Supplemental Table S2. Interaction/Sensitivity Analyses between HGI and HbA1c Parameters with Shorter/Longer Diabetes Duration (</≥8 Years) and Poorer/Better Glycemic Control (Mean HbA1c </≥7.5%), and Their Associated Risks in Stratified Analyses for the Future Occurrence of Macro- and Microvascular Complications and Mortality

HGI and HbA1c parameter	Diabetes duration, HR (95% CI)			Glycemic control during the 1st-year of follow-up, HR (95% CI)		
	<8 years (n=327)	≥8 years (n=360)	P for-interaction	Mean HbA1c <7.5% (n=339)	Mean HbA1c ≥7.5% (n=348)	P for-interaction
Total CVEs (n=215)	88	127		89	126	
Baseline HGI, continuous[d]	0.97 (0.79–1.21)	1.28 (1.10–1.50)[b]	0.106	1.22 (0.93–1.60)	1.07 (0.92–1.25)	0.442
Baseline HbA1c, continuous[d]	0.94 (0.73–1.21)	1.25 (1.06–1.49)[b]	0.265	1.12 (0.82–1.52)	1.04 (0.86–1.25)	0.782
Mean 1-year HGI, continuous[d]	1.32 (0.98–1.78)	1.23 (1.02–1.49)[c]	0.612	1.22 (0.63–2.35)	1.08 (0.87–1.33)	0.552
Mean 1-year HbA1c, continuous[d]	1.31 (1.00–1.71)[c]	1.33 (1.09–1.63)[b]	0.845	1.14 (0.54–2.42)	1.20 (0.96–1.52)	0.776
1-year HGI variability, continuous[d]	0.97 (0.77–1.21)	1.13 (0.96–1.32)	0.487	1.55 (0.90–2.65)	0.99 (0.85–1.16)	0.090
1-year HbA1c variability, continuous[d]	0.99 (0.78–1.27)	1.12 (0.96–1.31)	0.602	1.31 (0.75–2.26)	1.02 (0.87–1.20)	0.665
MACEs (n=176)	79	97		74	102	
Baseline HGI, continuous[d]	0.94 (0.75–1.18)	1.29 (1.08–1.55)[b]	0.032	1.16 (0.87–1.55)	1.04 (0.87–1.25)	0.346
Baseline HbA1c, continuous[d]	0.87 (0.66–1.15)	1.26 (1.03–1.53)[c]	0.056	1.08 (0.79–1.49)	0.97 (0.78–1.20)	0.424
Mean 1-year HGI, continuous[d]	1.27 (0.90–1.80)	1.12 (0.89–1.41)	0.902	1.31 (0.63–2.71)	0.97 (0.76–1.23)	0.468
Mean 1-year HbA1c, continuous[d]	1.30 (0.95–1.77)	1.24 (0.97–1.57)	0.866	1.36 (0.58–3.20)	1.05 (0.80–1.37)	0.482
1-year HGI variability, continuous[d]	1.01 (0.80–1.28)	1.20 (1.01–1.43)[c]	0.276	1.45 (0.79–2.65)	1.07 (0.91–1.26)	0.319
1-year HbA1c variability, continuous[d]	1.02 (0.78–1.34)	1.18 (1.00–1.40)[c]	0.452	1.16 (0.65–2.09)	1.09 (0.91–1.30)	0.847
Cardiovascular mortality (n=131)	54	77		55	76	
Baseline HGI, continuous[d]	0.91 (0.67–1.23)	1.31 (1.06–1.62)[c]	0.088	1.11 (0.76–1.64)	1.05 (0.86–1.28)	0.643
Baseline HbA1c, continuous[d]	0.84 (0.59–1.20)	1.30 (1.04–1.62)[c]	0.113	1.14 (0.76–1.72)	0.96 (0.76–1.22)	0.319
Mean 1-year HGI, continuous[d]	1.26 (0.83–1.93)	1.24 (0.96–1.62)	0.957	1.11 (0.48–2.55)	1.15 (0.87–1.51)	0.757
Mean 1-year HbA1c, continuous[d]	1.34 (0.94–1.93)	1.40 (1.07–1.85)[c]	0.898	1.45 (0.53–3.98)	1.25 (0.93–1.67)	0.856
1-year HGI variability, continuous[d]	1.05 (0.78–1.41)	1.23 (1.01–1.50)[c]	0.351	1.77 (0.90–3.48)	1.05 (0.86–1.29)	0.146
1-year HbA1c variability, continuous[d]	1.00 (0.72–1.41)	1.26 (1.04–1.51)[c]	0.218	1.15 (0.55–2.41)	1.13 (0.92–1.38)	0.918
All-cause mortality (n=269)	107	162		118	151	
Baseline HGI, continuous[d]	0.98 (0.79–1.20)	1.24 (1.06–1.45)[b]	0.257	1.24 (0.97–1.60)	1.02 (0.87–1.18)	0.102
Baseline HbA1c, continuous[d]	1.01 (0.79–1.28)	1.22 (1.04–1.44)[c]	0.637	1.25 (0.96–1.64)	0.97 (0.81–1.16)	0.066
Mean 1-year HGI, continuous[d]	1.25 (0.94–1.66)	1.17 (0.97–1.40)	0.228	0.93 (0.54–1.60)	1.06 (0.87–1.29)	0.387
Mean 1-year HbA1c, continuous[d]	1.31 (1.02–1.69)[c]	1.26 (1.05–1.53)[c]	0.296	0.92 (0.49–1.74)	1.14 (0.92–1.41)	0.382
1-year HGI variability, continuous[d]	0.93 (0.73–1.19)	1.16 (1.00–1.33)[c]	0.271	1.33 (0.82–2.16)	0.97 (0.83–1.13)	0.262
1-year HbA1c variability, continuous[d]	0.96 (0.75–1.24)	1.14 (0.99–1.31)	0.437	1.02 (0.61–1.70)	1.00 (0.86–1.17)	0.793
Microalbuminuria (n=126)	61	65		56	70	
Baseline HGI, continuous[d]	1.11 (0.83–1.48)	1.02 (0.80–1.30)	0.846	1.04 (0.69–1.55)	1.05 (0.83–1.32)	0.949
Baseline HbA1c, continuous[d]	0.95 (0.70–1.31)	0.99 (0.76–1.28)	0.578	1.01 (0.66–1.56)	0.92 (0.70–1.20)	0.731
Mean 1-year HGI, continuous[d]	1.24 (0.87–1.76)	1.15 (0.90–1.47)	0.617	0.96 (0.46–2.00)	1.17 (0.90–1.53)	0.798
Mean 1-year HbA1c, continuous[d]	1.19 (0.86–1.65)	1.25 (0.97–1.61)	0.368	0.80 (0.34–1.88)	1.34 (1.01–1.79)[c]	0.429
1-year HGI variability, continuous[d]	1.12 (0.84–1.48)	1.10 (0.88–1.38)	0.866	0.82 (0.39–1.72)	1.09 (0.89–1.33)	0.557
1-year HbA1c variability, continuous[d]	1.07 (0.79–1.46)	1.08 (0.88–1.34)	0.777	0.51 (0.22–1.20)	1.08 (0.90–1.31)	0.067

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Supplemental Table S2. Continued

HGI and HbA1c parameter	Diabetes duration, HR (95% CI)			Glycemic control during the 1st-year of follow-up, HR (95% CI)		
	<8 years (*n*=327)	≥8 years (*n*=360)	*P* for-interaction	Mean HbA1c <7.5% (*n*=339)	Mean HbA1c ≥7.5% (*n*=348)	*P* for-interaction
Renal failure (*n*=104)	35	69		42	62	
Baseline HGI, continuous[d]	1.34 (0.91–1.96)	1.32 (1.06–1.64)[c]	0.702	1.54 (1.05–2.26)[c]	1.19 (0.96–1.48)	0.206
Baseline HbA1c, continuous[d]	1.40 (0.93–2.10)	1.34 (1.07–1.68)[c]	0.586	1.52 (1.02–2.27)[c]	1.18 (0.93–1.51)	0.296
Mean 1-year HGI, continuous[d]	1.26 (0.79–2.02)	1.43 (1.12–1.81)[b]	0.242	1.59 (0.62–4.07)	1.44 (1.11–1.88)[b]	0.788
Mean 1-year HbA1c, continuous[d]	1.30 (0.86–1.96)	1.44 (1.12–1.85)[b]	0.219	2.58 (0.79–8.39)	1.54 (1.15–2.06)[b]	0.658
1-year HGI variability, continuous[d]	1.17 (0.84–1.65)	1.16 (0.94–1.43)	0.587	1.25 (0.57–2.72)	1.19 (0.97–1.45)	0.848
1-year HbA1c variability, continuous[d]	1.14 (0.78–1.66)	1.22 (1.01–1.48)[c]	0.543	1.34 (0.64–2.81)	1.26 (1.04–1.54)[c]	0.898
Retinopathy (*n*=161)	44	117		54	107	
Baseline HGI, continuous[d]	1.65 (1.20–2.28)[b]	1.08 (0.90–1.31)	0.019	1.16 (0.78–1.72)	1.15 (0.95–1.39)	0.443
Baseline HbA1c, continuous[d]	2.03 (1.43–2.87)[a]	1.09 (0.89–1.33)	0.006	1.01 (0.65–1.58)	1.19 (0.97–1.46)	0.968
Mean 1-year HGI, continuous[d]	1.74 (1.21–2.50)[b]	1.14 (0.94–1.38)	0.052	0.39 (0.18–0.85)[c]	1.33 (1.08–1.64)[b]	0.012
Mean 1-year HbA1c, continuous[d]	2.02 (1.47–2.78)[a]	1.14 (0.94–1.37)	0.011	0.93 (0.36–2.40)	1.31 (1.05–1.62)[c]	0.812
1-year HGI variability, continuous[d]	1.53 (1.19–1.96)[b]	1.15 (0.98–1.35)	0.033	2.16 (1.20–3.92)[c]	1.17 (1.00–1.36)[c]	0.114
1-year HbA1c variability, continuous[d]	1.52 (1.15–2.01)[b]	1.13 (0.97–1.32)	0.060	1.60 (0.93–2.75)	1.14 (0.98–1.33)	0.433
Peripheral neuropathy (*n*=177)	67	110		79	98	
Baseline HGI, continuous[d]	1.16 (0.88–1.53)	1.33 (1.10–1.60)[b]	0.077	1.22 (0.88–1.70)	1.26 (1.05–1.51)[c]	0.878
Baseline HbA1c, continuous[d]	1.31 (0.96–1.78)	1.45 (1.19–1.76)[a]	0.087	1.37 (0.99–1.89)	1.39 (1.13–1.71)[b]	0.962
Mean 1-year HGI, continuous[d]	1.55 (1.09–2.20)[c]	1.23 (1.01–1.51)[c]	0.969	1.10 (0.54–2.22)	1.36 (1.08–1.71)[c]	0.958
Mean 1-year HbA1c, continuous[d]	1.53 (1.11–2.10)[c]	1.23 (1.00–1.52)	0.857	1.21 (0.51–2.86)	1.40 (1.09–1.61)[b]	0.857
1-year HGI variability, continuous[d]	1.31 (1.02–1.68)[c]	1.11 (0.93–1.31)	0.938	1.55 (0.84–2.85)	1.08 (0.92–1.27)	0.527
1-year HbA1c variability, continuous[d]	1.32 (1.00–1.74)	1.12 (0.95–1.33)	0.902	1.37 (0.76–2.48)	1.12 (0.95–1.32)	0.708
Symptomatic hypoglycemia (*n*=90)	30	60		34	56	
Baseline HGI, continuous[d]	0.84 (0.55–1.27)	1.26 (0.90–1.78)	0.234	1.13 (0.73–1.75)	0.96 (0.69–1.32)	0.254
Baseline HbA1c, continuous[d]	0.97 (0.63–1.51)	1.48 (1.02–2.14)[c]	0.258	1.19 (0.76–1.86)	1.19 (0.83–1.71)	0.633
Mean 1-year HGI, continuous[d]	0.97 (0.53–1.78)	0.90 (0.65–1.24)	0.728	0.78 (0.24–2.54)	0.98 (0.70–1.38)	0.948
Mean 1-year HbA1c, continuous[d]	1.12 (0.66–1.91)	0.93 (0.66–1.30)	0.546	1.70 (0.43–6.69)	0.96 (0.65–1.41)	0.376
1-year HGI variability, continuous[d]	1.56 (0.98–2.48)	0.83 (0.58–1.18)	0.030	2.54 (0.93–6.97)	0.97 (0.73–1.29)	0.060
1-year HbA1c variability, continuous[d]	1.22 (0.75–1.97)	0.87 (0.60–1.24)	0.246	0.95 (0.34–2.65)	0.96 (0.72–1.30)	0.948

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.