

# **Chronic Heart Failure:** **The Size of a Worldwide Problem**

**Youngkeun Ahn, MD, PhD**

**Director of Cardiovascular Center  
Chonnam National University Hospital**

# Definition of Chronic Heart Failure

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**CHF is a Clinical Syndrome with the Following Features:**

**Symptoms typical of heart failure (shortness of breath at rest or during exertion, and/or fatigue)**

**Signs typical of heart failure (fluid retention such as pulmonary congestion or ankle swelling)**

**Objective evidence of a structural or functional abnormality of the heart at rest (cardiomegaly, third heart sound, etc)**

# Epidemiology and Prevalence of Chronic Heart Failure

**Overall Prevalence: 2–3%**

**Prevalence in 70–80-year-olds: 10–20%**

## **Mean Age of HF Patients**

- **75 years**

## **More Common in**

- **Elderly**
- **Females**
- **Hypertensives**
- **Diabetics**

# Morbidity and Mortality of Chronic Heart Failure

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## Morbidity

5% of all acute hospital admissions

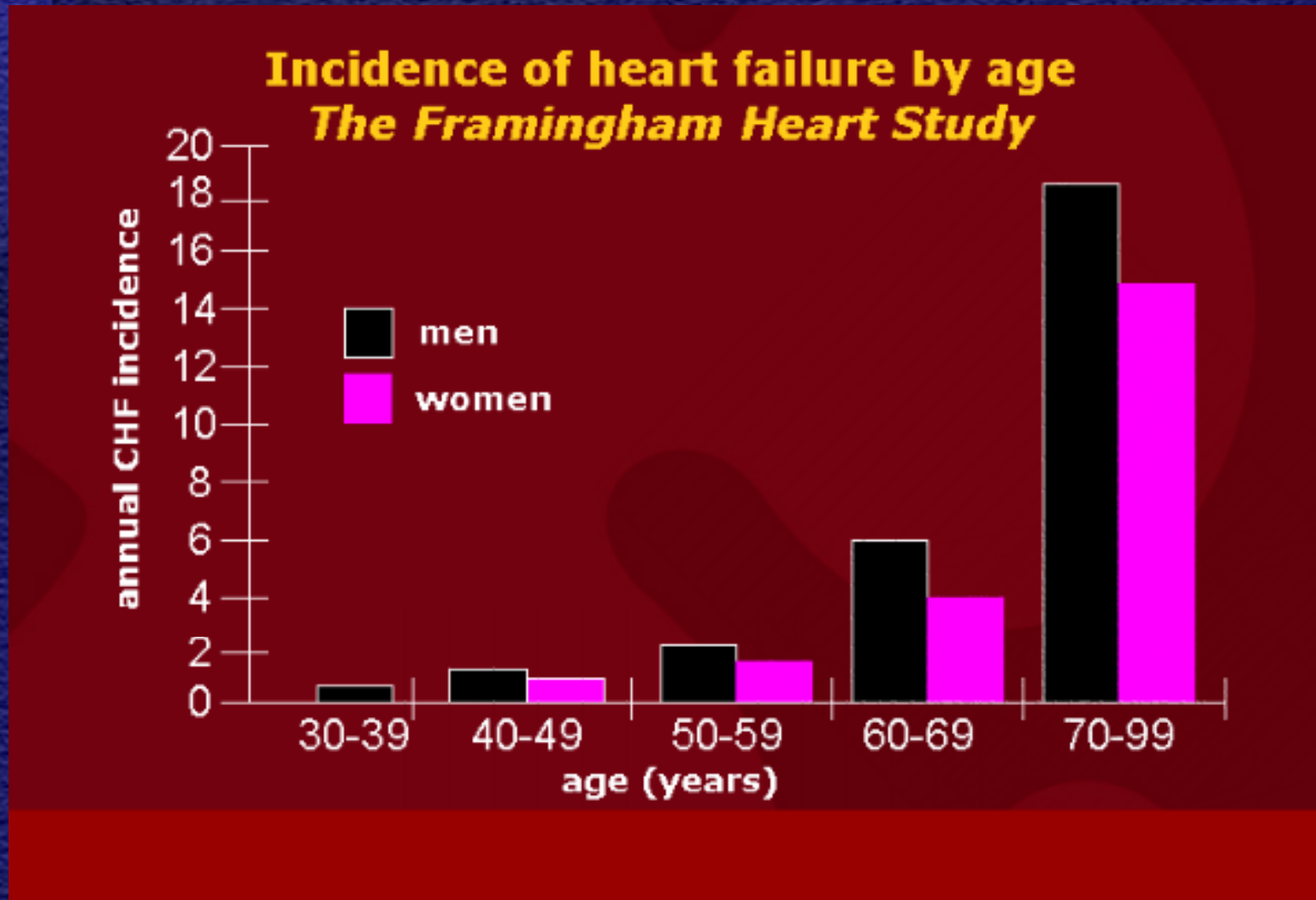
10% of patients occupying hospital beds

## Mortality

50% at 4 years

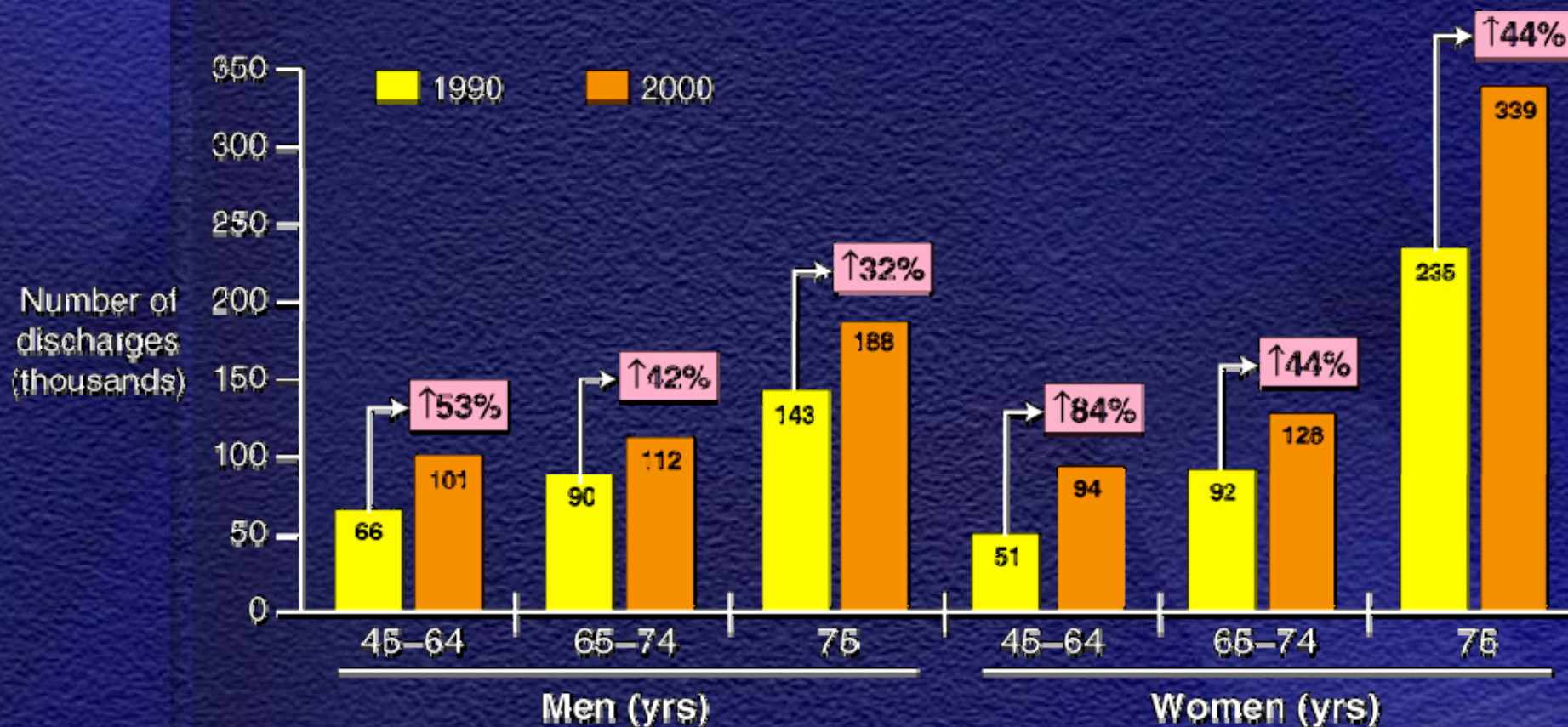
40% admitted have died or have been readmitted to hospital within 1 year

# Heart Failure Incidence: a Large Problem in the Elderly (Framingham Study)



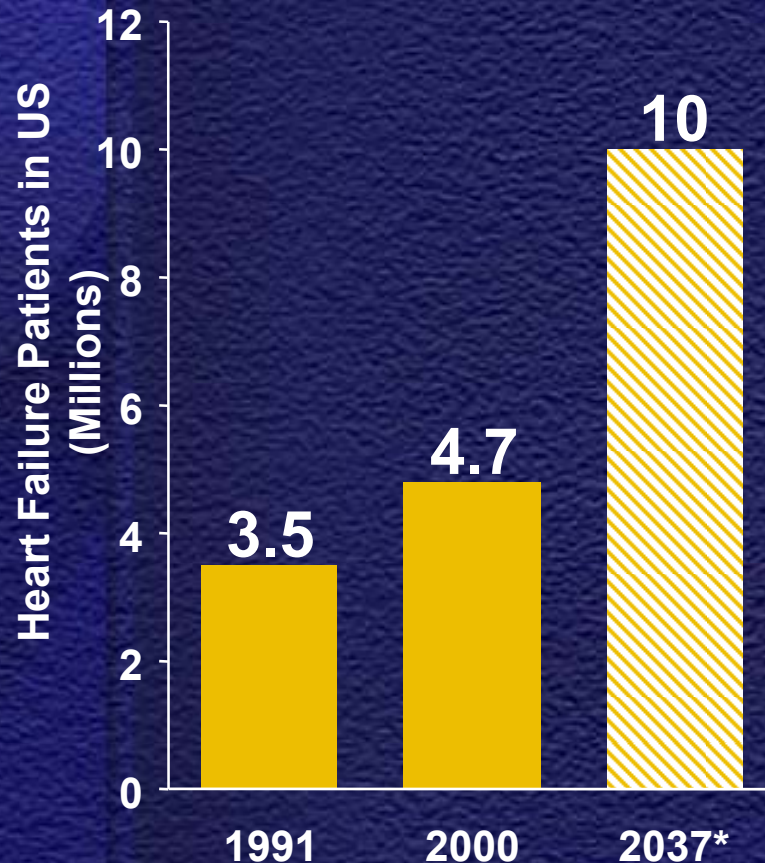
# HF is more increasing diagnosis

## Hospital discharges for HF by age: 1990 vs. 2000



CDC, National Center for Health Statistics,  
National Hospital Discharge Survey, 2002.

# Epidemiology of Heart Failure in the US



- More deaths from heart failure than from all forms of cancer combined
- 550,000 new cases/year
- 4.7 million symptomatic patients; estimated 10 million in 2037

\*Rich M. *J Am Geriatric Soc.* 1997;45:968–974.

American Heart Association. 2001 *Heart and Stroke Statistical Update.* 2000.

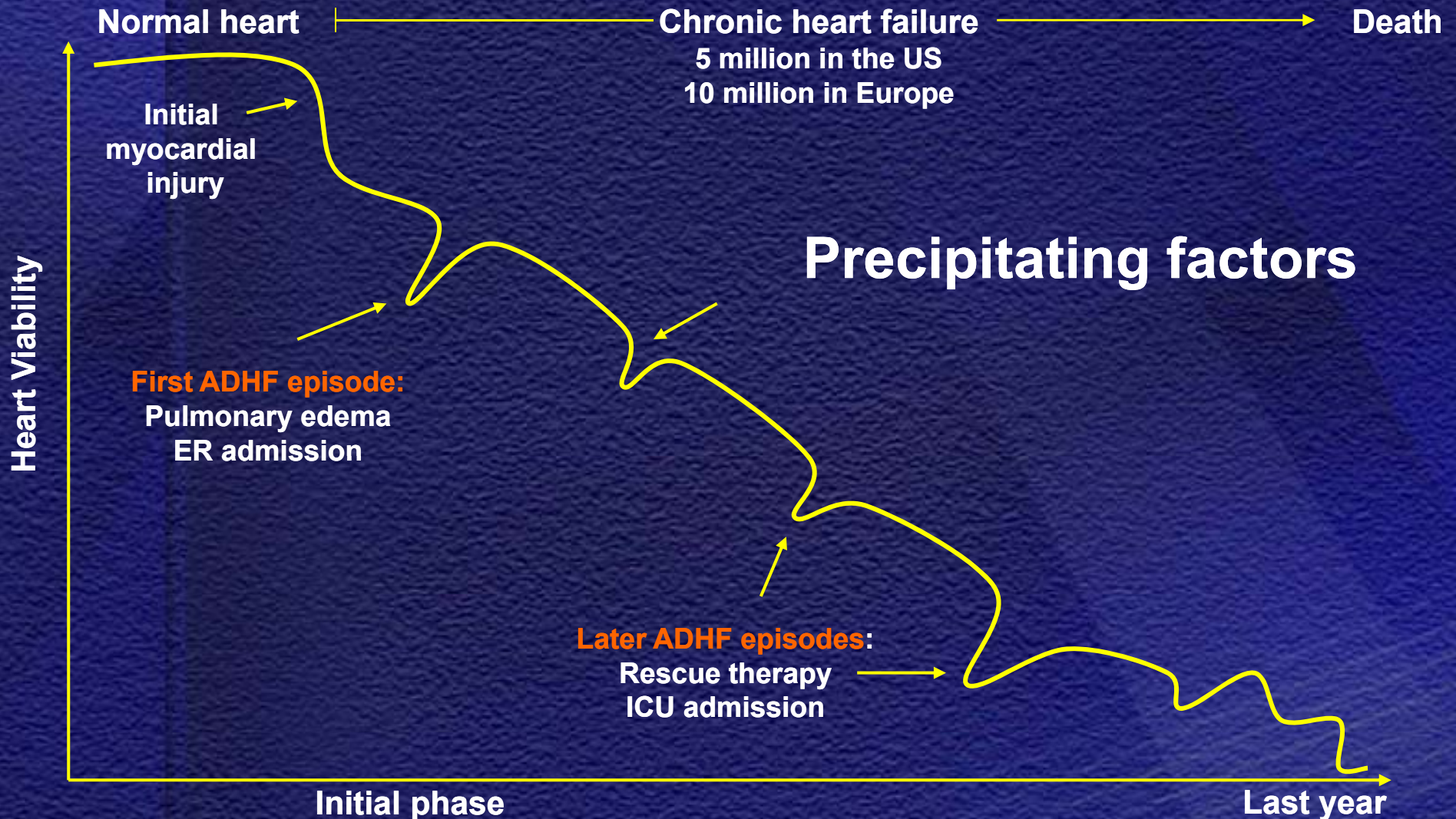
# Ethnic differences of heart failure

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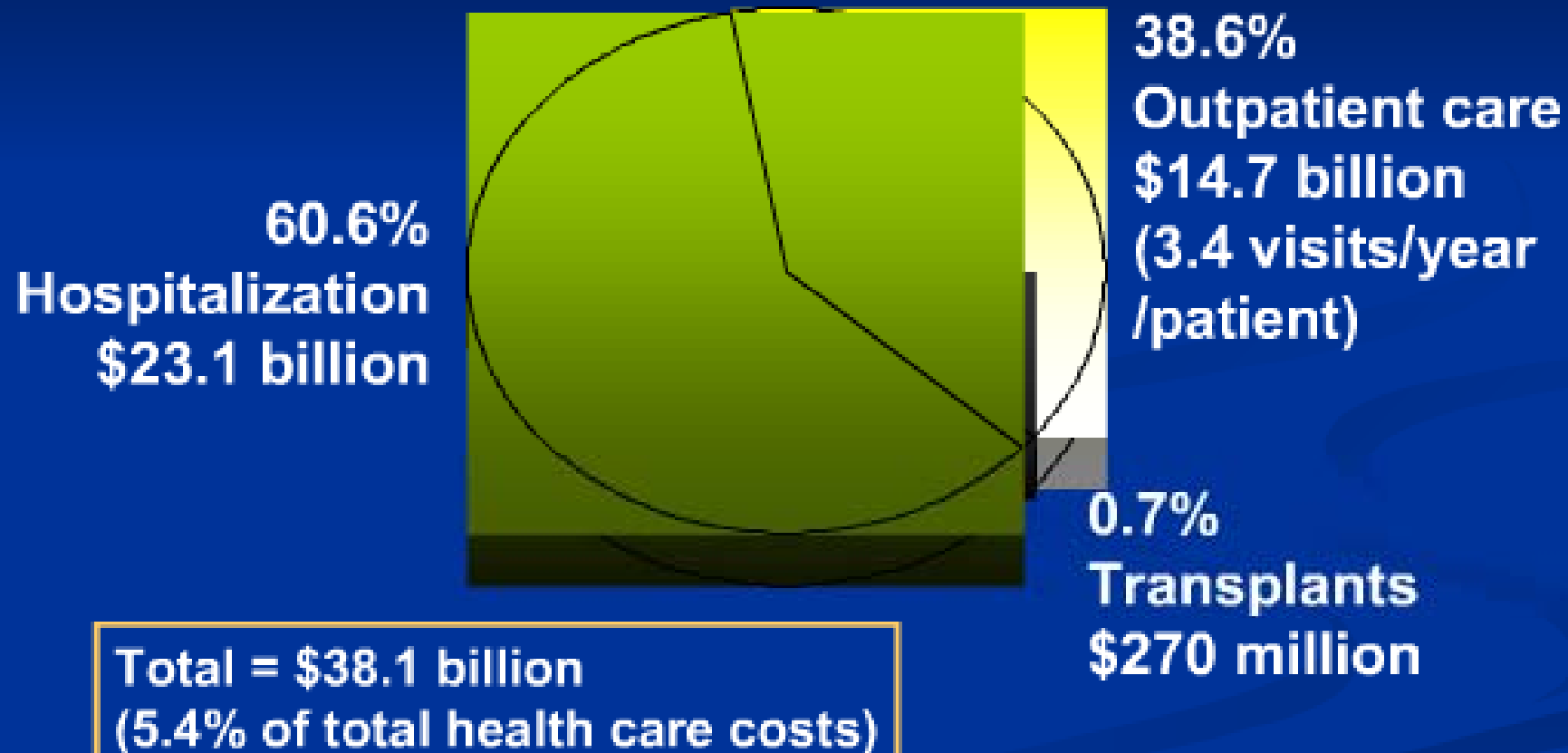
- In the United States, **African-American men** have been reported as having a 33% greater risk of being admitted to hospital for heart failure than white men; the risk for **black women** was 50%.
- In the United States mortality from heart failure at age <65 years has been reported as being up to 2.5-fold higher in **black patients** than in white patients.



# Natural History of Chronic and Acute Heart Failure



# Hospitalization: The Major Factor in Heart Failure Costs in the US



# A public health crisis: Heart failure hospitalizations have tripled in 25 years



NHLBI. *Morbidity and Mortality: 2000 Chartbook on Cardiovascular, Lung, and Blood Diseases*. Geneva: World Health Organization; 1996.

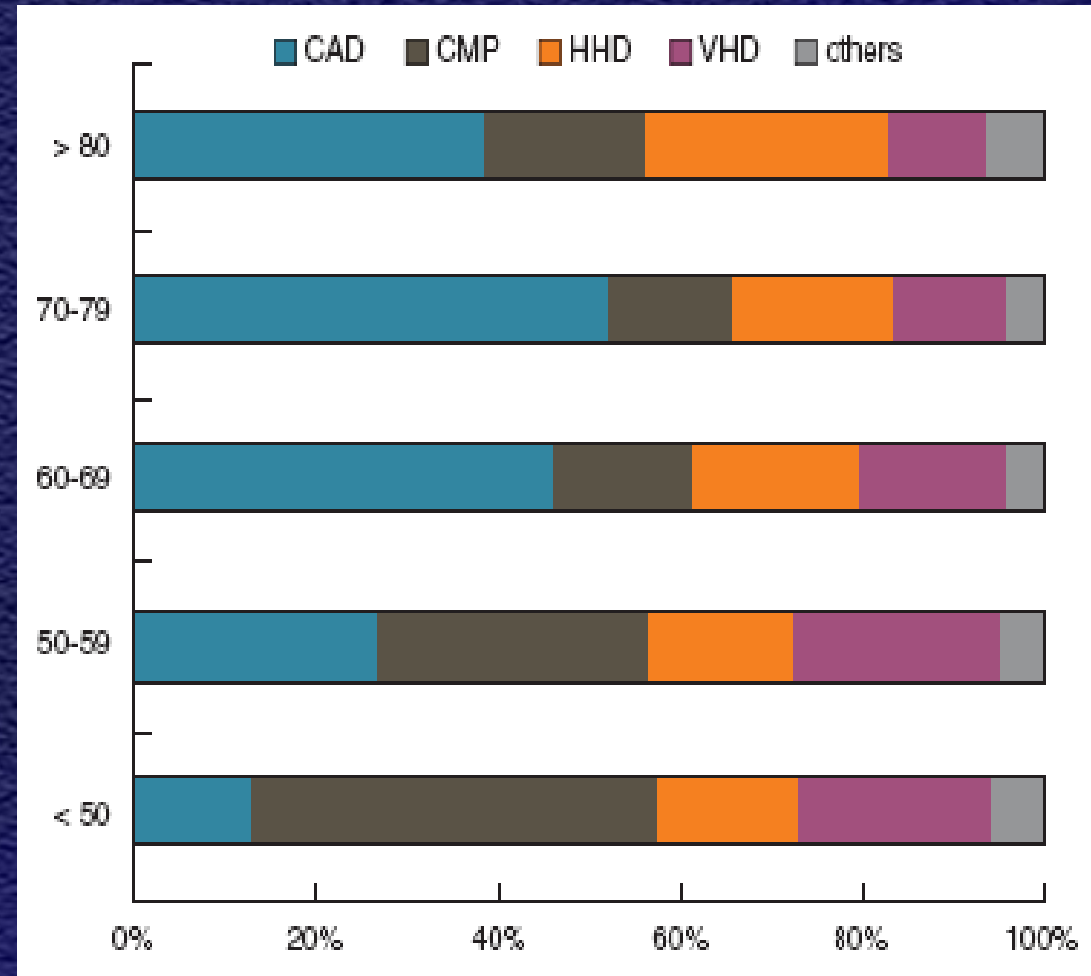
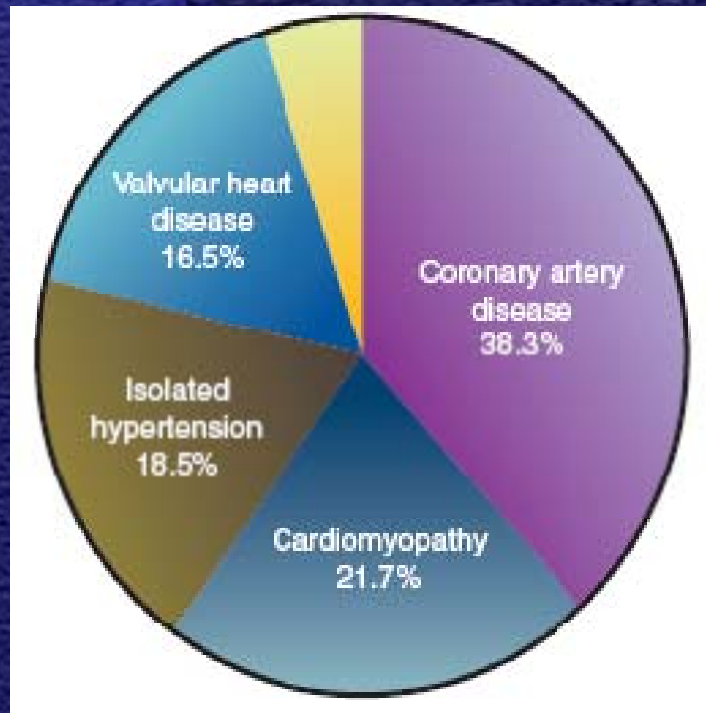
# Causes of HF in Western World

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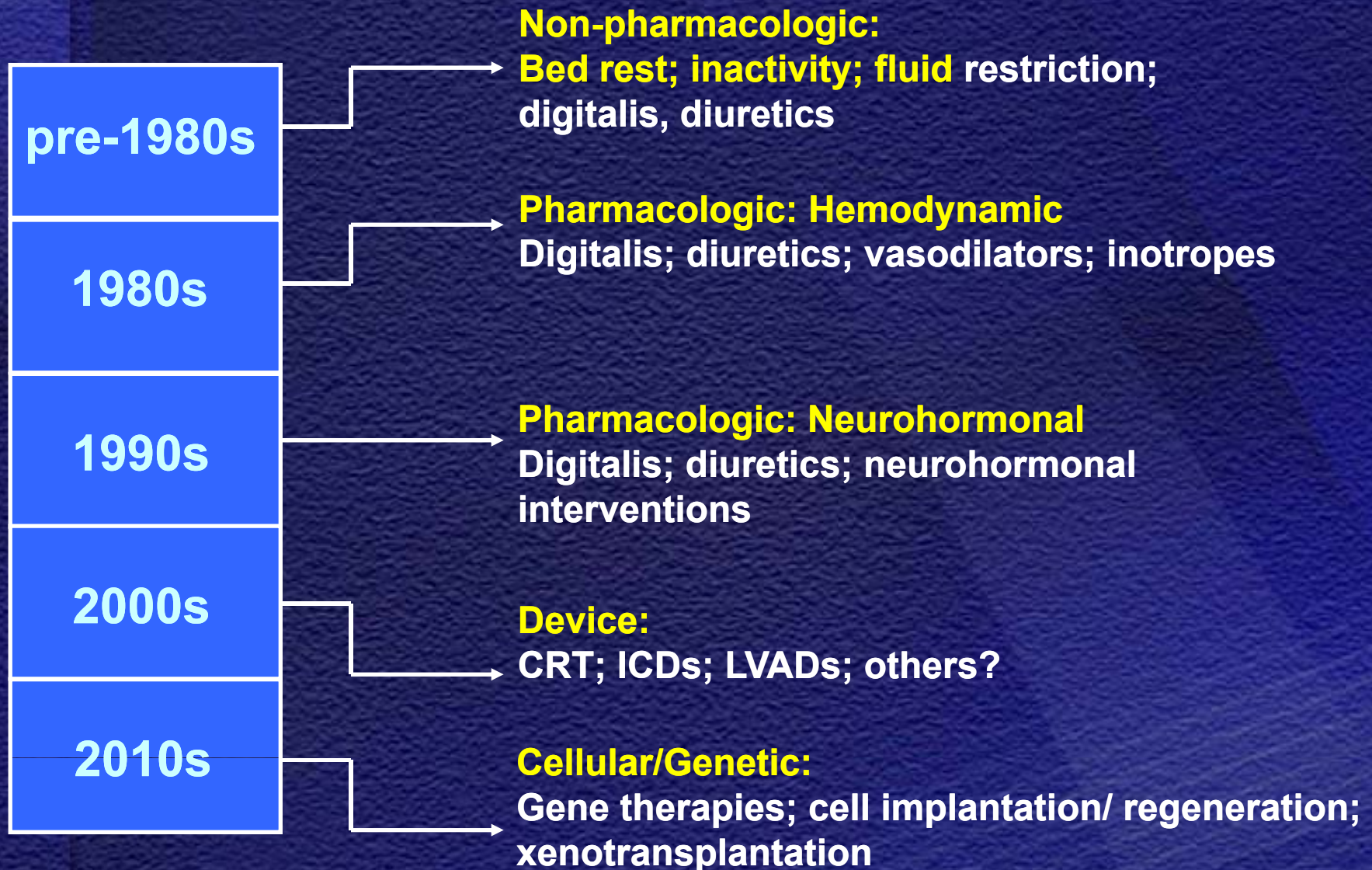
For a substantial proportion of patients, causes are:

1. **Coronary artery disease**
2. **Hypertension**
3. **Dilated cardiomyopathy**

# The Causes of Heart Failure in KOREA



# The Changes of Heart Failure Therapy



## At Risk for Heart Failure

### Stage A

At high risk for HF but without structural heart disease or symptoms of HF.

#### e.g.: Patients with:

- hypertension
  - atherosclerotic disease
  - diabetes
  - metabolic syndrome
- or
- Patients using cardiotoxins
  - with HFx CM

#### Therapy Goals

- Treat hypertension
- Encourage smoking cessation
- Treat lipid disorders
- Encourage regular exercise
- Discourage alcohol intake, illicit drug use
- Control metabolic syndrome

#### Drugs

- ACEI or ARB in appropriate patients (see text) for vascular disease or diabetes

Structural Heart Disease

### Stage B

Structural heart disease but without symptoms of HF.

#### e.g.: Patients with:

- previous MI
- LV remodeling including LVH and low EF
- asymptomatic valvular disease

#### Therapy Goals

- All measures under stage A

#### Drugs

- ACEI or ARB in appropriate patients (see text)
- Beta-blockers in appropriate patients (see text)

#### Devices in Selected Patients

- Implantable defibrillators

Development of Symptoms of HF

### Stage C

Structural heart disease with prior or current symptoms of HF.

#### e.g.: Patients with:

- known structural heart disease
- and
- shortness of breath and fatigue, reduced exercise tolerance

#### Therapy Goals

- All measures under stages A and B
- Dietary salt restriction
- Drugs for Routine Use
- Diuretic for fluid retention
- ACEI
- Beta-blockers

#### Drugs in Selected Patients

- Aldosterone antagonist
- ARBs
- Digitalis
- Hydralazine/nitrates

#### Devices in Selected Patients

- Biventricular pacing
- Implantable defibrillators

Refractory Symptoms of HF at Rest

## Heart Failure

### Stage D

Refractory HF requiring specialized interventions.

#### e.g.: Patients

who have marked symptoms at rest despite maximal medical therapy (e.g., those who are recurrently hospitalized or cannot be safely discharged from the hospital without specialized interventions)

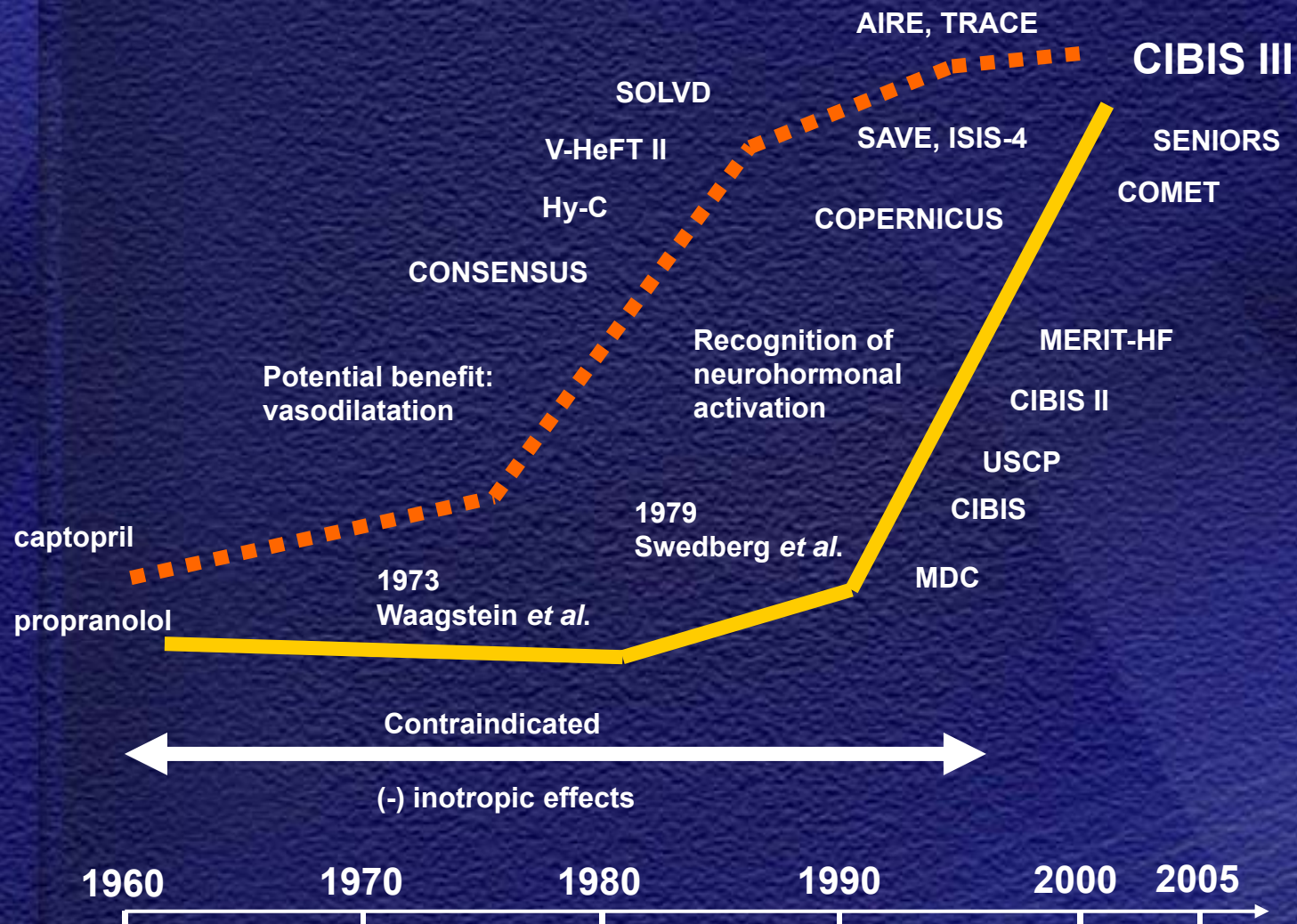
#### Therapy Goals

- Appropriate measures under stages A, B, C
- Decision re: appropriate level of care

#### Options

- Compassionate end-of-life care/hospice
- Extraordinary measures
- heart transplant
- chronic inotropes
- permanent mechanical support
- experimental surgery or drugs

# Development of Neurohormonal Antagonists in Treatment of CHF





# Pharmacological Therapy – Classes of Drugs

**Angiotensin-converting Enzyme (ACE) inhibitors**

**β-blockers**

**Aldosterone antagonists**

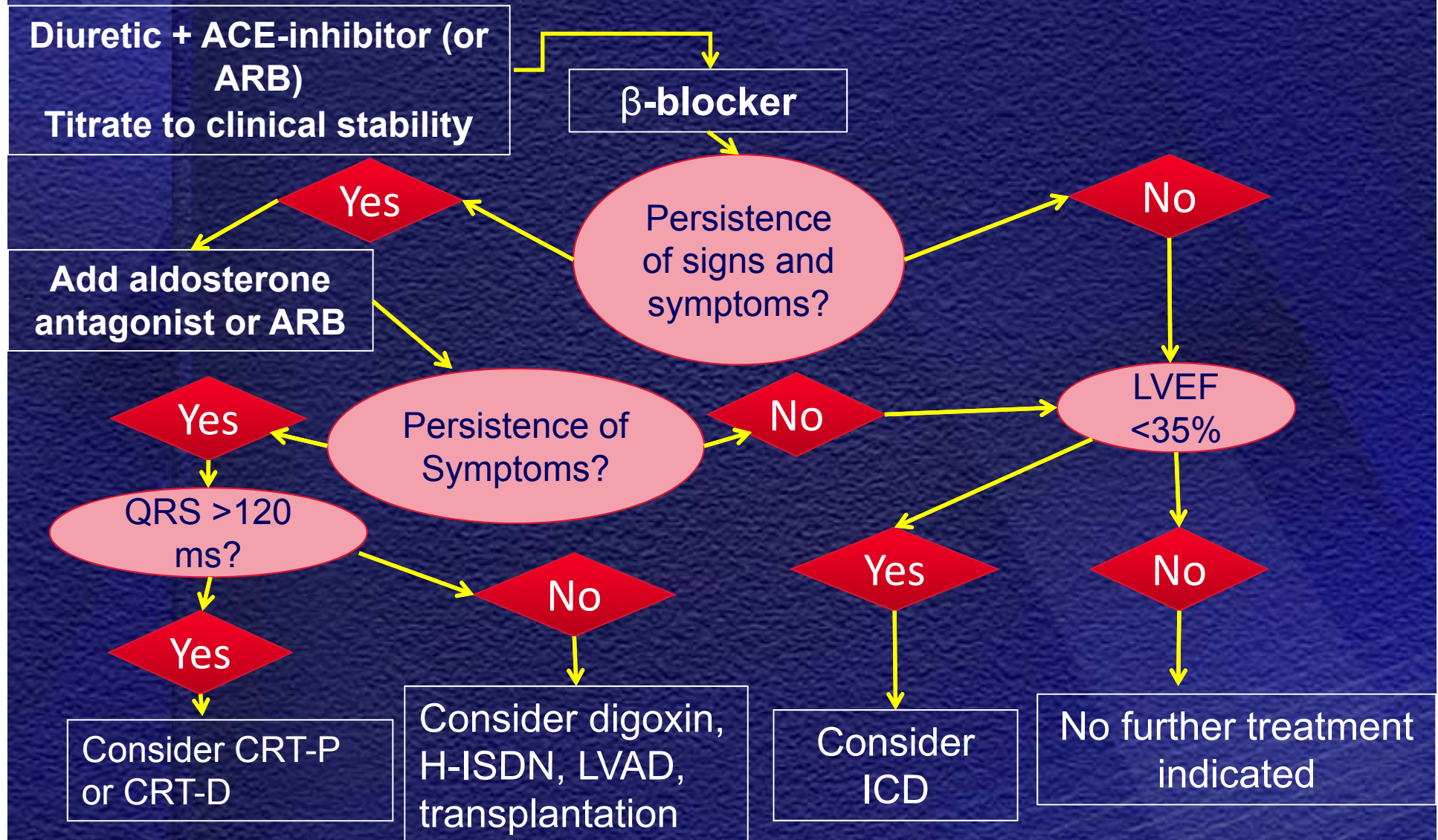
**Angiotensin Receptor Blockers (ARBs)**

**Hydralazine and isosorbide dinitrate (H-ISDN)**

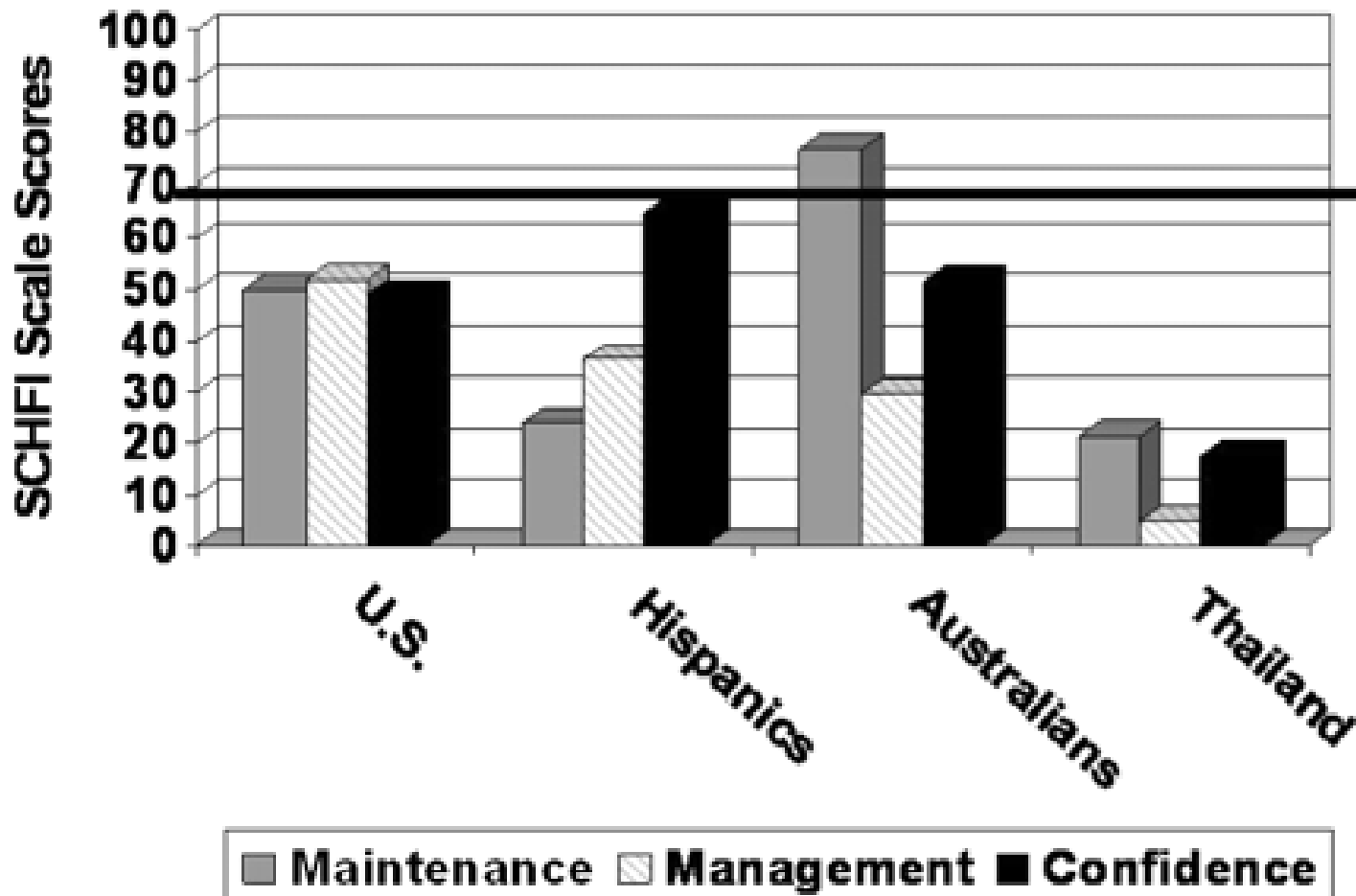
**Digoxin**

**Diuretics**

# Pharmacological Therapy



# Poor Heart Failure Self-Care



# Heart failure study finds more diastolic cases in older patients

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- Failure of relaxation
- In community studies ~ 50% of older patients with heart failure have preserved ejection fraction
- The incidence increases with age
  - Hypertension
  - Diabetes
  - In women

# Pharmacological Therapy – Patients with Preserved LVEF

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## No Convincing Reduction in Morbidity and Mortality

- Diuretics used to control sodium and water retention, and relieve breathlessness and edema
- Adequate treatment of hypertension and myocardial ischemia is important
- Control of ventricular rate in atrial fibrillation also important

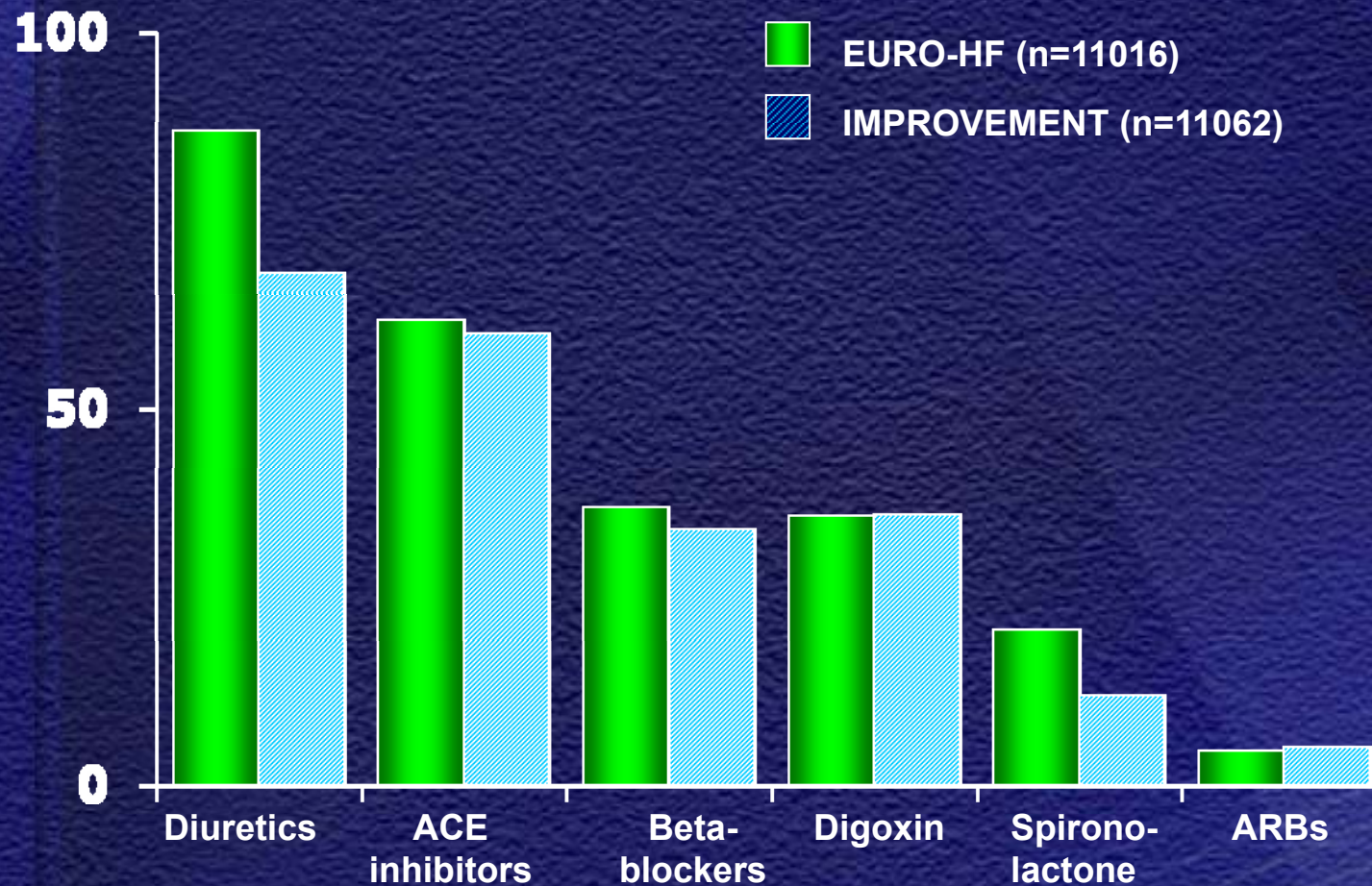
## CHARM-Preserved Trial

- No significant reduction in primary composite endpoint (adjudicated CV death or admission with HF)
- Significant reduction in investigator-reported admissions for HF

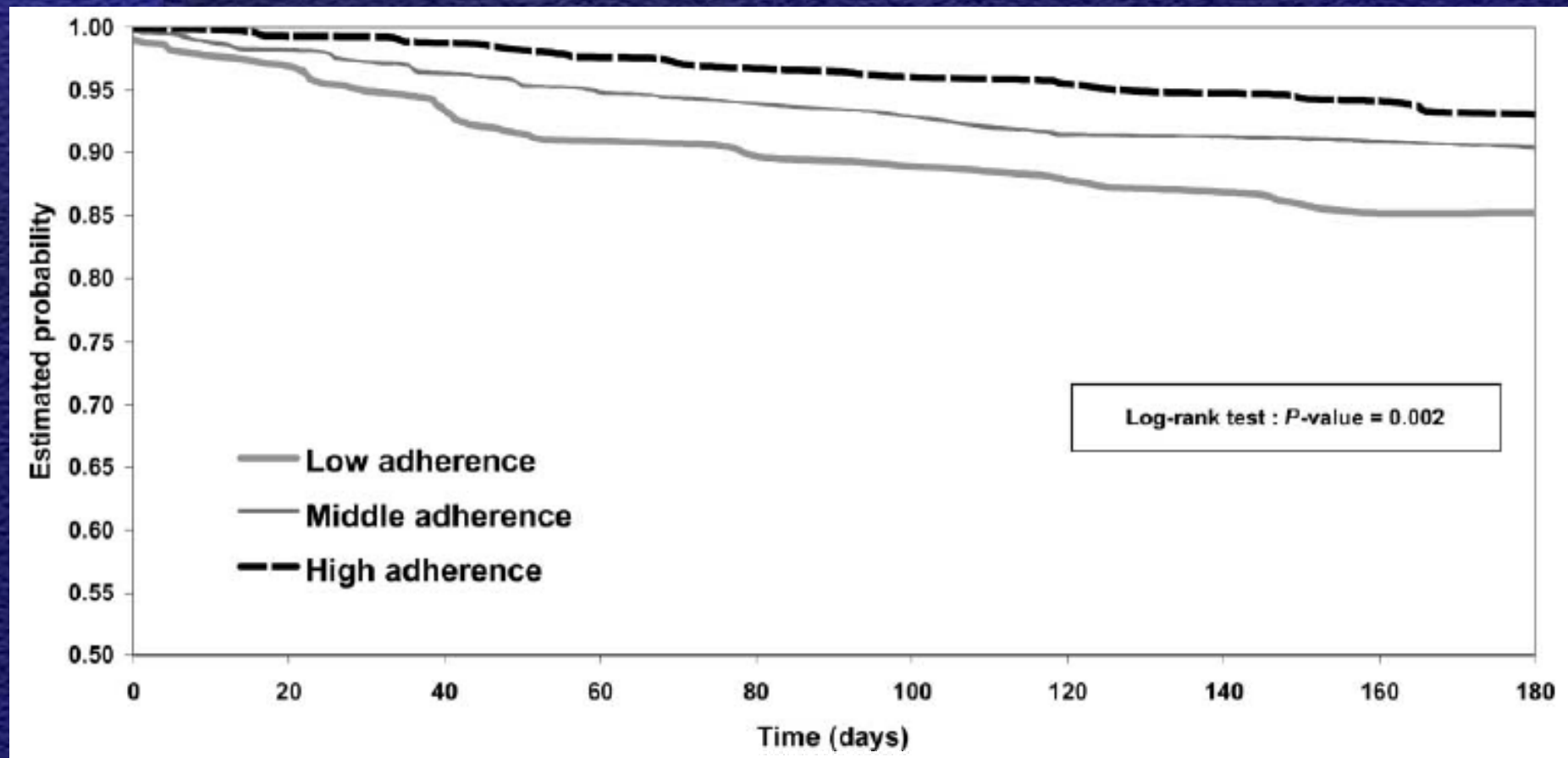
## PEP-CHF

- No reduction in primary composite end-point over total trial duration
- Significant reduction in CV death and HF hospitalizations after 1 year

# Prescribing of Heart Failure Drug Therapies in Clinical Practice



# Mahler Results: angiotensin-converting enzyme (ACE)-inhibitors, beta-blockers, spironolactone – Kaplan Meier Estimates for Cardiovascular Hospitalization



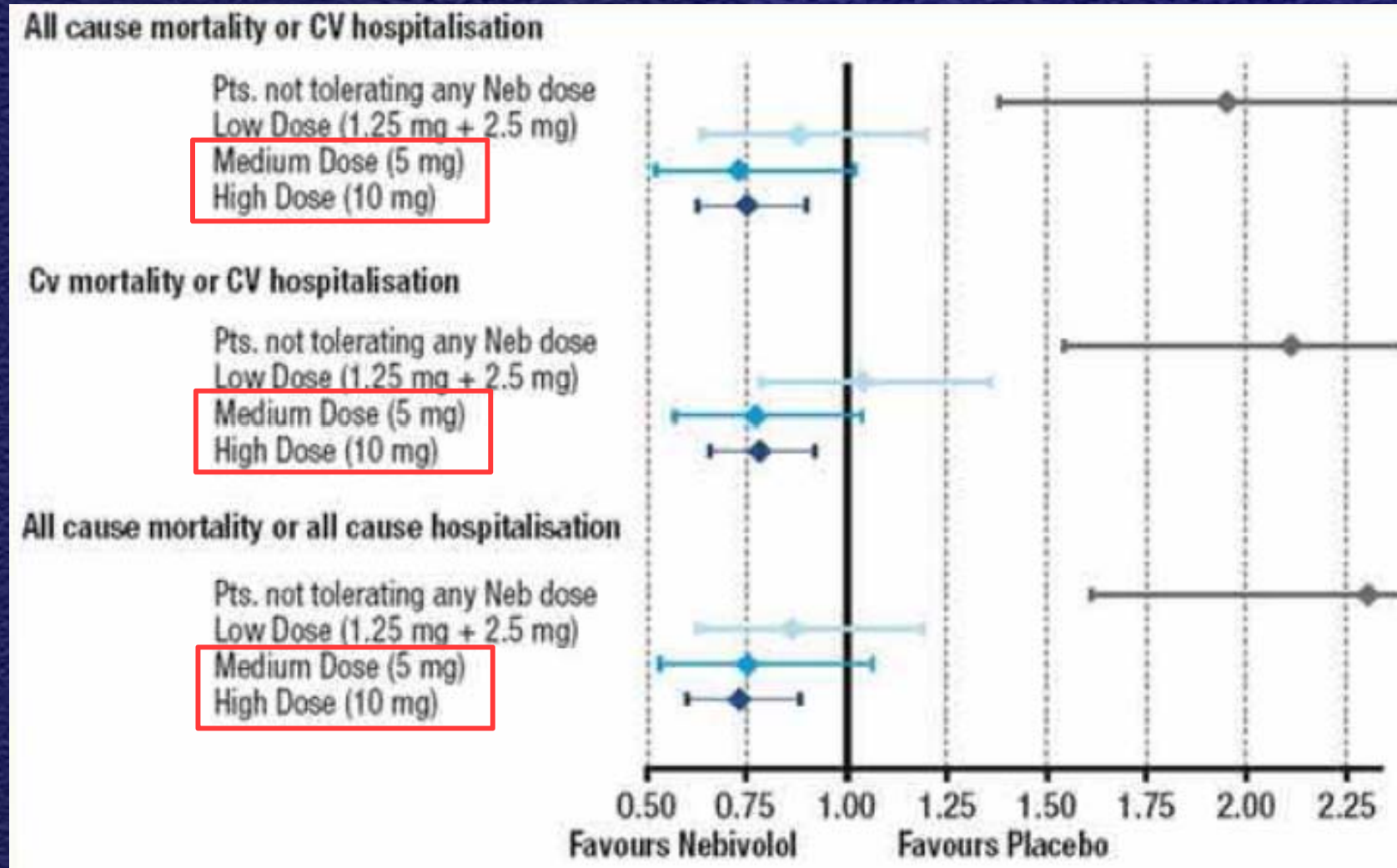
# Reasons for not prescribing a beta-blocker In The Euro HF Survey program Analysis of reasons for prescription (odds of receiving a beta-blocker)

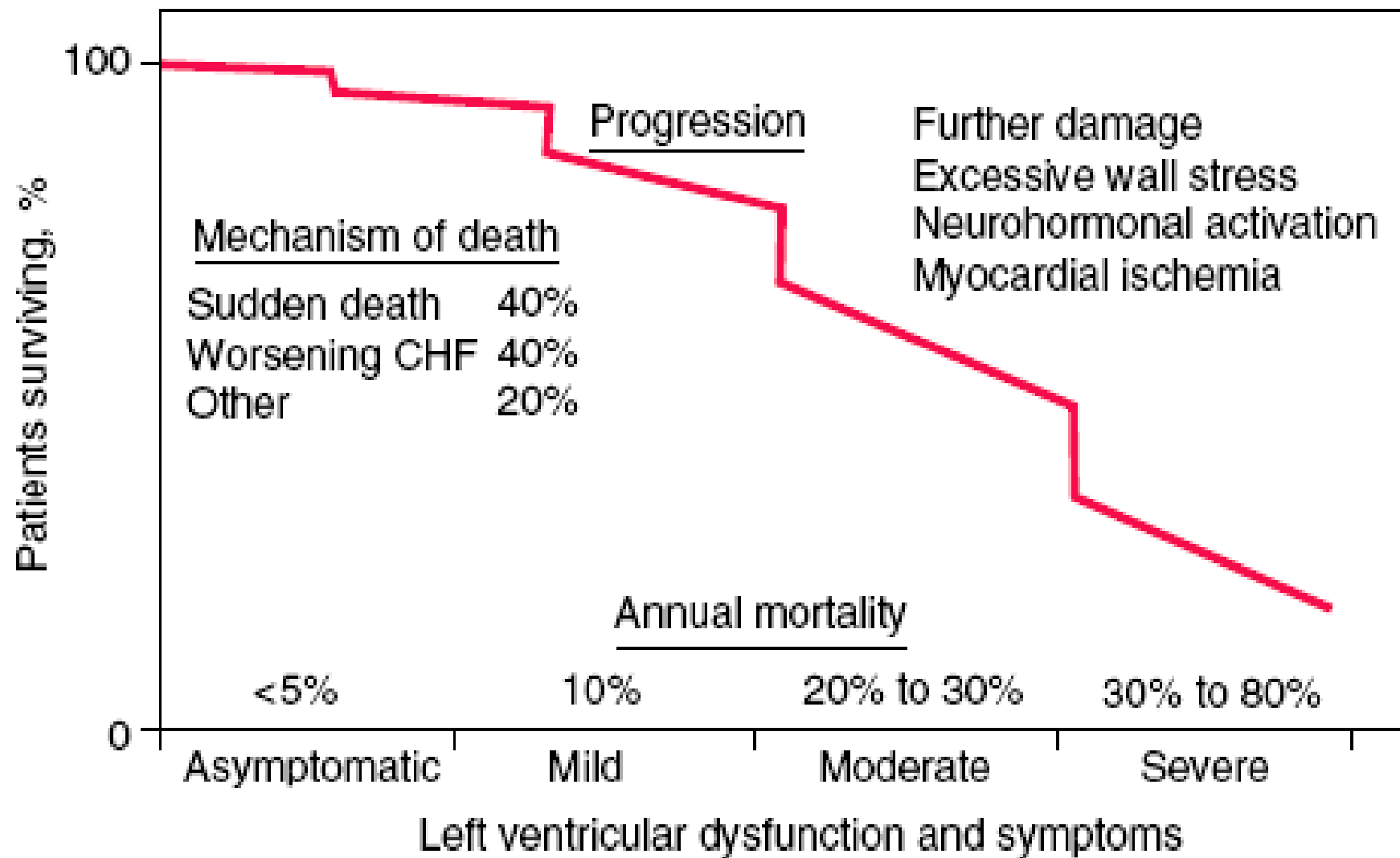
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- Respiratory/pulmonary disease 0.35 (0.30 to 0.40)
- Specialty at admission (Cardio vs int. med)  
2.69 (2.37 to 3.31)
- Ischemic heart disease 2.63 (2.32 to 2.99)
- Age group (>70 yr) 0.55 (0.49 to 0.61)
- Gender (being male) 1.16 (1.05 to 1.29)

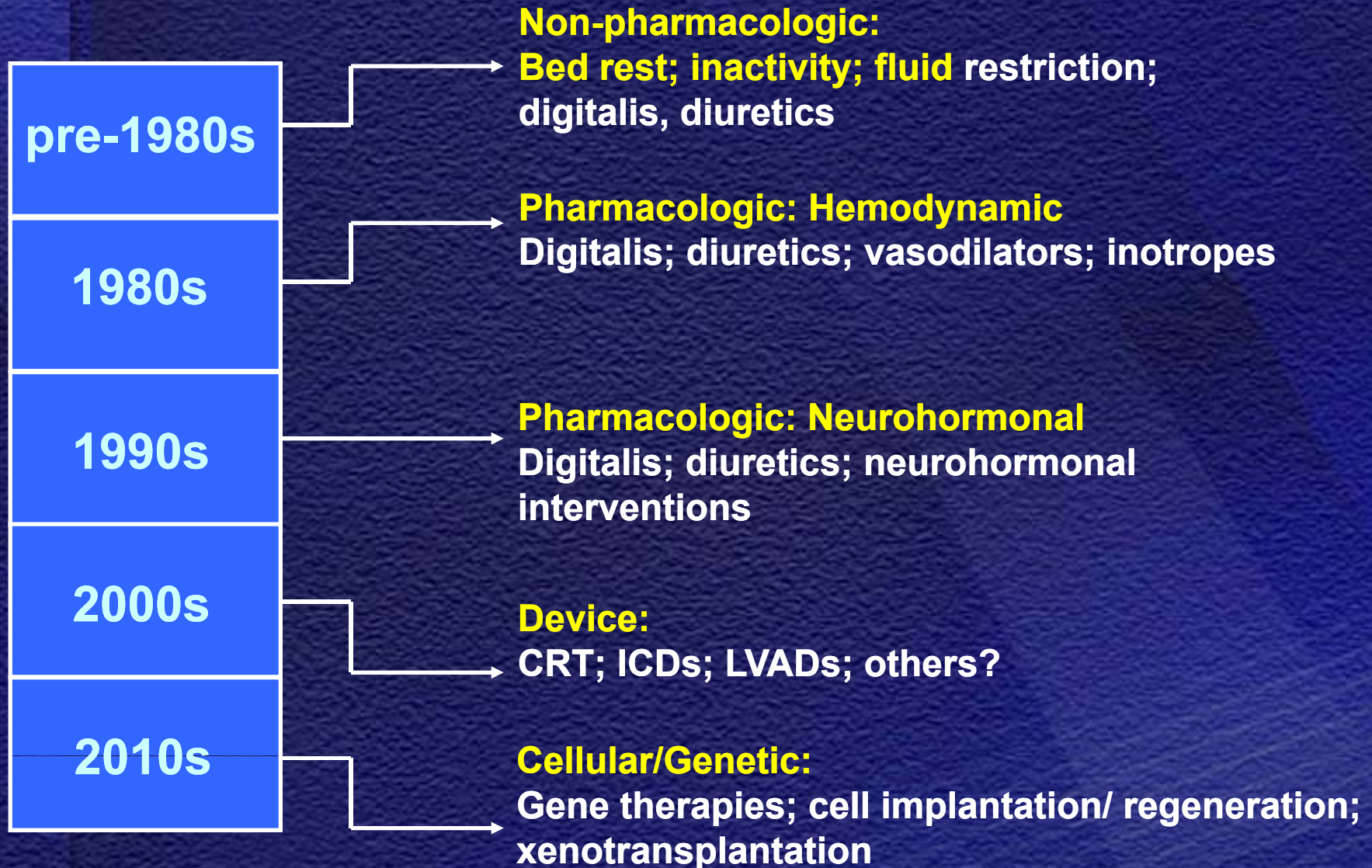


# Dose-related effects of Nebivolol in pts with CHF





# The Changes of Heart Failure Therapy



# Mesenchymal Stem Cells: Toward the Clinical Application

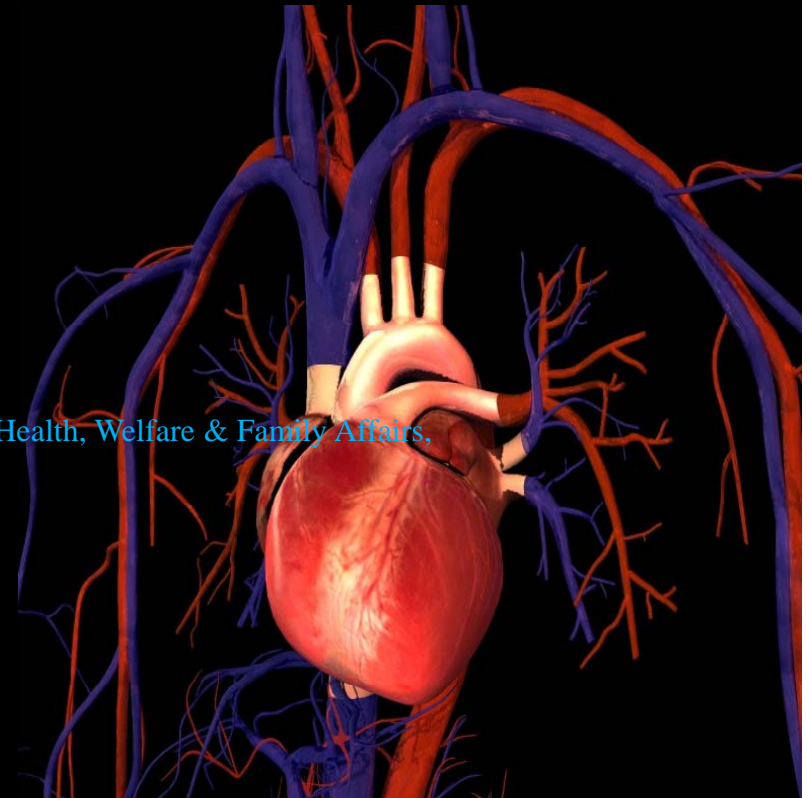
**Youngkeun Ahn, MD, PhD**

Cell and Gene Therapy Program

Heart Research Center, Korea Healthcare Technology R&D Project, Ministry for Health, Welfare & Family Affairs,

Chonnam National University Hospital

Department of Cardiology, Chonnam National University Hospital





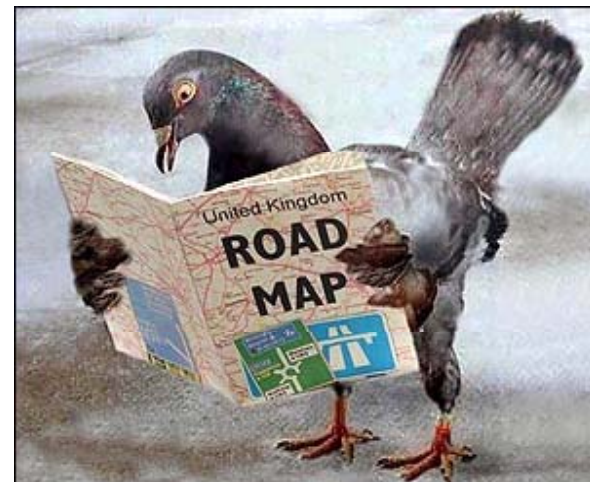
# Targeted Homing Proliferation Differentiation Functional Intercalation

Immobilization

Combination Therapy

Genetic Modification

Growth Factors, Cytokines



[Frontiers in Bioscience 14, 2845-2856, January 1, 2009]

*Artificial Organs*  
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## Promigratory Activity of Oxytocin on Umbilical Cord Blood-Derived Mesenchymal Stem Cells

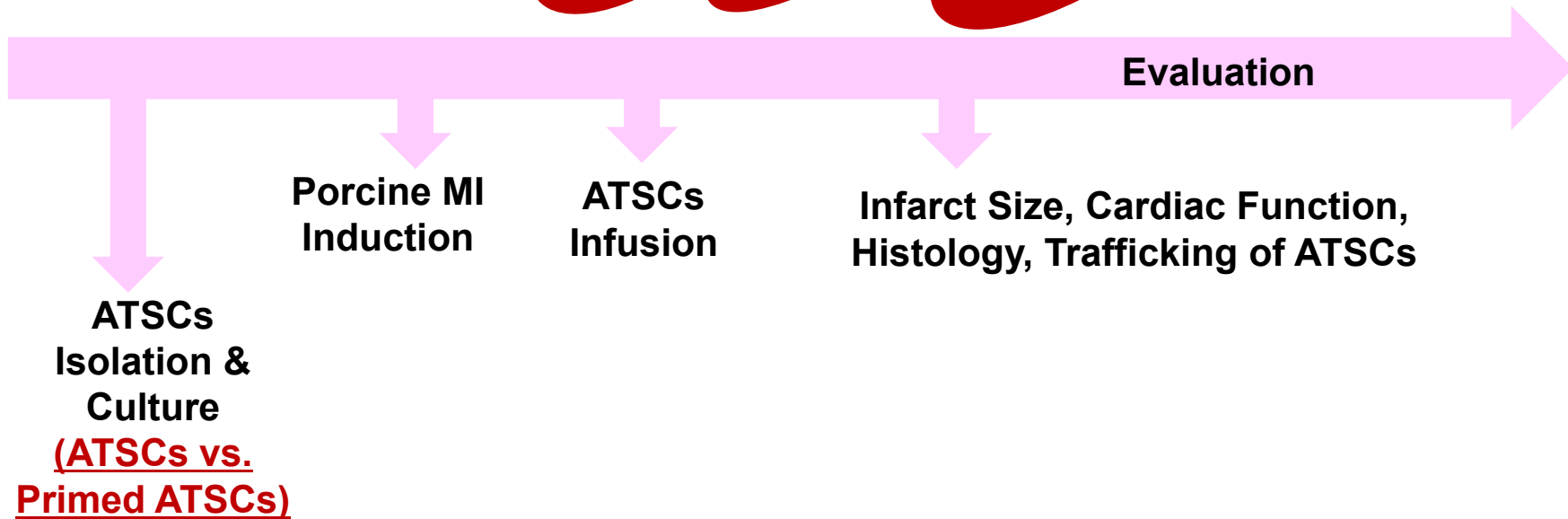
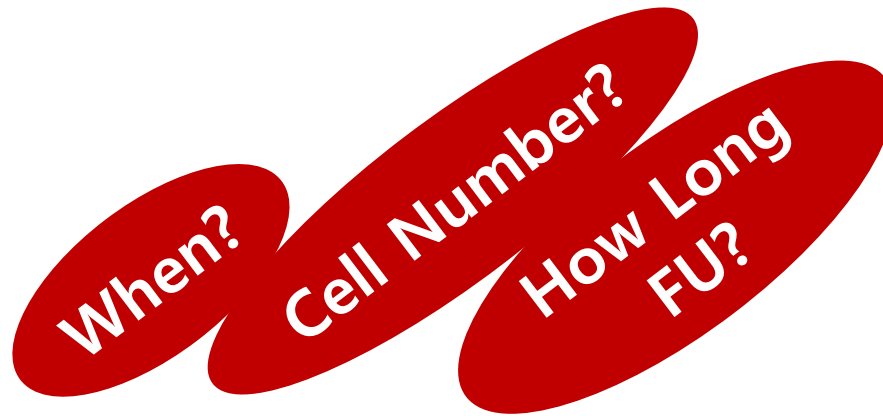
\*†Yong Sook Kim, \*†Jin Sook Kwon, \*†Moon Hwa Hong, ‡Jin Kim, ‡Chang Hun Song,  
\*†Myung Ho Jeong, \*Jeong Gwan Cho, \*Jong Chun Park, \*Jung Chae Kang,  
and \*†Youngkeun Ahn

*\*The Heart Center and †Heart Research Center of Chonnam National University Hospital, and ‡JB Stem Cell Institute,  
Inc., Gwangju, South Korea*

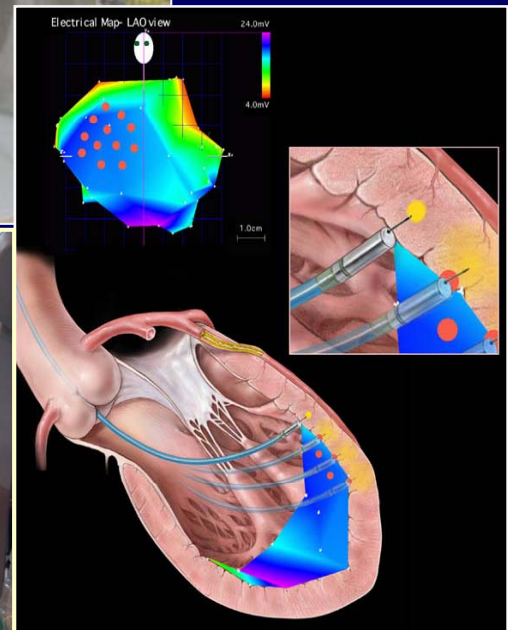
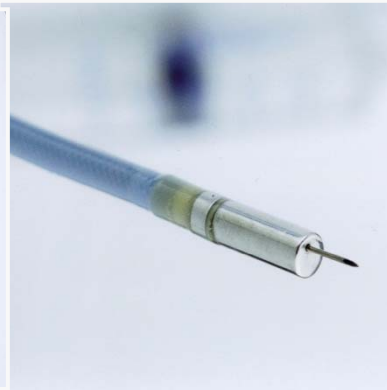
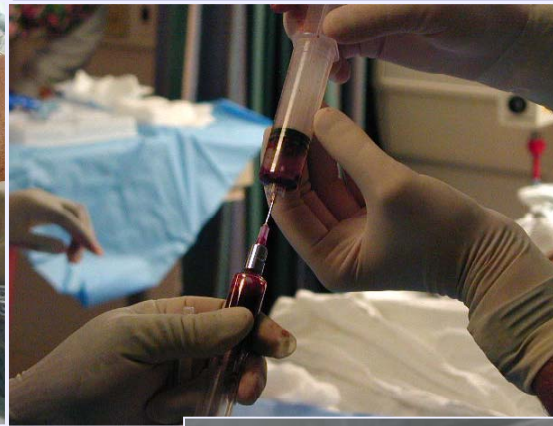
*rsity Hospital, Gwangju, South Korea*



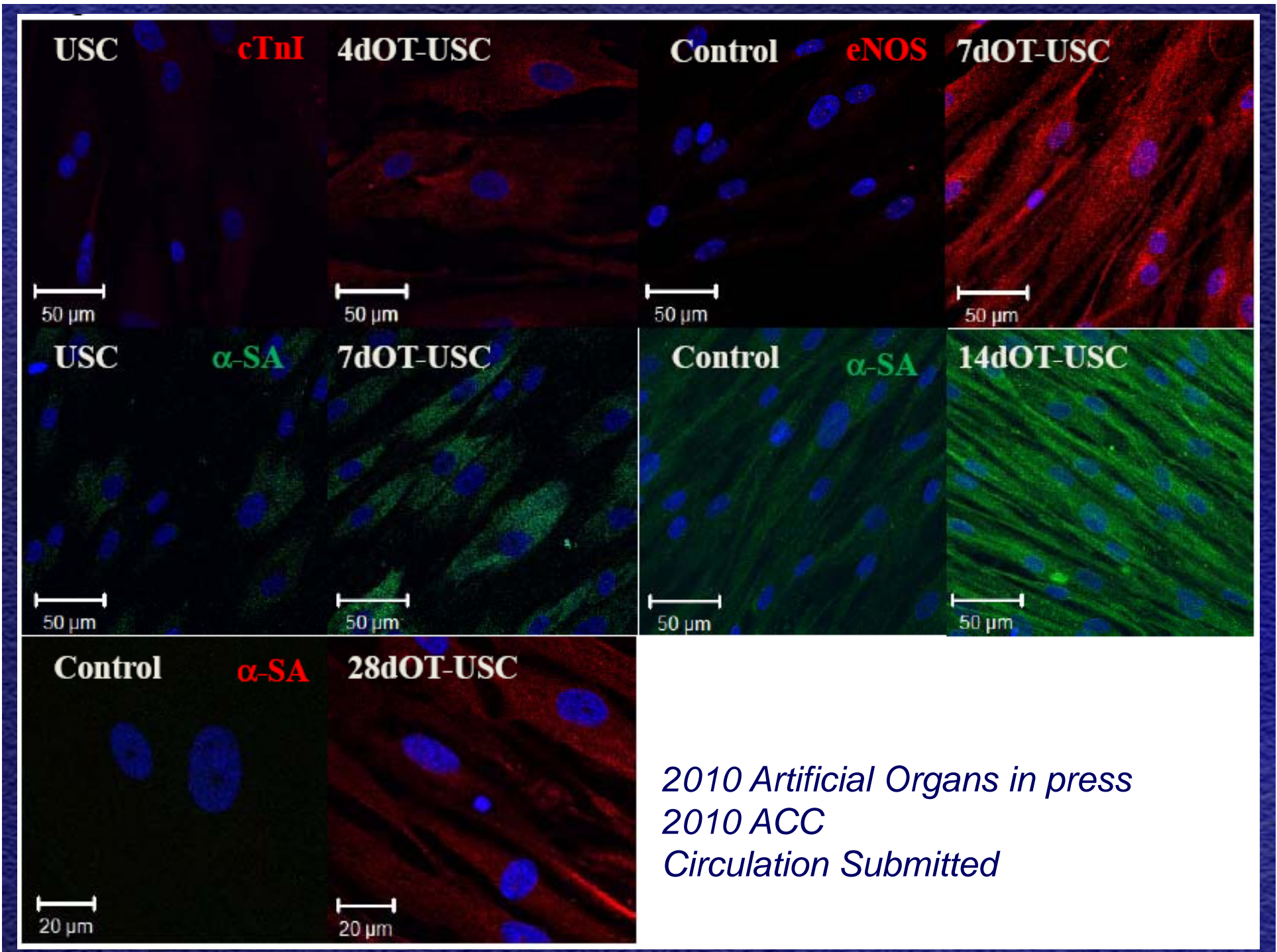
# Experimental Procedures



# *Transendocardial ABM Injection – Procedural Steps*







# Conclusion

- Chronic heart failure has become an enormous worldwide problem, particularly in elderly.
- Beta-blockers are still widely underused in this population.
- New therapeutic approach will be needed.





**Thank You for Your Attention!**

Celebrating for 100<sup>th</sup> Anniversary of Chonnam National University Hospital

INVITATION

## 2<sup>ND</sup> GWANGJU-BOSTON JOINT CARDIOLOGY SYMPOSIUM

*New Paradigm of Cardiovascular Therapeutics*

**Date :** April 23 (Fri), 2010

**Place :** Myung-Hak Hall, Chonnam National University Medical  
School, Hak-Dong, Gwangju, South Korea

**Course Directors :** Youngkeun Ahn, MD  
Anthony Rosenzweig, MD

**Organized by :** Heart Center, Chonnam National University Hospital  
The Honam Circulation Society of Korea

**Supported by :** National Research Foundation  
Ministry for Health, Welfare and Family Affairs  
Brain Korea 21 Project at CNUMS  
CNUH Research Institute of Clinical Medicine  
University Industry Liaison Office of CNU  
Foundation of Circulation Research

# 경청해 주셔서 감사합니다.