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RESEARCH ARTICLE

Rural residence across the life course and late-life cognitive decline in KHANDLE: A causal inference study

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Abstract

Background: Modifiable risks for dementia are more prevalent in rural populations, yet there is a dearth of research examining life course rural residence on late-life cognitive decline.

Methods: The association of rural residence and socioeconomic status (SES) in childhood and adulthood with late-life cognitive domains (verbal episodic memory, executive function, and semantic memory) and cognitive decline in the Kaiser Healthy Aging and Diverse Life Experiences cohort was estimated using marginal structural models with stabilized inverse probability weights.

Results: After adjusting for time-varying SES, the estimated marginal effect of rural residence in childhood was harmful for both executive function ($\beta = -0.19$, 95% confidence interval [CI] = –0.32, –0.06) and verbal episodic memory ($\beta = -0.22$, 95% CI = –0.35, –0.08). Effects of adult rural residence were imprecisely estimated with beneficial point estimates for both executive function ($\beta = 0.19$; 95% CI = –0.07, 0.44) and verbal episodic memory ($\beta = 0.24$, 95% CI = –0.07, 0.55).

Conclusions: Childhood rurality is associated with poorer late-life cognition independent of SES.

KEYWORDS
cognitive aging, cohort study, epidemiology, health disparities

1 | INTRODUCTION

Rural health disparities have been documented for many behaviors and conditions attributed to population risk of dementia.[1–3] Rural health disparities may arise due to persistent structural urbanism: the allocation of health care and public health–promoting resources that favors population centers, at the expense of rural communities.[4] Inequities arise from population-level programs that aim to impact large numbers and avoid the inefficiency of reaching more remote communities, which may limit cognition-promoting public goods (e.g., public libraries) in rural areas. At the same time, market-driven private resources, such as health-care systems and knowledge sectors employment opportunities, favor urbanized communities with a greater concentration of residents with higher socioeconomic status (SES). Structural urbanism theory thus suggests rural residence may impact dementia risk both through and independently of individual

RESEARCH IN CONTEXT

1. **Systematic Review**: Relevant scientific studies were reviewed on PubMed. Few studies have examined the relationship between rural residence and cognitive aging outcomes. Available studies suggest that rural residence in childhood or late life is associated with worse cognition after adjusting for markers of socioeconomic status (SES; e.g., education). These studies are appropriately cited.
2. **Interpretation**: Use of advanced causal inference methods allows for more accurate estimation of the effect of rural residence in the presence of time-varying SES. Our findings suggest a life-long effect of childhood rural residence, but not adulthood rural residence, on late-life cognition that is not explained by SES in childhood or adulthood.
3. **Future Directions**: The article recommends a thorough examination of community contextual factors (e.g., public libraries, pesticides) and individual mediating factors (e.g., cardiovascular health) that could explain the observed relationships and serve as public health intervention targets.

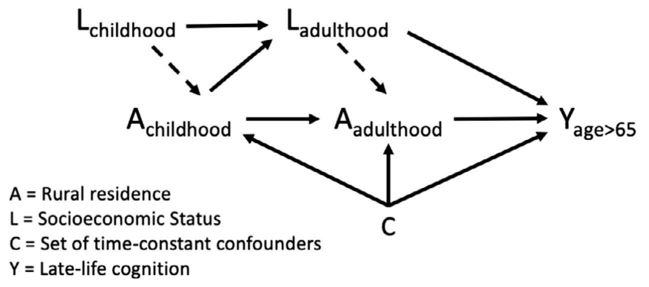

FIGURE 1 Directed acyclic graph demonstrating the relationships among time-varying rural residence, time-varying socioeconomic status, and late-life cognitive outcomes. Using inverse probability weights to estimate marginal structural models breaks paths from time-varying confounders to subsequent time-varying exposures, as represented by the dashed lines. This eliminates biased effects due to confounder–mediators and colliders

SES. Furthermore, life-course theory suggests the timing and duration of rural residence may also be important. The sensitive period model suggests that childhood, adolescence, and early adulthood are critical periods for cognitive development, and that exposures during these periods have a profound impact on later life cognitive outcomes.[5]

Few studies to date have considered the associations between rural contexts at different points in the life course and cognitive aging and dementia risk.[6–9] Participants of the Wisconsin Longitudinal Study who were rural dwelling in childhood had lower cognition in later life not explained by childhood SES or mid-life health risks.[6] In another study, older adults who moved from rural to urban areas within Mexico had better cognitive function than those who remained in rural areas after adjustment for health behaviors and SES.[8] A third study found that late-life rural residence in Canada was associated with lower baseline cognition, but not rate of cognitive decline over 10 years.[9] Other studies suggests the complexity of urban environments may have cognitive benefits in early/mid-life, but contribute to overstimulation and cognitive load deleterious for attention in late life.[10–12]

A major challenge for life-course research examining sensitive periods is accounting for time-varying confounders that may concurrently behave as mediators or contribute to collider bias, both of which can skew the true estimate of effect.[13,14] Consider our hypothesized relationship between individual SES and rural residence on late-life cognition, depicted in Figure 1. Rural dwellers are more likely to have lower SES. Because rural families and communities tend to have fewer resources, children from rural areas are more likely to become adults with lower SES.[4,15] In Figure 1, SES in adulthood is a mediator of childhood rural residence and late-life cognition and a confounder of mid-life rural residence and late-life cognition. Including SES in adulthood as a covariate, as done in conventional regression approaches, will adjust for confounding of the adult rural residence–cognition association. However, including this covariate will underestimate the association between childhood rural residence and late-life cognition, minimizing the ability to detect a sensitive period in childhood.

We build on prior research by implementing advanced statistical techniques that enable us to appropriately estimate the effect of rural residence as a time-varying (e.g., childhood or adulthood) social determinant of late-life cognition and cognitive decline in the presence of time-varying confounders that may concurrently behave as mediators (e.g., SES). We also examine potential heterogeneity in the effect of rurality on cognitive decline across the life course by accounting for geographic region of residence in childhood and adulthood.

2 | METHODS

The Kaiser Healthy Aging and Diverse Life Experiences (KHANDLE) cohort consists of 1712 community-dwelling older adults residing in the San Francisco Bay area and Sacramento Valley who are long-term members of Kaiser Permanente Northern California (KPNC). KPNC members demographically reflect residents in the region, though extreme tails of the income distribution are underrepresented.[16,17] KPNC members were contacted for study recruitment if they were age 65 or older on January 1, 2017; did not have an electronic medical record diagnosis of dementia or another health condition that would impede participation in study interviews (hospice activity in the past 12 months, history of severe chronic obstructive pulmonary disease in the past 6 months, congestive heart failure hospitalizations in the past 6 months, and/or history of end-stage renal disease or dialysis in the past 12 months); and had participated in one or more KPNC Multiphasic Health Checkups between 1964 and 1985 (optional medical visits offered as part of routine care).

In waves 1 and 2 (March 2017 to March 2020), participants were interviewed in their homes or at KPNC clinics. In March 2020, all interviews transitioned to phone due to COVID-19 protocol changes.

Approximately 4% of participants completed their Wave 2 interview by phone; all completed Wave 3 interviews by phone. The study was approved by the KPNC and University of California Davis institutional review boards. All enrolled participants provided written informed consent.

2.1 | Measures

2.1.1 | Cognition

Semantic memory, verbal episodic memory, and executive function were derived from the Spanish and English Neuropsychological Assessment Scales (SENAS).[18,19] This battery of cognitive tests was developed using item response theory methodology for valid comparisons of cognition and cognitive change across racial/ethnic and linguistically diverse groups. Administration procedures, development, and psychometric characteristics have been described in detail elsewhere.[18,19] The SENAS was administered in either English or Spanish, based on the participant's preference. After March 2020 the SENAS was administered by telephone under a separate protocol that adhered to safety precautions during the COVID-19 pandemic. The SENAS includes visual stimuli in the assessment of semantic memory, therefore only verbal episodic memory and executive function were collected during telephone visits and have sufficient repeated measures for longitudinal analysis. Each cognitive domain was z-standardized for analysis using the Wave 1 sample mean and standard deviation.

2.1.2 | Time-varying rural residence

Participants self-reported whether they resided "outside of town, in a rural area" at birth and ages 5, 10, 18, 30, 40, and 65. To test for sensitive periods, we classified participants as having a rural childhood if they reported a rural residence at birth, age 5, or age 10. Rural midlife/late life was classified as reporting residing in a rural area at ages 30, 40, or 65. We used self-reported rather than geocoded measures of rurality (e.g., the rural–urban continuum code published by the US Department of Agriculture) because 22% of our sample resided outside of the United States at age 10 and their childhood addresses could not be mapped to these codes.

2.1.3 | Time-varying socioeconomic status

SES in childhood and adulthood was captured through several participant-reported measures. Childhood SES variables were parental educational attainment and perceived childhood financial status. Maternal and paternal educational attainment were included as separate covariates, each coded continuously as years of education (range 0–20). Childhood financial status was based on a question about their family's financial status from their birth to age 16: "Would you say your family during that time was pretty well off financially, about average, or poor?" Responses were dichotomized as poor versus average/well off. Participants were additionally classified as "poor" if they reported ever having to go hungry because there was not enough money for food, regardless of the participant's response to the family financial status question.

SES in adulthood was based on educational attainment and late-life income. Participants reported years of education if they had completed less than a high school diploma, and the highest level of education completed if they had at least a high school diploma. We combined these two questions into a continuous variable indicating years of completed education (range 0–20; 16 = bachelor's degree). Late-life income was the self-reported income level of the participant and their spouse at KHANDLE Wave 1, categorized as <\$50k, \$50–99.9k, or ≥\$100k.

2.1.4 | Covariates

Covariates included Wave 1 age, sex (male/female), race/ethnicity (Asian, Black, Latino, and White), and whether the person was born in the United States. We coded geographic region in childhood based on the participant's state of residence at age 10, categorized as US-South, US-West, US-Northeast, and US-Midwest, or non-US. In adulthood, region was based on the participant's state of residence at age 30 and categorized as US-West, other US region, or non-US region, as most KHANDLE participants (88%) resided in California by age 30. Mode of interview was an indicator of whether the interview was conducted by phone or in person.

2.2 | Analysis

2.2.1 | Analytic sample

The baseline analytic sample was comprised of 1622 participants (95% of KHANDLE Wave 1) after participants were excluded for missing information on rural residence (n = 67), childhood family finances (n = 19), and region of residence at age 10 (n = 2). To account for high missingness on other covariates, we imputed theorized values based on the sample. We classified those who did not know their father's or mother's educational attainment (n = 171; 9.9%) as having maternal or paternal education of 0 years and differentiated these observations from participants with known values using indicator variables (1 = missing; 0 = not missing). Missingness on income at KHANDLE Wave 1 (n = 220; 12.8%) was imputed using income at KHANDLE Wave 2 when available (n = 84; 4.9%) or based on the sample mode (n = 136; 7.9%) specific to that person's race/ethnicity, educational attainment, and sex.

2.2.2 | Analytic procedures

Participant demographic data were examined overall and stratified by ever versus never residing in a rural area. Our primary models analyzed associations between time-varying rural residence and late-life cognition/cognitive decline using stabilized inverse probability weights

(IPWs) to estimate marginal structural models (MSM) for each cognitive domain (verbal episodic memory, executive function, and semantic memory). Using IPWs creates a pseudo-population in which rural or non-rural residence is statistically independent of time-varying confounders (SES; geographic region).[20] For both life-course periods, stabilized weights were calculated as: (1) the probability of residing in a rural area at that life-course period, given the history of characteristics preceding and up to that life-course period among those who resided in a rural area and (2) the probability of residing in a non-rural area at that life-course period, given the history of covariates, among those who did not reside in a rural area at that period. In childhood, weights were calculated based on age at KHANDLE wave 1 and childhood SES. In mid-life/late life, weights were calculated based on all variables used in the childhood IPW, plus adulthood SES. The estimated coefficients are the average treatment effects, $E[Y^{a1=1}]$-$E[Y^{a1=0}]$, which can be interpreted as the expected mean difference in cognitive function if everyone in the study had lived in a rural area at a given time point (childhood, mid-life/late life) or no one had lived in a rural area at that period.

Our primary analysis included two sets of outcome models. We estimated the total effect of childhood rural residence by applying the IPWs calculated based on childhood exposure and characteristics. We estimated the direct effect of childhood rural residence and the total effect of mid-life/late life rural residence by multiplying the childhood and adulthood IPWs and applying this IPW to the outcome models.

In secondary models, we examined the extent that geographic region confounded any associations between rural residence and late-life cognition and cognitive decline by replicating our primary analyses with the inclusion of region at age 10 in IPWs calculated for childhood exposures and the inclusion of region at ages 10 and 30 in IPWs for mid-life/late-life exposures. We conducted sensitivity analyses of our primary models with the sample of participants that did not have any values imputed due to missingness.

All outcome models were adjusted for sex, race/ethnicity, and mode of interview (phone vs. in person). We used model constraints to adjust for practice effects in longitudinal models, based on prior analyses in this cohort.[21] All analyses were performed in Stata 17 (StataCorp).

3 | RESULTS

Approximately 19% reported rural residence at one or more time points, with most occurring in childhood (n = 265; Table 1). At age 10, 55% resided in the West, while 21% resided outside of the United States. By age 30, 90% of participants resided in the West, predominately in California. Those who resided in a rural area in childhood were, on average, 3 years older (mean = 78.2; standard deviation [SD] = 7.1) at Wave 1 compared to those who never resided in a rural area (mean = 75.6; SD = 7.0). Those with a history of rural residence had lower SES in childhood and adulthood compared to those who never lived in a rural area. Nearly half of those who ever resided in a rural area reported being poor in childhood, compared to approximately one third (34%) of those who never resided in a rural area. Mean paternal and maternal education among rural dwellers was about 1 year lower compared to non-rural dwellers (rural maternal education mean = 7.6, SD = 5.5 vs. non-rural mean = 8.9, SD = 5.4), as was the participant's own educational attainment (rural mean = 13.9 years, SD = 3.5 vs. non-rural mean = 15 years, SD = 2.8).

3.1 | Verbal episodic memory

Estimates from our outcome models are interpreted as the expected mean difference had everyone in the sample had a rural residence compared to no one. In estimating the total effect of childhood rural residence on verbal episodic memory (Table 2, Model 1A) we did not observe an expected mean difference at baseline (–0.04; 95% confidence interval [CI] = –0.15, 0.14) or over time (β = –0.02; 95% CI = –0.09, 0.05). Had everyone in the sample resided in a rural area in adulthood, the total expected mean difference in baseline verbal episodic memory would be 0.24 SDs higher (95% CI = –0.07, 0.55) and rate of decline 0.08 SDs faster (95% CI = –0.17, 0.01), albeit these effects were not statistically significant due to the small sample size (Table 2, Model 2A). In models with IPWs that incorporated region of residence in childhood and mid-life, the expected mean differences in baseline verbal episodic memory due to adulthood rural residence were attenuated (Table 2, Model 2B).

3.2 | Executive function

We observed an expected mean difference in baseline executive function of –0.19 SDs (95% CI = –0.32, –0.06; Table 3, Model 1A) had everyone in the sample resided in a rural area in childhood. There was no difference in rate of decline in executive function by rural residence in childhood. We observed a non-significant expected mean difference in baseline executive function of 0.19 (95% CI = –0.07, 0.44; Table 3, Model 2A) had everyone resided in a rural area in adulthood. In models that incorporated region of residence, expected mean differences in baseline executive function due to childhood rural residence were attenuated and potential differences observed for adulthood rural residence were nullified (Table 3, Models 1B, 2B).

3.3 | Semantic memory

We observed an expected mean difference of approximately one fifth SD lower baseline semantic memory had everyone had a rural childhood (β = –0.22, 95% CI = –0.35, –0.08; Table 4, Models 1A, 2A). These effects were attenuated and made non-significant when region of residence was included in our IPWs (β = –0.10, 95% CI = –0.24, 0.04; Table 4, Models 1B, 2B) We had insufficient repeated measures of semantic memory to assess expected mean differences in cognitive change.

TABLE 1 Characteristics of Kaiser Healthy Aging and Diverse Life Experiences Study (KHANDLE) participants

Mean (SD) or *n* (%)	Overall (*n* = 1622, 100%)	Never resided in a rural area (*n* = 1319, 81.3%)	Resided in a rural area (*n* = 303, 18.7%)
Age	76.1 (7.1)	75.6 (7.0)	78.2 (7.1)
Sex: Female	959 (59)	771 (58)	188 (62)
Race			
Asian	401 (25)	333 (25)	68 (22)
Black	419 (26)	323 (25)	96 (32)
Latino	328 (20)	276 (21)	52 (17)
White	474 (29)	387 (29)	87 (29)
Paternal education (mean years, SD)	8.4 (6.3)	8.7 (6.3)	7.0 (6.0)
Paternal education missing (n, %)	380 (23)	305 (23)	75 (25)
Maternal education (mean years, SD)	8.7 (5.5)	8.9 (5.4)	7.6 (5.5)
Maternal education missing (n, %)	244 (15)	183 (14)	61(20)
Childhood family financial status			
Poor	598 (37)	452 (34)	146 (48)
Average	805 (50)	679 (52)	126 (42)
Well-off	219 (13)	199 (14)	31 (10)
Participant education (mean years, SD)	14.8 (3.0)	15.0 (2.8)	13.9 (3.5)
Late-life household income			
<US $50k	569 (35)	433 (33)	136 (45)
US $50k–99.9k	564 (35)	473 (36)	91 (30)
≥US 100k	489 (30)	413 (31)	76 (25)
Age 10 region of residence			
West	889 (55)	771 (58)	118 (39)
Northeast or Midwest	184 (11)	155 (12)	29 (9)
South	204 (13)	126 (10)	78 (26)
Outside of US	345 (21)	267 (20)	78 (26)
Age 30 region of residence			
West	1467 (90)	1203 (91)	264 (87)
Northeast, Midwest, or South	72 (4)	53 (4)	19 (6)
Outside of US	83 (5)	63 (5)	20 (7)

Abbreviation: SD, standard deviation.

3.4 | Sensitivity analyses

We re-estimated our primary models using complete case observations (n = 1044). Although the smaller sample size decreased the precision of our estimates, the overall pattern of findings remained consistent (Table S1 in supporting information).

4 | DISCUSSION

Applying IPWs to estimate MSM in a diverse sample, we estimated effects of residing in a rural context in childhood and adulthood on late-life cognition while appropriately accounting for time-updated mediating confounders (i.e., SES, region of residence). In primary models that accounted for time-varying SES, we found mean expected values for baseline executive function and semantic memory would be about one-fifth SD lower had everyone in the study lived in a rural area in childhood, supporting our hypothesis of a sensitive period in childhood. We observed a pattern whereby rural residence in adulthood was associated with higher (albeit non-significantly) baseline executive function and verbal episodic memory. Incorporating the region of residence into the IPWs in our secondary models attenuated observed effects of both childhood and adulthood rural residence in our outcome models. Neither childhood nor adulthood rural residence was associated with late-life cognitive change.

A key advantage of our methodological approach is accurately estimating the effects of time-varying rural residence in the presence of time-varying confounder–mediators. Specifically, our findings for rural

TABLE 2 Estimated mean difference in verbal episodic memory between rural residence versus non-rural residence in childhood and adulthood without (A) and with (B) adjustment for region of residence

Verbal episodic memory			
		A.	B.
1. Total effect of early life rurality	Rural childhood	−0.04 (−0.15, 0.14)	0.04 (−0.10, 0.18)
	Years between cognitive assessments	0.01 (−0.03, 0.04)	0.001 (−0.03, 0.04)
	Rural childhood x Years	−0.02 (−0.09, 0.05)	−0.04 (−0.10, 0.04)
2. Direct effect of early life rurality & total effect of mid-/late-life rurality	Rural childhood	0.01 (−0.14, 0.16)	0.05 (−0.09, 0.20)
	Rural adulthood	0.24 (−0.07, 0.55)	0.13 (−0.14, 0.41)
	Years between cognitive assessments	−0.01 (−0.05, 0.03)	0.001 (−0.04, 0.04)
	Rural childhood x Years	−0.02 (−0.09, 0.06)	−0.03 (−0.10, 0.04)
	Rural adulthood x Years	−0.08 (−0.17, 0.01)	−0.04 (−0.13, 0.05)

Notes: All models adjust for race/ethnicity, sex, and interview mode. 1A. IPW for childhood rural residence calculated using age at KHANDLE wave 1, maternal and paternal education, maternal and paternal education missing indicators, childhood family finances, and foreign birth. 2A. IPW for mid-life/late-life rural residence calculated using all variables for childhood IPW + participant education & late-life income. Mid-life/late-life IPW was multiplied with childhood IPW and applied to outcome models. 1B. IPW additionally adjusted for region of residence at age 10. 2B. IPW additionally adjusted for region of residence at ages 10 and 30.
Abbreviations: IPW, inverse probability weights; KHANDLE, Kaiser Healthy Aging and Diverse Life Experiences Study.

TABLE 3 Estimated mean difference in executive function between rural residence versus non-rural residence in childhood and adulthood without (A) and with (B) adjustment for region of residence

Executive function			
		A.	B.
1. Total effect of early life rurality	Rural childhood	−0.19 (−0.32, −0.06)	−0.10 (−0.23, 0.03)
	Years between cognitive assessments	−0.001 (−0.02, 0.02)	−0.01 (−0.03, 0.01)
	Rural childhood x Years	−0.01 (−0.04, 0.03)	−0.02 (−0.05, 0.02)
2. Direct effect of early life rurality & total effect of mid-/late-life rurality	Rural childhood	−0.19 (−0.32, −0.06)	−0.10 (−0.24, 0.04)
	Rural adulthood	0.19 (−0.07, 0.44)	−0.01 (−0.30, 0.32)
	Years between cognitive assessments	−0.001 (−0.02, 0.02)	−0.01 (−0.03, 0.02)
	Rural childhood x Years	−0.01 (−0.05, 0.03)	−0.03 (−0.06, 0.01)
	Rural adulthood x Years	0.03 (−0.02, 0.08)	0.05 (−0.02, 0.12)

Notes: All models adjust for race/ethnicity, sex, and interview mode. 1A. IPW for childhood rural residence calculated using age at KHANDLE wave 1, maternal and paternal education, maternal and paternal education missing indicators, childhood family finances, and foreign birth. 2A. IPW for mid-life/late-life rural residence calculated using all variables for childhood IPW + participant education & late-life income. Mid-life/late-life IPW was multiplied with childhood IPW and applied to outcome models. 1B. IPW additionally adjusted for region of residence at age 10. 2B. IPW additionally adjusted for region of residence at ages 10 and 30.
Abbreviations: IPW, inverse probability weights; KHANDLE, Kaiser Healthy Aging and Diverse Life Experiences Study.

TABLE 4 Estimated mean difference in semantic memory between rural residence versus non-rural residence in childhood and adulthood without (A) and with (B) adjustment for region of residence

Semantic memory			
1. Total effect of early life rurality	Rural childhood	−0.22 (−0.35, −0.08)	−0.09 (−0.23, 0.04)
2. Direct effect of early life rurality & total effect of mid-/late-life rurality	Rural childhood	−0.22 (−0.36, −0.08)	−0.10 (−0.25, 0.04)
	Rural adulthood	0.08 (−0.13, 0.29)	0.04 (−0.19, 0.26)

Notes: All models adjust for race/ethnicity, sex, and interview mode. 1A. IPW for childhood rural residence calculated using age at KHANDLE wave 1, maternal and paternal education, maternal and paternal education missing indicators, childhood family finances, and foreign birth. 2A. IPW for mid-life/late-life rural residence calculated using all variables for childhood IPW + participant education & late-life income. Mid-life/late-life IPW was multiplied with childhood IPW and applied to outcome models. 1B. IPW additionally adjusted for region of residence at age 10. 2B. IPW additionally adjusted for region of residence at ages 10 and 30.
Abbreviations: IPW, inverse probability weights; KHANDLE, Kaiser Healthy Aging and Diverse Life Experiences Study.

residence were independent of individual socioeconomic indicators, suggesting that living in a rural context in childhood—beyond its correlation with lower SES in childhood or adulthood—may contribute to worse late-life cognitive functioning. Our findings for rural childhood residence reflect those of Herd et al., who also concluded that childhood SES did not explain associations between childhood rural residence and late-life cognition.[6] Rather, evidence points to a sensitive period in childhood whereby rural contexts act as a social determinant of poor late-life cognition through other pathways. Possible explanations may be the differences in school quality and access to cognitively stimulating early life resources, such as public libraries.[22,23] Our findings also lend support to those of Helmes and Van Gerven,[9] who observed a steeper decline in Mini-Mental State Examination scores among late-life urbanites compared to rural dwellers. While our effects for cognitive decline were non-significant, our findings suggest that residing in a rural area in adulthood may provide protective baseline cognitive benefits, though we interpreted this finding cautiously due to the small sample who resided in a rural area as adults.

Importantly, rural contexts are not homogenous. In our study, we accounted for heterogeneity in rural contexts through weighting on region of residence in childhood and mid-life. We found that our estimates of lower baseline executive function and semantic memory associated with living in a rural area in childhood were attenuated and no longer significant with the inclusion of geographic region. In ad hoc analyses, we observed substantial heterogeneity in cognition between regions of residence in childhood and adulthood, though the pattern across regions between rural and non-rural residence was consistent (Figures S1–S6 in supporting information). This finding demonstrates that despite variations across rural areas (e.g., community investment, dominant economic industries), participants who were rural dwellers earlier in the life course consistently performed worse on late-life cognitive assessments than their non-rural counterparts.

We report several strengths. This study is among the first to consider associations between rural residence in both childhood and adulthood with late-life cognitive functioning. By using advanced causal inference techniques, we move closer to causal estimates of real-world conditions for which random assignment is impracticable and unethical. Compared to prior studies, our sample reflects the increasingly heterogeneous older adult population in the United States, with similar proportions of Asian, Black, Latino, and White participants and >20% of the sample immigrating to the United States after age 10. Additionally, our sample age range spans nearly 40 years with childhood residential experiences dating from 1910s to 1960s. Substantial changes to the living conditions in rural and non-rural contexts over this period suggest our findings are not driven by a cohort effect.

We note several limitations. We used self-reported rurality because one-fifth of our sample resided outside of the United States in childhood and could not be coded to commonly used US-based rurality measures. To examine the validity of our self-reported measure, we compared these responses to the rural–urban continuum codes (RUCC), an objective county-level measure published by the US Department of Agriculture from the 1970s onward. Between 67% and 92% of participant addresses could be mapped to the RUCC in each census decade from 1970 to 2010. Among these, we observed that approximately 97% of addresses were accurately self-reported as rural or non-rural, indicating participants are fairly accurate in determining rurality of prior residences. Because we don't have continuous residential information, we were unable to account for the duration of time residing in rural areas. Although we adjusted for race/ethnicity as a confounder, our sample size precluded examining effect modification by race/ethnicity. Doing so would have advanced our understanding of how racialized experiences may alter the pathways between rural residence and late-life cognition. Last, our sample is comprised of long-term members of KPNC, and regional heterogeneity and rural dwelling in adulthood are unlikely to represent the experiences of older adults across the United States.

Our findings have important implications. While the proportion of Americans residing in rural areas has decreased over the twentieth century, population aging is occurring at a more rapid rate in rural areas.[24] Rural populations face a greater burden of individual modifiable risk factors for dementia while increasing urbanization has often left rural areas with few resources for health at all stages of the life course.[2,25–28] Rurality may exacerbate cognitive aging and dementia risk through increased exposure to various social and physical contexts associated with dementia risk that may be more common in rural areas, such as fewer opportunities for cognitive stimulation or exposure to some pollutants (e.g., pesticides, mining contamination).[29–33]

This study is an important step toward understanding the relationship between life course rural residential contexts and late-life cognition. Using a causal inference approach, we attempted to disentangle estimates of rural residence at different life-course periods in the presence of time-varying confounder–mediators. Our study found associations where childhood rural residence was associated with worse late-life cognition beyond what is due to differences in individual SES in childhood and adulthood. Future steps include an examination of more nuanced measures of historical rural contexts, such as public-library access, that may provide insights into the specific contextual factors that contribute to lower late-life cognitive functioning. We also will extend this work to consider mediators, such as cardiovascular disease risk, that help to explain the relationships between contextual exposures and population outcomes.

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CONFLICTS OF INTEREST

The authors have no declarations of interest to disclose. Author disclosures are available in the supporting information.

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SUPPORTING INFORMATION

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

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