

Supplementary File 1

Supplementary Table S1: Candidate predictor missingness

ACCORD variable	Predictor definition	Missing n	Missing %
hist_quityrs	Years since quitting cigarettes	3777	55.11
hist_yrslipi	Years since hyperlipidemia diagnosis	1982	28.92
hist_yrstens	Years since hypertension diagnosis	1647	24.03
hist_retpathy	History of retinopathy	1036	15.12
hist_smokelif	History of smoking	818	11.94
med_othbol_insulin	Other bolus insulin use	708	10.33
hist_MNSIscore	Michigan Neuropathy Screening Instrument physical examination score	148	2.16
hist_yrsdiab	Years since diabetes diagnosis	58	0.85
hist_waist_cm	Waist circumference	57	0.83
hist_feeling	Feeling Thermometer score	54	0.79
med_cox2	COX-2 inhibitor use	30	0.44
med_estrogen	Estrogen use, excluding vaginal creams	30	0.44
med_bile_sequestrant	Bile-acid sequestrant use	30	0.44
med_thyroid	Thyroid medication use	30	0.44
med_aspirin	Aspirin use	30	0.44
med_progestin	Progestin use	30	0.44
med_antiarrhythmic	Antiarrhythmic medication use	30	0.44
med_oral_asthma	Oral asthma medication use, excluding steroids	30	0.44
med_digitalis	Digitalis preparation use	30	0.44
med_other_lipidmed	Other lipid-lowering medication use	30	0.44
med_nitrate	Nitrate use	30	0.44
med_other_cvmed	Other cardiovascular medication use	30	0.44
med_anti_depress	Antidepressant use	30	0.44
med_fibrate	Fibrate use at baseline	30	0.44
med_niacin	Niacin or nicotinic acid use	30	0.44
med_cholest_abi	Cholesterol absorption inhibitor use	30	0.44
med_other_med	Other prescribed medication use	30	0.44
med_herbal	Herbal or alternative medication use	30	0.44
med_platelet_agi	Antiplatelet medication use, excluding aspirin	30	0.44
med_otc	Over-the-counter medication use	30	0.44
med_anti_inflam	Nonsteroidal anti-inflammatory medication use, excluding aspirin	30	0.44
med_vitamin	Vitamin or nutritional supplement use	30	0.44
med_fluid_retention	Diuretic use for fluid retention	30	0.44
med_osteoporosis	Osteoporosis medication use	30	0.44
med_anti_psych	Antipsychotic medication use	30	0.44
med_anti_coag	Oral anticoagulant use	30	0.44
med_inhaled_asthma	Inhaled steroid use for asthma	30	0.44
med_oral_steroid	Oral steroid use	30	0.44
med_statin	Statin use	27	0.39
baseline_hr	Heart rate	27	0.39
baseline_dbp	Diastolic blood pressure	25	0.36
baseline_sbp	Systolic blood pressure	25	0.36
med_beta_blocker	Beta-blocker use	16	0.23
med_acei	Angiotensin-converting enzyme inhibitor use	16	0.23
med_reserpine	Reserpine use	16	0.23
med_vasodilator	Vasodilator use	16	0.23
med_central_agent	Central alpha-adrenergic agonist use	16	0.23

med_alpha_blocker	Peripheral alpha-blocker use	16	0.23
med_nondhp_ccb	Nondihydropyridine calcium-channel blocker use	16	0.23
med_dhp_ccb	Dihydropyridine calcium-channel blocker use	16	0.23
med_other_bpmed	Other antihypertensive medication use	16	0.23
med_a2rb	Angiotensin receptor blocker use	16	0.23
med_potassium	Potassium supplement use	16	0.23
med_ksparing	Potassium-sparing diuretic use	16	0.23
med_thiazide	Thiazide diuretic use	16	0.23
med_loop	Loop diuretic use	16	0.23
baseline_hba1c	Glycated hemoglobin (HbA1c)	7	0.10
baseline_potassium	Serum potassium	6	0.09
hist_edu	Highest level of education	3	0.04
baseline_bmi	Body mass index calculated from baseline height and weight	3	0.04
hist_alcohol	Number of alcoholic drinks consumed weekly	2	0.03
baseline_ldl	Low-density lipoprotein cholesterol	2	0.03
baseline_vldl	Very-low-density lipoprotein cholesterol	2	0.03
baseline_trig	Triglycerides	2	0.03
baseline_chol	Total cholesterol	2	0.03
hist_ht_cm	Height	2	0.03
hist_depressn	History of depression	1	0.01
baseline_hdl	High-density lipoprotein cholesterol	1	0.01
hist_wt_kg	Weight	1	0.01
hist_livealon	Lives with one or more adults	1	0.01
hist_ulcer	History of a foot ulcer requiring antibiotics	0	0.00
hist_hartfail	History of heart failure	0	0.00
hist_neuropat	History of neuropathy or nerve problems	0	0.00
hist_eyedisea	History of eye disease	0	0.00
hist_histhart	Family history of heart disease, heart attack, or stroke	0	0.00
hist_cigarett	Smoked cigarettes in the preceding 30 days	0	0.00
Female	Female sex	0	0.00
med_other_diabmed	Other diabetes treatment use	0	0.00
med_sulfonylurea	Sulfonylurea use	0	0.00
cvd_hx_baseline	History of cardiovascular disease at baseline	0	0.00
Raceclass	Race/ethnicity category	0	0.00
baseline_fpg	Fasting plasma glucose	0	0.00
baseline_alt	Alanine aminotransferase	0	0.00
baseline_cpk	Creatine phosphokinase	0	0.00
baseline_gfr	Estimated glomerular filtration rate	0	0.00
med_biguanide	Biguanide/metformin use	0	0.00
baseline_age	Age at randomization	0	0.00
med_meglitinide	Meglitinide use	0	0.00
med_ag_inhibitor	Alpha-glucosidase inhibitor use	0	0.00
med_nphl_insulin	NPH or L insulin use	0	0.00
med_tzd	Thiazolidinedione use	0	0.00
med_reg_insulin	Regular insulin use	0	0.00
med_la_insulin	Lispro or aspart insulin use	0	0.00
med_premix_insulin	Premixed insulin use	0	0.00

The three candidate history variables with greater than 20% missingness were excluded from the primary model. The remaining 91 predictors comprised the primary feature set.

Supplementary Table S2: Characteristics of the training, calibration, and held-out test sets.

Characteristic	Training	Calibration	Held-out test
Participants, n	4,111	1,371	1,371
Annualized eGFR change, mL/min/1.73 m ² per year, mean (SD)	-3.75 (6.61)	-3.70 (5.87)	-3.64 (5.61)
Rapid decline ($\leq$ -5 mL/min/1.73 m ² per year), n (%)	1,393 (33.9%)	465 (33.9%)	467 (34.1%)
Age, years, mean (SD)	62.7 (6.5)	62.7 (6.5)	62.7 (6.7)
Female sex, n (%)	1,606 (39.1%)	509 (37.1%)	534 (38.9%)
Baseline eGFR, mL/min/1.73 m ² , mean (SD)	91.3 (29.4)	92.4 (27.7)	91.1 (26.4)
HbA1c, %, mean (SD)	8.3 (1.1)	8.3 (1.0)	8.3 (1.1)
Systolic blood pressure, mmHg, mean (SD)	136.7 (16.8)	136.7 (16.9)	137.3 (16.4)
Triglycerides, mg/dL, mean (SD)	190.1 (141.7)	185.2 (141.1)	191.2 (162.5)
Creatine phosphokinase, U/L, mean (SD)	139.5 (122.9)	135.1 (120.2)	144.4 (160.6)

Supplementary Table S3: Paired test MAE differences

Comparator	RF minus comparator MAE	95% CI
DummyMean	-0.600	-0.756 to -0.450
RidgeCV	-0.146	-0.242 to -0.050
LassoCV	-0.129	-0.210 to -0.041
ElasticNetCV	-0.127	-0.209 to -0.041
HistGradientBoosting	-0.051	-0.102 to 0.001
XGBoost	-0.005	-0.060 to 0.049
Baseline eGFR alone	-0.303	-0.405 to -0.200
Clinical linear model	-0.178	-0.273 to -0.078

Supplementary Table S4: Demographic subgroup performance in the held-out test set.

Subgroup	n	MAE (95% CI)	90% interval coverage (95% CI)	Mean interval width (95% CI)
All participants	1,371	3.370 (3.221 to 3.527)	90.9% (89.2% to 92.3%)	14.706 (14.426 to 15.031)
Men	837	3.292 (3.110 to 3.480)	91.5% (89.4% to 93.2%)	14.302 (13.936 to 14.744)
Women	534	3.493 (3.238 to 3.781)	89.9% (87.0% to 92.2%)	15.340 (14.846 to 15.814)
Age <65 years	892	3.553 (3.360 to 3.753)	90.0% (87.9% to 91.8%)	15.177 (14.798 to 15.612)
Age $\geq$ 65 years	479	3.031 (2.794 to 3.272)	92.5% (89.8% to 94.5%)	13.829 (13.351 to 14.318)
White	881	3.253 (3.070 to 3.438)	91.3% (89.2% to 93.0%)	14.241 (13.881 to 14.650)
Black	260	3.719 (3.337 to 4.130)	90.0% (85.8% to 93.1%)	15.862 (15.177 to 16.615)
Hispanic	84	4.304 (3.409 to 5.274)	86.9% (78.1% to 92.5%)	15.411 (14.303 to 16.729)
Other race/ethnicity	146	2.922 (2.532 to 3.358)	92.5% (87.0% to 95.7%)	15.051 (14.097 to 16.079)

Supplementary Table S5: eGFR-conditioned interval-width analysis

Quintile	n	Mean baseline eGFR	Mean width	MAE	90% interval coverage	Rapid decline, %
Q1	280	90.858	10.526	3.158	0.839	35.0
Q2	271	89.852	12.664	3.339	0.900	31.7
Q3	269	90.498	14.198	3.232	0.929	33.5
Q4	271	91.387	15.930	3.693	0.908	35.4
Q5	280	92.806	20.168	3.434	0.968	34.6

Conditioned quintile score versus baseline eGFR: Spearman $\rho=0.004$ ($P=0.882$). Adjusted absolute-error difference per quintile: 0.063 mL/min/1.73 m² per year (95% CI -0.044 to 0.170; $P=0.250$). Adjusted rapid-decline OR per quintile: 1.006 (95% CI 0.923 to 1.095; $P=0.899$).