1

NT-proBNP and Heart Failure: How to Test and Analyze

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2

Disclosures

- Grant support from Novartis Pharmaceuticals, Applied Therapeutics, and Innolife
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- Clinical endpoint committees/data safety monitoring boards for Abbott, AbbVie, Amgen, CVRx, Janssen, MyoKardia, and Takeda
- Trustee, American College of Cardiology

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Before we start

- Biomarkers are a support to clinical judgment
- They do not replace clinical judgment
- They may inform useful information not otherwise obvious at the bedside

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Agenda

- Natriuretic peptide biology
- Established clinical applications
- Emerging uses

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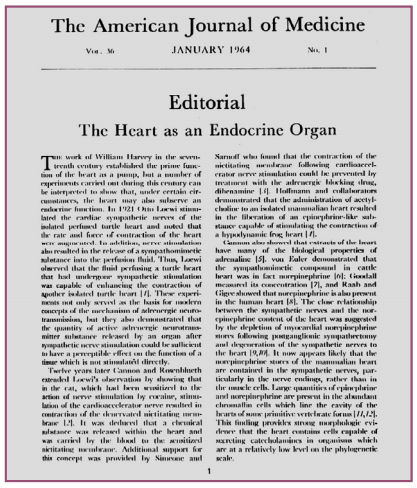
The heart as an endocrine organ



The American Journal of Medicine

Vol. 36 JANUARY 1964 No. 1

Editorial

The Heart as an Endocrine Organ

The work of William Harvey in the seventeenth century established the prime function of the heart as a pump, but a number of experiments carried out during this century can be interpreted to show that, under certain circumstances, the heart may also subserve an endocrine function. In 1921 Otto Loewi stimulated the cardiac sympathetic nerves of the isolated perfused turtle heart and noted that the rate and force of contraction of the heart were augmented. In addition, nerve stimulation also resulted in the release of a sympathomimetic substance into the perfusion fluid. Thus, Loewi observed that the fluid perfusing a turtle heart that had undergone sympathetic stimulation was capable of enhancing the contraction of another isolated turtle heart [1]. These experiments not only served as the basis for modern concepts of the mechanism of adrenergic neurotransmission, but they also demonstrated that the quantity of active adrenergic neurotransmitter substance released by an organ after sympathetic nerve stimulation could be sufficient to have a perceptible effect on the function of a tissue which is not stimulated directly.

Twelve years later Cannon and Rosenblueth extended Loewi's observation by showing that in the cat, which had been sensitized to the action of nerve stimulation by cocaine, stimulation of the cardioaccelerator nerve resulted in contraction of the denervated sensitizing membrane [2]. It was deduced that a chemical substance was released within the heart and was carried by the blood to the sensitized sensitizing membrane. Additional support for this concept was provided by Simeone and Sarnoff who found that the contraction of the sensitizing membrane following cardioaccelerator nerve stimulation could be prevented by treatment with the adrenergic blocking drug, dibenamine [3]. Hoffmann and collaborators demonstrated that the administration of acetylcholine to an isolated mammalian heart resulted in the liberation of an epinephrine-like substance capable of stimulating the contraction of a hypolysamic frog heart [4].

Cannon also showed that extracts of the heart have many of the biological properties of adrenaline [5]. von Euler demonstrated that the sympathomimetic compound in cattle heart was in fact norepinephrine [6]. Gaddall measured its concentration [7], and Raab and Gigee showed that norepinephrine is also present in the human heart [8]. The close relationship between the sympathetic nerves and the norepinephrine content of the heart was suggested by the depletion of myocardial norepinephrine stores following postganglionic sympathectomy and degeneration of the sympathetic nerves to the heart [9,10]. It now appears likely that the norepinephrine stores of the mammalian heart are contained in the sympathetic nerves, particularly in the nerve endings, rather than in the muscle cells. Large quantities of epinephrine and norepinephrine are present in the abundant chromaffin cells which line the cavity of the hearts of some primitive vertebrate forms [11,12]. This finding provides strong morphologic evidence that the heart contains cells capable of secreting catecholamines in organisms which are at a relatively low level on the phylogenetic scale.

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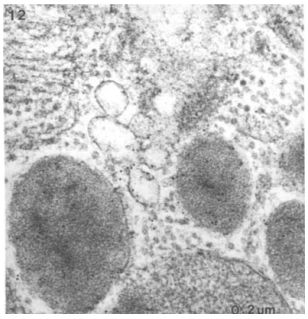

Braunwald, Am Jour Med, 1964

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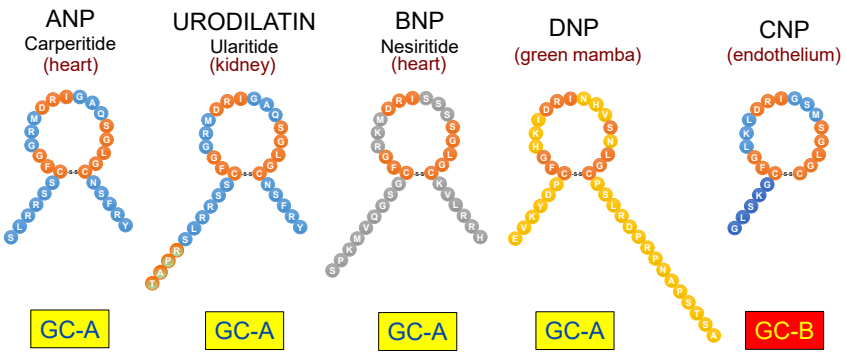
The Natriuretic Peptides: Particulate Guanylyl Cyclase (pGC) Activators



- Ring plays key role in receptor activation
- Alteration of the C-termini plays a role in providing resistance to enzymatic degradation

CNP, C-type natriuretic peptide; DNP, D-type natriuretic peptide; GC, guanylyl cyclase.
Meems LMG, Burnett JC Jr. *JACC: Basic Transl Sci.* 2016;1:557-567. Misono KS et al. *Biochem Biophys Res Commun*. 1984;123:444-51.

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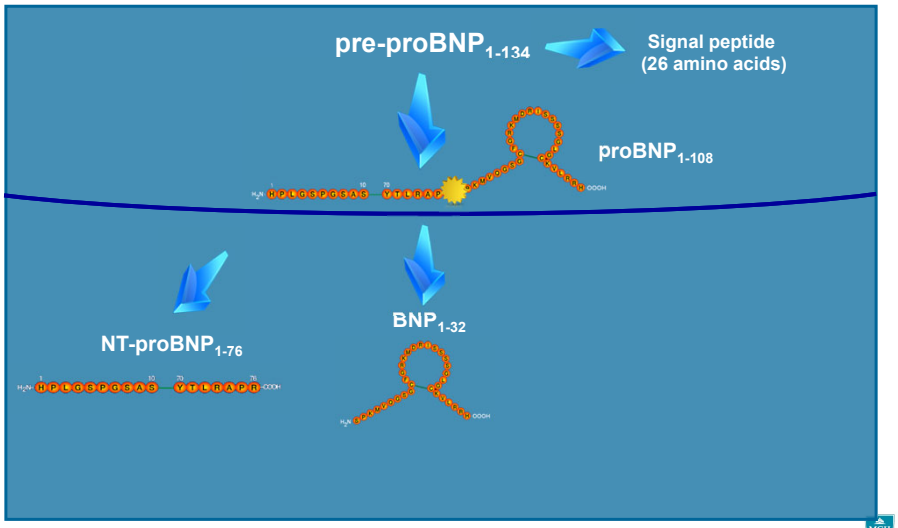
Biology of the NPs



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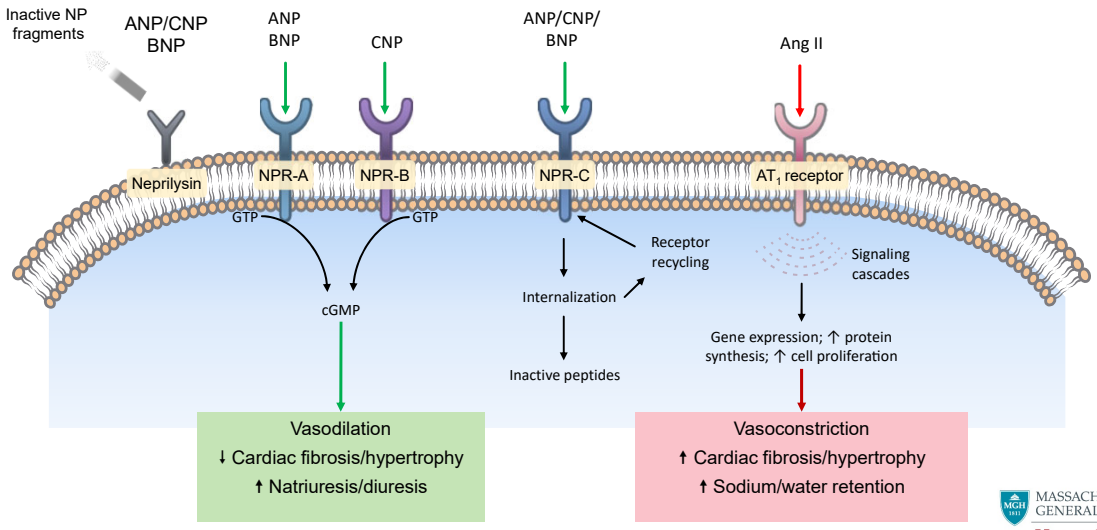
NPs oppose the RAAS



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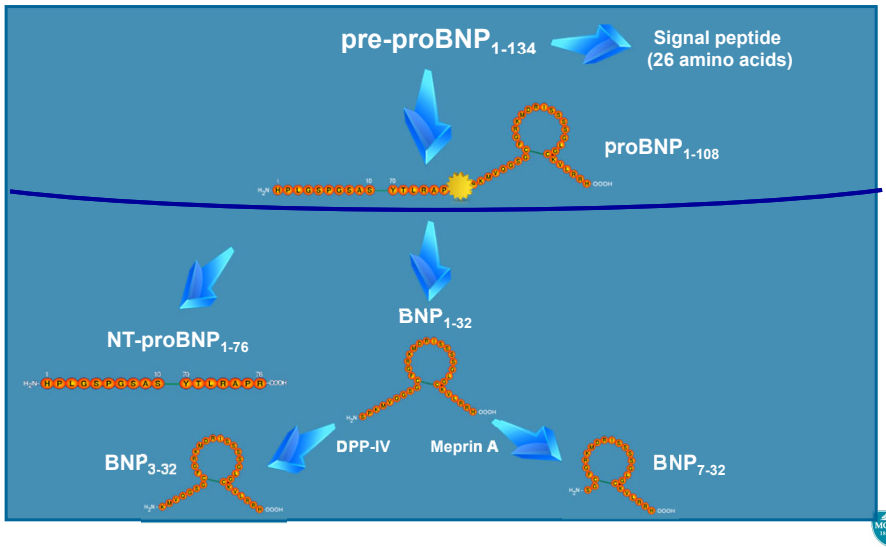
Biology of the NPs



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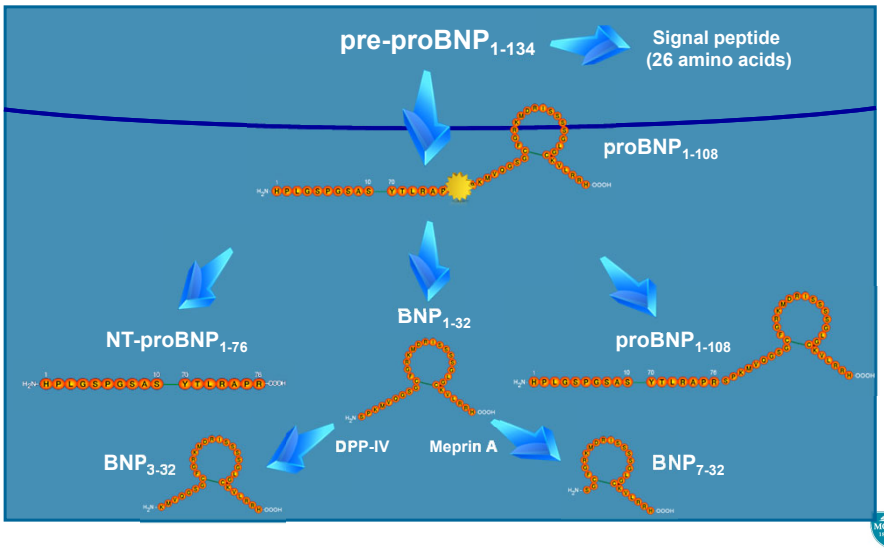
Biology of the NP System



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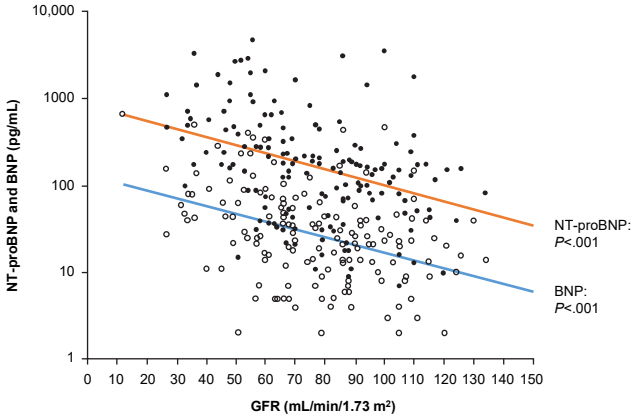
Natriuretic Peptide Clearance

- BNP[1]
  - NPR
  - Renal excretion
  - Neprilysin
- NT-proBNP[1,2]
  - Less well understood
  - Renal excretion partially responsible

BNP and NT-proBNP Clearance Are Equally Dependent on Renal Function[1,*]



BNP, B-type natriuretic peptide; GFR, glomerular filtration rate; NPR, natriuretic peptide receptor; NT-proBNP, N-terminal pro-brain natriuretic peptide.
*In patients with hypertension (N=165) undergoing renal arteriography with invasive renal plasma flow measurements and echocardiography.
1. van Kimmenade RRJ et al. *J Am Coll Cardiol.* 2009;53:884-890. 2. Palmer SC et al. *Eur J Heart Fail.* 2009;11:832-839.

12

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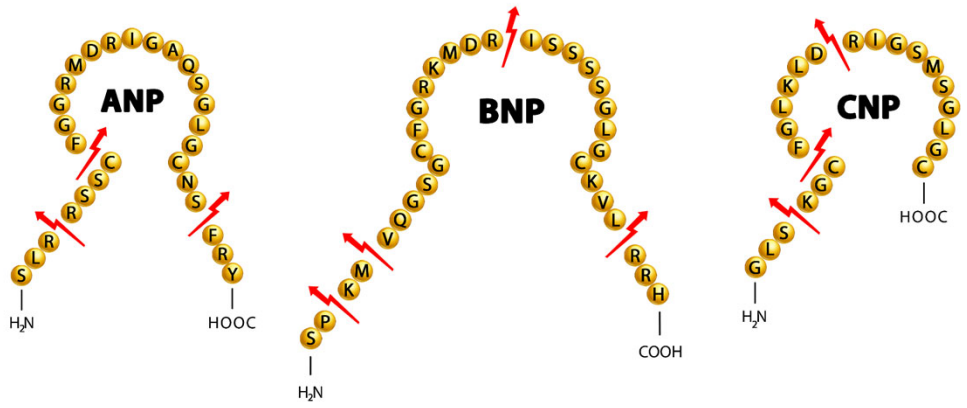
ANP, BNP, CNP Neprilysin Cleavage Sites



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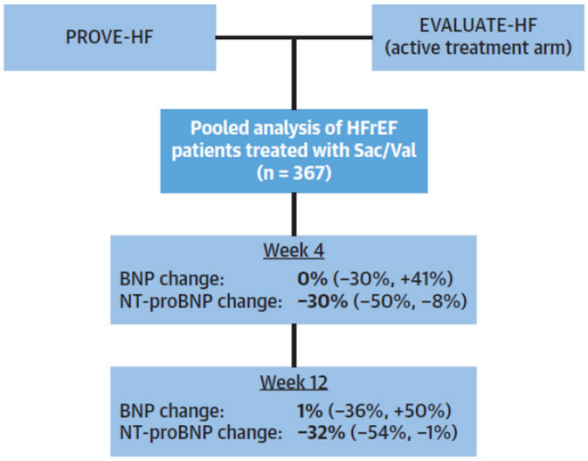
BNP change in PROVE-HF and EVALUATE-HF

PROVE-HF



- **Among 367 study participants treated with S/V for 12 weeks, the average BNP change was 0% and +1% respectively (compared to -30% and -32% reduction in NT-proBNP)**
- **This is in contrast to PARADIGM-HF, where the increase was +19%**
- **These results call into question the dogma that "BNP should significantly rise" after treatment with S/V**
- **But it didn't fall!**

Myhre PL, et al, JACC Heart Fail. 2022 Feb;10(2):119-128.

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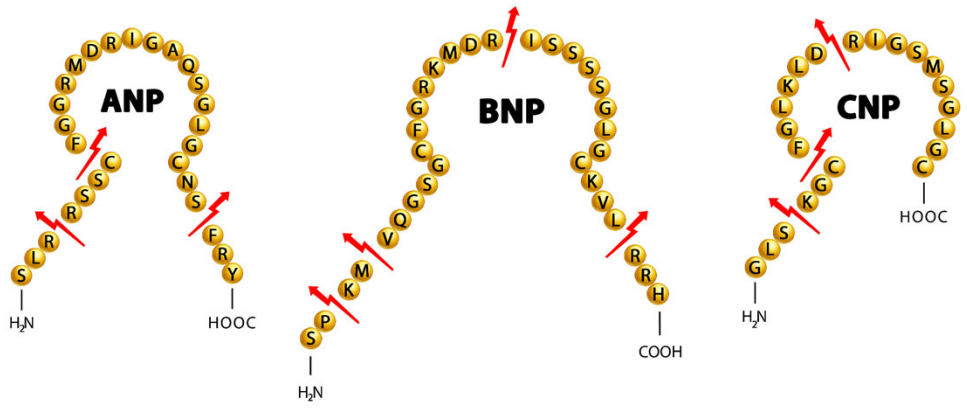
ANP, BNP, CNP Neprilysin Cleavage Sites



15

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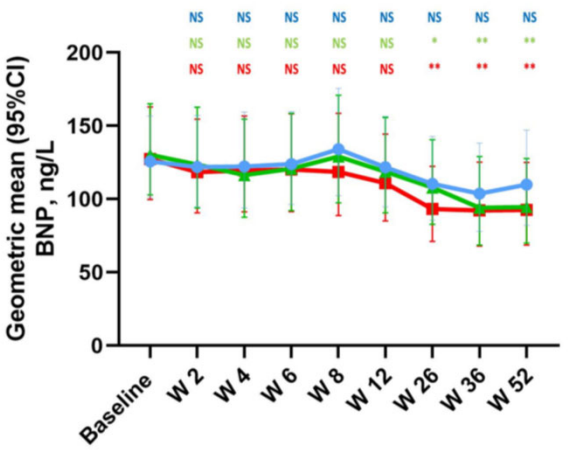
Does nep inhibition affect BNP assays differently?

PROVE-HF



- **These results provide reassuring evidence BNP methods are reasonably similar in their vulnerability to bias from neprilysin inhibition**
- **Use of the Siemens assay may result in modestly higher concentrations than other methods**

Myhre PL, et al, Clin Chem 2022

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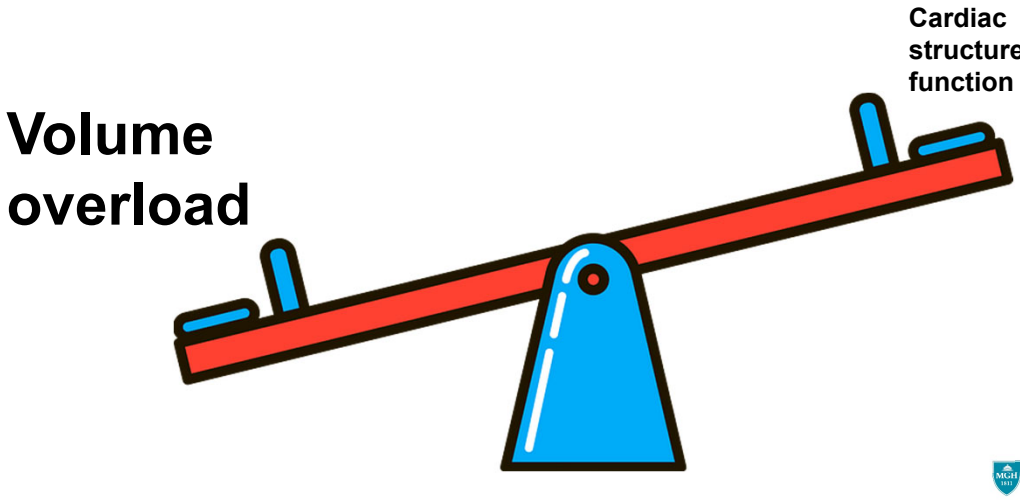
What drives NT-proBNP in acute heart failure?



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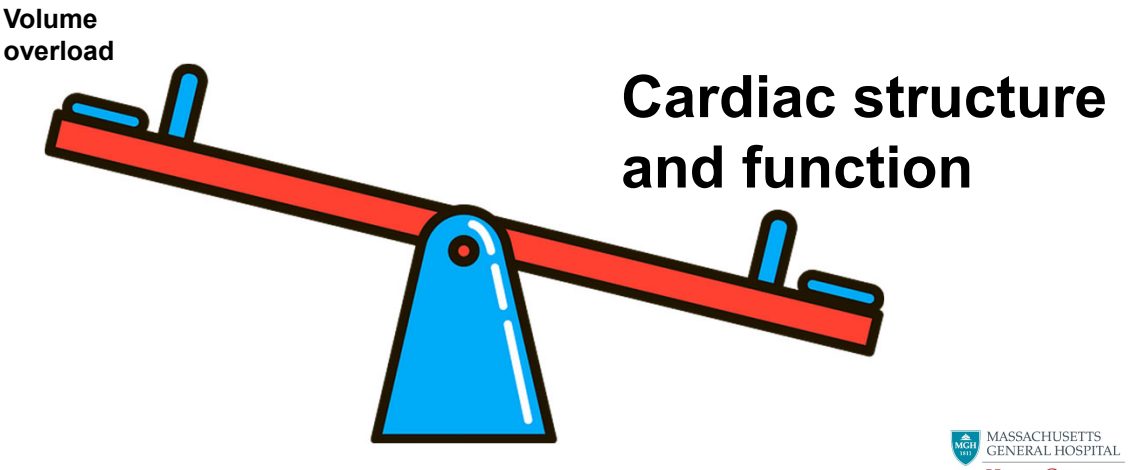
What drives NT-proBNP in chronic heart failure?



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Cardiac Correlates for NP Values

- Left ventricle
  - Systolic function
  - Diastolic function
  - Chamber size
  - Wall thickness
- Right ventricle
  - Systolic function
  - Chamber size
- Atria
  - Size
- Valves
  - AS, AI
  - MR, MS
  - TR, TS
- Filling pressures
  - Pulmonary
  - Left ventricle, left atrial
- Coronary ischemia
- Heart rhythm
- Aortic capacitance

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Clinical correlates of elevated NPs

- Heart failure

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Clinical correlates of elevated NPs

- Heart failure
- ACS
- Heart muscle disease
- Pericardial disease
- Valvular heart disease
- Atrial fibrillation
- Pulmonary hypertension
- Myocarditis
- Cardiac surgery
- Congenital heart disease
- Cardioversion
- Advancing age
- Anemia
- Pulmonary embolism
- Sleep apnea
- Critical illness
- Sepsis
- Burns
- Toxic-metabolic insults
- Renal failure

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21

HF Clinical Practice Guidelines

Indication	Class	LOE
NPs for diagnosis[1-3]	I	A
NPs for prognosis[1-3]	I	A
NPs for predischarge risk assessment[1-3]	IIa	B-NR
NPs to prevent HF onset[1-3]	IIa	B-R
NPs to guide HF therapy[4]	IIa	B

JACC Journal of the American College of Cardiology | Circulation Journal of the American Heart Association | Journal of Cardiac Failure

LOE, level of evidence.
1. Yancy CW et al. *J Am Coll Cardiol*. 2017. doi: 10.1016/j.jaac.2017.04.025. 2. Yancy CW et al. *Circulation*. 2017. doi: 10.1161/CIR.0000000000000509.
3. Yancy CW et al. *J Card Fail*. 2017. doi: 10.1016/j.cardfail.2017.04.014. 4. Yancy CW, et al. *Circulation*. 2013;e240-327.

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22

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3. Yancy CW et al. *J Card Fail*. 2017. doi: 10.1016/j.cardfail.2017.04.014. 4. Yancy CW, et al. *Circulation*. 2013;e240-327.

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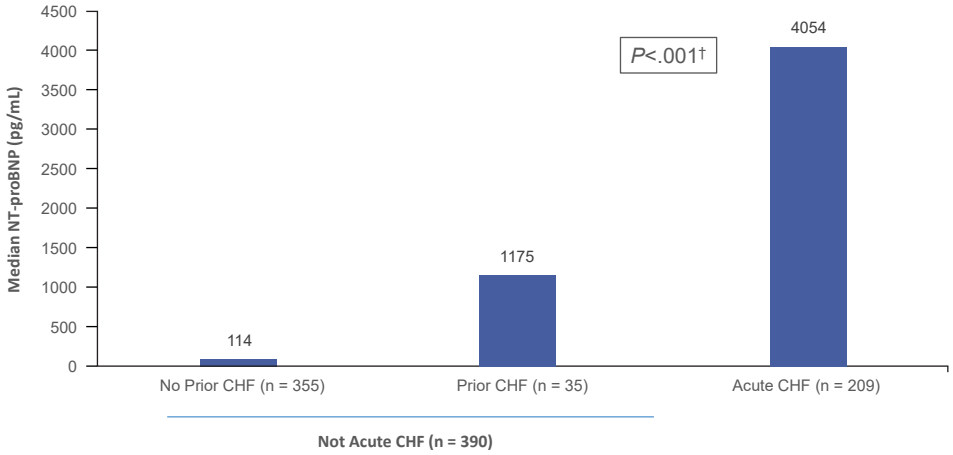
23

NT-proBNP Levels Were Elevated in Patients With Acute HF in the PRIDE Study*



CHF, congestive heart failure; PRIDE, N-Terminal Pro-BNP Investigation of Dyspnea in the Emergency Department.
*Patients (N = 599) were consenting adults ≥21 years of age presenting to the emergency department of the Massachusetts General Hospital with complain of dyspnea. †*P* value represents the comparison of acute CHF with patients with not-acute CHF.
Januzzi JL Jr et al. *Am J Cardiol.* 2005;95:948-954.

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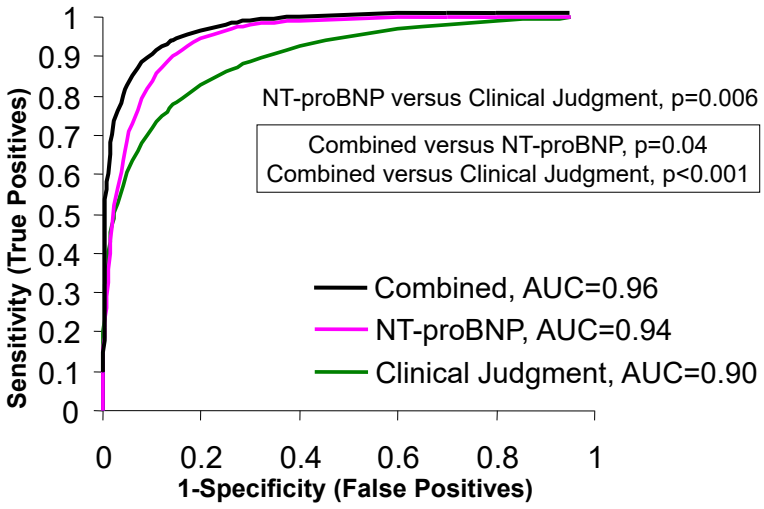
24

24

PRIDE Study



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25

Performance of BNP or NT-proBNP

When using a single cut-point strategy for BNP or NT-proBNP, we trade off reduced utility for simplicity!

Cut point	Sens	Spec	LR+	LR-
BNP, 100 ng/L	90%	76%	3.8	0.13
NT-proBNP, 900 ng/L	90%	85%	4.2	0.12

LR+ = Positive likelihood ratio; results >1 increase probability for disease; >10 is large increase

LR-= Negative likelihood ratio; results <1 reduce probability for disease; <0.10 is a large decrease

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Causes of lower PPV

Table 3. Variables associated with elevated BNP in the absence of acute heart failure.

Variable	Univariate OR	Univariate CI 95%	Multivariate OR	Multivariate CI 95%
Demographics				
Age/10-y increase	1.6	1.4–1.8	1.3	1.0–1.6
Medical history				
Chronic [illegible] heart failure	[illegible]	[illegible]		
Atrial				
Hype				
Clinic				
O_2 sa				
JVD				
Absen				
Murm				
Rales				
Body				
Ches				
Cardiomegaly	3.2	1.9–5.3	2.0	1.0–4.1
Pleural effusion	2.0	1.0–3.7		
Interstitial edema	2.5	1.1–5.8		
Blood value				
Creatinine (increase per mg/dL)	2.4	1.6–3.6		
Hemoglobin (decrease per g/dL)	1.3	1.2–1.4	1.2	1.1–1.4
ECG abnormal	3.0	2.0–4.4		

Variable	Multivariate OR	Multivariate CI 95%
Demographics		
Age/10-y increase	1.3	1.0–1.6

Among the most predictive variables for an elevated BNP in the absence of heart failure was age.

Per decade increase in age, a 30% adjusted risk for a BNP>100 was noted.

Knudsen, et al, Ann Emergency Med, 2005

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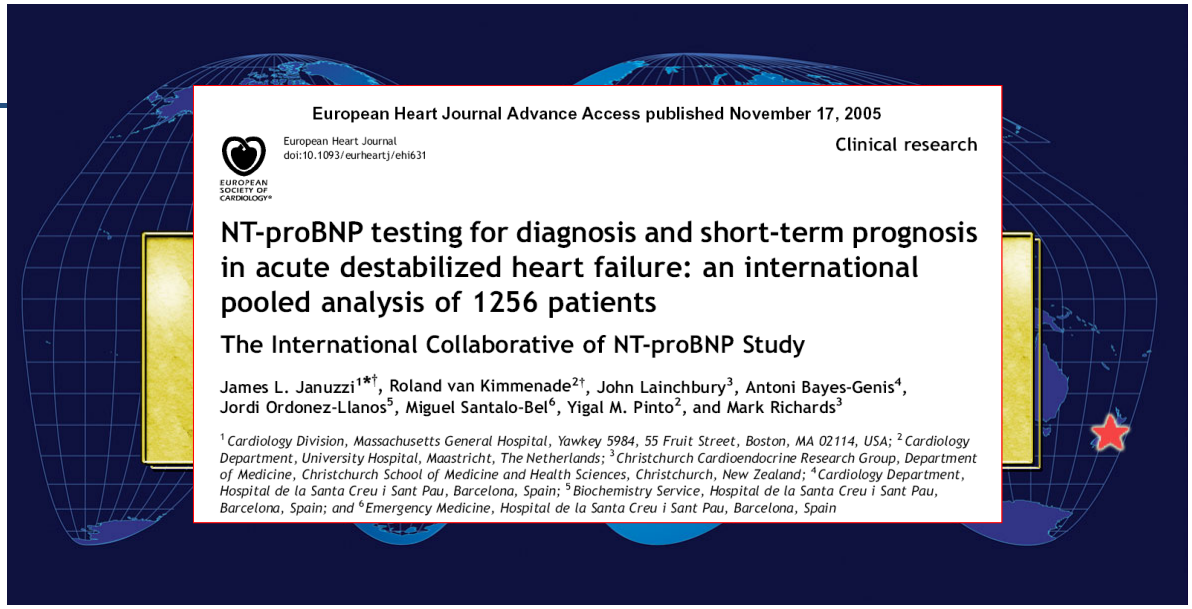

European Heart Journal Advance Access published November 17, 2005

European Heart Journal
doi:10.1093/eurheartj/ehi631

Clinical research

NT-proBNP testing for diagnosis and short-term prognosis in acute destabilized heart failure: an international pooled analysis of 1256 patients

The International Collaborative of NT-proBNP Study

James L. Januzzi[1*†], Roland van Kimmenade[2†], John Lainchbury[3], Antoni Bayes-Genis[4], Jordi Ordonez-Llanos[5], Miguel Santalo-Bel[6], Yigal M. Pinto[2], and Mark Richards[3]

[1] *Cardiology Division, Massachusetts General Hospital, Yawkey 5984, 55 Fruit Street, Boston, MA 02114, USA;* [2] *Cardiology Department, University Hospital, Maastricht, The Netherlands;* [3] *Christchurch Cardioendocrine Research Group, Department of Medicine, Christchurch School of Medicine and Health Sciences, Christchurch, New Zealand;* [4] *Cardiology Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain;* [5] *Biochemistry Service, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; and* [6] *Emergency Medicine, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain*

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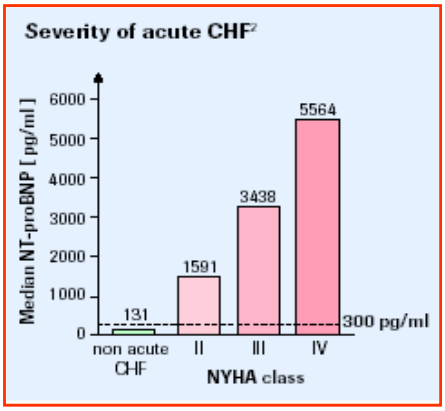
Age-independent "rule out" cut point

- **300 ng/L, age independent**
  - **99% sensitive**
  - **60% specific**
  - **LR- of 0.11**



Januzzi, et al, Eur H Jour 2006;27:330

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Age-stratified "rule in" cut point

To diagnose acute HF: the "triple cut point"

Age strata	Optimal cut-point	Sens	Spec	LR+
<50 years	450 ng/L	97%	93%	13.9
50-75 years	900 ng/L	90%	82%	5.0
>75 years	1800 ng/L	85%	73%	3.2
Overall		90%	84%	5.6

Age stratification was substantially superior to single cut-point strategy

Januzzi, et al, Eur H Jour 2006;27:330

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A new trial was needed to validate NT-proBNP cut-offs in the ED setting

International Collaborative of NT-proBNP:

Re-evaluation of Acute Diagnostic Cut-Offs in the Emergency Department

Gaggin,et al, Am Heart J, 2017; 192:26-37; Januzzi, et al, J Am Coll Cardiol, 2018;71(11):1191-1200

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Aims of the study

- The primary aim of this study was to validate the ICON cutoffs in the contemporary cohort.
  - Age-stratified “rule in” cut-offs
  - Age-independent “rule out” cut-off

Gaggin,et al, Am Heart J, 2017; 192:26-37; Januzzi, et al, J Am Coll Cardiol, 2018;71(11):1191-1200

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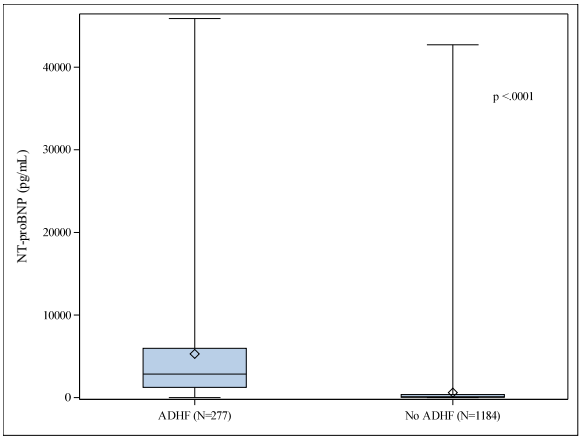
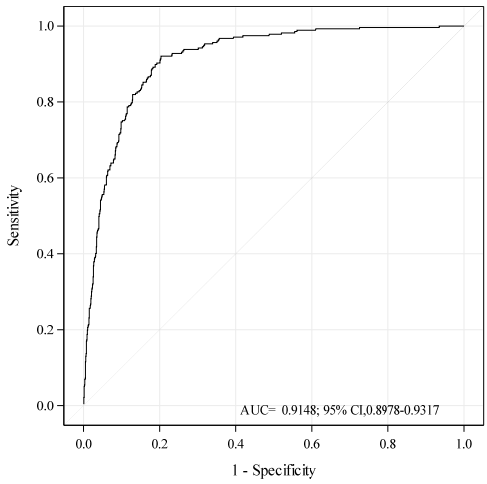
ICON-RELOADED Results: NT-proBNP





Januzzi, et al, J Am Coll Cardiol, 2018;71(11):1191-1200

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33

Performance of Cut-points

Category	Optimal Cut-Point	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	LR+	LR-
Confirmatory ('rule in') cut-points							
<50 years (n=462)	450 pg/mL	86%	94%	54%	99%	14.1	0.15
50-75 years (n=833)	900 pg/mL	79%	84%	58%	94%	4.96	0.25
>75 years (n=166)	1800 pg/mL	76%	75%	62%	85%	3.04	0.32
Rule in, overall		**79%**	**87%**	**58%**	**95%**	**5.97**	**0.24**
Exclusionary ('rule out') cut-point	**300 pg/mL**	**94%**	**72%**	**44%**	**98%**	**3.32**	**0.09**

Januzzi, et al, J Am Coll Cardiol, 2018;71(11):1191-1200

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ICON RELOADED in context

Study	AUC	LR+	LR-	Comment
Maisel, et al, 2002	0.91	2.6	0.05	Breathing Not Properly Multinational Study
Januzzi, et al, 2006	0.94	5.60	0.11	LR+ for age stratified cut off; LR- for 300 ng/L
Maisel, et al, 2010	0.91	2.51	0.07	Biomarkers in Acute Congestive HF Study
ICON-RELOADED	0.91	5.97	0.09	LR+ for age stratified cut off; LR- for 300 ng/L

Similar AUC compared with other studies

Januzzi, et al, J Am Coll Cardiol, 2018;71(11):1191-1200

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ICON RELOADED in context

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ICON-RELOADED	0.91	5.97	0.09	LR+ for age stratified cut off; LR- for 300 ng/L

The age-stratified diagnostic cut-point strategy provides comparable to superior LR+ compared with prior studies

Januzzi, et al, J Am Coll Cardiol, 2018;71(11):1191-1200

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ICON RELOADED in context

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ICON-RELOADED	0.91	5.97	0.09	LR+ for age stratified cut off; LR- for 300 ng/L

Rule out cut-point of 300 pg/mL provides excellent LR- to exclude acute HF

Januzzi, et al, J Am Coll Cardiol, 2018;71(11):1191-1200

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Managing unexpectedly high NPs

*For unexpectedly **HIGH** values:*

- Heart failure
- ACS
- Heart muscle disease
- Pericardial disease
- Valvular heart disease
- Atrial fibrillation
- Pulmonary hypertension
- Myocarditis
- Cardiac surgery
- Congenital heart disease
- Cardioversion, ablation
- Advancing age
- Anemia
- Pulmonary embolism
- Sleep apnea
- Critical illness
- Sepsis
- Burns
- Toxic-metabolic insults
- Renal failure

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Managing unexpectedly low NPs

*For unexpectedly **LOW** values:*

- Obesity
- HFpEF
- Mild acute heart failure
- Isolated right heart failure
- Treated heart failure

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Predictors of grey zone results

ICON

Characteristic	OR	95% CI	p-value
Cough	0.18	0.06-0.52	0.001
Use of loop diuretic on presentation	3.99	1.58-10.1	0.003
Paroxysmal nocturnal dyspnea	4.50	1.32-15.4	0.02
Jugular vein distension	3.05	1.06-8.79	0.04
Prior heart failure	2.63	1.02-6.80	0.05
Lower extremity edema	2.96	0.94-9.31	0.06
S3 Gallop	10.4	0.82-130.7	0.07
Prior COPD/Asthma	0.48	0.20-1.19	0.11
Orthopnea	2.06	0.73-5.83	0.17
Wheezing	0.81	0.29-2.22	0.17

Clinical variables assist with interpretation of grey zone NT-proBNP values!

van Kimmenade, et al, AJC, 2006

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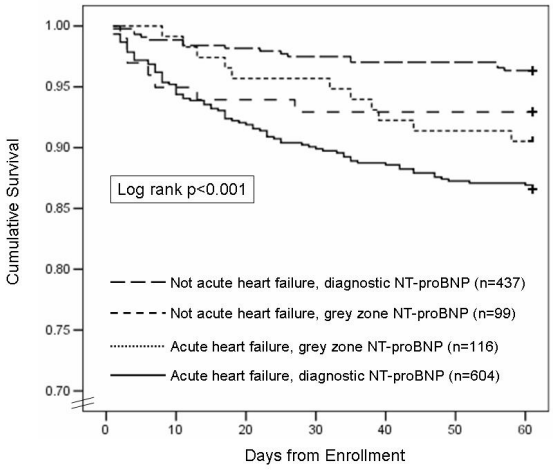
Grey zone results have prognostic meaning



Grey zone results have intermediate outcomes and should not be ignored!

van Kimmenade, et al, AJC, 2006

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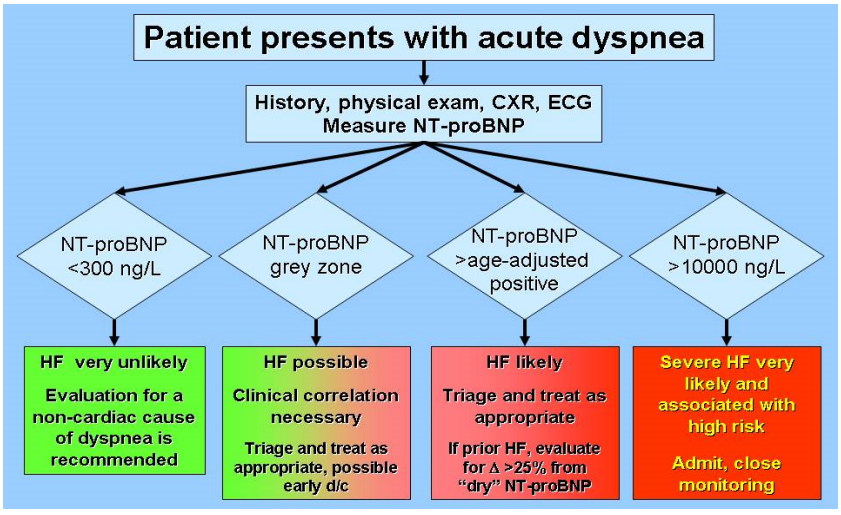
41

NT-proBNP Consensus Algorithm



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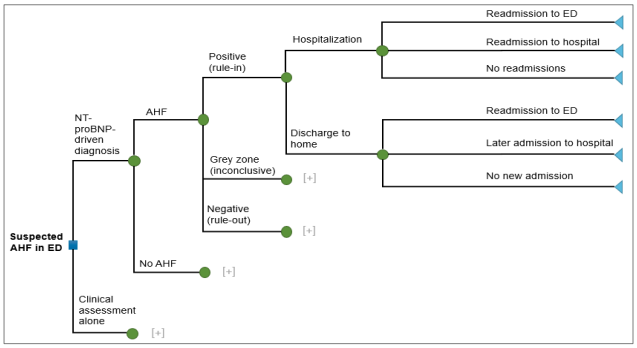
ICON-RELOADED Results: Cost-effectiveness



- 14% fewer initial hospitalizations
- 15% fewer admissions to cardiology or ICU
- 30% reduction in echocardiograms
- 26% fewer ED or hospital readmissions

Siebert, et al, Am Jour Cardiol, 2021

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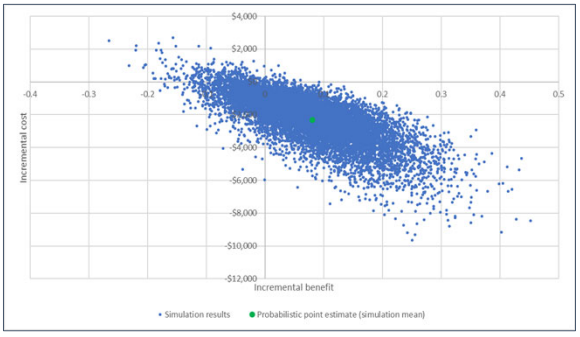
ICON-RELOADED Results: Cost-effectivess

- Use of NT-proBNP decreased the average inpatient management costs by a relative 10.4% ($20,247 vs. $22,584) and reduced the total length of stay in ED and hospital, yielding cost savings of $2,337/pt
- NT-proBNP reduced SAEs by 5.9% compared to clinical assessment alone



Siebert, et al, Am Jour Cardiol, 2021

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What about out-patient uses?

- For the outpatient evaluation of dyspnea in those without established heart failure, optimal application of NT-proBNP is:

✓To EXCLUDE the diagnosis (NPV-based)

✓Using much lower cut-points than in acute dyspnea

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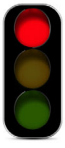
NT-proBNP: utility in outpatient dyspnea

History
Physical examination

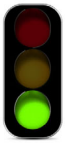
Measure NT-proBNP

NT-proBNP <125 pg/mL?



HF unlikely:
Seek alternative diagnosis

NT-proBNP ≥125 pg/mL?



HF possible:
Cardiac work up

Hildebrandt P, Collinson PO. Am J Cardiol. 2008 Feb 4;101(3A):25-8

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HF Clinical Practice Guidelines

Indication	Class	LOE
NPs for diagnosis[1-3]	I	A
NPs for prognosis[1-3]	I	A
NPs for predischarge risk assessment[1-3]	IIa	B-NR
NPs to prevent HF onset[1-3]	IIa	B-R
NPs to guide HF therapy[4]	IIa	B

JACC Journal of the American College of Cardiology | Circulation Journal of the American Heart Association | Journal of Cardiac Failure

LOE, level of evidence.
1. Yancy CW et al. *J Am Coll Cardiol*. 2017. doi: 10.1016/j.jaac.2017.04.025. 2. Yancy CW et al. *Circulation*. 2017. doi: 10.1161/CIR.0000000000000509.
3. Yancy CW et al. *J Card Fail*. 2017. doi: 10.1016/j.cardfail.2017.04.014. 4. Yancy CW, et al. *Circulation*. 2013;e240-327.

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47

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3. Yancy CW et al. *J Card Fail*. 2017. doi: 10.1016/j.cardfail.2017.04.014. 4. Yancy CW, et al. *Circulation*. 2013;e240-327.

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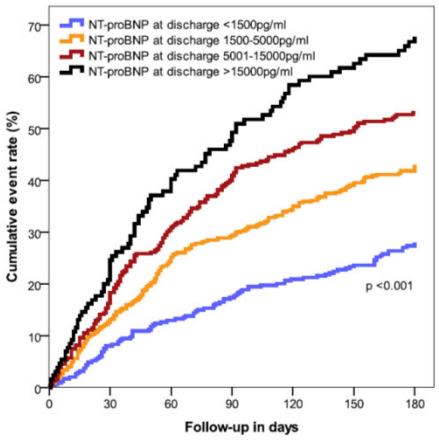
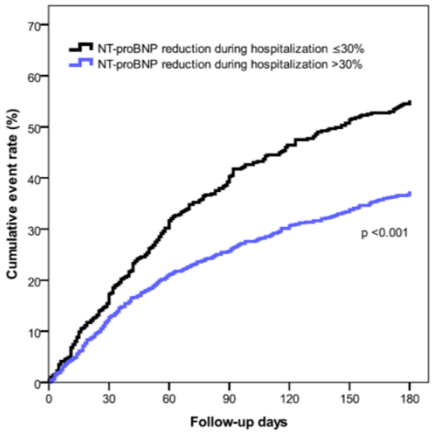
48

NT-proBNP and prognosis after ADHF treatment





Salah, et al, Heart, 2014

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NT-proBNP Monitoring in AHF

- **Two measurements:**
  - **<u>At presentation</u> for diagnosis, triage, and prognostication.**
  - **<u>At the end of hospitalization</u> to evaluate for treatment response and provide hospital to home link.**
    - ✓ **30% drop is desirable, and lower is always better**
    - ✓ **If baseline not available discharge NT-proBNP <4000 pg/mL is desirable**
    - ✓ **Non-falling or rising values identify a patient at imminent risk for rehospitalization and/or death**

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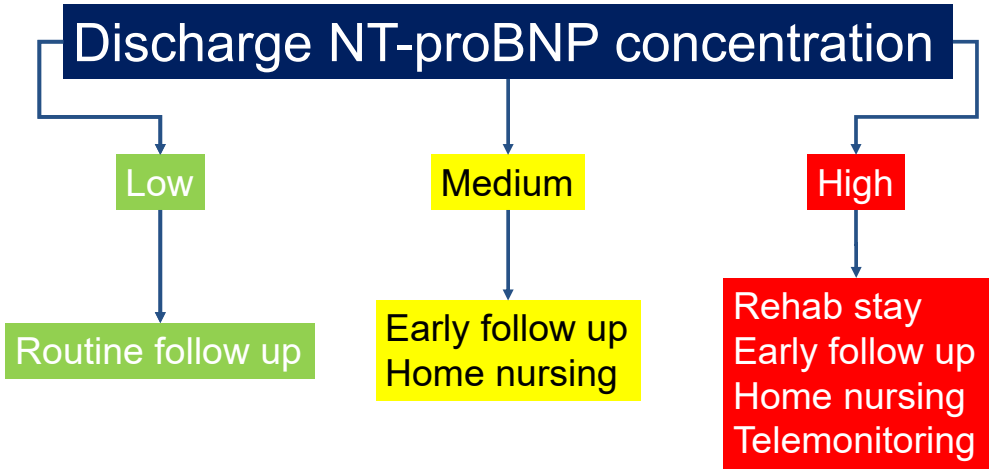
Individualized care based on discharge NT-proBNP



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NT-proBNP to bridge from hospital to home

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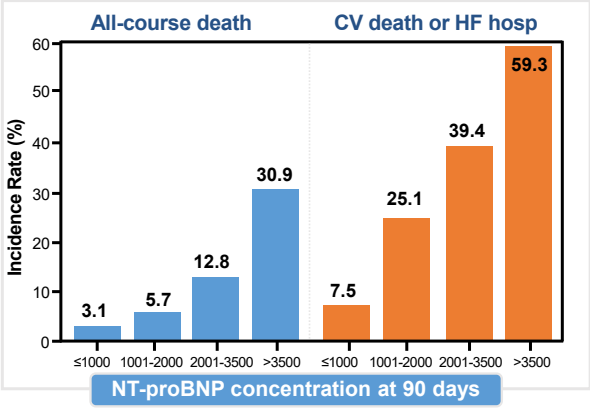
Outcomes and achieved NT-proBNP

Number of events per 100 patient-years of follow-up



Log2 of NT-proBNP at 90 days and clinical outcomes

	Adjusted	
Outcome	**HR (95% CI)**	**P-value**
All Cause Death[A]	0.58 (0.50–0.68)	<.001
HF Hosp/CV Death[B]	0.65 (0.57–0.73)	<.001

HR is with respect to halving of NT-proBNP

[A]Adjusted for history of ischemic heart disease, depression treated with medication, third heart sound, age, diastolic BP, congestion score, HF duration, heart rate, SpO2, sodium, and 6-minute walk distance.

[B]Adjusted for sleep apnea, depression treated with medication, Hispanic ethnicity, ICD or pacemaker, atrial fibrillation at baseline, Black race, history of ischemic heart disease, NYHA class, diastolic BP, creatinine, heart rate, potassium, and sodium.

BNP, B type natriuretic peptide; CI, confidence interval; CV, cardiovascular; HF, heart failure; HR, hazard ratio; NT-proBNP, N-terminal-pro-B type natriuretic peptide.
Januzzi J, et al. *J Am Coll Cardiol*.2019;74:1205-17.

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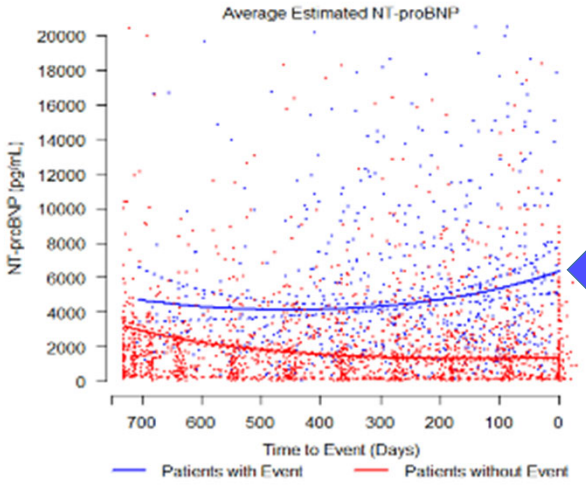
When does NT-proBNP rise relative to events?

GUIDE-IT



Serial results of NT-proBNP differed considerably among study participants with and without events (CV death/HF hospitalization)

Event happens here

Fuery M et al in preparation

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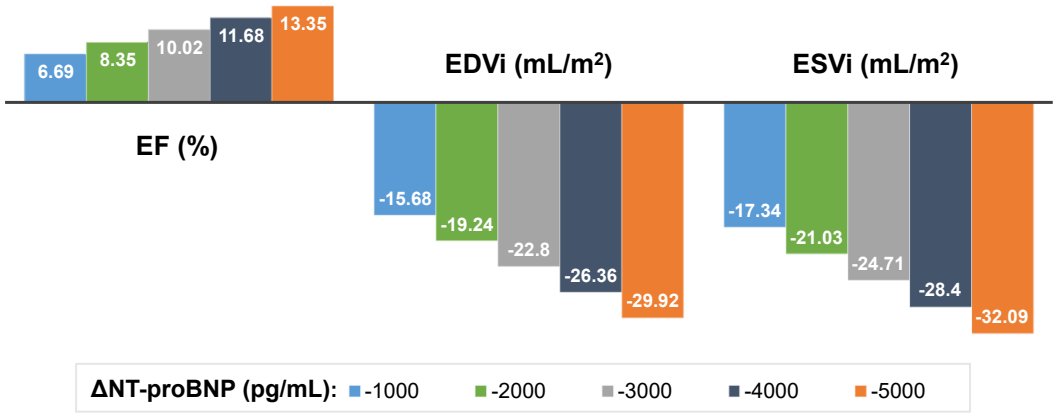
Change in LV structure and function at 1 year by NT-proBNP reduction



EF, ejection fraction; EDVi, end-diastolic volume index; ESVi, end-systolic volume index; LV, left ventricular; NTproBNP, N-terminal-pro-B type natriuretic peptide.
Daubert MA, et al. *JACC Heart Fail.* 2019;7:158–168.

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Operationalizing NP monitoring to enhance clinical decision-making in chronic HF

- **Hospital to home**: In recently decompensated patients, measure 1–2 weeks after discharge (office or home).
- **Outpatients**: measure every 3 months
  - Facilitates GDMT decision making (removal of diuretic after GDMT)
  - Stable concentrations <1000 pg/mL (NT-proBNP) or <100 pg/mL (BNP): imaging and other testing may be reasonably deferred
  - Elevated/rising concentrations: repeat imaging, further evaluations, review medication/lifestyle program and adjust as appropriate
  - **Markedly elevated concentrations**: Consider transplant referral, consider diagnoses associated with "unexpectedly elevated" NP (amyloidosis).

HF, heart failure; NT-pro-BNP, N-terminal pro-B type natriuretic peptide.
Yancy CW, et al. *J Am Coll Cardiol.* 2018;71:201–230.

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56

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3. Yancy CW et al. *J Card Fail*. 2017. doi: 10.1016/j.cardfail.2017.04.014. 4. Yancy CW, et al. *Circulation*. 2013;e240-327.

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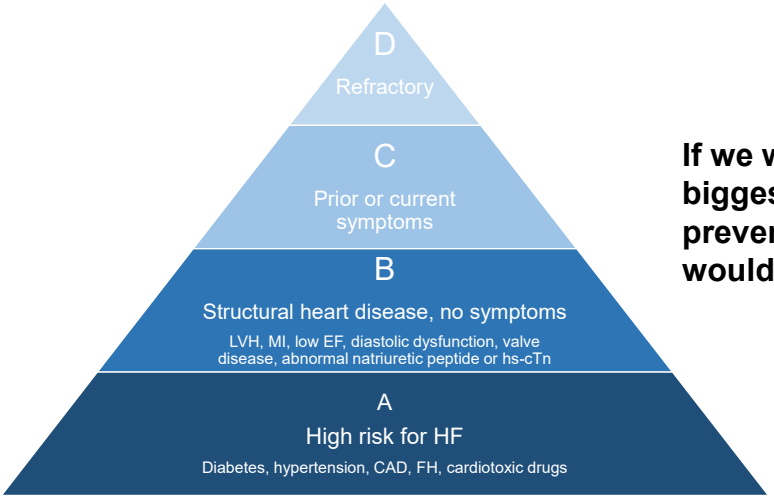
UDHF Stages of heart failure



If we were going to aim at the biggest opportunities for prevention of heart failure, where would we focus our energy?

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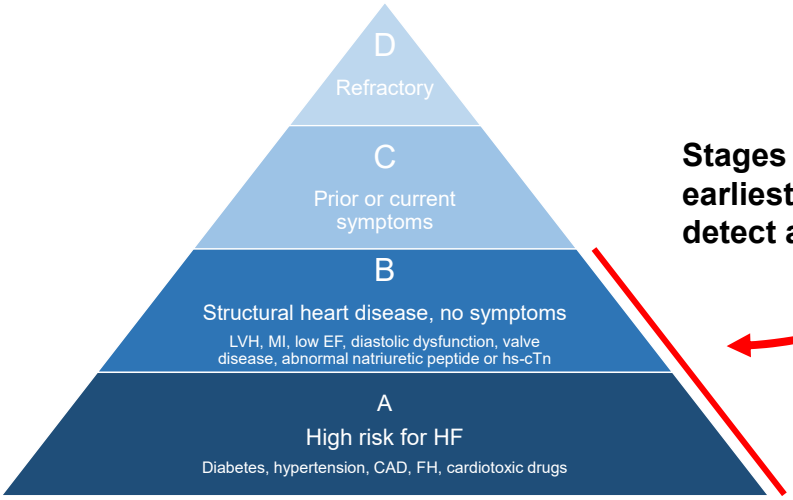
UDHF Stages of heart failure



Stages A and B represent the earliest and best opportunity to detect and prevent HF

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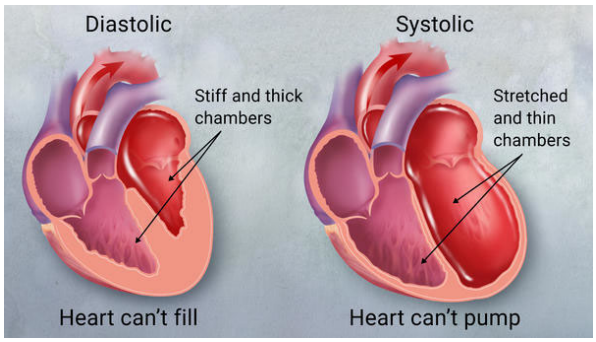
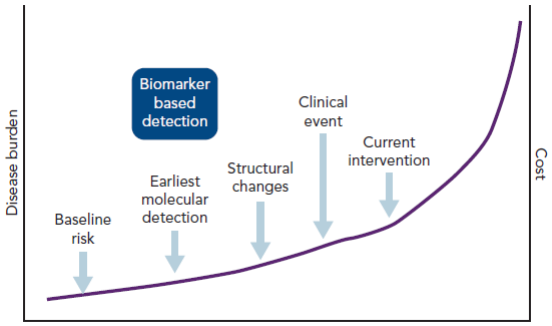
Stage B heart failure and biomarkers for early detection





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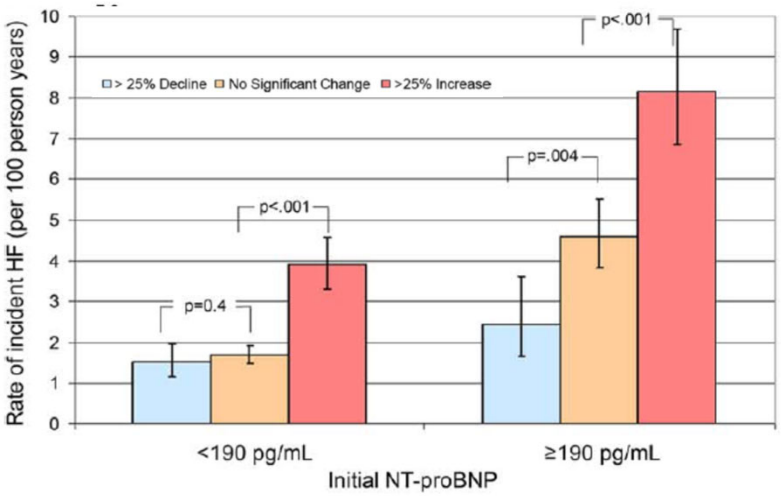
NT-proBNP and prognosis in Stage A HF



Seliger et al, JACC, 2010

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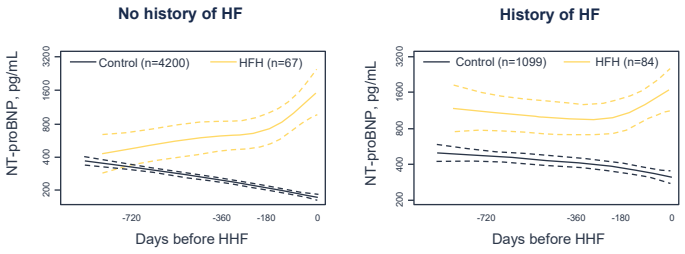
Sharp increase in NT-proBNP preceding hospitalization for heart failure in patients with T2D

- Randomized Phase 3 study including 5450 patients with T2D with a recent coronary event, with and without history of HF
- NPs measured at baseline and at 24 weeks
- Median follow-up: 26 months

- Levels of natriuretic peptides (BNP and NT-proBNP) were significantly greater when measured closer to the time of the event in those who experienced HF hospitalization (BNP, p<0.001; NT-proBNP, p<0.001).
- At the time of HHF, patients with and without a history of HF reached comparable levels of natriuretic peptides .

NP levels in the 6 months preceding heart failure hospitalization

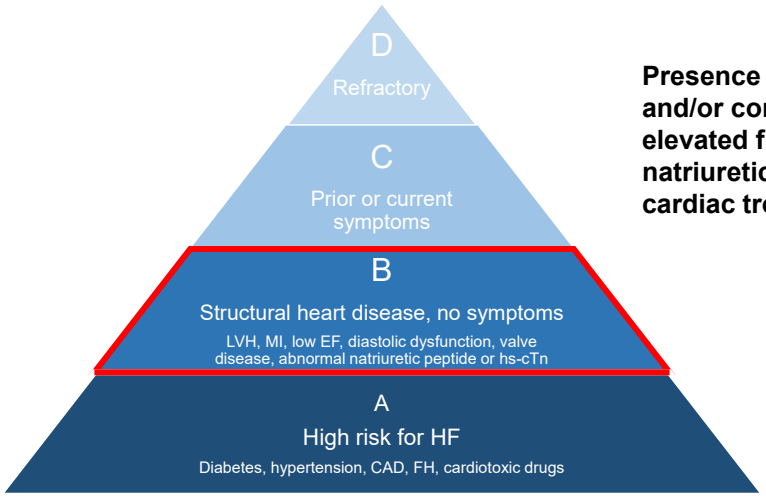


NT-proBNP may help identify patients with type 2 diabetes at risk for hospitalization for heart failure 6 months before the cardiac event, regardless of the history for heart failure

BNP, B-type natriuretic peptide; HHF, hospitalization for heart failure; NT-proBNP, N-terminal pro-B-type natriuretic peptide.
Wolsk et al. Circulation. 2017;136:1560-2.

62

Stages of heart failure: Stage B (pre-HF)



Presence of structural heart disease and/or congestion as evidenced by elevated filling pressures or abnormal natriuretic peptide or high sensitivity cardiac troponin

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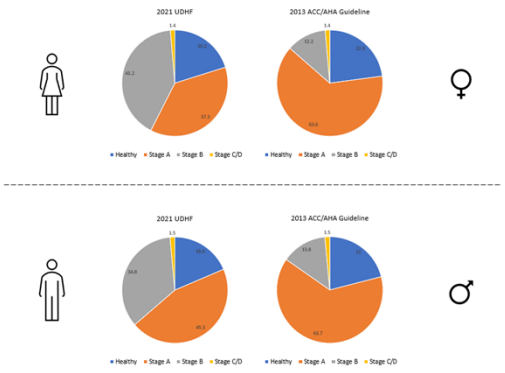
Impact of markers in Stage A→B

What is the impact of adding elevated biomarkers to the distribution of UDHF Stages in the community? And does it affect prognostication?



- With the 2021 definition, a more than doubling of the proportion of Stage B was observed
- Larger shift among women vs men
- Unique shifts in race / ethnic groups
  - Hispanic women
  - Black men

Mohebi R, et al, JACC Revised

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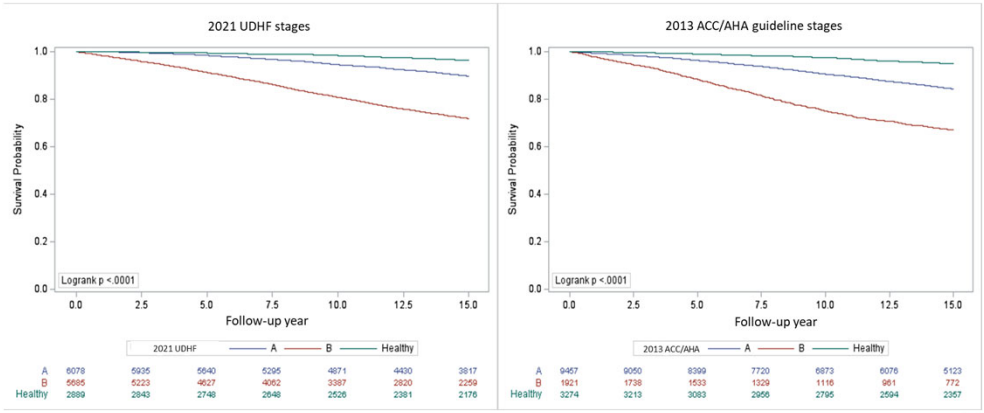

Transition to Stage C/D

Mohebi R, et al, JACC Revised

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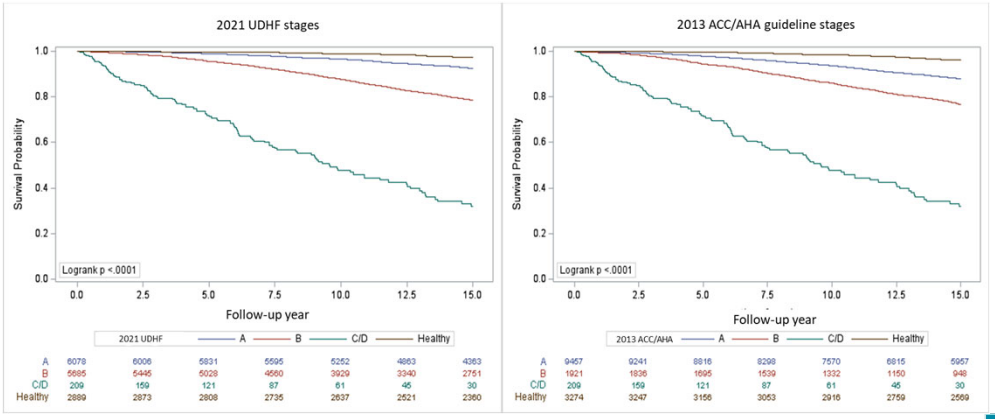

CV death

Mohebi R, et al, JACC Revised

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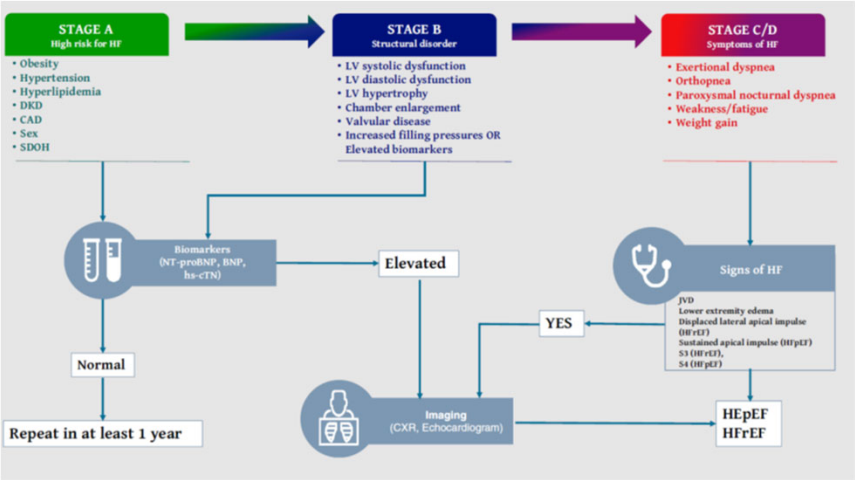
Evaluation and Diagnosis



- **Among those with diabetes, routine assessment for symptoms and control of risk factors is crucial**
- **Measurement of a natriuretic peptide or high sensitivity troponin at least yearly is recommended in Stages A/B**
- **In those with abnormal biomarkers and/or symptoms/signs of HF, referral for imaging is recommended**

Pop-Busui R, et al; Diabetes Care, 2022;45:1-21

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Agenda

- Natriuretic peptide biology
- Established clinical applications
- Emerging uses

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Conclusions

- In the past 20 years, NT-proBNP has gone from a curiosity to an essential tool in the everyday care of individuals with suspected heart failure
- Established uses of the biomarker include aid in diagnosis and prognosis of heart failure
- Emerging uses will include a role for prevention of heart failure onset in those at highest risk

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69