**SUPPLEMENTARY DOCUMENT**

Patients in NDR with a diagnosis of type 1 diabetes

(N = 54,004)

Excluded (N = 19): Patients died or had no clinic visit after 1 Jan 2002

Patients alive and have at least one clinic visit after 1 Jan 2002

(N = 53,985)

Excluded (N = 3,874): Patients with missing age at diagnosis

Patients with ages known at diagnosis

(N = 50,111)

Excluded (N = 22,270):

* Patients with an age at diagnosis ≥ 30 years (N = 18,786)
* Patients alive but had no prescriptions filled after 2005\*† (N = 123)
* Patients alive but received no insulin prescriptions after 2005\* (N = 1,545)
* Patients received medications other than insulin for diabetes treatment (N = 1,816)

Study cohort: patients with type 1 diabetes ascertained

(N = 27,841)

\* Year when the prescription records were available

† These patients might have left Sweden after 2005

Figure S1. Flow chart of the selection of the study cohort. NDR, Swedish National Diabetes Register.

Table S1. International Classification of Diseases [9th Revision (ICD-9) and 10th Revision (ICD-10)] and procedure code for major complications considered in the model

|  |  |  |  |
| --- | --- | --- | --- |
| **Event** | **ICD-9 code** | **ICD-10 code** | **Procedure code** |
| Myocardial infarction  (fatal, non-fatal and sudden death) | 410, 798.1, 798.2 | I210-4, I219, R96.0, R96.1 |  |
| Stroke | 431, 434, 436 | I61, I63-5, I67.9 |  |
| Heart failure | 428 | I50 |  |
| Amputation | 84.0, 84.1, 84.12, 84.15, 84.17, 84.19, 87.00. 87.01, 87.02, 87.11, 87.12, 87.50, 87.60, 87.70, 87.71, 87.80, 87.81 |  | NHQ09, NHQ11, NGQ09. NGQ19. NGQ99, NFQ09. NFQ19, NFQ99, NEQ19, NEQ99 |
| Peripheral vascular disease | 250F, 250G, 440A-X, 443A-X | I702, I731, I739, I792, E105, E115, E145 |  |
| Hypoglycaemia | 251A, 251C, 779C, 780A | E100, E106A, E110, E110C, E110X, E120, E130, E140, E116A, E159, E160, E161W, E162, R402 |  |
| Hyperglycaemia | 250B, 250C | E100A-B, E101, E101A-B, E101X, E110A-B, E111, E111A-B, E111X, E121, E131, E141 |  |
| End-stage renal disease | V56A, V42A, 54.98, 60.43, 60.70 | Z491, Z49B, Z992, E878A, Z94A | 3995, 5498, V9211-2, V9531-2, DR014-8, DR020, DR023-4, KAS10, KAS20, V9351-2 |
| Percutaneous coronary intervention |  |  | FNG0, FNG00, FNG02, FNG05, FNG06, FNG10, FNG30, FNG96, 0063, 0966, 0967, 3080 |
| Coronary artery bypass graft |  |  | FNA00, FNA10, FNA20, FNA96, FNB00, FNB20, FNB96, FNC10, FNC20, FNC30, FNC40, FNC50, FNC60, FNC96, FND10, FND20, FND96, FNE00, FNE10, FNE20, FNE96, FNF00, FNF10, FNF20, FNF30, FNF96, 3067, 3080, 3127, 3158 |

Table S2. Covariates considered in model selection

|  |  |  |
| --- | --- | --- |
| Variable | Description (unit) | Transformation applied before model fitting |
| Male | 1 for male; 0 for female |  |
| Age\_diag | Age at diagnosis of type 1 diabetes (years) | Age\_diag - 15 |
| Age | Age used in interaction terms with other covariates | Age - 50 |
| HbA1c | Current glycated haemoglobin (%), standardized based on the US National Glycohemoglobin Standardization Program (NGSP) | Ln(HbA1c) – Ln(8) |
| Lag\_HbA1c | One-year lagged value of HbA1c (%) | Ln(Lag\_HbA1c) |
| wHbA1c | Time-weighted mean HbA1c (%) of HbA1c measured over the past period from study entry to the time point immediately before the current time point | Ln(wHbA1c) – Ln(8) |
| BMI\* | Body biomass index (kg/m2) | BMI – 25 |
| Lag\_BMI\* | One-year lagged value of body biomass index (kg/m2) | Lag\_BMI - 25 |
| BMI\_cat1† | BMI (kg/m2) category 1, used as reference;  22.50 < BMI ≤ 25.00 |  |
| BMI\_cat2† | BMI (kg/m2) category 2;  BMI ≤ 20.00 |  |
| BMI\_cat3† | BMI (kg/m2) category 3;  20.00 < BMI ≤ 22.50 |  |
| BMI\_cat4† | BMI (kg/m2) category 4;  25.00 < BMI ≤ 27.50 |  |
| BMI\_cat5† | BMI (kg/m2) category 5;  27.50 < BMI ≤ 30.00 |  |
| BMI\_cat6† | BMI (kg/m2) category 6;  BMI > 30 |  |
| SBP | Systolic blood pressure (mmHg) | SBP - 130 |
| Lag\_SBP | One-year lagged value of systolic blood pressure (mmHg) | Lag\_SBP - 130 |
| Triglycerides | Triacylglycerol (mmol/L) |  |
| Lag\_Triglycerides | One-year lagged value of triacylglycerol (mmol/L) |  |
| HDL | High-density lipoprotein cholesterol (mmol/L) |  |
| Lag\_HDL | One-year lagged value of high-density lipoprotein cholesterol (mmol/L) |  |
| LDL | Low-density lipoprotein cholesterol (mmol/L) |  |
| Lag\_LDL | One-year lagged value of low-density lipoprotein cholesterol (mmol/L) |  |
| Microalbuminuria | Albumin/creatinine ratio 3–30 mg/mmol or urinary albumin excretion rate 20–200 μg/min or 20–300 mg/l, in two out of three consecutive tests |  |
| Macroalbuminuria | Albumin/creatinine ratio >30 mg/mmol or urinary albumin excretion rate >200 μg/min or >300 mg/l, in two out of three consecutive tests |  |
| eGFR | Estimated glomerular filtration rate (mL/min/1.73 m2) | Ln(eGFR) – Ln(90) |
| Lag\_ eGFR | One-year lagged value of Estimated glomerular filtration rate (mL/min/1.73 m2) | Ln(Lag\_eGFR) – Ln(90) |
|  |  |  |
| Smoker | 1 for current smoker; 0 otherwise |  |
| Ex-smoker | 1 for former smoker; 0 otherwise |  |
| Year | Number of years since study entry |  |
| Prior\_MI | 1 for a history of myocardial infarction; 0 otherwise |  |
| Time\_since\_MI | Time since the last occurrence of myocardial infarction | Ln(Time\_since\_MI) |
| Prior stroke | 1 for a history of stroke; 0 otherwise |  |
| Time\_since\_stroke | Time since the last occurrence of myocardial infarction if Prior\_stroke = 1; 1 otherwise | Ln(Time\_since\_stroke) |
| Prior\_HF | 1 for a history of heart failure; 0 otherwise |  |
| Time\_since\_HF | Time since the last hospitalisation due to heart failure if Prior\_HF = 1; 1 otherwise | Ln(Time\_since\_HF) |
| Prior\_PCI | 1 for a history of percutaneous coronary intervention; 0 otherwise |  |
| Time\_since\_PCI | Time since the last occurrence of percutaneous coronary intervention if Prior\_PCI = 1; 1 otherwise | Ln(Time\_since\_PCI) |
| Prior\_CABG | 1 for a history of coronary artery bypass graft; 0 otherwise |  |
| Time\_since\_CABG | Time since the last occurrence of coronary artery bypass graft if Prior\_CABG = 1; 1 otherwise | Ln(Time\_since\_CABG) |
| Prior\_ANG | 1 for a history of unstable angina; 0 otherwise |  |
| Time\_since\_ANG | Time since the last hospitalisation due to unstable angina if Prior\_ANG = 1; 1 otherwise | Ln(Time\_since\_ANG) |
| Prior\_PVD | 1 for a history of peripheral vascular disease; 0 otherwise |  |
| Time\_since\_PVD | Time since the last hospitalisation due to peripheral vascular disease if Prior\_PVD = 1; 1 otherwise | Ln(Time\_since\_PVD) |
| Prior\_AMP | 1 for a history of amputation; 0 otherwise |  |
| Time\_since\_AMP | Time since the last occurrence of amputation if Prior\_AMP = 1; 1 otherwise | Ln(Time\_since\_AMP) |
| Prior\_hypoGL | 1 for a history of hypoglycaemia; 0 otherwise |  |
| Time\_since\_hypoGL | Time since the last occurrence of hypoglycaemia if Prior\_hypoGL = 1; 1 otherwise | Ln(Time\_since\_hypoGL) |
| Prior\_hyperGL | 1 for a history of hyperglycaemia; 0 otherwise |  |
| Time\_since\_hyperGL | Time since the last occurrence of hyperglycaemia if Prior\_hyperGL = 1; 1 otherwise | Ln(Time\_since\_hyperGL) |
| Prior\_ESRD | 1 for a history of end-stage renal disease; 0 otherwise |  |
| Time\_since\_ESRD | Time since the last occurrence of end-stage renal disease if Prior\_ESRD = 1; 1 otherwise | Ln(Time\_since\_ESRD) |
| Prior\_x\_events | 1 if there were x events occurring in the past; 0 otherwise (x = 1, 2, …, 6) |  |

\* Used in the linear models for progression of other risk factors (see Tables S6 and S7).

† Used in the proportional hazards models for events (see Table S5)

Table S3. Baseline characteristics of the type 1 diabetes population used in the simulation (n = 27,841)

|  |  |
| --- | --- |
| Variable | Value\* |
| Male, % | 55.6 |
| Age | 36.98 (14.94) |
| Age at onset | 15.01 (7.60) |
| HbA1c, % | 8.10 (1.38) |
| Body biomass index, kg/m2 | 24.90 (3.71) |
| Systolic blood pressure, mmHg | 127.30 (16.91) |
| Triglycerides, mmol/L | 1.16 (0.85) |
| High-density lipoprotein cholesterol, mmol/L | 1.59 (0.46) |
| Low-density lipoprotein cholesterol, mmol/L | 2.72 (0.82) |
| Microvascular disease, % | 21.0 |
| Macrovascular disease, % | 8.3 |
| Estimated glomerular filtration rate, mL/min/1.73 m2 | 96.05 (26.52) |
| Current smoker, % | 13.6 |
| Former smoker, % | 4.3 |
| History of myocardial infarction, % | 2.9 |
| History of stroke, % | 1.8 |
| History of congestive heart failure, % | 1.3 |
| History of percutaneous coronary intervention, % | 1.4 |
| History of coronary artery bypass graft, % | 2.5 |
| History of ischemic heart disease, % | 1.0 |
| History of peripheral vascular disease, % | 3.7 |
| History of amputation, % | 4.2 |
| History of hypoglycaemia, % | 14.0 |
| History of hyperglycaemia, % | 14.2 |
| History of end-stage renal disease, % | 0.6 |

\* Values represent mean (standard deviation) except for those in per cents.

Table S4. Number of events, total patient-years and annual event rates in a cohort of 27,841 patients with type 1 diabetes

|  |  |  |  |
| --- | --- | --- | --- |
| Event/hospitalisation | Number of events | Total patient-years\* | Event rate (number of events per person-year) |
| Death | 2018 | 194,685.1 | 0.0104 |
| First MI | 1,308 | 191,671.2 | 0.0068 |
| Second MI | 375 | 2,312.6 | 0.1622 |
| Third MI | 152 | 488.3 | 0.3113 |
| First stroke | 671 | 192,725.1 | 0.0035 |
| Second stroke | 269 | 1,191.7 | 0.2257 |
| Third stroke | 120 | 432.1 | 0.2777 |
| First PCI | 715 | 192,176.1 | 0.0037 |
| Second PCI | 257 | 1,733.9 | 0.1482 |
| Third PCI | 105 | 461.1 | 0.2277 |
| First CABG | 461 | 192,884.9 | 0.0024 |
| Second CABG | 30 | 1,692.0 | 0.0177 |
| Third CABG | 9 | 75.6 | 0.1190 |
| First CHF hospitalisation | 737 | 193,034.8 | 0.0038 |
| Second CHF hospitalisation | 379 | 891.9 | 0.4254 |
| Third CHF hospitalisation | 219 | 323.7 | 0.6766 |
| First PVD hospitalisation | 1,237 | 190,371.5 | 0.0065 |
| Second PVD hospitalisation | 786 | 1,678.8 | 0.4682 |
| Third PVD hospitalisation | 529 | 968.4 | 0.5463 |
| First amputation | 721 | 192,695.1 | 0.0037 |
| Second amputation | 337 | 1,039.8 | 0.3241 |
| Third amputation | 171 | 450.0 | 0.3800 |
| First hypoglycaemia hospitalisation | 1,817 | 188,378.7 | 0.0096 |
| Second hypoglycaemia hospitalisation | 1,052 | 2,549.7 | 0.4126 |
| Third hypoglycaemia hospitalisation | 641 | 1,605.9 | 0.3992 |
| First hyperglycaemia hospitalisation | 1,627 | 189,001.1 | 0.0086 |
| Second hyperglycaemia hospitalisation | 1,005 | 2,182.5 | 0.4605 |
| Third hyperglycaemia hospitalisation | 614 | 1,438.7 | 0.4268 |
| First ESRD hospitalisation | 1,459 | 190,331.5 | 0.0077 |
| Second ESRD hospitalisation | 1,107 | 1,301.5 | 0.8506 |
| Third ESRD hospitalisation | 893 | 738.0 | 1.2100 |

\* For the first event, time at risk started from the first clinic visit; for the second or third events, time at risk started from the first or second event, respectively. CABG, coronary artery bypass graft; CHF, congestive heart failure; ESRD, end-stage renal disease; MI, myocardial infarction; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease.

Table S5. Functional forms, beta coefficients and parameters of the parametric proportional hazards models for estimating the probabilities of events. See Table S2 for description of the variables. Values in brackets are standard errors of the coefficient estimates

|  | **1st CVD (No prior HF)** | **1st CVD - Prior HF** | **2nd CVD** | **1st stroke** | **2nd stroke** | **HF (No prior MI)** | **HF (Prior MI)** | **PVD** | **1st amputation** | **2nd amputation** | **1st hypoGL** | **2nd hypoGL** | **1st hyperGL** | **2nd hyperGL** | **End-stage renal disease** | **Death** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Functional form**  **Variable** | Weibull | Weibull | Weibull | Gompertz | Weibull | Gompertz | Gompertz | Weibull | Weibull | Weibull | Gompertz | Gompertz | Weibull | Gompertz | Gompertz | Gompertz |
| Male |  |  |  |  |  | 0.298 (0.145) |  |  | 0.446 (0.101) | 0.473 (0.119) | 0.277 (0.068) | 0.223 (0.071) |  |  | 0.270 (0.072) | 0.352 (0.069) |
| Male \* Age |  |  |  |  |  |  |  | 0.024 (0.006) |  |  |  |  |  |  |  | -0.012 (0.004) |
| Age at diagnosis | -0.022 (0.004) |  |  |  |  | -0.024 (0.009) |  | -0.016 (0.006) | -0.017 (0.006) |  |  | -0.011 (0.005) |  |  |  |  |
| Age at diagnosis \* Age |  |  |  |  |  |  |  |  |  |  |  |  | -0.001 (0) |  |  |  |
| Ln(HbA1c) | 0.975 (0.288) |  |  |  | 1.144 (0.432) |  |  | 1.344 (0.422) |  | 1.301 (0.323) | 0.487 (0.229) |  | 3.465 (0.29) | 2.016 (0.297) |  |  |
| Ln(HbA1c) \* Age |  |  |  |  |  |  |  | -0.078 (0.023) |  |  | 0.043 (0.020) |  | -0.054 (0.015) | -0.032 (0.014) |  |  |
| Ln(wHbA1c) | 1.054 (0.32) |  |  | 1.312 (0.336) |  | 1.159 (0.504) |  | 2.892 (0.345) | 2.138 (0.347) |  |  |  |  |  | 0.652 (0.232) |  |
| Ln(wHbA1c) \* Age | -0.045 (0.019) |  |  |  |  |  |  |  |  |  | -0.060 (0.019) |  |  |  |  |  |
| bmicat2 (<= 20) |  |  | 0.390 (0.145) | 0.399 (0.163) |  |  |  |  |  |  |  | 0.508 (0.109) | 0.382 (0.133) |  | 0.279 (0.12) | 0.68 (0.084) |
| bmicat3 (>20 and <= 22.5 |  |  |  |  |  |  |  |  |  |  |  | 0.191 (0.083) | 0.233 (0.091) |  |  | 0.217 (0.07) |
| bmicat4 (> 25 and <= 27.5) |  |  | 0.124 (0.064) |  |  |  |  |  |  |  |  |  |  |  |  |  |
| bmicat5 (> 27.5 and <= 30) | 0.269 (0.083) |  |  |  |  |  |  |  |  |  |  |  |  |  | -0.240 (0.104) |  |
| bmicat6 (> 30) | 0.259 (0.085) |  |  |  |  | 0.558 (0.171) |  |  | -0.323 (0.145) |  |  |  |  |  |  | 0.308 (0.073) |
| bmicat2 \* Age |  |  | -0.016 (0.009) |  |  |  |  |  |  |  |  |  |  |  |  |  |
| SBP |  |  |  | 0.018 (0.003) |  |  |  | 0.007 (0.002) |  |  |  |  |  |  | 0.008 (0.002) |  |
| Triglycerides | 0.155 (0.037) |  | 0.068 (0.032) |  |  | 0.174 (0.081) |  | 0.167 (0.044) | 0.148 (0.055) |  |  |  | 0.121 (0.04) | 0.217 (0.028) | 0.1300 (0.033) | 0.097 (0.032) |
| Triglycerides \* Age |  |  |  |  |  |  |  |  |  |  |  |  |  |  | -0.008 (0.003) | -0.006 (0.002) |
| HDL | -0.264 (0.078) |  |  | -0.293 (0.120) |  |  |  |  |  |  | 0.134 (0.069) | 0.187 (0.071) | 0.296 (0.077) | 0.248 (0.071) |  | 0.225 (0.069) |
| HDL \* Age | 0.009 (0.004) |  |  | 0.022 (0.008) |  |  |  |  |  |  |  |  |  |  |  | -0.010 (0.004) |
| LDL | 0.223 (0.039) |  | 0.139 (0.037) |  |  |  |  |  |  |  |  |  |  |  |  |  |
| LDL \* Age | -0.009 (0.003) |  | -0.008 (0.003) |  |  |  |  |  |  |  |  |  |  |  | -0.009 (0.003) |  |
| Microalbuminuria | 0.229 (0.078) | 0.709 (0.258) | 0.239 (0.06) | 0.411 (0.121) |  | 0.594 (0.163) | 0.503 (0.156) | 0.480 (0.102) | 0.269 (0.11) |  |  | 0.205 (0.08) |  | 0.295 (0.104) | 0.975 (0.158) | 0.297 (0.067) |
| Microalbuminuria \* Age |  |  |  |  |  |  |  |  |  |  |  |  |  | 0.022 (0.006) | -0.024 (0.008) |  |
| Macroalbuminuria | 0.206 (0.100) |  |  | 0.433 (0.145) |  |  | 0.354 (0.159) |  |  |  |  |  |  |  | 0.329 (0.106) | 0.213 (0.075) |
| Macroalbuminuria \* Age |  |  |  |  |  |  |  |  |  |  |  | -0.016 (0.007) |  |  |  |  |
| Ln(eGFR) | -0.292 (0.030) | -0.150 (0.060) | -0.137 (0.026) | -0.163 (0.041) | -0.245 (0.056) | -0.943 (0.203) |  | -0.317 (0.036) |  |  | -0.258 (0.027) | -0.096 (0.027) |  | 0.505 (0.159) | -3.525 (0.084) |  |
| Ln(eGFR) \* Age |  |  |  | 0.027 (0.010) |  |  |  | 0.019 (0.01) |  | 0.011 (0.003) |  |  | -0.042 (0.009) |  |  |  |
| Smoking | 0.446 (0.094) |  |  |  |  | 0.445 (0.202) | 0.473 (0.188) | 0.388 (0.122) |  |  | 0.337 (0.089) | 0.191 (0.089) | 0.424 (0.096) |  |  | 0.408 (0.073) |
| Smoker \* Age | -0.021 (0.008) |  |  |  |  |  |  |  |  |  |  |  |  | -0.016 (0.004) |  |  |
| Ex-smoker | 0.200 (0.09) |  |  |  |  |  |  |  |  |  |  |  | 0.282 (0.113) |  |  | 0.16 (0.076) |
| Ex-smoker \* Age |  |  |  |  |  |  |  |  |  |  |  | 0.012 (0.007) |  | -0.014 (0.006) | 0.023 (0.008) |  |
| Year | -0.064 (0.012) |  | -0.026 (0.011) |  |  |  |  | -0.056 (0.018) |  |  |  |  |  |  | 0.14 (0.015) |  |
| Year \* Age |  |  |  | -0.002 (0.001) |  |  |  |  |  |  |  |  |  |  |  |  |
| Prior MI |  |  | 1.230 (0.117) |  |  |  |  | 1.182 (0.189) | 1.498 (0.27) |  |  | 0.476 (0.2) | 2.027 (0.242) | 1.676 (0.219) | 2.273 (0.175) | 4.364 (0.147) |
| Ln(Time\_since\_MI) |  |  | -0.694 (0.050) |  |  |  | -1.83 (0.096) | -0.652 (0.153) | -0.259 (0.117) |  |  | -0.322 (0.121) | -0.712 (0.177) | -0.883 (0.181) | -0.646 (0.086) | -2.211 (0.125) |
| Prior\_MI \* Age |  |  | 0.019 (0.006) | 0.039 (0.012) |  |  |  |  |  | 0.011 (0.007) | 0.034 (0.008) |  |  |  | -0.017 (0.008) | -0.046 (0.006) |
| Ln(Time\_since\_MI) \* Age |  |  |  | -0.021 (0.008) |  |  |  | 0.016 (0.007) |  |  |  |  | -0.023 (0.010) |  |  | 0.036 (0.006) |
| Prior\_stroke | 0.357 (0.108) |  | 0.256 (0.074) |  |  | 0.864 (0.178) |  | 0.619 (0.14) | 1.211 (0.215) |  | 1.474 (0.227) |  | 0.637 (0.169) |  | 2.034 (0.244) | 2.392 (0.139) |
| Ln(Time\_since\_stroke) |  |  |  |  | -0.887 (0.083) |  |  |  |  |  | -0.350 (0.135) |  |  |  | -0.776 (0.161) | -1.034 (0.107) |
| Prior\_stroke \* Age |  |  |  |  |  |  |  |  |  |  | -0.019 (0.011) |  |  |  | -0.045 (0.018) |  |
| Ln(Time\_since\_stroke) \* Age |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 0.035 (0.011) | 0.010 (0.005) |
| Prior\_HF |  |  | 1.053 (0.127) |  |  |  |  |  | 2.650 (0.372) | 0.789 (0.228) | 0.792 (0.280) |  |  |  | 1.814 (0.202) | 1.305 (0.138) |
| Ln(Time\_since\_HF) |  |  | -0.354 (0.066) |  |  |  |  |  | -1.173 (0.263) | -0.304 (0.144) | -0.476 (0.189) | 0.186 (0.081) |  |  | -0.351 (0.111) | 0.168 (0.087) |
| Prior\_HF \* Age |  |  | -0.014 (0.006) |  |  |  |  |  | -0.032 (0.017) |  |  |  |  |  |  |  |
| Ln(Time\_since\_HF) \* Age |  |  |  |  |  |  |  |  | 0.043 (0.014) |  |  |  |  |  |  | -0.012 (0.004) |
| Prior\_PCI |  |  | 0.810 (0.129) |  |  |  | -1.460 (0.211) |  | -1.241 (0.372) |  |  |  | -1.336 (0.476) | -0.630 (0.28) |  | -1.500 (0.15) |
| Ln(Time\_since\_PCI) |  |  | -0.527 (0.088) |  |  |  | 0.467 (0.146) |  | 0.52 (0.219) |  |  |  | 0.571 (0.274) |  |  | 0.712 (0.087) |
| Prior\_PCI \* Age |  |  | -0.024 (0.009) |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Ln(Time\_since\_PCI) \* Age |  |  | 0.019 (0.006) |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Prior\_CABG |  |  | -1.739 (0.168) | 1.772 (0.362) |  | 2.045 (0.410) | -1.516 (0.293) | 0.950 (0.201) |  |  |  |  | -0.661 (0.238) |  | -0.881 (0.291) | -1.532 (0.188) |
| Ln(Time\_since\_CABG) |  |  | 0.657 (0.075) | -0.906 (0.243) |  | -0.582 (0.216) | 0.660 (0.132) |  |  |  |  |  |  |  | 0.476 (0.135) | 0.694 (0.084) |
| Prior\_CABG \* Age |  |  |  | -0.065 (0.026) |  |  |  | -0.032 (0.013) |  |  |  |  |  |  |  |  |
| Ln(Time\_since\_CABG) \* Age |  |  |  | 0.04 (0.014) |  |  |  |  |  |  |  |  |  |  |  |  |
| Prior\_ANG |  |  | 2.459 (0.123) | 0.483 (0.211) |  | 0.779 (0.244) |  |  |  |  |  |  |  | 0.726 (0.244) | 1.458 (0.399) | 4.286 (0.193) |
| Ln(Time\_ since\_ANG) |  |  | -1.877 (0.126) |  |  |  |  |  | 0.467 (0.135) |  |  |  |  |  | -0.654 (0.255) | -2.221 (0.212) |
| Prior\_ANG \* Age |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | -0.048 (0.011) |
| Ln(Time\_since\_ANG) \* Age |  |  | 0.022 (0.007) |  |  |  |  |  |  |  |  |  |  |  | 0.022 (0.008) | 0.048 (0.010) |
| Prior\_PVD | 0.362 (0.094) |  |  | 0.777 (0.159) |  | 0.400 (0.194) | 0.529 (0.153) |  | 5.045 (0.183) |  | 0.974 (0.274) |  |  | 0.649 (0.280) | 1.157 (0.273) | 1.388 (0.175) |
| Ln(Time\_since\_PVD) |  |  |  |  |  |  |  |  | -1.248 (0.065) |  | -0.254 (0.123) | 0.098 (0.045) |  | -0.36 (0.142) | -0.227 (0.115) | -0.206 (0.066) |
| Prior\_PVD \* Age |  |  |  | -0.03 (0.011) |  |  |  |  |  |  |  |  |  |  | -0.063 (0.023) |  |
| Ln(Time\_since\_PVD) \* Age |  |  |  |  |  |  |  |  |  |  |  | -0.008 (0.003) |  | -0.026 (0.006) | 0.029 (0.010) |  |
| Prior\_AMP | 0.308 (0.093) |  |  | 0.988 (0.235) |  | 1.412 (0.312) | 0.339 (0.152) |  |  |  | 0.735 (0.234) |  | 0.445 (0.142) |  | 0.645 (0.12) | 1.888 (0.131) |
| Ln(Time\_since\_AMP) |  |  |  | -0.273 (0.108) |  | -0.391 (0.144) |  |  |  | -0.918 (0.073) | -0.309 (0.111) |  |  |  |  | -0.447 (0.048) |
| Prior\_AMP \* Age |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Ln(Time\_since\_AMP) \* Age |  |  |  |  |  |  |  |  |  | 0.007 (0.005) |  |  |  |  |  |  |
| Prior\_hypoGL |  |  |  | 0.284 (0.111) |  | 0.350 (0.158) |  | 0.294 (0.110) | 1.182 (0.279) | 0.176 (0.116) |  |  | 1.372 (0.172) | 0.649 (0.097) | 0.82 (0.19) | 2.6 (0.123) |
| Ln(Time\_since\_hypoGL) |  |  | 0.060 (0.031) |  |  |  |  |  | -0.344 (0.123) |  |  | -0.767 (0.037) | -0.53 (0.092) |  | -0.168 (0.082) | -0.867 (0.059) |
| Prior\_hypoGL \* Age |  |  |  |  |  |  |  |  | -0.048 (0.017) |  |  |  | 0.029 (0.01) | -0.019 (0.008) |  | -0.059 (0.006) |
| Ln(Time\_since\_hypoGL) \* Age |  |  |  |  |  |  |  |  | 0.024 (0.009) |  |  | 0.004 (0.002) | -0.018 (0.005) | 0.019 (0.003) |  | 0.03 (0.003) |
| Prior\_hyperGL | 0.711 (0.196) |  |  | 0.982 (0.258) | 0.536 (0.154) |  | -1.007 (0.392) | 0.379 (0.127) | 1.65 (0.279) |  | 1.735 (0.146) | 0.874 (0.135) |  |  | 1.119 (0.22) | 1.578 (0.142) |
| Ln(Time\_since\_hyperGL) | -0.266 (0.09) |  |  | -0.273 (0.117) |  |  | 0.430 (0.174) |  | -0.528 (0.114) |  | -0.508 (0.069) | -0.172 (0.062) |  | -0.831 (0.05) | -0.252 (0.087) | -0.309 (0.056) |
| Prior\_hyperGL \* Age |  |  |  |  |  |  |  |  | 0.030 (0.011) | 0.049 (0.017) |  |  |  |  |  |  |
| Ln(Time\_since\_hyperGL) \* Age |  |  |  |  |  |  |  |  |  | -0.022 (0.01) |  |  |  | 0.01 (0.003) |  | 0.005 (0.002) |
| Prior\_ESRD |  |  |  |  |  | -2.976 (0.843) |  |  | 2.060 (0.214) | 1.248 (0.145) |  |  | 1.532 (0.232) | 2.102 (0.716) |  | 1.198 (0.14) |
| Ln(Time\_since\_ESRD) |  |  | -0.171 (0.087) |  | -0.537 (0.211) |  |  |  |  |  |  |  | -0.897 (0.243) |  |  | 0.217 (0.075) |
| Prior\_ESRD \* Age | -0.035 (0.010) |  |  | 0.085 (0.045) |  |  |  | 0.071 (0.044) | -0.052 (0.011) |  |  |  | -0.169 (0.04) | -0.038 (0.013) |  |  |
| Ln(Time\_since\_ESRD) \* Age |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Prior\_2\_events |  |  |  |  |  |  |  |  | -0.575 (0.234) |  |  |  |  |  | -0.573 (0.154) | -0.327 (0.139) |
| Prior\_2\_events \* Age |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Prior\_3\_events |  |  |  |  |  |  |  |  | -1.491 (0.393) |  |  |  |  |  | -1.002 (0.250) | -1.118 (0.226) |
| Prior\_3\_events \* Age |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Prior\_4\_events |  |  |  |  |  |  |  |  | -2.248 (0.572) |  |  |  |  |  | -1.685 (0.361) | -2.399 (0.331) |
| Prior\_4\_events \* Age |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 0.026 (0.008) |
| Prior\_5\_events |  |  |  |  |  |  |  |  | -3.224 (0.764) |  |  |  |  |  | -2.156 (0.525) | -2.841 (0.412) |
| Prior\_5\_events\_5 \* Age |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Prior\_6\_events |  |  |  |  |  |  |  |  | -4.747 (1.134) |  |  |  |  |  | -3.647 (0.891) | -5.896 (0.617) |
| Prior\_6\_events \* Age |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 0.066 (0.022) |
| Constant | -19.36 (1.325) | -9.273 (1.524) | -5.992 (1.387) | -13.430 (0.624) | -2.830 (0.953) | -10.755 (0.326) | -2.951 (0.382) | -14.530 (0.865) | -13.526 (0.752) | -6.028 (1.545) | -5.825 (0.147) | -3.057 (0.197) | -5.064 (0.277) | -2.714 (0.192) | -10.633 (0.415) | -10.02 (0.417) |
| Shape parameter | 4.634 (0.341) | 2.550 (0.357) | 1.715 (0.322) | 0.075 (0.006) | 1.198 (0.209) | 0.082 (0.007) | 0.043 (0.007) | 3.293 (0.224) | 2.489 (0.191) | 1.870 (0.363) | 0.008 (0.003) | 0.010 (0.004) | 0.695 (0.057) | -0.011 (0.006) | 0.050 (0.011) | 0.095 (0.010) |

CVD, cardiovascular event including myocardial infarction, percutaneous coronary intervention and coronary artery bypass graft; HF, heart failure; MI, myocardial infarction; PVD, peripheral vascular disease; hypoGL, hypoglycaemia; hyperGL, hyperglycaemia; eGFR, estimated glomerular filtration rate.

Table S6. Beta coefficients in the linear regression models for progression of continuous risk factors. See Table S2 for description of the variables. Values in brackets are standard errors of the coefficient estimates

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Ln(HbA1c)** | **BMI** | **SBP** | **Triglycerides** | **HDL** | **LDL** | **Ln(eGFR)** |
| Ln(Baseline HbA1c) | 0.13889 (0.00249) |  |  |  |  |  |  |
| Baseline BMI |  | 0.13128 (0.00251) |  |  |  |  |  |
| Baseline SBP |  |  | 0.16201 (0.00278) |  |  |  |  |
| Baseline Triglycerides |  |  |  | 0.14095 (0.00274) |  |  |  |
| Baseline HDL |  |  |  |  | 0.16127 (0.00259) |  |  |
| Baseline LDL |  |  |  |  |  | 0.1035 (0.00253) |  |
| Ln(Baseline eGFR) |  |  |  |  |  |  | 0.08741 (0.00247) |
| Ln(Lag\_HbA1c) | 0.69852 (0.00256) |  |  |  |  |  |  |
| Lag\_BMI |  | 0.85065 (0.00241) |  |  |  |  |  |
| Lag\_SBP |  |  | 0.552 (0.00281) |  |  |  |  |
| Lag\_Triglycerides |  |  |  | 0.68599 (0.00264) |  |  |  |
| Lag\_HDL |  |  |  |  | 0.72296 (0.00254) |  |  |
| Lag\_LDL |  |  |  |  |  | 0.69561 (0.00258) |  |
| Ln(Lag\_eGFR) |  |  |  |  |  |  | 0.84762 (0.00236) |
| Male |  | 0.03552 (0.00729) | 1.11403 (0.06485) | 0.02871 (0.00257) | -0.03379 (0.0015) | 0.01599 (0.00295) | -0.00283 (0.00069) |
| Age | 0.00045 (0.00012) | -0.00072 (0.00164) | 0.21101 (0.0144) | 0.0006 (0.00009) | 0.00245 (0.00032) | 0.00278 (0.00067) | -0.00029 (0.00015) |
| Age2 | -0.00001 (0) | -0.00003 (0.00002) | -0.00108 (0.00015) |  | -0.00002 (0) | -0.00005 (0.00001) | -0.00001 (0) |
| Intercept | -0.00956 (0.00256) | 0.23228 (0.03669) | -8.4141 (0.32684) | 0.13782 (0.00498) | 0.14786 (0.00757) | 0.47719 (0.01517) | 0.03331 (0.00347) |

Table S7. Beta coefficients in the in the logistic regression for estimating the probability of binary variables. See Table S2 for description of the variables. Values in brackets are standard errors of the coefficient estimates

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Smoking initiation** | **Smoking cessation** | **Development of microalbuminuria (not from macroalbuminuria)** | **Development of microalbuminuria (from macroalbuminuria)** | **Remission of microalbuminuria** | **Development of macroalbuminuria (not from microalbuminuria)** | **Development of macroalbuminuria (from microalbuminuria)** | **Remission of macroalbuminuria** |
| Age at diagnosis | 0.007 (0.003) | -0.011 (0.003) | -0.025 (0.002) |  | 0.016 (0.003) | -0.027 (0.005) |  | 0.014 (0.006) |
| Male | -0.308 (0.045) |  | 0.162 (0.039) |  | -0.337 (0.041) | 0.27 (0.082) |  | -0.459 (0.089) |
| Age | -0.006 (0.002) |  | 0.025 (0.002) | 0.019 (0.003) | -0.005 (0.002) | 0.017 (0.003) |  | 0.008 (0.004) |
| Ln(HbA1c) | 1.438 (0.148) | -0.719 (0.144) | 2.204 (0.13) |  | -1.148 (0.137) | 2.473 (0.277) | 0.75 (0.228) | -1.682 (0.287) |
| BMI | -0.027 (0.006) | 0.039 (0.006) |  |  |  |  |  |  |
| SBP |  | -0.004 (0.001) | 0.011 (0.001) | -0.005 (0.002) | -0.003 (0.001) | 0.015 (0.003) | 0.011 (0.002) | -0.016 (0.003) |
| Triglycerides | 0.237 (0.025) | -0.122 (0.032) | 0.161 (0.024) | -0.165 (0.049) | -0.219 (0.034) | 0.255 (0.039) | 0.164 (0.039) | -0.349 (0.068) |
| HDL |  |  | -0.172 (0.044) |  |  |  |  |  |
| LDL |  |  | 0.059 (0.023) |  |  |  | 0.124 (0.04) |  |
| Ln(eGFR) | 0.214 (0.048) |  | -0.348 (0.039) | 0.518 (0.045) | 0.548 (0.066) | -0.768 (0.039) | -0.329 (0.035) | 0.519 (0.052) |
| Constant | -3.852 (0.087) | -1.497 (0.045) | -4.659 (0.129) | -2.696 (0.176) | -0.834 (0.097) | -6.234 (0.177) | -3.401 (0.125) | -1.839 (0.213) |



Figure S2. Observed (broken lines) and simulated (solid lines) progression of mean risk factors in four groups of patients categorized based on quartiles of the modelled baseline risk factors. Results were obtained from simulations using linear regression models for risk factor progression where histories of complications were not included as predictors. The graphs show good agreement between observed and predicted values across all risk factors.

A screenshot of a computer

Description automatically generated

Figure S3. Observed (broken lines) and simulated (solid lines) progression of mean risk factors in four groups of patients categorized based on quartiles of the modelled baseline risk factors. Results were obtained from simulations using linear regression models for risk factor progression where histories of complications were included as predictors. The graphs show instabilities of the simulated risk factor progression. In reference to Figure S2 where histories of complications were excluded from the list of predictors, this poor agreement between the observed and predicted values across all risk factors can be attributed to the complex interaction between events and risk factors, i.e. the occurrence of complications affects changes in risk factors and conversely changes in risk factors influence occurrence of complications.

Table S8. Functional forms, beta coefficients and parameters of the parametric proportional hazards models for estimating the probabilities of events where body mass index (BMI) was treated as a continuous variable. These models were fitted only for the purpose of comparing their behaviour with the behaviour of the models in the main analyses where BMI was treated as a categorical variable. The beta coefficients for BMI in the table below show that the higher the BMI is, the lower the risks of first CVD (in patients with prior heart failure), second CVD, second hypoglycaemia, first hyperglycaemia, end-stage renal disease and death are, holding other risk factors constant. When these equations were integrated into the simulation model, the simulated life expectancy in patients with a higher BMI, regardless of baseline BMI levels, was higher than that in patients with a lower BMI. This does not in line with previous studies which show the “U”or “J”-shape relationship between BMI and mortality (1,2). See Table S2 for description of the variables. Values in brackets are standard errors of the coefficient estimates.

|  | **1st CVD (No prior HF)** | **1st CVD - Prior HF** | **2nd CVD** | **1st stroke** | **2nd stroke** | **HF (No prior MI)** | **HF (Prior MI)** | **PVD** | **1st amputation** | **2nd amputation** | **1st hypoGL** | **2nd hypoGL** | **1st hyperGL** | **2nd hyperGL** | **End-stage renal disease** | **Death** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Functional form  Variable | Weibull | Weibull | Weibull | Gompertz | Weibull | Gompertz | Gompertz | Weibull | Weibull | Weibull | Gompertz | Gompertz | Weibull | Gompertz | Gompertz | Gompertz |
| Male |  |  |  |  |  |  |  |  | 0.406 (0.097) | 0.471 (0.111) | 0.278 (0.066) | 0.224 (0.072) |  |  | 0.223 (0.072) | 0.294 (0.069) |
| Male \* Age |  |  |  |  |  |  |  | 0.024 (0.006) |  |  |  |  |  |  |  | -0.010 (0.004) |
| Age\_diag | -0.021 (0.004) |  |  |  |  | -0.027 (0.009) |  | -0.016 (0.006) | -0.017 (0.006) |  |  | -0.010 (0.005) |  |  |  |  |
| Ln(HbA1c) | 1.044 (0.291) |  |  |  | 1.072 (0.400) |  |  | 1.345 (0.422) |  | 0.979 (0.387) | 0.476 (0.225) |  | 3.470 (0.289) | 2.094 (0.294) |  |  |
| Ln(HbA1c) \* Age |  |  |  |  |  |  |  | -0.078 (0.023) |  |  | 0.048 (0.019) |  | -0.054 (0.015) | -0.030 (0.014) |  |  |
| Ln(wHbA1c) | 1.114 (0.323) | 1.872 (0.66) |  | 1.493 (0.315) |  | 1.048 (0.497) |  | 2.891 (0.413) | 1.977 (0.335) | 0.646 (0.467) |  |  |  |  | 0.653 (0.237) |  |
| Ln(wHbA1c) \* Age | -0.048 (0.019) |  |  |  |  |  |  |  |  | -0.046 (0.029) | -0.068 (0.018) |  |  |  |  |  |
| BMI | 0.023 (0.008) | -0.061 (0.021) | -0.014 (0.007) |  |  | 0.041 (0.016) |  |  |  |  |  | -0.033 (0.010) | -0.032 (0.010) |  | -0.023 (0.008) | -0.016 (0.007) |
| BMI \* Age |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| SBP |  |  |  | 0.018 (0.003) |  |  |  | 0.007 (0.002) |  |  |  |  |  |  | 0.008 (0.002) |  |
| Triglycerides | 0.163 (0.036) |  | 0.072 (0.034) |  |  | 0.209 (0.061) |  | 0.167 (0.038) | 0.100 (0.045) |  |  |  | 0.071 (0.037) | 0.169 (0.025) | 0.152 (0.035) | 0.107 (0.028) |
| Triglycerides \* Age |  |  |  |  |  |  |  |  |  |  |  |  |  |  | -0.007 (0.003) | -0.004 (0.002) |
| HDL | -0.258 (0.079) |  |  |  |  |  |  |  |  |  | 0.167 (0.067) | 0.205 (0.072) | 0.241 (0.078) | 0.234 (0.071) |  | 0.269 (0.069) |
| HDL \* Age | 0.010 (0.004) |  |  |  |  |  |  |  |  |  |  |  |  |  |  | -0.011 (0.004) |
| LDL | 0.221 (0.039) |  | 0.125 (0.037) |  |  |  |  |  |  |  |  |  |  |  |  |  |
| LDL \* Age | -0.009 (0.003) |  | -0.007 (0.003) |  |  |  |  |  |  |  |  |  |  |  | -0.008 (0.003) |  |
| Microalbuminuria | 0.210 (0.079) | 0.704 (0.255) | 0.368 (0.084) | 0.435 (0.115) |  | 0.663 (0.16) | 0.461 (0.147) | 0.480 (0.100) | 0.302 (0.106) |  |  | 0.265 (0.079) |  | 0.287 (0.104) | 1.022 (0.163) | 0.306 (0.067) |
| Microalbuminuria \* Age |  |  | -0.01 (0.005) |  |  |  |  |  |  |  |  |  |  | 0.02 (0.006) | -0.023 (0.008) |  |
| Macroalbuminuria | 0.220 (0.101) |  |  | 0.451 (0.137) |  |  | 0.317 (0.151) |  |  |  |  |  |  |  | 0.327 (0.108) | 0.251 (0.075) |
| Macroalbuminuria \* Age |  |  |  |  |  |  |  |  |  |  |  | -0.016 (0.007) |  |  |  |  |
| Ln(eGFR) | -0.289 (0.030) | -0.146 (0.060) | -0.139 (0.026) | -0.201 (0.037) | -0.256 (0.051) | -0.848 (0.203) |  | -0.317 (0.035) |  |  | -0.263 (0.027) | -0.102 (0.027) |  | 0.470 (0.157) | -3.543 (0.085) |  |
| Ln(eGFR) \* Age |  |  |  | 0.031 (0.01) |  |  |  | 0.019 (0.01) |  | 0.008 (0.002) |  |  | -0.037 (0.009) |  |  |  |
| Smoking | 0.458 (0.095) |  |  | 0.251 (0.127) |  | 0.456 (0.203) | 0.470 (0.176) | 0.388 (0.119) |  |  | 0.301 (0.087) | 0.226 (0.088) | 0.419 (0.096) |  |  | 0.439 (0.072) |
| Smoker \* Age | -0.02 (0.008) |  |  |  |  |  |  |  |  | 0.02 (0.013) |  |  |  | -0.016 (0.004) |  |  |
| Ex-smoker | 0.199 (0.09) |  |  |  |  |  |  |  |  |  |  |  | 0.341 (0.116) |  |  | 0.152 (0.075) |
| Ex-smoker \* Age |  |  |  |  |  |  |  |  |  |  |  |  | 0.017 (0.008) | -0.014 (0.006) | 0.024 (0.008) |  |
| Year | -0.063 (0.012) |  |  |  |  |  |  | -0.056 (0.018) |  |  |  |  |  |  | 0.141 (0.015) |  |
| Year \* Age |  |  |  | -0.003 (0.001) |  |  |  |  |  |  |  |  |  |  |  |  |
| Prior MI |  |  | 1.406 (0.104) |  |  |  |  | 1.182 (0.186) | 1.441 (0.262) |  |  | 0.567 (0.2) | 2.071 (0.243) | 1.676 (0.218) | 2.333 (0.182) | 4.178 (0.125) |
| Ln(Time\_since\_MI) |  |  | -0.818 (0.066) |  |  |  | -1.859 (0.092) | -0.652 (0.151) | -0.205 (0.113) |  |  | -0.34 (0.12) | -0.776 (0.182) | -0.885 (0.18) | -0.655 (0.088) | -2.173 (0.124) |
| Prior\_MI \* Age |  |  |  | 0.031 (0.012) |  |  |  |  |  | 0.01 (0.007) | 0.03 (0.008) |  |  |  | -0.021 (0.009) | -0.045 (0.006) |
| Ln(Time\_since\_MI) \* Age |  |  | 0.012 (0.003) | -0.019 (0.008) |  |  |  | 0.016 (0.007) |  |  |  |  | -0.021 (0.010) |  |  | 0.032 (0.006) |
| Prior\_stroke | 0.362 (0.110) |  | 0.261 (0.076) |  |  | 0.815 (0.182) |  | 0.619 (0.136) | 1.237 (0.208) |  | 1.425 (0.226) |  | 0.669 (0.169) |  | 2.018 (0.253) | 2.234 (0.112) |
| Ln(Time\_since\_stroke) |  |  |  |  | -0.909 (0.078) |  |  |  |  |  | -0.332 (0.136) |  |  |  | -0.712 (0.164) | -1.021 (0.109) |
| Prior\_stroke \* Age |  |  |  |  |  |  |  |  |  |  | -0.017 (0.011) |  |  |  | -0.045 (0.019) |  |
| Ln(Time\_since\_stroke) \* Age |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 0.031 (0.012) | 0.010 (0.005) |
| Prior\_HF |  |  | 0.932 (0.104) |  |  |  |  |  | 2.665 (0.364) | 0.756 (0.220) | 0.809 (0.277) |  |  |  | 1.801 (0.211) | 1.086 (0.114) |
| Ln(Time\_since\_HF) |  |  | -0.367 (0.066) |  |  |  |  |  | -1.149 (0.262) | -0.284 (0.136) | -0.447 (0.182) | 0.190 (0.084) |  |  | -0.328 (0.115) | 0.195 (0.091) |
| Prior\_HF \* Age |  |  |  |  |  |  |  |  | -0.025 (0.017) |  |  |  |  |  |  |  |
| Ln(Time\_since\_HF) \* Age |  |  |  |  |  |  |  |  | 0.038 (0.014) |  |  |  |  |  |  | -0.011 (0.004) |
| Prior\_PCI |  |  | 0.553 (0.104) |  |  |  | -1.446 (0.194) |  | -1.221 (0.369) |  |  |  | -1.544 (0.503) | -0.562 (0.271) |  | -1.5 (0.15) |
| Ln(Time\_since\_PCI) |  |  | -0.333 (0.066) |  |  |  | 0.509 (0.133) |  | 0.510 (0.217) |  |  |  | 0.672 (0.281) |  |  | 0.711 (0.087) |
| Prior\_PCI \* Age |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Prior\_CABG |  |  | -1.781 (0.172) | 1.638 (0.362) |  | 2.252 (0.391) | -1.49 (0.267) | 0.95 (0.2) |  |  |  |  | -0.662 (0.239) |  | -0.873 (0.294) | -1.500 (0.203) |
| Ln(Time\_since\_CABG) |  |  | 0.663 (0.076) | -0.77 (0.238) |  | -0.687 (0.213) | 0.646 (0.122) |  |  |  |  |  |  |  | 0.426 (0.147) | 0.714 (0.087) |
| Prior\_CABG \* Age |  |  |  | -0.042 (0.025) |  |  |  | -0.032 (0.013) |  |  |  |  |  |  | 0.01 (0.012) | -0.006 (0.008) |
| Ln(Time\_since\_CABG) \* Age |  |  |  | 0.024 (0.013) |  |  |  |  |  |  |  |  |  |  |  |  |
| Prior\_ANG |  |  | 2.464 (0.123) | 0.538 (0.197) |  | 0.794 (0.239) |  |  |  |  |  |  |  | 0.714 (0.244) | 1.548 (0.395) | 4.066 (0.176) |
| Ln(Time\_ since\_ANG) |  |  | -1.93 (0.129) |  |  |  |  |  | 0.505 (0.129) |  |  |  |  |  | -0.684 (0.255) | -2.219 (0.215) |
| Prior\_ANG \* Age |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | -0.042 (0.011) |
| Ln(Time\_since\_ANG) \* Age |  |  | 0.023 (0.007) |  |  |  |  |  |  |  |  |  |  |  | 0.023 (0.008) | 0.044 (0.01) |
| Prior\_PVD | 0.375 (0.096) |  |  |  |  | 0.356 (0.195) | 0.543 (0.145) |  | 5.047 (0.179) |  | 0.909 (0.268) |  |  | 0.509 (0.279) | 1.196 (0.281) | 1.257 (0.153) |
| Ln(Time\_since\_PVD) |  |  |  | 0.283 (0.064) |  |  |  |  | -1.220 (0.062) |  | -0.214 (0.120) |  |  | -0.306 (0.140) | -0.257 (0.119) | -0.232 (0.065) |
| Prior\_PVD \* Age |  |  |  |  |  |  |  |  |  |  |  |  |  |  | -0.056 (0.023) |  |
| Ln(Time\_since\_PVD) \* Age |  |  |  | -0.011 (0.004) |  |  |  |  |  |  |  |  |  | -0.025 (0.006) | 0.028 (0.01) |  |
| Prior\_AMP | 0.316 (0.094) |  |  | 1.049 (0.214) |  | 1.440 (0.309) | 0.355 (0.144) |  |  |  | 0.718 (0.233) |  | 0.457 (0.142) |  | 0.679 (0.122) | 1.788 (0.124) |
| Ln(Time\_since\_AMP) |  |  |  | -0.299 (0.100) |  | -0.426 (0.144) |  |  |  | -0.945 (0.069) | -0.301 (0.110) |  |  |  |  | -0.468 (0.049) |
| Prior\_AMP \* Age |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | -0.006 (0.006) |
| Ln(Time\_since\_AMP) \* Age |  |  |  |  |  |  |  |  |  | 0.008 (0.004) |  |  |  |  |  |  |
| Prior\_hypoGL |  |  |  | 0.237 (0.107) |  | 0.427 (0.156) |  | 0.295 (0.108) | 1.334 (0.269) |  |  |  | 1.387 (0.172) | 0.648 (0.096) | 0.841 (0.195) | 2.369 (0.100) |
| Ln(Time\_since\_hypoGL) |  |  |  |  |  |  |  |  | -0.387 (0.120) |  |  | -0.765 (0.037) | -0.556 (0.093) |  | -0.168 (0.084) | -0.821 (0.058) |
| Prior\_hypoGL \* Age |  |  |  |  |  |  |  |  | -0.044 (0.016) |  |  |  | 0.029 (0.01) | -0.019 (0.008) |  | -0.057 (0.006) |
| Ln(Time\_since\_hypoGL) \* Age |  |  |  |  |  |  |  |  | 0.023 (0.008) |  |  | 0.006 (0.002) | -0.018 (0.005) | 0.019 (0.003) |  | 0.029 (0.003) |
| Prior\_hyperGL | 0.712 (0.197) |  | -0.326 (0.112) | 0.351 (0.124) | 0.513 (0.144) |  | -0.920 (0.365) | 0.379 (0.125) | 1.725 (0.271) |  | 1.704 (0.142) | 0.888 (0.134) |  |  | 1.077 (0.226) | 1.562 (0.123) |
| Ln(Time\_since\_hyperGL) | -0.261 (0.09) |  |  |  |  |  | 0.400 (0.160) |  | -0.501 (0.110) |  | -0.493 (0.067) | -0.194 (0.062) |  | -0.84 (0.05) | -0.232 (0.09) | -0.352 (0.059) |
| Prior\_hyperGL \* Age |  |  | 0.020 (0.008) |  |  |  |  |  | 0.029 (0.011) | 0.033 (0.016) |  |  |  | -0.027 (0.115) |  | -0.021 (0.008) |
| Ln(Time\_since\_hyperGL) \* Age |  |  |  |  |  |  |  |  |  | -0.013 (0.009) |  |  |  | 0.009 (0.003) |  | 0.013 (0.004) |
| Prior\_ESRD |  |  |  |  |  | -2.595 (0.846) |  |  | 2.120 (0.207) | 0.909 (0.204) |  |  | 1.432 (0.238) | 1.974 (0.705) |  | 1.028 (0.115) |
| Ln(Time\_since\_ESRD) |  |  | -0.181 (0.088) |  | -0.531 (0.187) |  |  |  |  | 0.236 (0.119) |  |  | -0.815 (0.244) |  |  | 0.181 (0.076) |
| Prior ESRD \* Age | -0.036 (0.01) |  |  | 0.096 (0.042) |  |  |  | 0.071 (0.043) | -0.048 (0.011) |  |  |  | -0.151 (0.041) | -0.037 (0.013) |  |  |
| Prior\_2\_events |  |  |  |  |  |  |  |  | -0.662 (0.224) |  |  |  |  |  | -0.61 (0.157) |  |
| Prior\_4\_events |  |  |  |  |  |  |  |  | -1.617 (0.378) |  |  |  |  |  | -1.076 (0.255) | -0.676 (0.101) |
| Prior\_4\_events\_4 |  |  |  |  |  |  |  |  | -2.447 (0.553) |  |  |  |  |  | -1.839 (0.374) | -1.745 (0.18) |
| Prior\_5\_events |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 0.027 (0.008) |
| Prior\_5\_events\_5 \* Age |  |  |  |  |  |  |  |  | -3.473 (0.741) |  |  |  |  |  | -2.243 (0.533) | -2.077 (0.202) |
| Prior\_6\_events |  |  |  |  |  |  |  |  | -5.064 (1.105) |  |  |  |  |  | -3.794 (0.895) | -4.803 (0.428) |
| Prior\_6\_events \* Age |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 0.066 (0.024) |
| Constant | -19.396 (1.341) | -11.316 (1.628) | -5.376 (1.332) | -9.518 (0.299) | -3.142 (0.878) | -10.62 (0.305) | -2.771 (0.342) | -15.252 (0.828) | -13.706 (0.742) | -5.416 (1.481) | -5.868 (0.14) | -2.927 (0.196) | -4.889 (0.277) | -3.502 (3.749) | -10.523 (0.432) | -9.995 (0.410) |
| Shape parameter | 4.655 (  0.345) | 3.034 (  0.383) | 1.561 ( 0.306) | 0.094 (0.009) | 1.277 (0.194) | 0.083 (0.007) | 0.040 (0.006) | 3.293 (0.215) | 2.539 (0.189) | 1.732 (0.345) | 0.008 (0.003) | 0.006 (0.004) | 0.710 (0.057) | 0.016 (0.115) | 0.044 (0.011) | 0.098 (0.010) |

CVD, cardiovascular event including myocardial infarction, percutaneous coronary intervention and coronary artery bypass graft; HF, heart failure; MI, myocardial infarction; PVD, peripheral vascular disease; hypoGL, hypoglycaemia; hyperGL, hyperglycaemia; eGFR, estimated glomerular filtration rate.

**References**

1. Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath Jr CW. Body-mass index and mortality in a prospective cohort of US adults. N Engl J Med 1999;341:1097-1105

2. Klatsky AL, Zhang J, Udaltsova N, Li Y, Tran HN. Body mass index and mortality in a very large cohort: is it really healthier to be overweight? The Permanente Journal 2017;21:16-142