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Trends in Alzheimer Disease Mortality Among American Indian and Alaska Native People Between 2011 and 2019

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Purpose: The number of American Indian and Alaska Native (AI/AN) people living with dementia is expected to increase 5-fold by 2060. Social determinants of health may explain disparities in the
incidence of Alzheimer disease (AD) but remain largely overlooked.

Methods: We examined the time trend of AD mortality rates an associations of the percentage of AI/ANs, density of primary care physicians and neurologists, area deprivation index, rurality, and Indian Health Service region with AD mortality in 646 purchased/referred care delivery area counties.

Results: AD mortality rates significantly increased over time. Counties with higher concentrations of AI/AN people had lower AD mortality. More deprived counties had 34% higher AD mortality compared with less deprived counties. AD mortality was 20% lower in nonmetro counties than in metro counties.

Conclusions: Findings have implications for prioritizing areas where more resources for AD care, education, or outreach are needed.

Key Words: Alzheimer disease, American Indian, Alaska Native, mortality, access to care, socioeconomic status, rurality

BACKGROUND

Alzheimer disease (AD) is an irreversible, progressive brain disease affecting 4.7 million Americans over 65 years of age in 2010, with a projected increase to 13.8 million cases by 2050.[1] In 2019, AD was the sixth leading cause of death in the United States.[2] The only longitudinal study of AD mortality rates by race and ethnicity showed that between 1999 and 2004, death related to AD increased by 80% among American Indian and Alaska Native people (AI/AN).[3] AI/AN people alone or in combination with other racial and ethnic groups comprise 7.1 million people or 2% of the U.S. population.[4] The Centers for Disease Control and Prevention (CDC) reports that 20% of AI/AN people aged 45 and over experience cognitive decline related to memory loss and predicts the number of AI/AN people aged 65 and over living with dementia will increase 5-fold by 2060.[5]

Previous research has largely focused on nonmodifiable or clinical risk factors for AD including aging, gene variants, family history, traumatic brain injury, hypertension, or diabetes.[6–9] Modifiable social determinants of health, such as access to health care, poverty, or rurality, may explain disparities in the incidence of AD and mortality related to AD but remain largely overlooked.[10] Primary care physicians (PCPs) and specialists play an important role in diagnosing and managing the needs of individuals with AD.[1,11] However, PCP and neurologist

shortage is an ongoing concern across the United States.[12] AI/AN people are particularly vulnerable to this shortage due to geographical or financial barriers related to accessing health care, lack of culturally competent providers, and distrust of medical professionals.[13]

Multiple studies in England, Wales, and the United States have revealed that living in socioeconomically deprived neighborhoods is associated with increased incident dementia,[14,15] incident AD,[16,17] and mortality related to dementia.14 Urban-rural disparities in mortality rates related to AD are also documented. Rural counties are experiencing a large and widening disparity in mortality related to AD compared with their urban counterparts.3,[18] These disparities may be associated with lower socioeconomic status, limited infrastructure, or larger prevalence of other chronic conditions that increase the risk of AD in socioeconomically deprived and rural areas.[18] Around 15% of AI/AN people live on reservations or other trust lands, most of which are geographically isolated with limited infrastructure.[19] This may render AI/AN people particularly vulnerable to AD.

In the absence of accurate incidence or prevalence data about AD, mortality data are commonly used to estimate the burden of AD in communities. Consistent with this approach, we conducted a longitudinal examination of AD mortality trends as a function of the percentage of AI/AN residents living in each county (hereafter AI/AN concentration), physician density, socioeconomic status, and rurality. We focused on AI/AN people as the nation's most rural population and a population understudied in AD
research.

METHODS

This longitudinal study was conducted at the level of the county in Indian Health Service (IHS) purchased/referred care delivery areas (PRCDA). These areas contain or are located adjacent to federally recognized tribal lands.[20] Approximately 62% of the AI/AN people live in PRCDA counties and race classification for AI/AN people is more accurate in these areas compared with other counties.[21] Figure 1 shows the location of PRCDA counties in the United States.

We used mortality data from the CDC National Vital Statistics System for the years 2011 to 2019. Counties are the smallest spatial unit, for which the CDC provides mortality data. Deidentified mortality data were obtained through a data-sharing agreement with the CDC.

Reported AD deaths were identified as either the underlying cause or contributing cause of death using the International Classification of Diseases 10th Revision codes of G30.0, G30.1, G30.8, or G30.9. A single underlying cause of death in addition to r20 additional contributing causes of death can be reported on the US standard Certificate of Death. We included decedents identified as AI/AN alone or in combination with other races or ethnicities. Race and ethnicity information on death certificates is collected from next of kin or by observation of a coroner or physician.[22]

Measures

The outcome variable was the number of AD deaths per county and year. All AI/AN decedents were 45 years or older at the time of death. No missing data were reported for age among AI/AN decedents with AD as the underlying or contributing cause of death.

Independent variables included year, percentage of AI/AN people, density of PCPs, density of neurologists, area deprivation index (ADI), rural-urban continuum codes (RUCC), and an indicator variable for PRCDA regions. We calculated the percentage of AI/AN people per county and year. This measure reflected the racial composition of counties in terms of the percentage of AI/ANs and has been used as an indicator for racial residential homogeneity and segregation.[23]

The Health Resources and Services Administration provided data on the number of nonfederal PCPs and neurologists by county.[24] These data were based on the American Medical Association Masterfile. Data on PCPs were available from 2011 to 2019. Data on neurologists were available for 2010, 2015, and 2018. The 2010 neurologists' data were merged with the 2011 to 2013 mortality data, the 2015 neurologists' data to 2014 to 2016 mortality data, and the 2018 neurologists' data to 2017 to 2019 mortality data. We approximated physician density by calculating PCP and neurology availability per 10,000 persons for each county and year.

We used ADI, a validated composite score of socioeconomic status, to represent the socioeconomic characteristics of counties.[25] This index is based on 17 census variables in 4 domains: poverty, housing, employment, and education. Scores range from 1 to 100, with higher scores reflecting more deprivation. We created a binary indicator of high deprivation (top 30%), as a surrogate for low socioeconomic status.[25] ADI data for 2015 were joined with mortality data from 2011 to 2019.

County rurality was defined by RUCC codes. Codes 1 to 3 were classified as metro; codes 4 to 9 were classified as nonmetro.26 The metro category includes large urban counties with a population of 250,000 or larger. The nonmetro category includes small urban areas with a population of 20,000 and rural areas with a population of 2500.26 RUCC data for 2013 were linked to mortality data from 2011 to 2019. PRCDA counties are typically grouped into 6 HIS regions including Alaska, East, Northern Plains, Pacific Coast, Southern Plains, and Southwest.[20] We combined Alaska with Pacific Coast because of the small number of cases. Members of federally recognized tribes may receive health care through this, clinics run by tribal governments, or private or federal insurance plans. IHS provides primary care only and for this reason, access to specialized health care and hospital care is generally not available on tribal lands.[27]

Statistical Analyses

Descriptive statistics included age-adjusted mortality rates for AD overall and by ADI, RUCC, and PRCDA region. Rates were calculated per 100,000 persons and are age-adjusted to the 2000 U.S. standard population.[20] We used generalized linear mixed models with zero-inflated negative binomial distribution to estimate the association between AD mortality and our independent variables. These were estimated as bivariable models (adjusted by time), for each independent variable separately, and as a multivariable model that included all independent variables together. All models included a fixed effect for time, a random intercept for county, and the log of AI/AN population by county and year as the offset variable. Less deprivation, metro

designation, and East were the reference categories for the ADI, RUCC, and IHS region variables. Results are reported as incidence risk ratios (IRR) with 95% CI. The significance level was set at 0.05 (2-tailed). All analyses were conducted by R software version 4.0.3 and the glmmTMB package.

RESULTS

Our data set included 3024 AD deaths in 646 PRCDA counties (Fig. 1). The average county was composed of 7.0% (interquartile range = 1.0% to 5.8%) AI/AN people in 2011 and 7.4% (interquartile range = 1.0% to 6.6%) AI/AN people in 2019. More counties were classified as less deprived compared with more deprived (62% vs 38%) or nonmetro compared with the metro (67% vs 33%). Overall age-adjusted AD mortality rate increased from 36.2 per 100,000 people in 2011 to 44.2 per 100,000 people in 2019, an increase of 22%. Increase in mortality rates was larger for more deprived counties versus less deprived counties (an increase of 30% vs 17%). Across RUCC designations, AD mortality rates increased from 44.7 per 100,000 people in 2011 to 54.9 per 100,000 in 2019 in metro counties and from 27.9 per 100,000 people in 2011 to 32.5 per 100,000 in 2019 in nonmetro counties (an increase of 23% in metro vs 16% in nonmetro counties). For IHS regions, the greatest increase in the AD mortality rate was observed in the Southern Plains followed by the East and Pacific Coast/Alaska in AD mortality. In contrast, the Northern Plains and Southwest experienced slightly decreased AD mortality rates. Table 1 shows age-adjusted AD mortality rates among AI/AN people by ADI, RUCC, and IHS region.

Table 2 depicts the results of bivariable and multivariable generalized linear mixed models. In bivariable models, time was associated with an increased incidence risk of AD. Every 10% increase in the percentage of AI/AN people was associated with a 15% lower risk for AD mortality (IRR = 0.85, 95% CI = 0.81-0.89). Nonmetro counties had a 31% lower risk for AD mortality compared with metro counties (IRR = 0.69, 95% CI = 0.57-0.83). Compared with IHS region East, the risk for AD mortality was 76% higher in Pacific Coast/Alaska (IRR = 1.76, 95% CI = 1.34-2.31), 98% higher in Southern Plains (IRR = 1.98, 95% CI = 1.47-2.66), and 35% lower in Southwest (IRR = 0.65, 95% CI = 0.47-0.91). Other county characteristics including PCP density, neurology density, and ADI were not significantly related to AD mortality in bivariable models.

Similar results were observed in multivariable models. AD mortality significantly increased over time (IRR = 1.08, 95% CI = 1.06-1.09). Every 10% increase in the percentage of AI/AN people was associated with a 14% lower risk for AD mortality (IRR = 0.86, 95% CI = 0.82-0.91). More deprived counties had a 34% higher risk for AD mortality compared with less deprived counties (IRR = 1.34, 95% CI = 1.06-1.70). Nonmetro counties had a 20% lower risk for AD mortality compared with metro counties (IRR = 0.80, 95% CI = 0.66-0.97). Compared with HIS region East, the risk for AD mortality was 2 times higher in Pacific Coast/Alaska (IRR = 2.16, 95% CI = 1.64-2.85) and Southern Plains (IRR = 2.25, 95% CI = 1.67-3.04) controlling for other county characteristics. None of the interactions between time and county characteristics were significantly related to AD mortality rates (results are not shown; available on request from authors).

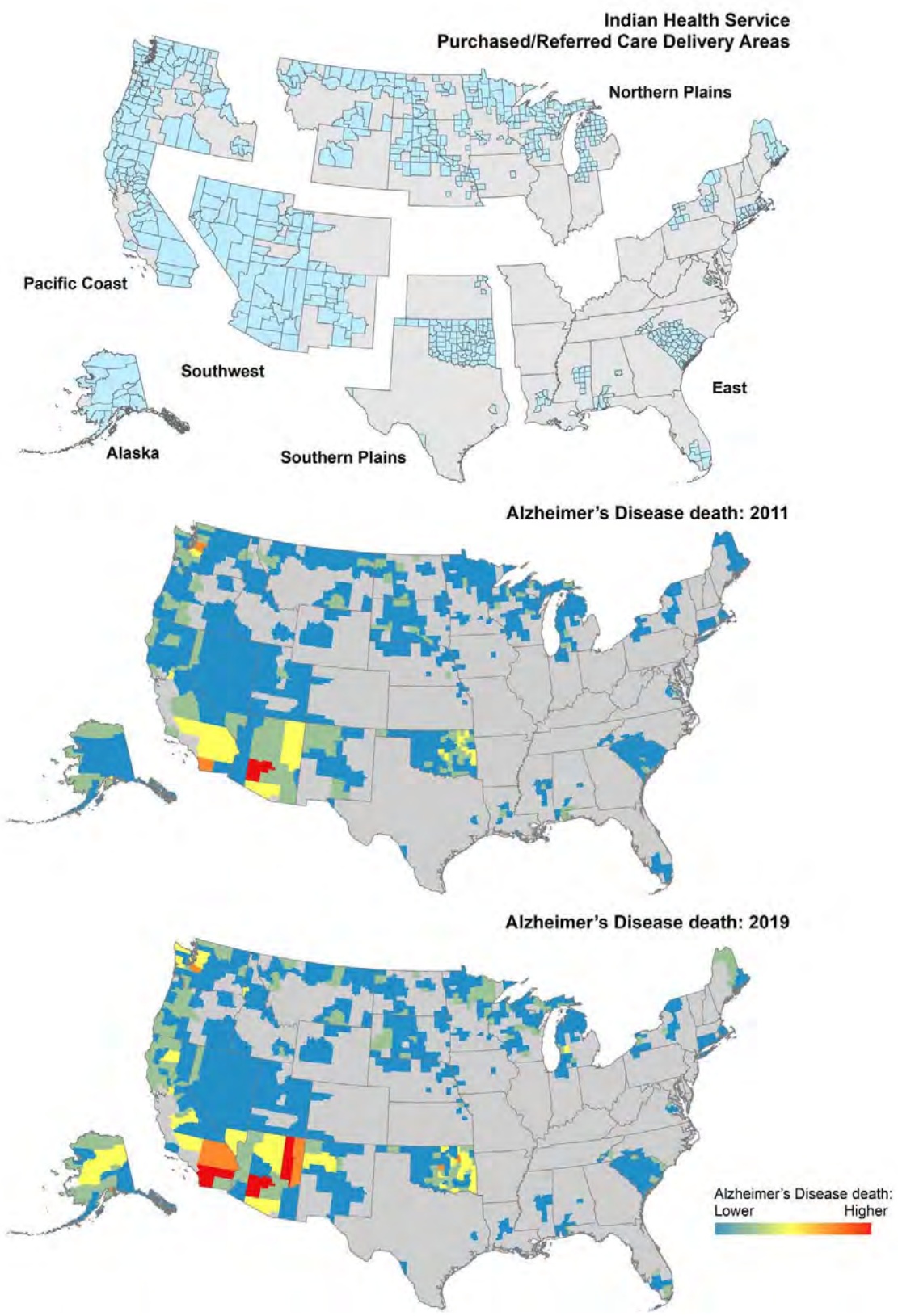

FIGURE 1. Alzheimer disease mortality among American Indian/Alaska Native people in purchased/referred care delivery area counties by Indian Health Service region.

TABLE 1. Age-adjusted Mortality Rates Related to AD Among AI/AN People by Rurality, Socioeconomic Status, and State, 2011 to 2019

Age-adjusted mortality rate (95% CI)	No. counties (%)	2011	2012	2013	2014	2015	2016	2017	2018	2019	Change (%)
No. deaths	646	238	239	270	305	350	385	410	416	411	—
Overall mortality rate	646	36.2 (31.6-41.1)	34.4 (30.1-39.1)	38.4 (33.9-43.3)	40.6 (36.1-45.5)	45.2 (40.5-50.2)	45.8 (41.3-50.7)	47.6 (43.1-52.5)	44.9 (40.6-49.5)	44.2 (39.9-48.7)	22
ADI											
Less deprived	398 (62)	40.8 (34.7-47.8)	38.5 (32.7-45.0)	46.3 (40.0-53.3)	49.3 (43.0-56.2)	49.0 (43.0-55.8)	51.2 (45.2-57.8)	52.2 (46.2-58.7)	49.2 (43.6-55.2)	47.8 (42.3-53.8)	17
More deprived	248 (38)	29.2 (22.9-36.7)	28.2 (22.2-35.3)	25.6 (19.9-32.5)	26.6 (20.9-33.4)	38.5 (31.7-46.4)	36.3 (29.8-43.9)	39.8 (33.1-47.5)	37.2 (30.8-44.5)	38.0 (31.7-45.2)	30
RUCC											
Metro	211 (33)	44.7 (37.6-52.8)	43.3 (36.5-51.0)	47.6 (40.5-55.5)	54.6 (47.2-62.8)	53.7 (46.6-61.5)	57.5 (50.3-65.3)	59.2 (52.2-67.0)	54.1 (47.6-61.2)	54.9 (48.4-62.0)	23
Nonmetro	435 (67)	27.9 (22.5-34.3)	25.6 (20.5-31.5)	29.2 (23.8-35.5)	27.0 (22-32.8)	36.2 (30.5-42.8)	33.9 (28.5-40.0)	35.6 (30.1-41.8)	35.3 (29.9-41.3)	32.5 (27.4-38.3)	16
IHS region											
East	127 (20)	20.0 (10.2-35.2)	< 10 cases	30.8 (17.5-50.2)	26.1 (14.1-44.0)	45.3 (29.0-67.2)	26.6 (14.9-43.4)	32.0 (18.8-50.4)	30.1 (17.3-48.5)	29.1 (17.0-46.0)	45
Northern Plains	227 (35)	40.0 (26.2-58.1)	38.8 (26.2-55.1)	46.3 (31.8-65.0)	38.8 (26.3-54.9)	30.6 (19.7-45.3)	39.9 (27.6-55.7)	39.7 (28.2-54.3)	29.6 (19.9-42.2)	39.5 (28.1-54.0)	−1
Pacific Coast/ Alaska	139 (22)	58.9 (46.9-73.0)	54.5 (43.6-67.2)	62.7 (51.3-75.8)	65.3 (54.3-78.0)	63.0 (52.5-74.9)	68.2 (57.7-80.1)	74.6 (63.4-87.2)	66.9 (56.8-78.3)	67.9 (57.6-79.5)	15
Southern Plains	84 (13)	42.4 (31.8-55.4)	46.4 (35.8-59.1)	39 (29.4-50.8)	40.6 (30.9-52.3)	66.2 (53.6-80.8)	61.2 (49.5-74.7)	81.4 (68.0-96.6)	73.9 (61.4-88.1)	68.6 (56.8-82)	62
Southwest	69 (11)	22.2 (16.6-29.1)	17.6 (12.6-23.8)	21 (15.7-27.6)	26.7 (20.8-33.7)	25.9 (20.2-32.6)	26.7 (21.1-33.3)	17.5 (13.2-22.9)	23.4 (18.5-29.2)	20.2 (15.7-25.6)	−9

Age-adjusted mortality rates were standardized to 2000 projected U.S. standard population.
95% CIs are included in parentheses for age-adjusted mortality rates.
AD indicates Alzheimer disease; ADI, area deprivation index; AI, American Indian; AN, Alaska Native; IHS, Indian Health Service; RUCC, rural-urban continuum codes.

TABLE 2. Bivariable and Multivariable Associations of County Characteristics Associated With AD Mortality Among AI/AN People in the United States, 2011 to 2019

Independent variables	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)
Time	1.08 (1.06-1.09)*	1.08 (1.06-1.09)*	1.08 (1.06-1.09)*	1.07 (1.06-1.09)*	1.08 (1.06-1.09)*	1.08 (1.06-1.09)*	1.08 (1.06-1.09)*	1.08 (1.06-1.09)*
10% increase in AI and AN population	—	0.85 (0.81-0.89)*	—	—	—	—	—	0.86 (0.82-0.91)*
PCP per 10,000 people	—	—	1.02 (1.00-1.05)	—	—	—	—	1.02 (0.99-1.05)
Neurologist per 10,000 people	—	—	—	1.29 (1.00-1.67)†	—	—	—	1.07 (0.81-1.40)
ADI								
Less deprived	—	—	—	—	Reference	—	—	Reference
More deprived	—	—	—	—	0.96 (0.79-1.17)	—	—	1.34 (1.06-1.70)‡
RUCC								
Metro	—	—	—	—	—	Reference	—	Reference
Nonmetro	—	—	—	—	—	0.69 (0.57-0.83)*	—	0.80 (0.66-0.97)‡
IHS region								
East	—	—	—	—	—	—	Reference	Reference
Northern Plains	—	—	—	—	—	—	0.92 (0.69-1.22)	1.25 (0.94-1.66)
Pacific Coast/Alaska	—	—	—	—	—	—	1.76 (1.34-2.31)*	2.16 (1.64-2.85)*
Southern Plains	—	—	—	—	—	—	1.98 (1.47-2.66)*	2.25 (1.67-3.04)*
Southwest	—	—	—	—	—	—	0.65 (0.47-0.91)‡	0.87 (0.63-1.21)

*$P < 0$.
†$P < 0.01$.
‡$P < 0.05$.
AD indicates Alzheimer disease; ADI, area deprivation index; AI, American Indian; AN, Alaska Native; IHS, Indian Health Service; IRR, incidence risk ratio; PCP, primary care physician; RUCC, rural-urban continuum code.

DISCUSSION

To our knowledge, this is the first longitudinal study to examine AD mortality trends as a function of county characteristics among AI/AN people. Our findings reveal that mortality rates associated with AD increased over time, a finding consistent with previous research.[3,28] This increase represents an actual increase in the number of AI/AN people dying from AD. This trend can also be attributed to the increase in the average life expectancy of this population, from 44 years in 1970 to 74 years in 2010, surviving to an age when the risk for developing AD or related dementias typically increases.[29,30] A variety of other factors, including improved diagnosis or awareness of AD, mandates in assessment for cognitive impairment, and changes in the perception of AD as a cause of death likely attributed to this increase.[31,32]

Our study showed that a higher concentration of AI/AN people in a county was associated with a lower risk for AD mortality. Even though AI/AN communities have experienced colonization, genocide, historical trauma, and poverty,[33] they have exhibited remarkable resilience in the face of overwhelming socioeconomic adversity and cultural change.[33] Thus, it may be the case that the sense of community through a larger presence of AI/AN people serves as a protective factor against developing AD. It may also be the case that AD is underreported and underdiagnosed in these communities. IHS or clinics run by tribal governments and funded by IHS provide health care to members of federally recognized tribes.[27] Even though previous research show that AD mortality is lower among AI/AN people compared with white or black people,[3,34] insights from HIS health care providers suggest that mortality data do not provide a complete picture of AD burden on AI/AN communities and that AD is underreported among this population.[35] In addition, studies that explored AI/AN people's knowledge of AD showed that AI/AN people are only moderately informed about AD.[36] Given that our findings describe lower AD mortality rates in counties with a larger percentage of AI/AN, community outreach and education should target raising awareness of AD in areas with a higher concentration of AI/AN people. Concurrently, future research should disentangle the extent, to which community resilience may be protective against the risk of AD among AI/AN people.

More deprived areas had higher AD mortality rates compared with less deprived areas. This finding is consistent with previous literature showing that the incidence and mortality related to dementia are higher in more deprived areas.[14–17,37] This disparity may reflect inequalities in diet, vascular risk factors, or access to health care among other characteristics that may be related to the clinical manifestation of dementia. An unexpected finding was that nonmetro counties had lower AD mortality rates compared with metro counties. This was inconsistent with previous research showing AD mortality mainly among white people.[3,18] The lower rate of AD in nonmetro areas may be confounded by lower physician density or limited/moderate information about AD.[11] Given that AI/AN people are less likely to be diagnosed with AD even when symptoms are present[13] and that clinical risk factors for AD including diabetes, hypertension, and obesity are prevalent among AI/AN people living in rural areas,[6,38] future efforts should increase access to care to improve diagnosis and management of AD. Developing systems to track the prevalence of AD and increasing awareness of the disease in rural areas is also warranted.

This analysis has several limitations. First, the misclassification of AI/AN people in vital statistics data is common.[39] This may have led to underestimating AD mortality among AI/AN people, hindering mortality status assessments, and impeding the planning, implementation, and

evaluation of public health strategies to address AD for this population. Second, AD deaths are typically underreported in vital statistics. AD is more likely to be reported on death certificates of individuals with severe AD or those living in long-term care facilities.[40] Third, we only had data on county of residence for decedents at the time of death. County at the time of death can only represent overall area characteristics at a single point in a decedent's lifetime. Using this information, we created a single timepoint measure of rurality, ADI, and access to PCPs, and neurologists but these measures may change over time. Fourth, our analysis included trends in the number of AD deaths adjusted by county population. We did not calculate age-adjusted mortality rate for PRCDA counties because of a small number of deaths among AI/AN people within some counties. Fifth, relying on mortality data to estimate the burden of AD in AI/AN or other communities may introduce bias. Accurate and timely data on the incidence and prevalence of AD and related dementias is essential not only for examining factors contributing to the development or progression of AD but also for estimating the community's needs and resources regarding AD. Lastly, our findings may not be generalizable to other settings with different population groups.

CONCLUSION

Mortality rates associated with AD among AI/AN people increased between 2011 and 2019. A higher risk for AD mortality was observed in counties with a lower concentration of AI/AN people, in more deprived, and in metro counties. These findings have implications for prioritizing areas where more resources for AD care, education, or outreach are needed.

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