

## **Geographic Inequalities in Rate of Memory Decline Among Older Adults in the United States**

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### **Brief Abstract**

Stark geographic inequalities in health and life expectancy divide the United States. Memory decline is the hallmark of Alzheimer's disease, a debilitating late-life health outcome. We evaluated whether rural-Southern childhood residence was associated with late-life memory decline among Health and Retirement Study participants (n=12,806) interviewed biennially from 1998-2016. Rural-Southern childhood residence was based on self-reported rurality (rural or non-rural) of childhood residence and state of childhood residence. Memory was assessed using immediate and delayed word list recall or the Informant Questionnaire for Cognitive Decline. In race-stratified linear mixed effects models (with age in decades as the timescale and linear splines), we estimated the effect of rural-Southern childhood residence on rate of memory decline, accounting for practice effects, sex, birth year, and parental education. On average, participants with rural-Southern childhood residence experienced approximately 9% faster rate of memory decline at ages >70 years for both Black and White participants.

## **Background and objective**

Stark geographic inequalities in health and life expectancy divide the United States (U.S.), with residents of the rural south experiencing some of the poorest health outcomes.<sup>1</sup> Lifecourse epidemiology suggests childhood place of residence may be relevant for late-life health,<sup>2</sup> but few studies have linked place of residence in childhood to late-life cognitive outcomes. Memory decline is the hallmark of progression of Alzheimer's disease and related dementias, a leading cause of morbidity and mortality among older adults with major caregiving and financial burdens on the individual, their family, and larger society.<sup>3,4</sup> We previously found that birth in a state with high stroke mortality (Southern U.S. states known as the "Stroke Belt" and Alaska) was associated with higher dementia incidence in Black and White residents in Northern California,<sup>5</sup> but this study could not disentangle effects of migration to Northern California from the effects of childhood place of residence. Here, our objective was to evaluate whether childhood residence in the rural Southern U.S. was associated with late-life memory decline among Black and White U.S.-born participants of a national cohort of adults age 51 years and older.

## **Data and methods**

*Sample.* The Health and Retirement Study (HRS) is an ongoing national cohort study of non-institutionalized adults ages 51 years and older and their spouses.<sup>6</sup> The present study includes n=12,806 Black and White HRS participants who participated in the 1998 study wave and were age 51 years or older at the time of interview. Study participants were interviewed approximately every 2 years between 1998 and 2016.

*Exposures.* The exposure of interest was rural-Southern childhood residence based on self-report. Rural childhood residence was based on self-report to a question that asked whether the participant lived in a "rural area" most of the time when they were a child. Southern childhood residence based on self-reported state of childhood residence classified by U.S. Census region, which includes the following states: DE, MD, DC, VA, WV, NC, SC, GA, FL, KY, TN, MS, AL, OK, TX, AR, LA. Race was based on self-report. All analyses were stratified by race because race and region of residence are highly correlated in the U.S. and place of residence may have different effects on health by race.<sup>7</sup>

*Outcome.* Memory was assessed by immediate and delayed recall of a 10-word list and the Informant Questionnaire for Cognitive Decline (IQCODE).<sup>8</sup> For individuals too impaired to directly participate in memory assessments, proxy informants, were asked to assess the participants' memory on a 5-item Likert scale and completed a 16-item IQCODE, which has been previously validated. We used a previously developed memory composite score combining proxy and direct memory assessments.<sup>9,10</sup> The composite memory scores were standardized (mean=0, standard deviation=1.0) to the baseline sample in 1998.

*Covariates.* We considered the following variables as potential confounders of the effect of place of childhood residence and cognitive decline: birth year, sex, maternal educational attainment (categorized as <8 years, ≥8 years, or "do not know"), paternal educational attainment (categorized as <8 years, ≥8 years, or "do not know"). We considered the following variables as potential mediators: participant educational attainment (in years) and history of stroke at baseline (yes/no). We considered the following variables as potential mediator-outcome confounders: poor childhood health (categorized as "fair" or "poor" versus "excellent," "very good," or "good") and childhood financial capital childhood financial capital (standard deviation units). All models are adjusted for practice effects with use of an indicator for the first cognitive visit.<sup>11</sup>

*Statistical analysis.* We used linear mixed effects models (with age in decades as the timescale and linear splines with a knot at age 70 years) to estimate effects of rural southern childhood residence on rate of memory decline. We selected this model specification because after comparing alternative models (linear, quadratic, and splines placed at alternative ages), this model form fit the data well and was easier to interpret than quadratic models. All analyses were stratified by race. We estimated several models adjusting for alternative covariate sets guided by our conceptual model (**Figure 1**). In Model 1, we adjusted for practice effects (indicator of first testing occasion), birth year, and sex. In Model 2, we additionally adjusted for parental educational attainment. In Model 3, we further adjusted for participant educational attainment, history of stroke at baseline, poor childhood health, and childhood financial capital. We conceptualized participant educational attainment and history of stroke at baseline as potential mediators and poor childhood health and childhood financial capital as potential mediator-outcome confounders. We tested for potential exposure-mediator interaction, but the estimates were imprecise; thus our final models do not include these interactions. We applied 1998 sampling weights to all models, so results are weighted to represent the community-dwelling U.S. population age 50 years and older in 1998.

## **Results**

Nearly half (48.9%) of Black participants reported rural-Southern childhood residence, and 17.5% of White participants reported rural-Southern childhood residence (Table 1). Parental educational attainment, childhood financial capital, and participant educational attainment tended to be lower and the prevalence of fair or poor childhood health and history of stroke were higher among Blacks versus Whites and among those with rural-Southern versus non-rural-Southern childhood residence.

Memory scores were lower for Blacks than Whites at all ages, but the rate of memory decline was similar in both race groups. Rural-Southern childhood residence was not associated with memory function at age 50, but was associated with faster rate of memory decline for both Blacks and Whites (Table 2, Figure 2). Results from mediation analyses suggest participant educational attainment and history of stroke contribute to this inequality in rate of memory decline by place of childhood residence for both Blacks and Whites.

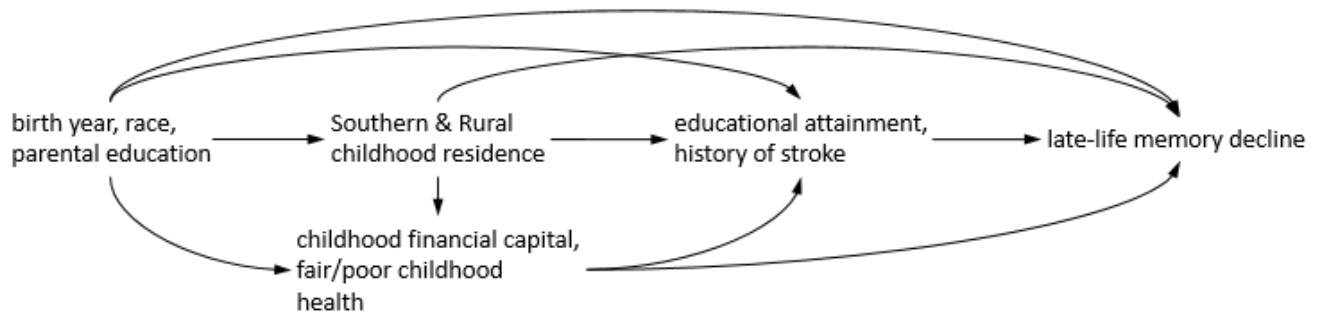
## **Conclusions**

In a large, nationally-representative sample, rate of memory decline was faster for Black and White older adults who spent their childhoods in the rural-Southern U.S. Participant educational attainment and history of stroke appeared to contribute to this inequality. This inequality was observed for both Black and White older adults, but rural-Southern childhood residence was more common among Black than White participants, so the potential population impact is greater for Black Americans. Our study confirms and extends our prior study comparing migrants from high stroke mortality states to other California residents.<sup>5</sup>

Limitations include the heterogeneous, self-reported measure of rural-Southern childhood residence. We were also limited by measuring memory with one brief measure of delayed word recall. Strengths of the study include the large, nationally-representative sample, and the lifecourse perspective of our analysis.

Childhood residence in the rural-Southern U.S. may influence late-life memory decline through multiple pathways, including educational environment and cardiometabolic health. Future studies are needed to investigate the lifecourse pathways driving this inequality, the extent to which geographic inequalities contribute to racial inequalities, and potential population-level interventions to promote equity in cognitive aging.

**Figure 1.** Conceptual diagram



Note: Sex is not included in the conceptual diagram, but it is included as a covariate in all models.

**Table 1.** Baseline characteristics of the sample (Health and Retirement Study participants 51 years and older at time of participation in the 1998 interview wave)

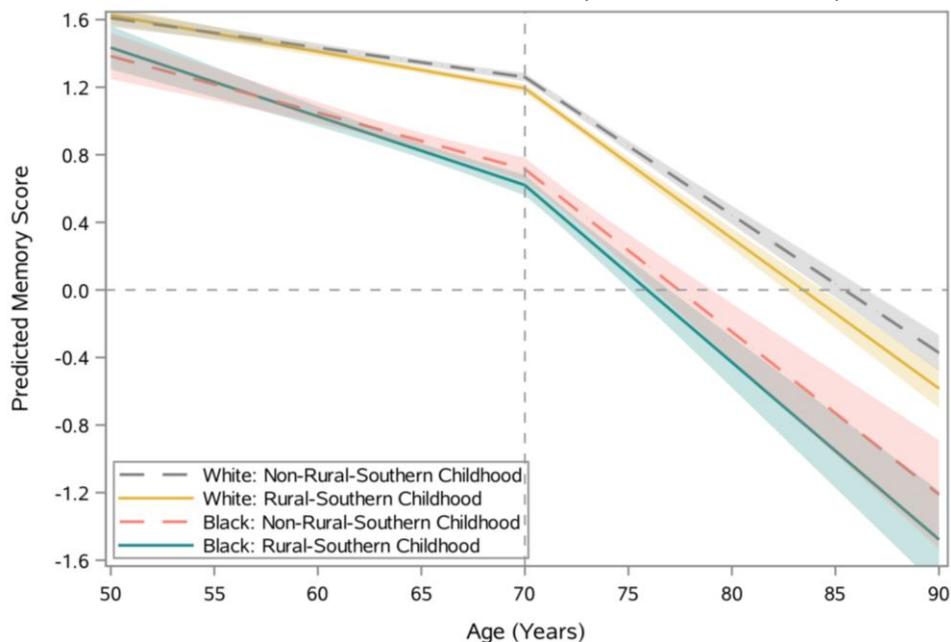
	Black Participants		White Participants	
	Southern-Rural Childhood Residence (n=517)	Non-Southern-Rural Childhood Residence (n=541)	Southern-Rural Childhood Residence (n=1,291)	Non-Southern-Rural Childhood Residence (n=6,079)
Baseline age (years), mean (SD)	61.6 (5.5)	60.2 (5.5)	61.6 (6.1)	61.3 (6.3)
Birth year, mean (SD)	1936 (5.4)	1937 (5.4)	1936 (6.0)	1936 (6.2)
Female, %	61.3	61.6	53.8	54.3
Father's education, %				
Do not know	25.5	17.7	14.7	8.9
<8 years	44.3	28.3	33.9	15.8
≥8 years	30.2	54.0	51.4	75.3
Mother's education, %				
Do not know	18.0	12.6	10.0	6.7
<8 Years	40.8	22.2	26.6	11.0
≥8 Years	41.2	65.3	63.4	82.3
Childhood financial capital, mean (SD)	-0.2 (0.9)	-0.08 (0.9)	-0.2 (1.0)	0.1 (1.0)
Fair or poor childhood health, %	9.7	7.4	6.7	5.3
Own education (years), mean (SD)	10.4 (3.1)	12.8 (2.5)	12.0 (3.0)	13.3 (2.4)
Stroke prevalence, %	5.2	4.1	3.2	3.0
Composite memory score, mean (SD)	0.8 (0.4)	0.9 (0.3)	1.2 (0.3)	1.3 (0.3)

Southern childhood residence based on self-reported state of residence classified by U.S. Census region, which includes the following states: DE, MD, DC, VA, WV, NC, SC, GA FL, KT, TN, MS, AL, OK, TX, AR, LA

**Table 2.** Estimated effect of place of childhood residence on late-life memory decline

	Model 1	Model 2	Model 3
<b>Black participants</b>			
Intercept (age 50 years)	1.38 (1.23, 1.52)	1.36 (1.21, 1.52)	1.33 (1.17, 1.48)
Rural-Southern Childhood	0.06 (0.01, 0.11)	0.05 (0.00, 0.10)	0.01 (-0.04, 0.07)
Age 50-70 years			
Decades	-0.32 (-0.41, -0.24)	-0.32 (-0.41, -0.23)	-0.29 (-0.38, -0.20)
Rural-Southern Childhood X Decades	-0.09 (-0.13, -0.05)	-0.07 (-0.11, -0.03)	-0.02 (-0.06, 0.02)
Age ≥70 years			
Decades	-0.96 (-1.10, -0.82)	-0.98 (-1.14, -0.82)	-0.97 (-1.14, -0.81)
Rural-Southern Childhood X Decades	-0.09 (-0.18, 0.01)	-0.09 (-0.18, 0.01)	-0.10 (-0.21, 0.01)
<b>White participants</b>			
Intercept (age 50 years)	1.69 (1.64, 1.74)	1.73 (1.67, 1.79)	1.72 (1.66, 1.78)
Rural-Southern Childhood	0.03 (0.00, 0.05)	0.02 (-0.01, 0.04)	0.00 (-0.02, 0.03)
Age 50-70 years			
Decades	-0.19 (-0.22, -0.16)	-0.24 (-0.27, -0.20)	-0.22 (-0.25, -0.19)
Rural-Southern Childhood X Decades	-0.06 (-0.08, -0.04)	-0.04 (-0.06, -0.02)	-0.02 (-0.04, 0.00)
Age ≥70 years			
Decades	-0.79 (-0.83, -0.76)	-0.82 (-0.67, -0.96)	-0.81 (-0.86, -0.75)
Rural-Southern Childhood X Decades	-0.08 (-0.12, -0.04)	-0.07 (-0.11, -0.03)	-0.06 (-0.10, -0.02)
Model 1 adjusted for practice effects, birth year (continuous, centered at 1924), and sex (reference = female). Model 2 additionally adjusted for parental education (reference = < 8 years education). Model 3 additionally adjusted for participant education (continuous, centered at 12 years), history of stroke at baseline (reference = no history of stroke), fair or poor childhood health (reference = better than fair or poor childhood health), childhood financial capital (continuous, centered at 0).			

**Figure 2.** Predicted memory score trajectories and 95% confidence interval bands by race and place of childhood residence, from a linear mixed effects model adjusted for practice effects, birth year, sex, and parental education. Shown for a woman born in 1924 whose parents each had <8 years of education.



### Literature Cited

1. Moy E, Garcia MC, Bastian B, et al. Leading Causes of Death in Nonmetropolitan and Metropolitan Areas-United States, 1999-2014. *Morbidity and mortality weekly report Surveillance summaries (Washington, DC: 2002)*. 2017;66(1):1-8.
2. Hayward MD, Gorman BK. The long arm of childhood: The influence of early-life social conditions on men's mortality. *Demography*. 2004;41(1):87-107.
3. Kelley AS, McGarry K, Gorges R, Skinner JS. The Burden of Health Care Costs for Patients With Dementia in the Last 5 Years of Life. *Annals of internal medicine*. 2015;163(10):729-736.
4. Association As. 2018 Alzheimer's disease facts and figures. *Alzheimer's & Dementia*. 2018;14(3):367-429.
5. Gilsanz P, Mayeda ER, Glymour MM, Quesenberry CP, Whitmer RA. Association between birth in a high stroke mortality state, race, and risk of dementia. *JAMA neurology*. 2017;74(9):1056-1062.
6. Sonnega A, Faul JD, Ofstedal MB, Langa KM, Phillips JW, Weir DR. Cohort profile: The health and retirement study (HRS). *International journal of epidemiology*. 2014;43(2):576-585.
7. Glymour MM, Manly JJ. Lifecourse social conditions and racial and ethnic patterns of cognitive aging. *Neuropsychology review*. 2008;18(3):223-254.
8. Jorm AF. The Informant Questionnaire on cognitive decline in the elderly (IQCODE): a review. *International Psychogeriatrics*. 2004;16(3):275-293.
9. Langa KM, Plassman BL, Wallace RB, et al. The Aging, Demographics, and Memory Study: study design and methods. *Neuroepidemiology*. 2005;25(4):181-191.
10. Wu Q, Tchetgen EJT, Osypuk TL, White K, Mujahid M, Glymour MM. Combining direct and proxy assessments to reduce attrition bias in a longitudinal study. *Alzheimer disease and associated disorders*. 2013;27(3):207.
11. Vivot A, Power MC, Glymour MM, et al. Jump, hop, or skip: modeling practice effects in studies of determinants of cognitive change in older adults. *American journal of epidemiology*. 2016;183(4):302-314.