg.

Risk Reduction of HF in Elderly Hypertensives in RCTs

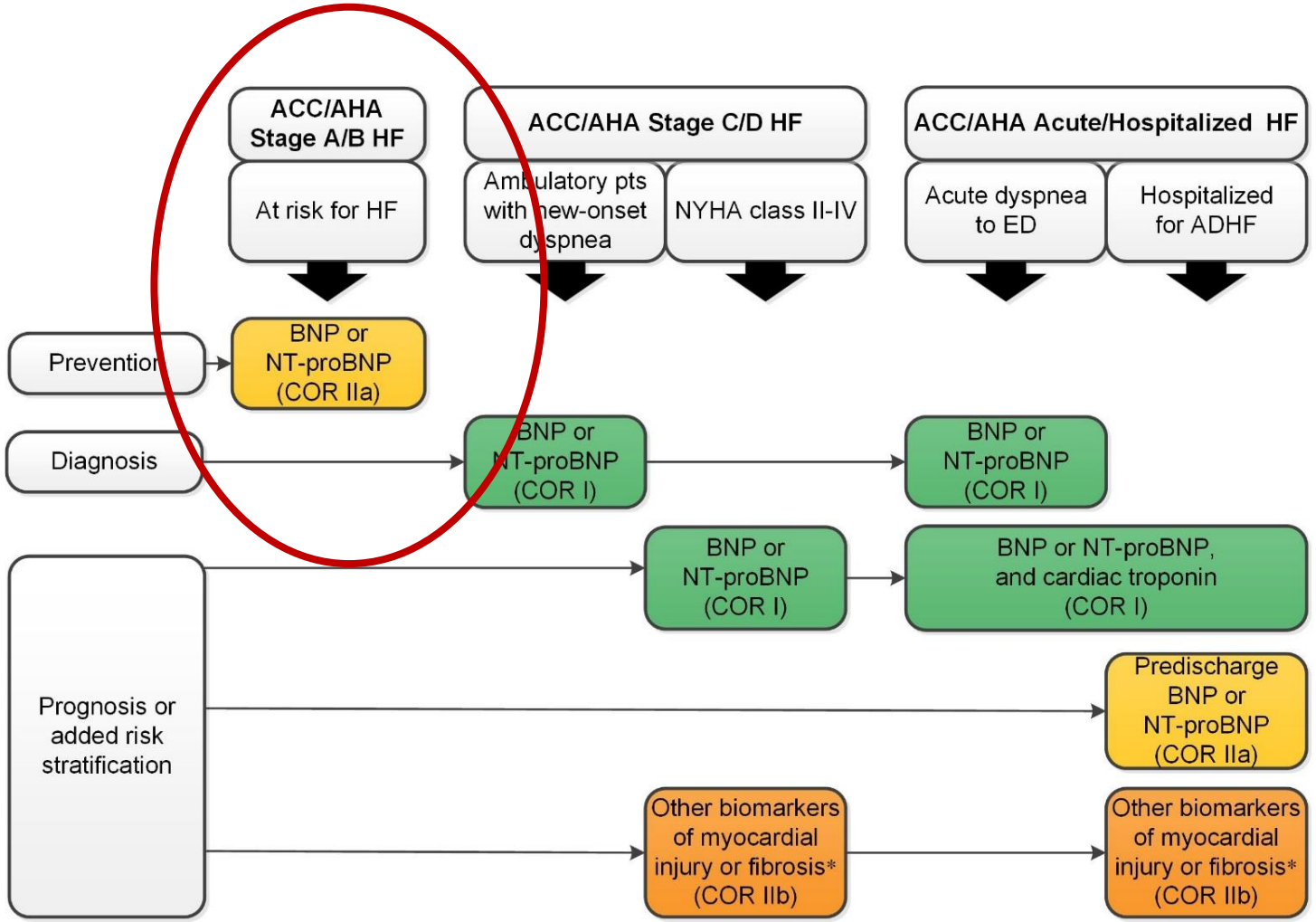


BP Thresholds and Recommendations for Treatment & FU



AHA/ACC Guideline on Hypertension, 2017

Biomarkers: Indications for Prevention



*Other biomarkers of injury or fibrosis include soluble ST2 receptor, galectin-3, and high-sensitivity troponin; ADHF, acute decompensated heart failure; BNP, B-type natriuretic peptide; COR, Class of Recommendation; ED, emergency department; HF, heart failure; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; and pts, patients.

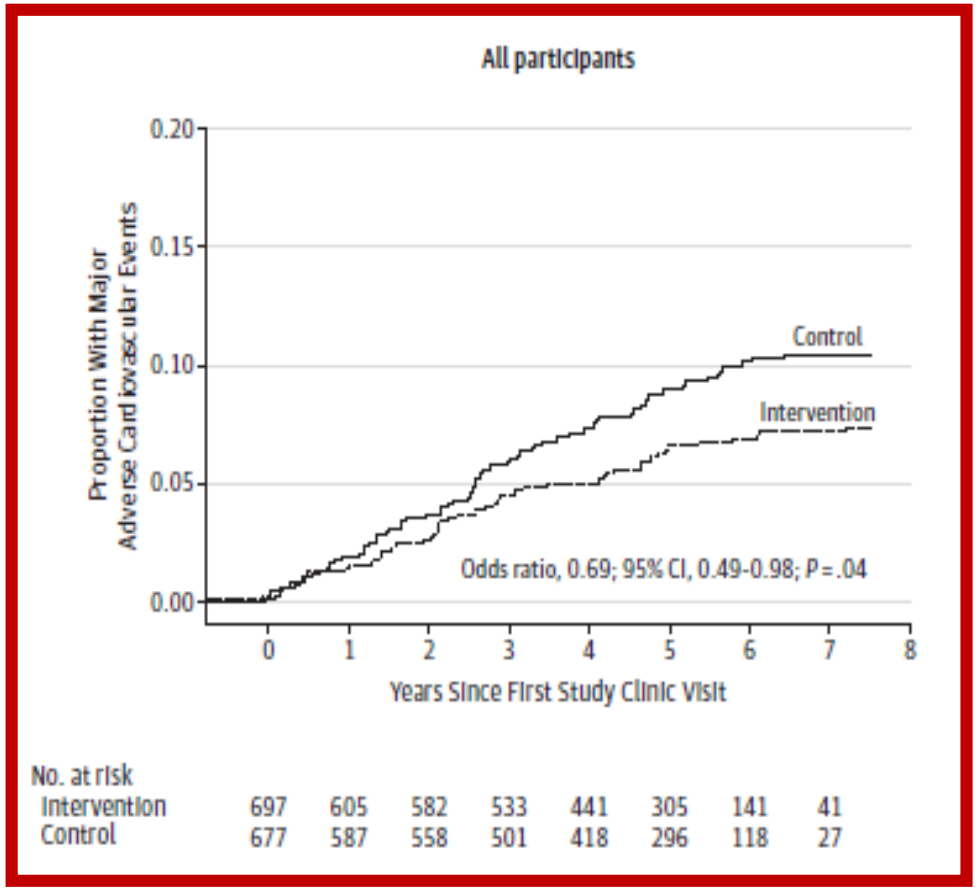
Biomarkers: Indications for Use in Prevention of HF

COR	LOE	Recommendation	Comment/ Rationale
		For patients at risk of developing HF, natriuretic peptide biomarker–based screening followed by team-based care, including a cardiovascular specialist optimizing GDMT, can be useful to prevent the development of left ventricular dysfunction (systolic or diastolic) or new-onset HF.	NEW: New data suggest that natriuretic peptide biomarker screening and early intervention may prevent HF.

STOP-HF (The St Vincent's Screening to Prevent Heart Failure)

- Large-scale (1374 individuals in Ireland), un-blinded study of patients at risk of HF (HTN, DM, or known vascular disease- stage A HF), but without established left ventricular systolic dysfunction or HF
- Patients randomly assigned to receive intervention based on screening BNP or usual primary care.
- Intervention group participants with BNP levels of >50 pg/mL had an echo and were referred to a cardiologist.

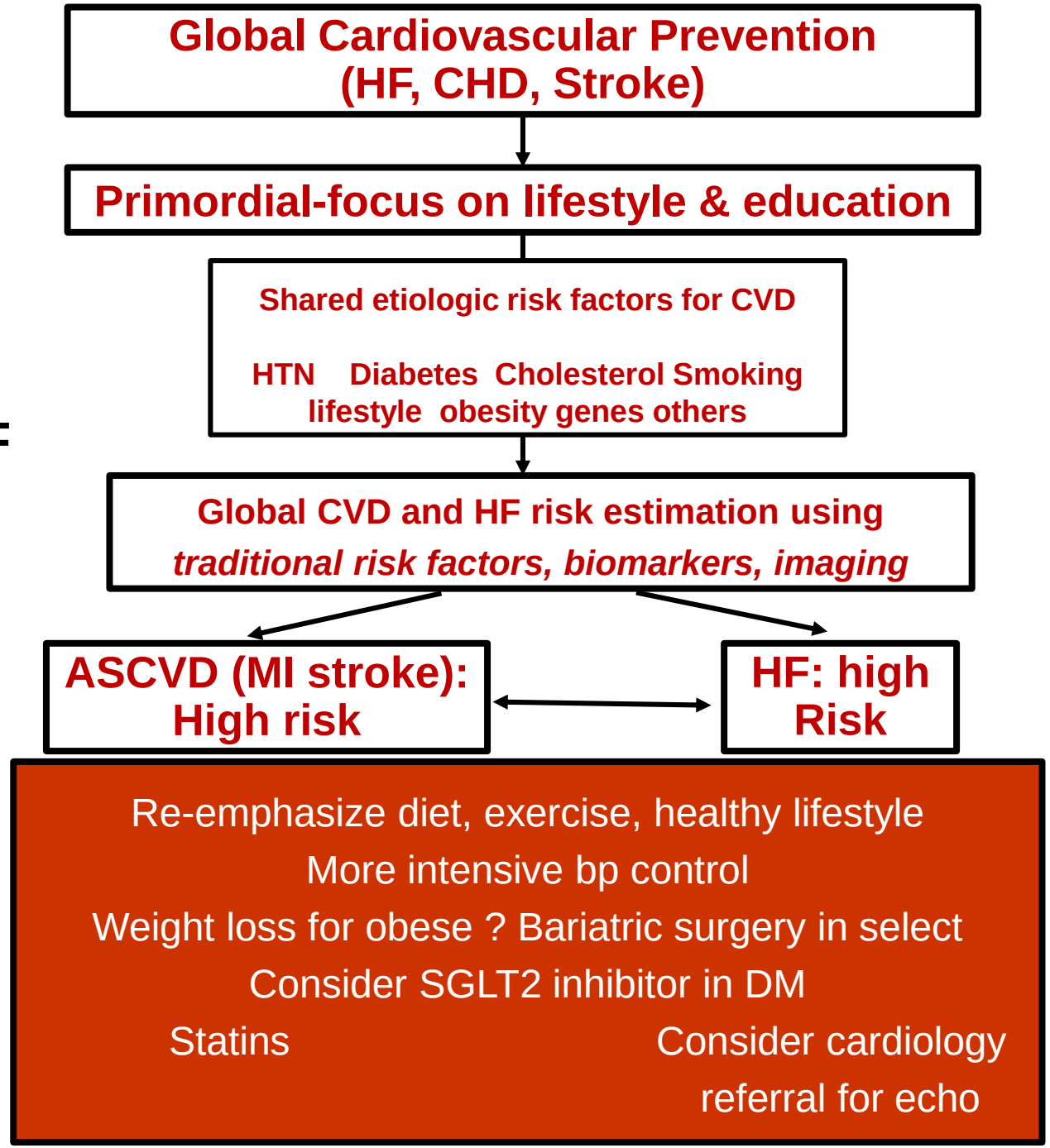
STOP-HF
(St Vincent's Screening to Prevent Heart Failure)



BNP-based screening reduced the composite endpoint of asymptomatic left ventricular (LV) dysfunction (systolic or diastolic) with or without newly diagnosed HF

Ledwidge M et al. JAMA 2013

Suggested Algorithm for Prevention of HF (Stage A)
(Not in guideline)



Nambi V, Deswal A et al. Circulation 2018;137:106–108

Prevention of Clinical HF in Stage B

(Structural cardiac abnormalities without clinical HF)

Recommendations	COR	LOE
In patients with a history of MI and reduced EF, ACE inhibitors or ARBs should be used to prevent HF	I	A
In patients with MI and reduced EF, evidence-based beta blockers should be used to prevent HF	I	B
In patients with MI, statins should be used to prevent HF	I	A
Blood pressure should be controlled to prevent symptomatic HF	I	A
ACE inhibitors should be used in all patients with a reduced EF to prevent HF	I	A
Beta blockers should be used in all patients with a reduced EF to prevent HF	I	C

Treat co-existing valvular heart disease and CAD as indicated

Initial Workup of Stage C HF

- Detailed history, including 3 generation family history (Class I)
- Initial laboratory evaluation:
  - CBC, urinalysis, CMP (including calcium and magnesium), fasting lipid profile, TSH (Class I)
  - Serial monitoring, when indicated, should include serum electrolytes and renal function (Class I)
  - Screening for hemochromatosis, HIV, amyloidosis, pheochromocytoma and other etiologies as indicated

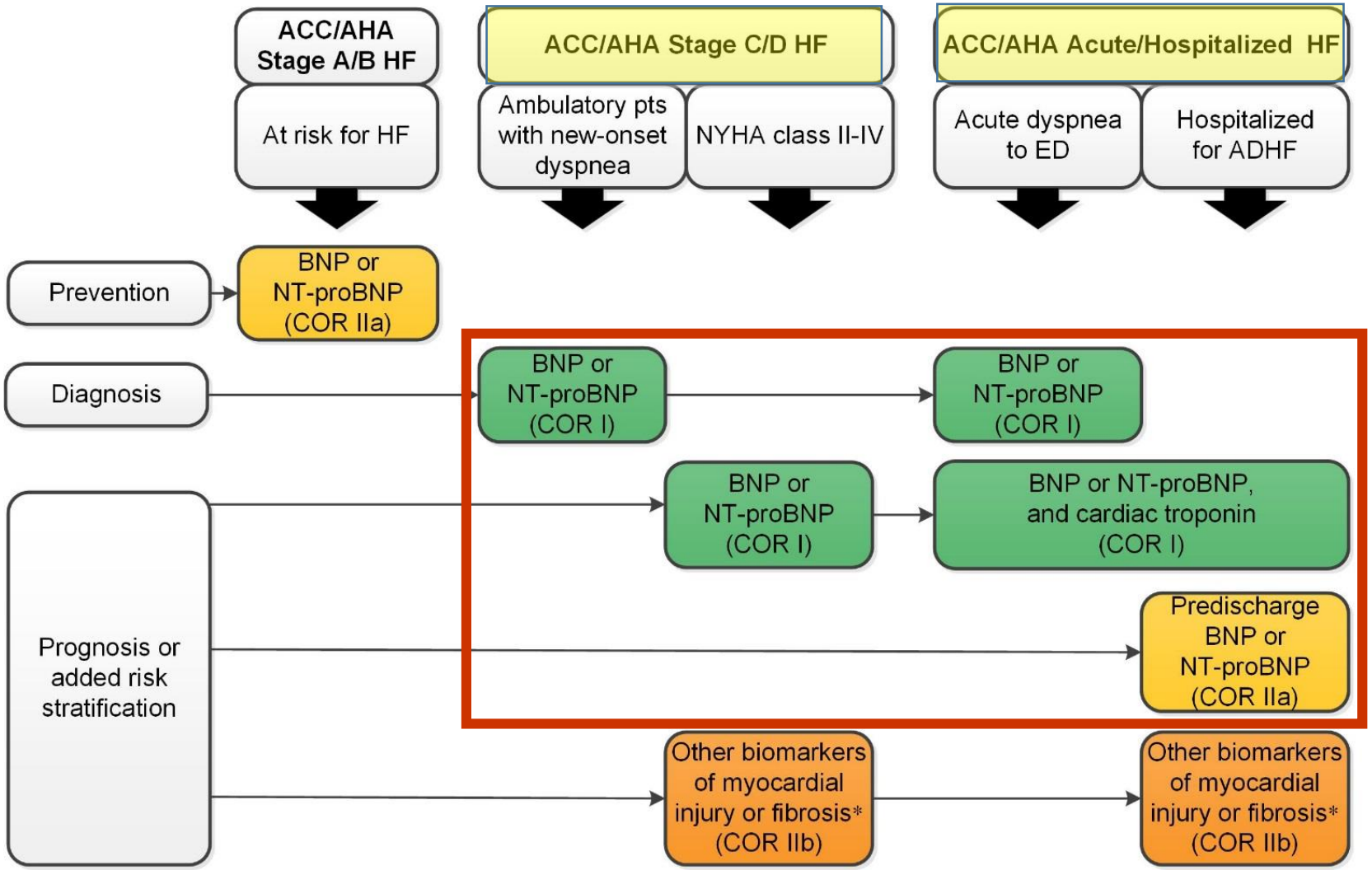
Workup of Stage C HF

- A 12-lead ECG, CXR should be performed initially on all patients presenting with HF.
- Echocardiogram in all patients with new dx of HF (MUGA in some)
- Noninvasive stress imaging or cardiac cath is reasonable in HF and suspected CAD
- Cardiac MRI is reasonable to assess LV volume, EF, myocardial infiltration, or scar

- Repeat echo usually for a significant change in clinical status or for consideration of changes after therapy or to evaluate for device therapy (Not done for routine follow up)

- Validated multivariable risk scores can be useful to estimate risk of mortality in ambulatory or hospitalized HF patients (Class IIa)

Biomarkers Indications for Use: Stage C



Non-Pharmacologic Management of Patients with Stage C HF

- Patients with HF should receive specific education to facilitate HF self-care (talk)

- Sodium restriction is reasonable for patients with symptomatic HF to reduce congestive symptoms. (COR IIa; *LOE C)*

  Controversial. Due to association between sodium intake and HTN, LVH, and CVD, the AHA recommendation for 1500 mg/d is applicable for stage A&B.

  Stage C&D: Lack of data. Since usual intake > 4 g/d, suggest < 3 g/d in HF for symptom improvement

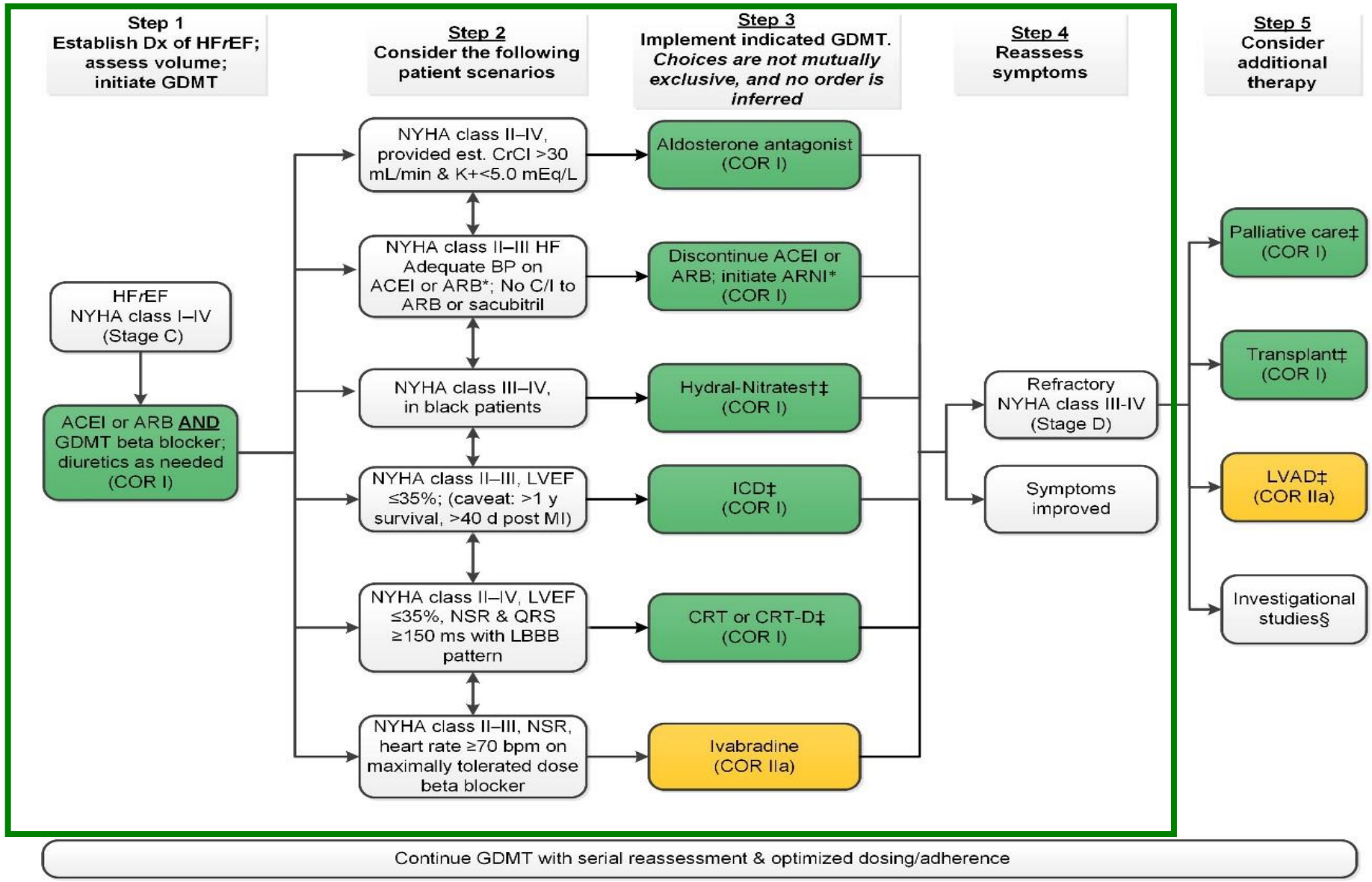
- Fluid restriction (1.5 to 2 L/d) is reasonable in stage D, especially in patients with hyponatremia, to reduce congestive symptoms. *(COR IIa; LOE C).*
  No recommendation for routine use of fluid restriction in all HF patients

Exercise and Cardiac Rehabilitation

- Exercise training (or regular physical activity) is recommended as safe and effective for patients with HF who are able to participate to improve functional status.

- Cardiac rehabilitation can be useful in clinically stable patients with HF to improve functional capacity, exercise duration, HRQOL, and mortality.

Guideline Directed Therapy for Stage C & D HF



Yancy et al. 2017 ACC/AHA/HFSA

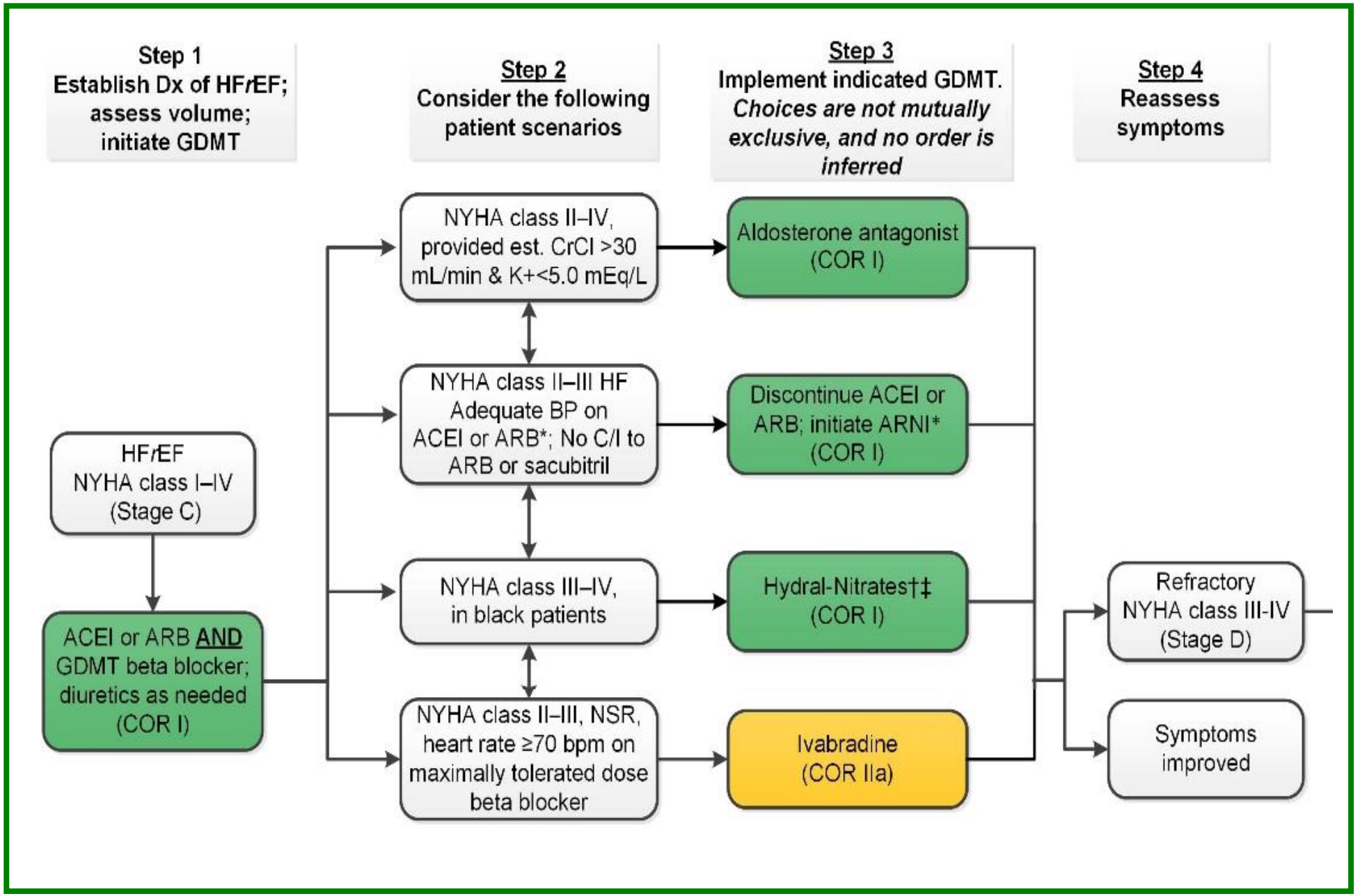
HFrEF: Medications & Devices

	Symptoms	Prevent Hospitalizations	Increase Survival
Diuretics	✓	? ✓	?
	✓	✓	✓
	✓	✓	✓
	✓	✓	✓
	✓	✓	✓
	✓	✓	✓
	✓	✓	X
	✓	✓	X
	✓	✓	✓
			✓

Medical Therapy for Stage C HFrEF: Magnitude of Benefit in RCTs

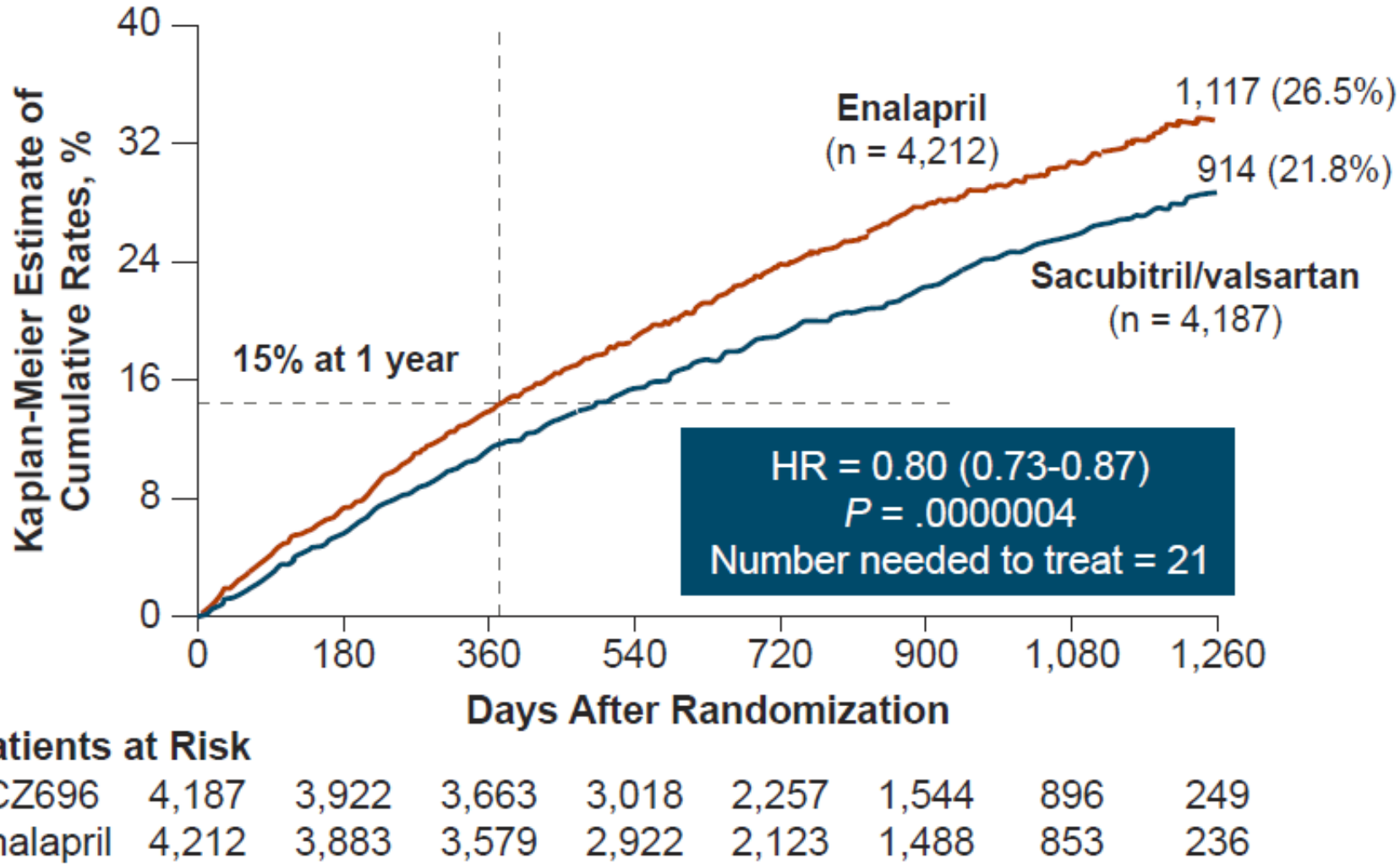
GDMT	RR ↓ Mortality	NNT for ↓ mortality (standardized 36 mo)	RR ↓ HF Hosp.
ACE Inhibitor or ARB	17%	26	31%
Beta-Blockers	34%	9	41%
Aldo-antagonists	30%	6	35%
HDZ/nitrate	43%	7	33%
Sacubitril/ valsartan (over ACE-I)	16%	21 (over 27 mo)	20%

Medical Therapy

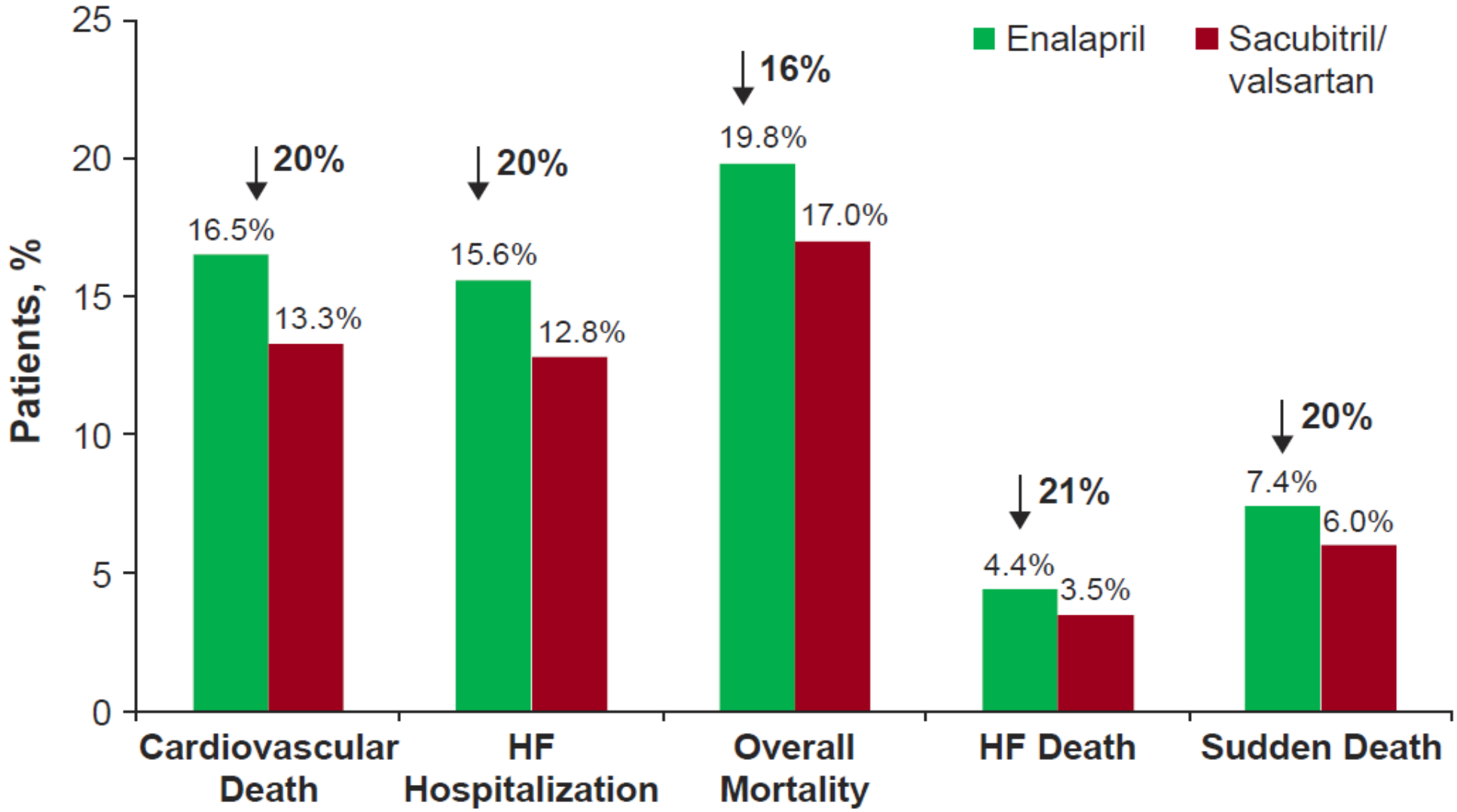


Yancy et al. 2017 ACC/AHA/HFSA

PARADIGM-HF: CV Death or HF Hospitalization

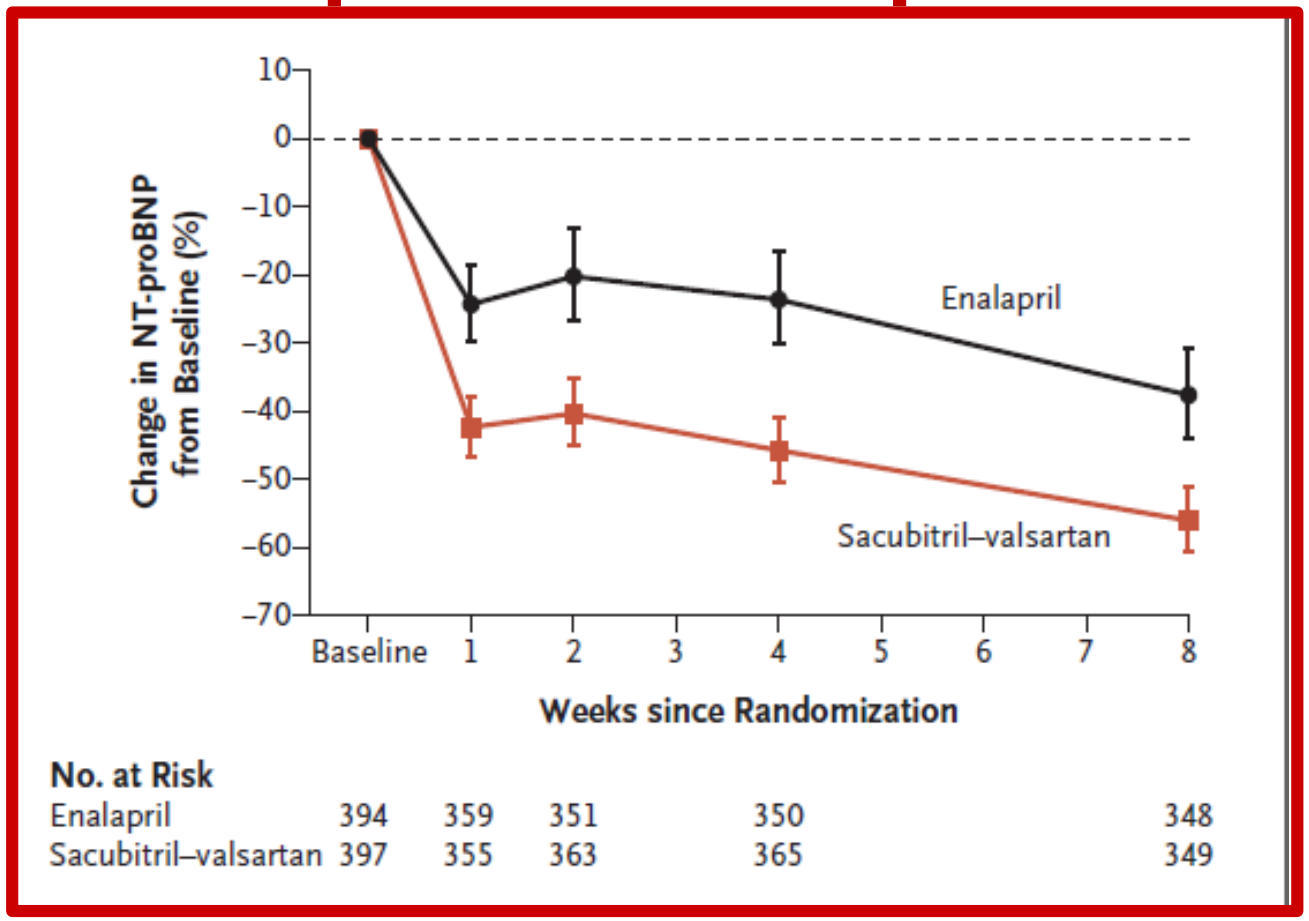


PARADIGM-HF: Other Key Endpoints



Desai AS et al. *Eur Heart J.* 2015;36:1990 1997. McMurray JJ et al. *N Engl J Med*. 2014;371:993 1004.

PIONEER-HF : Sacubitril-valsartan initiated in hospitalized HF patients



? De-novo ARNI without prior ACEI/ARB

No increase in adverse effects with sacubitril valsartan; secondary analyses with reduction in HF rehospitalization over 8 weeks

Practical Points for Using Ivabradine in HF

- FDA-approved indication: Reduce risk of HF hospitalization in patients with - stable, symptomatic chronic HFrEF, EF ≤ 35%,
  - SR with resting HR ≥ 70 bpm
  - on maximally tolerated doses of BBs
  - OR have a contraindication to BB

- Do not use in: ADHF or BP <90/50 mmHg, resting HR <60 bpm, pacemaker dependent, atrial fibrillation, severe heart block, severe hepatic impairment

- Interaction with CYP3A4 inhibitors
- Side effects: bradycardia, HTN, AF, and luminous phenomena (phosphenes)

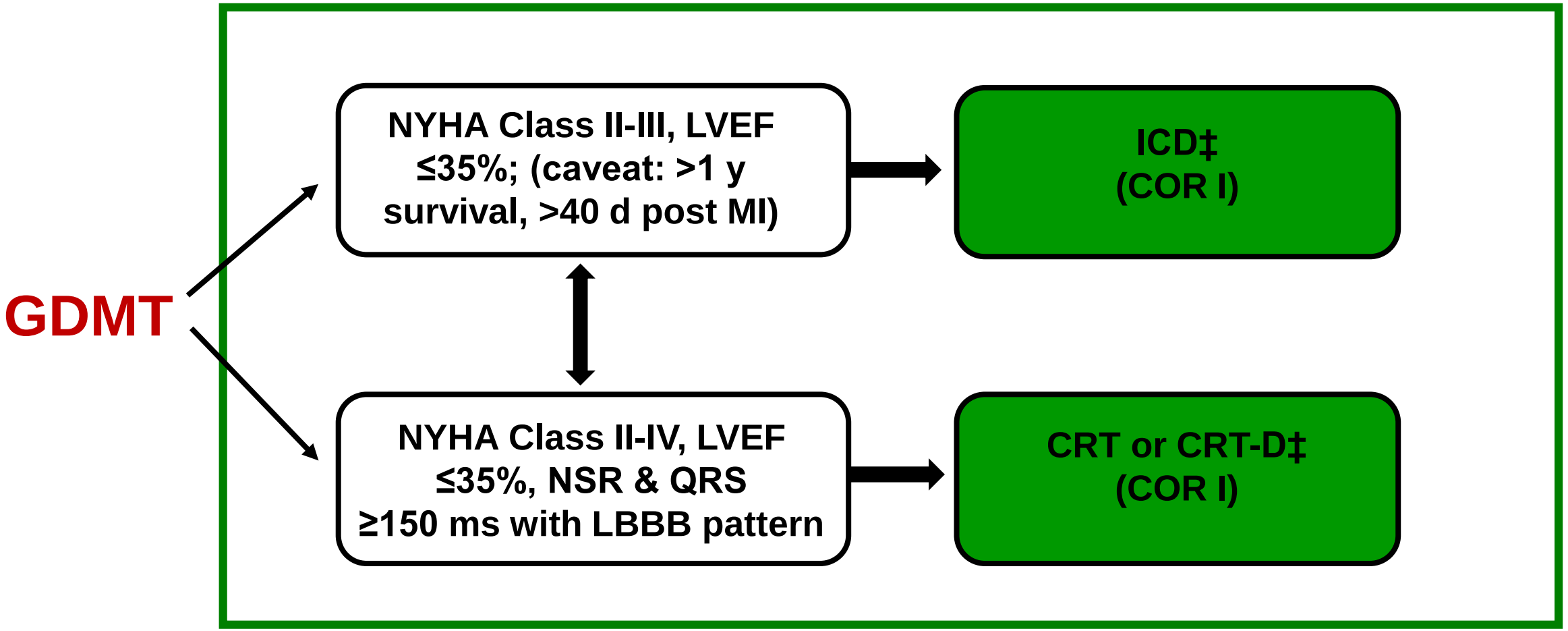
Corlanor Prescribing Information, April 2015.

Swedberg K, et al. *Lancet*. 2010;376:875

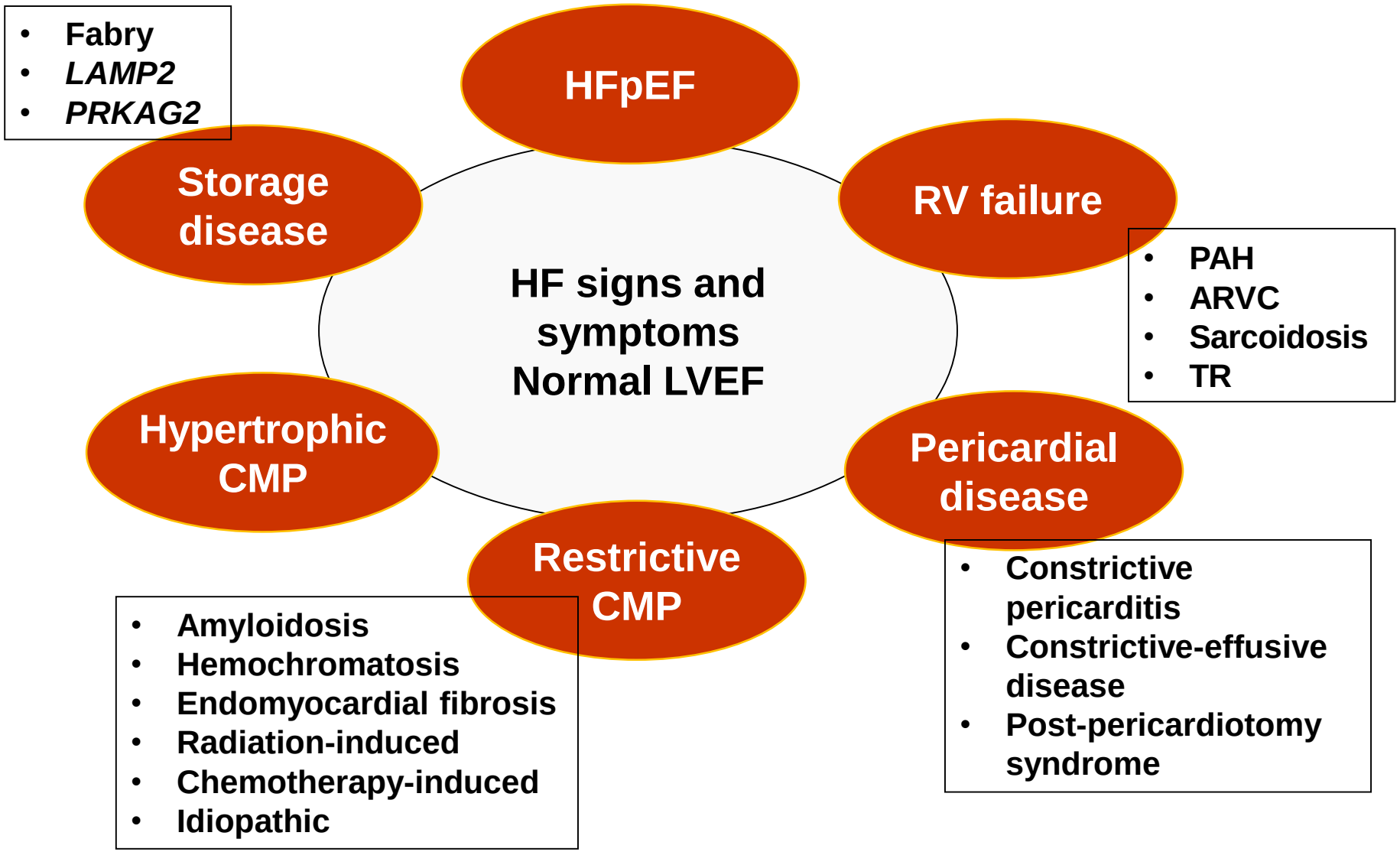
Harmful Drugs in HF (Class III)

- **NSAIDs**
- **Decongestants**
  e.g., pseudoephedrine
- **Thiazolidinediones**
- **Antiarrhythmics**
  Exceptions: amiodarone, dofetilide (different if ICD in place)
- **HFrEF: Diltiazem, Verapamil** (*amlodipine OK if needed for HTN or angina*)

Indications for AICD and BiV/CRT Pacing in HFrEF



HF With Preserved EF: Differential Diagnosis



Yancy CW et al. *J Am Coll Cardiol*. 2013;62:e147 e239.

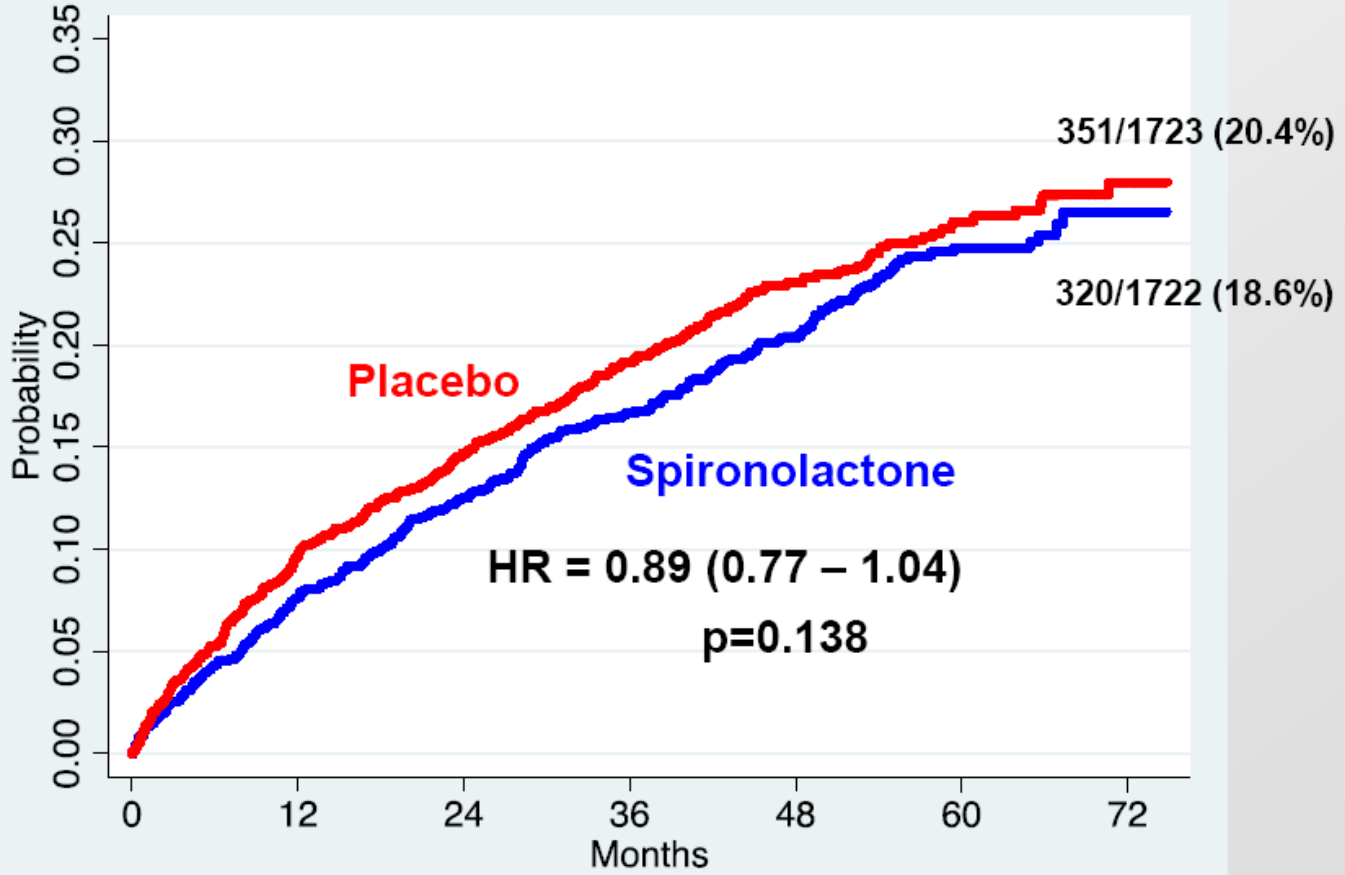
HFpEF

Trials have not shown significant mortality or morbidity benefit with use of ACEI/ARB specifically in HFpEF

1° Outcome
(CV Death, HF Hosp, or Resuscitated Cardiac Arrest)

TOPCAT

RCT of spiro. (15-45 mg) vs. placebo in HFpEF (LVEF >45%) +
- Prior HF hosp.
Or
- BNP > 100 pg/ml



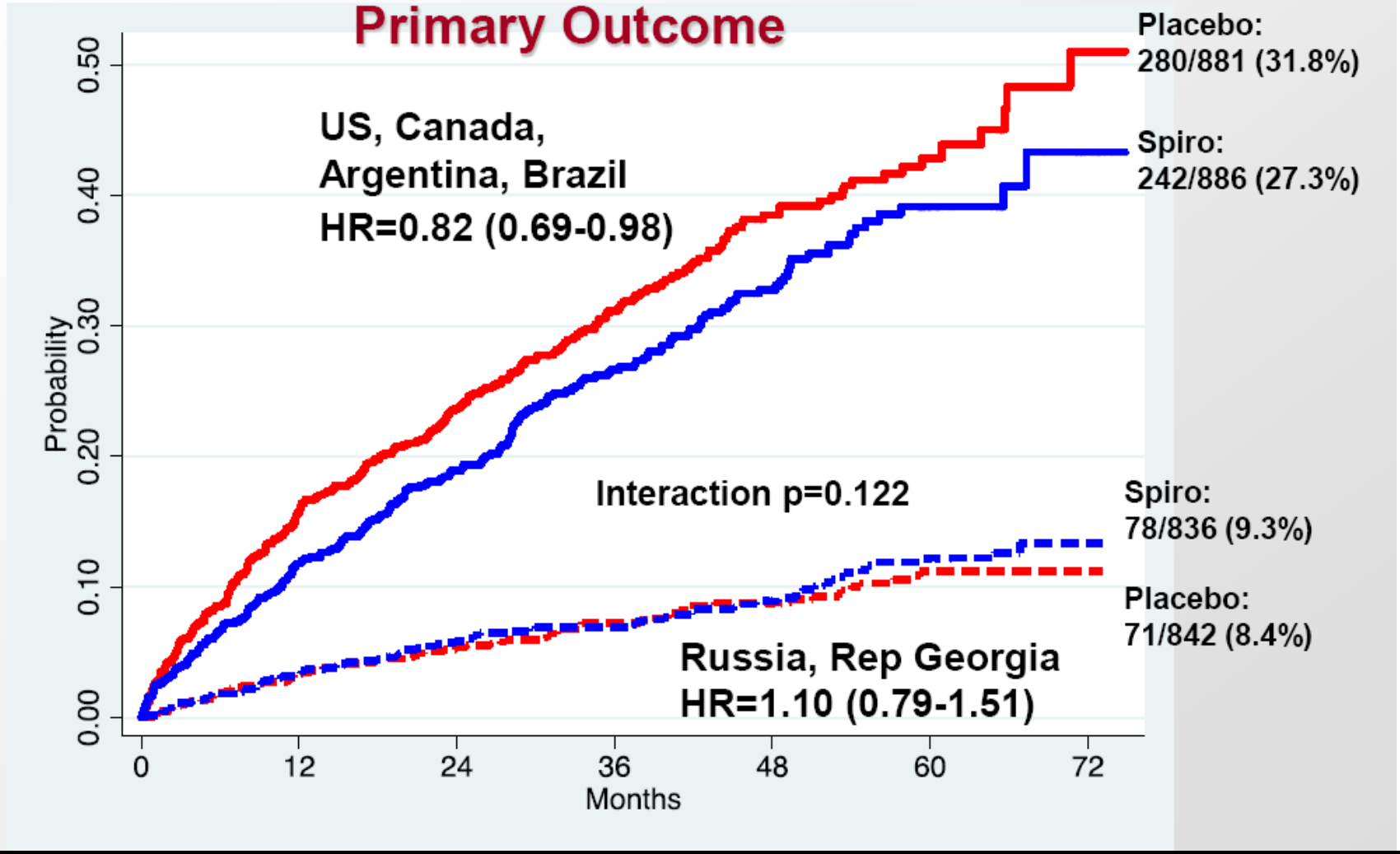
Number at risk

Spiro	1722	1502	1168	870	614	330	53
Placebo	1723	1462	1145	834	581	331	53

Pitt B, et al. N Engl J Med. 2014;370:1383–92

Exploratory-Post Hoc: Placebo vs. Spiro by Region

TOPCAT
Funded by the NHLBI



2017: Treatment of HFpEF

I	B	Systolic and diastolic blood pressure should be controlled in patients with HF*p*EF in accordance with published clinical practice guidelines to prevent morbidity
I	C	Diuretics should be used for relief of symptoms due to volume overload in patients with HF*p*EF.

IIa	C	The use of beta-blocking agents, ACE inhibitors, and ARBs in patients with hypertension is reasonable to control blood pressure in patients with HF*p*EF.

IIa	C	Coronary revascularization is reasonable in patients with CAD in whom symptoms (angina) or demonstrable myocardial ischemia is judged to be having an adverse effect on symptomatic HF*p*EF despite GDMT.
IIa	C	Management of AF according to published clinical practice guidelines in patients with HF*p*EF is reasonable to improve symptomatic HF.

Goal BP < 130/80 mm Hg

2017: Treatment of HFpEF

IIb	B-R	In appropriately selected patients with HF*p*EF (with EF ≥45%, elevated BNP levels or HF admission within 1 year, estimated glomerular filtration rate >30 mL/min, creatinine <2.5 mg/dL, potassium <5.0 mEq/L), aldosterone receptor antagonists might be considered to decrease hospitalizations.

III: No Benefit	B-R	Routine use of nitrates or phosphodiesterase-5 inhibitors to increase activity or QoL in patients with HF*p*EF is ineffective.
III: No Benefit	C	Routine use of nutritional supplements is not recommended for patients with HF*p*EF.

The NEW ENGLAND JOURNAL of MEDICINE

PARAGON-HF

Angiotensin–Neprilysin Inhibition in Heart Failure with Preserved Ejection Fraction

MULTICENTER, DOUBLE-BLIND, ACTIVE-COMPARATOR TRIAL (PARAGON-HF)

4822
Patients with NYHA class II–IV heart failure and EF ≥45%

Sacubitril–valsartan

97 mg + 103 mg (twice daily)

(N=2419)

Valsartan

160 mg (twice daily)

(N=2403)

Total hospitalizations for heart failure and cardiovascular death

894 events

1009 events

Rate ratio, 0.87; 95% CI, 0.75–1.01; P=0.06

Patients receiving sacubitril–valsartan more likely to have hypotension and angioedema but less likely to have hyperkalemia

S.D. Solomon et al. 10.1056/NEJMoa1908655

2017: Important Comorbidities in HF

Anemia

IIb	B-R	In patients with NYHA class II and III HF and iron deficiency (ferritin <100 ng/mL or 100 to 300 ng/mL if transferrin saturation is <20%), intravenous iron replacement might be reasonable to improve functional status and QoL.

III: No Benefit	B-R	In patients with HF and anemia, erythropoietin-stimulating agents should not be used to improve morbidity and mortality.

Comorbidities in HF: Sleep Apnea

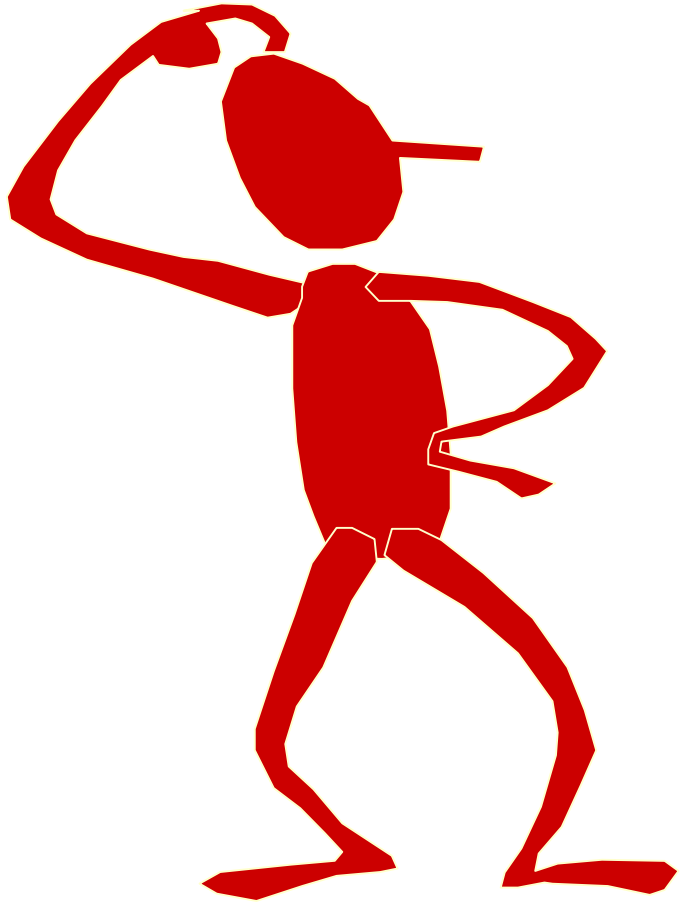
IIa	C-LD	In patients with NYHA class II–IV HF and suspicion of sleep disordered breathing or excessive daytime sleepiness, a formal sleep assessment is reasonable.
IIb	B-R	In patients with cardiovascular disease and obstructive sleep apnea, CPAP may be reasonable to improve sleep quality and daytime sleepiness.
III: Harm	B-R	In patients with NYHA class II–IV HF*r*EF and central sleep apnea, adaptive servo-ventilation causes harm.

Yancy C, et al. 2017 AHA/ACC/HFSA HF guideline

Summary

- Recognize risk factors (Stage A HF) and structural cardiac abnormalities (Stage B HF); recommend treatments
- Classify heart failure patients into stages and apply treatments, interventions and processes from the 2013 AHA/ACC/HFSA Heart Failure Guidelines / 2017 focused Update
- Review key pharmacological and non pharmacologic treatments for HFrEF and HFpEF

Thank you



Classification of Recommendations and Levels of Evidence (AHA/ACC Guidelines)

CLASS (STRENGTH) OF RECOMMENDATION

CLASS I (STRONG) — **Benefit >>> Risk**

Suggested phrases for writing recommendations:
- Is recommended
- Is indicated/useful/effective/beneficial
- Should be performed/administered/other
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is recommended/indicated in preference to treatment B
  - Treatment A should be chosen over treatment B

CLASS IIa (MODERATE) — **Benefit >> Risk**

Suggested phrases for writing recommendations:
- Is reasonable
- Can be useful/effective/beneficial
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is probably recommended/indicated in preference to treatment B
  - It is reasonable to choose treatment A over treatment B

CLASS IIb (WEAK) — **Benefit ≥ Risk**

Suggested phrases for writing recommendations:
- May/might be reasonable
- May/might be considered
- Usefulness/effectiveness is unknown/unclear/uncertain or not well established

CLASS III: No Benefit (MODERATE) — **Benefit = Risk**
(Generally, LOE A or B use only)

Suggested phrases for writing recommendations:
- Is not recommended
- Is not indicated/useful/effective/beneficial
- Should not be performed/administered/other

CLASS III: Harm (STRONG) — **Risk > Benefit**

Suggested phrases for writing recommendations:
- Potentially harmful
- Causes harm
- Associated with excess morbidity/mortality
- Should not be performed/administered/other

LEVEL (QUALITY) OF EVIDENCE‡

LEVEL A
- High-quality evidence‡ from more than 1 RCT
- Meta-analyses of high-quality RCTs
- One or more RCTs corroborated by high-quality registry studies

LEVEL B-R (Randomized)
- Moderate-quality evidence‡ from 1 or more RCTs
- Meta-analyses of moderate-quality RCTs

LEVEL B-NR (Nonrandomized)
- Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies
- Meta-analyses of such studies

LEVEL C-LD (Limited Data)
- Randomized or nonrandomized observational or registry studies with limitations of design or execution
- Meta-analyses of such studies
- Physiological or mechanistic studies in human subjects

LEVEL C-EO (Expert Opinion)

Consensus of expert opinion based on clinical experience

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR I and IIa; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

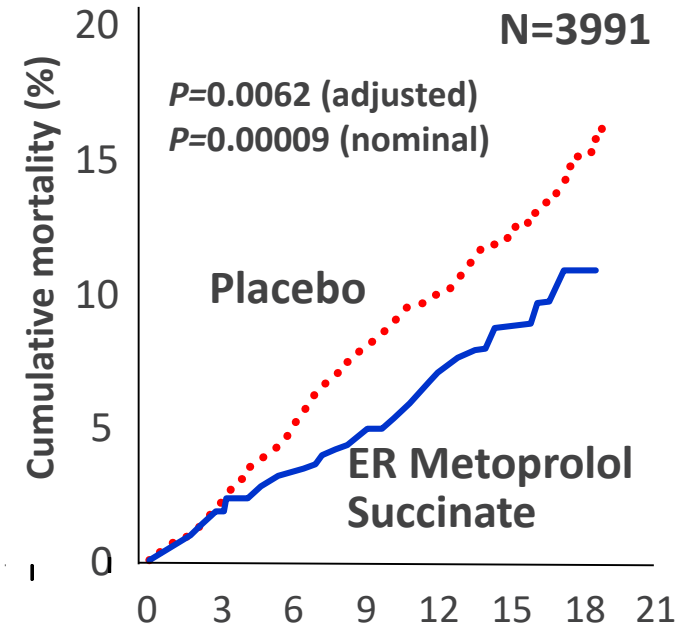
‡ The method of assessing quality is evolving, including the application of standardized, widely used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

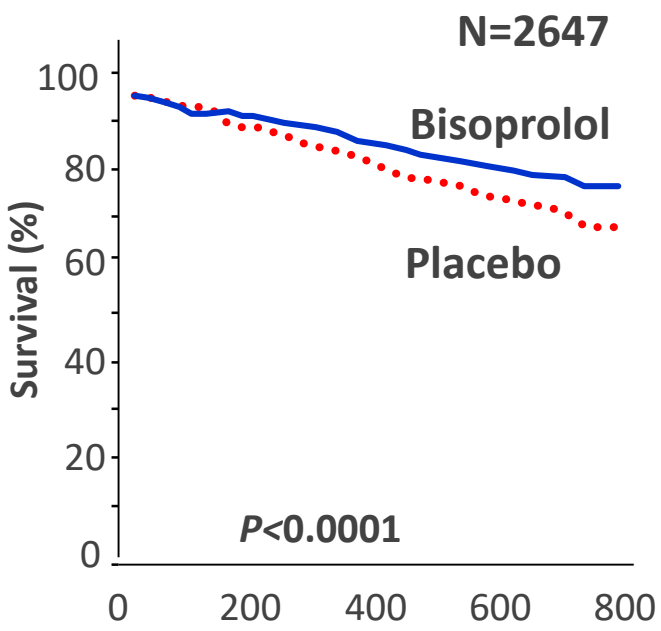
Mortality Benefit Using ACEIs in HF*r*EF

Mortality Benefit Using Beta Blockers in HF*r*EF

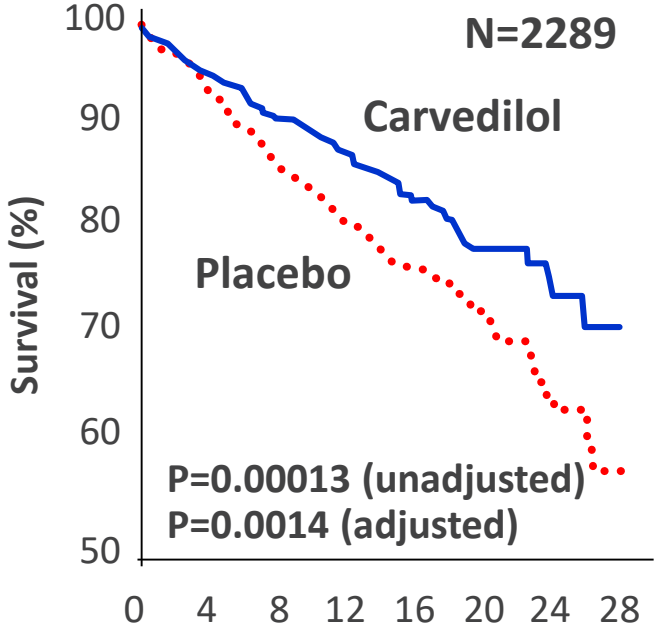
MERIT HF[1]



CIBIS II[2]



COPERNICUS[3]

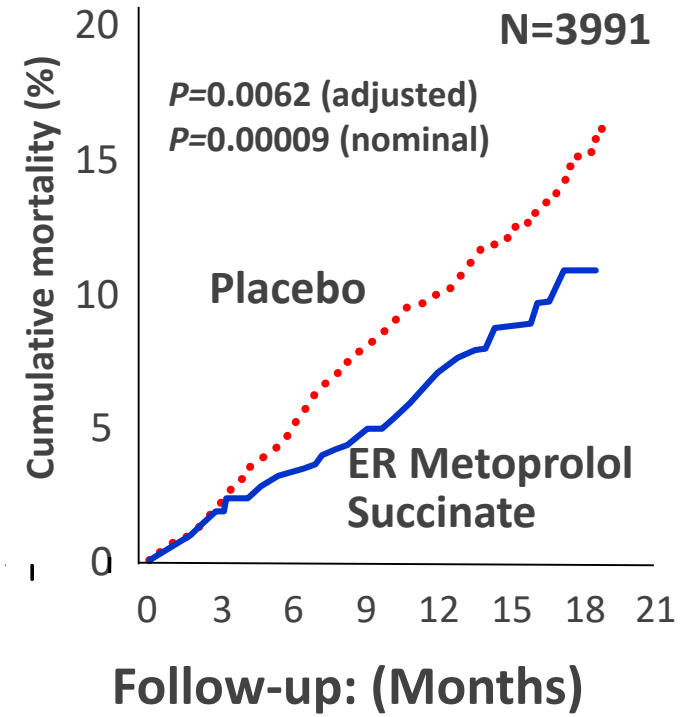


Mortality: ↓ 34% ↓ 34% ↓ 35%

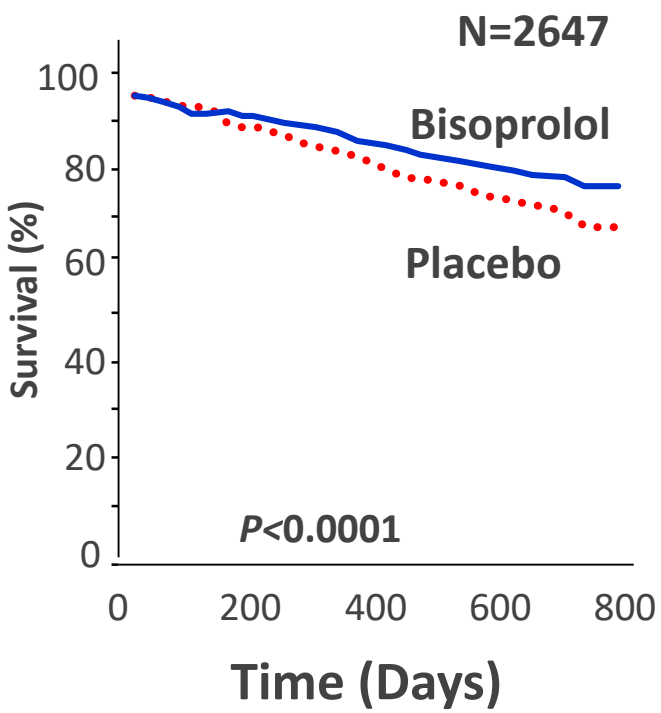
1. MERIT-HF Study Group. *Lancet*. 1999;353:2001-2007. 2. CIBIS-II Investigators. *Lancet*. 1999;353:913. 3. Packer M et al. *New Engl J Med*. 2001;344:1651 1658.

Mortality Benefit Using Beta Blockers in HF*r*EF

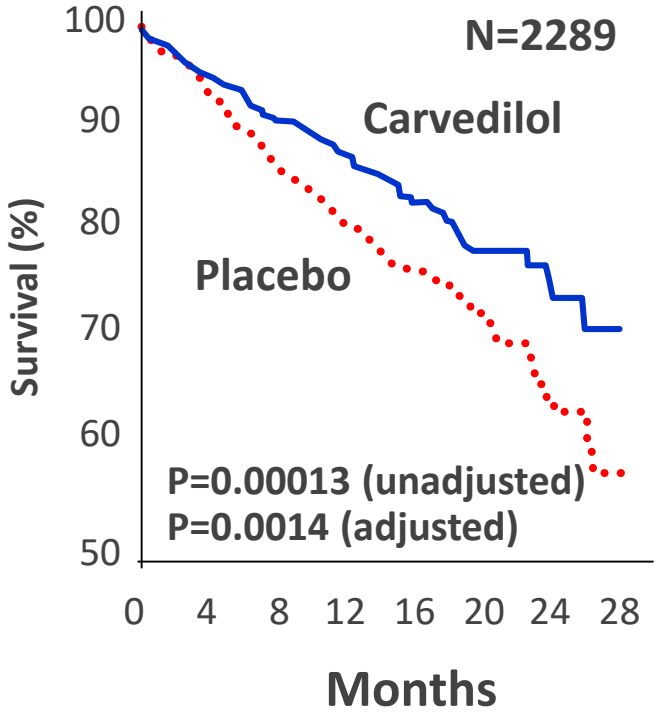
MERIT HF[1]



CIBIS II[2]



COPERNICUS[3]



Mortality: ↓ 34% ↓ 34% ↓ 35%

1. MERIT-HF Study Group. *Lancet*. 1999;353:2001-2007. 2. CIBIS-II Investigators. *Lancet*. 1999;353:913. 3. Packer M et al. *New Engl J Med*. 2001;344:1651 1658.