Supplemental Table S3. Interaction/Sensitivity Analyses between HGI and HbA1c Parameters with Absence/Presence of Macrovascular and Microvascular Diabetic Complications at Baseline, and Their Associated Risks in Stratified Analyses for the Future Occurrence of Macro- and Microvascular Complications and Mortality

HGI and HbA1c parameter	Macrovascular complications, HR (95% CI)			Microvascular complications, HR (95% CI)		
	Absent (n=483)	Present (n=204)	P for-interaction	Absent (n=314)	Present (n=373)	P for-interaction
Total CVEs (n=215)	114	101		80	135	
Baseline HGI, continuous[d]	1.23 (1.02–1.48)[c]	1.10 (0.92–1.32)	0.482	1.05 (0.81–1.35)	1.17 (1.01–1.36)[c]	0.297
Baseline HbA1c, continuous[d]	1.22 (1.00–1.47)[c]	1.05 (0.85–1.30)	0.397	1.07 (0.82–1.40)	1.16 (0.98–1.36)	0.418
Mean 1-year HGI, continuous[d]	1.36 (1.10–1.67)[b]	1.14 (0.87–1.49)	0.356	1.37 (0.98–1.91)	1.21 (1.00–1.46)[c]	0.887
Mean 1-year HbA1c, continuous[d]	1.46 (1.18–1.79)[a]	1.16 (0.90–1.51)	0.253	1.33 (0.97–1.82)	1.34 (1.10–1.62)[b]	0.532
1-year HGI variability, continuous[d]	1.16 (0.99–1.35)	1.03 (0.82–1.29)	0.376	1.11 (0.90–1.37)	1.11 (0.94–1.32)	0.749
1-year HbA1c variability, continuous[d]	1.15 (0.99–1.34)	1.01 (0.78–1.32)	0.407	1.11 (0.90–1.37)	1.14 (0.95–1.35)	0.626
MACEs (n=176)	91	85		66	110	
Baseline HGI, continuous[d]	1.13 (0.91–1.40)	1.19 (0.98–1.45)	0.508	1.03 (0.77–1.36)	1.17 (0.99–1.38)	0.341
Baseline HbA1c, continuous[d]	1.09 (0.88–1.37)	1.15 (0.91–1.45)	0.556	1.01 (0.75–1.36)	1.16 (0.96–1.40)	0.318
Mean 1-year HGI, continuous[d]	1.20 (0.94–1.54)	1.21 (0.90–1.64)	0.768	1.30 (0.91–1.88)	1.11 (0.90–1.38)	0.957
Mean 1-year HbA1c, continuous[d]	1.27 (1.00–1.62)	1.26 (0.94–1.69)	0.827	1.27 (0.89–1.80)	1.25 (1.00–1.55)[c]	0.658
1-year HGI variability, continuous[d]	1.20 (1.02–1.42)[c]	1.09 (0.85–1.39)	0.598	1.12 (0.91–1.39)	1.19 (0.99–1.44)	0.557
1-year HbA1c variability, continuous[d]	1.16 (0.99–1.37)	1.08 (0.81–1.44)	0.748	1.10 (0.89–1.36)	1.18 (0.97–1.44)	0.558
Cardiovascular mortality (n=131)	67	64		47	84	
Baseline HGI, continuous[d]	1.13 (0.86–1.47)	1.19 (0.96–1.47)	0.405	0.99 (0.69–1.43)	1.22 (1.00–1.47)[c]	0.366
Baseline HbA1c, continuous[d]	1.09 (0.83–1.44)	1.19 (0.93–1.52)	0.352	0.96 (0.65–1.42)	1.23 (1.00–1.51)[c]	0.347
Mean 1-year HGI, continuous[d]	1.19 (0.88–1.61)	1.43 (1.04–1.96)[c]	0.167	1.23 (0.79–1.91)	1.28 (1.00–1.64)	0.944
Mean 1-year HbA1c, continuous[d]	1.28 (0.95–1.73)	1.50 (1.11–2.03)[b]	0.161	1.28 (0.83–1.97)	1.46 (1.14–1.88)[b]	0.743
1-year HGI variability, continuous[d]	1.18 (0.95–1.47)	1.19 (0.92–1.55)	0.592	1.16 (0.88–1.53)	1.20 (0.97–1.50)	0.868
1-year HbA1c variability, continuous[d]	1.16 (0.94–1.43)	1.29 (0.96–1.74)	0.347	1.20 (0.91–1.58)	1.24 (0.99–1.54)	0.779
All-cause mortality (n=269)	150	119		90	179	
Baseline HGI, continuous[d]	1.23 (1.04–1.47)[c]	1.08 (0.91–1.28)	0.548	1.12 (0.86–1.44)	1.16 (1.01–1.34)[c]	0.846
Baseline HbA1c, continuous[d]	1.27 (1.06–1.51)[c]	1.05 (0.86–1.28)	0.497	1.15 (0.88–1.49)	1.18 (1.01–1.39)[c]	0.938
Mean 1-year HGI, continuous[d]	1.21 (0.99–1.47)	1.18 (0.93–1.51)	0.544	1.26 (0.91–1.75)	1.19 (1.00–1.42)[c]	0.946
Mean 1-year HbA1c, continuous[d]	1.33 (1.10–1.60)[b]	1.23 (0.97–1.55)	0.749	1.33 (0.97–1.81)	1.30 (1.09–1.54)[b]	0.988
1-year HGI variability, continuous[d]	1.11 (0.95–1.30)	1.06 (0.86–1.30)	0.921	1.11 (0.89–1.39)	1.10 (0.94–1.29)	0.878
1-year HbA1c variability, continuous[d]	1.11 (0.96–1.29)	1.11 (0.89–1.39)	0.642	1.12 (0.90–1.40)	1.13 (0.96–1.32)	0.628
Microalbuminuria (n=126)	92	34		51	75	
Baseline HGI, continuous[d]	1.21 (0.96–1.52)	0.95 (0.67–1.35)	0.198	1.02 (0.72–1.43)	1.09 (0.88–1.35)	0.409
Baseline HbA1c, continuous[d]	1.16 (0.93–1.46)	0.74 (0.45–1.21)	0.087	0.82 (0.57–1.20)	1.08 (0.86–1.37)	0.178
Mean 1-year HGI, continuous[d]	1.37 (1.09–1.70)[b]	0.52 (0.30–0.91)[c]	0.023	0.87 (0.58–1.30)	1.35 (1.07–1.71)[c]	0.065
Mean 1-year HbA1c, continuous[d]	1.48 (1.20–1.84)[a]	0.50 (0.29–0.86)[c]	0.008	0.91 (0.61–1.36)	1.42 (1.12–1.79)[b]	0.079
1-year HGI variability, continuous[d]	1.25 (1.05–1.49)[c]	0.60 (0.34–1.06)	0.019	1.06 (0.78–1.46)	1.16 (0.92–1.46)	0.577
1-year HbA1c variability, continuous[d]	1.18 (1.00–1.39)	0.62 (0.35–1.08)	0.084	0.89 (0.61–1.30)	1.22 (0.99–1.50)	0.123

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Supplemental Table S3. Continued

HGI and HbA1c parameter	Macrovascular complications, HR (95% CI)			Microvascular complications, HR (95% CI)		
	Absent (*n*=483)	Present (*n*=204)	*P* for-interaction	Absent (*n*=314)	Present (*n*=373)	*P* for-interaction
Renal failure (*n*=104)	62	42		24	80	
Baseline HGI, continuous[d]	1.17 (0.90–1.53)	1.35 (1.06–1.71)[c]	0.431	1.61 (0.95–2.73)	1.28 (1.06–1.55)[c]	0.643
Baseline HbA1c, continuous[d]	1.24 (0.94–1.62)	1.34 (1.02–1.78)[c]	0.607	1.36 (0.82–2.25)	1.31 (1.07–1.61)[c]	0.989
Mean 1-year HGI, continuous[d]	1.29 (1.00–1.67)[c]	1.48 (0.98–2.23)	0.723	0.67 (0.35–1.29)	1.49 (1.19–1.86)[b]	0.078
Mean 1-year HbA1c, continuous[d]	1.38 (1.07–1.78)[c]	1.29 (0.88–1.89)	0.754	0.87 (0.47–1.60)	1.48 (1.18–1.86)[b]	0.196
1-year HGI variability, continuous[d]	1.26 (1.04–1.53)[c]	0.88 (0.59–1.30)	0.095	0.90 (0.53–1.53)	1.32 (1.07–1.62)[b]	0.127
1-year HbA1c variability, continuous[d]	1.23 (1.02–1.48)[c]	1.12 (0.77–1.63)	0.669	0.96 (0.56–1.65)	1.36 (1.11–1.67)[b]	0.108
Retinopathy (*n*=161)	110	51		49	112	
Baseline HGI, continuous[d]	1.31 (1.07–1.60)[b]	1.02 (0.79–1.33)	0.049	1.39 (0.99–1.94)	1.16 (0.98–1.38)	0.297
Baseline HbA1c, continuous[d]	1.32 (1.07–1.63)[b]	1.10 (0.83–1.46)	0.144	1.34 (0.96–1.86)	1.19 (0.99–1.43)	0.512
Mean 1-year HGI, continuous[d]	1.40 (1.15–1.69)[b]	0.97 (0.69–1.37)	0.019	1.35 (0.93–1.98)	1.29 (1.06–1.57)[c]	0.586
Mean 1-year HbA1c, continuous[d]	1.47 (1.23–1.76)[a]	1.01 (0.73–1.40)	0.020	1.53 (1.07–2.18)[c]	1.31 (1.09–1.58)[b]	0.296
1-year HGI variability, continuous[d]	1.36 (1.17–1.57)[a]	1.09 (0.83–1.43)	0.078	1.28 (1.03–1.59)[c]	1.21 (1.02–1.44)[c]	0.688
1-year HbA1c variability, continuous[d]	1.30 (1.13–1.49)[a]	1.07 (0.79–1.45)	0.107	1.18 (0.92–1.50)	1.23 (1.04–1.44)[c]	0.796
Peripheral neuropathy (*n*=177)	119	58		64	113	
Baseline HGI, continuous[d]	1.34 (1.11–1.61)[b]	1.12 (0.87–1.45)	0.399	1.31 (0.95–1.80)	1.24 (1.04–1.48)[c]	0.856
Baseline HbA1c, continuous[d]	1.44 (1.18–1.76)[a]	1.29 (0.97–1.73)	0.677	1.60 (1.17–2.20)[b]	1.31 (1.08–1.58)[b]	0.857
Mean 1-year HGI, continuous[d]	1.26 (1.02–1.56)[c]	1.58 (1.10–2.27)[c]	0.429	1.36 (0.93–1.99)	1.32 (1.08–1.62)[b]	0.577
Mean 1-year HbA1c, continuous[d]	1.27 (1.03–1.56)[c]	1.44 (1.01–2.04)[c]	0.447	1.32 (0.93–1.87)	1.31 (1.06–1.61)[c]	0.532
1-year HGI variability, continuous[d]	1.14 (0.96–1.36)	1.07 (0.82–1.39)	0.689	1.24 (0.97–1.59)	1.09 (0.92–1.30)	0.908
1-year HbA1c variability, continuous[d]	1.15 (0.97–1.36)	1.14 (0.85–1.54)	0.587	1.15 (0.88–1.51)	1.15 (0.97–1.36)	0.588
Symptomatic hypoglycemia (*n*=90)	59	31		28	62	
Baseline HGI, continuous[d]	1.06 (0.78–1.45)	1.12 (0.70–1.78)	0.916	1.07 (0.69–1.66)	1.10 (0.81–1.51)	0.912
Baseline HbA1c, continuous[d]	1.27 (0.94–1.73)	1.22 (0.69–2.15)	0.728	1.29 (0.83–2.01)	1.22 (0.88–1.70)	0.627
Mean 1-year HGI, continuous[d]	0.92 (0.67–1.26)	1.15 (0.66–2.01)	0.609	0.87 (0.48–1.60)	0.97 (0.71–1.32)	0.994
Mean 1-year HbA1c, continuous[d]	0.97 (0.71–1.33)	1.17 (0.68–2.03)	0.649	1.03 (0.57–1.85)	1.03 (0.75–1.40)	0.802
1-year HGI variability, continuous[d]	0.92 (0.68–1.25)	1.36 (0.84–2.19)	0.167	1.25 (0.83–1.88)	0.86 (0.62–1.20)	0.061
1-year HbA1c variability, continuous[d]	0.88 (0.63–1.22)	1.32 (0.77–2.24)	0.205	1.17 (0.80–1.73)	0.82 (0.58–1.17)	0.086

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.