Trajectories in Leisure-Time Physical Activity and Risk of Stroke in Women in the California Teachers Study

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Background and Purpose—Whether changes in leisure-time physical activity (LTPA) over time are associated with lower risk of stroke is not well established. We examined the association between changes in self-reported LTPA 10 years apart, with risk of incident stroke in the CTS (California Teachers Study). We hypothesized that the risk of stroke would be lowest among those who remained active.

Methods—Sixty-one thousand two hundred and fifty-six CTS participants reported LTPA at 2 intensity levels (moderate and strenuous activity) at 2 time points (baseline 1995–96; 10-year follow-up 2005–2006). LTPA at each intensity level was categorized based on American Heart Association (AHA) recommendations (moderate, >150 minutes/week; strenuous, >75 minutes/week). Changes in LTPA were summarized as follows: (1) not meeting recommendations at both time points; (2) meeting recommendations only at follow-up; (3) meeting recommendations only at baseline; and (4) meeting recommendations at both time points. Incident strokes were identified through California state hospitalization records. Using multivariable Cox models, we examined the associations between changes in LTPA with incident stroke.

Results—Nine hundred and eighty-seven women were diagnosed with stroke who completed both questionnaires. Meeting AHA recommendations at both the time points was associated with a lower risk of all stroke (adjusted hazard ratio, 0.84; 95% confidence interval, 0.72–0.98). The protective effects for stroke were driven by meeting AHA recommendations for moderate activity and largely observed for ischemic strokes (adjusted hazard ratio, 0.70; 95% confidence interval, 0.55–0.88).

Conclusions—Meeting AHA recommendations for moderate activity had a protective effect for reducing ischemic stroke risk. Participants who met AHA recommendations at baseline but not at follow-up, however, were not afforded reduced stroke risk. **(*Stroke*. 2017;48:2346-2352. DOI: 10.1161/STROKEAHA.117.017465.)**

Key Words: epidemiology ■ exercise ■ hospitalization ■ risk ■ stroke prevention

Engaging in leisure-time physical activity (LTPA) has been consistently associated with a lower risk of stroke and cardiovascular disease.[1] As part of the American Heart Association (AHA)'s Life's Simple 7, engaging in at least 150 minutes of moderate intensity or 75 minutes per week of vigorous activity is recommended.[2] Several investigators who have examined the protective effect of LTPA on stroke have focused on single measurements of self-reported LTPA usually during mid-adulthood, with follow-up times ranging from 1 to 30 years.[3–9] There are several limitations of those prior analyses, however, including single measures of LTPA and incomplete ascertainment of stroke cases. A measurement of an exposure over several time epochs may provide more complete information about how protective or deleterious that exposure is.[10] For example, the cardiovascular effect of tobacco use is influenced in studies by whether participants are current, former, or never smokers and their pack-year history exposure.[11] Similarly, the patterns of LTPA that individuals engage in are not static but may change over time—some may engage in more activity as they age, while most tend to decline in the intensity and time spent on LTPA.[12] The degree to which changes in LTPA over the lifetime, such as sustained activity over a lifetime versus increasing activity in adulthood, influence the risk of stroke has not been well explored.

Here, we examined the association of self-reported LTPA measured at 2 time intervals, 10 years apart, with risk of stroke in the CTS (California Teachers Study) cohort, a large prospective cohort of female teachers and administrators in the state of California. We hypothesized that the risk of stroke would be highest among those who did not exercise in either time interval and that the effect would, thus, be smaller in magnitude but still present in those who transitioned from active to inactive over 2 time points.

Received March 24, 2017; final revision received July 18, 2017; accepted July 20, 2017.

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The online-only Data Supplement is available with this article at http://stroke.ahajournals.org/lookup/suppl/doi:10.1161/STROKEAHA.117.017465/-/DC1.

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Methods

Study Population

Details on recruitment of the CTS have been previously published.[13] In brief, the CTS is a prospective study established in 1995, comprising 133 479 current and retired female teachers and administrators who were active members of the California State Teachers Retirement System. Women were excluded if they were not residents of California at baseline (n=8866), had a prior history of stroke by self-report (n=1587) or California Office of Statewide Health Planning and Development diagnosis (97), were <26 years or >99 years old (n=1145), or had missing or invalid physical activity data (n=970). Of the 120 814 eligible CTS participants identified at baseline, 61 256 participants had complete physical activity data at both baseline (1995–96) and follow-up (2005–06) and comprised our final study population (Figure I in the online-only Data Supplement).

Data Collection

Baseline LTPA was obtained using a questionnaire outlining time spent and intensity of exercise (categorized as moderate or strenuous) performed during a typical week. Examples were provided regarding activities that could be categorized as moderate (brisk walking, golf, among others) or strenuous (swimming, aerobics, running) intensity. The questionnaire was first mailed out at enrollment in 1995, and the LTPA section was then repeated in the 2005 to 2006 follow-up questionnaire. Participants reported their mean hours per week and months per year (1–3, 4–6, 7–9, and 10–12 months) of participation at each level of activity in the past 3 years. For each intensity level, we created mean annual hours using per week for each period by multiplying the hours per week by the portion of the year engaged in the activity and calculated hours per week in which moderate or strenuous activity was engaged.[14] We dichotomized these measures by the AHA recommendations for ideal cardiovascular health (either 150 minutes/week for moderate activity or 75 minutes/week for strenuous activity). These categorical variables were used as the LTPA definition in our multivariate regression analyses.

In addition, we collected information on relevant stroke risk factors in the baseline questionnaire, including information on race/ethnicity, smoking history, alcohol consumption, hormone replacement therapy use, and history of hypertension and diabetes mellitus. Body mass index was calculated using self-reported measurements as weight in kilograms divided by height in meters squared. We used *International Classification of Diseases* Ninth Revision (ICD-9) codes 272.xx in California Office of Statewide Health Planning and Development through 1997 to capture hyperlipidemia at baseline. Socioeconomic status was estimated using baseline residential addresses that were geocoded to a 1990 census block group based on occupation, education, and income.

Stroke was defined as the following: incident total stroke, ischemic stroke, hemorrhagic stroke, and fatal stroke. Participants were identified through linkage with the California Office of Statewide Health Planning and Development hospital discharge database (http://www.oshpd.ca.gov/), the California state mortality file, and the National Death Index between 1995 and 2012, using the ICD-9, Clinical Modification. Stroke was defined as a hospitalization or death with an ICD-9, Clinical Modification code of 430, 431, 432.x (excluding 432.1), 433.x1, 434.xx (excluding 434.x0), or 436 in the principal diagnosis position only. Ischemic stroke was defined as hospitalization or death with ICD-9, Clinical Modification codes 433.x1, 434.xx (excluding 434.x0), or 436. Hemorrhagic stroke was defined as hospitalization or death with ICD-9, Clinical Modification codes 430, 431, or 432. These definitions were previously validated in the CTS based on expert neurologist reviews. (S.S. Wang, et al, unpublished data, submitted).

The study was approved by the institutional review boards at the City of Hope, University of Southern California, University of California at Irvine, and the Cancer Prevention Institute of California.

Statistical Analysis

Baseline characteristics of the cohort by change in LTPA were compared using χ^2 for categorical and *t* tests for continuous variables. For each stroke outcome (total, ischemic, hemorrhagic, and fatal separately), we examined the association of LTPA with incident stroke using Cox proportional hazards models, excluding event occurring before the second LTPA assessment. To examine how changes in LTPA are associated with incident stroke (total, ischemic, hemorrhagic, and fatal), we first examined the association of the single measure of LTPA obtained at the follow-up questionnaire (2005–2006) with subsequent stroke. Our primary analyses then examined changes in LTPA between the 2 questionnaires with risk of ischemic stroke. Specifically, we define 4 LTPA subgroups for each exercise patterns (moderate, strenuous, and moderate/strenuous), namely, not meeting recommendation at both time points (reference group), not meeting recommendation at baseline but meeting recommendation at follow-up (positive change), meeting recommendation at baseline but not at follow-up (negative change), and meeting recommendation at both times (high physical activity). The time scale (in days) was defined from age at enrollment to age at either incident stroke, death, a move out of California (for >3 months) or December 31, 2012, whichever came first. Cox proportional hazard models were stratified by age at baseline (in years) to adjust for calendar effects and adjusted for demographic risk factors (race–ethnicity, socioeconomic status), behavioral risk factors (tobacco use, alcohol use, body mass index), and clinical risk factors (hypertension, diabetes mellitus, dyslipidemia). We conducted sensitivity analyses using multiple imputation to assess the impact of missing physical activity data at follow-up. Analyses were done in SAS using PROC MI and PROC MIANALYZE, using 20 imputed data sets. Imputations were created using covariates (age, smoking status, race, diabetes mellitus, hypertension), the outcome (stroke), and all available physical activity measurements.

All statistical analyses were conducted using SAS v9.3 (Cary, NC) and R.

Results

Baseline Demographics

Table 1 outlines the baseline characteristics of all eligible participants by change in LTPA status. The mean age was 53±14 years, 88% were non-Hispanic White, and 79% had above median socioeconomic status. One third of participants reported meeting AHA-recommended physical activity at both time periods, with the majority because of meeting moderate activity guidelines. Characteristics of this study population included a low proportion of cardiovascular disease risk factors (<3% diabetic, 18% hypertensive). However, we note a few differences between those with and without the second LTPA assessment; those with missing data for the second visit were slightly older at study enrollment and had a slightly higher proportion of hypertension and current alcohol use as reported in their baseline questionnaire (Table I in the online-only Data Supplement); changes in LTPA are outlined in Table II in the online-only Data Supplement.

Association Between Stroke and LTPA Measured at 10-Year Follow-Up

The association of LTPA assessed at the second questionnaire with risk of stroke is outlined in Table 2. Engaging in moderate intensity activity was associated with a lower risk of all stroke, a result driven by a reduced risk of ischemic strokes. Specifically, engaging in at least 150 minutes per week of moderate activity versus not was associated with a lower risk of stroke (model 3: adjusted hazard ratio [HR], 0.84; 95%

Table 1. Baseline Characteristics of the California Teachers Study by Change in PA Status, Defined by Strenuous or Moderate Physical Activity From 1995–1996 to 2005–2006

	Participants With Physical Activity Data at Follow-Up (2005–06); (n=61 256); N (%)	Below AHA-Recommended PA Levels at Both Time Periods; (n=18 781); N (%)	Below AHA-Recommended PA Levels in 1995–96 to Meeting in 2005–06; (n=11 498); N (%)	Meeting AHA-Recommended PA Levels in 1995–96 and Below in 2005–06; (n=8609); N (%)	Meeting AHA-Recommended PA Levels at Both Time Periods; (n=22 368); N (%)
Age, y	52 (26–94)	51 (26–93)	51 (26–87)	52 (26–94)	52 (26–89)
Race/ethnicity					
White	54 023 (88)	16 140 (86)	10 001 (87)	7646 (89)	20 236 (90)
Black	1264 (2)	509 (3)	251 (2)	156 (2)	348 (2)
Hispanic	2280 (4)	828 (4)	481 (4)	323 (4)	648 (3)
Asian/Pacific Islander	2250 (4)	886 (5)	492 (4)	265 (3)	607 (3)
Other/missing	1439 (2)	418 (2)	273 (2)	219 (3)	529 (2)
SES					
Below median	11 940 (19)	4306 (23)	2204 (19)	1762 (21)	3668 (17)
Above median	48 591 (79)	14 266 (77)	9163 (81)	6735 (79)	18 427 (83)
Hypertension	11 092 (18)	4090 (22)	1936 (17)	1731 (20)	3335 (15)
Diabetes mellitus	1272 (2)	571 (3)	227 (2)	230 (3)	325 (1)
Hyperlipidemia	567 (1)	217 (1)	82 (1)	102 (1)	166 (1)
Body mass index, kg/m^2					
<20	6366 (10)	1626 (9)	1182 (11)	829 (10)	2729 (13)
20–<25	30 434 (50)	7750 (43)	5578 (50)	4148 (50)	12 958 (60)
25–<30	14 840 (24)	5124 (28)	2828 (25)	2313 (28)	4575 (21)
30+	7778 (13)	3687 (20)	1561 (14)	1063 (13)	1467 (7)
Tobacco use					
Current	2422 (4)	889 (5)	473 (4)	341 (4)	719 (3)
Former	17 667 (29)	4845 (26)	3163 (28)	2479 (29)	7180 (32)
Never	40 924 (67)	12 973 (69)	7807 (68)	5750 (67)	14 394 (65)
Alcohol use					
Current	40 152 (66)	11 109 (63)	7454 (68)	5660 (70)	15 929 (75)
Former	7125 (12)	2394 (14)	1360 (13)	1041 (13)	2330 (11)
Never	10 723 (18)	4188 (24)	2058 (19)	1442 (18)	3035 (14)
Hormone replacement therapy					
Current	23 564 (39)	6911 (37)	4631 (40)	3061 (36)	8961 (40)
Former	6646 (11)	2125 (11)	1121 (10)	1111 (13)	2289 (10)
Never	30 884 (50)	9699 (52)	5718 (50)	4404 (51)	11 063 (50)

Below AHA-recommended levels of physical activity for stroke prevention defined as <150 min/wk moderate activity and <75 min/wk strenuous activity; meeting or exceeding AHA-recommended levels: ≥150 min/wk moderate or 75 min/wk strenuous activity. AHA indicates American Heart Association; PA, physical activity; and SES, socioeconomic status.

confidence interval [CI], 0.73–0.96). Engaging in >75 minutes of strenuous activity was not statistically significantly associated with a lower risk of stroke (model 3: adjusted HR, 0.91; 95% CI, 0.77–1.07). The reduced stroke risk was largely driven by ischemic stroke risk, where meeting recommendations for AHA moderate activity resulted in nearly 20% decrease in risk (model 3: HR, 0.82; 95% CI, 0.70–0.96). Results are consistent when using baseline LTPA data (Table III in the online-only Data Supplement).

Association Between Stroke and Changes in LTPA Between Baseline and 10-Year Follow-Up

The primary outcome of interest in this analysis was incident strokes occurring after the follow-up questionnaire in 2005–2006 (Table 3). In all, there were 987 strokes (mean age of onset, 81 years), with 709 ischemic (mean age at onset, 81 years) and 221 hemorrhagic strokes (mean age at onset, 78 years). Of these, 247 were fatal strokes. The mean follow-up time after the second questionnaire was 6.5 years. In adjusted

Table 2. Risk Association (Hazard Ratio and 95% Confidence Interval) of Strenuous and Moderate Physical Activity, Dichotomized According to AHA Recommendations for Moderate (>150 min/wk) and Strenuous (>75 min/wk) Activity, Reported in 2005–2006 With Total, Ischemic, and Hemorrhagic Stroke and Stroke Mortality

Physical Activity	Total Stroke (n=987)	Ischemic Stroke (n=709)	Hemorrhagic Stroke (n=221)	Fatal Stroke (n=247)
Model 1: moderate activity				
≤150 min/wk	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
>150 min/wk	0.80 (0.70–0.91)*	0.77 (0.66–0.90)*	0.92 (0.70–1.21)	0.64 (0.48–0.84)*
Model 1: strenuous activity				
≤75 min/wk	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
>75 min/wk	0.88 (0.75–1.04)	0.85 (0.70–1.04)	0.95 (0.68–1.31)	0.94 (0.67–1.31)
Model 1: moderate/strenuous				
Neither recommendation met	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Either recommendation met	0.78 (0.69–0.89)*	0.77 (0.66–0.89)*	0.85 (0.65–1.11)	0.71 (0.55–0.93)*
Model 2: moderate activity				
≤150 min/wk	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
>150 min/wk	0.82 (0.72–0.94)*	0.80 (0.68–0.94)*	0.93 (0.70–1.22)	0.64 (0.48–0.85)*
Model 2: strenuous activity				
≤75 min/wk	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
>75 min/wk	0.90 (0.76–1.06)	0.87 (0.72–1.07)	0.96 (0.69–1.33)	0.93 (0.66–1.31)
Model 2: moderate/strenuous				
Neither recommendation met	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Either recommendation met	0.81 (0.71–0.93)*	0.80 (0.69–0.94)*	0.86 (0.65–1.13)	0.71 (0.55–0.93)*
Model 3: moderate activity				
≤150 min/wk	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
>150 min/wk	0.84 (0.73–0.96)*	0.82 (0.70–0.96)*	0.93 (0.70–1.23)	0.65 (0.49–0.87)*
Model 3: strenuous activity				
≤75 min/wk	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
>75 min/wk	0.91 (0.77–1.07)	0.89 (0.73–1.08)	0.96 (0.69–1.33)	0.95 (0.68–1.33)
Model 3: moderate/strenuous				
Neither recommendation met	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Either recommendation met	0.83 (0.73–0.94)*	0.82 (0.70–0.96)*	0.86 (0.65–1.13)	0.73 (0.56–0.95)*

Model 1: adjusted for age; model 2: model 1+adjusted for race, socioeconomic status, tobacco use, alcohol use, body mass index; model 3: model 2+adjusted for hypertension, diabetes mellitus, hyperlipidemia. AHA indicates American Heart Association.

analyses, we found that participants who did not meet AHA recommendations for LTPA at baseline but did meet AHA recommendations in follow-up had reduced risk of stroke (adjusted HR, 0.79; 95% CI, 0.65–0.97). Interestingly, this magnitude of risk was similar to that of participants who met AHA recommendations at both baseline and follow-up (adjusted HR, 0.84; 95% CI, 0.72–0.98). Notably, the reduced risks were significant only for moderate activity and ischemic stroke (adjusted HR, 0.78; 95% CI, 0.69–1.00). Participants who met AHA recommendations at baseline but did not meet recommendations in follow-up did not benefit from reduced stroke risk. Further, evaluation of LTPA in early adulthood (teenage years and early 20s) also did not affect stroke risk (data not shown), further supporting the notion that more recent moderate activity measured in adulthood was the relevant activity that offered benefits for reduced stroke risk. Because of the loss to follow-up, we performed imputation for missing data to examine whether the associations between change in LTPA was still associated with risk of stroke. Our results were similar, indicating a low likelihood that loss to follow-up biased our results (Table IV in the online-only Data Supplement).

Discussion

In the CTS, a prospective cohort designed to study risk factors for cancer but with a validated stroke adjudication process, we found that meeting AHA guidelines of moderate physical activity was associated with a lower risk of stroke, specifically ischemic stroke. Conversely, we did not detect an association between meeting AHA guidelines for strenuous activity and risk of risk. Several investigators have demonstrated a consistent association of LTPA with reduced risk of

Table 3. Risk Estimates for Total, Ischemic, Hemorrhagic, and Fatal Strokes by Exercise Patterns in Moderate, Strenuous, and Strenuous/Moderate Physical Activity Among 61 256 Women With Physical Activity Measurements in 1995–1996 and 2005–2006

	All Stroke, HR (95% CI)	Ischemic, HR (95% CI)	Hemorrhagic, HR (95% CI)	Fatal, HR (95% CI)
Exercise pattern*: moderate				
Recommendations not met at both time-points	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Not meeting recommendations at baseline but meeting recommendations in follow-up	0.73 (0.60–0.89)†	0.70 (0.55–0.88)†	0.76 (0.50–1.14)	0.65 (0.43–0.99)†
Meeting recommendations at baseline but not meeting recommendations in follow-up	0.96 (0.80–1.14)	0.94 (0.77–1.16)	1.00 (0.68–1.48)	0.97 (0.69–1.35)
Meeting recommendations at both time points	0.88 (0.74–1.05)	0.87 (0.71–1.07)	1.06 (0.75–1.50)	0.62 (0.43–0.90)†
Exercise pattern*: strenuous				
Recommendations not met at both time points	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Not meeting recommendations at baseline but meeting recommendations in follow-up	0.91 (0.72–1.16)	0.89 (0.67–1.19)	0.94 (0.58–1.53)	0.74 (0.42–1.30)
Meeting recommendations at baseline but not meeting recommendations in follow-up	1.12 (0.94–1.33)	1.11 (0.91–1.36)	1.10 (0.76–1.58)	1.17 (0.84–1.64)
Meeting recommendations at both time points	0.95 (0.76–1.17)	0.91 (0.70–1.18)	1.00 (0.65–1.52)	1.17 (0.78–1.76)
Exercise pattern*: strenuous and moderate				
Recommendations not met at both time points	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Not meeting recommendations at baseline but meeting recommendations in follow-up	0.79 (0.65–0.97)†	0.78 (0.69–1.00)†	0.75 (0.49–1.15)	0.73 (0.47–1.13)
Meeting recommendations at baseline but not meeting recommendations in follow-up	1.00 (0.83–1.19)	1.01 (0.82–1.24)	0.93 (0.62–1.37)	1.08 (0.77–1.51)
Meeting recommendations at both time points	0.84 (0.72–0.98)†	0.84 (0.70–1.01)	0.88 (0.63–1.22)	0.76 (0.55–1.05)

CI indicates confidence interval; and HR, hazard ratio.
*Adjusted for age, race, socioeconomic status, tobacco use, alcohol use, body mass index, hypertension, diabetes mellitus, hyperlipidemia.

stroke, with the magnitude of the effect differing by mean age of the cohort, intensity, or total calories.[15] For example, in the Northern Manhattan Study, the highest levels of total LTPA, factoring in intensity and time, were associated with a lower risk of ischemic stroke.[9] In the Nurse's Health Study, moderate intensity activities, such as walking for exercise, were also associated with a lower risk of stroke.[16] Few analyses, however, have examined the association of changes in physical activity with risk of stroke. In considering >1 time point of LTPA, we found that more recent activity better reflects reduction in stroke risk. Participants who met AHA guidelines at baseline but not in follow-up did not benefit from the same reduction in stroke risk.

It is now recognized that risk factor status in individuals is not a static process, but rather a dynamic process rarely accounted for in analyses of LTPA at a single time point with stroke risk. Our finding lend further evidence to the recommendation that individuals should increase exercise as an effective lifestyle modification for reducing the risk of stroke.[1,2] These findings also support the concept that low exercise levels performed at younger ages are not sufficient to counteract the risk of cardiovascular disease in the future but will need to be modified later in adulthood to gain a survival and cardiovascular mortality benefit.[17]

The lack of an association of risk of stroke with change in strenuous activity was unexpected. One possibility is that there is no clear dose–response relationship with exercise, and similar to other CVD outcomes, moderate-intensity activity is sufficient to reduce risk.[1] The effect of moderate-intensity activity on cardiometabolic profiles, such as dyslipidemia, diabetes mellitus, and obesity, has been well documented.[12,18–20] Similar to other large cohort studies, an analysis of the National Walkers' Health Study[21] showed a lower risk in multiple cardiovascular disease outcomes with even modest levels of activity (1.8–3.6 MET-hours/d—equivalent to 1 hour of light walking per day). In those analyses, there was a similar magnitude of an effect in comparison to the higher level of activities (MET-hours/d >3.6) for reducing risk of stroke, congestive heart failure, and cardiovascular disease mortality. A notable exception was the substantial benefit in higher intensity activities on diabetes mellitus–related mortality (63.8% reduction for moderate and 90.8% reduction for the highest level).[22]

The mechanism by which exercise reduces the risk of stroke is likely multifactorial. The effect of exercise on improving dyslipidemia, hypertension, weight, and diabetes mellitus have been well established; this is likely to be an only partial explanation because in multiple studies, adjustment for these risk factors in multivariable models does not alter the protective effect of LTPA. The independent benefit of exercise is likely from improving vascular and endothelial health, reducing inflammation, improving sympathetic tone, and maintenance of cerebral autoregulation.[23]

Our study has several strengths, including a large sample size, multiple measure of LTPA, a validated stroke outcome

ascertainment process, long duration of follow-up, and information available on multiple confounders. Several weaknesses, however, require discussion. Though the sample size was large, the overall proportion of participants with stroke, particularly hemorrhagic, is small. Our results may, therefore, not be generalizable to the general population with a higher baseline risk of stroke. Similarly, only 30% of participants met guidelines for strenuous activity, and we have been underpowered to detect a difference in that group. On the other hand, individuals in their fourth to sixth decade of life (middle age) have had a continued increase in the incidence of stroke in yearly trends, and our finding provide at least one intervention that could ameliorate that. We unfortunately do not have data on changes in other risk factors, notably body mass index, which may have acted as a confounder in our analyses. Similarly, we did not have further details on important confounders at baseline, such as blood pressure and diabetes mellitus control markers. We had a significant proportion of participants who were lost to follow-up between the first and second assessment, which could be a source of selection bias. The baseline characteristics of those lost to follow-up showed small increase in baseline risk factors for stroke such that those without second assessment may have been more likely to have an outcome event. On the other hand, we would expect that these results would bias our results toward the null and, yet, still noted an effect with changes in LTPA. Furthermore, we performed imputation analysis among those lost to follow-up, and our results were fundamentally similar. We did not objectively collect LTPA with the use of accelerometers, with several studies reporting significant reporting biases with self-reported questionnaires.[24,25] Participants may also tend to over-report the amount of activity they perform, which may bias our results to the null. Though commercial activity monitors have been increasing in use, most individuals are counseled in clinical practice based on their reported activity. Finer details of LTPA, such as differing intensities and frequencies, may provide a more nuanced understanding on how these components in combination may reduce the risk of stroke and cardiovascular disease.[26,27]

Summary/Conclusions

In summary, we find that starting and sustaining moderate-intensity LTPA in mid to late adulthood was associated with a lower risk of stroke. Our findings emphasize the importance of behavioral interventions centered on lifestyle, such as prescribing exercise in those who are inactive, for preventing stroke. Future studies are required to understand components and patterns of LTPA that are most likely to reduce the risk of stroke, likely informed by objective measures of LTPA.

Sources of Funding

NIH HL111195 provided funding for Dr Cheung. The California Teachers Study was funded by NH CA077398. Dr Willey was funded by NIH K23 NS 073104.

Disclosures

None.

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Stroke
Journal of the American Heart Association

Trajectories in Leisure-Time Physical Activity and Risk of Stroke in Women in the California Teachers Study

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Stroke. 2017;48:2346-2352; originally published online August 9, 2017;
doi: 10.1161/STROKEAHA.117.017465
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0039-2499. Online ISSN: 1524-4628

Supplemental Material

Supplemental Table I: Comparison of CTS participant characteristics for whom long-term physical activity data is available at two time points (1995-96 and 2005-06), compared to participants with long-term physical activity data at study enrollment (1995-96) only.

	Participants with available LTPA data at enrollment (1995-96) n = 120,814		Participants with available LTPA data at follow-up (2005-06) n = 61,256	Participants without LTPA data at follow-up (2005-06) n=59,558
Age (years)	53 (+/- 14)		52 (+/- 12)	54 (+/- 16)
Race-ethnicity				
White	104749 (87)		54023 (88)	50726 (85)
Black	3212 (3)		1264 (2)	1948 (3)
Hispanic	5028 (4)		2280 (4)	2748 (5)
Asian/Pacific Islander	4230 (4)		2250 (4)	1980 (3)
Other	3595 (3)		1439 (2)	2156 (4)
SES				
Below median	25523 (21)		11940 (19)	13583 (23)
Above median	93744 (78)		48591 (79)	45153 (76)
Hypertension	24912 (21)		11092 (18)	13820 (23)
Diabetes	3335 (3)		1272 (2)	2063 (3)
Hyperlipidemia	1468 (1)		567 (1)	901 (2)
Body mass index (kg/m2)				
<20	12590 (10)		6366 (10)	6224 (10)
20-25	57922 (48)		30434 (50)	27488 (46)
25-30	28862 (24)		14840 (24)	14022 (24)
30+	16258 (14)		7778 (13)	8480 (14)
Tobacco use				
Current	6102 (5)		2422 (4)	3680 (6)
Former	34703 (29)		17667 (29)	17036 (29)
Never	79328 (66)		40924 (67)	38404 (64)
Alcohol use				
Current	75952 (63)		40152 (66)	35800 (60)
Former	14554 (12)		7125 (12)	7429 (12)
Never	21773 (18)		10723 (18)	11050 (19)
Hormone replacement therapy				
Current	42632 (35)		23564 (39)	19068 (32)
Former	14732 (12)		6646 (11)	8086 (14)
Never	62921 (52)		30884 (50)	32037 (54)

Supplemental table II: Changes in physical activity pattern over time

	Did not meet strenuous activity guidelines at follow up (n = 43970)	Met strenuous activity guidelines at follow up visit (n = 17286)
Did not meet moderate activity guidelines at follow up (n = 35474)	27390	8084
Met moderate activity guidelines at follow up (n = 25782)	16580	9202

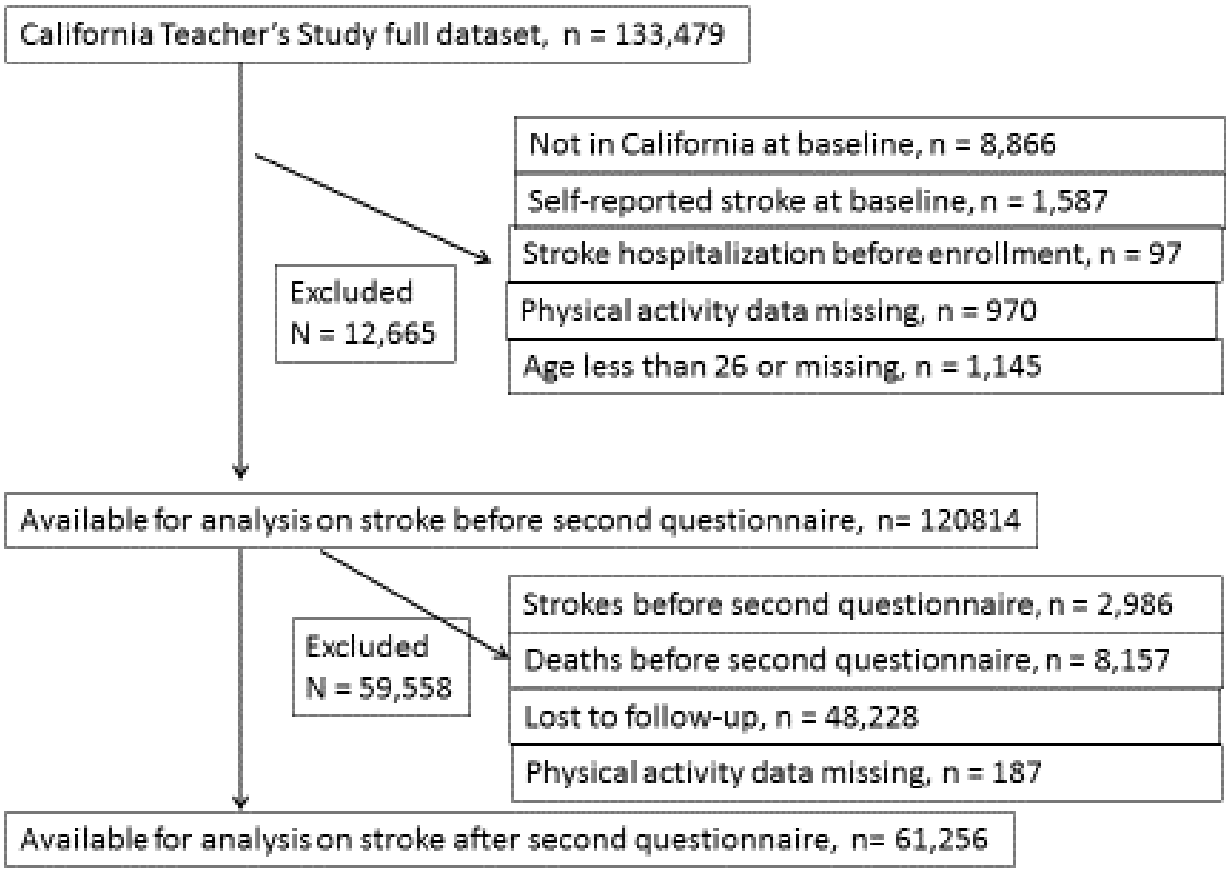
Supplemental Table III: Risk association (hazard ratio and 95% confidence interval) of strenuous and/or moderate physical activity at study enrollment (1995-96) with total, ischemic, and hemorrhagic stroke and fatal stroke (adjusted for age, race, SES, tobacco use, alcohol use, body mass index, hypertension, diabetes, hyperlipidemia).

Physical activity	**Total Stroke (n = 3,973)**	**Ischemic stroke (n = 2,808)**	**Hemorrhagic stroke (n = 812)**	**Fatal stroke (n = 1234)**
Moderate activity				
≤150 mins/week	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
>150 mins/week	**0.90 (0.84-0.96)**	**0.90 (0.83-0.98)**	0.96 (0.82-1.11)	**0.88 (0.77-1.00)**
Strenuous activity				
≤75 mins/week	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
>75 mins/week	0.99 (0.92-1.07)	0.96 (0.88-1.06)	1.06 (0.90-1.24)	0.97 (0.84-1.11)
Moderate/strenuous				
Neither recommendations met	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Either recommendation met	**0.89 (0.84-0.95)**	**0.88 (0.82-0.95)**	0.95 (0.82-1.09)	**0.88 (0.78-0.99)**

Supplemental Table IV: Risk association (hazard ratio and 95% confidence interval) of change in strenuous and/or moderate physical activity using imputation for missing physical activity assessment at follow up with total, ischemic, and hemorrhagic stroke and fatal stroke (adjusted for age, race, SES, tobacco use, alcohol use, body mass index, hypertension, diabetes, hyperlipidemia).

Physical activity	Total Stroke	Ischemic stroke	Hemorrhagic stroke	Fatal stroke
Exercise pattern* - Moderate				
Not met Q1 - Not met Q4	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Not met Q1 - Met Q4	**0.81 (0.70-0.94)**	**0.77 (0-64-0.93)**	0.81 (0.56-1.17)	0.84 (0.62-1.15)
Met Q1 - Not met Q4	0.97 (0.82-1.14)	0.96 (0.79-1.17)	1.01 (0.71-1.44)	1.01 (0.75-1.37)
Met Q1 - Met Q4	0.88 (0.77-1.01)	0.86 (0.73-1.01)	0.95 (0.71-1.29)	0.83 (0.62-1.10)
Exercise pattern* - Strenuous				
Not met Q1 - Not met Q4	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Not met Q1 - Met Q4	1.03 (0.86-1.23)	0.98 (0.78-1.23)	0.99 (0.66-1.49)	1.14 (0.81-1.60)
Met Q1 - Not met Q4	1.09 (0.93-1.28)	1.08 (0.91-1.31)	1.09 (0.80-1.53)	1.08 (0.80-1.48)
Met Q1 - Met Q4	1.04 (0.88-1.23)	0.99 (0.81-1.21)	1.06 (0.76-1.47)	1.21 (0.89-1.64)
Exercise pattern* - Stren+Mod				
Not met Q1 - Not met Q4	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Not met Q1 - Met Q4	0.92 (0.77-1.11)	0.92 (0.77-1.11)	0.92 (0.77-1.11)	0.92 (0.77-1.11)
Met Q1 - Not met Q4	0.98 (0.82-1.17)	0.98 (0.82-1.17)	0.98 (0.82-1.17)	0.98 (0.82-1.17)
Met Q1 - Met Q4	0.92 (0.78-1.08)	0.92 (0.78-1.08)	0.92 (0.78-1.08)	0.92 (0.78-1.08)

**Adjusted for age, race, socio-economic status, tobacco use, alcohol use, body-mass index, hypertension, diabetes, hyperlipidemia.*



Supplemental figure I: study flow of the California Teachers Study