SUPPLEMENTAL MATERIAL

Racial variation in stroke risk among women by stroke risk factors

Monik C. Jiménez, ScD; JoAnn E. Manson, MD, DrPH; Nancy R. Cook, ScD; Ichiro Kawachi, MD, PhD; Sylvia Wassertheil-Smoller, PhD; Bernhard Haring, MD, MPH; Rami Nassir, PhD; Jinnie J. Rhee, ScD; Shawnita Sealy-Jefferson, PhD, MPH; Kathryn M. Rexrode, MD, MPH

Materials and Methods
Women's Health Initiative

The observational study (WHI-OS) consisted of 93,676 women without CVD, at baseline, of which 8.2% were black or African American and 83.3% were white. Baseline clinical exams were conducted for all participants with follow-up contact varying by study through planned completion in 2005. At that time, 77% of eligible women were recruited for extended annual follow-up (n=115,403) through 2010. Therefore, in this sample, 74% of women provided follow-up through 2010, while follow-up ended in 2005 for the remainder.[1] Enrollment among eligible women differed by race with approximately 80% of white women enrolling compared to 63% of black women.[1] Overall, women who participated in the extended follow-up were younger, white, had higher levels of education and household income, and were less likely to report a history of hypertension and diabetes (Supplemental Table I). Response rates to annual questionnaires were greater than >90% as of August 2014.[2] Black women were significantly more likely to be excluded than white women for a history of stroke (2.7% vs 1.2%, p<0.0001), myocardial infarction (3.7% vs 2.2%, p<0.0001) or coronary bypass surgery or coronary angioplasty (2% vs 1.7%, p=0.005) with the greatest difference in prevalent disease among younger women.

Covariate Ascertainment

All participants completed baseline clinical exams with questionnaires on socio-demographic, lifestyle/behaviors, diet, medical history and medication inventory. Race/ethnicity (American Indian or Alaskan Native, Asian or Pacific Islander, black or African American, Hispanic/Latino, white [not of Hispanic origin] and other) and socioeconomic and lifestyle/behavioral variables (highest level of attained education, marital or partnership status, and last usual medical care provider visit within last year) were assessed by self-report at baseline. In this study, women who self-reported black or African American are referred to as black and white (not of Hispanic origin) women as white. Region of residence was assigned based on participant address at the baseline visit. Diet was assessed by the WHI food frequency questionnaire (FFQ), which has been validated in this and similar groups.[3, 4] Based on the baseline FFQ, the Healthy Eating Index-2005 (HEI-2005) was used to characterize a diet conforming to the 2005 U.S. Department of Agriculture dietary guidelines.[5] History of diabetes, atrial fibrillation and cancer were assessed by self-reported physician diagnosis and have been validated in this and similar cohorts.[6-8] Hypertension status (never, hypertensive non-treated, hypertensive treated) was defined based on self-reported physician diagnosis and treatment with anti-hypertensive medication. Certified staff used standardized procedures and instruments to measures systolic and diastolic blood pressure, height and weight, as previously described.[9] Updated values of systolic and diastolic blood pressure, body mass index (BMI) and hypertensive medication were available across all arms in the third year of follow-up. Time-varying age was calculated based on age at baseline and the date of stroke event.

Statistical Analyses

In analyses examining the association between race and stroke, we fit 3 nested multivariable models. Model 1 adjusted for age at baseline. Model 2 additionally adjusted for baseline values of socioeconomic-related variables (marital/partnership status, highest level of attained education, household income, region of residence at baseline, and last usual medical care provider visit within last year). Model 3 additionally adjusted for baseline stroke risk factors (smoking status, SBP, diastolic blood pressure [DBP], hypertension status, anti-hypertensive medication, hyperlipidemia medication, diabetes, atrial fibrillation, history of cancer, body mass index [BMI], hormone therapy use, alcohol consumption, HEI-2005, weekly minutes of physical activity, and family history of stroke).

Indicator variables were assigned for variables with missing values (smoking [n=1,585, 1%], hormone therapy use [3,244, 3%], history of hypertension [n=6,513, 5%], hyperlipidemia medication [n=6,873, 5%], diabetes [n=71 , 0.1%], atrial fibrillation [n=1,994, 2%], family history of stroke [n=6,855, 5%], education [n=878, 0.7%], household income [n=8,199, 6.5%], marital status [n=509, 0.04%] and last usual medical care provider visit within last year [n=3,929, 3%]).

Supplemental Tables

Table I. Baseline characteristics of participants by participation in the extended follow-up

	Overall		White women		Black women	
	No extended follow-up	**Extended Follow-up**	**No extended follow-up**	**Extended Follow-up**	**No extended follow-up**	**Extended Follow-up**
N	32890 (26%)	93128 (74%)	28124 (25%)	86505 (75%)	4766 (42%)	6623 (58%)
Age (years)	65 $\pm$ 7.6	63 $\pm$ 7.0	65 $\pm$ 7.5	63 $\pm$ 7.0	62 $\pm$ 7.4	61 $\pm$ 6.7
Follow-up among those without stroke (y)	8 [6-9]	14 [13-15]	8 [6-9]	14 [13-15]	7 [6-9]	14 [13-15]
Total Stroke events	1365	2979	1197	2737	168	242
Racial group, %						
Black	14	7	-	-	-	-
White	86	93	-	-	-	-
Smoking, %						
Never	48	50	48	50	49	49
Past	42	43	43	43	37	40
Current	9	6	8	5	12	10
Alcohol (g/day)	0.2 [0-2.4]	0.4 [0-3.2]	0.4 [0-2.7]	0.5 [0-3.5]	0 [0-0.4]	0 [0-0.6]
Physical Activity (mins/week)	30 [0-150]	60 [0-175]	30 [0-150]	60 [0-180]	0 [0-90]	10 [0-110]
Current hormone therapy Use, %	39	48	41	50	27	32
History of hypertension, %*	41	34	**38**	32	58	55
Current antihypertensive medication, %†	29	22	**26**	21	45	42
Systolic Blood Pressure	130 $\pm$ 18	126 $\pm$ 17	129 $\pm$ 18	126 $\pm$ 17	133 $\pm$ 18	131 $\pm$ 18
Diastolic Blood pressure	75 $\pm$ 9.5	75 $\pm$ 9.1	75 $\pm$ 9.4	75 $\pm$ 9.0	78 $\pm$ 9.7	78 $\pm$ 9.2
Pulse Pressure	54 $\pm$ 16	51 $\pm$ 14	54 $\pm$ 16	51 $\pm$ 14	55 $\pm$ 15	53 $\pm$ 15
Cholesterol lowering medication, %	13	11	**13**	11	15	13
BMI (kg/m²)	28 $\pm$ 6.3	28 $\pm$ 5.7	28 $\pm$ 6.0	27 $\pm$ 5.6	32 $\pm$ 6.9	31 $\pm$ 6.5
Diabetes, %	7	4	**6**	3	15	11
Atrial fibrillation, %	5	4	**5**	4	5	4
Family History of Stroke, %	37	36	**37**	36	37	37
Region of residence						

Northeast	21	25	22	26	18	18
South	28	25	25	23	44	48
Midwest	23	23	22	23	26	23
West	28	27	31	28	12	11
Educational attainment, %						
< HS diploma	6	3	5	2	15	7
HS diploma	19	15	20	16	15	12
Some college or vocational school	40	36	40	36	38	38
College or Postgrad	34	45	34	45	31	41
Household Income, %						
<$20,000	20	11	18	10	31	21
$20,000-<$50,000	43	41	44	41	39	41
$50,000-<$75,000	16	21	16	21	13	19
$>75,000	13	21	13	22	7	13
Partnership status‡, %						
Never married	5	4	5	4	6	6
Divorced or separated	17	15	15	13	30	29
Widowed	21	15	21	14	24	19
Married/Marriage like partnership	56	66	59	68	38	45
Last medical visit w/in past year, %	80	81	**80**	81	77	80
Treatment Arm, %						
Observational study only	69	60	70	61	66	46
Dietary modification trial only - Active	10	12	10	12	11	17
Dietary modification trial only - controls	13	19	12	18	15	24
Hormone therapy controls only	6	6	6	6	5	7
E-alone control	*2*	*2*	*2*	*2*	*3*	*4*
E+ P control	*3*	*4*	*3*	*4*	*2*	*3*
Hormone therapy controls and dietary modification trial	2	3	2	3	3	6

Relative frequencies and mean $\pm$ std or median [25th-75thpercentiles] presented; *t*-test, Wilcoxon rank-sum test or Chi-square test used as appropriate on non-missing values.

All characteristics significantly different by extension study enrollment ($p<0.05$)

* either treated or untreated self-reported hypertension; †Among those with self-reported hypertension

Table II. Baseline characteristics of participants by treatment arm

	Observational study	DM only: Active	DM only: Controls	HT controls only Overall	HT controls only E alone	HT controls only E + P	HT controls & DM	
	(n=78,458)	(n=14,536)	(n=21,700)	(n=7,885)	(n=2,947)	(n=4,938)	(n=3,439)	p-value
Age (years)	64 ± 7.3	62 ± 6.8	62 ± 6.8	64 ± 7.2	64 ± 7.4	64 ± 7.1	62 ± 6.9	<0.0001
White, %	92	89	89	91	86	94	85	<0.001
Follow-up among those without stroke (y)	13 [0-16]	13 [0-17]	14 [0.3-17]	13 [0-17]	13 [0.5-17]	13 [0-17]	14 [0.4-17]	<0.001
Total Stroke events	2,618	528	740	312	129	183	146	
Smoking, %								<0.001
Never	49	50	51	48	48	48	51	
Past	43	43	42	40	39	40	39	
Current	6	6	6	11	12	11	9	
Alcohol (g/day)	0.42 [0-127]	0.42 [0-63]	0.42 [0-65]	0.42 [0-94]	0.21 [0-94]	0.42 [0-65]	0.21 [0-42]	<0.001
Physical Activity (METs/week)	60 [0-1,330]	30 [0-1,090]	20 [0-1,330]	30 [0-1,330]	20 [0-1,090]	38 [0-1,330]	0 [0-1,120]	<0.001
Current hormone therapy Use, %	48	53	53	8	11	6	9	<0.001
History of hypertension, %	33	41	42	36	44	32	44	<0.001
Antihypertensive medication*, %	24	24	24	21	26	19	23	<0.001
Systolic Blood Pressure	126 ± 18	127 ± 17	127 ± 17	128 ± 18	130 ± 18	127 ± 17	129 ± 17	<0.001
Diastolic Blood pressure	75 ± 9.0	76 ± 9.1	76 ± 9.0	76 ± 9.2	76 ± 9.2	75 ± 9.1	77 ± 9.1	<0.001
Pulse Pressure	52 ± 15	51 ± 14	52 ± 14	53 ± 15	54 ± 15	52 ± 14	52 ± 14	<0.001
Cholesterol lowering medication, %	13	10	10	12	13	11	9	<0.001
BMI (kg/m^2)	27 ± 5.8	29 ± 5.8	29 ± 5.8	28 ± 5.9	29 ± 6.2	28 ± 5.7	31 ± 6.1	<0.0001
Diabetes, %	5	5	5	6	8	5	7	<0.001
Atrial fibrillation, %	4	4	4	3	4	3	3	<0.001

Family History of Stroke, %	36	35	35	37	37	36	37	0.07
Education, %								<0.001
< High school diploma	4	3	3	6	7	5	6	
High school diploma	16	17	17	20	22	20	21	
Some college or vocational school	36	39	39	40	44	37	42	
College or Postgrad	43	40	41	34	27	38	31	
Income, %								<0.001
<$20,000	13	12	12	19	24	17	18	
$20,000-<$50,000	41	43	43	47	47	47	49	
$50,000-<$75,000	19	21	20	16	14	18	17	
$≥75,000	20	19	19	12	10	13	11	
Partnership status, %								<0.001
Never married	5	4	4	4	3	4	4	
Divorced or separated	15	15	15	17	18	16	18	
Widowed	17	15	15	20	21	19	18	
Married/Partnered	63	65	66	59	57	60	60	

DM: dietary modification trial; HT: hormone therapy trials

Values are relative frequencies and sample, mean ± std, median [min-max]

t-test, Wilcoxon rank-sum test or Chi-square test used as appropriate

*Among those with self-reported hypertension

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