SUPPLEMENTAL MATERIAL

Neighborhood Disadvantage and Ischemic Stroke: The Cardiovascular Health Study (CHS)

Supplemental Methods:

The CHS is a longitudinal, population-based study of cardiovascular disease, as detailed previously.[1, 2] Briefly, participants were randomly sampled from Medicare eligibility lists in four U.S. communities: Forsyth County, North Carolina; Washington County, Maryland; Sacramento County, California; and Pittsburgh (Allegheny County), Pennsylvania. Eligible participants were 65 years or older, not institutionalized, and not requiring a proxy respondent at the time of recruitment. Approximately 57% of those eligible were enrolled in the study. The original cohort was recruited between 1989 and 1990 (N=5201, 94.7% white and 4.7% African American), and an additional African American cohort was recruited from the North Carolina, California, and Pennsylvania counties in 1992 (N=687, 100% African American). CHS collected survey and clinical data on study participants at regular intervals until 1999. We use data from continued surveillance for cardiovascular events and mortality through June 30, 2006, the end date for these analyses.

Ischemic Stroke. The primary outcome was first ischemic stroke. Detailed descriptions of the ascertainment methods for incident and prevalent strokes, transient ischemic attacks (TIAs), and deaths are described elsewhere.[1, 3, 4] Participants with prevalent strokes (N=205) and transient ischemic attacks (N=82) at baseline were

excluded from these analyses. Incident ischemic strokes were ascertained through interviews at annual visits, interim telephone contacts, notification of events by participants, and review of Medicare hospitalization and cause of death data. For suspected stroke events, inpatient and outpatient medical records, results of pertinent tests, and copies of brain images (CT and MRI) were obtained. All suspected strokes were adjudicated at periodic meetings of a cerebrovascular disease end-point committee that also classified stroke subtype (ischemic, hemorrhagic, and unknown type) and determined whether death was caused by stroke.[1, 3, 4]

Neighborhood Socioeconomic Status. CHS participants' baseline home addresses were geocoded, namely the geographic coordinates (longitude and latitude) were used to identify the residential census tract defined in the 1990 U.S. decennial Census. Census tracts were used as a proxy for neighborhood, given their relatively small spatial and population size. Although neighborhood definitions vary widely and are not perfectly captured by such administrative units, census tract characteristics have been shown to be robust predictors of health.[5]

The neighborhood socioeconomic status (NSES) index used in this study has been previously described in studies of the CHS population.[6, 7] It was constructed by summing the Z-scores of six census-derived SES indicators that represent the area's physical and social resources: 1) median household income; 2) median value of housing units; 3) % households with interest, dividend, or rental income; 4) % of residents $\geq$25 with a high school degree; 5) % of residents $\geq$25 with a college degree; and 6) % of residents in executive, managerial, or professional specialty occupations. Quartile 1 represented the highest residential NSES, and quartile 4, the lowest.

Neighborhood SES differed between African Americans and whites (Figure). Fewer than 25% of African Americans in the highest race-specific quartile overlapped with whites in the cohort, with even less overlap between the race-specific 2nd and 3rd quartiles of neighborhood SES for whites and African Americans. Thus, we constructed separate race-specific NSES index quartiles for whites and African Americans and conducted race-stratified analyses to examine neighborhood associations with stroke.

Covariates. Sociodemographic characteristics, including age, sex, race, income (median household income), and education were all reported in the baseline survey. Income was classified into 4 categories: <%12,000, $12-24,999, $25-34,999, and >=$35,000. Education was classified into 5 categories: < high school, complete high school or GED, some college, college graduate, and graduate or professional school.

Health behaviors reported in the interview included smoking history, physical activity, alcohol use, and diet. Smoking status was categorized as never smoked, former smoker, or current smoker. Participants were classified as non-smokers if they responded that they had smoked fewer than 100 cigarettes (or 5 packs of cigarettes) in their lifetime. Former smokers were those who reported having smoked at least 100 cigarettes or 5 packs of cigarettes in their lifetime but had not smoked during the prior 30 days. Alcohol use was categorized as none (less than one drink per week), 1-7 drinks per week, and more than 7 drinks per week. Physical activity, based on energy expenditure for leisure-time physical activity in the two weeks prior to the interview, was categorized into quartiles. For participants in the original cohort, dietary intake in the 12 months before the baseline survey was estimated using a standardized food frequency

inventory that was converted to nutrient intake per day.[8, 9] Cereal fiber was reported in grams and sodium in milligrams.

Biologic characteristics were obtained by combinations of participant report, medical record review, and CHS examination. Body mass index (BMI) was determined by height and weight measured during the examinations, and reported in kg/m^2. Blood pressure measurements were made in a standardized manner during the clinical examination. Hypertension was defined as systolic blood pressure (SBP)$\geq$160 mm Hg; diastolic blood pressure (DBP) $\geq$95 mm Hg; or both a reported diagnosis of hypertension and use of an anti-hypertension medication. "Borderline hypertension" was defined as SBP 140-159 mm Hg or DBP 90-94 mm Hg. We defined diabetes as a fasting blood glucose (FBG) $\geq$126 mg/dl on the clinical examination or both a reported diagnosis of diabetes and use of an oral anti-diabetic medication or insulin, using the American Diabetes Association definition.[10] Impaired fasting glucose was defined as a FBG between 100 and 126 mg/dl. Fasting lipid panels, that included Total Cholesterol (TC), LDL-cholesterol (LDL-c), and HDL-cholesterol (HDL-c), were measured in the study. A diagnosis of atrial fibrillation was based on self-report or electrocardiogram (EKG) readings. Subclinical cardiovascular disease was defined as evidence of any of the following: Ankle-arm index <0.9; Carotid stenosis >25%; internal carotid thickness >80th percentile; common carotid thickness >80th percentile; major EKG abnormalities; abnormal EF or wall motion on echocardiogram; and claudication or angina on Rose Questionnaire.[7]

Study Sample. Baseline data were available for 5888 participants (Appendix Figure). We excluded from the analyses 39 adults who neither African American nor

white. Of the 4925 whites, we excluded 875 participants whose addresses were not geocoded or whose addresses matched to block groups with fewer than 100 persons, fewer than 30 housing units per block, or with more than 33% persons in group quarters, e.g. military bases; 149 with prevalent stroke, and 67 with a prior TIA, leaving an analytic sample of 3834, with 652 incident ischemic stroke. Among the 924 African Americans, 68 could not be geocoded, 58 had a prevalent stroke, and 15 reported a prior TIA, resulting in an analytic sample of 785, 129 of whom had an incident ischemic stroke.

Supplemental Table 1: Characteristics at baseline of participants excluded from analysis by race*						
	Whites (n = 4925)			***African Americans (n = 924)***		
	Excluded from Analysis (N = 1091) N (%)or mean (SD)	Included in Analysis N = 3834 N (%) or mean (SD)	***P* - value**	Excluded from Analysis N = 139 N (%) or mean (SD)	Included in Analysis N = 785 N (%)or mean (SD)	***P* - value**
Demographics/ Individual SES						
Age, mean (SD)	73.3 (5.6)	72.7 (5.6)	0.004	73.9 (6.7)	72.7 (5.5)	0.06
Female	567 (58.0)	2223 (51.9)	0.0004	78 (56.1)	503 (64.1)	0.07
Education						
Less than high school	313 (28.7)	993 (25.9)	<0.0001	73 (52.5)	343 (44.0)	0.30
High school or GED	269 (24.7)	1147 (30.0)		26 (18.7)	170 (21.8)	
Some college	232 (21.3)	918 (24.0)		17 (12.2)	142 (18.2)	
College graduate	148 (13.6)	402 (10.5)		9 (6.5)	47 (6.0)	
Graduate/professional school	129 (11.8)	363 (9.5)		14 (10.1)	78 (10.0)	
Income						
Less than $12,000	233 (21.4)	770 (20.1)	0.002	78 (56.1)	375 (47.8)	0.20
$12,000 to less than $25,000	343 (31.4)	1336 (34.9)		32 (23.0)	207 (26.4)	
$25,000 to less than $35,000	141 (12.9)	611 (15.9)		11 (7.9)	81 (10.3)	
At least $35,000	301 (27.6)	872 (22.7)		14 (10.1)	69 (8.8)	
Missing income	73 (6.7)	245 (6.4)		4 (2.9)	53 (6.8)	
Behaviors						
Smoking status						
Never smoked	464 (42.6)	1796 (46.9)	0.01	68 (48.9)	384 (49.1)	0.71
Former smoker	510 (46.8)	1600 (41.7)		52 (37.4)	272 (34.8)	
Current smoker	115 (10.6)	437 (11.4)		19 (13.7)	126 (16.1)	
Alcohol use						
0 drinks per week	532 (49.0)	1777 (46.5)	0.32	89 (64.5)	515 (66.2)	0.23
1 – 7 drinks per week	418 (38.5)	1527 (39.9)		44 (31.9)	210 (27.0)	
>7 drinks per week	135 (12.4)	515 (13.5)		5 (3.6)	53 (6.8)	
Physical activity (kcals past two weeks)						
Lowest quartile (least activity)	298 (27.4)	832 (21.8)	0.0003	63 (45.7)	317 (40.5)	0.41
2nd	249 (22.9)	968 (25.3)		36 (26.1)	214 (27.3)	
3rd	283 (26.0)	962 (25.2)		28 (20.3)	154 (19.7)	
Highest quartile (highest activity)	258 (23.7)	1060 (27.7)		11 (7.9)	98 (12.5)	
Biologic factors						
Atrial fibrillation	96 (2.5)	45 (4.1)	0.005	5 (3.6)	8 (1.0)	0.02
Subclinical cardiovascular disease†	799 (73.2)	2494 (65.1)	<0.0001	116 (83.5)	552 (70.3)	0.001
Hypertension ‡						
Normal	442 (40.6)	1721 (44.9)	0.0005	28 (20.1)	204 (26.1)	0.10
Borderline	142 (13.0)	581 (15.2)		14 (10.1)	107 (13.7)	

Supplemental Table 1: Characteristics at baseline of participants excluded from analysis by race*						
	Whites (n = 4925)			***African Americans (n = 924)***		
	Excluded from Analysis (N = 1091) N (%)or mean (SD)	Included in Analysis N = 3834 N (%) or mean (SD)	***P* - value**	Excluded from Analysis N = 139 N (%) or mean (SD)	Included in Analysis N = 785 N (%)or mean (SD)	***P* - value**
Hypertensive	506 (46.4)	1528 (39.9)		97 (69.8)	472 (60.3)	
Diabetes (ADA) ||						
Normal	729 (67.1)	2784 (73.1)	0.0007	83 (62.4)	465 (61.5)	0.25
IFG	172 (15.8)	497 (13.0)		11 (8.3)	99 (13.1)	
Diabetes	185 (17.0)	530 (13.9)		39 (29.3)	192 (25.4)	
Total/HDL ratio , mean (SD)	4.3 (1.3)	4.2 (1.3)	0.007	4.1 (1.5)	3.8 (1.0)	0.05

*Excluded: unable to geocode, >= 30% of census tract resides in group quarters, stroke prior to baseline, TIA prior to baseline, other race/ethnicity.

†Ankle-arm index$\leq$0.9, carotid Stenosis > 25%, internal carotid thickness > 80th percentile, Major EKG abnormalities, abnormal EF or wall motion on echocardiogram, or claudication or angina on Rose Questionnaire.
‡ Hypertension categories: Normal = normotensive, Borderline = systolic blood pressure between 140 and 159 mm Hg or diastolic blood pressure between 90 and 94 mm Hg. Hyperstensive = systolic blood pressure above 160 mm Hg, diastolic blood pressure above 95 mm Hg.
|| Diabetes categories: Impaired fasting glucose = Fasting blood glucose 100-126 mm/dL. Diabetes = Fasting blood glucose above 126 mm/dL or diabetes diagnosis and diabetes medication.

Supplemental Table 2: Incident Ischemic stroke hazard ratios (HR) - all covariates shown					
	Unadjusted	**Model 1** (adjusted for age, sex, income and education)	**Model 2** (Model 1 + behavioral risk factors)	**Model 3** (Model 1 + biological risk factors)	**Model 4** (Model 1 + behavioral + biological risk factors)
Whites (n = 3834)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Neighborhood SES					
Q1 (Highest)	1.00	1.00	1.00	1.00	1.00
Q2	**1.33 (1.04 – 1.71)**	1.27 (0.98 – 1.63)	1.27 (0.98 – 1.64)	1.20 (0.93 – 1.56)	1.21 (0.93 – 1.56)
Q3	**1.42 (1.11 – 1.83)**	1.27 (0.92 – 1.65)	1.26 (0.97 – 1.64)	1.17 (0.90 – 1.52)	1.17 (0.90 – 1.52)
Q4 (Lowest)	**1.56 (1.22 – 2.00)**	**1.32 (1.01 – 1.72)**	1.30 (0.99 – 1.70)	1.16 (0.88 – 1.52)	1.15 (0.88 – 1.51)
Individual characteristics					
Age (5 year intervals)		**1.44 (1.34 – 1.56)**	**1.44 (1.33 – 1.56)**	**1.36 (1.25 – 1.47)**	**1.35 (1.24 – 1.46)**
Male		1.13 (0.95 – 1.35)	1.16 (0.96 – 1.40)	1.05 (0.88 – 1.26)	1.08 (0.89 – 1.31)
Education (ref: Grad/professional school)					
Less than high school		**2.07 (1.37 – 3.11)**	**1.96 (1.30 – 2.96)**	**1.85 (1.22 – 2.79)**	**1.80 (1.19 – 2.73)**
High school or GED		**1.92 (1.29 – 2.86)**	**1.88 (1.26 – 2.79)**	**1.70 (1.14 – 2.54)**	**1.68 (1.13 – 2.51)**
Some college		**1.80 (1.21 – 2.68)**	**1.76 (1.18 – 2.63)**	**1.70 (1.14 – 2.54)**	**1.68 (1.12 – 2.51)**
College graduate		1.34 (0.85 – 2.12)	1.32 (0.83 – 2.10)	1.31 (0.83 – 2.07)	1.30 (0.82 – 2.06)
Income(Ref: At least $35,000)					
Less than $12,000		1.08 (0.80 – 1.44)	1.08 (0.81 – 1.45)	1.10 (0.82 – 1.47)	1.13 (0.84 – 1.51)
$12,000 to less than $25,000		0.97 (0.75 – 1.25)	0.97 (0.75 – 1.26)	0.96 (0.75 – 1.25)	0.99 (0.76 – 1.28)
$25,000 to less than $35,000		0.95 (0.71 – 1.28)	0.97 (0.72 – 1.30)	0.99 (0.74 – 1.33)	1.01 (0.75 – 1.36)
Missing income		0.84 (0.56 – 1.28)	0.87 (0.57 – 1.31)	0.85 (0.56 – 1.29)	0.87 (0.57 – 1.33)
Behavioral risk factors					
Smoking status (ref: non-smoker)					
Former smoker			1.07 (0.88 – 1.30)		1.02 (0.84 – 1.23)
Current smoker			1.20 (0.89 – 1.60)		1.17 (0.87 – 1.58)
Alcohol use (ref: 0 drinks per wk)					
1 – 7 drinks per week			0.92 (0.76 – 1.11)		0.96 (0.79 – 1.16)
>7 drinks per week			0.92 (0.69 – 1.22)		0.98 (0.74 – 1.32)
Physical activity (ref: highest activity)					
1st (lowest activity)			**1.38 (1.09 – 1.74)**		1.24 (0.98 – 1.57)
2nd			0.88 (0.69 – 1.12)		0.83 (0.65 – 1.06)
3rd			1.00 (0.79 – 1.27)		0.99 (0.78 – 1.25)
Biologic risk factors					
Subclinical cardiovascular disease*				**1.75 (1.41 – 2.15)**	**1.75 (1.41 – 2.16)**
Atrial fibrillation (ref: normal)				**2.31 (1.57 – 3.39)**	**2.31 (1.57 – 3.40)**
Hypertension†					

Supplemental Table 2: Incident Ischemic stroke hazard ratios (HR) - all covariates shown					
	Unadjusted	**Model 1** (adjusted for age, sex, income and education)	**Model 2** (Model 1 + behavioral risk factors)	**Model 3** (Model 1 + biological risk factors)	**Model 4** (Model 1 + behavioral + biological risk factors)
Borderline				**1.52 (1.17 – 1.97)**	**1.55 (1.19 – 2.01)**
Hypertensive				**1.85 (1.52 – 2.26)**	**1.88 (1.54 – 2.29)**
Diabetes (ADA) (ref: normal) ‡					
IFG				1.20 (0.94 – 1.54)	1.20 (0.94 – 1.53)
Diabetes				**1.56 (1.24 – 1.95)**	**1.52 (1.21 – 1.92)**
Total cholesterol /HDL cholesterol ratio)				1.06 (0.99 – 1.13)	1.05 (0.98 – 1.13)
African Americans (n = 785)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Neighborhood SES					
Q1 (Highest) ref	1.00	1.00	1.00	1.00	1.00
Q2	0.74 (0.43 – 1.25)	0.68 (0.39 – 1.16)	0.66 (0.39 – 1.14)	0.70 (0.40 – 1.23)	0.68 (0.39 – 1.20)
Q3	0.84 (0.51 – 1.40)	0.70 (0.41 – 1.17)	0.63 (0.37 – 1.07)	0.72 (0.42 – 1.24)	0.64 (0.37 – 1.12)
Q4 (Lowest)	0.71 (0.41 – 1.25)	0.60 (0.33 – 1.07)	0.59 (0.33 – 1.08)	0.67 (0.37 – 1.22)	0.67 (0.36 – 1.23)
Individual characteristics					
Age (5 year intervals)		1.17 (0.97 – 1.40)	1.15 (0.94 – 1.40)	1.16 (0.95 – 1.42)	1.61 (0.94 – 1.44)
Male		0.75 (0.47 – 1.19)	0.78 (0.47 – 1.28)	0.74 (0.46 – 1.21)	0.76 (0.45 – 1.28)
Education (ref: Grad/professional school)					
Less than high school		1.03 (0.49 – 2.20)	0.95 (0.44 – 2.04)	0.85 (0.39 – 1.85)	0.73 (0.33 – 1.60)
High school or GED		0.73 (0.32 – 1.64)	0.68 (0.30 – 1.54)	0.67 (0.29 – 1.52)	0.60 (0.26 – 1.37)
Some college		0.83 (0.36 – 1.87)	0.82 (0.36 – 1.87)	0.70 (0.31 – 1.64)	0.69 (0.29 – 1.60)
College graduate		1.60 (0.66 – 3.90)	1.61 (0.66 – 3.94)	1.46 (0.59 – 3.62)	1.49 (0.60 – 3.68)
Income(Ref: At least $35,000)					
Less than $12,000		1.70 (0.65 – 4.44)	1.24 (0.41 – 3.68)	1.07 (0.35 – 3.28)	1.08 (0.35 – 3.33)
$12,000 to less than $25,000		2.31 (0.92 – 5.78)	2.32 (0.91 – 5.87)	2.10 (0.83 – 5.35)	2.18 (0.85 – 5.61)
$25,000 to less than $35,000		1.27 (0.43 – 3.74)	1.57 (0.59 – 4.18)	1.49 (0.56 – 3.98)	1.42 (0.52 – 3.85)
Missing income		1.22 (0.35 – 4.23)	1.09 (0.31 – 3.83)	1.26 (0.36 – 4.46)	1.17 (0.33 – 4.16)
Behavioral risk factors					
Smoking status (ref: non-smoker)					
Former smoker			0.89 (0.57 – 1.41)		0.90 (0.56 – 1.43)
Current smoker			0.67 (0.33 – 1.36)		0.76 (0.37 – 1.56)
Alcohol use (ref: 0 drinks per wk)					
1 – 7 drinks per week			**0.50 (0.29 – 0.89)**		**0.49 (0.27 – 0.87)**
>7 drinks per week			1.28 (0.58 – 2.81)		1.44 (0.64 – 3.22)
Physical activity (ref: highest activity)					
1st (lowest activity)			0.94 (0.49 – 1.81)		0.81 (0.42 – 1.58)

Supplemental Table 2: Incident Ischemic stroke hazard ratios (HR) - all covariates shown					
	Unadjusted	**Model 1** (adjusted for age, sex, income and education)	**Model 2** (Model 1 + behavioral risk factors)	**Model 3** (Model 1 + biological risk factors)	**Model 4** (Model 1 + behavioral + biological risk factors)
2nd			1.13 (0.58 – 2.20)		1.01 (0.52 – 1.98)
3rd			0.89 (0.43 – 1.85)		0.70 (0.32 – 1.49)
Biologic risk factors					
Subclinical cardiovascular disease*				1.31 (0.81 – 2.11)	1.33 (0.82 – 2.17)
Atrial fibrillation§				---	---
Hypertension (ref: normal) †					
Borderline				1.43 (0.69 – 2.98)	1.28 (0.60 – 2.71)
Hypertensive				1.60 (0.92 – 2.77)	1.61 (0.92 – 2.81)
Diabetes (ADA) (ref: normal) ‡					
IFG				1.22 (0.68 – 2.19)	1.18 (0.65 – 2.13)
Diabetes				0.99 (0.59 – 1.65)	0.96 (0.57 – 1.62)
Total cholesterol /HDL cholesterol ratio)				1.13 (0.93 – 1.37)	1.13 (0.93 – 1.37)

*Ankle-arm index≤0.9, carotid Stenosis > 25%, internal carotid thickness > 80th percentile, Major EKG abnormalities, abnormal EF or wall motion on echocardiogram, or claudication or angina on Rose Questionnaire.

† Hypertension categories: Normal = normotensive, Borderline = systolic blood pressure between 140 and 159 mm Hg or diastolic blood pressure between 90 and 94 mm Hg. Hypertensive = systolic blood pressure above 160 mm Hg, diastolic blood pressure above 95 mm Hg.

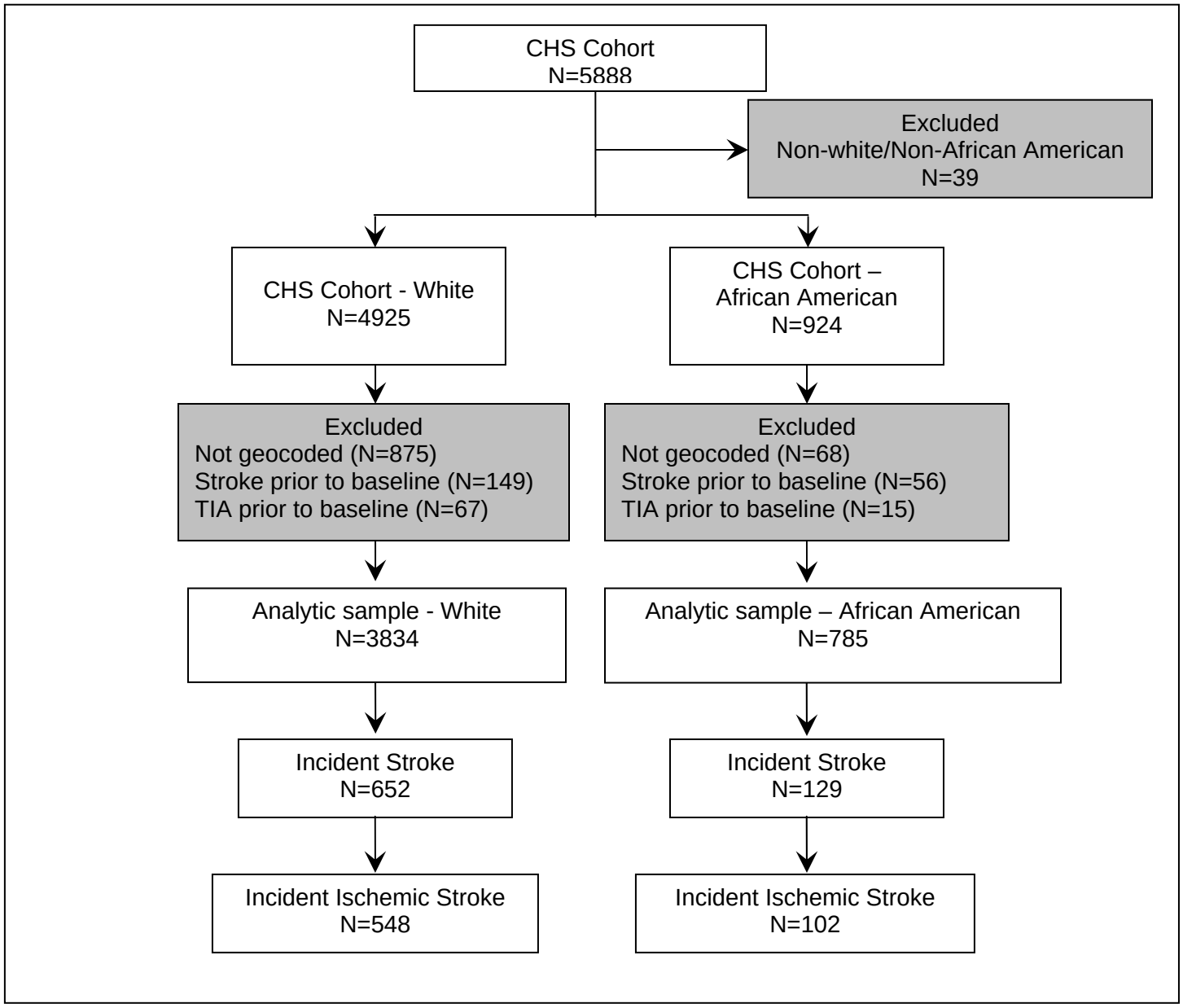
‡ Diabetes categories: Impaired fasting glucose = Fasting blood glucose 100-126 mm/dL. Diabetes = Fasting blood glucose above 126 mm/dL or diabetes diagnosis and diabetes medication. Diabetes = Fasting blood glucose above 126 mm/dL or diabetes diagnosis and diabetes medication.

§ Atrial fibrillation was not included in the African American model because too few participants had a diagnosis of atrial Fibrillation.

Supplemental Table 3: Summary of mediation analysis for Models of white participants with				
	Model 1 vs Model 2	**Model 1 vs Model 3**	**Model 2 vs Model 4**	**Model 3 vs Model 4**
Neighborhood SES quartile comparisons	Difference in Log(HR) between models (95% CI)	Difference in Log(HR) between models (95% CI)	Difference in Log(HR) between models (95% CI)	Difference in Log(HR) between models (95% CI)
Q2 vs. Q1 (highest)	-0.001 (-0.019, 0.051)	0.049 (-0.034, 0.117)	0.047 (-0.047, 0.110)	-0.003 (-0.030, 0.037)
Q3 vs. Q1 (highest)	0.009 (-0.023, 0.073)	**0.086 (0.004, 0.164)**	0.080 (-0.008, 0.148)	0.003 (-0.034, 0.056)
Q4 vs. Q1 (highest)	0.012 (-0.020, 0.092)	**0.130 (0.043, 0.210)**	**0.121 (0.016, 0.182)**	0.003 (-0.040, 0.058)

Confidence intervals around the difference of the Log(HR) were derived using 1000 replicate bootstrap samples. Model 1 is adjusted for individual SES, Model 2 is adjusted for individual SES and behavioral risk factors, Model 3 adjusted for individual SES and biologic risk factors, and Model 4 adjusted for individual SES and behavioral and biologic risk factors.

Supplemental Figure: Analytic Sample



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