

**Prediction of Incident Heart Failure in General Practice: The ARIC
Study**

Agarwal, ARIC Heart Failure Prediction Score

SUPPLEMENTARY MATERIALS

Appendix table 1. Discrimination and model fit characteristics of models predicting 10 years HF risk utilizing variables in respective rows

| Variables | AUC | Chi- Square |
|---|-------|-------------|
| Age, race, gender, diabetes | 0.714 | 66.0 |
| Age, race, gender, diabetes, glucose | 0.721 | 65.6 |
| Age, race, gender, antiHTN | 0.706 | 25.13 |
| Age, race, gender, SBP, antiHTN | 0.711 | 27.32 |
| Age, race, gender, diabetes, glucose, antiHTN, SBP | 0.741 | 63.8 |
| Age, race, gender, diabetes, BMI | 0.731 | 49.0 |
| Age, race, gender, diabetes, BMI, antiHTN | 0.742 | 41.8 |
| Age, race, gender, diabetes, BMI, antiHTN, SBP | 0.747 | 46.7 |
| Age, race, gender, diabetes, BMI, antiHTN, SBP, antiHTN*SBP | 0.747 | 39.0 |
| Age, race, gender, diabetes, BMI, antiHTN, SBP, glucose | 0.750 | 44.8 |
| Age, race, gender, diabetes, BMI, antiHTN, SBP, smoking status | 0.771 | 65.9 |
| Age, race, gender, diabetes, BMI, antiHTN, SBP, smoking status, COPD | 0.774 | 82.6 |
| Age, race, gender, diabetes, BMI, antiHTN, SBP, smoking status, pack-years | 0.775 | 74.0 |
| Age, race, gender, diabetes, BMI, antiHTN, prevalent CHD, smoking status | 0.780 | 52.5 |
| Age, race, gender, diabetes, BMI, antiHTN, prevalent CHD, smoking status, COPD | 0.781 | 78.6 |
| Age, race, gender, diabetes, BMI, antiHTN, SBP, smoking status, VHD | 0.755 | 59.2 |
| Age, race, gender, diabetes, BMI, antiHTN, SBP, smoking status, LVH | 0.755 | 39.0 |
| Age, race, gender, diabetes, BMI, antiHTN, SBP, smoking status, LVH, VHD | 0.755 | 66.8 |
| Age, race, gender, diabetes, BMI, antiHTN, SBP, smoking status, heart rate | 0.776 | 67.4 |
| Age, race, gender, diabetes, BMI, antiHTN, Prevalent CHD, SBP, smoking status, heart rate | 0.790 | 69.5 |
| Age, race, gender, diabetes, BMI, antiHTN, Prevalent CHD, SBP, smoking status, heart rate, VHD | 0.791 | 69.8 |
| Age, race, gender, diabetes, BMI, antiHTN, prevalent CHD, SBP, smoking status, heart rate, LVH | 0.792 | 74.8 |
| Age, race, gender, diabetes, BMI, antiHTN, prevalent CHD, SBP, smoking status, heart rate, LVH, BBB | 0.794 | 60.9 |
| Age, race, gender, diabetes, BMI, antiHTN, Prevalent CHD, smoking status, LVH, albumin | 0.789 | 63.3 |
| Age, race, gender, diabetes, BMI, antiHTN, Prevalent CHD, smoking status, LVH, albumin, VHD | 0.789 | 66.8 |
| Age, race, gender, diabetes, BMI, antiHTN, prevalent CHD, smoking status, LVH, albumin, BBB | 0.790 | 63.3 |
| Age, race, gender, diabetes, BMI, antiHTN, prevalent CHD, smoking status, LVH, albumin, BBB, VHD | 0.790 | 53.0 |
| Age, race, gender, diabetes, BMI, antiHTN, prevalent CHD, smoking status, heart rate, LVH, BBB, Albumin | 0.800 | 48.4 |
| Age, race, gender, diabetes, BMI, antiHTN, prevalent CHD, smoking status, heart rate, LVH, BBB, HDL | 0.802 | 39.0 |
| Age, race, gender, diabetes, BMI, antiHTN, prevalent CHD, smoking status, creatinine, HDL, albumin | 0.791 | 46.4 |
| Age, race, gender, diabetes, BMI, antiHTN, prevalent CHD, smoking status, glucose, creatinine, HDL, Albumin | 0.796 | 39.0 |

BMI = body mass index, SBP = systolic blood pressure, antiHTN = use of medication for hypertension, COPD = chronic obstructive pulmonary disease, LVH = left ventricular hypertrophy using Cornell voltage criteria from 10 second ECG, BBB = bundle branch block = QRS duration >120 ms on ECG.

Appendix Table 2: Discrimination and model fit statistics comparing several fits of NT-pro BNP to the ARIC HF risk score model

| Model | AUC | HL p value | GB p value | IDI | NRI (%) |
|-------------------------|----------------------|------------|------------|--------------------|-------------------|
| Without NT-proBNP | 0.772 (0.759, 0.787) | 0.031 | <0.001 | . | . |
| Categorical NT-proBNP | 0.802 (0.790, 0.817) | 0.005 | <0.001 | 0.056 (0.43, 0.73) | 12.7 (9.6, 20.1) |
| Ln (NT-proBNP) | 0.805 (0.792, 0.820) | 0.005 | <0.001 | 0.057 (0.43, 0.76) | 13.0 (10.2, 19.9) |
| Piecewise Polynomial I | 0.802 (0.791, 0.818) | 0.007 | <0.001 | 0.062 (0.48, 0.82) | 13.1 (10.1, 20.3) |
| Piecewise Polynomial II | 0.802 (0.791, 0.818) | 0.014 | <0.001 | 0.062 (0.48, 0.82) | 13.3 (10.1, 20.3) |

Results from the Atherosclerosis Risks in Communities Study 1996-98 through 2007

HL = Hosmer Lemeshow, GB = Gronessby Borgan

IDI = Intergrated discrimination index as comapred to the basic model

NRI = Net reclassification improvement as compared to the basic model

Without NT-proBNP = The ARIC HF risk score model

Continuous refers to log transformation of NT-proBNP

Piecewise polynomial II uses linear splines with knots at following percentiles: 5, 40, 60, 80, 95

Piecewise polynomial II uses linear splines with knots at following percentiles: 10, 40, 60, 80, 90

Appendix table 3 Heart Failure risk prediction at t years by race and gender: Proportion free of heart failure at time t for “null model” i.e., $S_0(t)$

| End of year | White Female | White Male | African American Male | African American Female |
|-------------|--------------|------------|-----------------------|-------------------------|
| 1 | 0.99988 | 0.99966 | 0.99948 | 0.99957 |
| 2 | 0.99969 | 0.99934 | 0.99882 | 0.99935 |
| 3 | 0.99945 | 0.99891 | 0.99836 | 0.99885 |
| 4 | 0.99916 | 0.99834 | 0.99736 | 0.99820 |
| 5 | 0.99881 | 0.99772 | 0.99628 | 0.99708 |
| 6 | 0.99838 | 0.99728 | 0.99514 | 0.99637 |
| 7 | 0.99802 | 0.99650 | 0.99341 | 0.99520 |
| 8 | 0.99768 | 0.99546 | 0.99135 | 0.99346 |
| 9 | 0.99718 | 0.99452 | 0.98980 | 0.99181 |
| 10 | 0.99671 | 0.99334 | 0.98800 | 0.99095 |

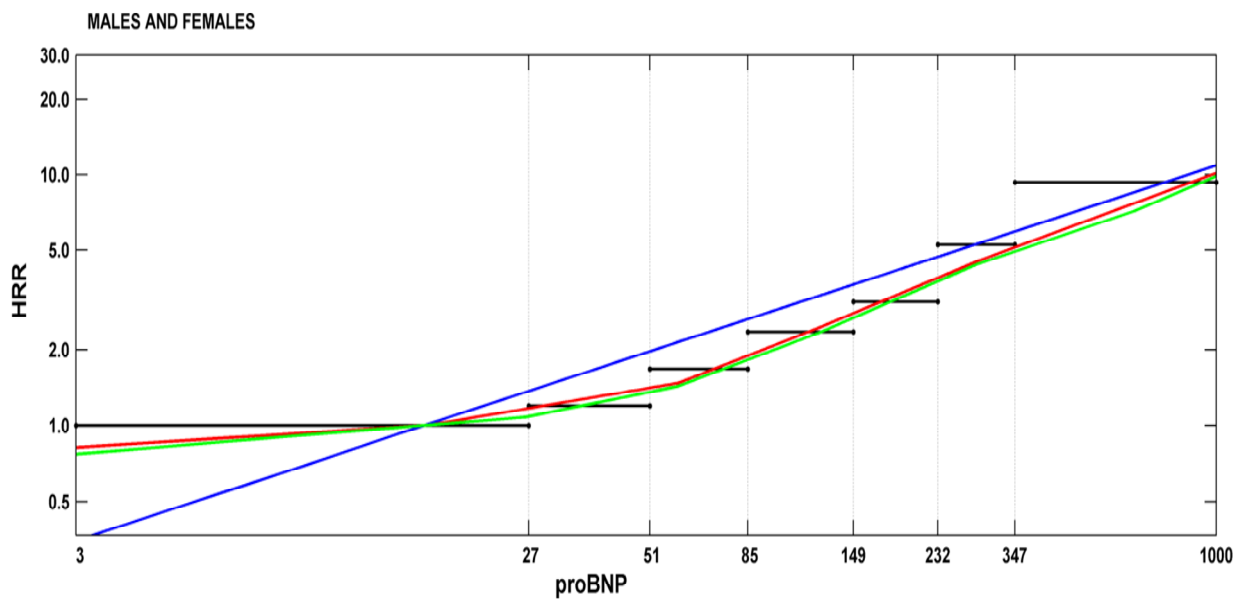
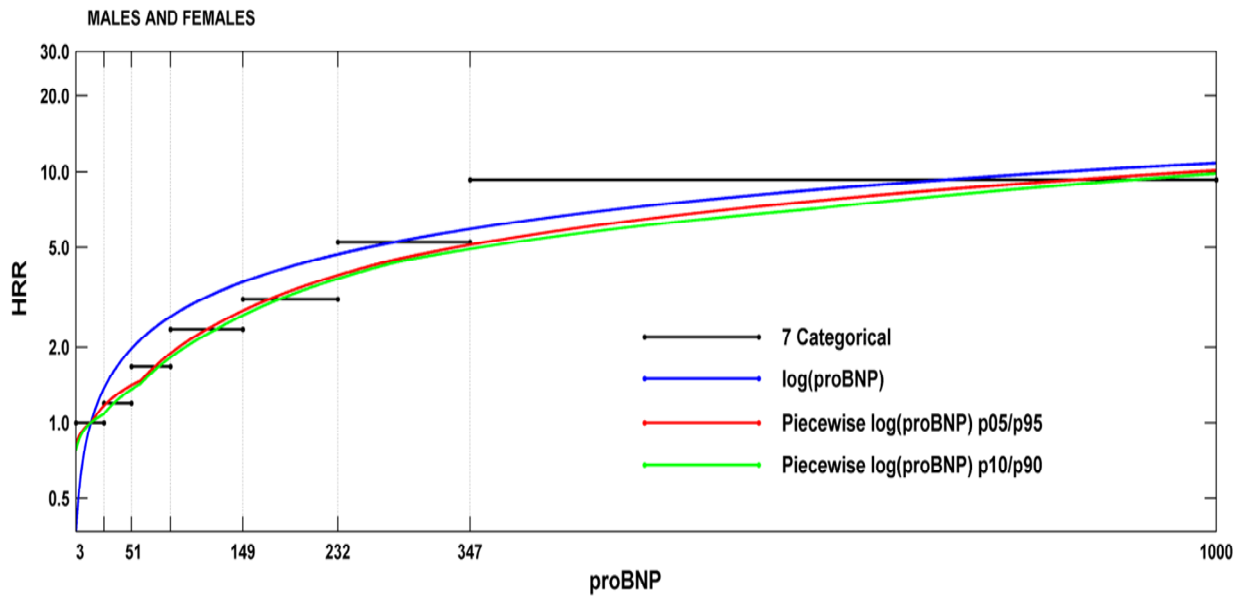
Risk at t years is given by $1 - S_0(t)^{\exp(XB)}$, where $\exp(XB) = e^{XB}$, and

$$XB = B_{age}*(age-65) + B_{cursmo}*CURSMO + B_{forsmo}*FORSMO + B_{HR}*(HR-60) + B_{prechd}*PRECHD + B_{hypmed}*HYPMED + B_{SBP}*(SBP-120) + B_{diabet}*DIABET + B_{BMI}*(bmi-25) + B_{logBNP}*(\log(BNP) - 1.6).$$

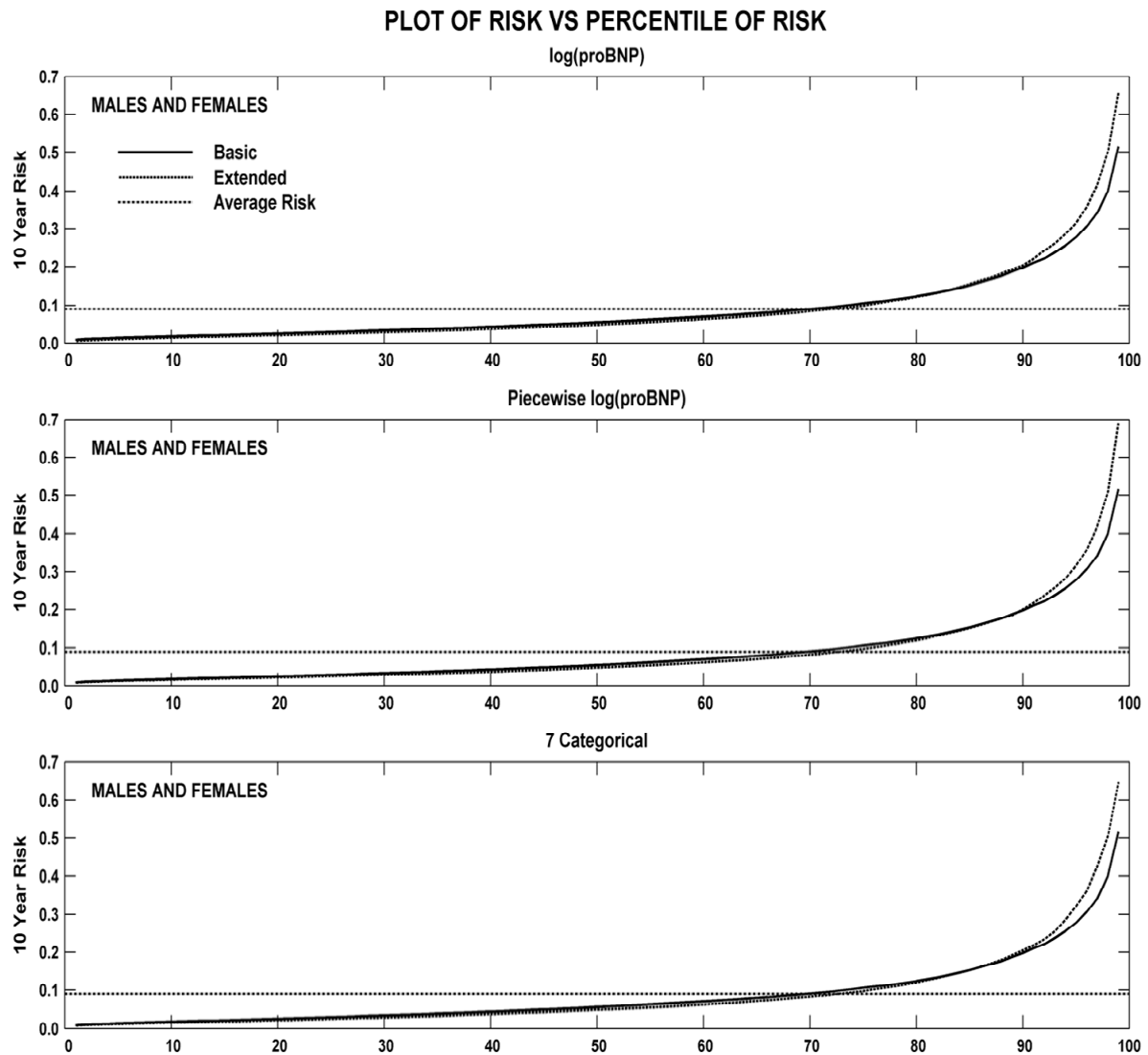
Above values correspond to S_0 at time t.

Where age is in years, cursmo = current smoker, forsmo = former smoker, HR = heart rate, prechd = prevalent CHD, hypmed = hypertension medication use, SBP = systolic blood pressure in mm of Hg, Diabet = diabetes, BMI = body mass index in kg/m², BNP = NT-proBNP.

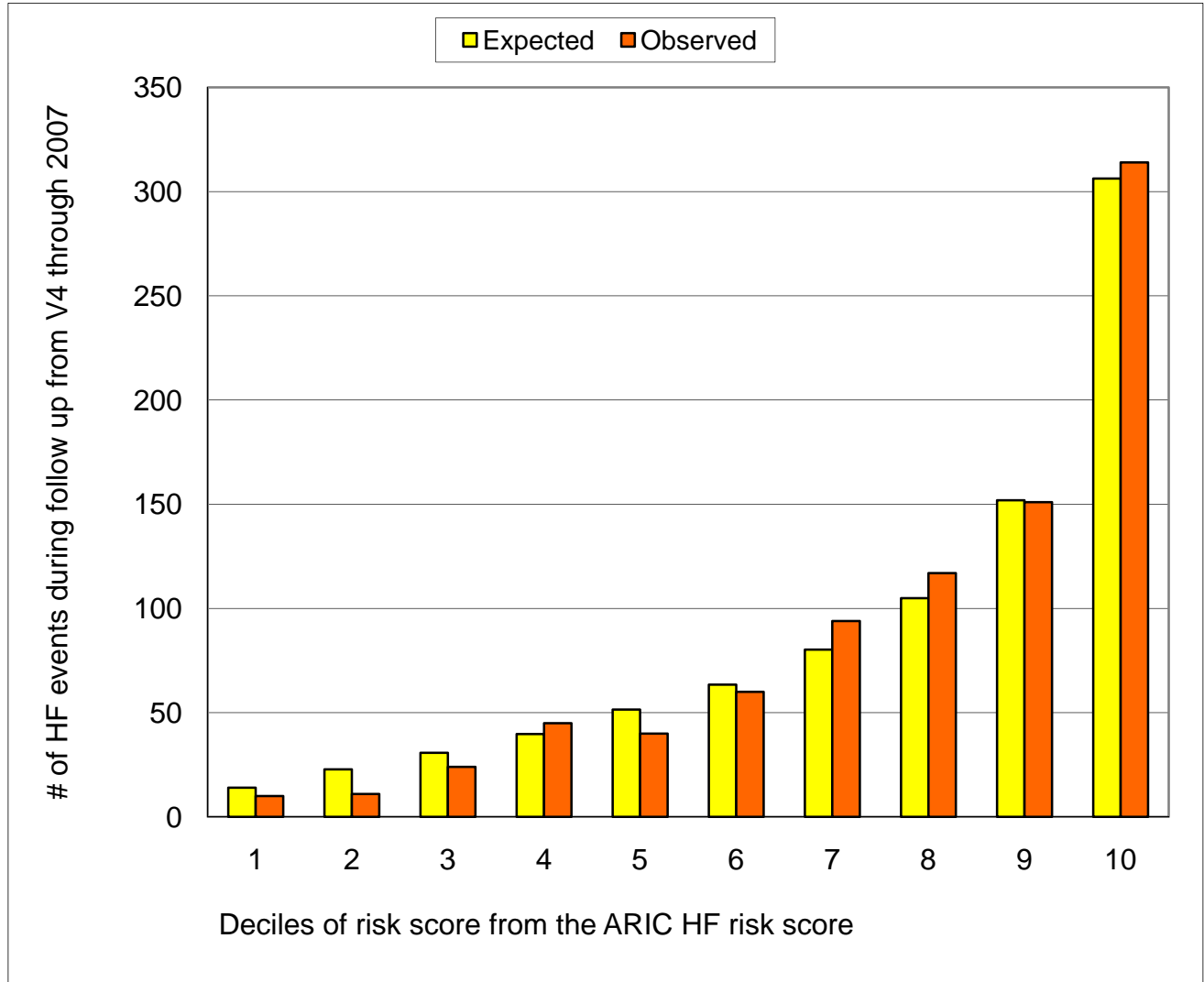
B_{age} , B_{cursmo} , etc are the sex/race-specific coefficients of the model, given in coefficients table 2 of the manuscript. $S_0(t)$, for $t=1, 2, \dots, 10$ are the “null model” survival i.e., $1 - \text{risk}$, values given in this table.



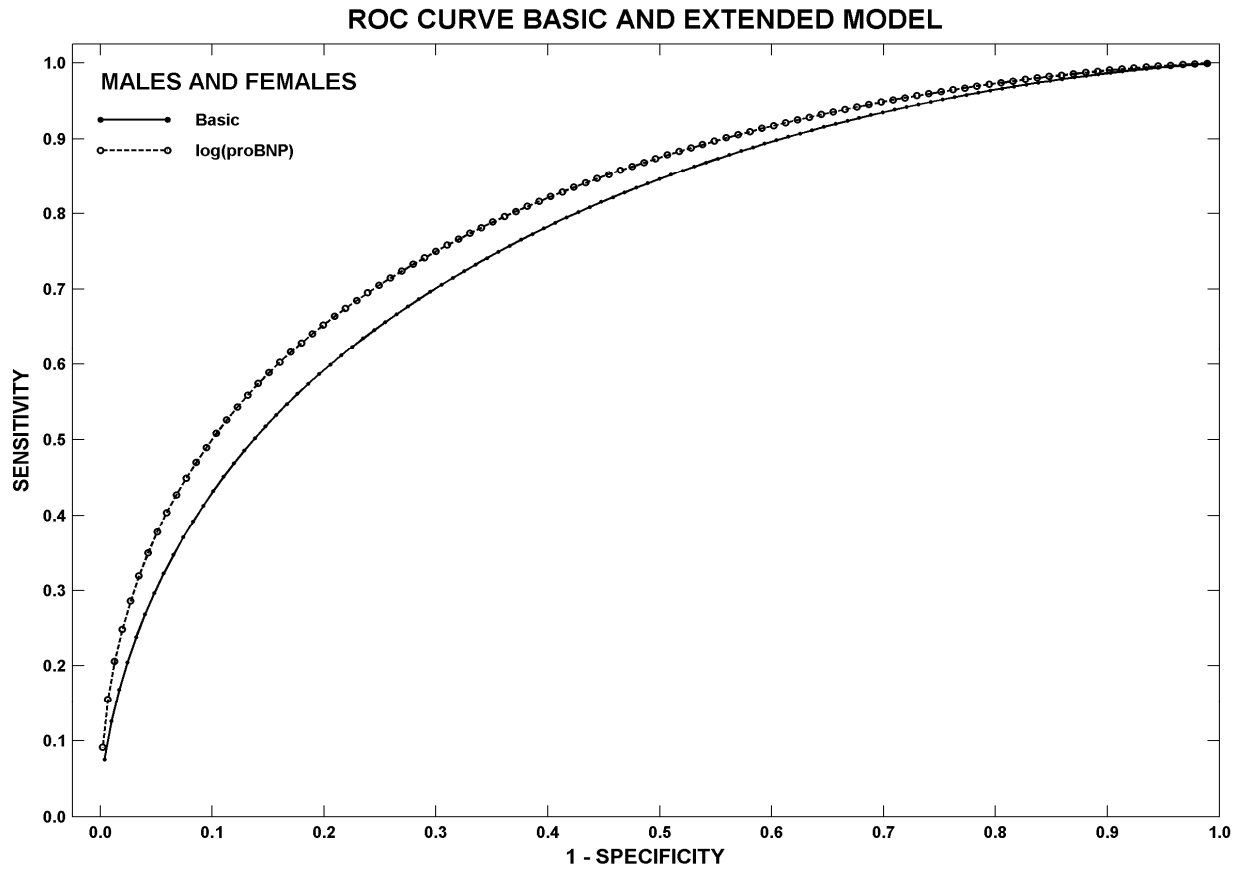
Appendix Figure 1.a Multivariable adjusted (variables in the ARIC study HF risk score) hazard ratios of heart failure from models fitting NT-proBNP in pg/mL and log(NT-proBNP, pg/mL) as: a) seven categories using NT-proBNP percentiles of 20, 40, 60, 80, 90, and 95, b) log (NT-proBNP), c) linear splines with knots at 10, 40, 60, 80, and 90th percentile, and d) linear splines with knots at 5, 40, 60, 80, and 95th percentile. In the upper panel the X-axis is on linear scale and in the lower panel its log transformed.



Appendix Figure 1.b Plot of risk vs. percentile of risk fitting NT-proBNP in pg/mL and log (NT-proBNP, pg/mL) in several ways: a). log (NT-proBNP), b). linear splines with knots at 5, 40, 60, 80, and 95th percentile, and c). seven categories using NT-proBNP percentiles of 20, 40, 60, 80, 90, and 95.



Appendix Figure 2. Number of observed versus predicted heart failure events during study follow up from visit 4 through 2007 by decile of the ARIC heart failure risk score. Each decile includes approximately 1010 individuals at start of follow up.



Appendix Figure 3. Receiver operating curves showing the sensitivity of the ARIC heart failure risk model (basic) over complete range of specificity and Area Under the Receiver Operating Curve as compared to model with addition of a variable NT-proBNP (extended). The Atherosclerosis Risk in communities study (1996-98 through 2007)