

## Supplemental Online Content

Wang W, Zhang MJ, Inciardi RM, et al. Association of echocardiographic measures of left atrial function and size with incident dementia. *JAMA*. doi:10.1001/jama.2022.2518

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

**eTable 1. Visit 1 Participant Characteristics According to Participant Follow-Up Status: The ARIC Study, 1987-1989**

	Attended visit 5 <sup>a</sup> (n=6,538)	Died before visit 5 was complete <sup>b</sup> (n=5,878)	Declined attending visit 5 <sup>c</sup> (n=3,376)
<b>Demographics</b>			
Age, mean (SD), years	52.1 (5.2)	56.8 (5.5)	53.6 (5.6)
Women, No. (%)	3845 (58.8%)	2716 (46.2%)	2149 (63.7%)
Men, No. (%)	2693 (41.2%)	3162 (53.8%)	1227 (36.3%)
Black race, No. (%)	1543 (23.6%)	1855 (31.6%)	868 (25.7%)
White race, No. (%)	4977 (76.1%)	4010 (68.2%)	2491 (73.8%)
Less than high school education, No. (%)	990 (15.1%)	1992 (33.9%)	785 (23.3%)
Current smokers, No. (%)	1170 (17.9%)	2182 (37.1%)	780 (23.1%)
<b>Clinical Characteristics</b>			
Body mass index, median (IQR), kg/m <sup>2</sup>	26.4 (23.8-29.7)	27.4 (24.0-30.5)	26.8 (24.0-30.5)
Systolic blood pressure, median (IQR), mmHg	115.0 (105.0-126.0)	124.0 (112.0-138.0)	118.0 (118.0-130.0)
Antihypertensive medication use, No. (%)	1471 (22.5%)	2406 (40.9%)	961 (28.5%)
Diabetes, No. (%)	386 (5.9%)	1206 (20.5%)	278 (8.2%)
>1 APOE ε4 allele, No. (%)	1830 (28.0%)	1876 (31.9%)	958 (28.4%)
Coronary heart disease, No. (%)	124 (1.9%)	561 (9.5%)	81 (2.4%)
Heart failure, No. (%)	168 (2.6%)	459 (7.8%)	125 (3.7%)
Anticoagulant medication use, No. (%)	14 (0.2%)	66 (1.1%)	9 (0.3%)

<sup>a</sup> Numbers for missing data are 11 for education level, 4 for body mass index, and 1 for systolic blood pressure.

<sup>b</sup> Numbers for missing data are 11 for education level, 15 for body mass index, and 2 for systolic blood pressure.

<sup>c</sup> Numbers for missing data are 5 for education level and 6 for body mass index.

Abbreviations: ARIC = Atherosclerosis Risk in Communities; SD = standard deviation; IQR = interquartile range; APOE = apolipoprotein E

**eTable 2. Baseline Participant Characteristics (Visit 5 Participants Missing LA Function Measures): The ARIC Study, 2011-2013**

	Analytic Study Population (n=4,096)	Visit 5 Participants Missing LA Function Measures <sup>a</sup> (n=850)
<b>Demographics</b>		
Age, mean (SD) years	75.0 (5.0)	75.2 (5.0)
Women, No. (%)	2443 (59.6%)	495 (58.2%)
Men, No. (%)	1653 (40.4%)	355 (41.8%)
Black race, No. (%)	895 (21.9%)	159 (18.7%)
White race, No. (%)	3201 (78.1%)	691 (81.3%)
Less than high school education, No. (%)	504 (12.3%)	90 (10.6%)
Current smokers, No. (%)	228 (5.6%)	53 (6.2%)
<b>Clinical Characteristics</b>		
Body mass index, median (IQR), kg/m <sup>2</sup>	27.7 (24.8-31.1)	28.7 (24.9-32.7)
Systolic blood pressure, median (IQR), mmHg	129.0 (118.0-140.5)	127.5 (117.0-140.0)
Antihypertensive medication use, No. (%)	2938 (71.7%)	645 (75.6%)
Diabetes, No. (%)	1187 (29.0%)	288 (33.8%)
>1 APOE ε4 allele, No. (%)	1119 (27.3%)	220 (25.8%)
Coronary heart disease, No. (%)	520 (12.7%)	124 (14.5%)
Heart failure, No. (%)	368 (9.0%)	90 (10.6%)
Anticoagulant medication use, No. (%)	90 (2.2%)	20 (2.3%)

<sup>a</sup> Numbers for missing data are 1 for education, 1 for systolic blood pressure, and 1 for body mass index.

Abbreviations: ARIC = Atherosclerosis Risk in Communities; SD = standard deviation; IQR = interquartile range; APOE = apolipoprotein E; LA = left atrial

**eTable 3. Baseline Participant Characteristics (Visit 5 Participants Without Echocardiograms): The ARIC Study, 2011-2013**

	Analytic Study Population (n=4,096)	Visit 5 Participants without Echocardiograms <sup>a</sup> (n=420)
<b>Demographics</b>		
Age, mean (SD), years	75.0 (5.0)	79.7 (5.5)
Women, No. (%)	2443 (59.6%)	303 (72.1%)
Men, No. (%)	1653 (40.4%)	117 (27.9%)
Black race, No. (%)	895 (21.9%)	211 (50.2%)
White race, No. (%)	3201 (78.1%)	209 (49.8%)
Less than high school education, No. (%)	504 (12.3%)	157 (37.4%)
Current smokers, No. (%)	228 (5.6%)	14 (3.3%)
<b>Clinical Characteristics</b>		
Body mass index, median (IQR), kg/m <sup>2</sup>	27.7 (24.8-31.1)	29.4 (25.6-35.3)
Systolic blood pressure, median (IQR), mmHg	129.0 (118.0-140.5)	135.0 (122.0-151.0)
Antihypertensive medication use, No. (%)	2938 (71.7%)	365 (86.9%)
Diabetes, No. (%)	1187 (29.0%)	181 (43.1%)
>1 APOE ε4 allele, No. (%)	1119 (27.3%)	143 (34.0%)
Coronary heart disease, No. (%)	520 (12.7%)	98 (23.3%)
Heart failure, No. (%)	368 (9.0%)	132 (31.4%)
Anticoagulant medication use, No. (%)	90 (2.2%)	63 (15.0%)

<sup>a</sup> Numbers for missing data are 1 for education level, 15 for systolic blood pressure, and 235 for body mass index.

Abbreviations: ARIC = Atherosclerosis Risk in Communities; SD = standard deviation; IQR = interquartile range; APOE = apolipoprotein E

**eTable 4. Baseline Participant Characteristics (Visit 5 Participants with Missing Covariates):  
The ARIC Study, 2011-2013**

	Analytic Study Population (n=4,096)	Visit 5 Participants with Missing Covariates <sup>a</sup> (n=228)
<b>Demographics</b>		
Age, mean (SD), years	75.0 (5.0)	76.0 (4.9)
Women, No. (%)	2443 (59.6%)	147 (64.5%)
Men, No. (%)	1653 (40.4%)	81 (35.5%)
Black race, No. (%)	895 (21.9%)	71 (31.1%)
White race, No. (%)	3201 (78.1%)	157 (68.9%)
Less than high school education, No. (%)	504 (12.3%)	50 (21.9%)
Current smokers, No. (%)	228 (5.6%)	19 (8.3%)
<b>Clinical Characteristics</b>		
Body mass index, median (IQR), kg/m <sup>2</sup>	27.7 (24.8-31.1)	30.1 (26.2-35.1)
Systolic blood pressure, median (IQR), mmHg	129.0 (118.0-140.5)	127.0 (117.0-141.5)
Antihypertensive medication use, No. (%)	2938 (71.7%)	192 (84.2%)
Diabetes, No. (%)	1187 (29.0%)	99 (43.4%)
>1 APOE ε4 allele, No. (%)	1119 (27.3%)	57 (25.0%)
Coronary heart disease, No. (%)	520 (12.7%)	30 (13.2%)
Heart failure, No. (%)	368 (9.0%)	33 (14.5%)
Anticoagulant medication use, No. (%)	90 (2.2%)	4 (1.8%)
<b>Echocardiogram Measures</b>		
LA reservoir strain, mean (SD), %	32.8 (7.7)	30.7 (7.8)
LA conduit strain, mean (SD), %	14.9 (5.6)	13.5 (5.4)
LA contractile strain, mean (SD), %	18.0 (5.5)	17.2 (6.1)
LA emptying fraction, mean (SD), %	58.3 (9.3)	56.5 (9.9)
LA passive emptying fraction, mean (SD), %	26.5 (10.4)	25.3 (10.8)
LA active emptying fraction, mean (SD), %	43.1 (10.5)	41.6 (11.3)
Maximal LA volume index, median (IQR), ml/m <sup>2</sup>	32.3 (26.0-39.7)	33.3 (27.0-40.3)
Minimal LA volume index, median (IQR), ml/m <sup>2</sup>	13.0 (9.7-17.7)	13.9 (10.2-19.9)
LV ejection fraction, median (IQR), %	66.1 (62.4-69.5)	63.3 (60.1-68.1)
LV mass index, median (IQR), %	75.2 (65.4-87.3)	77.4 (66.1-91.2)

<sup>a</sup> Numbers for missing data are 9 for education level, 15 for systolic blood pressure, 18 for body mass index, 58 for LA reservoir strain, 58 for LA conduit strain, 58 for LA contractile strain, 80 for LA emptying fraction, 80 for LA passive emptying fraction, 80 for LA active emptying fraction, 89 for maximal LA volume index, 89 for minimal LA volume index, 156 for LV ejection fraction, 51 for LV mass index.

Abbreviations: ARIC = Atherosclerosis Risk in Communities; IQR = interquartile range; APOE = apolipoprotein E; LA = left atrial; LV = left ventricular

**eTable 5. Association of Left Atrial Measures with Incident Dementia Stratified by Race: The ARIC Study, 2011-2019<sup>a</sup>**

	Black Participants (n=895)		White Participants (n=3201)	
	Incidence Rate (per 100PY)	Hazard Ratio (95% Confidence Interval)	Incidence Rate (per 100PY)	Hazard Ratio (95% Confidence Interval)
		Adjusted for age, sex, APOE ε4, education, body mass index, smoking status, diabetes, systolic blood pressure, antihypertensive medications, coronary heart disease, heart failure, anticoagulant use, incident atrial fibrillation incident stroke, LAVImin (for LA function measures only), left ventricular ejection fraction, left ventricular mass index		Adjusted for age, sex, APOE ε4, education, body mass index, smoking status, diabetes, systolic blood pressure, antihypertensive medications, coronary heart disease, heart failure, anticoagulant use, incident atrial fibrillation incident stroke, LAVImin (for LA function measures only), left ventricular ejection fraction, left ventricular mass index
<b>LA Reservoir Strain, %</b>				
<26.72	6.36	2.47 (1.27, 4.80)	4.29	1.91 (1.30, 2.82)
26.73 – 30.59	3.20	1.30 (0.70, 2.43)	1.72	0.86 (0.59, 1.26)
30.60 – 34.41	1.86	0.97 (0.49, 1.92)	1.68	0.96 (0.67, 1.37)
34.42 – 39.40	1.75	0.86 (0.42, 1.76)	1.40	0.92 (0.64, 1.32)
>39.41	1.88	Reference	1.49	Reference
<b>LA Conduit Strain, %</b>				
<9.90	5.43	1.68 (0.90, 3.13)	3.48	1.40 (0.96, 2.04)
9.91 – 13.06	3.31	1.46 (0.79, 2.70)	2.32	1.23 (0.85, 1.79)
13.07 – 15.89	2.53	1.13 (0.59, 2.17)	1.65	1.06 (0.73, 1.55)
15.90 – 19.52	2.17	1.31 (0.67, 2.55)	1.68	1.14 (0.79, 1.64)
>19.53	1.65	Reference	1.19	Reference
<b>LA Contractile Strain, %</b>				
≤13.47	4.99	1.92 (1.05, 3.53)	2.79	1.43 (1.00, 2.04)
13.48 – 16.62	2.32	0.99 (0.54, 1.81)	2.09	1.12 (0.80, 1.58)
16.63 – 19.17	2.27	1.04 (0.57, 1.92)	1.88	1.08 (0.77, 1.52)
19.18 – 22.37	3.13	1.35 (0.76, 2.41)	1.72	1.08 (0.77, 1.44)
>22.38	2.65	Reference	1.64	Reference
<b>LA Emptying Fraction, %</b>				
≤50.92	5.18	1.83 (0.94, 3.56)	3.85	1.85 (1.21, 2.81)
50.93 – 56.58	3.62	1.31 (0.72, 2.39)	1.92	1.10 (0.75, 1.61)
56.59 – 61.28	1.76	0.66 (0.34, 1.28)	1.85	1.26 (0.88, 1.82)
61.29 – 66.17	1.85	0.80 (0.41, 1.58)	1.48	1.11 (0.77, 1.59)
≥66.18	2.40	Reference	1.34	Reference
<b>LA Passive Emptying Fraction, %</b>				
≤17.63	4.73	1.47 (0.78, 2.76)	3.33	1.24 (0.87, 1.77)
17.64 – 23.66	2.95	1.15 (0.61, 2.20)	1.82	0.93 (0.65, 1.34)
23.67 – 28.68	2.73	1.12 (0.60, 2.12)	2.13	1.17 (0.83, 1.64)
28.69 – 35.20	2.65	1.32 (0.68, 2.53)	1.55	0.97 (0.68, 1.39)
>35.20	1.90	Reference	1.41	Reference

	Black Participants (n=895)		White Participants (n=3201)	
	Incidence Rate (per 100PY)	Hazard Ratio (95% Confidence Interval)	Incidence Rate (per 100PY)	Hazard Ratio (95% Confidence Interval)
<b>LA Active Emptying Fraction, %</b>				
<35.15	4.49	1.34 (0.72, 2.52)	2.92	1.38 (0.95, 2.01)
35.16 – 41.05	2.79	1.04 (0.58, 1.86)	2.14	1.15 (0.81, 1.64)
41.06 – 46.07	3.18	0.96 (0.55, 1.67)	1.77	1.01 (0.71, 1.45)
46.09 – 51.88	2.01	0.78 (0.41, 1.48)	1.73	1.04 (0.73, 1.46)
>51.89	2.59	Reference	1.56	Reference
<b>Maximal LA Volume Index, ml/m<sup>2</sup></b>				
<24.69	3.31	Reference	1.88	Reference
24.70 – 29.77	2.47	0.77 (0.44, 1.37)	1.66	0.76 (0.55, 1.07)
29.78 – 34.85	2.90	0.80 (0.47, 1.37)	1.70	0.74 (0.53, 1.04)
34.86 – 41.65	2.50	0.70 (0.40, 1.21)	1.94	0.75 (0.54, 1.05)
>41.66	4.06	0.79 (0.45, 1.36)	2.90	0.83 (0.59, 1.16)
<b>Minimal LA Volume Index, ml/m<sup>2</sup></b>				
<8.96	3.31	Reference	1.48	Reference
8.97 – 11.61	1.55	0.52 (0.27, 1.01)	1.60	0.94 (0.66, 1.33)
11.62 – 14.56	2.61	0.84 (0.48, 1.47)	1.65	0.78 (0.55, 1.11)
14.57 – 19.00	3.11	0.77 (0.45, 1.32)	2.34	1.09 (0.78, 1.53)
>19.01	4.45	0.88 (0.51, 1.52)	3.16	0.99 (0.70, 1.41)

<sup>a</sup> Quintile boundaries are based on the primary analysis. Incidence rates are unadjusted.

Abbreviations: ARIC = Atherosclerosis Risk in Communities; LA = left atrial; PY = person-years; APOE = apolipoprotein E

**eTable 6. Association of Left Atrial Measures with Incident Dementia Stratified by Sex: the ARIC Study, 2011-2019<sup>a</sup>**

	Males (n=1653)		Females (n=2443)	
	Incidence Rate (per 100PY)	Hazard Ratio (95% Confidence Interval)	Incidence Rate (per 100PY)	Hazard Ratio (95% Confidence Interval)
		Adjusted for age, race/center, APOE ε4, education, body mass index, smoking status, diabetes, systolic blood pressure, antihypertensive medications, coronary heart disease, heart failure, anticoagulant use, incident atrial fibrillation incident stroke, LAVImin (for LA function measures only), left ventricular ejection fraction, left ventricular mass index		Adjusted for age, race/center, APOE ε4, education, body mass index, smoking status, diabetes, systolic blood pressure, antihypertensive medications, coronary heart disease, heart failure, anticoagulant use, incident atrial fibrillation incident stroke, LAVImin (for LA function measures only), left ventricular ejection fraction, left ventricular mass index
<b>LA Reservoir Strain, %</b>				
≤26.72	5.39	2.55 (1.51, 4.31)	4.45	1.57 (1.02, 2.42)
26.73 – 30.59	2.21	1.21 (0.73, 2.00)	2.02	0.85 (0.57, 1.28)
30.60 – 34.41	2.15	1.33 (0.81, 2.17)	1.45	0.71 (0.46, 1.07)
34.42 – 39.40	1.37	0.93 (0.55, 1.56)	1.54	0.82 (0.55, 1.24)
≥39.41	1.48	Reference	1.61	Reference
<b>LA Conduit Strain, %</b>				
≤9.90	4.79	2.72 (1.57, 4.72)	3.36	0.98 (0.65, 1.47)
9.91 – 13.06	2.31	1.64 (0.93, 2.87)	2.74	1.12 (0.76, 1.64)
13.07 – 15.89	2.00	1.68 (0.96, 2.94)	1.71	0.81 (0.54, 1.22)
15.90 – 19.52	1.92	1.75 (0.99, 3.06)	1.68	0.89 (0.60, 1.32)
≥19.53	0.98	Reference	1.46	Reference
<b>LA Contractile Strain, %</b>				
≤13.47	3.44	1.64 (1.03, 2.62)	3.20	1.50 (0.99, 2.26)
13.48 – 16.62	2.52	1.09 (0.69, 1.72)	1.95	1.02 (0.69, 1.51)
16.63 – 19.17	2.22	1.17 (0.76, 1.82)	1.79	0.96 (0.64, 1.43)
19.18 – 22.37	1.92	1.06 (0.67, 1.66)	2.06	1.10 (0.75, 1.61)
>22.38	1.90	Reference	1.72	Reference
<b>LA Emptying Fraction, %</b>				
≤50.92	4.36	2.00 (1.16, 3.45)	4.10	1.76 (1.10, 2.82)
50.93 – 56.58	2.79	1.45 (0.88, 2.39)	2.04	1.01 (0.66, 1.55)
56.59 – 61.28	1.96	1.18 (0.72, 1.93)	1.74	0.99 (0.66, 1.51)
61.29 – 66.17	1.47	0.94 (0.57, 1.56)	1.61	1.07 (0.70, 1.62)
>66.18	1.58	Reference	1.45	Reference
<b>LA Passive Emptying Fraction, %</b>				
≤17.63	3.58	1.36 (0.83, 2.22)	3.73	1.17 (0.79, 1.72)
17.64 – 23.66	2.39	1.32 (0.81, 2.17)	1.82	0.77 (0.51, 1.16)
23.67 – 28.68	2.25	1.18 (0.72, 1.95)	2.29	1.15 (0.79, 1.68)
28.69 – 35.20	1.94	1.16 (0.69, 1.94)	1.66	0.94 (0.63, 1.40)
>35.20	1.45	Reference	1.50	Reference



	Males (n=1653)		Females (n=2443)	
	Incidence Rate (per 100PY)	Hazard Ratio (95% Confidence Interval)	Incidence Rate (per 100PY)	Hazard Ratio (95% Confidence Interval)
<b>LA Active Emptying Fraction, %</b>				
<35.15	3.47	1.44 (0.87, 2.37)	3.17	1.37 (0.90, 2.09)
35.16 – 41.05	2.49	1.21 (0.76, 1.91)	2.15	1.05 (0.70, 1.57)
41.06 – 46.07	2.33	1.12 (0.71, 1.76)	1.96	0.98 (0.66, 1.46)
46.09 – 51.88	1.91	1.05 (0.66, 1.66)	1.69	0.91 (0.60, 1.36)
>51.89	1.79	Reference	1.70	Reference
<b>Maximal LA Volume Index, ml/m<sup>2</sup></b>				
<24.69	2.20	Reference	2.07	Reference
24.70 – 29.77	2.02	0.77 (0.49, 1.21)	1.66	0.72 (0.49, 1.05)
29.78 – 34.85	1.93	0.79 (0.50, 1.25)	1.99	0.71 (0.49, 1.02)
34.86 – 41.65	2.32	0.84 (0.54, 1.33)	1.93	0.62 (0.43, 0.90)
>41.66	3.18	0.82 (0.52, 1.29)	3.18	0.72 (0.49, 1.04)
<b>Minimal LA Volume Index, ml/m<sup>2</sup></b>				
<8.96	1.96	Reference	1.64	Reference
8.97 – 11.61	1.53	0.85 (0.52, 1.39)	1.63	0.87 (0.58, 1.29)
11.62 – 14.56	2.01	0.89 (0.56, 1.40)	1.76	0.75 (0.51, 1.11)
14.57 – 19.00	2.43	1.04 (0.66, 1.63)	2.58	0.94 (0.65, 1.37)
>19.01	3.89	1.06 (0.67, 1.67)	3.22	0.85 (0.57, 1.25)

<sup>a</sup> Quintile boundaries are based on primary analysis. Incidence rates are unadjusted.

Abbreviations: ARIC = Atherosclerosis Risk in Communities; LA = left atrial; PY = person-years; APOE = apolipoprotein E

**eTable 7. Hazard Ratios for Dementia by Different Left Atrial Reservoir Strain Cutoffs: The ARIC Study, 2011-2019**

	No. dementia events / No. total	Hazard Ratio (95% Confidence Interval)	P value
		Adjusted for age, sex, race/center, APOE ε4, education, body mass index, smoking status, diabetes, systolic blood pressure, antihypertensive medications, coronary heart disease, heart failure, anticoagulant use, incident atrial fibrillation and incident stroke, LAVI <sub>min</sub> , left ventricular ejection fraction, left ventricular mass index	
Cutoff 1			
LA Reservoir <22%	78 / 311	1.69 (1.24, 2.30)	0.001
LA Reservoir ≥22%	453 / 3785	Reference	
Cutoff 2			
LA Reservoir <23%	96 / 375	1.91 (1.44, 2.55)	<0.001
LA Reservoir ≥23%	435 / 3721	Reference	
Cutoff 3			
LA Reservoir <24%	112 / 453	1.98 (1.52, 2.59)	<0.001
LA Reservoir ≥24%	419 / 3643	Reference	
Cutoff 4			
LA Reservoir <25%	134 / 558	2.08 (1.62, 2.68)	<0.001
LA Reservoir ≥25%	397 / 3538	Reference	
Cutoff 5			
LA Reservoir <26%	157 / 686	2.00 (1.57, 2.54)	<0.001
LA Reservoir ≥26%	374 / 3410	Reference	
Cutoff 6			
LA Reservoir <27%	199 / 864	2.10 (1.68, 2.61)	<0.001
LA Reservoir ≥27%	332 / 3232	Reference	
Cutoff 7			
LA Reservoir <28%	224 / 1071	1.80 (1.45, 2.24)	<0.001
LA Reservoir ≥28%	307 / 3025	Reference	
Cutoff 8			
LA Reservoir <29%	255 / 1271	1.80 (1.46, 2.22)	<0.001
LA Reservoir ≥29%	276 / 2825	Reference	
Cutoff 9			
LA Reservoir <30%	281 / 1485	1.63 (1.33, 2.00)	<0.001
LA Reservoir ≥30%	250 / 2611	Reference	
Cutoff 10			
LA Reservoir <31%	299 / 1719	1.41 (1.15, 1.72)	0.001
LA Reservoir ≥31%	232 / 2377	Reference	
Cutoff 11			

	<b>No. dementia events / No. total</b>	<b>Hazard Ratio (95% Confidence Interval)</b>	<b>P value</b>
LA Reservoir <32%	329 / 1945	1.41 (1.15, 1.73)	0.001
LA Reservoir ≥32%	202 / 2151	Reference	
Cutoff 12			
LA Reservoir <33%	350 / 2173	1.32 (1.08, 1.62)	0.008
LA Reservoir ≥33%	181 / 1923	Reference	
Cutoff 13			
LA Reservoir <34%	369 / 2376	1.23 (0.99, 1.51)	0.06
LA Reservoir ≥34%	162 / 1720	Reference	

Abbreviations: ARIC = Atherosclerosis Risk in Communities; LA = left atrial; APOE = apolipoprotein E

**eTable 8. Baseline Participant Characteristics (by Left Atrial Reservoir Strain <27% vs. ≥27%): The ARIC Study, 2011-2013<sup>a</sup>**

	LA Reservoir <27% (n=864)	LA Reservoir ≥27% (n=3,232)
<b>Demographics</b>		
Age, mean (SD), years	76.8 (5.3)	74.6 (4.7)
Women, No. (%)	527 (61.0%)	1916 (59.3%)
Men, No. (%)	337 (39.0%)	1316 (40.7%)
Black race, No. (%)	232 (26.9%)	663 (20.5%)
White race, No. (%)	632 (73.1%)	2569 (79.5%)
Less than high school education, No. (%)	155 (17.9%)	349 (10.8%)
Current smokers, No. (%)	46 (5.3%)	182 (5.6%)
<b>Clinical Characteristics</b>		
Body mass index, median (IQR), kg/m <sup>2</sup>	28.2 (25.1-31.9)	27.6 (24.8-31.0)
Systolic blood pressure, median (IQR), mmHg	131.5 (119.5-144.0)	128.5 (117.5-139.5)
Antihypertensive medication use, No. (%)	710 (82.2%)	2228 (68.9%)
Diabetes, No. (%)	323 (37.4%)	864 (26.7%)
>1 APOE ε4 allele, No. (%)	239 (27.7%)	880 (27.2%)
Coronary heart disease, No. (%)	187 (21.6%)	333 (10.3%)
Heart failure, No. (%)	179 (20.7%)	189 (5.8%)
Anticoagulant medication use, No. (%)	25 (2.9%)	65 (2.0%)
<b>Echocardiogram Measures</b>		
LA reservoir strain, mean (SD), %	22.5 (4.0)	35.5 (5.9)
LA conduit strain, mean (SD), %	9.8 (3.9)	16.2 (5.3)
LA contractile strain, mean (SD), %	12.8 (4.3)	19.3 (5.0)
LA emptying fraction, mean (SD), %	47.4 (8.2)	61.2 (7.2)
LA passive emptying fraction, mean (SD), %	19.9 (9.2)	28.3 (9.9)
LA active emptying fraction, mean (SD), %	33.9 (10.3)	45.6 (9.1)
Maximal LA volume index, median (IQR), ml/m <sup>2</sup>	39.5 (31.1-47.8)	30.8 (25.2-37.5)
Minimal LA volume index, median (IQR), ml/m <sup>2</sup>	20.3 (15.5-26.3)	11.9 (9.0-15.4)
LV ejection fraction, median (IQR), %	64.3 (59.8-68.5)	66.5 (63.1-69.7)
LV mass index, median (IQR), %	83.7 (72.2-101.3)	73.5 (64.2-84.5)

<sup>a</sup> Restricted to the analytic sample, which required participants to have an echocardiogram completed at visit 5 (2011-2013) and to not meet any exclusion criteria.

Abbreviations: ARIC = Atherosclerosis Risk in Communities; SD = standard deviation; IQR = interquartile range; APOE = apolipoprotein E; LA = left atrial; LV = left ventricular

**eTable 9. Association of Left Atrial Reservoir Strain (Binary Variable) with Incident Dementia: The ARIC Study, 2011-2019**

	Incidence Rate (per 100 PY)	Hazard Ratio (95% Confidence Interval)		
		Model 1: age, sex, race/center, APOE ε4, education, body mass index, smoking status, diabetes, systolic blood pressure, antihypertensive medications, coronary heart disease, heart failure, anticoagulant use	Model 2: adjusted for model 1 plus incident atrial fibrillation, incident stroke	Model 3: adjusted for model 2 plus LAVI <sub>min</sub> , left ventricular ejection fraction, left ventricular mass index
LA Reservoir Strain <27% (n=864)	4.72	2.21 (1.84, 2.67)	2.14 (1.77, 2.59)	2.10 (1.68, 2.61)
LA Reservoir Strain ≥27% (n=3,232)	1.68	Reference	Reference	Reference

Abbreviations: ARIC = Atherosclerosis Risk in Communities; LA = left atrial; PY = person-years; APOE = apolipoprotein E

**eTable 10. Brain MRI Measures (2011-13) Among Participants with Left Atrial Reservoir Strain <27%, Stratified by Dementia**

	<b>Dementia<sup>a</sup> (n=81)</b>	<b>No dementia (n=202)</b>	<b>P value</b>
White matter hyperintensity volume, mean (SD), cm <sup>3</sup>	23.4 (18.1)	19.2 (20.4)	0.11
Lacunar infarcts, No. (%)	21 (25.9%)	34 (16.8%)	0.08
Cortical infarcts, No. (%)	11 (13.6%)	23 (11.4%)	0.66
Any infarcts, No. (%)	29 (35.8%)	49 (24.3%)	0.04
Cerebral microbleeds, No. (%)	30 (37.0%)	63 (31.2%)	0.34

<sup>a</sup> Dementia was ascertained through 2019.

**eTable 11. Hazard Ratios for Dementia Among Participants Without Incident Atrial Fibrillation or Stroke: The ARIC Study, 2011-2019 (n=3,466)<sup>a</sup>**

		Hazard Ratio (95% Confidence Interval)	
	Incidence Rate (per 100PY)	Model 1: adjusted for age, sex, race/center, APOE ε4, education, body mass index, smoking status, diabetes, systolic blood pressure, antihypertensive medications, coronary heart disease, heart failure	Model 2: adjusted for model 1 plus left ventricular ejection fraction, left ventricular mass index
<b>LA Reservoir Strain, %</b>			
<26.72	4.16	2.08 (1.51, 2.86)	2.29 (1.55, 3.38)
26.73 – 30.59	1.76	0.98 (0.70, 1.37)	1.04 (0.73, 1.50)
30.60 – 34.41	1.59	0.95 (0.68, 1.34)	1.00 (0.70, 1.42)
34.42 – 39.40	1.37	0.90 (0.64, 1.28)	0.93 (0.65, 1.32)
>39.41	1.41	Reference	Reference
<b>LA Conduit Strain, %</b>			
≤9.90	3.16	1.56 (1.11, 2.18)	1.37 (0.96, 1.97)
9.91 – 13.06	2.14	1.32 (0.94, 1.87)	1.23 (0.86, 1.76)
13.07 – 15.89	1.70	1.08 (0.76, 1.54)	1.04 (0.73, 1.49)
15.90 – 19.52	1.56	1.09 (0.77, 1.54)	1.07 (0.75, 1.52)
≥19.53	1.24	Reference	Reference
<b>LA Contractile Strain, %</b>			
≤13.47	2.84	1.77 (1.29, 2.43)	1.75 (1.24, 2.48)
13.48 – 16.62	1.85	1.20 (0.86, 1.67)	1.20 (0.86, 1.68)
16.63 – 19.17	1.62	1.02 (0.73, 1.42)	1.02 (0.72, 1.43)
19.18 – 22.37	1.76	1.13 (0.82, 1.56)	1.12 (0.81, 1.56)
≥22.38	1.58	Reference	Reference
<b>LA Emptying Fraction, %</b>			
≤50.92	3.48	1.77 (1.28, 2.45)	2.06 (1.36, 3.13)
50.93 – 56.58	2.03	1.18 (0.84, 1.64)	1.28 (0.88, 1.86)
56.59 – 61.28	1.63	1.04 (0.74, 1.47)	1.11 (0.77, 1.59)
61.29 – 66.17	1.43	1.03 (0.73, 1.47)	1.06 (0.74, 1.52)
≥66.18	1.35	Reference	Reference
<b>LA Passive Emptying Fraction, %</b>			
≤17.63	3.01	1.42 (1.02, 1.97)	1.30 (0.91, 1.84)
17.64 – 23.66	1.68	0.96 (0.67, 1.37)	0.91 (0.63, 1.31)
23.67 – 28.68	2.04	1.23 (0.88, 1.71)	1.19 (0.85, 1.66)
28.69 – 35.20	1.55	0.98 (0.69, 1.39)	0.96 (0.68, 1.37)
≥35.20	1.36	Reference	Reference
<b>LA Active Emptying Fraction, %</b>			
<35.15	2.77	1.55 (1.12, 2.13)	1.59 (1.09, 2.30)
35.16 – 41.05	1.93	1.21 (0.87, 1.68)	1.22 (0.85, 1.73)
41.06 – 46.07	1.80	1.03 (0.74, 1.42)	1.03 (0.74, 1.46)
46.09 – 51.88	1.56	0.98 (0.70, 1.37)	0.98 (0.70, 1.38)

	Incidence Rate (per 100PY)	Hazard Ratio (95% Confidence Interval)	
		Model 1: adjusted for age, sex, race/center, APOE ε4, education, body mass index, smoking status, diabetes, systolic blood pressure, antihypertensive medications, coronary heart disease, heart failure	Model 2: adjusted for model 1 plus left ventricular ejection fraction, left ventricular mass index
>51.89	1.56	Reference	Reference
<b>Maximal LA Volume Index, ml/m<sup>2</sup></b>			
≤24.69	1.90	Reference	Reference
24.70 – 29.77	1.77	0.84 (0.61, 1.14)	0.81 (0.60, 1.11)
29.78 – 34.85	1.70	0.77 (0.56, 1.06)	0.75 (0.54, 1.03)
34.86 – 41.65	1.69	0.75 (0.54, 1.04)	0.71 (0.51, 0.99)
≥41.66	2.50	0.93 (0.67, 1.27)	0.84 (0.60, 1.17)
<b>Minimal LA Volume Index, ml/m<sup>2</sup></b>			
≤8.96	1.59	Reference	Reference
8.97 – 11.61	1.56	0.95 (0.68, 1.32)	0.92 (0.66, 1.28)
11.62 – 14.56	1.62	0.84 (0.60, 1.18)	0.81 (0.58, 1.13)
14.57 – 19.00	2.19	1.06 (0.77, 1.45)	0.99 (0.71, 1.36)
≥19.01	2.74	1.13 (0.81, 1.58)	1.01 (0.71, 1.43)

<sup>a</sup> Quintile boundaries are based on the primary analysis. Incidence rates are unadjusted.

Abbreviations: ARIC = Atherosclerosis Risk in Communities; LA = left atrial; PY = person-years; APOE = apolipoprotein E



**eTable 12. Hazard Ratios for Incident Dementia Among Participants Not Taking Anticoagulants: The ARIC Study, 2011-2019 (n=4,006)<sup>a</sup>**

		Hazard Ratio (95% Confidence Interval)		
	Incidence Rate (per 100PY)	Model 1: adjusted for age, sex, race/center, APOE ε4, education, body mass index, smoking status, diabetes, systolic blood pressure, antihypertensive medications, coronary heart disease, heart failure	Model 2: adjusted for model 1 plus incident atrial fibrillation, incident stroke	Model 3: adjusted for model 2 plus LAVI <sub>min</sub> (for LA function measures only), left ventricular ejection fraction, left ventricular mass index
<b>LA Reservoir Strain, %</b>				
<26.72	4.74	2.03 (1.53, 2.69)	1.94 (1.47, 2.58)	1.90 (1.36, 2.65)
26.73 – 30.59	2.12	1.02 (0.76, 1.38)	0.99 (0.74, 1.34)	1.00 (0.73, 1.37)
30.60 – 34.41	1.69	0.90 (0.66, 1.22)	0.89 (0.65, 1.21)	0.90 (0.65, 1.23)
34.42 – 39.40	1.47	0.86 (0.63, 1.19)	0.86 (0.62, 1.18)	0.86 (0.63, 1.19)
>39.41	1.58	Reference	Reference	Reference
<b>LA Conduit Strain, %</b>				
<9.90	3.89	1.79 (1.33, 2.42)	1.74 (1.28, 2.35)	1.48 (1.07, 2.04)
9.91 – 13.06	2.57	1.47 (1.08, 2.00)	1.40 (1.03, 1.92)	1.31 (0.95, 1.79)
13.07 – 15.89	1.86	1.16 (0.84, 1.61)	1.15 (0.83, 1.60)	1.11 (0.80, 1.54)
15.90 – 19.52	1.76	1.18 (0.86, 1.64)	1.19 (0.86, 1.64)	1.17 (0.85, 1.62)
>19.53	1.27	Reference	Reference	Reference
<b>LA Contractile Strain, %</b>				
<13.47	3.24	1.72 (1.30, 2.26)	1.67 (1.26, 2.20)	1.53 (1.12, 2.08)
13.48 – 16.62	2.12	1.13 (0.85, 1.51)	1.08 (0.80, 1.44)	1.03 (0.77, 1.39)
16.63 – 19.17	1.93	1.08 (0.81, 1.46)	1.09 (0.81, 1.46)	1.05 (0.78, 1.41)
19.18 – 22.37	2.04	1.16 (0.87, 1.55)	1.13 (0.85, 1.52)	1.10 (0.82, 1.48)
>22.38	1.82	Reference	Reference	Reference
<b>LA Emptying Fraction, %</b>				
<50.92	4.17	1.86 (1.40, 2.47)	1.77 (1.34, 2.36)	1.85 (1.29, 2.64)
50.93 – 56.58	2.33	1.19 (0.88, 1.60)	1.17 (0.87, 1.58)	1.20 (0.87, 1.65)
56.59 – 61.28	1.82	1.08 (0.79, 1.47)	1.07 (0.79, 1.46)	1.09 (0.79, 1.50)
61.29 – 66.17	1.56	1.02 (0.74, 1.41)	1.02 (0.74, 1.40)	1.03 (0.75, 1.42)
>66.18	1.50	Reference	Reference	Reference
<b>LA Passive Emptying Fraction, %</b>				
<17.63	3.63	1.49 (1.12, 1.99)	1.44 (1.08, 1.93)	1.27 (0.93, 1.73)
17.64 – 23.66	2.09	1.07 (0.78, 1.45)	1.06 (0.78, 1.44)	0.99 (0.73, 1.37)
23.67 – 28.68	2.28	1.25 (0.93, 1.69)	1.24 (0.92, 1.67)	1.17 (0.86, 1.59)
28.69 – 35.20	1.77	1.05 (0.77, 1.44)	1.06 (0.78, 1.45)	1.05 (0.76, 1.43)
>35.20	1.47	Reference	Reference	Reference
<b>LA Active Emptying Fraction, %</b>				

		Hazard Ratio (95% Confidence Interval)		
	Incidence Rate (per 100PY)	Model 1: adjusted for age, sex, race/center, APOE ε4, education, body mass index, smoking status, diabetes, systolic blood pressure, antihypertensive medications, coronary heart disease, heart failure	Model 2: adjusted for model 1 plus incident atrial fibrillation, incident stroke	Model 3: adjusted for model 2 plus LAVI <sub>min</sub> (for LA function measures only), left ventricular ejection fraction, left ventricular mass index
<35.15	3.24	1.56 (1.18, 2.05)	1.50 (1.14, 1.98)	1.41 (1.02, 1.95)
35.16 – 41.05	2.26	1.22 (0.92, 1.63)	1.17 (0.88, 1.57)	1.11 (0.81, 1.51)
41.06 – 46.07	2.15	1.12 (0.84, 1.50)	1.12 (0.84, 1.50)	1.07 (0.79, 1.44)
46.09 – 51.88	1.76	0.99 (0.73, 1.34)	0.99 (0.73, 1.34)	0.98 (0.72, 1.33)
>51.89	1.72	Reference	Reference	Reference
<b>Maximal LA Volume Index, ml/m<sup>2</sup></b>				
<24.69	2.10	Reference	Reference	Reference
24.70 – 29.77	1.79	0.75 (0.56, 0.99)	0.77 (0.57, 1.02)	0.74 (0.55, 0.99)
29.78 – 34.85	1.97	0.80 (0.60, 1.06)	0.82 (0.61, 1.09)	0.77 (0.58, 1.02)
34.86 – 41.65	2.10	0.80 (0.60, 1.06)	0.80 (0.60, 1.23)	0.72 (0.54, 0.96)
>41.66	3.14	0.98 (0.74, 1.28)	0.94 (0.71, 1.23)	0.76 (0.57, 1.02)
<b>Minimal LA Volume Index, ml/m<sup>2</sup></b>				
<8.96	1.76	Reference	Reference	Reference
8.97 – 11.61	1.59	0.87 (0.64, 1.18)	0.89 (0.65, 1.21)	0.86 (0.63, 1.17)
11.62 – 14.56	1.87	0.87 (0.65, 1.17)	0.89 (0.66, 1.19)	0.83 (0.62, 1.13)
14.57 – 19.00	2.53	1.08 (0.81, 1.43)	1.09 (0.82, 1.45)	0.98 (0.74, 1.31)
>19.01	3.46	1.22 (0.93, 1.62)	1.17 (0.88, 1.55)	0.94 (0.70, 1.26)

<sup>a</sup> Quintile boundaries are based on the primary analysis. Incidence rates are unadjusted.

Abbreviations: ARIC = Atherosclerosis Risk in Communities; LA = left atrial; PY = person-years; APOE = apolipoprotein E

**eTable 13. Hazard Ratios for Incident Dementia Among Participants Without Valvular Heart Disease<sup>a</sup>: The ARIC Study, 2011-2019 (n=3,973)<sup>b</sup>**

		Hazard Ratio (95% Confidence Interval)		
	Incidence Rate (per 100PY)	Model 1: adjusted for age, sex, race/center, APOE ε4, education, body mass index, smoking status, diabetes, systolic blood pressure, antihypertensive medications, coronary heart disease, heart failure, anticoagulant use	Model 2: adjusted for model 1 plus incident atrial fibrillation and incident stroke	Model 3: adjusted for model 2 plus LAVI <sub>min</sub> (for LA function measures only), left ventricular ejection fraction, left ventricular mass index
<b>LA Reservoir Strain, %</b>				
≤26.72	4.83	2.12 (1.59, 2.81)	2.01 (1.51, 2.68)	1.99 (1.42, 2.78)
26.73 – 30.59	2.05	1.00 (0.74, 1.36)	0.98 (0.72, 1.33)	0.99 (0.72, 1.36)
30.60 – 34.41	1.73	0.94 (0.69, 1.29)	0.93 (0.68, 1.27)	0.95 (0.69, 1.30)
34.42 – 39.40	1.45	0.87 (0.63, 1.20)	0.87 (0.63, 1.20)	0.87 (0.63, 1.21)
≥39.41	1.54	Reference	Reference	Reference
<b>LA Conduit Strain, %</b>				
<9.90	3.94	1.80 (1.33, 2.44)	1.75 (1.29, 2.37)	1.51 (1.09, 2.08)
9.91 – 13.06	2.51	1.41 (1.03, 1.93)	1.35 (0.98, 1.85)	1.25 (0.91, 1.72)
13.07 – 15.89	1.82	1.12 (0.81, 1.55)	1.12 (0.80, 1.55)	1.07 (0.77, 1.49)
15.90 – 19.52	1.77	1.17 (0.85, 1.62)	1.17 (0.85, 1.62)	1.16 (0.84, 1.60)
>19.53	1.27	Reference	Reference	Reference
<b>LA Contractile Strain, %</b>				
<13.47	3.29	1.79 (1.35, 2.36)	1.72 (1.30, 2.27)	1.59 (1.16, 2.17)
13.48 – 16.62	2.17	1.18 (0.88, 1.58)	1.12 (0.83, 1.49)	1.07 (0.80, 1.45)
16.63 – 19.17	1.88	1.09 (0.81, 1.48)	1.09 (0.81, 1.47)	1.05 (0.78, 1.43)
19.18 – 22.37	2.01	1.17 (0.88, 1.57)	1.15 (0.86, 1.54)	1.12 (0.83, 1.50)
>22.38	1.77	Reference	Reference	Reference
<b>LA Emptying Fraction, %</b>				
<50.92	4.19	1.93 (1.45, 2.56)	1.84 (1.38, 2.45)	1.95 (1.36, 2.79)
50.93 – 56.58	2.32	1.23 (0.91, 1.66)	1.21 (0.90, 1.64)	1.24 (0.90, 1.72)
56.59 – 61.28	1.82	1.11 (0.81, 1.51)	1.10 (0.81, 1.50)	1.12 (0.81, 1.55)
61.29 – 66.17	1.56	1.07 (0.77, 1.47)	1.07 (0.77, 1.47)	1.07 (0.77, 1.48)
>66.18	1.46	Reference	Reference	Reference
<b>LA Passive Emptying Fraction, %</b>				
<17.63	3.64	1.46 (1.10, 1.96)	1.43 (1.07, 1.91)	1.27 (0.93, 1.72)
17.64 – 23.66	2.04	1.01 (0.74, 1.38)	1.01 (0.74, 1.38)	0.95 (0.69, 1.31)
23.67 – 28.68	2.26	1.20 (0.89, 1.62)	1.20 (0.89, 1.62)	1.14 (0.84, 1.55)
28.69 – 35.20	1.72	1.00 (0.73, 1.37)	1.01 (0.74, 1.39)	0.99 (0.73, 1.37)
≥35.20	1.49	Reference	Reference	Reference
<b>LA Active Emptying Fraction, %</b>				
<35.15	3.27	1.61 (1.22, 2.13)	1.55 (1.17, 2.05)	1.48 (1.07, 2.05)
35.16 – 41.05	2.25	1.26 (0.94, 1.68)	1.21 (0.90, 1.62)	1.16 (0.85, 1.58)

	Incidence Rate (per 100PY)	Hazard Ratio (95% Confidence Interval)		
		Model 1: adjusted for age, sex, race/center, APOE ε4, education, body mass index, smoking status, diabetes, systolic blood pressure, antihypertensive medications, coronary heart disease, heart failure, anticoagulant use	Model 2: adjusted for model 1 plus incident atrial fibrillation and incident stroke	Model 3: adjusted for model 2 plus LAVI <sub>min</sub> (for LA function measures only), left ventricular ejection fraction, left ventricular mass index
41.06 – 46.07	2.14	1.15 (0.86, 1.54)	1.14 (0.85, 1.53)	1.09 (0.81, 1.48)
46.09 – 51.88	1.75	1.01 (0.74, 1.36)	1.02 (0.75, 1.38)	1.01 (0.74, 1.37)
>51.89	1.70	Reference	Reference	Reference
<b>Maximal LA Volume Index, ml/m<sup>2</sup></b>				
<24.69	2.14	Reference	Reference	Reference
24.70 – 29.77	1.79	0.73 (0.55, 0.98)	0.75 (0.56, 0.99)	0.72 (0.54, 0.96)
29.78 – 34.85	1.94	0.76 (0.57, 1.01)	0.78 (0.58, 1.03)	0.73 (0.55, 0.98)
34.86 – 41.65	2.09	0.77 (0.58, 1.02)	0.77 (0.58, 1.02)	0.69 (0.52, 0.92)
>41.66	3.10	0.93 (0.71, 1.23)	0.89 (0.68, 1.18)	0.73 (0.55, 0.98)
<b>Minimal LA Volume Index, ml/m<sup>2</sup></b>				
<8.96	1.77	Reference	Reference	Reference
8.97 – 11.61	1.58	0.85 (0.62, 1.16)	0.87 (0.64, 1.18)	0.84 (0.62, 1.14)
11.62 – 14.56	1.84	0.83 (0.62, 1.12)	0.85 (0.63, 1.14)	0.80 (0.59, 1.08)
14.57 – 19.00	2.54	1.06 (0.80, 1.41)	1.08 (0.81, 1.43)	0.97 (0.73, 1.30)
>19.01	3.44	1.20 (0.90, 1.59)	1.13 (0.85, 1.50)	0.93 (0.67, 1.25)

<sup>a</sup> Participants with moderate to severe valvular heart disease were excluded from this analysis.

<sup>b</sup> Quintile boundaries are based on the primary analysis. Incidence rates are unadjusted.

Abbreviations: ARIC = Atherosclerosis Risk in Communities; LA = left atrial; PY = person-years; APOE = apolipoprotein E

**eTable 14. Competing Risk<sup>a</sup> Subdistribution Hazard Models for Incident Dementia: The ARIC Study, 2011-2019 (n=4,096)<sup>b</sup>**

		Hazard Ratio (95% Confidence Interval)		
	Incidence Rate (per 100PY)	Model 1: adjusted for age, sex, race/center, APOE ε4, education, body mass index, smoking status, diabetes, systolic blood pressure, antihypertensive medications, coronary heart disease, heart failure, anticoagulant use	Model 2: adjusted for model 1 plus incident atrial fibrillation and incident stroke	Model 3: adjusted for model 2 plus LAVI <sub>min</sub> (for LA function measures only), left ventricular ejection fraction, left ventricular mass index
<b>LA Reservoir Strain, %</b>				
<26.72	4.80	1.54 (1.16, 2.05)	1.52 (1.14, 2.02)	1.51 (1.07, 2.14)
26.73 – 30.59	2.09	0.99 (0.74, 1.32)	0.96 (0.71, 1.28)	0.97 (0.71, 1.31)
30.60 – 34.41	1.72	0.91 (0.67, 1.23)	0.90 (0.66, 1.21)	0.91 (0.67, 1.24)
34.42 – 39.40	1.46	0.86 (0.63, 1.18)	0.85 (0.62, 1.16)	0.85 (0.62, 1.17)
>39.41	1.55	Reference	Reference	Reference
<b>LA Conduit Strain, %</b>				
<9.90	3.94	1.49 (1.10, 2.01)	1.47 (1.08, 1.98)	1.32 (0.96, 1.83)
9.91 – 13.06	2.57	1.35 (0.99, 1.82)	1.31 (0.97, 1.76)	1.25 (0.92, 1.70)
13.07 – 15.89	1.82	1.05 (0.76, 1.46)	1.05 (0.76, 1.45)	1.01 (0.73, 1.40)
15.90 – 19.52	1.77	1.22 (0.89, 1.68)	1.22 (0.89, 1.68)	1.20 (0.87, 1.66)
>19.53	1.28	Reference	Reference	Reference
<b>LA Contractile Strain, %</b>				
<13.47	3.29	1.43 (1.08, 1.88)	1.41 (1.07, 1.87)	1.35 (0.98, 1.86)
13.48 – 16.62	2.14	1.07 (0.79, 1.43)	1.04 (0.77, 1.40)	1.03 (0.76, 1.39)
16.63 – 19.17	1.96	1.06 (0.79, 1.41)	1.05 (0.79, 1.41)	1.04 (0.78, 1.40)
19.18 – 22.37	2.02	1.16 (0.87, 1.54)	1.14 (0.85, 1.52)	1.13 (0.85, 1.51)
>22.38	1.80	Reference	Reference	Reference
<b>LA Emptying Fraction, %</b>				
<50.92	4.20	1.60 (1.20, 2.14)	1.57 (1.18, 2.10)	1.79 (1.23, 2.62)
50.93 – 56.58	2.32	1.14 (0.85, 1.52)	1.12 (0.83, 1.50)	1.20 (0.87, 1.66)
56.59 – 61.28	1.83	1.06 (0.78, 1.45)	1.06 (0.78, 1.43)	1.11 (0.81, 1.52)
61.29 – 66.17	1.55	0.99 (0.73, 1.37)	0.99 (0.72, 1.35)	1.01 (0.73, 1.39)
>66.18	1.5	Reference	Reference	Reference
<b>LA Passive Emptying Fraction, %</b>				
<17.63	3.67	1.32 (0.99, 1.77)	1.31 (0.98, 1.75)	1.21 (0.89, 1.65)
17.64 – 23.66	2.06	0.97 (0.72, 1.32)	0.98 (0.72, 1.32)	0.95 (0.69, 1.29)
23.67 – 28.68	2.27	1.22 (0.91, 1.63)	1.22 (0.91, 1.64)	1.19 (0.89, 1.60)
28.69 – 35.20	1.77	0.99 (0.72, 1.35)	0.99 (0.73, 1.36)	0.98 (0.72, 1.34)
>35.20	1.49	Reference	Reference	Reference
<b>LA Active Emptying Fraction, %</b>				

<35.15	3.27	1.36 (1.03, 1.79)	1.34 (1.02, 1.78)	1.33 (0.96, 1.85)
35.16 – 41.05	2.28	1.15 (0.86, 1.53)	1.12 (0.84, 1.49)	1.12 (0.83, 1.52)
41.06 – 46.07	2.11	1.11 (0.84, 1.47)	1.10 (0.83, 1.46)	1.10 (0.82, 1.47)
46.09 – 51.88	1.78	0.96 (0.71, 1.30)	0.97 (0.72, 1.31)	0.97 (0.72, 1.32)
>51.89	1.74	Reference	Reference	Reference
<b>Maximal LA Volume Index, ml/m<sup>2</sup></b>				
<24.69	2.12	Reference	Reference	Reference
24.70 – 29.77	1.80	0.75 (0.56, 0.99)	0.76 (0.57, 1.02)	0.74 (0.55, 0.99)
29.78 – 34.85	1.96	0.79 (0.59, 1.05)	0.81 (0.61, 1.07)	0.77 (0.58, 1.03)
34.86 – 41.65	2.07	0.78 (0.59, 1.04)	0.78 (0.59, 1.04)	0.73 (0.55, 0.98)
>41.66	3.18	0.91 (0.68, 1.20)	0.90 (0.68, 1.19)	0.77 (0.57, 1.03)
<b>Minimal LA Volume Index, ml/m<sup>2</sup></b>				
<8.96	1.76	Reference	Reference	Reference
8.97 – 11.61	1.59	0.84 (0.62, 1.15)	0.86 (0.64, 1.17)	0.84 (0.62, 1.14)
11.62 – 14.56	1.86	0.86 (0.64, 1.15)	0.87 (0.65, 1.17)	0.84 (0.63, 1.13)
14.57 – 19.00	2.52	1.08 (0.82, 1.43)	1.09 (0.82, 1.44)	1.02 (0.77, 1.35)
>19.01	3.50	1.09 (0.82, 1.44)	1.07 (0.80, 1.42)	0.93 (0.69, 1.24)

<sup>a</sup> Competing risk of death

<sup>b</sup> Quintile boundaries are based on the primary analysis. Incidence rates are unadjusted.

Abbreviations: ARIC = Atherosclerosis Risk in Communities; LA = left atrial; PY = person-years; APOE = apolipoprotein E

**eTable 15. Hazard Ratios for Incident Dementia Among Participants with CRP Measures: the ARIC Study, 2011-2019 (n=4,057)<sup>a</sup>**

		Hazard Ratio (95% Confidence Interval)		
	Incidence Rate (per 100PY)	Model 1: adjusted for age, sex, race/center, APOE ε4, education, body mass index, smoking status, diabetes, systolic blood pressure, antihypertensive medications, coronary heart disease, heart failure, anticoagulant use, C-reactive protein	Model 2: adjusted for model 1 plus incident atrial fibrillation and incident stroke	Model 3: adjusted for model 2 plus LAVI <sub>min</sub> (for LA function measures only), left ventricular ejection fraction, left ventricular mass index
<b>LA Reservoir Strain, %</b>				
≤26.72	4.74	2.03 (1.53, 2.68)	1.94 (1.46, 2.57)	1.88 (1.35, 2.63)
26.73 – 30.59	2.10	1.01 (0.75, 1.37)	0.99 (0.73, 1.33)	0.99 (0.72, 1.36)
30.60 – 34.41	1.71	0.92 (0.68, 1.26)	0.91 (0.67, 1.24)	0.93 (0.68, 1.27)
34.42 – 39.40	1.45	0.86 (0.62, 1.18)	0.85 (0.62, 1.17)	0.85 (0.62, 1.18)
≥39.41	1.56	Reference	Reference	Reference
<b>LA Conduit Strain, %</b>				
<9.90	3.89	1.76 (1.30, 2.38)	1.71 (1.26, 2.30)	1.45 (1.05, 2.00)
9.91 – 13.06	2.59	1.45 (1.06, 1.96)	1.38 (1.02, 1.88)	1.28 (0.93, 1.75)
13.07 – 15.89	1.78	1.11 (0.80, 1.53)	1.10 (0.79, 1.52)	1.05 (0.76, 1.46)
15.90 – 19.52	1.79	1.19 (0.86, 1.64)	1.19 (0.86, 1.63)	1.17 (0.85, 1.61)
>19.53	1.28	Reference	Reference	Reference
<b>LA Contractile Strain, %</b>				
<13.47	3.27	1.74 (1.32, 2.29)	1.69 (1.28, 2.22)	1.55 (1.14, 2.11)
13.48 – 16.62	2.16	1.16 (0.87, 1.54)	1.10 (0.83, 1.47)	1.07 (0.79, 1.43)
16.63 – 19.17	1.98	1.13 (0.84, 1.52)	1.13 (0.85, 1.52)	1.09 (0.81, 1.47)
19.18 – 22.37	1.95	1.12 (0.83, 1.49)	1.09 (0.82, 1.46)	1.07 (0.79, 1.43)
>22.38	1.79	Reference	Reference	Reference
<b>LA Emptying Fraction, %</b>				
<50.92	4.18	1.87 (1.41, 2.47)	1.78 (1.34, 2.36)	1.82 (1.27, 2.59)
50.93 – 56.58	2.30	1.18 (0.88, 1.59)	1.17 (0.87, 1.57)	1.18 (0.86, 1.63)
56.59 – 61.28	1.84	1.10 (0.81, 1.50)	1.10 (0.81, 1.49)	1.11 (0.81, 1.52)
61.29 – 66.17	1.54	1.02 (0.74, 1.41)	1.01 (0.74, 1.40)	1.02 (0.74, 1.40)
>66.18	1.48	Reference	Reference	Reference
<b>LA Passive Emptying Fraction, %</b>				
<17.63	3.66	1.47 (1.10, 1.96)	1.43 (1.08, 1.91)	1.25 (0.92, 1.69)
17.64 – 23.66	2.06	1.03 (0.76, 1.40)	1.03 (0.76, 1.40)	0.96 (0.70, 1.32)
23.67 – 28.68	2.24	1.22 (0.90, 1.64)	1.21 (0.90, 1.63)	1.14 (0.84, 1.54)
28.69 – 35.20	1.76	1.03 (0.75, 1.40)	1.04 (0.76, 1.42)	1.02 (0.75, 1.39)
≥35.20	1.49	Reference	Reference	Reference
<b>LA Active Emptying Fraction, %</b>				
<35.15	3.27	1.58 (1.20, 2.08)	1.52 (1.15, 2.00)	1.42 (1.03, 1.96)
35.16 – 41.05	2.25	1.23 (0.92, 1.65)	1.18 (0.88, 1.58)	1.11 (0.82, 1.51)

		Hazard Ratio (95% Confidence Interval)		
	Incidence Rate (per 100PY)	Model 1: adjusted for age, sex, race/center, APOE ε4, education, body mass index, smoking status, diabetes, systolic blood pressure, antihypertensive medications, coronary heart disease, heart failure, anticoagulant use, C-reactive protein	Model 2: adjusted for model 1 plus incident atrial fibrillation and incident stroke	Model 3: adjusted for model 2 plus LAVI <sub>min</sub> (for LA function measures only), left ventricular ejection fraction, left ventricular mass index
41.06 – 46.07	2.12	1.12 (0.84, 1.50)	1.12 (0.84, 1.50)	1.07 (0.79, 1.44)
46.09 – 51.88	1.79	1.02 (0.75, 1.38)	1.02 (0.76, 1.38)	1.01 (0.75, 1.37)
>51.89	1.71	Reference	Reference	Reference
<b>Maximal LA Volume Index, ml/m<sup>2</sup></b>				
<24.69	2.10	Reference	Reference	Reference
24.70 – 29.77	1.77	0.74 (0.56, 0.99)	0.76 (0.57, 1.02)	0.74 (0.55, 0.99)
29.78 – 34.85	1.97	0.79 (0.60, 1.05)	0.81 (0.61, 1.08)	0.77 (0.58, 1.02)
34.86 – 41.65	2.08	0.79 (0.60, 1.05)	0.80 (0.60, 1.06)	0.72 (0.54, 0.96)
>41.66	3.18	0.99 (0.76, 1.30)	0.96 (0.73, 1.26)	0.78 (0.59, 1.04)
<b>Minimal LA Volume Index, ml/m<sup>2</sup></b>				
<8.96	1.74	Reference	Reference	Reference
8.97 – 11.61	1.59	0.87 (0.64, 1.18)	0.89 (0.65, 1.21)	0.86 (0.63, 1.17)
11.62 – 14.56	1.87	0.86 (0.64, 1.16)	0.88 (0.65, 1.18)	0.83 (0.62, 1.12)
14.57 – 19.00	2.48	1.06 (0.80, 1.40)	1.07 (0.81, 1.42)	0.97 (0.73, 1.29)
>19.01	3.51	1.25 (0.94, 1.65)	1.19 (0.90, 1.58)	0.97 (0.72, 1.30)

<sup>a</sup> Quintile boundaries are based on the primary analysis. Incidence rates are unadjusted.

Abbreviations: CRP = C-reactive protein; ARIC = Atherosclerosis Risk in Communities; LA = left atrial; PY = person-years; APOE = apolipoprotein E



**eTable 16. Association of Left Atrial Measures with Incident Dementia Using MICE: The ARIC Study, 2011-2019 (n=4,946)<sup>a</sup>**

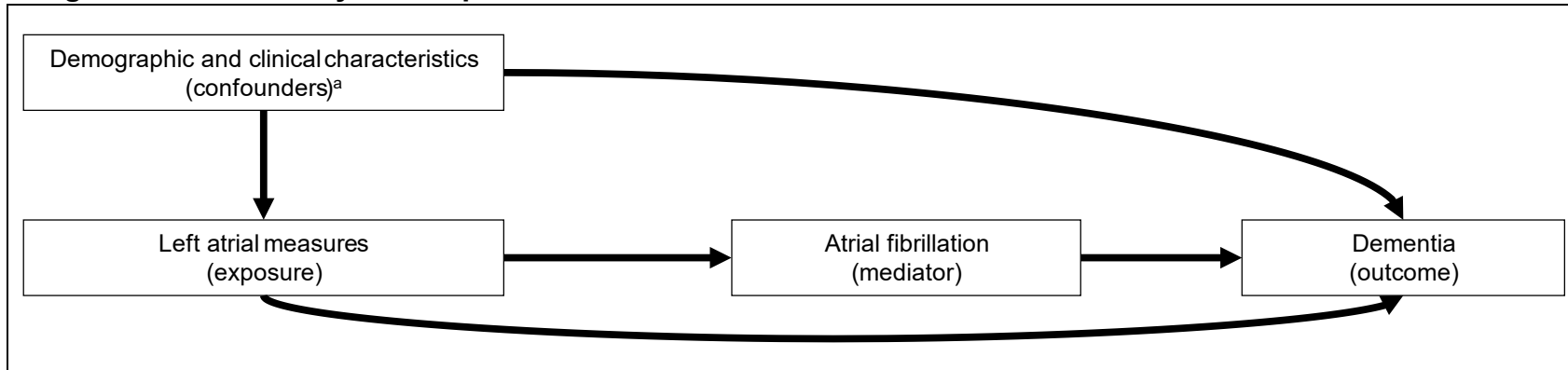
		Hazard Ratio (95% Confidence Interval)		
	Incidence Rate (per 100PY)	Model 1: adjusted for age, sex, race/center, APOE ε4, education, body mass index, smoking status, diabetes, systolic blood pressure, antihypertensive medications, coronary heart disease, heart failure, anticoagulant use	Model 2: adjusted for model 1 plus incident atrial fibrillation and incident stroke	Model 3: adjusted for model 2 plus LAVI <sub>min</sub> (for LA function measures only), left ventricular ejection fraction, left ventricular mass index
<b>LA Reservoir Strain, %</b>				
<26.72	4.57	1.92 (1.48, 2.47)	1.83 (1.42, 2.37)	1.74 (1.28, 2.38)
26.73 – 30.59	2.11	0.99 (0.75, 1.31)	0.97 (0.74, 1.28)	0.95 (0.71, 1.28)
30.60 – 34.41	1.69	0.87 (0.65, 1.16)	0.86 (0.64, 1.14)	0.86 (0.64, 1.16)
34.42 – 39.40	1.54	0.87 (0.65, 1.18)	0.87 (0.65, 1.17)	0.87 (0.64, 1.17)
>39.41	1.62	Reference	Reference	Reference
<b>LA Conduit Strain, %</b>				
<9.90	3.72	1.67 (1.27, 2.18)	1.60 (1.21, 2.10)	1.35 (1.01, 1.81)
9.91 – 13.06	2.62	1.40 (1.06, 1.86)	1.36 (1.03, 1.80)	1.25 (0.93, 1.66)
13.07 – 15.89	1.81	1.04 (0.77, 1.40)	1.04 (0.77, 1.39)	0.99 (0.73, 1.33)
15.90 – 19.52	1.81	1.15 (0.86, 1.54)	1.15 (0.86, 1.54)	1.12 (0.84, 1.50)
>19.53	1.36	Reference	Reference	Reference
<b>LA Contractile Strain, %</b>				
<13.47	3.15	1.65 (1.29, 2.13)	1.61 (1.25, 2.08)	1.46 (1.10, 1.93)
13.48 – 16.62	2.30	1.21 (0.94, 1.57)	1.17 (0.90, 1.51)	1.12 (0.86, 1.46)
16.63 – 19.17	1.90	1.07 (0.81, 1.41)	1.08 (0.82, 1.42)	1.03 (0.78, 1.37)
19.18 – 22.37	2.04	1.16 (0.89, 1.51)	1.14 (0.88, 1.49)	1.11 (0.85, 1.45)
>22.38	1.83	Reference	Reference	Reference
<b>LA Emptying Fraction, %</b>				
<50.92	4.00	1.76 (1.34, 2.32)	1.68 (1.27, 2.21)	1.63 (1.15, 2.31)
50.93 – 56.58	2.30	1.16 (0.86, 1.55)	1.14 (0.85, 1.53)	1.12 (0.80, 1.56)
56.59 – 61.28	1.87	1.06 (0.78, 1.44)	1.04 (0.77, 1.42)	1.03 (0.75, 1.42)
61.29 – 66.17	1.60	1.01 (0.73, 1.38)	0.99 (0.73, 1.36)	0.99 (0.72, 1.36)
>66.18	1.57	Reference	Reference	Reference
<b>LA Passive Emptying Fraction, %</b>				
<17.63	3.49	1.45 (1.09, 1.93)	1.40 (1.05, 1.87)	1.22 (0.90, 1.67)
17.64 – 23.66	2.17	1.07 (0.79, 1.46)	1.07 (0.79, 1.45)	0.99 (0.72, 1.36)
23.67 – 28.68	2.23	1.18 (0.87, 1.59)	1.16 (0.86, 1.57)	1.10 (0.81, 1.49)
28.69 – 35.20	1.81	1.03 (0.76, 1.39)	1.04 (0.77, 1.40)	1.01 (0.75, 1.37)
>35.20	1.56	Reference	Reference	Reference
<b>LA Active Emptying Fraction, %</b>				

		Hazard Ratio (95% Confidence Interval)		
	Incidence Rate (per 100PY)	Model 1: adjusted for age, sex, race/center, APOE ε4, education, body mass index, smoking status, diabetes, systolic blood pressure, antihypertensive medications, coronary heart disease, heart failure, anticoagulant use	Model 2: adjusted for model 1 plus incident atrial fibrillation and incident stroke	Model 3: adjusted for model 2 plus LAVI <sub>min</sub> (for LA function measures only), left ventricular ejection fraction, left ventricular mass index
≤35.15	3.19	1.50 (1.14, 1.97)	1.45 (1.10, 1.91)	1.31 (0.95, 1.80)
35.16 – 41.05	2.32	1.24 (0.94, 1.64)	1.19 (0.90, 1.58)	1.11 (0.82, 1.49)
41.06 – 46.07	2.08	1.07 (0.81, 1.42)	1.06 (0.80, 1.40)	1.00 (0.75, 1.33)
46.09 – 51.88	1.82	1.01 (0.74, 1.37)	1.01 (0.74, 1.37)	0.98 (0.72, 1.35)
≥51.89	1.77	Reference	Reference	Reference
<b>Maximal LA Volume Index, ml/m<sup>2</sup></b>				
≤24.69	2.05	Reference	Reference	Reference
24.70 – 29.77	1.84	0.81 (0.61, 1.07)	0.83 (0.63, 1.10)	0.81 (0.61, 1.06)
29.78 – 34.85	2.00	0.86 (0.64, 1.14)	0.88 (0.66, 1.17)	0.83 (0.63, 1.11)
34.86 – 41.65	2.12	0.86 (0.66, 1.13)	0.87 (0.67, 1.13)	0.80 (0.61, 1.04)
≥41.66	3.14	1.07 (0.83, 1.39)	1.04 (0.80, 1.35)	0.89 (0.68, 1.17)
<b>Minimal LA Volume Index, ml/m<sup>2</sup></b>				
≤8.96	1.77	Reference	Reference	Reference
8.97 – 11.61	1.63	0.89 (0.64, 1.22)	0.90 (0.68, 1.23)	0.87 (0.63, 1.19)
11.62 – 14.56	1.88	0.90 (0.67, 1.20)	0.91 (0.68, 1.22)	0.87 (0.65, 1.16)
14.57 – 19.00	2.47	1.10 (0.83, 1.45)	1.11 (0.86, 1.46)	1.01 (0.76, 1.34)
>19.01	3.42	1.29 (0.99, 1.67)	1.23 (0.94, 1.60)	1.04 (0.79, 1.38)

<sup>a</sup> Quintile boundaries are based on the primary analysis. LA measures were imputed for 850 participants. Incidence rates are unadjusted.

Abbreviations: ARIC = Atherosclerosis Risk in Communities; MICE = multiple imputation by chain equations; LA = left atrial; PY = person-years; APOE = apolipoprotein E

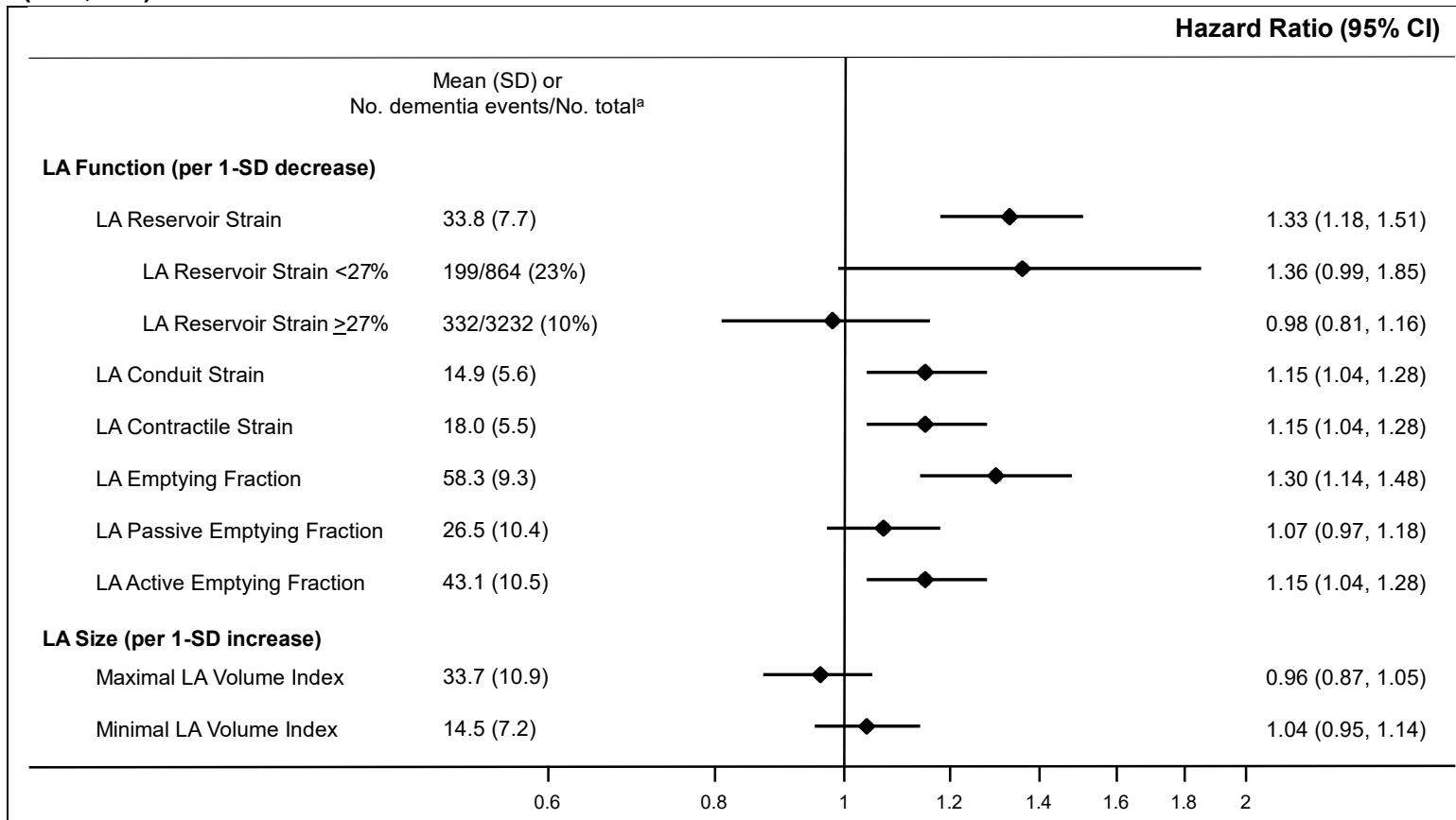
## eFigure 1. Directed Acyclic Graph



eFigure 1 illustrates the hypothesized associations among left atrial (LA) measures, dementia, atrial fibrillation (AF), and confounders. Specifically, in addition to AF mediating part of the association between LA measures and dementia, LA measures are also associated with dementia via a pathway that is independent of AF.

<sup>a</sup> Confounders include age, sex, race/center, education, body mass index, smoking status, diabetes, systolic blood pressure, antihypertensive medications, coronary heart disease, heart failure

**eFigure 2. Association of Left Atrial Measures with Incident Dementia: The ARIC Study, 2011-2019 (n=4,096)**



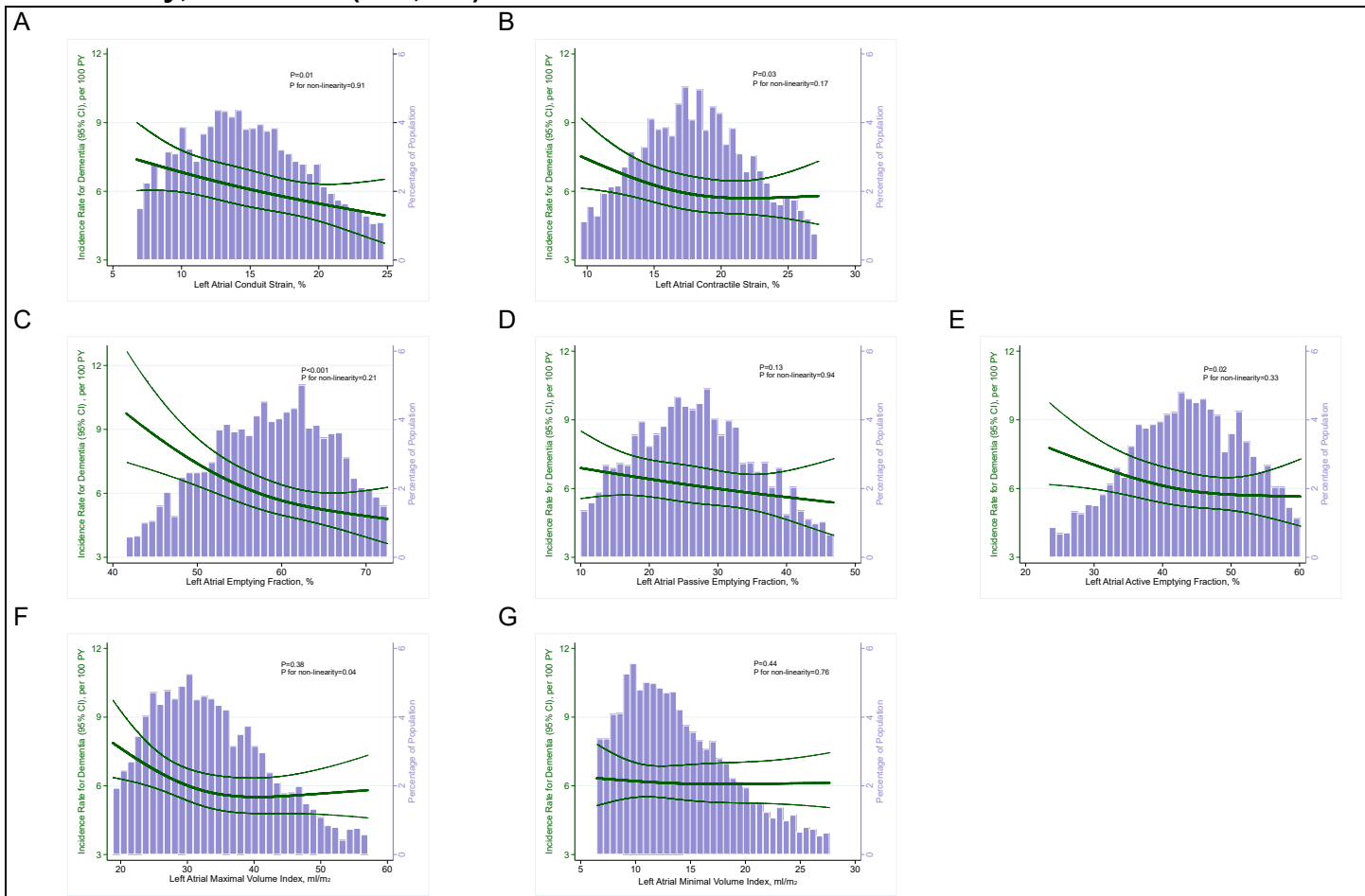
eFigure 2 depicts the association of left atrial measures (per 1-SD decrease or increase) and incident dementia. For continuous LA measures, hazard ratios are per 1-SD decrease or increase in LA measure. For example, each 1-SD decrease in LA conduit strain was associated with an increased risk of dementia (hazard ratio (95% CI): 1.15 (1.04, 1.28)).

Adjusted for age, sex, race/center, APOE ε4, education, body mass index, smoking status, diabetes, systolic blood pressure, antihypertensive medications, coronary heart disease, heart failure, anticoagulant use, incident stroke, incident atrial fibrillation, LAVI<sub>min</sub> (for LA function measures only), left ventricular ejection fraction, left ventricular mass index

<sup>a</sup> Data presented as mean (SD) for continuous variables and number of dementia events/total (%) for categorical variables. Units for LA function measures are %; units for LA size measures are ml/m<sup>2</sup>.

Abbreviations: ARIC = Atherosclerosis Risk in Communities; LA = left atrial; SD = standard deviation; CI = confidence interval

**eFigure 3. Restricted Cubic Splines Plotting Dementia Incidence by Left Atrial Measures: The ARIC Study, 2011-2019 (n=4,096)**



eFigure 3 depicts the association between LA measures and dementia incidence. *P* values are shown to indicate whether associations are significant and whether they are non-linear.

A: LA conduit strain; B: LA contractile strain; C: LA emptying fraction; D: LA passive emptying fraction; E: LA active emptying fraction; F: LA maximal volume index; G: LA minimal volume index

Adjusted for age, sex, race/center, APOE ε4, education, body mass index, smoking status, diabetes, systolic blood pressure, antihypertensive medications, coronary heart disease, heart failure, anticoagulant use, incident atrial fibrillation, incident stroke, LAVI<sub>min</sub> (for LA function measures), left ventricular ejection fraction, left ventricular mass index

Abbreviations: ARIC = Atherosclerosis Risk in Communities; LA = left atrial; PY = person-years