SUPPLEMENTARY DATA

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*** only involved in FRAM 1 study.**

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Supplementary Table 1. Prevalence of IGT by HIV Status and Smoking Status

Measure	**HIV-infected** (N = 309)*	**Controls** (N = 187)	**p-value**
IGT (2 hr >140 mg/dL)			
Current Smokers	16.7% (22/132)	22.7% (5/22)	0.54
Past Smokers	12.5% (9/72)	11.8% (4/34)	0.99
Never Smokers	20.0% (21/105)	10.7% (14/131)	0.064
Ever Smokers	15.2% (31/204)	16.1% (9/56)	0.84

Note: analyses above are age-restricted to 38-52 years.
Those with fasting glucose ≥ 126 mg/dL or on DM medication are excluded.
IGT = impaired glucose tolerance.

TECHNICAL APPENDIX

In HIV+ participants, GTT was performed on average within 9 days of other FRAM2 exam measurements. By contrast, for control participants, GTT was performed as part of the CARDIA year 20 exam, and occurred on average 234 days earlier than the rest of the FRAM2 exam measurements. A comparison of GTT fasting glucose (FG1) with the FRAM2 exam fasting glucose (FG2) revealed drift over time in control participants' fasting glucose measurements, and revealed that later glucose measurements were paradoxically lower, even though both FG1 and FG2 were performed by the same laboratory, Linco. This suggests laboratory drift, because the usual trend over time would be upward. We therefore sought to calibrate both FG1 and the 2 hour glucose (G2HR) to FG2, since 2 hour glucose was not performed as part of the FRAM2 exam for CARDIA participants.

Appendix Figure 1 shows the association between FG1 and FG2. We were limited in that almost all the fasting data available for calibration was below the range of interest; i.e., the cutpoint for IGT is at 140 mg/dL for 2 hour glucose, but most fasting values are below 140 mg/dL. This means that our calibration is essentially extrapolated. For control participants, we modeled FG2 in terms of FG1, with an externally estimated "age offset" (see below) added to reflect the impact of the differing dates of the FG1 and FG2 specimens (234 days apart, on average).

We first calculated a simple linear regression of FG2 on FG1, but found that the regression line tilted well below the line of equality (**Appendix Figure 1a**). There were few data points above 140 mg/dL, the cutpoint for impaired glucose tolerance, making extrapolation using the tilt very dubious. We therefore based our calibration on an intercept-only model which postulates a slope of 1 with a shift, i.e., the calibration line lies below the equality line, but is parallel (**Appendix Figure 1b**). Log-transformed versions were also considered, but model fit was similar. Heteroscedasticity checks suggested violation of homoscedasticity, so we used a trimmed mean to calculate a robust estimate of the intercept (Rosenberger and Gasko, 1983).

For each control participant, the calibrated GTT value was then determined by the estimated shift of the raw value, plus an age offset calculated using the MESA trajectory (**Appendix Table 1**). We estimated the effect of aging using unpublished MESA data for ~1300 men and women in the age range

of our control participants. Based on MESA data, we would expect glucose to increase by 1.57 mg/dL per year in men and 1.88 mg/dL in women, in the relevant age range. We applied the sex-specific rate to days between FG1 and FG2 to calculate a correction for each participant. Steeper and shallower versions of these rates were compared, but had little influence on the results.

We used calibrated GTT values for the 2 hour results reported in the paper, but also compared these results with analyses using uncalibrated values (**Appendix Table 2**). Covance fasting glucose values were reported in the paper since both HIV+ and Control participants had glucose measured by Covance, and values were collected at the same time as part of the FRAM2 exam, so that no fasting calibration was needed.

We analyzed both raw and calibrated 2 hour glucose values (**Appendix Table 2)**. Mean 2 hour glucose values in controls were 101.3 mg/dL calibrated and 105.9 mg/dL uncalibrated, compared with 108.9 mg/dL for HIV+. The estimated HIV effect was therefore larger in the calibrated analysis (7.6 mg/dL, p=0.012) than in the uncalibrated analysis (3.0 mg/dL, p=0.33). Comparisons of IGT prevalence in HIV+ vs. Control were not statistically significant in any calibrated or uncalibrated analysis. The prevalence of IGT in Controls was similar in the calibrated (12.3%) and uncalibrated (13.9%) analyses. When those with IFG were excluded, the prevalence of IGT in Controls was 8.2% in calibrated and 9.6% in uncalibrated analysis.

References:

Rosenberger, J.L. and Gasko, M., 1983, Comparing location estimators: trimmed means, medians and trimean, *Understanding Robust and Exploratory Data Analysis*, ed. D.C. Hoaglin, F. Mosteller and J.W. Tukey, John Wiley, NY.

Appendix Table 1. Sample calibration calculations
(intercept-only model, using trimmed mean to calculate intercept)

MESA trajectory is estimated as c=1.57 mg/dL increase/year in men, c=1.88 mg/dL per year in women, using ~1300 subjects aged 38-52 years old. offset = GTT FG + c * (FRAM2Date – GTTDate) / 365.24; Intercept = trimmed mean of (FRAM2 raw value minus offset) = -4.65775 (using middle 2/3 of data) Calibrated GTT 2 hour = -4.65775 + Raw GTT 2 hour	**Calibration equations:** With full MESA trajectory offset: Y = -4.65775 + X A glucose value of 70 will be converted to 65.3 A glucose value of 140 will be converted to 135.3 A glucose value of 200 will be converted to 195.3

Appendix Table 2. Analysis of GTT parameters by HIV Status: comparison of calibrated and uncalibrated results

Measure	HIV-infected (N = 309)	Controls (N = 187)	p-value
2 hr Glucose (mg/dL) (calibrated)			
Median (IQR)	105.0 (83, 128)	96.3 (78.3, 121.3)	
Mean ± SD	108.9 ± 35.9	101.3 ± 32.7	
Mean difference HIV+ vs. Controls (95% CI)			
Unadjusted	7.6 (1.7, 13.6)		**0.012**
Adjusted for demographics	7.3 (1.0, 13.5)		**0.023**
Final model with AT**	4.3 (-2.3, 10.8)		0.20
2 hr Glucose (mg/dL) (raw)			
Median (IQR)	105.0 (83, 128)	101.0 (83, 126)	
Mean ± SD	108.9 ± 35.9	105.9 ± 32.7	
Mean difference HIV+ vs. Controls (95% CI)			
Unadjusted	3.0 (-3.0, 8.9)		0.33
Adjusted for demographics	2.6 (-3.7, 8.9)		0.42
Final model with AT**	-0.40 (-6.9, 6.1)		0.90
Impaired Gluc Tol (2 hr >140 mg/dL) (calib.)	16.8% (52/309)	12.3% (23/187)	
OR for HIV+ vs. Controls (95% CI)			
Unadjusted	1.44 (0.85, 2.45)		0.17
Adjusted for demographics	1.32 (0.76, 2.30)		0.33
Final model with AT**	0.84 (0.44, 1.62)		0.61
Impaired Gluc Tol (2 hr >140 mg/dL) (raw)	16.8% (52/309)	13.9% (26/187)	
OR for HIV+ vs. Controls (95% CI)			
Unadjusted	1.25 (0.75, 2.09)		0.39
Adjusted for demographics	1.15 (0.67, 1.98)		0.60
Final model with AT**	0.74 (0.39, 1.39)		0.35
IGT (2 hr >140 mg/dL) (calib.) in those without IFG100 ‡	13.1% (33/252)	8.2% (12/146)	
OR for HIV+ vs. Controls (95% CI)			
Unadjusted	1.68 (0.84, 3.37)		0.14
Adjusted for demographics	1.61 (0.78, 3.33)		0.20
Final model with AT**	1.14 (0.50, 2.59)		0.76
IGT (2 hr >140 mg/dL) (raw) in those without IFG100 ‡	13.1% (33/252)	9.6% (14/146)	
OR for HIV+ vs. Controls (95% CI)			
Unadjusted	1.42 (0.73, 2.75)		0.30
Adjusted for demographics	1.39 (0.69, 2.78)		0.35
Final model with AT**	1.01 (0.46, 2.22)		0.98

Diabetes (2 hr >200 mg/dL)	1.3% (4/309)	0%*** (0/187)	0.65
OR for HIV+ vs. Controls (95% CI)	na		

* Note: all analyses are age-restricted to 38-52 years.
Those with fasting glucose ≥ 126 mg/dL or on DM medication are excluded.
IGT = impaired glucose tolerance; IFG = impaired fasting glucose; AT = adipose tissue.
‡ IFG100 is defined as fasting glucose > 100 mg/dL.
** Final model adjusts for demographics and adipose tissue.
*** There is only one CARDIA participant with 2 hr glucose > 200 (raw value is 203); all calibrations push this value below 200, so prevalence of 2hr DM is zero in all calibrated analyses.

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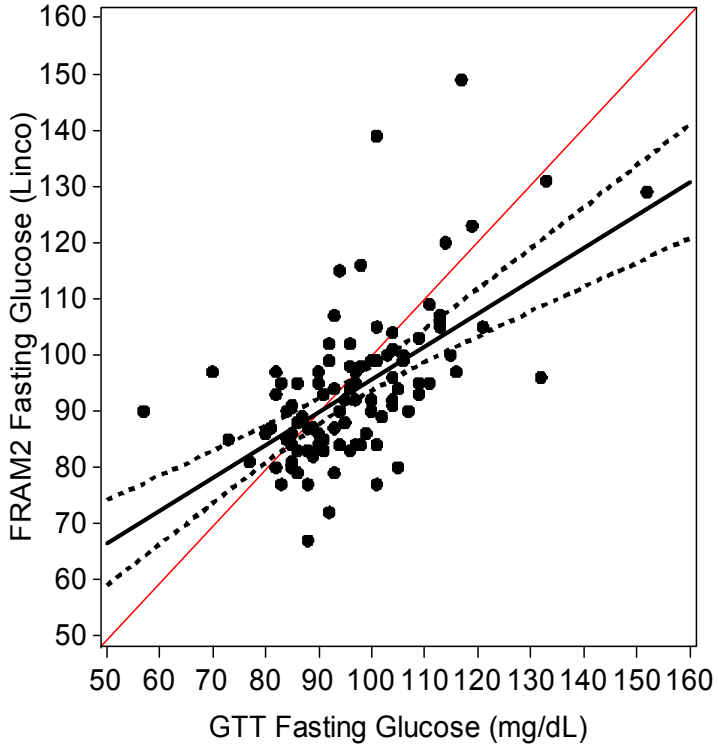
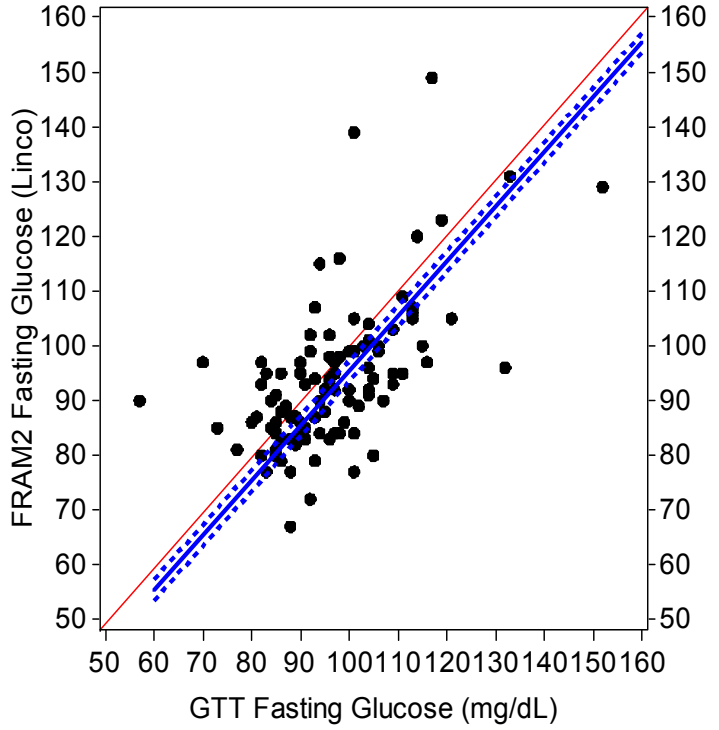
Appendix Figure 1. Regression of FRAM2 Fasting Glucose on GTT Fasting Glucose for Control Participants*

A. original equation, with 95% confidence limits



B. new intercept-only equation, with 95% confidence limits



Y = 37.29 + 0.585 X, Pearson r = 0.59, Spearman = 0.59
GTT FG: Mean = 96.7, SD = 13.3
FRAM2 FG: Mean = 93.8, SD = 13.1
Difference: Mean = 2.85, SD = 11.9
p = 0.017 (paired t-test), p = 0.0010 (signed rank)

Y = -4.65775 + X, SE = 0.913 for intercept
Offset = GTT FG + c * (FRAM2Date – GTTDate) / 365.24;
intercept = trimmed mean of (FRAM2 FG – offset)

* n=104. Those on DM medication were excluded. One outlier excluded (FRAM2 FG = 321, GTT FG = 112).