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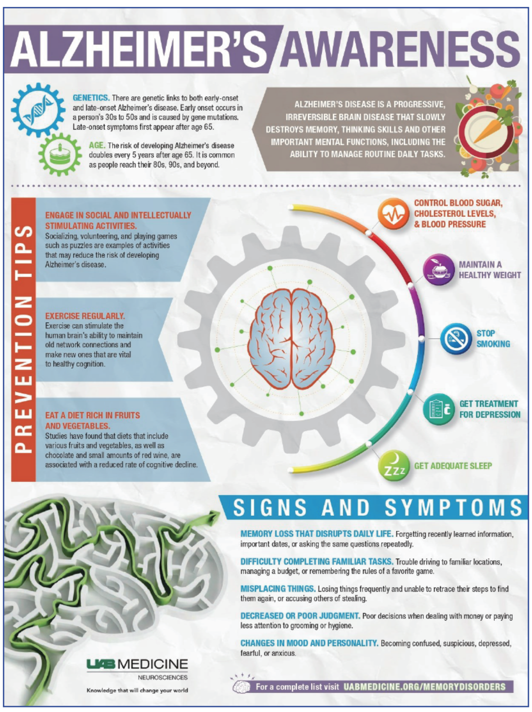

ALZHEIMER'S DISEASE ISSUE

Preplanned Studies

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Cover Image: adapted from Alzheimer's Disease Center at the University of Alabama at Birmingham, https://www.uab.edu/medicine/alzheimers/patient-care/resources/alzheimer-s-awareness.
This week's issue was organized by Guest Editor Xi Chen.

Preplanned Studies

Geographic Variation in Inpatient Care Utilization, Outcomes and Costs for Dementia Patients Aged 65 Years or Older — China, 2017–2019

Zhuoer Lin[1,&]; Fang Ba[1,&]; Heather Allore[2,3,4]; Gordon G Liu[5,6]; Xi Chen[1,4,6,7,#]

Summary

What is already known about this topic?

Dementia leads public health issues worldwide. China has the largest population of adults living with dementia in the world, imposing increasing burdens on the public health and healthcare systems. Despite improved access to health services, inadequate and uneven dementia management remains common.

What is added by this report?

The report documents the provincial-level geographic patterns in healthcare utilization, outcomes, and costs for patients hospitalized for dementia in China. Regional patterns demonstrate gaps in equity and efficiency of dementia care and management for dementia patients.

What are the implications for public health practice?

Public health policy and practices should consider geographic disparities in disease burden and healthcare provision to promote equitable allocation of resources for dementia care throughout China.

Globally, over 55 million people live with dementia, and the aggregate financial burden of the disease is over 1 trillion US dollars annually (*1–2*). This burden has been growing rapidly in China, which habilitates almost one-fourth of the total dementia cases worldwide (*3–4*). Prior research shows that the prevalence of dementia in China is high and differs geographically (*3–4*). However, no previous study has revealed the geographic patterns of dementia care and costs in China. To bridge that gap, we used administrative data from an extensive national database to characterize the geographic patterns in healthcare utilization, outcomes, and costs for patients hospitalized for dementia in China. We obtained novel estimates at both the provincial and national levels to enrich the understanding of the disease burden nationwide and facilitate the effective allocation of resources for dementia care. Our results demonstrated significant geographic disparities in inpatient care utilization, outcomes, and costs for patients hospitalized for dementia in China across provincial-level administrative divisions (PLADs). Specifically, we found notable geographic clusters in inpatient care costs and length of stay. These regional patterns imply gaps in equity and efficiency of dementia care and management for this rapidly growing population of dementia patients. Future policies and practices should consider these geographical disparities and promote a more equitable system for dementia care.

Hospital service data were obtained through the Data Center for High-Quality Hospital Management at Peking University Institute for Global Health and Development. The Center integrates data on healthcare services and management of representative hospitals in China for health policy and management research. The national sample covers 30 PLADs except for Xizang (Tibet) Autonomous Region; Taiwan, China; Hong Kong Special Administrative Region (SAR); and Macau SAR, making it a representative sample for understanding geographic variations. The dataset, spanning from June 2017 to June 2019, provides information on inpatient records, including admission type, dates of admission and discharge, primary and secondary diagnoses, comorbidities, and costs. To ensure that the care utilization and costs were related directly to dementia, we extracted inpatient records with primary diagnosis as dementia based on the International Classification of Disease (ICD) codes (Supplementary Table S1, available in http://weekly.chinacdc.cn).

Since dementia is an age-related condition, we restricted samples to patients aged 65 years or older at admission. Samples with a respective 2% of the highest and lowest total inpatient care costs were excluded from the analysis to mitigate the influence of extreme values; and the results were similar if we excluded extreme values based on other criteria (e.g., excluding 1% of the highest and lowest). Overall, 1,917 hospitals in the database had valid dementia cases (51,530 total cases), with 960 (50.1%) tertiary hospitals and 957 (49.9%) secondary hospitals or below. The distribution of hospitals and cases by PLAD is further illustrated in Supplementary Figure S1 (available in http://weekly.chinacdc.cn), where the total number of hospitals (and cases) and the proportion of types of hospitals are presented for each PLAD.

In this study, the inpatient care utilization, i.e., the number of hospital admissions due to dementia per 100,000 person-years, was first assessed for each PLAD. This assessment utilized our medical records data and data from China Statistical Yearbook for hospital admission and provincial population (*5*). Specifically, we scaled our total number of dementia admissions by the ratio of hospital admissions included in our database to the total hospital admissions from the Yearbook. The provincial population aged 65 or older and the observed periods were used as the denominator. Second, we evaluated the disease severity/urgency and outcomes of hospital admissions for dementia patients. Specifically, we used the percentage of emergency room (ER) admission and the number of comorbidities to reflect the disease severity/urgency of admission; and we used the percentage of in-hospital mortality as an indicator for care outcomes. The number of comorbidities was calculated as the sum of all coexisting diagnosed conditions documented at the time of admission using ICD codes. The in-hospital mortality was calculated as the proportion of patients who died during hospitalization among all dementia inpatient admissions. Third, we estimated the average total costs per admission based on the total hospital expenditure reported for each admission (including out-of-pocket and insurance-covered expenses), the average length of stay (LOS), and the average daily cost per admission to assess the care intensity during the hospitalization.

The quality of data was highly reliable, with limited missing records and extreme cases. Specifically, we found no missing data for all measures except for mortality outcome (with only <0.01% missing records). No extreme cases with values outside valid/possible ranges were found in our data. For each outcome, we calculated the national average, by averaging the provincial estimates of the outcome. Furthermore, using Moran's I statistic, we examined spatial autocorrelation and clustering using the distance decay parameter of 2. STATA (release 16.0, Stata Corp) and R (version 4.0.2, R Core Team) were used to perform the analyses.

Figure 1 displayed the geographic patterns of inpatient care utilization, severity/urgency, and outcomes. Panel A presented the number of dementia-related hospital admissions per 100,000 person-years for each PLAD. The national average number of dementia admissions was 111 [95% confidence interval (CI): 72–149] per 100,000 person-years. The utilization rate of care was higher in western PLADs and some central and southern PLADs, such as Xinjiang Uygur Autonomous Region (579), Yunnan Province (218), Guizhou Province (181), and Guangdong Province (273), but lower in northeastern PLADs. Panel B presented the percentage of ER admissions among all dementia admissions. The national average across PLADs was 19.5% (95% CI: 15.8%–23.2%). At the provincial level, the percentage of ER admissions ranged from 3.2% in Inner Mongolia Autonomous Region to 40.5% in Shanghai Municipality. Some PLADs with high percentages of ER admissions included Beijing Municipality (38.2%), Jilin Province (37.0%), Guizhou Province (33.4%), Qinghai Province (31.7%), Henan Province (31.3%), and Heilongjiang Province (30.3%). Panel C presented the average number of comorbidities per admission. Hospitalized dementia patients generally had multiple comorbidities. The national average across PLADs was 5.5 (95% CI: 4.9–6.1) comorbidities; and at the provincial level, the average number of comorbidities ranged from 3.1 in Liaoning Province to 9.5 in Yunnan Province. The average number of comorbidities in patients was higher in western PLADs and some eastern or northern PLADs, such as Xinjiang Uygur Autonomous Region (7.6), Qinghai Province (7.5), Fujian Province (8.9), Zhejiang Province (7.0), and Beijing Municipality (7.5), as compared to others. Lastly, for care outcomes, Panel D displayed the percentage of in-hospital mortality among all dementia-related admissions. The national average across PLADs was 1.0% (95% CI: 0.5%–1.4%). Northern PLADs had the highest percentage of in-hospital mortality, including Inner Mongolia Autonomous Region (6.5%), Heilongjiang Province (2.5%), Jilin Province (1.8%), and Liaoning Province (1.3%). The Moran's I statistics were all very small and no significant spatial autocorrelation was found for these measures except for the utilization rate.

Figure 2 further illustrated the geographic variation in average total costs, daily costs, and LOS per admission, as measures of care intensity and disease burden. Panel A presented the average total costs per admission. The national average total cost across

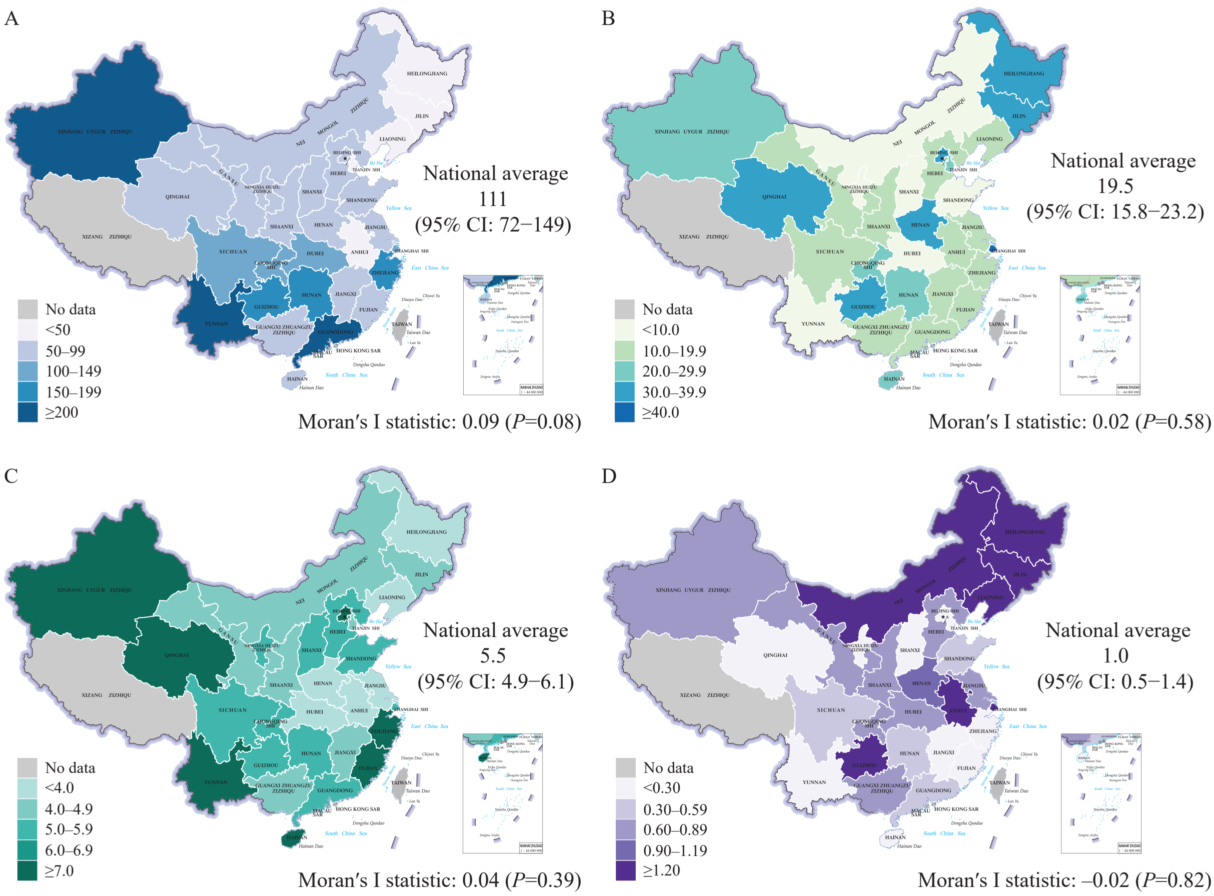

FIGURE 1. Geographical variation in health care utilization and outcomes for hospitalized dementia patients in China. (A) Number of hospital admissions due to dementia per 100,000 person-years; (B) percentage of emergency room admissions (%); (C) average number of comorbidities; (D) percentage of in-hospital mortality (%).
Note: In each panel, the sample period was from June 2017 to June 2019; and data were available for all PLADs except for Xizang (Tibet); Taiwan, China; Hong Kong SAR; and Macau SAR. Moran's I statistic for spatial autocorrelation is displayed at the bottom; and the national average across PLADs is displayed on the right with 95% CI presented in the parentheses. The following terms were used interchangeably: Xizang=Xizang (Tibet); Nei Mongol=Inner Mongolia; Zizhiqu=Autonomous Region.
Abbreviation: PLAD=provincial-level administrative division; SAR=Special Administrative Region; CI=confidence interval.

PLADs was 14,755 (95% CI: 12,738–16,772) CNY per admission which presented clear geographic patterns at the provincial level. Notably, the average total costs per admission were highest among Jing-Jin-Ji metropolitan area (i.e., Tianjin Municipality: 35,357; Beijing Municipality: 28,660; and Hebei Province: 15,618) and were consistently higher among eastern or southern coastal PLADs (e.g., Fujian Province: 22,072; Shanghai Municipality: 19,624; and Zhejiang Province: 17,406) than others. Panels B and C, presented the average daily costs and LOS per admission. At the national level, the average daily costs were 1,171 (95% CI: 965–1,377) CNY, and the average LOS was 15.5 (95% CI: 13.7–17.4) days per admission. At the provincial level, the average daily costs were higher among Jing-Jin-Ji metropolitan area and some northern PLADs than others, including Beijing Municipality (3,491), Tianjin Municipality (2,818), Hebei Province (1,385), Inner Mongolia Autonomous Region (1,442), and Jilin Province (1,175). The average daily costs were also relatively high in some coastal PLADs, such as Shanghai Municipality (1,385) and Guangdong Province (1,126). By contrast, the LOS was the highest among coastal areas and some western PLADs, such as Fujian Province (23.0), Zhejiang Province (23.0), Jiangsu Province (20.7), Shanghai Municipality (18.4), Sichuan Province (22.5), and Guizhou Province (21.0). The Moran's I statistics for average total costs, daily costs, and LOS were large and significant at 0.1% ($P<0.001$), indicating strong spatial correlation and clustering across PLADs.

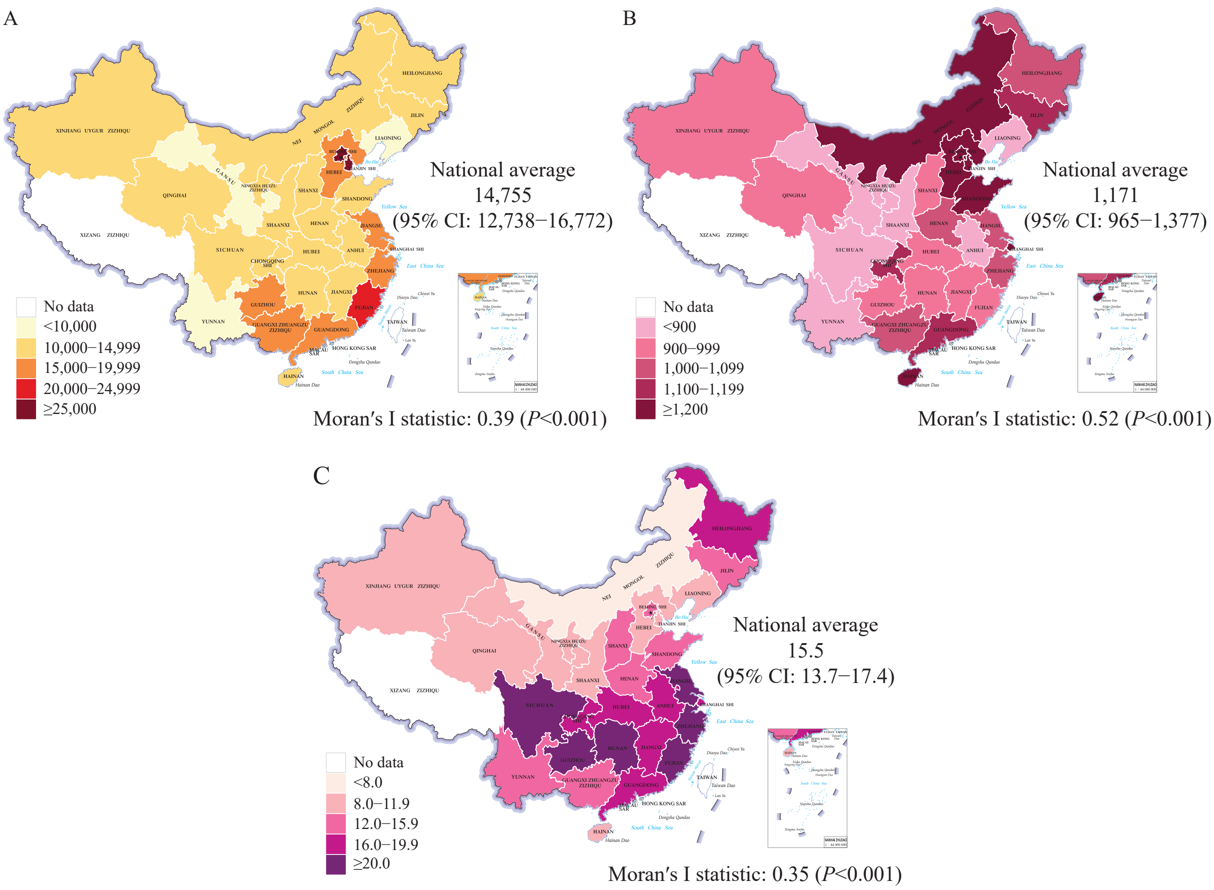

FIGURE 2. Geographical variation in health care costs, daily costs, and length of stay for hospitalized dementia patients in China. (A) Average total inpatient cost per admission (in CNY); (B) average daily cost per admission (in CNY); (C) average length of stay per admission (in days).

Note: In each panel, the sample period was from June 2017 to June 2019; and data were available for all PLADs except for Xizang (Tibet); Taiwan, China; Hong Kong SAR; and Macau SAR. Moran's I statistic for spatial autocorrelation was displayed at the bottom; and the national average across PLADs was displayed on the right with 95% CI presented in the parentheses. The following terms were used interchangeably: Xizang=Xizang (Tibet); Nei Mongol=Inner Mongolia; Zizhiqu=Autonomous Region.

Abbreviation: PLAD=provincial-level administrative division, SAR=Special Administrative Region, CNY=Chinese Yuan, CI=confidence interval.

DISCUSSION

The study demonstrated geographic variation in inpatient care utilization, disease severity/urgency, care outcomes, and costs for dementia patients in China. Several findings in the study warrant further discussion.

First, the geographical patterns of inpatient care utilization and costs overall were not entirely consistent with the patterns of disease prevalence, which may reflect the underlying disparities in dementia care and management (*4*). While some western PLADs with higher dementia prevalence showed greater utilization and disease burden, the patterns of other regions and PLADs differed in many other aspects. Such differences between utilization and prevalence could be partially explained by the regional variations in the proportion of older adults, economic development, healthcare infrastructure, disease awareness, and management. Varying levels of financial burden and coverage for dementia care may contribute to regional patterns (*4*).

Second, we showed that the regional patterns might vary across utilization measures, disease urgency/severity, outcomes, and costs, which deserves investigation in future research. For instance, while we observed greater utilization rates in western PLADs, the severity/urgency of the admissions (e.g., percentage of ER admissions) seemed to be higher in some other PLADs. Both demand and supply-side factors might explain these patterns. On the demand side, the utilization rate is mainly determined by disease prevalence and patients' care-seeking behaviors. Many demand-side factors, such as economic difficulties, low awareness, and social stigma, may impede dementia patients from seeking care and treatment at an early stage, which will consequently lead to greater severity/urgency of the diseases and higher rates of ER admissions (*1*–*2*,*4*). On the supply side, inpatient care utilization largely depends on prompt access and quality of care. The varying availability of well-trained specialists and dementia care facilities across PLADs may result in the differential capacity of clinical management and control, thereby shaping the patterns of utilization, disease outcomes, and costs. Additionally, the criteria for dementia admissions may vary across areas due to the uneven distribution of dementia care resources, leading to diverse patient compositions and care outcomes (*4*). Our initial evidence on the geographic patterns highlights the potential differences in various aspects of dementia care. Future studies should consider this and further disentangle the underlying causes of the patterns.

Third, we found strong geographic clustering of costs, daily costs, and LOS. The costs and the care intensity were consistently higher among more developed areas, such as Jing-Jin-Ji metropolitan area and eastern coastal PLADs, which reemphasized the regional disparities in dementia care and utilization across PLADs. As the demand for healthcare and nursing is intertwined, a lack of access to primary and long-term care, especially in less developed areas, has limited the care for people with dementia and enlarged their health inequities. Demographic shifts to a greater proportion of older adults and the rising burden of dementia suggest a need to establish and strengthen primary care and long-term care systems and affordable and equitable dementia caring models (*6*–*7*).

This study was subject to some limitations. First, only hospital admissions with dementia as the primary diagnosis were included. Yet restrictions by medical technology, dementia misdiagnosis and misclassifications may affect some PLADs more than others, leading to certain levels of geographic differences. The ubiquitous underdiagnosis of dementia may also apply to our study context for all PLADs. Moreover, dementia could have been a secondary diagnosis for admission, which was not examined in this study. Second, the underlying mechanisms for the geographic variations were not fully illuminated. Data on local policies and practices needs to be linked to the medical records to understand the mechanisms of the regional patterns.

Conflicts of interest: The authors have no conflicts of interest.

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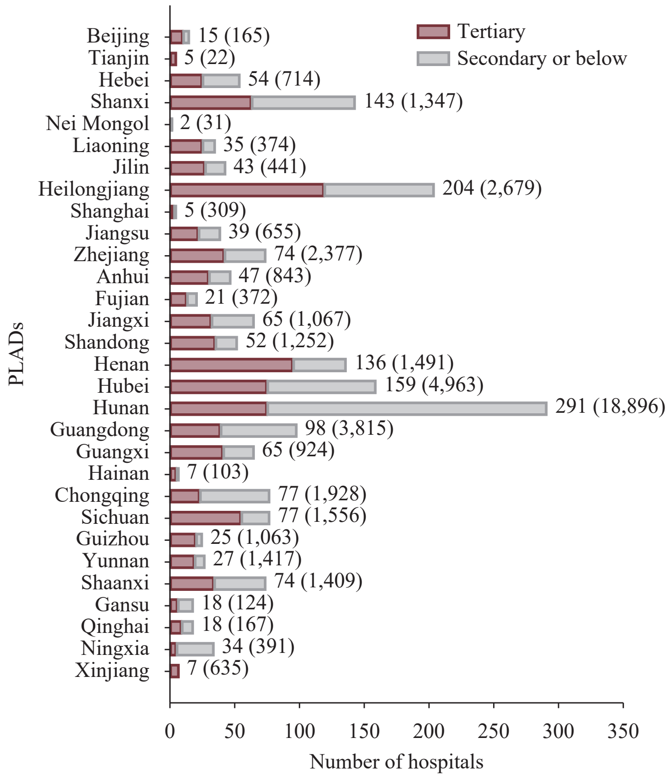
Supplementary Materials



SUPPLEMENTARY FIGURE S1. Distribution of hospitals and admitted dementia cases by PLADs.
Note: The figure displays the distribution of hospitals (and admitted dementia cases) by PLADs in our data. The horizontal bar represents the number of hospitals, where red color represents tertiary hospitals and gray color represents secondary hospitals or below. For each PLAD, the total number of hospitals is displayed next to the corresponding bar; and the number of dementia cases identified in the hospitals is shown in parentheses.
Abbreviation: PLADs=provincial-level administration divisions.

SUPPLEMENTARY TABLE S1. ICD codes for dementia diagnosis and classification.

	ICD-10 Codes	ICD-9 Codes
Alzheimer's Disease and Related Dementias	G30, F01, G31, G91, G93.7, G94, G23.8, F02, F03, F04, F05, F06, R41	331.0, 290.4, 290.0, 290.1, 290.2, 290.3, 290.8, 290.9, 294.x, 331.1–331.9, 333.0, 797

Abbreviation: ICD-10=International Classification of Diseases, 10th Revision; ICD-9=International Classification of Diseases, 9th Revision.

Preplanned Studies

COVID-19 Stay-At-Home Orders and Older Adults' Cognitive Health — United States, June 2018–Feburary 2022

Nam Sun Choi[1]; Tianzi Li[1]; Jingxiang Pan[1]; Selena Yue[1]; Jing Li[2,#]

Summary

What is already known about this topic?

Lack of social activities is known to negatively impact cognitive functioning and increase risk of cognitive impairment, including dementia, among older adults.

What is added by this report?

Coronavirus disease 2019 (COVID-19) stay-at-home orders implemented in the U.S. early during the pandemic were not found to negatively affect cognitive functioning of older adults.

What are the implications for public health practice?

There may have been no severe, unintended consequences of the COVID-19 stay-at-home orders in terms of their impact on cognitive functioning and risk of dementia among older adults, lending further support to use of such orders.

The global prevalence of cognitive impairment is estimated to be 19% (*1*), with more than 55 million people living with dementia worldwide (*2*) and 6.5 million in the U.S. (*3*). While lack of social activities is known to negatively impact cognitive functioning and increase risk of cognitive impairment including dementia among older adults (*4*), little is known on the effect of coronavirus disease 2019 (COVID-19) related stay-at-home orders on older adults' cognitive health. This study examined the impact of the COVID-19 stay-at-home orders implemented in certain states of the U.S. and the cognitive health of older adults. Stay-at-home orders requested residents to stay at home as much as possible, and many public shops and venues to close down temporarily (*5*). This research used data from the U.S. Understanding America Study (UAS), a longitudinal internet survey representative of individuals aged 50 and above in the U.S., and the COVID-19 State Policies (CUSP) database. A difference-in-differences (DID) approach was used to compare trajectories of four cognitive scores before and after state-specific stay-at-home orders were implemented between states with and without COVID-19 stay-at-home orders. This study found no significant relationship between state-specific stay-at-home policies and cognitive health of U.S. older adults.

This study conducted an observational retrospective cohort study. The study population included U.S. adults aged 50 and older who participated in UAS and answered survey questions relevant to cognitive health between June 2018 and February 2022. UAS is a nationally representative longitudinal internet panel survey of more than 9,000 adults older than 18 years. Our outcome variables were four cognitive scores from numbers, picture vocabulary, verbal analogies, and serial seven subtraction tests. The tests were designed to measure the respondent's quantitative reasoning and lexical knowledge according to the Woodcock-Johnson Tests of Cognitive Abilities (*6*). Survey questionnaires containing these tests were fielded in two waves, one in June 2018, and the other in July 2020. The respondents could take a test in each wave any time after it became available; only those who participated in the first wave were eligible to participate in the second wave. We included in our analyses all individuals who participated in at least one wave to improve precision of estimates, although only those who participated in both waves contributed to DID coefficients. The independent variable was implementation of stay-at-home orders from the CUSP database. Implementation was treated as a binary variable that equals 1 if the state issued a stay-at-home order (treatment group) and 0 if the state did not issue any order or issued but did not specifically restrict movement of the general public during the study period (control group). Our control variables included gender, age, immigration status, marital status, education, ethnicity, race, presence of other household members, employment status, and household income. These variables were also obtained from UAS.

This research examined summary statistics of key variables, and *t*-tests for continuous variables and Chi-squared tests for categorical variables were used to compare means between treatment and control groups. Our DID model specification was as follows:

$$y_{i,s,q} = \beta_0 + \beta_1 \left(d_s \times p_q\right) + X_{i,q}\gamma + \delta_q + \alpha_s + \varepsilon_{i,q,s} \quad (1)$$

where the dependent variable y is a cognitive test score for individual i, state s, and quarter q. d_s is an indicator for whether state s implemented strict stay-at-home orders. p_q is an indictor for whether quarter q is after the second quarter of 2020, since most states implemented stay-at-home orders between March and April 2020. $X_{i,q}$ contains individual-level sociodemographic control variables in quarter q. δ_q and α_s are quarter and state-fixed effects. $\varepsilon_{i,q,s}$ is the error term and is clustered at the state level. We conducted secondary analyses on subsamples stratified by age (65 or over *vs.* under 65), gender and whether the individual lived alone. All analyses were performed using Stata BE 17.0 (StataCorp, College Station, TX, U.S.A.).

Table 1 shows the numbers of state and person-wave observations for each of the four cognitive tests and the average test scores in states with stay-at-home orders (treatment group) and without stay-at-home orders (control group). Forty states out of 51 issued a stay-at-home order between March and April 2020. During the study period, the total number of observations per panel was about 8,000, of which over 80% were from the treatment group, with an average of approximately 170 observations per treatment state compared to approximately 100 per control state. The average cognitive test score was slightly higher in states with stay-at-home orders than in states without stay-at-home orders in all panels. Relative to the control states, treatment states had higher proportions of immigrants and unmarried people and higher average education levels and household incomes (Table 2). To assess selective attrition between Wave 1 and Wave 2, we compared summary statistics by the number of waves the respondent participated in (Supplementary Table S1, available in http://weekly.chinacdc.cn). Although we did not find large differences between those who participated in only one wave of cognitive assessment versus two, the former had somewhat higher socioeconomic status than the latter in terms of education and income. Table 3 shows the differential change in cognitive scores in states with stay-at-home orders relative to states without stay-at-home orders. None of the associations was statistically significant. In terms of coefficient magnitudes, stay-at-home orders were associated with lower numbers test and serial seven subtraction test scores compared to states without stay-at-home orders, by 0.184 points and 0.041 points, respectively. In contrast, stay-at-home orders were associated with increased picture vocabulary test and verbal analogies test scores by 0.221 and 0.757 points, respectively. Subgroup analyses yielded consistent results (not shown).

DISCUSSION

This study found no evidence that state-level COVID-19 stay-at-home orders in the U.S. led to significant changes in cognitive health of older adults. Previous studies of COVID-19 lockdown measures found adverse effects on mental health, such as

TABLE 1. Cognitive test score descriptive statistics, United States, June 2018–Feburary 2022.

Variable	Numbers test	Picture vocabulary test	Verbal analogies test	Serial seven subtraction test
Number of states, N	51	51	51	51
With stay-at-home order	40	40	40	40
Without stay-at-home order	11	11	11	11
Number of observations (%)	8,090 (100.0)	7,974 (100.0)	7,861 (100.0)	7,684 (100.0)
With stay-at-home order (%)	6,985 (86.3)	6,884 (86.3)	6,783 (86.3)	6,653 (86.6)
Without stay-at-home order (%)	1,105 (13.7)	1,090 (13.7)	1,078 (13.7)	1,031 (13.4)
Cognitive score, Mean (SD)	51.17 (9.10)	54.26 (8.48)	51.33 (8.89)	4.494 (1.078)
With stay-at-home order	51.24 (9.13)	54.28 (8.55)	51.35 (8.93)	4.494 (1.081)
Without stay-at-home order	50.72 (8.88)	54.13 (7.99)	51.21 (8.63)	4.493 (1.063)

Note: The 51 States includes the 50 states and the District of Columbia. Numbers, picture vocabulary, and verbal analogies scores reported in the Understanding America Study were converted to standardized scores, where 50 is the mean and 10 is the standard deviation. A score of 50 means that the person's cognitive ability is equal to that of the average person in the general population, a score of 60 means that the person's ability is one standard deviation above average, and a score of 40 means that the person's ability is one standard deviation below average. The serial seven subtraction test scores range from 0 to 5.

Abbreviation: SD=standard deviations.

TABLE 2. Summary statistics of individual characteristics, United States, June 2018–Feburary 2022.

Variable	Total	States with stay-at-home order	States without stay-at-home order	*P*-value
No. of observations (N)	8,090	6,985	1,105	
Age (Mean, SD)	63.1 (9.0)	63.2 (9.0)	62.6 (8.5)	0.036
Gender				0.19
Female (%)	4,389 (54.3)	3,762 (53.9)	627 (56.7)	
Male (%)	3,700 (45.7)	3,222 (46.1)	478 (43.3)	
Missing (%)	1 (0.0)	1 (0.0)	0 (0.0)	
Immigrant status				<0.001
Non-immigrant (%)	4,425 (54.7)	3,688 (52.8)	737 (66.7)	
First generation immigrant (%)	738 (9.1)	690 (9.9)	48 (4.3)	
Second or third generation immigrant (%)	2,757 (34.1)	2,462 (35.2)	295 (26.7)	
Missing (%)	170 (2.1)	145 (2.1)	25 (2.3)	
Marital status				<0.001
Never married (%)	782 (9.7)	720 (10.3)	62 (5.6)	
Married (%)	4,823 (59.6)	4,130 (59.1)	693 (62.7)	
Separated/divorced/widowed (%)	2,484 (30.7)	2,134 (30.6)	350 (31.7)	
Missing (%)	1 (0.0)	1 (0.0)	0 (0.0)	
Level of education				<0.001
High school graduate or under (%)	1,810 (22.4)	1,516 (21.7)	294 (26.6)	
Some college-no degree (%)	1,965 (24.3)	1,662 (23.8)	303 (27.4)	
Bachelor's degree (%)	2,935 (36.3)	2,578 (36.9)	357 (32.3)	
Master's degree and over (%)	1,380 (17.1)	1,229 (17.6)	151 (13.7)	
Hispanic ethnicity				0.59
No (%)	7,423 (91.8)	6,401 (91.6)	1,022 (92.5)	
Yes (%)	666 (8.2)	583 (8.3)	83 (7.5)	
Missing (%)	1 (0.0)	1 (0.0)	0 (0.0)	
Race				0.080
White only (%)	6,628 (81.9)	5,696 (81.5)	932 (84.3)	
Black only (%)	635 (7.8)	568 (8.1)	67 (6.1)	
Others (%)	798 (9.9)	695 (9.9)	103 (9.3)	
Missing (%)	29 (0.4)	26 (0.4)	3 (0.3)	
Employment status				0.20
Currently working (%)	3,293 (40.7)	2,825 (40.4)	468 (42.4)	
Retired (%)	2,798 (34.6)	2,443 (35.0)	355 (32.1)	
Others (%)	1,992 (24.6)	1,710 (24.5)	282 (25.5)	
Missing (%)	7 (0.1)	7 (0.1)	0 (0.0)	
Household income				0.001
Less than 30,000 USD	2,004 (24.8)	1,699 (24.3)	305 (27.6)	
30,000 to 59,999 USD	2,169 (26.8)	1,857 (26.6)	312 (28.2)	
60,000 to 99,999 USD	1,980 (24.5)	1,708 (24.5)	272 (24.6)	
100,000 USD or more	1,912 (23.6)	1,696 (24.3)	216 (19.5)	
Missing (%)	25 (0.3)	25 (0.4)	0 (0.0)	
Presence of other household members				0.071
No (%)	1,832 (22.6)	1,609 (23.0)	223 (20.2)	
Yes (%)	6,253 (77.3)	5,371 (76.9)	882 (79.8)	
Missing (%)	5 (0.1)	5 (0.1)	0 (0.0)	

Note: Values shown are numbers of individuals with percentages of individuals for each category in parentheses, unless otherwise indicated for continuous variables where means are shown with SD in parentheses.
Abbreviation: SD=standard deviations; USD=US dollar.

TABLE 3. DID estimates of stay-at-home order on cognitive health and loneliness, United States, June 2018–Feburary 2022.

Parameter	Cognitive Test Score			
	Numbers test	PV test	VA test	SSS test
DID estimate	−0.184 (0.436) [−1.060, 0.691]	0.221 (0.250) [−0.281, 0.722]	0.757 (0.582) [−0.412, 1.926]	−0.041 (0.041) [−0.124, 0.041]
R^2	0.266	0.295	0.234	0.078
N	8,090	7,974	7,861	7,684
States	51	51	51	51

Note: Difference-in-differences models were estimated with least squares and include controls listed in Table 2, state-fixed effects and quarter-fixed effects. Each observation is an individual-quarter. State-clustered standard errors are in parentheses and 95% confidence intervals are in brackets. None of the coefficients reached statistical significance.
Abbreviation: PV=picture vocabulary; VA=verbal analogies; SSS=serial seven subtraction; DID=difference-in-differences.

depression and anxiety (*7*), and worsening cognitive ability among those with dementia, albeit not in the U.S. (*8*). To our knowledge, ours is the first study to examine the impact of state-level stay-at-home policies on cognitive health among the general, older population in the U.S. Results of our study may help rule out any drastic impact on the cognitive health of older adults subject to state-wide stay-at-home orders, at least in the U.S. context and during the short-term. It is possible that older adults had alternative means to remain socially active in the presence of stay-at-home orders, for example, by telephone or internet. It could also be that the relatively short time horizon and relaxed measures of stay-at-home orders without strict enforcement were simply not severe enough to impact cognition health of older adults. However, our findings should not be construed to mean that no COVID-19 related restrictions can negatively impact the cognitive health of older adults. Further research is needed to better understand the longer-term consequences of COVID-19 related restrictions in different contexts, and whether there are effective coping methods already adopted or to be adopted by older adults, their families, and public health policy makers to mitigate unintended consequences.

The study had several limitations. First, we were unable to observe the exact extent to which study participants adhered to stay-at-home orders. Second, there was heterogeneity in the specific nature of stay-at-home order rules across states. For instance, some states allowed limited movement to conduct essential activities and others allowed movement for outdoor exercise. We were unable to study each scenario separately due to insufficient sample size, and our results should be interpreted as an average effect of these policies. Third, due to the relatively short study period, we were unable to examine long-term impact of the COVID-19 stay-at-home orders on cognitive health. Fourth, though UAS participants were broadly representative of the U.S. population, participation in individual surveys was voluntary. To the extent that those completing questionnaires on cognition were relatively cognitively healthy individuals, selection bias could have impacted the external validity of our findings. A related issue is that it is possible that those who participated in Wave 1 of each survey and experienced a larger decline in cognitive ability may have been less likely to participate in Wave 2, causing our DID estimates to be biased towards the null, although our supplementary analysis provides no direct evidence that this is the case. Finally, it is possible that COVID-19 illness may independently affect cognition, although our study design was robust to any impact of the COVID-19 pandemic common to the treated and control groups.

Despite of these limitations, our study is one of the first to show that U.S. COVID-19 related stay-at-home order did not have severe negative consequences on the cognitive health of older adults in the general population. It lends further support for such measures to be viable public health options for combating the spread of communicable diseases like COVID-19.

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SUPPLEMENTARY MATERIAL

SUPPLEMENTARY TABLE S1. Summary statistics of UAS respondents by number of participating cognitive test survey waves, United States, June 2018–Feburary 2022.

Variable n, %	One wave (N=2,102)	Both waves (N=2,994)	*P*-value of difference
Age, mean (SD)	61.8 (9.8)	62.6 (8.6)	<0.001
Score of Numbers Test, mean (SD)	50.9 (9.1)	51.4 (8.8)	0.11
Gender (n, %)			0.31
Female	1,168 (55.6)	1,609 (53.7)	
Male	934 (44.4)	1,384 (46.2)	
Missing	0 (0.0)	1 (0.0)	
Immigration status (n, %)			<0.001
Non-immigrant	1,117 (53.1)	1,654 (55.2)	
First generation immigrant	246 (11.7)	246 (8.2)	
Second or third generation immigrant	689 (32.8)	1,034 (34.5)	
Missing	50 (2.4)	60 (2.0)	
Marital status (n, %)			0.30
Never married	221 (10.5)	280 (9.4)	
Married	1,233 (58.7)	1,818 (60.7)	
Separated/divorced/widowed	648 (30.8)	895 (29.9)	
Missing	0 (0.0)	1 (0.0)	
Highest level of education (n, %)			0.034
High school graduate or under	437 (20.8)	683 (22.8)	
Some college-no degree	481 (22.9)	744 (24.8)	
Bachelor's degree	791 (37.6)	1,071 (35.8)	
Master's degree and over	393 (18.7)	496 (16.6)	
Hispanic ethnicity (n, %)			<0.001
No	1,886 (89.7)	2,769 (92.5)	
Yes	216 (10.3)	225 (7.5)	
Race (n, %)			0.62
White only	1,707 (81.2)	2,461 (82.2)	
Black only	167 (7.9)	234 (7.8)	
Others	218 (10.4)	290 (9.7)	
Missing	10 (0.5)	9 (0.3)	
Employment status (n, %)			0.020
Currently working	970 (46.1)	1,263 (42.2)	
Retired	683 (32.5)	998 (33.3)	
Others	447 (21.3)	730 (24.4)	
Missing	2 (0.1)	3 (0.1)	
Household income (n, %)			<0.001
Less than 30,000 USD	503 (23.9)	748 (25.0)	
30,000 to 59,999 USD	517 (24.6)	839 (28.0)	
60,000 to 99,999 USD	492 (23.4)	732 (24.4)	
100,000 USD or more	578 (27.5)	670 (22.4)	
Missing	12 (0.6)	5 (0.2)	
Other household members			0.090
No	514 (24.5)	654 (21.8)	
Yes	1,587 (75.5)	2,338 (78.1)	
Missing	1 (0.0)	2 (0.1)	

Note: Values shown are numbers of individuals with percentages of individuals for each category in parentheses, unless otherwise indicated for continuous variables where means are shown with SD in parentheses.
Abbreviation: UAS=Understanding America Study; SD=standard deviations; USD=US dollar.

Preplanned Studies

Polypharmacy Among People Living with Dementia — Israel and 24 Countries in European Union, 2015–2019

Shanquan Chen[1,#]; Xi Chen[2]; Huanyu Zhang[3]

Summary

What is already known about this topic?

With a growing number of people living with dementia (PLWD), the practice of taking multiple medications to manage symptoms or comorbidities, i.e., polypharmacy, among PLWD has become a global health challenge.

What is added by this report?

In 2015–2019, polypharmacy for PLWD varied substantially among 25 studied countries, with approximately 1 in 5 Estonian PLWD and 4 in 5 Cypriot PLWD having polypharmacy. In addition, Switzerland, Poland, Austria, and the Czech Republic have experienced a significantly increasing trend in polypharmacy for PLWD.

What are the implications for public health practice?

Countries should pay special attention to polypharmacy and make efforts to control polypharmacy among PLWD, especially in countries where the trend of polypharmacy among PLWD has been increasing.

People living with dementia (PLWD) often use multiple concurrent medications (a.k.a. polypharmacy) to treat symptoms of their comorbidities. However, polypharmacy was associated with negative health outcomes, such as adverse events, preventable and unplanned hospitalizations, frailty and impaired cognition (*1*–*2*). It was estimated that globally, the number of PLWD would increase from 57.4 million cases in 2019 to 152.8 million cases in 2050 (*3*). This rapid growth poses polypharmacy as a challenge to global health. Investigating variations in polypharmacy trajectories can be useful in designing interventions. Nevertheless, such investigation in PLWD is limited. We leveraged data from the Survey of Health, Ageing and Retirement in Europe (SHARE) collected from Israel and 24 European Union countries in 2015, 2017, and 2019, on 4,474 adults diagnosed with dementia. From 2015 through 2019, the percentages of polypharmacy ranged from 20.5% in Estonia to 84.6% in Cyprus among PLWD. After accounting for differences in sociodemographic characteristics, we found that the percentages of polypharmacy showed significantly increasing trends in Switzerland, Poland, Austria, and the Czech Republic, but significantly decreasing trends in Spain, Estonia, Denmark, Bulgaria, and the Netherlands. Therefore, public health planning efforts should pay attention to controlling polypharmacy among PLWD, especially in countries where the trend of polypharmacy has been rising.

The SHARE is a biennial social science, health, and multi-nationally individual survey of adults aged ≥50. Participants were interviewed by trained personnel. Interview questions included socio-demographic characteristics and health status. Detailed descriptions of the data, sampling methods and quality control procedures have been reported elsewhere (*4*). In this analysis, we used waves 6–8 of SHARE, because of the available information on the medications. The total sample sizes for sampled adults in each wave of SHARE were as follows: Wave 6 (2015, 72,660), Wave 7 (2017, 81,292), and Wave 8 (2019, 46,733), with a retention rate of approximately 80% in each country that was covered.

We only included those who once were diagnosed with dementia, determined by the following question, "Has a doctor ever told you that you had/currently have Alzheimer's disease, dementia, organic brain syndrome, senility, or any other serious memory impairment." SHARE also collected the total number of medications prescribed for their diseases. There is no single agreed definition of polypharmacy (*1*). Respondents were coded as having polypharmacy (=yes) if they took at least five medications (*5*–*6*).

Data were analyzed separately for each country. This made within-country comparisons robust to any cross-country differences. To estimate the temporal trend of the probability of polypharmacy, we fitted the data to country-specific logistic regression models (one model per country). We made polypharmacy (binary variable) the dependent variable and survey year (continuous variable) the critical predictor, controlling for age, sex, education, marital status, and wealth status. Survey weights were applied to account for sampling design (including the unequal probabilities of selection, clustering, and stratification) and generate representative estimates. The weight values were provided by SHARE (*7*). All the analyses were done by R (version 4.1.0, R Development Core Team, Vienna, Austria). The threshold for statistical significance was $P<0.05$.

Overall, 4,474 participants from 25 countries having at one time been diagnosed with dementia were included in the data for 2015, 2017, and 2019 (Table 1). The overall percentage of people having polypharmacy during 2015 and 2019 varied substantially between countries, with the lowest rate being in Estonia [20.5%, 95% confidence interval (CI): 7.9%, 43.9%] and highest rate being in Cyprus (84.6%, 95% CI: 64.9%, 94.3%) (Figure 1). After controlling for age, sex, marital status, education years, and wealth status, the probability of having polypharmacy had no significant trend in 16 of 25 countries, but increasing trends in Switzerland [adjusted odds ratio (AOR) 1.57, 95% CI: 1.01, 2.42], Poland (AOR 1.49, 95% CI: 1.12, 1.98), Austria (AOR 1.3, 95% CI: 1.04, 1.63), and Czech Republic (AOR 1.3, 95% CI: 1.01, 1.69), and decreasing trends in Spain (AOR 0.85, 95% CI: 0.72, 0.99), Estonia (AOR 0.72, 95% CI: 0.53, 0.99), Denmark (AOR 0.58, 95% CI: 0.34, 1.00), Bulgaria (AOR 0.33, 95% CI: 0.13, 0.84), and the Netherlands (AOR 0.15, 95% CI: 0.04, 0.61) (Figure 2B).

DISCUSSION

From 2015–2019, the percentage of PLWD having polypharmacy varied substantially among Israel and 24 European Union countries, with approximately 1 in 5 Estonian PLWD and 4 in 5 Cypriot PLWD having polypharmacy. In addition, this percentage showed significantly higher trends in 4/25 of the countries studied. The findings of this study call attention to the endangering impact of polypharmacy (e.g., frailty, and impaired cognition). They also reinforce the importance of efforts to control polypharmacy among PLWD, especially in countries with increasing trends. The high percentage and the increasing trend of polypharmacy we identified are consistent with previous studies. A cross-sectional study of older adults in Denmark indicated that 62.6% of PLWD had polypharmacy in 2014 (*8*). While, a prospective cohort study of women with dementia in Australia showed that the prevalence of polypharmacy increased from 57.7% in 2003 to 71.2% in 2014 (*5*). The increasing comorbidity and long-term treatments may contribute to the rising prevalence of polypharmacy among PLWD (*6*). Compared to people without dementia, adverse health outcomes of polypharmacy may be worse for PLWD. Typical dementia symptoms such as memory loss and language problems may prevent the early detection of adverse drug events, leading to more severe complications and subsequent hospitalizations (*2*). Therefore, it is essential to deprescribe inappropriate medications among PLWD with polypharmacy. Medication review (e.g., the implementation of a routine medication management review system in Australia) and increasing the awareness of potentially inappropriate medicine use in the older population (e.g., the introduction of the red-yellow-green list, a list of potentially inappropriate medications tailored toward use, in Denmark) could be helpful to slow or even reverse such increasing trends (*5*–*6*).

The percentage and the time trend of polypharmacy varied substantially among studied countries. The disparities in the health system (e.g., whether the health system covers medicines for dementia and other chronic conditions) could influence the number of medications patients take. For instance, the relatively lower percentage of polypharmacy in Estonia is consistent with a study conducted in the UK, which estimated 22.3% of polypharmacy in 2010 (*9*). However, we cannot exclude the possibility of underutilizing corresponding services among the Estonian elderly, as revealed by a previous study (*10*). Future studies are needed to explore the possible reasons for the substantial cross-country variation identified in our report by further considering the differences in the health systems, differences like the availability, accessibility, and affordability of related resources. A study conducted in Denmark also found an inconsistency in the time trend of polypharmacy. It indicated that after the initiative of increasing the awareness of potentially inappropriate medicine use in 2011, no significant time trend of polypharmacy was found between 2011 and 2014, compared to an increasing trend between 2000 and 2010 (*6*). Future studies involving the interventions (e.g., policy evaluations and scoping reviews) on polypharmacy are also needed.

This report possesses the following strengths. First,

TABLE 1. Summary statistics of people living with dementia across Israel and 24 European Union countries.

Country	Study period	N	Age Mean (SD)	Female n (%)	Marital status* n (%)	Education years Mean (SD)	Wealth status, n (%)						Proxy† n (%)
							Lowest 20% quartile	2	3	4	Highest 20% quartile	Don't know	
Austria	2015–2019	302	81.10 (9.20)	175 (57.9%)	138 (45.7%)	8.97 (4.48)	70 (23.2%)	63 (20.9%)	51 (16.9%)	48 (15.9%)	31 (10.3%)	39 (12.9%)	103 (34.1%)
Belgium	2015–2019	265	80.73 (9.96)	158 (59.6%)	164 (61.9%)	10.97 (3.64)	43 (16.2%)	61 (23.0%)	30 (11.3%)	31(11.7%)	15 (5.7%)	85 (32.1%)	143 (54.0%)
Bulgaria	2017–2019	44	78.27 (8.52)	28 (63.6%)	16 (36.4%)	8.73 (3.69)	20 (45.5%)	7 (15.9%)	9 (20.5%)	5 (11.4%)	2 (4.5%)	1 (2.3%)	13 (29.5%)
Croatia	2015–2019	93	75.74 (10.13)	61 (65.6%)	51 (54.8%)	7.49 (4.04)	29 (31.2%)	19 (20.4%)	13 (14.0%)	16 (17.2%)	12 (12.9%)	4 (4.3%)	51 (54.8%)
Cyprus	2017–2019	55	81.13 (8.70)	35 (63.6%)	35 (63.6%)	6.95 (3.66)	21 (38.2%)	15 (27.3%)	8 (14.5%)	4 (7.3%)	6 (10.9%)	1 (1.8%)	12 (21.8%)
Czech Republic	2015–2019	252	78.49 (8.54)	146 (57.9%)	143 (56.7%)	11.61 (3.28)	64 (25.4%)	54 (21.4%)	57 (22.6%)	38 (15.1%)	21 (8.3%)	18 (7.1%)	115 (45.6%)
Denmark	2015–2019	78	80.81 (7.57)	42 (53.8%)	41 (52.6%)	12.33 (3.98)	15 (19.2%)	12 (15.4%)	12 (15.4%)	5 (6.4%)	4 (5.1%)	30 (38.5%)	43 (55.1%)
Estonia	2015–2019	281	78.49 (9.62)	168 (59.8%)	140 (49.8%)	10.10 (3.79)	63 (22.4%)	67 (23.8%)	63 (22.4%)	45 (16.0%)	16 (5.7%)	27 (9.6%)	117 (41.6%)
Finland	2017–2019	57	78.77 (7.08)	32 (56.1%)	43 (75.4%)	8.68 (3.30)	19 (33.3%)	10 (17.5%)	11 (19.3%)	8 (14.0%)	6 (10.5%)	3 (5.3%)	19 (33.3%)
France	2015–2019	172	83.81 (8.23)	110 (64.0%)	83 (48.3%)	9.56 (3.92)	44 (25.6%)	37 (21.5%)	11 (6.4%)	21 (12.2%)	13 (7.6%)	46 (26.7%)	116 (67.4%)
Germany	2015–2019	211	78.50 (9.68)	97 (46.0%)	132 (62.6%)	11.82 (3.65)	55 (26.1%)	52 (24.6%)	33 (15.6%)	32 (15.2%)	18 (8.5%)	21 (10.0%)	104 (49.3%)
Greece	2015–2019	224	81.90 (6.99)	153 (68.3%)	117 (52.2%)	7.08 (4.34)	72 (32.1%)	54 (24.1%)	31 (13.8%)	33 (14.7%)	33 (14.7%)	1 (0.4%)	123 (54.9%)
Hungary	2017–2019	44	75.45 (8.60)	23 (52.3%)	21 (47.7%)	10.39 (3.58)	10 (22.7%)	11 (25.0%)	11 (25.0%)	5 (11.4%)	5 (11.4%)	2 (4.5%)	14 (31.8%)
Israel	2015–2019	256	81.61 (8.58)	160 (62.5%)	120 (46.9%)	10.27 (4.62)	70 (27.3%)	65 (25.4%)	53 (20.7%)	32 (12.5%)	16 (6.2%)	20 (7.8%)	189 (73.8%)
Italy	2015–2019	265	80.32 (8.89)	165 (62.3%)	139 (52.5%)	6.13 (4.12)	81 (30.6%)	52 (19.6%)	63 (23.8%)	28 (10.6%)	20 (7.5%)	21 (7.9%)	175 (66.0%)
Lithuania	2017–2019	81	75.86 (9.60)	54 (66.7%)	40 (49.4%)	8.31 (4.76)	18 (22.2%)	22 (27.2%)	23 (28.4%)	14 (17.3%)	3 (3.7%)	1 (1.2%)	20 (24.7%)
Luxembourg	2015–2019	98	76.67 (10.33)	50 (51.0%)	67 (68.4%)	10.28 (3.87)	22 (22.4%)	18 (18.4%)	17 (17.3%)	8 (8.2%)	12 (12.2%)	21 (21.4%)	42 (42.9%)
The Netherlands	2015–2019	90	76.33 (9.38)	48 (53.3%)	40 (44.4%)	10.26 (4.55)	21 (23.3%)	9 (10.0%)	10 (11.1%)	6 (6.7%)	3 (3.3%)	41 (45.6%)	50 (55.6%)
Poland	2015–2019	199	79.32 (9.76)	118 (59.3%)	101 (50.8%)	7.95 (3.09)	57 (28.6%)	34 (17.1%)	37 (18.6%)	29 (14.6%)	39 (19.6%)	3 (1.5%)	80 (40.2%)
Portugal	2015–2017	102	76.19 (8.67)	70 (68.6%)	74 (72.5%)	5.17 (3.44)	18 (17.6%)	18 (17.6%)	24 (23.5%)	18 (17.6%)	14 (13.7%)	10 (9.8%)	70 (68.6%)
Romania	2017–2019	37	77.38 (8.44)	21 (56.8%)	18 (48.6%)	6.68 (3.49)	10 (27.0%)	8 (21.6%)	8 (21.6%)	7 (18.9%)	4 (10.8%)	NA	14 (37.8%)
Slovenia	2015–2019	357	78.21 (8.89)	208 (58.3%)	219 (61.3%)	8.66 (3.18)	112 (31.4%)	74 (20.7%)	65 (18.2%)	44 (12.3%)	37 (10.4%)	25 (7.0%)	146 (40.9%)
Spain	2015–2019	624	83.23 (8.02)	399 (63.9%)	325 (52.1%)	6.30 (4.57)	155 (24.8%)	156 (25.0%)	84 (13.5%)	94 (15.1%)	56 (9.0%)	79 (12.7%)	435 (69.7%)
Sweden	2015–2019	210	80.45 (8.72)	112 (53.3%)	128 (61.0%)	10.10 (4.08)	48 (22.9%)	49 (23.3%)	35 (16.7%)	20 (9.5%)	9 (4.3%)	49 (23.3%)	91 (43.3%)
Switzerland	2015–2019	77	78.92 (10.00)	43 (55.8%)	45 (58.4%)	8.43 (5.43)	14 (18.2%)	12 (15.6%)	12 (15.6%)	9 (11.7%)	11 (14.3%)	19 (24.7%)	37 (48.1%)

Note: Statistics for categorical variables are reported in numbers (percentage), and those for continuous variables are reported in mean (SD). The quartiles of wealth status were generated based on all samples in each country, including people with or without dementia.

* Marital status means married, cohabiting or civil partnership.

† Proxy means proxy report.

Abbreviation: NA=not applicable; SD=standard deviations.

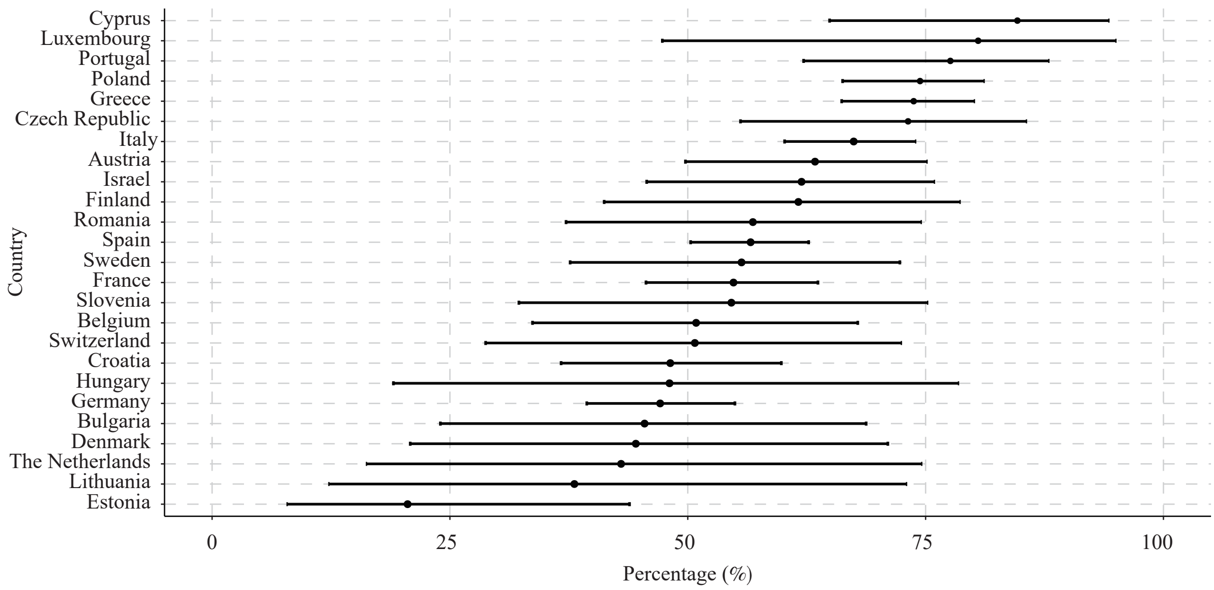

FIGURE 1. Pooled percentage of polypharmacy among people living with dementia across Israel and 24 European Union countries between 2015 and 2019.
Note: Points and horizontal lines show the percentages of polypharmacy and their 95% confidence intervals, respectively. The percentage was estimated by country by year, and then pooled by meta-analysis for each country. Survey weights were used to estimate the percentages and their 95% confidence intervals.

this is the first multi-country study to investigate the polypharmacy trajectory among PLWD, enriching our limited understanding of this global health challenge. Second, the measurement of polypharmacy was consistent among countries, which enhanced the reliability of the variations identified in this report.

However, this report is subject to at least three limitations. First, polypharmacy may not be problematic if medications are reasonably prescribed. The distinction between appropriate and problematic polypharmacy is critical for PLWD who may be taking anti-dementia medications, because other medications may play a necessary role in reducing the progression or suppressing the symptoms of dementia. Future studies are recommended to evaluate problematic polypharmacy due to pharmacological inappropriateness such as drug-drug interactions. Second, SHARE has no information on the types of medications (e.g., anti-dementia or antidepressants), which prevented us from exploring the trends in the composition of polypharmacy. Third, some countries' studies have apparent trends when only looking at point estimations in Figure 2, but no such significant odd ratios due to wide confidence intervals. These could be due to the potentially insufficient observations when studying dementia patients in each SHARE-covered nation. For instance, Luxembourg looks to be increasing but only had 98 participants in total. Although our primary findings on the high percentage and the increasing trend of polypharmacy we identified are consistent with previous studies as discussed above. Country-specific studies with more observations are needed.

In summary, future public health efforts must pay special attention to polypharmacy among PLWD. In countries with a higher prevalence of polypharmacy, healthcare providers should be aware of it when interacting with PLWD. They should also inform patients and their caregivers of the adverse effects of concurrent medications. Among countries with an increasing trend of polypharmacy, interventions and policies that promote medication review and awareness of potentially inappropriate medicine use should be considered.

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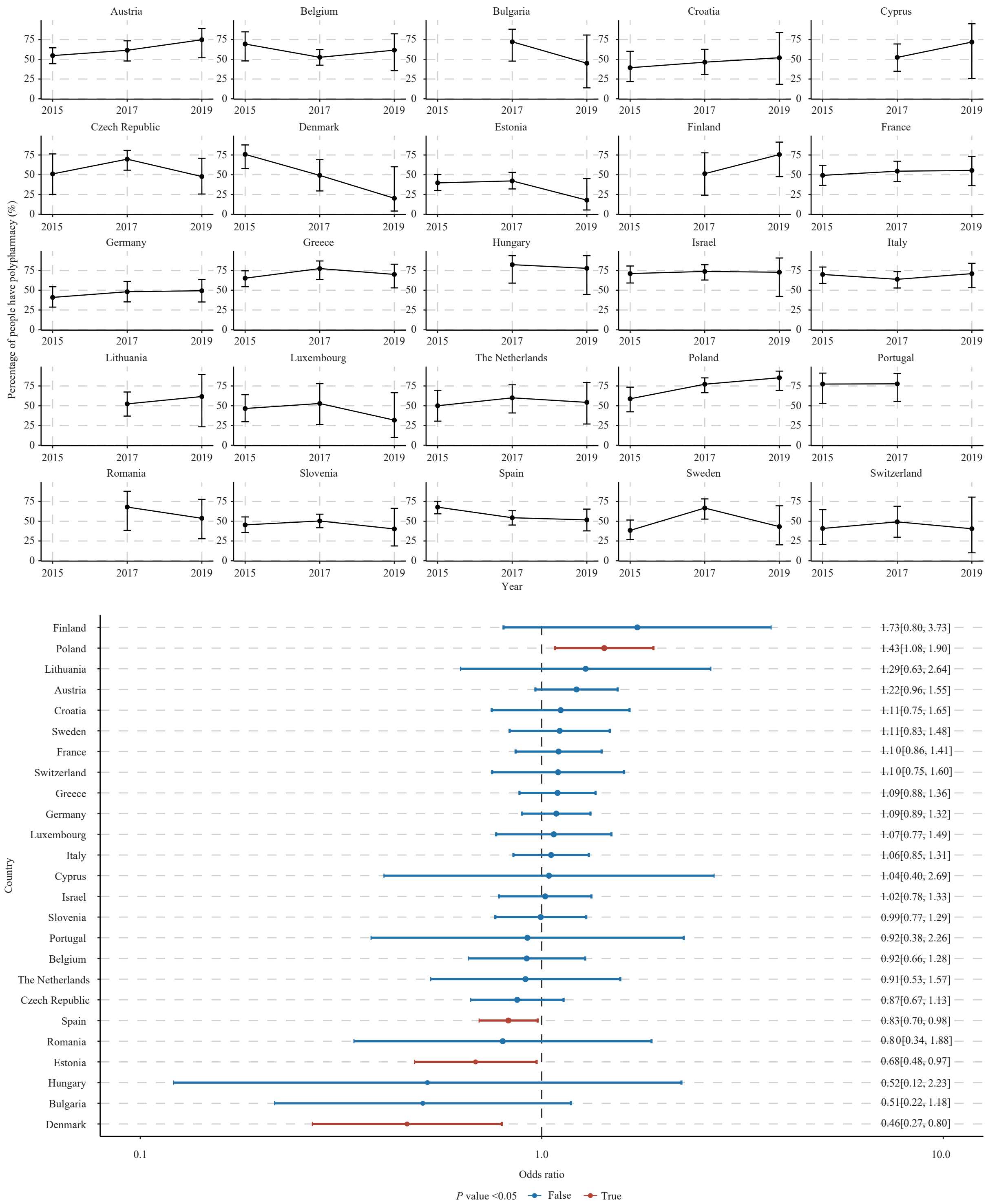

FIGURE 2. Time trend for percentage of polypharmacy among people living with dementia across Israel and 24 European Union countries during the study period. (A) Percentage of polypharmacy by country by year; (B) Adjusted odds ratios and their 95% confidence intervals of year.

Note: Panel A presents the percentages of polypharmacy and their 95% confidence intervals by country by year. Panel B presents the adjusted odds ratios and their confidence intervals, which were extracted from country-specific weighted logistic regression models (one model per country), with polypharmacy (binary variable) being the dependent variable and survey year (continuous variable) being the key predictor, controlling for age, sex, marital status, education, wealth status, and proxy.

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Preplanned Studies

Early-Life Circumstances and Cross-Country Disparities in Cognition Among Older Populations — China, the US, and the EU, 2008–2018

Binjian Yan[1]; Shuaifeng Gao[1]; Minlei Dai[1]; Thomas M. Gill[2]; Xi Chen[3,4,5,#]

Summary

What is already known about this topic?

Many health challenges have emerged due to rapid population aging, including declined cognitive ability among older adults.

What is added by this report?

Childhood circumstances have significant and lasting impacts on cognition in old age. This study compared cognition data from China with both the United States (U.S.) and the European Union (EU) during 2008–2018, finding that childhood circumstances could respectively explain 65.4% [95% confidence interval (CI): 59.4%, 71.4%] (China *vs.* the U.S.) and 38.2% (95% CI: 35.1%, 41.2%) (China *vs.* the EU) of the overall differences in cognition among older adults. Family socioeconomic status explained the largest share of differences among all considered childhood circumstances.

What are the implications for public health practice?

Large disparities in cognition should be addressed by mitigating childhood disadvantages.

With accelerated aging across the globe (*1*), it is critical to improving health in older populations (*2*), including in aspects relating to cognitive ability (*3*). Growing scientific evidence found associations between childhood circumstances and cognition in old age (*4–6*). However, it has yet to be discovered to what extent childhood circumstances may explain cross-country disparities in cognition in older populations, especially between countries in different stages of development. This study applied the Oaxaca-Blinder decomposition to a validated measure of cognition in harmonized global aging surveys to explore the contributions of childhood circumstances to cross-country differences in cognition. Our results demonstrated a large share of cross-country differences in cognition among older adults being explained by childhood circumstances. Specifically, childhood disadvantages contributed 65.4% to the China-US difference in cognition, while childhood disadvantages contributed 38.2% to the China-EU difference in cognition. In both cases, family socioeconomic status explained the largest share of cross-country differences in cognition. The large gap in the cognition of older adults across these countries and their risk factors in childhood stress the urgency of mitigating childhood disadvantages to achieve more equitable, healthy aging.

This study used three Health and Retirement Study (HRS)-family surveys: the China Health and Retirement Longitudinal Study (CHARLS); the U.S. HRS; and the Survey of Health, Aging, and Retirement in Europe (SHARE). In the past three decades, the U.S. National Institutes of Health and HRS-family survey teams in each country have collected and harmonized data for aging populations to offer an opportunity for cross-national comparisons (*7–8*). Our analysis was restricted to individuals aged 60 years and older, with no proxy respondents. We matched CHARLS Life History Survey 2014 (9,846 respondents) with CHARLS core survey 2018 (11,096 respondents); HRS Life History Mail Survey 2015/2017 (8,579 respondents) with HRS core survey 2016 (7,744 respondents); and SHARELIFE 2008/2017 (30,706 respondents) with SHARE core survey 2017 (27,173 respondents). For the three HRS-family surveys, the earliest and latest years in which cognition data were collected for this analysis were 2008 and 2018, respectively. To make the cognitive assessments most comparable across China, the U.S., and the EU, we measured cognitive ability using the validated Mini-Mental State Examination (MMSE). Our cognitive score included the typical dimensions and items across the three HRS-family surveys, ranging from 0 to 29. The larger the value, the better the cognitive ability. Considering salient differences in the distribution of cognitive scores between China and the U.S. and between China and the EU, standardized cognitive scores were measured. *Z*-scores were determined to facilitate cross-country comparisons, using the combined mean and standard deviation of cognition scores in all three HRS-family surveys. We used the Oaxaca-Blinder decomposition to estimate the extent of various childhood circumstances explained in the cognitive ability of older adults across countries (*9*). Originally proposed in 1973, the Oaxaca-Blinder decomposition offered a regression-based approach to attributing cross-country differences in cognition of older adults to differences in childhood circumstances (composition effect) *versus* differences in the effects of these circumstances (association effect) (*10*). A package *iop* in STATA (version16.0, Stata Corp, College Station, U.S.) was used to perform the analyses (*9*).

We measured cognitive ability among older populations in China, the U.S., and the EU, all of which exhibited rapid aging processes, though in different stages of development. While the cognitive scores of older adults in the U.S. and EU are relatively similar in level and distribution, Figure 1 displays the large differences with their Chinese counterparts who tended to have lower cognitive scores. As shown in Table 1, Chinese older adults in the sample also tended to receive lower education (on average 4.5 years, *versus* 12.0 years in the U.S. and 11.2 years in the EU). Education has been recognized as a profound, protective factor of cognitive ability (*11*).

TABLE 1. Summary statistics for older adults — China, the US, and the EU, 2008–2018.

Variables	Country	Obs	Mean	S.D.	Min	Max	Variable description
Cognition	CN	8,819	8.9	6.8	0	28	Continuous: include orientation, episodic memory, and calculating ability; possible values 0–29
	US	6,106	16.5	4.5	1	29	
	EU	18,540	17.5	4.3	0	29	
Standardized cognition score	CN	8,819	−1.0	1.1	−2.4	2.1	Measured in Z-scores, using mean and standard deviation of cognition scores in all three HRS-family surveys combined
	US	6,106	0.2	0.7	−2.2	2.2	
	EU	18,540	0.4	0.7	−2.4	2.2	
Male	CN	8,819	0.5	0.5	/	/	Dummy: males were assigned 1, females were assigned 0
	US	6,106	0.4	0.5	/	/	
	EU	18,540	0.4	0.5	/	/	
Age	CN	8,819	69.3	7.1	60	102	Continuous: selected samples aged ≥60 years
	US	6,106	76.1	7.2	60	100	
	EU	18,540	72.6	7.5	60	100	
Years of education	CN	8,819	4.5	4.0	0	16	Continuous: years of education the respondents received
	US	6,472	12.0	4.5	0	17	
	EU	15,709	11.2	4.2	0	25	
War or famine experiences	CN	8,819	0.2	0.4	/	/	Dummy: experienced World War II, the anti-Japanese war or famine in childhood assigned 1; 0 otherwise
	US	6,106	0.0	0.1	/	/	
	EU	18,540	0.0	0.2	/	/	
Family SES in childhood							
Father: no school	CN	8,819	0.6	0.5	/	/	Dummy: fathers did not attend school were assigned 1; 0 otherwise
	US	6,106	0.0	0.2	/	/	
	EU	18,540	0.0	0.2	/	/	
Father: below primary school	CN	8,819	0.2	0.4	/	/	Dummy: fathers did not finish primary school were assigned 1; 0 otherwise
	US	6,106	0.1	0.2	/	/	
	EU	18,540	0.1	0.2	/	/	
Father: primary school	CN	8,819	0.1	0.3	/	/	Dummy: fathers finished primary school were assigned 1; 0 otherwise
	US	6,106	0.1	0.4	/	/	
	EU	18,540	0.4	0.5	/	/	
Father: secondary school	CN	8,819	0.1	0.2	/	/	Dummy: fathers finished secondary school were assigned 1; 0 otherwise
	US	6,106	0.6	0.5	/	/	
	EU	18,540	0.2	0.4	/	/	

TABLE 1. (Continued)

Variables	Country	Obs	Mean	S.D.	Min	Max	Variable description
Father: university and above	CN	8,819	0.0	0.1	/	/	Dummy: fathers attended university or above were assigned 1; 0 otherwise
	US	6,106	0.2	0.4	/	/	
	EU	18,540	0.3	0.5	/	/	
Mother: no school	CN	8,819	0.9	0.3	/	/	Dummy: mothers did not attend school were assigned 1; 0 otherwise
	US	6,106	0.0	0.2	/	/	
	EU	18,540	0.0	0.1	/	/	
Mother: below primary school	CN	8,819	0.0	0.2	/	/	Dummy: mothers did not finish primary school were assigned 1; 0 otherwise
	US	6,106	0.0	0.3	/	/	
	EU	18,540	0.1	0.3	/	/	
Mother: primary school	CN	8,819	0.0	0.1	/	/	Dummy: mothers finished primary school were assigned 1; 0 otherwise
	US	6,106	0.1	0.3	/	/	
	EU	18,540	0.5	0.5	/	/	
Mother: secondary school	CN	8,819	0.0	0.1	/	/	Dummy: mothers finished secondary school were assigned 1; 0 otherwise
	US	6,106	0.7	0.5	/	/	
	EU	18,540	0.2	0.4	/	/	
Mother: university and above	CN	8,819	0.0	0.03	/	/	Dummy: mothers attended university or above were assigned 1; 0 otherwise
	US	6,106	0.1	0.3	/	/	
	EU	18,540	0.2	0.4	/	/	
Parental health							
Father: alive	CN	8,819	0.1	0.2	/	/	Dummy: fathers still alive assigned 1; 0 otherwise
	US	6,106	0.0	0.1	/	/	
	EU	18,540	0.0	0.1	/	/	
Father: lower lifespan than average	CN	8,819	0.4	0.5	/	/	Dummy: fathers died at below-average lifespan assigned 1; 0 otherwise
	US	6,106	0.4	0.5	/	/	
	EU	18,540	0.5	0.5	/	/	
Father: higher lifespan than average	CN	8,819	0.4	0.5	/	/	Dummy: fathers died at above-average lifespan assigned 1; 0 otherwise
	US	6,106	0.5	0.5	/	/	
	EU	18,540	0.4	0.5	/	/	
Mother: alive	CN	8,819	0.1	0.4	/	/	Dummy: mothers still alive assigned 1; 0 otherwise
	US	6,106	0.1	0.3	/	/	
	EU	18,540	0.1	0.3	/	/	
Mother: lower lifespan than average	CN	8,819	0.4	0.5	/	/	Dummy: mothers died at below-average lifespan assigned 1; 0 otherwise
	US	6,106	0.4	0.5	/	/	
	EU	18,540	0.4	0.5	/	/	
Mother: higher lifespan than average	CN	8,819	0.3	0.5	/	/	Dummy: mothers died at above-average lifespan assigned 1; 0 otherwise
	US	6,106	0.5	0.5	/	/	
	EU	18,540	0.4	0.5	/	/	
Childhood health	CN	8,819	2.7	1.0	1	5	Continuous: possible values 1–5, higher indicate poorer self-rated health in childhood
	US	6,106	1.7	0.9	1	5	
	EU	18,540	2.3	1.1	1	5	
Child abuse	CN	8,819	0.3	0.4	/	/	Dummy: beaten by parents during childhood were assigned 1; 0 otherwise
	US	6,106	0.1	0.2	/	/	
	EU	18,540	0.3	0.4	/	/	

Note: This table presents summary statistics for cognitive assessments, demographic, and childhood circumstance variables. The 10th, 25th, 50th, 75th, 90th percentiles of cognitive score (for CN) are 0, 3, 8, 14, 18, respectively.

Abbreviation: CN=China; US=the United States; EU=the European Union; SD=standard deviation; SES=socioeconomic status; HRS= Health and Retirement Study.

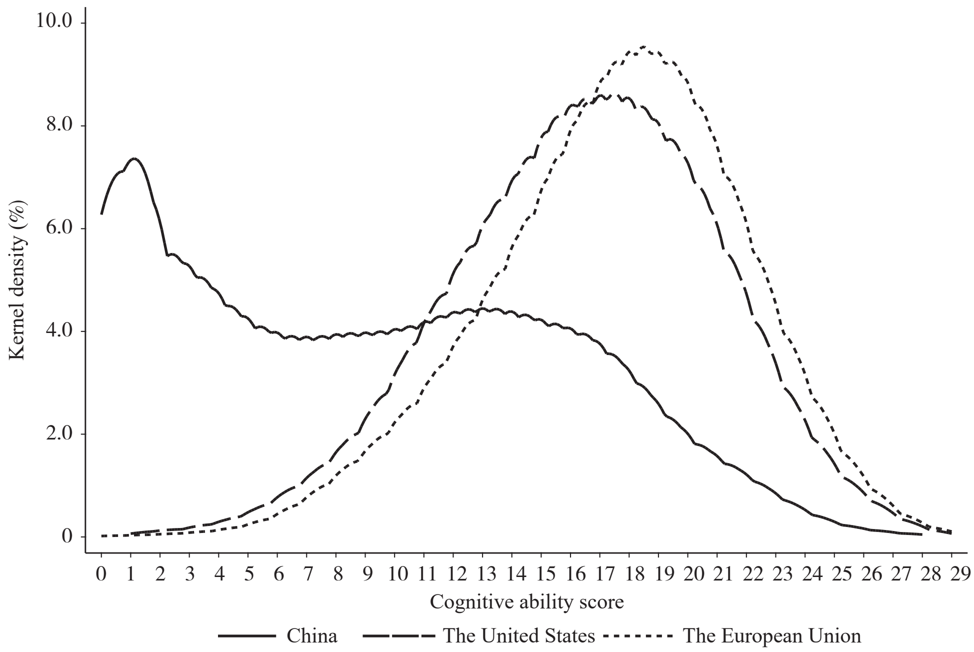

FIGURE 1. Distributions of cognitive score for older adults — China, the United States, and the European Union, 2008–2018.

Notes: The kernel density plots represent the distributions of assessed cognitive ability for older adults in China, the US, and the EU. This figure is plotted using raw cognitive assessment data without accounting for differences in education across the countries. The MMSE score was calculated based on common items in three dimensions in the CHARLS, HRS and SHARE surveys. Specifically, the cognitive ability score ranges from 0 to 29, and the larger the value, the better the cognitive ability. The three dimensions included functions of orientation to time and attention, episodic memory, and computational ability. There were 4 points for orientation function, i.e., correct answers to the year, month, day, and day of the week; 20 points for episodic memory, i.e., 10 points for immediate memory and 10 points for delayed memory; and 5 points for computational ability, i.e., subtracting 7 from 100 for five consecutive times, and the number of correct answers is the computational ability score.

Abbreviation: MMSE=Mini-mental State Examination; CHARLS=China Health and Retirement Longitudinal Study; HRS=Health and Retirement Study; SHARE=the Survey of Health, Aging, and Retirement in Europe.

In addition to the gaps in educational attainment, a key predictor of cognitive disparities for older populations, other economic and social development aspects may also widen the cross-country cognitive disparities. To better understand these economic and social conditions at an individual level, we considered the role of various childhood circumstances of our study subjects before completing their education. Table 1 shows the summary statistics, a significantly higher proportion of Chinese older adults experienced war or famine compared to those in the U.S. and the EU. Five levels of schooling were created across China, the U.S., and the EU to indicate parental educational attainment to harmonize parental educational data for comparison. There were significant cross-country differences in parental education. Specifically, for older Chinese adults above age 60, about 60% of their fathers and 90% of their mothers received no formal education. By contrast, only 3% of fathers and 3% of mothers of older U.S. adults received no formal education. Similar differences existed when comparing other childhood circumstances, including parental and individual health. Chinese and European older adults experienced more abuse in childhood than their U.S. counterparts. Childhood circumstance variables in Table 1 were defined according to the literature (*12*).

Using the three HRS-family surveys and the Oaxaca-Blinder decomposition based on the standardized cognitive scores (Z-scores), Table 2 further illustrates the differences in cognition of the elderly and the contribution of childhood circumstances: 1) Chinese older persons had significantly lower assessed cognition (8.9 out of a total score of 29) than their U.S. and EU counterparts, respectively, at 16.5 and 17.5 (Table 1); 2) comparing China to the U.S. and the EU, overall childhood circumstances respectively explained 65.4% [95% confidence interval (CI): 59.4%, 71.4%] and 38.2% (95% CI: 35.1%, 41.2%) of the China-US and China-EU disparities in cognitive ability; 3) various childhood

TABLE 2. Differences in cognitive score between countries explained by childhood circumstances.

Item	CN and US				CN and EU			
	Overall gap	Explained gap	Explained proportion (%)	95% confidence interval (%)	Overall gap	Explained gap	Explained proportion (%)	95% confidence interval (%)
Difference (standardized score of cognitive score)	1.2	0.80	65.40	(59.4, 71.4)	1.4	0.50	38.20	(35.1, 41.2)
War / famine experiences		0.02	1.30	(0.7, 1.9)		0.02	1.60	(1.3, 2.0)
Parental health		0.04	3.50	(2.6, 4.4)		0.01	0.60	(0.2, 1.0)
Father: alive		−0.00	−0.07	(−0.4, 0.2)		−0.00	−0.20	(−0.4, −0.01)
Father: < average lifespan		−0.00	−0.20	(−0.4, −0.09)		−0.00	−0.20	(−0.3, −0.09)
Mother: alive		−0.01	−1.10	(−1.0, −0.6)		−0.01	−0.70	(−0.9, −0.6)
Mother: < average lifespan		0.00	0.01	(−0.04, 0.06)		−0.00	−0.07	(−0.1, 0.007)
Family SES		0.70	57.60	(51.8, 63.4)		0.50	35.00	(31.9, 38.0)
Father: < primary school		−0.30	−3.80	(−4.4, −3.1)		−0.03	−2.50	(−3.1, −1.9)
Father: primary school		0.10	0.90	(0.6, 1.2)		0.05	3.70	(2.8, 4.5)
Father: secondary school		1.40	18.40	(15.4, 21.5)		0.05	3.70	(3.2, 4.3)
Father: college and above		0.50	5.90	(4.9, 6.9)		0.10	8.20	(7.2, 9.3)
Mother: < primary school		0.02	0.20	(0.02, 0.4)		0.00	0.20	(−0.003, 0.3)
Mother: primary school		0.20	2.40	(1.7, 3.1)		0. 10	9.20	(7.7, 10.7)
Mother: secondary school		2.00	26.80	(21.7, 31.8)		0.09	6.60	(5.8, 7.4)
Mother: college and above		0.50	6.80	(5.6, 8.0)		0.08	5.90	(5.2, 6.5)
Childhood health		0.30	4.40	(3.2, 5.6)		0.01	1.00	(0.8, 1.3)
Child abuse		−0.10	−1.40	(−2.1, −0.7)		−0.00	−0.04	(−0.08, 0.0007)

Notes: The reference group for parental health is "Father (Mother): Higher lifespan than average", and the reference group for family SES in childhood is "Father (Mother): No school".
Abbreviation: CN=China, US=the United States; EU=the European Union; SES=Socioeconomic Status.

circumstances significantly contributed to cross-country differences in the cognitive ability of older adults. Of the childhood circumstances considered, family socioeconomic status, measured by parental educational attainment, contributed the largest — 57.6% (95% CI: 51.8%, 63.4%) to the China-US difference and 34.9% (95% CI: 31.9%, 38.0%) to the China-EU difference in cognitive ability. Of the other factors, individual health, parental health, and war or famine experiences respectively explained 4.4% (95% CI: 3.2%, 5.6%), 3.5% (95% CI: 2.6%, 4.4%), and 1.3% (95% CI: 0.7%, 1.9%) of the China-US difference, while war or famine experiences, individual health, and parental health explained 1.6% (95% CI: 1.3%, 2.0%), 1.0% (95% CI: 0.8%, 1.3%), and 0.6% (95% CI: 0.2%, 1.0%) of the China-EU difference.

DISCUSSION

Using harmonized data from HRS-family surveys conducted in China (CHARLS), the U.S. (HRS), and the European Union (SHARE), this study examined cross-country disparities in the cognitive ability of older adults, with a focus on the influences of childhood circumstances. The three countries were chosen due to their high levels of population aging but different stages of socioeconomic development, which provided a clear basis for comparisons. We found that childhood circumstances explained large shares of differences in the cognitive ability of older persons across countries. Further decomposing these cross-country disparities, we specifically showed that the contributions of childhood circumstances amounted to 65.4% of the China-US and 38.2% of the China-EU differences in cognitive ability in older age, respectively.

Among all domains considered, we identified that family socioeconomic status was the most significant contributor to these differences. Striving for parental educational equity may compensate for cognitive disparities resulting from other childhood disadvantages. Although modest, parental health status during childhood also contributed to disparities in cognitive ability. Relative to mothers' lifespan, fathers' lifespan was much more statistically significant but only slightly larger in terms of the size of cross-country differences. In addition to indicating inherited health endowments from parents, men's health explained slightly more as they often constituted the primary labor force and were expected to bring in substantial resources for their families. Therefore, long-term cognitive ability may be influenced more by the health status of their fathers. Other childhood circumstances, including war or famine experiences and individual health, also had statistically significant but modest contributions.

Overall, our main finding of childhood circumstances contributing substantially to the cross-country disparities in the cognitive ability of older populations highlights the value of taking a life-course perspective to study health inequalities. In the meantime, the economic theory of equality of opportunity calls for public policies to offer more equitable childhood circumstances and compensate for those who had adverse childhood circumstances to improve cognitive health in older age. These policies can potentially narrow the differences between developing and developed countries that promote global health equity.

This study had some limitations. First, while we used a comprehensive and harmonized MMSE for cross-country comparisons, the lack of clinical diagnosis data prevented us from directly assessing the link between childhood circumstances and cognitive impairment using validated clinical criteria. Second, the self-reported childhood circumstances data can be subject to recall error. Third, considering the nature of cross-country comparisons, we included early life circumstance indicators that are more consistent across the three surveys, which indicate a lower bound, and therefore a conservative estimate.

Conflicts of interest: No conflicts of interest.

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