The Heart Failure Management Paradigm: From the Emergency Department to Hospital Admission and Discharge

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Pre-Activity Assessment Question 1

Sacubitril, which is now coformulated with valsartan in a new combination medication, takes action via a novel pathway by inhibiting neprilysin, which breaks down brain (or B-type) natriuretic peptide (BNP). Which of the following statements is *false* regarding neprilysin?

A. Neprilysin breaks down atrial natriuretic peptide (ANP), BNP, and C-type natriuretic peptide (CNP)
B. Neprilysin is an enzyme
C. N-Terminal pro-BNP (NT-proBNP) is not a substrate for neprilysin
D. In a clinical trial, valsartan/sacubitril *decreased* BNP levels but *increased* NT-proBNP levels

Pre-Activity Assessment Question 2

Which of the following acute heart failure treatments has class I, level A (the best!) supporting evidence?

A. Angiotensin-converting enzyme (ACE) inhibitors
B. Nitroglycerin
C. Furosemide
D. None of the above
E. A, B, and C

Pre-Activity Assessment Question 3

A 67-year-old man with a history of HFpEF, hypertension (HTN), COPD, and morbid obesity presents short of breath (SOB) and 10 lb heavier. No wheezing; no URI complaints. Heart rate, 87 bpm; BP, 157/85; oxygen saturation, 87% right atrial (RA). No wheezing on exam. Labs show a Cr of 1.1, a troponin of <0.02, and an NT-proBNP level of 288 (previous level was 9000 during a prior hospitalization). CTA of chest was negative for pulmonary embolism (PE) and pneumonia. After providing supplemental oxygen with a nasal cannula, what would be the next best step?

A. High-dose intravenous (IV) diuretics
B. IV vasodilator
C. Steroid, antibiotic, and bronchodilator therapy
D. Noninvasive positive pressure ventilation

BP=blood pressure; bpm=beats per minute; BUN=blood urea nitrogen; COPD=chronic obstructive pulmonary disease; Cr=creatinine; CTA=computed tomography angiography; HFpEF=heart failure with preserved ejection fraction; URI=upper respiratory tract infection.

Pre-Activity Assessment Question 4

Which of the following would be an example of an acute HF patient who could be placed in an observation unit?

A. A 60-year-old man with a history of myocardial infarctions (MIs) and renal insufficiency who is confused and has cool, mottled extremities.
B. An 84-year-old woman with minimal residual dyspnea post treatment who has mild dementia and lives by herself.
C. A 63-year-old woman accompanied by her son (with whom she lives) who responds well to emergency department (ED) treatment and has no high-risk features identified during ED evaluation.
D. A 71-year-old man who, after treatment in the ED, remains markedly hypertensive with significant dyspnea at rest.

Learning Objectives

- **Identify** heart failure (HF) patients by their clinical profiles and phenotypes and assess comorbid conditions
- **Produce** the diagnosis of acute heart failure (AHF) based on clinical presentation, history, laboratory assessment, and radiographic findings
- **Integrate** the data of related clinical trials and the evidence to support the use of current therapies as well as novel therapies that are in development for AHF
- **Collaborate** with the interdisciplinary team to properly assess when HF patients need to be admitted to the hospital, placed in observation status, or discharged
- **Distinguish** the importance of early re-initiation of guideline-directed medical therapy, including beta blockers, and discuss the initiation or continuation of newer FDA-approved treatments for patients admitted to the hospital or placed in observation status
- **Describe** **evidence-based practices, including methods to improve care transitions for AHF patients once they are ready for discharge from the hospital**

Introduction to the Epidemic

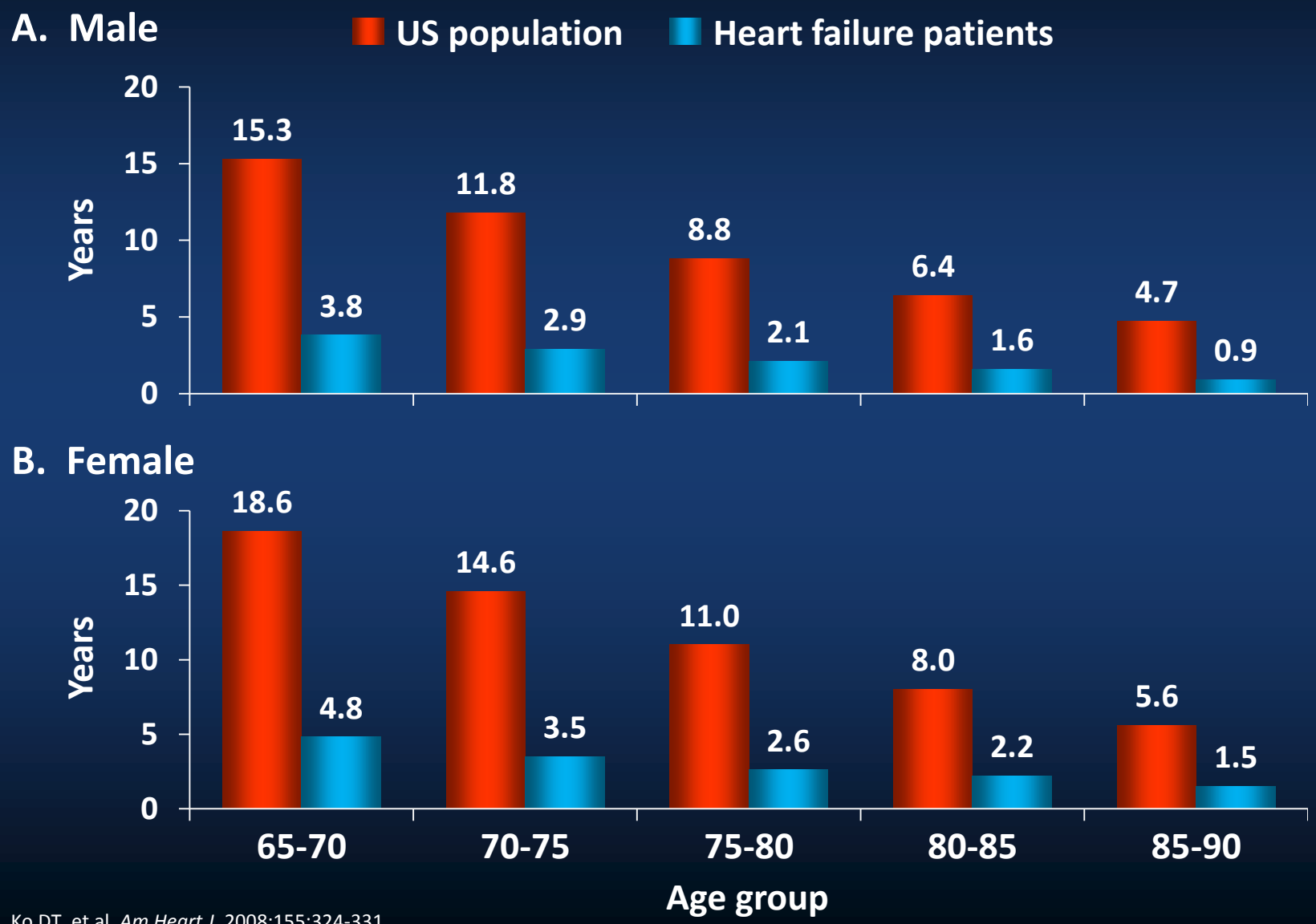
AHA Statistical Update—Heart Disease and Stroke Statistics 2014 Update

- 825,000 new HF cases annually
- At 40 years of age, the lifetime risk of developing HF for both men and women is 1 in 5
- The lifetime risk for people with BP >160/90 mm Hg is double that of those with BP <140/90 mm Hg

AHA=American Heart Association.

Go AS, et al. *Circulation*. 2014;129(3):e28-e292.

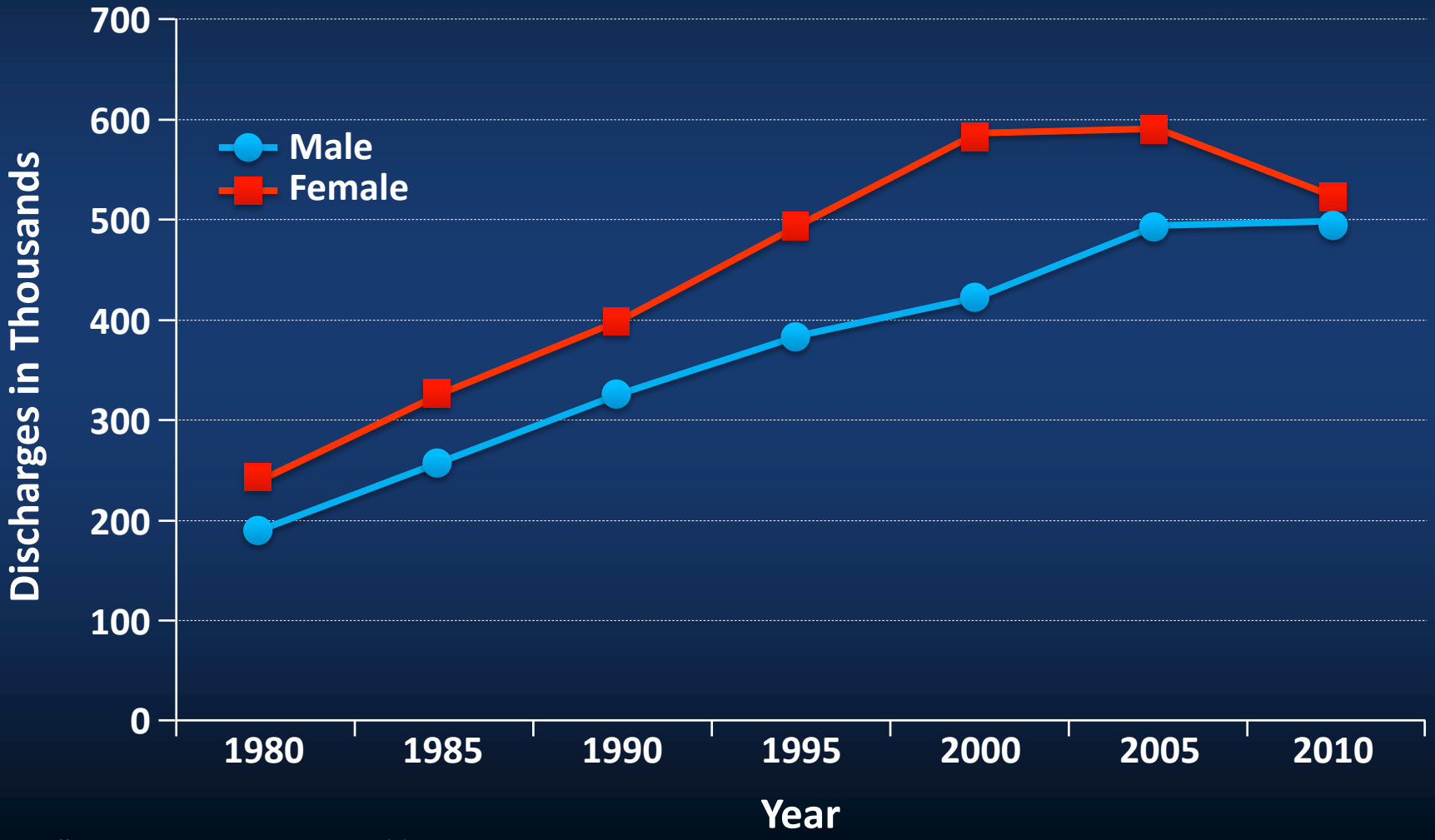
Median Survival



Ko DT, et al. *Am Heart J*. 2008;155:324-331.

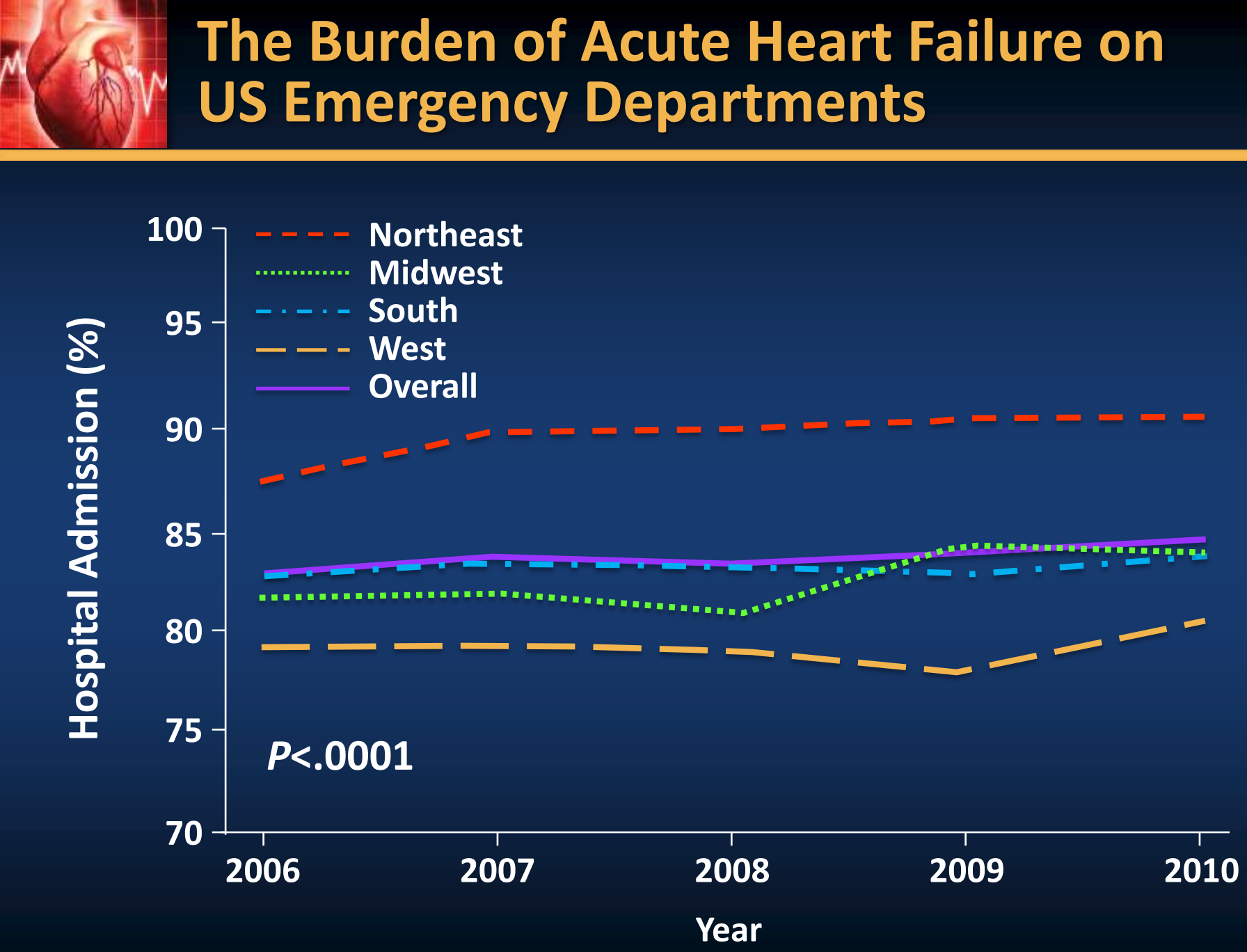
AHA Statistical Update—Heart Disease and Stroke Statistics 2014 Update

Hospital discharges for heart failure by sex (United States: 1980-2010)



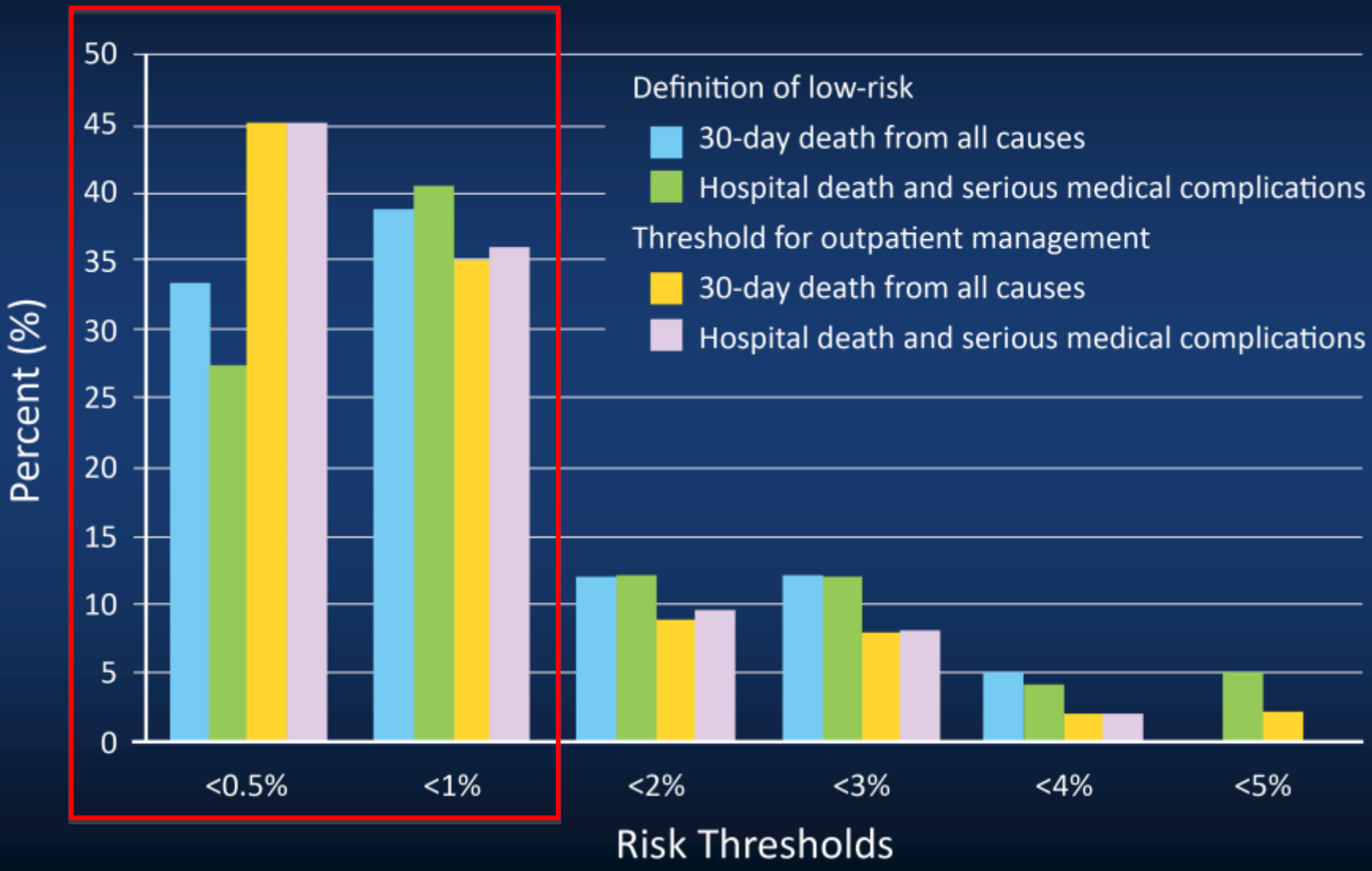
Mozaffarian D, et al. *Circulation*. 2015;131(4):e29-e322.

The Burden of Acute Heart Failure on US Emergency Departments



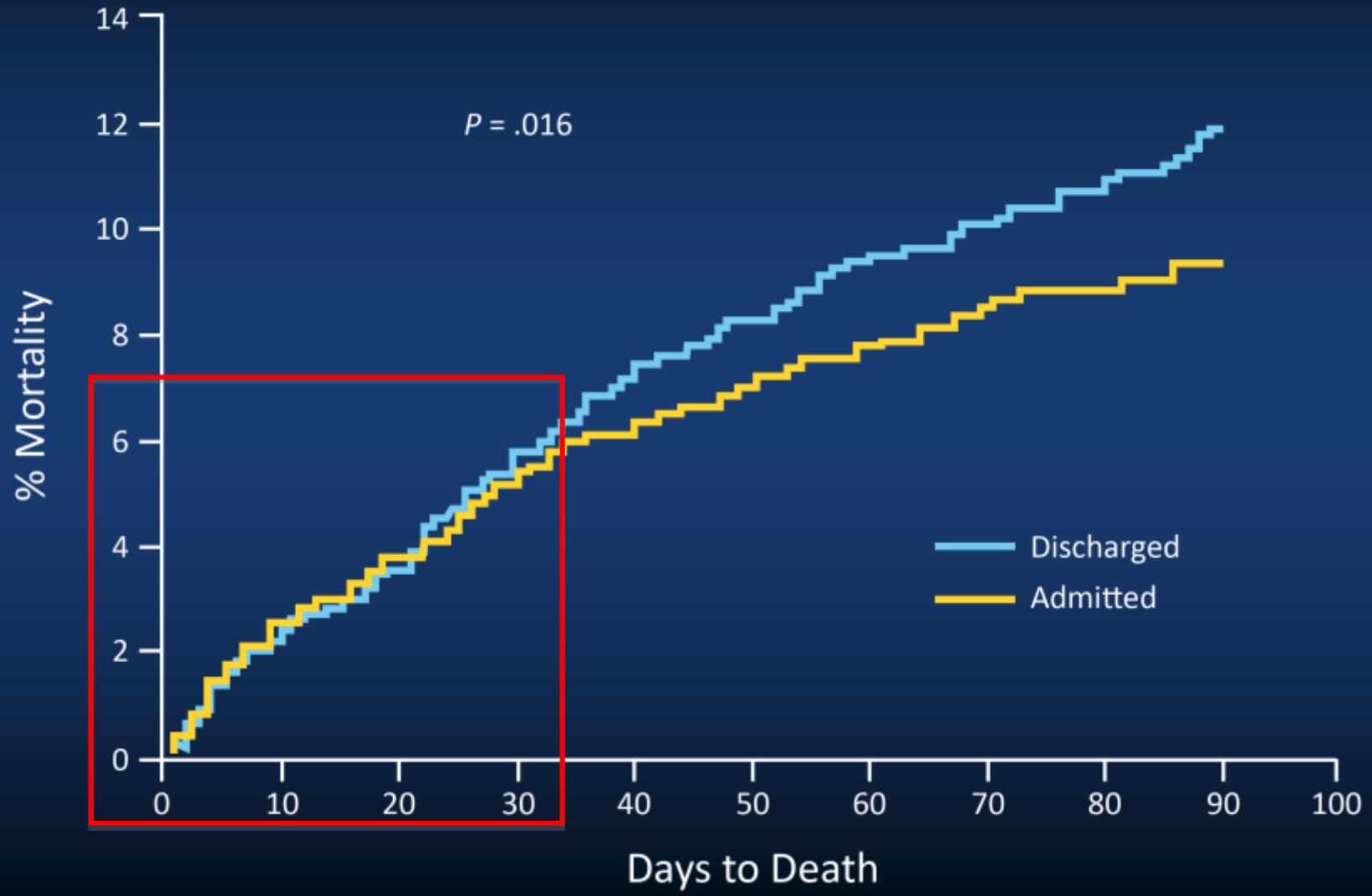
Storrow AB, et al. *JACC Heart Fail*. 2014;2(3):269-277.

Emergency Room Doctors Are Risk-Averse!



McCausland B, et al. *Acad Emerg Med.* 2010;17:108-110.

Early Deaths in Patients With Heart Failure Discharged From the Emergency Department: A Population-Based Analysis



Lee DS, et al. *Circ Heart Fail.* 2010 3:228-235.

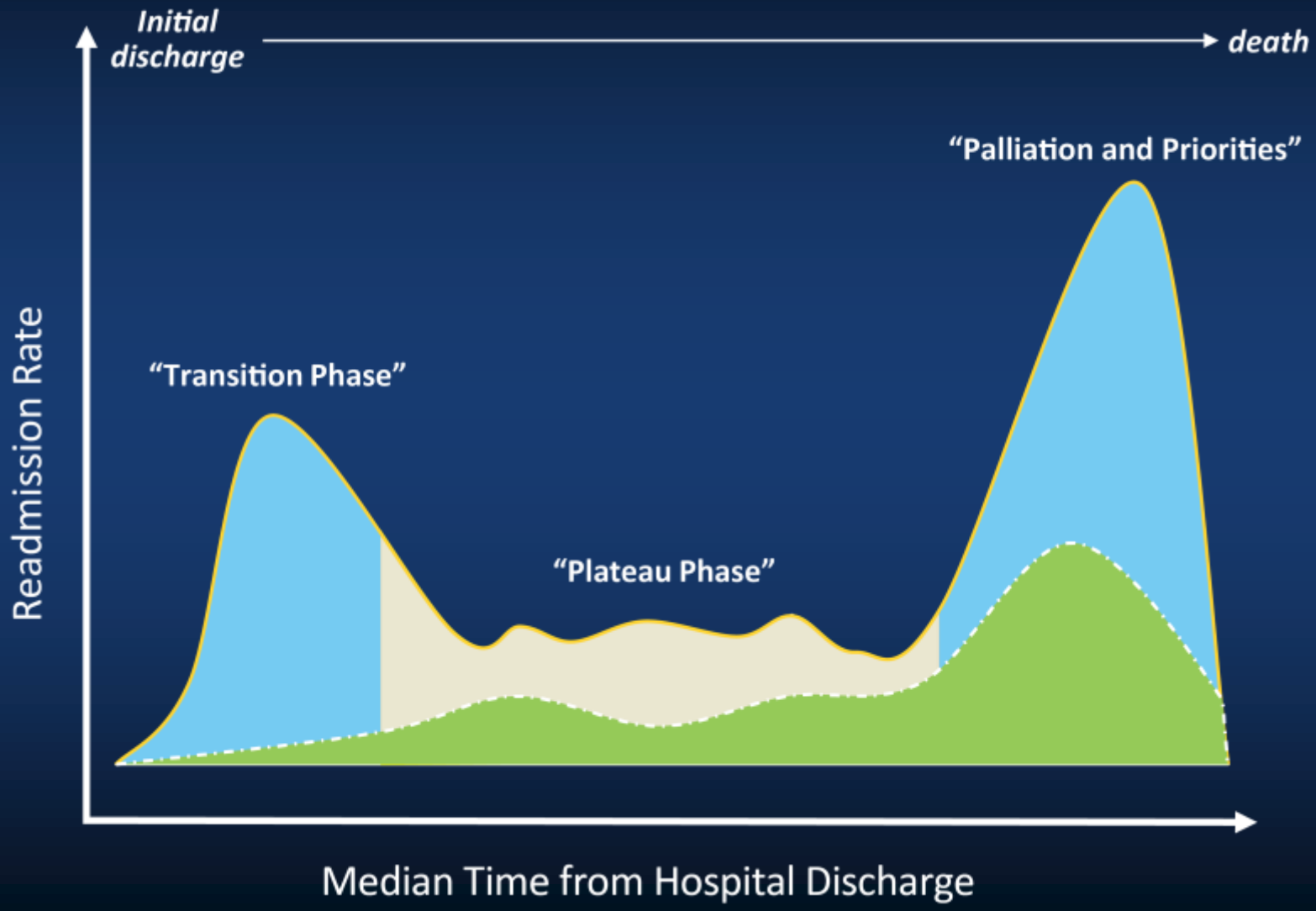
Rehospitalizations Among Patients in the Medicare Fee-for-Service Program

	Percent		Most Frequent	Second Most Frequent
MEDICAL				
All	21.0	77.6	Heart failure (8.6)	Pneumonia (7.3)
Heart failure	**26.9**	**7.6**	**Heart failure (37.0)**	**Pneumonia (5.1)**
Pneumonia	20.1	6.3	Pneumonia (29.1)	Heart failure (7.4)
COPD	22.6	4.0	COPD (36.2)	Pneumonia (11.4)
Psychoses	24.6	3.5	Psychoses (67.3)	Drug toxicity (1.9)
GI problems	19.2	3.1	GI problems (21.1)	Nutrition-related or metabolic issues (4.9)
SURGICAL				
All	15.6	22.4	Heart failure (6.0)	Pneumonia (4.5)

COPD=chronic obstructive pulmonary disease; GI, gastrointestinal.

Jencks SF, et al. *N Engl J Med.* 2009;360:1418-1428.

Readmission Risk After Heart Failure Hospitalization



Desai AS, Stevenson LW. *Circulation.* 2012;126:501-506.

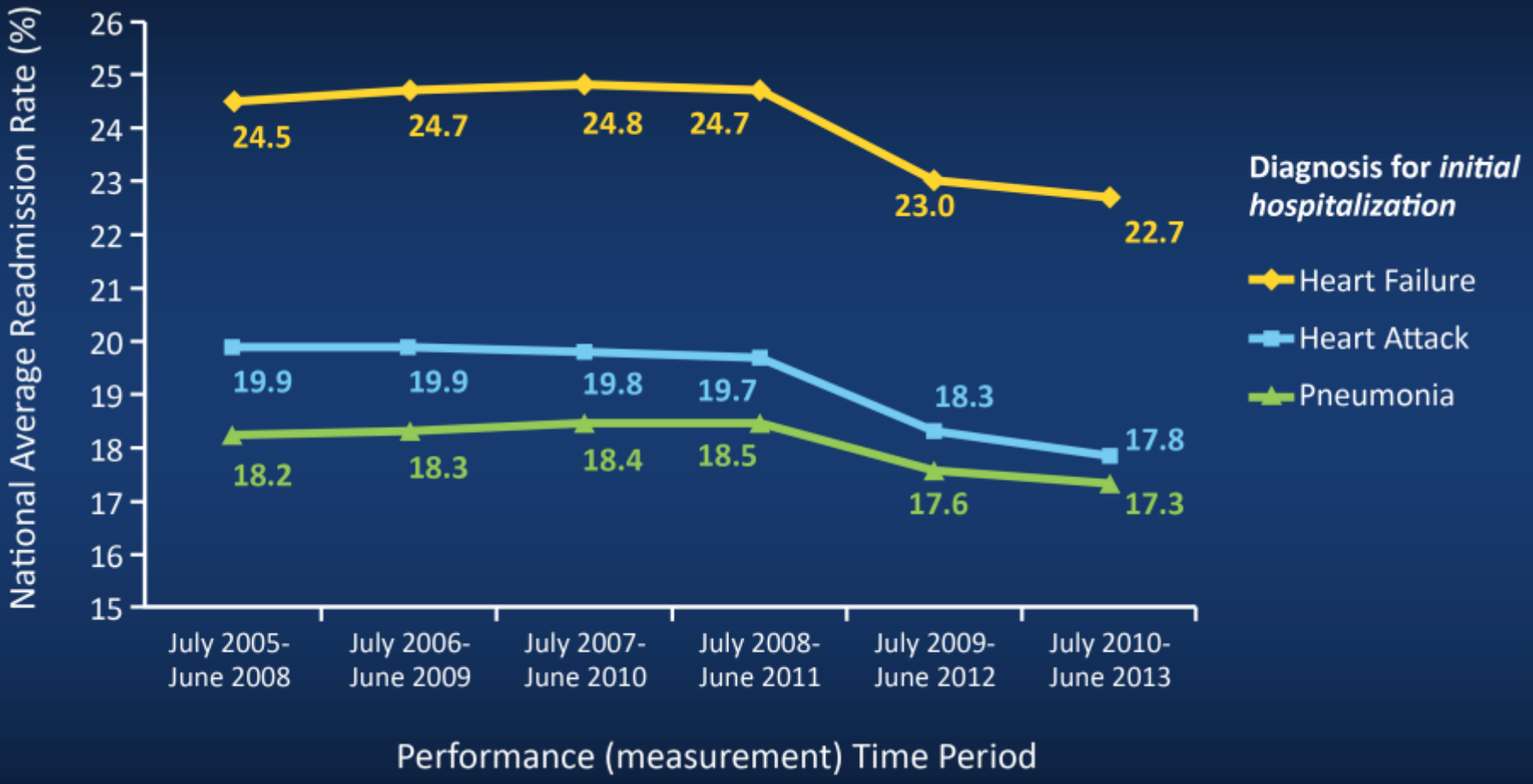
The Relationship Between Hospital Admission Rates and Rehospitalizations

Predictor	30 Days After Index Discharge		60 Days After Index Discharge		90 Days After Index Discharge	
	Univariate Analysis	Multivariate Analysis*	Univariate Analysis	Multivariate Analysis*	Univariate Analysis	Multivariate Analysis*
	Percent of variance in readmission rates explained					
Congestive heart failure						
Case mix	11.0	2.6	15.0	2.4	17.8	3.1
Discharge planning	10.5	1.0	12.9	1.0	12.9	1.0
HRR-level supply variables						
PCPs per 100,000 population	0.1	0.5	0.3	0.7	0.4	0.6
Cardiologists per 100,000 population	11.6	0.8	13.6	1.0	15.4	1.9
Hospital beds per 1000 population	5.6	0.7	8.1	0.2	8.9	0.4
All-cause admission rate	27.5	16.0	33.5	20.4	37.4	23.6

HRR=hospital referral region; PCPs=primary care physicians.

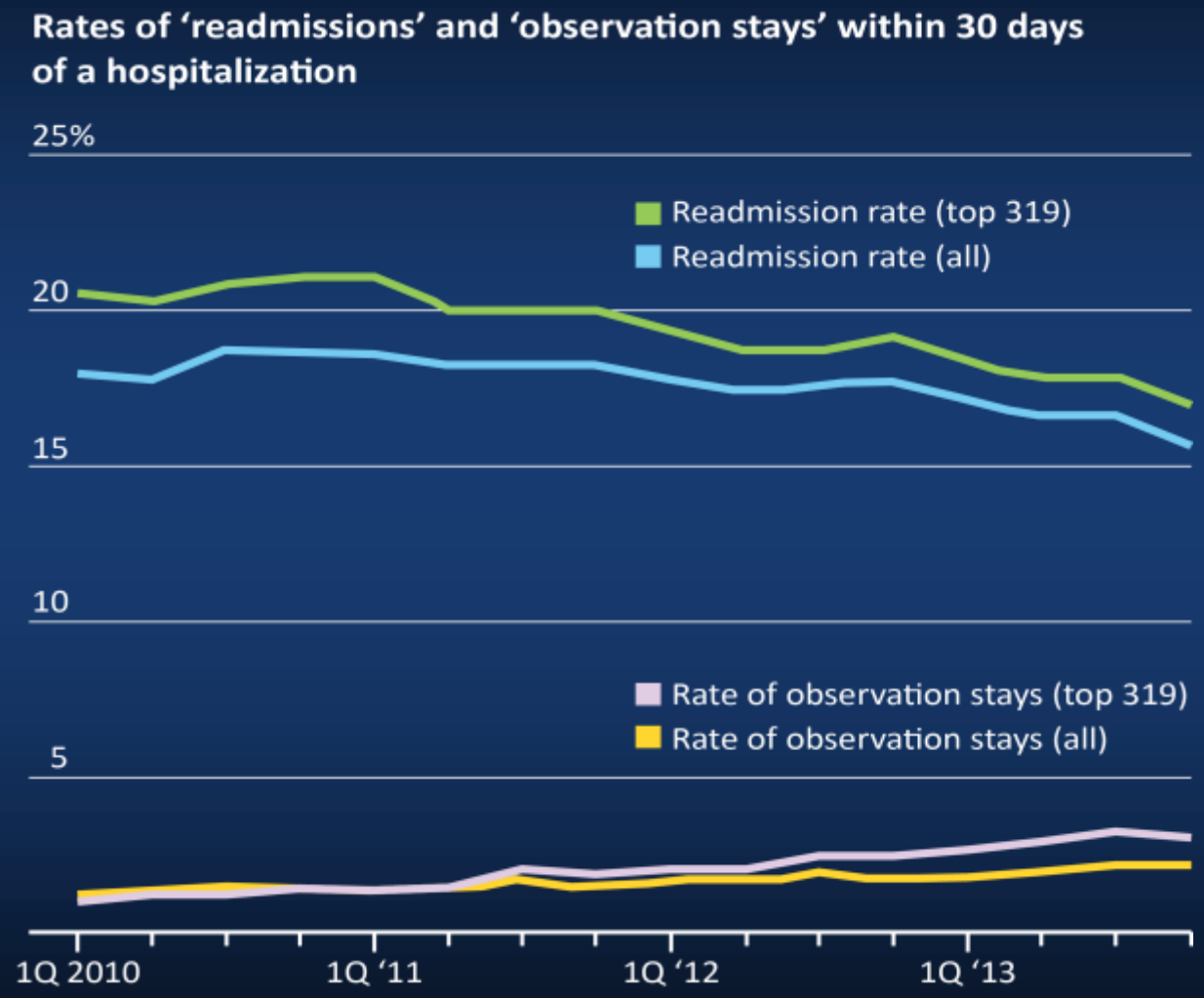
Epstein AM, et al. *N Engl J Med*. 2011;365:2287-2295.

Aiming for Fewer Hospital U-Turns: The Medicare Readmission Reduction Program



Boccuti C, Casillas G. http://kff.org/medicare/issue-brief/aiming-for-fewer-hospital-u-turns-the-medicare-hospital-readmission-reduction-program/. January 29, 2015.

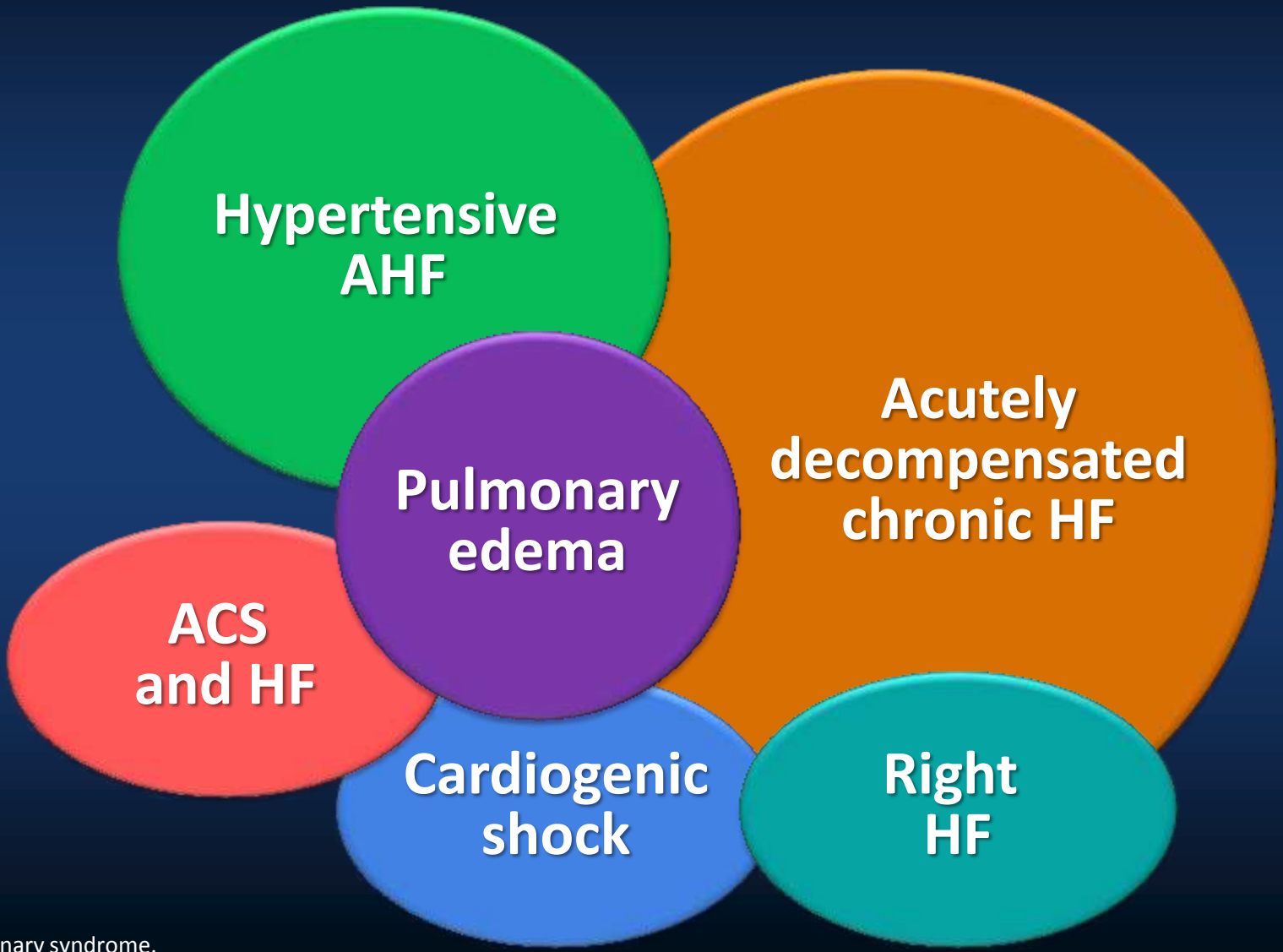
Going Back to the Hospital



Weaver C, et al. *Wall Street Journal.* December 1, 2015. http://www.wsj.com/articles/medicare-rules-reshape-hospital-admissions-1449024342.

Evaluating Acute Heart Failure Patients in the ED—Initial Approach

Recognizing Acute Heart Failure (AHF)



ACS=acute coronary syndrome.

Pang PS, et al. *Eur Heart J*. 2010;31:784-793.

Is Clinical Examination Really Useful?

	Pooled		Summary Likelihood Ratio (95% CI)	
Finding	**Sensitivity**	**Specificity**	**Positive**	**Negative**
Initial clinical judgment	0.61	0.86	4.4 (1.8-10.0)	0.45 (0.28-0.73)
Physical examination				
Third heart sound (ventricular filling gallop)	**0.13**	**0.99**	**11 (4.9-25.0)**	**0.88 (0.83-0.94)**
Abdominojugular reflux	0.24	0.96	6.4 (0.81-51.0)	0.79 (0.62-1.0)
Jugular venous distension	0.39	0.92	5.1 (3.2-7.9)	0.66 (0.57-0.77)
Rales	0.60	0.78	2.8 (1.9-4.1)	0.51 (0.37-0.70)
Any murmur	0.27	0.90	2.6 (1.7-4.1)	0.81 (0.73-0.90)
Lower-extremity edema	0.50	0.78	2.3 (1.5-3.7)	0.64 (0.47-0.87)
Valsalva maneuver	0.73	0.65	2.1 (1.0-4.2)	0.41 (0.17-1.0)
Systolic blood pressure <100 mm Hg	0.06	0.97	2.0 (0.60-6.6)	0.97 (0.91-1.0)
Fourth heart sound (atrial gallop)	0.05	0.97	1.6 (0.47-5.5)	0.98 (0.93-1.0)
Systolic blood pressure ≥150 mm Hg	0.28	0.73	1.0 (0.69-1.6)	0.99 (0.84-1.2)
Wheezing	0.22	0.58	0.52 (0.38-0.71)	1.3 (1.1-1.7)
Ascites	0.01	0.97	0.33 (0.04-2.9)	1.0 (0.99-1.1)

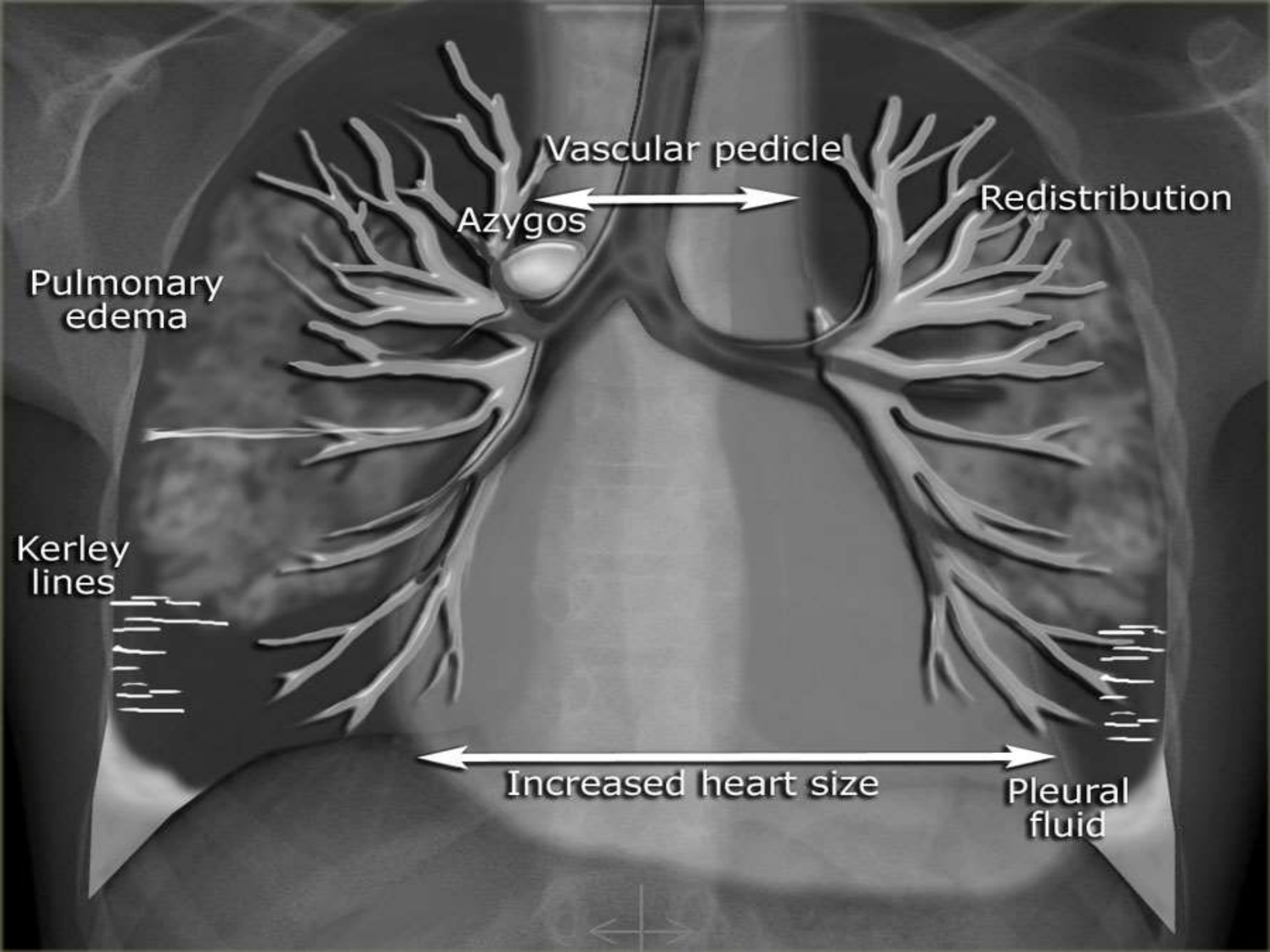
Wang S, et al. *JAMA*. 2005;294:1944-1956.

Diagnosing Acute Heart Failure in the Emergency Department: A Systematic Review and Meta-Analysis

	No. of Studies	No. of Patients	% AHF (95% CI)	Sensitivity, % (95% CI)	Specificity, % (95% CI)	LR+ (95% CI)	LR– (95% CI)
Electrocardiogram							
Ischemic changes	2	1138	42.6 (39.8-45.5)	34.0 (29.8-38.4)	84.2 (81.2-86.9)	2.9 (1.2-7.1)	0.78 (0.73-0.84)
T-wave inversion	1	709	69.4 (65.9-72.7)	10.0 (7.5-13.0)	95.9 (92.3-98.1)	2.4 (1.2-4.8)	0.94 (0.90-0.98)
Atrial fibrillation	6	2242	55.8 (53.7-57.8)	20.5 (18.3 -22.9)	89.9 (87.9-91.7)	2.2 (1.4-3.5)	0.88 (0.85-0.91)
ST depression	2	1024	60.8 (57.8-63.8)	5.6 (3.9-7.7)	96.5 (94.2-98.1)	2.0 (1.0-3.8)	0.97 (0.95-1.00)
Normal sinus rhythm	3	1207	39.6 (36.9-42.4)	55.4 (50.9-60.0)	17.8 (15.1-20.8)	0.7 (0.5-0.9)	2.88 (1.26-6.57)
ST elevation	1	219	61.2 (54.6-67.4)	5.2 (2.1-10.5)	91.8 (83.8-96.6)	0.6 (0.2-1.7)	1.03 (0.96-1.11)
Chest radiograph							
Kerley B lines	2	814	46.8 (43.4-50.2)	9.2 (6.5-12.5)	98.8 (97.3-99.6)	6.5 (2.6-16.2)	0.88 (0.69-1.13)
Interstitial edema	3	2001	48.3 (46.2-50.5)	31.1 (28.2-34.2)	95.1 (93.6-96.3)	6.4 (3.4-12.2)	0.73 (0.68-0.78)
Cephalization	5	1338	54.0 (51.3-56.6)	44.7 (41.1-48.4)	94.6 (92.6-96.3)	5.6 (2.9-10.4)	0.53 (0.39-0.72)
Alveolar edema	3	2001	48.3 (46.2-50.5)	5.7 (4.7-6.9)	98.9 (98.4-99.3)	5.3 (3.3-8.5)	0.95 (0.94-0.97)
Pulmonary edema	15	4393	46.6 (45.1-48.1)	56.9 (54.7-59.1)	89.2 (87.9-90.4)	4.8 (3.6-6.4)	0.48 (0.39-0.58)
Pleural effusion	5	1326	55.1 (52.4-57.8)	16.3 (13.7-19.2)	92.8 (90.4-94.7)	2.4 (1.6-3.6)	0.89 (0.80-0.99)
Enlarged cardiac silhouette	12	3515	51.7 (49.4-52.7)	74.7 (72.9-76.5)	61.7 (59.4-63.9)	2.3 (1.6-3.4)	0.43 (0.36-0.51)

AHF, acute heart failure; LR+, likelihood ratio of a positive test; LR–, likelihood ratio of a negative test.

Martindale JL. *Acad Emerg Med*.2016;23:223-242.


Vascular pedicle
Azygos
Redistribution
Pulmonary edema
Kerley lines
Increased heart size
Pleural fluid

Diagnosing Acute Heart Failure in the ED: A Systematic Review and Meta-Analysis *(cont'd)*

	No. of Studies	No. of Patients	% AHF (95% CI)	Sensitivity, % (95% CI)	Specificity, % (95% CI)	LR+ (95% CI)	LR– (95% CI)
Lung ultrasound							
Positive B-line scan	8	1914	48.2 (46.0-50.5)	85.3 (82.8-87.5)	92.7 (90.9-94.3)	7.4 (4.2-12.8)	0.16 (0.05-0.51)
Pleural effusion(s)	2	155	40.7 (33.2-48.5)	63.5 (50.4-75.3)	71.7 (61.4-80.6)	2.0 (1.4-2.8)	0.49 (0.22-1.10)
Bedside echocardiography							
Restrictive mitral pattern	1	125	43.2 (34.9-52.0)	81.5 (68.6-90.7)	90.1 (80.7-95.9)	8.3 (4.0-16.9)	0.21 (0.12-0.36)
Reduced ejection fraction (EF)	3	325	41.2 (36.0-46.7)	80.6 (72.9-86.9)	80.6 (74.3-86.0)	4.1 (2.4-7.2)	0.24 (0.17-0.35)
Increased LV end-diastolic dimension	1	84	58.3 (47.7-68.3)	79.6 (65.7-89.7)	68.6 (50.7-83.1)	2.5 (1.5-4.2)	0.30 (0.16-0.54)

AHF, acute heart failure; LR+, likelihood ratio of a positive test; LR–, likelihood ratio of a negative test; LV, left ventricle.
Martindale JL. *Acad Emerg Med*.2016;23:223-242.

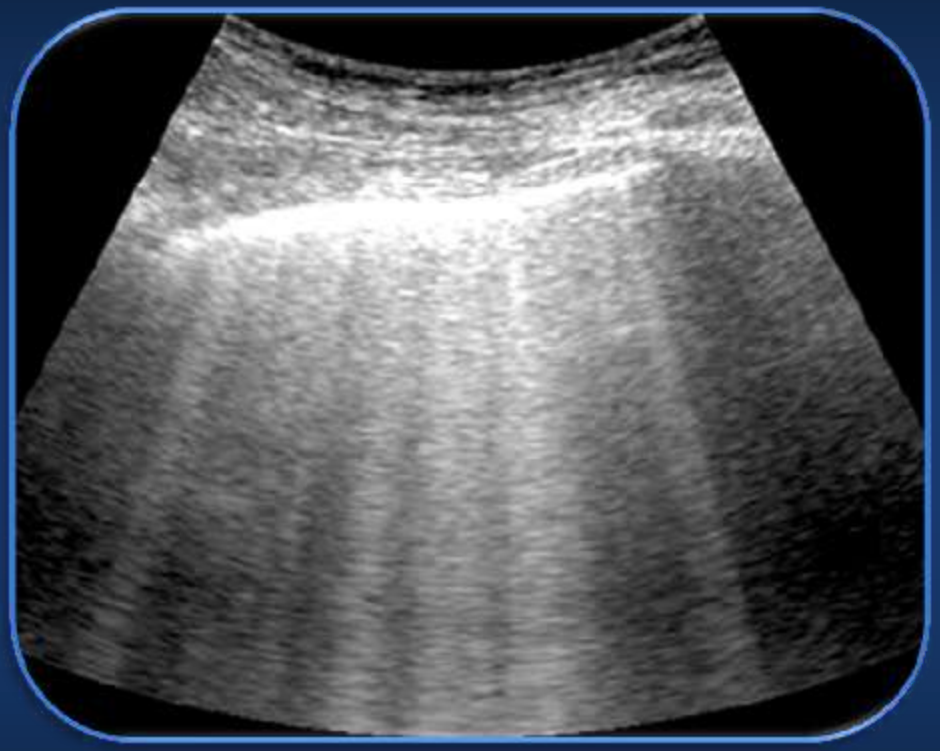
Chest Ultrasonography: Another Useful Adjunct?

Mid-axillary	Anterior axillary	Mid-clavear	Para-sternal	Inter-costal space	Para-sternal	Mid-clavear	Anterior axillary	Mid-axillary
				2				
				3				
				4				
				5				

Gargani L, et al. *Eur J Heart Fail*. 2008;10:70-77.

Ultrasound Lung Comets

Normal



Acute Heart Failure

Soldati G, et al. *Intern Emerg Med*. 2008;3:37-41.

Diagnosing Acute Heart Failure in the ED: A Systematic Review and Meta-Analysis *(cont'd)*

Assay	Cutoff (pg/mL)	N	n	% AHF (95% CI)	Specificity % (95% CI)	Specificity % (95% CI)	LR+ (95% CI)	LR– (95% CI)
BNP								
Triage	100	19	9143	44.7 (43.7-45.8)	93.5 (92.6-94.2)	52.9 (51.6-54.2)	2.2 (1.8-2.7)	0.11 (0.07-0.16)
	200	11	3279	50.4 (48.7-52.1)	85.9 (84.2-87.6)	72.2 (69.9-74.4)	3.1 (2.3-4.0)	0.18 (0.12-0.27)
	500	8	3.915	46.7 (45.1-48.3)	67.7 (65.5-69.9)	89.8 (88.5-91.1)	9.1 (4.1-20.2)	0.34 (0.26-0.45)
AxSym	100	4	684	52.3 (48.6-56.1)	93.3 (90.2-95.7)	53.1 (47.5-58.6)	1.9 (1.5-2.4)	0.15 (0.08-0.29)
iSTAT	100	2	585	42.6 (38.6-46.6)	94.4 (90.7-96.9)	64.6 (59.2-69.7)	3.0 (1.2-7.4)	0.05 (0.02-1.23)
NT-proBNP								
Elecsys	300	10	3498	45.0 (43.4-46.7)	90.4 (88.9-91.8)	38.2 (36.0-40.4)	1.8 (1.4-2.2)	0.09 (0.03-0.34)
	1000	8	2988	44.8 (43.0-46.6)	84.8 (82.8-86.7)	65.5 (63.2-67.8)	2.7 (1.9-3.9)	0.20 (0.12-0.33)
	1550	9	3043	37.3 (35.6-39.0)	75.5 (73.4-77.9)	72.9 (70.6-75.0)	3.1 (2.3-4.3)	0.32 (0.20-0.51)
Dimension	300	1	401	30.4 (26.0-35.2)	95.9 (90.7-98.6)	48.0 (42.0-54.1)	1.9 (1.6-2.1)	0.09 (0.04-0.20)

AHF, acute heart failure; BNP, brain (or B-type) natriuretic peptide; LR+, likelihood ratio of a positive test; LR–, likelihood ratio of a negative test; NT-proBNP, N-Terminal pro-BNP.

Martindale JL. *Acad Emerg Med*.2016;23:223-242.

Diagnosing Acute Heart Failure in the ED: A Systematic Review and Meta-Analysis *(cont'd)*

BNP Value (pg/mL)	Interval LR	N (%)	NT-proBNP (pg/mL)	Interval LR	N (%)
0-100	0.14 (0.12-0.18)	617 (28)	0-100	0.09 (0.05-0.17)	150 (7.5)
100-200	0.29 (0.23-0.38)	308 (14)	100-300	0.23 (0.16-0.33)	205 (10.2)
200-300	0.89 (0.67-1.17)	188 (9)	300-600	0.28 (0.20-0.39)	212 (10.5)
300-400	1.34 (0.98-1.83)	148 (7)	600-900	0.63 (0.46-0.87)	151 (7.5)
400-500	2.05 (1.47-2.84)	148 (7)	900-1500	0.84 (0.67-1.06)	249 (12.4)
500-600	3.50 (2.30-5.35)	115 (5)	1500-3000	1.49 (1.19-1.86)	273 (13.6)
600-800	4.13 (3.01-5.68)	218 (10)	3000-5000	2.36 (1.81-3.08)	225 (11.2)
800-1000	5.00 (3.21-7.89)	130 (6)	5000-10,000	2.48 (1.91-3.21)	239 (11.9)
1000-1500	7.12 (4.53-11.18)	160 (70)	10,000-15,000	2.84 (1.90-4.23)	112 (5.6)
1500-2500	8.33 (4.60-15.12)	105 (5)	15,000-30,000	2.93 (1.95-4.39)	111 (5.5)
2500-5001	8.91 (4.09-19.43)	65 (3)	30,000-200,000	3.30 (2.05-5.31)	86 (4.3)
		2202 (100)			2013 (100)

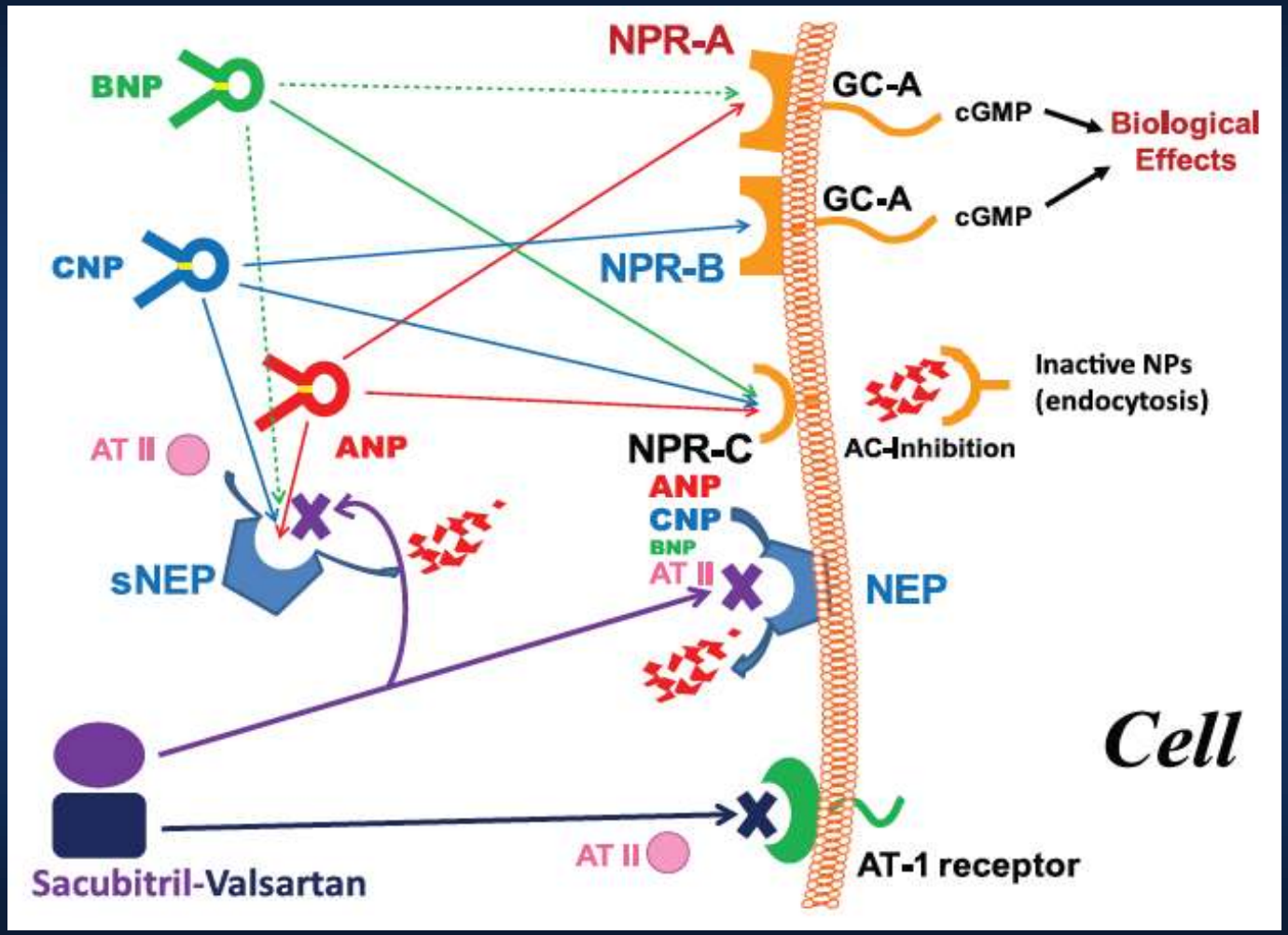
BNP=brain (or B-type) natriuretic peptide; LR=likelihood ratio; NT-proBNP=N-Terminal pro-BNP.

Martindale JL. *Acad Emerg Med*.2016;23:223-242.

Natriuretic Peptide Caveats

- Relative increase in women
- Inverse relationship with body mass index (BMI)
- Higher with renal dysfunction

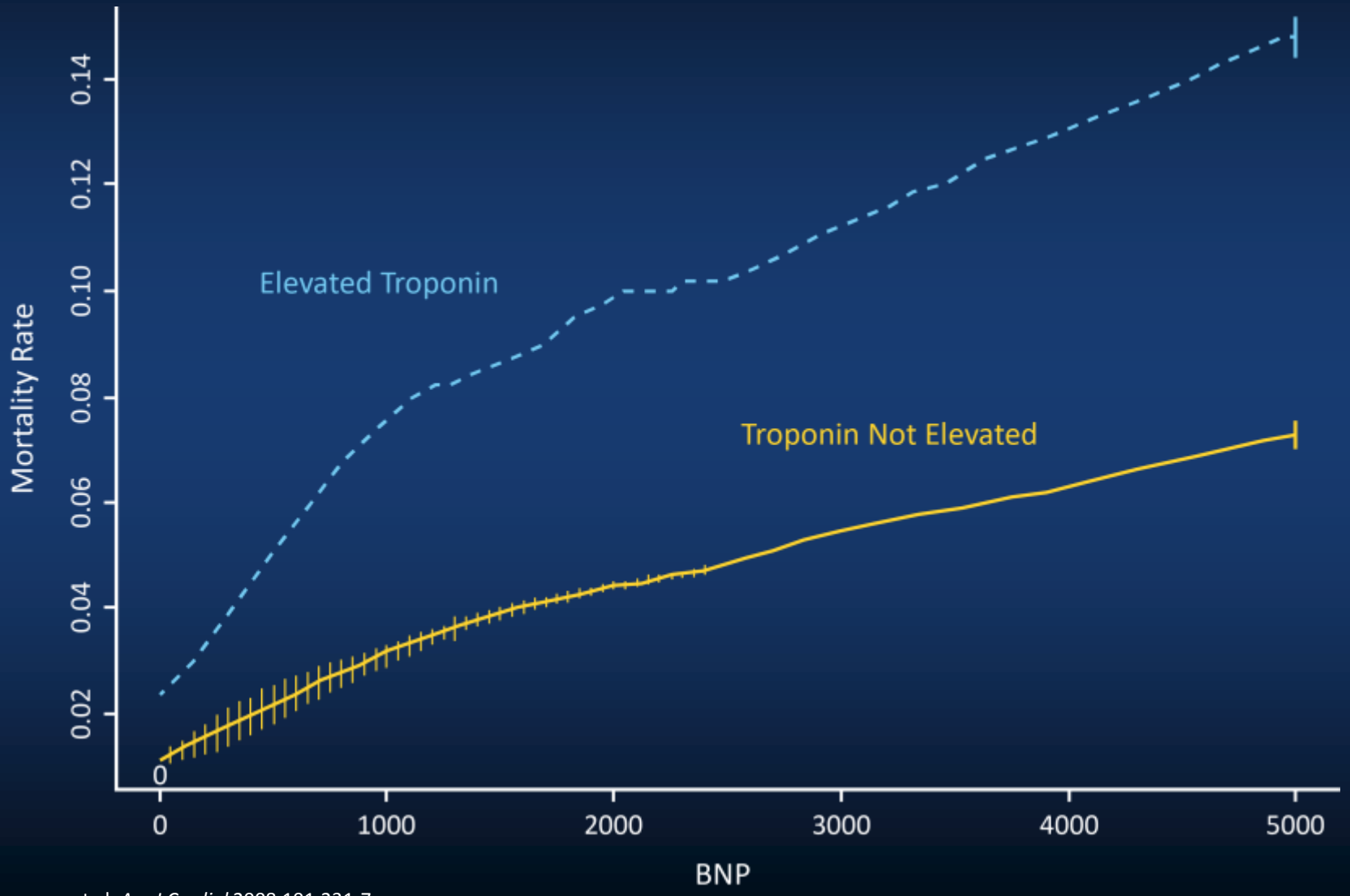
Potential Impact of Sacubitril/Valsartan



AC=adenylate cyclase; ANP=A-type natriuretic peptide; BNP=B-type natriuretic peptide; cAMP=cyclic adenosine monophosphate; cGMP=cyclic guanosine monophosphate; CNP=C-type natriuretic peptide; NEP=neutral endopeptidase; NP=natriuretic peptide; NPR=natriuretic peptide receptor.

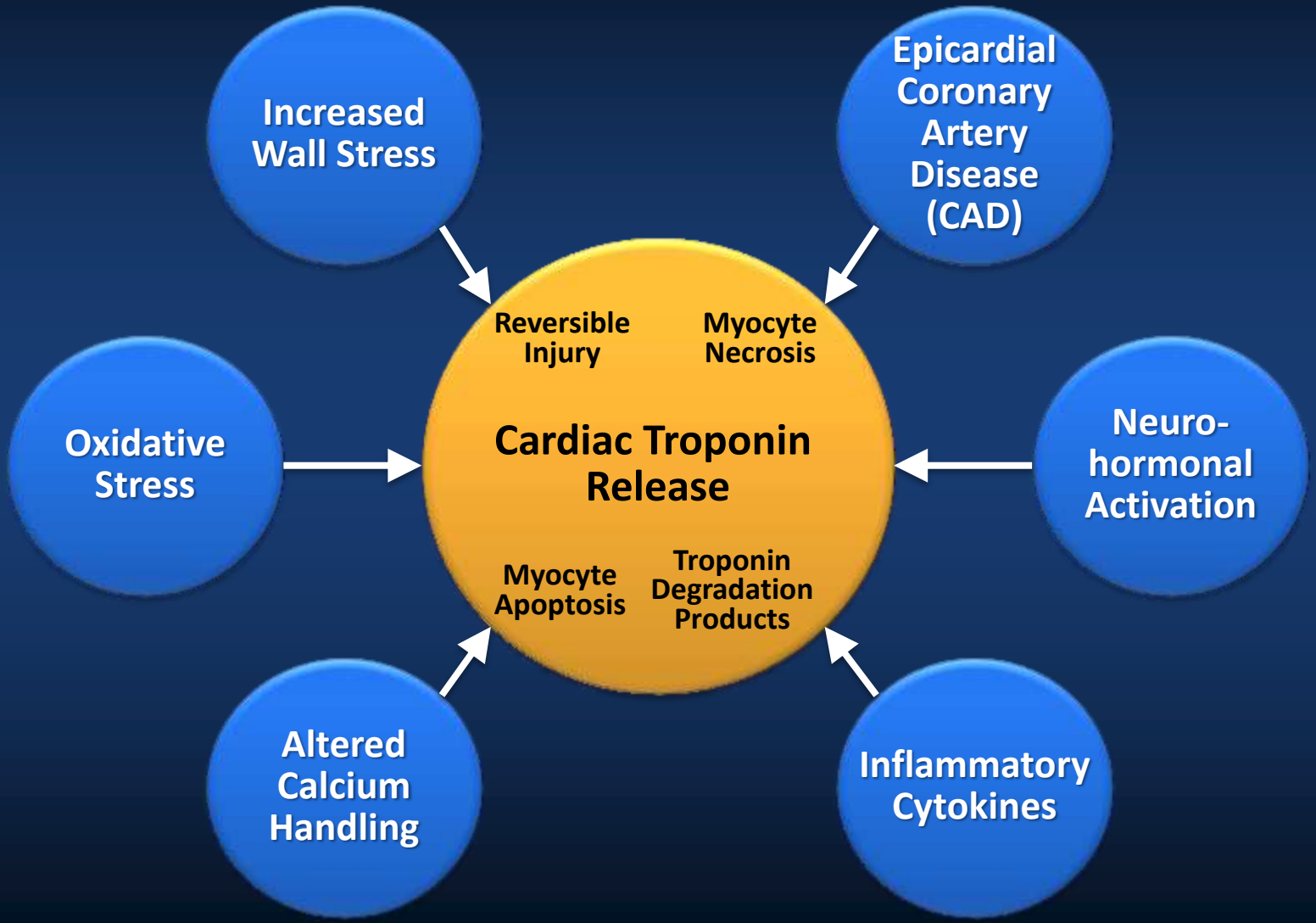
Mair J, et al. [Published online January 12, 2016.] *Eur Heart J Acute Cardiovasc Care*. pii: 2048872615626355.

Rising Levels = Worse Prognosis



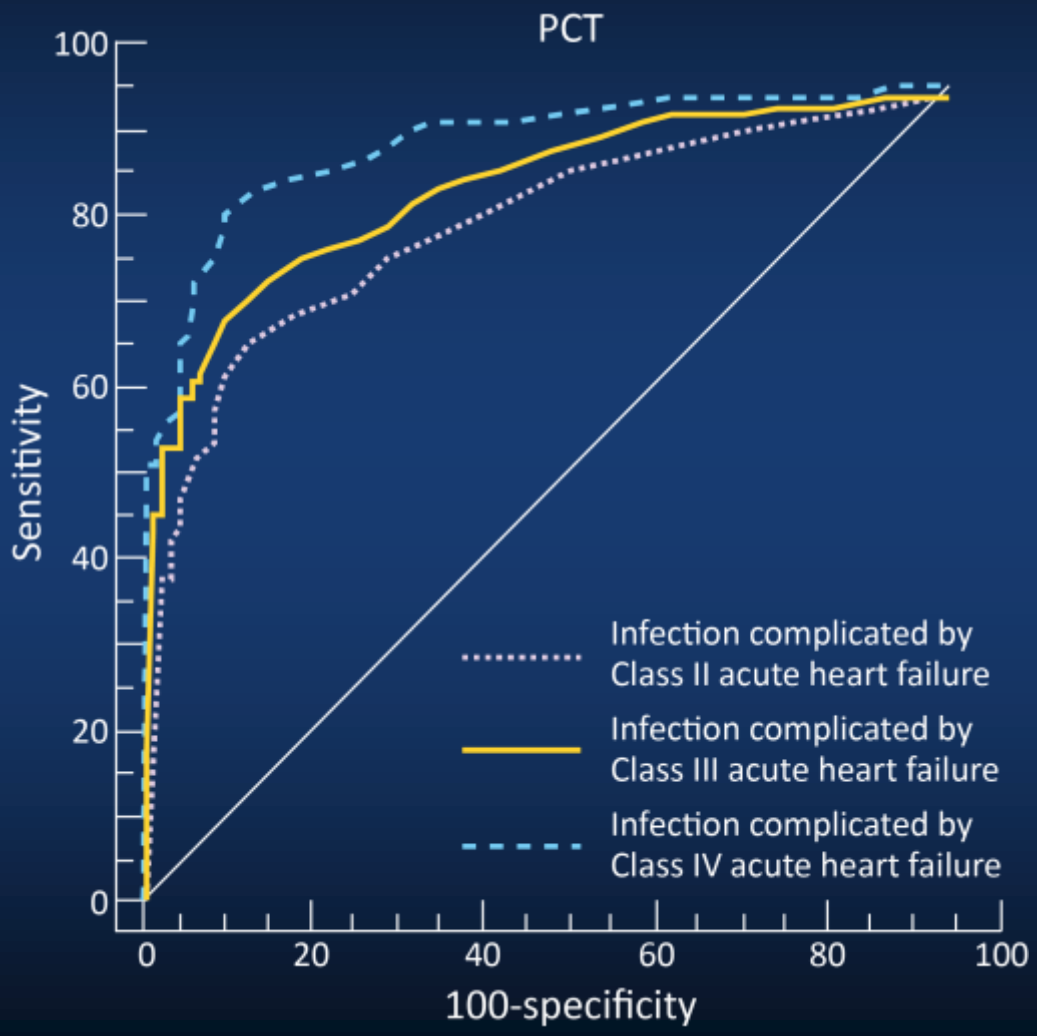
Fonarow et al. *Am J Cardiol* 2008;101:231-7.

Mechanism of Cardiac Troponin Release in Heart Failure



Kociol RD, et al. *J Am Coll Cardiol.* 2010;56:1071-1078.

Procalcitonin Testing for Diagnosis and Short-term Prognosis in Bacterial Infection Complicated by Congestive Heart Failure



- Receiver operating characteristic curve for procalcitonin (PCT)-based diagnosis of infections complicated by different classes of heart failure
- As depicted, PCT had high areas under the receiver operating characteristic curve in each heart failure group; however, the best cutoff values for each group were different

Wang W, et al. *Crit Care.* 2014;18(1):R4.

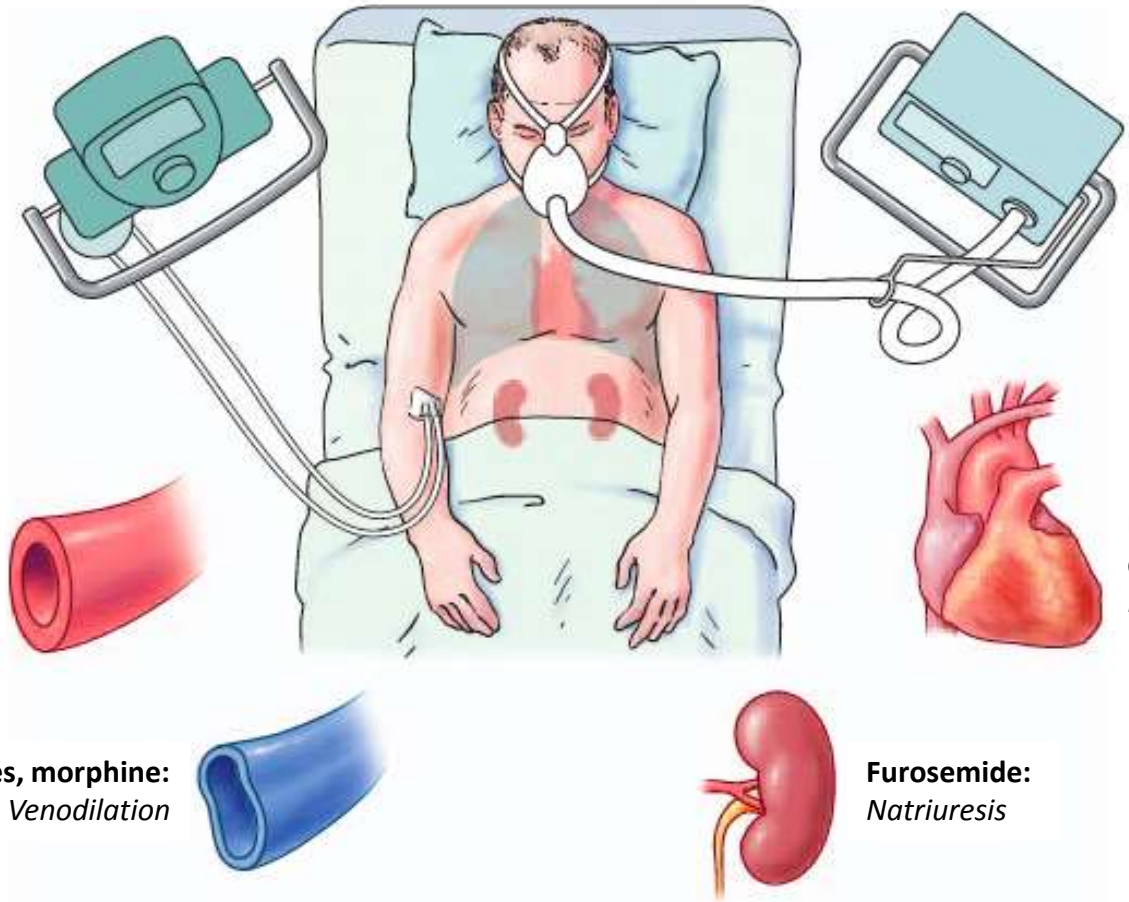
Triggers and Treatment for the Failing Heart

Overview of Acute Therapy

Ultrafiltration:
Aqua/natriuresis

Nitrates, nitroprusside, dobutamine:
Arterial vasodilation

Nitrates, morphine:
Venodilation



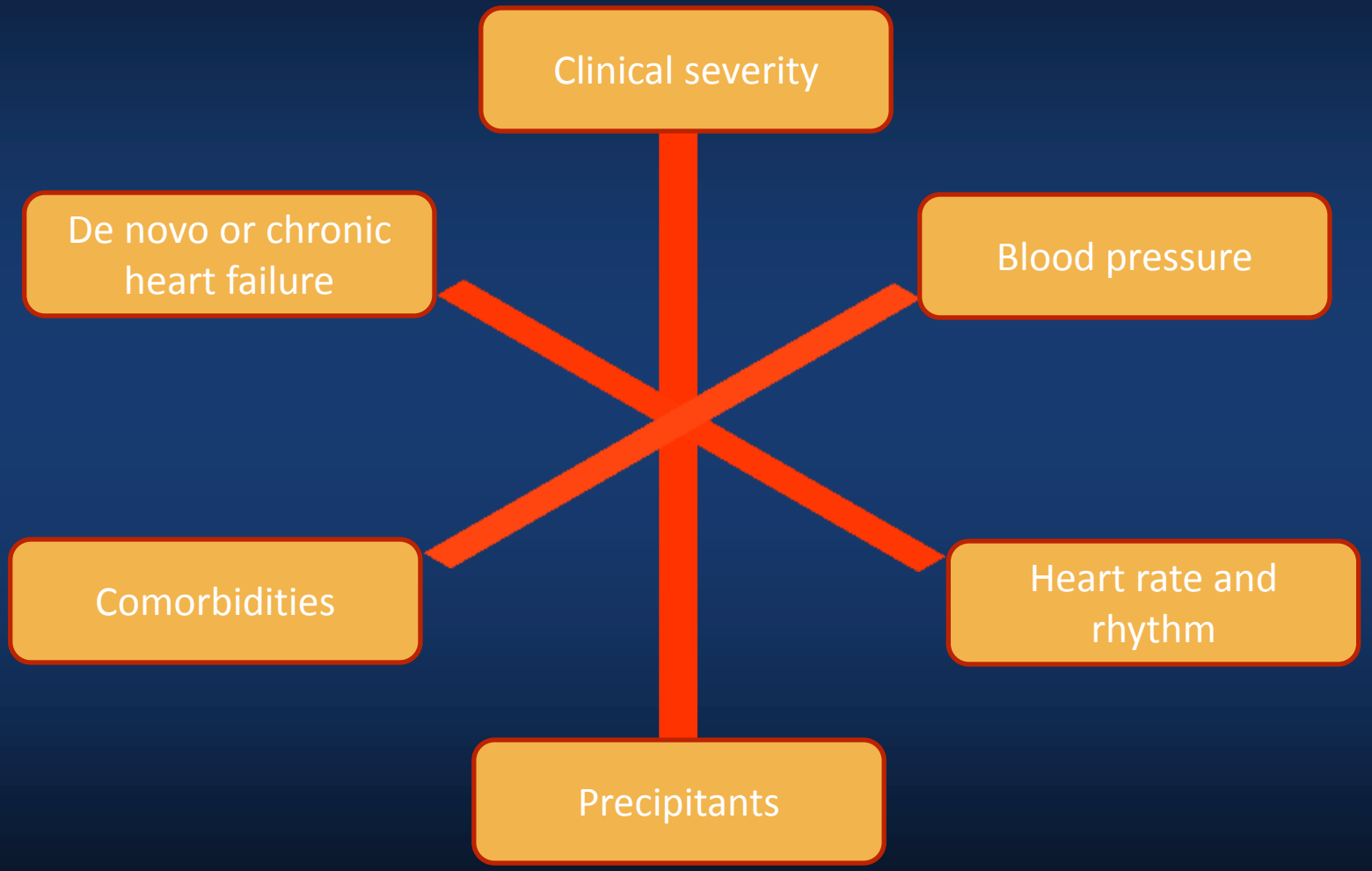
Bilevel or continuous positive airway pressure:
Preload reduction

Dobutamine, dopamine, milrinone:
Increased inotropy

Furosemide:
Natriuresis

Allen LA, O'Connor CM. *CMAJ* 2007;176:797-805.

A Proposed Model for Initial Assessment and Management of Acute Heart Failure Syndromes



Gheorghiade M, Braunwald E. *JAMA.* 2011;305:1702-1703.

ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012

Suspected Acute Heart Failure

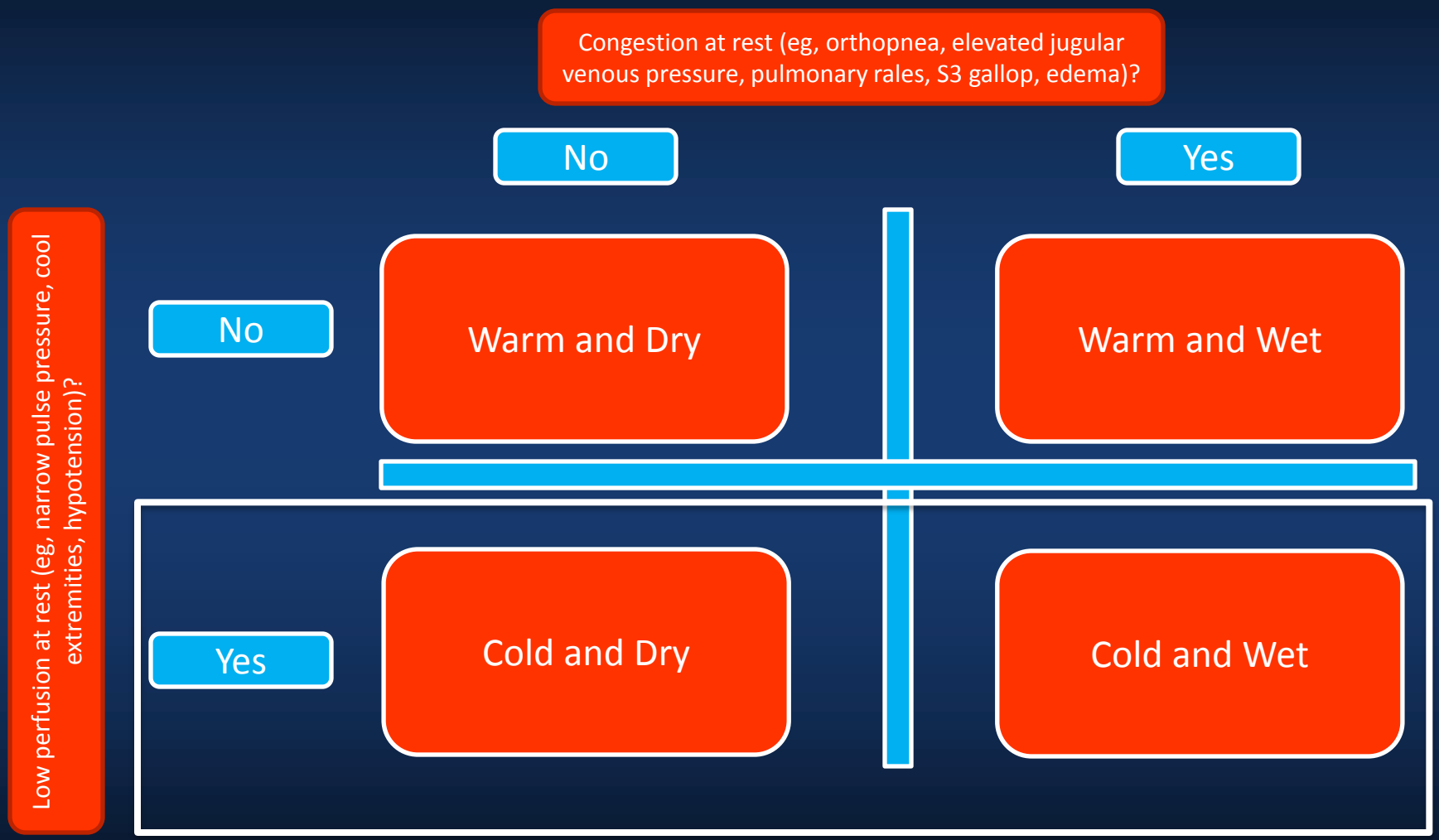
History/Exam (including blood pressure and respiratory rate)
Chest X-Ray
Echocardiogram or NP (or both)
Blood Chemistry
ECG
Oxygen Saturation
Complete Blood Count

Simultaneously assess for:	Ventilation/ systemic oxygenation inadequate?	Life-threatening arrhythmia/ bradycardia?	Blood pressure <85 mm Hg or shock	Acute coronary syndrome (ACS)	Acute mechanical cause/severe valvular disease
Urgent action if present:	- Oxygen - NIV - ETT and invasive ventilation	- Electrical cardioversion - Pacing	- Inotrope/ vasopressor - Mechanical circulatory support (eg, IABP)	- Coronary reperfusion - Antithrombotic therapy	- Echocardiography - Surgical/ percutaneous intervention

McMurray JJ, et al. *Eur Heart J*. 2012;14:803-869.

McMurray et al. Eur J Heart Fail 2012; 14:803–69.

Medical Management of Advanced Heart Failure



Adapted from: Nohria A, et al. *JAMA*. 2002;287:628-640.

ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 (cont'd)

Suspected Acute Heart Failure

History/Exam (including blood pressure and respiratory rate)
Chest X-Ray
Echocardiogram or NP (or both)
Blood Chemistry
ECG
Oxygen Saturation
Complete Blood Count

Simultaneously assess for:

Ventilation/ systemic oxygenation inadequate?	Life-threatening arrhythmia/ bradycardia?	Blood pressure <85 mm Hg or shock	Acute coronary syndrome (ACS)	Acute mechanical cause/severe valvular disease

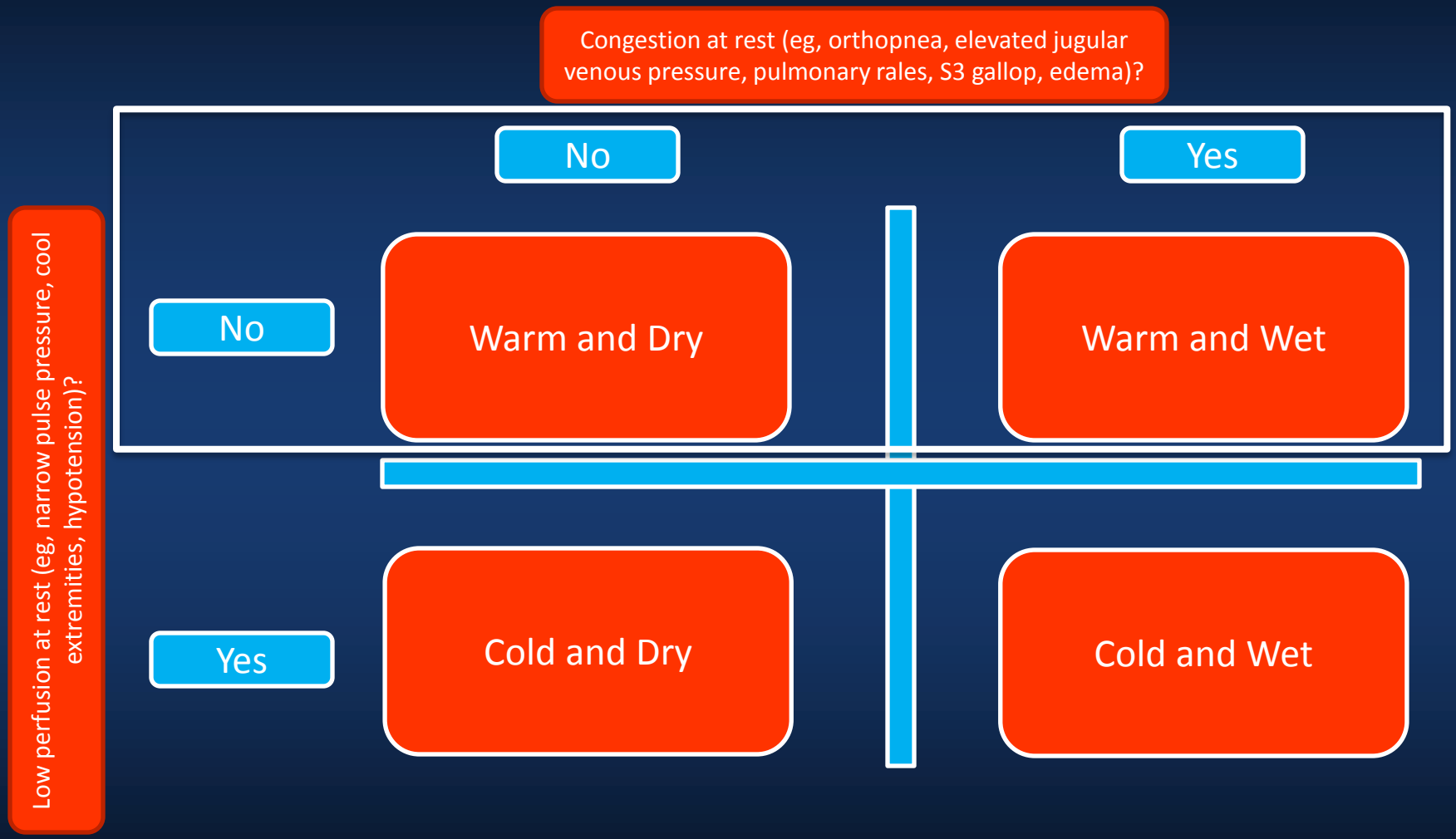
Urgent action if present:

- Oxygen - NIV - ETT and invasive ventilation	- Electrical cardioversion - Pacing	- Inotrope/ vasopressor - Mechanical circulatory support (eg, IABP)	- Coronary reperfusion - Antithrombotic therapy	- Echocardiography - Surgical/ percutaneous intervention

McMurray JJ, et al. *Eur Heart J*. 2012;14:803-869.

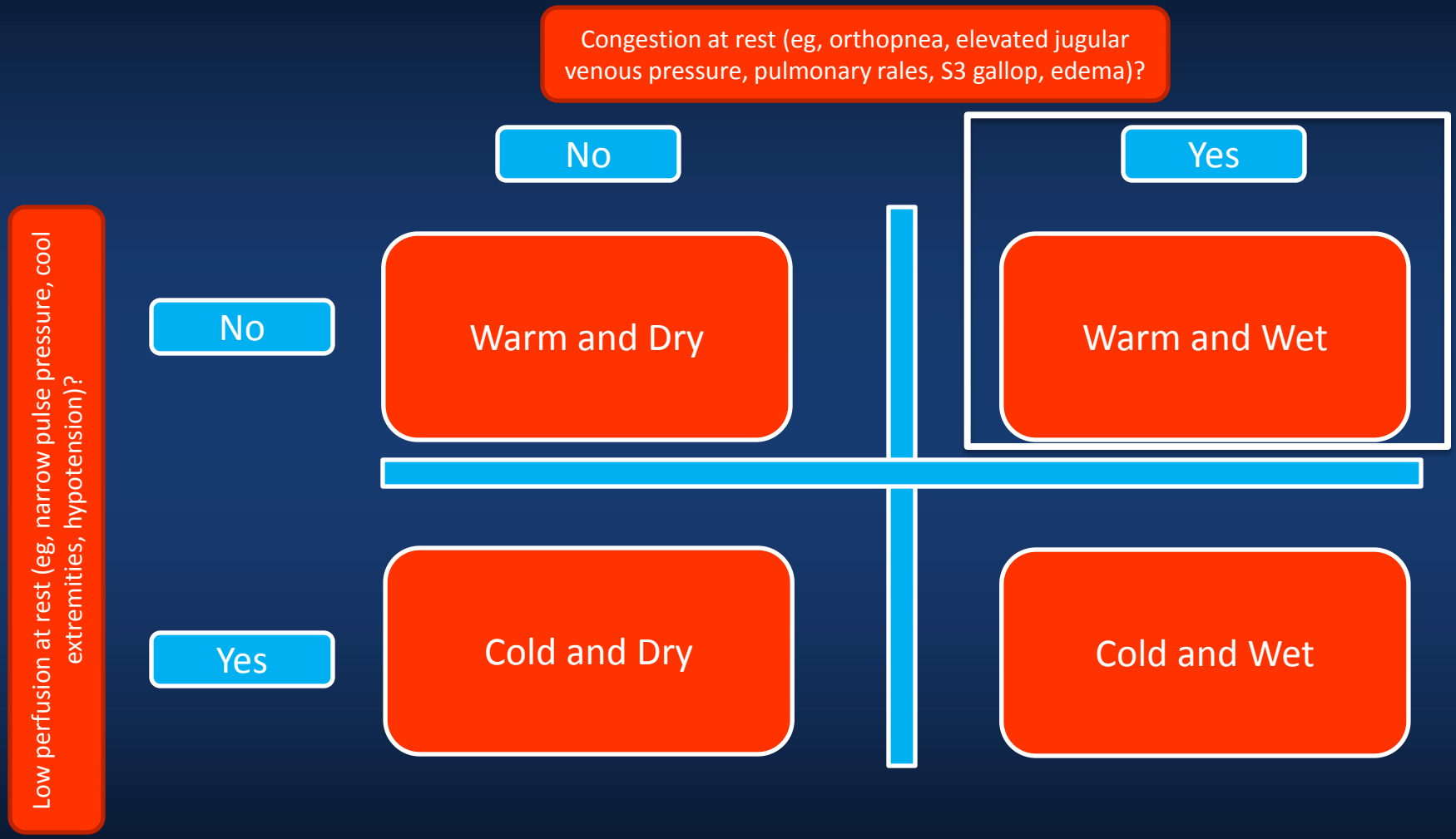
McMurray et al. Eur J Heart Fail 2012; 14:803–69.

Medical Management of Advanced Heart Failure (cont'd)



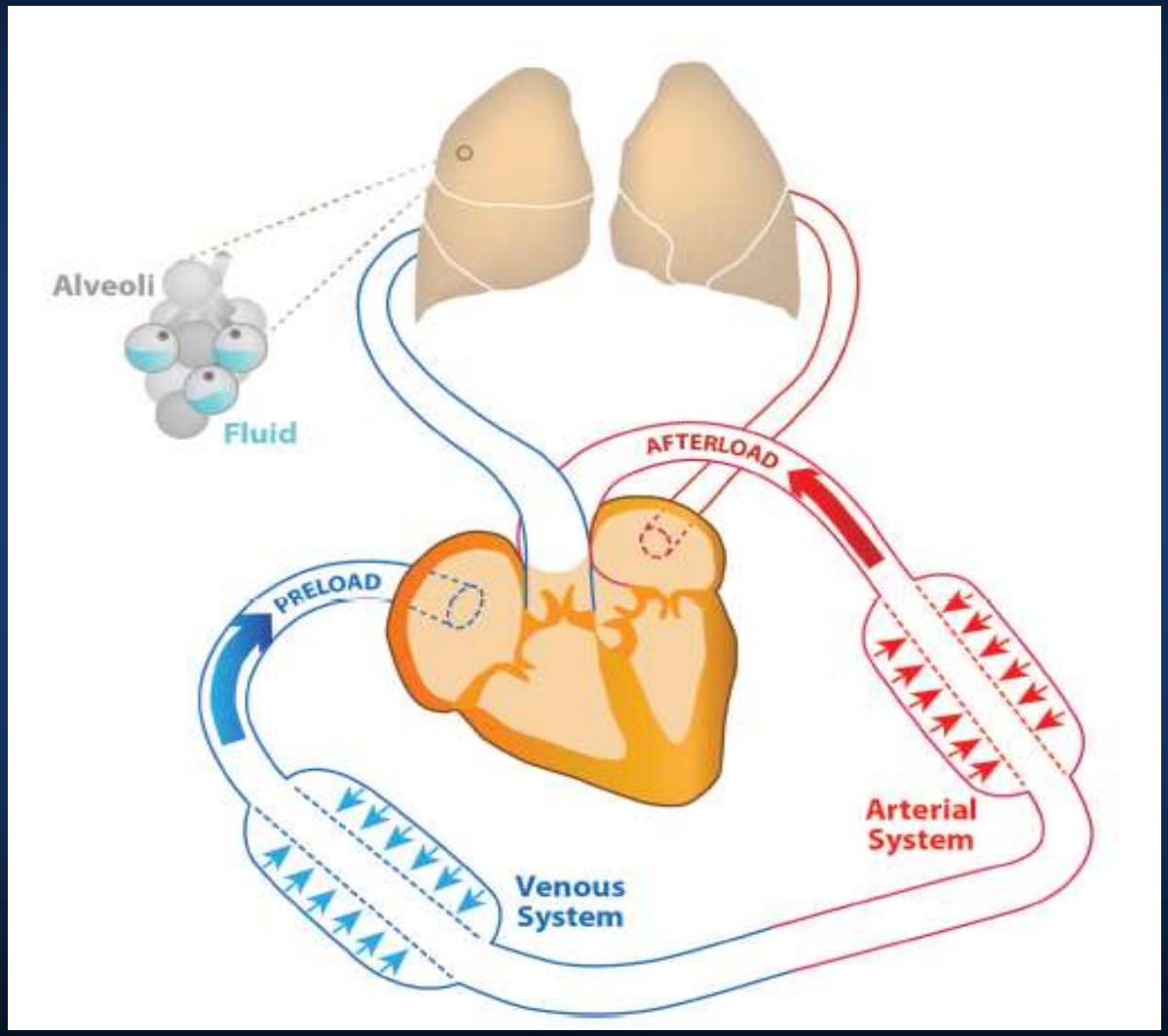
Adapted from: Nohria A, et al. *JAMA*. 2002;287:628-640.

Medical Management of Advanced Heart Failure (cont'd)



Adapted from: Nohria A, et al. *JAMA*. 2002;287:628-640.

The Pathophysiology of Acute Heart Failure



Viau DM, et al. *Heart*. 2015;101(23):1861-1867.

Normotensive Phenotype: Systolic Blood Pressure 100-140 mm Hg

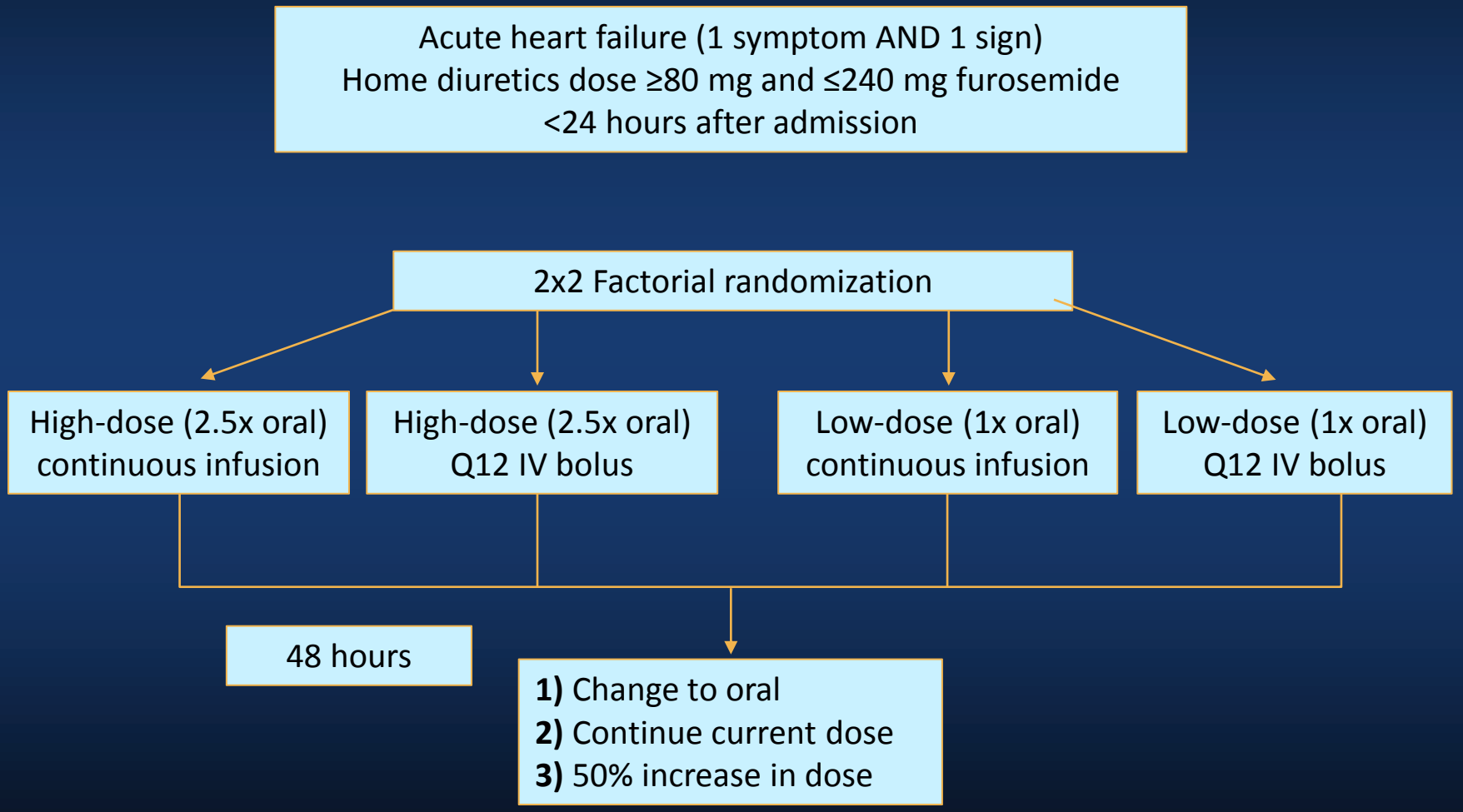
- Primary treatment
  - Diuresis
    - Furosemide
    - Bumetanide
    - Torsemide

Diuretic Dosing

- Furosemide
  - 40-mg intravenous (IV) push
  - Age + BUN
  - DOSE trial

BUN=blood urea nitrogen.

Diuretic Strategies in Patients With Acute Decompensated Heart Failure



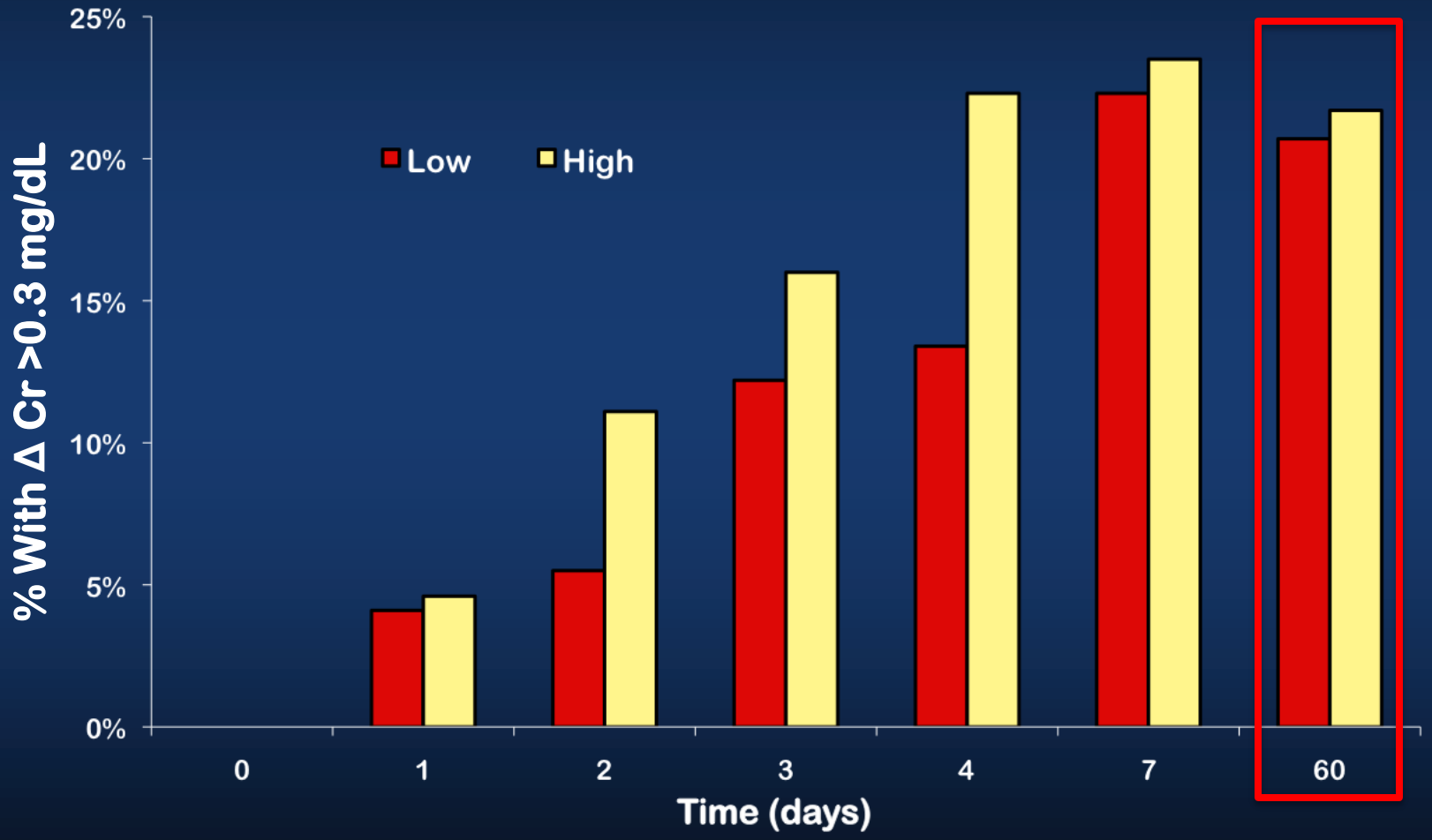
Felker GM, et al. *N Engl J Med.* 2011;364:797-805.

Diuretic Dosing

End Point	Bolus Every 12 Hours (N=156)	Continuous Infusion (N=152)	*P* Value	Low Dose (N=151)	High Dose (N=157)	*P* Value
AUC for dyspnea at 72 hours	4456±1468	4699±1573	0.36	4478±1550	4668±1496	0.04
Freedom from congestion at 72 hr No./total no. (%)	22/153 (14)	22/144 (15)	0.78	16/143 (11)	28/154 (18)	0.09
Change in weight at 72 hr (lb)	−6.8±7.8	−8.1±10.3	0.20	−6.1±9.5	−8.7±8.5	0.01
Net fluid loss at 72 hr (mL)	4237±3208	4249±3104	0.89	3575±2635	4899±3479	0.001
Change in NT-proBNP at 72 hr (pg/mL)	−1316±4364	−1773±3828	0.44	−1194±4094	−1882±4105	0.06
Worsening or persistent heart failure No./total no. (%)	38/154 (25)	34/145 (23)	0.78	38/145 (26)	34/154 (22)	0.40
Treatment failure No./total no. (%)	59/155 (38)	57/147 (39)	0.88	54/147 (37)	62/155 (40)	0.56
Increase in Cr of >0.3 mg/dL within 72 hr No./total no. (%)	27/155 (17)	28/146 (19)	0.64	20/147 (14)	35/154 (23)	0.04
Length of stay – hospital			0.97			0.55
Median (days)	5	5		6	5	
Interquartile range (days)	3-9	3-8		4-9	3-8	
Alive and out of the hospital			0.36			0.42
Median (days)	51	51		50	52	
Interquartile range (days)	42-55	38-55		39-54	42-56	

AUC=area under the curve; Cr=creatinine; NT-proBNP=N-Terminal pro-BNP (brain [or B-type] natriuretic peptide).
Felker GM, et al. N Engl J Med. 2011;364:797-805.

Worsening Renal Function Persistent in Both Groups



Felker GM, et al. *N Engl J Med.* 2011;364:797-805.

Hypertensive Phenotype: Systolic Blood Pressure >140 mm Hg

- Primary treatment
  - Nitrates
    - Topical/Sublingual (SL)
    - IV
- Secondary treatment
  - Diuretics

Nitrate Dosing

- Nitroglycerin (NTG)
  - Typical infusion range: 10-20 mcg/min
  - Increase by 5 mcg/min every 5 min as needed up to 400 mcg/min
- High dose
  - Repeat 2 mg bolus

	HD NTG	Controls	*P* Value
Mechanical vent	20.7%	46.7%	0.023
ICU admit	37.9%	80.0%	<0.001
Hospital LOS (days)	4.1±3.4	6.2±7.3	0.171
NSTEMI	17.2%	28.9%	0.254
Low BP	3.4%	0%	0.210

HD=high-dose; ICU=intensive care unit; LOS=length of stay; NSTEMI=non-ST-elevation myocardial infarction; BP=blood pressure.

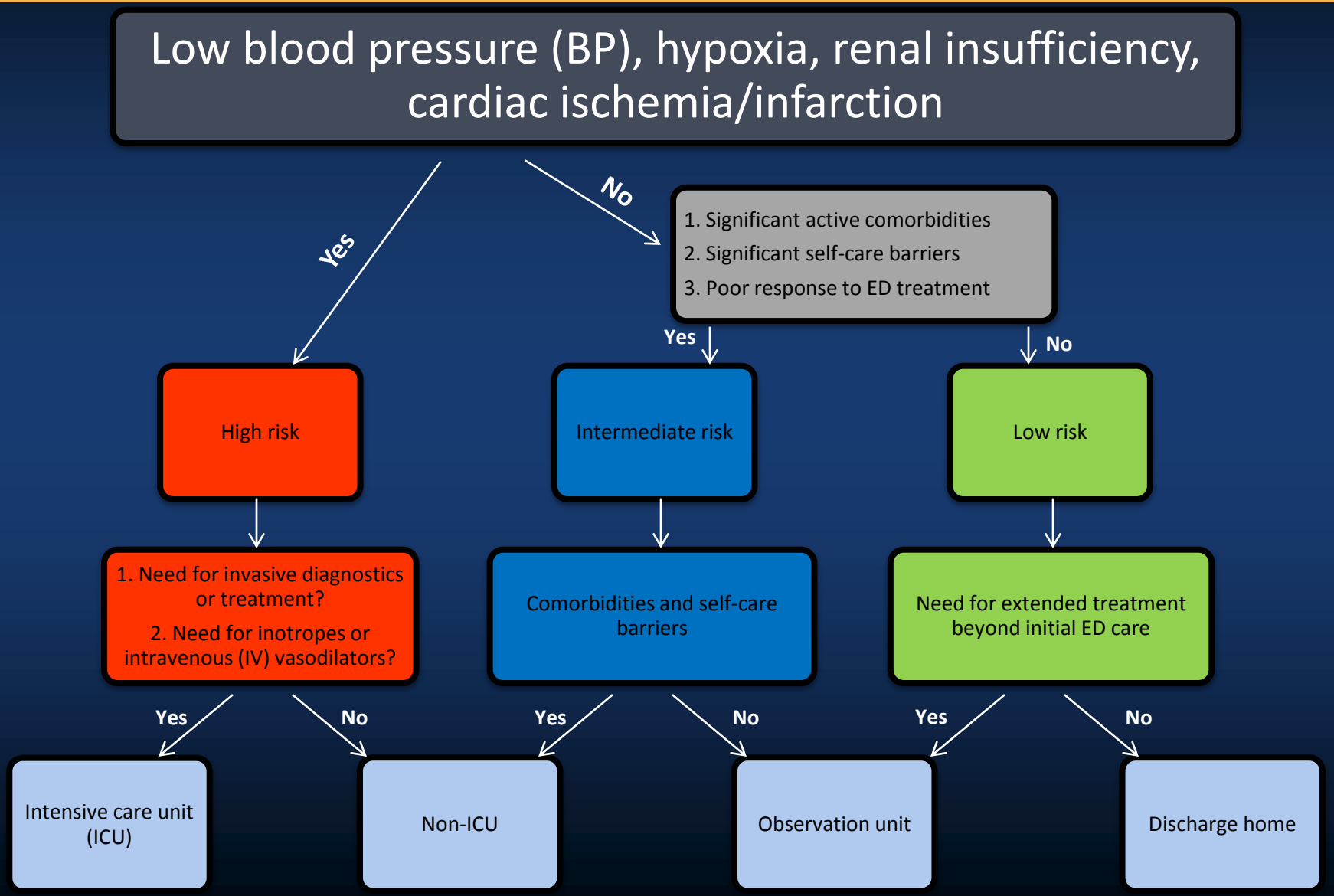
Levy P, et al. *Ann Emerg Med*. 2007;50:144-152.

Next-Generation Vasodilators?

- RELAX-AHF 2
  - Serelaxin
- TRUE AHF
  - Ularitide
- BLAST-AHF
  - TRV027
- PRONTO
  - Clevidipine

Disposition

Acute Heart Failure in the Emergency Department (ED)



Collins SP, et al. *Acad Emerg Med*. 2015;22:94-112.

Sample Observation Unit Protocol

- SBP >160 mm Hg
- Duration of symptoms: 24-48 h
- Euvolemic/mild hypervolemic

Observation unit monitoring
- Continuous-pulse oxygen and ECG
- Weigh patient
- Intake & output
- Fluid restriction (2000 mL/d)
- 2-g sodium diet
- Place on home dose of ACEI/ARB and β-blocker
- Consider echocardiogram

- SBP 100-160 mm Hg
- Duration of symptoms: days to weeks
- Hypervolemic

- Vasodilator NTG 0.4 mg, SL q5min x 3 doses then NTP 1"-2"
- Diuretic (moderate dose)

Treatment

- Diuretic (aggressive dose)
- Consider vasodilator if hypertensive

Reassess every 4 to 6 hours

Improved
- Good urine output
- SBP normalized at 100-120 mm Hg
- Improved symptoms
- Serum sodium >135 mEq/L

Partial response
- Consider repeat diuretic
- Consider IV vasodilator

Worse
- Poor urine output
- SBP <90 mm Hg or >160 mm Hg
- Increased symptoms
- Serum sodium <135 mEq/L

Discharge, prescribe, and document
- ACEI/ARB (LVEF <40%)
- β-blocker
- Education
- Aftercare

Admit to hospital

Fermann GJ, Collins SP. *Curr Heart Fail Rep.* 2010;7:125-133.

Inpatient Management

Therapeutic Goals

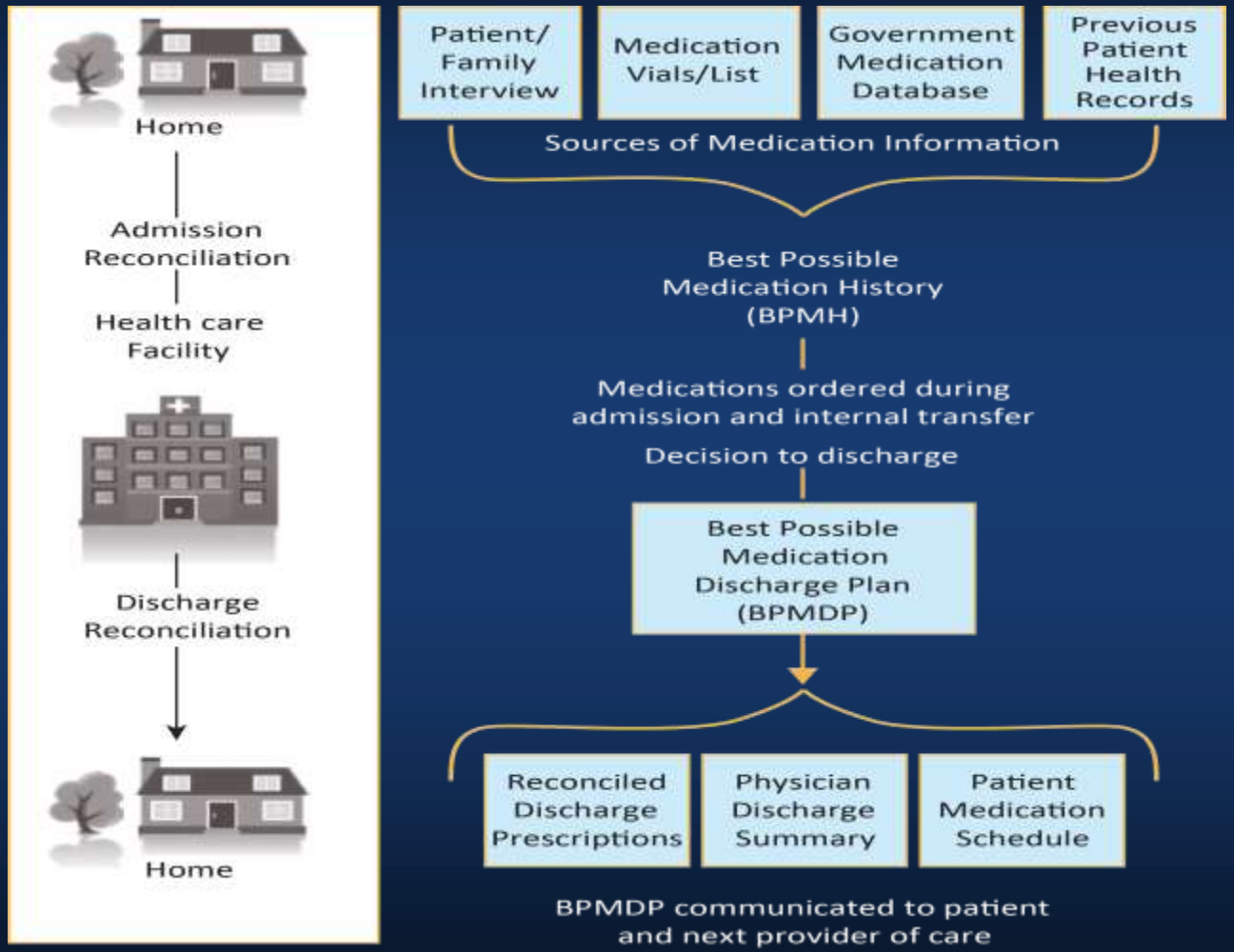
- Stabilization phase (first 24-48 hours)
  - Improve symptoms
  - Balance hemodynamics
  - Achieve euvolemia
  - ***Avoid harm!***
    - Myocyte injury
    - Renal damage
- Implementation phase (>48 hours)
  - Initiate lifesaving interventions
    - Angiotensin-converting enzyme (ACE) inhibitors, β-blockers, etc

Gheorghiade M, et al. *Am J Cardiol.* 2005;96(suppl):11G-17G.

Stabilization Phase

- Achieve euvolemia
  - Adjust dose/frequency of diuretics as needed
- Monitoring
  - Standing weight
  - Intake and output (I & O)
  - Heart and lung exam
  - Electrolytes and renal function
  - Telemetry
  - Serial inferior vena cava (IVC) measurements/IVC collapsibility index (IVCCI)
- Ensure proper medication reconciliation on admission

Medication Reconciliation During Transitions of Care as a Patient Safety Strategy

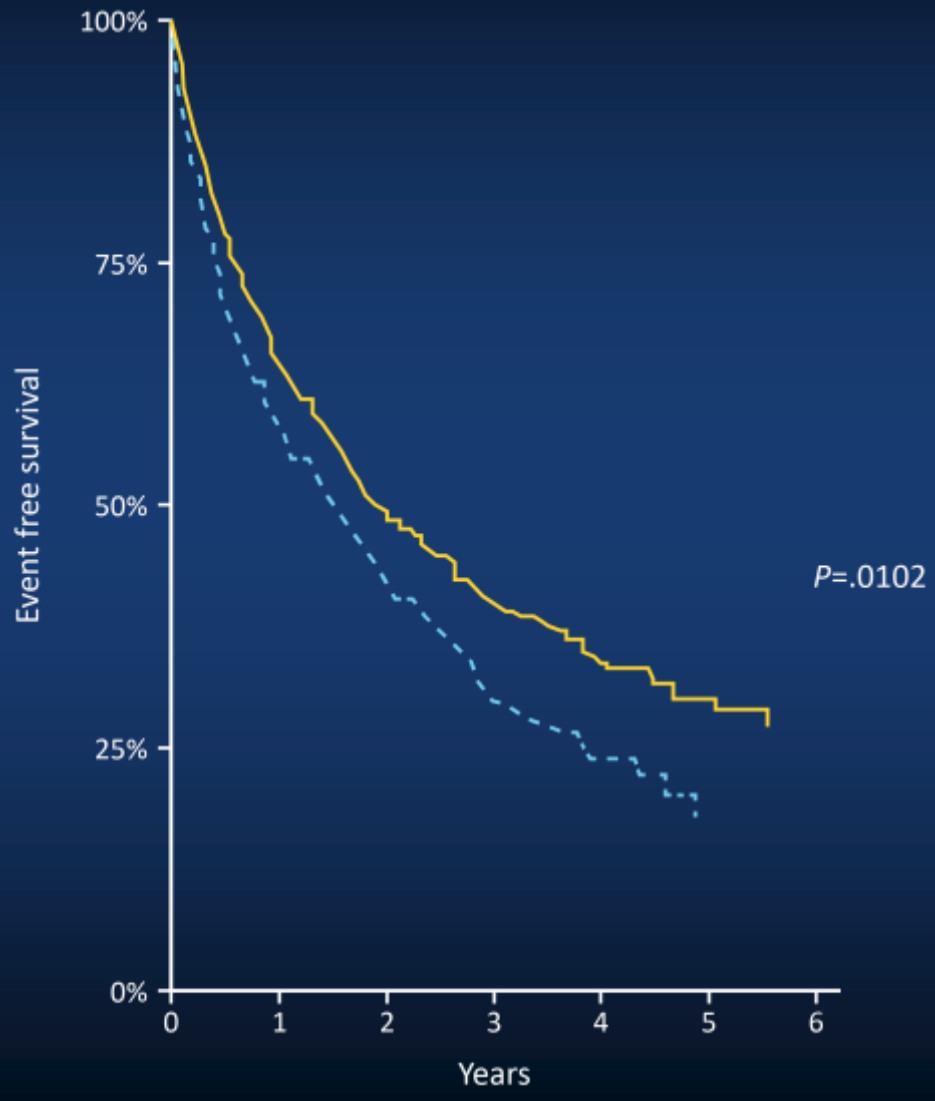


Kwan JL, et al. *Ann Intern Med.* 2013;158(5 part 2):397-403.

Stabilization Phase

- Identify trigger of exacerbation
  - Nonadherence to diet
  - Nonadherence to medications
  - Progression of disease
  - Ischemia
  - Arrhythmia

Impact of Medication Nonadherence on Hospitalizations and Mortality in Heart Failure



Fitzgerald AA, et al. *J Card Fail.* 2011;17(8):664-669.

If Not Improving, Reassess Diagnosis

10 Most Common Pairs of Discrepant Admission and Primary Discharge Diagnosis Codes			
Admission Diagnosis		**Principal Discharge Diagnosis**	
Code	**Description**	**Code**	**Description**
786.05	Shortness of breath	428.08	Congestive heart failure, unspecified
786.50	Chest pain, unspecified	786.59	Chest pain, other
786.05	Shortness of breath	486	Pneumonia, organism unspecified
780.6	Fever	486	Pneumonia, organism unspecified
780.6	Fever	996.62	Infection and inflammatory reaction due to other vascular device, implant, or graft
789.00	Abdominal pain, unspecified site	577.0	Acute pancreatitis
780.6	Fever	599.0	Urinary tract infection, site not specified
786.05	Shortness of breath	491.21	Obstructive chronic bronchitis with acute exacerbation
786.05	Shortness of breath	415.19	Pulmonary embolism and infarction, other
786.05	Shortness of breath	493.22	Chronic obstructive asthma with acute exacerbation

Johnson TM, et al. *J Hosp Med*. 2009;4(4):234-239.

Implementation Phase: Long-term Therapy

At Risk for Heart Failure (HF)

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

eg, Patients with:
- Hypertension (HTN)
- Atherosclerotic disease
- Diabetes mellitus (DM)
- Obesity
- Metabolic syndrome

or

Patients:
- Using cardiotoxins
- With family history of cardiomyopathy

THERAPY

Goals
- Heart-healthy lifestyle
- Prevent vascular, coronary disease
- Prevent LV structural abnormalities

Drugs
- ACEI or ARB in appropriate patients for vascular disease or DM
- Statins as appropriate

Structural heart disease

STAGE B
Structural heart disease but without signs or symptoms of HF

eg, Patients with:
- Previous MI
- LV remodeling, including LV hypertrophy (LVH) and low EF
- Asymptomatic valvular disease

THERAPY

Goals
- Prevent HF symptoms
- Prevent further cardiac remodeling

Drugs
- ACEI or ARB as appropriate
- Beta-blockers as appropriate

In selected patients
- Implantable cardioverter-defibrillator (ICD)
- Revascularization or valvular surgery as appropriate

Development of symptoms of HF

Heart Failure

STAGE C
Structural heart disease with prior or current symptoms of HF

eg, Patients with:
- Known structural heart disease, *and*
- HF signs and symptoms

HF*p*EF

THERAPY

Goals
- Control symptoms
- Improve HRQoL
- Prevent hospitalization
- Prevent mortality

Strategies
- Identification of comorbidities

Treatment
- Diuresis to relieve symptoms of congestion
- Follow guideline-driven indications for comorbidities, eg, HTN, AF, CAD, DM
- Revascularization or valvular surgery as appropriate

HF*r*EF

THERAPY

Goals
- Control symptoms
- Patient education
- Prevent hospitalization
- Prevent mortality

Drugs for routine use
- Diuretics for fluid retention
- ACEI or ARB
- Beta-blockers
- Aldosterone antagonists

Drugs for use in selected patients
- Hydralazine/isosorbide dinitrate
- ACEI and ARB
- Digoxin

In selected patients
- CRT
- ICD
- Revascularization or valvular surgery as appropriate

Refractory symptoms of HF at rest despite GDMT

STAGE D
Refractory HF

eg, Patients with:
- Marked HF symptoms at rest
- Recurrent hospitalizations despite guideline-determined medical therapy (GDMT)

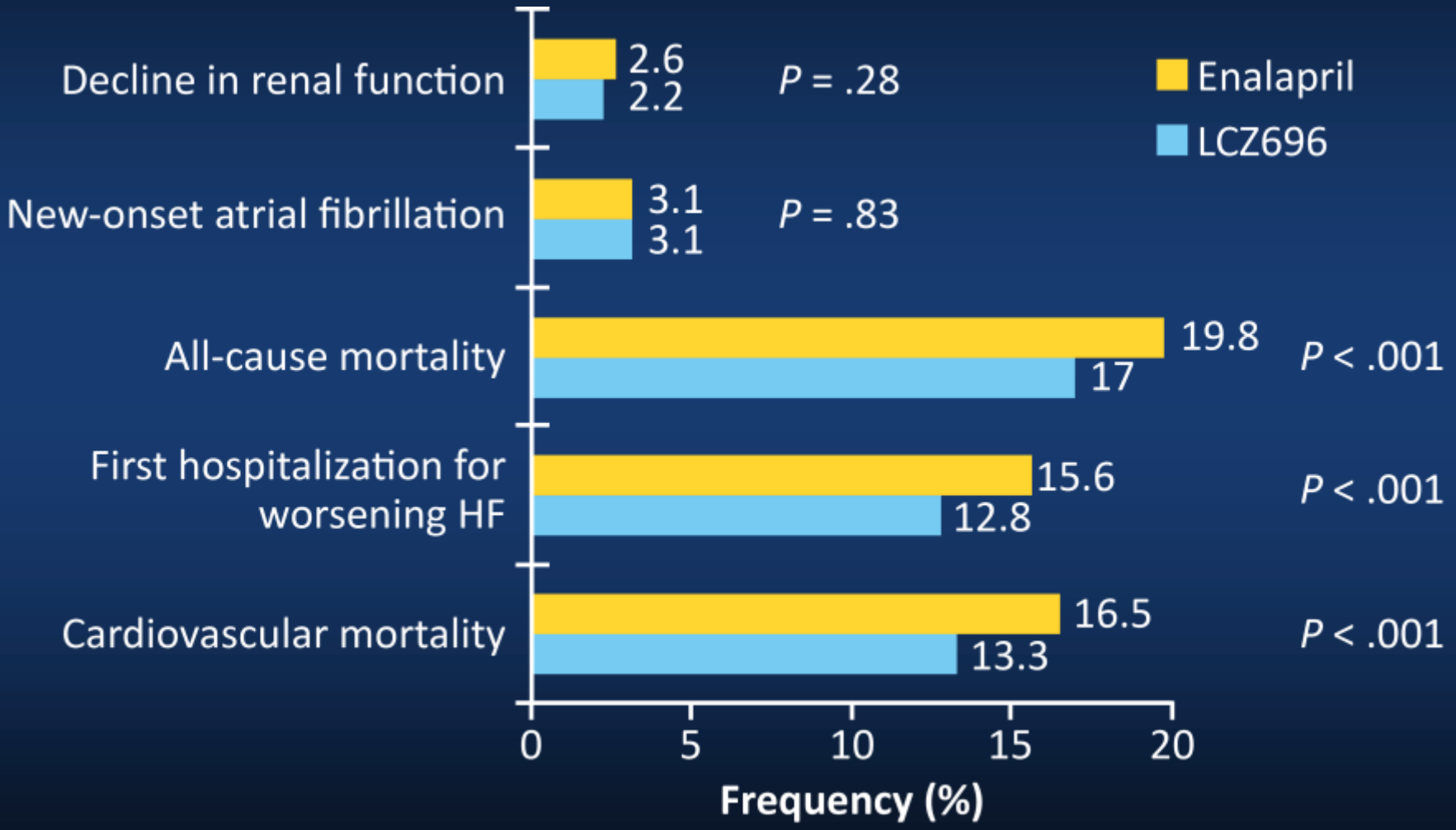
THERAPY

Goals
- Control symptoms
- Improve HRQoL
- Reduce hospital readmissions
- Establish patient's end-of-life goals

Options
- Advanced care measures
- Heart transplant
- Chronic inotropes
- Temporary or permanent mechanical circulatory support (MCS)
- Experimental surgery or drugs
- Palliative care and hospice
- ICD deactivation

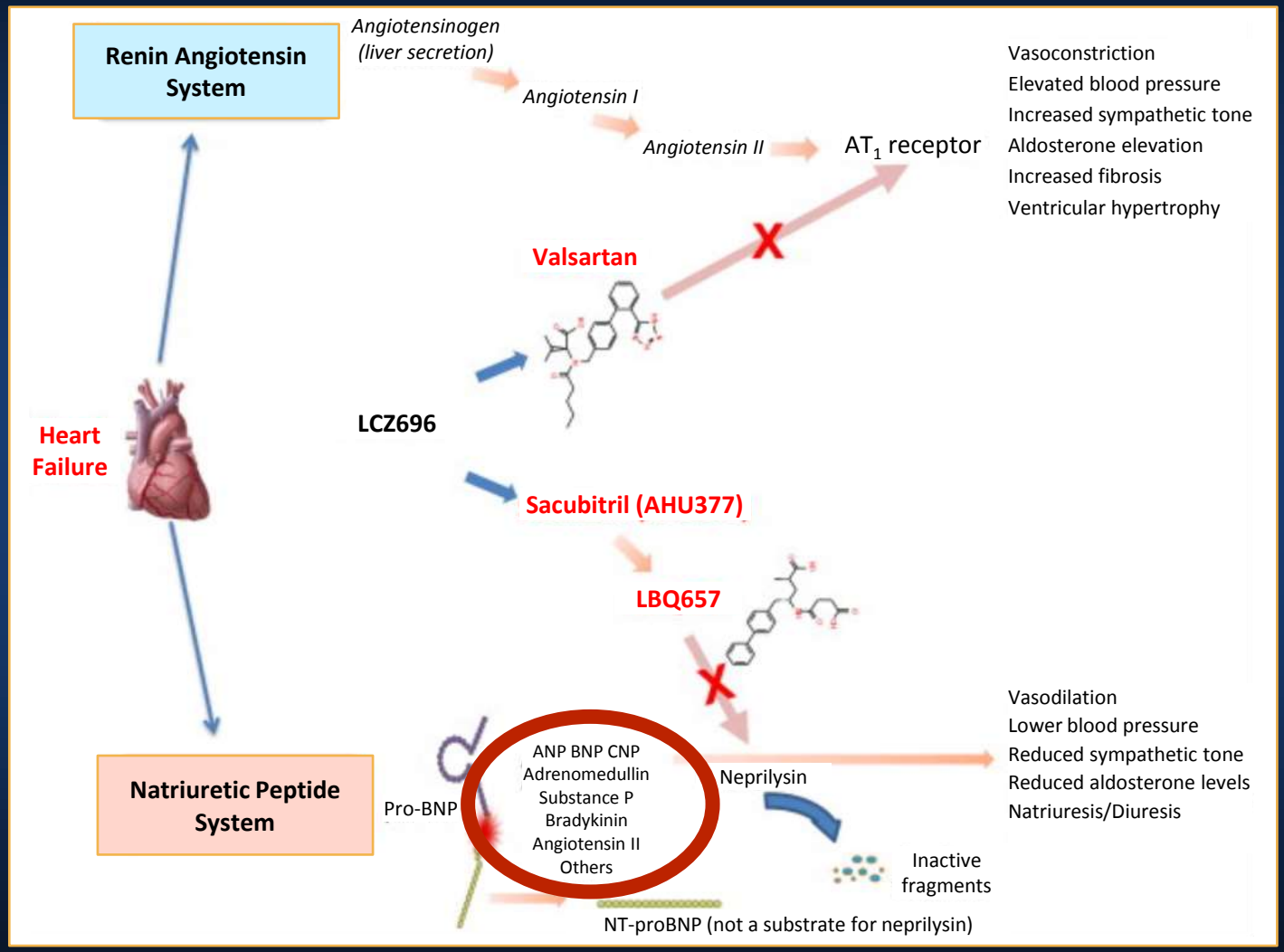
Yancy CW, et al. *J Am Coll Cardiol*. 2013;62(16):e147-e239.

Primary and Secondary Outcomes in the PARADIGM-HF Clinical Trial



Minguet J, at al. *Exp Opin Pharmacother*. 2015;16,:435-446.

Sacubitril/Valsartan



Vardeny O, et al. *JACC Heart Fail*. 2014;2(6):663-670.

Discharge Planning

Is this patient medically ready for discharge today?

When to Discharge?

BNP, IVC Size, Collapsibility in All Patients and 2 Subgroups

	All Patients			Admission			Discharge		
	Admission	Discharge	*P* Value	No Readmit	Readmit	*P* Value	No Readmit	Readmit	*P* Value
BNP (pg/mL)	6139 (9714)	3497 (4824)	-	6177 (10,091)	5982 (9208)	-	2106 (3298)	4888 (5112)	-
logBNP	3.8±0.5	3.5±0.6	<.001	3.7±0.6	3.8±0.5	.28	3.3±0.7	3.6±0.4.0	.04
IVCmax (cm)	2.3±0.5	2.0±0.6	<.001	2.2±0.5	2.4±0.4	.02	1.7±0.6	2.3±0.5	.001
IVCsniff (cm)	1.7±0.7	1.2±0.8	<.001	1.5±0.7	1.9±0.6	.03	0.9±0.7	1.5±0.7	<.001
IVCCI (%)	27±21	45±27	<.001	31±23	23±16	.10	57±27	36±22	.002

BNP=brain natriuretic peptide; IVC=inferior vena cava; IVCCI=inferior vena cava collapsibility index; IVCmax=maximum diameter of the inferior vena cava; IVCsniff=minimum diameter of the inferior vena cava; logBNP=log-transformed values for brain natriuretic peptide.

Goonewardena AN, et al. *JACC Cardiovasc Imaging*. 2008;1(5):595-601.

Factors Associated With Readmission Preventability as Determined by Patient Opinion

Variable	No. (%) Total Sample (N=98)	Preventable Readmission or Undecided (n=30)	Nonpreventable Readmission (n=68)	*P* Value
Felt they were discharged before ready	**(n=96)**	**(n=29)**	**(n=67)**	<.001
No	67 (70)	9 (31)	58 (87)	
Yes	29 (30)	20 (69)	9 (13)	
Felt all concerns were addressed before discharge	**(n=93)**	**(n=27)**	**(n=66)**	<.001
No	28 (30)	18 (67)	10 (15)	
Yes	65 (70)	9 (33)	56 (85)	

Howard-Anderson J, et al. *JAMA Intern Med.* 2014;174(11):1870-1872

Howard-Anderson et al. JAMA Internal Medicine 2014 [10.1001/jamainternmed.2014.4782].

Clear Discharge Instructions

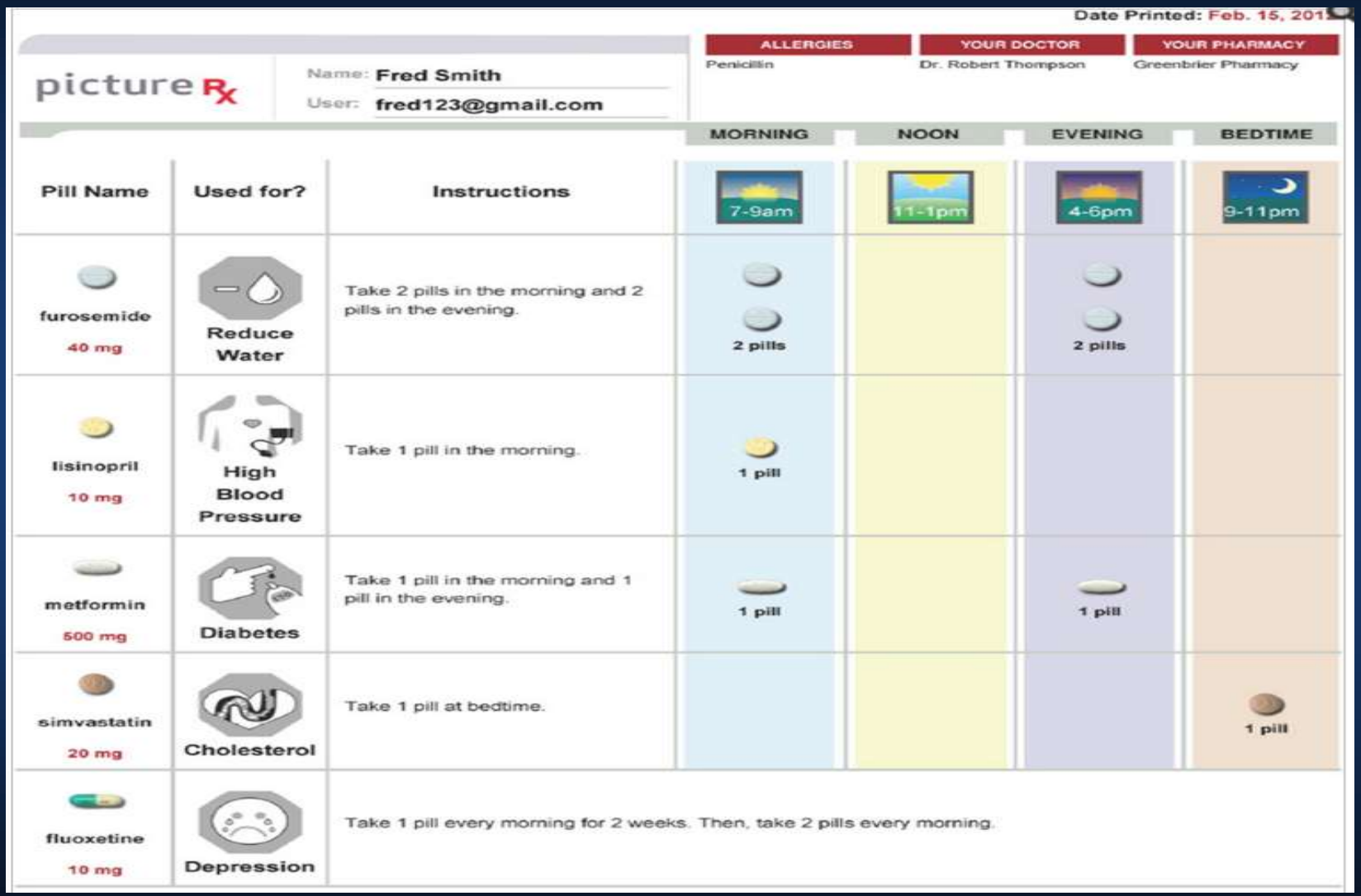
PICTOGRAPHS WITH THE NON-WEIGHTED LOWEST SCORES	Non-Weighted Score	Source
 Diabetes Education	8%	RWJF
 Social Service	24%	RWJF
 Outpatient	30%	RWJF

PICTOGRAPHS WITH THE HIGHEST NON-WEIGHTED SCORES	Non-Weighted Score	Source
 Take this drug with food	100%	Authors
 Do not drink more than 2 liters of fluid per day	100%	Authors
 Do not operate any machinery while taking this drug	96%	Authors

Pictographs with the lowest and highest recognition scores

Atkinson N, et al. *J Med Internet Res*. 2009;11(1):e4.

Discharge Medication Reconciliation



Date Printed: Feb. 15, 201

picture Rx

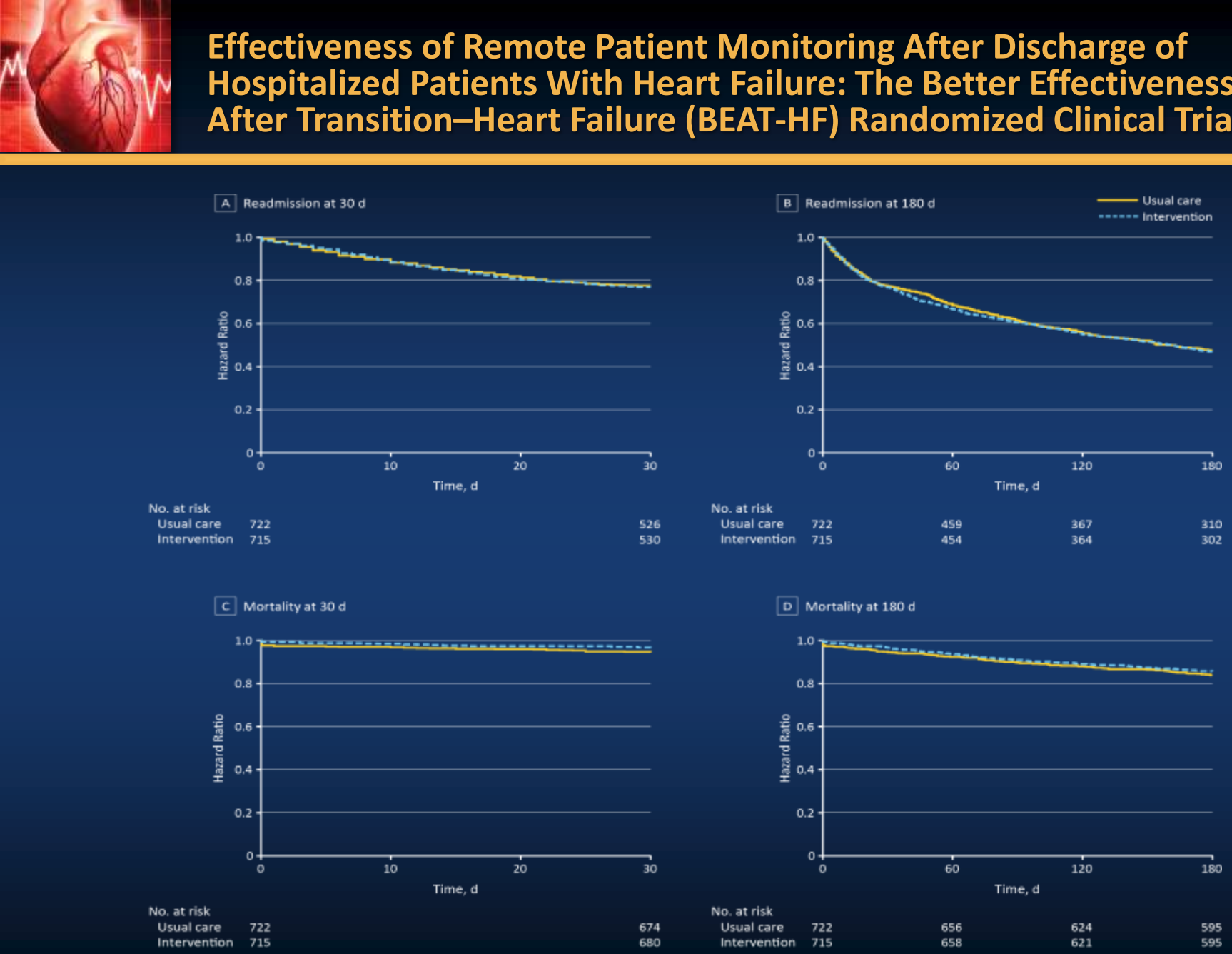
Name: Fred Smith
User: fred123@gmail.com

ALLERGIES	YOUR DOCTOR	YOUR PHARMACY
Penicillin	Dr. Robert Thompson	Greenbrier Pharmacy

Pill Name	Used for?	Instructions	MORNING 7-9am	NOON 11-1pm	EVENING 4-6pm	BEDTIME 9-11pm
furosemide 40 mg	Reduce Water	Take 2 pills in the morning and 2 pills in the evening.	2 pills		2 pills	
lisinopril 10 mg	High Blood Pressure	Take 1 pill in the morning.	1 pill			
metformin 500 mg	Diabetes	Take 1 pill in the morning and 1 pill in the evening.	1 pill		1 pill	
simvastatin 20 mg	Cholesterol	Take 1 pill at bedtime.				1 pill
fluoxetine 10 mg	Depression	Take 1 pill every morning for 2 weeks. Then, take 2 pills every morning.				

Martin D, et al. *J Gerontol Nurs.* 2012;38(6):24-37.

Effectiveness of Remote Patient Monitoring After Discharge of Hospitalized Patients With Heart Failure: The Better Effectiveness After Transition–Heart Failure (BEAT-HF) Randomized Clinical Trial



Ong MK, et al. *JAMA Intern Med.* 2016;176(3):310-318.

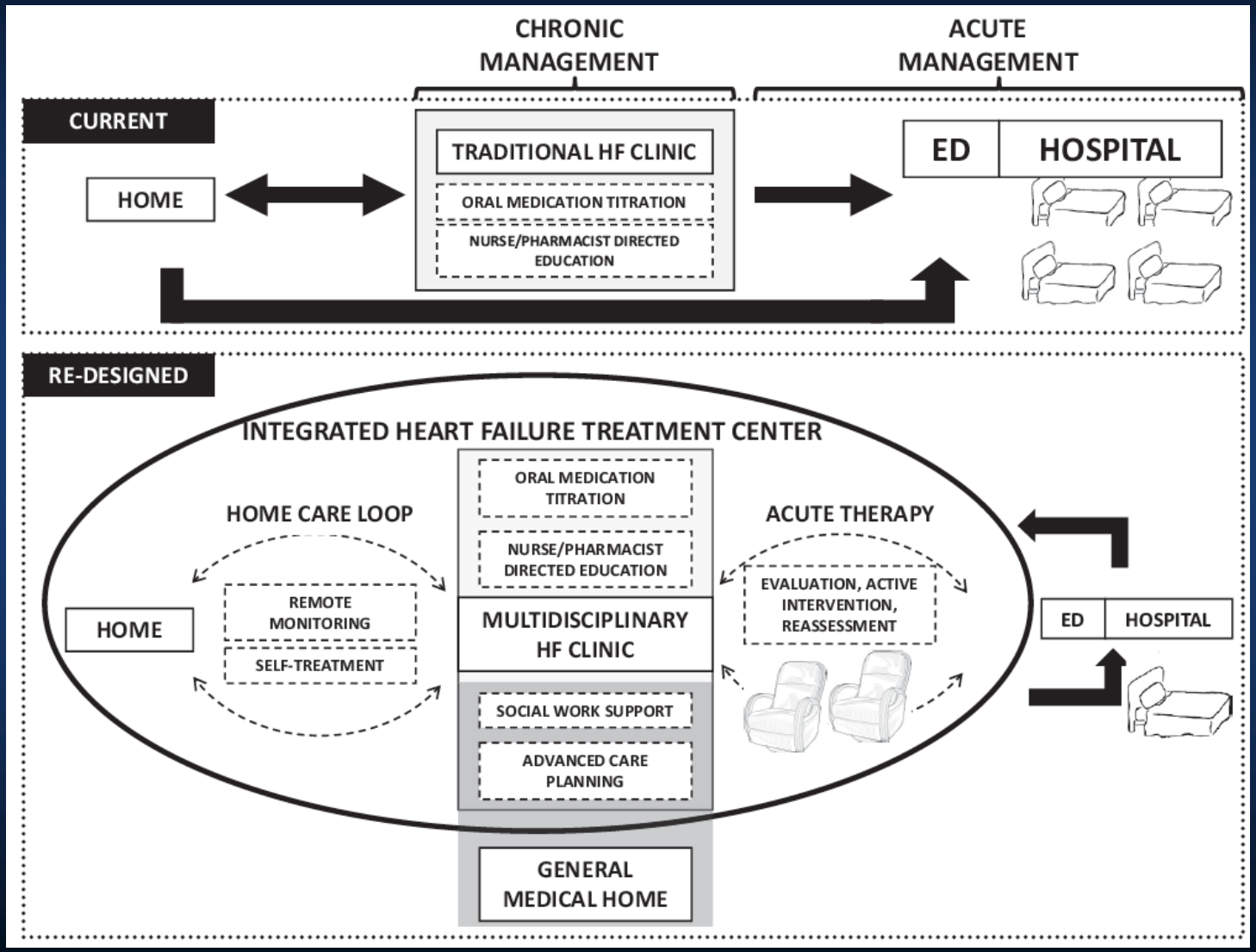
Unadjusted and Adjusted Relationships Between Early Physician Follow-up by Quartile and 30-Day All-Cause Readmission

Quartile (% of follow-up)	Unadjusted HR (95% CI)	*P* Value	Adjusted HR (95% CI)	*P* Value
Model 1: Early follow-up with a physician				
1 (<32.4)	1 [reference]		1 [reference]	
2 (32.4-37.9)	0.86 (0.78-0.94)	.001	0.85 (0.78-0.93)	<.001
3 (38.3-44.5)	0.85 (0.76-0.94)	.002	0.87 (0.78-0.96)	.005
4 (>44.5)	0.87 (0.79-0.95)	.002	0.91 (0.83-1.00)	.05
Model 2: Early follow-up with a cardiologist				
1 (<4.1)	1 [reference]		1 [reference]	
2 (4.1-7.4)	0.91 (0.82-1.02)	.09	0.92 (0.83-1.02)	.09
3 (7.5-13.8)	0.91 (0.82-1.00)	.05	0.91 (0.82-1.00)	.05
4 (>13.8)	0.91 (0.82-1.00)	.06	0.95 (0.85-1.05)	.30
Model 3: Early follow-up with the same physician				
1 (<13.5)	1 [reference]		1 [reference]	
2 (13.5-17.5)	0.93 (0.84-1.04)	.20	0.96 (.86-1.05)	.36
3 (18.1-24.1)	0.91 (0.81-1.02)	.11	0.94 (0.84-1.04)	.23
4 (>24.1)	0.93 (0.83-1.03)	.16	0.97 (0.87-1.08)	.54
Model 4: 14-Day follow-up with a physician				
1 (<56.6)	1 [reference]		1 [reference]	
2 (56.6-64.5)	0.88 (0.80-0.97)	.01	0.89 (0.81-0.97)	.01
3 (64.6-70.0)	0.87 (0.78-0.97)	.009	0.90 (0.81-1.00)	.04
4 (>70.0)	0.87 (0.79-0.96)	.004	0.93 (0.84-1.02)	.13

HR=hazard ratio.

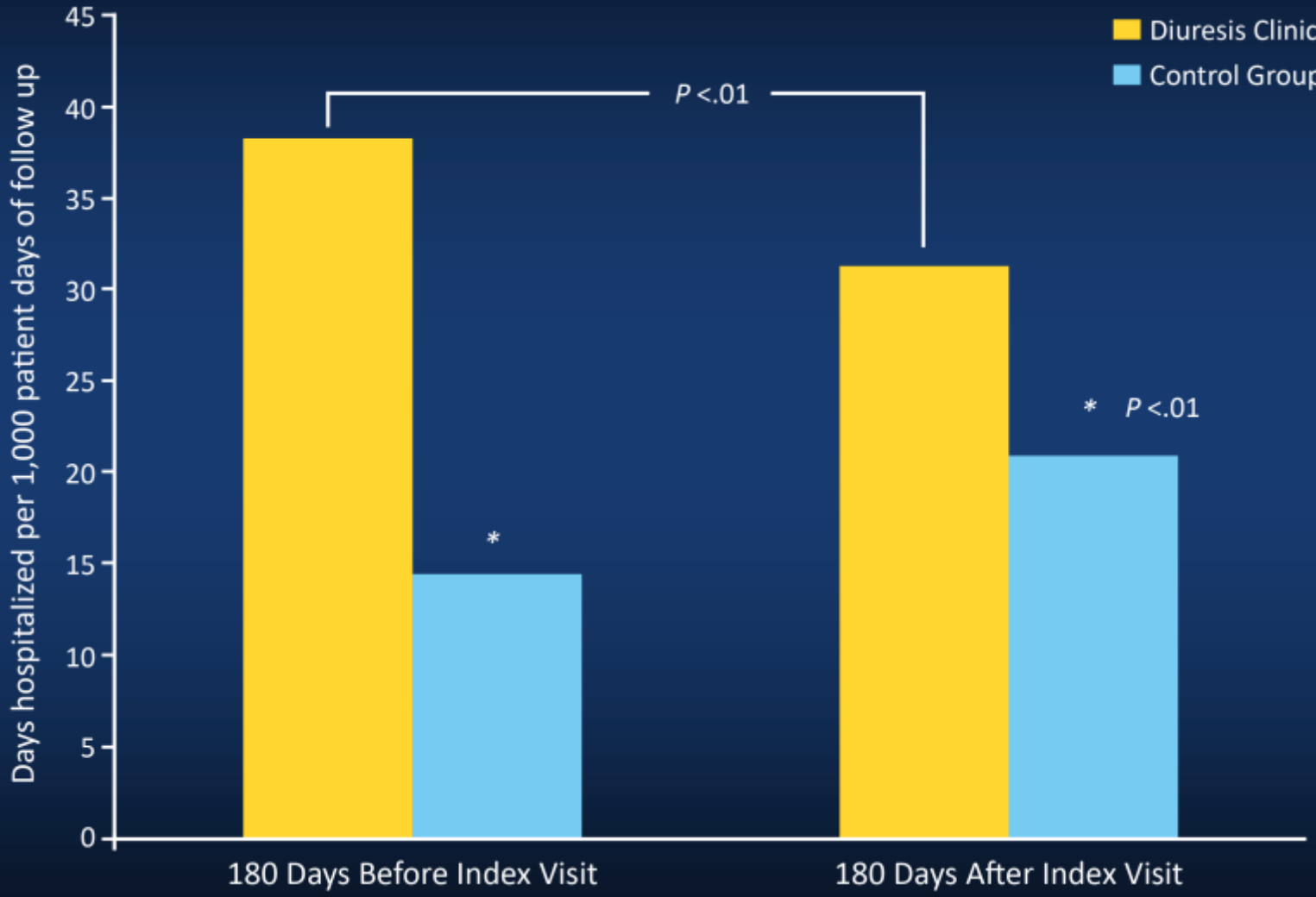
Hernandez AF, et al. *JAMA.* 2010;303(17):1716-1722.

Transition to Outpatient Care



Desai AS, Stevenson LW. *Circulation.* 2012;126:501-506.

The Diuresis Clinic: A New Paradigm for the Treatment of Mild Decompensated Heart Failure



Makadia S, et al. *Am J Med.* 2015;128(5):527-531.

Pre-Activity Assessment Question 1

Sacubitril, which is now coformulated with valsartan in a new combination medication, takes action via a novel pathway by inhibiting neprilysin, which breaks down brain (or B-type) natriuretic peptide (BNP). Which of the following statements is *false* regarding neprilysin?

A. Neprilysin breaks down atrial natriuretic peptide (ANP), BNP, and C-type natriuretic peptide (CNP)
B. Neprilysin is an enzyme
C. N-Terminal pro-BNP (NT-proBNP) is not a substrate for neprilysin
D. In a clinical trial, valsartan/sacubitril *decreased* BNP levels but *increased* NT-proBNP levels

Pre-Activity Assessment Question 2

Which of the following acute heart failure treatments has class I, level A (the best!) supporting evidence?

A. Angiotensin-converting enzyme (ACE) inhibitors
B. Nitroglycerin
C. Furosemide
D. None of the above
E. A, B, and C

Pre-Activity Assessment Question 3

A 67-year-old man with a history of HFpEF, hypertension (HTN), COPD, and morbid obesity presents short of breath (SOB) and 10 lb heavier. No wheezing; no URI complaints. Heart rate, 87 bpm; BP, 157/85; oxygen saturation, 87% right atrial (RA). No wheezing on exam. Labs show a Cr of 1.1, a troponin of <0.02, and an NT-proBNP level of 288 (previous level was 9000 during a prior hospitalization). CTA of chest was negative for pulmonary embolism (PE) and pneumonia. After providing supplemental oxygen with a nasal cannula, what would be the next best step?

A. High-dose intravenous (IV) diuretics
B. IV vasodilator
C. Steroid, antibiotic, and bronchodilator therapy
D. Noninvasive positive pressure ventilation

BP=blood pressure; bpm=beats per minute; BUN=blood urea nitrogen; COPD=chronic obstructive pulmonary disease; Cr=creatinine; CTA=computed tomography angiography; HFpEF=heart failure with preserved ejection fraction; URI=upper respiratory tract infection.

Pre-Activity Assessment Question 4

Which of the following would be an example of an acute HF patient who could be placed in an observation unit?

A. A 60-year-old man with a history of myocardial infarctions (MIs) and renal insufficiency who is confused and has cool, mottled extremities.
B. An 84-year-old woman with minimal residual dyspnea post treatment who has mild dementia and lives by herself.
C. A 63-year-old woman accompanied by her son (with whom she lives) who responds well to emergency department (ED) treatment and has no high-risk features identified during ED evaluation.
D. A 71-year-old man who, after treatment in the ED, remains markedly hypertensive with significant dyspnea at rest.

Thank you!

- Thank you for joining us in the CME activity, we hope this presentation was valuable to you and the way you practice.

- Please complete the CME post-test and evaluation to receive your CME credit.