UNIVERSITY OF CALIFORNIA

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Cognitive Aging in Marginalized Populations

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Doctor of Philosophy in Epidemiology

by

Adiba Hassan

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ABSTRACT OF THE DISSERTATION

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Doctor of Philosophy in Epidemiology

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Professor Susan D. Cochran, Co-Chair

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Introduction: Dementia is a progressive condition marked by a decline in cognitive abilities, impairing an individual's daily functioning and leading to dependence. Currently, there are over 55 million dementia cases globally, with over 60% of cases concentrated in low- and middle-income countries (LMICs). The population in LMICs is particularly vulnerable for risk of dementia from exposure to indoor air pollutants due to highly prevalent use of biomass fuel for cooking and heating. Additionally in the United States, nearly half of the 16.5 million living military veterans are men 65 years or older who are vulnerable for dementia due to various hazardous exposures during their time in service. With an aging global population, it is imperative to focus on preventing and delaying the onset of dementia, including among individuals in LMICs and former US service members. This dissertation aimed to further characterize the risk of impaired cognitive function by exposure to indoor air pollutants and veteran status among marginalized populations in India and the US, respectively.

Method: Using data obtained from a nationally representative cross-sectional survey in India, I estimated the effect of exposure to reported use of unclean cooking fuel compared with clean cooking fuel on culturally appropriate measures of cognitive function and prevalence of neurocognitive disorder among older Indian women and evaluated the extent to which type of housing (permanent vs. semi-permanent construction materials) modified this effect. Additionally, I estimated the effect of exposure to reported use of unclean cooking fuel within the household on cognitive function and prevalence of neurocognitive disorder among older Indian adults and identified whether this association differed by sex. I used generalized linear models to estimate mean differences in cognitive factor scores and prevalence of neurocognitive disorder by type of cooking fuel within the sample. I added an interaction term between type of cooking fuel and housing type, and type of cooking fuel and sex, to assess for effect modification by type of housing and sex, respectively.

Using data from two harmonized cohort studies, Kaiser Healthy Aging and Diverse Life Experiences and Study of Healthy Aging in African Americans, I assessed late-life cognitive function and rate of cognitive change among US male veterans compared with non-veterans, and the extent to which veteran status modified the effect of a self-reported lifetime encounter with blasts/explosions on late-life cognitive function and rate of cognitive change. I used linear mixed effects models with age as the timescale to evaluate the extent to which average cognitive function and rate of cognitive change differed by veteran status. To assess for possible effect modification by veteran status on the association between reported lifetime exposure to

blasts/explosions and cognitive measures, I conducted a subgroup analysis by veteran status and a pooled analysis with interaction terms between veteran status, reported lifetime exposure to blasts/explosions and age.

Result: In the population of older Indian women, overall and domain specific cognitive factor scores were worse for women who reported use of unclean cooking fuel compared with women who reported using clean cooking fuel. There was modest evidence that type of housing modified this relationship, namely, women living in homes made with semi-permanent construction materials performed poorer in the specific domains of executive function, language/fluency, and memory (*P-value* for interaction <0.10). The prevalence ratio (PR) of neurocognitive disorder was modestly consistent with a higher prevalence for women who reported use of unclean cooking fuel (PR: 1.16, 95% CI 0.97, 1.40), but the confidence intervals were consistent with values ranging from little or no effect to moderate increase in prevalence. When assessing whether the association between reported household use of unclean cooking fuel on late-life cognitive function differed by sex, mean differences in cognitive factor scores were slightly greater for women in the overall and specific domains of orientation, language/fluency, and visuospatial ability (*P*-value for interaction <0.10). Among men, reported household use of unclean cooking fuel was associated with higher prevalence of neurocognitive disorder (PR: 1.41, 95% CI 1.09, 1.83). However, among women, this association was moderately consistent with higher estimates (PR: 1.18, 95% CI 0.93, 1.50), but the confidence intervals were consistent with values ranging from little or no effect to moderate increase in prevalence.

Among US men, average verbal episodic memory scores at age 75 years were slightly higher among veterans compared to non-veterans (Coefficient: 0.12, 95% CI 0.01, 0.23). There were no differences in average executive function scores at age 75 years (Coefficient: 0.06, 95% CI -0.06, 0.18) or in the annual rate of change in either cognitive domains comparing veterans to non-veterans. The overall association between reported lifetime exposure to blasts/explosions and late-life cognitive trajectory was null for the full sample and did not reveal robust evidence for effect modification by veteran status.

Conclusion: Among older Indian women, upgrading homes made with semi-permanent materials to permanent materials and transitioning to sustainable use of clean fuel may help reduce risk of late-life cognitive impairment. Further exploration of potential confounders is needed including exploring possible effects of outdoor air pollution and other early and mid-life socio-economic factors to rule out alternative explanations for the association observed among men and to accurately determine differences in effect by sex. In the US, rate of cognitive change by veteran status should remain an important measure to monitor in a rapidly aging veteran population, with further work needed towards correctly assessing potential resilience mechanisms and heterogeneity within the veteran population.

The dissertation of Adiba Hassan is approved.

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This dissertation is dedicated to the children in the slums of Dhaka, Bangladesh who bravely battle for daily survival, and to Parveen, a 15-year-old who asked me during my time working there how I was going to help. I don't yet fully know, but I am hoping this is a step closer.

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General Introduction

Background

Dementia is a progressive syndrome, characterized by decline in cognitive skills that disrupt an individual's ability to perform daily activities and ultimately leading to disability and dependency.[1] Dementia is a major global public health challenge, with substantial physical, psychological, social, and economic costs to societies and individuals.[1] Globally, the number of people 60 years and older are projected to outnumber the number of children under ten years by 2030.[2] This trend reflects global achievements in reduction in mortality, birth rates and an increase in global life expectancy up to 72.6 years as of 2019.[3] But this longevity comes with new economic burdens. The population in low-and-middle income countries (LMIC) will age faster than the institutional capacity to manage the growing number of older people and their need for health and social care services.[4] In 2019, dementia cost the global economy 1.3 trillion US dollars,[1] and that is expected to rise to 2 trillion US dollars by 2030.[4] The World Health Organization (WHO) and the World Bank estimates that by 2030, 40 million new health and social care jobs and 18 million more health workers will be needed, primarily in LMIC, to treat and care for people living with dementia.[5] Currently, over 55 million people are living with dementia globally, and 71% of all new cases are expected to occur in LMIC by 2050.[4]

This dissertation focuses on investigating risk factors for dementia in two understudied populations: older adults living in India, a lower-middle-income country in South Asia, and military veterans in the United States (US). Concerning older Indians, this dissertation examines reports of their exposure to indoor air pollution which is a major public health concern in LMIC because of the prevalent use of biomass fuel for cooking and heating.[6,7] In rural communities, women and older adults are exposed to higher levels of indoor air pollution from combustion of biomass fuel due to prolonged time spent at home or in enclosed kitchen spaces,[6,8] impacting their health and potentially cognitive function.[9-12] Concerning US Military veterans, this dissertation examines the rate of cognitive change for veterans compared with non-veterans, and the possible modifying role of veteran status on the association between reported lifetime exposure to blasts/explosions and late-life cognitive trajectory. Of the 16.5 million veterans living in 2021, almost 50% (8.1 million) were men aged 65 years or older.[13] These service members share many risk factors for dementia including traumatic brain injuries (TBI),[14-17] post-traumatic stress disorder (PTSD),[18,19] and exposure to environmental hazards[20] which can compound risk and accelerate neurodegenerative processes.

Summary of gaps in the literature

Most research on dementia and cognitive aging has been conducted in high-income countries (HIC), and within these HIC studies, respondents with relatively high levels of education tend to be overrepresented. In LMIC, family structure, education and economic opportunities vary drastically from HIC,[21,22] leaving a wide gap in understanding potential risk mechanisms and protective factors for older populations in LMIC.[23] It is estimated that 41% of dementia cases in India are attributable to modifiable risk factors, including air pollution.[22] The Indian National Family Health Survey 2019-2021 reported almost 56% of rural homes used unclean cooking fuel[24] despite recent policies such as the Pradhan Mantri Ujjwala Yojana that aimed to promote use of clean fuel in India.[25,26] Indoor air pollution from combustion of solid fuels continues to be a major contributor of many chronic conditions in LMIC,[7] but only recently have studies started to investigate how this exposure relates to cognitive function.[9-12] To broaden the focus of this dissertation, I also investigate another high risk group in the US: military veterans, of whom the majority are Vietnam War veterans between 77–79 years old[13] and rapidly aging.[27] Little is known of their risk of cognitive impairment and whether it is similar or different compared with non-veterans.

Aims and Hypothesis

This dissertation further characterizes the risk of impaired cognitive function among marginalized populations in India and the US with the following aims:

Aim 1: To estimate the effect of exposure to reported use of unclean cooking fuel (kerosene, charcoal, coal, dung cake, etc.) compared with clean cooking fuel (electric, biogas, liquified petroleum gas) on cognitive function and neurocognitive disorder among older Indian women and to evaluate the extent to which type of housing may modify this effect.

> *Hypothesis 1:* Reported use of unclean cooking fuel will be associated with lower cognitive function and higher prevalence of neurocognitive disorder among older women as compared to women reporting use of clean cooking fuel.
>
> *Hypothesis 2:* The association between reported use of unclean cooking fuel and cognitive function will be stronger for women living in homes made with semi-permanent material (kutcha) than permanent (pucca) homes.

Method: Cross-sectional data were obtained from women aged ≥60 years who participated in the baseline wave of the Harmonized Diagnostic Assessment of Dementia for the Longitudinal Aging Study in India (LASI-DAD), a nationally representative study of older adults in India launched in 2017. In the current study, generalized linear models estimated the effect of unclean cooking fuel on (a) culturally appropriate continuous measures of cognitive function and (b) prevalence of neurocognitive disorder. An interaction term between reported use of unclean cooking fuel and living in a kutcha home assessed the extent to which type of housing modified the effect of type of cooking fuel on cognitive measures.

Aim 2: To estimate the effect of reported exposure to use of unclean cooking fuel within the household on cognitive function and prevalence of neurocognitive disorder among older Indian adults and identify if this association differs by sex.

Hypothesis 1: Reported use of unclean cooking fuel within the household will be associated with lower cognitive function and higher prevalence of neurocognitive disorder among older Indian adults compared with those living in households that reported use of clean cooking fuel.

Hypothesis 2: The association between reported use of unclean cooking fuel within household and cognitive function will be stronger for women than men.

Method: Cross-sectional data were obtained from women and men aged ≥60 years who participated in the baseline wave of the LASI-DAD, a nationally representative study of older adults in India launched in 2017. Generalized linear models estimated the effect of reported use of unclean cooking fuel within households on (a) culturally appropriate continuous measures of cognitive function and (b) prevalence of neurocognitive disorder. An interaction term between reported use of unclean cooking fuel within household and sex assessed the extent to which the effect of reported use of cooking fuel within the household and cognitive measures differed by sex.

Aim 3: To assess whether male US veterans who served during the Korean and Vietnam war eras evidence a faster rate of late-life cognitive change compared with male non-veterans, and to examine the extent to which veteran status may modify the effect of reported lifetime encounter with blasts/explosions on late-life rate of cognitive change.

Hypothesis 1: Late-life baseline cognitive function will be higher, and rate of cognitive change will be faster among veterans compared with non-veterans.

Hypothesis 2: The estimated effects of a reported lifetime encounter with blasts/explosions on late-life rate of cognitive change will be greater for veterans than non-veterans representing the likely greater intensity of exposure to this feature.

Method: Data were obtained from men participating in two harmonized cohort studies of older Kaiser Permanente Northern California members: the Kaiser Healthy Aging and Diverse Life Experiences (KHANDLE) (up to 4 cognitive assessments, 2017-2023) and the Study of Healthy Aging in African Americans (STAR) (up to 3 cognitive assessments, 2017-2021). Linear mixed effects models with age as the timescale estimated cognitive function at 75 years of age and the rate of cognitive change among veterans compared with non-veterans. Subgroup analysis by veteran status and a pooled analysis with three-way interaction term between veteran status, age, and reported lifetime exposure to blasts/explosions and two-way interaction term between veteran status and reported lifetime exposure to blasts/explosions assessed the extent to which veteran status modified the effect of reported lifetime exposure to blasts/explosions on late-life rate of cognitive change.

Aim 1: Effect of reported use of unclean cooking fuel on cognitive measures among older women in India: a cross-sectional analysis from LASI-DAD

Abstract

Introduction: Women in resource-limited settings are disproportionately at risk for dementia due to low levels of early-life human capital investments in girls. In this aim, I explore the possible contributions of reported exposure to use of unclean cooking fuel (kerosene, charcoal, lignite, coal, dung cake) compared with clean cooking fuel (biogas or liquified petroleum gas) on cognitive measures among older Indian women. I use culturally appropriate and harmonized measures of cognitive function as well as reports of type of home construction to assess the latter's possible modifying effect.

Methods: I used data obtained from 2,144 women aged ≥60 years surveyed in the nationally representative Harmonized Diagnostic Assessment of Dementia for the Longitudinal Aging Study in India (LASI-DAD). Generalized linear models estimated the effect of reported use of unclean cooking fuel on overall and domain-specific cognitive factor scores, and the prevalence of neurocognitive disorder per DSM-5 definition, adjusted for potential early and mid-to-late-life confounders. As type of home effects ventilation and kitchen location, an interaction term between reported use of unclean cooking fuel and type of home assessed for possible effect measure modification.

Results: Overall and domain specific cognitive factor scores were worse for women who reported use of unclean cooking fuel compared to women who reported use of clean cooking fuel. Type of home slightly modified this relationship; mean differences in executive function, language/fluency, and memory factor scores by reported type of cooking fuel were greater for women living in kutcha vs. pucca homes (*P* for interaction <0.10). The prevalence ratio (PR) of neurocognitive disorder was modestly higher for women who reported use of unclean cooking fuel (PR: 1.16, 95% CI 0.97, 1.40), but the confidence intervals were consistent with values ranging from little or no effect to moderate increase in prevalence. After restricting the analyses to only women who indicated involvement in household cooking and cooked indoors in a sensitivity analysis, among women living in kutcha homes, those who reported use of unclean cooking fuel had twice the prevalence (PR: 2.09, 95% CI 1.33, 3.29) of neurocognitive disorder compared with those who reported use of clean cooking fuel. While among women living in pucca homes, there was no difference in the prevalence of neurocognitive disorder comparing women who reported use of unclean cooking fuel with women who reported use of clean cooking fuel (PR: 1.10, 95% CI 0.73, 1.67).

Conclusion: Transitioning to sustainable use of clean cooking fuel may help reduce risk of cognitive impairment among older Indian women. It is possible that upgrading kutcha homes might also prove beneficial, however additional studies are needed to clarify its contributory effects.

Introduction

Global indoor air pollution from biomass fuel

In 2020, an estimated 3.2 million deaths globally were attributed to indoor air pollution, almost as many deaths as attributed to outdoor air pollution.[28] Indoor air pollution is responsible for 4% of the global burden of disease worldwide[29] including respiratory illnesses,[30] cancer,[31] cardiovascular diseases, low birth weight,[32] cataracts and blindness[33] and more recently, cognitive decline.[10-12,34] While indoor air pollution is a global problem, strategies to mitigate indoor air quality requires local understanding of construction materials, climate, energy sources, human behavior, and cultural practices, which vary within and across countries. Indoor air pollution disproportionately affects people from poor and marginalized communities, who tend to have higher prevalence of chronic conditions and higher exposure to outdoor air pollution.[35] In rural and lower socioeconomic status neighborhoods of low and middle income countries (LMIC), wood, charcoal, dried twigs, crop residues, and animal dung cakes, collectively called biomass fuels, are commonly used for cooking and heating and serve as an additional threat to indoor air pollution. An estimated 3.8 billion people worldwide, mostly from LMICs, use biomass fuels as their primary energy source for cooking because these are inexpensive and readily available.[36] Biomass fuel is considered unclean because of the incomplete combustion that emits carbon monoxide (CO), nitrogen dioxide, sulfur dioxide, formaldehyde, polycyclic aromatic hydrocarbons, volatile organic compounds, chlorinated dioxins, free radicals and large amounts of particulate matter < 10 microns in aerodynamic diameter (PM_{10}) with potential inflammatory and carcinogenic properties.[8,34,37] Particulate matter and carbon monoxide are the most measured pollutants from cookstoves.[38] The World Health Organization (WHO) recommendations for 24-h indoor mean $PM_{2.5}$ and PM_{10} concentrations are <25μg/m^3 and <50μg/m^3, respectively.[39] However, there is growing evidence that there may not be a safe level of exposure to $PM_{2.5}$ and many LMICs peak indoor concentration of PM_{10} is often over 2000μg/m^3.[40,41] The 2023 International Energy Agency (IEA) report estimates there are currently 760 million people living without access to electricity and 2.3 billion without access to clean cooking fuel.[42] Exposure to indoor air pollution from biomass cookstoves was responsible for 2.3 million deaths in 2019.[36]

Indoor air pollution from biomass fuel in India

In Indian culture, women spend more time dedicated to household chores and meal preparation compared to men, who are primarily responsible for household earnings. On average, girls begin helping with kitchen duties at 15 years of age, and spend four to six hours daily in a kitchen.[43,44] Girls and women are more at risk of exposure to indoor air pollution from biomass cooking fuel due to this extended time dedicated to cooking in enclosed kitchen spaces.[6,8] Over a lifetime, women aged 15-40 years have the highest exposure to pollutants from biomass fuel as they are most likely to be involved in cooking.[43] Older adults are also at risk of exposure to indoor air pollution due to prolonged time spent at home.[45] The Indian National Family Health Survey 2019-2021 reports almost 56% of rural households used unclean cooking fuel, with 49% cooking inside their homes in a separate room, 27% cooking inside their homes without a separate kitchen, 14% cooking in a separate building, and 10% cooking outdoors.[24] The location of the kitchen, fuel sources, type of ventilation, and concentration of pollutants, which can vary by type of housing, play a critical role in health. Permanent homes built with solid long-lasting materials such as brick or concrete are termed “pucca” homes while semi-permanent homes built with natural resources like mud or wood are termed “kutcha” homes. Kutcha homes are typically single units where cooking is done in shared living spaces. Lack of ventilation, overcrowding, and use of firewood and kerosene as the main cooking fuel are common in kutcha homes.[24] Kutcha homes tend to have lower average floor space compared with pucca homes and are often built in areas without access to electricity.[46] As floor space is negatively correlated with indoor $PM_{2.5}$ levels, kutcha homes are also more prone to high $PM_{2.5}$ levels compared with pucca homes.[46]

Global risk of dementia

Dementia is a syndrome caused by various etiologies that affect the brain, destroying nerve cells and leading to deterioration of cognitive function - the ability to process thoughts and perform daily activities. Dementia is the seventh leading cause of death globally and one of the major causes of disability and dependency among older people.[1] While age is the strongest risk factor for dementia, not all people will develop dementia as they age.[1] Current putative risk factors for dementia include high blood pressure,[47] high blood sugar,[48] being overweight or obese,[49] smoking,[50] excessive alcohol consumption,[51] physical inactivity,[52] low education attainment,[53] social isolation,[54] and depression.[1,22]

Risk of dementia in India

Per the 2011 Indian Census, 8.6% (103 million) of the Indian population was 60 years and older.[55] By 2050, this is projected to increase to 20% (319 million) per the UN World Population Prospect estimates,[56] reflecting the almost doubling of life expectancy in India from 37 years in

1950 to 69 years in 2020,[57] and up to 75 years in 2050.[58] Development of basic health infrastructure, economic growth, and increase in literacy rates have contributed to increasing life expectancy in India.[55] This increase in life expectancy also increases the number of individuals at risk of developing dementia. As of 2022, an estimated 8.8 million adults 60 years and older in India were living with dementia.[59] The aging index, calculated as the ratio of number of people aged 65 years and older to 100 children under 15 years, is expected to increase from 8.4 in 1950 to 74.5 by 2050,[58] signifying rapid aging and concomitantly high burden of dementia in India. The pace of aging varies regionally in India, with a greater proportion of older adults (age 65 years and above) in the developed southern states and a greater proportion of children (age 0-14 years) population in the less developed northern states than the national average.[56] As the aging population in the world's most populous country of 1.42 billion[60] people continues to grow, the need for prevention and risk reduction strategies is key to managing the expected strain on India's healthcare system.

Current studies on indoor air pollution and cognitive measures in India

Recent studies in India have suggested that indoor air pollution may be negatively associated with cognitive performance.[9,11,12,34,61] A community-based study in rural south India of middle-aged to older adults who reported exposure to indoor air pollution, defined as use of biomass or kerosene fuel for cooking compared with liquefied petroleum gas (LFG), observed double the risk of cognitive impairment among those exposed.[61] A second study from a nationally representative survey in India reported that men and women living in households reporting use of solid and unclean fuel had lower mean composite cognitive scores.[34] In another nationally representative study in India, 19% of rural women reported living in households exposed to indoor air pollution, and these women performed lower on cognitive functional abilities compared with women unexposed to indoor air pollution.[12] In both of these nationally representative studies, use of unclean fuel or exposure to indoor air pollution was defined as households reporting use of unclean such as crop residue, wood, dung cake, kerosene, etc., for domestic activities (cooking, boiling water for bathing, lighting, etc.) inside the house, or cooking in traditional stoves, or in open space without ventilation.[12] In the WHO Study of Global AGEing and adult health (SAGE), Indian participants aged 50 years and older who reported use of solid fuel were also more likely to perform lower on cognitive scores.[11] The magnitude of this association was greater for older women, individuals belonging to lower caste, and those living in rural areas, but interestingly, living in a home with ventilation and living in a home with a separate kitchen were not associated with cognitive function.[11] Cross country comparison of unclean energy sources and cognitive assessments from China, Mexico and India also showed lower cognitive performance among middle-aged and older adults exposed to unclean energy sources.[10] Women continue to be at increased risk of dementia due to sex disparities in early-life socioeconomic conditions that give girls low priority and support for advancement in educational and occupational achievements,[62] while also experiencing greater exposure to household air pollution due to longer time spent at home and/or cooking, in closed, crowded spaces with poor ventilation.[63]

Gaps and impact

While the above recent studies have shown older Indian adults reporting use of unclean cooking fuel have lower average cognitive test scores,[10,11,34,64] measures of cognitive performance vary, only one has looked into the association with type of housing,[65] but none have investigated the possible modifying role of type of housing. The current study aim adds to the existing knowledge of indoor air pollution and cognitive performance among older Indians by: 1) Focusing specifically on women as they have differential risk in exposure to both indoor air pollution and cognitive impairment; 2) Including culturally appropriate measures of overall and domain specific cognitive function and assessment of mild or major neurocognitive disorder; and, 3) Identifying possible modification by type of housing. Overall findings from this aim will have implications for guiding strategies to minimize exposure to indoor air pollution from unclean cooking fuel by upgrading to clean fuel and/or homes with permanent construction materials.

Objective and hypothesis

In this aim, I estimate the effect of reporting use of unclean cooking fuel compared with reporting use of only clean cooking fuel on cognitive measures (overall and domain specific cognitive function and prevalence of mild/major neurocognitive disorder) among older Indian women. Additionally, I evaluate the extent to which type of housing may modify the effect of reporting use of unclean cooking fuel on cognitive measures. Housing type collectively represents home construction characteristics, amenities, and financial opportunities of individuals living in these homes. Type of housing can also influence home ventilation as the concentration of air pollutants resulting from indoor sources can reach higher concentrations in homes without ventilation.[46] I hypothesize that reporting use of unclean cooking fuel will be negatively associated with late-life cognitive measures, and the estimated effects will be stronger for women living in semi-permanent (kutcha) compared with permanent (pucca) homes as kutcha homes tend to be smaller, lack ventilation and are less likely to have a separate kitchen space.

Methods

Data and population

This aim included women assessed in the Harmonized Diagnostic Assessment of Dementia for the Longitudinal Aging Study in India (LASI-DAD) who were subsampled from the larger LASI survey. The larger LASI survey is a multipurpose population-based study that interviewed 72,250 individuals aged 45 years and older drawn from 44,949 Indian households. Topics assessed included information on health, economic and social well-being. Data for wave 1 was collected from October 2017 to March 2020 by home interviewers in rural and urban areas across 18 states and union territories. The LASI sample is fully representative of adults aged 45 years and older in India, and in each state and union territory, with an overall individual response rate of 87%. The main goal of LASI was to collect longitudinal data on disease burden, functional health, healthcare utilization, and social and economic wellbeing of older adults that is comparable to international standards. All measures in LASI were specific and sensitive to the Indian population and harmonized to the U.S. Health and Retirement Survey (HRS) and international sister studies on aging and retirement. Detailed information on the LASI study protocol, sampling design, data collection and methodologies has been previously published.[66]

LASI-DAD included a subsample of 4,096 participants, aged 60 years and older, drawn from the larger LASI study by two-stage stratified sampling with oversampling of participants with high risk of cognitive impairment to ensure sufficient number of participants with dementia and mild cognitive impairment.[66] LASI-DAD participants were interviewed at home or in participating hospitals according to preference and had an overall response rate of 83%. LASI-DAD included additional data on late-life cognition and dementia collected using a battery of cognitive tests and informant interviews, health examination, venous blood assays, and genotyping. The LASI-DAD cognitive tests allowed for international comparisons and were suitable for illiterate and innumerate populations. The details of the LASI-DAD selected cognitive tests have been described elsewhere.[67] The main goals of LASI-DAD were to: 1) Collect, analyze and disseminate high-quality data on late-life cognition, dementia, and their risk factors, with the objective of analyzing prevalence and determinants of dementia in India, and 2) Enable cross-country analysis of late-life cognition and dementia with the Harmonized Cognitive Assessment Protocol (HCAP) of the HRS and other sister studies.[68] The present aim used cross-sectional data from baseline LASI-DAD interviews which took place from 2017 to 2020. Of 2,207 women included in the LASI-DAD, 8 were excluded as they reported not cooking at home, leaving 2,199 women eligible for inclusion including 2,144 women with complete data.

Exposure

The primary exposure of interest was self-reported type of cooking fuel used at time of survey which is used as a proxy for lifetime exposure to pollutants from use of unclean cooking fuel. Reported use of unclean cooking fuel was categorized as “yes” if the self-reported main source of cooking fuel was kerosene, charcoal, lignite, coal, crop residue, wood or shrub, dung cake.

Reported use of unclean cooking fuel was categorized as “no” if the self-reported main source of cooking fuel was liquefied petroleum gas (LPG), biogas, or electric.

Outcomes

Cognitive function was assessed via in-depth cognitive and neuropsychological test batteries administered during an hour-long face-to-face interview. The cognitive test battery was adapted from the tests in HCAP[69] and modified for cultural appropriateness and validity with innumerate and low-literacy populations.[70] For example, backward counts and number series were dropped in LASI-DAD as they were difficult to administer to a largely innumerate population. Instead, additional tests designed for illiterate and innumerate populations such as the Hindi Mental State Exam, symbol cancellation and Go-No-Go test were included.[66] The tests were grouped into broad domains of well-accepted categories of cognitive functioning[71] based on a priori knowledge and Cattell-Horn-Carroll (CHC) theory of human cognitive abilities.[72]

Overall cognitive function was estimated with a LASI-DAD calculated summary factor score for general cognitive performance using a previously-developed hierarchical multiple domain factor analysis including factor scores from both narrow and broad domains.[70] Additionally, domain-specific cognitive function was separately assessed in five broad domains including: 1) orientation, 2) executive function, 3) language/fluency, 4) memory, and 5) visuospatial skills based on a factor analysis determined latent structure of the LASI-DAD cognitive battery.[70] The orientation domain factor score employed five questions on orientation to time (name the current month, year, season), orientation to place (state, city), and one question on orientation to current events (naming the Prime Minister). The executive function domain factor score drew from tests on numeracy task, backwards day counting, symbol cancellation, Digit Span Forward and Backward, Ravens progressive matrices task, clock drawing, and two trials of the Go-No-Go test. The language/fluency domain factor score was calculated from test performance tasks including animal naming, writing or saying a sentence, phrase repetition, naming of common objects by sight (watch, pencil), naming of common objects by description (elbow, hammer, scissors, coconut, window), following a verbal or acted command to close one's eyes, and completing a 3-stage task. The memory domain factor score was based on immediate, delayed, and recognition recall of a 10-word list; immediate, delayed, and recognition recall of the Logical Memory test, immediate and delayed recall of the Brave Man story learning test, and a three-word recall task. Lastly, the visuospatial domain factor score was based on constructional praxis tests (drawing a circle, rectangle, cube, and diamond) and interlocking pentagons.

A binary measure of mild or major neurocognitive disorder was scored using DSM-5 criteria including objective cognitive function, informant-rated cognitive decline, informant-rated functional decline, and exclusion of schizophrenia, active delirium or major depression.[73] Objective cognitive function was estimated using summary factor scores representing specific domains of memory, language, executive function and visuospatial ability evaluating an individual’s ability to remember, think, or attend to stimuli.[70] Cutoffs of 1 or 1.5 standard deviations (SD) below the mean on each cognitive domain score was identified using a normative sample without functional limitations or other exclusionary criteria.[73] Informant-rated cognitive decline was ascertained using the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE), a screening instrument used to assess change in cognitive and functional ability compared with 10 years ago, validated for LASI-DAD.[74] Informant-rated functional decline in everyday activities was ascertained using the Blessed Dementia Rating Scale Parts 1 (instrumental activities of daily living) and II (activities of daily living).[75] Mild neurocognitive disorder was defined as: 1) A functional score of ≤1 SD in one or more domain, 2) No activities of daily living impairment, and no or minimal loss in Blessed Part I, or discordant informant reports for Blessed Part I vs. Part II, 3) IQCODE score of ≥3.2 or poor self-rated memory, and 4) Absence of meeting criteria for schizophrenia, active delirium during testing, or a positive history of major depression. Major neurocognitive disorder was defined as: 1) Functional score of a) ≤1.5 SD in at least two domains, or b) ≤1.5 SD in one domain, and ≤1 SD in two or more domains, 2) Any activities of daily living impairment, Blessed Part I score of ≥2, or Blessed Part 2 score of ≥1, 3) IQCODE score of ≥3.5 and poor self-rated memory, and 4) Absence of schizophrenia, active delirium during testing or history of major depression. Due to the small number of women with major neurocognitive disorder, the mild and major neurocognitive disorder categories were collapsed into a single category referred to as neurocognitive disorder.

Effect modifier

Type of housing was defined as “kutcha” if the interviewer reported the woman living in a home constructed with a combination of temporary and permanent materials or only temporary materials such as grass, thatch, palm leaf, bamboo, plastic, polythene sheeting, mud, dung, palm, un-burnt brick, wood, or handmade tiles. Type of housing was defined as “pucca” if the interviewer reported the woman living in a home where the roof, walls, and floors were made of permanent materials (cement, concrete, oven-burnt bricks, hollow cement or ash bricks, stone, stone blocks, jackboards, iron, zinc or other metal sheets, timber, tiles, slate, corrugated iron, asbestos cement sheet, veneer, plywood, artificial wood of synthetic material, and polyvinyl chloride material). This variable was conceived as a proxy measure of other important home features that contribute to the concentration of indoor air pollution including ventilation, home size and separation between kitchen and other parts of the home.[24]

Covariates

Covariates included early-life sociodemographic variables (caste, paternal education level as proxy for childhood socio-economic status, education in years), and mid-to-late life sociodemographic variables (age, urbanicity, annual household income in Rupees and housing type). These were collected at baseline and used to control for potential confounding, selected a priori and based on the causal diagram (Figure 1.1). Everyday life in India has been significantly shaped by social institutions like the caste system. Within the Indian caste system, scheduled castes/tribes and other backward class are considered lower-ranked social groups with health and social outcomes reflective of social disadvantage.[76] For the purpose of this aim, caste was recoded into scheduled castes/scheduled tribes, other backward class, or not one of these castes. Childhood socioeconomic status was assigned using paternal educational attainment (never attended school, primary school [grade 7] or less, middle school [grade 8] or higher, missing) as a proxy. Highest educational attainment of the respondent in years was included as it can influence roles within households, lead to or reflect residency in underdeveloped areas, and limit economic opportunities,[11,64] collectively prolonging exposure to unclean fuel. Residence at time of interview (urban community vs. rural village), annual household income in Rupees, and housing type (kutcha vs. pucca) were also included as other measures of socioeconomic status that can influence both type of cooking fuel used and cognitive measures. Age (years) was included as it is a well-known risk factor for cognitive impairment.[1] Since 99% of women were married and 80% were not working at time of survey, marital status (married vs. never married) and current employment status (employed, unemployed, and never worked) were excluded from analytical models. Other sources of air pollutants, including use of mosquito coils/incense sticks/smoker (yes vs. no), current job around burning material, exhaust or smoke (yes vs. no), and current job close to chemicals, pesticides or herbicides (yes vs. no) were also excluded from analytical models as they do not influence type of cooking fuel or fall in the causal pathway. Religion (Hindu, Muslim, Christian, Sikh, and Buddhist/Jain/None), number of people in household, main lifetime occupation (senior professionals, service/shop/craft workers, agriculture/forestry/fishery, plant/machine operators, elementary occupations, other, and never worked), and difficulty hearing or seeing (yes vs. no) were included to describe the sample.

Statistical analysis

Characteristics of the sample population were first summarized for the full sample of women and by combined use of unclean cooking fuel and type of housing. Generalized linear models with an identity link function were then used to estimate mean differences in overall and domain-specific factor scores of cognitive performances (continuous outcomes) between women who reported use of unclean cooking fuel compared with those who reported using clean cooking fuel. Generalized linear models with a log link function and Poisson distribution[77] estimated the prevalence ratio of neurocognitive disorder (binary outcome) between women who reported use of unclean cooking fuel compared with those reporting using clean cooking fuel. Covariates mentioned earlier were included to control for potential confounding of the association between reported use of unclean cooking fuel and late-life cognitive measures. The primary model was adjusted for early-life potential confounders (caste, paternal education as proxy for childhood socioeconomic status, highest education attainment in years) with subsequent models additionally adjusted for mid-to-late-life potential confounders (urbanicity, age at interview, annual household income and housing type) (Figure 1.1). An interaction term between reported use of unclean cooking fuel and living in a kutcha home was included to assess the extent to which type of housing may modify the effect of reported use of unclean cooking fuel on cognitive measures. Results were stratified by kutcha and pucca homes and a *P*-value of the interaction is reported. All analyses were adjusted for the complex sampling design of the LASI-DAD to account for stratification and clustering using survey estimation procedures and appropriate weights were utilized.[56,78] All analyses were conducted using Stata 18 SE (College Station, TX).

Sensitivity Analysis

To account for variations in exposure to pollutants from reported use of unclean cooking fuel, sensitivity analyses were conducted with a restricted sample of women and a modified definition of the exposure. As household help with cooking and cleaning is common practice in

Indian society, all analyses were repeated with a restricted sample of women who responded "yes" to involvement in household cooking at time of interview. Additionally, as exposure to pollutants may differ between indoor and outdoor cooking space, the restriction was extended to only include women who indicated their usual place of cooking as "inside the house" or "in a separate building," excluding women who reported cooking outdoors. To identify sufficient levels of exposure to unclean cooking fuel, a second set of analyses was repeated with a modified definition of the exposure combining type of primary cooking fuel and hours of any additional type of fuel used for either cooking, boiling water, heating or other purposes into reporting categories of: 1) Clean fuel use only, 2) Clean fuel use as primary, some hours of unclean fuel use, 3) Only unclean fuel use of ≤2.5 hours, 4) Only unclean fuel use of >2.5 hours. The median hours of reported unclean cooking fuel of 2.5 hours per day was used as the cutoff.

Data availability

LASI-DAD data used for analyses are available from the Gateway to Global Aging Data website (https://g2aging.org/home).

Results

The analytic sample included 2,144 women with complete data (weighted count=2,453) (98% of all women) aged 60 years and older. Mean age at interview was 69 years (SD 8). Nearly all (99%) women were married, with the majority being Hindu (81%), had never attended school (69%), never worked outside the home or were currently unemployed (80%), and lived in rural villages (58%). Sixty nine percent of women identified as belonging to the lower castes (scheduled caste/tribe or other backward class) (Table 1.1). Unclean cooking fuel was reported as the primary fuel by 40% of all women. Among women living in kutcha homes, the majority (60%) reported using unclean cooking fuel, while among women living in pucca homes, the majority (74%) reported using clean cooking fuel. A higher proportion of women who reported using unclean cooking fuel lived in rural villages, came from disadvantaged socioeconomic backgrounds, and had lower median annual household income compared with women who reported using clean cooking fuel. A little over half of all women (52%) reported having difficulty with hearing or seeing; this proportion was equally distributed by type of housing and reported type of cooking fuel use. Mean baseline overall and domain specific cognitive factor scores were lower for women who reported using unclean cooking fuel compared with women who reported using clean cooking fuel, and lowest among women who reported using unclean cooking fuel in kutcha homes (Figure 1.2). Prevalence of neurocognitive disorder was 26% for all women, it was highest (31%) among women who lived in kutcha homes and reported using unclean cooking fuel (Table 1.1).

Estimates from generalized linear models using an identity link function (Table 1.2) adjusted for early-life potential confounders (model 1) suggested lower mean overall and domain specific cognitive factor scores for women who reported using unclean cooking fuel compared with clean cooking fuel. After fully adjusting (model 2), the mean difference in overall cognitive factor score was -0.15 (95% CI -0.21, -0.09) for women who reported using unclean compared with clean cooking fuel. Mean domain specific cognitive factor scores were also consistently lower for women who reported using unclean compared with clean cooking fuel and ranged from -0.09 (95% CI -0.16, -0.01) in the language/fluency domain to -0.14 (95% CI -0.21, -0.07) and -0.14 (-0.21, -0.08) in the orientation and executive functioning domains, respectively. Estimates from the generalized linear model using a log link function and Poisson distribution suggested prevalence of neurocognitive disorder was modestly associated with women who reported use of unclean cooking fuel (Prevalence Ratio [PR]: 1.16, 95% CI 0.97, 1.40) after adjusting for early and mid-to-late-life confounders (model 2). However, the data were consistent with values ranging from little or no effect to moderate increase in prevalence (Table 1.3).

Upon stratifying by home type, there was minimal evidence that the association between reported use of unclean cooking fuel and cognitive function may differ by kutcha (semi-permanent material) and pucca (permanent material) homes (Table 1.4). Specifically, among those living in kutcha homes, women who reported using unclean cooking fuel had a lower mean executive functioning (Coefficient: -0.20, 95% CI -0.28, -0.11), language/fluency (Coefficient: -0.15, 95% CI -0.25, -0.05) and memory (Coefficient: -0.19, 95% CI -0.31, -0.07) factor scores compared with women who reported using clean cooking fuel. These mean differences in factor scores for executive functioning (Coefficient interaction term: -0.10; 95% CI -0.22, 0.01; *P*-value: 0.086), language/fluency (Coefficient interaction term: -0.12; 95% CI -0.25, 0.01; *P*-value: 0.081), and memory (Coefficient interaction term: -0.16; 95% CI -0.32, -0.004; *P*-value: 0.044) domains were only slightly larger among women living in kutcha homes than in pucca homes. Interestingly, the effect of unclean cooking fuel on visuospatial factor score was greater for women living in pucca homes (Coefficient: -0.21, 95% CI -0.30, -0.13) than in kutcha homes (Coefficient: -0.04, 95% CI -0.13, -0.06) with a *p*-value of the interaction term of 0.005. There was no evidence of effect modification by housing type on the association between reported use of unclean cooking fuel and neurocognitive disorder (Coefficient interaction term: 0.20; 95% CI -0.14, 0.53; *P*-value: 0.251) (Table 1.5).

Sensitivity Analyses

To consider possible variations in exposure to pollutants from reported use of unclean cooking fuel, sensitivity analyses were conducted restricting the sample to 1,147 (weighted n: 1,290) women who indicated involvement in household cooking and cooking indoors. Women who reported not being involved in cooking at time of survey were dropped from this restricted analysis and were on average older (72 [SD 9] vs. 67 [SD 6] years), had larger families (5-7 vs. 2-6 members in household), had lower levels of formal education (74% vs. 61% never attended school), and reported a higher median annual household income (60,000 vs. 18,000 Rupees) compared to the women included the sensitivity analysis (Appendix Table S1.1).

After restricting the analyses to only women who indicated involvement in household cooking and cooked indoors, mean overall and domain specific cognitive factor scores remained consistently lower for women who reported using unclean cooking fuel compared with clean fuel (Appendix Table S1.2). The estimated effect was slightly greater among women living in kutcha homes than in pucca homes in the memory domain (Coefficient interaction term: -0.18; 95% CI -0.40, 0.03; *P*-value for interaction: 0.098) (Appendix Table S1.4). Prevalence of neurocognitive disorder was higher for women who reported use of unclean versus clean cooking fuel after adjusting for early-life (PR: 1.60, 95% CI 1.23, 2.07) and additionally for mid-to-late-life (PR: 1.51, 95% CI 1.13, 2.02) potential confounders, although these estimates are imprecise encompassing a wide range from possibly low to high prevalence (Appendix Table S1.3). Unlike findings from the main analysis, there was evidence of effect modification by housing type on neurocognitive disorder (Coefficient interaction term 0.65; 95% CI 0.07, 1.22; *P*-value: 0.029) (Appendix Table S1.5). Namely, among women living in kutcha homes, those who reported use of unclean cooking fuel had twice the prevalence (PR: 2.09, 95% CI 1.33, 3.29) of neurocognitive disorder compared with those who reported use of clean cooking fuel. While among women living in pucca homes, there was no difference in the prevalence of neurocognitive disorder comparing women who reported use of unclean cooking fuel with women who reported use of clean cooking fuel (PR: 1.10, 95% CI 0.73, 1.67).

Upon repeating the analysis with the full sample of 2,144 women using a categorical exposure combining type of primary cooking fuel and hours of unclean fuel use, estimates of overall and domain specific cognitive factor scores suggested lower mean scores for women who reported using unclean cooking fuel either as their primary or additional fuel source compared with women who reported only using clean cooking fuel when adjusted for all potential confounders (Appendix Table S1.6). Prevalence of neurocognitive disorder was also higher (PR: 1.27, 95% CI 1.01, 1.61) for women who reported use of unclean cooking fuel ≥2.5 hours per day compared with women who reported use of only clean cooking fuel when adjusted for all potential confounders (Appendix Table S1.7).

Discussion

In a nationally representative sample of Indian women aged 60 years and older, late-life overall and domain specific cognitive function scores were worse for women who reported use of unclean cooking fuel compared to clean cooking fuel. Evidence for effect modification by type of housing (kutcha and pucca homes), which can influence concentration of pollutants in a home through ventilation and location of kitchen, was modest at best, with slightly stronger effects in the domains of executive function, language/fluency, and memory. Overall, women living in kutcha homes rather than in pucca homes showed some evidence of lower performance in these cognitive domains when comparing those who reported using unclean versus clean cooking fuel. The prevalence ratio of neurocognitive disorder was moderately consistent with higher estimates for women who reported use of unclean cooking fuel compared with women reporting use of clean cooking fuel, although this finding lacked precision and the confidence intervals were consistent with values ranging from little or no effect to moderate increase in prevalence. The association between reported use of unclean cooking fuel and neurocognitive disorder and the modifying role of home type on this association was more evident after restricting the analyses to only women who indicated involvement in household cooking and cooked indoors.

I hypothesized that women who reported using unclean cooking fuel would have lower overall and domain specific cognitive factor scores and higher prevalence of neurocognitive disorder compared with women who reported using clean cooking fuel. This was based on recent studies from the main LASI survey in India that found that older adults exposed to indoor air pollution from solid fuels[24-26] and other sources[51] had lower average standardized cognitive test scores. Findings from the current aim are consistent with previous studies showing moderately large associations between reported use of unclean cooking fuel and standardized scores of cognitive function. The two measures of cognitive function in this aim capture different aspects of a woman's cognitive performance. The overall and domain specific factor scores are based solely on individual test performances and calculated from a previously-developed hierarchical multiple domain factor analysis.[70] In contrast, neurocognitive disorder in this survey is defined by an algorithm of both objective test scores and informant reports incorporating elements of daily function beyond what would be captured in the cognitive function tests alone. Inconsistencies in findings between the two cognitive measurements can be attributed to the difference in construction of these two cognitive measures. Additionally, the solely cross-sectional test based cognitive performance scores can be more vulnerable to residual confounding from early-life differences in socioeconomic factors.[79] As such, poor cognitive test scores among older Indian women may not necessarily represent decline from peak lifetime cognitive function or imply that they struggle with daily activities, especially considering the cultural expectation of women to take lead in household chores and activities.

This aim used self-reported type of cooking fuel at time of interview between 2017-2020 as a proxy for cumulative measure of lifetime exposure to pollutants from unclean cooking fuel. However, it is unlikely that women who reported using clean cooking fuel were lifetime users. On average, women who reported use of clean cooking fuel were 69 years of age, suggesting most were born around 1948 and were involved in kitchen activities by 1960's. While clean cooking fuel using LPG in India has been available since 1955, accessibility and uptake has been slow.[80] It was not until the United Nations Sustainable Development Goals in 2015 that India pledged to ensure universal access to affordable, reliable, and modern energy services by 2030.[26] In 2016, India launched a central scheme called the Pradhan Mantri Ujjwala Yojana (PMUY) to increase access to clean cooking fuel among poor and rural families.[25] PMUY aimed to provide 80 million LPG connections to rural families living below the poverty line and contributed to extensive replacement of traditional biomass fuel. However, sustaining the use of clean cooking fuel and transitioning households away from traditional use of biomass fuel has been challenging.[81] By 2019, there was a sharp increase in the number of inactive LPG connections from 35.8 million inactive connections in 2017 to 43.2 million in 2019**.**[25] In the 2019-2021 National Family Health Survey, 41% of households reported using unclean fuel as their primary source for cooking.[24] This suggests that the 58% of women surveyed here who reside in rural households were unlikely to have exclusively used clean cooking fuel over their lifetime, and may only have had access as early as 2016 with the possibility of interrupted use. As such, the modest results from this aim should be interpreted with consideration that harmful exposure to pollutants from unclean cooking fuel cannot be ruled out even for women who reported use of clean cooking fuel. That is, this is likely to be a measure of recent versus cumulative lifetime exposure. This misclassification of the exposure of type of cooking fuel is likely to bias results towards the null.

It is also important to note that reporting use of unclean cooking fuel may be an inexact measurement of sufficient exposure to harmful pollutants; there was no direct measurement of indoor air pollution in the LASI-DAD. Exposure to pollutants from unclean cooking is directly related to hours spent cooking which can be influenced by several factors including type of stove, number of household members, household ventilation, or other women available to help or share cooking responsibilities. In this sample of women, number of household members were similar across groups of women using unclean or clean cooking fuel, however, annual household income was not. Women who reported use of unclean cooking fuel ≤2.5 hours a day also had the lowest median annual household income of 6,000 Rupees, suggesting household income could be a limiting factor for availability and affordability of unclean fuel or food, indirectly minimizing time spent cooking. Results from the sensitivity analyses on reported hours of unclean cooking fuel use suggest longer duration of exposure to pollutants from reported use of unclean cooking fuel may be associated with late-life neurocognitive disorder. However, these findings are sensitive to accurate recall of hours exposed to pollutants from unclean cooking fuel and subject to variability over a lifetime.

To my knowledge, this aim is the first to assess the modifying role of home type on the effect of unclean cooking fuel on late-life cognitive measures. In a recently published paper of older adults from the main LASI survey, home type (kutcha, semi-pucca vs. pucca) and characteristics associated with kutcha home (lack of electricity and separate kitchen space) were associated with lower mean cognitive performances.[65] While home type can be a proxy for socioeconomic status as higher household income is associated with pucca homes and lower income with kutcha homes, my interest was whether characteristics of the home influences exposure to pollutants from cooking fuel through differences in ventilation and dilution. In this sample, not all women living in pucca homes reported use of clean cooking fuel and not all women living in kutcha homes reported use of unclean fuel. Though there was no evidence of modification by house type on the prevalence of neurocognitive disorder in the main analysis, upon restricting the sample to only women who reported being involved in cooking indoors, prevalence of neurocognitive disorder was higher for women who reported use of unclean cooking fuel among those living in kutcha homes.

Given the differences in background of women between the restricted sample of women who indicated involvement in household cooking and cooked indoors and the full sample, there are multiple reasons why women included in the full sample may have reported no longer being involved in cooking at time of survey. First, they may have been removed from cooking responsibilities due to limitations or impairment as they were somewhat older. Second, they may have passed primary cooking responsibilities to younger household members since they were from larger families. Third, those with wealthier background may never have been involved in cooking which was done by hiring outside help. Without additional information on why these women were not involved in household cooking, it is difficult to conclude if the higher prevalence of neurocognitive disorder associated with reported use of unclean cooking fuel in the restricted sample of women who indicated involvement in household cooking and cooked indoors is driven by higher cumulative lifetime exposure to pollutants from unclean cooking fuel or other factors.

This study has several additional limitations worth considering in interpreting the results reported here. First, as with all aging studies, these findings are subject to some degree of survival bias arising from selective survival of women up to 60 years of age. While it is not empirically possible to test if type of cooking fuel influences survival to old age, it is reasonable to assume that women reporting cooking with unclean cooking fuel are poorer, and those included in LASI-DAD are healthy survivors who could potentially bias results towards the null. Second, exposure to contaminants from unclean cooking fuel is subject to misclassification as there was no direct measurement of indoor air pollution and reported use of unclean fuel may not correspond with lifetime use or harmful exposure duration or levels. Additionally, unclean cooking fuel has been historically prevalent due to ease of accessibility, low cost, and cultural preference, so it is likely many women reporting primary use of clean cooking fuel were also exposed to unclean cooking fuel at some point over their lifetime. Third, kutcha homes also include semi-pucca homes as there were few purely constructed kutcha homes in sample. Effect modification by home type may be different if it were strictly restricted to purely kutcha homes that generally have poor ventilation and lack separate kitchen space. Fourth, as harmonized cognitive function measures were assessed at a single time point, it was not possible to assess rate of cognitive change over time; wave two data collection of LASI-DAD is currently ongoing. Cross-sectional measures of cognitive function are more subject to confounding by early-life factors as between person variation in late-life cognitive function is heavily influenced by pre-morbid differences in cognitive function.[82] Last, as neurocognitive disorder is defined per the DSM-5 criteria, it was operationalized using survey information and not by trained clinicians or a panel of neuropsychologists or neurologists. It is important to interpret DSM-5 classification of neurocognitive disorder separate from a clinical diagnosis.

At the same time, this study also has multiple strengths. These include using data from a large, nationally representative sample of Indian women assessed by harmonized measures of cognitive function. Overall and domain specific cognitive factor scores allowed for identification of variations within specific domains in addition to overall cognitive score. Additionally, inclusion of a DSM-5 structured measure of neurocognitive disorder allowed for assessment of cognitive impairment incorporating both objective cognitive functional scores and informant reports of cognitive and functional decline.

Findings from this study using a nationally representative survey add to the growing evidence that exposure to pollutants from unclean cooking fuel is negatively associated with cognitive function among older Indian women. It additionally suggests housing type may play a modifying role in this association highlighting the importance for policies supporting clean fuel to reach a greater proportion of women in India, including those from poorer backgrounds. Effective targeting of the poorest of the poor who are more likely to use unclean fuel may need to also consider issues of accessibility and affordability of clean cooking fuel. Further, solutions may need to include improved ventilation in primary areas of cooking. It is important moving forward to explore the possible effects of outdoor air pollution as well and other early and mid-life socio-economic factors that could be driving these observed associations.

Tables and Figures

Table 1.1. Weighted counts and weighted column percentages of demographic, socio-economic, and cognitive performance measures of Indian women aged ≥60 years from the LASI-DAD by type of main cooking fuel and housing.

	All	Kutcha Home		Pucca Home	
Primary Cooking Fuel		Clean	Unclean	Clean	Unclean
Weighted N (row %)	**2,453**	**395 (16)**	**588 (24)**	**1,089 (44)**	**381 (16)**
Unweighted N (row %)	2,144	307 (14)	500 (23)	958 (45)	379 (18)
Demographic characteristics					
Urbanicity, n (%)					
Urban community	1019 (42)	167 (42)	64 (11)	737 (68)	51 (13)
Rural village	1434 (58)	227 (58)	525 (89)	352 (32)	330 (87)
Age at interview, mean (SD)	69 (8)	69 (8)	68 (7)	69 (8)	69 (9)
Marital status, n (%)					
Never married	16 (1)	1 (0)	3 (0)	10 (1)	3 (1)
Married	2432 (99)	392 (100)	586 (100)	1076 (99)	378 (99)
Religion, n (%)					
Hindu	1982 (81)	296 (75)	499 (85)	848 (78)	338 (89)
Muslim	301 (12)	61 (16)	69 (12)	144 (13)	27 (7)
Christian	73 (3)	15 (4)	8 (1)	42 (4)	9 (2)
Sikh	60 (2)	14 (3)	12 (2)	29 (3)	5 (1)
Buddhist/Jain/None	38 (2)	8 (2)	0 (0)	28 (3)	2 (1)
Number of people in household, median (IQR)	5 (3-6)	5 (2-6)	4 (2-6)	5 (3-6)	5 (3-7)
Socio-economic status					
Caste system, n (%)					
No or other caste	757 (31)	74 (19)	104 (18)	467 (43)	113 (30)
Scheduled caste/tribe	594 (24)	116 (29)	209 (36)	165 (15)	103 (27)
Other backward class	1101 (45)	205 (52)	275 (47)	457 (42)	165 (43)
Paternal education, n (%)					
Never attended school	1739 (71)	288 (73)	474 (81)	685 (63)	292 (77)
Primary school (grade 7) or less	362 (15)	69 (17)	50 (8)	206 (19)	38 (10)
Middle school (grades 8) or more	186 (8)	17 (4)	24 (4)	129 (12)	16 (4)
Missing	166 (7)	21 (5)	40 (7)	69 (6)	36 (9)
Highest educational attainment, n (%)					
Never attended school	1684 (69)	294 (74)	499 (85)	583 (54)	308 (81)
Primary school (grade 7) or less	492 (20)	76 (19)	79 (13)	283 (26)	54 (14)
Middle school (grades 8) or more	277 (11)	25 (6)	10 (2)	223 (20)	18 (5)
Years of education, mean (SD)	2 (4)	1.5 (3)	0.6 (2)	3.4 (4)	1 (3)
Current employment status, n (%)					
Unemployed	713 (29)	106 (27)	189 (32)	286 (26)	132 (35)
Employed	491 (20)	119 (30)	162 (27)	128 (12)	82 (22)
Never worked	1249 (51)	169 (43)	237 (40)	675 (62)	167 (44)
Main lifetime occupation, n (%)					
Senior professionals	52 (2)	3 (1)	4 (1)	42 (4)	4 (1)
Service, shop, craft workers	151 (6)	41 (10)	24 (4)	75 (7)	11 (3)
Agricultural/forestry/fishery	509 (21)	69 (18)	201 (34)	134 (12)	105 (28)
Plant and machine operators	8 (0)	1 (0)	0 (0)	5 (1)	2 (0)
Elementary occupations	313 (13)	84 (21)	71 (12)	100 (9)	58 (15)
Other	166 (7)	27 (7)	51 (9)	56 (5)	32 (8)
Never worked	1249 (51)	169 (43)	237 (40)	675 (62)	167 (44)
Annual household income (Rupees), median (IQR)	30,000 (0-120,000)	30,000 (0-104,000)	14,000 (0-63,000)	60,000 (0-180,000)	15,000 (0-75,000)
Other indoor/outdoor air pollutants					
Mosquito coils, incense, smoker, n (%)					
No	214 (9)	23 (6)	65 (11)	85 (8)	40 (11)
Yes	2239 (91)	371 (94)	523 (89)	1004 (92)	340 (89)

Table 1.1. Weighted counts and weighted column percentages of demographic, socio-economic, and cognitive performance measures of Indian women aged ≥60 years from the LASI-DAD by type of main cooking fuel and housing.

	All	Kutcha Home		Pucca Home	
Primary Cooking Fuel		Clean	Unclean	Clean	Unclean
Weighted N (row %)	**2,453**	**395 (16)**	**588 (24)**	**1,089 (44)**	**381 (16)**
Unweighted N (row %)	2,144	307 (14)	500 (23)	958 (45)	379 (18)
Current job around burning material, exhaust, or smoke					
No	396 (16)	94 (24)	135 (23)	105 (10)	62 (16)
Yes	95 (4)	26 (7)	27 (5)	23 (2)	19 (5)
Not Working	1958 (80)	275 (70)	427 (73)	959 (88)	297 (78)
Current job close to chemicals, pesticides, or herbicides					
No	358 (15)	86 (22)	113 (19)	103 (9)	56 (15)
Yes	133 (5)	33 (8)	49 (8)	25 (2)	26 (7)
Not Working	1958 (80)	275 (70)	427 (73)	959 (88)	297 (78)
Sensory impairment					
Difficulty hearing or seeing					
No	1170 (48)	179 (46)	259 (44)	550 (51)	182 (48)
Yes	1276 (52)	214 (54)	327 (56)	536 (49)	199 (52)
Cognitive measure					
General cognitive factor score, mean (SD)	-0.32 (0.85)	-0.33 (0.74)	-0.67 (0.62)	-0.04 (0.94)	-0.57 (0.74)
Orientation factor score, mean (SD)	-0.36 (0.79)	-0.37 (0.70)	-0.66 (0.65)	-0.12 (0.83)	-0.55 (0.75)
Executive functioning factor score, mean (SD)	-0.32 (0.81)	-0.32 (0.68)	-0.65 (0.61)	-0.06 (0.90)	-0.54 (0.70)
Language/fluency factor score, mean (SD)	-0.20 (0.78)	-0.20 (0.73)	-0.46 (0.69)	-0.01 (0.79)	-0.34 (0.75)
Memory factor score, mean (SD)	-0.12 (0.95)	-0.07 (0.87)	-0.40 (0.76)	0.09 (1.01)	-0.33 (0.94)
Visuospatial factor score, mean (SD)	-0.22 (0.75)	-0.29 (0.71)	-0.39 (0.59)	-0.03 (0.82)	-0.47 (0.67)
DSM-5 neurocognitive disorder, n (%)					
No neurocognitive disorder	1806 (74)	302 (76)	408 (69)	825 (76)	272 (71)
Mild/major neurocognitive disorder	647 (26)	93 (24)	180 (31)	264 (24)	109 (29)

LASI-DAD: Harmonized Diagnostic Assessment of Dementia for the Longitudinal Aging Study in India.
Kutcha: Homes made with raw/semi-permanent materials.
Pucca: Homes made with solid/permanent materials.
Unclean cooking fuel: Kerosene, charcoal, lignite, coal, crop residue, wood/shrub, or dung cake as main cooking fuel.
Clean cooking fuel: Electric, biogas, or liquified petroleum gas as main cooking fuel.

Table 1.2. Association between primary cooking fuel and late-life overall and domain specific cognitive function among Indian women aged ≥60 years from the LASI-DAD.

	Coefficient (95% CI)		
	Crude	**Model 1**	**Model 2**
Overall cognitive factor score			
Clean cooking fuel	Ref	Ref	**Ref**
Unclean cooking fuel	-0.51 (-0.58, -0.44)	-0.18 (-0.24, -0.12)	-0.15 (-0.21, -0.09)
Orientation factor score			
Clean cooking fuel	Ref	Ref	Ref
Unclean cooking fuel	-0.43 (-0.50, -0.36)	-0.18 (-0.25, -0.12)	-0.14 (-0.21, -0.07)
Executive functioning factor score			
Clean cooking fuel	Ref	Ref	Ref
Unclean cooking fuel	-0.48 (-0.55, -0.41)	-0.18 (-0.24, -0.12)	-0.14 (-0.21, -0.08)
Language/fluency factor score			
Clean cooking fuel	Ref	Ref	Ref
Unclean cooking fuel	-0.35 (-0.42, -0.28)	-0.11 (-0.18, -0.05)	-0.09 (-0.16, -0.01)
Memory factor score			
Clean cooking fuel	Ref	Ref	Ref
Unclean cooking fuel	-0.42 (-0.50, -0.34)	-0.14 (-0.22, -0.06)	-0.11(-0.19, -0.02)
Visuospatial factor score			
Clean cooking fuel	Ref	Ref	Ref
Unclean cooking fuel	-0.32 (-0.39, -0.26)	-0.10 (-0.16, -0.04)	-0.13 (-0.20, -0.06)

LASI-DAD: Harmonized Diagnostic Assessment of Dementia for the Longitudinal Aging Study in India.
Model 1: Adjusted for early-life variables including caste, paternal education, and education in years.
Model 2: Additionally adjusted for age, annual household income, housing type, and urbanicity.
Unclean cooking fuel: Kerosene, charcoal, lignite, coal, crop residue, wood/shrub, or dung cake as main cooking fuel.
Clean cooking fuel: Electric, biogas, or liquified petroleum gas as main cooking fuel.

Table 1.3. Association between primary cooking fuel and prevalent late-life neurocognitive disorder among Indian women aged ≥60 years from the LASI-DAD.

	Prevalence Ratio (95% CI)		
	Crude	**Model 1**	**Model 2**
Neurocognitive disorder			
Clean cooking fuel	Ref	Ref	Ref
Unclean cooking fuel	1.24 (1.07, 1.45)	1.16 (0.99, 1.37)	1.16 (0.97, 1.40)

LASI-DAD: Harmonized Diagnostic Assessment of Dementia for the Longitudinal Aging Study in India.
Prevalence ratio estimated using GLM with Poisson distribution and log link function.
Model 1: Adjusted for early-life potential confounders including caste, paternal education, and education in years.
Model 2: Additionally adjusted for age, annual household income, housing type, and urbanicity.
Unclean cooking fuel: Kerosene, charcoal, lignite, coal, crop residue, wood/shrub, or dung cake as main cooking fuel.
Clean cooking fuel: Electric, biogas, or liquified petroleum gas as main cooking fuel.

Table 1.4. Association between primary cooking fuel and late-life overall and domain specific cognitive function stratified by type of house among Indian women aged ≥60 years from the LASI-DAD.			
	Kutcha House Weighted N=983	**Pucca House** Weighted N=1,470	
	Coefficient (95% CI)	**Coefficient (95% CI)**	***P* for Interaction**
Overall cognitive factor score			
Clean cooking fuel	Ref	Ref	0.175
Unclean cooking fuel	-0.19 (-0.28, -0.11)	-0.11 (-0.22, -0.04)	
Orientation factor score			
Clean cooking fuel	Ref	Ref	0.216
Unclean cooking fuel	-0.18 (-0.28, -0.09)	-0.10 (-0.20, -0.01)	
Executive functioning factor score			
Clean cooking fuel	Ref	Ref	0.086
Unclean cooking fuel	-0.20 (-0.28, -0.11)	-0.10 (-0.18, -0.01)	
Language/fluency factor score			
Clean cooking fuel	Ref	Ref	0.081
Unclean cooking fuel	-0.15 (-0.25, -0.05)	-0.03 (-0.13, -0.06)	
Memory factor score			
Clean cooking fuel	Ref	Ref	0.044
Unclean cooking fuel	-0.19 (-0.31, -0.07)	-0.03 (-0.14, 0.09)	
Visuospatial factor score			
Clean cooking fuel	Ref	Ref	0.005
Unclean cooking fuel	-0.04 (-0.13, -0.06)	-0.21 (-0.30, -0.13)	

LASI-DAD: Harmonized Diagnostic Assessment of Dementia for the Longitudinal Aging Study in India.
Adjusted for caste, paternal education, education in years, age, annual household income, and urbanicity.
P for interaction: *P*-value of the interaction term between reported use of unclean cooking fuel and kutcha home.
Kutcha: Homes made with raw/semi-permanent materials.
Pucca: Homes made with solid/permanent materials.
Unclean cooking fuel: Kerosene, charcoal, lignite, coal, crop residue, wood/shrub, or dung cake as main cooking fuel.
Clean cooking fuel: Electric, biogas, or liquified petroleum gas as main cooking fuel.

Table 1.5. Association between primary cooking fuel and prevalent late-life neurocognitive disorder stratified by type of house among Indian women aged ≥60 years from the LASI-DAD.

	Kutcha Home Weighted N=983		**Pucca Home** Weighted N=1,470		
	Weighted events/n	**Prevalence Ratio (95% CI)**	**Weighted Events/n**	**Prevalence Ratio (95% CI)**	***P* for Interaction**
Neurocognitive disorder					
Clean cooking fuel	93/395	Ref	264/1089	Ref	0.251
Unclean cooking fuel	180/588	1.29 (0.98, 1.69)	110/381	1.06 (0.84, 1.34)	

LASI-DAD: Harmonized Diagnostic Assessment of Dementia for the Longitudinal Aging Study in India.
Prevalence ratio estimated using GLM with Poisson distribution and log link function.
Adjusted for caste, paternal education, education in years, age, annual household income, and urbanicity.
P for interaction: *P*-value of interaction term between reported use of unclean cooking fuel and kutcha home.
Kutcha: Homes made with raw/semi-permanent materials.
Pucca: Homes made with solid/permanent materials.
Unclean cooking fuel: Kerosene, charcoal, lignite, coal, crop residue, wood/shrub, or dung cake as main cooking fuel.
Clean cooking fuel: Electric, biogas, or liquified petroleum gas as main cooking fuel.

Figure 1.1. Directed acyclic graph (DAG) illustrating the effect of type of cooking fuel on late-life cognitive impairment among Indian women aged ≥60 years from the LASI-DAD study.

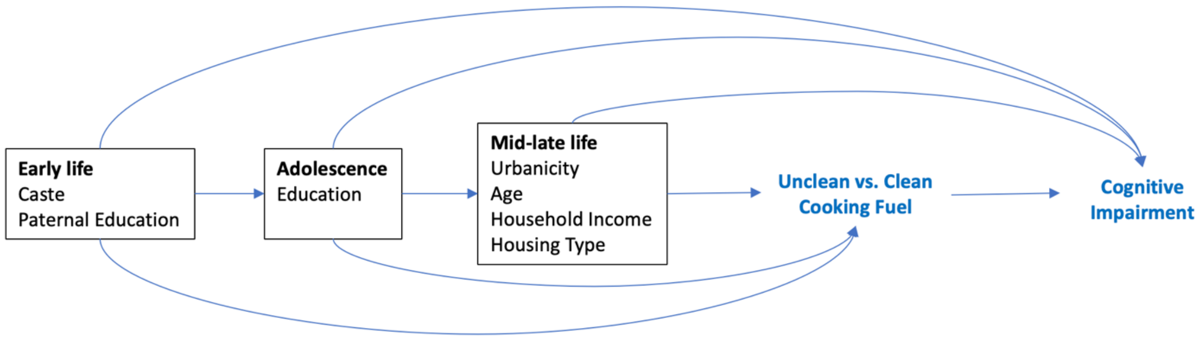
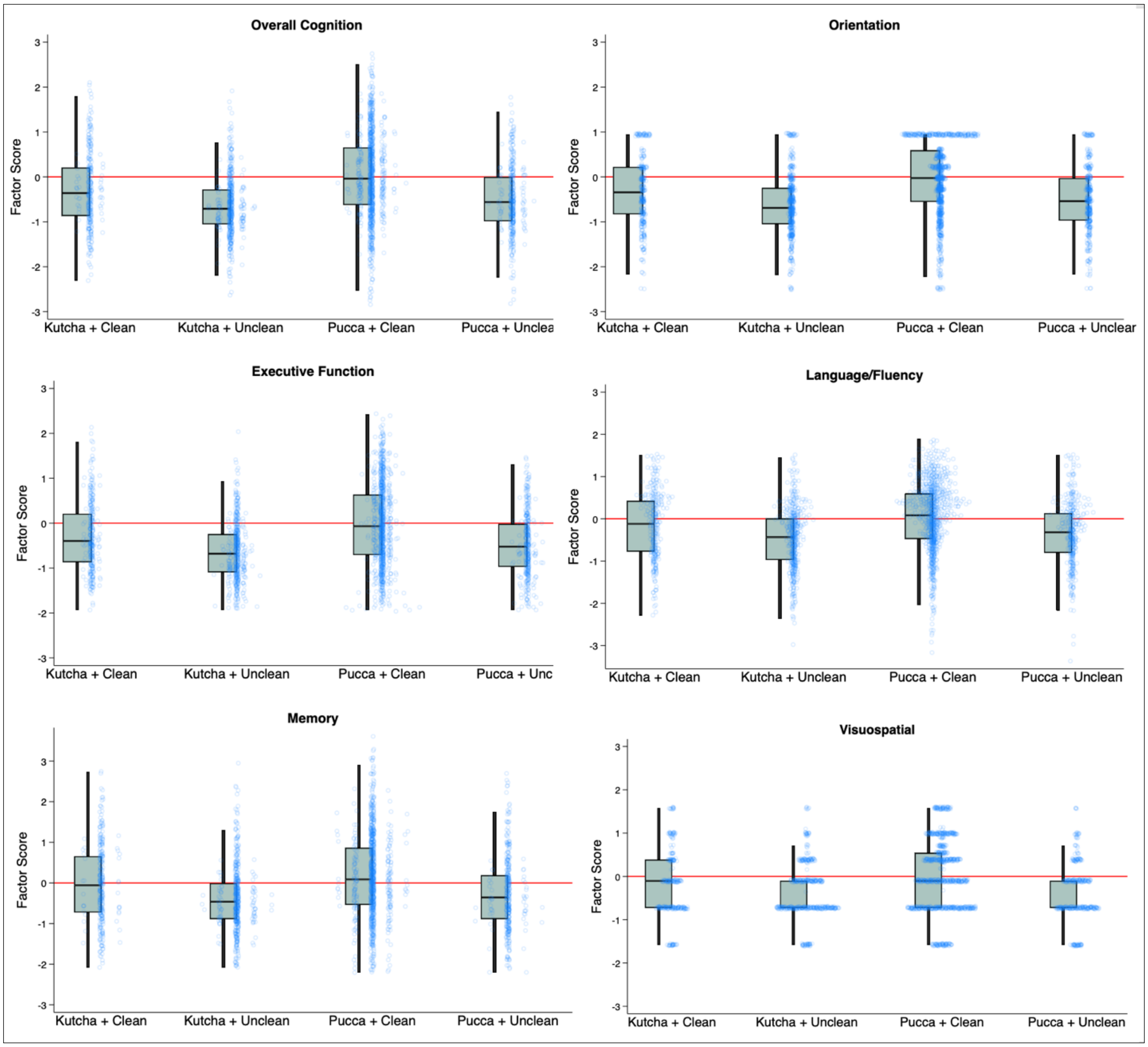


Figure 1.2. Summary box and jitter plots of overall and domain specific cognitive factor scores by type of cooking fuel (clean vs. unclean) and type of home (kutcha vs. pucca) for Indian women aged ≥60 years from the LASI-DAD study.



Appendix

Table S1.1. Weighted counts and column percentages of demographic, socio-economic, and cognitive performance measures of Indian women aged ≥60 years from the LASI-DAD study by involvement in household cooking and cooking indoors at time of survey.

	Involvement in Household Cooking and Cooking Indoors	
	No	Yes
Unweighted N (row %)	780 (41)	1,147 (59)
Weighted N (row %)	901 (41)	1,290 (59)
Demographic characteristic		
Urbanicity, n (%)		
Urban community	314 (42)	512 (47)
Rural village	466 (58)	635 (53)
Age at interview, mean (SD)	72 (9)	67 (6)
Marital status, n (%)		
Never married	5 (1)	10 (1)
Married	773 (99)	1135 (99)
Religion, n (%)		
Hindu	604 (80)	886 (80)
Muslim	115 (14)	155 (12)
Christian	19 (2)	56 (4)
Sikh	32 (3)	35 (2)
Buddhist/Jain/None	10 (2)	15 (2)
Number of people in household, median (IQR)	6 (5-7)	4 (2-6)
Socio-economic Status		
Caste system, n (%)		
No or other caste	298 (34)	412 (32)
Scheduled caste/tribe	174 (23)	256 (23)
Other backward class	308 (43)	479 (44)
Type of home, n (%)		
Pucca (permanent)	526 (66)	715 (60)
Kutcha (semi-permanent)	254 (34)	432 (40)
Paternal education, n (%)		
Never attended school	569 (73)	750 (68)
Primary school (grade 7) or less	101 (13)	209 (17)
Middle school (grades 8) or more	58 (7)	119 (9)
Missing	52 (7)	69 (6)
Highest educational attainment, n (%)		
Never attended school	555 (74)	646 (61)
Primary school (grade 7) or less	156 (18)	282 (23)
Middle school (grades 8) or more	69 (7)	219 (16)
Years of education, mean (SD)	2 (3)	3 (4)
Current employment status, n (%)		
Unemployed	221 (30)	299 (28)
Employed	68 (10)	246 (24)
Never worked	491 (60)	602 (48)
Main lifetime occupation, n (%)		
Senior professionals	13 (1)	42 (3)
Service, shop, craft workers	27 (4)	80 (8)
Agricultural/forestry/fishery	107 (16)	204 (20)
Plant and machine operators	1 (0)	3 (0)
Elementary occupations	92 (13)	141 (13)
Other	49 (6)	74 (7)
Never worked	491 (60)	602 (48)

Table S1.1. Weighted counts and column percentages of demographic, socio-economic, and cognitive performance measures of Indian women aged ≥60 years from the LASI-DAD study by involvement in household cooking and cooking indoors at time of survey.

	Involvement in Household Cooking and Cooking Indoors	
	No	Yes
Unweighted N (row %)	780 (41)	1,147 (59)
Weighted N (row %)	901 (41)	1,290 (59)
Annual household income (Rupees), median (IQR)	60,000 (0-150000)	18,000 (0-100000)
Mosquito coils, incense, smoker, n (%)		
No	63 (7)	106 (9)
Yes	717 (93)	1041 (91)
Current job around burning material, exhaust, or smoke		
No	57 (8)	192 (19)
Yes	11 (2)	54 (5)
Not working at time of survey	710 (90)	900 (76)
Current job close to chemicals, pesticides, or herbicides		
No	51 (8)	178 (18)
Yes	17 (2)	68 (6)
Not working at time of survey	710 (90)	900 (76)
Sensory Impairment		
Difficulty hearing or seeing		
No	298 (39)	618 (55)
Yes	480 (61)	526 (45)
Cognitive measures		
General cognitive factor score, mean (SD)	-0.53 (0.84)	-0.11 (0.84)
Orientation factor score, mean (SD)	-0.51 (0.81)	-0.20 (0.76)
Executive functioning factor score, mean (SD)	-0.48 (0.77)	-0.14 (0.82)
Language/fluency factor score, mean (SD)	-0.37 (0.81)	-0.04 (0.73)
Memory factor score, mean (SD)	-0.34 (0.93)	0.08 (0.95)
Visuospatial factor score, mean (SD)	-0.39 (0.73)	-0.08 (0.76)
DSM-5 neurocognitive disorder, n (%)		
No neurocognitive disorder	517 (66)	899 (79)
Mild/major neurocognitive disorder	263 (34)	248 (21)

Table S1.2. Association between primary cooking fuel and late-life overall and domain specific cognitive function among Indian women aged ≥60 years from the LASI-DAD restricted to women who reported involvement in cooking and cooking indoors at time of survey.	
	Coefficient (95% CI)
Overall cognitive factor score	
Clean cooking fuel	**Ref**
Unclean cooking fuel	-0.17 (-0.25, -0.09)
Orientation factor score	
Clean cooking fuel	Ref
Unclean cooking fuel	-0.18 (-0.27, -0.09)
Executive function factor score	
Clean cooking fuel	Ref
Unclean cooking fuel	-0.13 (-0.21, -0.05)
Language/fluency factor score	
Clean cooking fuel	Ref
Unclean cooking fuel	-0.11 (-0.21, -0.02)
Memory factor score	
Clean cooking fuel	Ref
Unclean cooking fuel	-0.12(-0.24, -0.004)
Visuospatial factor score	
Clean cooking fuel	Ref
Unclean cooking fuel	-0.22 (-0.31, -0.13)

LASI-DAD: Harmonized Diagnostic Assessment of Dementia for the Longitudinal Aging Study in India.
Model adjusted for caste, paternal education, and education in years, age, annual household income, housing type, and urbanicity.
Unclean cooking fuel: Kerosene, charcoal, lignite, coal, crop residue, wood/shrub, or dung cake as main cooking fuel.
Clean cooking fuel: Electric, biogas, or liquified petroleum gas as main cooking fuel.

Table S1.3. Association between primary cooking fuel and prevalent late-life neurocognitive disorder among Indian women aged ≥60 years from the LASI-DAD restricted to those who reported involvement in cooking and cooking indoors at time of survey.

	Prevalence Ratio (95% CI)		
	Crude	**Model 1**	**Model 2**
Neurocognitive disorder			
Clean cooking fuel	Ref	Ref	Ref
Unclean cooking fuel	1.56 (1.23, 1.99)	1.60 (1.23, 2.07)	1.51 (1.13, 2.02)

LASI-DAD: Harmonized Diagnostic Assessment of Dementia for the Longitudinal Aging Study in India.
Prevalence ratio estimated using GLM with Poisson distribution and log link function.
Model 1: Adjusted for early-life potential confounders including caste, paternal education, and education in years.
Model 2: Additionally adjusted for age, annual household income, housing type, and urbanicity.
Unclean cooking fuel: Kerosene, charcoal, lignite, coal, crop residue, wood/shrub, or dung cake as main cooking fuel.
Clean cooking fuel: Electric, biogas, or liquified petroleum gas as main cooking fuel.

Table S1.4. Association between primary cooking fuel and late-life overall and domain specific cognitive function stratified by type of house among Indian women aged ≥60 years from the LASI-DAD restricted to women who reported involvement in cooking at time of survey and cooked indoors.

	Kutcha Home Coefficient (95% CI)	Pucca Home Coefficient (95% CI)	*P* for Interaction
Overall cognitive factor score			
Clean cooking fuel	Ref	Ref	0.395
Unclean cooking fuel	-0.20 (-0.31, -0.10)	-0.14 (-0.25, -0.02)	
Orientation factor score			
Clean cooking fuel	Ref	Ref	0.973
Unclean cooking fuel	-0.18 (-0.30, -0.06)	-0.18 (-0.31, -0.05)	
Executive function factor score			
Clean cooking fuel	Ref	Ref	0.143
Unclean cooking fuel	-0.19 (-0.30, -0.07)	-0.07 (-0.19, 0.06)	
Language/fluency factor score			
Clean cooking fuel	Ref	Ref	0.195
Unclean cooking fuel	-0.16 (-0.29, -0.04)	-0.05 (-0.18, 0.07)	
Memory factor score			
Clean cooking fuel	Ref	Ref	0.098
Unclean cooking fuel	-0.21 (-0.37, -0.05)	-0.02 (-0.19, 0.14)	
Visuospatial factor score			
Clean cooking fuel	Ref	Ref	0.036
Unclean cooking fuel	-0.13 (-0.26, -0.01)	-0.32 (-0.44, -0.19)	

LASI-DAD: Harmonized Diagnostic Assessment of Dementia for the Longitudinal Aging Study in India.
Adjusted for caste, paternal education, education in years, age, annual household income, and urbanicity.
P for interaction: *P*-value of interaction term between reported use of unclean cooking fuel and kutcha home.
Kutcha: Homes made with raw/semi-permanent materials.
Pucca: Homes made with solid/permanent materials.
Unclean cooking fuel: Kerosene, charcoal, lignite, coal, crop residue, wood/shrub, or dung cake as main cooking fuel.
Clean cooking fuel: Electric, biogas, or liquified petroleum gas as main cooking fuel.

Table S1.5. Association between primary cooking fuel and prevalent late-life neurocognitive disorder stratified by type of house among Indian women aged ≥60 years from the LASI-DAD restricted to women who reported involvement in cooking at time of survey and cooked indoors.

	Kutcha Home		Pucca Home		
	Weighted events/n	**Prevalence Ratio (95% CI)**	**Weighted Events/n**	**Prevalence Ratio (95% CI)**	***P* for Interaction**
Neurocognitive disorder					
Clean cooking fuel	32/239	Ref	114/608	Ref	0.029
Unclean cooking fuel	84/282	2.09 (1.33, 3.29)	36/161	1.10 (0.73, 1.67)	

LASI-DAD: Harmonized Diagnostic Assessment of Dementia for the Longitudinal Aging Study in India.
Prevalence ratio estimated using GLM with Poisson distribution and log link function.
Adjusted for caste, paternal education, education in years, age, annual household income, and urbanicity.
P for interaction: *P*-value of the interaction term between reported use of unclean cooking fuel and type of house.
Kutcha: Homes made with raw/semi-permanent materials.
Pucca: Homes made with solid/permanent materials.
Unclean cooking fuel: Kerosene, charcoal, lignite, coal, crop residue, wood/shrub, or dung cake as main cooking fuel.
Clean cooking fuel: Electric, biogas, or liquified petroleum gas as main cooking fuel.

Table S1.6. Association between primary cooking fuel and late-life overall and domain specific cognitive function among Indian women aged ≥60 years from the LASI-DAD.	
	Coefficient (95% CI)
Overall cognitive factor score	
Clean fuel use only	Ref
Clean fuel use primarily, some hours of unclean fuel	-0.09 (-0.17, 0.01)
Only unclean fuel use ≤2.5 hours	-0.19 (-0.27, 0.10)
Only unclean fuel use >2.5 hours	-0.20 (-0.28, -0.11)
Orientation factor score	
Clean fuel use only	Ref
Clean fuel use primarily, some hours of unclean fuel	-0.09 (-0.18, -0.01)
Only unclean fuel use ≤2.5 hours	-0.17 (-0.26, -0.09)
Only unclean fuel use >2.5 hours	-0.21 (-0.29, -0.12)
Executive function factor score	
Clean fuel use only	Ref
Clean fuel use primarily, some hours of unclean fuel	-0.09 (-0.17, -0.001)
Only unclean fuel use ≤2.5 hours	-0.17 (-0.26, -0.09)
Only unclean fuel use >2.5 hours	-0.21 (-0.29, -0.12)
Language/fluency factor score	
Clean fuel use only	Ref
Clean fuel use primarily, some hours of unclean fuel	-0.03 (-0.13, 0.06)
Only unclean fuel use ≤2.5 hours	-0.05 (-0.16, 0.05)
Only unclean fuel use >2.5 hours	-0.16 (-0.26, -0.06)
Memory factor score	
Clean fuel use only	Ref
Clean fuel use primarily, some hours of unclean fuel	0.01 (--0.11, 0.12)
Only unclean fuel use ≤2.5 hours	-0.15 (-0.26, -0.03)
Only unclean fuel use >2.5 hours	-0.06 (-0.17, 0.06)
Visuospatial factor score	
Clean fuel use only	Ref
Clean fuel use primarily, some hours of unclean fuel	-0.11 (-0.21, -0.02)
Only unclean fuel use ≤2.5 hours	-0.18 (-0.27, -0.09)
Only unclean fuel use >2.5 hours	-0.18 (-0.26, -0.09)

LASI-DAD: Harmonized Diagnostic Assessment of Dementia for the Longitudinal Aging Study in India.
Model adjusted for caste, paternal education, and education in years, age, annual household income, housing type, and urbanicity.
Unclean cooking fuel: Kerosene, charcoal, lignite, coal, crop residue, wood/shrub, or dung cake as main cooking fuel.
Clean cooking fuel: Electric, biogas, or liquified petroleum gas as main cooking fuel.

Table S1.7. Association between primary cooking fuel and prevalent late-life neurocognitive disorder among Indian women aged ≥60 years from the LASI-DAD.

	Crude	Model 1	Model 2
	Prevalence Ratio (95% CI)	Prevalence Ratio (95% CI)	Prevalence Ratio (95% CI)
Type and hours of cooking fuel use			
Clean fuel use only	Ref	Ref	Ref
Clean fuel use primarily, some hours of unclean fuel	1.15 (0.92, 1.45)	1.10 (0.87 - 1.39)	1.09 (0.85 - 1.39)
Only unclean fuel use ≤2.5 hours	1.24 (1.01, 1.51)	1.15 (0.92, 1.42)	1.15 (0.89 - 1.47)
Only unclean fuel use >2.5 hours	1.38 (1.13, 1.70)	1.28 (1.03, 1.58)	1.27 (1.01 - 1.61)

LASI-DAD: Harmonized Diagnostic Assessment of Dementia for the Longitudinal Aging Study in India.
Prevalence ratio estimated using GLM with Poisson distribution and log link function.
Model 1: Adjusted for early-life potential confounders including caste, paternal education, and education in years.
Model 2: Additionally adjusted for age, annual household income, housing type, and urbanicity.
Unclean cooking fuel: Kerosene, charcoal, lignite, coal, crop residue, wood/shrub, or dung cake as main cooking fuel.
Clean cooking fuel: Electric, biogas, or liquified petroleum gas as main cooking fuel.

Aim 2: Reported use of unclean cooking fuel and late-life cognitive measures among older adults in India: Does the association differ by sex?

Abstract

Introduction: Recent studies have highlighted an association between indoor air pollutants and cognitive measures among older Indian adults.[34,61] Most include both men and women, however, men in India are not customarily responsible for household cooking and are likely to spend more time away from the kitchen and outside of the house than women. In this aim, I assessed whether the effect of reported household use of unclean cooking fuel (kerosene, charcoal, lignite, coal, dung cake) on cognitive functioning among older Indian adults differs by sex. To do so, I again use culturally appropriate and harmonized measures of cognitive function.

Methods: I used data from individuals (N = 4,000 men and women aged ≥60 years) surveyed in the nationally representative Harmonized Diagnostic Assessment of Dementia for the Longitudinal Aging Study in India (LASI-DAD). Generalized linear models estimated the effect of reported household use of unclean cooking fuel on overall and domain-specific cognitive factor scores, and prevalence of neurocognitive disorder per DSM-5 definition, after adjusting for potential early and mid-to-late-life confounders. An interaction term included in the model between reported household use of unclean cooking fuel and sex assessed for effect measure modification.

Results: Among older men and women, reported household use of unclean cooking fuel compared to clean cooking fuel was associated with poorer late-life cognitive function. This effect estimate was slightly greater among women for overall and domain specific cognitive factor scores for orientation, language/fluency, and visuospatial ability (*P*-value for interaction <0.10). In contrast, among men, reported household use of unclean cooking fuel was associated with a higher prevalence of neurocognitive disorder (PR: 1.41, 95% CI 1.09,1.83). Among women, this association was consistent with slightly higher prevalence (PR: 1.18, 95% CI 0.93, 1.50), but the confidence intervals were consistent with values ranging from no effect to moderate increase in prevalence.

Conclusion: Among older men and women, exposure to pollutants from reported household use of unclean cooking fuel is negatively associated with late-life cognitive measures with modest differences by sex. Further understanding of early-life sex-based disparities in socioeconomic opportunities and differential exposure to outdoor pollutants is needed to better assess whether differences in household labor activities have differential consequences for men and women.

Background

Air pollution and risk of dementia in India

Air pollution is a major global health risk, and India is estimated to experience very high levels.[83] In 2019, air pollution was linked to 1.67 million deaths in India, 0.61 million of these cases (37%) were from exposure to household air pollutants.[84] The prevalent use of biomass fuel such as wood, charcoal, dried twigs, crop residues, and animal dung cakes for cooking, heating, and boiling water in Indian society, especially in rural settings, contribute to the threat of exposure to indoor air pollutants.[37] In Indian culture, women spend more time dedicated to household chores, and have a greater exposure to pollutants from biomass fuel than men as they are more likely to be involved in cooking for a substantial part of each day.[43] Polluted air once inhaled can eventually damage the lungs, heart, and brain, causing inflammation and neuronal dysfunction.[85] Recent studies in India have highlighted how indoor air pollution from unclean or solid fuel use is negatively associated with poor cognitive performance.[9,11,12,34,61] Most of these studies include both men and women, but it is unlikely that men are similarly exposed to the harmful effects of pollutants from unclean cooking fuel compared to women.

Differences in cognitive measure in India by sex

India is rapidly aging and carries a high burden of dementia.[58] As of 2022, an estimated 8.8 million adults 60 years and older were living with dementia in India.[59] Older women continue to be at a disadvantage for cognitive functioning compared to men in developing countries as India.[86,87] Age-standardized prevalence of dementia is higher among older Indian women (9.63%, 95% CI 8-11) than men (5.77%, 95% CI 5-8).[59] As education has a strong protective effect on cognitive functioning in later life,[88,89] early-life socio-economic disparities and gaps in educational opportunities and nutrition are likely important contributors to sex-based differences observed in cognitive abilities.[90] Educational opportunities for women since independence in 1947 has been slow to emerge.[91,92] Indeed, it was not until 2009 that education was made compulsory and free for all Indian children aged 6-14 years.[93] However, these changes have not benefitted the present generation of older Indian women. Men and women not only differ in educational opportunities, but also in economic and employment opportunities that follow this which might contribute towards additional differences in cognitive functioning.[62,94] Due to sex differences in the distribution of labor,[94,95] men may find themselves in the labor market where there is additional opportunities for intellectual stimulation,[62,94] or in jobs outdoor with other sources of environmental exposure to pollutants,[96-98] while women may be more restricted to indoor activities.[99,100] I anticipate that exposure to a female-linked exposure factor, such as cooking fuel, should have more impact on women than on men.

Objective and hypothesis

In this aim, I evaluate the extent to which the association between reported use of unclean cooking fuel within household and late-life cognitive function and prevalence of neurocognitive disorder may differ by sex. As Indian men are typically not tasked with household cooking responsibilities, their exposure to indoor air pollutants from cooking fuel should be less compared with women. As such, I hypothesize that exposure to pollutants from reporting use unclean cooking fuel within a household will be negatively associated with late-life cognitive measures and this effect will be stronger among older Indian women than men.

Methods

Data and population

This aim uses data obtained from men and women assessed in the Harmonized Diagnostic Assessment of Dementia for the Longitudinal Aging Study in India (LASI-DAD); participants were selected from the larger LASI baseline survey. The LASI survey itself is a population-based panel study that initially interviewed 72,250 individuals aged 45 years and older drawn from 44,949 Indian households. Topics included information on health, economic and social well-being. Data for wave 1 was collected from October 2017 to March 2020 by home interviewers in rural and urban areas across 18 states and union territories. The LASI sample is fully representative of India, and of each state and union territory, with an overall individual response rate of 87%. The main goal of LASI is to collect longitudinal data on disease burden, functional health, healthcare, and social and economic wellbeing of older adults that is comparable to international standards. All measures in the baseline LASI were specific and sensitive to the Indian population and harmonized to the Health and Retirement Survey (HRS) and international sister studies on aging and retirement. Detailed information on the baseline LASI study protocol, sampling design, data collection and methodologies have been previously published.[66]

LASI-DAD included a subsample of 4,096 participants aged 60 years and older drawn from the larger LASI study by a two-stage stratified sampling design with oversampling of participants with high risk of cognitive impairment. This was done to ensure a sufficient number of participants with dementia and mild cognitive impairment.[66] LASI-DAD participants were interviewed at home or in participating hospitals according to their preference. Overall, the response rate for the LASI-DAD was 83%. The LASI-DAD obtained additional data on late-life cognition and dementia using a battery of cognitive tests and informant interviews, health examination, venous blood assays, and genotyping. The LASI-DAD cognitive tests were selected to allow for international comparisons and are suitable for administration to illiterate and innumerate populations. The details of the LASI-DAD cognitive tests have been described elsewhere.[67] The main goal of LASI-DAD is to: 1) Collect, analyze and disseminate high-quality data on late-life cognition, dementia, and their associated risk factors, with the objective of estimating prevalence and identifying determinants of dementia in India, and 2) Enable cross-country analysis of late-life cognition and dementia within the Harmonized Cognitive Assessment Protocol (HCAP) of the HRS and other sister studies.[68] The present aim used newly available cross-sectional data from baseline LASI-DAD interviews from 2017 to 2020. A total of 2,207 women and 1,889 men were eligible for inclusion in this aim and 2,152 women and 1,848 men with complete data were included in the current analyses associated with this aim.

Exposure

The primary exposure of interest was self-reports of exposure to pollutants from reported household use of unclean cooking fuel. This was assessed using a proxy of self-reported type of cooking fuel used within the household at time of survey. Unclean cooking fuel was categorized as “yes” if the self-reported main source of cooking fuel was kerosene, charcoal, lignite, coal, crop residue, wood or shrub, dung cake. Otherwise, use of unclean cooking fuel was categorized as “no” if the main source of cooking fuel was reported as liquefied petroleum gas (LPG), biogas, electric, or the participant indicated that do not cook at home.

Outcomes

Cognitive function was assessed via in-depth cognitive and neuropsychological test batteries administered during an hour-long face-to-face interview. The cognitive test battery was adapted from the tests in the Harmonized Cognitive Assessment Protocol [69] and modified for cultural appropriateness and validity with innumerate and low-literacy populations.[70] For example, backward counts and number series were dropped in LASI-DAD as they were difficult to administer to a largely innumerate population. Instead, additional tests designed specifically for illiterate and innumerate populations, such as the Hindi Mental State Exam, symbol cancellation and Go-No-Go test, were included.[66] The tests were grouped into broad domains of well-accepted categories of cognitive functioning[71] based on a priori knowledge and Cattell-Horn-Carroll (CHC) theory of human cognitive abilities.[72]

LASI-DAD also calculated an overall cognitive function summary factor score for general cognitive performance using a previously developed hierarchical multiple domain factor analysis. These analyses generates factor scores from both narrow and broad domains.[70] Additionally, domain-specific cognitive function was separately assessed in five broad domains including: 1) orientation, 2) executive function, 3) language/fluency, 4) memory, and 5) visuospatial skills based on a factor analysis determined structure of the LASI-DAD cognitive battery.[70] The orientation domain factor score was derived from responses to three questions on orientation to time (name the current month, year, season), two questions on orientation to place (state, city), and one question on current events (name the Prime Minister). The executive function domain factor score was derived from test scores on a numeracy task, backwards day counting, symbol cancellation, Digit Span Forward and Backward, Ravens progressive matrices task, clock drawing, and two trials of the Go-No-Go test. The language/fluency domain factor score was calculated from scores based on tests on animal naming, writing or saying a sentence, phrase repetition, naming of common objects by sight (watch, pencil), naming of common objects by description (elbow, hammer, scissors, coconut, window), following a verbal or acted command to close one's eyes, and completing a 3-stage task. The memory domain factor score was based on immediate, delayed, and recognition recall of a 10-word list; immediate, delayed, and recognition recall of the Logical Memory test, immediate and delayed recall of the Brave Man story learning test, and a three-word recall task. Lastly, the visuospatial domain factor score was derived from scores based on constructional praxis tests (drawing a circle, rectangle, cube, and diamond) and interlocking pentagons.

A binary measure of mild or major neurocognitive disorder was derived using DSM-5 criteria defined by objective cognitive function, informant-rated cognitive decline, informant-rated functional decline, and exclusion of schizophrenia, active delirium or major depression.[73] Objective cognitive function was estimated using summary factor scores representing specific domains of memory, language, executive function and visuospatial ability that tests an individual’s ability to remember, think, or attend to stimuli.[70] Cutoffs of 1 or 1.5 standard deviations (SD) below the mean on each cognitive domain score were identified using a normative sample without functional limitations or other exclusionary criteria.[73] Informant-rated cognitive decline was ascertained using the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE), a screening instrument used to assess change in cognitive and functional ability compared with 10 years ago, validated for LASI-DAD.[74] Informant-rated functional decline in everyday activities was ascertained using the Blessed Dementia Rating Scale Parts 1 (instrumental activities of daily living) and II (activities of daily living).[75] Mild neurocognitive disorder was defined as: 1) Functional score of ≤1 SD in one or more domain, 2) No activities of daily living impairment, and no or minimal loss in Blessed Part I, or discordant informant reports for Blessed Part I vs. Part II, 3) IQCODE score of ≥3.2 or poor self-rated memory, and 4) No schizophrenia, active delirium during testing or history of major depression. Major neurocognitive disorder was defined as: 1) Functional score of a) ≤1.5 SD in two domains, or b) ≤1.5 SD in one domain, and ≤1 SD in two or more domains, 2) Any activities of daily living impairment, Blessed Part I score of ≥2, or Blessed Part 2 score of ≥1, 3) IQCODE score of ≥3.5 and poor self-rated memory, and 4) No schizophrenia, active delirium during testing or history of major depression. Due to a small number of people with major neurocognitive disorder, mild and major neurocognitive disorder were collapsed into a single category referred to as neurocognitive disorder.

Effect modifier

Male or female sex was coded by the interviewer, and only asked of the respondent if sex was not clear to the interviewer.

Covariates

Several variables in the LASI-DAD were used in analyses as potential confounders. This included early-life (caste, paternal education level as proxy for childhood socio-economic status, education in years) and mid-to-late life (age, urbanicity, annual household income in Rupees, housing type and employment status) demographic and socioeconomic status measures. These variables were collected at baseline, selected a priori, and based on the causal diagram (Figure 2.1). Everyday life in India is significantly shaped by social institutions like the caste system. Within the Indian caste system, scheduled castes/tribes and other backward class have been considered lower-ranked social groups and these individuals typically experience disadvantaged health and social outcomes.[76] For the purpose of this aim, caste was recoded into scheduled castes/scheduled tribes, other backward class, or not one of these castes. Childhood socioeconomic status was considered using paternal educational attainment (never attended school, primary school [grade 7] or less, middle school [grade 8] or higher, missing) as a proxy. Highest education attainment of the respondent in years was included as it can influence sex-roles within households, lead to or maintain residency in underdeveloped areas, and contribute towards economic and job opportunities,[11,64] collectively influencing exposure to unclean cooking fuel. Residence at time of interview (urban community vs. rural village), annual household income in Rupees, housing type (kutcha vs. pucca) and current employment status (employed, unemployed, and never worked) were also included as other measures of socioeconomic status that can influence both type of cooking fuel and cognitive measures. Age (years) was included as it is a well-known risk factor for cognitive impairment.[1] Since 99% of men and women were married and main lifetime occupation was highly aggregated, marital status (married vs. never married) and main lifetime occupation (senior professionals, service/shop/craft workers, agriculture/forestry/fishery, plant/machine operators, elementary occupations, other, and never worked) were excluded from all analytical models. Reported use of mosquito coils/incense sticks/smoker in house (yes vs. no), current job around burning material, exhaust, or smoke (yes vs. no), and current job close to chemicals, pesticides, or herbicides (yes vs. no) were also excluded from analytical models as they do not influence type of cooking fuel or fall in the causal pathway. Religion (Hindu, Muslim, Christian, Sikh and Buddhist/Jain/None), number of people in household, and difficulty with hearing or seeing (yes vs. no) were only included to describe the sample.

Statistical analysis

Characteristics of the sample were summarized separately for men and women and by type of cooking fuel. Generalized linear models with an identity link function estimated the mean differences in overall and domain-specific factor scores of cognitive performances (continuous measures) for people who reported household use of unclean cooking fuel compared with clean cooking fuel. Generalized linear models with a log link function and Poisson distribution[77] estimated the prevalence ratio of neurocognitive disorder for people who reported household use of unclean cooking fuel compared with clean cooking fuel. Covariates mentioned earlier were included to control for potential confounding assuming the confounding structure were similar between men and women. Models included an interaction term between reported household use of unclean cooking fuel and sex to assess whether the association differed between men and women and a *P*-value of the interaction term was reported. The primary model was adjusted for early-life potential confounders (caste, paternal education as proxy for childhood socioeconomic status, education in years) with subsequent models additionally adjusted for mid-to-late-life (urbanicity, age, annual household income and housing type, with and without employment status) potential confounders (Figure 2.1). As employment status may not have the same confounding structure for men as for women, fully adjusted models excluding employment status (model 2) were considered the main models in this aim. All analyses were adjusted for the complex sampling design of LASI-DAD to account for stratification and clustering using survey estimation procedures and appropriate weights were utilized.[56,78] All analyses were conducted using Stata 18 SE (College Station, TX).

Data availability

LASI-DAD data used for analyses are available from the Gateway to Global Aging Data website (https://g2aging.org/home).

Results

The analytic sample included 1,848 men (weighted count = 2,212) (98% of all men) and 2,152 women (weighted count=2,462) (98% of all women) for a total sample of 4,000 participants (weighted count=4,674) aged 60 years and older with complete data (Table 2.1). Mean age of the sample at interview was 69 years (SD=8), nearly all were married (99%), with majority being Hindus (82%), residing in rural villages (61%), and identified as belonging to the lower castes (scheduled caste/tribe or other backward class) (70%). Forty percent of the sample reported using unclean cooking fuel as their primary fuel source for the household. Among men, 41% reported using unclean cooking fuel in their household and among women, 39% reported using unclean cooking fuel in their household. The majority of men and women who reported using unclean cooking fuel in their household lived in rural villages (Men: 90%, Women: 88%) and came from lower socioeconomic background with most never having attended school (Men: 50%, Women: 83%), resided in kutcha homes (Men: 63%, Women: 61%), and earned a lower median annual household income (Men: 15,000 Rupees, Women: 15,000 Rupees). Very few men reported having never worked for wages in their lifetime (5%), in contrast, 51% of women reported never having worked outside the home in their lifetime. Agriculture, forestry, or fishery work were the most frequent lifetime occupations among both men and women. Only 32% of respondents reported being employed at the time of survey, 8% reported working near burning materials, exhaust or smoke and 11% in jobs close to chemicals, pesticides or herbicides.

Mean overall and domain specific cognitive factor scores at baseline were consistently lower for those who reported household use of unclean cooking fuel compared with clean cooking fuel; women performed consistently lower than men across all domains. Prevalence of neurocognitive disorder in the overall sample was 25%; prevalence was higher among men and women who reported household use of unclean cooking fuel (Men: 30%, Women: 30%) compared with their counterparts who reported using clean cooking fuel in their household (Men: 20%, Women: 24%).

Among women, reported household use of unclean cooking fuel compared with clean cooking fuel was associated with lower performance across overall and all specific cognitive domains (Table 2.2). When adjusted for early and mid-to-late life potential confounders (model 2), women who reported household use of unclean cooking fuel had on average lower overall cognitive factor scores than women who reported household use of clean cooking fuel (Coefficient: -0.17, 95% CI -0.23, -0.11). This trend was consistent over the five specific cognitive domains among women. In contrast, men who reported household use of unclean cooking fuel had lower average factor scores only in the executive functioning domain than men who reported household use of clean cooking fuel (Coefficient: -0.09, 95% CI -0.16, -0.02). There was modest evidence of effect modification by sex on the overall cognitive factor score (*P*-value for interaction: 0.011) and domain specific factor scores for orientation (*P*-value for interaction: 0.002), language/fluency (*P*-value for interaction: 0.009), and visuospatial ability (*P*-value for interaction: 0.004) where the mean differences in cognitive performance scores comparing reported household use of unclean cooking fuel versus clean cooking fuel were greater among women than men.

Reported household use of unclean cooking fuel was associated with a higher prevalence of neurocognitive disorder among men, and possibly among women (Table 2.3). Among men, estimates from the model after adjusting for early and mid-to-late-life confounders (model 2) suggested reported household use of unclean cooking fuel was associated with a higher prevalence of neurocognitive disorder compared with men who reported household use of clean cooking fuel (Prevalence Ratio [PR]: 1.41, 95% CI 1.09,1.83). Among women, this association was moderately consistent with higher estimates when adjusted for early (PR: 1.22, 95% CI 0.98, 1.51), and additionally for mid-to-late-life confounders (PR: 1.18, 95% CI 0.93, 1.50), but the parameter estimates ranged from no effect to 50% increase in prevalence. There was no evidence of effect modification by sex in the association between reported household use of unclean cooking fuel and prevalence of neurocognitive disorder (*P*-value for interaction: 0.273).

Discussion

In a nationally representative sample of Indian men and women aged 60 years and older, reported household use of unclean cooking fuel was negatively associated with late-life cognitive function compared with reported household use of clean cooking fuel. This effect was slightly stronger among women for overall and three specific cognitive domains when using continuous measures of cognitive functions. However, there was no difference by sex when assessing prevalence of neurocognitive disorder by type of reported household cooking fuel. Men who reported household use of unclean cooking fuel had higher prevalence of neurocognitive disorder compared with men who reported household use of clean cooking fuel. Results for women were consistent with values ranging from little or no effect to a moderate increase in prevalence.

As men in India are not customarily responsible for household cooking and may be more likely than women to spend time away from the kitchen and outside of the home, I hypothesized that the exposure to pollutants from household use of unclean cooking fuel would be lower for men than for women. Evidence for this effect was seen primarily in the findings of overall and domain specific cognitive factor scores (Table 2.2) where mean differences in cognitive factor scores by reported type of household fuel were consistently larger across all domains for women than for men. However, even after adjusting for education attainment, the test-based performance scores in these continuous measures of cognitive function may be subject to a greater degree of residual confounding by education among women than in men. In this sample, 50% of men who reported household use of unclean cooking fuel had never attended school, but only 6% reported never having worked over their lifetime. In contrast, 83% of women who reported household use of unclean cooking fuel had never attended school and 42% reported never having worked outside the home during their lifetime. As such, the lower cognitive test scores among women may be partially driven by systemic sex-based differences in opportunities in social investment and upward mobility for girls in Indian society compared to boys.[62,64] In fact, participation of women in the Indian labor force has been consistently low and in 2018 only 21% of women were working.[101] Primary barriers for women in the workforce include a conservative culture and social stigma that emphasizes a women's place is at home.[102] When women are employed, many occupy jobs in domestic or unskilled work associated with high manual labor.[102] The sex-based differences in upward mobility such as employment opportunities despite educational attainment is reflected in this sample.

Even though men are less likely to be directly exposed to pollutants from household cooking fuel, there are two possibilities that could be driving the effect of reported household use of unclean cooking fuel on higher prevalence of neurocognitive disorder observed among men. First, most men from households using unclean cooking fuel primarily lived in kutcha homes (63%), in rural areas (90%), and had a lifetime occupation in agriculture, forestry, or fishery (52%) earning a median annual household income of 15,000 Rupees (Interquartile range [IQR]:

0, 66,000). In contrast, men from households reporting use of clean cooking fuel primarily lived in pucca homes (76%), in urban areas (55%), and had a lifetime occupation in office-based jobs such as senior officials, service or shop managers (39%) earning a median annual household income of 40,000 Rupees (IQR: 0, 144,000). As such, men reporting household use of unclean cooking fuel came from poorer backgrounds, worked outdoors and were more likely to be exposed to outdoor sources of air pollutants compared with men from households reporting use of clean cooking fuel. Second, 23% of men reporting household use of unclean cooking fuel were employed in jobs close to chemicals,[103] pesticides,[104,105] or herbicides,[106] compared with 12% of men from households reporting use of clean cooking fuel. As such, it is likely there is possible under controlled confounding by occupational exposure to environmental pollutants such as outdoor air pollution and pesticides in the associations observed among men.

The difference in findings between continuous and binary cognitive measures can be attributed to the differences in construction of these two measures. Neurocognitive disorder was defined by an algorithm of objective cognitive function scores and informant reports incorporating elements of daily function beyond what would be captured in the cognitive function tests alone. In contrast, continuous cognitive function scores were exclusively test-driven and these cross-sectional measures are more subject to confounding by early-life socio-economic factors, as between-person variation in late-life cognitive function is heavily influenced by pre-morbid differences in cognitive function.[79] As such, poor results in cognitive tests, which may be partially driven by early-life sex-based disparities, may not necessarily correspond with lower functioning in daily activities.

This aim used self-report of the type of cooking fuel used within the household at the time of interview during 2017-2020. This was treated as a proxy for cumulative lifetime exposure to pollutants from household use of unclean cooking fuel. However, it is unlikely that both men and women who reported household use of clean cooking fuel were lifetime users because universal access to clean fuel in India was only recently initiated. In 2016, the Pradhan Mantri Ujjwala Yojana (PMUY) initiative aimed to increase universal access to clean cooking fuel among poor and rural families.[81] As such, the measurement in this study is likely to represent current, but not lifetime exposure to pollutants from unclean cooking fuel. This type of misclassification of the exposure is likely to bias results towards the null in this aim. Additionally, variations in the level of exposure to pollutants from reported household use of unclean cooking fuel remain unknown for both men and women. As men are not directly involved in cooking activities, their exposure to pollutants from unclean cooking fuel is dependent upon factors such as the amount and timing of exposure within the home and whether the kitchen is in a separate room. Without more information on the variations and level of exposure among men, it is difficult to be specific as to the direction of bias in study findings.

This underscores some of the limitations of the current aim. First, exposure to reported household use of unclean cooking fuel is subject to misclassification as the LASI-DAD does not include a direct measurement of indoor air pollution. Further, reported use of certain fuel within households may not correspond with lifetime use or harmful exposure duration or levels. Second, there are limited early and mid-life socio-economic status measures that may not accurately capture the complex structure of early-life sex-based differential socio-economic opportunities in India leading to inadequate control of potential confounding factors. Third, as harmonized cognitive function measures were assessed at a single time point, it was not possible to assess rate of cognitive change. Fourth, as with all aging studies, these findings are subject to some degree of survival bias arising from selective survival of both men and women up to 60 years of age. As poorer households are more likely to use unclean cooking fuel and poverty is associated with increased mortality,[107] it is possible that participants from households reporting use of unclean cooking fuel included in the study are more selected for resilience to surviving the effects of poverty compared to those who died earlier. However, given that there is no difference in the mean age in this sample by type of cooking fuel reported within households or by sex, it is unlikely survival bias is a significant contributing factor to these findings. Last, as the DSM-5 criteria is operationalized using survey information and not by trained clinician or panel of neuropsychologists or neurologists, it is important to interpret DSM-5 classification of neurocognitive disorder separate from a clinical diagnosis.

There are also multiple strengths of this aim. These include using data from a large, nationally representative sample of Indian men and women with harmonized measures of cognitive measures. Overall and domain specific cognitive factor scores allowed for identification of variations within specific domains. Additionally, inclusion of the DSM-5-based measure of neurocognitive disorder captured assessment of cognitive function incorporating both objective cognitive functional scores and informant reports.

Given recent findings of the association between indoor air pollutants and cognitive measures among older adults in India,[34,61] this aim further investigated whether the effect of exposure to reported use of unclean cooking fuel within households differed by sex. While there is modest evidence of differences by sex, findings suggest the need to further disentangle the effects of early-life socio-economic disparities and differential exposure to outdoor and workplace pollutants to better understand how late-life cognitive function may vary for men and women. Further understanding of these mechanisms will be beneficial in developing policy recommendations specific to men and women to minimize exposure to harmful pollutants.

Tables and Figures

Table 2.1. Weighted/unweighted counts and weighted column percentages of demographic, socio-economic and cognitive performance measures of Indian men and women aged ≥60 years from the LASI-DAD study by primary household cooking fuel and sex.

	All	Men		Women	
		Weighted N: 2,212 Unweighted N: 1,848		Weighted N: 2,462 Unweighted N: 2,152	
Primary Cooking Fuel		Clean	Unclean	Clean	Unclean
Weighted N (row %)	**4,674 (100)**	**1,300 (28)**	**912 (20)**	**1,493 (32)**	**969 (20)**
Unweighted N (row %)	4,000 (100)	1,092 (27)	756 (19)	1,273 (32)	879 (22)
Demographic characteristics					
Urbanicity, n (%)					
Urban community	1,835 (39)	717 (55)	95 (10)	908 (61)	115 (12)
Rural village	2,839 (61)	583 (45)	817 (90)	585 (39)	854 (88)
Age at interview, mean (SD)	69 (8)	69 (7)	69 (7)	69 (8)	68 (8)
Marital status, n (%)					
Never married	43 (1)	16 (1)	12 (1)	10 (1)	6 (1)
Married	4,597 (99)	1,260 (99)	897 (99)	1,477 (99)	964 (99)
Religion, n (%)					
Hindu	3,833 (82)	1035 (80)	811 (89)	1150 (77)	838 (86)
Muslim	533 (11)	167 (13)	63 (7)	206 (14)	96 (10)
Christian	128 (3)	39 (3)	15 (2)	58 (4)	16 (2)
Sikh	112 (2)	37 (3)	16 (2)	42 (3)	17 (2)
Buddhist/Jain/None	67 (1)	22 (2)	7 (1)	36 (2)	2 (0)
Number of people in household, median (IQR)	5 (2-6)	5 (3-6)	5 (2-6)	5 (3-6)	5 (2-6)
Socioeconomic status					
Caste system, n (%)					
No or other caste	1,400 (30)	454 (35)	186 (20)	543 (36)	217 (22)
Scheduled caste/tribe	1,171 (25)	250 (19)	323 (35)	286 (19)	313 (32)
Other backward class	2,103 (45)	596 (46)	403 (44)	664 (44)	440 (45)
Type of home, n (%)					
Pucca (permanent)	2800 (60)	987 (76)	340 (37)	1093 (73)	381 (39)
Kutcha (semi-permanent)	1874 (40)	313 (24)	572 (63)	400 (27)	588 (61)
Paternal education, n (%)					
Never attended school	3,284 (70)	814 (63)	722 (79)	982 (66)	766 (79)
Primary school (grade 7) or less	764 (16)	283 (22)	119 (13)	275 (18)	87 (9)
Middle school (grades 8) or more	346 (7)	136 (10)	24 (3)	146 (10)	40 (4)
Missing	280 (6)	67 (5)	46 (5)	90 (6)	76 (8)
Highest educational attainment, n (%)					
Never attended school	2,523 (54)	372 (29)	460 (50)	884 (59)	807 (83)
Primary school (grade 7) or less	1,115 (24)	319 (25)	303 (33)	360 (24)	134 (14)
Middle school (grades 8) or more	1,035 (22)	609 (47)	149 (16)	248 (17)	29 (3)
Years of education, mean (SD)	4 (5)	7 (5)	3 (4)	3 (4)	1 (2)
Current employment status, n (%)					
Unemployed	1,797 (38)	696 (54)	386 (42)	395 (26)	321 (33)
Employed	1,511 (32)	545 (42)	475 (52)	247 (17)	244 (25)
Never worked	1,366 (29)	59 (5)	52 (6)	851 (57)	404 (42)
Main lifetime occupation, n (%)					
Senior professionals	333 (7)	248 (19)	32 (4)	44 (3)	8 (1)
Service, shop, craft workers	491 (11)	256 (20)	84 (9)	116 (8)	35 (4)
Agricultural/forestry/fishery	1,303 (28)	320 (25)	473 (52)	205 (14)	306 (32)
Plant and machine operators	119 (3)	92 (7)	19 (2)	6 (0)	2 (0)
Elementary occupations	669 (14)	202 (16)	154 (17)	185 (12)	129 (13)
Other	381 (8)	120 (9)	94 (10)	83 (6)	83 (9)
Never worked	1,366 (29)	59 (5)	52 (6)	851 (57)	404 (42)

Table 2.1. Weighted/unweighted counts and weighted column percentages of demographic, socio-economic and cognitive performance measures of Indian men and women aged ≥60 years from the LASI-DAD study by primary household cooking fuel and sex.

	All	Men		Women	
		Weighted N: 2,212 Unweighted N: 1,848		Weighted N: 2,462 Unweighted N: 2,152	
Primary Cooking Fuel		Clean	Unclean	Clean	Unclean
Weighted N (row %)	**4,674 (100)**	**1,300 (28)**	**912 (20)**	**1,493 (32)**	**969 (20)**
Unweighted N (row %)	4,000 (100)	1,092 (27)	756 (19)	1,273 (32)	879 (22)
Annual household income (Rupees), median (IQR)	27,000 (0-117000)	40,000 (0-144000)	15,000 (0-66000)	50,000 (0-150000)	15,000 (0-70000)
Other indoor/outdoor air pollutants					
Mosquito coils, incense, smoker, n (%)					
No	394 (8)	90 (7)	88 (10)	111 (7)	106 (11)
Yes	4280 (92)	1210 (93)	824 (90)	1382 (93)	864 (89)
Current job around burning material, exhaust, or smoke					
No	1,151 (25)	414 (32)	341 (38)	199 (13)	197 (20)
Yes	361 (8)	132 (10)	134 (15)	49 (3)	46 (5)
Not working at time of survey	3,147 (68)	748 (58)	431 (48)	1,244 (83)	724 (75)
Current job close to chemicals, pesticides, or herbicides					
No	1,014 (22)	385 (30)	270 (30)	190 (13)	169 (17)
Yes	498 (11)	161 (12)	205 (23)	58 (4)	75 (8)
Not working at time of survey	3,147 (68)	748 (58)	431 (48)	1,244 (83)	724 (75)
Sensory impairment					
Difficulty hearing or seeing					
No	2293 (49)	679 (53)	443 (49)	731 (49)	441 (46)
Yes	2363 (51)	614 (47)	466 (51)	758 (51)	526 (54)
Cognitive measures					
General cognitive factor score, mean (SD)	-0.05 (0.93)	0.48 (0.91)	-0.07 (0.79)	-0.12 (0.90)	-0.63 (0.68)
Orientation factor score, mean (SD)	-0.08 (0.82)	0.39 (0.68)	-0.001 (0.71)	-0.19 (0.81)	-0.62 (0.70)
Executive functioning factor score, mean (SD)	-0.04 (0.91)	0.49 (0.89)	-0.06 (0.80)	-0.13 (0.86)	-0.61 (0.66)
Language/fluency factor score, mean (SD)	-0.04 (0.80)	0.27 (0.79)	-0.06 (0.74)	-0.07 (0.79)	-0.41 (0.72)
Memory factor score, mean (SD)	-0.04 (0.95)	0.24 (0.97)	-0.22 (0.82)	0.04 (0.99)	-0.37 (0.84)
Visuospatial factor score, mean (SD)	-0.02 (0.83)	0.33 (0.86)	0.03 (0.78)	-0.10 (0.81)	-0.42 (0.63)
DSM-5 neurocognitive disorder, n (%)					
No neurocognitive disorder	3,495 (75)	1,040 (80)	642 (70)	1,133 (76)	680 (70)
Mild/major neurocognitive disorder	1,179 (25)	260 (20)	270 (30)	360 (24)	290 (30)

LASI-DAD: Harmonized Diagnostic Assessment of Dementia for the Longitudinal Aging Study in India.
Unclean cooking fuel: Kerosene, charcoal, lignite, coal, crop residue, wood or shrub, or dung cake as primary cooking fuel.
Clean cooking fuel: Electric, biogas, liquified petroleum gas, or does not cook at home.

Table 2.2. Association between primary household cooking fuel and late-life overall and domain specific cognitive function among Indian men and women aged ≥60 years from the LASI-DAD study.

	Crude Coefficient (95% CI)		Model 1 Coefficient (95% CI)		Model 2 Coefficient (95% CI)		Model 3 Coefficient (95% CI)	
	Men	Women	Men	Women	Men	Women	Men	Women
Overall cognitive factor score								
Clean	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Unclean	-0.55 (-0.64, -0.47)	-0.51 (-0.58, -0.44)	-0.11 (-0.18, -0.04)	-0.23 (-0.29, -0.17)	-0.06 (-0.13, 0.01)	-0.17 (-0.23, -0.11)	-0.07 (-0.13, 0.003)	-0.17 (-0.23, -0.11)
P for interaction		*0.416*		*0.011*		*0.011*		*0.012*
Orientation factor score								
Clean	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Unclean	-0.40 (-0.47, -0.32)	-0.43 (-0.50, -0.36)	-0.09 (-0.15, -0.02)	-0.23 (-0.29, -0.16)	-0.04 (-0.11, 0.03)	-0.18 (-0.24, -0.11)	-0.04 (-0.11, 0.02)	-0.18 (-0.25, -0.11)
P for interaction		*0.538*		*0.002*		*0.002*		*0.002*
Executive functioning factor score								
Clean	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Unclean	-0.55 (-0.64, -0.47)	-0.47 (-0.54, -0.41)	-0.14 (-0.21, -0.07)	-0.21 (-0.27, -0.15)	-0.09 (-0.16, -0.02)	-0.15 (-0.21, -0.09)	-0.09 (-0.16, -0.02)	-0.15 (-0.21, -0.09)
P for interaction		*0.157*		*0.128*		*0.153*		*0.145*
Language/fluency factor score								
Clean	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Unclean	-0.34 (-0.41, -0.26)	-0.35 (-0.42, -0.28)	-0.03 (-0.11, 0.04)	-0.16 (-0.22, -0.00)	-0.01 (-0.09, 0.06)	-0.13 (-0.20, -0.07)	-0.02 (-0.09, 0.06)	-0.13 (-0.20, -0.06)
P for interaction		*0.847*		*0.009*		*0.009*		*0.020*
Memory factor score								
Clean	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Unclean	-0.46 (-0.55, -0.37)	-0.41 (-0.50, -0.33)	-0.11 (-0.19, -0.02)	-0.19 (-0.26, -0.11)	-0.07 (-0.15, 0.02)	-0.14 (-0.22, -0.06)	-0.07 (-0.15, 0.02)	-0.14 (-0.22, -0.06)
P for interaction		*0.443*		*0.149*		*0.168*		*0.160*
Visuospatial factor score								
Clean	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Unclean	-0.30 (-0.38, -0.22)	-0.32 (-0.38, -0.25)	0.02 (-0.06, 0.09)	-0.12 (-0.18, -0.06)	0.02 (-0.06, 0.10)	-0.12 (-0.18, -0.06)	0.02 (-0.06, 0.09)	-0.12 (-0.19, -0.05)
P for interaction		*0.733*		*0.005*		*0.004*		*0.004*

P for interaction: *P*-value of the interaction term between reported household use of unclean cooking fuel and sex.

Model 1: Adjusted for early life factors including caste, paternal education, and education in years.

Model 2: Additionally adjusted for age, annual household income, housing type, and urbanicity.

Model 3: Additionally adjusted for employment status.

Unclean cooking fuel: Kerosene, charcoal, lignite, coal, crop residue, wood or shrub, or dung cake as main source of cooking fuel.

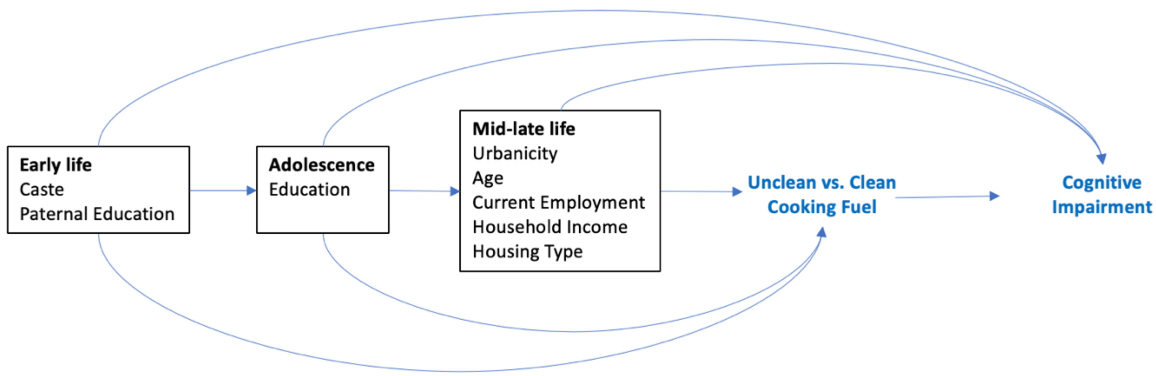
Clean cooking fuel: Electric, biogas, liquified petroleum gas, or does not cook at home.

Table 2.3. Association between primary household cooking fuel and prevalent late-life neurocognitive disorder among Indian men and women aged ≥60 years from the LASI-DAD study.

	Crude Prevalence Ratio (95% CI)		Model 1 Prevalence Ratio (95% CI)		Model 2 Prevalence Ratio (95% CI)		Model 3 Prevalence Ratio (95% CI)	
	Men	Women	Men	Women	Men	Women	Men	Women
Neurocognitive disorder								
Household cooking fuel								
Clean	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Unclean	1.69 (1.34, 2.14)	1.35 (1.09, 1.66)	1.45 (1.14, 1.85)	1.22 (0.98, 1.51)	1.41 (1.09, 1.83)	1.18 (0.93, 1.50)	1.45 (1.12, 1.89)	1.17 (0.92, 1.48)
P for interaction		*0.156*		*0.278*		*0.273*		*0.180*

Prevalence ratio estimated using GLM with Poisson distribution and log link function.
P for interaction: *P*-value of the interaction term between reported household use of unclean cooking fuel and sex.
Model 1: Adjusted for early life factors including caste, paternal education, and education in years.
Model 2: Additionally adjusted for age, annual household income, housing type, and urbanicity.
Model 3: Additionally adjusted for employment status.
Unclean cooking fuel: Kerosene, charcoal, lignite, coal, crop residue, wood or shrub, or dung cake as main cooking fuel.
Clean cooking fuel: Electric, biogas, liquified petroleum gas, or does not cook at home.

Figure 2.1. Directed acyclic graph (DAG) illustrating the effect of type of cooking fuel on late-life cognitive impairment among Indian men and women aged ≥60 years from the LASI-DAD study.



Aim 3: Late-life rate of cognitive change among veterans serving during the Korean and Vietnam War era: A longitudinal analysis using information from the KHANDLE and STAR cohorts

Abstract

Introduction: Military veterans are exposed to numerous hazards during time in service that put them at increased risk of mental and physical health problems, including possibly dementia in later life. In this aim, I investigated whether male US veterans who served during the Korean and Vietnam war eras experienced a faster rate of late-life cognitive change compared with male non-veterans. I also examined the extent to which veteran status may modify the effect of a reported lifetime encounter with blasts/explosions on rate of cognitive change.

Methods: I used data obtained from 921 men aged ≥50 years who participated in two harmonized cohort studies of older Kaiser Permanente Northern California members: the Kaiser Healthy Aging and Diverse Life Experiences (KHANDLE) (up to 4 cognitive assessments, 2017-2023) and the Study of Healthy Aging in African Americans (STAR) (up to 3 cognitive assessments, 2017-2021). Linear mixed effects models with age as the timescale estimated cognitive functioning and rate of cognitive change among veterans and non-veterans. A two-way interaction term between veteran status and self-reported exposure to reported lifetime blasts/explosions and a three-way interaction term between veteran status, age, and reported lifetime exposure to blasts/explosions assessed the extent to which veteran status modified the effect of reported lifetime exposure to blasts/explosions on cognitive function and rate of cognitive change.

Results: Average verbal episodic memory scores at age 75 years were slightly higher among veterans compared to non-veterans. There was no appreciable difference in average executive function scores at age 75 for veterans compared to non-veterans. There was no difference in the annual rate of cognitive change in either cognitive domain by veteran status. Investigating the possible modifying role of veteran status in the association between reported lifetime exposure to blasts/explosions on late-life cognitive function did not reveal robust evidence for effect modification.

Conclusion: Despite the lack of evidence in differences in rate of cognitive change by veteran status, this remains an important measure to monitor in a rapidly aging veteran population. Further work is needed to correctly assess mechanisms of potential resilience and heterogeneity within the veteran population that can impact cognitive trajectory during later life.

Introduction

Wars fought in Europe and Asia since 1941 have substantially shaped the composition of the US veteran population living today. Of the 16.5 million living veterans in 2021, almost 50% (8.1 million) are men aged 65 years or older,[13] collectively representing wartime experiences of World War II, Korean War, and Vietnam War. Among older veterans, the largest cohort are Vietnam War veterans who were 18-20 years of age in 1964 when the United States (US) entered the Vietnam War.[13] As the veteran population ages, risk of dementia is concerning as veterans frequently present with associated risk factors for dementia including posttraumatic stress disorders (PTSD),[18,19] functional disability,[108] sleep disturbances,[109,110] traumatic brain injury (TBI),[14-17] multiple sclerosis,[111] and trauma-related psychological symptoms[112] that can compound risk and accelerate neurodegenerative processes.

Epidemiological studies have continued to highlight the negative effects of the Korean[113,114] and Vietnam War[115-117] on the mental health of US veterans. Lifetime prevalence of Vietnam veterans with combat-related PTSD has been estimated as 20-30%,[118] while 12% of World War II and Korean veterans reported PTSD 45 years after experiencing combat.[119] Compared with non-veterans, Vietnam veterans have a higher prevalence of depression, anxiety, and alcohol abuse or dependency,[117] as well as higher incidence of aggression, violence, and resistance to authority.[120] Furthermore, 14% of Vietnam combat veterans sustained brain injury during their tour of duty [121] and were more likely than previous war veterans to show behavioral disturbances associated with PTSD,[122] both of which can contribute to cognitive decline.[18] In addition to these mental health challenges, Vietnam War veterans faced a number of challenges upon their return in 1973 that was exacerbated by the lack of public support for the war,[123] including lack of social support,[124] stigmatization,[125] and economic difficulties.[126]

Veteran status and cognitive function

There are several reasons why veteran status may be positively associated with late-life levels of cognitive function. Veterans can be expected to have better late-life cognitive function compared with non-veterans as military selection and service are associated with factors such as higher educational attainment, physical fitness, and cognitively engaging activities which collectively contribute to higher cognitive reserve.[127] Individuals with greater cognitive reserve have greater ability to resist the onset of symptoms related to degenerative brain changes linked to dementia than individuals with lower cognitive reserve.[128] Selection into military service is restricted to individuals with good physical, mental and moral standards in their youth, those with poor health are usually rejected from enlisting or commissioning.[129] Also, many veterans served during times when military drafts were present.[13] During military service, service members have access to additional training and educational opportunities as a requirement of their military occupational specialty, or through benefits such as the GI Bill.[130] Military service also ensures healthcare, stability in income, earnings opportunity through the VA loan program,[131] and other resources that can improve living conditions.[132] The physical training and comradery built during training can have long-term beneficial effects on overall health and wellbeing ultimately improving cognitive function.[133] Ultimately, military service can set up unharmed veterans on a better life trajectory that may be associated with better cognition in later life.

There are also many reasons why veteran status may be negatively associated with late-life levels of cognitive function. Military service can have adverse effects on late-life cognition due to service-related injuries, hazardous exposures and prevalent unhealthy behaviors that impair health and well-being. For example, military environments often foster heavy alcohol or substance use, contributing to unhealthy behaviors.[134,135] Veterans also have a higher prevalence of potential risk factors for cognitive decline[22] compared to the general population, including sleep disorders,[136] cardiovascular disease, [137] diabetes[135], sensory impairment,[138] depression,[136] traumatic brain injury (TBIs),[139,140] and post-traumatic stress disorder (PTSD).[113] PTSD can accelerate memory decline in older adults and is associated with twice the risk of dementia.[141] In a recent review article, four studies on US military service members highlighted that veterans diagnosed with PTSD or major depressive disorder are at greater risk of developing dementia than healthy controls.[18] TBI from explosions and blasts can also be a potential catalyst for cognitive decline.[142] In a nationally representative sample of 188,000 older veterans, TBI was associated with 60% higher risk of dementia over a nine year period.[15] In addition, the effects of repeated low- to medium-level blasts on the brain experienced during military training and combat deployments[143] has been associated with hearing loss,[144] and accelerated time to dementia.[145] The cumulative burden of TBIs can vary by type of exposure ranging from military combat, sports injuries, to car accidents. TBIs are marked by neural changes,[146] vascular injuries,[147] and structural alterations,[148] that can interact with normative aging to lower cognitive reserve and influence decline.[149] Taking into consideration all these possibilities, the positive factors associated with military enlistment and service which can contribute towards higher cognitive reserve may be countermanded by the potential negative effects of veteran status.

Current studies

Much of the extant scientific literature on dementia among veterans focuses on life-course consequences of military service and chronic conditions[150] and cognitive changes within the veteran population.[151] Cognitive aging research on veterans has examined effects of disadvantaged neighborhood and time to dementia,[152] sex differences and incident dementia,[153] diabetes-associated genetic variants and dementia,[154] agent orange and dementia,[20] and adverse childhood socioeconomic status and dementia.[155] A longitudinal study of older male veterans found that at age 66 years, Vietnam veterans had poorer health (high blood pressure, diabetes, cancer, lung disease, heart disease, stroke, psychiatric conditions, and arthritis) compared with veterans of other wars, but experienced fewer limitations in activities of daily living and reported better health in older age.[156] Only one study evaluated differences in rate of cognitive decline, in this case between female veterans versus non-veterans;[157] this study reported that female veterans experienced more pronounced rate of cognitive decline compared to non-veterans. One of the few studies comparing late-life cognitive trajectories of men aged 65 years or older by veteran status found World War II and the Korean War veterans experienced better cognitive function compared with non-veterans at retirement age, but their cognitive performance declined more rapidly over time.[133] A recent study of primarily White veterans, most of whom served before the start of World War II, and non-veterans, found no effect of veteran status on cognitive decline over a 10-year period.[158] Further, there was no effect modification by TBI.[158] In summary, previous studies suggest that within the veteran population, the prevalence and risk of dementia are high among veterans exposed to various chronic and socioeconomic conditions. However, when comparing veterans to non-veterans, there are conflicting findings.

Gaps and impact

In general much of the previous research comparing cognitive aging by veteran status has been limited to primarily White respondents with small sample sizes and short duration of follow-up.[159,160] Only a few have compared cognitive trajectories[133,157,158] with opposing findings. Some studies did not have non-veteran respondents losing the opportunity to determine the role that veteran status plays in cognitive capacity among old ages. This is an important gap to bridge as military service has been associated with protective factors that can initially help preserve cognitive function,[13] but can potentially lead to faster rate of cognitive decline as the underlying risks from years of military service eventually prevail.[157] Additionally, it is important to include a diverse sample of veterans as minoritized racial and ethnic groups are increasingly represented in veteran cohorts[161] and experience more social stressors to health.[162] This aim adds to existing literature by identifying differences in cognitive trajectories among a racially and ethnically diverse group of male veterans compared with male non-veterans.

Objective and hypothesis

In this aim, I investigate potential differences in late-life cognitive functioning and rate of cognitive change by veteran status. Additionally, I examine the extent to which veteran status may modify the association between reported lifetime encounter with blasts/explosions and late-life rate of cognitive change. I hypothesized that late-life cognitive scores will be higher, but rate of cognitive change will be faster among veterans compared with non-veterans. Additionally, I hypothesized that the effect of a reported lifetime encounter with blasts/explosions on late-life rate of cognitive change will be stronger for veterans than non-veterans reflecting possibly greater intensity of exposure to this risk if it occurs.

Methods

Data and population

This aim used harmonized data from the Kaiser Healthy Aging and Diverse Life Experiences (KHANDLE) and Study of Healthy Aging in African Americans (STAR) cohorts with up to four waves of measurements on participants' executive function and verbal episodic memory. KHANDLE participants included long-term members of Kaiser Permanente Northern California from San Francisco Bay and Sacramento areas of California who were 65 years or older as of January 1, 2017, spoke English or Spanish, and were former participants of Kaiser Permanente multiphasic health checkup exams between 1964 to 1985. Recruitment of KHANDLE participants was accomplished by stratified random sampling (race/ethnicity, educational attainment) from their Kaiser Permanente records. Classification of self-reported race and educational attainment was obtained from information collected routinely during health checkup exams. Recruitment was done with a goal of equal representation of Asian, Black, Latino, and White participants with a diversity of educational attainment patterns. KHANDLE aimed to evaluate how race/ethnicity and life course health and sociocultural factors influence late-life brain health and cognitive decline. At baseline, KHANDLE had 1,712 participants, (April 2017 to December 2018), including 689 men who were included in this study.

STAR participants included Black Americans residing in the San Francisco Bay area of California who had been long-term members of the Kaiser Permanente Northern California STAR cohort study. All identified as Black or African American, were aged 50 years or older as of January 1, 2018, and were former participants in Kaiser Permanente multiphasic health check-up exams from 1964 to 1985. STAR recruitment was completed from Kaiser Permanente health records using stratified random sampling by age and educational attainment with a goal for equal representation of Black or African American individuals ages 50-64 and 65 and older. STAR aimed to evaluate how life course health and sociocultural factors influence cognitive aging and trajectories among Black and African Americans. STAR included 764 participants at baseline (November 2017 to March 2020) of whom 232 were men aged 50 years and older that met criteria for the current study. Over third (36%) of STAR participants had immigrated to California from Southern states, with 53% born outside of California.

Exclusion criteria for KHNALDE/STAR participants were electronic medical record notation of: 1) a diagnosis of dementia or other neurodegenerative disease (frontotemporal dementia, Lewy body disease, Pick's disease, Parkinson's disease with dementia, Huntington's disease) prior to forming the cohort, and 2) health conditions that would limit participation, such as 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.

For the current aim, I included all male participants in KHANDLE/STAR (N = 921) of whom 367 (40%) reported a history of service in the United States military.

Exposure

For the current aim, the primary exposure of veteran status was identified by participant's response to the question "Have you ever served in the active military of the US?" Participants who responded "yes" were categorized as veterans, and those answering "no" as non-veterans. The secondary exposure of reported lifetime encounter with blasts/explosions was identified by participant's response to the question "Have you ever been nearby when an explosion or a blast occurred?" Participants who responded "yes" was categorized as exposed to blasts/explosions, and those answering "no" as not exposed.

Outcome

This aim investigated two cognitive domains: executive function and verbal episodic memory which were assessed using repeated measures drawn from the Spanish and English Neuropsychological Assessment Scales (SENAS), a validated battery of cognitive tests for comparisons across racial/ethnic and linguistically diverse groups.[163,164] Executive function is sensitive to cerebrovascular disease and brain changes.[165] The SENAS executive function score is derived from subscale scores on tests of fluency, phonemic/letter fluency, and working memory (digit span backward and two list sorting). Verbal episodic memory is most sensitive to brain changes, and the SENAS verbal episodic memory score is derived from two Word List

Learning tests.[166,167] Neither domains were limited by ceiling or floor effect.[168] Additional details of SENAS psychometric scales[164] and characteristics[168] have been described elsewhere.

In the STAR cohort, executive function and verbal episodic memory scores were available for three waves of data collection from November 2017 to November 2021. In the KHANDLE, four waves of assessment conducted between April 2017 through June 2023 were available. Due to the Covid-19 pandemic, KHANDLE assessments were switched from in-person to telephone mode during Wave 3 (June 2020 to June 2021), with future waves including the option of telephone assessments. Cognitive domain scores were z-standardized to the pooled KHANDLE and STAR baseline sample.

Effect modifier

Veteran status (veteran vs. non-veteran) was also included as a possible modifier of the association between reports of lifetime exposure to blasts/explosions on late-life cognitive measures.

Covariates

For this aim, early life measures collected at baseline as covariates were conceptualized as potential confounders of the effect of veteran status and reported lifetime exposure to blasts/explosions on rate of cognitive decline (Figure 3.1). All potential confounders occurred prior to achieving veteran status and may have influenced propensity to join military service.[169,170] They may also be associated with late-life cognitive function. The features include:

1) self-reported nativity (US vs. foreign born),

2) self-reported birth in the Southern US (south vs. not south US Census region),[171,172]

3) self-reported paternal education (less than college vs. some college and more)[173] and childhood family finances (average or more vs. poor)[174] which were proxies for childhood socioeconomic status,

4) self-reported educational attainment recoded as less than college vs. some college and more,[53,171] and,

5) exposure to childhood adversity as indexed by an adverse childhood experience (ACE) measure.[175] This included responses to nine separate experiences from birth to 16 years of age (experiences of parents' divorce or separation, a parent remarrying, witnessing domestic violence, substance abuse by a family member, loss of a job by a parent, a parent going to jail, serious illness of a family member, death of mother, and death of father). The ACE score was included as the sum of ACEs reported and categorized into 0, 1, or 2+ events.

Other measures from the parent cohort study were also utilized. As measures of executive function and verbal episodic memory were conducted both in person and by phone, an indicator variable for interview mode was also included in all analytical models. I also used several measures to further characterize the sample, but excluded these from analytic models as they are likely to fall in the causal pathway between veteran status/exposure to blasts or explosions and cognitive measure.[176,177] These measures included self-reported rating of individual health (poor or fair vs. good or better), hearing (poor or fair vs. good or better) and vision (poor or fair vs. good or better) at baseline, marital status (never married, married/living with partner, separated/divorced/widowed), and annual household income (<$35,000, $35,000-$74,999, $75,000-$99,999, and $100,000 or more).

Statistical analysis

Characteristics of the sample were first summarized for the full sample and then by veteran status. Next, to generate estimates between each exposure and rate of cognitive decline, linear mixed effects models with current age (in years, centered at age 75) as the timescale and random intercepts were used for each cognitive domain. Base models were adjusted for interview mode, study-specific practice effect offset derived in accordance with prior work,[178] current age centered at 75 years, veteran status, and interaction between current age centered at 75 years and veteran status. Adjusted models further included nativity, race and ethnicity, birth in the southern US, childhood socioeconomic status proxies (paternal education and family finances), educational attainment, and adverse childhood experiences. These were all considered as potential confounders as mentioned earlier and illustrated in Figure 3.1. The possible modifying role of veteran status on the association between reported lifetime exposure to blasts/explosions on cognitive measures was assessed in two ways: 1) a subgroup analysis for men by veteran status, and 2) a pooled analysis with a two-way interaction term between veteran status and report of lifetime exposure to blasts/explosions and a three-way interaction term between reports of lifetime exposure to blasts/explosions, veteran status, and current age. A *P*-value of the interaction term is reported below. In addition, for each model, four critical features in standard units were reported to estimate executive functioning and verbal episodic memory: a) mean cognitive score of non-veterans at age 75, b) mean annual rate of change in cognitive score for non-veterans, c) mean difference in cognitive score at age 75 for veterans versus non-veterans, and d) mean difference in annual rate of change in cognitive score for veterans versus non-veterans. The latter two (c and d) were the primary effects of interest. The other measures were reported to derive the mean score for veterans at age 75 (a + c) and the mean annual rate of change in cognitive score for veterans (b + d). All analyses were conducted using Stata 18.0 SE (College Station, TX).

Data availability

KHANDLE and STAR cohort data used in analyses are available upon request to the KHANDLE/STAR/LA90 study site (https://sites.google.com/g.ucla.edu/khandle-study-site/home). Permission is typically granted to researchers who provide a methodologically sound proposal that does not substantially overlap with existing project (unless the goal is replication).

Results

The analytical sample included 921 men (92% of all male participants) with complete data, 75% of the sample were KHANDLE participants. Mean age at enrollment was 74 years (SD 8); 40% were veterans and 23% reported having a lifetime encounter with blasts/explosions. The overall sample included 38% who self-identified as Black/African American, 79% were born in the US, and 21% were born in the southern region of the US. The majority (71%) were married, with some college or higher level of education (82%) and a large proportion (38%) reported an annual household income of $100,000 or more. While over half (54%) the sample reported that their father's highest education was less than college, 61% recalled their family finances to be middle class or more. Adverse childhood experiences of two or more events were reported by 44% of men, with the majority rating their health (81%), hearing (66%) and vision (76%) to be good or better than that at enrollment. Compared to non-veterans, veterans were on average older, more likely US born, and with a higher proportion born in the south (Table 3.1). Veterans indicated that they came from more disadvantaged childhood socioeconomic backgrounds than non-veterans. A higher proportion of veterans compared to nonveterans reported lifetime exposure to blasts/explosions (38% vs. 13%) and having fair or poor hearing (38% vs. 29%). Interviews and assessments were all completed in-person at enrollment, and follow-up data were available for 79%, 81%, and 30% of participants at waves 2, 3, and 4, respectively. At study baseline, veterans had lower scores on mean standardized executive function (-0.25, SD=1) and verbal episodic memory (-0.43, SD=0.9) compared with non-veterans (Figure 3.2).

Estimates from linear mixed effects models adjusted for mode, practice effects, and age centered at 75 years (base model) suggested modestly higher average executive function scores (Coefficient: 0.16, 95% CI 0.03, 0.28) at age 75 years for veterans compared with non-veterans. After additionally adjusting for other potential confounders, there were no appreciable differences in average executive function scores by veteran status at age 75 years (Coefficient: 0.06, 95% CI -0.06, 0.18). For verbal episodic memory, veterans had slightly higher average verbal episodic memory scores in the base model (Coefficient: 0.11, 95% CI -0.004, 0.22) and fully adjusted model (Coefficient: 0.12, 95% CI 0.01, 0.23) when compared with non-veterans at age 75 years. There were no differences in the average rate of cognitive change in either executive function or verbal episodic memory by veteran status (Table 3.2).

Estimates of the association between reported lifetime exposure to blasts/explosions and cognitive functions in a subsequent analysis by veteran status showed that among veterans, there were no difference in scores for executive function or verbal episodic memory at age 75 years by reported lifetime exposure to blasts/explosions. Average rate of change in executive function also did not differ by reported lifetime exposure to blasts/explosions among veterans. Interestingly, there was some evidence that veterans who reported lifetime exposure to blasts/explosions may have a slightly slower annual rate of cognitive change in verbal episodic memory (Coefficient: 0.03 SD units, 95% CI 0.004, 0.05) compared with veterans who indicated they were unexposed, but the results were statistically consistent with parameter values ranging from no difference in annual rate of change to a slightly slower annual rate of change. Findings among non-veterans were null for both cognitive domains (Table 3.3). When additionally evaluating the possible modifying role of veteran status on the association between reported lifetime exposure to blasts/explosions and cognitive functions using pooled models with interaction terms, there remained no evidence of effect modification by veteran status in either executive function (*P*-value for 2- and 3-way interaction terms: 0.627 and 0.698, respectively) or verbal episodic memory (*P*-value for 2- and 3-way interaction terms: 0.534 and 0.169, respectively) (Table 3.4).

Discussion

Using information available in the diverse KHANDLE and STAR cohorts, this aim investigated whether veteran status was associated with late-life cognitive measures among male veterans from the Korean and Vietnam War eras. Average executive function scores at 75 years were only slightly higher in the base model for veterans compared with non-veterans, but there were no appreciable differences when these models were fully adjusted. In contrast, average verbal episodic memory scores were modestly higher for veterans compared to non-veterans in the base and fully adjusted models after standardizing the effects to age 75 years. There were no differences in annual rate of cognitive change by veteran status in either cognitive domain. There was no robust evidence that veteran status modified the association between reported lifetime exposure to blasts/explosions on late-life cognitive function or change.

While there have been many studies comparing cognitive measures by various exposures within the veteran population, few have assessed cognitive trajectories comparing veterans to non-veterans.[133,158] This aim in the dissertation was motivated by the need to fill this gap in the literature. I hypothesized that veteran status would be associated with higher cognitive level at baseline, but faster cognitive change based on the many risk factors[22,179] highly prevalent within the veteran population including TBI/blast[15,180,181] and PTSD[182] that have been associated with cognitive measures. This hypothesis was derived from findings in a study that used 10-year measurements of male participants in the Health and Retirement Study (HRS). In that study, World War II and Korean War veterans had higher cognition scores compared with non-veterans at retirement age, but declined more rapidly.[133] In contrast, a recent study including male and female participants aged 65 years and older from the Adult Changes in Thought (ACT) cohort observed military employment was not associated with rate of cognitive decline, incident dementia or incident Alzheimer's disease dementia, and there was no evidence of effect modification by traumatic brain injury where there had been loss of consciousness.[158]

The overall null association between veteran status and cognitive change reported here aligns with findings from the ACT cohort,[158] while higher cognitive scores at 75 years are more consistent with earlier findings from the HRS cohort.[133] Unlike the ACT cohort, which was composed of primarily White male and female veterans with service prior to World War II, and the HRS cohort which primarily included World War II (1941-1946) and Korean War (1950-1955) male veterans, the KHANDLE/STAR participants studied here included a racially diverse cohort of only male veterans who primarily served during the Korean and Vietnam War (1955-1975) eras.

The absence of differences in cognitive change comparing veterans to non-veterans observed in the current study is contrary to what was hypothesized. There are several possible explanations for this. First, among veterans there is likely heterogeneous exposure to risk on cognitive functioning. In this aim, detailed information related to military service necessary to sufficiently investigate features of military service that might affect cognitive decline in late-life were unavailable. This includes age at military enlistment, duration of service, number of combat deployments, training and duties performed, and exposure to environmental pollutants or chemicals. These distinctions are critical. For example, a veteran whose military occupational specialty was in administration and management might be expected to have lower levels of hazardous training and service hardship during their military career compared with a veteran assigned to a military occupational specialty in infantry or related.[183] A second factor that may have made detection of differences in cognitive decline problematic is the relatively short follow-up period of the current study. Median follow-up time was 2.6 years (IQR 1-4) which was much shorter compared to the 11-year follow-up in the HRS cohort.[133] A longer follow-up time may be necessary to conclusively project cognitive trajectory. A third factor of relevance is that the KHANDLE/STAR cohorts represent a generally well-educated and wealthier group of older adults and may not generalize to the overall veteran and non-veteran population in the US. Finally, as with all aging studies, findings are subject to survival bias. Participation in study requires survival to older ages and given that life expectancy can be shorter for veterans then non-veterans,[184] it is possible that veterans in KHANDLE and STAR cohorts are more highly selected for vitality than were non-veterans. As a result, if military service truly generated a faster rate of cognitive change, results could be biased towards the null due to this differential selection process. It is important to note while this aim did not find any evidence of cognitive change by veteran status, it remains an important heath outcome to monitor in a rapidly aging veteran population.[27,185]

Encounter with blast/explosion during combat can leave harmful long-term impact on cognitive abilities. Assuming veterans are more likely to be exposed to such explosions and who respond with a positive answer to a single question about exposure to blast/explosion would reflect a higher intensity of exposure,[181,186] I hypothesized that the effect of reported lifetime exposure to blasts/explosions would be greater among veterans than non-veterans. Findings from this aim suggests the contrary. This is unexpected and may be due to several possible factors. First, this finding could just be due to a poorly assessed exposure measurement of reported lifetime exposure to blasts/explosions. This seems likely in this instance as the question provided in the KHANDLE/STAR questionnaire was imprecise. Although veterans were more likely to report exposure to an explosive blast providing some validity to using this measure, the inexactness of the severity of the blast or whether the exposure was frequent or rare underscores how tentative the exposure classification likely was. It is possible that this exposure includes a range of severity by including both combat and non-combat related lifetime exposure to blasts/explosions reported among veterans. Second, this finding could be due to a healthy survivor effect. Survival rates among veterans following an encounter with a blast/explosion could be different between those exposed and not exposed, and the slower rate of cognitive change observed could reflect higher cognitive resiliency among veterans who survived an encounter with a blast/explosion.

Despite the absence of evidence here for harmful effects of blast/explosion exposures, this should remain a concern going forward. It may especially be relevant among post-9/11 service members who served in Iraq, Afghanistan, and later. Blast exposures are common among recent service members, with current estimates by the Defense and Veterans Brain Injury Center (DVBIC) of 413,858 service members diagnosed with a TBI between 2000 to 2019.[187] In a Veterans Affairs study evaluating blast exposures among post-9/11 combat veterans, over 70% reported a history of blast exposure.[188] Despite this high prevalence, little is known about how the effects of exposure to a blast are associated with cognitive trajectories, especially in later life. Future studies could benefit from establishing well defined parameters constituting what is considered a sufficient exposure to a blast/explosion to cause harm, including measures of frequency and intensity of exposure as well as distinguishing between combat (i.e. improvised explosive device or other explosives) and non-combat (routine infantry and/or artillery training) exposures.

The current study also has several strengths worth mentioning. In comparison with previous studies comparing cognitive trajectories by veteran/military employment status, this cohort included 367 (40%) male service members, fewer than the HRS study with 4,028 (59%) veterans, but greater than the ACT cohort with 262 (6%) participants with military employment. Unlike the ACT and HRS cohorts which included veterans from periods when minoritized racial and ethnic groups were less likely to be in the military, the current sample is more diverse and includes a higher representation of African American veterans. This aim also includes up to four waves of repeated cognitive assessments on two cognitive domains which allow for assessment of cognitive change accounting for practice effects and early-life measures that can potentially influence both military selection and cognitive measure.

This aim fills current gaps in literature on cognitive trajectories by veteran status, but more work is needed to evaluate potential resilience mechanisms and heterogeneity within the veteran population. Studies directly comparing veterans with non-veteran populations are needed to better understand the long-term consequences of military service. The largest cohort of veterans who served decades ago are part of the aging population today. It is our responsibility to understand and fulfill their needs to adequately serve our military service members and prepare for the future wave of post-9/11 veterans as they age.

Tables and Figures

Table 3.1. Characteristic of analytic sample by veteran status using data from the combined Kaiser Healthy Aging and Diverse Life Experiences (KHANDLE) and Study of Healthy Aging in African Americans (STAR) cohorts.

	All	Non-veteran	Veteran
	N=921	N=554	N=367
Age at baseline, (years), mean (SD)	74 (8)	72 (7)	78 (7)
Race/ethnicity, n (%)			
Black/African American	346 (38)	206 (37)	140 (38)
Asian	181 (20)	125 (23)	56 (15)
White	199 (22)	108 (19)	91 (25)
Latino or other	195 (21)	115 (21)	80 (22)
Nativity, n (%)			
US born	727 (79)	392 (71)	335 (91)
Foreign born	194 (21)	162 (29)	32 (9)
Birth in southern United States, n (%)			
Not South	501 (54)	286 (52)	215 (59)
South	193 (21)	87 (16)	106 (29)
Missing	227 (25)	181 (33)	46 (13)
Marital status, n (%)			
Never married	51 (6)	36 (6)	15 (4)
Married/living with partner	658 (71)	396 (71)	262 (71)
Separated, divorced, widowed	204 (22)	118 (21)	86 (23)
Refused	8 (1)	4 (1)	4 (1)
Highest educational attainment, n (%)			
Less than college	170 (18)	104 (19)	66 (18)
Some college and more	749 (82)	449 (81)	300 (82)
Annual household income range, n (%)			
Less than $35,000	52 (8)	35 (9)	17 (6)
$35,000 - $74,999	191 (28)	100 (25)	91 (31)
$75,000 - $99,999	103 (15)	59 (15)	44 (15)
$100,000 or more	265 (38)	155 (39)	110 (38)
Refused/Don't know	78 (11)	48 (12)	30 (10)
Paternal highest educational attainment, n (%)			
Less than college	493 (54)	291 (53)	202 (55)
Some college and more	228 (25)	158 (29)	70 (19)
Not applicable/administered/Refused	200 (22)	105 (19)	95 (26)
Self-recall of family finances, n (%)			
Poor	358 (39)	193 (35)	165 (45)
Average or more	563 (61)	361 (65)	202 (55)
Adverse childhood experience, n (%)			
None	279 (30)	171 (31)	108 (29)
One event	239 (26)	146 (26)	93 (25)
Two or more events	403 (44)	237 (43)	166 (45)
Lifetime exposure to blasts/explosions, n (%)			
No	694 (77)	470 (87)	224 (62)
Yes	207 (23)	70 (13)	137 (38)
Individual rating of health at wave 1, n (%)			
Poor/fair	174 (19)	101 (18)	73 (20)
Good or better	738 (81)	447 (82)	291 (80)
Self-rated hearing at wave 1, n (%)			
Poor/fair	300 (33)	162 (29)	138 (38)
Good or better	612 (66)	387 (70)	225 (61)
Don't know/refused	9 (1)	5 (1)	4 (1)
Self-rated vision at wave 1, n (%)			
Poor/fair	211 (23)	130 (23)	81 (22)
Good or better	701 (76)	419 (76)	282 (77)

Table 3.1. Characteristic of analytic sample by veteran status using data from the combined Kaiser Healthy Aging and Diverse Life Experiences (KHANDLE) and Study of Healthy Aging in African Americans (STAR) cohorts.

	All	Non-veteran	Veteran
	N=921	N=554	N=367
Don't know/refused	9 (1)	5 (1)	4 (1)
Cohort, n (%)			
KHANDLE	689 (75)	397 (72)	292 (80)
STAR	232 (25)	157 (28)	75 (20)
Wave 1 total participants, n (%)	921 (100)	554 (100)	367 (100)
Wave 2 total participants, n (%)	729 (79)	433 (78)	296 (81)
Wave 3 total participants, n (%)	742 (81)	452 (82)	290 (79)
Wave 4 total participants, n (%)	276 (30)	151 (27)	125 (34)
Follow up time on study (years), median (IQR)	2.6 (1-4)	2.6 (2-4)	2.6 (1-4)
Interview mode at wave 1, n (%)			
In-person	921 (100)	554 (100)	367 (100)
Wave 1 Executive Function (z-score), mean (SD)	-0.16 (1)	-0.11 (1)	-0.25 (1)
Wave 1 Verbal Episodic Memory Function (z-score), mean (SD)	-0.34 (0.9)	-0.28 (0.9)	-0.43 (0.9)

Table 3.2. Mean differences (SD units) in cognitive test scores at 75 years and annual rate of cognitive change comparing veteran to non-veteran using age as the timescale. N=921		
	Base	Adjusted
	Coefficient (95% CI)	Coefficient (95% CI)
Executive function		
Mean score for non-veterans at age 75 (intercept)	-0.22 (-0.30, -0.14)	-0.35 (-0.53, -0.16)
Annual change in score for non-veterans	-0.05 (-0.06, -0.05)	-0.06 (-0.07, -0.05)
Mean difference in score at age 75 for veterans vs. non-veterans	0.16 (0.03, 0.28)	0.06 (-0.06, 0.18)
Mean difference in annual rate of change for veterans vs. non-veterans	0.001 (-0.01, 0.02)	0.002 (-0.01, 0.02)
Verbal episodic memory		
Mean score for non-veterans at age 75 (intercept)	-0.36 (0.40, 0.51)	-0.65 (-0.83, -0.48)
Annual change in score for non-veterans	-0.05 (-0.05, -0.04)	-0.05 (-0.06, -0.04)
Mean difference in score at age 75 for veterans vs. non-veterans	0.11 (-0.004, 0.22)	0.12 (0.01, 0.23)
Mean difference in annual rate of change for veterans vs. non-veterans	-0.006 (-0.02, 0.008)	-0.000 (-0.01, 0.01)

Base: Adjusted for mode, practice effects, age centered at 75 years, and interaction between age and veteran status.
Adjusted: Adjusted for mode and practice effects, age centered at 75 years, race and ethnicity, southern US birth, nativity, childhood SES measures (family financial status and paternal education), education, and adverse childhood experience with interaction between age and veteran status.

Table 3.3. Subgroup analysis of veterans and non-veterans comparing mean differences (SD units) in cognitive test scores at baseline and annual rate of cognitive decline by reported lifetime exposure to blasts/explosions using age as the timescale.

	Veteran N=361		Non-Veteran N=540	
	Base	Adjusted	Base	Adjusted
	Coefficient (95% CI)	Coefficient (95% CI)	Coefficient (95% CI)	Coefficient (95% CI)
Executive Function				
Mean score for no blasts/explosions at age 75 (intercept)	-0.11 (-0.24, 0.02)	-0.51 (-0.83, -0.18)	-0.24 (-0.32, -0.15)	-0.66 (-0.93, -0.39)
Annual change in score for no blasts/explosions	-0.05 (-0.07, -0.04)	-0.05 (-0.07, -0.04)	-0.06 (-0.07, -0.05)	-0.06 (-0.07, -0.05)
Mean difference in score at age 75 for blasts/explosions vs. no blasts/explosions	0.10 (-0.10, 0.30)	0.09 (-0.10, 0.27)	0.19 (-0.05, 0.43)	0.02 (-0.20, 0.23)
Mean difference in annual rate of change for blasts/explosions vs. no blasts/explosions	0.003 (-0.02, 0.03)	0.004 (-0.02, 0.03)	0.009 (-0.02, 0.04)	0.004 (-0.02, 0.03)
Verbal Episodic Memory				
Mean score for no blasts/explosions at age 75 (intercept)	-0.18 (-0.29, -0.06)	-0.65 (-0.96, -0.34)	-0.37 (-0.45, -0.30)	-0.85 (-1.11, -0.59)
Annual change in score for no blasts/explosions	-0.06 (-0.07, -0.05)	-0.06 (-0.08, -0.05)	-0.05 (-0.06, -0.04)	-0.05 (-0.06, -0.04)
Mean difference in score at age 75 for blasts/explosions vs. no blasts/explosions	-0.13 (-0.31, 0.04)	-0.15 (-0.32, 0.03)	0.02 (-0.19, 0.23)	-0.05 (-0.25, 0.15)
Mean difference in annual rate of change for blasts/explosions vs. no blasts/explosions	0.03 (0.004, 0.05)	0.03 (0.004, 0.05)	0.006 (-0.03, 0.03)	0.004 (-0.03, 0.03)

Base: Adjusted for mode, practice effects, age centered at 75 years, and interaction between age and exposure to blasts/explosions.
Adjusted: Adjusted for mode and practice effects, age centered at 75 years, southern US birth, nativity, childhood SES measures (family financial status and paternal education), education and adverse childhood experience with interaction between age and exposure to blasts/explosions.

Table 3.4. Result of pooled analysis with interaction terms to assess potential modifying role of veteran status on the association between reported lifetime exposure to blasts/explosions and cognitive test scores (SD units) at 75 years and annual rate of change using age as the timescale. N=921		
	Coefficient (95% CI)	*P*-value for interaction
Executive Function		
Difference in mean scores at age 75 for exposure to blasts/explosions vs. no blasts/explosion by veteran status	0.07 (-0.21, 0.35)	0.627
Difference in annual rate of change for exposure to blasts/explosions vs. no blasts/explosions by veteran status	0.004 (-0.01, 0.02)	0.698
Verbal Episodic Memory		
Difference in mean scores at age 75 for exposure to blasts/explosions vs. no blasts/explosion by veteran status	-0.08 (-0.35, 0.18)	0.534
Difference in annual rate of change for exposure to blasts/explosions vs. no blasts/explosions by veteran status	0.01 (-0.01, 0.03)	0.169

P-value for interaction: *P*-value of 2-way interaction term between reported lifetime exposure to blasts/explosions and veteran status, and 3-way interaction between reported lifetime exposure to blasts/explosions, veteran status, and age.
Models adjusted for mode and practice effects, age centered at 75 years, southern US birth, nativity, childhood SES measures (family financial status and paternal education), education and adverse childhood experience with interactions between reported lifetime exposure to blasts/explosions, age, and veteran status.

Figure 3.1. Directed acyclic graph (DAG) illustrating the relationship between veteran status, reported lifetime exposure to blasts/explosions, and cognitive measures among male participants from the Kaiser Healthy Aging and Diverse Life Experiences (KHANDLE) and the Study of Health Aging in African Americans (STAR) cohorts.

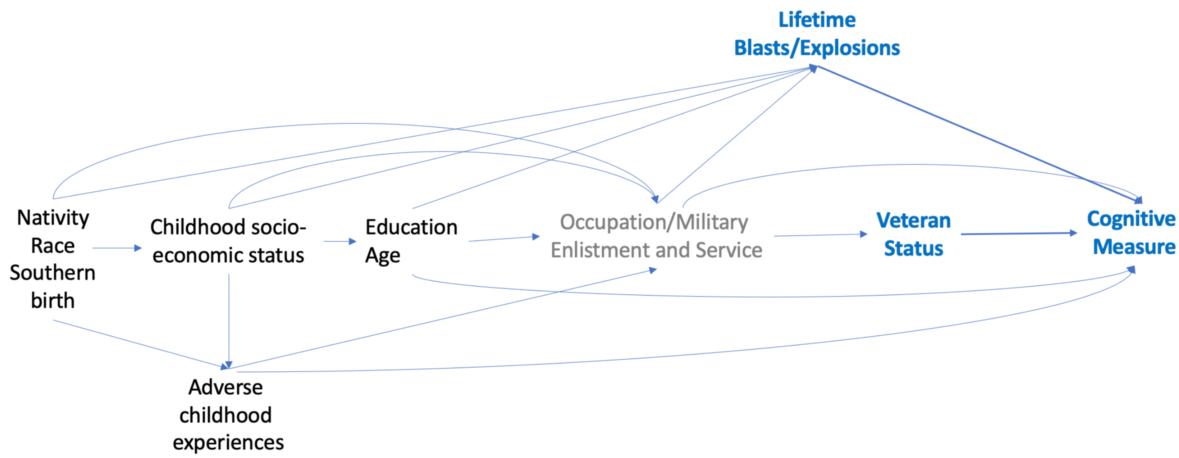
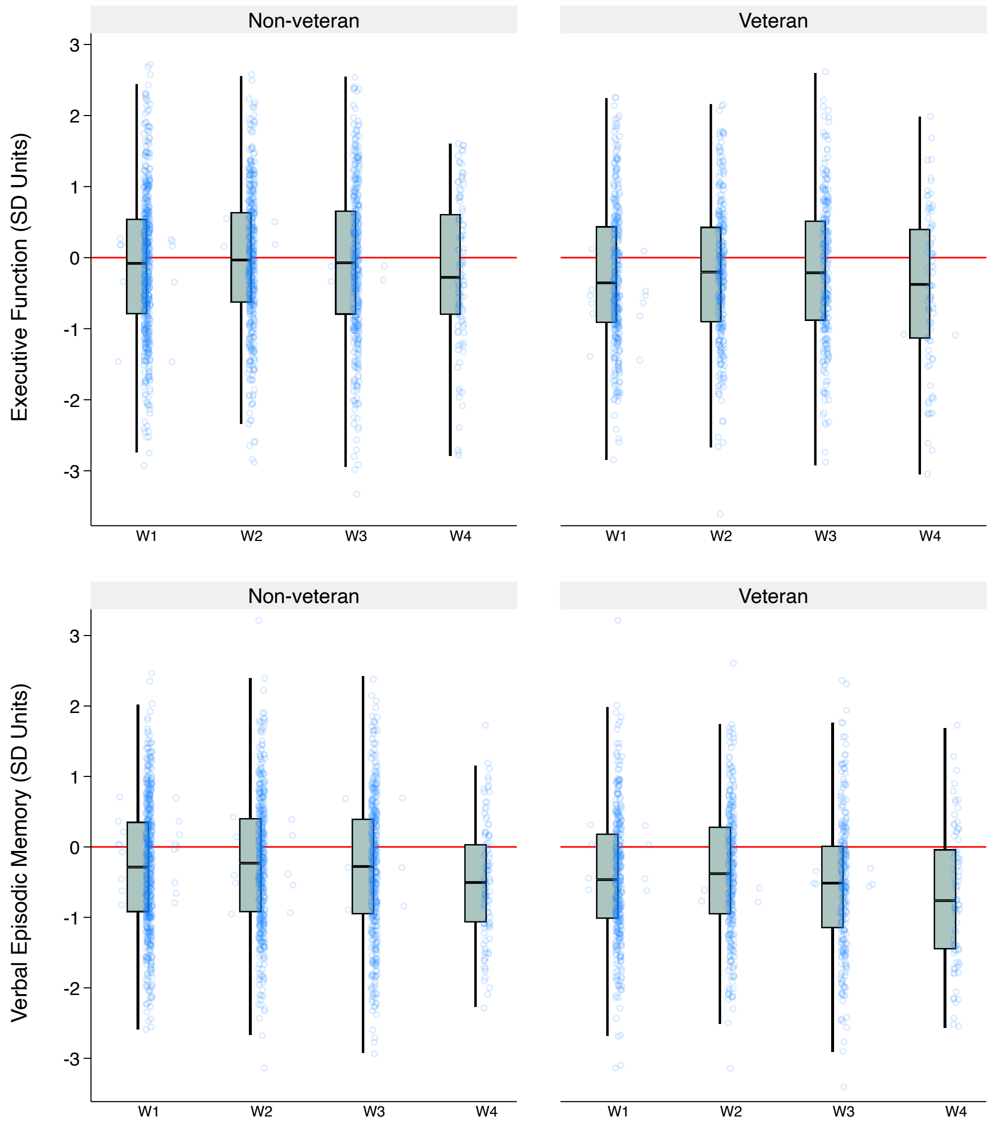


Figure 3.2. Summary box and jitter plots of standardized cognitive performance scores by veteran status on four waves of data from the combined Kaiser Healthy Aging and Diverse Life Experiences (KHANDLE) and Study of Healthy Aging in African Americans (STAR) cohorts. N=921



Potential impact of dissertation

With an overall goal to study cognitive measures in marginalized populations, this dissertation adds to the diversity and inclusivity of dementia prevention research. Most current studies on dementia are observed among a majority White population and there is a need to know how these findings relate and compare towards a more racially diverse population. Without studies on underrepresented groups such as military veterans and men and women in low-and-middle income countries, valuable insights on risk factors influencing cognitive measures in an aging population will be missed, especially for populations in low- and middle-income countries where the aging population is likely to be concentrated in the future. This is crucial for the development of inclusive and effective prevention strategies in a rapidly aging world.[189]

The findings from this dissertation underscore the need to address existing gaps in accurately assessing cognitive measures within marginalized and underserved populations. First, there is a pressing need for improved measurement and definition of exposure to indoor air pollution from unclean cooking fuel in Indian households, and lifetime exposure to blasts and explosions among veteran and non-veteran populations in the US. Improving precision of these measures is paramount to capturing the severity, frequency, and context of such exposures. Second, accounting for other sources of confounding, including early life socio-economic factors accounting for sex-based differences in low- and middle-income countries and heterogeneity within the veteran population is essential to mitigating bias in the assessment of cognitive measures. Third, it is imperative to consider the contribution of outdoor air pollution and hazardous environmental exposures in populations spending significant time working outdoors to comprehensively understand the influence of other potential drivers of cognitive measures. Last, expanding sample sizes to include larger and more diverse groups is crucial for detecting potential interactions by race/ethnicity, housing type, and other culturally relevant factors. Accounting for these limitations can offer important information on representative populations, shed light on the counterintuitive findings observed in this dissertation, and advance understanding of potentially modifiable risk factors contributing towards cognitive measures.

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