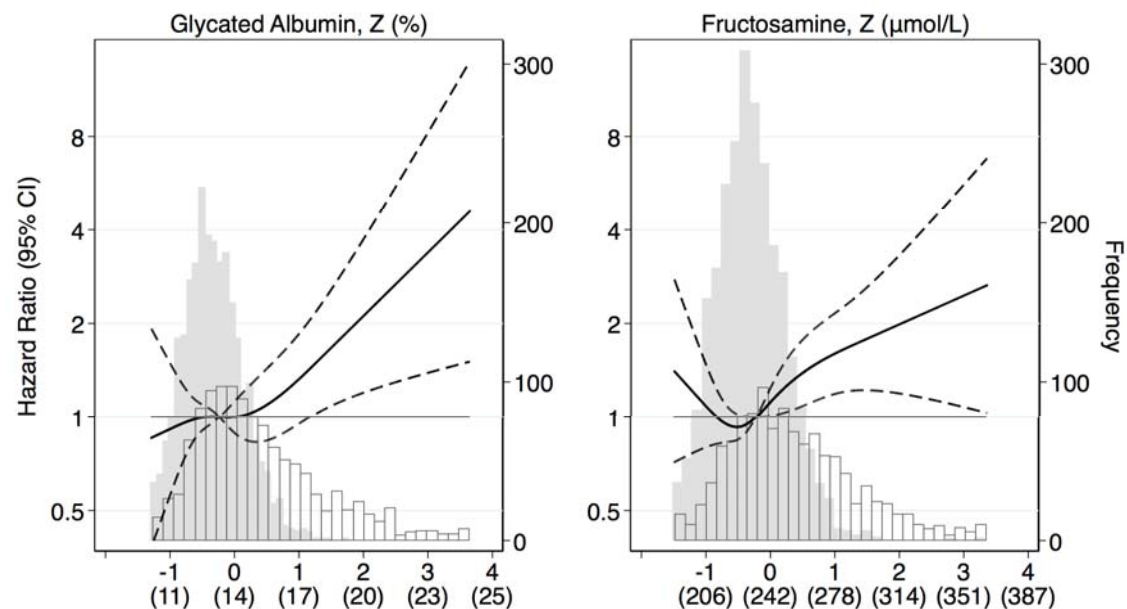SUPPLEMENTARY DATA

Supplementary Figure S1. Adjusted hazard ratios (95% CI) glycated albumin and fructosamine with incident dementia – with additional adjustment for HbA1c

Legend: Biomarker values are shown as Z scores (original units). Hazard ratios (solid line) and 95% confidence intervals (dashed lines) are from Cox proportional hazard regression, adjusted for age, race, sex, education level, cigarette smoking status (current/former/never), drinking status (current/former/never), APOE e4 (0,1, or 2 alleles), hypertension (yes/no), history of stroke (yes/no), history of CHD (yes/no), and HbA1c. HbA1c was modeled using a restricted cubic spline with knots at the 10th (5.2%), 50th (5.7%), and 90th (6.9%) percentiles.
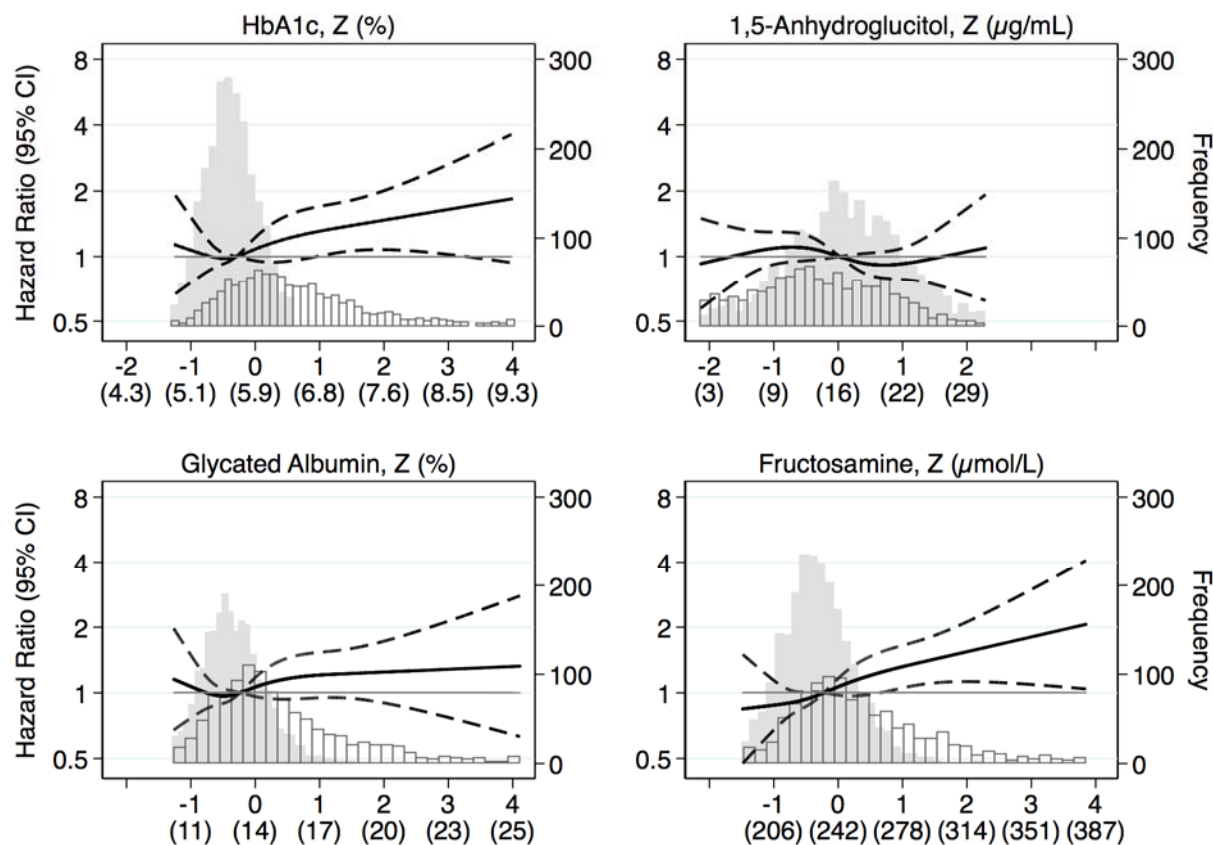Each biomarker was modeled using a restricted cubic spline, with knots at the 5th, 35th, 65th, and 95th percentiles, and centered at the median.
Histograms of each biomarker are shown separately for persons without (solid bars) and with (outline bars) diabetes
Abbreviations: CI, confidence interval; HbA1c, hemoglobin A1c.

SUPPLEMENTARY DATA

Supplementary Figure S2. Adjusted hazard ratios (95% CI) for HbA1c, 1,5-anhydroglucitol, glycated albumin, and fructosamine with incident mild cognitive impairment

Legend: Biomarker values are shown as Z scores (original units). Hazard ratios (solid line) and 95% confidence intervals (dashed lines) are from Cox proportional hazard regression, adjusted for age, race, sex, education level, cigarette smoking status (current/former/never), drinking status (current/former/never), APOE e4 (0,1, or 2 alleles), hypertension (yes/no), history of stroke (yes/no), and history of CHD (yes/no).
Each biomarker was modeled using a restricted cubic spline, with knots at the 5th, 35th, 65th, and 95th percentiles, and centered at the median.
Histograms of each biomarker are shown separately for persons without (solid bars) and with (outline bars) diabetes
Abbreviations: CI, confidence interval; HbA1c, hemoglobin A1c.

SUPPLEMENTARY DATA

Supplementary Table S1. Adjusted hazard ratios (95% CI) for incident dementia among dementia-free persons with diabetes by baseline age tertiles and diabetes duration

Baseline age (years)	Diabetes duration (years)	n/N	Adjusted HR (95% CI)	Adjusted HR (95% CI) comparing duration within age tertile
<72.8	<6	11/186 (5.9%)	1 (reference)	1 (reference)
<72.8	6-12	15/199 (7.5%)	1.44 [0.66, 3.14]	1.44 [0.66, 3.14]
<72.8	>12	26/196 (13.3%)	2.49 [1.23, 5.06]*	2.49 [1.23, 5.06]*
72.8 – 77.9	<6	16/163 (9.8%)	2.19 [1.01, 4.74]*	1 (reference)
72.8 – 77.9	6-12	25/199 (12.6%)	2.70 [1.33, 5.51]**	1.23 [0.66, 2.31]
72.8 – 77.9	>12	29/199 (14.6%)	3.23 [1.61, 6.47]**	1.47 [0.80, 2.72]
>77.9	<6	27/116 (23.3%)	5.02 [2.48, 10.16]***	1 (reference)
>77.9	6-12	28/152 (18.4%)	4.94 [2.44, 9.98]***	0.98 [0.58, 1.67]
>77.9	>12	45/168 (26.8%)	5.73 [2.95, 11.14]***	1.14 [0.70, 1.85]

Models are adjusted for age, race-center, sex, and education level
Diabetes was defined based on self-reported diagnosis, use of glucose lowering medication, or HbA1c of ≥6.5% (48 mmol/mol).
* p-valule < 0.05 ** p-value < 0.01 *** p-value <0.001

SUPPLEMENTARY DATA

Supplementary Table S2. Adjusted hazard ratios (95% CI) for cognitive outcomes by glycemic – among participants who were cognitively normal at visit 5, using three categories of HbA1c

Diabetes and glycemic control	Incident dementia		Incident MCI	
No Diabetes	164/2690 (6.1%)	1 (reference)	301/1938 (15.6%)	1 (reference)
Diabetes, A1c <7%	77/968 (8.0%)	1.03 [0.78, 1.38]	105/655 (16.0%)	1.11 [0.88, 1.40]
Diabetes, A1c 7-7.9%	16/225 (7.1 %)	0.95 [0.57, 1.61]	31/142 (21.8%)	1.65 [1.13, 2.42]**
Diabetes, Ac1 ≥8%	16/111 (14.4%)	1.68 [0.95, 2.98]	17/76 (22.4%)	1.89 [1.14, 3.14]*

Models are adjusted for age, race-center, sex, education level, cigarette smoking status (current/former/never), drinking status (current/former/never), APOE e4 (0,1, or 2 alleles), hypertension (yes/no), history of stroke (yes/no), and history of CHD (yes/no)

Diabetes was defined based on self-reported diagnosis, use of glucose lowering medication, or HbA1c of ≥6.5% (48 mmol/mol). HbA1c of 7% is equivalent to 53 mmol/mol, HbA1c of 8% is equivalent to 64 mmol/mol.

Abbreviations: HR, hazard ratio; MCI, mild cognitive impairment.

* p-valule < 0.05 ** p-value < 0.01 *** p-value <0.001

Supplemental Table S3. Adjusted hazard ratios (95% CI) for cognitive outcomes by baseline cognitive status, using three categories of HbA1c

Diabetes and glycemic control	Incident cognitive impairment† among participants dementia free at baseline		Incident dementia among participants with MCI at baseline	
No Diabetes	638/3344 (19.1%)	1 (reference)	169/639 (26.4%)	1 (reference)
Diabetes, A1c <7%	264/1276 (20.7%)	1.06 [0.91, 1.23]	81/305 (26.6%)	1.03 [0.78, 1.35]
Diabetes, A1c 7-7.9%	72/306 (23.5%)	1.17 [0.91, 1.50]	25/80 (31.3%)	1.20 [0.77, 1.85]
Diabetes, Ac1 ≥8%	47/153 (30.7%)	1.95 [1.42, 2.66]***	14/42 (33.3%)	1.91 [1.08, 3.36]*

† Cognitive impairment includes incident MCI in persons cognitively normal at baseline and incident dementia in persons cognitively normal or MCI at baseline

Models are adjusted for age, race-center, sex, education level, cigarette smoking status (current/former/never), drinking status (current/former/never), APOE e4 (0,1, or 2 alleles), hypertension (yes/no), history of stroke (yes/no), and history of CHD (yes/no)

Diabetes was defined based on self-reported diagnosis, use of glucose lowering medication, or HbA1c of ≥6.5% (48 mmol/mol). HbA1c of 7% is equivalent to 53 mmol/mol, HbA1c of 8% is equivalent to 64 mmol/mol.

Abbreviations: HR, hazard ratio; MCI, mild cognitive impairment;

* p-value < 0.05 ** p-value < 0.01 *** p-value <0.001