

Natriuretic Peptides

The Cardiologists View

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Disclosures

Research support: Alere, BG Medicine, Critical Diagnostics, Roche Diagnostics, and Singulex

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Poll Question

Learning Objectives

- Review the recently published recommendations from the 2013 American College of Cardiology/ American Heart Association Guidelines for Heart Failure for natriuretic peptide testing.
- Evaluate the diagnostic accuracy and optimal patient selection for natriuretic peptide testing to diagnose acute heart failure and differentiate from other etiologies of dyspnea.
- Identify a role for serial natriuretic peptide testing in-hospital and how to best utilize these levels for prognosis and predict readmission.
- Consider the state of the evidence for serial natriuretic peptide outpatient testing to optimize the prognosis of ambulatory heart failure patients.

Why Should Cardiologists Pay More Attention to the Natriuretic Peptide Values in Patients with Heart Failure?

The Cardiologist and Emergency Department
Same game, but different perspective

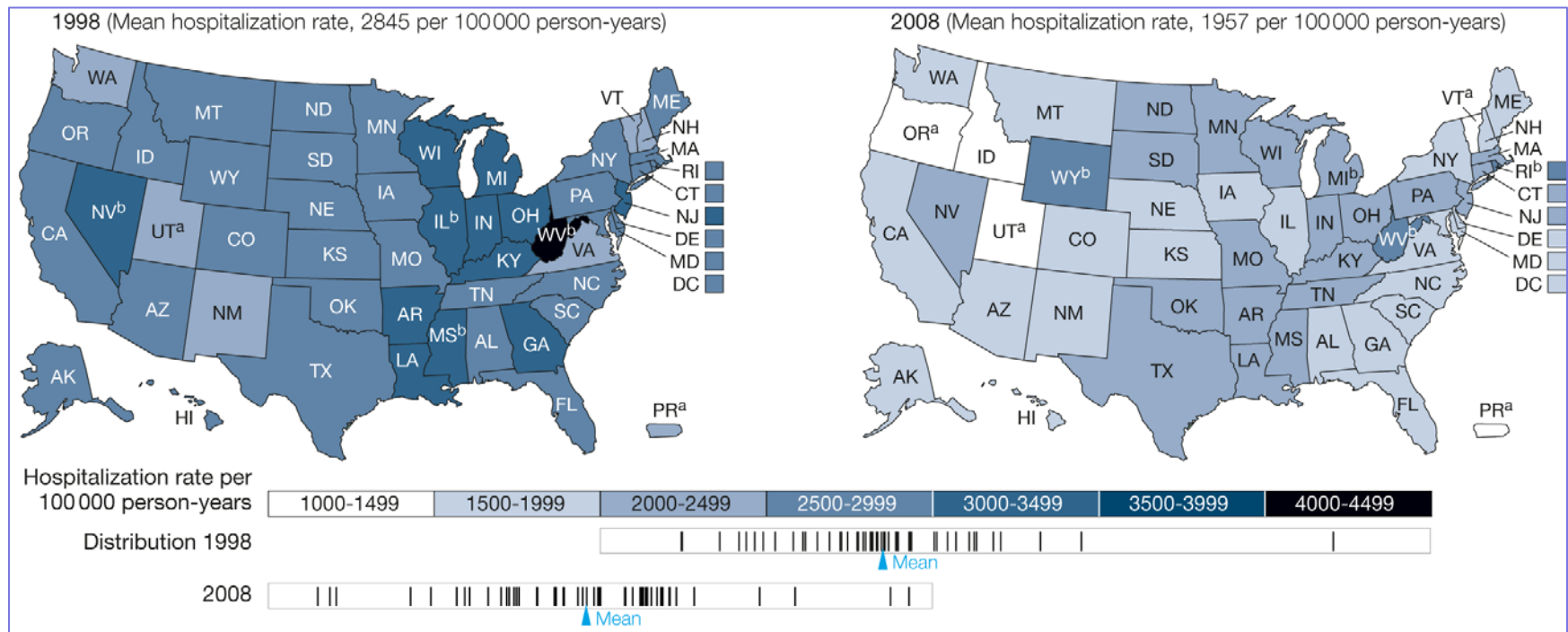


The Cardiologist: the long view

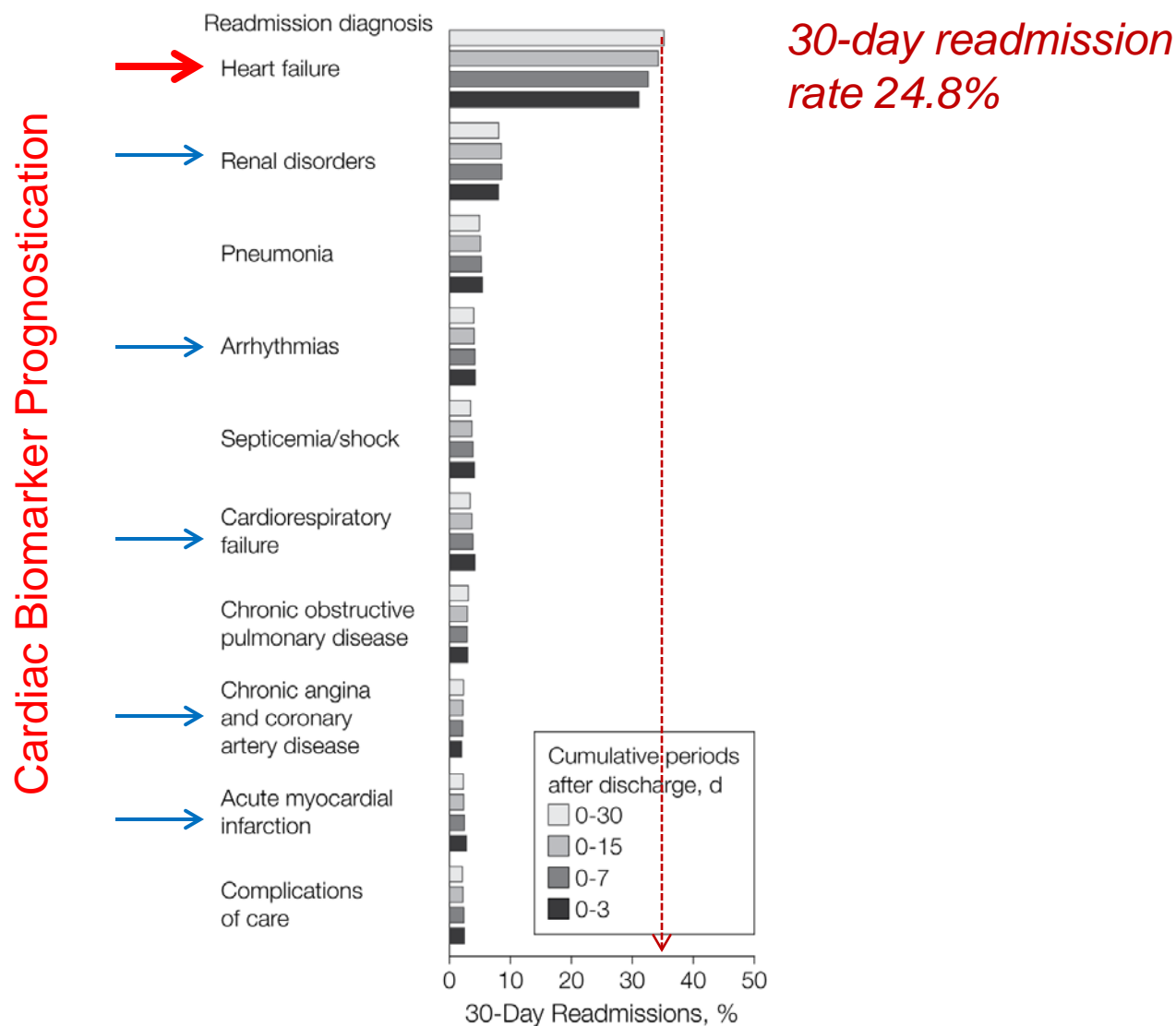


**The Emergency Department:
short-term diagnostic accuracy**

Trends in Heart Failure Hospitalization Rates for Medicare Beneficiaries 1998-2008



Diagnoses of 30-Day Readmissions After Hospitalization for Acute HF

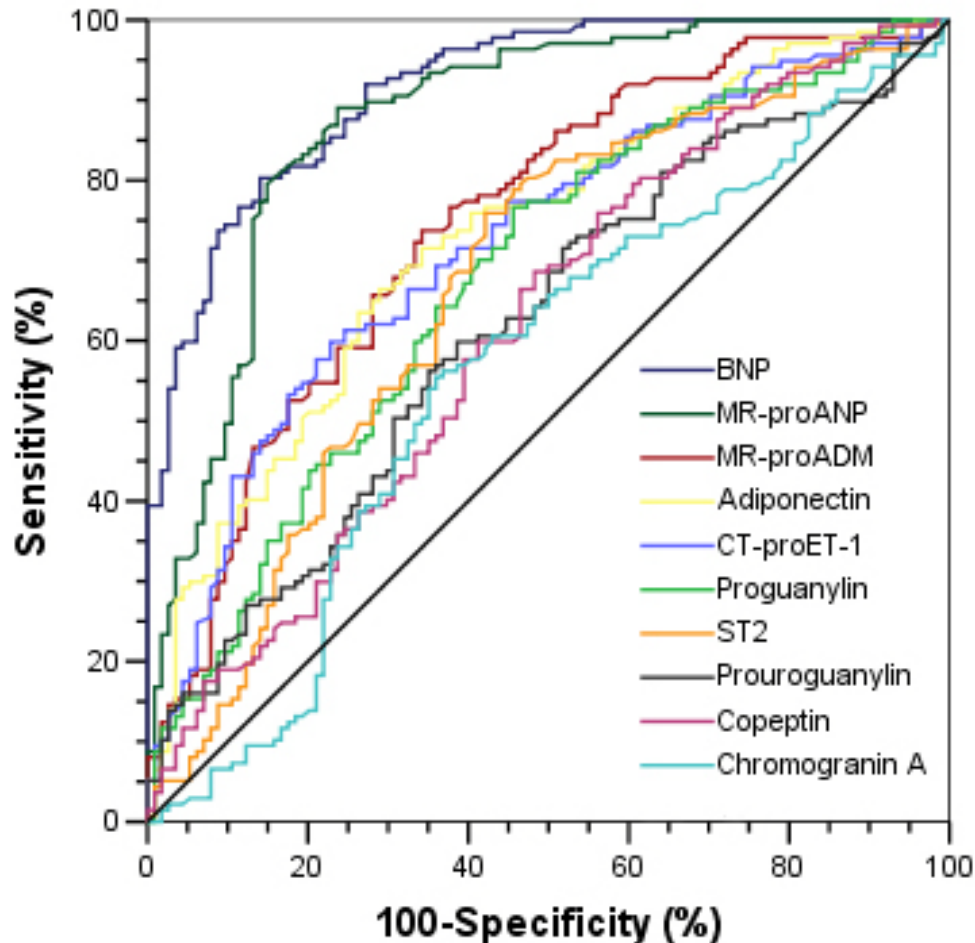


Poll Question

Integrating Natriuretic Peptides into Cardiology Practice

- Hospital based practice
 - Diagnosis and prognostication at presentation
 - Inpatient management and discharge planning
- Outpatient clinic based practice
 - Utilizing natriuretic peptide levels to optimize chronic heart failure management
 - Identifying at-risk patients prior to heart failure symptom onset

Biomarkers – diagnosis of Acute HF in ED



ROC curves for the biochemical diagnosis of acute destabilized HF by established and novel biomarkers in short-of-breath patients presenting to the emergency department.

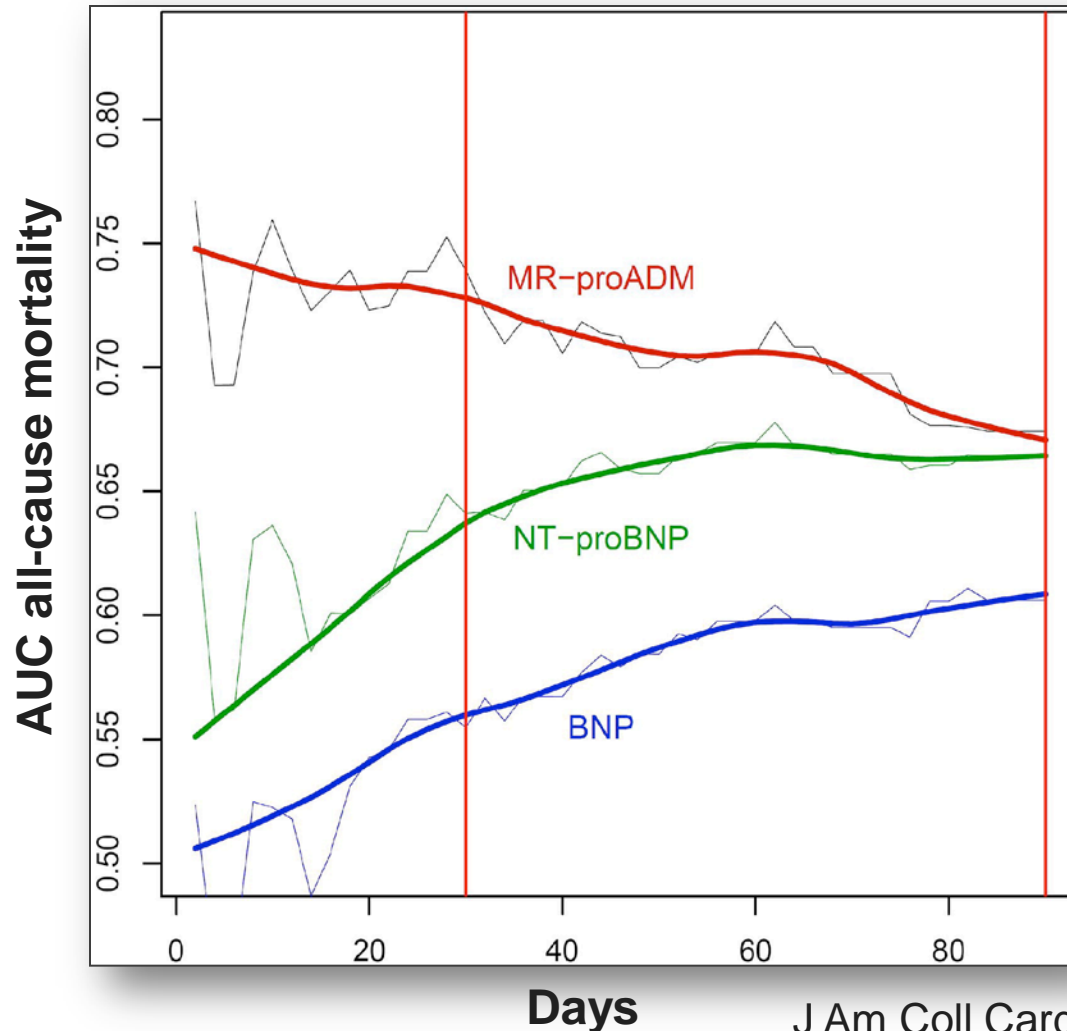
n=251 in total,
HF=137, non-HF=114

areas under the curve:

BNP, 0.92 (95% CI, 0.87-0.95)
sST2, 0.62 (95% CI, 0.55-0.69)

Limitation of natriuretic peptides at presentation for early prognosis

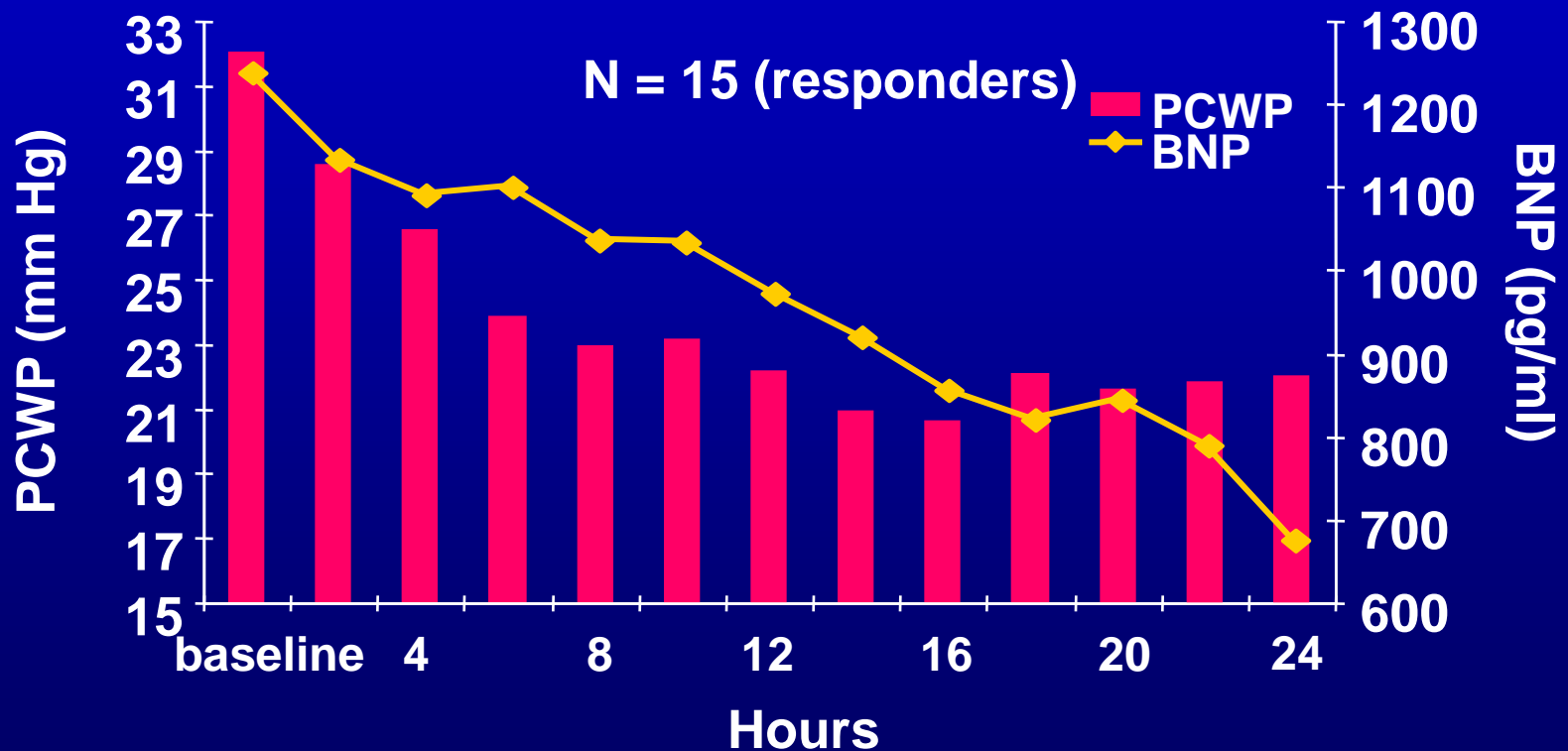
Results of the BACH study



Integrating Natriuretic Peptides into Cardiology Practice

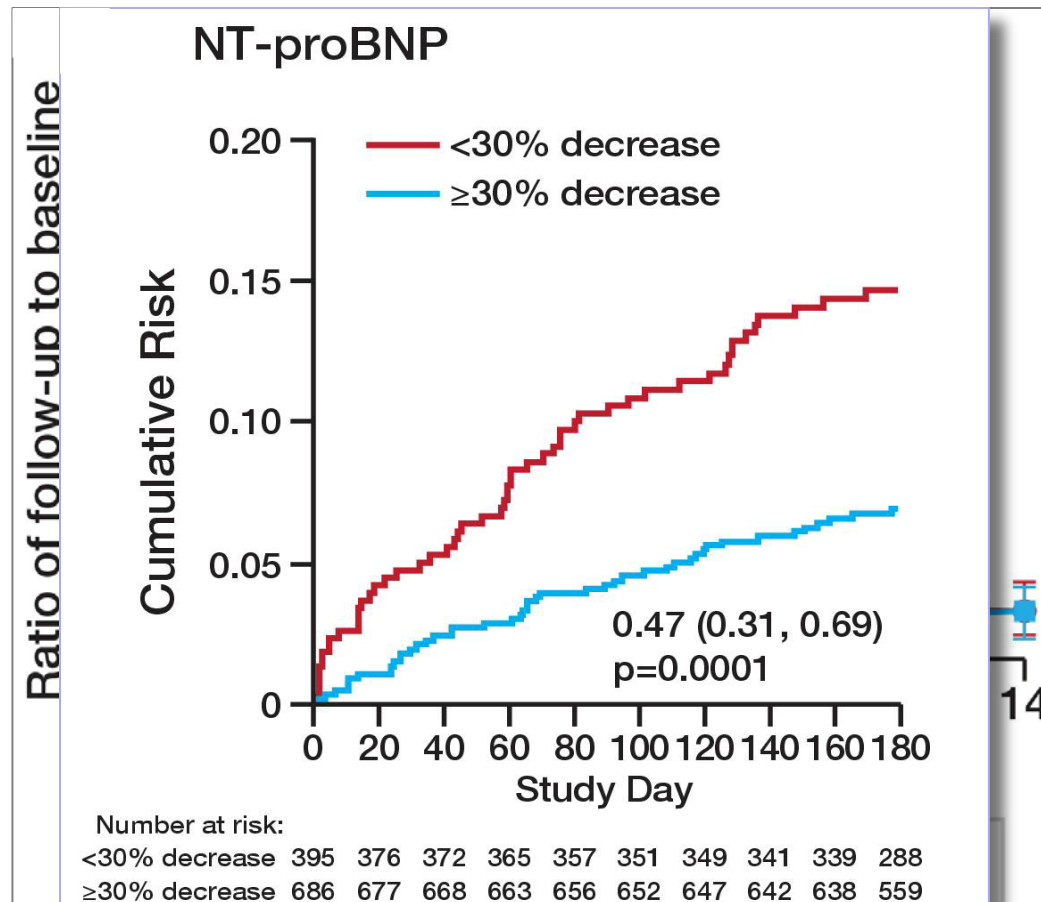
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Changes in BNP and Pulmonary Capillary Wedge Pressure (PCWP) During 24 Hours of Treatment



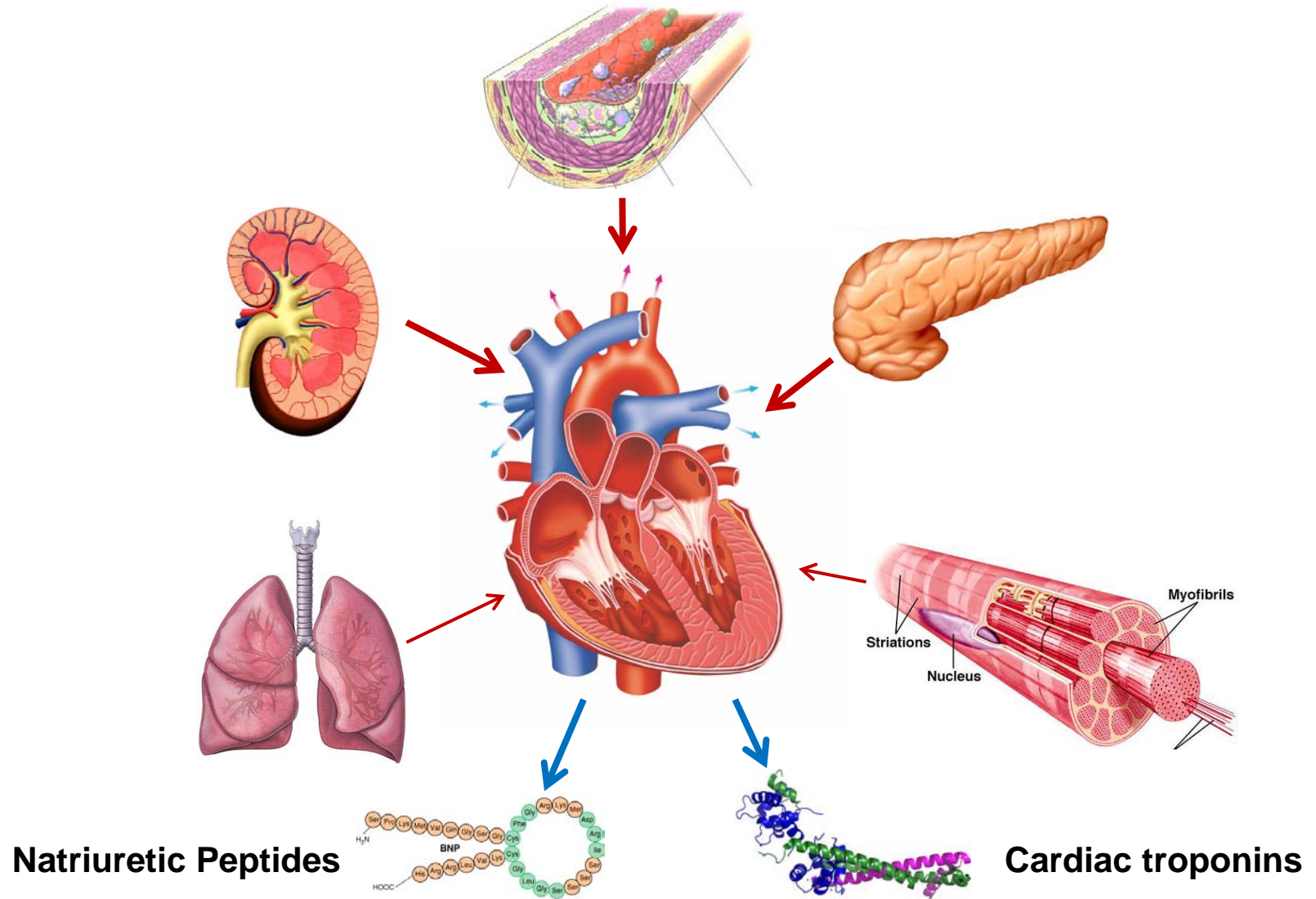
NT-proBNP change during acute HF hospitalization

Insights from RELAX-AHF





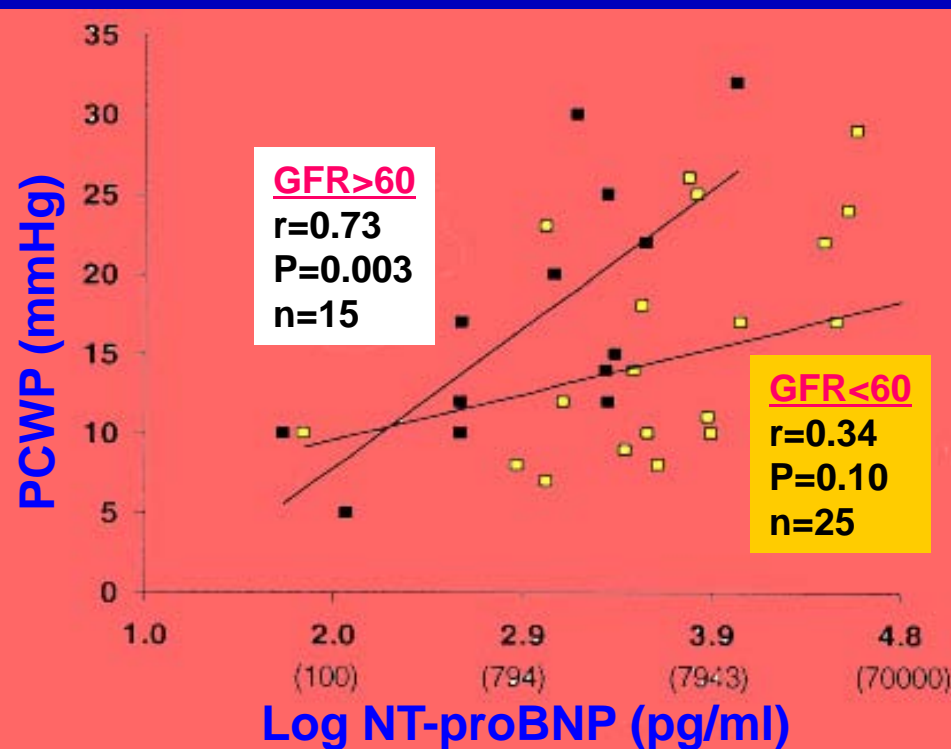
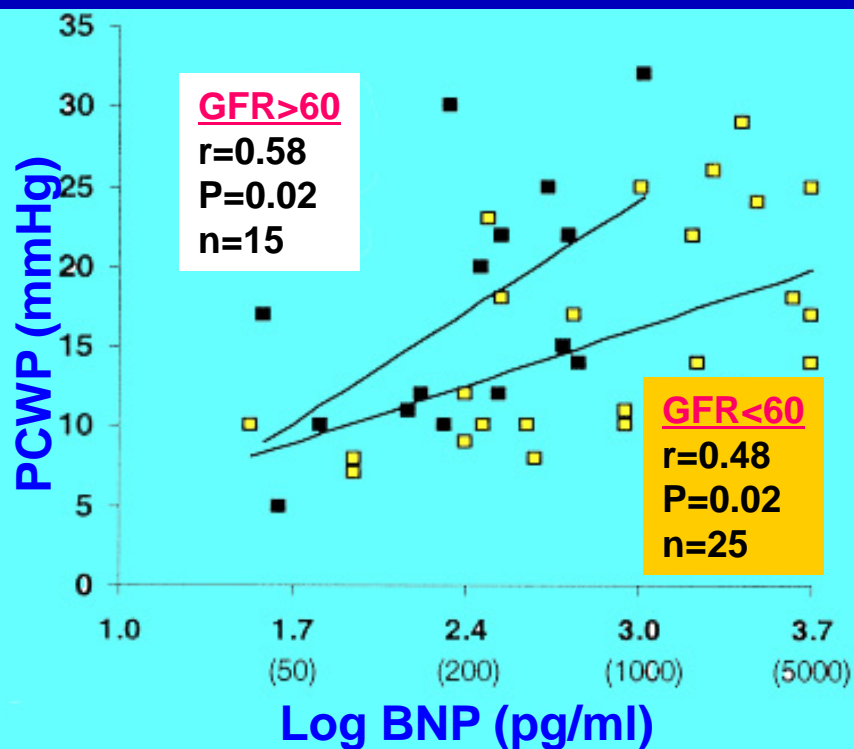
Cardiac biomarker levels represent a summation of the influence of acute and chronic comorbidities



NT-proBNP/BNP Levels Without Acute Decompensated HF

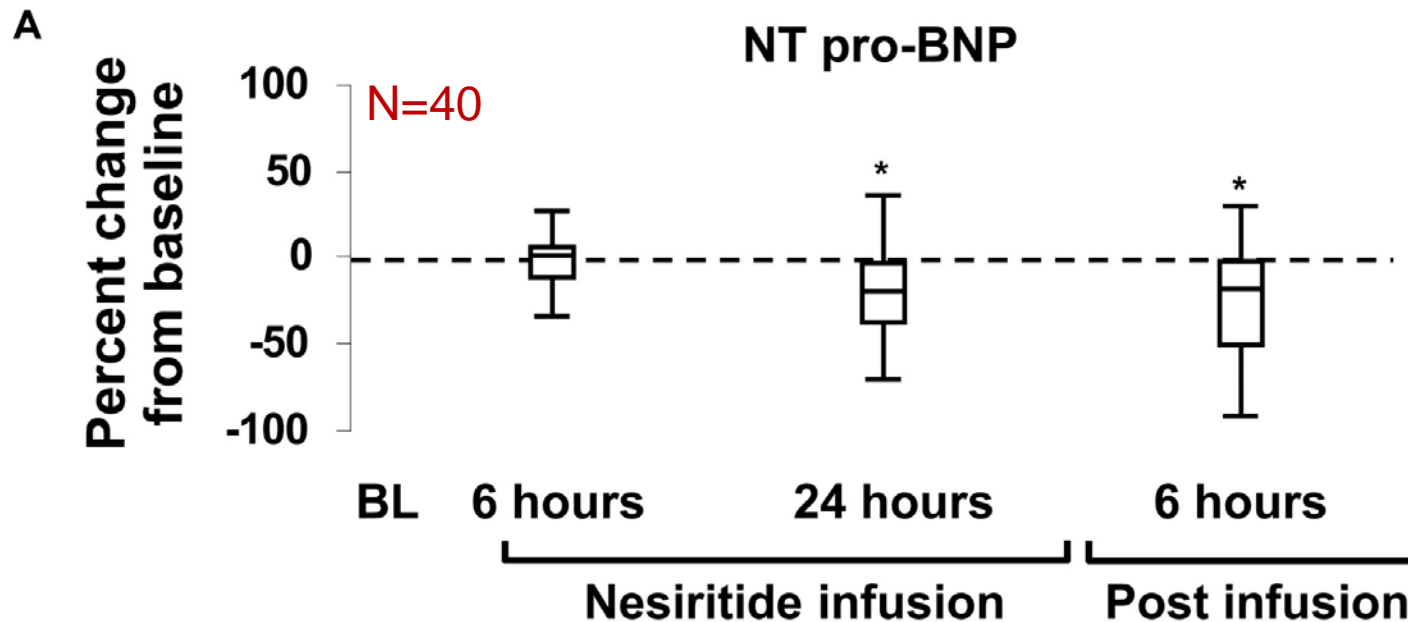
<u>Clinical State</u>	<u>Effect on (NT-pro)BNP Value</u>
Acute coronary syndrome/CAD	↑
Pulmonary embolism	↑
Right ventricular overload	↑
Obesity	↓
Age	↑
Renal failure	↑
Critical illness	↑
Chronic heart failure	↑ or ↓

Correlation between PCWP and natriuretic peptide levels in the ICU



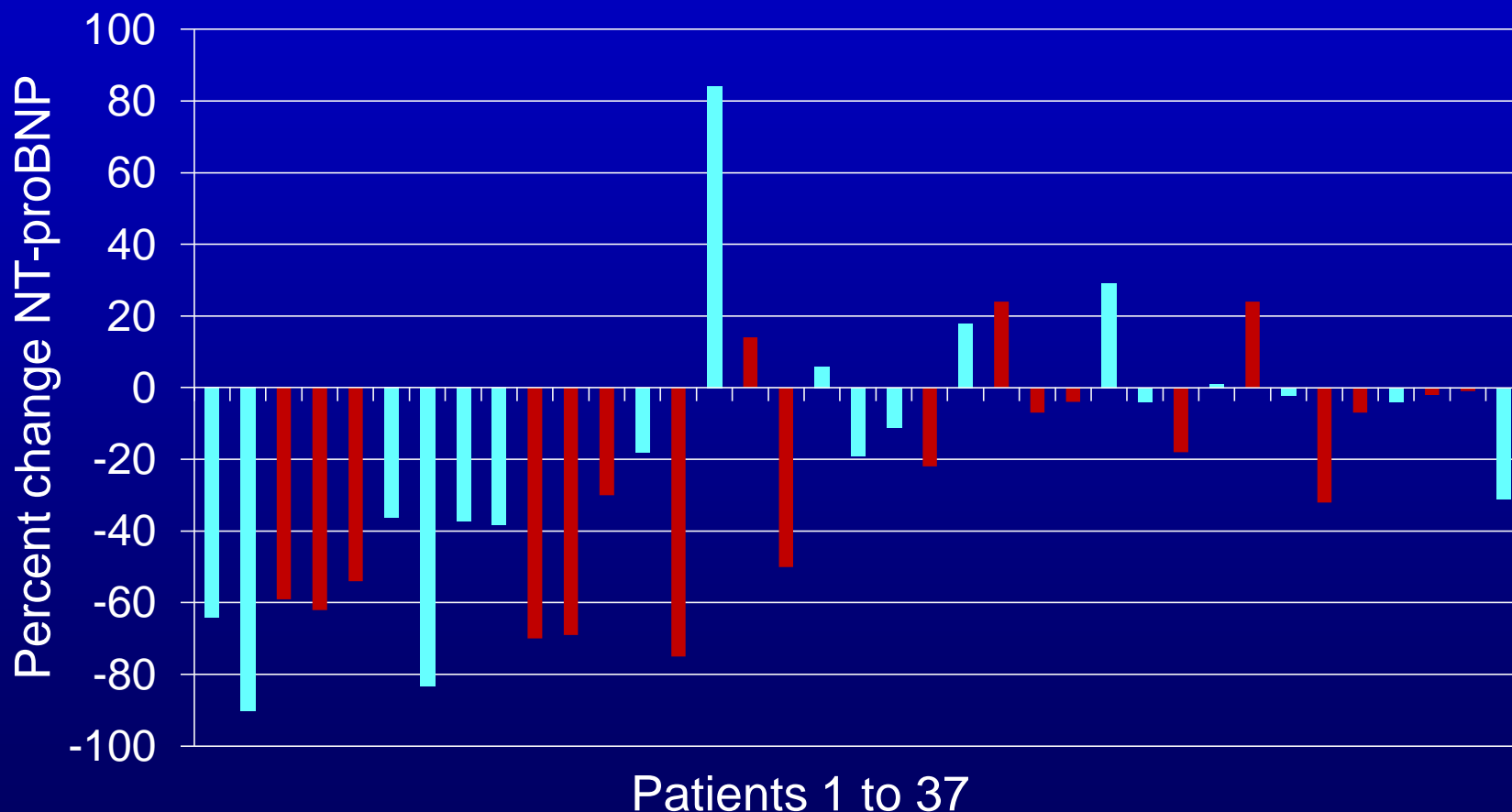
Yellow boxes indicate patients with a GFR < 60 ml/min
Closed boxes indicate patients with a GFR \geq 60 ml/min

NT-proBNP Response to Nesiritide Therapy in Patients with Acute Heart Failure



Percent change in NT-proBNP concentration from baseline to 6 hours post nesiritide infusion

Change in NT-proBNP level is unrelated to other clinical findings



■ >4 Kg weight loss

■ ≤4 Kg weight loss

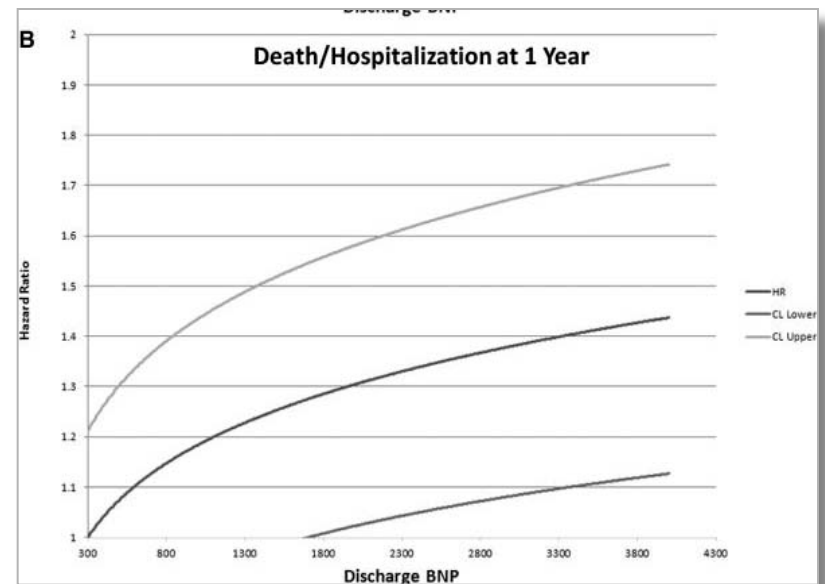
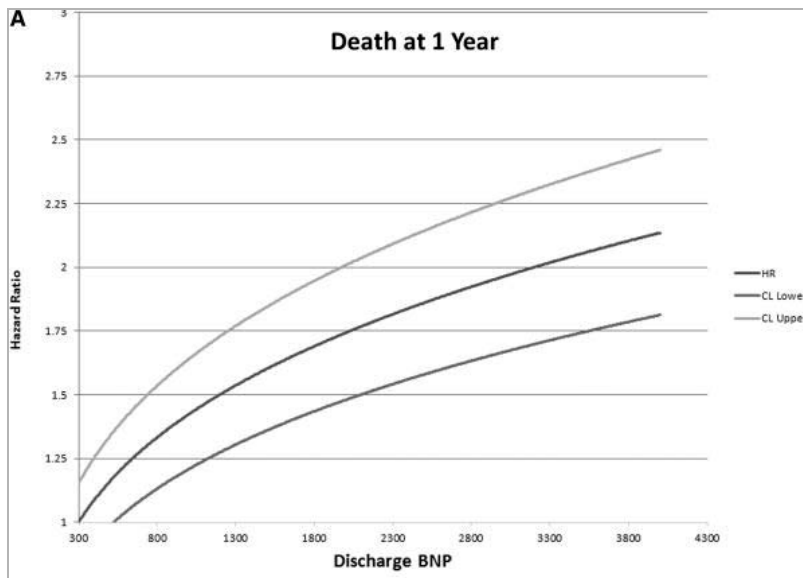
Prognosis summary for natriuretic peptides based on timing of measurement during index hospitalization for acute HF

Author	Year	Subjects	Outcome	NP	Admit	Pre D/C	Change
Bettoncourt	2004	182	6 mo M/R	NT-pro	X	X	X
Logeart	2004	202	6 mo M/R	BNP	0.69	0.80	0.76
Verdiani	2006	100	30-day R	BNP	X	X	NA
Waldo	2008	164	90-day M	NT-pro	0.788	0.834	NA
SURVIVE	2009	1038	6 mo M	BNP	NA	0.70	0.71
ESCAPE	2010	255	6 mo M	BNP	X	0.76	NA
Novean	2011	171	12 mo M	NT-pro /BNP	0.67	0.77	NA
OPTIMIZE-HF	2011	7039	12 mo M	BNP	0.684	0.694	0.680
RELAX-AHF	2013	1161	6 mo M	NT-pro	NA	NA	X

Legend: M, mortality; R, readmission; red= not significant, yellow=significant, green=significant and most prognostic. Numbers are area under the curve. X is any alternative prognostic statistic other than c-statistic. NA=Not assessed in publication

OPTIMIZE-HF discharge BNP level

Adjusted hazard ratios for one-year outcomes

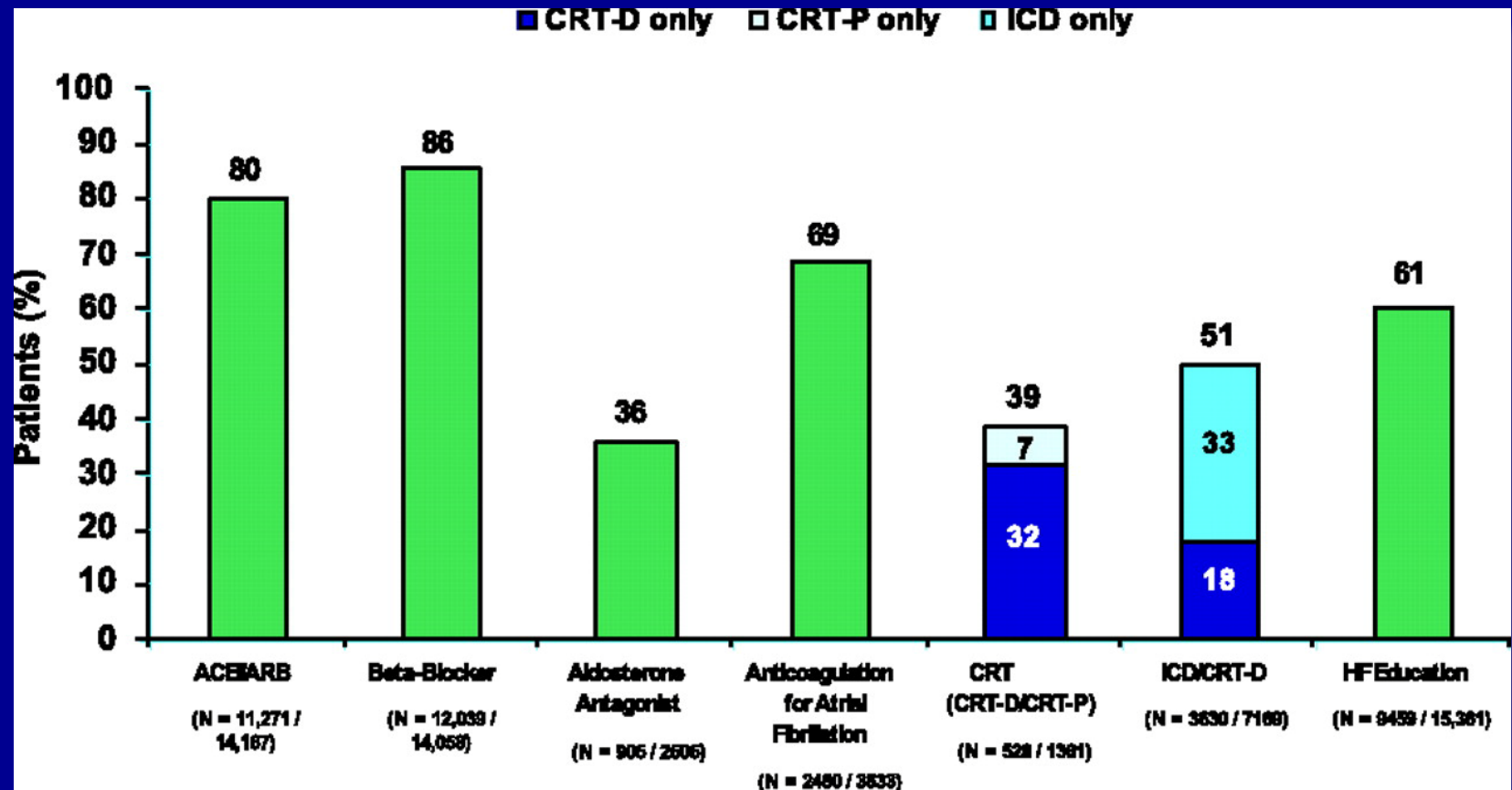


Integrating Natriuretic Peptides into Cardiology Practice

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Proportion of HF patients achieving therapy targets

IMPROVE HF care metrics at baseline

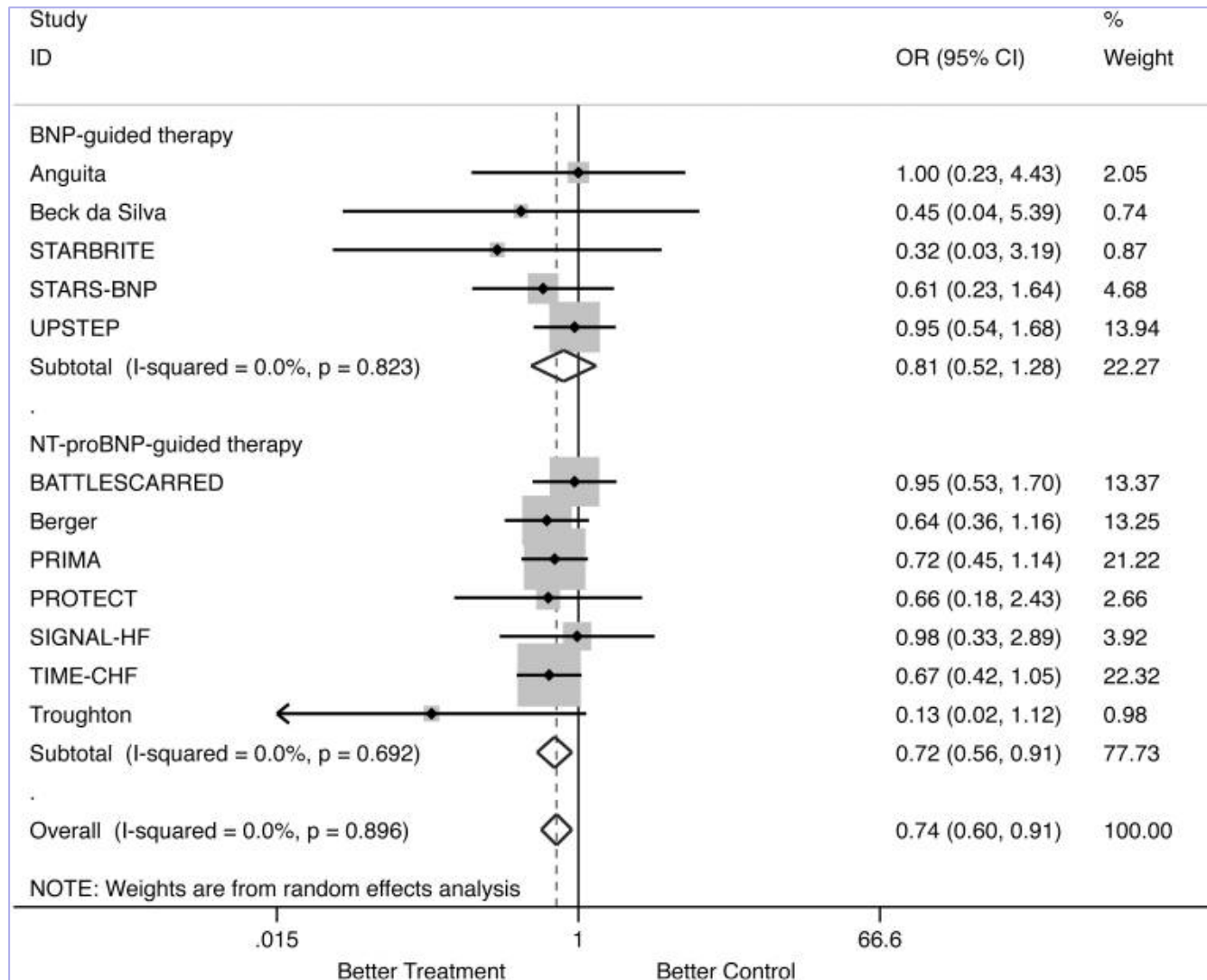


Potential efficacy of a biomarker adjunctive approach to clinical judgment for management of outpatient HF therapy

- Better achievement of guideline recommended medications and doses
 - Improve patient compliance with prescribed therapy by providing quantitative feedback
 - Overcome provider limitations of reliance on signs and symptoms in “stable” patients

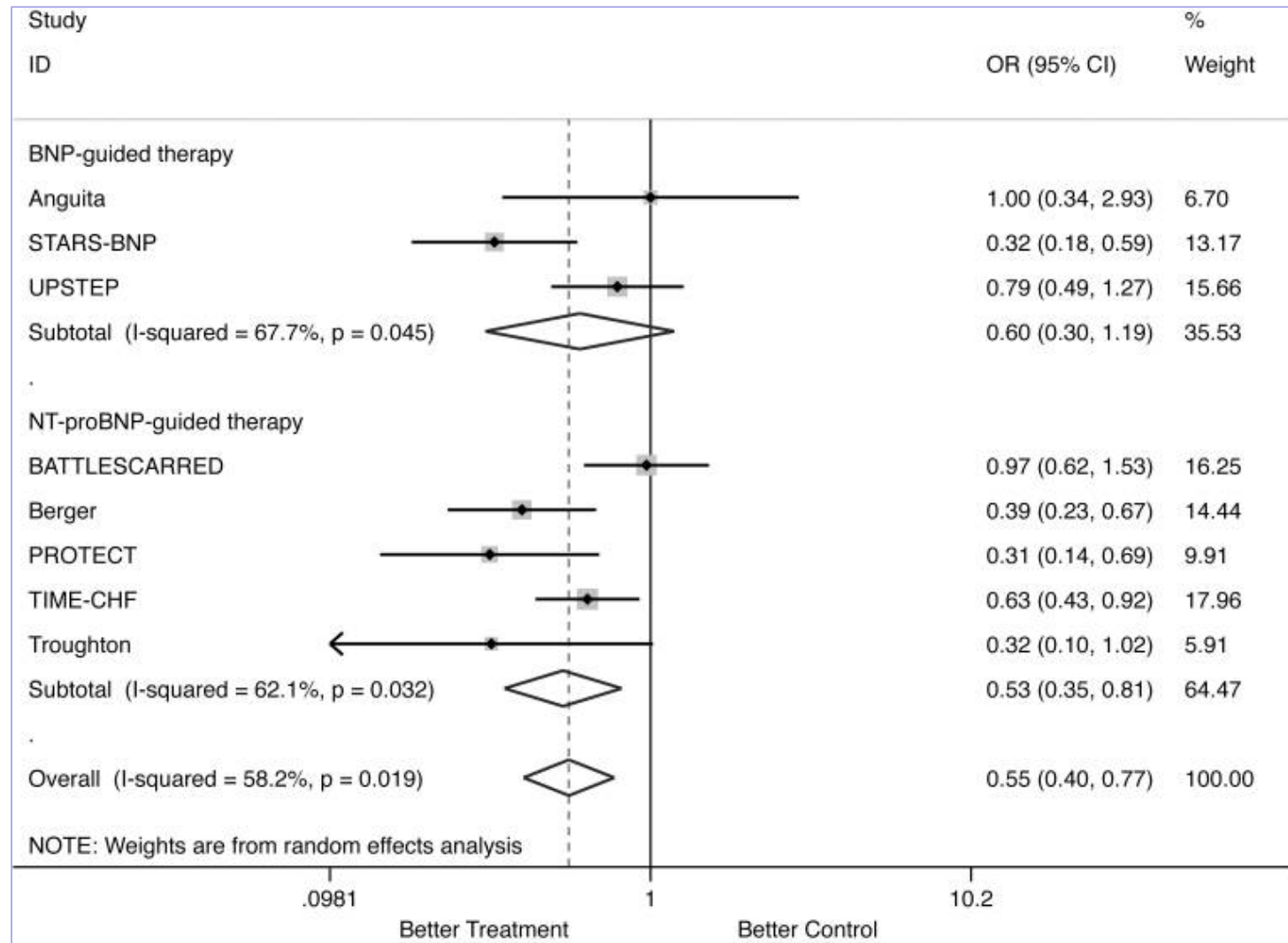
B-Type Natriuretic Peptide-Guided Heart Failure Therapy: A Meta-analysis

All-Cause Mortality



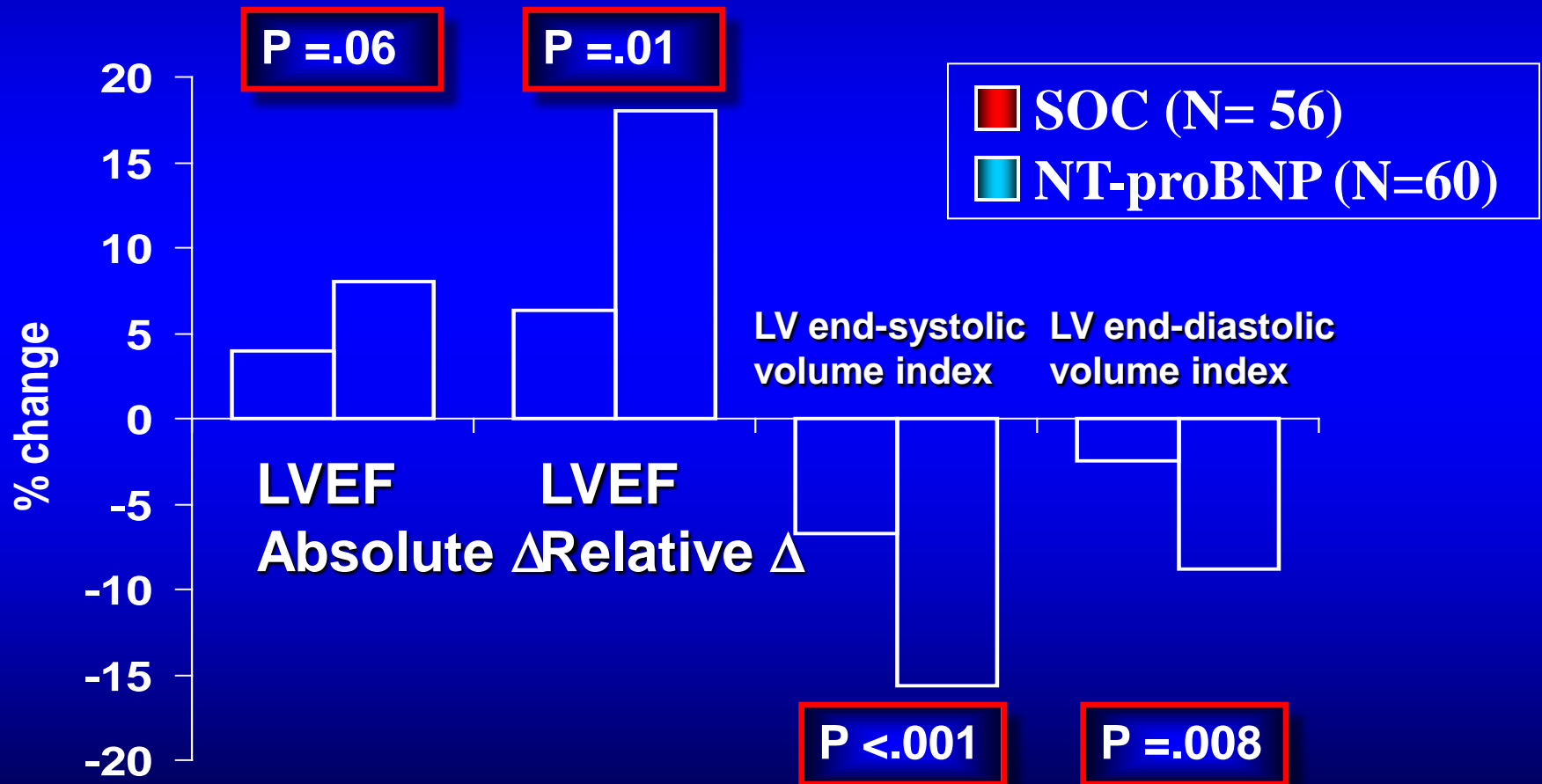
B-Type Natriuretic Peptide-Guided Heart Failure Therapy: A Meta-analysis

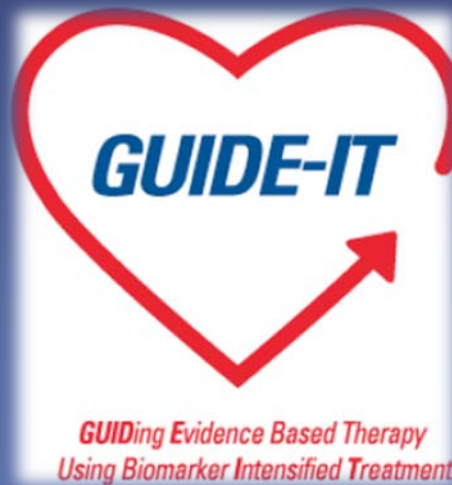
Heart Failure related Hospitalization





Selected echo results



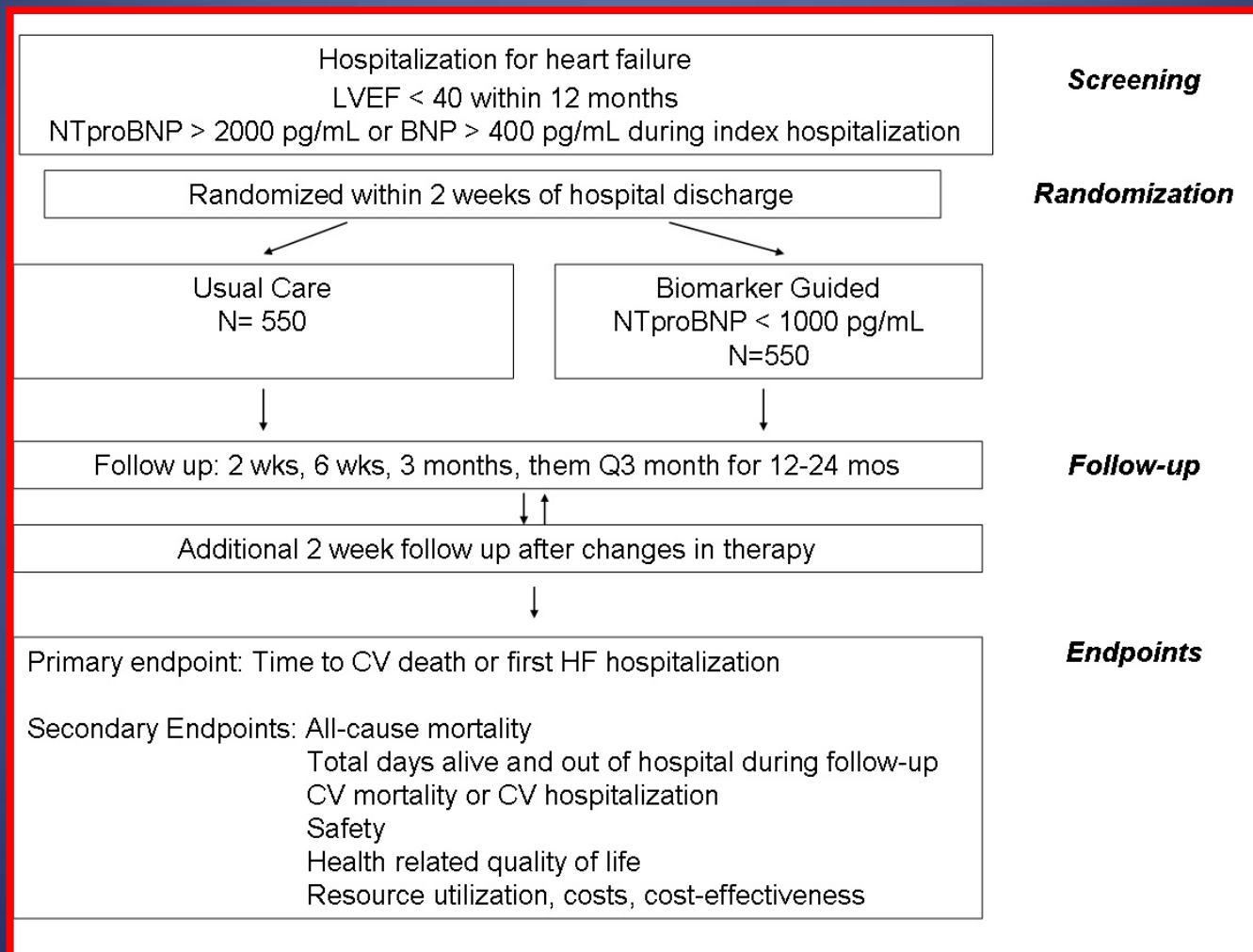


Primary Hypothesis of NIH GUIDE-IT trial

- In high risk heart failure patients with LV systolic dysfunction, a strategy of titrating medical therapy based on minimizing natriuretic peptide levels will be superior to usual care with regard to the composite endpoint of heart failure hospitalizations or CV mortality



GUIDE-IT Study Design Overview



The Poll Results

2013 ACCF/AHA Guideline for the Management of Heart Failure

Table 9. Recommendations for Biomarkers in HF

Biomarker, Application	Setting	COR	LOE	References
<i>Natriuretic peptides</i>				
Diagnosis or exclusion of HF	Ambulatory, Acute	I	A	(212, 217-223, 245-250)
Prognosis of HF	Ambulatory, Acute	I	A	(222, 224-229, 248, 251-258)
Achieve GDMT	Ambulatory	IIa	B	(230-237)
Guidance for acutely decompensated HF therapy	Acute	IIb	C	(259, 260)
<i>Biomarkers of myocardial injury</i>				
Additive risk stratification	Acute, Ambulatory	I	A	(238-244, 248, 253, 256-267)
<i>Biomarkers of myocardial fibrosis</i>				
Additive risk stratification	Ambulatory	IIb	B	(238, 240-244, 280)
	Acute	IIb	A	(248, 253, 256, 257, 261-267)

COR indicates Class of Recommendation; GDMT, guideline-directed medical therapy; HF, heart failure; and LOE, Level of Evidence.

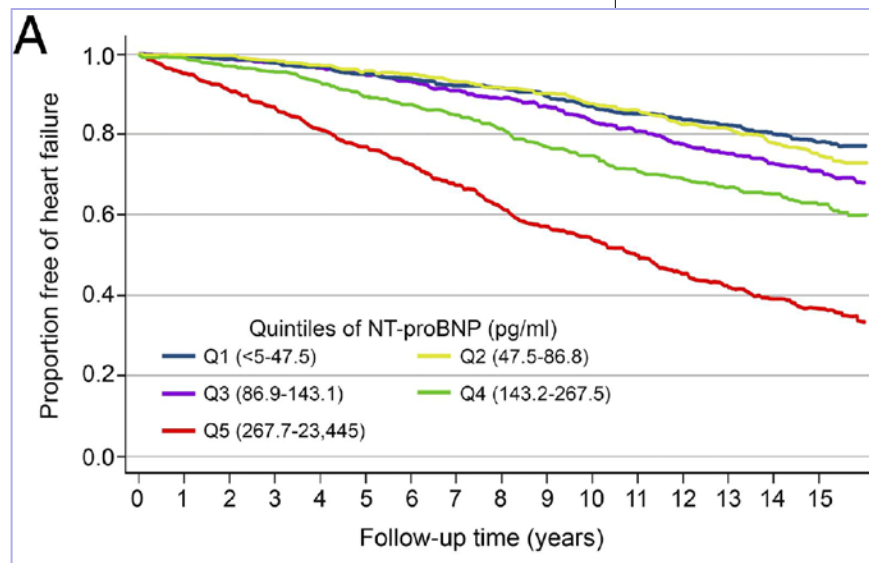
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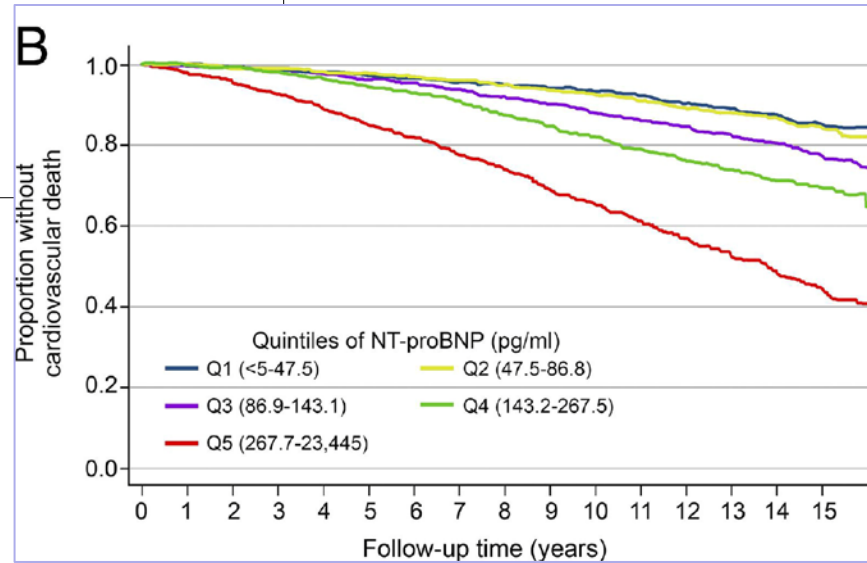
NT-proBNP predicts cardiovascular outcomes in asymptomatic community dwelling older adults

The Cardiovascular Health study (n=4312)

Time to new-onset heart failure



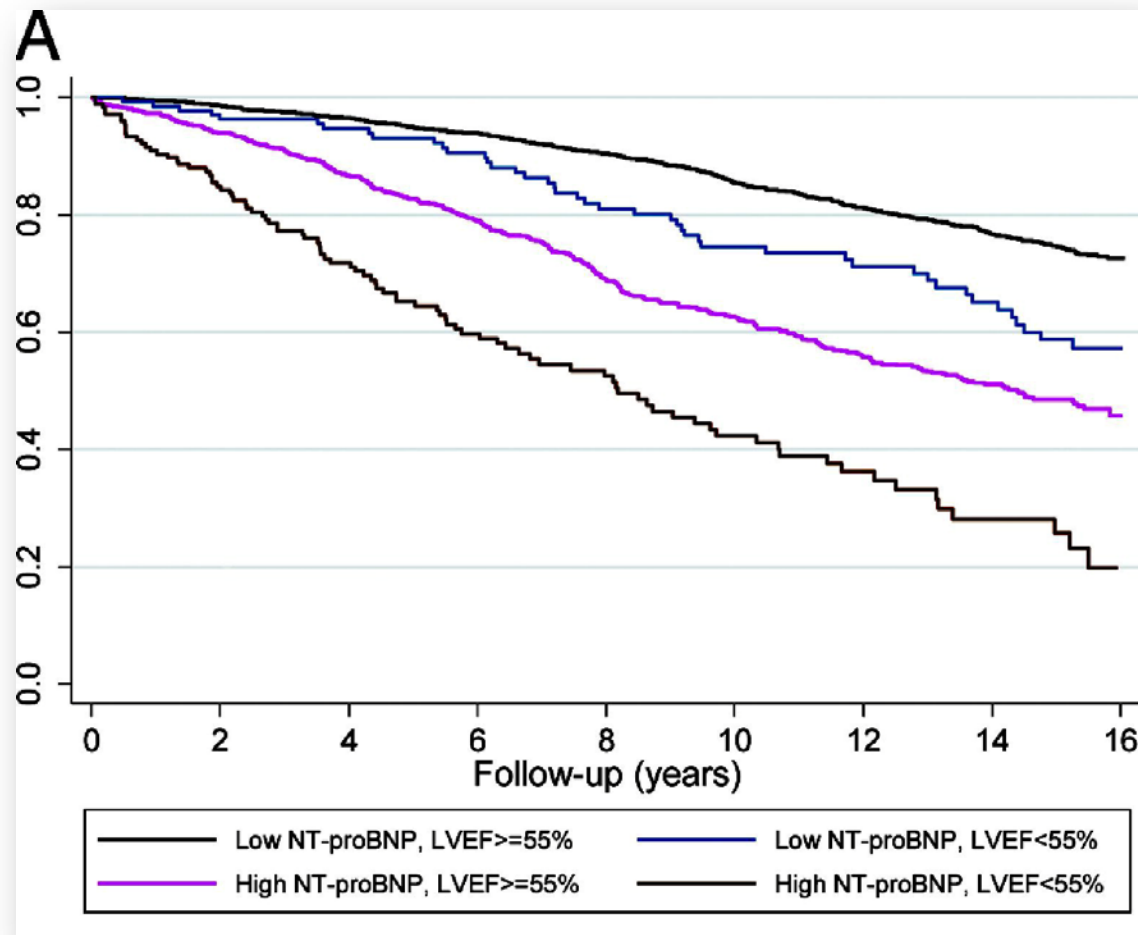
Time to Cardiovascular Death



NT-proBNP and Echocardiography together to predict new-onset heart failure

The Cardiovascular Health study

Time to new-onset heart failure



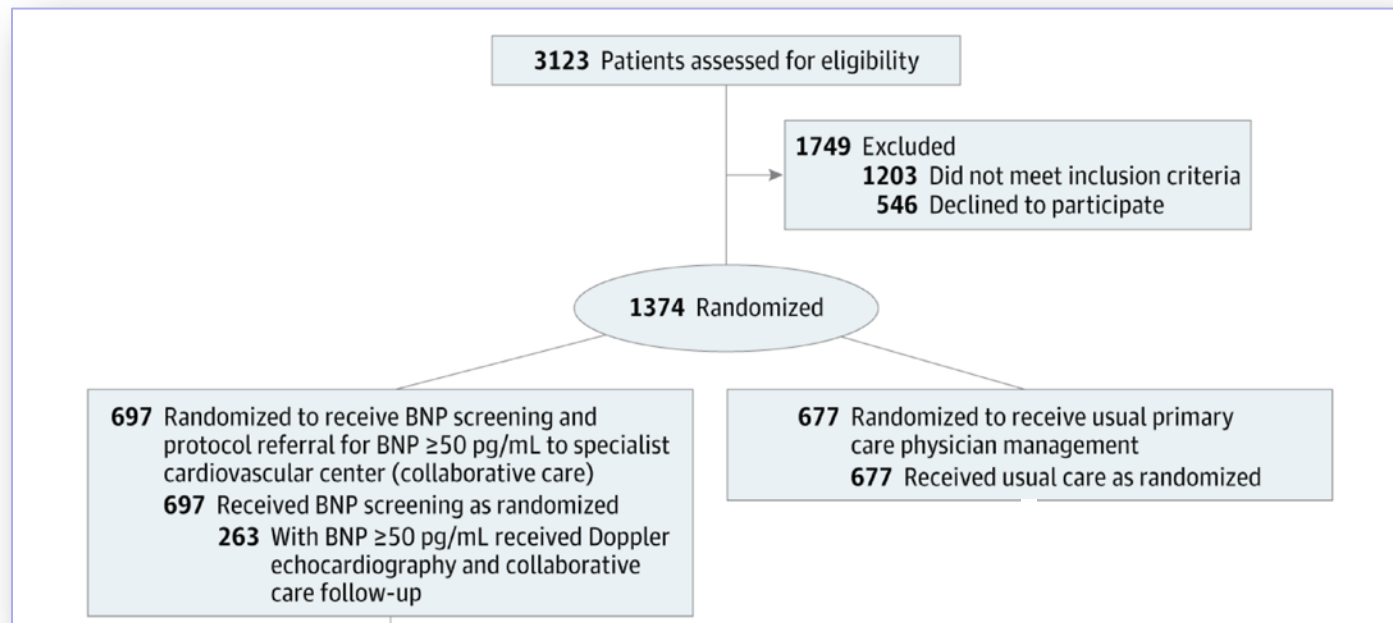
Using natriuretic peptide levels to guide primary prevention of cardiovascular events

The next big thing?

- The STOP-HF randomized trial
- The PONTIAC randomized controlled trial

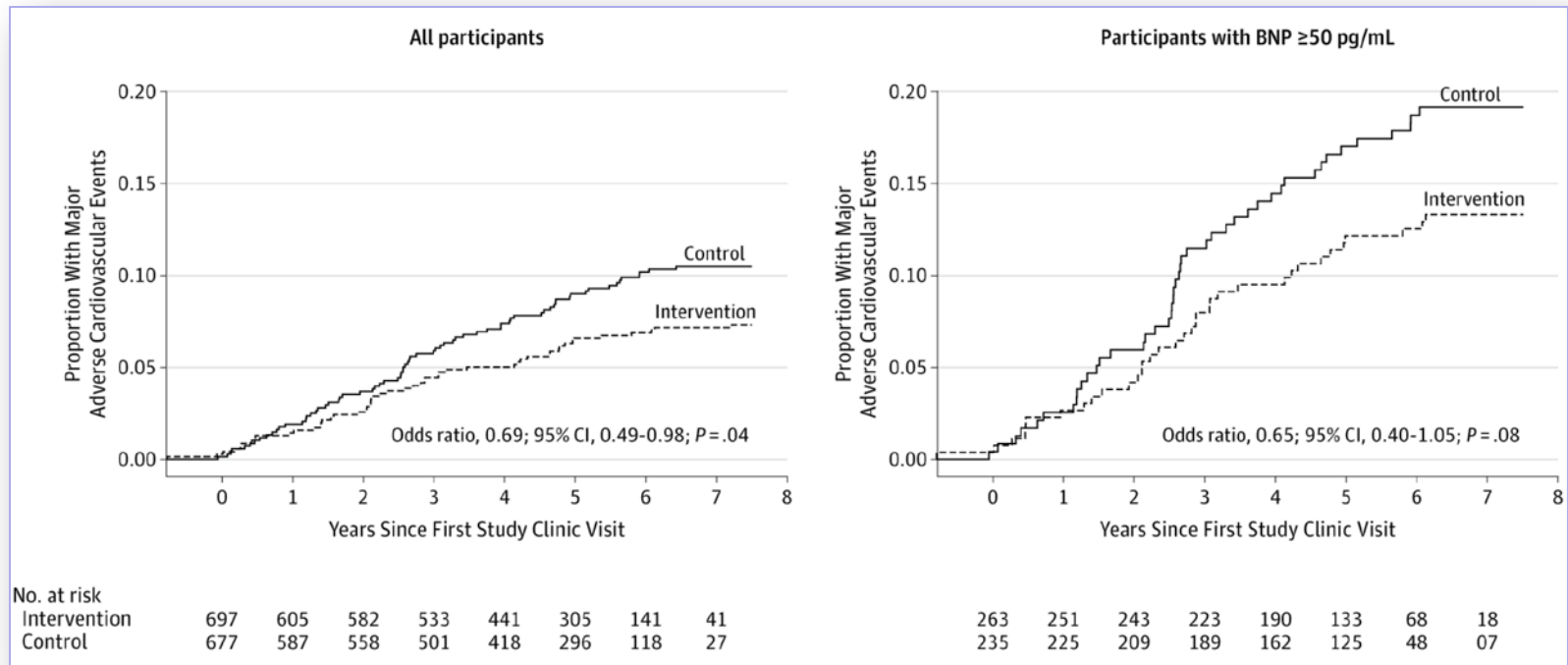
Natriuretic Peptide-Based screening and collaborative care for heart failure

The STOP-HF randomized trial study design



The STOP-HF randomized trial

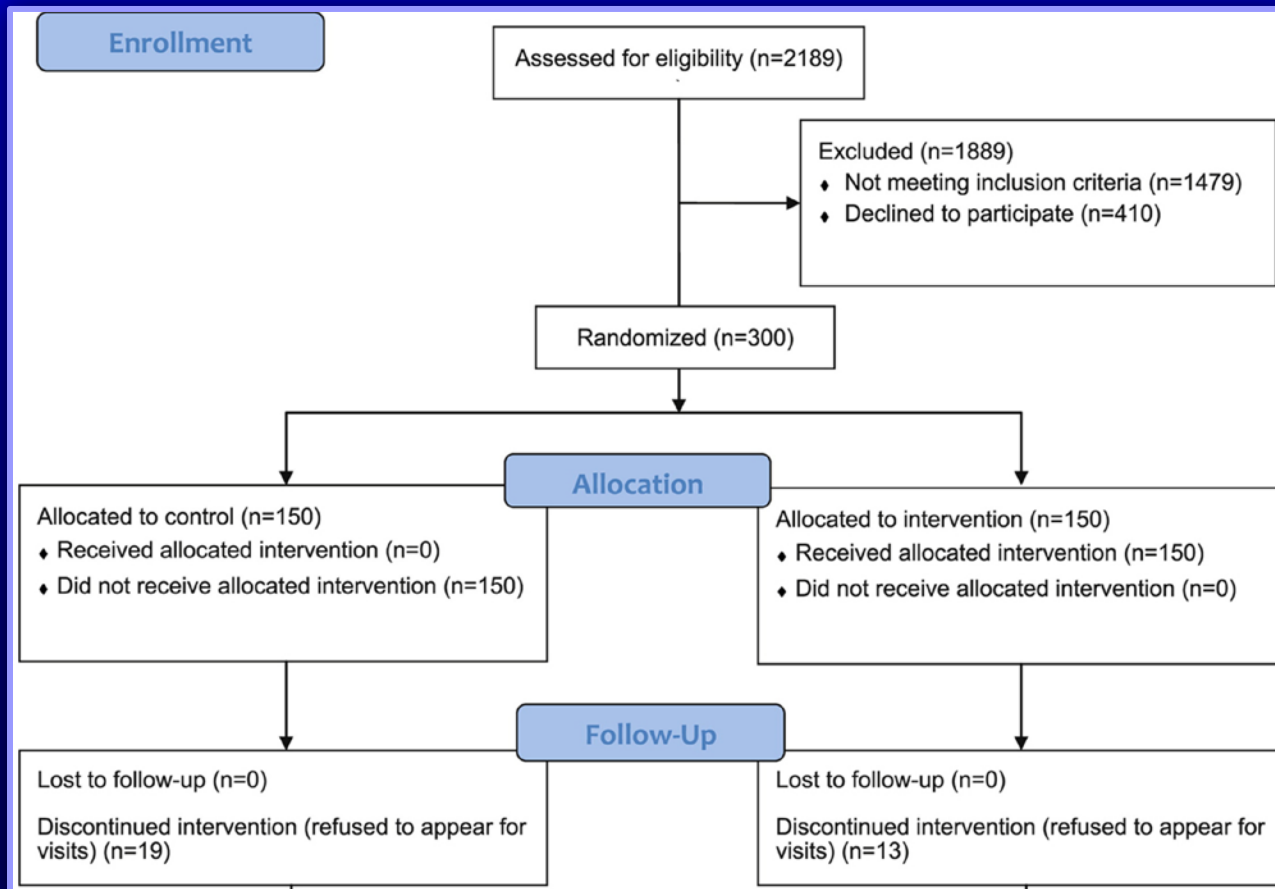
Outcomes



Admission for major adverse cardiovascular event

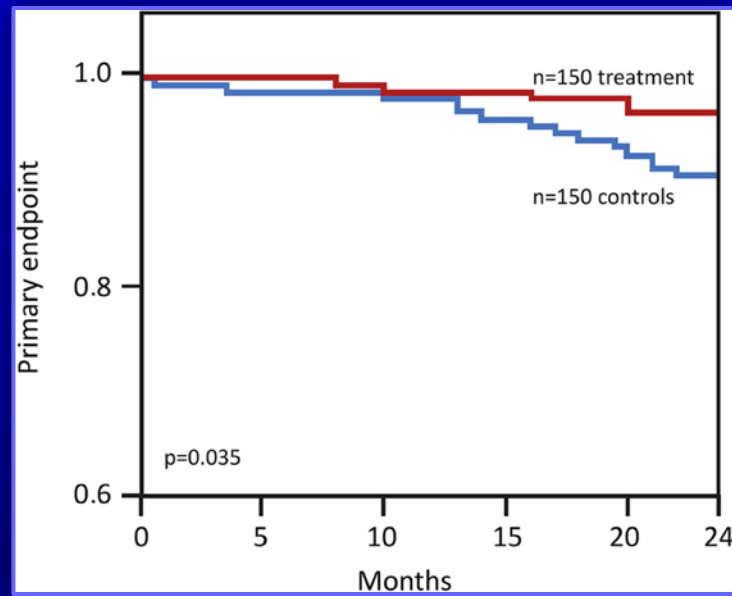
PONTIAC (NT-proBNP Selected Prevention of cardiac events in a population of diabetic patients without A history of Cardiac disease)

A Prospective Randomized Controlled Trial



The PONTIAC Study

Two-Year Outcomes



Hospitalization Due to	All	Control	Intensified	p Value
Any reason	135 (45%)	77 (51%)	58 (39%)	0.02
Cardiovascular event	25 (8%)	18 (12%)	7 (5%)	0.02
Cardiac event	19 (6%)	14 (9%)	5 (3%)	0.03
Heart failure	8 (3%)	7 (5%)	1 (1%)	0.003

Integrating Natriuretic Peptides into Cardiology Practice

Conclusions

- NP's have excellent accuracy to differentiate acute HF from other causes of dyspnea
- Discharge, more than admission, NP levels are powerful prognosticators for cardiovascular outcomes
- BNP and NT-proBNP are promising tests to optimize outpatient chronic HF management to reduce readmissions and death
- NP's can identify "at-risk" asymptomatic individuals in the community and may be useful to direct more intensive interventions to reduce cardiovascular hospitalizations