| Table I-3. Summary of diagnostic properties of studies that evaluated NT-proBNP in patients with symptoms suggestive of HF in the primary care settings | | | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author**  **Year**  **Country** | **Study Design (Companion Study)**  **Ethnicity**  **Comorbidities**  **Reference Standard(S)** | **Objectives/end-points** | **BNP (Methods)** | **Sample Characteristics** | **Index Cutpoint (pg/ml)** | **Sensitivity (%)** | **Specificity (%)** | **LR+** | **LR-** | **AUC** |
|
| Christenson,4  2010  United States | Cross-Sectional (Independent Study)  Ethnicity: African-American (n=246)  Comorbidities:  HBP (n=209), CAD (n=227), AF (n=147), Diabetes (n=245), Prior HF (n=236)  Reference Standard: 1 Cardiologist | Adjudicated acute HF, all-cause mortality  (evaluated the accuracy of NTproBNP and BNP across a range of BMIs for diagnosis of decompensated HF in a community-based dyspneic patient population; also investigated whether the prognostic accuracies of NT-proBNP and BNP concentrations differed based on BMI for predicting 1-year all-cause mortality) | NT-proBNP (ELECSYS -proBNP Immunoassay) | Dyspnea (decompensated HF, overall)  n=675  mean age= NR  %males= NR  HF Prev=NR%; Age specific cutoffs, 450 pg/ml for age <50yrs, 900 pg/ml for 50-75yrs and 1800 pg/ml for >75yrs | Age specific | NR | NR | NA | NA | 0.72 |
| Dyspnea (decompensated HF, Normal Weight, BMI <25 kg/m  n=211  mean age= 69.8y (15.5)  %males=5  HF Prev=36%; Age specific cutoffs, 450 pg/ml for age <50yrs, 900 pg/ml for 50-75yrs and 1800 pg/ml for >75yrs | Age specific | 88 | 50 | 1.76 | 0.24 | NR |

| Table I-3. Summary of diagnostic properties of studies that evaluated NT-proBNP in patients with symptoms suggestive of HF in the primary care settings (continued) | | | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author**  **Year**  **Country** | **Study Design (Companion Study)**  **Ethnicity**  **Comorbidities**  **Reference Standard(S)** | **Objectives/end-points** | **BNP (Methods)** | **Sample Characteristics** | **Index Cutpoint (pg/ml)** | **Sensitivity (%)** | **Specificity (%)** | **LR+** | **LR-** | **AUC** |
|
| Christenson,4  2010  United States  (cont’d) | (repeated data)  Cross-Sectional (Independent Study)  Ethnicity: African-American (n=246)  Comorbidities:  HBP (n=209), CAD (n=227), AF (n=147), Diabetes (n=245), Prior HF (n=236)  Reference Standard: 1 Cardiologist | (repeated data)  Adjudicated acute HF, all-cause mortality (evaluated the accuracy of NTproBNP and BNP across a range of BMIs for diagnosis of decompensated HF in a community-based dyspneic patient population; also investigated whether the prognostic accuracies of NT-proBNP and BNP concentrations differed based on BMI for predicting 1-year all-cause mortality) | (repeated data)  NT-proBNP (ELECSYS -proBNP Immunoassay) | Dyspnea (decompensated HF, Over Weight, BMI 25-30 kg/m  n=193  mean age= 66.6y (13.8)  %males=58  HF Prev=37%; Age specific cutoffs, 450 pg/ml for age <50yrs, 900 pg/ml for 50-75yrs and 1800 pg/ml for >75yrs | Age specific | 68 | 51 | 1.39 | 0.63 | NR |
| Dyspnea (decompensated HF, Obese, BMI >30 kg/m  n=280  mean age= 62.5y (14.6)  %males=38  HF Prev=32%; Age specific cut offs, 450pg/ml for age <50yrs, 900pg/ml for 50-75yrs and 1,800pg/ml for >75yrs | Age specific | 69 | 64 | 1.92 | 0.48 | NR |
| Fuat,5  2006  United Kingdom | Cross-Sectional (Independent Study)  Ethnicity: NR  Comorbidities:  HBP (n=102), AF(n=56), COPD (n=69), Diabetes (n=27), Historical Mi (n=39), Ischemic (n=87)  Reference Standard: Gps,15% Of Echo Verified By Cardiologists | To test and compare the diagnostic accuracy and utility of B-type natriuretic peptide (BNP) and N-terminal B-type natriuretic peptide (NT proBNP) in diagnosing HF due to left ventricular systolic dysfunction | NT-proBNP (ELECSYS -proBNP Immunoassay) | Suspected HF referred by GPs  n=297  mean age= (patients with LVSD) 73.5y; (patients with no LVSD) 74y,  %males=37  HF Prev=38% | 150 | 94 | 40 | 1.57 | 0.15 | NR |
| Goode,13  2007  United Kingdom | Cross-Sectional (Independent Study)  Ethnicity: NR  Comorbidities:  HBP (n=283), Diabetes (n=82),IHD (n=140), Ankle Oedema Or Worse (n=31), Previous MI (n=144), Angina (n=65),  Reference Standard:  1 Cardiologist | LVSD (to assess the univariate and multivariable utility of NT-proBNP, QRS duration, symptoms and evidence of myocardial infarction (MI) to detect LVSD) | NT-proBNP (ELECSYS -proBNP Immunoassay) | HF (LVSD)  n=427  mean age= 70y (8)  %males=57  HF Prev=8% | 150 | 84 | 45 | 1.52 | 0.35 | NR |
| Using upper 97.5th centile of normal population after Galasko et al; men <60yrs (100pg/ml);women <60yrs (164pg/ml); men ≥60yrs (172pg/ml); Women ≥60yrs (255pg/ml) | Age/Sex specific | 84 | 53 | 1.79 | 0.29 | NR |
| NR | NR | NR | NA | NA | 0.72 |
| Goode,14  2008  United Kingdom | Cohort (INDEPENDENT STUDY)  Ethnicity: NR  Comorbidities:  HBP (n=52), AF(n=14), COPD (n=9), Diabetes (n=12), Historical MI (n=17), IHD (n=31), Angina (n=9), Anemia (n=17), GFR<30 Ml/Min/1.73 ^2 (n=3)  Reference Standard:  1 Cardiologist | To assess the diagnostic utility of NT-proBNP and QRS width (independently and in combination) as the initial investigation for patients in whom the primary-care physician suspected HF | NT-proBNP (ELECSYS -proBNP Immunoassay) | HF (Overall)  n=94  mean age= 77y\* (70-81(IQR))  %males=46.8  HF Prev=19% | NR | NR | NR | NA | NA | NR |
| HF (Major LVSD)  n=94  mean age= 77y\* (70-81(IQR))  %males=46.8  HF Prev=19%; Prevalence of HF and threshold for NT-proBNP based on Original Echo Scoring | <178 | NR | 47 | NA | NA | 0.88 |
| Goode,14  2008  United Kingdom  (cont’d) | (repeated data)  Cohort (INDEPENDENT STUDY)  Ethnicity: NR  Comorbidities:  HBP (n=52), AF(n=14), COPD (n=9), Diabetes (n=12), Historical MI (n=17), IHD (n=31), Angina (n=9), Anemia (n=17), GFR<30 Ml/Min/1.73 ^2 (n=3)  Reference Standard:  1 Cardiologist | (repeated data)  To assess the diagnostic utility of NT-proBNP and QRS width (independently and in combination) as the initial investigation for patients in whom the primary-care physician suspected HF | (repeated data)  NT-proBNP (ELECSYS -proBNP Immunoassay) | HF (Major LVSD)  n=94  mean age= 77y\* (70-81(IQR))  %males=46.8  HF Prev=16%; Prevalence of HF and threshold for NT-proBNP changed due to revised Echo scoring | <464 | NR | 72 | NA | NA | 0.91 |
| HF (Any LVSD)  n=94,  mean age= 77y\* (70-81(IQR))  %males=46.8  HF Prev=32%; Prevalence of HF and threshold for NT-proBNP based on Original Echo Scoring | <25 | NR | 3 | NA | NA | 0.82 |
| HF (Any LVSD)  n=94  mean age= 77y\* (70-81(IQR))  %males=46.8  HF Prev=30%; Prevalence of HF and threshold for NT-proBNP changed due to revised Echo scoring | <76 | NR | 24 | NA | NA | 0.79 |
| Goode,14  2008  United Kingdom  (cont’d) | (repeated data)  Cohort (INDEPENDENT STUDY)  Ethnicity: NR  Comorbidities:  HBP (n=52), AF(n=14), COPD (n=9), Diabetes (n=12), Historical MI (n=17), IHD (n=31), Angina (n=9), Anemia (n=17), GFR<30 Ml/Min/1.73 ^2 (n=3)  Reference Standard:  1 Cardiologist | (repeated data)  To assess the diagnostic utility of NT-proBNP and QRS width (independently and in combination) as the initial investigation for patients in whom the primary-care physician suspected HF | (repeated data)  NT-proBNP (ELECSYS -proBNP Immunoassay) | HF (Major Structural heart disease)  n=94  mean age= 77y\* (70-81(IQR))  %males=46.8  HF Prev=36%; Prevalence of HF and threshold for NT-proBNP based on Original Echo Scoring | <93 | NR | 35 | NA | NA | 0.91 |
| HF (Major Structural heart disease)  n=94,  mean age= 77y\* (70-81(IQR))  %males=46.8  HF Prev=35%; Prevalence of HF changed due to revised Echo scoring | <93 | NR | 35 | NA | NA | 0.91 |
| Gustafsson,15  2003  Denmark | Cross-Sectional (Independent Study)  Ethnicity: NR  Comorbidities:  HBP (n=68), AF(n=15), COPD (n=25), Diabetes (n=7), Ischemic (n=47)  Reference Standard:  NR | Diagnosis of LVSD | NT-proBNP (ELECSYS -proBNP Immunoassay) | Suspected HF (All)  n=367,  mean age= 68.8y\* (39.0-84.0)  %males=0  HF Prev=9% | NR | NR | NR | NA | NA | NR |
| Suspected HF (LVEF > 40%)  n=334  mean age= 68.0y\* (38.0-84.5)  %males=43  HF Prev=NR% | NR | NR | NR | NA | NA | NR |
| Gustafsson,15  2003  Denmark  (cont’d) | (repeated data)  Cross-Sectional (Independent Study)  Ethnicity: NR  Comorbidities:  HBP (n=68), AF(n=15), COPD (n=25), Diabetes (n=7), Ischemic (n=47)  Reference Standard:  NR | (repeated data)  Diagnosis of LVSD | (repeated data)  NT-proBNP (ELECSYS-proBNP Immunoassay) | Suspected HF (LVEF ≤ 40%)  n=33  mean age= 70.3y\* (38.4-84.0)  %males=76  HF Prev=NR% | 125 | 97 | 46 | 1.80 | 0.07 | NR |
| Suspected HF (LVEF ≤ 40%)  n=33  mean age= 70.3y\* (38.4-84.0)  %males=76  HF Prev=NR%;  Age specific cutoffs, 125 pg/ml for age <75yrs or 450 pg/ml for age ≥ 75yrs | Age specific | 91 | 60 | 2.28 | 0.15 | NR |
| Suspected HF (LVEF ≤ 40%)  n=33  mean age= 70.3y\* (38.4-84.0)  %males=76  HF Prev=NR%;  Sex specific cut offs, 144pg/ml for Females and 93pg/ml for males | Sex specific | 91 | 60 | 2.28 | 0.15 | NR |
| Suspected HF (LVEF ≤ 30%)  n=14  mean age= 67.0y\* (51.0-84.0)  %males=86  HF Prev=NR% | 125 | 100 | 56 | 2.27 | 0.00 | NR |
| Gustafsson,15  2003  Denmark  (cont’d) | (repeated data)  Cross-Sectional (Independent Study)  Ethnicity: NR  Comorbidities:  HBP (n=68), AF(n=15), COPD (n=25), Diabetes (n=7), Ischemic (n=47)  Reference Standard:  NR | (repeated data)  Diagnosis of LVSD | (repeated data)  NT-proBNP (ELECSYS -proBNP Immunoassay) | Suspected HF (LVEF ≤ 30%)  n=14  mean age= 67.0y\* (51.0-84.0)  %males=86  HF Prev=NR%; Age specific cut offs, 125pg/ml for age <75yrs or 450pg/ml for age ≥ 75yrs | Age specific | 100 | 58 | 2.38 | 0.00 | NR |
| Suspected HF (LVEF ≤ 30%)  n=14  mean age= 67.0y\* (51.0-84.0)  %males=86  HF Prev=NR%; Sex specific cut offs, 144 pg/ml for Females and 93 pg/ml for males | Sex specific | 100 | 44 | 1.79 | 0.00 | NR |
| Gustafsson,16  2005  Denmark | Cross-Sectional (Independent Study)  Ethnicity: NR  Comorbidities:  HBP (n=68), Obstructive Lung Disease (n=25), AF(n=15), Diabetes (n=7),IHD (n=47)  Reference Standard: Blinded Investigator | Mortality and diagnosis | NT-proBNP (ELECSYS -proBNP Immunoassay) | Suspected CHF (LVSD)  n=367  mean age= 68.8y  %males=46  HF Prev=9% | 125 | 97 | 46 | 1.80 | 0.07 | 0.87 |
| LVSD (Age specific)  n=367  mean age= 68.8y  %males=46  HF Prev=9%; Age specific cut off values , 125pg/ml for Age <75yrs and 450pg/ml for Age ≥ 75yrs | Age specific | 91 | 60 | 2.28 | 0.15 | NR |
| Gustafsson,16  2005  Denmark  (cont’d) | (repeated data)  Cross-Sectional (Independent Study)  Ethnicity: NR  Comorbidities:  HBP (n=68), Obstructive Lung Disease (n=25), AF(n=15), Diabetes (n=7),IHD (n=47)  Reference Standard: Blinded Investigator | (repeated data)  Mortality and diagnosis | (repeated data)  NT-proBNP (ELECSYS -proBNP Immunoassay) | Severe LVSD (LVEF ≤ 30 %)  n=367  mean age= 68.8y  %males=46  HF Prev=4% | 125 | 100 | 56 | 2.27 | 0.00 | 0.93 |
| Severe LVSD (Age specific)  n=367  mean age= 68.8y  %males=46  HF Prev=4%; Age specific cut off values , 125pg/ml for Age <75yrs and 45pg/ml for Age ≥ 75yrs | Age specific | 100 | 58 | 2.38 | 0.00 | NR |
| Hobbs,17  2004  United Kingdom | Cross-Sectional (Echoes)  Ethnicity: Caucasian (n=573), Other (n=98)  Comorbidities:  HBP (n=232), Prior Ami/Angina (n=127), Diabetes (n=68), Historical Mi (n=87)  Reference Standard: NR | no specified endpoint, diagnostic study | NT-proBNP (ELECSYS -proBNP Immunoassay) | All  n=591  mean age= 65.8y (10.7)  %males=54  HF Prev=6%. Prevalence for HF (LVSD, n=33) reported in overall population  n=59 but not for individual groups | NR | NR | NR | NR | NR | NR |
| General population over 45yrs  n=307  mean age= NR  %males= NR  HF Prev=NR% | 40 pmol/L | 80 | 73 | 2.96 | 0.27 | 0.76 |
| Hobbs,17  2004  United Kingdom  (cont’d) | (repeated data)  Cross-Sectional (Echoes)  Ethnicity: Caucasian (n=573), Other (n=98)  Comorbidities:  HBP (n=232), Prior Ami/Angina (n=127), Diabetes (n=68), Historical Mi (n=87)  Reference Standard:  NR | (repeated data)  no specified endpoint, diagnostic study | (repeated data)  NT-proBNP (ELECSYS -proBNP Immunoassay) | Pts with previous HF diagnosis  n=103  mean age= NR  %males=NR  HF Prev=NR% | 40 pmol/L | 100 | 18 | 1.22 | 0.00 | 0.7 |
| Pts on diuretics  n=87  mean age= NR  %males= NR  HF Prev=NR% | 40 pmol/L | 86 | 40 | 1.43 | 0.35 | 0.81 |
| Pts at high risk for HF  n=133  mean age= NR  %males= NR  HF Prev=NR% | 40 pmol/L | 100 | 46 | 1.85 | 0.00 | 0.73 |
| Kelder,7  2011  Netherlands | Cross-Sectional  (Uhfo-Ia)  Ethnicity: NR  Comorbidities:  HBP (n=88), AF(n=8), COPD (n=47), Diabetes (n=29), Stroke , TIA (n=15), MI, PCI, CABG (n=9)  Reference Standard: Expert Panel (1 Cardiologist, 1 Pulmonologist, And 1 Gp | Data on the comparative performance of 3 popular automated assays in patients suspected of new slow-onset HF | NT-proBNP (ELECSYS -proBNP Immunoassay) | HF  n=172  mean age= 70.2y (11.3)  %males=34  HF Prev=30% | NR | NR | NR | NA | NA | NR |
| Koschack,18  2008  Germany | Cross-Sectional (Independent Study)  Ethnicity: NR  Comorbidities: Dyslipidemia (n=282), HBP (n=468), Cad (n=166), Diabetes (n=170), Historical Mi (n=41), Family History Heart Disease (n=231)  Reference Standard:  1 Cardiologist | Diagnostic power of the NT-proBNP assessment in ruling out left ventricular systolic dysfunction and compared it to a risk score derived from a logistic regression model of easily acquired clinical information | NT-proBNP (ELECSYS -proBNP Immunoassay) | HF (LVSD)  n=542  mean age= (noLVSD) 63y (62-63); (LVSD) 69y (66-73)  %males=57.55  HF Prev=4% | <98.5 | 91 | 46 | 1.69 | 0.20 | 0.83 |
| Lim,19  2007  United Kingdom | Cross-Sectional (Independent Study)  Ethnicity: NR  Comorbidities:  HBP (n=78), AF(n=19), Diabetes (n=24), History HID/MI (n=32)  Reference Standard: Echo (Physician) | Determine cost effectiveness assessment of patients suspected HF | NT-proBNP (ELECSYS -proBNP Immunoassay) | Suspected HF (overall)  n=137  mean age= 71y (13)  %males=50  HF Prev=24% | 20 pmol/L | 91 | 62 | 2.39 | 0.15 | NR |
| LVSD  n=137,  mean age= 71y (13)  %males=50  HF Prev=14% | 20 pmol/L | 100 | 57 | 2.33 | 0.00 | NR |
| LVDD  n=137,  mean age= 71y (13)  %males=50  HF Prev=9% | 20 pmol/L | 75 | 69 | 2.42 | 0.36 | NR |
| Lim,19  2007  United Kingdom  (cont’d) | (repeated data)  Cross-Sectional (Independent Study)  Ethnicity: NR  Comorbidities:  HBP (n=78), AF(n=19), Diabetes (n=24), History HID/MI (n=32)  Reference Standard: Echo (Physician) | (repeated data)  Determine cost effectiveness assessment of patients suspected HF | (repeated data)  NT-proBNP (ELECSYS -proBNP Immunoassay) | LVSD + LVDD  n=137  mean age= 71y (13)  %males=50  HF Prev=23% | 20 pmol/L | 90 | 60 | 2.25 | 0.17 | NR |
| VHD or RVD  n=137  mean age= 71y (13)  %males=50  HF Prev=4% | 20 pmol/L | 100 | 51 | 2.04 | 0.00 | NR |
| Mikklesen,20  2006  Denmark | Cross-Sectional (Independent Study)  Ethnicity: NR  Comorbidities:  HBP (n=64), Diabetes (n=16),IHD (n=44)  Reference Standard: History, Physical Exam, Chest Xray, Echo | Diagnosis of LVD | NT-proBNP (ELECSYS -proBNP Immunoassay) | Suspected cardiac dyspnea (Left ventricular dysfunction (LVD) = LVSD + IDD )  n=150  mean age= (LVSD) 70y\*  %males= (IDD) 68y\*  HF Prev=53% | ≥87 | 95 | 76 | 3.96 | 0.07 | 0.95 |
| LVD (male)  n=82  mean age= NR  %males= NR  HF Prev=NR% | ≥85 | 95 | 71 | 3.28 | 0.07 | NR |
| LVD (female)  n=68  mean age= NR  %males= NR  HF Prev=NR% | ≥110 | 98 | 88 | 8.17 | 0.02 | NR |
| LVSD  n=150  mean age= 70y\*  %males=54.6  HF Prev=15% | ≥270 | 100 | 85 | 6.67 | 0.00 | 0.98 |
| Mikklesen,20  2006  Denmark  (cont’d) | (repeated data)  Cross-Sectional (Independent Study)  Ethnicity: NR  Comorbidities:  HBP (n=64), Diabetes (n=16),IHD (n=44)  Reference Standard: History, Physical Exam, Chest Xray, Echo | (repeated data)  Diagnosis of LVD | (repeated data)  NT-proBNP (ELECSYS -proBNP Immunoassay) | LVSD (male)  n=82  mean age= NR  %males= NR  HF Prev=NR% | ≥270 | 100 | 85 | 6.67 | 0.00 | NR |
| LVSD (female)  n=68  mean age= NR  %males= NR  HF Prev=NR% | ≥595 | 100 | 96 | 25.00 | 0.00 | NR |
| Nielsen,21  2004  Denmark | Cross-Sectional (Independent Study)  Ethnicity: NR  Comorbidities:  COPD (n=166)  Reference Standard: Combination Of History, Physical Exam, ECG Chest X-Ray Exam, Lung Spirometry, Echocardiography And Blood Tests (Blood-Haemoglobin, Thyroid Hormones, Creatinine, Sodium, Potassium And Glucose). | Diagnosis of HF | NT-proBNP (not stated) | Patients with dyspnoea, all  n=345  mean age= 65y (18-89)  %males=5  HF Prev=24% | NR | NR | NR | NR | NR | NR |
| male patients ≥50 years  n=146  mean age= NR  %males= NR  HF Prev=NR% | 9 pmol/L | 100 | 60 | NR | NA | NR |
| 11 pmol/L | 96 | 67 | NA | NA | 0.93 |
| 18 pmol/L | 89 | 79 | NA | NA | NR |
| 8 pmol/L | 100 | 27 | NA | NA | NR |
| 17 pmol/L | 94 | 69 | NA | NA | 0.9 |
| 26 pmol/L | 91 | 84 | NA | NA | NR |
| Olofsson,22  2010  Sweden | Cross-Sectional (Independent Study)  Ethnicity: NR  Comorbidities:  HBP (n=43), AF(n=19), Historical MI (n=22), Valvular Heart Disease (n=18), Angina (n=37)  Reference Standard:  1 Cardiologist | “Main outcome measures. NPV, PPV, sensitivity, specificity, and cut off levels. To explore the negative predictive value (NPV), positive predictive value (PPV), sensitivity, and specificity of natriuretic peptides, cut-off levels, and the impact of sex and age in elderly patients with systolic HF | NT-proBNP (ELECSYS -proBNP Immunoassay) | Dyspnoea (HF)  n=109  mean age= (HF) 79y (6.4); (noHF) 76y (8.6),  %males=32  HF Prev=44% | 100 ng/L | 96 | 18 | 1.17 | 0.22 | NR |
| 200 ng/L | 92 | 46 | 1.70 | 0.17 | NR |
| 300 ng/L | 81 | 69 | 2.61 | 0.28 | NR |
| 400 ng/L | 75 | 82 | 4.17 | 0.30 | NR |
| 500 ng/L | 73 | 87 | 5.62 | 0.31 | NR |
| Park,11  2010  Korea | Cross-Sectional (Independent Study)  Ethnicity: NR  Comorbidities: Arrhythmia (n=90), Dyslipidemia (n=139), Diastolic Dysfunction (n=676), HBP (n=544), Diabetes (n=259), Ischemic (n=664), Valvular Heart Disease (n=22), Hypothyroidism (n=155), Hyperthyroidism (n=34), Cardiomyopathy (n=90)  Reference Standard:  2 Cardiologists | The detection of left ventricular systolic dysfunction (LVSD) or diastolic dysfunction (LVDD) in the symptomatic patients, To assess the direct correlation and its independent determinants between the BNP/NT BNP; to identify the factors that might influence the discrepancies between them | NT-proBNP (ELECSYS -proBNP Immunoassay) | Dyspnea or chest discomfort (Overall)  n=1,032  mean age= 62.0y (13.0)  %males=54  HF Prev=10% | NR | NR | NR | NA | NA | NR |
| Men, LVSD  n=555  mean age= NR  %males=100  HF Prev=10% | 510 | 81 | 81 | 4.22 | 0.23 | 0.867 |
| Men, advanced DD  n=555  mean age= NR  %males=100  HF Prev=7% | 1,678 | 83 | 81 | 4.41 | 0.22 | 0.879 |
| Women, LVSD  n=477  mean age= NR  %males=100  HF Prev=10% | 431 | 87 | 87 | 6.87 | 0.15 | 0.925 |
| Park,11  2010  Korea  (cont’d) | (repeated data)  Cross-Sectional (Independent Study)  Ethnicity: NR  Comorbidities: Arrhythmia (n=90), Dyslipidemia (n=139), Diastolic Dysfunction (n=676), HBP (n=544), Diabetes (n=259), Ischemic (n=664), Valvular Heart Disease (n=22), Hypothyroidism (n=155), Hyperthyroidism (n=34), Cardiomyopathy (n=90)  Reference Standard:  2 Cardiologists | (repeated data)  The detection of left ventricular systolic dysfunction (LVSD) or diastolic dysfunction (LVDD) in the symptomatic patients, To assess the direct correlation and its independent determinants between the BNP/NT BNP; to identify the factors that might influence the discrepancies between them | (repeated data)  NT-proBNP (ELECSYS -proBNP Immunoassay) | Women, advanced DD  n=477  mean age= NR  %males=100  HF Prev=7% | 860 | 85 | 85 | 5.51 | 0.18 | 0.878 |
| Age ≥ 65, LVSD  n=NR  mean age= NR  %males= NR  HF Prev=NR% | 1,446 | 82 | 81 | 4.32 | 0.22 | 0.875 |
| Age ≥ 65,advanced DD  n=NR  mean age= NR  %males= NR  HF Prev=NR% | 1,356 | 84 | 83 | 4.91 | 0.19 | 0.894 |
| Age < 65, LVSD  n=NR  mean age= NR  %males= NR  HF Prev=NR% | 379 | 84 | 84 | 5.26 | 0.19 | 0.912 |
| Age < 65, advanced DD  n=NR  mean age= NR  %males= NR  HF Prev=NR% | 276 | 83 | 82 | 4.73 | 0.20 | 0.893 |
| BMI ≥ 25, LVSD  n=NR  mean age= NR  %males= NR  HF Prev=NR% | 771 | 85 | 87 | 6.44 | 0.17 | 0.947 |
| BMI ≥ 25,advanced DD  n=NR  mean age= NR  %males= NR  HF Prev=NR% | 309 | 80 | 80 | 4.02 | 0.25 | 0.893 |
| Park,11  2010  Korea  (cont’d) | (repeated data)  Cross-Sectional (Independent Study)  Ethnicity: NR  Comorbidities: Arrhythmia (n=90), Dyslipidemia (n=139), Diastolic Dysfunction (n=676), HBP (n=544), Diabetes (n=259), Ischemic (n=664), Valvular Heart Disease (n=22), Hypothyroidism (n=155), Hyperthyroidism (n=34), Cardiomyopathy (n=90)  Reference Standard:  2 Cardiologists | (repeated data)  The detection of left ventricular systolic dysfunction (LVSD) or diastolic dysfunction (LVDD) in the symptomatic patients, To assess the direct correlation and its independent determinants between the BNP/NT BNP; to identify the factors that might influence the discrepancies between them | (repeated data)  NT-proBNP (ELECSYS -proBNP Immunoassay) | BMI < 25, LVSD  n=NR  mean age= NR  %males= NR  HF Prev=NR% | 830 | 81 | 81 | 4.21 | 0.23 | 0.869 |
| BMI<25,advanced DD  n=NR  mean age=NR  %males=NR  HF Prev=NR% | 682 | 81 | 81 | 4.29 | 0.23 | 0.885 |
| Hb ≥ 12, LVSD  n=NR  mean age=NR  %males=NR  HF Prev=NR% | 512 | 83 | 84 | 5.11 | 0.20 | 0.901 |
| Hb ≥ 12,advanced DD  n=NR  mean age=NR  %males=NR  HF Prev=NR% | 389 | 83 | 84 | 5.03 | 0.20 | 0.906 |
| Hb < 12, LVSD  n=NR  mean age=NR  %males=NR  HF Prev=NR% | 2,464 | 83 | 82 | 4.63 | 0.21 | 0.856 |
| Hb < 12,advanced DD  n=NR  mean age=NR  %males=NR  HF Prev=NR% | 1,912 | 77 | 77 | 3.27 | 0.30 | 0.82 |
| eGFR ≥ 60, LVSD  n=NR  mean age=NR  %males=NR  HF Prev=NR% | 418 | 84 | 84 | 5.41 | 0.18 | 0.915 |
| Park,11  2010  Korea  (cont’d) | (repeated data)  Cross-Sectional (Independent Study)  Ethnicity: NR  Comorbidities: Arrhythmia (n=90), Dyslipidemia (n=139), Diastolic Dysfunction (n=676), HBP (n=544), Diabetes (n=259), Ischemic (n=664), Valvular Heart Disease (n=22), Hypothyroidism (n=155), Hyperthyroidism (n=34), Cardiomyopathy (n=90)  Reference Standard:  2 Cardiologists | (repeated data)  The detection of left ventricular systolic dysfunction (LVSD) or diastolic dysfunction (LVDD) in the symptomatic patients, To assess the direct correlation and its independent determinants between the BNP/NT BNP; to identify the factors that might influence the discrepancies between them | (repeated data)  NT-proBNP (ELECSYS -proBNP Immunoassay) | eGFR ≥ 60,advanced DD  n=NR  mean age=NR  %males=NR  HF Prev=NR% | 276 | 83 | 82 | 4.65 | 0.20 | 0.889 |
| eGFR < 60, LVSD  n=NR  mean age=NR  %males=NR  HF Prev=NR% | 1,981 | 78 | 78 | 3.55 | 0.28 | 0.832 |
| eGFR < 60,advanced DD  n=NR  mean age=NR  %males=NR  HF Prev=NR% | 1,733 | 78 | 76 | 3.32 | 0.28 | 0.836 |
| Shelton,23  2006  United Kingdom | Cross-Sectional (Independent Study)  Ethnicity: NR  Comorbidities: Cerebrovascular (n=91), HBP (n=585), Diabetes (n=276), IHD (n=707)  Reference Standard: Echo, MSHD Classification(No Mention Of Clinicians) | Diagnostic Accuracy | NT-proBNP (ELECSYS -proBNP Immunoassay) | Suspected HF / Dyspnea  n=1321  mean age= (MSHD-AF) 74.5y; (No-MSHD with AF) 72.6y; (SR-MSHD) 69.7y; (SR-No MHSD) 69.1y,  %males=58  HF Prev=60% | NR | NR | NR | NA | NA | NR |
| MSHD with AF  n=276  mean age=NR  %males=6  HF Prev=40% | 400 | 99 | 7 | 1.06 | 0.14 | NR |
| 500 | 99 | 11 | 1.11 | 0.09 | NR |
| 600 | 98 | 23 | 1.27 | 0.09 | NR |
| 800 | 92 | 32 | 1.35 | 0.25 | NR |
| 1,000 | 90 | 50 | 1.80 | 0.20 | NR |
| 1,200 | 81 | 60 | 2.03 | 0.32 | NR |
| 1,400 | 77 | 68 | 2.41 | 0.34 | NR |
| 1,600 | 74 | 75 | 2.96 | 0.35 | NR |
| 1,764 | 69 | 77 | 3.01 | 0.40 | 0.784 |
| MSHD with SR  n=1,045  mean age=NR  %males=57  HF Prev=57% | 365 | 75 | 75 | 2.95 | 0.34 | 0.794 |
| MSHD with AF (Age > 75)  n=140  mean age=NR  %males=NR  HF Prev=75% | 757 | 100 | 3 | 1.03 | 0.00 | NR |
| 1,764 | 69 | 61 | 1.75 | 0.51 | NR |
| MSHD with AF (Age ≤ 75)  n=136,  mean age=NR  %males=NR  HF Prev=72% | 125 | 100 | 0 | 1.00 | NR | NR |
| 1,758 | 70 | 90 | 7.12 | 0.33 | NR |
| Shelton,23  2006  United Kingdom  (cont’d) | (repeated data)  Cross-Sectional (Independent Study)  Ethnicity: NR  Comorbidities: Cerebrovascular (n=91), HBP (n=585), Diabetes (n=276), IHD (n=707)  Reference Standard: Echo, MSHD Classification(No Mention Of Clinicians) | (repeated data)  Diagnostic Accuracy | (repeated data)  NT-proBNP (ELECSYS -proBNP Immunoassay) | MSHD with SR (Age ≤ 75)  n=725  mean age=NR,  %males=NR  HF Prev=56% | 125 | 89 | 43 | 1.56 | 0.26 | NR |
| 357 | 73 | 79 | 3.43 | 0.34 | NR |
| MSHD with SR (Age>75)  n=320  mean age=NR  %males=NR  HF Prev=58% | 450 | 75 | 68 | 2.34 | 0.37 | NR |
| 652 | 69 | 79 | 3.23 | 0.39 | NR |
| Sivakumar,24 2006  United Kingdom | Cross-Sectional (Independent Study)  Ethnicity: NR  Comorbidities:  BP (n=35), AF (n=35), Diabetes (n=10), IHD (n=38)  Reference Standard:  1 Clinician | Diagnosis: systolic dysfunction, diastolic dysfunction, AF, and valve HD | NT-proBNP (ELECSYS -proBNP Immunoassay) | suspected HF/valvular disease (LVSD)  n=100  mean age=82.4y  %males=40  HF Prev=25% | 424 | 96 | 45 | 1.75 | 0.09 | 0.71 |
| 1,226 | 68 | 68 | 2.13 | 0.47 | NR |
| 1,689 | 60 | 76 | 2.50 | 0.53 | NR |
| 6,180 | 44 | 96 | 11.00 | 0.58 | NR |
| Valvular disease only  n=75  mean age= NR  %males= NR  HF Prev=29% | 227 | 91 | 43 | 1.60 | 0.21 | NR |
| 334 | 91 | 53 | 1.94 | 0.17 | NR |
| 424 | 82 | 55 | 1.82 | 0.33 | NR |
| Stahrenberg,25  2010  Germany | Cohort (DIAST/CHF)  Ethnicity: NR  Comorbidities:  HBP (n=210), CAD (n=94), AF(n=58), Diabetes (n=75), Hyperlipidemia (n=122, HF Patients Only)  Reference Standard: Physicians, Framingham | Investigated the clinical relevance of GDF-15 plasma levels in HFnEF. ROC curves were constructed for discrimination between controls and subjects with HFnEFESC or HFnEFNew and sensitivity, specificity, and odds ratios HFnEF were calculated. | NT-proBNP (ELECSYS -proBNP Immunoassay) | Chronic HF (HFnEFESC)  n=416  mean age= (HFnEFESC Grp) 73y (66-78); (HFrEF Grp) 71y (66-75); (Controls) 56y (52-63)  %males=44.7;  HF Prev=34%; Discrimination of HFnEFESC (HF normal Ejection Fraction) from healthy controls, Prevalence NR in paper but calculated using info on N’s | >220 ng/L | 65 | 97 | 20.34 | 0.36 | NR |
| Discrimination of HFnEFESC (HF normal Ejection Fraction) from healthy controls, Prevalence NR in paper but calculated using info on N’s | NR | NR | NR | NA | NA | 0.88 |
| Specificity Fixed, Prevalence NR in paper but calculated using info on N’s | 120 ng/L | 74 | 80 | 3.70 | 0.33 | NR |
| Sensitivity Fixed, Prevalence NR in paper but calculated using info on N’s | 220 ng/L | 55 | 97 | 18.33 | 0.46 | NR |
| Prevalence NR in paper but calculated using info on N’s | NR | NR | NR | NA | NA | 0.859 |
| Valle,26  2005  Italy | Cohort  Ethnicity: NR  Comorbidities:  HBP (n=27), AF(n=8), COPD (n=3), Diabetes (n=10), Ischemic (n=7), Renal Disease (n=2), Valve Disease (n=6)  Reference Standard: Framingham | Diagnosis HF, Deaths, hospitalization for chronic HF and cases of acute HF without hospitalization. | NT-proBNP(ELECSYS -proBNP Immunoassay) | suspected HF in elderly  n=101,  mean age= 84(9)y,  %males=20); HF  HF Prev=13% | NR | NR | NR | NA | NA | NR |
| LVD (LVSD + DDF)  n=101  mean age= 84y (9)  %males=20  HF Prev=42%; 230 is optimal to distinguish between patients with or without some kind of ventricular dysfunction | 150 | 93 | 41 | 1.58 | 0.17 | NR |
| 200 | 83 | 53 | 1.77 | 0.32 | NR |
| 230\* | 80 | 60 | 2.00 | 0.33 | 0.78 |
| 250 | 76 | 60 | 1.90 | 0.40 | NR |
| 300 | 73 | 66 | 2.15 | 0.41 | NR |
| 350 | 70 | 70 | 2.33 | 0.43 | NR |
| LVSD + restrictive diastolic pattern  n=101  mean age= 84y (9)  %males=20  HF Prev=NR%; 530 is optimal threshold distinguish between patients with serious systolic and /or diastolic ventricular dysfunction | 350 | 100 | 65 | 2.86 | 0.00 | NR |
| 400 | 95 | 70 | 3.17 | 0.07 | NR |
| 500\* | 95 | 82 | 5.28 | 0.06 | 0.93 |
| 550 | 90 | 84 | 5.63 | 0.12 | NR |
| 600 | 85 | 84 | 5.31 | 0.18 | NR |
| Zaphiriou,12  2005  United Kingdom | Cross-Sectional (Independent Study)  Ethnicity: NR  Comorbidities: Dyslipidemia (n=67), HBP (n=168), Stroke (n=35), COPD (n=58), Diabetes (n=58),  MI (n=42), PVD (n=20), Angina (n=80), CABG(n=18),  PCI (n=7)  Reference Standard:  1 Cardiologist | Sensitivity, specificity, positive and negative predictive values (PPV and NPV) and positive and negative likelihood ratios for BNP, NTproBNP and the ECG for the diagnosis of HF. Area under the ROC curves for the two natriuretic peptides | NT-proBNP (ELECSYS -proBNP Immunoassay) | Suspected HF referred by GPs (all)  n=306  mean age= 74y\* (52-87)  %males=4  HF Prev=34% | ≥125 | 98 | 35 | 1.51 | 0.06 | 0.85 |
| ≥166 | 96 | 43 | 1.68 | 0.09 | NR |

**Abbreviations:** AF = Atrial Fibrillation; AMI = Acute myocardial infarction; AUC = Area Under the Curve; BMI = Body Mass Index; BNP = B-Type Natriuretic Peptide; CAD = Coronary Artery Disease; CAGB = Coronary Artery Bypass Graft; CHF = Congestive Heart Failure; COPD = Chronic obstructive pulmonary disease; DD = Diastolic dysfunction; DDF = Diastolic dysfunction; DIAST-CHF = Diastolic congestive heart failure; ECG = Electrocardiogram; ECHO = Echocardiogram; ECHOES = Echocardiographic Heart of England Screening; eGFR = Estimated glomerular filtration rate; GDF-15 = Growth differentiation factor 15; GFR = Glomerular filtration rate; GP = General practitioner; Hb = Hemoglobin; HBP = High Blood Pressure/Hypertension; HF = Heart Failure; HFnEF = Heart failure with normal ejection fraction; HFnEFESC = Heart failure with normal ejection fraction recommended by European Society of Cardiology; HFnEFNew = Heart failure with normal ejection fraction recommended by American Society of ; HFrEF Grp Heart failure with reduced ejection fraction group; echocardiography; IDD = Isolated diastolic dysfunction ; IHD = Ischemic Heart Disease; IQR = Interquartile range; kg/m2 = Kilograms per metre squared; LR- = Negative Likelihood Ratio; LR+ = Positive Likelihood Ratio; LVD = Left ventricular dysfunction; LVDD = Left ventricular diastolic dysfunction; LVEF = Left Ventricular Ejection Fraction; LVSD = Left ventricular systolic dysfunction ; MI = Myocardial Infarction; mL/min/1.73m2 = Millilitre per minute per 1.73 metres squared; MSHD = Major structural heart disease; NA = Not applicable; ng/L = Nanogram per litre; NPV = Negative predictive value; NR = Not reported; NT-proBNP = N-Terminal proBNP; PCI = Percutaneous coronary intervention; pg/mL = Picograms per millilitre; pmol/L = Picomol per litre; PPV = Positive predictive value ; Pts = Patients; QRS = QRS complex on electrocardiogram; ROC = Receiver operating characteristic ; RVD = Right ventricular dysplasia; SOB = shortness of breath; SR = Sinus rhythm; TIA = Transient ischemic attack; UHFO-IA = Utrecht Heart Failure Organisation – Initial Assessment; VHD = Valvular heart disease; yrs = Years