

Supplementary Information

Quan J, Pang D, Li TK, Choi CH, Siu SC, Tang SY, Wat NM, Woo J, Lau ZY, Tan KB, Leung GM. Risk prediction scores for mortality, cerebrovascular, and heart disease among Chinese people with type 2 diabetes (2019).

The HKU-SG risk scores

Supplemental Table 1. Predictors included in the mortality, cerebrovascular disease and ischemic heart disease risk scores

Predictors	Mortality				Cerebrovascular disease					Ischemic heart disease				
	HKU	HKU-SG	JADE	RECODE	HKU	HKU-SG	JADE	UKPDS 60	UKPDS 82	HKU	HKU-SG	JADE	UKPDS 56	UKPDS 82
Age	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Duration	✓	✓			✓	✓		✓		✓	✓	✓	✓	
Gender	✓	✓	✓	✓		✓		✓	✓	✓	✓	✓	✓	✓
Smoking	✓	✓		✓	✓	✓		✓	✓	✓	✓	✓	✓	
Body mass index		✓	✓			✓					✓			
Systolic blood pressure		✓		✓		✓		✓	✓	✓	✓		✓	✓
Diastolic blood pressure		✓				✓					✓			
Mean arterial pressure					✓									
HbA1c		✓		✓	✓	✓	✓		✓	✓	✓		✓	
Lipid ratio (Total:HDL)								✓					✓	
Total cholesterol				✓						✓				
HDL cholesterol				✓						✓				✓
LDL cholesterol		✓				✓			✓		✓			✓
Non-HDL cholesterol												✓		
Creatinine	✓			✓	✓					✓				
Estimated GFR			✓						✓			✓		✓
Urine ACR			✓	✓			✓					✓		
Microalbuminuria									✓					
Hemoglobin	✓		✓											
White blood cells	✓				✓				✓	✓				
Heart rate (resting)										✓				
Atrial fibrillation		✓			✓	✓		✓	✓		✓			
Cancer	✓		✓											
Chronic kidney disease		✓				✓					✓			
Ischemic heart disease		✓				✓	✓		✓					
Cerebrovascular disease	✓	✓									✓			
Congestive heart failure	✓									✓				✓
Peripheral arterial disease			✓											✓
Cardiovascular disease				✓										
Amputation									✓					✓
Diabetic complications	✓									✓				
Diabetes medication	✓				✓					✓				
Insulin use			✓											
Antihypertensive medication	✓			✓						✓				
Statin use				✓						✓				
Anticoagulant other than aspirin				✓										

Supplemental Appendix 1.

Data sources and study participants

We used the Hong Kong Hospital Authority's electronic health records (Clinical Management System) to identify all people with diabetes in the public health care system. All residents are eligible to use public health care services at highly subsidized rates. Public sector services are provided by the Hospital Authority, which accounts for the majority of inpatient care (90% total bed-days and 80% of admissions), 50% of specialist outpatient care, and 30% of first-contact outpatient services in the overall Hong Kong health system.^{21–23} The electronic health records comprised of all 6.4 million unique individuals who used public health care services from 1 January 2006 to 31 December 2014. Each individual has two unique identifiers (Hong Kong Identity Card number and hospital patient number) to allow tracking and data linkage. Data collected included demographic information and inpatient records from 1997, specialist outpatient and emergency room data from 2000; and primary care, clinical laboratory and medications data from 2006. Diagnoses were coded according to the International Classification of Disease 9th revision (ICD-9) for secondary care; and the International Classification of Primary Care 2nd Edition (ICPC-2) for primary care.

Data for Singapore were obtained from Ministry of Health administrative datasets covering 1 January 2008 to 31 December 2016. Singapore also has a mixed public-private health care system, with public hospitals providing the majority of inpatient care (85.5% of total bed-days and 76.0% of admissions) and private sector general practitioners providing up to 80.6% of primary care.^{24,25} The administrative datasets capture hospitalizations and visits at public institutions, hospitalizations and day surgeries at private institutions as well as selected private outpatient visits that were covered by Medisave (national medical savings scheme) and MediShield (national health insurance scheme). Data for private specialist outpatient visits and private primary care visits are lacking, except for visits covered under the Community Health Assistance Scheme subsidy for lower- and middle-income households from 2012. Diagnoses were defined by recorded ICD-9 diagnosis codes (pre-2012) and ICD-10 diagnosis codes (2012 and after).

All cases of type 2 diabetes were confirmed by any one of: (a) HbA1c $\geq 6.5\%$ (≥ 48 mmol/mol); (b) fasting plasma glucose ≥ 7.0 mmol/l (≥ 126 mg/dl); (c) oral glucose tolerance test (OGTT) ≥ 11.1 mmol/l (200 mg/dl); (d) random plasma glucose ≥ 11.1 mmol/l (≥ 200 mg/dl) on two separate occasions; (e) diagnosis code for diabetes (ICD-9 codes 250, 357.2, 366.41 and 362.01–362.0; or ICPC codes T89 and T90); (f) prescription of antihyperglycemic medication (including insulins, metformin, thiazolidinediones, sulfonylureas, incretin mimetics / glucagon-like peptide-1 analogues, glucosidase inhibitors, and dipeptidyl peptidase inhibitors).

Predictors

The laboratory values considered as candidate predictors were Hemoglobin A1c (HbA1c), Lipid ratio (total:HDL cholesterol), total cholesterol, HDL cholesterol, LDL cholesterol, Non-HDL cholesterol, serum creatinine, estimated glomerular filtration rate (eGFR), hemoglobin, and white blood cell count.

Missing data

Our Hong Kong derivation and Singapore validation cohort had missing values as summarized in Supplemental Table 2 and 3. Due to a high proportion of missing values, we excluded urine albumin-creatinine ratio from our candidate predictors.

Supplemental Table 2. Distribution of and mean values of missing values in the Hong Kong derivation cohort

Variable	Non-missing			Imputed			
	n	Mean	SD	n	%	Mean	SD
Body mass index	297,770	26.0	4.3	380,980	56.1%	25.6	4.2
Systolic blood pressure	450,000	138.4	19.6	228,750	33.7%	138.8	20.1
Diastolic blood pressure	450,116	76.4	11.6	228,634	33.7%	76.3	11.5
Mean arterial pressure	450,118	97.1	12.5	228,632	33.7%	97.1	12.5
HbA1c	521,322	7.6	1.9	157,428	23.2%	7.5	1.8
Total cholesterol	492,337	5.1	1.2	186,413	27.5%	5.2	1.1
HDL-cholesterol	481,155	1.2	0.4	197,595	29.1%	1.2	0.4
LDL-cholesterol	477,622	3.1	1.0	201,128	29.6%	3.1	0.9
Lipid ratio	480,647	4.4	1.5	198,103	29.2%	4.7	1.4
Hemoglobin	442,275	13.1	2.1	236,475	34.8%	13.5	1.8
Triglycerides	487,227	1.8	1.6	191,523	28.2%	2.0	1.6
White cell count	438,577	8.6	4.1	240,173	35.4%	8.2	3.4
Urine albumin:creatinine ratio	151,171	12.2	51.5	527,579	77.7%	56.0	124.3
Creatinine	580,876	96.6	90.9	97,874	14.4%	94.2	75.6
Estimated GFR	580,876	100.9	52.0	97,874	14.4%	99.5	32.6

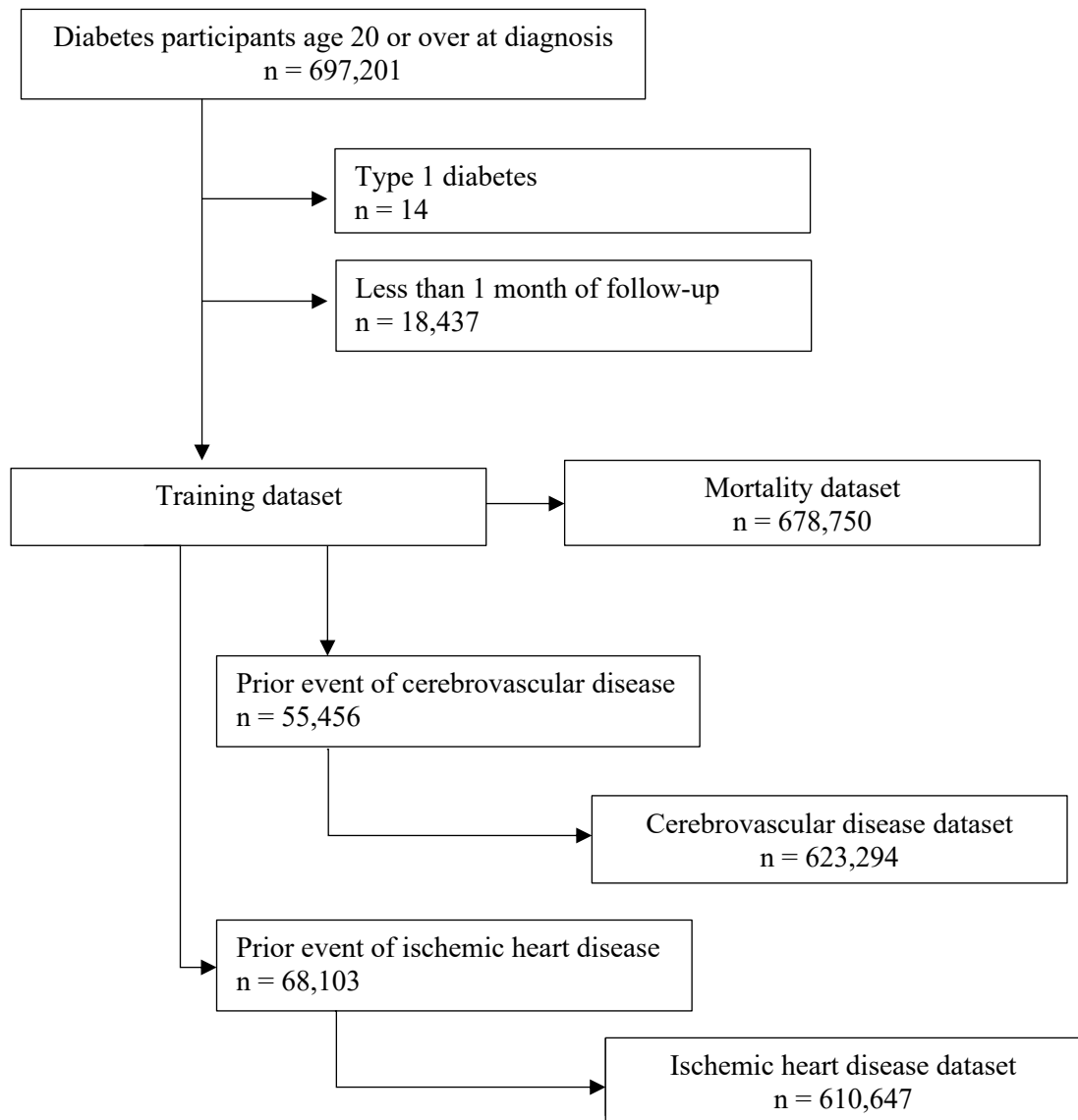
Supplemental Table 3. Distribution of and mean values of missing values in the Singapore validation cohort

Variable	Non-missing			Imputed			
	n	Mean	SD	n	%	Mean	SD
Body mass index	101,665	26.7	5.0	284,760	73.7%	26.8	5.1
Systolic blood pressure	250,889	132.8	17.4	135,536	35.1%	132.2	15.6
Diastolic blood pressure	250,925	74.9	10.1	135,500	35.1%	75.2	15.0
Mean arterial pressure	250,882	94.2	10.8	135,543	35.1%	94.2	10.0
HbA1c	222,590	7.6	1.8	163,835	42.4%	7.6	1.9
LDL-cholesterol	205,074	3.0	0.9	181,351	46.9%	3.0	0.9

Supplemental Table 4. External validation of HKU-SG risk scores for the Singapore validation cohort (Chinese ethnicity subgroup): model performance measured by Harrell's c-index

	Singapore validation cohort	
	With imputation	Complete cases
Mortality	0.783 (0.781-0.786)	0.775 (0.767-0.782)
Cerebrovascular disease	0.704 (0.699-0.710)	0.701 (0.690-0.711)
Ischemic heart disease	0.652 (0.648-0.657)	0.638 (0.629-0.650)

Supplemental Figure 1. Flow diagram outlining the cohort selection.

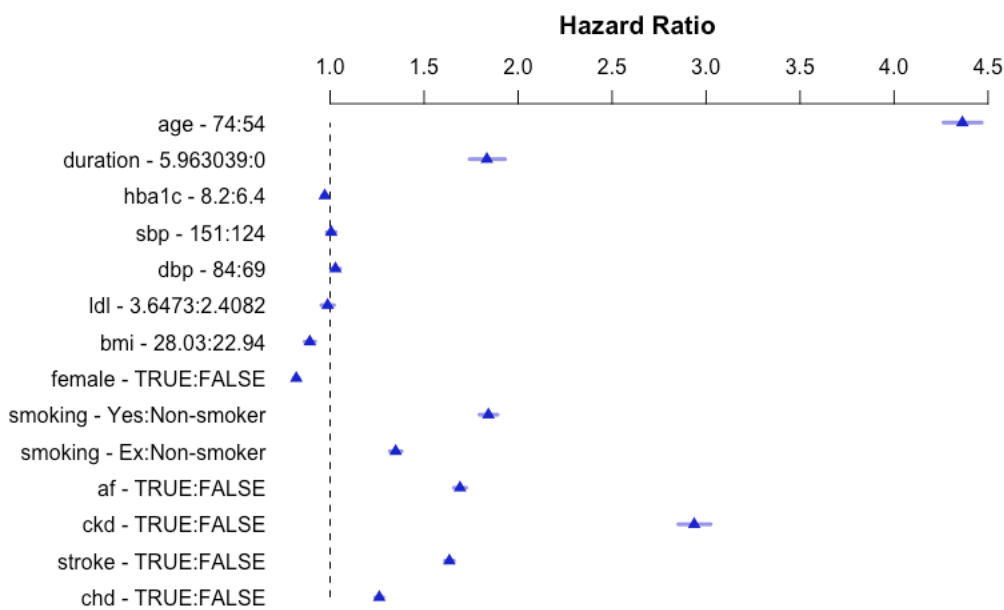


Supplemental Figure 2. Hazard ratios

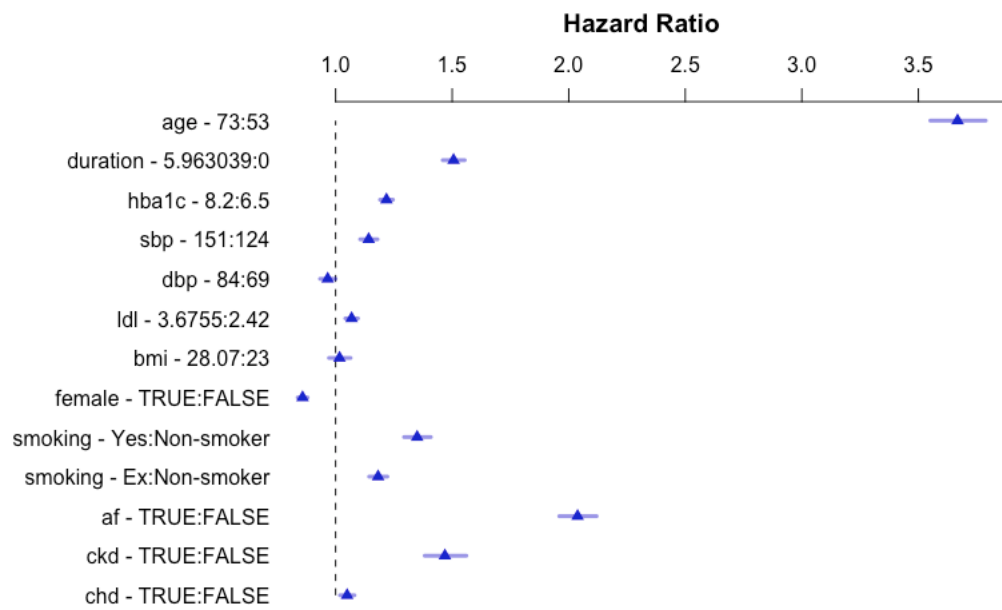
Forest plots of the HKU-SG models. The filled triangles indicate the hazard ratio of each variable, adjusted for all other variables in the model. Horizontal bars indicate 95% confidence intervals. For the continuous variables hazard ratios are estimated for the third vs the first quartile. All continuous variables were included as restricted cubic splines with four knots at the respective 5th, 35th, 65th and 95th sample percentiles.

Abbreviations: duration = duration of diabetes (years), hba1c = hemoglobin A1c (%), sbp = systolic blood pressure (mmHg), dbp = diastolic blood pressure (mmHg), ldl = LDL-cholesterol (mmol/L), bmi = body mass index, smoking = current smoking status (yes/ex-smoker/no), af = atrial fibrillation, ckd = chronic kidney disease, stroke = cerebrovascular disease, chd = ischemic heart disease.

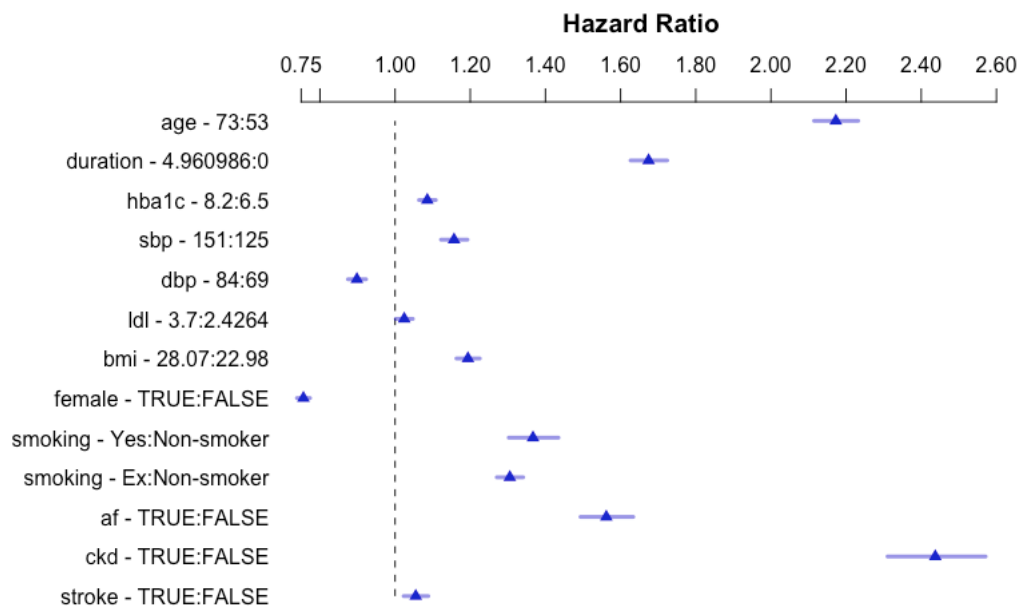
Mortality



Cerebrovascular disease



Ischemic heart disease



Supplemental Appendix 2. HKU-SG risk equations

Abbreviations: duration = duration of diabetes (years), smoking = current smoking status (yes/ex-smoker/no), af = atrial fibrillation, ckd = chronic kidney disease, cvd = cerebrovascular disease, chd = ischemic heart disease, hba1c = hemoglobin A1c (%), sbp = systolic blood pressure (mmHg), dbp = diastolic blood pressure (mmHg), ldl = LDL-cholesterol (mmol/L), bmi = body mass index.

Mortality

$$\begin{aligned} &100*(1-0.912^{\exp(2.727159} \\ &\quad +0.02659452*age+4.075628e-5*(age-41)^3-0.0001070358*(age-58)^3 \\ &\quad +7.311264e-5*(age-70)^3-6.833147e-6*(age-85)^3 \\ &\quad +0.2650322*duration-0.01608406*(duration-0.04654346)^3 \\ &\quad +0.01883374*(duration-0.9609856)^3-0.00277583*(duration-6.466804)^3 \\ &\quad +2.614735e-5*(duration-22.96235)^3 \\ &\quad -0.1983312*(female==TRUE) \\ &\quad -0.3118533*(smoking=="Ex- smoker")-0.6109742*(smoking=="Non-smoker") \\ &\quad +0.5252391*(af==TRUE) \\ &\quad +1.077321*(ckd==TRUE) \\ &\quad +0.4913603*(cvd==TRUE) \\ &\quad +0.2324324*(chd==TRUE) \\ &\quad -0.3320009*hba1c+0.06135776*(hba1c-5.6)^3-0.1198288*(hba1c-6.6)^3 \\ &\quad +0.05774934*(hba1c-7.6)^3+0.0007216831*(hba1c-11.6)^3 \\ &\quad -0.006923551*sbp+3.548158e-6*(sbp-108)^3-8.185037e-6*(sbp-130)^3 \\ &\quad +4.343557e-6*(sbp-145)^3+2.93321e-7*(sbp-174)^3 \\ &\quad -0.00510383*dbp+8.585339e-6*(dbp-58)^3-1.604159e-5*(dbp-71)^3 \\ &\quad +4.674797e-6*(dbp-80)^3+2.781449e-6*(dbp-96)^3 \\ &\quad -0.1802774*ldl+0.03426755*(ldl-1.62)^3-0.06139979*(ldl-2.6606)^3 \\ &\quad +0.01499461*(ldl-3.3636)^3+0.01213762*(ldl-4.73)^3 \\ &\quad -0.0506029*bmi+0.0003252084*(bmi-19.7)^3-0.0004954199*(bmi-23.95)^3 \\ &\quad +2.750309e-5*(bmi-26.83)^3+0.0001427083*(bmi-33.08)^3)) \end{aligned}$$

Cerebrovascular disease

$100 * (1 - 0.956^{\exp(-2.064696 + 0.04760847 * \text{age} + 2.588852e-5 * (\text{age} - 41)^3 - 0.0001133716 * (\text{age} - 57)^3 + 0.000129855 * (\text{age} - 69)^3 - 4.237201e-5 * (\text{age} - 84)^3 + 0.1577806 * \text{duration} - 0.008730594 * (\text{duration} - 0.04654346)^3 + 0.0102011 * (\text{duration} - 0.9609856)^3 - 0.001469774 * (\text{duration} - 6.38193)^3 - 7.300185e-7 * (\text{duration} - 22.96235)^3 - 0.1529727 * (\text{female} == \text{TRUE}) - 0.1325478 * (\text{smoking} == \text{"Ex-smoker"}) - 0.2999421 * (\text{smoking} == \text{"Non-smoker"}) + 0.7119795 * (\text{af} == \text{TRUE}) + 0.3844405 * (\text{ckd} == \text{TRUE}) + 0.04812592 * (\text{chd} == \text{TRUE}) - 0.2098922 * \text{hba1c} + 0.06664091 * (\text{hba1c} - 5.6)^3 - 0.1429844 * (\text{hba1c} - 6.6)^3 + 0.07876916 * (\text{hba1c} - 7.6)^3 - 0.00242565 * (\text{hba1c} - 11.6)^3 + 0.001670955 * \text{sbp} + 1.651687e-6 * (\text{sbp} - 108)^3 - 4.057867e-6 * (\text{sbp} - 130)^3 + 2.397451e-6 * (\text{sbp} - 145)^3 + 8.728936e-9 * (\text{sbp} - 173)^3 - 0.004012801 * \text{dbp} - 1.040069e-6 * (\text{dbp} - 58)^3 + 2.512736e-5 * (\text{dbp} - 72)^3 - 3.756894e-5 * (\text{dbp} - 81)^3 + 1.348164e-5 * (\text{dbp} - 96)^3 - 0.02585389 * \text{ldl} + 0.01522244 * (\text{ldl} - 1.61573)^3 - 0.0270327 * (\text{ldl} - 2.6818)^3 + 0.005895536 * (\text{ldl} - 3.3936)^3 + 0.005914729 * (\text{ldl} - 4.716)^3 + 0.006860727 * \text{bmi} - 4.236023e-5 * (\text{bmi} - 19.77)^3 + 6.894357e-5 * (\text{bmi} - 24)^3 - 1.031967e-5 * (\text{bmi} - 26.88)^3 - 1.626367e-5 * (\text{bmi} - 33.19)^3)$

Ischemic heart disease

$100 * (1 - 0.940^{\exp(-2.369324 + 0.05279655 * \text{age} - 1.113892e-5 * (\text{age} - 40)^3 + 2.355396e-5 * (\text{age} - 57)^3 - 9.722953e-6 * (\text{age} - 69)^3 - 2.692082e-6 * (\text{age} - 84)^3 + 0.1900872 * \text{duration} - 0.009881304 * (\text{duration} - 0.04654346)^3 + 0.01164563 * (\text{duration} - 0.9609856)^3 - 0.001751162 * (\text{duration} - 5.963039)^3 - 1.31642e-5 * (\text{duration} - 21.96304)^3 - 0.2796647 * (\text{female} == \text{TRUE}) - 0.04617688 * (\text{smoking} == \text{"Ex-smoker"}) - 0.3125719 * (\text{smoking} == \text{"Non-smoker"}) + 0.4459626 * (\text{af} == \text{TRUE}) + 0.8908878 * (\text{ckd} == \text{TRUE}) + 0.05348183 * (\text{cvd} == \text{TRUE}) - 0.06588639 * \text{hba1c} + 0.02325631 * (\text{hba1c} - 5.6)^3 - 0.04966861 * (\text{hba1c} - 6.6)^3 + 0.02718206 * (\text{hba1c} - 7.6)^3 - 0.0007697539 * (\text{hba1c} - 11.7)^3 + 0.001559869 * \text{sbp} + 2.09833e-6 * (\text{sbp} - 108)^3 - 5.63889e-6 * (\text{sbp} - 130)^3 + 3.7886e-6 * (\text{sbp} - 145)^3 - 2.480404e-7 * (\text{sbp} - 173)^3 - 0.01556448 * \text{dbp} + 9.790044e-6 * (\text{dbp} - 59)^3 - 9.663981e-6 * (\text{dbp} - 72)^3 - 8.686406e-6 * (\text{dbp} - 81)^3 + 8.560342e-6 * (\text{dbp} - 96)^3 - 0.1870673 * \text{ldl} + 0.04221539 * (\text{ldl} - 1.6273)^3 - 0.09174528 * (\text{ldl} - 2.6945)^3 + 0.04208207 * (\text{ldl} - 3.4)^3 + 0.007447821 * (\text{ldl} - 4.7573)^3 + 0.03542997 * \text{bmi} + 6.105394e-5 * (\text{bmi} - 19.73)^3 - 0.0005459628 * (\text{bmi} - 23.97)^3 + 0.0006664542 * (\text{bmi} - 26.87)^3 - 0.0001815454 * (\text{bmi} - 33.19)^3)$

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