

## Supplementary Online Content

Lacy ME, Wellenius GA, Sumner AE, et al. Association of sickle cell trait with hemoglobin A<sub>1c</sub> in African Americans. *JAMA*. doi:10.1001/jama.2016.21035

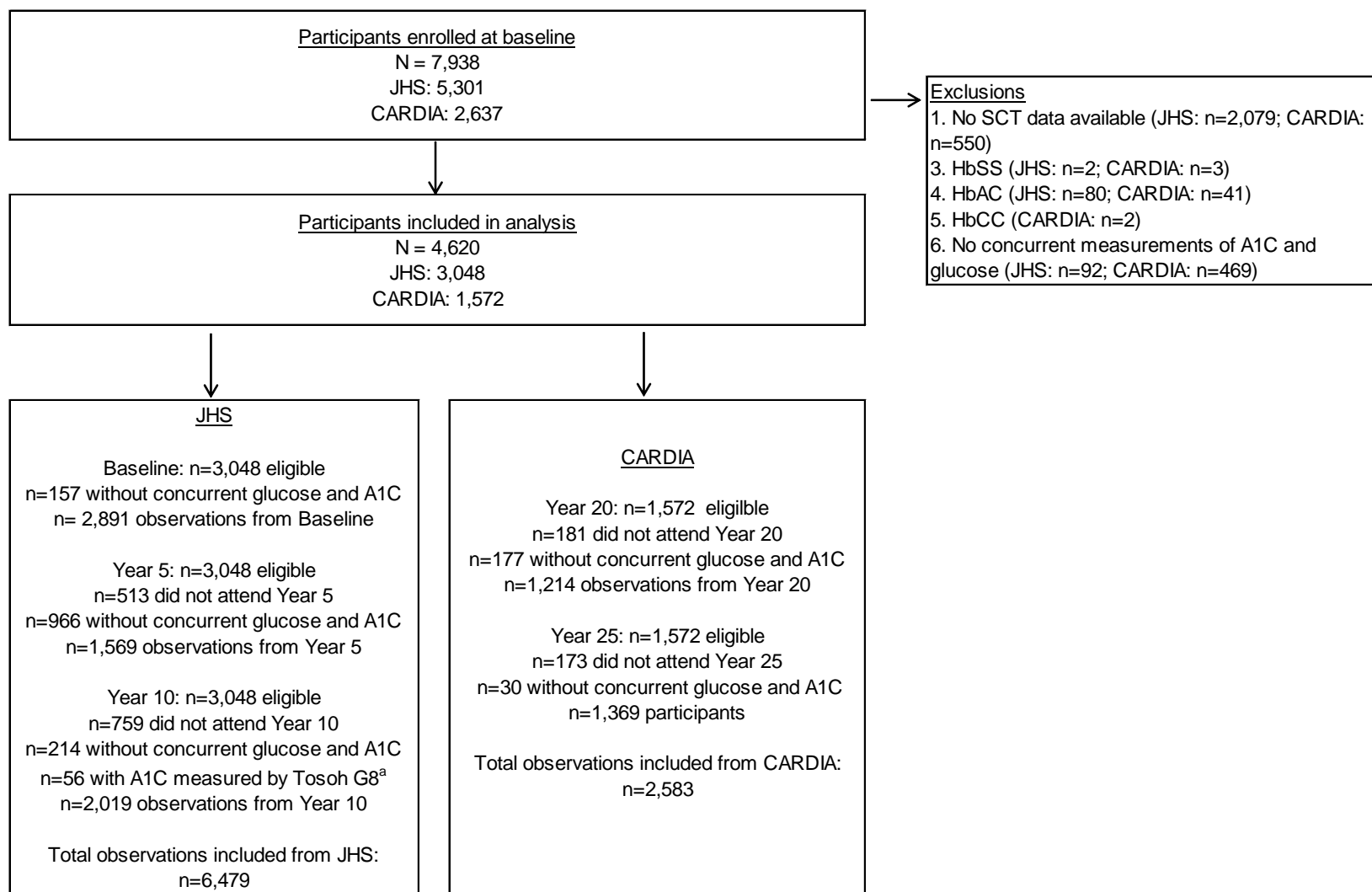
**eFigure 1.** Analytic sample: inclusion and exclusion criteria for participants from CARDIA and JHS

**eTable 1.** Detailed information on A<sub>1c</sub> and glucose measures from CARDIA and JHS

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This supplementary material has been provided by the authors to give readers additional information about their work.



**eFigure 1 – Analytic sample: Inclusion and exclusion criteria for participants from CARDIA and JHS**

eFigure 1 Footnotes:

Abbreviations: CARDIA, Coronary Artery Risk Development in Young Adults Study; JHS, Jackson Heart Study; A1C, hemoglobin A1c

<sup>a</sup> Due to recent interference from SCT, all observations using the Tosoh G8 were excluded from analyses (n=56).

**eTable 1. Detailed information on A1C and glucose measures from CARDIA and JHS**

Measure	Study	Visit	Years	Method	Lab	High/Low Control	CV (%)
A1C	CARDIA	Year 20 follow-up	2005-2006	HPLC, Tosoh G7 (variant mode)	University of Minnesota	High Low	1.2% 1.9%
A1C	CARDIA	Year 25 follow-up	2010-2011	HPLC, Tosoh G7 (variant mode)	University of Minnesota	Mean <sup>d</sup> Mean <sup>d</sup>	1.3%
A1C	JHS	Baseline	2000-2004	HPLC, Tosoh 2.2 analyzer	University of Mississippi Medical Center	High Low	1.4% 1.9%
A1C	JHS	Year 5 follow-up	2005-2008	HPLC, Tosoh G7 (variant mode)	University of Minnesota	High Low	1.4% 1.9%
A1C	JHS	Year 10 follow-up	2009-2013	HPLC, Tosoh G7 (variant mode) <sup>c</sup>	University of Minnesota	High Low	1.4% 1.9%
Fasting glucose <sup>a</sup>	CARDIA	Year 20 follow-up	2005-2006	Hexokinase, Cobas Mira Plus	University of Minnesota	High Low	1.8% 3.8%
Fasting glucose <sup>a</sup>	CARDIA	Year 25 follow-up	2010-2011	Hexokinase, Cobas Mira Plus	University of Minnesota	Mean <sup>d</sup> Mean <sup>d</sup>	1.9%
Fasting glucose <sup>a</sup>	JHS	Baseline	2000-2004	Glucose oxidase, Vitros colorimetric	University of Mississippi Medical Center	Range <sup>d</sup>	3.6%
Fasting glucose <sup>a</sup>	JHS	Year 5 follow-up	2005-2008	Hexokinase, Roche Modular P	University of Minnesota	High Low	1.6% 3.3%
Fasting glucose <sup>a</sup>	JHS	Year 10 follow-up	2009-2013	Hexokinase, Roche Modular P	University of Minnesota	High Low	1.6% 3.3%
2-hour glucose <sup>b</sup>	CARDIA	Year 20 follow-up	2005-2006	Hexokinase, Cobas Mira Plus	University of Minnesota	Mean <sup>d</sup> Mean <sup>d</sup>	3.5%
2-hour glucose <sup>b</sup>	CARDIA	Year 25 follow-up	2010-2011	Hexokinase, Cobas Mira Plus	University of Minnesota	Mean <sup>d</sup> Mean <sup>d</sup>	3.5%

eTable 1 Footnotes—

Abbreviations: CARDIA, Coronary Artery Risk Development in Young Adults Study; JHS, Jackson Heart Study; A1C, hemoglobin A1c; HPLC, high-performance liquid chromatography; CV, coefficient of variation

<sup>a</sup> To be eligible for fasting glucose, participants must have been fasting for at least 8 hours.

<sup>b</sup> To be eligible for 2-hour glucose (CARDIA only), participants must have been fasting for at least 8 hours and could not be on any diabetes medications.

<sup>c</sup> In addition to the Tosoh G7, the Tosoh G8 was used at JHS year 10 follow-up for some participants. However, due to recent interference from SCT, all observations using the Tosoh G8 were excluded from analyses (n=56).

<sup>d</sup> Quality control data on the CV was usually reported as the CV for high and low values. When indicated as 'Mean,' data was obtained as the CV on labs from a subset of participants that were obtained one month apart and the CV was calculated based on the difference between the mean values at the time of exam and quality control data from one month later. When indicated as 'Range,' the CV was calculated on data across the range of values.

**eTable 2. Characteristics at enrollment of study participants who were excluded from analyses versus those who were included in the final analytic sample**

Characteristic <sup>b</sup>	Excluded from analysis <sup>a</sup>	Included in analysis	p-value
	n=3,190	n=4,620	
Male, n (%)	1,249 (39.2)	1,785 (38.6)	0.64
Age, mean (SD), y	45.3 (18.2)	44.9 (18.1)	0.31
BMI, mean (SD)	29.4 (7.2)	29.8 (7.5)	0.01
Fasting glucose, mean (SD), mg/dL	93.6 (32.0)	94.0 (29.4)	0.64
A1C, mean (SD), % <sup>c</sup>	6.0 (1.3)	6.0 (1.3)	0.68
eGFR, mean (SD), mL/min/1.73m <sup>2,d</sup>	94.2 (22.1)	94.1 (21.8)	0.85
Diagnosed diabetes, n (%) <sup>e</sup>	394 (12.4)	532 (11.5)	0.26
Physical Activity <sup>f</sup>			
Poor Health	1,073 (33.6)	1,528 (33.1)	0.85
Intermediate Health	900 (28.2)	1,321 (28.6)	
Ideal Health	1,214 (38.1)	1,769 (38.3)	
Diet <sup>g</sup>			
Poor Health	2,022 (63.4)	2,973 (64.3)	0.74
Intermediate Health	1,091 (34.2)	1,555 (33.7)	
Ideal Health	27 (0.9)	35 (0.8)	
Smoking <sup>h</sup>			
Poor Health	674 (21.1)	886 (19.2)	0.08
Intermediate Health	69 (2.2)	108 (2.3)	
Ideal Health	2,396 (75.1)	3,573 (77.3)	

eTable 2 Footnotes:

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); A1C, hemoglobin A1c; eGFR, estimated glomerular filtration rate (calculated using the CKD-EPI equation).

<sup>a</sup>Participants who were excluded on the basis of missing data.

<sup>b</sup>Comparisons are based on data from study enrollment for CARDIA and JHS.

<sup>c</sup>Hemoglobin A1c is only available at study enrollment in JHS (not CARDIA), n=2,022 out of a total 3,188 in those excluded from analysis and n=3,034 out of a total of 4,620 in those included in analysis.

<sup>d</sup>eGFR is only available at study enrollment in JHS (not CARDIA), n=2,081 out of a total of 3,188 in those excluded from analysis and n=3,047 out of a total of 4,621 in those included in analysis.

<sup>e</sup>Diagnosed diabetes is defined as self-report of a prior physician's diagnosis of diabetes.

<sup>f</sup>Physical Activity is defined as Poor, Intermediate or Ideal based on minutes/week of moderate or vigorous physical activity. Poor Health (0 minutes/week); Intermediate Health (>0 - <150 minutes/week); Ideal Health (≥150 minutes/week).

<sup>g</sup>Diet is defined as Poor, Intermediate or Ideal based on the number of diet components achieved. Components: ≥4.5 cups of fruits and vegetables/day; ≥198 g of fish/week; <1500 mg of sodium/day; <450 calories/week of sugar-sweetened beverages; ≥3 servings/day of whole grains. Poor Health (0-1 components); Intermediate Health (2-3 components); Ideal Health (4-5 components).

<sup>h</sup>Smoking is defined as Poor, Intermediate or Ideal based on current and former smoking status. Poor Health (Current smoker); Intermediate Health (Quit < 12 months ago); Ideal Health (Never smoked or quit ≥12 months ago).

**eTable 3. Regression coefficients from generalized estimating equations<sup>a</sup> examining the association between SCT and A1C**

	Fasting glucose (CARDIA and JHS)							
	Overall		Excluding participants currently using diabetes medications		CARDIA only		JHS only	
	Unadjusted	Adjusted <sup>b</sup>	Unadjusted	Adjusted <sup>c</sup>	Unadjusted	Adjusted <sup>b</sup>	Unadjusted	Adjusted <sup>b</sup>
	$\beta$ (95% CI)	$\beta$ (95% CI)	$\beta$ (95% CI)	$\beta$ (95% CI)	$\beta$ (95% CI)	$\beta$ (95% CI)	$\beta$ (95% CI)	$\beta$ (95% CI)
# of observations	9,062	8,460	7,777	7,241	2,583	2,219	6,479	6,241
Model fit (QIC)	9085.6	8502.2	7803.0	7289.2	2606.0	2266.8	6504.1	6292.5
Intercept	6.01 (5.99, 6.03)	5.94 (5.91, 5.97)	5.93 (5.91, 5.95)	5.95 (5.92, 5.97)	5.90 (5.87, 5.93)	5.92 (5.85, 5.98)	6.06 (6.04, 6.09)	5.95 (5.92, 5.99)
SCT	-0.28 (-0.35, -0.22)	-0.32 (-0.39, -0.26)	-0.29 (-0.25, -0.23)	-0.35 (-0.41, -0.29)	-0.23 (-0.32, -0.13)	-0.33 (-0.43, -0.23)	-0.32 (-0.40, -0.24)	-0.32 (-0.40, -0.24)
Fasting glucose	0.027 (0.026, 0.028)	0.025 (0.023, 0.026)	0.029 (0.028, 0.031)	0.028 (0.026, 0.030)	0.026 (0.024, 0.029)	0.023 (0.020, 0.027)	0.028 (0.026, 0.029)	0.025 (0.024, 0.027)
SCT x Fasting glucose	-0.004 (-0.008, -0.0009)	-0.005 (-0.009, -0.001)	-0.006 (-0.001, -0.002)	-0.009 (-0.013, -0.005)	-0.003 (-0.007, 0.0002)	-0.005 (-0.008, -0.001)	-0.005 (-0.010, 0.0002)	-0.005 (-0.010, 0.001)
	Overall		2-hour glucose (CARDIA only)					
	Unadjusted	Adjusted						
	$\beta$ (95% CI)	$\beta$ (95% CI)						
	$\beta$ (95% CI)	$\beta$ (95% CI)						
# of observations	2,001	1,715						
Model fit (QIC)	2005.0	1781.9						
Intercept	5.65 (5.62, 6.67)	5.66 (5.60, 5.73)						
SCT	-0.28 (-0.36, -0.20)	-0.36 (-0.44, -0.27)						
2-hour glucose	0.011 (0.009, 0.013)	0.011 (0.008, 0.014)						
SCT x 2-hour glucose	-0.004 (-0.008, 0.001)	-0.004 (-0.009, 0.001)						

eTable 3 Footnotes:

Abbreviations: SCT, sickle cell trait; A1C, hemoglobin A1c; CARDIA, Coronary Artery Risk Development in Young Adults Study; JHS, Jackson Heart Study; QIC, quasi-likelihood under independence model criterion;  $\beta$ , beta coefficient from regression model; SE, standard error of  $\beta$  coefficient.

<sup>a</sup> All continuous variables were centered at the population mean. Adjusted models for "Overall," "CARDIA only" and "JHS only" were adjusted additionally for sex, age, BMI, ferritin, eGFR, study cohort, self-reported physician diagnosis of diabetes and current use of diabetes medications

<sup>b</sup> Adjusted models for "Overall," "CARDIA" only and "JHS only" were adjusted additionally for sex, age, BMI, ferritin, eGFR, study cohort, self-reported physician diagnosis of diabetes and current use of diabetes medications.

<sup>c</sup> Adjusted models for subgroup analysis excluding those currently on diabetes medications were adjusted additionally for sex, age, BMI, ferritin, eGFR, study cohort and self-reported physician diagnosis of diabetes.