SUPPLEMENTARY DATA

Supplementary Table 1. Counts (%) of the baseline cohort vital status at subsequent visits

	Baseline (1990-1992)	Visit 4 (1996-1998)	Visit 5 (2011-2013)
Visit Status			
Attended	12,996 (100)	10,461 (80.5)	5,898 (45.4)
Alive did not attend	0	2,972 (22.9)	3,441 (26.5)
Deceased by visit	0	437 (3.4)	3,657 (28.1)

Values shown as counts (%), where % is of the original baseline cohort.

SUPPLEMENTARY DATA

Supplementary Table 2. Baseline* participant characteristics by vital status at visit 5

	Attended visit 5		Alive but did not attend visit 5		Deceased by visit 5	
1,5-AG, µg/mL	≥10	<10	≥10	<10	≥10	<10
N (%)						
Age, years	55.0	55.1	57.2	57.8	59.6	59.8
Female, %	59.3	64.4	61.0	66.9	44.1	52.4
Black, %	20.8	36.2	21.0	34.9	25.4	42.6
Measures of glycemia						
1,5-AG, µg/mL	19.1	5.8	19.5	5.4	19.8	4.4
Fasting glucose, mg/dl	102.8	157.0	104.7	172.0	107.5	209.7
HbA1c, %	5.4	7.1	5.5	7.4	5.6	8.5
HbA1c, mmol/mol	35.8	53.8	36.6	57.8	38.0	69.9
Body mass index, kg/m^2	27.5	28.9	27.9	30.2	27.9	30.4
Diabetes, %	3.7	46.0	6.6	58.9	10.7	78.1
Hypertension, %	26.5	34.7	34.9	45.7	45.6	62.3
eGFR, mL/min/1.73 m^2	97.9	100.4	96.5	99.8	93.8	90.4
Incident events after baseline						
Dementia, %	5.1	8.3	14.4	21.2	12.2	14.0
Stroke, %	4.1	5.7	7.5	11.4	11.9	23.2
Myocardial infarction, %	7.3	11.2	10.0	16.9	16.1	26.4
Chronic kidney disease†, %	28.9	44.7	17.0	28.9	23.1	45.3
End-stage renal disease, %	0.6	2.6	1.2	2.9	3.0	15.5
Global Z score	0.25	0.04	0.00	-0.22	-0.30	-0.64

* Values shown are measured at baseline except for “incident events after baseline”
† CKD was defined in persons with eGFR >60 mL/min/1.73 m^2 at baseline as eGFR <60 mL/min/1.73 m^2 and a 25% or greater decrease in GFR from baseline or kidney disease-related hospitalization based on cohort surveillance.

SUPPLEMENTARY DATA

Supplementary Table 3. Mean (SD) and change in cognitive function across study visits by dementia status during follow-up

	Dementia during follow-up	No Dementia during follow-up
Visit 2	-0.43 (1.06)	0.04 (0.98)
Visit 4	-0.61 (1.08)	0.02 (0.96)
Visit 5	-2.29 (0.95)	-0.52 (0.95)
Change: v4 - v2	-0.30 (0.68)	-0.12 (0.58)
Change: v5 - v4	-2.01 (0.98)	-0.74 (0.69)

Abbreviations: SD, standard deviation; v4, visit 4; v2, visit 2.

SUPPLEMENTARY DATA

Supplementary Table 4. Adjusted HRs (95% CI) for the association of 1,5-anhydroglucitol categories with incident dementia – stratified analyses by diabetes and HbA1c category

		Events/N	Model 1 HR (95% CI)	p-value†	Model 2 HR (95% CI)	p-value†
No Diabetes	1,5-AG ≥10 µg/mL	829/10708 (7.7%)	1 (reference)	0.959	1 (reference)	0.717
	1,5-AG <10 µg/mL	48/576 (8.3%)	1.01 (0.75, 1.35)		1.06 (0.79, 1.42)	
Diabetes* HbA1c < 7%‡	1,5-AG ≥10 µg/mL	60/535 (11.2%)	1 (reference)	0.400	1 (reference)	0.202
	1,5-AG <10 µg/mL	19/125 (15.2%)	1.26 (0.74, 2.15)		1.45 (0.82, 2.56)	
HbA1c ≥ 7%‡	1,5-AG ≥10 µg/mL	19/176 (10.8%)	1 (reference)	0.035	1 (reference)	0.110
	1,5-AG <10 µg/mL	130/876 (14.8%)	1.68 (1.04, 2.73)		1.53 (0.91, 2.58)	

Abbreviations: HR, hazard ratio; CI, confidence interval; HbA1c, hemoglobin A1c; 1,5-AG, 1,5-anhydroglucitol. HRs and CIs were estimated using Cox proportional hazards regression over a median follow-up of 21 years.
Model 1: Adjusted for age, sex, education, and race-center
Model 2: Adjusted for the variables in model 1 plus hypertension, history of stroke, history of coronary heart disease, cigarette smoking status, drinking status, APOE4, and HbA1c
* Diabetes was defined as a self-reported physician diagnosis of diabetes, use of glucose lowering medication, or an HbA1c ≥ 6.5% (48 mmol/mol)
† p-value for test of the difference in HR between 1,5-AG ≥10 µg/mL to 1,5-AG <10 µg/mL within diabetes status and HbA1c category
‡ Equivalent to HbA1c of 53 mmol/mol

SUPPLEMENTARY DATA

Supplementary Table 5. Adjusted HRs (95% CI) for the association of 1,5-anhydroglucitol categories with incident dementia by diabetes status among ARIC participants with at least one hospitalization, N=10,646

		Events/N	Model 1 HR (95% CI)	p-value†	Model 2 HR (95% CI)	p-value†
No Diabetes						
	1,5-AG ≥10 µg/mL	792/8589 (9.2%)	1 (reference)	0.793	1 (reference)	0.567
	1,5-AG <10 µg/mL	44/473 (9.3%)	1.05 (0.73, 1.51)		1.11 (0.77, 1.60)	
Diabetes*						
HbA1c < 7%‡	1,5-AG ≥10 µg/mL	57/483 (11.8%)	1.33 (0.96, 1.83)	0.881	1.28 (0.92, 1.78)	0.730
	1,5-AG <10 µg/mL	19/119 (16.0%)	1.39 (0.80, 2.43)		1.43 (0.82, 2.51)	
HbA1c ≥ 7%‡	1,5-AG ≥10 µg/mL	19/159 (11.9%)	1.48 (0.85, 2.57)	0.227	1.29 (0.72, 2.32)	0.122
	1,5-AG <10 µg/mL	125/823 (15.2%)	2.11 (1.69, 2.63)		2.08 (1.36, 3.19)	

Abbreviations: HR, hazard ratio; CI, confidence interval; HbA1c, hemoglobin A1c; 1,5-AG, 1,5-anhydroglucitol. HRs and CIs were estimated using Cox proportional hazards regression over a median follow-up of 21 years.

Model 1: Adjusted for age, sex, education, and race-center

Model 2: Adjusted for the variables in model 1 plus hypertension, history of stroke, history of coronary heart disease, cigarette smoking status, drinking status, and APOE4

* Diabetes was defined as a self-reported physician diagnosis of diabetes, use of glucose lowering medication, or an HbA1c ≥ 6.5% (48 mmol/mol)

† p-value for test of the difference in HR between 1,5-AG ≥10 µg/mL to 1,5-AG <10 µg/mL within diabetes status and HbA1c category

‡ Equivalent to HbA1c of 53 mmol/mol

SUPPLEMENTARY DATA

Supplementary Table 6. Adjusted HRs (95% CI) for the association of 1,5-anhydroglucitol categories with incident dementia by diabetes status among ARIC participants – stratified analysis by sex

		Female			Male		
		Events/N	HR (95% CI)	p-value†	Events/N	HR (95% CI)	p-value†
No Diabetes							
	1,5-AG ≥10 µg/mL	481/5950 (8.1%)	1 (reference)	0.973	348/4758 (7.3%)	1 (reference)	0.604
	1,5-AG <10 µg/mL	31/378 (8.2%)	0.99 (0.69, 1.43)		17/198 (8.6%)	1.14 (0.70, 1.86)	
Diabetes*							
HbA1c < 7%‡	1,5-AG ≥10 µg/mL	37/311 (11.9%)	1.17 (0.83, 1.66)	0.375	23/224 (10.3%)	1.61 (1.05, 2.47)	0.889
	1,5-AG <10 µg/mL	9/60 (15.0%)	1.64 (0.84, 3.18)		10/65 (15.4%)	1.70 (0.90, 3.21)	
HbA1c ≥ 7%‡	1,5-AG ≥10 µg/mL	12/117 (10.3%)	1.11 (0.62, 1.98)	0.029	7/59 (11.9%)	1.59 (0.74, 3.40)	0.163
	1,5-AG <10 µg/mL	56/501 (11.2%)	2.19 (1.69, 2.84)		54/375 (14.4%)	2.79 (2.08, 3.76)	

Abbreviations: HR, hazard ratio; CI, confidence interval; HbA1c, hemoglobin A1c; 1,5-AG, 1,5-anhydroglucitol. HRs and CIs were estimated using Cox proportional hazards regression over a median follow-up of 21 years.
Models were adjusted for age, education, race-center, hypertension, history of stroke, history of coronary heart disease, cigarette smoking status, drinking status, and APOE4
* Diabetes was defined as a self-reported physician diagnosis of diabetes, use of glucose lowering medication, or an HbA1c ≥ 6.5% (48 mmol/mol)
† p-value for test of the difference in HR between 1,5-AG ≥10 µg/mL to 1,5-AG <10 µg/mL within diabetes status and HbA1c category
‡ Equivalent to HbA1c of 53 mmol/mol

SUPPLEMENTARY DATA

Supplementary Table 7. Adjusted HRs (95% CI) for the association of 1,5-anhydroglucitol categories with incident dementia by diabetes status among ARIC participants – stratified analysis by race

		Black			White		
		Events/N	HR (95% CI)	p-value†	Events/N	HR (95% CI)	p-value†
No Diabetes	1,5-AG ≥10 µg/mL	225/2180 (10.3%)	1 (reference)	0.168	604/8528 (7.1%)	1 (reference)	0.524
	1,5-AG <10 µg/mL	18/148 (12.2%)	1.41 (0.87, 2.29)		30/428 (7.0%)	0.89 (0.61, 1.28)	
Diabetes* HbA1c < 7%‡	1,5-AG ≥10 µg/mL	27/232 (11.6%)	1.12 (0.74, 1.70)	0.953	33/303 (10.9%)	1.47 (1.03, 2.10)	0.231
	1,5-AG <10 µg/mL	5/41 (12.2%)	1.09 (0.45, 2.67)		14/84 (16.7%)	2.16 (1.27, 3.69)	
HbA1c ≥ 7%‡	1,5-AG ≥10 µg/mL	12/102 (11.8%)	1.26 (0.70, 2.27)	0.045	7/74 (9.5%)	1.52 (0.72, 3.22)	0.202
	1,5-AG <10 µg/mL	74/421 (17.6%)	2.36 (1.80, 3.10)		56/455 (12.3%)	2.54 (1.91, 3.37)	

Abbreviations: HR, hazard ratio; CI, confidence interval; HbA1c, hemoglobin A1c; 1,5-AG, 1,5-anhydroglucitol. HRs and CIs were estimated using Cox proportional hazards regression over a median follow-up of 21 years.
Models were adjusted for age, education, race-center, hypertension, history of stroke, history of coronary heart disease, cigarette smoking status, drinking status, and APOE4
* Diabetes was defined as a self-reported physician diagnosis of diabetes, use of glucose lowering medication, or an HbA1c ≥ 6.5% (48 mmol/mol)
† p-value for test of the difference in HR between 1,5-AG ≥10 µg/mL to 1,5-AG <10 µg/mL within diabetes status and HbA1c category
‡ Equivalent to HbA1c of 53 mmol/mol

Supplementary Table 8. Adjusted HRs (95% CI) for the association of 1,5-anhydroglucitol categories with incident dementia by diabetes status among ARIC participants – stratified analysis by presence of APOE e4 alleles

		0 APOE e4 alleles			1 or 2 APOE e4 alleles		
		Events/N	HR (95% CI)	p-value†	Events/N	HR (95% CI)	p-value†
No Diabetes	1,5-AG ≥10 µg/mL	438/7103 (5.8%)	1 (reference)	0.927	391/2779 (12.3%)	1 (reference)	0.829
	1,5-AG <10 µg/mL	25/363 (6.4%)	1.05 (0.70, 1.57)		24/165 (12.7%)	1.06 (0.69, 1.61)	
Diabetes* HbA1c < 7%‡	1,5-AG ≥10 µg/mL	42/335 (11.1%)	1.86 (1.34, 2.57)	0.548	18/141 (11.3%)	0.76 (0.46, 1.24)	0.067
	1,5-AG <10 µg/mL	8/84 (8.7%)	1.33 (0.66, 2.71)		11/22 (33.3%)	2.02 (1.10, 3.71)	
HbA1c ≥ 7%‡	1,5-AG ≥10 µg/mL	6/109 (5.22%)	0.97 (0.43, 2.18)	0.067	12/48 (21.3%)	1.57 (0.89, 2.77)	0.879
	1,5-AG <10 µg/mL	81/547 (12.9%)	2.43 (1.83, 3.24)		49/199 (19.8%)	2.02 (1.41, 2.90)	

Abbreviations: HR, hazard ratio; CI, confidence interval; HbA1c, hemoglobin A1c; 1,5-AG, 1,5-anhydroglucitol. HRs and CIs were estimated using Cox proportional hazards regression over a median follow-up of 21 years.
Models were adjusted for age, education, race-center, hypertension, history of stroke, history of coronary heart disease, cigarette smoking status, drinking status, and APOE4
* Diabetes was defined as a self-reported physician diagnosis of diabetes, use of glucose lowering medication, or an HbA1c ≥ 6.5% (48 mmol/mol)
† p-value for test of the difference in HR between 1,5-AG ≥10 µg/mL to 1,5-AG <10 µg/mL within diabetes status and HbA1c category
‡ Equivalent to HbA1c of 53 mmol/mol