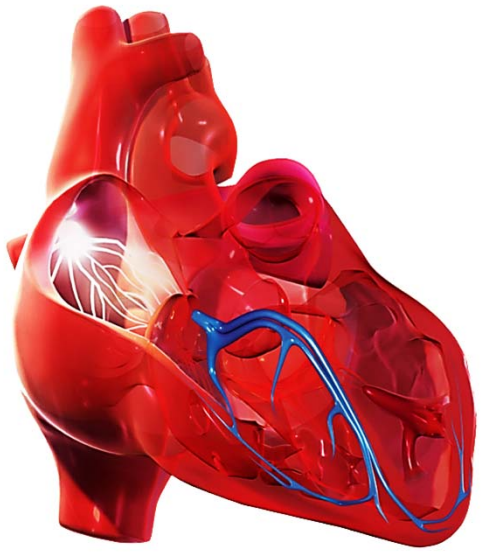

OVERVIEW OF CHRONIC HEART FAILURE

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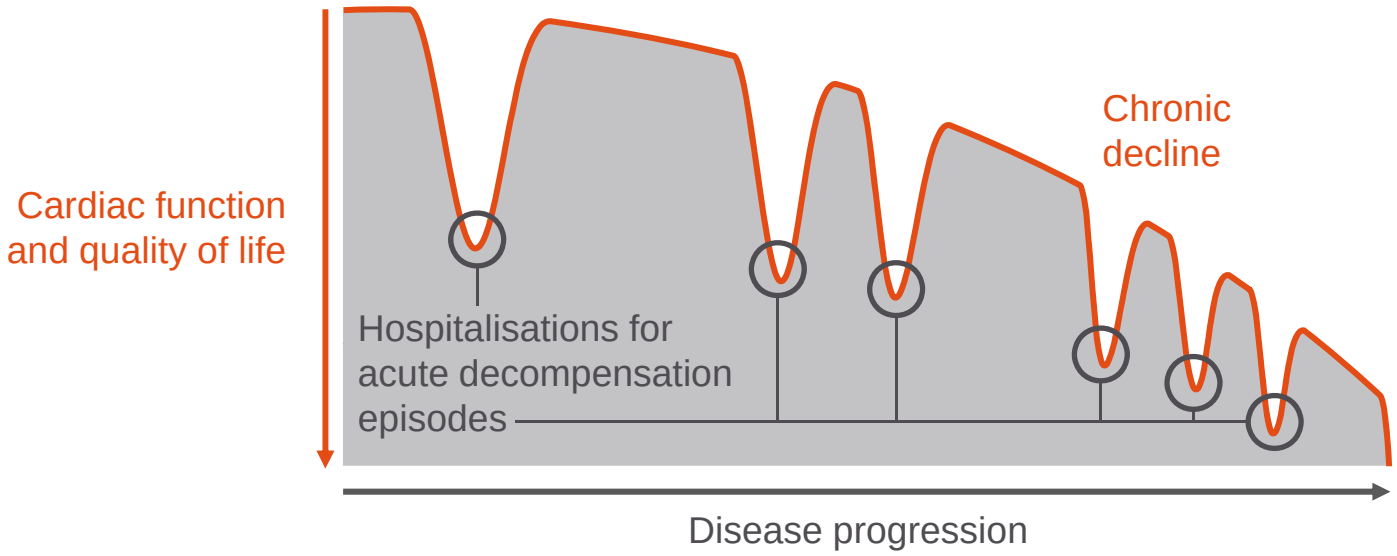
21-1-2018

Heart Failure is a complex syndrome involving multiple organ systems and is associated with a high morbidity and mortality.

- Heart failure (HF) is a chronic condition, punctuated by acute episodes
- Each acute event results in further organ damage: may contribute to progressive left ventricular and/or renal dysfunction
- Increasing frequency of acute events with disease progression leads to higher rates of hospitalization and increased risk of mortality



Adapted from Gheorghiade et al. Am J Cardiol 2005;96:11–17; Gheorghiade and Pang. J Am Coll Cardiol 2009;53:557–73

Heart failure, a worldwide burden

26 million

Number of heart failure patients worldwide.[1]

1-2%

Health care expenditure attributed to heart failure in Europe and North America.[2]

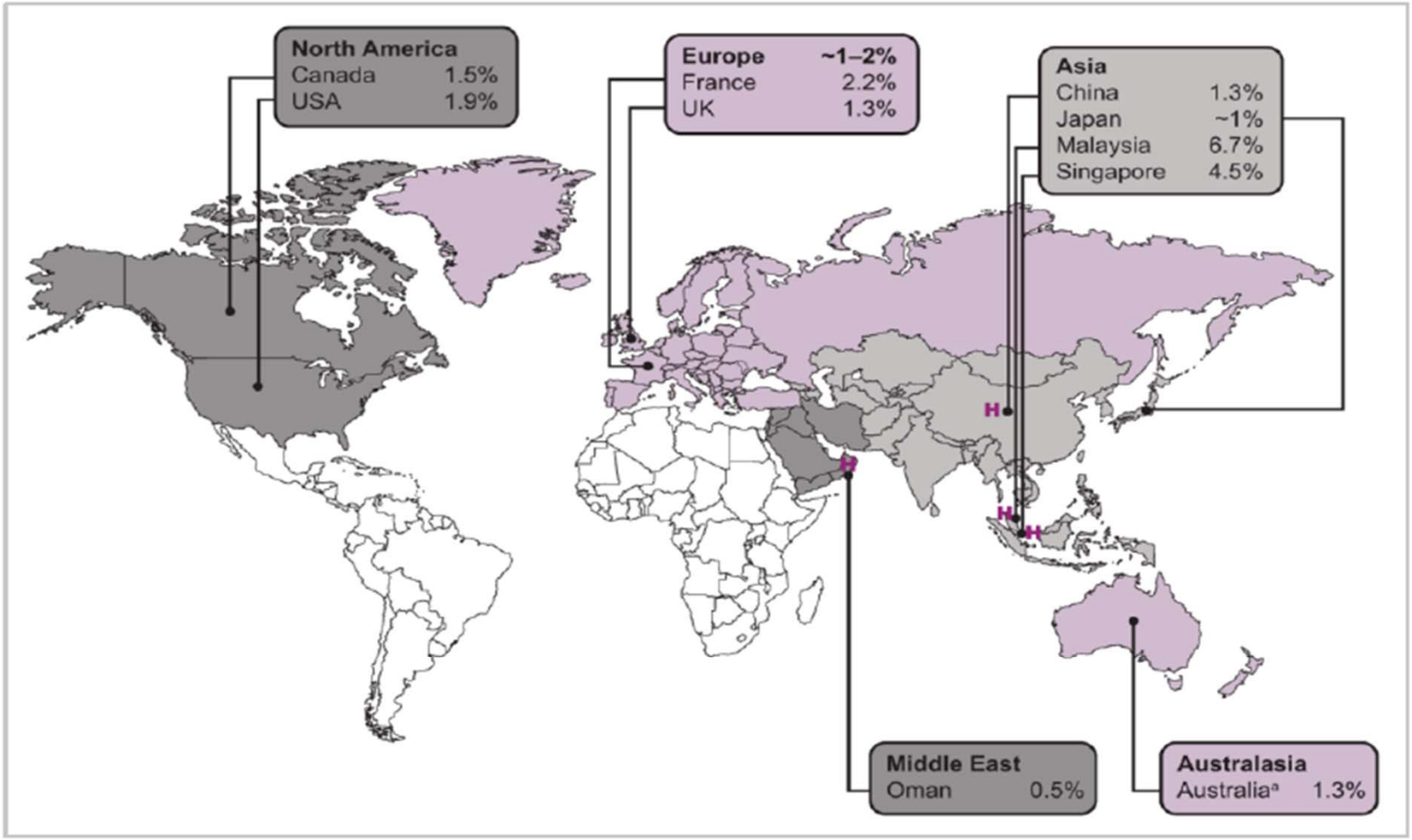
74%

Heart failure patients suffering from at least 1 comorbidity: more likely to worsen the patient's overall health status.[3]

1. Ambrosy PA et al. The Global Health and Economic Burden of Hospitalizations for Heart Failure. Lessons Learned From Hospitalized Heart Failure Registries. *J Am Coll Cardiol.* 2014;63:1123–1133. **2.** Cowie MR et al. Improving care for patients with acute heart failure. 2014. Oxford PharmaGenesis. ISBN 978-1-903539-12-5. Available online at: http://www.oxfordhealthpolicyforum.org/reports/acute-heart-failure/improving-care-for-patients-with-acute-heart-failure **3.** van Deursen VM et al. Co-morbidities in patients with heart failure: an analysis of the European Heart Failure Pilot Survey. *Eur J Heart Fail.* 2014;16:103-111.

Prevalence of HF

GLOBAL HEART FAILURE AWARENESS PROGRAMME



Heart failure is a major and growing public health problem

Prevalence[1]

1-3%

of the population in Asia have HF[1]

As many as **1 in 5** people aged 70–80 years have HF[1]

Growth[2]

Increasing prevalence of risk factors[5,6]

Aging population[5]

Improved post-MI survival[5]

General socioeconomic and health expenditure data for the regions

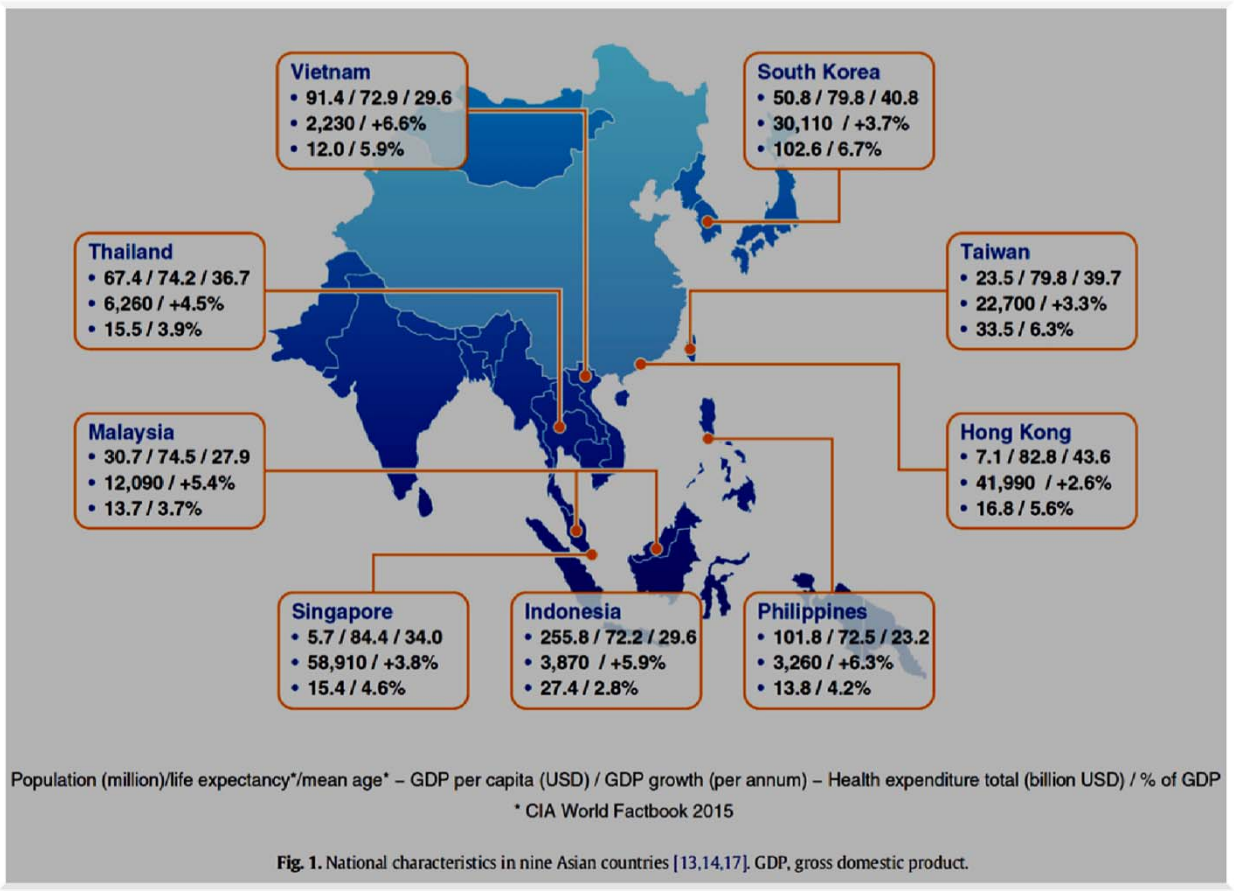


Fig. 1. National characteristics in nine Asian countries [13,14,17]. GDP, gross domestic product.

1. Heart failure across asia: same healthcare burden but difference in organization of care; International journal of cardiology 223(2016) 163-167 2. Hunt et al. J Am Coll Cardiol 2009;53:e1–90; 6. Kearney et al. Lancet 2005; 365:217–23

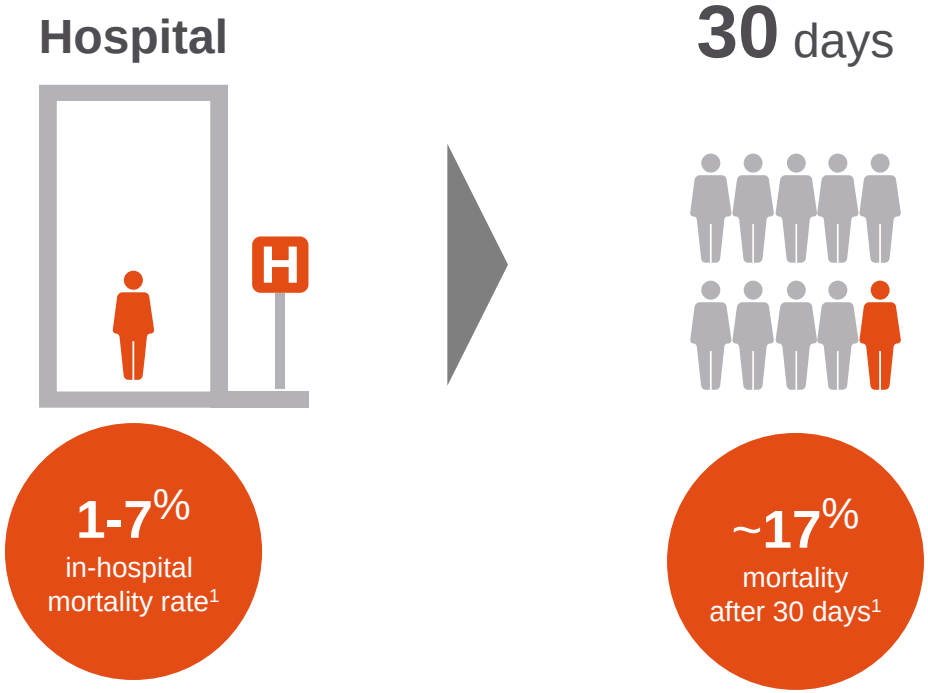
Prevalence of Heart Failure, demographic characteristics of patients and etiology in 9 Asian regions

Prevalence or characteristic	Asia								
	Hong Kong	Indonesia	Malaysia	Philippines	Singapore	South Korea	Taiwan	Thailand	Vietnam
Prevalence of HF	2%–3%[a]	5%	-	1%–2%	-	0.6%	6%	0.4%	-
Demographic characteristics of HF patients									
Male	45%	66%	75%	57%	64%	55%	72%	-	59%
Female	55%	34%	26%	43%	36%	45%	28%	-	41%
Mean age at admission (years)	76.8	57.8	61.8	60	66.6	69	64	67	59
Cardiovascular risk factors									
Ischemic heart disease	29%	35%	68%	52%	37%	37%	44%	45%	32%
Valvular/rheumatic heart disease	6%	18%	29%	20%	-	14%	8%	19%	18%
Cardiomyopathy (non-ischemic)	1%	2%	28%	11%	-	21%	34%	14%	21%
Hypertensive heart disease	70%	8%	2%	6%	-	4%	7%	12%	21%
Other causes[b]		2%	5%	7%	-	11%	7%	-	-

1. Heart failure across asia: same healthcare burden but difference in organization of care; International journal of cardiology 223(2016) 163-167

Morbidity and mortality in Heart failure

HF is associated with significant mortality



Heart Failure hospitalization and mortality in 9 Asian countries or regions

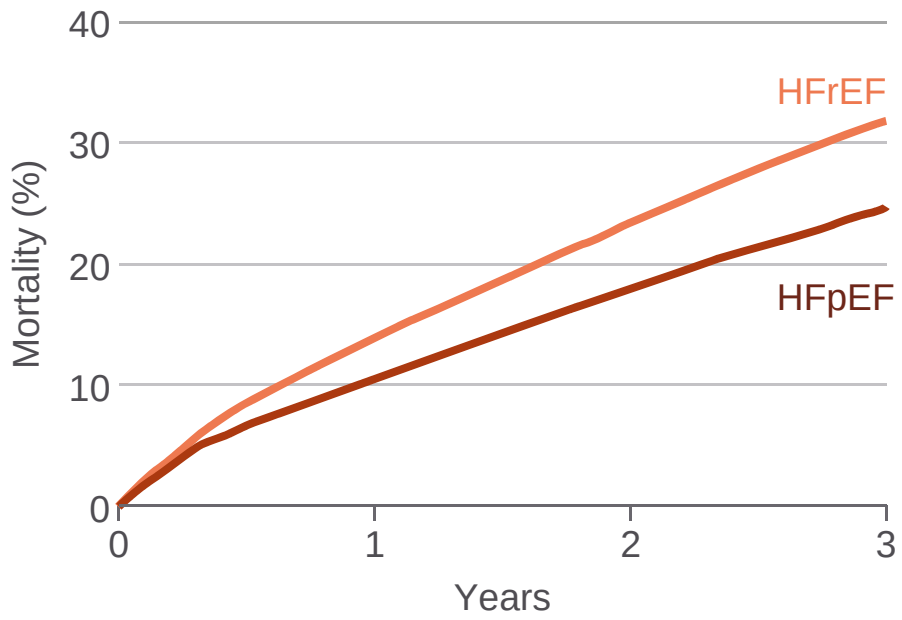
Mortality	Indonesia	Malaysia	Philippines	Singapore	South Korea	Thialand	Vietnam
Inpatient	3%	6%	7%	1.1%	6.1%	6%	7%
Within 30 days of discharge	17%	1%	10%	-	-	-	2%-3%

HF=heart failure

1. Heart Failure hospitalization and mortality in 9 Asian countries or regions :International journal of Cardiology 223 (2016) 163-167

Morbidity and mortality in Heart failure

HF with reduced EF and HF with preserved EF are associated with high levels of morbidity and mortality



The **prognosis** for patients with **chronic HF and preserved EF** is **substantially worse** than that for **patients with other conditions that increase CV risk**‡[2]

No therapies are **proven** to reduce **morbidity and mortality** in **chronic HF with preserved EF**[3]

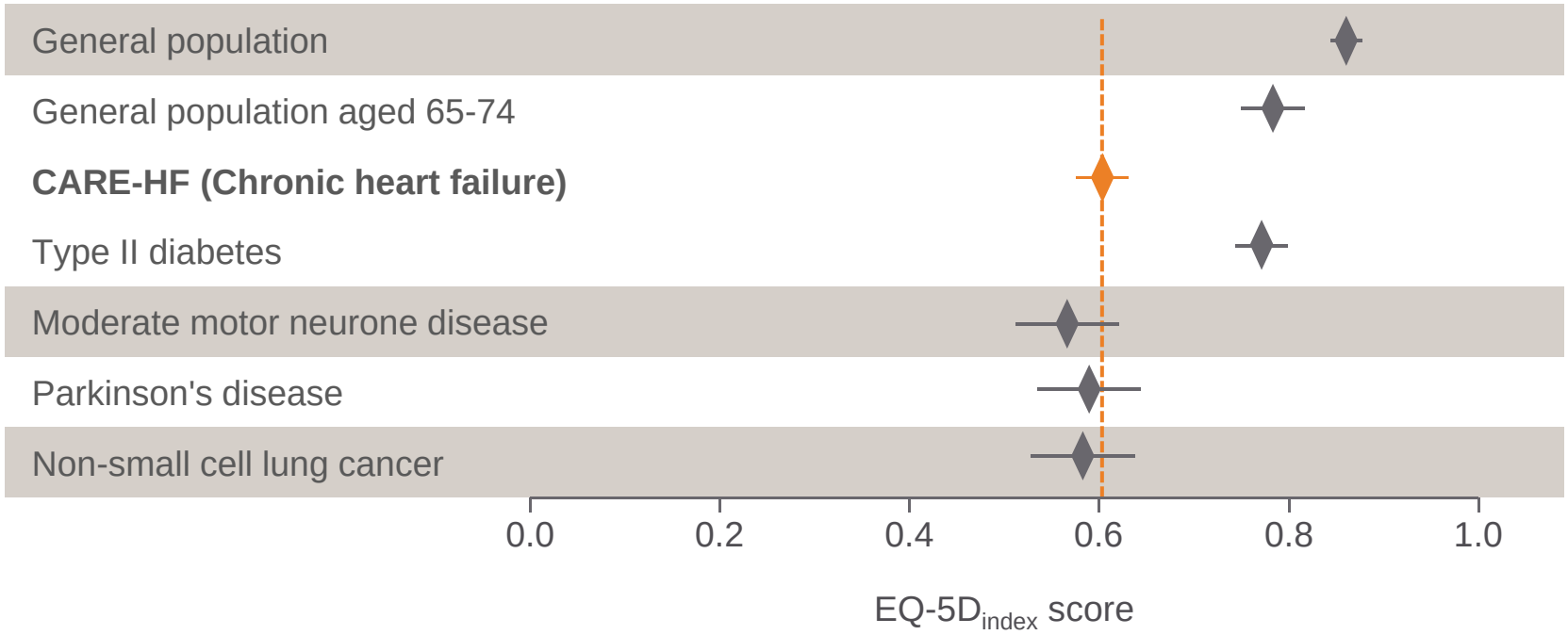
‡Based on data comparing mortality and HF hospitalization rates from clinical trials in patients with HFpEF (n=3 trials) with similar data from clinical trials in patients of without HF but who were of a similar age, comorbidity profile and had other conditions that increase CV risk (stable angina pectoris [n=1 trial], diabetes [n=1 trial] or hypertension [n=5 trials])

CV=cardiovascular; EF=ejection fraction; HF=heart failure; HFpEF=heart failure with preserved ejection fraction; HFrEF=heart failure with reduced ejection fraction; LVEF=left ventricular ejection fraction

1.Meta-Analysis Global Group In Chronic heart failure (MAGGIC). Eur Heart J 2012;33:1750–7;
2. Campbell et al. J Am Coll Cardiol 2012;60:2349–56; 3. McMurray et al. Eur Heart J 2012;33:1787–847

Heart failure has a significant impact on quality of life

Quality of life among patients with HF compared with the general population and other chronic conditions*



*Data from patients receiving optimal medical therapy with chronic heart failure due to left ventricular systolic dysfunction and dysynchrony enrolled in the CARE-HF trial EQ-5D™ is a standardized instrument for use as a measure of health outcome, providing a simple descriptive profile and a single index value for health status Reprinted from the European Journal of Heart Failure, 7(2), Calvert MJ, et al. The impact of chronic heart failure on health-related quality of life data acquired in the baseline phase of the CARE-HF study, 243–51, Published on behalf of the European Society of Cardiology. All rights reserved, Copyright (2005) the authors, with permission of John Wiley & Sons, Inc. CARE-HF=CArdiac REsynchronisation in Heart Failure; HF=heart failure Calvert et al. Eur J Heart Fail 2005;7:243–51

HEART FAILURE ADMISSION
NOGTH CARDIOLOGY DEPARTMENT 2017

H	TOTAL	HF	HF (%)	TOTAL MORTA
B, MARCH,	782	107	13.7%	31 (3.96%)
UNE, JULY, AUG	743	97	13.05%	51 (6.86%)
T, NOV,	770	102	13.25%	42 (5.45%)
	2295	306	13.3%	124 (5.4%)

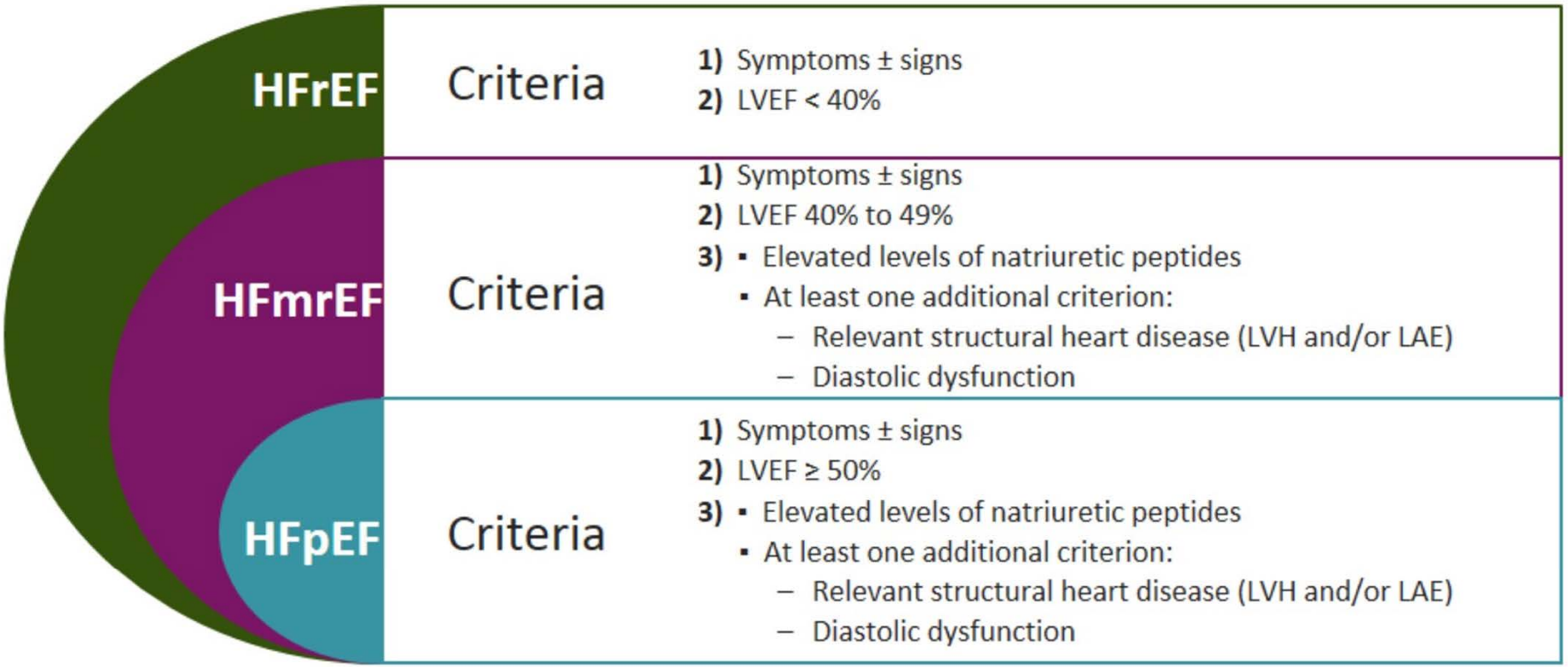
Definition of Heart Failure

Classification	Ejection Fraction	Description
I. Heart Failure with Reduced Ejection Fraction (HF*r*EF)	≤40%	Also referred to as systolic HF. Randomized clinical trials have mainly enrolled patients with HF*r*EF and it is only in these patients that efficacious therapies have been demonstrated to date.
II. Heart Failure with Preserved Ejection Fraction (HF*p*EF)	≥50%	Also referred to as diastolic HF. Several different criteria have been used to further define HF*p*EF. The diagnosis of HF*p*EF is challenging because it is largely one of excluding other potential noncardiac causes of symptoms suggestive of HF. To date, efficacious therapies have not been identified.
a. HF*p*EF, Borderline	41% to 49%	These patients fall into a borderline or intermediate group. Their characteristics, treatment patterns, and outcomes appear similar to those of patient with HF*p*EF.
b. HF*p*EF, Improved	>40%	It has been recognized that a subset of patients with HF*p*EF previously had HF*r*EF. These patients with improvement or recovery in EF may be clinically distinct from those with persistently preserved or reduced EF. Further research is needed to better characterize these patients.

Classification of Heart Failure

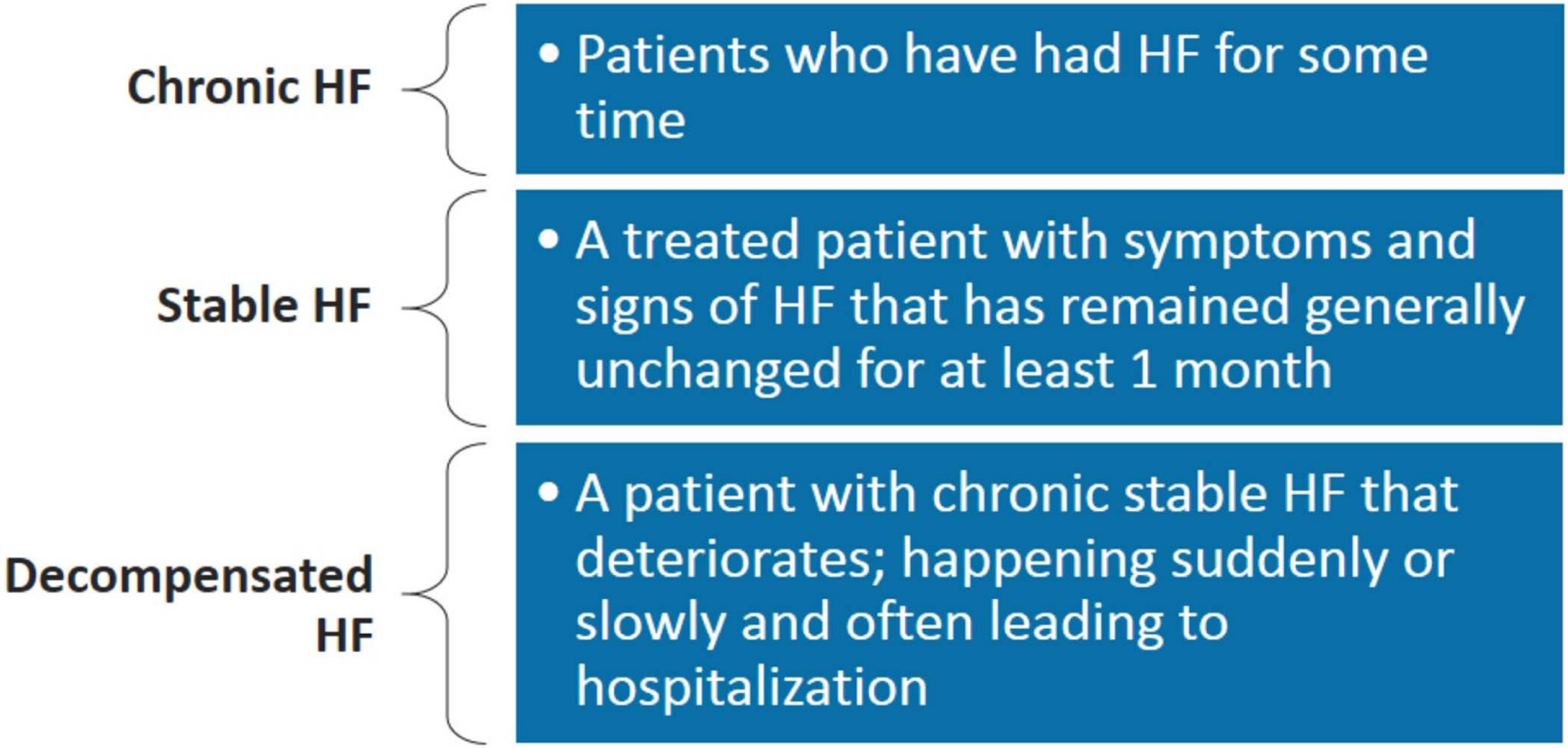
ACCF/AHA Stages of HF		NYHA Functional Classification	
A	At high risk for HF but without structural heart disease or symptoms of HF.	None	
B	Structural heart disease but without signs or symptoms of HF.	I	No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF.
C	Structural heart disease with prior or current symptoms of HF.	I	No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF.
		II	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in symptoms of HF.
		III	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes symptoms of HF.
		IV	Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest.
D	Refractory HF requiring specialized interventions.		

Definition of the Type of HF



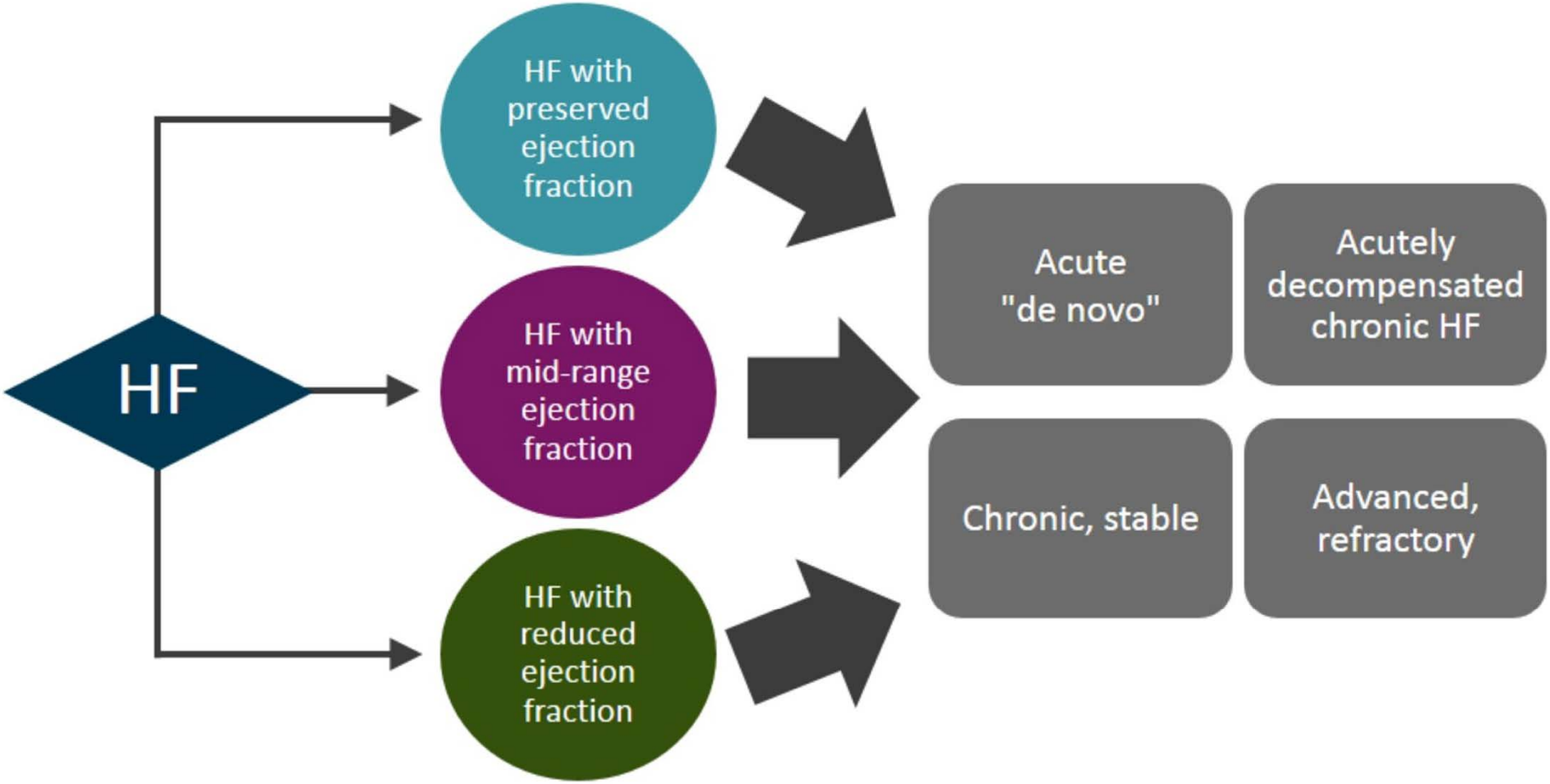
Ponikowski P, et al. *Eur Heart J.* 2016;18:891-975.

Terminology Within Heart Failure



Ponikowski P, et al. *Eur Heart J.* 2016;18:891-975.

HF: More Than Just LV Systolic Function



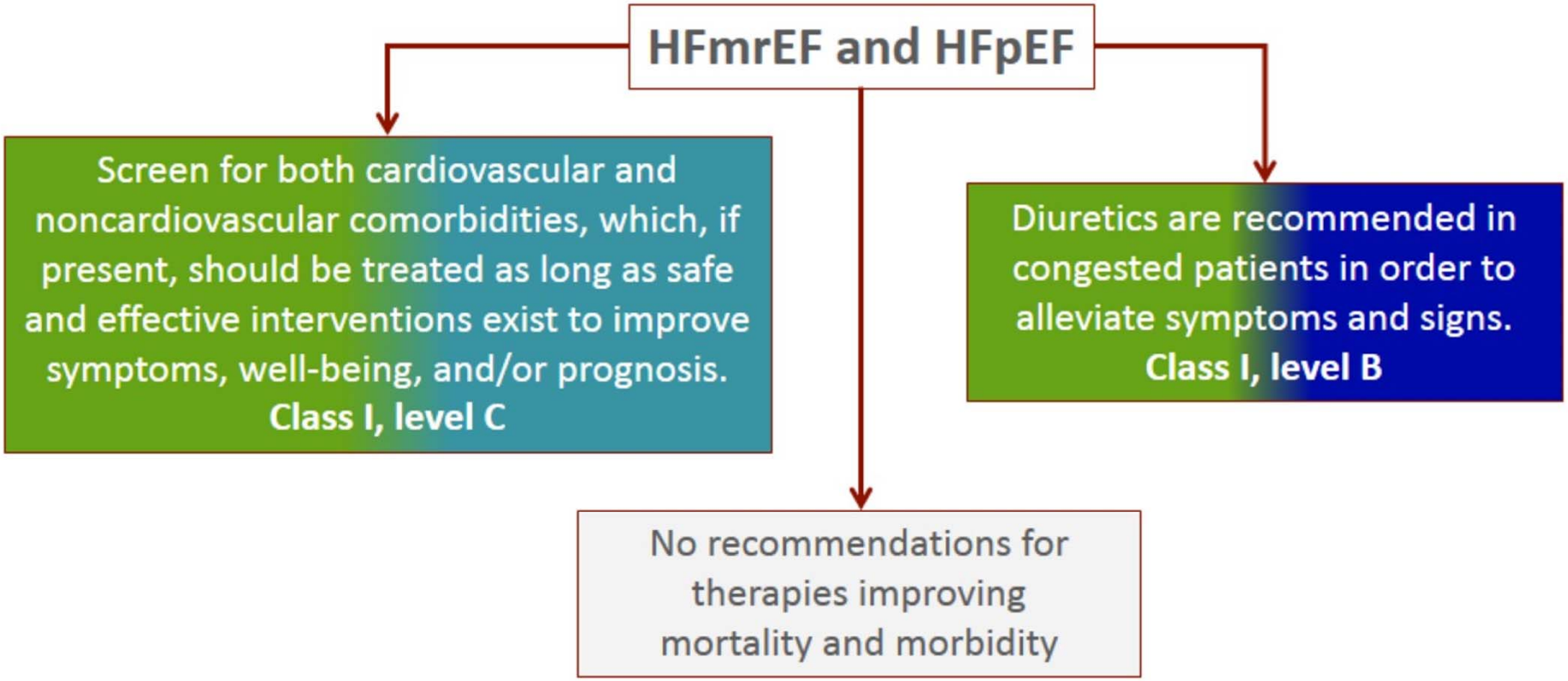
Ponikowski P, et al. *Eur Heart J.* 2016;18:891-975.

What We Do Know About HFmrEF

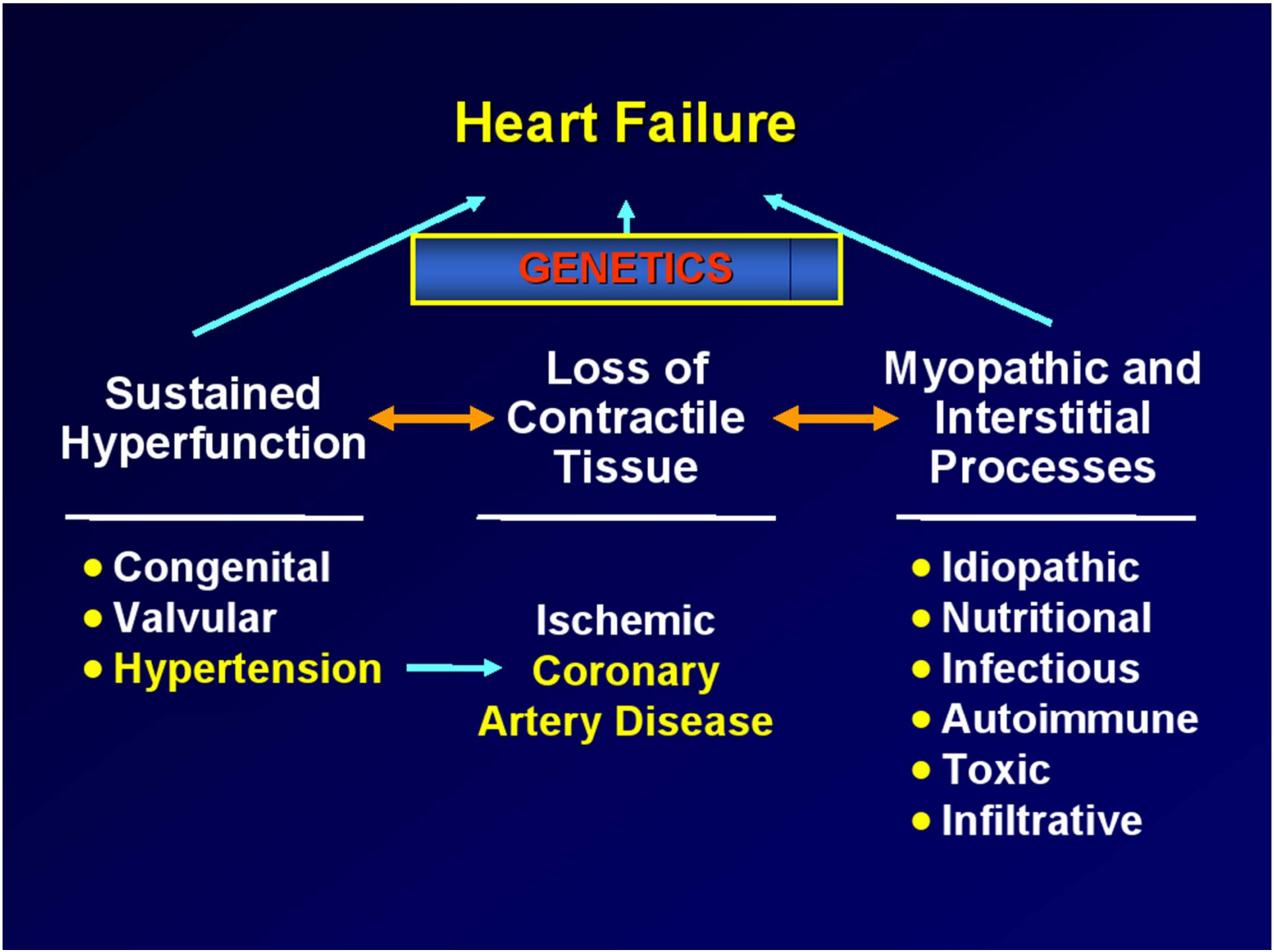
- The EF is not normal
- There are no treatments available to reduce morbidity and mortality
- There are limitations to using the measurement of EF but it is what clinicians use
- Drugs used in HFrEF are not indicated in HFpEF
- HFmrEF is a lot like HFrEF in terms of
  - Underlying causes
  - Clinical presentation
  - Biomarkers
- Patients with HFmrEF usually have a better prognosis than patients with HFrEF

What Is New in the Therapeutic Algorithm?

Recommendations for treatment of patients with HFpEF and HFmrEF



Ponikowski P, et al. *Eur Heart J.* 2016;18:891-975.


Heart Failure
GENETICS
Sustained Hyperfunction
Loss of Contractile Tissue
Myopathic and Interstitial Processes
• Congenital
• Valvular
• Hypertension
Ischemic Coronary Artery Disease
• Idiopathic
• Nutritional
• Infectious
• Autoimmune
• Toxic
• Infiltrative

Symptoms of HF

Symptoms

Typical

- Breathlessness
- Ankle swelling
- Orthopnea
- Fatigue, tiredness, increased time to recover after exercise
- Paroxysmal nocturnal dyspnea
- Reduced exercise tolerance

Less Typical*

- Nocturnal cough
- Syncope
- Wheezing
- Palpitations
- Bloated feeling
- Confusion

Signs

More Specific

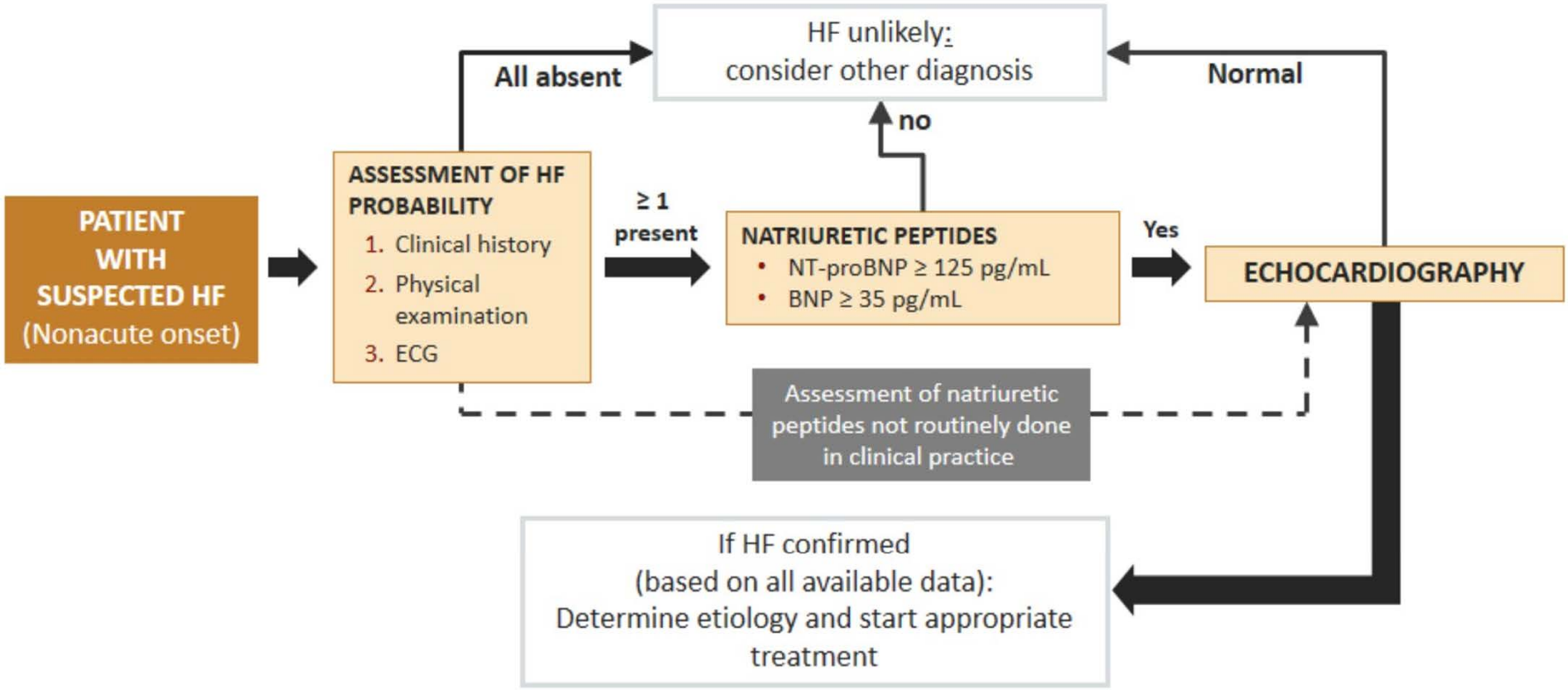
- Laterally displaced apical impulse
- Elevated jugular venous pressure
- Third heart sound (gallop rhythm)
- Hepatojugular reflux

Less Specific*

- Weight gain
- Tissue wasting (cachexia)
- Peripheral edema (ankle, sacral, scrotal)
- Hepatomegaly
- Pulmonary crepitations
- Irregular pulse
- Reduced air entry and dullness to percussion at lung bases (plural effusion)

*For complete list of symptoms and signs, refer to Table 4.1 in:
Ponikowski P, et al. *Eur Heart J.* 2016;18:891-975.

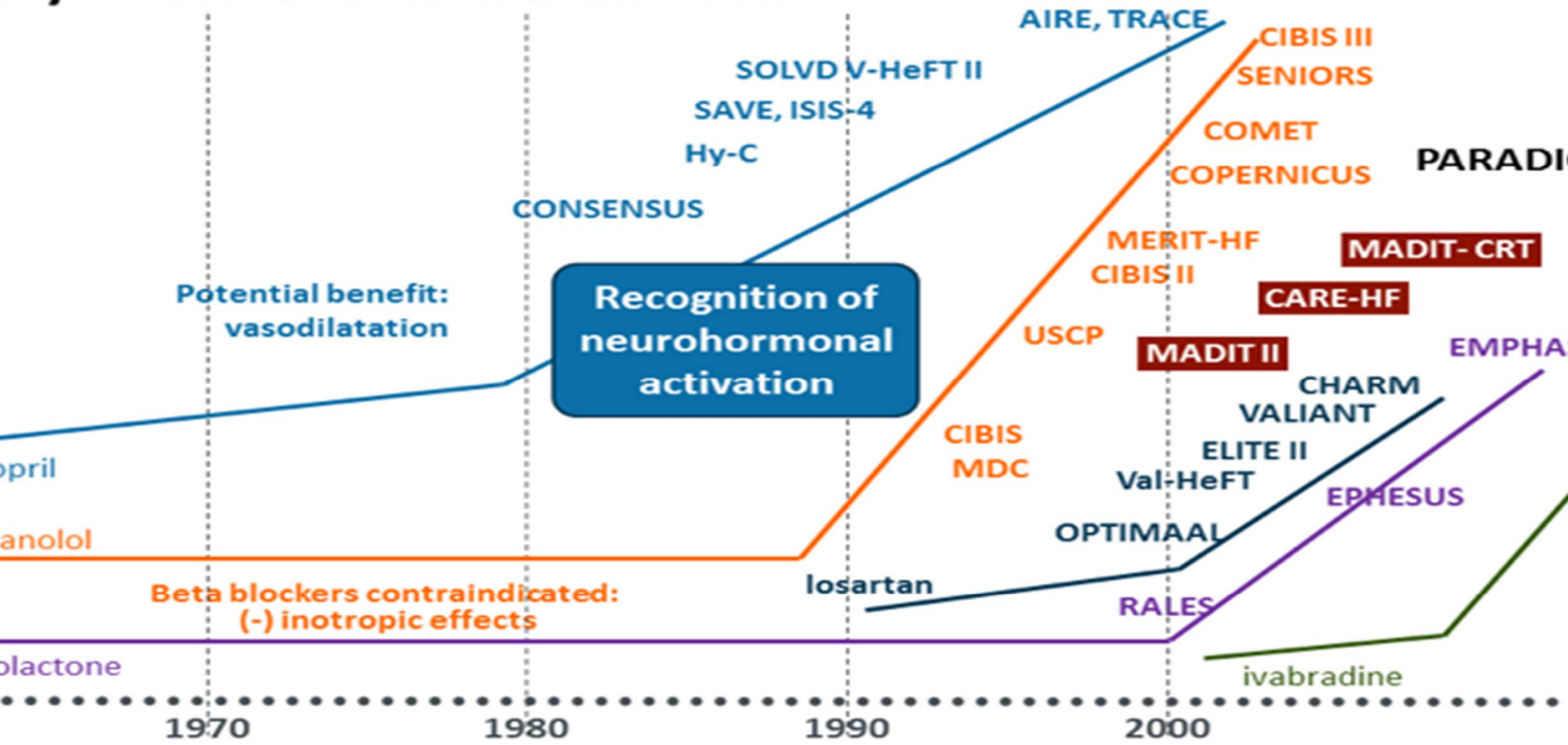
ESC Guidelines: Management of Suspected HF



Ponikowski P, et al. *Eur Heart J.* 2016;18:891-975.

andscape at the Beginning of 21st Century: H
reatable and Preventable Disease

ory of the landmark trials in HF



HF: Becoming a Preventable Disease

The goals of treatment in patients with HF:

- **Reduce mortality**
- Prevent hospital admission
- Improve clinical status, functional capacity, and quality of life
- In the year 2016 (…) by applying all evidence-based discoveries, **HF** is becoming a preventable and treatable disease

"…preventing HF hospitalization and improving functional capacity are important benefits to be considered if a mortality excess is ruled out…"

Ponikowski P, et al. *Eur Heart J.* 2016;18:891-975.

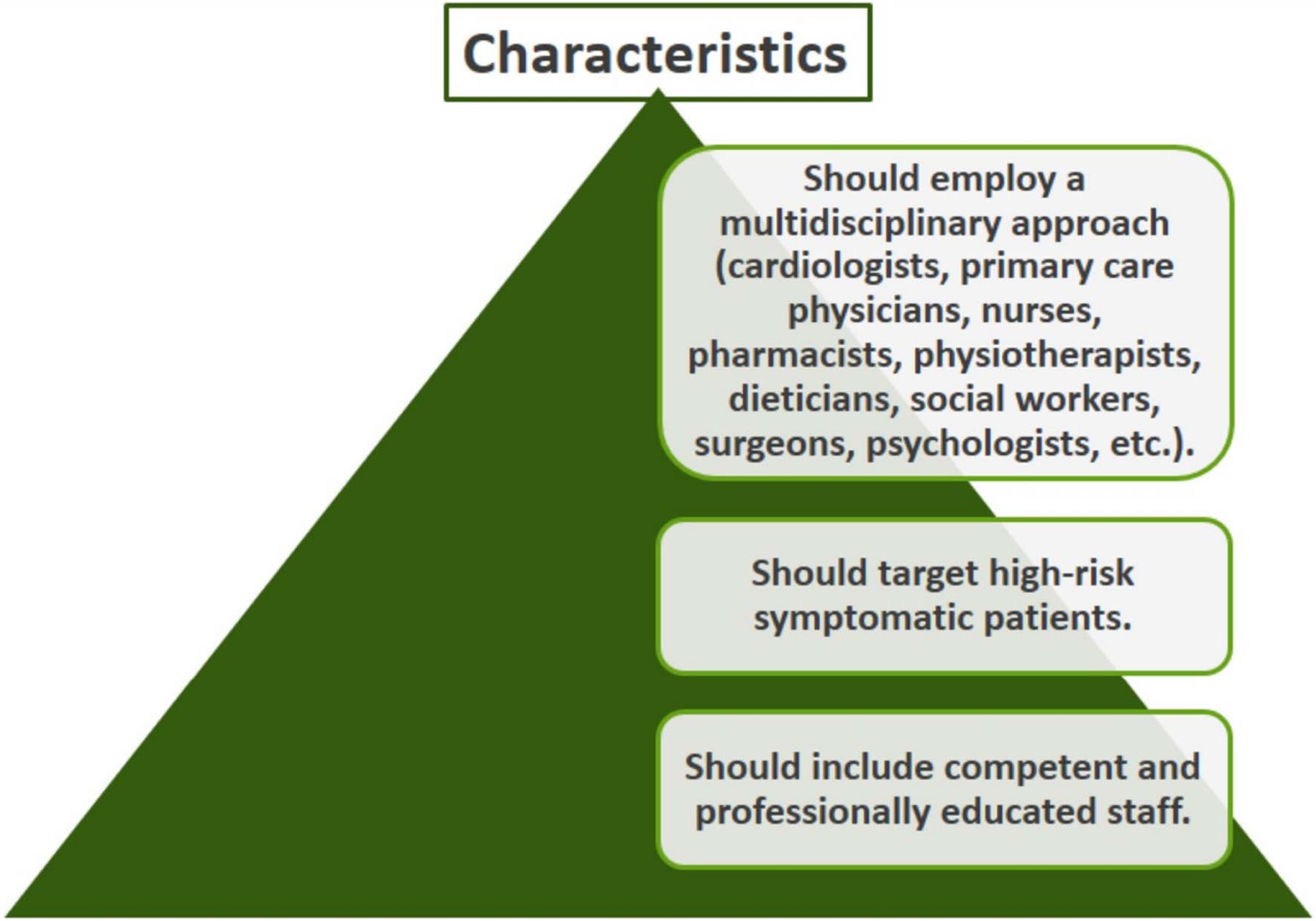
2016 ESC HF Guidelines: Prevention

To prevent or delay onset of HF and prolong life, the following are recommended

- Treatment of arterial hypertension
- Use of statins in patients with or at high risk of CAD
- Use of ACEi in patients with asymptomatic LV dysfunction
- Use of BBs in those with asymptomatic LV dysfunction and a history of myocardial infarction

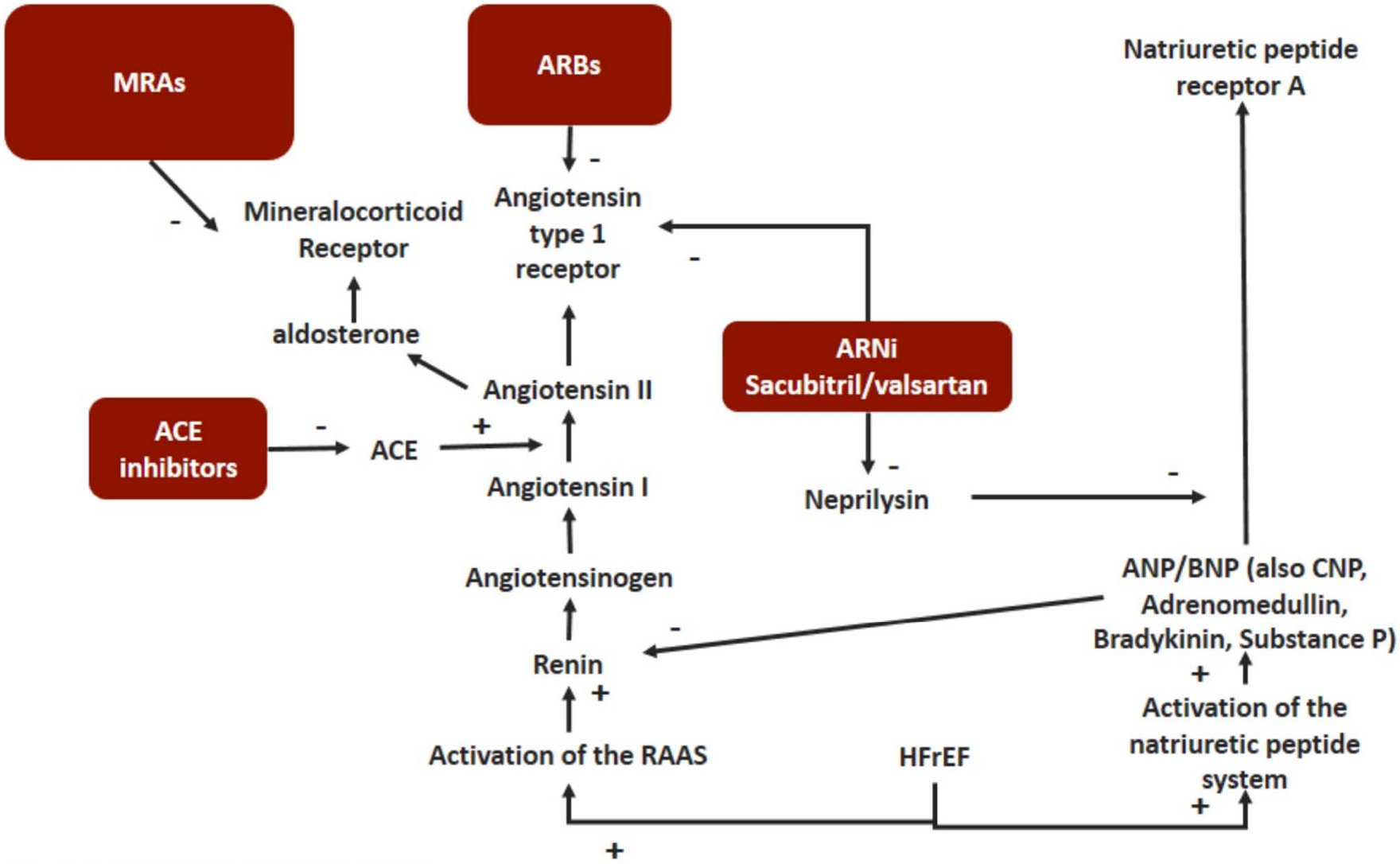
Ponikowski P, et al. *Eur Heart J.* 2016;18:891-975.

Multidisciplinary Approach to HF Management



Ponikowski P, et al. *Eur Heart J.* 2016;18:891-975.

Pathways Blocked by Pharmacological Therapies in HF



Jhund P, et al. *BJM*. 2016;102:1342-1347.

ARN Inhibition: Sacubitril/Valsartan

Heart Failure

Vasoactive peptide system

pro-BNP

NT-proBNP

ANP BNP CNP

Adrenomedullin
Bradykinin
Substance P
(angiotensin II)

NEP

Vasodilation

- ↓ blood pressure
- ↓ sympathetic tone
- ↓ aldosterone levels
- ↓ fibrosis
- ↓ hypertrophy

Natriuresis/diuresis

LCZ696

Sacubitril (AHU377)

↓

LBQ657

Stable at pH 5-7
Breaks apart after ingestion

Inactive fragments

Valsartan

LCZ696 is a novel crystalline complex consisting of the molecular moieties of valsartan and sacubitril in an equimolar ratio

RAS

Angiotensinogen (liver secretion)

Angiotensin I

Angiotensin II

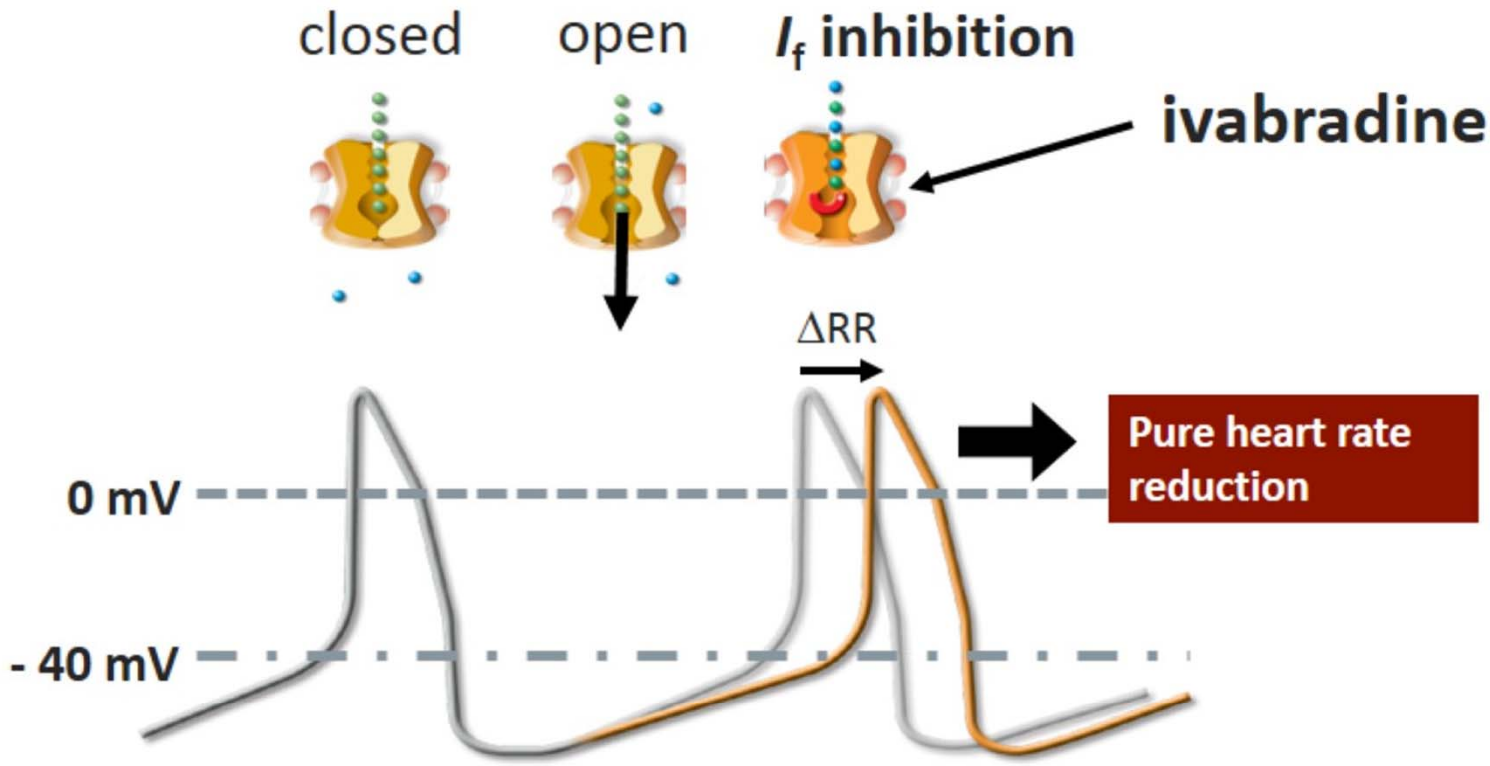
AT_1 receptor

Vasoconstriction

- ↑ blood pressure
- ↑ sympathetic tone
- ↑ aldosterone
- ↑ fibrosis
- ↑ hypertrophy

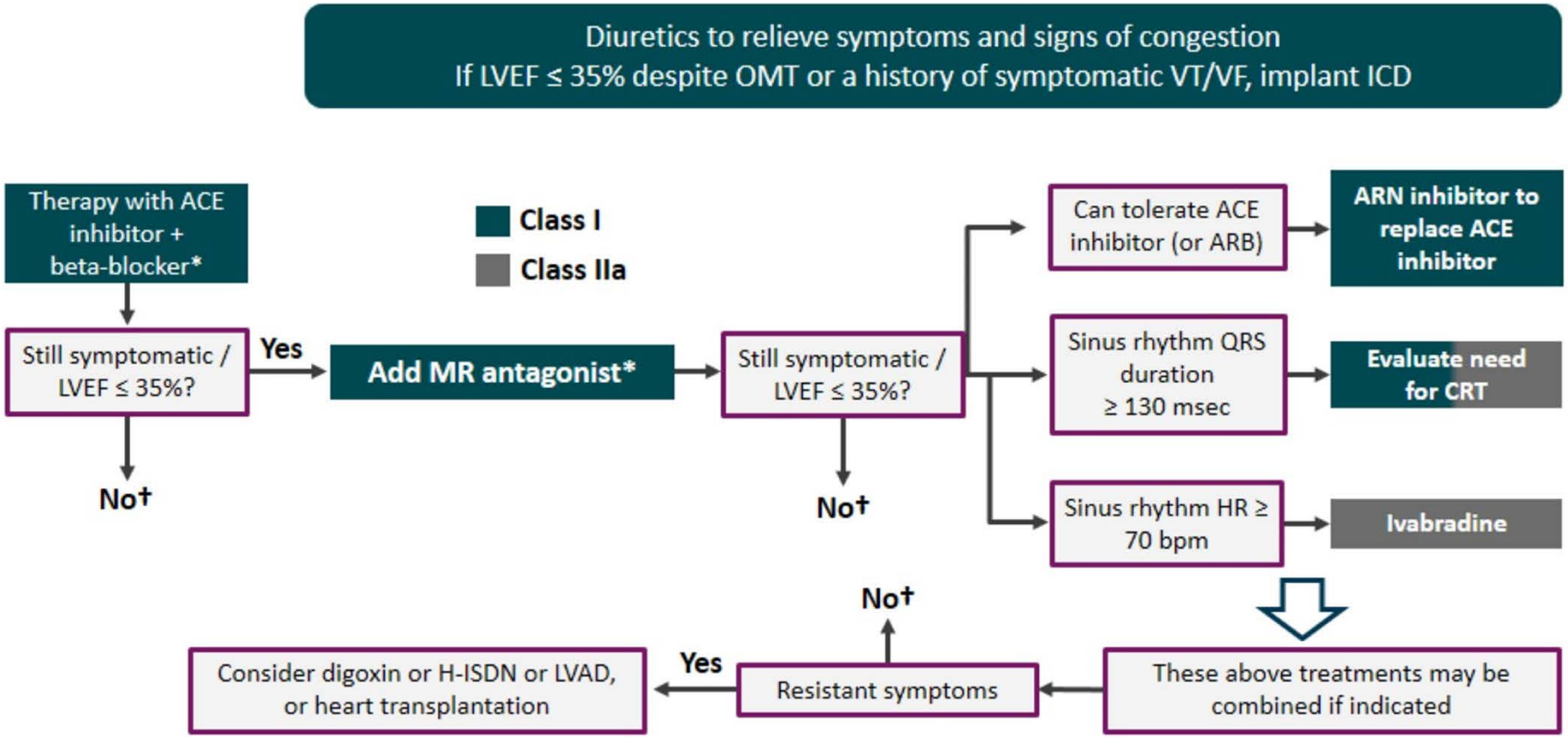
Vardeny O, et al. *JACC Heart Fail.* 2014;2:663-670.

Pure Heart Rate Reduction Through I_f Current Inhibition



Thollon C, et al. *Br J Pharmacol*. 1994;112:37-42.
DiFrancesco A, et al. *Drugs*. 2004;64:1757-1765.
Image courtesy of Jeffrey S. Borer, MD.

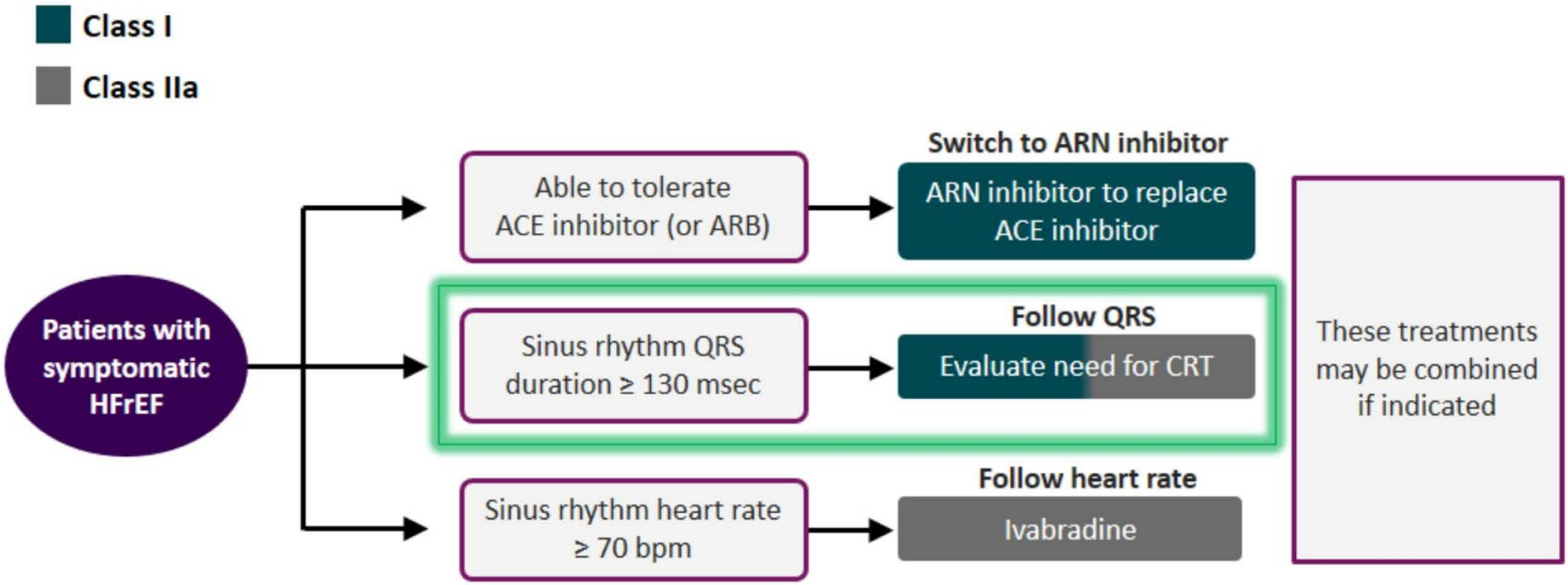
ESC Guidelines for HF: Patient With Symptomatic HFrEF



*Up-titrate to maximum tolerated evidence-based doses; †No further action required, Consider reduction diuretic dose.

Ponikowski P, et al. Eur Heart J. 2016;18:891-975.

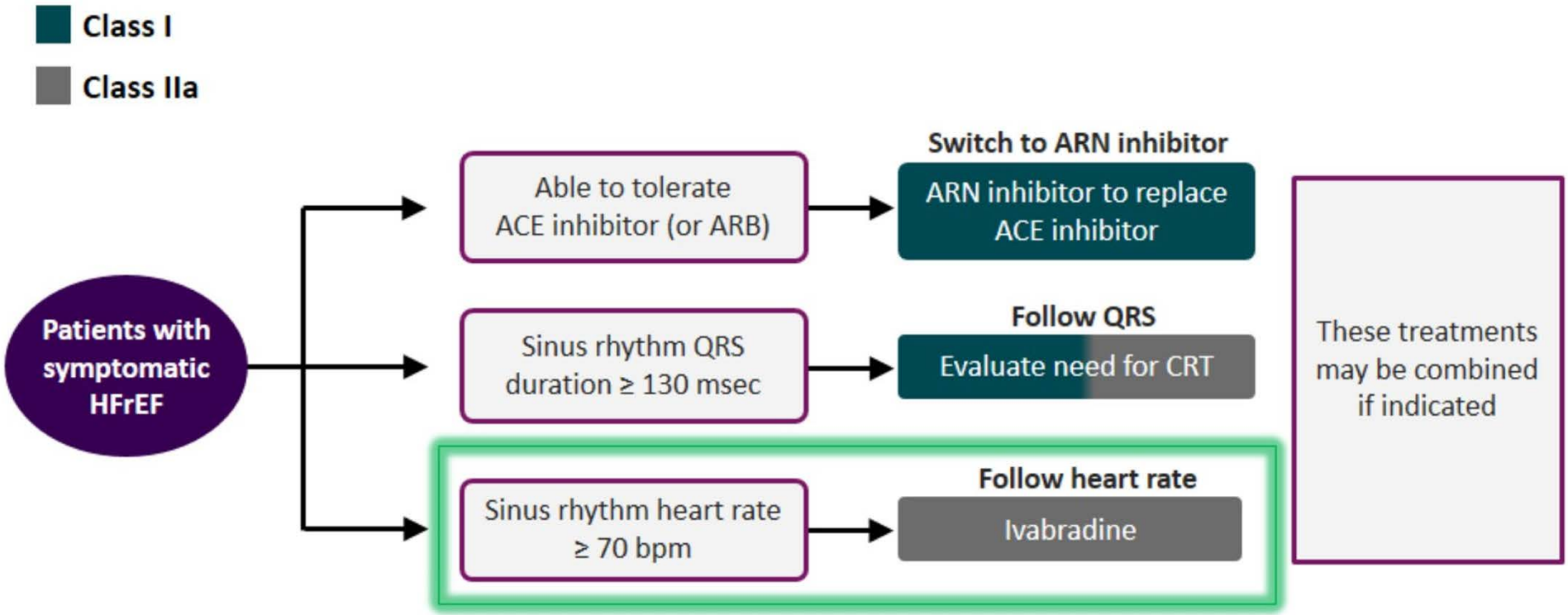
Guidelines: Therapy for Symptomatic HFrEF (cont)



Consult published guidelines for additional treatment recommendations.

Ponikowski P, et al. *Eur Heart J.* 2016;18:891-975.

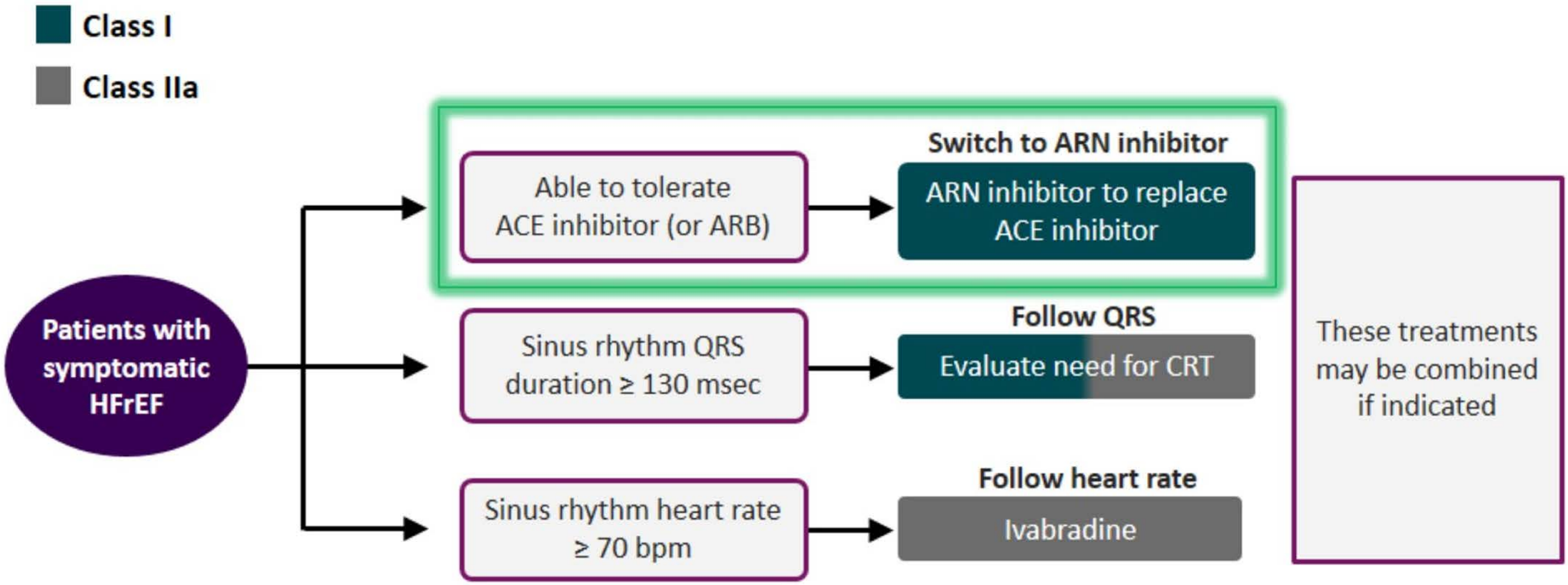
ESC Guidelines: Therapy for Symptomatic HFrEF (cont)



Consult published guidelines for additional treatment recommendations.

Ponikowski P, et al. *Eur Heart J*. 2016;18:891-975.

ESC Guidelines: Therapy for Symptomatic HFrEF (cont)



Consult published guidelines for additional treatment recommendations

Ponikowski P, et al. Eur Heart J. 2016;18:891-975.

ESC Guidelines: Therapy for Symptomatic HFrEF (cont)

ACE-Inhibitor

Recommendation

An ACE-I is recommended, in addition to a beta-blocker, for symptomatic patients with HFrEF

Class I

Level A

Beta-Blocker

Recommendation

A beta-blocker is recommended, in addition an ACE-I, for patients with stable, symptomatic HFrEF

Class I

Level A

Mineralocorticoid-Antagonist

Recommendation

An MRA is recommended for patients with HFrEF, who remain symptomatic despite treatment with an ACE-I and a beta-blocker

Class I

Level A

Ponikowski P, et al. *Eur Heart J.* 2016;18:891-975.

Pharmacological Treatments Recommended in Selected Patients With Symptomatic (NYHA Class II-IV) HFrEF

Diuretics

Recommendation

- Diuretics are recommended to improve symptoms and exercise capacity in patients with signs and/or symptoms of congestion. **Class** I **Level** B
- Diuretics should be considered to reduce the risk of HF hospitalization in patients with signs and/or symptoms of congestion. **Class** IIa **Level** B

ARN Inhibitor

Recommendation

- Sacubitril/valsartan is recommended as a replacement for an ACE inhibitor to further reduce the risk of HF hospitalization and death in ambulatory patients with HFrEF who remain symptomatic despite optimal treatment with an ACE inhibitor, a beta-blocker and MRA. **Class** I **Level** B

I_f-channel Inhibitor

Recommendation

- Ivabradine should be considered to reduce the risk of HF hospitalization and cardiovascular death in symptomatic patients with LVEF ≤35%, in sinus rhythm and a resting heart rate ≥70 bpm **Class** IIa **Level** B
- Ivabradine should be considered to reduce the risk of HF hospitalization and cardiovascular death in symptomatic patients with LVEF ≤35%, in sinus rhythm and a resting heart rate ≥70 bpm who are unable to tolerate beta-blockers. Patients should also receive an ACE inhibitor (or ARB) and an MRA (or ARB). **Class** IIa **Level** C

ARB

Recommendation

- An ARB is recommended to reduce the risk of HF hospitalization and cardiovascular death in symptomatic patients unable to tolerate an ACE inhibitor (Patients should also receive a beta-blocker and an MRA). **Class** I **Level** B
- An ARB is recommended to reduce the risk of HF hospitalization and CV death in symptomatic patients despite optimal medical treatment. **Class** IIb **Level** C

Ponikowski P, et al. *Eur Heart J.* 2016;18:891-975.

The Conundrum of Inotropic Therapy

Applying Inotropic Therapy: Risk of Inducing Pro-arrhythmia

Inotropic Agents: Dobutamine, Dopamine, Levosimendan, Phosphodiesterase III (PDE III) Inhibitors

- Short-term, IV infusion of inotropic agents may be considered in patients with hypotension (SBP <90 mmHg) and/or signs/symptoms of hypoperfusion **Class** IIb **Level** C
- Inotropic agents are not recommended unless the patient is symptomatically hypotensive or hypoperfused because of safety concern. **Class** III **Level** A

Vasopressors

Concern of Increased Mortality

- A vasopressor (norepinephrine preferably) may be considered in patients who have cardiogenic shock -- despite treatment with another inotrope -- to increase blood pressure and vital organ perfusion **Class** IIb **Level** B
- It is recommended to monitor ECG and blood pressure when using inotropic agents and vasopressors, as they can cause arrhythmia, myocardial ischemia **Class** I & IIb **Level** C

Ponikowski P, et al. *Eur Heart J.* 2016;18:891-975.

ESC Guidelines: HF Education

Education Topic	Professional Behaviors
Symptom monitoring and self-care	• Provide individual information to support self-management such as: – In the case of increasing dyspnea or edema or a sudden unexpected weight gain of > 2 kg in 3 days, patients may increase their diuretic dose and/or alert their healthcare team – Use of flexible diuretic regime – Self-care support aids such as dosette box when appropriate
Diet and alcohol	• Individualize information on fluid intake to take into account body weight and periods of high heat and humidity. Adjust advice during periods of acute decompensation and consider altering these restrictions towards end-of-life • Tailor alcohol advice to etiology of HF; eg, abstinence in alcoholic cardiomyopathy • Normal alcohol guidelines apply (2 units per day in men or 1 unit per day in women). 1 unit is 10 mL of pure alcohol (eg, 1 glass of wine, ½ pint of beer, 1 measure of spirit).
Smoking and recreational substance use	• Refer for specialist advice for smoking cessation and drug withdrawal and replacement therapy • Consider referral for cognitive behavioral theory and psychological support if patient wishes support to stop smoking
Exercise	• Advice on exercise that recognizes physical and functional limitations, such as frailty, comorbidities • Referral to exercise program when appropriate

Ponikowski P, et al. *Eur Heart J.* 2016;18:891-975.

Polypharmacy and Comorbidities

- Need for adjustment of therapies to reduce polypharmacy due to comorbidities and drug interactions
  - Example: arthritis and HF-therapy

Sleep Apnea

Recommendation

Adaptive servo-ventilation is not recommended in patients with HFrEF and a predominant central sleep apnea because of an increased all-cause and CV mortality **Class** III **Level** B

Diabetes

Recommendation

Thiazolidinediones (glitazones) are not recommended in patients with HF, as they increase the risk of HF worsening and HF hospitalization **Class** III **Level** A

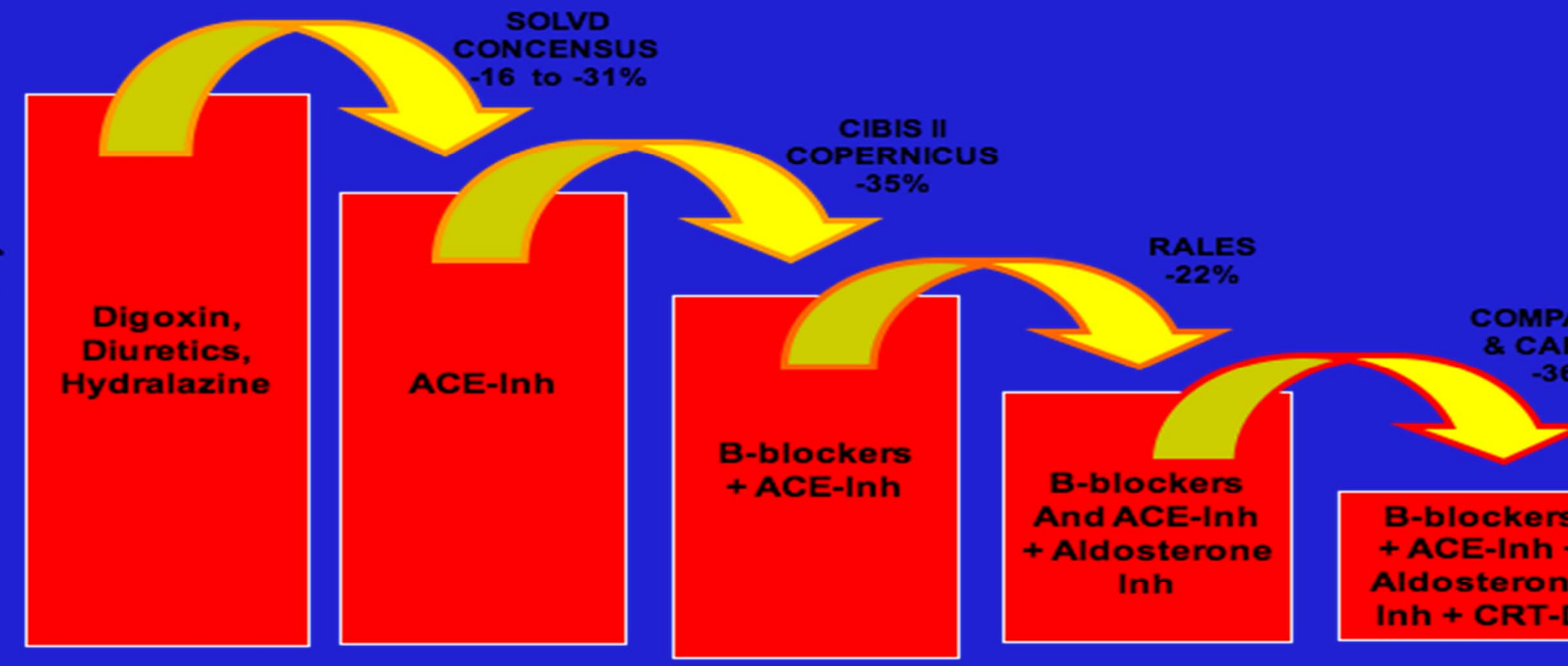
Arthritis

Recommendation

NSAIDs or COX-2 inhibitors are not recommended in patients with HF, as they increase the risk of HF worsening and HF hospitalization **Class** III **Level** B

Ponikowski P, et al. *Eur Heart J.* 2016;18:891-975.

Improving survival of Heart Failure Patient



Kashani et al- JACC Dec05;46(12):218

Conclusions

- HF most likely contributes to significant disease burden in Asia as a result of increasing prevalence of risk factors.
- Controlling the risk factors ; mainly HT, smoking & DM and treating heart disease optimally will prevent the burden of HF
- Over the last 40 years, treatment of chronic heart failure has improved dramatically.
- A series of randomized controlled trial have led to change in standard of medical care.
- Further improvement should hopefully replace old by new therapies more than adding them.

THANK YOU