

# Walking Speed and Risk of Incident Ischemic Stroke Among Postmenopausal Women

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**Background and Purpose**—Walking speed is a simple, reliable, and valid measure of functional status that has been shown to be strongly correlated with age-related outcomes and may be an indicator of subclinical cerebrovascular disease. However, few studies have investigated the association of walking speed with risk of incident ischemic stroke.

**Methods**—The present analyses included 13 048 postmenopausal women (mean age 65 years) from the Women's Health Initiative free of stroke at baseline, 264 of whom had incident ischemic strokes on follow-up. Cox proportional hazards regression was used to obtain hazard ratios (HRs) and 95% confidence intervals (CIs) to assess the relationship between performance on a timed walk and risk of incident ischemic stroke. Multivariate adjustment included age, race/ethnicity, body mass index, waist-hip ratio, depression, arthritis, hypertension, smoking, systolic blood pressure, treated diabetes, hormone use, NSAID use, aspirin use, self-reported general health, and history of coronary heart disease.

**Results**—Slower walking speed was a significant predictor of incident ischemic stroke. After multivariate adjustment, the hazard for incident ischemic stroke was increased for the slowest walking speed tertile compared to the fastest walking speed tertile (HR=1.69, 95% CI: 1.21, 2.36). Additional adjustment for other physical function variables (grip strength and chair stands) did not change the association significantly.

**Conclusions**—Slow walking speed was found to be a strong predictor of increased risk of incident ischemic stroke among postmenopausal women independent of other established risk factors for stroke. (*Stroke*. 2008;39:1233-1239.)

**Key Words:** physical function ■ stroke ■ walking speed ■ women

Functional status, as measured by tests of physical performance, has been found to be predictive of important age-related outcomes. Walking speed is a simple, reliable, and valid measure of functional status that is considered a surrogate for the overall quality of gait and motor function, and even short distance walking tests have the ability to measure motor control, strength, balance, and adaptations in the gait pattern.<sup>1</sup> Walking speed in itself has been shown to be strongly correlated with age-related outcomes such as falls,<sup>2</sup> development of functional disability,<sup>3,4</sup> hospitalizations,<sup>5</sup> dementia,<sup>2,6</sup> and risk for mortality.<sup>3,4</sup>

Additionally, walking speed has been shown to be strongly associated with white matter hyperintensities<sup>7</sup> and lacunar infarcts<sup>8</sup> on cranial MRI, and may thus be an indicator of subclinical cerebrovascular disease.<sup>9</sup> Subclinical cerebrovascular disease on imaging studies in turn have been associated with increased risk of future clinical strokes.<sup>10</sup> Despite these

findings, few studies have investigated the association of walking speed with risk of stroke, and prior population-based investigations are primarily based on one cohort of elderly men and women, the Cardiovascular Health Study (CHS). In one study of CHS participants, after 3.3 years of follow-up, physical performance measures of walking speed (time to walk 15 feet) and number of chair stands were independently associated with risk of incident stroke.<sup>11</sup> In another study of CHS participants, after 7 years of follow-up, slower walking speed was an independent predictor of death attributable to all stroke and ischemic stroke.<sup>12</sup>

Stroke is one of the leading causes of death in the United States for both men and women, particularly in the elderly,<sup>13</sup> and leads to serious long-term disabilities among survivors.<sup>14</sup> Frailty, a complex measure consisting of several components, including unintentional weight loss, weakness, poor endurance, slowness, and low activity levels, has been shown to be

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related to but distinct from disability and comorbidities.<sup>15,16</sup> In CHS it was found that in those without a history of cardiovascular disease (CVD), subclinical measures of CVD (measured by carotid ultrasound, ankle-arm index, left ventricular hypertrophy by ECG and echocardiography, and cerebral MRI) was related to frailty.<sup>17</sup> Given that walking speed, a component of frailty, is simple to perform and inexpensive with little burden on physician or patient and has also been shown to be associated with subclinical cerebrovascular disease, it may prove to be a valuable routine test to help aid in the prediction of strokes among elderly patients.<sup>9</sup> Thus, the purpose of this study was to assess walking speed as a risk factor for incident ischemic stroke in postmenopausal women without a history of stroke at baseline in the Women's Health Initiative (WHI) Study. Other measures of physical performance, hand grip strength and number of chair raises, are also evaluated.

## Methods

### Study Population

The WHI Study has both an observational and a clinical trials component, the methods of which are described in detail elsewhere.<sup>18,19</sup> Briefly, the WHI was designed to examine the impact of a number of factors on many of the major causes of morbidity and mortality in postmenopausal women. Women eligible for the study were 50 to 79 years of age at baseline, were postmenopausal, had no medical conditions associated with a predicted survival of less than 3 years, and were likely to continue to reside in the vicinity of a WHI clinical center for at least 3 years. Women also had to be able and willing to provide informed consent to be a part of the study. Exclusion criteria for the clinical trial component (which examined postmenopausal hormone therapy, low-fat diet, or calcium supplementation) included alcohol or drug dependency, mental illness including severe depression or dementia, and additional exclusions based on safety adherence and retention concerns.<sup>18</sup> Women ineligible or not interested in the clinical trial components were given an opportunity to enroll in the observational study; other women were specifically invited to participate in the observational study. 93 676 women enrolled in the Observational Study, and an additional 68 133 women were randomized in the clinical trials portion of the study from October 1993 through December 1998.<sup>19</sup> Participants in the WHI completed clinic visits at baseline and periodic follow-up visits (observational study at year 3, clinical trials annually) and also completed mail questionnaires periodically to update data on key health status measures, and were followed longitudinally for the occurrence of major health events (including stroke) and death.

### Data Collection

All WHI participants completed visits at baseline to determine eligibility and collect data including questionnaires, physical examinations, collection of biological specimens, and laboratory tests. Medical history questionnaires asked participants if a doctor ever told them that they had any of several medical conditions, including stroke, myocardial infarction, angina, peripheral arterial disease, congestive heart failure, coronary revascularization, high blood pressure, arthritis, and Parkinson Disease. These questionnaires also asked about cardiovascular risk factors (high cholesterol requiring pills, treatment for diabetes, smoking), postmenopausal hormone use, depression (measured by the shortened CES-D<sup>20</sup>), and self-reported general health. At the baseline clinic visit, trained and certified staff obtained blood pressure and anthropometric measures including height, weight, and waist and hip circumferences. From these clinic measurements, body mass index (weight in kg/height in m<sup>2</sup>) and waist to hip ratio were calculated. Hypertension was defined using a combination of self-reported physician diagnosed high blood pressure and clinical measurements (systolic blood pressure

≥140 mm Hg or diastolic blood pressure ≥90 mm Hg). History of coronary heart disease was defined as physician diagnosed stroke, myocardial infarction, angina, peripheral arterial disease, coronary revascularization, or congestive heart failure.

Women were also asked to bring all of their currently used prescription medications, over-the-counter medications, and vitamins and supplements in their original bottles to the baseline visit and information from these bottles was entered into a medication inventory database. From this inventory, information on use of aspirin and nonsteroidal antiinflammatory drugs (NSAIDs) was obtained for each woman. NSAID use was dichotomized as any versus none and aspirin use was dichotomized at 81 mg per day.

Measures of usual physical activity, cognitive impairment, and ability to complete activities of daily living were only obtained for a subset of women. Physical activity was measured as the total expenditure of weekly recreational activity from self-report, cognitive impairment was measured using the modified mini-mental status examination (3MSE),<sup>21</sup> and activities of daily living was measured using 4 items asking about the amount of help (no help, some help, totally dependent) needed to eat, dress and undress, get in and out of bed, and take a bath or shower.

Walking speed was assessed at baseline by measuring the time in seconds that it took to complete a 6-meter walk, performed at usual pace. Other measures of physical function included repeated chair stands and handgrip strength. The number of chair rises able to be performed in 15 seconds was measured to assess lower extremity muscle strength and balance. Participants were asked to sit in a straight-backed chair with arms folded across their chest and to stand as many times as they could in 15 seconds. Handgrip strength of the dominant hand measured voluntary muscle strength using a hydraulic hand grip dynamometer. Women performed each of these tests of physical function twice at the baseline visit, and the average of the repeated tests were used in these analyses.

### Outcome Ascertainment

The outcome of interest for the present study was incident ischemic stroke defined as the rapid onset of a persistent neurological deficit attributed to an obstruction in the brain arterial system, lasting more than 24 hours and without evidence for other causes. Only stroke events that required hospitalization were considered as potential outcomes. All potential stroke outcomes were identified primarily through self-report at semiannual contacts for clinical trial participants, annual contacts of observational study participants, and through third-party reports by family members and proxies.<sup>22</sup> Specific details of the illness and hospitalizations are obtained via a standardized questionnaire administered by phone, in-person interview, or self-completed form. Medical records were obtained for potential strokes and other predefined health events, and adjudication was conducted at the local clinical centers by a trained physician adjudicator who assigned a diagnosis according to standard criteria for all strokes requiring a hospital stay. Central adjudication was also performed on all strokes arising from the Hormone Replacement Clinical Trial to document and improve the accuracy of diagnosis, and to provide continuity of diagnostic decisions in this long clinical trial. Additionally, a portion of the locally adjudicated end points were also referred for central adjudication for quality control purposes and the percent agreement between central and local adjudication was 91%. Only confirmed incident ischemic strokes were considered as an outcome. Transient ischemic attacks (TIAs), hemorrhagic strokes, or strokes of indeterminate etiology were not included in the definition of stroke outcome.

### Statistical Analyses

Walking speed was calculated as meters per second. In preliminary analyses, we examined the distribution of walking speed to assess the normality of this variable and identify outlying values. Walking speed had a skewed distribution toward the left, and though all analyses were repeated using the log of walking speed as the outcome with similar results, we present the data by tertile of walking speed for ease of interpretability. We then identified variables associated with walking speed by comparing these vari-

ables across tertiles of walking speed and noting the *P* for trend. The relationship between walking speed and risk of incident ischemic stroke was evaluated using Cox proportional hazards regression to obtain hazard ratios (HRs) and 95% confidence intervals (CIs). Multivariate adjustment was performed with those variables that were significantly associated with walking speed in univariate analyses: age, race/ethnicity, body mass index (BMI), waist-hip ratio, depression, arthritis, hypertension, smoking, systolic blood pressure, treated diabetes, hormone use (never, past, present), NSAID use, aspirin use, self-reported general health, and history of coronary heart disease. Additional adjustment for handgrip strength and number of chair stands was also performed. All correlations between multivariate adjustment variables (including arthritis) and walking speed, handgrip strength, and number of chair stands were  $<0.20$  indicating no multi-collinearity concerns. Correlations between arthritis and NSAID use were also minimal ( $<0.25$ ). We found no evidence for departures from the model assumption of proportional hazards.

All Cox proportional hazards models were stratified within the model by clinical trial component or observational study to account for the fact that stroke incidence rates may have varied among these populations. Because information on physical activity, cognitive impairment, and activities of daily living limitations, which are potentially important confounders, was not available on all women, subgroup analyses that incorporated these variables were also performed for those women with available data, noting limitations in power attributable to the decreased sample sizes.

Sensitivity analyses were performed by conducting analyses with serial exclusions for (1) women with baseline disease that may have affected walking ability or speed: emphysema, angina, myocardial infarction, congestive heart failure, peripheral arterial disease, Parkinson Disease, Multiple Sclerosis, and Amyotrophic Lateral Sclerosis; (2) women with TIA at baseline; and (3) unusually slow walking speeds (below the 1st percentile:  $<0.46$  meters per second). The results were not affected by these serial exclusions. The interaction of age with walking speed was nonsignificant in the final models and assessment of a nonlinear association of age and walking speed was modeled with age as a linear-plus-quadratic variable with no effect on the point estimates. Additionally, statistical interactions between walking speed and hand grip strength and chair stands were highly nonsignificant ( $P=0.95$  and  $P=0.87$ , respectively). Interactions between arthritis and walking speed ( $P=0.69$ ), chair stands ( $P=0.09$ ), and handgrip strength ( $P=0.23$ ) were also found to be nonsignificant, and further adjustment for these interaction variables did not change the results compared to the full model that is presented.

Because walking speed is likely to be associated with a greater risk of death or a greater loss to follow-up or stopped follow-up (ie, refusals), bias may result in the point estimates derived from survival analyses attributable to an unequal proportion of censored data among the tertiles of walking speed. In this dataset the rate of lost to follow-up (tertile 1: 1.1%, tertile 2: 1.3%, tertile 3: 1.3%) and stopped follow-up (tertile 1: 2.7%, tertile 2: 3.4%, tertile 3: 3.2%) was fairly constant between walking speed tertiles. However, bias may be introduced as the rate of unrelated deaths increased with declining walking speed (tertile 1: 4.7%, tertile 2: 6.4%, tertile 3: 10.3%), however this bias would be toward the null, resulting in conservative estimates.

## Results

Walk speed was assessed at baseline on a subsample of 14 990 participants in the WHI. 197 (1.3%) were excluded because of self-report of stroke at baseline, and an additional 53 (0.4%) were excluded because of implausible walk speeds ( $>3$  meters per second). Thus these analyses included 14 740 women, of whom 12 360 were the clinical trials component and 2 380 women from the observational study component of the WHI. Cox models were based on complete-case analyses limiting the sample size to 13 048, of which 264 had incident

ischemic stroke on follow-up. Median follow-up time was 5.2 years for cases and 9.4 years for censored individuals.

Women with faster walking speeds were significantly younger, more likely to be white, taller, self-report better health, and to have lower BMI and waist-hip ratio (Table 1). Women with faster walking speeds were also less likely to be hypertensive, present smokers, under treatment for diabetes or high cholesterol, or to have a history of arthritis or coronary heart disease. Additionally, faster walking speeds were associated with present use of hormones, increased number of chair stands, and higher grip strengths.

In unadjusted models, slower walking speed was a significant predictor of incident ischemic stroke (Table 2). Compared with the fastest walk speed tertile, the HR (95% CI) for incident ischemic stroke was 1.53 (1.09, 2.14) for the second tertile of walking speed and 2.49 (1.81, 3.42) for the slowest walking speed tertile. Adjustment for age and race attenuated the association between walking speed and ischemic stroke; however, even after additional multivariate adjustment (full model) the hazard for incident ischemic stroke remained statistically significant for the slowest walking speed tertile compared to the fastest walking speed tertile (HR=1.69, 95% CI: 1.21, 2.36; *P* for trend= $<0.01$ ). The Figure depicts the cumulative hazards for the full model with the number of women at risk at each time point. Other variables in the full model with significant or borderline significant associations with ischemic stroke include: age (HR=1.07, 95% CI: 1.05 to 1.10), hypertension (HR=1.39, 95% CI: 0.99 to 1.96), systolic blood pressure (HR=1.02, 95% CI: 1.01 to 1.03), history of CHD (HR=1.40, 95% CI: 0.98 to 2.01), and prevalent diabetes (HR=1.70, 95% CI: 1.07 to 2.70).

Additional adjustment for other physical functioning variables (grip strength and chair stands) did not change the association between walking speed and ischemic stroke significantly (Table 2). However, number of chair stands was an independent predictor of ischemic stroke, with an increased risk of stroke in the range of HR=1.4 to 1.6 comparing the bottom 3 quartiles to the highest (referent) quartile ( $>7.5$  chair stands in 15 seconds). Hand grip strength was not associated with risk of incident ischemic stroke (data not shown).

Adjustment of the full model for physical activity, activities of daily living or cognitive function limited the sample size, however the results were not significantly affected (adjustment for physical activity: tertile 3 versus tertile 1: HR=1.63, 95% CI: 1.08, 2.47, *P* for trend=0.02; adjustment for activities of daily living tertile 3 versus tertile 1: HR=1.55, 95% CI: 1.01, 2.39, *P* for trend=0.04; cognitive function tertile 3 versus tertile 1: HR=1.41, 95% CI 0.67, 3.11, *P* for trend=0.14).

## Discussion

Among more than 13 000 postmenopausal women in the WHI, slower walking speeds at baseline were associated with higher risk of incident ischemic stroke. In multivariate analyses, compared to women in the fastest tertile of walking speed, those with walking speeds in the second tertile (1.06m/s to 1.24 m/s) had a 29% increase in incident ischemic stroke risk (95% CI: 0.92 to 1.82), and those in the slowest

**Table 1. Baseline Characteristics of WHI Participants Without Prior Stroke at Baseline, by Walking Speed**

	Walking Speed (meters per second)						P Value
	Tertile 1 (faster: >1.24 m/s)		Tertile 2 (1.06 m/s–1.24 m/s)		Tertile 3 (slower: <1.06 m/s)		
	n	Mean (SD) or %	n	Mean (SD) or %	n	Mean (SD) or %	
Age, y	4928	63.5 (7.2)	4907	65.0 (7.1)	4905	67.2 (6.7)	<0.001
Race/ethnicity							<0.001
White	4529	91.9	4401	89.7	3985	81.2	
Black	175	3.6	294	6.0	589	12.0	
Hispanic	100	2.0	108	2.2	184	3.8	
Other/Unknown	124	2.5	104	2.1	147	3.0	
Self-reported General Health							<0.001
Excellent	1102	22.6	828	17.0	450	9.3	
Very good	2275	46.6	2062	42.3	1708	35.3	
Good	1330	27.2	1669	34.3	1986	41.0	
Fair	172	3.5	296	6.1	646	13.3	
Poor	5	0.1	14	0.3	55	1.1	
Smoking							0.001
Never smoked	2617	53.5	2502	51.4	2475	51.2	
Past smoker	1971	40.3	2038	41.9	1973	40.8	
Current smoker	301	6.2	325	6.7	388	8.0	
Depression	352	7.3	433	9.0	554	11.6	<0.001
History of arthritis	2037	42.5	2257	47.1	2747	57.6	<0.001
History of Parkinson disease	5	0.2	7	0.3	13	0.4	0.32
History of CHD	286	5.8	396	8.1	603	12.3	<0.001
Hypertension	1565	31.8	1834	37.4	2386	48.6	<0.001
Treated diabetes	114	2.3	173	3.5	329	6.7	<0.001
High cholesterol requiring pills	339	14.3	398	16.0	515	17.3	0.01
Aspirin use	923	18.7	916	18.7	945	19.3	<0.001
NSAID use	872	17.7	1008	20.5	1187	24.2	<0.001
Hormone use							<0.001
Never used	2379	48.3	2432	49.6	2612	53.3	
Past user	896	18.2	917	18.7	1016	20.7	
Current user	1649	33.5	1555	31.7	1276	26.0	
Repeated chair stands	4882	7.6 (1.9)	4823	6.9 (1.7)	4609	6.2 (1.7)	<0.001
Quartile 1: ≤5.5	634	13.0	1138	23.6	1950	42.3	
Quartile 2: 6.0 to 6.5	1035	21.2	1287	26.7	1206	26.2	
Quartile 3: 7.0 to 7.5	1205	24.7	1156	24.0	812	17.6	
Quartile 4: >7.5	2008	41.1	1242	25.8	641	13.9	
Handgrip strength, kg	4910	25.9 (5.8)	4898	24.8 (5.7)	4882	23.2 (5.9)	<0.001
Quartile 1: ≤20.5	870	17.7	1074	21.9	1616	33.1	
Quartile 2: 21 to 24	1107	22.5	1274	26.0	1297	26.6	
Quartile 3: 24.5 to 28	1296	26.4	1298	26.5	1106	22.7	
Quartile 4: >28	1637	33.3	1252	25.6	863	17.7	
Height, cm	4911	162.2 (6.3)	4881	161.6 (6.5)	4882	160.4 (6.4)	<0.001
Body mass index, kg/m <sup>2</sup>	4909	27.0 (4.8)	4874	28.0 (5.2)	4876	29.9 (6.0)	<0.001
Waist-hip ratio	4915	0.80 (0.08)	4886	0.81 (0.08)	4885	0.83 (0.08)	<0.001
Physical activity, kcal/week	2508	14.5 (15.0)	2640	12.0 (12.9)	3089	8.9 (11.2)	<0.001
Activities of daily living score (4–12)	2258	4.02 (0.19)	2402	4.02 (0.23)	2875	4.04 (0.24)	0.01
Cognitive function score (0–100)	662	95.7 (3.9)	680	95.1 (4.5)	909	94.1 (5.4)	<0.001

(Continued)

Table 1. Continued

	Walking Speed (meters per second)						P Value
	Tertile 1 (faster: >1.24 m/s)		Tertile 2 (1.06 m/s–1.24 m/s)		Tertile 3 (slower: <1.06 m/s)		
	n	Mean (SD) or %	n	Mean (SD) or %	n	Mean (SD) or %	
Systolic blood pressure, mm Hg	4928	126.8 (17.3)	4907	129.2 (17.4)	4905	132.8 (18.2)	<0.001
Diastolic blood pressure, mm Hg	4927	75.1 (9.0)	4905	75.3 (9.2)	4901	75.5 (9.4)	0.13

Depression measured by the shortened CES-D. History of CHD includes history of myocardial infarction, angina, congestive heart failure, peripheral arterial disease, or revascularization at baseline.

Repeated Chair Stands: # of chair rises able to be performed in 15 seconds (mean of 2 measures).

Handgrip Strength: hydraulic hand grip dynamometer measure of dominant hand (mean of 2 measures).

Physical Activity: total expenditure of weekly recreational activity from self-report.

Activities of Daily Living Score: sum of the amount of help (no help, some help, totally dependent) needed to eat, dress and undress, get in and out of bed, and take a bath or shower.

Cognitive Function Score: modified mini-mental status examination (3MSE).

m/s indicates meters per second; SD, standard deviation; CHF, congestive heart failure; MI, myocardial infarction; PAD, peripheral arterial disease; NSAID, nonsteroidal antiinflammatory drug.

tertile (<1.06 m/s) had a 69% increased incident ischemic stroke risk (95% CI: 1.21 to 2.36). This relationship persisted after adjustment for other tests of physical performance and was not affected by exclusion of women with baseline disease that may have affected walking ability or speed, or those who had exceptionally slow walking speeds. Notably, the strength of the association of walking speed with incident ischemic stroke in this group of women is independent of and comparable, if not stronger, to established risk factors for stroke, including hypertension and diabetes.

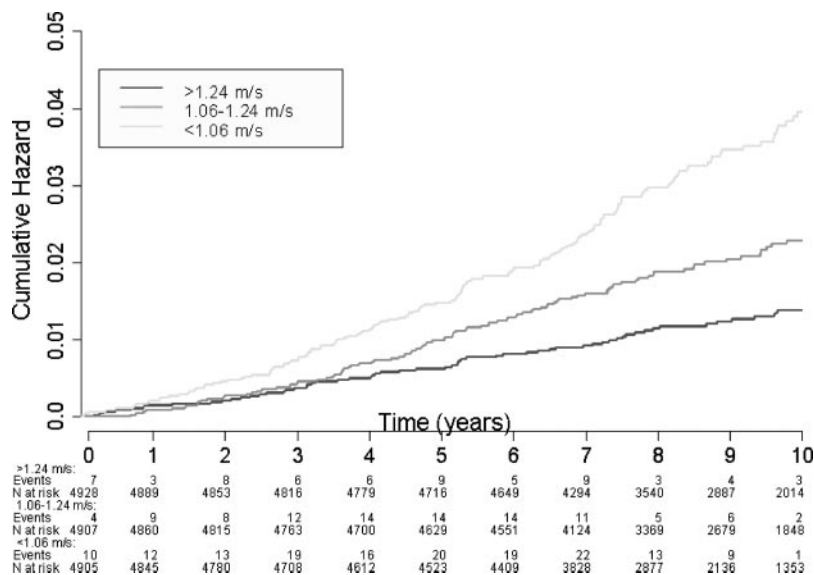
Stroke is one of the leading causes of death and disability,<sup>13</sup> and improved ability to identify subjects at risk would be valuable for prevention and early treatment, especially among older adults. Our findings confirm those of others suggesting that slow walking speed is a preclinical marker that identifies older adults at high risk for stroke. Time to walk 15 feet was directly related to risk of incident stroke<sup>11</sup> and to the risk of death attributable to incident stroke,<sup>12</sup> among men and women in the CHS. It is fundamental to confirm the findings from CHS in a separate population, such as the WHI, to

Table 2. Hazard Ratios (95% Confidence Intervals) for the Association Between Walking Speed and Risk of Incident Ischemic Stroke

	Walking Speed (meters per second)			P Trend
	Tertile 1 (faster: >1.24 m/s)	Tertile 2 (1.06 to 1.24)	Tertile 3 (slower: ≤1.06 m/s)	
#Strokes/#censored	57/4433	84/4339	123/4012	
Unadjusted				
HR	1	1.53	2.49	
95% CI	(reference)	(1.09, 2.14)	(1.81, 3.42)	<0.0001
Age and race/ethnicity adjusted				
HR	1	1.36	1.92	
95% CI	(reference)	(0.97, 1.94)	(1.41, 2.69)	<0.0001
Multivariate* adjusted				
HR	1	1.29	1.69	<0.01
95% CI	(reference)	(0.92, 1.82)	(1.21, 2.36)	
Multivariate* adjusted plus grip strength, chair stands				
HR	1	1.25	1.63	<0.01
95% CI	(reference)	(0.89, 1.77)	(1.16, 2.30)	

\*Multivariate adjustment variables include: age, race/ethnicity, body mass index, waist-hip ratio, depression, arthritis, hypertension, smoking, systolic blood pressure, history of coronary heart disease (myocardial infarction, angina, congestive heart failure, peripheral arterial disease, or revascularization), treated diabetes at baseline, hormone use, NSAID use, aspirin use, and self-reported general health.

NOTE: All models are stratified within the model by clinical trial component (estrogen+progestin active, estrogen-alone active, hormone therapy placebo, clinical trial participant not randomized to hormone therapy trial) or observational study to account for the fact that stroke incidence rates may have varied among these populations.



**Figure.** Cumulative hazards for ischemic stroke by tertile of walking speed.

suggest a simple, clinically relevant approach to identifying older persons at high risk for strokes. Notably, this population was limited to postmenopausal women and had a younger age distribution (mean age 65 years) than did the CHS (mean age 73 years).

Several studies have reported that subclinical white matter alterations, brain infarcts, and measures of ventricular enlargement detected on brain MRI are associated cross-sectionally with measures of lower extremity performance, including walking speed.<sup>7,8,23</sup> A more recent study has assessed this association both cross-sectionally and longitudinally, and showed that increasing severity of common subclinical brain MRI abnormalities was associated with greater rate of walking speed decline.<sup>24</sup> We hypothesize that slower walking speeds among high-functioning older adults may be the consequence of brain infarcts or subclinical white matter alterations that fail to cause symptoms or signs that are clinically recognized as stroke. Thus, using slow walking speeds among the elderly as a proxy for underlying subclinical cerebral manifestations may help identify those at risk for overt stroke in the future.

Studies have also shown that balance and gait dysfunction is associated with gradual onset of white matter disease.<sup>25</sup> This is in concordance with our finding of chair stands, a measure of balance, as an independent predictor of ischemic stroke, with fewer chair stands associated with increased risk of stroke.

It is important to note that there is the possibility for misclassification bias resulting from underreporting of strokes in this study because potential outcomes are identified primarily through self-report by the study participants. We used the National Death Index to search for otherwise unreported deaths and to ascertain causes of death. Furthermore, an attempt is made to obtain information on any outcomes occurring between the participant's last routine contact and her date of death through third party proxies (family members or other contacts given by the participant at baseline study visit). Lastly, the percentage of women in this sample who were lost to follow-up (1.2%) or stopped

follow-up (3.2%) was minimal, thus every effort has been made to minimize bias introduced by misclassification of stroke in this study. Nonhospitalized strokes were not captured in our case identification method, which is a limitation.

In summary, slow walking speed was found to be a strong predictor of increased risk of incident ischemic stroke among postmenopausal women in this study. We found that this association persisted after multivariate adjustment for known stroke risk factors, including diabetes and hypertension, variables associated with walking speed, and other physical functioning variables. Thus, the present study supports prior research that slow walking speed is an independent risk factor for identifying older women with incident ischemic stroke, suggesting a clinically relevant approach to identifying older women at high risk for strokes; however, further investigations should evaluate the discriminatory ability of walking speed as a predictor of stroke.

## Appendix

### Participating WHI Investigators and Institutions

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**Disclosures**

None.

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