Glycaemic markers and all-cause mortality in older adults with and without diabetes: The Atherosclerosis Risk in Communities (ARIC) Study

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ESM Table 1. Pearson's correlation coefficient for glycemic biomarkers according to diagnosed diabetes in the ARIC study, 2011–13

No Diagnosed Diabetes				
	HbA_{1c}	Fructosamine	Glycated Albumin	Fasting Glucose
HbA_{1c}	1	-	-	-
Fructosamine	0.193	1	-	-
Glycated Albumin	0.278	0.663	1	-
Fasting Glucose	0.364	0.150	0.142	1
Diagnosed Diabetes				
	HbA_{1c}	Fructosamine	Glycated Albumin	Fasting Glucose
HbA_{1c}	1	-	-	-
Fructosamine	0.748	1	-	-
Glycated Albumin	0.809	0.918	1	-
Fasting Glucose	0.640	0.529	0.540	1

ESM Table 2. Determinants of low HbA$_{1c}$ and low HbA$_{1c}$ percentile equivalences for fructosamine and glycated albumin by diagnosed diabetes status in the ARIC study, 2011–2013

	OR (95% CI)*					
	No Diagnosed Diabetes†			Diagnosed Diabetes†		
Determinants	**Low HbA$_{1c}$**	**Low Fructosamine**	**Low Glycated Albumin**	**Low HbA$_{1c}$**	**Low Fructosamine**	**Low Glycated Albumin**
BMI categories						
Underweight, <18.5 kg/m^2	1.61 (0.43-6.00)	1.15 (0.15-9.01)	3.22 (0.39-26.8)	0.27 (0.03-2.70)	–	–
Ideal, 18.5–<25 kg/m^2	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Overweight, 25–<30 kg/m^2	0.94 (0.60-1.46)	1.00 (0.62-1.62)	0.43 (0.19-0.96)	0.68 (0.49-0.95)	1.26 (0.85-1.88)	1.16 (0.81-1.65)
Obese, ≥30 kg/m^2	0.76 (0.44-1.29)	2.44 (1.56-3.81)	1.83 (0.97-3.48)	0.42 (0.30-0.59)	1.28 (0.86-1.88)	1.13 (0.80-1.60)
eGFR <60 mL/min/1.73m^2						
No	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Yes	1.59 (1.05-2.42)	1.36 (0.95-1.95)	2.02 (1.17-3.50)	0.91 (0.72-1.15)	0.96 (0.74-1.24)	0.95 (0.75-1.21)
Prevalent CVD						
No	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Yes	1.95 (1.26-3.01)	1.39 (0.93-2.08)	1.43 (0.75-2.71)	0.88 (0.69-1.14)	0.64 (0.48-0.86)	0.67 (0.52-0.87)
ALT						
Not elevated	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Elevated	0.57 (0.17-1.87)	0.51 (0.18-1.40)	0.97 (0.30-3.16)	0.84 (0.51-1.37)	0.59 (0.35-0.99)	0.71 (0.45-1.11)
AST						
Not elevated	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Elevated	0.45 (0.14-1.47)	0.67 (0.27-1.67)	1.03 (0.32-3.34)	0.82 (0.50-1.35)	0.93 (0.53-1.62)	1.05 (0.64-1.71)
GGT						
Not elevated	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Elevated	1.28 (0.54-3.06)	0.78 (0.31-1.96)	1.14 (0.35-3.73)	0.95 (0.58-1.53)	0.60 (0.33-1.06)	0.66 (0.40-1.09)
Frailty						
No	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Yes	0.64 (0.43-0.96)	0.50 (0.35-0.70)	0.52 (0.31-0.90)	1.17 (0.92-1.48)	1.12 (0.86-1.46)	1.17 (0.92-1.48)
Anemia‡						
No Anemia	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Mild Anemia	1.12 (0.67-1.86)	1.72 (1.14-2.58)	1.70 (0.86-3.39)	0.62 (0.47-0.82)	0.53 (0.39-0.72)	0.50 (0.37-0.66)
Moderate/Severe	3.34 (1.76-6.35)	2.52 (1.14-5.56)	3.00 (0.87-10.31)	0.83 (0.51-1.33)	0.60 (0.32-1.12)	0.60 (0.34-1.04)
Diabetes duration						
<10 years	–	–	–	1 (Ref)	1 (Ref)	1 (Ref)
≥10 years	–	–	–	0.52 (0.41-0.67)	0.39 (0.29-0.52)	0.43 (0.33-0.55)
Diabetes medications						
None	–	–	–	1 (Ref)	1 (Ref)	1 (Ref)
Oral only	–	–	–	0.25 (0.20-0.33)	0.41 (0.32-0.54)	0.44 (0.34-0.56)

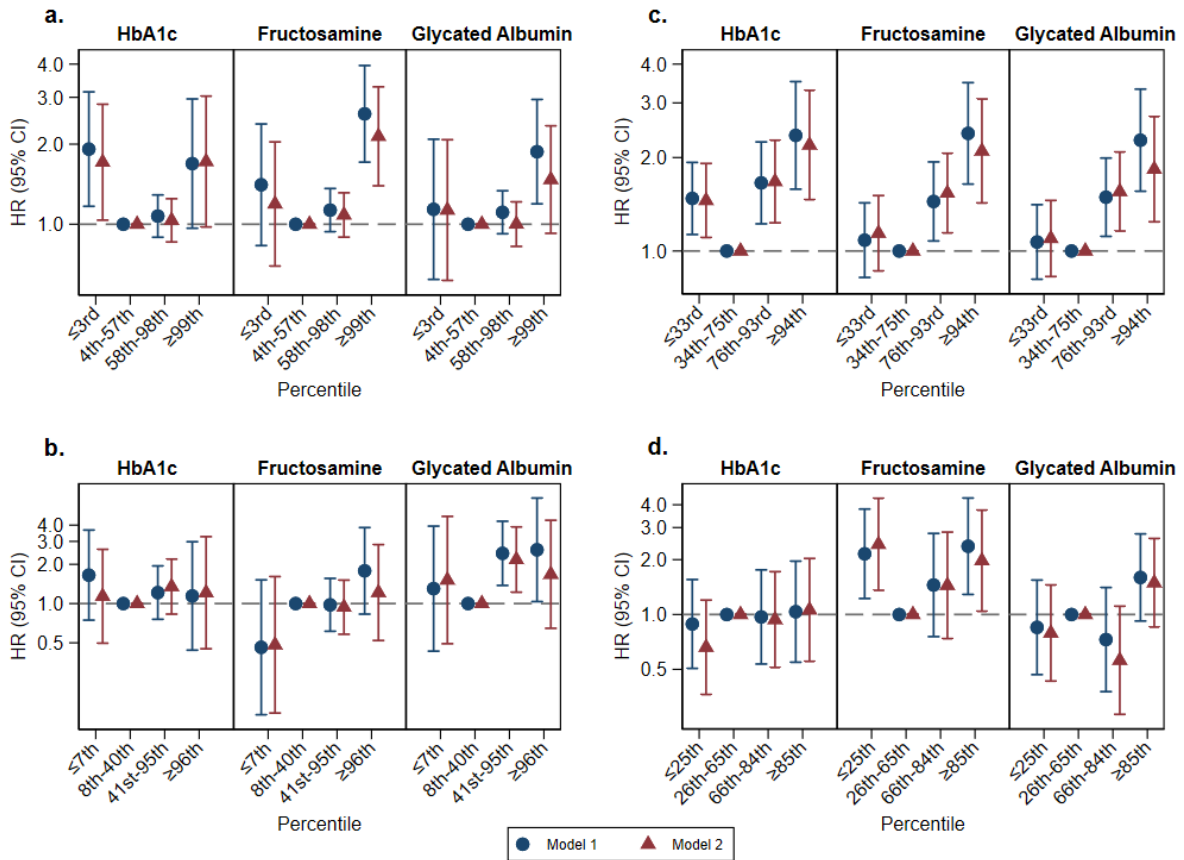|						
Insulin only	–	–	–	0.18 (0.09-0.37)	0.14 (0.05-0.42)	0.27 (0.12-0.58)
Insulin and oral	–	–	–	0.20 (0.09-0.45)	0.05 (0.01-0.21)	0.19 (0.09-0.40)

* Adjusted for age, sex, and race-center; dependent variable = glycemic variable (low vs normal (ref))

† HbA$_{1c}$ categories and percentile equivalences for fructosamine and glycated albumin correspond to <31 vs 31–<39 mmol/mol (ref) [<5.0% vs 5.0–<5.7% (ref)] in individuals without diabetes, and <42 vs 42–<53 mmol/mol (ref) [<6.0% vs 6.0–<7.0% (ref)] in individuals with diabetes.

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ESM Fig. 1 Study participant flow chart


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        ┌─────────────────────┐
        │  ARIC Study Visit 5 │
        │       N=6538        │
        └─────────────────────┘
                  │
                  │        ┌──────────────────────────────────────────┐
                  │        │              Exclusions                  │
                  ├───────▶│  - Missing glycemic markers (N=439)      │
                  │        │  - Non-fasting blood draw (N=247)        │
                  │        │  - Missing model covariates (N=181)      │
                  │        │  - Race other than white or black, &     │
                  │        │  blacks at the MN & MD center (N=35)     │
                  ▼        └──────────────────────────────────────────┘
        ┌─────────────────────┐
        │   Analytic Sample   │
        │       N=5636        │
        └─────────────────────┘
              │         │
        ┌─────┘         └─────┐
        ▼                     ▼
┌──────────────┐      ┌──────────────┐
│ No Diagnosed │      │  Diagnosed   │
│   Diabetes   │      │   Diabetes   │
│   N=3866     │      │   N=1770     │
└──────────────┘      └──────────────┘
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ESM Fig. 2a-d Race stratified HRs (95% confidence intervals) for HbA₁c categories in individuals **a)** without diabetes – whites; **b)** without diabetes – blacks; **c)** with diabetes – whites; **d)** without diabetes – blacks*†
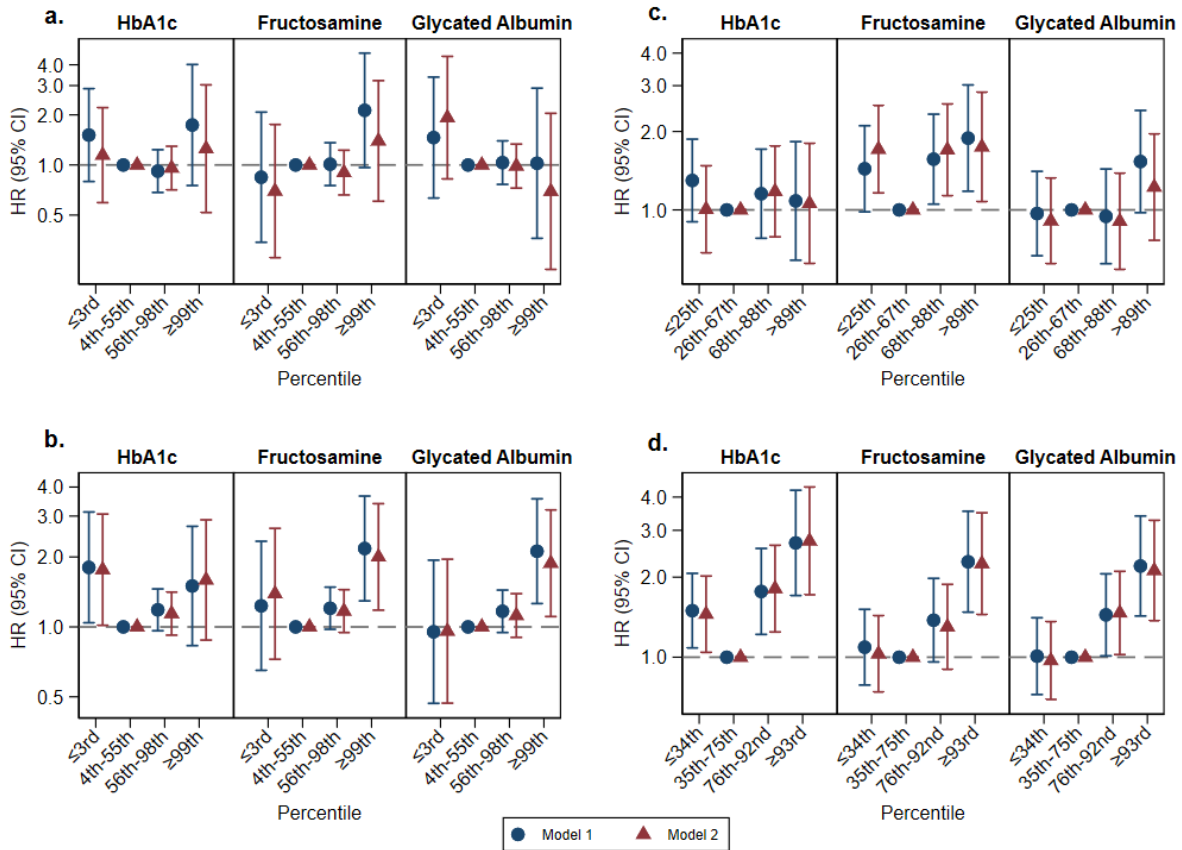

* Diabetes defined as self-report physician diagnosis or current medication use for diabetes
† Model 1 = age, sex, center
Model 2 = Model 1 + current smoking status, current drinking status, BMI, systolic blood pressure, antihypertension medication use, eGFR (spline knot at eGFR <60 mL/min/1.73m²), HDL, total cholesterol, lipid-lowering medication use, hemoglobin

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ESM Fig. 3a-d Anemia stratified HRs (95% confidence intervals) for HbA$_{1c}$ categories in individuals **a)** without diabetes – anemia; **b)** without diabetes – no anemia; **c)** with diabetes – anemia; **d)** without diabetes – no anemia*†‡
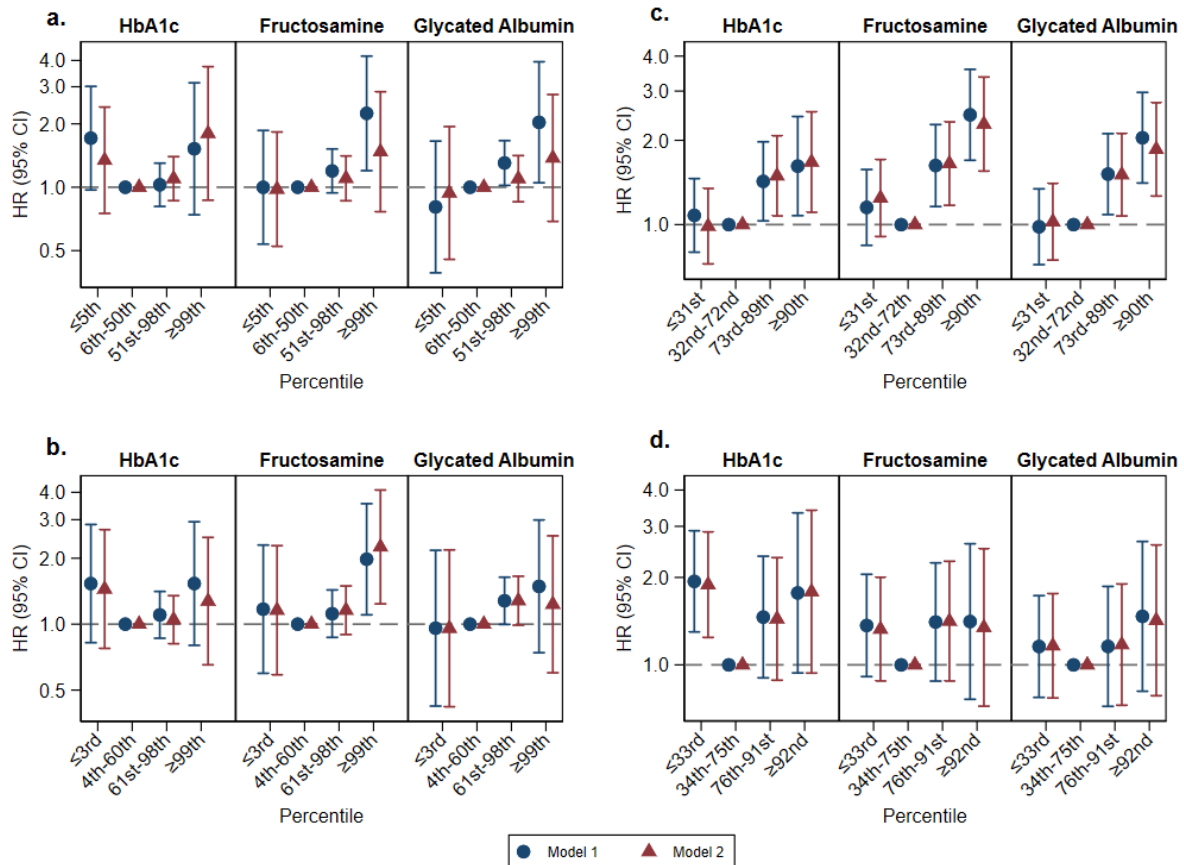

* Anemia = males hemoglobin <135 g/l, females hemoglobin <120 g/l
† Diabetes defined as self-report physician diagnosis or current medication use for diabetes
‡ Model 1 = age, sex, race-center
Model 2 = Model 1 + current smoking status, current drinking status, BMI, systolic blood pressure, antihypertension medication use, eGFR (spline knot at eGFR <60 mL/min/1.73m^2), HDL, total cholesterol, lipid-lowering medication use

ESM Fig. 4a-d Chronic kidney disease stratified HRs (95% confidence intervals) for HbA$_{1c}$ categories in individuals **a)** without diabetes – CKD; **b)** without diabetes – no CKD; **c)** with diabetes – CKD; **d)** without diabetes – no CKD*†
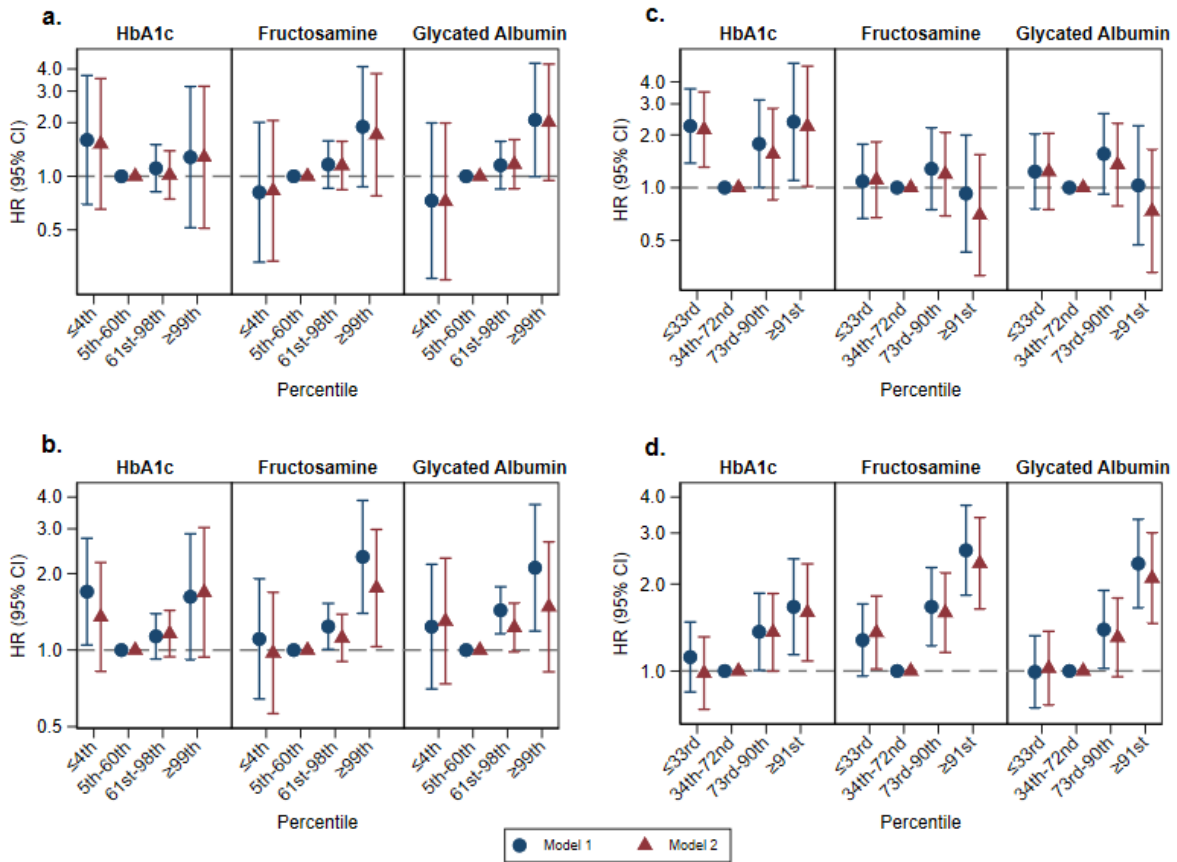

* Diabetes defined as self-report physician diagnosis or current medication use for diabetes
† Model 1 = age, sex, race-center
Model 2 = Model 1 + current smoking status, current drinking status, BMI, systolic blood pressure, antihypertension medication use, eGFR (spline knot at eGFR <60 mL/min/1.73m^2), HDL, total cholesterol, lipid-lowering medication use, hemoglobin

ESM Fig. 5a-d Frailty stratified HRs (95% confidence intervals) for HbA$_{1c}$ categories in individuals **a)** without diabetes – frail; **b)** without diabetes – not frail; **c)** with diabetes – frail; **d)** without diabetes – not frail*†

* Diabetes defined as self-report physician diagnosis or current medication use for diabetes
† Model 1 = age, sex, race-center
Model 2 = Model 1 + current smoking status, current drinking status, BMI, systolic blood pressure, antihypertension medication use, eGFR (spline knot at eGFR <60 mL/min/1.73m^2), HDL, total cholesterol, lipid-lowering medication use, hemoglobin