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# Physical activity, but not body mass index, predicts less disability before and after stroke

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## ABSTRACT

**Objective:** To determine whether physical activity and body mass index (BMI) predict instrumental or basic activities of daily living (I/ADL) trajectories before or after stroke compared to individuals who remained stroke-free.

**Methods:** Using a prospective cohort, the Health and Retirement Study, we followed adults without a history of stroke in 1998 ( $n = 18,117$ ) for up to 14 years. We estimated linear regression models of I/ADL trajectories comparing individuals who remained stroke-free throughout follow-up ( $n = 16,264$ ), those who survived stroke ( $n = 1,374$ ), and those who died after stroke and before the next interview wave ( $n = 479$ ). We evaluated whether I/ADL trajectories differed by physical activity or BMI at baseline (before stroke), adjusting for demographic and socioeconomic covariates.

**Results:** Compared to those who were physically active, stroke survivors who were physically inactive at baseline had a lower probability of independence in ADLs and IADLs 3 years after stroke (risk difference =  $-0.18$  and  $-0.16$  for ADLs and IADLs, respectively). However, a similar difference in the probability of independence was also present 3 years before stroke, and we observed no evidence that physical activity slowed the rate of decline in independence before or after stroke. Unlike the results for physical activity, we did not observe a consistent pattern for the probability of independence in ADLs or IADLs comparing obese stroke survivors to normal-weight or to overweight stroke survivors 3 years before stroke or 3 years after stroke.

**Conclusions:** Physical inactivity predicts a higher risk of being dependent both before and after stroke. *Neurology*® 2017;88:1718-1726

## GLOSSARY

**ADL** = activities of daily living; **BMI** = body mass index; **CI** = confidence interval; **HRS** = Health and Retirement Study; **IADL** = instrumental activities of daily living.

Identifying modifiable factors that may ameliorate the functional consequences of stroke is a high research priority. Retrospective studies indicate that stroke patients who reported regular exercise before stroke onset have milder strokes or better functional outcomes after stroke.<sup>1-5</sup> Some evidence indicates that mortality risk is lower and functional outcomes are better among obese or overweight compared to normal-weight or underweight stroke patients,<sup>6-14</sup> although higher body mass index (BMI) increases the risk of ischemic stroke.<sup>15-20</sup>

Most prior research on the influence of prestroke physical activity and BMI on poststroke outcomes enrolled stroke survivors and retrospectively assessed prestroke characteristics. However, retrospective reports may be inaccurate,<sup>21</sup> and such designs cannot evaluate how functional status changed as a result of stroke, e.g., whether physical activity or prestroke BMI modifies the change in functioning associated with stroke onset. Additionally, these studies cannot examine functioning years before stroke to determine whether differences in poststroke functioning are driven by prestroke functioning. Prior research also could not compare functioning in stroke patients or

Supplemental data  
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those who later develop a stroke to functioning in healthy individuals. There is evidence that even years before stroke diagnosis, cerebrovascular processes may impair functioning.<sup>22</sup>

To determine whether physical activity and BMI predict disability trajectories before and after stroke compared to individuals who remain stroke-free, we compared instrumental activities of daily living (IADL) and activities of daily living (ADL) changes in a cohort with up to 12 years of follow-up on adults who were all stroke-free at baseline.

**METHODS** The Health and Retirement Study (HRS) is a nationally representative cohort of individuals >50 years old and their spouses.<sup>23,24</sup> For this study, we included individuals born between 1900 and 1947 who were interviewed in 1998; participants were interviewed biennially through 2012. We excluded 1,449 individuals with a history of stroke in 1998 and 305 respondents missing covariate information, which left 18,117 individuals for our analyses.

**I/ADL assessment.** At each biennial interview, participants or their proxy respondents were asked to report whether they had difficulty completing 5 ADLs (getting across a room, dressing, bathing, eating, getting in and out of bed) and 5 IADLs (taking medications as prescribed, grocery shopping, using the telephone, preparing meals, managing money) in the previous 30 days. Response options were “yes,” “no,” “don’t do,” or “refused.” We analyzed ADL and IADL limitations separately. We used the RAND version of the HRS data, focusing on binary indicator variables for any reported ADL limitation and any reported IADL limitation.<sup>25</sup> “Don’t do” and “refused” are treated as no limitation in the RAND coding. Our coding allows participants to become disabled and subsequently recover independence.

**Stroke assessment.** Stroke events were self- or proxy-reported at biennial interviews. During the interviews, respondents were asked, “Has a doctor ever told you that you had a stroke?” They were also asked for the month and year of stroke events. If a participant died or could not complete the interview, proxy respondents answered questions on stroke events. On the basis of the responses, we categorized participants as never stroke (no stroke during follow-up), stroke survivor (had a stroke and survived), or stroke decedent (had a stroke and did not survive to the next interview wave).

For the small number of respondents missing stroke month, we used the midpoint of the last known stroke-free date and the date when the stroke was first reported.<sup>22</sup> If a participant reported multiple strokes, only the first stroke was included in our analyses, and all follow-ups after the first stroke were defined as poststroke.

For each interview, we calculated the months until stroke date and the months since stroke date. We estimated the association between months until and months since stroke variables and I/ADL independence. We converted all coefficients to years to facilitate comparison with the rate of change in I/ADL independence among stroke-free participants per year of age.

**Modifiers.** We were interested in whether physical activity and BMI modify the association between stroke and I/ADL independence. At baseline in 1998, participants were asked, “On average over the last 12 months, have you participated in vigorous

physical activity or exercise 3 times a week or more? By vigorous physical activity, we mean things like sports, heavy housework, or a job that involves physical labor.” Participants were categorized as active (vigorous physical activity  $\geq 3$  times a week) or inactive (vigorous physical activity  $< 3$  times a week). In addition, participants were asked at baseline to report their current height and weight. This information was used to calculate the participant’s BMI, which was then categorized according to World Health Organization cut points: underweight ( $< 18.5$  kg/m<sup>2</sup>), normal weight (18.5–24.9 kg/m<sup>2</sup>), overweight (25–29.9 kg/m<sup>2</sup>), or obese ( $\geq 30.0$  kg/m<sup>2</sup>). There is a high correlation between self-reported and measured BMI in HRS ( $r = 0.921$ ,  $p \leq 0.0001$ ).<sup>26</sup> We present results of overweight and obese (reference group is normal weight); there were too few underweight respondents (2% of sample) to present their results.

**Covariates.** We considered the following covariates as assessed in 1998 as potential confounders: age (continuous), race (black, other, white), male sex, marital status (never married, divorced/separated, widowed, married), Southern birthplace (yes or no as defined by Census region), education (less than high school, General Education Development, high school, some college, college graduate), mother’s education (missing indicator,  $< 8$  or  $\geq 8$  years), per capita household wealth (quartiles), and number of comorbidities (0–8; includes high blood pressure, diabetes mellitus, cancer, lung disease, heart disease, stroke, psychiatric problems, and arthritis). Continuous variables were centered at the group mean. For categorical variables, the most prevalent group was used as the reference category. Our reference group was 75-year-old, white, married women who were not born in the South, whose mothers had  $\leq 8$  years of education, and who themselves had lowest-quartile household wealth, less than a high school education, and no comorbidities.

**Statistical analysis.** Although this was not our primary interest in this study, we first estimated risk differences for baseline physical activity and BMI categories on stroke incidence using linear models.

For our primary analysis of interest, we used linear regression to estimate I/ADL independence trajectories, estimating separate models for ADL and IADL independence. We adjusted all models for the covariates described above. Coefficients are interpreted as differences in the probability of being independent associated with each risk factor (risk differences). When describing the association between our modifiers and the probability of being independent, we use the term predict because this term describes an association in which there is a temporal order between the exposure and outcome as in these analyses. To compare the trajectory of changes in independence before and after stroke by baseline modifier status, we estimated separate models stratified by either baseline physical activity or BMI categories including stroke survivors, stroke decedents, and stroke-free participants. We used age as the time scale, centered at age 75 years. For stroke survivors, time was specified by a slope for the annual rate of change in probability of I/ADL independence for each year of age before nonfatal stroke, a discontinuity term for change in probability of independence at the time of stroke, and a slope for rate of change in probability of independence in the years after stroke, with additional adjustment for age at stroke. For stroke decedents, time was specified by a slope for change in probability of independence for each year of age before stroke, with additional adjustment for age at stroke. For stroke-free participants, time was specified by a slope of change in probability of independence for each year of age. We also used these models to compare the prevalence of independence 3 years before stroke (for stroke survivors and stroke decedents), just before stroke (for stroke decedents), and 3 years after stroke (for stroke survivors), as well as

the loss of independence at stroke onset (for stroke survivors) (see appendix e-1 at Neurology.org for models and appendix e-2 for an example calculation). We graphed predicted trajectories of I/ADL independence for a reference respondent.

We formally tested for differences in I/ADL independence by baseline physical activity and BMI categories on the multiplicative scale by including an interaction term (e.g., modifier × time) in pooled models.

Primary analyses were conducted in Stata 13 with repeated-measures linear regression models (i.e., generalized estimating

equations), applied baseline (1998) sampling weights to make the HRS sample representative of the 1998 US population born 1947 or earlier, and used robust standard errors.

**Standard protocol approvals, registrations, and patient consents.** HRS was approved by the University of Michigan Health Sciences Human Subjects Committee.

**RESULTS** Respondents were followed up for an average of 12.04 years. Table 1 shows the characteristics of

**Table 1** Baseline characteristics of study population by stroke status during follow-up

Variable	Ever stroke (n = 1,853)				Never stroke (n = 16,264)	
	Survivors (n = 1,374)		Decedents (n = 479)		Mean, n	SD, %
	Mean, n	SD, %	Mean, n	SD, %		
Age at stroke, y	75.0	9.6	80.9	9.4		
Age at baseline, y	68.7	9.6	74.5	9.6	65.6	9.9
Male	619	45.1	181	37.8	7,112	43.7
White	1,098	79.9	371	77.5	13,550	83.3
Black	240	17.5	92	19.2	2,148	13.2
Other	36	2.6	16	3.3	566	3.5
<b>Marital status</b>						
Married	883	64.3	222	46.3	11,333	69.7
Divorced/separated	112	8.2	48	10.0	1,634	10.0
Widowed	338	24.6	194	40.5	2,829	17.4
Never married	41	3.0	15	3.1	468	2.9
Southern birthplace	256	18.6	99	20.7	2,551	15.7
<b>Wealth quartile</b>						
1	403	29.3	163	34.0	3,963	24.4
2	355	25.8	117	24.4	4,059	25.0
3	286	20.8	120	25.1	4,126	25.4
4	330	24.0	79	16.5	4,116	25.3
<b>Education</b>						
Less than high school	443	32.2	213	44.5	4,282	26.3
GED	52	3.8	13	2.7	695	4.3
High school graduate	439	32.0	130	27.1	5,170	31.8
Some college	248	18.0	67	14.0	3,178	19.5
College graduate	192	14.0	56	11.7	2,939	18.1
No. of comorbidities (0-8)	1.8	1.2	2.1	1.3	1.4	1.2
<b>Mother's education</b>						
≥8 y	647	47.1	202	42.2	8,284	50.9
Missing	162	11.8	65	13.6	1,673	10.3
Physically active	595	43.3	124	25.9	7,353	45.2
<b>BMI category</b>						
Underweight	18	1.3	21	4.4	341	2.1
Normal weight	473	34.4	182	38.0	5,752	35.4
Overweight	549	40.0	173	36.1	6,441	39.6
Obese	334	24.3	103	21.5	3,730	22.9

Abbreviations: BMI = body mass index; GED = General Education Development; HRS = Health and Retirement Study.

individuals included in this study by stroke status: those who survived their stroke (survivors,  $n = 1,374$ ), those who had a stroke and died before the next interview wave (decedents,  $n = 479$ ), and those who remained stroke-free throughout follow-up ( $n = 16,264$ ).

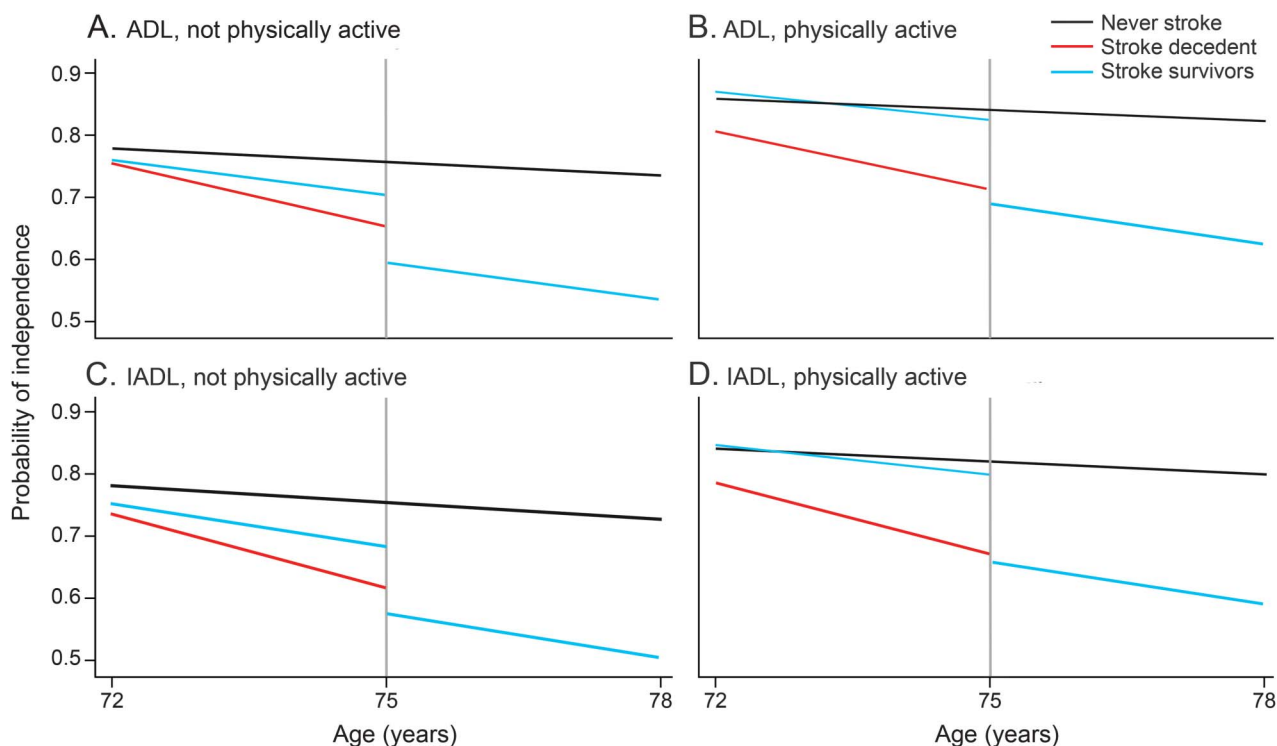
**Physical activity.** Baseline physical activity was not associated with risk of stroke. However, among those who had stroke, baseline physical activity was associated with a decreased risk of dying after that stroke and before the next interview ( $\beta = -0.110$ , 95% confidence interval [CI]  $-0.154$  to  $-0.067$ , table e-1).

Figure 1 shows the predicted trajectories of ADL independence by physical activity status for stroke survivors, stroke decedents, and stroke-free participants. Among stroke survivors, those who were physically inactive at baseline had a lower probability of being independent 3 years after stroke than those who were physically active at baseline (risk difference =  $-0.089$ , 95% CI  $-0.144$  to  $-0.035$ , figure 1, A and B and table 2). However, this difference in the probability of independence between physically inactive

and active stroke survivors was also seen 3 years before stroke (risk difference =  $-0.109$ ; 95% CI  $-0.156$  to  $-0.063$ , table 2). Our design allowed us to explore why differences in the probability of independence 3 years after stroke were similar to differences in the probability of independence 3 years before stroke. We observed that physical activity does not change the rate of decline in independence (table e-2), and compared to physically active individuals, physically inactive individuals experienced a similar decline at stroke event (risk difference =  $-0.012$ , 95% CI  $-0.073$  to  $0.050$ ), suggesting that being physically active does not protect against the disabling effects of a stroke itself. We observed no differences between stroke decedents who were physically active and those who were physically inactive 3 years before stroke or just before the stroke event.

Our design also allows us to compare the trajectories of individuals who experience a stroke to those who remain stroke-free. Compared to those who were physically active at baseline and remained stroke-free, physically active stroke survivors and physically active stroke decedents had faster rates of decline in ADL

**Figure 1** Probability of I/ADL independence by stroke status and baseline physical activity



Predicted probability of independence in all I/ADLs (an indicator of self-reported difficulty with any of the 5 individual ADLs and 5 individual IADLs) stratified by baseline physical activity status: (A) ADL, physically inactive, (B) ADL, physically active, (C) IADL, physically inactive, and (D) IADL, physically active by stroke status over follow-up (never/survivor/decedent): HRS, 1998–2012. Reference group is defined as 75-year-old, white, married women who were born in the South, whose mothers had  $\leq 8$  years of education, and who themselves had the lowest quartile of education, less than a high school education, and no comorbidities. Vertical line represents the transition at the time of stroke for stroke patients, with predicted probabilities of independence modeled for someone whose stroke occurred at age 75. Regression model point estimates and confidence intervals underlying this figure are reported in table e-2. ADL = activities of daily living; HRS = Health and Retirement Study; IADL = instrumental activities of daily living; — = date of stroke (vertical line).

**Table 2** Estimated RDs and bootstrapped SEs<sup>a</sup> comparing I/ADL outcomes by physical activity status

Outcome	RD comparison groups	Time point in stroke trajectory at which estimated probabilities of independence were tested	RD	SE	z Score	p Value	95% CI
ADL	Physically inactive vs physically active	Survivors 3 y before stroke	-0.109	0.024	-4.64	<0.001	-0.156 to -0.063
		Survivors, loss at stroke	-0.012	0.031	-0.38	0.70	-0.073 to 0.050
		Survivors 3 y after stroke	-0.089	0.028	-3.22	0.001	-0.144 to -0.035
		Survivors, difference-in-difference, 3 y before stroke-3 y after stroke	-0.020	0.026	-0.77	0.44	-0.072 to 0.031
		Decedents 3 y before stroke	-0.051	0.052	-0.99	0.32	-0.152 to 0.050
		Decedents just before stroke	-0.060	0.079	-0.76	0.45	-0.214 to 0.095
IADL	Physically inactive vs physically active	Survivors 3 y before stroke	-0.094	0.022	-4.32	<0.001	-0.137 to -0.051
		Survivors, loss at stroke	-0.018	0.032	-0.57	0.57	-0.080 to 0.044
		Survivors 3 y after stroke	-0.086	0.027	-3.22	0.001	-0.139 to -0.034
		Survivors, difference-in-difference, 3 y before stroke-3 y after stroke	-0.008	0.026	-0.30	0.77	-0.059 to 0.043
		Decedents 3 y before stroke	-0.050	0.037	-1.36	0.18	-0.123 to 0.022
		Decedents just before stroke	-0.055	0.059	-0.93	0.35	-0.171 to -0.061

Abbreviations: ADL = activities of daily living; CI = confidence interval; IADL = instrumental activities of daily living; RD = risk difference; SE = standard error.

Risk differences shown in this table compare a reference respondent (75-year-old, white, married woman who was not born in the South, whose mother had  $\leq 8$  years of education, who herself had lowest-quartile household wealth, who had less than a high school education, and who had no comorbidities) who is physically active to a reference respondent who is not physically active.

<sup>a</sup>Bootstrapped SEs are from 1,000 replications.

independence before stroke and after stroke. Similarly, compared to individuals who were physically inactive at baseline and remained stroke-free, physically inactive stroke survivors and physically inactive stroke decedents had faster rates of decline in ADL independence before stroke and after stroke (table e-2). This suggests that individuals who later experience a stroke may have other underlying pathophysiology that causes their faster decline and that this decline occurs even among those who are physically active.

In general, patterns were similar in magnitude and trend for IADL independence and for ADL independence (figure 1, C and D).

**Weight status.** Compared to those with normal weight at baseline, obese individuals had an increased risk of stroke ( $\beta = 0.014$ , 95% CI 0.001–0.027); overweight individuals did not have an increased risk of stroke (table e-1).

Among stroke survivors, we observed no differences in rates of decline or in the probability of being independent before or after stroke comparing individuals who were normal weight at baseline to those who were overweight. Those who were obese at baseline had a lower probability of independence 3 years before stroke (risk difference =  $-0.074$ , 95% CI  $-0.144$  to  $-0.004$ ), but this difference did not persist 3 years after stroke. Rates of decline were similar for those who were obese compared to those who were normal weight.

Among stroke decedents, we observed no differences in the probability of independence 3 years before stroke or just before stroke between overweight and normal-weight participants or between obese and normal-weight participants (table 3).

Compared to those who did not experience a stroke and were normal weight, normal-weight stroke survivors and normal-weight stroke decedents had faster rates of decline in ADL independence before stroke and after stroke. Similar results were seen among those who were overweight or obese (tables e-3–e-6).

There were no differences in the probability of IADL independence either before or after stroke in a comparison of normal-weight, overweight, and obese stroke survivors and stroke decedents (figure 2 and table 3).

**DISCUSSION** Stroke survivors who were physically inactive at baseline had lower probability of independence in ADLs and IADLs 3 years after stroke, whereas no clear pattern of functional independence after stroke was found by baseline weight status. The difference in the probability of I/ADL independence after stroke by baseline physical activity mirrored the differences before stroke.

Several retrospective studies among cohorts of stroke patients suggest that physical activity before stroke is associated with milder strokes or better functional outcomes after stroke.<sup>1–5</sup> A large, prospective cohort study of participants with incident stroke



**Table 3** Estimated RD and bootstrapped SEs<sup>a</sup> comparing I/ADL outcome by weight status

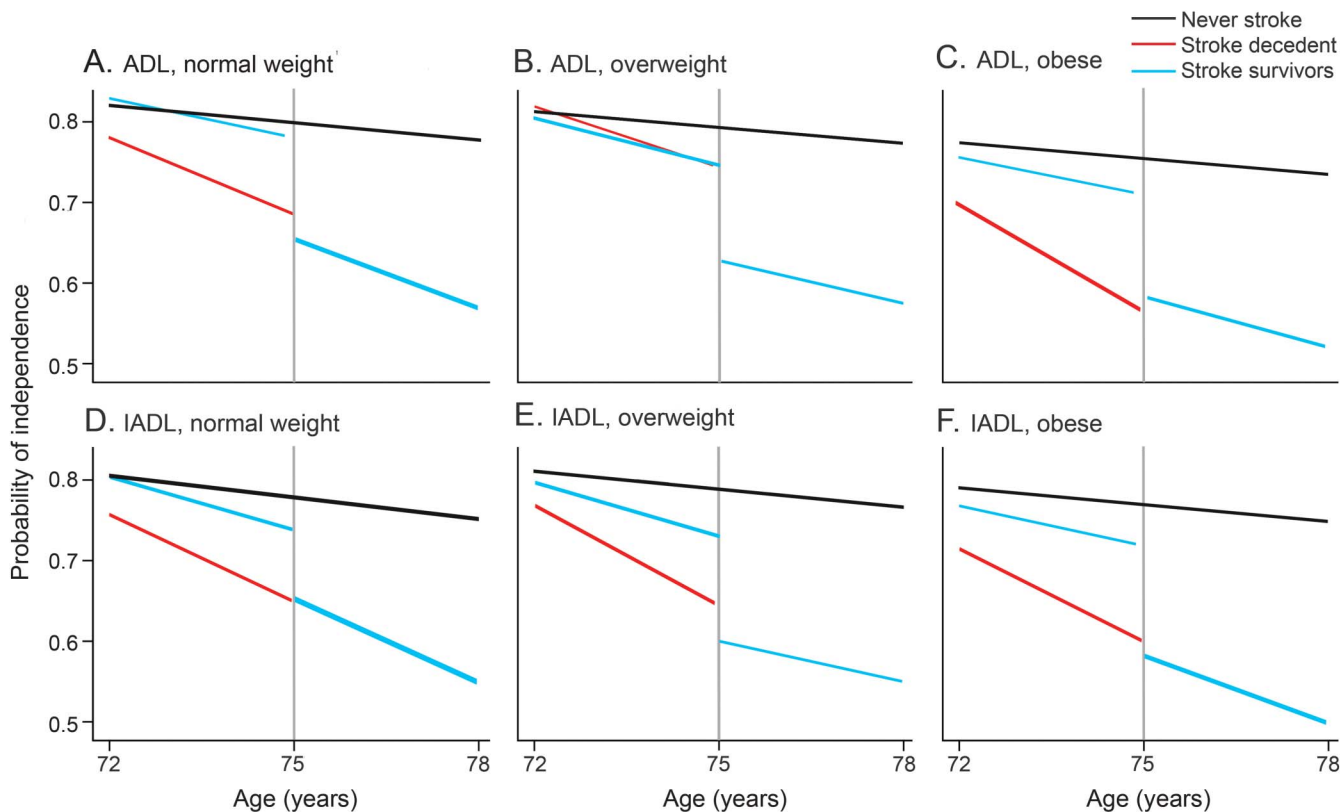
Outcome	RD comparison groups	Time point in stroke trajectory at which estimated probabilities of independence were tested	RD	SE	z Score	p Value	95% CI
ADL	Overweight vs normal weight	Survivors 3 y before stroke	-0.024	0.026	-0.90	0.369	-0.075 to 0.028
		Survivors, loss at stroke	-0.022	0.037	-0.58	0.559	-0.095 to 0.051
		Survivors 3 y after stroke	0.006	0.033	0.19	0.851	-0.058 to 0.070
		Survivors, difference-in-difference, 3 y before stroke-3 y after stroke	-0.030	0.030	-1.01	0.313	-0.088 to 0.028
		Decedents 3 y before stroke	0.039	0.047	0.83	0.409	-0.054 to 0.132
		Decedents just before stroke	0.059	0.072	0.82	0.411	-0.082 to 0.201
	Obese vs normal weight	Survivors 3 y before stroke	-0.074	0.036	-2.07	0.038	-0.144 to -0.004
		Survivors, loss at stroke	-0.029	0.043	-0.67	0.501	-0.114 to 0.056
		Survivors 3 y after stroke	-0.050	0.037	-1.35	0.177	-0.123 to 0.023
		Survivors, difference-in-difference, 3 y before stroke-3 y after stroke	-0.024	0.036	-0.66	0.511	-0.094 to 0.047
		Decedents 3 y before stroke	-0.084	0.064	-1.30	0.194	-0.210 to 0.042
		Decedents just before stroke	-0.122	0.094	-1.31	0.191	-0.306 to 0.061
	Obese vs overweight	Survivors 3 y before stroke	-0.050	0.034	-1.48	0.138	-0.117 to 0.162
		Survivors, loss at stroke	-0.007	0.041	-0.18	0.861	-0.088 to 0.074
		Survivors 3 y after stroke	-0.057	0.037	-1.53	0.126	-0.129 to 0.016
		Survivors, difference-in-difference, 3 y before stroke-3 y after stroke	0.006	0.035	0.18	0.858	-0.062 to 0.074
		Decedents 3 y before stroke	-0.123	0.057	-2.14	0.032	-0.235 to -0.010
		Decedents just before stroke	-0.182	0.085	-2.14	0.033	-0.348 to -0.015
IADL	Overweight vs normal weight	Survivors 3 y before stroke	-0.008	0.025	-0.34	0.738	-0.058 to 0.041
		Survivors, loss at stroke	-0.064	0.036	-1.81	0.071	-0.134 to 0.005
		Survivors 3 y after stroke	0.001	0.029	0.04	0.972	-0.057 to 0.059
		Survivors, difference-in-difference, 3 y before stroke-3 y after stroke	-0.010	0.030	-0.32	0.749	-0.068 to 0.049
		Decedents 3 y before stroke	0.011	0.044	0.24	0.810	-0.076 to 0.098
		Decedents just before stroke	-0.004	0.068	-0.06	0.956	-0.137 to 0.129
	Obese vs normal weight	Survivors 3 y before stroke	-0.040	0.032	-1.23	0.220	-0.103 to 0.024
		Survivors, loss at stroke	-0.061	0.041	-1.48	0.138	-0.143 to 0.020
		Survivors 3 y after stroke	-0.052	0.034	-1.52	0.129	-0.119 to 0.015
		Survivors, difference-in-difference, 3 y before stroke-3 y after stroke	0.012	0.036	0.33	0.739	-0.059 to 0.083
		Decedents 3 y before stroke	-0.043	0.048	-0.91	0.362	-0.137 to 0.050
		Decedents just before stroke	-0.050	0.076	-0.66	0.509	-0.200 to 0.099
	Obese vs overweight	Survivors 3 y before stroke	-0.031	0.031	-1.01	0.314	-0.092 to 0.030
		Survivors, loss at stroke	0.003	0.042	0.06	0.948	-0.079 to 0.084
		Survivors 3 y after stroke	-0.053	0.035	-1.52	0.127	-0.121 to 0.015
		Survivors, difference-in-difference, 3 y before stroke-3 y after stroke	0.022	0.036	0.61	0.545	-0.048 to 0.092
		Decedents 3 y before stroke	-0.054	0.048	-1.13	0.257	-0.148 to 0.039
		Decedents just before stroke	-0.047	0.077	-0.61	0.544	-0.197 to 0.104

Abbreviations: ADL = activities of daily living; CI = confidence interval; IADL = instrumental activities of daily living; RD = risk difference; SE = standard error.

Risk differences shown in this table compare a reference respondent (75-year-old, white, married woman who was not born in the South, whose mother had ≤8 years of education, and who herself had lowest-quartile household wealth, less than a high school education, and no comorbidities) in one body mass index (BMI) category to a referent respondent in another BMI category.

<sup>a</sup>Bootstrapped SEs are from 1,000 replications.

**Figure 2** Probability of I/ADL independence by stroke status and baseline weight status



Predicted probability of independence in all I/ADLs (an indicator of self-reported difficulty with any of the 5 individual ADLs and 5 individual IADLs) stratified by weight status: (A) ADL, normal weight, (B) ADL, overweight, (C) ADL, obese, (D) IADL, normal weight, (E) IADL, overweight, and (F) IADL, obese and by stroke status over follow-up (never/survivor/decedent): HRS, 1998–2012. Reference group is defined as 75-year-old, white, married women who were born in the South, whose mothers had  $\leq 8$  years of education, who themselves had lowest quartile of education, height, and household wealth, and who had no comorbidities. Vertical line represents the transition at the time of stroke for stroke patients, with predicted probabilities of independence modeled for someone whose stroke occurred at age 75. Regression model point estimates and confidence intervals underlying this figure are reported in tables e-3 and e-4. ADL = activities of daily living; HRS = Health and Retirement Study; IADL = instrumental activities of daily living; — = date of stroke (vertical line).

observed that baseline physical activity was associated with a marginally nonsignificant increase in having a Barthel Index score  $\geq 95$  compared to a Barthel Index score  $< 95$  (relative risk = 1.49, 95% CI 0.99–2.24) up to 5 years after stroke.<sup>27</sup> Similar to our study, this finding suggests that those who are physically active before stroke maintain a reduced risk of disability years after stroke.

The current study helps elucidate whether the association between physical activity and improved poststroke outcomes is due to slower rates of decline among those who are physically active or whether the better poststroke outcomes merely reflect higher levels of functioning before the stroke event. We observed that the lower probability of independence seen among physically inactive individuals is not driven by faster rates of decline before stroke or by the harmful effects of the stroke events. Instead, it is driven by differences in the probability of independence 3 years before stroke between physically active and physically inactive individuals.

Almost all research on BMI and stroke outcomes has been in cohorts of stroke patients and used the modified Rankin Scale score to measure disability. Studies are inconsistent, with some reporting a protective effect of obesity on disability<sup>7,12,13</sup> and others finding higher prevalence of disability among obese participants<sup>16,19</sup> or no association.<sup>20</sup> The only prospective cohort study in initially healthy individuals observed no association between BMI and modified Rankin Scale score at hospital discharge after ischemic stroke.<sup>18</sup> We add to the existing literature by examining the probability of independence before stroke onset and rates of decline in independence over time. We observed few effects of BMI on independence 3 years before stroke or on rates of decline in independence after stroke.

Unlike most prior studies, our cohort enrolled individuals without stroke at baseline and examined disability trajectories as measured by ADL and IADL limitations both before and after stroke. This design rules out reverse causation from stroke severity to



physical activity or BMI or biases implicit in retrospective reporting. Examining IADL limitations substantially adds to the existing literature because many prior studies were unable to examine risk factors for IADL limitations among stroke patients. IADLs may be a major determinant of quality of life among stroke patients,<sup>28,29</sup> making it important to identify factors that may reduce the risk of IADL limitations. Similar to prior results in the general population<sup>30</sup> or among those with cognitive impairment,<sup>31</sup> physical activity was associated with a reduction in the probability of IADL dependence among those who experience a stroke in this study. Given that IADLs are more cognitively demanding than ADLs<sup>32</sup> and that physical activity may help to maintain cognitive function,<sup>33,34</sup> it is possible that physical activity before stroke may protect against IADL limitations through its effects on cognitive function.

Limitations to this study include the use of self- or proxy-reported strokes and lack of information on stroke subtypes. However, prior research has shown similar stroke incidence rates in HRS and in cohorts that used physician-verified stroke.<sup>35</sup> The lower number of fatal stroke events compared to nonfatal stroke events resulted in lower power for the fatal stroke analyses. We focused only on a dichotomous measurement of I/ADL limitations and did not examine individual I/ADL limitations or a count of the number of limitations. We also chose to measure risk differences instead of relative risks because risk differences may be more meaningful from a clinical and public health perspective.<sup>36</sup> Additionally, mortality in the stroke-free group may have posed a competing risk to observing incident disability, potentially leading to an underestimation of the incident disability rate in the stroke-free. To preserve clarity of temporal order, we used baseline values of BMI and physical activity, but this precluded exploring how changes in these factors may influence disability trajectories before and after stroke. Additionally, individuals may have developed functional limitations before baseline that prevented them from being physically active at baseline. Therefore, the results seen among the physically active individuals may not represent a causal effect of physical activity on independence before stroke but may instead reflect the better overall health and functioning of individuals who are able to be physically active before stroke. Finally, our measure of physical activity was coarse and did not measure the type or frequency of exercise in detail.

Strengths to this study include the use of a large, nationally representative cohort study with prospective ascertainment of physical activity and BMI and repeated ascertainment of I/ADL limitations over up to 12 years of follow-up. Additionally, all participants were stroke-free at baseline. This allowed us to

examine disability trajectories both before and after stroke and to consider separately stroke survivors, stroke decedents, and those who never experienced a stroke.

Physical inactivity before stroke predicts higher risk of being dependent both before and after a stroke event. Future research directions include exploring the association between physical activity intensity and stroke outcomes to help inform public health recommendations and whether changes in physical activity patterns also predict stroke outcomes.

## AUTHOR CONTRIBUTIONS

Pamela M. Rist drafted the manuscript for content and interpreted the data. Benjamin D. Capistrant revised the manuscript for content, designed the study, and analyzed and interpreted the data. Elizabeth Rose Mayeda revised the manuscript for content and analyzed and interpreted the data. Sze Y. Liu revised the manuscript for content and interpreted the data. M. Maria Glymour revised the manuscript for content, designed the study, analyzed and interpreted the data, obtained study funding, and supervised the study.

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## DISCLOSURE

The authors report no disclosures relevant to the manuscript. Go to [Neurology.org](http://Neurology.org) for full disclosures.

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