



Original Contribution

Life-Course Socioeconomic Position and Incidence of Dementia and Cognitive Impairment Without Dementia in Older Mexican Americans: Results From the Sacramento Area Latino Study on Aging

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There have been few investigations of the link between changes in life-course socioeconomic position (SEP) and cognitive decline or incidence of dementia. The authors examined the impact of changes in life-course SEP on incidence of dementia and cognitive impairment but not dementia (CIND) over a decade of follow-up. Participants of Mexican origin ($n = 1,789$) were members of the Sacramento Area Latino Study on Aging cohort. Incidence of dementia/CIND was ascertained by using standard diagnostic criteria. SEP indicators at 3 life stages (childhood, adulthood, and midlife) were used to derive a measure of cumulative SEP (range, 0 to 8) and SEP mobility. Nearly 24% of the sample maintained a low SEP throughout life. Hazard ratios and 95% confidence intervals were computed from Cox proportional hazards regression models. In fully adjusted models, participants with a continuously high SEP had lower hazard ratios for dementia/CIND compared with those with a continuously low SEP at all 3 life stages (hazard ratio = 0.49, 95% confidence interval: 0.24, 0.98; $P = 0.04$). In age-adjusted models, participants experienced a 16% greater hazard of dementia/CIND with every 1-unit increase in cumulative SEP disadvantage across the life course (hazard ratio = 1.16, 95% confidence interval: 1.01, 1.33; $P = 0.04$). Early exposures to social disadvantage may increase the risk of late-life dementia.

aged; dementia; longitudinal studies; Mexican Americans; social class; socioeconomic factors

Abbreviations: CIND, cognitive impairment but not dementia; SALSA, Sacramento Area Latino Study on Aging; SEP, socioeconomic position.

There is a wealth of literature that suggests that low socioeconomic position (SEP), which is assessed by using a range of measures, including educational attainment (1–13) and occupation (2, 13–17), is associated with late-life dementia. These associations have been increasingly linked to early life socioeconomic environment (18–21), which may influence brain and cognitive development (19, 22–26) and potentially increase the risk of dementia later in life (19). Accordingly, the influence of SEP on dementia is best described within a life-course context.

The proportion of older US Hispanics is growing quickly (27), and 66% are of Mexican descent. Mexican Americans and some other ethnic minority groups in the United States are disproportionately burdened with dementia (3, 28–30)

and dementia risk factors, such as hypertension and type 2 diabetes (31–33), compared with non-Hispanic whites. The life-course socioeconomic experience of US Hispanics is complex; for example, beneficial changes in SEP trajectories from childhood to adulthood have been documented (34–35) to have protective effects on cognitive function (34). However, most of the work examining racial/ethnic differences in dementia in the United States has focused on either non-Hispanic white or black populations (1, 30, 36–40), and less is known about dementia among Mexican Americans (29, 41).

To our knowledge, there have been no studies to date that examined the association between changes in SEP across the life course and dementia incidence among Mexican

Americans. In the present analysis, we examined the association between life-course SEP trajectory and incident dementia and cognitive impairment but not dementia (CIND) in a cohort of older Mexican Americans.

MATERIALS AND METHODS

Study population

Participants in this analysis were members of the Sacramento Area Latino Study on Aging (SALSA) cohort. SALSA is a longitudinal cohort study of 1,789 community-dwelling Mexican Americans residing in California's Sacramento Valley who were 60–101 years of age at baseline in 1998–1999. The study population and the participant recruitment procedure have been described elsewhere (41). SALSA was approved by the institutional review boards of the University of Michigan and the University of California, Davis. Clinical data were collected about participants in home visits every 12–15 months for a total of 7 follow-up visits. Participants reported health conditions and lifestyle and sociodemographic risk factors. Participants with dementia/CIND at baseline ($n = 155$) were excluded from this analysis, and the remaining participants ($n = 1,634$) were followed for an average of 6.3 years (standard deviation, 3.1). Monitoring of participants deaths is still ongoing.

Measures

Dementia/CIND diagnosis. A multistage screening process was used. In the first stage, the Modified Mini-Mental State Examination, a 100-point global cognitive test (42), and the Spanish and English Verbal Learning Test, a memory word list recall test (43), were administered. If participants scored below the 20th percentile on either test or if their Modified Mini-Mental State Examination or Spanish and English Verbal Learning Test scores declined by more than 8 points or 3 points, respectively, from the previous examination, participants were referred for further neuropsychological testing. In the second stage, the neuropsychological test battery (Spanish and English Neuropsychological Assessment Scales) (44) and the Informant Questionnaire on Cognitive Decline in the Elderly were used to determine the need for further neurologic examination on the basis of the following criteria: a score ≥ 3.40 on the Informant Questionnaire on Cognitive Decline in the Elderly and a score below the 10th percentile on at least 1 of the Spanish and English Neuropsychological Assessment Scales tests, a score below the 10th percentile on at least 4 Spanish and English Neuropsychological Assessment Scales tests, or a score >4.0 on the Informant Questionnaire on Cognitive Decline in the Elderly. In the third stage, neurologists and neuropsychologists diagnosed potential cases of dementia based on the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (45) and the National Institute of Neurologic and Communicative Disorders and Stroke-Alzheimer Disease and Related Disorders Association (46) criteria. Participants were classified as normal, cognitively impaired but not demented, or demented. Participants with dementia were

subject to further magnetic resonance imaging and laboratory tests. In the present analysis, dementia and CIND were combined into a single outcome, dementia/CIND.

Life-course SEP. We included measures from 3 life stages. Parental educational level and occupation, food deprivation while growing up, and childhood sibling mortality were measures of childhood SEP. As conceptualized here, participant's educational attainment and lifetime occupation were measures of early adulthood and midlife SEP, respectively. Both maternal and paternal educational levels were classified as low (less than elementary school) or high (elementary school or beyond). Maternal occupation was classified as low (manual or housewife) or high (nonmanual), as was paternal occupation (manual or unemployed vs. nonmanual). Participants reported how often they did not have enough to eat while growing up, and their responses were coded as low (ever lacked enough to eat) or high (never). Participants reported whether any of their siblings died in childhood, and those answers were classified as present or absent. Participants with no siblings (1.93%) were classified as having no sibling mortality. All childhood SEP variables were assigned a score of 0 (high SEP) or 1 (low SEP) and then added together into a composite measure that estimated overall childhood SEP. Total childhood SEP score (range, 0–6) was split at the median and recoded into 0 (high SEP) or 1 (low SEP). Participants' educational levels were obtained by asking them how many years of education they completed, and the responses were classified as low (less than elementary school) or high (elementary school or beyond). Participants reported their major lifetime occupation, which was classified as low (manual, unemployed, or housewife) or high (nonmanual).

A 4-level SEP trajectory measure was created, with each level representing a distinct trajectory from childhood to early adulthood and midlife (Figure 1): 1) low SEP at all stages (referent category; low childhood SEP, low early adulthood SEP, and low midlife SEP); 2) downward SEP (high childhood SEP, low early adulthood SEP, and low midlife SEP; low childhood SEP, high early adulthood SEP, and low midlife SEP); 3) upward SEP with low educational level (low childhood SEP, low early adulthood SEP, and high midlife SEP or high childhood SEP, low early adulthood SEP, and high midlife SEP); and 4) high SEP at all stages or upward SEP with high educational level (high childhood SEP, and high early adulthood SEP, and high midlife SEP or low childhood SEP, high early adulthood SEP, and high midlife SEP) (47, 48). Given the established importance of education in predicting dementia/CIND (1–4, 6–7, 14, 49–52), participants with an upward SEP with a high educational level were separated from those with a low educational level. Furthermore, those with high educational levels were merged with participants whose trajectory was always high because they had statistically similar hazards of dementia/CIND.

Cumulative SEP disadvantage. A variable measuring cumulative disadvantage (range, 0–8) was constructed by summing dichotomous childhood, early adulthood, and midlife SEP measures. A higher score represents a greater disadvantage.

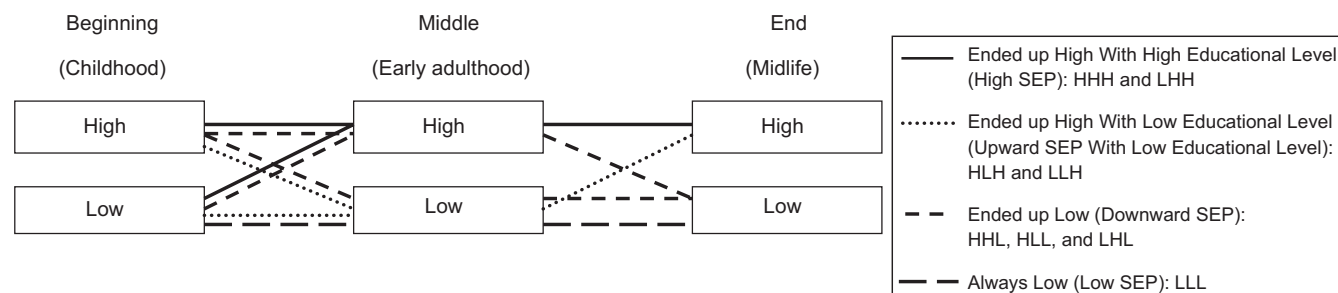


Figure 1. Conceptual framework of socioeconomic position (SEP) trajectories in the Sacramento Area Latino Study on Aging, 1998–2008. HHH, high childhood SEP, high early adulthood SEP, and high midlife SEP; HHL, high childhood SEP, high early adulthood SEP, and low midlife SEP; HLH, high childhood SEP, low early adulthood SEP, and high midlife SEP; HLL, high childhood SEP, low early adulthood SEP, and low midlife SEP; LHH, low childhood SEP, high early adulthood SEP, and high midlife SEP; LHL, low childhood SEP, high early adulthood SEP, and low midlife SEP; LLH, low childhood SEP, low early adulthood SEP, and high midlife SEP; LLL, low childhood SEP, low early adulthood SEP, and low midlife SEP.

Covariates

Native country was categorized based on participants' reports of their country of birth. Participants either were born in the United States or were born in Mexico or another Latin American country and then immigrated to the United States. Nearly all immigrants were born in Mexico. Nativity was coded as US-born or Mexican-born. Participants reported their past-month household income, which was split at the median and classified as low (income <\$1,500) or high (income \geq \$1,500). Fasting blood glucose levels were measured and blood pressure was monitored at each home visit. Incidence of diabetes was ascertained as a self-report of having received a diagnosis from a medical doctor, use of diabetes medication, and/or a fasting glucose level \geq 126 mg/dL (53). Hypertension was ascertained as a self-report of having received a diagnosis from a medical doctor, use of medication, a systolic blood pressure $>$ 140 mm Hg, and/or a diastolic blood pressure $>$ 90 mm Hg (54). A stroke event was ascertained as a self-report of having received a diagnosis from a medical doctor, including hospitalization for stroke. Anthropometric measures such as height (in cm) and weight (in kg) were measured. Body mass index (weight in kilograms divided by height in meters squared) was derived and classified as normal ($<$ 25.0), overweight (25.0–29.9), or obese (\geq 30). Waist circumference (in cm) was measured and classified into sex-specific tertiles, the values of which were then combined for men and women. Participants reported whether they had health insurance, their baseline smoking status (ever or never), and their alcohol consumption (never, $<$ 2 drinks/week, or \geq 2 drinks/week).

Statistical analyses

All statistical analyses were performed using SAS, version 9.2 (55). Cox proportional hazards models were used with the PHREG procedure to examine the risk of dementia/CIND. Participants contributed observed time at risk beginning with their enrollment in the study (56). Time was considered as participants' age (57), and accordingly an entry point (age at enrollment) and an ending point (age at dementia/CIND diagnosis or censoring) were modeled in an attempt to address

left-truncation, the time at which participants contributed unobserved time at risk. Ties were handled using the discrete option, which assumes no underlying ordering for 2 events that occur at the same time. Participants without a dementia/CIND diagnosis by the end of the study period were censored at the age of their last available contact. A total of 27 deaths with dementia listed as a cause occurred during the study period and were identified from mortality surveillance. These participants were censored at their age of death.

Cox proportional hazards models were used to examine bivariate associations between covariates, selected based on the literature, and the risk of dementia/CIND. A series of Cox proportional hazards models were also used to evaluate the associations between life-course SEP measures and the risk of dementia/CIND and were adjusted for age, income, alcohol consumption, diabetes, and stroke. Inclusion of covariates at the multivariate level was based on their association with dementia/CIND at the bivariate level and their association with life-course SEP. Hazard ratios, 95% confidence intervals, and 2-sided *P* values were computed. Interactions between nativity, age at enrollment, and life-course SEP measures were tested separately. These interactions were not significant and were not included in the final models. Monthly household income often declines with retirement and is not an accurate measure of past income. It was not included in the SEP trajectory but was adjusted for as a covariate in the multivariate analyses. We differentiated between diabetic participants who were treated and those who were untreated. Indicator variables for treated, untreated, and nondiabetic (reference) subjects were used. Incidence rates of dementia/CIND (per 1,000 person-years) by SEP trajectory were calculated by dividing the number of dementia/CIND cases in each SEP trajectory by the number of person-years at risk contributed by participants within that trajectory.

Data imputation

Before data imputation, one-fourth of the participants had missing data at any point during the study follow-up time. Most of this was due to death ($n = 522$). We performed sensitivity analyses using the nonimputed SALSA data

Table 1. Incidence Rates (per 1,000 Person-Years) of Dementia/Cognitive Impairment but Not Dementia by Socioeconomic Position Trajectory Group, Sacramento Area Latino Study on Aging, 1998–2008.

SEP Trajectory	No. of Cases	Person-Years at Risk	Incidence Rate	95% Confidence Interval	Incidence Rate Ratio ^a
High SEP: HHH and LHH	19	1,860.8	10.4	–1.2, 22.0	0.3
Upward SEP with low educational level: LLH and HLH	14	496.2	29.0	–8.1, 66.1	0.9
Downward SEP: LHL, HHL, and HLL	126	5,530.4	22.8	12.8, 32.8	0.7
Low SEP: LLL	75	2,338	32.1	12.7, 51.5	1.0
Total	234	10,225.4	23.0	14.1, 31.9	

Abbreviations: HHH, high childhood SEP, high early adulthood SEP, and high midlife SEP; HHL, high childhood SEP, high early adulthood SEP, and low midlife SEP; HLH, high childhood SEP, low early adulthood SEP, and high midlife SEP; HLL, high childhood SEP, low early adulthood SEP, and low midlife SEP; LHH, low childhood SEP, high early adulthood SEP, and high midlife SEP; LHL, low childhood SEP, high early adulthood SEP, and low midlife SEP; LLH, low childhood SEP, low early adulthood SEP, and high midlife SEP; LLL, low childhood SEP, low early adulthood SEP, and low midlife SEP; SEP, socioeconomic position.

^a Low SEP was the reference category.

set. Similar conclusions were found, with unchanged statistical significance compared with the analysis using multiple imputations. A multiple-imputation approach was performed for the entire SALSA data set to accommodate incomplete data points. It was a sequential regression multivariate imputation approach that conditions on all observed variables as predictors (58, 59). The different imputations were run in a cyclic manner that overwrote previously drawn values and built interdependence between the imputed values. By using all available variables, the multiple-imputation approach provided less biased estimates while improving efficiency compared with other alternative analytical approaches, such as the listwise deletion analysis. Although such alternative approaches assume that data are missing completely at random, an assumption that is rarely valid in epidemiologic studies (60), the sequential regression multivariate imputation approach used in this analysis imposes a less restrictive assumption. The efficiency of the estimates levels off after the production of a few imputed data sets (58), and thus 5 imputations were produced for the SALSA data set by using Imputation and Variance Estimation Software (61). Data from baseline and 6 follow-up examinations were used in this analysis.

RESULTS

Incidence rates of dementia/CIND are presented in Table 1 by SEP trajectory. A total of 234 participants developed dementia/CIND over the study period, for an overall incidence rate of 23.0 per 1,000 person-years at risk. Whereas dementia/CIND incidence rates were lowest among participants with high SEP trajectories, incidence rates were highest among those with low SEP trajectories, followed by those with upward SEP trajectories with low educational levels and those with downward SEP trajectories.

Figure 2 illustrates the adjusted survival curves to dementia/CIND diagnosis by SEP trajectory based on age at diagnosis. Participants with high SEP trajectories showed better survival curves than did those with low SEP trajectories. Participants with upward SEP trajectories with low educa-

tional levels or downward SEP trajectories had curves similar to those of participants with low SEP trajectories.

Baseline life-course socioeconomic characteristics of the study population are presented in Table 2, both overall and by SEP trajectory. Most of the participants had a manual occupation and a past-month income <\$2,500. The majority of the participants had mothers and fathers with less than an elementary education, and most fathers had a manual occupation. Nearly all mothers worked at home. Over 21% of the participants experienced food deprivation when growing up, and 49.3% reported death of a sibling in childhood. Overall, participants experienced a mean cumulative SEP disadvantage of 5.4 (standard deviation, 1.5). SEP variables differed significantly across the 4 SEP trajectory groups. Participants with more disadvantaged SEP trajectories were more likely to have parents with low educational levels and manual occupations, to have experienced food deprivation when growing up, and to have experienced childhood sibling mortality.

Baseline characteristics of the study population and their bivariate associations with dementia/CIND from Cox proportional hazards models are presented in Table 3. Participants had a mean age of 70.1 years at enrollment (standard deviation, 6.7 years). The majority of participants were women, and about half of the participants were born in Mexico (45%) or another Latin-American country (5.5%). At baseline, nearly all participants reported having health insurance. The majority of the participants smoked and consumed alcohol. Higher alcohol consumption was associated with a lower hazard of dementia/CIND compared with no alcohol consumption. Over two-thirds of the participants were either overweight or obese. About a third of the participants had diabetes at baseline, over two-thirds had hypertension, and 7.7% reported a baseline stroke. Being treated for diabetes was associated with a greater hazard of dementia/CIND compared with those without diabetes. Baseline stroke was associated with a greater hazard of dementia/CIND. We further examined the associations between individual SEP factors and risk of dementia/CIND. Participants with lower SEP characteristics showed increased hazards of dementia/CIND compared with those who had higher SEP

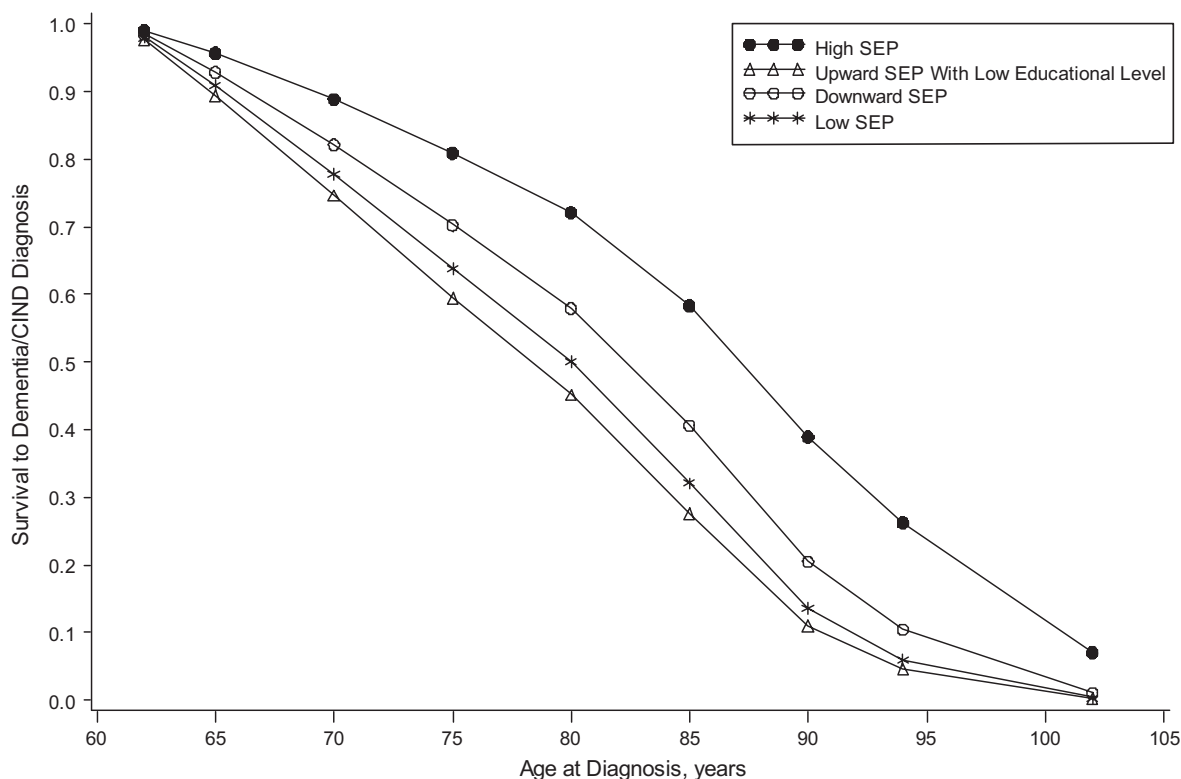


Figure 2. Survival to dementia/cognitive impairment but not dementia (CIND) by socioeconomic position (SEP) trajectory group in the Sacramento Area Latino Study on Aging, 1998–2008. Results were adjusted for age at enrollment, alcohol consumption, type 2 diabetes, and stroke.

characteristics, with statistical significance only for early adulthood SEP (Appendix Table 1).

Table 4 shows the results of multivariate Cox proportional hazards models for the association of SEP trajectories with dementia/CIND. In the age-adjusted model (model 1), participants who maintained high or upward SEP trajectories with high educational levels had lower hazards of dementia/CIND than did participants who maintained low SEP trajectories. Although not significant, participants with downward SEP trajectories had lower hazards of dementia/CIND than did those with low SEP trajectories. In the fully adjusted model (model 2), the hazard of dementia/CIND among participants who maintained high or upward SEP trajectories with high educational levels increased slightly (0.43–0.49) but remained significant compared with participants who maintained low SEP trajectories. The hazards of dementia/CIND for participants in other SEP trajectories remained nonsignificant. The hazard of dementia/CIND was lower in participants who consumed alcohol than in those who never consumed alcohol. The hazard of dementia/CIND was greater among diabetic subjects who were being treated than among non-diabetic participants and among participants with reported stroke than among those who had not had a stroke.

For the measure of cumulative SEP disadvantage, the hazard of dementia/CIND increased by 16% with every increase in 1 unit of SEP disadvantage in the age-adjusted model (model 1) (hazard ratio = 1.16, 95% confidence in-

terval: 1.01, 1.33; $P = 0.04$). In the fully adjusted model (model 2), the association between cumulative SEP disadvantage and dementia/CIND was attenuated (hazard ratio = 1.12, 95% confidence interval = 0.97, 1.30; $P = 0.12$).

DISCUSSION

In the present study of a population-based sample of older Mexican Americans, we found evidence of an association between life-course SEP and the risk of dementia/CIND. In comparison with participants who maintained low SEP trajectories, those who maintained high SEP trajectories or had upward trajectories with high educational levels had a 51% lower risk of dementia/CIND. Participants with low educational levels who experienced upward trajectories and participants with downward trajectories had a risk of dementia/CIND similar to that of participants who maintained low SEP trajectories. Increased cumulative socioeconomic disadvantage was associated with increased risk of dementia/CIND in age-adjusted models. Adjustment for alcohol consumption and cardiometabolic risk factors attenuated the associations between trajectories of SEP and risk of dementia/CIND.

Our results from the SEP trajectory analyses support the well-established literature that has reported that childhood experience is not the only determinant of late-life cognitive health; life-course socioeconomic experiences also play a

Table 2. Life-Course Socioeconomic Characteristics of the Study Population Free of Dementia/Cognitive Impairment but Not Dementia at Baseline ($n = 1,634$), by Socioeconomic Position Trajectory Group, Sacramento Area Latino Study on Aging, 1998–2008

SEP Covariate	All		High SEP (HHH and LHH)		Upward SEP/ Low Educational Level (LLH and HLH)		Downward SEP (LHL, HHL, and HLL)		Low SEP (LLL)		P Value
	No.	%	No.	%	No.	%	No.	%	No.	%	
Overall	1,634	100	262	16.6	78	4.9	865	54.8	375	23.7	
Adulthood and midlife characteristics											
Education, years ^a	7.3 (5.3)		14.6 (2.8)		6.7 (3.4)		6.7 (4.7)		3.9 (3.2)		<0.0001
Major lifetime occupation											<0.0001
Manual	1,262	78.6	0	0.0	0	0.0	865	100.0	375	100.0	
Nonmanual	343	21.4	262	100.0	78	100.0	0	0.0	0	0.0	
Monthly old-age household income											<0.0001
Low (<\$1,500)	1,043	63.9	60	22.9	49	62.8	595	68.8	302	80.5	
High (≥\$1,500)	588	36.1	202	77.1	29	37.2	270	31.2	73	19.5	
Childhood characteristics											
Paternal educational level											<0.0001
Less than elementary school	1,171	72.9	171	65.3	46	59.0	576	66.6	357	95.2	
Elementary school or more	435	27.1	91	34.7	32	41.0	289	33.4	18	4.8	
Maternal educational level											<0.0001
Less than elementary school	1,167	72.7	154	58.8	55	70.5	584	67.5	357	95.2	
Elementary school or more	439	27.3	108	41.2	23	29.5	281	32.5	18	4.8	
Paternal occupational level											<0.0001
Manual or unemployed	1,416	88.2	229	87.4	68	87.2	726	83.9	371	98.9	
Nonmanual	190	11.8	33	12.6	10	12.8	139	16.1	4	1.1	
Food deprivation while growing up	342	21.3	50	19.1	15	19.2	100	11.6	170	45.3	<0.0001
Sibling mortality	791	49.3	128	48.9	44	19.2	300	34.7	304	81.1	<0.0001
Life-course cumulative SEP ^a	5.4 (1.5)		3.7 (1.1)		4.8 (1.1)		5.3 (0.9)		7.2 (0.4)		<0.0001

Abbreviations: HHH, high childhood SEP, high early adulthood SEP, and high midlife SEP; HHL, high childhood SEP, high early adulthood SEP, and low midlife SEP; HLH, high childhood SEP, low early adulthood SEP, and high midlife SEP; HLL, high childhood SEP, low early adulthood SEP, and low midlife SEP; LHH, low childhood SEP, high early adulthood SEP, and high midlife SEP; LHL, low childhood SEP, high early adulthood SEP, and low midlife SEP; LLH, low childhood SEP, low early adulthood SEP, and high midlife SEP; LLL, low childhood SEP, low early adulthood SEP, and low midlife SEP; and SEP, socioeconomic position.

^a Data are expressed as mean (standard deviation).

role (7, 47, 48, 52, 62–64). The late-life effects of a participant's disadvantaged childhood on dementia/CIND may be buffered by upward mobility in later life stages. High educational attainment in particular may provide a buffer, as marked by the lower hazard compared with those who maintained low SEP trajectories. The protective effects of an advantaged childhood or early adulthood may be diluted by downward mobility in later life stages, as marked by the similar hazard compared with those with low SEP trajectories.

These findings are in agreement with previous studies that examined cognitive outcomes, one of which examined Alzheimer disease. In a community-based longitudinal study of Swedish participants ≥75 years of age, Karp et al. (13) found significant associations between occupation-based socioeconomic mobility and risk of Alzheimer disease. These associations became nonsignificant after accounting for educational level. Results from the SALSA study (34) found that older Mexican Americans with more

advantaged childhood-to-adulthood SEP trajectories experienced slower cognitive decline as measured by using the Modified Mini-Mental State Examination and short-term verbal memory test than did those with disadvantaged trajectories. Results from a population-based study among middle-aged Finnish men (47) showed that the effect of childhood SEP disadvantages on cognitive function may be buffered by upward mobility in later life stages. Similarly, Luo and Waite (48) showed an association between life-course SEP mobility and cognitive function among participants ≥50 years of age in the Health and Retirement Study.

Further results from the SEP trajectory analyses provided evidence that educational level plays a uniquely important role in the pathway linking life-course SEP and dementia/CIND who maintained acts as a decisive transition in one's life-course trajectory. Whereas participants with upward trajectories with high educational levels had hazard coefficients similar to those of participants who

Table 3. Baseline Covariates of the Study Population Free of Dementia/Cognitive Impairment but Not Dementia at Baseline ($n = 1,634$), Sacramento Area Latino Study on Aging, 1998–2008

Baseline Covariate	No.	%	Hazard Ratio	95% Confidence Interval	P Value
Age at enrollment ^a	70.1 (6.7)		0.82	0.79, 0.86	<0.01
Gender					
Male	681	41.7	0.86	0.65, 1.15	0.32
Female	953	58.3	1.00		
Nativity					
Mexican-born	821	50.5	1.05	0.79, 1.41	0.72
US-born	806	49.5	1.00		
Health insurance					
Yes	1,477	90.6	0.77	0.42, 1.42	0.39
No	154	9.4	1.00		
Smoking status					
Ever	876	53.7	1.02	0.77, 1.36	0.90
Never	755	46.3	1.00		
Alcohol consumption					
≥2 drinks/week	307	18.8	0.55	0.33, 0.92	0.02
<2 drinks/week	584	35.8	0.64	0.44, 0.94	0.02
Never	740	45.4	1.00		
Body mass index ^b					
≥30	716	44.2	0.75	0.52, 1.10	0.14
25.0–29.9	600	37.0	0.82	0.53, 1.27	0.36
<25.0	305	18.8	1.00		
Waist circumference, cm					
High tertile	547	33.5	0.92	0.61, 1.40	0.68
Middle tertile	569	34.9	1.00	0.68, 1.47	0.99
Low tertile	515	31.6	1.00		
Diabetes treatment					
Diabetic with treatment	331	20.3	1.96	1.23, 3.12	0.01
Diabetic without treatment	195	12.0	1.56	0.88, 2.77	0.12
Not diabetic	1,105	67.7	1.00		
Hypertension					
Yes	1,005	61.5	0.93	0.70, 1.25	0.65
No	629	38.5	1.00		
Stroke					
Yes	125	7.7	2.07	1.34, 3.20	0.00
No	1,509	92.3	1.00		
Systolic blood pressure, mm Hg ^a	138.4 (18.8)		1.00	0.99, 1.01	0.74
Diastolic blood pressure mm Hg ^a	76.0 (10.7)		0.99	0.98, 1.01	0.29

^a Data are expressed as mean (standard deviation).

^b Weight in kilograms divided by height in meters squared.

maintained high SEP trajectories, participants with upward trajectories with low educational levels did not differ from those who maintained low SEP trajectories. We also examined the impact of education on the downward trajectory by comparing those with high and low educational levels. Participants with high educational levels had lower hazards of dementia/CIND than did those with low educational levels (data not shown). A growing body of literature describes the protective effect of educational attainment on

cognition and dementia/CIND (1–4, 6–7, 14, 49–51). A stimulating learning exposure at early stages in life may result in better brain development due to increased neuronal branching and synaptic density (65, 66). At older ages, maintenance of cognitive function is more common than neurogenesis. Early experiences may contribute in old age to “brain reserve” or capacity through compensating strategies that help to maintain function and delay the clinical manifestation of dementia/CIND.

Table 4. Associations Between Life-Course Socioeconomic Position Trajectory and Risk of Dementia/Cognitive Impairment but Not Dementia, Sacramento Area Latino Study on Aging, 1998–2008

Independent Variable	Model 1 ^a			Model 2 ^a		
	HR	95% CI	P Value	HR	95% CI	P Value
SEP trajectory ^b						
High SEP (HHH and LHH)	0.43	0.23, 0.84	0.01	0.49	0.24, 0.98	0.04
Upward SEP with low educational level (LLH and HLH)	1.13	0.55, 2.32	0.74	1.17	0.56, 2.43	0.67
Downward SEP (LHL, HHL, and HLL)	0.79	0.54, 1.15	0.21	0.80	0.54, 1.18	0.25
Low SEP (LLL)	1.00			1.00		
Monthly old-age household income						
Low				1.06	0.72, 1.58	0.75
High				1.00		
Alcohol consumption						
≥2 drinks/week				0.67	0.38, 1.15	0.14
<2 drinks/week				0.70	0.47, 1.04	0.08
Never				1.00		
Diabetes						
Diabetic with treatment				1.70	1.10, 2.63	0.02
Diabetic without treatment				1.48	0.82, 2.66	0.18
Not diabetic				1.00		
Stroke						
Yes				1.82	1.16, 2.86	0.01
No				1.00		

Abbreviations: CI, confidence interval; HR, hazard ratio; SEP, socioeconomic position.

^a All models were adjusted for age at enrollment in the study.

^b HHH, high childhood SEP, high early adulthood SEP, and high midlife SEP; HHL, high childhood SEP, high early adulthood SEP, and low midlife SEP; HLH, high childhood SEP, low early adulthood SEP, and high midlife SEP; HLL, high childhood SEP, low early adulthood SEP, and low midlife SEP; LHH, low childhood SEP, high early adulthood SEP, and high midlife SEP; LHL, low childhood SEP, high early adulthood SEP, and low midlife SEP; LLH, low childhood SEP, low early adulthood SEP, and high midlife SEP; LLL, low childhood SEP, low early adulthood SEP, and low midlife SEP.

Results from the cumulative SEP disadvantage analyses showed a relation between continuity of disadvantaged exposure over the life course and risk of dementia/CIND in age-adjusted models. Our results are in agreement with reports from other studies. For example, results from the Sao Paulo Ageing and Health Study found a dose-response relation between cumulative adversity and prevalent dementia (7). With regard to cognitive function, few studies have shown an association between cumulative socioeconomic disadvantage and worse cognitive functioning (47, 48). Lynch et al. (67) discussed similar associations that showed a direct association between sustained economic hardship and cognitive function.

Our results are in accordance with other longitudinal studies that showed a greater risk of dementia/CIND in those with cardiometabolic risk factors (32, 68–75). Such risk factors could act as mediators on the pathway between life-course SEP and dementia/CIND. Accounting for them attenuated but did not eliminate the association between high SEP trajectory in particular and dementia/CIND. Results from this analysis are also in agreement with the literature emphasizing the importance of alcohol consumption as a protective factor for dementia/CIND via underlying cardiovascular mechanisms (76). In this study, participants

with high SEP trajectories were 2 times more likely to have consumed alcohol than were participants with low SEP trajectories.

There were few limitations to this study. First, participants had to survive until at least 60 years of age to be eligible. Moreover, because of the longitudinal nature of the study, participants who died or dropped out were likely to be more socioeconomically disadvantaged and to show worse cognitive functioning. Consequently, the observed associations were likely smaller than what they might have been in the absence of such attrition. Second, childhood socioeconomic measures were self-reported, which likely resulted in some reporting bias. To address this concern, we created a composite measure based on various childhood SEP indicators. Third, SEP could be a marker for other unmeasured factors that influence dementia/CIND, such as chronic malnutrition or environmental risk factors, thus possibly contributing to residual confounding. Despite these limitations, to our knowledge, this is the first study to examine changes in life-course SEP and incidence of dementia/CIND in a cohort of older Mexican Americans followed for over a decade. The current study expands a body of literature on dementia/CIND that is mainly cross-sectional (47) or that lacks SEP measures across the life course (8, 13).

The current analysis did not rely on self-reporting of type 2 diabetes and hypertension, which are important risk factors for dementia/CIND. Furthermore, the diagnosis of dementia/CIND followed a thorough multistage process. Finally, even though the overall variability in SEP indicators was generally lower in this population than in non-Hispanic whites, an effect of life-course SEP on dementia/CIND was identified. Therefore, the results may be more pronounced in other racial/ethnic groups where there is more variability in SEP.

Findings in the present study demonstrate an association between life-course SEP and dementia/CIND, further highlighting the fact that neurodegeneration processes are shaped by life-course experiences. This study provides evidence that diabetes and stroke are important risk factors for dementia/CIND and account for part of the SEP-dementia/CIND gradient. These findings are of crucial importance to US Hispanics because they are increasingly burdened with cardiometabolic risk factors (31, 33). Health care providers should begin trying to prevent dementia/CIND early in life by developing interventions targeted at delaying its onset as well as strategies for maintaining cognitive functioning throughout life.

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REFERENCES

- Callahan CM, Hall KS, Hui SL, et al. Relationship of age, education, and occupation with dementia among a community-based sample of African Americans. *Arch Neurol.* 1996; 53(2):134–140.
- Evans DA, Hebert LE, Beckett LA, et al. Education and other measures of socioeconomic status and risk of incident Alzheimer disease in a defined population of older persons. *Arch Neurol.* 1997;54(11):1399–1405.
- Kukull WA, Higdon R, Bowen JD, et al. Dementia and Alzheimer disease incidence: a prospective cohort study. *Arch Neurol.* 2002;59(11):1737–1746.
- Hall KS, Gao S, Unverzagt FW, et al. Low education and childhood rural residence: risk for Alzheimer's disease in African Americans. *Neurology.* 2000;54(1):95–99.
- Caamaño-Isorna F, Corral M, Montes-Martínez A, et al. Education and dementia: a meta-analytic study. *Neuroepidemiology.* 2006;26(4):226–232.
- Ngandu T, von Strauss E, Helkala EL, et al. Education and dementia: what lies behind the association? *Neurology.* 2007; 69(14):1442–1450.
- Sczufca M, Menezes PR, Araya R, et al. Risk factors across the life course and dementia in a Brazilian population: results from the Sao Paulo Ageing & Health Study (SPAH). *Int J Epidemiol.* 2008;37(4):879–890.
- Qiu C, Bäckman L, Winblad B, et al. The influence of education on clinically diagnosed dementia incidence and mortality data from the Kungsholmen Project. *Arch Neurol.* 2001; 58(12):2034–2039.
- Goldbourt U, Schnaider-Beeri M, Davidson M. Socioeconomic status in relationship to death of vascular disease and late-life dementia. *J Neurol Sci.* 2007;257(1-2): 177–181.
- Bottino CM, Azevedo D Jr, Tatsch M, et al. Estimate of dementia prevalence in a community sample from São Paulo, Brazil. *Dement Geriatr Cogn Disord.* 2008;26(4): 291–299.
- Peters R, Beckett N, Geneva M, et al. Sociodemographic and lifestyle risk factors for incident dementia and cognitive decline in the HYVET. *Age Ageing.* 2009;38(5): 521–527.
- De Ronchi D, Fratiglioni L, Rucci P, et al. The effect of education on dementia occurrence in an Italian population with middle to high socioeconomic status. *Neurology.* 1998; 50(5):1231–1238.
- Karp A, Kåreholt I, Qiu C, et al. Relation of education and occupation-based socioeconomic status to incident Alzheimer's disease. *Am J Epidemiol.* 2004;159(2):175–183.
- Stern Y, Gurland B, Tatemichi TK, et al. Influence of education and occupation on the incidence of Alzheimer's disease. *JAMA.* 1994;271(13):1004–1010.
- Qiu C, Karp A, von Strauss E, et al. Lifetime principal occupation and risk of Alzheimer's disease in the Kungsholmen project. *Am J Ind Med.* 2003;43(2):204–211.
- Smyth KA, Fritsch T, Cook TB, et al. Worker functions and traits associated with occupations and the development of AD. *Neurology.* 2004;63(3):498–503.
- Andel R, Crowe M, Pedersen NL, et al. Complexity of work and risk of Alzheimer's disease: a population-based study of Swedish twins. *J Gerontol B Psychol Sci Soc Sci.* 2005; 60(5):P251–P258.
- Huang TL, Carlson MC, Fitzpatrick AL, et al. Knee height and arm span: a reflection of early life environment and risk of dementia. *Neurology.* 2008;70(19):1818–1826.
- Moceri VM, Kukull WA, Emanuel I, et al. Early-life risk factors and the development of Alzheimer's disease. *Neurology.* 2000;54(2):415–420.
- Moceri VM, Kukull WA, Emanuel I, et al. Using census data and birth certificates to reconstruct the early-life socioeconomic environment and the relation to the development of Alzheimer's disease. *Epidemiology.* 2001;12(4):383–389.
- Wilson RS, Scherr PA, Hoganson G, et al. Early life socioeconomic status and late life risk of Alzheimer's disease. *Neuroepidemiology.* 2005;25(1):8–14.
- Cravioto J, Delicardie ER, Birch HG. Nutrition, growth, and neuro-integrative development: an experimental and ecologic study. *Pediatrics.* 1966;38(2):319–372.

23. Paine P, Dorea JG, Pasquali L, et al. Growth and cognition in Brazilian schoolchildren: a spontaneously occurring intervention study. *Int J Behav Dev.* 1992;15(2):169–183.
24. Bradley RH, Corwyn RF, McAdoo HP, et al. The home environments of children in the United States part I: variations by age, ethnicity, and poverty status. *Child Dev.* 2001;72(6):1844–1867.
25. Fernald LC, Neufeld LM, Barton LR, et al. Parallel deficits in linear growth and mental development in low-income Mexican infants in the second year of life. *Public Health Nutr.* 2006;9(2):178–186.
26. Hackman DA, Farah MJ. Socioeconomic status and the developing brain. *Trends Cogn Sci.* 2009;13(2):65–73.
27. Office of Minority Health, US Department of Health and Human Services. *Hispanic/Latino Profile.* Rockville, MD: US Department of Health and Human Services; 2009. (<http://minorityhealth.hhs.gov/templates/browse.aspx?lvl=3&lvlid=31>). (Accessed January 12, 2010).
28. Tang MX, Stern Y, Marder K, et al. The APOE-epsilon4 allele and the risk of Alzheimer disease among African Americans, whites, and Hispanics. *JAMA.* 1998;279(10):751–755.
29. Gurland BJ, Wilder DE, Lantigua R, et al. Rates of dementia in three ethnorracial groups. *Int J Geriatr Psychiatry.* 1999;14(6):481–493.
30. Lopez OL, Kuller LH, Fitzpatrick A, et al. Evaluation of dementia in the cardiovascular health cognition study. *Neuroepidemiology.* 2003;22(1):1–12.
31. Carter JS, Pugh JA, Monterrosa A. Non-insulin-dependent diabetes mellitus in minorities in the United States. *Ann Intern Med.* 1996;125(3):221–232.
32. Luchsinger JA, Tang MX, Stern Y, et al. Diabetes mellitus and risk of Alzheimer's disease and dementia with stroke in a multiethnic cohort. *Am J Epidemiol.* 2001;154(7):635–641.
33. Egede LE, Dagogo-Jack S. Epidemiology of type 2 diabetes: focus on ethnic minorities. *Med Clin North Am.* 2005;89(5):949–975.
34. Haan MN, Zeki Al Hazzouri A, Aiello AE. Life course socioeconomic trajectory, nativity and cognitive aging in Mexican Americans: the Sacramento Area Latino Study on Aging. *J Gerontol B Psychol Sci Soc Sci.* In press.
35. Colón-López V, Haan MN, Aiello AE, et al. The effect of age at migration on cardiovascular mortality among elderly Mexican immigrants. *Ann Epidemiol.* 2009;19(1):8–14.
36. Hendrie HC, Osuntokun BO, Hall KS, et al. Prevalence of Alzheimer's disease and dementia in two communities: Nigerian Africans and African Americans. *Am J Psychiatry.* 1995;152(10):1485–1492.
37. Fillenbaum GG, Heyman A, Huber MS, et al. The prevalence and 3-year incidence of dementia in older black and white community residents. *J Clin Epidemiol.* 1998;51(7):587–595.
38. Fitzpatrick AL, Kuller LH, Ives DG, et al. Incidence and prevalence of dementia in the Cardiovascular Health Study. *J Am Geriatr Soc.* 2004;52(2):195–204.
39. Plassman BL, Langa KM, Fisher GG, et al. Prevalence of dementia in the United States: the Aging, Demographics, and Memory Study. *Neuroepidemiology.* 2007;29(1-2):125–132.
40. Potter GG, Plassman BL, Burke JR, et al. Cognitive performance and informant reports in the diagnosis of cognitive impairment and dementia in African Americans and whites. *Alzheimers Dement.* 2009;5(6):445–453.
41. Haan MN, Mungas DM, Gonzalez HM, et al. Prevalence of dementia in older Latinos: the influence of type 2 diabetes mellitus, stroke and genetic factors. *J Am Geriatr Soc.* 2003;51(2):169–177.
42. Teng EL, Chui HC. The Modified Mini-Mental State (3MS) examination. *J Clin Psychiatry.* 1987;48(8):314–318.
43. González HM, Mungas D, Haan MN. A semantic verbal fluency test for English- and Spanish-speaking older Mexican-Americans. *Arch Clin Neuropsychol.* 2005;20(2):199–208.
44. Mungas D, Reed BR, Crane PK, et al. Spanish and English Neuropsychological Assessment Scales (SENAS): further development and psychometric characteristics. *Psychol Assess.* 2004;16(4):347–359.
45. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders.* 4th ed. Washington, DC: American Psychiatric Association; 1994.
46. McKhann G, Drachman D, Folstein M, et al. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's disease. *Neurology.* 1984;34(7):939–944.
47. Turrell G, Lynch JW, Kaplan GA, et al. Socioeconomic position across the lifecourse and cognitive function in late middle age. *J Gerontol B Psychol Sci Soc Sci.* 2002;57(1):S43–S51.
48. Luo Y, Waite LJ. The impact of childhood and adult SES on physical, mental, and cognitive well-being in later life. *J Gerontol B Psychol Sci Soc Sci.* 2005;60(2):S93–S101.
49. Zhang MY, Katzman R, Salmon D, et al. The prevalence of dementia and Alzheimer's disease in Shanghai, China: impact of age, gender, and education. *Ann Neurol.* 1990;27(4):428–437.
50. Letenneur L, Gilleron V, Commenges D, et al. Are sex and educational level independent predictors of dementia and Alzheimer's disease? Incidence data from the PAQUID project. *J Neurol Neurosurg Psychiatry.* 1999;66(2):177–183.
51. Christensen H, Hofer SM, Mackinnon AJ, et al. Age is no kinder to the better educated: absence of an association investigated using latent growth techniques in a community sample. *Psychol Med.* 2001;31(1):15–28.
52. Whalley LJ, Dick FD, McNeill G. A life-course approach to the aetiology of late-onset dementias. *Lancet Neurol.* 2006;5(1):87–96.
53. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care.* 2006;29(suppl 1):S43–S48.
54. American Heart Association. *High Blood Pressure.* Dallas, TX: American Heart Association; 2010. (<http://www.americanheart.org/presenter.jhtml?identifier=4623>). (Accessed March 19, 2010).
55. SAS Institute, Inc. SAS statistical software, release 9.2. Cary, NC: SAS Institute, Inc; 2005.
56. Allison P. *Survival Analysis Using SAS: A Practical Guide.* Cary, NC: SAS Press; 1995.
57. Commenges D, Letenneur L, Joly P, et al. Modelling age-specific risk: application to dementia. *Stat Med.* 1998;17(17):1973–1988.
58. Rubin DB. *Multiple Imputation for Nonresponse in Surveys.* New York, NY: John Wiley & Sons; 1987.
59. Raghunathan TE, Lepkowski JM, Van Hoewyk J, et al. A multivariate technique for multiply imputing missing values using a sequence of regression models. *Surv Methodol.* 2001;27(1):83–95.
60. Rubin DB. Inference and missing data. *Biometrika.* 1976;63:581–590.
61. *IVeware: Imputation and Variance Estimation Software* [computer program]. Ann Arbor, MI: University of Michigan; 2009.
62. Singh-Manoux A, Richards M, Marmot M. Socioeconomic position across the lifecourse: how does it relate to

- cognitive function in mid-life? *Ann Epidemiol.* 2005;15(8):572–578.
63. Joseph KS, Kramer MS. Review of the evidence on fetal and early childhood antecedents of adult chronic disease. *Epidemiol Rev.* 1996;18(2):158–174.
 64. Maguire EA, Gadian DG, Johnsrude IS, et al. Navigation-related structural change in the hippocampi of taxi drivers. *Proc Natl Acad Sci U S A.* 2000;97(8):4398–4403.
 65. Mohammed AK, Winblad B, Ebendal T, et al. Environmental influence on behaviour and nerve growth factor in the brain. *Brain Res.* 1990;528(1):62–72.
 66. Albert MS. How does education affect cognitive function? *Ann Epidemiol.* 1995;5(1):76–78.
 67. Lynch JW, Kaplan GA, Shema SJ. Cumulative impact of sustained economic hardship on physical, cognitive, psychological, and social functioning. *N Engl J Med.* 1997;337(26):1889–1895.
 68. Awad N, Gagnon M, Messier C. The relationship between impaired glucose tolerance, type 2 diabetes, and cognitive function. *J Clin Exp Neuropsychol.* 2004;26(8):1044–1080.
 69. Luchsinger JA, Reitz C, Honig LS, et al. Aggregation of vascular risk factors and risk of incident Alzheimer disease. *Neurology.* 2005;65(4):545–551.
 70. Sun MK, Alkon DL. Links between Alzheimer's disease and diabetes. *Timely Top Med Cardiovasc Dis.* 2006;10E24.
 71. Craft S. The role of metabolic disorders in Alzheimer disease and vascular dementia: two roads converged. *Arch Neurol.* 2009;66(3):300–305.
 72. Ott A, Stolk RP, van Harskamp F, et al. Diabetes mellitus and the risk of dementia: the Rotterdam Study. *Neurology.* 1999;53(9):1937–1942.
 73. Peila R, Rodriguez BL, Launer LJ. Type 2 diabetes, APOE gene, and the risk for dementia and related pathologies: the Honolulu-Asia Aging Study. *Diabetes.* 2002;51(4):1256–1262.
 74. Haan MN. Therapy insight: type 2 diabetes mellitus and the risk of late-onset Alzheimer's disease. *Nat Clin Pract Neurol.* 2006;2(3):159–166.
 75. Schnaider Beerli M, Goldbourt U, Silverman JM, et al. Diabetes mellitus in midlife and the risk of dementia three decades later. *Neurology.* 2004;63(10):1902–1907.
 76. Anstey KJ, Mack HA, Cherbuin N. Alcohol consumption as a risk factor for dementia and cognitive decline: meta-analysis of prospective studies. *Am J Geriatr Psychiatry.* 2009;17(7):542–555.

Appendix Table 1. Bivariate Associations Between Life-Course Socioeconomic Conditions and Risk of Dementia/Cognitive Impairment Without Dementia Over the Study Follow-up Period, Sacramento Area Latino Study on Aging, 1998–2008

Covariate	Hazard Ratio	95% Confidence Interval	P Value
Childhood SEP			
Maternal educational level (less than elementary school vs. elementary school or more)	1.44	0.75, 2.75	0.24
Paternal educational level (less than elementary school vs. elementary school or more)	1.04	0.77, 1.41	0.78
Maternal occupation (manual or housewife vs. nonmanual)	1.57	0.34, 7.31	0.53
Paternal occupation (manual or unemployed vs. nonmanual)	1.11	0.56, 2.22	0.75
Food deprivation while growing up (ever vs. never)	1.13	0.78, 1.64	0.51
Childhood sibling mortality (yes vs. no)	1.09	0.71, 1.67	0.66
Early adulthood SEP			
Participants' educational level (less than elementary school vs. elementary school or more)	1.70	1.16, 2.51	0.01
Midlife SEP			
Major lifetime occupation (manual vs. nonmanual)	1.45	0.89, 2.33	0.13

Abbreviation: SEP, socioeconomic position.