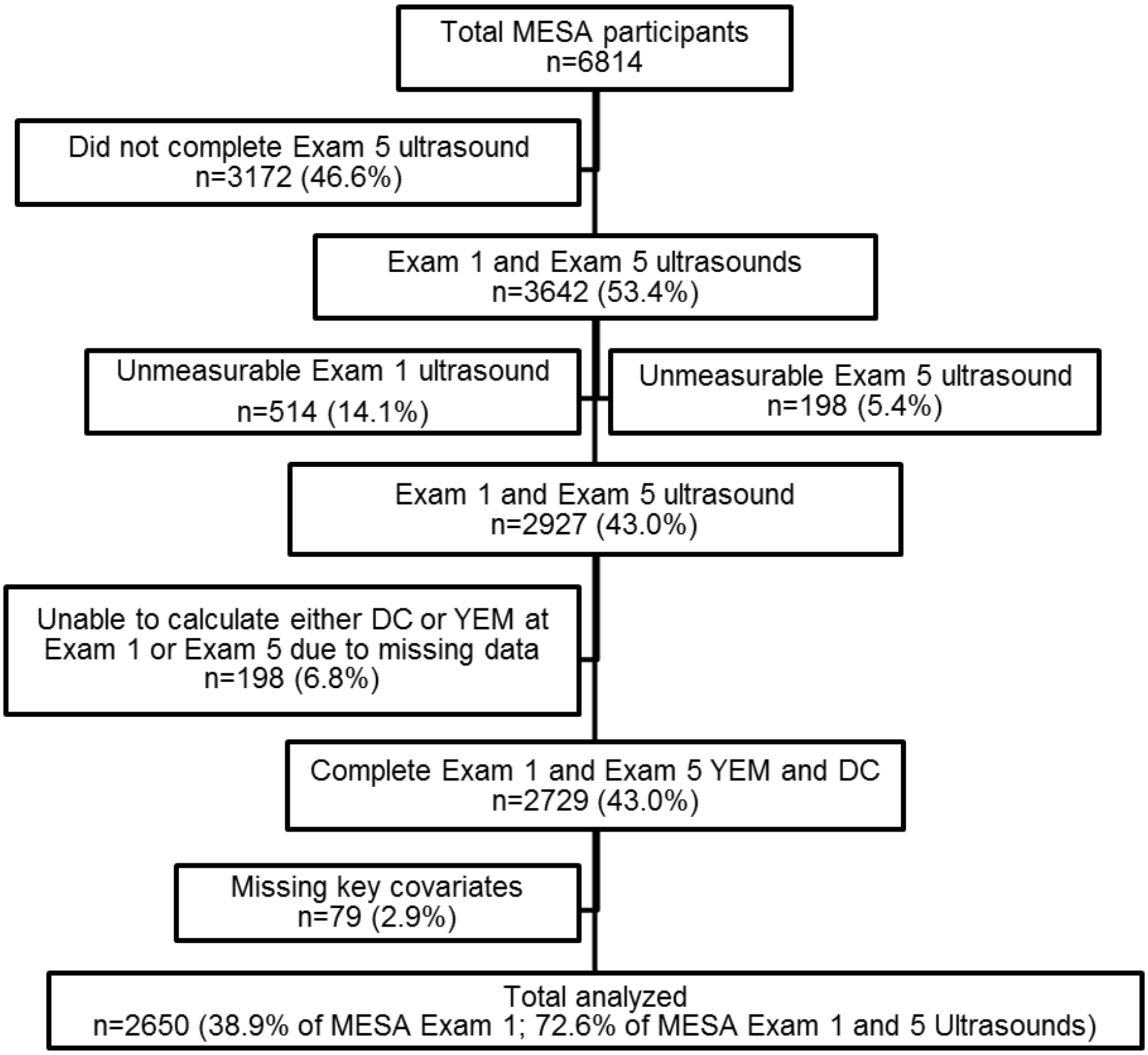
SUPPLEMENTAL MATERIAL

Supplement I: 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 II: 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:

$$YEM = \left(\frac{\frac{Dd}{h}}{DC}\right)$$

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 <0.001).

Supplement III: Intra- and Inter-reader Reproducibly

Reproducibility measurements were performed by a single reader with 25 representative images selected from each field center. 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 ($r=0.989$). 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. The means and standard deviations of the differences in blinded re-readings are below:

Intra-reader differences	**Differences, reading 1 - reading 2**				
	Peak Systolic Internal Diameter	**End-Diastolic Internal Diameter**	**End-Diastolic External Diameter**	**Change in Diameter**	**Thickness**
Mean (mm)	0.0089	0.0178	0.0409	-0.0089	0.0231
SD (mm)	0.0561	0.0488	0.0655	0.0636	0.0492
Inter-reader differences	**Differences, reader 1 - reader 2**				
Mean (mm)	0.064	0.055	0.122	0.009	0.067
SD (mm)	0.070	0.058	0.075	0.062	0.090

The intra-reader intra-class correlation coefficient for intra-reader wall thickness was 0.98 and for delta diameter it was 0.85. The inter-reader intra-class correlation coefficients were very similar; for intra-reader wall thickness it was 0.92 and for delta diameter it was 0.87. Of note, each reader read both sets of distensibility studies for each subject, so there is no bias by reader within subjects, which is the basis of all of our analyses

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 video stream ($p=0.660$). 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 t-test, 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).

Data Supplement IV

Supplementary Table IV-A: Multivariable Linear Regression Models for Change in Distensibility Coefficient (DC) without Adjustment for Baseline DC

Significant Predictors	Men		Women	
	Beta (10^{-3} mm Hg^{-1})	**P-value**	**Beta (10^{-3} mm Hg^{-1})**	**P-value**
Age	0.0076	**0.04**	0.0003	0.95
Baseline systolic blood pressure	0.0049	**0.01**	0.0074	**<0.001**
Total cholesterol, mg/dL	0.0023	**0.02**	-0.0003	0.72

Models were adjusted for baseline distensibility coefficient, age, ethnicity, education, diabetes mellitus, smoking, total and high-density lipoprotein cholesterol, body-mass index, systolic blood pressure, antihypertensive treatment, and menopausal status (in models restricted to females).

Supplementary Table IV-B: Multivariable Linear Regression Models for Change in Young's Elastic Modulus (YEM) without Adjustment for Baseline YEM

Significant Predictors	Men		Women	
	Beta (mmHg)	**P-value**	**Beta (mmHg)**	**P-value**
Age	12.5	**0.003**	10.9	**0.03**
High school graduate	84.3	0.56	-408.4	**0.001**
Greater than high school education	-31.7	0.80	-258.2	**0.03**

Models were adjusted for baseline Young's Elastic Modulus, age, ethnicity, education, diabetes mellitus, smoking, total and high-density lipoprotein cholesterol, body-mass index, systolic blood pressure, antihypertensive treatment, and menopausal status (in models restricted to females).

Supplementary Table IV-C. Male Participant Characteristics by Race/Ethnicity

	Caucasian	Chinese	African American	Hispanic	P-value
Number (%)	498 (40.3)	195 (15.8)	275 (22.2)	268 (21.7)	
Age (years)	60.2 (9.2)	60.9 (9.4)	59.6 (9.1)	59.1 (9.7)	0.17
Blood pressure parameters					
Systolic blood pressure	122.3 (17.2)	122.3 (18.5)	127.6 (18.5)	122.4 (18.4)	<0.001
Diastolic blood pressure	74.1 (8.8)	75.5 (9.5)	77.5 (9.0)	74.6 (9.0)	<0.001
Hypertension (%)	183 (36.8)	73 (37.4)	148 (53.8)	88 (32.8)	<0.001
Use of antihypertensive medications (%)	151 (30.3)	52 (26.7)	120 (43.6)	69 (25.8)	<0.001
Lipids (mg/dL)					
Total cholesterol	186.7 (32.1)	187.6 (30.1)	183.5 (35.8)	192.2 (35.6)	0.03
High-density lipoprotein cholesterol	44.6 (11.3)	46.1 (11.8)	46.6 (12.7)	42.4 (9.4)	<0.001
Lipid-lowering meds (%)	106 (21.3)	25 (12.8)	41 (14.9)	33 (12.3)	0.003
BMI (kg/m^2)	27.7 (3.7)	24.0 (3.0)	28.4 (4.2)	28.2 (3.8)	<0.001
Diabetes mellitus status (%)	22 (4.4)	24 (12.3)	33 (12.0)	40 (14.9)	<0.01
Impaired fasting glucose	58 (11.7)	45 (23.1)	42 (15.3)	39 (14.6)	
Untreated	6 (1.2)	5 (2.6)	9 (3.3)	5 (1.9)	
Treated	16 (3.2)	19 (9.7)	24 (8.7)	34 (12.7)	
Smoking (%)					<0.001
Former	230 (46.2)	70 (35.9)	127 (46.2)	112 (41.8)	
Current	49 (9.8)	13 (6.7)	44 (16.0)	39 (14.6)	
Education					<0.001
Less than high school education	9 (1.8)	29 (14.9)	15 (5.5)	96 (35.8)	
High school graduate	57 (11.5)	19 (9.7)	42 (15.3)	50 (18.7)	
Greater than high school education	432 (86.8)	147 (75.4)	218 (79.3)	122 (45.5)	
Income (annual)					<0.001
Less than $20,000	28 (5.6)	56 (28.7)	27 (9.8)	72 (26.9)	
Up to $39,000	65 (13.1)	38 (19.5)	63 (22.9)	92 (34.3)	
Up to $74,999	153 (30.7)	50 (25.6)	99 (36.0)	77 (28.7)	
Greater than $75,000	252 (50.6)	51 (26.2)	86 (31.3)	27 (10.1)	
Distensibility Coefficient at Exam 1 (10^{-3} mmHg^{-1})	3.3 (1.2)	2.9 (1.1)	2.9 (1.2)	2.9 (1.2)	<0.001
Δ Distensibility Coefficient (10^{-3} mmHg^{-1})	-0.42 (1.2)	-0.48 (1.0)	-0.40 (1.1)	-0.35 (1.1)	0.65
Young's Elastic Modulus at Exam 1 (mmHg)	1488 (761)	1750 (958)	1662 (1095)	1746 (965)	<0.001
Δ Young's Elastic Modulus (mmHg)	172 (1080)	220 (1061)	173 (1649)	83 (1159)	0.67
Carotid wall thickness (cm)	0.074 (0.015)	0.072 (0.016)	0.080 (0.016)	0.074 (0.016)	<0.001
Peak systolic internal diameter (cm)	0.661 (0.075)	0.643 (0.080)	0.656 (0.083)	0.646 (0.065)	0.01
End-diastolic internal diameter (cm)	0.611 (0.070)	0.602 (0.073)	0.610 (0.078)	0.603 (0.060)	0.28

Supplementary Table IV-D. Female Participant Characteristics by Race/Ethnic Group

	Caucasian	Chinese	African American	Hispanic	P-value
Number (%)	541 (38.3)	185 (13.1)	385 (27.2)	303 (21.4)	
Age (years)	59.7 (9.4)	60.1 (9.2)	59.9 (9.2)	59.7 (9.7)	0.96
Blood pressure parameters					
Systolic blood pressure	118.9 (20.9)	121.0 (21.4)	129.5 (20.3)	124.0 (22.1)	<0.001
Diastolic blood pressure	66.2 (9.8)	68.8 (10.5)	72.5 (9.6)	68.1 (9.1)	<0.001
Hypertension (%)	196 (36.2)	61 (33.0)	215 (55.8)	130 (42.9)	<0.001
Use of antihypertensive medications (%)	146 (27.0)	44 (23.8)	180 (46.8)	102 (33.7)	<0.001
Lipids (mg/dL)					
Total cholesterol	203.2 (35.4)	195.7 (32.6)	194.7 (33.5)	203.6 (37.0)	<0.001
High-density lipoprotein cholesterol	59.6 (15.8)	53.6 (13.6)	58.3 (15.3)	54.8 (15.1)	<0.001
Lipid-lowering meds (%)	72 (13.3)	24 (13.0)	58 (15.1)	41 (13.5)	0.86
BMI (kg/m^2)	27.2 (5.6)	23.8 (3.2)	30.5 (5.9)	28.9 (4.9)	<0.001
Diabetes mellitus status (%)	14 (2.3)	14 (7.6)	46 (12.0)	35 (11.6)	<0.001
Impaired fasting glucose	37 (6.8)	22 (11.9)	37 (9.6)	37 (12.2)	
Untreated	2 (0.4)	2 (1.1)	5 (1.3)	8 (2.6)	
Treated	12 (2.2)	10 (5.4)	39 (10.1)	27 (8.9)	
Smoking (%)					<0.001
Former	206 (38.1)	4 (2.2)	124 (32.2)	67 (22.1)	
Current	63 (11.7)	3 (1.6)	55 (14.3)	31 (10.2)	<0.001
Education					
Less than high school education	15 (2.8)	51 (27.6)	21 (5.5)	127 (41.9)	<0.001
High school graduate	100 (18.5)	37 (20.0)	76 (19.7)	69 (22.8)	0.52
Greater than high school education	426 (78.7)	97 (52.4)	288 (74.8)	107 (35.3)	<0.001
Income (annual)					<0.001
Less than $20,000	48 (8.9)	74 (40.0)	60 (15.6)	124 (40.9)	
Up to $39,000	128 (23.7)	46 (24.9)	134 (34.8)	112 (37.0)	
Up to $74,999	183 (33.8)	29 (15.7)	134 (34.8)	55 (18.2)	
Greater than $75,000	182 (33.6)	36 (19.5)	57 (14.8)	12 (4.0)	
Distensibility Coefficient at Exam 1 (10^{-3} $mmHg^{-1}$)	3.4 (1.3)	3.1 (1.3)	2.9 (1.2)	3.0 (1.3)	<0.001
Δ Distensibility Coefficient (10^{-3} $mmHg^{-1}$)	-0.47 (1.2)	-0.37 (1.2)	-0.33 (1.1)	-0.33 (1.0)	0.22
Young’s Elastic Modulus at Exam 1 (mmHg)	1388 (874)	1716 (1038)	1607 (969)	1635 (852)	<0.001
Δ Young’s Elastic Modulus (mmHg)	156 (1050)	229 (1677)	242 (1537)	85 (989)	0.39
Carotid wall thickness (cm)	0.071 (0.014)	0.070 (0.013)	0.077 (0.015)	0.071 (0.014)	<0.001
Peak systolic internal diameter (cm)	0.598 (0.061)	0.621 (0.074)	0.603 (0.068)	0.601 (0.059)	<0.001
End-diastolic internal diameter (cm)	0.549 (0.057)	0.577 (0.070)	0.559 (0.065)	0.556 (0.056)	<0.001

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.