Congestive Heart Failure Treatment & Update 2018

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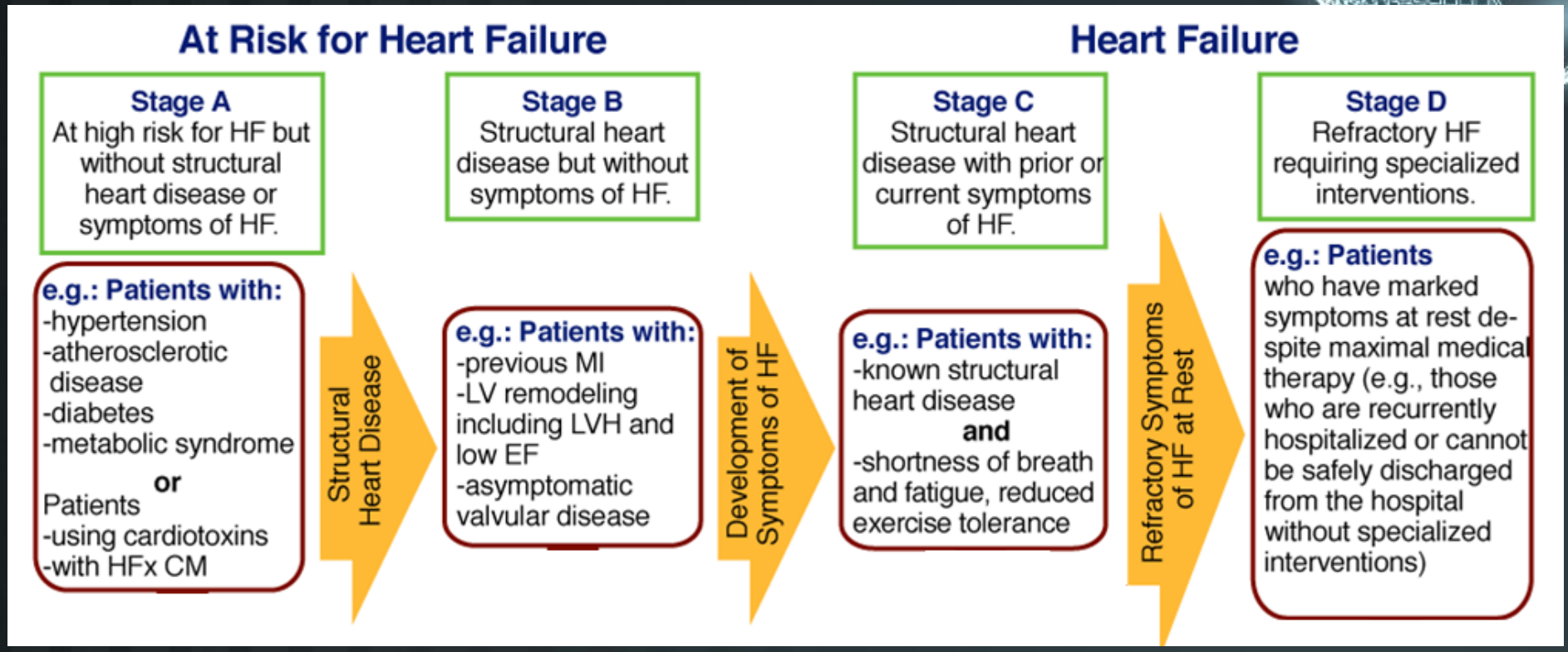
Objectives

- Define Heart Failure (HF).
- New classification. Stages: ESC 2016.
- Identify current assessment and treatment modalities for heart failure.

Heart Failure Definition

- HF is a clinical syndrome characterized by typical symptoms (*breathlessness, ankle swelling and fatigue*)
- May accompanied by signs (*elevated juglar venous pressure, pulmonary crackles and peripheral edema*)
- Caused by *structural* and /or *functional* cardiac abnormalitiy, resulting in a *reduced C.O* or *elevated intracardiac pressure* at rest or stress.

Stages of Heart Failure



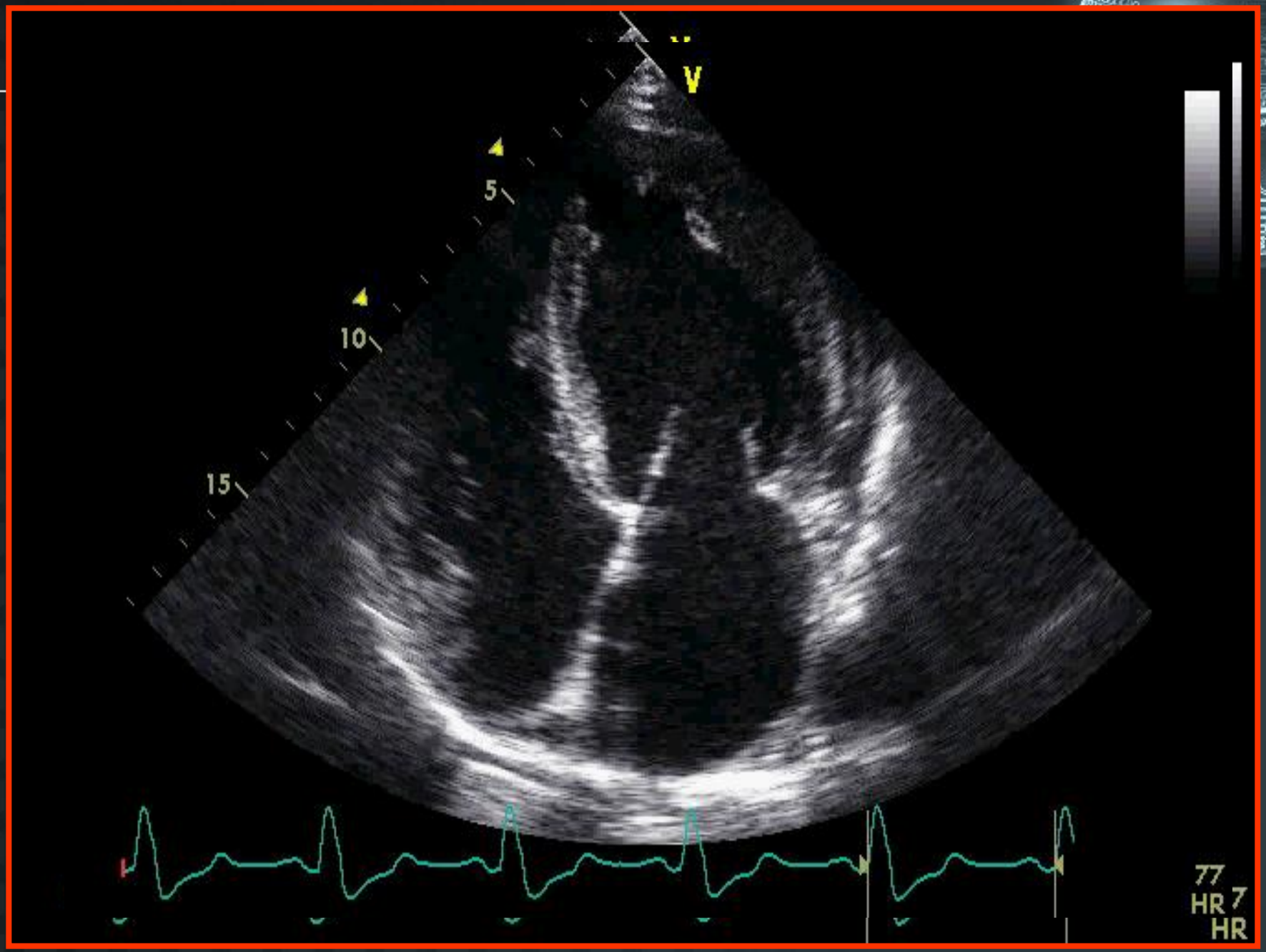
- Progressive nature of LV dysfunction
- Progress in *one* direction due to cardiac remodeling
- Patient can *move between* NYHA classes

Case Presentation

-53 years nice lady , was referred for evaluation
- Effort dyspnea, Cough, PND, in the last year.
- Medical history:
- 1 - Ca of breast S/P Rt mastectomy, complete chemotherapy courses.
- 2-HTN 3- Bronchial Asthma
- ECG: NSR; QRS=120msec; Normal axis.
- Treatment: Enaladex10mg*1; Symbicort inh. Prednison 5mg*1

Physical exam:Prominent JVP; Lungs:- Bilaterale rales

Heart : Regular sounds, S3 Gallop.


V
5
10
15
77
HR
7
HR

Case Presentation

- What would you recommend for this patient?
- 1-Dimitone 3.125mg*2& stop prednisone.

  2- Aldacone 12.5mg*1& stop Symbicort
- 3- Enaladex 10mg*2 & Fusid 40mg
- 4- All of the above.

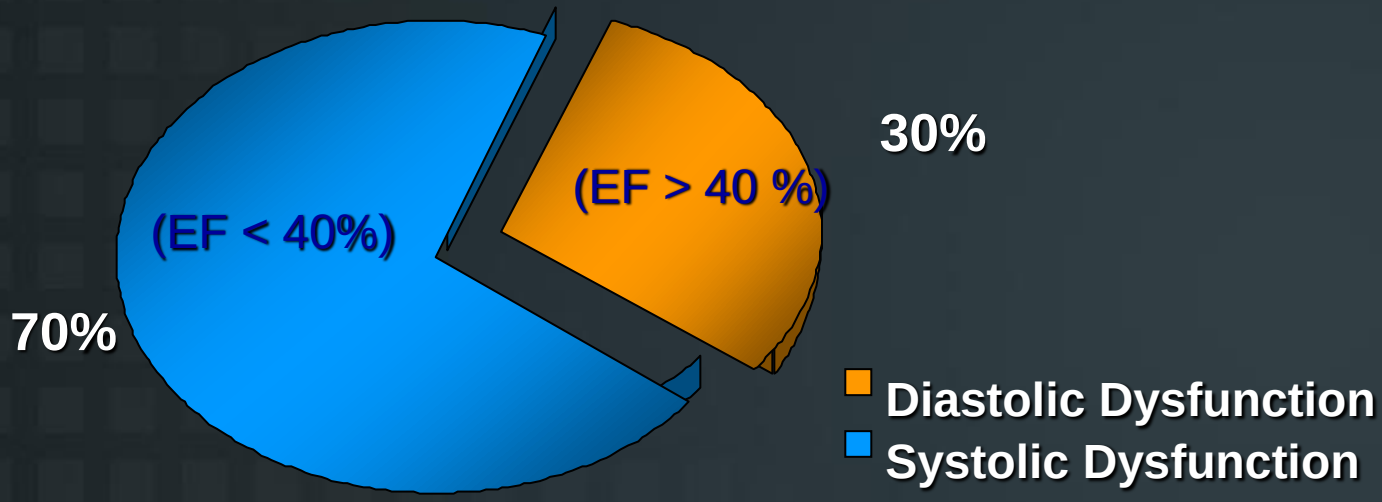
CHF – FC II

- **At follow up few months later she came back with Mild symptoms.**
- **What is the next step?**

- 1- Send the patient for Cardiac Transplant?
- 2- Stop enaladex, give Entresto 50mg*2 ?
- 3- Evaluate for CRT-D?
- 4- Will answer at the end of Presentation?

Left Ventricular Dysfunction

- **Systolic:** Impaired contractility/ejection
  - Approximately two-thirds of heart failure patients have systolic dysfunction[1]
- **Diastolic:** Impaired filling/relaxation



1 Lilly, L. Pathophysiology of Heart Disease. Second Edition p 200

Definition of heart failure with preserved (HFpEF), mid-range (HFmrEF) and reduced ejection fraction (HFrEF) of heart failure

Type of HF		HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs[a]	Symptoms ± Signs[a]	Symptoms ± Signs[a]
	2	LVEF <40%	LVEF 40–49%	LVEF ≥50%
	3	–	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).

BNP= B-type natriuretic peptide; HF= heart failure; HFmrEF= heart failure with mid-range ejection fraction; HFpEF = heart failure with preserved ejection fraction; HFrEF= heart failure with reduced ejection fraction; LAE =left atrial enlargement; LVEF =left ventricular ejection fraction; LVH =left ventricular hypertrophy; NT-proBNP =N-terminal pro-B type natriuretic peptide.

aSigns may not be present in the early stages of HF (especially in HFpEF) and in patients treated with diuretics. bBNP>35 pg/ml and/or NT-proBNP>125 pg/mL

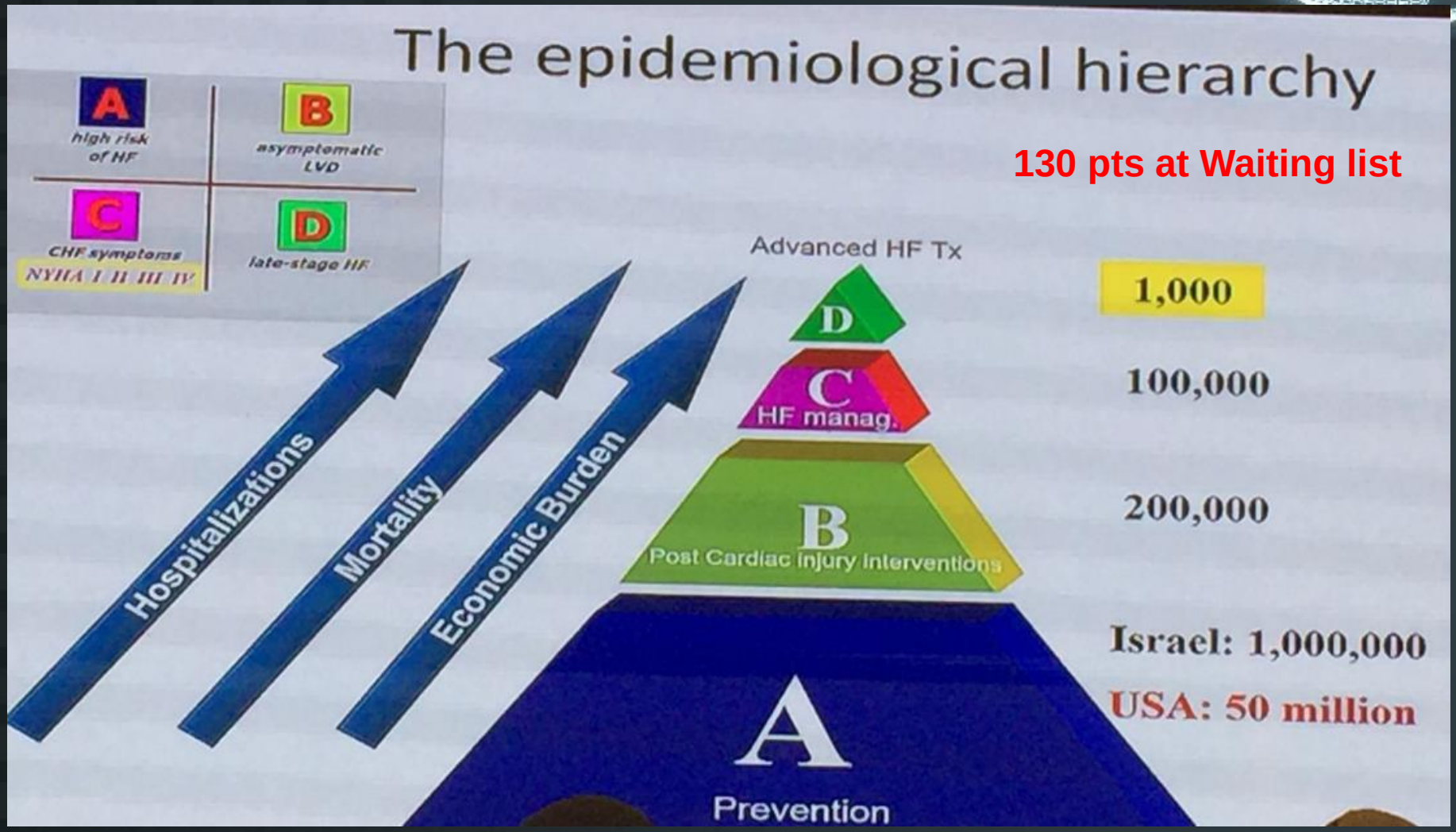
2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Heart Failure

- Prevalence
  - Worldwide, 22 million[1]
  - United States, 5.5 million[2]
- Mortality
- The absolute mortality rates for HF remain approximately 50% within 5 years of diagnosis
- 50% of these deaths occur suddenly

1 World Health Statistics, World Health Organization,

2 American Heart Association Heart and Stroke Statistical Update.

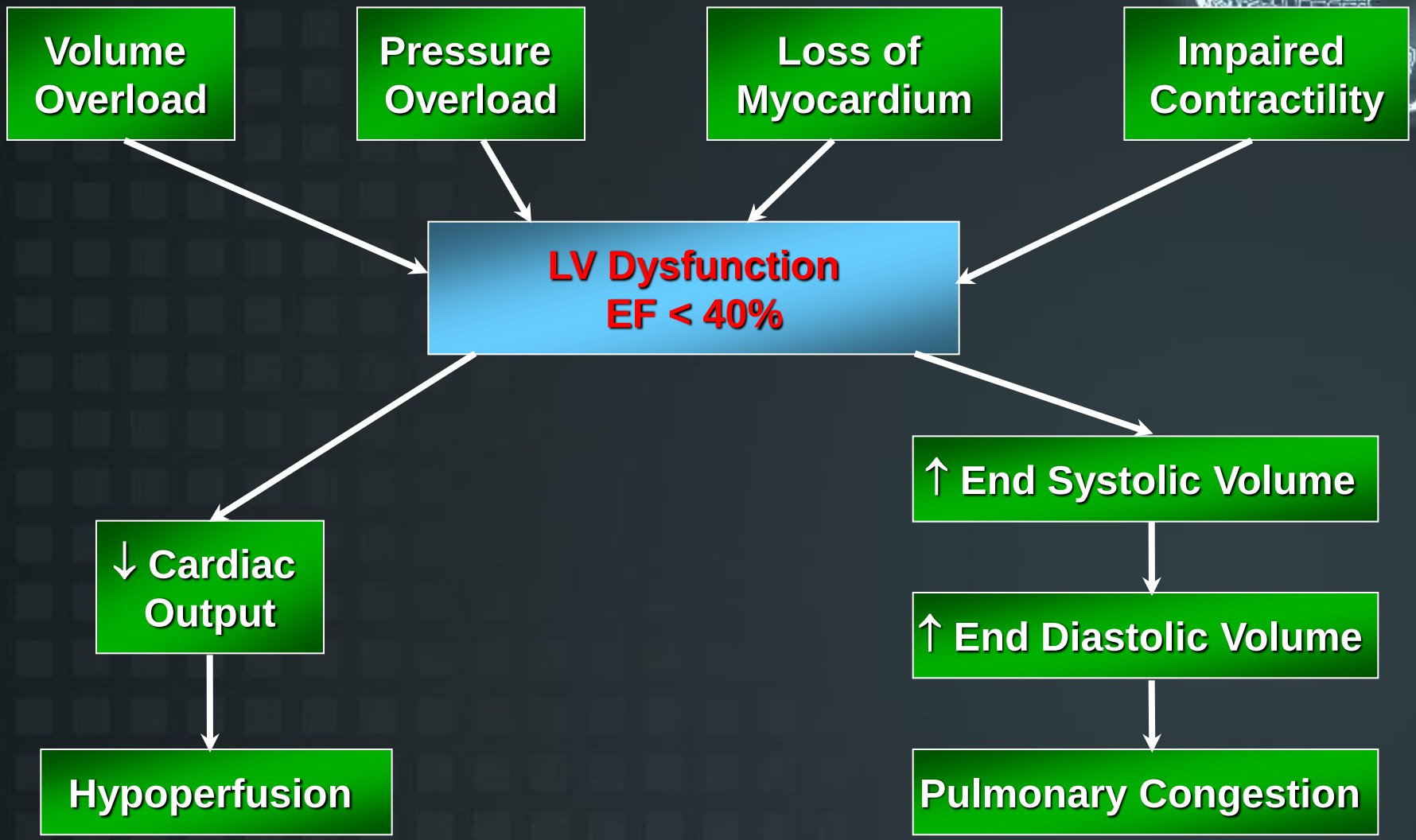

The epidemiological hierarchy
A
high risk of HF
B
asymptomatic LVD
C
CHF symptoms
NYHA I II III IV
D
late-stage HF
130 pts at Waiting list
Advanced HF Tx
D
C
HF manag.
B
Post Cardiac Injury Interventions
A
Prevention
Hospitalizations
Mortality
Economic Burden
1,000
100,000
200,000
Israel: 1,000,000
USA: 50 million

Etiology of Heart Failure

What causes heart failure?

- The loss of a critical quantity of functioning myocardial cells after injury to the heart due to:
  - Ischemic Heart Disease
  - Hypertension
  - Idiopathic Cardiomyopathy
  - Infections (e.g., viral myocarditis, Chagas' disease)
  - Toxins (e.g., alcohol or cytotoxic drugs)
  - Valvular Disease
  - Prolonged Arrhythmias

Left Ventricular Dysfunction



Left Heart Failure

- Elevated LVEDP
  - LAP
  - PVP
- Pulmonary congestion
- Dyspnea
- Orthopnea
- Cough
- Tiredness and lethargy

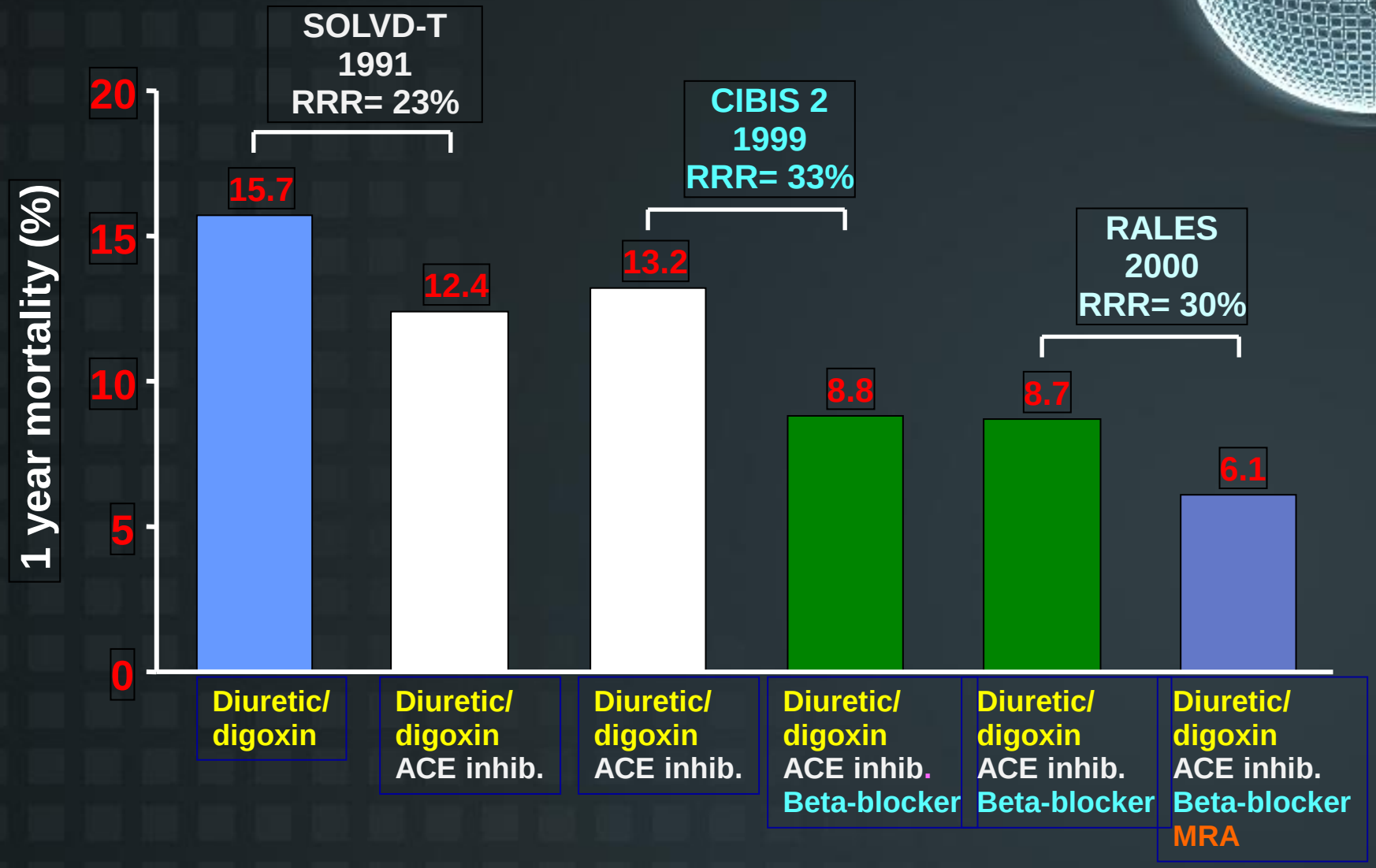
HFrEF-Medical therapy

DIGOXIN ***1785 Dr William Wethering***
DIURETICS

ACEI 1990
ARB
BB
MRA
HYDRALAZINE-ISOSORBIDE DINITRATE **2003**
Ivabradine ***2010***

ARNI=Entresto ***2016***

Cumulative benefit of poly-pharmacy in HF

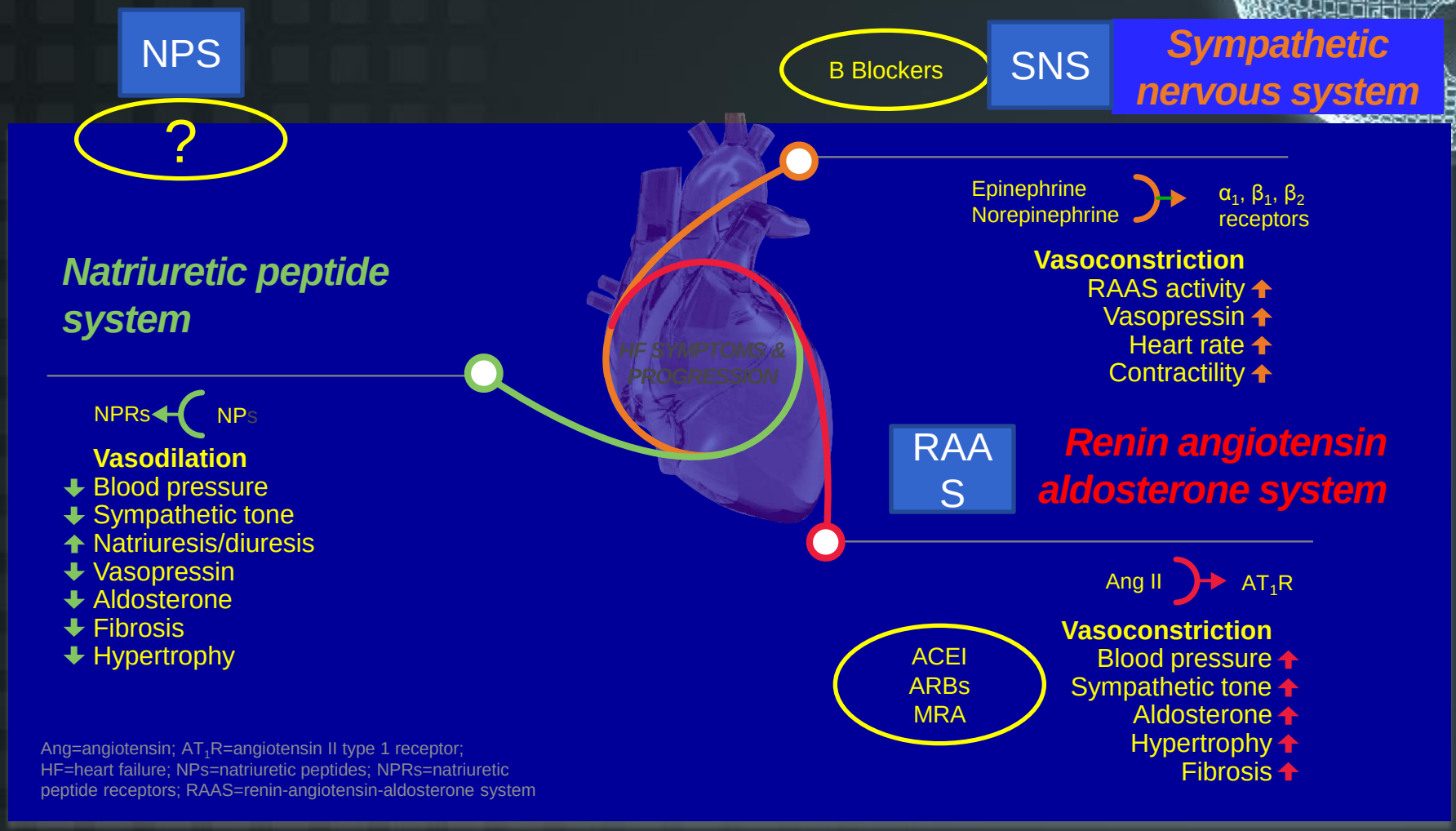


Ivabradine chronic heart failure) (selective sinus-node inhibitor) SHIFT Study

- 6558 patients were randomly assigned to treatment groups (3268 ivabradine, 3290 placebo).EF<35%
- The primary endpoint: Composite of CV death or hospital admission for worsening HF.
  - **24% vs 29% -18%**
    (HR 0·82, 95% CI 0·75-0·90,p<0·0001).
- Hospital admissions for worsening HF
  - **21% *vs* 16% -26%**
    (HR 0·74, 0·66—0·83; p<0·0001)

Swedberg k lancet 2010 Sep 11;376(9744):875-85

Pathophysiology of HFrEF



Ang=angiotensin; AT_1R=angiotensin II type 1 receptor; HF=heart failure; NPs=natriuretic peptides; NPRs=natriuretic peptide receptors; RAAS=renin-angiotensin-aldosterone system

1. Levin ER., et al. Natriuretic peptides. N Engl J Med 1998;339:321–8. 2. Nathisuwan S. & Talbert RL. A Review of Vasopeptidase Inhibitors: A New Modality in the Treatment of Hypertension and Chronic Heart FailurePharmacotherapy 2002;22:27–42. 3. Kemp CD. & Conte JV. The pathophysiology of heart failure Cardiovascular Pathology 2012;365–71. 4. Schrier RW. & Abraham WT. Hormones and hemodynamics in heart failur Engl J Med 2009;341:577–85.

PARADIGM-HF

The NEW ENGLAND JOURNAL of MEDICINE

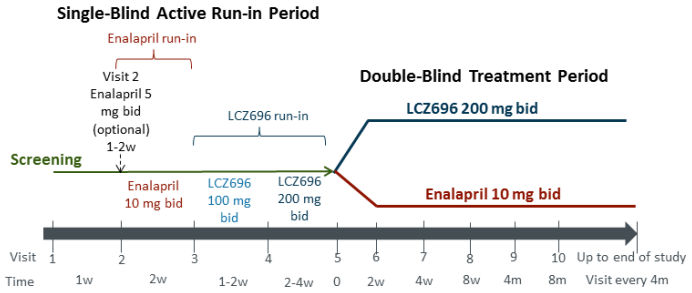
ESTABLISHED IN 1812 SEPTEMBER 11, 2014 VOL. 371 NO. 11

Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure

John J.V. McMurray, M.D., Milton Packer, M.D., Akshay S. Desai, M.D., M.P.H., Jianjian Gong, Ph.D., Martin P. Lefkowitz, M.D., Adel R. Rizkala, Pharm.D., Jean L. Rouleau, M.D., Victor C. Shi, M.D., Scott D. Solomon, M.D., Karl Swedberg, M.D., Ph.D., and Michael R. Zile, M.D., for the PARADIGM-HF Investigators and Committees*

PARADIGM-HF: Design

- Double-blind
- NYHA class II-IV CHF with EF ≤40% (n=8442)
- Patients entered a single-blind enalapril run-in period (titrated to 10 mg bid), followed by a LCZ696 run-in period (100 mg titrated to 200 mg bid)
- 8442 patients were randomly assigned 1:1 to enalapril 10 mg bid or LCZ696 200 mg bid
- The primary outcome was a composite of CV death or hospitalization for HF



McMurray JJ, et al. *N Engl J Med.* 2014;371:993-1004.

PARADIGM-HF: Significant Reductions in the Primary Endpoint With LCZ696 vs Enalapril

- Data monitoring committee recommended early termination, after a median follow-up of 27 months
- LCZ696 was superior to enalapril in reducing the primary endpoint of CV death or HF hospitalization

Outcome	LCZ696	Enalapril	HR (95% CI)	*P*
Primary composite outcome, %				
Death from CV causes or first hospitalization for worsening HF	21.8	26.5	0.80 (0.73-0.87)	<.001
Death from CV causes	13.3	16.5	0.80 (0.71-0.89)	<.001
First hospitalization for worsening HF	12.8	15.6	0.79 (0.71-0.89)	<.001

- The effect of LCZ696 was consistent across most prespecified subgroups

McMurray JJ, et al. *N Engl J Med.* 2014;371:993-1004.

2016 ESC Guideline - Sacubitril/valsartan

Pharmacological treatments indicated in patients with symptomatic (NYHA Class II-IV) HFrEF

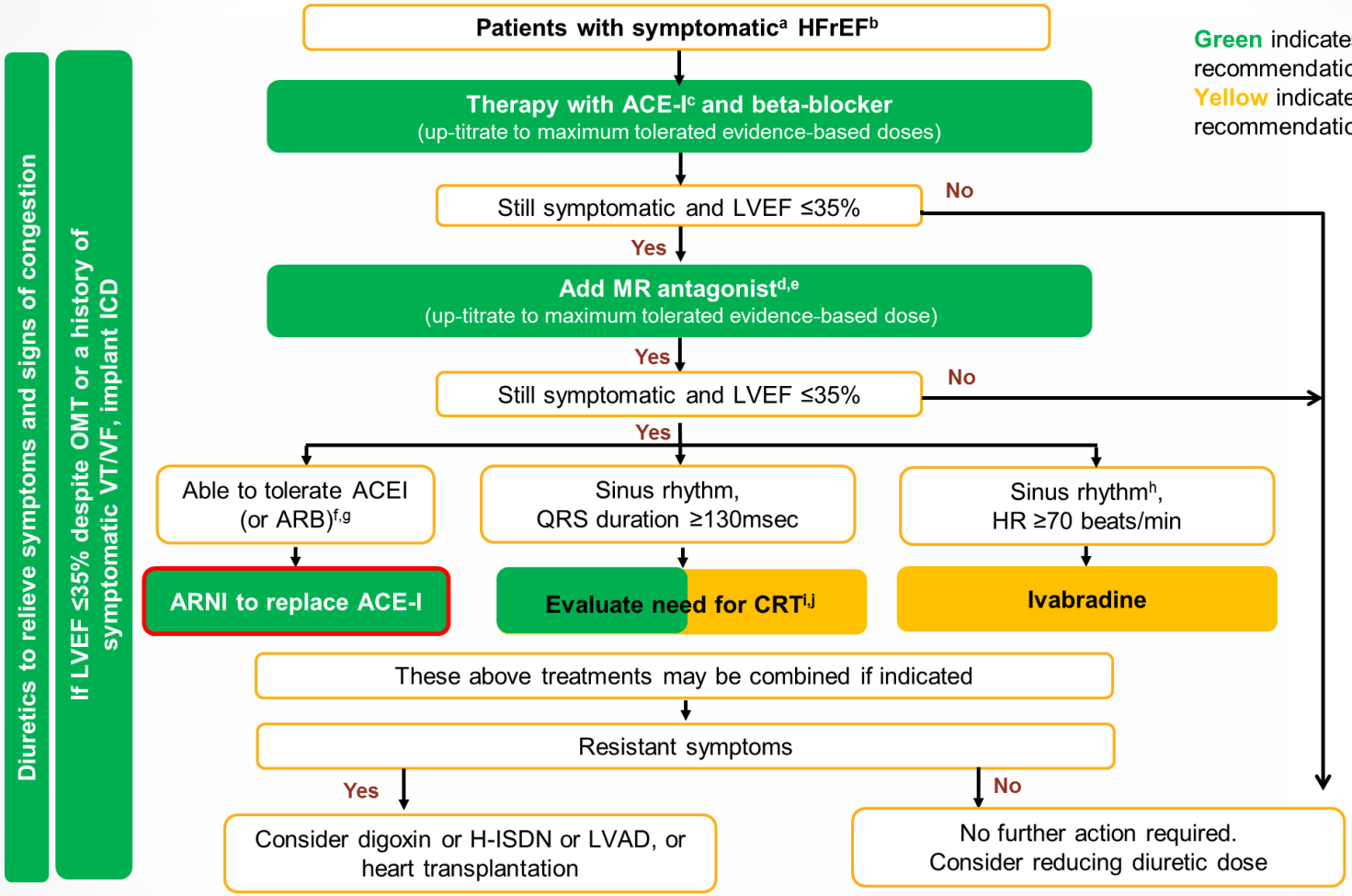
An **ACEi** is recommended, in addition to a beta blocker, for symptomatic patients with HFrEF to reduce the risk of HF hospitalization and death	I	A
A **beta blocker** is recommended, in addition an ACEi, for patients with stable, symptomatic HFrEF to reduce the risk of HF hospitalization and death	I	A
An **MRA** is recommended for patients with HFrEF, who remain symptomatic despite treatment with an ACEi and a beta-blocker, to reduce the risk of HF hospitalization and death	I	A
Sacubitril/valsartan is recommended as a **replacement for an ACEi** to further reduce the risk of HF hospitalization and death in ambulatory patients with HFrEF who remain symptomatic despite optimal treatment with an ACEi, a beta-blocker and an MRA*	I	B

**Patient should have elevated natriuretic peptides (plasma BNP ≥150 pg/mL or plasma NT-proBNP ≥600 pg/mL, or if HF hospitalization within the last 12 months, plasma BNP ≥100 pg/mL or plasma NT-proBNP ≥400 pg/mL) and able to tolerate enalapril 10 mg b.i.d.*

ACC, American College of Cardiology; AHA, American Heart Association; ACEI, angiotensin-converting-enzyme inhibitor; ARB, angiotensin II receptor blocker, ARNI, angiotensin receptor neprilysin inhibitor; CV, cardiovascular; ESC, European Society of Cardiology; HF, heart failure; HFSA, Heart Failure Society of America; HFrEF, HF with reduced ejection fraction; NYHA, New York Heart Association

Ponikowski et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure Eur Heart J. 21 May 2016. doi:10.1093/eurheartj/ehw128
;

2016 ESC Guideline
Treatment Algorithm



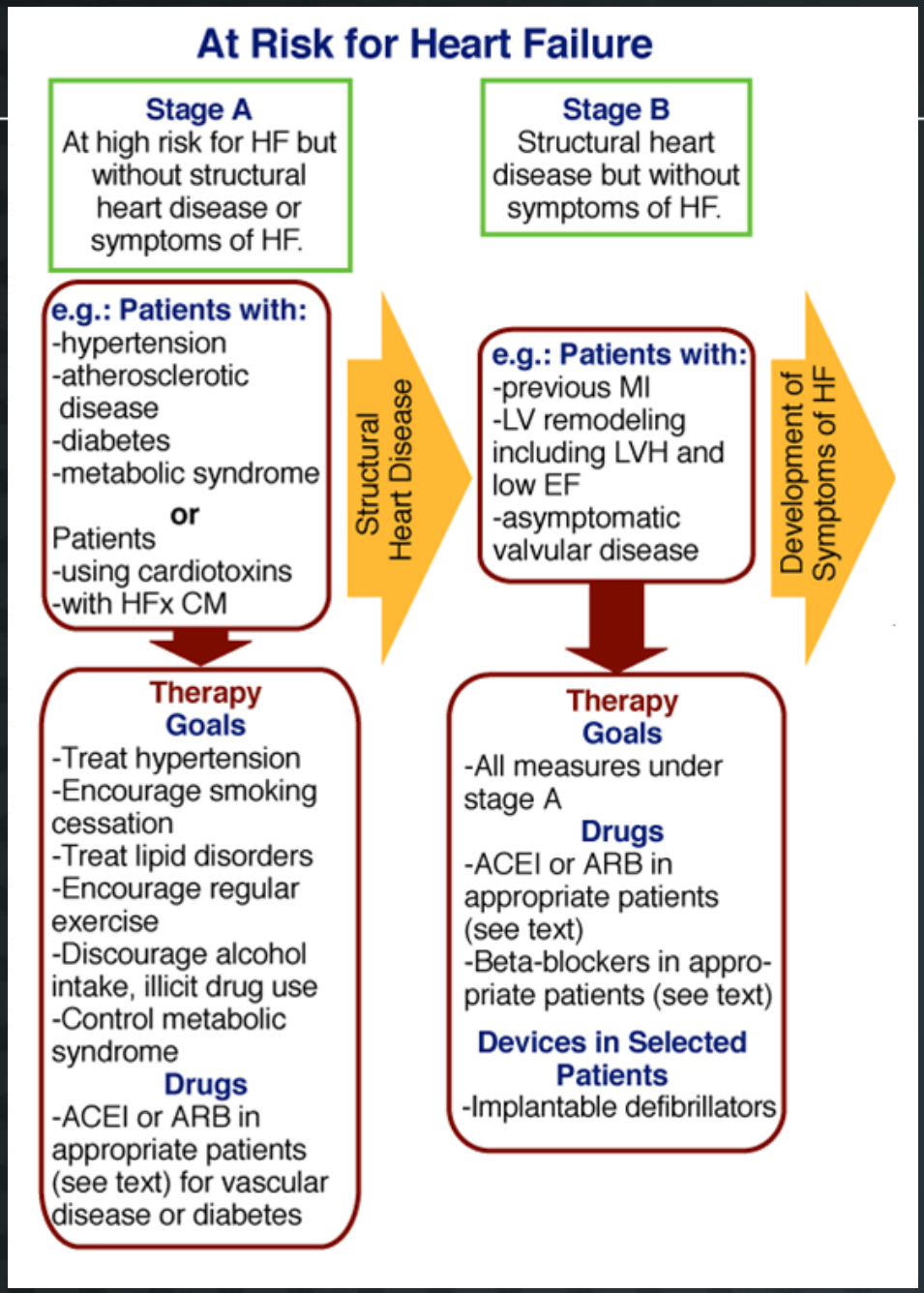
Green indicates a **class I** recommendation;
Yellow indicates a **class IIa** recommendation.

[a]Symptomatic=NYHA Class II-IV; [b]HFrEF=LVEF<40%; [c]If ACEI not tolerated/contra-indicated, use ARB; **[d]If MR antagonist not tolerated/contra-indicated, use ARB; [e]With a hospital admission for HF within the last 6 months or with elevated natriuretic peptides (BNP >250 pg/ml or NTproBNP >500 pg/ml in men and 750 pg/ml in women); [f]With an elevated plasma NP level (BNP ≥150 pg/mL or plasma NT-proBNP ≥ 600 pg/mL, or if HF hospitalization within recent 12 months plasma BNP ≥ 100 pg/mL or plasma NT-proBNP ≥ 400 pg/mL); [g]In doses equivalent to enalapril 10 mg *b.i.d.*;** [h]With a hospital admission for HF within the previous year; [i]CRT is recommended if QRS ≥ 130 msec and LBBB (in sinus rhythm); [j]CRT should/may be considered if QRS ≥ 130 msec with non-LBBB (in a sinus rhythm) or for patients in AF provided a strategy to ensure bi-ventricular capture in place (individualized decision)

Ponikowski et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure Eur Heart J. 21 May 2016. doi:10.1093/eurheartj/ehw128

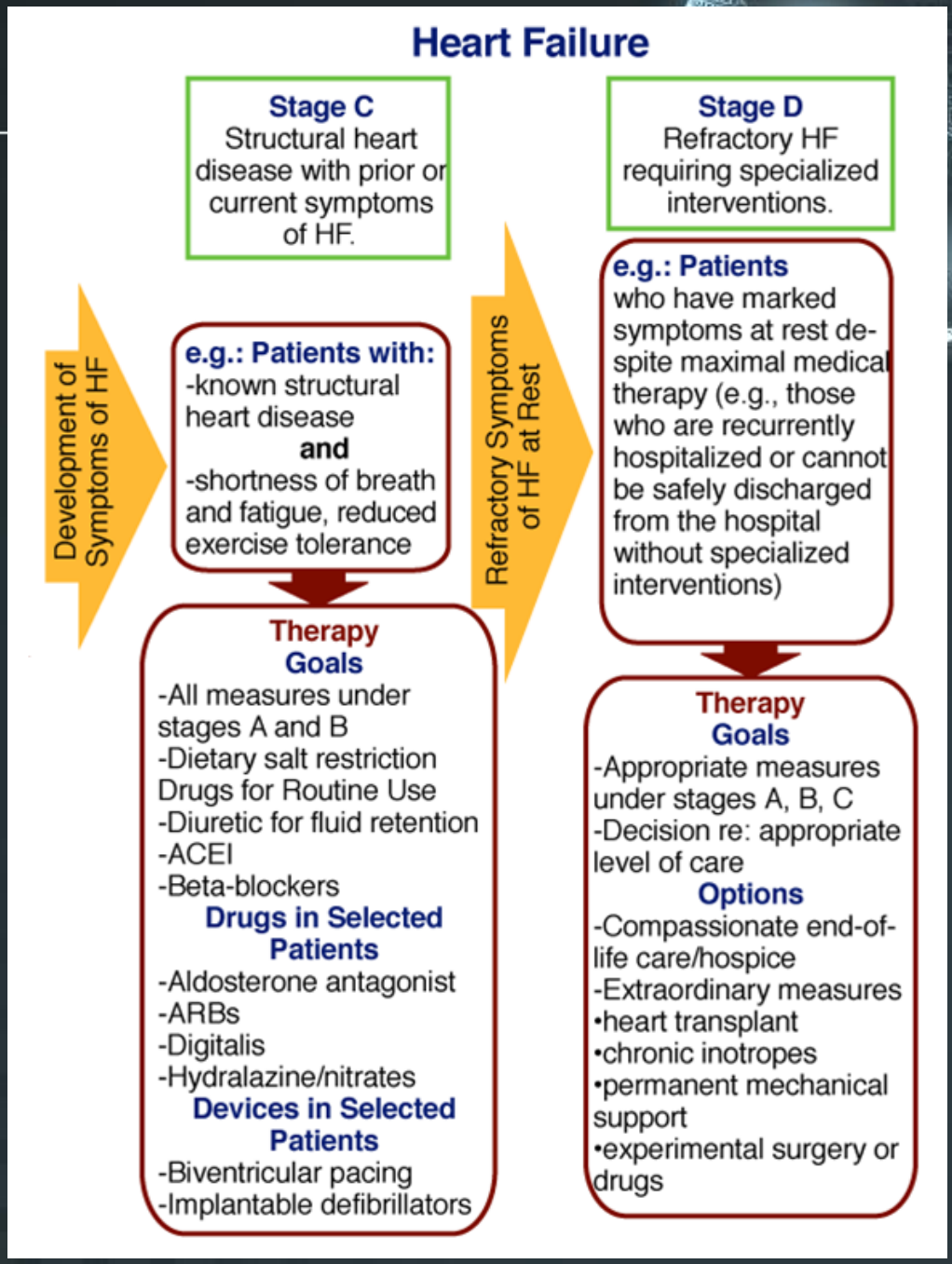
Cardiac Failure - Community Approach

- The nurses role
- Input and output charts
- Telephone conversations
- Daily weights
- Home biochemical monitoring
- 24 hour ECG monitoring



- Stage A emphasizes *preventability*
- Stage B is asymptomatic LV dysfunction

- "typical" patient is in Stage C
- Increasing numbers of patients with Stage D
  - Palliation is appropriate



Case Presentation

- **What is the next step?**

- 1- Add diuretics Disothiazide 25mg?
- 2- Stop enaladex, give Entresto 50mg*2 ?
- 3- Send the patient for cardiac Transplant?
- 4- Evaluate for CRT-D?

Take Home Messages

- Heart failure is a chronic, progressive disease that is generally not curable, but treatable. It is detectable in the community and preventable.
- consumes a considerable proportion of health care resources
- Recent guidelines promote lifestyle modifications and medical management with ACE inhibitors or **ARNI Entresto,** beta blockers, MRA, and diuretics. It is estimated 15%-20% of all heart failure patients may be candidates for cardiac resynchronization therapy.
- Close follow-up of the heart failure patient is essential, with necessary adjustments in max. medical management

Challenges for - 2019

- Increase the numbers with an accurate diagnosis.
- Establish pts on evidence based therapies.
- Avoiding adverse effect from treatment.
- Working in a team with **FP specialist and nurses.**


תודה רבה