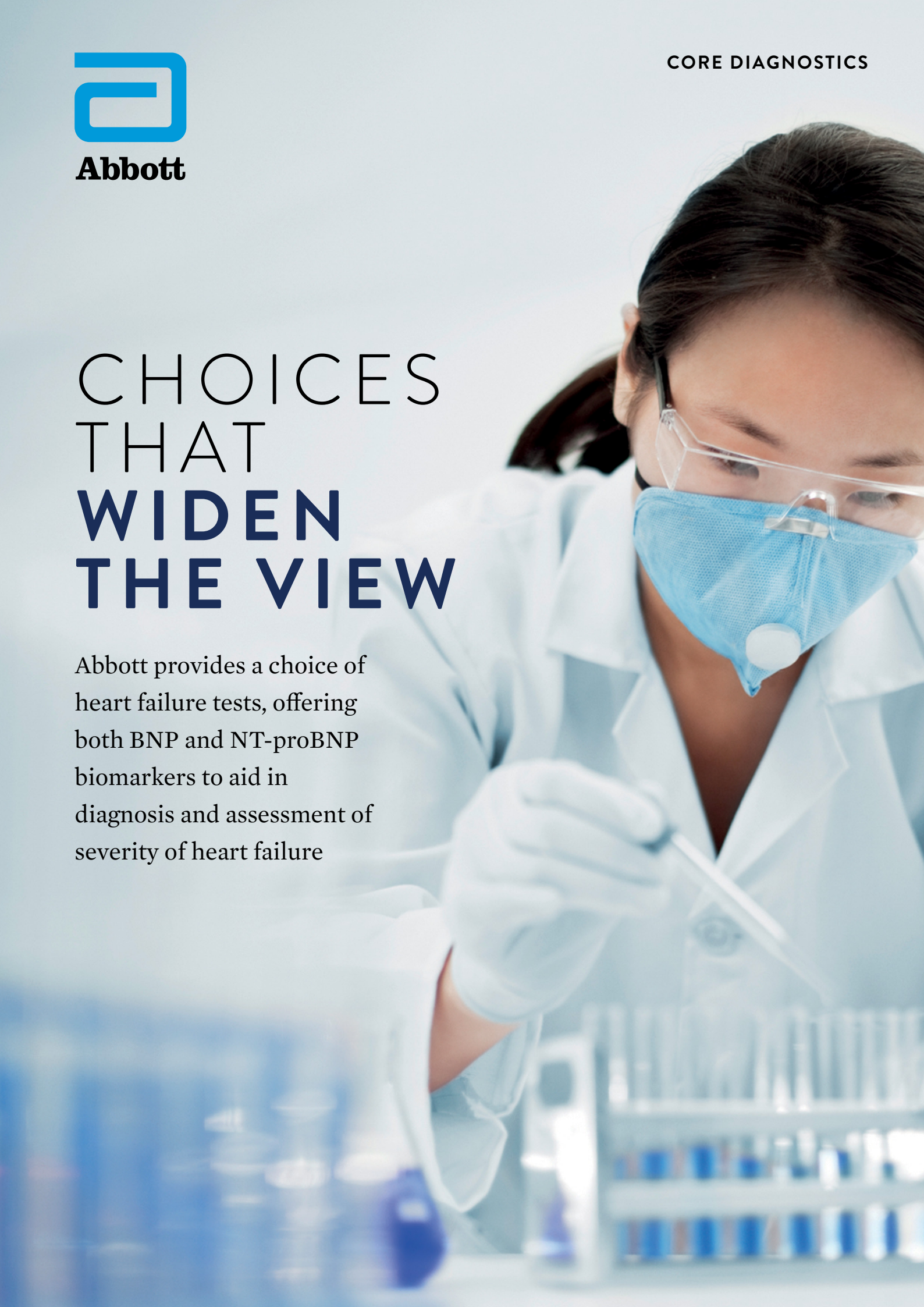
Abbott

CORE DIAGNOSTICS



CHOICES THAT **WIDEN THE VIEW**

Abbott provides a choice of heart failure tests, offering both BNP and NT-proBNP biomarkers to aid in diagnosis and assessment of severity of heart failure

THE VALUE OF NATRIURETIC PEPTIDES (NPs) IN ADDRESSING THE HEART FAILURE CHALLENGE

Measuring NPs—specifically B-type natriuretic peptide (BNP) and N-terminal pro B-type natriuretic peptide (NT-proBNP)—has shown benefit in almost every aspect of heart failure care.[1–5]

WHAT IS THE HEART FAILURE CHALLENGE?

- Heart failure can be difficult to diagnose since its presentation is complex, with many nonspecific signs and symptoms, such as shortness of breath[9]
- Misdiagnosis can lead to morbidity, and in-hospital mortality and re-admission rates are high.[6,8]

64.3 million people living with heart failure worldwide[6,7]

Prevalence of known heart failure in developed countries is estimated at **1–2%** of the adult population[6]

46% predicted rise in heart failure prevalence by 2030[8]

Heart failure results in significant clinical, societal and economic burden globally.[10,11]

Abbott's range of high-performance tests are free from biotin interference and enable identification of levels of either BNP or NT-proBNP which, when used in conjunction with clinical assessment, enables more accurate diagnosis of heart failure patients.[1–4]

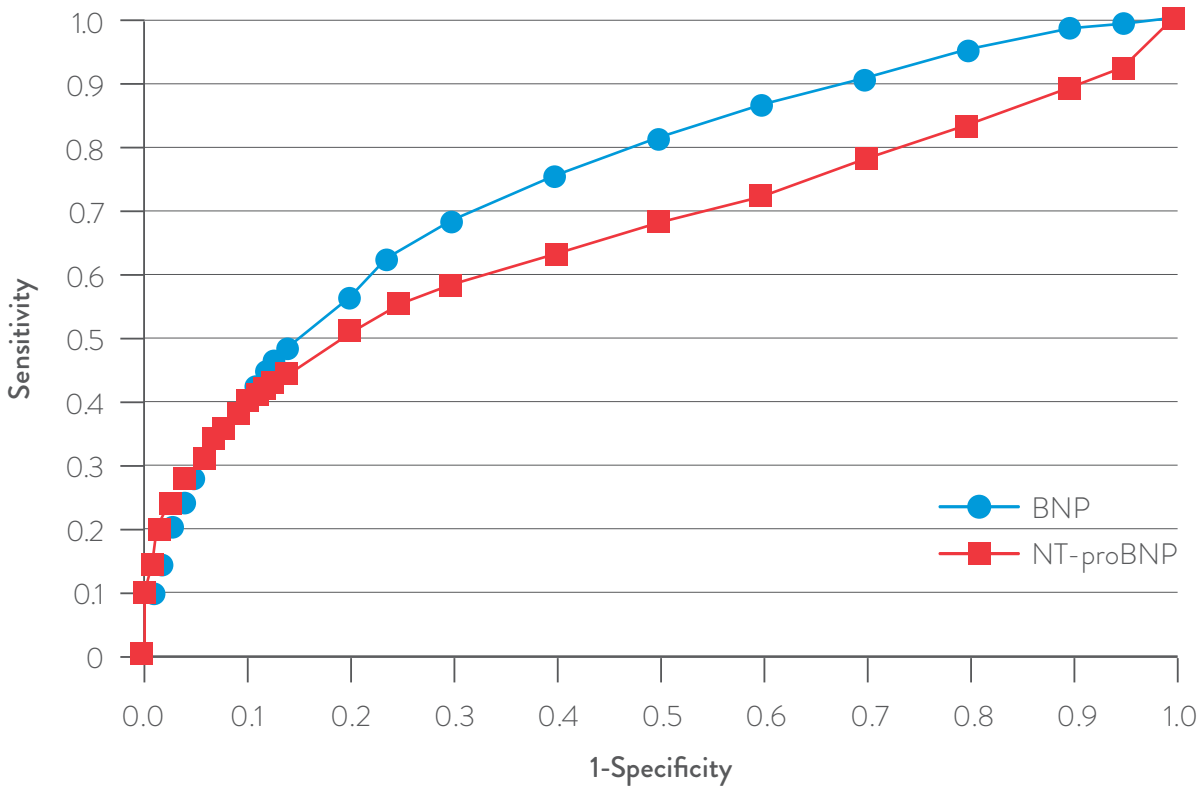
- NPs are useful in conjunction with clinical evaluation for the diagnosis or exclusion of acute heart failure in dyspneic patients[12]
- NPs used in assessment of dyspnea can lead to improved patient care while providing substantial cost savings by reducing hospitalizations and length of stay[10,13]
- NP measurement following heart failure treatment identifies patients at highest risk for death or rehospitalization.[11]

Diagnostic studies comparing measurements of NPs against a reference standard diagnosis of heart failure (or alternative diagnosis) have consistently shown that NP levels have high diagnostic accuracy for heart failure.[14–16]

NPs IN HEART FAILURE DIAGNOSIS

Assays for BNP and NT-proBNP have been increasingly used to establish the presence and severity of heart failure. The value of NP testing is particularly significant when the etiology of dyspnea is unclear.[15]

FIGURE 1: DIAGNOSIS AND EXCLUSION OF ACUTE HEART FAILURE IN DYSPNEIC PATIENTS[17]



Adapted from Roberts et al., 2016

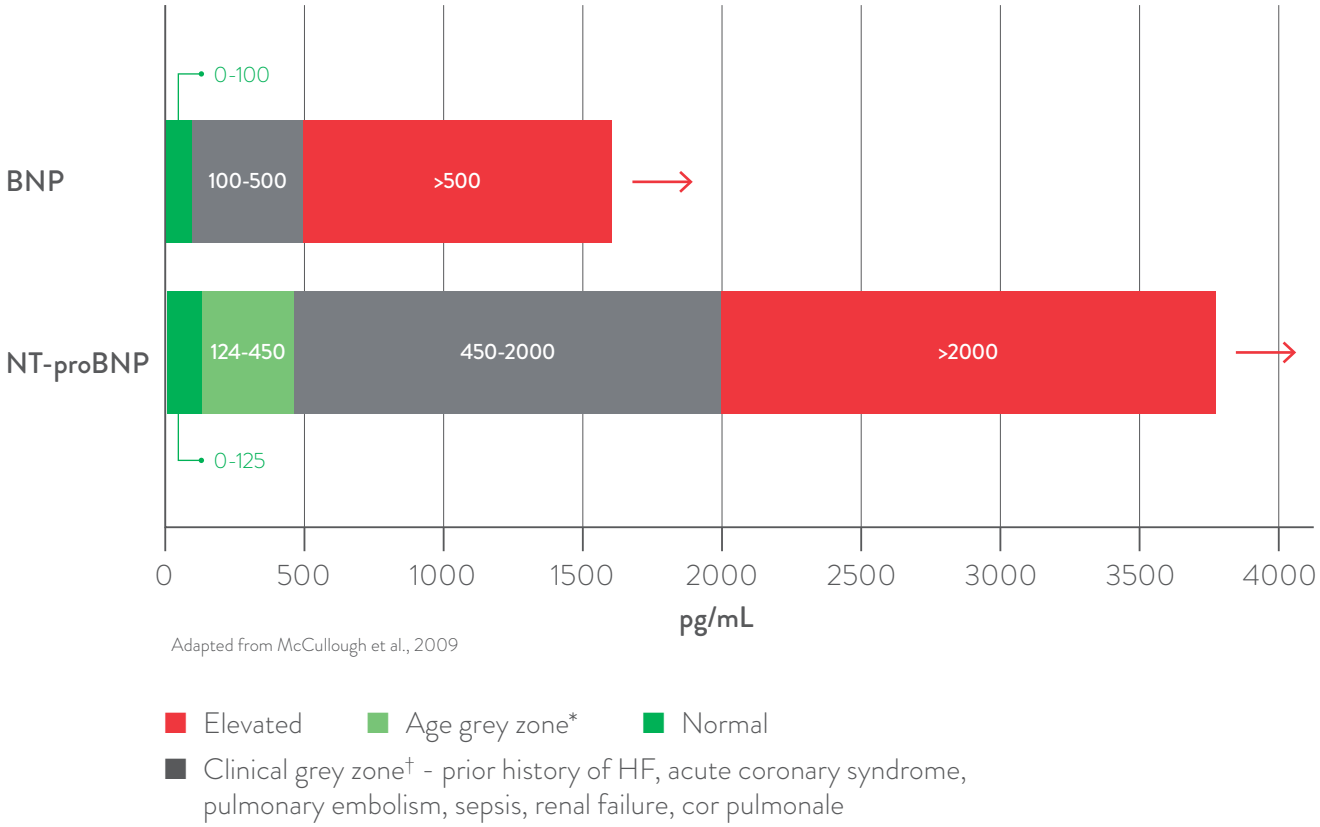
Comparison of area under the receiver operating characteristic curve (AUC) for BNP and NT-proBNP in the diagnosis of reduced left ventricular ejection fraction.

BNP AUC = 0.83;
NT-proBNP AUC= 0.79.[18]

DIFFERENT NP ASSAY CUTOFFS

BNP and NT-proBNP values are reasonably correlated, and either can be used in patient care settings as long as their respective absolute values and cut points are not used interchangeably.[19]

FIGURE 2: BNP AND NT-proBNP CLINICAL DECISION POINTS[17]



For BNP, all manufacturers currently suggest a single-decision cut off of 100 pg/mL1.[20]

For NT-proBNP, multiple age-related cut offs are used:[3]
125 pg/mL <75 yrs
450 pg/mL ≥75 yrs

ICON study recommends several cut offs for NT-proBNP:[13]

Rule out:	300 pg/mL
Rule in:	450 pg/mL <50 yrs
	900 pg/mL 50-75 yrs
	1800 pg/mL >75 yrs

Concentrations of both BNP and NT-proBNP that are below any of the decision cut offs can rule out the presence of heart failure with a high degree of confidence due to the sensitivity of the tests.[17,21]

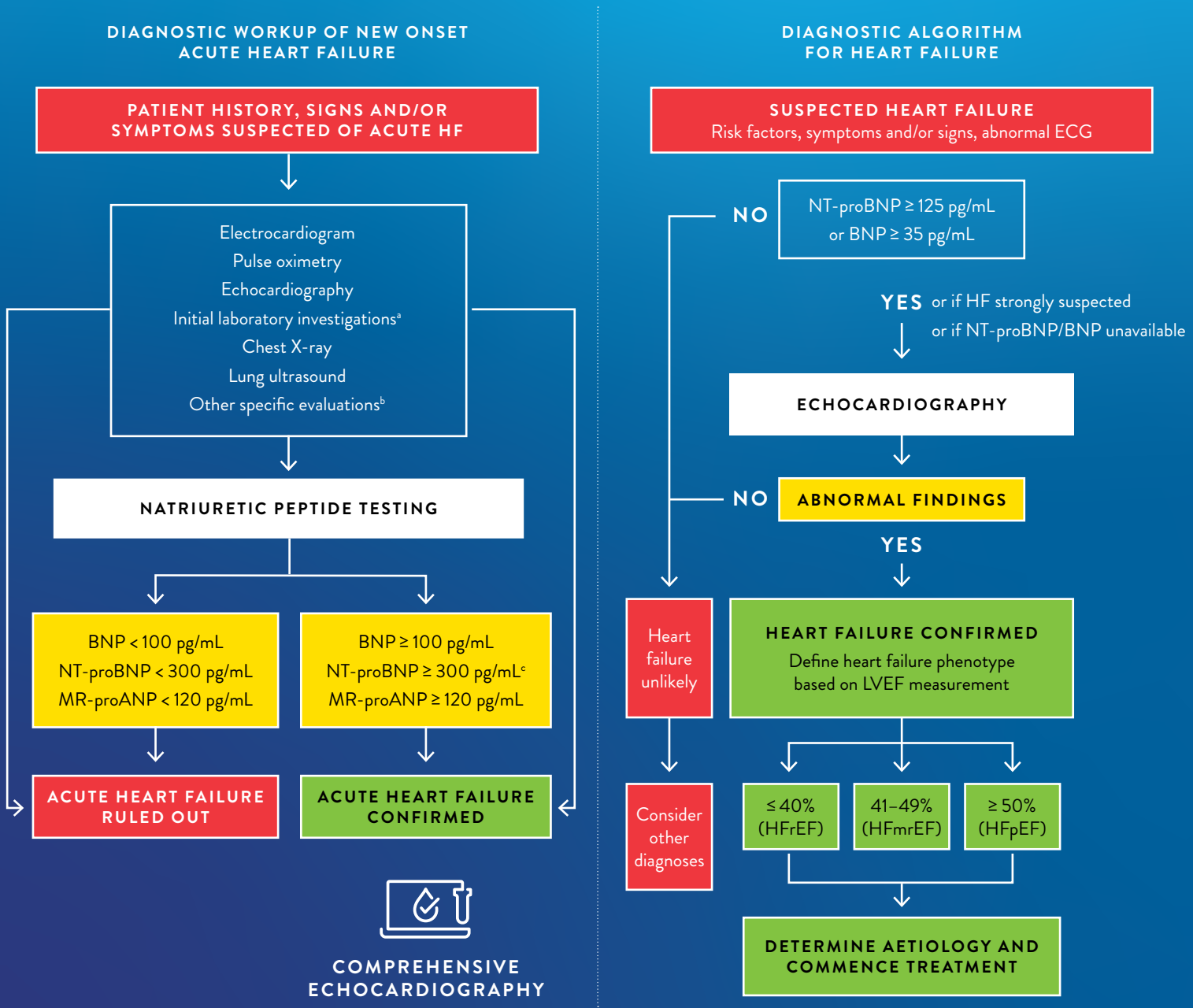
* Age over 50 years or renal dysfunction.
† Other non-heart failure conditions may be contributing to elevation.

USING CARDIAC BIOMARKERS IN CLINICAL PRACTICE

NP measurement can assist clinicians in differentiating acute heart failure (AHF) from other causes of acute shortness of breath.[11,21,22]

BNP or NT-proBNP measurement is a simple method to either exclude heart failure or identify patients who require more diagnostic testing to determine if heart failure is present.[21,22]

FIGURE 3: ESC GUIDELINES HEART FAILURE 2021[21]



Adapted from ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. McDonagh et al European Heart Journal 2021.

NPs HELP IMPROVE PATIENT OUTCOMES AND REDUCE COSTS*

Both BNP and NT-proBNP levels have been shown to correlate well with patient prognosis:

- In one study patients with BNP levels >350 pg/mL , were 5 times more likely to die or be readmitted for heart failure if discharged[20]
- Patients with BNP levels >700 pg/mL had 15 times the risk of death or readmission[20]
- Studies using NT-proBNP in heart failure patients during treatment suggested an absence of a decrease in levels during hospitalization correlates with mortality or readmission within 6 months of discharge.[20]

NPs used in assessment of dyspnea can lead to improved patient care while providing substantial cost savings by reducing hospitalizations and length of stay.[12,22]

In a study by Mueller et al, the use of BNP was associated with:[22]

- Improved time to treatment
- Improved time to discharge
- Decreased rate of hospitalization by 10%
- Reduced total cost of treatment by 26%.

In a study by Siebert et al, the use of NT-proBNP was associated with:[12]

- 1% relative reduction in mortality post discharge
- 58% reduction in echocardiography
- Prevention of hospitalizations by 13%
- Reduced length of stay by 12%.

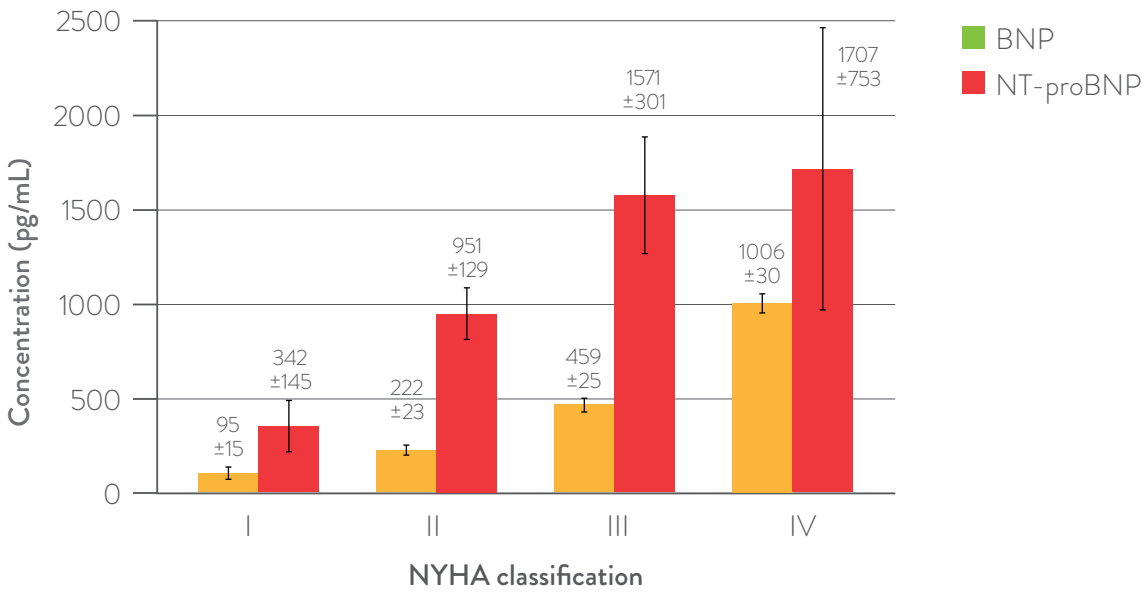
* Relates specifically to reduction in the number of hospitalizations and length of hospital stay.

GUIDELINE RECOMMENDATIONS FOR USE OF NPs

European Society of Cardiology and the American Heart Association guidelines recommend that NPs should be measured in all patients presenting with symptoms suggestive of new onset or worsening of heart failure, such as dyspnea and/or fatigue, as their use facilitates both early diagnosis or the early exclusion of heart failure.[21,30]

Baseline measurements correlate closely with the New York Heart Association (NYHA) heart failure functional classification and can be useful for prognosis in acutely decompensated patients.[18]

FIGURE 4: BNP AND NT-proBNP LEVELS REFLECT HEART FAILURE SEVERITY[18]



Adapted from McCullough et al., 2004

ABBOTT'S OFFERING

BENEFITS OF BNP AND NT-PROBNP

Alinity BNP and ARCHITECT BNP assays are additive tools that, when used in conjunction with clinical information, can enable physicians to make timely and more informed clinical decisions in the diagnosis and management of their heart failure patients, leading to improved outcomes at reduced cost.[1,2,23]

Alere NT-proBNP for Alinity i and Alere NT-proBNP for ARCHITECT can improve lab operational efficiency, while providing accurate and reliable results that enable physicians to confidently rule out patients with non-cardiac dyspnea, and aid in the diagnosis and management of heart failure.[3,4]

INTENDED USES

ALINITY i BNP

The Alinity i BNP assay is a chemiluminescent microparticle immunoassay (CMIA) used for the quantitative determination of human B-type natriuretic peptide (BNP) in human EDTA plasma on the Alinity i analyzer.[2]

The Alinity i BNP assay is to be used as an aid in the diagnosis and assessment of severity of heart failure.[2]

ALERE NT-proBNP FOR ALINITY i

The Alere NT-proBNP for Alinity i[3] assay is a chemiluminescent microparticle immunoassay (CMIA) for the *in vitro* quantitative determination of N-terminal pro B-type natriuretic peptide (NT-proBNP) in human serum and plasma on the Alinity i analyzer.[4]

The Alere NT-proBNP for Alinity i assay is to be used as an aid in the diagnosis of individuals suspected of having CHF and detection of mild forms of cardiac dysfunction. The test also aids in the assessment of heart failure severity in patients diagnosed with CHF.[4]

The Alere NT-proBNP for Alinity i assay is further indicated for the risk stratification of patients with ACS and CHF, and it can also be used for monitoring the treatment in patients with left ventricular dysfunction.[4]

TABLE 1: DIFFERENCES BETWEEN BNP AND NT-proBNP

	ALINITY I BNP	ALERE NT-proBNP FOR ALINITY i	COMMENTS
Claims[1,4]	Less	More	NT-proBNP has additional claims for risk stratification of acute coronary syndrome (ACS) and congestive heart failure (CHF), in addition to treatment monitoring
Cutoffs[1,4]	One-off cutoff for diagnosis (>100 ng/mL)	Multiple age-related cutoffs for diagnosis	With one diagnostic cutoff for all ages, BNP is simpler to interpret
Grey zone[19]	Narrow	Wider	BNP has narrower grey zone, so less patients have indeterminate values
Renal dysfunction[19]	BNP less affected by renal dysfunction	NT-proBNP more affected by renal dysfunction	Often patients with heart failure have renal dysfunction. BNP results are less affected than NT-proBNP by renal dysfunction, as NT-proBNP is solely cleared through the kidneys
Sample stability[1,4]	4 hours (room temperature) 24 hours (2–8°C)	3 days (room temperature) 6 days (2–8°C)	BNP has several advantages over NT-proBNP but may not be suitable for all testing situations due to sample stability (test within 4 hours at room temperature or 24 hours at (2–8°C)
Sample type[1,4]	EDTA plasma	Plasma/serum	NT-proBNP can be measured on multiple sample types

* Blue denotes advantages.

CONFOUNDING FACTORS IN THE MEASUREMENT OF NPs

Several disease processes and patient characteristics can confound the results of NP assays – clinicians must interpret the NP measurements with caution in these clinical scenarios. NT-proBNP is more susceptible to elevations in patients with kidney disease than BNP, because NT-proBNP is eliminated primarily by the kidneys.[20] In severe kidney disease, BNP is also affected, but NT-proBNP continues to be more severely altered.[20]

Several studies have also documented that NT-proBNP is increased in patients with atrial fibrillation; because this is a common comorbidity in patients with heart failure, clinicians must consider this when evaluating NT-proBNP measurements.[23,24] Increasing age and female gender both appear to increase the NP measurements regardless of underlying cardiac function, whereas obesity may decrease measured NP concentrations.[25]

DIFFERENCES IN NP ASSAY TYPES

Although most studies indicate that BNP and NT-proBNP assays have similar sensitivity and specificity, clinicians should be aware of several differences.[20] For example, NT-proBNP has a longer half-life than BNP, although this does not appear to have significant clinical implications.[20]

In addition, because the normal value ranges differ between the two types of assays, NT-proBNP concentrations measure higher and have more variability than BNP concentrations. It is essential that clinicians be aware of which assay is being used in the facility and be familiar with normal ranges of both tests (Figure 2).[20] Notably, BNP and NT-proBNP values are not interchangeable: there is no recognized "conversion factor" that works to convert a BNP result into an NT-proBNP result.[19]

Finally, all commercially available BNP assays standardize to an upper limit of normal of 100 pg/ml.[20] However, there is no universal cutpoint for normal for NT-proBNP. Most laboratories give a spectrum of upper limit values based on age categories ranging from 125 pg/mL to 2000 pg/mL, depending on the study population and assay used.[20]

ORDERING INFORMATION[2,4,26–29]

PRODUCT DESCRIPTION	LIST NUMBER
Alinity i BNP Reagent Kit 2 cartridges x 100 tests	08P24-20
Alinity i BNP Reagent Kit 2 cartridges x 500 tests	08P24-30
Alinity i BNP Calibrator Kit	08P24-01
Alinity i BNP Controls	08P24-10
ARCHITECT BNP Reagent, 1x 100 Test Kit	8K28-28
ARHITECT BNP Reagent, 1x 500 Test kit	8K28-36
ARCHITECT BNP Calibrators, 6 bottles (4 mL each)	8K28-04
ARCHITECT BNP Controls, 3 bottles (8 mL each)	8K28-13
Alere NT-proBNP for Alinity i Reagents, 2 x 100 Test Kit	04S79-20
Alere NT-proBNP for Alinity i Reagents, 2 x 500 Test Kit	04S79-30
Alere NT-proBNP for Alinity i Calibrators, 6 bottles (3 mL each)	04S79-01
Alere NT-proBNP for Alinity i Controls, 3 bottles (8 mL each)	04S79-10
Alere NT-proBNP for ARCHITECT Reagents, 1 x 100 Test Kit	02R10-25
Alere NT-proBNP for ARCHITECT Reagents, 1 x 500 Test Kit	02R10-35
Alere NT-proBNP for ARCHITECT Calibrators, 6 bottles (4 mL each)	02R10-01
Alere NT-proBNP for ARCHITECT Controls, 3 bottles (8 mL each)	02R10-10

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For *in vitro* diagnostic use only.

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