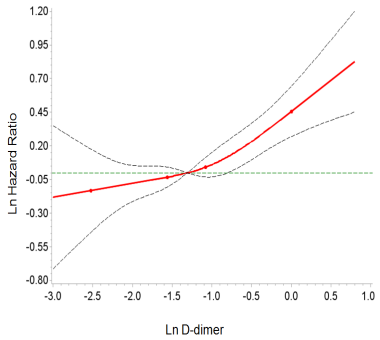
SUPPLEMENTAL MATERIAL

Supplemental Table I. Incidence Rates (95% CI) and Hazard Ratios (95% CI) of Definite and Probable Total Stroke in Relation to D-dimer, the ARIC Study, 1993-2012.

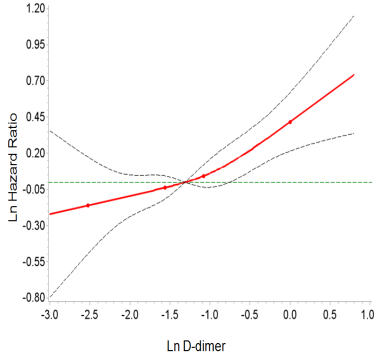
	D-dimer Quintiles, μg/ml						Continuous D-dimer
Total Stroke	Q1 (≤ 0.14)	Q2 (0.15-0.22)	Q3 (0.23-0.32)	Q4 (0.33-0.49)	Q5 (> 0.49)	P_{TREND}	Per 1-SD Log_e increment*
Definite plus probable stroke							
Events, n	114	123	151	127	204		
Incidence rate†	3.0 (2.5-3.6)	3.0 (2.5-3.6)	4.1 (3.5-4.8)	3.9 (3.3-4.7)	6.1 (5.3-6.9)		
Model 1 HR	1 (Referent)	0.92 (0.71-1.18)	1.13 (0.88-1.45)	0.99 (0.76-1.28)	1.43 (1.12-1.82)	0.001	1.11 (1.03-1.20)
Model 2 HR	1 (Referent)	0.89 (0.69-1.16)	1.04 (0.81-1.33)	0.86 (0.66-1.12)	1.30 (1.02-1.67)	0.001	1.09 (1.002-1.18)
Model 3 HR	1 (Referent)	0.90 (0.70-1.17)	1.04 (0.81-1.34)	0.85 (0.65-1.11)	1.30 (1.02-1.67)	0.002	1.08 (1.00-1.17)
Definite stroke							
Events, n	93	95	122	101	157		
Incidence rate†	2.4 (2.0-3.0)	2.3 (1.9-2.9)	3.3 (2.8-4.0)	3.1 (2.6-3.8)	4.7 (4.0-5.5)		
Model 1 HR	1 (Referent)	0.86 (0.65-1.15)	1.10 (0.83-1.45)	0.95 (0.71-1.26)	1.33 (1.01-1.74)	0.004	1.09 (0.99-1.18)
Model 2 HR	1 (Referent)	0.85 (0.64-1.13)	1.02 (0.77-1.34)	0.84 (0.62-1.12)	1.24 (0.94-1.63)	0.011	1.07 (0.97-1.17)
Model 3 HR	1 (Referent)	0.85 (0.64-1.14)	1.02 (0.77-1.34)	0.83 (0.62-1.12)	1.22 (0.93-1.61)	0.016	1.06 (0.97-1.16)
Probable stroke							
Events, n	21	28	29	26	47		
Incidence rate†	0.5 (0.4-0.8)	0.7 (0.5-1.0)	0.8 (0.6-1.1)	0.8 (0.5-1.2)	1.4 (1.0-1.9)		
Model 1 HR	1 (Referent)	1.14 (0.64-2.00)	1.25 (0.71-2.20)	1.16 (0.64-2.08)	1.86 (1.09-3.18)	0.008	1.20 (1.02-1.41)
Model 2 HR	1 (Referent)	1.09 (0.62-1.92)	1.11 (0.62-1.97)	0.92 (0.50-1.69)	1.57 (0.91-2.70)	0.044	1.16 (0.97-1.38)
Model 3 HR	1 (Referent)	1.11 (0.63-1.97)	1.13 (0.63-2.00)	0.92 (0.50-1.69)	1.63 (0.94-2.81)	0.033	1.17 (0.98-1.39)

Model 1: Hazard ratio (HR) with 95% confidence interval from Cox proportional hazards model adjusted for age, sex and race–field center.
Model 2: Model 1 additionally adjusted for education level, smoking status, alcohol intake, body mass index, systolic blood pressure, antihypertensive medication use, diabetes status, total and HDL cholesterol.
Model 3: Model 2 additionally adjusted for prevalent left ventricular hypertrophy, atrial fibrillation, peripheral artery disease and heart failure.
* 1 Log_e standard deviation (SD) = 0.97 log_e μg/ml.
† Unadjusted incidence rate per 1,000 person-years with 95% confidence interval.
ARIC, Atherosclerosis Risk in Communities; CI, confidence interval; HR, hazard ratio; SD, standard deviation.

Supplemental Figure IA. Restricted cubic spline depicting relationship between log D-dimer and incident total stroke adjusted for age, sex, race and center. Reference value = -1.347 (median).
95% confidence intervals displayed in broken lines. Knots shown as dots set at 5th, 35th, 65th, and 95th percentiles. (Test for non-linear relation = 0.19.)



Supplemental Figure IB. Restricted cubic spline depicting relationship between log D-dimer and incident ischemic stroke adjusted for age, sex, race and center. Reference value = -1.347 (median).
95% confidence intervals displayed in broken lines. Knots shown as dots set at 5th, 35th, 65th, and 95th percentiles. (Test for non-linear relation = 0.42.)



Supplemental Figure IC. Restricted cubic spline depicting relationship between log D-dimer and incident cardioembolic stroke adjusted for age, sex, race and center. Reference value = -1.347 (median). 95% confidence intervals displayed in broken lines. Knots shown as dots set at 5th, 35th, 65th, and 95th percentiles. (Test for non-linear relation = 0.80.)