Supplemental Table S1. Interaction/Sensitivity Analyses between HGI and HbA1c Parameters with Younger/Older Age (</≥ 60 Years) and Sex, and Their Associated Risks in Stratified Analyses for the Future Occurrence of Macro- and Microvascular Complications and Mortality

HGI and HbA1c parameter	Age, HR (95% CI)			Sex, HR (95% CI)		
	<60 years (n=348)	≥60 years (n=339)	P for-interaction	Female (n=420)	Male (n=267)	P for-interaction
Total CVEs (n=215)	93	122		124	91	
Baseline HGI, continuous[d]	1.22 (1.03–1.44)[c]	1.03 (0.86–1.25)	0.328	1.20 (1.00–1.44)	1.11 (0.92–1.35)	0.461
Baseline HbA1c, continuous[d]	1.23 (1.01–1.49)[c]	1.00 (0.82–1.22)	0.198	1.16 (0.94–1.43)	1.14 (0.93–1.39)	0.910
Mean 1-year HGI, continuous[d]	1.51 (1.21–1.87)[a]	0.99 (0.77–1.28)	0.028	1.33 (1.07–1.65)[c]	1.29 (0.99–1.67)	0.823
Mean 1-year HbA1c, continuous[d]	1.39 (1.12–1.72)[b]	1.15 (0.89–1.49)	0.217	1.37 (1.11–1.70)[b]	1.39 (1.07–1.82)[c]	0.934
1-year HGI variability, continuous[d]	1.00 (0.83–1.20)	1.32 (1.05–1.64)[c]	0.099	1.08 (0.91–1.29)	1.21 (0.99–1.48)	0.456
1-year HbA1c variability, continuous[d]	1.03 (0.85–1.25)	1.25 (1.01–1.54)[c]	0.276	1.14 (0.95–1.37)	1.14 (0.94–1.38)	0.977
MACEs (n=176)	70	106		101	75	
Baseline HGI, continuous[d]	1.14 (0.94–1.39)	1.11 (0.91–1.35)	0.837	1.17 (0.95–1.43)	1.10 (0.89–1.37)	0.632
Baseline HbA1c, continuous[d]	1.09 (0.86–1.38)	1.08 (0.88–1.33)	0.968	1.10 (0.87–1.40)	1.13 (0.90–1.42)	0.881
Mean 1-year HGI, continuous[d]	1.24 (0.96–1.61)	1.10 (0.83–1.44)	0.517	1.21 (0.95–1.54)	1.18 (0.87–1.61)	0.755
Mean 1-year HbA1c, continuous[d]	1.20 (0.93–1.55)	1.22 (0.92–1.62)	0.896	1.27 (1.00–1.61)	1.28 (0.94–1.75)	0.887
1-year HGI variability, continuous[d]	1.06 (0.86–1.30)	1.34 (1.05–1.71)[c]	0.238	1.13 (0.94–1.37)	1.22 (0.98–1.50)	0.656
1-year HbA1c variability, continuous[d]	1.07 (0.86–1.33)	1.28 (1.01–1.62)[c]	0.377	1.21 (0.99–1.47)	1.10 (0.90–1.36)	0.547
Cardiovascular mortality (n=131)	44	87		78	53	
Baseline HGI, continuous[d]	1.11 (0.86–1.44)	1.13 (0.91–1.42)	0.838	1.17 (0.91–1.52)	1.15 (0.89–1.48)	0.966
Baseline HbA1c, continuous[d]	1.05 (0.77–1.43)	1.13 (0.90–1.42)	0.725	1.14 (0.86–1.51)	1.17 (0.89–1.53)	0.582
Mean 1-year HGI, continuous[d]	1.09 (0.76–1.58)	1.52 (1.05–2.19)[c]	0.245	1.29 (0.98–1.71)	1.34 (0.93–1.92)	0.948
Mean 1-year HbA1c, continuous[d]	1.31 (0.95–1.80)	1.40 (1.02–1.92)[c]	0.589	1.35 (1.03–1.77)[c]	1.66 (1.14–2.41)[b]	0.432
1-year HGI variability, continuous[d]	1.07 (0.82–1.39)	1.35 (1.03–1.76)[c]	0.411	1.12 (0.89–1.41)	1.33 (1.03–1.71)[c]	0.436
1-year HbA1c variability, continuous[d]	1.13 (0.86–1.48)	1.31 (1.02–1.69)[c]	0.531	1.25 (0.99–1.57)	1.21 (0.94–1.56)	0.837
All-cause mortality (n=269)	91	178		154	115	
Baseline HGI, continuous[d]	1.09 (0.90–1.31)	1.16 (0.99–1.36)	0.562	1.15 (0.96–1.38)	1.14 (0.96–1.35)	0.829
Baseline HbA1c, continuous[d]	1.12 (0.90–1.38)	1.15 (0.98–1.36)	0.962	1.19 (0.98–1.45)	1.14 (0.95–1.37)	0.679
Mean 1-year HGI, continuous[d]	1.21 (0.98–1.49)	1.13 (0.90–1.41)	0.222	1.23 (1.01–1.49)[c]	1.24 (0.96–1.59)	0.923
Mean 1-year HbA1c, continuous[d]	1.22 (0.99–1.50)	1.28 (1.02–1.60)[c]	0.387	1.33 (1.11–1.60)[b]	1.36 (1.05–1.77)[c]	0.752
1-year HGI variability, continuous[d]	0.97 (0.80–1.18)	1.22 (1.01–1.48)[c]	0.571	1.11 (0.94–1.30)	1.10 (0.90–1.36)	0.943
1-year HbA1c variability, continuous[d]	1.04 (0.85–1.27)	1.20 (1.00–1.44)	0.742	1.18 (1.01–1.39)[c]	1.04 (0.85–1.28)	0.422
Microalbuminuria (n=126)	67	59		74	52	
Baseline HGI, continuous[d]	1.27 (1.00–1.62)[c]	0.78 (0.56–1.10)	0.023	1.07 (0.83–1.39)	1.11 (0.84–1.46)	0.465
Baseline HbA1c, continuous[d]	1.17 (0.91–1.50)	0.76 (0.53–1.10)	0.082	1.00 (0.77–1.31)	1.05 (0.78–1.42)	0.317
Mean 1-year HGI, continuous[d]	1.30 (1.02–1.65)[c]	1.06 (0.73–1.53)	0.447	1.27 (0.97–1.67)	1.14 (0.83–1.58)	0.768
Mean 1-year HbA1c, continuous[d]	1.37 (1.08–1.74)[c]	1.17 (0.81–1.70)	0.668	1.30 (1.00–1.68)	1.27 (0.91–1.77)	0.434
1-year HGI variability, continuous[d]	1.19 (0.96–1.47)	1.09 (0.78–1.53)	0.722	1.04 (0.80–1.35)	1.19 (0.94–1.52)	0.232
1-year HbA1c variability, continuous[d]	1.12 (0.90–1.38)	1.11 (0.83–1.49)	0.897	1.09 (0.86–1.40)	1.09 (0.85–1.40)	0.689

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Supplemental Table S1. Continued

HGI and HbA1c parameter	Age, HR (95% CI)			Sex, HR (95% CI)		
	<60 years (n=348)	≥60 years (n=339)	P for-interaction	Female (n=420)	Male (n=267)	P for-interaction
Renal failure (n=104)	51	53		65	39	
Baseline HGI, continuous[d]	1.23 (0.95–1.58)	1.35 (1.04–1.76)[c]	0.998	1.44 (1.12–1.85)[b]	1.28 (0.93–1.77)	0.156
Baseline HbA1c, continuous[d]	1.25 (0.95–1.64)	1.34 (1.03–1.76)[c]	0.942	1.42 (1.09–1.86)[b]	1.44 (1.02–2.02)[c]	0.543
Mean 1-year HGI, continuous[d]	1.35 (1.05–1.74)[c]	1.40 (0.93–2.10)	0.877	1.47 (1.14–1.89)[b]	1.09 (0.69–1.73)	0.246
Mean 1-year HbA1c, continuous[d]	1.40 (1.08–1.82)[c]	1.28 (0.84–1.93)	0.481	1.47 (1.15–1.88)[b]	1.03 (0.65–1.61)	0.268
1-year HGI variability, continuous[d]	1.14 (0.89–1.45)	1.31 (0.93–1.86)	0.642	1.17 (0.95–1.44)	1.08 (0.76–1.53)	0.568
1-year HbA1c variability, continuous[d]	1.22 (0.96–1.54)	1.28 (0.93–1.76)	0.802	1.33 (1.08–1.64)[b]	0.87 (0.59–1.27)	0.072
Retinopathy (n=161)	89	72		107	54	
Baseline HGI, continuous[d]	1.44 (1.18–1.75)[a]	0.94 (0.72–1.23)	0.012	0.98 (0.79–1.22)	1.51 (1.20–1.90)[b]	0.042
Baseline HbA1c, continuous[d]	1.49 (1.20–1.84)[a]	0.97 (0.73–1.29)	0.025	1.06 (0.85–1.33)	1.46 (1.15–1.85)[b]	0.162
Mean 1-year HGI, continuous[d]	1.49 (1.22–1.83)[a]	1.00 (0.71–1.42)	0.322	1.06 (0.87–1.30)	1.63 (1.20–2.21)[b]	0.043
Mean 1-year HbA1c, continuous[d]	1.57 (1.30–1.91)[a]	1.00 (0.72–1.38)	0.133	1.12 (0.92–1.35)	1.81 (1.33–2.47)[a]	0.015
1-year HGI variability, continuous[d]	1.32 (1.14–1.53)[a]	1.03 (0.78–1.36)	0.145	1.25 (1.05–1.49)[c]	1.32 (1.07–1.65)[c]	0.717
1-year HbA1c variability, continuous[d]	1.31 (1.13–1.50)[a]	1.00 (0.77–1.30)	0.095	1.20 (0.99–1.44)	1.26 (1.03–1.53)[c]	0.657
Peripheral neuropathy (n=177)	94	83		115	62	
Baseline HGI, continuous[d]	1.23 (1.01–1.49)[c]	1.31 (1.03–1.68)[c]	0.379	1.31 (1.07–1.60)[b]	1.22 (0.95–1.57)	0.910
Baseline HbA1c, continuous[d]	1.39 (1.11–1.73)[b]	1.38 (1.08–1.75)[b]	0.856	1.57 (1.27–1.94)[a]	1.21 (0.92–1.60)	0.678
Mean 1-year HGI, continuous[d]	1.35 (1.08–1.69)[b]	1.20 (0.87–1.67)	0.619	1.20 (0.97–1.50)	1.64 (1.18–2.27)[b]	0.112
Mean 1-year HbA1c, continuous[d]	1.29 (1.03–1.62)[c]	1.29 (0.93–1.79)	0.906	1.21 (0.98–1.50)	1.53 (1.09–2.15)[c]	0.134
1-year HGI variability, continuous[d]	1.05 (0.86–1.28)	1.35 (1.03–1.78)[c]	0.312	1.11 (0.93–1.32)	1.09 (0.84–1.41)	0.593
1-year HbA1c variability, continuous[d]	1.12 (0.92–1.35)	1.26 (0.96–1.65)	0.669	1.06 (0.88–1.29)	1.20 (0.96–1.47)	0.189
Symptomatic hypoglycemia (n=90)	57	33		65	25	
Baseline HGI, continuous[d]	0.90 (0.67–1.21)	1.46 (0.88–2.45)	0.052	0.82 (0.59–1.13)	1.63 (1.06–2.52)[c]	0.010
Baseline HbA1c, continuous[d]	1.04 (0.76–1.41)	1.78 (1.06–2.98)[c]	0.033	1.07 (0.77–1.48)	1.71 (1.07–2.73)[c]	0.058
Mean 1-year HGI, continuous[d]	0.98 (0.72–1.35)	0.81 (0.47–1.37)	0.984	0.99 (0.72–1.34)	0.94 (0.56–1.58)	0.618
Mean 1-year HbA1c, continuous[d]	1.01 (0.74–1.37)	0.84 (0.48–1.49)	0.923	1.05 (0.78–1.43)	0.92 (0.54–1.57)	0.698
1-year HGI variability, continuous[d]	1.06 (0.81–1.39)	0.95 (0.52–1.72)	0.931	1.06 (0.79–1.42)	1.14 (0.71–1.85)	0.683
1-year HbA1c variability, continuous[d]	1.03 (0.77–1.37)	0.81 (0.44–1.51)	0.716	0.99 (0.72–1.37)	1.09 (0.69–1.73)	0.619

Values are expressed as adjusted HR and their 95% CI, estimated for standardized increments of 1-standard deviation in each parameter by Cox analyses: except for hypoglycemia outcome, which were adjusted odds ratios by logistic regressions. Models were adjusted for age, sex, body mass index (body height in neuropathy analyses), diabetes duration, smoking status, physical inactivity, number of antihypertensive drugs in use, presence of micro- and macrovascular complications at baseline, systolic blood pressure, high-density lipoprotein and low-density lipoprotein cholesterol levels, and use of insulin, statins and aspirin. Analyses of renal outcomes were further adjusted for baseline albuminuria and estimated glomerular filtration rate.
HGI, hemoglobin glycation index; HbA1c, glycated hemoglobin; HR, hazard ratio; CI, confidence interval; CVE, cardiovascular event; MACE, major adverse cardiovascular event.
[a]P<0.001; [b]P<0.01; [c]P<0.05; [d]HR calculated for 1-standard deviation.