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Temporal trends in stroke-related memory change: results from a US national cohort 1998–2016

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Abstract

Background and Purpose: Findings from the Framingham Heart Study suggest that declines in dementia incidence rates over recent decades are partially due to decreases in stroke incidence and mortality; however, whether trends of declining dementia rates extend to survivors of incident stroke remains unclear. We investigated evidence for temporal trends in memory change related to incident stroke in a nationally representative cohort.

Methods: Adults age 50+ in the Health and Retirement Study (HRS) were followed across three successive six-year epochs (Epoch 1: 1998–2004, n=16,781; Epoch 2: 2004–2010, n=15,345; Epoch 3: 2010–2016; n=15,949). Participants were included in an epoch if they were stroke-free at the start of that epoch. Annual rates of change in a composite z-standardized memory score were compared using demographic-adjusted linear regression models for stroke-free participants, those who survived after stroke, and those who died after stroke, considering memory change prior to stroke, at the time of stroke, and for years following stroke.

Results: Crude stroke incidence rates decreased from 8.5 per 1,000 person-years in Epoch 1 to 6.8 per 1,000 person-years in Epoch 3. Rates of memory change before and following stroke onset were similar across epochs. Memory decrement immediately after stroke onset attenuated from −0.37 points (95% CI: −0.44, −0.29) in Epoch 1 to −0.26 (95% CI: −0.33, −0.18) points in Epoch 2 and −0.25 (95% CI: −0.33, −0.17) points in Epoch 3 (p-value for linear trend = 0.02).

Conclusions: Decreases in stroke-related dementia in recent years may be partially attributable to smaller memory decrements immediately after stroke onset. Findings suggest reductions in

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Supplemental Materials
Online Table I

stroke incidence and improvements in stroke care may also reduce population burden of dementia. Further investigations into whether temporal trends are attributable to improvements in stroke care are needed.

Indexing terms:

stroke; cognition; cognitive decline; epidemiology; trends

Subject terms:

epidemiology; cognitive impairment

Introduction:

Stroke is a major cause of long-term cognitive impairment and dementia. Nearly one in four stroke survivors is diagnosed with dementia and an additional one in three shows signs of cognitive impairment.[1–5] Both stroke and dementia incidence rates in the US and other high-income countries have declined in recent years.[3,6,7] Stroke mortality rates have also declined, leading to the hypothesis that reductions in stroke severity or improvements in quality of stroke care may contribute to decreases in post-stroke dementia.[8] However, whether trends of declining dementia rates extend to survivors of incident stroke remains unclear.[6,9]

Acute stroke is often preceded by accumulating cerebrovascular disease, causing memory decline years prior to stroke diagnosis. Additionally, immediate decrements in memory functioning at stroke onset suggest that evaluating links between stroke and memory requires consideration of the entire trajectory of memory performance.[10–14] Few studies have longitudinal data to evaluate whether trends of cognitive impairment before and after stroke have changed in recent decades. Results examining temporally nonoverlapping epochs (time periods) in the Framingham Study, corresponding with resampling waves, found that risk of dementia after stroke decreased from a 4.72 (95% CI: 2.17, 10.23) times higher risk of dementia in stroke survivors compared to stroke-free participants between 1992 to 1998 to a 1.43 (95% CI: 0.20, 10.37) times higher risk between 2004 to 2008.[7]

We evaluated whether post-stroke cognitive outcomes have improved in recent years by defining three successive epochs corresponding with study resampling periods in the nationally representative Health and Retirement Study (HRS). Treating each epoch as a distinct cohort for that time period, we estimated cognitive trajectories prior to stroke, immediate change at stroke onset, and longer-term post-stroke cognitive trajectory. We compared epoch-specific memory trajectories in people who experienced stroke to memory trajectories in stroke-free participants to assess temporal trends in stroke-related cognitive change, and to explore when changes occur in the development of stroke-related deficits.

Methods:

Study design:

HRS is a study of community-dwelling middle-aged and older adults in the US, initiated in 1992. Enrollment was modified in 1998 to achieve a nationally representative sample of US adults over age 50 and has fielded additional enrollment waves every six years to represent subsequent generational birth cohorts. Study recruitment and design have been published elsewhere.[15,16] Biennial interviews are ongoing, typically conducted via telephone. Proxies complete “exit interviews” after death of a participant to provide information on major health events preceding the participant’s death (such as a fatal stroke). HRS is sponsored by the National Institute on Aging, National Institutes of Health and conducted by the University of Michigan, Ann Arbor. All study participants gave informed consent and HRS was approved by the institutional review board at the University of Michigan. The current study, as a secondary analysis of deidentified publicly available HRS data, was certified as exempt from review by the University of California, San Francisco Institutional Review Board. All data and materials have been made publicly available through the Institute for Social Research at the University of Michigan, Ann Arbor and can be accessed at https://hrsdata.isr.umich.edu/data-products/public-survey-data.

Three epochs with temporally non-overlapping periods of eligibility, corresponding with new HRS enrollments in 1998, 2004, and 2010, were examined with epoch 1 spanning the period from 1998 to 2004, epoch 2 from 2004 to 2010, and epoch 3 from 2010 to 2016. Full epoch inclusion is shown in Figure 1. Epochs included participants completing the baseline wave of each epoch [1998 for Epoch 1 (n=19,819), 2004 for Epoch 2 (n=18,523), and 2010 for Epoch 3 (n=20,185)] and up to 6 years of follow-up. Respondents were excluded if they had history of a stroke at baseline for that epoch [Epoch 1 (1998): 1,461; Epoch 2 (2004): 1,356; Epoch 3 (2010): 1,544] or no information on date of stroke experienced during the epoch (Epoch 1: 2; Epoch 2: 41, Epoch 3: 54). Participants were further excluded if missing memory scores across all waves in an epoch (Epoch 1: 1,530, Epoch 2: 1,725; Epoch 3: 2,532) or missing covariates (EP1: 45; EP2: 56; EP3: 106) for a final analytic sample of 16,781 in Epoch 1, 15,345 in Epoch 2, and 15,949 in Epoch 3.

Dependent variable:

Immediate and delayed (5-minute) recall tests of a verbally given 10-word list of common nouns were used to assess memory. Previous findings have shown that verbal memory may be the strongest predictor of impairment after incident stroke.[17] If individuals were too impaired to participate in assessments, proxy informants such as spouses rated participant’s memory on a 5-point Likert scale and the Jorm Informant Questionnaire for Cognitive Decline,[18,19] for which validity and reliability have been documented elsewhere.[20,21] A previously created composite score combining proxy and direct memory measurements for HRS was used as the measure of memory at each data collection wave.[22,23] Memory scores were z-standardized using the population-weighted mean and standard deviation of the full 1998 sample. The final standardized measures ranged from −6.02 to 3.14, with each point corresponding to a one standard deviation change in the 1998 population.

Independent variable:

Stroke status was determined using self-reported doctor's diagnosis of stroke answering the question, "Has a doctor ever told you that you had a stroke?" If patients were unavailable for direct interview or deceased, proxy informants reported patients' stroke status. Prior analyses of stroke in HRS have found that self-reported stroke incidence does not differ greatly from physician-verified strokes.[24] All memory reports after date of first stroke were considered post-stroke cognition; information was not collected on subsequent strokes or stroke subtypes, and transient ischemic attacks were not measured.

Participants were classified into three categories for each epoch: (1) stroke survivors: participants experiencing stroke during epoch who survived to participate in a subsequent interview; (2) stroke decedents: participants experiencing stroke who did not survive to participate in subsequent interviews (i.e. who died from any cause including but not restricted to stroke); and (3) stroke-free participants: those reporting no stroke during the epoch. Participants were included in an epoch if newly enrolled into HRS and not reporting a previous stroke, or if already-enrolled and stroke-free as of the previous epoch (stroke survivors or decedents were automatically ineligible for inclusion in subsequent epochs as baseline exclusion criteria restricted each epoch to stroke-free participants at the start of each epoch). Trajectories for stroke survivors and stroke decedents were calculated using months prior to stroke or months since stroke for each memory measurement ascertainment. For stroke-free participants, trajectories of memory were calculated for age-related memory decline.

Covariates:

Models adjusted for stroke-free participants' interview age or age at stroke for those experiencing stroke, centered at 75 years. The following demographics were collected at HRS entry: race (white, black, other), gender, birthplace region (Census-defined Northeast, Midwest, South, West, or outside US), years of attained education (range: 0 to 17+ years), and mother's education (<8 years, 8+ years, unknown). Height, marital status (married/partnered, separated/divorced/widowed, never married), and wealth were updated at the start of each epoch (1998 for Epoch 1, 2004 for Epoch 2, and 2010 for Epoch 3). Analyses further adjusted for practice effects of repeated memory testing indicating the wave of individuals' first cognitive assessment.

Statistical Analysis:

Longitudinal trajectories of memory scores were estimated using linear mixed models with random intercepts. Models were estimated separately for each epoch, with the following epoch-specific predictors: stroke status (stroke survivor, stroke decedent, stroke-free), time until stroke for stroke survivors and decedents, time since stroke for stroke survivors, age at stroke or stroke-free age, and covariates noted above. A discontinuity indicator for immediate decrement in memory performance at the time of first stroke was included for participants who survived stroke, representing acute decreases in memory at stroke onset. Changes in memory were thus estimated as a function of time until stroke for participants who experienced stroke and additionally as time following stroke for stroke-survivors, estimating separate pre- and post-stroke slopes, and as age-related memory

decline for stroke-free participants. Predicted memory scores were calculated for all stroke categories, with the intercept representing an epoch-specific stroke-free 75-year-old individual. A pooled model including all stroke variables interacted with an epoch indicator was used to assess trends across epochs. Supplementary analyses assessed patterns of stroke-related memory using only direct cognitive assessments (excluding proxy informant memory reports) instead of the previously published imputed memory score. To obtain estimates representative of the community-dwelling US population over age 50, analyses were weighted to be nationally representative of baseline for each epoch. Analyses were conducted in SAS 9.4 (SAS Institute, Cary, NC).

Results:

Across all epochs, 2,434 individuals experienced a first stroke: 1,844 nonfatal and 590 fatal. Average baseline age was 66.3 (SD: 10.0) years in Epoch 1, 67.1 ± 10.2 years in Epoch 2, and 66.5 ± 10.8 year in Epoch 3. Other characteristics are presented in Table 1.

Age-adjusted stroke incidence rates for nonfatal strokes, using 2000 census estimates as the referent population, decreased from 6.6 per 1,000 person-years in Epoch 1 to 6.1 per 1,000 person-years in Epoch 2 and 5.3 per 1,000 person-years in Epoch 3 (Table 2). Age-adjusted incidence rates for fatal strokes similarly decreased, from 1.9 per 1,000 person-years in Epochs 1 and 2 to 1.4 per 1,000 person-years in Epoch 3.

Estimates for the relationship between stroke and memory trajectories are shown in Table 3 and used to calculate predicted memory scores shown in Figures 2 and 3. Average memory scores in stroke-free participants at age 75 improved from −0.60 (95% CI: 0–0.65, −0.55) points per year in Epoch 1 to −0.57 (95% CI: 0.61, −0.52) in Epoch 2 and −0.46 (95% CI: −0.50, −0.42) in Epoch 3 (P-value for trend: <0.01); memory decline for stroke-free individuals was similar across epochs at −0.07 points per year. For Epoch 1 participants who subsequently had stroke, average pre-stroke memory score was −0.17 (95% CI: −0.24, −0.09) points worse than stroke-free participants; in Epoch 3, average pre-stroke memory score among stroke survivors was −0.11 (95% CI:−0.18, −0.03) points worse than stroke-free individuals (P-value for trend across epochs: <0.01). Among stroke decedents, average pre-stroke memory at age 75 in Epoch 1 was 0.45 (95% CI: −0.59, −0.31) points lower than stroke-free participants; −0.33 (95% CI: −0.45, −0.20) points lower in Epoch 2; and −0.38 (95% CI: −0.53, −0.23) points lower in Epoch 3 (P-value for trend: <0.01). In sensitivity analyses restricted to direct memory assessments (no proxies), patterns of pre-stroke memory disadvantage compared to people who did not have stroke attenuated over time, matching primary analyses. The discontinuity at the time of stroke attenuated over time (p=0.025) though the temporal trend was less pronounced than in primary analyses. (Supplementary Table A1).

Figure 2 shows pre- and post-stroke decline in stroke survivors and pre-stroke decline in decedents. Memory decline rates prior to stroke for survivors was similar across epochs at −0.12 (95% CI: −0.14, −0.10) points per year prior to stroke in Epoch 1, −0.13 (95% CI: −0.15, −0.11) in Epoch 2, and −0.12 (95% CI: −0.14, −0.10) in Epoch 3 (p-value for trend: 0.63). These coefficients indicate that over a 1-year period prior to stroke, we expect

similar memory decline as 1.7 years among stroke-free participants. At the time of stroke, the immediate decrement in memory was −0.37 (95% CI: −0.44, −0.29) points in Epoch 1 but only −0.26 (95% CI: −0.33, −0.18) points in Epoch 2 and −0.25 (95% CI: −0.33, −0.17) points in Epoch 3 (p-value for trend: 0.02). Following stroke, average annual memory decline was −0.08 (95% CI: −0.11, −0.06) points per year in Epoch 1, −0.13 (95% CI: −0.15, −0.10) points in Epoch 2, and −0.10 (95% CI: −0.13, −0.08) points in Epoch 3 (p-value for trend: 0.16), or a 1-year post stroke decline being approximately equivalent to a 1.1-year decline in stroke-free participants. Prior to stroke for decedents, average annual memory decline was −0.21 (95% CI: −0.25, −0.17) points in Epoch 1, −0.18 (95% CI: −0.21, −0.14) in Epoch 2, and −0.20 (95% CI: −0.25, −0.16) in Epoch 3 (p-value for trend: 0.08), or a 1-year decline prior to stroke in decedents being approximately equivalent to a 3.3-year decline in stroke-free participants.

Predicted memory scores after stroke onset in survivors and age-related decline in stroke-free participants are shown in Figure 3. Average memory scores for the referent 75-year-old stroke-free individual [−0.60 (95% CI: −0.65, −0.55) points in Epoch 1, −0.57 (95% CI: −0.61, −0.52) points in Epoch 2, and −0.46 (95% CI: −0.50, −0.42) points in Epoch 3] were higher than a similar individual experiencing a nonfatal stroke at age 75 across all epochs (Figure 3, Panel A). In Epoch 1, absolute differences in memory decline between stroke-free participants and stroke survivors were stable across the three years following stroke (following age 75 for stroke-free participants). Differences between stroke-free and stroke survivors were narrower in Epochs 2 and 3 than Epoch 1; however, this attenuation was more pronounced 1-year post-stroke, with an increasing difference between estimates observed 3-years post-stroke (Figure 3, Panel B).

Discussion:

Consistent with previous research, stroke patients had worse memory and faster pre-stroke decline than stroke-free participants in this large, nationally representative cohort. Across successive epochs, the pre-stroke memory disadvantage of people with stroke compared to people without stroke had attenuated. The short-term decrement in memory scores associated with stroke onset was also attenuated by 0.11 points across epochs, a 35% reduction in memory decrement (approximately equivalent to 2 years of age-related decline in stroke free participants). Rate of post-stroke memory change did not substantially change across epochs but for 1-year post-stroke and to a lesser extent, 3-years post-stroke, the gap between stroke-survivors and stroke-free individuals was attenuated.

Our findings are consistent with reduced incidence of stroke in recent years and reduced impact of stroke on memory impairment and related conditions. We observed a decrease in fatal and nonfatal stroke incidence rates across epochs, consistent with previous studies demonstrating downward trends in incidence of first stroke.[25–28] The observed decreased incidence from Epoch 1 to Epoch 3 also mirrors reported decreases in stroke deaths from the U.S. National Vital Statistics System, showing a 3.5% annual decline for national age-standardized stroke death rates from 2000 to 2015 among people aged 65–74 and age 75–84.[8] Improved control of smoking and other vascular risk factors that contribute to stroke has been highlighted as potential contributors for concurrent declines in stroke incidence and

subsequent mortality, but existing evidence on associations between vascular risk factors and post-stroke dementia is conflicting.[3]

Our findings suggest that pre-stroke memory functioning for individuals who experience stroke is better in recent years than earlier periods. Explanations for this change are uncertain but may indicate that determinants of stroke are less strongly associated with memory than in the past. Recent decreases in stroke-related dementia are also likely partially attributable to smaller memory decrements in the immediate aftermath of stroke. The attenuation of short-term adverse consequences of stroke on memory observed in Epochs 2 and 3 compared to Epoch 1 may be due to improvements in acute stroke care across the last few decades as documented in Get With the Guidelines–Stroke initiatives,[29] including wider adoption of tissue plasminogen activator (tPA), which is reported to have doubled from 2003 to 2011, and reduced door-to-needle times which improve the efficacy of this treatment.[30,31] It is also possible that improved risk factor profiles in people at high risk of stroke - such as improved hypertension control, diabetes management, or increases in physical activity – led to decreases in stroke severity. This may have resulted in an increasing proportion of mild strokes or of subtypes with smaller cognitive consequences. Increases in detection of mild strokes would have similar consequences, but is unlikely given the overall decline in incidence rates. Reduced stroke recurrence would not have contributed to our results because we evaluated only first strokes. .[32,33]

This study contributes significantly to our understanding of trends in post-stroke dementia. Previous studies used retrospective samples of only stroke survivors or populations that may not be generalizable to the U.S. population. A major strength of this study is that each epoch was aligned with study resampling, allowing us to mimic continuous monitoring over an extended period of observation corresponding with re-enrollments using consistent recruitment and study procedure methods. Considering pre- and post- stroke trajectories is critical in understanding progression of memory decline around stroke, as long-term outcomes of stroke survivors reflects both consequences of stroke and cognitive status of individuals prior to stroke. By examining how trajectories differ both before and after stroke onset, we may differentiate between improvements in age-related cognitive decline and changes in acute or post-stroke care.

Our study aimed to evaluate temporal trends by emulating continuous monitoring in a nationally representative sample. Consistent with recent trends observed in the Framingham Study, we observed improvements in cognitive functioning after stroke in recent years.[7] However, we found that improvements in post-stroke memory functioning were driven primarily by lessening of immediate memory deficits at the time of stroke onset, not differences in memory decline around stroke onset. Furthermore, Framingham Study results compared time periods from 1977 and 2008; our results extend findings through 2016.

Important limitations of this study include self-report of stroke status and inability to differentiate between stroke sub-types or consider transient ischemic attacks. Our results reflect a weighted average effect of different stroke types and likely represent more common ischemic strokes. As with many self-report measures, self-reported strokes are subject to recall bias and overreporting such as possible misclassification of TIAs or other related

cardiovascular conditions, the frequency of which may also differ across epochs.[24,34] However previous investigations have suggested that misreporting of strokes in HRS is nonsystematic with a sensitivity of 74% and specificity of 93% to detect strokes recorded through Centers for Medicare and Medicaid Services.[35] Though imperfect, self-reported strokes in HRS allowed us to estimate trends across the US in the absence of a national infrastructure for systematic stroke reporting.[24] Second, we had insufficient data to explore potential mediation of secular trends by vascular risk factors and other comorbidities such as depression, known contributors to post-stroke dementia, although previous reports have shown that vascular risk factors do not significantly predict cognitive change after stroke and therefore were unlikely to affect our findings.[17,36] Third, our results are limited to the cognitive domain of verbal memory after stroke. Though our measure of immediate and delayed recall have been previously shown to be associated with diagnoses of post-stroke dementia and can more easily be used to assess large population cohorts than full cognitive batteries, we were unable to determine whether temporal trends in other domains or overall cognition were present. Finally, follow-up time within epochs, available only in two-year intervals with a maximum of 6 years, may have been insufficient to capture the full effects of stroke on subsequent memory decline. Through sensitivity analyses, we concluded that inclusion of follow-up outside of each epoch biased our results towards healthier participants, as those with lesser decline and better memory performance were more likely to remain eligible across epochs.

This work adds to current knowledge of stroke-related decline by considering potential trends in the relationship between stroke and cognition across almost two decades. In the HRS, stroke onset was associated with a smaller decrement in memory for stroke survivors in recent epochs (2004–2010 and 2010–2016) compared to stroke survivors in the first period we observed (1998–2004). Although improvements in quality of care for stroke survivors may explain trends in post-stroke memory outcomes, further research with direct measures of quality of care and other possible mediators are needed. Future studies may consider the impact of specific changes in stroke care during this study period to further address possible underlying mechanisms behind these observed trends.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Disclosures:

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Non-standard Abbreviations and Acronyms:

HRS	Health and Retirement Study

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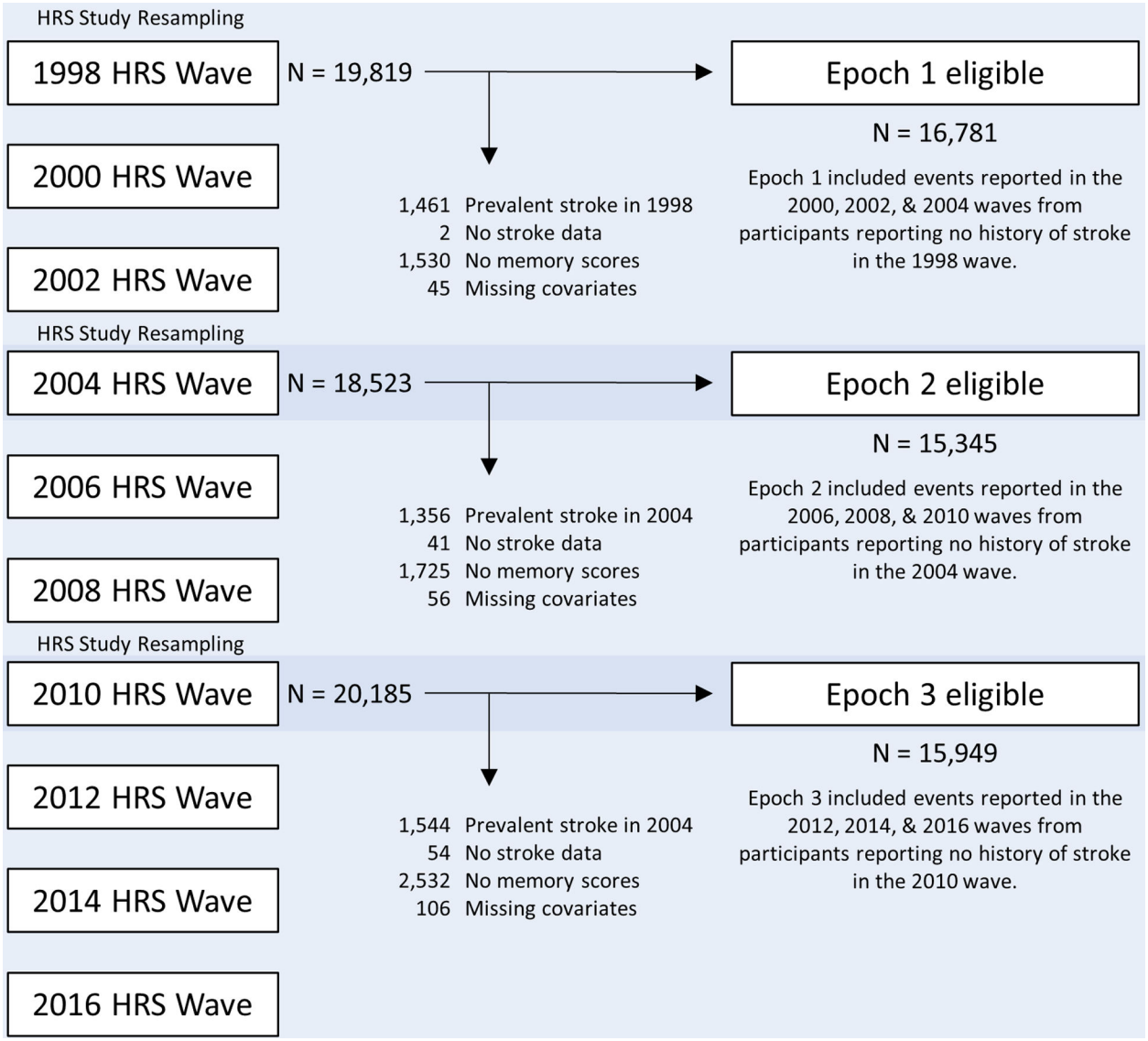

Figure 1.

Epoch eligibility: each epoch included baseline wave and up to 3 waves of biennial follow-up. Participants with prevalent baseline strokes excluded from that epoch to mirror separate cohorts of stroke-free individuals. For example, individuals enrolling in 1998 and reporting first stroke in 2004 would be considered as having a stroke in Epoch 1 and would be ineligible for Epoch 2. A similar individual enrolling in 1998 but experiencing a first stroke in the 2006 wave would be considered stroke-free in Epoch 1 and as having a stroke in Epoch 2.

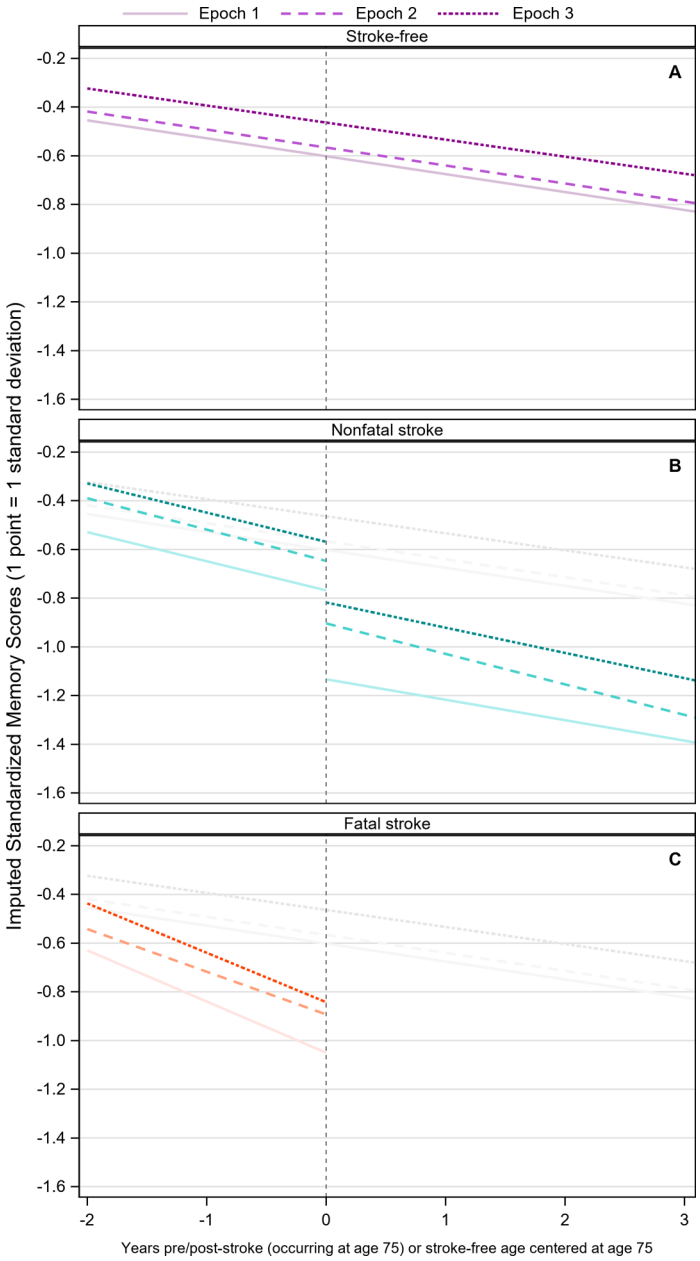

Figure 2.

Trends in memory decline across epochs for (A) stroke-free participants, (B) stroke survivors, and (C) stroke decedents: solid curves represent trends in Epoch 1, dashed curves represent Epoch 2, and dotted curves represent Epoch 3. Time 0 indicates stroke onset for participants who experienced incident stroke at 75 years of age (survivors and decedents), or age 75 for stroke-free participants. For (B) stroke survivors and (C) decedents, curves to the left of stroke onset indicate change in memory before stroke onset and curves to the right indicate change after stroke; panels (B) and (C) include stroke-free trends in light grey.

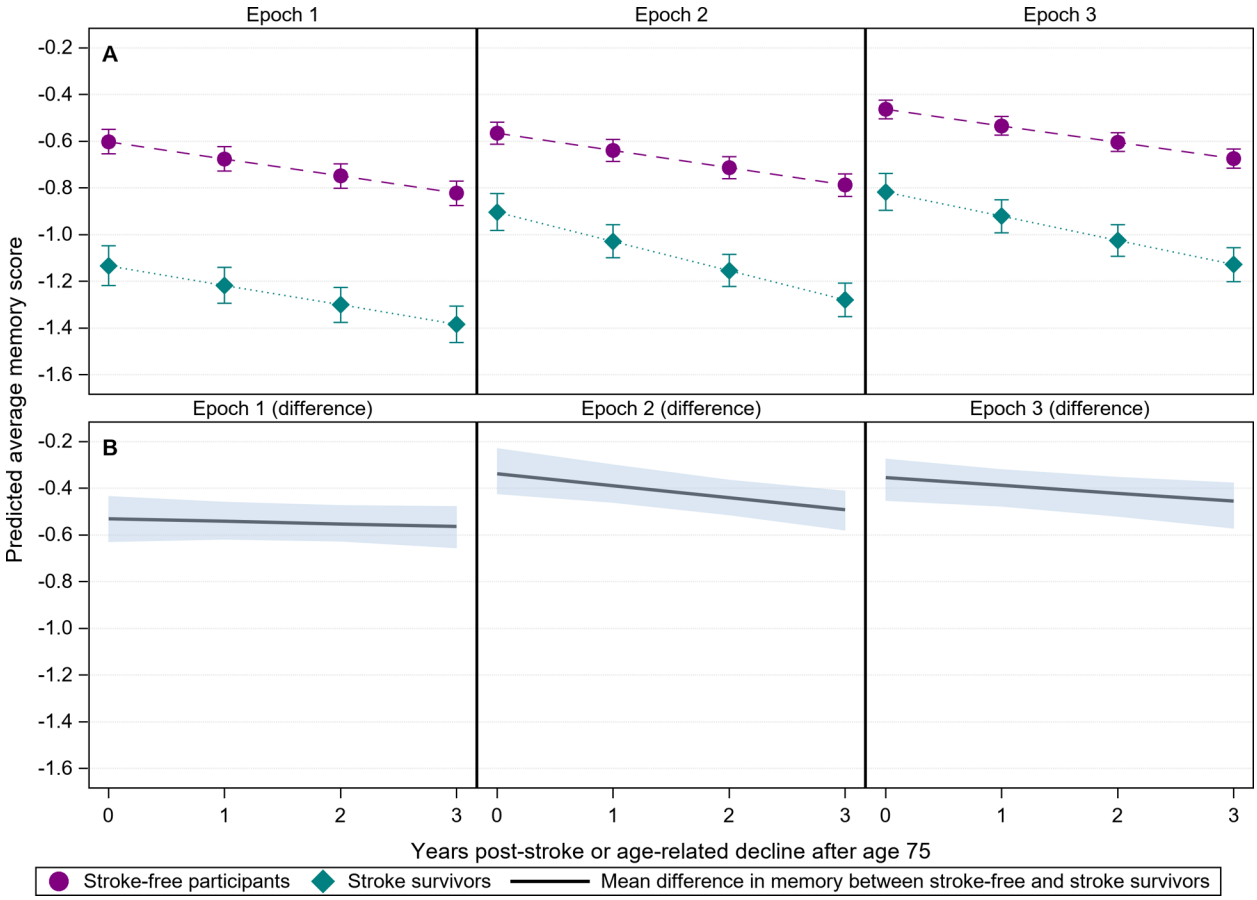

Figure 3.

Predicted memory scores for stroke-free participants and post-stroke decline in stroke survivors. Time 0 indicates time of stroke onset for stroke survivors experiencing a stroke at age 75 or age 75 for stroke-free participants. Row A shows trajectories (dashed curves for stroke-free participants, dotted curves for stroke survivors) of decline at 0, 1, 2, and 3 years post-stroke or post-age 75. Row B shows trends in mean absolute difference and 95% confidence interval between average memory scores of stroke survivors and stroke-free participants at 0, 1, 2, and 3 years post-stroke or post-age 75.

Table 1.

Unweighted baseline demographic characteristics

	Epoch 1 (1998 – 2004) N = 16,781		Epoch 2 (2004 – 2010) N = 15,345		Epoch 3 (2010 – 2016) N = 15,949		P-value for differences across epochs
	N/Mean	SD / %	N/Mean	SD / %	N/Mean	SD / %	
Stroke Status							<.0001
Stroke Free	15,890	94.69%	14,493	94.45%	15,258	95.67%	
Stroke Survivors	672	4.00%	636	4.14%	536	3.36%	
Stroke Decedents	219	1.31%	216	1.41%	155	0.97%	
Memory Score *	1.01	0.56	0.99	0.55	0.99	0.54	0.0448
Age	66.28	9.99	67.07	10.24	66.52	10.83	<.0001
Gender							0.7994
Male	7,214	42.99%	6,553	42.70%	6,802	42.65%	
Female	9,567	57.01%	8,792	57.30%	9,147	57.35%	
Race							<.0001
White	13,979	83.30%	12,627	82.29%	11,983	75.13%	
Black	2,445	14.57%	2,316	15.09%	3,396	21.29%	
Other	357	2.13%	402	2.62%	570	3.57%	
Marital Status							<.0001
Married/Partnered	11,499	68.52%	10,271	66.93%	10,203	63.97%	
Divorced/Separated	1,638	9.76%	1,704	11.10%	2,231	13.99%	
Widowed	3,154	18.80%	2,879	18.76%	2,678	16.79%	
Never Married	490	2.92%	491	3.20%	837	5.25%	
Years of Education	12.32	3.01	12.79	2.84	13.17	2.62	<.0001
Mother's Education							<.0001
< 8 years	7,883	46.98%	6,387	41.62%	5,689	35.67%	
8+ years	8,898	53.02%	8,958	58.38%	10,260	64.33%	
Wealth (median, per $1,000)	74.00	IQR (23.33, 183.00)	102.50	IQR (29.81, 265.50)	86.50	IQR (16.56, 263.00)	<.0001
Height (meters)	1.69	0.10	1.69	0.10	1.69	0.10	0.0001
Southern birthplace	2,864	17.07%	2,479	16.16%	2,930	18.37%	<.0001

SD: standard deviation. IQR: interquartile range. P-value for differences across epoch calculated using chi-square statistic for categorical covariates and analysis of variance (ANOVA) for continuous covariates.

* Memory scores z-standardized to 1998 sample mean and SD; 1-unit change represents 1 standard deviation.

Table 2.

Age-Standardized[*] Stroke Incidence Rates[†] (weighted to be representative for US community-residing individuals aged 50 and older at the start of each epoch)

	Epoch 1 (1998 – 2003) N = 16,781		Epoch 2 (2004 – 2009) N = 15,345		Epoch 3 (2010 – 2015) N = 15,949	
Total person-time (years)	**300,758,176**		**370,590,983**		**402,748,397**	
	Events	**Incidence Rate**	**Events**	**Incidence Rate**	**Events**	**Incidence Rate**
All strokes	2,777,349	8.49	3,155,683	7.97	2,805,609	6.75
Stroke survivors only	2,125,213	6.58	2,387,825	6.05	2,207,419	5.33
Stroke decedents	652,136	1.91	767,858	1.91	598,190	1.42

[*] Standardized to the US population according to 2000 US census estimates.

[†] Presented as incidence per 1,000 person-years

Table 3.

Covariate-adjusted associations between stroke-status and memory scores in population-weighted mixed linear regression models

	Epoch 1 (1998 – 2004) N=16,781			Epoch 2 (2004 – 2010) N=15,345			Epoch 3 (2010 – 2016) N=15,949			P-value (linear trend across epochs)
	Beta	95% CI		Beta	95% CI		Beta	95% CI		
		Lower	Upper		Lower	Upper		Lower	Upper	
Intercept[†]	−0.60	−0.65	−0.55	−0.57	−0.61	−0.52	−0.46	−0.50	−0.42	
Stroke-Free Participants										
Age (years)	−0.07	−0.07	−0.07	−0.07	−0.07	−0.07	−0.07	−0.07	−0.07	<0.0001
Stroke Survivors										
Indicator[‡]	−0.17	−0.24	−0.09	−0.08	−0.15	−0.01	−0.11	−0.18	−0.03	<0.0001
Age of stroke (years)	−0.10	−0.10	−0.09	−0.09	−0.10	−0.09	−0.09	−0.10	−0.09	<0.0001
Time until stroke (years)	−0.12	−0.14	−0.10	−0.13	−0.15	−0.11	−0.12	−0.14	−0.10	0.6342
Discontinuity at time of stroke[§]	−0.37	−0.44	−0.29	−0.26	−0.33	−0.18	−0.25	−0.33	−0.17	0.0196
Time since stroke (years)	−0.08	−0.11	−0.06	−0.13	−0.15	−0.10	−0.10	−0.13	−0.08	0.1599
Stroke Decedents										
Indicator[‡]	−0.45	−0.59	−0.31	−0.33	−0.45	−0.20	−0.38	−0.53	−0.23	<0.0001
Age of stroke (years)	−0.09	−0.10	−0.08	−0.10	−0.10	−0.09	−0.11	−0.12	−0.10	<0.0001
Time until stroke (years)	−0.21	−0.25	−0.17	−0.18	−0.21	−0.14	−0.20	−0.25	−0.16	0.0831

[*] Adjusted for gender, race, memory practice effects, marital status, wealth, education, height, birthplace, mother's education.

[†] Average memory score in stroke-free participants at age 75 who are female, white race, married/partnered, not born in the Southern US with 12 years of education, mother's education of less than 8 years, and median income and height for that epoch.

[‡] Indicator coefficients represent difference in average memory for this stroke group immediately compared to otherwise similar stroke-free individuals, assuming stroke occurred at age 75.

[§] Discontinuity at time of stroke is a binary indicator for assessments taken after stroke representing short-term post-stroke decrement in cognition associated with stroke onset.