

BACKGROUND

This study aims to define the analytical characteristics, perform Method Comparisons and establish valid Reference Limits for the novel Access NT-proBNP assay that will be widely available for clinical management of patients. Measurements were conducted with the Access NT-proBNP assay on the Dxl 9000 Immunoassay Analyzer* with LiHep plasma samples.

STUDY DESIGN

Analytical Characteristic	Result(s)	Guidance Followed	Comment
Limit of Blank (LoB)	1.1 ng/L	CLSI EP17-A2	4 reagent lots tested; 240 NT-proBNP-free data points
Limit of Detection (LoD)	4.8 ng/L	CLSI EP17-A2	4 Li-hep samples between LoB and 4.5-fold higher.
Limit of Quantitation (LoQ)	4.8 ng/L	NTproBNP level @ 20% CV	NT-proBNP concentration at 20% CV of assay
Imprecision	3.0 to 7.9% Reproducibility; Table 1	CLSI EP05-A3	3 reagent lots@ 3 labs; 7 concentrations 38 ng/L to 23,847 ng/L
Linearity	38 ng/L to 25,000 ng/L	CLSI EP06-Ed2	3 reagent lots; 5 replicates of 15 samples across assay range
Interferences / Cross reactivity	No interferences	CLSI EP07-A3	74 drugs and substances & 15 biologicals tested.
Method Comparison	Figure 1 & 2; Table 2	CLSI EP09C-ED3:2018	210 Residual Li-Hep samples; Passing Bablok linear regress; Bland Altman bias plots
Reference Interval Study	Table 3 & 4; Figure 3	CLSI EP28-A3c & IFCC 2019	306 males and 369 Females

Table 1. Imprecision of Access NT-proBNP across the Analytical Measuring Range

LiHep Sample	N	Mean ng/L	Between Site /Lot, CV (SD)	Between Day CV (SD)	Between Run CV (SD)	Repeatability CV (SD)	Reproducibility CV (SD)
Sample1	60	38.24	6.9% (2.6)	0.0% (0.0)	1.7% (0.7)	3.5% (1.3)	7.9% (3.0)
Sample2	59	127.31	5.6% (7.1)	0.6% (0.8)	0.0% (0.0)	2.9% (3.6)	6.3% (8.0)
Sample3	59	288.19	4.9% (14.0)	1.6% (4.7)	0.7% (2.0)	2.7% (7.8)	5.8% (16.8)
Sample4	60	428.00	4.1% (17.4)	0.0% (0.0)	1.7% (7.3)	1.5% (6.5)	4.7% (20.0)
Sample5	60	1708.42	0.3% (5.2)	1.4% (23.2)	1.7% (29.5)	2.0% (33.7)	3.0% (50.7)
Sample6	60	11096.6	1.4% (159.7)	0.8% (91.7)	1.2% (135.2)	1.7% (191.6)	2.7% (298.2)
Sample7	60	23848.6	1.4% (334.0)	0.0% (0.0)	1.5% (367.5)	2.2% (527.5)	3.0% (724.4)

METHOD COMPARISON

Figure 1. Passing-Bablok Regression- Method Comparison between Access NT-proBNP and Elecsys NT-proBNP assays

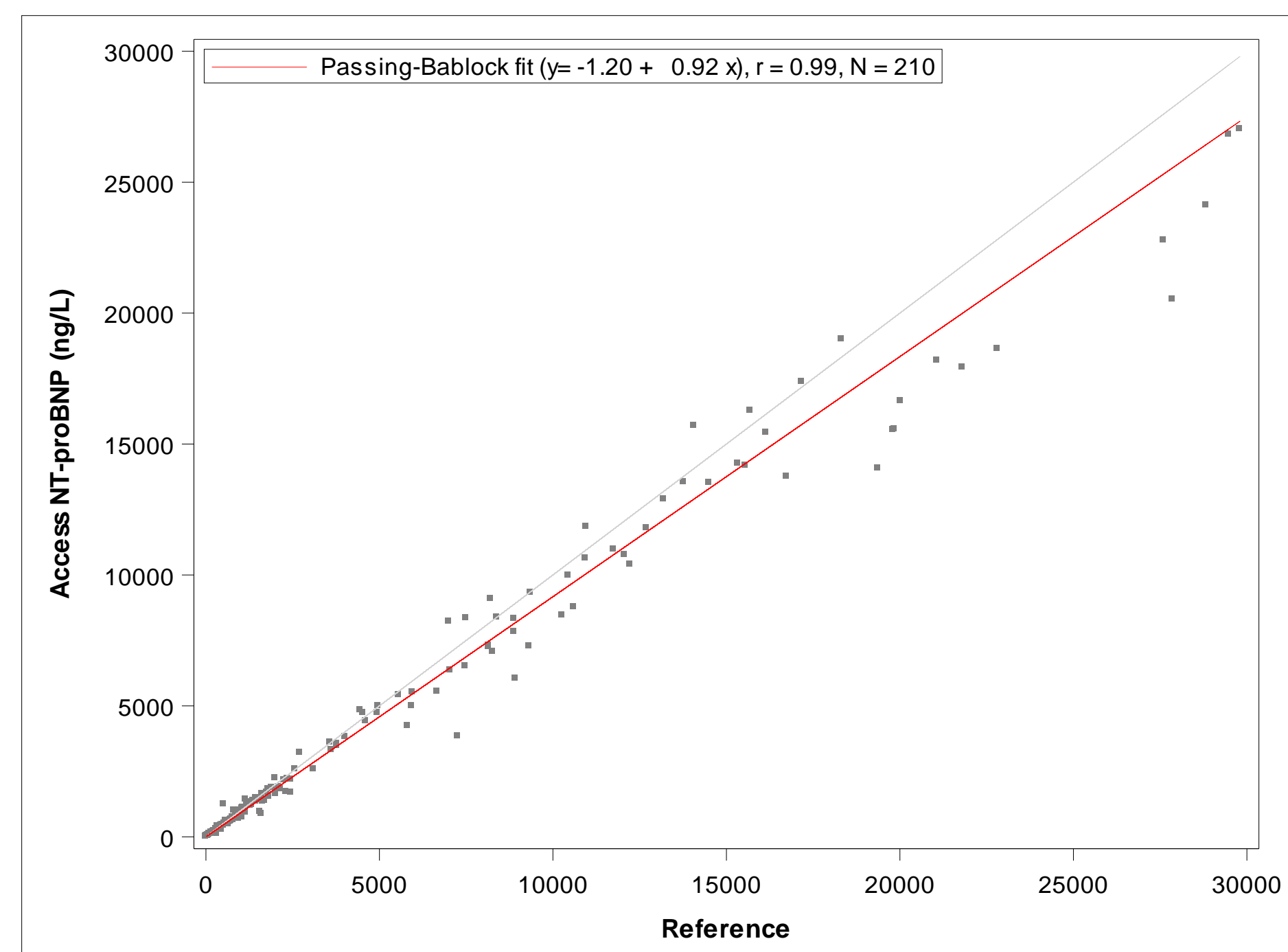


Figure 2. Bland-Altman Bias Plot comparing the Access and Elecsys NT-proBNP assays

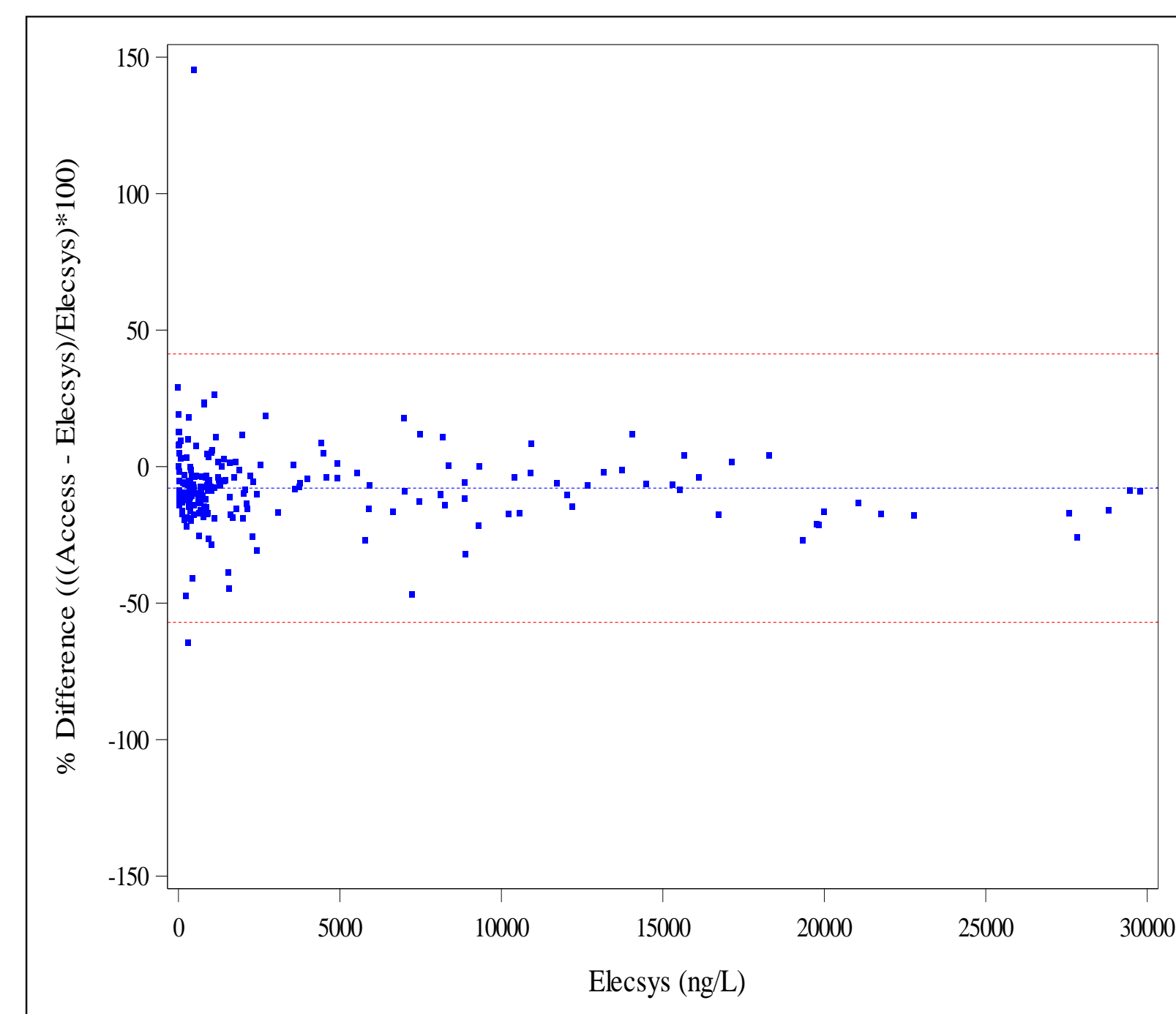


Table 2. Positive (PPA), Negative (NPA), & Overall (OPA) Method Agreement at Critical Decision Points

Cutoff, ng/L	PPA		NPA		OPA	
	%	95% CI	%	95% CI	%	95% CI
125	97.9	94.8–99.2	100.0	82.4–100.0	98.1	95.2–99.3
300	97.7	94.3–99.1	100.0	89.6–100.0	98.1	95.2–99.3
450	96.6	92.4–98.6	100.0	94.1–100.0	97.6	94.5–99.0
900	91.4	84.9–95.3	96.8	91.0–98.9	93.8	89.7–96.3
1800	94.9	87.7–98.0	100.0	97.2–100.0	98.1	95.2–99.3

REFERENCE INTERVAL STUDY

Table 3. Characteristics of Enrolled Reference Population

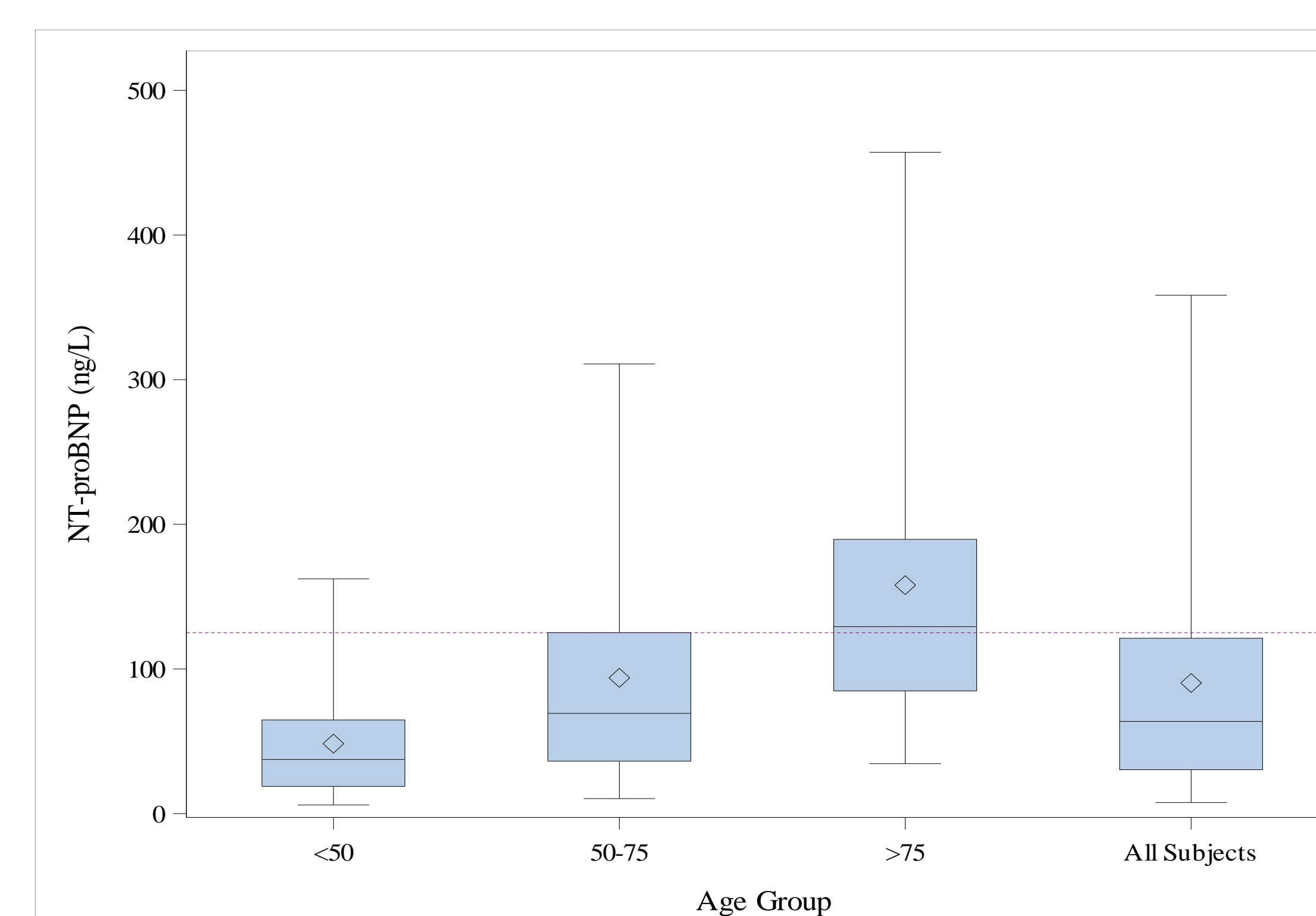
	Female (N=369)	Male (N=306)	Total (N=675)
Age (years)	62 (39, 75)	54 (37, 72)	57 (38, 74)
hsTnl (ng/L)	2 (2, 3)	3 (2, 5)	3 (2, 4)
Overweight (25+)	27.85%	29.04%	56.89%
eGFR (60+)	51.56%	43.26%	94.81%
White	47.56%	31.56%	79.11%
Non-Hispanic or Latino	44.59%	37.33%	81.93%

Table 4. Age and Sex Stratified Access NT-proBNP Values in a Healthy Population.. NHANES data in right-most column

Age category (years)	Sex	N	Access NT-proBNP			NHANES 50 th Percentile (95% CI)
			2.5 th Percentile (95% CI)	97.5 th Percentile (95% CI)	50 th Percentile (95% CI)	
21–29	Female	46	11 (7.9, 12.7)	152 (148.1, 162.3)	51 (39.9, 66.6)	44 (41, 47)
	Male	38	3 (3.1, 6.6)	108 (75.4, 107.5)	22 (15.6, 28.2)	16 (15, 18)
30–39	Female	51	12 (11.3, 14.9)	152 (140.6, 178.2)	54 (44.0, 64.9)	50 (47, 54)
	Male	52	6 (4.6, 6.3)	103 (84.1, 118.1)	23 (14.6, 30.8)	21 (19, 23)
40–49	Female	38	16 (16.4, 22.3)	215 (205.8, 215.1)	53 (44.6, 68.6)	59 (54, 55)
	Male	42	5 (4.6, 6.0)	103 (92.1, 364.1)	23 (18.8, 31.0)	24 (21, 27)
50–59	Female	42	17 (4.9, 19.1)	273 (199.3, 369.8)	60 (39.8, 76.2)	71 (61, 81)
	Male	55	8 (3.9, 10.1)	188 (185.0, 266.8)	31 (27.7, 43.8)	41 (35, 46)
60–69	Female	19	25 (3.9, 10.1)	247 (185.0, 266.8)	82 (54.4, 123.4)	90 (75, 105)
	Male	19	9 (3.9, 10.1)	169 (185.0, 266.8)	51 (36.1, 67.0)	61 (49, 75)
70–93	Female	173	31 (20.2, 40.5)	443 (376.5, 521.0)	136 (121.2, 152.1)	177 (141, 222)
	Male	100	19 (9.5, 28.0)	411 (283.6, 461.8)	100 (77.8, 117.6)	155 (123, 193)

CONCLUSIONS

Figure 3. Box and Whisker Plot for Reference Interval by Age Group and All-ages



Upper bound of the whisker indicates 97.5th Percentile Upper Reference Limit

- The novel Access NT-proBNP assay offers robust analytical performance as an aid to acute HF management
- Imprecision of assay is acceptable (Table 1)
- Agreement with a reference assay is ≥94% (Table 2)
- Reference interval study shows that median results for all age and sex strata very similar to the NHANES national study. (Table 4)
- NT-proBNP Upper Reference Limit varies substantially with age, precluding use of a single URL for all patients (Figure 3)

*Full name: Dxl 9000 Access Immunoassay Analyzer