Supplementary Appendix

**Supplementary table 1**

ICD-10 codes included in Charlson co-morbidity index

Diagnostic categories, ICD-10 codes

Codes

Condition Weights ICD-10

Peripheral vascular disease 1 I70, I71, I74, I790, I739

Cerebral vascular accident 1 I60, I61, I62, I63, I65, I66, I67, I68, I69, G450, G451, G452, G458, G459, I64, G454 ,G46 I670, I671, I672, I674, I675, I676, I677, I678, I679,

I682, I688, I681

Dementia 1 F00, F01, F02, G30, G31

Pulmonary disease 1 J40, J41, J42, J43, J44, J45, J46, J47, J67, J60, J61, J62, J63, J64, J65,

J66, J67

Connective tissue disorder 1 M32, M34, M331, M053, M058, M059, M060, M063, M069, M050,

M051, M052, M353

Peptic ulcer 1 K25, K26, K27, K29, K221

Liver disease 1 K702, K703, K704, K73, K717, K740, K742, K746, K743, K744, K745

Diabetes complications 2 E102, E112, E132, E142, E103, E113, E133, E143, E104, E114, E134,

E144

Paraplegia 2 G81, G041, G820, G821, G822, T144

Renal disease 2 N03, N052, N053, N054, N055, N056, N072, N073, N074, N01, N18,

N19, N25, N17, R34, I12, I13, Z992, N04, T858, T859

Cancer 2 C0, C1, C2, C3, C40, C41, C43, C45, C46, C47, C48, C49, C5, C6, C70,

C71, C72, C73, C74, C75, C76, C80, C81, C82, C83, C84, C85, C883,

C887, C889, C900, C901, C91, C92, C93, C940, C941, C942, C942,

C9451, C947, C95, C96

Metastatic cancer 3 C77, C78, C79, C80

Severe liver disease 3 K729, K766, K767, K721, B150, B160, B190, K711

HIV 6 B20, B21, B22, B23, B24

**Supplementary table 2**

***ICD-10 codes used in outcome and baseline variables***

|  |  |
| --- | --- |
| Heart Failure | *I50* |
| Myocardial infarction | *I21, I22, 410 (ICD-8)* |
| Pacemaker Implantation | *BFCA01, BFCA03, BFCA07, BFCA61, ZZ4050A, ZZ405B* |
| Atrial fibrillation | *I48* |
| Cardiovascular Death | *I00-I99* |
| Valvular heart disease | *I05, I06, I34, I35, KFK, KFM* |

***ICD-10 codes used in combined variables with medication***

|  |  |
| --- | --- |
| Hypertension | *I10, I15* |
| Diabetes Mellitus | *E10, E11* |

***ATC-codes used for defining medical therapy***

|  |  |
| --- | --- |
| Beta-blocker | C07A, C07B, C07C, C07D, C07F |
| Loop diuretics | C03C, C03EB |
| Calcium channel antagonist | C08, C09BB, CO9DB |
| RAS-inhibitor | C09AA, C09BA, C09BB, C09CA, C09DA, C09DB, C09XA02, C09XA52 |
| Non-loop diuretics | C02L, C02DA, C07D, C09XA52, C03A, C03EA, C03B, C03X, C07C, C08G, C09BA, C09DA, C03D, C03E, C03EB |
| Anti-diabetic medication | A10A, A10B |

**Supplementary table 3** - Number of events of adverse cardiovascular outcomes per BBB subtype during follow-up.

**Men**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **BBB subtype** | **CV Death**  **No.** | **HF**  **No.** | **Pacemaker implantation**  **No.** | **MI**  **No.** | **AF**  **No.** |
| **IRBBB (n = 887)** | 37 | 53 | 14 | 38 | 67 |
| **RBBB (n = 2,297)** | 244 | 276 | 156 | 137 | 258 |
| **LBBB (n = 358)** | 56 | 118 | 34 | 30 | 44 |
| **NIVCD (n = 1,979)** | 216 | 343 | 124 | 144 | 197 |

**Women**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **BBB subtype** | **CV Death**  **No.** | **HF**  **No.** | **Pacemaker implantation**  **No.** | **MI**  **No.** | **AF**  **No.** |
| **IRBBB (n = 426)** | 26 | 26 | 14 | 11 | 31 |
| **RBBB (n = 1,213)** | 163 | 167 | 77 | 54 | 136 |
| **LBBB (n = 679)** | 82 | 167 | 32 | 52 | 99 |
| **NIVCD (n = 1,071)** | 172 | 255 | 69 | 92 | 126 |

**Supplementary table 4 -** Brier scores for all models and outcomes with 95% confidence intervals.

**Men**

|  |  |  |
| --- | --- | --- |
| **Outcome** | **Conventional model**  **Brier score (95%CI)** | **BBB Model**  **Brier score (95%CI)** |
| CV Death | 0.0438 (0.0378-0.0499) | 0.0439 (0.0378-0.0499) |
| HF | 0.0607 (0.0528-0.0686) | 0.0603 (0.0525–0.0681) |
| Pacemaker implant | 0.0157 (0.0132-0.0183) | 0.0155 (0.0130-0.0181) |
| MI | 0.0514 (0.0444-0.0583) | 0.0514 (0.0444-0.0583) |
| AF | 0.0735 (0.0646-0.0824) | 0.0735 (0.0646-0.0824) |

**Women**

|  |  |  |
| --- | --- | --- |
| **Outcome** | **Conventional model**  **Brier score (95%CI)** | **BBB Model**  **Brier score (95%CI)** |
| CV Death | 0.0461 (0.0395–0.0527) | 0.0461 (0.0395–0.0527) |
| HF | 0.0546 (0.0469-0.0623) | 0.0544 (0.0468–0.0621) |
| Pacemaker implantation | 0.0116 (0.00941-0.0138) | 0.0115 (0.00938-0.0137) |
| MI | 0.0312 (0.0262–0.0363) | 0.0312 (0.0262–0.0362) |
| AF | 0.0697 (0.0608-0.0787) | 0.0697 (0.0608-0.0787) |

**Supplementary table 5** - Cox models used in risk prediction of the outcomes of pacemaker implantation and heart failure as well as the corresponding competing outcomes of event-free mortality.

***Heart Failure:***

|  |  |  |  |
| --- | --- | --- | --- |
|  | Beta-coefficient | Standard  Error | P-value |
| No BBB | [Ref] | [Ref] | [Ref] |
| BBB RBBB | 0.37502 | 0.04923 | < 0.001 |
| BBB LBBB | 1.30553 | 0.06057 | < 0.001 |
| BBB NIVCD | 1.02830 | 0.04271 | < 0.001 |
| BBB IRBBB | 0.09672 | 0.11449 | 0.398 |
| Male sex | 0.43830 | 0.01968 | < 0.001 |
| Age 40-49 | [Ref] | [Ref] | [Ref] |
| Age 50-59 | 0.63929 | 0.04637 | < 0.001 |
| Age 60-69 | 1.34767 | 0.04386 | < 0.001 |
| Age 70-79 | 2.09015 | 0.04327 | < 0.001 |
| Age 80-89 | 2.63039 | 0.04561 | < 0.001 |
| Age 90-99 | 3.08874 | 0.06962 | < 0.001 |
| Comorbidity | 0.55792 | 0.01970 | < 0.001 |

H0(10)= 0.051525 (10-year baseline cumulative hazard)

***Competing event (Death from all causes without heart failure)***

|  |  |  |  |
| --- | --- | --- | --- |
|  | Beta-coefficient | Standard  Error | P-value |
| No BBB | [Ref] | [Ref] | [Ref] |
| BBB RBBB | 0.04168 | 0.03176 | 0.1894 |
| BBB LBBB | 0.02021 | 0.06043 | 0.7381 |
| BBB NIVCD | 0.09338 | 0.03707 | 0.0118 |
| BBB IRBBB | 0.11049 | 0.06653 | 0.0968 |
| Male sex | 0.38599 | 0.01188 | < 0.001 |
| Age 40-49 | [Ref] | [Ref] | [Ref] |
| Age 50-59 | 0.77976 | 0.03146 | < 0.001 |
| Age 60-69 | 1.49193 | 0.02995 | < 0.001 |
| Age 70-79 | 2.45022 | 0.02916 | < 0.001 |
| Age 80-89 | 3.35215 | 0.02972 | < 0.001 |
| Age 90-99 | 4.27201 | 0.03749 | < 0.001 |
| Comorbidity | 0.44902 | 0.01171 | < 0.001 |

H0(10)= 0.13285 (10-year baseline cumulative hazard)

***Pacemaker implantation***

|  |  |  |  |
| --- | --- | --- | --- |
|  | Beta-coefficient | Standard  Error | P-value |
| No BBB | [Ref] | [Ref] | [Ref] |
| BBB RBBB | 1.44882 | 0.07190 | < 0.001 |
| BBB LBBB | 1.48645 | 0.12629 | < 0.001 |
| BBB NIVCD | 1.60717 | 0.07699 | < 0.001 |
| BBB IRBBB | 0.82529 | 0.19074 | < 0.001 |
| Male sex | 0.49830 | 0.04394 | < 0.001 |
| Age 40-49 | [Ref] | [Ref] | [Ref] |
| Age 50-59 | 1.04940 | 0.14186 | < 0.001 |
| Age 60-69 | 2.11864 | 0.13329 | < 0.001 |
| Age 70-79 | 2.99222 | 0.13173 | < 0.001 |
| Age 80-89 | 3.40676 | 0.13642 | < 0.001 |
| Age 90-99 | 3.70429 | 0.19077 | < 0.001 |
| Comorbidity | 0.29514 | 0.04320 | < 0.001 |

H0(10) = 0.0080481 (10-year baseline cumulative hazard)

***Competing event (Death from all causes without pacemaker implantation)***

|  |  |  |  |
| --- | --- | --- | --- |
|  | Beta-coefficient | Standard  Error | P-value |
| No BBB | [Ref] | [Ref] | [Ref] |
| BBB RBBB | 0.05888 | 0.02949 | 0.0458 |
| BBB LBBB | 0.10609 | 0.05142 | 0.0391 |
| BBB NIVCD | 0.18861 | 0.03230 | < 0.001 |
| BBB IRBBB | 0.11394 | 0.06278 | 0.0695 |
| Male sex | 0.39957 | 0.01108 | < 0.001 |
| Age 40-49 | [Ref] | [Ref] | [Ref] |
| Age 50-59 | 0.79474 | 0.03041 | < 0.001 |
| Age 60-69 | 1.53413 | 0.02888 | < 0.001 |
| Age 70-79 | 2.50249 | 0.02811 | < 0.001 |
| Age 80-89 | 3.40871 | 0.02860 | < 0.001 |
| Age 90-99 | 4.31612 | 0.03565 | < 0.001 |
| Comorbidity | 0.46710 | 0.01093 | < 0.001 |

H0(10)= 0.14387 (10-year baseline cumulative hazard)

**Supplementary table 6 -** Landmark analysis of outcome of incident HF only including individuals with event free survival at 1 year of follow-up.

|  |  |  |
| --- | --- | --- |
|  | **LBBB** | **NIVCD** |
| **Main model** | HR 3.96 (95% CI 3.30 - 4.76, P<0.001) | HR 2.37 (95% CI 2.12-2.65, P<0.001) |
| **Landmark model** | HR 3.58 (95% CI 2.84-4.52, p <0.001) | HR 1.95 (95% CI 1.69-2.25, P <0.001) |

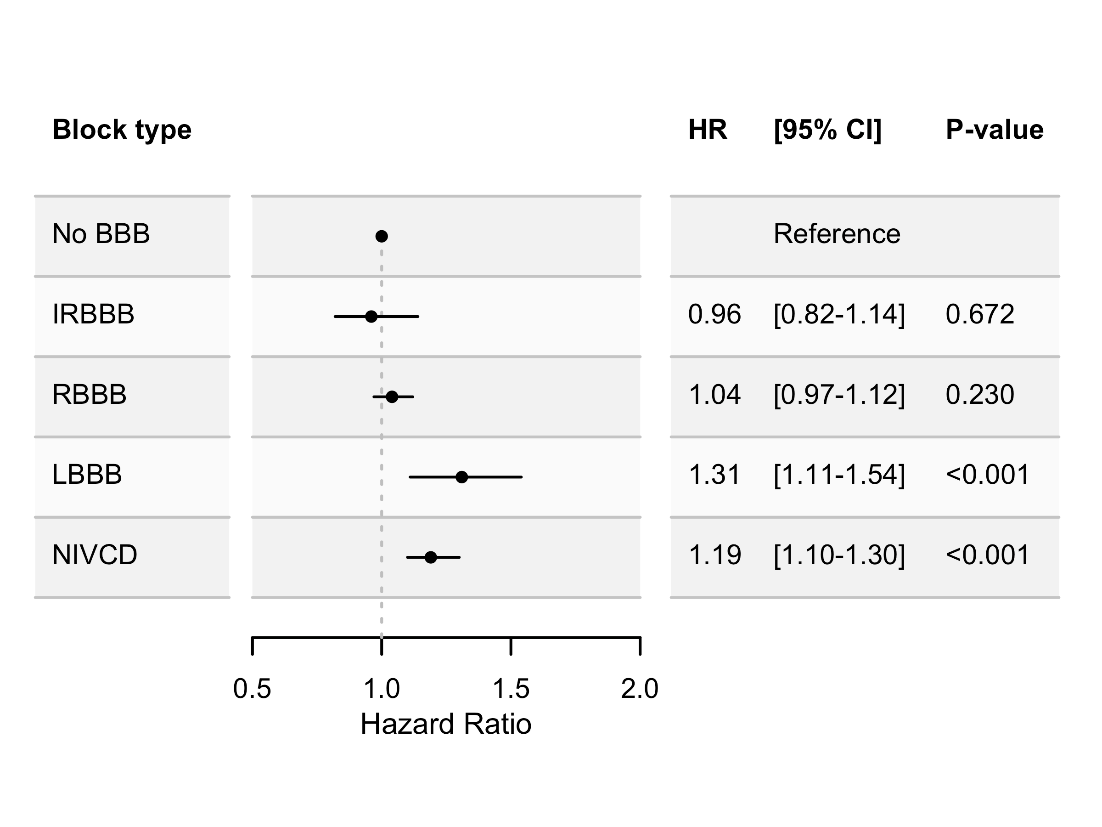
**Men**

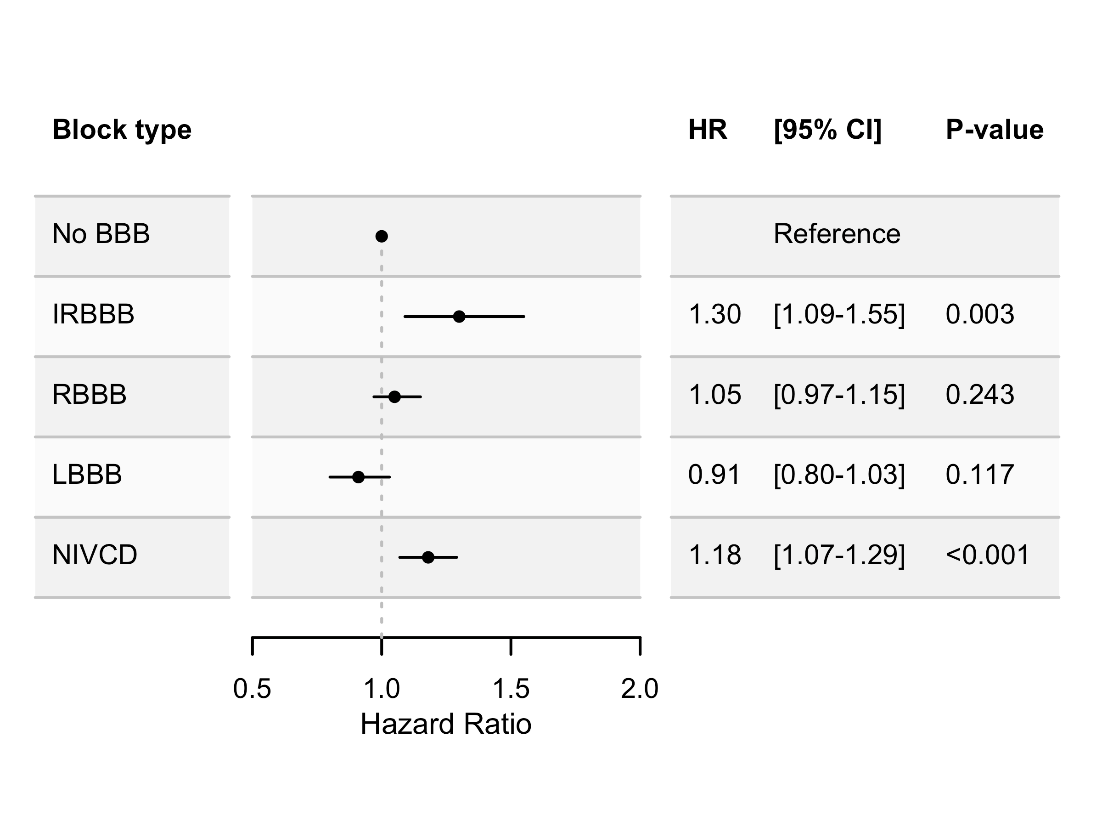
|  |  |  |
| --- | --- | --- |
|  | **LBBB** | **NIVCD** |
| **Main model** | HR 2.51 (95% CI 2.15 – 3.94, P<0.001) | HR 2.80 (95% CI 2.47-3.18, P<0.001) |
| **Landmark model** | HR 2.33 (95% CI 1.92-2.82, P <0.001) | HR 2.56 (95% CI 2.19-3.00, P <0.001) |

**Women**

**Supplemental figure S1**

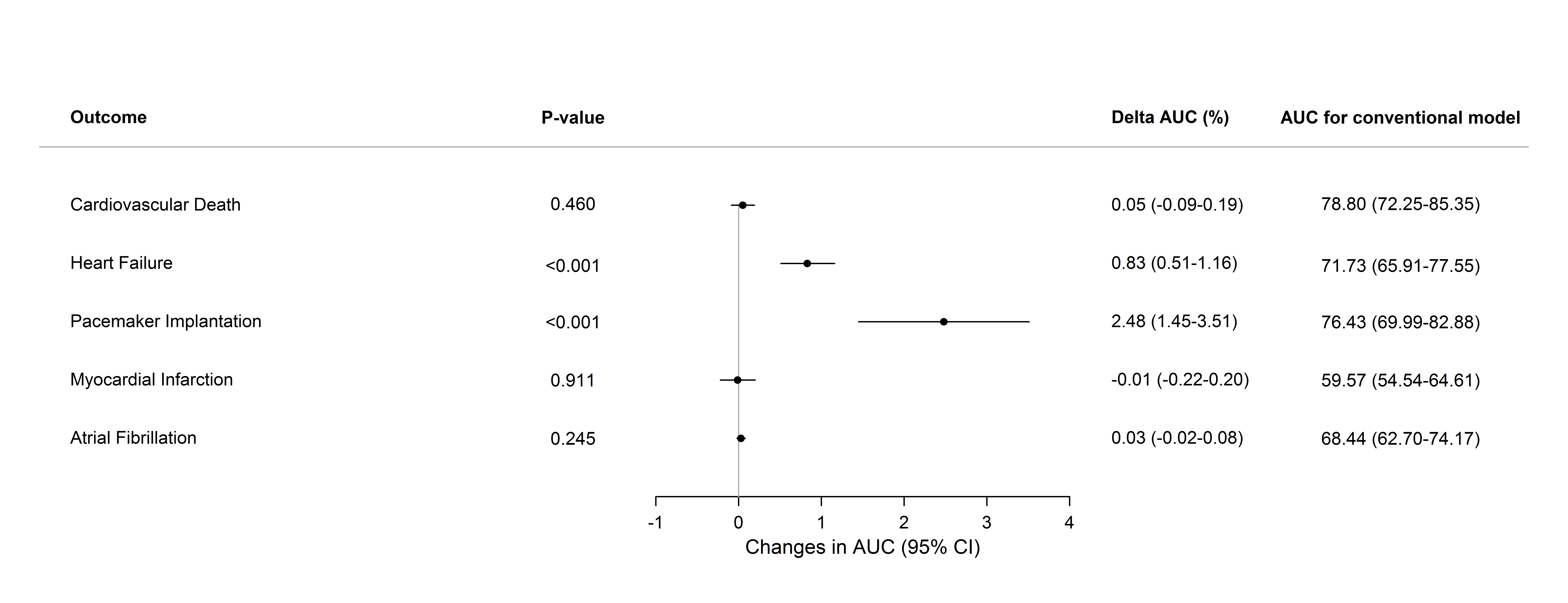
Forest plots depicting multivariable-adjusted hazard ratios by bundle branch blocks and sex for the outcome all-cause mortality

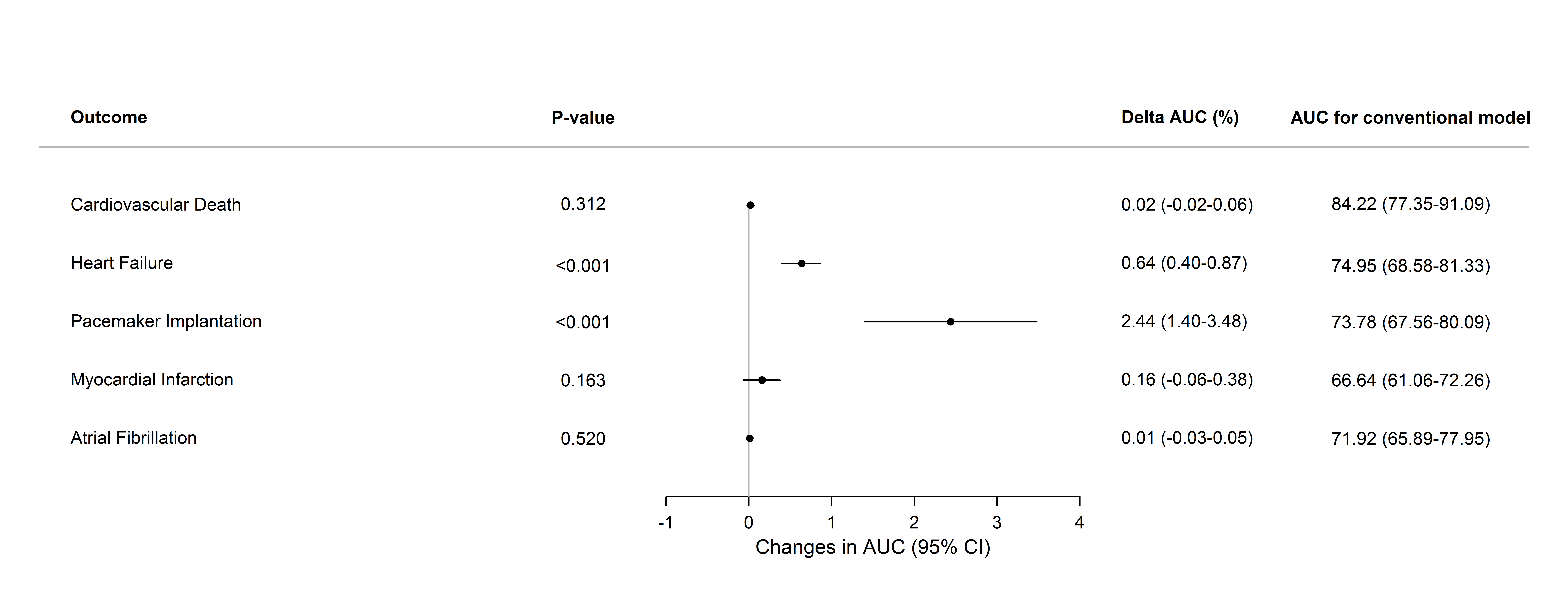
**Men**

**Women**

**Supplemental figure S2**

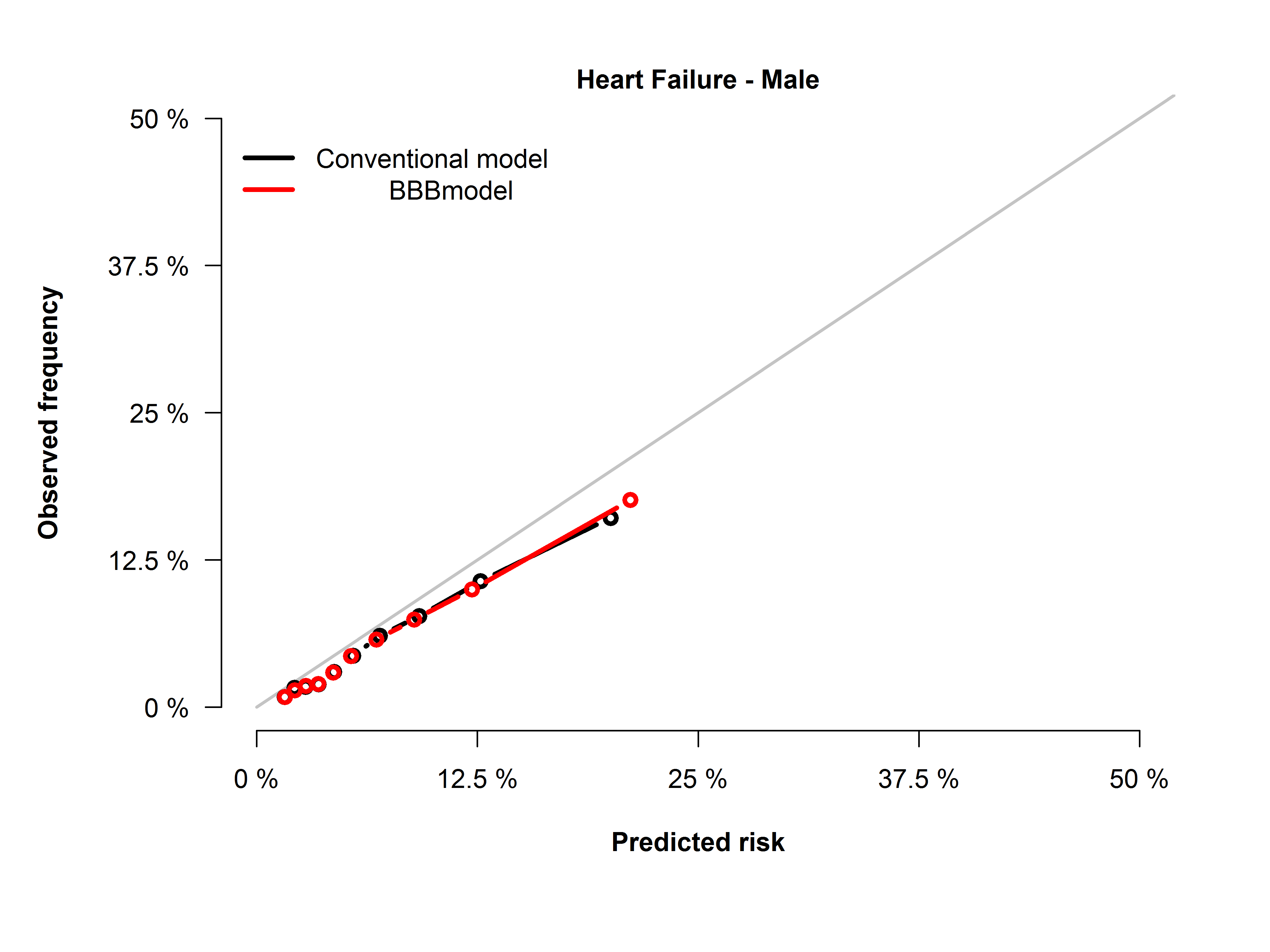
Absolute AUC for conventional risk models for cardiovascular outcomes as well as differences in AUC with p-values for model comparison when introducing BBB subtypes to the conventional risk models.

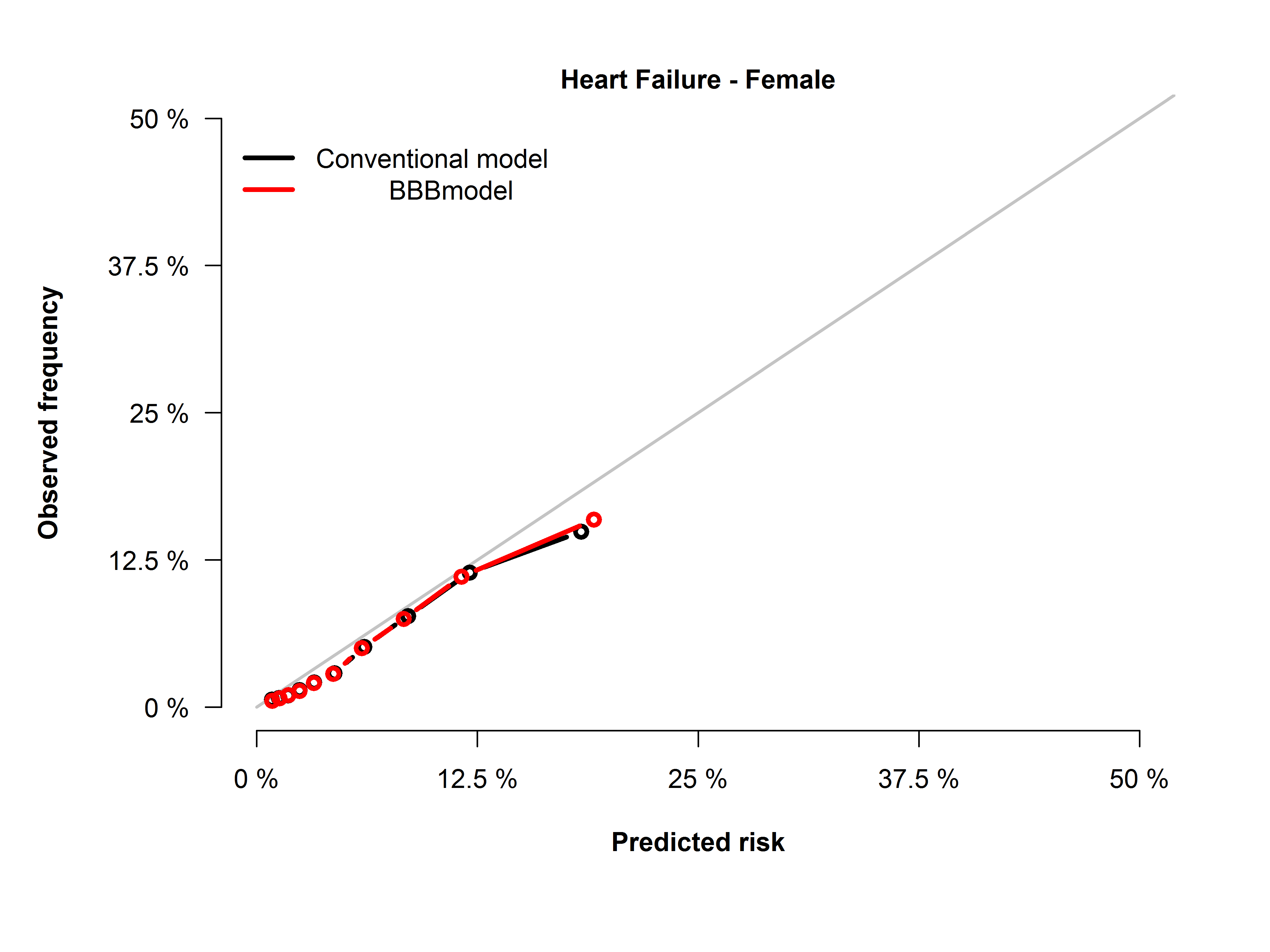
**Men**

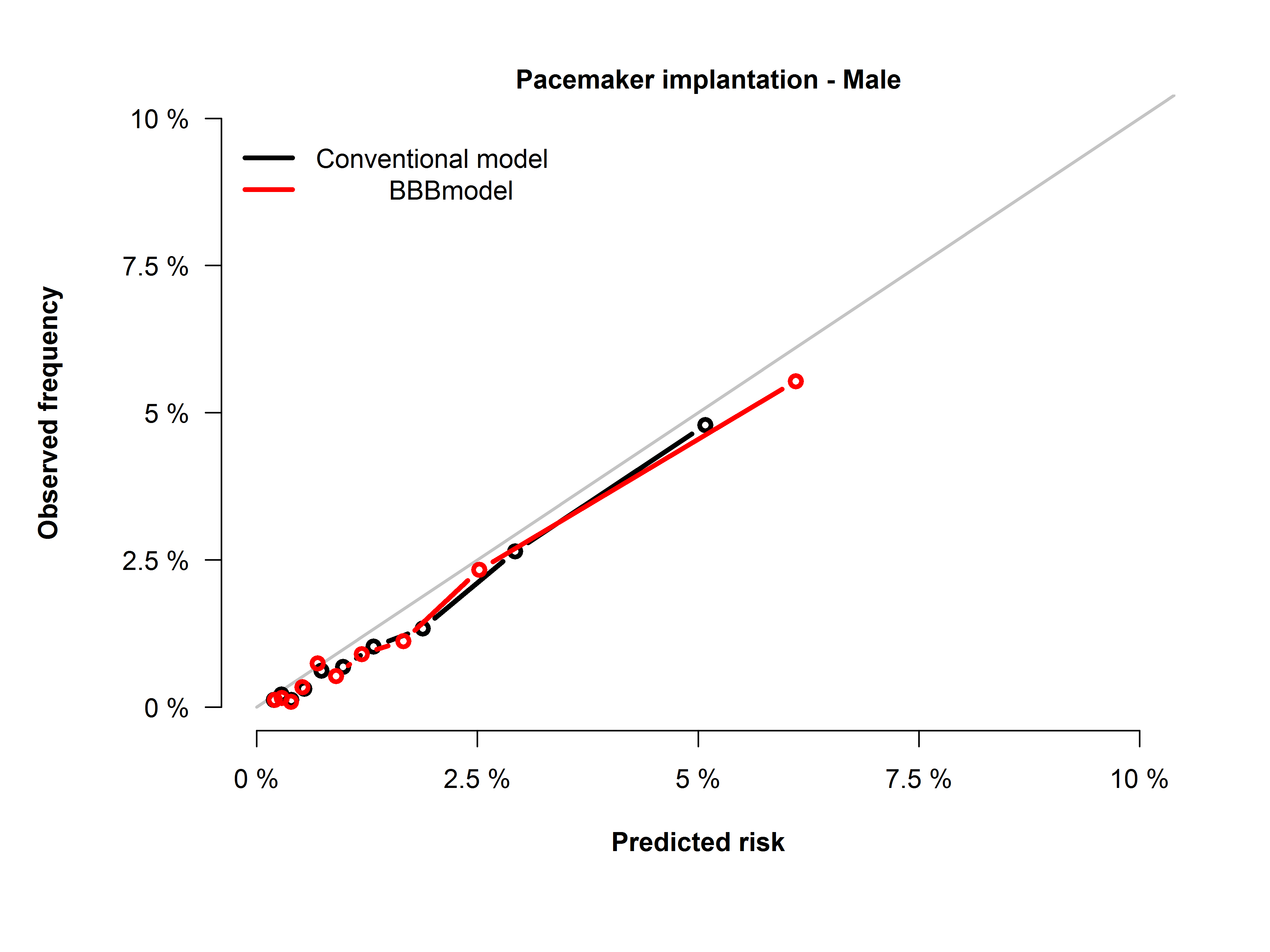
**Women**

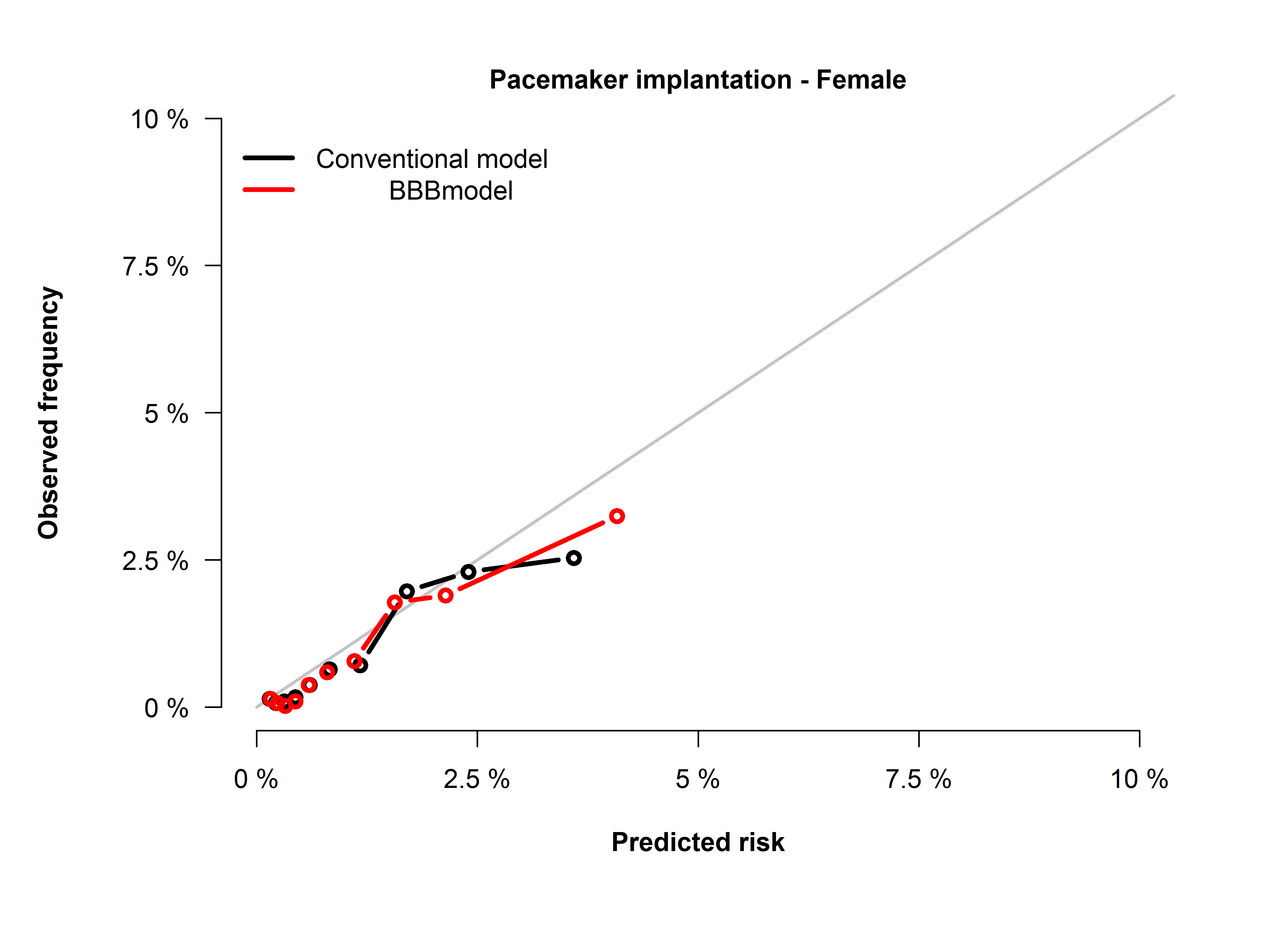
**Supplementary figure S3**

Plots depicting model calibration for the outcomes heart failure and pacemaker implantation for both men and women. Shown are the predicted risks against the observed frequency of the outcome in question with the expected status obtained in groups defined by quantiles of the predicted risks.

A)

B)

C)

D)