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Rising Hyperlipidemia and Dementia Related Mortality Among Older Adults: United States Epidemiological Trends (2000–2023)

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Abstract

Background

Hyperlipidemia (HL) and dementia represent significant health burdens among older adults, with established pathophysiological links. This study examined mortality trends among older adults with both conditions in the United States from 2000 to 2023.

Methods

We analyzed CDC WONDER Multiple Cause of Death data for decedents aged ≥ 65 years with HL (E78.1-E78.5) and dementia (F01, F03, G30) listed as contributing or underlying causes. Age-adjusted mortality rates (AAMRs) per 100,000 population were calculated and stratified by sex, race/ethnicity, geographic region, and urbanization. Temporal trends were assessed using Joinpoint regression analysis.

Results

From 2000 to 2023, 216,705 HL and dementia-related deaths occurred among older adults. The AAMR increased over six-fold from 2.8 (95% CI: 2.6-3.0) in 2000 to 17.8 (95% CI: 17.7–17.9) in 2023 (AAPC: 11.8%; $p < 0.001$). Mortality accelerated sharply from 2018–2021 (APC: 16.3%), followed by a slight decline. Women consistently exhibited higher AAMRs than men. Non-Hispanic Black individuals experienced the highest burden and most rapid increase (AAMR: 2.0 to 40.4). Geographic disparities were pronounced, with Southern states and non-metropolitan areas demonstrating elevated mortality. Most deaths occurred in nursing homes (43.7%) or decedents' homes (27.3%).

Conclusions

HL and dementia-related mortality among older Americans has risen dramatically over two decades, with marked disparities by race, sex, and geography. These findings underscore an escalating public health crisis requiring targeted interventions for vulnerable populations.

Introduction

Hyperlipidemia (HL), characterized by elevated levels of cholesterol and triglycerides in the blood, represents one of the most prevalent cardiovascular risk factors globally, with 39% of the world adult population affected by elevated blood cholesterol according to the World Health Organization [1]. The burden of hyperlipidemia is particularly pronounced among older adults, with prevalence increasing substantially with age [2,3]. In the United States, HL affects a disproportionate number of adults aged 65 and older, representing a critical health concern as this demographic continues to expand [4].

Dementia poses an even more acute challenge for older adult populations, with its incidence doubling approximately every 5–6 years after age 65. Current estimates indicate that 57.4 million people worldwide were living with dementia in 2019, with this number projected to reach 152.8 million cases by 2050 [5]. Most dementia cases occur in adults aged 65 and older, with age representing the strongest known risk factor for cognitive decline [6]. Together, hyperlipidemia and dementia represent substantial health and economic burdens that disproportionately impact aging populations and strain healthcare systems designed to serve older adults.

A well-documented relationship exists between HL and cognitive decline in older adults, with extensive research demonstrating significant associations between cholesterol levels and dementia risk [7,8]. The cholesterol-dementia

connection has been consistently observed across multiple population studies, with elevated cholesterol levels showing clear associations with increased risk of cognitive deterioration [9]. This relationship is particularly relevant for adults aged 65 and older, where both conditions reach their highest prevalence and clinical significance [10]. Recent research has explored the intricate interplay between lipid metabolism and neurodegeneration specifically in aging populations, identifying shared pathophysiological mechanisms such as age-related vascular dysfunction, chronic neuroinflammation, and altered amyloid processing that become increasingly prevalent after age 65 [11,12].

This study examines mortality trends linked to hyperlipidemia and dementia among U.S. adults aged 65 + from 2000 to 2023, using CDC WONDER data. Analyses assess variations by sex, race, urbanization, and region to clarify how these conditions shape evolving mortality patterns in the aging population.

METHODS

We analysed mortality data related to hyperlipidemia and dementia obtained from the Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiologic Research (CDC WONDER) Database [13]. CDC-WONDER is a comprehensive database that contains death certificate data from all fifty states and the District of Columbia. We used the Multiple Cause of Death Public Use Record to retrieve data about patients who died with both hyperlipidemia and dementia as either an underlying cause or contributing cause of death in the United States from 2000 to 2023. We collected death records for patients aged 65 and older using the following International Classification of Diseases, 10th Revision, Clinical Modification codes: E78.1-E78.5 for Hyperlipidemia and F01.x, F03.x, and G30.x for dementia. Other researchers have used these same codes to identify Hyperlipidemia and Dementia in administrative databases. Additionally, we followed the guidelines [14,15] established by the reporting standards of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) [16]. The study did not require approval from the local institutional review board because it used an anonymous public data set provided by the government.

2.1 Data extraction

The extracted data included population, year, and demographics such as sex, race/ethnicity, and regional details. Race/ethnicity was classified into the following categories: Hispanic or Latino, Non-Hispanic (NH) Black or African American, NH White, and NH Asian or Pacific Islander. The Urban–Rural classification was based on the National Center for Health Statistics Urban–Rural Classification Scheme. The population was divided into urban (large metropolitan area, medium/small metropolitan area) and rural (population < 50,000) HL and Dementia-Related mortality counties according to the 2013 U.S. census classification [17]. Regions were classified as Northeast, Midwest, South, and West based on U.S. Census Bureau definitions [18].

2.2 Statistical analysis

The crude and age-adjusted mortality rates (CMRs and AAMRs) per 100,000 individuals from 2000 to 2023 were calculated to analyse the trends in mortality related to HL and dementia. CMRs were calculated by dividing the deaths related to HL and dementia by the total U.S. population each year. AAMRs were calculated by standardizing HL and dementia-Related deaths to the 2000 U.S. population, with 95% confidence intervals [19]. The AAMRs were used to analyse mortality patterns across various demographic classifications. The trends in AAMR were determined using the Joinpoint Regression Program (Joinpoint Version 5.1.0, National Cancer Institute) that reported annual percentage change (APC) along with 95% CI [20]. Significant changes in AAMR over time were assessed using log-linear regression models to examine temporal variations. APCs were considered to increase or decrease if the slope representing the change in mortality significantly deviated from zero, as determined by 2-tailed t-tests. A P-value of less than 0.05 indicated statistical significance.

Results

Between 2000 and 2023, a total of 216,705 deaths related to Hyperlipidemia and Dementia were recorded **(Supplementary Table 1)**. The AAMR for Hyperlipidemia-related deaths in Dementia patients was 2.8 (95% CI: 2.6 to 3) in 2000 and increased to 17.8 (95% CI: 17.7 to 17.9) in 2023, reflecting a significant rise over the two decades with an AAPC of 11.8% (95% CI: 10.5 to 13.0; p < 0.001). The AAMR exhibited distinct trends across different periods. From 2000 to 2007, the trend increased (APC: 23.6%; 95% CI: 21.0 to 26.2; p < 0.001), followed by an increase from 2007 to 2012 (APC: 11.2%; 95% CI: 8.3 to 14.1; p < 0.001). It continued to rise between 2012 and 2018 (APC: 2.1%; 95% CI: 0.6 to 3.6; p < 0.001). From 2018 to 2021, the trend again increased (APC: 16.3%; 95% CI: 10.0 to 22.9; p < 0.001), followed by a decrease from 2021 to 2023 (APC: − 1.6%; 95% CI: − 6.3 to − 3.3; p < 0.001). (**Supplementary Table 3)**

3.1 Sex

Throughout the study period, men and women exhibited similar AAMR trends. In 2000, the AAMR for men was 2.1 (95% CI: 1.9 to 2.4), which increased to 35.4 (95% CI: 34.6 to 36.3) in 2023. Similarly, the AAMR for women increased from 3.1 (95% CI: 6.93 to 7.24) in 2000 to 39.7 (95% CI: 15.44 to 15.83) in 2023. (Fig. 1, **Supplementary Table 3**)

In men, the AAMR demonstrated an inclining trajectory, between 2000 and 2005 (APC: 29.2%, 95% CI: 21.3 to 37.5; p < 0.001). This was followed by an increase in AAMR (APC: 14.4%, 95% CI: 10.8 to 18.0; p < 0.001) till 2011.It continued to rise from 2011 to 2021 but increased greatly between 2018 and 2021 (APC: 16.9%, 95% CI: 7.8 to 26.7; p < 0.001) Finally, there was a decline till 2023 (APC: -3.2%, 95% CI: -10.0 to 4.1; p < 0.001). Females displayed analogous trajectories, with increasing AAMR until 2021, followed by subsequent decline. **(**Fig. 1**)**

3.2 Race

When stratified by race/ethnicity, the greatest increase in AAMRs was seen among NH Black patients, rising from 2.0 (95% CI: 1.5 to 2.6) in 2000 to 40.4 (95% CI: 38.5 to 42.3) in 2023. NH White patients followed, increasing from 2.9 in 2000 (95% CI: 2.7 to 3.1) to 39.8 (95% CI: 39.2 to 40.4) in 2023, then Hispanic or Latino from 1.7 (95% CI: 1.1 to 2.5) to 31.7 (95% CI: 30.0 to 33.3), and NH Asian or Pacific Islander patients from 3.4 (95% CI: 2.1 to 5.2) to 23.7 (95% CI: 21.9 to 25.6) respectively (Fig. 2, **Supplementary Table 4, Supplementary Table 8**).

For NH Black or African Americans, the AAMR demonstrated an inclined trajectory, between 2000 and 2008 (APC = 24.2, 95% CI: 13.0 to 35.4). This was followed by another increase in AAMR (APC = 7.5, 95% CI: 6.1 to 8.8) till 2023. For Hispanic or Latinos AAMR showed increasing trends. From 2000 to 2010, the trend increased (APC: 22.5%; 95% CI: 18.3 to 26.8; p < 0.001), followed by an increase from 2000 to 2018 (APC: 3.3%; 95% CI: 1.0 to 5.7; p < 0.001). It continued to rise between 2018 and 2021 (APC: 22.1%; 95% CI: 8.5 to 37.4; p < 0.001), followed by a decrease from 2021 to 2023 (APC: − 5.6%; 95% CI: − 14.7 to 4.6; p < 0.001). NH Whites and NH Asian or Pacific Islanders displayed analogous trajectories, with increasing AAMR until 2021, followed by subsequent decline. **(**Fig. 2**)**

3.3 Census Region

Throughout the study period, all regions showed increasing AAMRs, Northeast from 2.0 (95% CI: 1.7 to 2.4) in 2000 to 34.3 (95% CI: 33.2 to 35.5) in 2023. The South followed, increasing from 2.7 (95% CI: 2.4 to 3.0) to 42.2 (95% CI: 41.2 to 43.1), then the West from 3.1 (95% CI: 2.7 to 3.5) to 38.3 (95% CI: 37.2 to 39.4), and finally the Midwest, rising from 3.2 (95% CI: 2.8 to 3.6) to 33.8 (95% CI: 32.7 to 34.9) (AAPC: 11.0%; 95% CI: 9.1 to 13.0; p < 0.001).

Northeast region exhibited increasing AAMR trends. From 2000 to 2010 AAMR increased (APC: 21.3%; 95% CI: 15.3 to 27.5; p < 0.001), AAMR further increased from 2010 to 2023 (APC: 6.9%; 95% CI: 5.4 to 8.4; p < 0.001). Midwest and South regions exhibited similar AAMR trends, increasing throughout the study period. For West the trend increased from 2000 to 2006 (APC: 25.6%; 95% CI: 21.6 to 29.8; p < 0.001), followed by an increase from 2006 to 2012 (APC: 11.3%; 95% CI: 8.8 to 13.8; p < 0.001). It continued to rise between 2012 and 2018 (APC: 0.3%; 95% CI: -1.4 to 2.1; p < 0.001). From 2018 to 2021, the trend again increased (APC: 15.7%; 95% CI: 8.2 to 23.7; p < 0.001), followed by a decrease from 2021 to 2023 (APC: − 2.1%; 95% CI: -7.8 to 3.9; p < 0.001). (Fig. 4, **Supplementary Tables 7**).

3.4 Urbanization

Non-metropolitan areas had higher AAMRs than metropolitan areas. AAMRs in non-metropolitan areas increased from 3.1 (95% CI: 2.7 to 3.5) in 2000 to 43.4 (95% CI: 42.1 to 44.8) in 2020. In comparison, metropolitan areas increased from 2.7 (95% CI: 2.5 to 2.9) to 35.5 (95% CI: 35.0 to 36.1).

The trends for non-metropolitan areas can be divided into four segments. The initial phase from 2000 to 2008 exhibited an increase in AAMR (APC:23.7% 95% CI: 21.4 to 25.9; $p < 0.001$). This was followed by a rise until 2014 (APC:7.3% 95% CI: 5.2 to 9.5; $p < 0.001$). AAMR continued to rise between 2014 and 2020, most rapidly from 2018 to 2020 (APC:21.6% 95% CI: 14.2 to 29.5; $p < 0.001$). Similarly, metropolitan areas showed similar trends, increasing throughout the period between 2000 and 2020 (**Supplementary Fig. 1, Supplementary Table 5**).

3.5 State

A significant difference in AAMRs was observed across different states, with the AAMRs ranging from 7.3 (95% CI: 6.6 to 8.0) in Nevada to 50.5 (95% CI: 47.4 to 53.6) in Vermont. States that fell into the top 90th percentile, such as Vermont, Nebraska, Hawaii, Oregon, and North Dakota, had significantly higher AAMRs compared to states in the lower 10th percentile, including Arizona, Utah, Georgia, Massachusetts, and the Nevada (Fig. 3, **Supplementary Table 6**).

3.6 Place of Death

Information on the location of death was available for 216,705 deaths during the study period (2000–2023). Of these, 103,697 deaths (43.7%) occurred in nursing homes/long-term care facilities, 56,920 deaths (27.3%) in decedent's homes, 23,858 deaths (11.4%) in medical facility-inpatient, 15,308 deaths (7.3%) in other locations, 8,427 deaths (4.0%) in hospice facility, 7,759 deaths (3.7%) in medical facility-outpatient or ER, 436 deaths (0.2%) as dead on arrival, and 300 deaths (0.1%) in unknown locations (**Supplementary Table 2**).

Discussion

This study provides a comprehensive analysis of mortality in the United States where HL and dementia were co-involved among older adults (aged ≥ 65 years) from 2000 to 2023, identifying crucial temporal trends and demographic disparities. Our findings reveal a dramatic and deeply concerning escalation in the age-adjusted mortality rate (AAMR), which surged more than six-fold over the two-decade study period. This trend was not uniform; it was marked by a sharp acceleration between 2018 and 2021, followed by a slight but notable decline. Most of these deaths occurred outside of acute medical settings, taking place primarily in long-term care facilities or the decedent’s home. The analysis underscores profound inequities: NH Black individuals consistently bore the highest mortality burden and experienced the fastest rate of increase. Geographically, the mortality burden was most concentrated in the Southern states and in nonmetropolitan areas, the latter of which also saw a more rapid rise in mortality compared to urban regions. **(**Table 1**)**

The pathophysiological link between HL and Dementia involves a triad of vascular, molecular, and inflammatory insults on the brain. The most direct assault is vascular: chronic hyperlipidemia fuels the atherosclerosis that causes cerebral hypoperfusion and ischemic damage, setting the stage for vascular dementia [21]. Beyond this, the pathology extends into the molecular architecture of Alzheimer’s disease. Elevated cholesterol can alter the processing of amyloid precursor protein to favor the creation of neurotoxic amyloid-beta (Aβ) peptides [22]. This risk is dangerously magnified in carriers of the ApoE4 allele, a variant of the brain's lipid transporter that critically impairs the clearance of Aβ from the brain [23]. Completing this triad, dyslipidemia compromises the blood-brain barrier, which ignites a chronic neuroinflammatory state that accelerates neuronal death and synaptic failure [24]. These mechanisms become particularly destructive within the context of the aging brain. Natural senescence fosters a vulnerable environment characterized by arterial stiffening [25], a decline in the brain's protein clearance efficiency [26], and a state of chronic, low-grade inflammation known as "inflammaging" [27]. HL acts as a

potent catalyst in this environment, transforming the slow, sub-clinical processes of brain aging into a rapid, pathological cascade that culminates in dementia.

The multi-phasic mortality trend among older adults reflects key shifts in geriatric medicine and public health. The initial steep rise in deaths is likely a documentation artifact from growing clinical awareness of the dementia-lipid link in this age group [28]. This was followed by a decade-long stabilization, coinciding with the widespread adoption of statin therapies for seniors, which may have blunted the most severe cerebrovascular outcomes [29]. This stability was abruptly reversed by the COVID-19 pandemic. The sharp mortality spike after 2018 points unequivocally to this crisis, as the virus's systemic inflammatory effects proved catastrophic for the neurologically vulnerable elderly [30]. The most recent downturn is likely not a sign of recovery but a "mortality displacement" effect, a demographic echo of the pandemic's disproportionate toll on older adults [31].

Our analysis confirms a persistent sex disparity in mortality among older adults, with women consistently facing a higher burden. This heightened vulnerability in women stems from a complex interplay of factors. Beyond greater longevity and post-menopausal hormonal shifts that reduce neuroprotection [32], women may exhibit a brain hypometabolism pattern from midlife that signals early risk [33]. This can be compounded by a more pro-inflammatory cerebral immune response [34], a greater dementia risk conferred by the ApoE4 allele [35], and an accelerated vascular decline in late life which increases susceptibility to lipid-related brain injury [36]. Yet, the most telling insight is not the disparity itself, but the near identical rate at which mortality has escalated for both sexes. This parallel trend suggests that while older women carry a higher baseline risk, the systemic forces that have recently driven up mortality, most notably the COVID 19 pandemic, have impacted older men and women with equal severity.

This study uncovers profound racial and ethnic inequities in mortality among older adults. The most severe burden falls upon Non-Hispanic (NH) Black individuals, who exhibited both the highest death rate and the most rapid rate of increase. This disparity is multifactorial. It stems from a higher lifelong burden of cardiometabolic comorbidities [37] and the impact of structural inequities that impede quality care [38]. This is compounded by the "weathering" effect, where chronic stress from systemic racism may accelerate biological aging, increasing late-life vulnerability to neurodegeneration [39]. Furthermore, the ApoE4 allele, the strongest genetic risk factor for Alzheimer's, is more prevalent in populations of African ancestry, contributing to a higher baseline risk at the population level [40]. While the crisis is most acute for Black seniors, the exceptionally high mortality among NH White older adults underscores this as a broad societal failure. In contrast, rates were lower among Hispanic and Asian or Pacific Islander (API) older adults. The finding for the Hispanic population may reflect a weakening "Hispanic Paradox," given their rapid mortality increase [41]. The lower API rate should be interpreted with caution, as this broad category masks significant heterogeneity in risk among its distinct subgroups [42].

The role of geography in this mortality crisis is crucial. The burden on older adults is not evenly spread across the nation but is instead heavily concentrated in the Southern United States. This regional hotspot aligns with the well-documented "Diabetes Belt," suggesting a deep-rooted foundation of metabolic risk factors that become particularly lethal in late life [43]. Driving this pattern is a profound rural-urban disparity. Non-metropolitan areas consistently show higher death rates, and this gap is widening, as older adults there struggle against known barriers to the specialized care this dual diagnosis requires [44]. A puzzling counter-narrative emerges in the Northeast; despite a lower overall burden, this region saw the fastest mortality increase, a dynamic that points toward unique and accelerating pressures on its aging population [45].

At the state level, the picture becomes even more complex. The sheer scale of this local variation is stark: an older adult's risk of dying from this condition was seven times higher in Vermont than in Nevada during the study period. This is a powerful testament to how 'place' can shape survival. Hotspots like Vermont and Nebraska dismantle the idea of a simple Southern problem, highlighting instead diverse archetypes of risk, perhaps rooted in the distinct challenges of rural aging in different parts of the country [46]. Ultimately, these state-level differences show that outcomes for the elderly are not

predetermined but are critically shaped by a mosaic of local policies, economic conditions, and the quality of regional healthcare systems [47].

The analysis of death locations for these older adults reveals a clear end-of-life trajectory that largely unfolds outside of acute hospital settings. The plurality of deaths in nursing homes or long-term care facilities (43.7%) is expected, as this setting often provides the necessary intensive, late-stage dementia care [48]. Equally significant is the substantial portion of deaths at the decedent's home (27.3%), a figure reflecting both the preference for aging in place and the profound burden on family caregivers [49]. In stark contrast, inpatient hospital deaths were relatively uncommon (11.4%). This likely represents a welcome shift in geriatric care away from burdensome interventions and toward a palliative approach for older adults with terminal dementia [50].

This study's findings demand a crucial shift in focus: from solely preventing dementia to improving care for older adults already living with it. For clinicians, this means moving beyond routine lipid management to a more nuanced, palliative-focused approach that actively involves family caregivers in the complex risk-benefit decisions surrounding statin use in frail, multi-morbid patients [51,52]. For policymakers, the data is a mandate to bolster the infrastructure of care outside hospital walls, by investing in workforce training for long-term care facilities and providing tangible support for the family caregivers who shoulder this immense burden [53]. Finally, researchers must pivot. The urgent questions are no longer just about prevention, but about efficacy and implementation. Can lipid-lowering therapies improve quality of life for patients who already have cognitive impairment [54]? And how can we effectively deliver integrated care to the high-risk, underserved older adults identified in this study [55]? Answering these questions is critical to addressing the real-world complexities of this growing public health crisis.

This study is limited by its reliance on death certificates, which are subject to diagnostic misclassification and coding errors that may misrepresent the true mortality burden in older adults [56]. As an ecological analysis, the study demonstrates population-level associations, not individual causality. Furthermore, the lack of granular clinical data (such as disease severity, medication use, or other comorbidities) precludes a more detailed, confounder-adjusted analysis, while the broad demographic categories may mask important subgroup heterogeneity. Despite these constraints, the study's strength is its population-wide scope, offering a vital, high-level view of a worsening public health crisis among America's older adults.

Conclusion

Over the past two decades, mortality at the intersection of hyperlipidemia and dementia in older Americans has risen more than six-fold, underscoring an escalating public health crisis. This is not a uniform trend. Its trajectory has been shaped by the competing forces of pharmacological intervention and the acute shock of the COVID-19 pandemic, while its devastating burden falls disproportionately on women, Non-Hispanic Black individuals, and those in Southern and rural communities. These are not disconnected statistics; they are the downstream consequences of a fragmented healthcare system struggling to manage the complexities of multi-morbidity in an aging and inequitable society. Therefore, these findings must serve as a catalyst, shifting the focus from simply documenting this crisis to the urgent implementation of integrated, equitable strategies that protect the brain health of America's older adults.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

The data supporting the findings of this study were obtained from the CDC WONDER online database (Centers for Disease Control and Prevention Wide-ranging Online Data for Epidemiologic Research). The datasets used and analyzed during the current study are publicly available and can be accessed at *https://wonder.cdc.gov*.

Competing interests

All authors declare no competing interests.

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Table 1

Table 1 is available in the Supplementary Files section.

Figures

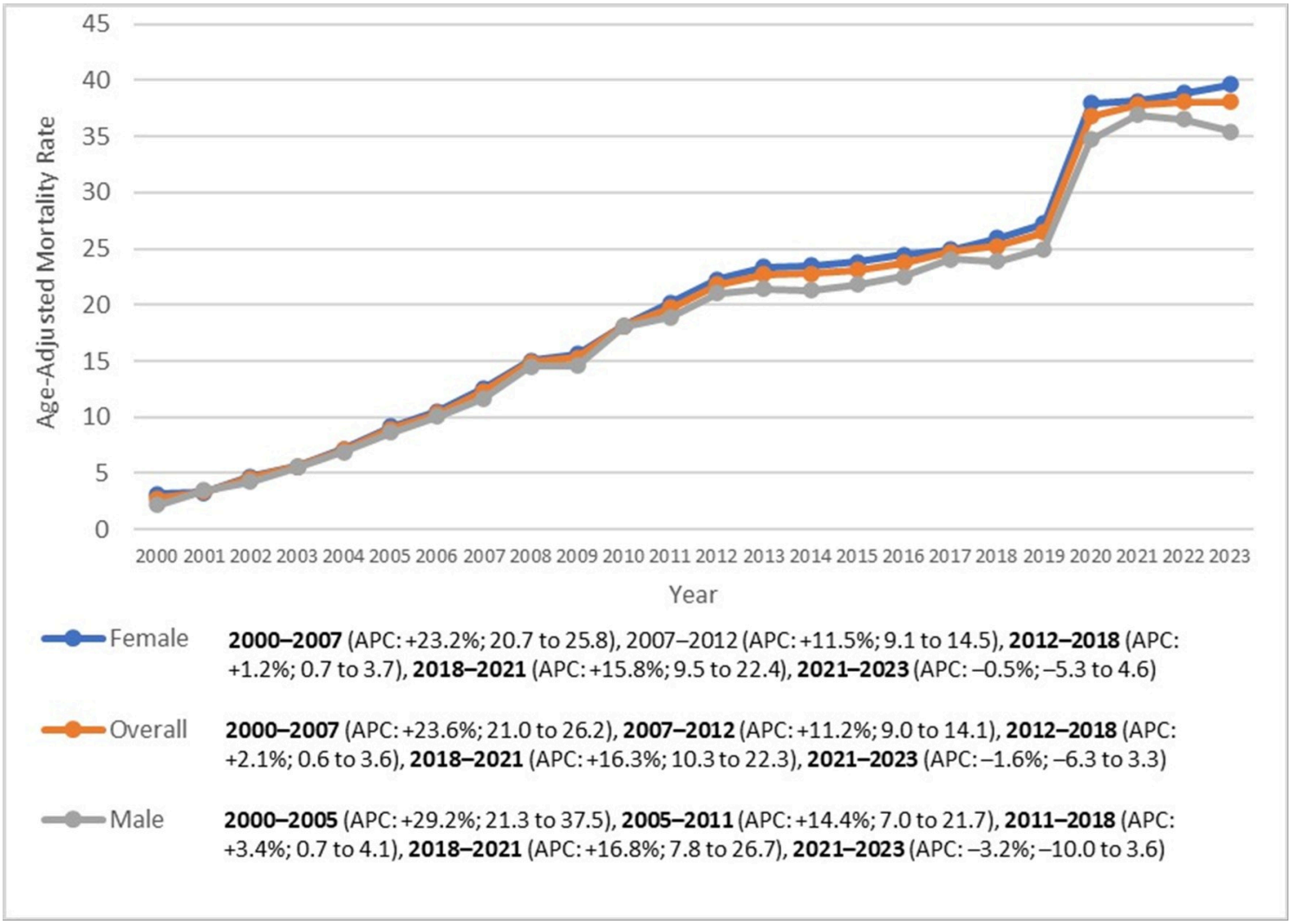


Figure 1

Overall and sex-stratified Dementia and Hyperlipidemia-related Age-Adjusted Mortality Rates (AAMRs) per 100,000 individuals in the United States, 2000–2023.

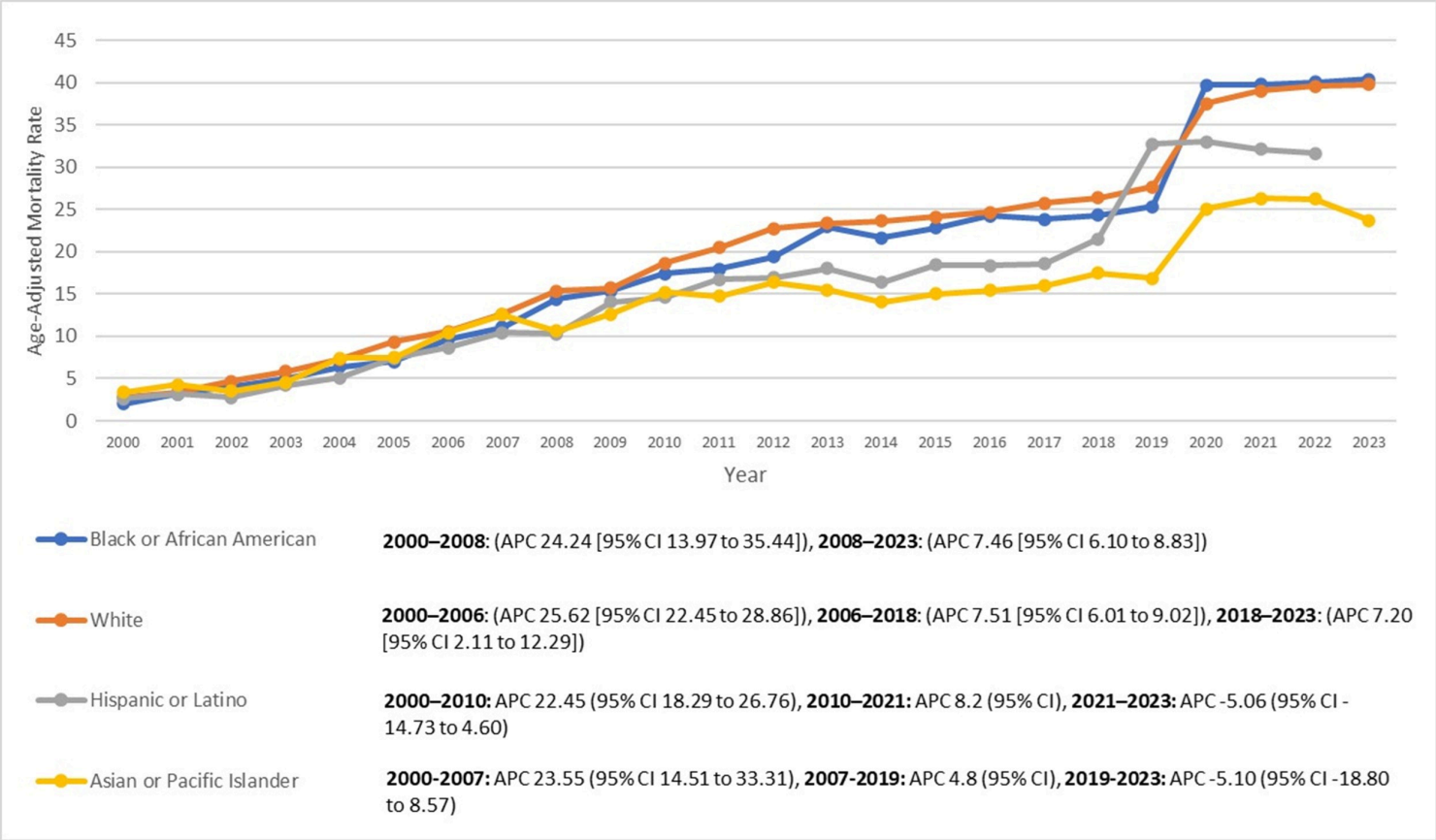


Figure 2

Dementia and Hyperlipidemia-Related Age-Adjusted mortality rates (AAMRs) per 100,000 individuals stratified by race and ethnicity in the United States, 2000–2023.

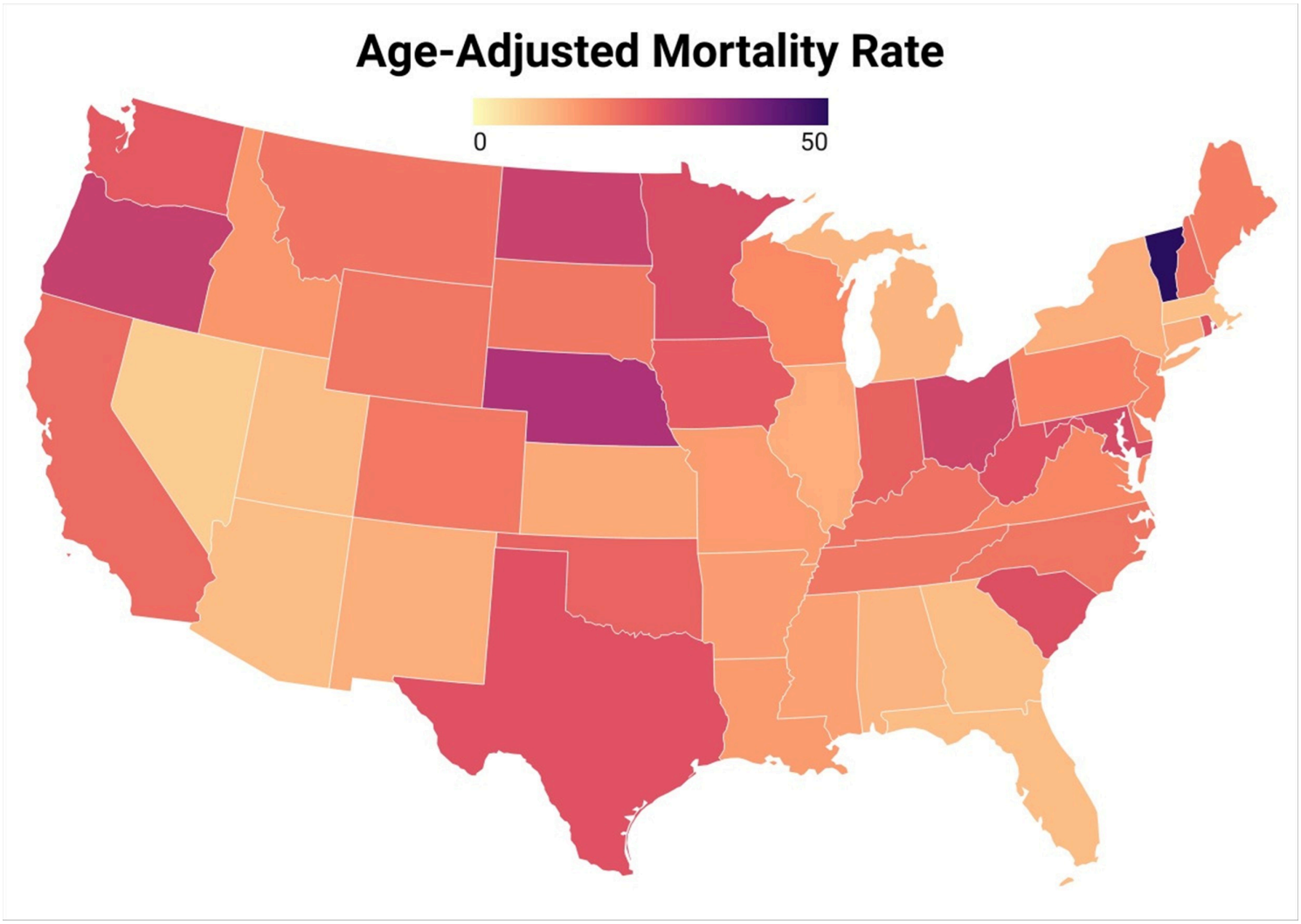


Figure 3

Dementia and Hyperlipidemia-Related related mortality in adults in the United States stratified by state, 2000 to 2023

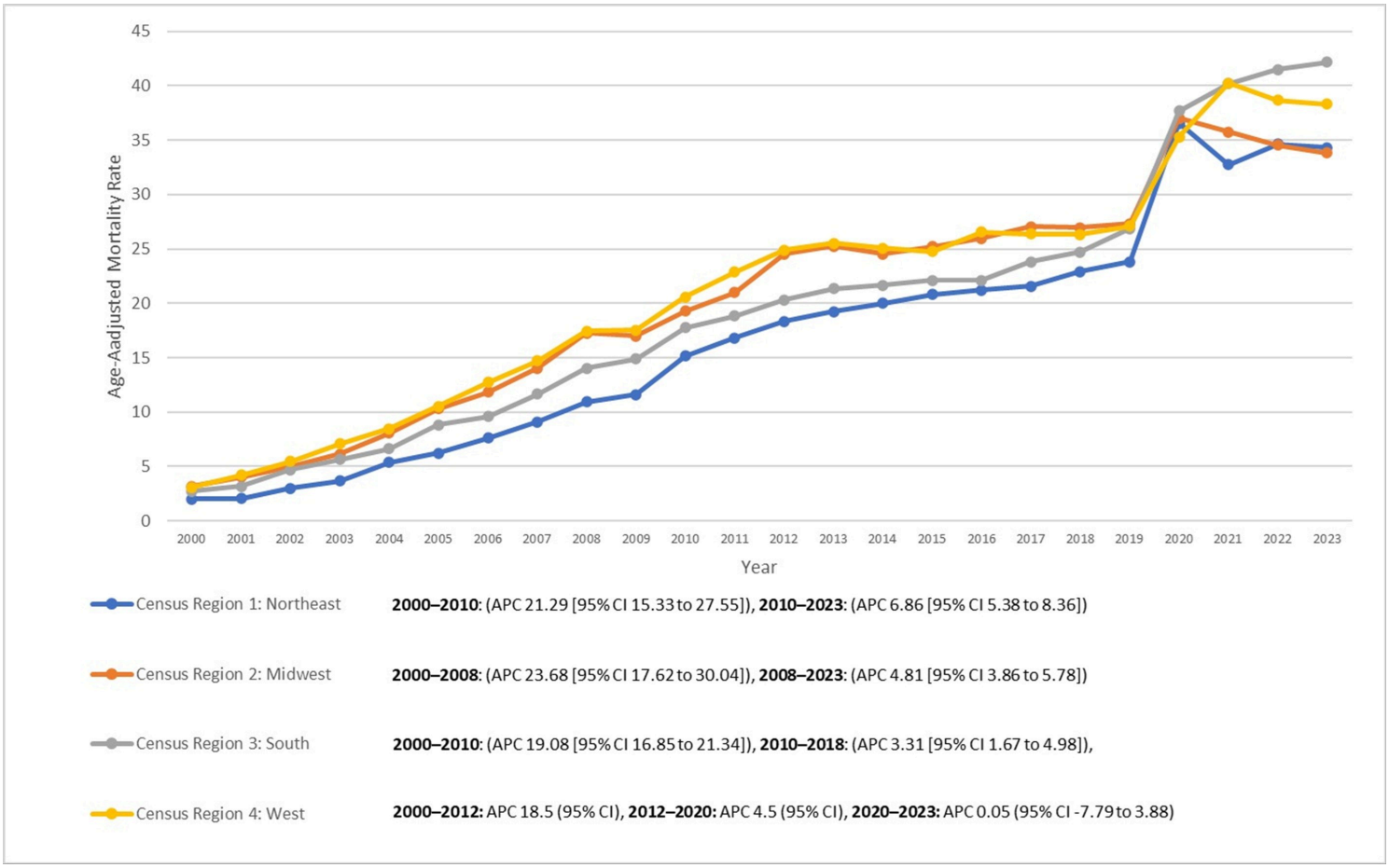


Figure 4

Dementia and Hyperlipidemia-Related age-adjusted mortality rates (AAMRs) per 100,000 individuals stratified by census Region in the United States, 2000–2023.

Supplementary Files

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- TablesHLDandDementianew.docx
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