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RESEARCH ARTICLE

Alzheimer's disease and related dementias and related health conditions among American Indian and Alaska Native Medicare beneficiaries

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Abstract

INTRODUCTION: Alzheimer's disease and related dementias (ADRD) and its associated factors are not well understood in the American Indian and Alaska Native (AI/AN) population.

METHODS: We analyzed Medicare 2019 data for 112,280 AI/AN and 1,010,862 White beneficiaries aged 68+, examining the prevalence of ADRD-related health conditions and their associations with ADRD through logistic regressions.

RESULTS: AI/AN beneficiaries had higher age-adjusted ADRD prevalence (15.6% vs. 13.3%), and a higher prevalence of 5 of 9 Lancet risk factors: diabetes, alcohol use disorder (AUD), tobacco use disorder, visual and hearing impairments. Traumatic brain injury (TBI), AUD, and visual and hearing impairments had stronger associations with ADRD among AI/AN beneficiaries, while depression, diabetes, and hypertension had stronger associations among White beneficiaries.

DISCUSSION: Our findings highlight disparities in ADRD and related health conditions between AI/AN and White beneficiaries, potentially due to social and systematic health-care inequalities. Addressing these gaps requires culturally tailored prevention and care strategies.

KEYWORDS
Alzheimer's disease, American Indian and Alaska Native peoples, chronic conditions, disparities, Medicare

Highlights

- American Indian and Alaska Native (AI/AN) Medicare beneficiaries had higher age-adjusted Alzheimer's disease and related dementias (ADRD) prevalence than White beneficiaries.
- AI/AN beneficiaries had higher prevalence for most Lancet risk factors.

- The links of ADRD with some top-ranked risk factors were stronger among AI/AN adults.
- Sex differences were observed in the associations of health conditions with ADRD.

1 | BACKGROUND

Alzheimer's disease (AD) and related dementias (ADRD) affect ≈ 7 million Americans aged ≥ 65, with an anticipated increase to 13.9 million by 2060.[1] The older American Indian and Alaska Native (AI/AN) population is projected to experience the fastest growth among all racial groups, nearly tripling between 2016 and 2060.[2] Consequently, ADRD has emerged as a major health concern in AI/AN communities.[1,3–5]

Current epidemiologic evidence suggests that ADRD prevalence and incidence may be higher among AI/AN peoples compared to non-Hispanic White adults. Age-adjusted ADRD prevalence among AI/AN (9.7%) has been found to be higher than non-Hispanic White (7.7%) Medicare beneficiaries.[6] Kaiser Permanente Northern California reported higher dementia incidence and shorter survival post-diagnosis among its AI/AN members than most other racial and ethnic groups.[7–9] The Strong Heart Study found a dementia prevalence of 10% among tribal members aged 70 to 95 years.[10] Health-care system–based estimates also point to a substantial burden; Indian Health Service (IHS) data identified 2.3% new dementia cases in FY2010 to 2013, although prevalence was not reported.[11] These findings may reflect systemic inequalities in health-care access, socioeconomic opportunity, and environmental exposures, as well as historical trauma, rather than inherent biological differences.[12]

In the absence of a cure, understanding and mitigating risk factors offer a crucial opportunity to reduce ADRD burden, particularly in under-resourced AI/AN communities.[13,14] The 2024 Lancet Commission identified 14 potentially modifiable dementia risk factors, including less education, hypertension, hearing loss, smoking, obesity, depression, physical inactivity, diabetes, social isolation, excessive alcohol consumption, traumatic brain injury (TBI), air pollution, untreated vision loss, and high low-density lipoprotein (LDL) cholesterol.[15,16] Our understanding of ADRD and its related factors among AI/AN peoples remains limited compared to White adults.[17] Hypertension, depression, hyperlipidemia, diabetes, cardiovascular disease, and air pollution have been associated with increased ADRD risk among AI/AN individuals.[11,18–20] However, nationally representative data on relevant health conditions and their associations with ADRD in this population remain scarce.

Two recognized data sources on AI/AN health are IHS, Tribal, and Urban Indian Health Organization (hereafter IHS/Tribal) data and Medicare data. Approximately one third of AI/AN peoples obtain services from IHS/Tribal clinics and hospitals.[21,22] According to US Census data, > 95% of the AI/AN population aged ≥ 65 is enrolled in Medicare,[23] making it a robust national dataset for studying AI/AN health conditions in this age group. Furthermore, IHS/Tribal providers obtain Medicare reimbursement for Medicare covered services provided to beneficiaries. Thus, Medicare data include IHS/Tribal service data as well as data for services, such as outpatient and inpatient specialty care services, obtained elsewhere, providing a broad view of diagnosed ADRD. Using Medicare data, we estimated the prevalence of ADRD-related health conditions and examined their associations with ADRD among AI/AN beneficiaries and compared these results to their White counterparts to explore potential disparities.

2 | METHODS

2.1 | Data and study population

Data were drawn from the 2019 Medicare master beneficiary summary file (MBSF) from the Centers for Medicare and Medicaid services (CMS). The MBSF includes one record per beneficiary per enrollment year with information on health plan enrollment, age, sex, race and ethnicity, the date of death, ZIP code of residence, and chronic conditions.

We focused our analysis on AI/AN beneficiaries, who remain understudied in ADRD research, and compared them to White beneficiaries, the largest racial group in Medicare. Limiting the analysis to a single comparison group allowed us to anchor interpretation while maintaining a clear focus on AI/AN disparities. Broader comparisons involving additional racial and ethnic groups, many of which have been examined in prior studies,[24–26] were outside the scope of this analysis and will be explored in future research.

The study population included Medicare beneficiaries aged 68+ in the 50 states or Washington, DC, excluding territories, with fee-for-service (FFS) coverage for 11 to 12 months or while alive in 2019. We restricted the sample to 68+ years to ensure more complete case identification by allowing at least 3 years of health condition information because many beneficiaries enroll in Medicare at age 65. We included all eligible AI/AN beneficiaries and a 5% random sample of non-Hispanic White (White) beneficiaries.

2.2 | Health conditions

Two categories of health conditions were included. The first category comprised 9 of the 14 ADRD-related factors drawn from the 2024 Lancet Commission report (referred to as Lancet Factors). The second

RESEARCH IN CONTEXT

1. **Systematic review**: We reviewed PubMed for studies on Alzheimer's disease and related dementias (ADRD) among American Indian and Alaska Native (AI/AN) populations. Studies have shown higher ADRD burden among the AI/AN communities compared to non-Hispanic Whites, but nationally representative data on relevant health conditions and their associations with ADRD in this population are scarce.
2. **Interpretation**: Our study revealed higher ADRD prevalence and a greater burden of multiple ADRD-related factors among AI/AN than White beneficiaries. Stronger associations with ADRD were observed for traumatic brain injuries, alcohol use disorder, and visual and hearing impairment in AI/AN beneficiaries, while depression, diabetes, and hypertension had stronger associations with ADRD in White beneficiaries.
3. **Future directions**: Future longitudinal studies should explore the social, biological, and sex-specific determinants underlying ADRD disparities. Culturally tailored interventions might be needed to address modifiable factors such as visual and hearing impairment to reduce ADRD and related health disparities.

category (Other Health Factors) consisted of 13 additional conditions shown to be associated with ADRD.[27–33] These terms are capitalized to denote specific groupings of conditions as defined and used within this study. The 9 Lancet Factors available in MBSF Chronic Conditions Segment are: diabetes, hypertension, depression, hearing loss, TBI, alcohol use disorder, tobacco use disorders, hyperlipidemia, and blind or visual impairment (visual impairment). It is important to note that our study used the Chronic Conditions Warehouse (CCW) constructed variables available in MBSF, which in some cases are proxies for the specific Lancet definitions. This represents a methodological divergence due to data availability. For example, we used the CCW claims-based definitions for "alcohol use disorder," "tobacco use disorder," and "hyperlipidemia," whereas the Lancet Commission specified "excessive alcohol consumption" (> 21 units/week), "smoking," and "high LDL cholesterol," respectively.

Other Health Factors extend beyond the Lancet Commission's framework and capture broader clinical conditions that are downstream complications of diabetes (cardiovascular, renal disease) and disproportionately affect AI/AN communities. Including these factors allows us to characterize the overall comorbidity burden relevant to ADRD without overlapping with the Lancet factors. The Other Health Factors that are previously shown to be associated with ADRD and therefore included in the study are: end-stage renal disease (ESRD);[27] chronic kidney disease (CKD) without ESRD;[27] chronic obstructive pulmonary disease (COPD);[28] cancers;[29] liver disease;[30] drug use disorder;[31] other mental health disorders (other than depression);[31] and cardiovascular conditions,[32,33] specifically acute myocardial infarction (AMI), ischemic heart disease (IHD), heart failure (HF), atrial fibrillation (AFib), peripheral vascular disease (PVD), and stroke or transient ischemic attack (TIA). Several other Lancet Factors were examined but excluded due to their low prevalence or unclear definitions. For instance, we excluded obesity from our analysis. Although available in the MBSF, claims-based prevalence of obesity was substantially lower than national survey estimates, suggesting significant under-reporting. This is a documented issue in Medicare claims data, which have been shown to have low sensitivity for identifying obesity.[34,35] This discrepancy raised concerns about the validity of this measure for our analysis, leading to its exclusion. Similarly, although the MBSF includes diagnostic flags for glaucoma, cataract, and visual impairment, we only included visual impairment because glaucoma and cataract indicators do not distinguish treated from untreated cases, whereas identifying untreated vision loss is essential to match the Lancet Commission's definition.

All conditions, including ADRD, were identified using variables extracted from the MBSF Chronic Conditions Segment, and the Other Chronic or Potentially Disabling Conditions Segment.[36] For each condition, we used the end-of-year indicator, which is created from Medicare claims data from 2017 to 2019 using published algorithms based on International Classification of Disease Tenth Revision (ICD-10) codes.[37,38] These algorithms generally define a condition as present if a beneficiary has at least one inpatient claim or one to two other claims (e.g., outpatient or carrier) with a qualifying diagnosis code within a specified period, in addition to having sufficient FFS coverage.

2.3 | Outcome

The outcome, diagnosis of ADRD, was determined using the ADRD end-of-year condition code from the 2019 MBSF Chronic Condition Segment. This definition is based on published and validated algorithms that use ICD-10 codes from claims data (see Table S1 in supporting information).[37] We chose this definition for consistency and comparability to other large-scale epidemiological studies using Medicare data.[39] Previous studies have shown that Medicare claims data have a sensitivity of 0.85 and specificity of 0.89 for identifying clinically diagnosed dementia, and a sensitivity of 0.64 and specificity of 0.95 for AD.[40]

2.4 | Other covariates

Other covariates include age, sex, and race drawn from the MBSF.

2.5 | Statistical analysis

We first present descriptive summary statistics, displayed as frequencies (*n*) and percentages (%) for AI/AN and White beneficiaries.

These statistics, which include percentages of demographic categories and health conditions (ADRD and all related factors), appear in a table (Table 1) stratified first by race, and then within each race by ADRD status. The overall column within each racial group effectively represents the prevalence or percentage specific to that racial group.

We calculated the age-adjusted prevalence of ADRD among AI/AN adults using direct standardization, with the age distribution of the White beneficiaries as the standard population. To examine associations with ADRD, we first fit a series of age-adjusted logistic regression models for each condition, calculating odds ratios (ORs) and 95% confidence intervals (CIs). We then conducted our main multivariable logistic regression analysis to examine the association between the Lancet Factors and ADRD. This analysis proceeded in three sequential steps: (1) An initial model using the full sample, including the 9 Lancet Factors, age, sex, and a race variable (AI/AN vs. White), to examine the overall effect of race. (2) Given significant interactions between many Lancet Factors and race, we subsequently fit race-stratified models (for AI/AN and White groups separately) to examine differential associations. (3) Within each racial group, we further fit sex-stratified models. As an additional analysis, we expanded race-specific models to include the "Other Health Factors" along with the Lancet Factors, age, and sex.

All statistical analyses were performed using Stata, SE 14.2. Consistent with recommendations to use more stringent thresholds for p values in large samples,[41] we report p values but only emphasize results with $p < 0.001$ while mainly focusing on effect magnitude and clinical interpretation.

3 | RESULTS

3.1 | Sample characteristics and prevalence of conditions

A total of 112,280 AI/AN and 1,010,862 White Medicare FFS beneficiaries 68+ were included in this study. After age adjustment, ADRD prevalence was higher among AI/AN (15.6%) than White (13.3%) beneficiaries (Table 1). Descriptive demographics and the unadjusted prevalences of all health conditions by ADRD status are also provided in Table 1. AI/AN beneficiaries were relatively younger, with nearly half in the youngest (68–74) age category. AI/AN beneficiaries exhibited substantially higher prevalences for 5 out of 9 Lancet Factors: diabetes (43.5% vs. 26.3%), alcohol use disorder (2.8% vs. 1.5%), tobacco use disorder (11.9% vs. 6.8%), hearing loss (9.8% vs. 7.6%), and visual impairment (0.7% vs. 0.4%), but a lower prevalence of hyperlipidemia (41.3% vs 54.3%). Both groups had a similar prevalence of hypertension, depression, and TBI. The prevalence of Other Health Factors differed little between AI/AN and White beneficiaries, except ESRD (1.9% vs. 0.5%), drug use disorder (3.3% vs. 2.0%), and CKD without ESRD (31.7% vs. 26.6%).

3.2 | Age-adjusted associations between individual factors and ADRD

The bivariate age-adjusted analyses (Table 2) showed that each condition was associated with elevated odds of ADRD in both groups. Associations between these conditions and ADRD were similar across racial groups, except for TBI, which had a much stronger association with ADRD among AI/AN (OR = 12.20, 95% CI: 9.93–14.98) than White (OR = 8.50, 95% CI: 7.93–9.10) beneficiaries. In both groups, TBI, depression, alcohol use disorder, stroke/TIA, and visual impairment were among the stronger ADRD predictors.

3.3 | Multivariable models

The age-adjusted association between race (AI/AN vs. White) and ADRD in the overall sample revealed that ADRD odds were 25% higher in AI/AN than White beneficiaries (OR = 1.25, 95% CI: 1.22–1.27). Figure 1 (and Table S2A in supporting information) presents the ORs for race (AI/AN vs. White) from the multivariable regression analysis that also included age, sex, and the Lancet Factors. AI/AN beneficiaries still had higher adjusted odds of ADRD compared to White beneficiaries (adjusted OR = 1.17, 95% CI: 1.14–1.19). Interactions of all Lancet Factors except visual impairment and tobacco use disorder with race were significant, leading to race-stratified analyses of the Lancet Factors with ADRD. Figure 1 shows stronger associations of TBI, alcohol use disorder, visual impairment, and hearing loss with ADRD in AI/AN beneficiaries, and stronger associations of depression, diabetes, and hypertension in White beneficiaries.

Unlike other Lancet Factors, hyperlipidemia was associated with lower ADRD odds among White beneficiaries, but an OR close to 1 among AI/AN beneficiaries. In sensitivity analyses, the association for hyperlipidemia became positive in both groups after removing hypertension and diabetes from the model (Table S2B). This pattern suggests that hyperlipidemia may act as an upstream cardiometabolic marker whose association with ADRD is largely captured through downstream conditions such as hypertension and diabetes; when these conditions are included in the model, the remaining direct association of hyperlipidemia is attenuated. We also formally assessed multicollinearity among covariates and found no evidence that it meaningfully affected the model estimates.

3.4 | Sex-specific associations

Table 3 presents sex-specific ORs for the Lancet Factors from multivariable models. After sex stratification, statistically significant associations (except hyperlipidemia among AI/AN) remained evident. Among AI/AN beneficiaries, the largest sex difference was for TBI (OR = 10.69 for males vs. 6.40 for females). Males also showed stronger associations for depression (OR = 4.73 vs. 3.66) and alcohol use disorder

TABLE 1 Characteristics of American Indian and Alaska Native (AI/AN) and non-Hispanic White (White) Medicare beneficiaries aged 68 years and older by ADRD status, 2019.

	AI/AN			White		
	ADRD (*N* = 15,598)	No ADRD (*N* = 96,682)	Overall (*N* = 112,280)	ADRD (*N* = 135,237)	No ADRD (*N* = 875,625)	Overall (*N* = 1,010,862)
Age-adjusted ADRD prevalence	–	–	15.6%	–	–	13.3%
Sample characteristics	*N* (%)	*N* (%)	*N* (%)	*N* (%)	*N* (%)	*N* (%)
Age groups						
68–74	3315 (21.3%)	51,667 (53.4%)	54,982 (49.0%)	20,103 (14.9%)	423,184 (48.3%)	443,287 (43.9%)
75–84	6629 (42.5%)	35,506 (36.7%)	42,135 (37.5%)	50,804 (37.6%)	335,304 (38.3%)	386,108 (38.2%)
85–94	4930 (31.6%)	8872 (9.2%)	13,802 (12.3%)	52,989 (39.2%)	106,244 (12.1%)	159,233 (15.8%)
95+	724 (4.6%)	637 (0.7%)	1361 (1.2%)	11,341 (8.4%)	10,893 (1.2%)	22,234 (2.2%)
Sex						
Female	9870 (63.3%)	56,464 (58.4%)	66,334 (59.1%)	85,210 (63.0%)	485,201 (55.4%)	570,411 (56.4%)
Male	5728 (36.7%)	40,218 (41.6%)	45,946 (40.9%)	50,027 (37.0%)	390,424 (44.6%)	440,451 (43.6%)
Health conditions						
Lancet factors						
Hypertension	11,944 (76.6%)	59,580 (61.6%)	71,524 (63.7%)	105,132 (77.7%)	533,217 (60.9%)	638,349 (63.1%)
Diabetes	7695 (49.3%)	41,108 (42.5%)	48,803 (43.5%)	46,504 (34.4%)	219,597 (25.1%)	266,101 (26.3%)
Hyperlipidemia	7379 (47.3%)	39,017 (40.4%)	46,396 (41.3%)	76,900 (56.9%)	472,477 (54.0%)	549,377 (54.3%)
Depression	5530 (35.5%)	12,173 (12.6%)	17,703 (15.8%)	56,684 (41.9%)	115,463 (13.2%)	172,147 (17.0%)
Tobacco use disorder	2176 (14.0%)	11,136 (11.5%)	13,312 (11.9%)	10,487 (7.8%)	58,673 (6.7%)	69,160 (6.8%)
Hearing loss	2547 (16.3%)	8495 (8.8%)	11,042 (9.8%)	17,831 (13.2%)	59,094 (6.8%)	76,925 (7.6%)
Alcohol use disorder	902 (5.8%)	2218 (2.3%)	3120 (2.8%)	4033 (3.0%)	11,078 (1.3%)	15,111 (1.5%)
Visual impairment	305 (2.0%)	426 (0.4%)	731 (0.7%)	1909 (1.4%)	2231 (0.3%)	4140 (0.4%)
Traumatic brain injury	259 (1.7%)	178 (0.2%)	437 (0.4%)	2104 (1.6%)	1828 (0.2%)	3932 (0.4%)
Other health factors						
CKD without ESRD	7558 (48.5%)	28,022 (29.0%)	35,580 (31.7%)	61,585 (45.5%)	206,882 (23.6%)	268,467 (26.6%)
AMI/IHD	7130 (45.71%)	27,632 (28.58%)	34,762 (30.96%)	64,489 (47.69%)	256,540 (29.30%)	321,029 (31.76%)
HF/AFib	6270 (40.20%)	17,774 (18.38%)	24,044 (21.41%)	57,867 (42.79%)	166,307 (18.99%)	224,174 (22.18%)
COPD	3529 (22.6%)	12,439 (12.9%)	15,968 (14.2%)	29,479 (21.8%)	96,746 (11.1%)	126,225 (12.5%)
PVD	4085 (26.2%)	9526 (9.9%)	13,611 (12.1%)	46,331 (34.3%)	102,877 (11.8%)	149,208 (14.8%)
Any cancer	1407 (9.0%)	7302 (7.6%)	8709 (7.8%)	15,646 (11.6%)	93,578 (10.7%)	109,224 (10.8%)
Other mental health disorder	1738 (11.1%)	6018 (6.2%)	7756 (6.9%)	18,632 (13.8%)	78,110 (8.9%)	96,742 (9.6%)
Liver disease	1265 (8.1%)	5437 (5.6%)	6702 (6.0%)	7612 (5.6%)	38,678 (4.4%)	46,290 (4.6%)
Stroke/TIA	1598 (10.2%)	2916 (3.0%)	4514 (4.0%)	15,308 (11.3%)	27,818 (3.2%)	43,126 (4.3%)
Drug use disorder	807 (5.2%)	2847 (2.9%)	3654 (3.3%)	4595 (3.4%)	15,698 (1.8%)	20,293 (2.0%)
ESRD	503 (3.2%)	1669 (1.7%)	2172 (1.9%)	1332 (1.0%)	3657 (0.4%)	4989 (0.5%)

Notes: Conditions were listed in descending order of prevalence among AI/AN beneficiaries. Visual impairment includes blindness and or visual impairment. Other mental health disorder included diagnoses of anxiety, bipolar disorder, post-trauma stress disorder, or schizophrenia and other psychotic disorders, but without a diagnosis of depression. Any cancer included diagnoses of breast, colorectal, prostate, lung, or endometrial cancers.

Abbreviations: ADRD, Alzheimer's disease and related dementias; AFib, atrial fibrillation; AMI, acute myocardial infarction; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; ESRD, end-stage renal disease; HF, heart failure; IHD, ischemic heart disease; PVD, peripheral vascular disease; TIA, transient ischemic attack.

TABLE 2 Sex-stratified bivariate age adjusted associations of all health conditions with ADRD among American Indian and Alaska Native (AI/AN) and non-Hispanic White (White) Medicare beneficiaries aged 68 years and older.

	AI/AN			White		
	Female (*N* = 66,334)	Male (*N* = 45,946)	All (*N* = 112,280)	Female (*N* = 570,411)	Male (*N* = 440,451)	All (*N* = 1,010,862)
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Lancet factors						
Hypertension	1.70 (1.61–1.79)	1.90 (1.78–2.03)	1.78 (1.71–1.85)	1.68 (1.65–1.71)	1.90 (1.86–1.95)	1.77 (1.74–1.79)
Diabetes	1.49 (1.43–1.56)	1.54 (1.45–1.63)	1.51 (1.45–1.56)	1.69 (1.66–1.72)	1.71 (1.67–1.74)	1.67 (1.65–1.69)
Hyperlipidemia	1.40 (1.33–1.46)	1.39 (1.31–1.47)	1.39 (1.34–1.44)	1.10 (1.08–1.12)	1.28 (1.26–1.31)	1.16 (1.15–1.18)
Depression	4.12 (3.91–4.34)	5.90 (5.48–6.34)	4.53 (4.35–4.73)	4.85 (4.76–4.93)	6.47 (6.32–6.62)	5.31 (5.24–5.39)
Tobacco use disorder	1.77 (1.65–1.90)	1.99 (1.84–2.15)	1.85 (1.76–1.96)	1.81 (1.75–1.87)	2.00 (1.93–2.06)	1.88 (1.83–1.92)
Hearing loss	1.39 (1.30–1.50)	1.70 (1.58–1.84)	1.51 (1.43–1.59)	1.31 (1.27–1.34)	1.65 (1.61–1.70)	1.43 (1.41–1.46)
Alcohol use disorder	4.05 (3.50–4.69)	4.67 (4.20–5.18)	4.35 (4.00–4.74)	3.87 (3.62–4.13)	3.93 (3.74–4.13)	3.76 (3.62–3.91)
Visual impairment	2.74 (2.21–3.39)	4.22 (3.29–5.41)	3.27 (2.78–3.85)	2.76 (2.53–3.01)	3.62 (3.23–4.06)	3.05 (2.85–3.27)
Traumatic brain injury	9.51 (7.26–12.46)	16.87 (12.27–23.20)	12.20 (9.93–14.98)	7.14 (6.52–7.83)	10.70 (9.63–11.88)	8.50 (7.93–9.10)
Other health factors						
CKD w/out ESRD	1.98 (1.89–2.07)	2.15 (2.03–2.28)	2.03 (1.96–2.11)	2.08 (2.05–2.11)	2.26 (2.22–2.31)	2.11 (2.09–2.14)
AMI/IHD	1.96 (1.87–2.06)	1.78 (1.68–1.88)	1.84 (1.77–1.90)	1.91 (1.88–1.94)	1.84 (1.81–1.88)	1.79 (1.77–1.82)
HF/AFib	2.30 (2.19–2.42)	2.39 (2.25–2.54)	2.32 (2.24–2.41)	2.18 (2.14–2.21)	2.21 (2.16–2.25)	2.15 (2.12–2.18)
COPD	1.96 (1.85–2.08)	1.96 (1.83–2.10)	1.95 (1.86–2.04)	2.06 (2.02–2.10)	2.20 (2.15–2.26)	2.11 (2.07–2.14)
PVD	2.86 (2.70–3.03)	2.72 (2.54–2.92)	2.79 (2.67–2.92)	2.78 (2.73–2.83)	2.73 (2.67–2.79)	2.73 (2.69–2.77)
Any cancer	1.21 (1.11–1.32)	1.09 (0.99–1.20)	1.14 (1.07–1.21)	1.01 (0.98–1.04)	1.07 (1.04–1.10)	1.02 (1.00–1.04)
Other mental health disorder	1.70 (1.58–1.83)	2.58 (2.32–2.86)	1.95 (1.84–2.08)	1.40 (1.37–1.43)	2.27 (2.19–2.34)	1.66 (1.63–1.69)
Liver disease	1.66 (1.52–1.82)	2.44 (2.20–2.70)	1.95 (1.82–2.09)	1.52 (1.47–1.58)	1.85 (1.78–1.93)	1.65 (1.61–1.70)
Stroke/TIA	3.38 (3.09–3.69)	3.72 (3.35–4.14)	3.51 (3.28–3.76)	3.07 (2.97–3.16)	3.65 (3.52–3.77)	3.29 (3.21–3.36)
Drug use disorder	2.63 (2.35–2.93)	2.94 (2.58–3.36)	2.76 (2.53–3.00)	2.68 (2.56–2.81)	3.00 (2.83–3.17)	2.82 (2.72–2.92)
ESRD	2.73 (2.37–3.13)	2.37 (2.01–2.80)	2.57 (2.31–2.85)	3.27 (2.96–3.62)	2.89 (2.64–3.17)	2.98 (2.79–3.19)

Notes: Other mental health disorder included diagnoses of anxiety, bipolar disorder, post-trauma stress disorder, or schizophrenia and other psychotic disorders, but without a diagnosis of depression.
Any cancer included diagnoses of breast, colorectal, prostate, lung, or endometrial cancers.
Abbreviations: ADRD, Alzheimer's disease and related dementias; AFib, atrial fibrillation; AMI, acute myocardial infarction; CI, confidence interval; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; ESRD, end-stage renal disease; HF, heart failure; IHD, ischemic heart disease; OR, odds ratio; PVD, peripheral vascular disease; TIA, transient ischemic attack.

(3.40 vs. 2.90) compared to females. Among White beneficiaries, sex differences were generally smaller but followed similar patterns, with males exhibiting higher ORs for several factors, including depression (5.46 vs. 4.43) and hearing loss (1.38 vs. 1.15). These results indicate that although the direction of associations is consistent across sexes, the magnitude tends to be larger in males for several key conditions.

3.5 | Further adjusted models including other health factors

Results from the multivariable regression that included both Lancet and Other Health Factors are presented in Table 4. Controlling for both sets of factors, AI/AN adults had 23.6% (CI: 21.1–26.2) greater odds of having ADRD. The relationships between the Lancet Factors with ADRD were attenuated by the inclusion of the Other Health Factors. Among the Other Health Factors, end-stage renal disease, other mental health disorder, peripheral vascular disease, and stroke or TIA had the strongest associations with ADRD in both populations.

4 | DISCUSSION

Our results show that the age-adjusted prevalence of ADRD was higher among AI/AN Medicare beneficiaries aged 68+ than their White counterparts in 2019. This association remained after further adjusting for multiple factors. Similarly, the prevalence was higher among AI/AN than White beneficiaries for 5 of the 9 Lancet Factors examined, including diabetes, alcohol and tobacco use disorders, visual impairment, and hearing loss. The conditions that had a particularly strong

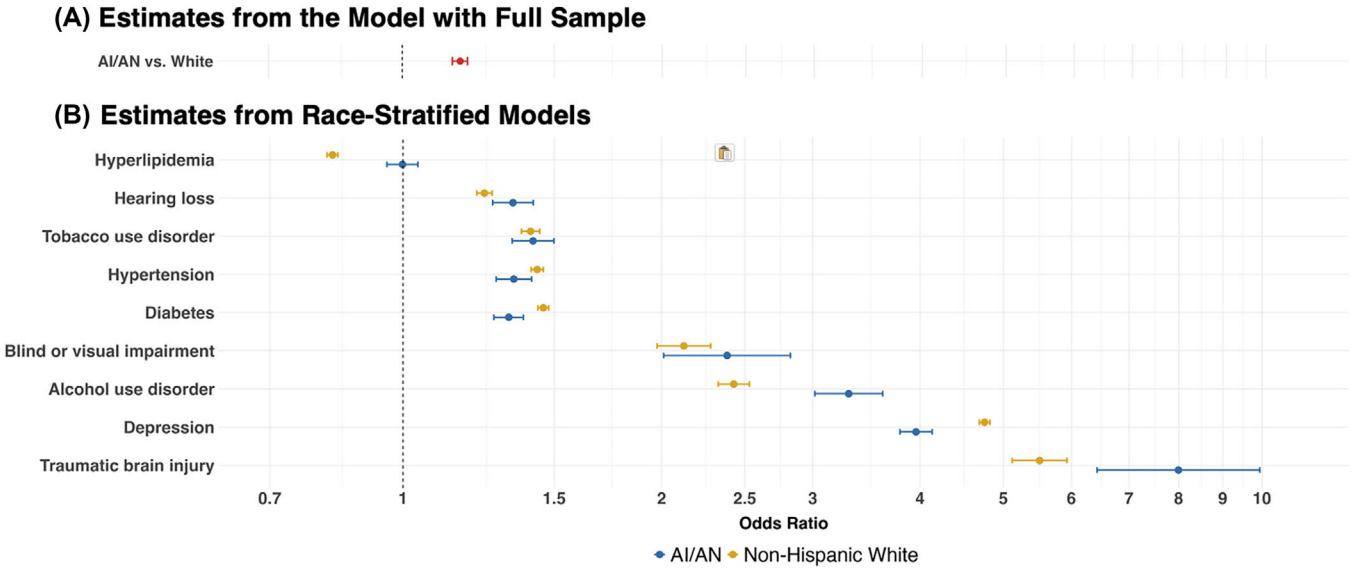

FIGURE 1 Multivariable regression: ORs for ADRD by Lancet Factors, among AI/AN and non-Hispanic White Medicare beneficiaries in 2019. A, The OR for AI/AN versus White was from an overall multivariable logistic regression model that includes both AI/AN and White beneficiaries. The independent variables of that model included age, sex, race (AI/AN vs. White) and all 9 Lancet Factors: traumatic brain injury, depression, alcohol use disorder, blind or visual impairment, diabetes, hypertension, tobacco use disorder, hearing loss, and hyperlipidemia. B, ORs for Lancet Factors are from a race-stratified multivariable model that included age, sex, and all 9 Lancet Factors. ADRD, Alzheimer's disease and related dementias; AI/AN, American Indian and Alaska Native; OR, odds ratio.

association with ADRD, such as TBI, also had stronger association with ADRD among AI/AN than White beneficiaries.

The finding of higher age-adjusted ADRD prevalence among AI/AN (15.6%) compared to White beneficiaries (13.4%) in our study is consistent with a recent study by Haye et al., which reported a prevalence of 9.7% in AI/AN and 7.7% in White beneficiaries in 2017 among adults aged 65+ years.[6] The higher absolute prevalence observed in our study may reflect differences in case identification algorithms. Specifically, Haye et al. required an ADRD diagnosis code plus at least one additional confirming diagnosis code within 1 to 2 years, whereas the CCW algorithm used in our study classifies ADRD based on a single qualifying diagnosis. This less restrictive algorithm is expected to capture more cases and may contribute to the higher prevalence estimates. Differences in age inclusion criteria (≥ 68 vs. ≥ 65 years) and data years (2019 vs. 2017) may also contribute.

Furthermore, it is important to interpret our prevalence estimates with caution. Claims-based algorithms for ADRD are known to have relatively low sensitivity, which may lead to an underestimation of the true prevalence across all groups.[42] This underestimation may be particularly pronounced for the AI/AN population due to factors like differences in health-care–seeking behaviors, health-care access barriers, cultural competency, and diagnostic delays, which can also result in under-ascertainment of conditions in claims data.[43]

Our findings that AI/AN beneficiaries had a higher prevalence of many ADRD-related health conditions than White beneficiaries were also consistent with the literature.[44] A study using Behavioral Risk Factor Surveillance System (BRFSS) data[13] found higher self-reported prevalence of several risk factors, including hearing loss, diabetes, smoking, and hypertension in AI/AN than in White individuals. However, the prevalence of depression was higher in AI/AN individuals, which was contrary to our findings based on Medicare data. Discrepancies in the prevalence of depression may reflect the self-reported nature of BRFSS data and age differences between populations, limiting direct comparisons.

Both our age-adjusted and multivariable analysis showed statistically significant higher odds of ADRD in AI/AN than White beneficiaries, suggesting the disparities in rates of ADRD cannot be fully accounted for by disparities in health conditions. Rather, they may reflect systemic inequalities in socioeconomic opportunity, health-care access, and environmental factors, as well as historical and intergenerational trauma experienced by AI/AN peoples, not inherent biological differences.[12] Indeed, two previous studies comparing White and Black populations examined the association of race and ADRD through a series of regression analyses and found that the differences in dementia risk may be mainly attributable to socioeconomic status.[25,26]

The associations between health conditions and ADRD among AI/AN people have been understudied. Consistent with two recent studies,[18,19] we found positive associations of several important factors, such as diabetes and depression, with ADRD among AI/AN beneficiaries. Several ADRD-related conditions showed stronger associations among AI/AN beneficiaries than among White beneficiaries. This pattern may reflect broader structural and life-course factors: AI/AN individuals experience earlier onset and greater severity of cardiometabolic and sensory conditions,[45] higher cumulative exposure to socioeconomic adversity,[14] and more limited access to timely specialty care.[46] These contextual factors can amplify the downstream cognitive consequences of chronic conditions, resulting in larger effect estimates even when prevalences are similar. TBI provides such an example.

TABLE 3 Sex-stratified multivariable logistic regression of Lancet Factors on ADRD among American Indian and Alaska Native (AI/AN) and non-Hispanic White (White) Medicare beneficiaries aged 68 years and older.

Characteristics	AI/AN				White			
	Female (*N* = 66,334)		Male (*N* = 45,946)		Female (*N* = 570,411)		Male (*N* = 440,451)	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Demographics								
Age	1.15*	1.14–1.15	1.13*	1.13–1.14	1.14*	1.14–1.14	1.13*	1.13–1.14
Lancet factors								
Hypertension	1.29*	1.21–1.37	1.44*	1.33–1.56	1.39*	1.36–1.42	1.49*	1.45–1.53
Diabetes	1.34*	1.27–1.41	1.30*	1.22–1.39	1.48*	1.45–1.50	1.43*	1.40–1.46
Hyperlipidemia	1.02	0.97–1.08	0.96	0.90–1.03	0.80*	0.79–0.82	0.87*	0.85–0.89
Depression	3.66*	3.47–3.85	4.73*	4.39–5.10	4.43*	4.35–4.51	5.46*	5.33–5.59
Tobacco use disorder	1.44*	1.33–1.55	1.38*	1.26–1.50	1.38*	1.33–1.42	1.43*	1.38–1.48
Hearing loss	1.26*	1.17–1.36	1.45*	1.34–1.57	1.15*	1.12–1.18	1.38*	1.34–1.42
Alcohol use disorder	2.90*	2.48–3.38	3.40*	3.03–3.81	2.37*	2.21–2.53	2.38*	2.26–2.51
Blind or visual impairment	2.07*	1.65–2.58	2.88*	2.22–3.75	1.99*	1.82–2.18	2.39*	2.12–2.69
TBI	6.40*	4.82–8.50	10.69*	7.59–15.06	4.74*	4.30–5.21	6.70*	5.98–7.50

Notes: The sex and race-stratified multivariable models included the independent variables presented in the table: age, hypertension, diabetes, hyperlipidemia, depression, tobacco use disorder, hearing loss, alcohol use disorder, blind or visual impairment, and TBI.
Abbreviations: ADRD, Alzheimer's disease and related dementias; CI, confidence interval; OR, odds ratio; TBI, traumatic brain injury.
*$P < 0.001$.

Although its prevalence was low in late-life Medicare claims for both groups, prior research shows that AI/AN populations experience higher rates of traumatic injury and TBI earlier in adulthood,[47] resulting in a greater lifetime burden that is not captured in older-adult administrative data. Under-ascertainment of earlier injuries can therefore produce stronger observed associations with ADRD despite similar or lower measured prevalence at older ages. Together, these findings suggest that lifetime exposure severity and socio-structural context may underlie the stronger associations observed in AI/AN beneficiaries.

We also found that among the Lancet Factors, TBI, depression, alcohol use, and visual impairment were most strongly associated with ADRD among AI/AN and White beneficiaries. However, these factors were not among the top contributors to population attributable risk (PAR) for AI/AN peoples in another study.[13] This is likely because PAR considers both the strength of association and the prevalence of risk factors. For example, although TBI showed the strongest association with ADRD among both AI/AN and White beneficiaries in our study, its low prevalence (0.4%) in both populations limited its contribution to the overall ADRD burden.

While prior studies have examined ADRD in the AI/AN population,[13,48–50] our study more comprehensively examined a wide range of health conditions and their associations with ADRD using recent national Medicare data, helping to better contextualize the overall burden of ADRD-related comorbidities in this population. Our findings confirmed that the AI/AN population has a higher prevalence of conditions that may lead to increased risk of ADRD compared to their White counterparts. This is particularly true for several Lancet Factors (e.g., diabetes) that are classified as potentially modifiable midlife risk factors. For example, AI/AN adults experience early onset of diabetes.[45] Therefore, understanding the burden of these conditions and their associations with ADRD can facilitate prevention efforts for this population.

Key strengths of this study include leveraging data from a large, geographically diverse Medicare beneficiary sample with nearly continuous Part A and Part B enrollment, ensuring complete claims capture and statistical power.[40,51] Additionally, we systematically evaluated a wide array of Lancet-identified factors and captured nuanced heterogeneity through race-specific, sex-stratified logistic regression models.

Despite these strengths, our study has several limitations. First, the cross-sectional design of our study prohibits causal conclusions and the inference of temporal sequence. Many of the examined health conditions may represent co-pathologies or even consequences of the underlying neurodegenerative process, rather than being true etiological factors. For example, conditions like stroke or TIA may share an underlying vascular pathology with dementia; this is a particularly important consideration for the AI/AN population, given their high burden of vascular disease.[10,52,53] Other conditions, such as depression, could be a prodromal symptom of ADRD. Our findings should therefore be interpreted as associations, not as causal relationships.

Second, AI/AN populations have higher premature mortality rates (before 65 years),[54] which likely contributes to their observed age distribution in our older adult sample, with a disproportionately higher number in younger age categories. This suggests a survivor

TABLE 4 Multivariable logistic regression of all examined health conditions among American Indian and Alaska Native (AI/AN) and non-Hispanic White (White) Medicare beneficiaries aged 68 years and older.

	Race stratified				Overall sample	
	AI/AN (*N* = 112,280)		White (*N* = 1,010,862)		(*N* = 1,123,142)	
Characteristics	OR	95% CI	OR	95% CI	OR	95% CI
Demographics						
Race					1.24*	1.21–1.26
Age	1.13*	1.13–1.14	1.12*	1.123–1.13	1.13*	1.12–1.13
Male	0.99	0.95–1.04	0.96*	0.95–0.98	0.97*	0.96–0.98
Lancet factors						
Hypertension	1.07	1.02–1.12	1.10*	1.08–1.12	1.09*	1.07–1.11
Diabetes	1.09*	1.04–1.14	1.16*	1.15–1.18	1.16*	1.14–1.17
Hyperlipidemia	0.82*	0.78–0.86	0.72*	0.71–0.73	0.73*	0.72–0.74
Depression	3.91*	3.73–4.09	4.93*	4.85–5.01	4.81*	4.74–4.88
Tobacco use disorder	1.16*	1.09–1.23	1.07*	1.05–1.10	1.08*	1.06–1.11
Hearing loss	1.29*	1.22–1.36	1.14*	1.11–1.16	1.16*	1.14–1.18
Alcohol use disorder	2.84*	2.58–3.12	2.11*	2.02–2.20	2.22*	2.13–2.31
Blind or visual impairment	1.98*	1.67–2.35	1.69*	1.57–1.82	1.74*	1.62–1.86
TBI	7.03*	5.63–8.78	4.59*	4.26–4.95	4.79*	4.46–5.14
Other health factors						
CKD w/o ESRD	1.43*	1.36–1.49	1.40*	1.38–1.42	1.40*	1.38–1.42
AMI/IHD	1.08*	1.04–1.13	1.15*	1.13–1.16	1.14*	1.12–1.16
HF/AFib	1.38*	1.31–1.44	1.32*	1.30–1.34	1.32*	1.30–1.34
COPD	1.06	1.00–1.11	1.18*	1.16–1.20	1.16*	1.15–1.18
PVD	1.68*	1.60–1.77	1.76*	1.74–1.79	1.76*	1.73–1.78
Any cancer	0.91	0.85–0.97	0.86*	0.84–0.87	0.86*	0.84–0.88
Other mental health disorder	2.51*	2.35–2.68	2.53*	2.48–2.59	2.53*	2.48–2.58
Liver disease	1.11	1.03–1.20	1.00	0.97–1.03	1.01	0.98–1.04
Drug use disorder	1.25*	1.14–1.38	1.16*	1.12–1.21	1.17*	1.13–1.22
Stroke/TIA	2.20*	2.05–2.37	2.17*	2.12–2.23	2.17*	2.12–2.23
ESRD	1.81*	1.60–2.04	1.73*	1.61–1.86	1.74*	1.64–1.85

Notes: The independent variables of the race-stratified models included age, sex, the 9 Lancet Factors (traumatic brain injury, depression, alcohol use disorder, blind or visual impairment, diabetes, hypertension, tobacco use disorder, hearing loss, and hyperlipidemia) and the 13 Other Health Factors (CKD without ESRD, AMI or IHD, HF or AFib, COPD, PVD, any cancer, other mental health disorders, liver disease, drug use disorder, stroke or TIA, and ESRD). The overall model included the same variables with the addition of race. Other mental health disorders included diagnoses of anxiety, bipolar disorder, post-trauma stress disorder, or schizophrenia and other psychotic disorders, but without a diagnosis of depression. Any cancer included diagnoses of breast, colorectal, prostate, lung, or endometrial cancers.

Abbreviations: ADRD, Alzheimer's disease and related dementias; AFib, atrial fibrillation; AMI, acute myocardial infarction; CI, confidence interval; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; ESRD, end-stage renal disease; HF, heart failure; IHD, ischemic heart disease; OR, odds ratio; PVD, peripheral vascular disease; TIA, transient ischemic attack.

*$p < 0.001$.

bias toward healthier individuals in the AI/AN population. Consequently, our findings may be influenced by residual confounding related to age, or an underestimation of disparities if the surviving AI/AN population is systematically healthier or has different disease profiles.

Third, the MBSF provides a single variable to identify race and ethnicity. Using the Research Triangle Institute Race Code, 4.5% of adults were classified as "unknown" or "other" in 2019. According to Census data, 60.8% of AI/AN individuals report two or more races, and 30.8% identify as Hispanic.[22] Thus, we may have under-identified AI/AN adults and were more likely to identify non-Hispanic AI/AN adults who reported one race. Racial and ethnic misclassification is well documented in electronic health record and claims data, with lower sensitivity for identifying AI/AN individuals in Medicare data leading to underreporting of health outcomes.[55] This could bias our results through selection bias if correctly classified AI/AN individuals dif-

fer systematically from those misclassified (e.g., stronger health-care engagement or tribal affiliation).

Fourth, our study excluded Medicare Advantage (MA) enrollees, who now comprise approximately half of all Medicare beneficiaries.[56] This exclusion impacts generalizability, as MA enrollees may differ from the FFS population and may have lower socioeconomic status and a higher prevalence of certain risk factors like diabetes as well as ADRD.[6,57,58] This could lead to an underestimation of the true ADRD burden in the overall Medicare population.

Lastly, we recognize the importance of socioeconomic status (SES) in understanding health disparities. However, we could not incorporate individual-level social determinants of health, such as income and education, due to data limitations. The absence of these crucial covariates may influence the estimated racial disparities. We plan to incorporate area-level SES measures to better capture socioeconomic context.

In conclusion, older AI/AN beneficiaries had a higher prevalence of ADRD and multiple related factors compared to White beneficiaries, with some factors showing stronger associations with ADRD among AI/AN populations. Future studies should investigate social determinants of health and other behavioral, environmental, and genetic factors potentially contributing to ADRD disparities. Longitudinal studies enabling stronger causal inference are also needed.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

CONSENT STATEMENT

This study used de-identified Medicare data. Because the data were de-identified and no contact with human subjects occurred, informed consent was not required.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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