

RESEARCH ARTICLE

Alzheimer's disease medication use and adherence patterns by race and ethnicity

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Abstract

Background: We examined racial and ethnic differences in medication use for a representative US population of patients with Alzheimer's disease and related dementias (ADRD).

Methods: We examined cholinesterase inhibitors and memantine initiation, non-adherence, and discontinuation by race and ethnicity, using data from the 2000–2016 Health and Retirement Study linked with Medicare and Medicaid claims.

Results: Among newly diagnosed ADRD patients ($n = 1299$), 26% filled an ADRD prescription ≤ 90 days and 36% ≤ 365 days after diagnosis. Among individuals initiating ADRD-targeted treatment ($n = 1343$), 44% were non-adherent and 24% discontinued the medication during the year after treatment initiation. Non-Hispanic Blacks were more likely than Whites to not adhere to ADRD medication therapy (odds ratio: 1.50 [95% confidence interval: 1.07–2.09]).

Discussion: Initiation of ADRD-targeted medications did not vary by ethnoracial group, but non-Hispanic Blacks had lower adherence than Whites. ADRD medication non-adherence and discontinuation were substantial and may relate to cost and access to care.

KEYWORDS

acetylcholinesterase inhibitors, Alzheimer's disease, anti-dementia medication, cognitive health, dementia, health disparities

HIGHLIGHTS

- Initiation of anti-dementia medications among newly diagnosed Alzheimer's disease and related dementias (ADRD) patients was low in all ethnoracial groups.
- ADRD medication non-adherence and discontinuation were substantial and may relate to cost and access to care.
- Compared to Whites, Blacks and Hispanics had lower use, poorer treatment adherence, and more frequent discontinuation of ADRD medication, but when controlling for disease severity and socioeconomic factors, racial disparities diminish.

- Our findings demonstrate the importance of adjusting for socioeconomic characteristics and disease severity when studying medication use and adherence in ADRD patients.

1 | BACKGROUND

Although Alzheimer's disease and related dementias (ADRD) have no cure, several medications approved by the US Food and Drug Administration (FDA) may slow progression of ADRD symptoms. These medications include acetylcholinesterase inhibitors (donepezil, galantamine, and rivastigmine) and an N-methyl-D-aspartate receptor antagonist (memantine). While the evidence for these medications is modest and limited to short-term follow-up studies that showed small improvements in cognitive functioning and maintenance of global functioning,^{1,2} the use of these therapies is indicative of how patients may use new drugs developed in the future.

Analyses of Medicare claims have found that roughly one third to one half of eligible patients use anti-dementia drugs, with lower rates among Asians, Blacks, and Hispanics than among Whites.³⁻⁶ Other studies found that initiation of anti-dementia medication differed across racial groups in the United Kingdom,⁷ as well as in a US health-care system.⁸ Another study reported discontinuation rates in the United States for the three acetylcholinesterase inhibitors ranging from 39% to 59% after 18 weeks, although this study did not investigate discontinuation by race or ethnicity.⁹ Studies using the Medicare Current Beneficiary Survey have documented racial/ethnic disparities in the use of medications to treat dementia after adjusting for basic demographic, economic, health status, or health-care use factors.^{5,10,11} While most studies of racial disparities have controlled for basic demographic characteristics and socioeconomic factors, they have not incorporated measures of ADRD symptom severity and cannot tell us whether the treatment is less timely for some groups.

This study assesses anti-dementia medication treatment by race and ethnicity in a nationally representative population. Unlike prior studies that used administrative data alone, we adjusted for ADRD symptom severity and socioeconomic factors, leveraging national surveys linked to claims data. We investigated the timeliness of anti-dementia medication initiation and symptom severity at treatment initiation by race and ethnicity among newly diagnosed patients. We also compared medication adherence and discontinuation rates within the first year of treatment by race and ethnicity.

2 | METHODS

2.1 | Study sample and data sources

Our study included participants aged 65 years and older from the Health and Retirement Study (HRS) from 2000 to 2016, limiting atten-

tion to individuals with (1) linked Medicare claims data for the years 2000 to 2015; (2) Medicaid Analytic Extract (MAX) and summary files for the years 2000 to 2012 for individuals enrolled in Medicaid; and (3) complete data on sex, race, and ethnicity ($n = 23,128$).

The HRS is a national survey that currently interviews approximately 20,000 individuals living in the United States over the age of 50 every 2 years, collecting economic, health, and psychosocial information.¹² By linking longitudinal HRS data and administrative health claims data, we can associate individual socioeconomic, cognitive, and functional characteristics with their diagnoses, medications, and services paid for by Medicare and Medicaid. The HRS oversamples non-White populations, making it well suited to study racial and ethnic health disparities.

Our analysis included Medicare claims files for Part A (i.e., inpatient, skilled nursing facility, hospice, and home health), Part B (i.e., physician visits, outpatient care, and durable medical equipment), Part D (prescription medications), and MAX files for inpatient, long-term care, other services, and medications covered by Medicaid for qualified beneficiaries.

2.2 | Anti-dementia drug initiation

For our treatment initiation analyses, we identified HRS participants who had an incident ADRD diagnosis in any of their claim records during the years 2006 to 2015 (International Classification of Diseases [ICD]-9/10 diagnosis codes in Appendix Table 1).^{13,14} We defined newly diagnosed cases using a 12-month look-back period to ensure the individual had no prior ADRD diagnosis for at least 12 months before the incidence date observed within the available data. Subjects were required to be enrolled in Medicare/Medicaid and have at least one medical claim during the look-back period to establish that they were in contact with the health-care system. We also required the individuals to have at least 12 months of enrollment in Medicare, Medicare Part D drug coverage, or in Medicaid after their initial ADRD diagnosis.

We identified claims for anti-dementia drugs in Medicare Part D and Medicaid claims using National Drug Codes for donepezil, galantamine, rivastigmine, memantine, and their combinations. We analyzed the proportion of individuals who had a billing claim for anti-dementia drugs with a fill date within 90 days after their initial diagnosis date, or whose initial diagnosis date was between their first prescription's fill date and run-out date—defined as the fill date plus the days of supply. Further, we analyzed the time from ADRD diagnosis to the first anti-dementia drug claim after diagnosis. Because the FDA indications for anti-dementia drugs in our analysis are specific to treatment

of Alzheimer's disease (AD), we also performed a subgroup analysis that restricted the sample to individuals with AD diagnosis (ICD-9-CM code: 331.0).

2.3 | Anti-dementia drug non-adherence

To assess treatment non-adherence and discontinuation, we identified individuals who filled at least one prescription for an anti-dementia medication and required the subjects to be continuously enrolled in Medicare Part D or Medicaid for at least 12 months after their initial prescription fill date.

We defined an individual as non-adherent if their "proportion of days covered" for anti-dementia medications was less than 80% during that year.¹⁵ We calculated "proportion of days covered" as the number of days for which a patient had any ADRD medication prescriptions (including dual usage of memantine and cholinesterase inhibitors) during a year divided by 365 days.

2.4 | Anti-dementia drug discontinuation

We examined treatment discontinuation during the 12 months after the initial fill date for the anti-dementia medication prescription. We classified a patient as discontinuing treatment if they (1) had no additional prescription for any anti-dementia medication within 45 days after the index medication run-out date and (2) did not switch to a different anti-dementia medication within 45 days after the run-out date.¹⁶ We defined the index treatment run-out date as the prescription fill date plus the number of days of supply for the index drug.

2.5 | Cognitive and functional impairment

The HRS measured cognitive function using the Telephone Interview for Cognitive Status (TICS) for self-respondents and the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) short form for respondents who used a proxy. The HRS data set provides imputed cognitive data for self-respondents to make up for item-level non-response using standardized methodology.¹⁷ We quantified cognitive impairment on a 0 to 10 scale (where 0 represents no impairment, and 10 represents high impairment) by combining normalized TICS scores and IQCODE scores.

We assessed functional status based on the number of Activities of Daily Living (ADL) limitations and Instrumental Activities of Daily Living (IADL) limitations. ADLs include getting dressed, walking across the room, bathing, eating, getting in and out of bed, and using the toilet; IADLs include preparing meals, grocery shopping, using the telephone, taking medication, and managing personal finances.

2.6 | Covariates

Covariates in the multivariable statistical models included demographic factors (i.e., age and sex); the year of diagnosis; number of

RESEARCH IN CONTEXT

- **Systematic Review:** We searched the published literature on medication treatment and adherence patterns for dementia and/or Alzheimer's disease.
- **Interpretation:** Our analyses showed:
 1. Overall use of Alzheimer's disease and related dementias (ADRD)-targeted medication treatment is low, and treatment adherence is poor:
 - Initiation of ADRD-targeted medications among newly diagnosed patients was low in all ethnographic groups, with nearly two-thirds having no prescription for cholinesterase inhibitors or memantine during their first year post-diagnosis.
 - ADRD medication non-adherence and discontinuation were substantial and may relate to cost and access to care.
 2. By racial/ethnic group: unadjusted results revealed significantly lower use, poorer treatment adherence, and more frequent discontinuation among Blacks and Hispanics than among Whites newly diagnosed with ADRD, but when controlling for socioeconomic factors and disease severity, racial disparities diminish.
- **Future Directions:** Researchers should further explore upstream socioeconomic factors and health system biases contributing to disparities in ADRD diagnosis and treatment.

comorbidities; and socioeconomic factors: nursing home status, dual eligibility for Medicare and Medicaid, education, and income. We adjusted for each subject's comorbidity burden, which we quantified in terms of the number of conditions they reported having in response to the HRS survey (0–8), including high blood pressure, diabetes, cancer, lung disease, heart disease, stroke, psychiatric problems, and arthritis. Finally, we adjusted for dementia symptom severity, quantified in terms of functional and cognitive measures, as described in Section 2.5.

2.7 | Statistical analysis

2.7.1 | Anti-dementia treatment initiation

This analysis used data for patients newly diagnosed with ADRD (N = 1299). Univariate analysis compared the proportion of individuals filling an ADRD-targeted medication within the 90 days after diagnosis across racial/ethnic groups. A parsimonious logistic regression model compared the likelihood of having an ADRD prescription within the 90 days after diagnosis, adjusted for race and ethnicity, age, sex, and the year of diagnosis. An expanded model controlled for additional covariates: cognitive impairment, functional limitations, number of comorbidities, nursing home status, dual eligibility for Medicare and Medicaid, education, and income.

We used cumulative incidence function curves to examine the proportion of individuals who filled an anti-dementia prescription within the first year after an ADRD diagnosis. We calculated the unadjusted, average time between first ADRD diagnosis and first anti-dementia prescription filled across racial/ethnic groups. In adjusted analyses, we estimated the average time to treatment initiation controlling for the same covariates included in the treatment initiation model described above, using a generalized linear model with a gamma distribution and log link function.

2.7.2 | Non-adherence and discontinuation

We used data for patients who received an anti-dementia medication, regardless of ADRD diagnosis status, within our study period ($n = 1431$). We used logistic regression to compare medication non-adherence or discontinuation across groups. As with the treatment initiation outcomes, we used a parsimonious model that adjusted for basic demographics, and an expanded model. The expanded model added ADRD diagnosis (as reported in medical claims) to the list of covariates.

We used Stata Statistical Software Release 16 for all data analyses. The Tufts Medical Center/Tufts University Health Sciences Institutional Review Board approved this study.

3 | RESULTS

3.1 | Sample characteristics

Our subjects were an average age of 82 years old at the time of first ADRD diagnosis, and 67% were female (Table 1). Compared to non-Hispanic Whites, Hispanics and non-Hispanic Blacks had lower educational attainment ($P < .01$), a lower median income ($P < .01$), and lower out-of-pocket spending for Part D medications ($P < .001$). Non-Hispanic Blacks and Hispanics were almost twice as likely to qualify for dual eligibility for Medicare and Medicaid services compared to non-Hispanic Whites ($P < .01$), and a greater proportion reported having trouble filling a medication prescription for financial reasons ($P < .01$).

A higher proportion of non-Hispanic Whites than non-Hispanic Blacks or Hispanics resided in a nursing home ($P = .03$), though the proportion of respondents who responded by proxy did not differ by race or ethnicity. Comorbidity burden was similar across racial/ethnic groups. Non-Hispanic Blacks and Hispanics had lower cognitive function and more functional limitations at ADRD diagnosis, although the differences were modest in magnitude ($P < .01$).

3.2 | Initiation of anti-dementia treatment within 90 days

Among individuals with newly diagnosed ADRD, 26% filled an ADRD prescription ≤ 90 days and 36% ≤ 365 days past diagnosis (Table 2, Figure 1). These proportions and the likelihood of initiating treatment

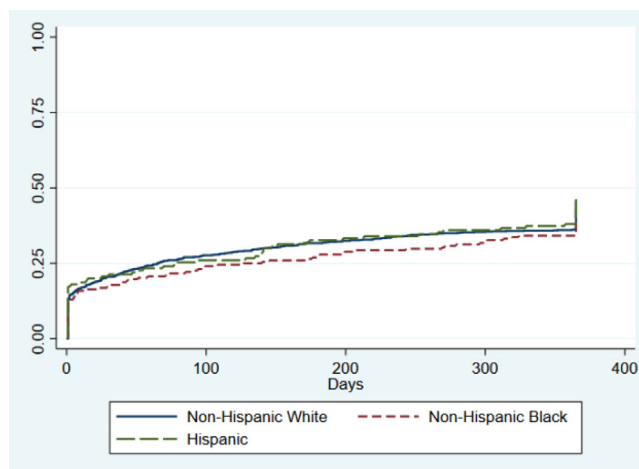


FIGURE 1 Proportion of individuals initiating an anti-dementia medication within the first year after initial Alzheimer's disease and related dementias diagnosis by race or ethnicity (cumulative incidence function curves; total $n = 1299$).

within 90 days, controlling for patient characteristics, were similar across racial/ethnic groups (Table 3).

In subgroup analyses of individuals with AD-specific diagnosis, 52% initiated treatment within 90 days, and initiation rates did not differ by race or ethnicity.

3.3 | Time to anti-dementia treatment initiation

Treatment delays did not differ by race or ethnicity in either the unadjusted or adjusted analyses (Table 2 and Figure 1). The mean unadjusted time from initial ADRD diagnosis to first anti-dementia drug prescription fill date within 12 months ranged from 62 days for non-Hispanic Whites, to 76 days for Hispanics and 82 days for non-Hispanic Blacks ($P = NS$). The median time to treatment initiation ranged from 14.5 days for Hispanics, to 18 days for non-Hispanic Whites and 29.5 days for non-Hispanic Blacks (Table 2).

3.4 | Cognitive and functional impairment at the time of treatment initiation

For three of four measures, ADRD severity at treatment initiation did not differ across racial/ethnic groups. Among self-respondents, non-Hispanic Blacks and Hispanics had worse cognitive function at treatment initiation than did non-Hispanic Whites ($P < .01$; Table 2). Subgroup analyses restricted to individuals with AD-specific diagnosis showed the same patterns.

3.5 | Non-adherence to anti-dementia drug treatment

Non-adherence rates for non-Hispanic Blacks and Hispanics exceeded corresponding rates for non-Hispanic Whites (50% and 51% vs. 42%,

TABLE 1 Characteristics of Health and Retirement Study respondents diagnosed with ADRD in Medicare or Medicaid claims at the time of first ADRD diagnosis

	Non-Hispanic White	Non-Hispanic Black	Hispanic	P-value
N (%)	941 (72%)	208 (16%)	150 (12%)	
Female	620 (66%)	149 (72%)	101 (67%)	.28
Age—mean	82.3	80.3	80.3	<.01
65–74	192 (20%)	70 (34%)	42 (28%)	<.01
75–84	379 (40%)	78 (38%)	65 (43%)	
+85	370 (39%)	60 (29%)	43 (29%)	
Education				<.01
Less than high school	273 (29%)	126 (61%)	119 (79%)	
High school	381 (41%)	58 (28%)	19 (13%)	
More than high school	286 (30%)	24 (12%)	12 (8%)	
Income—mean (median)	\$107,471 (\$21,624)	\$16,572 (\$12,700)	\$15,738 (\$11,815)	.45
Income quartiles				<.01
1 st quartile	144 (15%)	85 (41%)	65 (43%)	
2 nd quartile	211 (22%)	48 (23%)	35 (23%)	
3 rd quartile	229 (24%)	39 (19%)	30 (20%)	
4 th quartile	357 (38%)	36 (17%)	20 (13%)	
Dual eligible status	256 (27%)	107 (51%)	78 (52%)	<.01
Mean number of Medicare Part D claims per person	63	59	64	.9
Annual out-of-pocket payments for Part D medications—mean (median)	\$734 (\$361)	\$269 (\$72)	\$297 (\$75)	<.01
Ever reported having trouble filling any prescription due to financial reasons	238 (27%)	84 (43%)	60 (42%)	<.01
Comorbidities—mean	3.1	3.2	3.1	.63
Nursing home residence	145 (17%)	22 (11%)	14 (10%)	.03
Proxy respondent in HRS	144 (17%)	37 (19%)	33 (24%)	.15
Cognitive and functional status at first ADRD diagnosis:				
TICS score—mean	16.5	13.1	14.3	<.01
IQCODE score—mean	4.02	3.7	3.7	.02
ADL limitations—mean	1.2	1.6	1.6	<.01
IADL limitations—mean	1.4	1.6	1.7	<.01

Abbreviations: ADL, Activities of Daily Living; ADRD, Alzheimer's disease and related dementias; HRS, Health and Retirement Survey; IADL, instrumental activities of daily living; IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly; TICS, Telephone Interview for Cognitive Status.

Notes: TICS: Only for participants who did not have a proxy respondent (self-reported). Scale from 0 to 35; higher scores indicate higher cognitive function. IQCODE: Only for participants who had a proxy respondent. Scale from 0 to 5; Lower scores indicate higher cognitive function. ADL: Numbers are the reported number of activities (6 total) participants have difficulty performing; lower scores indicate higher functional ability. IADL: Numbers are the reported number of activities (5 total) participants have difficulty performing; lower scores indicate higher functional ability. We quantified comorbidity burden in terms of the number of conditions each subject reported having in response to the HRS survey (0–8), including high blood pressure, diabetes, cancer, lung disease, heart disease, stroke, psychiatric problems, and arthritis.

$P = .01$; Table 4). After controlling for patient characteristics, non-Hispanic Blacks were less likely to adhere to anti-dementia medication treatment than non-Hispanic Whites, while adherence rates for Hispanics and Whites did not differ (Table 3). Non-adherence increased with comorbidity burden, but was lower for nursing home residents and for individuals with an ADRD diagnosis coded in their claims.

3.6 | Discontinuation of anti-dementia drug treatment

Anti-dementia medication discontinuation rates for non-Hispanic Blacks and Hispanics exceeded corresponding rates for non-Hispanic Whites (32% and 27% vs. 21%, $P = .001$; Table 4). After controlling for

TABLE 2 Anti-dementia medication treatment initiation rates, cognitive function, and functional status at treatment initiation by race or ethnicity (N = 1299 individuals newly diagnosed with ADRD)

	Non-Hispanic White	Non-Hispanic Black	Hispanic Black	P-value
Individuals diagnosed with ADRD: N (% of total)	941 (72%)	208 (16%)	150 (12%)	
Anti-dementia medication initiation				.18
Treated at or within 90 days from index ADRD diagnosis	27%	22%	25%	
Late treatment (after 90 days)	19%	23%	21%	
No treatment	54%	55%	53%	
Filled an anti-dementia prescription during the first 12 months after diagnosis	337 (36%)	70 (34%)	56 (37%)	.76
Days from index ADRD diagnosis to first prescription mean (median), unadjusted	62 (18)	82 (29.5)	76 (14.5)	.18
Days from index ADRD diagnosis to first prescription, adjusted mean*	63	75	74	
Cognitive function at first prescription				
TICS score ¹ (n = 438 self-respondents)	15.87	11.30	14.54	<.00
IQCODE score ² (n = 106 proxy respondents)	4.13	3.69	4.14	.14
Functional status at first prescription (n = 559)				
Number of ADL limitations ³	1.11	1.10	1.16	.97
Number of IADL limitations ⁴	1.38	1.42	1.44	.96

Abbreviations: ADL, Activities of Daily Living; ADRD, Alzheimer's disease and related dementias; HRS, Health and Retirement Survey; IADL, instrumental activities of daily living; IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly; TICS, Telephone Interview for Cognitive Status.

Notes: *Estimates adjusted by age, sex, year of diagnosis, number of comorbidities, nursing home residence, cognitive function, functional limitations, and dual eligibility for Medicaid and Medicare. TICS: Only for participants who did not have a proxy respondent (self-reported). Scale from 0 to 35; higher scores indicate higher cognitive function. IQCODE: Only for participants who had a proxy respondent. Scale from 0 to 5; lower scores indicate higher cognitive function. ADL: Numbers are the reported number of activities (6 total) participants have difficulty performing; lower scores indicate higher functional ability. IADL: Numbers are the reported number of activities (5 total) participants have difficulty performing; lower scores indicate higher functional ability.

patient characteristics, discontinuation rates for non-Hispanic Blacks and Hispanics and Whites did not differ (Table 3).

Subgroup analyses restricted to individuals with AD-specific diagnosis showed the same patterns.

4 | DISCUSSION

Our study of anti-dementia medication use in newly diagnosed ADRD patients found that initiation of ADRD-targeted medications was low in all ethnorracial groups, with nearly two thirds having no prescription for cholinesterase inhibitors or memantine during the first year after their diagnosis. Even among patients with a specific AD diagnosis, only half initiated anti-dementia medication. Rates of ADRD medication non-adherence and discontinuation were also substantial across ethnorracial groups.

Prior investigations in the United States have found that anti-dementia medication initiation rates vary across the country, but are generally in the same range as in our study sample.^{16,18} Furthermore, previous studies have reported high discontinuation rates for all three acetylcholinesterase inhibitors (donepezil, galantamine, and rivastigmine) after 18 weeks, ranging from 39% to 59%, with most discontinuation explained by adverse events or the cost of medication.⁹

Donepezil, galantamine, and rivastigmine have been commercially available in generic form since 2012 to 2014, and generic memantine became available in 2015. Our analyses accounted for use of these medications through 2016, regardless of whether they were available as branded or generic formulations. As more data become available, future research should investigate whether the availability of generic memantine has affected usage after 2016. Prior studies have also found that both Hispanics and Blacks discontinue medication use at a faster rate than Whites.⁶ Whether the reasons for discontinuation differ by race or ethnicity, however, remains unclear. It would be useful to conduct interviews or further surveys with members of different racial and ethnic groups to shed light on this issue.

We found no difference in treatment initiation by race. ADRD symptom severity, specifically, poorer cognitive status and better functional status, were associated with medication initiation within 90 days. After controlling for other factors, initiation of anti-dementia medication was *more* likely among people with greater cognitive impairment; on the other hand, it was *less* likely among people with more ADL limitations. A prior analysis of Medicare data found that Hispanics are more likely than Whites and Blacks are equally likely as Whites to initiate anti-dementia medications.⁶ Other studies reported that Black, Asian, and Hispanic individuals were all less likely to use anti-dementia drugs than Whites.³ Cognitive and functional status, which was not

TABLE 3 Factors associated with anti-dementia medication use patterns: Treatment within 90 days, days to initiation, therapy non-adherence, and discontinuation

	Treatment initiation within 90 days of ADRD diagnosis		Days from ADRD diagnosis to treatment initiation during the first 12 months after diagnosis ^a		Treatment non-adherence		Treatment discontinuation	
	OR	95% CI	exp(b)	95% CI	OR	95% CI	OR	95% CI
Parsimonious model (N)	N = 1299		N = 463		N = 1431		N = 1431	
Race and Ethnicity								
Non-Hispanic White	Reference		Reference		Reference		Reference	
Non-Hispanic Black	0.77	(0.54, 1.11)	1.29	(0.90, 1.85)	1.73	(1.27, 2.38)	1.37	(1.03, 1.82)
Hispanic	0.90	(0.60, 1.34)	1.26	(0.85, 1.89)	1.32	(0.92, 1.90)	1.43	(1.04, 1.97)
Additional covariates for parsimonious model: sex, age, year of index ADRD diagnosis or first anti-dementia prescription								
Expanded model (N)^b	N = 1156		N = 408		N = 1258		N = 1258	
Race and ethnicity								
Non-Hispanic White	Reference		Reference		Reference		Reference	
Non-Hispanic Black	0.72	(0.47, 1.09)	1.31	(0.85, 2.00)	1.50	(1.07, 2.09)	1.83	(0.98, 2.51)
Hispanic	0.87	(0.53, 1.38)	1.45	(0.88, 2.39)	1.39	(0.94, 2.05)	1.18	(0.68, 2.16)
Sex								
Male	Reference		Reference		Reference		Reference	
Female	1.04	(0.76, 1.4)	1.16	(0.84, 1.60)	1.17	(0.91, 1.5)	1.19	(0.9, 1.92)
Age								
65-74	Reference		Reference		Reference		Reference	
75-84	1.25	(0.87, 1.79)	0.74	(0.51, 1.06)	0.96	(0.71, 1.29)	1.10	(0.87, 2.11)
85+	0.67	(0.44, 0.99)	0.88	(0.58, 1.32)	1.16	(0.83, 1.6)	0.70	(0.41, 1.14)
Year of index ADRD diagnosis	1.00	(0.94, 1.05)	0.99	(0.93, 1.04)				
Year of first anti-dementia prescription					1.00	(0.95, 1.04)	0.96	(0.88, 1.01)
Cognitive impairment^c	1.27	(1.15, 1.39)	0.96	(0.87, 1.06)	0.94	(0.87, 1.01)	0.96	(0.82, 1.03)
ADL limitations	0.86	(0.76, 0.96)	0.94	(0.84, 1.06)	1.04	(0.94, 1.14)	1.02	(0.91, 1.2)
IADL limitations	0.98	(0.86, 1.09)	1.01	(0.89, 1.14)	0.97	(0.87, 1.06)	0.99	(0.87, 1.14)
Comorbidities^d	0.97	(0.88, 1.06)	1.05	(0.95, 1.16)	1.14	(1.05, 1.23)	1.09	(0.96, 1.22)
Nursing home residence	1.06	(0.67, 1.64)	0.98	(0.60, 1.62)	0.50	(0.34, 0.72)	0.69	(0.4, 1.16)
Dual eligibility status	0.76	(0.54, 1.06)	1.43	(1.01, 2.03)	0.99	(0.74, 1.32)	0.74	(0.52, 1.02)
Education								
Less than high school	1.06	(0.7, 1.58)	0.94	(0.61, 1.46)	0.96	(0.68, 1.33)	1.23	(0.83, 1.79)
High school	1.13	(0.78, 1.63)	1.06	(0.71, 1.57)	1.05	(0.78, 1.42)	1.14	(0.79, 1.61)
More than high school	Reference		Reference		Reference		Reference	
Income quartiles								
1 st quartile	1.08	(0.68, 1.7)	0.57	(0.35, 0.92)	1.15	(0.82, 1.6)	1.29	(0.86, 1.9)
2 nd quartile	0.99	(0.65, 1.51)	0.77	(0.50, 1.17)	0.96	(0.67, 1.37)	1.36	(0.89, 2.06)

(Continues)

TABLE 3 (Continued)

	Treatment initiation within 90 days of ADRD diagnosis		Days from ADRD diagnosis to treatment initiation during the first 12 months after diagnosis ^a		Treatment non-adherence		Treatment discontinuation	
	OR	95% CI	exp(b)	95% CI	OR	95% CI	OR	95% CI
3 rd quartile	0.92	(0.61, 1.36)	0.66	(0.44, 1.00)	1.01	(0.67, 1.49)	1.07	(0.67, 1.7)
4 th quartile	Reference		Reference		Reference		Reference	
ADRD Diagnosis					0.56	(0.39, 0.8)	1.35	(0.87, 2.07)

Note: Values shown in bold are statistically significant results at 0.05 significance level.

Abbreviations: ADL, Activities of Daily Living; ADRD, Alzheimer's disease and related dementias; CI, confidence interval; HRS, Health and Retirement Survey; IADL, instrumental activities of daily living; IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly; OR, odds ratio; TICS, Telephone Interview for Cognitive Status.

^aDays to treatment initiation is a continuous outcome.

^bThe sample sizes for expanded models may be slightly smaller than for parsimonious models for the same outcomes because a small number of patients had missing data for some of the additional variables. All models used complete case analysis.

^cCognitive impairment measured on a 0–10 scale (where 0 represents no impairment, and 10 represents high impairment) by combining normalized TICS scores and IQCODE scores.

^dWe quantified comorbidity burden in terms of the number of conditions each subject reported having in response to the HRS survey (0–8), including high blood pressure, diabetes, cancer, lung disease, heart disease, stroke, psychiatric problems, and arthritis.

TABLE 4 Anti-dementia medication treatment non-adherence and discontinuation by race/ethnicity, unadjusted (N = 1343 individuals who filled anti-dementia prescription regardless of diagnosis)

	Non-Hispanic White	Non-Hispanic Black	Hispanic	P-value
Individuals who filled anti-dementia prescription: N (% of total)	1010 (71%)	240 (17%)	181 (13%)	
Anti-dementia medication non-adherence	42%	50%	51%	<.01
Anti-dementia medication discontinuation	21%	32%	27%	.01

available in these previous analyses, is an important factor influencing anti-dementia treatment initiation.

While we found no difference in anti-dementia treatment initiation by race or ethnicity for patients who have received an ADRD diagnosis, disparities in treatment access may still exist. Black and Hispanic populations may experience more missed and delayed ADRD diagnoses and have poorer cognitive function and more functional limitations at the time of their diagnosis.¹⁹ Moreover, because of these disparities, disease diagnosis for non-Hispanic Blacks and Hispanics occurs at more severe stages, when medication may be less effective at slowing disease progression. Differential diagnosis delays and the consequent differences in patient disease severity at the time of diagnosis may contribute to disparities in anti-dementia medication use by race/ethnicity. Another factor that may contribute to these disparities is the differential access to dementia specialists by patient race and ethnicity.^{3,8,14} Our data lacked detailed information on prescribing physician specialty and care setting (e.g., specialty practices or memory centers) or the specialty of physicians that the patients accessed for their medical care. Further research should explore the role of provider specialty, care setting, anti-dementia medication use, and adherence.¹⁸

The FDA's recent approval of aducanumab (aduhelm), a promising but expensive anti-dementia therapy, raises concerns about equitable care access for all ethnorracial groups. Furthermore, because aducanumab is indicated for early stages of disease, missed and delayed

diagnoses have the potential to exacerbate disparities in access to timely care. Future research should further explore how socioeconomic factors, explicit and implicit bias, and structural racism may contribute to disparities in ADRD diagnosis and treatment.

While we found differences in medication adherence and discontinuation by race and ethnicity, statistical significance of these differences diminished when controlling for disease severity and socioeconomic factors. Odds ratios of discontinuation for Non-Hispanic Blacks versus non-Hispanic Whites and odds ratios for non-adherence for Hispanics versus non-Hispanic Whites increased slightly after controlling for other factors, even though the odds ratios became non-significant. The lack of significance may relate to the smaller sample size contributing to the expanded model and increase in number of covariates in the model.

Further, socioeconomic characteristics of our subjects varied across racial/ethnic groups. For example, non-Hispanic Black and Hispanic populations had less education and lower incomes than non-Hispanic Whites. A greater proportion of Blacks and Hispanics qualified for dual eligibility for Medicare and Medicaid services, reported having trouble filling a medication prescription for financial reasons, and had lower out-of-pocket spending for Part D medications, compared to Whites. These measures indicate a higher degree of financial hardship that interferes with access to medications for non-Hispanic Blacks and Hispanics compared to Whites. Because most ADRD patients have

multiple comorbidities, their out-of-pocket medication expenses can quickly add up.

Differences in anti-dementia medication adherence and discontinuation after controlling for ADRD symptom severity and socioeconomic status represent ethnoracial health-care *disparities* per definition of the Institute of Medicine, which focuses on the effects of the health-care systems and operations, as well as discrimination, rather than differences in treatment due to clinical appropriateness criteria and patient preferences.²⁰ Although research suggests that ADRD concerns, knowledge, and beliefs vary across racial and ethnic groups, there is no documentation of differences that should influence treatment. For example, one study found that beliefs differ among Whites, Blacks, and Latinos regarding the role of genetics, stress, and mental activity as factors that influence the risk of developing AD.²¹ Research has also identified differences in attitudes toward family caregiving and access to institutional services across racial and ethnic groups. For example, Blacks tend to place greater value than do Whites on family caregiving and tend to have larger family and community support networks.^{22,23} Hispanic families may experience obstacles to accessing health-care services, including language barriers, a lack of formal support and services, and cultural perceptions by providers that Hispanic caregivers prefer not to use formal services.^{23,24} Whether there are ethnoracial differences in attitudes specifically toward anti-dementia medications remains unclear. Further qualitative and quantitative research is critical to understanding factors that contribute to differences in ADRD medication use by race and ethnicity and to suggesting strategies to reduce ethnoracial disparities and inequity.

4.1 | Limitations

First, our analysis of medication use relied on prescription fill data. Based on billing claims we could not ascertain whether patients actually took the medications they received. Our analysis of adherence and discontinuation measures relied on prescription fill date and runout date data as proxies for medication usage. Because some subjects may have filled prescriptions but not taken the medications, we may have overestimated adherence rates. There is, however, no reason to believe that this factor biases our comparison of adherence rates across ethnoracial groups.

Second, when we conducted our analysis, HRS-linked Medicare claims were available for fee-for-service beneficiaries only. Future research should investigate Medicare Advantage enrollees, as there are indications that their patterns of care may differ from those covered by traditional Medicare, especially for beneficiaries with ADRD.²⁵

Third, because our analysis relied on medication prescription data from Part D and Medicaid, we could not quantify use for patients not covered by these services. However, a high proportion of Medicare beneficiaries are enrolled in Part D (55% of non-Hispanic White, 66% of Black, and 71% of Hispanic beneficiaries), so our findings represent the majority of this population.²⁶

Finally, our sample size was insufficient for us to analyze Asian American, Pacific Islander, American Indian, Alaska Native, or other

racial/ethnic groups, or for us to analyze subcultures or various countries/regions of origin for non-Hispanic Blacks (e.g., American-born, Caribbean, or African-born) and Hispanics (e.g., Mexican, Puerto Rican, or central American in origin).

4.2 | Conclusions

Our study showed that once diagnosed with ADRD, treatment initiation does not differ by race or ethnicity. Missed or delayed ADRD diagnosis, which disproportionately affects non-Hispanic Blacks and Hispanics, may drive disparities in anti-dementia treatment access. Non-adherence and discontinuation of ADRD-targeted medication treatment is more prevalent among non-Hispanic Blacks than in Whites, but not among Hispanics, when controlling for patient factors. Socioeconomic factors play an important role in driving ethnoracial disparities, and financial hardship, lower income, and education level disproportionately affect non-Hispanic Blacks and Hispanics. Providers and policy makers should work to identify factors limiting timely diagnosis and access to care for ADRD and develop and implement strategies to overcome those barriers.

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CONFLICTS OF INTEREST

The authors report no conflicts of interest. [Author disclosures](#) are available in the supporting information.

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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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APPENDIX A

TABLE A1 ICD-9/10 diagnosis codes for dementia

ICD-9 codes	331.0, 331.11, 331.19, 331.2, 331.7, 290.0, 290.10, 290.11, 290.12, 290.13, 290.20, 290.21, 290.3, 290.40, 290.41, 290.42, 290.43, 294.0, 294.10, 294.11, 294.20, 294.21, 294.8, 797, 331.82, 331.89, 331.9, 290.8, 290.9, 294.9
ICD-10 codes	G30.0, G30.1, G30.8, G30.9, F01.50, F01.51, F02.80, F02.81, F03.90, F03.91, F04, G13.8, F05, F06.1, F06.8, G31.1, G31.2, G31.01, G31.09, G94, R41.81, R54, G31.83, G31.89, G31.9

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Abbreviation: ICD, International Classification of Diseases.