

# UCSF

## UC San Francisco Previously Published Works

### Title

Gender differences in the association between education and late-life cognitive function in the LifeAfter90 Study: A multiethnic cohort of the oldest—old

### Permalink

<https://escholarship.org/uc/item/5wh091q0>

### Journal

Alzheimer's & Dementia, 20(11)

### ISSN

1552-5260

### Authors

Lam, Jennifer O  
Whitmer, Rachel A  
Corrada, Maria M  
[et al.](#)

### Publication Date

2024-11-01

### DOI

10.1002/alz.14217

### Copyright Information

This work is made available under the terms of a Creative Commons Attribution License, available at <https://creativecommons.org/licenses/by/4.0/>

Peer reviewed

## RESEARCH ARTICLE

# Gender differences in the association between education and late-life cognitive function in the LifeAfter90 Study: A multiethnic cohort of the oldest-old

Jennifer O. Lam<sup>1,2</sup> | Rachel A. Whitmer<sup>3,1</sup> | Maria M. Corrada<sup>4,5</sup> | Claudia H. Kawas<sup>4,6</sup> | Katherine E. Vieira<sup>1</sup> | Charles P. Quesenberry<sup>1</sup> | Paola Gilsanz<sup>1</sup>

<sup>1</sup>Division of Research, Kaiser Permanente Northern California, Pleasanton, California, USA

<sup>2</sup>Department of Health Systems Science, Kaiser Permanente Bernard J. Tyson School of Medicine, Pasadena, California, USA

<sup>3</sup>Department of Public Health Sciences, University of California Davis School of Medicine, Davis, California, USA

<sup>4</sup>Department of Neurology, University of California Irvine, Orange, California, USA

<sup>5</sup>Department of Epidemiology and Biostatistics, University of California Irvine, Irvine, California, USA

<sup>6</sup>Department of Neurobiology and Behavior, University of California Irvine, Irvine, California, USA

## Correspondence

Jennifer O. Lam, Division of Research, Kaiser Permanente Northern California, 4480 Hacienda Drive, Pleasanton, CA 94588, USA. Email: [Jennifer.O.Lam@kp.org](mailto:Jennifer.O.Lam@kp.org)

## Funding information

PI: Gilsanz, Grant/Award Number: R01 AG066132; PI: Gilsanz, Grant/Award Number: The Judy Fund/2019-AARGD-644788; MPIs: Whitmer, Corrada, Gilsanz, Grant/Award Number: R01AG056519; PI: Lam, Grant/Award Number: K01AI157849

## Abstract

**INTRODUCTION:** Few studies have examined the relationship between education and cognition among the oldest-old.

**METHODS:** Cognitive assessments were conducted biannually for 803 participants (62.6% women) of LifeAfter90, a longitudinal study of individuals  $\geq 90$  years old. Gender differences in associations between education ( $<$  high school, high school, some college, and  $\geq$  college) and cognition (verbal episodic memory, semantic memory, and executive function) were examined at baseline and longitudinally using linear mixed models.

**RESULTS:** Higher education levels were associated with better cognitive performance at baseline for both men and women. College completion was more strongly associated with better baseline executive function among women. Education-cognition associations for baseline verbal episodic memory and baseline semantic memory did not differ by gender. Education was not associated with a decline in any domain-specific cognitive scores, regardless of gender.

**DISCUSSION:** Education is associated with cognitive function among the oldest-old and varies by gender and cognitive domain at baseline but not over time.

## KEYWORDS

aging, cognition, cognitive function, disparity, education, gender

## Highlights

- In the oldest-old, higher education was associated with better cognitive function.
- College completion was more strongly associated with executive function in women.
- Education was not associated with cognitive decline after age 90 regardless of gender.
- Improving education could decrease gaps in cognitive level among older individuals.

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial-NoDerivs](https://creativecommons.org/licenses/by-nc-nd/4.0/) License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2024 The Author(s). *Alzheimer's & Dementia* published by Wiley Periodicals LLC on behalf of Alzheimer's Association.

## 1 | BACKGROUND

Educational attainment is one of the strongest determinants of cognitive function in later life.<sup>1-3</sup> General population data consistently show that lower educational attainment is associated with poorer cognitive functioning and a greater risk of dementia in older age.<sup>1-4</sup> Further, given that women have historically had fewer educational opportunities than men due to systemic inequities in access to education, lower cognitive performance among older women has been attributed in part to gender disparities in early-life educational attainment.<sup>5-9</sup>

It is well accepted that the effects of education in earlier life can persist through adulthood.<sup>3</sup> However, the extent to which these effects persist into very old age remains unclear. Indeed, while a recent review article concluded that associations between education and cognitive ability are apparent throughout the adult life span and across the full range of education levels, it did not include any studies of the oldest-old (i.e., individuals aged  $\geq 90$  years).<sup>3</sup> Additionally, data are lacking on gender differences in the education-cognition relationship among the oldest-old but would be important to investigate because disparities in years of formal education between men and women were likely the greatest in this age group.

To address this gap in the literature, we conducted a study among participants in the LifeAfter90 study, a diverse sample of community-dwelling individuals aged  $\geq 90$  years. Our objectives were to: (1) examine the association between educational attainment and both baseline cognitive level and cognitive change over time, and (2) determine whether these associations differed by gender.

## 2 | METHODS

### 2.1 | Study design and population

LifeAfter90 is an ongoing longitudinal cohort study of long-time members of Kaiser Permanente Northern California (KPNC), an integrated health-care delivery system in the United States. LifeAfter90 participants are at least 90 years old and reside in the San Francisco and Sacramento areas of California. The overall goal of the LifeAfter90 study is to investigate dementia incidence, cognitive decline, neuropathologic changes, and brain imaging markers in an ethnically diverse cohort of the oldest-old.

KPNC members were eligible for recruitment into the study if they were at least 90 years old, were KPNC members at some point between 1964 and 1992, and had English or Spanish language proficiency. Participants were excluded if they were unable to provide informed consent, if they had a medical condition that would interfere with their participation in study interviews (e.g., in hospice care, on dialysis), or if they had a pre-existing diagnosis of dementia or other neurodegenerative disease in their KPNC medical record at the time of study recruitment. Consistent with other studies of life course risk factors of dementia among KPNC members,<sup>10,11</sup> dementia and other neurodegenerative diseases were identified using International Classification of Diseases (ICD) 9 and 10 codes in the electronic health record (EHR;

### RESEARCH IN CONTEXT

- 1. Systematic review:** The authors used PubMed to review the literature on education and later life cognitive function. While there is significant literature showing that educational disparities may drive female cognitive disadvantage in older age, the literature related to education and cognitive function among the oldest-old is sparse.
- 2. Interpretation:** We found that the association of educational attainment with later life cognitive function is present among the oldest-old population and that the association appears to vary by gender and cognitive domain. However, there was no notable association of education with cognitive decline after age 90 regardless of gender.
- 3. Future directions:** Future work examining gender differences in exposures that lie on the pathway between education and late-life cognition (e.g., occupational type and complexity), and whether these vary by gender, could inform interventions aimed at healthy brain aging.

ICD-9: 290.0, 290.1x, 290.2x, 290.3, 290.4., 294.1x, 294.2x, 294.8, 331.0, 331.1x, 331.82x, 333.4; ICD-10: F01.50, F01.51, F02.8x, F03.90, F03.91, G10.x, G30.0, G30.1, G30.8,4 G30.9, G31.01, G31.09, G31.83).

Study enrollment began in July 2018, and non-White participants were oversampled to achieve a racially diverse study population. The study sample for the current paper included the first 819 participants who were enrolled and completed baseline visits at KPNC and the University of California, Davis (UCD), an affiliated site for the study, through February 26, 2021. Participants were excluded if they were missing all the cognitive measures ( $n = 2$ ), missing self-reported educational attainment ( $n = 4$ ), or missing self-reported race and ethnicity ( $n = 10$ ), resulting in a final analytic sample of 803 participants. The study was approved by the KPNC and UCD Institutional Review Boards, and all enrolled participants provided informed consent.

Study visits were conducted at 6-month intervals. Before the start of the coronavirus disease 2019 (COVID-19) pandemic, study visits were conducted in person at participants' homes or in KPNC clinics and shifted to phone-based visits from May 18, 2020, through the end of the study period for this paper (February 26, 2021).

### 2.2 | Educational attainment

Educational attainment was assessed at baseline interviews and defined as the last grade or highest level in school completed. Participants were considered to have an education level of "less than high school" if the highest level of education completed was  $< 12$  years, "high school degree" if they graduated high school or received a General Education Development diploma, "some college" if they

attended university but did not receive a bachelor's degree, and "college degree or more" if they received a bachelor's degree or higher. Completion of certifications was also obtained, and those who completed a certification but not a formal education degree were placed in the "technical/trade school" category. Education was examined as a categorical variable defined by degrees earned rather than years of schooling because the social credentialing earned by the obtainment of degrees could have a substantial impact on late-life cognition and may differ by gender.

### 2.3 | Cognitive function assessment

Cognitive assessments were administered at each visit by trained interviewers using Spanish and English Neuropsychological Assessment Scales (SENAS). The SENAS is a battery of cognitive tests encompassing the domains of verbal episodic memory, semantic memory, and executive function that have been validated for comparisons of cognitive change across racial/ethnic and linguistically diverse groups.<sup>12,13</sup> The cognitive assessments were administered in English or Spanish by a language-concordant interviewer. A verbal episodic memory score was derived from a multi-trial word list learning test in which the interviewer read a list of words and asked the participant to say all the words he/she could remember. Semantic memory was measured using a composite score derived from verbal (object-naming) and non-verbal (picture association) tests. An executive function composite score was obtained using component tasks of category fluency, phonemic (letter) fluency, and working memory (digit-span backward, list sorting). The score for each cognitive domain (i.e., verbal episodic memory, semantic memory, executive function) was *z* standardized using the overall baseline sample mean and standard deviation. To reduce practice effects, the SENAS word list learning test had three different versions, and participants were randomly assigned to complete one of these versions at each study visit. Details of the administration procedures, development, and psychometric characteristics have been extensively described in previous publications.<sup>12,13</sup> The semantic memory assessment section of SENAS uses visual cues that cannot be administered via phone so was assessed during in-person (i.e., pre-COVID-19) visits only.

To tailor the lengthy battery of tests to a study population aged  $\geq 90$ , we did not administer the picture association test, the visual-span backward test, the vegetable fluency test, or the "L" phonemic fluency test. We decreased the number of lists in the word list learning test from five to three and did not administer the second list in the list sorting test. Using shortened versions allowed us to measure verbal episodic memory and executive function with less burden for the  $\geq 90$ -year-old individuals in this study while maintaining high levels of measurement reliability (0.80 for executive function and 0.88 for verbal episodic memory). We also added a visual stimuli card during the word list learning test to assist participants with hearing impairment. During the test, the interviewer showed the participant the written words on the visual stimuli card while speaking the words included in the list. This was first done in a random sample of 200

people so that the test scores could be mapped to word list scores without visual aids and then it was implemented for all subsequent participants.

### 2.4 | Gender

Sex was obtained from the EHR and served as a proxy for gender.

### 2.5 | Covariates

Self-reported race and ethnicity were collected during the first study visit and were categorized as Asian, Black, Latino, White, more than one race (i.e., multiple race), or other racial/ethnic group. Participants' ages at baseline were calculated using the visit date and their birth date obtained from the EHR.

### 2.6 | Statistical methods

Participants' characteristics were compared by gender, and gender differences were evaluated using chi-square tests. For analyses of the association between education and domain-specific SENAS scores, educational attainment was categorized ordinally as "less than high school" (reference group), "high school degree," "some college," and "college degree or more."

For each cognitive domain, linear mixed models with random intercepts and slopes were used to estimate the association between education and domain-specific SENAS scores, adjusting for time since baseline (years), time  $\times$  education (to capture differential effects of education on cognitive decline), gender, baseline age (continuous and centered at the sample mean age of 92.6 years), race/ethnicity, and mode of cognitive test administration (phone vs. in person; to account for the potential influence of mode effects on cognitive test scores). Based on prior analyses examining model effects in this cohort, we used model constraints to adjust for gender-specific practice effects.<sup>14</sup> To assess gender differences, models were evaluated separately for men and women. Additionally, interaction terms were added to the overall model to assess gender differences in the association of education with baseline cognitive scores (i.e., education  $\times$  gender) and cognitive decline (i.e., education  $\times$  gender  $\times$  time). A sensitivity analysis reran analyses with the "college or more" category separated into two groups: "college completion" and "graduate school completion." Analyses were conducted in SAS 9.4 (SAS Institute).

## 3 | RESULTS

The study included 503 (62.6%) women and 300 (37.4%) men (Table 1). The average age at baseline was 92.6 years (standard deviation [SD] = 2.4 years; range: 90.1–104.7 years); 28.5% of participants identified as White, 23.9% as Asian, 22.5% as Black, 17.4% as Latino, and

**TABLE 1** Characteristics of participants by gender: the LifeAfter90 Study.

Characteristic	Women n (%)	Men n (%)	Overall n (%)
No. of participants	503 (62.6)	300 (37.4)	803 (100)
Mean age at baseline, years (range)	92.7 (90, 103)	92.6 (90, 105)	92.6 (90, 105)
Educational attainment			
Less than high school	62 (12.3)	41 (13.7)	103 (12.8)
High school	104 (20.7)	35 (11.7)	139 (17.3)
Technical/trade school	24 (4.8)	21 (7.0)	45 (5.6)
Some college	163 (32.4)	75 (25.0)	238 (29.6)
College or more	150 (29.8)	127 (42.3)	277 (34.5)
Race and ethnicity			
White	138 (27.4)	91 (30.3)	229 (28.5)
Asian	107 (21.3)	85 (28.3)	192 (23.9)
Black	127 (25.2)	54 (18.0)	181 (22.5)
Latino	89 (17.7)	51 (17.0)	140 (17.4)
Other or multiple	42 (8.3)	19 (6.3)	61 (7.5)
Follow-up time, years (range)	1.06 (0, 2.5)	0.99 (0, 2.4)	1.03 (0, 2.5)
No. of visits (range)	2.8 (1, 5)	2.7 (1, 5)	2.7 (1, 5)

7.5% another racial or ethnic group or as multiple race or ethnicity. Women were more likely than men to have their highest level of education be high school completion (20.7% of women vs. 11.7% of men) or some college (32.4% of women vs. 25.0% of men). Women were less likely than men to have their highest level of educational attainment be technical/trade school (4.8% vs. 7.0%) or to have graduated college (29.8% of women vs. 42.3% of men; chi-square for overall education distribution by gender  $p < 0.001$ ). Participants were followed for an average of 1 year and up to 2.5 years (one to five study visits; mean = 2.7 visits; SD = 1.5).

Compared to men and women with less than a high school education, higher baseline cognitive test scores were observed among those with a high school degree or technical/trade school for semantic memory (high school degree:  $\beta = 0.51$ ; 95% confidence interval [CI] = 0.26, 0.76; technical/trade school:  $\beta = 0.50$ ; 95% CI = 0.17, 0.84) and executive function (high school degree:  $\beta = 0.48$ ; 95% CI = 0.25, 0.70; technical/trade school:  $\beta = 0.46$ ; 95% CI = 0.15, 0.76) but not episodic memory (high school degree:  $\beta = 0.22$ ; 95% CI = -0.03, 0.47; technical/trade school:  $\beta = 0.11$ ; 95% CI = -0.22, 0.44), accounting for gender, time since baseline, baseline age, race/ethnicity, mode of cognitive test administration, and practice effects (Table 2). A similar pattern of results was observed for those who completed some college (Table 2). Completion of a college degree or more was associated with better performance on all cognitive domains examined, including higher baseline verbal episodic memory ( $\beta = 0.36$ , 95% CI = 0.13, 0.58), semantic memory ( $\beta = 0.75$ , 95% CI = 0.51, 0.98), and executive function scores ( $\beta = 0.90$ , 95% CI = 0.69, 1.11).

In gender-stratified models, point estimates for the association between education and baseline domain-specific cognition varied by

gender (Table 2). However, these differences were only statistically significant for baseline executive function ( $P$  for interaction = 0.03) but not for baseline verbal episodic memory ( $P$  for interaction = 0.32) nor baseline semantic memory ( $P$  for interaction = 0.57). Among women, we observed a dose-response relationship between education and executive function. Compared to women with less than a high school degree, higher baseline executive function scores were observed for those with a high school degree ( $\beta = 0.45$ , 95% CI = 0.17, 0.73), some college ( $\beta = 0.55$ , 95% CI = 0.28, 0.82), and college degree or more ( $\beta = 1.00$ , 95% CI = 0.73, 1.28; Table 2). The difference in baseline executive function scores between women with some college and women with college degrees was also significant ( $\beta = 0.45$ , 95% CI = 0.25, 0.65;  $p < 0.0001$ ; results not shown in table). Among men, those with a high school degree, some college, or a college degree or more all had higher baseline executive function scores ( $\beta = 0.54$ , 95% CI = 0.15, 0.94;  $\beta = 0.80$ , 95% CI = 0.46, 1.14; and  $\beta = 0.78$ , 95% CI = 0.46, 1.11, respectively) than those with less than a high school degree. However, unlike among women, the baseline executive function scores did not significantly differ between men with some college and those with a college degree or more ( $\beta = -0.01$ , 95% CI = -0.26, 0.24;  $p = 0.92$ ; results not shown in table).

In overall models of cognitive change over time, semantic memory scores among our reference group of men who had less than high school education declined over a mean follow-up period of 1.5 years ( $\beta = -0.22$ , 95% CI = -0.43, -0.02) but there was no significant change in executive function ( $\beta = 0.03$ , 95% CI = -0.09, 0.14) or verbal episodic memory ( $\beta = -0.16$ , 95% CI = -0.34, 0.02). Educational attainment levels were not associated with cognitive decline in any of the three domains in a full cohort or gender-stratified models (Figure 1). We

**TABLE 2** Association between education and domain-specific cognitive function.

	Verbal episodic memory $\beta$ (95% CI)	Semantic memory $\beta$ (95% CI)	Executive function $\beta$ (95% CI)
<b>Overall sample</b>			
Less than high school	Ref	Ref	Ref
High school	0.22 (−0.03, 0.47)	0.51 (0.26, 0.76)	0.48 (0.25, 0.70)
Technical/trade school	0.11 (−0.22, 0.44)	0.50 (0.17, 0.84)	0.46 (0.15, 0.76)
Some college	0.13 (−0.10, 0.36)	0.73 (0.50, 0.96)	0.62 (0.41, 0.83)
College degree or more	0.36 (0.13, 0.58)	0.75 (0.51, 0.98)	0.90 (0.69, 1.11)
Less than high school × time since baseline	Ref	Ref	Ref
High school × time since baseline	0.00 (−0.21, 0.21)	0.00 (−0.24, 0.25)	−0.09 (−0.22, 0.05)
Technical/trade school × time since baseline	−0.07 (−0.36, 0.21)	0.02 (−0.28, 0.33)	−0.19 (−0.38, −0.01)
Some college × time since baseline	0.04 (−0.16, 0.23)	−0.07 (−0.30, 0.15)	−0.10 (−0.23, 0.02)
College degree or more × time since baseline	−0.06 (−0.25, 0.13)	−0.04 (−0.26, 0.19)	−0.12 (−0.24, 0.00)
<b>Among women</b>			
Less than high school	Ref	Ref	Ref
High school	0.10 (−0.21, 0.41)	0.47 (0.17, 0.77)	0.45 (0.17, 0.73)
Technical/trade school	−0.14 (−0.61, 0.33)	0.52 (0.06, 0.98)	0.36 (−0.07, 0.78)
Some college	0.00 (−0.30, 0.30)	0.65 (0.36, 0.93)	0.55 (0.28, 0.82)
College degree or more	0.30 (−0.01, 0.61)	0.76 (0.47, 1.06)	1.00 (0.73, 1.28)
Less than high school × time since baseline	Ref	Ref	Ref
High school × time since baseline	0.10 (−0.17, 0.38)	−0.04 (−0.36, 0.29)	−0.14 (−0.30, 0.02)
Technical/trade school × time since baseline	−0.02 (−0.43, 0.39)	0.00 (−0.42, 0.43)	−0.21 (−0.45, 0.02)
Some college × time since baseline	0.14 (−0.11, 0.40)	−0.04 (−0.34, 0.26)	−0.12 (−0.27, 0.03)
College degree or more × time since baseline	0.04 (−0.21, 0.29)	−0.06 (−0.35, 0.24)	−0.13 (−0.28, 0.01)
<b>Among men</b>			
Less than high school	Ref	Ref	Ref
High school	0.43 (0.01, 0.85)	0.61 (0.15, 1.06)	0.54 (0.15, 0.94)
Technical/trade school	0.46 (−0.02, 0.94)	0.55 (0.03, 1.07)	0.62 (0.17, 1.08)
Some college	0.38 (0.02, 0.74)	0.91 (0.50, 1.31)	0.80 (0.46, 1.14)
College degree or more	0.49 (0.14, 0.83)	0.71 (0.32, 1.10)	0.78 (0.46, 1.11)
Less than high school × time since baseline	Ref	Ref	Ref
High school × time since baseline	−0.19 (−0.53, 0.15)	0.06 (−0.34, 0.46)	0.05 (−0.22, 0.31)
Technical/trade school × time since baseline	−0.21 (−0.60, 0.18)	0.05 (−0.41, 0.51)	−0.17 (−0.48, 0.13)
Some college × time since baseline	−0.14 (−0.44, 0.16)	−0.16 (−0.53, 0.20)	−0.08 (−0.31, 0.15)
College degree or more × time since baseline	−0.23 (−0.52, 0.05)	−0.02 (−0.36, 0.32)	−0.09 (−0.31, 0.13)
<i>P</i> for interaction, education × gender	0.32	0.57	0.03

Note: Models included terms for education, time since baseline (years), time × education, gender, baseline age (continuous and centered at the sample mean age of 92.6 years), race/ethnicity, and mode of administration (phone vs. in person). Models accounted for random intercepts and models with verbal episodic memory or executive function as the outcome were constrained to account for gender-specific practice effects. Interaction term *p* values were from Type III tests of fixed effects in models with men and women in the sample.

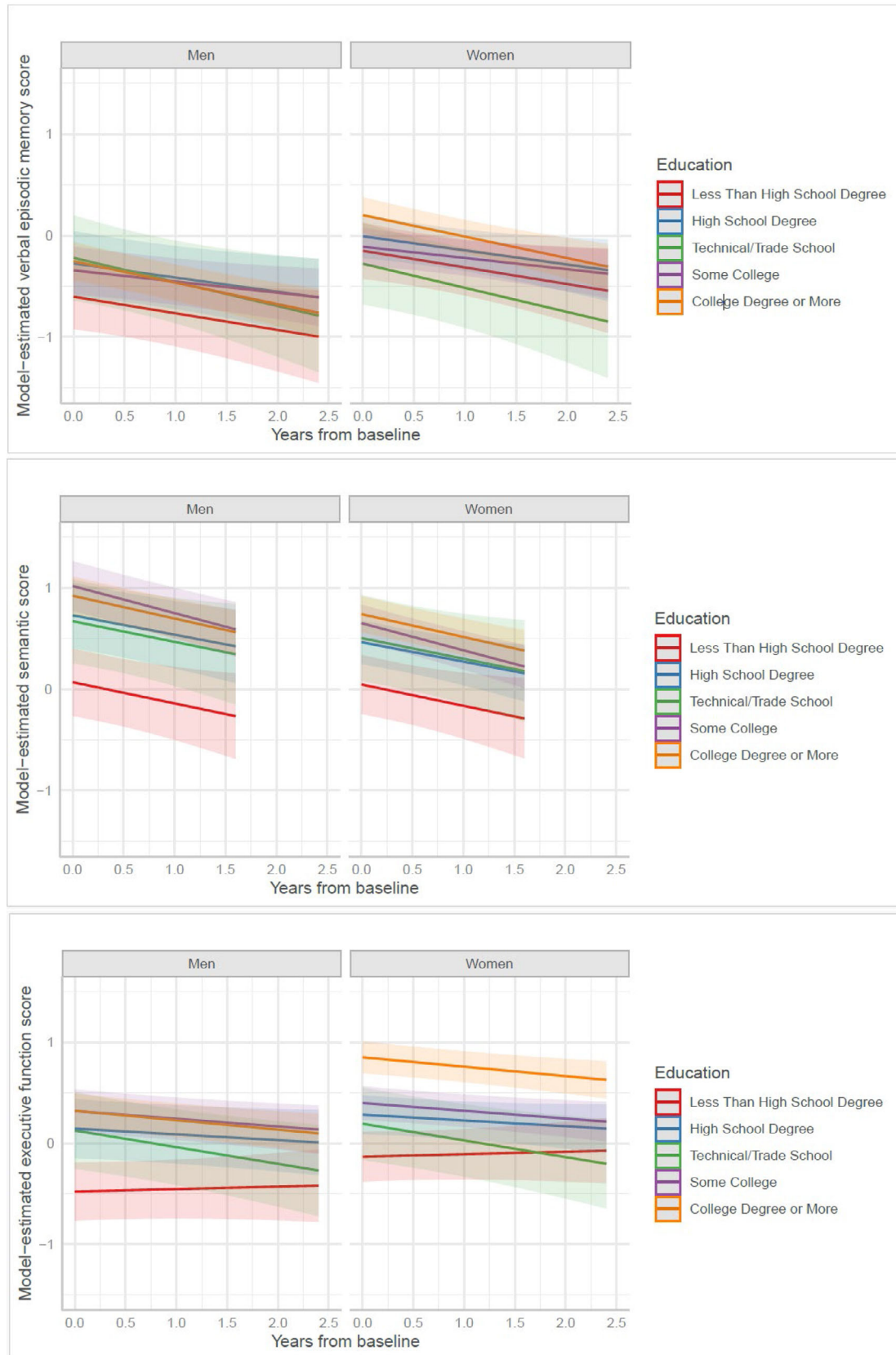
Abbreviation: CI, confidence interval.

found no evidence of gender-by-education interaction for cognitive decline in any of the cognitive domains (all *p* values for the interaction term of education × gender × time since baseline > 0.64).

In sensitivity analyses that separated the “college degree or more” group into those who completed college and those who completed

graduate school, both groups had higher baseline cognitive scores across all three domains compared to those with less than a high school degree with the exception of a non-significant association between graduate degree and verbal episodic memory (Table S1 in supporting information). Though point estimates for the association between





**FIGURE 1** Model-estimated verbal episodic memory, semantic memory, and executive function scores by gender. Semantic memory was assessed during in-person, pre-COVID-19 visits only and was therefore modeled only for a 1.5-year period.

graduate school and baseline cognitive function were lower than those for college degrees, these differences were not statistically significant, with the exception of the point estimates for verbal episodic memory. As in the main analyses, there were no associations between education and cognitive decline.

## 4 | DISCUSSION

In this analysis of a large, multiethnic cohort of US adults aged  $\geq 90$  years, we evaluated gender differences in the association between education and late-life cognitive level and change over time. Among LifeAfter90 participants, women were less likely than men to be college graduates (30% vs. 42%). The association between education and baseline executive function differed by gender, primarily due to the completion of a college degree appearing more protective among women. On the other hand, we found no evidence that the association between education and baseline verbal episodic memory or baseline semantic memory differed by gender. We also found no evidence of an association between education and cognitive decline in any of the cognitive domains examined during the mean follow-up period of 1.5 years, regardless of gender.

Our finding that the effect of education on executive function in late life differed by gender is consistent with a study of 2061 Korean Americans that found a positive association between completion of at least a high school degree and cognitive function, assessed with the Mini-Mental State Examination (MMSE); furthermore, this association was more pronounced among women than men in their sample.<sup>15</sup> These findings build on prior work demonstrating differential effects of education on other health outcomes (e.g., self-rated health,<sup>16</sup> depression,<sup>17</sup> and physical impairment<sup>18</sup> by gender). Our findings also complement prior prospective studies of younger cohorts (i.e., youngest age of inclusion ranging from 45 to 70 years) in diverse geographic settings<sup>8,19–23</sup> that have found that differential educational attainment by gender is a possible driver or mediator of later life gender disparities in cognitive outcomes but which have not specifically examined effect modification by gender.

Possible reasons for gender differences in the relationship of education with cognitive outcomes include differences in social and structural forces influencing postcollege opportunity across genders. The association of more education with better executive function was weaker among men suggesting that women may have reaped a greater benefit than men from obtaining higher education. Other potential explanations include gender-specific selection into educational opportunities or gender-based educational experiences, although evidence has been limited and mixed.<sup>5,20</sup> Notably, the advantage of college completion was only observed among women who completed all years of college and obtained a degree; a similar gender advantage was not observed among women who only completed some college but did not graduate. This suggests that the credentialing signaled by a college degree, and perhaps the greater occupational and socioeconomic benefits it provided, were an additional potential mechanism. Indeed, the 1950s US Census<sup>24</sup> showed that women who completed high school or

some college were less likely than men to participate in the labor force (27.9% vs. 13.6%; calculations done by authors). We interpret these findings with caution given the small sample size, but it nevertheless adds to the limited literature in this area suggesting that returns of educational attainment may differ not only by gender but also by cognitive domain.<sup>23,25</sup> It remains unclear why these results were observed only for executive function and not for verbal episodic memory or semantic memory, an unexpected finding that warrants further study in larger samples.

We found that educational attainment was not strongly associated with cognitive decline in individuals aged  $\geq 90$ , consistent with some prior studies that have not found substantial associations between early-life education and rates of cognitive decline in the general population.<sup>26</sup> Potential explanations include relatively short duration of study follow-up, changing risk factor associations over time including accumulation of age-related comorbidities, competing risks, selective mortality, and differing prevalence of neuropathologies across population subgroups.<sup>27,28</sup> Variability in the association of educational attainment with cognitive decline across cognitive domains, and across ethnically or geographically diverse study populations, would also be important to investigate in larger cohorts.<sup>29</sup> Given the focus of our study on a smaller segment of the older population (aged  $\geq 90$ ), our observations may reflect a healthy survivor effect and/or mortality inequality earlier in life. In other words, our participants may represent a “survival cohort” of exceptionally healthy older individuals, which could have diminished our ability to distinguish cross-group variability in cognitive decline.

LifeAfter90 is an ongoing study with continued recruitment and additional SENAS administrations; as more data are collected, we will be better powered to provide additional insights on the association of education and cognitive decline over longer periods of time and across more granular levels of higher education. Future work in larger cohorts of individuals  $\geq 90$  should also investigate education–cognition associations accounting for the intersectionality of participant identities, such as at the intersection of gender race, and ethnicity, which may be particularly relevant as educational opportunities in the United States have historically differed across racial groups.<sup>30–32</sup> For example, some participants in the study population may have completed school in the US South during a time in which Southern US state laws allowed school segregation until 1954. Overall, our results emphasize the importance of investment in education for reducing differences in levels of later-life cognitive function. Encouragingly, recent reports show that secular changes in access to education have resulted in narrowing gaps in cognitive function between men and women in younger generations.<sup>8,23</sup>

A key strength of the study was the well-defined cohort of people  $\geq 90$  with stable follow-up. Repeated measures of cognitive performance approximately every 6 months maximized the ability to capture cognitive change while minimizing data loss due to attrition between study periods.<sup>33</sup> Another strength was the inclusion of a racially and ethnically diverse study population though we were underpowered to examine possible differential effects of education on cognition by race, ethnicity, and gender concurrently. Furthermore, we acknowledge



that gender identity may not align with an individual's biological sex and that there may be heterogeneity in gender identities not captured by our definitions of "men" and "women," which was based on the patient's sex recorded in the EHR. There could also be heterogeneity within categories of educational attainment including gender differences in academic discipline, years of informal schooling, and quality of schooling which could also contribute to cognitive functioning. Our results may not generalize to other populations or countries with different educational systems and socioeconomic conditions that could lead to different life course experiences by gender. However, there is evidence that the education-cognition association is strong across populations with different educational systems after controlling for social circumstances.<sup>34</sup> And last, we began conducting phone visits during the COVID-19 pandemic to increase participant safety. There may be residual differences in cognitive test results not captured by statistical adjustment for mode of cognitive test administration.

In summary, this study found that the association of educational attainment with later-life cognitive function is present among the oldest-old population and that the association appears to vary by gender and cognitive domain. On the other hand, there was no notable association of education with cognitive change over time after age 90 for any of the cognitive domains, regardless of gender. Overall, the findings from this study underline the importance of improving education access to decrease gaps in cognitive levels among older individuals. Future work examining the effects of experiences on the pathway between education and late-life cognition—such as occupational type and complexity, for example, and potential differences by gender, race, and ethnicity, could inform strategies to reduce disparities in healthy brain aging.

## ACKNOWLEDGMENTS

This work was supported by funding from The Judy Fund/2019-AARGD-644788 (PI: Gilsanz), the National Institute on Aging (R01 AG066132, PI: Gilsanz; R01AG056519, MPls: Whitmer, Corrada, Gilsanz), and the National Institute of Allergy and Infectious Diseases (K01 AI157849, PI: Lam). We thank Dr. Joseph Roscoe and Andrew Hirst for assistance with data analyses.

## CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest. Author disclosures are available in the [supporting information](#).

## CONSENT STATEMENT

The study was approved by the Kaiser Permanente Northern California and University of California at Davis Institutional Review Boards, and all enrolled participants provided informed consent.

## REFERENCES

- Baumgart M, Snyder HM, Carrillo MC, Fazio S, Kim H, Johns H. Summary of the evidence on modifiable risk factors for cognitive decline and dementia: a population-based perspective. *Alzheimers Dement*. 2015;11(6):718-726. doi:10.1016/j.jalz.2015.05.016
- Beydoun MA, Beydoun HA, Gamaldo AA, Teel A, Zonderman AB, Wang Y. Epidemiologic studies of modifiable factors associated with cognition and dementia: systematic review and meta-analysis. *BMC Public Health*. 2014;14:643. doi:10.1186/1471-2458-14-643
- Lövdén M, Fratiglioni L, Glymour MM, Lindenberg U, Tucker-Drob EM. Education and cognitive functioning across the life span. *Psychol Sci Public Interest*. 2020;21(1):6-41. doi:10.1177/1529100620920576
- Lipnicki DM, Makkar SR, Crawford JD, et al. Determinants of cognitive performance and decline in 20 diverse ethno-regional groups: a COSMIC collaboration cohort study. *PLoS Med*. 2019;16(7):e1002853. doi:10.1371/journal.pmed.1002853
- Ford KJ, Leist AK. Returns to educational and occupational attainment in cognitive performance for middle-aged South Korean men and women. *Gerontol Geriatr Med*. 2021;7:23337214211004366. doi:10.1177/23337214211004366
- Zhang Z. Sex differentials in cognitive impairment and decline of the oldest old in China. *J Gerontol B Psychol Sci Soc Sci*. 2006;61(2):S107-115. doi:10.1093/geronb/61.2.s107
- Angrisani M, Jain U, Lee J. Sex differences in cognitive health among older adults in India. *J Am Geriatr Soc*. 2020;68 Suppl 3(Suppl 3): S20-S28. doi:10.1111/jgs.16732
- Lei X, Hu Y, McArdle JJ, Smith JP, Zhao Y. Sex differences in cognition among older adults in China. *J Hum Resour*. 2012;47(4):951-971. doi:10.3368/jhr.47.4.951
- Bonsang E, Skirbekk V, Staudinger UM. As you sow, so shall you reap: sex-role attitudes and late-life cognition. *Psychol Sci*. 2017;28(9):1201-1213. doi:10.1177/0956797617708634
- Hayes-Larson E, Mobley TM, Mungas D, et al. Accounting for lack of representation in dementia research: generalizing KHANDLE study findings on the prevalence of cognitive impairment to the California older population. *Alzheimers Dement*. 2022;18(11):2209-2217. doi:10.1002/alz.12522
- Jimenez MP, Gause EL, Hayes-Larson E, et al. Racial and ethnic differences in the association between depressive symptoms and cognitive outcomes in older adults: findings from KHANDLE and STAR. *Alzheimers Dement*. 2023;20(5):3147-3156. doi:10.1002/alz.13768
- Mungas D, Reed BR, Crane PK, Haan MN, González H. Spanish and English neuropsychological assessment scales (SENAS): further development and psychometric characteristics. *Psychol Assess*. 2004;16(4):347-359. doi:10.1037/1040-3590.16.4.347
- Mungas D, Reed BR, Haan MN, González H. Spanish and English neuropsychological assessment scales: relationship to demographics, language, cognition, and independent function. *Neuropsychology*. 2005;19(4):466-475. doi:10.1037/0894-4105.19.4.466
- Chen R, Calmasini C, Swinnerton K, et al. Pragmatic approaches to handling practice effects in longitudinal cognitive aging research. *Alzheimers Dement*. 2023;19:4028-4036. doi:10.1002/alz.13067
- Choi EY, Jang Y, Chiriboga DA. Sex as a moderator of the effect of education and acculturation on cognitive function: a study of older Korean immigrants. *J Aging Health*. 2020;32(10):1659-1666. doi:10.1177/0898264320950554
- Ross CE, Masters RK, Hummer RA. Education and the sex gaps in health and mortality. *Demography*. 2012;49(4):1157-1183. doi:10.1007/s13524-012-0130-z
- Ross CE, Mirowsky J. Sex differences in the effect of education on depression: resource multiplication or resource substitution? *Soc Sci Med*. 2006;63(5):1400-1413. doi:10.1016/j.socscimed.2006.03.013
- Ross CE, Mirowsky J. Sex and the health benefits of education. *Sociol Q*. 2010;51(1): doi:10.1111/j.1533-8525.2009.01164.x
- Cagney KA, Lauderdale DS. Education, wealth, and cognitive function in later life. *J Gerontol B Psychol Sci Soc Sci*. 2002;57(2):P163-172. doi:10.1093/geronb/57.2.p163
- Maurer J. Education and male-female differences in later-life cognition: international evidence from Latin America and the Caribbean. *Demography*. 2011;48(3):915-930. doi:10.1007/s13524-011-0048-x

21. Yount KM. Sex, resources across the life course, and cognitive functioning in Egypt. *Demography*. 2008;45(4):907-926. doi:[10.1353/dem.0.0034](https://doi.org/10.1353/dem.0.0034)
22. Lee J, Shih R, Feeney K, Langa KM. Sex disparity in late-life cognitive functioning in India: findings from the longitudinal aging study in India. *J Gerontol B Psychol Sci Soc Sci*. 2014;69(4):603-611. doi:[10.1093/geronb/gbu017](https://doi.org/10.1093/geronb/gbu017)
23. Bloomberg M, Dugravot A, Dumurgier J, et al. Sex differences and the role of education in cognitive ageing: analysis of two UK-based prospective cohort studies. *Lancet Public Health*. 2021;6(2):e106-e115. doi:[10.1016/s2468-2667\(20\)30258-9](https://doi.org/10.1016/s2468-2667(20)30258-9)
24. United States Census Bureau. Census of Population: 1950. US Government Printing Office; 1953.
25. Reas ET, Laughlin GA, Bergstrom J, Kritz-Silverstein D, Barrett-Connor E, McEvoy LK. Effects of sex and education on cognitive change over a 27-year period in older adults: the Rancho Bernardo Study. *Am J Geriatr Psychiatry*. 2017;25(8):889-899. doi:[10.1016/j.jagp.2017.03.008](https://doi.org/10.1016/j.jagp.2017.03.008)
26. Seblova D, Berggren R, Lövdén M. Education and age-related decline in cognitive performance: systematic review and meta-analysis of longitudinal cohort studies. *Ageing Res Rev*. 2020;58:101005. doi:[10.1016/j.arr.2019.101005](https://doi.org/10.1016/j.arr.2019.101005)
27. Kaplan GA, Haan MN, Wallace RB. Understanding changing risk factor associations with increasing age in adults. *Annu Rev Public Health*. 1999;20:89-108. doi:[10.1146/annurev.publhealth.20.1.89](https://doi.org/10.1146/annurev.publhealth.20.1.89)
28. Kawas CH, Legdeur N, Corrada MM. What have we learned from cognition in the oldest-old. *Curr Opin Neurol*. 2021;34:258-265. doi:[10.1097/wco.0000000000000910](https://doi.org/10.1097/wco.0000000000000910)
29. Lipnicki DM, Crawford JD, Dutta R, et al. Age-related cognitive decline and associations with sex, education and apolipoprotein E genotype across ethnocultural groups and geographic regions: a collaborative cohort study. *PLoS Med*. 2017;14(3):e1002261. doi:[10.1371/journal.pmed.1002261](https://doi.org/10.1371/journal.pmed.1002261)
30. Kimbro RT, Bzostek S, Goldman N, Rodríguez G. Race, ethnicity, and the education gradient in health. *Health Aff*. 2008;27(2):361-372. doi:[10.1377/hlthaff.27.2.361](https://doi.org/10.1377/hlthaff.27.2.361)
31. U.S. Census Bureau. Educational Attainment in the United States: 2022. US Government Printing Office; 2022. Accessed June 18, 2024. <https://www.census.gov/data/tables/2022/demo/educational-attainment/cps-detailed-tables.html>
32. Chiang AY, Schwartz G, Hamad R. School segregation and health across racial groups: a life course study. *J Adolesc Health*. 2024;75:323-332. doi:[10.1016/j.jadohealth.2024.04.014](https://doi.org/10.1016/j.jadohealth.2024.04.014)
33. Corrada MM, Brookmeyer R, Paganini-Hill A, Berlau D, Kawas CH. Dementia incidence continues to increase with age in the oldest old: the 90+ study. *Ann Neurol*. 2010;67(1):114-121. doi:[10.1002/ana.21915](https://doi.org/10.1002/ana.21915)
34. Zhang J, Lu N, Wang W. Does education moderate the relationship between social capital and cognitive function among older adults? Evidence from Suzhou city, China. *Int J Environ Res Public Health*. 2020;17(18). doi:[10.3390/ijerph17186560](https://doi.org/10.3390/ijerph17186560)

### SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

**How to cite this article:** Lam JO, Whitmer RA, Corrada MM, et al. Gender differences in the association between education and late-life cognitive function in the LifeAfter90 Study: A multiethnic cohort of the oldest-old. *Alzheimer's Dement*. 2024;1-9. <https://doi.org/10.1002/alz.14217>