

**Fig. 1**  
**Summary Stats**  
**1 Year Mortality**

| Variable       | Outcome=0           |         | Outcome=1          |         | KW Test<br>P Value | sHR(Raw)         |            | sHR(ln)          |            | AuROC | Most     |
|----------------|---------------------|---------|--------------------|---------|--------------------|------------------|------------|------------------|------------|-------|----------|
|                | Median [IQR]        | Missing | Median [IQR]       | Missing |                    | Est [95% CI]     | log-rank p | Est [95% CI]     | log-rank p |       |          |
| NTproBNP pg/ml | 1210[458.5-2866]    | 0       | 2775.5[1682-5774]  | 0       | <0.001             | 1.24 [1.12-1.38] | <0.001     | 2.04 [1.63-2.55] | <0.001     | 0.702 | Gaussian |
| cTnT1          | 21.09[9.74-37.44]   | 13      | 41.16[29.81-67.44] | 2       | <0.001             | 1.21 [1.11-1.33] | <0.001     | 2.09 [1.7-2.56]  | <0.001     | 0.742 | ln       |
| Creatinine     | 1.46[1.17-1.97]     | 3       | 1.68[1.31-2.29]    | 0       | 0.002              | 1.1 [0.96-1.25]  | 0.18       | 1.26 [1.06-1.51] | 0.009      | 0.602 | ln       |
| eGFR           | 42.13[29.36-58.99]  | 13      | 29.02[21.96-45.73] | 2       | <0.001             | 0.52 [0.39-0.69] | <0.001     | 0.66 [0.55-0.78] | <0.001     | 0.663 | ln       |
| SBP            | 125[110-140]        | 9       | 120[103.75-140]    | 2       | 0.051              | 0.81 [0.65-1.02] | 0.075      | 0.8 [0.64-0.99]  | 0.044      | 0.565 | ln       |
| DBP            | 70[63-80]           | 9       | 65.5[60-75]        | 2       | 0.004              | 0.7 [0.55-0.89]  | 0.004      | 0.7 [0.56-0.88]  | 0.002      | 0.596 | ln       |
| HGB g/dl       | 13[11.8-14.3]       | 0       | 11.95[10.72-13.28] | 0       | <0.001             | 0.63 [0.52-0.76] | <0.001     | 0.74 [0.65-0.83] | <0.001     | 0.656 | Raw      |
| Age Yr         | 69.6[59.6-76.4]     | 0       | 77.2[68.7-83.3]    | 0       | <0.001             | 2.23 [1.68-2.96] | <0.001     | 2.4 [1.71-3.37]  | <0.001     | 0.695 | Raw      |
| ST2 ng/ml      | 37.1[30.4-48.9]     | 0       | 53.3[38.45-89.1]   | 0       | <0.001             | 1.39 [1.27-1.52] | <0.001     | 1.82 [1.56-2.13] | <0.001     | 0.705 | ln       |
| LVEF           | 34[26-43]           | 0       | 35[25.25-43]       | 0       | 0.494              | 1.08 [0.88-1.33] | 0.456      | 1.1 [0.89-1.36]  | 0.386      | 0.522 | ln       |
| BMI            | 27[24.5-30.7]       | 13      | 25.15[22.8-27.92]  | 2       | <0.001             | 0.61 [0.47-0.8]  | <0.001     | 0.64 [0.51-0.8]  | <0.001     | 0.625 | ln       |
| NYHA           | 1=64;2=54;3=188;4=8 | 0       | 1=1;2=39;3=44;4=2  | 0       | <0.001             |                  | <0.001     |                  |            |       |          |
| Ethnicity      | 1=800;2=5           | 0       | 1=86               | 0       | 1                  | 0 [0-Inf]        | 0.475      |                  |            |       |          |
| Sex            | 0=230;1=575         | 0       | 0=23;1=63          | 0       | 0.802              | 1.1 [0.68-1.77]  | 0.707      |                  |            |       |          |
| CAD            | 0=327;1=478         | 0       | 0=39;1=47          | 0       | 0.421              | 0.82 [0.54-1.26] | 0.362      |                  |            |       |          |
| Diabetes       | 0=523;1=282         | 0       | 0=47;1=39          | 0       | 0.076              | 1.5 [0.98-2.29]  | 0.061      |                  |            |       |          |
| HTN            | 0=316;1=489         | 0       | 0=31;1=55          | 0       | 0.642              | 1.12 [0.72-1.74] | 0.616      |                  |            |       |          |

Fig. 2  
Summary Stats  
Study Mortality

| Variable       | Outcome=0             |         | Outcome=1           |         | KW Test<br>P Value | SHR(Raw)         |            | SHR(In)          |            | AuROC | Most |
|----------------|-----------------------|---------|---------------------|---------|--------------------|------------------|------------|------------------|------------|-------|------|
|                | Median [IQR]          | Missing | Median [IQR]        | Missing |                    | Est [95% CI]     | log-rank p | Est [95% CI]     | log-rank p |       |      |
| NTproBNP pg/ml | 969.65[364.12-2313.5] | 0       | 2233[922.4-5174]    | 0       | <0.001             | 1.27 [1.19-1.35] | <0.001     | 2 [1.77-2.25]    | <0.001     | 0.684 | In   |
| cTnT1          | 15.65[7.92-30.78]     | 7       | 34.18[20.81-53.64]  | 8       | <0.001             | 1.21 [1.15-1.28] | <0.001     | 2.01 [1.8-2.24]  | <0.001     | 0.725 | In   |
| Creatinine     | 1.37[1.12-1.86]       | 3       | 1.67[1.33-2.37]     | 0       | <0.001             | 1.13 [1.06-1.21] | <0.001     | 1.36 [1.24-1.49] | <0.001     | 0.643 | In   |
| eGFR           | 47.73[32.75-65.07]    | 4       | 32.45[22.55-44.32]  | 11      | <0.001             | 0.47 [0.4-0.54]  | <0.001     | 0.63 [0.57-0.69] | <0.001     | 0.711 | In   |
| SBP            | 123[110-140]          | 5       | 125[110-145]        | 6       | 0.409              | 0.99 [0.89-1.11] | 0.879      | 0.99 [0.88-1.1]  | 0.817      | 0.517 | In   |
| DBP            | 70[65-80]             | 5       | 70[60-78]           | 6       | <0.001             | 0.82 [0.73-0.92] | 0.001      | 0.81 [0.72-0.91] | <0.001     | 0.571 | In   |
| HGB g/dl       | 13.2[12-14.5]         | 0       | 12.1[11.1-13.6]     | 0       | <0.001             | 0.68 [0.62-0.75] | <0.001     | 0.78 [0.73-0.83] | <0.001     | 0.654 | Raw  |
| Age_Yr         | 66.05[56.58-74.32]    | 0       | 75.5[69.6-80.85]    | 0       | <0.001             | 2.26 [1.95-2.61] | <0.001     | 2.5 [2.1-2.97]   | <0.001     | 0.737 | Raw  |
| ST2 ng/ml      | 35.45[29.37-45.4]     | 0       | 44.7[34-61.1]       | 0       | <0.001             | 1.29 [1.22-1.37] | <0.001     | 1.62 [1.48-1.77] | <0.001     | 0.662 | In   |
| LVEF           | 34[26-42.25]          | 0       | 34[25-44]           | 0       | 0.865              | 0.98 [0.88-1.09] | 0.705      | 0.95 [0.85-1.06] | 0.344      | 0.503 | In   |
| BMI            | 27.1[24.7-30.7]       | 5       | 26.4[23.6-29.8]     | 10      | 0.005              | 0.79 [0.7-0.9]   | <0.001     | 0.78 [0.7-0.88]  | <0.001     | 0.558 | In   |
| NYHA           | 1=60;2=418;3=91;4=3   | 0       | 1=5;2=166;3=141;4=7 | 0       | <0.001             |                  | <0.001     |                  |            |       |      |
| Ethnicity      | 1=567;2=5             | 0       | 1=319               | 0       | 0.166              | 0 [0-Inf]        | 0.163      |                  |            |       |      |
| Sex            | 0=154;1=418           | 0       | 0=99;1=220          | 0       | 0.215              | 0.92 [0.73-1.17] | 0.494      |                  |            |       |      |
| CAD            | 0=242;1=330           | 0       | 0=124;1=195         | 0       | 0.321              | 1.07 [0.86-1.34] | 0.537      |                  |            |       |      |
| Diabetes       | 0=387;1=185           | 0       | 0=183;1=136         | 0       | 0.003              | 1.45 [1.16-1.8]  | 0.001      |                  |            |       |      |
| HTN            | 0=237;1=335           | 0       | 0=110;1=209         | 0       | 0.045              | 1.3 [1.04-1.64]  | 0.024      |                  |            |       |      |

Fig. 3 Linearity Check: NT-proBNP

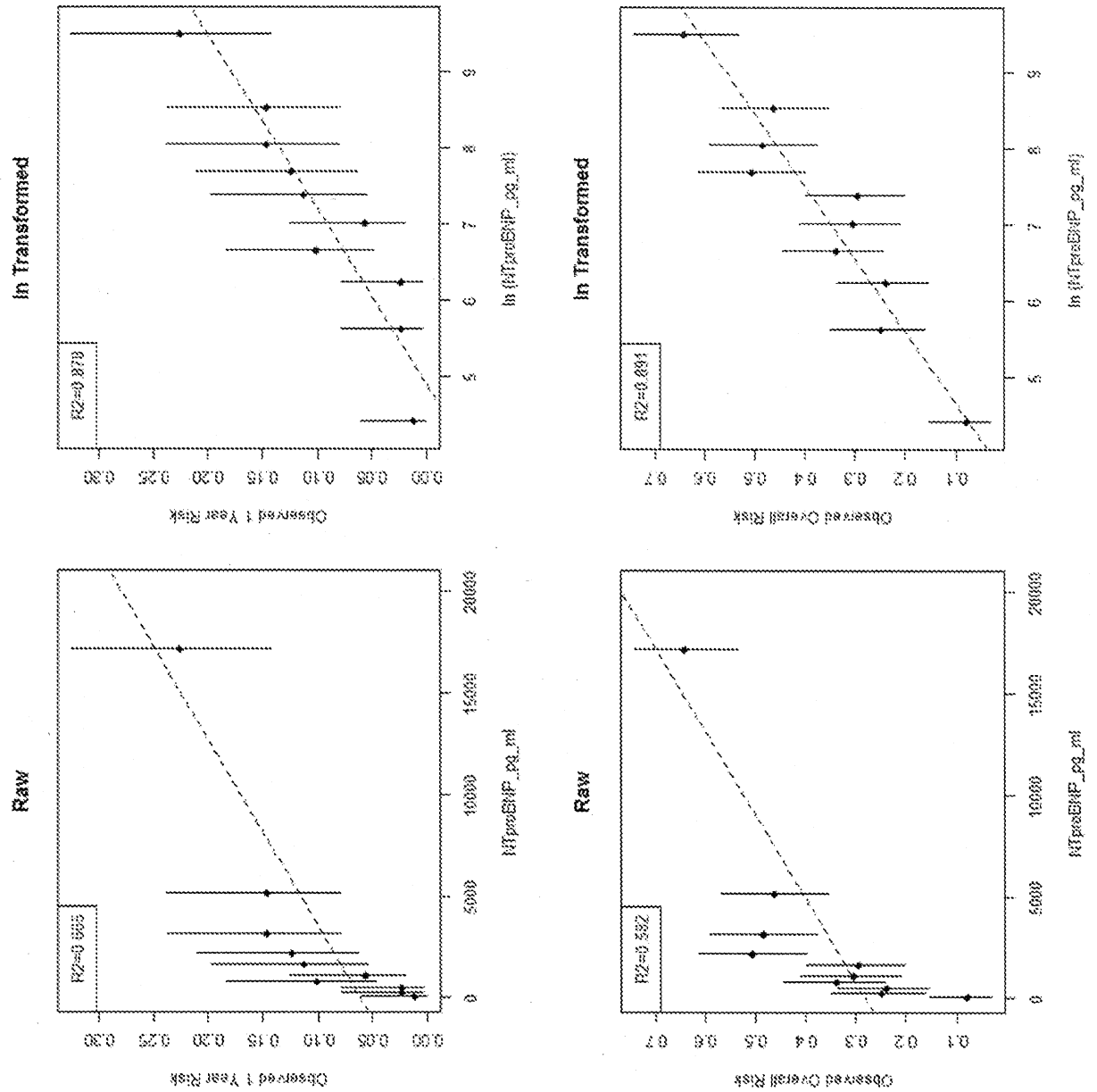


Fig. 4 Cut-Point Evaluation  
NT-proBNP

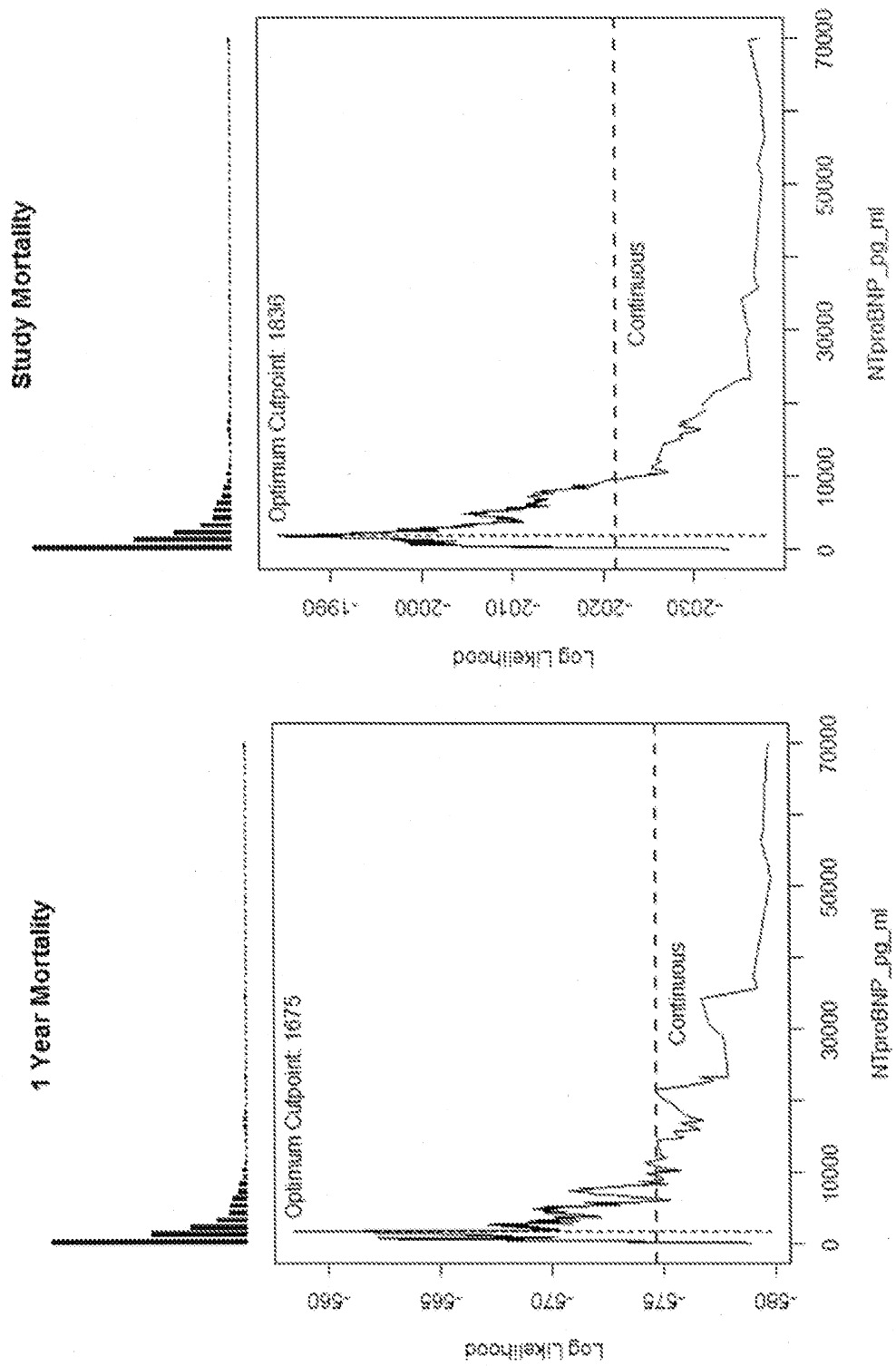


Fig. 5 Linearity Check: Troponin

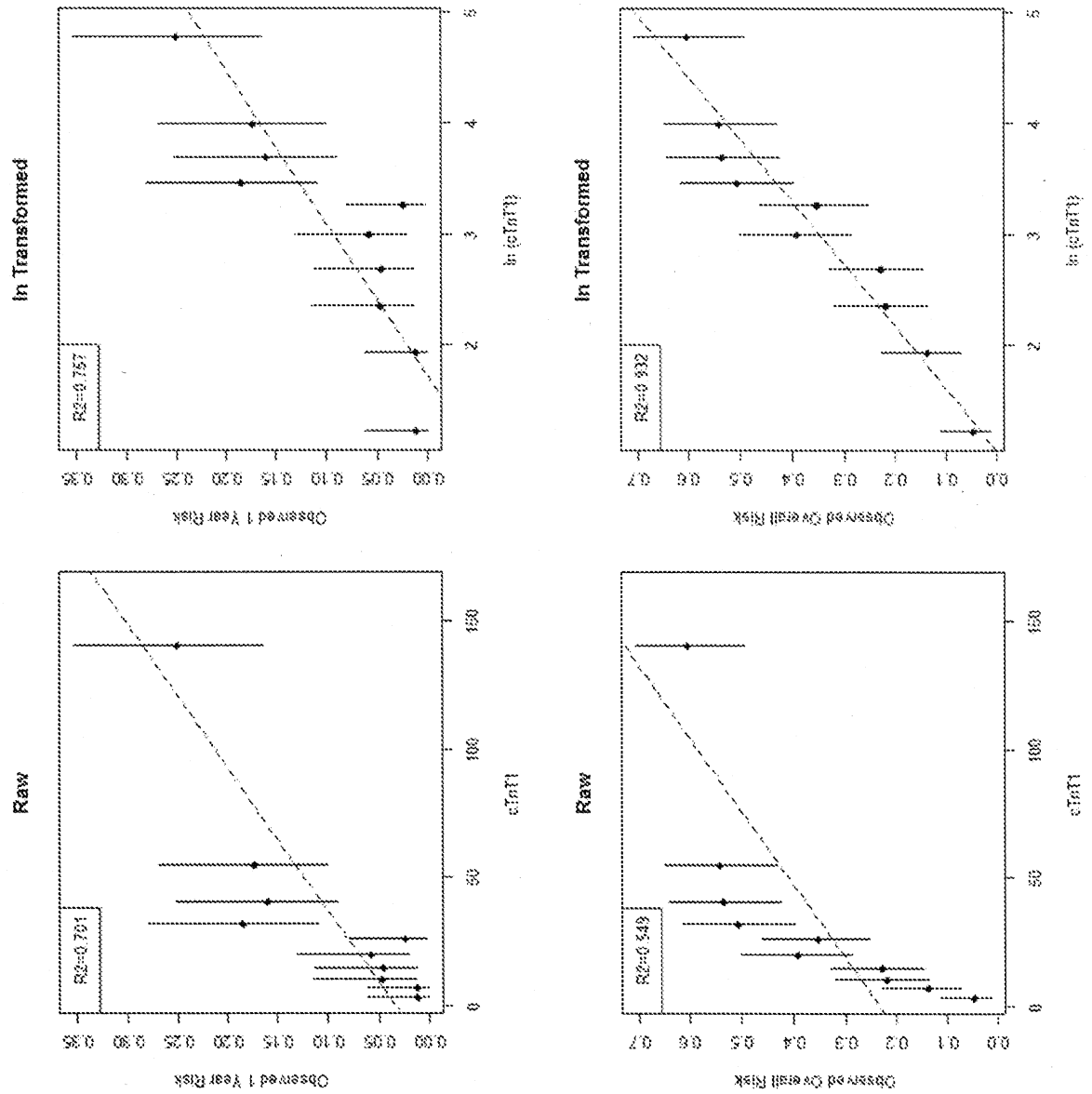


Fig. 6 Cut-Point Evaluation Troponin

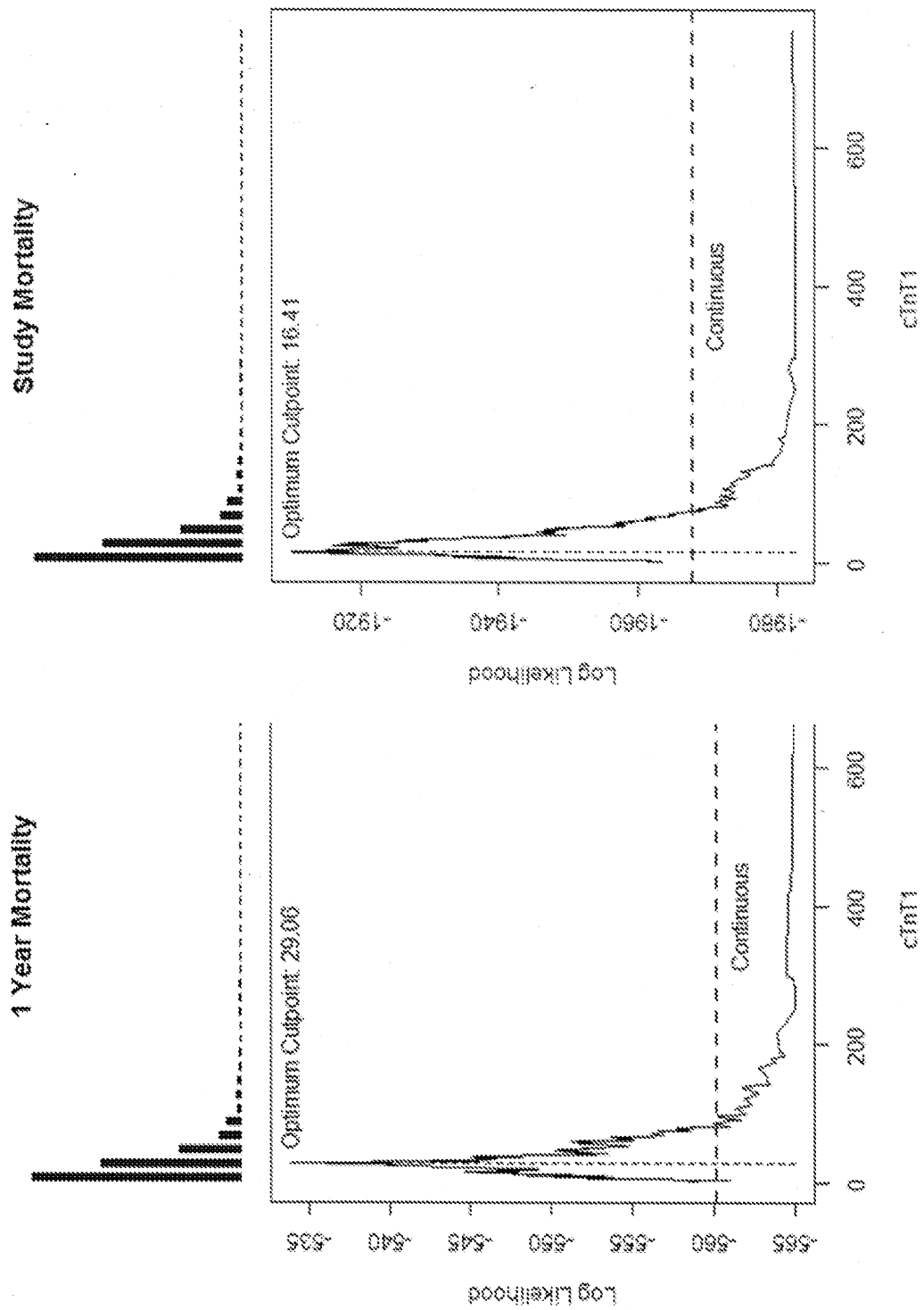


Fig. 7 Linearity Check: Creatinine

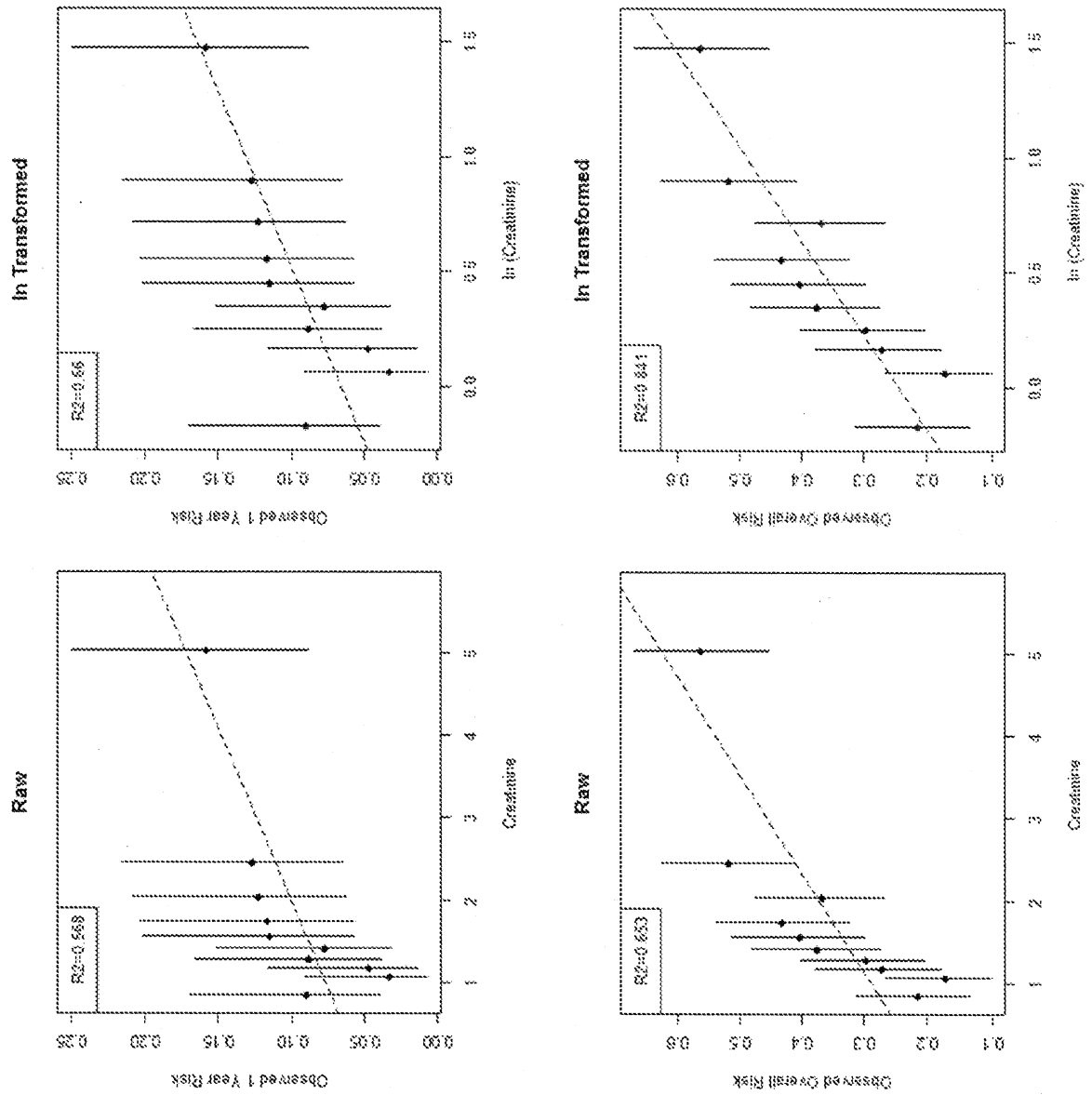


Fig. 8 Cut-Point Evaluation Creatinine

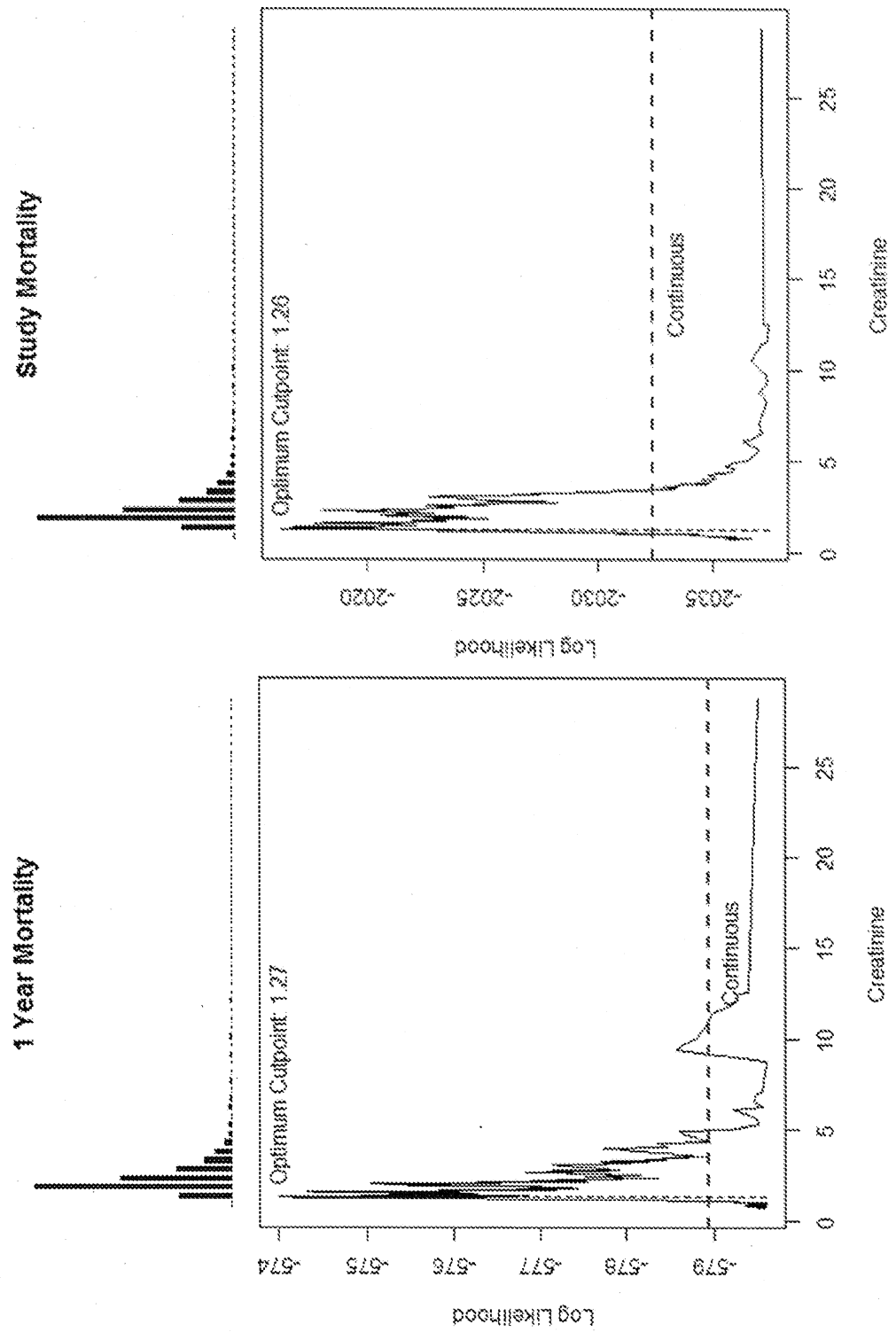


Fig. 9 Linearity Check: eGFR

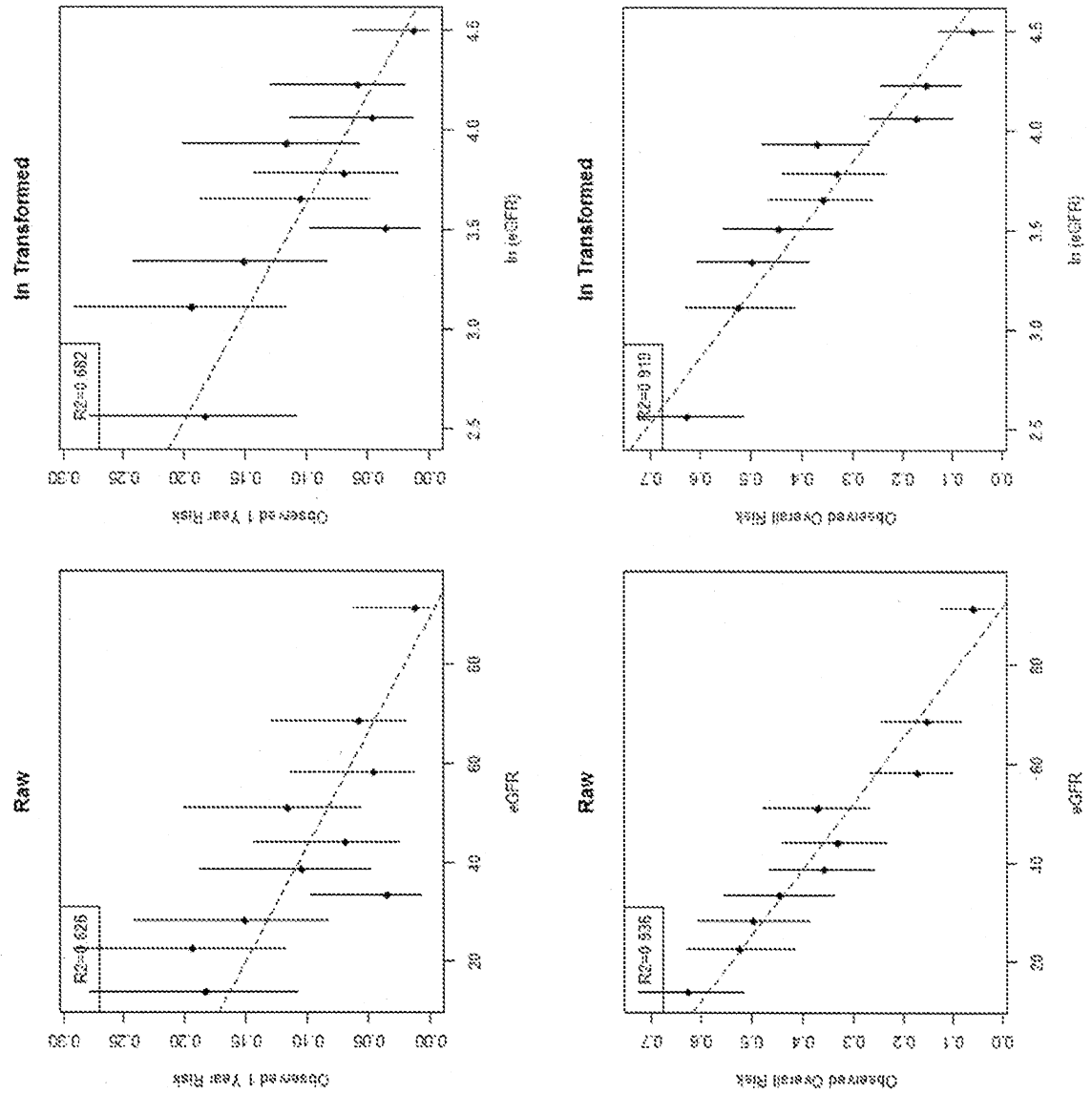


Fig. 10 Cut-Point Evaluation eGFR

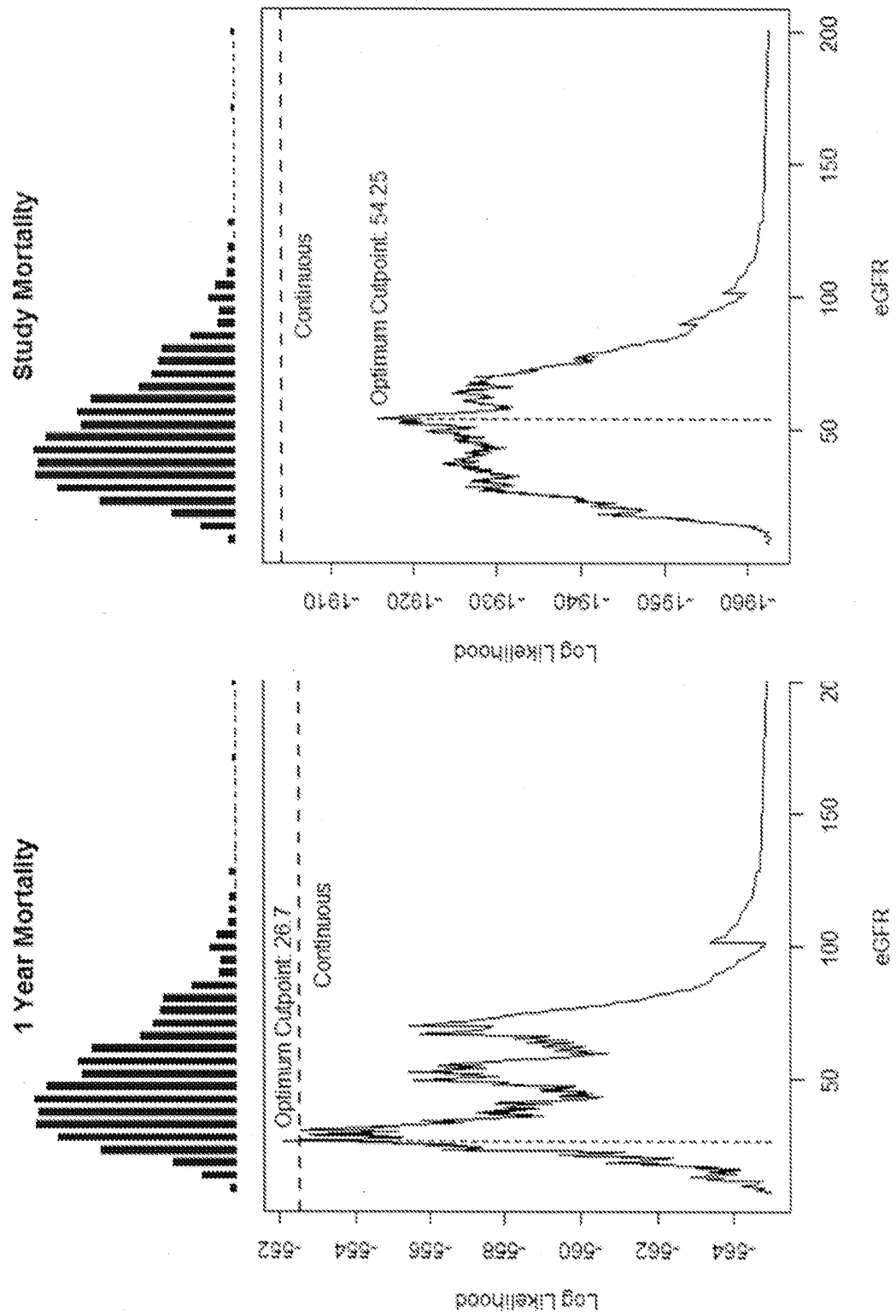


Fig. 11 Linearity Check: SBP

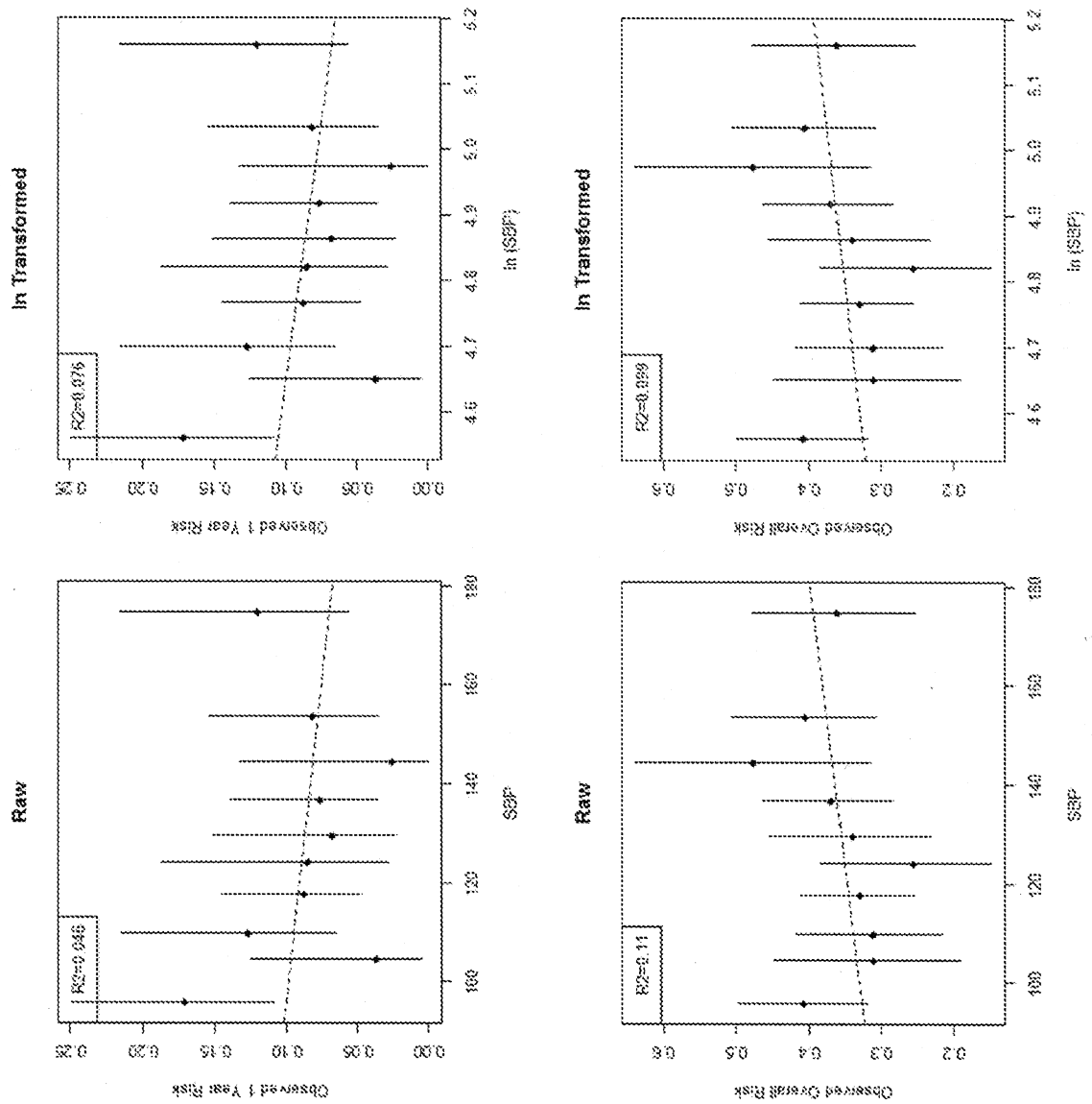


Fig. 12 Cut-Point Evaluation SBP

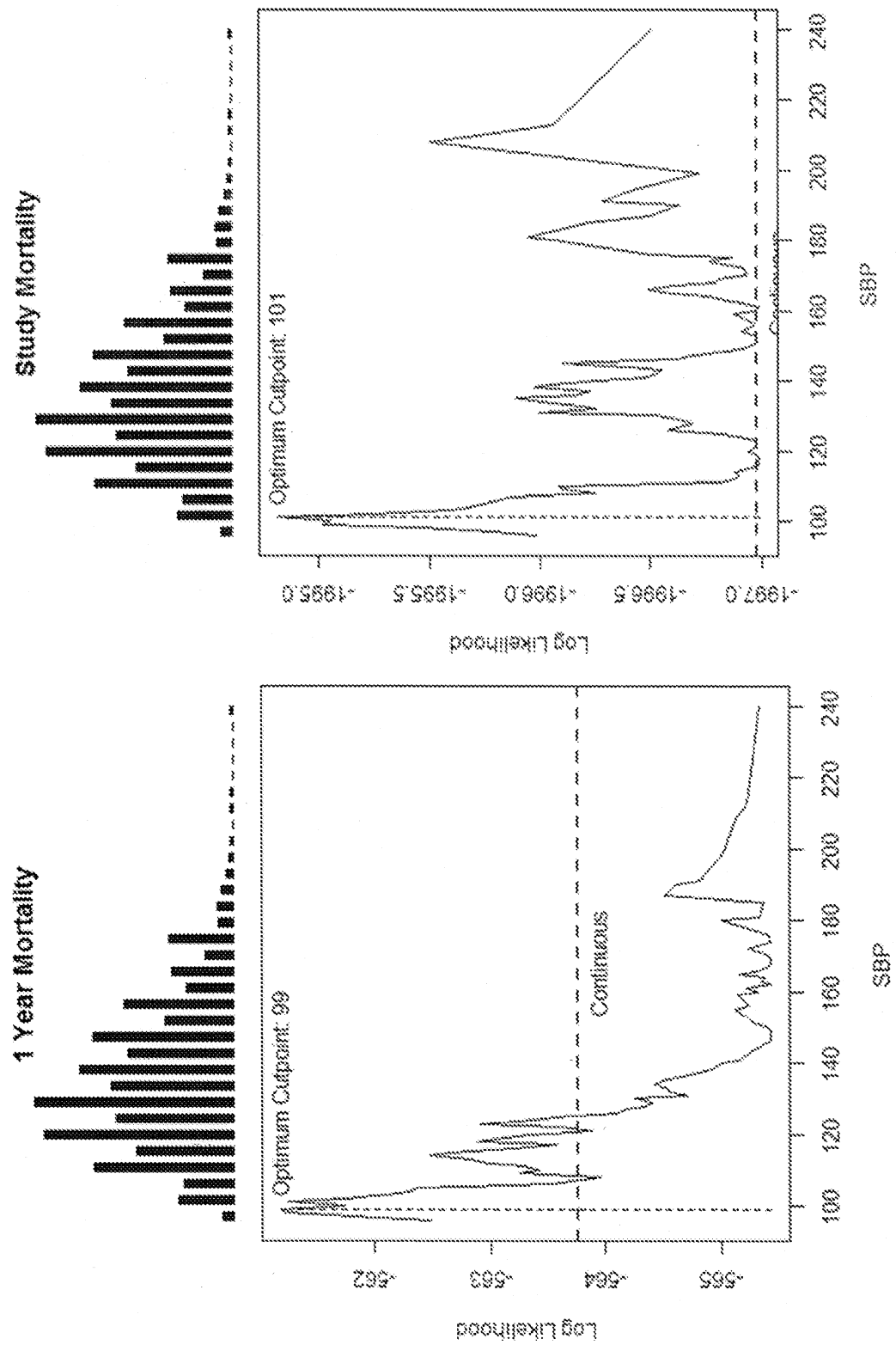


Fig. 13 Linearity Check: DBP

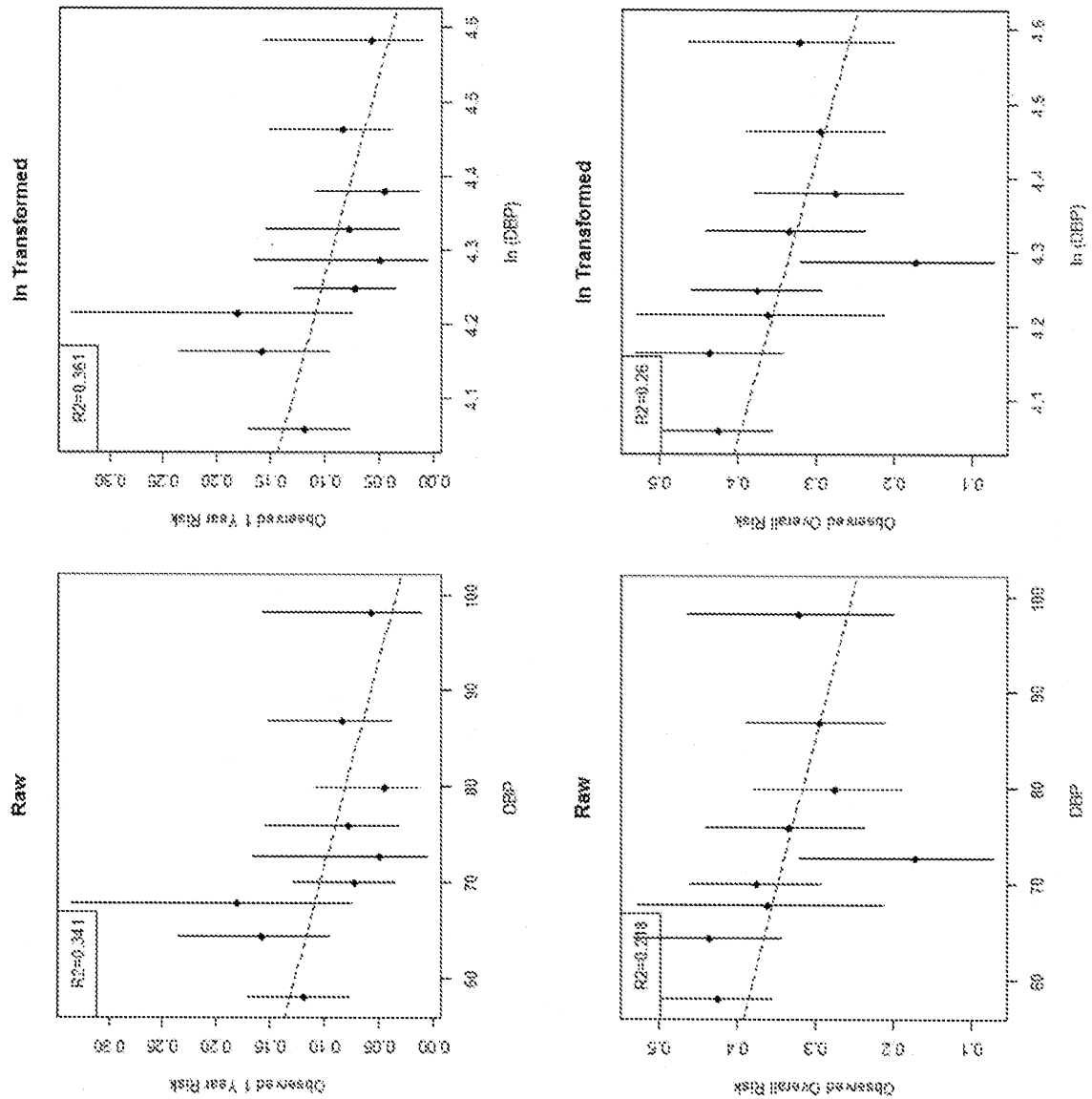


Fig. 14 Cut-Point Evaluation DBP

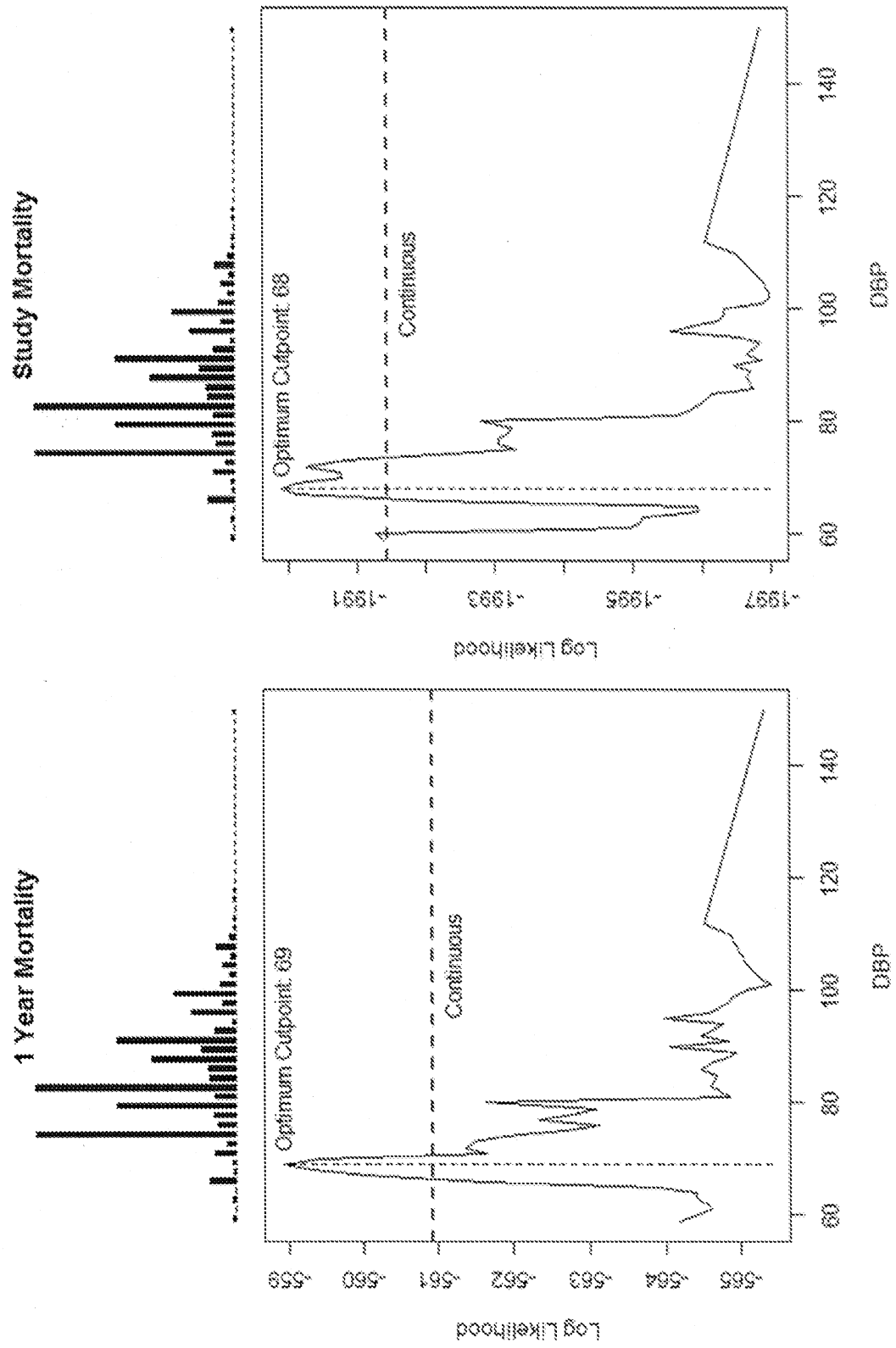


Fig. 15 Linearity Check: Hgb

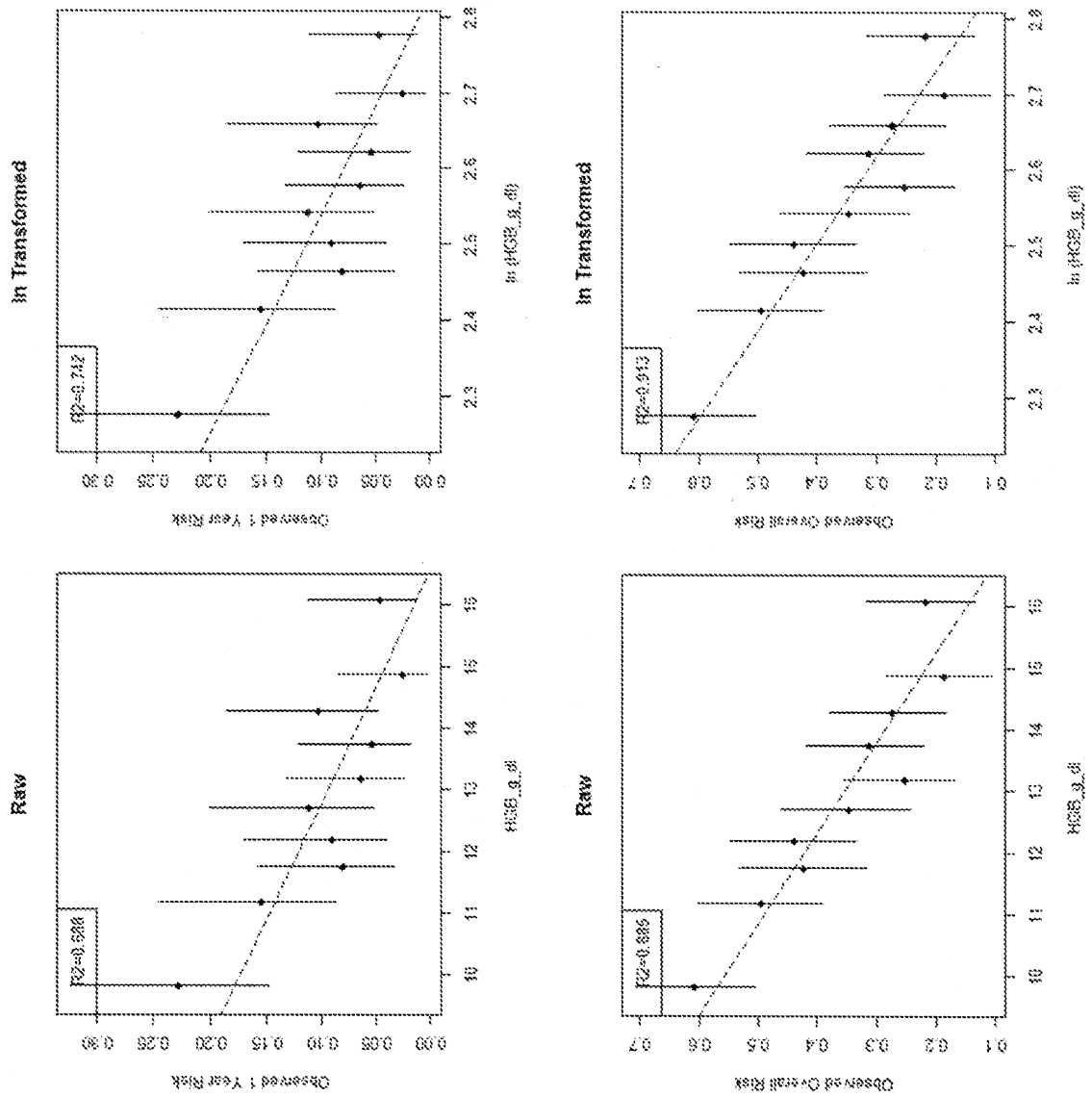


Fig. 16 Cut-Point Evaluation Hgb

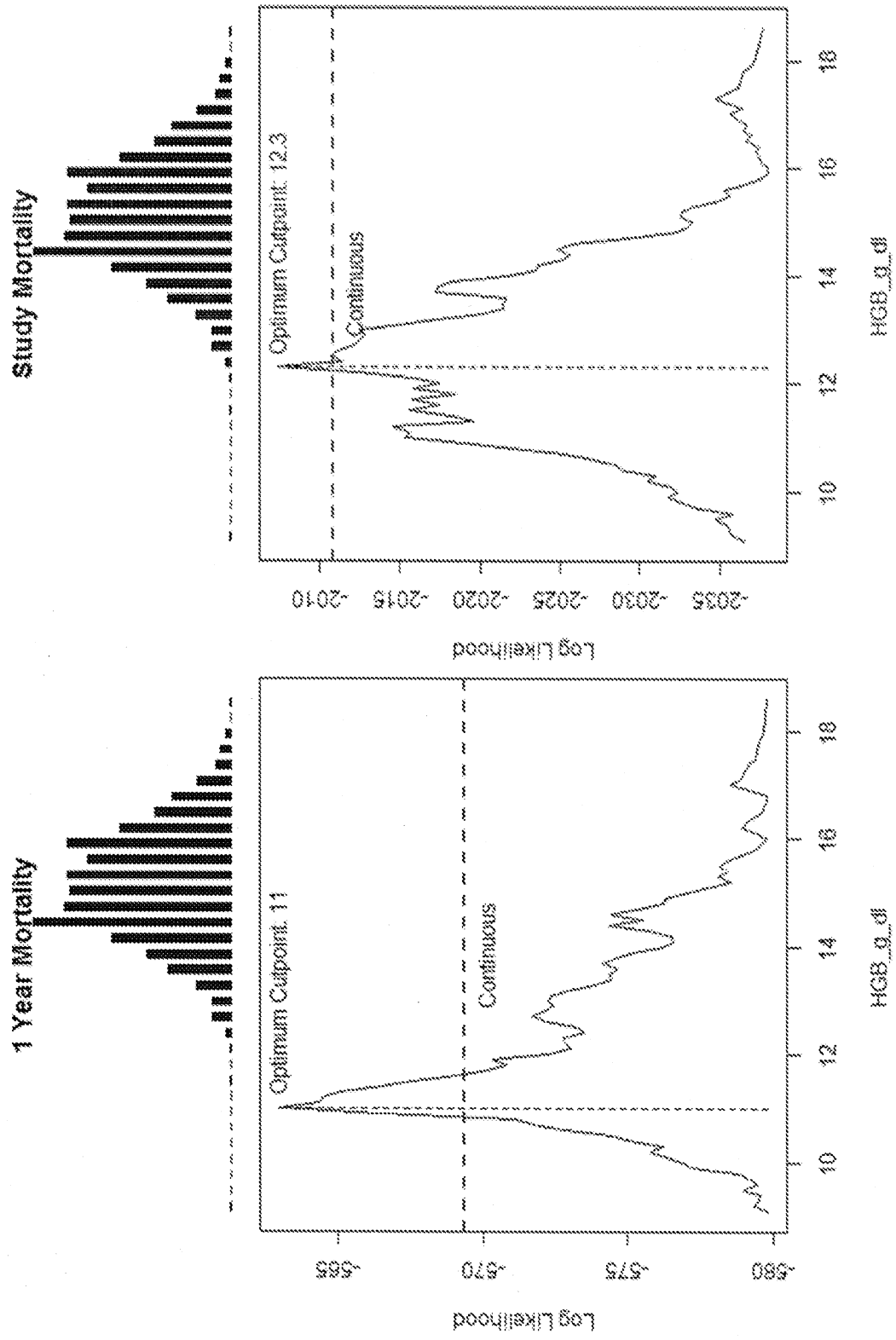


Fig. 17 Linearity Check: Age

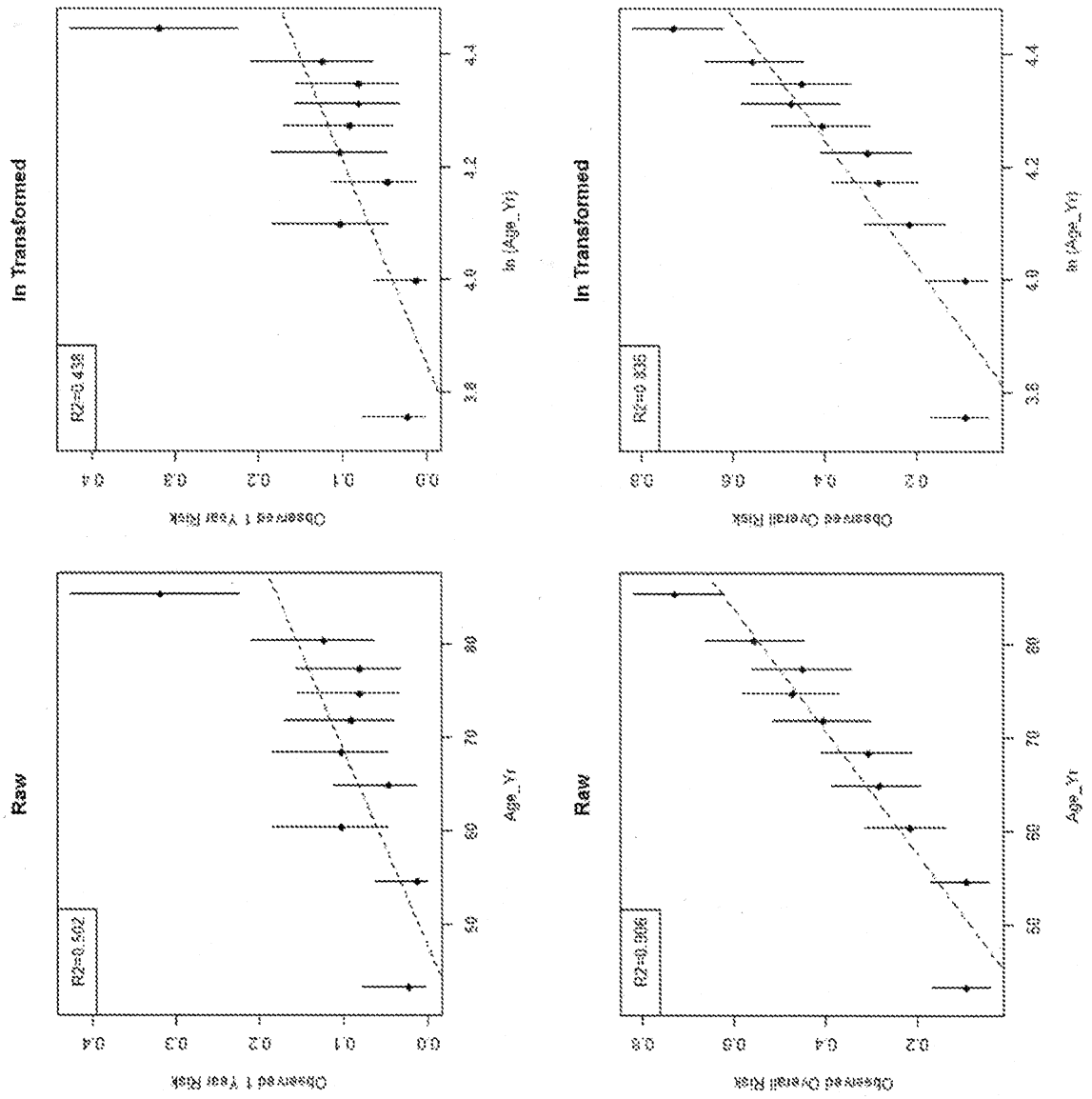


Fig. 18 Cut-Point Evaluation Age

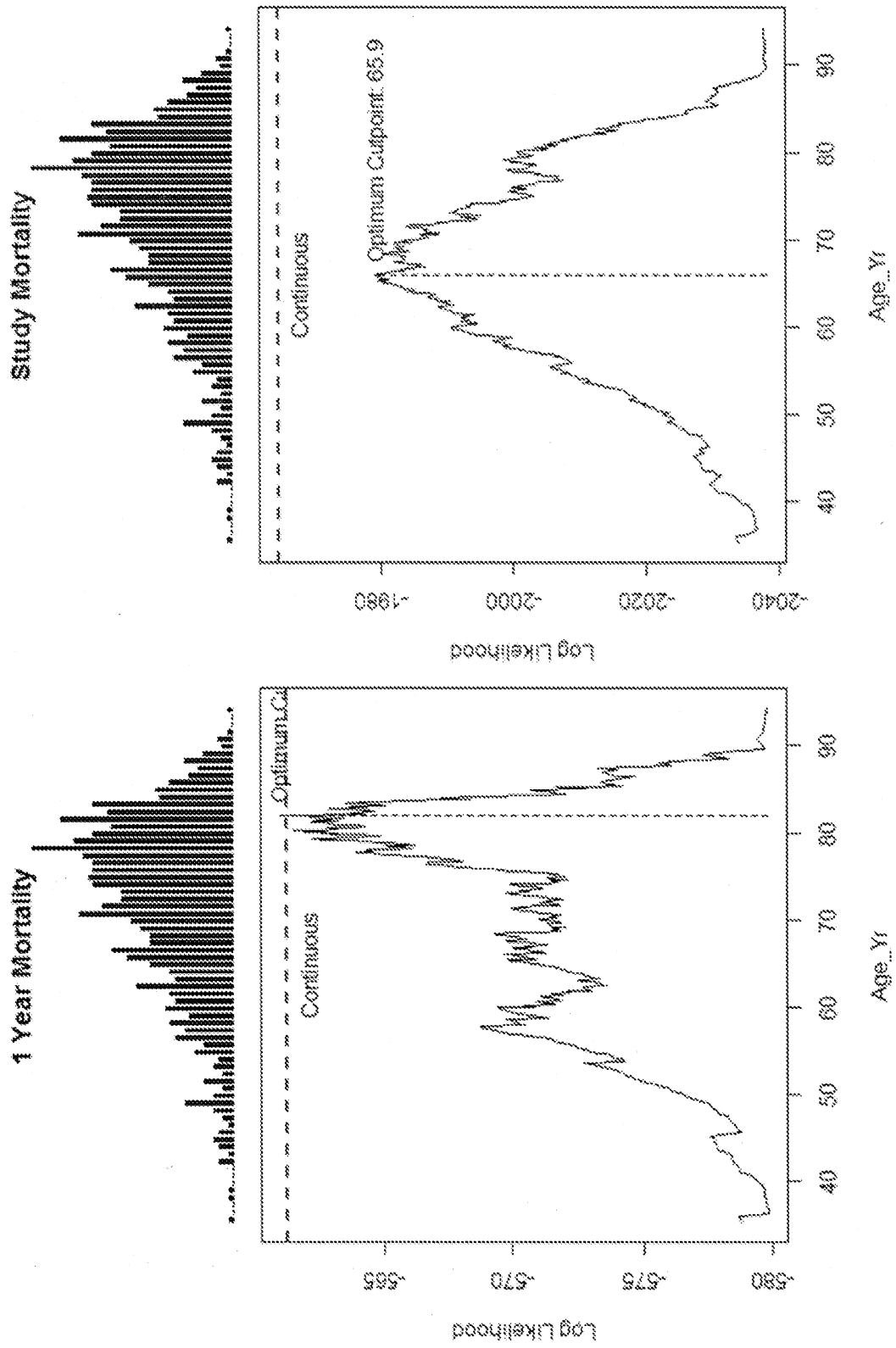


Fig. 19 Linearity Check: ST2

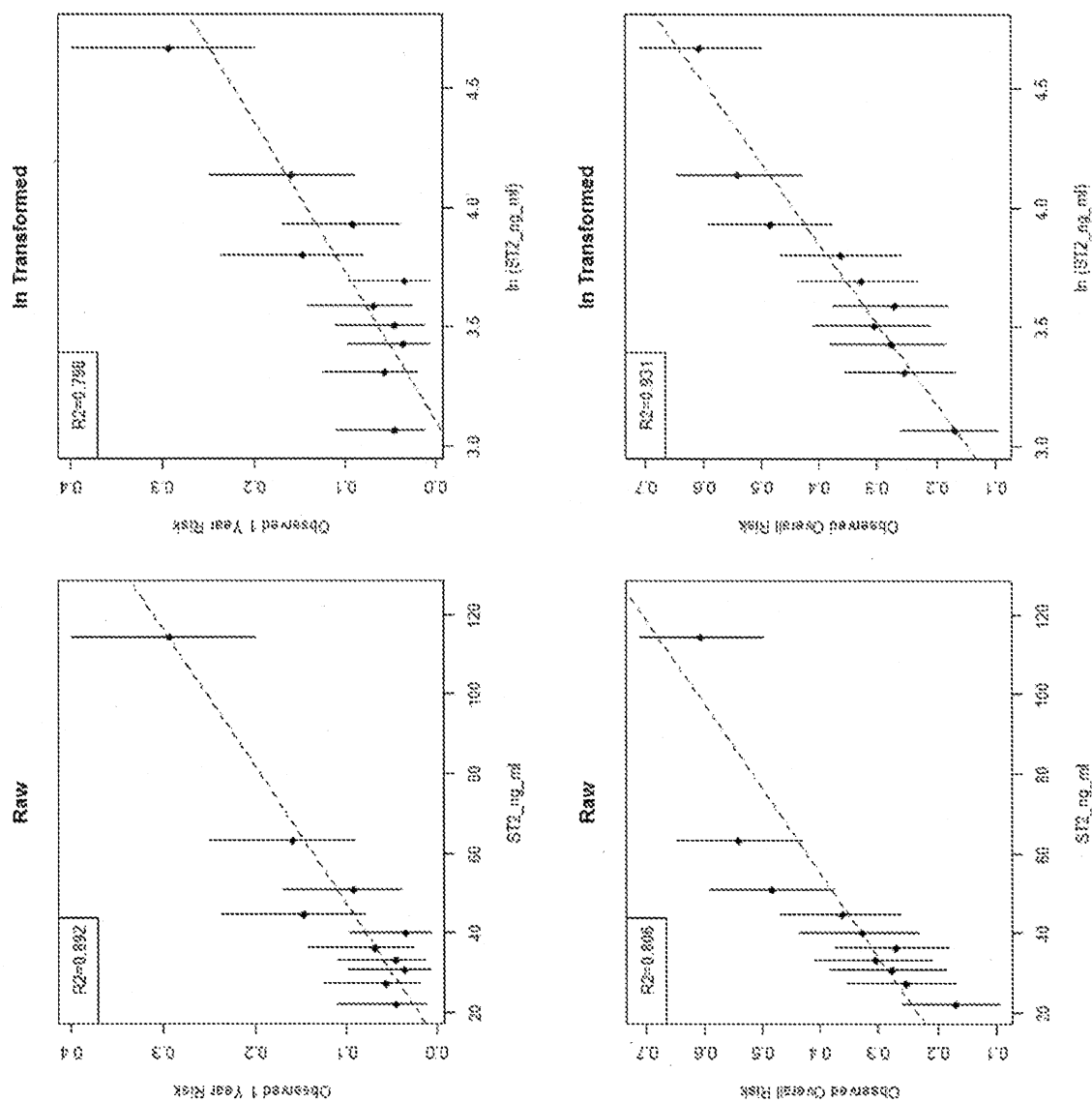


Fig. 20 Cut-Point Evaluation ST2

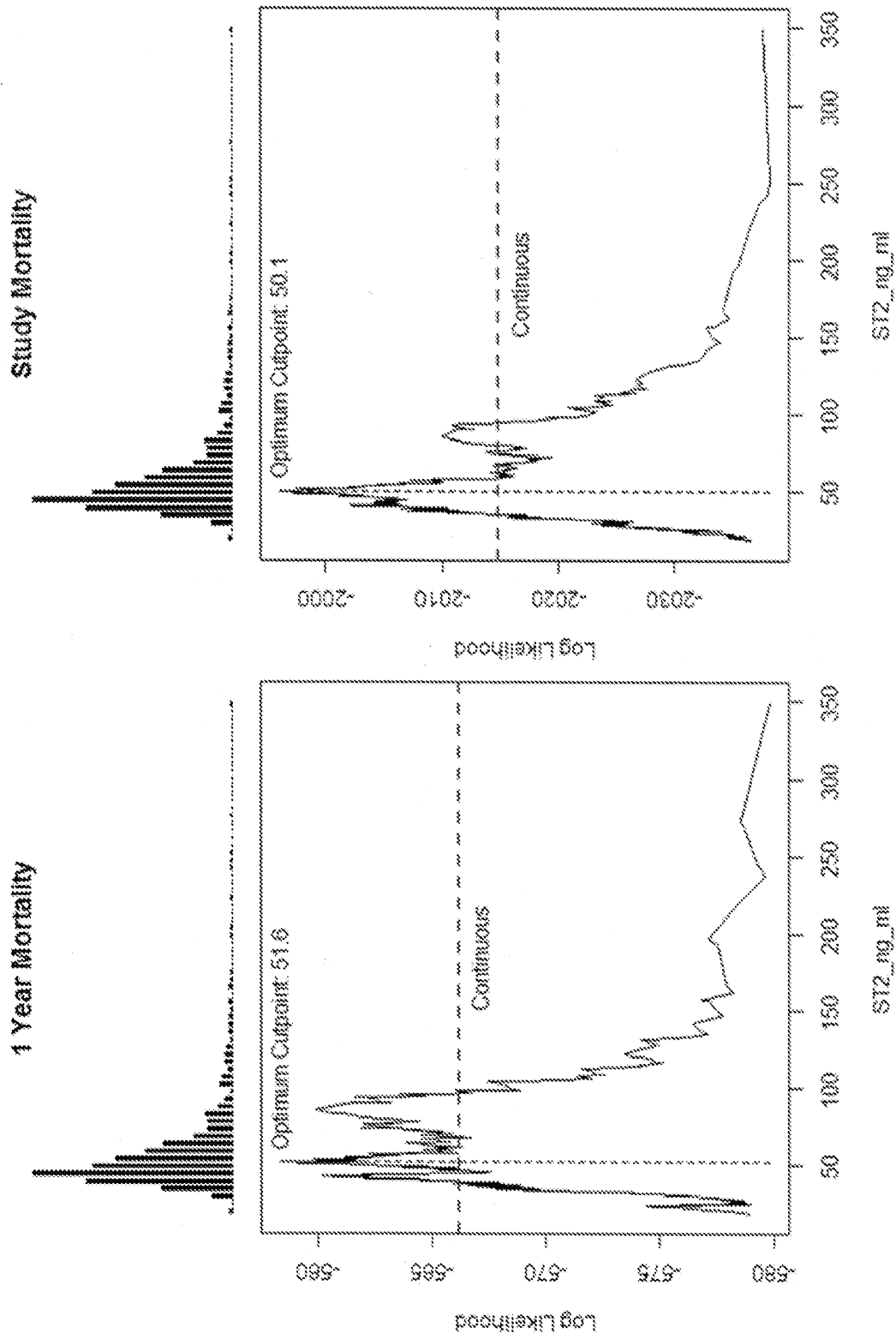


Fig. 21 Linearity Check: LVEF

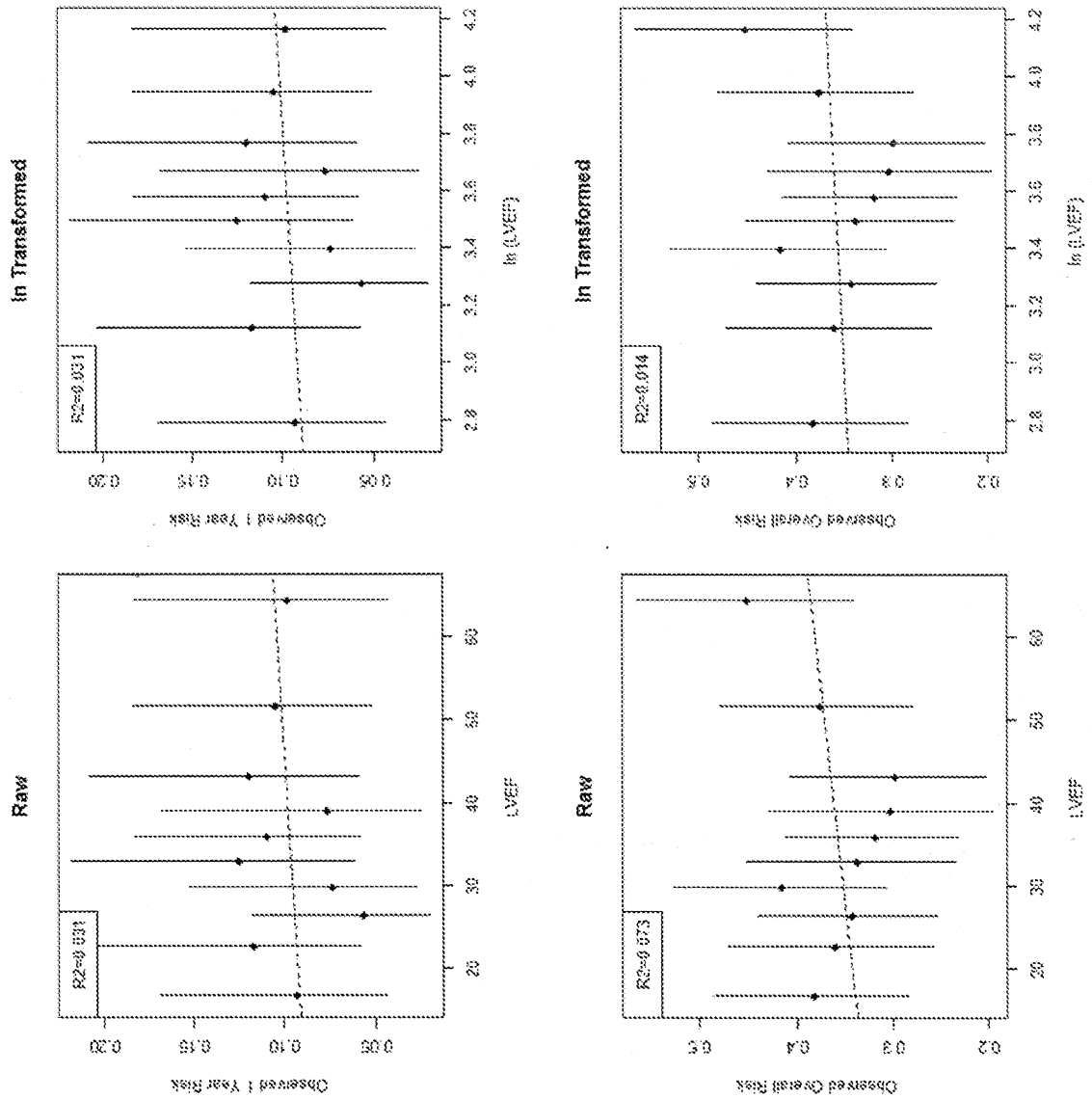


Fig. 22 Cut-Point Evaluation LVEF

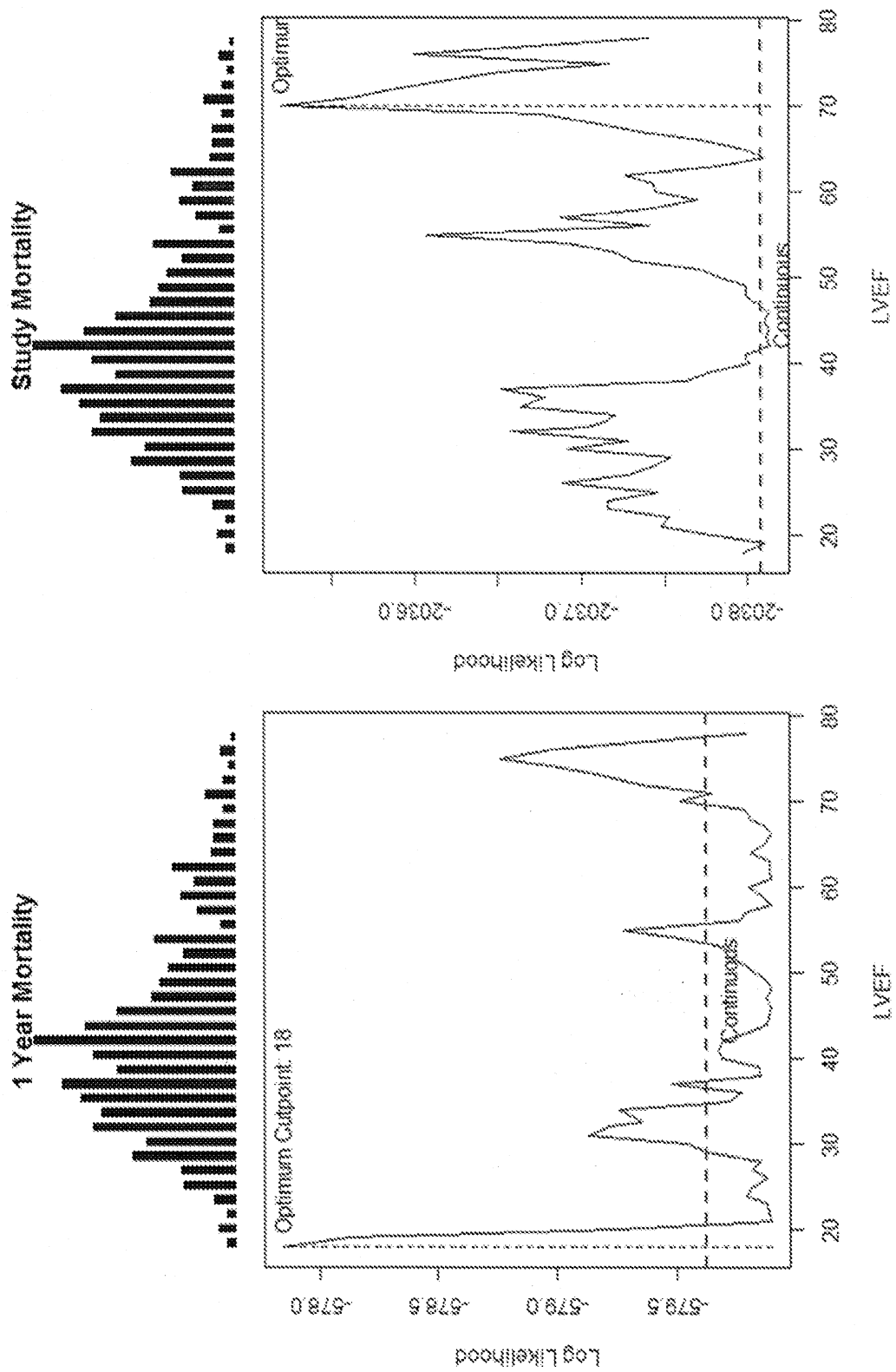


Fig. 23 Linearity Check: BMI

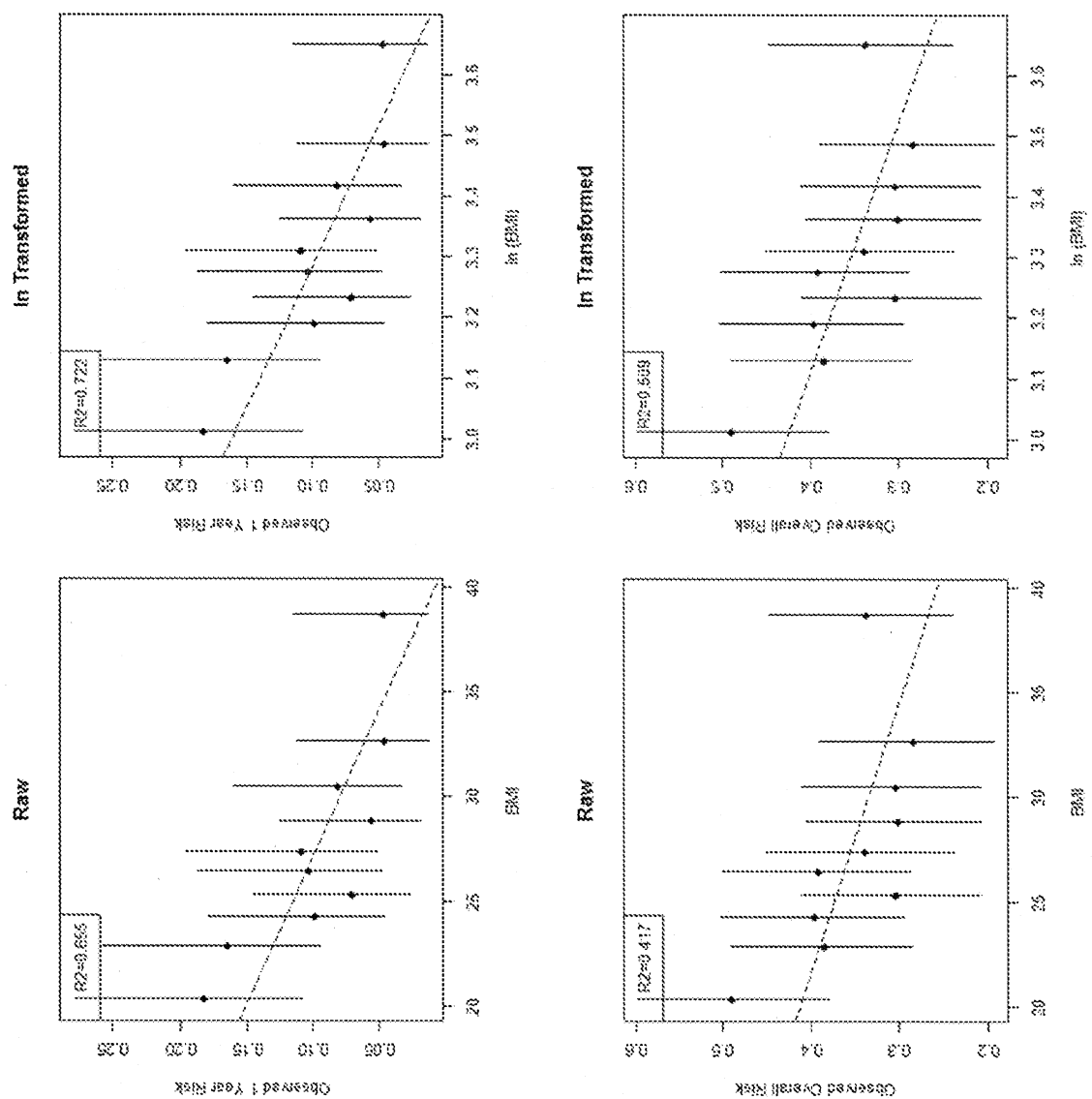


Fig. 24 Cut-Point Evaluation BMI

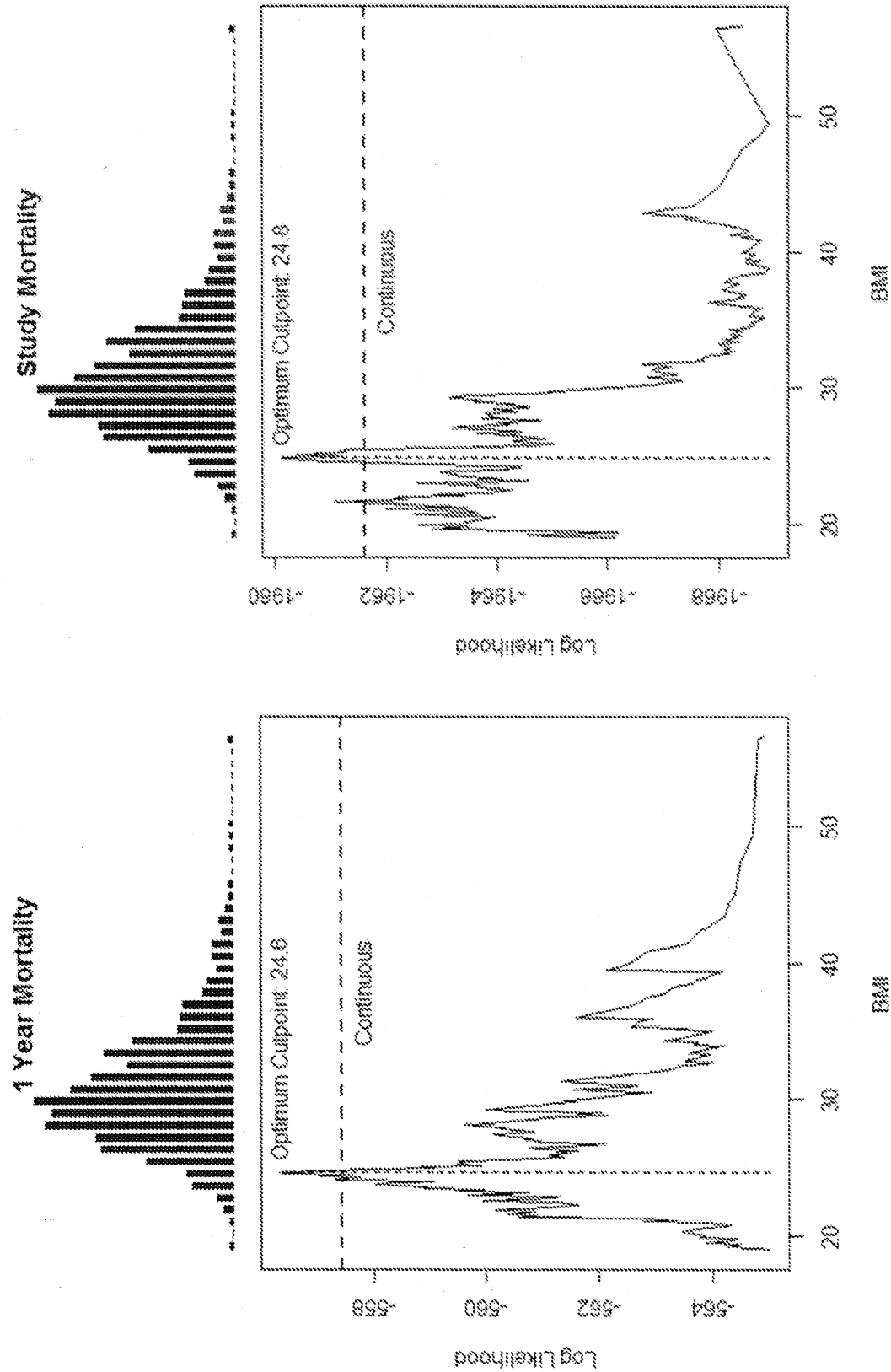


Fig. 25 Summary of Results

| Variables      | 1-Yr Cut | Study-Cut | Selected Cut | Transformed | Comments                                  |
|----------------|----------|-----------|--------------|-------------|-------------------------------------------|
| NTproBNP_pg_ml | 1675     | 1836      | 1700         | Yes         |                                           |
| cTnT1          | 29.06    | 16.41     | 16           | Yes         | Consistent with cutpoint identified       |
| Creatinine     | 1.27     | 1.26      | None         | Yes         | Not enough observations ion the low group |
| eGFR           | 26.7     | 54.25     | 50           | Yes         | Moderate decrease in GFR                  |
| SBP            | 99       | 101       | 120          | No          | Selected for historical comparison        |
| DBP            | 69       | 68        | None         | No          | Not enough observations ion the low group |
| HGB_g_dl       | 11       | 12.3      | None         | Yes         | Not enough observations ion the low group |
| Age_Yr         | 82       | 65.9      | None         | No          | Not nearly as good as continuous          |
| ST2_ng_ml      | 51.6     | 50.1      | 35 / 50      | Yes         | Try two different Cuts                    |
| LVEF           | 18       | 70        | None         | No          | Not enough observations ion the low group |
| BMI            | 24.6     | 24.8      | 25           | No          | Overweight cutoff                         |

Fig. 26 Summary of Variables

- Continuous
  - Ln NT-proBNP
  - LN Troponin
  - LN Creatinine
  - LN eGFR
  - SBP
  - DBP
  - LN Hgb
  - Age
  - LN ST2
  - LVEF
  - BMI
- Discrete
  - NT-proBNP $\geq$ 1700
  - Troponin $\geq$ 16
  - eGFR $<$ 50
  - SBP $<$ 120
  - ST2 $\geq$ 35
  - ST2 $\geq$ 50
  - ST2 3 Groups
  - BMI $\geq$ 25
  - NYHA $\geq$ 3
  - Sex
  - CAD
  - Diabetes
  - Hypertension

Fig. 27 Top 10 Models  
1 Year Outcomes (Size =1-5)

| Standardized Hazard Ratios |       |          |         |             |           |      |      |         |         | Model Fit |       |          | Discrimination |        |        |       |       |       |       |
|----------------------------|-------|----------|---------|-------------|-----------|------|------|---------|---------|-----------|-------|----------|----------------|--------|--------|-------|-------|-------|-------|
| ST2                        |       | Troponin | NYHAgt3 |             | SBPtt120  | CAD  | BMI  | BMIgt25 | InNTpro | InCreat   | InHGB | Diabetes | logLik         | AIC    | BIC    | AUC   | bsAUC | LCI   | UCI   |
| Age_Yr                     | INST2 | ST2gt50  | ST2.3g  | InTroponin1 | Troponin6 |      |      |         |         |           |       |          |                |        |        |       |       |       |       |
| 13488 5                    | 1.66  | 1.48     |         | 1.53        | 1.29      | 0.85 |      |         |         |           |       |          | -532.0         | 1074.1 | 1098.0 | 0.802 | 0.795 | 0.734 | 0.855 |
| 16905 5                    | 1.74  | 1.45     |         | 1.45        | 1.29      | 1.18 |      |         |         |           |       |          | -532.0         | 1074.1 | 1098.0 | 0.804 | 0.794 | 0.738 | 0.850 |
| 11944 5                    | 1.76  | 1.50     |         | 1.51        |           |      |      |         |         |           | 1.18  |          | -534.0         | 1077.9 | 1101.9 | 0.801 | 0.792 | 0.731 | 0.854 |
| 16189 5                    | 1.69  | 1.47     |         | 1.50        | 1.30      |      | 0.81 |         | 0.99    |           |       |          | -533.2         | 1076.4 | 1100.3 | 0.800 | 0.792 | 0.728 | 0.856 |
| 16825 5                    | 1.61  | 1.42     |         | 1.46        | 1.36      |      |      | 1.16    |         |           |       |          | -533.8         | 1077.7 | 1101.6 | 0.795 | 0.792 | 0.725 | 0.859 |
| 13506 5                    | 1.64  | 1.54     |         | 1.64        | 1.32      | 0.87 |      |         |         |           |       |          | -533.3         | 1076.6 | 1100.6 | 0.799 | 0.792 | 0.713 | 0.871 |
| 3524 4                     | 1.65  |          | 1.57    | 1.57        | 1.34      |      |      |         |         |           |       |          | -534.0         | 1076.0 | 1095.2 | 0.796 | 0.790 | 0.734 | 0.846 |
| 16987 5                    | 1.68  | 1.43     |         | 1.53        | 1.35      | 1.19 |      |         |         |           |       |          | -533.1         | 1076.2 | 1100.1 | 0.798 | 0.789 | 0.732 | 0.847 |
| 11372 5                    | 1.62  | 1.45     |         | 1.43        | 1.32      |      | 0.78 |         |         |           |       |          | -531.3         | 1072.6 | 1096.5 | 0.804 | 0.789 | 0.715 | 0.863 |
| 16650 5                    | 1.84  | 1.48     |         | 1.46        | 1.22      |      |      | 0.78    |         |           |       |          | -532.1         | 1074.2 | 1098.2 | 0.797 | 0.789 | 0.723 | 0.855 |

Markers Not Selected:

Ln (eGFR)

SBP

DBP

LVEF

NT-proBNP>=1700

GFR<50

ST2 >= 35

Sex

Hypertension

Fig. 28 Top 10 3 Parameter Models  
1 Year Outcome

| Model No |   | Standardized Hazard Ratios |         |        |          |               | Model Fit |             |      | Discrimination |        |        |        |       |       |       |       |
|----------|---|----------------------------|---------|--------|----------|---------------|-----------|-------------|------|----------------|--------|--------|--------|-------|-------|-------|-------|
|          |   | ST2                        | ST2ge50 | Age_Yr | Troponin | NTROPININge16 | NYHAgte3  | NTBNPge1700 | BMI  | BMIge25        | logLik | AIC    | BIC    | AUC   | bsAUC | LCI   | UCI   |
| 476      | 3 | 1.62                       |         | 1.81   |          |               |           | 1.47        |      |                | -538.6 | 1083.2 | 1097.6 | 0.781 | 0.780 | 0.716 | 0.844 |
| 477      | 3 | 1.62                       |         | 1.84   |          |               | 1.38      |             |      |                | -538.6 | 1083.1 | 1097.5 | 0.789 | 0.779 | 0.725 | 0.832 |
| 481      | 3 | 1.60                       |         | 1.78   |          | 1.70          |           |             |      |                | -538.1 | 1082.3 | 1096.6 | 0.786 | 0.778 | 0.706 | 0.849 |
| 474      | 3 | 1.53                       |         | 1.80   | 1.57     |               |           |             |      |                | -536.6 | 1079.2 | 1093.6 | 0.789 | 0.777 | 0.710 | 0.844 |
| 320      | 3 | 1.69                       |         | 1.91   |          |               |           |             | 0.80 |                | -541.1 | 1088.3 | 1102.6 | 0.782 | 0.776 | 0.714 | 0.838 |
| 1933     | 3 | 1.52                       |         |        | 1.51     |               |           | 1.39        |      |                | -542.6 | 1091.2 | 1105.6 | 0.773 | 0.775 | 0.709 | 0.841 |
| 1934     | 3 | 1.48                       |         |        | 1.59     |               | 1.39      |             |      |                | -540.4 | 1086.8 | 1101.2 | 0.783 | 0.774 | 0.705 | 0.844 |
| 299      | 3 | 1.68                       |         | 1.88   |          |               |           |             | 0.74 |                | -540.9 | 1087.9 | 1102.3 | 0.778 | 0.773 | 0.700 | 0.847 |
| 1978     | 3 |                            | 1.49    |        | 1.67     |               | 1.45      |             |      |                | -540.8 | 1087.5 | 1101.9 | 0.779 | 0.773 | 0.708 | 0.838 |
| 490      | 3 |                            | 1.46    | 1.76   | 1.69     |               |           |             |      |                | -539.2 | 1084.4 | 1098.8 | 0.782 | 0.771 | 0.693 | 0.850 |

Markers Not Selected:

Ln (NT-proBNP)

Ln Creatinine

Ln (eGFR)

SBP

DBP

Ln (Hgb)

LVEF

GFR<50

SBP<120

ST2 >= 35

ST2 3 Groups

Fig. 29 Selected Models Based on AIC

| 1 Year Outcome                                 |      |                                                |         |
|------------------------------------------------|------|------------------------------------------------|---------|
| Fitted AUC:0.821<br>bsAUC: 0.751 [0.677-0.824] |      | Fitted AUC:0.818<br>bsAUC: 0.751 [0.677-0.824] |         |
| Backward Selection                             |      | Stepwise Selection                             |         |
|                                                | HR   | 95% CI                                         | P       |
| ln (Troponin)                                  | 1.34 | 1.01-1.78                                      | 0.0423  |
| ln (Creatinine)                                | 0.08 | 0.02-0.26                                      | <0.0001 |
| ln (eGFR)                                      | 0.09 | 0.03-0.28                                      | <0.0001 |
| ln (Hgb)                                       | 0.28 | 0.07-1.03                                      | 0.056   |
| ln (ST2)                                       | 2.05 | 1.37-3.08                                      | 0.0005  |
| LVEF                                           | 1.02 | 1-1.04                                         | 0.028   |
| NTproBNP>=1700                                 | 1.53 | 0.87-2.66                                      | 0.1377  |
| SBP<120                                        | 1.55 | 0.98-2.44                                      | 0.06    |
| NYHA>=3                                        | 1.67 | 1.06-2.64                                      | 0.028   |
| Sex                                            | 3.76 | 1.95-7.26                                      | <0.0001 |
| Diabetes                                       | 1.44 | 0.92-2.25                                      | 0.11    |
| Fitted AUC:0.818<br>bsAUC: 0.751 [0.677-0.825] |      |                                                |         |
| Forward Selection                              |      |                                                |         |
|                                                | HR   | 95% CI                                         | P       |
| ln (Troponin)                                  | 1.43 | 1.11-1.84                                      | 0.0053  |
| ln (ST2)                                       | 2.26 | 1.51-3.38                                      | <0.0001 |
| Age                                            | 1.05 | 1.02-1.07                                      | 0.0002  |
| NYHA>=3                                        | 1.69 | 1.07-2.65                                      | 0.0239  |
| ln (HGB)                                       | 0.27 | 0.07-1.02                                      | 0.0535  |
| BMI>=25                                        | 0.63 | 0.41-0.98                                      | 0.0408  |
| SBP<120                                        | 1.46 | 0.93-2.28                                      | 0.0977  |
| Diabetes                                       | 1.6  | 1.01-2.53                                      | 0.047   |
| CAD                                            | 0.68 | 0.44-1.06                                      | 0.0855  |
| Hypertension                                   | 0.67 | 0.41-1.07                                      | 0.0942  |

Fig. 30 Selected Models Based on BIC  
1 Year Outcome

|                                                |      |           |         |                                                |      |           |         |
|------------------------------------------------|------|-----------|---------|------------------------------------------------|------|-----------|---------|
| Fitted AUC:0.818<br>bsAUC: 0.796 [0.756-0.836] |      |           |         | Fitted AUC:0.817<br>bsAUC: 0.797 [0.757-0.837] |      |           |         |
| Backward Selection                             |      |           |         | Stepwise Selection                             |      |           |         |
|                                                | HR   | 95% CI    | P       |                                                | HR   | 95% CI    | P       |
| ln (Troponin)                                  | 1.45 | 1.12-1.88 | 0.0043  | ln (Troponin)                                  | 1.49 | 1.18-1.89 | 0.0008  |
| ln (Creatinine)                                | 0.09 | 0.03-0.29 | <0.0001 | ln (ST2)                                       | 2.34 | 1.59-3.47 | <0.0001 |
| ln (eGFR)                                      | 0.09 | 0.03-0.27 | <0.0001 | Age                                            | 1.04 | 1.02-1.07 | 0.0004  |
| ln (ST2)                                       | 2.23 | 1.48-3.35 | 0.0001  | NYHA>=3                                        | 1.82 | 1.16-2.85 | 0.0091  |
| NYHA>=3                                        | 1.86 | 1.18-2.92 | 0.0074  |                                                |      |           |         |
| Sex                                            | 3    | 1.62-5.57 | 0.0005  |                                                |      |           |         |
| Fitted AUC:0.817<br>bsAUC: 0.798 [0.758-0.837] |      |           |         | Forward Selection                              |      |           |         |
|                                                | HR   | 95% CI    | P       |                                                | HR   | 95% CI    | P       |
| ln (Troponin)                                  | 1.49 | 1.18-1.89 | 0.0008  | ln (Troponin)                                  | 1.49 | 1.18-1.89 | 0.0008  |
| ln (ST2)                                       | 2.34 | 1.59-3.47 | <0.0001 | ln (ST2)                                       | 2.34 | 1.59-3.47 | <0.0001 |
| Age                                            | 1.04 | 1.02-1.07 | 0.0004  | Age                                            | 1.04 | 1.02-1.07 | 0.0004  |
| NYHA>=3                                        | 1.82 | 1.16-2.85 | 0.0091  | NYHA>=3                                        | 1.82 | 1.16-2.85 | 0.0091  |

Fig. 31 Top 10 Models  
Study Outcomes (Size =1-5)

| Model No | K | Age_Yr | ST2gte50 | NYHAgte3 | Troponin | InTropoin |      |      |      |      | Model Fit |      |      |      |      | Discrimination |      |      |      |      |
|----------|---|--------|----------|----------|----------|-----------|------|------|------|------|-----------|------|------|------|------|----------------|------|------|------|------|
|          |   |        |          |          |          |           |      |      |      |      |           |      |      |      |      |                |      |      |      |      |
| 16776    | 5 | 1.67   | 1.39     | 1.34     | 1.65     | 1.65      | 1.65 | 1.65 | 1.65 | 1.65 | 1.65      | 1.65 | 1.65 | 1.65 | 1.65 | 1.65           | 1.65 | 1.65 | 1.65 | 1.65 |
| 16581    | 5 | 1.60   | 1.37     | 1.35     | 1.65     | 1.65      | 1.65 | 1.65 | 1.65 | 1.65 | 1.65      | 1.65 | 1.65 | 1.65 | 1.65 | 1.65           | 1.65 | 1.65 | 1.65 | 1.65 |
| 16692    | 5 | 1.71   | 1.36     | 1.30     | 1.70     | 1.70      | 1.70 | 1.70 | 1.70 | 1.70 | 1.70      | 1.70 | 1.70 | 1.70 | 1.70 | 1.70           | 1.70 | 1.70 | 1.70 | 1.70 |
| 17095    | 5 | 1.69   | 1.38     | 1.35     | 1.70     | 1.70      | 1.70 | 1.70 | 1.70 | 1.70 | 1.70      | 1.70 | 1.70 | 1.70 | 1.70 | 1.70           | 1.70 | 1.70 | 1.70 | 1.70 |
| 13616    | 5 | 1.68   | 1.38     | 1.36     | 1.70     | 1.70      | 1.70 | 1.70 | 1.70 | 1.70 | 1.70      | 1.70 | 1.70 | 1.70 | 1.70 | 1.70           | 1.70 | 1.70 | 1.70 | 1.70 |
| 16317    | 5 | 1.68   | 1.37     | 1.36     | 1.64     | 1.64      | 1.64 | 1.64 | 1.64 | 1.64 | 1.64      | 1.64 | 1.64 | 1.64 | 1.64 | 1.64           | 1.64 | 1.64 | 1.64 | 1.64 |
| 3526     | 4 | 1.72   | 1.36     | 1.33     | 1.70     | 1.70      | 1.70 | 1.70 | 1.70 | 1.70 | 1.70      | 1.70 | 1.70 | 1.70 | 1.70 | 1.70           | 1.70 | 1.70 | 1.70 | 1.70 |
| 3610     | 4 | 1.68   | 1.38     | 1.36     | 1.70     | 1.70      | 1.70 | 1.70 | 1.70 | 1.70 | 1.70      | 1.70 | 1.70 | 1.70 | 1.70 | 1.70           | 1.70 | 1.70 | 1.70 | 1.70 |
| 16497    | 5 | 1.66   | 1.35     | 1.33     | 1.71     | 1.71      | 1.71 | 1.71 | 1.71 | 1.71 | 1.71      | 1.71 | 1.71 | 1.71 | 1.71 | 1.71           | 1.71 | 1.71 | 1.71 | 1.71 |
| 15971    | 5 | 1.70   | 1.38     | 1.36     | 1.71     | 1.71      | 1.71 | 1.71 | 1.71 | 1.71 | 1.71      | 1.71 | 1.71 | 1.71 | 1.71 | 1.71           | 1.71 | 1.71 | 1.71 | 1.71 |

Markers Not Selected: LVEF      SBP<120      Sex

Ln (NT-proBNP)      BMI      Diabetes

DBP      NT-proBNP>=1700      ST2 3 Group

Ln (ST2)      GFR<50      BMI >=25

Fig. 32 Top 10 3 Parameter Models  
Study Outcomes

|          |   | ST2    | Trponin  |        | Model Fit |              |            | Discrimination |         |        |        |       |       |       |       |
|----------|---|--------|----------|--------|-----------|--------------|------------|----------------|---------|--------|--------|-------|-------|-------|-------|
| Model No | K | Age_Yr | ST2gte50 | ST2.3g | lnST2     | TRPONINgte16 | lnTroponin | NHAgte3        | logLik  | AIC    | BIC    | AUC   | bsAUC | LCI   | UCI   |
| 514      | 3 | 1.73   |          |        |           | 1.81         |            | 1.36           | -1904.8 | 3815.6 | 3830.0 | 0.799 | 0.797 | 0.763 | 0.831 |
| 513      | 3 | 1.89   | 1.48     |        |           |              |            | 1.42           | -1913.0 | 3832.0 | 3846.4 | 0.799 | 0.795 | 0.757 | 0.832 |
| 511      | 3 | 1.90   |          | 1.53   |           |              |            | 1.39           | -1914.0 | 3833.9 | 3848.3 | 0.794 | 0.794 | 0.756 | 0.832 |
| 477      | 3 | 1.90   |          |        | 1.44      |              |            | 1.38           | -1915.8 | 3837.7 | 3852.0 | 0.798 | 0.794 | 0.754 | 0.833 |
| 488      | 3 | 1.85   | 1.39     |        |           |              | 1.69       |                | -1900.2 | 3806.3 | 3820.7 | 0.793 | 0.793 | 0.754 | 0.831 |
| 531      | 3 | 1.82   | 1.38     |        |           | 1.77         |            |                | -1903.2 | 3812.4 | 3826.7 | 0.795 | 0.792 | 0.755 | 0.829 |
| 490      | 3 | 1.84   | 1.35     |        |           |              | 1.70       |                | -1901.2 | 3808.4 | 3822.8 | 0.796 | 0.791 | 0.751 | 0.831 |
| 484      | 3 | 1.79   |          |        |           |              | 1.72       | 1.31           | -1903.2 | 3812.4 | 3826.7 | 0.797 | 0.791 | 0.754 | 0.828 |
| 529      | 3 | 1.83   | 1.43     |        |           | 1.75         |            |                | -1903.1 | 3812.2 | 3826.6 | 0.793 | 0.790 | 0.757 | 0.824 |
| 481      | 3 | 1.83   |          |        | 1.36      | 1.74         |            |                | -1904.7 | 3815.4 | 3829.8 | 0.794 | 0.790 | 0.744 | 0.836 |

Markers Not Selected:

Ln (NT-proBNP)

Ln Creatinine

Ln (eGFR)

SBP

DBP

Ln (Hgb)

LVEF

BMI

NT-proBNP >=1700

GFR<50

SBP<120

ST2 >= 35

BMI>=25

SEX

CAD

Diabetes

Hypertension

Fig. 33 Models Based on AIC  
Study Outcome

| Backward Selection                             |      |           |         | Stepwise Selection                             |      |           |         |
|------------------------------------------------|------|-----------|---------|------------------------------------------------|------|-----------|---------|
| Fitted AUC:0.808<br>bsAUC: 0.741 [0.665-0.816] |      |           |         | Fitted AUC:0.800<br>bsAUC: 0.743 [0.666-0.837] |      |           |         |
|                                                | HR   | 95% CI    | P       |                                                | HR   | 95% CI    | P       |
| ln (NT-proBNP)                                 | 1.13 | 1.01-1.27 | 0.0407  | ln (Troponin)                                  | 1.2  | 1-1.45    | 0.0534  |
| ln (Troponin)                                  | 1.19 | 0.99-1.44 | 0.0695  | Age                                            | 1.04 | 1.03-1.05 | <0.0001 |
| ln (Creatinine)                                | 1.69 | 0.91-3.15 | 0.0953  | ST2 >=50                                       | 1.87 | 1.47-2.38 | <0.0001 |
| ln (eGFR)                                      | 1.58 | 0.85-2.94 | 0.1483  | NYHA >= 3                                      | 1.84 | 1.45-2.32 | <0.0001 |
| ln (Hgb)                                       | 0.34 | 0.17-0.68 | 0.002   | Troponin >=16                                  | 1.88 | 1.25-2.8  | 0.0022  |
| Age                                            | 1.05 | 1.03-1.07 | <0.0001 | ln (Hgb)                                       | 0.34 | 0.18-0.68 | 0.0019  |
| Troponin >=16                                  | 1.88 | 1.26-2.8  | 0.0021  | ln (NT-proBNP)                                 | 1.12 | 1.01-1.26 | 0.0401  |
| ST2 >=50                                       | 1.89 | 1.49-2.4  | <0.0001 | Sex                                            | 1.2  | 0.94-1.54 | 0.1522  |
| NYHA >= 3                                      | 1.84 | 1.46-2.32 | <0.0001 |                                                |      |           |         |
| Forward Selection                              |      |           |         | Fitted AUC:0.800<br>bsAUC: 0.744 [0.667-0.821] |      |           |         |
|                                                | HR   | 95% CI    | P       |                                                | HR   | 95% CI    | P       |
| ln (Troponin)                                  | 1.2  | 1-1.45    | 0.0534  | ln (Troponin)                                  | 1.2  | 1-1.45    | 0.0534  |
| Age                                            | 1.04 | 1.03-1.05 | <0.0001 | Age                                            | 1.04 | 1.03-1.05 | <0.0001 |
| ST2 >=50                                       | 1.87 | 1.47-2.38 | <0.0001 | ST2 >=50                                       | 1.87 | 1.47-2.38 | <0.0001 |
| NYHA >= 3                                      | 1.84 | 1.45-2.32 | <0.0001 | NYHA >= 3                                      | 1.84 | 1.45-2.32 | <0.0001 |
| Troponin >=16                                  | 1.88 | 1.25-2.8  | 0.0022  | Troponin >=16                                  | 1.88 | 1.25-2.8  | 0.0022  |
| ln (Hgb)                                       | 0.34 | 0.18-0.68 | 0.0019  | ln (Hgb)                                       | 0.34 | 0.18-0.68 | 0.0019  |
| ln (NT-proBNP)                                 | 1.12 | 1.01-1.26 | 0.0401  | ln (NT-proBNP)                                 | 1.12 | 1.01-1.26 | 0.0401  |
| Sex                                            | 1.2  | 0.94-1.54 | 0.1522  | Sex                                            | 1.2  | 0.94-1.54 | 0.1522  |

# Fig. 34 Selected Models Based on BIC

## 1 Year Outcome

**Fitted AUC:0.818**

**bsAUC: 0.798 [0.757-0.839]**

**Fitted AUC:0.818**

**bsAUC: 0.800 [0.760-0.841]**

| Backward Selection |      |           |         | Stepwise Selection |      |           |         |
|--------------------|------|-----------|---------|--------------------|------|-----------|---------|
|                    | HR   | 95% CI    | P       |                    | HR   | 95% CI    | P       |
| ln (Troponin)      | 1.3  | 1.1-1.54  | 0.0022  | ln (Troponin)      | 1.3  | 1.1-1.54  | 0.0022  |
| ln (Hgb)           | 0.35 | 0.18-0.69 | 0.0021  | Age                | 1.04 | 1.03-1.05 | <0.0001 |
| Age                | 1.04 | 1.03-1.05 | <0.0001 | ST2 >=50           | 2    | 1.58-2.52 | <0.0001 |
| Troponin >=16      | 1.95 | 1.31-2.9  | 0.001   | NYHA >=3           | 1.83 | 1.45-2.3  | <0.0001 |
| ST2 >=50           | 2    | 1.58-2.52 | <0.0001 | Troponin >=16      | 1.95 | 1.31-2.9  | 0.001   |
| NYHA >=3           | 1.83 | 1.45-2.3  | <0.0001 | ln (Hgb)           | 0.35 | 0.18-0.69 | 0.0021  |

**Fitted AUC:0.818**

**bsAUC: 0.801 [0.760-0.841]**

| Forward Selection |      |           |         |
|-------------------|------|-----------|---------|
|                   | HR   | 95% CI    | P       |
| ln (Troponin)     | 1.3  | 1.1-1.54  | 0.0022  |
| Age               | 1.04 | 1.03-1.05 | <0.0001 |
| ST2 >=50          | 2    | 1.58-2.52 | <0.0001 |
| NYHA >=3          | 1.83 | 1.45-2.3  | <0.0001 |
| Troponin >=16     | 1.95 | 1.31-2.9  | 0.001   |
| ln (Hgb)          | 0.35 | 0.18-0.69 | 0.0021  |



Fig. 36 Univariate Performance

| Variable       | Outcome=0<br>Median [IQR] | Outcome=1<br>Median [IQR] | Test<br>P Value | sOR(Raw)<br>Est [95% CI] | LRT p  | sOR(ln)<br>Est [95% CI] | LRT p  | AuROC |
|----------------|---------------------------|---------------------------|-----------------|--------------------------|--------|-------------------------|--------|-------|
| Age_Yr         | 73.5[61.5-81]             | 80[74-85]                 | 0.001           | 1.75 [1.25-2.55]         | <0.001 | 1.84 [1.27-2.8]         | <0.001 | 0.641 |
| Sex            | 0=70;1=78                 | 0=32;1=29                 | 0.544           | 0.81 [0.45-1.48]         | 0.497  |                         |        |       |
| Ethnicity      | 1=13;5=11;6=5;7=1         | 1=56;5=2;6=3              | 0.646           |                          | 0.502  |                         |        |       |
| Is_Black       | 0=137;1=11                | 0=59;1=2                  | 0.354           | 0.42 [0.06-1.63]         | 0.231  |                         |        |       |
| SBP            | 140[124-156.25]           | 130[110-151]              | 0.022           | 0.68 [0.48-0.93]         | 0.016  | 0.68 [0.49-0.92]        | 0.013  | 0.601 |
| DBP            | 75[66-86.25]              | 74[61-83]                 | 0.411           | 0.91 [0.67-1.23]         | 0.553  | 0.9 [0.66-1.21]         | 0.474  | 0.536 |
| BMI            | 26.98[23.88-32]           | 26.61[21.92-29.75]        | 0.036           | 0.65 [0.45-0.9]          | 0.009  | 0.67 [0.48-0.92]        | 0.012  | 0.592 |
| HTN            | 0=55;1=93                 | 0=21;1=40                 | 0.754           | 1.13 [0.61-2.13]         | 0.708  |                         |        |       |
| Diabetes       | 0=85;1=63                 | 0=36;1=25                 | 0.878           | 0.94 [0.51-1.71]         | 0.833  |                         |        |       |
| CAD            | 0=93;1=55                 | 0=28;1=33                 | 0.031           | 1.99 [1.09-3.67]         | 0.025  |                         |        |       |
| LVEF           | 52[36-62]                 | 51[30-67]                 | 0.844           | 0.94 [0.7-1.27]          | 0.685  | 0.9 [0.67-1.22]         | 0.491  | 0.509 |
| eGFR           | 54.69[40.99-79.85]        | 48.91[35.7-60.53]         | 0.008           | 0.59 [0.4-0.83]          | 0.002  | 0.64 [0.46-0.87]        | 0.005  | 0.617 |
| Creatinine     | 1.2[0.9-1.6]              | 1.4[1.1-1.5]              | 0.065           | 1.35 [1-1.82]            | 0.047  | 1.41 [1.04-1.93]        | 0.027  | 0.581 |
| BUN            | 23[17-32]                 | 31[24-41]                 | <0.001          | 1.64 [1.22-2.27]         | <0.001 | 1.77 [1.29-2.48]        | <0.001 | 0.669 |
| HGB_g_dl       | 12.7[11-14.3]             | 11.3[10.1-12.5]           | 0.001           | 0.63 [0.46-0.87]         | 0.004  | 0.68 [0.49-0.91]        | 0.01   | 0.641 |
| cTnT1          | 0[0-0.03]                 | 0.03[0-0.06]              | 0.002           | 0.92 [0.55-1.24]         | 0.611  | 1.01 [0.72-1.34]        | 0.932  | 0.628 |
| NTproBNP_pg_ml | 3122.5[1401-7947.25]      | 9020[3366-12991]          | <0.001          | 1.61 [1.15-2.43]         | 0.004  | 2.03 [1.46-2.9]         | <0.001 | 0.685 |
| CRP_mg_ml      | 11.9[3.77-36.12]          | 36.5[9.5-92.2]            | <0.001          | 1.61 [1.21-2.2]          | 0.001  | 1.85 [1.34-2.61]        | <0.001 | 0.666 |
| ST2_ng_ml      | 37.02[23.43-64.69]        | 67.39[41.62-97.23]        | <0.001          | 1.77 [1.31-2.48]         | <0.001 | 1.9 [1.37-2.69]         | <0.001 | 0.692 |

Recall in the entire PRIDE data set, missing LVEF was not random. In this subpopulation only 6 subjects have missing LVEF data (4 cases and 2 controls)->OR=5.07 (p=0.06)

BUN looks strongest in a univariate sense

Fig. 37 Linearity Evaluation: Age

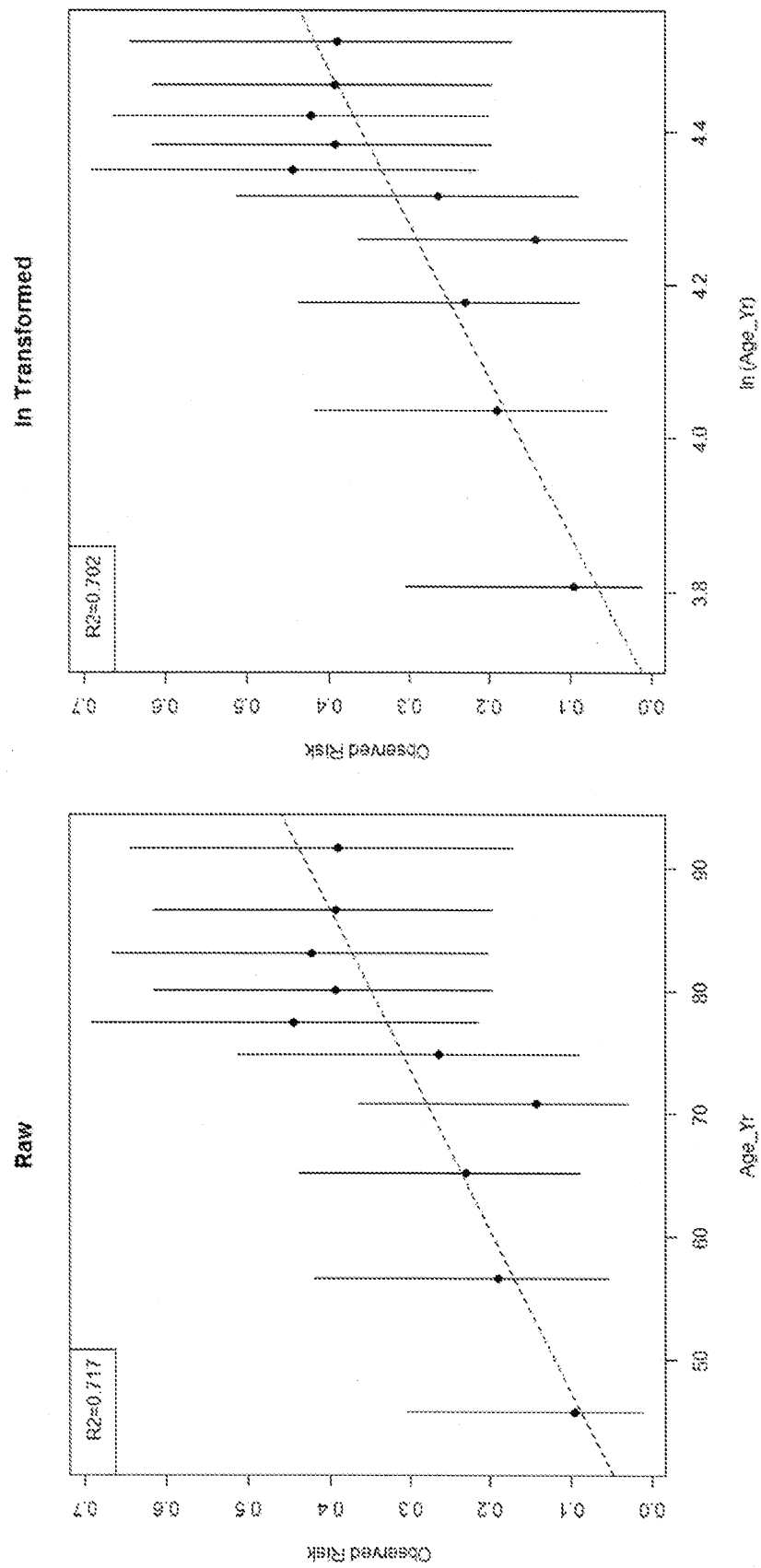


Fig. 38 Linearity Evaluation: SBP

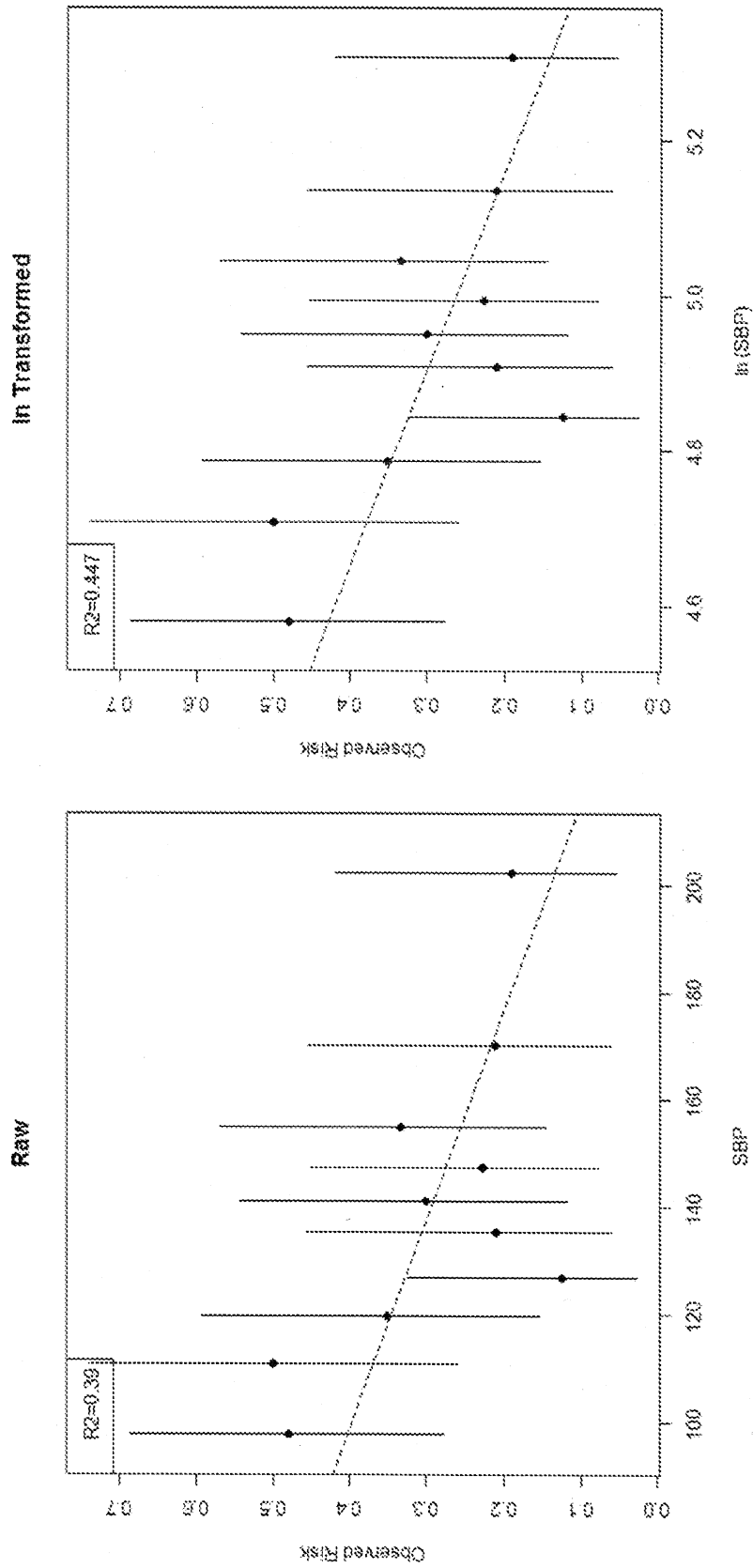


Fig. 39 Linearity Evaluation: DBP

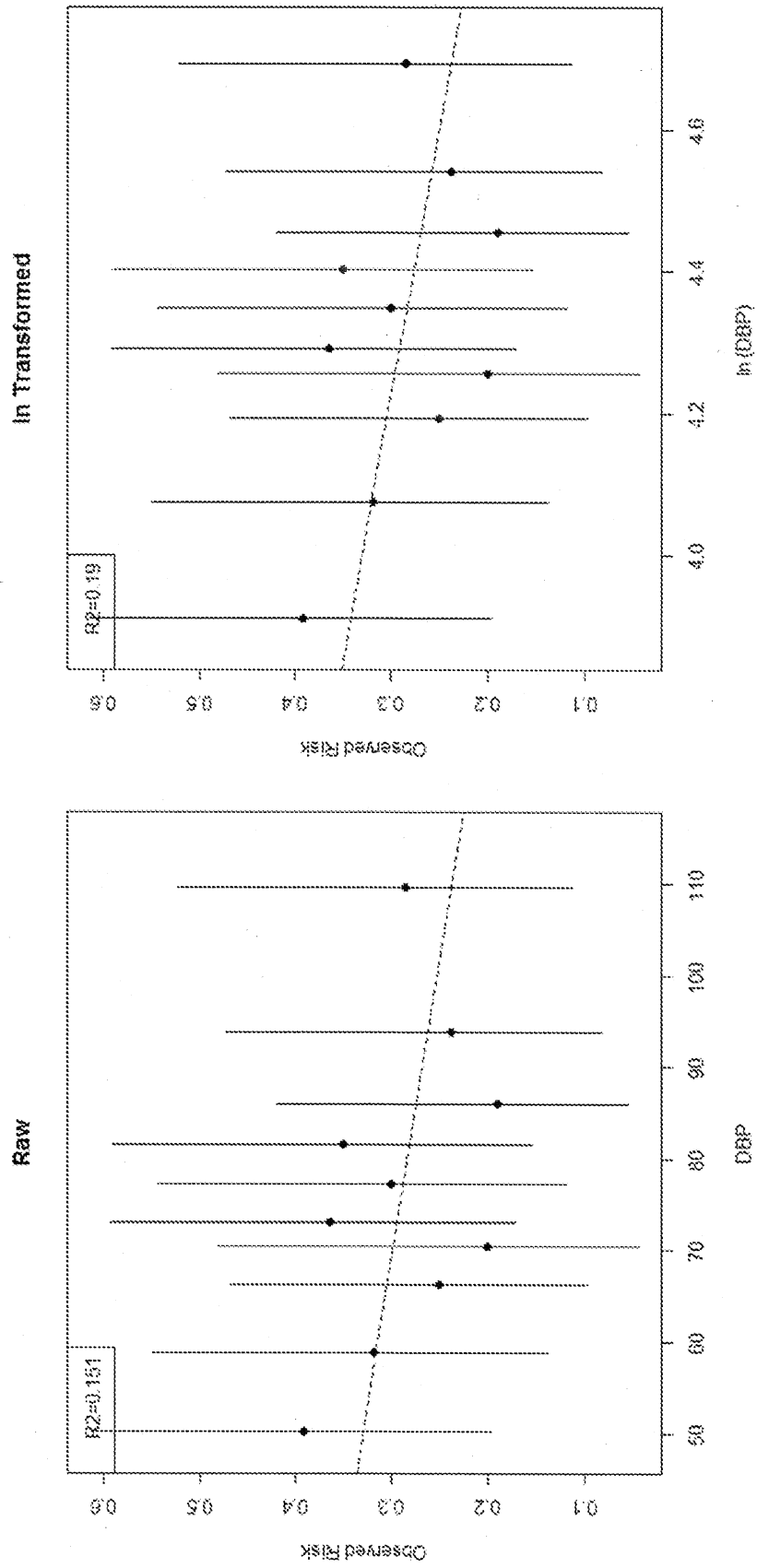


Fig. 40 Linearity Evaluation: BMI

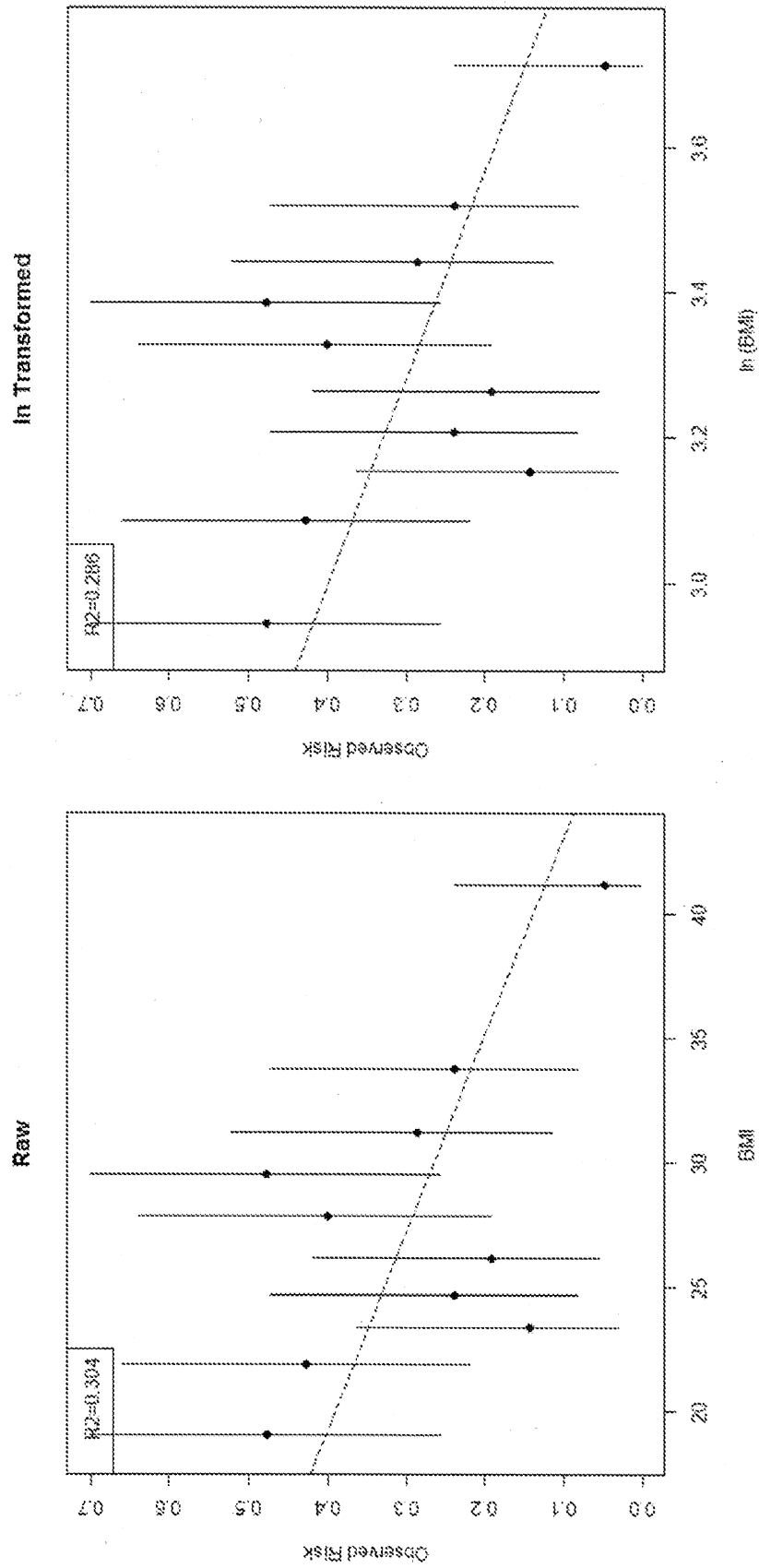


Fig. 41 Linearity Evaluation: LVEF

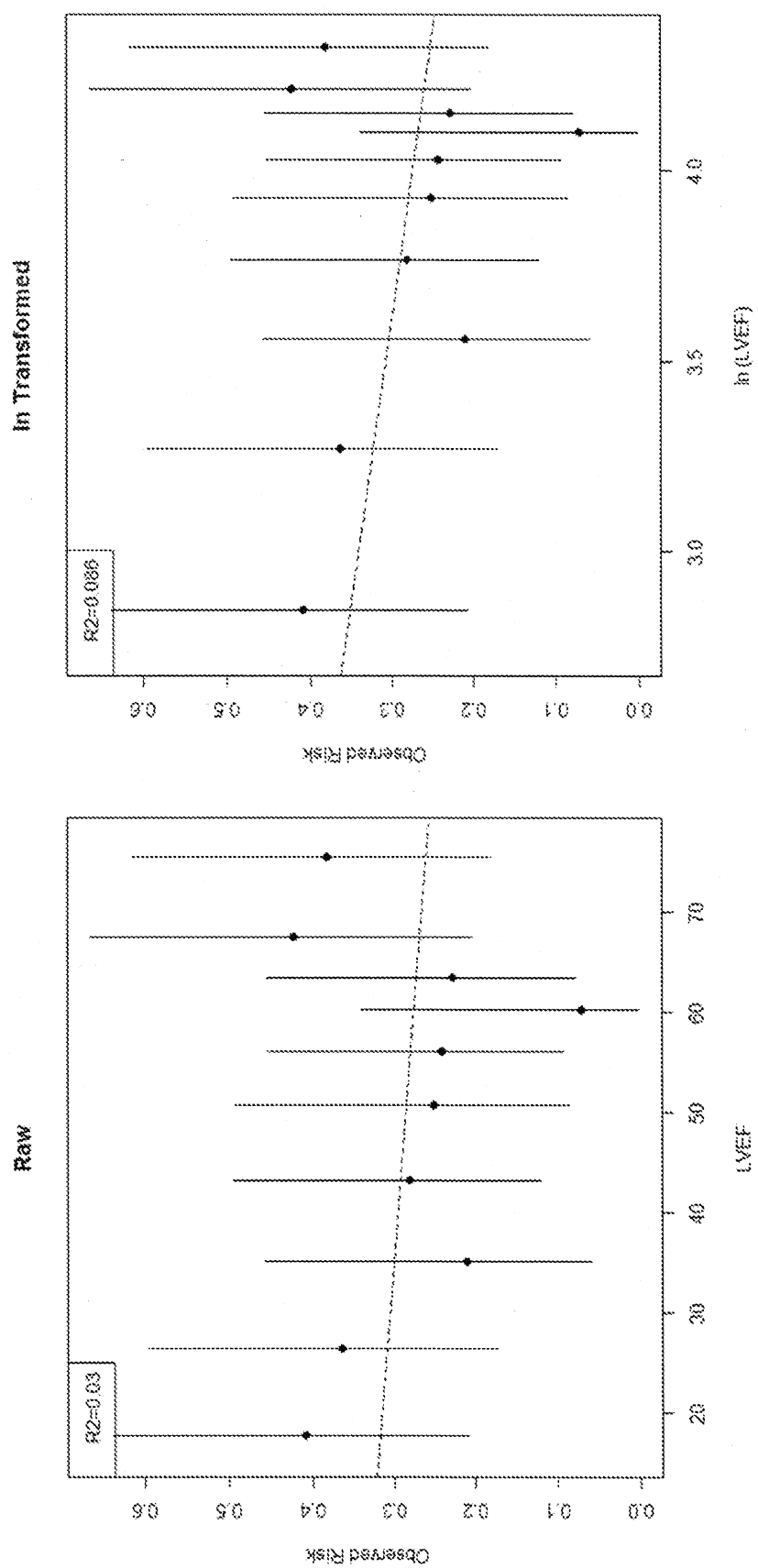


Fig. 42 Linearity Check: eGFR

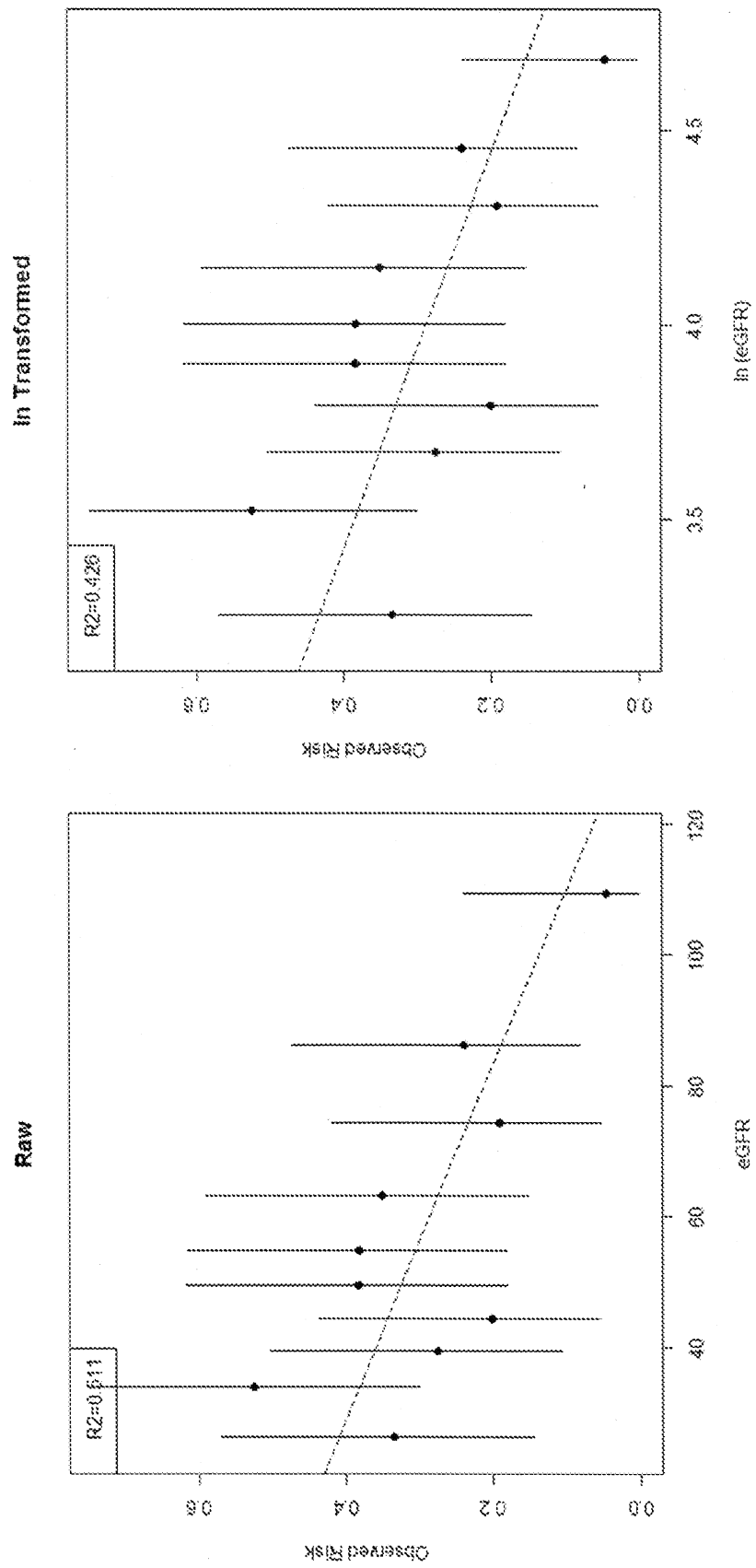


Fig. 43 Linearity Check: Creatinine

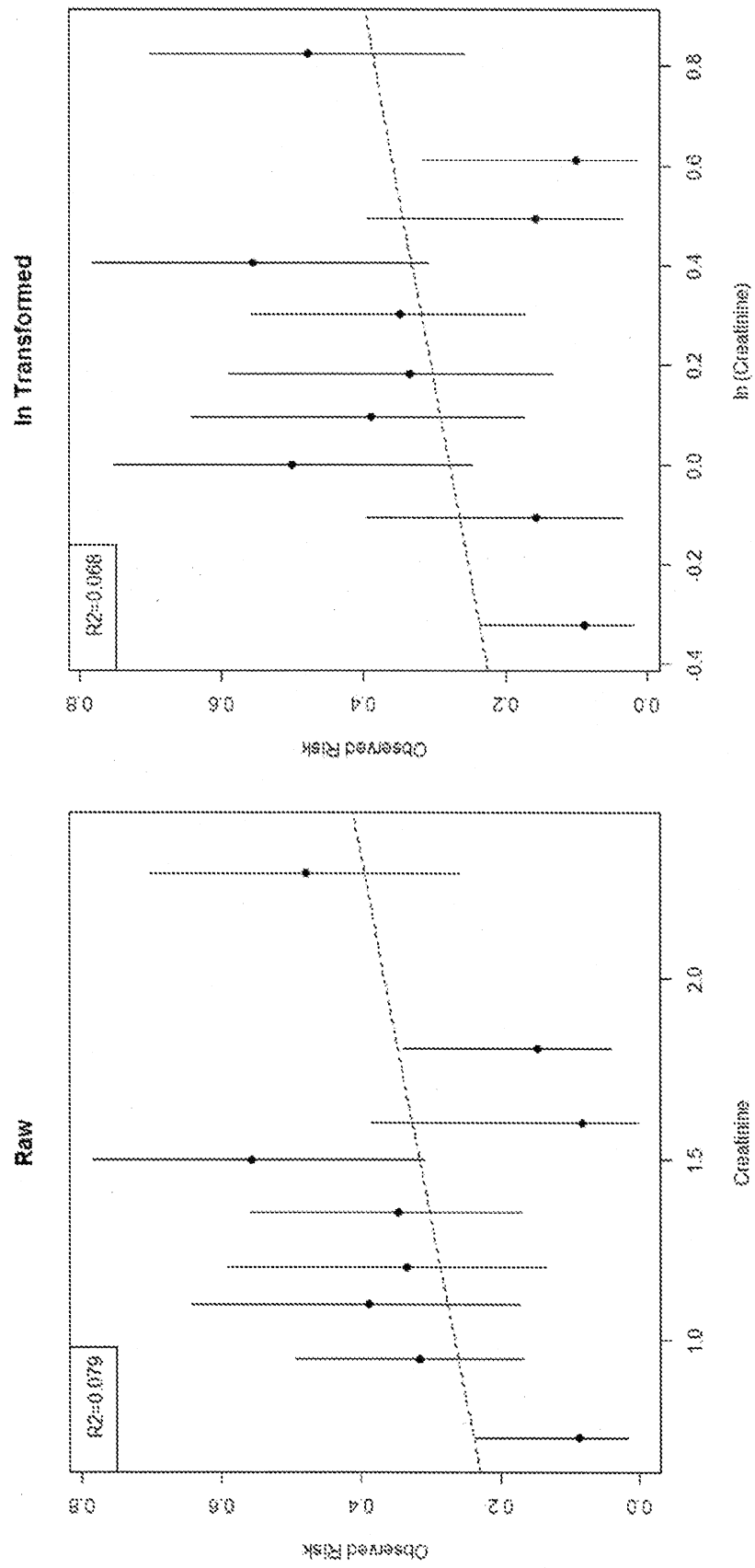


Fig. 44 Linearity Check: BUN

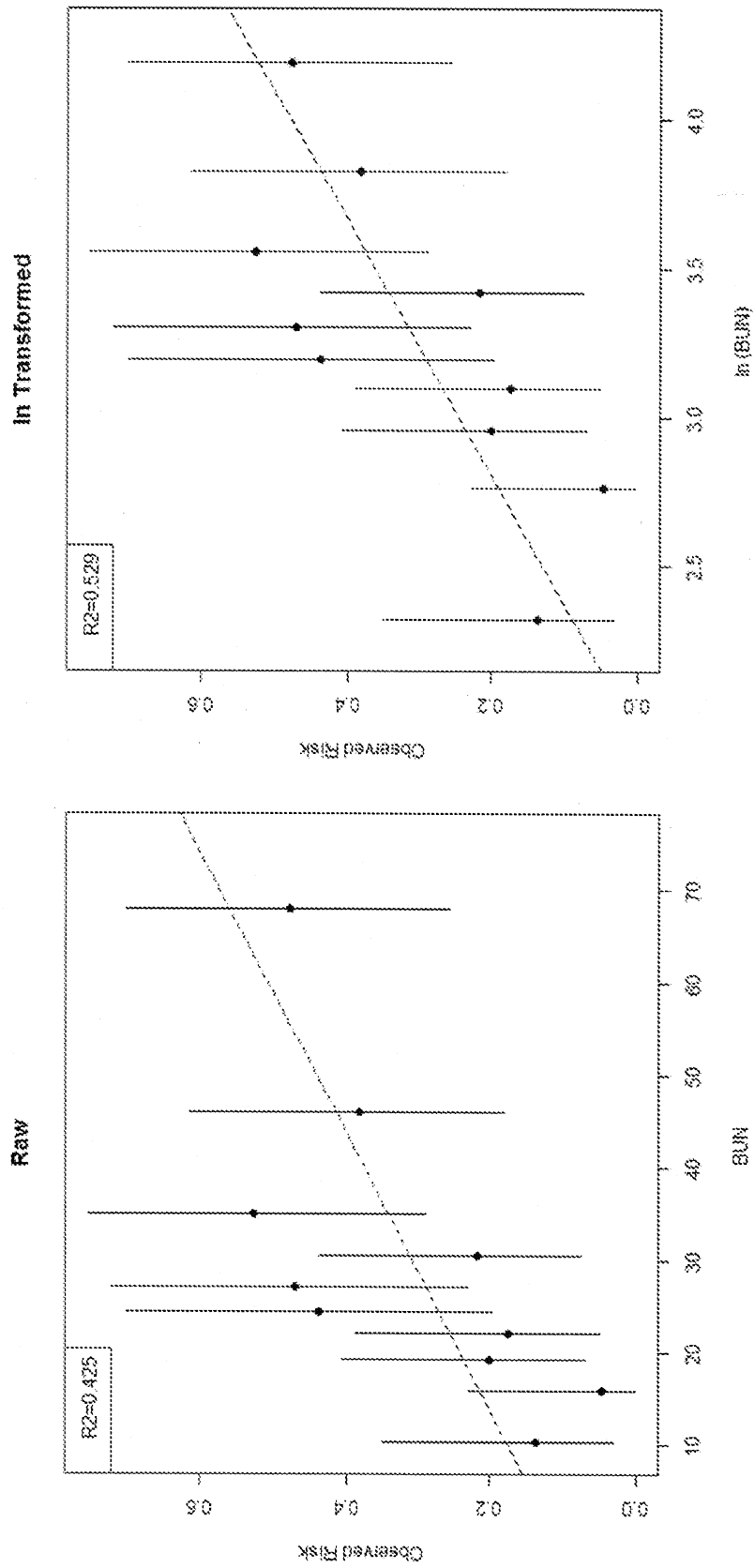


Fig. 45 Linearity Check: Hemoglobin

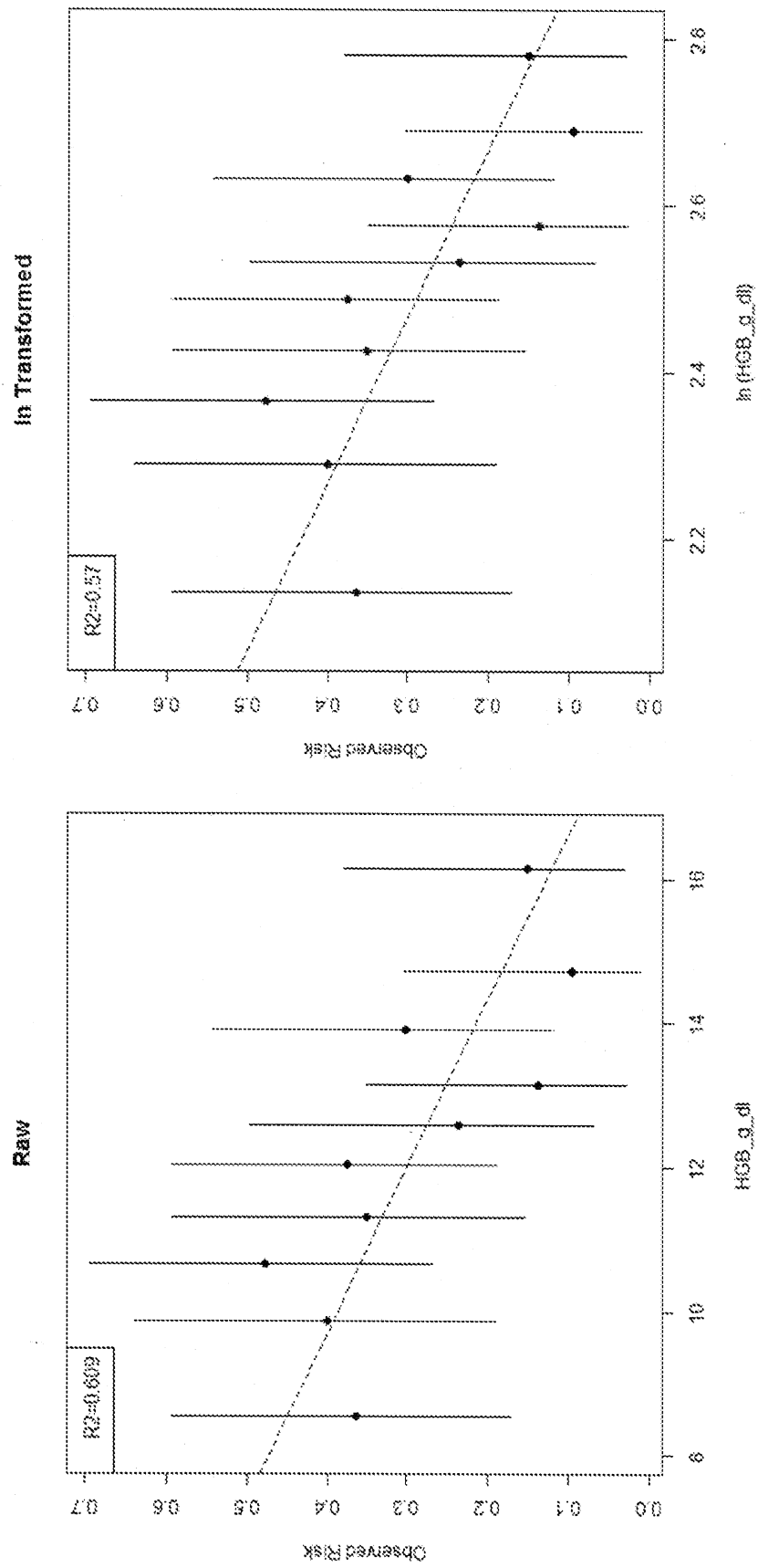


Fig. 46 Linearity Check: Troponin

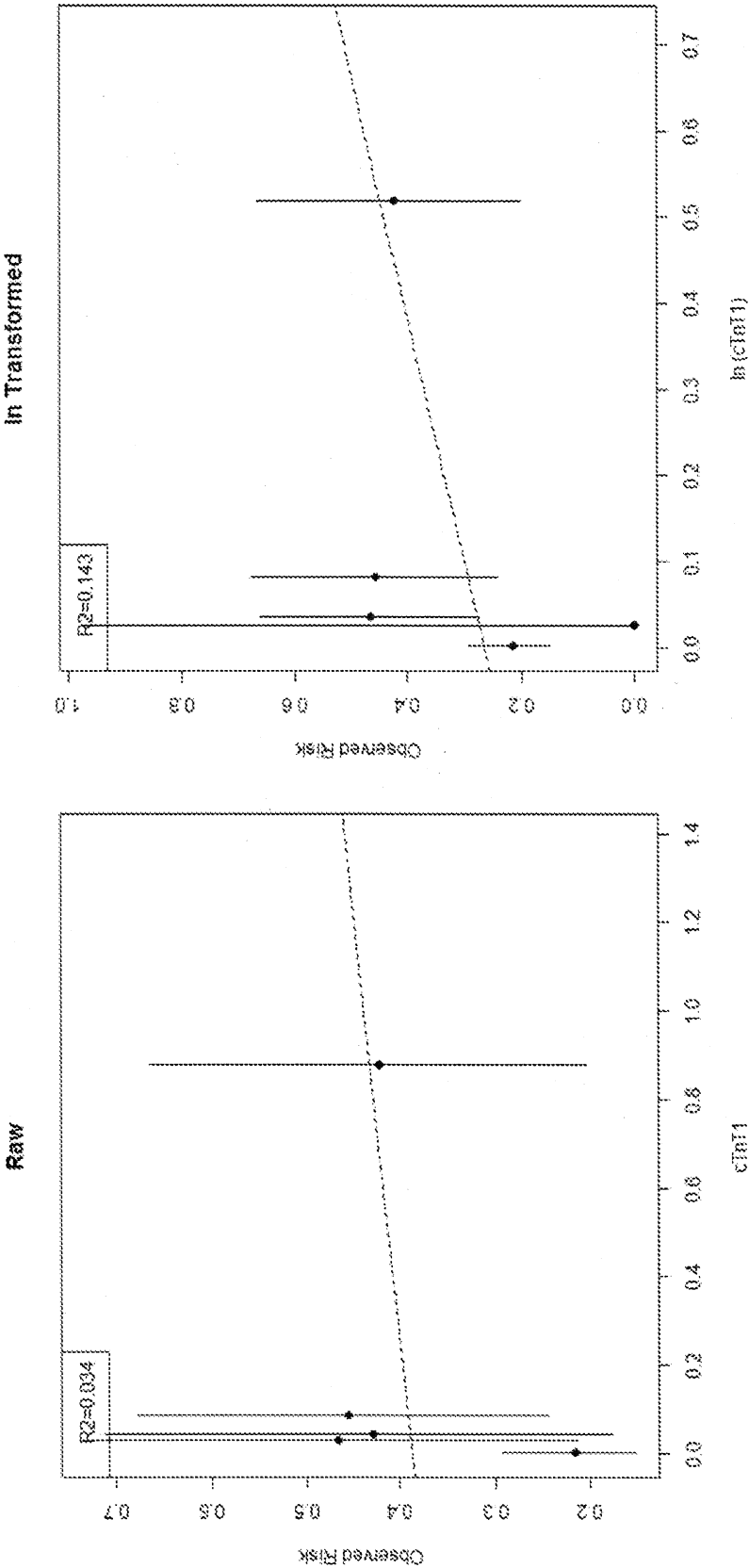


Fig. 47 Linearity Check: NT-proBNP

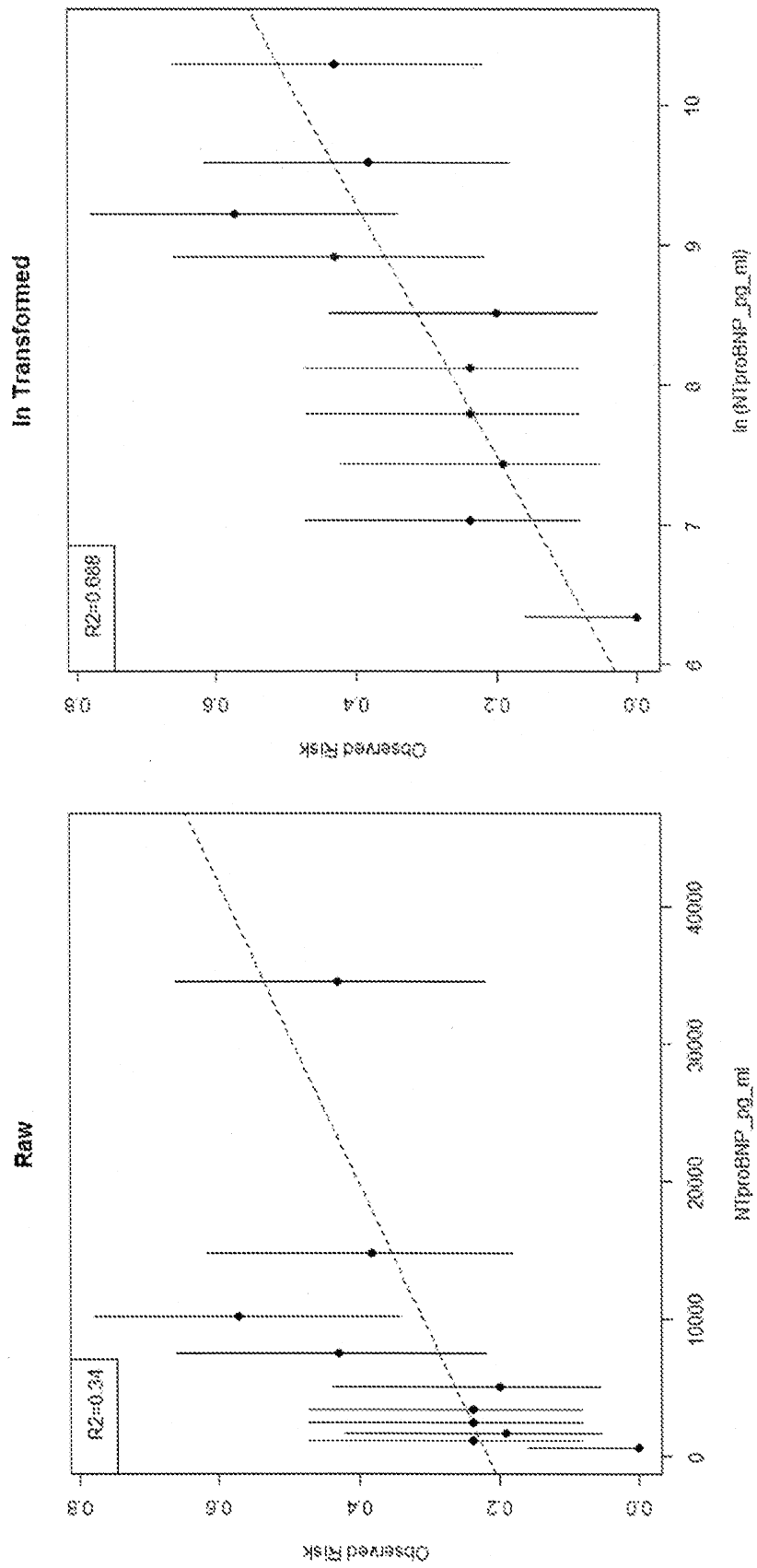


Fig. 48 Linearity Check: CRP

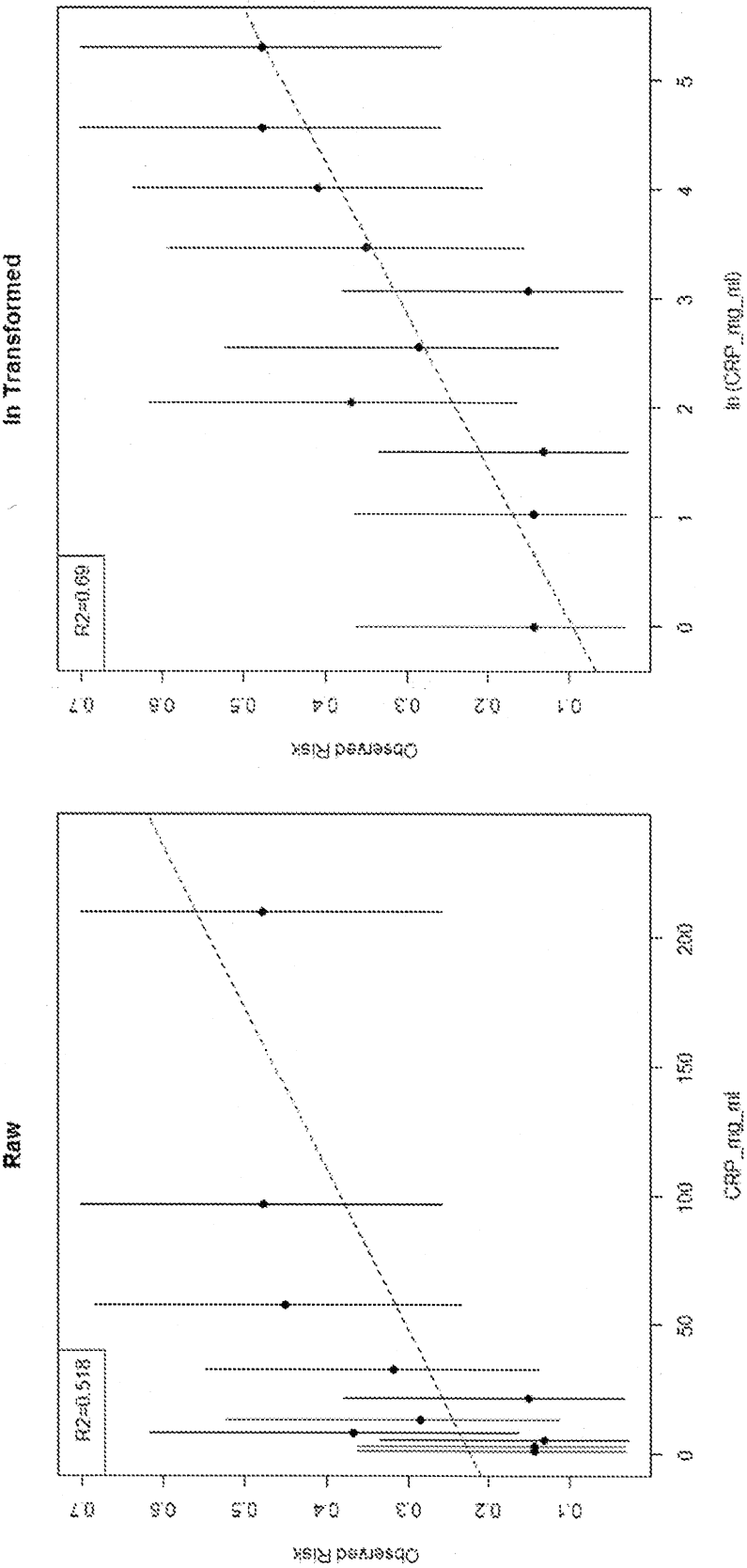


Fig. 49 Linearity Check: ST2

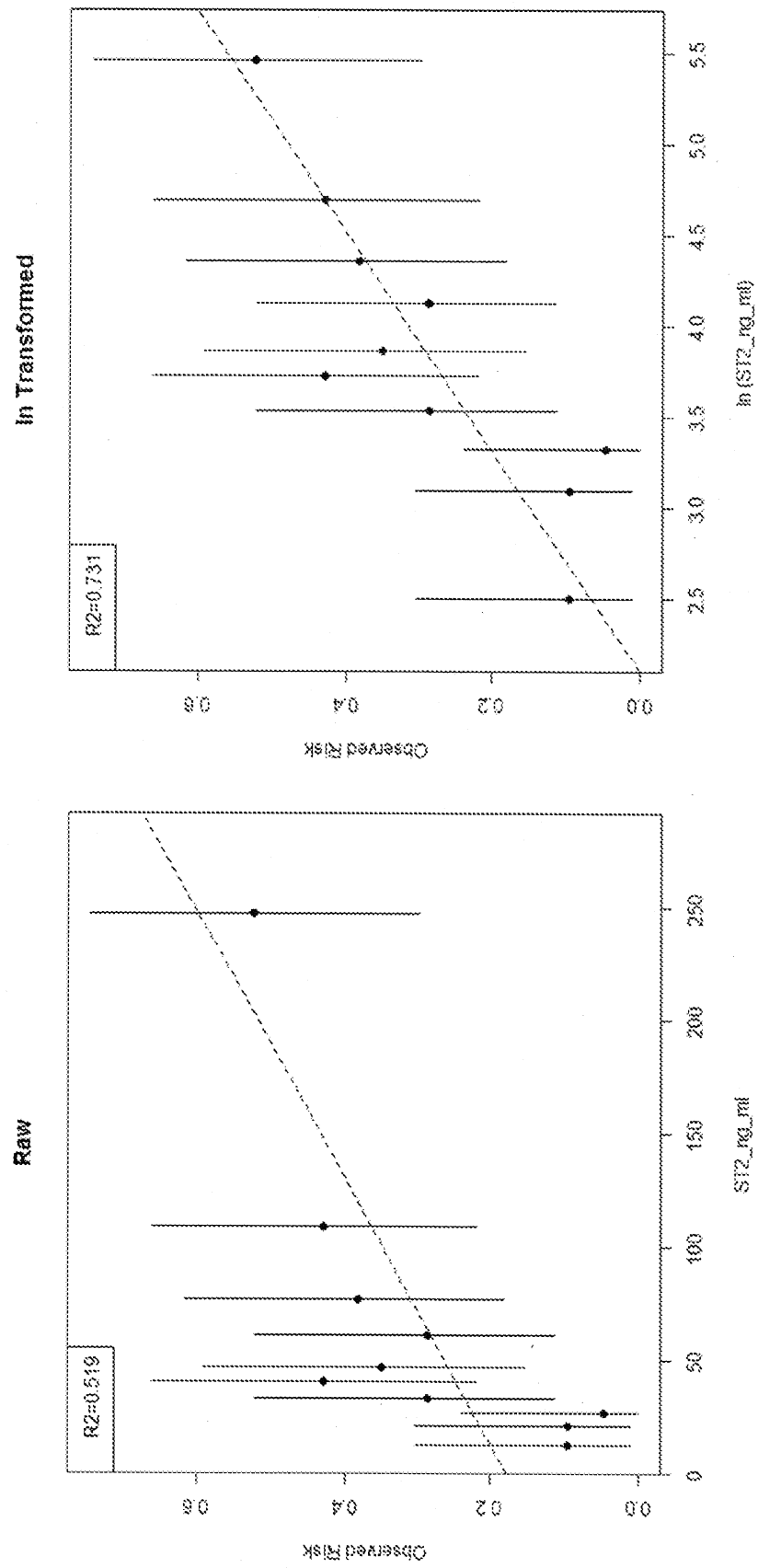


Fig. 50 Summary

|            | AIC           |               | Other         | Comment | Graph |
|------------|---------------|---------------|---------------|---------|-------|
|            | Raw           | Log           |               |         |       |
| Age        | 245.31        | <b>245.14</b> |               |         | Raw   |
| SBP        | 250.6         | <b>250.2</b>  | <b>245.85</b> | >120    | log   |
| DBP        | 256.04        | <b>255.88</b> |               |         | log   |
| BMI        | <b>249.49</b> | 250.1         |               |         | Raw   |
| LVEF       | 256.23        | <b>255.92</b> |               |         | ?     |
| eGFR       | <b>246.93</b> | 248.39        |               |         | Raw   |
| Creatinine | 252.44        | <b>251.53</b> |               |         | Raw   |
| BUN        | 245.5         | <b>243.6</b>  |               |         | log   |
| Hemoglobin | <b>248.07</b> | 249.81        |               |         | Raw   |
| Troponin   | 256.14        | 256.39        | <b>247.08</b> | >0      | ?     |
| NT-proBNP  | 247.98        | <b>237.46</b> |               |         | log   |
| CRP        | 245.74        | <b>241.77</b> |               |         | log   |
| ST2        | 241.74        | <b>240.61</b> | <b>238.15</b> | >=35    | log   |

• Parameter Space

- Age
- Log(SBP)
- SBP>120
- Log(DBP)
- BMI
- Log(LVEF)
- Log(BUN)
- Hemoglobin
- Troponin
- Troponin>0
- Log(NT-proBNP)
- Log(CRP)
- Log(ST2)
- ST2>=35
- Other factors (Sex, Race, Diabetes, HTN,CAD,IS\_Black)

AIC (Smaller is better) generally agrees with graphical approach. Bins will be considered for ST2, SBP, and Troponin

Fig. 51 Marker Selection (AIC)

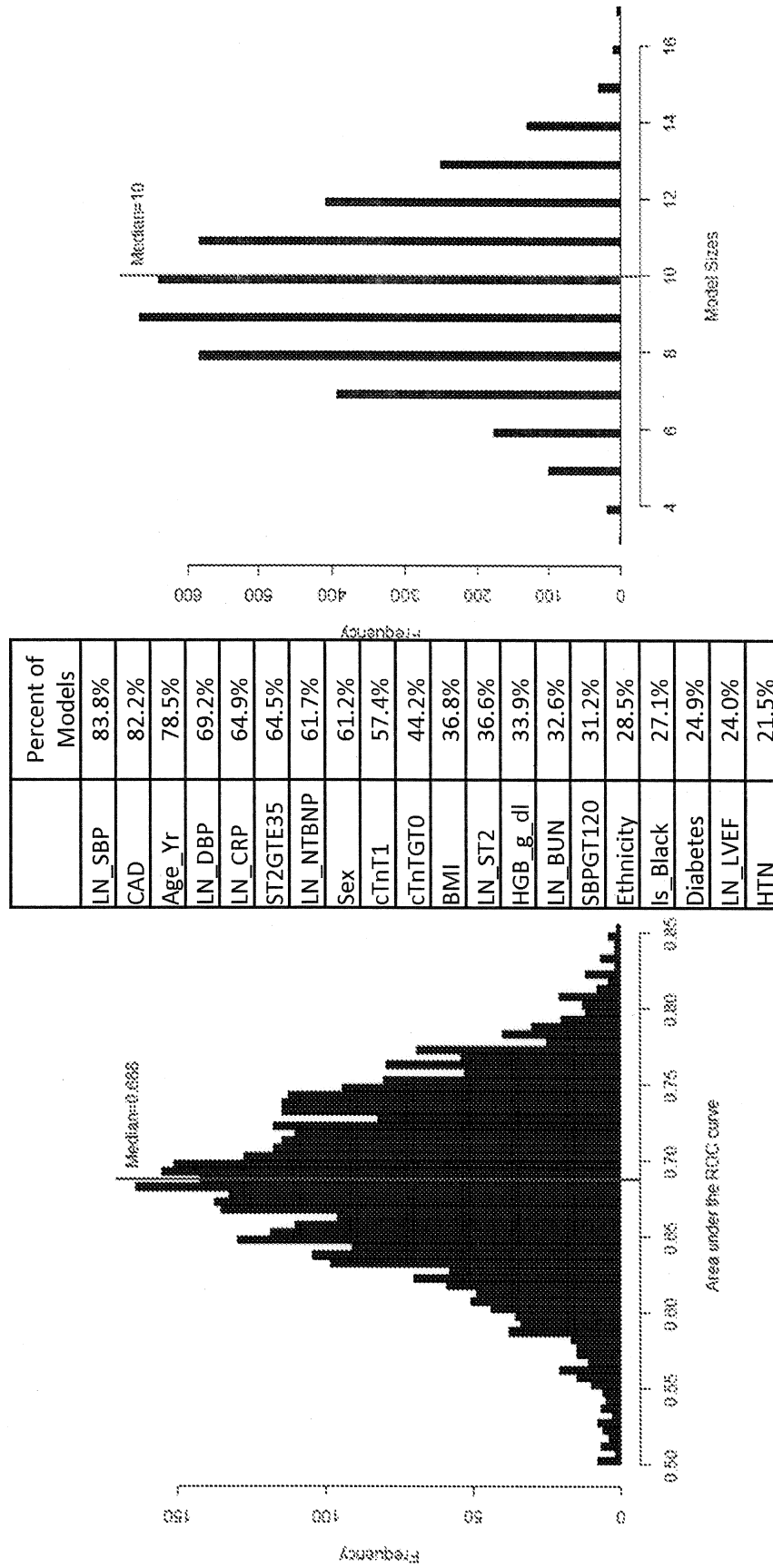


Fig. 52 BIC Based Marker Selection

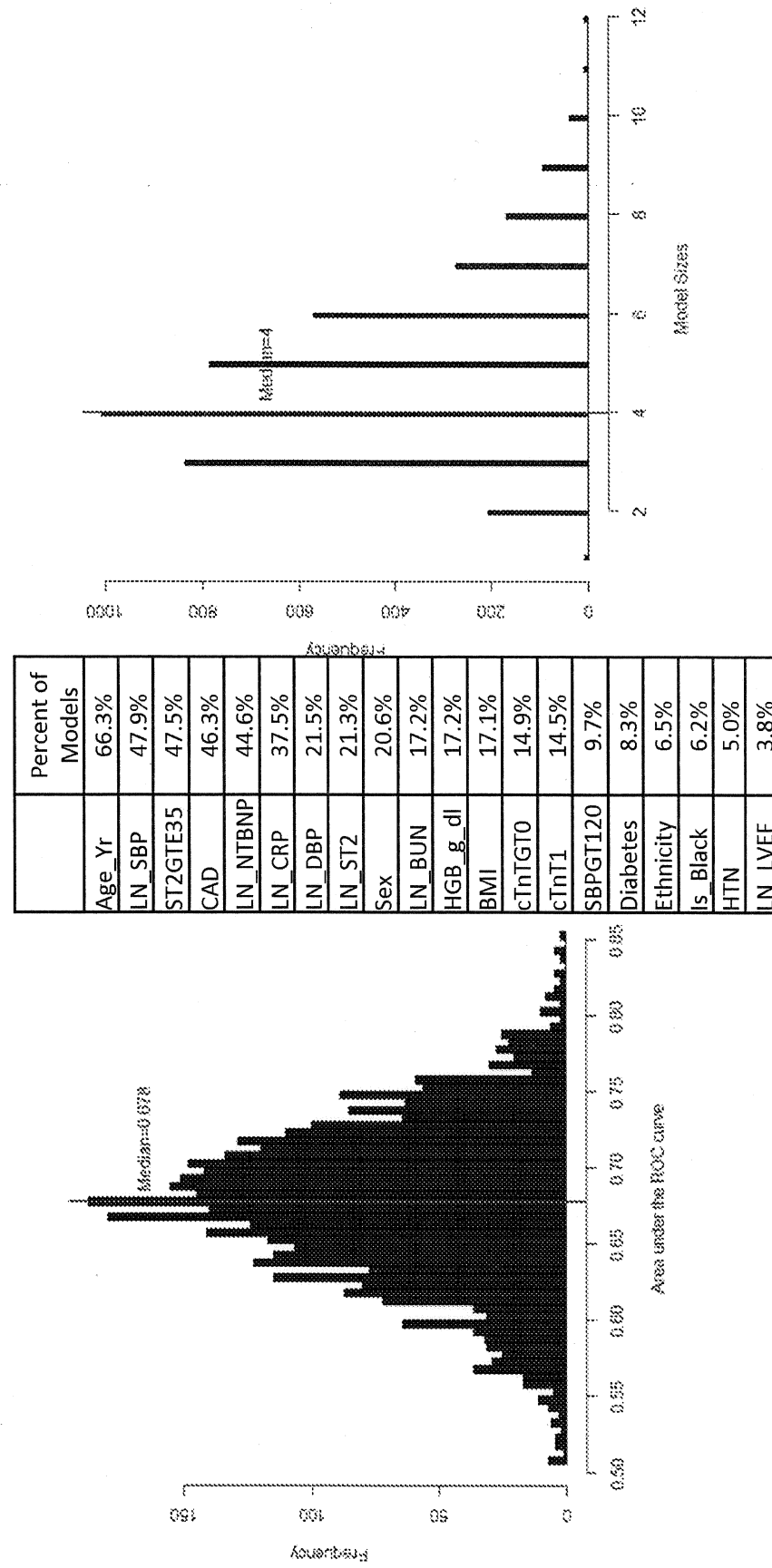


Fig. 53 Comparison of the Two Models

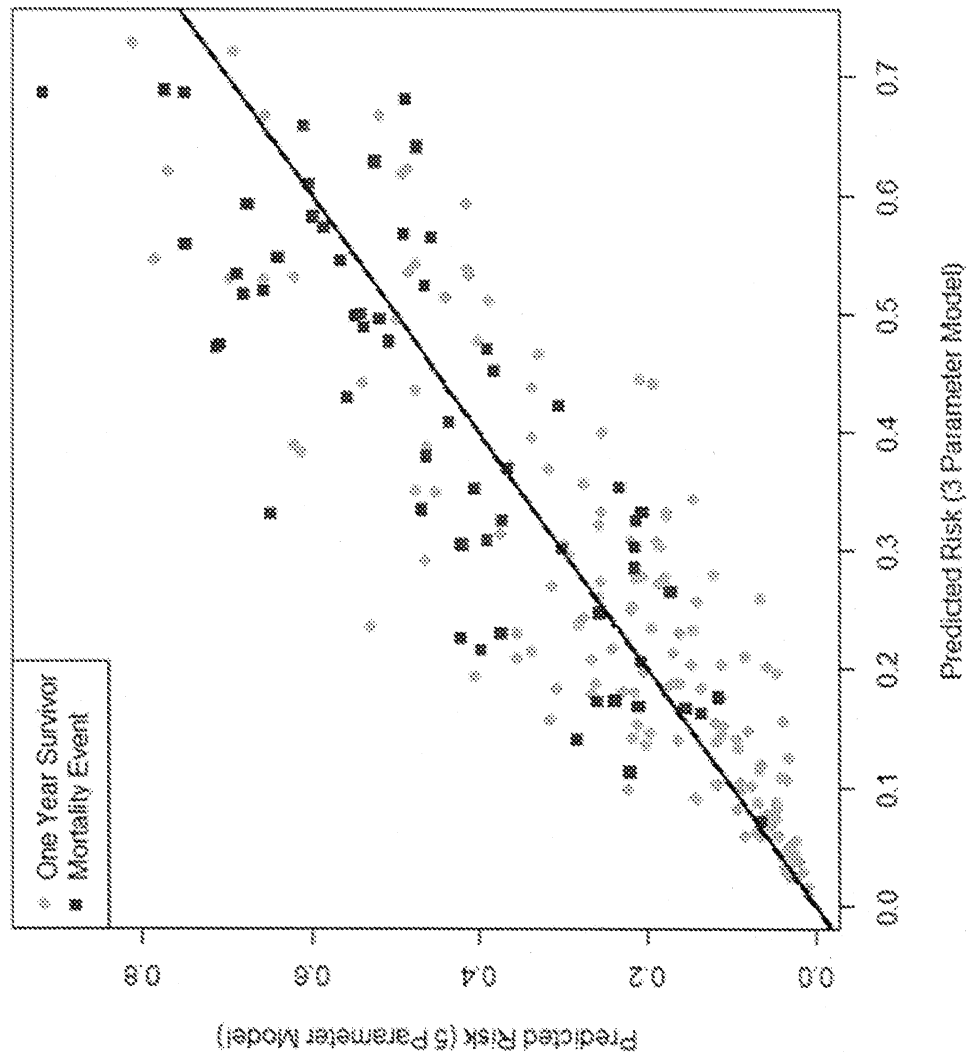


Fig. 54 ROC Curves

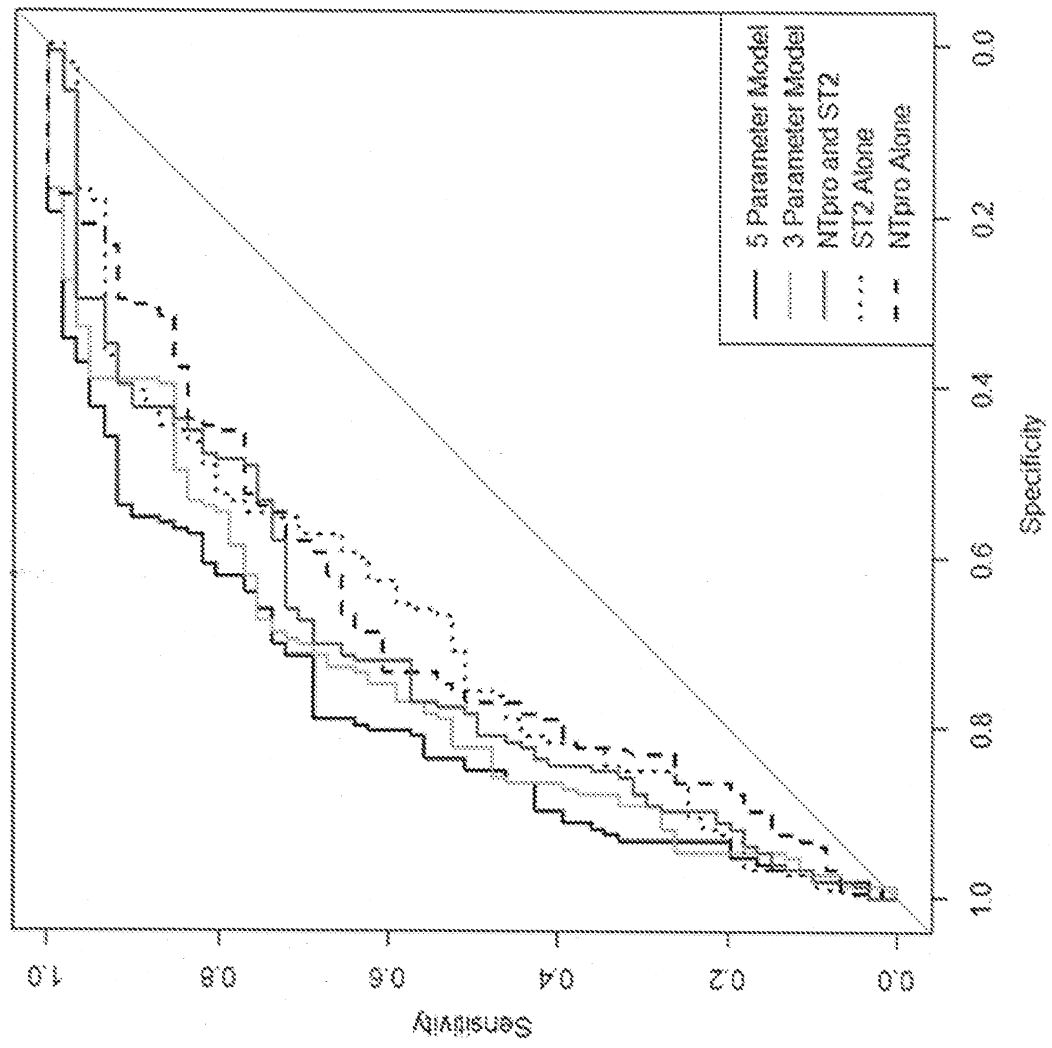


Fig. 55 Bootstrap AUC  
"Out of Bag" estimates

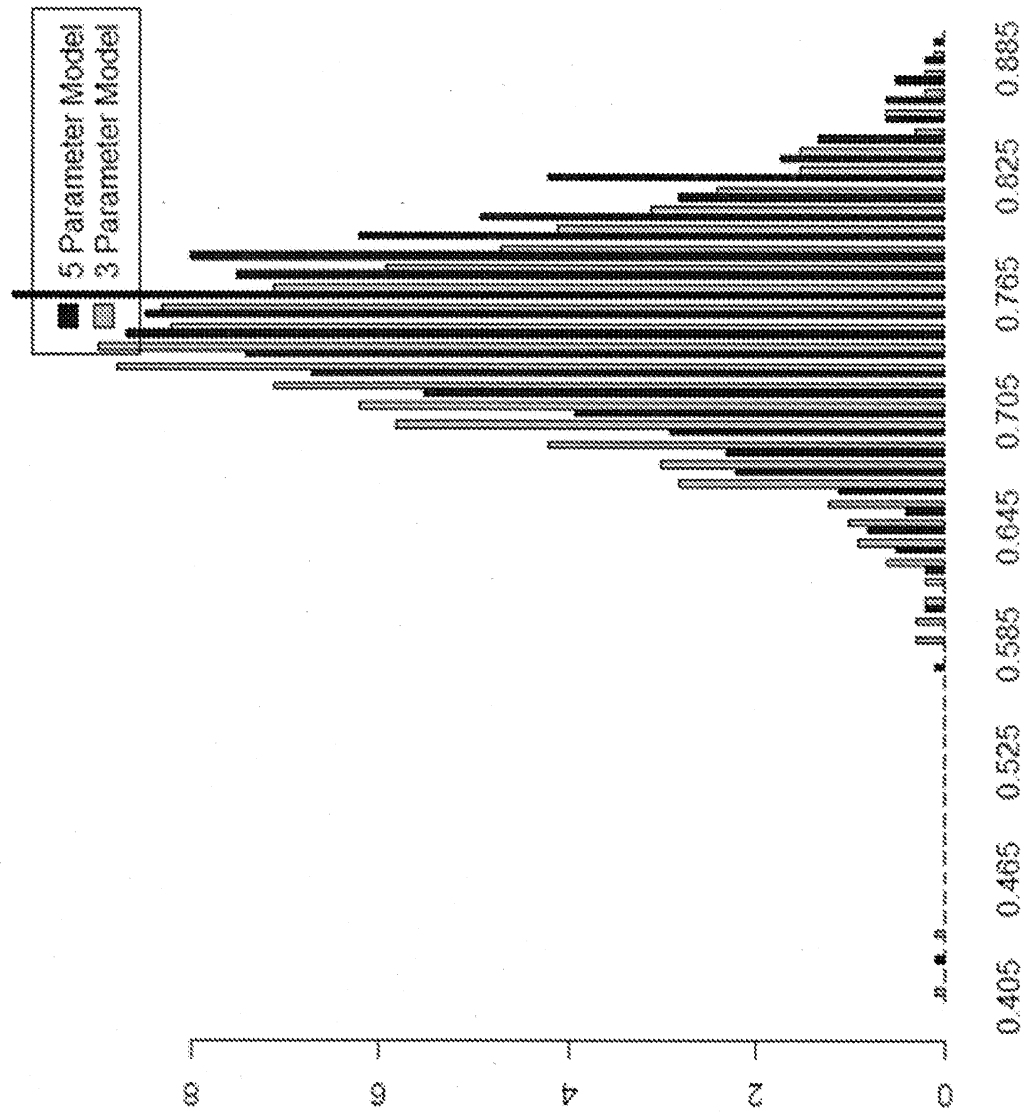


Fig. 56 Model Calibration

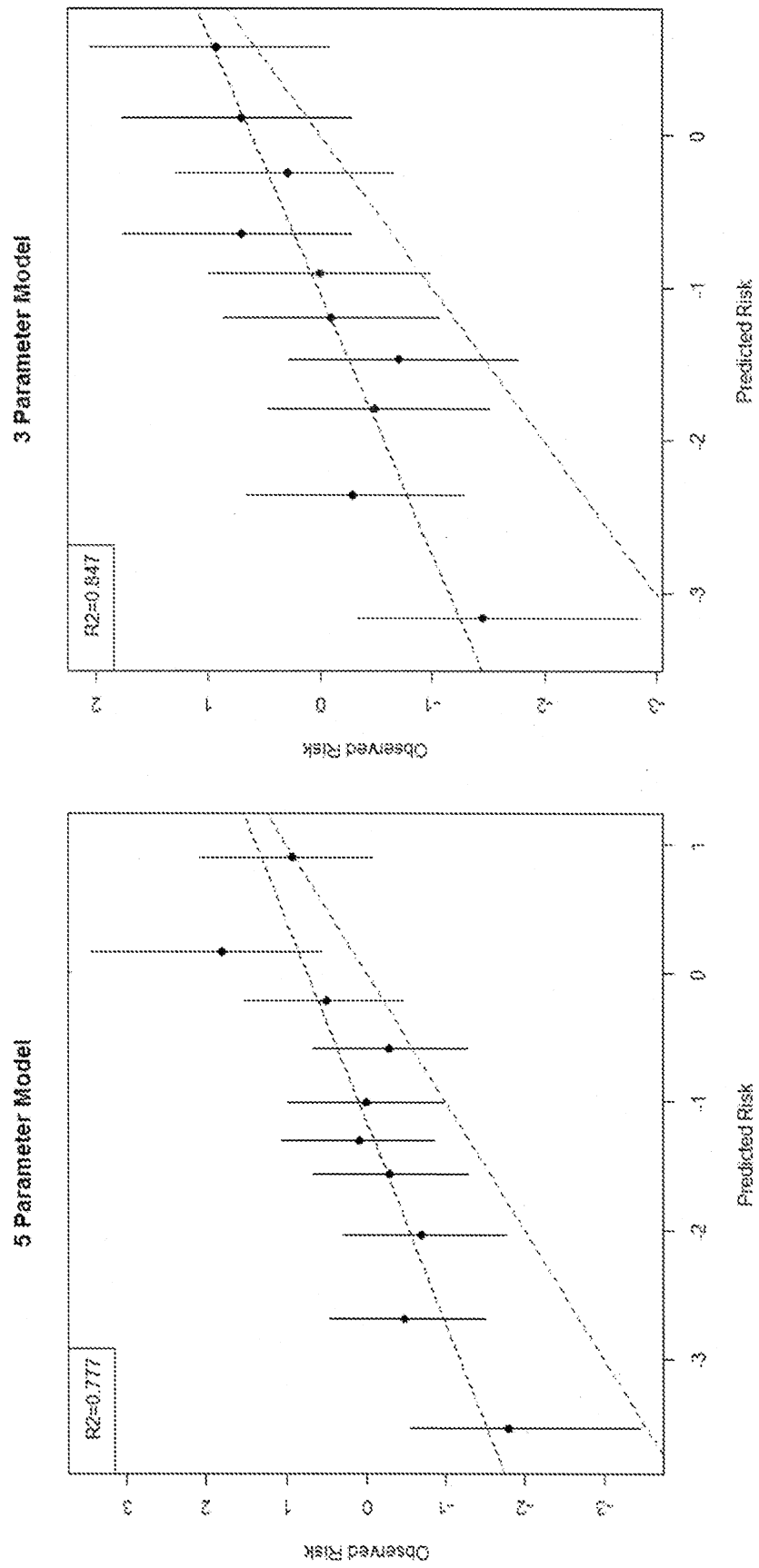


Fig. 57 Model Parameters

## 5 Parameter Model

```

Coefficients:
              Estimate Std. Error z value Pr(>|z|)
(Intercept)    1.6996    4.3544     0.39  0.6963
Age_Yr         0.0403    0.0154     2.62  0.0087 **
LN_SBP        -2.1065    0.8663    -2.43  0.0150 *
CAD           0.7824    0.3607     2.17  0.0301 *
ST2GTE35      1.3846    0.4384     3.16  0.0016 **
LN_NTBNP      0.4023    0.1668     2.41  0.0159 *
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

```

## 3 Parameter Model

```

Coefficients:
              Estimate Std. Error z value Pr(>|z|)
(Intercept)  -8.3383    1.6970    -4.91  8.9e-07 ***
Age_Yr       0.0426    0.0144     2.96  0.0030 **
ST2GTE35     1.2656    0.4164     3.04  0.0024 **
LN_NTBNP     0.3998    0.1586     2.52  0.0117 *
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

```