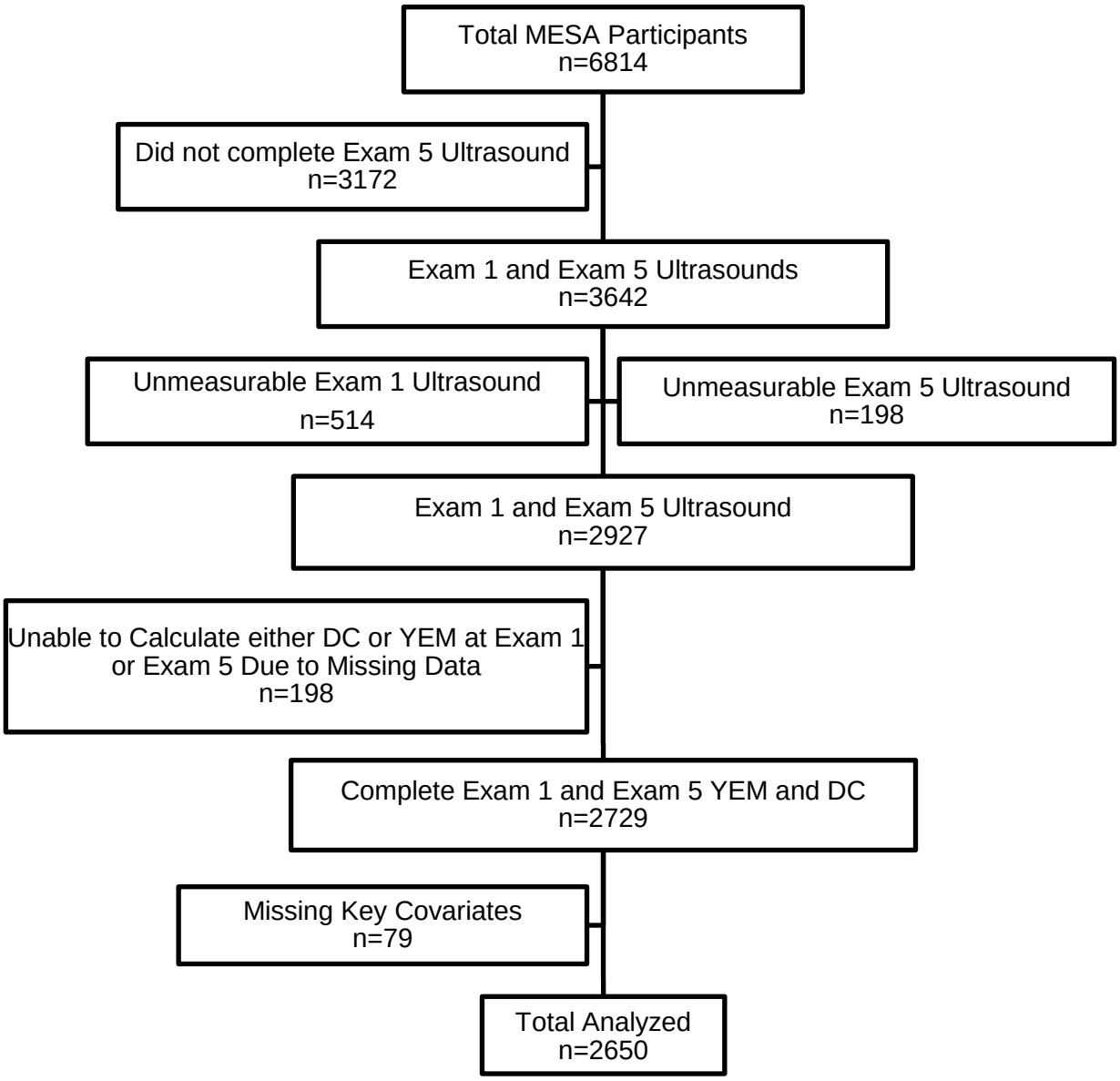
SUPPLEMENTAL MATERIAL

Supplement A: Flow diagram for Participant Inclusion



As is typically seen in longitudinal epidemiological studies, the 2650 subjects included in our analysis were healthier than the entire MESA sample. They were younger, had higher education levels, less diabetes mellitus, lower blood pressure, lower body-mass index, and fewer smoked. Since the subjects analyzed were healthier, our analyses would be expected to create a bias towards the null.

Supplement B. Measurement of Carotid Distensibility and Young's Elastic Modulus

The carotid distensibility coefficient (DC) was calculated as:

$$DC = \frac{(Ds^2 - Dd^2)}{\Delta p \cdot Dd^2}$$

Ds represents the internal arterial diameter at peak systole, *Dd* represents the internal diameter at end-diastole, and *Δp* represents the difference between the systolic and diastolic measurements (pulse pressure).[1] Young's elastic Modulus (YEM), the ratio of stress and circumferential strain in the arterial wall, was calculated as:

$$YEM = \frac{Dd/h}{DC}$$

Dd is the arterial diameter at end-diastole, *h* is the arterial wall thickness at end-diastole (external carotid artery diameter minus internal carotid artery diameter).[1, 2] YEM and DC are inversely related, thus increased arterial stiffness corresponds to a lower DC and a higher YEM. The derived wall thickness (*h*) was strongly correlated with the far wall carotid IMT values measured directly using a semi-automated border detection program ($r=0.78$, $p < 0.0001$).

Supplement C: Intra- and Inter-reader Reproducibly

Reproducibility measurements were performed by a single reader with 25 representative images. Reproducibility was excellent: $p<0.0001$ for all measurements: internal end-diastolic diameter ($r=0.998$), peak systolic internal diameter ($r=0.998$), end-diastolic external diameter ($r=0.997$), change in diameter ($r=0.925$) and wall thickness ($r=0.989$).

Paired, blinded measurements of the diameter of an ultrasound phantom containing a simulated blood vessel showed mean (standard deviation) diameters of 3.47 (0.02) mm for digitized videotape and 3.47 (0.01) mm for digitized videostream (t-test $p=0.660$). The size of a digitized pixel using the Medical Digital Recording device was 0.056 mm. A systematic bias of <

1/2 digital pixel (0.028 mm) was statistically rejected using the two, one-sided test (TOST), thus demonstrating equivalence of both measurements using digitized videotape and digitized video stream.[3,4] Based on these findings and the visual appearance of essentially superimposable images from digitized videotape and video stream, even if a very small bias existed, it would not affect the relationships between the covariates (it only would affect the absolute values of the measurements).

Approximately 90% of readings were performed by two readers. Inter-reader correlations were 0.99 for all 3 diameter measurements and 0.96 for wall thickness. Of note, each reader read both sets of distensibility studies for each subject, so there is no bias by reader within subjects, which the basis of all of our analyses

Supplement References

1. Laurent S, Cockcroft J, Van Bortel L, Boutouyrie P, Giannattasio C, Hayoz D, Pannier B, Vlachopoulos C, Wilkinson I, Struijker-Boudier H. Expert consensus document on arterial stiffness: Methodological issues and clinical applications. *Eur Heart J*. 2006;27:2588-2605
2. Reneman RS, Meinders JM, Hoeks AP. Non-invasive ultrasound in arterial wall dynamics in humans: What have we learned and what remains to be solved. *Eur Heart J*. 2005;26:960-966
3. Hsu J, Hwang J, Liu H-K, Ruberg S. Confidence intervals associated with tests for bioequivalence. Biometrika 1994;81:103-114.
4. Chow S, Liu J. Design and analysis of bioequivalence studies. New York: Marcel Dekker; 1992.

Supplementary Table I. Multivariate ANCOVA Regression Models for Change in Young's Elastic Modulus without Adjustment for Baseline Young's Elastic Modulus

	Significant predictors	β	p-value
Model 1 R^2=0.0236	Age	10.9	0.0004
	Education level (compared to those who did not graduate high school)		
	Greater than high school	-200.2	0.03
	Use of antihypertensive medication at baseline	112.8	0.05
Model 2 R^2=0.0272	Age	11.2	0.0002
	Education level (compared to those who did not graduate high school)		
	Greater than high school	-202.6	0.03
	Stopping antihypertensive medication	398.4	0.006

Model covariates are the same as in Table 2.

Supplementary Table II. Multivariate ANCOVA Regression Models for Change in Distensibility Coefficient without Adjustment for Baseline Distensibility Coefficient

	Significant predictors	β	p-value
Model 1 $R^2 = 0.046$	Study site		
	University of Minnesota	4.0×10^{-4}	<0.0001
	Columbia	3.4×10^{-4}	<0.0001
	University of California – Los Angeles	2.0×10^{-4}	0.02
	Active smoker at baseline	-2.0×10^{-4}	0.008
	Activity Level (compared to the least active subjects, quartile 1)		
	Quartile 2	-1.5×10^{-4}	0.02
	Baseline systolic blood pressure (per mmHg)	7.7×10^{-6}	<0.0001
Model 2 $R^2 = 0.053$	Study site		
	University of Minnesota	3.9×10^{-4}	<0.0001
	University of California – Los Angeles	1.9×10^{-4}	0.03
	Active smoker at baseline	-2.0×10^{-4}	0.007
	Activity Level (compared to the least active subjects, quartile 1)		
	Quartile 2	-1.4×10^{-4}	0.02
	Baseline systolic blood pressure (per mmHg)	6.0×10^{-6}	<0.0001
	Starting antihypertensive medication	2.2×10^{-4}	0.0002

Model covariates are the same as in Table 2.

Supplementary Table III. Participant Characteristics by Ethnic Group

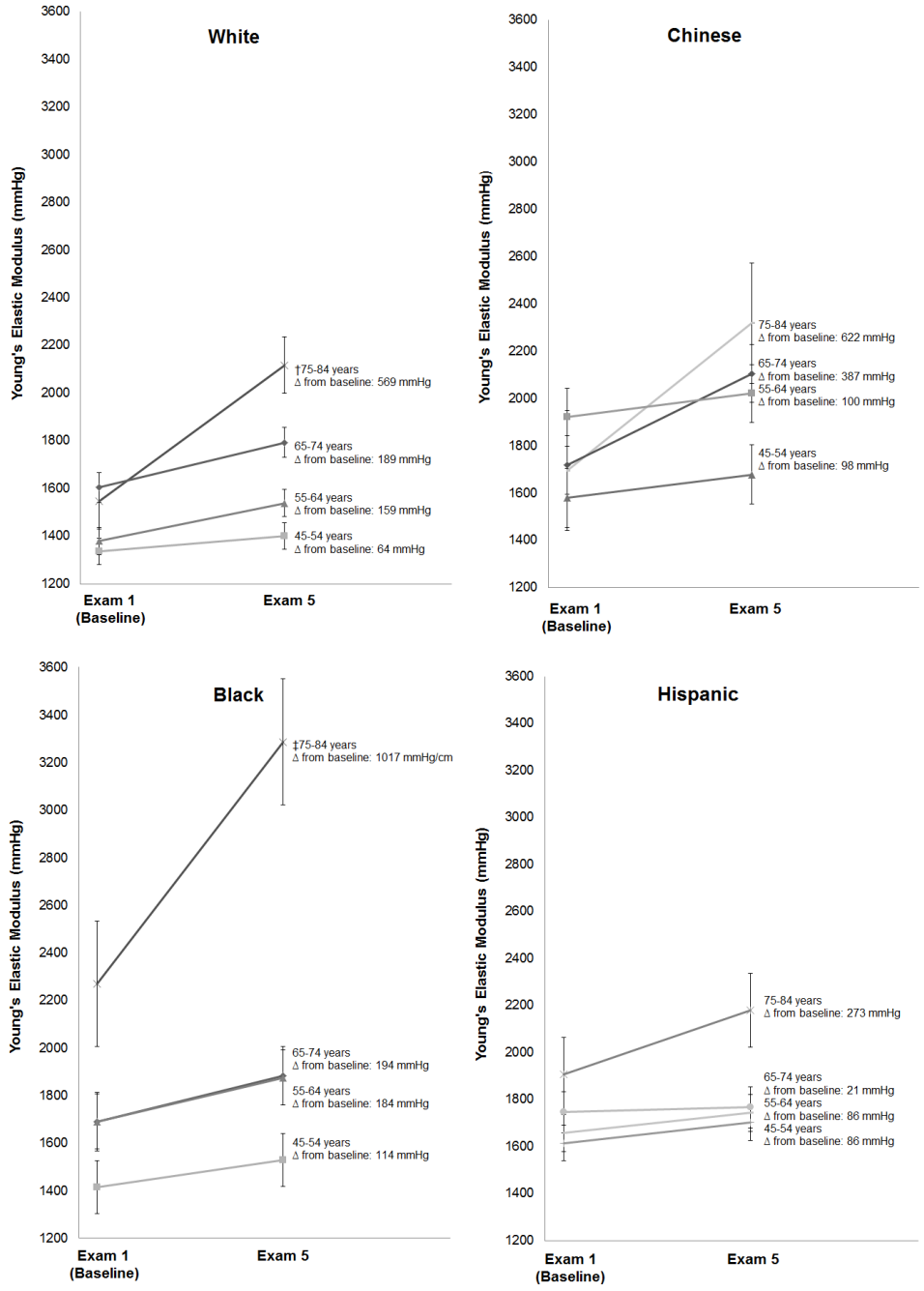
	Baseline					Exam 5				
	White N=1039	**Black N=660**	**Chinese N=380**	**Hispanic N=571**	**P**	**White N=1039**	**Black N=660**	**Chinese N=380**	**Hispanic N=571**	**P**
Age (years)	59.9 (9.3)	59.8 (9.2)	60.5 (9.3)	59.4 (9.7)	0.359	69.4 (9.2)	69.1 (9.1)	70.1 (9.2)	68.9 (9.5)	0.22
Female sex (%)	541(52.1)	385 (58.3)	185 (48.7)	303 (53.1)	0.014					
Study Site (%)										
Wake Forest	240 (23.1)	213 (32.3)	0 (0.0)	1 (0.2)						
Columbia	112 (10.8)	164 (24.9)	2 (0.5)	241 (42.2)						
John Hopkins	133 (12.8)	110 (16.7)	0 (0.0)	0 (0.0)						
U Minnesota	254 (24.5)	0 (0.0)	0 (0.0)	157 (27.5)	<0.0001					
Northwestern	251 (24.2)	117 (17.7)	184 (48.4)	0 (0.0)						
UCLA	49 (4.7)	56 (8.5)	194 (51.1)	172 (30.1)						
Blood pressure parameters (mmHg)										
SBP	120.5 (19.3)	128.7 (19.6)	121.7 (19.9)	123.2 (20.5)	<0.0001	120.7 (19.5)	128.0 (21.0)	122.3 (20.0)	124.9 (21.1)	<0.0001

DBP	70.0 (10.1)	74.6 (9.7)	72.0 (10.5)	71.2 (9.6)	<0.0001	67.1 (10.0)	70.6 (10.5)	68.0 (9.4)	68.4 (10.3)	<0.0001
Pulse Pressure	50.5 (15.1)	54.2 (15.7)	49.6 (14.8)	52.1 (16.4)	<0.0001	53.5 (16.3)	57.4 (17.2)	54.3 (17.2)	56.5 (17.5)	<0.0001
HTN (%)	385 (37.1)	371 (56.2)	138 (36.3)	224 (39.2)	<0.0001	570 (54.9)	491 (74.4)	198 (52.1)	337 (59.1)	<0.0001
HTN meds (%)	297 (28.6)	300 (45.5)	96 (25.3)	171 (30.0)	<0.0001	493 (47.5)	435 (65.9)	173 (45.5)	289 (50.6)	<0.0001
Diabetes mellitus status (%)										
IFG	95 (9.1)	79 (12.0)	67 (17.6)	76 (13.3)		197 (19.1)	111 (17.0)	104 (27.5)	145 (25.5)	
Untreated	8 (0.8)	14 (2.1)	7 (1.8)	13 (2.3)	<0.0001	13 (1.3)	8 (1.2)	9 (2.4)	11 (1.9)	<0.0001
Treated	28 (2.7)	63 (9.6)	29 (7.6)	61 (10.7)		91 (8.8)	139 (21.3)	69 (18.3)	121 (21.3)	
Lipids (mg/dL)										
Total cholesterol	195.3 (34.9)	190.1 (34.9)	191.5 (31.6)	198.2 (36.7)	0.0002	182.8 (37.1)	184.7 (36.1)	186.1 (36.7)	182.5 (36.8)	0.34
Low-density lipoprotein cholesterol	116.8 (29.0)	117.2 (32.2)	114.4 (28.4)	119.9 (32.4)	0.0524	104.2 (31.8)	107.9 (32.4)	106.6 (31.5)	106.0 (32.0)	0.15
High-density lipoprotein cholesterol	52.4 (15.8)	53.4 (15.4)	49.7 (13.2)	49.0 (14.2)	<0.0001	57.4 (17.9)	59.0 (18.2)	55.4 (14.8)	52.6 (15.5)	<0.0001
Triglycerides	130.2 (80.0)	97.6 (52.7)	139.2 (81.9)	150.0 (100.4)	<0.0001	106.0 (56.2)	90.3 (48.7)	123.4 (75.9)	121.3 (63.9)	<0.0001
Lipid-lowering meds (%)	178 (17.1)	99 (15.0)	49 (12.9)	74 (13.0)	0.0773	431 (41.5)	228 (34.6)	123 (32.4)	211 (37.0)	0.003

BMI (kg/m^2)	27.4 (4.8)	29.6 (5.3)	23.9 (3.1)	28.5 (4.4)	<0.0001	27.7 (5.1)	29.7 (5.4)	24.0 (3.2)	28.9 (5.1)	<0.0001
Waist (cm)	96.8 (14.2)	99.4 (13.7)	86.4 (9.5)	98.0 (11.9)	<0.0001	98.4 (14.3)	101.1(13.4)	88.2 (10.0)	99.2 (12.3)	<0.0001
Smoking (%)										
Former	436 (42.0)	251 (38.0)	74 (19.5)	179 (31.4)	<0.0001	528 (51.0)	319 (48.5)	99 (26.1)	259 (45.8)	<0.0001
Current	112 (10.8)	99 (15.0)	16 (4.2)	70 (12.3)		77 (7.4)	74 (11.3)	11 (2.9)	32 (5.7)	
YEM (mmHg)	1436 (823)	1630 (1023)	1733 (996)	1687 (908)	<0.0001	1600 (1065)	1843 (1722)	1958 (1375)	1771 (1044)	<0.0001
DC (10^{-3} $mmHg^{-1}$)	3.4 (1.3)	2.9 (1.2)	3.0 (1.2)	3.0 (1.2)	<0.0001	2.9 (1.2)	2.5 (1.1)	2.6 (1.0)	2.6 (1.1)	<0.0001
Carotid wall thickness (cm)	0.145 (0.029)	0.156 (0.032)	0.141 (0.029)	0.145 (0.031)	<0.0001	0.161 (0.030)	0.173 (0.033)	0.154 (0.031)	0.163 (0.035)	<0.0001
PSI Diameter (cm)	0.628 (0.075)	0.625 (0.079)	0.633 (0.078)	0.622 (0.066)	0.15	0.646 (0.081)	0.639 (0.083)	0.658 (0.084)	0.635 (0.068)	<0.0001
EDI Diameter (cm)	0.579 (0.071)	0.580 (0.075)	0.590 (0.073)	0.578 (0.063)	0.03	0.599 (0.077)	0.597 (0.079)	0.617 (0.080)	0.592 (0.065)	<0.0001

See Table 1 for abbreviations

Supplementary Figure I. Change in Young's Elastic Modulus by Ethnicity



† p=0.002; ‡ p=0.010 for age group x exam interaction term

Supplementary Figure II. Change in Distensibility Coefficient by Ethnicity