# Trajectories in HbA1c and other risk factors among adults

# with type 1 diabetes by age at onset

Supplemental material

Supplemental material

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**Supplementary table S1 - ICD-9 and ICD-10 codes for comorbidities at baseline**

| Diagnosis | Inpatient registry (ICD-9) | Inpatient registry (ICD-10) |
|---|---|---|
| Cardiovascular disease | 431, 432X, 433, 434, 436, 437X | I21, I61, I62.9, I63, I64, I67.9 |
| Heart failure | 428 | I50 |
| Renal dialysis or transplantation | V42A, V45B, V56A, V56W | Z94.0, Z49, Z99.2 |
| Amputation | | NHQ09, NHQ11, NHQ12, NHQ13, NHQ14, NHQ16, NHQ17, NHQ99, NGQ09, NGQ19, NGQ99, NFQ19, NFQ99 |

Diagnosis used from the inpatient registry according to the International Classification of Diseases (ICD) system.

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**Supplementary table S2 - Baseline characteristics among patients with type 1 diabetes stratified by age at onset and by sex**

| | 0-10 years (Men) | 0-10 years (Women) | 11-15 years (Men) | 11-15 years (Women) | 16-20 years (Men) | 16-20 years (Women) | 21-25 years (Men) | 21-25 years (Women) | 26-30 years (Men) | 26-30 years (Women) |
|---|---|---|---|---|---|---|---|---|---|---|
| n | 5142 | 5100 | 4445 | 3719 | 3196 | 2189 | 2803 | 1919 | 2078 | 1414 |
| Women - n (%) | 0 (0.0) | 5100 (100.0) | 0 (0.0) | 3719 (100.0) | 0 (0.0) | 2189 (100.0) | 0 (0.0) | 1919 (100.0) | 0 (0.0) | 1414 (100.0) |
| Age (years) | 30.5 (12.5) | 30.8 (12.8) | 31.3 (13.1) | 32.8 (13.9) | 33.3 (14.2) | 34.8 (14.4) | 36.7 (13.1) | 38.2 (13.7) | 40.6 (12.0) | 41.7 (12.5) |
| Diabetes duration (years) | 24.2 (12.8) | 24.3 (13.0) | 18.2 (13.2) | 20.1 (13.8) | 15.4 (14.1) | 16.9 (14.5) | 13.7 (13.0) | 15.2 (13.6) | 13.1 (11.9) | 14.2 (12.5) |
| Debut age of diabetes (years) | 6.3 (2.7) | 6.5 (2.7) | 13.1 (1.4) | 12.7 (1.4) | 17.9 (1.4) | 17.9 (1.4) | 23.0 (1.4) | 23.0 (1.4) | 27.5 (1.1) | 27.5 (1.1) |
| HbA1c (mmol/mole)/(%) | 68.2 (14.6)/8.4 (1.3) | 68.8 (15.3)/8.4 (1.4) | 66.6 (14.6)/8.2 (1.3) | 67.1 (15.6)/8.3 (1.4) | 63.0 (15.4)/7.9 (1.4) | 64.3 (16.3)/8.0 (1.5) | 62.7 (16.4)/7.9 (1.5) | 63.3 (16.5)/7.9 (1.5) | 62.5 (16.1)/7.9 (1.5) | 63.6 (16.7)/8.0 (1.5) |
| Total cholesterol (mmol/L) | 4.5 (1.0) | 4.8 (1.0) | 4.6 (1.0) | 4.8 (1.0) | 4.5 (1.0) | 4.8 (0.9) | 4.7 (1.0) | 4.8 (1.0) | 4.8 (1.0) | 4.8 (1.0) |
| LDL cholesterol (mmol/L) | 2.6 (0.8) | 2.7 (0.8) | 2.6 (0.8) | 2.6 (0.8) | 2.6 (0.8) | 2.6 (0.8) | 2.7 (0.8) | 2.6 (0.8) | 2.8 (0.9) | 2.7 (0.8) |
| Body Mass Index (kg/m2) | 24.6 (3.4) | 24.9 (3.7) | 24.7 (3.5) | 24.7 (3.8) | 24.6 (3.5) | 24.5 (4.1) | 25.0 (3.6) | 24.6 (4.2) | 25.2 (3.4) | 25.0 (4.4) |
| Systolic blood pressure (mmHg) | 126.8 (14.9) | 122.1 (15.8) | 126.9 (15.0) | 123.0 (16.5) | 127.1 (15.4) | 123.0 (16.7) | 128.1 (15.7) | 124.1 (17.3) | 128.0 (15.5) | 125.6 (17.9) |
| Smokers - n (%) | 514 (10.9) | 682 (14.4) | 484 (11.8) | 528 (15.4) | 315 (10.8) | 295 (14.6) | 348 (13.5) | 285 (16.0) | 268 (14.0) | 226 (17.4) |
| Albuminuria - n (%) | | | | | | | | | | |
| No albuminuria | 3319 (80.8) | 3362 (82.6) | 2999 (84.4) | 2502 (85.1) | 2220 (86.9) | 1597 (89.8) | 1923 (86.0) | 1418 (90.7) | 1444 (87.3) | 1042 (90.7) |
| Microalbuminuria | 473 (11.5) | 434 (10.7) | 323 (9.1) | 263 (8.9) | 201 (7.9) | 113 (6.4) | 185 (8.3) | 99 (6.3) | 141 (8.5) | 66 (5.7) |
| Macroalbuminuria | 316 (7.7) | 276 (6.8) | 231 (6.5) | 175 (6.0) | 134 (5.2) | 68 (3.8) | 128 (5.7) | 47 (3.0) | 69 (4.2) | 41 (3.6) |
| eGFR (mL/min/1.73m$^2$) | 104.6 (28.4) | 97.0 (28.8) | 107.3 (27.8) | 97.7 (29.7) | 105.2 (28.3) | 95.5 (27.9) | 100.7 (26.0) | 94.1 (27.5) | 98.0 (24.8) | 90.2 (24.9) |
| Antihypertensives - n (%) | 1020 (21.2) | 924 (19.3) | 815 (19.5) | 627 (17.9) | 537 (17.9) | 323 (15.7) | 479 (18.0) | 295 (16.2) | 361 (18.3) | 249 (18.6) |

| Statins - n (%) | 413 (8.8) | 379 (8.2) | 356 (8.8) | 299 (8.8) | 279 (9.5) | 196 (9.8) | 309 (12.0) | 182 (10.4) | 260 (13.6) | 157 (12.1) |
| Insulin pump | 639 (24.7) | 738 (30.1) | 413 (19.1) | 362 (21.8) | 109 (7.3) | 99 (10.3) | 52 (4.4) | 56 (7.5) | 35 (4.2) | 42 (7.7) |
| Treatment: Insulin | 5142 (100.0) | 5100 (100.0) | 4445 (100.0) | 3719 (100.0) | 3196 (100.0) | 2189 (100.0) | 2803 (100.0) | 1919 (100.0) | 2078 (100.0) | 1414 (100.0) |

Data are *n* (%) for categorical variables and mean (SD) for continuous variables unless otherwise indicated.

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**Supplementary table S3 – Imputed baseline characteristics among patients with a diabetes duration >1 year from onset, stratified by age at onset and by sex**
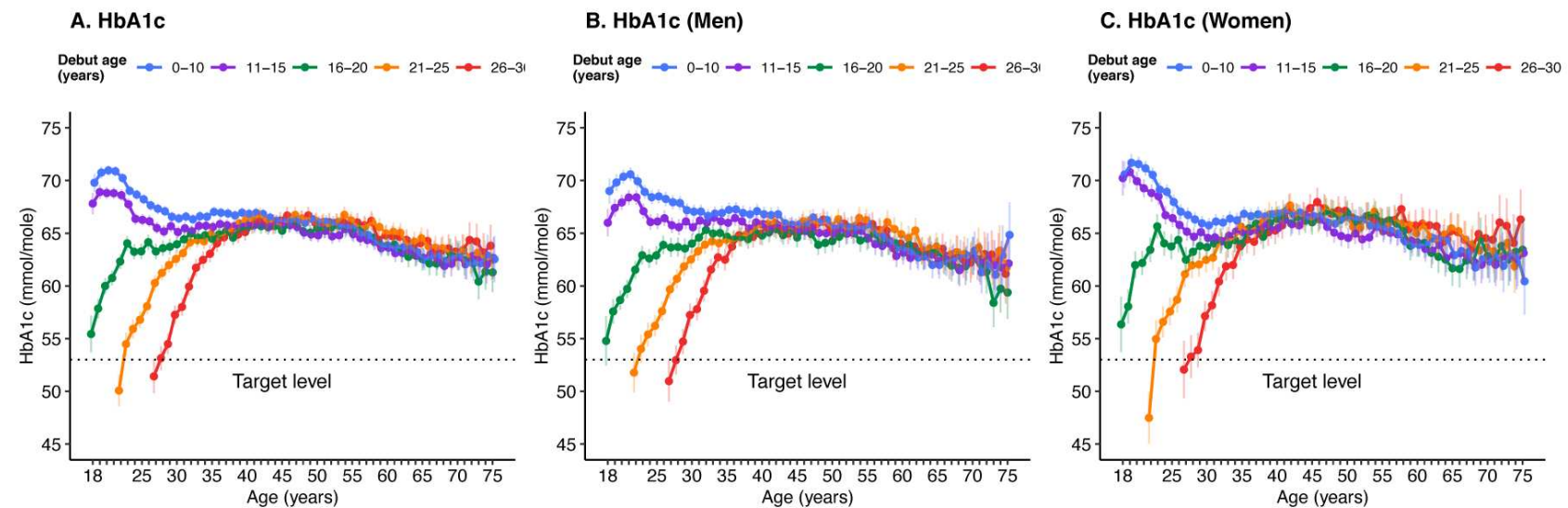
|  | 0-15 years (Men) | 0-15 years (Women) | 16-30 years (Men) | 16-30 years (Women) |
|---|---|---|---|---|
| n | 9581 | 8811 | 7194 | 5015 |
| Age (years) | 30.9 (12.8) | 31.6 (13.3) | 38.0 (13.5) | 39.2 (13.8) |
| *Marital status - n (%)* | | | | |
| Married | 1961 (20.5) | 2214 (25.1) | 2563 (35.6) | 2101 (41.9) |
| Single | 7156 (74.7) | 5925 (67.2) | 4022 (55.9) | 2297 (45.8) |
| Divorced | 437 (4.6) | 591 (6.7) | 570 (7.9) | 527 (10.5) |
| Widowed | 27 (0.3) | 81 (0.9) | 39 (0.5) | 90 (1.8) |
| *Education - n (%)* | | | | |
| 9 years or less | 2200 (23.0) | 1812 (20.6) | 1446 (20.1) | 944 (18.8) |
| 10 to 12 years | 5410 (56.5) | 4842 (55.0) | 3793 (52.7) | 2551 (50.9) |
| College or university | 1971 (20.6) | 2157 (24.5) | 1955 (27.2) | 1520 (30.3) |
| *Income (hundreds, SEK)* | | | | |
| Q1 | 2417 (25.2) | 2227 (25.3) | 829 (11.5) | 652 (13.0) |
| Q2 | 1657 (17.3) | 2295 (26.0) | 1000 (13.9) | 1168 (23.3) |
| Q3 | 1606 (16.8) | 2017 (22.9) | 1265 (17.6) | 1236 (24.6) |
| Q4 | 1889 (19.7) | 1332 (15.1) | 1763 (24.5) | 1130 (22.5) |
| Q5 | 2012 (21.0) | 940 (10.7) | 2337 (32.5) | 829 (16.5) |
| Swedish born - n (%) | 9298 (97.0) | 8488 (96.3) | 6816 (94.7) | 4702 (93.8) |
| Cardiovascular disease | 236 (2.5) | 194 (2.2) | 214 (3.0) | 131 (2.6) |
| Heart failure | 58 (0.6) | 68 (0.8) | 55 (0.8) | 41 (0.8) |
| Diabetes duration (years) | 21.4 (13.3) | 22.5 (13.5) | 15.9 (13.0) | 17.2 (13.4) |
| Age at onset | 9.4 (4.1) | 9.1 (3.8) | 22.1 (4.1) | 22.0 (4.1) |
| HbA1c (mmol/mole) | 67.5 (14.7) | 68.1 (15.4) | 62.8 (15.0) | 64.0 (15.8) |
| LDL cholesterol (mmol/L) | 2.6 (0.8) | 2.7 (0.8) | 2.7 (0.8) | 2.7 (0.8) |
| Body Mass Index (kg/m$^2$) | 24.6 (3.5) | 24.8 (3.8) | 25.0 (3.5) | 24.8 (4.1) |
| Systolic blood pressure (mmHg) | 126.6 (14.9) | 122.3 (16.0) | 128.6 (15.7) | 124.7 (17.2) |
| Diastolic blood pressure (mmHg) | 73.5 (9.1) | 71.8 (8.7) | 74.8 (9.0) | 72.8 (8.6) |
| Smokers - n (%) | 1078 (11.3) | 1320 (15.0) | 942 (13.1) | 817 (16.3) |
| *Albuminuria - n (%)* | | | | |
| No albuminuria | 7962 (83.1) | 7436 (84.4) | 6193 (86.1) | 4495 (89.6) |
| Microalbuminuria | 978 (10.2) | 863 (9.8) | 620 (8.6) | 331 (6.6) |
| Macroalbuminuria | 641 (6.7) | 512 (5.8) | 381 (5.3) | 189 (3.8) |
| eGFR (mL/min/1.73 m$^2$) | 98.3 (26.4) | 89.5 (27.2) | 92.4 (24.4) | 84.4 (24.4) |
| Antihypertensives - n (%) | 1896 (19.8) | 1604 (18.2) | 1415 (19.7) | 887 (17.7) |

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| | | | | |
|---|---|---|---|---|
| Statins - n (%) | 829 (8.7) | 727 (8.3) | 897 (12.5) | 570 (11.4) |
| Insulin pump | 1051 (11.0) | 1099 (12.5) | 193 (2.7) | 193 (3.8) |

Data are *n* (%) for categorical variables and mean (SD) for continuous variables unless otherwise indicated.
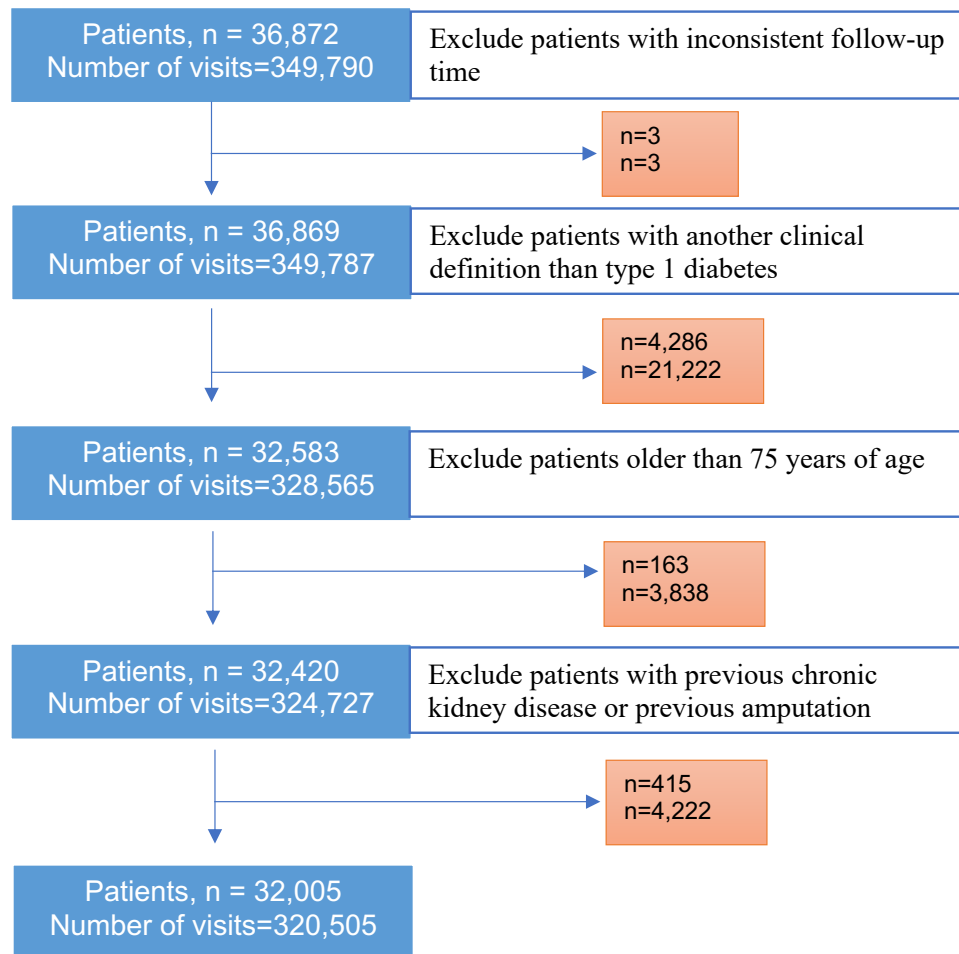
**Supplementary Figure S1**

Flow chart

**Distributions before imputation**
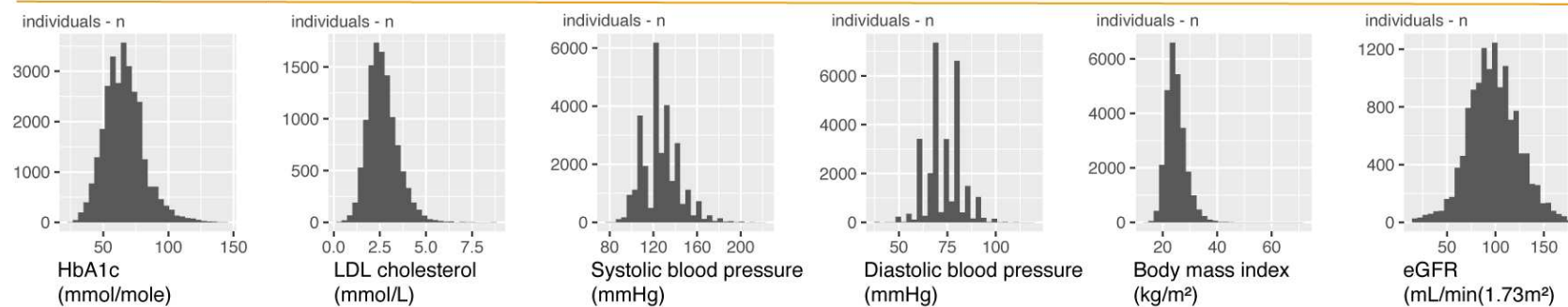


**Distributions after imputation**
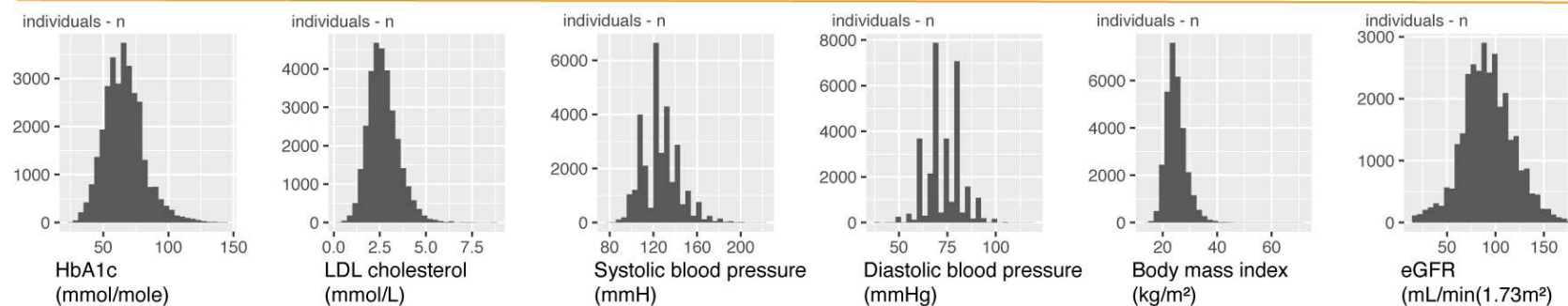


**Supplementary Figure S2**

Subample of variables describing distributions before and post imputation of baseline variables.

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**Supplementary Figure S3 - Trends for HbA1c associated with type 1 diabetes between 18-75 years of age stratified by age at onset and sex**

Analyses were performed with Mixed Linear Regression and Generalized linear mixed model. Age, age at onset and the interaction between age and age at onset were set as fixed effects, with a random participant effect. Panel A was adjusted for sex.
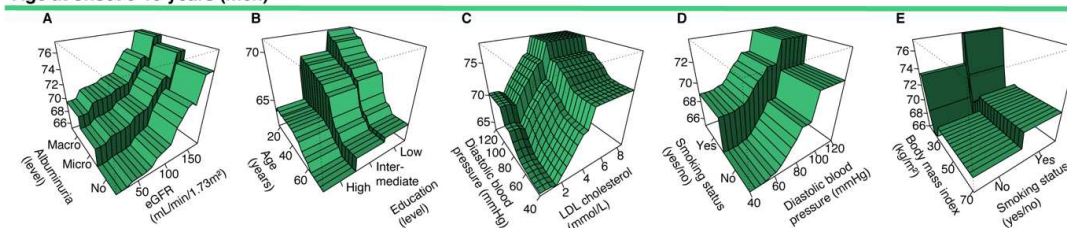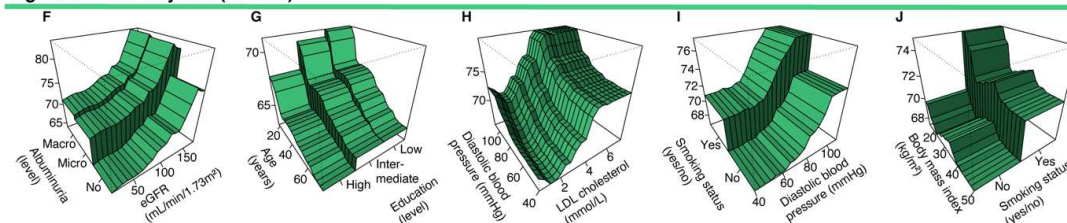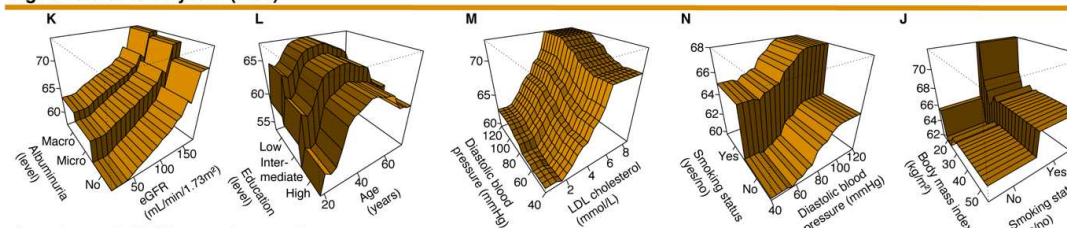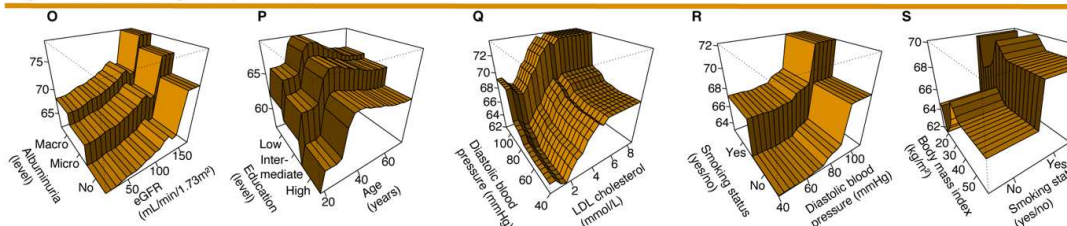
**Supplementry Figure S4 - Partial dependence plots, showing interaction effects for the most important variables presented in Figure 3**

3D partial dependence plots showing the adjusted average target response from the top predictors. Plots were generated from the Gradient boosting machines prediction presented in Figure 3. Panels A-E, F-J, K-J and O-S contains interactions of features in following order: albuminuria*eGFR; age*education; diastolic blood pressure*LDL cholesterol; smoking status*diastolic blood pressure; body mass index*smoking status.
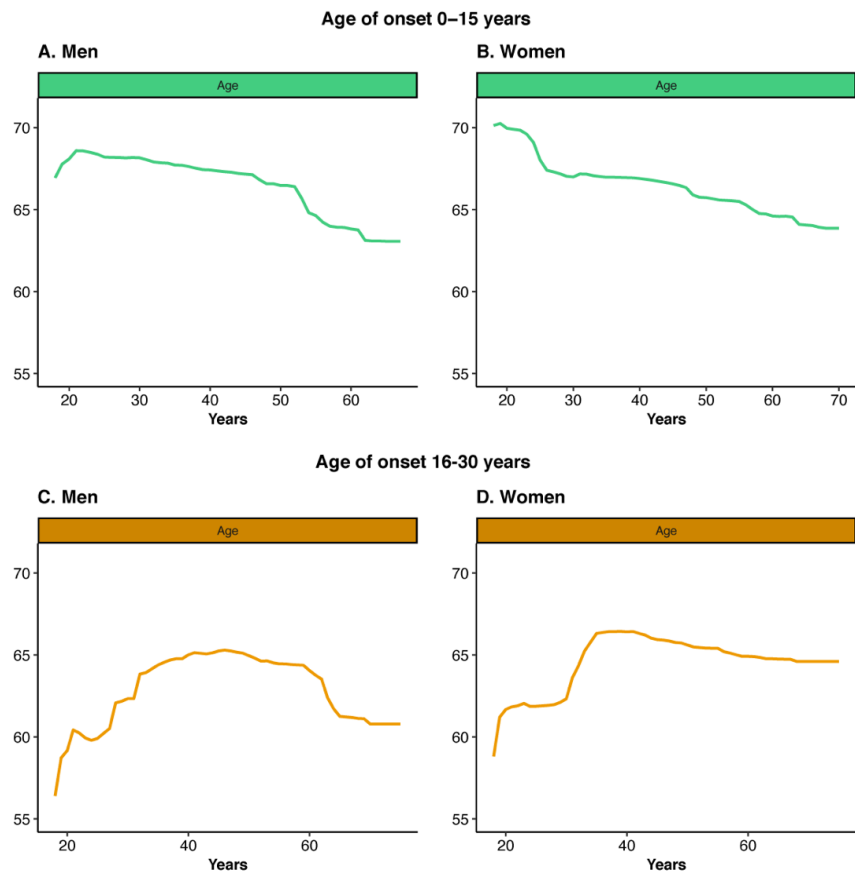
**Supplementary Figure S5 – Single Partial dependence plot containing age based on GBM models presented in Figure 3**

Single partial dependence plots showing the adjusted average target response from age. Plots were generated from the Gradient boosting machines prediction presented in Figure 3.