SUPPLEMENTARY DATA

Fasting glucose variability in young adulthood and cognitive function in middle age: The Coronary Artery Risk Development in Young Adults (CARDIA) Study

Short-title: Glucose variability and cognitive function

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Supplementary Table 1. Multivariable association between fasting glucose average real variability during young adulthood with cognitive function in middle age

Difference in Cognitive Test Score at Year 25 according to 1 SD ARV-FG (95% CI)					
	Model 1[*]	Model 2[†]	Model 3[‡]	Model 3A[§]	Model 3B[‖]	Model 3C[¶]
DSST, n=3292	-0.72 (-1.22, -0.23)	-0.54 (-1.00, -0.07)	-0.54 (-1.01, -0.07)	-0.53 (-1.01, -0.06)	-0.56 (-1.04, -0.09)	-0.51 (-0.98, -0.03)
RAVLT, n=3287	-0.10 (-0.20, 0.00)	-0.08 (-0.18, 0.02)	-0.08 (-0.18, 0.02)	-0.08 (-0.18, 0.02)	-0.08 (-0.18, 0.03)	-0.08 (-0.18, 0.02)
Stroop, n=3280	-0.06 (-0.41, 0.30)	-0.17 (-0.53, 0.18)	-0.17 (-0.52, 0.18)	-0.16 (-0.52, 0.19)	-0.15 (-0.51, 0.21)	-0.15 (-0.51, 0.20)
Global z, n=3254	-0.03 (-0.06, -0.001)	-0.02 (-0.05, 0.01)	-0.02 (-0.05, 0.01)	-0.02 (-0.05, 0.01)	-0.02 (-0.05, 0.01)	-0.02 (-0.05, 0.01)

Abbreviations: ARV (average real variability), DSST (Digit Symbol Substitution Test), FG (fasting glucose), RAVLT (Rey-Auditory Verbal Learning Test). A 1-standard deviation (SD) unit increment in ARV-FG at year 25 is 0.14. Adjustments: [*]Model 1: age, sex, race, field center. [†]Model 2: Model 1 plus highest level of educational attainment, and cumulative values for: number of years as a current smoker, grams of weekly alcohol consumption, body mass index, physical activity, systolic blood pressure, use of blood pressure-lowering medications, low-density lipoprotein cholesterol, and cholesterol-lowering medications. [‡]Model 3: Model 2 plus weighted average of fasting glucose. [§]Model 3A: Model 3 plus the incidence of diabetes, diabetes medication use, and diabetes duration. [‖]Model 3B: Model 3 plus change in fasting glucose level during variability measurement. [¶]Model 3C: Model 3 plus year 25 fasting glucose level.

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Supplementary Table 2. Multivariable association between fasting glucose average real variability during young adulthood with cognitive function at examination year 30 (2015-2016)

	Difference in Year 30 Cognitive Test Score per 1 SD ARV-FG (95% CI)					
	Model 1[*]	Model 2[†]	Model 3[‡]	Model 3A[§]	Model 3B[‖]	Model 3C[¶]
DSST, n=**2996**	-0.67 (-1.21, -0.13)	-0.38 (-0.90, 0.13)	-0.39 (-0.91, 0.12)	-0.39 (-0.91, 0.13)	-0.44 (-0.97, 0.08)	-0.35 (-0.87, 0.17)
RAVLT, n=**3011**	-0.03 (-0.14, 0.08)	0.01 (-0.09, 0.12)	0.02 (-0.09, 0.12)	0.02 (-0.09, 0.13)	0.02 (-0.09, 0.13)	0.02 (-0.09, 0.13)
Stroop, n=**2939**	-0.05 (-0.45, 0.35)	-0.19 (-0.59, 0.21)	-0.19 (-0.59, 0.21)	-0.20 (-0.60, 0.20)	-0.17 (-0.58, 0.23)	-0.20 (-0.60, 0.20)
MoCA, n=**2994**	0.02 (-0.11, 0.14)	0.07 (-0.05, 0.19)	0.07 (-0.05, 0.19)	0.06 (-0.06, 0.18)	0.06 (-0.06, 0.18)	0.07 (-0.05, 0.19)
Category Fluency, n=**2986**	-0.09 (-0.28, 0.10)	-0.03 (-0.21, 0.16)	-0.02 (-0.21, 0.16)	-0.05 (-0.24, 0.13)	-0.05 (-0.23, 0.14)	-0.04 (-0.22, 0.15)
Letter Fluency, n=**2938**	-0.21 (-0.66, 0.24)	-0.04 (-0.48, 0.40)	-0.04 (-0.48, 0.40)	-0.10 (-0.55, 0.34)	-0.07 (-0.52, 0.37)	-0.04 (-0.49, 0.40)
Global *z*, n=**2852**	-0.01 (-0.05, 0.02)	0.00 (-0.02, 0.03)	0.00 (-0.02, 0.03)	0.00 (-0.03, 0.03)	0.00 (-0.03, 0.03)	0.01 (-0.02, 0.03)

Abbreviations: ARV (average real variability), DSST (Digit Symbol Substitution Test), FG (fasting glucose), MoCA (Montreal Cognitive Assessment), RAVLT (Rey-Auditory Verbal Learning Test). A 1-standard deviation (SD) unit increment in ARV-FG at year 30 is 0.13. Adjustments: [*]Model 1: age, sex, race, field center. [†]Model 2: Model 1 plus highest level of educational attainment, and cumulative values for: number of years as a current smoker, grams of weekly alcohol consumption, body mass index, physical activity, systolic blood pressure, use of blood pressure-lowering medications, low-density lipoprotein cholesterol, and cholesterol-lowering medications. [‡]Model 3: Model 2 plus weighted average of fasting glucose. [§]Model 3A: Model 3 plus the incidence of diabetes, diabetes medication use, and diabetes duration. [‖]Model 3B: Model 3 plus change in fasting glucose level during variability measurement. [¶]Model 3C: Model 3 plus year 30 fasting glucose level.

SUPPLEMENTARY DATA

Supplementary Table 3. Multivariable association between fasting glucose coefficient of variation during young adulthood with cognitive function at examination years 25 (2010-2011) and 30 (2015-2016) stratified by diabetes status at the time of cognitive assessment

Difference in Year 25 Cognitive Test Score per 1 SD CV-FG (95% CI)				
Model 1[*]	Model 2[†]	Model 3[‡]	Model 3A[§]	Model 3B[‖]
DSST at Year 25 (Y25)				
Diabetes by Y25, n=366				
0.80 (-0.35, 1.95)	0.47 (-0.62, 1.56)	0.46 (-0.66, 1.57)	0.37 (-1.01, 1.75)	0.46 (-0.66, 1.57)
No Diabetes by Y25, n=2926				
-1.48 (-2.03, -0.92)	-0.91 (-1.44, -0.37)	-0.89 (-1.42, -0.35)	-1.33 (-2.00, -0.67)	-1.07 (-1.62, -0.51)
P for interaction = 0.43				
RAVLT at Year 25				
Diabetes by Y25, n=367				
0.06 (-0.16, 0.28)	-0.01 (-0.22, 0.20)	-0.04 (-0.25, 0.18)	-0.05 (-0.32, 0.22)	-0.04 (-0.25, 0.18)
No Diabetes by Y25, n=2920				
-0.20 (-0.31, -0.08)	-0.13 (-0.24, -0.01)	-0.14 (-0.26, -0.03)	-0.18 (-0.32, -0.03)	-0.15 (-0.27, -0.03)
P for interaction = 0.28				
Stroop Test at Year 25				
Diabetes by Y25, n=366				
-0.13 (-1.06, 0.80)	-0.01 (-0.93, 0.91)	0.06 (-0.88, 1.00)	0.78 (-0.38, 1.94)	0.06 (-0.88, 1.00)
No Diabetes by Y25, n=2914				
0.53 (0.13, 0.92)	0.28 (-0.11, 0.68)	0.26 (-0.13, 0.65)	0.41 (-0.08, 0.91)	0.36 (-0.05, 0.78)
P for interaction = 0.36				
Global _z_ score at Year 25				
Diabetes by Y25, n=362				
0.02 (-0.05, 0.09)	-0.004 (-0.07, 0.07)	-0.01 (-0.07, 0.06)	-0.04 (-0.12, 0.04)	-0.01 (-0.07, 0.06)
No Diabetes by Y25, n=2892				
-0.09 (-0.12, -0.05)	-0.05 (-0.08, -0.02)	-0.05 (-0.08, -0.02)	-0.07 (-0.11, -0.03)	-0.06 (-0.09, -0.03)
P for interaction = 0.28				
Difference in Year 30 Cognitive Test Score per 1 SD CV-FG (95% CI)				
DSST at Year 30 (Y30)				
Diabetes by Y30, n=303				
0.37 (-0.89, 1.62)	0.12 (-1.11, 1.35)	0.30 (-0.94, 1.54)	-0.06 (-1.61, 1.50)	0.24 (-1.00, 1.48)
No Diabetes by Y30, n=2693				
-1.22 (-1.84, -0.59)	-0.55 (-1.14, 0.05)	-0.51 (-1.11, 0.08)	-0.96 (-1.71, -0.21)	-0.56 (-1.17, 0.06)
P for interaction = 0.77				
RAVLT at Year 30				
Diabetes by Y30, n=307				
0.05 (-0.19, 0.29)	0.03 (-0.21, 0.28)	0.02 (-0.23, 0.27)	-0.03 (-0.35, 0.28)	0.01 (-0.24, 0.26)
No Diabetes by Y30, n=2704				
-0.19 (-0.32, -0.06)	-0.08 (-0.21, 0.04)	-0.09 (-0.22, 0.04)	-0.11 (-0.27, 0.05)	-0.09 (-0.22, 0.05)

P for interaction = 0.57

Stroop Test at Year 30					
Diabetes by Y30, n=299	0.21 (-0.96, 1.37)	0.25 (-0.91, 1.41)	0.22 (-0.95, 1.40)	0.97 (-0.49, 2.43)	0.27 (-0.90, 1.44)
No Diabetes by Y30, n=2640	0.19 (-0.26, 0.64)	-0.15 (-0.59, 0.30)	-0.14 (-0.59, 0.30)	-0.22 (-0.78, 0.34)	-0.17 (-0.63, 0.29)
P for interaction = 0.56					
MoCA at Year 30					
Diabetes by Y30, n=303	0.03 (-0.26, 0.31)	-0.02 (-0.29, 0.25)	-0.04 (-0.31, 0.24)	-0.08 (-0.43, 0.26)	-0.03 (-0.31, 0.24)
No Diabetes by Y30, n=2691	-0.29 (-0.43, -0.14)	-0.13 (-0.27, 0.00)	-0.12 (-0.26, 0.01)	-0.24 (-0.41, -0.07)	-0.13 (-0.27, 0.01)
P for interaction = 0.39					
Category Fluency at Year 30					
Diabetes by Y30, n=301	-0.16 (-0.57, 0.25)	-0.21 (-0.61, 0.18)	-0.23 (-0.64, 0.17)	-0.42 (-0.93, 0.08)	-0.24 (-0.65, 0.17)
No Diabetes by Y30, n=2685	-0.19 (-0.40, 0.03)	-0.06 (-0.27, 0.15)	-0.07 (-0.28, 0.14)	-0.18 (-0.45, 0.09)	-0.11 (-0.34, 0.11)
P for interaction = 0.08					
Letter Fluency at Year 30					
Diabetes by Y30, n=297	-0.63 (-1.72, 0.46)	-0.81 (-1.87, 0.25)	-0.74 (-1.81, 0.34)	-1.11 (-2.46, 0.24)	-0.78 (-1.85, 0.30)
No Diabetes by Y30, n=2641	-0.34 (-0.86, 0.17)	0.05 (-0.45, 0.56)	0.06 (-0.44, 0.57)	-0.03 (-0.66, 0.61)	0.14 (-0.39, 0.66)
P for interaction = 0.17					
Global *z* score at Year 30					
Diabetes by Y30, n=286	-0.03 (-0.10, 0.05)	-0.04 (-0.11, 0.03)	-0.04 (-0.11, 0.04)	-0.08 (-0.17, 0.01)	-0.04 (-0.11, 0.03)
No Diabetes by Y30, n=2566	-0.06 (-0.09, -0.02)	-0.01 (-0.05, 0.02)	-0.01 (-0.05, 0.02)	-0.02 (-0.06, 0.02)	-0.01 (-0.05, 0.02)
P for interaction = 0.79					

Abbreviations: CV (coefficient of variation), DSST (Digit Symbol Substitution Test), FG (fasting glucose), MoCA (Montreal Cognitive Assessment), RAVLT (Rey-Auditory Verbal Learning Test). A 1-standard deviation (SD) unit increment in CV-FG at year 25 is 3.4% and at year 30 is 3.3%. Adjustments: [*]Model 1: age, sex, race, field center. [†]Model 2: Model 1 plus highest level of educational attainment, and cumulative values for: number of years as a current smoker, grams of weekly alcohol consumption, body mass index, physical activity, systolic blood pressure, use of blood pressure-lowering medications, low-density lipoprotein cholesterol, and cholesterol-lowering medications. [‡]Model 3: Model 2 plus weighted average of fasting glucose. [§]Model 3A: Model 3 plus change in fasting glucose level during variability measurement. [‖]Model 3B for individuals with diabetes: Model 3 plus diabetes medication use and duration before cognitive assessment. [‖]Model 3B for individuals without diabetes: Model 3 plus year fasting glucose level at the time of cognitive assessment.

Supplementary Table 4. Multivariable association between fasting glucose variability during young adulthood with cognitive function at Year 25 in middle age restricting to individuals with 5 or 6 glucose measurements or diabetes free through Year 30

Restricting to 5 or 6 Glucose Measurements

Difference in Cognitive Test Score at Year 25 according to 1 SD CV-FG (95% CI)

	Model 1[*]	Model 2[†]	Model 3[‡]	Model 3A[§]	Model 3B[‖]	Model 3C[¶]
DSST, n=2317	-1.81 (-2.50, -1.13)	-1.05 (-1.71, -0.39)	-1.02 (-1.68, -0.36)	-1.07 (-1.73, -0.40)	-1.38 (-2.22, -0.54)	-1.22 (-1.92, -0.52)
RAVLT, n=2310	-0.24 (-0.38, -0.09)	-0.16 (-0.30, -0.02)	-0.16 (-0.31, -0.02)	-0.17 (-0.31, -0.03)	-0.26 (-0.44, -0.08)	-0.18 (-0.33, -0.03)
Stroop, n=2310	0.48 (0.01, 0.94)	0.13 (-0.33, 0.59)	0.10 (-0.36, 0.56)	0.12 (-0.34, 0.58)	0.23 (-0.37, 0.82)	0.28 (-0.21, 0.77)
Global z, n=2295	-0.09 (-0.13, -0.06)	-0.05 (-0.09, -0.01)	-0.05 (-0.09, -0.01)	-0.05 (-0.09, -0.02)	-0.08 (-0.12, -0.03)	-0.06 (-0.10, -0.02)

Difference in Cognitive Test Score at Year 25 according to 1 SD ARV-FG (95% CI)

	Model 1[*]	Model 2[†]	Model 3[‡]	Model 3A[§]	Model 3B[‖]	Model 3C[¶]
DSST, n=2317	-1.55 (-2.20, -0.90)	-0.96 (-1.58, -0.33)	-0.98 (-1.61, -0.36)	-1.03 (-1.66, -0.40)	-0.97 (-1.60, -0.33)	-1.02 (-1.65, -0.39)
RAVLT, n=2310	-0.27 (-0.40, -0.13)	-0.21 (-0.34, -0.08)	-0.21 (-0.34, -0.07)	-0.22 (-0.35, -0.08)	-0.21 (-0.35, -0.08)	-0.21 (-0.34, -0.08)
Stroop, n=2310	0.16 (-0.28, 0.60)	-0.12 (-0.56, 0.31)	-0.10 (-0.54, 0.33)	-0.09 (-0.52, 0.35)	-0.10 (-0.54, 0.34)	-0.05 (-0.49, 0.38)
Global z, n=2295	-0.08 (-0.12, -0.05)	-0.05 (-0.09, -0.01)	-0.05 (-0.09, -0.01)	-0.05 (-0.09, -0.02)	-0.05 (-0.09, -0.01)	-0.05 (-0.09, -0.02)

Restricting to individuals who did not develop diabetes by Year 30

Difference in Cognitive Test Score at Year 25 according to 1 SD CV-FG (95% CI)

	Model 1[*]	Model 2[†]	Model 3[‡]	Model 3A[§]	Model 3B[‖]	Model 3C[¶]
DSST, n=2872	-1.39 (-1.96, -0.83)	-0.86 (-1.40, -0.32)	-0.83 (-1.38, -0.29)	NA	-1.28 (-1.96, -0.61)	-1.01 (-1.58, -0.44)
RAVLT, n=2866	-0.18 (-0.30, -0.06)	-0.11 (-0.23, 0.00)	-0.13 (-0.24, -0.01)	NA	-0.16 (-0.31, -0.02)	-0.14 (-0.26, -0.02)
Stroop, n=2860	0.51 (0.11, 0.92)	0.28 (-0.12, 0.68)	0.26 (-0.14, 0.66)	NA	0.44 (-0.06, 0.94)	0.37 (-0.05, 0.78)
Global z, n=2838	-0.08 (-0.11, -0.05)	-0.05 (-0.08, -0.02)	-0.05 (-0.08, -0.02)	NA	-0.07 (-0.11, -0.03)	-0.06 (-0.09, -0.03)

Difference in Cognitive Test Score at Year 25 according to 1 SD ARV-FG (95% CI)

	Model 1[*]	Model 2[†]	Model 3[‡]	Model 3A[§]	Model 3B[‖]	Model 3C[¶]
DSST, n=2872	-0.76 (-1.32, -0.20)	-0.55 (-1.08, -0.02)	-0.56 (-1.08, -0.03)	NA	-0.57 (-1.10, -0.03)	-0.58 (-1.11, -0.05)
RAVLT, n=2866	-0.10 (-0.21, 0.02)	-0.08 (-0.19, 0.04)	-0.07 (-0.19, 0.04)	NA	-0.07 (-0.18, 0.04)	-0.07 (-0.19, 0.04)
Stroop, n=2860	0.00 (-0.39, 0.40)	-0.09 (-0.48, 0.29)	-0.09 (-0.48, 0.30)	NA	-0.08 (-0.48, 0.31)	-0.07 (-0.46, 0.32)
Global z, n=2838	-0.03 (-0.07, 0.00)	-0.02 (-0.05, 0.01)	-0.02 (-0.05, 0.01)	NA	-0.02 (-0.05, 0.01)	-0.02 (-0.05, 0.01)

Abbreviations: ARV (average real variability), CV (coefficient of variation), DSST (Digit Symbol Substitution Test), FG (fasting glucose), RAVLT (Rey-Auditory Verbal Learning Test). A 1-standard deviation (SD) unit increment in CV-FG at year 25 is 3.4% and a 1-SD unit increment in ARV-FG at year 25 is 0.14. Adjustments: [*]Model 1: age, sex, race, field center. [†]Model 2: Model 1 plus highest level of educational attainment, and cumulative values for: number of years as a current smoker, grams of weekly alcohol consumption, body mass index, physical activity, systolic blood pressure, use of blood

pressure-lowering medications, low-density lipoprotein cholesterol, and cholesterol-lowering medications. [‡]Model 3: Model 2 plus weighted average of fasting glucose. [§]Model 3A: Model 3 plus the incidence of diabetes, diabetes medication use, and diabetes duration. [‖]Model 3B: Model 3 plus change in fasting glucose level during variability measurement. [¶]Model 3C: Model 3 plus year 25 fasting glucose level.

Supplementary Table 5. Multivariable association between fasting glucose variability during young adulthood with cognitive function at Year 30 in middle age restricting to individuals with 6 or 7 glucose measurements

Difference in Cognitive Test Score at Year 30 according to 1 SD CV-FG (95% CI)

	Model 1[*]	Model 2[†]	Model 3[‡]	Model 3A[§]	Model 3B[‖]
DSST, n=1822	-1.61 (-2.43, -0.78)	-0.65 (-1.45, 0.14)	-0.65 (-1.45, 0.14)	-0.99 (-1.99, 0.00)	-0.90 (-1.75, -0.05)
RAVLT, n=1828	-0.14 (-0.32, 0.03)	-0.01 (-0.18, 0.16)	-0.01 (-0.18, 0.16)	-0.01 (-0.22, 0.21)	-0.03 (-0.22, 0.15)
Stroop, n=1795	0.46 (-0.13, 1.04)	-0.04 (-0.62, 0.54)	-0.03 (-0.61, 0.54)	-0.27 (-0.99, 0.46)	-0.05 (-0.67, 0.56)
MoCA, n=1819	-0.38 (-0.56, -0.19)	-0.17 (-0.35, 0.01)	-0.17 (-0.35, 0.01)	-0.28 (-0.50, -0.06)	-0.22 (-0.41, -0.03)
Category Fluency, n=1821	-0.26 (-0.56, 0.04)	-0.07 (-0.37, 0.23)	-0.07 (-0.37, 0.23)	-0.14 (-0.52, 0.23)	-0.09 (-0.41, 0.23)
Letter Fluency, n=1797	-0.35 (-1.06, 0.36)	0.18 (-0.52, 0.88)	0.18 (-0.52, 0.88)	0.12 (-0.76, 1.00)	0.40 (-0.34, 1.15)
Global z, n=1754	-0.08 (-0.13, -0.03)	-0.02 (-0.06, 0.02)	-0.02 (-0.06, 0.02)	-0.02 (-0.08, 0.03)	-0.02 (-0.07, 0.03)

Difference in Cognitive Test Score at Year 30 according to 1 SD ARV-FG (95% CI)

	Model 1[*]	Model 2[†]	Model 3[‡]	Model 3A[§]	Model 3B[‖]
DSST, n=1822	-1.55 (-2.33, -0.78)	-0.78 (-1.52, -0.04)	-0.81 (-1.55, -0.06)	-0.82 (-1.57, -0.07)	-0.84 (-1.59, -0.10)
RAVLT, n=1828	-0.19 (-0.35, -0.02)	-0.08 (-0.24, 0.08)	-0.08 (-0.24, 0.09)	-0.08 (-0.24, 0.09)	-0.08 (-0.24, 0.08)
Stroop, n=1795	0.26 (-0.29, 0.80)	-0.16 (-0.70, 0.38)	-0.18 (-0.72, 0.36)	-0.22 (-0.76, 0.33)	-0.19 (-0.73, 0.36)
MoCA, n=1819	-0.25 (-0.42, -0.07)	-0.07 (-0.24, 0.10)	-0.08 (-0.25, 0.09)	-0.08 (-0.25, 0.09)	-0.09 (-0.25, 0.08)
Category Fluency, n=1821	-0.30 (-0.58, -0.02)	-0.15 (-0.43, 0.12)	-0.16 (-0.44, 0.12)	-0.17 (-0.45, 0.12)	-0.16 (-0.44, 0.12)
Letter Fluency, n=1797	-0.79 (-1.45, -0.12)	-0.35 (-1.01, 0.30)	-0.36 (-1.01, 0.30)	-0.39 (-1.06, 0.27)	-0.32 (-0.98, 0.33)
Global z, n=1754	-0.07 (-0.12, -0.03)	-0.02 (-0.07, 0.02)	-0.02 (-0.07, 0.02)	-0.02 (-0.07, 0.02)	-0.02 (-0.07, 0.02)

Abbreviations: ARV (average real variability), CV (coefficient of variation), DSST (Digit Symbol Substitution Test), FG (fasting glucose), RAVLT (Rey-Auditory Verbal Learning Test). A 1-standard deviation (SD) unit increment in CV-FG at year 30 is 3.3% and a 1-SD unit increment in ARV-FG at year 30 is 0.13. Adjustments: [*]Model 1: age, sex, race, field center. [†]Model 2: Model 1 plus highest level of educational attainment, and cumulative values for: number of years as a current smoker, grams of weekly alcohol consumption, body mass index, physical activity, systolic blood pressure, use of blood pressure-lowering medications, low-density lipoprotein cholesterol, and cholesterol-lowering medications. [‡]Model 3: Model 2 plus weighted average of fasting glucose. [§]Model 3A: Model 3 plus change in fasting glucose level during variability measurement. [‖]Model 3B: Model 3 plus year 30 fasting glucose level.

Supplementary Figure 1. Forest plot of the association between a 1-standard deviation unit increment (1 SD = 3.4%) in fasting glucose coefficient of variation with z score (95% confidence limits) for the (A) Digit Symbol Substitution Test, (B) Rey Auditory Verbal Learning Test, (C) Stroop Test, and (D) Global *z* score, at year 25. A negative *z* score represents worse cognitive performance. Model adjustments: Demographics: age, sex, race, field center. Cumulative Risk Factors: Demographics plus highest level of educational attainment, and cumulative values for: number of years as a current smoker, grams of weekly alcohol consumption, body mass index, physical activity, systolic blood pressure, use of blood pressure-lowering medications, low-density lipoprotein cholesterol, and cholesterol-lowering medications. Average FG: Cumulative Risk Factors plus and weighted average of fasting glucose. T2DM Dx & duration: Average FG plus incidence of diabetes, diabetes medication use, and diabetes duration. FG Change: Average FG plus change in fasting glucose level during variability measurement. Y25 FG level: Average FG plus year 25 fasting glucose level.
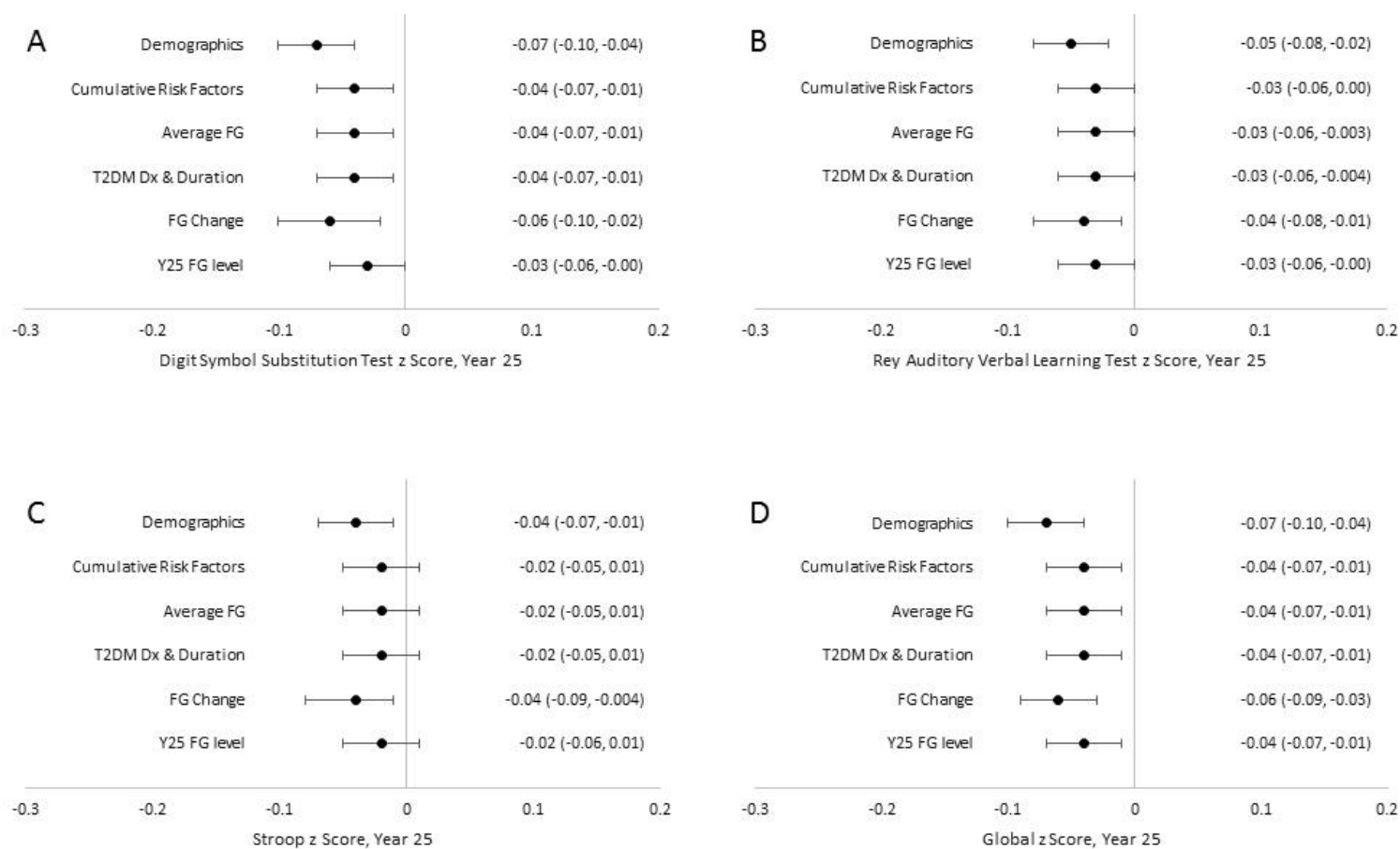
SUPPLEMENTARY DATA

Supplementary Figure 2. Forest plot of the association between a 1-standard deviation unit increment (1 SD = 3.3%) in fasting glucose coefficient of variation with z score (95% confidence limits) for the (A) Digit Symbol Substitution Test, (B) Rey Auditory Verbal Learning Test, (C) Stroop Test, (D) Montreal Cognitive Assessment, (E) Category Fluency Test, (F) Letter Fluency Test, and (G) Global *z* score, at year 30. A negative *z* score represents worse cognitive performance. Model adjustments: Demographics: age, sex, race, field center. Cumulative Risk Factors: Demographics plus highest level of educational attainment, and cumulative values for: number of years as a current smoker, grams of weekly alcohol consumption, body mass index, physical activity, systolic blood pressure, use of blood pressure-lowering medications, low-density lipoprotein cholesterol, and cholesterol-lowering medications. Average FG: Cumulative Risk Factors plus and weighted average of fasting glucose. T2DM Dx & duration: Average FG plus incidence of diabetes, diabetes medication use, and diabetes duration. FG Change: Average FG plus change in fasting glucose level during variability measurement. Y30 FG level: Average FG plus year 30 fasting glucose level.