Abbott

IT'S MORE THAN A TEST.

IT'S THE INSIGHT TO HELP ENHANCE THE DIAGNOSIS AND MANAGEMENT OF HEART FAILURE.

How the BNP and NT-proBNP assays from Abbott can **aid in the diagnosis and assessment of severity of heart failure** – a physician resource.[1-4]

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

The measurement of 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 can be complex, with many non-specific signs and symptoms, such as dyspnea.**[6,7]
- **Misdiagnosis can lead to morbidity, and in-hospital mortality and readmission rates are high.**[8,9]

64.3 million people worldwide are living with heart failure[10,11]

5–10 days is the average length of stay in hospital for heart failure patients.[12]

Heart failure prevalence is predicted to **rise by 46%** by 2030[13]

HEART FAILURE RESULTS IN SIGNIFICANT CLINICAL, SOCIAL AND ECONOMICS BURDEN GLOBALLY.[10,11]

Abbott's range of high-performance tests are designed not to intefere with biotin, enabling the accurate detection of BNP and NT-proBNP. The results, when used in conjunction with other clinical information, **help to facilitate the timely diagnosis of heart failure.**[1–4]

- NPs are useful in conjunction with clinical evaluation for the **diagnosis or exclusion of acute heart failure in dyspneic patients**[14,15]
- NPs used in assessment of dyspnea can lead to improved patient care while providing **substantial cost savings by reducing hospitalizations and length of stay**[16,17]
- NP measurement following heart failure treatment **identifies patients at highest risk for death or rehospitalization.**[18]

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.[19–21]

INTENDED USES[1–4]

BNP

The Alinity i and ARCHITECT BNP assays are chemiluminescent microparticle immunoassays (CMIA) used for the quantitative determination of human B-type natriuretic peptide (BNP) in human EDTA plasma on the Alinity i analyzer and ARCHITECT iSystem.

The Alinity i and ARCHITECT BNP assays are to be used as an aid in the **diagnosis and assessment of severity of heart failure.**

Alere NT-proBNP

The Alere NT-proBNP for Alinity i and ARCHITECT assays are chemiluminescent microparticle immunoassays (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 and ARCHITECT iSystem with STAT protocol capability.

The Alere NT-proBNP for Alinity i and ARCHITECT assays are to be used as an aid in the **diagnosis of individuals suspected of having congestive heart failure and detection of mild forms of cardiac dysfunction.** The tests also aid in the assessment of heart failure severity in patients diagnosed with congestive heart failure.

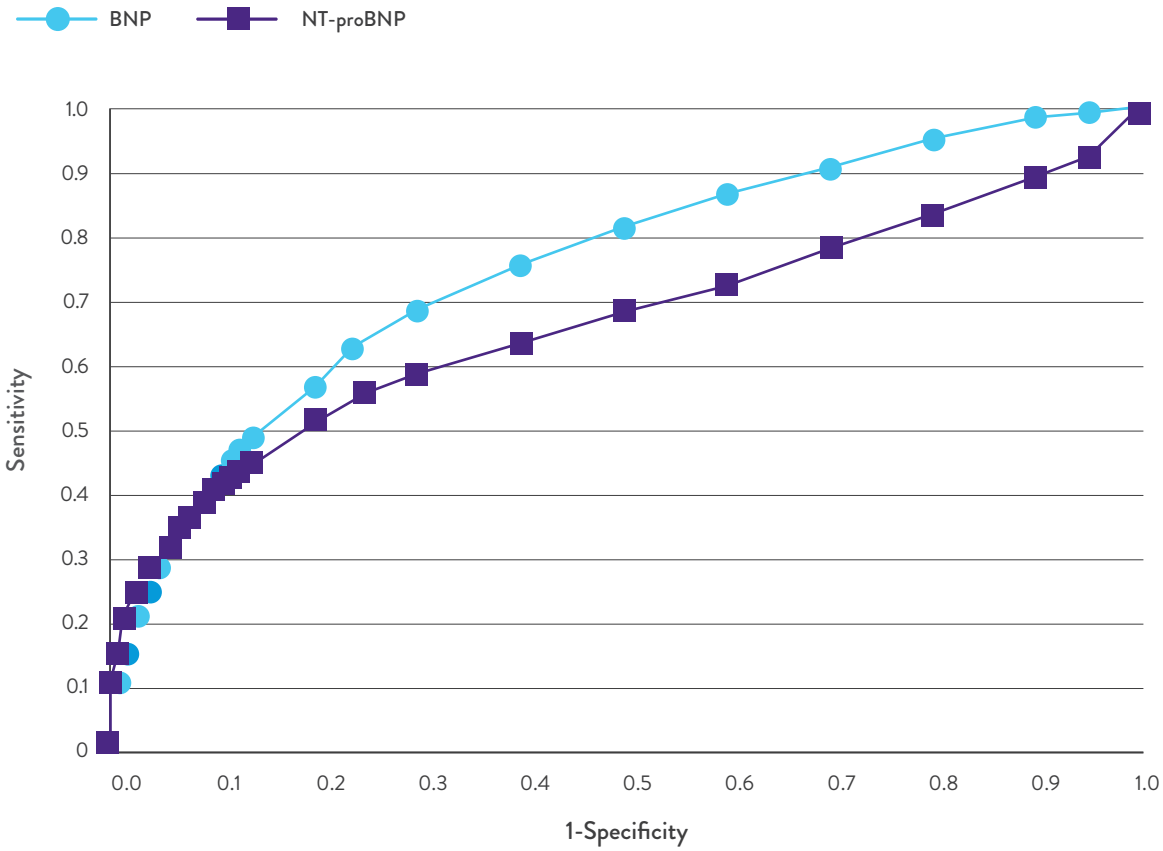
The Alere NT-proBNP for Alinity i and ARCHITECT assays are further indicated for the risk stratification of patients with acute coronary syndrome and congestive heart failure, and it can also be used for monitoring the treatment in patients with left ventricular dysfunction.

NPs IN HEART FAILURE DIAGNOSIS

There is a significant body of evidence endorsing the utilization of NPs for ruling out heart failure as the underlying cause of indicative symptoms, both in ambulatory and ED settings.[14,15,22]

Not only can elevated NP levels can suggest heart failure, but they also prove valuable for predicting outcomes and allow clinicians to consider other avenues that result in raised concentrations.[14,15,22] The value of NP testing is **particularly significant when the etiology of dyspnea is unclear.**[20]

FIGURE 1: DIAGNOSIS AND EXCLUSION OF ACUTE HEART FAILURE IN DYSPNEIC PATIENTS[9]



Adapted from McCullough P, et al. 2003.[9]

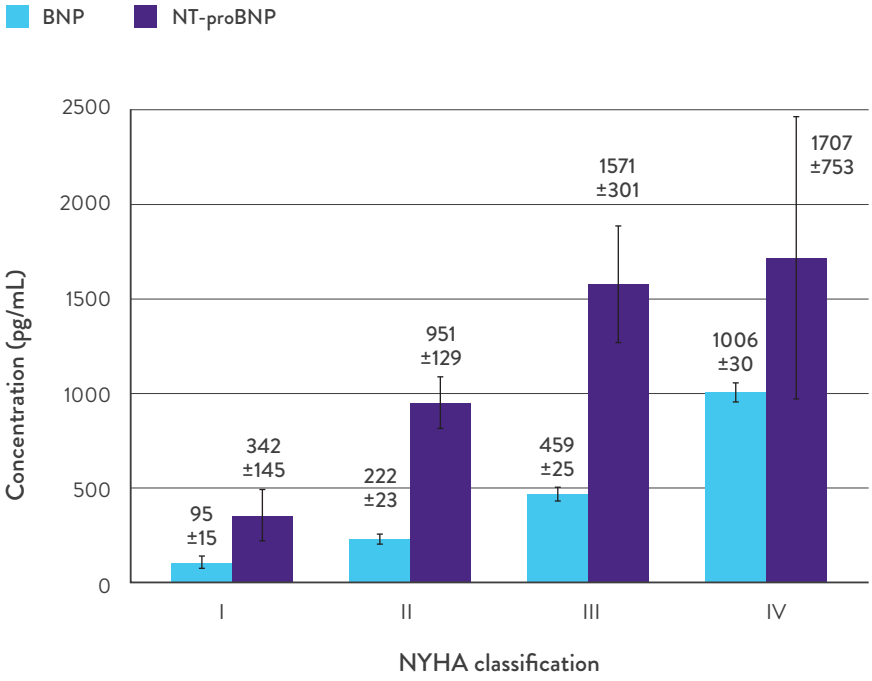
Comparison of area under the receiver operating characteristic curve (AUC) for BNP and NT-proBNP in the diagnosis of reduced left ventricular ejection fraction. **BNP AUC** = 0.83; **NT-proBNP AUC** = 0.79.[9]

GUIDELINE RECOMMENDATIONS FOR USE OF NPs

The European Society of Cardiology (ESC) and American Heart Association (AHA) 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 or fatigue, as their use **facilitates both early diagnosis or the early exclusion of heart failure.**[14,15]

Baseline NP measurements correlate closely with the New York Heart Association (NYHA) heart failure functional classification and can be useful for prognosis in acutely decompensated patients.[9]

FIGURE 2: BNP AND NT-proBNP LEVELS REFLECT HEART FAILURE SEVERITY[9]



Adapted from McCullough P, et al. 2003.[9]

ABBOTT'S OFFERING

Benefits of BNP

The Alinity i 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 evaluation and treatment of patients at reduced cost.[1,2,8,23]

Benefits of NT-proBNP

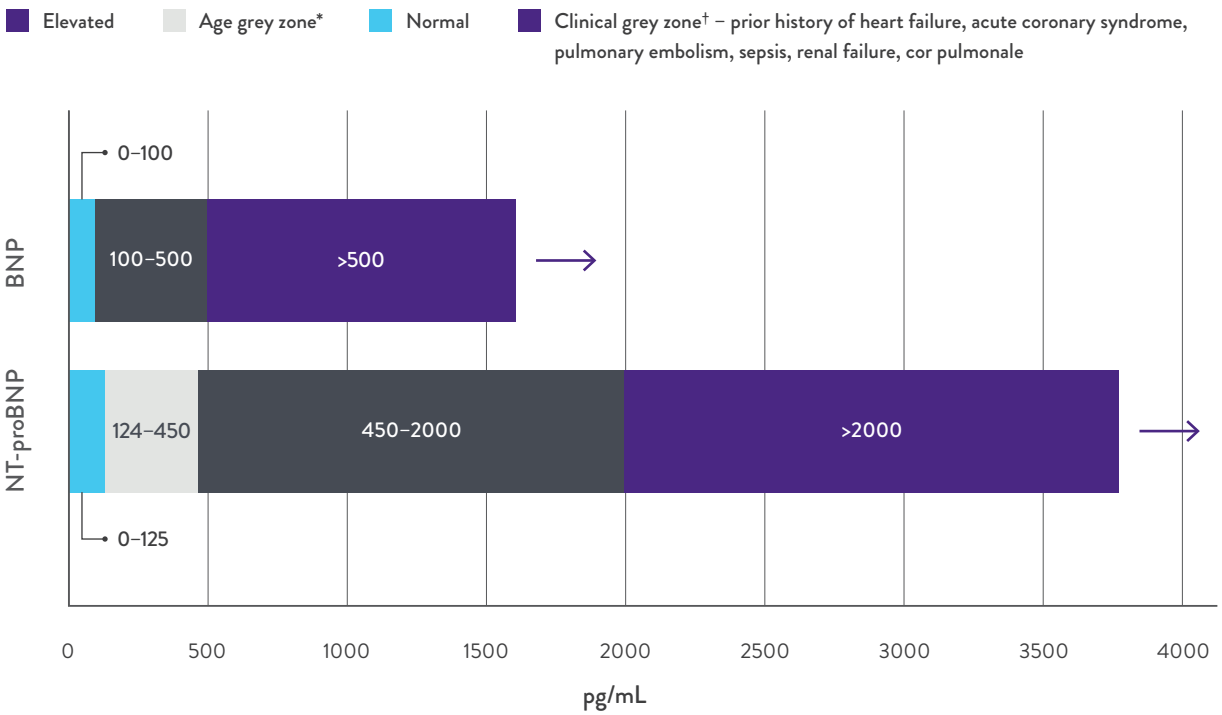
Alere NT-proBNP for Alinity i and ARCHITECT can improve lab operational efficiency, while providing accurate and reliable results that **enable physicians to confidently rule out patients with non-cardiac dyspnea,** and aid in the diagnosis and management of heart failure.[3,4]

UNDERSTANDING DIFFERENT NP ASSAY CUT-OFFS

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-off points are not used interchangeably.[24]

There is no recognized "conversion factor" that works to convert a BNP result into an NT-proBNP result.[22]

FIGURE 3: BNP AND NT-proBNP CLINICAL DECISION POINTS[22]



Adapted from McCullough et al., 2009[22]

For BNP, all manufacturers currently suggest a single-decision cut off of 100 pg/mL.[22]

For NT-proBNP, multiple age-related cut-offs are used:[3,4]
125 pg/mL < 75 yrs
450 pg/mL ≥ 75 yrs

ICON study recommends several cut offs for NT-proBNP:[17]

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

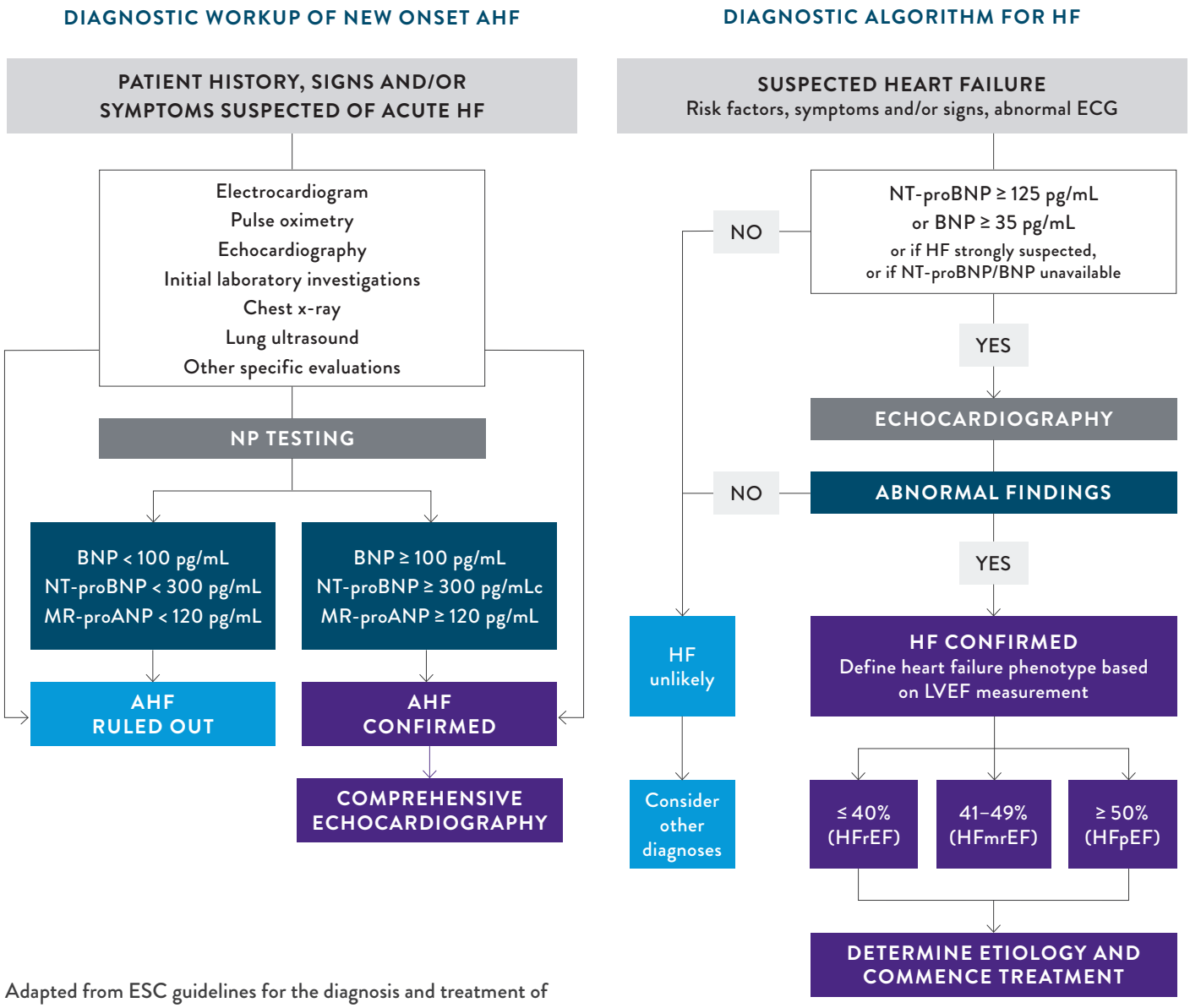
Concentrations of both BNP and NT-proBNP that are below any of the decision cut-offs can rule out the presence of heart failure with a high degree of confidence due to the sensitivity of the tests.[7,25]

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

USING CARDIAC BIOMARKERS IN CLINICAL PRACTICE

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.[7,26]

FIGURE 4: ESC GUIDELINES HEART FAILURE 2021[15]



Adapted from ESC guidelines for the diagnosis and treatment of acute and chronic heart failure.[15]

AHF = acute heart failure; **ECG** = electrocardiogram; **ESC** = European Society of Cardiology; **HF** = heart failure; **HFmrEF** = heart failure with mid-range ejection fraction; **HFpEF** = heart failure with preserved ejection fraction; **HFrEF** = heart failure with reduced ejection fraction; **LVEF** = left ventricular ejection fraction; **NP** = natriuretic peptide.

NPs HELP IMPROVE PATIENT OUTCOMES AND REDUCE COSTS*

Both BNP and NT-proBNP levels have been shown to **correlate well with patient prognosis:**[22]

- In one study patients with BNP levels >350 pg/mL, were **five-times more likely** to die or be readmitted for heart failure if discharged.
- Patients with BNP levels >700 pg/mL had **15-times the risk of death or readmission.**
- 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.

NPs used in assessment of dyspnea can lead to improved patient care while providing substantial cost savings by reducing hospitalizations and length of stay.[16,17]

IN A STUDY BY MUELLER ET AL., THE USE OF BNP WAS ASSOCIATED WITH:[26]

- An improved time to treatment
- An improved time to discharge
- A 10% decrease in the rate of hospitalizations
- A 26% reduction in total cost of treatment.

IN A STUDY BY SIEBERT ET AL., THE USE OF NT-proBNP WAS ASSOCIATED WITH:[12]

- A 1% relative reduction in mortality post discharge
- A 58% reduction in echocardiography
- The prevention of hospitalizations by 13%
- A 12% reduction in length of stay.

USE OF BNP IN THE EVALUATION AND MANAGEMENT OF ACUTE DYSPNEA[26]

END POINT	B-Type Natriuretic Peptide Group (N=225)	Control Group (N=227)
Time to Treatment (min)† Median Interquartile Range	 63 16–153	 90 20–205
Time to Discharge (days) Median Interquartile Range	8.0 1.0–16.0	11.0 5.0–18.0
Hospitalization: # (%)	169 (75%)	193 (85%)
Admission to Intensive care: # (%)	33 (15%)	54 (24%)
Cost of intensive care (USD) Median 95% Confidence Interval	 874 423–1,324	 1,516 989–2,043
Total treatment cost (USD) Median 95% Confidence Interval	 5,410 4,516–6,304	 7,264 6,301–8,227

* Relates specifically to reduction in the number of hospitalizations and length of hospital stay.
† The time to treatment was defined as the interval from presentation at the ED to the initiation of the appropriate therapy according to the final discharge diagnosis.

DIFFERENCES BETWEEN BNP AND NT-proBNP

In the hospital setting, NPs can assist in distinguishing the cause of acute shortness of breath, determine praognostic information about mortality risk in acute heart failure and, **when measured at discharge, can identify long-term prognosis after an acute heart failure admission.**[7,18,24]

They can also be used as a screening tool in the outpatient setting to rule out heart failure, as well as provide long-term prognostic information for patients with chronic heart failure.[7,18,24]

Although most studies indicate that BNP and NT-proBNP assays have similar sensitivity and specificity, **clinicians should be aware of several differences between the assays.**[22]

	Alinity i BNP	Alere NT-proBNP for Alinity i	COMMENTS
Claims[1,4]	Fewer	More	NT-proBNP has additional claims for risk stratification of acute coronary syndrome and congestive heart failure, in addition to treatment monitoring.
Cut-offs[1,4]	One cutoff for diagnosis (>100 ng/mL)	Multiple age-related cut-offs for diagnosis	With one diagnostic cutoff for all ages, BNP is simpler to interpret.
Grey zone[22]	Narrow	Wider	BNP has a narrower grey zone so less patients have indeterminate values.
Renal dysfunction[22]	BNP less affected by renal dysfunction	NT-proBNP affected more by renal dysfunction	Often patients with HF 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)	NT-proBNP has greater sample stability in comparison to BNP.
Sample Type[1,4]	EDTA plasma	Plasma/serum	NT-proBNP can be measured on multiple sample types.

Advantage

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.[22] In severe kidney disease, BNP is also affected, but NT-proBNP continues to be more severely altered.[22]

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.[23,28]

Increasing age and female gender both appear to increase the NP measurements regardless of underlying cardiac function, whereas obesity may decrease measured NP concentrations.[29]

DIFFERENCES IN NP ASSAY TYPES

Understanding the **differences between BNP and NT-proBNP** is vital when implementing either assay.

For example, NT-proBNP has a longer half-life than BNP, although this does not appear to have significant clinical implications.[22] 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 3).[22]

Furthermore, all commercially available BNP assays standardize to an upper limit of normal of 100 pg/ml.[22] 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.[22]

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At Abbott, we know that accurate and timely diagnostic results play a pivotal role in **achieving improved clinical outcomes for your patients.** As your trusted healthcare partner, you can rely on Abbott's diagnostic solutions to provide this, so you can make clinical decisions with confidence, for the benefit of your patients.

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