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RECEIVED 14 February 2024

ACCEPTED 31 July 2024

PUBLISHED 14 August 2024

CITATION

McCandless MG, Dharia AA, Wicks EE and
Camarata PJ (2024) Geo-demographic trends
in nontraumatic subarachnoid
hemorrhage-related mortality among older
adults in the United States, 1999–2020.
Front. Neurol. 15:1385128.
doi: 10.3389/fneur.2024.1385128

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Geo-demographic trends in nontraumatic subarachnoid hemorrhage-related mortality among older adults in the United States, 1999–2020

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Introduction: Nontraumatic subarachnoid hemorrhage (ntSAH) often results from a ruptured aneurysm and correlates with significant morbidity and mortality, particularly among the older population. Despite its impact, limited comprehensive studies evaluate the longitudinal trends in ntSAH-related mortality in older adults in the United States (US).

Methods: The authors conducted a retrospective analysis using the CDC WONDER database from 1999 to 2020, analyzing Multiple Cause-of-Death Public Use death certificates to identify ntSAH as a contributing factor in the death of adults aged 65 years and older. We calculated age-adjusted mortality rates (AAMR) and annual percent change (APC) to examine trends across demographic variables such as sex, race/ethnicity, urbanization, and states/census region.

Results: A total of 78,260 ntSAH-related deaths (AAMR 8.50 per 100,000 individuals) occurred among older adults in the US from 1999 to 2020. The overall AAMR for ntSAH decreased from 9.98 in 1999 to 8.67 in 2020 with an APC of -0.7% [95% CI $(-1.0, -0.3)$]. However, the authors observed a noticeable rise from 2013 to 2020 with an APC of 1.7% [95% CI $(0.8, 2.6)$]. Sex, racial, and regional disparities were evident with higher mortality rates for ages 85 or greater (crude mortality rate 16.6), women (AAMR 9.55), non-Hispanic Asian or Pacific Islander (AAMR 12.5), and micropolitan areas (AAMR 8.99), and Western US (AAMR 8.65).

Conclusion: Mortality from ntSAH increases with age, affects women disproportionately, and occurs more often in an inpatient setting. These findings necessitate targeted, multi-dimensional health policies and clinical interventions. Specialties beyond neurosurgery can utilize this data for improved risk stratification and early treatment. Policymakers should focus on equitable resource allocation and community-level interventions to mitigate these trends effectively.

KEYWORDS

epidemiology, subarachnoid hemorrhage, elderly, mortality, disparities

Introduction

The risk of nontraumatic subarachnoid hemorrhage (ntSAH) rises sharply with age (1–3). Due to aging demographics in the United States (US), ntSAH warrants a more focused epidemiological evaluation by American neurosurgeons. Especially among adults aged 65 years and older, the morbidity and mortality associated with ntSAH represent a considerable clinical and economic burden (4, 5). Age-specific data on ntSAH-related mortality among the older population in the US remains minimal (6). The lack of comprehensive analysis could impede the formation of targeted health policy measures aimed at reducing mortality and improving the quality of life in this vulnerable group (7).

Given the demographic shifts and the aging population's susceptibility to ntSAH, we investigate how trends in ntSAH-related mortality continue to evolve among adults aged 65 and above. To address this question, this study performs an in-depth analysis of data from the Centers for Disease Control and Prevention's Wide-ranging Online Data for Epidemiologic Research (CDC WONDER) database. By dissecting these trends, we aim to contribute to existing knowledge on ntSAH epidemiology, thereby informing clinical guidelines and health policy initiatives to mitigate the impact of ntSAH-related mortality among the older population.

Methods

Data source

This study investigated the number of deaths associated with nontraumatic subarachnoid hemorrhages (ntSAH) from ages 65 years and older in the United States from 1999 to 2020. The study used the CDC WONDER database (8). This study was exempt from institutional review board approval due to the public and anonymous nature of the database and was compliant with STROBE guidelines.

This study analyzed Multiple Cause-of-Death Public Use death certificates to identify ntSAH as a contributing factor in the death. The authors obtained the number of annual deaths related to ntSAH and the corresponding population sizes. The data were separated into categories based on sex, race/ethnicity, 10-year age groups, level of urbanization, and state. The study used the *International Statistical Classifications of Diseases, Tenth Revision* (ICD-10) code for ntSAH (I60.x) (9).

The sex, ethnicity, and race were recorded on the death certificates in compliance with the US Office of Management and Budget (10). Ethnicity and race were divided into separate categories, including Hispanic or Latino, non-Hispanic Black or African American, non-Hispanic Asian or Pacific Islander, or Non-Hispanic White patients. Although we included the individuals who did not fall into the categories of Hispanic or Latino or non-Hispanic in the overall analysis, we omitted these from the subgroup analysis due to the suppression of data with too few individuals in CDC WONDER.

Urbanization was defined in compliance with the 2013 National Center for Health Statistics Urban-Rural Classification Scheme for Counties (11). Metropolitan was subdivided into

large central metros (population >1 million and completely contain or are entirely contained by the largest city or contain at least 250,000 residents of any city within the statistical area), large fringe metros (population >1 million and not central metro), medium metros (population 250,000–999,999), and small metros (population <250,000). Nonmetropolitan counties are subdivided into micropolitan (population 10,000–49,999) and noncore (population <10,000). The data for each state excluded the District of Columbia. The place of death was subdivided into inpatient, nursing home, home, hospice facility, and other/unknown.

Statistical analysis

The crude mortality rate (CMR) and age-adjusted mortality rates per 100,000 (AAMR) were calculated using the US 2000 standard population (12). To evaluate mortality trends, Joinpoint Regression Program (v4.9.1.0; National Cancer Institute, 2022) (13) was employed to analyze the overall population and subgroup segments. The Monte Carlo permutation test was employed to determine the annual percent change (APC) in mortality with 95% confidence intervals at identified segments linking join points. The slopes of APCs were then calculated and assessed using a two-sided *t*-test against a null value of 0. Statistical significance was determined by a *P*-value < 0.05. Analysis was conducted in October 2023.

Results

A total of 78,260 ntSAH-related deaths (AAMR 8.50 per 100,000 individuals) occurred among older adults in the United States from 1999 to 2020. Of the total deaths, 26,285 (33.9%) were men, 51,359 (66.1%) were women. Of the known ethnic and racial groups 60,151 (76.9%) were Non-Hispanic White patients, 6,873 (8.8%) were non-Hispanic Black or African American, 4,118 (5.3%) were non-Hispanic Asian or Pacific Islander, and 5,963 (7.6%) were Hispanic or Latino. Of the 75,928 known locations of death, 59,122 (75.6%) were inpatient facilities, 8,004 (10.2%) were nursing homes, 4,911 (6.3%) were in the decedent's home, and 3,891 (5.0%) were in hospice facilities. Among diagnosis, age, sex, race and ethnicity, and urbanization, the highest mortality rates were seen in those 85 or older (CMR 16.9), women (AAMR 9.55), non-Hispanic Asian or Pacific Islander adults (AAMR 12.5), micropolitan populations (AAMR 8.99), and in the Western US (AAMR 8.65; Table 1, Supplementary Table 1).

The overall AAMR for ntSAH in older adults decreased from 9.98 in 1999 to 8.67 in 2020 with an average annual percent change (AAPC) of -0.7% , 95% CI (-1.0 , -0.3). The AAMR decreased from 1999 to 2013 [APC, -1.8% 95% CI (-2.2 , -1.5)] followed by a rise from 2013 to 2020 [APC, 1.7% 95% CI (0.8 , 2.6)]. NtSAH-related mortality remained stable for men but decreased for women. Specifically, the AAMR in men changed from 7.40 in 1999 to 7.89 in 2020, while the AAMR for women decreased from 11.7 in 1999 to 9.27 in 2020. Although the AAMR for both men and women decreased from 1999 to 2014 and 1999 to 2011, respectively, the AAMR for men increased from 2014 to 2020 [APC, 2.9%

TABLE 1 Demographics of nontraumatic subarachnoid hemorrhage-related mortality.

Characteristics	Deaths (%) ^a	CMR or AAMR (95% CI)
Total	78,260 (100)	AAMR: 8.50 (8.44, 8.56)
10-year age groups		CMR
65–74 years	27,905 (35.9)	5.47 (5.40, 5.53)
75–84 years	29,591 (38.1)	9.91 (9.80, 10.0)
85+ years	20,148 (26.0)	16.9 (16.6, 17.1)
Gender		AAMR
Men	26,285 (33.9)	6.94 (6.86, 7.03)
Women	51,359 (66.1)	9.55 (9.47, 9.63)
Race/Ethnicity		AAMR
Non-Hispanic White patients	60,151 (76.9)	8.06 (8.00, 8.13)
Non-Hispanic Black or African American	6,873 (8.78)	8.87 (8.66, 9.08)
Hispanic or Latino	5,963 (7.62)	9.67 (9.42, 9.92)
Non-Hispanic Asian or Pacific Islander	4,118 (5.26)	12.5 (12.2, 12.9)
Non-Hispanic Native American or Alaska Native	385 (0.49)	8.73 (7.83, 9.62)
Other/unknown	770 (0.98)	
Urbanization		AAMR
Noncore	6,071 (7.81)	8.19 (7.99, 8.40)
Micropolitan	8,259 (10.6)	8.99 (8.80, 9.19)
Small Metro	7,889 (10.2)	8.53 (8.34, 8.71)
Medium Metro	16,978 (21.9)	8.59 (8.46, 8.72)
Large Fringe Metro	17,428 (22.5)	8.03 (7.91, 8.15)
Large Central Metro	21,019 (27.1)	8.46 (8.35, 8.58)
Census region		AMMR
Northeast	15,209 (19.4)	8.34 (8.21, 8.48)
Midwest	17,768 (22.7)	8.54 (8.41, 8.66)
South	27,799 (35.5)	8.32 (8.22, 8.42)
West	16,868 (21.6)	8.65 (8.51, 8.78)
Unknown	616 (0.79)	–
Location of death		
Inpatient	59,122 (75.6)	–
Nursing Home	8,004 (10.2)	–
Home	4,911 (6.28)	–
Hospice Facility	3,891 (4.97)	–
Other/Unknown	2,332 (2.98)	–

CMR, crude mortality rate per 100,000 individuals; AAMR, age-adjusted mortality rate per 100,000 individuals.

^aPercentage may not sum to 100 due to rounding.

95% CI (1.7, 4.2)] while the AAMR for women had a statistically insignificant rise from 2011 to 2020 [APC, 0.6% 95% CI (–0.1, 1.3); Figure 1]

AAMR decreased for all ethnic and racial groups. Asian or Pacific Islander adults had the highest AAMR which decreased from 17.2 in 1999 to 12.0 in 2020. The AAMR for White, Black, and Asian or Pacific Islander adults decreased from 1999 to 2012, 2013, and 2014, respectively, followed by a statistically significant increase to 2020 for White and Black adults. The AAMR for Asian or Pacific Islander adults had a statistically insignificant increase [APC, 1.1% 95% CI (–1.4, 3.7)], while the AAMR for Hispanic or Latino adults decreased from 13.7 in 1999 to 9.30 in 2020 (Figure 2).

Subgroup analysis showed that CMR in those 65 and older decreased from 9.93 in 1999 to 8.32 in 2020. The CMR for adults 65–74 and 75–84 years old decreased from 1999 through 2020 while the CMR in adults 85 or older increased from 16.0 in 1999 to 19.3 in 2020 (Supplementary Figure 1). From 1999 through 2020, the proportions of ntSAH-related deaths decreased in inpatient facilities (86.0%–66.7%). In contrast, the proportion of ntSAH-related deaths increased in homes (3.7%–11.4%), nursing homes (9.3%–9.9%), and hospice facilities (0.4% in 2003 to 9.6% in 2020; Supplementary Table 2, Supplementary Figure 2). The AAMR of ntSAH as the underlying cause of death decreased from 1999 to 2013 [APC, –2.5% 95% CI (–2.7, –2.2)] before stabilizing from 2013 to 2020 [APC, 0.2% 95% CI (–0.4, 0.9); Supplementary Table 3, Supplementary Figure 3].

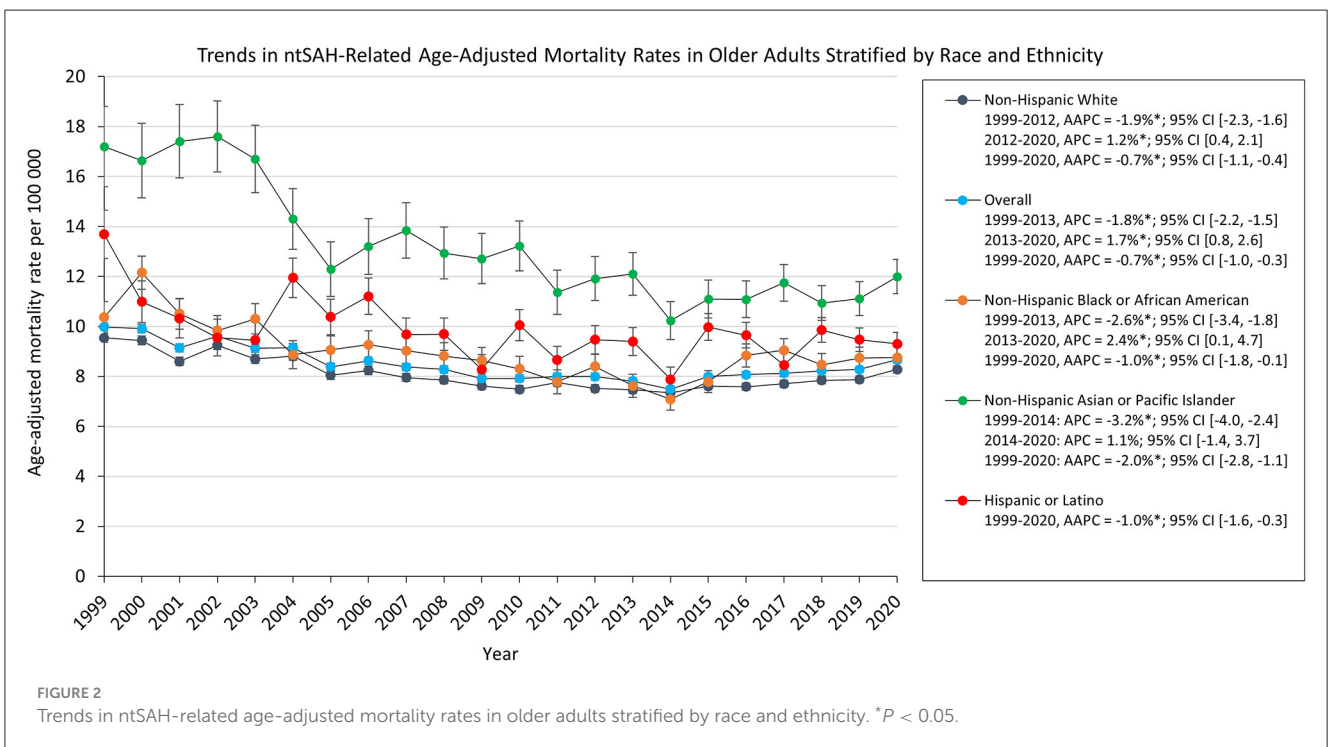
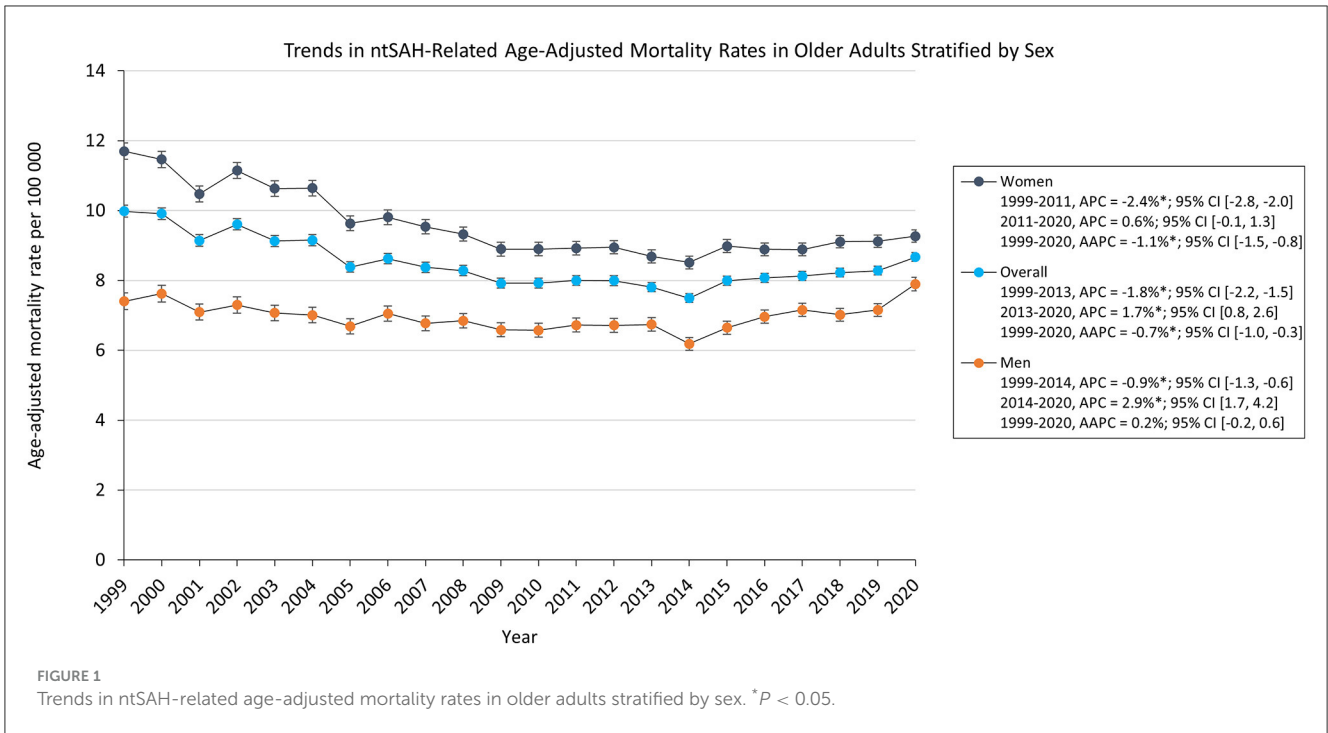
Mortality rates for all urbanization groups decreased from 1999 to 2020 except for micropolitan and noncore areas which remained stable. Micropolitan areas had the highest AAMR which decreased from 11.2 in 1999 to 9.93 in 2020. All urbanization groups decreased from 1999 to the 2010s. The AAMR for noncore, micropolitan, and medium metropolitan areas increased from 2008, 2011, and 2012 through 2020, respectively, while medium metropolitan, large fringe and large central areas remained stabilized from 2012 and 2014 through 2020, respectively (Figure 3).

There were significant regional differences in the burden of ntSAH-related mortality with the Western US having a significantly higher mortality burden compared to the remaining census regions (Table 1, Supplementary Table 4). The top five states (Hawaii, Tennessee, West Virginia, Alaska, and Washington) with the highest ntSAH-related mortality had much higher mortality than those in the bottom five states (Kansas, New Hampshire, Arizona, Florida, and Maine; Figure 4).

Discussion

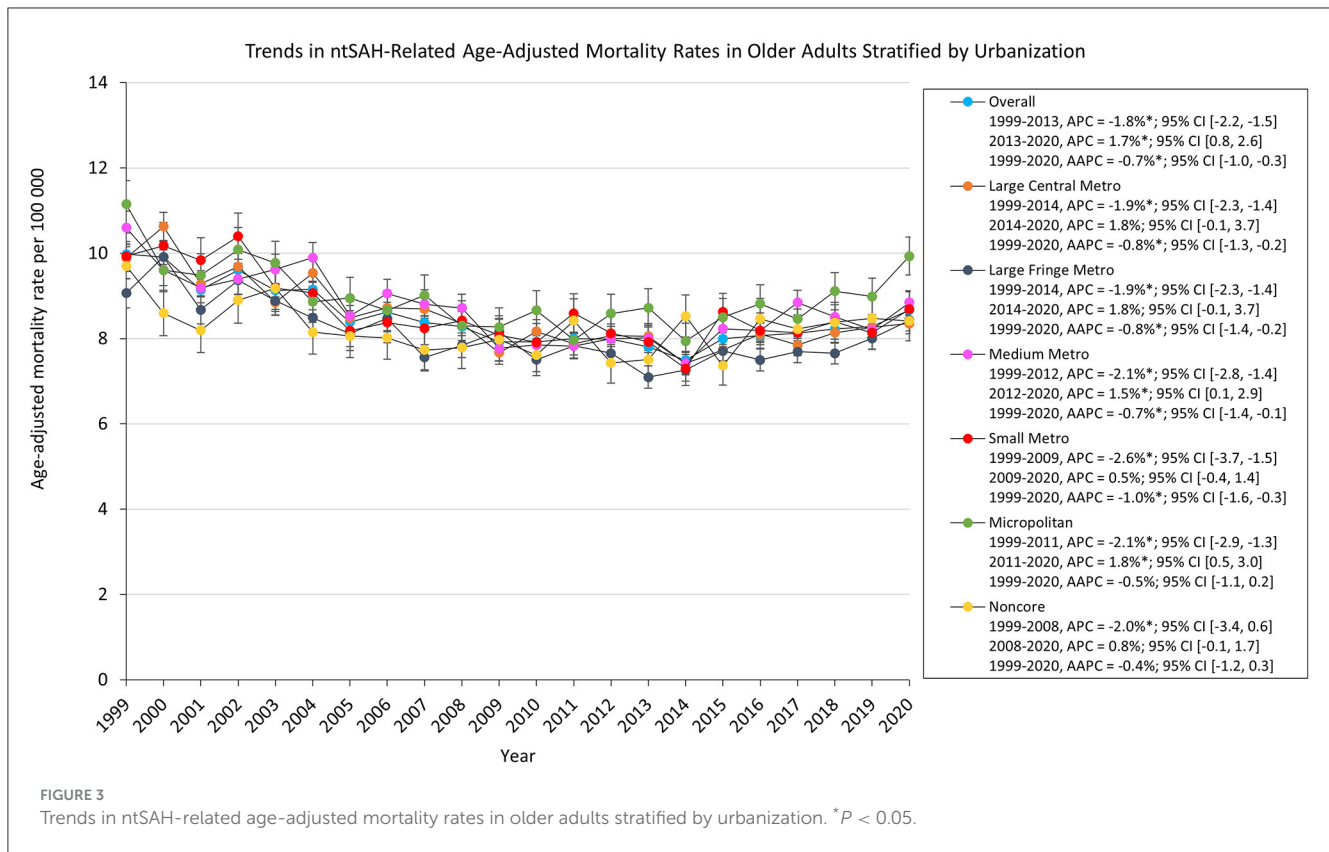
This comprehensive analysis of ntSAH-related mortality among adults aged 65 years and older from the CDC WONDER database from 1999 to 2020 demonstrates a complex trajectory. While the overall AAMR exhibited an annual decline of –0.7%, the overarching figure conceals dynamic changes over the span of 2 decades. An initial decline in mortality was observed from 1999 to 2013, followed by a concerning rise from 2013 to 2020. This resurgence in mortality rates, despite advancements in neurosurgical interventions and medical management, signals a need for further investigation into evolving risk factors and healthcare disparities in this vulnerable population.

The increase in mortality related to ntSAH in elder men observed in our study is relevant for several reasons. The results



confirm that this increase is a significant trend. This suggests that understanding trends in ntSAH mortality in elder men may help target public health interventions including increasing awareness and potentially different treatment strategies for this high-risk population. This trend also encourages further research to explore underlying causes, such as biological differences, lifestyle factors, comorbidities, or access to healthcare, which might contribute to higher mortality (14–16).

As patient demographics have shifted toward an older age with overall improvements in health care and longer life expectancies, clinical practice has also evolved with more elderly ntSAH patients referred to neurosurgical centers than ever before. Nearly two decades after the publication of the International Subarachnoid Aneurysm Trial (ISAT), which highlighted the utility of endovascular interventions over traditional microsurgical clipping and craniotomy for ruptured cerebral aneurysms, the



treatment of ntSAH has changed dramatically (17). In support of aggressive management of cerebral aneurysms and accommodation of elderly patients unable to tolerate surgery, the ISAT results have led to the explosive growth of endovascular coiling in the elderly SAH population. Although increasing technological sophistication has led to increased device costs and healthcare expenditures, we are now better equipped to treat patients with ntSAH (18).

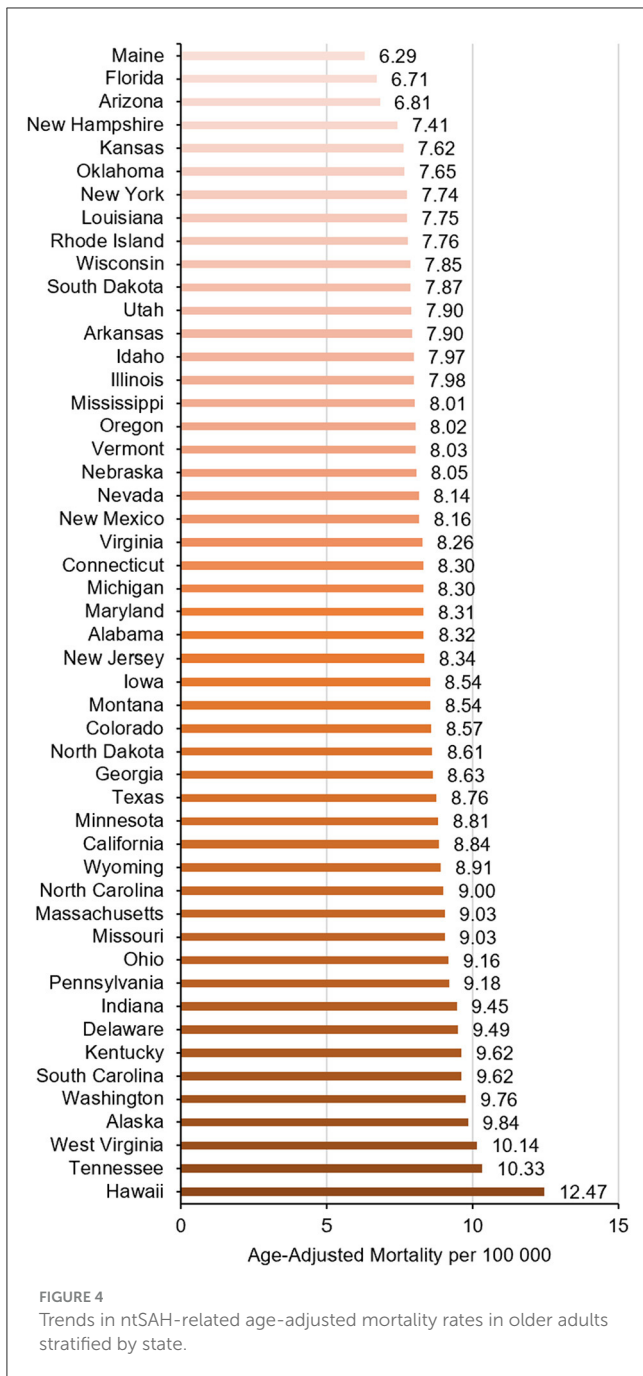
Several studies have cited advancing age, along with the severity of clinical presentation on admission, as two of the strongest prognostic factors for predicting poor functional outcomes (19–23). Age negatively impacts survival and recovery as older patients have a greater number of co-morbidities and systemic complications. Moreover, ntSAH has a unique pathophysiology in elderly patients. Elderly patients have greater degrees of brain atrophy, vessel calcification or stenosis, and hypertension, which may affect the pattern and extension of blood after a rupture. Additionally, elderly patients have lower cerebral blood flow and lower cardiac output. While less elasticity of the vessels may lower the probability of vasospasm after ntSAH, elderly patients have a high likelihood of mortality and cardiovascular events compared with the younger healthy population (24–26). Although these age-related pathophysiologic differences may account for greater mortality in elderly patients, the increasing mortality rate since 2013 within the cohort is alarming. A greater number of treatments, especially endovascular interventions enhanced by rapidly advancing technologies, are now offered to elderly patient more than at any previous time. The authors suspect that with improved access to tertiary care centers and greater number of elderly patients considered for treatment, more deaths are now

coded appropriately as ntSAH. This is compounded by the number of elderly individuals or family members who may choose to withdraw care and clinicians who forgo treatment understanding the poor functional outcomes within this cohort.

With respect to racial and ethnic stratification, all groups exhibited a decrease in AAMR, albeit to varying extents. Xia’s article, which spanned between 2007 and 2017, showed an unchanged incidence of spontaneous SAH in Asian, Hispanic, and Non-Hispanic White patients but an increased incidence in Black patients. This possibly suggests that either incidence has particularly increased in the Asian cohort since 2017, or that there is greater mortality in this cohort after hemorrhage recently.

The findings in this study illuminate geographical discrepancies related to urbanization. While all urbanization groups witnessed a decrease in mortality rates from 1999 to 2020, micropolitan areas remained persistently higher, and along with noncore areas stabilized instead of decreasing. Regional variances further complicate the landscape of ntSAH mortality, with the Western US exhibiting significantly higher mortality. Interestingly, significant differences were noted at the state level, highlighting the influence of local healthcare infrastructure, policy, and possibly environmental factors.

Regional and urban differences in mortality may reflect different levels of access to healthcare resources. Micropolitan areas have a greater incidence of vascular risk factors, such as cigarette smoking, diabetes, and hypertension, which have been associated with greater predisposition to, and worse outcomes following ntSAH (27). Mariajoseph et al. (28) contend that this may explain the higher rates of mechanical ventilation seen



in non-metropolitan location transfers after aneurysmal SAH, which yields greater rates of rebleeding due to delays in transfer. Furthermore, ntSAH care requires unique expertise, which has led to greater regionalization among higher-volume centers. Changes in mortality may suggest delayed transport to comprehensive stroke centers, which perform highly specialized endovascular and surgical procedures and have neuro-intensive care units. Care at high-volume teaching hospitals is more likely to reduce mortality and readmissions with multidisciplinary team-based interventions involving neurointensivists, neurosurgeons, endovascular specialists, nursing care, social work, and rehabilitation services.

Older patients with ntSAH may require prompt consideration for referral to high-volume teaching hospitals to reduce this mortality.

Limitations

There are inherent limitations to this study that warrant consideration. The employment of the ICD codes and the dependency on death certificates for data collection may engender some level of misclassification of ntSAH as a cause of death. Additionally, advancement in diagnostic capabilities and the increasing use of electronic health records may contribute to changes in the recording of ntSAH on death certificates, potentially influencing trends without necessarily reflecting actual changes in ntSAH-related mortality rates among the older population. The study has limitations in identifying the primary driver(s) of the U-shaped trends in mortality from 2009 to 2020. We believe that reporting the cause of death was affected by the adoption of the electronic medical records due to the enactment of the Health Information Technology for Economic and Clinical Health Act (29). Additionally, CDC WONDER does not capture subgroups with smaller populations as described by Tiwari et al. (30). The CDC WONDER database from which this study draws its data lacks granularity on disease characteristics such as clinical symptoms, laboratory markers, imaging studies, or other prognostic indicators. These limitations collectively circumscribe the ability to draw definitive conclusions and suggest that the findings should be interpreted cautiously.

Conclusions

The study reveals that after an initial period of decline, the AAMR for ntSAH-related mortality among older adults has discernibly increased from 2013 to 2020 in the United States. This rise is nuanced by demographic variables such as sex, race and ethnicity, and geographic location, necessitating a multi-dimensional approach for its interpretation and management. Targeted health policy measures are imperative to address the escalating burden of ntSAH in the older population, with an emphasis on refined risk stratification, timely intervention, and the mitigation of persistent disparities.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent from the patients/participants or patients/participants' legal guardian/next of kin was not required to participate in this study in accordance with the national legislation and the institutional requirements.

Author contributions

MM: Conceptualization, Data curation, Formal analysis, Methodology, Software, Visualization, Writing – original draft, Writing – review & editing. AD: Writing – original draft, Writing – review & editing. EW: Writing – original draft, Writing – review & editing. PC: Funding acquisition, Supervision, Writing – original draft, Writing – review & editing.

Funding

The author(s) declare that no financial support was received for the research, authorship, and/or publication of this article.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships

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that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fneur.2024.1385128/full#supplementary-material>

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